Constructive Technology Assessment of Emerging Nanotechnologies

Experiments in Interactions

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CONSTRUCTIVE TECHNOLOGY ASSESSMENT OF EMERGING NANOTECHNOLOGIES

EXPERIMENTS IN INTERACTIONS

DISSERTATION

to obtain
the degree of doctor at the University of Twente,
on the authority of the rector magnificus,
prof.dr. H. Brinksma,
on account of the decision of the graduation committee,
to be publicly defended
on Thursday the 25th of November 2010 at 13h15

by

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This dissertation is approved by the promotor prof.dr Arie Rip

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PART I

Chapter 1 Topic and theme of the thesis

1.0 Introduction

In January 2003, the Dutch R&D consortium NanoNed (at first supported by special NanoImpulse funding) started its work, and from the beginning it included a component on Technology Assessment and Societal Aspects of Nanotechnology, organized as an additional "flagship", labelled TA NanoNed. The pre-history of the consortium is interesting in its own right (and a glimpse is offered in Robinson, Rip & Mangematin, see Ch. 2). Important for the topic of this dissertation is that the proposal to have such a component on Technology Assessment and Societal Aspects of Nanotechnology was an initiative of the nano-scientists who pushed for the consortium, who had seen the discussions in the US and wanted to make sure that societal aspects of nanotechnology would be considered at an early stage. To begin with they invited Arie Rip (University of Twente), who had a record of working on technology assessment, to draw up a research program, building on the approach of Constructive Technology Assessment (see further below, 1.2.2 and 1.2.3). That research program was the framework for the work presented in this dissertation.

In this program, Constructive TA is conducted at an early stage of technology development, so as to be able to feed back into ongoing choices and strategies, i.e. to contribute to the ongoing construction of the new technology. It has three components: (1) analysis and diagnosis of ongoing developments, including expectations about the potential embedding in society; (2) anticipation on further developments and their embedding in society; (3) feedback of insights into ongoing discussions and choices. When doing concrete Constructive TA projects, one, or another, component can be emphasized over others. In the work for this dissertation, a decision was made at an early stage to take component (3) as an integral part of the methodology through the "insertion" (see 1.3) of the work into the world of nanoscientists and nanotechnologists. As it turned out, the European Network of Excellence Frontiers was receptive to this approach, and willing to fund the interactive exercises that were part of the methodology.

With this brief introduction, it is visible already that in the case of nanotechnology, Constructive TA need not just be an exercise done by an analyst and then offered to technology developers and other actors interested in the emerging technology. These exercises are actually welcomed (and funded) by the technology developers and technology promoters, who see them as necessary to anticipate on societal

embedding, including possible reactions from various societal actors. In more theoretical terms: there is always co-evolution of technology and society, but anticipations are becoming more important, so that the co-evolution will be more reflexive. This overall change towards more reflexive co-evolution is the backdrop against which the work for this dissertation was carried out. It shaped the thinking about, and the design of, the approach, which is now formulated as contributing to increasing reflexivity of co-evolution, in addition to the concrete aims of improving technological development by having broader aspects taken into account. And it made such an approach feasible; because actors were recognizing the importance of being reflexive, even while they would also be constrained by their identification with further technological development (what I will call an 'enactor' perspective (see 1.2.3)).

This first chapter will discuss the backdrop developments and on that basis, formulate research themes for the CTA approach. It will also offer a selective review of relevant literature, and define what needs to be done to turn the overall and somewhat programmatic CTA approach into an empirical venture that can be evaluated as to what it is able to achieve. Finally, it will specify the empirical approach that was developed and applied, including the element of "insertion" in the nanoworld.

The next four chapters are published papers that present the analytic and diagnostic approach (component 1) and tools for anticipation (component 2). Chapters 6 and 7 present findings: insights derived from insertion in the nano-world, and insights based on analysis of the dedicated exercises that were done (the details are provided in the Appendices). Chapter 8, the final chapter, offers overall conclusions, and returns to the question of co-evolution of technology and society becoming more reflexive.

1.1 Emerging holes in the wall separating nanotechnology developments and society

1.1.1 Promising nanoscale technology

Novel science and technologies emerge with both promises of enabling tremendous innovation potential and recognition of (and even warnings about) the enormous uncertainties and often unknowns. "NST" (nanoscience and nanotechnology) covers a range of such potentially enabling new science and technology. In contrast with biotechnology or neuro-cognitive science, NST is not a domain with substantial coherence. It is about everything interesting that is observable, or is

being engineered, at the nanoscale; the prefix ‘nano’ can be used to specify a focus, e.g. within electronics or biology. While there are several definitions of these nanoscale technologies, there is some convergence towards a definition of nanotechnologies as technologies which include components that have at least one dimension between 1 and 100 nm, and display unique characteristics due to this scale.

Unlike previous high-technology waves induced by biotechnology and genomics, nanotechnology covers diverse fields of sciences and engineering with very different dynamics, and crosses boundaries by its utilization of fundamental characteristics of matter by manipulation and control at the nanoscale. The broad term “nanotechnology” continues to be used because of the rhetorical and resource-mobilization force it has. (Rip 2006)

Speculation and anticipation abound in the activities within and around nanotechnology. The past 10 years has seen an explosion of interest for the area. Already at an early stage, promises have led to high expectations about fruits that could be harvested from the development of and investment into nanotechnology. Large amounts of funding have been made available for national nanotechnology initiatives in the US, in Europe and elsewhere. One sees a “funding race” (rather than an innovation race) where countries compare their R&D expenditure and on that basis argue they should invest more.

Research and development at the nanoscale both require and enable a large degree of integration, from convergence of research disciplines in new fields of enquiry to new linkages between start-ups, research centres, infrastructure and facilities. There is a multitude of visions of what nanotechnology *is*, or could be. Such framings of nanotechnology can emphasize:

a) the gradual improvement of instrumentation for visualising and interacting with the nanoscale,

b) an enabling technology that will enable many applications in many industrial sectors,

c) the total control and manipulation of matter at the atomic scale.

While the various nanotechnologies that are envisioned draw on combinations of disciplines, nanotechnologies induce reshaping of the existing organizational arrangements amongst many industries and technology chains. Much anticipation is focused on how nanotechnology will disrupt existing, or create new industries. Various technological fields are emerging beneath the umbrella term. Some areas are extensions of what was already happening, for instance the scaling down of

silicon-based integrated circuits (the backbone of the International Technology Roadmap Semiconductors) towards the nanoscale has led to nano-scale lithography and nano-scale conducting structures (Schubert and Meyer 2009). But in the same domain of semi-conductors, an alternative approach, bottom-up nano-electronics, is emerging which is no longer an extension, but an alternative approach to developing electronic circuits and structures. (Schaller 1997) In addition, new networks are forming based around expectations and promises of altogether new technologies made possible by manipulation at the nanoscale.

Besides providing space for interaction between various technological fields the 'nanohype' leads to support for further development of nanotechnology through government programmes and financial investments mobilised through utopian visions and high expectations. At the same time, the promised far-reaching impacts of nanotechnology touted by both proponents and critical commentators of the emerging field create a pressure to do something about them. This includes exploration of the possible and desirable directions for the field of nanotechnology with a focus on governance of the interactions between nanotechnology and society (Renn & Roco 2006). What was already clear at the time when this PhD project started in 2004, is that there is anticipation on societal impacts, not only through exaggerated promises that are part of resource mobilisation strategies of technology developers, but also in how governmental agencies, non-governmental organisations and societal actors respond.

Thus, nanotechnology is a going concern for industrial actors, policy makers, societal actors and research institutions alike, even if they will have different interests and perspectives. In that way, it constitutes a rich site for exploring dynamics and conditions of the emergence of novel science and technology in real-time, shaped by the force-fields between science and technology, industry, and society.

1.1.2 Changing relationship between technology development and society

The traditional distinction between technology development and societal uptake is itself part of a historically evolved regime where technology development became a separate task, at a distance from uptake and use – the heritage of the Industrial Revolution of the 18th and 19th centuries (Rip, Misa and Schot 1995). Over time, engineers and other technology actors were seen, and saw themselves, as having a mandate to develop new technologies and confront users – 'society' - with them, as long as this could be presented as progress (Van Lente 1993). This link to ideals of

progress legitimated a space for technology development, somewhat protected against societal selection pressures, as well as the establishment of separate institutions, and later also government departments, which reflected a division of labour between promoters of new technology and regulators. This led to a particular regime of technology development and assessment, because the divisions of labour and legitimation became entrenched into the way technology was handled in society.

There are now signs, in NST but also other fields of science and technology, that the institutional separation of technology development and selection based on (projected) societal impact is becoming bridged. At least, there are pressures to bridge and various attempts at handling these pressures. One can argue that the emergence of Technology Assessment as a government responsibility since the early 1970s is a first step in this direction. Constructive TA explicitly aims to bridge the separation (Schot and Rip 1997). What is new is that anticipation on societal impacts is now also seen as a responsibility of technology developers.

One example is that the encounters between nanotechnologists and government and societal actors around concerns arising from the uncertainties of NST have led (and continue to lead) to a new discourse on 'responsible innovation' (the label of 'responsible development' is also used). The idea carried by the label 'responsible innovation' is that innovation activities should take social aspects, desirability and acceptability into account. With the emphasis on societal impact and embedment of nanotechnology applications, and the recent general acceptance of possibilities of environmental and health risks of nanomaterials, there is an extension to 'responsible research' (for example, in the Code of Conduct for Nanoscience Research, proposed by the European Commission to the Member States in 2008) which may become a locked-in part of the discourse of Nanotechnology R&D.

The notion of 'responsible innovation' can be read in two ways. There can be emphasis on innovation, which requires some responsibility to be successful/acceptable, and thus a licence to continue. This reading is common with technology developers and other insiders to the nano-world. The other reading emphasizes responsible, which may go as far as halting developments along questionable R&D lines. The proposed moratorium on nano-particles R&D (ETC 2003) would be an example – and it had repercussions even while no moratorium was established (Rip and Van Amerom 2009). The second reading, which puts responsible upfront, is usual with societal actors who are outsiders to the nano-world.

While the dichotomies (innovation vs. responsible, insiders vs. outsiders) are visible, there are interactions and mixtures, and the situation evolves. There is widespread uncertainty about impacts and risks, while there are also proposals for regulation, and NGOs which advocate a precautionary approach. There is additional uncertainty about consumer and citizen reactions to new nanotechnology-enabled products and processes, which includes fears of innovators about a public backlash and about barriers to public acceptance. This can then be channelled, even locked-in, in a specific direction, as appears to happen now in the strong political push for labelling of products when they "contain" nanotechnology.

A key dynamic is that innovation actors can choose to be responsive and may be asked by societal actors to account for what they do. This will set articulation processes in motion, and let responsible innovation emerge as the responsibility of innovation actors, in interaction with various societal actors. In general, it is not one type of actor, which can and should be held responsible. Responsibilities are distributed, just like technological development itself (Von Schomberg 2007). One could speak of 'distributed responsible development' to keep this aspect explicit, whatever the actual pattern is (e.g. whether 'responsible' will be foregrounded or backgrounded).

Continuing the focus on the position and perspective of nanotechnology enactors, four kinds of pressures on nanotechnology development activities can be identified, which lead to some integration in ongoing work and broader activities:

a. a pressure to translate research into applications that will benefit the economy and benefit society (a responsibility to innovate);

b. a pressure to be strategic, in particular to undertake anticipatory coordination activities up to roadmapping and agenda building;

c. a pressure to be transparent and pay attention to public outreach, up to early ("upstream") public engagement;

d. a pressure to engage with, and include, ethical and societal aspects of technology development activities (in a move towards responsible research and innovation);

Even when there are no dedicated activities in response to these pressures, they are felt. Over the past 5-10 years, they have become an integral part of the context of nanotechnology development. By now, one sees various responses. There are public outreach activities, ranging from lectures, science cafés, exhibitions and

videos to dialogue activities as the recent Dutch Societal Dialogue on Nanotechnology (www.nanopodium.nl). There is strategic agenda building, also with a view to resource mobilisation for nanotechnology R&D. The European Technology Platforms, in particular the one on nanomedicine, are interesting in this respect because they mobilize a wide range of actors. Engaging with ethical and societal aspects occurs, but in *ad hoc* ways, except for the occurrence of ELSA (Ethical, Legal and Social Aspects) programmes as a complement to nanotechnology R&D programmes.

The inclusion of ELSA in R&D programmes has its origins in the early 1990s, when the Human Genome Program (in the US) included studies of ethical, legal and social issues in its funding. Such a component is now a regular feature of genomics funding programmes all over the world, and not limited to genomics anymore. ELSA (along with environmental and economic aspects) is becoming expected as a component in national and international funding programmes, research networks and other R&D activities, and the acronym need not be spelled out anymore. Prudent/proactive nanotechnologists can stimulate such initiatives themselves, on a small scale by hiring a social scientist to work in the lab, or on a larger scale as when the Dutch nanotechnology consortium included a Technology Assessment program.

There is a reflexive moment here: the work for this dissertation is part of this move to include ELSA in nanotechnology R&D programmes, but also studies it and develops ways to do better. To articulate better approaches and work on them, a more detailed diagnosis is necessary (in 1.2.3). At a later stage (in Section 1.3 and in Chapter 6), I will show how my "insertion" in ongoing developments and interactions is not just a circumstance that requires some methodological reflection. It is actual a methodology in its own right, which makes patterns in the co-evolution of technology and society visible, and thus enables co-evolution to become more reflexive.

1.1.3 Real-world interactions in the face of uncertainties presented by NST

How to address issues of responsible innovation against the backdrop of co-evolution of technology and society? Let me start (as has been usual in discussions of TA and Constructive TA) with Collingridge's (1980) knowledge and control dilemma. At an early stage there is little knowledge about eventual outcomes of technological development and their effects, but the technology pathways are not yet entrenched, and steering is relatively easy. When effects have become visible,

however, and criteria for assessment can be specified, developments will be entrenched, there are vested interests and stabilized practices, so it will be difficult to change much about the technology. Collingridge advocates flexibility, and keeping options open, but does not offer further guidance other than reference to a pro-active role of government.

In fact, the dilemma is visible already within any innovation process (or "innovation journey"; Van de Ven 1999) where one has to shift from exploration to exploitation and foreclose options at a moment when not enough is known (March 1991). Verganti (1999) has analyzed this as the flexibility dilemma. This analysis can be extended to later stages of the innovation journey where again options, now about markets, regulation, and uptake and impact, will be foreclosed before enough is known to do this with certainty (Rip and Schot 2002). Recognition of the many choices (and by different actors) that are involved shifts the challenge from the strong dichotomy that Collingridge presents (and which can be heard as a message of despair) to a wide range of choices over time, where actors will be making their assessments. These choices add up to *de facto* directions of development, including emerging irreversibilities (Van Merkerk and Robinson 2006). Thus, Technology Assessment can, and should, come in everywhere, and help modulate the overall process by introducing anticipation and feedback to actors facing their 'little' dilemmas of knowledge and control.

There is a further limitation of the original Collingridge dilemma, which is the absence of consideration of what would be desirable directions and impacts. There is a third horn, and the dilemma is actually a trilemma: at an early stage, it is not clear what the dimensions of desirability should be, because the promised novelty may well transcend existing ethical and political evaluations. By the time ethics and politics have caught up, *les faits sont accomplis*, and there is little or no steering possible anymore, other than say 'no' (or better, attempts to say 'no'). The third horn becomes a concrete challenge when 'responsible innovation' is put on the agenda. It is exacerbated by the complex multi-actor situations with distributed powers (and lack of power) of control in which NST and other new science and technology emerge.

One cannot escape the dilemma (or trilemma). But the challenge is not to better forecast the future, it is to anticipate the range of possible developments in such a way that prudent selection of strategies in real time becomes possible. There are tools and approaches to do so, and I have developed more sophisticated versions like multi-path mapping (see Ch 4). Such tools may not be appreciated by technology developers, however, because they position themselves as pursuing a

promising option, rather than anticipating on issues of societal embedding (Deuten et al. 1997). In this sub-section, I offer an analysis of roles and interactions of types of interactions which will also help to understand this situation. This analysis will then allow me to formulate concrete research questions in the next sub-section.

There is an asymmetry between technology developers, at the source of (and at a distance to) potential impacts. One might call them "impactors", and those who will feel the impacts, "impactees". At an early stage, technology developers know more, and have invested more in specific pathways of development, whereas impactees and spokespersons for society have to wait and see, and thus can react only after the fact. This is the social configuration linked to Collingridge's dilemma. One can accept it as a division of assessment and of technology-shaping labour, but the division of labour is hampered (and thus not as productive as it should be) by technology developers being "insiders" and not knowing (or not concerned about knowing) very much about the "outside" world.

This point has been made by Garud and Ahlstrom (1997), and further developed by them in a way that I can build on.[1] They show how technology developers are working in an 'enactment frame', which leads to a concentric approach to product development: "get the product right, then the market and the regulation, and only after that we will start worrying about public acceptability". (cf. Deuten et al. 1997). Technology 'enactors' look at the world as a challenge, and when not responsive, as a barrier to be overcome. The enactors may be in for surprises, though, as when cochlear implants for deaf people, touted as a promise that the deaf community would embrace, were not accepted, for one thing because it would take deaf people out of their own culture (Reuzel 2004).

One can understand how enactors, i.e. technology developers and promoters, who try to realize (i.e. enact) new technology, construct views (up to informal scenarios) of progress. They thus work and think in 'enactment cycles' which emphasize positive aspects. This includes a tendency to disqualify opposition as irrational or misguided, or following their own agendas.[2] While enactors identify

[1] Here I draw heavily on the work of Arie Rip on folk theories in nanotechnology, see e.g. Rip 2006.

[2] Enactors will get irritated, because for them, explaining the promise of their technological option should be enough to convince consumers/citizens. For nanotechnology, enactors now also anticipate on obstacles similar to the ones that occurred for Genetically Modified Organisms) in agriculture and food, cf. Colvin (2003). But the structure of the situation remains the same, that of an enactment cycle.

with a technological option and products-to-be-developed, and see the world as waiting to receive this product, "the world" may well see alternatives, and take a position of comparing and selecting.

Thus, the other main position to be distinguished is the one of comparative selectors (not necessarily critics). There are professional comparative selectors (regulatory agencies like the US Food and Drug Administration) which use indicators, and develop calculations to compare the option with alternatives (e.g. versions of cost-benefit analysis). There are also citizens, consumers etc as *amateur* comparative selectors – who can range more freely because they are not tied to certain methods, and to accountability. Further, spokespersons for consumers or citizens can react and oppose rather than just select. And some NGOs became enactors for an alternative (as when Greenpeace Germany pushed for a better fridge, and helped to realize it)[3]

Enactors can, and sometimes must, interact with comparative selectors. Formally as with the US Food and Drug Administration, or informally as in marketing and in the recent interest in interactions between strategic management of firms and spokespersons for environment and civil society (see e.g. Doubleday 2004). There is also a "domesticated" version in test-labs like Philips Home-Lab (Philips Research – Technologies) and the RFID (Radio-Frequency Identification Device) - filled shop (RFID Journal 2003) in which people are invited to try out the new products, services and infrastructure.

One sees how the asymmetries in knowledge, in timing and power to shape between enactors and selectors give rise to a *de facto* division of TA labour where enactors (or "insiders" as Garud & Ahlstrom call them) articulate 'promotion' and selectors (or "outsiders" as Garud & Ahlstrom call them) 'control'. This is how Collingridge's dilemma is addressed in practice. But the practice is not fully satisfactorily, to put it mildly. The next step is to explore possible bridging of promotion and control. This occurs already but is distributed and patchy.

[3] Interestingly, pressures to substitute fluorochlorocarbons as coolants were ineffective until Greenpeace Germany and an ailing refrigerator company in former East-Germany got together and created a technical alternative, Greenfreeze, which shifted the balance of forces, at least in Europe (Verheul & Vergragt 1995). There is a technology dynamics point here as well: Van de Poel (1998, 2003) has shown more generally that it is important to have a technological alternative, a configuration that actually works, to effect regime change.

It will be clear that Garud and Ahlstrom's analysis can be developed further to create a theory of actors and interaction dynamics around new and emerging technologies. For the moment, their further point about 'bridging events' is important: occasions where, insiders meet outsiders and can learn about their perspectives and 'selection cycles'. Conversely, for the outsiders, learning can occur about the options being developed within enactment cycles. Garud & Ahlstrom offer a diagram which visualizes the positions and possible interactions, which is reproduced below, with a small modification.

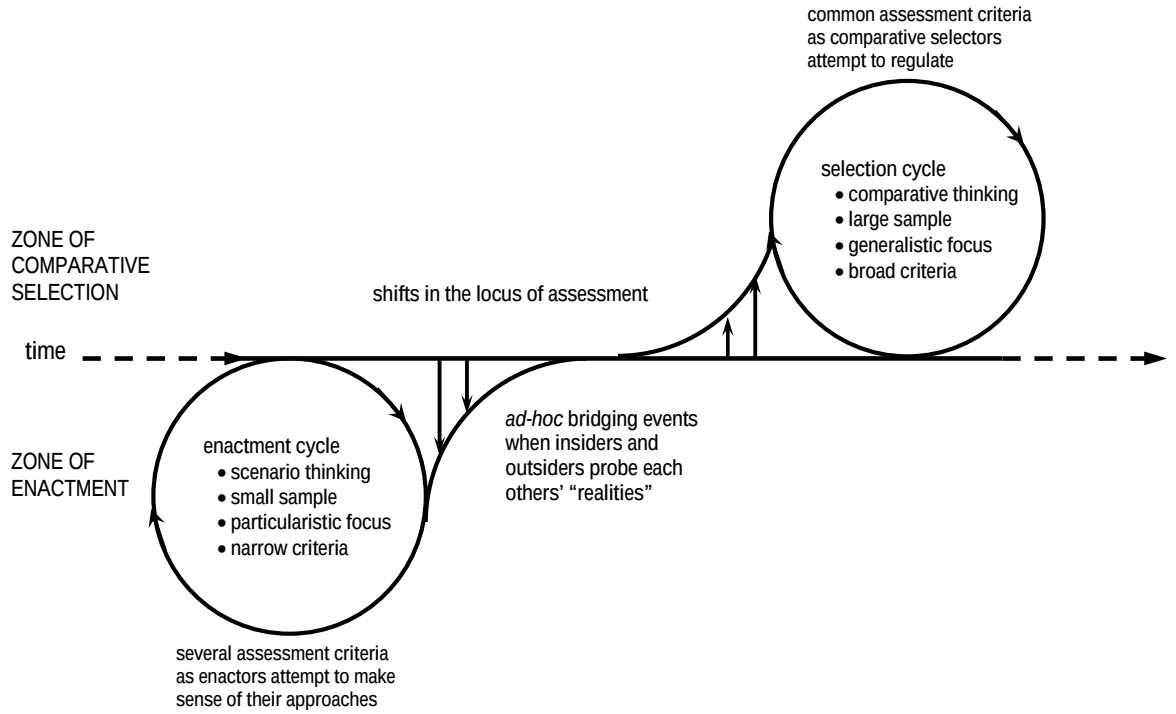

Figure 1.1: Enactment and Selection – adapted from Garud and Ahlstrom 1997

The modification is to speak of zones of enactment and comparative selection (at the left-hand side of the diagram), rather than "insiders" and "outsiders", because the latter terminology refers to boundaries and memberships rather than to type of activity and role. The crucial point is then that these zones interfere in various ways, including through bridging events. Another such interference (and with a more structural character) is Cowan (1987)'s analysis in terms of a consumption junction. Interference may not be productive, or will just reproduce the differences that were there already. To help bridging promotion and control, one can start by identifying (possible) interference locations and events and what can happen there. These can then be supported, and one could also be pro-active and create (or better,

contribute to the creation of) bridging events. Over time, some institutionalization might occur.

As indicated earlier, a weakening of, or holes appearing in, the division between technology development and society, is occurring. Ad-hoc bridging is visible in nanotechnology, and is now actively pushed by policy makers and some nanotechnology enactors. It may become a general trend for other new fields of technology development. At the time when the work reported in this thesis started (in 2004) the bridging events when they occurred were located outside of the enactment zones of nanoscientists, in somewhat neutral territory, and there was little feedback of the outcomes of bridging activities into the ongoing activities of nanoscientists. Thus, there was a need as well as an opportunity to do better.

The added value of the Garud and Ahlstrom inspired analysis in terms of interference and bridging events is that it is not just about discussion of a particular issue (for example, the extent to which the precautionary principle should be applied), but also about experience and recognition of different perspectives. In this way, a basis for further and more productive "interference" may emerge.

In other words, designing and orchestrating bridging events would be an important way to develop and apply Constructive TA in practice. This would allow broadening by including more aspects and perspectives at an early stage. The learning about handling "interference" that would occur would enable doing better the next time, and perhaps lead to some institutionalization. This would amount to co-evolution of technology and society becoming more reflexive. That cannot be a goal of the thesis, of course. The aim is to develop practical ways to do Constructive TA for newly emerging technologies, with a particular focus on broadening "enactment cycles". But we should recognize that this can be a contribution to broader change.

1.1.4 Research themes

Given the location of this study as part of TA NanoNed, and the observations and arguments developed in 1.1.2 and 1.1.3, my entrance point is how ongoing developments in nanotechnology are shaped by enactment cycles, and how such enactment cycles can be broadened. This implies two types of activities: analysis of dynamics (and develop tools for better analysis and diagnosis) and design and experiment with bridging events. Analysis and design/experiment will feed into each other.

To articulate the research themes, I start with observations about the present situation. In 1.1.2 I identified four pressures (without going into further analysis of what kind of pressures these are and where they come from):

a. a pressure to translate research into applications that will benefit the economy and benefit society (a responsibility to innovate); ‘

b. a pressure to be strategic, in particular to undertake anticipatory coordination activities up to roadmapping and agenda building;

c. a pressure to be transparent and pay attention to public outreach, up to early (“upstream”) public engagement;

d. a pressure to engage with, and include, ethical and societal aspects of technology development activities (in a move towards responsible research and innovation);

So the historical division between technology development and society is becoming less strong, and bridging occurs already at early stages. Such bridging is not limited to the nanotechnology enactors which feel these pressures, but the enactors play a particular role because of their knowledge and the possibilities to shape developments (through choices, through networking).

Nanotechnology being at a very early stage, the assessments must rely on anticipations: anticipations about future developments and performance of nano-materials and nano-devices, and about eventual societal uptake and impact. This is a challenge in its own right, and leads to the need to develop tools for such controlled speculation, as well as the need to broaden anticipatory activities, in particular of and for nanotechnology enactors. The latter is additionally important because nanoscientists and nanotechnologists work within a concentric perspective, which structures their anticipations of future developments.

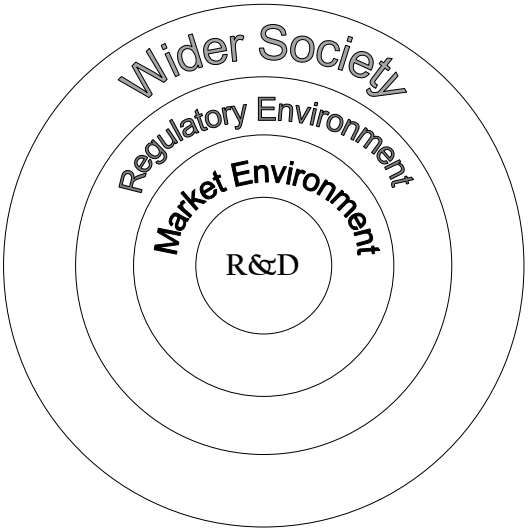

Figure 2.1: The environments of the technology embedment process as concentric layers around R&D (adapted from Deuten et al. 1997)

For example in the case of the development of new products, product managers often view the environment as concentric layers around the development of a new product, from the business environment to eventually the wider society.

While alignments with all layers need to be made, the product manager often deals with them sequentially, starting first with clarifying functional aspects of the product, before addressing broader aspects (Deuten et al. 1997).

For nanotechnology, at its early stage, nanotechnologists occupy a very powerful role, albeit slightly eroded due to the pressures outlined above. But the nanotechnologists as "insiders" know very little about the "outside" and in fact, structure their position in the process of value creation and "technology transfer" in terms of the linear model, and thus frame their activities in a concentric way. [4]

How to anticipate better? A key point is that nanotechnologies are enabling technologies and their eventual uptake will be as elements (although perhaps key ones) in products (e.g. sun screens, nanotextiles, advanced memory chips, drug delivery systems) and services (e.g. advanced analytical tools with nanoscale resolution, nanofabrication processes and foundries). The impact of nanotechnology therefore will depend on what happens in these sectors. In other words, nanotechnology impacts are co-produced. Analysis and controlled speculation must therefore focus on this co-production including expectations and how these evolve, shape and eventually form agendas, and on the parallel emergence of R&D networks, industrial consortia and how these support particular directions or pathways) of development over others. The combination of evolving

[4] Thus, another asymmetry, now in the enactors' limited understanding of the processes of production of potential societal impacts. Put positively, nanotechnologists, if they are serious about considering and anticipating on societal embedment processes, have something to gain by engaging in bridging.

agendas and emergent structures, and the irreversibilities that arise, sets patterns for further developments. Such patterns shape further actions and choices, and in that way, embody 'endogenous futures', and are predictors for what may happen. But the issue is not just about predictability and thus better management (broadly speaking), but also about broadening the development of nanotechnology.

Doing this at an early stage requires broadening the concentric bias and includes non-linear models of innovation. Such approaches require inputs from science, technology and innovation studies, in particular evolutionary economics and industrial economics. In my brief literature review in Section 1.2 I will argue that further work is necessary. I will do some dedicated work on this point (see Part II of this study for the published results).

These observations allow me to formulate the first two research themes:

Research Theme 1: Exploring the dynamics and patterns that are part of the emergence of nanotechnologies (in real time) with a view to understanding enactment processes (cycles) and how they shape the emerging development pathways of nanotechnology

Research Theme 2: Developing tools to support controlled speculation on the co-evolution of nanotechnology and its embedment into (or rejection by) society

Work on these two themes will contribute to relevant literatures, and be important for all actors concerned. Broadening enactment cycles, the other main goal, has enactors as first-round audience and target group. There is little earlier experience to guide us there, other than some Constructive TA studies and exercises on technologies at a later stage of development. This implies that I have to develop research approaches for the design and experiment part of my work (see Section 1.3).

What I can say already is that the exercises must be embedded, or "inserted" as I will call it later, in ongoing activities of nanotechnology enactors. A similar requirement holds for action research, but for action research there is an immediate change goal shared with actors who are themselves involved in doing the research (Reason 2001). In my Constructive TA exercises designed as bridging events, there is a stronger role of analysis, and only a mediated change goal. The participants in the exercises will learn, including recognition of perspectives of other actors, and this will inform and shape their later choices and interactions in their own contexts. As observed in Section 1.1.2, at the current stage of emergence

of nanotechnology, there are definitely openings for exploring interactions and events to support the broadening of enactment cycles.

This informs my formulation of the last two research themes. They include specific items which will be developed a bit further in Section 1.3.

Research Theme 3: Designing of productive bridging events, embedded in the ongoing activities of nanotechnologists, and with an emphasis on anticipatory technology assessment and strategy articulation.

Research Theme 4: Orchestrating and subsequently evaluating such events, structured around controlled speculation and relevant dimensions of bridging.

In doing this, and reflecting on what happens, also in wider contexts of my work on the Constructive TA exercises, I can observe co-evolution of technology and society at work in real time, and speculate about it becoming more reflexive. This is not a research theme that will be addressed as such, but I will return to these considerations in my concluding chapter.

1.2 Relevant bodies of literature

Much of the relevant literature is mobilized and reviewed in the articles that make up Chapters 2 to 5. Here, the focus will be on the key points of the first two Research Themes (Section 1.1.4): tracing emergence and anticipating better. The two are linked through the phenomenon of emerging patterns (which embody irreversibilities), because this phenomenon implies that futures are partly "endogenous". Existing literature offers important insights already, particularly in evolutionary approaches to techno-economic change and in Actor-Network Theory, but more should be done. Similarly, future-oriented technology analysis has been developed but should be extended by introducing more complexity – which can be done on the basis of evolutionary economics and sociology of technical change, with some Actor Network theory added. This will be argued below, and I can then (in section 1.2.3) to briefly position Constructive TA.

1.2.1 Emerging patterns and their stabilization

The key question has been formulated by Callon (1992) as the dynamics of "hot" (open, fluid) situations and "cold" (articulated and in that sense closed, stable)

situations. His interest then (as more generally in Actor-Network Theory) was mainly in showing the fluidity of "hot" situations, not in the transition from "hot" to "cold". In the literature on economics of technology and innovation, there has been a strong interest in the emergence of dominant designs, but with a bias toward looking for success factors. In SCOT, there is an interest in process and ongoing closure, which has led to interesting case studies but less attention to possible patterns.

For my research themes, I can use these literatures, but critically. In developing an approach that addresses "emergence" directly, I can build on earlier work on quasi-evolutionary approaches and the role of expectations (Van den Belt and Rip 1987, Van Lente 1993), on studies of technology dynamics (Van de Poel 1998, Deuten 2003). There is further relevant work, but these are some key references. Recent work on path dependence and path creation is also very relevant, and I have been involved in it (Robinson 2006a, Rip and Robinson 2006, Rip, Robinson and Te Kulve 2007).

Let me start with a brief discussion of the emergence of scientific-technical fields (which might well be applicable to nanoscience), rather than with technological innovation.

The first stages of a possible new field, is the emergence of what can be called a socio-technical world[5]. This first manifestation of this world is the demarcation of what is inside and what is outside the world. There, the naming of the world becomes important, as is visible in nanotechnology as it became a dominant label after 2000 (including struggles what is to be counted in – is heterogeneous catalysis which existed already now nanotechnology? But supramolecular chemistry existed already as well, and tends to be included under the nanotechnology label without much discussion). A further characteristic of an emerging socio-technical world is that the actors involved are interested in continuing their membership and maintenance of this world. It can also be the case that other actors wish not to be part of the world, which also contributes to the definition of the boundaries of the socio-technical world.

As these socio-technical worlds become more coherent, more actors become involved and are mutually dependent, a *cultural repertoire* emerges which includes

[5] I use the term socio-technical world to emphasise that the ongoing technological component of the emerging world of actors is part of the analysis. The technological aspect be it embodied in expectations, shared visions, problems to be solved, etc., shapes (and is itself shaped by) the actors in the socio-technical world.

stable reputations, champions of the field and a shared agenda of what is important to do and why. There is an ongoing activity to find solutions to problems, identified as important by the actors within the world. While scientific directions become articulated, their technological complements may well remain diffuse and varied.

At this time, networks begin to emerge. Such networks may take the form of actors which are connected through shared beliefs, expectations, visions, evaluation routines, guiding artefacts, shared agendas etc. (Garud & Rappa 1994).When this stabilizes, those who try to explore a new option which is incompatible with the evaluation routines and beliefs currently held by the actors in the network will find it difficult to mobilise resources to enable exploration and creation of a new technological path.

The stabilization of such enabling and constraining networks occurs through actors becoming connected through mutual translation in/through the exchange of intermediaries such as scientific articles, software, technological artefacts, instrumentation and technology platforms, money, contracts etc. [6] All this gets entangled i.e. cannot move completely independently anymore (Rip and Robinson 2006, Rip 2010).

For technological innovation, other dynamics are important, but irreversibilities will emerge again. A useful entrance point to analyse and understand socio-technical entanglement is the notion of alignment, in particular across contexts and levels. This builds on the seminal work of Abernathy and Clark (1985), and also draws inspiration from Fujimura (1987) about how alignment across levels can be actively sought.

When a novelty is recognized and introduced in an existing order, this requires de-alignment (of existing linkages and competencies) and then (but in the same movement) re-alignment (cf. Abernathy and Clark 1985, and our extension of their approach by including societal embedment). Technological interrelatedness and sunk investments can (and should) be studied in these terms. (cf. Rip, Robinson and Te Kulve 2007 for more detailed argument and examples.)

Fujimura has shown how research becomes doable because of alignment across levels (work in the lab, the institute, the wider world, especially sponsors of

[6] This is the important insight from Actor-Network Theory. “An intermediary is anything that passes from one actor to another, and which constitutes the form and the substance of the relation set up between them.” Callon (1992)

research). Similarly, nanotechnology paths become "doable" when there is alignment:

- of ongoing work (and the practices this is embedded in), also across locations,
- of the relevant institutions and networks that are directly involved, but also "third parties" who can provide or withhold credibility and legitimation (examples would be insurance companies, NGOs and critical or activist groups – the cluster of socio-technical paths of nano-particles is strongly shaped by these third parties),
- of overall institutions, arrangements and authorities in our society (like patent law and patenting practices, which were important for the azo-dyes trajectory in the late 19th century (Rip and van den Belt 1987), and again with biotechnology; but also issues of public/private collaboration).

Alignment across contexts is important for the innovation chains from laboratory to products and applications, and eventual societal embedding. What has to be done to achieve alignment is easier to recognize when the actors are known, their relationships functioning, regulation is largely unambiguous and the technology field is well understood. This is the case in "cold" situations. For new and emerging fields of science and technology where architectural (radical) innovations might occur (terminology from Abernathy & Clark 1985), conditions of high technology and market (and societal) uncertainty are typical – a "hot" situation. In practice, actors address this situation by 'muddling through' and capitalising on fortuitous events. At the same time, in an age of strategic science and high-investment projects scientists and decision makers need to identify possible and promising directions and options at an early stage. This then leads to attempt of actors and (not just the formal decision makers) to reduce uncertainty through anticipatory alignment. Presently fashionable roadmapping exercises are an example, European Technology Platforms and other such forums are social locations for anticipatory alignment (which can be seen actively pursued, as in the European Technology Platform Nanomedicine).

Alignment refers to the eventual entanglement of actors and activities in such a way that there is some mutual dependency; they cannot move completely independently. There is some mutual accommodation, like parts fitting together, creating a configuration that works. Alignment can emerge because actors and activities accommodate to the same environmental constraints. It can also be actively pursued, and institutional entrepreneurs will then play an important role

(Garud et al. 2007). Actor-network theory with its interest in "enrolment" and "obligatory passage points" has offered useful case studies (Latour 1987).

Alignment across levels is particularly important because it introduces vicarious stabilisation: if actors or circumstances appear to move in other directions and might actually be able to do so on their own level, they will still be constrained by the links to another level with its own dynamics, which makes it more difficult for these actors to effect change at the other level. The implication is that actors who can work at two (or more) levels – in Rip, Robinson and Te Kulve (2007), we called them *linking-pin entrepreneurs* – play a key role in multi-level alignment. Dutch nanoscientist David Reinhoudt, driving force of the NanoNed consortium, is an interesting example (see Robinson 2007, reprinted as Chapter 2).

The insights from the literature presented (and integrated) here can be positioned as an evolutionary approach, but with more complexity (multi-level, role of change agents) than is usual in the literature on evolutionary economics of technical change where variation/selection is taken as the basic mechanism (e.g. Metcalfe 1998), and firms are the basic unit (Nelson and Winter 1977). That literature has itself evolved, however. Particularly interesting for my theme is how early ideas about what I called emerging and stabilizing patterns of alignment have been developed further. In the same movement, the role of actors and anticipations became more visible.

Using different terminology, Dosi (1982) and Nelson and Winter (1977) – the latter can be considered to be founders of the evolutionary approach to technical change – showed there are particular patterns in technical change. Dosi proposed to speak of technical paradigms which direct activities in technology development and thus are rules that guide heuristics as well as strategic resources to move further (from the actor perspective).

> "Technical paradigms are 'models' and 'patterns' for finding solutions to *selected* technological problems, based on *selected* principles derived from natural sciences and on *selected* material technology (…). A technological paradigm embodies strong prescriptions on the *directions* of technical change to pursue and those to neglect." (Dosi, 1982, p 152)

Nelson & Winter used the example of airplane construction to show that different firms shared particular search and development routines, which add up to what they term as a technical trajectory at the sector level: The DC-3 aircraft in the 1930s was the template for over 20 years for innovation in aircraft design around piston powered planes with metal skin and low wings. The potential of these

elements was incrementally exploited, improving the engines, enlarging the planes, making them more efficient.

In the DC-3 (and further) case engineers were singled out as the drivers of the development. In other situations, it may be a continuing product-use combination (cf. the recent trajectory of mobile telephony), or industry structures (such as the energy sector) or strategic games (as with Moore's Law for semiconductors).

While Nelson and Winter (1977) and Dosi (1982) positioned their approach as evolutionary, their cases showed that the variations produced were not blind. Van den Belt and Rip (1987) developed this further, and showed (with the help of the case of emergence of synthetic dye paradigms) how expectations about new possibilities, as well as attempts to "domesticate" harsh selection environments played key roles. Their so-called quasi-evolutionary (but in any case, sociological) approach has been developed further, up to analysis of so-called technological transitions (Geels 2002a).

A key point is "For new technologies, these expectations have the form of 'diffuse scenarios', sketching a possible future world for the product. These scenarios involve assumptions about users, markets, regulation, technical progress etc. So, already in an early stage, actors anticipate on future 'actor-worlds' to use a term from actor-network theory (Callon, 1986). Such expectations provide guidance to R&D activities, especially when translated into field agendas and search heuristics. Furthermore, expectations and scenarios are used strategically by product champions, who make promises to attract attention and resources from other actors." (Geels and Schot 2007)

Phrased this way, one sees an important element of the dynamics of emergence and stabilization, and one which can also be an entrance point for consideration of future-oriented technology analysis, because it puts methodologies like scenario building and roadmapping in their social contexts.

A similar message can be drawn from the literature on path dependence in technological change (which is often seen as part of the evolutionary economics approach). In the economics literature, the concept of path dependence was introduced by David (1985) and in a slightly different way by Arthur (1990), for the purpose of explaining why certain technologies become dominant even though they may be sub-optimal. David's paradigmatic case of the QWERTY typewriter layout which became impossible to replace even into the time that typewriters were replaced by computer consoles is the most quoted example. They explain the occurrence of such a self-reinforcing process beyond the control of the actors involved in terms of increasing returns after a first and perhaps fortuitous

advantage which then create a lock-in because of sunk investments and embedding in strongly aligned and widely dispersed networks.

The point about sub-optimality has been softened and the concept of path dependence is now used in sociology and history to indicate the difficulty to break out of an established path. This can then further dissolve into the empty claim that history matters.

Halfway between sub-optimal lock-ins and "history matters" is the concept of emerging and stabilizing irreversibilities which informed my earlier discussion of emergence and stabilization.[7] This may lead to a cluster of irreversibilities which then constitutes a path, the strength of which can still vary. How "strong" the path is, i.e. how difficult it is to deviate, is not given once and for all, but depends on changing contexts and initiatives of actors.

Garud & Karnøe (2001) have made a strong point about agency in arguing that there is 'path creation' just as much as 'path dependence':

> *entrepreneurs may intentionally deviate from existing artifacts and relevance structures, fully aware they may be creating inefficiencies in the present, but also aware that such steps are required to create new futures. Such a process of mindful deviation lies at the heart of path creation. (Garud & Karnøe 2001, p.6.)*

In such a situation, vision, analysis/diagnosis, and willingness to take risks go together. Thus, there is an element of informal future-oriented technology analysis involved. This can be supported by more formal methods to anticipate, but it remains the context for such dedicated exercises.

The combination of emerging irreversibilities and stabilising shared expectations (related to formal and informal future-oriented technology analysis) can be combined and thought of in terms of entangled activities[8], directions to go,

[7] The idea of emerging irreversibilities emerged in the 1990s in the work of Michel Callon and Arie Rip (Callon 1991, Callon 1992, Rip 1995, Rip and Kemp 1998) through research into the dynamics of emerging fields. The notion of emerging irreversibilities combines emerging structure (as in path dependence literature) with agency (as in path creation literature) by looking at indicators of alignment and stabilisation in the evolution of new and emerging science and technology. It is a way to trace the transition from "hot" to "cold".

[8] Entanglements are "associations that last longer than the interactions that formed them" (Callon and Latour 1981: 283) emphasizing that actors and activities can become mutually

emerging but precarious patterns, all of which can be conceived as actual or possible paths. A 'path' then becomes an actor's claim about actual and possible order of the socio-technical world, a claim to which other actors may well respond, reinforcing or undermining it. The claim may turn into provisional reality. This is how Moore's Law (for semiconductor development) started in the 1960s – to become a reference point in strategic games, and the backbone of the International Semiconductor Technology Roadmapping exercises, thus reproducing itself.

Looking at emerging and stabilising paths in this way, as ingredients of a complex, heterogeneous, and multi-level socio-technical world, shifts the attention to the socio-technical entanglements as the entrance point to study the emergence and co-evolution of nanotechnology developments.

1.2.2 Methods to improve anticipation and interaction

Methods range from future-oriented technology analysis/assessment and bridging approaches, up to Constructive TA. There is a large literature, from earlier technological forecasting (still alive and kicking, but difficult to apply in the case of emerging technologies) to technology foresight and what is now called future-oriented technology analysis (the series of IPTS conferences)[9]. There are limitations to this literature, for one thing because of their neglect of ongoing informal anticipations in concrete situations which will be the context for eventual uptake of such dedicated exercises. I highlighted this already towards the end of the preceding subsection.

There is another limitation in the literature, which is the neglect of ongoing sociotechnical dynamics while this should be an integral part of any dedicated attempt at anticipation. This is particularly clear in roadmapping, when it backcasts from envisioned product-market combinations to set priorities for ongoing research and action (cf. Fiedeler et al 2004, and Fleischer et al 2004). There is little attention to the actual road to be followed to get there, and to the dynamics that will be

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dependent: they cannot move independently anymore. These associations can be related to the ways of handling risk, or of ELSA, foresight, public engagement and agenda building.

[9] The International Seville Conference on Future-Oriented Technology Analysis (FTA) is a conference held every two years brings together FTA experts, practitioners, researchers and decision-makers in the field. It is based on conference papers and approximately 14 are chosen from the 80 or so papers to be published in high ranked peer-reviewed journals. http://foresight.jrc.ec.europa.eu/fta.html

involved.[10] They assume "makeability": if we outline what we want, and put in a concerted effort, we will achieve – somehow. When they are not part of actual organized anticipatory coordination, as is the case with the International Semiconductor Technology Roadmap (www.itrs.net) roadmapping exercises remain just that, a report filed and left lying on a shelf.

If one does include sociotechnical dynamics, future-oriented technology analysis becomes more complex (in Chapter 6 I will present a way how to do that with 'complexity scenarios'). The key entrance point are the emerging and stabilising patterns, approaches, and interactions as discussed in the preceding subsection. These will shape, tentatively at first, what actors will do and how interactions will be perceived and taken up in further actions. Ongoing dynamics thus shape the future, or at least create affordances for particular futures. In other words, futures are "endogenous" in the present dynamics. This is not determinism: actors are reproducing the patterns or occasionally deviating. But it is an opportunity to do better future-oriented technology analysis, taking into account the complexities of the past, as well as how to understand them. This then allows reflexive anticipation (Geels 2002). Reflexive anticipation can still take different forms, using different kinds of methodological and professional support.

Garud and Karnøe (2001) make an evocative point:

> "*the role of agency [in path dependency literature] can be viewed as one of entrepreneurs watching the rear view mirror and driving forward*" (page 7)

In other words, actors are driven by their past rather than driving themselves. To some extent they are: the emerging and stabilizing patterns and trajectories at the collective level shape what individual actors will do. Or at least, create gradients where it is easier to do some things rather than others. Insight into the nature of these co-constructed processes allows to "deviate", not because one wants to achieve a better future (while that may play a role), but because one recognizes opportunities to do something different.

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[10] There are a few interesting discussions about roadmapping. Walsh (2004) suggests that, rather than considering the product-market paradigm, the technology product paradigm is the entrance point into roadmapping: a company uses a technology to form a 'core product', which is then used as a platform to derive application-specific products from (cf. also the concept of 'generic richness' developed in the ATBEST project, see Spinardi and Williams (2005))

Another route starts with analysis. The relevant literature is inspired by Actor-Network Theory and the idea of transition from hot to cold. The EU-funded project SOCROBUST was an attempt at creating anticipatory management and assessment tools for analysis and improving the societal embedding of innovations (Larédo et al. 2002). Contexts were captured in term of 'Techno-Economic Networks' (Callon et al. 1991). Thus, what had been seriously neglected, "the processes of solidification and partial irreversibilisation turning the fluid into the stabilised", should now be taken up. Building on a further assessment tool, 'future scripts' (De Laat 2000), it is proposed to create a picture of the future as embedded in the actions and views of the project, and then confront it with information about what is actually going on, and perhaps may have to be modified.

Scenario approaches are attractive, since they can capture complexities in a story and indicate lateral movements in the development. In the literature, and in actual scenario exercises, there is a strong tendency to create a possible future first, and only then ask (if at all) how to get there (Wack P. 1985a, 1985b). However useful such scenarios are to set the mind free of preconceptions, there is a distance to the scenarios embedded in ongoing developments. To make the latter explicit, including important emerging patterns and dilemmas, will also set the mind free, but now in terms of what could be done to modulate developments, up to actual deviation.

Up until now, I have focused on anticipation from within the world of technology development. This interacts with initiatives "from the outside in" (Rip 2007) and may lead to bridging events (see section 1.1.3). In terms of methods of anticipation and interaction, the evolution of TA is instructive. As Rip (2001) describes it:

> TA exercises can be oriented to the public arena more generally, and focus on articulation and building an agenda for handling new technology in society. This most recent strand takes up the increasing calls for participation (at least by so-called new stakeholders like environmental groups). While it is particularly visible and more or less institutionalised in some European countries (Denmark, the Netherlands), participatory methods like consensus conferences have been taken up all over the world (Guston and Bimber 1997). Agenda-building TA has a longer history, however, given that controversies over new projects or new technologies (and the studies and documents produced in the course of the controversy) induce learning about potential impacts and articulation of the value of the technology. Agenda-building TA merges into informed consultation processes to reach agreement on the value of new technology. Thus, there

is overlap between TA and more general political and policy approaches for articulation and learning.

There is, by now, a range of approaches to technology assessment. Foresight and future visioning emphasise the open future, and there are now proposals for 'vision assessment' (Grin and Grunwald, 2000). At the other end of the spectrum there is the comparison of existing technological options by firms and R&D institutions in order to select the promising ones. Within the range of approaches, a cluster of approaches and methodologies have been developed and piloted over the last 10–15 years, which emphasise real time interaction and learning. There are various labels, including Interactive TA (Grin and Van de Graaf 1996, Grin et al.1997), Real-Time TA (Guston and Sarewitz 2002), and Constructive TA (Rip et al. 1995).

Constructive TA places an emphasis on contributing to the actual construction of new technologies and the way these become more or less embedded in society – rather than simply waiting for the changes and then trying to map possible impacts. Historically, CTA grew out of developments in the Netherlands during the early 1980s, with the 1984 Policy Memorandum on Integration of Science and Technology in Society including an interest in broadening processes of technological development. In other words, rather than waiting for technology to enter society (when impacts would be visible), assessment would be done earlier and the results should feedback into other actual developments of technology, and therefore playing a constructive role.

The approach shifts the focus of future oriented technology assessment away from the reliance on processes of prediction in its strictest sense, and shifts towards a process of reflexive anticipation through controlled speculation based on exploring the underlying dynamics of emergence. Constructive Technology Assessment (Schot and Rip 1997, Rip and Schot 2002) was developed with an emphasis on anticipation, articulation and feedback into ongoing processes. While actors will always take enabling and constraining factors in the situation into account, Constructive TA adds to this because of a broader & deeper understanding of socio-technical dynamics.

For early stages, such as that for nanotechnology, one needs analysis of processes of emergence and partial stabilisation in order to control speculation. This is the analysis and diagnosis part of the equation, and I have outlined approaches (including sociotechnical scenarios) in discussion with relevant literatures. Constructive TA also includes feedback to ongoing technology developments, but it has remained programmatic as to active attempts at feedback. This is where experiments in interaction are in order. There is literature on action research, but

this has a different focus (see below, section 1.3.1). Given the choice to experiment with bridging events (section 1.1.3); there is some literature to draw on for inspiration. Particularly relevant is the design and evaluation of an interactive TA exercise about genetically modified vines (Marris et al. 2008), because it addresses a key issue for designing and orchestrating bridging events: these are microcosms in which some dynamics of the real world occur, and learning may take place. But the macrocosm has its own dynamics, and this will determine eventual feedback of the exercise.

1.3 Research Approaches and Organisation of the Thesis

The general approach outlined in section 1.1 has to be specified further, and with the benefit of my selective *tour d'horizon* of the literature in section 1.2. Since the primary goal is broadening of enactment cycles, this requires embedding of the activities in the evolving world of nanotechnology (requirements 1 and 2), as well as positioning them as experiments that can be evaluated (requirement 3).

1.3.1 Embedding of Constructive TA in ongoing developments of nanotechnology – requires insertion

In the world of nanotechnology, there is an interest in anticipation and coordination so as to choose right directions. The actual and potential stakeholders are attempting to shape emerging nanotechnology developments, in different fora and with a variety of strategies. For CTA-projects to be legitimate, for them to be accepted as part of the world of nanotechnology developers, they must be link up with their world – i.e. make reasonable claims about the present, recent past and potential future developments. This requires more than distantiated study. Visiting locations of nanotechnology R&D and of anticipatory coordinating activities that are shaping nanotechnology developments is the first step. One could characterize this as 'moving about' in the world of nanotechnology. There should be interactions as well, and the CTA analyst/agent should enter into the substance of the developments and concerns so as to be a legitimate partner. This second step can be characterized as 'insertion' in the world of nanotechnology. Insertion is the process of becoming a temporary member of the field (a recognised visitor). The inserted analyst should not go native; this requires constant reaffirmation that the analyst is a visitor and not a full member. (Cf. also my remarks in 1.1.4 about the difference with action research.)

The 'insertion' approach is oriented towards data collection by being around and occasionally probing, and towards creating legitimacy (or at least recognition) for

Constructive TA exercises. It is not a dedicated change action, even if it cannot avoid introducing changes in the situation. As I noted before, there is a background goal of increasing reflexivity of co-evolution of technology and society, but that is possible effect, rather than a dedicated goal.

There is an interesting link with Lindblom's (1990) plea for inquiry (rather than a search for truth as such) in relation to change.[11] People probe the world (probe into situations, into other actor's perspectives, into problems and possible solutions) in order to change it, and this is a kind of inquiry, and the resulting insights can be formulated as such, somewhat independent of proposed actions. Social scientists may not have a strong change perspective, but they also probe the world. Lindblom emphasizes that there is no epistemological difference between probing by citizens, by government functionaries and by social scientists. However, the latter may well have more honed and articulated probing skills. When one scales down the scope of Lindblom's argument from society in general to the world of nanotechnology development, it constitutes a justification of the 'insertion' approach and allows further specification in terms of probing: by the social scientists, but also as something that actors do, and is important to support because it produces practical knowledge and understanding. Garud and Ahlstrom's (1997) notion of 'probing each other's realities' (see Figure 1) fits with Lindblom's perspective on inquiry, and my approach to the Constructive TA exercises, with scenarios built on social-science insights which will improve the quality of mutual probing in the workshops, is a further step where the more honed and articulated probing skills of the social scientist are packaged so as to improve the quality of the interactions of the actors..

1.3.2 Understanding the nanotechnology world – requires analysis of emergence

The targeting and embedding CTA into the ongoing activities of nanoscientists must be legitimate (accepted into the world of nanoscientists) and well informed (necessary for legitimation). Thus, the CTA must be supported by data which is:

(a) **timely** – the rapidly changing context of nanotechnology emergence requires a (near or fully) real-time assessment of nanotechnology activities and the co-evolution

[11] Charles E. Lindblom, Inquiry and Change. The Troubled Attempt to Understand and Shape Society. New Haven, CT: Yale University Press, 1990

(b) **accurate** – as close to the actual activities (including the shifting expectations and agendas) in relation to nanotechnology development

(c) **broad and deep** – that it covers a wide enough field to capture the dynamics of co-evolution and deep enough to be able to identify and address relevant issues and dilemmas in the field

This requires the analysis of how nanotechnologies are emerging and how technology developers are anticipating and acting (the stuff of enactment cycles). The study of the processes of emergence can apply concepts such as emerging irreversibilities (through exploring entanglements) and the sociology of expectations.

The next step: 'endogenous futures' as the basis for scenarios about possible further developments. Such scenario building must take co-production of outcomes and non-linearities into account, and can thus be seen as a speculative application from insights of technology dynamics and evolutionary economics (with my own twists).

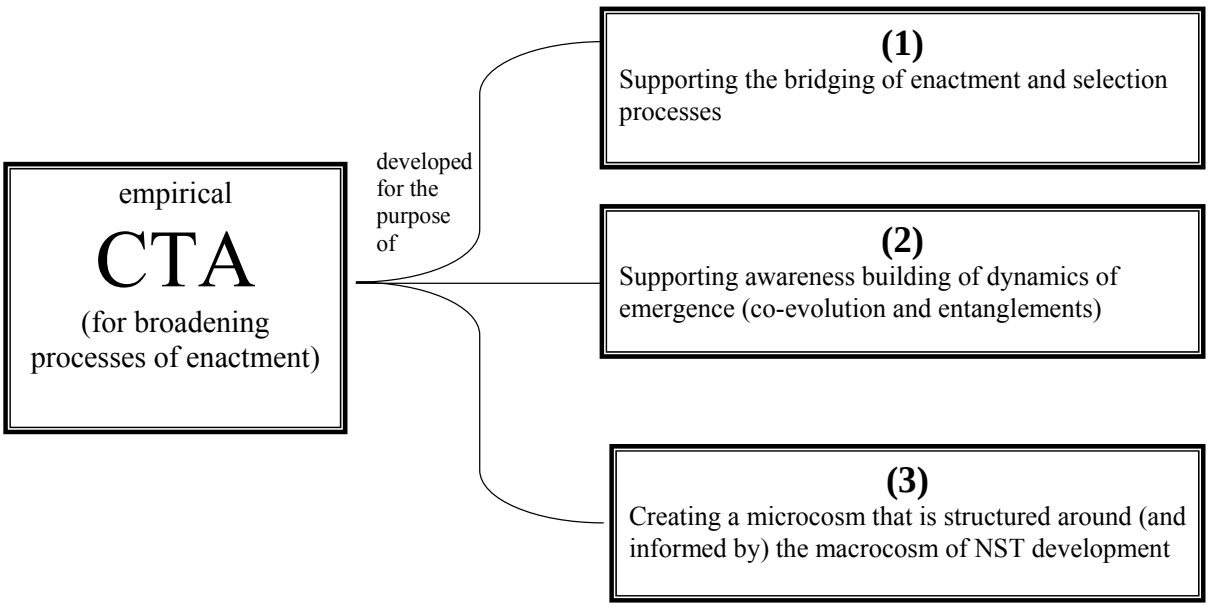
Such scenarios also serve to make participants in the exercise more aware of complexities, and allows them to think more broadly about challenges and dilemmas. To reach the main target audience, nanotechnology enactors, the scenarios are written from an enactor position, but without the concentric bias. They have to mitigate the effects of the unavoidable concentric bias of enactors.

1.3.3 The CTA approach operationalized: requires testing

Can bridging events be embedded successfully into the ongoing activities of nanotechnologists and can they lead to broadening enactment cycles? This can only be answered by conducting CTA experiments in the world of nanotechnology development, exploring the productivity of controlled speculation processes and orchestrated bridging events. The actual methodologies of creating sociotechnical scenarios and using them in the workshops that function as bridging events, up to the organisation of the workshop and the "animation" during it (by the moderator chairing the workshop and by the domain and CTA expert), will be discussed in Chapter 7 and shown in some detail in the Appendices. Here, I limit myself to noting that there is a large experience with focus groups, which overlap to some extent with the aims and the dynamics of my workshops. The main difference is the use of pre-circulated scenarios to support discussion of substantial issues rather than just offering viewpoints.

A broadening of enactment processes is afforded when competences (and motivation) are developed and in place to anticipate and articulate issues relating to the technology beyond the concentric bias and recognising (taking up and using insights) broader dynamics of co-evolution, of the nonlinearity of innovation, and of non-enactor assessment worlds.

The exercises in empirical CTA for broadening the enactment process have three aims. Each aim leads to requirements in designing and doing the exercises, and to dimensions along which the exercises can be evaluated (these will be specified in detail in Chapter 7).



1.3.4 Organization of the thesis

The three activities outlined earlier have to be (and were) undertaken in parallel, in order to capture elements of nanotechnology emergence in real-time. This poses challenges for writing up (and for the reader), however there are distinct (albeit overlapping) types of research activity which allow separation into different parts:

Part II: Analysis of Nanotechnology

Part III: CTA by insertion in the nano-world

Appendix: Reports on five CTA projects as experiments

Briefly put, these cover:

PART II – Analysis of Nanotechnology

This part presents my studies of nanotechnology through my participation in a number of research activities. This includes the key papers that were written during this PhD project. As contributions in of themselves to the TA NanoNed programme they also provide insights into emergence of nanotechnology and the shaping roles of expectations dynamics, emerging irreversibilities, of institutional entrepreneurship and multi-level entanglements. They also present two tools that were developed in the context of my CTA activities for harnessing the insights gained from applying concepts from technology studies and innovation studies and translating this intelligence into forms that can be useful for CTA purposes. The chapters describe in great depth the construction and application of the tools (which will not be covered in such depth elsewhere in this volume).

PART III – CTA by insertion into the nanoworld

This part comprises three chapters. The first describes my moving about and insertion into the nanoworld, in conferences, meetings and other nanoactivities. It describes the creation of what would become a programme of CTA-activities within a nanotechnology R&D consortium, and how it evolved amidst the co-evolution of the R&D consortia and the multi-level alignment activities occurring in the world of nanotechnology development. The chapter provides insights into the shifts and orientations of nanotechnology development and the incorporation or exclusion of elements of responsible innovation. It also describes the tensions, contingencies and opportunities that faced me as an inserted CTA-agent.

The following chapter explores the CTA projects as experiments. Five CTA-projects were conducted (each described in full in the Appendices). This chapter compares the findings from the five workshops paying attention to the initiation and preparation of the CTA workshops, the dynamics that occur within CTA workshops and the productivity of the workshops. The overall question of how productive these attempts were at broadening and bridging will be explored.

The remaining chapter of this part provides the overall conclusions and discussion from this PhD activity.

Appendix –Reports of CTA projects as experiment

To allow the reader of this thesis to see the development and execution of each CTA experiment in detail, I place a case study account of each CTA-project in the appendices. These are substantial in detail and are individual chapters in of themselves. In PART III I draw on these Appendices as source material (this is

why they are in the appendices). Each CTA-project is written chronologically to allow the reader to see the construction of the CTA-project and is split into three sections: (1) the details of the focus topic and the contingencies that shape CTA embedded in the nanoworld and also traces how the contingent factors, (2) the design of the CTA and (3) the undertaking of CTA workshops. All three elements influence the productivity of such CTA.

PART II

Chapter 2 Technology agglomeration and emergence of nanodistricts[12]

Abstract

Research and development at the nanoscale requires a large degree of integration, from convergence of research disciplines in new fields of enquiry to new linkages between start-ups, regional actors and research facilities. Based on the analysis of two clusters in nanotechnologies (MESA+ (Twente) and other centres in the Netherlands and Minatec in Grenoble in France), the paper discusses the phenomenon of technological agglomeration: co-located scientific and technological fields associated to coordinated technology platforms to some extent actively shaped by institutional entrepreneurs. Such co-location and coordination are probably a pre-requisite for the emergence of strong nano-clusters.

Introduction

There is a rich literature on high-tech clusters and districts. Case studies have been done, comparisons have been made, and general (even if tentative) conclusions have been formulated, e.g. the role of centres of excellence and star scientists (Zucker et al., 1998, 2002), the size of the existing market (Feldman and Ronzio, 2001, Autant-Bernard et al., 2006) or the role of incumbents and large firms (Agrawal and Cockburn 2003). These studies have often taken biotechnology as their entrance point.

There is an additional dynamic, which we will provisionally call 'technological agglomeration *i.e.* the geographic co-location of different scientific and technological fields. Technological opportunities as well as requirements on further technological development (e.g. a next generation of chips) stimulate linkages and coordination amongst different fields, and this may create cumulative advantages for clusters in which a wide range of scientific areas is explored. Thus, there is a technological driver in the agglomeration of actors and activities in a geographical region, and more generally, in clusters building on proximity.

[12] This chapter was published as: Robinson D. K. R., Rip A. and Mangematin V. (2007) Technological agglomeration and the emergence of clusters and networks in nanotechnology. Special issue on Nanoscale research. Research Policy 36 (2007) 871–879

Technology agglomeration and emergence of nanodistricts

Technological agglomeration is a general phenomenon, but it is particularly visible in newly emerging nanotechnology-linked developments. We will use our ongoing studies of regions with a high concentration of nanotechnology-linked activities to show the importance of technological agglomeration for the overall dynamics of development. Our analysis of these techno-institutional dynamics and related changes in networks of firms, research centres, and regional actors and policy makers, takes technology infrastructures and in particular, technology platforms as the main entrance point. Technology platforms are increasingly recognized as important in enabling innovation, as a key part of business models of (high-tech) start-ups, and as having dynamics and requirements of their own.

In this note, we present a first analysis of the role of technological agglomeration in the evolution of nano-clusters in the Netherlands and in Grenoble.

The research note contributes first to the empirical understanding of how technological characteristics are leading to geographic agglomeration of scientific activities. It specifically highlights the role of technological platforms in the agglomeration process. Second, it presents two different processes of agglomeration, a centralised one in France and a distributed one in the Netherlands. Third, our note illustrates the multilevel character of such technological agglomeration.

The Technological agglomeration and technology platforms

The past ten years have seen an explosion of interest for the area of science and technology labelled "nanotechnology". Nanotechnologies are defined as technologies which include components that have at least one dimension between 1-100 nm, and display unique characteristics due to being at this scale. Unlike previous high-technology waves, nanotechnology covers a diverse field of sciences and engineering, crosses boundaries between them and aims to utilize the very fundamental characteristics of matter by manipulation and control at the nanoscale.

As they cross many disciplines, also many industries and technology chains, nanotechnologies reshape the existing organisational arrangements amongst actors. Technological agglomeration *i.e.* the co-location of scientific and technological supports the development of nanotechnologies within the area. They also involve large investments in infrastructures. Bigger and better clean rooms, atomic force microscopes for observation and manipulation at the nanoscale, e-beam lithography and nano-imprint lithography to make the channels, pores, and circuits needed for the research. Organisationally, it requires the sharing of facilities, equipment and skilled technicians for these very different technology/research fields. Since such

facilities are expensive and take some time to construct, they need high investment (both financially and in training of manpower) over a period of time.[13]

Developments in most fields of nanotechnologies are tied to technical facilities, that is the instrumentation itself and the skills that are needed to operate them. In addition, a lot of nanotechnology research involves development, construction and implementation of new instruments. In other words, nanotechnology must be a field that allows us to study the phenomenon of technological agglomeration.

Actually, the infrastructural requirements add up to a basic set of technologies and skills, which allow, when in place, a variety of further work and product development. In other words, there is a technological platform *i.e.* a set of instruments which enables scientific and technological production: it allows exploration and exploitation of a variety of options, for strategic research, technology development, and sometimes also product development. Such a basic set of technical infrastructure is somewhat independent of the team which originally built and assembled it. It is recognized by others as important, and assembled to be able to profit from the variety of purposes it can be put to. It is not focused, however, on appropriating part of the value added in producing goods or services, but to enable innovation and valorisation (and appropriate the resulting technological options, for example in publications, patents, and as core competence of a start-up firm).

A technology platform is not just a collection of equipment. It enables and constrains further actions. Furthermore, the recognition of the possibility of such platforms incites actions to realize them. As product platform (Gawer and Cusumano, 2002) focuses on the standardisation of interfaces which makes it compatible with the other modules, technological platforms appear as enablers of R&D, of families of technological options, and of successive product development. A sector can then be viewed not in terms of a dominant design and related industry structures, but as a patchwork of technology platforms and related coordination, up to aggregation. Peerbaye (2004) shows how genomics platforms emerged in R&D institutions and some R&D companies (e.g. micro-arrays), but took on a further feature in France when public financing was made available provided there was some geographical concentration and provisions for access (*'dispositif instrumental partagé'*).

[13] An example would be the state-of-the art Extreme Ultra-Violet lithography platform which is priced in the order of $40 million (ASML 2005).

Technology agglomeration and emergence of nanodistricts

In nano R&D and product development, the range runs from the basic set necessary for manipulating at the nanoscale (STM, AFM, surface analysis instrumentation, nano-fabrication including clean room facilities) to further technological (and social) infrastructure necessary for nano-production. This will be different for different types of products: coatings vs. biochips vs. nano-electronics. Such products are not (and most often cannot) be exclusively nano: for example, micro-systems enabled by nano-inputs (components, modifications). When the new industries have become articulated and stabilized, the technology platforms turn into platforms enabling product families in the traditional sense (Tatikonda 1999). What is still distinctive is that these product families are defined by the technology rather than the sector. Start-up companies basing themselves on a technology platform can identify and follow-up opportunities in different sectors.

Technological platforms, when sought after, are intentional opportunity structures. They are also part of evolving (or emerging) techno-industrial networks and help structure them. This note argues that technological agglomeration is the effect of technological platforms being set up, used and expanded. Because of the coordination (*de facto* through the nature of the platform, as well as intentional, e.g. when organizing access) that is involved, there is a proximity effect and some clustering will occur. There are two main routes of technological agglomeration (and one may find other routes in between, a mix of the two main routes).

- building interrelated and interdependent networks, where technological opportunities and platforms get assembled by being available at the same time ("off the shelf"), and allow various exploitations. This can then be recognized for what is happening, optimised, and packaged to be used elsewhere & elsewhen. Already in the region Twente, but definitely the Netherlands (the second case study), one finds a number of nanotechnology value chains (*filières*), some still only emerging. In new fields such a bottom-up fabrication, and to a certain extent bio-nanotechnology, previous arrangements are absent, or are more diffuse. A technological *filière* is not there yet, in contrast to the situation in micro/nano-electronics. Still, one sees technology platforms being constructed and exploited.

- building co-localised facilities and scientific and technological competencies (geographic concentration), where the technology platforms are expansions of existing facilities. They have to be articulated and designed as such, which requires a concerted effort from the beginning. The second route often builds on what has been happening in the first route, in particular when a certain threshold of articulation and stabilization has been passed. The French public policy which supported the creation of technological platforms within the Genopole programme

is an example of such articulation allowing further steps to be made (Peerbaye 2004). The Minatec project in Grenoble (our first case study) was conceived as a major new step, but derived its legitimacy from what was happening already in the region.

In both cases, technology platforms need to be located near a research centre or university. The high investment of monetary and human capital into such technology platforms, and the possibility of many various diffuse technology chains to cross at a technological platform, imply that it is attractive to locate the various technology platforms at the same location, near skilled workforce (and a workforce that evolves with the evolution of the technology platform). Small and large companies could then locate themselves nearby and profit from this agglomeration. Platform agglomeration is also an enabling tool to run complementary experiments and to explore different scientific fields. In addition to scientific and technological convergence in nanotechnologies (Roco and Bainbridge, 2002), generic platforms appear to be the locus of hybridization amongst technologies (Avenel *et al.*, 2006), where teams from different traditions and disciplines can meet around technological facilities. Platforms are a hub for the different disciplines to meet (Carlile, 2004), a sharing facility which play the role of a boundary object (Carlile, 2002; Star and Griesemer, 1989).

There will be path dependencies, in the sense that earlier investments and competencies shape what can be done later. Sometimes, such path dependencies are actively constructed by institutional entrepreneurs who mobilize a variety of resources to create a new and major lab (Jean Therme and Minatec in Grenoble) or a distributed set of lab facilities (David Reinhoudt in Twente, and his colleagues in Groningen and Delft, in the Netherlands), which will then have a life of their own. Initiatives from such institutional entrepreneurs will be the other entrance point for our case studies, because these project futures and actively combine resources from different levels. In a particular locality or region, combinations of disciplines and infrastructures can be assembled and exploited that is adapted to existing competencies and networks. For example, Grenoble focuses on nano-electronics and the Twente region in the Netherlands on materials and sensors.

Illustrative case studies

To explore the agglomeration, we focus on two clusters, Grenoble and the surrounding areas and the cluster/network in the Netherlands. These two cases have been chosen as they are part of the most visible areas involved in nanotechnologies

in the world. According to Kahane *et al.*,[14] Grenoble and the Netherlands are two of between 20 and 30 most visible concentrated areas in nanotechnologies, of which nine are in the US and fifteen in Europe (see Figure 1). In the chart (Figure 1), the profiles of the two clusters are quite different as Grenoble exhibits a high specialisation in physics while the Netherlands appears to be rather specialised in biotechnology.

For each case study, archival and documentary data were used, including project and funding proposals, consortia agreements, websites, and qualitative and quantitative data on publications and patents. We also interviewed main actors, traced the activities of the promoters of each cluster (Jean Therme and David Reinhoudt), and inventoried firms involved in the clusters and universities.

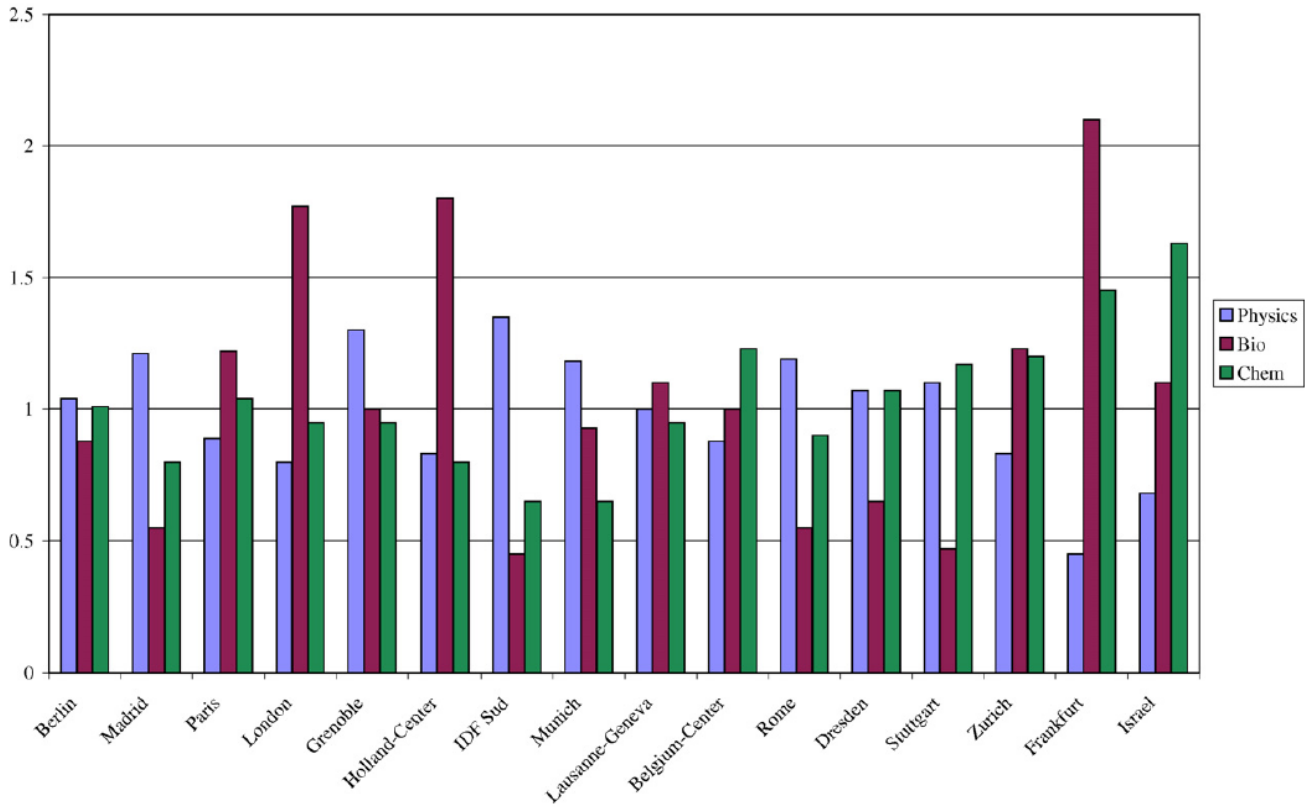


Figure 2.1: Comparison of European regions selected from Kahane et al.

Orchestrating technological agglomeration in Grenoble

Technological agglomeration has been occurring in the Grenoble region for a long time. During the early 1980s, LETI (*Laboratoire d'Electronique de Technologie de l'Information*, a semi-public technological institute dedicated to applied

14 http://www.nanodistrict.org/events/Workshop%20in%20March/nanotec/Kahane.pdf

microelectronic research), Thomson Semiconductor (a nationally leading firm at the time) and the Universities of Grenoble formed an alliance to develop research and development capabilities to be able to design and produce wafers of 100mm. They set up shared clean rooms for R&D while production facilities were installed in the neighbourhood of Grenoble to make the transfer of knowledge and know how between R&D and production facilities easier. During the 1990s, the consortium was enlarged to include France Telecom Research Centre (also located in Grenoble) and to build larger research facilities dedicated to silicon applications, optronics labs and software security (cryptography). In addition, dedicated research and training facilities which belong to different public research organisations (LETI, Universities of Grenoble, European synchrotron research Facility, Leo Langevin Institute) are co-located within the so-called scientific polygon. Micro and nano electronics, structural chemistry, nanobiotechnology, structural biology and generic biotechnology have been developed and formed a local network of interrelated platforms. Actors agreed to share access to the technological platforms and to design rules to manage intellectual property rights, to share the costs of running such platforms (pricing) and to plan the renewal and update of existing facilities as well as the development of new ones. Some of these facilities have been used by start-ups such as Soitec to develop their technologies. So-called 'common labs' between LETI and firms were created later.

In the late 1990s, Minatec was conceived: a new building with shared facilities as well as a collaborative project, promoted by LETI and orchestrated by Jean Therme (Delemarle, 2005), in which the different universities of Grenoble are involved, as well as national labs. Minatec has been formulated as a large and generic scientific and technological facility. It underlines geographic proximity to stimulate scientific and hybridisation amongst the different disciplines which form nanotechnologies. It covers scientific, technological and economic dimensions to support the development of micro- and nanotechnologies. It is not only a hub for scientific teams and firms to collaborate but also an umbrella which groups different the public research organisations. The project was justified by, and could build on four pillars. The first three are a continuum of research organisations, from universities to industry, including LETI as a bridge between basic research and industry; training, with large university campus where engineers and scientists are trained; and a dense network of technology based firms from large multinationals such as Philips or Motorola to recent start-ups like Trixell, Xenocs or Soitec. The fourth pillar is the agglomeration of technological platforms.

The architecture of the building was designed so as to encourage close links between upstream, technology and applied research allocating a central position to

technological platforms. Platforms have been assembled in the 20,000 sq meters of Minatec. The actual platforms derive from various groups in the regional scientific (firms and academia) community which opted to share their specific tools of increasing sophistication. Minatec then groups some of them together in the new building, and plans to upgrade them when they are installed in the building during 2006. It also organises platform management facilities and facilitates access to interrelated platforms located in the area. During the resource mobilisation and design phases, centres and their links to other technological resources were already defined, from LETI,[15] and from the region more generally.[16] There is overlapping technological agglomeration. Minatec projected, and now implements, agglomeration of facilities. Characterisation facilities are a further important component, and the idea of "common labs" including special Intellectual Property Right rules was successfully pushed by Jean Therme.

The emergence of Minatec is based on the high concentration of scientific and technological actors. The organisation of the work around the different and coupled technological platforms fosters pluridisciplinarity and problem solving approaches. Minatec emerged from different public research organisations and universities as a hub to produce simultaneously basic research and targeted collaborations with industries. Meanwhile, firms around Grenoble have grown and have decided to realise a joint venture so as to share the costs and the risks in nanoelectronics fabrication. Around SGS Thomson (later to become ST Microelectronics), firms allied to develop a new labfab to produce wafers around 200nm. In 2000, the alliance grew up, including ST Microelectronics, Philips and Motorola to build a

[15] The Advanced Microelectronics Project Centre (CPMA) enables it to access LETI resources such as the PLATO technology platform (Plasma technology, Lithography: EUV, Nanoimprint, Dielectric materials, Nanomaterials (Si, Ge, Magnetics) and Near field microscopy), the Very Low Temperature Research centre (CRTBT), the Centre for Basic research in condensed materials and the Nanofab which is specialised in the nanofabrication of objects larger than 50nm by particle based (electron and ion beam) lithography, deposition and etching (See Minatec Newsletter, July 2003, at www.minatec.com). It is a keystone of a large number of scientific projects in nano-optics, nanomagnetism or nanoelectronics.

[16] Minatec benefits from the presence of major European facilities, such as Institut Laue Langevin (ILL, neutron source), the European Synchrotron Facility (ESRF), the European Molecular Biology Laboratory (EMBL) and the Grenoble High Magnetic Field Laboratory (GHMFL) enabling atoms to be observed in fine detail and experiments to be performed which are essential to progress in nanosciences. They are located nearby (less than ½ miles away).

new labfab to deal not only with submicronic like in the previous generation but also with nanoelectronics to produce wafers of 200/300 mm. in the same time, one of the world leader in electricity, Schneider Electric decided to set up a new research centre to benefit from the spillovers and from the infrastructure around Grenoble. In 2005, the French government recognized the ensemble which groups Minatec, the fabrication alliance between STMicroelectronics, Philips and Motorola named Crolles 2 and the Schneider new research centre as a world class Pole de competitivité, which implies some preferential treatment.

In the Minatec newsletters (www.minatec.com) there is also reference to the linkages between the research facilities, research and training. About 4,000 employees are to work in Minatec, including 1000 students from Grenoble universities and 2,000 researchers, engineers and teaching staff. Promoted by LETI and universities of Grenoble (especially the engineering, physics and microelectronics departments), it has been positioned as making Grenoble an international centre of nanoscience (Minatec newsletter n°5, January 2004).

This is a success story in the resource mobility and the construction of a rich supply of research and technological opportunity. The question which looms on the horizon is whether to work towards the next integrated set of technological platforms, or to step out of the race altogether. The Crolles 2 production facility is in place; there are some 50 of such facilities worldwide. Actors are already projecting a next "generation", Crolles 3 (of which there will be some 20 worldwide), and negotiate and struggle about what is to be done, and who should take the lead.

What we sketched here is the dominant dynamic in the Grenoble region centred around micro- and nano-electronics, one which clearly shows the strong role of technological platforms and evolving industry structures which need nodes where synergies are exploited. There are other activities in the region, e.g. in bionanotechnology. These are much more dispersed but do show signs of emerging technology chains anchored and linked by more or less generic technology platforms. Such a dynamic is clearly visible, and intentionally sought after in our second case, Twente and the Netherlands.

Emerging distributed technological agglomeration in Twente and the Netherlands

Our second case is played out at two levels, regional and national. The geographical scope is perhaps less important for this distinction (the Netherlands is a small country, and could be seen as a region), than the difference in roles of regional actors and authorities, and national level public authorities. The two levels

have become linked in two main ways: the mutual positioning of the key nanoscience and technology centres in the Netherlands, and the emergence of a national nanotechnology consortium "NanoNed", which includes a distributed "NanoLab". We shall study the developments in Twente in some detail, as these are centred around a world-level nano-science research institute, MESA+, in the University of Twente, and show some technological agglomeration. For the national consortium, we focus on "NanoLab". There are other interesting aspects including institution building (in which the director of MESA+, David Reinhoudt, played a major role) and its intended and unintended effects (Mangematin et al. 2005), to which we only refer in passing.

There is mutual positioning of the research institutes, with Groningen as a hub for bionanotechnology, Twente for nanomaterials and manufacture, and Delft for micro- and nano-electronics. We will discuss Twente in more detail below. The Groningen region and University focus on facilities related to preparation, manipulation and detection of cells and biomolecules. In the Technical University of Delft, there is basic nano-science (now organized as a Kavli Institute) as well as work on lithography and nano-electronics, which complements activities of TNO-TPD, a division of the public applied research organisation TNO located in Delft.

Small microtechnology and nanotechnology companies, mainly start-ups, are playing a role in the regions, intertwined with the workings and evolution of the technical platforms. In Twente, where most start-ups are located, they are at the moment both users of facilities and providers of service. Examples include MicronIt, Lionix, and CapilliX, which use the facilities to create micro and nanofluidic platforms for use within the university or by other start-ups, such as Medimate. However, there is still only limited demand for their service in providing tools for R&D. "Killer applications" may arrive, allowing for expansion. None of the bigger firms in the three regions are at present active in nanotechnology, so there is little involvement of what might otherwise be anchor tenants (Agrawal and Cockburn, 2003). There are, of course, non-regional links with big firms like Philips Company.

The history of micro- and nano-research in Twente shows the importance of evolving and overlapping technology platforms. The research institute MESA in the University of Twente, established in 1990, building on an earlier conglomerate of groups and institutes with research in the general area of sensors, actuators and micro-systems. By the end of 1999, further mergers with electronics, optics, and materials research groups led to the establishment of MESA+, with special investments in extensive clean room facilities and linked to a TechPark (itself

building on predecessors from the early 1990s). This gradual convergence of fields and the eventual uptake of the 'nanotechnology' banner had much to do with the availability of overlapping technology platforms and the possibility of their expansion – which required institute leaders with particular entrepreneurial characteristics. The competencies built up over the last 20 years include microfabrication, microfluidics and sensors and actuators. MESA+ has high international visibility as it is embedded in networks of excellence, international collaborations and consortia.

For MESA+, spin-offs from the University have become an integral part of micro and nano developments in the region. In the University of Twente research into microfluidics and lab-on-a-chip revolves around the manufacture and manipulation of chip devices both in silica and polymer. Over the last 25 years, University of Twente has built up skills in micromachining to fluidic chips, leading to three spin off companies (LioniX, MicronIt and CapiliX) who develop and produce fluidic chips. The production of the chips occurs in the university cleanroom facilities which are rented by the two companies. Overall, 33% of time of the cleanroom time is rented to companies, limiting the time available for ongoing research at the University of Twente. In addition, 33% of the use of the various technology platforms housed within the MESA+ DANNALAB complex and Central Materials Analysis Laboratory, is allocated to the small companies for characterisation and analysis of products such as pharmaceuticals, nanomaterials, coatings and polymers.

The existence of companies that produce chips on demand, and the mixture of other small companies, which have expertise in thin films, microsieves etc. along with research lines in MESA+ are a further input into an emerging cluster based on (and exploiting) micro and nanofabrication – a national hub and European leader of nanofabrication.

In parallel to these developments, and building on them, a series of initiatives were taken at the national level which would lead, after a number of shifts, to the present R&D consortium NanoNed which draws on government funding. The original aim was to create a stronger position for the three partner centres from the Universities of Twente, Groningen and Delft, in which provision of advanced technical infrastructure was to play a key part. From the 2000 "Masterplan Nanotechnology" onward, a distributed NanoLab, i.e. facilities to be located in the three centres, featured in the plans and proposals. This contains a number of generic technology platforms, not co-located but coordinated across a few locations.

Technology agglomeration and emergence of nanodistricts

Shifts occurred to address resource mobilisation opportunities, in particular the expansion of the original group of three centres, including, by that time, a division, located in Delft, of the national applied research organization TNO, with centres in four more universities (necessary to avoid accusations of preferential treatment of the original three centres), and eventually also Philips Company. Alignment of the various participants was a challenge, and meeting it (even if precariously) was part of the challenge for the institutional entrepreneurship of David Reinhoudt (Scientific Director of MESA+) in which he was helped by the promise of major funding. Important also was the need to achieve some semblance of coordination between participants who otherwise might see themselves in outright competition. This was done by positioning participants according to their specializations with cross-cutting "flagships" at the consortium national level. NanoLab continued to be a core element, with some 35% of the envisaged resources of the consortium devoted to it. While to be located at the three main centres, it would offer access to other NanoNed participants.

Contrary to Minatec (and Crolles 2) which emphasises co-location to creation a dense cluster of nanotechnologies organised around platforms, the technological agglomeration visible in the so-called NanoLab occurs within dense and highly coordinated networks in the Netherlands. It emphasizes existing competencies and the promise of creating four overlapping generic technology platforms. The Table below shows how the actors themselves described the "hubs" (Figure 2).

By the end of 2005, NanoLab has invested 20% of its €90 million budget. The project has stimulated larger integration/coordination by the inclusion of Philips NatLab which has now joined NanoLab and is part of the decision making structure for the coordination of investments. Representatives of the five participants (MESA+, DIMES, TNO, MSC+ in Groningen, and Philips) form the board of NanoLab and coordinate the final investments during 2006. This includes the decision for investments, and the fees for use. Thus, it is not just a matter of getting new resources and dividing the spoils. A certain coherence at the level of technical infrastructures is established.

Tensions remain, however, and not just between the university groups. Philips Company, formally part of the NanoNed consortium, continues to pursue its own interests, such as the growth of the research campus it has created on its premises and its avowed goal to push for a micro- and nanotech triangle between Eindhoven (where major research labs are located), Louvain in Belgium (with IMEC) and

Aachen in Germany.[17] Since December 2005, the concentration of high tech activities in Eindhoven is recognized by the Dutch government as a "pole de competitivité", and IMEC (Louvain) has established a branch in Eindhoven. The network thickens. And one can speculate about a further form of distributed technological agglomeration, now at the level of the "Low Countries" (Netherlands, Belgium, and the German lower-Rhine region).

Twente: MESA+ focuses on the research and realisation of complex materials, devices and systems, on the processes used for the production of these and on the integration into complex devices and complete systems. Thus it aims to become the Dutch hub for nanofabrication.
Groningen: MSC+ / Biomade has a fast intensifying focus on the development of (bio)molecular (nano) electronics through a combination of fundamental and applied research. Using the present infrastructure, new functional molecular elements and materials are designed and synthesized. Within the NanoLab NL programme, the MSC+ / Biomade infrastructure is designed to function as: the Dutch centre for bottom-up (bio) molecular electronics and functional (bio) molecular nanostructures. Local organizations putting effort and in such a facility MSC+, Biomade, and the Groningen Academic Hospital (AZG).
Delft: DIMES has expertise in the field of Micro- and Nano-electronics, mostly using cryogenic techniques, and expertise in Nano-fabrication in many applications. With NanoLab NL, DIMES will provide a facility for nano-fabrication for broad use (and for all sorts of material-systems), using high-resolution e-beam lithography, different wet processing, oven-processes, thin film growth, dry-etch, and all sorts of nano-inspection techniques.
Delft: TNO TPD is primarily focused on production and analysis instrumentation on behalf of mass-fabrication of nano-chips. For this type of research, one needs to be able to measure, develop and experiment on (sub) nanometer scale. Within NanoLab NL the aim is the development of competencies in lithography.

Figure 2.2: Investment and consolidation plan for instrumentation within the NanoLab programme. (edited version of text from NanoNed proposal to ICES-KIS 2003)

[17] As Philips Company phrases it: "Initiatives by governments, industries and knowledge institutions are rapidly transforming the region between Aachen, Leuven and Eindhoven from an industry-based area to a technology- and knowledge-based economy with potential to rival some of the world's most prestigious regions of excellence." *Philips Research Password*, 19 (April 2004).

Discussion

While the starting situation and the strategies of key actors are different, the cases of Minatec/Grenoble and Twente/Netherlands both illustrate emerging technological agglomeration. The agglomeration process builds on existing technological competencies, research and training institutions and facilities, but is driven by the recognition of opportunities offered by technological platforms for research as well as for new and existing firms, and by the activities of institutional entrepreneurs mobilising resources for further infrastructure, and creating coordination across actors at the same time. Institutional entrepreneurs like Jean Therme and David Reinhoudt have to act at different levels (organizational, regional, national) at the same time. They mobilize support, networks are built and allocation decisions are made, which create a virtual presence of Minatec and NanoLab before actual building occurs. The virtual presence and the promise of new technological opportunities orients actors.

While co-location of the technology platforms is the important and recurrent phenomenon, there are different routes. In Grenoble, in the Minatec project, Jean Therme (and his allies) pools existing infrastructure in the neighbourhood, upgrades those that are needed and adds new ones. In the Netherlands, the strategy of key actors, with David Reinhoudt in the lead, is to reinforce existing competencies by overlaying the facilities with funding for key focal areas, leading to different nano-hubs.

Local arrangements can differ and the 'business models' for the generic platforms must evolve further. In the Netherlands, there are tensions about availability of clean-room time for researchers, dictated by the policy of 33% of the time being made available for small companies. This is compounded by responsibilities of the local hubs to the national NanoLab. In Minatec the organisation of the clean room and related facilities is different: there will be dedicated staff to do fabrication and analysis as a service to a customer. The realisation of actual co-location of equipment from the original institutions and their staff will not be easy though.

The further development may not be conforming to the promises and projections that were made. But it is clear already that there will be effects. Links between universities, public research institutes and firms (small, medium and large) become more important. Regional actors and policy makers become part of the techno-institutional dynamics and changes in industrial networks. Clustering on the basis of technology platforms does not only shape emerging nanotechnology regions, but is also important for the distribution of hubs and Poles de Competitivité at the national level and probably also at the European level. Hybrid roles emerge, for

start-ups (see LioniX and MicronIt), and in coordination of facilities with industry (Philips and examples from Minatec) as both users of facilities and providers of a service.

What remains to be clarified is whether this reinforces and balances the creation of clusters based on instrumentation, or whether novel combinations between nano centres, nano networks and nano alliances may appear. The strong claim that agglomeration of technology platforms is a pre-requisite for a nano-cluster needs to be verified further. Further case studies are planned, and while the complexity of developments in the real world will make it difficult to make general claims about factors and drivers, we will disentangle some of the complexity by working with contrasting case studies. The results described above already give an indication that clustering in nanotechnology has interesting dynamics and that the success and failure of a cluster to be stimulated will in part be related to the degree of success in agglomeration of technology platforms.

Chapter 3 Tracking the evolution of new and emerging S&T via statement-linkages [18] [19]

Abstract

The past 10 years has seen an explosion of interest for the area of science and technology labelled "nanotechnology." Although at an early stage, nanotechnology is providing a space for the creation of new alliances and the forging of new ties in many actor arenas, initiated based on promises and high expectations of the fruits that could be harvested from development and investment into nanotechnology. Those trying to characterise the dynamics of emerging ties and networks within this field are faced with a number of complexities which are characteristic of the nanotechnology umbrella term, which covers many technologies, various mixes of disciplines and actors, and ongoing debates about definitions of fields and terminology.

In this paper we explore an approach for capturing dynamics of emergence of a particular area of nanotechnology by investigating visions of possible futures in relation to molecular mechanical systems (molecular machines). The focus of this text is to outline an approach used to map and analyse visions in an emerging field by taking as the unit of analysis linkages made in statements in texts, and the agglomeration of linkages around certain nodes. Taking the linkage, rather than node, allows one to probe deeper into the dynamics of emergence at early stages when definitions and meanings of certain words/nodes are in flux and patterns of their use change dramatically over short periods of time.

As part of a larger project on single and macromolecular machines we explore the dynamics of visions in the field of molecular machines with the eventual aim to elucidate the shaping strength of visions within nanotechnology.

[18] This chapter was published as: Robinson, D.K.R., Ruivenkamp M. and Rip A. (2007) Tracking the evolution of new and emerging S&T via statement-linkages: Vision assessment in molecular machines. Scientometrics, 70(3): 831–858

[19] Some of the elements of the methodology of statement linkages were tested by Rutger van Merkerk, Arie Rip and myself as part of another TA NanoNed investigation into lab-on-a-chip technologies. Elements of this unpublished work are described in van Merkerk and Robinson 2005.

Tracking the evolution of new and emerging S&T via statement-linkages

Introduction

The past 10 years has seen an explosion of interest for the area of science and technology labelled "nanotechnology." Already at an early stage, promises have led to high expectations of the fruits that could be harvested from the development and investment into nanotechnology. Various technological fields are emerging beneath the umbrella term, some are extensions of what was already happening (cf. CMOS progressing along the ITRS roadmap towards the nanoscale) but in many cases new networks are forming based around expectations and promises of altogether new technologies made possible by manipulation at the nanoscale. Besides providing space for interaction between various technological fields the 'nanohype' offers opportunities for further development of nanotechnology through government programmes and financial investments mobilised through utopian visions and high expectations.

The far-reaching impacts of nanotechnology touted by both proponents and opponents of the emerging field calls for a need to assess possible directions for the field of nanotechnology with a focus on governance of the co-evolution of nanoscience, nanotechnology and society (Renn & Roco 2006).

For effective steering a deeper understanding of the characteristics of this emerging field is needed in order to develop a robust map for an emerging situation, but also as part of the ongoing assessments which need to be evaluated based on dynamics of path emergence.

Mapping dynamics of nanotechnologies is complex. First of all, the ambiguity in nanotechnology's ontology provides opportunities for relabeling of a variety of technologies as nanotechnology. Secondly, within the field of nanotechnology terms such as nanomedicine, nanoelectronics, bionanotechnology etc. have different meanings and different usages depending on the context and actor using them. Nanotechnologies cover many industry chains, many sectors and many research disciplines which become even more complex at the nexus of convergence of these chains sectors and disciplines.

As part of a larger programme on technology assessment (TA NanoNed) we are interested analysing indicators of emerging structures within the field of nanotechnology, and develop ways of using such knowledge to improve governance processes.

As a first step, we investigate a particularly interesting field of nanotechnology, that of molecular machines. This field has been linked to the discussions on nanotechnology since the famous lecture of Richard Feynmann (Feynmann 1959)

and the now infamous book of Eric Drexler *Engines of Creation* (Drexler 1986). The field of molecular machines is also an interesting case due to the very early stages of the field, the different (often separate) research communities investigating and discussing possibilities of molecular machines.

For molecular machines, drawing boundaries around a molecular machine research community is difficult. From first round interviews with a number of researchers in the field of molecular mechanics, we see a number of camps, which need not be opposed, but originate from a different discipline with their own specific search heuristics, expectations and agendas; Biologists investigating protein machinery, chemists making interesting molecules, physicists looking at individual molecule dynamics etc. Thus there are, at the moment, a number of spheres of science which are forming molecular machine communities.

The nanohype has also provided a space for further development of molecular machines and the building of new linkages between previously disparate research communities. There is a convergence of communities with a broad notion of harnessing molecular mechanisms to do work – molecular machines.

Beyond the realms of scientific research, the nanohype has also allowed space for (enabled) other actors to enter the debate on molecular machine futures such as: Non-governmental organisations (such as the ETC Group and Greenpeace), futurists, consumer groups and even the British Royal family (Charles the Prince of Wales[20]). Thus at very early stages of emergence there is a great diversity of actors involved in articulating hopes and fears in the expected futures related to molecular machines.

Visions and expectations of possible futures for molecular machines are interesting as they shape activities in both the research sphere and in broader societal debate. This study, which is part of a larger project on vision assessment, is carried out through the application of a tool to systematically map expectations and visions concerning molecular machines. The aim of this pilot project is to explore the robustness of this tool by using a data set taken from the reference list of a recent review article on molecular machines in the 1st issue of *Nature Nanotechnology*. This core data set will be further contrasted with a smaller data set taken from the database of articles of the British popular science magazine *New Scientist*.

These datasets will be used to analyse linkages made in texts by various actors, who, by doing so link different actants together. By using this tool, which will be

[20] The Prince of Wales published an article on nanotechnology risks and responsibility in the Independent on Sunday, a British newspaper, on 11th July 2004.

elaborated below, we wish to map the expectations and visions within the datasets, through analyses of statement linkages, and evaluate the types of visions presented.

Such mapping can reveal dynamics of emergence at early stages, before more formal ties are present. This is advantageous for steering activities, which is attractive for prospective nanotechnologies which are touted to be breakthrough science and technologies.

The aim of this paper is to present a new approach to mapping dynamics of an emerging field based on statement-linkages. We demonstrate this tool through a pilot project based upon two data sets, reflective of the forms of data that will form the basis of a larger study of nanotechnologies based around vision assessment.

Statement Linkages as a relevant unit of analysis

There is a rich literature of the use of words in texts to map the dynamics of science and technology. Word occurrence and co-occurrence has been used to map for instance the growth of a field, identifying research communities and taking words as actants tracking words as indicators of shaping effects within the field.

We will not review this wealth of literature here, but highlight that what all of these analyses have in common is the focus on keywords as nodes of the network and the co-occurrence of these words being the attribute of a linkage. Some of these words may become macro-actors in the sense they begin to dominate co-word maps with many linkages being made. Due to the very early stage of nanotechnology, such co-word analysis may be misleading as analysis occurs as the field is emerging, where we are still located in very early stages in the lifetime of nanotechnology. In accordance with this, the contexts in which terms are used in emerging S&T are constantly in flux.

For example, in nanotechnology terms such as nanomedicine, nanoelectronics, bionanotechnology etc. have different meaning and different usages depending on context and actor using them. We will not go into the problems posed by the definition of nanotechnology term here, however it can be generalised that in nanotechnology new terms have fluctuating meanings depending on the context in which they are embedded. Thus, for nanotechnology (and perhaps more broadly to new and emerging S&T) the linkage itself, made by an author in a text, becomes interesting. Thus a refocusing from co-occurrence of terms, to the linkage that joins them seems promising.

When making a statement in a text, an author may link actants[21] together by making a linkage between them. We claim that one can look for specific types of linkages related to emergence of a technology and use them to characterise the emergence of the field itself. In addition, for an emerging field one can attempt to gauge the modality of the linkage, which may enable the analysis of the evolution of a specific linkage over time, i.e. if it is taken up and used by other actors. Focus on the statement-linkage allows one to get deeper into the translations that are going on in an emerging field. The actants that are involved which are defined and positioned by the linkages made by authors.

Below is an example of a statement linkage taken from an article concerning molecular machines.

> "Biological molecular motors are capable of performing specific tasks in response to specific external energy sources in a highly sophisticated fashion and thus may soon be utilized in nanoscopic devices." Holland et al. 2003, page 2015

Here *biological molecular motors* are connected with (near) future *nanoscopic devices* through a statement linkage made by Holland et al. The statement was made in a peer-reviewed journal for the study of macromolecules and positioned *naturally occurring protein molecular motors* as a component of a synthetic device.

A focus on such vision-based linkages, statements about the future, is useful for gauging activities during *very* early stages of an emerging field of science and technology where decisions and actions are based on promises and expectations against the backdrop of institutional settings and actor networks. For S&T under the umbrella term of nanotechnology, many actors who would traditionally be involved in the field later on in the innovation chain are becoming involved at the outset, articulating their own expectations and agendas, and shaping the directions for activities which contribute to the emergence of the new technology field.

Thus, the monitoring of such linkages seems attractive as it may allow the systematic exploration of a data set, pulling out indicators of emerging alignment based on visions, expectations and agendas. This is important for very early stages

[21] Actants are the network nodes in Actor-Network Theory (Callon et al. 1986) where the actor-network is the sum of the translations occurring between actants at a particular time. The term *actant*, rather than actor is used to denote that the node may be a not only be a person or institution etc. but can also be an artifact that shapes the network through translation.

of a nascent technology field, as visions and expectations guide activities (to varying degrees) prior to agenda setting and concrete activities.

Visions as guiding forces during early stages of emergence

Due to the immaturity of many nanotechnology fields, expectations and promises play a dominant role by mobilising resources and action in the shaping of an emerging S&T. Over the last 10 years, the sociology of expectations has argued about the structuring of action by expectations, especially at early stages where the situation is fluid and there are opportunities to create new ties and positions (van Lente 1993, van Lente & Rip 1998, Brown & Michael 2003, van Merkerk & Robinson, Borup et al. 2006). In nanotechnology, one can argue that expectations are particularly important, since resources are being mobilised into investing in nanotechnology based on promises rather than concrete products or proofs of principle, and in so doing structuring and guiding action.

In addition to expectations, there is another type of promise, which can be linked to visions. Visions can take the form of images or texts, and stretch from a near term vision (close to expectations) to science fiction. Vision linkages in text may have varying degrees of facticity in various communities, but in the emerging field of nanotechnology, even the science-fiction visions have strength, by shaping public debate and activities even though the vision is accepted as a fantasy.

A recent stream of activities under the heading of Vision Assessment (Grin & Grunwald, 2000; Grunwald, 2004) seeks to explore the role of visions in the co-evolution of science, technology and society. The idea behind Vision Assessment is not to create new visions that may shape socio-technical systems, but

> *that visions exist already in most societal sectors, that these visions tend to reproduce the ways in which these sectors have developed hitherto, and that a critical discussion of these visions is a prerequisite for changing the course of development (Decker, et al., 2000;1)*

In this way it is sought to contribute to a reflexive development of emerging technologies through a constructive assessment, not only of actual technological practices, but also of future visions and the underlying presuppositions of these technological practices as well.

As part of the larger project on the emergence of nanotechnologies[22] we are interested in emerging alignment and networks within the field of nanotechnology for particular streams of development (such as drug delivery, nanoelectronics etc.). The analysis of the population of nodes and linkages, its configuration and the modality of the linkages can give indicators into path dynamics (Robinson 2006a) such as a dominant vision aligning actors, or path creation (Garud and Karnøe 2001) in a community.

Monitoring such indicators is essential for enabling real-time evaluation and steering of an evolving and emerging field of technology, a key component of the Technology Assessment programme.

Scope of this pilot study

The first round approach, which is described in this paper, is applied to the field of molecular machines, as part of a project which aims to map the dynamics of the emerging field of controlled molecular motion. In line with this special issue, we apply the tool for the mapping the field of molecular machines as described in a recent review article published in the first issue of *Nature Nanotechnology*. In addition to this focus dataset, statement linkages are tracked in a complimentary dataset of articles relating to molecular machines in the popular science magazine *New Scientist.* Reasons for this complimentary dataset will be described in the following.

Data

The field of molecular machines is discussed in many different settings and in many different arenas. In this article two specific fora have been selected in which statement linkages have been tracked. Firstly, the reference list of a review article published in the recent first issue of *Nature Nanotechnology* has been examined. Secondly, several search items were used to demarcate the field of molecular machines in the popular science magazine *New Scientist*. The interest in including this complimentary data set is to ascertain if there is a different modality spread of the linkages made in these fora, but also to see the types of nodes and linkages made with a view to our claim that this tool can handle heterogeneous data sets in a systematic way.

Nature Nanotechnology

In early October 2006 a new supplement to the journal *Nature* was launched with a specific focus on nanotechnology. *Nature Nanotechnology* can be seen as a

[22] See the technology assessment programme within the Dutch nano consortium, NanoNed led by Arie Rip, University of Twente, The Netherlands. http://www.nanoned.nl/ta

landmark, as a recognised forum for research in nanotechnology originating from any natural science discipline.

In the first issue of *Nature Nanotechnology* (6th October 2006) a review article covering the last 5-6 years of investigations into molecular machines was published. Of the two authors (who are supramolecular chemists) Ben Feringa of Groningen is a recognised world leader in artificial molecular motors. Wesley Browne is a Post Doctoral Student in the Feringa group.

For this pilot study we take the reference list of this review article to map the visions of the molecular machines community bounded by Ben Feringa through his review article. There is a natural bias, both Browne and Feringa are chemists, but since this is a review article in the first *Nature Nanotechnology*, they highlight relevant work and make a claim on which visions they deem relevant and which they do not.

New Scientist

Since the broader project will also investigate linkages outside peer-reviewed fora, which may inhibit some of the more visionary types of linkages, we also apply our tool on another forum for the discussion of scientific endeavour in molecular machines – the popular science magazine *New Scientist*. *New Scientist* is a weekly publication for the interested lay audience and students of science. It is a forum for many different actors mainly through journalists but also authored by other actors from NGOs (such a *Greenpeace*) to supramolecular chemists (such as Vincenzo Balzani editor of the book Molecular Machines – Balzani et al. 2003). There is no peer review, but a need for newness and by the very nature of the journal, a need for less conservative claims in order to attract the interest of the reader. Nonetheless, scientists who publish here are taken to be spokespersons for the field.

To be able to demarcate the field of molecular machines among the many different topics discussed in the *New Scientist*, it has first of all been chosen to search for articles in *New Scientist Tech*, a web service which provides all articles from the *New Scientist* since 1989. The search terms where based on key words chosen relating to the number of definitions of molecular machine and nanomachine taken from literature and from interviews.

Below are two examples of the types of definitions of molecular machine available in the literature.

> *"A machine is defined as "an assembly of parts that transmit and modify forces, motion, and energy one to another in a predetermined manner". When the word "parts" is replaced by "molecules", a machine turns into a molecular or supramolecular machine. Therefore, a molecular machine is defined as an assembly of a distinct number of molecular components designed*

> *to perform machine-like movements in response to an appropriate external stimulus. In addition, a molecular machine has features characteristic of the molecules. In biological systems, there are many molecular and/or supramolecular machines, such as enzymes, antibodies, and viruses."* Harada 2001, p 456
>
> *"At the heart of every machine is its motor. The Oxford Dictionary of English defines a motor as "a thing that imparts motion"; work as "the operation of a force in producing movement or other physical change"; and motion as "the condition of a body, when at each successive point in time it occupies a different position or orientation in space". Perhaps, a more utilitarian definition of a motor is a device that converts fuel, be it chemical, thermal or light, into kinetic energy in a controlled manner — that is, it makes things move."* Browne and Feringa 2006, p 26

Thus we take a molecular machine to be a molecule, or an assembly of molecules, which converts chemical, thermal or light energy into kinetic energy in a controlled manner. We also took a similar definition for nanomachine where "assemblies of molecules" was replaced with "assemblies of nanoscale components". This led to a number of search terms which were fed into the search engine of the New Scientist Archive which stretched from 1989 to the present (October 1st 2006). This provided to 97 articles.

List of search terms for New Scientist archive		
• Molecular Machine • Molecular Machines • Molecular Motor • Molecular Motors • Molecular Rotor • Molecular Rotors • Molecular Motion	• Nanomachine • Nanomachines • Nanomotor • Nanomotors • Nanorotor • Nanorotors • Nanobot	• Nanobots • Nano robot • Nano robots • Nano assembler • Grey Goo

We use this tightly focussed exploration as a basis for further refinement of the approach for the mapping of a broader molecular machine data set, and later for other nanotechnology fields, which is work in progress conducted by the lead author. For this project, exploration of trajectories of nanotechnology, or more broadly nanotechnology paths (Robinson 2005, Robinson 2006a) are important. A

deeper understanding in the dynamics which lead to certain paths becoming dominant rather than others is a key asset to foresight and strategy articulation exercises (Rip et al. 1995, Robinson and Propp 2006, Robinson 2006b).

The following section describes the method used to understand the evolution of an emerging field, as it is defined through linkages made in texts, and their modalities. The objective is to investigate how expectations of the future evolve (or fail to evolve) into agenda setting activities and concrete action within a socio-technical network. Mapping of expectations and shared agendas allows one to explore emerging patterns leading to alignment within the field and possible irreversibilities, which can set in.

Methodology

Recalling the outline of the process described above, the tool has been designed and used in this pilot study to get a handle on the dynamics and evolution of emergence in the field of molecular machines. The focal data point that we take is the *statement-linkage* that is a connection made between two nodes/keywords by an author of a text. The node can either be an actor or technology component/characteristic. The linkages we are interested in pertain to visions and expectations.

Linkages and modalities

As mentioned previously we take linkages which describe claims about future activities within the field of molecular machines. We have drawn on the literature of sociology of expectations (van Lente 1993, van Lente & Rip 1998, Brown & Michael 2003, van Merkerk & Robinson, Borup et al. 2006) and Vision Assessment (Grin & Grunwald, 2000; Grunwald, 2004) to develop a classification of the modality of linkage from proof of concept through to science fiction.

> **Science Fictions** indicate long-term fictional ideas, which are accepted as fantasy without demands of feasibility. An example of a Science Fiction linkage could be: "*The dark side of nanotechnology is "grey goo" - the nightmare possibility that "nano-robots" could be programmed to gobble up their surroundings and turn everything on Earth into more nano-robots*" (Park, 2003).
>
> **Visionary Linkages** indicate long-term technological possibilities, which are accepted as reality-based fantasies, which *could* claim feasibility. An example of a Visionary Linkage could be: "*The behaviour of devices at*

these scales could eventually mean fundamental changes in the way we build things, forcing us to abandon old ideas" (Cho, 2001).

Guiding Visions denote more technical and plannable technological futures (Grin & Grunwald, 2000) such as their *paperless office*. An example from the world of molecular machines would be *"Powering nanoscale machinery by nanosized motors that move by in situ conversion of stored chemical energy is one of the most interesting challenges facing nanotechnology."* (Kline et al. 2005 p744).
The difference between Guiding Visions and Visionary Linkages is that Guiding Visions imply action, although no actor is positioned to undertake it (a more general statement).

An **expectation linkage,** of a constituent of the future molecular machine world. An example of an expectation linkage could be: "*We expect that the successful formation of fully functional surface-mounted rotors will enable investigation of the concerted action of a large ensemble of unidirectional molecular motors, and that this system might be a first step towards the construction of more elaborate and functional nanosized mechanical devices." (*Van Delden et al 2005. p1340).

A shared **agenda (goal)** of what future action should or will be taken. An example of an agenda statement could be: "*This paper is the first step towards our goal of creating artificial complex systems composed of large numbers of components that move autonomously and that self assemble."(*Ismagilov, R. F. et al. 2002 p654).

Proof: Technological developments that have been demonstrated and are accepted as fact or reality. An example of a proof-linkage could be: "*Nature already provides us with a wide range of biological nanomotors*" (Hess, et al., 2004, p2111).

These six types of linkage can be tabulated as statement linkage modalities (see table below).

A database was constructed of linkages made by authors in the data set described. The first step entailed the identification of a statement based on whether the sentence referred directly to the field of molecular/nanomachines. Once we identified such a statement, we determined whether the statement housed one or more of the six types of linkage outlined above.

Once a relevant linkage was found, this was entered along with details of the author (name, institution and country), the title of the article, the journal name and

the page number. Each node was entered along with the linkage modality and the whole statement.

Statement linkage modality	Description	Action implied
Science Fiction	It may happen **(accepted as fantasy)**	No
Visionary linkage	It may happen **(accepted as reality based fantasy)**	No
Guiding vision	It may happen	Yes
Expectation linkage	It will happen	Yes
Agendas (goals)	We are gonna make it happen	Yes
Proof (Proven and/or demonstrated)	We have made it happen **(accepted as fact/reality)**	Yes

Visualizing the statement-linkages

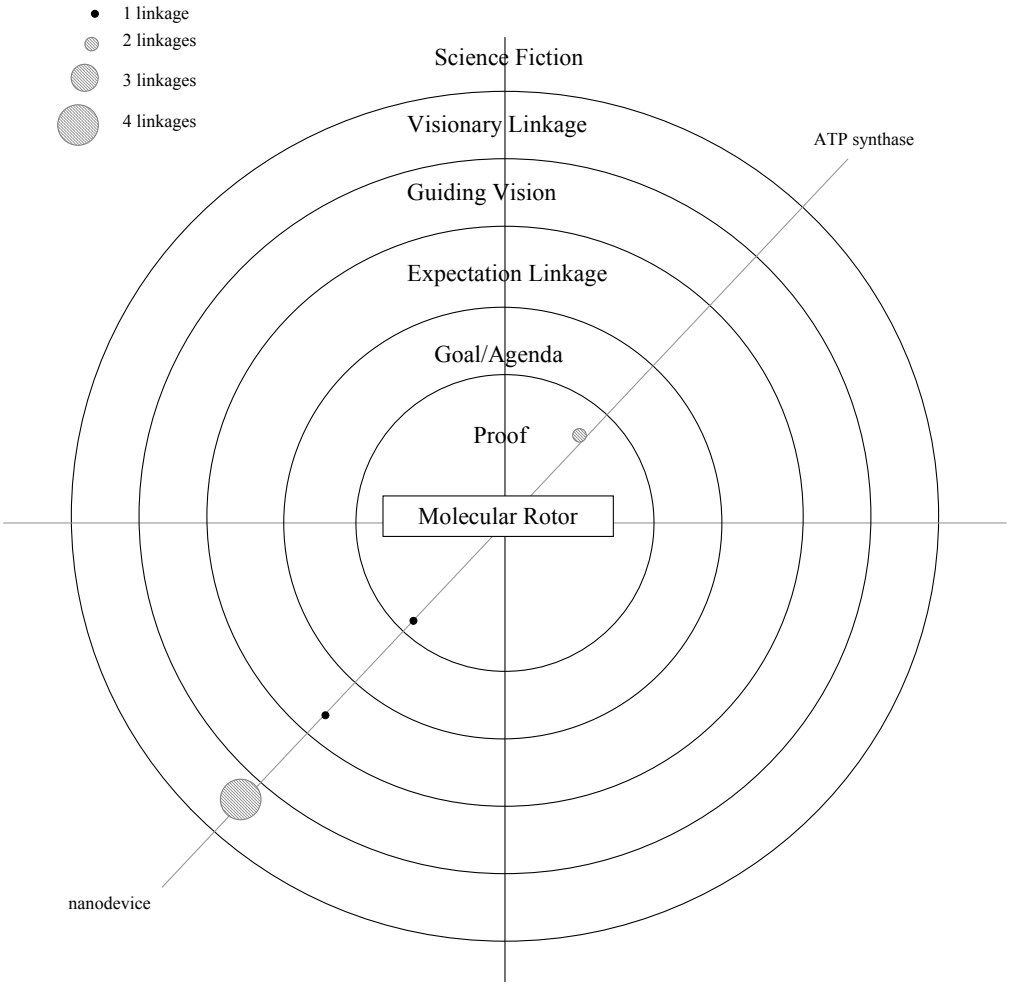


Figure 3.1: Modality-map showing linkages to molecular machines.

In this pilot we will use a simple ring structure representing the six different modalities mentioned above. Each modality map will map the nodes and linkages related to a specific node, selected from the dataset for being of particular interest. In Figure 1 you can see an example. For each node there is a line. The line may stretch across a number of rings, which shows that there is a mix of modalities for this linkage. Along this line are circles, the larger the circle, the more linkages there are. This visual allows you to get a glimpse at what is in the database related to a particular node. In the fictitious example in figure 1, we can see two type of linkages mapped. Molecular-rotor to ATP-synthase and Molecular-rotor to nanodevice. For the ATP-synthase linkage we see that 2 linkages with the *Proof* modality. For the nanodevice linkages, we see 4 linkages with a *Visionary Linkage* modality, 1 with an *Expectation Linkage* modality and 1 with a *Proof* modality.

Full modality maps would show all the linkages made to a particular node.

Illustrative case – Mapping vision linkages in Molecular Machines

Richard P. Feynmann speech *There is Plenty of Room at the Bottom* is often referred to as the first speech on nanotechnology. In this famous address to the Meeting of the American Society of Physics in 1959, the Nobel Laureate in Physics not only considered the possibility of direct manipulation of individual atoms, but laid down the challenge to construct mechanical machines at the nano (molecular) scale as well.

> *"What are the possibilities of constructing molecular-scale mechanical machines?... An internal combustion engine of molecular size is impossible. Other chemical reactions, liberating energy when cold, can be used instead.... Lubrication might not be necessary; bearings could run dry; they would not run hot because heat escapes from such a small device very rapidly..."* (Feynmann, 1959).

The notion of molecular machines was further brought under attention by Eric K. Drexler in 1986. In *Engines of Creation*, Drexler describes molecular assemblers as devices capable of building products from the atom up, thus with absolute precision and without pollution. However, according to Drexler (1986), to be able to do so, these assemblers need to be able to reproduce themselves as well, something that could happen at considerably high frequency. Assuming that the first assembler could make a copy in one thousand seconds,

> *the two replicators then build two more in the next thousand seconds, the four build another four, and the eight build another eight. At the end of ten hours, there are not thirty-six new replicators, but over 68 billion. In less than a day, they would weigh a ton; in less than two days, they would outweigh the Earth*; (Drexler, 1986).

This idea led to the apocalyptic scenario of the 'Grey Goo', in which the process of self-replication gets out of control and the assemblers 'eat up' all life forms on earth. The 'Grey Goo' scenario was fiercely attacked by 1996 Nobel Prize winner in Chemistry Richard E. Smalley, who expressed his objections against molecular assemblers through what he called the 'fat fingers' and the 'sticky fingers' problems (Smalley, 2001).

While the possibilities of assemblers were debated on a scientific and public level, the discovery of a family of moving proteins labelled as biological molecular machines attracted a lot of attention from, biologists, chemists and physicists (Vallee & Hook, 2003; Schliwa & Woehlke, 2003). It was argued that "these proteins [could] perform directed or programmed motions, similar to many tools and machines used in our daily life" (Kinbara & Aïda, 2005; 1377). The integration

of biomolecular motors into synthetic environments has been described as one of the three possible ways to construct machines able to perform work at the nanoscale. Other "paths taken in the quest for nanoscale generation of mechanical work [are] the bottom-up design of molecular motors by chemical synthesis, [and] the top-down fabrication of miniaturized electric motors by lithography" (Hess & Bachand, 2005).

In the last two decades the first biomolecular machines have been controlled to perform specific tasks, and machinery has artificially been built at the nanoscale. Nowadays the progress in the construction of molecular machines is being categorized in generations of molecular machines. For example the first generation of light driven molecular motors were characterized by their ability to perform unidirectional rotary motion upon energy uptake for which molecular chirality turned out to be an essential feature (Koumara, et al., 2002). "Further important structural features in this first generation light-driven molecular motor are the identical nature of the upper and lower parts of the tetrahydrobiphenanthrylidene and the all-carbon framework of the molecule" (Koumara, et al., 2002). In second generation light driven molecular motors, the structure of the stator-parts and the rotor-parts are different, "enabling additional components to be attached to either the top or the bottom half and surface attachment of the stator" (Browne & Feringa, 2006).

For this study, we are interested in the visions of the present and future generations of development of molecular machines. The modality of the visions can tell us about the degree of acceptance of specific characteristics a future molecular machine generation may hold.

In this case study we explore vision linkages by investigating two data sets, the core set taken from the reference list of Browne and Feringa 2006 as a representative review of the scientific exploration and development of synthetic, natural and hybrid molecular machines. The second data set represents the scientific press, where broader debate without peer review is undertaken, thus we have selected articles from the archive of the *New Scientist* magazine. The latter data set could give insight into the uptake of the notion of nanomachine and the linkages made to these bolstered by the nano-hype in recent years societal debate[23] on the societal impacts of nanotechnology.

[23] Perhaps phrasing it as "debate on behalf of society" would be a more appropriate term to use.

Results

A total of 486 statement-linkages where obtained with the *Browne and Feringa* data set and 129 statement-linkages with the *New Scientist* data set. The diversity of phrasing within the dataset meant that some grouping of nodes was necessary resulting in the list of nodes given in Table 3 below.

One immediate comparison of the types of linkages in both data sets (see charts in Figure 2 below) shows a weighting more to *Proof* modalities for the Browne and Feringa data, which comprised mostly of peer-reviewed articles. The New Scientist data set shows a clear weighting to more visionary modalities such as *Guiding Visions, Visionary Linkages* and *Science-Fiction* linkages. This supports the reasoning for taking a complimentary data set to allow for statement linkages across the *range* of modalities.

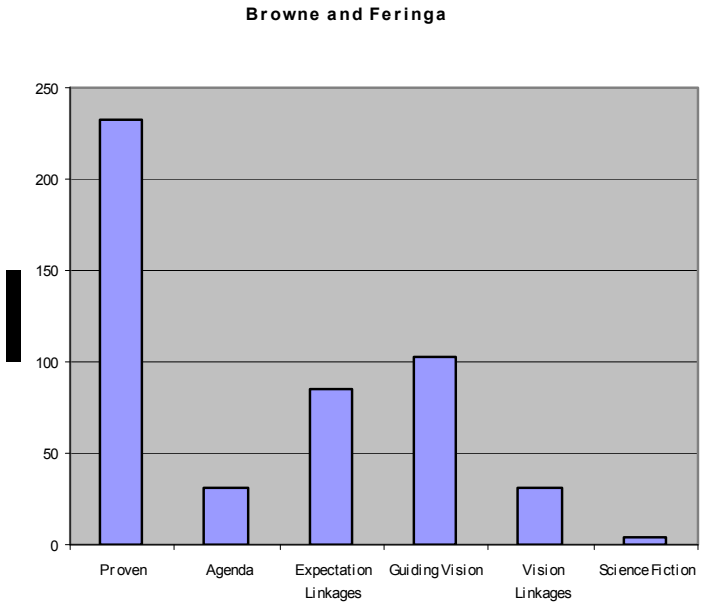
Of particular note was the amount of linkages to three nodes molecular machines, molecular motors and nanomachines. We chose to focus the analysis on the linkages to these three nodes due to the limited dataset.

The following two sections will describe the linkage ecology related to these three nodes in the two datasets. Discussion of content of the linkage ecology will take place in section 5.4.

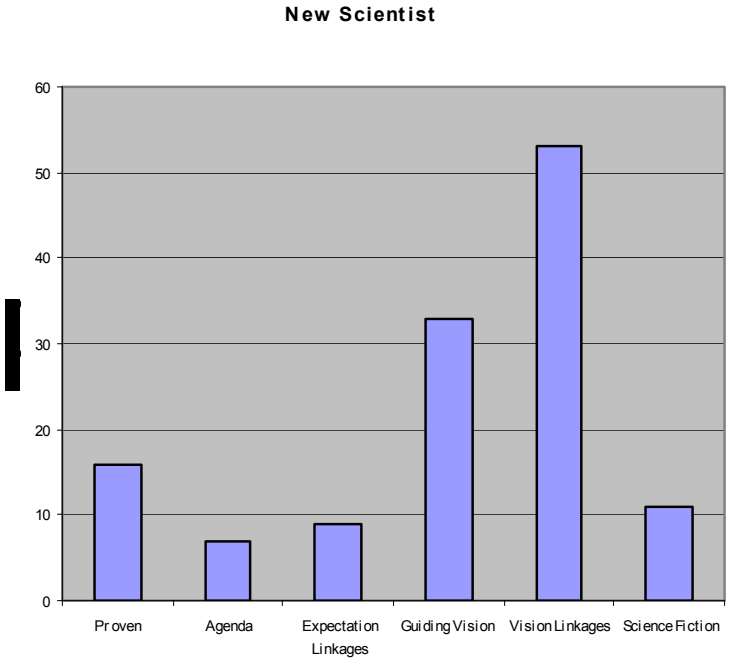
List of nodes in the statement linkage dataset			
(supra)molecular species	endergonic chemical	molecular components	polymer motors
1C and 1T interconversion	reactions energy conversion	molecular design	positioning on surface
amphidynamic crystals	engineering	molecular electronics	power generator
antibodies	engineers	molecular elevator	power sources
apoptosis	enzymers	molecular gear	Powering nanoscale
application of photoswitches	Eric Drexler	molecular gyroscopes	machinery
artifical molecular machine	experimental system	molecular machines	Prince Charles
artifical rotor	factories on a chip	molecular manipulation	proteins
artificial molecular motor	family of compounds	molecular memory	prototype
artificial molecular rotor	fears	molecular microchips	pseudorotaxanes
artificial structures	feringa motor	molecular models	quantum mechanics
artificial surface-mounted	fluctuation driven transport	molecular motions,	ratchets
motor	fluidic gears	molecular motor array	real issues
assemblers	friction	molecular motors	retrieval systems
assemblies	fuelled molecular motions	molecular muscles	reversible helicity
ATP synthase	functional molecules	molecular piston	revolution
autonomous	future applications	molecular pumps	ribosomes
balance	gears	molecular ratchet	Richard Feynman
Bioelectronics	global ecophagy	molecular rotors	rotational motion
biofuel cell	Grey goo	molecular scissors	Rotors
biological molecular	helicases	molecular shuttles	self assembly
machines	hormone	molecular sorters	self-healing materials
biomolecular motor	human enhancement	molecular structure	self-replicating
biological purification	human implant	molecular switches	nanomachines

biological systems	hybrid molecular machines	molecular-scale	sensors
biology	immortality	molecules	shafts
biomimicry	immune systems	Montemagno	shuttles
biomotron	inorganic materials	Moore	similar propulsion
biosensors	input	motion coupling	mechanism
bioweapons attack	integration	movement of a small ring	simple electron transfer
bottom-up construction	intramolecular mechanism	muscle linear motor	processes
brakes	junction	muscles	single molecule device
Brownian motion	Kinesin	myosin	single-molecular machine
Brownian motor	Lieber	nano assembler	small machines
buckyball	life	nanoactuators	Smalley
cantenanes	lifts	nanobots	smart surfaces
cargo carrying	light powered	nanocar	society
catalytic reactions	linear motor	nanodevices	speed of rotation
cells	living cells	nanofabrication	statistical theories
chemical fuel	logic operations	nanofluidics	steam engine,
chemical receptor	machines	nanomachines	stereogenic center
chemical synthesis	macroscopic analogues	nanomotor	studying toxic surfaces
chemists	macroscopic change	nanorod	submarines
chirality	major endeavors	nanoscale electronics	submolecular fragment
cis-trans isomerization	mall metal complex	nanoscale elevator	submolecular motion
cogwheels	material scientists	nanoscale	supramolecular
combination	materials at the bulk leve	nanoscale systems	organization in materials
commercial product	mechanical actuator	nanoscale thermite	surface of gold
communication	mechanical devices	nanoscale wheels	nanoparticles
complex tasks	mechanical systems	nanostructures	switch
computation	mechanical-like movements	nanosubmarines	synthetic oxygen
computational scientists	mechanically linked rotor	Nanotechnologists	system
controllable molecular	medicine	nanotechnology	top-down fabrication
motion	memory chips	nanotrains	trans-cis isomerizations
controlled chemical reactions	metallacarboranes	nanotubes	transport
crystalline molecular	microfluidics	nanovalves	tweezers
machines	micromachnes	nanowalker	unidirectional rotary
crystals	microrobots	nano-welding	motion
cyclodextrin	microrotors	nanowidget	universal fabricator
cytoskeletal motor	microscopic wind farm	natural molecular	useful work
device	miniature “engines	machines	valve
DNA	miniature electronic circuits	nature	variety of environments
DNA device	miniaturisation	new technology	(environments)
drug delivery	molecular assembler	optomechanical energy	viruses
electrical energy	molecular assemblies	Overheating	
electrodes	molecular bonding	physicists	
electromagnetic radiation		pivots	
electron transfer processes			
electronic and nuclear			
rearrangements			

Table 3: Technology component or characteristic nodes in the statement-linkage database



Proven = 232
Agenda = 31
Expectation Linkages = 85
Guiding Vision = 103
Vision Linkages = 31
Science Fiction = 4
Total = 486



Proven = 16
Agenda = 7
Expectation Linkages = 9
Guiding Vision = 33
Vision Linkages = 53
Science Fiction = 11
Total = 129

Figure 3.2: Linkage modality distribution in both data sets

Browne & Feringa 2006

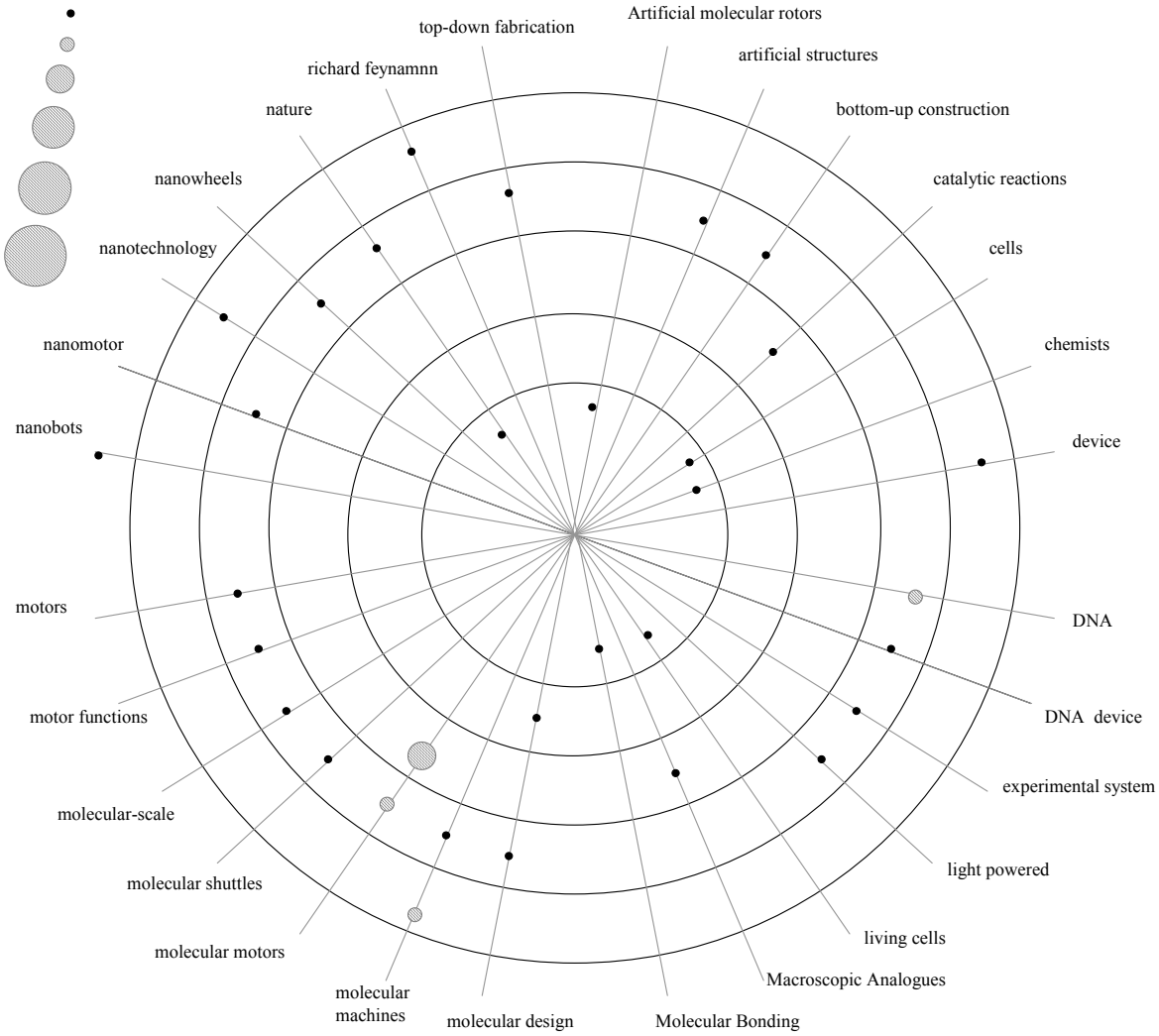


Figure 3.3: Modality-map for nanomachines (Browne and Feringa 2006)

Figure 3 shows the modality map for nanomachines. Over the 111 reference articles in Browne and Feringa the linkages made where in the main guiding visions for the second and third generation of nanomachines. We see in the map that components of nanomachines prevail (molecular shuttles, molecular motors,

DNA, nanowheels etc.) and desired functionalities (light powered, catalytic reactions). There are few linkages to devices or applications.

Figure 4 below shows the modality map for molecular motors. Molecular motors differ from molecular machines in that they are a component, and in some case may be a single molecule).

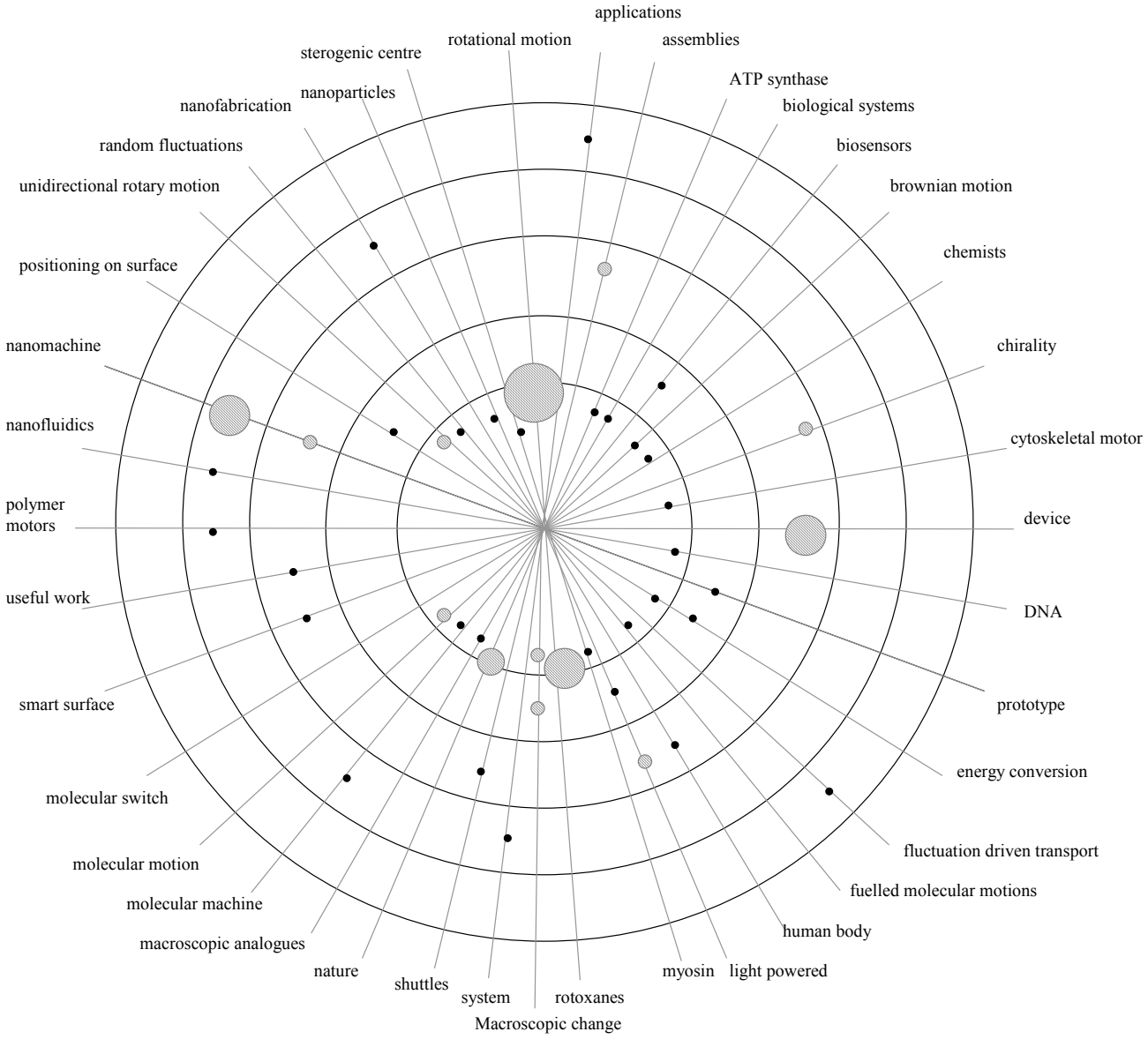


Figure 3.4: Modality-map for molecular motors (Browne and Feringa 2006)

Here we see a greater spread of linkages made than with nanomachines. Many links to desired functions (rotational motion, unidirectional motion, light powered) and more focus on devices (device, smart surface, nanomachine, molecular switch, biosensors etc.). The modality of linkages is much more centralised with proof and guiding vision dominating. We see a number of linkages being stated a number of times pertaining to the dominant investigations into molecular machines (rotoxanes and rotors) and visions of application (device, nanomachine).

Figure 5 shows the modality map for molecular machines. There were 56 types of linkage to molecular machines, with a modality spread in the main between *Proof* and *Guiding Vision*. Within the *Guiding Vision* and *Visionary Linkage* rings one can see a dominance of linkages to applications (computation, device, antibodies, energy conversion, human enhancement, drug delivery). Actor linkages are more prevalent here (chemists, physicists, engineers, material scientists).

New Scientist 1989-2006

The number of linkages made in the articles was dramatically less than in the previous dataset. This is due to the size of the texts (approximately 1-2 pages). Figure 6 shows the modality maps of nanomachines, molecular motors and molecular machines respectively.

In all three maps one can see a more diverse spread of linkages, dipping closer into the *Science Fiction* and *Visionary Linkage* rings. Desired functionalities do not occur, and the focus is more on applications (nanowalkers, nanomachines, grey goo) and actors (chemists. engineers, nanotechnologists).

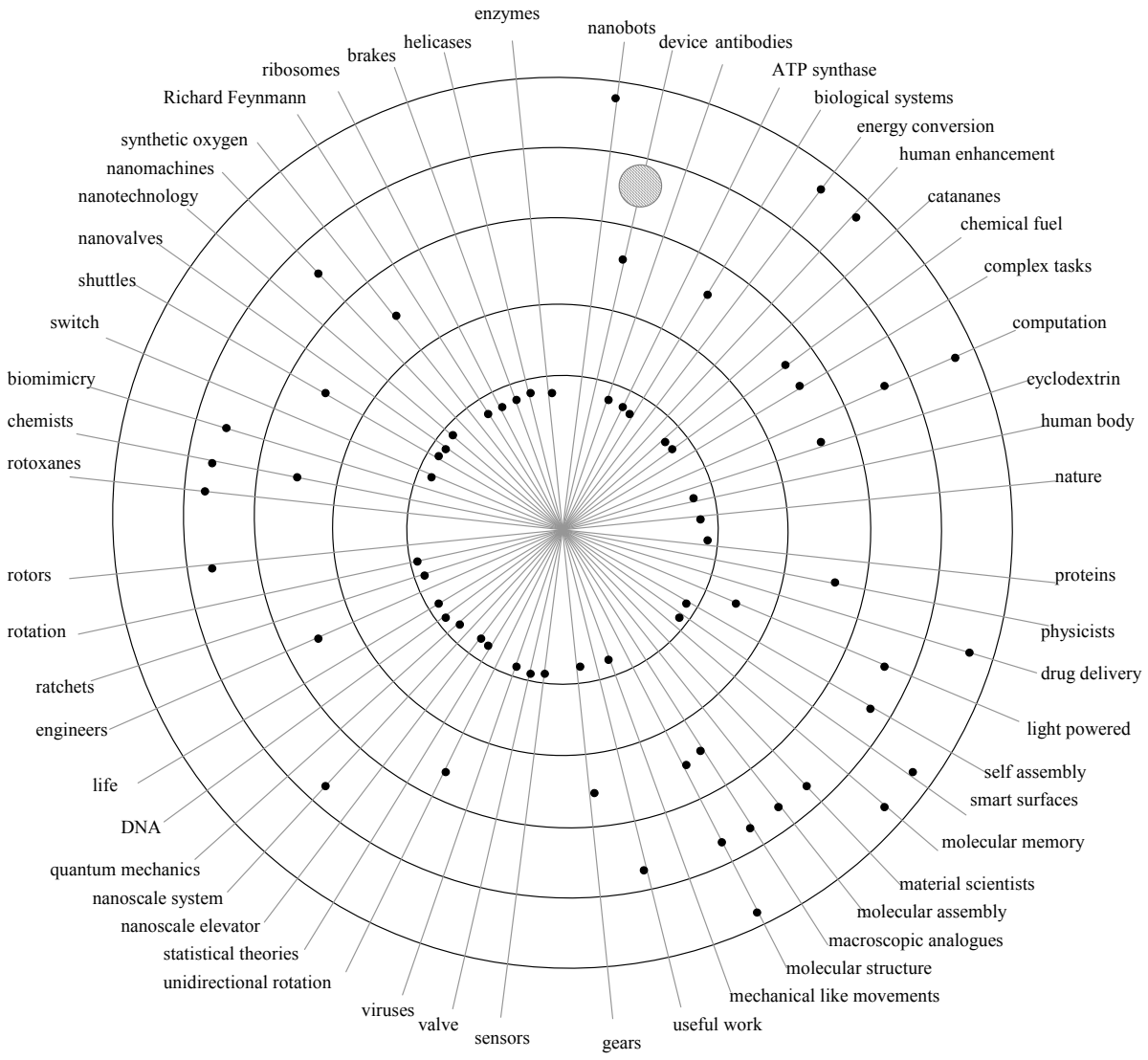


Figure 3.5: Modality-map for molecular machines (Browne and Feringa 2006)

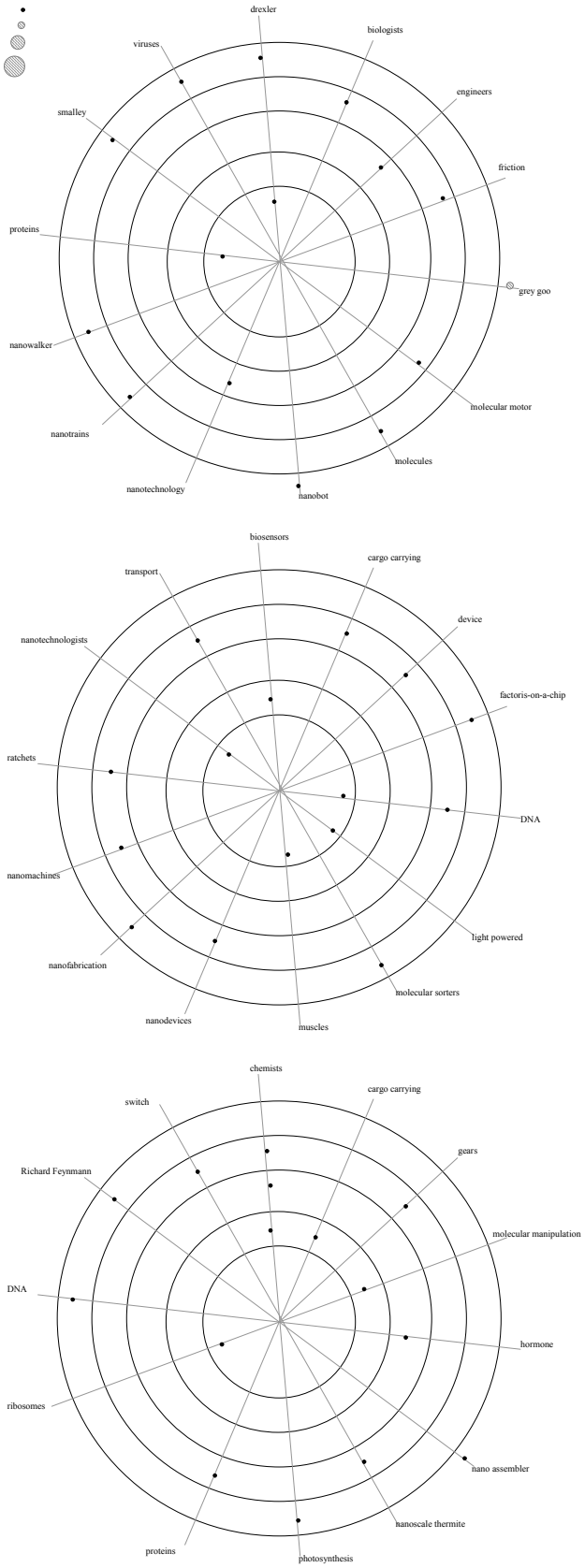


Figure 3.6: From top to bottom, modality-maps for nanomachines, molecular motors & molecular machines (New Scientist)

Discussion

The modality maps show the linkage ecology of three particular nodes selected from the database. They illustrate the spread and modality of the linkages about such nodes. From the data we see a large diversity in the types of linkages made. In addition, there are few obviously dominating linkages. In figures 3 and 5 for example, there is a dominance of single linkages whereas in figure 4 we see the beginnings of the restating of certain linkages.

Can we see agglomeration in the ecology of linkages in the field of molecular machines? The three nodes where selected from the dataset due to the large percentage of linkages made to them, but a larger dataset will be necessary to truly be able to evaluate agglomeration. From the research community, physicists (mostly dealing with single molecule mechanics) and biologists (dealing in the main with protein motors) where considerably underrepresented in the data set and thus visions need to be mapped. A similar peer-reviewed journal approach would be useful here, however, as has been shown, the peer-reviewed journals may not stimulate the articulation of Visionary Linkages or Science Fiction linkages. The New Scientist data showed that here such linkages prevailed. Considering that certain authors made linkages in both data sets (J. Fraser Stoddart and Vincenzo Balzani both leading researchers in molecular machine chemistry) these provide different fora for creating linkages. Thus an interesting research question would be to track certain actors and their linkages in different fora.

An important step needs to be taken in exploring the boundaries imposed in different fora for linkage making. An example would be the ETC-group, an NGO active in the nanotechnology debate especially focussed on Grey and Green Goo, where they currently use the vision of Green Goo as a possible future outcome for nanobiotechnology.

Their major forum for making linkages is on websites. The legitimacy and shaping strength of such linkages comes into question, and thus a necessary further step for the tool would be to link fora for linkage making and shaping strength on the field.

From the database we can observe that there are distinct generations in the perceived futures of molecular machines. 1st generation (the present) in chemistry creation of artificial motors, rotors and walkers in solution and statistical analysis of their movements is the going concern. Biologists in the 1st generation are attempting to understand the mechanics of natural macromolecular machines such as ATP-synthase and other protein based molecular machines.

The 2nd generation is the positioning of molecular machines onto surface to allow useful work to be done. 1st generation artificial molecular machines where in

solution and thus floating aimlessly and not transferring their kinetic energy. The 2nd generation is perceived to be a point where different communities can actively cooperate. Biologists working with chemists and material scientists to position natural motors into a synthetic environment.

The 3rd generation is envisioned to see the first devices with functionalised surfaces of molecular machines. It also sees the construction of larger artificial assemblies of molecular machines into the perceived nanomachines and nanodevices.

These generations are reflected in the modality of visions. However, since the linkages where mostly taken from the chemistry community (in the case of Browne and Feringa 2006), a further investigation into other community's visions is in order, to test the robustness and/or further define the generations of molecular machines and the perceived time frame.

The modality maps allow us to see the visions articulated by the producers of scientific and technical knowledge in the field of molecular machines, and allows us to tap into this and see the visions that guide the field.

The next step beyond this pilot study, is to undertake a study over time, to understand the dynamics of development and the to investigate the evolution of vision linkages. This would be interesting to monitor in a number of communities, especially with those deemed to be converging.[24]

An important next step in the exploration should be the visualisation of the authors of the linkage. Perhaps certain linkages come to dominate in a specific field, or perhaps, even more enticing, a community may be identified by those who make similar linkages. For the field of molecular machines this is an interesting entry point and one which the authors will pursue.

Conclusions

We have demonstrated the tool for a very specific question: what linkages are being made about visions, expectations and agendas in a specific data set (Browne and Feringa 2006) and contrasted it with a smaller data set taken from the New Scientist.

The tool allows one to gauge dynamics of an early field where data is heterogeneous and many activities are based on expectations of possible developments. Handling

[24] There are indications from our data set that the chemists and biologists are beginning to create the same linkages, and initiate collaboration on hybrid molecular machines.

heterogeneity is essential for understanding the dynamics for early stage new and emerging science and technology. In the above, we have outlined a tool to help in measuring the types of linkages made in statements about the emerging field of molecular machines, which could not be obtained easily with other methods. We have investigated the modality to allow us to gauge the (perceived) degree of development of the field. The statement-linkage approach particularly lends itself to rapidly evolving and fluctuating fields, such as those found in nanotechnology.

Its usefulness is in getting a handle on the dynamics of linkages rather than nodes, which presently is a lacuna that needs to be filled within the literature for studies of emerging science and technology fields when the definition of terms and actor communities (nodes) fluctuate. This is certainly the case for nanotechnology, which like the mythical many-headed hydra, sprouts more and more terms and definitions by the time one has conquered a specific term. One can see this at all levels of nanotechnology, from the definition of the umbrella term itself, to sub-fields based on application (Nanomaterials, Nanomedicine etc.), to technology developments (nanpatterned surfaces, functionalised nanoparticles etc.) to scientific disciplines (nanofluidics, bionanotechnology). Thus focussing on linkages perhaps bypasses the problem of taming the many sprouting heads of hydra by accepting the diversity of terms and focussing on the linkage.

The visualisation approach of the *modality map* used to present some of the data can be expanded to include changes over time, and networks of linkages. An obvious extension of this approach would be to track linkages in other data sets, such as conferences papers, policy documents, company reports, press releases etc. dependent on which community you wish to explore. This data set could be linked in a dynamic network mapping approach, which could capture the change of types and modality of linkages over time as well as the linkage/node ecology. The full application of the tool to the emerging field of molecular machines would focus on the various communities articulating visions and doing research in the field of molecular machines. This means heterogeneous data set (as outlined above). However, a comparison can be made about the modality of the linkages in each data set, the nodes which are dominant (depending on no. linkages and modality) and the evolution over time. This is in fact part of the extended programme of Molecular Machine mapping, and is work in progress.

Another characteristic, which can be mapped, is the positioning that occurs when and actor makes a linkage in a statement. Following from the work of Harré, van Langenhove and others (Harré et al. 1992, 1999, 2003 and van Langenhove and Berloznik 1999) one can see how networks emerge based on how the actor

positions himself with respect to the linkage (the author may make a negative or positive linkage thus positioning himself through making this claim). This data may be interesting for unveiling actor strategies in path emergence (Garud and Karnøe 2001, Rip and Robinson 2006, Robinson 2006a)

There are a number of limitations to this approach. The qualitative approach to selecting and coding the statements is dependent on the analyst and thus may not be directly reproducible. The determination of the modalities is also somewhat subjective. This could be lessened by conducting more mapping projects, the further refinement of the coding protocol and improvements on the visualisation techniques will thus be a goal of the authors.

In section 1 we described some of the challenges faced when investigating science and technology domains which lie beneath the umbrella term of *nanotechnology*. The approach illustrated through this pilot study shows promise for application to other domains of nanotechnology which lie at early stages such as bionanotechnologies, nanoelectronic devices etc. The strength of this tool is to get a handle on the types of expectations and visions in circulation in an emerging field in a systematic way. It is an important step for early stage technologies in order to inform further investigations and to provide the basis for selection of appropriate tools to explore the field further.

By looking at modality of linkages dynamically one can observe the evolution of nodes and linkages and emerging stabilities and irreversibilities that may occur. Such insights into expectation dynamics and emerging irreversibilities coming from such linkage mapping can be integrated into foresight, technology assessment and strategy articulation activities with actors. For a recent example of how this could be done, see Robinson and Propp 2006 or Robinson 2006a.

In conclusion, the methodology presented should be considered as the starting point for a much more elaborated statement-linkage mapping toolbox. It shows promise in getting a handle on dynamics of an emerging field at very early stages by enabling a systematic exploration of expectations and visions being articulated by various communities. Broader exploration and testing is needed on a more exhaustive data set and is indeed the intention of the authors.

Chapter 4 Multi-path mapping as a tool for reflexive alignment in emerging S&T[25]

Abstract

Roadmapping serves both short and long-term (strategic) alignment in science and technology (S&T). Forecasts of the likely future development of S&T are generated; then research and development (R&D) efforts necessary to realize various goals are backcast. But for new and emerging S&T this trusted principle does not work: the likely products are not articulated yet. A promising approach however is building mapping tools based on underlying patterns and indicators of the dynamics of emergence. This paper discusses, based on a first round application in the field of micro and nanotechnologies for single-cell-analysis, the methodology of such a new approach. The work is linked to a programme of Future oriented Technology Assessment (FTA) activities coordinated within a European nanotechnology research network.

Our paper addresses well-known lacunae of alignment tools from the viewpoints of the path creation/dependency literatures. We then apply these insights to lab-on-a-chip devices for cell analysis. Dynamics of emerging paths can be used to articulate a future structured in terms of prospective innovation chains and potential paradigms. We demonstrate a plausible variety of paths, which provides a broader set of strategic choices. This enables management of expectations and hype by which emerging S&T are characterised, and leads to alignment of actors. Our tool can be applied in strategic management of research and R&D at the level of science-to-industry networks. These are becoming an important element in European S&T policy but will only be successful if ways are found for closing gaps in the innovation chain.

[25] This chapter was published as: Robinson, D.K.R. and Propp T. (2008) Multi-path mapping as a tool for reflexive alignment in emerging S&T. Technological Forecasting and Social Change 75 517 538.

Lacunae and prospects of assessment and alignment tools for emerging science and technology

For innovation to succeed actor alignment in the form of innovation chains from laboratory to products and applications is necessary. Alignment is easier to achieve where the actors are known, their relationships functioning, regulation is largely unambiguous and the technology field is well understood. This is the case with incremental innovation in established technological paradigms. For new and emerging fields of science and technology (S&T) where architectural (radical) innovations might occur (Abernathy & Clark 1985), conditions of non-linearity and high technology and market uncertainty are typical (Rip 1995). This often leaves actors with the alternative of 'muddling through' and capitalizing on fortuitous events until such time that there is a feeling of stabilization and assessments and forecasts have become more reliable. However, in an age of strategic science and high-investment projects decision makers need to identify possible and promising directions and options and influence technology emergence in advance.

These are challenges for current strategic technology intelligence and forward-looking assessment tools. This is especially the case for the recent European Networks of Excellence and Technology Platforms which have been created around new and emerging S&T and have to develop strategies in the early stages of an emerging situation. Our project is embedded in a particular network of excellence on nanotechnology called *Frontiers*. Among the central aims of the Frontiers Network-of-Excellence (NoE) programme[26] are

a. the **coordination of research activities** in the research institutes that comprise the NoE (alignment); and

b. the **enabling of interactions** between industry in creating and sustaining an innovation chain.

These aims pose tremendous **managerial challenges**: NoEs have to combine 'vertical' or bottom-up management of a portfolio of research projects with

[26] The EC 6th Framework Programme Network of Excellence Frontiers is a network of 14 European research institutes, which aim to coordinate activities in enabling nanotechnologies for research in the life sciences. The Technology Assessment Programme is part of the Science to Industry work package and the Ethical and Societal Aspect package, and is led by Douglas K. R. Robinson.

'horizontal' stimulation of science-to-industry innovation chains. This includes actors outside the network, in the case of nanotechnology, start-ups and small-to-medium sized enterprises (SMEs), which have a lot at stake in entering such risky innovation chains. Many networks and platforms have dedicated working groups or programmes on foresight, strategic planning and anticipation of societal and ethical hurdles to innovation based on emerging technologies. Frontiers initiated in 2006 one such programme of Future oriented Technology Assessment activities (FTA). **FTA** is used here as an umbrella term for similar forward-looking and/or interactive characteristics of TA approaches. Another term, with a similar outlook but not limited to technology only, is **strategic intelligence** (SI)[27] which can be produced in evaluation, foresight, or TA projects and comparative studies of national and regional innovation systems etc.

Activities in the FTA programme focus on designing tools and support systems which allow the Frontiers network to develop strategies for a number of different issues relevant to particular areas within nanotechnologies for the life sciences. Our paper centres on one Frontiers FTA project on the stimulation of alignment to allow for the creation of innovation chains in the field of micro and nanotechnology. The project has added benefit at two levels:

1. developing recommendations for the **Frontiers research network**; and

2. exploring strategies for **specific actor groups** (SMEs and researchers).

At both intra-organizational (department-level) and inter-organizational levels in technology and industry, roadmapping has become a fashionable alignment tool. In general it combines forecasts and business strategies.[28] Ubiquitous as it may be, the advantages (and disadvantages) of roadmapping depend on the context in which it is applied.

There is a wealth of literature focusing on the functions, uses and tools of roadmaps in high-technology companies and multi-national corporations (MNCs) (Albright et al. 2003, Barker et al. 1995, Brady et al. 1997, Duus 1999, Groenveld 1997, Hussey 1997, Kappel 2001, Kostoff 1999, Kostoff & Schaller 2001, Lee & Park 2005, Lichtenthaler 2005, McCarthy 2003, Matzler et al. 2005, Phaal 2004, Probert & Radnor 2003, Rigby 2001, Rigby & Gillies 2000, Savioz & Blum 2002).

[27] Cf. (Kuhlmann, S et al. 2005)

[28] We note in passing that 'roadmaps' in the public sector often seem to be no more than outlooks on the future of a field or sector, using Delphi tools, or the more loosely structured 'prospectives'.

In contrast, analyses of assessment practices of researchers and start-ups (who constitute the larger part of Frontiers) seem rare. This lacuna may be explained with respect to the situation of new and emerging S&T. In exploration and early exploitation of new developments, assessment tools (market forecasts; knowledge of the technology and market drivers) are generally uncertain (Kappel 2001, Myers et al. 2002, Walsh 2004). New S&T are not defined by eventual application but characterized by 'generic richness', by linking up with a number of different fields a number of new innovations are enabled (Spinardi & Williams 2005). New and emerging S&T are often assessed in terms of their potential to "break through" recognized frontiers, or "disrupt" existing technology-product linkages (Walsh 2004, Kassicieh 2002, Kostoff 2004) – but this might be affected by hyped expectations. In some MNCs separate roadmaps are developed based on anticipation of multiple future scenarios (Lichtenthaler 2005) cf. also (Lizaso & Reger 2004). In the world of research, scientists undertake assessments all the time; these assessments are functioning if not always characterized by breadth of focus (a broader view of the field) and depth of vision (i.e. possible applications in the long term). There is also a general resistance against linearity towards applications imposed upon research: linearity contradicts the open-endedness and uncertainty of cutting-edge research.[29] From our own involvement in Frontiers and interviews done in conjunction with the work discussed here, we can add that unless start-ups and SMEs are part of networks which are able to commission roadmaps for dissemination among their members[30], they are in a difficult situation to develop or buy roadmaps of the fields they work in.

Literature in the management of innovation, expectations management and sociology-of-technology fields has stressed repeatedly that for assessments during early stages of technological emergence, more 'open-ended', flexible yet effective strategies may be useful. This element of open-endedness has been discussed by Fiedeler et al 2004a and Fleischer et al. 2004b and implemented in MANCEF's (proprietary) roadmap[31] (Walsh 2004). Beyond a diagnosis of the situation and suggestions, few assessment tools seem to have been **developed** and made

[29] Even though group leaders may use roadmap-type forecasts to organize financial support for their research.

[30] As the Dutch MinacNed consortium did in 2006 with their 'Roadmap Micro/Nanotechnology in Food'; cf http://www.minacned.nl/nl/activiteiten/roadmap_mnt_food_nutrition.php.

[31] MANCEF is the US based Micro and Nanotechnology Commercialization and Education Foundation; cf http://www.mancef.org/

available to actors. The FP6-NEST 'ATBEST' project addressed this problem in a workshop with practitioners but at a too general level.[32]

The point we make is that technological uncertainty is linked back to the underlying dynamics of the emergence of S&T. These dynamics can be explained by the concept of "socio-technical path" (Rip & Robinson 2006m Deuten 2003): multiple actors follow their own paths-as-strategies towards a future of possible (if competing, or mutually exclusive) paths-as-sociotechnical paradigms. Whilst following their paths actors consider a number of factors 'along the road' (which contribute a considerable amount of uncertainty, and demand flexibility). The aggregate outcome of actor strategies is the path-as-paradigm. These different paths at the different levels can be anticipated and mapped to some degree. The resulting maps can support in a very early stage (spinning-off of start-ups; portfolio creation) reflections on what road to take (for actors such as research groups, or start-ups), or which roads to support (for programme managers). A map of paths can be embedded as a central element in a support system to articulate the most robust[33] strategy for research groups, start-ups and programme committees (strategic/strategy support system, SSS). An ongoing strategy support system needs to stay aware of the field, allowing the assessment of whether the current strategy is optimum or a transition is needed to another strategy open to this particular actor.

In the paper we report on the (ongoing) development and application of the '*multi-path mapping' (MPM)* toolset. We explore the prospects of MPM, which provides strategic intelligence and would allow reflexive alignment. Specifically, we focus on the stimulation of innovation chains in the field of cell-on-a-chip devices.[34] This field is interesting because perceived products/applications would need a high

[32] Cf Rip et al 2005 'Assessment' and 'alignment' can be used somewhat interchangeably where they refer to tools that help assessing actions on the way to an anticipated future - tools for 'anticipatory coordination' (learning curves of 'disruptive technologies'; 'hype-cycles'; roadmaps). In other contexts it may be useful to differentiate, such as with 'anticipatory tools' (foresight exercises, bibliometric analyses, scenario planning, etc); and tools for portfolio and project management.

[33] Robust in the sense that it is informed by knowledge of path dynamics of new and emerging S&T.

[34] Cell-on-a-chip devices are integrated laboratories on a chip (Lab-on-a-chip) dedicated to cell analysis and manipulation. They combine many components and approaches from the macro-scale laboratory equivalent: sample preparation, pre-treatment, analysis, manipulation and removal.

degree of coordination to enable integration of a large number of technology innovations into a platform which itself could be tailored to various applications. In addition, over the 15 years of research and development into Lab-on-a-chip devices, larger industry has been reluctant to invest in stimulating *and maintaining* a Lab-on-a-chip innovation chain. Research and development of the components of Lab-on-a-chip continue, however innovations in terms of products are few and far between.

The long term aim is to package MPM as a *strategic support system* for start-up (and more mature) companies. This system comprises a number of tailored FTA/SI tools. It is being built around the notion of the '*deployment cycle*', which mirrors dynamics underlying technology S-curves: in early stages of technology emergence, the more flexible multi-path mapping is used; in later stages, when the technological, regulatory and business context of the (hopefully) growing start-up/SME has matured, the company can switch towards *roadmapping* for incremental innovation.

Before delving into the context of lab-on-a-chip for cell analysis we explore what the literature can tell us with regards to insights into emerging path dynamics stemming from sociology of S&T, evolutionary economics and organization studies. After selecting a particular (tailored) model from the menu on offer, we delve into the innovation context by setting the scene for the multi-path mapping exercise. We then present two forms of multi-path mapping undertaken in this project. We close with a discussion and outlook for the multi-path mapping approach.

Insights from studies of path dynamics and alignment

In more or less stable situations, affordance structures (Deuten 2003) are stabilised which frame possibilities and activities.[35] For new and emerging S&T, many paths are possible and thus speculation is needed. Thus, for developing an FTA relating to paths into the future, knowledge of path dynamics need to be integrated into a process of controlled speculation in combination with other analyses. There is now a substantial (and growing) literature on dynamics of path emergence and

[35] Affordance structures suggest directions of action, without determining them. Using the metaphor of landscape, "The affordance structure is in the situation, and frames possibilities for action while not determining them. The metaphor of landscape is useful… why climb over steep mountains, if you can follow a path through a valley (if you know the path is there)?" (Deuten 2003, page 14).

stabilisation. Here we can only focus on the main lines of research and highlight relevant notions.

Insights from the literature into the notion of path

From literature on evolutionary economics, notions of technical change were developed in the context of the firm. In his seminal paper, Dosi (Dosi 1982) argued that *technical paradigms* direct activities in technology development and thus are both rules that guide heuristics and strategic resources to move further (from the actor perspective).

> "Technical paradigms are 'models' and 'patterns' for finding solutions to *selected* technological problems, based on *selected* principles derived from natural sciences and on *selected* material technology (…). A technological paradigm embodies strong prescriptions on the *directions* of technical change to pursue and those to neglect." (Dosi, 1982, p 152)

In their paper investigating the airplane construction regime, Nelson & Winter (Nelson & Winter 1977) argued that when different firms share particular search and development routines, these routines add up to a *technological regime*. The shared direction of search processes adds up to what they term as a technical trajectory at the sector level: The DC-3 aircraft in the 1930s was the template for over 20 years for innovation in aircraft design around piston powered planes with metal skin and low wings. The potential of these elements was incrementally exploited, improving the engines, enlarging the planes, making them more efficient.

In the DC-3 case engineers were singled out as the drivers of the development. In other situations, it may be a continuing product-use combination (cf. the recent trajectory of mobile telephony), or industry structures (such as the energy sector) or strategic games (as with Moore's Law for semiconductors). Van den Belt and Rip (Van den Belt & Rip 1987) extended the Nelson-Winter-Dosi models for the late 19th synthetic dye industry, and in particular the new azo-dyes regime. What came together in the *co-construction of a trajectory* were, (1) heuristics, (2) an exemplary product, (3) a cultural matrix of expectations, and (4) the drive of a "promise champion". The environment had to change and be re-aligned so as to accommodate to the new trajectory and its promises.

Studies in economic history, organisational dynamics and institution theory have also given rise to the notion of *paths*. The concept of *path dependency* was first mentioned by Paul David (David 1985) and later by Brian Arthur (Arthur 1990).

The aim was to explain what microeconomics at the time was unable to do: Why do certain technologies become dominant even though they may be sub-optimal (such as the use of the QWERTY typewriter layout in computer consoles)? Path dependency is argued to be a self-reinforcing process beyond the control of the actors involved leading to lock-in. Small events can trigger a technological path that is then sustained by "increasing returns". As a result, momentum begins to build up and the path enters into irreversibility. This model argues that a path comes into existence behind the backs of all actors concerned and suggests this may be uncontrollably so.

As opposed to pure path dependency, *path creation* is a stream of research that remains sensitive to lock-in while modelling emergence on the basis of interactions of actors and their environment. Path creation acknowledges agency in the form of 'mindful deviation' and the mobilising of resources by actors leading to the creation of new paths (Garud & Karnøe 2001). Of particular interest for us, are the two main foci of the approach: (1) acknowledging mindful deviation as part of the emerging processes, implying that (2) real-time modulation of processes is possible. This broadens the previous notions of path from lock-in to the co-evolution of interactions of networks of actors with attempts at mindful deviation.[36]

Characteristics of path dependency and path creation are combined in a research line in S&T studies around the notion of *socio-technical paths* (Rip & Robinson 2006, Dosi 1982, Robinson et al 2007). This model seeks to conceptualise path dynamics both at the actor and aggregate level (similar to technical paradigms).[37] It was developed as a framework to study emerging alignments and entanglements in the field of nanotechnology, and looks at socio-technical paths as emerging outcomes of actor alignments within and across multi-levels.[38]

[36] Which can have unintended consequences as Anthony Giddens (Giddens 1984) points out "Merton has provided perhaps the classical discussion of the issue. He points out, entirely correctly, that the study of unintended consequences is fundamental to the sociological enterprise" (Giddens 1984, page 12).

[37] Path creation and path dependence studies are also merged in the Free University of Berlin doctoral programme on organisational paths of the semiconductor consortia (Meyer & Schubert 2005).

[38] Research becomes doable because of alignment across levels (the lab, institute, or wider world; Fujimura (Fujimura 1987)). Similarly, socio-technical paths become "doable" when there is alignment.

Researchers working with the concept of socio-technical paths have recently taken up the notion of *emerging irreversibilities*. Increasing alignment and entanglement in the concept of socio-technical paths can be linked to *emerging irreversibilities* (Callon 1991, Callon 1992, Rip & Kemp 1998, van Merkerk & van Lente 2005, van Merkerk & Robinson 2006). Emerging irreversibilities are punctuations in the evolution of a technological field, which both guide and drive it. They can be defined as '*socio-technical entanglements which over time enable and constrain alignments and activities of persons, institutions and artifacts. As these entanglements become tighter, options are reduced, facilitating certain paths whilst inhibiting others.*'[39] Irreversibilities grow over time, shaping and being shaped by the historical affordance structures which guide path dynamics.

The concept of emerging irreversibilities combines emerging structure (as in path dependency literature) with agency (as in path creation literature) by looking at indicators of alignment and stabilisation in the evolution of affordance structures that guide activities in new and emerging S&T. Thus over time as the S&T field becomes more stabilised, the patchwork of emerging irreversibilities become part of the affordance structure that shapes ongoing dynamics within the socio-technical path. This model has a crucial advantage: by repositioning the notion of path as something that is evolving/emerging in real-time, one can attempt to modulate/steer dynamics towards the more desirable actor arrangements and entanglements.

The models of path used in this project

For this project we draw on the notion of socio-technical path in its two forms: paths as **macro-level paradigms** characterised by socio-technical alignments and entanglements; and path as **micro-level actor strategies** projected towards a future paradigm.

With respect to the first notion a path lies at the domain level. The forward-propelling dynamics of incremental innovation act as a disincentive or even boundary to radical options. Entanglements of socio-technical actors and factors are both causes and effects of these dynamics. Predictions and projections of all sorts can be made (as in roadmaps) – outlining the future *path* of socio-technical development. In the case of cell-on-a-chip this notion of path can be taken as a projected socio-technical path in the overall field of cell-on-a-chip, where current

[39] This is in keeping with the 'actants' notion as network nodes in Actor-Network Theory (Callon et al. 1986).

projections, activities and search heuristics add up to an e*merging socio-technical path.* We emphasise the "emerging" part to it since a socio-technical path can only occur when there is multiple alignment across and between levels (c.f. Fujimura 1987, and Rip and Robinson 2006).

The second notion of path is from the perspective of an actor making decisions, developing strategies and taking action. In this case path is like a business model, a plan to connect the present to the future. In both cases managing for the most desirable path is the goal, be it on the individual actor level (such as an entrepreneur) or on the level of the paradigm (national agencies, international consortia).

Setting the scene: Lab-on-a-chip devices for cell analysis

The vision of performing laboratory experiments at a micro or even nanoscale was first posed by Terry (Terry 1975) who linked the idea of integrated microelectronics to the notion of integrated microfluidics for chromatography. The notion of a laboratory on a chip based on integrated microfluidics and micro-devices remained for some time as a general notion in the microfabrication community. In 1990 Manz (Manz et al. 1990) posed that integrated microfluidics could be harnessed to create complex systems that integrate all necessary analysis steps on one chip, labelled as a *Micro Total Analysis System* (μTAS). The agenda was set to miniaturise existing laboratory analysis instrumentation and in the early 1990s high expectations were raised about the possibilities of performing (bio)chemical analysis at any Lab-on-a-chip and at anytime, for example, total blood analysis at the patient's bedside (Point-of-care testing). In 1993, Harrison and Manz (Harrison et al. 1993) reported on a breakthrough regarding the successful miniaturisation of the analytical technique of capillary electrophoresis, which provided impetus to the field and stimulate a proliferation of research projects towards the vision of μTAS.

In the mid 1990s other scientific communities (synthetic chemists; biologists) were attracted to the field, foreseeing that this technology could aid them in their work or enable new lines of research, such as microscale reactors on chip or experiments with living cells (cellomics). The new and broader notion *Lab-on-a-chip* became widely accepted. Around 2000 nanotechnology started entering this field, offering improvements to existing possible chip components, but also providing novel concepts for separation and detection, cell analysis, cell manipulation etc.

Also, in the field of biomedical research, off the back of the Human Genome Project[40], a major emphasis in cell biology over the last decade has been focused on in areas related to genomics, proteomics, medical diagnostics, and detection of trace amounts of biological agents. High-throughput screening and microarray technologies are now in common use for measuring gene and protein expression and for assessing biological activity of potential drug targets.

For the field of Lab-on-a-chip there is a general agreement of four consecutive phases of technological development (see figure 1). Currently most developments still remain in phase 2.

Phase 1	Involves R&D in individual processes, instrumentation or devices, such as microfluidic research, pumps, valves, mixers, etc. – elements of an integrated system.
Phase 2	Experimental integration of some of the elements in phase 1 for analysis in the laboratory. These systems are complex and difficult to manage and thus are confined to research laboratories.
Phase 3	Integrated platforms which have refined the experimental integration into a chip sized system which can be incorporated into a device and used by a consumer.
Phase 4	Product tailored for a specific application. This is a customized and packaged lab-on-a-chip based device for analysis or synthesis. Examples could be point-of-care diagnostics of blood samples, or DNA analysis device for crime scene investigations.

Figure 4.1: Phases of materialization of the vision of lab-on-a-chip.

This can be translated into a prospective innovation chain diagram (see Figure 2) where we see scientific and technological research on the left-hand side of the diagram, where ad hoc integrations of a number of the necessary systems for lab-on-a-chip devices are explored and tested as technologies in of themselves as specific capabilities, techniques or devices. Examples could be a microfluidic channel, a fluid mixing system, a sample injector, positioner, sensor etc. In this dotted bubble, researchers attempt to develop and bridge the technology hurdle of integrating these proof-of-principle devices and combine them into an experimental platform for systems research such as protein analysis in the lab (moving from phase 1 to phase 2). Such an integration of a number of devices into an experimental system is usually undertaken in a university laboratory. Such

[40] http://www.ornl.gov/sci/techresources/Human_Genome/home.shtml.

integrated systems are bulky and complicated to handle, operate and maintain, and thus are only suitable for laboratory use. This activity is a bit further down the line from the initial cutting-edge research, and demarcates in many (but not all) laboratory settings the boundary between where research ends, and technology development begins.

The central bubble describes the further technical development of an experimental integration of elements into a working lab-on-a-chip device (transition from phase 2 to phase 3). This development is the largest stumbling block over the past years (as described in the history above) since there are a number of routes The decision has to be taken, sooner or later, whether to go for a highly application specific product (one purpose only), a product that is somewhat more generic and would allow for a number of distinct yet still similar operations, or a highly generic, versatile LoC device for many purposes (for instance through a *plug-in-and-play* platform which can be tailored to specific needs through the substitution of components).

The grey crescent represents the present barrier which must be crossed in order to produce an integrated lab-on-a-chip device. This barrier will be explored later in the paper as the main gap in the innovation chain for the last 15 years, relegating developments of LoC to remaining in phase 2.

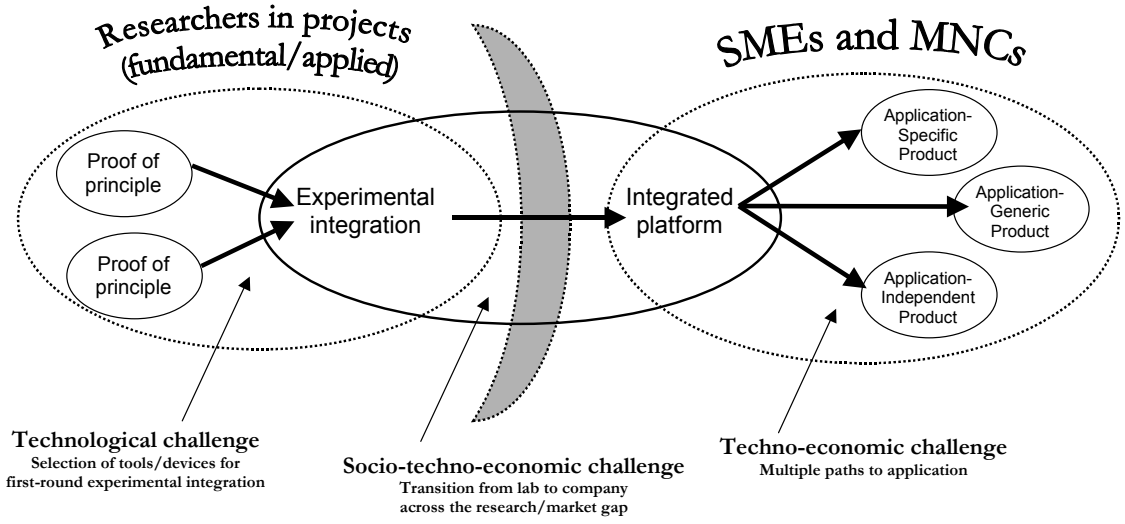


Figure 4.2: Broader innovation issues of the transition from research lab to company in the single cell analysis innovation chain

The final large bubble represents the evolution of an integrated platform to a product application. Application driven innovation chains would find that what we term *integrated platform* and *product application* being one-and-the-same. However, the various possible prospective innovation chains include the notion of generic integrated microfluidics platform which can be tailored for specific applications and thus we make the division in the diagram.

For single cell analysis, nanotechnology based tools are beginning to emerge as promising devices for single cell and subcellular analysis. Although current microtechnologies (including microfluidics) provide a foundation for creating a nanotechnology interface with single cells, both the integration of multiple functions and automated analysis and data handling remain to be accomplished in a self-contained cell-on-a-chip. Besides the challenge of integrating many components and devices, a more general challenge is how to bridge technology research with start-ups and/or multi-national corporations to allow technology applications suited to market demands and more broadly, societal needs: Who will be the key actors in stimulating the innovation chain (noting the reluctance of larger industry to stimulate innovation chains) and creating a platform?

With a multitude of projections of technology configurations and possible applications in circulation, and the lack of successful innovation chains meaning lab-on-a-chip remains at the research level, with this in mind, a project was set up under the framework of the Frontiers Technology Assessment Programme to:

1. explore and develop tools to map possible futures for the *field* of cell-on-a-chip with a focus on single cell analysis and identify possible promising paths for the technology;
2. use analysis of path dynamics and other strategic intelligence to explore the robustness of specific paths located within the field map; and
3. evaluate which paths show the most promise of successfully bridging the gaps in the innovation chain for single cell analysis with lab-on-a-chip technology.

Thus, multi-path mapping necessitates a deeper understanding of path emergence. This is in order to develop a robust map for an emerging situation, but also as part of the ongoing assessments which need to be evaluated based on dynamics of path

emergence. In our project we developed multi-path mapping in two ways: (MPM-1) the technical dimension of the MPM was based on desk research as a map to be used for the Frontiers network to aid strategy articulation in research and science-to-industry linkages, and (MPM-2) was used in an interactive way with practitioners as part of a workshop on bridging gaps in the innovation chain from the perspective of practitioners. We fed MPM-1 into the process of developing MPM-2 to combine both field level MPM with practitioner specific MPM. The workshop was used for the co-construction of the organizational dimension of the MPM, where the underlying path dynamics could be illustrated and discussed. In the following two sections we will describe both MPMs, focusing on their utility.

MPM-1: technical dimension

Lab-on-a-chip specifically for cell analysis is particularly relevant for Frontiers research lines due to its focus on instrumentation based on nanotechnologies for the life sciences. Of particular interest is the proliferation of research and development of nanotechnologies for cell analysis the laboratory, the proliferation of expectations regarding applications for such cell-on-a-chip devices, but no real bridging of the gap between experimental integration and integrated platform (cf. figure 2). Thus our first aim with the FTA project was to prospect possible socio-technical paths based on projections of the relevant communities involved in research and the prospected innovation chains. Cell-on-a-chip development is at a very early stage; much of the discussion of cell-on-a-chip development remains at the level of projections and claims.

For Frontiers, the abilities to map possible emerging socio-technical paths and use them to direct the portfolio of research lines within the network would be attractive (management issue 1 – see section 1). In addition, such a multi-path-map would allow plotting of possible innovation chains and enable the network to constructively stimulate innovation chains stemming from its research choices. Eventually, this would allow targeting of research and the negotiation with various relevant innovation chain actors.

For cell-on-a-chip, research areas are based around the perceived functions for cell handling and analysis conducted today in a macro-scale laboratory:

(1) cell culture;

(2) sample treatment;

(3) selection of what you want from the treated sample;

(4) lysis or incubation of the cell;

(5) separation of cell lysate (or single cells); and

(6) Analysis.

Relevant research for instrumentation and approaches for each of these stages is positioned in the proof of principle section (phase 1) of the innovation chain shown in Figures 1 and 2. Such areas of research have proliferated over the last 10 years (Andersson & van den Berg 2003, El-Ali et al. 2006).

Each of these six functions houses scientific research and technology development. We want to point out that within the six functions attributed to a cell-focused laboratory on a chip, research is ongoing with many variations and techniques being attempted or planned within each functional area. Examples for selection of cell would include optical manipulation of cells in microfluidic devices, including the parallel manipulation of cells using optical tweezers, optical switching of cells in fluidic channels and patch clamp devices. Recently, microfluidics for cell culture, flow cytometers, and other microscale flow-based cell analysis systems have been investigated for cell detection. Microfluidic devices for cell treatment, which includes cell lysis, cell culture and cell electroporation, electrofusion, and optoporation, are also under investigation.

In a number of cases, some of these devices have been integrated into a simple experimental system (cf. Wheeler *et al.* and the Fluidigm Corporation (Wheeler et al. 2003)). This has stimulated hopes for the field of single cell analysis, and promises about tissue engineering on a chip, stem cell analysis and possible production, single cell based biosensors etc, are now being circulated by many of both the μTAS and biology communities. Aside from these *relatively* simple experimental integrations there is the same gap in the innovation chain which we have diagnosed in Section 3 – a gap in full experimental integration and its evolution into an integrated platform. The visions of lab-on-a-chip devices still remain a promise just out of reach. With many start-ups and SMEs focusing on individual components related to the six functions, there is a sense of urgency in creating a platform for integrating various components into Lab-on-a-chip devices for cell (or any) analysis. We come back to this in the next section where we look at specific innovation chains for cell-on-a-chip.

This part of the project was to develop a tool to be able to gauge the ongoing developments articulated related to the possibility of cell-on-a-chip devices. Using literature analysis and a number of semi-structured interviews we constructed a

map of the actual and possible technological and application paths for chip-based cell analysis platforms (cf Figure 3). The map indicates that actors can select between two distinct yet general clusters of technological paths within cell analysis: using multiple cells for analysis (MCA), detection, or as 'cell factories', and using single cells (SCA). The former has already been realized to the extent of experimental integration (Wheeler et al. 2003, Schilling 2002). Single cell analysis in itself can be achieved using lysed cells (i.e. cells where the membranes have been intentionally ruptured) or intact cells. Multiple cell analysis is a technology path in as far as platforms and instruments are constructed around the principle of using multiple cells; compared with single cell analysis this has certain advantages and disadvantages in terms of application that need not be discussed here. Any cell analysis technique however can use different approaches and technologies shown in the lowest band on the diagram. Each decision is strategic as it requires investments and expertise on the parts of actors involved which constrain lateral freedom (at a certain point it will be difficult for SMEs to switch to another approach) but propel activities along a trajectory, such as the patch-clamping path. That is why there are always more paths as defined by underlying physical principles within the larger path.

There can be a number of technological paths towards one application area. This is because the labels ('medical diagnostics'; 'drug delivery') are abstract. Nevertheless more defined purposes require more specific technologies and hence, particular technological paths.

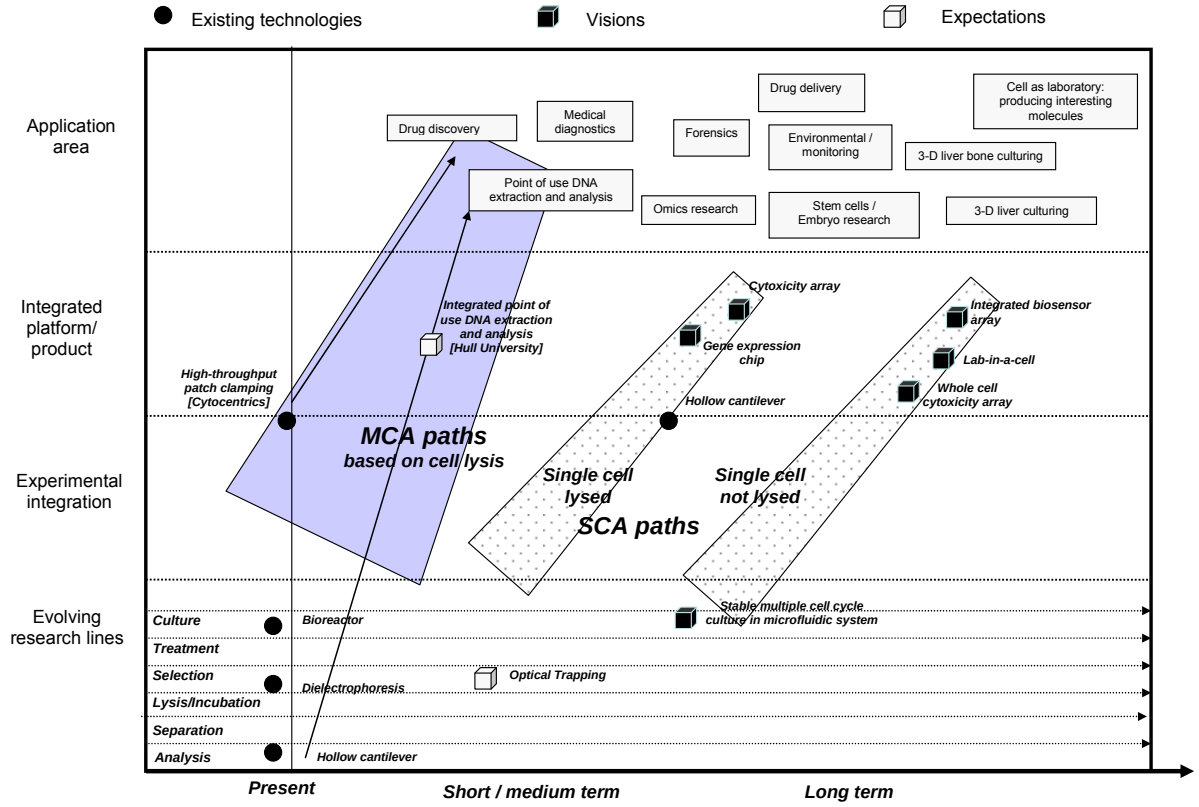


Figure 4.3: Technological multi-path map for cell-on-a-chip

The map shows the possible paradigms that can emerge. In the future, drug delivery could be based on socio-technical entanglements created around multiple cell analysis. These entanglements would be based on, and in reverse maintain, the existence of innovation chains around MCA linking actors in research, experimental integration, integration into platforms, and heterogeneous users in drug discovery. To the extent that this path would also comprise benevolent regulation and S&T policies, what we show here as the possible future path/paradigm at the level of an application area (drug discovery) may also be called an innovation system.

Because of all the contingencies related to gaps in the prospective innovation chain, in addition to regulatory/ethical uncertainty we did not specify how long it would take for something to occur. For this reason, the time axis is left open-ended with some divisions into short-term and long-term. This was done intentionally as, for the purpose of the MPM-1 was to be a platform on which to build during an

interaction between multiple stakeholders, we actually wanted to avoid specific dates and offer a contingency map rather than a roadmap.[41]

The existing technologies and the visions we have mapped here refer to results, or visions, of actors involved in the innovation process. Actors can and do link up with application areas such as those mapped in the top section of the Figure. The Figure also implies that, from a technical point of view, the future path of drug delivery can either be dominated by MCA or SCA. However, it is only the aggregate effect of actors linking up with visions of application, as well as each other, and responding to external events, which redefines an application area as a socio-technical path. In order to really change a paradigmatic path, concerted and sustained interaction of actors in and around the innovation chains is necessary.

The resulting first-round MPM shown in figure 3, brings together into the same space:

(1) research projections;

(2) applications;

(3) possible integrated platforms;

(4) possible paths; and

(5) general time axis and stages of innovation chain.

The actual MPM would show many more specific paths plotted within the clusters of MCA and SCA outlined here. We have plotted two actor-strategy paths into the map to illustrate some of the details that can be included in such a map. The first path shows a technology that is already present within a start-up company (as a prospective component of an integrated system) and its own projection of a path where it should go. This path originates at the interface of experimental integration

[41] Also, terms such as *short-term* and *long-term* are defined in particular organizational contexts. For example, there is anecdotal evidence that in highly competitive business contexts, long term begins at 5 years, but in fundamental research it can be 10 because of all the uncertainties. There is probably no a priori definition but partners in innovation chains will negotiate deadlines and durations of projects, and hence in the process co-define what must be achieved in the 'short' and the 'long term', respectively. Probably they will take into consideration the complexity of the goal to be achieved: a simple goal might be achieved in a single, short term project (1-2), but a more complex one requires both sequencing and 'stacking' of projects, so they would automatically speak of 3-4-5 years.

and integrated platform since it is a specific device searching for integration but having been demonstrated as possible within the laboratory (Cytocentrics B.V., Eindhoven). The second path comes from a research project at the University of Hull (UK), where government support has been granted to refine existing technologies and develop an integrated platform for DNA analysis, with a particular focus on point-of-use. This integrated platform has been funded to develop "*At scene of crime DNA characterization*" with the aim of demonstrating an integrated platform and then securing funding to turn this into a product for crime scene investigations.[42]

Such an MPM-1 can be useful for developing a portfolio of research projects and targeting the stimulation of innovation chains. This links up with management challenge 1 for Frontiers: creation and ongoing analysis of a portfolio of relevant research. Innovation chains are specific and there is a lot at stake for those who attempt at creating (or becoming a part of) an innovation chain. Looking at specifics of innovation chains addresses the management challenge 2, development and maintenance of science-to-industry links through stimulation of innovation chains.

For the purpose of aiding development to strategic research area setting within Frontiers, this map (and any future evolution) is and will be integrated in the *Frontiers Roadmapping Initiative*. The initiative is a programme focussing on aiding research foci in the link to applications. The next step of our project was to focus more intently on the second management issue – that of innovation chains.

MPM-2: innovation chain dynamics

Referring to the two management challenges of Frontiers, section 4 described and explored a use of MPM as support for the articulation and ongoing assessment of *Strategic Research Areas* based on dynamics of the field as a whole. The second challenge for Frontiers, that of stimulation of relevant innovation chains, is the subject of this section. Whereas MPM-1 was based on the FTA-analyst mapping of the emerging field, MPM for various possible innovation chains requires insights from practitioners who have experience and something at stake in creating and maintaining innovation chains.

To this end, we facilitated a practitioner strategy articulation workshop. The workshop focussed on mapping possible innovation chains and challenges for

[42] Cf. EPRSC project reference EP/D040930/1.

progressing down the number of possible options. The two aims of the workshop were:

1. Developing strategic information for the Frontiers network to include within the framework of MPM-1 in order to direct research and seek out possible actors who could co-construct an innovation chain based on the *Strategic Research Areas* of Frontiers
2. Broadening the perspectives of the practitioners participating in the exercise to test the robustness of MPM as part of a strategy support system for prospecting innovation chains.

Building off MPM-1, we conducted interviews based on perspectives and projections of the field of lab-on-a-chip for single cell applications. Along with the MPM-1 it was important to insert details of affordance structures and their co-evolution with emerging irreversibilities, in order to evaluate and assess possible paths within the prospective socio-technical paths. To this end, we used s*ocio-technical scenarios* to house some of the more detailed path dynamics and issues that came from interviews and desk research (on socio-technical scenarios in general (Geels 2002, Elzen et al. 2002, Elzen et al 2005). These scenarios in themselves contained reliable information on the current situation and selected prospective chronologies of innovations in cell-on-a-chip (rather than possible choices to go for). Their purpose was also to prepare participants to the kind of anticipatory work that was one of the workshop's aims.

From the interviews and the work already done on MPM-1 we identified the central bubble in Figure 2 as the greatest challenge to overcome for cell-on-a-chip (and lab-on-a-chip more generally). As possible participants we identified (1) researchers in microfluidics, microfabrication and nanotechnology tools for cell analysis and (2) start-up companies and small- and medium-sized enterprises (SMEs) relating to specific cell analysis techniques and lab-on-a-chip technology. Fourteen selected practitioners attended the workshop on 12 June 2006 in Amsterdam. Due to the aims and constraints of this paper we have to describe the

details of the workshop process elsewhere.[43] Here we focus on the results relating to the MPM-2.

The group identified a number of existing (or attempts at) innovation chains in the broader microfluidic/cell analysis fields:

- *In-house R&D of a multinational corporation (MNC)*
- *Technology development conducted by SMEs but stimulated by an MNC*
- *Start-ups finding opportunities and becoming the integrator*
- Separate integrators and design houses
- Research device is picked up by someone
- *Groups of heterogeneous actors coming together in a cluster*

The four options shown in italic where chosen to be discussed in more detail; cf Figure 5. The MPM scaffold allowed organizational challenges and technical challenges to be placed side by side with the goal of prospecting innovation chains. In this case we left the technical steps in the chain as part of the axis whilst the content of the map focused on organizational arrangements and roles of actors at different stages of the chain. We overlaid on top of the chains the challenges and hurdles linked with each chain. On this basis the chains were evaluated.

Within the group there was an agreement that multi-national corporations, such as Siemens or Philips have the capability to undertake research into components and integrate them into a Lab-on-a-chip technology platform. But ***innovation chain 1*** was said to have a key stumbling block - no clear market is visible for return on investment. Identifying the end user is one clear approach to selecting the components and configurations of a technology innovation chain. However one of the participants described the hedging of bets on a particular end user as dangerous because the innovation chain is precarious and may collapse. Flexibility is attractive for developing sustainable innovation chains but requires a belief in the technology. The participants agreed that this is lacking in MNCs due to previous hype-disappointment cycles – such as in biosensors. Another issue is that cell biology is diverse and so for cell-on-a-chip many niche markets will be the key. Large industry will be unwilling to invest in such niche markets (such is the case in

[43] For some more information on this and other elements of the Frontier FTA programme, contact Douglas K. R. Robinson or go to the programme website: www.technology-assessment.eu

pharmaceutical industry). Perhaps when a generic platform is the target large companies may invest, but application focus for cell-on-a-chip will be niche market oriented.

However, the large risk of little return-on-investment has stimulated another form of innovation chain initiated by MNCs shown in ***innovation chain 2***. This shifts the risk to SMEs which the MNC contracts for risky projects. Thus MNCs attempt at shifting the risk to start-up companies which build on their own ties with the research community and attempt to develop the technology. Intellectual property (IP) is shared with the MNC. Major issues here were agreed in the workshop to relate to the relationship between MNC and start-ups: for example the sustenance of the innovation chain is wholly dependent on the whim of the MNC. Moreover the concern was raised about the protection of IP: although the IP can be shared MNCs have the capability to turn it into a product and defend any IP issues based on their large resource base. One of the participants gave a case example: a large multi-national pharmaceutical company initiated the development of a prototype integrated device for chemical analysis with a number of start-up companies but then proceeded to outsource the further development of the possible product to another company with the end effect of the start-up companies being dissolved.

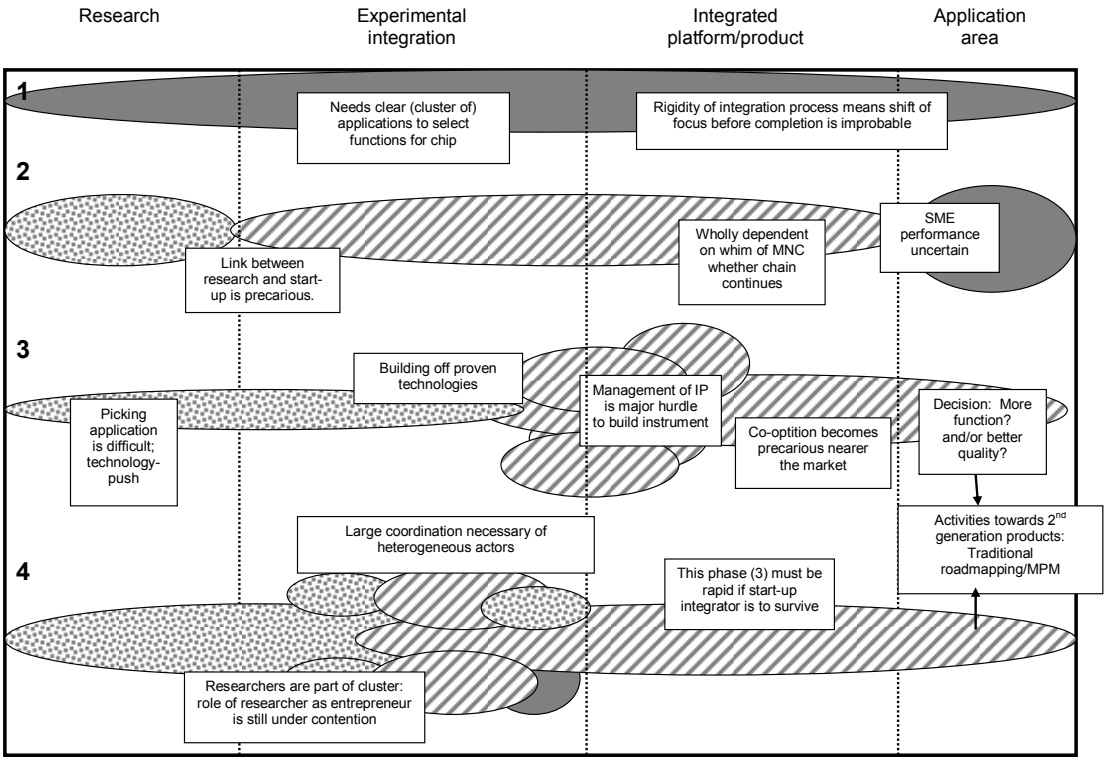


Figure 4.4:**(1)** MNC (dark grey) in-house; **(2)** SMEs (shaded) chain stimulated by MNC; **(3)** Start-ups creating network; **(4)** Heterogeneous clusters

Another obstacle came from the MNC perspective based on the risk of outsourcing the development of an integrated platform to SMEs: the performance of the SME is uncertain. The group posed innovation chains 3 and 4 and explored these as ways of bypassing any MNC lack of interest in integration by new forms of innovation chain.

In ***innovation chain 3*** a consortium of start-up companies would be the initiator for bridging the gap by attempting a generic integrated platform which could then be tailored for specific applications. This proposal was based on a view from the Netherlands: here similar SMEs waiting for the integrated platform to arrive are struggling to survive and are motivated to take action. Networks of start-ups and SMEs related to micro and nanotechnology (cf MinacNed) already exist. Thus a form of co-optition would be the desired goal to take the step of integration together and then competing based on tailored products and added value. The workshop participants agreed that the attractiveness of this innovation chain would be tempered again by IP issues – a large number of companies, distributed IP, difficult to see how each member as well as the collective could capitalise on the developments. The degree of complexity of an integrated lab-on-a-chip platform would mean a clear application driver for the SME-consortium or the move towards a generic platform in which all would benefit would be needed as a guiding vision. The idea of a generic platform is still contended (this contention was included in one of the three socio-technical scenarios) and thus mobilising the resources to create a generic platform may be tempered by uncertainty of whether generic platform (rather than specific application tailored innovation chains) is the path to take.

An alternative to this path was ***innovation chain 4*** which focussed on heterogeneous clusters. Since a large investment is needed in integration, there are specific advantages to be gained by building on proximity relations. This comes from building up capacity based on resources in the region, as well as a funnel for innovations coming from university research. Thus such a heterogeneous cluster would centre around university research and fabrication facilities[44], where start up companies (and perhaps larger companies) would form the constituents of the heterogeneous cluster. On the one hand, a large investment in coordination is

[44] This agglomeration effect of technology platforms is particularly strong for nanotechnologies [67]. For cell-on-a-chip devices, access to a large number of facilities is needed from microfabrication equipment, to bio labs, to instrumentation such as optical tweezers.

necessary and mobilising and coordinating resources is a key issue. On the other hand, advantages of such an approach are that new innovations will be occurring within the cluster, and proximity will allow for knowledge exchange and the building up of trust.

The workshop participants pointed out that there are attempts at all four innovation chains. ***Innovation chain 1*** has been attempted by large companies such as Siemens for relatively simple integrated microfluidics. One participant mentioned a "Lab-cow": an interesting integrated microfluidic device was designed first and then began the search for an application, leading to more loss of confidence in such ventures by MNCs. ***Innovation chain 2*** has occurred with companies such as Glaxo-Smith-Kline[45] and spin-offs such as those University of Hull (UK) and Yole Developpement, a French MEMS business development consultancy.[46] There are attempts in the Netherlands for ***innovation chain 3*** building off micro and nanotechnology SME networks such as MinacNed.[47] ***Innovation chain 4*** is currently occurring at the University of Twente (NL) where a start-up company with a specific sensor is acting as platform integrator.

Each of these innovation chains are possible, but 3 and 4 were agreed to be the most plausible ways forward (based on past failures of innovation chains 1 and 2). The participants also raised more general issues which came up as part of the exploration of the possible innovation chains. A major point was IP for distributed development of an integrated platform, the agreement being that new organisational models need to be sought. For innovation chain 3 this is indeed a challenge. For innovation 4 however this can be handled if there is one system integrator which targets a specific application and builds its network based around this. The IP issue can be generalised to many projected nanotechnology innovations, where technologies cannot be products in themselves but must be part of a system of technologies to be enabled.[48] Furthermore, the workshop participants recognized the difficulty of researchers in public institutions getting credit in developing integrated platforms. Although pressure is on them to provide research that can be turned into innovation chains, there is little acknowledgement of time

[45] Source: workshop participant.

[46] http://www.yole.fr/.

[47] www.minacned.nl.

[48] Examples are targeted drug delivery, implants, sensors etc. enabled through nanotechnology. Exceptions however include coatings and catalysts, which can in themselves be turned into innovations.

spent on doing this as opposed to research and teaching.[49] One way of doing this is developing an integrated platform based on an interesting experiment. For example, the University of Hull's crime scene forensic device is one case where funding was given to develop a prototype device for DNA analysis, with the added advantage of demonstrating integration possibilities for a cell-on-a-chip device.

The outcome of the workshop was that innovation chain 4 is agreed to be the most promising approach to creating an integrated lab-on-a-chip platform. Salient issues of the management of socio-technical aspects of this particular innovation chain were also highlighted. In the University of Twente case, we see a spin-off company becoming the system integrator for a specific application. In the University of Hull case, we see a research group becoming the systems integrator and building its network around them with a view to transition to a company after proof of concept.

Discussion and outlook for multi-path mapping as strategic intelligence for reflexive alignment

We have reported on a tool to provide ongoing strategic intelligence on evolving actor paths and emerging paradigms related to new and emerging S&T. Its methodological development and shaping owes its robustness to both a study of the relevant literature and interaction with practitioners.

Tools for assessment/alignment have been discussed in bodies of literatures as diverse and heterogeneous as: strategic management of S&T; the strategy literature; the general R&D, innovation management and management literatures; futures studies; organization studies; the S&T policy literature; and bibliometrics, scientometrics, and patent analysis. For the conceptual development of MPM, our self-set task was to integrate insights from roadmapping, dynamics of emerging S&T and expectations, and path dynamics. We argued that for new and emerging S&T path dynamics (Robinson 2006) should be addressed, and can be integrated into FTA activities enhancing the quality of assessment/alignment activities. We mapped initial, potential multiplicity paradigms with path characteristics, as well as the strategies that companies actually use. Shifts of entanglements are possible for actors for some time but otherwise they are more or less constrained as they are caught up in the very path dynamics at strategy and emerging paradigm level observed here. Multi-path mapping allows one to bring technical and organizational perspectives of path emergence and dynamics together in one

[49] This also a general issue in relation to the current situation of strategic science and application oriented research.

related space. MPM-1 was developed to map technology-based complexities of future projections from various communities and for various phases of a prospective innovation chain. We tailored this particular MPM with the generally acknowledged phases specific to lab-on-a-chip technology.

The project to which the tool development was linked was characterized by interactions with practitioners around forward-looking discussions. We organized a highly interactive workshop following the premises of Constructive Technology Assessment (CTA) (Rip et al. 1995), where insights into technology dynamics are explored with actors in order to broaden at an early stage the decision making process. The MPM-2 project involved a collective mapping of projected *actor-strategy paths* (or actors' paths-into-the-future) and a reflection on the future socio-technical path or entanglements which are foreseen or sought. The multi-path map allows the group to physically map some of the projections, however beneath these projections complex socio-technical arrangements and dynamics - which will enable or constrain some of these actor-strategy paths - could be brought into view. If path creation at the level of application areas is the aggregate outcome of activities at actor levels, then any of the innovation chains identified can create the matrix of entanglements constitutive of the new technology-application paradigm: cell analysis based medical diagnostics could be driven by MNC based innovation, SME based innovation, etc. From the outset no preference can be given to any chain, even if each of these has its own characteristic challenges to respond to.

Because of the exploratory nature of this first project of Frontiers' FTA programme, we positioned ourselves as experts in the field of S&T dynamics and path creation vis-à-vis the field-level expertise of the workshop participants. For reflexive alignment within research networks or firms it would seem advantageous that a 'strategy support system' (SSS) should be developed as a toolbox to be used without external help. This generic term denotes a toolbox specifically addressing the needs of organizations and networks of organizations with respect to strategic intelligence, possibilities for alignment, and exploitation of the generic richness of new and emerging S&T. The strategy support systems will be further developed for different technology fields being investigated within the framework of the Frontiers research programme. This network level strategy support system is somewhat abstract from specific technological issues, such as cell-on-a-chip; in a way it is a bottom-up way of methodology/tool building, growing with each new FTA exercise at this network level.

MPM can be of use at the level of research group leaders, portfolio managers, and start-up companies. Through analysis of socio-technical scenarios, emerging paths

and emerging irreversibilities in the field of research can be anticipated and investigated. Strategic flexibility means different things for different actors and situations, programme managers in particular can use it to be flexible in the selection of projects into a portfolio, monitor them, and over time, reshape the portfolio. MPM helps answering relevant questions such as: What specific kinds of innovation chains can be stimulated? What happens – technologically, organizationally - along the way and needs strategic rethinking? What are upcoming issues for regulation? The maps can be used to train programme officers/portfolio managers on anticipated issues along respective innovation chains, enabling some sort of strategic management including decisions whether to deviate from strategies shown or go along with them.

For a company or specific project leader, the *path analysis* is with respect to developments in research, the business environment, possible users, as well as regulation. The path they wish to develop strategy for is their company path.

The tool can also be used in communities outside of research and technology development but related to its financing, such as venture capitalists. Here it could act as anticipation and mapping tool guiding decisions on what innovation chain to invest in, or which actor strategies of building up such chains to support. It can be linked with assessments of hype cycles, by contrasting the hype surrounding particular paths with the kinds of path-typical challenges that can be anticipated.

With respect to our tool (but also any other tools developed by social sciences scholars exposed to research reality) we encourage diffusion into the wider public and private domains. There are numerous examples where research and R&D intelligence is separate from strategic management intelligence embodied in specialized technology consultancies but both cooperate in the context of alignment exercises. For example, there have been numerous Strategic Support Actions (SSA) of the Sixth European Framework Programme (FP6) Thematic Areas that supported roadmap building and where consultancies were involved. Therefore, what would suffice is to articulate a generic SSS sufficiently enough so that consultancies can take it ‘off the shelves’ of scholarly research and apply it. Such diffusion could be accelerated with support of FP7 Activity Areas.

At the time of writing (March 2007) we can undertake some preliminary impact assessment because the conceptual development and refinement of the MPMs was linked up with an interactive workshop. The workshop participants accepted our diagnosis given in MPM-1 and scenarios as well as the MPM-2 tool as relevant. This allowed discussion to go ahead on forms of innovation chain and ways of bridging the gaps. Therefore we would claim *immediate usability* as a positive

impact indicator. At the level of Frontiers the tool has been taken up in official documents as MPM-1 was included in the first round strategic planning document known as the Frontiers Roadmap for 2006/2007. This *acknowledgement* is another positive impact indicator. Further developments of MPM-2 will be included in the following evolutions of the Roadmap; however monitoring the affect and further developments of the MPM-1 approach is an ongoing task.

A very *concrete* impact on strategy articulation comes from one of the participants, a young start-up company initiated in January 2006 with intentions to be the systems integrator of a lab-on-a-chip device focused on a specific application in the medical sector. This start-up company is attempting innovation chain 4 (heterogeneous clusters) based on an application oriented innovation chain where users are already involved in the design process. As a consequence of their use of this tool, they have approached the authors in order to further apply the management tool to see if they can gain extra insights on organisational innovation chains (as well as the technology paths), and thus a tailoring of the tool for the start-up company is currently ongoing.

Chapter 5 Co-evolutionary Scenarios[50]

Abstract

Potentially breakthrough science and technologies promise applications which may radically affect society. Nanotechnology is no exception, promising many benefits through nano-enabled applications across multiple sectors and with the potential of affecting many parts of our society.

At present, during its early stages, a wide variety of actors are anticipating both on the potential benefits and risks of the development of nanotechnologies and their embedment into markets and into society.

Those wishing to coordinate and develop appropriate governance strategies for nanotechnologies need to consider both the wide spectrum of nanotechnology research and development lines, the governance landscape surrounding nanotechnology and the application areas it will affect, and how these may co-evolve with each other.

This paper presents a research project that took the recent activities in and around the notion of *Responsible Research and Innovation* of nanotechnologies as an opportunity to develop support tools for exploring potential co-evolutions of nanotechnology and governance arrangements. This involved the inclusion of pre-engagement analysis of potential co-evolutions in the form of scenarios into interactive workshop activities, with the aim of enabling multi-stakeholder anticipation of the complexities of co-evolution.

Introduction

The path to innovation is journey-like, certainly so for radical innovation. Trodden more often, the activities along the path will become more predictable (as with incremental innovation). Retrospective studies of emerging technology applications/products (from disciplines of Management and Sociology of Innovation) reveal that the journeys twist and turn, are non-linear and recursive

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and are contingent on a variety of forces and dynamics in the environments the hopeful technology may encounter.

For those wishing to enable beneficial technology applications stemming from potentially breakthrough areas of science and technology, such as nanotechnology, this complexity increases as we shift from retro- to prospective analysis of potential paths to innovation and the journeys that will be taken from idea to technical application well embedded in society.

In the field of nanotechnology these challenges are further compounded due to the early stage of nano developments, where promises proliferate around the benefits and risks that may become reality as nanotechnology matures. It is uncertain what sort of sectors will be impacted (or created) by nanotechnology innovations and how the regulatory, economic and societal landscapes will co-evolve.

Therefore, those wishing to develop strategies for managing nanotechnology emergence not only face the general challenge of prospecting possible pathways for innovation they also are challenged to prospect the changing environments and framing conditions that will determine whether an innovation will move from a hopeful proof-of-principle to a product well embedded in our society.

Anticipatory coordination for the responsible development of nanotech

These general challenges become very specific in the case of nanoscience and nanotechnology. There is a call for anticipatory governance (Barben 2007) often phrased as the need for responsible development of nanotechnology or responsible innovation in nanotechnology,[51] where activities are underway to enable those nanotechnologies which would provide benefit whilst constraining those that may cause harm. But the potential breakthrough nature of nanotechnologies as enablers of radically new applications may mean a complex reconfiguration of the environments that a nanotechnology innovation may traverse during its 'lifetime' from concept to well embedded technology in our society. The challenge then is how to be aware of the underlying forces shaping this reconfiguration. Only then

[51] The phrase 'responsible innovation' refers to innovation activities in which social aspects, desirability and acceptability are taken into account. Innovation actors will be responsive and may be asked by societal actors to account for what they do, and in this way responsible innovation is the responsibility of innovation actors, in interaction with various societal actors.

can effective strategies be developed to shape the emerging nanotechnology governance arrangement.

Such an emerging reconfiguration of actor relations, their roles and responsibilities is particularly striking in nanotechnology in the diverse activities in and around *"Responsible Research and Innovation of Nanotechnology"*.[52] That is why it became the subject of a research project and workshop within a programme of future-oriented technology analysis (FTA) in a nanotechnology research network called Frontiers.[53] The FTA activities in this network revolve around multi-(potential) stakeholder workshops where the aim is to explore the complex dynamics in and around specific areas of nanotechnology important for the Frontiers Network of Excellence (Frontiers NoE). The objective of the programme was to gain a deeper understanding of issues, perspectives and dynamics in order to develop smarter strategies.

As mentioned elsewhere (Kulve & Rip 2007, Kulve & Rip 2008) such interactive workshops are not an easy task. The focus topics are complex, uncertain and involve multiple actors working at multiple levels shot through with anticipatory strategies and expectations on risks and benefits of the emerging technology field. This creates a requirement for rich and easy to digest strategic intelligence for which can prepare the ground for interactive workshops on complex and highly uncertain topics such as nanotechnology.

This article focuses on the preparation and content of what we term co-evolutionary scenarios - those which focus on revealing underlying dynamics of co-evolution rather than articulating and placing emphasis on desirable end points. This approach is developed as a support tool for Constructive Technology Assessment (Constructive TA), see Box 1, and incorporates what we call

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[52] This term was created by the author for the purposes of the project, encompassing the notions of responsible development, responsible innovation and including the notion that this umbrella term covers research, product development and embedment. Responsible (research &) innovation can be read in two ways: one with an emphasis on innovation, which requires some responsibility to be successful/acceptable, or another with an emphasis on responsible up to and including halting developments along particular R&D or product lines.

[53] The FP6 funded Network of Excellence **Frontiers** is a network of 14 European research institutes, which aim to coordinate activities in enabling nanotechnologies for research in the life sciences. The Technology Assessment Programme was part of the Science to Industry work package and the Ethical and Societal Aspect package, and was led by the author.

"endogenous futures" into scenarios which take actors' initiatives and interactions into account. The latter is important because this form of scenario confronts participants in multi-stakeholder workshops with choices and dilemmas, allowing for more informed strategy articulation through deepening and broadening the understanding of socio-technical dynamics.

Scenarios have often been used to create a synthesis of future-oriented aspects prior to an interactive workshop, and there are many roles that scenarios can play i.e. offering possible alternative futures to assess and evaluate, or for presenting the playing outs of complex processes. The latter is interesting for us, and requires what Haico te Kulve and Arie Rip have termed "pre-engagement" through socio-technical scenario building (Kulve & Rip 2007). It involves the combination of exploration of dynamics using theoretical models and deep case research (Geels 2002) into scenario narratives which place emphasis on the "how" paths to the future may unfold whilst reducing (but not removing) the emphasis on the "where" the paths will lead to.

The why and how of co-evolutionary scenarios

In recent years, governance of new and emerging nanotechnologies has become a highly visible debate, disagreements on efficacy of current governance arrangements proliferate, new alliances have been (or are in the process of being) formed to shape possible new configurations of roles and responsibilities in the development of nanotechnology.

Within this context, a key issue for many potential stakeholders, and most of those that were the subject of this FTA exercise **was what sort of stabilized governance structure would emerge or would be desirable:** What processes would lead to stabilisation, what options are there, should stabilisation be sought at this time or should exploration under uncertainty continue?

The task of creating open-ended and context-rich scenarios encompasses a trade-off between recognizing the complexity of actual dynamics of innovation and the need to reduce complexity, without falling back on the linear model of innovation. Such scenarios should highlight both the multi-level/multi-actor dynamics AND the unfolding innovation journeys of technology development have not been developed to date. Such scenarios require insight into co-evolutionary dynamics, of actor activities (including anticipation in the form of agendas and strategies) and of enabling and constraining factors which shape the direction and pace of the co-evolution.

There is increasing recognition that innovation emergence is a non-linear process, not only in the management and sociology of technology and innovation communities, but also by international and global actors.[54] To capture this non-linearity of innovation processes, the metaphor of the 'innovation journey' has been used; it refers to the complex twists and turns in the emergence of a new product (van de Ven et al. 1999). Innovation is non-linear, and characterized by learning processes of actors about artefacts and actants.

Elements include the convergence and coupling of emerging technical and organisational elements, forks in to a number of potential paths (especially at early stages although forks can be triggered at later stags), dead-ends, setbacks etc. Other characteristics such as shifts and branches are also linked with the metaphor, and are considered part and parcel of the actor-network that carries the innovation as well as the broader landscape which over-time shifts

[54] Braun for example describes the early notions of innovation as being "characterised by a 'linear' view of innovation as an automatic spill-over process between basic knowledge and technological application" whilst recent notions regard innovation as being "non-linear and recursive interactions between a variety of actors participating in the quest for innovation".

Box 1 – The Constructive Technology Assessment goal of reflexivity rather than prediction

For early stage and highly uncertain fields of technology development, prediction is a tough task. Another approach would be to shift the focus of strategy articulation away from relying on prediction in its strictest sense, and stimulate a process of reflexive anticipation through controlled speculation based on exploring the underlying dynamics of emergence. Constructive Technology Assessment (Constructive TA) (Robinson & Propp 2008, Rip & Schot 2002, Schot & Rip 1997, van Merkerk & Robinson 2006, van Merkerk & Smits 2008) as a reflexive strategy articulation support system taking as its starting point ongoing socio-technical dynamics is particularly suitable for such a purpose.

The creation of visions of possible futures in Constructive TA is based on analysis rather than brainstorming. This is possible because there are emerging irreversibilities in ongoing socio-technical developments, based on shared agendas, mutual dependencies and network ties - there is an "endogenous future" (Larédo et al. 2002). While actors will always take enabling and constraining factors in the situation into account, Constructive TA adds to this because of a broader & deeper understanding of socio-technical dynamics.

In the case of the Frontiers NoE for nanotechnology, the programme involved research and preparation of these scenarios a input to 1-day multi-stakeholder workshops, where the complexities of the case, as well as the exploration of positions, stances and perspectives of the stakeholders, where probed and explored.

The interaction of the participants with the scenarios and each other are important aspects of the Constructive TA. Different types of participant have different assessment routines and practices, and one must acknowledge these bring them out in the scenarios and create opportunities to become more reflexive of how the different participant groups make assessments. Garud and Ahlstrom (Rip 1995) describe two perspectives of such technology assessment, those of technology developers and promoters they term "insiders" (that focus on innovation through enactment cycles) and "outsiders" (who focus on comparing and selecting options through selection cycles). This has been developed further by Rip (Rip 2008) and colleagues into a way of framing various ways of assessing technical novelty and its development. Rip and Garud et al. speak of bridging events, where real learning occurs when insiders and outsiders meet and probe each other's assessment worlds. The bridging events can occur in an ad-hoc way, or could be orchestrated – the

method put forward in the Constructive TA within Frontiers.

In this way, Constructive TA is an instance of the general shift in management (and tailored foresight) away from prediction towards reflexive anticipation and strategy making. If van de Ven's comment is true "Management can't control innovation success, only its odds" (van de Ven et al. 1999) then this implies a shift from deterministic approaches to foresight and strategy towards the creation of circumstances and conditions which enhance the chance of success. Good preparation and anticipation of possible problems in the innovation journey increase these chances of success. (Rip 1995)

To this end, Constructive TA develops endogenous futures into scenarios which not only take actors' initiatives and interactions into account but also the surrounding or ensuing dynamics and shifts in agendas that slowly become irreversible. Scenarios are not used anymore to extrapolate particular developments into the future but rather, to enhance the reflexivity of actors regarding strategic decisions which can modulate these developments, and larger lock-ins (irreversibilities) which constrain such actions and impact on unforeseen or sub-optimal trajectories of socio-technical developments. This reflexivity allows for a trying out of different possible paths, and this actor learning is captured in the term 'complexity'. This learning links up with the complexity of evolving (governance and other) environments. Working with such scenarios in strategy-articulation workshops is a means of testing the scenarios while probing and modulating participants' worldviews.

If we accept that paths to innovation is journey like, for the scenarios we must also recall there may be many potential pathways to innovation (Robinson & Propp 2008) and each of the journeys down the pathways could involve forks, setbacks, convergence etc. (the stuff of innovation journeys). However, for breakthrough technologies, the factors that shape the pathways may be evolving too! An example could be the regulatory landscape which would enable certain technology options and constrain others. The arrangements of the industrial sector could also enable and constrain certain technology options. Of course the technology options themselves may shape the landscapes that they encounter – could initiate a change in industrial sectors, in regulation etc.

Nanotechnology, even at this nascent stage, is stimulating a lot of speculation on shifts in these landscapes[i] leading to a desire to explore the potential mutual co-evolution of nanotechnologies and the various environments (industrial, market,

society, regulation, research, etc.).[55] To this end it was necessary to create a scenario method which incorporated these relationships and how they may play out in the future.

Co-evolutionary Scenarios were developed as a theory-informed approach to capture the complexities of innovation journeys and (co-) evolving environments whilst still allowing the formulation of strategies and concrete steps to take action. The key point here is that novelties do not traverse a *static* landscape made up of various selection environments (such as regulations, markets, policy etc.), but that this landscape is actively shaped in response to anticipations on development and impact of the novelties. The co-evolutionary scenarios should reflect this, and the discussions and interactions in the workshop will, in a sense, be a further, albeit small, element in the co-evolution of innovation and the surrounding selection landscape.

This is a key aspect of modern FTA – connecting complexities of ongoing innovations (and the conditions which frame the creation and selection of options) with the real issue of developing strategic agendas and plans that will lead to action. Some of the implications (including opportunities) of infusing complexity into FTA practices will be discussed.

Prospecting innovation: theory and concepts

Recent thinking about innovation adds up to a general idea that technology emergence is a process of innovation and selection shot through with anticipations (c.f. quasi evolutionary model (van den Belt & Rip 1987, Green et al. 1999) and sociology of expectations) (van Merkerk & Robinson 2006, Bakker et al. 2009, van Lente 1993). Evolutionary theories of technical changes emphasise that for innovation one should think of variation and selection (and retention of those selections). The outcome can stabilise into paradigms (Dosi 1982) and regimes (Nelson & Winter 1977)] Variation (or rather novelty creation) and selection however does not occur at random, actors anticipate on futures and these expectations influence their attempts to shape activities (van Lente & Rip 1998). Recent projects such as Socrobust (Larédo et al. 2002) were an attempt at creating anticipatory management and assessment tools for the analysis and improvement of the societal embedding of innovations. Socrobust emphasised the difference between hot unarticulated, open-ended ('fluid/hot') situations and more structured

[55] These environments, which enable and constrain certain technology options, I will call selection environments.

and well articulated, stable ('cold') situations (Callon 1991). So far there **has been limited investigation into to the transition from one state to the other**: what has been seriously "neglected are the processes of solidification and partial irreversibilisation turning the fluid into the stabilised" (van Merkerk & Robinson 2006). Future Scripts (de Laat 1996), which focus on actors' estimates about desired futures, also neglects these processes.

In this section I use three building blocks to construct a framework for prospecting innovation: evolutionary models of technical change; the 'innovation chain+', and endogenous futures. This framework which can help in structuring large amounts of heterogeneous data, aid the construction of complexity scenarios, and aid in locating and targeting Constructive TA activities. I begin by exploring evolutionary approaches and what they have to offer.

Lacunae in evolutionary models of technical change

How do innovations come to be selected from a number of possible options; how do some prevail whilst others diminish? Paradigms, trajectories and expectations offer partial understanding of how new technologies emerge, but have not answered these questions, nor have they given insights into the transition from unstable to stable situations. The idea from evolutionary economics of a 'selection environment' indicates the part played by economic, institutional and social factors in shaping a technology.

Sociologically inclined innovation scholars have focused on analysing and prospecting innovation/selection activities, studying open-ended situations of emergence, and other topics. Against this background I propose that there is a clear gap in the literature so far regarding the shifting natures of selection environments and how they co-evolve and shift with respect to unfolding innovation journeys.

There is a gap in capturing the shifting natures of the selection environments and mechanisms of action (Green et al. 1999, Glynn 2002, Freeman & Perez 1988). As Rip and Schot noted (Schot & Rip 1997), there is a lack of models that can capture this, with little or no focus on the actual shaping dynamics on the innovation journey in the literature. The authors suggest to acknowledge and embrace these dynamics of selection environments but go no further.

Green et al. (Green et al. 1999) in their comparison of the techno-economic networks (micro level analysis stemming from sociology) and techno-economic paradigms (macro-level analysis stemming from evolutionary economics similar to Nelson & Winters natural trajectories) critique both analyses for missing the

interplay between both. They suggest the quasi-evolutionary approach citing that Constructive TA could act as a middle point.

Robinson and Propp made a first step through exploring path dynamics. They developed a multi-path mapping approach which would combine path dynamics (David 1985, Arthur 1990, Garud & Karnøe 2002) with the sociology of expectations (Borup et al. 2006) to prospect micro level innovation chains. They acknowledged the concentric bias of the enactor perspective (technology developers and promoters who project a linear path from their technology option into the future described in Box 1) and attempted to broaden this concentric bias by taking into consideration open-ended nature of their projections and structured explorations of the journey-like nature of actual emergence.

In this project on RRI we add a further conceptualization using the idea of arenas of innovation and selection, with their (evolving) practices and rules. To show continuity with the earlier work, we have sometimes called it "innovation chain plus (IC+)", but it is actually a mosaic of arenas through which innovations traverse (including anticipation on further selections). The advantage of this conceptualization is that it allows selection environments and framing conditions to be an explicit part of the mapping.

Innovation Chain+: A mosaic of arenas for innovation and selection

At the time of the Constructive TA project, a method of combining ideas of innovation journeys amidst evolving landscapes (co-evolution of innovation/selection processes and framing conditions) was not available but was crucial in order to get close to the real issues being explored through the CTA. Building of the notions and gaps given above, the Innovation-Chain+ model was developed.[56]

Whilst every innovation has its journey, it is dependent on the techno-institutional landscape. This landscape will have different characteristics at different stages of technology/product emergence and is shaped by broader framing conditions and by anticipatory coordination on the part of technology developers and promoters, as well as those who seek to control and select options. With this in mind, I propose the Innovation-Chain+ framework as a way of presenting this situation. It allows the positioning of the complexities inherent to the reality of innovations, paths and landscapes, whilst allowing the link to the linear-model (reducing complexity to achieve outcomes).

[56] I add the "+" to indicate the broader framing conditions. Robinson and Propp 2008 used the innovation chain concept in the context of path dynamics.

It is complementary to the widely used value chain approach, which focuses on stabilised chains of product development. The Innovation-Chain+ is designed for new product creation and thus is useful for locating and framing shifts within certain areas of the chain, in the framing conditions (see coordinating mechanisms) or the whole system, the latter being typical for potentially radical and breakthrough innovations).

Detailing in brief, in this visualization an innovation 'traverses' a complex mosaic of arenas of innovation and selection which are affected by broader aspects. Within this mosaic certain technology options are enabled whilst others are constrained. The arenas for innovation and selection are shown as bubbles where each arena represents a particular socio-technical configuration carrying and being carried by the technical option traversing it. These configurations are entanglements (sometimes regular networks) of many actors, interacting based on regimes of activities.

Thus the innovation journey (represented in figure 1 as a branching line) is made up of a path to innovation (a pathway represented by the bubbles in the centre of figure 1) where the emerging technology itself which journeys through these bubbles.[57] The technology (and its socio-technical network) shifts and reconfigures based on the arenas it encounters, which themselves are influenced. This model is a complex mix of perspectives, and is a combination of technology studies, innovation and management studies, and path dynamics which adds up to a mosaic of arenas, or game-boards, broadening (although not removing) the linear perspective of chains.

Unlike the linear model, the emergence of an innovation is not pre-determined, it is more reactive and responsive and 'journey'-like, hence the van de Ven metaphor is very useful here.[58] The IC+ diagram broadens the value chain model but does not show details of the socio-technical networks. This is a reduction of complexity. However it is important to remember these are backgrounded in the IC+ representation (not removed).

[57] Here I make a distinction. Technical innovation is more than a box or device made up of material components and is part of a socio-technical network of actors, artifacts and infrastructures which evolve with the innovation. This reads like actor-network theory (Callon et al on TEN) and so innovation itself is an outcome of alignment and configuration of actors, artifacts and infrastructures. In line with innovation-chain+ nomenclature, one could call this innovation+.

[58] Still the focus of technology developers in their FTA activities is on paths (such as roadmapping) rather than journeys. Robinson and Propp expand this path perspective to a multi-path one. In this paper, we shift discussions to the journeys themselves and the arenas that will shape and be shaped by the journeys.

For structuring the co-evolutionary scenario narratives, the IC+ provides a "game board" for locating emerging technologies and evolving arenas and thus a way of framing our scenarios. The next step is to introduce evolution over time, so as to address the other main gap in the literature: how does eventual stabilization occur? For controlling our speculations of actions and co-evolutions of technologies and the IC+ we need some indications of how paths-to-innovation may emerge and how the IC+ may evolve. Paths to the future do not fall out of the sky; they are based on the dynamics of the present: there are endogenous futures embedded in the present which can give indications and insights into the transition from present into future.

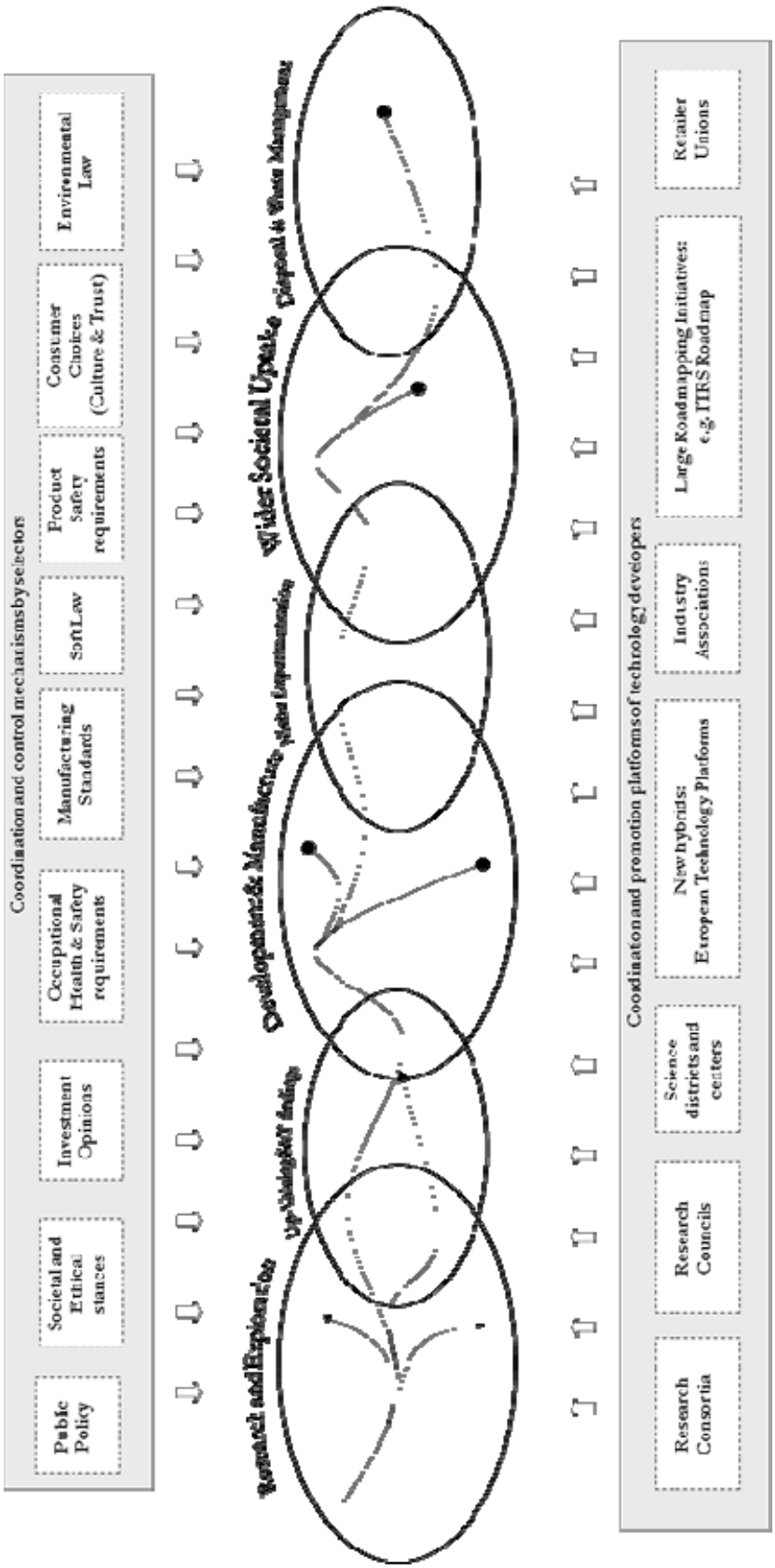


Figure 5.1: Innovation-Chain+ as a mosaic of co-evolving arenas of innovation and selection with innovation journeys showing coupling, shifting, dead-ends

Endogenous Futures

While new (emerging) science and technology introduce novelties, and thus potentially breaking up existing orders to some extent, subsequent developments create new patterns that may lead to stable situations. As mentioned in brief earlier in this section, emerging irreversibilities facilitate specific technological paths – making it easier to act and interact – whilst constraining others – making it more difficult to do something else. Emerging irreversibilities can manifest in a number of forms. Entanglements such as sunk investments (and the anticipations on which investments are based) and industry standards are some examples. Emerging irreversibilities are a general feature of social life, and the sociological concept of 'institutionalization' captures a large part of what happens. When technology is involved, irreversibilities are further solidified in configurations that work (Rip & Kemp 1998). The concept of 'configuration that works' applies to artefacts and systems, and includes (in principle) social linkages and alignments as well.

Another aspect of endogenous futures is linked with anticipation of actors. Expectations can give indications of directions and can transform into agendas which shape action (this is emphasized in the quasi-evolutionary model mentioned earlier). Van Merkerk and Robinson (van Merkerk & Robinson 2006) show examples from the field of lab-on-a-chip technology and how expectations have an effect on selection choices of pathways to follow, enabling some options and constraining others. This can occur also at through anticipatory coordination.[59] Studies also show how expectations can prestructure actions through prospective structures (van Lente & Rip 1998).

Paths and other stable patterns enabling and constraining actions and views, will shape further development. Thus, they span up an "endogenous future". The idea of "endogenous future" is midway between attempts at prediction (which are always precarious) and the suggestion that everything is still possible (and it is just a matter of actors deciding on what they want to work towards). Further developments are predicated on the pattern of the present situation. Not in a deterministic way: there are always choices and contingencies.

It is here that analysis comes in: of evolving patterns, of dynamics extending into the future, including irreversibilities that arise. This is the task of scenario builder.

Coupling endogenous futures with characteristics of innovation journeys (from historical case studies) within the framework of the IC+ framework helps us structure the complexities and control our speculation in order to make effective

[59] For example the nanoelectronics industry coordination efforts described in which would lie in the coordinating body's box of the IC+ diagram. Also describe Nanodistricts and the role of technology platforms which came about through institutional entrepreneurship between the framing conditions, the bubbles and the coordinating bodies.

and high quality scenarios. The following section will bring us away from conceptual explorations to the real-world of FTA and creating scenarios for a CTA exercise.

Evolving selection environments, and their internalization

A project is initiated

In autumn 2007 (as still the case two years on) there was an increasing emphasis on societal impact and embedment of nanotechnology applications. Ideas of responsible development of nanotechnology have been in circulation for a while now, but by the end of 2007 they were solidifying into policy and regulation. Thus, there was an occasion to launch a technology assessment exercise, with the aim of bringing together actual and potential players involved in nanotechnology governance to share perspectives, explore possibilities and draw out some recommendations to guide both the Nanotechnology R&D network (Frontiers) who initiated the project as others exploring potential governance approaches.

As part of the project within Frontiers, I carried out case research into the field, analyzed the recent history and current situation and developed three *co-evolutionary scenarios* showing plausible playings out of technology innovations and how they emerged and co-evolved with shifting regulatory, economic, societal landscapes. These provided input into a day-long multi-stakeholder interactive workshop where the complex interactions of potential governance arrangements and stakeholder strategies were explored.

At the time of the workshop (December 2007) the situation in and around nanotechnology involved mostly the discussion of Environment, Health and Safety aspects (EHS/HES) and other nanotoxicity related discussions, in addition, a call for standards in definitions. Actors such as governmental agencies, industry and NGOs were increasingly held accountable for addressing societal concerns, feeling pressures to incorporate ELSA and HES into their ongoing activities (similarly with corporate social responsibility). Thus, at the time, there was something at stake for these actors and a willingness to participate in discussions and workshops on the nano governance issue.

It is not in the scope of this paper to detail the case history of the emergence of RRI for nanotechnology, but to highlight some of the key aspects which informed the scenarios. For a detailed account of the developments of the nano risk debate and the key elements of RRI see van Amerom and Rip (Rip & van Amerom 2009) and Kearnes and Rip (Kearnes & Rip 2009).

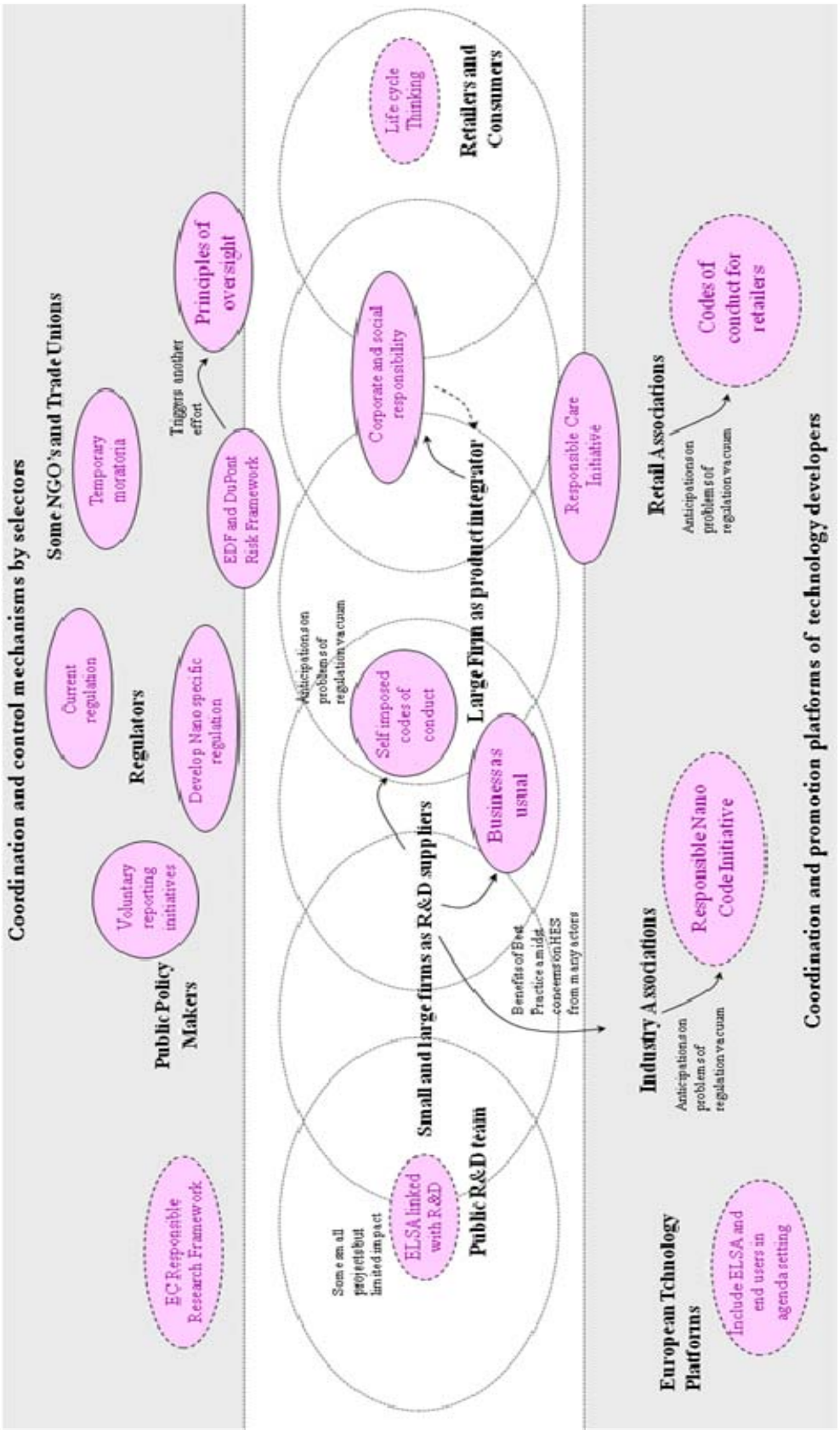


Figure 5.2: Here I position (in the IC+ framework) the actors that were active at the time of the workshop and RRI elements that were visible. The key question in this Constructive TA exercise: how will these elements add up and shape innovation and selection processes?

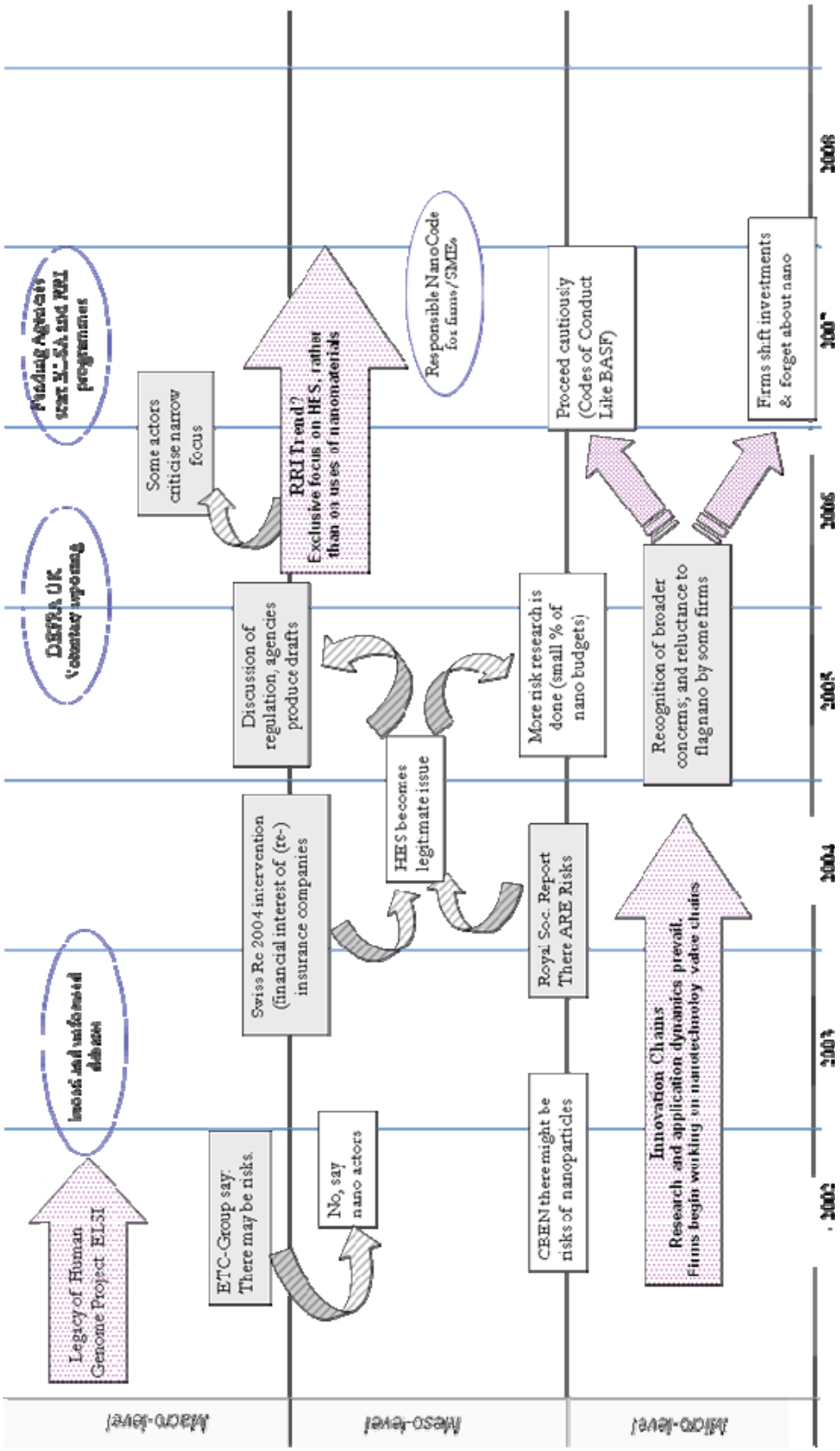


Figure 5.3: Evolution of governance, 2000-2008

By the end of 2007 a large number of soft law proposals were on the table, including codes of conduct for nanotechnology, some prepared by authorities like the European Commission, others offered by one or another firm, or proposed by a consortium. The proposed codes of conduct were the tip of an iceberg of a larger movement towards responsible innovation, increased political and public scrutiny, and the need to explore and develop recommendations for what one could call good nano-practice.

At the same time, researchers (for example in the Frontiers NoE) and other actors in and around the nano-world were becoming concerned about hype and bubbles bursting, about pressures towards valorisation of research as well as lack of uptake in sectors that could profit from the possibilities offered by nanoscience and nanotechnology. There was a widely recognised uncertainty about the potential impacts and risks, whilst in the meantime proposals for regulation were being formulated and various NGOs were taking positions, often advocating a precautionary approach (cf. Principles of Oversight) up to a moratorium (cf. ETC-Group and others). And there was additional uncertainty about consumer and citizen reactions to new nanotechnology-enabled products and processes – fears of a public backlash and of barriers to public acceptance.

The scope of the workshop and the nano context at the time

From the situation outlined in section 3.1, responsible (research &) innovation can be read in two ways. One with an emphasis on **innovation**, which requires some responsibility to be successful/acceptable, or another with an emphasis on **responsible** up to and including halting developments along particular R&D lines. Figure 2 takes Figure 1 and shows some of the activities in terms of coordination, promotion and control. This shows the status of the IC+ game board at the time of the workshop and was the starting point for the development of realistically complex scenarios.

Emerging paths and patterns that shape (enable and constrain) the future are particularly visible in the coupled evolution of research, production and use of nano-particles and the consideration of risks of nanotechnology.[60] Figure 3

[60] I have placed innovation journeys at the micro-level, technology developer coordination attempts at the meso-level and selector coordination and control at the macro-level. This is for ease of showing linkages and emerging entanglements across levels. Conceptual development of this multi-level perspective has been explored elsewhere.

visualizes this (up to 2008). We can see the importance of "new actors" in the shaping of emerging governance patterns and industry structure, of NGOs such as the ETC-Group, and of re-insurance companies shaping the emerging path of RRI. Dynamics are visible at all three levels, although there is little alignment yet. The repeated occurrences and acceptance of acronyms such as ELSA (Ethical, Legal, Social Aspects) and HES (Health, Environmental, Safety) in discourse on, and governance of, nanotechnology research and in the mobilisation of funding, indicates emerging alignment between societal concerns & allocation of resources.

There is an opening for consideration of soft law due to actors (firms in the main) anticipating (and thus proceeding with caution). Also, regulators recognise that there are openings but are unclear on how to target nano broadly beyond the current focus on nanoparticles. Firms are reluctant to start reporting – the DEFRA voluntary reporting initiative was mentioned as having limitations – but there are also voluntary initiatives in the pipeline and new ways of managing them e.g. the Risk Framework for Nanotechnology put forward by the unusual alliance of DuPont and Environmental Defence.

Irreversibilities are visible already. There is a lock in around RRI in the focus on HES issues. This would have consequences for other elements as resources are shifted away from them (path dynamics). Engagement with various publics is on the agenda (UK government initiatives and elsewhere) but have been ad-hoc and mainly centred around technology developer outreach programmes. Also, there is something like a **regulation void**, and commentators have suggested that the soft law initiatives and voluntary codes occur exactly because of this void. Others (like the Commission of the European Communities) argue that there is no real void, because existing law and regulation is sufficient, at least for the time being. Thus codes are on the agenda, although there is anticipation that proliferation of codes of conduct and other forms of soft law, may remove the pressure to develop regulation.

These elements provide building blocks to create three scenarios each of them a plausible story about how they might play out (including twists and turns). In the next section I show one of the scenarios, which focuses on evolving governance mixes. The other two scenarios focused on engagement and actor strategies, and on hype and mobilizing resources (promise requirement dynamics).

Summary of the Scenarios

Taking figure 2 as the game board, identification of some of the endogenous futures,[61] three co-evolutionary scenarios where created and fed into a Constructive TA workshop. The scenarios hang together with many elements being interchangeable. They do their job by emphasising tensions occurring in the Innovation Chain+ frame and place into context possible playings out, based on expectations and path dependencies that are crystallising out of the present (endogenous futures). They not only provide a platform for positioning the tensions, but also the perspectives (shown in figure 2 and 3) which allow for location of actual selection forces and mechanisms of action. This is important, especially in this workshop due to the focus on governance. What mechanisms should be modulated or augmented? Can we include forms of anticipatory actions or FTA mechanisms that are reflexive of the wider complexities of new and emerging technologies? Who should be involved and when?

Contrary to many traditional scenario building techniques, these co-evolutionary scenarios do not present mutually exclusive futures. In this way they are similar to the functions of expectations – the scenarios can be read and discussed as anticipations (1st order learning), but they also have a performative function in that they can lead to 2nd order learning on how to build more context-fitting scenarios.

Below I summarise the three scenarios developed for and in the workshop in the form of key threads and storylines. For reasons of space only one example (scenario 3) is given in full in section 5. The example helps to illustrate elements such as 'paths' and 'endogenous futures'.

The three scenarios

At the time of the workshop, in general most public engagement activities initiated by R&D actors focused more on enlightening the general public on the potentials of nanotech R&D – engagement as a lubricant against public friction. Stirling (Stirling 2003) identified three motivations for engagement which I adapt slightly below: (1) Instrumental motivations – legitimising R&D activities as a policy to ensure that technology is not held back by public scepticism; (2) Normative motivations – participation is a good thing in itself; (3) Substantive motivations – can lead to a better end product (Laurent 2008). The scenario in box 2 revolves around these three meanings and links them up with overall strategies in

[61] This was done through interviews and case analysis to find expectations of various actor groups and entanglements between groups and particular elements of RRI.

motivations for engagement around nanotechnology.[62] The scenario focused on the engagement aspects of RRI, the roles of various actor groups, the strategies and how the interactions played out.

Box 2 – Scenario 1 summary

The nano umbrella term becomes more specific (in funding mechanisms) - now defined in terms of potential sectors that will be impacted by R&D lines. In turn, potential consumers (and other impactees) can now be identified (the general public translates to specific publics) and technology developers begin to start anticipating on societal acceptance of products.

Proliferation of engagement/communication approaches at the micro-level allows justification of "societal awareness" as a strategy for ensuring "societal acceptance". Concerns are voiced by media, by civil society on effects on Food, Lifestyle, Health, Privacy and Human rights – an outcome of the increased specificity of nano. At the micro-level these broad discussion are termed as "a separate issue for longer term speculation".

Ad-hoc public engagement exercises act as a lubricant to continue nanotechnology developments across the board. However, one project in particular captures people's attention, named "NanoDiaBlog" - it is created as a web-based discussion forum (based on a Wikipedia model transparency is enhanced). Over time, the NanoDiaBlog project actually fulfils the promise made by its initiators (much to their surprise) as creating an informed general public, in addition it forms a community of scrutiny and debate, both positive and critical. Although not an official body, the NanoDiaBlog community is deemed a high quality indicator of the populace (in any case the populace who takes an interest) and principles such as precaution, inclusiveness (transparency), integrity (protection for whistle blowers), ongoing assessment (constant vigilance), and the need to interface promoters and

[62] NanoDiaBlog crosses all three motivations for engagement. The normative motivation is set down in the EU Action plan and leads to instrumentalist approaches being used when engagement is operationalized for R&D activities. This approach to engagement stems from an anticipation by nanotech developers of public friction, which leads to enlightenment and legitimisation strategies. NanoDiaBlog provides a space for other actors to shape the context from instrumental to constructive criticism (whistle blowers have a space to proclaim and civil society to discuss and mobilise opinion). One technology entrepreneur uses the NanoDiaBlog with a substantive motivation for engagement – to improve the product. Using the space to probe concerns, he incorporated the option of peel off RFID labels to empower the consumer with "the right to choose".

selectors, arrive on governmental agendas. Thus perfunctory public engagement exercises have the unintended outcome of creating a sustainable forum for engagement and action.

Taking advantage of this, a firm developing food-packaging sensors uses the blog to collect data on user preferences allowing targeting strategies. One outcome is with Radio-Frequency Identity Devices (RFID) tracking of goods through food packaging contains labels, similar to health risk labelling with the privacy risk label "This product is system tracked" placed on food packaging (a response to bloggers' insistence on transparency). Acceptance of the label was initially turbulent but general agreement of labelling and the "right to choose" (the label could be peeled off and so no further tacking possible) enabled wider uptake.

The scenario in box 3 looks at a specific cluster of innovations in nanoparticle based drug delivery. Tensions in this scenario include the issues of timeliness of engagement - when to incorporate actors? Early stage technologies are fragile and too early selection may inhibit novel solutions. The same for regulation – nanocodes enable in this scenario but the lack of regulation and eventual loss of the support of public organisations means limited access to the novel therapy. Again it describes actor strategies and the eventual entanglement of actors and the RRI elements to allow certain paths and inhibit others. In this case a technology option emerges but is only available for a limited number of people. It integrates elements of hype cycles, roles and responsibilities of researchers and the issues around risk of nanoparticles.

The scenario in box 4 will be shown in more detail in section 5.

Box 3 – Scenario 2 summary

Drug delivery becomes a key driver in nanotechnology. Rapid developments in nano means the consequent burgeoning number of delivery methods leads to increasingly bewildering regulatory protocols. Anticipation on further regulatory delays sees shift in private investments from nano to other promising technologies. NGOs, concerned about 2nd generation effects of nanoparticles argued for a moratorium on nanoparticles for medical purposes until toxicity tests tailored for these particles would be done.

In reaction to these concerns Dr Würzel (a researcher on nano therapies) argues on the ZDF TV news show that successes have outweighed the fatalities: "Fatalities occur all the time! My staff are combating a serious disease which causes

hundreds of thousands of deaths per year in Europe alone. It would be unethical to stop clinical trials for a drug that works better than others." The following Spring, as a response to the prior press coverage and the ZDF news item, many patients with lung cancer go to the lab. As ever more patients converge on his lab, coverage shifts towards headlines like "From battling disease to battling the health authorities": regulatory authorities become the enemy, obstacles to patient therapy. In the meantime, for the health authorities, the issue of proper clinical trials became an ever-increasing issue.

Lack of lifecycle thinking in nanoparticles and engineered tissue causes real concerns by both environmental agencies (the former) and clinicians (the latter). Production, storage and distribution in both the manufacture of nanoparticle based therapeutics and use in the clinics is an ongoing concern, as well as quality control of nanoparticles and bioaccumulation uncertainties (particularly in liver, spleen and bone marrow).

Public funding agencies form a blanket ban on financing nanoparticulate delivery systems. Private sector continues, voluntary reporting prevails but confidentiality of development hampers transparency (issues of competition) and thus watchdogs find it difficult to access data to assess practices. SME's, already severely hampered by lack of public financing (linked with university ties) can't cope on own with voluntary regulations, bypass it (for purposes of survival).

By 2012, health care authorities would not certify the approach without clinical testing. This leads to precaution by health insurance companies to cover the procedure. The further effect is that this medical option becomes available only to those who can obtain it in another way through private clinics.

The effect of these scenarios in the workshop

The three scenarios together covered the various positions and expectations of those actors active in the debate around RRI. The day long workshop was comprised of a number nanotechnology researchers, a ministry of health representative, a large chemical company, a trade union representative, a nanotechnology industry association, researchers interested in NGO activities, and a number of technology assessment scholars.

The elements and actors were recognised by the participants, with praise about the plausibility of such scenarios. Analysing the scenarios in depth in the workshop was not part of the exercise, but the participants were asked which elements they found the most striking or important. These provided the basis for the discussions

in the workshop which covered locating the responsibility of risk evaluation in the value chain, the ethics of promising (by researchers and firms), the ethics of engagement (not incorporated in the scenarios but stemming from the discussions) where including NGOS and civil society in research agenda setting causes tensions for the R&D agents (who work in an open-ended manner, shifting and adapting their agendas – where if they agree societally desirable end points, their open-endedness is reduced somewhat).

Box 4 – Scenario 3 summary

By mid 2008 the patchwork of codes of conduct, best practices and measures of responsible innovation remains misaligned, but allows progress in technology development through self-regulation and self quality control. The codes are particularly enabling for medical devices, providing some guidelines for nano alongside existing regulation of medical devices and so self regulation of new nano-enabling components can continue.

A case of focused alignment of R&D agendas in national initiatives can be seen. One example, Finland begins to invest in nanotechnology for paper processing (a major contributor to the Finnish economy). The specificity of the case related to opportunities to cut costs, reduce use of chemicals and improve manufacture. The lack of standards helps this growth and large investments are made leading to positive gains.

Early engagement exercises and high profile projects such as Nano Jury UK and others lead to the inclusion of "engagement programmes" in technology R&D programmes to inform and communicate the benefits of nanotechnology. There is a proliferation of such projects across (and initiated by) the nano R&D domain focussing on enabling public acceptance. Although no linkages between the projects occurs there the ethical and risk debate, begins to separate to "real issues" (of health, environmental and safety issues of nano production) and speculation on broader ethical debates around Human Enhancement, Justice, and theological issues.

Monitoring signatory compliance becomes a major issue. Code initiators attempt annual monitoring through direct contact to signatories, by asking them to volunteer time to report. Comparative and systematic methods do not exist. There is a lack of watchdogs; self-regulation and voluntary reporting go unchecked. The Precautionary Principle is promoted within codes but framed by self-assessment

mechanisms (degree of precaution unclear). Innovation actor's quality not assured. Voluntary codes align best practice but have little effect on worst practice due to regime of patchwork of codes (so good become better, worst remain worst).

Gaps in regulation widen as nanotechnologies become increasingly more complex – existing laws which could be applied to products (medical devices) are less equipped to oversee products and processes such as active nanostructures which cross many sectors and can be applied in many settings.

The accident with the Finnish worker opens up nano governance once again and a number of lines of R&D grind to a halt pending further investigation. Those wishing to exact change are faced with an entangled web of best practices, codes with varying degrees of transparency in how they are acted upon.

By 2014 the proliferation of nano and its increasing complexity hits home when consumer organisations try to target concerns, no inroads. Liability becomes the issue. When problems begin to occur with certain products secondary effects, lack of regulation means it's difficult to find who is liable. Public remains sceptical, voicing failures such as "lack of transparency" and "unclear accountability".

Governmental watchdogs begin to emerge and the clamour to catch up leads to numerous temporary moratoria. Regulatory actions retroactively cover all Nanomaterials and products on the market become identified and recalled pending certification.

The co-evolution of regulatory approaches and technology options was also discussed throughout the workshop, although not directly quoted in the discussions, the co-evolutions described in all three scenarios where picked up and discussed.

What was important in such a multi-stakeholder setting was the inclusion of all active actors in the scenarios. This meant that for certain actor strategies, say a firm or ministry, they could refer to scenario elements and discuss around these, allowing an easier route to some of the key issues.

A full analysis of the workshop interactions will be given elsewhere. In the following section I will give a full scenario (Scenario 3) with annotations showing the key elements in the narrative. I will then in section 6 discuss the technique and how it fits into the emerging menu of socio-technical scenarios.

An annotated scenario

Below is shown a full scenario. It is difficult to find the best way of annotating the text. Here I insert the comments within the narrative. This makes for difficult reading, but reveals the various elements of the scenarios as they appear. The annotations are given within the scenario text, after the relevant section of the narrative, in square brackets and in italic. At the beginning of an annotation, an indication of the type of dynamic involved in the scenario text is given, emphasized by underlining the comment.

By mid 2008 the regulation void continues and soft law is taken as an interim solution to allow nano to go ahead [*Observed Misalignment: There is no new nano specific regulation so soft law is taken as a solution. This was one vision of the future proposed by a number of codes of conduct tabled in the December 2007 EU meeting. Unresolved tension: This element linked up with the difference between two regulation reviews in the UK during 2006. HSE executive saying current regulation was enough. DEFRA saying there are gaps (Mayer Brown 2007)*]. Industrial consortia and research networks develop agreed best practices, which are self-imposed and a number of codes emerge and are agreed to [*Coordination of governance stemming from technology promoters – see figure 1.*]. Government instigated voluntary reporting, after the initial disappointment in the UK, begins to increase moderately. Reporting (when it happens) goes through the consortia (which act as a broker to maintain anonymity) [*Unresolved tension: Government actors attempt voluntary initiatives but there are tensions. This was the case at the time of writing w.r.t. the UK voluntary initiative. Attempts at coordination from selectors has limits. Thus technology promoters dominate.*].

Not all actors in R&D sign up to the codes, the broadness of principles causes concerns with some actors - a large pharmaceutical company states, "The lack of clarity and small print is unsettling for early stage technologies. Uncertainty in possible inroads for litigation and liability is not covered by such codes, for this reason our company will not sign up" [*A strong position: This is a stylized quote announced by a large pharmaceutical company in a meeting in November 2007 on Nanomedicine (Delemarle et al. 2005).*]. Conversely, code promoters state that "The breadth of codes is what gives it validity in current climate of high uncertainty" [*An opposed strong position: In debates I have observed, code promoters argue that the broadness is the reason why codes are good. This was taken from interactions I had with code developers Mayer Brown 2007)*].

The patchwork of codes of conduct, best practices and measures of responsible innovation remain misaligned, but allow progress in technology development through self-regulation and self quality control [*Misalignments enabling for some: A continuation of the situation given in figure 3 becoming an emerging irreversibility (not quite path dependency but a situation becoming increasingly entrenched of a patchwork of soft-law options. Pressure to consider broader*

(ELSA) aspects: Researchers and technology developers do not feel pressure and continue with their R&D unabated. This was inspired by interviews at an annual meeting of the Frontiers NoE, where researchers were anticipating that the EU responsible development code may affect funding.].

The codes are particularly enabling for medical devices, providing some guidelines for nano alongside existing regulation of medical devices (such as ISO 14971 for Medical Devices), and so self regulation of new nano-enabling components can continue [*Enabling aspect of soft law entrenchment: The codes are positioned here as useful additions to existing (well regulated) areas like medical devices (Robinson & Propp 2008).*]. By the end of 2008 advanced cantilever arrays and the long-awaited integrated micro-fluidic devices (lab-on-a-chip) begin to enter prototype phase with start-ups begin to emerge (and flourish) to take the university research to the market, with the prospect of takeover by larger firms in three to four years [*Aspects of translation through Innovation Chain*: *Innovation Journeys shift from gestation period to start-up phase. This section also illustrates techno start-up strategies.*]. Similar developments can be seen for crime scene investigation and civil security technologies, where advanced diagnostics, forensics and identification technologies were the focus – stimulate by government grants, small companies begin to commercialise this technology [*Broader context of comparable innovation journeys*: *These other fields are added to compare to the medical device innovation journeys later in the scenario.*].

A case of focussed national initiatives can be seen. One example, Finland begins to invest in nanotechnology for paper processing (a major contributor to the Finnish economy) [*Anticipatory coordination and lock-in: In Finland, sunk investments enable further development (but create constraints later on in the scenario)*]. Focused investments included nanofiltration (for effluent treatment), nanocoatings (for pigment and texture) and nanodiagnostics (for monitoring quality) and nanocharacterisation (for deeper understanding of paper materials). The specificity of the case related to opportunities to cut costs, reduce use of chemicals and improve manufacture. The lack of standards helps this flourish and large investments are made leading to positive gains [*A governance option of no standards*: There is a tension, s*tandards enable because they reduce uncertainty but also constrain variety and new ventures. This section shows a playing out of a continuation of the current situation*].

Other governments look at Finland's targeted explorations and developments in nanotechnology for the paper sector [*Lock-in as path enabling*: *Other governments look on with envy at the focus of Finnish nanotechnology. This is a mirror of anticipatory coordination in other geographical regions (Robinson 2007b, Nordmann 2007)*]. Government official "Nanotechnology promises to revolutionise all industry sectors, paper production could seriously be enhanced through nanotechnology and as a small country, Finland should focus resources on what is most beneficial for us." Other national governments look with envy at the rapidity of developments of the targeted nano programmes of Finland.

Early experiments and high profile projects such as Nano Jury UK and other engagement exercises lead to the inclusion of "engagement programmes" in technology R&D programmes to inform and communicate the benefits of nanotechnology. There is a proliferation of such projects across (and initiated by) the nano R&D domain focussing on enabling public acceptance. Although no linkages between the projects occurs, the ethical and risk debate begins to separate to "real issues" (of health, environmental and safety issues of nano production) and speculation on broader ethical debates around Human Enhancement, Justice, and theological issues [*Forking and division of RRI labour*: RRI topics begin to fork as actors focus either on *Speculative Ethics [41] and near-term Health Safety and Environment issues. This creates a gap in ethics of the present and near-future.*].

Monitoring signatory compliance becomes a major issue [*Tension: observed in many discussions of voluntary codes.*]. Code initiators attempt yearly monitoring through direct contact to signatories, by asking them to volunteer time to report.

Comparative and systematic methods do not exist. There is a lack of watchdogs; self-regulation and voluntary reporting go unchecked. Responsible actors, who have followed a particular code of conduct, flag their level responsibility by highlighting the following of codes as a sign of good governance [*Tension: I imply in the text that the "good guys" can make themselves visible through such initiatives whilst the "bad guys" remain below the radar.*].

2009 – 2010 Nano Development Boom

The self-imposed standards for manufacture work as a minimum safety requirement, but are at a considerably low level (minimum damage but some damage all the same) [*Selectors attempt at modulating governance arrangements*: *The narrative shifts into the perspective of NGOs and Trade Unions. The question of risk thresholds is often discussed especially around consumer safety and occupational health and safety. Here the NGOs and Trade Unions try to shape but have little effect because of the lock-in enabling technology development but constraining comparative selector input.*]. Some issues of workers safety voiced but related to non-nano issues and passed to others. Calls for moratoria continue from a number of civil society and labour organisations based on some occupational health issues but have little effect. This is in part due to the governance arrangements being firmly centred on industry consortia [*Tension: Del Stark (ENTA) in a meeting in Brussels pointed out that trade secrets in manufacturing would be a problem for voluntary reporting of use and processing of nanomaterials. He suggested that an industry association (such as his own) could play that role.*].

Emergence of platform technologies with applications in multiple sectors and comprising of ever increasing complexity of functional nano-elements (multifunctional tailored nanoparticles, highly integrated Lab on a chip, Moore

than More integrating of semiconductors and molecular electronics [*Tension: Increasing complexity of governance of platform technologies. This highlights another issue of where to locate responsibility for nanotechnology in applications, as nano is an enabling technology, and just contributes to the functioning of a large system. Key question: why focus on nano?*].

2011 – 2012 Nanoproducts proliferate

The Precautionary Principle is promoted within codes but framed by self-assessment mechanisms (i.e. the actual degree of precaution is unclear) [*Tension*: *Here the precautionary principle is placed up front in the text, and to emphasize that there can be degrees of precaution. Having been to a number of meetings on risk, I see that many technology promoters take an adverse stance towards precaution, connecting it to a halt (moratoria) on technology progress. This was placed in the text to provoke a discussion.]*. Innovation actor's quality not assured. Voluntary codes align best practice but have little effect on worst practice due to regime of patchwork of codes (so good become better, worst remain worst) [*Dilemma*: *Attempts to regulate through voluntary initiatives aimed at temporary governance of developments are expected to reduce pressure on regulators – so not supplanting regulation but inhibiting it all the same (regardless of good intentions). Taken from a discussion with a representative of Greenpeace UK*.].

Codes are not intended to supplant regulation but in practice reduce pressure on regulators causing delays in regulatory mechanics. Regulators rely on current law (or modifications of them) for nanomaterials and applications. REACH[63] is used but is identified as a blunt instrument by labour organisations as it fails to cover certain substances in very small quantities [*Differing positions between enactors and comparative selectors*: *REACH has been positioned as enough already by manufacturers, whereas labour organizations are concerned that it isn't refined enough.*].

A regulatory task force is set up by the British Government to identify possible regulatory gaps that could be filled [*Potential path shifting event*: *Taking a trigger from the labour organizations, UK government explores regulatory landscape. The report shows various gaps and issues (this was the case with the DEFRA report already. However in this scenario it is not immediately taken up. Here it is recognized as a good report but no further action initiated (until circumstances change).*]. The report pushing for mandatory government oversight, identifies many gaps but the major emphasis lies on the fact that nano regulation is difficult due to increasing complexity. - law is less equipped to oversee products and

[63] REACH Regulations – Registration, Evaluation, Authorisation and Restriction of Chemical substances (EC 1907/2006) – which entered into force on 1 June 2007. Reach applies to chemical products above a certain volume of production (1 tonne), while some nanomaterials will be produced below that level.

processes such as active nanostructures which cross many sectors and can be applied in many setting.

2013 House of Cards collapses

As ever-increasing complexity of nano, and various incidents cause concerns, the governance arrangements become questioned and regulatory concerns begin to emerge in many countries as calls for further investigation [*Lock-in becomes more visible as selectors wish to coordinate action*: *As nano develops, civil society, NGOs and governments become more concerned but find no clear inroads into the governance arrangements – a lock-in which is difficult to open up without major investment of resources.*]. However, there is alignment in the complicated relationships between technology platforms (multi-functionalised nanoparticles, and other functional macromolecular systems) and the various applications/sectors (they have become embedded), and this befuddles GOs, NGOs, and Civil Society.

Then a worker in paper factory, being treated for liver damage because of alcohol abuse, is found to have peculiar lesions of the liver tissue not related to alcohol abuse. Further diagnostics reveal nanoparticulate aggregation directly linked with the Finnish paper mill (specificity of tailored nanoparticles enables the identification of source of particle) [*Trigger creating window of opportunity for repositioning and realignment of nanotechnology governance: a triggering event occurs which raises the issue of toxicity and exposure. This element of the narrative was inspired by NIOSH 2004 which raised concerns around the manufacturing of nanoparticles. I do not mention that nanotoxicity is the cause of liver damage here, I leave it open. Because hazards and exposure issues are not known, it is difficult to decide whether nano is the problem or not. The uncertainty it the issue*].

In the field of medical diagnostics, nano-enabled chips were beginning to be integrated into clinical practice [*What previously enabled technology development constrains its embedment into markets*: *As medical nano enters the clinics user issues begin to emerge (previously unarticulated requirements come about). The issue of MRSA links up to discussions on new standards for medical devices. This example is linked to a presentation given by manufacturing firm in the London meeting November 2007 on Nanomedicine*]. The lack of nano specific regulation allowed innovations to proliferate but transition into the clinic became fraught with many other challenges related to user needs and user practices. Methicillin-Resistant Staphylococcus Aureus was found on a number of devices, which led to an enquiry on methods of sterilisation and exploration of bio-fouling. Technical complexity becomes an issue.

A number of legal actions were filed against medical device companies, which in turn causes health insurance companies to withdraw their backing of the devices in their coverage. One medic was quoted saying “The technologists missed the boat

early on, they should have listened to user needs rather than contemplating far off utopian and dystopian sci-fi futures" [C*onsequence of division of RRI labour*: *Clear issue of speculative ELSA in contrast to near-term ELSA]*. In contrast diagnostics for crime prevention and other non-health related applications continue to flourish [*A fork: Other devices are enabled whilst the medical devices are constrained.*].

The Finnish case sparks of a chain of enquiries into nano-regulation, and a number of lines of R&D grind to a halt pending further investigation [*Finnish case triggers a temporary moratorium: Because of huge sunk investment Finland begins to suffer.*]. Finnish economy begins to suffer due to the high sunk investments into nanotechnology based infrastructure. Public outcry as consumer organisations identify major issues in a number of sectors which could hold potential risk with no protection for the consumer (the house of cards collapses) [W*indow of opportunity for selectors: Consumers and NGOs are able to raise concerns, the lock-in can now be unlocked, and previous (technology promoter dominated) governance arrangements collapse.*].

Total recall

By 2014 Nanotech employs approximately 2.3 million workers globally. Nano has become a many headed hydra which is difficult to tame, one popular scientific journal headlines "One look at the Nano Medusa turns regulators to stone". This is picked up by other media, and phrased and framed in different ways. The proliferation of nano and its increasing complexity hits home when consumer organisations try to target concerns, no inroads. Liability becomes the issue [*Entrenched patchwork and lack of standards causes complication*: *Complexity of nano and the lack of coherent regulatory infrastructure means big delays for certain areas.*]. Reference to UK government report of 2012 identifying gaps – stimulates finger pointing at regulators for not following up. When problems begin to occur with certain products (secondary effects), the lack of regulation means it is difficult to find who is liable. Public remains sceptical, voicing failures such as "Lack of transparency" and "unclear accountability".

Governmental watchdogs emerge and in the clamour to catch up this leads to numerous temporary moratoria. Regulatory actions retroactively cover all Nanomaterials and products on the market become identified and recalled pending certification.

Whilst regulators scramble to catch up, the ever-increasing complexity delays the process even more. Whilst for nanomedicine and bionanotechnology the clamour for tests and rapid certification hampers technological progress, other nano-promises as in "Beyond Moore" (nanoelectronics and nanophotonics) take the lead – for the time being [*Winners and losers are mentioned here. Highlighting that*

this is not a dark scenario, but a situation which enables some options and constrains others.].

Evaluation and Discussion

These co-evolutionary scenarios can prepare the ground for discussion of complex potential radical technologies via the combination of endogenous futures, the IC+ framework and deep case research into actors and their activities. The process provides a means for the creation of rich, context aware and plausible scenarios, which are accepted as legitimate and controlled speculations by participants of Constructive TA workshops. In this case they were used by participants as a resource for discussing the complexities of potential multi-actor multi-level de/re alignments and the effects on nanotechnology emergence.

Here they show that the patterns that were becoming stabilized by 2007 (identified through exploring endogenous futures) continue to shape development and that twists and turns are to be expected as well (characteristic of innovation journeys). While in the annotated scenario, the Finnish worker case, and some of the actions and reactions given are contingent, there is a certain plausibility to their occurrence, and the responses and eventual outcomes are shaped by what is in place already, and thus not completely contingent.

In that scenario I could include anticipations from the world of nano, fears of being locked out of the debate through lack of transparency, of maintaining a patchwork of soft law options to facilitate nanotechnology innovation, positions taken on precaution, the emergence of windows of opportunity for action (stemming from the Finnish worker case being part of the co-evolution of emerging nanotechnology options in paper production and risk and regulation landscape), entanglements due to sunk investments (Finnish policy), collective decision on technology developer side for soft law, etc.

As some of the annotations indicate, the scenario introduces actors and their activities, responses and shifts that have a certain plausibility given what is happening already. Because of this, participants in the workshop can't dismiss them; they have to reflect on them.

Participants in the workshop recognized the dynamics given in the scenario narratives. Elements were picked up, and further responsibility issues were discussed, like how governance arrangements affect cowboy firms (and other organizations) versus good firms. This scenario worked well in terms of showing interactions and outcomes shaped by earlier patterns ("endogenous futures"), and

in terms of encompassing variation and contingencies. The scenarios also worked well in terms of stimulating productive discussion in the workshop. This can be seen as a stakeholder 'endorsement' of the approach (which is an important indicator how well workshops like these are working). The evaluation of my workshops for Frontiers show that learning about other perspectives occurs, however it does not yet mean that the scenario method has proved practical in the long term (in the practices of the participants), this is part of ongoing assessment.

However, as mentioned in section 4.2, these types of scenarios do stimulate discussions, and provide both a place for exploring different actors' positions and strategies as well as providing key elements and aspects in context. The context is important as it shows the co-evolutionary nature of emergence.

Making some of the emerging pathways explicit, through exploration of endogenous futures and their playings out in scenarios, helps in creating more reflexive strategies. It does this in a form that is usable and makes sense. IC+ emphasizes the overlapping mosaic of arenas of innovation and selection shape and are shaped by the innovations that pass through them and so helps in identifying actors and their strategies. This aids the scenario creator, in my case I could place amidst the three scenarios some major stances and strategies of various actors, and based on expectations analysis and the concept of emerging irreversibilities, show how actors interactions and reactions would co-evolve with the broader IC+ landscape.

A new member to the socio-technical scenario family

Co-evolutionary scenarios can be created and are productive as an input in Constructive TA type workshops. Their productivity depends on the trade-off between the need to reduce complexity to make it manageable (while keeping the complexity visible), and the risk of bowing to the concentric bias of enactors who need scenarios to guide them to identify and overcome barriers to introduce "their" nanotechnology into society. The IC+ framework provides a gameboard to bring together linear/concentric perspectives with complexity, and thus helps with the creation of scenarios.

These scenarios embrace complexity by referring to the emerging natures of both the innovation chains and their environment. Both are complex, and there is co-shaping. So the scenarios provide a grip on complexity –through actors pro-actively shaping chains and governance, and through lock-ins and selection. In workshop situations they act as a way to provide controlled speculation into easier

to handle forms, to enable those who do not have a propensity towards elaborate anticipation to observe patterns, evaluate the scenarios and interact within multi-stakeholder workshops.

The scenarios use endogenous futures, not as a way of extrapolating trajectories but to foreground what may happen as activities play out, and certain entanglements of actors and their activities prevail in one direction or another.

The co-evolutionary scenario approach is a contribution to the growing field of socio-technical scenarios. Other members of the family include regime transition scenarios,[64] broadened concentric scenarios,[65] multi-level scenarios for evolving industrial sectors[66] [67], and actor-centric scenarios revealing the visions carried by various actors.

Co-evolutionary scenarios make a modest, but important, contribution to this family by combining concentric and multi-level approaches through emphasizing co-evolution. As is already clear from the evaluation of the workshop, such scenarios support strategic anticipation. If that informs interactions, it will lead to anticipatory governance.

[64] Targeted (and used) for transition policy.
[65] Used for open-ended roadmapping by technology developers at early stages of development.
[66] Used for exploring industrial/sectoral alignment/misalignments
[67] See Haico te Kulve's work on Food Packaging for a thorough description of this approach. Also see the work of Alireza Parandian, Delft University (NL) on multi-level analysis of body area networks (to be published in 2010). Also the multi-level approach similar to was used in one of the Frontiers Constructive TA exercises on the drug delivery sector, but from a researchers perspective (the tension of exploration and exploitation).

PART III

Chapter 6 Insertion as a necessary element of CTA

This chapter reports on my observations and interactions while developing a programme of CTA activities through insertion into the nanoworld. As I noted in Chapter 1, insertion is also a way of data collection. Moving about in the nano-world allows one to observe the ongoing developments and probe the positions (and forcefields) in that world. The latter occurs also, and especially, when intervening, e.g. when preparing a CTA workshop. While probing occurs in micro-interactions, up to informal conversations, some of these interactions take place at the meso-level, as in board meetings of an EU Network of Excellence, and thus offer a view of what happens at that level. Over the course of five years, it is possible to see longer-term changes, in particular (and using terminology introduced in Chapter 1) increasing reflexivity in the co-evolution of nanotechnology and society.

As in accounts of ethnographical research, the narrative is often done in diary style. While this will read in places as sharing the vicissitudes of working on a PhD research project, it is a way to make situations and developments in the nano world come alive. The data that are collected through insertion are heterogeneous, and need to be contextualized.

This constitutes a separate chapter because it is more than telling the complexities of preparing for the CTA workshops. That is part of it, and I will draw on the detailed reporting that is done in the Appendices. There is also the development over time, and diagnosis of what is happening. This is connected to my point in Chapter 1.3.1, that insertion is a methodology. It is experimenting in real-world interactions.

Insertion is a necessary element of CTA as an empirical program. I have developed it as a methodology by trying it out (building on some general insights). It involves becoming a visitor to the world of nanotechnology developments, and moving about to both capture what is going on and target, tailor and embed CTA projects. Given that CTA projects require some fit to evolving circumstances in order to be accepted as legitimate/plausible exercises, but also some stretching of these circumstances so as to broaden enactment processes and stimulate reflexive learning, the visitor moving about is doing more than sightseeing. Fitting and stretching requires deep knowledge of dynamics and contexts. Along with the rapidly evolving developments in and around nanotechnology such knowledge can only be garnered by immersion. This is more than an anthropologist, also a visitor

by definition, would do; the CTA agent moving about in the nano-world is also formulating diagnoses about what is happening and could happen.

While this chapter details my experiences in the nanoworld in so far as these are relevant to understand the history of the embedded programmes of CTA activities and what this can tell us about dynamics in and around the nano-world, it also allows a first evaluation of the methodology of insertion and what it has achieved. Of course, this cannot be a simple case of tracing outcomes and attributing them to my activities. Outcomes are co-produced, and in fluid situations it is difficult to identify what might have made a difference. Overall changes have more to do with pressures on the nano-world (cf. Chapter 1.1.2) than with CTA activities. These CTA activities, however, do create openings for handling these pressures. It is the latter that can be evaluated.

The first section of this Chapter outlines the different spaces for nanotechnology development processes from a multi-layered perspective. This will allow me to locate my insertion activities, and explore the co-evolution of these spaces and the activities within them. Here I can also detail the insertion methodology using general insights. A key point is that insertion is not a way to achieve objectives of the CTA agent, but a combination of reconnoitring the lay of the land and on that basis, creation of circumstances that stimulate actors to reflect, act and interact in ways that might well achieve the CTA agent's objectives.

Section 6.2 offers a detailed narrative of my insertion in the nanoworld in terms of 'stretches' that occur in the process.[68] This section also helps position the individual CTA projects (reported in Chapter 7) in the evolving context of nanotechnology developments. And thirdly, it shows increasing reflexivity of actors in the nano-world and how new institutions emerge. The final section draws out what can be learned from the insertion narrative, including an informal evaluation of overall effects of my activities.

6.1 CTA-by-insertion

6.1.1 Capturing the entanglements between nanotechnology and society

Embedding CTA into the ongoing nanotechnology development processes requires knowledge of the co-evolution of nanotechnology development processes

[68] "Stretches" represent a period of time identified as a specific period in the chronology of events. Breaking down into stretches gives an indication of the intensity of various types of activities, of insertion, and of the evolution of nanotechnology developments and allows the structuring of the presentation of findings from insertion (see 6.1.3).

themselves. As articulated in Chapter 1, a first entrance point to analyse and understand co-evolution of nanotechnology and society, and how it is becoming more or less entangled, is the notion of alignment, in particular across contexts and levels. When a novelty is recognized and introduced in an existing order, this requires de-alignment (of existing linkages and competencies) and then (but in the same movement) re-alignment (cf. Abernathy and Clark 1985, and the extension of their approach by including societal embedment).

Insights into these alignment processes can be obtained by capturing the "entanglements" that are emerging and which will shape the way nanotechnology development processes will materialize. I distinguish three layers of nanotechnology activities which must align to make nanotechnology doable. As indicated in section 1.2.1, alignment spanning the layers is particularly important because it introduces vicarious stabilisation. Capturing such dynamics in and around the co-evolution of nanotechnology developments and society will allow me to detail the "landscape" in which my insertion is taking place.

Alignments, visible through entanglements and their stabilization, occur within the layers, and also across layers. This framing will be used to identify interesting activities that I encounter during my insertion activities, but also to locate my activities in the overall dynamics.

The **top layer is** of broader activities related to public policy, regulation and societal debate. This includes overall institutions, arrangements and authorities in our society.
The **middle layer** is located in collectives of actors, relevant institutions and networks that are directly involved in nanotechnology development through coordination and agenda setting.
The **bottom layer** represents ongoing practices and projects (often shaped by enactment cycles). For nanotechnology these may occur in publicly funded research laboratories, universities, and large or small firms.

At the start of this research project in 2004, there were no clear communities of nanotechnologists. For example during my first explorations in the nanoworld (see later in this chapter) most researchers didn't refer to themselves as nanoscientists or

nanotechnologists[69] but as researchers in more traditional domains such as material science, biotechnology, supramolecular chemistry etc.

In short, traditional methods, suitable for relatively well established technology fields, cannot be the whole story for early stage emerging science and technologies and particularly for nanotechnologies. The usual approach in science and technology studies is to do interviews with lots of actors, in the hope of capturing what is happening. This is what I have done as well, but I have added to it, and in two ways.

First, I take the doing of interviews as part of moving about in the nano-world, and collecting data that way. For example, the negotiations about getting an interview tell just as much (and sometimes more) about the dynamics and forces in the field than what an interviewee is willing to say about them. Thus, the 'insertion' approach is oriented towards data collection by moving around and occasionally probing.

Second, interviews and other insertion activities create visibility and (hopefully) legitimacy for the analyst. This helps to make interactions productive, and also, in my case, creates legitimacy (or at least recognition) for the programme of Constructive TA exercises. Clearly, insertion introduces changes in the situation. That is not a problem (except for methodology purists) as long as the insertion activities are documented and made part of the analysis and interpretation. This is another reason for the detailed reconstruction of my insertions in this chapter.

There is a third element. Social scientists moving about in the world of a scientific specialty or domain will set the members of that world thinking about what is happening, and about patterns that enable or constrain.[70] This is relevant for the overall CTA goal of increasing reflexivity of co-evolution of technology and society. My moving about in the nano-worlds may have such an effect, but it was not a dedicated aim, which structured what I was doing. I will come back to this in the concluding Ch 8.

[69] Many researchers were often cynical about the term NANOTECHNOLOGY positioning it as a buzz-word that allows more funding into interesting research – which is a valid point even if it is not the whole story.

[70] A well-known example are Harry Collins' studies, over the years, of the gravitational waves specialty (Collins 1998)

6.1.2 Insertion as a methodology

Insertion into the world of nanotechnology development requires the active circulation of the analyst in locations were actors are shaping the emerging paths of nanotechnology R&D. This can include research laboratories, conferences, workshops, agenda setting meetings, roadmapping events, public debates anticipating on issues related to technology developments.

My insertion is composed of four types of activities:

1. Moving about (within) in the world of nanotechnology development
2. Aggregation of my findings and presenting them
3. (Visibly) Moving in and moving out of the world of nanotechnology development
4. Embedding and negotiating CTA projects within the activities that shape nanotechnology developments

I will briefly elaborate on these four elements.

Moving about (within) the nanoworld combines the moving about in data sources linked to research desk research (for example through archives and online data bases, through reports other publications) with visiting and participating in physical spaces where nanotechnology development is taking place. There are different types of spaces and arenas that shape nanotechnology development in each layer. This requires visiting and moving around the arenas in these layers (which include workshops, public debates, roadmapping events, conferences etc.) quizzing and probing what is occurring, observing patterns and/or indicators of entanglements and expectation dynamics. It requires proactive involvement in data gathering, and requires effort and time.

Arenas for coordination and debate were occurring in the three layers, but with differences within specific layers. For example, public debate on societal aspects of applications stemming from nanotechnology R&D at the time my PhD activities started was, if it occurred at all, almost fully in the top layer, in the public governance layer. Nanotechnologists participate in this layer as experts, but the link back into the ongoing activities of nanotechnology R&D was not clear.

Aggregation and presentation. Part of the work of an analyst is to gather and aggregate information in the form of maps, diagrams, analyses etc. For many of the arenas that play an important role in nanotechnology development, there is a requirement that some form of presentation, poster or paper is necessary to allow you to enter/participate in this forum. This is particularly the case for workshops

and conferences. Therefore aggregation of the data gathered from moving about within the nanoworld is necessary to enter arenas.[71] This aggregation and presentation is an opportunity to get more feedback and data from those in the arena seeing/reading the aggregation of data that you present, and thus an additional source of data and a platform for further interaction in the nanoworld. Aggregation is therefore not just a matter of tactics, of getting entry, it is part of my analysis, and this is what the insertion approach adds, rather than just doing rounds of interviews.

Aggregation and presentation in the nanoworld is an entry ticket and a way of getting feedback, but there is the danger of being positioned as part of the nanoworld (going native) or positioned in a service role to the nanoworld (which will limit the freedom of movement). This means that there is another requirement to distinguish myself in the nanoworld as a visitor (or stranger) and this forms the third part of my insertion methodology that is moving in and moving out of the nanoworld.

Moving in allows interactions with actors, and the various elements described in the first element of the Insertion approach. **Moving out** is also important in order to maintain the role of researcher/analyst rather than being a full member of the nanoworld. This can be part of self-positioning in conversations with the subject (nanotechnologists) but can also be achieved through visibly moving out via aggregation and presentation outside of the nanoworld. For example, as will be described later in this chapter, after the first CTA workshop, I wrote up findings on methodology for preparing the workshop and processes that occurred within it in two international conferences in STS and in future-oriented technology analysis. Upon moving in once again into the nanoworld, these papers where publicly available (online) and I announced them in my presentations to Frontiers. This contributed to a clearer (although not fully articulated) distinction between myself and the nanoworld.

Embedding and negotiating CTA projects within the activities that shape nanotechnology developments. This element involves the linking up of my interests in experimenting with empirical CTA and requires negotiating the inclusion of CTA into ongoing nanotechnology activities. CTA is tailored in the context of the specific arena but also both informed and shaped by the broader developments in the three layers described above.

[71] Rip 2000 describes this moving about and aggregation in terms of actor-network theory.

6.1.3 Presentation of the insertion data

The data will be presented as a narrative, an account divided into "stretches". I call them stretches rather than periods to emphasize the similarity with my use of 'stretches' in Chapter 7, where they indicate stretches of interaction within the microcosm of the workshops. Here it characterises particular stretches of interaction in the macrocosm of the real-world as seen through my insertion activities. These insertion activities range widely, but over time, there is a focus on my endeavour to insert concrete CTA into the Frontiers Network of Excellence. Other activities, for example related to another Network of Excellence Nano2Life, will be recounted as well.

Presenting my data as a narrative allows me to provide a temporal ordering of my activities in the nanoworld, the ongoing developments of the CTA programme and the co-evolving multi-layered "backdrop" of governance of nanotechnology developments (Pentland 1999, Ansari and Garud 2009). In this way, I can explore the factors that shaped the embedment of my programme of CTA activities and the broader governance entanglements as these become clear through my insertion activities. Rather than report on everything that occurred during my five or so years of insertion during this PhD project, I will build the narrative on the most significant events that occurred (cf. Miles and Huberman 1994).

6.2 The narrative of insertion

During my insertion into the world of nanotechnology development, I moved about in the three layers of governance, gathered data and created a programme of CTA projects within the Frontiers Network of Excellence. The narrative of my insertion activities thus presents the descriptions, and the entanglements, of a number of activities. These include the developments in real-time that were visible during my moving about in the nano-world, the aggregation and presentation of my findings in real-time within the nano-world and outside the nanoworld and the emergence and (co) evolution of my programme of CTA projects in the nanoworld.

Each stretch commences with two tables showing the key arenas in the nanoworld I visited during the stretch and the aggregation and presentation activities inside and outside of the nanoworld. The text itself will read similar to a diary, necessarily so because of the nature of the data. In this way, the role that insertion played in the embedding of CTA in the nanoworld can be made more visible.

Stretch 1: The first excursion into the nanoworld

Period: August 2004 – December 2004

Insertion in the nanoworld

Activity type	Date	Details
Circulation & interactions only	23-25 August 2004	Frontiers Kick-off Meeting Enschede, NL
Poster Pres.	08-12 October 2004	iNano, Nanoscience PhD graduate school Aarhus, DK
Poster Pres.	2 December 2004	NanoImpuls Annual Meeting Delft, NL

Activity outside nanoworld

Activity type	Date	Details
Report	November 17th 2004	"Twente/Netherlands as a possible nanodistrict" Work package report to the PRIME Nanodistrict project. PISA.

The first steps

The start of this insertion activity began around the same time as the (so-called) Royal Society Report appeared in July 2004,[72] was released with a message to be cautious with introduction of nanoparticles in the environment because of the knowledge gaps about health and environmental impacts. During the previous

[72] In 2003 the UK government approached the Royal Society and the Royal Academy of Engineering to conduct a joint inquiry into the health and safety, environmental, ethical and societal implications, and other possible uncertainties of nanotechnologies. The report "Nanoscience and Nanotechnologies: Opportunities and Uncertainties" was published in 2004.

year, anticipation of potential issues related to Ethical, Legal, Societal and safety aspects were emerging on a number of fronts. Bioethicisits began to call for inclusion of ELSA issues in nanotechnology R&D (Mnyusiwalla et al. 2003). Meetings such as the International dialogue on Responsible Innovation (a first meeting in 2004) were being organised by the US and EU. ***T***he understanding of new properties from manipulating the nanoscale started becoming the object of specific actors in the toxicology community and NGOs (CBEN and ETC-group. In addition other actors, for example the re-insurer Swiss Re began reporting on anticipations of potential risks. Through 2004 there was an increasing number of reports on nanoparticle specific toxicity issues in the scientific peer-reviewed journals. A number of programmes and symposia were launched for toxicity of nanoparticles. The 1st symposium on Nano and occupational health was held by NIOSH (US) and HES (UK) followed by the launch of the International Council for Nanotechnology (ICON) coordinated from Rice University. Although, these discussions remained mostly outside of the nanotechnologists laboratories, broad programmes on Nano and societal aspects were emerging at the Woodrow Wilson Centre for Scholars and the Dutch nanotechnology research consortium NanoNed.

Against this backdrop, my insertion started shortly after I began my PhD project in the Nanoimpuls programme, and this could be divided into three activities. One was to further articulate my CTA objectives and target them by learning more about the nanoworld. This involved a considerable amount of desk research, but also going to presentations and attending meetings when they were available (in this period I attended three). The second activity was part of the PRIME Network of Excellence project NANODISTRICT, where I was investigating the Netherlands (and the Twente region in particular) on how nanotechnology districts were emerging.[73] The third activity was with my colleague PhD student in the NanoImpuls programme, Rutger van Merkerk, who had chosen bionanochips[74] as a core topic of his research project and who had invited me to collaborate with him on his first exploration into the field, and to undertake research jointly.

Moving in

The first activity involved moving about in the Frontiers kick off meeting in late August. The Frontiers network consisted of 12 partners from across Europe. The scope of the network was to support: Research, processes and facilities directed at instrumentation for manufacturing and analysis of single molecules, individual nano structures and 2-3 D architectures of them, targeted at life sciences.

[73] The results of this activity lead to findings presented in Chapter 2.
[74] This would later be further refined and labelled as “lab-on-a-chip”.

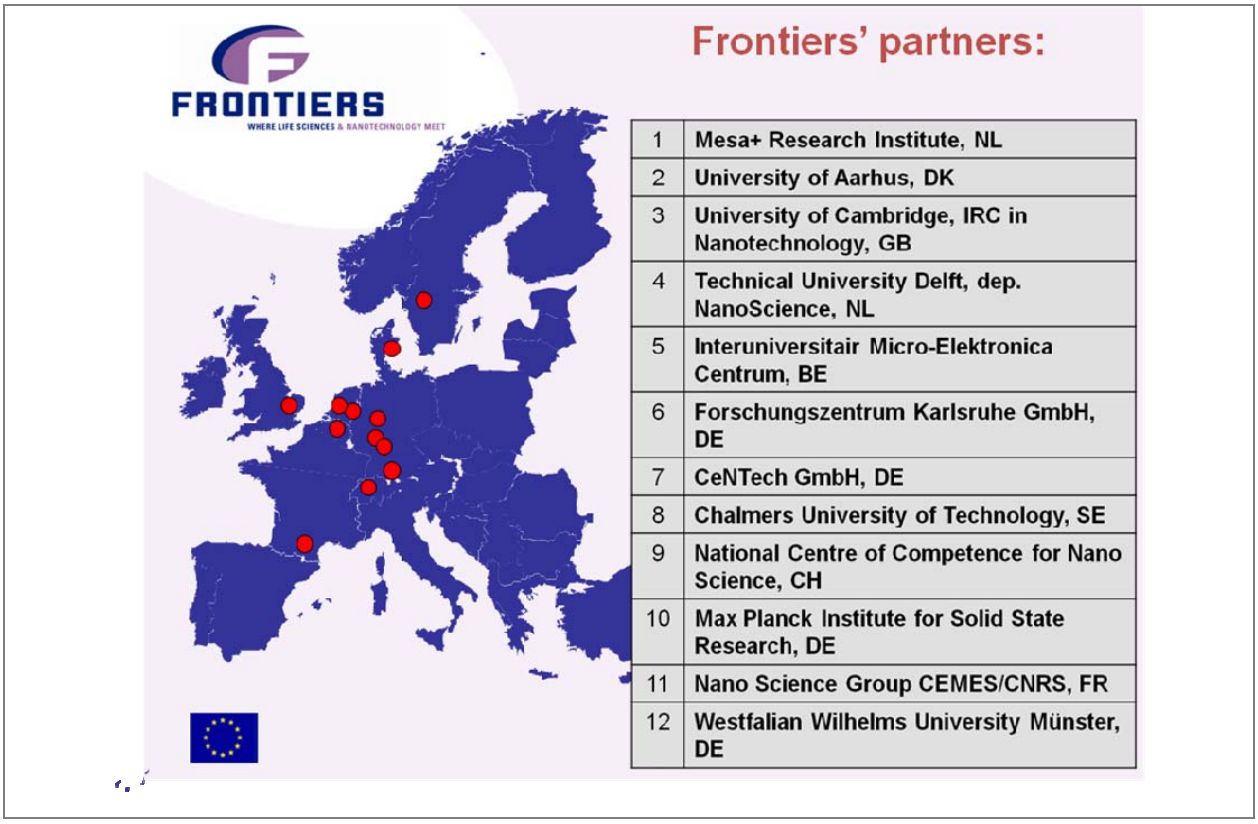


Figure 6.1: The partner institutes of the Frontiers Network of Excellence

It was here that I began my discussions with nanoscientists, around posters, during lunch etc. An advantage that the kick-off meeting being in the Netherlands was that many of the nanoscientists were from the Netherlands and knew about NanoImpuls (the project in which my PhD was part at that time). I was invited to participate in the internal partner meetings to discuss the following (and first) year's activities of the network. It was a curious setting for me since (as can be seen from the figure below) I found myself in a small meeting with all the contact persons for each partner institute and the workpackage leaders in the network. This was a small group, and my presence (and introduction of myself during the roundtable) meant that I became visible in Frontiers - I was a recognised member of the network, even though my role in it was not clear to most of the participants. It was after this meeting that I discussed with Robert Doubleday (a researcher in Science, Technology and Society employed in the NanoScience Laboratory at Cambridge University) about my CTA interests. During the meeting Robert had been appointed leader of the Ethics Workpackage, and we agreed that as my CTA project developed further we should interact more.

Figure 6.2: Kick off meeting of Frontiers; I was invited to observe the planning for the first year

After these first interactions, and in the same vein, I applied to the iNANO autumn school in Aarhus, DK, to both improve my knowledge of nanotechnology (nano schools were quite rare at that time) and also to meet a wider range of nanoscientists and discuss my own research. I wanted to find out how CTA could be connected with the real/actual activities of nanoscientists. This was very interesting, since, up until then, I was discussing mainly with small firms in the MESA+ Techno park and the senior staff of MESA+, and my interest in nanodistricts (and clusters) was recognised aspect of the nanoworld (at the meso-level of coordination). The Aarhus school was for PhD and Post Doctoral researchers in nanoscience. When I first put in my application to attend, there were concerns that a social scientist would not fit in. This position was a difficult one to shift. It was clear that in their view a social scientist had no role in such a meeting, and there was suspicion why I would want to attend at all. They agreed to allow me to attend based on the fact that I had a degree in physics from my earlier academic life.[75] I attended the meeting and on the first day presented my poster on the research questions of my PhD activity, concerning CTA and nanotechnology.

[75] This was not so strange at the time. Few programmes of research in the social sciences were looking at nanotechnology, and TA NanoNed (or as it was at that time, part of NanoImpuls) was ahead of the curve. Later on (see stretch 6 in spring 2007 for example) I would come across a few other social scientists attending meetings of nanoscientists.

The discussions with nanoscientists in the meeting were my first real exposure to the forcefields at play. The poster acted as a nucleus for discussions (I showed S-curves of the technology development cycle and discussed early stage assessment based on that representation). The participants (mostly nanoscientists that spent their working life in the laboratories) could not position my work at all, it was alien to them. The tendency was to try to position my work into a world that they knew. Comments such as "So you want to educate the public about nanotechnology?" or "You're looking at commercialisation of nanotechnologies?" were the main questions, but more interesting for me were the questions on responsibility. I announced in the poster the CTA aim of broadening the development process at an early stage, by bringing in more issues and more actors. This was uncomfortable for the nanoscientists, and in some cases, triggered responses verging on the aggressive – stressing the position that scientists should be left alone to get on with their research and not have to deal with societal issues.

The second activity involved research for the nanodistrict project. As part of this exercise, in September and October, I conducted some interviews at MESA+ and, after the interview with the then commercial director of MESA+ (Kees Eijkel) I was allowed to access the archive. I became a visible part of the MESA+ office: the archive was next to the coffee machine, and in this way I became acquainted with a number of the small firms, the technical and commercial director of MESA+ and some of the other senior researchers. I wrote up a first round analysis of the study of MESA+ and the Netherlands for a PRIME Nanodistrict meeting in PISA. In this activity I was seen as a student looking at research coordination (often the small firms asked if I worked in management studies). I was recognized as a visitor, mostly a curious exhibit near the coffee machine. From these insertions and document studies I could see that, in the Netherlands (as well as elsewhere in Europe) nanoscientists were attempting to coordinate research activities, create infrastructure and shape national funding programmes. Part of this is written up in Chapter 2, and also in Delemarle et al 2005 (see next stretch). The institutional entrepreneurs were shaping/structuring the nature of nanotechnology developments, and coordinating through building nanodistricts and networks. Since this process was ongoing, I thought that locating CTA into such development processes the programmes and coordination activities could be interesting - rather than doing CTA of individual technology projects.

The third activity involved a number of interviews based around our first round desk research on the topic of lab-on-a-chip. Rutger van Merkerk and I created a number of maps and tables of the field; one example is given in the figure below

(presented in Van Merkerk and Robinson 2005). When we showed this mindmap in our initial interviews, the interviewees found this representation very appealing, added to it, and given the breadth and scope of the map, asked whether we could give them suggested trends (predictions) of potential winning pathways. The mindmap that was presented and further developed through the interviews Rutger and I conducted was presented at the annual NanoImpuls[76] meeting.

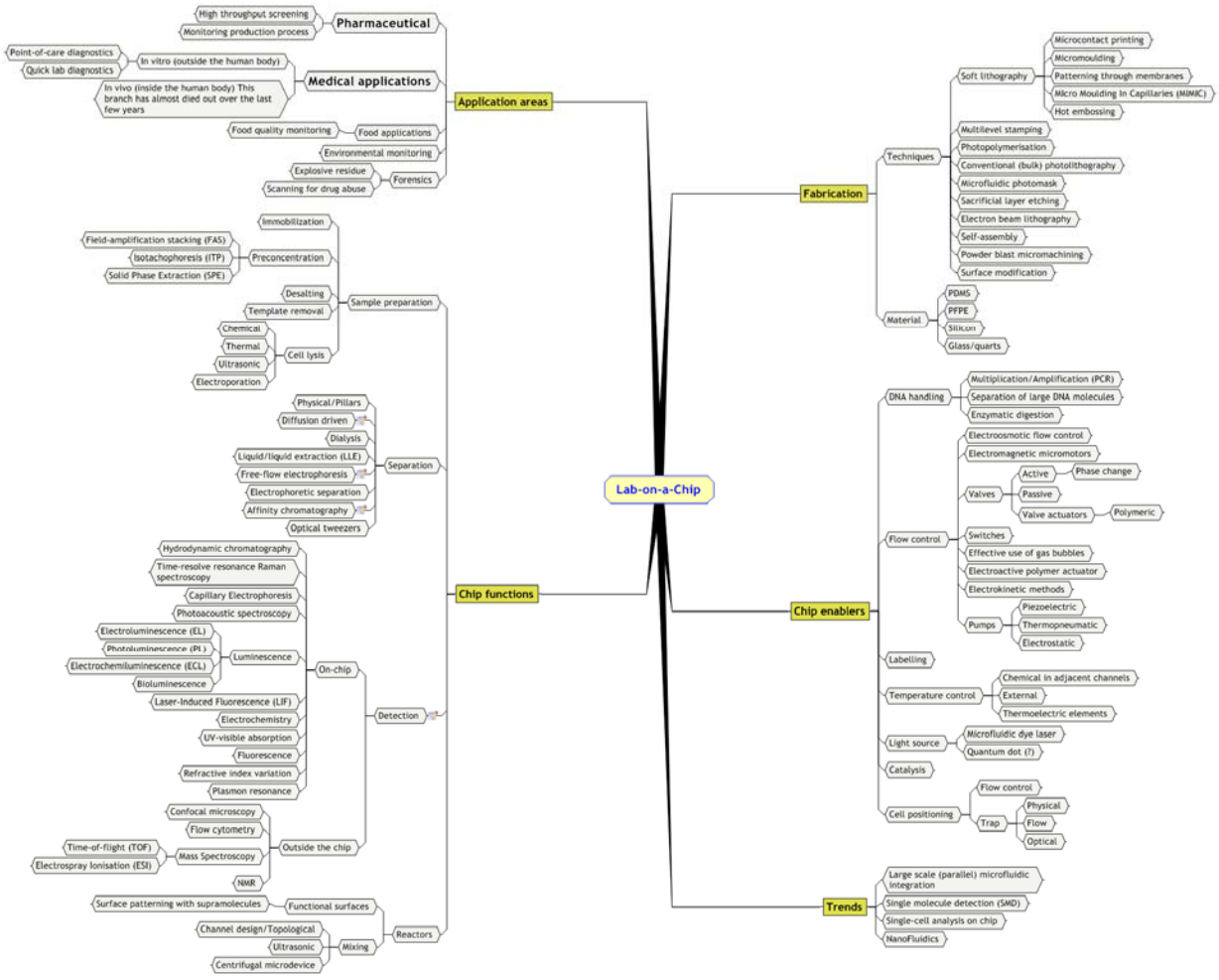


Figure 6.3: Lab-on-a-chip Mindmap presented as a poster in the NanoImpuls annual meeting. (Taken from van Merkerk and Robinson 2005)

Presenting ourselves as social scientists in a community of nanoscientists was received with some curiosity by the participants who came to our poster, and asked us what we were doing in such a forum and probed us on the elements of the mindmap. We too were able to probe, informally with drinks, the world of lab-on-

[76] NanoImpuls was the forerunner to the NanoNed consortium, in which Rutger's and my PhD projects were embedded.

a-chip and nanotechnology more broadly and were able to collect lots of important anecdotal details of the field as well as leads for our research.

Stretch 2: An attempt at integrating CTA into nanotechnology R&D activities

January 2005 – December 2005

Insertion in the nanoworld

Activity type	Date	Details
Circulation & interactions only	March 2nd – 3rd 2005	1st Nano2Life Annual Meeting, Münster, DE
Poster Pres.	April 18th – 20th 2005	1st International Nanofluidics Workshop Boekelo, NL
Oral Pres. and Poster	September 18th -21st 2005	1st Frontiers Annual Meeting Karlsruhe, DE
Poster Pres.	September 29th 2005	MESA+ Annual Meeting Enschede, NL
Poster Pres.	October 19th - 21st 2005	Nano2Life scientific meeting Enschede, NL
Poster Pres.	December 8th – 9th 2005	NanoNed-MicroNed Annual Symposium Groningen, NL

Activity outside nanoworld

Activity type	Date	Details
Publication (conference)	January 2005	New methods for studying the dynamics of emerging technologies: the case of Lab-on-a-chip technology, Rutger O. van Merkerk and Douglas K.R. Robinson, Paper presented at the DRUID Academy Winter 2005 PhD Conference, Aalborg, Denmark, 27-29 January 2005
Publication (conference)	May 2005	Building a nanodistrict: Technology platforms and institutional entrepreneurship, Delemarle A., Robinson

		D., Mangematin, V., Rip, A., Paper presented at the Triple Helix Conference, Turin, 18-21 May 2005
Publication (conference)	September 2005	Identifying and measuring loci of increasing irreversibility in the emergence of nanotechnology paths. Douglas K. R. Robinson. Working paper for the Berlin meeting "Measuring Path Dependency: the social-constructivist challenge", Berlin, 5th and 6th September 2005

An important event in this year was the release of the EU Action Plan on Nanosciences and Nanotechnologies (with its interesting use of the plural in the title). It can be seen as an indication that nanotechnology was approached more systematically at the macro-level.

A visible visitor

Following on from my diagnosis that nanoscientist-led coordination activities would be an interesting location for embedding CTA, I began my attempts to both further understand these coordination activities and to interact with those involved to see whether there were opportunities to create such a programme. In March 2005, one opportunity became available. The 1st annual meeting of another Network of Excellence (Nano2Life[77]) was to be held very close to the University of Twente, in Münster. I attended the meeting, and discussed with many of the researchers their activities discovering that there was a foresight work package as well as an ethics workpackage. I made some useful contacts, and had e-mail correspondence over the following months, although connecting up with the workpackage leaders was not as forthcoming as in the Frontiers meeting.

[77] Nano2Life was the first European Network of Excellence in nanobiotechnology supported by the 6th Framework Programme. Its aim was to merge existing European expertise in the field of nanobiotechnology combining 23 partners from across Europe, with an aim of (within 4 years of its initiation) set the basis of a virtual European Nanobiotech Institute (EIN). The EIN was planned to investigate possible applications in several areas such as in the field of integrated novel sensor technologies, health care, pharmaceuticals, environment, security and food safety. Therefore coordination of research was directed under visions of applications rather than the underlying science.

Meanwhile**,** my collaboration with Rutger continued at full pace in 2005. We wrote a conference article together (van Merkerk and Robinson 2005) in January and began our interviews and mapping. We asked if we could attend the 1st International Conference on Nanofluidics in Boekelo (NL), and were invited to attend for free, even allowed to present a poster of the latest results of our work (by that time Rutger and I had completed more than 25 interviews). This was a chance to test the robustness of our analysis of statements in texts and our interviews in a preliminary construction of a lab-on-a-chip timeline.

The conference experience was easy going, since many of our interviewees were present and we were greeted warmly by interested and curious members of the lab-on-a-chip (and in this meeting the nanofluidics) community. We were introduced by these actors to others (including visitors from the US) as graduate students looking at emerging innovation.

Our poster stimulated a lot of discussion; the maps were attractive to the participants (especially the figure shown below). Most discussions led eventually to what we were going to do with the data? Advise policy makers and funding agencies? Circulate to the general public? In some cases (particularly with junior researchers) there was the "why is this useful?" question. Actually, this was a standard question during my moving about. Sometimes confrontational, but mostly probing. Such a question required me to position myself in relation to the implicit or explicit assumption that I would be a service to the nanoscientists: "why is this useful for us [nanoscientists]?" One researcher was vociferous about social scientists interfering in the real work of nanotechnologists. The heated discussion that followed, in front of our poster in the meeting, led to a truce, which finally led to the researcher being present in one of my CTA workshops.

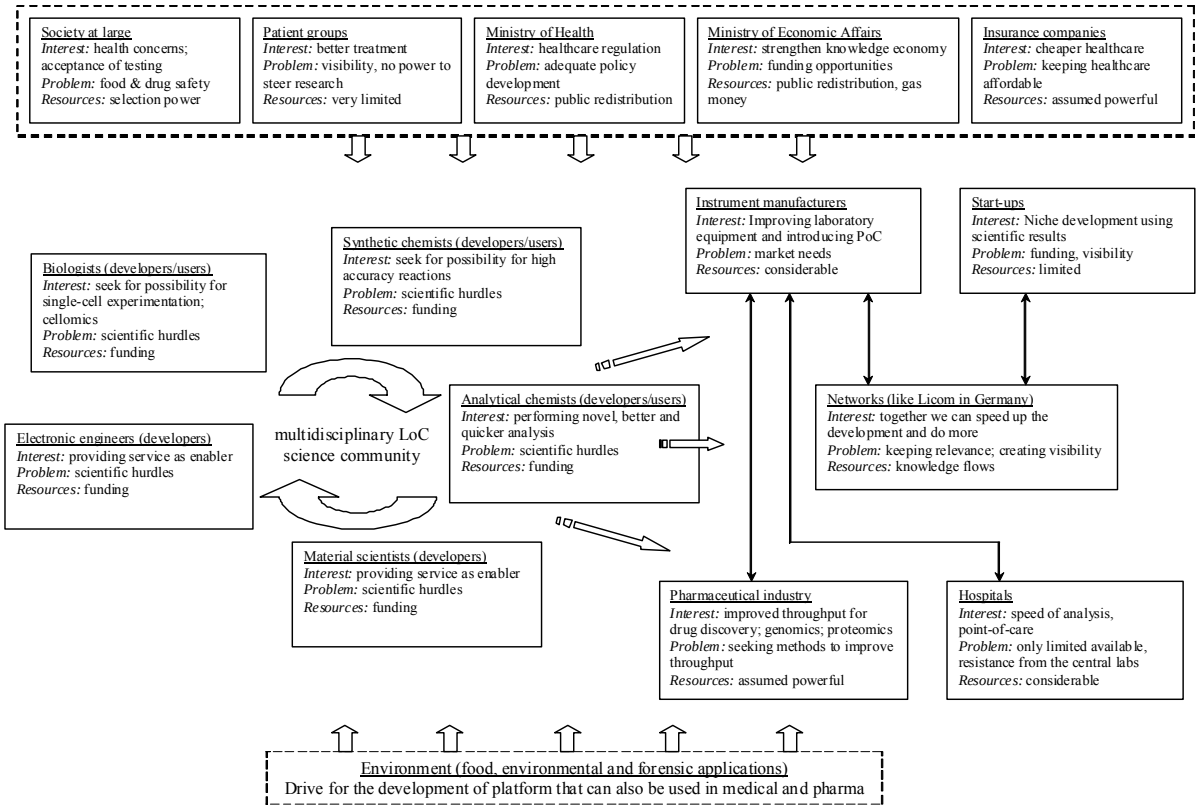


Figure 6.4: Mapping of actors and some relationships. Presented in the poster in the Nanofluidics conference, reproduced from van Merkerk and Robinson 2005.

Presenting the philosophy of CTA to the Frontiers Network of Excellence

Following the kick-off meeting of the Frontiers Network of Excellence I kept in touch with Robert Doubleday. I mentioned that the first concept of the CTA activities I wanted to explore were emerging and that I would like to test them in Frontiers or elsewhere. Robert was interested in the scope of the CTA projects, but unsure of how it would fit in the Frontiers network (no real future-oriented activity in Frontiers, unlike Nano2life which had a dedicated foresight package). By the time the 1st Annual Meeting of Frontiers arrived, I was asked to fill in for Robert since he could not be available for the meeting. My task was to report on the engagement exercises that had taken place in the UK Nanojury project (in which Robert had been involved) and to present my ideas for CTA as linking prospective innovation chains and exploring the societal embedment issues and processes. Robert suggested that it would be good to make visible my interest in running projects within Frontiers.

For the presentation I took a linear-model approach to innovation, using the upstream/downstream metaphor. I knew very few people in the network at that point and arrived as the only social scientist in the 100 person strong meeting. I had some discussions with some of the members during the evening, and they found it very difficult to position me. When I was called to make my presentation the following day, the Chair of the session introduced me as someone who will help the Frontiers Network to deal with ELSA issues. I had to reposition myself, explicitly in the discussion, as an STS researcher, with my own research interests and my own world. My presentation got the most discussion out of all the presentations during that day. The questions were a mixture of quizzing about my knowledge on ELSA issues, but also probing of my world as a social scientist, why was I there? What role do I play? Was I against nanotechnology or for it?

Figure 6.5: Presenting to the nanoscientists (photos taken during my talk)

Some nanoscientists in the audience vented their rage at the outside world pushing ethics on them and another nanoscientist suggested that sociologists like myself are better positioned to talk about ethics than nanoscientists so perhaps it is best left to the ethics expert. A senior research scientist in MESA+, knowledgeable about TA NanoNed's general aims and familiar with CTA, did focus on CTA pointing out the practical issues of operationalising CTA type projects, that it had been theoretical and that although it is promising, there has been little demonstration or application of it. He found it worthwhile to explore the value it could add.

In the wine tasting event after these sessions, there were lots of discussions with professors, with students etc continuing along the same lines. They were probing my world and the world of STS (since in the presentation I mentioned that understanding the underlying dynamics of technology emergence underpinned the CTA activity I had in mind). A distinct division in position was clear. Researchers working in the laboratories, including the Post Docs and PhD students, could not easily position me in their world, sometimes explicitly voicing that my work was without any value, and becoming obnoxious about it. Senior researchers could position me, but still not easily: "are you an ethicist?", "do you mean outreach as engagement?"

The ambiguity in my role in their world visible in most of the conversations had to do with three roles that I might be seen to be playing. (1) An *Ethicist* who will solve their ethical issues for them and help protect them from those ethicists (and ethical committees) who scrutinise their work, (2) a *Provider of Roadmaps* and checklists for success (3) a *Conductor of Public Engagement* in a narrow definition of engagement meaning the deficit model of educating the general public about nano promises. In this Frontiers meeting, and regardless of my positioning attempts, there was always recourse to one of these three roles (or a blurry mix), except for the senior Nanoscientist who was familiar with the TA NanoNed programme.

There was no real discussion of a CTA programme during the Karlsruhe meeting. My presentation was only one small part of the meeting, but I followed it up with emails, and face to face meetings to see if there was a way of running a CTA exercise.

A CTA foot in the enactor's doorway

After the Karlsruhe meeting I attended two large nanotechnology meetings within six weeks, both held at MESA+ (where also the Frontiers management team was located). I presented a number of posters in the MESA annual meeting and the Nano2Life scientific meeting. During the MESA+ meeting, it was clear that I was becoming more visible. There were more comments about the posters, more actors that I had met earlier introducing others to me and my work. Seeing the attention to the poster, and my comments, the coordinator of Frontiers (who was present) was visibly excited and enthusiastic and asked for us to meet up with the management team for a discussion.

We did so a few days later, I presented the ideas behind CTA and the sort of thing I wanted to do. By this time I was in my 2nd year as a PhD, and they asked me about my research activities. I had by then a few conference papers and circulated those

(van Merkerk and Robinson 2005 on Lab-on-a-chip, Delemarle et al. 2005 on Nanodistricts and Robinson 2005 on Path emergence in nanotechnologies). In later correspondence the coordinator mentioned he was pleased with my responses to his questions in my presentation in the first annual meeting and during the social events in the meetings and would like to support one workshop as a trial, and no discussion of any more funding until after the pilot. However he mentioned that he could not confirm financial support at that time, as it would have to be coordinated with the partners of the network in order to release finance for it. This was October 2005 and the issue of funding became a serious one, I couldn't do anything without some degree of external financing. Through my desk research, I found some of the research in converging technologies as being interesting for CTA, and began to explore Neuron-Computer interfacing.

Trying other doors

At the close of this year, I attended two more events. Nano2Life had what they called a "scientific meeting" between their annual meetings, which they held in Enschede, NL. I did the usual moving around and gathering information. Two things are important to note. The first is that Nano2life were attempting to coordinate cross-partner collaborations by envisioning broader application areas for the nanotechnology research that was being done at the partner institutes. The second was that I presented a poster on the TA NanoNed programme and CTA in particular. It caught the eye of those active in the Foresight workpackage and we sat down to discuss my and their activities. They liked the approach, but did not want to try experimental tools, only tried and tested ones (those coordinating the Foresight workpackage worked as foresight professionals in CEA). The doorway to embedding CTA in Nano2Life was closed, but the possibility of Frontiers still seemed promising.

I took the same poster to the annual NanoNed meeting in Groningen and received a lot of comments. It was in the NanoNed meeting that I met and discussed, following a presentation, some lead researchers on molecular machines (what I would later relabel as supramolecular machines). The discussion revealed that there was a lot of activity in this field in chemistry, and in molecular biology using a different approach. We discussed images of nanotechnology, as in their presentation they ridiculed nanobots (attributed to Drexler) as nonsense, but to me their labelling of these rotoxanes as molecular machines conjured up the imagery of machines and robots. When my colleague PhD student Martin Ruivenkamp

started the following January I suggested that we run a joint project on exploring molecular machines.[78]

Stretch 3: Coordination and roadmapping

January 2006 – June 2006

Insertion in the nanoworld

Activity type	Date	Details
Circulation & interactions only	March 27th – 29th 2006	2nd Nano2Life Annual Meeting Sitges, ES
Poster Pres.	May 15th -18th 2006	2nd International Nanotechnology Conference on Communication and Cooperation, Arlington, US
CTA Workshop (Appendix 1)	June 12th 2006	Technology Assessment Workshop, Cell-on-a-Chip Amsterdam, NL

A visible visitor in Nano2life

By this time I had been to two Nano2Life meetings, presented posters and met some of the participants in other meetings (such as NanoNed, or MESA+ meetings). Although the door to incorporating my CTA into the Nano2Life activities was closed, I was still a member of the network (being affiliated with MESA+) and also designated to represent my supervisor (Prof. Arie Rip) who was part of the Nano2Life Ethics board, in the 2nd Annual Meeting in Sitges.

I played a passive role in the meeting, watching the conference presentations, quizzing nanoscientists. What was striking was that the whole meeting was now arranged around a matrix, which Dr. Martin Bennink (of MESA+) had created to organise the previous scientific meeting. There was considerable lock-in in the way the matrix began shaping the collaboration and orientation of activities in Nano2Life (see matrix below). I, and a colleague PhD student Haico te Kulve (also in TA NanoNed), interviewed Martin Bennink earlier in the year about the organization of this matrix. At the time Martin mentioned that it was a visualization to help organize discussions at the scientific meeting. The framework

[78] This finally led to both Chapter 3 and Appendix 3.

persisted until mid 2008 (the end of Nano2Life and became a means of evaluating gaps in the portfolio of activities).

SRPA	SRPT					
	bioanalytics instrumentation Peter-Katalinic	in vitro cell and tissue analysis Marin Bennink	in vivo imaging Pierre Le Ber	surface functionalisation Pascal Colpo	nano-assemblies Ehud Gazit	protein, DNA & cell chip Paul Galvin
Drug delivery incl theranostics Rafi Korenstein						
Cancer related diagnostics Jürgen Schnekenburger						
NBIC applied to neurodegenerative medicine Mira Markus-Kalish						
Environment monitoring & security Shimshon Belkin						
Cell biology Kristina Riehemann						
In vitro toxicology Maurice Wheelan						

Figure 6.6: The mNano2Life matrix coordinating Strategic Research Projects in Technologies (SRPT) and in Applications (SRPA)

Coordination in Nanoelectronics

For exploring coordination processes in nanotechnology, I began looking at fields outside of nanobiotechnology. It turned out that in nanoelectronics coordination is consciously aimed for. There was already a long history of coordination through the ITRS roadmap, but as the manufacturing processing and infrastructure costs increase, coordination and cooperation shifted. Since nanoelectronics in of itself was still under development additional fora where visible. An important example was ENIAC, the European Technology Platform for Nano-electronics, with strong involvement of key industrial actors like Siemens and Philips.

The nano-electronics challenges are taken up globally, with key actors attempting to find places/spaces to interact and coordinate, or at least be able to adjust own strategies knowing about the strategies of other important actors. One such concrete "space" is the International Nanotechnology Conference on

Communication and Cooperation (INC). Its origin was the tentative interactions between the US semiconductor firms (especially Intel) and the USA National Nanotechnology Initiative led by Mihail Roco, to discuss envisaged paths for nanoelectronics.

I visited this event and, compared to what I saw in nanobiotechnology, was surprised at the degree of coordination that was taking place. One example is given below, the Nanoelectronics Roadmap commonly referred to in ENIAC and other Nanoelectronics fora. There is increasing agreement at the level of large industry (Philips, Siemens, Intel etc.) that coordination beyond the semiconductor manufacturing is necessary.

> "For the More than Moore business, there is a clear need to standardise and commoditise some of the required technologies and designs in order to enable product manufacturing to be quickly ramped up to an economic scale. This can only be achieved by establishing structured cooperation within the electronics sector." (ENIAC Strategic Research Agenda 2006)

The notion of heterogeneous integration, where systems-in-a-package (SiP) will be necessary to add value to Moore's Law, is another driver.

Note that the major part of the roadmap addresses micro, rather than nano. In a sense, that is as it should be, because the eventual effects of nano depend on how it can be taken up at the micro (and meso) level.

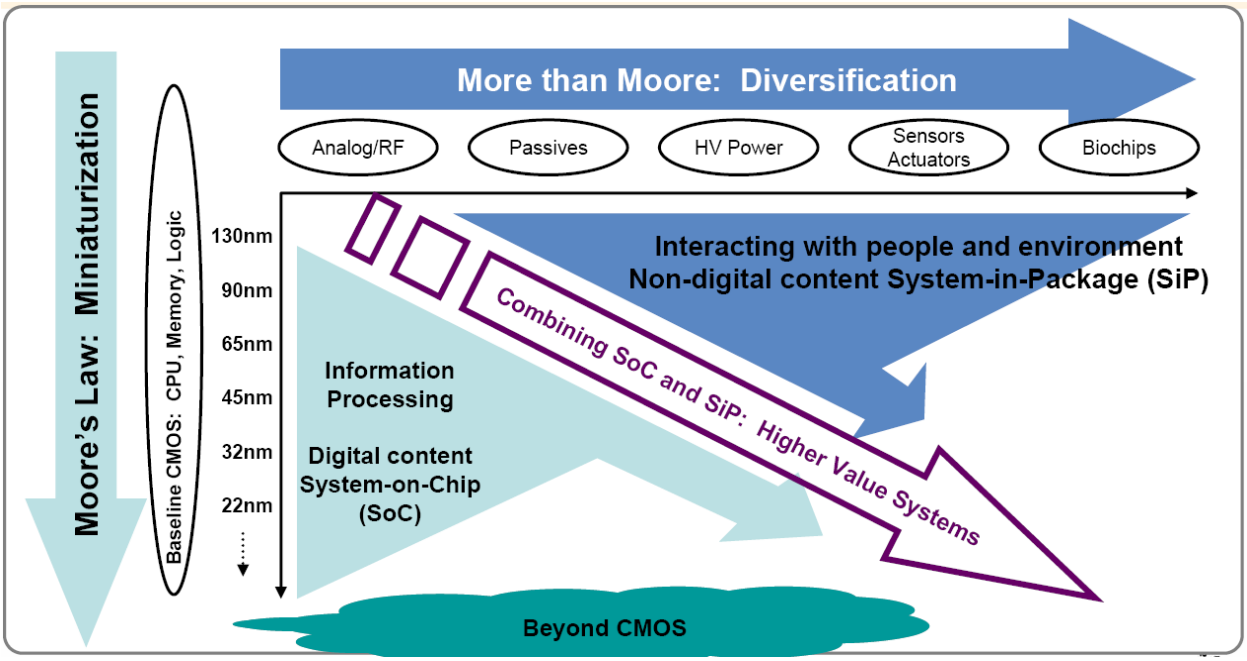


Figure 6.7: The Nanoelectronics Roadmap (www.eniac.eu)

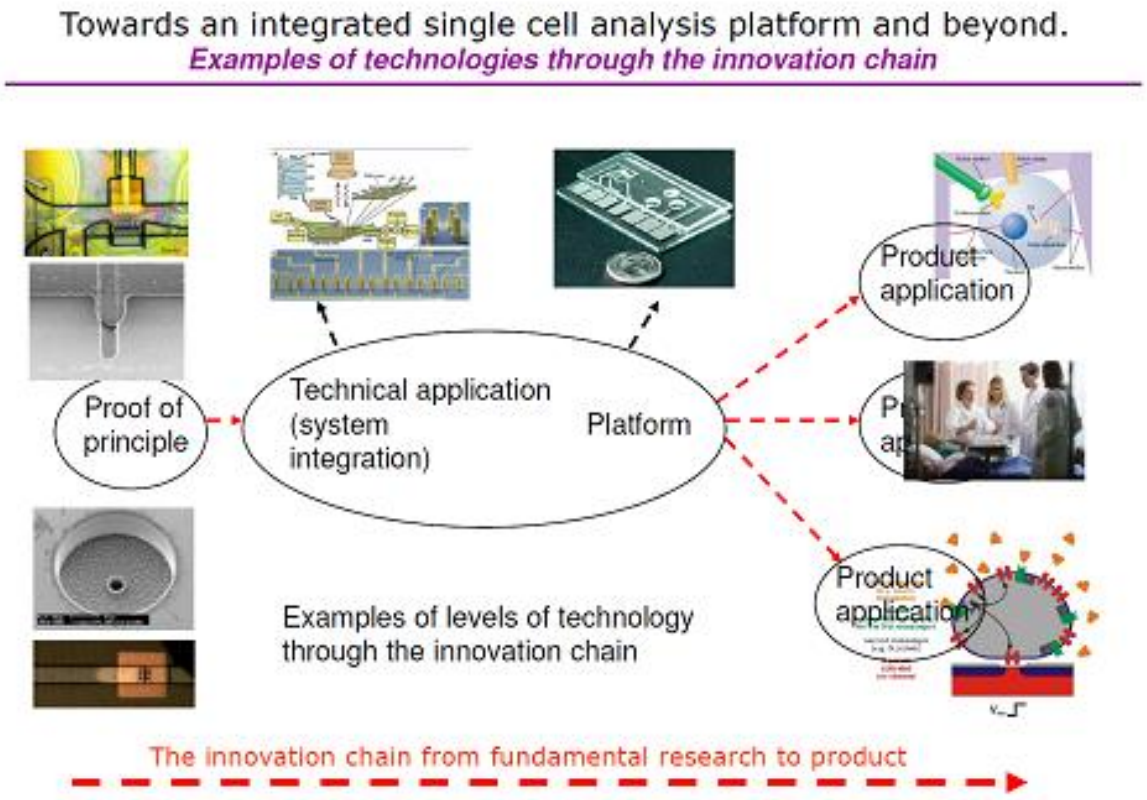
The CTA project on anticipatory coordination of multiple paths

Regarding the CTA projects, at the beginning of 2006, there was some verbal support from the head of the Frontiers Ethics workpackage and the coordinator of the project, offering support in theory for one pilot CTA project, I began to explore potential candidates for a first CTA project. My initial candidate was brain-computer interfacing. During January and February I began research into this field and began interviewing some key researchers in the community, all of which were interested in the notion of CTA but, as reported in Appendix 1, this would not work out as a first CTA project, the case itself was rich, but the main researchers in the field would not participate in such a project (although they were happy to provide information) because of earlier experiences in workshops and meetings "we have had our fingers burnt with ethical debates" was one comment from a telephone interview with a key researcher in Munich.

I had spent considerable time and energy by this stage in research which did not lead to a project and the pressure was on to provide a CTA case that would be rich enough to fulfill my interests as a PhD researcher, would be in line with the Frontiers focus on nanotechnology for investigating the life sciences and would provide enough promising experience to allow for more CTA projects to be funded.

I chose lab-on-a-chip for cell analysis based on the year-long study Rutger van Merkerk and I had done, and also on my own research into nanotechnology for biology (part of my desk research to map the various facets of nanotechnology research). At the end of February 2006 I began to create a workshop concept with my Twente colleague Tilo Propp (also of the TA-NanoNed programme) - the full description of the topic and the negotiations are given in Appendix 1.

In our interviews and desk research, two topics became interesting: (1) the innovation gap and strategies to overcome it and (2) cell-on-a-chip visions and potential ELSA issues. We constructed a diagram of the issue and started structuring our development of the CTA around this topic.



Many of the participants of Frontiers were involved in microfluidics and recognized the innovation gap when we showed them the visualization, and especially in the meeting with the central management team of Frontiers in MESA+ on March 7th 2006. The ability to map possible emerging paths from a lab-on-a-chip platform to potential applications was seen to be attractive by the leader of the science-to-industry workpackage and he proposed that this could be linked to the Frontiers roadmapping activity.

Still there was the issue of resources, which was not settled until the beginning of April. Following the go-ahead, at the beginning of April I embarked on a targeted invitation campaign; due to limited funding and timing, I focused on researchers and firms mainly in the Netherlands, and Frontiers members involved in Lab-on-a-chip or single cell analysis. I had the opportunity to interview all of the participants prior to the meeting by telephone or by face-to-face meeting (due to the CTA pilot project being held in the Netherlands).

The CTA workshop was held in Amsterdam on June 16. I discussed with some of the participants immediately after the event, over drinks, and then the following week through email and some face-to-face interactions. One of the participants, a nanobiotechnologist (from Nano2Life), found the scenarios useful recognising some of dynamics embedded in the scenarios as *'useful fictions'*, which help

prospecting the future.[79] The multi-path mapping and the innovation chain diagrams were taken up by a small firm that participated, applying this tool to their own situation of developing an electrolyte analyser.

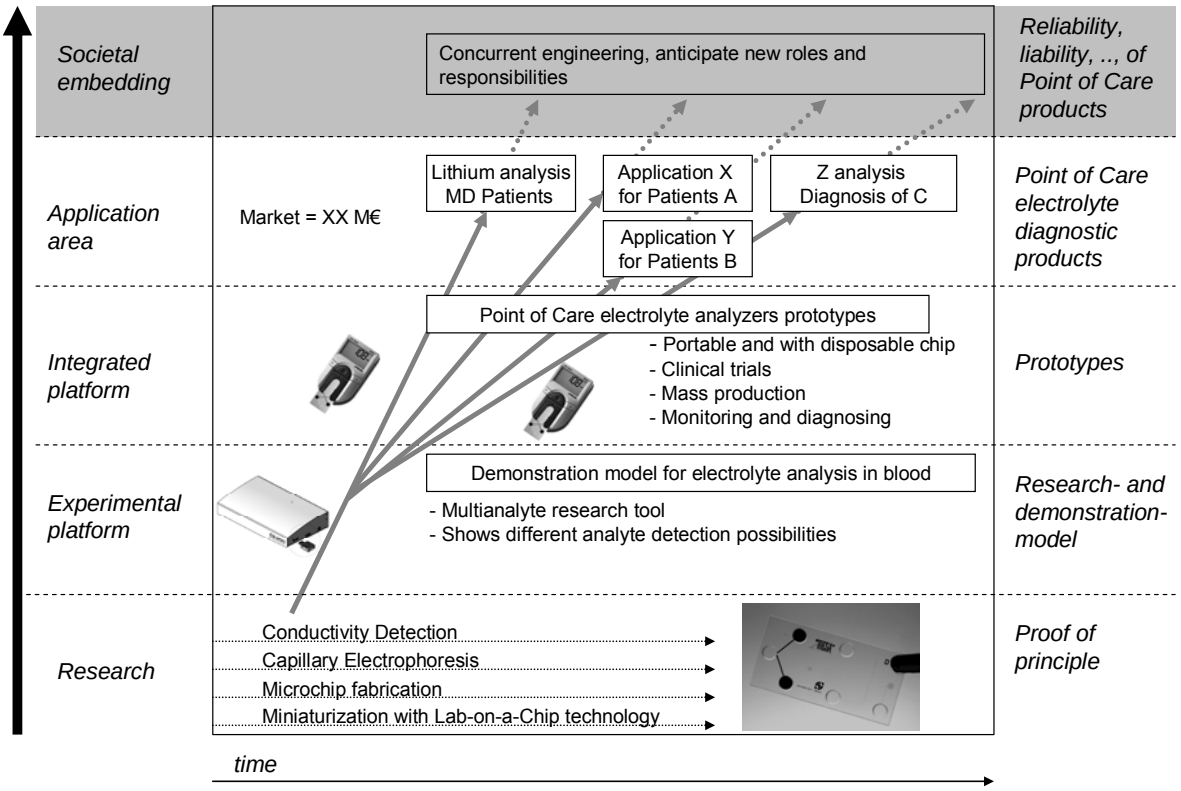


Figure 6.8: Multi-path map created afterwards by small firm Medimate, one of the workshop participants, to structure their strategic thinking,

[79] This was further backed up when I went through in detail his hand written feedback that was summarised during the workshop (see Stretch 2 in Section 3 of Appendix 1)

Stretch 4: Moving out

June 2006 – September 2006

Activity outside nanoworld

Activity type	Date	Details
Publication (peer reviewed)	July 2006	The interaction between expectations, networks and emerging paths: a framework and an application to Lab on a chip technology for medical and pharmaceutical applications. Rutger O. van Merkerk & Douglas K. R. Robinson. Technology Analysis and Strategic Management, Volume 18, Numbers 3-4, -4/July-September 2006, pp. 411-428(18).
Publication (conference)	July 2006	Cluster Institutionalising Entrepreneurs in the Emerging Field of Nanotechnologies. Vincent Mangematin, A. Rip, A. Delemarle and Douglas K.R. Robinson. 22nd EGOS Colloquium, "The Organizing Society", Bergen, July 6 - 8, 2006
Presentation (conference)	August 2006	Balancing asymmetry in the division of technology assessment labour: Broadening upstream strategy articulation in European nanotechnology research networks through CTA. Douglas K. R. Robinson. European Association for the Study of Science and Technology (EASST) Conference. Reviewing Humanness: Bodies, Technologies and Spaces. University of Lausanne, Switzerland 23rd-26th August 2006
Publication (conference)	September 2006	Multi-path roadmapping as a tool for reflexive alignment in emerging S&T. Douglas K. R. Robinson & Tilo Propp. Second International Seville Seminar on Future-Oriented Technology Analysis (FTA), 28th-29th September 2006, Joint Research Centre, IPTS, Seville

This summer period saw few nanotechnology meetings, and provided a convenient time to write up some findings, present them to my own community of STS and further underscore my position as visitor to the nanoworld.

Aggregating and presenting findings from (and outside of) the nanoworld

During this period I wrote up some of the findings from the first CTA workshop and presented it to others in the STS community studying nanotechnology at the EASST 2006 meeting in Lausanne. Comments from the audience related to the richness of the data (because of the specificity of the case and the types of actors present in the workshop). It was striking how few there were studying the specificities of the bottom layer and middle layer of the three-layer framework (see section 6.1); the focus was on the top layer, of broader debates and evolutions (in policy, in the media).

A quick write up of a paper for the IPTS conference was done by myself and Tilo Propp by the first week of July, and presented in September as PhD research. This paper on the methodology of multipath mapping and some of the findings of the workshop was selected as one of the best in the conference and was to be published in a special issue of TF&SC. This was reported back to the Frontiers management board, for the purpose of underscoring that I was a visitor, but also to show some impact of the CTA project.

During this period, my co-authored paper with Rutger van Merkerk (the first publication of the TA NanoNed programme) was published, and we circulated it to those who we'd interviewed. Some of these were in Frontiers, and circulated it a little bit more widely for example; the Frontiers management board got it).

These three activities, along with the conference publication in EGOS, provided a platform for discussion when I returned to the nanoworld. I could refer to these papers, and show them, as evidence of that I was doing serious analysis. It reaffirmed my role as a visitor and further clarified my interests as a PhD student. Just as important was that the form of activity was recognisable to the nanoscientists: conference presentations and peer-reviewed articles are the currency of social and natural sciences. Thus, the fact that some of the Frontiers activities would be in a peer-reviewed article was reported in the annual assessment meeting, explicitly mentioning my role as TA researcher.

Stretch 5: A programme of CTA is initiated

October 2006

Insertion in the nanoworld

Activity type	Date	Details
Presentation	October 23rd – 24th 2006	Frontiers Assessment Meeting Sicily, IT
Presentation and Poster	October 24th – 26th 2006	2nd Frontiers Annual Meeting Sicily, IT
Participation in roundtable	October 24th 2006	Frontiers Ethics board meeting Sicily, IT

In the 2nd Annual Meeting of Frontiers, held in Sicily during October 2006, I was asked to participate in both the internal management board meeting (including the annual assessment by the European Commission) and the annual meeting itself. In the internal meeting and the annual meeting, a number of issues were particularly visible. Issues of (1) managing R&D around particular therapeutic applications, (2) the stress on research centres to innovate as well as provide excellence in research and training and (3) the variety of mechanisms, means and pathways of commercialising nano-enabled therapies (the link with large firms, and spin out companies were discussed).

In the internal meeting, these issues were discussed as a matter of "indicators of quality" of the activities coordinated in the network of excellence. In the annual meeting it emerged in the presentations of the technology, discussions in the coffee breaks, during the long lunches and evening meals. Through my discussions, especially with researchers from Karlsruhe, Stuttgart, Aarhus and MESA+, a number of pressures that were not related to "usual" research practices became visible. These included discussions about links with patients with one research group leader mentioning that family relations to patients of a particular disorder would come to presentations and ask, in some cases well-informed, questions about the promising therapy. A researcher from Karlsruhe noted that this is not only uncomfortable, in the sense that they are not used to these interactions with the "general public", but it "also forces a more realistic picture." My own response to this in the meeting was to chat about scientific promising versus therapy promising. This spurred a discussion in one of the conference meals about hype, which forms part of the dynamics in the scenarios shown later.

A disconnection from the macro-level responsible innovation debates

With cocktails later that evening, along with Martin Ruivenkamp, another PhD student from the TA-NanoNed programme, I discussed issues of toxicity with the heads of most of the Frontiers Partner institutes. The research group leaders had limited knowledge about many of the debates and meetings on these topics. Martin and I decided to probe into this further by discussing the International Risk Governance Council report released a couple of months earlier (Renn & Roco 2006)

We also brought the discussion around to the ETC-group and their Nano Label competition that was running at the time of the meeting. The research group leaders were oblivious to these initiatives. I probed a little bit further and proposed the general idea of a workshop on "risk governance" a term that was being used by IRGC and others during that time. The Frontiers partners thought risk discussions generally may be interesting because of the Drexler scares "people are scared of grey goo". When Martin asked "What about toxicity and regulation?" one of the researchers, chuckling, held up his glass of Orangeade and said "I'm drinking nanoparticles now...the colorants in this glass are nanoscale. Nano is not new." There was some low-level chuckling from the group of research scientists.

Clearly, we had been moving about in other worlds than the nano-scientists, so we saw different things.

The following day, my presentation proposing risk governance based CTA project was greeted with enthusiasm by the technology transfer experts and start-up companies in the room, but the researchers seemed indifferent. Building on the enthusiasm of "commercial" participants I began to construct a CTA workshop concept based on the preliminary diagnosis given above. I proposed that four more CTA projects should be undertaken over the following 2 years.

After my presentation, a representative of CEMES (a CNRS research institute in Toulouse, France) made a presentation on molecular machines as the lead institute of the Strategic Research Area "Molecular Machines" in Frontiers. My colleague PhD student in the TA NanoNed programme, Martin Ruivenkamp, with a particular interest in images of the nanoscale, and I had conducted a small study on molecular machines through a vision assessment exercise (see chapter 3), and Martin had joined me in attending the Frontiers annual meeting to chat with nanoscientists and to see the presentation on molecular machines. The presentation

on molecular machines was very revealing; in that even in such a meeting as a scientific research network, the presentation was full of macroscopic analogies (wheelbarrows, rack and pinions, trucks) of the nanoscale.

After the presentation Martin and I asked some questions (as part of the audience) about images of molecular machines and how they are picked up in the media. This triggered a long response from the speaker about misrepresentation of nanoscale research by media (referring to nanobots in blood vessels.). When the round of questions from the audience had concluded, Martin and I chatted with the speaker to discuss whether a CTA project on images and visions of molecular machines would be interesting for this Frontiers Strategic Research Area. Because of the research Martin and I had already done for our article including some interviews with world leaders in molecular machine research (Alberto Credi and Vincenzo Balzani) and some interactions in the Netherlands with Ben Feringa during a NanoNed annual meeting, we could reference a lot of research activities. This seemed to soothe his, at first, suspicious posture to us and encouraged him to think with us a bit and brainstorm a possible workshop. The presenter [EM] asked us to send an email to the head of his group [GP] and we would move on from there.

Later in the day, a lead researcher at the University of Aarhus presented his group's work on drug delivery under the framework of a Strategic Research Area of Frontiers on drug delivery which they were leading. In this conference keynote presentation, he described the potential of nanodelivery systems for RNAi therapy (a mechanism of using a molecule similar to DNA for interfering with intracellular communication systems, disrupting the manifestation of disease when a cell is infected). I could see that drug delivery would be interesting for a CTA-project, because those in the Frontiers NoE involved in nanoparticle drug delivery would have to be linked with envisaged therapies in order to create potentially useful delivery systems. As was clear in early discussions there was an innovation issue and an expectation management issue. I decided to explore the potential of CTA workshop on this topic. After some discussions with the drug delivery research group leader and some of the senior researchers in the Aarhus group present at the meeting, a CTA concept began to take shape in my mind, that interfacing research with therapy development seemed an interesting and relevant topic. To avoid a general discussion of drug delivery, such a workshop would get closer to issues through focusing on a particular therapy area (or family of therapies) utilising the RNAi.

Stretch 6: Negotiating three additional projects

December 2006 – June 2007

Insertion in the nanoworld

Activity type	Date	Details
Circulation & interactions only	March 19th – 21st 2007	3rd Nano2Life Annual Meeting Saarbrücken, DE
Discussions	April10th - 12th 2007	Visit to iNano to create siRNA CTA outline Aarhus, DK
Poster pres.	April 16th - 19th 2007	3rd International Nanotechnology Conference on Communication and Cooperation (INC3) Brussels, BE
Negotiation about CTA Molmach	May 9th – 11th 2007	Frontiers Research Meeting Toulouse, FR
CTA Workshop (Appendix 2)	May 31st 2007	Technology Assessment Workshop, siRNA Aarhus, DK
CTA Workshop (Appendix 3)	June 11th 2007	Technology Assessment Workshop, Molmach Toulouse, FR
Participation in roundtable	June 12th 2007	Frontiers Management Board Meeting Münster, DE

Activity type	Date	Details
Publication (peer reviewed)	April 2007	Tracking the evolution of new and emerging S&T via statement-linkages: Vision Assessment of Molecular Machines. Douglas K. R. Robinson, Martin Ruivenkamp and Arie Rip. The Journal Scientometrics, Vol. 70, No. 3. 2007.

In March 2007 I participated in the third annual meeting of Nano2Life. For the first time, I met another STS researcher participating such a forum. His research, located in a nanoscience research laboratory in Newcastle, rarely took him to

coordination level forums. He was interested in attending and gathering data for his own PhD studies, quizzing the nanoscientists on technical details (which they could provide) or on questions of democracy (which non-plussed them).

Negotiating a CTA on drug delivery

On 1st April 2007, iNANO confirmed that they would host the workshop, and I flew to Aarhus for a visit from 10th – 12th April to co-create the outline of the CTA project. During this meeting I met with my main point of contact whose background is in pharmaceutical research, a research group leader with a background in molecular biology, and a number of PhD students at iNANO working on drug delivery. As described in section 1 of Appendix 2, the first meeting with the nanoscientist revealed some of the position and forcefields present. During the day and a half of discussion, the early difficulties of communication (in the sense of concepts on CTA and likewise on technical details of siRNA delivery) were decreased through probing each other's worlds. There was excitement, but also a short preparation time of 5 weeks or so.

The return of a CTA on brain-computer interfacing

During the Third International Nanotechnology Conference on Communications and Cooperation, held in Brussels, 16-19 April 2007, I presented two posters, one on the TA NanoNed programme, and one on the CTA initiatives underway in Frontiers. By this time I had completed one workshop, and had just returned from discussing in Aarhus the concept of the second workshop on drug delivery. I met a senior researcher at IMEC, , who was working on bioelectronics and was interested in the poster, where I argued that ELSA and innovation can be bridged with awareness of co-evolutionary dynamics and could be done with controlled speculation and interactive workshops. The researcher and I began to discuss some of our mutual interests in brain-machine interfacing. I described my experiences with my first attempt at developing a CTA on brain-machine interfacing, and he was not surprised:

"...some of those high up in the field had been involved in discussions about computer-brain interfacing and there was a lot of discussion on ethics back then."

He went on to say that the research had a lot of "scary press" and so it was unsurprising that they were cautious to get into such issues. He mentioned, however, that he was impressed with the concept outlined in the poster, and invited me to visit him in IMEC; after the summer, since I mentioned that I was busy working on three other CTAs at that time.

Intense preparations

After the INC3 meeting I entered into an extremely intense period of work. I had six weeks to prepare and execute three CTA workshops, one on risk governance (planned for 9th May), one on drug delivery (planned for 31st May) and one on molecular machines (planned for 11th June).

I did my research and socio-technical mapping (see further the appendices) and began preparing scenarios. In parallel, I started circulating flyers and invitations for participants to attend the meeting.

The risk governance workshop had, by the end of April, only two participants, I chose to cancel the workshop (if I had a poor turnout, that wouldn't bode well for the future projects and also perhaps I could use the promised resources for a risk workshop at a later date). I attended the scientific meeting of Frontiers, which was held in Toulouse, and so I could discuss with some of the co-organisers of the

molecular machine workshop. The scientific meeting itself was poorly attended; workshop fatigue (too many meetings away from core activities) was the diagnosis of various participants with whom I talked. It was difficult to get a measure whether the reason for lack of participation in my risk governance workshop was workshop fatigue or lack of relevance for the Frontiers network partners. In interviews I did receive comments such as: "The workshop topic was interesting but I was too busy."

In the research meeting, I met up with the molecular machinists with whom I was co-organising the workshop. We agreed on the general theme, although on specifics we disagreed. More importantly for me, the time for my CTA was reduced to being approximately three hours instead of six. This was because they had the obligation of coordinating a scientific meeting on molecular machines and had pushed for the CTA workshop to be combined with it. I resisted but was overruled (I had less manoeuvrability since I was amidst four people from the same department which created a difficult negotiating position).

Two workshops conducted

In a period of two weeks I held the siRNA workshop and the MolMach workshop (full details in the appendices). The two workshops differed in how they were co-developed. In the siRNA case, during the visit to Aarhus, there was much miscommunication at the beginning but probing and negotiating allowed some broadening of my understanding of the world of siRNA research and development and their ideas of what CTA is and the broader issues that may be involved in their R&D activities. A trust as to methods (trust in my experience) and topics (I took some of their advice about a focus on diseases for siRNA). For molecular machines the visit to Toulouse showed a difficult negotiation about scope and structure of the workshop (albeit friendly, the partners from Toulouse were very hospitable).

Post workshop, the participants from Aarhus were quite happy with the outcome, although the majority found it a curious workshop. As one participant phrased it:"there were lots of items and I experienced and learned a lot, but specifically I can't put my finger on the take-home-message.

The leading figures were interested in the background of the scenarios (the material and structuring that went into them) and there were some email interactions following the event.

For the molecular machine workshop, it was very difficult to get any feedback after the workshop. Most of the participants went on holiday, or were away at conferences during June, and after summer there was little enthusiasm for feedback. I discussed the workshop with two participants at the Frontiers Annual Meeting in Leuven, and they said they found it interesting. When I asked them about their strategies in creating images of molecular machines and whether the workshop helped or changed their approaches, they replied in the negative.

Stretch 7: The return of the responsible innovation project

July 2007 – December 2007

Insertion in the nanoworld

Activity type	Date	Details
Circulation & interactions only	October 7th – 11th 2007	MicroTAS 2007 The 11th International Conference on Miniaturized Systems for Chemistry and Life Sciences Paris, FR
Presentation	October 2nd – 23rd 2007	Frontiers Assessment Meeting Leuven, BE
Participation in roundtable	October 23rd 2007	Seminar on Knowledge Exploitation Leuven, BE
Presentation	October 23rd - 25th 2007	3rd Frontiers Annual Meeting Leuven, BE
Circulation & interactions only	November 28th – 29th 2007	Investing in Medical Nanotechnologies II London, UK
Circulation & interactions only	December 5th 2007	Debate on Governance Initiatives for the European Nanotechnology Community in the Public and Private Sectors Brussels, BE
CTA Workshop (Appendix 4)	December 18 2007	Technology Assessment Workshop, RRI Enschede, NL

Activity outside nanoworld

Activity type	Date	Details
Publication (peer review)	July 2007	Technological agglomeration and the emergence of clusters and networks in nanotechnology. Douglas K. R. Robinson, Arie Rip and Vincent Mangematin. Research Policy. Accepted for publication in special issue on Nanoscale research. Research Policy 36 (2007) 871–879
Publication (conference)	September 2007	Multi-level emergence and stabilisation of paths of nanotechnology in different industries/sectors. Paths of Developing Complex Technologies: Insights from Different Industries", Rip A., Robinson D. K. R. and te Kulve H. Berlin, September 17-18. 2007. Sponsored by the Volkswagen Foundation

Multi-layered responsible innovation debate

In autumn 2007 there was an increasing emphasis on societal embedment of nanotechnology applications, which provided a window of opportunity to relaunch a CTA workshop on risk and governance. During the 3rd Annual Meeting in October 2007, held in Leuven, Belgium (where I also had a chance to chat with a few people who had participated in the molecular machines or drug delivery workshop), I presented a new concept for the workshop with reference to the proliferation of governance proposals: calls for input into codes of conduct, discussion of regulation, and pressure for the precautionary principle to be put into practice.

In September 2007, the situation in the macro (and meso) level of nanotechnology debates on governance was becoming more visible (across the three layers). There was an increasing reference to 'responsible innovation' in government documents (particularly of the European Commission) and in some industry statements. It was clear that what constituted 'responsible innovation', or what was given the most priority in discussions and debate, differed across actor groups. For instance, in European Commission documents, the responsible development of nanotechnology was positioned as operationalized through transparency and some public engagement. In the case of industry, it was positioned as a responsibility for safe

handling of nano-production and nano-products. Also at that time, there was a visible initiative toward a 'Responsible Nanotechnologies Code', led by the UK Royal Society, an NGO (Insight Investment), the Nanotechnology Industries Association, and supported by a network organised by the UK Department of Trade and Industry, in which societal impacts were explicitly included.

Taking as the entrance point this emphasis on engagement, on societal impact, EHS (Environmental, Health and Safety aspects) and soft law, i.e. voluntary measures, I proposed in the meeting of Frontiers that "Responsible Research & Innovation" would be something interesting for Frontiers, now that these issues were becoming more visible (I presented some of my observations with regards to codes of conduct development).

I said that,

> "The main issue, particularly from the side of researchers and research organisations like the Frontiers Network of Excellence, was what can be done and should be done? At the very least, developments in RRI could be understood better, and be taken into account in strategic decisions. And in this way a CTA workshop would be advantageous and could [itself] be regarded as a minimal level of 'responsible' research and innovation."

The general thrust of my presentations during the meeting, and which was picked up in the discussions I had afterwards, was that the notion of responsibility is now encompassing and affecting research, hence the term RRI and the need to understand it better, so that Frontiers could participate in a more informed manner. This would require the bringing together of actors outside of the network which are involved in shaping the elements of RRI and/or would be affected by it.

It was agreed to be a good topic by the new director of the Frontiers Network, Vinod Subramaniam and the new manager Rolf Vermeij.

A meeting of codes of conduct developers (and stakeholders)

By the end of 2007 the situation involved mostly EHS and nanotoxicity related discussions, and a number of soft law proposals. December 5th in Brussels saw the meeting of three major efforts in defining soft law guidelines, the EU Code of Conduct for nano research, the UK Responsible Nano Code Initiative and the Principles of Oversight formulated by a group of labour unions and NGOs.

The EU had proposed a Code of Conduct for responsible nanosciences and nanotechnologies targeted specifically at research:

> "In order to promote safe and responsible nanotechnology research and pave the way to its safe and responsible application and use, the European Commission is planning to adopt a voluntary Code of Conduct for Responsible Nanosciences and Nanotechnologies Research ("the Code of Conduct"). This Code of Conduct would take the form of a European Recommendation and would invite the Member States, industry, universities, funding organisations, researchers and other interested parties to follow its principles. The Commission itself would follow these principles in its own action under the Community research policy…The Code of Conduct would offer those following it recognition of a responsible approach towards nanosciences and nanotechnologies research, making their actions more visible at a European Level."

The group I mentioned already, comprising the Royal Society, Insight Invest, the Nanotechnology Industries Association (and others), proposed a principles-based Code of Conduct that might be adopted by businesses and research institutions involved in developing, manufacturing and retailing products using nanotechnologies.

> "Like other principles-based codes, it will illustrate expected behaviours and processes, not standards of performance. Indicators of compliance could be developed at a later stage. The Code is not intended, however, to be an auditable standard, it will not detail levels of performance expected of companies, nor will it give guidance on definitions, characterisation and measurement. … The Responsible Nano Code aims to stimulate organisations to consider all aspects of their involvement with nanotechnologies, including the broader social and ethical issues."

Developed earlier, but now placed into context alongside the EU and the Responsible Nanotechnologies Code proposals, was the proposal created by a broad coalition of civil society, public interest, environmental and labour organizations, the "Principles for the Oversight of Nanotechnologies and Nanomaterials." The document declared eight fundamental principles that they proposed must provide the foundation for adequate and effective oversight and assessment of the emerging field of nanotechnology, including those nanomaterials that are already in widespread commercial use.

The three codes although originating from different areas (policy makers, industry/investment community and NGOs respectively) and targeted at different

actors (researchers, industry, and the whole innovation chain respectively) they had many parallels, albeit with a differing breadth and scope. The discussions during the Brussels meeting confirmed that the topic of responsible innovation was timely in the wider world, and also that different actors were still seeking for productive ways of addressing the issues. This situation had made it relatively easy to find participants for the CTA workshop.

On December the 18th we held the CTA workshop on Responsible Research and Innovation at MESA+, Enschede, NL. Details of the event are given in full in Appendix 4. The participants included persons from regulation, industry and the world of trade unions (some of whom were regular participants in meetings and discussions like the Brussels one), and nanoscientists some of whom had been involved in strategic discussions as in the European Technology Platform Nanomedicine. Thus, for some participants the workshop was an occasion for further positioning and discussion of the issues. There was also quizzing of the "regulars" by the nanoscientists present.

Stretch 8 – The final CTA

January 2008 – April 2008

Insertion in the nanoworld

Activity type	Date	Details
Participation in roundtable	January 8th 2008	Frontiers Management Board Meeting Schiphol, NL
Participation in roundtable	January 16th 2008	General Assembly of the ETP Nanomedicine Brussels, BE
Circulation & interactions only	April 1st 2008	Micro and Nanotechnologies for Neurosciences. Organised by the Observatory of Micro and Nano Technologies (OMNT) Paris, FR
CTA Workshop (Appendix 5)	April 7th 2008	Technology Assessment Workshop, DBS Leuven, BE

After the Christmas break, I had little chance to write up the workshop findings thoroughly before I was to report to the management board the findings. I could only present the main findings from the RRI project, and the planning for the final one. At this point, there was no clear leader of the Ethics workpackage, Robert Doubleday had left, no real candidate was there to replace him (a nanoscientist from the Cambridge partner was told to substitute – and they were seeking guidance from me). I was asked to become head of the workpackage, but I declined saying that I had too many PhD responsibilities.

Shortly after this meeting, there was a meeting in Brussels of the European Technology Platform Nanomedicine. I was interested in attending to see what sort of activities take place at such events. The set up was of presentations and break-out sessions. I was recognized by a number of people there and asked to participate in the break-out session on ELSA issues, which I did. There were seven participants – "the usual suspects" dealing with ELSA issues. The characterization of "usual suspects" had come up in the RRI workshop, and some names were mentioned by the workshop participant; and these were now sitting around the table. This showed how the discussion of ELSA of nanotechnology had become regularized (people are recognized for it) as well that there are still only few regulars (they're drawn on again and again). Actually, from what I have been reporting about my being recognized and invited, it is clear that I was becoming a "usual suspect" as well (although on my own terms).

The final of the five

In February 2008 I visited IMEC, and discussed the possibilities. The group at IMEC were about to develop a portfolio of research activities for the next 10 years, and was thinking of targeting the bio-electronics work to brain disorders, to focus the effort and perhaps deliver technologies that would have therapeutic use. The senior researcher emphasised his excitement about the CTA project, since in his opinion, the research community was oblivious to many of the factors that are important to developing therapeutic technologies such as brain implants, and about user practices. I showed some of the details of the past four TAs and we agreed that a look at broadening the linear model (using the innovation chain idea) and exploring generations of technology development in deep-brain-implants would allow the use of the multi-path mapping tool – both these visualisations spoke to his way of thinking, he mentioned this explicitly when describing his attempts over the previous two months to develop a kind of roadmap which had an unclear end point. The agreed date was April 7th in Leuven, Belgium.

The details are given in Appendix 5. The workshop went smoothly, possibly because of the focus on innovation.

Stretch 9: The conclusion of Frontiers, the birth of NaBiA

May 2008 – February 2009

Insertion in the nanoworld

Activity type	Date	Details
Presentation	June 23rd – 26th 2008	Frontiers Research Meeting Heraklion, GR
Circulation & interactions only	June 25th – 27th 2008	Nano2Life Scientific Meeting Heraklion, GR
Circulation & interactions only	September 23rd -25th 2008	Nanotech Northern Europe 2008 Copenhagen, DK
Presentation	November 26th 27th 2008	Conference: 21st Century Medicine: Breakthroughs and Challenges London, UK
Circulation & interactions only	December 2nd - 3rd 2008	European Nanoelectronics Forum Paris, FR
Presentation and Round table meeting	January 26th 2009	End of Frontiers Assessment Meeting Brussels, BE
Presentation and Round table meeting	January 27th 2009	NanoBio Alliance Kick Off meeting Brussels, BE

Activity outside nanoworld

Activity type	Date	Details
Publication (peer review)	May 2008	Multi-path roadmapping as a tool for reflexive alignment in emerging S&T. Douglas K. R. Robinson & Tilo Propp. Technological Forecasting & Social Change

		75 (2008) 517–538
Publication (conference)	October 2008	Complexity Scenarios for Emerging Techno-Science: Addressing Strategy-Context fit by prospecting level dynamics of governance. Douglas K. R. Robinson. (2008) Paper presented at the third International Seville Seminar on Future-Oriented Technology Analysis: Impacts and implications for policy and decision-making – Seville 16-17 October 2008

At the Frontiers and Nano2life joint meeting in June 2008 I was given a large slot to present. I had become a regular in this world, as was additionally clear when Nano2Life invited me to sit with the coordinators and discuss projects on ELSA and TA, along with foresight. Along with this, I was invited to a Nanomedicine conference in November 2008 in London, to talk about CTA and foresight and TA (not on ELSA).[80] What was visible in this period was that, the Nanomedicine research community was merging and that I was recognised as an actor close to the field (knowledgeable about Nanomedicine) with my own interests in prospecting futures with a view to (Constructive) Technology Assessment.

In January 2009, during the final Frontiers assessment with the European Commission, my work was presented as a regular and important part of Frontiers (to the European Commission Project Officer Heico Frima), and my publications were included in the listing of products as relevant research in its own right. This was not just an attempt to make a good impression with the European Commission (which was pushing for a Code of Conduct for nanoscience and technology research). In the successor to Frontiers and Nano2Life, NanoBioAlliance (NaBiA), the CTA idea was an integral part (a sort of cross-pollination into Nano2Life of my Frontiers legitimacy) and I was invited to be part of the working group on TA and ELSA for NaBiA.

It is not clear yet what NaBiA (and its CTA part) might become. I was struck with the difference in level and ways of coordination compared with nano-electronics when I attended the ENIAC Annual Meeting in Paris (see Stretch 3 for a characterization of ENIAC which is a European Technology Platform). Nanoelectronics has highly structured arrangements with lots of private sector funding going into the coordination.

[80] My invitation on this basis continues to date, one instance is the participation and assistance in running a foresight/TA workshop in the following Nanomedicine event: *Nanomedicine: Visions for the Future, Amsterdam, 24 - 25th February, 2010*

Stretch 10: Post Frontiers insertion

March 2009 – October 2009

Insertion in the nanoworld

Activity type	Date	Details
Circulation & interactions only	September 18th -22nd 2009	36th Annual meeting and exposition of the controlled delivery society Copenhagen, DK
Presentation	April 1st – 2nd 2009	Third international conference: Active and Intelligent Packaging Chipping Campden, UK
Circulation & interactions only	June 10th 2009	Trans Atlantic Consumer Dialogue: "Regulating Nanotechnologies in Food and Consumer Products: Developing a Consumer-focused Transatlantic Approach" Brussels, BE
Circulation & interactions only	September 10th 2009	Scientific Hearing on Risk Assessment of Nanotechnologies Brussels, BE
Participation in roundtable	October 12th - 13th 2009	EURONanoBio Roadmapping Workshop Milan, IT

Activity outside nanoworld

Activity type	Date	Details
Publication (peer review)	November 2009	Robinson, D. K. R. (2009). Co-evolutionary Scenarios: An application to prospecting futures of the responsible development of nanotechnology. Technological Forecasting and Social Change, Volume 76, Issue 9, November 2009, Pages 1222-1239

My insertion continued, now as a regular, and independent of my PhD activities. One new activity was my work for the ObservatoryNANO project, a European Commission funded project led by the Institute of Nanotechnology, Glasgow.

There, my focus was more on identifying directions and challenges than CTA questions like openings for broadening. Based on that work I was sometimes invited to give a presentation, as in April 2009, I was invited to give a talk on nanotechnology in the food sector for an international conference being run by a food and beverage industry association. This allowed me to see (again) ambivalence about engagement with consumers ("fingers may get burned") and how companies went for caution, mentioning often that they would not apply nanotechnology until clear regulatory procedures were in place.

When I attended the controlled delivery society meeting, the world biggest and most recognized forum on research and development in drug delivery technologies, many of the participants in my siRNA workshop were present and I had a chance to discuss with some of them. In particular, the group leader was happy to discuss some the developments since our workshop. He mentioned his satisfaction with the workshop, and when probed, said that the workshop was good to discuss things that were already in the back of their minds. Further development of siRNA therapy was now occurring through an international network including some companies. I was allowed to sit in on some negotiation around coffee, and when a lead scientist and a company person looked concerned that I was there, he said: "Dougi's ok, he's helped us before".

There appeared to be a general movement towards regularization. The Trans Atlantic Consumer Dialogue (TACD) meeting on the 10th of June was an international event which covered all sorts of industrial and commercial sectors, this time focusing on nanotechnology. Some of the nanoworld regulars gave presentations alongside consumer organizations, environmental NGOs, and regulatory agencies. What was striking also was how many scholars studying nanotechnology were present. I had started meeting these people in various events in 2008, in the world of STS and in nanotechnology meetings related to governance and in other non-technical meetings. Now, I was the only one personally recognizable to many of the nanoscientists present, but we were recognized as a collective, often described or introduced as "social scientists" to other people. During lunch and in coffee breaks, whilst the "social scientists" chatted and shared notes and experiences, various actors would approach one (or a number of us) and start discussing projects they were working on, concerns about certain aspects of regulation or societal issues etc. Social scientists were not foreigners anymore.

Later in the year I attended the "Nanohearing" which was focused on the EHS issues of nanotechnology. The meeting was jam-packed. Some of the social scientists from the "nano-circuit" were present, but the majority were members of

industry, industry associations and toxicity and risk experts. In October 2009 I was invited to attend what was termed a Roadmapping event for the project EuroNanoBio (linked to core partners of NaBiA). Other social scientists were invited as well, especially to give their opinions and insight on what the organizers called "Ethics". I was invited by the leader of the project (formerly active in Nano2Life) who knew about the CTA projects I had run in Frontiers. And thus invited with regards to foresight and innovation (including societal aspects). There was also reference (by a member of Frontiers) to my paper on multi-path mapping which he had read, and how the type of roadmapping I had done could be used. Clearly, there is diffusion and uptake in the nano-world. One of the organizers of the meeting (a senior scientist from MESA+), of his own accord, said: "we should anticipate on societal embedment issues".

My activities moving in and out of the nanoworld continue to-date, but for the purpose of evaluating the CTA-by-insertion, I end the narrative here.

6.3 Discussion

I have reported on my moving about in the nano-world and my negotiating and embedding of CTA projects. Forcefields of different kinds were experienced, and changes over time. Particularly striking was how my role evolved from 'foreigner' to 'regular'. This had to do with my activities which became gradually accepted: visible, and in some circles, legitimate. It was also part of an overall change in which social scientist and other non-technical actors were welcomed into the nano-world. While there were different reasons to do so, one strong idea was that some of these non-technical actors could be of some help (in innovation dynamics and roadmapping, for example). The other driver, of course, was the pressures on the nano-world, as visible in the discussion of risk and of responsible development.

Insertion as a methodology turned out to have different facets. Moving in, but also moving out to maintain some independence, are both important. It turned out that aggregation and presentation, in particular the possibility to refer to own social-science publications which could be helpful to nanoscientists and nanotechnologists, was a very good way to create legitimacy. There is more to say, but given the vicissitudes of insertion, including the need to work under time pressure, it is difficult to offer general comments. Insertion will always have ad-hoc elements.

Insertion as necessary for CTA, the claim with which I started, was confirmed at the level of individual CTA projects, their preparation and their fate. It was also confirmed at the meso- and macro-level in how over time CTA projects, but really the idea of doing CTA-type activities ("anticipating on societal embedment issues") in general, became accepted and embedded. The steps that occurred can be traced in the reporting. One factor, important at first, were pressures, in the case of Frontiers pressure from the European Commission to do something about ethics, which required some action, symbolic or otherwise. By now, the action is not just symbolic anymore.

Chapter 7 Developing empirical CTA

Introduction

Five CTA projects were successfully conducted around nano topics that are connected with the ongoing developments of nanotechnology activities in the member organizations of the Frontiers nanotechnology consortium. This was an opportunity to develop the methodology of empirical CTA in the context of nanotechnology. The opportunity came with constraints, because of the link with the Frontiers consortium. This is actually a general aspect of empirical CTA: insertion is important to create opportunities for broadening, but implies being responsive to the shifting conditions and circumstances of the field of investigation. Still, one can speak of a methodology since there are steps in the approach, and since one can, albeit only to some extent, link elements of the approach to productivity in achieving aims. Since the approach requires contextualization, my reporting on the CTA projects and the subsequent analysis in terms of methodology must show the contextualization in some detail. The detailed reporting and some first round analysis is given in the appendices. This chapter focuses on the analysis and tentative conclusions.

The key part of each CTA project was an interactive workshop, organized as a bridging event (see Ch. 1.1.3). Table 7.1 lists the workshops, the acronyms I will use when referring to a workshop, and the appendix in which it is located.

The CTA projects were conducted within the evolving R&D consortium Frontiers, itself an example of a relatively new form of research coordination by the European Commission. The challenge (and opportunity) was to include CTA experiments within an evolving situation – for most of the nanoscientists involved in Frontiers the notion and activity of a Network of Excellence was a new one, and therefore, not a stable entity. This is an institutional point, but it reflects the overall challenge of CTA of emerging technologies which are still in flux. In nanoscience and nanotechnology, the enactors try to get a grasp of what is happening and which directions to go. This will also affect how they see CTA projects (as was clear in their appreciation of tools to structure the future).

Table 7.1: The five CTA experiments

	Acronym	Full title of the project	Date
Appendix 1	CellChip	Integrated microfluidics for single and multiple cell analysis	16 June 2006
Appendix 2	siRNA	siRNA delivery innovation providing new tensions and opportunities	31 May 2007
Appendix 3	MolMach	The role of images of molecular machines inside and outside the lab	12 June 2007
Appendix 4	RRI	Responsible research and innovation as part of nanotechnology governance	18 December 2007
Appendix 5	DBS	Socio-technical and innovation issues and opportunities in implant R&D	7 April 2008

The CTA projects were orchestrated experiments in interaction, and an occasion to develop a methodology for such projects. Each experiment was different; they were initiated at different times, on different topics, with a variety of contingencies and design strategies. However, each CTA-project followed a stepwise process of development and execution which was part of a reasoned design of the project. This is the basis for evaluating the productivity of the CTA projects. I will elaborate the various evaluations in the subsequent sections. Here I indicate the overall approach.

First, there is comparison across the CTA projects, focusing on the important elements that defined and shaped each CTA-project during the three stages of development:

i) Initiation of the project
ii) Preparation of the CTA
iii) Execution of the CTA

During each of these stages, the process was similar, and the description can be ordered in a systematic way and compared. The thick description is given in the Appendices. Here, I use summary tables, which allow comparison. They are arranged according to the three stages of development (sections 7.1, 7.2 and 7.3).

Second, there is evaluation of productivity within each CTA project. Dimensions of productivity are:

i The degree of bridging of enactment and selection processes
ii The degree of awareness building of dynamics of emergence (co-evolution and entanglements)
iii The effectiveness of orchestrating a microcosm that is structured around (and informed by) the macrocosm of NST development

These dimensions will be further specified in section 7.4. There, I also explore relations between starting conditions and process variables, and with eventual outcomes in terms of productivity.

7.1 Initiating and creating an inserted-CTA project

When exploring the initiation of a CTA project, there are three interests at play. As a CTA agent I must link-up and link-in with the ongoing activities of the nanotechnologists, maintain enough distance to be able to remain, and take advantage of being, external to the situation and also incorporate my own interests as a PhD researcher. Then, there are the interests of the Frontiers management board which govern the R&D consortium (this is linked to their own interests and the strategic aims and obligations of the network itself). And there are the researchers who are members of the network and will participate in my CTA projects have their own interests as part of the network and within their individual activities in their home institution.

To determine topics/subjects for CTA projects, and for them to be productive, these interests have to be managed. For my attempts at creating CTA projects, negotiating the starting conditions, in both senses of the phrase, was necessary to fit the CTA to the context I was working in and actually *do* CTA. (I had to negotiate with important actors in Frontiers with regard to the topic of the CTA and it's financing. But also, in the sense of negotiating an obstacle course; part of my insertion was to identify tensions and dilemmas, windows of opportunities etc. through moving about the nanoworld within Frontiers and outside.)

For each workshop I will describe:

- The emergence of the initial CTA-project concept
- The negotiation and state of alignment of my CTA interests and the Frontiers partners
- The contingencies and ramifications of the starting conditions

This is important as each of these three elements may affect the productivity of each CTA-project.

7.1.1 First diagnosis of concept

For Frontiers, I was restricted to topics within their remit, thus nanobiotechnologies, molecular mechanics and ELSA (the latter because the workshops were created as part of the Frontier's ELSA work package). I used two criteria when exploring whether an emerging CTA-project concept was viable:

- Richness of the case: Was it a viable case? Were there enough issues and dynamics to explore in a workshop?

- Something at stake, for potential participants, be they the nanoscientists in Frontiers, societal or other actors. This was also practically important since the CTA project had to be seen as addressing an issue of relevance to stakeholder groups (particularly nanoscientists) in order to attract participation – which was voluntary (no monetary recompense).

The Table 7.2 details how the five workshops scored on these criteria.

In all cases except MolMach I could identify something at stake now. Potential MolMach stakes were linked to the recent historical discourse around grey goo and images of nanobots and self-replication, and the current developments in the field which get close to the original notions of nanobots, such as molecular walkers, nanocars, nanotrucks etc. This did not appear to be an important stake for the nanoscientists, but as a CTA-analyst I could see the potential of a near-future shift in stakes as the field of molecular machines becomes more articulated and the relegation of control at the nanoscale, and potential loss of control, can no longer be relegated to the realms of science fiction.

The limited stake in the DBS case had to do with the fact that the project was initiated as a way of doing better, rather than solving an issue or dilemma. Further exploring broader design requirements and potential innovation journeys would be a way of identifying pathways to invest in. As long as interesting research was to be done, the scientists were OK, and there appeared to be little external pressure (other than consideration of opportunity costs).

Table 7.2: Identifying whether there is something at stake and the potential richness of the case

	My diagnosis of the topic richness	Could I identify something at stake?
CellChip	There were many issues that could be explored, a substantial history in the field of lab-on-a-chip, with visible dynamics relating to expectations and emerging irreversibilities.	**Yes,** there were two stakes that I could identify: (1) an innovation gap between laboratory and prototype (small firms' very survival depended on this) and (2) the platform nature of the technology meant many possible applications and many potential routes of societal embedment.
siRNA	The combination of gene therapy and nanotechnology for targeted delivery could provide lots of innovation and societal embedment issues. Clinical trials of siRNA (not nano) were underway at the time of the project and a variety of potential vectors for delivery were being developed around the world.	**Yes**, new pressures on researchers involved in this field were visible in my discussion with them. In particular with regards to the exploitation of research and on societal implications. The stake (that was visible in the discussions) was, to what extent should nanoscientists link up with these new possibilities for exploitation and the responsibilities that go with it?
MolMach	A variety of representations and associated meanings of molecular machines in multiple disciplines was visible in an earlier research project (Chapter 3). Coupled with images of nanomachines and nanobots from the early days of nanotechnology (and persisting to this day) and their circulation there was a reasonable amount of material for the case, but no explicit elements relating to societal embedding or innovation aspects.	There was **little** at stake at the time of the workshop, but potentially in the near future. In the early days of nanotechnology, molecular machines were linked with self-replication and images representing molecular machines proliferated. They were later disregarded as sci-fi. However our research in TA-NanoNed indicated that molecular machines as an issue of control at the nanoscale could re-ignite the earlier debate on self-replication and grey goo.
RRI	A very rich case, anticipatory coordination and debate was occurring concerning which governance arrangements would be the most appropriate for nanotechnology. Questions on risk, ethics, soft law, hard law etc. were proliferating around a theme of responsible development of nanotechnology (cf. EU Nano Action Plan)	**Yes,** the potential institutionalization of new roles and responsibilities of all nano stakeholders was under discussion, and was a hot topic of debate at the time, but could cool off and be locked in at any time. Therefore, the argument of being aware and potentially becoming involved in the shaping of the attribution of roles and responsibilities was the entrance point to this workshop.

DBS	There were a limited number of issues since the project was focused, in the main, around a particular technology option for a particular form of medical disorder. However, experimental neurosurgeons were active in the field and could potentially be involved in the CTA, which made it potentially rich by bringing together medical device manufacturers and neurosurgeons to broaden the perspective of the Frontiers researchers.	**Medium**, there was an issue of opportunity costs in choosing the research portfolio for the next 10 years. Therefore, a further articulation of enactment, selection and how innovation journeys play out would be enlightening and potentially useful. A research group in the Frontiers network was developing R&D plan and was proactive in attempting to anticipate on broader issues (rather than wait and see what will happen).

7.1.2 Aligning interests though negotiation

Each CTA project was created in the framework of Frontiers, either with a lead partner in the network, or with the management team themselves. After my preliminary diagnosis (7.1.1) the next step was the further development of the CTA concept and the agreement that it would be financed and endorsed by the Frontiers management team. This was dependent on the further articulation and alignment of mine and Frontiers interests, requiring discussion and negotiation, and this differed from case to case

For the first workshop of the series, (CellChip), the negotiation of the subject "Integrated microfluidics for single and multiple cell analysis" was negotiated with the coordinator of the Frontiers Network-of-Excellence. His interest at the time (2006) was in having a productive workshop that would a) fulfill some of the obligations of the Ethics Workpackage in Frontiers, b) would be relevant for the members of the network (both as participants and/or users of the findings) and c) would be appreciated by the European Commission (and particularly the Project Officer who monitored the network and its constituent workpackages). The CellChip project became a pilot exercise, relatively low risk and closer to nanoscientists than to societal actors.

The other four workshops could be broader in scope, and the objective was to provide a CTA that would allow linking ELSA and innovation aspects in and around a particular nano topic in Frontiers. A criterion was that there could be no repeat of a workshop, so each CTA-project would be on a different topic. Then, the interest of nanoscientists, members of Frontiers, became important.

As can be seen in the table below, for siRNA and DBS there was eagerness on the parts of the lead partner involved, however the MolMach case had a large number of difficulties.

Table 7.3: Relative alignment or tension between Frontiers partner and CTA-agent interests

	Alignment of Frontiers partner and my CTA interests
CellChip	The CTA concept was to explore innovation and societal embedment processes and how they would shape (and be shaped) by emerging socio-technical entanglements. The presentation of this idea around the (broadened) linear framework of the innovation chain (see slides in section 1 of Appendix 1) presented the topic in enactor terms, therefore there was little friction because of the enactor framing and the appreciation that there was something immediately at stake (the innovation gap) along with something at stake beyond the immediate (societal embedment), although the former "stake" was given a higher degree of relevance in the discussions with the Frontiers management team.
siRNA	This project was more of a negotiation (even though it was framed in a similar way as the CellChip project) around innovation and societal embedment issues. To convince the lead partners required some mutual probing of each other's understanding of the stakes and the processes of R&D and innovation in drug delivery, but the lead partners did not have any strong opinions with respect to the form and objective of the CTA and thus it was more like further targeting and refinement of my original CTA interests.
MolMach	For this project there was misalignment from the outset. My interest was to understand how visions of molecular machines (particularly those represented in images) shaped anticipation and ongoing activities in the emerging field. The Frontiers partners involved disagreed with the breadth and scope of the workshop concept and preferred a seminar-type discussion on public engagement strategies or "how to communicate better with the general public". This disagreement persisted throughout the preparation and execution of the CTA-project and required active "repair work" from the side of CTA-agents
RRI	In the first attempt at developing a workshop concept there was little interest from the nanoscientists in the Frontiers network, however the industry-linked partners found it interesting and agreed with the CTA interests. Following the first failed attempt to run a workshop, when presenting the concept in the 3rd Frontiers Annual Meeting there was a lot of interest across the board, with general agreement to the CTA aims presented during that meeting.

DBS	This project concept was easier to negotiate, perhaps because four workshops had already taken place and could be referred to by both the CTA-agent and lead partner in Frontiers. Multi-path mapping and the innovation chain (CellChip) framed the negotiation of what could be achieved in the CTA and there was agreement from both sides that, a productive CTA would focus on broadening the concentric bias through a broadened linear model (Innovation Chain) supported by more complex scenarios.

7.1.3 Contingencies and ramifications of the starting conditions

There were formal and informal organizational constraints based on the requirements, restrictions and other circumstances placed on the CTA-projects by the Frontiers network. These are important to mention as they shaped the starting conditions quite dramatically. In particular, the concept for a CTA-workshop could be developed but only after a decision by the Frontiers network and the release of resources could the project be initiated. In most cases this led to a very short turnaround time for each CTA project, in some cases approximately a month to develop the concept further, do case analysis, gather participants and develop the preparation material. At the outset there was pressure to deliver a CTA concept rapidly and to execute a full CTA-project before the summer of 2006, if I was to obtain a legitimate position in Frontiers (as part of a workpackage) and to obtain financial and political support from the Frontiers Management Team for future workshops. (I could manage this by drawing on my deep case research undertaken jointly with Rutger van Merkerk (van Merkerk and Robinson 2005a, van Merkerk and Robinson 2006) on lab-on-a-chip and of nanofluidics.)

The often contracted time for initiating and executing the CTA-projects had implications for preparation. The dedicated interviewing that was necessary had to be arranged in a short period of time. Thus became even more difficult because of the process of gathering participants. Relevant actor communities could be identified, and participants individually sought out or circular invitations sent to message boards or communities etc, but in most cases many of the participants finally agreed to participate not earlier than a week before the workshop event. In addition, given that my projects were part of the Frontiers network, members of the board would suggest approaches to the workshop, recommend participants or requested certain people to be invited, often near or in the final stages (one could see the difference in worlds: “Bums on seats” was very important for the

Management Team as a criterion, and the mix of types of participants had less priority for them.).

Table 7.4: Table of contingencies and ramifications

	CellChip	siRNA	MolMach	RRI	DBS
Explicit requirements and constraints from the Frontiers network	Frontiers needed a workshop before July 2006. The topic had to be clearly linked to Frontiers activities. Funding could be provided for Frontiers partners and a very limited amount for external parties.	Funding could be provided for Frontiers partners and a very limited amount for external parties.	No external nanoscientists were allowed which seriously restricted the potential diversity of participants.	External parties could be invited with hotel and travel paid for by Frontiers due to the non-technical nature of the topic.	There should be a multi-path map as an output. Funding could be provided for Frontiers partners and a very limited amount for external parties.
Level of control over the topic and process by CTA organiser	**High** level of control .	**High** level of control	**Low** level of control	**High** level of control	**Medium** level of control
Amount of time to prepare the project	7 weeks	5 weeks	4 weeks	7 weeks	5 weeks
Gathering participants	**Very easy** to gather enactors because of the innovation gap	**Difficult** to get people from outside of Denmark.	**Very difficult** to get people from outside of Toulouse	**Very difficult** during the first attempt **Very easy** during 2nd attempt	**Medium** but only nanoscientists from the host institution

For the first three workshops and the first (and failed) attempt at a risk workshop (see Appendix 4 for the story), it was stipulated by the Frontiers Management Team that most of the participation had to come from the Frontiers NoE. They positioned the CTAs as a support tool or educational seminar almost like a mini course on ELSA. It was only after demonstrating, through the first few workshops, that they were something else, that my CTA projects were recognized as a process for supporting interactive learning with the requirements of including more kinds of actors (increased heterogeneity) and insight in dynamics (well researched and well structured support material)

7.2 Preparation prior to the CTA workshop

I will use the term microcosm to emphasize the special characteristics of a CTA-workshop. The workshop is built on knowledge and insight of the actual activities and dynamics in the real-world (the macrocosm) which have to be present or at least visible in the somewhat protected (and orchestrated) space of the workshop. Thus, it is a micro-cosm in which elements of the macrocosm can be explored and actors and dynamics are brought more closely together than in the macrocosm. The setting of the workshop also allows actors to step outside of their macrocosm roles or augment probing of the worlds of other actors who they may not usually meet face-to-face or only in a situation where positions (and potential interaction mechanisms) are already locked-in. Preparing for a CTA microcosm requires mapping the important issues, dynamics and actors, i.e. socio-technical mapping. It also includes the orchestration of the microcosm through bringing together (a) key actors and (b) provide support tools and material for the reflection on the potential co-evolution of issues, dynamics and actors. Such preparation will play a role in the productivity of the CTA microcosm, along with the actual interactions between the actors and their interaction with the support tools and material (and including the activities of the CTA-agent as animator in the microcosm).

Socio-technical mapping was conducted for all five CTA-projects. This mapping produced findings in their own right, but this chapter is not the place to outline them. They are described (in part) in the appendices, when the scenarios are presented. Each socio-technical mapping also included dynamics, capturing key elements of the emerging socio-technical entanglement in the field of nanotechnology, or at least in and around the topic chosen for the CTA project:

i) The current and potential actors in the area;

ii) The expectations about the direction and emergence of the field, the anticipated dilemmas and stakes; and
iii) Emerging irreversibilities as indicators of stabilising entanglements (which contribute to path dependencies, cf. Ch. 1.2).

Such data was captured through multiple means, necessarily so since for emerging fields, with little history, there is limited systematic data available and what data there is, is distributed across a variety of sources. Thus desk research (peer reviewed articles (including reviews), grey literature and in some cases information from websites) is combined with dedicated interviews and insertion (which includes the visiting and participation in a variety of forums, conferences, meetings in and around an area of nanotechnology). Details of the methodology of tracing expectations, of mapping the actors and capturing indicators of emerging irreversibilities were already given in Chapters 2-5.

7.2.1 Orchestrating the microcosm

The mapping allowed the identification of actors and dynamics in the macrocosm of the real world. The next step was to use this knowledge to prepare a microcosm that would function as a temporary space to explore and probe dynamics of the real world because it was structured and informed by knowledge of dynamics, patterns and emerging entanglements in this world. This translates into two main steps: (A) Identifying relevant actors and gathering them for the workshop and (B) creating the preparatory material for the participants – socio-technical scenarios and other support materials.

(A) Identifying relevant actors and gathering them for the workshop

One way of working towards broadening the concentric bias is to facilitate probing through co-locating different types of actors. The Table below presents the actor composition in each workshop.

The mixes were different. As the table shows, MolMach and CellChip were homogeneous (in terms of enactor/non-enactor mix) whereas the others were heterogeneous. To what extent does the composition affect the productivity of the microcosm? Conventional wisdom would suggest that the more heterogeneous the composition the more effective would be the interactions and more productive the interactions. But there are trade-offs.

Indeed, one needs heterogeneity to avoid the situation where the "in-crowd" or "experts" can just repeat their own preconceptions without being challenged, or at least probed. However, with too much heterogeneity, the potential to go deep into issues and the incentive to probe may be less, leading to a situation where there will belittle productive interaction.

All of the five workshops never contained less than 2/3 enactors, this was the most I could achieve within the organizational constraints (see 7.1.3).

Table 7.5: Composition and degree of heterogeneity of each CTA workshop

	Actual composition of actors present at the workshop	Degree of heterogeneity
CellChip	5 senior LoC researchers, 1 junior researcher, 5 small firms, 3 organisers and 2 observers	Strongly homogenous
siRNA	3 senior researchers, 6 junior researchers, 1 firm, 1 medical doctor, 1 technology transfer expert, 1 EHS expert and 2 organisers.	Heterogeneous
MolMach	11 Senior Researchers, 2 junior researchers, 3 organisers, 1media representative, 1 sociologist, 1 philosophy of technology scholar.	Homogenous. Mostly enactors from CEMES
RRI	1 senior researcher, 3 junior researchers, 1 large firm, 1 industry association, 1 labour organisation, 1 public agency, 1 communications scholar, 2 observers and 2 organisers.	Heterogeneous
DBS	2 large firms, 2 SME's, 1 senior researcher, 3 junior researchers, 2 neurosurgeons, 1 technology transfer expert, 3 organisers	Heterogeneous

(B) Scenarios and the role of other support material

Scenarios are often used to create a synthetic picture of a possible future, and the emphasis is on the nature of that future, rather than the route towards it (although there have been so-called 'back-casting' projects (see for example Loeber's 2004 analysis). In the socio-technical scenario approach that I follow, socio-technical mapping, interactions with actors, and the exploration of dynamics using theoretical models and case research and, are translated into scenario narratives which place emphasis on the "how" paths into the future may unfold. Evaluations of desirability or undesirability of a future state can then be coupled immediately to features of the path that led to them, and induce strategic reflection and subsequent choices.

In each of my CTA-projects, three socio-technical scenarios were created. Each scenario narrative unfolded in a different way, highlighting a particular dynamic. Thus, the scenarios need not be mutually exclusive, elements of each of them can co-occur, reflecting the complexity of the real world.

The preparation of the socio-technical scenarios is – as far as possible – built on in-depth studies of the technical field, of actor arrangements and socio-technical entanglements. This ensures accuracy and scenarios of high quality in terms of plausibility, not probability). The scenarios must also be plausible for the workshop participants; otherwise the workshop organisers will lose legitimacy. In all five workshops the quality of the scenarios was recognized, and occasionally applauded. (The extent to which they were mentioned in the workshop itself will be indicated in 7.3).

Socio-technical scenarios are a means to explore the relationships between emerging technologies and those who are involved in the development or who will be affected in some way by the emergence of a new technology. As an input into the workshops, their primary role is to integrate a lot of analysis of the complexities of technology emergence and controlled speculation as a platform for the exploration of issues and the probing of the worlds of the various participants. All scenarios are given in the relevant appendices, and annotated so as to make clear the dynamics and elements that were incorporated into them. A description of the construction of the socio-technical scenarios has been given in Chapter 5.

Other support material mobilised

In a number of the workshops, additional representations capturing elements and dynamics of socio-technical emergence were used. In CellChip and DBS multi-path mapping and representations of the innovation chain where used to mirror the linear/concentric perspective of enactors, but also to locate broadening possibilities and dynamics in a frame that was recognisable for the participants. In siRNA and RRI I framed some of the co-evolutions in the form of multi-level diagrams, for siRNA they were used to show the multi-level dynamics in each scenario, and in RRI it was used to present the case history (see Appendix 2 and 4 respectively). The construction of multi-path maps is described in Chapter 4. The innovation chain and multi-level diagrams as representative of concentric and co-evolutionary perspectives, respectively, were presented in Chapter 5.

7.3 The dynamics in CTA workshops

The workshops play a central role in the CTA projects. If conducted satisfactorily, they act as a microcosm of the real world and allow the mingling of actor-roles and experiences of those participating and the aggregated intelligence from the analysts who orchestrate the microcosm. They are also an opportunity to bring closer those elements (actors, issues, roles, dynamics) that may be quite distant (or invisible) to the participant's traditional activities in the real-world. The concentration of these elements into an arena for interaction is only one aspect, interactions can occur in a variety of ways and conversations may be hard coming in a workshop with a diversity of participants) that may not usually communicate directly with each other).

The first step in evaluating this is to analyse the dynamics that occurred in the five CTA workshops. Inspired by Garud and Ahlstrom (1997) and the notion of bridging (see Ch. 1.1.3), I introduce the notion of a productive arena for interaction. One aspect was already discussed: the opportunity for probing each other's worlds. Thus, the degree and frequency of probing that occurs in the workshop setting is an important indicator.

Another aspect of productivity of the arena is issue articulation. CTA workshops go beyond brainstorming by exploring interrelations and dynamics, supported by scenarios that are informed by the scholarly literature and dedicated data collection. The degree of issue articulation will be related to recognition of patterns and dynamics of co-evolution. This indicator of a productive arena speaks to the CTA

goals of awareness of co-evolution dynamics and the linking of the microcosm to the macrocosm.

A third indicator of a productive arena is not specific to CTA, but applies to all interactive workshop settings: the flow and intensity of discussion. But there is a specific CTA element as well: the links between the microcosm of the workshop and the macrocosm in which the participants live. The flow may ebb and wane, and the CTA agent, in particular the chair of the workshop, must act as an animator to keep the flow going, but also occasionally bring in insights from the preparatory research. The latter relates to the nature of the microcosm which concentrates a variety of actors, dynamics and perspectives into a one-day event where the CTA agent may be more knowledgeable about the overall co-evolution than each individual participant in the workshop. Thus, linkages from the microcosm to the macrocosm and vice versa can be made by the CTA agent (organizer or animator), which then provide openings for discussion (or sometimes a means to refocus a discussion that detracts from the core theme of the workshop).

Managing the flow in real-time requires ad hoc decisions by the animator whether to let the discussion flow or intervene. To do so effectively requires legitimacy of the animator sufficient to be accepted as someone who can shape the discussion, and sufficient knowledge of the domain and the issues to make sure that the intervention is substantially correct. It is not just the animator who intervenes. Participants will respond to the flow of the discussion, continuing it or introducing another perspective or topic. Thus, further ‘stretches’ in the discussion can be initiated by the organizers as well as the participants. Given the importance of probing each other’s world in the ‘bridging event’, there is a further task for the animator. If participants just recourse to the positions and roles they have in the macrocosm of the real world, the animator can intervene and open up the discussion. In my cases, this is particularly important when nanoscientists recourse back to technical details. The animator can intervene, e.g. by asking other participants for comment. Or abstain from intervening, to see whether one or another participant will rise to the occasion (this actually happened in the RRI workshop).

These three aspects, linked to indications of what was happening will be discussed in the following sub-sections.

7.3.1 Probing

Probing differs from questioning in that it not only involves one actor asking another actor about their opinion, it goes further in that the act of probing combines this with an attempt to understand the positioning and framing of the person being questioned along with the content of the response. Probing doesn't directly lead to broadening (which includes the uptake of more dynamics and/or more actor perspectives) but does indicate that there is a bridging event going on. The degree of probing therefore is an indication that productive interaction is occurring.

To identify the level of probing in each of the workshop, I differentiate between three forms of questioning:

> 1 – Quizzing. This is when a question is posed to get a factual answer based on a participant's expertise or experience.
>
> 2 – Asymmetric probing. This is when probing occurs but is restricted to a specific type of actor, for example a workshop on innovation where all the participants probe the world of an actor from a large firm about the behaviour and activities of his organisation.
>
> 3 – Mutual probing. This occurs when there is questioning on facts and on perspectives between a variety of actors. This provides a different dynamic than that of asymmetric probing as there is no dominant actor being probed.

Table 7.6 shows which form of questioning was visible in each CTA workshop. As is visible in the table, mutual probing occurred in three of the five workshops. Quizzing occurred in all but one of the workshops, the exception being RRI which had the most diverse mix of participants.

7.3.2 Issue articulation and recognition of dynamics

A key point in any CTA is the creation of a richer description of the topic through identifying key elements, dilemmas, issues and the forceful dynamics at play. The socio-technical scenarios added a future dimension. The evaluation question then is what actually happened in the workshops (and why). In Table 7.7 I outline the main issues that were articulated and discussed in the workshops. If issues were raised by individual participants and not taken up in the discussion, I have not included them in the list. I have also indicated next to the list whether the issues were already included in the scenarios or not.

In each workshop, there was always issue articulation, the frequency of issues did not differ greatly across the cases (there was always a flow and discussions) the types of issues did vary and is linked with various perspectives (concentric or otherwise). The table shows the types of issues that were raised in each workshop. Note that for DBS, the number of stretches (Table 7.8) does not seem to match the number of issues presented in table 7.7. This is because the stretches are shown chronologically, but the issues are gathered together (in DBS the new stretches returned to issues discussed earlier).

	Quizzing	Asymmetric Probing	Mutual Probing
CellChip	**Yes** Quizzing occurred in the session before lunch. This was partly due to the setup of the workshop, where the organisers tried to structure the interactions around the scenarios and the multipath maps. The stretches that emerged were based on quizzing. For example in stretches 3 and 4 there is a collective building of a richer picture, with agreements or mild disagreements. The participants spoke in the morning session in a manner of imparting knowledge, as if informing the organisers.	**No.** There were only two types of enactors, small firms and researchers and thus no dominating actor.	**No/Limited.** The homogeneity of the group meant that the worlds were more or less known. Specific experiences of individuals were explored. After lunch when there was a reconfiguration of the seating, and a topic was targeted for joint exploration, when discussing the hypothetical application of gene diagnostic and therapy on a chip, difference of opinions were made clearer and probing of each other's experiences in the macro world were shared.
siRNA	**Yes.** There was a lot of quizzing especially before lunch. In Stretch 1 there is quizzing between the participants in the round of introduction. During this extended round of introductions there is no	**No.** There was no dominating group, including the resear chers themselves, which were diverse.	**Yes.** Probing began after the extended round of introductions in stretch 2 (initiated by a firm to researchers). In stretch 3 for example, a medical doctor probes the world of some of the researchers.
MolMach	**Yes.** In the presentation and between the "guest" research participants and CEMES	**Yes.** The non-enact ors attempted to probe the world of the relatively homo genous enactors.	**No.** There were a few attempts in stretch 1 after a long discussion of the effects of images on the general public, a sociologist asks why nanoscientists want public attention, but gets no response.

RRI	**No.** There was little quizzing.	**Yes.** In stretch 4 there is some asymmetric probing as participants probe the two of their company who are involved in the ETP-Nanomedicine. This led to a large stretch of the discussion and you can see the shift in discussion dynamic to asymmetry.	**Yes.** Lots of probing. Some examples include stretch 1 where the labour organisation probes the industry association on interpretation of responsibility. In stretch 2 there is probing across a boundary between participants on the role of soft law (c.f. the discussion of good and bad guys).
DBS	**Yes/limited**	**No.** There was no dominating group. However [KM] a representative of a large multi-national medical device manufacturer did speak often on the behalf of large firms.	**Yes.** There was substantial probing in this meeting, in terms of firms and how they determine product platform strategies (especially from neurosurgeons who probed about the reasoning behind the asymmetry between technical advances in research, and what they could actually buy on the market. Junior researchers probed the speculation boundaries of large firms. The senior researcher probed the firms on the role of small and large firms and their relationship with researchers in R&D. Also mutual probing on issues of ethics and hype (especially in stretch 11).

Table 7.7: Issue articulation

	Major issues articulated in the workshop	Included in the scenarios?
CellChip	Promise of lab-on-a-chip platforms persists (even though they have not materialised over the past 18 years)	Yes
	The technical elements (for the system) are there but needs to be integrated though alignment around a killer application, coordination and resources – all three are lacking.	Yes
	Does the potential coordination activity focus on creating a flexible platform or on a specific killer application?	Yes
	Currently potential applications are poorly articulated.	No
	Anticipated ethical issues around certain potential applications shape what lab-on-a-chip options are feasible.	Yes
	Who or what can be the alignment actor in the creation of a lab-on-a-chip device and value chain?	No
siRNA	Changing requirements on PhD (and other) researchers Patent as well as publications in a system geared towards peer-review	Yes
	How much to promise? Where are the lines to be drawn on hyping?	Yes
	Infrastructure for patenting and commercialising not sufficient currently in universities. Also training for this.	No
	Hype strategies are different for research and for innovation contexts. Need to be aware if this when researchers become innovators.	No
	When to explore, when to exploit?	Yes
	Regulatory loopholes. Advantage or disadvantage for R&D.	Yes
	Good laboratory practice needed if university researchers begin to develop.	No
MolMach	Circulation of images, between scientific communities can shape the outcome of research, including research agendas	Yes
	Misrepresenting/misleading images designed for the general public. When does "dumming down" become a	No

	deception?	
	There are parallels, such as in lab-on-a-chip were visionary images persist and shape the direction of the field.	No
	Reduction in the complexity (e.g.in Scenario 1) enables communication but is somewhat misleading. How to handle this tension?	Yes
	Interpretation of an image may differ across communities (including different scientific communities).	Yes
RRI	Role (strength) of public agencies in the governance of nano	Yes
	Where does the responsibility for toxicity assessment lie? With the manufacturers of nanomaterials?	No
	Monitoring compliance with standards and codes of conduct are a challenge	Yes
	There is asymmetry in evaluating potential risk and potential benefit	No
	There is anticipatory coordination of governance arrangements	Yes
	If enactors engage with selectors to set agendas, can enactors change them without consulting the selectors once more? An issue of the ethics of engagement.	No
	Where is the location of nanotechnology responsibility in a nanoenabled value chain? Nano is but one part of a system of components, when is it nano?	No
DBS	Researchers have to promise big leaps, even though their main contribution will be in the many small steps.	No
	Where does the money for incremental innovation come from? Is this a major issue in an age of focussing on rapid radical innovation?	No
	Lots of niche patient groups are candidates for DBS. One knowledgeable participant mentioned that large medical device manufacturers go for broad platform suitable (but not optimised for) a wide selection of niche applications. Difficult to prove good ROI on niche markets.	No
	There is a "waiting game": large firms waiting for breakthroughs and not going for them themselves.	No
	Improved technologies for surgery can mean more resources (inc time) required. Treatment cost analysis – must include all aspects (this is a major challenge)	Yes

	including logistics during and after treatment. Neurosurgeons have sensible reluctance towards the new tech. Surgeons need to trust new therapies	
	Mismatch of expectations (patients believe sci-fi, can lead to disappointment and in some cases to aggression when they believe you are not giving them access to all options)	Yes
	Labels such as "brain chips" get taken up by actors and create their own reality.	Yes
	There are different planning frames Researchers (10 years +) large firms 2-5 years. How can you manage this when planning paths to follow.	No

7.3.3 The flow of the discussion

Keeping the discussion and exchange alive is part of a productive CTA-workshop. The organisers must stimulate discussion, but also allow it to flow on its own, allowing issues to be brought to light by participants themselves. The animator can intervene if the flow of discussion is stalling, or goes in an unproductive direction. The challenge for the animator is to assess correctly what stalling of the discussion means. Is it that a topic is not considered relevant enough; or that mutual probing has been so successful as to have led to recognition of possible counterproductive effects? Decisions have to be made during the discussions, about allowing stretches to unfold, keeping the discussion on the general track of the topic of the workshop, but allowing room for manoeuvre.

Table 7.8 summarises the flow of discussion for each of the workshops. A new stretch can be initiated by the organizers (O) or a participant (P). As to the further coding: When a + is added, there is active take-up, when a – is added, there is little take-up

Table 7.8: The flow of the discussions in the workshop

CellChip	**Overall flow of the discussion:** The flow of the discussion before lunch was somewhat strained. Quizzing dominated. After lunch, participants started initiating stretches when there was a shift from a situation of "expert providing information" (before lunch) to "participant in an exploratory process"**.** Not everybody was involved in the discussion, 4 persons remained relatively silent. **Emergence of stretches:** O/O/P+/P+/O/P+/P In the morning session, the stretches were stimulated by the organizers. This was somewhat due to the confusion of the participants to the role they should play. Only enactors were present and concentric style problem solving was expected. **Did attempts by the organizers to intervene work out?** The organizers had to trigger stretches of discussion in the morning session. The afternoon session was particularly animated. Soon after lunch the discussion started to move away from ELSA and societal embedment issues (of gene analysis on a chip) to innovation challenges. The organisers decided to go with the flow (away from the explicit broadening opportunity of ELSA and societal embedment discussions) and move towards innovation processes (with the hope of implicit broadening in the animation of the discussion).
siRNA	**Overall flow of the discussion:** The flow of the discussion before lunch was based on a round of introductions combined with comments on the scenarios and the context of the workshop. There were lots of comments and everybody got involved in the discussion. **Emergence of stretches:** O+/P+/O+/O+/O+ The general pattern was that the organisers stimulated a stretch, but that this was soon taken up by the participants. **Did attempts by the organizers to intervene work out?** Yes. Perhaps too much so, very few participants initiated stretches.
MolMach	**Overall flow of the discussion:** The flow of the discussion was somewhat limited. The setup of the workshop was different to the other four workshops in that there were two technical presentations and two small CTA sessions, on either side of lunch. **Emergence of stretches:** O+/O+/P+ Few stretches and mostly from the organisers. **Did attempts by the organizers to intervene work out?** No. The organizers

	attempts to open up the discussion based around imaging strategies were not picked up fully.
RRI	**Overall flow of the discussion:** Very good. Everybody got involved in the discussion, and lots of probing. **Emergence of stretches:** O+/P+/P+/O+/O+ Initiation of stretches by organizers and participants were taken up and run with. **Did attempts by the organizers to intervene work out?** Yes.
DBS	**Overall flow of the discussion:** There were a lot of small stretches in this workshop, partly because of the diversity and the willingness to bring up information for the discussion (almost everyone excepting the shy junior researchers) got involved. **Emergence of stretches:** P+/P+/P+/P+/O-/P+/O/P+/P+/P+/O+/P-/P/P/O+/O+/O Mostly participant led. This workshop was co-organized with a lead partner, and thus the main nanoscientist there had invited some of the participants. The discussion did go into broader details, but often with recourse to the concentric model, and many stretches were based around this (broadened) concentric framing. **Did attempts by the organizers to intervene work out?** No. Of particular note was the lack of effect of direct shifting of discussions. In Stretch 5 (O-) [AR] linked the discussion with dynamics with only short responses. [DR] following on from this had little luck when discussion dynamics, when a participant returned to an earlier stretch on product development strategies. Again between stretch 9 and 10 there was an attempt by the organisers to discuss dynamics explicitly, which was not taken up.

7.4 Were these CTA-projects productive?

In Chapter 1, the original, and programmatic, aim of CTA to support reflexive co-evolution by including more dynamics and more actors, was further articulated to enable the development and execution of empirical CTA for newly emerging technologies, for which enactors (and in my case specifically Frontiers nanoscientists and nanotechnologists) are the most prominent actors.

Any CTA approach should provide an opportunity to encounter more perspectives and more dynamics. For a workshop setting, this means representing the macrocosm of actual socio-technical dynamics in the real-world into the microcosm of a workshop.

For my role as CTA agent in the nanoworld, translating this global CTA aim to the specifics of supporting enactors in their involvement in reflexive co-evolution, leads to two (still broad) objectives:

> (A) Develop a CTA support system to provide an environment for interaction between actors and (a) other actors and (b) issues within their and other's actor-worlds, amidst broader co-evolutionary processes
>
> (B) Develop a CTA support system which acts as a platform for broadening the concentric bias[81]

Broadening the concentric bias may occur at anytime in the CTA-project, it may be temporary or it may persist. To find out about eventual persistence, post-workshop interaction with the participants is necessary. But this turned out to be difficult; they were distributed across many countries, and had varying degrees of enthusiasm in participating in follow up discussions. For most of the participants, the CTA project was equal to the workshop and thus my own interest in the impact of the workshop and of our interactions was second to their own benefit taken from the workshop. In addition, attribution of eventual broadening to the workshop experience is not simple. Many of the participants engaged in other outreach, ELSA, and TA–type activities which would contribute to broadening their perspective.

In this section I will focus on the productivity of the CTA-projects in terms of process, by assessing how (if) they were successful in creating a microcosm adequate to the real-world, and in creating an arena for bridging.

[81] This does not mean to say that enactors should broaden their concentric perspective all the time; in fact the concentric perspective provides certain advantages for enacting technologies. However, reflexive co-evolution can be augmented if enactors are aware of broader dynamics and can locate actor strategies and co-evolutionary dynamics to create "broadened" concentric strategies.

7.4.1 The representation of the macrocosm in the microcosm of a workshop

The aim is to provide the participants in the workshop the opportunity to explore the macrocosm more easily than they normally do limited as they are in their roles in the real-world. This is relevant for nanoscientists who rarely see in detail the activities and value of co-evolution from the perspective of other actors. Most of the partners in Frontiers had limited knowledge of the world outside of nanotechnology research.

For the CTA-project to be productive, it should thus start by providing a richer and more coherent picture of the actor arrangements and entanglements and its potential development. This was done in the preparation, including the construction of scenarios that reflect relevant actor-strategies. One question then is whether this was recognized. I take as an indication the recognition of broader macrocosm dynamics (as available in the preparatory material) during the workshop. This is an interpretative question, because it relates to situation and context, and my experience in preparing the workshop is one input.

The CellChip workshop was a pilot workshop, and the focus on dynamics was restricted to the world of enactors (the concentric bias still remained even if it was reduced through the recognition of feedback loops, forks in the road, multiple paths etc.). The CellChip workshop was only comprised of enactors, the material provided focused on making more explicit the dynamics within the world of enactors through scenarios, multipath maps and innovation chain diagrams. During the workshop there was little reference to non-enactor frames.

The MolMach workshop had limited macrocosm – microcosm linking as well, but for other reasons. It was an enactor dominated workshop. More importantly, in the negotiation phase of the workshop, there was active reduction of the issues by the key Frontiers partner to a specific issue, communication to the public, and from the physicist's perspective on molecular machines (mono-molecular machines on a surface). In spite of my negotiations about other perspectives, these would not be represented in the workshop, although I did include them in the scenarios. While the macrocosm was included in the preparatory material, and the animator and moderator attempted to create openings for discussions of broader issues, these were not taken up in the workshop.

	(a) Recognition of dynamics of the macrocosm in starting concept by key Frontiers partner	(b) Macrocosm dynamics included in the preparatory material	(c) Macrocosm dynamics recognised in workshop discussions
CellChip	Not  applicable		
siRNA			
MolMach			
RRI	Not  applicable		
DBS			

Table 7.9: Representing the macrocosm in the workshop setting. CellChip is shaded grey since it was a special case (a pilot). "Not applicable" indicates that negotiations were conducted with the Board of Frontiers, rather than the key partner for the workshop

From this brief discussion, it is clear that three variables should be considered when one tries to explain the outcome. Participant composition (if enactors dominate, the link with macrocosm may be backgrounded), starting conditions (in particular negotiation of the scope of the workshop), and the "flow" of the workshop as orchestrated by the moderator.

Participant composition is not an explanation. Also in the positive cases of siRNA and DBS, there were no less than 66% enactors. The difference derives from what became clear in the negotiation phase. As is clear from Appendix 2 (siRNA) and Appendix 5 (DBS) the key Frontiers partner was willing to discuss broader aspects (even if they were unarticulated and the person involved acknowledged a lack of knowledge/understanding). Also, I made a day-long visit to negotiate, interact and

co-develop a project that would be mutually interesting, allowing some probing and learning to take place already at the initiation of the CTA process. For the CellChip case and the RRI case there were no key Frontiers actors to interact with, and negotiation was at the level of the Frontiers Management Team.

The role of animator/moderator, however important for the actual flow of the workshop, did not appear to make a systematic difference. In the MolMach case, animator interventions did not work out; in the CellChip case it was mixed. In the DBS case, animator interventions did not work out, yet macrocosm dynamics were recognized in the workshop.

7.4.2 An arena for bridging?

The bridging dynamics that we orchestrate for include (a) probing and (b) issue articulation. A further element (c) is maintaining a healthy flow of discussion, allowing threads of conversation to emerge, as well as motivating those who do not participate. This is, of course, best practice of general workshop moderation, but takes a specific form because moderation now also draws on insights in the substance of the issues.

(A) Probing and quizzing

For each CTA project, the intention was to have a mix of actors that would reflect the dynamics in the macrocosm and support the reflexive co-evolution through enabling mutual probing between the various actors. The actual participant mix differed across the cases, so one can trace possible effects even if the workshops were not organized to have systematic variation on the dimension of the participant mix (it became a natural experiment).

Drawing on Tables 7.5 (composition of participants) and Table 7.6 (presence of probing) a 2x2 matrix can be constructed.

Clearly, homogeneity in the participant mix is linked to absence of probing and heterogeneity is linked to presence of probing. Why would this be the case? It is not automatic that heterogeneity leads to more probing: too much heterogeneity may make productive communication difficult. One could speak of optimal

heterogeneity, somewhere between homogeneity and extreme heterogeneity.[82] The location of the "optimum" would of course depend on the situation and the forcefields. The preparatory material will also play a role.

		Presence of mutual probing	
		No	Yes
Participant Mix	Homogenous	MolMach, CellChip	
	Heterogeneous		RRI, DBS, siRNA

Figure 1: Participant mix and presence of probing

Absence of probing when there is a homogenous participant mix is not the only explanatory factor. In a CTA workshop on Organic Large Area Electronics in Heidelberg, organized by another PhD student in the TA NanoNed programme, Alireza Parandian, there was homogeneity and participants knew each other. But there was also probing, because the topics of discussion prepared in the scenarios were ones they didn't usually talk about

Probing combines an attempt to understand the position and framing of the person being questioned along with the content of the response. This more than just quizzing (see 7.3.1). As a check, I also create a 2x2 matrix for quizzing.

Quizzing occurred in all workshops except in the RRI workshop. The topic there was governance in relation to risks and responsibilities, which invited probing, and made simple quizzing about specifics less interesting.

[82] Thus, there would be an inverted U-curve for extent of probing. Such an analysis, but then for innovation, has been made for innovation (Nooteboom 1999), and Garraway (2007) has applied this to interaction between different communities of practice, and added the idea of a 'learning space' that can emerge.

		Presence of Quizzing	
		No	Yes
Participant Mix	Homogenous		MolMach, CellChip
	Heterogeneous	RRI	DBS, siRNA

Figure 2: Participant mix and presence of quizzing

(B) Issue articulation and recognition of co-evolutionary dynamics

Issue articulation was important for workshop participants (cf. 7.3 + my comment to the Table there), that was what they wanted to do because there was something at stake for them. The frequency of issue articulation was more or less the same for all workshops. In order to trace effects, if any, of the preparation and orchestration of the workshops, I can differentiate between issues that were visible already in the preparatory material and those which weren't (cf. Table in 7.3). This is not a simple measure, though. Participants may not have read the scenarios (some of them took part at a late stage only), or read them only perfunctorily. So the issues that they articulated might have come from them, rather than from the preparatory material. Still, we can explore possible explanations for the extent of new issue articulation. The mix of participants does not appear to play a role (Figure 3):

An intervening variable, the intervention of the organizers during the workshop, may explain part of the outcome. For MolMach and siRNA, the organizers asked the participants to comment on the scenarios during the workshop (siRNA during the round of introductions, MolMach after lunch), and thus induced issue articulation as visible already in the preparatory material. What remains is the question what the results for the other three workshops mean. Were there important issues for participants who for one reason or another were not taken up in the preparatory materials? Was that a limitation that should be corrected when applying the methodology in the future?

		Amount of issues that were not in preparatory material	
		<50%	>50%
Participant Mix	Homogenous	MolMach	CellChip
	Heterogeneous	siRNA	RRI, DBS

Figure 3: Participant mix and additional issue articulation

Another take on insights achieved in the workshop is the recognition of co-evolutionary dynamics. Figure 4 shows the correlation between co-evolutionary dynamics mentioned by participants and the reference to preparatory material.

		Co-evolutionary dynamics mentioned by participants?	
		No	Yes
Reference to preparatory material by participants?	No	CellChip, MolMach	
	Yes		DBS, RRI, siRNA

Figure 4: Reference to preparatory material and mention of co-evolutionary dynamics

The first-round interpretation of this finding is that participants actually needed the preparatory materials to recognize co-evolutionary dynamics. By themselves, they would be limited by their various enactor perspectives. For the CellChip workshop, the preparatory materials did not push co-evolutionary dynamics, so there were no incentives. For the MolMach workshop, the scenarios did emphasize co-evolution, but there was active resistance against such insights.

(C) Flow of discussion

The flow of discussion is an important element in and of itself. A characterization of the flow in terms of stretches was offered in Table 7.8. These are the result of interactions among the participants, in combination with the moderator's and expert CTA agent's role to animate and moderate the discussion, reacting in real-time, allowing stretches of conversation to continue (go-with-the-flow) or intervening (bringing in a new topic or quizzing a participant).

Stretches of discussion emerge, gel and become temporary platforms for probing and quizzing. How long this last depends on the interactions between the participants and the reactions of the moderator of the workshops. The activity of the moderator within the workshops was also aimed at stimulating discussion on broader topics, like co-evolutionary dynamics and what I called entanglements (Chapter 1, Chapter 6). The Table below focuses on interventions and their effects.

CellChip	This workshop was formed around the world of enactors, and so there was no intervention in opening up stretches of conversations of co-evolution
siRNA	Interventions were successful, although much of the moderator's action was to go with the flow
MolMach	Interventions by the moderator and animator did not lead to stretches related to co-evolution
RRI	Interventions were successful, although much of the strategy was to go with the flow
DBS	There was a lot of interaction, and lots of small stretches. Interventions did not work out by the animator and moderator.

These interventions can be traced in more detail in the reports of the workshops in the Appendices. No simple causal links can be established between such interventions and probing and issue articulation. The moderator creates affordances; it is up to the participants what to do with them.

7.5 Broadening and reflections on methodology

I have explored the productivity of the CTA projects in process terms, analyzing how they supported bridging, raised awareness about broader dynamics and issues, and were able to link up with the macrocosm of nanotechnology development. On these accounts, my evaluation is generally positive, and lessons, up to guidelines for further application of the approach could be specified.

The overall aim of the CTA-projects was to provide an opportunity for broadening the concentric bias that comes with the enactor perspective. Some indications of broadening may be visible in and through the conversations, in the positioning and probing in the CTA workshops.

Broadening entails an exploration of possible new linkages beyond one's own perspective. The CTA workshops were tailored to support broadening of enactors' worlds, so broadening would be the articulation and exploration of linkages (and their dynamics) outside of the enactor perspective, such as user demands, and issues of political and societal acceptability. Broadening enactors' perspectives is more than improving the enactment processes of getting a specified technology embedded into (a now more specified) society, it also incorporates an understanding of the values of other actors, and the perspectives they have (this is facilitated by probing, and can be an occasion to explore new linkages). The CTA-projects should contribute to this.

Capturing indications of these effects in the real world is difficult. An interview directly after the workshop will not suffice, since it will only show the intra-mural effect of the workshop. It requires some time to trace actual uptake in perspectives and diagnoses of actors, and their eventual choices in their institutional and other contexts. Then there is the problem of attribution. Nanoscientists feel pressures to engage in activities such as ELSA, and engage in anticipatory coordination. Also, the participants in the workshops will participate in other events and meetings, and one cannot disentangle what are the sources for their positioning and action. They themselves will be hard put to link elements from the CTA workshop to specific

decisions they make. They continue to also live in the macro-level nano world, and will attribute their insights to various circumstances and events.

So how can one capture the impact on broadening? One way is to trace from the initial starting conditions of each workshop, how actors positioned themselves, articulate issues and were aware of dynamics and how that changed during the process of the CTA and somewhat after.

There are limitations, not all participants could be contacted or had time to be involved in follow up. The limited data that I have are anecdotal evidence, but such evidence is a "window on the [nano-] world" and is plausible because of the story it tells (Rip 2003). I start with two exhibits where I tell the stories of two participants.

Exhibit 1:

[HK] was the key actor in the siRNA CTA project, with which I negotiated the project scope. My first interaction with [HK] was in the iNANO autumn school in 2004 (see 6.2 Stretch 1), where he gave a general presentation on the promise of drug delivery which followed a typical enactor approach – he identified functional requirements of a drug delivery system that would be effective on the body. In our next meeting in Sicily (see 6.2 Stretch 5) we had further discussions, were he positioned his interest as foresight where the objective a would be to explore the right path to clinics for the technology.

As part of the eventual CTA-project, I visited Aarhus (the potential host of the CTA workshop) and discussed with [HK] the first evening in a restaurant (as reported in Appendix 2). [HK] found it difficult to get a handle on the way I was framing the pathway from laboratory research to clinics. We continued the following day, and at first the visible differences in perspective remained. I presented some representations (aggregations of my first desk research in drug delivery, see Appendix 2, Figure 1) to discuss the potential CTA project. In the course of that day, [HK] started using these representations to frame his introductions of me to others, and in the brainstorming of potential topics for the workshop.

During the workshop itself [HK] brought up a number of issues, perspectives and dynamics that he had found difficult to get a handle on during my earlier visit to Aarhus. He drew on the scenarios to discuss hype strategies, the challenge of balancing exploration/exploitation and of regulation in relation to the speed of translation of lab research into clinics (see Stretch 1 of the workshop report in

Appendix 4). He drew on these elements throughout the workshop, in responding to quizzing and probing and in presenting his position (Stretches 3 and 4).

Immediately after the workshop, I had discussions with [HK] and he was satisfied with the "interesting discussions", and when I prompted him further about actual items, he mentioned that it was difficult to identify specific issues (although he waved a few sheets of papers of notes).

Post workshop, I had the opportunity to have substantial interaction with [HK] through email, and then on two occasions during trips to Denmark as part of my insertion activities (see 6.2 Stretches 9 & 10). By this time, his research group had expanded their research portfolio, were developing two spin-out entities, and participating in a number of networks. We discussed the exploration/exploitation issues, the perspectives of patients and how he and the group were dealing with this. What struck me during these discussions, was the ease in which [HK] could position the issues. He didn't mention the findings from the CTA project, but framed his descriptions of the activities of the RIGHT Network of Excellence (focusing on siRNA research) and plans for a new R&D consortium together with firms (which I cannot detail here) in the terms that he had started to use in the CTA project .

He certainly had broadened his perspective since I first met him, since my workshop; however, he had participated in a number of networks, and met more nanoscientist dealing with nanomedicine, so it is difficult to unambiguously position the broadening as impact of the workshop.

Exhibit 2:

Similar effects were visible in another case. [AW], of start-up company Medimate, was a former Masters student from MESA+ who, with the assistance of a star scientist in MESA+ had acquired some funding to commercialize a microfluidics technology concept from MESA+ into a platform to develop sensors to measure electrolyte concentrations. The company was officially founded and registered with the chamber of commerce only 4 months before the workshop.

During the workshop [AW] participated actively in the discussions, quizzing the more mature firms, and the senior scientists present. Immediately after the workshop, he used ideas from the workshop (multipath mapping, and various platform strategies) to develop his own maps and diagrams about how to (A) have an open-ended roadmap given the flexible platform, and (B) how to identify non-

technological aspects – he had taken the multipath mapping idea further than presented in the workshop, and used it to articulate issues and challenges (one of the first multipath maps for Medimate is shown in 6.2, Stretch 3). Of course, this was a concentric approach but a broadened one. I interacted with [AW] regularly for a year after the workshop (and continued to meet him during my insertion activities). Post workshop, he began expanding his interactions with potential intermediaries and users where other electrolytes than lithium (sodium or potassium) were to be measured. He began linking up with other social scientists, and set up Masters Projects with industrial design students to design user interfaces for his device etc.

To date Medimate has a core technology, a spin out company and a network of social scientists and designers exploring and feeding back insights. They could ally themselves with health insurance company Achmea to create a trial at the Trimbos Institute (the National Institute of Mental Health and Addiction in the Netherlands). Also, in an innovative move, they established an advisory board of societal stakeholders. If you ask [AW] about impact of the CTA project, he will show the multi-path map, which framed a lot of the early strategy of Medimate and lead to certain entanglements. Another aspect was becoming sensitized to CTA-agents and social scientists, because these had created opportunities for [AW] to probe and learn other perspectives and make them work for his (essentially) concentric approach.[83]

In these two Exhibits, I tell a complete story. There are also partial stories to tell, for example about early indications of broadening within the "walls" of the workshop setting. An example occurred in the RRI workshop where (in Stretch 4) [RvdW] shifts from his original stance about incorporating more comparative selectors (especially patient groups) and about European Technology Platform Nanomedicine as a lubricant to ease mobilisation of funding (complying with some of the criteria of the European Commission) to a reconsideration of the issues. [RvdW] had been confronted in that Stretch with different perspectives, one of comparative selectors, through reference to patient groups which were involved in

[83] I say essential here to emphasize for such small firms, their survival is paramount. That [AW} spent a substantial amount of his time in engaging with broader aspects (through participating in workshops and meeting, not just my CTA project) reveals the importance he place on this.

agenda setting and agreed to certain roads in the roadmap, and one of enactors, where coordination within ETP Nanomedicine reduced the risks of open- R&D.

Another partial story about broadening plays out at the meso-level. A large number of nanoscientists in Frontiers, seeing the CTA-programme and following (albeit passively) the development of the programme could link up with broader changes in the nano landscape. One example is the way a very critical nanoscientist (from Stuttgart) after my presentation in Karlsruhe (see 6.2, Stretch 2). He thought that social scientists were "fanning the flames" of public interference with research. When I met him later, in the Sicily meeting of Frontiers (see 6.2 Stretch 5) he approached me and began describing his concerns about how to discuss/describe his research to audiences outside of the technology domain. "How will the public or NGOs read my research? Especially when I work with viruses on self assembly!" The issues he was raising were present in the nanoworld, before our discussion, but I became a focal point for articulating the issues and sensitizing him to them. This actually led to further interactions up to a chapter in a joint conference proceedings on Vision and Image Assessment as part of (or preparation for) public engagement about nano self-assembly with Tobacco-Mosaic Viruses.

Reflections

CTA can create broadening, modestly, so much is clear. It can also have an effect on framing conditions, in particular in and through the Network of Excellence Frontiers. Frontiers could eventually locate CTA and appreciate it as being relevant, up to promoting it in the continuation of Frontiers together with Nano2life. Of course, this is not only due to the modest contribution I made in the CTA projects, but also relates to changing circumstances (compare the pressures that I identified in Chapter 1). This is part of the overall co-evolution of technology and society, the backdrop against which I located my CTA projects as contributing to the co-evolution becoming more reflexive.

Having noted this, further questions can be raised. One immediate question is whether external pressures had created a window for modulating enactment processes which will close again after achieving a modest amount of reflexivity in the co-evolution. This would apply to embedded CTA projects which are now accepted in the bionanotechnology world of NaBiA (see Chapter 6), but also to integration of ELSA and anticipation of societal aspects in nanotechnology research proposals.

Emerging technologies like nanoscience and nanotechnology are still in flux, and the enactors try to get a grasp of what is happening and which directions to go. This was clear in how they take up results from CTA projects: they appreciate tools that help them to structure the future and broadening is a side-effect (cf. the two Exhibits above). In my CTA projects I have been willing to support this enactor's perspective, and had developed tools that could be used for that purpose.

This leads to another question, about strategy for doing CTA projects, now and in the future. I have to come back to this question in the concluding Chapter 8; here I focus on the methodological aspect.

There is a trade-off between insertion (and thus closeness to ongoing developments) and purity (so as to reach clear conclusions, but perhaps of limited scope). An independent-CTA activity (as opposed to one embedded in the nanoworld) could perhaps spend more time in preparation and in the gathering of participants (including interviewing all potential participants beforehand). There would be less pressure to follow a timeline and less restrictions on choice of participants – which would also help in evaluation, for example of learning because differences in insight and positioning of each participant before and after CTA workshops could be ascertained. Such context-independent-CTA would allow for the systematic evaluation of broadening as it occurred during and immediately after the workshops. It would also depend on whatever individual participants might do later for effects on the processes of nanotechnology development. Insertion of CTA projects (and of the CTA agents) in the nano-world will be exposed to (suffer from, but also encounter opportunities in) the contingencies of embedding. Broader effects of institutionalizing CTA-based support of nanotechnology developments can be realized that way – at the price of having to be modest, and (in terms introduced in the beginning of Chapter 6) follow fit strategies with only occasional attempts at stretch strategies.

Chapter 8 Conclusions and reflections

The overall approach to Constructive TA that I advocated and developed is captured by the four research themes outlined in Chapter 1

Research Theme 1: Exploring the dynamics and patterns that are part of the emergence of nanotechnologies (in real time) with a view to understanding enactment processes (cycles) and how they shape the emerging development pathways of nanotechnology

Research Theme 2: Developing tools to support controlled speculation on the co-evolution of nanotechnology and its embedment into (or rejection by) society

Research Theme 3: Designing of productive bridging events, embedded in the ongoing activities of nanotechnologists, and with an emphasis on anticipatory technology assessment and strategy articulation.

Research Theme 4: Orchestrating and subsequently evaluating such events, structured around controlled speculation and relevant dimensions of bridging.

I have shown that this approach is doable. And in doing so, I created two types of findings. First, I developed tools (cf. Research Theme 2) as shown in Chapters 2-5, and showed actual and possible dynamics and patterns in emerging nanotechnology (cf. Research Theme 1). The latter is visible in Chapter 2 and in the fifteen scenarios which are given in full in the appendices (see also Chapter 5 for a discussion of building complex scenarios). Second, I designed and orchestrated dedicated bridging events and identified evaluation dimensions (cf. Research Themes 3 and 4). I also traced the larger and evolving context of which they were part through my experiences as a CTA agent inserting himself in the world of emerging nanotechnology (see Chapter 6).

What I did can be positioned as “experiments in interactions”. The dedicated bridging events were experiments in interactions, among the participants but also with the CTA agents. I was able to show that some of the intended processes and outcomes occurred, even if there are no simple recipes to produce them. While the

experimental phase of this methodology is now concluded – one can specify the steps and the tools and the guidelines (as I will do in section 8.1), and others can use them (and have been doing so already, e.g. in other projects in the TA NanoNed programme, and elsewhere) – in a sense every application will (and should) remain an experiment in interactions.

There is another sense to "experiments in interactions" in this study. As I noted when articulating my research approaches, a deeper understanding of the nanotechnology world requires (real-time) analysis of nanotechnology emergence, and the embedding of Constructive TA in the ongoing developments of nanotechnology requires insertion in the world of nanotechnology development. This indicated an experimental approach, but not in the sense of creating controlled conditions and trying out variations to see what happens. It was experimenting by moving about, observing and probing, being visible as an interested visitor and getting reactions. Thus, there were experiments in interactions which produced data and insights and allowed diagnosis. The latter is where this "methodology" clearly differs from participant observation. I put quotes around methodology here because it did not start as a fully-fledged methodology positioned with respect to other methodologies in the literature. My experiences and reflection on them have turned into a methodology (now without quotes), and I will offer brief considerations on the methodology in 8.2 which build on what I presented already in Chapter 1.3.

Looking back at my experiences and results, I can now also offer some insights in the co-evolution of nanotechnology and society, the backdrop which motivated and informed my CTA study (Chapter 1.1), and reflect on the role of CTA agents in this co-evolution.

8.1 How to do CTA of emerging technologies

The philosophy behind previous (and mostly programmatic) writings on Constructive TA (van den Belt & Rip 1987, Schot & Rip 1997, Schot & Rip 2001) has at its core the analysis of dynamics and actor-networks (of technology emergence and co-evolution), speculation of future co-evolutions and the feedback of these insights into the processes of co-evolution. In this way Constructive TA would add more (knowledge about) dynamics into the development of a new technology and in this way support reflexive co-evolution. Another (related) element was to include more actors at the early stages of development to broaden design processes at early stages by bringing in various perspectives and knowledge about different stages and processes of co-evolution (including the societal robustness of a new technology). An approach proposed in Schot and Rip 1997

was to do this by supporting interactions between the technology developers and a variety of other actors (such as societal actors). In this way Constructive TA was to add more (knowledge about) dynamics into the development of a new technology and in this way support reflexive co-evolution.

The steps of actually ***doing Constructive TA*** have not been made clear in the literature to-date, particularly so for newly emerging technologies such as nanotechnology. Both capturing the elements and dynamics of the newly emerging field, and identifying the actors (and potential actors) have not been detailed. On top of this, the mechanisms of feedback into the ongoing developments of technology development had not been explored or developed.

In Chapter 1 to fill these lacunae (and others) I proposed to explore how to do ***empirical*** Constructive TA. I took the opportunity of investigating in real-time the field of nanotechnology as an occasion to develop the Constructive TA approach for the particular context of newly emerging technologies.

I originally stated that Constructive TA has three components: (1) analysis and diagnosis of ongoing developments, including expectations about embedding in society; (2) anticipation on further developments and their embedding in society; (3) feedback of insights into ongoing discussions and choices. These I explored through five CTA experiments, embedded in the Frontiers Network of Excellence. Each experiment was developed and executed in four steps, the details of which are given in the appendices and compared in Chapter 7.

After five embedded CTA experiments, what guidelines can I provide for those wishing to do CTA for newly emerging technologies?
The table below gives an indication of the activities related to each step in the CTA process and the experience and guidelines this has provided (which I will further outline in the rest of this section).

Step in CTA experiments	What this meant in practice	Related experience and guidelines (I will present in this section)
(i) Initiation of the project	This required the diagnosis and locating oneself strategically and tactically in the macrocosm of nanotechnology developments, a preliminary selection of the topic and scope, aligning of interests (and shifts in topic/scope), mobilizing participants, facing contingencies	8.1.1 Participant composition and working with contingencies
(ii) Preparation of the CTA 'bridging event'	This required socio-technical mapping, preparing for microcosm by gathering participants (also in step 1), preparing scenarios and other support material	8.1.2 Socio-technical scenarios and other support material
(iii) Execution of the CTA 'bridging event'	This required organizing and orchestrating the workshop, i.e. the microcosm (this could (and did) have different forms and processes but should (and did) remain a microcosm).	8.1.3 Interactions within workshops
(iv) Evaluation and some follow-up	Required analysis of step 1 through step 3 and insertion in both the Frontiers Network of Excellence and the world of nanotechnology development more broadly, to capture indications of uptake and broadening.	8.1.4 Broadening enactment cycles and the (modest) change aim of CTA

Experiences and guidelines

8.1.1 Participant composition and working with contingencies

In my experiments with CTA, I focused on the nanoworld and inserted a programme of CTA projects within an R&D network, to (A) be close to the actual

activities of nanoscientists and (B) to link in to the actual activities (providing a support tool for broadening enactment processes).

CTA involves actors. But which actors should be involved is dependent on the location and scope of the subject of CTA. One can choose these by identifying the key actors in the emerging socio-technical network or identifying the key target group of your CTA (enactors, comparative selectors, third parties etc.).

Actors may not wish to become involved. In Chapter 6 I describe an incident of neuron-computer interfacing where enactors, although interested in the CTA would not participate. Societal actors, with strong positions may not wish to participate in a forum which could reinforce one technology option and reduce the breadth of choice.

The possibility of gathering actors can also be dependent on the location of the CTA. Embedding CTA in the Frontiers network allowed getting closer to the action, but meant that I had to relinquish some control of the experiments. In particular, limitations on the diversity of actors in the workshop which is important to reflect the real world, trade-off A.

Trade-off A is linked to the contingencies of embedding CTA. There is another trade-off, trade-off B, that is a matter of orchestrating the CTA workshop and which is related to probing.

If the diversity of participants in a CTA (workshop) is limited participants feel no need to probe (bridging is not necessary). If the diversity is high, probing may become difficult and orchestrating for probing may lead to artificial situations with little bridging. For a productive bridging event there has to be optimal diversity (i.e. the dependence on diversity will have the shape of an inverted. U-curve, as Nooteboom (1999) presented for innovation and which was then taken up by Garraway (2007) and developed for interactions between different social worlds). What is optimal depends also on the field and the stage of development.

There were other strong effects of being embedded in Frontiers, in particular how short timelines were part and parcel of my life as an inserted CTA agent. This is not just an effect of the specific circumstances (my dependence on NoE Frontiers). It shows that one cannot be isolated from the realities of ongoing nano activities.[84]

[84] These included the link to its annual cycle of activities and assessments, the process of releasing resources, the nature of the management board and the decisions to support a CTA project, in kind and /or with resources. These limitations are only part of the picture, not only were resources made available, not just money for the venue and travel and accommodation for participants, but also advertisement, and inclusion in the official

One has to take them into account, in real-time, fit to the circumstances or actively stretch them to suit the goals of the CTA-agent. Even consultants doing a CTA "job" for a client have a professional responsibility to do a good job, and so stretch the situation if necessary.

Should these strong effects be avoided? And can they be avoided?

Creating a distance from the constraints of embedment would mean freedom to invite the mix of participants one would like[85] and to frame the workshop topic and scope how one would like (regardless of the interests of nano (or other) actors). But it would also create distance to ongoing dynamics. Thus, there is a trade-off.

Trade off B reveals that there will be an optimum level of heterogeneity, and the diversity and weight (relative number) of participant types will depend on the location and scope of the CTA exercise. For example, CTA embedded in the zone of comparative selection (Section 1.1.3 Figure 1) may be heavily weighted with comparative selectors (perhaps a diverse mix of them) and with limited enactors. [86] Embedding means that trade off A is dependent on the negotiation power of the CTA-agent and the circumstances in which he/she has to fit to or stretch.

8.1.2 Socio-technical scenarios and other support material

Socio-technical scenarios can be created and are productive as an input in Constructive TA type workshops. Important is the creation of scenarios that speak to what is at stake in the domain of the nano-world that is the topic of the workshop is to build on insights from insertion activities. This allows productive reduction of complexity while keeping it visible (for example, to avoid linearity in developments). It also allows to manage the risk of identifying too much with enactors so as to get them involved, but then bowing to the concentric bias of enactors who need scenarios to guide them to identify and overcome barriers to introduce "their" nanotechnology into society.

In workshops with heterogeneous composition, scenarios also provide an introduction to the situations and ongoing developments which allows participants with less involvement in the nano-world to participate more knowledgeably in the interactions. This can be a further consideration in writing up the scenarios. Also,

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programme of activities. All of which provided legitimacy for my programme, and a ***link in*** with the activities of the R&D network.

[85] Whether they would accept the invitation is another issue.

[86] Section 7.3 and 7.4 detail participant mix in my enactor weighted workshops.

when the desired heterogeneity (or mix) of participants isn't met (through various contingencies, trade-off A mentioned in the previous sub-section) socio-technical scenarios can mitigate the lack of perspectives by including them in the scenarios. Forcefields, relationships, entanglements etc. can be presented in workshop settings, and participants can react (reveal their own experience) an occasion to reflect and articulate.

It is important to put effort in creating high-quality scenarios. The scenarios should be plausible, have recognisable "anchors" for the target audience, be rich enough to provide a platform for discussion and include a number of threads and forks in the road. The latter element is important for workshop interactions. Rather than scenarios that afford the reader a binary assessment of the text (I agree with it/I don't) socio-technical scenarios are designed to open up discussion, have many different paths/stories/innovation-journeys in each scenario. Another element is to make the scenarios non-mutually exclusive. This reduces the recourse to a binary assessment of the scenarios.[87]

Creating socio-technical scenarios requires knowledge of the domain and the dynamics of its development and embedding in society. It also requires experience/expertise in constructing controlled speculation. This includes sensitivity to non-linear socio-technical dynamics, forks in the road, interactions, as well as creativity in constructing the narratives.

The preparation of socio-technical scenarios is useful for both the participants and the animators of the CTA workshops. The animator can draw on elements that are in the scenarios, the journeys that are described, etc.

I have also used various support materials: representations of elements of socio-technical dynamics like innovation chain diagrams, and tools like multi-path mapping.[88] In preparing the bridging event, such support materials can be selected and developed for presentation, but they should be used sparingly, because they

[87] Three scenarios were developed for each CTA workshop, and each of the three had elements that ran in parallel, or could equally occur in the other scenario.

[88] This tool has now been taken up elsewhere (Georgia Tech, Beijing Institute of Technology, Cardiff University for a grand challenge project). The reason is that it captures broader dynamics of co-evolution and emergence, but does so in enactor terms. It can thus be used as a soft broadening tool (also by enactors themselves). I have collaborated with those institutes mentioned above and the application of this method in other contexts has been written up (Robinson et al 2010).

can draw the attention away from the probing and interactive consideration of future developments and strategies.[89]

8.1.3 Interactions within workshops

In the interactions in workshops, stretches of conversation emerge where there is mutual reference, up to a shared topic. Such mutual reference can "gel" around a position or a question, and a stage or platform for probing emerges. Other participants start taking positions or querying positions. A clear example where suddenly a platform emerged to talk about the "good guys" and what they do occurred in Workshop 4. I quote the text in the box to show how a focus emerged which allowed mutual probing.

> **Excerpt from Appendix 4, Section 3, Stretch 2.**
>
> Unsure of what responsibility of manufacturer's means, [GdB] asks whether costs are an issue. [RvdW] responds by positioning it as depending on the one hand where there could be liability and on the other what can you achieve in a particular context. [GdB] replied that he was not talking about "good' and "bad" guys; three others [RvdW] [GM] [WdJ] emphatically replied "We are".
>
> [RvdW], underlining that his company is indeed one of the good guys, mentions that his company had "gone one step further by signing the Responsible Care Program." He also asked why all this discussion surrounds nanotechnology specifically, "responsible R&D innovation holds for everything, not just nano."
>
> [GM] stressed that "we *are* talking about good guys and bad guys and this is what codes of conduct are about." [GdB] "As a consumer I don't feel assured by value-based codes. When industry says that they are trying to do some good, I am more interested in what they are actually doing!", further underscoring his position that transparency is needed.

The moderator can sense such opportunities and stimulate them, or take a pro-active role. In the back of his mind will be notions of what is important to get out of the workshop, so while s/he tends to let the discussion flow by itself (within the

[89] If the emphasis is not on increasing reflexive co-evolution generally, but on moderate broadening of enactor agenda setting, such representations can be applied less sparingly. This was the case when the Multipath mapping approach was used in the UK EPSRC and MRC financed *Grand Challenge Project for Information Driven Health* "An innovative multidisciplinary patient-centric early detection care model" Cardiff School of Computer Science & Cardiff School of Medicine (Primary Care, Cardiology, Respiratory Disease, Diabetes)

constraints of the overall orchestration of the workshop), s/he will also give or create attention for some items rather than others.[90]

To handle this in the real-time situation of a workshop, I have found it useful (after my first workshop) to split the role of moderator up into that of moderator/animator and that of expert organiser. The moderator is responsible for the flow of the workshop, including specific CTA goals like making sure that there are opportunities for probing. The expert organiser (i.e. me) can intervene tactically and use his knowledge of the domain and of the actors and their background to make sure that important aspects do not remain invisible, or that unproductive interaction is given a productive turn. In the detailed reporting of the workshops in the Appendices a number of examples can be found.

Identifying stretches in the post-workshop analysis is a useful way of observing the "gelling" around a specific topic in a discussion. Quizzing and probing will be part of such gelling, and positioning around these discussions is made more visible (including forcefields).

8.1.4 Broadening enactment cycles and the (modest) change aim of CTA

Broadening, and particularly broadening enactment cycles (see 1.1.3), is an overall goal of CTA, but it can be reached only in small steps, and when external pressures are present. The goal should be kept visible, at least at the side of the CTA agent, but the envisaged changes will have to be modest.

CTA-workshops as microcosms provide an opportunity for bridging, there are others occurring in the nanoworld (some are tailored for a specific purpose, but most are ad-hoc). The CTA-projects I have worked on reveal the challenges of tailoring CTA as a support tool for enactors. Because of the lacunae, in the zone of enactment (1.1.3), with regards to embedded opportunities for bridging, CTA was seen as unusual, and negotiation, positioning and probing was necessary for both CTA-agent and the enactors.

This has implications for the focus on workshops as bridging events. In terms of the change aim, workshops suffer from the intra-mural effect: All sorts of interesting interactions occur within the walls of the meeting room, but then participants go back to their own situation with its opportunities and constraints. The eventual impact of the embedding with ongoing activities is not automatic.

[90] This occurs in focus groups, unavoidably as Lezaun (2007) has shown admirably.

Thus, one should consider stepping out of the box, i.e. not (or not only) focus on bridging events in the form of dedicated events/microcosms. Then, my moving about in the nano-world, and becoming legitimate in what I was doing (see conclusion of Ch 6) also contributes to broadening enactment cycles, albeit in a diffuse way which is difficult to trace. But impacts occur (if at all) in the macrocosm of the world of nanotechnology developments. Thus, evaluation and follow up of the workshops remains important to capture and consolidate the learning that occurred.

8.1.5 Reflections on doing CTA

Doing empirical (and embedded) CTA has to be context-dependent. Dependent on the dynamics of the field which is the topic of the CTA, dependent on the actors that could participate in the CTA and, if closely tied to actual activities of a certain group of actors, is dependent on the relationship between CTA-agent and those actors.

Contingencies play a strong role, necessarily so because they are part-and-parcel of being "close to the action". This should not be taken as a message of despair (to TA methodology purists), but taken as a starting point for tailoring effective tools and approaches for doing CTA within the co-evolution of technology and society. This means each CTA will be different, context dependent and riddled with contingencies.[91]

Is there a "good" method for doing empirical CTA? The question cannot be of a best approach, but could (and should) be a question of what is a satisficing approach (Simon 1956). A satisficing approach is necessary because identifying a broadly applicable best solution in such conditions would require high costs in terms of resources spent. This is even more so for early stage emerging technologies, where the co-evolution is rapid, and conditions will change.[92]

In this study I have developed tools and approaches that can be applied to early stage emerging technologies, but to be effective, they require tailoring to the context in which they are applied. I have shown how these were tailored (see Chapter 4, 5 and 6) and the effect of their application (Chapter 7 and the appendices).

[91] Insertion has been put forward as a means of handling these issues better (although not overcoming them).

[92] See how the changing conditions in the nanoworld shaped the attempts at embedding a CTA workshop on Responsible Research and Innovation (Chapter 6 and Appendix 4)

Therefore, application of empirical and embedded CTA will always require experiments with interactions. An approach to aid this experimentation - for informing, targeting and legitimising CTA - is that of "insertion". It was originally put forward as a means to an end (of inserting CTA into the nanoworld), and became an object of research in of itself. In the next section, I go deeper into insertion as a methodology.

8.2 Insertion in ongoing co-evolution as a methodology

Insertion is a combination of broadening knowledge and understanding of co-evolution and creating change. There were experiments in interactions which produced data and insights and allowed diagnosis. The latter is where this "methodology" clearly differs from participant observation.

What is special about insertion as a methodology? It is more dirty than some methodologies because contingencies play a strong role, but is more appropriate for specific situations, in particular early stage emerging fields of technology development, because it combines probing and affording change through feedback.

In Chapter 1 I linked this with Lindblom's (1990) plea for inquiry in relation to change. In my case, probing into situations and actors perspectives in order to change them. Moving about in the nanoworld (Chapter 6) revealed that actors probe all the time, even if they do not have well developed skills to do so.

Probing is also taken as an approach to inquiry by social scientists to obtain knowledge and insights, and there will be a change effect linked to this. This was a reason for insertion to be further developed in this study, not only to suit my own practical requirements of doing empirical CTA, but for developing this methodology for more general application when studying and shaping (modulating) co-evolution in emerging fields.

Reflecting on my experiences, I can now position insertion as a methodology. One key point is that moving about in the nanoworld requires moving in and moving out. Moving about in the nanoworld allows capturing entanglements in co-evolution as they occur. Of course, a large amount of desk research is a necessary prerequisite. The next step is the identification of arenas and events to insert oneself in. This is a challenge in of itself, and requires more than just visiting the nanoworld as a passive observer. One aspect of identifying arenas requires drawing

tentative boundaries around communities.[93] At an early stage, in 2004, there were no clear communities of nanotechnologists. Many of the "nanotechnologists" felt more comfortable with traditional labels and communities (physicists, chemists, material scientists, also biologists). This changed over time, and was often only visible in the informal interactions, encountered when moving about and probing. One further phenomenon is the emergence of forums and events where actors in these emerging communities aggregate.[94]

Insertion reveals the meetings and fora as these are encountered, but this is not the whole story. Nanotechnology developments occur across the world, conferences, seminars, and roadmapping events are part of activities of international communities of nanoscientists, across the globe. Thus, "hearsay" is also important to trace overall developments. In addition, judicious selection where and how to move, and exploiting opportunities – "smart" insertion.

Moving within the nanoworld goes beyond active observation; it requires probing in the interactions with the subjects (in my case mainly nanotechnology enactors and others related to nanotechnology developments). Probing doesn't come easily, especially when social scientists are (as until recently) very much seen as strangers.

The combination of active observation, in moving about, and probing gives indications of the forcefields at play and the type of bridging that is occurring in the nanoworld. Already the presence of a social scientist in the world of nanotechnology development can be an occasion for enactors to speculate on, and position, the roles of comparative selectors and other types of actors (including social scientists).

Success of moving about (interacting, probing and being visible, garnering feedback, positioning oneself as analyst) can easily lead to attempts of enactors to enrol the analyst into their worlds (this is visible in the narrative in Ch 6). Indeed, social scientists even when not going native, can provide intelligence to enactors,

[93] In my case this involved "nano" communities whether they be the nanobiotechnology community (itself a diverse community covering many disciplines) or a more focused community such as nanofluidics.

[94] For example in nanotechnology for drug delivery, the most recognised meeting with regards to research and development is the annual meeting of the Controlled Delivery Society (see Stretch 10 in Chapter 6). For Lab-on-a-chip, the most recognised meeting is MicroTAS (See stretch 7). These two fora have grown to be the most attended and recognised locations for exchange of information. Nanofluidics, an early-stage field of research, was distributed amongst a number of disciplines, and through insertion, we discovered (in Stretch 1) that a first meeting on this topic would be held and that it would bring together those "in the community". Insertion can reveal these important details for early stage fields of research.

"to do better" as they would phrase it. The analyst should maintain some independence, however (this in fact is what sophisticated consultants do while providing intelligence to their clients). Thus, there are two further elements to insertion. One element is not to offer a direction to be taken, but to support the exploration of options. The social scientist augments articulation, reflection and learning (the stuff of CTA), rather than identifying a "right" path. The other element is that the social scientist while inserting, must be proactive in the maintenance of some distance from the nanoworld through underscoring his/her position as a visitor, or an involved stranger. One way to do so is through visibly leaving it. Moving in has to be complemented by moving out.

One way to affirm the involved stranger's role is to do distantiated analysis, aggregating findings into an overall picture, publish them in their own right, and then presenting them in the nanoworld.[95] The social scientist makes clear one role he/she is playing, the role of an analyst. Such aggregation and presentation of analysis is a feedback into the nanoworld, and may shape developments to a certain degree.[96]

Enactors may not find publications in the "home" discipline of the social scientist enlightening, but the fact that they are accepted publications (and therefore accredited), legitimises the visiting social scientist in terms that work in both worlds, i.e. peer-reviewed publications). That the peers are different makes little difference.

Insertion tactics as outlined here are a means of gaining legitimacy in the world the social scientist is visiting, which then allows him/her to gain further access, as well as successfully negotiate participation of enactors in events s/he wishes to organize (in my case, CTA workshops.

Insertion has been positioned as a methodology for capturing details of co-evolution and affording opportunities to modulate it. Even if the change aim is not a focus of the activity, there will be a change because of the probing which will modify views and choices of actors, and because of the recognition of the added-value of insights of an actor, here a social scientist, who has been moving about in

[95] For example, fora such as 4S, EASST are locations for presenting findings to the STS community for feedback in a visible forum. Another is to publish findings in peer-reviewed journals (or as conference papers). This becomes a visible means of moving out of the nanoworld when such publications are shown to the enactors in the nanoworld as evidence of the social scientist being located in a "home" discipline.

[96] The degree that it shapes is dependent on many factors, the standing of the social scientist, the location of the presentation, the frame in which the analysis is given (enactor frame, or otherwise) etc.

other worlds. Methodologically, the fact that there are effects of being present is not a problem as long as the insertion activities are documented and made part of the analysis and interpretation.

Probing is mutual, and an effect of a social scientist being a visitor in the nanoworld sensitizes nano-actors to other framings of issues. While I have emphasized the importance of the social scientist offering analysis and diagnosis, if only to legitimize him/herself, the fact of having somebody around in the nanoworld who is different, and offers different perspectives is also important. It unsettles received perspectives, even if at first only in the form of queries about what this social scientist is doing (cf. Chapter 6). When Rip (2006) discussed co-evolution of technology and society, and how it can become more reflexive, he identified the role of tricksters in unsettling received patterns. Social scientists, in my case CTA agents, inserting themselves in the nano-world, are modest ("soft") tricksters. They don't play tricks on their audience, but induce some unsettling just because of their presence and their questions.

8.3 Co-evolution and the role of CTA agents

The eventual trajectory of an emerging technology, or more accurately the eventual varied entanglements of socio-technical networks, cannot be predicted beforehand. The socio-technical networks (co-)evolve reflecting the interactions and the irreversibilities that emerge during the development, production, uptake and embedment processes.

A new technology option emerges against a background of existing technological and societal regimes. Over time, as investments are made (material, symbolic) irreversibilities emerge (Chapter 4, Chapter 5). There are patterns in the irreversibilities, multi-level entanglements (Chapter 5, Chapter 6) which create opportunities and constraints for further development (cf. the notion of 'endogenous futures'). Still, it will be the interactive processes of co-evolution which will determine the outcomes.

Some entanglements are more desirable than others. This is where CTA should play a role, to improve the chances of the more desirable entanglements through supporting reflexive co-evolution. It does not, by itself, specify what is desirable.

Co-evolution of nanotechnology and society is the backdrop against which my CTA projects were shaped and performed. The experiences in the CTA projects offered insights in the forcefields and dynamics of co-evolution. In section 1.1.2 the preliminary diagnosis of nanotechnology emergence showed that there are

already some elements of reflexive co-evolution (in particular, in the spread of the discourse and perhaps the practice of responsible innovation). During my insertion (Chapter 6) this was visible, also in how my own moving about became part of larger developments, at first being constrained, but then being enabled by them in the sense that there was more acceptance. At the same time my activities also contributed to these larger developments by showing that something interesting and useful could be done.

This perspective on co-evolution and entanglement then leads to questions whether further arenas for bridging do emerge and are being taken up. One indication is how in coordination activities like the European Technology Platforms, societal aspects and health and safety aspects are included e.g. as working groups (see ETP Nanomedicine in Chapter 6 and in Appendix 4 Stretch 4). Arenas for bridging might also occur in the various nanodialogues that are being organized and orchestrated. These nanodialogue activities are still quite distant from actual technology development (in terms of ability to shape enactment cycles). In so far nanotechnologists and other enactors are involved, it is as experts invited to participate in the dialogues, on temporary leave from their nanotech activities. Codes of Conduct and voluntary reporting and other soft law all of which envisage soft governance, lead to measures and rules, but it is not clear whether they will lead to bridging events. In my fourth CTA project I did create a bridging event about new roles and responsibilities in governance of development of nanotechnologies. From that experience it is clear that there were effects for the actors that participated, but not for governance, or at least for governance in the traditional sense where legitimate and effective rules and measures have to be established.[97]

While not necessarily leading to new arenas and bridging events, these activities are definite indications of increasing entanglement. The consideration of eventual impacts is being taken up in ongoing nanotechnology developments. One example is the repeated occurrences and acceptance of acronyms such as ELSA (Ethical, Legal, and Societal Aspects) and EHS (Environmental, Health, Safety) in discourse on, and governance of, nanotechnology research as well as in the mobilisation of resources for research. In principle, this indicates emerging alignment between societal concerns and allocation of resources.

[97] There has been a proposal to consider *de facto* governance, which is actual social ordering with some legitimacy (Rip 2010b). Bridging events as well as the insertion of CTA agents in the nanoworld are examples of activities leading to *de facto* governance.

Conclusions

In the nanotechnology world, actors such as governmental agencies, industry and NGOs are increasingly held accountable for addressing societal concerns – a new emerging rule within the multi level processes. Over time, the rules of the game might change into: "you should not only (promise to) take EHS and ELSA into account, but also incorporate them into your research and thus live up to your promises." Whether this will happen is another question, and possibilities might be pursued by creating scenarios of future co-evolution.

The implication of this is that socio-technical paths will occur in a world in which EHS considerations have become forceful (Mantovani et al 2009), and which thus have to be taken into account (see also Chapter 6, Stretch 10 for examples).

With regards to enactors, the few studies that have been carried out show that protection from the outside world is still their main consideration – which is actually functional for pursuing research without interference. See for example earlier and ongoing studies by Erik Fisher, who developed and experimented with the concept of midstream modulation (Fisher et. al. 2006; Schuurbiers and Fisher 2009).

If these trends continue, the various specific paths that emerge will share the inclusion of societal aspects (anticipating on embedding, as such or because of credibility pressures). This would be like what Nelson & Winter (1977, 1982) called a 'natural trajectory': a long-term trend like mechanisation (since 19th century), or miniaturisation (since 1960s). In this case, one might label it 'societal robustness'. Such broader trends can be seen as second-order paths, and in the case of societal robustness, one that is only a possibility at the moment (see further Rip 2010b).

The implication of brief diagnosis is that there are changes in the processes of enactment – many are independent from my activities, but in some cases individual CTA projects (or the programme of CTA projects) can play a role.

So what about the role of CTA agents? I used insertion as a method to become a CTA agent who was a recognized visitor (was visible as an STS researcher doing my research and being part of a separate community) but was also shaping ongoing processes. This to a greater or lesser degree is part of many STS studies of nanotechnology (which involves some form of interaction with nanotechnology actors or for that matter those other enactors, governmental actors or societal actors involved in shaping the outcome of nanotechnology development). The dual approach is also nicely visible in how the Dutch Rathenau Institute inserted itself in ongoing developments of, and debates on, nanotechnology, taking the stage of

development and debate into account when to decide what to do and what to postpone (van Est & Walhout 2010).

CTA-agents can find openings for their activities in the pressures for responsible innovation, and orchestrate bridging events in various loci in the (co-) evolving socio-technical networks. STS scholars have a particular challenge, when interacting with their subjects, in my case enactors in the nanoworld, to make their analysis and its representation recognizable and acceptable. The nanotechnologists often have more power and a higher status with regards to opinions on nanotechnology developments than the STS analysts. When the analysts limit themselves to presenting their products within their own circles they can escape this issue. In my insertion activities, there were many feedback loops. Part of my moving in and moving out involved aggregating my findings and presenting them in the form of posters, oral presentations, reports, conference papers and peer-reviewed articles, in both the world of nanotechnology development and the world of STS and innovation studies (see Chapters 2 - 5). The visibility of my aggregation in both the nanoworld and STS world was essential in positioning myself as a visitor, a welcome (and sometimes unwelcome) stranger to the field. Also the opportunity for the nanoscientist to probe my world was important during insertion; the early stages of my interactions with Frontiers participants involved much mutual probing and positioning between myself and the participants. As the programme of CTA projects emerged, and my moving in and moving out became more visible, my position as a welcome stranger was reinforced.

This links up with the methodology of insertion (8.2). But there is also a normative point, related to the third horn of the Collingridge "trilemma" (1.1.3). This "third horn" is that at an early stage, it is not clear what the dimensions of desirability should be, because the promised novelty may well transcend existing ethical and political evaluations. The CTA-agent should not resolve the trilemma by specifying what is desirable, but enter the emerging field with what might be called a second-order normativity: increase reflexivity of co-evolution (Schot & Rip 1997).

Even so, linking up with actors in a particular location in the socio-technical network is inevitable for inserted CTA. Also inevitably, the CTA-agent has to fit to the circumstances of this location but not at the expense of the overall aim of CTA to increase reflexive co-evolution. This is not easy, as the five experiments in CTA reported in the appendices have shown. Negotiation will occur, and insertion can help in managing these tensions (but not remove them).

In this study I have shown the nature of such interactions during my experiences in the nano-world. Insertion is a method to help position (or better articulate) the role of social scientists interacting with the nanoworld, for the benefit of the social sciences and the nanoworld alike. Through experiments in interactions, both through insertion in the nanoworld, and the orchestration of workshops tailored for bridging, empirical CTA is now available for application and further development and tailoring.

APPENDICES

Appendix 1 - Integrated microfluidics for single and multiple cell analysis

1 Starting Conditions

1.1 Preparation through field analysis and insertion into the ELSA work package agenda

At the beginning of 2006 when there was some verbal support from the head of the Frontiers Ethics work package and the coordinator of the project, offering support in theory for one pilot CTA project, I began to explore potential candidates for a first CTA project. My initial candidate was brain-computer interfacing which was both part of the speculations in and around NANOTECHNOLOGY and NBIC, but also actively worked on in a number of laboratories. During January and February I began research into this field and began interviewing some key researchers in the community, all of which were interested in the notion of CTA but would not attend a workshop – citing their experiences with "Ethical harassment" at such projects in 2001 – 2003. I revisited this case in the final CTA project at IMEC in Belgium (see Appendix 5), but for the sake of the pilot project for Frontiers by the end of February 2006, with the collapse of the first concept through potential participants fear of ethical harassment, I had to provide a proposal within 2 weeks to the Frontiers network organisers and the head of the Ethics workpackage. During 2004 and 2005 I had spent a considerable amount of time investigating the field of microfluidics in collaboration with another colleague in the TA-NanoNed programme, Rutger van Merkerk (Van Merkerk and Robinson 2006, Van Merkerk 2007). In this study Rutger and I noticed that there was an innovation gap, large promises prevailing since the early 1990s had carried the field so far, with ever increasing activity at the research side, followed by a burst in the hype when large firms in the early 2000s pulled out, disappointed by the delays and unclear applications. The hype still remained for lab-on-a-chip, but activity remained at the level of research with the wait for the "killer application" which was expected to align actors and create value chains. There were a number of small firms sprouting up, which would be able to provide one part of a lab-on-a-chip platform, but required other parts (other actors) to create a device. In early 2006, medical point of care was the main vision, but with a burgeoning number of start-ups, and the innovation gap identified above, there was a feeling of almost desperation in

some of the interviews I conducted with small companies – their very survival was at stake.

It was with this idea of 'something real being at stake for real actors' that I began constructing a workshop concept. I could see a number of areas within the field of microfluidics that were related to the research activities of Frontiers. These could be classified into a number of interrelated subthemes:

- Lab-on-a-chip as a hand held point-of-use device (LoC);
- Integrated microfluidics systems for analysis and chemical synthesis (MicroTAS and Microreactors, respectively); and
- Micro to Nanofluidics

Similar insights from a TA cousin

During the same period (1st quarter of 2006) Rutger van Merkerk, a fellow PhD in the TA NanoNed programme, also explored this perceived "something at stake" and building on the work that we had done together in 2004/2005 he created a regional focused constructive technology assessment exercise solely on lab-on-a-chip in the Netherlands. In his work he built on the socio-technical mapping we conducted (reported in Van Merkerk and Robinson 2005 and Van Merkerk and Robinson 2006) and sought to augment alignment across this innovation gap through interviewing key actors identified in the socio-technical map (in the Netherlands). Through these interviews he captured their individual perspectives on the socio-technical network of lab-on-a-chip currently and in the future. Through presenting and confronting the actors with their own (and others') socio-technical visions of the future (in a controlled workshop setting) he attempted to stimulate alignment through revealing positions and perspectives. Our approaches to constructive technology assessment, although cousins, differ in the sense that alignment was not the goal of my workshops, but broadening and probing *was*, thus an element of mirroring back at actors their own strategies and positions plays a role in my approach. Revealing co-evolutionary dynamics and dynamics of path emergence are also a major part of my approach.

The recognized innovation gap in lab-on-a-chip had meant no commercial product has arrived on the market (beyond microarrays) although a large number of techno start-ups had formed in this area. One of the main questions concerning this gap was the technology and innovation strategy:

> *Go for a multifunctional flexible platform of integrated microfluidics that could be configured for many applications?*
>
> *Or, go for a specific application and shape the technology around that?*

At the time of the workshop this was an open question. For microreaction technology, there is less pressure to create individual platforms, more on improving technology and exploring interesting new reactions. For micro to nanofluidics,

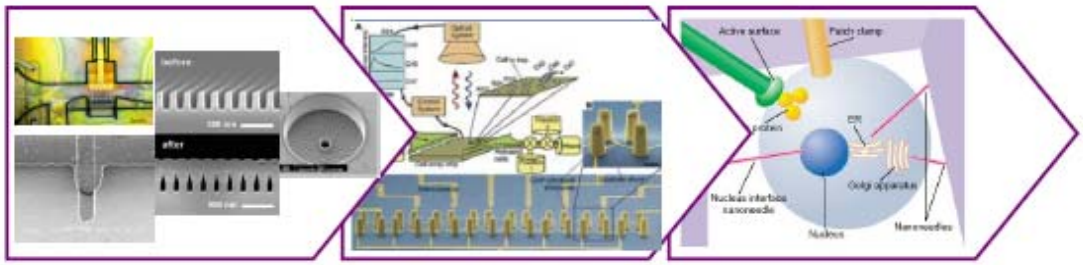
single cell analysis has become a target for (A) the better understanding of living cells internal dynamics and processes (B) for developing nanotools and (C) understanding nanofluidics (a large component of cell dynamics). Visions of applications of single cell analysis included cancer diagnostics, harnessing cells as laboratories ('lab-in-a-cell') or as workhorses ('cell-as-a-factory'). There was a rich territory for discussion of ELSA through medical applications, harnessing cellular processes, etc.

Therefore two topics became interesting: (1) the innovation gap and strategies to overcome it and (2) cell-on-a-chip visions and potential ELSA issues.

With this in mind, in February 2006 I began to create a workshop concept with a colleague Tilo Propp (then post-doc in the TA-NanoNed programme) to further explore these two topics, whilst I waited for the approval from the Frontiers management team. Based on the large amount of interviews undertaken during the collaboration with Rutger van Merkerk, I and Tilo began constructing a diagram that would depict the situation from this data, and we took this to a couple of targeted interviews with a firm and a senior researcher in MESA+ (University of Twente, NL). The issues were recognized and Tilo and I tailored this diagram (what we termed as the 'Innovation Journey') and created a proposal for the Frontiers management team. Below I give the slides (6 in total) that were presented to the management team on March 7th 2006. At this point it was clear that if we were to get funding, we would have to undertake the project before July. It was in this meeting in March 7th 2006, that the concept for the workshop became locked in; Tilo and I had to behave as if it was going to happen even though we had no confirmed financial support, no participants and no venue.

Getting further with micro and nano tools for single cell analysis

Strategy tools for creating linkages in the innovation chain



Towards an integrated single cell analysis platform and beyond.

12th June 2006, De Rode Hoed, Amsterdam,

Towards an integrated single cell analysis platform and beyond.

Dealing with evaluations of future paths for emerging science and technologies is problematic. Uncertainty is high, expectations are powerful and visions of future directions guide actions (and reactions) from many different scientific, industrial and societal communities.

Not only this, those in the research community dealing with emerging technologies such as biotechnology and nanotechnology, today deal with broader challenges than the purely scientific and technical, such as coordination of between the mix of fields and research communities which converge under the banner of nanotechnology, from motivations towards application oriented research to industry relations being part of the R&D landscape along with pressure to deal with social, ethical and legal issues regarding possible applications of fundamental science and technologies.

As part of the Frontiers network of excellence "Technology Assessment Project", this 1 day workshop will bring together actors from the research community, start ups, users and strategy & planning experts to evaluate and determine strategies **towards an integrated single cell analysis platform**.

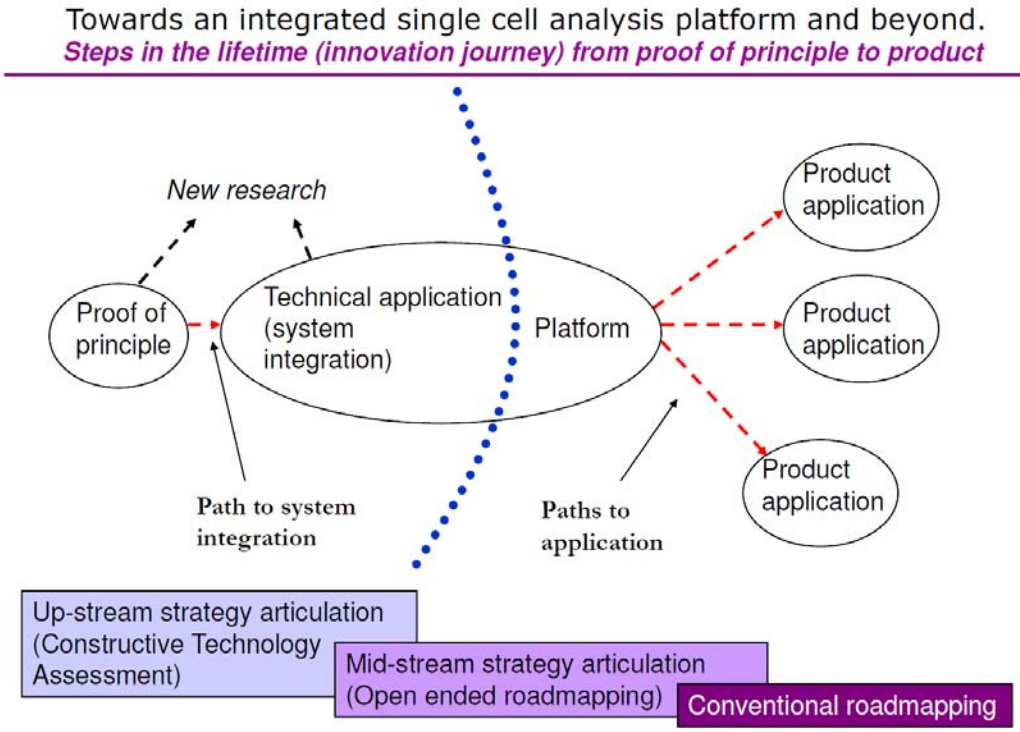
In this workshop we use two tools to evaluate ongoing research and strategies in fields relating to mciroand nano tools that could be used for single cell analysis, we develop possible scenarios and strategies towards a single cell analysis integration of tools and use open-ended roadmapping for exploring where such a research platform could link up with industry to become a product platform .

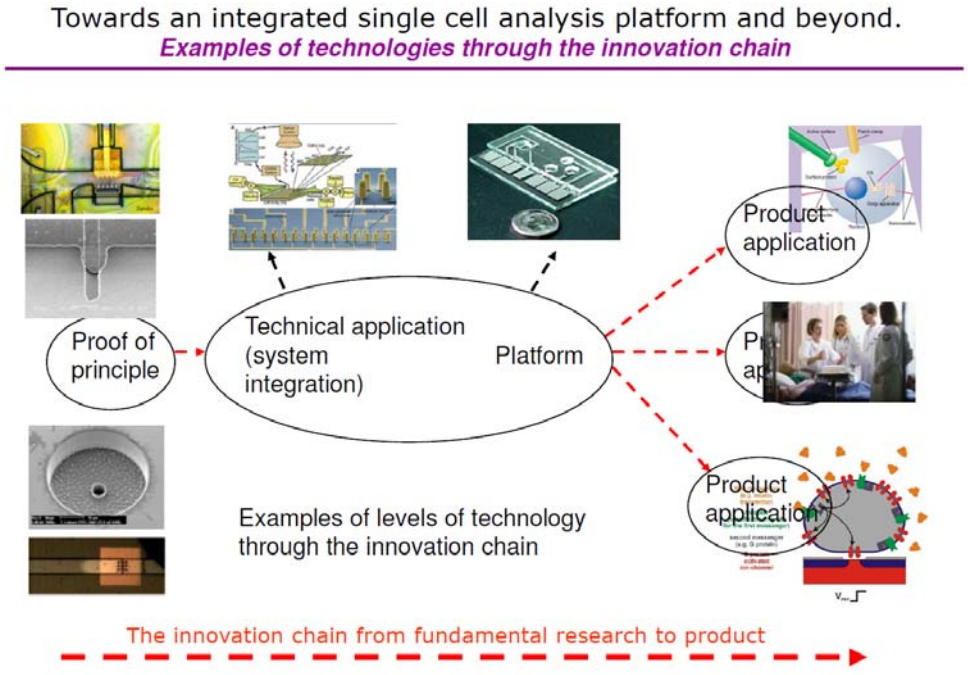
Steps in the life time of a single cell analysis

A brief explanation of the following diagrams (page 3 and 4 of this note). You see a number of stages in the lifetime: (1) micro and nano tools developed on their own, (2) integration into a system for further research (3) a single cell platform for further development by industry and (4) final applications (perhaps lab-in-a-cell or other application).

The blue dotted in separates the boundary were the research community has control on the shape and directions of the single-cell platform (left) and industry has control (right).

Conventional roadmapping is relevant for later stages towards a product application, but what about the present?


Towards an integrated single cell analysis platform and beyond.
Steps in the lifetime (innovation journey) from proof of principle to product
New research
Proof of principle
Technical application (system integration)
Platform
Product application
Product application
Product application
Path to system integration
Paths to application
Up-stream strategy articulation (Constructive Technology Assessment)
Mid-stream strategy articulation (Open ended roadmapping)
Conventional roadmapping


Towards an integrated single cell analysis platform and beyond.
Examples of technologies through the innovation chain
Proof of principle
Technical application (system integration)
Platform
Product application
Product application
Examples of levels of technology through the innovation chain
The innovation chain from fundamental research to product

Towards an integrated single cell analysis platform and beyond.

What we will do in the project

- Evaluate present day state-of the art micro and nano tools that can be used for single cell analysis
- Develop scenarios of how these (and other emerging) tools may develop and be combine into a technology platform.
- Collectively explore the possible futures and develop strategies for action towards a technology platform
- Explore via open-ended roadmapping, product applications stemming from single-cell analysis systems.

Workshop Timetable, June 12th 2006

08h45 – 09h15

Reception

09h15 – 10h45

Session I: Feedback on scenarios formicro and nano tools

- Presentation of scenarios
- Evaluation and further development of scenarios – group

10h45 – 11h00 *Comfort break*

11h00 – 12h30

Session II: From scenarios to strategy articulation for research on tools.

- Identification of problematic issues
- List of difficulties for coordination

12h30 – 13:15 Lunch

13h15 – 14h15

Session III: From strategy articulation to alignment via roadmapping

- Action points for handling challenges; recommendations; strategy: what is the outcome for the people, the network? Think about transition points, obligatory passage points – Discussion; animateur: DR
- Open-ended roadmapping, Part 1: Premises – Report TP
- Open-ended roadmapping, Part 2: Vignette – OER for fluidic chips – Report TP, DR

14h45 – 15h00 *Comfort break*

15h00 – 16h30

Session IV: Possibilities for roadmap-based alignment in Frontiers; summary and conclusions

16:30 *Depart*

That lab-on-a-chip and single cell analysis issues were combined into a single CTA workshop was seen as interesting by the Frontiers management team. One of the Frontiers management team mentioned that "Lab-on-a-chip specifically for cell

analysis is particularly relevant for Frontiers research lines due to Frontiers' focus on instrumentation based on nanotechnologies for the life sciences." For me, what was particularly interesting was the difference between, on one hand, the proliferation of research and development of nanotechnologies for cell analysis in research laboratories and the concurrent proliferation of expectations regarding applications for such cell-on-a-chip devices, and on the other, there being no real bridging of the gap between experimental integration and integrated platform (cf. Innovation Journey diagram in slide 3). Cell-on-a-chip development is at a very early stage; much of the discussion in peer reviewed literature and in between peers around the development of cell-on-a-chip remains at the level of projections and claims. Thus my first aim with the CTA project was to prospect possible socio-technical paths based on projections of the relevant communities involved in research and the prospected innovation chains.

Many of the participants of Frontiers are involved in microfluidics and recognize the innovation gap; in addition single cell analysis, as an objective, provides a reason to develop nanotools and a better understanding on nanofluidics. This was mentioned in the March 7th meeting as a common objective within Frontiers NoE. With this in mind, the ability to map possible emerging socio-technical paths and use them to direct the portfolio of research lines within the Frontiers network was seen to be attractive by the leader of the science-to-industry workpackage and he proposed that this could be linked to the Frontiers roadmapping activity.

Still there was the issue of resources, which was not settled until the beginning of April. Following the go-ahead, at the beginning of April I embarked on a targeted invitation campaign; due to limited funding and timing, I focused on researchers and firms mainly in the Netherlands, and Frontiers (or Nano2Life) members involved in Lab-on-a-chip or single cell analysis. I had the opportunity to interview all of the participants prior to the meeting by telephone or by face-to-face meeting (due to the CTA pilot project being held in the Netherlands).

Below, two tables summarizing aspects of the insertion process are presented. The first presents seven criteria that were used to both determine the starting concept of the CTA-project and its suitability for the various interested parties involved. The second table shows the contingencies that were an outcome of the negotiation of the project concept with the programme level actors in Frontiers, the context of the subject, my degree of control over the shape of the project, etc.

1.2 Summary tables

Key field elements that contributed to the initial idea for the CTA	There was a recognized innovation gap between proof-of-principle in the laboratory and a prototype device suitable for transfer to applications. Also, there was a recognized need for alignment between a large number of R&D and innovators to create a device (since like integrated electronic circuits, integrate microfluidics devices are multi-component platform technologies) Nanotools for cell analysis were a growing area in nanotechnology, and particularly interesting for Frontiers. Analysis and manipulation (up to the harnessing) of living cells on chips provided potential ethical and societal issues (especially with regards to stem cells or with embryo creation on a chip). Thus, ELSA issues around cell-on-a-chip were another topic salient in the field.
Stage of development of the field?	Large amount of development over a 15 year period with a vast number of research groups working on microfluidics. For the previous 5 years the field has been expected to provide devices as products, but as yet these have not materialised.
An identifiable community or socio-technical network?	**Yes.** There were a large number of actors up to and including insurance companies becoming involved in assessing the potential of the device. A recognisable research community and networks of microfluidics firms are visible.
Is there something at stake recognisable to some of the actors in the emerging community or socio-technical network?	The survival of small firms is at stake if the innovation gap is not bridged Identification of the expected "killer application" was seen as necessary for success and thus bridging the gap between technology development and users (seen by researchers and firms) was deemed very important. Researchers in nanotools for cell analysis and manipulation anticipated on potential ethical discussions (manifesting in a public backlash) stemming from living-cell based devices.
Amount of material to work with? *(as perceived during the early stages of the CTA project*	A very rich data set. Lots of visions, high expectations of cell-on-a-chip devices, plus the recognised innovation gap provided a lot of material and dynamics to explore. The three focus topics were discussed with the lead lab-on-a-chip expert in the Netherlands (and potentially a world leader). This expert who was embarking on the first steps in a plan to explore cell-on-a-

development)	chip was particularly relevant for the workshop and thus he agreed to attend.98
Is it interesting for my study of inserted CTA targeted at broadening enactors' perspectives?	It seemed that broadening the enactor perspective was possible here. Since the expectation that alignment of an innovation chain was the key to success, but was confounded by something (perhaps a waiting game, perhaps a lack of killer application) a broadening of the concentric perspective could be helpful in understanding why there is an innovation gap and a potential waiting game situation. Focussing on cell-on-a-chip (a much younger field than lab-on-a-chip) would allow a study of expectation dynamics and their role in co-evolution in an area further away from the present innovation issues, and allow an opening for ELSA.
Response of key negotiation actors	The arrangement of the content and focus of the meeting was presented and agreed to by the Frontiers management team.

Table 1: Identifying and negotiating an area to apply CTA to

Organizational requirements and constraints from the Frontiers network	The Ethics workpackage needed a workshop by the end of June 2006. The CTA had to be on a core topic of the Frontiers network (instrumentation or enabling technologies for life sciences of medical applications), and had to have some ELSA issues as part of it. Little money would be made available to non Frontiers partners.
Strategies chosen by the CTA analyst to respond to effects of organizational requirements	The organisation and arrangement was with the management board of the Frontiers network and the head of the Ethics work package. I had strong control over this project once the general topic of cell-on-a-chip was agreed to. There was a relatively short period of time from the initial go-ahead from the Frontiers management board on 7th March 2006, but extra delays as funding was not agreed until mid April 2006. This left a 7 week window for preparing the

[98] As will be outlined later, this expert dropped out of the workshop a matter of hours before it began. This had consequences for the discussion as the workshop was designed with this expert providing key expertise (that of cell-on-a-chip) and without his participation the discussion on this topic was significantly reduced.

	whole project. Because of the rapid agreement to attend the workshop of almost 100% of those invited, it was possible to undertake interviews with all participants during April, some fact-to-face and some by telephone. As little money would be made available to non Frontiers partners, participants from the Frontiers partner institutes had to be the bulk of the participants. For firms I had to draw on local firms (in the Netherlands) if I could.
Strategies chosen by the CTA analyst to respond to field problems	Because of the recognised innovation gap there was a lot at stake for small firms and so almost half of the participants were firms.
Topic-specific preparation of the CTA analyst(s)	Since the research field of lab-on-a-chip has grown exponentially since the early 90s, there was a lot of data (as reported in Van Merkerk and Robinson 2006). For cell-on-a-chip this was more limited at that time, although the authors of the leading review articles of the field agreed to attend the workshop, and so interviews provided a lot of data that wasn't as yet published.

Table 2: Contingencies and ramifications

2 Preparation

2.1 The promising technology

The vision of performing laboratory experiments at a micro or even nanoscale was first posed by Terry[99] who linked the then recent developments of integrated microelectronics to the idea of integrated microfluidics for chromatography. The notion of a laboratory on a chip based on integrated microfluidics and micro-devices remained for some time as a vision in the backdrop of the activities gaining increasing momentum in the microfabrication community working closely with fluids. In 1990 Manz[100] posed that integrated microfluidics could be harnessed to create complex systems that integrate all necessary analysis steps on one chip, labelled as a *Micro Total Analysis System* (μTAS). The agenda was set to miniaturise existing laboratory analysis instrumentation and in the early 1990s high expectations were raised about the possibilities of performing (bio)chemical

[99] Terry, S. C. Ph.D. Thesis, Stanford, Stanford, CA, 1975.

[100] Manz, A.; Miyahara, Y.; Miura, J.; Watanabe, Y.; Miyagi, H.; Sato, K. Sens. Actuators 1990, B1, 249-255.

analysis at any place and at anytime, for example, total blood analysis at the patient's bedside (Point-of-Care testing). In 1993, Harrison and Manz[101] reported on a breakthrough regarding the successful miniaturisation of the analytical technique of capillary electrophoresis, which provided impetus to the field and stimulate a proliferation of research projects towards the vision of μTAS.

In the mid 1990s other scientific communities (synthetic chemists; biologists) were attracted to the field, foreseeing that this technology could aid them in their work or enable new lines of research, such as microscale reactors on chip or experiments with living cells (cellomics). The new and broader notion *Lab-on-a-chip* became widely accepted by research scientists who used the term μTAS and Lab-on-a-chip interchangeably. Large industrial actors saw promise in the vision of Lab-on-a-chip and a number of activities were initiated. Around 2000 nanotechnology started entering this field. However the promise of a lab-on-a-chip manifested into microarrays which focused on screening only, with very little complex functionality on the chips (see Agilent chips). For complex lab-on-a-chip systems (those providing a number of steps in the preparation and analysis of a sample) there was no clear 'killer application' and the many large industrial players who had initially invested in the lab-on-a-chip vision began to withdraw resources from the projects.

The Lab-on-a-chip vision however did not die; it was bolstered by increasing activity in public research laboratories (Van Merkerk and Robinson 2006) show this increasing activity in some detail). With the advent of nanotechnology, microfluidics systems were seen as powerful interfaces between the nanoworld and the macroworld. By the end of 2005, one area of particular growth was the area of cellular analysis with microfluidic systems utilising nanotools. Cells are of the order of microns, and cellular components (the organelles and other constituents of cells) are in the 1 – 100s nanometre scale. Cells provided interesting challenges for the micro and (now) nanoscientists; separating cells from tissue or samples such as blood or urine, detection, cell manipulation, lysis and lysate management. This meant in many cases a retraining in biological systems since historically the MicroTAS community were composed of micromachining engineers and chemists.

[101] Harrison, D.J.; Fluri, K.; Seiler, K.; Fan, Z.; Effenhauser, C.S.; Manz, A.; 'Micromachining a Miniaturized Capillary Electrophoresis Based Chemical Analysis System on Chip', Science, 261(5123), (1993).

At the same time (2005) in the field of biomedical research, off the back of the Human Genome Project[102], there was a major emphasis in cell biology research (growing over the previous 10 years) focusing on areas related to genomics, proteomics, medical diagnostics, and detection of trace amounts of biological agents. High-throughput screening and microarray technologies are now (2010) in common use for measuring gene and protein expression and for assessing biological activity of potential drug targets. The microarrays mentioned earlier were being used for studies of certain components and in 2005 the shift was to improve these microarray platforms from genomics to proteomics. Thus there was a lot of interest still in the microfluidic platform idea as an interface between the nanoworld and the macroworld.

2.2 Pre-workshop diagnosis

The earlier disappointments of the lab-on-a-chip platform and reduced funding from large industrial actors was somewhat insulated from the research community through the combination of two other hypes (See Gartner group (Fenn 2008)):

- the NANOTECHNOLOGY hype where the microfluidics platform (the core part of lab-on-a-chip) could potentially provide a platform for nanotools to be put to work and thus interfacing the nanoworld with the macroworld via the microworld; and
- PROTEOMICS where advanced high throughput screening techniques were necessary for continuing research.

However, although many large industrial actors withdrew funding in the early 2000s, many small industrial actors remained. These comprised mainly of techno start-ups from universities, having started during the peak of the Lab-on-a-chip hype in the commercial sector and specialising in one element of a lab-on-a-chip system, for example a sensor or a microfluidics channel fabrication method or a microreaction chamber for mixing two fluids.[103]

By 2005 many were still remaining, getting by through collaboration with their parent universities, or through national and European research grants until a time

[102] http://www.ornl.gov/sci/techresources/Human_Genome/home.shtml; last accessed on 12-07-2010

[103] Mixing fluids at the microscale is a non-trivial task; the challenges are related to the types of fluid flows that are (or are not) possible in micro and nanochannels.

when a "killer application" would be found by somebody (anybody), align actors and provide a market for their device or technique.

To explain this (hopeful) expectation in the world of small industrial actors in the world of lab-on-a-chip, a further unravelling and elaboration of the expectation is needed.

Phase 1	Involves R&D in individual processes, instrumentation or devices, such as microfluidic research, pumps, valves, mixers, etc. – elements of an integrated system.
Phase 2	Experimental integration of some of the elements in phase 1 for analysis in the laboratory. These systems are complex and difficult to manage and thus are confined to research laboratories.
Phase 3	Integrated platforms which have refined the experimental integration into a chip sized system which can be incorporated into a device and used by a consumer.
Phase 4	Product tailored for a specific application. This is a customized and packaged lab-on-a-chip based device for analysis or synthesis. Examples could be point-of-care diagnostics of blood samples, or DNA analysis device for crime scene investigations.

Figure 1: Peer consensus (in 2005) on the phases of materialization of the vision of lab-on-a-chip.

In 2005 (and also at the time of writing in spring 2010) in the field of Lab-on-a-chip there is a general agreement by technology developers of four consecutive phases of technological development (see the figure above).[104] At the time of this CTA project (in the first half of 2006) most activities were concentrated in phase 2.

This table of phases can be further divided into regions of activities of particular actors in the innovation chain, and in this way can be represented in the form of a prospective innovation chain diagram (see Figure 2) where scientific and

[104] Here I use the 4-stage table as a form of diagnostic tool, but it is should be highlighted that it expresses the consensus of peers at the time, a diagnosis on the situation's inherent expectations, so there is promise-requirement conversion

technological research is placed on the left-hand side of the diagram, where ad hoc integrations of a number of the necessary systems for lab-on-a-chip devices are explored and tested as technologies in of themselves as specific capabilities, techniques or devices. Examples could be a microfluidic channel, a fluid mixing system, a sample injector, positioner, sensor etc. In this dotted bubble, researchers attempt to develop and bridge the technology hurdle of integrating these proof-of-principle devices and combine them into an experimental platform for systems research such as protein analysis in the lab (moving from phase 1 to phase 2). Such an integration of a number of devices into an experimental system is usually undertaken in a university laboratory. Such integrated systems are bulky and complicated to handle, operate and maintain, and thus are only suitable for laboratory use.

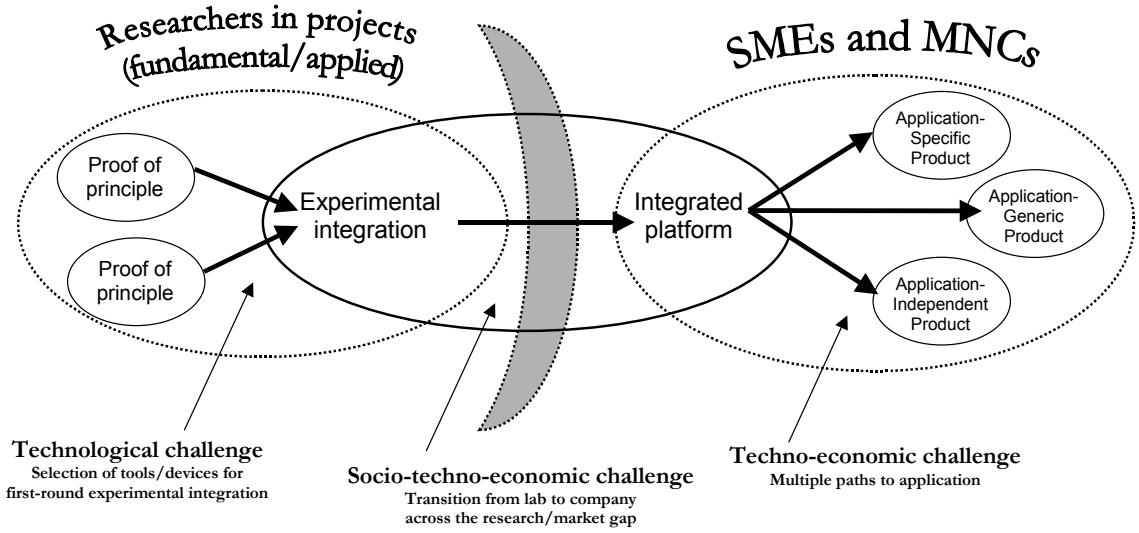


Figure 2: Broader innovation issues of the transition from research lab to company in the single cell analysis innovation chain

The central bubble represents the further technical development of an experimental integration of elements into a working lab-on-a-chip device (transition from phase 2 to phase 3). This development was seen in both the research and commercial communities in 2005 as the largest stumbling block in the previous years. This represents a fork in the road which required a decision: since there are a number of routes to development (many configurations of elements in a lab-on-a-chip platform) and an as yet unclear user community, there was a feeling by many of the actors in the field of lab-on-a-chip that a decision had to be taken sooner or later whether to go for

- (1) a highly application specific product (one purpose only with a clearly identifiable user/customer);
- (2) a product that is somewhat more generic and would allow for a number of distinct yet still similar operations; or
- (3) a highly generic, versatile LoC device for many purposes (for instance through a *plug-in-and-play* platform which can be tailored to specific needs through the substitution of components).

The final bubble represents the evolution of an integrated platform to product applications. From the interviews with firms in 2005 and early 2006, **application driven innovation chains** would find that what we term *integrated platform* and *product application* are one-and-the-same. For **generic integrated microfluidics platform driven innovation chains** they are still separate where the *integrated platform* could be tailored for specific applications and therefore a distinction is made explicit in the diagram.

Alongside the innovation chain issues, there is an element of new research territory in terms of cell analysis and manipulation. For single cell analysis, nanotechnology based tools were emerging as promising devices for single cell and subcellular analysis. Although microtechnologies (including microfluidics) provided a foundation for creating a nanotechnology interface with single cells, both the integration of multiple functions and automated analysis and data handling still remained to be accomplished in a self-contained cell-on-a-chip at the time of the CTA-project.

Along with the research and development challenges of integrating many components and devices, a more general challenge is how to bridge technology research with start-ups and/or multi-national corporations to allow technology applications suited to market demands and more broadly, societal needs: Who will be the key actors in stimulating the innovation chain and creating a platform?

Having presented the preliminary diagnosis in the following section I will describe the translation into a workshop topic and support material.

2.3 Translating diagnosis into workshop topic and scenarios

Workshop Rationale

With a multitude of projections of technology configurations and possible applications in circulation, and the lack of successful innovation chains, lab-on-a-

chip remained at the research level. This CTA project was conceptualized as follows:

4. **Intention** wise, I wanted to explore and develop tools to map possible futures for the *field* of cell-on-a-chip with a focus on single cell analysis and identify possible promising paths for the technology.
5. **Theory (model)** wise, I wanted to explore the robustness of specific paths located within the field map based on an analysis of path dynamics and other strategic intelligence.
6. **Methodology**-wise, I wanted to orchestrate a workshop to co-evaluate with practitioners which paths showed the most promise of successfully bridging the gaps in the innovation chain for single cell analysis with lab-on-a-chip technology.

This meant developing a tool or approach to do this mapping and also to translate it into a way of presenting the important dynamics and dilemmas to the workshop participants. For the development of tools I made use of insights from studies in the fields of (technological) path dependency, expectations dynamics, and scenario building

Theoretical background of workshop tools

While in general new (emerging) science and technology introduce novelties, and thus potentially breaks up existing orders to some extent, subsequent developments create new patterns that may lead to stable situations. Irreversibilities emerge, which will be reinforced when actors invest in the paths that appear to emerge. The emerging irreversibilities afford specific technological paths – making it easier to act and interact – whilst constraining others – making it more difficult to do something else (Van Merkerk and Robinson 2006). Irreversibilities grow over time, shaping and being shaped by the historical affordance structures which shape path dynamics. Emerging irreversibilities can manifest in a number of forms. Entanglements such as sunk investments (and the anticipations on which investments are based) and industry standards are some examples.

Another path shaping element, emphasized in the quasi-evolutionary model, is expectations. Expectations can transform into agendas which shape action. Van Merkerk and Robinson 2006 show examples of how expectations have an effect on selection choices of paths to follow, enabling some options and constraining others.

This can occur also through anticipatory coordination.[105] Van Lente and Rip 1998 also show how expectations can pre-structure actions through prospective structures.

These insights into endogenous futures can be applied to lab-on-a-chip devices for cell analysis. Dynamics of emerging paths are used to articulate a future structured in terms of prospective innovation chains and potential paradigms. We demonstrate a plausible variety of paths in a world, where deeper exploration and assessment can take place in the workshop.

To prospect plausible futures the support material for the workshop was developed in two parts. The first is socio-technical scenarios which combine complexities of emergence and actual dynamics within narratives linked with the actual context of cell on a chip. The scenarios include some of the shaping factors which will enable or constrain paths (emerging irreversibilities) the shaping effects of visionary expectations (think of the emphasis on "killer applications" and the previous lab-on-a-chip hype and disappointment).

Because of the enactor dominated participation in the workshop and the focus on bridging the gap, the scenarios are developed in a concentric manner (Deuten et al. 1997) where innovation journeys span out from the present into the future. Technically, the scenarios are based on available LoC literature. The innovation journeys in the scenarios are shaped by broader forces stemming from co-evolution of the technology path and the multi-level socio-technical entanglements that are emerging. They are written to speak to enactors, and bring in these broader issues.

Since the scenarios (and the planned workshop interactions) are created to broaden the enactors concentric bias and to be aware of co-evolution dynamics, it was seen as appropriate (by Tilo Propp and myself) to provide some form of mapping that would speak to the enactors, but would allow openings for discussion of expectations, broader issues and the uncertainty of innovation journeys.

Therefore the second support material was a multi-path map of a number of technology routes to go in the field, in a world where the majority of expectations can become reality. This will be described in section 2.6. The following section

[105] For example the Nanoelectronics industry coordination efforts described in which would lie in the coordinating bodies box of the IC+ diagram. Also (Robinson et al 2007) describe Nanodistricts and the role of technology platforms which came about through institutional entrepreneurship. This mobilization of resources through institutional entrepreneurship created a locus for techno-organisational agglomeration, and emerging irreversibility based on sunk costs and the anticipations based on them.

gives three short summaries of the scenarios. This is followed by the full scenarios with key elements, dynamics and issues shown in annotations.

2.4 Scenario summaries

Scenario 1

This scenario foregrounds dynamics such as the polarization of visions of different applications and subsequent lock-in of one of these visions, constraining the further development of the other vision. Earlier research aimed at the development of a chip that can be used for analysis of cells, with application to point-of-care diagnostics, slows down because the promises are not achieved in the short term, and support is withheld. Instead, new research lines are opened when pharmaceutical companies start to invest in this technology platform for drug screening applications, using arrays of cells that act as biosensors. A key factor stimulating pharmaceutical firms to invest in this type of technology are increased safety requirements on drugs and a general (political) trend to move away from animal testing. After a time, sunk investments in this new area of applications make it difficult to pursue the initial vision of single cell analysis (for point-of-care diagnostics or any other use). Although, as the scenario explains, breaking out of this dominant path is possible, and is demonstrated by a number of small dedicated devices, but mobilising resources for a dedicated single cell analysis platform becomes too high a challenge.

Scenario 2

This scenario focuses instead on the dynamics of specific design paradigms and their impact on technological paths. The promise of a cell analysis platform to enable the "measurement" of living cells in real time serves as a bridging opportunity between cell-on-a-chip research and cell biologists. Two different approaches towards the development of such a chip emerge. One approach emphasizes the development of a generic platform for cell-on-a-chip and a modular design. This approach turns out to work well for research, but less for the commercialisation of a chip. A number of actors link up to establish a fictive start up company named 'CellTron', linked to existing facilities and attempting to coordinate them, to develop lab-in-a-cell into a product family, (large firms are not prepared to invest, they need a clear prospect of profitable applications). It explores various possibilities, but finds it difficult to push particular applications when they emerge, and can survive only by further speculative investments. The other

approach is to focus on an application-specific platform. Spin-offs from universities and public labs try out possibilities, and some survive. A portable DNA testing device based on lab-in-a-cell is successful. Although profitable applications remain limited, it acts as a stimulus for other application-based research projects and start-ups exploiting them.

Scenario 3

This scenario foregrounds the effect of overall promise and disappointment trends in nanotechnology. In the research world, there is clear interest in improved understanding of sub-cellular mechanisms via cell-on-a-chip technology. But this is not enough to carry on, now that the general high expectations around nanotechnology are deflated. To survive and grow, cell-on-a-chip technology must link up with concrete promises (for example drug delivery) and thus shift from the development of a platform for general research to applications. However, potential applications are difficult to identify. Since the relevance for general research remains clear, the field survives, but as a niche development. There is some support of funding agencies because of the articulated fundamental interests, and there are incidental applications developed by start-ups.

2.5 Full scenarios with annotations

This section contains the full scenarios (left column), with key elements, dynamics and issues highlighted – and their intended purpose for the workshop interactions detailed - in annotations in the right column.

Scenario 1: Vision polarisation and lock-in

For the first years the MicroTAS community leads the innovation chain by continuing research into apoptosis on a chip, nanotools, nanofluidics, BioMEMS electroporation, needles for injection/extraction, trapping and sorting, cell division, patch clamp etc.[i] Attempts at integration of the tools and techniques to provide interesting chips succeed in part by having working prototypes which can be exploited locally and commercialised. [ii] There are attempts to link MicroTAS research lines with life scientists through appeals in Lab-on-a-chip journal, discussions within conferences and exhibits in international conferences.[iii] The approach of the MicroTAS community is to find interesting biological problems and direct research in construction of tools to solve these problems.[iv]

Due to delays in fulfilling promises of point-of-care diagnostics the Lab-on-a-chip bubble eventually bursts. [v]

Nearly simultaneously, because of interesting problems in, and clear applications of microreaction technology, the pharmaceutical industry begins to invest at a large scale, and so this technology begins to dominate in the field of LoC. [vi]

A prototype device is developed for detection of certain pathogens in the water supply by integrating a cell-based assay, which only needs maintenance every 4 weeks. The device is installed in many water pipes and enables improved water safety. This approach uses large arrays of cells as whole-cell biosensors for toxicity effects, where the process focuses more on detection than the effects and complex mechanisms that are occurring in individual cells. [vii]

With the EU chemicals policy (REACH) and the 7th Amendment to the Cosmetics Directive, significant burden is placed on pharmaceutical companies to improve the safety assessment process on their products.[viii] In addition, a general move away from animal testing means a robust alternative is needed. [ix] This is followed by large-pharmaceutical industries

[i] MicroTAS is a recognised research community emerging during the early 90s. This comment highlights research as the main location for innovation at this point. This has come out in interviews.

[ii] There have been a number of lab-top integrated devices as prototypes, and the formation of some companies to try to develop these further. I mention commercialisation here, but do not mention anything about success.

[iii] In reality such attempts of bringing another research/user community into the field of lab-on-a-chip have occurred before with the active inclusion of synthetic chemists into the field. microreaction technology research was the main reason for this, which shaped the notion of MicroTAS to Lab-on-a-chip. Although tensions still remain. (van Merkerk and Robinson 2006)

[iv] Design driver comes from biological research "what are interesting biological problems".

[v] Here I insert hype/disappointment dynamics

[vi] Two elements here: (a) the design driver comes from industry and (b) visions (and direction of resources) can become dominant and affect other technology paths.

[vii] I include a specific example: whole-cell biosensors as a promise in research seen in my literature review; water supply pathogens is my own construct.

[viii] This is pressure is recognised as an opportunity by some lab on a chip researchers I interviewed – the need for better diagnostics.

[ix] Political shifts create a

driving a project for high throughput cell based drug screening, based on prototype from the water toxicity project. [x]

Following this, the needs of drug screening etc. become a dominant driver for micro fabricated devices. The success of this drives research towards extending the cell based sensor array approach.[xi] In industry and policy spheres, the polarisation of vision of cell analysis creates numerous devices, whereas less attention is paid to more advanced and tricky single cell analysis platforms due to the sunk investment (investments in fabrication facilities, trained workforce, knowledge base and networks such as in collaborations) which meant momentum was built up along this line which constrains research in this direction.[xii] Breaking out of this dominant path is possible, and is demonstrated by a number of small dedicated devices, but mobilising resources for a dedicated single cell analysis platform become too high a challenge. [xiii]

Without a dedicated single cell analysis platform, cell biologists find other ways of researching cell systems biology: multiple cell analysis with cell lysis, computer modelling, lysate arrays (focussed on specific substance, proteins for example).

Scenario 2: Design paradigm successes and failures along the innovation chain

The idea that new micro and nanotechnologies in an integrated cell analysis platform could allow the analysis of multiple parameters in individual undisturbed living cells in real time become a bridging opportunity between cell biologists and the MicroTAS community. [xv] Promises are voiced of an integrated platform for the maintenance of living cells (both eukaryotic and prokaryotic), automated handling and trapping of cells, highly sensitive detection of proteins and small molecules, and a cell-lysis module with downstream processing capabilities.[xvi] Many devices (single tools) are being researched and the questions raised are more of the type: which functions do we want on a chip? Two approaches begin to arise at the same

window of opportunity for devices.

[x] Cell-based sensors become an industrial interest.

[xi] Guiding vision for developments comes from improved drug screening.

[xii] Here I show path dynamics. Lock in to the drug screening vision, where innovation is on optimising system for this area, at the expense of other more complex devices (which interest the research community).

[xiii] Some break free, but not all.

[xiv] Other research becomes interesting and feasible to solve interesting biological problems.

[xv] Shared vision provides an opportunity for joint agenda setting by MicroTAS and biology community.

[xvi] I sprinkle in some expectations in research, from interviews and desk research.

[xvii] There is a feeling of saturation at the research side of various components of a lab-on-a-chip platform. So the question shifts to what do we want the chip to do? (from interview with workshop participant)

[xviii] One design path, making sense in the research world (from many interviews in universities), is that of a modular “plug-in-and-play” idea of lab-on-a-chip. Creating a flexible system where you can tailor your chip to the functions you wish by choosing components from the plethora already available.

time.

One of the approaches involves a *modular* approach to single cell analysis and is research focussed with the aim for a generic platform for lab-in-a-cell (not factory approach but for systems biology). The concept is drawn from developments in the electronics and semiconductor industry, Systems-on-chip concept, which is a design paradigm actively pushed by large industrial actors such as Philips. The systems-on-a-chip approach to modular design not only makes sense (to the systems engineer who designs the chip) but also historically the MicroTAS concept of integrated miniaturised solutions emerged from the microelectronics area. (Terry (PhD) 1975 and Terry et al. 1979). [xviii]

This platform works well for research, spinning off a lot of research projects, publications and PhDs, however, bridging the gap between such a highly technical piece of instrumentation (one that needs fiddling in laboratory conditions and skilled staff to get it working) as well as systems integration on a streamlined chip makes it difficult to spin-off into a product. [xix] A group of university researchers sets up a company CellTron to commercialise the idea.

They assume that large firms would not invest in a generic product without quick market exploitation (Why invest lots of cash in a product where others will exploit the results just as much as they?).[xx] Thus their strategy is to stimulate a network of start-ups to create the platform.[xxi]

Overtime, as new markets and new discoveries in various research lines emerge, the CellTron network has to modify their product. This becomes difficult due to their investment in building up a network of ties and sharing of fabrication facilities. These sunk investments remain a constraining factor for CellTron.[xxii]

An alternative approach to designing a platform is a more *holistic* approach focussing on a specific application, and systems integration succeeds in breaking the boundary. [xxiii] A research team at the University of Hull as part of the EPSRC Crime

Previous comment refers to saturation at research side, but no comment on the utility and reliability of these components.

[xix] This is an observation from my own insertion. Research publications proliferate, and a number of spin-offs are emerging, but from interviews with some of these small companies, the transition of a complex system of devices in the lab, to a usable lab-on-a-chip is difficult. Not only technically, user requirements mean that design and use must be streamlined. Thus requires significant investment of resources.

[xx] This point came up in an interview with one of the workshop participants, a long term small-firm working in microfluidics.

[xxi] The same small firm at the time of the workshop wished to go along this route of stimulating a network of start-ups to create the platform.

[xxii] I insert some path dynamics here. As the environment changes (user preferences, industry structures etc.) so must the emerging device be tailored. This becomes difficult as the network of start-ups has to change its agenda and shift resource expenditure (but there have already been sunk investments in terms of resources and network ties). This is left to trigger discussions on flexibility and open-ended roadmapping (drivers for the multi-path mapping process)

[xxiii] Another approach that has been mentioned in interviews and in the literature is the focus on a “killer application”. Create a first device around a clear need, and then broaden to cover niches or create more complex

Technology Programme, successfully develops a point-of-use integrated portable DNA testing device. The dedicated devices (designed from the beginning taking the whole process into account) integrates functions such as macro to micro interfacing, cell separation, cell lysis and controlled DNA analysis. The design team combines expertise in chemistry, chemical engineering, cell biology, physics and engineering from the start to make the holistic design approach achievable. This demonstration in the field of forensics, acts as a stimulus for focussed effort in integration for other application based research including stem cell analysis and tissue analysis. [xxiv]

The successful integration of cell analysis stimulates other research in the field of integrated cell analysis systems using the holistic approach.

Visions of tissue engineering up to artificial organs which circulated prior to 2005 begin to be reinforced as both researchers, industry and societal actors begin to link up with the promises. One vision which is actively pursued is that of "stem-cell production units" capable of growing, incubating and harvesting large amounts of stem cells for therapeutic use. Even though fears of ethical problems and societal backlash on stem cell production hinder industry investment, ethical issues do not play a major role as the stem cell debate focuses on embryonic stem cells and their harvesting. Stem cell production units provide an alternative to embryo harvesting. [xxvi]

For tissue engineering however, the ethical debate provides serious issues on the uses and regulation of tissue engineering and regenerative medicine. Questions are raised of where the line is drawn between medical treatment and human enhancement.

devices and versatile devices.

[xxiv] The dedicated platform provides proof of principle, making way for other dedicated platforms to be developed.

[xxv] Tissue engineering becomes a promising application for cell-on-chip devices. Stem cell production units.

[xxvi] In this element of the scenario, I give an opening for ethics. In this case, the cell-on-a-chip for stem cell production does not cause new ethical issues. It actually solves some, by providing an alternative to embryo harvesting.

[xxvii] Instead of biologists, MicroTAS researchers are the drivers here.

[xxviii] The lab-in-a-cell concept is a vision which requires intermediate developments to be made. Such intermediate steps include tools for single cell analysis, micro and nanofluidics control (for environmental control) etc. And so is a useful guiding vision for the MicroTAS researchers to show as an aim.

[xxix] More details on the interest of the whole cell biosensor is given as a near term vision.[106]

[xxx] Another example of

[106] In fact, this vision manifested itself into a prototype at the time of writing up this manuscript, see: Alonso J., Greenway G. M, Hardege J. D. and Haswell S. J. (2009). A prototype microfluidic chip using fluorescent yeast for detection of toxic compounds. Biosensors and Bioelectronics 24 (2009) 1508–1511

Scenario 3: Harnessing sub-cellular mechanisms

The MicroTAS community continue to push for improving BioMEMS and other processes to enable single cell analysis and manipulation.[xxvii]

The idea of using the cell as a sensor, bioreactor or production unit is encompassed in the notion of Lab-in-a-cell. Cell biologists become interested in the lab-in-a-cell concept as it would allow them a deeper understanding of systems biology.[xxviii]

Others in the micro and nanotechnology community see opportunities for whole cell based biosensors. An interesting reason for using cells as a biosensor unit is that the cell as a component means it is possible to obtain functional information, i.e. information about the effect of a stimulus on a living system. This can be contrasted with analytical information, which answers the question of how much of a given substance is present. Thus, the understanding of function is interesting for more thorough toxicity and drug screening processes. [xxix]

The nanotechnology umbrella term (one could perhaps call it hype) begins to deflate and focus areas underneath the umbrella term begin to crystallise out, such as nanoelectronics, nanomedicine, functional materials and surfaces and nanofabrication and processes.[xxx] The emergence of the umbrella term nanomedicine puts more strain on the field of Lab-on-a-chip, and Lab-in-a-cell has to link up closer with applications, as newer promises come into circulation: nano applications for drug targeting and delivery, theranostics etc.

Thus Lab-in-a-cell has to rely on linking up with these promises (some link with applications, some don't [and suffer]). The growth in the field of single-cell analysis within the concept of Lab-in-a-cell has to shift emphasis towards applications rather than on integration of devices of general research. [xxxi] This becomes problematic since potential applications for a large market are not clearly visible, whereas in the research field the utility of such a research platform is undeniable.

bursting bubbles but with the nano term becoming more specific. This means lab-on-a-chip (which has been able to draw resources from the vast nano research programmes in the past) has to link up closer with applications.

[xxxi] The lab-in-a-cell concept as a research driving vision now has to be replaced by an application one, which is problematic as there is no clear market for it.

[xxxii] Another hype, but for systems biology may provide the saviour of lab-in-a-cell concept.

[xxxiii] The lack of large market provides opportunities for small companies dedicated to niche markets.

[xxxiv] Lab-in-a-cell vision circulates in research community but goes no further. I put this in as a trigger to link up with other promises in lab-on-a-chip which have still to come to fruition – such as true point-of-care diagnostics.

[xxxv] The gap in the innovation chain remains.

Although industry is not willing to invest in a single cell platform (not seeing applications in the short term) the field gains support from funding agencies due to the fundamental nature of systems biology and the understanding of various types of cells (stem cells, cancer cells, neurons etc.).[xxxii]

The field of single cell analysis is carried by application specific devices, which are strung together in a modular and ad-hoc way in the research lab. Start-up companies proliferate as they profit from their individual devices, while they can avoid being bought up by larger firms due to there not being a larger market. [xxxiii]

The general vision of single cell analysis for the purpose of understanding sub-cellular mechanisms for research purposes and then at a further level by harnessing these mechanisms for use by controlling the cell and analysing what is going on, continues to circulate within research community but is not developed fully because of lack of interest from financiers. [xxxiv]

There is a gap in the innovation chain, as progress in the research level continues with ad-hoc innovations, no dedicated integrated platform is possible thus concepts such as single-cell based sensor and the production of various biochemicals and materials by using the cell as a factory or chemical reaction chamber remain visions circulating in the research level.

Important actors outside of the concentric approach (from diagnosis)	Which ones were included in the preparatory material	Actor communities outside of the concentric approach represented in the workshop
Potential Users, particularly the medical community due the strong expectation that point of care diagnostics would be the "killer application". **Medical Insurance companies,** as gate keepers to allow or reject a new medical technology such as a lab-on-a-chip point of care device. **Public funding agencies**, these have been the life line to Lab-on-a-chip R&D since the pull out of large firms. **Regulators**, which set safety guidelines **General Public/Citizens**, en masse as opposed to specific user groups, potentially important because of the anticipated (by enactors) public backlash.	**Regulators** are included in Scenario 1 – role involved shaping the regulatory landscape so as to enable some paths and constrain others **Public funding agencies** are included in Scenario 1, 2 and 3 – role involved shaping through financial support for one pathway over another **General Public/Citizens** are included in Scenario 2 – role played as comparative selectors (as opposed to emotional and uninformed citizens – a folk legend that proliferates in the world of enactors)	None of them. The workshop was composed of small firms and researchers only.

What elements were chosen and highlighted in the scenarios?	• Vision polarisation towards a particular product application (exploring the situation of a potential killer application vision that drives innovation – as expected in the field of lab-on-a-chip. • Emerging irreversibilities in terms of network ties, shared expectations and agendas and sunk investments. • Hype/disappointment dynamics, how they come about and the consequences. • The different types of lab-on-a-chip platform and how the socio-technical configuration of which it becomes a part, shapes its development and societal embedment. • Roles played by important actors outside the world of enactors and how they could shape the field (e.g. regulators, citizens, public funding agencies
What stakes were chosen and highlighted in the scenarios?	The stakes included (1) the fate of small firms and (2) the fate of a desired application during the emergence of the field. In the scenarios there were successes and failures, but elements could easily be interchangeable – an opening for discussion. The successes and failures could be included as forks in the road of innovation journeys, this showed implicitly that there were possible situations in these futures were choices had to be made, and based on actor strategies AND the external circumstances they succeeded or failed. In this way another stake was (3) that it is necessary to be aware of the external circumstances and how they shape the success or failure of innovation journeys.
Structural difficulty in creating scenarios	Due to the homogeneity of the workshop participants (purely enactors) the workshop preparatory material had to provide an opening of broader issues (which could have been provided in part by other actors). This made it relatively clear cut for deciding which stakes should be made visible. However, it meant for scenarios that would broaden enactor's perspective but also speak to them. Since this was the first time such scenarios were attempted in the TA NanoNed programme, we kept them relatively close to the world of enactors.
Other support material mobilised? If yes, what and	Multi-path mapping. As a form of open-ended mapping, it projects potential pathways through the innovation chain over time. Although framed in a linear perspective (so as to speak to enactors) the cont is based on path analysis and studies of expectations. It also allows

why?	locating issues that may affect the pathway at the different stages of the innovation chain. In this way, the objective would be to locate issues, obstacles etc. envisioned by the enactors in the workshop and to probe deeper into the dynamics that would lead to such outcomes – an entrance point again into co-evolutionary dynamics.

2. 7 A Multi-Path Map

Based on literature analysis and a number of semi-structured interviews we constructed a map of the actual and possible technological and application paths for chip-based cell analysis platforms (cf Figure 3). This 'multi-path map' (MPM) indicates that actors can select between two distinct yet general clusters of technological paths within cell analysis: using multiple cells for analysis (MCA), detection, or as 'cell factories', and using single cells (SCA). The former has already been realized to the extent of experimental integration.[107] Single cell analysis in itself can be achieved using lysed cells (i.e. cells where the membranes have been intentionally ruptured) or intact cells. Multiple cell analysis is a technology path in as far as platforms and instruments are constructed around the principle of using multiple cells; compared with single cell analysis this has certain advantages and disadvantages in terms of application that need not be discussed here. Any cell analysis technique however can use different approaches and technologies shown in the lowest band on the diagram. Each decision is strategic as it requires investments and expertise on the parts of actors involved which constrain lateral freedom (at a certain point it will be difficult for SMEs to switch to another approach) but propel activities along a trajectory, such as the patch-clamping path.

There can be a number of technological paths towards one application area. This is because the labels ('medical diagnostics'; 'drug delivery') are general.

[107] Schilling, E.; Kamholz, A.; Yager, P.; Cell lysis and protein extraction in a microfluidic device with detection by a fluorogenic enzyme assay, Anal. Chem. 74 (2002)

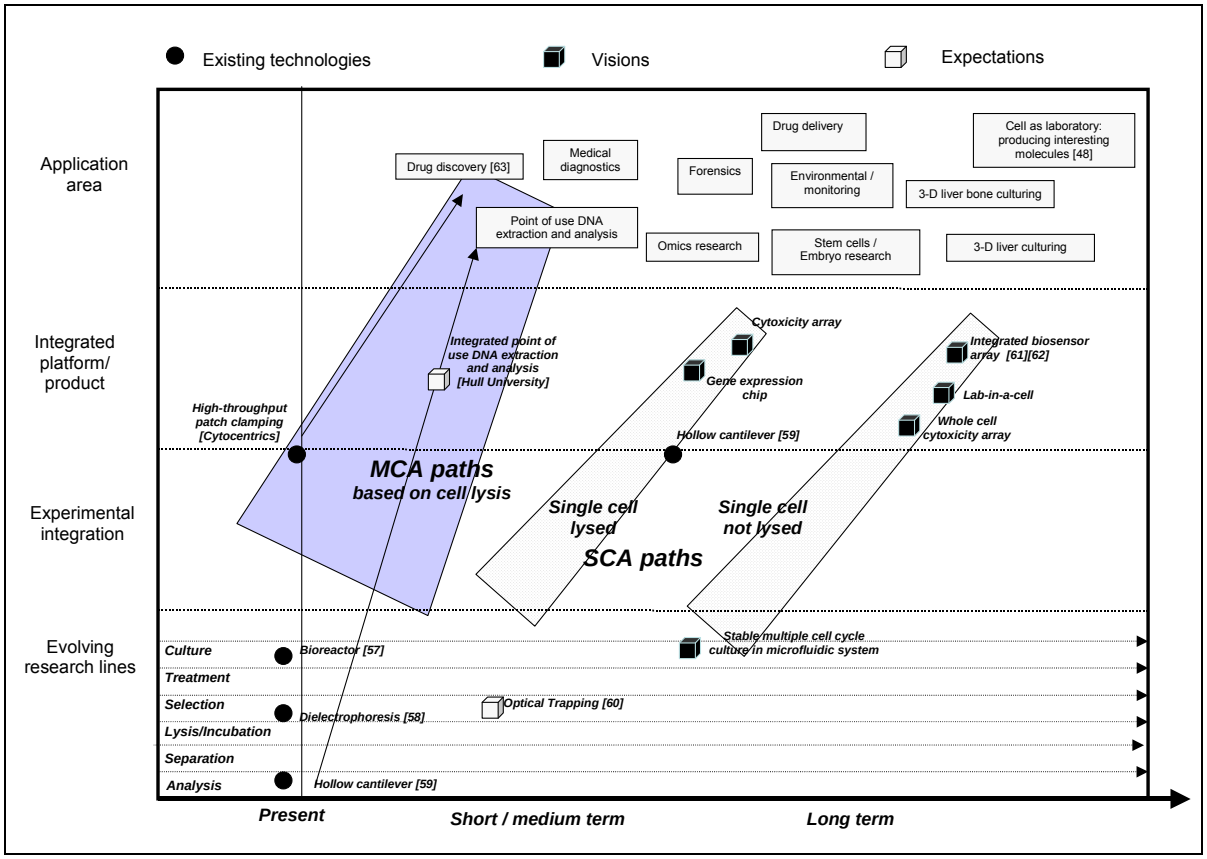


Figure 3: Technological multi-path map for cell-on-a-chip

The resulting first-round MPM shown in figure 3, brings together into the same space (non-exhaustive list):

(6) research projections;

(7) applications;

(8) possible integrated platforms;

(9) possible paths; and

(10) general time axis and stages of innovation chain

The map shows the possible paths that can emerge. In the future, drug delivery could be based on socio-technical entanglements created around multiple cell analysis. These entanglements would be based on, and subsequently maintain, the existence of innovation chains around MCA linking actors in research, experimental integration, integration into platforms, and heterogeneous users in drug discovery.

Because of all the contingencies related to gaps in the prospective innovation chain, in addition to regulatory/ethical uncertainty we did not specify how long it would take for something to occur. For this reason, the time axis is left open-ended

with only a division into short-term and long-term. This was done intentionally as, the purpose of the MPM is to be a platform on which to build during an interaction between multiple stakeholders, and we actually wanted to avoid specific dates and offer a contingency map rather than a roadmap.[108]

The existing technologies and the visions we have mapped here refer to results, or visions, of actors involved in the innovation process. Actors can and do link up with application areas such as those mapped in the top section of the Figure. The Figure also implies that, from a technical point of view, the future path of drug delivery can either be dominated by MCA or SCA. However, it is only the aggregate effect of actors linking up with visions of application, as well as each other, and responding to external events, which defines an application area as a socio-technical path.

A more detailed MPM would show many more specific paths plotted within the clusters of MCA and SCA outlined here. We have plotted two actor-strategy paths into the map (line arrows) to illustrate some of the details that can be included in such a map. The first path shows a technology that is already present within a start-up company (as a prospective component of an integrated system) and its own projection of a path where it should go. This path originates at the interface of experimental integration and integrated platform since it is a specific device still searching for integration but having been demonstrated as possible within the laboratory (Cytocentrics B.V., Eindhoven). The second path comes from a research project at the University of Hull (UK), where government support has been granted to refine existing technologies and develop an integrated platform for DNA analysis, with a particular focus on point-of-use. This integrated platform has been funded to develop "*At scene of crime DNA characterization*" with the aim of demonstrating an integrated platform and then securing funding to turn this into a product for crime scene investigations.[109]

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[108] Also, terms such as *short-term* and *long-term* are defined in particular organizational contexts. For example, there is anecdotal evidence that in highly competitive business contexts, long term begins at 5 years, but in fundamental research it can be 10 because of all the uncertainties. There is probably no a priori definition but partners in innovation chains will negotiate deadlines and durations of projects, and hence in the process co-define what must be achieved in the 'short' and the 'long term', respectively. Probably they will take into consideration the complexity of the goal to be achieved: a simple goal might be achieved in a single, short term project (1-2), but a more complex one requires both sequencing and 'stacking' of projects, so they would automatically speak of 3-4-5 years.

[109] Cf. EPRSC project reference EP/D040930/1.

3 The workshop

3.1 The participants

For this workshop we intended to get industrial actors attempting to develop cell analysis tools or LoC and researchers in the area of LoC and single cell analysis. In the world of industry, small start-up firms are the dominant actors in LoC. All but one of our invitees declined the invitation. However [FMB] cancelled his attendance less than 5 hours before the start of the workshop. This had serious ramifications, since he was leading a group in the Netherlands on LoC for cell analysis, and was a leading scientist in this area internationally.

Code	Institute	Invited as:
[FMB]	**Frederick Mount-Batten** MESA+ BIOS Group	Lab-on-a-chip researcher
[SPB]	**Sophie Peble-Brox** MESA+ BIOS Group	Lab-on-a-chip researcher
[RT]	**Rupert Twosheds** Cambridge University	Invited as observer
[JA]	**Jeffrey Arkleseizure** Glasgow University.	Researcher linked with Industry
[JG]	**Jaap Gallumbits** Technical University of Delft. Sensor Lab	Lab-on-a-chip researcher
[QRD]	**Questula Rontok Desiato** Start-Up focusing on dielectrophoresis of cells	Chief technical officer, (was before CEO) of Start-Up
[MR]	**Marvin Rabotet** University of Leiden	Research Group Leader in Lab-on-a-chip (interest in cell)
[AF]	**Art Fenton** University of Newcastle	Spin off company
[BS]	**Barty Slartvast**	SME linked with microfluidics and lab-on-a-chip
[AW]	**Arnie Woop**	Fresh start up focusing on lab-on-a-chip for lithium measurement
[JL]	**Joop Loonquawl** Cytocentrics	SME
[RP]	**Renault Praefectus** Chalmers	Researcher interested in creating a start up.
[AT]	**Anije Thrashbarg** MESA+ and Stockholm Uni	Research group leader in cell on a chip
[AR]	**Arie Rip**	Moderator

	University of Twente	
[DR]	**Douglas Robinson** University of Twente	Workshop organiser
[TP]	**Tilo Propp** University of Twente	Observer interested in technology assessment
[GS]	**Glenn Sterenborg** Harvard University	Colleague acting as observer

3.2 The workshop interactions as stretches

The one-day workshop took place on 16 June 2006 in Amsterdam's 'De Rode Hoed' conference facility. People were sat around a long table. Feedback, which we asked for in the preparatory material on the scenarios and on the field generally, was handed to the organisers by a number of the participants in the form of notes in various formats. These notes were then compiled during the first session by an observer/assistant [GS].

Stretch 1: Positioning in the innovation chain

One of the organisers [DR] begins the day by introducing the objectives of the meeting with a PowerPoint presentation, but is interrupted very quickly by a participant wishing for clarification on terminology. In particular the participant, an SME [BS], questioned the organisers' use of "integrated platform". From his experience the, "Terminology in microelectronics sector is that a modular approach can be taken in creating an integrated platform." This provided an opening for other participants to query terminology used by the organisers. Another small firm [QRD] pointed out that the separation between single/multiple cell analysis is blurry, pointing out that, single cell resolution can be on a multiple-cell sample. Responding that in this meeting we are interested in the analysis and control of single cells (which can be on a multi-cell sample) the organiser returns to introduce the goal of the meeting.

[Rather than initiate a round of introductions] the organiser, *[in an attempt to frame the meeting around innovation chain]* presents the slide (shown below) and starts locating some of the participants in this diagram.

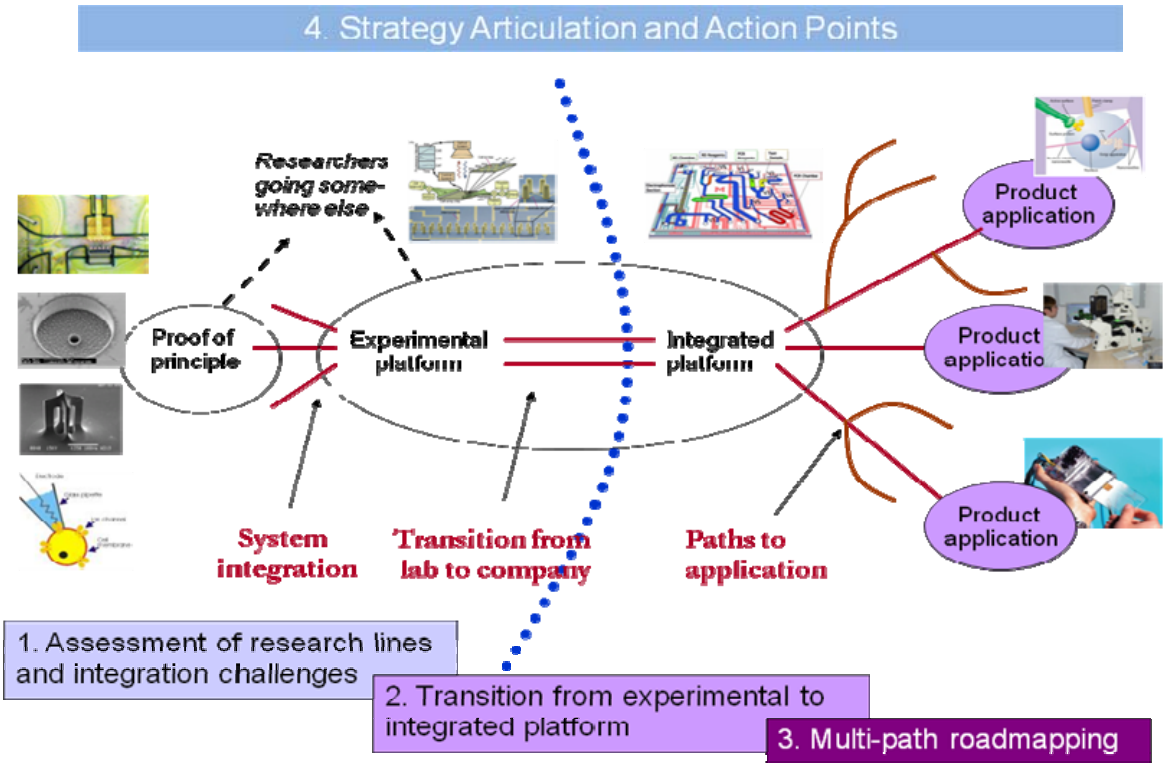


Figure 4: Slide presented to the participants

He describes one small firm [AW] as an example of a company wishing to cross the (dotted) boundary from experimental to integrated platform. [AW] nods in agreement whilst [DR] points to another company currently straddling this boundary [BS]. This elicits a response concerning the positioning and [BS] interjects "we're a technology provider; we don't make our own product". Agreeing and reformulating the positioning [DR] responds, "but you do work with others to cross this boundary?" which receives a nod of agreement.

Moving further around the oval table and shifting his approach from positioning to questioning, [DR] points to another participant [QRD] "how did *you* make the transition from research to company?" [QRD] describes his position as using European Commission research funding to support the start-up company in its R&D. EC financing helped stimulate a network of partners around an R&D challenges "we didn't know much about microfluidics, but this we got through it with partners for example those in CEA Grenoble".

[DR] continues, as the animator, positioning and prompting. Moving to another participant whose core technology had also recently originated from academia, [DR] asks about the origins of another firm [JL]. In this case the original technology came from post-doctoral research in patch clamp technology. After acquiring capital through prizes they won, they began looking for markets. Three and a half years later they are on the first generic prototype machine and currently further developing this generic prototype for customers (he predicts another year and a half).

The animator still positioning and setting the scene draws on another participant, who positions themselves [AF] "We are a sort of a proto company, commercialising technologies stemming from research in our university".
Moving to the final participant "And [JA], before we move on, you're the last victim of this round. You're linked to larger industry? SMEs and big pharmaceutics (including SMEs delivering to pharmaceutical firms)?"

By this point, the organiser has shown that he is familiar with the topic and the background of the participants. Through introducing the participants in the frame of the innovation chain diagram, and positioning (eliciting responses and repositioning) the first probing – albeit the animator with each individual participant – has taken place, with the intention of others picking up on the probing.

Having outlined the three sessions for the day, there follows a long round of introductions, this takes 20 minutes. As we get close to the time announced for the first coffee break, an organiser [TP] introduces the reasons for development of the multi-path approach. Noting that roadmapping is a fashionable term, it still means different things. Summarising the small introduction:

> "There are limitations to roadmapping, it is geared towards identified ideal end points and so cannot deal with open-ended situations were such end points are not easy to identify, or when there are many routes to innovation. We have developed a multipath mapping approach, with the innovation chain elements on the vertical-axis, with time on the horizontal, and have located some of the specific technological expectations, and the (broader) application visions on the diagram. In this map ([*TP] shows the MPM diagram shown in the figure below*), everything is possible, it is an idealised world. Once this is done we can assess each route to innovation. This is what we intend to do in the final session of the day. First, after the coffee break, we will explore the complexities that will affect this idealised world and then zoom into specific paths."

The group adjourn for a coffee break. During the break [GS] groups the participants input, into topics and challenges that the participants think are relevant for cell-on-a-chip innovation chains.

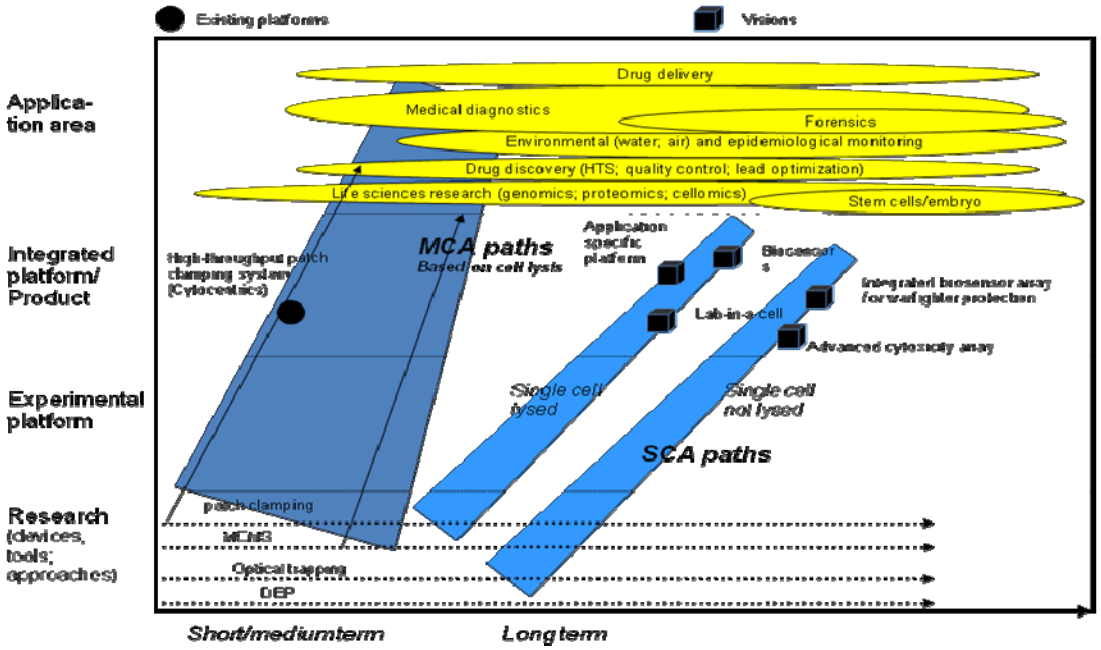


Figure 5: Slide presented to the participants

----------COFFEE BREAK----------

Stretch 2: Probing the complexities of a non-ideal world

When the participants are seated once again, [TP] begins to introduce the scenario technique, announcing that this is done with the intent of opening up the discussion on scenarios, "Let me do some sociological rambling about scenarios". [TP] begins to describe some of his observations as a scholar of technology assessment regarding scenarios and their use, the heterogeneity and the limitations. He outlines the scenario approach for this workshop, using the cell metaphor given below.

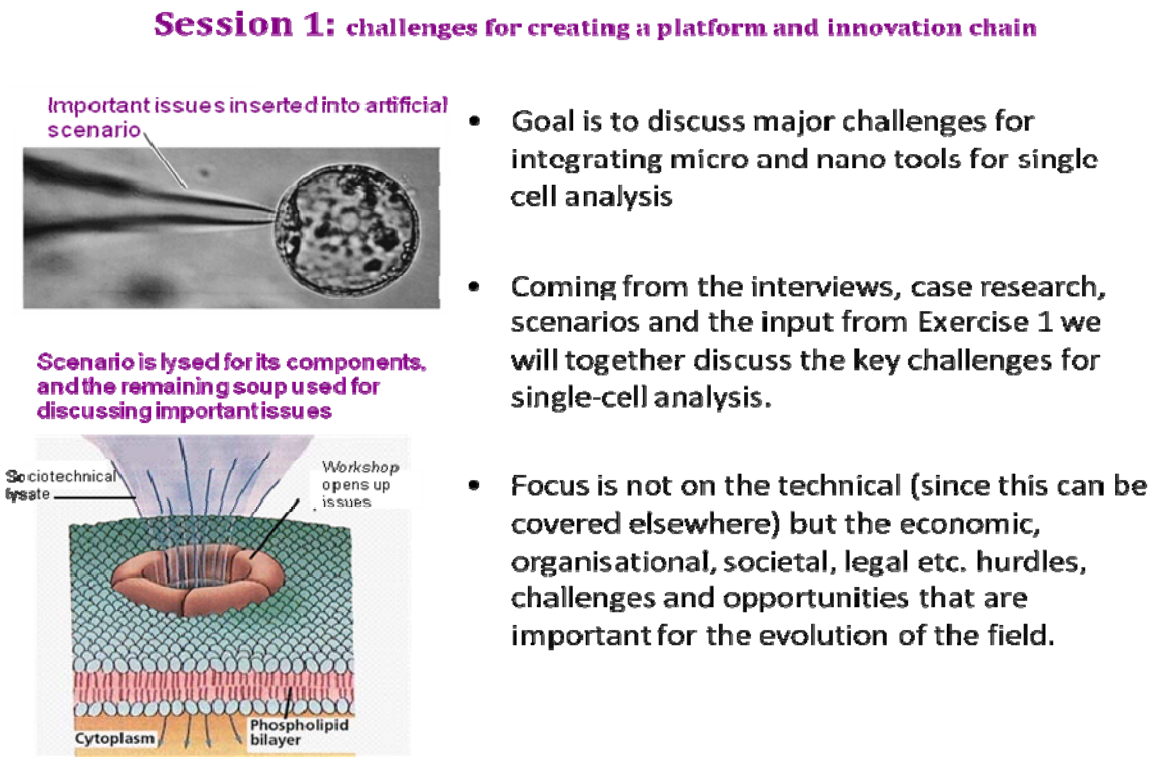


Fig 6: Slide shown to the participants: "Important issues inserted into artificial scenario. Scenario is lysed for its components, and the remaining soup is used for discussing important issues."

The interest of [TP] in scenarios and roadmapping shines through, but another workshop organiser observes that the posture and general body language of the participants indicates a disinterest or disconnection from the topic of the discussion (which is in the frame of a scholarly presentation). [DR] attempts to shift the setting from presentation to interaction.

[DR] interrupts by addressing the group "What do *you* think are major challenges to achieve integrated SCA). Are there lots of niche markets?"

After being asked for clarification, [DR] shows the list of challenges coming from the participants homework (collated by an assistant [GS]). There are a lot of suggestions, too many to discuss in detail in the workshop. Commenting on this fact, he shows the list to the participants "There is too much here, what can you (the audience) make of it?" *(See Box below showing an extract of the response from the participants).*

The group begins to shape the setting for the interactions. One of the researchers [JA] suggests segmenting the list in terms of applications such as diagnostics, screening and forensics. After some silence, [BS] noting that biosensors is on the list, speaks from his experience recalling that "...the promise of biosensors from the 1980s is only now accepted as (economically) interesting – and even then most of near market stuff is R&D" (there is nodding of [JA] in agreement),

[MR] (a research group leader) reacting to this speaks of research agenda setting.

> "You should have lower goals so that you can go for (and achieve) a killer application. Remember that most of the functions can be fulfilled by other tools, so be clear what Single Cell Analysis (SCA) value is. One clear area where SCA has value is on streamlining electrophysiology research in pharmaceutical companies."

This comment initiates a stretch of discussion in the group on challenges of progressing along innovation chains and potential organisational configurations for cell-on-a-chip devices (generic device or many application oriented devices). There is little prompting needed from the organisers as the discussion begins to roll.

Box: Collated answers to two of the questions from the preparatory report (the input filed 26 PowerPoint slides)

Q: What gaps do you see in possible innovation chains (from research to product)?
(From the scenarios but also from your own experience).

- Sunk investments: pressure to make sure equipment is used so returns can be seen and future investment attracted, making it difficult to move outside the MicroTAS line of research
- FDA type regulations, market is not ready for new technologies
- additional factors related to e.g. embryonic / stem cell ethical questions
- there is often incompatibility in outcome and time scales of academic research and industrial R&D.
- engineers do not really know which problems are most important to solve for biologists or medical doctors, and biologists/doctors do not really know which benefits/solutions they can expect from available micro/nano technologies
- "Wow" factors both enable and constrain possible designs, as these affect VCs and politicians
- Industry is NOT convinced by market numbers – Bio-diagnostics is filled largely with lots of niche markets: Isn't attractive for large firms
- Academic research community lack the understanding of market dynamics and needs
- Emphasis on delivering the academic promise with near term returns, this has stifled novelty/innovation and led to relatively low risk research
- There is a trend of integrating components at the end, conceptually integration should be considered first and based on a process, not modules, but this requires dedicated goal.
- packaging is often neglected by the ideas-people who kick these projects off. It's often done late and costly
- For some of the diagnostic type applications/visions circulating at the moment, is

the information coming from them of sufficient quality to be trusted to undertake actions esp. with appreciation of litigation risks

- Technical challenges: Primary cell culture for single cells, electrical measurement from primary cells, Intracellular nanosensors, Creating the correct microenvironment for the cell (flow, metabolites etc)

Q: In an *ideal* world, advances in the field of single cell analysis would be picked up by industry and commercialized, giving rise to new application areas or impacting on existing ones. Such products would still take a number of years to appear due to problem solving and iterations in research, R&D and scaling up. But given that any problems whatsoever could be solved within a short time frame, what such new application areas can you envision to arise within the next five and the next ten years from now on related to the various cell analysis tools?

5 yrs:

- Doing screening targeting
- Point-of-care diagnostics
- High throughput diagnostics
- Cell diagnostics circulating tumor stem cells
- Pharma & basic research tumor stem cells
- flow cell geometry with or without DEP for point-of-care/deployed sensing (e.g. pathogens @ borders)
- Organ maintenance systems
- Multidrug/multiparameter drug screening parallel systems

10 yrs:

- Genetic manipulation of cells
- On-chip colonies
- Cell therapy
- Single cell analysis for systems biology
- Lab in a cell for precise manufacturing of new drugs
- Complete tissue development (growth) systems from stem cells

Stretch 3: Challenges of development time

[JL] agrees with [MR] that it does indeed take a long time for technology to get to the end users. Speaking from his own position, his company has the technology but incumbent firms and value chains have no need for new products. This is why a you need killer applications. [JL] also points out that the screening market is a different market from diagnostics. He goes on to suggest that a generic platform may be the solution then tailor for a lot of niche markets.

[JA] agrees, but is not so pessimistic about incumbent value chains being a barrier to new technologies such as the patch clamp of [JL] "drug companies all have the same competencies; they're all looking for a little edge". One of the workshop organisers asks whether this long lead time, such as in biosensors, is a general phenomenon? [BS] responds with an emphatic "Yes".
[JL] elaborates "You need couple of years to get the technology functioning, and there is reluctance since the market needs to get accustomed to the novel idea (another few years), then you have to adapt it to users' needs." .
[JA] "Professionals now accept point-of-care biosensors like glucose. So I would say it could take from 2 years, like [JL], to 20 years as [BS] has said.
A start-up company [AW], having registered as a firm 3-months prior to the workshop, is not so pessimistic, noting that ICT innovations will speed up these development times.
Seizing on this comment, [DR] comes in with a prompt "the innovation landscape is changing; including the role of start-ups. This could reduce the time to market."
[MR] comments on timing, "The human genome project went very fast. The problem is rather hype and disappointment, and also [*connected with this*] if you develop faster you may also stop faster, cf. proteomics in companies."

Stretch 4: Integrated platform

Almost out of the blue, another participant [BS] comes in [*with a comment which triggers another stretch in the conversation*]; "There will be no integrated platform. I promise you that." "There will be many integrated platforms" mutters [JA]. [DR] "But people *do* talk about integrated platforms such as academics, European Commission Framework Programme projects etc." [AF] nods agreement acknowledging that there is generally an academic buzz, but that companies are more reluctant. [BS] comments "this is an aspect of the new landscape."

[AF] [*with an unannounced history in biotechnology research but mentioned in the interviews with [DR]]* comments on how the application context shapes the innovation challenges [AF] "Biology is so diverse, so there are different provisions (each of them expensive). There are <u>real</u> [*he says this emphatically*] niches for point of care: sexually transmitted diseases for example."

[AR] makes a brief summary "So from the discussion we see there (are lots of niche markets, but no killer application yet. But aren't killer applications necessary to get real development of technology as [MR] mentions?" [BS] responds that technology is not the problem. [QRD] concurs by adding that all the technical elements are developed but it is financial resources that are needed which are the main issue. [JL] highlights the attractiveness of having a platform which you can tailor for niches requiring marginal alterations for each application.

[QRD] remains sceptical about a generic platform:

> "Venture Capitalists require quick return on investment and thus identifiable large turnovers. Present incentives from investment world assume that you're selling something already. This is a major bottleneck for radical innovations. The only way you can do this is to bring the blocks together: you need to own everything, network & consolidate. This is where aid from public agencies can help (decreasing risks) for example DARPA: requiring semi-conductor companies to share masks."

[[QRD] *speaks from his experience of benefiting as a start-up from EC Framework financial assistance*]

[AR] mentions that working towards these larger futures (with large revenues) will also create other opportunities. [AF] agrees, adding that one often touted driver is the ageing population with the general theme of monitoring their own lifestyle. [JA] describes an instance where this hasn't worked. One example of poorly articulated end application is the Siemens, "lab cow" for genetic analysis. Medical Solutions Siemens, made the device first, only now is looking for application. Additionally, small companies cannot do such risky business.

There are nods of agreement from [AF] and [QRD], [AF] commenting that other large firms like Philips have similar approaches.

The organisers connect up this stretch of discussion with the innovation chain diagram shown earlier. "You can see a fragmentation of technology, because of the dynamics (niche markets, biology, SMEs, big companies and their various strategies)." *There is nodding in the audience, the participants recognise this.*

[BS] comments on specifics of innovation chains, that you must distinguish product companies and service innovation. The larger companies buy the technology when they need it. Smaller sized companies are embedded in supplier chains. Still wishing to focus the discussion, [JA] voices his concerns that we should distinguish between application areas so we can anchor the discussion, i.e. homeland security, R&D, diagnostics, forensics. [BS] disagrees "For all these applications, you use similar tools, because we (my company) supplies chips in all of these sectors you mention)

[AW] (returning to the earlier stretch on challenges of innovation chain) comments that additional expertise are also necessary in the various stages, SME can't cover the whole development trajectory.

An organiser [TP] decides to shift the broad discussion towards the ideas of multi-path mapping and the planned session. Another organiser adds [DR] "Start Ups

need a framework to support strategic decisions. Rather than specific detailed roadmaps. Sort of socio-technical map (changing over the years) but this is difficult to create and difficult to get hold of."

[TP] suggests three areas (to focus) on stemming from our literature review and interviews. Which one to choose for this afternoon's discussion?

- Tissue Engineering/Stem Cells
- SCA for systems biology
- High-throughput screening
  (or impose a choice)

The group begin to discuss with the striking suggestion put forward by [BS] that high-throughput in-vitro fertilisation is a good example of product which could be, but isn't. Others have some qualms [JA] "I wouldn't want to work towards it, too many ethical issues disturbing the technology." [BS] But currently it is done manually injecting sperm into egg cell. 5 years ago a US Start-Up wanted a single cell analysis in-vitro fertilisation bioreactor for in-vitro fertilisation? But then the Bush Administration clamped down on this sort of research. [BS] and [AF] It is just automation, replacing technicians by a machine. What about prenatal diagnostics?

Lunchtime has arrived, and we concluded that "Gene Analysis/Therapy (of a single cell) on a chip" would be broad enough and specific enough for the afternoon session.

LUNCH

During the lunch break, one of the organisers [DR] mingles with the participants and queries about the workshop process. A number of participants voice their concern about finding it difficult to find an entrance point to the discussion. The large oval table doesn't help with this, commented one participant [MR].

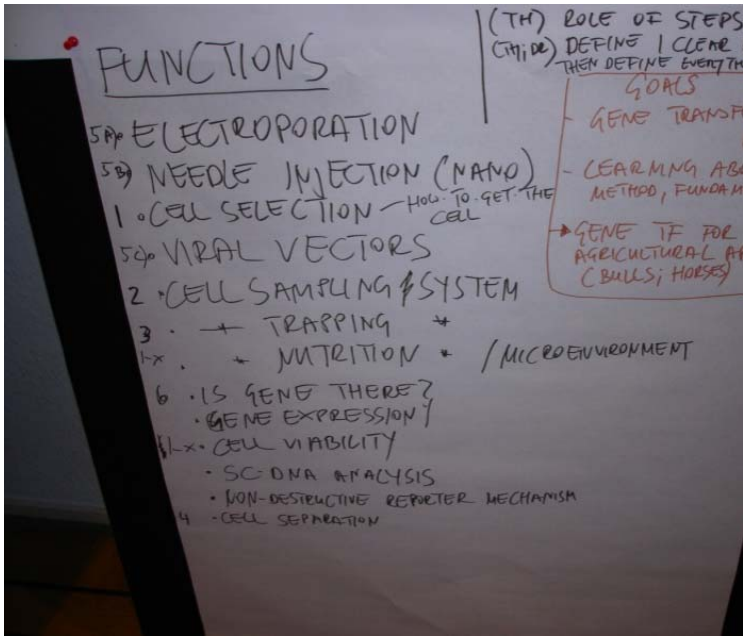
This triggers some rapid redesign of the workshop setup, to move more quickly into interactive and joint development of the MPM. [DR] foregoing his lunchtime sandwich, reconfigures the seating (whilst the participants are at lunch) around a large version of the MPM, and some flipcharts. People are placed in close proximity to each other and the map.

Stretch 5: Moving towards the multipath map

Fig 7: Participants are seated around a flip chart (left) and empty multipath map (center; green, with post it notes). It brings everyone together and focuses on lists and maps. This proves a more amenable workshop approach to the enactor participants (as opposed to round table discussions).

[TP] introduces the session. "First we will discuss (brainstorm) a little bit about the functions that are necessary for cell on a chip, and then we can move on to multi-path mapping and explore the challenges for the innovation chain in the context of cell on a chip."

In this period, participants started listing functions needed and some technology components of a cell-on-a-chip device. People discuss amongst themselves in a similar fashion to a focus group.



Functions necessary:

- electroporation, nanoneedles,
- selection of cells (for therapy).
- Cell sampling (getting them – from a soup, from a tissue),
- cell trapping,

Goals

- Micro-environment sampling
- Injection/electroporation
- Analysis: is gene therapy.
- Proteins. Bioreactors?

Fig 8: Photo of the flip chart with some of the selected functions and goals listed.

At this point the dynamic is quite slow and forced. This is observed by all organisers, unlike stretches 3 and 4. It requires concerted effort by [DR] seated amidst the participants to draw on his experience doing the case research and interviews that was undertaken in preparation for this meeting.

[AT] (Her first and only comment) notes that ideally we would have an application where we learn about mechanisms. This is one of the major causes of very low success rates of present gene transfection (so not create a new product but a better current one) i.e. gene transfection on a chip.

[AF] questions the point of being able to work with one single transfected cell. "What is the use?" [JA] suggests that for a case example we take as overall product, gene transfection for bulls, race horses (artificial insemination). So avoid immediate link with humans. "I am uncomfortable talking about gene transfection on a chip or embryo analysis."

[QRD] has different concerns and asks the organisers: "What do you put on a chip?" He goes on to elaborate. Systems-on-a-chip (CMOS) can accommodate only so much. So systems-in-a-package is what microelectronics goes for. Partitioning what you put on the chip and what you have in the surrounding device is important. For example placing an expensive part in the device opens the way

for disposable cartridges. This means you have to work with polymers – giving you a design requirement.

[BS] notes that there is a question on success rate "for medical applications you need 100%". [JA] agrees "For animals, you can accept 99% success rate. You don't have to work for another two or three years to improve success rate. (1% just have another cow) All components can be made by university groups but quality and continuity of production is not guaranteed. For a product you need integration and thus a big company - they can do it in house."

[JA] continues, commenting that the UK attempted at creating a value chain of industry and foundries, to create SME suppliers. He notes that SMEs can't do that as it requires upfront investment to store all the building blocks and maintain the skills.

The organiser [DR] decides go with the flow of conversation around the organisation of actors for innovation on cell-on-a-chip (rather than the types of technical configuration of chips which was decided earlier). The discussion livens up, a large number of participants find an entrance point.

Stretch 6: Innovation Chains and organisational form of MPM

The group identified a number of existing (or attempts at) innovation chains in the broader microfluidic/cell analysis fields:

- *In-house R&D of a multinational corporation (MNC)*
- *Technology development conducted by SMEs but stimulated by an MNC*
- *Start-ups finding opportunities and becoming the integrator*
- Separate integrators and design houses
- Research device is picked up by someone
- *Groups of heterogeneous actors coming together in a cluster*

The four options shown in italic where agreed to be discussed in more detail. One of the organisers [DR], changing from the original plan, took the original MPM scaffold and sketched out the four organisational paths. This allowed organizational challenges and technical challenges to be placed side by side with the goal of prospecting innovation chains. In this case we left the technical steps in the chain as part of the axis whilst the content of the map focused on organizational

arrangements and roles of actors at different stages of the chain. We overlaid on top of the chains the challenges and hurdles linked with each chain (see photo below). On this basis the chains were evaluated.

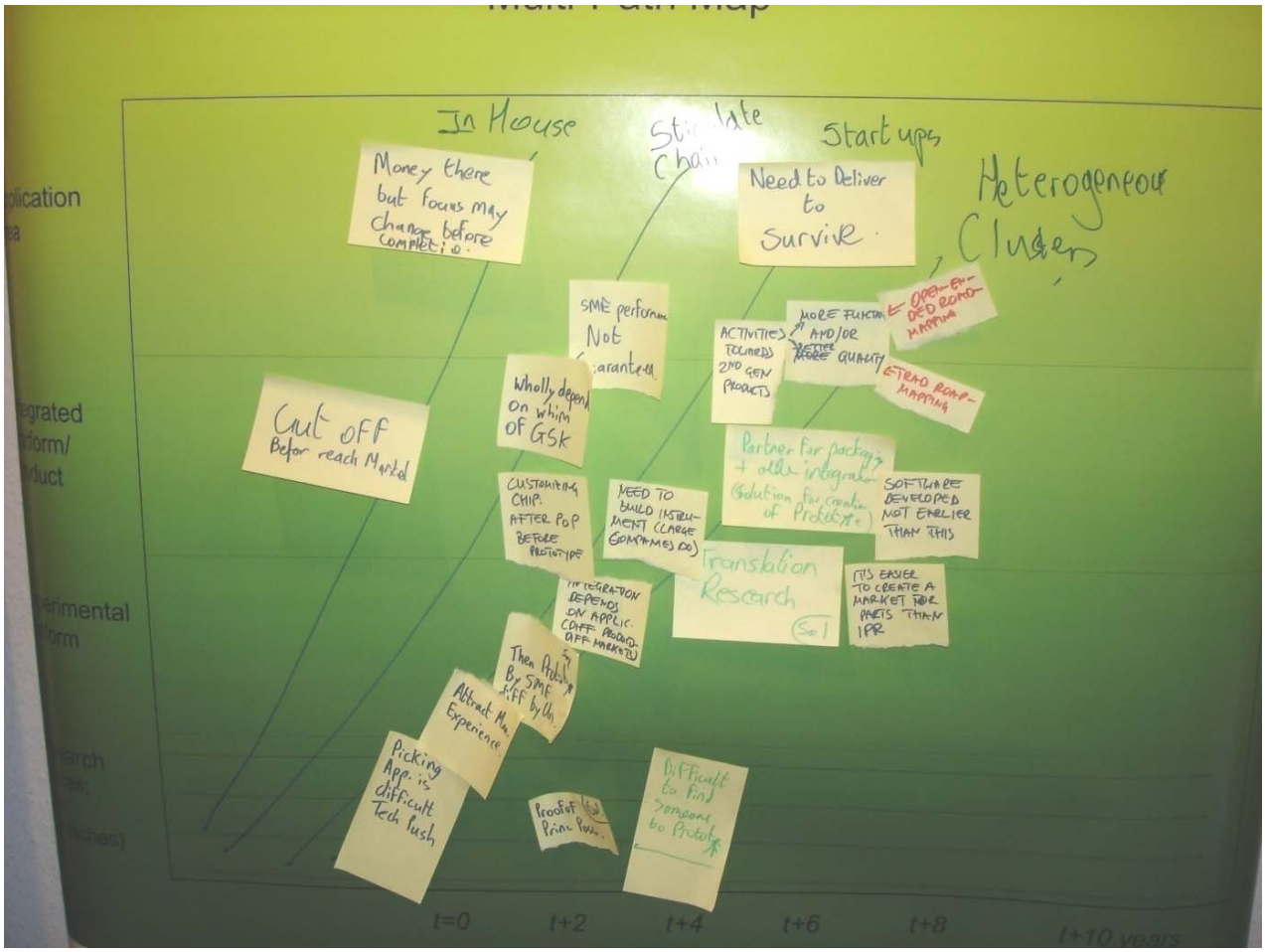


Fig 9 Photo of the possible configurations of innovation chains (as non mutually exclusive pathways)

Within the group there was an agreement that multi-national corporations, such as Siemens or Philips have the capability to undertake research into components and integrate them into a Lab-on-a-chip technology platform. But ***innovation chain 1*** (see figure below) was said to have a key stumbling block - no clear market is visible for return on investment. Identifying the end user is one clear approach to selecting the components and configurations of a technology innovation chain. However one of the participants described the betting on a particular end user as dangerous because the innovation chain is precarious and may collapse. Flexibility is attractive for developing sustainable innovation chains but requires a belief in the technology. The participants were in agreement that this is lacking in MNCs due to previous hype-disappointment cycles – such as in biosensors. Another issue is that cell biology is diverse and so for cell-on-a-chip many niche markets will be the key. Large industry will be unwilling to invest in such niche markets (such is the

case in pharmaceutical industry). Perhaps when a generic platform is the target large companies may invest, but application focus for cell-on-a-chip will be niche market oriented.

However, the large risk of little return-on-investment was agreed in the group to have stimulated another form of innovation chain initiated by MNCs labelled as ***innovation chain 2***. This shifts the risk to SMEs which the MNC contracts for risky projects. Thus MNCs attempt at shifting the risk to start-up companies which build on their own ties with the research community and attempt to develop the technology. Intellectual property (IP) is shared with the MNC One participant [JA] gave an example from Glaxo Smith Kline in a project which he was involved in. Major issues voiced in the discussion related to the relationship between MNC and start-ups: for example the sustenance of the innovation chain is wholly dependent on the whims of the MNC [AF]. Moreover, the concern was raised about the protection of IP: although the IP can be shared MNCs have the capability to turn it into a product and defend any IP issues based on their large resource base.

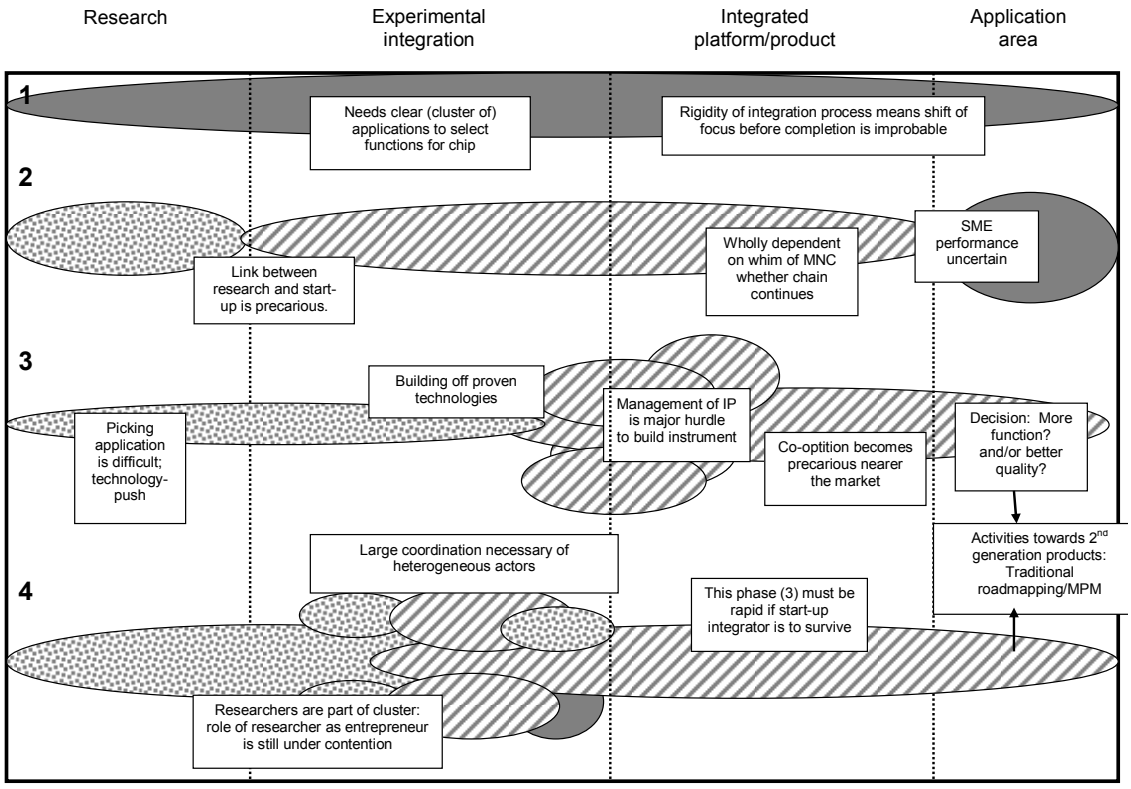


Figure 10: A summary of the sketched out innovation chains. (1) MNC (dark grey) in-house; (2) SMEs (striped) chain stimulated by MNC; (3) Start-ups creating network; (4) Heterogeneous clusters

One of the participants gave a case example: a large multi-national pharmaceutical company initiated the development of a prototype integrated device for chemical analysis with a number of start-up companies but then proceeded to outsource the further development of the possible product to another company with the end effect of the start-up companies being dissolved.

The discussions continued, [JA] highlighted that there is a risk for MNCs when outsourcing the development of an integrated platform to SMEs: the performance of the SME is uncertain. The other two suggested configurations of the innovation chain (chains 3 and 4) had little or no reliance on MNCs.

In ***innovation chain 3*** a consortium of start-up companies would be the initiator for bridging the gap by attempting a generic integrated platform which could then be tailored for specific applications. This was proposed by a technology focussed SME which has a history of connecting up with other SMEs in product development processes [BS]. He gave an example where similar SMEs in the Netherlands are waiting for the integrated platform to arrive are struggling to survive and are motivated to take action. Networks of start-ups and SMEs related to micro and nanotechnology (cf MinacNed) already exist. Thus a form of co-optition would be the desired goal to take the step of integration together and then competing based on tailored products and added value. The workshop participants agreed that the attractiveness of this innovation chain would be tempered again by IP issues – a large number of companies, distributed IP, difficult to see how each member as well as the collective could capitalise on the developments. The degree of complexity of an integrated lab-on-a-chip platform would mean a clear application driver for the SME-consortium or the move towards a generic platform in which all would benefit would be needed as a guiding vision. One of the organisers [DR] pointed out that the idea of a generic platform is still contended [*this contention was included in one of the three socio-technical scenarios*] and thus mobilising the resources to create a generic platform may be tempered by uncertainty of whether going for a generic platform (rather than specific application tailored innovation chains) is the path to target.

An alternative to this path was ***innovation chain 4*** which focussed on heterogeneous clusters. Since a large investment is needed in integration, there are specific advantages to be gained by building on proximity relations. This comes from building up capacity based on resources in the region, as well as a funnel for innovations coming from university research [AW]. Thus such a heterogeneous cluster would centre on university research and fabrication facilities, where start up companies (and perhaps larger companies) would form the constituents of a

heterogeneous cluster. On the one hand, a large investment in coordination is necessary and mobilising and coordinating resources is a key issue. On the other hand, advantages of such an approach are that new innovations will be occurring within the cluster, and proximity will allow for knowledge exchange and the building up of trust.

The workshop participants pointed out that there are attempts at all four innovation chains:

- ***Innovation chain 1*** has been attempted by large companies such as Siemens for relatively simple integrated microfluidics. One participant [JA] mentioned a "Lab-cow": which he describes as "an interesting integrated microfluidic device was designed first and then began the search for an application, leading to more loss of confidence in such ventures by MNCs".

- ***Innovation chain 2*** has occurred with companies such as Glaxo-Smith-Kline[110] and spin-offs such as those from University of Hull (UK) and Yole Development, a French MEMS business development consultancy.[111]

- There are attempts in the Netherlands for ***innovation chain 3*** building off micro and nanotechnology SME networks such as MinacNed.[112]

- ***Innovation chain 4*** is currently occurring at the University of Twente (NL) where a start-up company with a specific sensor is acting as platform integrator.

The groups agreed that each of these innovation chains are possible, but 3 and 4 are the most plausible ways forward (based on past failures of innovation chains 1 and 2). The participants also raised more general issues which came up as part of the exploration of the possible innovation chains. A major point was IP for distributed development of an integrated platform, the agreement being that new organisational models need to be sought. The IP issue can be generalised to many projected nanotechnology innovations, where technologies cannot be products in themselves but must be part of a system of technologies to be enabled. For innovation chain 3 this is indeed a challenge. For innovation 4 however this can be handled if there is one system integrator which targets a specific application and builds its network based around this.

[110] Source: workshop participant.

[111] http://www.yole.fr/.

[112] www.minacned.nl.

Stretch 7: Final discussions at the close of the meeting

The participants recognised the difficulty of researchers in public institutions actually getting any credit in developing integrated platforms – it is outside of the evaluation criteria for their profession. Although pressure is on them to provide research that can be turned into innovation chains, there is little acknowledgement of time spent on doing this as opposed to research and teaching. One way of doing this is developing an integrated platform based on an interesting experiment. [DR] mentioned that, for example, the University of Hull's crime scene forensic device is one case where funding was given to develop a prototype device for DNA analysis, with the added advantage of demonstrating integration possibilities for a cell-on-a-chip device. Innovation chain 4 was agreed by the group to be the most promising approach to bridging the gap in the innovation chain.

Seeing that the end of the meeting is imminent [AF], returning to the technological multipath map, refers to possible strategies for product development for cell on a chip: "First generation products shows that the device works, and is aimed at a market niche. You use this to learn how to make the second generation device with more quality and more targeted. You should stagger (and increase the level) of functionality on the chip (so do not saturate the market with the 1st generation, allow opportunity for second generation)".

He goes onto suggest a key technical bottleneck in cell on a chip. "Sample preparation technologies – may take us quite some years. Will we have time before the bubble bursts?"

In response, a techno start-up [QRD] replies "The bubble has burst already; people don't want to invest in the technology (in general, in this area). Standard biosensors are available; cell analysis may not be able to compete."

With that final comment, the time allotted for the meeting is over and the meeting adjourned.

3.3 Summary table

Actual composition	5 senior LoC researchers, 1 junior researcher, 5 small firms, 3 organisers and 2 observers
Degree of heterogeneity	Homogenous (100% enactors)
Last minute cancellations of participation and its impact.	1 senior researcher (not counted above) dropped out a matter of hours before the commencement of the meeting. This had serious consequences as he was recognised as an international expert in the field flying the flag of cell-on-a-chip as an important vision. This flag flying was only

	shared by one other participant in the workshop [AT] who remained silent throughout the whole workshop. This meant one major topic (that of cell-on-c-hip and thus societal embedment issues) was sidelined.
Stretches in the discussions Organiser initiated and taken up = O+ Organiser initiated not taken up = O- Participants initiated and taken up = P+ Participant initiated not taken up = P-	O/O/P+/P+/O/P+/P Stretch 6 was particularly animated. At the end of stretch 5 the discussion started to move away from ELSA and societal embedment issues (of gene analysis on a chip) to innovation challenges. The organisers decided to go with the flow (away from the explicit broadening opportunity of ELSA and societal embedment discussions) and move towards innovation processes (with the hope of implicit broadening in the animation of the discussion).
Explicit reference and use of the scenarios	= They did not refer to the scenarios explicitly in the discussions except when in the comments handed in as "homework" regarding the preparatory material. The questions and collected answers are given in the box in stretch 2.
Implicit reference and use of the scenarios	+ They refer to the hype/disappointment cycle in stretch 3 They describe the difference between generic and integrated platform
Quizzing between homogenous actor group (or with those who knew each other prior to the workshop)	Yes in Stretches 3 and 4 there is a collective building of a richer picture, with agreements or mild disagreements. The participants speak as if informing the organisers. At the end of stretch 4 there is a particularly striking difference in perspective on ELSA issues around a potential application (high throughput in-vitro fertilisation).
Asymmetric probing of the majority group (perceived as experts)	Yes between the small firms and the researchers
Mutual probing in	Probing occurred after lunch in stretches 5 and 6.

heterogeneous group	Stretch 5 revolved around the hypothetical application of gene diagnostic and therapy on a chip, where difference of opinions where made clearer and probing of each other's experiences in the macroworld were shared. Stretch 6 revolved around individuals' experience. Although all part of a similar community, each participant was in a specific (and separate) institution or firm, and in some cases from different countries. Thus once a common issue was found (the innovation gap) they began exploring together the issue and Therefore, although not heterogeneous per se, in stretch 6 in particular, they found a situation where within their own enactor based world they found enough differences to probe.
Do participants get into broader aspects or do they recourse back to their usual positions.	They recourse back to their usual positions (or are forced to). At the end of Stretch 4 when [JA] mentions his unwillingness to discuss a hypothetical case because of ELSA issues (in the real world) this is not really picked up. There is not enough heterogeneity in the group to build momentum on a non technical or innovation chain issue, so potential stretches that could have flowed from the beginning of stretch 5 when we discussed gene therapy on a chip did not fire up, and there was recourse back to the technical and innovation issues.

Appendix 2 - siRNA delivery innovation providing new tensions and opportunities

1 Starting Conditions

1.1 Preparation through insertion and analysis

In the 2nd Annual Meeting of Frontiers, held in Sicily during October 2006, I was asked to participate in both the internal management board meeting (with annual assessment by the European Commission) and the annual meeting itself. In the internal meeting and the annual meeting, a number of issues were particularly visible, such as

- Managing R&D around particular therapeutic applications;
- The stress on research centres to innovate as well as provide excellence in research and education; and
- The variety of mechanisms, means and pathways of commercialising nano-enabled therapies (the link with large firms, spin out companies).

In the internal meeting, these issues were discussed as a matter of "indicators of quality" of the activities coordinated in the network of excellence. In the annual meeting it emerged both in the presentations of the technology presentations with discussions in the coffee breaks, during the long lunches and evening meals.

Through my discussions, especially with researchers from Karlsruhe, Stuttgart, Aarhus and MESA+, I felt a number of pressures that were not related to "usual" research practices. These included discussions about links with patients, with one research group leader mentioning that family relations to patients of a particular disorder would come to presentations and ask - in some cases well-informed - questions about the promising therapy. A researcher from Karlsruhe noted that this is not only uncomfortable, in the sense that they are not used to these interactions with the "general public", but it "also forces a more realistic picture."[113]

During this meeting, a lead researcher at the University of Aarhus presented his group's work on drug delivery under the framework of a *Strategic Research Area* of Frontiers under the same name (which they were leading). In this conference

[113] My own response to this in the meeting was to talk about scientific promising versus therapy promising. This spurred a discussion in one of the conference meals about hype, which forms part of the dynamics in the scenarios shown later.

keynote presentation, he described the potential of nanodelivery systems for RNAi therapy (a mechanism of using a molecule similar to DNA for interfering with intracellular communication systems, disrupting the manifestation of disease when a cell is infected).

I could see that drug delivery would be interesting for a CTA-project, because those in the Frontiers NoE involved in nanoparticle drug delivery would have to be linked with envisaged therapies in order to create potentially useful delivery systems. In addition through early discussions there was an innovation issue and an expectation management issue. I decided to explore the potential of a CTA workshop on this topic.

After some discussions with the drug delivery research group leader and some of the senior researchers in the Aarhus group present at the meeting, a CTA concept began to take shape in my mind, that interfacing research with therapy development seemed an interesting and relevant topic, where rather than a broad discussion of drug delivery, it could get closer to issues through focusing on a particular therapy area (or family of therapies) utilising the RNAi.

From these initial insertion activities, and some further desk research around RNAi and nanodelivery platforms, I decided to propose a workshop. For this workshop I also wanted to focus on the implications of the new roles and responsibilities if there was a shift towards exploitation. The issue of linking with therapies would be the entrance point, which in turn would be an opportunity for exploring reflexive co-evolution through prospecting innovation chains from the laboratory to the clinic, thus combining

- Discussions of the tensions in academic research centres (such as those represented in the Frontiers NoE); and

- Anticipations of the plausible journeys of nanodelivery systems for RNAi more broadly than technology development but on regulation, patient culture, medical practices etc.

My plan, as described to the Frontiers management team regarding the programme of CTA projects, was framed around exploring the potential for stimulating reflexive co-evolution in R&D networks through creating a temporary space for (1) probing the assessment worlds and criteria from multiple actor perspectives, and (2) exploring possible innovation journeys in order to unveil (based on collective experience and knowledge co-located in the workshop) issues and challenges along the innovation journey.

An additional objective of the programme of CTA workshops[114] was to embed the workshops more into the ongoing dynamics of the Frontiers network;[115] I remained flexible to negotiations on the shape and content of the workshop. With this in mind, the two anchor points (mentioned in the previous paragraph) and the philosophy of CTA (broadening design processes and stimulating reflexivity and learning about broader socio-technical dynamics) were kept as central to the emerging workshop concept.[116]

During the period between October 2006 and March 2007, it was unclear whether finance would be available from the Frontiers management board for further workshops. The interest was there, based on the output of the first workshop on cell-on-a-chip and also the enthusiasm of the science-to-industry workpackage leader on bridging innovation with ELSA[117], but confirmation of resources were delayed.[118] At the end of March, the confirmation of resources came, but the timing for organising the workshop was very tight[119] (a 1-day window!) since the only opportunity for a workshop before July 2007 was May 31st and I had to go forward on that basis.

On 1st April 2007, iNANO confirmed that they would host the workshop, and I flew to Aarhus for a visit from 10th – 12th April to co-create an outline CTA project. During this meeting I met with [HK] (my main point of contact) whose background is in pharmaceutical research, [SB] a research group leader with a background in molecular biology, and a number of PhD students at iNANO working on drug delivery.

The first contact was on the evening of the 10th in downtown Aarhus, when [HK] and I went for a meal and a few drinks. During this meal we discussed a number of

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[114] For clarification, at the time (2006), I had in mind five or six workshops for the programme including the pilot project described in Appendix 1.

[115] The CellChip workshop was organised for the Frontiers NoE with the management team. Thus the topic was decided by me. At the time of the pilot CTA project, there were no Strategic Research Areas in Frontiers. Now that there were, it seemed an opportunity for greater embedding of CTA into Frontiers activities.

[116] In the agreement with Aarhus I made it clear that the CTAs had a dual role, one as a project for Frontiers and the other and part of my PhD research in the TA-NanoNed programme.

[117] A term I used in my presentation and a key slogan in the TA NanoNed programme.

[118] It is important to note here that at this point that my proposal was to conduct two workshops in the 3rd year of Frontiers (before July 2007) and two in the final year (before July 2008) and consequently the delay in agreeing to resources was for the programme and not one particular workshop activity.

[119] Based on the agenda of the agreed host institution, iNANO, University of Aarhus, Denmark.

things unrelated to the workshop, but quickly turned to the focus of the meeting. There was much confusion when I mentioned the notion of prospecting innovation chains, anticipating on issues etc. [HK] admitted he was confused by the concepts and my explanation but could see merit in the project and mentioned, "As a minimum it would be *seen* as useful by organisations such as the European Commission"[120], and therefore he was willing to run with the project and apply himself to it. During breakfast the following day, recalling [HK]'s confusion and remembering that the topic of the workshop would co-evolve with my meetings with [HK] and [SB] that day, I drafted models of the extended transition path from research to therapy as well as the concentric/multi-level view (see figures below)

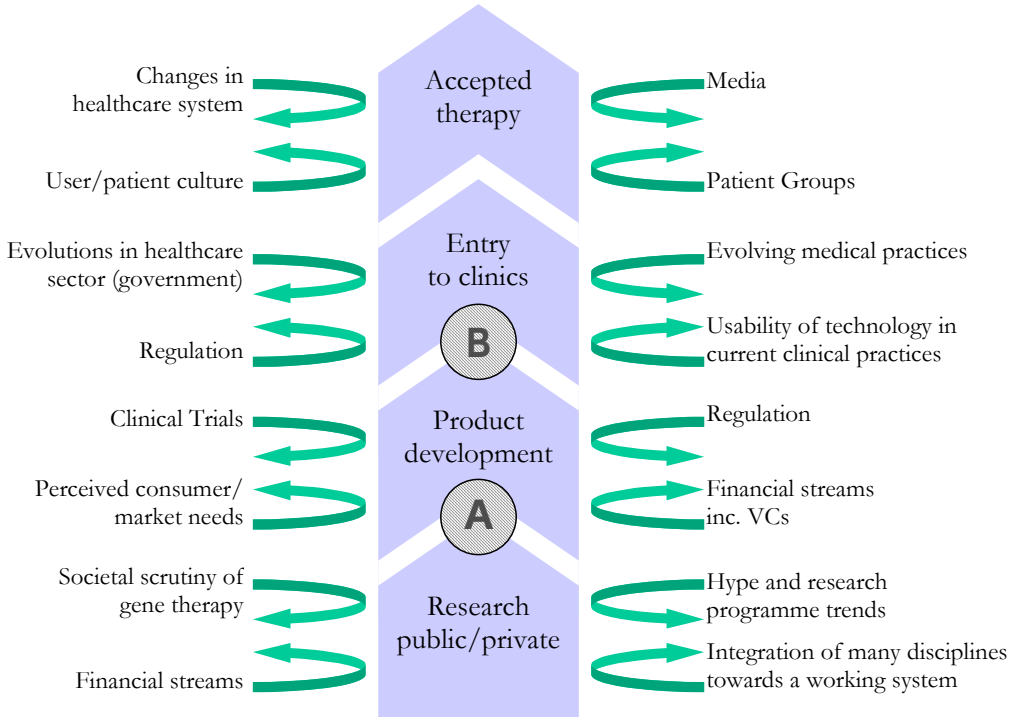


Figure 1: The extended transition path from research to therapy.

In Figure 2 the concentric view is represented by vertical arrows, and interacts with the multi-level view (horizontal arrows). Actors must combine both in their strategy making. Arrows (green) show some of the many dynamics that will influence the chance of successful transition along the chain. Two important gaps are located: the gap between research and industry (A), and the gap between

[120] During the meal he mentioned the increasing emphasis in calls for proposals for R&D funding to include ethical aspects and public engagement. In a separate stretch of our discussion he also mentioned pressure to patent and spin out companies.

industry and clinical needs (B). This diagram is an unmodified version of the figure I showed in the meeting.

In Figure 1 I depicted the innovation chain as usually perceived from the scientists point of view (left), with the arrow as the innovation chain (concentric view). Referring to the right hand-side I mentioned that this is what actually happens, that the innovation chain emerges out of multiple interactions between all segments. I proposed that the workshop would allow representatives from each segment to be able to interact at the same time ("a temporary space for exchange of ideas and perspective"). This diagram is an unmodified version of the figure I showed in the meeting.

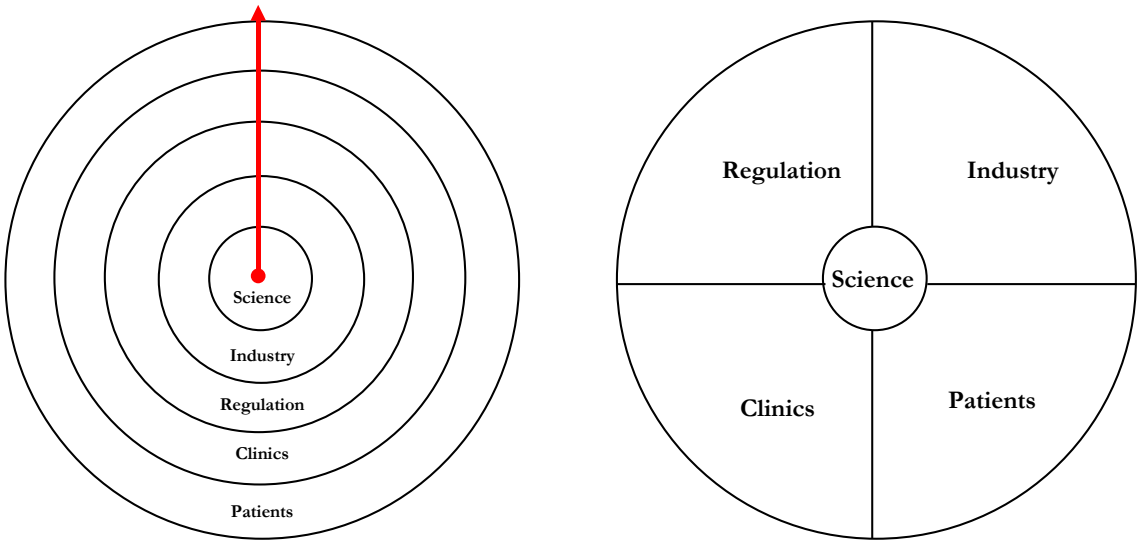


Figure 2: Concentric (left) and concurrent interaction views (right) of knowledge production and uptake (adapted from Deuten et al 1997)

In the discussions during the day I described that the concentric view is how scientists usually view the world when making plans, but that in practice (and often recognised by those developing technologies) that many groups are involved, with varying degrees of strength, from the very beginning, with feedback loops, setbacks etc. The point of the workshop, I proposed, would be to manage and explore these interfaces by exploring (in a temporary space) possible innovation journeys and how each of these groups affect (and are affected by) the emerging innovation. The notion of temporary space was picked up (both jovially and

seriously)[121] especially by [HK] who liked the term and was one of the aspects that stuck in his mind.[122]

The rest of the visit in Aarhus I was introduced to the fundamentals of siRNA research and development at iNANO, to the commercialisation and technology transfer activities at iNANO through discussions with a consultant they used to advise them in their patenting and private sector collaborations. I also had many interactions with PhD students on some of the aspects of research. The group were considering developing therapy candidates for influenza, arthritis, and pulmonary disease; although at that point they were unsure to what extent they would develop the therapy themselves. This provided a prospective context for the workshop; they were envisioning applications and shaping their research agendas, choice of nanoparticle and payloads around this. They already had links with a small biotechnology firm to provide the raw payload (the siRNA) which they would modify.

The outcome of the one and a half day meeting was that there was a recognisable tension around the issue of exploitation and exploration, that siRNA as a gene therapy raises many issues, both societal (with respect to the failures and tragedies of some previous gene therapies) and also on innovation: "the gene therapy bubble has not burst but has been deflated". The objective of the CTA project was then for the further contextualizing of the envisioned innovation journeys, currently planned for using the concentric view, through creating an opportunity for recognition and reflection of the broader/overall dynamics that effect innovation journeys.

After the negotiation, and exploration of the first workshop concept in the context of iNANO and siRNA research, it was agreed by myself, [SB] and [HK], that the workshop would look at the tensions of exploration vs. exploitation on research groups/centres in the field of nanotechnology drug delivery, and stimulate reflexivity on the roles and responsibilities involved in the variations of the exploration/exploitation theme. This would be useful for them and the Frontiers

[121] Jovially in the sense that it was deemed a language that the European Commission would understand and get excited about ([KH]). Seriously in the sense that once I elaborated on the notion (one is free to think out of one's professional box and explore different perspectives) it was dubbed a worthwhile initiative although risky – "people may not want to think outside of their box" [KH].

[122] I qualify this claim by noting how [KH] introduced the project he and I were to run during the number of meetings and chats we had with colleagues and friends during the day at iNANO. The notion of temporary space and prospecting innovation journeys to optimise drug delivery innovation were the key aspects brought up. He also mentioned at the end of the day that the diagrams helped him get a grasp on what I was going on about.

network, as the results and findings could be applied more broadly to other nano contexts in the Frontiers' research portfolio. The group were already envisioning target ailments to broadly guide their research and development agenda, and the CTA would attempt to bring these visions into context by creating scenarios unfolding from the present to the delivery of some of the treatments they were envisioning and thus linking with the second broad theme of dynamics that play a role in the translation of therapies from research into clinical practice.

I suggested, and it was agreed, that we would use the budget allocated for the project to bring in representatives of the relevant actors that would be involved in the plausible innovation journeys that from the present. This translated into an official outline submitted to the Frontiers Management board to sign off on:

- The CTA project will dig deeper into the exploration/exploitation tension and its consequences on the research team.
- The CTA project will dig deeper into the dynamics that will affect the emergence and embedment of nano-enabled therapies.
- The CTA project will create an opportunity for reflexivity and learning via:
    - Providing socio-technical scenarios showing some of the shaping dynamics in the drug delivery context, and
    - Creating an opportunity for probing the assessment worlds of different actors who would be involved in the innovation journey.

Below two summary tables are presented. The first present's seven criteria that were used to both determine the starting concept of the CTA-project and its suitability for the various interested parties involved. The second table shows the contingencies that where an outcome of the negotiation of the project concept, the context of the subject, my degree of control over the shape of the project etc.

1.2 Summary Tables

Key elements that contributed to the initial idea for the CTA.	Nanotechnology enabled drug delivery and the broader shifts in drug development coincide creating new opportunities and challenges for researchers. This leads to potential changing roles of research scientists in R&D to actually participate in drug development practices (the tension between exploration and exploitation)
Is it interesting for my study of inserted CTA targeted at broadening enactor's perspectives?	The linear model of innovation is prominent in the drug development process, part of the process of aligning actors and activities over a long development process (e.g. the steps in clinical trials). But cases reveal societal embedment issues along the chain, which provide examples of broader dynamics

	at play. Along with the discussions at iNANO, it seemed possible to link broadening the concentric bias with broader multi-level shifts in drug development sector (where delivery has become a key strategic activity) and to do this be prospecting the possible co-evolution of innovation journeys in the field and the broader context.
Frontiers partner interests?	**Key negotiation actors:** Key nanoscientists at iNANO [HK] and [SB] iNANO at the University of Aarhus has a young but internationally recognised group in nano-enabled drug delivery research with a view to targeting their research to particular therapies. Their interest was how to do better as researchers being involved in potential therapies. They had mentioned a number of societal and innovation pressures which they thought the workshop could help them with.
Stage of development of the field?	Rapidly growing with the announcement in 2007 of a Nobel prize for siRNA research.
An identifiable community or socio-technical network?	Yes. A complex mix of nanotechnology delivery mechanisms and siRNA research, many different approaches to delivery and many different targets for the siRNA therapy. For siRNA there was another European Network called RIGHT in which Aarhus was a member. Thus [SB] and I proposed to the RIGHT network to make the CTA project a joint project (Frontiers with its emphasis on Nanotechnology and RIGHT with its emphasis on siRNA).
Is there something at stake recognisable to some of the actors in the emerging community or socio-technical network?	There was recognition of the exploration/exploitation issues in nanotechnology based drug development research and as a matter of prudence it is worthwhile investing time in the CTA project. Also, since siRNA is a gene therapy, there were overtones of the controversies in the 90s and early 2000's and so a matter of prudence on ELSA issues too.
Amount of material to work with? *(as perceived during the early stages of the CTA project development)*	A very rich data set. A first scan of the literature revealed that a second path of drug development may be emerging around what was then labelled as "Bophirima" where genomic drugs or other molecular based medicines were developed with delivery being a key factor. The emphasis on delivery is part of the very nature of biomolecular drugs – most of the molecules need protection from the human body's defences and/or controlled release and targeting because of potentially

	toxic off target effect. A division in the set up of the innovation chains could be seen, were large pharmaceutical companies dominate the currently dominant generic and block buster approaches to drug development. In the Biopharma regime development would be on a large number of drugs (as opposed to the relatively few developments on generics) and the development would be led by networks of smaller firms, biotech companies, drug delivery firms (particularly in areas of nanoparticle development) and academic research centres with large pharmaceutical firms providing the gateway to markets. Thus there is a potential shift in the drug development landscape which would effect biopharma and research centres.

Table 1: Identifying and negotiating an area to apply CTA to

Requirements and constraints from the Frontiers network	The workshop finances would be mainly for Frontiers members. We made use of linking with a firm, a clinician and someone from an environmental agency (on risk and toxicity) from Denmark, the location of the workshop.
Level of control over the topic and process by CTA organiser	It was a negotiation, since the theme of exploration/exploitation and ELSA issues around a nano-enabled gene therapy came about during my visit to Aarhus. However, my diagnosis of the situation and suggested topics, after some elaboration and discussions during my 1 ½ day visit to Aarhus were accepted without much modification.
Amount of time to prepare the project	This project had a very tight timeframe. Since the funds were only made available 5 weeks before the agreed date of the workshop, finding participants and doing the research, creating scenarios was very tight and I was under a lot of pressure. Also, during the last 3 weeks of this 5 week period, I had a 3rd CTA project to prepare for (see Appendix 3).
Gathering participants	Two strategies were applied, one of an invitation to Frontiers partners, and another more targeted (in order to get a diverse mix of participants). However, most participants only confirmed less than a week before the actual workshop.
Possibility to interview participants	The limited time meant that I could do little more interviewing than the 1½ day visit to Aarhus (which was quite extensive anyway). This was unfortunate since I

	wanted to do interviews similar to the cell-on-a-chip workshop. An additional limitation was that many participants agreed to attend less than a week before the actual workshop.
Available document data	A lot of information, although for nano-enabled siRNA delivery specifically, it was a HOT field at the time and so few review papers were available and I had to go deep into technical papers to get an overview of the field.

Table 2: Contingencies and ramifications

2 Preparation

2.1 Two promising technologies – Nano-based delivery and RNAi therapies

The field of drug delivery is developing rapidly and is gaining the attention of scientists, pharmaceutical researchers and industry alike. The development of effective drug delivery systems that can transport and deliver a drug precisely and safely to its site of action has become the 'holy grail' of developers of new drugs. Indeed, a great number of new delivery technologies surface each year and nearly every part of the body has been studied as a potential route for administrating both classical and novel medicines.

Consequently, promises of new ways of delivering poorly soluble drugs, peptides and proteins are attracting a great deal of attention and one of the many possibilities includes nanoparticle-enabled drug delivery and targeting. In addition, alternative drug delivery technologies are currently under intensive study (transdermal patches, nanodevices, bioadhesive systems, implants, microfabricated systems, cell encapsulation devices and novel nasal drug delivery systems).

Research in nanotechnology for drug delivery is diverse, expanding and accelerating, with some of the most active areas including: polymer conjugates, nanogels, dendrimers, liposomes, micelles, lipid nanoparticles, nanoemulsions, polysaccharide nanoparticles (such as chitosan), magnetic nanoparticles, ceramic nanoparticles, nanoshells, cyclodextrin nanosponges, nanocrystals. A variety of companies are entering clinical trials such as Magforce (based in Berlin) and Nanobiotix (based in Paris) both targeting cancer. An important element of this is that the candidate nanodelivery system is developed along with the drug candidate, they co-evolve. But why is there such interest in this field?

Most of today's pharmaceuticals are based on systemic delivery, that is, a tablet, capsule, spray or liquid is taken either orally, nasally, as a suppository or via injection; the drug then circulates through a system (blood, lymph, digestive) and travels to the site of an ailment. There are many issues and challenges which therapies based on systemic delivery have to face:

- Concentration – the drug will dissolve or react in the various environments it will encounter during its journey through the body;
- The body's defence – kidneys, liver and macrophages – all of which scrub foreign objects; or
- Toxic or other side effects – the drugs may concentrate in a location other than that which they are designed for, leading to unwanted side effects.

Thus delivery is a serious issue for pharmaceutical based therapies. In the area of medicine, nanotechnologies for drug delivery has been one of the most touted promises for Nanomedicine, with a lot of activity at the level of research and with first attempts at commercialisation occurring.

One important aspect of nanotechnology based drug delivery systems is that they cannot be developed in total isolation in a research laboratory, they have to link up with those developing the therapeutic "cargo" to allow conjugation (to fasten the cargo to the delivery system) and to explore the mechanisms of controlled release which are particular to the drug/carrier conjugate. This requires knowledge of the pharmacokinetics of the drugs as well as knowledge of the disease/disorder to maximise targeting efficiency and minimise toxic effects.

Therefore the development of effective drug delivery systems that can transport and deliver a drug precisely and safely to its site of action continues to be the 'holy grail' of pharmaceutical researchers. Indeed, a great number of new delivery technologies surface each year and nearly every part of the body has been studied as a potential route for administrating both classical and novel medicines.

Nanodelivery systems also promise to offer a new lease of life to off-patent (or near to off patent) generics (or blockbuster drugs) which form the mainstay of the large pharmaceutical firms. Large pharmaceutical companies are losing a great deal of money as patents expire and they are beginning to explore new positions in the innovation chain, focussing efforts on better deliver of already developed drugs. The usual development time of a drug from discovery to market is approximately 15 years. Since a patent lifetime is for 20 years, this means that the time available for firms to gain a return on investment before competitors can step in, is 5 years. New delivery options can add to the exploitation of the original

drugs by adding new functionalities, the drug/delivery system can then be marketed once again, giving a strategic edge in the exploitation of the original drug.

Patents for several blockbuster drugs are scheduled to expire in the near future, so new delivery technologies are one way that companies could repackage products and avoid competition.[123] As a result of these and other advances, the market for drug delivery is changing drastically. Benefits from new formulations that offer a competitive edge after the expiry of patent, market extension, and reduction of the drug development budget, which have increased demand, are contributing to creating a new market in the field of drug delivery.

Aside from extending the Blockbuster drug paradigm by adding a new lease of life, nanotechnology based delivery systems promise functionalities which could boost the biotechnology-based pharmaceutical industry (Biopharma).

Research groups in nanoparticulates inspired by the promise of short interfering RNA (siRNA) as a therapeutic have begun to explore methods for drug delivery using particles as delivery systems for diverse diseases such as arthritis, influenza and cancer. siRNA play a role in the process of RNA interference (RNAi) which takes place in the cell cytoplasm, and acts through silencing the expression of a disease by interfering with the communication processes within a cell that has been infected. Such therapy does not prevent the infection of a cell but intercepts communication processes (messenger RNA) and thus prevents expression of the disease. RNAi was found to work in mammalian cells, and research quickly focused on harnessing this powerful endogenous and specific mechanism of gene silencing for human therapy.

Gene silencing has become one of the most promising potential therapies in recent years. Two strategies can introduce small RNAs into the cytoplasm of cells, where they are active – a **drug approach** where double stranded RNAs are administered in complexes designed for intracellular delivery and a **gene therapy approach** to express precursor RNAs from viral vectors. Phase 1 clinical studies have already begun to test the therapeutic potential of small RNA drugs that silence disease-related genes by RNAi.

However, for deep seated regions of the body, issues of transport have become a major issue and so new methods of delivery are called for. Thus, many

[123] When Pfizer's angina drug Procardia approached the end of its patent a few years ago, the company re-released Procardia, this time in the form of sustained-release tablets.

biotechnology drugs, such as those that were developed for gene therapy such as antisense and plasmid therapies, have issues related to delivery. Getting the drug into the cytoplasm of a living cell within the human body has many challenges, crossing many barriers such as the endosome; navigate the circulatory system and the extracellular matrix whilst avoiding defence systems such as kidney filtration, macrophages which engulf the foreign agent or the charged serum properties which bind to the drugs. This brings the requirement for therapy development to avoid these barriers (recently a term coined in the field is to include "stealth characteristics"), targeting (to get where they want to be) and controlled release of the drug at the target.

Summarising, nanotechnologies for drug delivery is a promising technology because of:

- The potential for large pharmaceutical firm's interest for extending patent-life.
- They provide delivery options for biotech drugs to deep seated regions of the body as well as potential new therapies based on targeted and controlled delivery

2.2 Preliminary diagnosis

A recent amendment to the FDA drug development regulations has allowed the possibility of so-called Phase 0 trials.[124] Phase 0 is a pre-clinical testing phase and allows human testing of a very low dose of a drug prior to entering the expensive pre-clinical trial phase. Such a phase would be 7 – 10 days and would sit before animal testing. This was greeted with enthusiasm, especially in the UK, by those against animal testing.

Phase 0 allows for cheaper initial exploration, meaning universities and small SMEs have the opportunity to develop drugs with these initial human trials. Phase 0 studies do not examine safety or effectiveness; instead they gather data on the targeting, action and metabolism of a drug in the body. The goal is twofold: two allow drug makers to identify or jettison failing candidates early, and to generate

[124] "The problem is that researchers conducting very early studies were required to follow the same manufacturing procedures as companies that mass-produce products for broad-scale distribution" explains Janet Woodcock, the FDAs deputy commissioner for operations. "The changes should benefit academics, she notes, by allowing them to make small batches of experimental drugs and do early testing in people – giving them a better shot at snaring industrial partners to take drugs further".

data that will help them design smarter Phase 1 studies for promising compounds. In this way Phase 0 offers a new role for academic researchers in the innovation process.

In conclusion, for those involved in siRNA therapy R&D using nanotechnologies, there are a number of issues that are (becoming) important:

1. **Advanced (nano-enabled) delivery system development goes hand-in-hand with the development of therapeutic agents** – requiring much more integration of delivery system developers in the early stages of therapy development

2. **The drug development regime is diversifying** – there is a shift in large generic drugs to more specific drugs requires increased knowledge on pharmacokinetics, of toxicokinetics and other metabolic effects. As the *FDA Critical Path* report showed, this means more types of actors with more advanced technologies.

3. **Academic researchers are becoming more embedded in drug development** - a consequence of the need for advanced analytical processes and the potential of micro dosing (the so called Phase 0) means that there are opportunities for academic research centres with limited resources to become involved. Moreover, there are expectations in research and elsewhere (FDA for example) that they should become involved in drug innovation.

4. Related to (3), whilst many researchers are exploring delivery systems tailored for particular therapies in an academic setting, there is an increasing number of academic drug development centres emerging. **This is a shift in the balance of research centres in exploration versus exploitation,** and thus new mixes of roles and responsibilities.

5. Beyond the technical, there are issues of putting the therapy to use, **societal embedding,** details of patients and of medical practices, of health insurance which is linked with regulation and costs. For nanotechnology based delivery systems, disciplines which were previously separate are now becoming directly involved, for example material scientists in drug delivery now work with medical doctors in order to understand the requirements. Unlike those previously working on therapy innovations, nanoscientists are now being confronted by non-technical actors, such as patients, regulators as well as receiving much greater media attention.

2.3 Translating diagnosis into workshop topic and scenarios

Workshop Topic

Together all these factors lead to an interesting situation for nanoparticle-based delivery of siRNA. As part of iNANO's drug delivery project, and for the Frontiers Network of Excellence, it seemed timely to open up the discussion and consider obstacles, opportunities and other dynamics which were important for turning research findings from the Frontiers partners generally (and iNANO in particular) into societally robust technologies.

We announced the intention of the workshop was to reveal insights into two areas:

- The roles that could/should be played by university labs, SMEs, large industry, regulatory bodies and medical centres in the diversifying drug development regime

- The major issues for the many nano-enabled drug delivery options (specifically for siRNA) in the translation from laboratory to patients

The invitation to participants stated that "For the participants the added value is to see the whole innovation chain from lab-to-clinic, learning how to get the broader picture, learn how to anticipate complex issues and how to assess them and take action."

To prospect plausible futures the support material for the workshop was developed in two parts. The first part was socio-technical scenarios which combine complexities of emergence and actual dynamics within narratives linked with the actual context of siRNA delivery system development and embedment. The scenarios include some of the shaping factors which may enable or constrain paths (emerging irreversibilities) the shaping effects of expectations and hype and the previous issues related to gene therapy development.[125]

Because of the enactor dominated participation in the workshop and the focus on exploring the potential issues, dilemmas and dynamics involved in developing nano-based therapies for siRNA delivery, the scenarios were developed in a concentric manner (Deuten et al. 1997; cf Figure 2 above) where innovation journeys span out from the present into the future. The innovation journeys in the

[125] Recall that siRNA delivery is a gene therapy, albeit a gene therapy aimed at interfering with the communication pathways in a cell.

scenarios are shaped by broader forces stemming from co-evolution of the technology path and the multi-level socio-technical entanglements that are emerging. They are written to speak to enactors, and bring in these broader issues.

With this in mind, we also provided a depiction of each scenario in the form of multi-level dynamics, to locate some of the elements which appear in the scenarios as forces which shape innovation journeys. These will be described in section 2.6. The following section gives three short summaries of the scenarios. This is followed by the full scenarios with key elements, dynamics and issues shown in annotations.

2.4 Scenario summaries

Scenario summary 1

Anticipating on opportunities for small players due to the new possibilities of biopharma coupled with the possibility of participating in early stage drug development through Phase 0, a number of academic centres become active in siRNA therapy development. In this scenario two university spin-offs (which remain on the site of their respective universities) embrace the Phase 0 opportunities and take different routes to development. The company Deliverenz takes the fast-tech approach, with the aim of providing therapy as quick as possible. Reading the patients and doctors needs for a therapy they go through rapid Phase 0 trialling and attract partners to create a platform. When price per unit (compared with other less effective therapies) becomes an issue, Deliverenz finds it cannot reshape its technology platform due to sunk investments in the partnerships, and has to resort to changing its business plan (more expensive treatment used for a specific group only). In contrast, the company Xylenz opts for the slow-tech approach, undergoes longer term Phase 0 and uses the advantages of the academic setting to do multi-pronged research on various criteria – technology platform, user needs etc. The slow pace allows for learning and more reflexive partnership building, but at a cost of a longer development time (this is not mentioned explicitly in the scenario but is left as an opening for the workshop).

Scenario summary 2

Recognising that delivery is the most important bottleneck to resolve in novel therapy development, activity in the area of controlled and targeted drug delivery

begins to grow. Governmental boosts and support for delivery technologies, coupled with the enthusiasm around nanotechnologies provides abundant R&D resources for nanotechnology enabled delivery systems. By the end of 2007 this has resulted in an abundance of small firms. The rise in R&D activity and the proliferation of small firms working in the area outpaces regulation. As the wide variety of potential innovative solutions to the delivery problem is worked upon, regulators find it difficult to find inroads to regulating a diverse field, with no standard definition and many technologies involved.

The issue of how to regulate is underlined when a report describes the characteristics of a nanoparticle based delivery system which could be regulated as a drug, a device or a biologic. NGOs, which have had concerns earlier, find an opportunity to be heard, underlining their stance for a moratorium until toxicity and toxicokinetics of nanoparticles in the human body is known. Less staunch opposers from the NGO sector and other selector communities begin to plea for comparative analysis of the delivery methods both risk and benefits – this in the absence of standards, a cross comparison is seen as a logical assessment approach.

Life cycle analysis with respect to hazard and exposure is picked out by a government report as well as a need for quality control reinforced by standards. Other researchers (competing with nanoscientists) in the siRNA field link some of the issues with early tragedies of gene therapy warning that precaution is necessary.

Firms continue along their development paths, due to heavy upfront investment. But as regulation begins to shift, some firms begin to feel the effects. In particular the lack of standards becomes an issue. This regulatory and standards roadblock stifles development of nanoparticle based delivery systems, and investors begin to look into alternatives.

Scenario summary 3

Trialling through Phase 0 becomes routine practice in academic settings. Large interest in siRNA related to high profile diseases such as cancer. Star scientists who begin to be involved in innovation activities (due to the Phase 0 possibility) become spokes persons, communicating the promises of new therapies based on advances in science. Due to the high general public interest, an animal trial, where 150 mice died, becomes news-worthy. Against the protestations of the scientific researchers that this is usual in trials, speculation on the safety of the potential therapy begins to mount. Health care authorities advise caution on the part of the researchers eliciting a response from the high profile scientists who positions the

ethical stances as: Slow-technology delays the many benefits for those terminal patients who will die if this therapy is not made available. Thus Fast-track technology is the best option for saving lives. Patients begin to converge on the laboratories to voice their support for the therapy, announcing that they are willing to take the risk along with the promised benefit.

When another research group shows that siRNA therapy in general has a number (and potentially many) unintended side effects which will require further research. However, developers convinced at Clinical Trial Phase 1 voice their position – that delaying the benefit will cost lives, and that the therapy should be fast tracked. As an outcome speed of development of the siRNA therapy outpaces treatment protocols and procedural standards. Health care authorities do not certify the treatment and insurance companies follow suit, refusing to reimburse the treatment until the gaps in protocols is filled. Treatment becomes available though, to a limited few who can obtain it through private clinics

2.5 Scenarios

Scenario 1: Exploration versus Exploitation

Anticipating on a shift in the roles of large pharmaceutical companies where the majority of drug development would not be done by large pharmaceutical companies but by biotech SMEs, a large number of research groups and small-medium enterprises (SMEs) began to emerge [i].

In early 2008, opportunities opened up for smaller players to explore new drugs and drug delivery lines through the cheaper Phase 0 testing[ii], University groups and biotech firms grasp opportunities, and take up the challenge of developing drug. In one region, the region centering on the University of Munich saw the initiation and eventual spin-off of a number of activities to capitalise on this shift: *Xylenz* a spin-off focussing on chitosan as a delivery system for siRNA for pulmonary disease and *Deliverenz* focussing on liposomes [iii].

Deliverenz sought to jump start the process of mobilising resources for it's' innovation and compete with *Silence Therapeutics PLC* (formerly *Atugen*) through a rapid Phase 0. *Deliverenz* linked up with regional biotech firms and an SME developing improved nebulisers. Shared intellectual property rights on the system *Nebulon* (a dedicated nebuliser device for liposome delivery of siRNA through the lung) attract large investments from pharmaceutical companies. The shared technical platform is a strategy to enter the market swiftly and exploit research findings. So resources where shifted away from exploration of options to exploitation.

Xylenz focussing on a chitosan-based delivery system took an alternative strategy of exploring conjugates of

[i] Shared expectations create a shift in strategies of a number of actors which reinforce an emerging "biopharma" path.

[ii] Window of opportunity for smaller players to get into drug discovery coincides (and in part is linked|) with the emerging biopharma path (and reinforce it).

[iii] Nanodistrict in Munich supports emergence of a number of start ups, and at such early stages there is some flexibility in innovation approach. Here two different approaches are possible (a fork in the innovation journey).

possible drug formulations through Phase 0. This is done in collaboration with the university from which the company originated and a number of regional biotech firms. The approach, although time consuming, allowed exploration of a diverse set of lines, and some candidates became interesting. However, *Xylenz* remains as a small research team, due to limited turnover and awards from the government. Conversely, *Deliverenz* increases its staff and sets up an organisational infrastructure.

In early 2010, indications from other attempts at improving drug delivery through inhalable powders caused concerns for *Deliverenz* partners [iv]. *Inhalable Therapeutics*, a US firm developing inhalable powders discovered it has other hurdles to jump. D'Augustino of Boston consultancy points out that although insulin's market is large; the profit margins on selling the drug are rather small. Most diabetics, he says, currently pay only about $1 a day for their medication. That means the inhalable formulation will likely need to be priced similarly. That could be a problem, particularly is the devices deliver only 20% to 50% of their drug cargo to the lungs and then only a fraction of that is absorbed into the bloodstream. Thus the technology may be great, but if the system is not economical it will not gain market share.

Deliverenz taking this judgement onboard explored a number of avenues, high-cost drugs (so economics where not as severe as the insulin case) and alternative modes of delivery (which higher efficacy). *Deliverenz* attempted to link up with other companies; however the sunk investment into a *Nebulon* platform both in money, intellectual capital and expertise meant that it became difficult to attract new partners or to build up a new technology platform. *Deliverenz* was tied to *Nebulon* and hoped for a lowcost drug which would benefit from its delivery system [v].

[iv] Circumstances change as a company with a similar technology strategy (in a parallel domain) discovers problems with its market plan.

[v] Company flexibility is reduced due to earlier investment into a particular delivery platform for a particular situation (which has now shifted). Innovation strategy is then to keep delivery platform and search for a low cost d (but widely used) drug that would gain added value through their delivery platform.

[vi] Alternative innovation path (beyond the original fork in the road) finds different opportunities and challenges. Choice of delivery platform is left open

[vii] Xylenz, using a broadened concentric perspective, engages with patients and clinicians to aide their strategy upstream.

[viii] Xylenz uses a strategy visible in other nanotechnology university spin-offs, of using proximity to a University to create mutually beneficial research projects. This can be low cost for the SME and can explore areas outside of their

Xylenz and its partners had other issues on the table, Phase 0 tests allowed drug selection, however the delivery route and system became the hurdle [vi]. Phase 0 tests were conducted through injections. A number of technological options were on the table, the *Nebulon* platform is one possibility, but there are others.

In late 2010, seeing the problems of *Deliverenz*, *Xylenz* began to invest in research into patient habits for particular disease, to learn about patient and clinical practices [vii]. Relational ties between the University and the local hospital were drawn upon and *Xylenz* began to exploit the free labour of research students through its strong ties to the University [viii]. The possibility to see which diseases are an issue both for new drugs, better targeting and transport within the body and delivery systems (to improve patients quality of life, or to streamline clinical practices by easing burden on medics) were brought to light.

By 2012, this new orientation meant that university groups in the fields of pharmaceutical chemistry and molecular biology were drawn closer into the drug development and delivery process, meaning a fundamental change in roles of researchers in public institutions. Xylenz begins to grow as it invests in a technology platform along with a number of University groups built of knowledge gained over the past 4 years.

core expertise.

[ix] This is one of the central issues of the workshop inserted into this scenario. Reflecting the situation of the research group in Aarhus (and similar groups across the world). This makes explicit the potential fundamental shift (or broadening) of role of public funded R&D centres.

Scenario 2: Controversies about drug delivery options

Driven by the limitations of existing delivery methods and the emergence of new classes of genomic drugs, companies begin to flock to the growing drug delivery industry [x].

[x] Drug delivery emerges as a key enabling technology amidst a broader emergence – that of biotechnology-based and genomic pharmaceuticals (Biopharma).

"The synthesis of the medicine is only part of the drug. Without delivery you just won't have a successful treatment," announces Robert Langer, a chemical engineering professor at the Massachusetts Institute of Technology and past chairman of the US Food and Drug Administration (FDA)'s science advisory board.

This new emphasis on delivery coincided with the evolution of drug delivery with micro and nanoparticles. Boosted by the promises of nanotechnology in industry and national agency, large research funds where available and a new space for institutes to focus on drug delivery as a distinct topic [xi]. By the end of 2007, predictions of large drug delivery turnover initiated a proliferation of small firms eager to enter the drug delivery market [xii].

In 2008, the consequent burgeoning number of delivery methods lead to increasingly bewildering regulatory protocols. Government agencies struggle to evaluate unprecedented delivery approaches through traditional channels. As a result, many revolutionary technologies languish just out of reach, trapped in a regulatory stranglehold [xiii].

“All the clever ideas for delivering therapies may never evolve into real products unless clear-cut guidelines emerge to smooth their regulatory path,” says FDA Spokesperson Xavier Windeler “Regulatory agencies are becoming increasingly befuddled over how to evaluate the bulk of new delivery methods. In the US, for instance, the FDA has three separate centers devoted to evaluating drugs, devices and biologics.” [xiv]

By the end of 2008 NGOs, concerned about 2nd generation effects of nanoparticles argued for a moratorium on nanoparticles for medical purposes until toxicity tests tailored for nanoparticles would be done. Pleas for comparative testing with other delivery methods, patches, implants, time release capsules etc.

[xi] The confluence of a general increase of interest in drug delivery and new nanotechnology options fire’s up enthusiasm, which manifests into funding programmes – making DRUG DELIVERY a research field in its own right.

[xii] Hype begins to build as the promise or the field of drug delivery becomes taken up by industrial actors,

[xiii] As nanotechnology enabled delivery systems become more diverse and complex, governmental agencies and regulatory bodies lag behind causing a serious bottleneck for market entry of new therapies.

[xiv] At the time of the workshop in 2007 (and at the time of writing in 2010) drug delivery approaches could be placed in all of three different regulatory categories: drug, device or biomaterial. Often it is down to the innovator themselves to choose which regulatory pathway they will follow.

[xv] In this part of the scenario I shift the discussion away from comparison within nanotechnology options, to other non nano options. I bring in a non-technical actor to introduce this as a call for a broader comparison (comparative selectors attempt to shape enactors).

[xvi] The call for a moratorium

[xv].

The regulatory issues brought to light by cases like *Cypher*, and NGO concerns stimulate a commission to investigate the rapid growth of drug delivery with nanoparticulates to explore the broader issues linked to the promise of nanoparticle based therapeutics [xvi]. In the meantime small companies surged ahead, starting pre clinical trials.

Early 2010 saw the release of the commission report, constructed by risk assessment, public officials, the FDA and social scientists identified a number of issues based around nanoparticulate base drug delivery mechanisms [xvii]. Production, storage and distribution in both the manufacture of nanoparticle based therapeutics and use in the clinics was a going concern. Quality control of nanoparticles and bioaccumulation uncertainties (particularly in liver, spleen and bone marrow). The safety of others became another key issue – for inhalable approaches, concerns of free particles in the air in mist forms either direct from drug delivery device (pump) or from sneezing, coughing etc.

In reaction to this, in the August 2010 edition of the Economist, Augustus Milverton renowned for his work on siRNA delivery direct to the eye described nanoparticle based systems as: "A blindfolded man with a machine gun shooting at targets. Sure he will hit the target but where do the other bullets go? - we just don't know yet" [xviii]

He brought up the case of 2006 when viral vectors were planned for siRNA delivery (labelled as safe virus). Adeno-associated virus (AVV) as RNAi vector kills 150 mice. High investment was put into this research line based on preclinical trials "but the outcomes speak for themselves", says Milverton.

An article in Scientific American "Magic bullet with a deadly coating?" sparked wide debate concerning the effects of viral and nanoparticle based delivery had the

triggers an opening up of assessment of nanoparticle based therapeutics. This shift in "external conditions" does not seem to affect the world of enactors and small companies surge ahead in the development of nanoparticle-based therapeutics.

[xvii] The broad shift in "external conditions" becomes more specific through a commission report. EHS issues and quality assurance become issues. Occupational Health concerns are raised.

[xviii] A leading research scientist, a spokesperson for the field, speaks as a scientist but in the media. By highlighting the unknowns in nanoparticle enabled delivery systems, he can be read (by readers of the Economist) as taking a position, creating an issue that can be picked up (as an entrance point for non-technical actors) to get into the debate.

[xix] Another popular scientific journal picks up on the Economist article and probes deeper into the debate (mentioned in the previous annotation). This compares issues with other (at the time high profile) catastrophes.

[xx] Industrial actors do not feel the effects of the debate (is

unknown secondary effects of the delivery system itself. A link is made to that of viral vectors for gene therapy as AVV is known to combine with DNA (as that which happened to the two children in Necker, Paris with fatal consequences). This led to a "public outcry", according to a Canadian based NGO, and greater scrutiny of drug delivery research and development ensued [xix].

Those developing siRNA delivery do not feel impaired by the societal deliberations on safe delivery [xx]. *Sirna Therapuetics* (US) in 2011 continues: "The firm has spent a hell of a lot of time and effort putting siRNAs into animals and non-human primates, and we haven't seen anything like this". They continue for human trials.

A direct competitor of *Sirna Therapeutics*, *RiNO*, anticipating on a quick transition through clinical trials, began to feel regulatory bottle necks emerging whilst entering phase 2 of clinical trials. When questioned about this during an interview, an FDA spokesperson mentioned that "the absence of systematic comparative performance data is a major hurdle. No standardised trial for drug delivery (due to regulatory classification issues) has been developed" [xxi].

With classification issues causing a regulatory roadblock, and the societal debate on nanoparticulate and viral vector toxicity, large pharmaceuticals were forced into looking at other options. Implants seem the most promising and investment occurs there [xxii].

Beyond 2002 companies focussing on nanoparticles struggle for survival as biotech companies, with motivation from larger pharmaceuticals and patient groups, move towards implantable delivery systems.

outside of their world) and they continue on human trials.

[xxi] The enabling nature of no nano specific regulation or standards becomes a constraint when it comes to trials. There is no standardised trial or means of evaluating the effects and safety of nano-enabled drugs.

[xxii] The regulatory bottlenecks cause delays and coupled with the "external conditions" regarding safety concerns, large industrial actors (who manage a portfolio of products) begin to look at technologies which suit the market and regulatory conditions.

Scenario 3: Safety and success by popular vote?

In 2008, with Phase 0 trials becoming usual practice, university groups developing and testing of new drug options begins to proliferate [xxiii].

By the end of 2009, Klaus Würzel, leader of the research team at the University of Gottingen developed a spray for inhalation of siRNA directly into the lung without vector. Targeting non-small lung cancer, initial trials on mice showed promising results. These results were published in *Science*, and Würzel began to appear in the press as "Würzel battling lung cancer".[xxiv]

Preclinical studies on mice and lower-primates showed optimistic results. Human trials begin.

During autumn 2009, in the US a study using AVV for siRNA transfection caused 150 mice to die. Initial concerns about the vector being the problem are quickly doused by research teams who show that the deaths resulted from an excess of siRNA. Questions are raised concerning the reactions to too much siRNA in cells and the effects of reactions with mRNAs and consequently cell function. Health care authorities concerned about the siRNA approach and advise caution in the move to human trials. [xxv]

In reaction to these concerns Würzel argues on ZDF news that successes have outweighed the fatalities, "Fatalities occur all the time! My staff is combating a serious disease which causes hundreds of thousands of deaths per year in Europe alone. It would be unethical to stop clinical trials for a drug that works better than others."[xxvi]

As a response to the prior press coverage and the ZDF new item, many patients with lung cancer go to the lab the following spring. Würzel points the finger at the

[xxiii] The possibility of research groups in Universities conducting preliminary trials of drugs becomes a widespread (albeit nascent) practice.

[xxiv] A researcher gets visibility when succeeding in what is currently thought of as the low hanging fruit of siRNA delivery (easy to access parts of the body meaning no delivery system is needed)

[xxv] A research study using one specific delivery system (a modified virus) causes fatalities in the lab. This triggering event causes concern which leads to health care authorities scrutinising the whole field of siRNA and advising a precautionary approach.

[xxvi] A researcher steps out of his laboratory to give an interview as a spokesperson for the field. He highlights the dangers of the precautionary approach with regards to therapy – a delay will allow more fatalities which could potentially be prevented. (This shows common position of enactors in therapeutic fields, and is shown here as friction between an enactor (the researcher) and a comparative selector (the health care authority).

[xxvii] Researcher in his role

health authorities, "This is evidence of a patient revolt. Clinical testing and current protocol stand in the way of these sick people getting better!" [xxvii].

As ever more patients converge on lab, coverage shifts towards headlines like "From battling disease to battling the health authorities" regulatory authorities become the enemy, obstacles to healing. In the mean-time, for the health authorities, the issue of proper clinical trials became an ever-increasing issue.

Mid 2010, another group in the US working with siRNA mentioned that although initial reports suggested that siRNAs would have previously unheard of specificity for their targets, several mechanisms have since been described that can lead to unintended off-target effects on gene expression (such as those experienced with the AVV experiments) and need to be seriously considered in developing RNAi based drugs. Perhaps more serious are unanticipated off-target effects that occur by siRNA recognition of other mRNAs bearing only partial homology.

Researchers working on the system maintained that the evidence suggests that the tests worked on animals and initial patients (with a few exceptions) and that it would be unethical to continue with the arduous clinical trials of phase 2 and 3 – sentencing more people to death that could be cured by this new drug.

By the end of 2011, Würzels' team has mobilised some $100 million through deals with large pharmaceuticals, and anticipates on larger investment.

However, a challenge remains with the transferral of Würzels' siRNA system to the clinics. Health Authorities emphasised that not seeking large samples and following proper protocol, meant that testing processes are confounded. Patients might not receive optimal treatment as a new therapy or drug will not be properly evaluated. "Patients and press determined the drugs validity by popular vote and shouting rather than

has spokesperson can mobilise resources (in this case patients and families of patients) to back his claim. (This is included to reveal an alternative role of a researcher – more than developing technology in his lab. It is in part a way of holding up a mirror to ambivalent researchers who on the one hand argue that they just stick to the science but on the other take advantage, stimulate or fuel hype).

[xxviii] Challenges remain with bringing the therapy to actual patients. The health care authority's precautionary position and concern about standardised clinical testing approaches causes insurance companies to be cautious also in covering this new therapy. Regardless of the success shown by researchers in the clinical trials, insurance

scientific method”

Würzels’ team argue that they have evidence that system works and has improved on its initial efficacy through further refinements during pre clinical trials.

2012, health care authorities would not certify the approach without clinical testing leading to private insurance companies unwilling to cover this procedure [xxviii]. The medical option becomes available only to those who can obtain it by other means, such as private clinics, in stark contrast to Würzels’ vision of siRNA delivery for all patients who want it.

companies wait for more robust evidence. Without the insurance companies backing, the therapy is then only available for private clinics

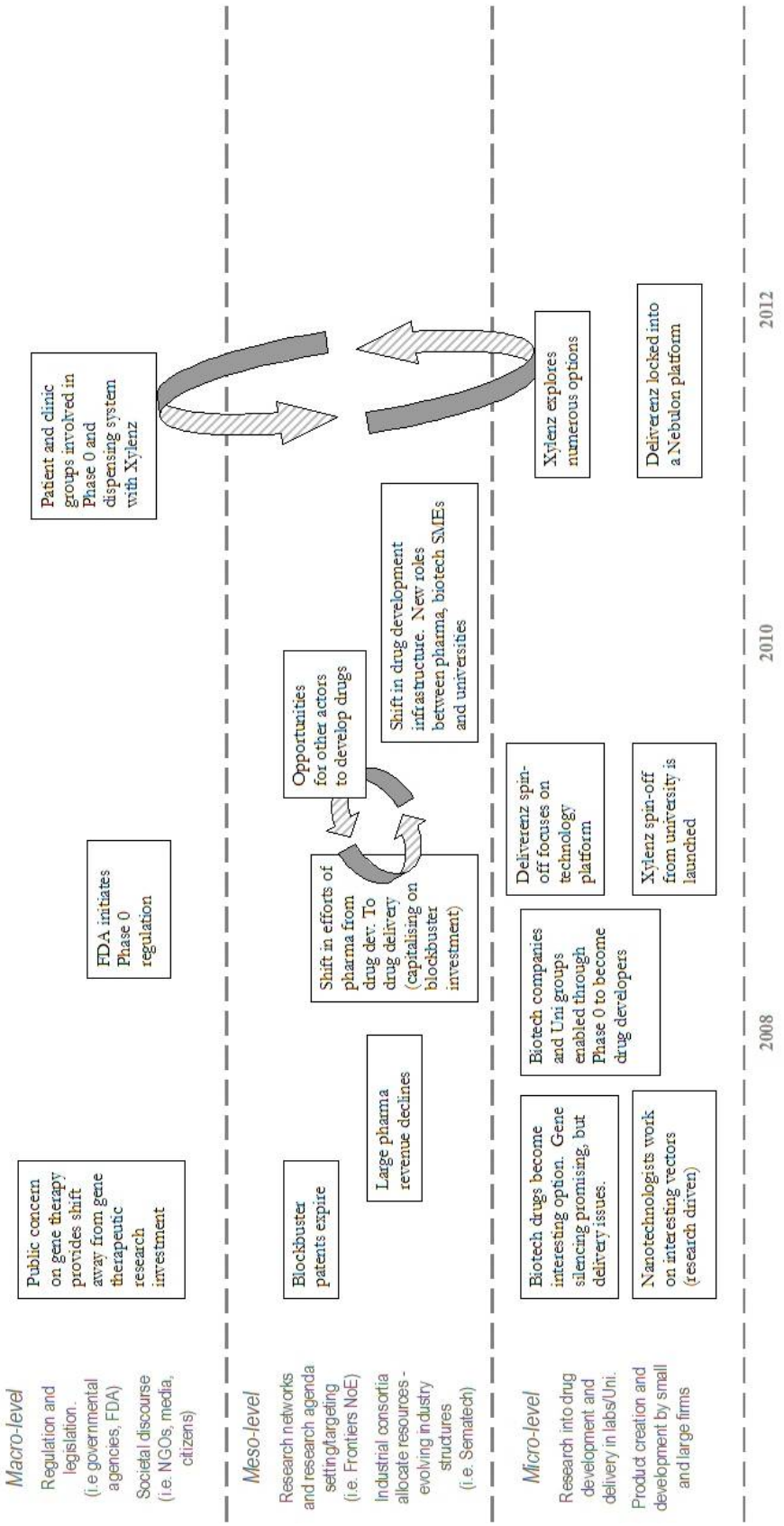
2.6 Other Support material

As announced in the invitation to participants, the aim was to go beyond the linear model and to expand the perspective to include more dynamics and more actors. Since developments at different levels influence each other and create complex dynamics, such as the connections between specific projects, shifting industry structures, and policy and societal changes. A tool to visually map these (as an alternative to the scenarios based on innovation journeys) was seen to be important. Thus we created three 'multi-level diagrams' to represent the scenarios.

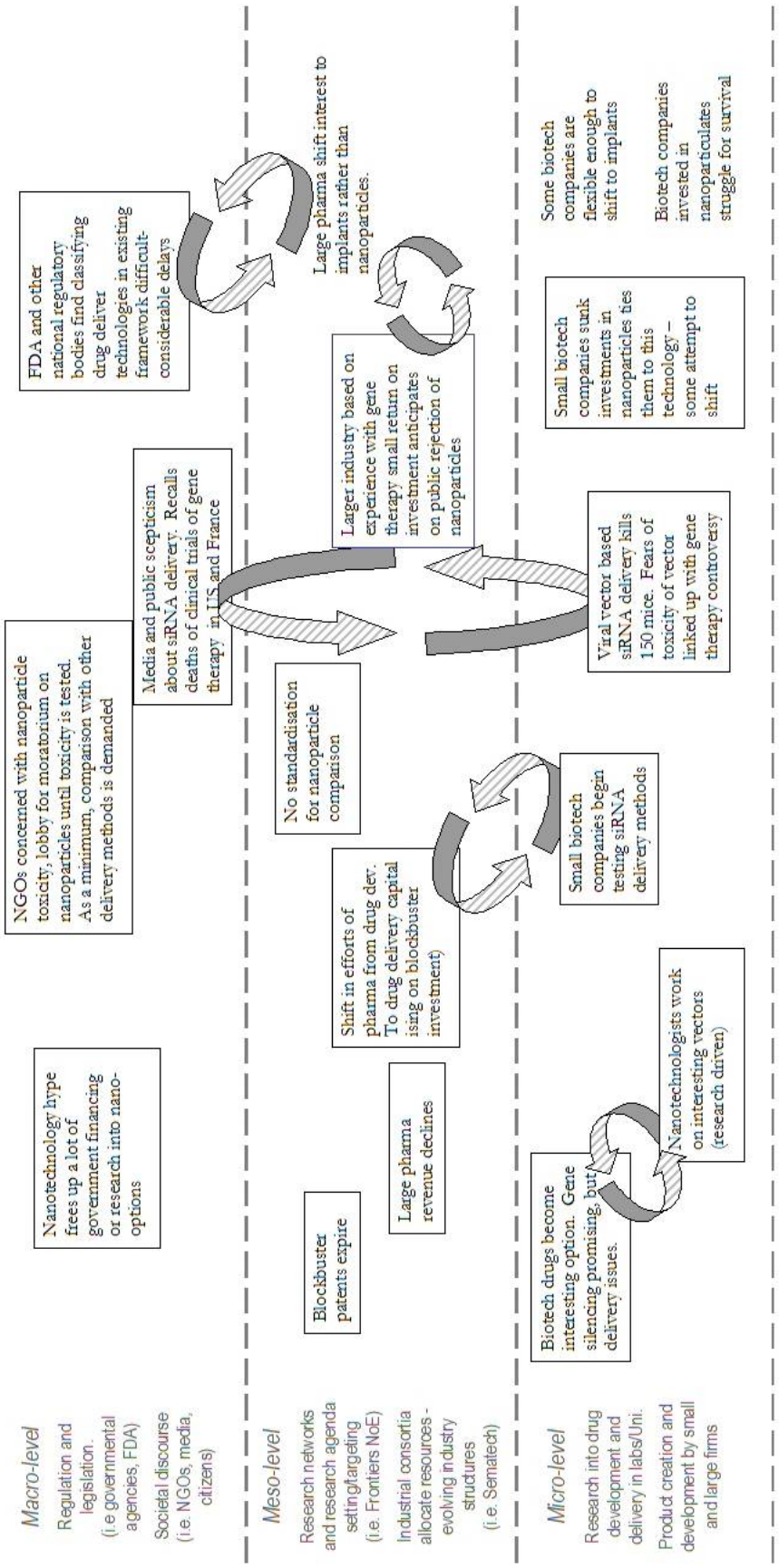
The lowest (or **micro**) level represented the individual R&D projects in public and private R&D. In our case this could be the exploration of possible drug delivery systems or of the drugs themselves. Management, coordination, but also assessment of ongoing developments elsewhere stay at the level of the research team, and are included in the project.

The middle (or **meso**) level describes collective developments of consortia. Industry associations for example, coordinate activities; it is at this level one can place the industry standards and market trends. Coordination attempts at this level can include anticipatory coordination by way of roadmaps (the International Technology Roadmap for Semiconductors); networks of public research centres (the Dutch NanoNed consortium); or research 'networks of excellence' (Frontiers). Management and coordination stays at the network level.

The top (or **macro**) level describes governmental and more formal regulation; it is at this level that regulation is made, NGOs lobby, societal debate occurs, consumers choose to consume or not to consume (market governance) etc. Management and coordination lies at the governmental level and consumer level, with the many actors such as NGOs, regulatory agencies, consumer groups, citizen associations etc. shaping agendas. The three multi-level maps are given below.


Macro-level
Regulation and legislation. (i.e governmental agencies, FDA)
Societal discourse (i.e. NGOs, media, citizens)
Meso-level
Research networks and research agenda setting/targeting (i.e. Frontiers NoE)
Industrial consortia allocate resources - evolving industry structures (i.e. Sematech)
Micro-level
Research into drug development and delivery in labs/Uni.
Product creation and development by small and large firms
Public concern on gene therapy provides shift away from gene therapeutic research investment
FDA initiates Phase 0 regulation
Blockbuster patents expire
Large pharma revenue declines
Shift in efforts of pharma from drug dev. To drug delivery (capitalising on blockbuster investment)
Opportunities for other actors to develop drugs
Shift in drug development infrastructure. New roles between pharma, biotech SMEs and universities
Patient and clinic groups involved in Phase 0 and dispensing system with Xylenz
Biotech drugs become interesting option. Gene silencing promising, but delivery issues.
Nanotechnologists work on interesting vectors (research driven)
Biotech companies and Uni groups enabled through Phase 0 to become drug developers
Deliverenz spin-off focuses on technology platform
Xylenz spin-off from university is launched
Xylenz explores numerous options
Deliverenz locked into a Nebulon platform
2008
2010
2012

SCENARIO 1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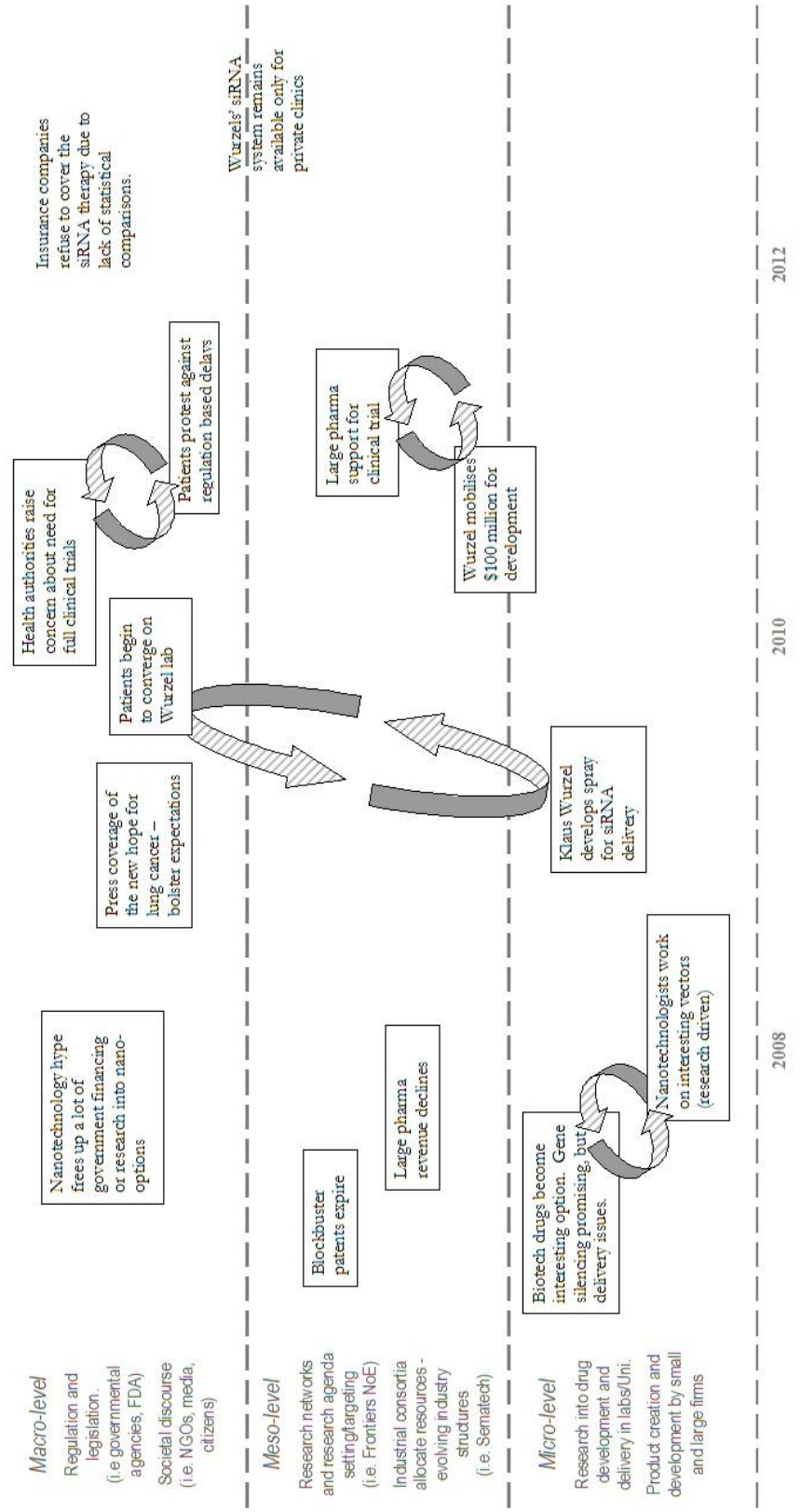
Micro-level
Research into drug development and delivery in labs/Uni.
Product creation and development by small and large firms
Nanotechnology hype frees up a lot of government financing or research into nano-options
NGOs concerned with nanoparticle toxicity, lobby for moratorium on nanoparticles until toxicity is tested. As a minimum, comparison with other delivery methods is demanded
Blockbuster patents expire
Large pharma revenue declines
Media and public scepticism about siRNA delivery. Recalls deaths of clinical trials of gene therapy in US and France
No standardisation for nanoparticle comparison
Shift in efforts of pharma from drug dev. To drug delivery capital ising on blockbuster investment)
Biotech drugs become interesting option. Gene silencing promising, but delivery issues.
Nanotechnologists work on interesting vectors (research driven)
Small biotech companies begin testing siRNA delivery methods
FDA and other national regulatory bodies find classifying drug deliver technologies in existing framework difficult- considerable delays
Larger industry based on experience with gene therapy small return on investment anticipates on public rejection of nanoparticles
Viral vector based siRNA delivery kills 150 mice. Fears of toxicity of vector linked up with gene therapy controversy
Large pharma shift interest to implants rather than nanoparticles.
Small biotech companies sunk investments in nanoparticles ties them to this technology – some attempt to shift
Some biotech companies are flexible enough to shift to implants
Biotech companies invested in nanoparticulates struggle for survival
2008
2010
2012

SCENARIO 2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Micro-level
Research into drug development and delivery in labs/Uni.
Product creation and development by small and large firms
2008
2010
2012
Nanotechnology hype frees up a lot of government financing or research into nano-options
Blockbuster patents expire
Large pharma revenue declines
Press coverage of the new hope for lung cancer – bolster expectations
Patients begin to converge on Wurzel lab
Health authorities raise concern about need for full clinical trials
Patients protest against regulation based delays
Insurance companies refuse to cover the siRNA therapy due to lack of statistical comparisons.
Wurzels' siRNA system remains available only for private clinics
Large pharma support for clinical trial
Wurzel mobilises $100 million for development
Klaus Wurzel develops spray for siRNA delivery
Biotech drugs become interesting option. Gene silencing promising, but delivery issues.
Nanotechnologists work on interesting vectors (research driven)

SCENARIO 3

Important actors outside of the concentric approach (from diagnosis)	Which ones were included in the preparatory material	Actor communities outside of the concentric approach
R**egulators**, which set safety guidelines and standards **Health care authorities**, choose between potential approaches to an issue such as disease by exploring many options, and targeting policy and funding programmes around their choices **Medical Insurance companies,** as gate keepers to allow or reject a new medical technology or therapy. **Environmental NGOs**, concerned about the fate of nanoparticle and nanomaterials that are used in nanomedicines or other nano-based products **Patient associations**, who lobby for access to the best therapies for their particular disease or disorder **Private investment community**, these are quite interested in the potential of nano-based delivery systems (that can add life to drugs). **Medics and Clinicians**, those who implement the new therapies (first round user) **Patients**, as recipients of the novel therapies that are envisioned.	**Regulators** are included in Scenario 1 – role involved shaping the regulatory landscape so as to enable some paths and constrain others **Health care authorities** are included in Scenario 3 – role involved attempting to shape R&D standards amidst public pressures to allow a new less well tested therapy to be made available **Insurance companies** are included in Scenario 3 – role involved shaping acting as a gatekeeper to new therapies **Environmental NGOs** are included in scenario 2 – role played as promoting a precautionary approach to R&D along with supporting an exploration and assessment of alternatives. **Medics and Clinicians**, mentioned as co-developers or spokespersons for the field **Patients** are included in Scenario 1 and 3 – role played as voicing their support for promising new approaches since they have a lot at stake. In scenario 3 they converge en masse at a research laboratory to show their support (which is taken advantage of).	**Medics and Clinicians,** a medic at the University Hospital **Environmental Agency,** a member of the Danish National Environmental Research Institute

What elements were chosen and highlighted in the scenarios?	• Exploration/exploitation tensions in academic R&D groups and for spinout firms. • Hype strategies by researchers, made explicit in scenario 3 with a maverick scientist. Hyping is a recognized part of academic research, but hyping outside of academia can be read as promising to deliver. This has ramifications for the researcher/innovator with a view to responsible innovation • The positives and negatives of fast and slow technology development with regards to opportunities to support reflexivity, but also with the real issue of surviving (such as in the first years of a spin out firm). There is an issue of the ethics of delaying medical benefit (especially for those patients with terminal conditions) and ethics of going too fast (risking lack of knowledge through limited study and reflection). Therefore, an important dilemma for academic drug development. • Phase 0 as an opportunity and a pressure on academic research organisations to be involved in therapy development. • Issues of societal embedding, such as details of patients and medical practices, of health insurance which is linked with regulation and costs. For nanotechnology based delivery systems, disciplines which were previously separate are now becoming involved directly, for example material scientists in drug delivery work are connected with medical doctors in order to understand the requirements.
What stakes were chosen and highlighted in the scenarios?	Key points that were included which speak to the participants included (1) the success of development of nano-enabled therapies is based on the balance of exploration/exploitation by technology developers, (2) the fate of societal embedment of nano-based therapies are part of broader dynamics and go far beyond the power of technology developers alone (health care authorities, insurance companies, patient culture etc.)
Structural difficulty in creating scenarios	The main issue was that participants didn't confirm their attendance until the week preceding the workshop (in some cases it was a matter of days). This meant that scenarios could be made somewhat i9n advance but had to remain unfinished until the very last week before the workshop in order to be targeted to the group.

siRNA

Other support material mobilised? If yes, what and why?	Developments at different levels influence each other and create complex dynamics, such as the connections between specific projects, shifting industry structures, and policy and societal changes. To reflect this, multi-level mapping was used as an aid in broadening with respect to the participant's appreciation of the multi-actor multilevel nature of emergence. Since the scenarios in this workshop are told as innovation journeys, many of the elements and non-enactor characters in the narratives play a role that is linked to the multi-level dynamics of the field.

3 The workshop

3.1 The participants

The aim was to get as diverse a mix as possible. In the short period of 6 weeks from concept to execution, getting such a mix was difficult. However, the final mix had representation from the main actor groups; research, industry, regulation and risk, medical profession, but was heavily weighted on the side of researchers. The challenge therefore was to create good scenarios which would give intelligence on important dynamics of the context of the topic AND provide a starting point for the participants to build on (especially for those areas under represented in the participant mix). The final list was as follows:

Code	Institute	Invited as:
[JS]	**Janne Savolainen** MESA+ Optical SS Group	Nanoscientist
[GD]	**Georg Dalager** NERI, Aarhus	EH&S Considerations
[MB]	**Manray Bungle** University of Chalmers	Innovation Strategy
[GK]	**Gudrun Keelo** University of Twente	Researcher delivery
[HK]	**Harold Kane** iNANO	Researcher delivery
[SB]	**Stig Brandes** iNANO	Researcher siRNA
[KAO]	**Karen Adler-Olsen** iNANO	Researcher siRNA
[OB]	**Ole Bendy** University Hospital	Medical Doctor
[JvdB]	**Jelle van den Broek** University of Twente	Researcher delivery

[PH]	**Pal Høeg**	Biotech firm
[TFJ]	**Tove Fink-Jensen** iNANO	Researcher biomaterials
[RCN]	**Rab C. Nesbitt** iNANO	Researcher delivery
[JB]	**Jussi Blixen** iNANO	Researcher biomaterials
[AR]	**Arie Rip** University of Twente	Moderator
[DR]	**Douglas Robinson** University of Twente	Workshop organizer

3.2 The workshop interactions as stretches

People began arriving early to the workshop. [HK] and [SB] were waiting for us. They mentioned that the scenarios were interesting but scenarios generally were a technique new to them and they found it difficult to position them in the context of the meeting. [DR] mentioned that he would introduce this once again in at the start of the meeting (although it was described in the preparatory report).

The workshop began on time. One of the organisers [DR] opened the meeting by describing the origins of the workshop, the interest from [HK] on how to link the Technology Assessment with siRNA delivery. [DR] briefly introduces the scenarios and the approach.

> "At iNANO (a Frontiers partner) nano research is being coupled with siRNA for possible drug delivery for gene silencing with promises for pulmonary disease, inflammatory disease etc. As an entrance point to the broader discussions of the shifting structure of drug development innovation chains Frontiers in consultation with iNANO chose this topic to be the anchor point for discussions – to allow deeper probing into the issues before moving to the general. In a day long workshop we cannot map the whole drug development and delivery R&D landscape. What we *can* do is collectively anticipate the possible new situations coupled with new research lines."

Ending this small introduction [DR] introduced the timetable for the day:

10:00 – 12:30	Reacting on the pre-circulated scenarios, a round of introductions and presentation of exercise 1 from the participants. This will be feedstock for further discussion and additions through the morning session
12:30 – 13:15	Buffet lunch
13:15 – 16h15	Mapping of future situation and exploration of roles and responsibilities of all the major players, researchers, industry, regulators etc.

Figure 3: The timetable of the meeting.

Linking back to comments on lack of familiarity of the scenario approach, [DR] goes on to differentiate between types of scenarios (for example, the scenario approach used by Shell), where possible broad futures are identified for comparison and evaluation versus Socio-technical scenarios (those used here) where we explore emerging technologies in contexts (co-evolution) and thus the evolutionary paths of emerging technologies are the focus, not the comparison of potential endpoints.

Stretch 1: Round of introduction: some first probing

To start of the discussion the participants were asked to introduce themselves and mention some of the key elements that they drew from the preparatory material (beyond technical aspects of siRNA delivery systems.

[JS] is a chemist in his mid 30s working in photo-physics; currently speculating on potential application of his research to therapy (links up with drug delivery possibilities). Has an interest in broadening his view (beyond the technical). He goes on to make a diagnosis of the scenarios. In Scenario 1 he sees that there is a change in how research is done. He notes from his own experience (as a PhD student) that there are changing PhD requirements. Patents instead of papers! Meaning a new type of pressure on young researchers in a system geared towards peer-review. He has an open question to the group: "Are University groups capable of doing phase 0?" What was a key point in scenario 2, for him, was the link between unknown toxicity and unclear regulation. For scenario 3 the dilemma of how much to promise? What are the researcher's responsibilities? More

importantly, in his view, what is the real advantage? He suspects too much of a rush for development in scenario 3.

[JvdB] is a 22 year old researcher working on new polymeric gene carriers for RNA "for fighting cancer". He sees in scenario 1 two different approaches taken, bold vs. more cautious. Scenario 2 shows the impact of negative media hype; he suggests that you could prevent this by telling the public about your research at an early stage so they know about it "this would act as a buffer")

[TFJ] is a Post-Doctoral researcher working on scaffolds for tissue engineering including Nanoparticles and positions himself as in-between clinic and nano-particle development-people. He says he has no real comments as yet, since he hadn't had time to read the preparatory report, but as a general comment emphasises the need for infrastructure at the University to support university groups and SMEs in translational research.

[PH] is a medicinal chemist and co-founder of a small SME, initiated 8 months previous, utilising infrastructure of the university for the development of a modified siRNA (he is the inventor). He has some more IPR and will start working on new products also for drug delivery. He is also involved in the FP6 RIGHT network. His comments on the preparatory report and scenarios is that the role of researchers is important (then, also more credibility, so as prevent media hype). Phase 0 very appealing from his point of view, drug development becomes knowledge based. In the scenarios he sees too much forced/rushed development. As a strategy, researchers exaggerate (as in the scenario) but you have to do this in university; it is part of research life: "Beware of stupid press releases!" Communication is difficult; the general public cannot understand the details.

[HK] is a pharmaceutical researcher at the university. He established a drug delivery group from scratch, and so was not limited by the "traditional pharmaceutical approach". They are working on a number of systems. One of the most important is on siRNAdelivery. As a research group, we get a lot of hype and media attention. From the preparatory material he can see the pressure of managing exploration/exploitation. In his opinion you should do both, the question is of timing

> "When should you research and when should you exploit? As a research group we have to choose, which means pressure on forecasting the right directions. In our case, we have an interdisciplinary team which allows us to be a little bit better at forecasting what is interesting."

siRNA

For [HK] Scenario 2 and 3 are linked, in that they suggest that you need clear guidelines from the regulatory authorities. In his opinion Phase 0 is not such a big thing; you always need toxicity testing. "Picking up on [PH]" [HK] says that "if something is good you should get it out to the public. Even if it is somewhat toxic, that is where delivery comes in, targeted delivery reduces doses." KH goes on to say"you can use/exploit hype: media attention" adding "You can get across your message, but too much hype is a problem"

[OB] is a medical doctor/consultant. In his opinion, proof of concept for the research done at the university has no real problems; they can just go down the usual route. There are many good ideas around, but not recognised for their clinical value (need to get stronger links with the clinics) [*this is interpreted as lots of ideas in the universities and the clinicians are unaware of them*]. "What is attractive is to skip part of the laborious testing if therapy is promising (will save lives). Also, if drug can be used for X, it might be used for whole panel of disease, melanoma for example melanoma."

[KAO] is a PhD student running tests on mice, preparing new protocols (for reaching the brain, penetrating the brain/blood barrier). She anticipates on later uptake of her research by companies, "but you need to know what is out there. And know about cross linking, broader applications"

An organiser [DR] interrupts the round of introductions "[PH] is an example?" [PH] responds "we provide siRNA, won't develop further steps".

[RCN] is a researcher looking at how siRNA moves in a cell, with the aim of exploring how to target the carrier better. Did not read the report as he only knew he was coming that morning, so had no direct comments, but has a question "Is Phase 0 accepted now?"

[DR] responds **"**Yes, Nature articles say it is done. You still need toxicity tests on animals - but not on lost causes anymore."

[SB] highlights that you have to build a human model anyway, to see how people respond. "That's not Phase 0". You can't go about it by effectively taking people into a hotel room, exposing them to certain circumstances. But testing is not such an issue, companies such as Sirna and Alnylam compete on patents but collaborate on testing.

[HK] continues along this thread from his position, "our delivery systems are dual like in the scenario. So more difficult to test? This is especially so for controlled release system. Need to know the toxicity of drug and toxicity of polymer carrier."

[SB]: But Phase 0 is only after animal testing? [DR]: No, is testing low doses on humans.

The round of introductions continues with [JB], a molecular biologist working on scaffolds to include nanoparticles to induce differentiation of stem cells. "This is interesting stuff". The big issue is that the translation into a product is a long process and a difficult one - see Scenario 1. Scenario 2 shows influence of society and the effect of preconceived opinions. But you have to validate the performance before you can go to clinical quality. How can you do this if you don't know enough about your product at early stages?"

[DR] queries this "In Denmark you can do an industrial PhD?" [JB] "Yes, mixed: basic research and getting it into a product"

[DR] sums ups [JB]'s suggestions: early reporting → transparency → better public reactions

[GK] is a chemical engineer working on synthesis. "Deliverenz is the real innovator, taking big risks by moving quickly. Xylenz is more cautious in it wants to understand it product before going to market. In scenario 2 the viral approach is perceived as risky with respect to contamination, you should differentiate present delivery from it (it is an unfair comparison) to polymer based therapeutics."

The participants respond to this starting a small stretch in the conversation.

Sub-stretch A

[JS] responds to [GK] "But the requirements for safety are the same for virus or polymeric". An organiser [AR] reframes the comment "so this is more of an institutional issue, the question isn't about the difference but can we trust the testing." This is not picked up by any of the participants and [GK] continues with his diagnosis of the 3rd scenario mentioning that media hype is the issue here. Drawing lessons from this, he thinks that researchers should do more explaining about what they do, for example to high school students.

Since [JS] sets a precedent for interrupting the round of introductions and scenario reflections, other participants comment.

Returning to the initial contention from [JS], [HK] questions [GK]'s statement on media management "Will you denounce viral in the media? Drug delivery is complex". [SB] notes that "it is dependent on risk thresholds, and that acceptable costs are different. Viral approaches are cheap and effective so would be more economical. Polymerics are more expensive, so you wouldn't use that for the common cold."

[OB] the medic concurs that you do need do the same tests, but acceptability of results/risks will change if you promise that a deadly disease may be treated, "say cancer, that would speed up development."

[GK] reacts to this technology push strategy identifying some loop hole that drug delivery developers can exploit. He identifies particularly that drug delivery slips through FDA classifications. Nodding in agreement [TFJ] adds "Yes, the Cypher case in the preparatory report is an example of this"

[SB] adds that the delivery system may fall through the loop hole, but there is the drug you are delivering, so even if you have the vector accepted, you still have to test the drug (gene therapy).

Participants follow this by giving examples of the blurred nature of regulatory routes for products. [OB] describes the example of a plastic device to avoid pregnancy. This is a device but was tested like a drug. [MB] also adds that there are other issues to consider if you have devices. For example a slow drug releasing implanted device; after drug has gone, the device is still there. "This causes complications and so has to be removed surgically. So there are lifecycle issues. So depending on drug and delivery system, different regulatory hurdles and issues."

One of the participants [GK] sums up "there is a consensus now that the distinction of drug/delivery is too simple" [SB] adds "in our research we're mixing the two, increasingly we do this and rely on the mutual influence of carrier and drug"

[[SB]*'s work on chitosan nanoparticles for siRNA delivery is interesting here, since the chitosan delivery system also has therapeutic effects – chitosan is an antimicrobia*l]

[PH] (An siRNA company) turns to [OB] (a medic) and asks "How will it go?" [OB] responds "everything will be tested as a drug".

[SB] points out that siRNA is a generic drug. "Would you need approval for the approach as such?"

There is some silence signalling the end of this sub-stretch, and [AR] initiates the round of introductions by beckoning to the next participant in line.

Return to Stretch 1

[SB] is a professor of molecular biology interested in siRNA. As drugs, siRNAs are extremely potent if you can get them to the right place, so his interest focuses on targeted delivery. From the preparatory material, he sees that product

development should stay close to academia. That effective use of the media is important, but transparency more generally is important for long-term projects to pay off.

[DR] (With some knowledge of the history of some of the participants) probes further with a triggering comment " With incumbents you can have IP problems"

[SB] "Yes, Small start-ups are important, you must set them up to commercialise what you have. In our case, as researchers, perhaps a paper company is suitable where you can deal with other companies through this form." [SB] goes on to suggest that in the field of drug development you could do more with simulations, run computer simulations to test the drugs. "This has not yet taken off, but it is promising." [SB] adds that his group are also involved with environmental researchers for toxicity of nano-particles. However, they're just interested in size, not in difference between the particles. This is illustrative of a key issue, "if you can't explain it to environmental scientists, how can publics understand?"

[HK] adds that "As researchers geared towards peer-review, we have to learn to be less open and go for patents." Another researcher [TFJ] adds details on infrastructure, "you need to have sufficient critical mass, and so clusters of SMEs/University research groups, AND some exchange between them."

The round of introductions continues. [MB] works in a department for Technical Transfer in a University. He has worked for Volvo, Ericsson, and a Venture Capital company. He only just got the scenarios from another participant, and so has no direct comments on them. But referring back to the discussion. "If you don't make business, you won't get therapies. So train people in such aspects, they need to be trained in exploitation as well as exploration". Following on from other comments already voiced, in his opinion you have to be guarded when dealing with the media "don't let anyone talk to the media!" This triggers nods and a lot of chuckles. In his experience journalists can and do distort and therefore should only be allowed to talk with seasoned/skilled people. One of the organisers [DR] points out that [HK] benefited from media attention "He already mentioned that hype has helped." There is some slow nodding around the table, and [MB] shrugs and looks to the last person to introduce himself, the acting chair [AR] who briefly introduces himself as a former chemist who shifted to philosophy, chemistry and society, and now looks at many things in and around nanotechnology, technology assessment risk.

Stretch 2: Exploration and Exploitation

[AR] concludes his introduction of himself and summarises the threads that have emerged during the round of introductions. "As a researcher you go for a mix of exploration and exploitation, this is covered in Scenario 1. Also the relationships between universities and SMEs."

At this point, one participant [PH] raises a concern, about an earlier comment by another participant [SB].

> "Be careful with academics and paper companies. What is the ownership then? And do your students work for the university or the paper company. For your own company, everything is transparent, there are rules. Who owns the patents of your research group?"

[TFJ] comments that in their institute they have people dedicated to developing patents and maintaining links with companies, "This is especially useful in the present situation of our siRNA delivery research." [MB] "It comes down to why/how is a company started? It is not just to earn money. It requires well defined economics. You need to be an entrepreneur."

[DR] refers to a case he knows about regarding two participants [PH] and [SB] from his visit to iNANO in Aarhus a month earlier "You two were approached by a third party with regards to development no?"

[PH] and [SB] "Yes we had a patent and sold it to the third party. They will do all of the commercialisation part". [TFJ] notes that by going through this process they became familiar with the rules, "we now have experience." He raises his concern that this isn't taught to young researchers, especially PhDs.

[MB] (From a different institute) shares details from his situation. "We have a start up competence/excellence centre with both, researchers and companies. We have three people in it, giving advice about patentability, supporting researchers and how to handle the patents."

[DR] "At what stage do they become involved? " [MB] "Early on. There are no simple guidelines or teaching, about this."

[PH] Denmark funds the transition from proof of concept to product. It is important that academics should remain involved. This way you can keep the development process knowledge there. [MB] nods agreement" indeed, don't lose the researchers"

[SB] "Yes start the company in the university (can use facilities). There have been issues with university-company IPR issues, but this has been changing over the last

five or so years. But there are national differences. In Sweden and Italy for example the academic researchers own the patent. Can lead to misguided exploitation [PH] so ownership by university is better."

A lady pops her head around the open doorway and mentions that lunch is ready and [AR] suggests the group to adjourn for lunch.

----------LUNCH----------

Stretch 3: Shifting and blurring roles in research and product development

After lunch, the organisers reintroduce the topic of changing roles and responsibilities in therapy development, one striking example included in the preparatory report being the potential of Phase 0 testing.

Responding, [SB] mentions that clinical testing only occurs after the start-up company has been launched and seed money for feasible product is obtained. Good laboratory practice will still be required. University laboratories are certified so that they can reliably sell nanotubes to a company for 20,000 Euros per year.

[HK] (A colleague of [SB]) mentions that the pharmaceutical industry has had such good laboratory practice all along. However, [SB] anticipates that there will be more applied/relevant research in the area and in development and thus also more need for good laboratory practice in both public research and for small companies. [MB] adds that in his [*geographic*al] region they see the need to set up a dedicated good laboratory practice and good medical practice lab.

[OB] comes in with another line of discussion "is your stuff anything else than clinical? (like veterinarian) this would be easier in terms of regulation. Then you won't be imprisoned in the promise to cure cancer. You can focus on animals and get the proof of concept there. You're already doing animal experiments anyway." [DR] links with the similar ideas in the field of nano-enabled medical devices (from the cell-on-a-chip workshops. [JS] notes that if you do this, then you step down from your earlier promises of delivering drug delivery. [JS] continues with a question of his own "But will the regulation change? Do you anticipate on changes and factor that into your strategy?" [*Question to [SB], [PH], [MB] and [OB]*]

[MB] responds first, mentioning that as a business, you have to know and follow existing regulatory directives"

[GD] (A researcher from the Danish National Environmental Agency who only arrived after lunch) anticipates that environment/health regulation will not change very much to address nanotechnology. Also, he believes that basic research can be

a separate issue because of longer timeframes. You could include anticipation on (new) regulation to define research direction however. [HK] agrees that you should anticipate - otherwise waste of effort. [GD] responds "But then your research agenda will be totally applied" he goes on to emphasise that you should keep an interest in mechanisms (basic research), "I'd hate if you would become as applied as me!"

[HK]/[SB] together note that in their line of work, you are developing delivery systems to deliver something, and so are inherently tied up with the application. So go for a system or purpose close to treatment. In this case you have to know a bit about the regulatory landscape. [PH] concurs and adds that "you should forget about the distinction basic/applied development, it never existed and certainly isn't useful today."

Stretch 4: Media and Hype

At this point the chair of the meeting, [AR], announces that from the topics discussed before lunch Media and Hype was mentioned as important in the route for new products from lab to clinics.

[HK] is the first to comment, "there is a too negative a view of nanoparticles, you should tell about the benefits, e.g. cancer treatment" [PH] agrees but reminds [HK] that scientists have been promising, but not delivering, so many other people such as politicians are disappointed. [GD], "For example, the GMO promises backfired". [PH] questions the group "Is there really negative perception of nano?"

[GD] says no, referring to a UK study finding that public perception of nanotechnology is OK; however technology is positioned as negative. "I agree" says [KAO] "if I say to friends I do nano, they say "wonderful" I don't see any issues."

[PH] but research programmes now must contain HES elements and ELSA etc. Not because scientists believe in the toxicity issue, it comes from outside. [HK] responds, "But we know our particles are safe" [SB] points out that this is a very strange discussion (referring to the broad debate on toxicity) as in the lab they test for toxicity and "more importantly our particles are supposed to have toxic effects".

[GK] suggests that you could pre-empt by publishing yourself rather than leave it to journalists. [AR] comments "Like in Scenario 3?" [SB] "But there are always

countries with less regulation". [JB] "And then people would then get treatment in another country?" [AR] "But that will reflect on the field. A space for maverick scientists?" [HK] thinks that there will be a shift in production to other countries and other countries with less regulation, but [PH] has no qualms about this "Over time it will even out. Such discussions of transferring development and production to other less regulated countries should become more based on fact than fear."

3.3 Summary table

Actual composition	3 senior researchers, 6 junior researchers, 1 firm, 1 medical doctor, 1 technology transfer expert, 1 EHS expert and 2 organisers.
Degree of heterogeneity	Heterogeneous (66% enactors)
Last minute cancellations of participation and its impact.	No last minute cancellations. But last minute additions (3 junior researchers)
Stretches in the discussions Organiser initiated and taken up = O+ Organiser initiated not taken up = O- Participants initiated and taken up = P+ Participant initiated not taken up = P-	O+/P+/O+/O+/O+ The general pattern was that the organisers stimulated a stretch, but that this was soon taken up by the participants.
Explicit reference and use of the scenarios	++ Prior to the start of the workshop there were questions from the participants. In addition the morning session was orchestrated by the organisers as a long round of introductions with each participant commenting on the scenarios.
Implicit reference and use of the scenarios	+ Particularly in stretch 4. The organisers announce these implicit references when they are made (see the behaviour of [AR] in the text)
Quizzing between homogenous	In the main, this workshop there was more quizzing

actor group (or with those who knew each other prior to the workshop)	than probing. You can see this in the alignment of the discussion around technology-push strategies and barriers to overcome. Comments on people comments or general questions voiced to the group as a whole. In Stretch 1 there is quizzing between the participants in the round of introduction. During this extended round of introductions there is no real probing, but discussion of general questions (as issues) with no direction at a particular person until after the round of introductions. A sub stretch in this stretch 1 was initiated.
Asymmetric probing of the majority group (perceived as experts)	No there was no dominating group. Moreover since the researchers themselves were diverse (analytical chemists, synthetic chemists, molecular biologists).
Mutual probing in heterogeneous group	Probing began after the round of introductions in stretch 2 (initiated by a firm to researchers). *In this interaction (regarding paper companies –see quote at the beginning of Stretch 2) one of the organisers further stimulated the discussion using his own knowledge of a commercialisation situation unannounced by some of the participants.* Stretch 3 Medical doctor probes the researchers.
Do participants get into broader aspects or do they recourse back to their usual positions.	Yes they do get into broader aspects but not through probing it seems. Due to the set up of the first half of the workshop (introductions with comments on the scenarios) important elements as seen by the participants were voiced and comments and questions made based on these. There were many instances of reframing issues and elements of the scenarios with examples from their own world, and their own experiences. In some cases comments were raised based on unannounced positions which the organisers were aware of (such as some of the researchers having legal issues with a commercial partner in a technology transfer arrangement).

Appendix 3 - The role of images of molecular machines inside and outside the lab

1 Starting Conditions

1.1 Preparation through insertion and analysis

During the annual meeting in October 2006 in Sicily, a representative of CEMES (a CNRS research institute in Toulouse, France) made a presentation on molecular machines as the lead institute of the Strategic Research Area "Molecular Machines" in Frontiers. My colleague in the TA NanoNed programme, Martin Ruivenkamp, and I had conducted a small study on molecular machines through a vision assessment exercise (some of which is published in Robinson, Ruivenkamp and Rip 2007), and Martin joined me in attending the Frontiers annual meeting to chat with nanoscientists and to see the presentation on molecular machines (with his particular interest in images of the nanoscale).

The presentation on molecular machines was very revealing, even in such a meeting as a scientific research network, the presentation was full of macroscopic representations of the nanoscale.

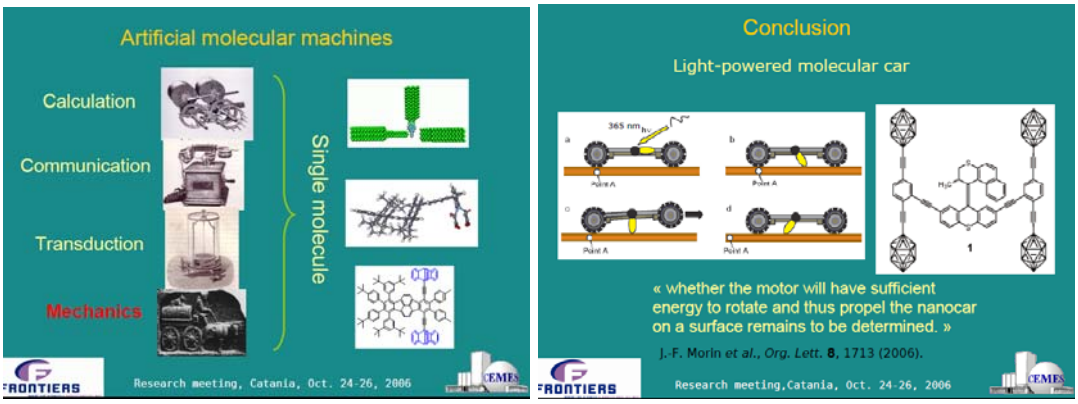

Figure 1: Two of the slides presented by a representative of CEMES at the Frontiers Annual Meeting 2006

After the presentation Martin and I asked some questions (as part of the audience) about images of molecular machines and how they are picked up in the media. This triggered a long response from the speaker (mostly critical) of the misrepresentation of nanoscale research by media (referring to nanobots in blood vessels.).

Martin and I found this intriguing since we had just witnessed a form of misrepresentation in the connection of macroscale devices with the nanoscale in the presentation. When the round of questions from the audience had concluded, Martin and I chatted with the speaker to discuss whether a CTA project on images and visions of molecular machines would be interesting for this Frontiers Strategic Research Area. Because of the research Martin and I had already done for our article in the special issue of the Journal of Scientometrics on nanotechnology (Robinson, Ruivenkamp and Rip 2007)[126], we could reference a lot of research activities. This seemed to soothe his, at first, suspicious posture to us and encouraged him to think with us a bit and brainstorm a possible workshop. The presenter [EM] asked us to send an email to the head of his group [GP] and we would move on from there.

In the remainder of the meeting in Sicily, Martin and I did some brainstorming before contacting [GP] about what we thought would be interesting. In our own research, Martin and I had noticed that there were distinct communities of researchers on molecular machines rooted in different disciplines:

- supramolecular chemistry;
- molecular biology; and
- physics.

Each had their own interpretation of what a molecular machine is and different ways of representing. All three groups making macro-scale comparisons which were circulating in the media, in nanotechnology presentations and even in policy documents. The creation and circulation of images, their reinterpretation and the power of images as they take up a life of their own was the starting point that Martin and I took to the "negotiating table."

Following the annual meeting, we had a number of phone calls with [JC] about the content of the meeting. [JC] is a very active researcher who participates in ethics discussions in France and has strong opinions. Being a member of the "physics community"[127] of molecular machine researchers in our telephone interviews he

[126] Including some interviews with world leaders in molecular machine research (Alberto Credi and Vincenzo Balzani) and some interactions in the Netherlands with Ben Feringa during a NanoNed annual meeting.

[127] Note that although the distinct communities are recognizable, the term "physics community" is one that Martin and I created.

repeatedly commented on our definition of molecular machines – he strongly suggests that "single molecule motors, rotors and walkers are the only true definition of molecular machine". Not wanting to focus purely on the imaging strategies of one of the groups (since the aim of the CTA projects were to broaden and look at co-evolution) Martin and I resisted this attempt to focus only on single molecular machines (what we termed as the 'physicist community interpretation').

Although the disagreement on definition of molecular machine remained, and required continuous reminders of the definition by the CTA organisers, including on the day of the workshop, the workshop was delayed because of agreement of financing. Even though in early November 2006 Martin and I were "ready to roll" with a CTA project proposal, it wasn't until mid April 2007 (as described in Appendix 2) that funding could be confirmed. Since there was a Frontiers research meeting planned in Toulouse on 9 May 2007, we decided to meet together in Toulouse and create the CTA-project concept. In the meantime, Martin and I explored some key players in the different molecular machine communities that we would like to have in our workshop.

Fig 2: In Toulouse May 9th – 11th The Molecular machine workshop concept was given the go ahead (4 weeks before what would be the date of the workshop)

In Toulouse on May 9th, some key researchers from CEMES [AD], [GP] and [EM] were present along with myself and the Frontiers Management team. Together we agreed that a workshop on Vision and Image assessment, the circulation of images would be the focus (the original proposal) but that only researchers from Frontiers would be funded, other actors could be funded. Also [EM] and [GP] who had the obligation of coordinating a meeting of the Strategic Research Agenda on molecular machines pushed for the CTA workshop to be combined with the

technical meeting. I resisted but was overruled as there was an argument that workshop fatigue was setting in the Frontiers network and that more people would be likely to attend the CTA-project if it was combined with a technical meeting. Although the logic was reasonable, Martin's and my wish to have representatives from all three major molecular machine communities was squashed – since the only Frontiers members doing research on molecular machines were CEMES themselves (the physicists). The only date before summer that was possible was June 12th and so the deadline was set for a 4 week preparation and attempt to attract participants from the Frontiers network.

Below two summary tables are presented. The first present's seven criteria that were used to both determine the starting concept of the CTA-project and its suitability for the various interested parties involved. The second table shows the contingencies that where an outcome of the negotiation of the project concept, the context of the subject, my degree of control over the shape of the project etc.

1.2 Summary tables

Key elements that contributed to the initial idea for the CTA.	Imaging of the nanoscale. How the representations of molecular machines made by a number of distinct communities of molecular machinists were translated, were (re)represented and put into circulation in the media, in conferences etc, and how these shaped both the research in the laboratories and the co-evolution of the field of molecular machines and society.
Is it interesting for my study of inserted CTA targeted at broadening enactor's perspectives?	Exploring co-evolution dynamics by analysing the role images play in shaping research agendas, perspectives and vision assessment of molecular machines.
Frontiers partner interests?	**Key negotiation actors:** Research group leader at the host institution How to communicate better with the media, and to educate its members on this.[128]
Stage of development of the field?	Fundamental research in the case of supramolecular and physicist approaches. Biomolecular machines are being

[128] Note that this strongly contrasts with the CTA goal and Martin and I positioned this as less important for the CTA and perhaps would be an additional, but not necessary, outcome of the CTA. The point was that it was supposed to be a space for probing and broadening, and not a seminar.

	used in devices in the laboratory but could be argued to be close to application, but rely on microtechnology and microfluidics (the biomolecular machines have to be in liquids).
An identifiable community or socio-technical network?	Yes, a number of distinct communities were visible in physics, biomolecular sciences and supramolecular chemistry.
Is there something at stake recognisable to some of the actors in the emerging community or socio-technical network?	The link between molecular machines and grey goo (prominent in the 1990's) has disappeared and so there is little pressure on the molecular machinists, so there was little at stake specific to molecular machines at the time of the workshop. For CEMES their interest was in communication and educating the general public on what is reality of molecular machine research.
Amount of material to work with? *(as perceived during the early stages of the CTA project development)*	There was lots of work in three main scientific disciplines on molecular machines (physicists, molecular biologists and supramolecular chemists). Another community that conceptualised molecular machines is the Foresight Institute, initiated by Eric Drexler focusing on molecular machines built atom-by-atom. Visions of molecular machines were at the very heart of the initial hype and debate about nanotechnology, and so even though molecular machines are still very much basic research, they have an important position in the collection of visions underneath the umbrella term NANOTECHNOLOGY.

Table 1: Identifying and negotiating an area to apply CTA to

Requirements and constraints from the Frontiers network	No non-Frontiers researchers, therefore no representatives from the biomolecular sciences and supramolecular chemistry. This meant our intended molecular machine community diversity was not possible.
Level of control over the topic and process by CTA organiser	Very little control. Our choice of participants was rejected, the length of time for the workshop cut (due to the blending with a Technical meeting). A disagreement on the real objective of the workshop continued until the actual event.
Amount of time to prepare the	Very tight. 4 weeks from the final decision to go ahead.

project	Although the CTA organisers could draw on some earlier research they had done, which reduced some of the preparation load.
Gathering participants	Very difficult. Only MESA+ had some people contemplating work on molecular machines. Gathering non-scientists proved ok, but limited budget meant only one representative of the media (from Paris)
Possibility to interview participants	Not possible due to time constraints.
Available document data	A lot of research and review papers were available.

Table 2: Contingencies and ramifications

2 Preparation

2.1 The promising technology

During the last 5-10 years there has been a rapid development in the control, and harnessing of, mechanical molecular motion. This includes the isolation, exploration and manipulation of natural macromolecular motors such as ATP-ase[129] and motor proteins,[130] in supramolecular chemistry there has been development in seen light driven artificial ratchets, shuttles and rotoxanes[131] and in

[129] Boyer, P. D. Molecular motors: What makes ATP synthase spin? Nature 402, 247–249 (1999). Hess, H. & Bachand, G. D. Biomolecular motors. Nanotoday 8, 22–29 (2005).

[130] Hess, H. & Vogel, V., Molecular shuttles based on motor proteins: active transport in synthetic environments. Rev. Mol. Biotechnol. 82, 67–85 (2001).

[131] Vincenzo Balzani V., Miguel C.-L., Credi A., Ferrer B., Venturi M., Flood A, Stoddart J. F.. Autonomous artificial nanomotor powered by sunlight. PNAS 2006;103;1178-1183 Kelly, T. R., De Silva, H. & Silva, R. A. Undirectional rotary motion in a molecular system. Nature 401, 150–152 (1999). Koumura, N. Zijlstra, R. W. J., van Delden R. A., Harada, N. & Feringa, B. L. Light-driven molecular rotor. Nature 401, 152–155 (1999). Feringa, B. L. In control of motion: from molecular switches to molecular motors. Acc. Chem. Res. 34, 504–513 (2001).Leigh, D. A., Wong, J. K. Y., Dehez, F. & Zerbetto, F. Unidirectional rotation in a mechanically interlocked molecular rotor. Nature 424, 174–179 (2003).Hernandez, J. V., Kay, E. R. & Leigh, D. A. A reversible synthetic rotary molecular motor. Science 306, 1532–1537 (2004). Fletcher, S. P., Dumur, F., Pollard, M. M. &

addition, the isolation and control of mono-molecular machines on surfaces through AFM and STM.[132]

Presently the field is entering the next step in the development of molecular mechanical control, and witnesses a convergence of goals within the above research lines (albeit with different approaches). One such goal is the harnessing of such molecules by positioning on surfaces to do work with the aim of enabling exciting new devices.[133]

"Linear and rotary molecular motors have been anchored to surfaces without loss of function — a significant step towards future nanomachines and devices".

Alongside these developments, we have seen the rise of the nanotechnology hype, which has permeated, and caused much debate, across scientific, industrial and societal communities on the promise of what nanotechnology can deliver. Exploration of what we broadly term as *molecular machines* has been inextricably linked with the promises of nanotechnology.

Visions and promises of molecular machines abound, from the Drexler links to atomic and molecular nanoassemblers[21], to the now "taboo" notion of grey goo to more "down-to-earth" promises of functionalised materials and processes which current research trajectories can enable. The developments under the banner of

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Feringa, B. L. A reversible, unidirectional molecular rotary motor driven by chemical energy. Science 310, 80–82 (2005).

[132] Rapenne G.. Synthesis of technomimetic molecules: towards rotation control in single-molecular machines and motors. Org. Biomol. Chem. 2005,3, 1165-1169. C. Joachim, H. Tang, F. Moresco, G. Rapenne, G. Meyer. The design of a nanoscale molecular barrow. Nanotechnology 2002, 13, 330-335. Rapenne G, Launay J. P. and Joachim C. Design and synthesis of mono-molecular machines. J. Phys.: Condens. Matter 18 (2006) Rapenne G., Grill L., Zambelli A, Stojkovic S.M., F. Ample F., Moresco F., C. Joachim C. Launching and landing single molecular wheelbarrows on a Cu(100) surface. Chemical Physics Letters 431 (2006) 219–222

[133] Hess, H., & Bachand, G.D. (2005). Biomolecular Motors. Nanotoday, 8, page 28. Kinbara, K., & Aïda, T. (2005). Toward Intelligent Molecular Machines: Directed Motions of Biological and Artificial Molecules and Assemblies. Chemical Reviews, 105, 1377 – 1400. van Delden, R. A., ter Wiel, M. K. J., Pollard, M. M., Vicario, J., Koumara, N. & Feringa, B. L. (2005). unidirectional molecular motor on a gold surface. Nature 437, 1337–1340. Credi A. Artificial nanomachines based on interlocked molecules. J. Phys.: Condens. Matter 18 (2006) Browne, W.R., & Feringa, B.L. (2006). Making Molecular Machines Work. Nature Nanotechnology, 1, page 33

'molecular machines' are shot through with promises and visions of possible next steps in the development of the field and of future applications.[134]

Research on all fronts of molecular machines is broadening its agenda, from proof of control to putting molecules to work on surfaces and in MEMS.

2.2 Preliminary diagnosis

The idea of molecular machines, as we use the term in the Vision Assessment Workshop, is to put molecules to work, trying to understand dynamics and perhaps using them for applications. Thus we use the umbrella term of molecular machines to cover, mono-molecular motors, rotors and walkers, mono-molecular machines, supramolecular and macromolecular machines. For research into these molecular machines, nanoscience, nanotechnology and the media have constructed high expectations, both for understanding phenomena at this level and for the promise of harnessing molecular mechanics to do work in the macro-world in which we live.

Research into molecular motors and rotors in fields such as physics, chemistry, biology and material sciences have their own dynamics but also appear to converge towards a vision of harnessing mechanical motions (through functionalised surfaces, crystals and NEMS). Images play an important role in research and in communication about research, also to wider audiences. Their uptake and circulation is an issue in its own right, and may well have repercussions, both on the directions of research and on expectations and public reception.

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[134] Browne, W.R., & Feringa, B.L. (2006). Making Molecular Machines Work. Nature Nanotechnology, 1, page 33 Even though there are ongoing attempts to separate the two and to clarify what is or what is not nanotechnology: See Joachim C. To be nano or not to be nano? Nature Materials | VOL 4 | February 2005 Joachim 2005 & Grimsdale A. C., Müllen K. Die Chemie organischer Nanomaterialien. Volume 117, Issue 35 , 2005. Pages 5732 - 5772

Drexler, K. E. (1999). Building molecular machine systems. Trends in Biotechnology, 17, 5-7. Joy, B. (2000).Why the future doesn't need us. Wired, 8, 238-262. Smalley, R. E. (2000). Nanotechnology, education, and the fear of nanobots. In M. C. Roco & W. S. Bainbridge (Eds.), Societal implications of nanoscience and nanotechnology: A report on the September 28-29, 2000 NSET Workshop. Arlington, VA: National Science Foundation.

With its link to nanotechnology, leading to both fantastic visions of nanomachines and more nearer term visions of improved functions and devices, the field of molecular machines is shot through with promises.

Currently an increasing amount of work is being done in functionalised or controlled molecular transports on surfaces, providing opportunities for convergence of a number of fields of research in mono and macro-molecular machines moving closer to the realization of nanomachines and molecular-devices. With this renewed promise, it is timely to probe visions of the field (both in the various streams of research and outside the lab – in the media and elsewhere).

2.3 Translating diagnosis into workshop topic and scenarios

Workshop Topic

This workshop seeks to take stock of the current promises and visions of the field of molecular machines, to explore past dynamics and to extrapolate future relations between research into molecular machines in its various disciplinary flavours.

By exploring visions (and associated images) of the potentials of harnessing molecular machines, from the many streams of research inside the lab as well as those outside the lab, we can anticipate on some of the challenges inside research as well as gain a deeper understanding of the relationships between science, technology and society.

The questions to be addressed in the workshop include:

- Which visions and images (of molecular machines) are viable in the convergence/divergence of research communities stemming from biotechnology, material sciences and supramolecular chemistry?

- Which visions and images are viable promises in circulation in the media (and elsewhere) in the industrial and societal debate on the promise of molecular machine based devices and nanomachines?

- What role do such visions and images play in the emergence of new technology and what strategies could be taken to optimize the uptake and use of such visions?

The idea is not to reach a consensual answer to these questions, but to articulate the various points of view and possible strategies.

There are two parts to such investigation and exploration:

1. Analysis of vision and image dynamics by the organisers and creation of scenarios of plausible futures for the field of molecular machines and some possible interactions between visions, research and societal debate.

2. Interactive workshop were relevant participants are drawn from the field of molecular machine research, researchers into the sociology of visions of technology and representatives of the media.

The objective of this workshop is to explore the visions in circulation in the many streams of research in the field. ***Which visions are plausible goals to follow?***

In addition, we look at visions of nanomachines outside the laboratory, in mass media, industry and policy worlds. ***What can these speculative visions tell us about the future of development and role of nanomachines?***

As an entrance point to this discussion, we present three scenarios, built on case study research and insights into the role of visions on the co-evolution of technology and society. The following section gives three short summaries of the scenarios. This is followed by the full scenarios with key elements, dynamics and issues shown in annotations.

2.4 Scenario summaries

Scenario summary 1

In 2010 research focused on the transportation of cargo and information across nanoscale surfaces. This new emphasis coincided with the release of nanoSimCity, a popular computer simulation game allowing players to develop a virtual nanoscape by laying down roads, bridges, tunnels, car parks and mass-transit lines using molecules and nanoscale machines. The computer game stimulated a lot of interest in the field of molecular machines and was further bolstered by the large amount of press coverage through articles referring to *molecular cities.* Although labelled as an interesting fantasy by some researchers, others seize the media and public interest in molecular cities and start tailoring their public outreach programmes. They do this by blending the key elements of their research activities with visualisations and examples from nanoSimCity.

The images capture the imagination of the press and a broad public audience and research scientists start linking their research directions ever closer to the fantasy world of nanoSimCity, this is visible in governmental research funding proposals As the notion of molecular city gained momentum, tying together many disparate research lines in the field of molecular mechanics, and by 2012 the molecular city concept still remains strong, attracting other research lines and industrial interest for the purpose of advance logic and mass storage solutions via nanoscale transport.

Scenario summary 2

By the end of 2009 the nanotechnology umbrella term dwindles and the nano-label dissolved into its sub-fields relating to application, Nanoelectronics, Nanomedicine etc. As the hype (and associated financing) begins to focus on specific areas, researchers in the field of molecular machines find it increasingly difficult to link up to research funding programmes (a victim of being too involved in the nano-hype). This shift in fortunes comes as a shock to molecular machinists who have benefited from the Nanotechnology umbrella label. Feeling this pressure, research groups increasingly have to work on promotion and communication activities to gain interest and support. Different strategies are tried out; modest visions of putting molecular machines to work but with a long-time to application in the macro-world receive little attention. Another is to try early visions once again, through recycling Drexler's nanoassembler idea, now with more findings (20 years on). This is picked up with some interest in the media, but technology developers and other researchers have concerns about the potential repercussions of such visioning strategies and distance themselves from those touting a modified Drexlerian vision. Anticipating on the growth of this field, insurance companies voice their concerns about the control and containment of these active nanodevices. The debate about control of molecular machines inside and outside the lab begins to be a key discussion around molecular machines.

Scenario summary 3

By the end of 2008, the once diffuse field of research into molecular machines, now begins to solidify with identifiable groups of researchers, however, rather than definition or disciplinary based distinctions, research agenda based distinctions became more characteristic. Groupings included (1) Research on mono-molecular machines for purpose of physics and chemistry (2) Research on functionalised surfaces and smart materials and (3) Research on NEMS/MEMS harnessing macromolecular motors. The three strategies are developed in parallel. With

devices getting closer to the market, based on macromolecular machines, attention shifts away from mono-molecular machines. Thus research and development began to stabilise at the larger end of the nanoscale. This had consequences on research directions within the field; macromolecular machine research receives a lot of funding, whereas the focus on mono-molecular machines focuses on imaging techniques to understand the science that is occurring at the single molecular level.

2.5 Scenarios

Scenario 1: Nanoscapes

By 2010 research into molecular machines began to focus on the movement of information and cargo across surfaces. Research agendas targeted simple systems of nano vehicles or biomolecular shuttles.[i]

This new emphasis on increasingly complex systems of molecular machines on surfaces coincided with the release of nanoSimCity, a popular computer simulation game allowing players to develop a virtual nanoscape by laying down roads, bridges, tunnels, car parks and mass-transit lines. The objective of the game is to lay down, at the nanoscale, components that are the equivalents of roads, tunnels and lines of mass-transit, and to use them to move cargo between regions in a device. The 'cargo' might be colloidal particles in suspensions, fluids inside microfluidic pipes, quanta of electricity (electrons), or quanta of magnetic flux (superconducting vortices) [ii]. An example from the game was an electrical capacitor — effectively a 'car park' to temporarily store electrons, which could be eventually moved elsewhere.

The computer game stimulated a lot of interest in the field of molecular machines and was further bolstered by the large amount of press coverage through articles referring to *molecular cities*, and public attention turns with interest to the laboratories.[iii]

A senior research fellow at Rice University, in response to the buzz around nanoSimCity stated "these computer games are wonderful, but nothing to do with what we do in the laboratory".

Elsewhere, other researchers began publishing research with the term molecular city, as a vague but interesting goal for their very specific research.

[i] Here I bring in one particular community of molecular machines (those working on harnessing living systems such as kinesin and dynesin). It also equates communication (information transmission) with physical movement (which is a vision of molecular machine usage for computation or other "intelligent" technologies.

[ii] A computer game was created taking molecular transport and nanoscale landscapes as the platform for creating a working nanoscale world. Like similar style console games, the objective was to create the most imaginative and best functions world (in this case efficiency).

[iii] The relative popularity of the game, provide an easy simile for nanoscientists working in this field. Images of these landscapes (from the computer game) became emblems of possible future nanotechnology potentials. (similar to the image of the nanobot (a microscale robot) pinching a blood cell with its nanopincers)

[iv] Researchers react proactively in two ways. One broad group positions their work as far from the representations given in the computer game. The other broad group of researchers embrace the attention in popular press and media and

Taking the large public interest in molecular cities as an opportunity, Dr. Rickstein, of Purdue University, creates a number of graphic visualisations of molecular cityscapes with nanocars moving between factories and biomolecular cargo transports. The images capture the imagination of the press and a broad public audience and a discussion of the potentials of molecular cities ensued. These visions, he claimed, were within reach of current research lines.[v]

Early 2011 Rickstein built on the molecular city idea with his work on molecular communications. Key features of molecular communication included the use of molecules as a communication carrier and biochemical reactions caused by the information molecules at the receiving side. Unlike existing communication where encoded information such as voice, text, and video is interpreted at the receiver, in molecular communication it Rickstein posed that information molecules cause some reaction at the receiver and recreate a phenomenon and/or chemical status that the sender transmits [vi].

"Harnessing molecular communications through the construction of complex systems on nanomachines, "molecular cities" if you will, promise to revolutionise the way we think about computation and memory storage."

"Nano-engineers and nano-architects will create cityscapes where molecular shuttles, nanotrucks will exchange cargo and information to and from processing centers meaning super control of processes at the nanoscale….the possibilities are endless from advanced molecular computing to smart surfaces!"

The notion of molecular city gained momentum, tying together many disparate research lines in the field of molecular mechanic, and nanocar is inextricably linked with this vision. Bolstering research into molecular machines, but with the goal of cargo transport and

use some of the terms such as "molecular city" from the game to frame their public engagement and outreach programmes.

[v] A leading researcher creates visualisations (images) of nanoscale landscapes, with topography and nanocars, and trucks moving between storage depots. This captures the imagination of the press and garners interest. The researcher emphasises that this vision could become a reality. (such images are used in articles about single molecular machines – see the Rice University nanocars, or the nanoshuttles in on biomolecular machines using kinesin motors on microtubules).

[vi] The researcher builds on this first imaginary (and visioning) world depicted in his images to hypothesise that information could truly be transmitted in an analogue format.

[vii] The notion of molecular city becomes widely used as a vision for nanotechnology in the press and in science enthusiastic publics, which in turn provides impetus to funding agencies to invest more in this growing hype. (vision is shared across a large area of society and referred to, enabling further research, but

communications [vii].

Senior researchers at Rice react "although Rickstein's vision is interesting, understanding the actual processes occurring at the nanometre scale should be the focus of research. This is a serious bottleneck in exploration of true nanomachines".

By 2012 the molecular city concept still remains strong, attracting other research lines and industrial interest for the purpose of advance logic and mass storage solutions.

constraining it inline with this vision).

Scenario 2: Managing Hype

By the end of 2009 the nanotechnology umbrella term had dwindled and the nano-label dissolved into its sub-fields [viii]. As the hype (and associated financing) begins to focus on specific areas, researchers in the field of molecular machines find it increasingly difficult to link up to research funding programmes (a victim of being too involved in the nano-hype) [ix].

Feeling this pressure, research groups increasingly had to work on promotion and communication activities to gain interest and support [x].

In one case, the further development of nanovehicles, a molecular truck was designed and used to transport cargo from on site to another. In conjunction with his nanotruck/cargo findings, Prof. F. Beringer presented his vision of the challenges for nanomachines in the popular science magazine New Scientist, "The first primitive artificial molecular motors have been constructed and it has been demonstrated that energy consumption can be used to induce controlled and unidirectional motion. Major challenges in the development of useful nanomachines remain, such as the development of fast and repetitive movement over

[viii] The nano umbrella term which carried broad visions dissolves into specific sector focused umbrella terms such as nanoelectronics and nano-medicine (this has already been observed in part in Chapter 3)

[ix] Molecular machines, which could be referred to as an enabling nanotechnology field, suffers from the collapse of the nano hype (visions of nanorobots and molecular machines were part and parcel of the first hype of NANOTECHNOLOGY).

[x] Researchers reacting to pressures to justify their work (and anticipating on future reduced funding) begin to create outreach programmes to garner support for molecular machine research.

[xi] A start scientist connects the technical challenges of molecular machines with a vision of molecular transport, (These challenges incidentally have been given by leaders in the field in 2007 at the time of

longer time frames, directional movement along specified paths, integration of fully functional molecular motors into nanomachines and devices, catalytic molecular motors, systems that can transport cargo etc." [xi]

the workshop and so this was an opportunity to prompt the molecular machine researchers into this mix of visions and research challenges)..

Contrary to expectations, this discovery didn't receive much interest. Prof. Beringer and other members of his group write a number of monographs for newspapers and popular magazines, with little follow up.

[xii] Another researcher strategy is to link up with an earlier debate (hijack tactic) – that of molecular self-assembly. Going back to the roots of the original NANOTECHNOLOGY hype, he recalls the vision of Drexler as relevant (regardless of the actual research done by Drexler himself)

In another institute, Prof. G. Bennet, anticipating on his groups research findings begins promoting his work on molecular self-assembly and replication for nanodevices through building up recognition of their research by linking up with former debates on self-replication. "Even though his notion of nano-assemblers is physically and chemically flawed, Drexler's vision should not be abandoned because it holds a number of promising ideas of where to go and what to do in the future. Drexler's core idea of self-replicating nanorobots, however, may be challenged by alternative and more natural concepts of implementation. Chemistry has been looking into this direction for a number of years—the first demonstration of a chemical self-replicating system was reported in the same year when Drexler's book came out."

[xiii] The vision of self-replicating nanomachines (previously rejected by the scientific community) garners support from enthusiastic public – the environment for such visions has changed and the vision now represents a positive future, versus the previous representation of out of control nanomachines and grey goo.

Professor Bennet freely quotes George Whitesides, a critic of Drexlers nanoassemblers, in his argument that self-assembly is a promising manufacturing strategy.[135] This speculative vision of a return to the

[ix] The question of control comes to the fore as insurance

[135] The quote being "In the 21st century, scientists will introduce a manufacturing strategy based on machines and materials that virtually make themselves; what is called self-assembly is easiest to define what it is not. A self-assembling process is one in which humans are not actively involved, in which atoms, molecules, aggregates of molecules and components arrange themselves into ordered, functioning entities without human intervention […] People may design the process, and they may launch it but once under

core of Drexler's vision of self-replicating nanomachines raises concerns in much of the scientific world. However the notion was picked up by the broader public with optimism.[xiii]

A number of research scientists react with comments such as "We do not want to return to the pointless discussions of Grey Goo." And "With these claims, self-assembly and replication is becoming a media sensation once again. Engineers need feasible concepts to work with, and these claims are just confusing the issue.

Anticipating on the growth of this field, insurance companies drawn into the nano debate through earlier risk assessment of nanotoxicity raise their concerns: "We are concerned with the control and containment of these active nanodevices. This provides the biggest risk concern in nanotechnology next to the toxicity of nanoparticles"

The debate about control of molecular machines inside and outside the lab begins to be a key discussion around molecular machines. Tensions still remain however, whether researchers should create long term vague and speculative visions (where there is less control on the interpretation of the vision) or for very specific visions of overcoming a near-term technical hurdle.

companies raise concerns about so called "active" nanotechnology (Active nanotechnology as self replicating structures and/or nano actuators as a truly different family of nanotechnology to passive nanotechnology options such as nanomaterials and nanosensors).

[x] The concerns about self replication and control, and the promise of active nanotechnology systems (the original visions of nanotechnology) return once more in the field of molecular machines. However, they are more articulated due to the overall development of NANOTECHNOLOGY and awareness across most communities, but also due to further specific discoveries of particular nanotechnologies – the fear of lack of control of the nanotechnologies (rather than toxicity issues) returns.

Scenario 3: Vision lock-in in R&D

By the end of 2008, research into mono and macro-molecular machines has provided a plethora of molecular components. The once diffuse field of research into molecular machines now begins to

[xi] The fields of molecular machines have grown enough to be identifiable (and bounded) communities in their own right (1 group of

way it proceeds according to its own internal plan, either toward an energetically stable form or toward some system whose form and function are encoded in its parts": George Whitesides (1995) Self-assembling materials, Scientific American, September p146-149

solidify with identifiable groups of researchers [xi].

Rather than definition or disciplinary based distinctions, research agenda based distinctions became more characteristic. Groupings included (1) Research on mono-molecular machines for purpose of physics and chemistry (2) Research on functionalised surfaces and smart materials and (3) Research on NEMS/MEMS harnessing macromolecular motors [xii].

Work on primitive artificial nanomachines continues. Those lines of research actively linking up with applications, such as research on NEMS and smart materials based on functionalised surfaces, gains interest from media and industry [xiii].

In 2009, with the macromolecular hybrid MEMS for molecular sensing, being successfully demonstrated, venture capitalists see opportunities for useful devices on the horizon, and the first tentative investments are made into hybrid devices.

With devices getting closer to the market, based on macromolecular machines, attention shifts away from mono-molecular machines. Thus research and development began to stabilise at the larger end of the nanoscale [xiv].

By 2011 the net effect was not a lack of investment into the development of molecular motors (such as the nanocar) but the much needed nano-scale imaging probes, which provides a bottleneck to the further exploration of this line of investigation. Because of the limitations of the tools for nanoscience, a detailed single-molecule study on a surface is limited to atomically flat solid surfaces that are suitable for scanning probe microscopy observational techniques. Progress is stifled in this area, whilst momentum builds up in harnessing of natural macromolecular motors for interesting devices and smart materials.

supramolecular chemistry origins, another from biomolecular sciences another from physics and maths).

[xii] The distinctions shift from origins to research agendas and shared visions.

[xiii] Application oriented molecular machine research garners the most support and interest from industry and the general public. (there are indications of this trend and in interviews with the participants there were concerns about such a shift – it would jeopardize some of the research directions they were interested in)..

[xiv] Attention is more and more focused on the macromolecular machines (such as the biomolecular machines) due to the shift in “external conditions”.

[xv] The limited funds that are available for the monomolecular machines R&D is focussed on the major stumbling block that of imaging instrumentation. In this way monomolecular machines are merely the site for developing instrumentation with little science actually conducted on the monomolecular machines themselves.

Important actors outside of the concentric approach (from diagnosis)	Which ones were included in the preparatory material	Actor communities outside of the concentric approach represented in the workshop
The media, who take up and modify images and visions of molecular machines and circulate them. **The general public,** we see and interpret these images **Research funding bodies,** who include visions in their assessment of funding proposals **Non-governmental Organisations**, who interpret such visions and react to them through support or opposition	**The media,** who promote interesting new things to a wider audience (Scenario 2. **The general public,** we see and interpret these images **Research funding bodies,** play a role in choosing to invest in certain visions as opposed to others based on a number of criteria (see Scenario 3)	**The media,** a writer for the popular science magazine La Recherche

What elements were chosen and highlighted in the scenarios?	• The strategic use of images to mobilise support, resources and to communicate with other communities. • The blurring of reality and fiction in imaging strategies of one community of actors (e.g. molecular biologists), and the consequences for other communities (a member of the public) who interpret them • Hype/Disappointment cycles • Lock-in to a particular concept/notion of molecular machine due to a dominant vision.
What stakes were chosen and highlighted in the scenarios?	The original stakes would have been the lock-in of the R&D agendas based on images and vision strategies of different molecular machine communities. This could have been integrated but we judged that, based on our long arguments with the core Frontier partner on this topic about definitions, that it would be rubbished or ignored. Therefore we had to work with what we had, looking at an individual (relatively homogenous) group of molecular machinists visioning, and how the circulation of the images and/or visions would be part of the co-evolution of the field. In effect, as mentioned in section 1, there was little at stake.
Structural difficulty in creating scenarios	The original idea of exploring how images of molecular machines are constructed by nanoscientists and how they can shape the development of their field was quashed by the fact that we could only have one very homogenous group of molecular machinists from the physics community at the workshop. This put enormous pressure on the scenario writing since one of the most interesting elements of the workshop (the one where there was something at stake for the enactors in the VERY early stages of emergence) was not present. The emerging irreversibilities and the co-evolution of images, expectations, agendas and actions (see van Merkerk and Robinson 2006) would have been a good platform for broadening and could have been represented in the scenarios. The effect was that the story lines had to focus around the interface between nanoscientists on the one side and the media/general public on the other. Making it very difficult not to reinforce this boundary division between insiders doing the science and the outsiders interpreting it. In other words it was difficult to include elements of co-evolution.

3 Workshop

3.1 The participants

The aim of getting a diverse mix of participants was confounded by the time horizon for organizing the workshop (4 weeks) and the limited number of research groups in the Frontiers network who worked on molecular machines. Since one of the restrictions for the budget of these workshops was that money for participants external to Frontiers should be limited to funding those skills or expertise not within the Frontiers network, my argument for a diverse mix of molecular machinists did not succeed and only single-molecular machinists attended and mainly from the host institution. We did bring other non technology actors together, some sociologists, a philosopher of science, a representative from the media, but the relative homogeneity of the meeting and the quick turnaround of the project (4 weeks from the go ahead) meant a difficult environment for broadening and exploring dynamics of co-evolution. Another issue was of the combination of the CTA project with a Technology focused brainstorming meeting. Thus all of the non-CEMES researchers attended the CTA as an additional aside to the technical meeting – there was little at stake for them. The final list was as follows:

Code	Institute	Community
[NP]	**Nicolas Symphorien** La Recherche (F)	Media
[EV]	**Elena Valeriani** University of Catania (I)	Sociologist of images
[AP]	**Agnan Prauquier** Université of Paris I (F)	Philosopher of science
[WP]	**William Postlethwaite** Laboratoire de Photophysique Moléculaire, Paris, (F)	Researcher on single molecular motors
[LL]	**Louisette Leiris** University of Twente (NL)	Research on lab on chip (interest in molecule machines on surfaces)
[MES]	**Marie-Edwige Sarraute** University of Twente (NL)	Researcher on single molecular motors
[MR]	**Martin Ruivenkamp** University of Twente (NL)	Sociologist of Images and co-organiser
[DR]	**Douglas Robinson** University of Twente (NL)	Organiser
[AR]	**Arie Rip** University of Twente (NL)	Organiser
[EM]	**Eudes Modeste** CEMES/CNRS (F)	Researcher on single molecular motors
[GP]	**Geoffroy Pompon**	Researcher on single

	CEMES/CNRS (F)	molecular motors
[MS]	**Mathieu Sooge** CEMES/CNRS (F)	Researcher on single molecular motors
[AD]	**Alceste Dubruit** CEMES/CNRS (F)	Researcher on single molecular motors
[CD]	**Clotaire Ducrin** CEMES/CNRS (F)	Researcher on single molecular motors
[JD]	**Joachim Desnos** CEMES/CNRS (F)	Researcher on single molecular motors
[RSE]	**Rex de Saint-Exupéry** CEMES/CNRS (F)	Researcher on single molecular motors
[MD]	**Maixent Dhôtel** CEMES/CNRS (F)	Researcher on single molecular motors
[RR]	**Rufus Rabearivelo** CEMES/CNRS (F)	Researcher on single molecular motors

3.2 The workshop interactions as stretches

The workshop began a little late whilst the visitors to CEMES-CNRS searched for the workshop room. Since the meeting was a joint event, under the aegis of Frontiers, [EM] introduced the main details of the Frontiers Network of Excellence and the objective of the technical meeting and its role in the Frontiers NoE (should contribute to the Strategic Research Agenda of Frontiers). This was followed by an introduction to the programme of CTA projects in Frontiers by [DR] and the focus of the day "Vision Assessment and the role of images in molecular machines".

[DR] "What are visions? From research experts they are guiding ideas that shape the directions of research. In part they can be of a particularly desired scientific goal, or on the future application of scientific findings in society. They are always speculative, they are about the unknown, and are often mediated by images. We can see this in molecular machines, in biomolecular machines of shuttles, to nanocars in the work you do here in CEMES, to molecular switches etc." [DR] showed some examples (given below) of natural and artificial molecular machines.

[DR] "The idea of molecular machines, as we use the term in this Vision Assessment Workshop, is to put molecules to work, trying to understand dynamics and perhaps using them for applications. Thus we use the umbrella term of molecular machines to cover, mono-molecular motors, rotors and walkers, mono-molecular machines, supramolecular and macromolecular machines."

[DR] "For molecular machines and nanomachines visions are often mediated by images – meaning this will be quite prominent in our discussions today. Visions as

ideas or images can affect the development of science and technology as well as the uptake (or lack thereof) of applications stemming from a new technology. Thus understanding the dynamics of visions may lead to optimizing the emergence of S&T as well as the relationship between S&T and society." Ending this small introduction [DR] introduced the timetable for the day:

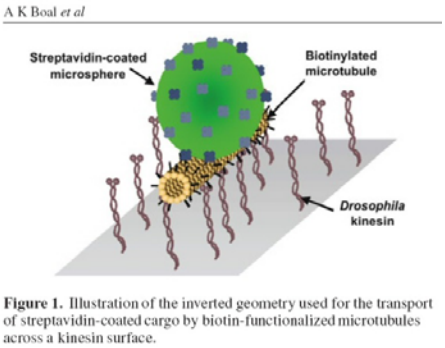
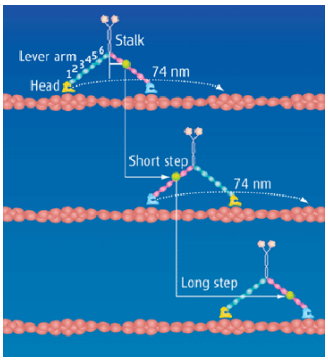
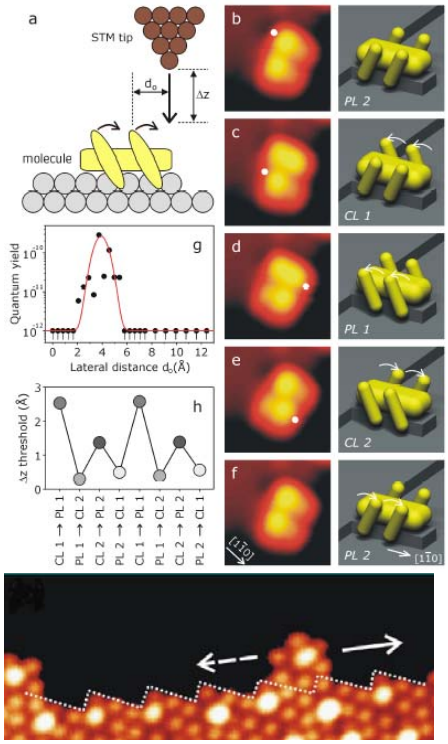


Figure 1. Illustration of the inverted geometry used for the transport of streptavidin-coated cargo by biotin-functionalized microtubules across a kinesin surface.



Examples of natural molecular machines



Examples of artificial molecular machines

09:00 – 09:45	Introduction to the day by the organisers and round of introductions
09:45 – 10:45	Two presentations on technical aspects of molecular machines (20 minutes plus questions)
11:00 – 12:30	**Vision Assessment discussion:** Promises in the research laboratory
12:30 – 13:30	lunch
13:30 – 15:30	**Vision Assessment discussion:** Promises of nanomachines

15:30 – 16:00	coffee break
16:00 – 18:00	SRA – Technical meeting

Figure 4: The timetable of the meeting. Note that for the CTA there are two slots appointed for the discussions entitled "Vision Assessment discussion" with the rest being part of the Technical meeting.

A
tl
afternoon coffee break and opened up the floor for the first technical presentation.

First presentation

[WP] A researcher from the Paris region, worked on manipulating single molecules on semiconductor surfaces – with Scanning Tunnelling Microscopes (and with the STM collaborated with CEMES) – the vision of his research being the electronic control of single molecule dynamics. Control here meant control of motion and luminescence. To do this there are a number of options; (1) push or pull (lateral displacement), (2) field exploration (vertical displacement), (3) inelastic electron effects (do this by fragmenting the molecule), (4) direct contact or (5) by using photons to induce manipulation.

In his work in the Paris region, [WP] had been working on a bottom-up nanomachines project were three benzene rings (creating a small wire) had ketones attached the end. Oxygen atoms were attached to the centre piece. This nanomachine was sensitive to small changes, and so the investigation focused on the motion of this nanomachine, which is sensitive to small changes in voltage, what happens is still unclear. Can we control positions?

[WP] ends this small introduction and the chair opens up the floor for questions.

[LL] a research scientist investigating integrated microfluidics systems asks "When you move the single molecular nanomachine, you can also change the molecule. How do you control for that?" [WP] nodding "Yes that is true, but not for this particular molecule. We know there is no change because the molecular reaction we undertook in the construction of the nanomachine is irreversible."

[AP] A philosopher of science who had been investigating molecular machines as a case study asks a technical question, "Your nanomachine shows four different states, changed by the absorption of hydrogen?" [WP] "Yes, one of our PhD students saw the images and saw dark patches that couldn't be explained. They didn't look like the silicon (part of the nanomachine) and so thought it may be hydrogen. That stimulated us to look further,"

[DR] asks a question "You mentioned the calculations indicate which combinations of molecule and surface will work, how does that go in experimental practice? The combination of calculation, experimentation and interpretation?" [WP] "Our present calculations are about electronic structure of absorption. At RTP we can't chemically identify it (no direct way of visualising it) and so have to calculate."

At this point two late comers arrive at the meeting [NP] from La Recherche (a popular scientific magazine in France) and [AD], an active member of the CEMES research team.

Second presentation

The chair asks the newcomers to introduce themselves and then gives the floor to the second speaker, a lead researcher in the group [GP].

[GP] announces that he will give an overview of the field of molecular machines, a little technical with a little bit of other aspects. "There are a number of ideas of what a molecular machine is. Macromolecule machines (which are easier to imagine) can be found in biology or perhaps in macromolecular chemistry. The others are single-molecule molecular machines (or nanomachines). The Frontiers visions oscillate between them."

It is curious phrasing by [GP] as he positions a Frontiers vision of what molecular machines are. Since CEMES is the only institute active in molecular machines in the whole network it can be assumed by the "Frontiers vision" he means the workshop organisers definition – which was co-constructed with himself.

[GP] continues, "Molecular machines have roots in molecular computing. One interesting point in this history was the work, and impact of the work, of Aviram and Ratner 1974, with their molecular rectifier. A key issue for them was how to pass on such ideas as the molecular rectifier to the public. They used diagrams, derived from semiconductors (because available, not because they were correct). There was a mixture of chemistry and physics depictions of the phenomena which made no sense in either discipline but which had an effect"

"Concerning molecular mechanics, the discovery and exploration of the biomolecular machine ATP-synthase (Boyer 1965) coincided more or less with the famous book (in Nanotechnology circles) of Isaac Asimov's, Fantastic Voyage 1966. Depictions of molecular machines carry on to this day along the same vein up until 2000's virtual nanomedicine images such as the Nanobot. Questions have always been, how can we diffuse our ideas and new concepts? One way is to use

modernistic, shiny structures of robots doing a job vs. chemistry's space-filling molecule models." [GP] shows another depiction that he likes, a Lego-movie for kids, with the underlying message that is possible to fix DNA atom by atom.

"Coming back to reality" says [GP] "there is the issue of access to atomic scale." [GP] shows an image of the molecular wheelbarrow which they have been working on in their lab.

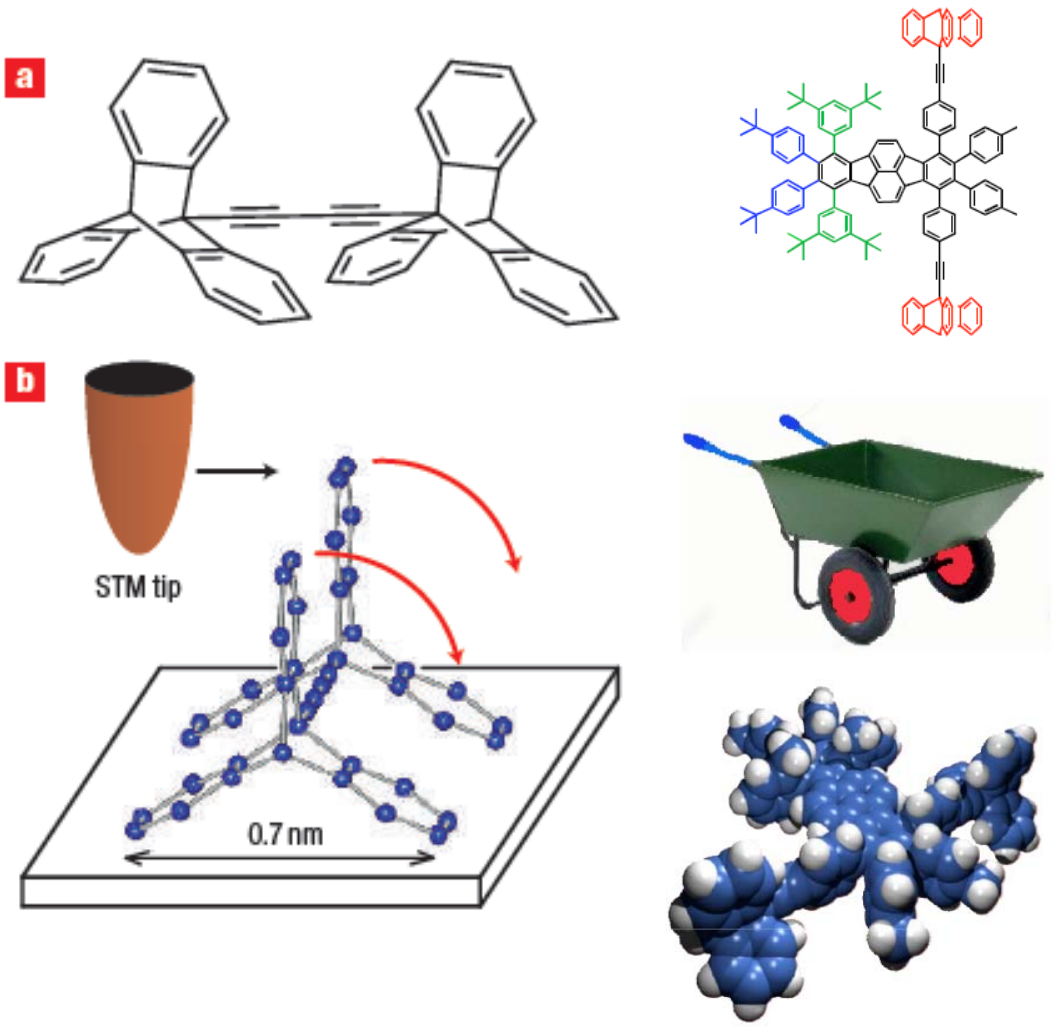


Figure 5: Molecular Wheelbarrows as depicted by [GP]

In the research project [GP] and group have been pushing a wheelbarrow-like molecule across a surface using a Scanning Tunnelling Microscope. "We used a number of ways of depicting it as you can see. You see the molecular model, space-filled depiction and we thought we could explain the idea by adding a picture of a wheelbarrow – in a scientific publication! We also did a molecular pinion on a

rack – for newspapers, you have to offer a macroscopic equivalent. You see Rice University doing similar things with their nanocars."

[AD] interrupts the presentation, "You present molecular machines as being constructed atom by atom (physics) and molecular (biology) so chemistry has disappeared."

[GP] "Yes, the image of chemistry, was: manipulating molecules (which they didn't!). About representing it as building atom by atom, that was for an article in a Ladies journal: cosmetics atom by atom. I wanted to explain it to the readers."

"But this is WRONG" [AD] exclaims "you can't build anything atom by atom, you need materials science." He continues to grumble at the back of the room, muttering sardonically with a smile "Don't manipulate the atom, that is sacrilege."

Some of this behaviour may be related to a tension between [AD] and [GP] who work together in the same institute, [GP] being higher in the hierarchy and [AD] soon becoming unemployed as his temporary contract runs out – data stemming from informal interviews the month before the workshop.

[MR] a co-organiser of the CTA project interested in images of nanotechnology, comes in with a question "You explained that you needed a macroscopic image and that you are not sure what impact images may have. How do you select the image?"

[GP] "Trial and learning. That's how we got the wheelbarrow."

[MR] follows up "So the idea of transporting cargo was the goal! Like a wheelbarrow. Also to get support from publics/funders?" [GP] doesn't answer, but responds with a shrug of the shoulders [*interpreted as I don't know*].

[DR] picks up on [MR]'s thread "Can you get trapped by such pictures? You need them even if scientists don't like them." Another social scientist comes in adding to the thread (before anyone can answer). [AP] "How much of the message in images shapes your research directions?"

[GP] "It does for molecular mechanics, not for electronics". "But does it limit your creativity?" continues [AP]. [GP] "Not really, we can shift from wheels to legs".

[AP] "So it is just to communicate with publics? "

New Stretch

There is no answer. The chair [AR] comes in, announcing that "This is a good time to begin the next part of the schedule on Vision Assessment. We have discussed a little about visions and the imaging strategies of researchers. I turn to the rest of the participants now; do you have any comments on what has been discussed?"

[LL] "In the Lab-on-a-chip field we use macroworld images – such as laboratory equipment on the palm of a hand. The image is now all over the world and has no real link to the technology."

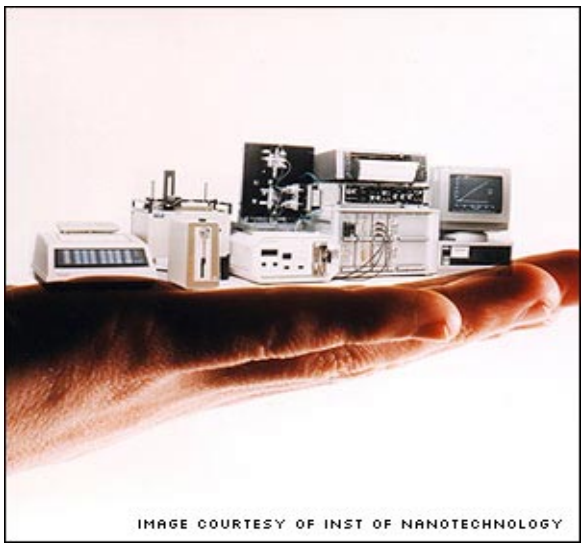


Figure 6: The image [LL] is referring to

[DR] "But there was a historic move around 1993 from microfluidics. Actuators etc. to integrated micro total analysis systems. This was a vision. Do such images (and general visions) shape your research?"

"Yes", answers [LL] "Currently in my field, the medical applications are placed up front then the MicroTAS details and chemical synthesis. The problem with such things is that the hard work and research findings in the lab are not visible. The question is always - What can it do (for society)?" [DR] responds "but this is like pressure to deliver on a promise that was made in the field, but now continues without the hype surrounding lab-on-a-chip in the 1990s". [LL] nods in agreement, "Indeed and it is failing. The medical point of care vision is not a problem for ongoing research in the laboratories. We do have some examples, such as the

lithium chip of Medimate, but the responsibility is on the spin outs and commercial sector".

[GP] picks up on this bilateral interaction on lab-on-a-chip and brings the discussion back to molecular machines. "We see similar strategies elsewhere, like the Lego movie, manipulating DNA and shown today in a playful way. It lightens up the subject, rather than being so serious about it. This was fantastic in 1998, not anymore. Lego put it away, no traces can be found. I guess for ethical reasons?" He looks around the room.

[MES], a post doctoral researcher at the University of Twente whose activities include engineering materials, "I am an outsider to nano and its images." She now looks at nanomechanical properties of single polymer chains. "We use macroscopic analysis but it can be limiting to your own thinking (not comparable). [DR] "It can be enabling as well as constraining?" [MES] "Actual underlying work is not visible. I'm not a physicist, so may have more problems, when this happens I go to the physicist who is my boss." [MES] sits back in her seat looking embarrassed about commenting.

[AP] "In my research [*as a philosopher*], a lot of nanoscientists present their work as linking up to nanomedicine applications, seems almost easy. But I think it limits the focus on important scientific problems. There is an assumption that you need to link up with applications to link up with general public's. One strategy could be to create informed publics." Nobody responds to this suggestion.

[LL] leaning forward in her chair asks the group "Why did nano make such a public impact, and microtech did not?"

[GP] "Images were not used so much 15 years ago. We didn't have the visualisation techniques (nor animations).

The chair asks [NP], a representative of the media who until this points has remained silent, "What do you think?" [NP] "La rechérche is friendly to nano. Our readers like science, so we don't emphasize bad sides." [AR] prompting the media representative further responds "I'm not so sure in France generally. There's a fear of nanotechnology (as [GP] says). If there is a fear, it is of chemistry?"

[NP] responds with a shrug of his shoulders, "I am skeptical about the promises of nanomachines and nano in general. There is a fundamental interest in novel ways of doing things with molecules which will lead in the end to new applications. Nano at the moment tries to have both, lots of applications and lots of hard work in

fundamental science needed. This is especially visible in molecular machines. You can' really have both together. Separate the two!"

[NP] continues "Metaphors can remain implicit. For example the May Issue of La Recherche [*The month previous to the workshop*], Un moteur un taille de molecule. It was a proposal of scientist X. He never mentioned this was in a liquid (+Brownian motion); this had to be made explicit. Also during our editing phase we cut out the too strong promises. We needed a nice picture on the first page. To attract the reader you can't always have "right" images. Although, personally, I wouldn't have included it myself".

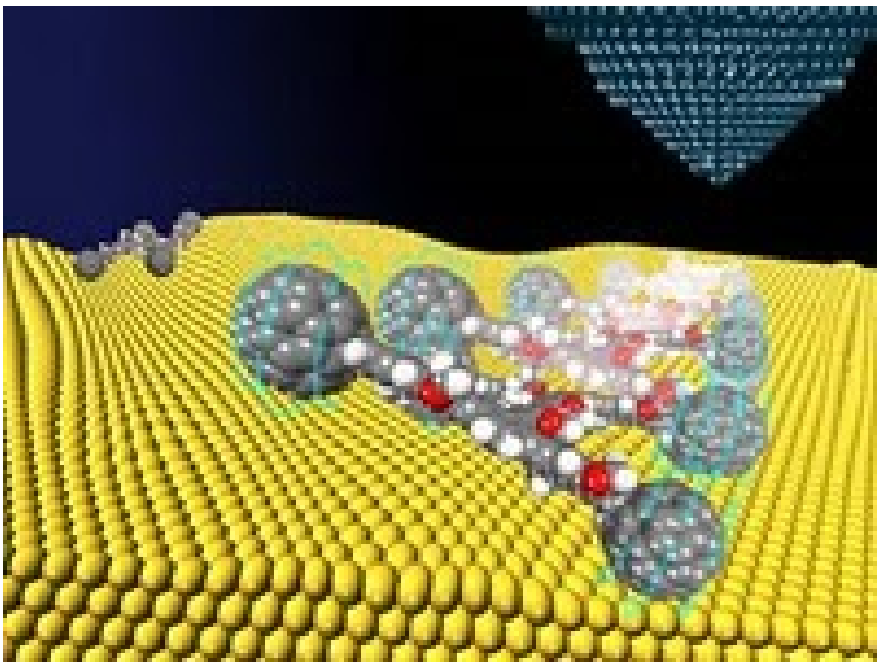


Figure 7: Image resembling the front cover picture [NP] refers to and showed in the meeting

"These are half-way pictures" says [AD]. [EV] mentions that in her opinion, the wheelbarrow work doesn't convey any real innovation. Is good science but not innovation. [NP] nods agreement.

[GP] elaborates a little on the wheelbarrow image. "This image [*of a wheelbarrow*] was presenting findings and was re-presented. There was similar work in Birmingham (UK) on a molecular wheelbarrow where they diffused their work in the press. The ECHO (a local newspaper) had an ugly picture of a wheelbarrow on purpose – linking the work with nanotoxicology"

[WP] a British citizen working in Paris "I read that article, wasn't frightened at all. Didn't think picture was ugly. Nanotoxicity didn't come to my mind at all. Just a

clearly written article. When I first saw the wheelbarrow (when I arrived in the group) I was shocked: it was too crude a picture."

[EV] a sociologist studying images of nanotechnology, continues to voice her opinion "My impressions are that the pictures and language used have a lot to do with control. There is no place for complexity or uncertainty. This was the same in biotechnology, it was presented as mechanistic manipulation. There, we see the limits of the linear paradigm. Should we discuss this for nanotechnology? I think we talk too quickly about concerns and fear with publics and too little about awareness."

[AR] adds to this "Or marvel, there are rhetorics of control – so a dichotomy" [EV] "Indeed, but why do you want public attention?" She asks the nanoscientists in the room. Nobody responds.

[MR] shifts the discussion back to the pictures La recherché, "There is an issue of attractiveness versus scientific correctness. You can have a stepwise presentation (cf. Christian on car). This image of the nanocar was produced by scientists X, and is now reproduced in many other contexts. Is this picture of the nanocar dominant because they made it attractive?"

[AD] "It is a survival technique – Legitimacy" [AP] "but the image is a lie, lots of things are missing!"

[DR] mentions in passing that the image looks like devices in space, like a moonlander. There is a general mumbling of agreement and nodding of heads.

[AP] still concerned about the deceptiveness of the image "This image misleads about what a machine is. Andrew's pictures focussed on operative principles and discoveries, not it's utility. When it does not function, it is occasion for further discovery. New options yes, but not application driven (is this a third type of research between fundamental and applied)?"

[AD] with body language signalling exasperation "It is to fuel hype so get more money... and it is a successful strategy. [GP] recognises this." [*A jibe at [JC] once again but elicits no response].*

[WP] "The difficulty is that we scientists have (and this is visible at the end of scenario 2 in the prep material) a long-term speculative approach as opposed to short-term concrete ones. So these images are halfway between an STM image and a real car (in movies) which signals some sort of innovation. As scientists we have to be careful because it hides a lot of what is there, as [NP] mentioned. In the

nanocar, the wheels actually don't turn around they flop around like teddy bears strapped to the chassis"

[AD] "Aaah, but remember legitimacy comes not from press, but from public attention." "and it works" says [WP] "Scientist X gets millions for his nanocar"

[LL] "All the same, Lab-on-a-chip actually meant something. A current vision in my lab, Lab-in-a-cell is confusing, just as molecular machine is confusing"

[AR] "There is an essence of control imagery – you need to control the messiness": control imagery (control the messiness). [WP] "Our objective is to control. I did simplify the complexity when I created my own images, but was also partly a lack of understanding."

[LL] "In biology one accepts the lack of full control."

The secretary pops her head in and cajoles [GP] to get everyone moving to have lunch.

Lunch

The lunch was a very nice affair but lasted longer than planned. The CTA organizers had no control over this, it was organized by CEMES and after all, the day was not purely for the CTA project. The service was of three courses, and took time, so that everybody had to wait until the final serving of the last course was available. Many drank wine. This long lunch, although pleasant reduced the time available for the workshop. In addition, many of the CEMES people who attended the morning session had another meeting planned in the afternoon. This was only visible upon returning to the workshop room, where approximately 10 of the participants vanished. [GP] mentioned that there was another meeting.

Post lunch stretch

The session began slowly, the large dinner, wine, and the long break had a soporific effect on the group. The chair began the session by introducing the scenarios. [AR] "Let's look at the scenarios. Scenario three show molecular machine developments as small steps only (not too much development pulled along by large speculations). Let's start with [LL]", [AR] beckons to [LL] to comment.

[LL] "The interdisciplinary aspect is very important (especially at the nano scale) "molecular city" helps there in locating entrance points for different disciplines in a collective effort. How can we trigger events? The molecular shuttle comes in there but how does it move? Where is the sound, light?"

[DR] the author of this scenario feels he should comment "These factors weren't made explicit, but the shuttle was a form of molecular communication (has already been discussed today) here they go for promise visions rather than technical feasibility."

[AD] "The *Nanoscapes* scenario is most positive on molecular machines" [LL] nods her head, "yes, it reduces complexity but in order to support understanding"

[AP] comes in with his reading of the scenarios "There are three distinct uses of images in each particular scenario. In scenario 1 there is a global reference to molecular city (it is Drexler's vision really including cybernetics and communication). In scenario 3 scientific images are foregrounded and in scenario 2: there is little on the role of images per se but of other representations of visionary hype and grey goo.

[MES] a research scientist prefers scenario 3 "It seems more solid. Scenario 1 is too crazy!" [EV] responds to that remark "Scenario 1 goes with market I think? But also with the playfulness of the video game. The notion of a *Molecular City* unifies the field – but may pass away as a metaphor and then discipline will disunify."

[AD] "Dominant views are to be seen in popular science. These are worked on because of the fundamental nature of creating a toy, playfulness is part of science". [EV] "Indeed, grey goo is another unifying picture"

[AP] "Second life is also a manipulation". [NP] shakes his head and asks the group "But why would anybody else but nerds want to play nano Sim city?"

[MES] "Generally visions can be created from outside the nano world, for example the images of nanobots circulating in the blood, repairing"

[AD] "This image is similar to viruses, halfway between life and machine"

[LL] "If we showed the reality, these images circulate, and have a life of their own."

[GP] "Yes but they have a finite lifetime." [LL] "Maybe, but they can persist, for example the image of lab-on-a-chip (the equipment on the palm of a hand) has circulated for more than 10 years and is still powerful today"

[AP] "There is more freedom in artist impressions, more meaning can be put in. In reality there is less freedom. In the Nanoscapes scenario reality and the imaginary

is mixed/confused, as happens in the real world." [EV] "Scientists can profit from the confusion"

[GP] comments on his groups drawings for a TV programme. "These are outside sphere of influence, so not the responsibility of us nanoscientists" [AD] and others retort "But they have effects!"

[MR] builds on collective disagreement "There is a role and responsibility of actors, how they circulate and propagate images, especially journalists and the media". [NP] "If too far away from reality it will be counterproductive. If you do fundamental science, far removed from any application you still think about it because of prudence/GM example

[GP] "For the first time in history we get negative feedback before we actually achieve something."

With that final comment the secretary pops in her head again and mentions that coffee is ready. The chair thanks the participants and the meeting adjourns for coffee (some participants continue to the technical meeting).

3.3 Summary table

Actual composition	11 Senior Researchers, 2 junior researchers, 3 organisers, 1media representative, 1 sociologist, 1 philosophy of technology scholar.
Degree of heterogeneity	Mostly enactors from CEMES
Last minute cancellations of participation and its impact.	No, but a last minute additions of 2 junior researchers and some senior researchers
Stretches in the discussions Organiser initiated and taken up = O+ Organiser initiated not taken up = O- Participants initiated and taken up = P+ Participant initiated not taken up = P-	The setup of the workshop was somewhat different. There were two technical presentations and two small CTA sessions, one either side of lunch. O+/O+/P+
Explicit reference and use of the scenarios	Yes – In stretch 1 {AJM] refers to scenario 2 drawing on it in his discussion. In the stretch directly after lunch, after a suggestion by [AR] to discuss the scenarios there is a lot of discussion between many

	participants. In this situation the previous "guests" quizzing "hosts" dynamic disappears as the scenarios become the focus (a curiosity for all participants)
Implicit reference and use of the scenarios	The many explicit references and the shortness of time for the CTA meant little if any implicit references.
Quizzing between homogenous actor group (or with those who knew each other prior to the workshop)	Yes. In the presentation and between the "guest" research participants and CEMES
Asymmetric probing of the majority group (perceived as experts)	Yes. There was little quizzing or probing of non-enactors.
Mutual probing in heterogeneous group	There was no dominating group. However [KM] a representative of a large multi-national medical device manufacturer did speak often on the behalf of large firms.
Do participants get into broader aspects or do they recourse back to their usual positions.	Yes. They try to make sense of the circulation, uptake and (re)representations of images.

Appendix 4 - Responsible research and innovation as part of nanotechnology governance

1 Starting Conditions

1.1 Preparation through insertion and analysis

The occasion for this project came directly from my insertion in the nano-world, where I attempted to disaggregate the nanotechnology umbrella term and explore the dynamics. It was clear that at the macro-level, governance of new and emerging nanotechnologies had become a highly visible debate, disagreements on efficacy of current governance arrangements were proliferating, new alliances were being (or were in the process of being) formed to shape possible new configurations of roles and responsibilities in the development of nanotechnology. Inclusion of Environmental, Health and Safety aspects (EHS) in technological developments at an early stage seemed to be stabilising.

Multi-level dynamics were also visible in the coupled evolution of nano-particles (research and production and use) and risks of nanotechnology. The repeated occurrences and acceptance of acronyms such as ELSA (Ethical, Legal, Social Aspects) and EHS in discourse on, and governance of, nanotechnology research and in the mobilisation of resources, indicates emerging alignment between societal concerns and allocation of resources.

Actors such as governmental agencies, industry and NGOs were increasingly being held accountable for addressing societal concerns – a new emerging rule within this multi level process. Over time, the rules of the game might change into: you should not only (promise to) take EHS and ELSA into account, but also incorporate them into your research and thus live up to your promises

It was with these observations that a concept for a workshop on these multi-level shifts in governance arrangements began to emerge. The force of EHS (up to the use of just the acronym) is itself the outcome of what one could call an emerging and stabilised path, now at the meso/macro levels.

Therefore the force of EHS at various levels was the starting point for the development of a workshop concept beginning in the 2nd annual meeting of the Frontiers network in Sicily, where I proposed a rough outline of a project exploring potential implications for research and spin offs of EHS and broader societal issues, linking up with the debate at the macro-level of governance approaches

In 2nd annual meeting in Sicily, during my presentation in the public part of the event (as opposed to the management meeting the day previous) I proposed that 4 more CTA projects should be undertaken over the next 2 years. During the management meeting the day before I proposed this idea in a presentation and during the coffee breaks where I mingled with the partner institution representatives and began gauging what topics were "hot" and interesting for them. This was done in order to shape my hypothesised programme of 4 CTAs.

With cocktails later that evening, along with Martin Ruivenkamp from the TA-NanoNed programme, I discussed the issues of toxicity with the heads of the Frontiers Partner institutions. Martin who hadn't had much experience of insertion in the nano-world up until this point was surprised to find that the research group leaders had limited knowledge about many of the debates and meetings that were so visible in our world of science and technology studies of nanotechnology. Martin and I decided to probe into this further by discussing the International Risk Governance Councils report (released a couple of months earlier). We also brought the discussion around to the ETC-group and their Nano label competition that was running at the time of the meeting. The research group leaders were absolutely oblivious to these initiatives. I probed a little bit further and proposed the general idea of a workshop on "risk governance" a term that was being used by IRGC and others during that time. The Frontiers partners thought risk discussions generally may be interesting because of the Drexler scares "people are scared of grey goo". When Martin asked "What about toxicity and regulation?" One of the researchers, chuckling, held up his glass of Orangeade and said "I'm drinking nanoparticles now... the colourants in this glass are nanoscale. Nano is not new." There was some low-level chuckling from the group of research scientists.

Martin and I could see all these shifts in the risk governance discussions, but even at the research coordination level, this gaggle of research group leaders did not seem to be aware of these debates – perhaps they were not receiving the signals? Or perhaps not tuned in to receiving them? In our discussion, over more cocktails, Martin and I considered why this group of researchers were oblivious to these issues. We concluded that it is part of our practices of insertion; we are free to move around different arenas and at multiple levels and see various dynamics and actor strategies in different contexts.

The following day, my presentation proposing a risk governance based CTA project was greeted with enthusiasm by the technology transfer experts and start-up companies in the room, but the researchers seemed indifferent. Building on the

enthusiasm of "commercial" participants I began to construct a CTA workshop concept based on the preliminary diagnosis given above.

The first workshop concept

During the period from November 2006 to March 2007 I developed a workshop concept and an invitation. At this point there was no confirmation of finance for the workshop, although there was still interest from the Technology Transfer experts, in particular CeNTech, based in Muenster, Germany. To reduce spending, the Frontiers director suggested that I hold the workshop as an extra part of the Frontiers Scientific meeting (a science focused meeting to be held May 9th -11th 2007 in Toulouse). The agreement came on the 1st April, and since Frontiers members automatically could have the costs covered for the scientific meeting, I did not have to wait for the go ahead for financing. I had 5 weeks to gather participants and develop the preparatory material for the target date of 9th May in Toulouse. The essence of the project can be seen in the extract from the invitation which I circulated, see box below.

Because of the limited time, and the connection with the Frontiers scientific meeting, I decided to create a workshop for Frontiers members only, so it would be an enactor based workshop probing multilevel dynamics via a concentric perspective. I proceeded on an active invitation campaign. However, by the end of April I only had two participants, the enthusiastic representative of CeNTech and the official Ethics workpackage leader from Cambridge. I had to cancel the workshop, but attended the scientific meeting anyway (as described in Appendix 3 for the creation of the CTA workshop on molecular machines). The scientific meeting itself was poorly attended, and in a number interactions with different participants the general idea was of workshop fatigue (too many meetings away from core activities). It was difficult to get a measure whether workshop fatigue or lack of relevance for the Frontiers network partners was the reason for lack of participation in my CTA workshop. In interviews I received comments such as: *The workshop topic was interesting but I was too busy*.

In autumn 2007 there was an increasing emphasis on societal embedment of nanotechnology applications, which provided a window of opportunity to relaunch this CTA workshop. At the 3rd Annual meeting in October 2007, held in Leuven, Belgium, I presented a new concept for the workshop based on the proliferation of calls for input into codes of conduct, for regulation, for precautionary principle to be put into practice.

The Frontiers Technology Assessment Programme would like to invite members of Frontiers partner institutes to take part in their foresight project on prospecting the nanotechnology risk debate beyond nanotoxicity. Current risk and responsibility debates around nano S&T across science, industry, government and societal domains has focused on toxicity and environmental hazards that could be the consequence of natural and artificial nanomaterials. As research moves from interesting nanomaterials to functional systems and devices, we predict that the risk and responsibility debate will broaden beyond toxicity once again and return to the impact and risks of nanotechnology devices and applications. Thus, the current focus on the technical and safety aspects of nanomaterials will broaden once again to the societal, economic, regulatory and ethical aspects of nanodevices and applications.

With the recent EU push for responsible innovation in its action plan, the recently launched 7th Framework Programme and a growing recognition of the potential benefits and risks of nano enabled technologies – we predict a renewed scrutiny of R&D in nanoscience and nanotechnology which will influence all nanotechnology actors – including natural and applied scientists!

This project takes this prediction as an occasion to explore ways that the Frontiers research community can be proactive in entering the new risk debate of nanotechnology (rather than being drawn into it and being placed into a position rather than choosing it). We will investigate the possible new roles and responsibilities related to nanotechnology and risks and develop and evaluate possible strategies for action on the part of the research community.

Figure 1: Extract of the invitation to the May 7th Risk workshop (which was cancelled)

Taking as the entrance point the emphasis, at the time, on societal impact and embedment of nanotechnology applications, the general acceptance of potential environmental and health risks of nanomaterials and the call for nano codes of conduct during the situation of a regulation vacuum, I presented "Responsible Research & Innovation" as something that could become locked into the very substance of nanotechnology R&D and shape its eventual uptake and embedment into society.

The notion of "Responsible Research and Innovation" (RRI) was my own term capturing the thrust of responsible development of nanotechnology in research and in the translation of that research into societally embedded applications.

I proposed in the meeting that:

> "responsible research & innovation could be read in two ways. One with an emphasis on innovation, which requires some responsibility to be successful/acceptable, or another with an emphasis on responsible up to and including halting developments along particular R&D lines."

In the presentations of the proposed workshop[136], I said that researchers (in Frontiers and elsewhere) and other actors in and around the nano-world are concerned about hype, about pressures towards valorisation of research as well as lack of uptake in sectors that could profit from the possibilities offered by nanoscience and technologies. I also mentioned that there is uncertainty about impacts and risks, while proposals for regulation are formulated and various NGOs take positions, often advocating a precautionary approach up to a moratorium (cf. ETC-Group and others). And there is additional uncertainty about consumer and citizen reactions to new nanotechnology-enabled products and processes – fears of a public backlash and of barriers to public acceptance.

I described that,

> "the main issue, particularly from the side of researchers and research organisations like the Frontiers Network of Excellence, was what can be done and should be done? At the very least, developments in RRI could be understood better, and be taken into account in strategic decisions. And in this way a CTA workshop would be advantageous and could be regarded as a minimal level of 'responsible' research and innovation."[137]

The general thrust of my presentations, which was picked up through the discussions I had afterwards, was that the notion of responsibility is now encompassing and affecting research, hence the term RRI and the need to understand it better, so that Frontiers could participate in a more informed manner. This would require the bringing together of actors outside of the network which are involved in shaping the elements of RRI and/or would be affected by it.

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[136] Both in the annual management meeting (at this point I was coordinating and running Workpackage 8 on Ethics and Societal Aspects on behalf of Cambridge, even though my position was not formal. This included the presentation to the whole network in the main meeting and so I had become the point of contact for the ELSA workpackage.

[137] I also mentioned that in fact, there is external pressure to do such explorations, with the inclusion of (still undefined) requirements for "responsible innovation" and "inclusion of societal impact assessments" in EU and US science policy as well as in statements [by organisations such as insurance companies and NGOs.

It was agreed as a good topic by the new director of the Frontiers Network, Vinod Subramaniam and the manager Rolf Vermeij.

The entrance point for this CTA was to explore plausible evolutions of the present situation and probe the various visions and proposals put forward for the implementation of responsible research and innovation by various stakeholders. The phrase that I created 'responsible research and innovation' was coined as an encompassing term referring to activities in which social aspects, desirability and acceptability are taken into account. Ideas of responsible development of nanotechnology had been in circulation for a while, but only by the time that the 3rd Frontiers annual meeting was held were they solidifying into policy and regulation. Through the various levels of insertion, in Frontiers, in Nano2life, in EC meetings, in social science circles, this trend was visible to me but it seemed that only weak signals were reaching the researcher on the laboratory floor. In the management meeting, coinciding with the 3rd annual meeting in Leuven, it was clear that a number of the research group leaders, especially those involved in activities such as the ETP-Nanomedicine, were aware of the EC code for responsible development of nanotechnology.[138]

Therefore if RRI would become an integral part of R&D, technology developers could be asked by societal actors to account for what they do, and in this way responsible innovation would be the responsibility of technology developers, in interaction with various societal actors. It was on this basis that the workshop was locked down: exploring the possible elements of RRI, based around different positions and stances on what RRI could entail, and how different mixes of these elements would shape the development of nanotechnologies (and those involved in development of nanotechnology).

Below two summary tables are presented. The first present's seven criteria that were used to both determine the starting concept of the CTA-project and its suitability for the various interested parties involved. The second table shows the

[138] More broadly that the EU code of conduct there were also others: the principles for the oversight of nanotechnology 2007 (Greenpeace, Friends of the Earth and others) and codes of conduct (BASF, European Nanotechnology Trade Alliance, the Nano Industries Association and others), there was almost a convergence of various actors around this terms such as "responsible development" (confirmed by the meeting held in the European Commission on December 5th).

contingencies that where an outcome of the negotiation of the project concept, the context of the subject, my degree of control over the shape of the project etc.

1.2 Summary tables

Key elements that contributed to the initial idea for the CTA.	The notion of responsible development of nanotechnology was emerging in risk assessment, governmental and non-governmental organisation circles as well as around some prudent industrial actors and associations (anticipating on a consumer backlash if appropriate measures to limit risk were not taken at early stages). At this time, toxicity was become stabilised as a major societal issue to handle around nanotechnology, whereas other elements were being discussed as well, relating to the application of nanotechnology to products and services.
Is it interesting for my study of inserted CTA targeted at broadening enactor's perspectives?	This workshop topic explores directly the pressures on enactors to become involved in the co-evolution of nanotechnology and society at early stages. How this manifests and how enactors engage in this co-evolution is the question. At the outset, it seemed the researchers in Frontiers felt some distant expectation that they should engage, but no pressure to pick up responsible development, at least at the start of the CTA concept development.
Frontiers partner interests?	**Key negotiation actors:** Frontiers management team Those partners closer to industry found it relevant, those closer to fundamental research found it intriguing but not directly relevant.
Stage of development of the field?	The term Responsible Research and Innovation, that I constructed as an encompassing term of the various governance elements being discussed at the time was at a turning point, or seemingly so. With many soft law options arriving on the table (for example in a well attended symposium in Brussels on 5th December 2007) there was a lot of activity and debate around options. There were dissatisfactions about the speed of regulatory development, and an emphasis on the precautionary principle from many NGOs, up to a moratorium.
An identifiable community or socio-technical network?	Not applicable
Is there something at stake recognisable to some of the actors in the emerging community or socio-technical network?	Yes a lot at stake, the governance configuration and entanglements was in a fluid state at the time of the workshop, but could very easily become locked in. In the invitation texts I proposed that Frontiers researchers would better be engaged and shape what will in time shape their activities before it does get locked in.
Amount of material to	Very rich. Especially in Autumn/Winter 2007 when many different actors and communities were putting forward different governance options in and

work with? *(as perceived during the early stages of the CTA project development)*	around the notion of responsible development of nanotechnology.

Table 1: Identifying and negotiating an area to apply CTA to

Requirements and constraints from the Frontiers network	The Frontiers management team, who had by this time had become very involved in EC activities, events and calls for proposals for nanotechnology projects, found the topic very relevant . There was recognition that the topic of the workshop could not be covered by Frontiers partners alone and thus there was less of a restriction on the people I could invite.
Level of control over the topic and process by CTA organiser	Full control over the topic.
Amount of time to prepare the project	7 weeks.
Gathering participants	Comparatively easy. Everyone invited agreed to come (except those with other engagements). The diversity of participants reflected the interest in the field.
Possibility to interview participants	No real opportunity to interview the majority of participants, because of their schedules (most external participants were in positions of high authority in their organisation). So email correspondence only.
Available document data	There was a lot of information available, especially close to the time of the workshop as reports on soft law, on codes of conduct and studies of gaps in regulation were being published.

Table 2: Contingencies and ramifications

2 Preparation

In the following section I give a brief history of the emergence of the notion of responsible research and innovation (RRI) in relation to nanotechnology.

2.1 Anticipation amidst a changing governance arrangement

During the early days of nanotechnology, nano promises were dominated by visions of molecular manufacture as total control at the nanoscale. Concerns on the speculative nature were voiced from much of the research community but remained as mutterings as slowly the focussed finances rose. Debate whether molecular manufacture was feasible was mentioned but was not picked up and promises of nanotechnology were abound. The Clinton administration began the preparations for the National Nanotechnology Initiative (NNI). An article in Wired magazine sparked a debate about nanotechnology ("Why the future doesn't need us" – Bill Joy 2000) and became referred to as representative of concerns of nanotechnology and control.

Self-replication and control became a key focus in the discussions. After the launch of the US National Nanotechnology Initiative in 2000, a series of NNI meetings on the societal implications of nanotechnology were held and a number of issues began to dominate the discussion. The grey goo term began to be used as a banner for self-replication issues, and became widely referred to (name some elements). In addition, the lack of ***control <u>of</u>*** the nanoscale became embodied in discussions on arms race (Altmann 2002) and nano divide (between industrialised and developing nations (Rocco and Bainbridge 2001). National and European nanotechnology initiatives began to emerge.

In 2003 issues of RRI were emerging on a number of fronts. Bioethicists began to call for inclusion of ELSA issues in nanotechnology R&D ("Mind the Gap", Mnyusiwalla et al. 2003). Meetings such as the International Dialogue on Responsible Innovation 1st Meeting 2003 were being organised by the US and EU.

Control <u>at</u> the nanoscale (understanding new properties from manipulating the nanoscale) became the object of specific actors in the toxicology community and NGOs (CBEN and ETC-group). 2003 ended in the Smalley/Drexler debate December 2003 - where Smalley (a renowned nanoscientist) questioned the scientific basis of molecular manufacture (thick and sticky fingers issue) and outright rejected grey goo. Other actors began to argue against the scientific basis of grey goo (such as Lord Sainsbury of UK).

When the issue of health and environmental risks of nano-particles was raised, and further highlighted by the NGO the ETC Group (2003), the immediate response

was negation, and anger at the ETC proposal for a moratorium on nanoparticles. In a news feature article in *Nature*, it was noted that 'the debate is clearly gathering pace', while 'some researchers (..) feel that they don't need to join in the argument: "They don't really see what the hoop-la is about" (Brumfiel 2003, p. 247).

Inputs from toxicologists and epidemiologists (and scientists like Vicky Colvin of CBEN) introduced some moderation, but the gut reaction remained. It was not legitimate to seriously discuss such risks, because that would only create a roadblock.

By the time the (so-called) Royal Society Report appeared in July 2004,[139] with its message to be cautious with introduction of nanoparticles in the environment because of the knowledge gaps about health and environmental impacts, it had become more difficult to just claim that nanoparticles were no cause for concern. The balance shifted, irreversibly, after the appearance of re-insurer Swiss Re's report in April 2004. Discussing (and researching) risks of nanoparticles then became fully legitimate. One irony, played upon by ETC Group and Swiss Re alike, was "size matters": if the small size is what gives nanoparticles their interesting properties, these same size-dependent properties can also create harm.

By the end of 2004 there were an increasing number of reports on nanoparticle specific toxicity issues in the scientific peer-reviewed journals. A number of programmes and symposia were launched for toxicity of nanoparticles. The 1st symposium on Nano and occupational health was held by NIOSH (US) and HES (UK) followed by the launch of the International Council for Nanotechnology (ICON) coordinated from Rice University. More broad programmes on Nano and societal aspects were seen at the Woodrow Wilson Centre for Scholars and the Dutch nanotechnology initiative Technology Assessment programme (TA-NanoNed).

[139] In 2003 the UK government approached the Royal Society and the Royal Academy of Engineering to conduct a joint inquiry into the health and safety, environmental, ethical and societal implications, and other possible uncertainties of nanotechnologies. The report "Nanoscience and Nanotechnologies: Opportunities and Uncertainties" was published in 2004.

Consolidation around HES/Institutionalisation (2005/2006)

In response to the Royal Society recommendations, a number of nano-engagement exercises were initiated. The Cambridge Nanoscience Centre, in collaboration with the University of Newcastle, Greenpeace and the Guardian Newspaper organized Nano Jury UK in the summer of 2005, held a citizens jury on nanotechnology over a period of six weeks in Halifax, North of England. Following this, the British Government launched its "Programme for Public Engagement on Nanotechnologies". The European project Nanologue an 18-month European Commission-funded project designed to support dialogue on the social, ethical and legal implications of nanoscience and nanotechnologies. Although having different remits, targeted at different publics, and leading to different forms of outcomes, the projects did receive some attention but it is unclear how they have affected nanotechnology policy.

In a meeting run by The Innovation Society, Swiss Re proposed risk dialogue and self-regulation as the solution with adaptation of governmental laws only desirable for longer term issues. At the same time the Magic Nano incident, fuelled discussions on Nanotoxicity. There are renewed calls for moratoria from ETC group and from Friends of the Earth (the latter on commercial release of Nanomaterials in personal care products and cosmetics). The immediate effects of this lock-in were two-fold: more risk research was done, and regulatory agencies start moving (one question is whether existing regulation can be used to address the issues of nanotechnology). That created a focus, almost a lock-in, on HES issues (cf. also recent activities of OECD), and backgrounding of broader questions about the actual use of nanotubes, and nanoparticles in general.

In parallel, firms started to have second thoughts about flagging nano for their products. If something untoward would happen under the label nanotechnology that might then also reflect on their products, even if there was no cause for concern. Some firms stepped out of the nanomaterial business altogether, others proceeded, but more prudently.

Also in the UK, this has led to a *de facto* alliance between firms and the regulatory agency DEFRA (Department for Environment, Food and Rural Affairs), where DEFRA is experimenting with voluntary reporting ('soft law'). In other countries, regulatory authorities are still considering what to do, or, as in the USA, need to show that they do something because of criticisms levelled at them.

The notion of 'responsible innovation' is in the air, in documents of the European Commission, and now also in the US, as in the proposal for a Nanotechnology Advancement and New Opportunities (NANO) Act by Rep. Honda (D-San Jose).

"The NANO Act requires the development of a nanotechnology research strategy that establishes research priorities for the federal government and industry that will ensure the development and responsible stewardship of nanotechnology."

Governance mixes and the rise of soft law: Spring 2007 – Winter 2007

In the meantime Risk governance landscape continues to evolve. September saw the launch of number of initiatives. Soft law is a major part of risk governance. When the EC code consultation is launched, EC funded Frontiers would be affected by such a code and thus being aware (and perhaps shaping this code is developed.

There is now also increasing reference to 'responsible innovation' in government documents (particularly of the European Commission) and some industry statements. While this may invite nano-promotors to consider broader issues, and allow other actors to raise questions about directions of development, 'responsible innovation' is presently operationalised as transparency and some public engagement. And in the case of industry, as a responsibility for safe handling of nano-production and nano-products.[140] The recent (September 2007) initiative toward a 'Responsible Nanotechnologies Code', led by the UK Royal Society, an NGO (Insight Investment), the Nanotechnology Industries Association, and supported by a network organised by the UK Department of Trade and Industry,[141] is much broader, but it is not clear if and how it will be taken up.

By the end of 2007 the situation involves mostly discussion of HES and other nanotoxicity related discussions, in addition, a call for standards in definitions. In addition actors such as governmental agencies, industry and NGOs are increasingly held accountable for addressing societal concerns. The increase in accountability may mean that, over time, the rules of the game might change into: you should not only (promise to) take HES and ELSA into account, but also incorporate them into your research and thus live up to your promises.

This is particularly pertinent for the number of soft law proposals in circulation at the end of 2007. December 5th in Brussels saw the meeting of three major efforts in defining soft law guidelines, the EU code of conduct for nano research, the UK

[140] Degussa's website on nanotechnology has an item to this extent on responsibility (www.degussa-nano.com/nano), and BASF's Code of Conduct has a similar thrust.

[141] See www.responsiblenanocode.org.

Responsible Nano Code Initiative and the Principles of Oversight. To end the timeline we outline (very briefly) the three proposals.

The EU has proposed a code of conduct for responsible nanosciences and nanotechnologies targeted specifically at research:

"In order to promote safe and responsible nanotechnology research and pave the way to its safe and responsible application and use, the European Commission is planning to adopt a voluntary Code of Conduct for Responsible Nanosciences and Nanotechnologies Research ("the Code of Conduct"). This Code of Conduct would take the form of a European Recommendation and would invite the Member States, industry, universities, funding organisations, researchers and other interested parties to follow its principles. The Commission itself would follow these principles in its own action under the Community research policy…The Code of Conduct would offer those following it recognition of a responsible approach towards nanosciences and nanotechnologies research, making their actions more visible at a European Level."

Another group, comprising the Royal Society, Insight Invest, the Nanotechnology Industries Association (and others) proposed a principles-based Code of Conduct that may be adopted by businesses and research institutions involved in developing, manufacturing and retailing products using nanotechnologies.

"Like other principles-based codes, it will illustrate expected behaviours and processes, not standards of performance. Indicators of compliance could be developed at a later stage. The Code is not intended, however, to be an auditable standard, it will not detail levels of performance expected of companies, nor will it give guidance on definitions, characterisation and measurement. … The Responsible Nano Code aims to stimulate organisations to consider all aspects of their involvement with nanotechnologies, including the broader social and ethical issues."

In addition, a broad coalition of civil society, public interest, environmental and labour organisations have created the "Principles for the Oversight of Nanotechnologies and Nanomaterials." The document declares eight fundamental principles that they propose must provide the foundation for adequate and effective oversight and assessment of the emerging field of nanotechnology, including those nanomaterials that are already in widespread commercial use.

The three codes although originating from different areas (Policy makers, Industry/Investment community and NGOs respectively) and targeted at different actors (Researchers, Industry, and the whole innovation chain respectively) they

had many parallels, albeit with a differing breadth and scope. December sees additions to the codes with reporting to take place in Spring 2008.

2.2 Preliminary diagnosis

Reviewing the history of RRI, figure 4 shows some of the key elements that are important for the history for RRI emergence.[142] Figure 5 shows some of the elements of the evolution of RRI.[143] We can see the importance of "new actors" in the shaping of emerging governance patterns and industry structure, of NGOs such as the ETC-Group, and of re-insurance companies shaping the emerging path of RRI. Dynamics are visible at all three levels (although there is little alignment yet) in the coupled evolution of nano-particles (research and production and use) and risks of nanotechnology. The repeated occurrences and acceptance of acronyms such as ELSA (Ethical, Legal, Social Aspects) and HES (Health, Environmental, Safety) in discourse on, and governance of, nanotechnology research and in the mobilisation of funding, indicates emerging alignment between societal concerns & allocation of resources.

What was clear at the time of the workshop was that there is an opening for consideration of soft law due to actors (firms in the main) anticipating (and thus proceeding with caution) and also that regulators recognise that there are openings but are unclear on how to target nano broadly beyond the current focus on nanoparticles[144]. Firms are reluctant to start reporting, the DEFRA voluntary reporting initiative was mentioned as having limitations – but there are voluntary initiatives in development and new ways of managing them e.g. the Risk Framework for Nanotechnology put forward by the alliance of DuPont and Environmental Defense. Also there are specific nano codes of conduct (such as the one formulated by BASF to broaden its corporate responsibility programme to

[142] For a more detailed description, see Rip and van Amerom 2009

[143] I have placed innovation journeys at the micro-level, technology developer coordination attempts at the meso-level and selector coordination and control at the macro-level. This is for ease of showing linkages and emerging entanglements across levels. Conceptual development of this multi-level perspective has also been given in the CTA project on siRNA delivery and so will not be repeated here.

[144] Emphasised in a meeting at the European Commission DG Research on Nano codes. Mayer Brown. (2007) Minutes of 'Debate on Governance Initiatives for the European Nanotechnology Community in the Public and Private Sectors' European Commission, Brussels. 5th December 2007

include societal aspects. The European Commission proposed to circulate its Code to Member States.

Certain elements give indications of endogenous futures. Figure 5 shows a potential lock in around RRI in the focus on EHS issues. This would have consequences for other elements as resources are shifted away from them (path dynamics). Engagement with various publics is on the agenda (UK government initiatives, and elsewhere) but have been ad-hoc and mainly centred around technology developer outreach programmes (there are some exceptions but these are again ad-hoc). What would happen if engagement was integrated more thoroughly in the evolving socio-technical entanglement?[145] Also, there is something like a regulation void, and commentators have suggested that the soft law initiatives and voluntary codes occur exactly because of this void. Others (like the Commission of the European Communities) argue that there is no real void, because existing law and regulation is sufficient, at least for the time being. Still others see a void, but welcome the opportunity for experimentation and learning.

[145] This was explored in one of the scenario the scenarios. In that scenario, a platform for communication in the form of a NanoDiaBlog was taken up by many stakeholders and became a forum for assessing technologies, exchanging opinions and in the end shaping policy.

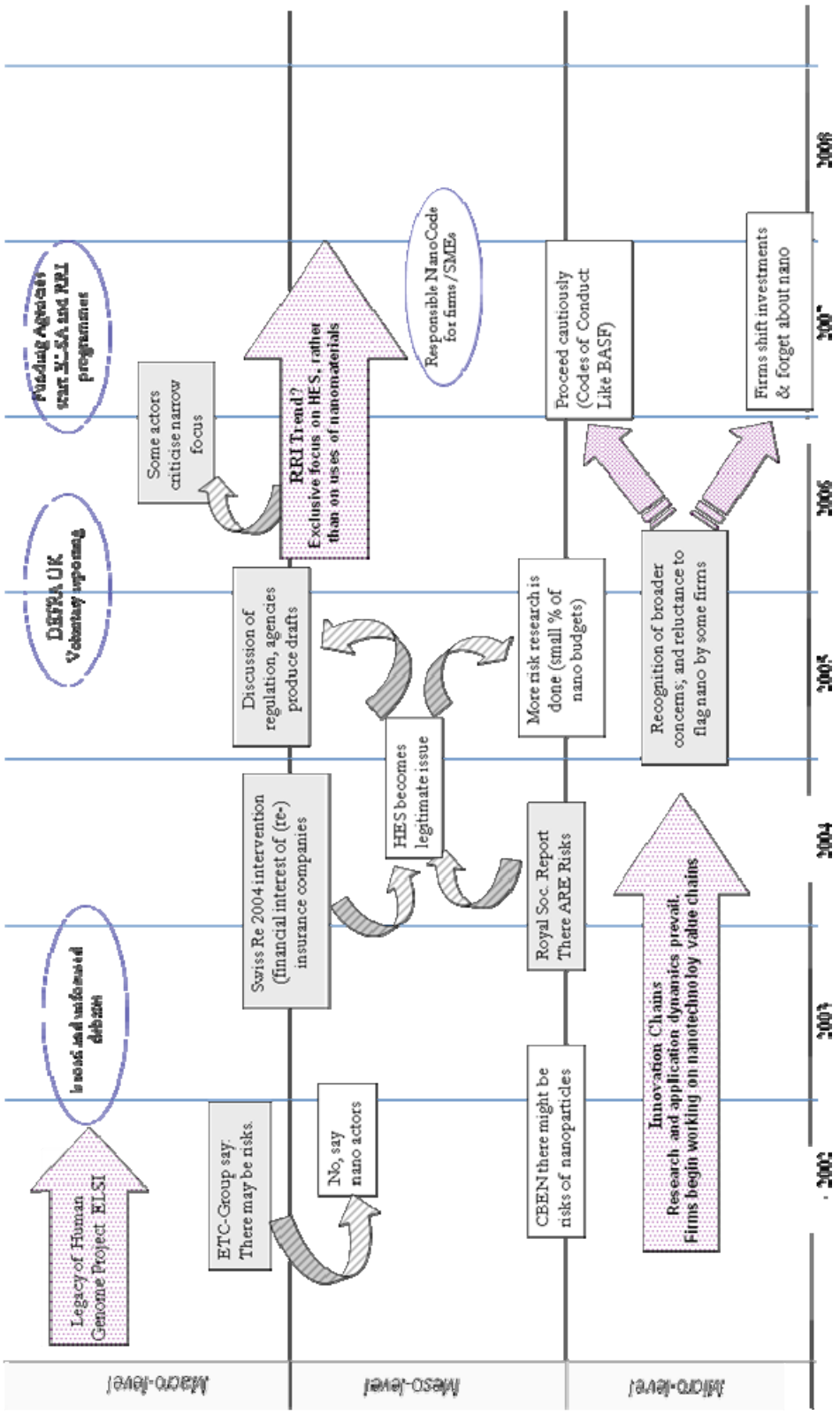

Figure 2: Dynamics of governance, 2000-2008

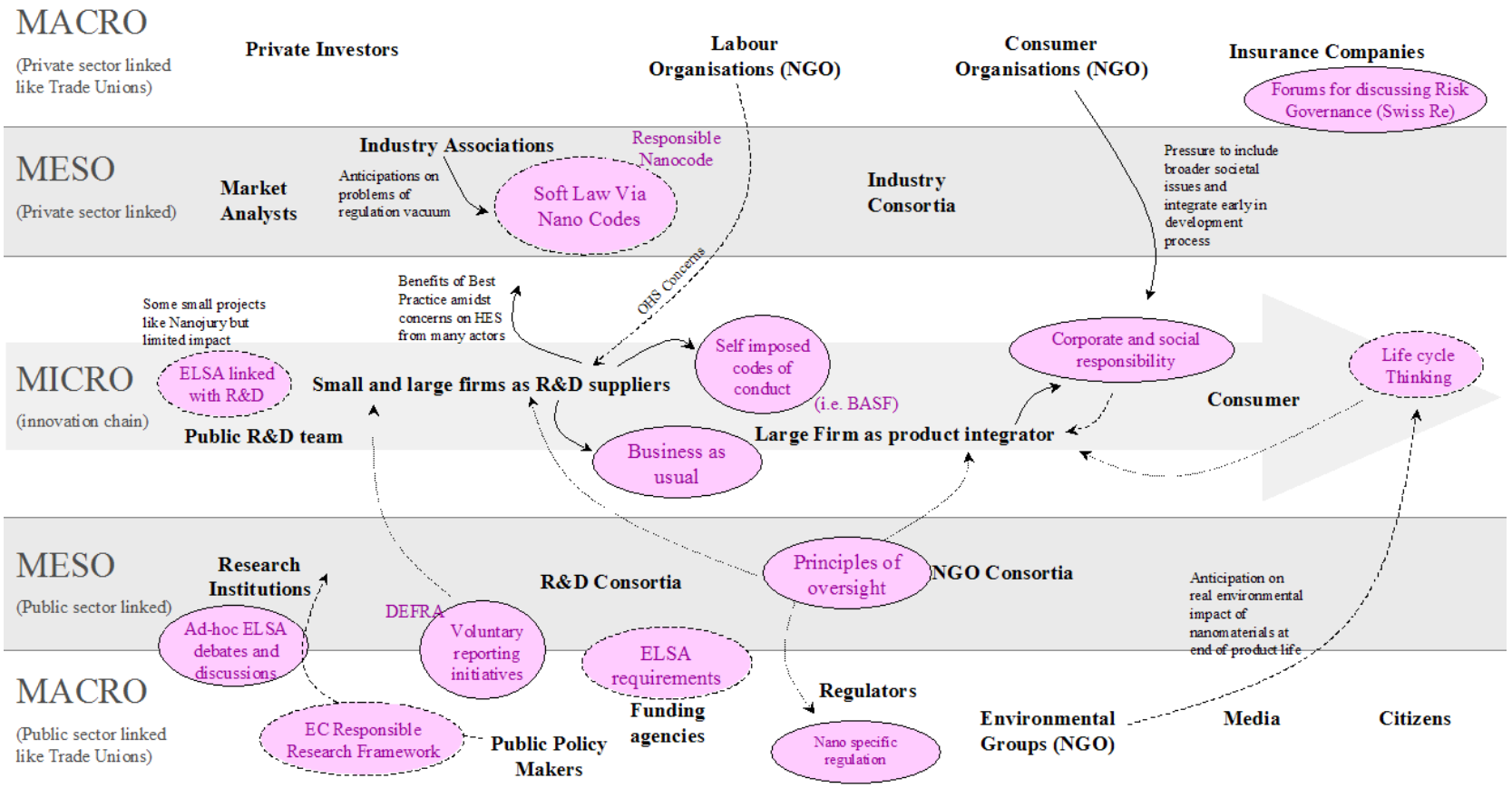

Figure 3: In this snapshot of the activities occurring in RRI, I have put key actors (both currently and potentially) in appropriate positions and in the pink bubbles I have placed potential elements of responsible innovation currently on the table and where they originated. As a backdrop in the micro-level, the large grey arrow represents the direction of the innovation chain. Full arrows are actual actions (responses to pressures), dashed lines are pressures to do something and the dotted (thin) arrows represent pressure attempts that have shown little effect so far.

Another interesting phenomenon is how certain arenas overlap and actor roles become mixed or blurred. One example are government actors with a regulatory responsibility who attend meetings and generally, take part in a variety of arenas where informal societal agendas are built. Similarly, industrial actors mingle with other kinds of actors, especially if a somewhat neutral space is provided (Rip and van Amerom). An interesting example is the meeting organized by Swiss Re and the International Risk Governance Council in Zürich in July 2006.

Thus codes are on the agenda, although there is anticipation that proliferation of codes of conduct and soft law, may remove the pressure to develop regulation.

2.3 Translating diagnosis into workshop topic and scenarios

Workshop Topic

With the current emphasis on societal impact and embedment of nanotechnology applications, the general acceptance of potential environmental and health risks of Nanomaterials and the call for nano codes of conduct during the present situation of a regulation vacuum, "Responsible Research & Innovation" at the time of the workshop was becoming locked into the very substance of Nanotechnology R&D and will shape its eventual uptake and embedment into society.

The notion of "Responsible Research and Innovation" (RRI) could well be here to stay, the question now is, how to implement RRI and what to expect from it? Different actors will have different visions and expectation, and one can imagine different futures.

This was the announced reason for the CTA project within the Frontiers Network of Excellence. By analysing the current situation and co-locating different stakeholders I proposed that, with the support of scenarios, we could explore plausible evolutions of the present situation and probe the various visions and proposals put forward for RRI implementation by various stakeholders.

The objective then is to explore possible elements of RRI through scenarios and sharing of opinions and positions and collectively develop ideas for implementation of RRI.

The proposed codes of conduct could be the tip of an iceberg of a larger movement towards responsible innovation, increased political and public scrutiny, and the need to explore and develop recommendations for what one could call **good nano-practice**.

Developments in RRI should be understood better, and be taken into account in strategic decisions. That will be a minimal level of 'responsible' research and innovation, and could be further developed into best practices in the nano-world. In fact, as has been outlined earlier in this section, there is external pressure to do so, with the inclusion of (still undefined) requirements for "responsible innovation" and "inclusion of societal impact assessments" in EU and US science policy as well as in statements by organisations such as insurance companies and NGOs.

To support the controlled speculation of the potential configuration of roles and responsibilities in RRI, socio-technical scenarios where developed which combine complexities of emergence and actual dynamics within narratives linked with the actual context nanotechnology development and embedment. The scenarios include some of the shaping factors which may enable or constrain paths (emerging irreversibilities), multi-level dynamics and the various actor strategies and governance approaches that are being developed or are anticipated.

The following section gives three short summaries of the scenarios. This is followed by the full scenarios with key elements, dynamics and issues shown in annotations.

2.4 Scenario summaries

Scenario summary 1

By mid 2008 the patchwork of codes of conduct, best practices and measures of responsible innovation remains misaligned, but allows progress in technology development through self-regulation and self quality control. The codes are particularly enabling for medical devices, providing some guidelines for nano alongside existing regulation of medical devices and so self regulation of new nano-enabling components can continue.

A case of focussed alignment of R&D agendas in national initiatives can be seen. One example, Finland begins to invest in nanotechnology for paper processing (a major contributor to the Finnish economy). The specificity of the case related to opportunities to cut costs, reduce use of chemicals and improve manufacture. The lack of standards helps this growth and large investments are made leading to positive gains.

Early engagement exercises and high profile projects such as Nano Jury UK and others lead to the inclusion of "engagement programmes" in technology R&D programmes to inform and communicate the benefits of nanotechnology. There is

a proliferation of such projects across (and initiated by) the nano R&D domain focussing on enabling public acceptance. Although no linkages between the projects occurs there the ethical and risk debate, begins to separate to "real issues" (of health, environmental and safety issues of nano production) and speculation on broader ethical debates around Human Enhancement, Justice, and theological issues.

Monitoring signatory compliance becomes a major issue. Code initiators attempt annual monitoring through direct contact to signatories, by asking them to volunteer time to report. Comparative and systematic methods do not exist. There is a lack of watchdogs; self-regulation and voluntary reporting go unchecked. The Precautionary Principle is promoted within codes but framed by self-assessment mechanisms (degree of precaution unclear). Innovation actor's quality not assured. Voluntary codes align best practice but have little effect on worst practice due to regime of patchwork of codes (so good become better, worst remain worst).

Gaps in regulation widen as nanotechnologies become increasingly more complex – existing laws which could be applied to products (medical devices) are less equipped to oversee products and processes such as active nanostructures which cross many sectors and can be applied in many settings.

The accident with the Finnish worker opens up nano governance once again and a number of lines of R&D grind to a halt pending further investigation. Those wishing to exact change are faced with an entangled web of best practices, codes with varying degrees of transparency in how they are acted upon.

By 2014 the proliferation of nano and its increasing complexity hits home when consumer organisations try to target concerns, no inroads. Liability becomes the issue. When problems begin to occur with certain products secondary effects, lack of regulation means it's difficult to find who is liable. Public remains sceptical, voicing failures such as "lack of transparency" and "unclear accountability".

Governmental watchdogs begin to emerge and the clamour to catch up leads to numerous temporary moratoria. Regulatory actions retroactively cover all Nanomaterials and products on the market become identified and recalled pending certification.

Scenario summary 2

The nano umbrella term becomes more specific (in funding mechanisms) - now defined in terms of potential sectors that will be impacted by R&D lines. In turn, potential consumers (and other impactees) can now be identified (the general

public translates to specific publics) and technology developers begin to start anticipating on societal acceptance of products.

Proliferation of engagement/communication approaches at the micro-level allows justification of "societal awareness" as a strategy for ensuring "societal acceptance". Concerns are voiced by media, by civil society on effects on Food, Lifestyle, Health, Privacy and Human rights – an outcome of the increased specificity of nano. At the micro-level these broad discussion are termed as "a separate issue for longer term speculation".

Ad-hoc public engagement exercises act as a lubricant to continue nanotechnology developments across the board. However, one project in particular captures people's attention, named "NanoDiaBlog" - it is created as a web-based discussion forum (based on a Wikipedia model transparency is enhanced). Over time, the NanoDiaBlog project actually fulfils the promise made by its initiators (much to their surprise) as creating an informed general public, in addition it forms a community of scrutiny and debate, both positive and critical. Although not an official body, the NanoDiaBlog community is deemed a high quality indicator of the populace (in any case the populace who takes an interest) and principles such as precaution, inclusiveness (transparency), integrity (protection for whistle blowers), ongoing assessment (constant vigilance), and the need to interface promoters and selectors, arrive on governmental agendas. Thus perfunctory public engagement exercises have the unintended outcome of creating a sustainable forum for engagement and action.

Taking advantage of this, a firm developing food-packaging sensors uses the blog to collect data on user preferences allowing targeting strategies. One outcome is with Radio-Frequency Identity Devices (RFID) tracking of goods through food packaging contains labels, similar to health risk labelling with the privacy risk label "This product is system tracked" placed on food packaging (a response to bloggers' insistence on transparency). Acceptance of the label was initially turbulent but general agreement of labelling and the "right to choose" (the label could be peeled off and so no further tacking possible) enabled wider uptake.

Scenario summary 3

Drug delivery becomes a key driver in nanotechnology. Rapid developments in nano means the consequent burgeoning number of delivery methods leads to increasingly bewildering regulatory protocols. Anticipation on further regulatory delays sees shift in private investments from nano to other promising technologies. NGOs, concerned about 2nd generation effects of nanoparticles argued for a

moratorium on nanoparticles for medical purposes until toxicity tests tailored for these particles would be done.

In reaction to these concerns Dr Würzel (a researcher on nano therapies) argues on the ZDF TV news show that successes have outweighed the fatalities: “Fatalities occur all the time! My staff are combating a serious disease which causes hundreds of thousands of deaths per year in Europe alone. It would be unethical to stop clinical trials for a drug that works better than others.” The following Spring, as a response to the prior press coverage and the ZDF news item, many patients with lung cancer go to the lab. As ever more patients converge on his lab, coverage shifts towards headlines like “From battling disease to battling the health authorities”: regulatory authorities become the enemy, obstacles to patient therapy. In the meantime, for the health authorities, the issue of proper clinical trials became an ever-increasing issue.

Lack of lifecycle thinking in nanoparticles and engineered tissue causes real concerns by both environmental agencies (the former) and clinicians (the latter). Production, storage and distribution in both the manufacture of nanoparticle based therapeutics and use in the clinics is an ongoing concern, as well as quality control of nanoparticles and bioaccumulation uncertainties (particularly in liver, spleen and bone marrow).

Public funding agencies form a blanket ban on financing nanoparticulate delivery systems. Private sector continues, voluntary reporting prevails but confidentiality of development hampers transparency (issues of competition) and thus watchdogs find it difficult to access data to assess practices. SME’s, already severely hampered by lack of public financing (linked with university ties) can’t cope on own with voluntary regulations, bypass it (for purposes of survival). By 2012, health care authorities would not certify the approach without clinical testing. This leads to precaution by health insurance companies to cover the procedure. The further effect is that this medical option becomes available only to those who can obtain it in another way through private clinics.

2. 5 Scenarios

Scenario 1: Increasing socio-technical complexity

By mid 2008 the regulation void continues and soft law is taken as an interim solution to allow nano to go ahead [i]. Industrial Consortia and Research networks (NoE) develop agreed best practices, which are self-imposed and a number of codes emerge and are agreed to. [ii] Government instigated voluntary reporting, after the initial disappointment in the UK, begins to increase moderately. Reporting (when it happens) goes through the consortia (act as a broker to maintain anonymity). [iii]

Not all actors in R&D sign up to the codes, broadness of principles causes concerns with some actors - a large pharmaceutical company states, "The lack of clarity and small print is unsettling for early stage technologies. Uncertainty in possible inroads for litigation and liability is not covered by such codes, for this reason our company will not sign up"[iv]. Conversely, code promoters state that "The breadth of codes is what gives it validity in current climate of high uncertainty". [v]

The patchwork of codes of conduct, best practices and measures of responsible innovation remain misaligned, but allow progress in technology development through self-regulation and self quality control.[vi]

The codes are particularly enabling for medical devices, providing some guidelines for nano alongside existing regulation of medical devices (such as ISO 14971 for Medical Devices), and so self regulation of new nano-enabling components can continue.[vii] By the end of 2008 advanced cantilever arrays and the long-awaited integrated micro-fluidic devices (lab-on-a-chip) begin to enter prototype phase with start-ups begin to emerge (and flourish) to take the university research into market, with the prospect of takeover by larger firms in three to four years [viii]. Similar developments can be seen for crime scene investigation and civil security technologies, where advanced diagnostics, forensics and identification technologies were the focus – stimulate by government grants, small companies begin to

[l] No new nano specific regulation so soft law is taken as a solution. This was one vision of the future proposed by a number of codes of conduct on the table in December 2007. This element linked up with the difference between two regulation reviews in the UK during 2006. HSE executive saying current regulation was enough. DEFRA saying there are gaps.[56]

[ii] Governance is located by enactors at the meso-level of coordination (see figure 4).

[iii] Government actors attempt voluntary initiatives but there are tensions. This was the case at the time of writing with respect to the UK voluntary initiative[56]

[iv]Concerns on litigation in roads cause hesitation for some firms. This is a stylized quote announced by a large pharmaceutical company in a meeting in November 2007 on Nanomedicine [57[

[v] Code promoters argue broadness is why codes are good. This was taken from interactions I had with code developers.[36]

[vi] A continuation of the situation given in figure 4. Researchers and technology developers do not feel pressure and continue with their R&D unabated. Taken from interviews at the Frontiers NoE Annual Meeting, Leuven, October 2007. Researchers were anticipating that the EU responsible dev. Code may affect funding.

[vii] Codes are useful

commercialise this technology [ix].

A case of focussed national initiatives can be seen. One example, Finland begins to invest in nanotechnology for paper processing (a major contributor to the Finnish economy).[x] Focussed investments included nanofiltration (for effluent treatment), nanocoatings (for pigment and texture) and nanodiagnostics (for monitoring quality) and nanocharacterisation (for deeper understanding of paper materials). The specificity of the case related to opportunities to cut costs, reduce use of chemicals and improve manufacture. The lack of standards helps this flourish and large investments are made leading to positive gains. [xi]

Other governments look at Finland's targeted explorations and developments in nanotechnology for the paper sector [xii]. Government official "Nanotechnology promises to revolutionise all industry sectors, paper production could seriously be enhanced through nanotechnology and as a small country, Finland should focus resources on what is most beneficial for us." Other national governments look with envy at the rapidity of developments of the targeted nano programmes of Finland.

Early experiments and high profile projects such as Nano Jury UK and other engagement exercises lead to the inclusion of "engagement programmes" in technology R&D programmes [xiii] to inform and communicate the benefits of nanotechnology. There is a proliferation of such projects across (and initiated by) the nano R&D domain focussing on enabling public acceptance. Although no linkages between the projects occurs there the ethical and risk debate, begins to separate to "real issues" (of health, environmental and safety issues of nano production) and speculation on broader ethical debates around Human Enhancement, Justice, and theological issues.[xiv]

Monitoring signatory compliance becomes a major issue [xv]. Code initiators attempt yearly monitoring through direct contact to signatories, by asking them to volunteer time to report.

Comparative and systematic methods do not exist. There is a lack of watchdogs, self-regulation and voluntary

additions to existing (well regulated) areas like medical devices. Taken from interviews and research in and around a CTA on lab-on-a-chip technologies [5]

[viii] Innovation Journeys begin to start moving. From gestation period to start-up phase. This section also illustrates techno-startup strategies.

[ix] Another field is added for context and to compare to the medical device innovation journeys later in the scenario (an actual project at Hull University, UK)

[x] Anticipatory coordination in Finland. Sunk investments enables (but constrains later on in the scenario)

[xi] Argument whether standards are desirable by various actors.

[xii] Other governments look on with envy at the focus of Finnish nanotechnology. This is a mirror of anticipatory coordination in other geographical regions. [34][58]

[xiii] Proliferation of engagement activities presented here in the perspective of communication and outreach (to educate the public). Public Acceptance.

[xiv] Separation in types of issues discussed. Speculative Ethics [59] and near-term Health Safety and Environment issues.

[xv] Issue /Tension. Was debated in the Dec 5th meeting [36] and is reported in the minutes but no agreement on mechanism [see own notes]. Here I mimic one suggested approach.[60]

[xvi] Here I leave unsaid but imply that the good guys shout out loud whilst the bad

reporting go unchecked. Responsible actors, who have followed a particular code of conduct, flag their level responsibility by highlighting the following of codes as a sign of good governance [xvi].

2009 – 2010 Nano Development Boom

The self-imposed standards for manufacture work as a minimum safety requirement, but are at a considerably low level (minimum damage but some damage all the same) [xvii]. Some issues of workers safety voiced but related to non-nano issues and passed to others. Calls for moratoria continue from a number of civil societies and labour organisations based on some occupational health issues but have little effect. This is in part due to the governance arrangements being firmly centred on industry consortia (which become specialised under sector rather than on enabling technology which adds another issue of lack of transparency (especially where platforms are concerned)) [xviii].

Emergence of platform technologies with applications in multiple sectors and comprising of ever increasing complexity of functional nano-elements (multifunctional tailored nanoparticles, highly integrated Lab on a chip, Moore than More integrating of semiconductors and molecular electronics. [xix]

2011 – 2012 Nanoproducts proliferate

The Precautionary Principle is promoted within codes but framed by self-assessment mechanisms (degree of precaution unclear) [xx]. Innovation actor's quality not assured. Voluntary codes align best practice but have little effect on worst practice due to regime of patchwork of codes (so good become better, worst remain worst) [xxi].

Codes not intended to supplant regulation [xxi], in practice reduces pressure on regulators causing delays in regulatory mechanics. Regulators rely on current law (or modifications of them) for nanomaterials and

guys remain silent.

[xvii] Shift into NGO and Trade Union perspective. Risk thresholds. NGOs and Trade Unions try to shape but have little effect because of lock-in.

[xviii] This is a key issue. Del Stark (ENTA) in the Dec 5th meeting pointed out that trade secrets in manufacturing would be a problem for voluntary reporting of use and processing of nanomaterials. He suggested that an industry association (such as his own) could play that role[36]

[xix] More examples of technologies that can enter multiple sectors. This highlights another issue of where to locate responsibility for nanotechnology in applications, as nano is an enabling technology and is in the main part of larger systems of technology – why focus on nano?

[xx] Degree of precaution unclear

[xxi] Emphasizing the concern by some actors that the good guys get better and the bad guys remain bad.

[xxii] In a discussion I had with a representative of Greenpeace UK, he mentioned his concern that it will reduce pressure on regulators – so not supplanting regulation but inhibiting it all the same (regardless of good intentions).

[xxiii] REACH has been positioned as enough already by manufacturers and 3rd parties, whereas labor organizations are concerned that it isn't refined enough. This came from informal discussions I had in the Dec

applications. REACH[146] is used but is identified as a blunt instrument by labour organisations as it fails to cover certain substances in very small quantities. [xxiii]

A regulatory task force is set up by the British Government to identify possible regulatory gaps that could be filled [xxiv]. The report pushing for mandatory government oversight identifies many gaps but the major emphasis lies on the fact that nano regulation is difficult due to increasing complexity. - law is less equipped to oversee products and processes such as active nanostructures which cross many sectors and can be applied in many setting.

2013 House of Cards falls

As ever-increasing complexity of nano and various incidents cause concerns, the governance arrangements become questioned and regulatory concerns begin to emerge in many countries as calls for further investigation [xxv]. However, there is alignment already and GOs, NGOs, and Civil Society become befuddled by the complicated relationships between technology platforms (multi-functionalised nanoparticles, and other functional macromolecular systems) and the various applications/sector (they have become embedded).

A worker in paper factory, being treated for liver damage because of alcohol abuse, is found to have peculiar lesions of the liver tissue not related to alcohol abuse. Further diagnostics reveal nanoparticulate aggregation directly linked with the Finnish paper mill (specificity of tailored nanoparticle enables the identification of source of particle) [xxvi].

In the field of medical diagnostics, nano-enabled chips were beginning to be integrated into clinical practice [xxvii]. The lack of nano specific regulation allowed innovations to proliferate but transition into the clinic

5th meeting with representatives from Greenpeace and a participant linked to Trade Unions.

[xxiv] Taking a trigger from the labour organizations, UK government explores regulatory landscape. Report shows various gaps and issues (this was the case with the DEFRA [61]. However in this scenario it is not immediately taken up. Good report but no further action initiated (until circumstances change).

[xxv] As nano develops, civil society, NGOs and governments become more concerned but find no clear inroads into the governance arrangements – lock-in due to earlier dynamics which is difficult to unpick (without major investment of resources).

[xxvi] A triggering event occurs which brings up the issue of toxicity and exposure. This was linked to NIOSH 2004 which raised concerns around the manufacturing of nanoparticles. I do not mention that nanotoxicity is the cause of liver damage here, I leave open. Implicit in this phrasing is that because hazards and exposure issues are not known, it is difficult to decide whether nano is the problem or not.

[xxvii] As medical nano enters the clinics user issues begin to emerge (previously unarticulated requirements come about). I took the then current issue of MRSA which links up to discussions on new standards for medical devices.

[146] "REACH Regulations – Registration, Evaluation, Authorisation and Restriction of Chemical substances (EC 1907/2006) – which entered into force on 1 June 2007. Reach applies to chemical products above a certain volume of production (1 tonne), while some nanomaterials will be produced below that level."

became fraught with many other challenges related to user needs and user practices. Methicillin-Resistant Staphylococcus Aureus was found on a number of devices, which led to an enquiry on methods of sterilisation and exploration of bio-fouling. Technical complexity becomes and issues.

A number of legal actions were filed against medical device companies, which in turn causes health insurance companies to withdraw their backing of the devices in their coverage. One medic was quoted saying "The technologists missed the boat early on, they should have listened to user needs rather than contemplating far off utopian and dystopian sci-fi futures" [xxviii]. In contrast diagnostics for crime prevention and other non-health related applications continue to flourish.[xxix]

Finnish case sparks of a chain of enquiries into nano-regulation, and a number of lines of R&D grind to a halt pending further investigation [xxx]. Finnish economy begins to suffer due to the high sunk investments into nanotechnology based infrastructure. Public outcry as consumer organisations identify major issues in a number of sectors which could hold potential risk with no protection for the consumer (the house of cards falls) [xxxi].

Total recall

By 2014 Nanotech employs approximately 2.3 million workers globally. Nano has become more complex, a many headed hydra which is difficult to tame, one popular scientific journal headlines "One look at the Nano Medusa turns regulators to stone". This is picked up by other media, and phrased and framed in different ways. The proliferation of nano and its increasing complexity hits home when consumer organisations try to target concerns, no inroads. Liability becomes the issue [xxxii]. Reference to UK government report of 2012 identifying gaps – stimulates finger pointing at regulators for not following up. When problems begin to occur with certain products secondary effects, lack of regulation means it's difficult to find who is liable. Public remains sceptical, voicing failures such as "Lack of transparency" and "unclear accountability".[xxxiv]

This example is linked to a presentation given by manufacturing firm in the London meeting November 2007 on Nanomedicine.[62] This element was to introduce an opening in discussion on methods of anticipating. It also showed shifts, forks and setbacks.

[xxviii] Clear issue of speculator ELSA and near-term ELSA.[59]

[xxix] Other devices are enabled whilst the medical devices are constrained.

[xxx] Finnish case cause temporary moratorium. Because of huge sunk investment Finland begins to suffer (effects of path dependency and emerging irreversibilities).

[xxxi] Window of opportunity for consumers and NGOs, to raise concerns. Lock-in is unlocked, previous governance arrangements collapse.

[xxxii] Complexity of nano and the lack of coherent regulatory infrastructure mean big delays for certain areas.

[xxxiv] Public remains sceptical, voicing failures such as "Lack of transparency" and "unclear accountability". This is placed as a trigger for discussion – good guys and bad guys (technology developer), versus transparency and accountability (civil society).

[xxxv] Retroactive regulation as an outcome.

[xxxvi] Winners and losers mentioned here. Highlighting that this is not a dark scenario, but a situation which enables some options and constrains others.

Governmental watchdogs begin to emerge and in the clamour to catch up leads to numerous temporary moratoria. Regulatory actions retroactively cover all Nanomaterials and products on the market become identified and recalled pending certification. [xxxv]

Whilst regulators scramble to catch up, the ever-increasing complexity delays the process even more. Promises in "Beyond Moore" nanoelectronics and nanophotonics begin to dominate whilst nanomedicine and bionanotechnology clamour for tests and rapid certification. [xxxvi]

Scenario 2: Rules of engagement & the engagement of rules

In 2008, nanotechnology developments continue to grow, spawning an ever-increasing amount of sub-disciplines and interest of multiple industries as research results dealing with specific projects become available. As funding schemes launched near the beginning of the major nanotechnology impetus in 2003 (see timeline) a second wave of funding instruments from public financing organisations begins (European Commission FP7 and 2nd round national programmes) [xxxvii].

Nanotechnology as a term has become more articulated (in its plethora of specific research lines and possible impacting sectors) but the umbrella term still covers many enabling technologies, many potential application sectors and many visions of possible societal changes based on nano [xxviii].

The rise in interest of existing sectors such as textiles, energy, transport, cosmetics [xxxix], etc. brings more focus on consumers – the public begins to become less general and specific targeting begins in particular sectors[XL]. The concerns in a number of sectors where consumers are particularly sensitive, food and health care, cause an additional impetus to focussed

[xxxvii] 2nd wave of funding. Implicitly linking up to assessment, evaluation and lessons learned from the 1st wave. Also hype-disappointment as a possibility here, or hype replaced by hype?

[xxxviii] Nano vagueness becomes more specific (more articulated) as old vagueness and umbrella term doesn't bring any benefit anymore [Links back to Drexler's umbrella term, used by researchers at the time but then criticized when there was little use for it…Rip and van Amerom]

[xxxix] Trend of positioning nano in terms of sectors it could impact rather than scientific platform.

[XL] Comparative selectors can be more easily identified by enactors and 3rd parties. Nanotechnologies can be seen by comparative selectors making it easier to anticipate on potential impacts.

[XLI] Anticipation of concern [Nano phobia phobia] triggers societal acceptance strategies by enactors.

efforts on enabling the societal acceptance of technologies [XLI].

The locus of such broad engagement initiatives is placed on public investment actors and research institutions; whereas industry actor's focus on particular elements of the innovation chain through recognised market survey practices.

Proliferation of engagement/communication approaches at the micro-level allows justification of "societal awareness" as a strategy for ensuring "societal acceptance". Concerns are voiced by media, by civil society on effects on Food, Lifestyle, on Health, on Privacy and Human rights. This has little connection with ongoing nano practices ("a separate issue for longer term speculation"). Ad-hoc public engagement exercises act as a lubricant to progress in nanotechnology developments.

A contributor to the Royal Society Report (a recognised report referred to in ongoing nano developments) captures the climate of engagement perfectly, "We warmly welcome breadth of participation. Our report has not yet been assailed four years on, is robust because of inclusion of stakeholders" [XLII].

[XLII] This is a stylized quote from a meeting [Dec 5th 2007 meeting] Enactors strategies of engagement as a token gesture.

Ambivalence of nanotechnology comes out in a major governmental engagement report: "Novel properties of nano will enable benefits in health, energy, and other sectors [XLII]. True control and harnessing of these unique processes will usher in a new industrial revolution." In contrast, the report goes onto say with regards to risks of nanotechnology on Environment, Health and Society, "Nanomaterials already occur in nature, there is nothing new."

[XLII] Ambivalence of novelty of nanotechnology: (a) promises wonderful new things and (b) risks are positioned as nothing new. [From Folk theories of Nano paper?]

Developers at the early stage development of technologies begin to implement their own codes of conduct to the manufacture of nanomaterials [XLIII]. Codes of conduct are a way of bridging the gap between a vacuum in regulatory mechanisms and a

[XLIII] Enactors use CoCs to guide but do not take a position on risk.

solid legal framework. Upon questioning of what are the actual dangers of such particles, the response was "more research is needed".

2009 From communication to multi-logue

By the end of 2008, as part of a new initiative in response to the EU Action Plan [XLIV] and responsible governance mandate, an online public engagement exercises designed to communicate nanotechnology research is initiated and linked up with the evolving European Technology Platforms. The project, named "NanoDiaBlog", becomes a platform for informing whoever wishes to read the weblog and allowing comments and discussions [XLV]. Taking the lessons of Wikipedia (possibility of historical memory) transparency is enhanced (one of the requisites of the EU Nano Action Plan). It also allows anyone to start a question thread. The five topics with the most comments each day are listed in the daily feed to those who join the NanoDiaBlog community mailing lists. [XLVI]

Early 2009, after a short period of intense reporting by researchers on technical developments and possible solutions to today's problems that may arise from the research, comments start trickling in and question threads from outside the R&D community begin to emerge. [XLVII]

Examples of early entries include "Nano is not new" originating from an international NGO spokesperson, emphasises that "we do not have the luxury of early stage. Products are here already!" Such question threads are not picked up. General positive feeling of the promises of nanotechnology continues to be the main discussion topic. [XLVIII]

One legal actor starts a topic (question thread) focussing on the limitations of self-regulation currently

[XLIV] EC interest in responsible development of nanotechnology.

[XLV] ELSA dialogue online.

[XLVI] Token gesture?

[XLVII] Enactors use it as a promotion platform to talk of benefits nano can bring.

[XLVIII] Some comparative selectors use this space for debate to move discussion away from future benefits to present day issues – Nano is here already! But here I have it not taken up…similar to other events occurring around the time of the workshop.

[XLIX] This is linked to an informal interview with a lawyer from Mayer-Brown. If there is nothing new about risks of nano, why need a new code? Also codes have little effect on wrong doers unless certain elements are in place.

prevalent in nanotechnology innovation development. [XLIX] Pointing out two flaws in nano codes of conduct. "If there is nothing new about nanomaterials, then why have a new code? The codes do not seem to have any consequence for not following the code. Wrong doers will not be affected. Right doers will be promoted and perhaps gain prestige, but announcing the following of the code can attract litigation." Legitimation of codes as a soft alternative to hard law begins to diminish, but there is nothing to replace them. The legal actors question thread makes it into the top 5 topics for a few days and then fades away.

By mid 2009, the NanoDiaBlog server has to be upgraded and a dedicated team is set up under the FP7 Science and Society programme. The NanoDiaBlog fulfils its task as creating an informed general public, in addition forms a community of scrutiny and debate, both positive and critical. [L]

[L] Engagement and debate becomes more than a token gesture – is picked up and the NanoDiaBlog as a space for interactions and positioning gets a life of its own.

[LI] This can said to be comparative selector thinking. Looking at applications and how nano will enable broader societal shifts.

2010: An informed society

[LII] Enactor strategy explain technology that it could be used for great benefits

A new topic entitled The Nano-Panopticon discussing a comment that nanotechnology for security and surveillance will be faster, cheaper and more pervasive than other previous technologies. This raises concerns, and comparisons proliferate with examples such as CCD cameras, ID cards with embedded chips and mobile phone cameras as pervasive surveillance. [LI]

[LIII] Whistleblowers personal concerns about database and control of such knowledge. This is a case of an enactor using comparative selector thinking -> not nanocentric thinking but looks at situation as not inevitable but choices that can be made.

One actor, attempting to dispel the notion of many invisible cameras everywhere, uses NanoDiaBlog to quell fears by explaining the research on nanosensors that can be embedded in clothing to detect poisonous gases, to locate lost children and other improvements on current situations. [LII]

[LIV] link to real example of personal database lost by government [REF]

[LV] Enactors: "broad discussions, removed from Nano"
Comparative Selectors "Nano contributes/exacerbates this, is a nano issue"

One blogger (turns out to be a medical researcher [whistle blower]) links the advances in personalised medicine to expanding details of patients. [LIII]

[LVI] Arena becomes recognized space. Token

"Comparisons need to be made and thus a database must exist – questions of access to this database emerge (especially with regards to health insurance companies who push for access to this data for "targeting" cover)." She mentions UK Government Blunder of 2 CDs of 3 million child benefit claimants data lost in the post. [LIV] Data protection becomes a major discussion point on the NanoDiaBlog, much to the bemusement (and frustration) of nanotechnology developers who wish to refocus the discussion on more specific issues of health and safety risks and on lifecycle issues for nanomaterials. [LV]

By early 2010, the NanoDiaBlog serves to create an informed and critical public and also creates a community where some DiaBloggers are voted online as representatives of the virtual community in the "real world". This entity begins to mobilise support for targeted moratoriums and lobbying public policy and regulation. [LVI]

In the meantime food and food packaging sector, previously sceptical, begin to take an interest in nanotechnology opportunities but tread carefully due to perceived public rejection of new technologies (often cites biotech failure). [LVII]

2011 Constructive criticism: constraining and enabling innovation

One firm developing food-packaging sensors uses the blog to collect date on user preferences. Allows targeting strategies. One outcome is with RFID tracking of goods through food packaging contains labels, similar to health risk labelling with the privacy risk label "This product is system tracked" placed on food packaging (a response to bloggers insistence on transparency). Acceptance of the label was initially

gesture has become a reality, but the way it emerged and eventual characteristics were unintended by the initiators and is part of the co-evolution of interactions, and circumstances described in this scenario-tale.

[LVII] Here I use some of case research into expectations in the food sector to help in creating a shift in the scenario-tale.

[LVIII] Arena becomes a locus for virtual niche testing. RFID outcome direct. Nanotechnology innovation linked to user values and firm develops a targeted societal embedment strategy.

[LIX] This community of transparent debate becomes semi-official and recognized as a reference point. Elected representatives lobby at national level to shape policy. Principles emerge – transparency, integrity etc. [These mirror the principles of oversight – REFERENCE and was a means of putting these perspectives in a future where they had guiding power].

[LX] Is part of governance landscape linked with governments and firms.

turbulent but general agreement of labelling and the "right to choose" allowed discussions to focus not on moratoria on RFID but on allowing "the right to choose" by limiting monopoly of tracking system for a two year period to allow for exploration of positives and negatives. [LVIII]

A set of principles emerges through the NanoDiaBlog and representatives present them to national governments to follow national code. Although not an official body, the NanoDiaBlog community is deemed a high quality indicator of the populace (in any case the populace who take an interest) and principles such as precaution, inclusiveness (transparency), integrity (protection for whistle blowers), ongoing assessment (constant vigilance), and the need to interface promoters and selectors, arrive on governmental agenda. [LIX]

2012: Enabling and Rejecting

The evolution of governmental codes for funding leads to point where some technologies are deemed unsuitable for public funding. Learning from RFID experience of 2011 firm, other firms follow suit in interaction with users. Food and Packaging flourish (linked with early bridging) albeit at a slow pace due to regulation and "niche testing" , however regulation can be targeted due to transparency, and de facto roadmapping on regulation occurs which allows alignment and coordination to take place. [LX]

FP8 Requirement to develop such weblogs to promote transparency (as in earlier Responsible Nano Code for Researchers). By 2014 nanotechnology in most sectors proceeds cautiously, with watchdogs evolving with the many branches of nanoscience and nanotechnology.[LXI]

[LXI] Participating and augmenting such diablogs becomes a core part of responsible development ideas and are translated into requirements for the FP8 Framework Programme.

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Scenario 3: Controversies about drug delivery options

2009 Drug delivery boom

Driven by the limitations of existing delivery methods and the emergence of new classes of genomic drugs, companies began to flock to the growing drug delivery industry. [xxxvii]

[xxxvii] Drug delivery emerges as a key enabling technology amidst a broader emergence – that of biotechnology-based and genomic pharmaceuticals (Biopharma).

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"The synthesis of the medicine is only part of the drug. Without delivery you just won't have a successful treatment," announces Robert Langer, a chemical engineering professor at the Massachusetts Institute of Technology and past chairman of the US Food and Drug Administration (FDA)'s science advisory board.

[xxxix] Convergence of delivery hype with promising nanotechnology options

This new emphasis on delivery coincided with the evolution of drug delivery with micro and nanoparticles. Boosted by the promises of nanotechnology in industry and national agency. [xxxix] Engagement exercises and Ethical debates on the future impact of nanotechnologies on society began to emerge in scientific programmes, business networks, etc. [xxxx]

[xxxx] ELSA activities in the form of engagement become part of the fabric of Nano R&D programmes

[xxxxi] Promising technology fuels drug delivery hype.

Large research funds were made available due to the large promise of nanotechnology and a new space for institutes to focus on drug delivery as a distinct topic. By the end of 2009, predictions of large drug delivery turnover initiated a proliferation of small firms eager to enter the drug delivery market.[xxxxi] Large pharmaceutical companies saw in drug delivery the promise to extend the lease of life of existing drugs (through better targeting) and a backlog of research which failed to progress through clinical testing due to targeting issues.[xxxxii]

[xxxxii] Nano promises to extend drug exploitation time. From discussions with representatives of Glaxo Smith Kline, Pfizer and Roche

[xxxxiii] Regulatory loop hole

During this period, the recognition (by a number of scientists) of drug delivery by particles having a dual nature of being both a medical technology and a drug, was publicized but no new regulations where developed. [xxxxiii]

[xxxxiv] As nanotechnology enabled delivery systems become more diverse and complex, governmental

2010 Regulation struggles

In 2010, the consequent burgeoning number of delivery methods led to increasingly bewildering regulatory protocols. Government agencies struggled to evaluate unprecedented delivery approaches through traditional channels. As a result, many revolutionary technologies languished just out of reach, trapped in a regulatory stranglehold.[xxxxiv] Soft law options, stemming from civil society and public funding bodies began to be developed to bridge the gap and allow some alignment in "best practices" of development. [xxxxv]

"All the clever ideas for delivering therapies may never evolve into real products unless clear-cut guidelines emerge to smooth their regulatory path," says FDA Spokesperson Xavier Windeler "Regulatory agencies are becoming increasingly befuddled over how to evaluate the bulk of new delivery methods. In the US, for instance, the FDA has three separate centres devoted to evaluating drugs, devices and biologics." [xxxxvi]

In the middle of 2010, a key Investment firm announced it was stopping all nano investments due to its failure to deliver any return on investment. This lead to a domino effect of investment firms imposing an internal ban on nano funding. [xxxxvii]

This coincided with Phase 0 trials becoming usual practice, university groups developing and testing of new drug options began to proliferate and small firms had the opportunity to develop technologies with the added advantage of "pre" pre-clinical testing. [xxxxviii] This created opening for maverick scientists to explore new options, and publicize them.

Small firms take the lead

Autumn 2010, Klaus Würzel, leader of the research team at the University of Gottingen developed a spray

agencies and regulatory bodies lag behind causing a serious bottleneck for market entry of new therapies.

[xxxxv] Soft law supports tentative alignment in best practices during a period of a regulatory void.

[xxxxvi] At the time of the workshop in 2007 (and at the time of writing in 2010) drug delivery approaches could be placed in all of three different regulatory categories: drug, device or biomaterial. Often it is down to the innovator themselves to choose which regulatory pathway they will follow.

[xxxxvii] Bandwagon/domino effects as investment firm wirthdraws.

[xxxxviii] As private financiers pull out, publicly funded academic laboratories can expand their scope for dug dev elopement via Phase 0 microdosing.

[iL] A researcher gets visibility when succeeding in what is

for inhalation of siRNA directly into the lung without a vector. Targeting non-small lung cancer, initial trials on mice showed promising results. These results were published in Science, and Würzel began to appear in the press as "Würzel battling lung cancer".[iL]

Preclinical studies on mice and lower-primates showed optimistic results, and human trials began.

By the end of 2010 NGOs, concerned about 2nd generation effects of nanoparticles argued for a moratorium on nanoparticles for medical purposes until toxicity tests tailored for nanoparticles would be done. Pleas for comparative testing with other delivery methods, patches, implants, time release capsules etc. [L]

The regulatory issues brought to light by cases like Cypher , combined with NGOs becoming restive stimulated a commission to investigate the rapid growth of drug delivery with nanoparticulates to explore the broader issues linked to the promise of nanoparticle based therapeutics. [Li] In the meantime small companies surged ahead, some starting pre clinical trials.

During autumn 2010, in the US a study using AVV (a virus) for siRNA transfection caused 150 mice to die. Initial concerns about the vector being the problem were quickly doused by research teams who show that the deaths resulted from an excess of siRNA. Questions were raised concerning the reactions to too much siRNA in cells and the effects of reactions with mRNAs and consequently cell function. Health care authorities concerned about the siRNA approach and advise caution in the move to human trials.[Lii]

In reaction to these concerns Würzel argues on ZDF news that successes have outweighed the fatalities, "Fatalities occur all the time! My staff are combating a serious disease which causes hundreds of thousands of deaths per year in Europe alone. It would be unethical

currently thought of as the low hanging fruit of siRNA delivery (easy to access parts of the body meaning no delivery system is needed)

[L] In this part of the scenario I shift the discussion away from comparison within nanotechnology options, to other non nano options. I bring in a non-technical actor to introduce this as a call for a broader comparison (comparative selectors attempt to shape enactors).

[Li] The call for a moratorium triggers an opening up of assessment of nanoparticle based therapeutics. This shift in "external conditions" does not seem to effect the world of enactors and small companies surge ahead in the development of nanoparticle-based therapeutics.

[Lii] A research study using one specific delivery system (a modified virus) causes fatalities in the lab. This triggering event causes concern which leads to health care authorities scrutinising the whole field of siRNA and advising a precautionary approach.

[Liii] A researcher steps out of his laboratory to give an interview as a spokesperson for the field. He highlights the dangers of the precautionary approach with regards to therapy – a delay will allow more fatalities which could potentially be prevented. (this shows common position of enactors in therapeutic fields, and is shown here as friction between an enactor (the researcher) and a comparative

to stop clinical trials for a drug that works better than others." [Liii]

The following spring, as a response to the prior press coverage and the ZDF news item, many patients with lung cancer go to the lab. Würzel points the finger at the health authorities, "This is evidence of a patient revolt. Clinical testing and current protocol stand in the way of these sick people getting better!" [Liv]

As ever more patients converge on his lab, coverage shifts towards headlines like "From battling disease to battling the health authorities": regulatory authorities become the enemy, obstacles to patient therapy. In the meantime, for the health authorities, the issue of proper clinical trials became an ever-increasing issue.

2011 Little Fish can survive the regulatory net

First wave of delivery systems which entered the clinical testing in 2002, pass human trial entered the market. One environmental group found evidence showing the specific delivery system would effect crustaceans and phytoplankton (key elements of the biosphere). Further explorations (by the environmental group) shows that no lifecycle tests were attempted both inside and outside of the patient and thus failed to pre-empt flora and fauna risks. [Lv]

Clinicians working on regenerative medicine, building off the environmentalist uproar begin to look at lifecycle issues of engineered cells for regenerative medicine. The clinician community begin to show concerns of cells lifecycle "where do they go? Where do they end up? Nobody knows!" These events add up to a turning point. [Lvi]

Early 2011 saw the release of the commission report, by risk assessment, public officials, the FDA and social scientists identified a number of issues based around nanoparticulate base drug delivery mechanisms. [Lvii]

selector (the health care authority).

[Liv] Researcher in his role has spokesperson can mobilise resources (in this case patients and families of patients) to back his claim. (This is included to reveal an alternative role of a researcher – more than developing technology in his lab. It is in part a way of holding up a mirror to ambivalent researchers who on the one hand argue that they just stick to the science but on the other take advantage, stimulate or fuel hype).

[Lv] Environmental group do their own scientific research and discover potential ecological risk. This sort of research is done by Greenpeace UK at the University of Exeter for example.

[Lvi] A user community (clinicians) is outraged at the lack of life cycle research.

[Lvii] The broad shift in "external conditions" becomes more specific through a commission report. EHS issues and quality assurance become issues. Occupational Health concerns are raised.

[Lviii] Public agencies call for a moratorium

Production, storage and distribution in both the manufacture of nanoparticle based therapeutics and use in the clinics was an ongoing concern, as well as quality control of nanoparticles and bioaccumulation uncertainties (particularly in liver, spleen and bone marrow). The safety of others became another key issue – for inhalable approaches, concerns of free particles in the air in mist forms either direct from drug delivery device (pump) or from sneezing, coughing etc.

Public funding agencies formed a blanket ban on financing nanoparticulate delivery systems.[Lviii] Private sector continues, voluntary reporting prevails but confidentiality of development hampers transparency (issues of competition) and thus watchdogs find it difficult to access data to assess practices.[Lix] SME's, already severely hampered by lack of public financing (linked with university ties) can't cope on own with voluntary regulations, bypass it (for purposes of survival).[Lx]

An article in Scientific American "Magic bullet with a deadly coating?" sparked wide debate concerning the effects of viral and nanoparticle based delivery and the unknown secondary effects of the delivery system itself. A link is made to that of viral vectors for gene therapy as AVV is known to combine with DNA (as that which happened to the two children in Necker, Paris). This led to a "public outcry", according to a Canadian based NGO, and greater scrutiny of drug delivery research and development ensued.[Lxi]

Those developing siRNA delivery in the private sector do not however feel impaired by the societal deliberations on safe delivery. [Lxii] Sirna Therapeutics (US) in 2011 continues: "The firm has spent a hell of a lot of time and effort putting siRNAs into animals and non-human primates, and we haven't seen anything like this". They continue for human trials.

A vociferous member of the church community looking

[Lix] This issue was raised by Del Stark (ENTA) during his presentation at the December 2007 meeting in Brussels and was discussed during the presentation and between participants in the coffee breaks.

[Lx] This was a concern of an SME I interviewed.

[Lxi] Another popular scientific journal picks up on the Economist article and probes deeper into the debate (mentioned in the previous annotation). This compares issues with other (at the time high profile) catastrophes.

[Lxii] Industrial actors do not feel the effects of the debate (is outside of their world) and they continue on human trials.

[Lxiii] Stylised quote from the Brussels meeting, December 2007.

at the ethics of nanotechnology, to the surprise of nanotechnology developers voices his criticism of the public funding agencies ban on drug delivery "The ban is preposterous. We saw the same thing in the US a few years ago with stem cell research, and now we have a wide mistrust of private enterprises and the governance of stem cells. A blanket ban, rather than broader regulation and guidance, will jeopardize safety as well as the consumer. Will the private sector follow their own codes? Please do not go the same way as US Stem Cells!" [Lxiii]

Entering the market

Mid 2011, another group in the US working with siRNA mentioned that although initial reports suggested that siRNAs would have previously unheard of specificity for their targets, several mechanisms have since been described that can lead to unintended off-target effects on gene expression (such as those experienced with the AVV experiments) and need to be seriously considered in developing RNAi based drugs. Perhaps more serious are unanticipated off-target effects that occur by siRNA recognition of other mRNAs bearing only partial homology.

Researchers working on the Würzel system maintained that the evidence suggests that the tests worked on animals and initial patients (with a few exceptions) and that it would be unethical to continue with the arduous clinical trials of phase 2 and 3 – sentencing more people to death that could be cured by this new drug.

By the end of 2011, Würzel's team has mobilised some $100 million through deals with large pharmaceutical companies, and anticipates on larger investment.

However, a challenge remains with the transferral of Würzel's siRNA system to the clinics. Health Authorities emphasised that not seeking large samples

and following proper protocol, meant that testing processes are confounded. Patients might not receive optimal treatment as a new therapy or drug will not be properly evaluated. "Patients and press determined the drugs validity by popular vote and shouting rather than scientific method"

Würzel's team argue that they have evidence that the system works and have improved on its initial efficacy through further refinements during pre clinical trials.

By 2012, health care authorities would not certify the approach without clinical testing. This led to caused precaution by health insurance companies to cover the procedure. [Lxiv] The further effect is that this medical option becomes available only to those who can obtain it in another way through private clinics. In stark contrast to Würzel's vision of siRNA delivery for all patients who want it

Beyond 2012 companies focussing on nanoparticles struggle for survival as biotech companies, with support from larger pharmaceuticals and patient groups, move towards implantable delivery systems.

[Lxiv] Challenges remain with bringing the therapy to actual patients. The health care authority's precautionary position and concern about standardised clinical testing approaches causes insurance companies to be cautious also in covering this new therapy. Regardless of the success shown by researchers in the clinical trials, insurance companies wait for more robust evidence. Without the insurance companies backing, the therapy is then only available for private clinics

2.6 Summary Tables

Important actors outside of the concentric approach (from diagnosis)	Which ones were included in the preparatory material	Actor communities outside of the concentric approach
Regulators, which set safety guidelines and standards **Governmental risk assessment agencies**, explore environmental, health and safety ricks. **Public funding and research and innovation policy agencies**, choose between potential approaches to an issue such as disease by exploring many options, and targeting policy & funding programmes **Insurance companies,** act as gate keepers to allow or reject a new technology. **Labour organisations and trade unions** **Environmental NGOs**, concerned about the fate of nanoparticle and nanomaterials that are used in nanomedicines or other nano-based products **Consumer/User associations**, who lobby for access to, or a particular level of safety of, a new technological product. . **Private investment community** **Users** those who make use of the new technology	**Regulators**, dealing with the complexities of nanomaterials in a variety of industrial settings **Governmental risk assessment agencies**, explore environmental, health and safety risks. **Public funding and research and innovation policy agencies**, an example in scenario 1 is Finland, which plays a prominent role in shaping the nanotechnology research agenda. **Labour organisations and trade unions,** lobby for certain standards in safety for workers in nanomaterial manufacturing facilities. **Environmental NGOs**, promote a precautionary approach to nanomaterial R&D **Consumer/User associations** **Users**, in scenario 1 clinicians bring to attention a design flaw that risks health. In scenario 2 they play a strong role in scrutinising and debating nanotechnology developments via the NanoDiaBlog platform	**Governmental (risk assessment) agencies**, we had a representative from the Dutch National Institute of Public Health and the Environment (RIVM) **Labour organisations and trade unions, we had a representative of a Labour organisation** which provides advice for Trade Unions with regards to Occupational Health and Safety issues.

What elements were chosen and highlighted in the scenarios?	• Codes of conduct and voluntary reporting schemes • The role of intermediaries at the meso-level of coordination (such as industry associations, and research consortia) • Public engagement as part of the governance landscape (in a weak form (scenario 1) and in a strong form (scenario 2) • Health and Safety issues in a number of locations (particularly in nanomaterial manufacturing plants) • Monitoring compliance to codes of conduct and other forms of soft law • Anticipation by all actors is occurring during the early stages of nanotechnology emergence, thus in the scenarios comparative selectors and third parties are involved in the co-evolution at early stages of emergence (in the beginnings of the scenarios). • The role of researchers in this new landscape, through mobilising resources, coordinating consortia and hyping outside of the research domain (to industry, to the public). Another role is as whistleblower.
What stakes were chosen and highlighted in the scenarios?	The stakes included related to the emerging governance configurations and entanglements that could occur based on the outcomes of interactions between particular actors and co-evolving institutions.
Structural difficulty in creating scenarios	The challenge was to write scenarios focussing on co-evolution of governance arrangements, rather than co-evolution from the perspective of a technology innovation journey. This meant that reduction of complexity was more difficult and lead to longer scenarios.
Other support material mobilised?	No

3 The workshop

3.1 The participants

The response to the invitations was very positive from firms, industry associations, labour organizations, but very limited from the researcher side.

Code	Institute	Invited as:
[JV]	**Joppy Vla** MESA+ Optical SS Group	Nanoscientist
[RvdW]	**Rens van der Westhasen** DSM	Company representative
[DS]	**Dilip Shakrabarty** Max Planck Institute	PhD Nanoscientist
[BO]	**Boudewijn Oude** National Institute of Public Health and the Environment (RIVM)	Public Agency
[WK]	**Wolfgang Kehl** Advice for Trade Unions. Occupational Health and Safety. Regulation interest.	Labour Organisation
[GM]	**Gisela Mann** Industry Association (specializing in nanotechnologies)	Industry Association
[JHS]	**Jan-Hein Schmulders** University Amsterdam	NGO dialogue
[GdB]	**Gilles de Boobe** Max Planck, Stuttgart	Nanoscientist interested in Sci-Applications
[RB]	**Rajesh Bouri** MESA+	Research group leader in nanoscience.
[AR]	**Arie Rip** University of Twente	Moderator
[DR]	**Douglas Robinson** University of Twente	Workshop organiser
[CSE]	**Clare Shelley-Egan** University of Twente	Observer interested in ethics
[TP]	**Tilo Propp** University of Utrecht	Observer interested in technology assessment

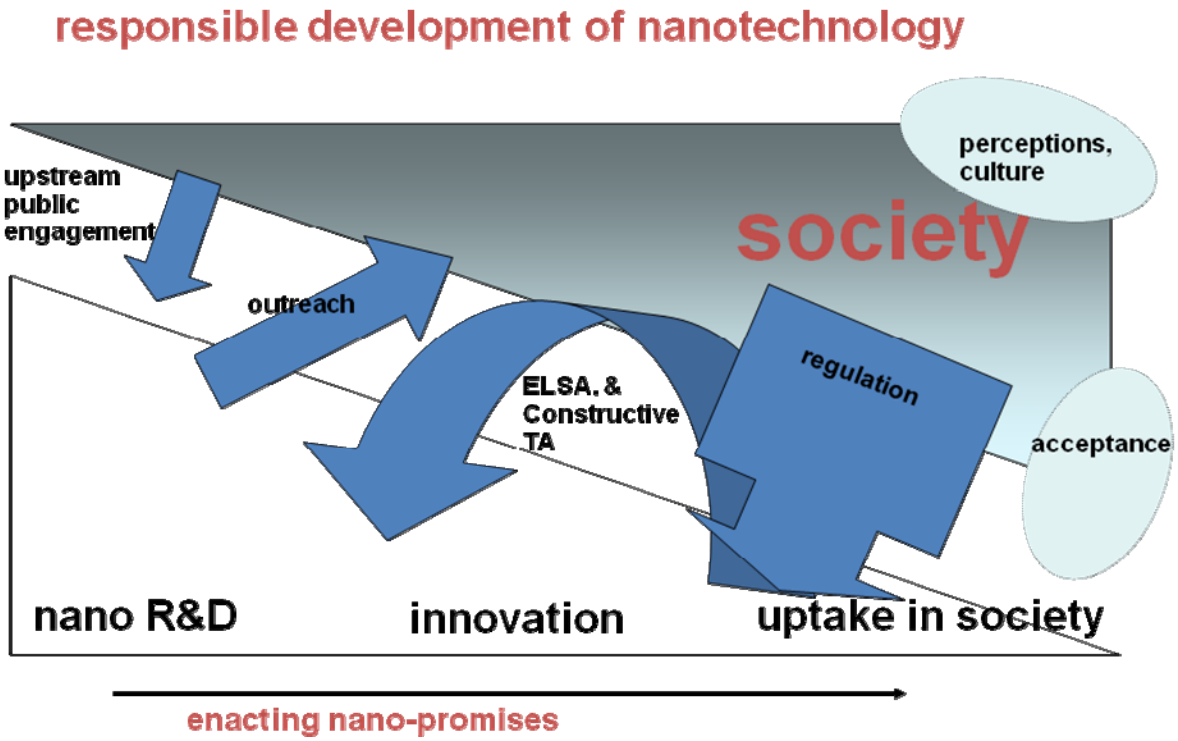
3.2 The workshop interactions as stretches

The workshop started on time, and in the round of introductions it appeared that some participants had been interacting already, while others were relatively new to discussions about nanotechnology. The atmosphere was constructive with participants who were interested in discussing and seeing what they could learn. The organizers presented the premise of the workshop, the exploration of possible configuration of governance arrangements in terms of the emerging interest in

Responsible Research and Innovation in nanotechnology. The Chair emphasized the importance of "probing each other's realities" The aim of the workshop was not to reach consensus but to stimulate learning.

One participant, [GM] who works for an industry association, wanted to clarify the status of the discussion and what parts of it will be used later. The chair [AR] proposed to follow the (UK) Chatham House rules, as had been done in earlier workshops. There was agreement that insights and views can be used by other participants, but not attributed. The other question about the report for Frontiers would be handled practically, by checking the draft text with participants.

The organizers began the first session with [AR] presenting a slide on the trend toward responsible development of nanotechnology, and then pointing out that this paints a "rosy picture" of a possible trend. The aim of the workshop could thus be to make this picture more complex.



The discussion was then opened up for comments on the scenarios but it shifted almost immediately to substantial discussion.

Stretch 1 Limited role of public agencies

The participants thought of the scenarios as having good content overall while they said some elements and specific issues needed further discussion. A first stretch in the discussion was initiated by a nanoscientist [GdB] saying that the content of the

scenarios was very good, but that public agencies seemed to be impotent in the scenarios. [AR] asked whether, "this impotency was an artifact of the scenarios or if it is actually present in the world of nanotechnology?" A participant from a public agency regarding health [BO] responded, "Governments are not impotent but cautious." He continued saying that, "Governments are hesitant to implement regulation too soon. Also current regulation, especially the EU REACH, also covers nanotechnology and nanoproducts so that manufacturers have a responsibility."

Another research scientist [RB] recognizes this and then reframes it by adding that "public agencies are acting in a pragmatic fashion because they don't want to stifle innovation." [RB] points out that as most of the existing legislation covers nanoparticles in general terms, the responsibility lies with the manufacturer; so until there is hard evidence available, governments would naturally be reluctant to go into hard legislation and prefer learning to occur.

Picking up the point of evidence and learning, [GdB] reacted by mentioning examples of use of nanoparticles (in micro and nanoelectronics) and the fact that there are already indications of specific nanotoxicity as opposed to bulk forms of the same material. *[So one can start regulating ...]* [BO] responds: "there will be a natural regulation lag: if nanotoxicity can be proven, micro regulation wouldn't cover this and then (only then) must regulation step in".

Participants positioned themselves (with [GdB] almost as a devil's advocate) and mutual probing began, pushed further by [GdB]. [GdB] follows with "but who is responsible?" A participant from the NGO world [JHS] answers "Employers are responsible until such time that toxicity can be proven – then regulation is needed." This leads to a question, from [GM], about further clarification of this issue, "especially because of differences in context: the differences in existing legislation in Europe and US have implications."

At this point a participant linked to trade unions who had worked on regulatory issues generally, [WK], intervened by asking for clarification from [GM], and the rest of those who had spoken already, about "what 'responsibility lies with the manufacturer' actually means and how regulations are fulfilled?" He thought "there is a mix of regulation and employer responsibility", and proposed that it is important to look at the interaction between soft law and regulation and the overall effect of such interactions, and also that the issue of compliance and who monitors should not be forgotten.

After articulating important questions for the overall theme of the workshop, [WK] went on to comment on the scenarios, and in doing so, got responses which in effect created a new stretch.

Stretch 2 Zooming in on risk management and responsibilities

Shifting back to the scenarios themselves, [WK] commented that the use of "nanotechnology" in scenarios as a general label is a bit confusing. This drew a partial defence of the scenarios by [GM]: she felt that the scenarios were "very good quality but also, from her position, rather grim reading - in the sense that no stable and productive regulation emerged." Some elements of the scenarios were unlikely according to [GM]; in Scenario 1 for example she mentioned that it was unlikely that industry would still be using self-imposed standards in 2009. [RvdW] (from a large chemical firm and an ISO working party member) heard her saying that industrial standards would be in place soon, and thus questioned her optimism. [BO], coming from risk regulation, added that, "Only for areas which already have good standards, for example, the medical devices sector, will the regulation be easy." As an expert, he noted that the scenarios positioned standards as 'soft law', but that this is not correct as compliance with standards is obligatory.[147]

Compliance with standards was then picked up by [GdB] to raise the issue whether there are checking mechanisms? [BO] replies, "The checking mechanism depends on the particular product." [BO] shifted the conversation to the specifics of free nanoparticles "the risky area of production of free nanoparticles – products have already been a long time on the markets". [RvdW] and [GM] join [BO] in emphasizing that risk is not the same as hazard (toxicity as such), it includes exposure. "No exposure no risk", thus nanomaterials embedded in products are safe. [BO] modified this by referring to accidents and leakage leading to exposure: so toxicity needs to be known, and it may lead to regulation.

[RvdW] positions his company as responsible: we don't use powders - this is a "forbidden situation". He goes on to say "why pick on nano? Is just another product?" [GdB] responds that he sees a window of opportunity to shape regulation and governance more broadly.[148]

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[147] While the situation may be clear cut in principle, in practice discussions continue, as was clear in the **December 5 workshop in Brussels**. The scenarios were built also on the way various actors took positions in this workshop.

[148] The question posed by enactors - Why pick on Nano? - occurs very often in the nano-world. Comparative selectors see that: nano is new, receiving lots of resources (and growing), has a high degree of uncertainty (hazards – c.f. [WdJ]'s statement, and exposure

Unsure of what responsibility of manufacturer's means, [GdB] asks whether costs are an issue. [RvdW] responds by positioning it as depending on the one hand where there could be liability and on the other what can you achieve in a particular context. [GdB] replied that he was not talking about "good' and "bad" people; [RvdW] [GM] [BO] emphatically replied "We are".

[RvdW], underlining that his company is indeed one of the good guys mentions that his company had "gone one step further by signing the Responsible Care Program." He also asked why all this discussion surrounds nanotechnology specifically, "responsible R&D innovation holds for everything, not just nano."

[GM] stressed that "we *are* talking about good guys and bad guys and this is what codes of conduct are about." [GdB] "As a consumer I don't feel assured by value-based codes. When industry says that they are trying to do some good, I am more interested in what they are actually doing!", further underscoring his position that transparency is needed. [GM] asked [GdB] what he would like to see if he doesn't trust value-based codes. [GdB] stated that he would like to see a system where tensions are balanced institutionally (e.g. judge and jury).

At this point shared positions are emerging. At this stage only AV plays the role of comparative selector.

Stretch 3 Asymmetry of Risk/Benefit (Benefit vs. potential benefit)

Switching gear from discussions of risk assessment, [RB] observes that the group were only talking about risks and asked "what about the benefits?" He felt that very often the benefits get lost in the debate and that benefits should be part of the discussion.

With regards to benefits, [RB] also stresses that, "The discussion surrounding risks come from a very Western perspective; in other parts of the world, the consideration of risks and benefits are completely different." [GdB] agrees that the

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and end of life issues), there are a lot of statements from enactors about the promising applications and how they would influence society. For this reason nano receives a lot of attention. He positions himself as a consumer…therefore a comparative selector. As an interested consumer (the way [AV] will position himself a little later) nano is one emerging thing where there are unknowns and some people are concerned and so there is some pressure to do it right from the very beginning based on the fact that it receives a lot of attention and resources at an early stage. There is an opportunity to talk about life-cycle costs for example. This notion of a window of opportunity was included in the scenarios (nano as a tech not the reason to be victimised, but nano as promising enabling technology where people are anticipating on risks and benefits).

benefits do have to be taken into account and that questions surrounding distribution have to be posed, however, he felt that it was fair that the Western ”rich country” perspective was the dominant one as the West is developing nanotechnology. [RB] outraged mentions that he originates from the developing world and goes on to describe some of the transformative potential of new technologies on the developing world. One of the workshop organizers [AR] commented “It appears from this discussion that the benefits and risks of nanotechnology are not just a matter of the absence of techniques but also related to issues of distributive justice.”[149]

Moving away from the heated confrontation with [GdB] went on to say that thresholds of risk are very different in different situations and that “it is not possible to have a code that takes all these thresholds into account.” He goes on to say “The current problem that technology absorption is immediately at the global scale. There’s no time to wait and see.”

[WK] points out that “Before risk/benefit analysis can be carried out, it is necessary to think about benefits vs. *potential* benefits; there is a need to analyse what was predicted and what was the outcome.”

Whilst other participants appeared to accept his point, they do not pick up on the issue of asymmetry in current speculations on the future. One of the Frontiers Adminstration staff (Monique ‘The Mo’ Snippers) pops her head around the doorway to announce that lunch will be served, and the meeting is adjourned.

LUNCH

Stretch 4 Ethics of promising and ethics of engagement

Lunch was a hot/cold buffet allowing the break to keep more or less to time. When the participants were seated, [AR] launched this session by handing out a 2 page extract from the European Technology Platform for Nanomedicine (ETP) Strategic Research Agenda as a discussion point on creating R&D strategic agendas and roadmaps. In the extract, some visions of what was planned for the ETP were shown.

This example was chosen due to the organiser interest in anticipatory coordination (included in the Scenario 1 as a story line involving the Finnish Government). The ETP Nanomedicine was chosen as a visible organisation anticipating futures, creating visions etc. More importantly although an enactor focussed agenda

[149] Organiser diffuses tension by opening up the floor.

building consortium, the ETP engages and includes selectors such as patient associations, ethics and society scholars etc. – in a contributory role. This could then be a topic where we could see probing and forcefields being played out. [150]

[AR] shows the rough diagram of an innovation system that was in the preparatory material.

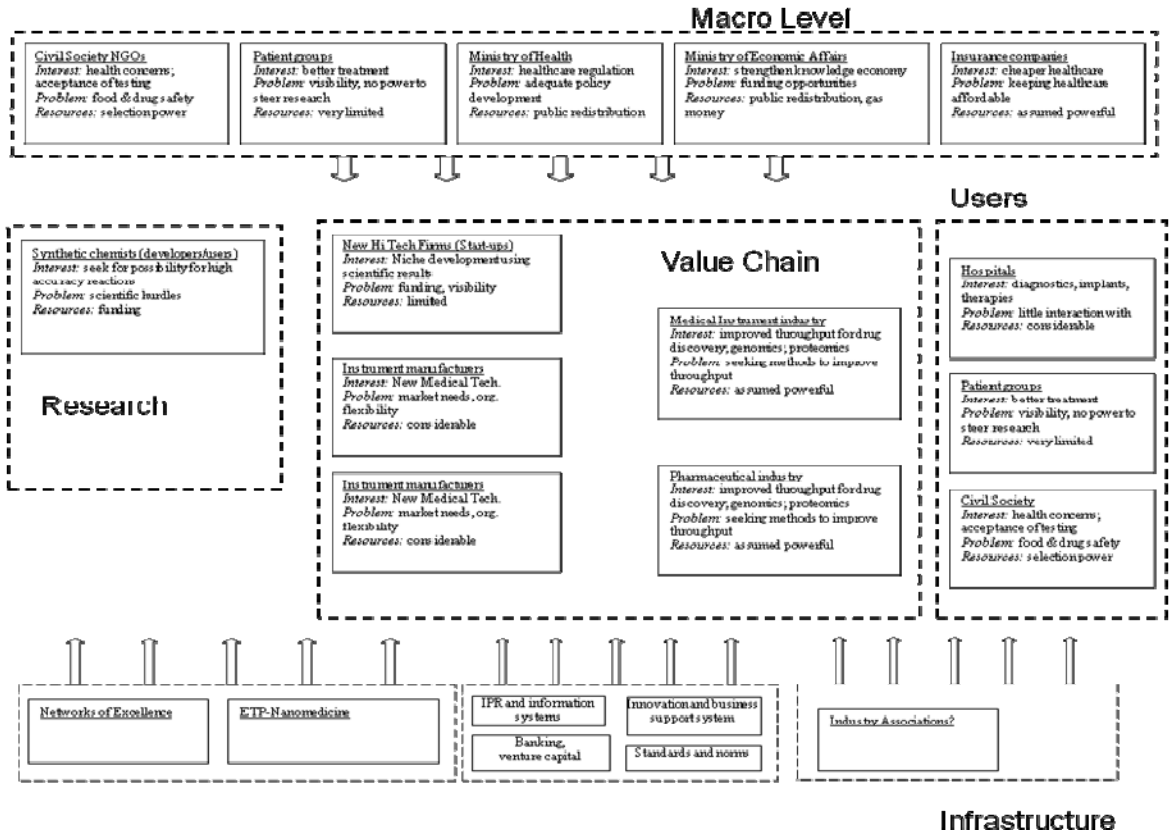

Figure 5: A rough outline of an innovation system presented as a starting point for the afternoon discussions

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[AR] opens up the discussion with the question "looking at the overall system. What sort of responsibilities and roles can you identify and locate? There are unclear projections of ETP which seem inflexible with respect to changing scenarios of the larger socio-technical environment."

Acknowledging the diagnosis as accurate, [RB], who participates actively in this ETP defends it by rationalizing the process in which the timelines for technology development were developed. Highlighting that the strategic research agenda (SRA) was pragmatic and that the timelines were flexible (*in his perspective)*, he comments that the targets for the first two years were achievable while the targets

[150] Also, two of the participants took part in the ETP Nanomedicine visioning exercise ([VS] and [GV])

for five years were "blue sky thinking". "The vision/agenda document was not the place for considering negative aspects". Furthermore, he said that, in his view, the document is there as a living document that will be adapted to circumstances.

This comment by [RB] focused the discussion on the ETP itself rather than rather than on the responsibilities in the overall innovation system diagram.

Emphasizing that the goal of the document was to shape EC funding [RvdW] went on to say that "Ethical aspects had to be included in the SRA in order for the EC to accept it, thus making the inclusion of ethics tactical ploy – don't take it too seriously!" [RvdW] went on to say that the reality is that promises where necessary to get funds, "This is also the way to bring the next generation of research about." [RB] Agrees that the inclusion of ethical, societal and corporate responsibility issues was "only a token inclusion."

[GdB] asks [RvdW] and [RB] whether other paths/routes to the envisioned benefits (such as the five year goals) are in place? Any "contingency plans"?[151] Responding emphatically [RB] states that "this is a living document" and "one must revise the vision if the reality doesn't fit".

One of the organizers [AR] mentions that the ETP is still anticipatory coordination and hence a new actor – realizing the benefits of nanotechnology. [AR] goes on to say that that although ETPs bring different European players together to work towards achieving consensus, it could be better; the platforms give social scientists, etc. a natural platform to introduce ethical, societal issues, etc. For example, the Ethics Board of Nano2Life was involved in drawing up the ETP Nanomedicine document.[152]

[V]S agrees that the ETP approach provides platforms to inject new approaches *and thus new opportunities for responsible innovation*

At this stage, [DR] sees that there is some discomfort in the audience. Discussions are dominated by those two involved in the ETP. [DR] and [AR] signal to each other that the strategy should be to let the conversation flow a little bit longer and if little interaction occurs then they should intervene.

Perhaps feeling this discomfort (through silence from the other participants) [RvdW] announces that perhaps more explanation is required on ETPs that "They

[151] Research scientist positions himself as a selector_ probing the world of enactors.

[152] This comment was made in order to open up the discussion to those not involved in the ETP by highlighting the fact that it is a new actor, making claims, shaping emergence. It also links up with the overall question of roles and responsibilities (the original question for the afternoon).

are constructed so as to write proposals for the European Commission Framework Programmes. They do not do their own research or put in their own money."

[JHS], who has been silent all afternoon, asks whether it a kind of "lobbying machine"? [*with regards to first pickings of the European Commission Funds*]. [BO] draws attention to the fact that those involved in setting the agenda in the ETP are sitting "in the front row" when the funding is handed out. [AR] clarifies that it is not a traditional lobby but still is a lobby and a transparent one, producing vision documents. [BO] (with a note of skepticism) asks: "Writing proposals for which the money goes to others? " He looks around, particularly at [RvdW] and [RB], but nobody picks up his gauntlet.

[JHS] probes further about the role of this new actor, "Will they limit themselves to agenda-setting or do additional things?" As an example he ask whether the ETP plays a role in the acceptance of nanotechnology and how does the ETP determine the agenda?

[RB] asserts that there is a role for the ETP and with that in mind "There were many people involved, for example, through a public consultation and the involvement of the usual suspects like the Ethics Board of Nano2Life." He went on to remind the other participants what the goal of the document was to provide justification (to the EC, politicians, etc.) for investment in nanotechnology.

[AR] shifts the discussion to regulation by asking the group whether national regulatory agencies are interested in ETPs? [BO] adds to this question, "Do intermediaries advising these agencies assess whether a particular product safe to use? "

[RB] makes a separation:"Regulation details have no place in SRAs. These initiatives are only about direction." An organizer [DR] pushes him a little bit: 'With ethical WPs on board there is also voluntary reporting'. [RB] after reiterating the general goals of the ETP to be setting direction, mentions that some patient organizations were also involved.

This triggers a shift in the conversation, and opening for probing by comparative selectors.

Building on the claim that some patient organisations are involved in the SRAs, one of the organizers decides to push further into this inclusion of selectors in

enactor anticipatory coordination. He wanted to know how the patient organizations were included in the ETP.[153]

One of the observers [TP] felt that there could be an ethical conflict between patient organizations and the visions set out by the ETP: How do you reconcile involvement of patient organizations with flexible roadmapping? Is it ethical to change roadmaps?

The two vociferous participants who frame their interactions as comparative selectors find an opening into the discussion. – an opportunity to probe.

[WK] wanted to know how patient organizations are used. [RB] replied that patient organizations are used as a means to incorporate ELSA issues. [GdB] wanted to know whether broader measures of benefit such as health, safety and lifestyle issues were being considered in the targeting of particular beneficial applications in the SRA. There was no substantial response except reiterating the role of ETP as a way of directing funding.[154]

Breaking his silence [RvdW], who earlier positioned ethics as a tactical ploy not to be taken seriously, picks up on the points made by [GdB] and [WK]. He felt that an ethical question was visible in terms of ETP and incorporating patient organizations and other societal actors – is it ethical for researchers to team up with these patient organizations and change their documents willy-nilly?

This shift of a key enactor in the workshop, jars the discussion. At this point you can see some positioning. TP also mentioned the ethics of enrolling selectors to justify one's own ends but not living up to the bargain. The issue has been elaborated on by [GdB] and [WK] in their role as comparative selectors, which gave occasion to the enactor [RvdW] to consider his ethical stance on engaging.

[RB] doesn't react directly to the question but returns to the potential for including such associations through reference to the US "patient advocacy groups are very influential in legislation in the US"; this phenomenon, he said, is only somewhat developed in Europe but "it's on its way".

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[153] The question was framed to explore what were the consequences of their engagement. Consequences of engagement are included in all three scenarios (a) token gesture with zero effect – Scenario1, (b) token gesture turning into something more substantial: Scenario2 and(c) individual attempts to mobilise resources through enrolling patients – Scenario 3.

[154] Forcefields are made more apparent as probing continues. Here and NGO probes research scientists on his opinion on a specific issue.

[GdB] doesn't allow the topic to be closed and brings up the issue of making promises be they explicit promise of a roadmap/SRA in the ETP, or implicit promises to patient organisations 'if you give us your input we will use it and respect it'. [GdB], "Don't you think the ETP is playing down these promises?"

[RB] admitted that individual scientists do sometimes indulge in "flights of fancy" when writing their research proposals, however experts in the field can distinguish between hype and reality. One of the observers [CSE] responded to this, "What happens with other stakeholders who can't distinguish hype?" [RB] answers by referring to mavericks, "The actions of a scientist who hypes up their research when talking to a journalist cannot be condoned."

A coffee break closed this stretch of conversation, however, during the break, one of the organizers followed up on this and asked [RB] how nanoscientists can be held accountable for hype; he replied that the peer review is the method of accountability for research scientists.

Stretch 5 What governance mix and who is responsible.

At this point (after the coffee break) the organisers shift the discussion back towards the central questions posed in the preparatory material "What elements of responsible research and innovation make sense to the group? What dilemmas are there and what could be done. What roles and responsibilities and where should they be located?"

The first reply to this comes from [RvdW], who replied responsibility lies "all over the place". A workshop organizer pushing [RvdW] for further elaboration (and using an example of the case of nanomaterials and whether we should go towards existing regulation?) [RvdW] replies that he felt that the responsibility is spread over a range of actors who should take the lead, "One can look to the European level to cover all aspects of health and safety for society." He went on to say that, "Ideally, this should be done at a global level; the OECD has that role and they are quite successful but they should do more".

Linking back to earlier discussions, in particular the [RB]/[GdB] on 3rd world framing of risk/benefits , [RvdW] goes on to say that the judgment of the safety of a compound can't depend on the country, as the application or use may be acceptable in certain societies.

[RB] adds that he felt that large multinationals corporations are pragmatic; companies make decisions based on questions such as: is the use of a particular

technology acceptable in a particular culture? Also they won't break the law. [RvdW] adds to this by stating that his multinational chemical firm has a universal approach to safety across the countries in which it operates.

[WK], *with his previously announced interest in the interplay between regulation and codes*, asks "What about voluntary codes? From a regulation point of view (enforcement agency) you can scrutinize companies without codes." [GM] (*who was involved in a code of conduct project at the time of the workshop*): "Voluntary codes don't substitute regulation but are complementary. The "downside" to codes is that they can give rise to litigation cases. That's why codes should be complementary to proactive regulation. US companies are reluctant to sign-up."

[AR] "Nanomedicine is an easy case, we can switch to more challenging cases. Nanomaterials is more of a going concern."

[GM] changes the course of discussion to firms and the difference in national regulations and legislation culture, "It's a huge administrative burden for multinational companies to have different rules for different countries or one policy." [BO] comes in with his own diagnosis, mentioning that "The burden of responsible innovation isn't only on the companies: *RESPONSIBILITY* is all over the place but there are also different clusters of activities. In nanomaterials for example: there is too much variety in the production methods - so you can't make homogeneous claims.

[GM] continues to defend codes of conduct, "The medical sector and pharmaceutical industry are so highly regulated, they are the least controversial. Codes can be implemented tomorrow along the supply chain. Part of the code of conduct is not to do reverse engineering."

[BO] rebukes this remark, "That's ridiculous. You need/want to know what is *in* a product". Having said that [BO] doesn't offer an alternative to the codes and points out that regulation will always lag behind science and technology development. [RvdW] stresses that this means that the supplier has the responsibility to guarantee safe products. [BO] responds by adding that the end-used must also have the relevant information.

[GM] follows on from this by highlighting that nanotechnology as an enabling technology and one elements of broader and more complex value chains, "Because companies are in supply chains, they cannot act in their own regulatory vacuum. Codes don't say don't do x, y, z."

[AR] responds, "Voluntary codes have problems identifying who is in the club." [GM] says "Nanotechnology is neither industry nor market but an enabling

technology." She gives an example, "suppliers may not be nano, company may be nano, customers are not a nano-company. So is it nano? Because of this situation the code has to be flexible. A code is no exemption for regulation present or future."

[DR] questions how signatories to the code can be monitored? [WK] rapidly following up on [DR]'s wanted to know if there is an overview of companies who are not adopting the codes and whether regulation could be augmented by codes through directing regulatory activities on those companies.

[BO] zooms into the case of the Responsible Nano Code effort lead by the UK, feeling that there are issues in the specific details. In his opinion, "only very big companies can adopt the Responsible Nano Code, in particular, Principle 4". *("Each Organisation should carry out thorough risk assessments and minimize any potential public health, safety and environmental risks relating to its products using nanotechnologies.").*

[RvdW] responds that if a company is not able to carry out risk assessment, they cannot bring out a product, thus regulation won't matter, small companies are no exception - if a company can't do that it shouldn't market the products. [AR] suggests giving risk assessment support for SMEs in order to fulfil Principle 4.

[BO] comes back out of the specifics, "Let's not forget that only a small fraction of chemical compounds currently on the market are (sufficiently) characterised in terms of toxicology."

Seeing an opening, [GdB] builds on this diagnosis with historical precedence's which may be paralleled by nanotechnology, "There are instances, he said, such as Tobacco, Asbestos, VioXX, where there was knowledge about risks but not made public. Perhaps whistleblowers[155] should be protected in order to make that K accessible." [AR] points out that this sort of protection can also be abused.

[RB] returns to the issue of national differences and risk thresholds mentioning that risk recognition is intertwined with national litigation procedures. [BO] argues that, "However precise regulation is (size 100, 200, 500 nm) companies will find ways to circumvent regulation." "So there is a place for codes and best practices", replies [AR] "soft law is an attempt to solve that problem".

The allotted time for the meeting is up, this is announced by [AR] but [GdB] indicates that he wants to make a comment. "What I would like to see is a place where civil society, small companies can ask for knowledge about toxicity and

[155] Note that whistleblowers and their activities where described in Scenario 2.

risks, and linked with that a space for asking for the production of new knowledge, as well as a role for lay knowledge."

With that final comment, which has summarized some of these discussions of the day, the session is closed and participants depart.

3.3 Summary table

Actual composition	1 senior researcher, 3 junior researchers, 1 large firm, 1 industry association, 1 labour organisation, 1 public agency, 1 communications scholar, 2 observers and 2 organisers.
Degree of heterogeneity	Heterogeneous (66% enactors)
Last minute cancellations of participation and its impact.	Yes, one SME who worked on the site of the workshop (MESA+) cancelled during the morning of the workshop (5 minutes before the start of the first session).
Stretches in the discussions Organiser initiated and taken up = O+ Organiser initiated not taken up = O- Participants initiated and taken up = P+ Participant initiated not taken up = P-	O+/P+/P+/O+/O+
Explicit reference and use of the scenarios	++ For example, in stretch 1 the participants drew on elements of the scenarios and in stretch 2 participants pull out specific elements of the scenarios, evaluating their quality and discussing the 3 scenarios as a whole (cf. [GM] applauding the quality of the scenarios but also noting that they were in her opinion grim reading).
Implicit reference and use of	=

the scenarios	There were many explicit links to the scenarios. Participants seemed to be aware of the content and the elements, the nature of the stretches of discussion meant that the preference was explicit reference to the scenarios.
Quizzing between homogenous actor group (or with those who knew each other prior to the workshop)	Little quizzing, mostly probing.
Asymmetric probing of the majority group (perceived as experts)	In stretch 4 there is some asymmetry as participants probe the two of their company who are involved in the ETP-Nanomedicine.
Mutual probing in heterogeneous group	Lots of probing. In stretch 1 the labour organisation probes the industry association on interpretation of responsibility. In stretch 2 there is probing across a boundary between participants on the role of soft law (c.f. the discussion of good and bad guys).
Do participants get into broader aspects or do they recourse back to their usual positions.	Yes. The probing over the interpretation of "responsibility" by different participants showed some broadening. Also in the recognition of the asymmetry between risks and benefits (a comparative selector [WK] noted that benefits do not seem to be labelled as "potential benefits" at early stages were as risks always are labelled as "potential risks".

Appendix 5 - Socio-technical and innovation issues and opportunities in implant R&D

1 Starting Conditions

1.1 Preparation through insertion and analysis

The first ideas for this workshop began in April 2007, when I was attending the Third International Nanotechnology Conference on Communications and Cooperation, held in Brussels, 16-19 April 2007. I presented two posters there, one on the TA NanoNed programme, and one on the CTA initiatives underway in Frontiers. At that point I had completed one workshop, and had just returned from discussing in Aarhus the concept of the second workshop on drug delivery (4 days previous).

During this meeting I met a senior researcher at IMEC, BE, who was working on bioelectronics and was interested in the posters thrust, which argued that ELSA and innovation can be bridged with awareness of co-evolutionary dynamics and controlled speculations, to identify productive strategies in the present. The researcher, who I will name for reasons of anonymity, [KS], and I began to discuss some of our mutual interests in brain-machine interfacing. I mentioned my first attempt at developing a CTA on the subject, and he recognised some of the behaviour of the researchers who were cautious to get into such issues. He mentioned, however, that he was impressed with the concept outlined in the poster, and that perhaps, since he was in theory a member of Frontiers, we could do something together. He invited me to visit him in IMEC after summer, since I mentioned that I was busy working on three other CTAs at that time (drug delivery, molecular machines and what would become the first attempt at a responsible development workshop in May).

We had some email contact and planned to discuss further at the 3rd Annual Meeting of Frontiers in October 2007, since this would be hosted by IMEC in Leuven. We met at the event, and discussed with his department leader about the potential project, she was enthusiastic having seen that three had been done already by that time.

We agreed to do something in the new year, since I was busy preparing for the Responsible Research and Innovation workshop. I put forward the idea to the heads of Frontiers, and they agreed to look into the financial situation.

DBS

In February 2008 I visited IMEC, and discussed with [KS] the possibilities. [KS] outlined that his group was about to develop a portfolio of research activities for the next 10 years, and was thinking of targeting the bio-electronics work to brain disorders, to focus the effort and perhaps deliver technologies that would have therapeutic use. He emphasised his excitement about the CTA project, since in his opinion, the research community was oblivious to many of the factors that are important to developing therapeutic technologies such as brain implants, and about user practices. I showed some of the details of the past four TAs and we agreed that a look at broadening the linear model (using the innovation chain idea) and exploring generations of technology development in deep-brain-implants would allow the use of the multi-path mapping tool – both these visualisations spoke to his way of thinking, he mentioned this explicitly when describing his attempts over the previous two months to develop a kind of roadmap which had an unclear end point.

Thus the idea was to get more insight into potential innovation journeys stemming from the currently envisioned research trajectories they were discussing at the time, to understand what factors should be considered, which research trajectories were more suitable, and who to involve in the development process and when. One thing that came out of the visit (which was about 4 hours long, with a tour of the facilities included) was that [KS] took the notion of design as the important part of the CTA, broadening and being aware were important, but what was at stake for him was the development of a reflexive strategy for the group. We had limited budget for the project, and so we decided to focus efforts on gathering participants locally (this also would have the advantage in [KS]'s eyes of possibly allowing connections to be made for future collaboration).

We discussed then and there who we could invite, two experimental neurosurgeons in Belgium had been attending IMEC colloquia on brain-interface technologies, two large medical device firms also (one in Belgium, one in the US and Netherlands). We decided that these could be the core to build our workshop around. The neurosurgeons and firms agreed to attend, and I began the task of researching the field, creating scenarios and a workshop concept and promoting the workshop through the Frontiers network.

Below two summary tables are presented. The first present's seven criteria that were used to both determine the starting concept of the CTA-project and its suitability for the various interested parties involved. The second table shows the contingencies that where an outcome of the negotiation of the project concept, the context of the subject, my degree of control over the shape of the project etc.

1.2 Summary tables

Key elements that contributed to the initial idea for the CTA.	Bio-electronic interfacing was becoming a growing field. One way interfacing – electronic stimulation of muscles, nerves etc was already applied. Micro and nanotechnology was enabling the possibility of two way interfacing. A number of elements made brain interfacing interesting: Nano-enabled bioelectronics was promising advanced interfacing with the larger promise of closed loop implants (those that would detect, decide on a reaction and react to a situation). For the brain, one-way interfacing Deep-brain stimulation had been applied for about 10 years for Parkinson's disease and only in the previous 5 years was it being explored in the labs and in clinics for other disorders. IMEC wished to do create an agenda of research activities that would be useful for applications in the clinics. And so a deeper understanding of innovation journeys, of issues and aspects that are important for clinicians, neurosurgeons, regulators etc would be interesting.
Is it interesting for my study of inserted CTA targeted at broadening enactor's perspectives?	The topic seemed similar in scope as the CellChip and siRNA workshop, in the sense that a research group was about to embark (for the first time) on clinically targeted research and thus link up with innovation and ELSA issues. There was an appreciation by the core researcher [KS] that they work in the concentric frame and for this workshop looking at all aspects is important since they would develop an agenda that would be aware of issues that may become important during the timeline of their programme. Thus anticipation, articulation of issues and probing seemed very possible in this project.
Frontiers partner interests?	**Key negotiation actors:** A key researcher at IMEC [KS] A CTA workshop which would articulate potential issues, user needs and perhaps technical requirements in order to have a more reflexive research agenda for the next 10 years.
Stage of development of the field?	Simple DBS were entering the clinics and for Parkinson's being used in a large population. Micro and Nanoelectronics for interfacing with biological matter was a very small field but growing and gaining a lot of attention under the banner of CONVERGING TECHNOLOGIES
An identifiable community or socio-technical network?	Yes, a small one of microelectronics researchers moving into the field of bioelectronics. For the users there was the area of experimental neurosurgery where neuromodulation technologies (such as deep-brain and Vagus nerve stimulators) were underdevelopment.

DBS

Is there something at stake recognisable to some of the actors in the emerging community or socio-technical network?	No strong external pressure, but recognition from IMEC that non-technical issues would determine the societal embedment of the technologies to be worked on in this field.
Amount of material to work with?	Rich enough. I had in mind an innovation chain and multipath map supported workshop (broadened concentric diagrams) which could be broadened further via more dynamics (in scenarios) and more actors (in the workshop).

Table 1: Identifying and negotiating an area to apply CTA to

Requirements and constraints from the Frontiers network	There was limited budget left in the kitty, and so we had to keep the workshop relatively local.
Level of control over the topic and process by CTA organiser	Full control over the topic, with active interactions with [KS].
Amount of time to prepare the project	5 weeks
Gathering participants	It was difficult to get many people from the Frontiers network involved. However, for non enactors it was easier and in the end had 3 commercial actors and 2 neurosurgeons. However, the commercial partners and neurosurgeons tentatively agreed at first and 4 of the 5 only confirmed a week before the actual workshop that they would indeed attend.
Possibility to interview participants	People were too busy to pin down for interviews. I interviewed the IMEC participants during my visit to IMEC, and also one of the industrial participants on the phone, but the rest didn't have time for interviews.
Available	There was a lot of information available on DBS for Parkinson's

document data	Disease, but little on the rest. It required some extensive desk research to gather information on DBS for disorders other than Parkinson's. Also, there was very little information available on micro and nanoelectronic interfacing with nerve cells or brain tissue (because it was a very early stage field). I attended a 1 day conference prior to the workshop in Paris on nanotechnologies for neuro and cognitive sciences – but it was mostly related to the microelectronic deep-brain-stimulation.

Table 2: Contingencies and ramifications

2 Preparation

2.1 The promising technology

The need for treatment options combined the growing number of patients and, as a consequence, an increased burden on institutions led to a health care crisis in the early 1930s, which provided an impetus to explore various approaches to medical treatment for a variety of diseases and ailments. During this time many physicians were more than willing to pursue a therapy that might successfully treat these disorders and reduce the burden on the institutions, and one area in particular, that of psychiatric disorders, there was much interest in the potential of surgical treatments of the disorder. The impact of lobotomy on the field of psychiatric disorder treatment was explosive and widespread. By the 1950s however, the major detrimental effects of the approach were recognized and alternatives to lobotomy were explored.

In the 1960s, ablative stereotactic surgery was developed and used for a variety of movement disorders and psychiatric conditions. Although largely abandoned in the 1970s because of highly effective drugs, such as Levodopa for Parkinson's disease, and also due to reaction against psychosurgery now sullied with the disasters of the frontal lobotomies, the field has undergone a revival, augmented by an improved understanding of brain microcircuitry and the abnormalities underlying movement disorders such as Parkinson's and neuropsychiatric conditions, such as obsessive compulsive disorder.

Aside from surgical and pharmacological approaches, the first deep brain stimulation dates back to around 1950 were Poole treated depression in a patient with Parkinson's disease. Modern day high-frequency electrical DBS of specific

targets, presented in 1987 by Alim-Luis Benabid and his team in Grenoble, led to the introduction in the early 1990s of DBS for Parkinson's, and has now become widespread with more than 35,000 patients having been implanted to date. The positive aspects, as opposed to other approaches is the argument that the therapy is less invasive, reversible, and has the means of adjustment post operation.

DBS holds several significant advantages over traditional pharmacological approaches to the management of neuropsychiatric disorders. Most notably, electrical stimulation boasts far better spatial and temporal resolution than pharmacological agents. Pharmaceutical approaches focus on systems, and although targeting is improving (see recent advances in drug delivery with polymers and liposomes) targets are still at system level.

Electrode placement, by contrast, can be *sufficiently* specific to stimulate one functional region of a given brain structure while avoiding adjacent populations of neurons. However, size, number and spacing of electrodes determine the spatial accuracy and to-date is a limiting factor. In addition, wave forms remain as simple square waves and one can assume with increased experience of stimulating certain regions of the brain, waveforms could be tailored to be more efficacious that the simple square wave.

Today, DBS is under clinical investigation for a broad selection of neurological and psychiatric conditions, such as epilepsy, dystonia, Tourette's syndrome, depression, obsessive-compulsive disorder, and cluster headache.

Although knowledge of the mechanism of action of DBS is as yet undecided, developments to improve and refine the stimulation process is underway, augmented by technological advances in fields such as microfabrication, imaging and improvement of stereotactic methods to name a few. Although still a niche technology, with applications to patients who have no alternative therapy, the promise of DBS has prompted industrial development in Parkinson's (Medtronic), epilepsy (Medtronic and Neuropace) and in other disorders too

2.2 Preliminary diagnosis

One interesting field of technology R&D focuses on neurotechnologies for stimulating specific areas deep within the brain for motor and psychiatric disorders. Deep brain stimulation (DBS), the chronic implantation of stimulating electrodes in deep brain structures such as the subthalamic nucleus (STN) and globus pallidus (GP), has emerged as a leading treatment for Parkinson's disease, essential tremor, and several other motor disorders over the past decade.

The field is still in its early stages, a niche application focussing on areas where there are no other pharmaceutical based options, but still has a reasonable amount of history to draw upon. Since the first successful thalamic DBS for Parkinson's (Benabid et al. 1987), to date over 50,000 patients have been implanted with deep brain stimulating electrodes.[156] DBS is perceived as having an advantage over prior surgical procedures (such as ablation, lesioning) and neuropharmaceuticals (which often have irreversible effects). Despite limited understanding of its mechanisms of action, DBS has proven effective for a number of movement and psychiatric disorders.

As neurotechnologists look to treat pharmaco-resistant patients in other disorders[157] with DBS, and technology developers rise to the many challenges posed by potential clinical/surgical applications, it seemed timely to address some of the challenges faced by neurosurgeons and neurologists on the one hand, and issues for technology/product development processes on the hand.

In addition, for a treatment to be fully embedded into practice, regulatory and ethical issues need to be explored, shifting health care structures and patient needs/expectations need to be catered to or moderated, and broader societal and policy issues need to be explored. There has already been some experience from DBS already (20 years for Parkinson's and almost 10 years in OCD and epilepsy) but the majority of issues have yet to come – and therefore discussions of issues will be prospective. In addition future studies can swiftly move towards the fantastical and so controlled speculation along with interfacing/integrating experience, perspectives and other knowledge is vital.

2.3 Translating diagnosis into workshop topic and scenarios

Workshop Topic

If managing for the optimum transition of novel technologies from concept to clinical practices is the goal it should be recognised that the many technologies currently on the R&D laboratory tables have a long development time, with many twists and turns, hurdles, barriers and possible setbacks. A useful simplification of this journey is visualised in the figure below. Here the evolution of the technology from proof of principle to embedment in society is charted with the relevant stages to be passed through plotted.

[156] The majority targeted at Parkinson's.
[157] In some cases DBS is thought practical enough to replace some drug-based therapies.

It should be noted that the simplification removes the many feedback and feed-forward mechanisms between stakeholders that reside at various lengths of the chain.

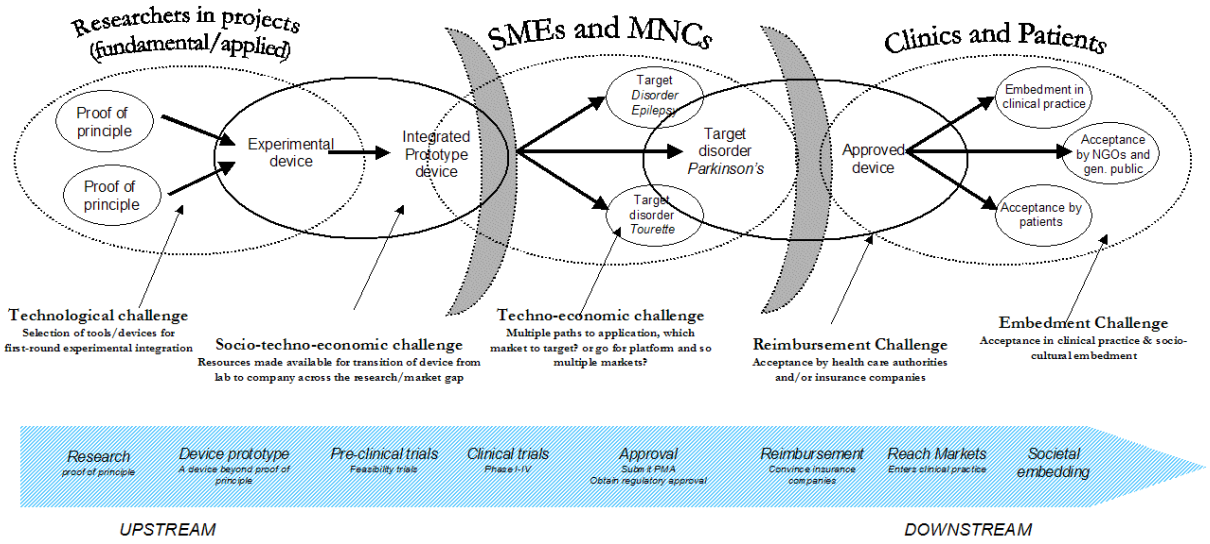

Figure 1: The medical device innovation chain

Looking at figure 1, it shows the necessary milestones to be achieved, but gives little indication of the interactions between stakeholders at each length of the chain, the challenges that are faced at each step, the dynamics at play or the broader issues in which this innovation chain is embedded (broader changes in regulation, in user practices, in innovation policy etc.).

Our focus is on the DBS technology innovation chain, which shows promise for a large number of disorders such as Parkinson's, epilepsy, obsessive-compulsive disorder to name but a few, but many complications are still to be to be resolved. Compounding these challenges, as the DBS devices promise to get ever more complex, they bring with them a variety of other issues and challenges, including

- hardware issues (lead fracture, infection, patient compliance, some cases of frequent battery change etc.),
- side effects affecting mental well being (severe depression, suicidal and manic states, diminishing cognitive function);
- physical effects (headaches, kindling of seizures etc.).
- surgical procedure;
- patient assessment;
- regulatory issues;
- organisational challenges (issues of integration of a number of technologies for example); and

- ethics, broader societal issues (on control) and more specific societal issues (responsibility).

In this project we planned to broaden the linear perspective of figure 1 to include dynamics stemming from co-evolution which manifest in the innovation journeys that occur. The proposed goal was announced as:

> "... by anticipating on the types of issues listed above[158] between all the stakeholders, and remaining sensitive to broader changes in user practices, regulation and policy shifts, present day action can be informed and lead to a better journey navigating the landscape of challenges, opportunities and bottlenecks."

I used a schematic diagram to show the innovation chain with a time-axis, which allowed some issues to be shown, and perhaps entice participants to attend and become involved in the CTA project.

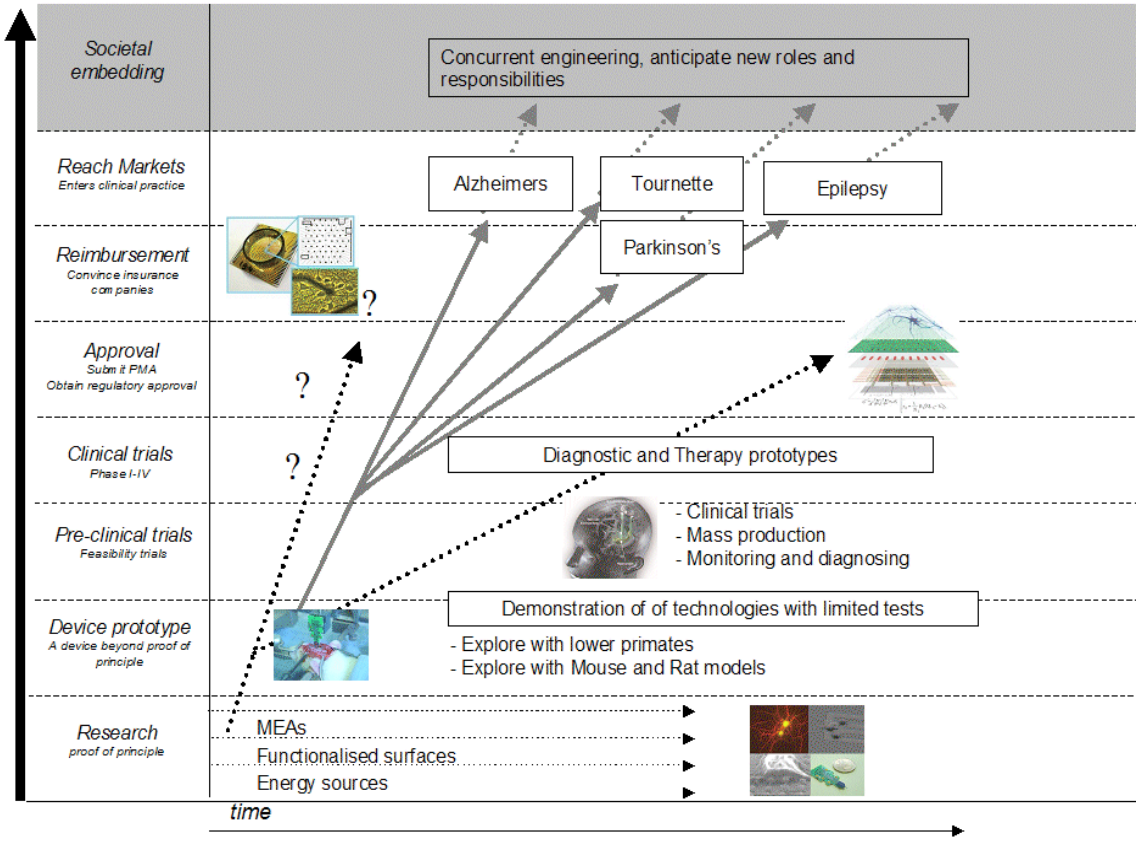

Figure 2: A Schematic of DBS innovation pathways with elements of the innovation chain on the y-axis, and time on the x-axis.

[158] This is not an exhaustive list.

DBS

The following section gives three short summaries of the scenarios that were circulated prior to the workshop. This is followed by the full scenarios with key elements, dynamics and issues shown in annotations.

2.4 Scenario summaries

Scenario summary 1

DBS becomes entwined with national healthcare needs and gains support from public agencies. With the increased focus, like nanotechnology, NEUROTECHNOLOGY becomes a focus of debate. Initial focus on far future transhumanism garners irritation from practitioners who plea for a more focussed and real-time debate. Their wish becomes true, but near-term ethical and societal horizon scanning has consequences for both public support and investment into bringing new technologies into mainstream clinical practice.

In the preparatory report this scenario was visualised with the diagram shown in section 2.6 in Box 1

Scenario summary 2

By end of 2009 Neurologists have a rich and varied menu of options for treating neurodegenerative diseases. A focussed effort on epilepsy in the Netherlands forces practitioners to consider the options on the table and possible near-term solutions. Trials of new DBS devices for epilepsy are successful but cause pressures on management of the clinical cycle and pressures on costs of healthcare (sunk investments across the board needed if radical change is decided upon). As patient requirements move from treatment to improved quality of life more issues arise with a more selective and demanding patient group. Health Insurers remain sceptical and cautious, leading to delays in the proliferation of some medical solutions.

In the preparatory report this scenario was visualised with the diagram shown in section 2.6 in Box 2

Scenario summary 3

Micro and nanotechnologists see many opportunities to contribute to the emerging field of neurotechnologies. Promising technology research lines abound, but little is known about how they will be integrated into clinical practice. Incremental steps

at improving current technologies fare quite well, more radical and elegant innovations fare less well with slow acceptance by neurosurgeons, conservative positions taken by insurance companies with regards to reimbursement and difficulty in obtaining investments.

One team decides to create a platform technology with no claims about applications (an attempt to circumvent laborious medical device regulation) they are successful and enter the market for anyone to use. Regulators struggle to keep up with the diversity of regulation regimes for treatment of the same disorder (for pharma it is extremely long and rigorous, medical device shorter duration, technology platform negligible regulatory procedure).

Technology is ready but investment community remains sceptical and investment in DBS remain with incremental advances – those where markets are already proven, and regulatory process known. Thus improved electrode arrays do make it to market and provide better control (location) and better control of stimulation (spatial and temporal).

2. 5 Scenarios

Scenario 1 – Policy perspective

As part of the UK Healthcare System Initiative in late 2008 experts were invited to present state-of-the-art and future prospects. [i] The aim was to aid the targeting of policy through communication between experts and policy makers.

In a session on *Healthcare System Challenges for Neurodegenerative and Psychiatric Disorders*, one major medical device manufacturer highlighted a number of issues. "The answer lies in new technologies, such as micro and nanotechnologies, Information technology and improved screening."[ii]

One expert: There is a large potential for Alzheimer's disease next-generation acetyl-cholinesterase (AChE) inhibitors combining anti-amyloid activity – thereby tying up two previously separated strands of AD treatment. This can be augmented through advances in drug-delivery as a bolt-on to current bio-pharma approaches

Another example was presented by Neurosurgeon from Scotland college Ally McSmithy. Presents surgical options and Deep-Brain-Stimulation as a reversible and controllable method which has been growing over the past decade and a half [iii]. Shows videos of patients before/after, implant switched on and off. Heroic stories! [iv]

"Truly spectacular" says one policy maker who will be backing this approach. "We are under serious pressure to provide suitable health care for a rapidly ageing population. Neurodegenerative disorders and dementia are key challenges in this case and DBS promises to make a large impact in mitigating this healthcare burden."[v]

[i] An opportunity for tech developers to showcase options and to shape policy accordingly

[ii] Industrial actor in a major event anticipates that new technologies will provide solutions for problems in Neurodegenerative and Psychiatric disorders.

[iii] A number of innovation pathways are possible at the early stage. Pharmaceutical options (AChE) and surgical options.

[iv] (I actually witnessed such videos in a conference I attended in neurodegenerative disease where a teenage boy with Parkinson's was implanted with a stimulating device, they showed him in continuous state of spasm, turned on device and he was still, turned off and he spasms again. This was greeted by a kind of applause by the audience – with no discussion of side effects of such treatment).

[v]Policy maker impressed by what the researcher has shown (unawares of what he hasn't shown) see a possible solution to a key healthcare challenge.

[vi]Once policy interest is fired up, research community accept that more research is needed and ask for funding for further scientific research. (This element was included so as to make visible the ambivalent

The underlying principles need further investigation. More research is needed. Government finances Neuroscience programme. Neu-roads forecasting project set up to scan for possible applications and attract investors.[vi]

Media picks up on the neuroscience wave and draws parallels with other potential technology waves such as nanotechnology and the hybrid discussions of NBIC-Converging Technologies. [vii] NBIC has attracted great interest on potential societal and reflections on ethical issues of human enhancement and transhumanism.

This provides feedstock for the community of researchers in philosophy and ethics of science and technology.

One vociferous Professor in Philosophy of Science "Considering the potential impact of neuroscience and neurotechnologies on future society, it is amazing that such discussions of potential ethical implications hasn't been addressed. In nanotechnology and NBIC there are large numbers of projects bringing together ethicists, philosophers and technology developers."

Dr. Peter Pailthorpe, Neurologist at the University of Hull voices criticism of the new hype and advocates cautious optimism: [ix]

"Neuromodulation with High-Frequency Deep Brain Stimulation is a tool which has the potential to be used in facilitating or possible enhancing normal functions in non-diseased brains. This raises serious questions for us today as the field of Neurotechnology grows rapidly through growing research activities and financing with the consequence of DBS technologies potentially becoming more readily available"

nature of DBS. On the one hand they see a positive effect," switch on the device and the boy is fine", on the other hand in research community itself they acknowledge they do not understand the underlying functions of the brain and do not understand truly why electric stimulation works"

[vii] Hype around deep brain stimulation gets impetus from other hypes (NBIC) and so garners interest. It also inherits concerns and debates in and around these other hypes.

[viii] Here another actor which is part of the nanotechnology world (sociologist or academic of humanities) becomes involved/ it is unclear whether they speak as citizens or as academic analysts but nonetheless they are part of the of the debate (especially visible in discussions of converging technologies).

[ix] A researcher recognises hype dynamics and tries to manage them through promoting "cautious optimism"

[x] Two types of ELSA debates are identified, speculative discussions on far future societies related to

When questioned on future prospects for the technology and ethical issues:

"These far-fetched transhumanist societies which are mentioned in these reports have little to do with present day concerns … what is needed are discussions relevant to current and near-term practices. Speculation on far futures is drawing attention away from real issues for today and tomorrow."[x]

In a plenary session in a prestigious (and thus well attended) annual meeting for neurosurgeons, neurosurgeons were asked to raise their hands for or against certain issues. No one raised their hand for enhancement. One plenary panel member noted "This is conclusive proof that neurosurgeons will not be going down the path of augmenting healthy brain functions." [xi]

Following the early unexpected discovery of augmenting memory during DBS treatment of a 50 year old man with severe Obesity, a project was initiated to explore the potentials of these findings [xii].

Ally McSmithy "It just goes to show how interesting is the field of Neuroscience and how much more we have to learn. More research is needed. – these are very exciting times."

One critical voice (NGO) coins the term Brain Bricolage – the lack of understanding of the actual basis of the research [xiii]. This lack of knowledge and "brain bricolage" is picked up by other actors and used to discredit such practices – emphasising that little is known about the actual processes that DBS cause. Researchers acknowledge the surprising nature of their research – "we know so little about the functioning – there is much more work to be

transhumanism and another on near-term practices.

[xi] This is an abridged quote of one of the Neurosurgeons who had confirmed that they would participate in the CTA project. It reveals a stance of the Neurosurgeons in this meeting, but not of mavericks or in other branches of the community.

[xii] Surprising finding when experimenting with DBS. This is included to highlight that unintended positive effects are expected and highlighted by the researchers, and symmetrically unintended negative effects are expected although asymmetrically they are not highlighted.

[xiii] The notion of Brain Bricolage was included here to highlight the different assessment processes of comparative selectors. Whereas the enactors accept their world of surprising findings and open-ended explorations – including experiments with patients – others see it in a different light.

[xiv] The slogan "Trial and success" is pick up by others, but read in a somewhat different way – focusing attention on standardisations of clinical trials.

done. This is the basis of scientific research."

Media picks up on this. One major broadsheet newspaper publishes article: "Brain Bricolage – A case of trial and success?" It criticises the approach of DBS as a process "Trial and success" and draws on criticisms elsewhere in the scientific community which highlight the lack of standardisations, of repeatable controlled trials and on biased follow up methods [xiv].

The reporter goes on to claim "Although we are much more advanced today in procedures, the lack of control of neurotechnologies is reminiscent of the barbaric approaches of Freeman and Watts in the late 30s. Are we heading for a repeat of the Lobotomy scandal?" [xv].

Outrage from Neuroscience community about the parallels, the damage to credibility is done and the article, igniting scepticism and suspicion in the general public, reinforces the growing disappointment with evidence based medicine [xvi]. The debate around this article stimulates caution by policy makers who refuse to discuss the neurotechnologies per se." We will seek solutions to the healthcare needs of today and tomorrow, and are willing to consider any suitable option".

As public funding becomes spread more widely over options for Dementia and Neurodegenerative disorders (food & health approaches and genomics in addition to neurosurgical, neuropharma and electrostimulation), DBS developers look to the private sector but the investment community remains cautious [xvii]. One analyst captures the mood in a comment to BBC World Service:

"The issue is of whether first-in-the-class is best-in-the-class. We are in the early stages where focus is

[xv] A reporter links up the experimental neurosurgery to the now infamous neurosurgery of the 1930s relating to Lobotomy. This is a fear still present today in DBS, and in most presentations I have seen on the topic try to highlight the difference "we are doing it better than the 1930s" is often said.

[xvi] The latent fear of being linked to Lobotomy causes researchers to react with outrage at the connection made by the reporter. This draws attention from other media and, following this, the general public. Policy makers follow suit as concerns are raised and enthusiasm for DBS begins to wane.

[xvii] Public funding is spread over many options for improving Dementia and Neurodegenerative disorders across the population (preventative approaches also are on the table).

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[xviii] A cautionary approach is taken by investors, "wait and see"

[xix] Ethical debate divide into near-term and futuristic discussions become distinct areas of discussion. Having had fingers burnt, researchers stay away from day-to-day issues of neurosurgery and discuss distance futures (well away from their practice). (This was the case in the first attempt

on building an Intellectual Property portfolio and knowledge infrastructure… at such early stages risks are difficult to quantify and with such large investments, venture capitalists and other investors are waiting to see what happens."[xviii].

By the end of 2010, Neurotechnology R&D continues but at a relatively modest pace. The ethical debate has split in two. One branch focuses on transhumanism and augmented functions still draws the public attention, and tech developers still invited to attend (and do so). Another branch stays closer to current practices, with a proliferation of projects focusing on near-term horizon scanning of ethical issues targeted at clinicians, researchers and technology developers. These have poor turnout. Many burnt fingers with the early neurotechnology hype and "Brain Bricolage" article means that little is done to feedback into ongoing practices. Transhumanism discussions become more comfortable for technology developers and a means of voicing their vision for the future [xix]

at a neurosurgery based CTA project in 2006. When I discussed with lading research scientist about brain-machine interface and CTA, they did not want to attend such workshops because of previous workshops they had attended "I have already had my fingers burnt" said a world leading researcher in the field.)

Scenario 2 – Healthcare perspective

By the end of 2009, for those dealing with, and managing, Parkinson's disease and other motor disorders the selection of options has never been so varied. With developments in Neuropharma, imaging techniques allowing improved stereotactic methods and ablation, and the promise of DBS (and other stimulation approaches) Neurologists have a large and varied menu for the treatment neurodegenerative diseases.

A focussed effort on Epilepsy in the Netherlands forces practitioners to consider the options on the table and possible near-term solutions.

With promising results from initial SANTE (Stimulation of the Anterior Nucleus of the Thalamus in Epilepsy) trials with Medtronic Intercept™ device for partial-onset epilepsy in 2008, a consortium of neurology institutes, start-ups and more mature small enterprises coordinate an effort to develop a device for medical refractory epilepsy [xxi].

Trials are successful and by 2013 the technology begins to be used in a number of clinics around the globe.

As more and more patients benefit from the new device, a number of issues arise which cause issues relating to extra burden for healthcare managers [xxii].

As insurers demand more accuracy in the diagnosis, and advanced imaging technologies become available, data analysis and management become major challenges for an already over burdened

[xx] Many innovation pathways are being investigated for Parkinson's disease. (Note that Parkinson's was the first disorder to be investigated with regards to DBS and is the disorder were DBS is currently applied the most)

[xxi] (This was included to link up with current promises, an actual development of DBS for epilepsy by a large firm, Medtronic) This activity triggers more activity by small enterprises who, following Medtronic's lead, attempt to leap frog through developing more advanced technologies (a strategy announced in an interview with a spin-off company [GB]).

[xxii] The embedment of a new technology in clinical practice is dependent on more than an improvement in technology accuracy, but on organisational issues and clinical practices.

healthcare system [xxiii].

Clinics find it difficult to keep pace with new technologies; specialist training requirements and large cost of instruments mean that clinics seek return on sunk investments before upgrading [xxiv].

One study shows the clinical cycle as an ever-expanding spiral of requirements and responsibilities. Improved diagnostics through imaging and other screening methods for patient selection require an enormous amount of investment or resources. Training issues alone prove a potential burden [xxv].

As an answer to some of the problems, alternatives to open-loop systems (where the device is tuned by neurologist team in the months post operation and throughout the following years during follow up) are foreseen. Closed loop systems where diagnostic – stimulation – analysis and feedback are closed into the same device are the future of such devices [xxvi].

Another device developer mentions:

"We talk of closing the loop for stimulation and diagnostics, another loop that can be closed is patient-clinician-device post operation. It is well known that many epileptics can feel the onset of a seizure in advance, in many cases before our current devices do. We could take advantage of this by allowing patient to control the device, restricting use to when needed thus reducing burden on clinician follow up and using less battery power – and so reducing the need for battery replacement and further surgery."[xxvii]

Although device gains regulatory approval, health insurers remain sceptical:

"Closing the loop of in such a way brings up many

[xxiii] Insurance companies do not want to fund the new technology without clinicians having more accurate data (incorrect diagnosis or use of the technology would be costly to the insurance company). This means more information which has to be used by clinicians, therefore increasing the burden.

[xxiv] Technology continuously improves, but the high cost of inserting it into clinical infrastructure and practice (when resources have already been spent on earlier versions of the technology) mean that clinics remain using older generation technology. Technology outpaces the user.

[xxv] Training of users is an expensive effort (as mentioned in interviews prior to the workshop).

[xxvi] (Closing the loops is vision of the group at IMEC, and was the entrance point to this exercise – is closing the loop appropriate for DBS? Which loops should be closed?)

[xxvii] A number of loops can be closed (or opened). For example the current technology used in DBS, the surgeon sets the pulse rate during the surgical procedure, and cannot change it unless they undertake a further operation. An additional loop would be modulation of the pulse of the device post operation. This could be integrated into the device (closed loop) or shaped by wireless communication – or in the case of this scenario – by the patient themselves.

issues that we have seen already in point-of-care diagnostics and therapies. Responsibility moving from clinician to patient – who is responsible when treatment fails? This is still unclear for PoC devices." [xxviii]

[xxviii] Different ways of closing the loop lays responsibility on different actors.

Evaluation of efficacy of devices shifts emphasis onto quality-of-life indicators. Patients demand more from their device than reducing seizures "Every seizure has a detrimental effect" says one representative of Epilepsy Patient Association. Patients associations begin to lobby health insurance companies to cover costs of Patient controlled devices [xxix].

[xxix] Evaluation of devices shifts from technical functions to quality of life indicators. Patient Associations get involved.

By 2015 tremendous sales in devices and small medical device companies begin to proliferate, linking up with a few key large medical device manufacturers and marketing firms.

Shifting patient expectations and easier comparison of clinics technological portfolio lead to a number of legal cases where patients linked side effects of their treatments to lack of modern technologies [xxx]. This is linked to strategies of clinics to handle the increasing number of new technologies which have led to three routes:

[xxx] Growing patient awareness leads to more articulated demand through legal cases against health authorities on detrimental effects of not using the new technologies.

1. Invest in new technologies and changing clinical practice;
2. not invest and wait and see;
3. have a hybrid centre of tech R&D and neurosurgery

The latter strategy is very successful in adapting new technologies, but state-of-the-art is restricted to regional clusters and thus limited to the few who can afford (both in terms of money and time) to have treatment in these places.

This creates tensions on the healthcare sector where

patients demand choice and top of the range.

Delays in reimbursement agreements mean that closed-loop systems still remain in the realm of R&D or the rich patient.

Scenario 3 – Technology developer perspective

By mid 2008 the rise in interest in, and research funding made available for, neuroscience and neurotechnology means many opportunities for technology developers in micro and nanotechnology.

One research group leader emphasises the opportunities "The needs of surgeons are massive. Compared to current advances in micro, nano and information technology there is a rich resource of possible innovations. Neurosurgeons require; better electrode, better biocompatibility, better control of wave form, better data management, better data management approaches, and speed" [xxxi]

A number of flagship projects are supported through the first wave of funding. Flexible polymer probes are developed with the aim of improving biocompatibility and acceptance of probe and leads in the brain. Other project includes advanced imaging diagnostics and also exploring possible configurations of MEAs for surgical applications to the deep brain are explored [xxxii].

By end of 2009 all three projects have positive results. With the trend in valorisation at research institutions in Europe, these research projects start sprouting spin off companies to commercial their findings.

Polymer probe prototype enters pre-clinical trials. The polymer probe developers are confounded by the conservatism of some surgeons who say,

> *"the biocompatible advantage of the polymer probe doesn't make up for the fact that during surgery I don't know where the bloody hell it is going!*

[xxxi] Researcher see opportunities for micro and nanotechnology for solving some issues he thinks are important for neurosurgeons. (Parallel to the key researcher at IMEC who helped organise the CTA project).

[xxxii] Some more technical details are added, based on expectations and agenda in the research world (stemming from desk research and interviews prior to the workshop). Here three different research paths are followed.

[xxxiii] The pressure for researchers on new technologies to commercialise is high.

[xxxiv] Innovation in technology meets user's practices. Some neurosurgeons highlight the negative aspects, another see positives.

[xxxv] Hearing both positive and negative, venture capitalists behave more cautiously but suggest the

During operation and after!" [xxxiv]

Other neurosurgeons counter this by mentioning the post-operative advantages. Venture capitalists are not convinced "we want to see the flexible probe augmented by better imaging technologies and microprobe technology for positioning the electrode before we will invest."[xxxv]

The MEA project as an incremental improvement on current developments, positions itself as an enabling platform technology with no direct connection with medical world [xxxvi]. This frees it up from arduous and expensive medical device regulation process. The device designed to be versatile becomes very popular.

One group of neurosurgeons in South Africa use the platform technology to improve their DBS for obsessive compulsive disorder. "The reduction in size and the increase control is crucial for our control of psychiatric disorders such as obsessive compulsive disorder and depression".

One of these first South African test patients, on a trip to Austria has a skiing accident. Imaging technique in Accident & Emergency Dept. of Infirmary interfered with device and caused interruption of stimulation and remission of symptoms. Surgery needed to replace the device meant high trauma for the patient who was already suffering from the accident.

This was picked up by the media as a going concern. On the one hand reversibility (the option of turning off the stimulation) is now linked up to being an issue (constant fear of remission?) and the issues of international standards and awareness of DBS and its specifications [xxxviii]. The South African group counter that in most cases there were no problems with patients and that this statistically doesn't affect the quality of the approach. "It is the only available

technologies are improved with the voiced user needs in mind – imaging technologies to help position the floppy probe.

[xxxvi] (This is a strategy that has been mentioned a number of times during my interviews and insertion in the nanoworld. In particular, one neuroscientist in a conference in Paris told me that companies selling nutraceutical and neurocognitive technologies that do not make specific claims about treating or curing a particular disease can market products without gaining regulatory approval required for medical treatments and technologies.)

[xxxvii] A non-medical device accident creates a circumstance not anticipated by the surgeons (the patient was healthy enough to go skiing and broke their leg and comes across other technology that causes device failure).

[xxxviii] (Reversibility is one of the selling points of DBS over other forms of neurosurgery. That a device can be switched off creates an option of control. I inserted this to show that other circumstances could lead to what is now touted as THE advantage of DBS over surgery could, in certain circumstances be viewed as problematic).

solution for a group of pharma-resistant patients who would otherwise lead a miserable existence."

The DBS for OCD accident is drawn upon by insurance companies, who already cautious due to complexity of DBS implants one insurer was quoted saying: "Implants are EXTREMELY risky anyway! This is because of the number of components and reliance on perfect interaction between devices (even the current "simple" Medtronic brain pacemakers have three devices (battery in chest, pulse regulator and recording device in cranium and stimulating probe in the deep brain (and don't forget the leads that connect them all up)." [xxxix] One ablative (lesioning) specialist notes that: "It is all very well to have a device that can mimic ablation that you can turn off when you like. But irreversibility has advantages too… batteries may run out, or there may be interference."

One researcher from University of Pittsburgh says he has the answer "Biofuel batteries which draw power from natural metabolic pathways are a serious option." Such proposals are not taken seriously by many clinicians. "Research can look great but usually when test enters the real-world it (a) may not be useful (b) will not work". Key issues remain with data management and communication with the user remains the most prominent challenge.

[xxxix] (This is a stylised quote from a Dutch Ministry risk assessment organisation in an interview I had in preparation for this workshop).

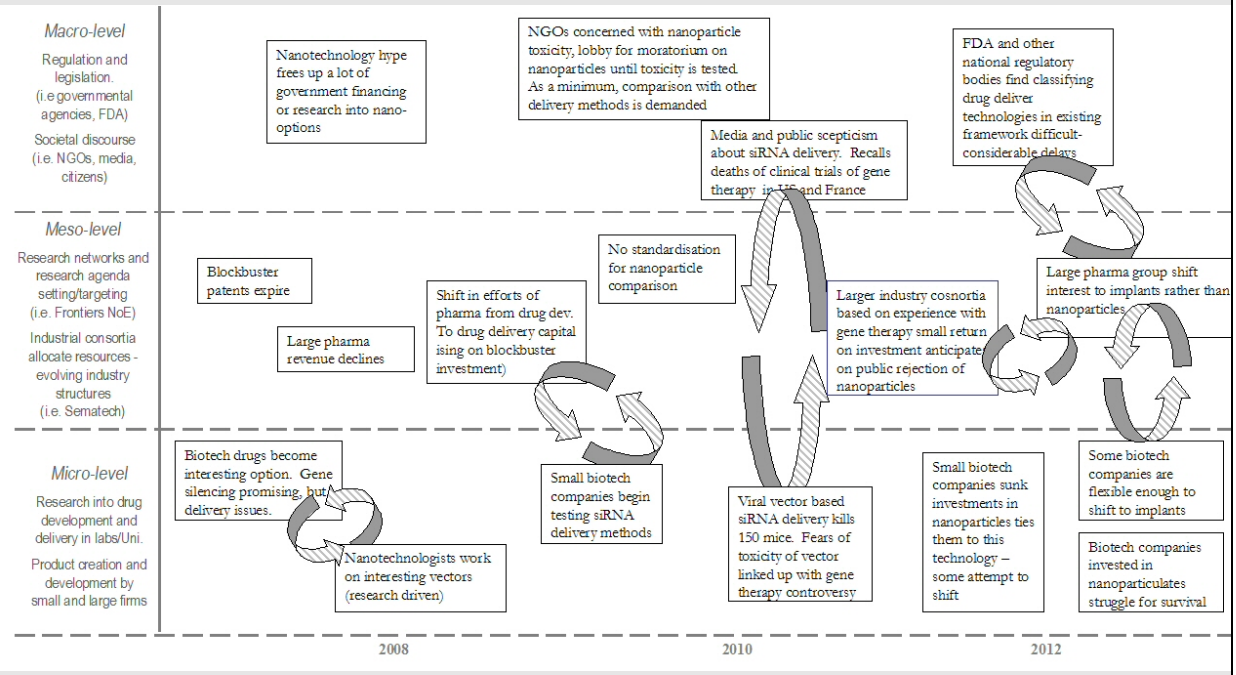
2.6 Other Support material

Additional aspects – Visualising the scenario perspectives in the workshop.

Box 1: Awareness of developments at multiple levels

In the workshop we will use a number of diagrams to visualise the scenarios and issues for the discussion. These relate to the perspective that are sued in the scenarios and that are important for the workshop exercises. We present the format of the visualisations in three boxes here and we will use them in the workshop as a means of visualising the scenarios and linking them together in the case study in the afternoon. Box 1: Awareness of developments at multiple levels

In innovation, developments at different levels influence each other and create complex dynamics, such as the connections between specific projects, shifting industry structures, and policy and societal changes. A tool to map these important dynamics is the 'multi-level diagram' introduced shown below (example drawn from workshop on drug delivery).



The lowest (or **micro**) level shows individual R&D projects in public and private R&D. In our case this could be the exploration of a flexible probes or retinal implants. Management, coordination, but also assessment of ongoing developments elsewhere stay at the level of the research team, and are included in the project.

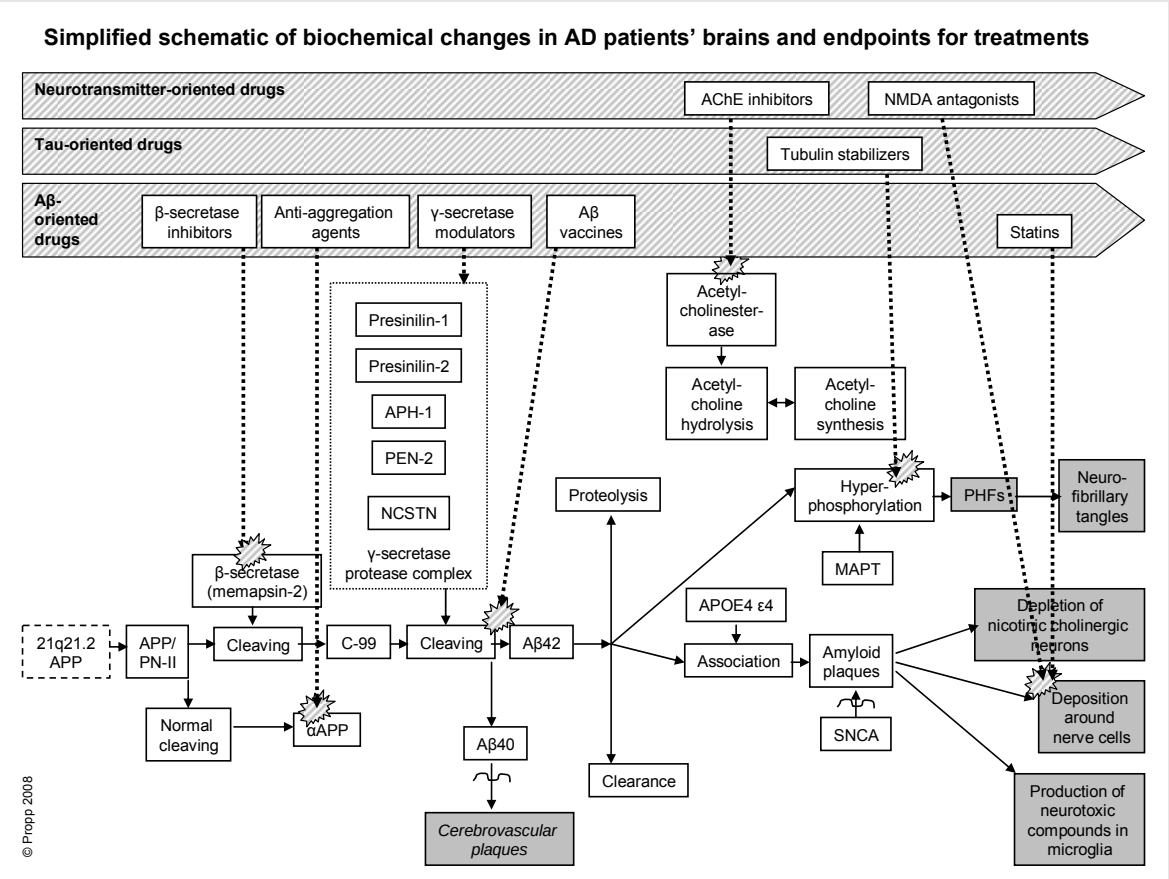
The middle (or **meso**) level describes collective developments of consortia. Industry associations for example, coordinate activities; it is at this level one can place the industry standards and market trends. Coordination attempts at this level can include anticipatory coordination by way of roadmaps (the International Technology Roadmap for

Semiconductors); networks of public research centres (the Dutch NanoNed consortium); or research 'networks of excellence' (Frontiers). Management and coordination stays at the network level.

The top (or **macro**) level describes governmental and more formal regulation; it is at this level that regulation is made, NGOs lobby, societal debate occurs, consumers choose to consume or not to consume (market governance) etc. Management and coordination lies at the governmental level and consumer level, with the many actors such as NGOs, regulatory agencies, consumer groups, citizen associations etc. shaping agendas,.

Box 2: Introducing the user perspective

Those working in the health care sector related to neurodegenerative and psychiatric disorders have many choices to make in terms of diagnostic and therapeutic approaches. Health care managers have to make a trade-off based on technology reliability, surgical procedure; clinical cycle costs (pre-operative, surgical and post operative costs to name but a few).

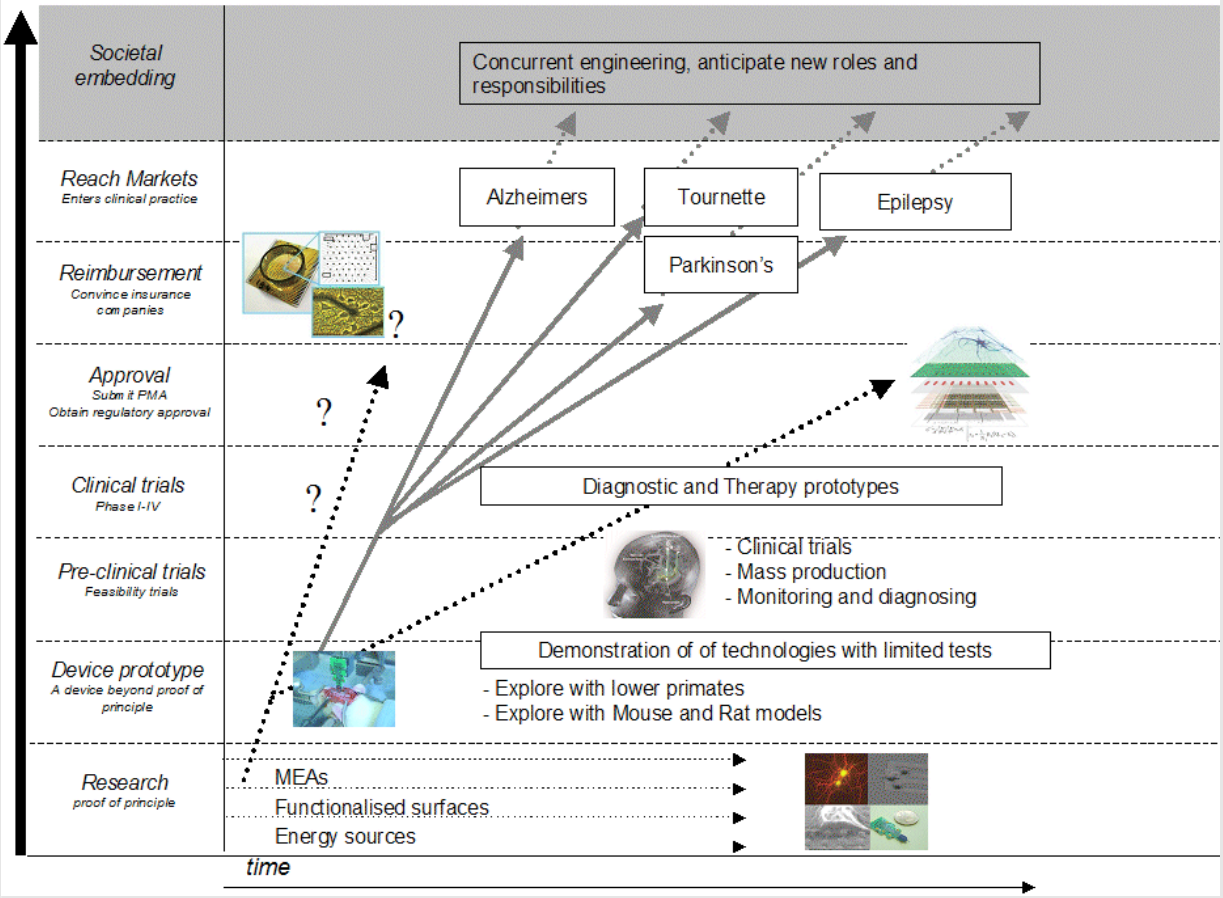


This simplified diagram shows some of the options in treatment of Alzheimer's Disease linked with biochemical changes in the brains of AD sufferers (part of an ongoing exercise at the University of Utrecht). In the workshop we will look at the options open for those dealing with neurodegenerative and psychiatric disorders. Three main streams are can be identified, surgical, electro/magnetic neuromodulation of the brain (or elsewhere) and pharmaceuticals. These are not mutually exclusive and options from all three streams can be components of a clinical procedure.

One interesting question for the workshop could be: what selection criteria are being made (or could be made) in the choice of option for a particular patient or group of patients?

Box 3: Introducing the technology developer perspective

Conventional roadmaps only chart one path of technology development into the future. However, new and emerging technologies have multiple possible futures, which can all be charted into the same visual space. This 'multi-path map', which is another cTA tool, allows for entrepreneurs to reflect on the variety of available strategies, each being an optimum given the particular business, market, regulation, and societal contexts. These futures also include follow-up generations, i.e. improved and augmented versions of a technology (remember the first-, second-, third- etc generation mobile phones).



We will use this diagram as a central component to the case study exploration. By plotting the possible innovation chains we can overlay issues, challenges and bottlenecks (linked with dynamics from the other diagrams and perspectives described above) and develop strategies for action upstream.

2.6 Summary Tables

Important actors outside of the concentric approach (from diagnosis)	Which ones were included in the preparatory material	Actor communities outside of the concentric approach represented in the workshop
Neurosurgeons, neurologists and other clinicians, those who implement the new therapies (first round user) **Patients**, as recipients of the novel therapies that are envisioned. **Patient associations**, who lobby for access to the best therapies for their particular disease or disorder **Regulators**, which set safety guidelines and standards **Health care authorities**, choose between potential approaches to an issue such as disease by exploring many options, and targeting policy and funding programmes around their choices **Medical Insurance companies,** as gate keepers to allow or reject a new medical	**Neurosurgeons, neurologists and other clinicians,** evaluate DBS in terms of their practices, their infrastructure and patients needs **Patients**, evaluate new technologies not on the improved performance, but on quality of life (see scenario 2). **Patient associations**, lobby for insurance companies to make available the DBS technology (scenario 2) **Health care authorities**, c targeting policy and funding programmes in favour of deep-brain stimulation (see scenario 1) **Medical Insurance companies** act as gatekeepers and use this to demand improved performance, e.g. greater accuracy in imaging technology (see scenario 2).	**Neurosurgeons, neurologists and other clinicians,** we had two neurosurgeons in the workshop

What elements were chosen and highlighted in the scenarios?	• Various criteria that users (patients and clinicians) consider when determining their position (for/against) a new medical technology • The role of hype and expectations in different communities • That other actors enable and constrain the potential development and embedment of new technologies, such as insurance companies and patient associations. • The role of the media and the shaping power of labels. In the field of DBS for psychiatric disorders there is a phobia of a phobia against surgical approaches, linked historically to lobotomy.
What stakes were chosen and highlighted in the scenarios?	The stakes were on the successful societal embedding of a new therapy enabled by nanotechnology. Through making explicit the various dilemmas, evaluation mechanisms of the various actors and potential competing options the scenarios showed plausible outcomes of developments and causal relationships if certain aspects were (not) taken into account.
Structural difficulty in creating scenarios	The challenge was to create openings for three different views, one the technology developers perspective of optimising a technology trajectory (scenario 3), a users perspective of comparing and selecting options for a specific task (scenario 2), and a broader multi-level perspective (scenario 1).
Other support material mobilised? If yes, what and why?	Three different visualisations were provided in the preparatory material in order to underscore the tailoring of each scenario to a different perspective.

3 The workshop

3.1 The participants

Code	Institute	Invited as:
[UW]	**Udo Wokkels** Company dealing in cochlear implants	Large firm
[KS]	**Kaled Skaro** IMEC, Bioelectronics group	Senior researcher
[GS]	**Gilbert Slipvis** University of Chalmers	Technology transfer expert
[GB]	**Gerhard Bonko** EPFL (CH) and Start-Up in Neurotherapeutics	SME
[TG]	**Tamsin Ghopal** IMEC	Junior researcher
[DZ]	**Davros Zyberman** Medical Device Manufaturer	Large firm
[KK]	**Kristof Kwak** IMEC	Junior researcher
[PDK]	**Pieter De Koninck** KU Leuven?	Neurosurgeon
[MD]	**Michiel Duvel** University of Gent	Neurosurgeon
[MC]	**Marjon Chimay** IMEC	Junior researcher
[TP]	**Tilo Propp** Utrecht University	Organiser
[WP]	**Wurzel Pertwee** Business partner of an SME in Boston and a venture capitalist	SME
[DR]	**Douglas Robinson** University of Twente	Organiser
[AR]	**Arie Rip** University of Twente	Organiser

3.2 The workshop interactions as stretches

People began to arrive at the Begijnhof in Leuven early, and milled around the coffee and cakes. Some exchanges where already underway between a small start-up firm and a neurosurgeon. When the participants are seated, one of the organizers ([AR] who plays the role of chair in the meeting) mentions that the day is organized to be flexible but would like to stay as close to the announced schedule as possible. There is a short round of introductions which is followed by a presentation by another organizer [DR].

[DR] points out when discussing deep-brain stimulation or implants, there is a speculation gap in the debate: (i) transhumanism vs. (ii) present challenges. There is also an anticipation dilemma, "what are relevant directions and what is the trade off between anticipation of applications and research decisions? The workshop rides this dilemma."

[DR] shows a slide of an innovation chain. "There are challenges along the innovation chain (different actors). You can see three main groups involved in technology development in this diagram; Researchers, medical device producers and clinics/patients. This is what we will do in the workshop, we will explore what are the issues are for various participating groups

[DR] "For deep brain stimulation, we can see some development paths in terms of the innovation chain (y-axis) and broad time frames (x-axis). There are a number of challenges that could affect the potential paths, and exploring these challenges and opportunities is the goal of this meeting." [AR] thanks [DR] for the introduction and adds "By end of the morning session we'll have an overview. In the afternoon we shall try to build a richer picture, a "composite scenario" where differences between participating groups will become visible and will be entrance points for mutual learning."

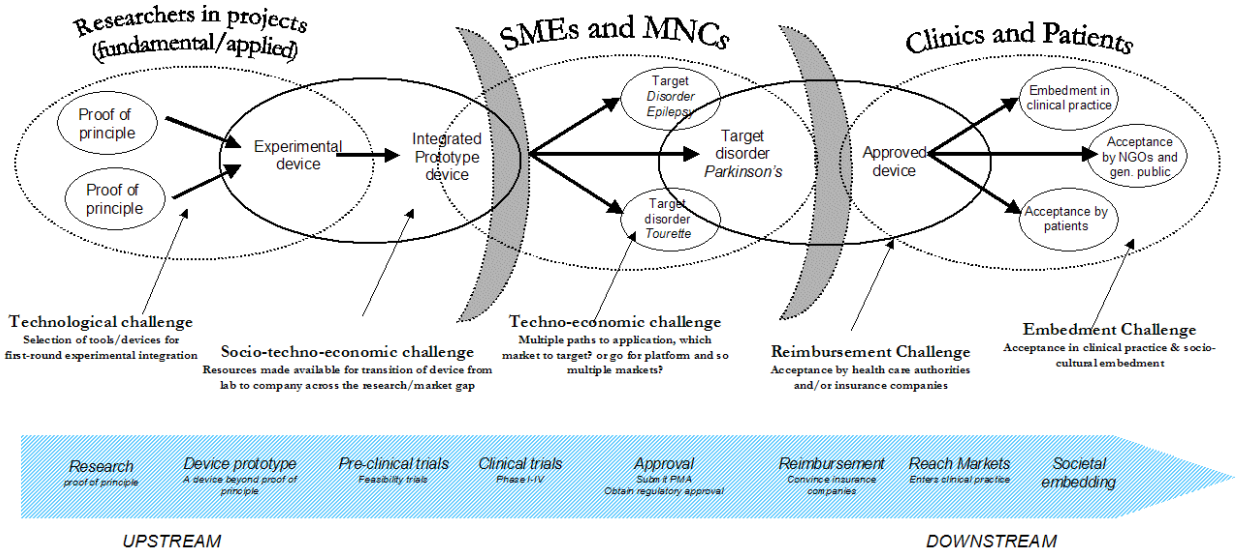
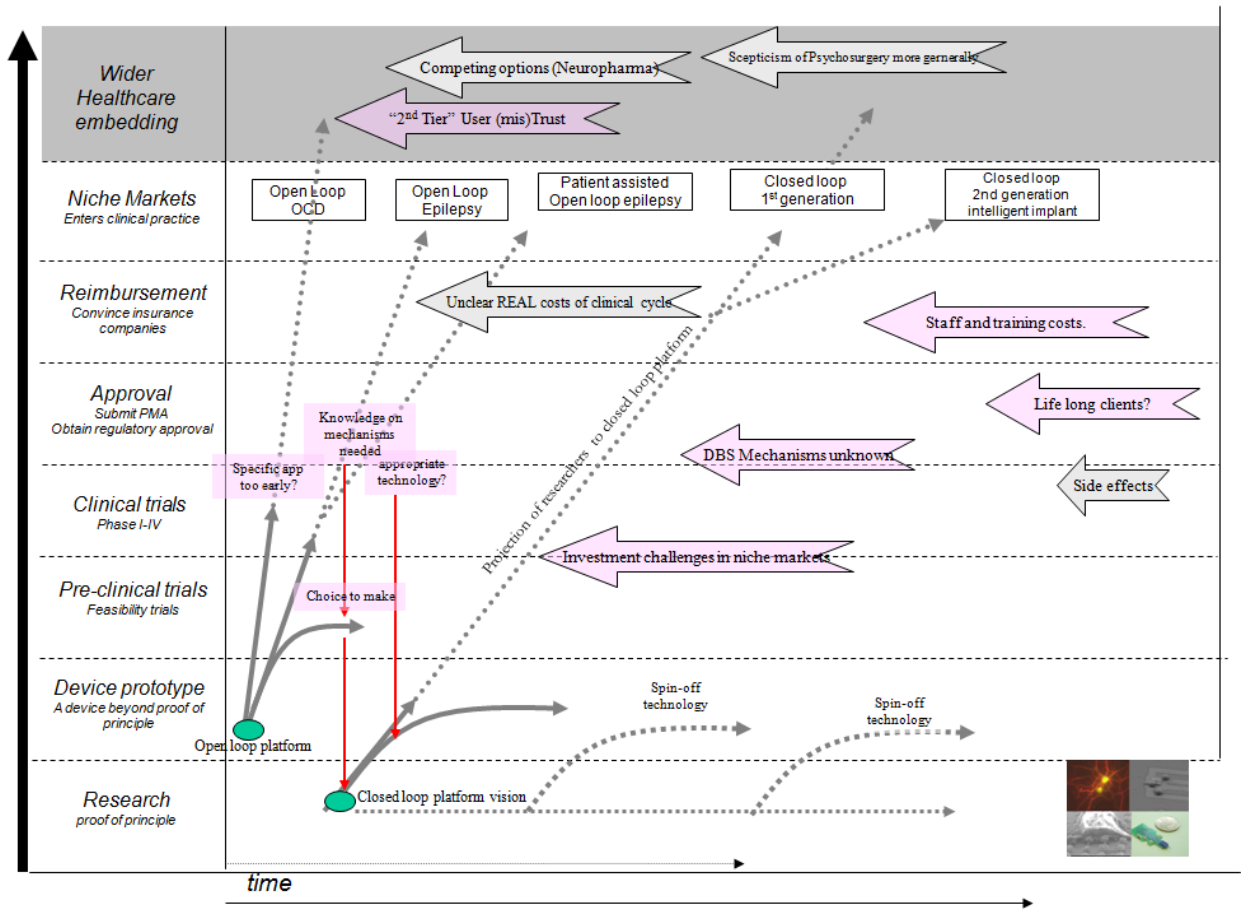


Fig 4: Slide shown in the introduction



One of the participants announces a conflict of interest, [GS] "We work with a competitor of the medical manufacturer in the room; my background is with dental implants in 60s and 70s". The organisers suggest Chatham House rules as in previous workshops.

Stretch 1: Challenges for embedding Deep Brain Stimulation into standard practices

An organiser [DR] recalls that as part of the preparatory work he asked participants to jot down what they thought were the most important elements in the scenarios. "Who has done this?" [GS] raises his hand. [DR], "can you summarise your notes for us?"

[GS] notes that one key aspect is that "Neurosurgeons need to trust new therapies as an obvious treatment choice and as a toolbox. That means proven reliability is important." He highlights that education tools and training for neurosurgeons is important. [GS] looks at the group and says "I do not know who is responsible for providing such training for neurosurgeons faced with a new device." Another key point he mentions is that intelligent treatment-cost analysis is needed which should include all aspects such as logistics during and after new treatment at hospital.

[DZ] agrees with [GS], responding to his question that large medical device manufacturers are responsible for supplying information and training, "As a large medical device manufacturer, we provide the training to our clients." [DZ] goes on to say that in his opinion, neurosurgeons are second-tier adopters. "There are occasional users, such as experimental neurosurgeons, like [PDK] here, but standard surgeons need to be persuaded, that is an important aspect to consider in augmenting the acceptance of deep-brain stimulation devices by the average neurosurgeon."

The chair, [AR], seizes on this comment and poses it to the group "Maybe there's a reason why surgeons don't accept?" An experimental neurosurgeon [PDK] answers, "Yes, there are reasons – you need positive results of random trials – these are later stages in medical device development, we aren't there yet – we're still experimenting."

Stretch 2: User expectations

Another experimental neurosurgeon [MD] enters the discussion. [MD] sees two important aspects. "Firstly there are issues of broad acceptance in standard practices for certain disorders and secondly there are the expectations of people to consider, that is potential patients and their families." He goes on to describe a case of an illiterate Anatolian woman, who after an accident was quadriplegic. Her family (two sons) came to him expecting bionic arms: "In Turkey you can get bionic arms". [MD] "These expectations are science fiction but shape patients' perceptions and their expectations. Of course they are disappointed."

There are nods and murmurs of agreement around the table and [MD] continues "In my opinion, closed loop systems are the next stage. Closed loop systems like the heart defibrillator are fully integrated devices; however this will be very different for the situation of the brain." [DZ] murmurs agreement. [MD] goes on "Also, sometimes closed loop systems may not be advantageous, for example in treatment of chronic pain. For instance in the case of epilepsy I have my doubts since for epilepsy there are 300 activations in the brain a day, and so the device has to handle a lot of noise. For the brain – do we only want to counter symptoms? Or do we want to reverse underlying disease? This is not clear. Therefore in my opinion it is better to focus on technology options at hand – not closed loops. CLS yield no better effects than open loop systems"

An observer [TP], who in his own research is interested in the role played by expectations, asks whether expectations of patient organisation are as unrealistic as those of individual patients, "or is there some sort of expectations management?"

From his experience, [MD] thinks that patient organisations are narrow minded "...they push for their disease. But basic research works differently, it is open-ended." In his opinion, these patient organisations have science fiction type expectations and "researchers have then to deal with such visions of speculative applications. Health Organisations use labels such as 'brain chips' – these get taken up by other actors and create their own reality." [GB] a researcher[159] agrees that patient expectations are unrealistic.

Stretch 3: Which loops?

[DZ] notes that, "Closing the loops aren't too difficult, but the focus should be on developing the physiology lab for understanding the brain, not on creating a better technology lab, it is the physiology lab that needs investment."

Most of the participants nod. [MD] doesn't nod but his response to [DZ] is in partial agreement, "You can't just inject additional electrical signals into the brain. When the brain becomes epileptogenic, this disorder remodels synapses. You need continuous intervention to reverse such remodelling."

[159] It should be noted that [GB] does not announce that he is also starting up a company for fear of some of the large medical device manufacturers present in the room. He discussed this with the organisers, who agreed not to announce this unless he did but for the purpose of the meeting [GB] must not mislead the medical device manufacturers present. This was a curious situation as [GS] announced his relation to a competitor of the medical device manufacturer [DZ].

Another medical device manufacturer, [UW], emphasises that for the brain there is no one-to-one mechanism, and so there is a complex interplay of signalling going on, "this is similar to my field of cochlear implants"

[KS] comes in enthusiastically (in defence of closed loop), "Closed-loop can also work as an open loop you need some technology to work in the physiology lab. But there is no sense in making a closed-loop system if we don't know how to interpret responses. Better to build a platform that can evolve through generations. This is why there should be investments in the physiology side. Advances in biomedical research provide incentives for advancing technology. There is a lot of know-how in implants which comes from technology and user design."

At this stage, about 50 minutes into the discussion, participants respond to each other, involving [UW], [KS], [DZ], [MD].

[MD] agrees that, "Closed loop systems are appealing from engineering point of view but still you have to know where and what to measure as the brain (approximately 6 layers) is complex." [PDK] agrees with both [MD] and [KS], and draws on the example of a Nobel Prize winner, who received his prize in science because of better technology (in this case a centrifuge) which "...enabled the science. So technology is an important driver in biomedical research!"

[DR] refers to workshop goals set out in the initial presentation and poses some questions to the group: "What *are* the tools in neurosurgery? What are opportunities for incremental innovation?" [GB] announces that he is an answer for incremental innovation (*recall that [GB] is a researcher developing electrodes for implanting in the brain and at the time of the workshop, was creating a start up*).

Stretch 4: Asymmetry between product supply and R&D advances

[MD] speaks from his perspective as an experimental neurosurgeon: "There is a contrast between expectations and reality. The density of contacts on electrodes is a real issue; we still use the same four point electrode!" He gesticulates emphatically. "Improving this is a simple engineering project, but this has been a longstanding need from our side. For example meso-temporal lobe electronic implants need more flexibility, that is, more contacts per centimetre. This is a project which we are doing in cooperation with [DZ]'s large medical device manufacturer."

[PDK] says he agrees with [MD] and that he is happy with the technology available and the cooperation with medical device manufacturers, he smiles and nods to [DZ]. But "I would like to know why is it difficult to get a question like [MD]'s answered – is it an engineering problem or FDA approval? Engineers can achieve anything."

[KS] says it is a regulatory barrier not an engineering one. [DZ] agrees: "Yes it is about regulation and market.You don't put wires in people's brains without a strong need, only a small group of patients, at late end disorder stage, get treated with implants." He goes on to say that "each of the small patient groups with a specific disorder have unique needs but the technologies can't be configured accordingly to each one, it is too great a financial burden, and too time consuming. So as a medical device manufacturer you have to go with a general (less specific) general purpose stimulator (platform). This you can get regulatory approval for rather than many approvals for many devices for many small groups. For example as a company, how can we know that deep-brain stimulation for epilepsy will be a potentially successful therapy?"

Stretch 5: Failed attempt to discuss dynamics explicitly

[AR] responds to this asking whether there is something of a waiting game occurring?
"When it is clearer there is a need, you will invest?" [GB] chips in noting that there is an issue of "...who can risk waiting? Large multinationals like [DZ]'s firm can take more risks but smaller companies have to survive!" [DZ] agrees "Indeed, and we watch what the small companies do."

At this stage 11h08, some participants give examples from their practice – a way of characterising issues.

[MD] points out a knowledge asymmetry on the users side "There is a dilemma if you don't have the right product to use, as a user such as myself, you don't know what you're missing." Nobody picks up on this and a brief silence descends on the group.

Stepping in to get the discussion flowing once more, [DR] asks the group "What about a modular system? Also how does DBS compare with other therapy options? At your company [*looking at [DZ]*] how do you map technology options? Do you stay open, wait and see what other companies develop? For example risks could be placed on SMEs"[160]

[DZ] shrugs his shoulders and doesn't comment. [*Too direct a question?]*

[160] [DR] already knows part of the answer as it has been mentioned earlier in the interchange between [GB] and [DZ] when they discussed risk taking by small and large firms.

DBS

[DR] tries again, shifting to companies more generally "Ok, How sits epilepsy with other disorders? What made the companies invest in these options?"

[MD] responds, "At my medical University, DBS for epilepsy was chosen based on selection criteria, specifically treatment resistant epilepsy, and so is seen as a last resort and thus experimenting with this is accepted. There are reasonable results in this case for deep-brain stimulation for such refractory epilepsy."

Stretch 6: Product development challenges

Returning to the issue of product development, [GS] comments, "There is a difference between approaches. The driving force of multi-nationals, MNCs in the [*Innovation Chain*] diagram, is shareholder value. For SME's there is a completely different force that is technology development. The focus is on up-valuing the technology using investment capital."

[GB] leans forward and adds emphatically, "SME's take greater risks and need to make money as return on venture capital. So they have the same driving force as larger firms!"

[KS] looking around the table, poses a question to the whole group "Are there differences between when in the innovation process SMEs and MNCs should be involved? Is there a model, for example, first SME and then after sometime the option is taken up by a big firm who is better positioned to develop it further?"

One of the medical device manufacturers [UW] answers "Small companies also need to look at government funding for development projects. For example my company working on cochlear implants could have been in another country but it chose this one because of governmental funding opportunities. In general I think there needs to be more projects funded from governments that target niches, areas where multi-nationals may not have much interest because they are exactly that, currently unprofitable niches. In that way the government funding would augment the building up of expertise in those niches."

[AR] links back to an earlier stretch of the discussion "There <u>is</u> then, something like a waiting game. Companies waiting for research breakthrough, watching other companies activities. How to overcome this? We need to come back to this in the afternoon."

[DZ] responds "Our company did take a risk; we took a risk with [PDK] and got into neuropsychiatry – in spite of the lobotomy association. And so we are investing in psychiatric disorders and devoting resources into engaging with

psychiatrists. Also, you should be aware that in large companies you have small groups of people working, under the radar, on new technologies. But generally in our case, I prefer to take one step at a time, using standard products, i.e. those which are FDA-approved."

[MD] looking astonished at this comment "But you can miss something that way!"

Stretch 7: Junior researchers probe into time horizons of firms

[AR] in his position as chair, sums up and opens up to others in the room "There seems to be a 'sensible reluctance' of picking up technology solutions. But there is silence from many of the young IMEC researchers? Is there a future for their work?" [AR] smiles encouragingly at the group of PhD students who are clustered together on one side of the table.

One of the PhD students [MC] takes up the invitation to comment, "Neurosurgeons are motivated to invest in technology, a tool to do better. But companies seem to be hesitant." [DZ], shifting in his seat he sits up straighter and responds to the comment, "But there are precedence's, go back into the history of neuromodulation. The use of radiofrequency technology for neurostimulators began in 1967. There were great risks – lots of technology choices, what frequency to use for example. But technology development allowed us to cross bridges."

The PhD student, slightly shyly, continues, "But company's talk about 10 year time frames, but researchers work in ~50 year frames. I thought that these long-term issues are/should/would be the workshop topic"

[DR] mentions that "We will get to this topic of future developments and possible paths in the afternoon, so there is a place for discussion of long-term goals. We chose closed-loop systems because of the long-term interest in the bioelectronics research community, stemming from IMEC in our arrangement of this workshop". [DR] shifts to another topic "Coming back to your [MC] comments on companies, proof of concept projects need not be funded by large companies. They can be publicly funded." [DR] looks around at the two firms [UW] and [DZ] and the technology transfer expert [GS], but the issue is not taken up.

Stretch 8: Recourse to technical requirements of a closed-loop system

[DZ] shifts the discussion by offering an alternative to closed loop systems as a research end goal (he does not believe they will work out in the long run). He

suggests that "There should be greater research into novel waveforms. Not metronomic signalling because heart beats do not beat that regularly. Also a focus on more equally effective/efficient ways of stimulating neurotissues would be interesting."

[KS] responds to the announcement of technical requirements, "Yes, we could think about that in our agenda, including waveforms."

[DZ] continues suggesting research directions, now targeted towards [KS] "Also our therapies take too much of the doctors time. Surgeons of course, but especially neurologists. So things like self titrating systems would be interesting. For example for pain doctors, patient is part of the loop – the patient is involved in his own therapy. What do you think [*he nods towards [PDK]*]?" [PDK] "I agree."

[GB] points out that the systems [DZ] is suggesting are almost closed loop, just a different kind of loop.

Stretch 9: Risk assessment

[MD] announces that he wants to make two comments. "Firstly, the risks that companies take is about use in humans – questions arise such as 'would application be financed by healthcare?' There are different structures, for example in France any simple injection is bought by patient in the pharmacy. Secondly, we should work with animal models. If sufficiently characterised biologically/technically then we can move to applications in humans. So there should be more focus on animal models." [MD] sits back in his chair awaiting a reaction.

[DZ] shakes his head slightly "We always start with human trials. When we have first positive indications then we study mechanisms with animals prior to full clinical trials." [GB] (exasperated) agrees "How do you do psychological experiments with animals?" He goes on to comment that in his lab animal experiments were a waste of time (he gave an example of difficulty of handling Rats). Their lab gave up on them. [DZ] nods in agreement with [GB] stating that "Animals are always a challenge. My company sponsors animal research only after they know that the treatment works."

Two hours into the discussion, the chair announces that he wants to introduce another point. "In the scenarios – there are 'non-linear' dynamics about responses in society (linear technology options, obstacles). What are your responses to these parts of the scenario? You might say it is out of your hands – but there may also be other experiences."

Stretch 10: Consequences of past-generation implants still being in living patients

[UW] short circuits this opening for scenario discussion by bringing up another issue that he thinks is important which is not in scenarios but which he thinks is relevant. "'Backwards compatibility' in implanted patients is an issue. You have to support patients with implanted technology over the remaining period of their life time. As technology progresses, you need to maintain production of older technologies or allow for compatibility. This is a reimbursement issue."

[MD] nods and cites an example of early implants of pacemakers, "If the external system breaks down it has to be replaced. There were cases where parts needed to be replaced, but the parts where no longer available." Silence ensues.

Stretch 11: Psychosurgery and ethical debates around DBS

[DR] comes in with another issue (*based on a conversation he overheard between some participants during coffee before the session began*) "Are you wary of the term psychosurgery?" The chair adds to [DR]'s comment: "The workshop was positioned as 'Deep-Brain Stimulation' , this term sounds nice. If it is positioned as neuro/psychosurgery it sounds different."

[PDK] responds "I was, at the beginning, very afraid of possible psychosurgery risks (such as those in lobotomy), and so was reluctant to work on it, but then I saw patients suffering. Now there is no resistance to exploring psychosurgical options such as DBS, in fact there are actually too high expectations. But I have no problem with talking about neurosurgery."

[MD] adds to this "Neurologists involved in research, and patients, describe neurosurgery as being a painful experience. DBS and neurosurgery are the same thing, have similar risks. In some fields existing neurosurgery is very effective. Alternatives might be more risky. Although the perception that anything that is not conventional neurosurgery is better is in my opinion the wrong way of thinking about it."

[DR] "Do you *[MD]* feel any patient pressure?" [MD] "For fundamental research (not clinical research) these experiences are reasons to do new things"

[AR] mentions that this is about the ethics of promises. Speculative ethics about good/bad sides of things you could do in future. He poses a question to the Neurosurgeons "What do think about the role of professional ethicists?"

[PDK] "I just don't care about this. You have to stand with both feet on the ground." [*not speculate*]. [MD], "I agree, professional ethicists are invading more and more the clinical life (our labs and hospital), the most trivial things are now being regulated by ethics committees. I refuse to do some things asked of me. Ethics committees may jeopardise some things that are not yet true."

[PDK] has never had problems with ethical committees, "On the contrary ethical committees sometimes say it would be unethical not to do something." He goes on to question: Does [MD] think there's ever going to be a situation where ethical committees would prohibit nano-surgery? [AR] reminds the participants that nanotechnology is a not a particular technology, contrary to genetic technology.

[DZ] sits up and looks around the table with an expression of excitement "Where is the line between therapy and enhancing a function? For examples, is there a difference between combating memory decline versus memory enhancement?" [PDK] is of the opinion that standardised scales are needed to decide who is to receive treatment. He doesn't think that people should go further with it "...this is an ethicist's issue. You should go as quickly as possible from research to devices."

[DR] "But the line between treatment/enhancement is relevant. Where do you stop?" [PDK] responds that he doesn't see this as a problem for now. "At this moment, we're not ready for enhancement, but it can become an issue. We (researchers) need not go into this heavily, especially not yet." [DZ] nods agreement adding that "currently it is not about human enhancement, only on correcting deficiencies."

[MD] sighs and sits up straight "There are examples of Parkinson's patients with DBS experiencing personality changes...personality changes going further than immediate release from the disorder, up to changes in sexual desire. In one case this has led to divorce! We can warn patients that we can shut the brain stimulator off, but they don't want to anymore - in this example the patient liked the sex." There are chuckles around the table, and some nodding from the medical device manufacturers. [PDK] adds in defence of stimulators that "all medications have some issues, side effects are nothing unusual."

[DZ] considers this "If a depressed patient with DBS feels happy is that enhancement?" [AR] looking at the clock, announces that he wants to stop the extended morning session and announces a further adapted programme (lunch has been shifted) and so asks the participants to read the case example which has been

handed out to the participants [*This is a 3 page compilation of extracts of a review of neroengineering and devices for epilepsy by Stacey and Litt 2008*] [AR] asks [MD] [*who has to leave at lunch time*] to comment on the questions of the case study.

[MD] "These texts are real, they are contrary to the scenario texts which where…imagined? "

[AR] does not respond to the half question and beckons to [MD] to continue. "There are two categories of epilepsy and there is an issue of which nuclei to target. The open loop "SANTE" project is interesting. But for closed loop, the system for epilepsy does not work well. The device will start up several 100 times a day, because of many false positives, whereas EEG shows there are much fewer seizures. There have been attempts at prediction, a study in Bonn of 20 computers in parallel. That's loads of computational power, which enabled prediction (to the hour) of seizures but these IT investments are unfeasible for many patients.and the patient has to be hooked up to the 20 computers all day long." He smiles at the absurdity of that situation.

[AR] looking at [MD] but also glancing at [PDK] and [DZ] "Are there any harmful effects of such unnecessary stimulation? Regarding false positives, what are the issues of liability – could a patient due for compensation for suffering unnecessary seizures?" [MD] suggests that one approach could be to allow the patient to have some control.

13h08 the chair closes morning session and the participants head to lunch.

LUNCH BREAK

The chair opens the afternoon session with a small introduction. "The aim of this afternoon is to think about the area of DBS. What sort of future world could it create in terms of different activities? As an outcome of this afternoon we should have ingredients to create a composite scenario or richer picture of potential futures. Kicking off the discussion, in the morning session we saw an issue of mutual demand articulation: for example SMEs saying what surgeons, researchers should do."

Stretch 12: Demand Articulation

Before [AR] can continue his introduction, [PDK] jumps in, "You need a [DZ]! A friendly person from industry with whom researchers can communicate, a person that can communicate with all kinds of different stakeholders." Smiling modestly [DZ] adds to this noting that "This is what can be called 'intrapreneur' a person

within a larger company who can think like an 'entrepreneur'". [UW] agrees, "It took my company sometime to realise that recording devices are needed. This is a way of creating a feedback loop for patients. SME's have this intrapreneurship already."

[AR] comments "If you take the case of nanoparticles, there are no general approaches to regulation, it is much more ad-hoc trial-observation regulation."

Stretch 13: Operational issues of a telematic closed loop system

[TG] a PhD student who remained silent during the morning session asks a technical question "Are there telematic closed loop systems so that surgeons can do distant (internet based) check-ups with minimal patient irritation?"

[KS] nods approvingly [*to his PhD student*] "this links up with [DZ]'s concern about taking up surgeons time" but "where can we stop realistically? Do we feed telematic data to GP or specialised doctor? And when is this external analysis needed? What are emergencies in fact? This is the case if there is no closed loop system."

[AR] summarises "So the loop should not be closed too early because this makes learning about the meaning of signals impossible. How much time would this learning require, 5 years, 10 years?" *Directed at [KS]*

[KS], "Currently it is not the technology but the surgical people who can interpret recorded data and provide input into the technology development done by researchers. Depending on this input they [*the researchers*] move into that direction, so it is not a decision taken by the researchers themselves. You should have the loop semi-closed – so that surgeons etc. can check on what is happening. Don't close the loop, keep learning. Focus on what is really relevant. Always have some human decision – until we have learned enough. How much time necessary? I don't know, we need more evidence. This requires sharing of data, there is no funding for that. But research organisations like IMEC and EPFL [*he waves a hand towards [GB]*] have to promise cool technologies – even when clinicians think this is ridiculous. However, the medical community <u>should</u> articulate requirements to help guide technology developers!"

Stretch 14: Innovation gaps

[GB] agrees but adds that physiologists should articulate requirements also. He suggests that "You should have more multi-disciplinary interactions like these

workshops to develop both realistic and promising proposals." [KS] agrees with [GB] "You can't [*as a researcher]* have too many incremental steps, funding agencies like novelty, breakthrough and portfolio concentration"[161]

[DR] observes that there is a tension visible here in the discussion between exploration – exploitation. Looking around the table [DR] asks, "Is there too little money about for the incremental steps in technology development?"

"Yes" says [GB] "Clinicians are sometimes astonished about how disconnected technology developers can be from clinical practice. Researchers sometimes have to make unreasonable promises, outstanding to reviewers." [GS] agrees but emphasises that money is also needed. "I think there should be a shift in how these things are done. Companies need to fund researchers and not just have public agencies fit the bill."

[AR] comes in, "What [GB] is saying is a 'pushing game' rather than a 'waiting game' we discussed before lunch"

[PDK] comments that "What is key is that important stakeholders need to come and stay together at and from the very beginning. So that technology developers learn what is needed and clinicians see what is possible. This creates realism"

[KS] agrees in one sense but links up with his own context – the world of researchers "Yes, but funding agencies can't fund too many incremental steps. A conglomerate of projects, bundles different trajectories and guarantees that things can be achieved" [GS] nods agreement, "This is portfolio management." [GB] agrees about the suggested strategy "In EU Funding you must 'shoot for the stars' promise huge steps – hoping to achieve small/incremental change along the way. So making radical promises in order to enable incremental research advances is the only strategy in the current setup"

[DR] "Again, this discussion is about exploration/exploitation shift but now also how SME's will get ahead. The gap remains, where does the money come from for incremental steps?" [GB] responds "For public funding you have to 'out smart' the reviewers. For private funding venture capitalists will expect huge steps. So you have to make these promises." [KS] adds "Incremental research steps often happen as side effects of intermediary steps in the research process."

It is approximately an hour before the end of the allotted time. The chair summarises the discussion so far.

[161] Research scientist articulates a dilemma from his own world – of the need to promise new research findings offering radical advances, but need the incremental steps – who fits the bill for incremental steps?

Stretch 15: Anticipatory coordination needed?

*"*So we are talking of a portfolio of activities and projects which overtime makes sure something will come out. But coordination is also necessary. Anticipatory coordination can happen with much promising (this is the case with ETP for nanomedicine). Could IMEC start an informal consortium on coordination and communication?"

[KS] thinks that people are pragmatic/cautious about both top-down and bottom-up coordination. "At the beginning an initiative must remain local – not too much visibility, then again without visibility and marketing, not much will be achieved. What sort of time horizon for this consortium? At least 5 years, I would think."

[DR] suggests a different way of probing this issue "If you take an example, say [UW]'s adding recording function to your device, that would provide a lot of the information for researchers looking into closed-loop devices, no?" He looks around the table.

[DZ] leaning back in his chair comes in "I cannot talk details, but I will give an imaginary case. Suppose we invest 50 million dollars into including recording function into device. That would mean, more or less, a 30% price increase. Our company would put the recording feature in the product if there was an advantage for healthcare, not just researchers"

An organiser ask [UW] about cochlear implants [*his company's speciality*]. "Recording is a fancy new option" says [UW] "In our company, it got momentum after a while. We put recording function into the device because it improved market share and penetration and thus higher sales. But there are other new possibilities coming in laterally, like polymer probes which we are looking into."[162]

[GB] [*in a quite confrontational manner*] points at [DZ] and says that "[DZ] assumes there is no clear clinical benefit of including a recording device." [DZ] still slouching back in his chair [*and seemingly relaxed*] responds to [GB]'s comment but looks at others around the table "There is another aspect; a big company has a greater burden of proof. The FDA looks for credibility. Smaller companies sometimes have it easier certainly for Basal Stem.[163] It is another type

[162] Recall that polymer probes were a topic in the scenarios.
[163] This is another area of neurostimulation devices, one which has a greater level of development.

of stimulation, not necessarily deep-brain stimulation. The tall tree catches the wind." He nods sagely.

The chair summarises, "Researchers create a portfolio of activities to catch some possibilities. Companies do the same. Does a close link between these portfolios foreclose exploration? Long-term opportunities may be missed out on?"

[DZ] "Clear advantages come from 'jump shift' rather than the incremental strategies of larger organisations, in my company disruptive technologies are threatening technologies, they displace incumbents which have already been invested in."

Stretch 16: Learning and evaluation in therapy development

[AR] responds "The question then is which threats are real, and which won't affect the situation? This could become part of the composite scenario/responses" He continues, announcing that he wants to steer discussion towards learning once more, evidence-based medicine, controlled trials. "If learning is important can you do so via controlled trials, in order to satisfy regulation, or is learning in a grey zone? How important will evidence based medicine be given that patient organisations will want to profit from new opportunities, jump at them?"

[UW], "You need to think with different points of view. Patients will always value improvements. There is an issue of regulation for safety 'make sure that the cables don't break'."

[GB] "as a North American [*Canadian*] evidence based medicine is big in America." [WP] [*a venture capitalist who has remained silent but who has taken many notes*] adds to this "But there is no need for calls for evidence based medicine in neurodegenerative disorders, there are immediate behavioural changes – It works! Anyway, evidence based medicine is a misnomer as it is about cost-benefit calculations."

[PDK]'s experience is different. "From the first obsessive compulsive disorder patient we had a protocol – but it was flexible." He outlines that when he started they had protocols for each patient that were adaptable from patient to patient. For new medicine it is important to document evidence.

Stretch 17: Rounding off

The chair rounds up the meeting "We haven't created the 'composite scenario' yet. What actions are required? Where are the responsibilities" [AR] shows the innovation chain diagram. "[PDK], as a neurosurgeon do you have recommendations for the researchers?"

[PDK], "You need to develop something that works, is interesting enough, and promises future breakthroughs. Can't add much more to what has been said. The place for start ups depends on what you want to develop. At what time do you decide for collaborating/going it alone." [AR], "So start-ups must fairly soon realise that they can't stand on their own (especially for long term projects)." [PDK], "Yes, you should go as quick as possible, but also as good as possible."

[KS] voices his opinion "For researchers it is important to have many entrance points for companies to respond to. Researchers can create openings for research leading to incremental changes, which in turn leads to incremental product development in companies. Radical changes aren't always necessary. You can't propose a 10 year research project to "midstream people" in large companies, but the right person may be an intrapreneur. I would recommend to a company to give this person higher visibility."

[GB] smirking adds "But the age of 'intrapreneurs' may be a bygone era. Intrapreneurs are leaving companies and going it alone, but the medical device corporations can squash these." [*This seems to be targeted at [DZ] specifically.*]

[MC] [*Bringing back her earlier suggestion*] recommends more research should be done on animal models. [DZ] nods but adds, "There are problems there too. Technology developed on insights into animal models that is thought to be translatable into humans may not actually work in humans. A case that did work however was vagal nerve stimulation. But there should always be human models, for example OCD and depression – difficult to measure those in animals."

With an air of wrapping up the discussion, [AR] looks around the table and asks whether there are any other issues?

[DZ] suggests some elements that would be interesting for him to be on the research agenda "Novel wavelength, Data acquisition, transition and use, closed-loop systems or (use above to improve stimulation), open-loop systems. Improved computing power to predict seizures (at feasible energy levels) that is what might be interesting future possible technology developments."

With that the chair closes the session.

At this point [GB] pulls out a laptop and begins to show a demonstration of his technology to [PDK] and the PhD students, while [DZ] is out of the room. [WP] shuffles across [Is in league with [GB] in the possible start-up initiative involving advanced multi-electrode arrays for neuromodulation.

3.3 Summary Table

Actual composition	2 large firms, 2 SME's, 1 senior researcher, 3 junior researchers, 2 neurosurgeons, 1 technology transfer expert, 3 organisers
Degree of heterogeneity	Heterogeneous (a balanced mix, excepting that there was only one senior researcher).
Last minute cancellations of participation and its impact.	No last minute cancellations.
Stretches in the discussions Organiser initiated and taken up = O+ Organiser initiated not taken up = O- Participants initiated and taken up = P+ Participant initiated not taken up = P-	P+/P+/P+/P+/O-/P+/O/P+/P+/P+/O+/P-/P/P/O+/O+/O There were a lot of stretches in this workshop, partly because of the diversity and the willingness to bring up information for the discussion (almost everyone excepting the shy junior researchers) got involved. Of particular note was the lack of effect of direct shifting of discussions. In Stretch 5 (O-) [AR] linked the discussion with dynamics with only short responses. [DR] following on from this had little luck when discussion dynamics, when a participant [GS] returned to an earlier stretch on product development strategies. Again between stretch 9 and 10 there was an attempt by the organisers to discuss dynamics explicitly, which was not taken up.
Explicit reference and use of the scenarios	-- There was no direct reference to the scenarios. This could be for a number of reasons, perhaps the heterogeneity of the participants meant that

	there was less reliance on the scenarios and more probing and quizzing of participants (this is very visible in the number of participant initiated stretches). There was also reference to the innovation chain diagram, which was referred to a number of times, and the terminology use to frame questions and discussions.
Implicit reference and use of the scenarios	= Many of the issues and dynamics from the scenarios were mentioned in the discussion, but it is very difficult to see a link, since in the main, these seem to have come from participants experience and described through examples from their own world.
Quizzing between homogenous actor group (or with those who knew each other prior to the workshop)	Some quizzing, but there was little homogeneity and so there was more probing.
Asymmetric probing of the majority group (perceived as experts)	There was no dominating group. However [DZ] a representative of a large multi-national medical device manufacturer did speak often on the behalf of large firms.
Mutual probing in heterogeneous group	There was substantial probing in this meeting, in terms of firms and how they determine product platform strategies (especially from neurosurgeons who probed about the reasoning behind the asymmetry between technical advances in research, and what they could actually buy on the market. Junior researchers probed the speculation boundaries of large firms. The senior researcher probed the firms on the role of small and large firms and their relationship with researchers in R&D. Also mutual probing on issues of ethics and hype (especially in stretch

	11).
Do participants get into broader aspects or do they recourse back to their usual positions.	Yes, a large number of issues are brought up. As opposed to Workshop 2 and 3, the enactors in the room were mainly industrial actors who are linked to users (less of a concentric bias?). Although [KS] the sole senior researcher did a reasonable amount of probing.

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Summary

Already in its present early stage, nanotechnology is stimulating debates, dialogue, promotion and protest. Particularly important is the anticipation of potential future technology development societal impacts and their co-evolution.

Nanoscientists and nanotechnologists ('nanotechnologists' for short), as enactors of nanotechnology, play an important role in this early stage of the development process. They experience a variety of pressures, all requiring anticipation. There is a pressure to translate research into applications that will benefit the economy and benefit society (a responsibility to innovate); a pressure to be strategic, in particular to undertake anticipatory coordination activities up to roadmapping and agenda building; a pressure to be transparent and pay attention to public outreach, up to early ("upstream") public engagement; and a pressure to engage with, and include, ethical and societal aspects of technology development activities. The latter is related to the move towards responsible research and innovation.

This provides fertile ground for Constructive Technology Assessment (CTA), with its focus on analysis of socio-technical dynamics (including embedding in society) and feeding such analysis back into the processes of design of new technologies, and the development and societal embedment of new technologies. CTA, first proposed in the early 1980s, remained a promising approach for quite some time. There was conceptual development, especially with regard to a deeper understanding of socio-technical dynamics and interventions in such dynamics (van den Belt & Rip 1987, Rip, Misa and Schot 1995, Schot & Rip 1997, Rip & Schot 2002). Actual CTA exercises were limited, however.

This situation changed when the Dutch nanoscience research consortium NanoNed included technology assessment (and societal aspects) of nanotechnology as one of its "flagship" programmes. The main thrust of this program was to do CTA of a number of areas of nanoscience and nanotechnology, and in doing so, further develop the methodology. This was the starting point for the research that is reported in this thesis. It is a contribution to the empirical programme of CTA, and thus advances the empirical turn in CTA.

Part I Nano "enactors" and their role in shaping nanotechnology and society

In Chapter 1, I explore the changing relationship between technology development and society and how indications of this shift are explicit in the nascent field of

nanotechnology. I identify a number of pressures and processes that show that, although more actors at multiple levels are influencing, to a greater and lesser extent, the development paths of nanotechnology, that nanotechnologists themselves are still the most powerful actors. After a focused review of the literature of technology and innovations studies and technology assessment I formulate the three components of my study:

(1) A deeper understanding of the nanoworld and emergence (PART II)

(2) The embedding of constructive technology assessment in the ongoing developments of nanotechnology (PART III)

(3) A deeper understanding of operationalizing and conducting constructive technology assessment (APPENDICES)

PART II Analyzing nanotechnology and tools for more reflexive anticipation

Chapter 2 analyses two cases of a nano-district (an industrial district with nanotechnology as a core activity), the Grenoble region in France and the Dutch centres for nanotechnology (which had also joined forces in NanoNed Institutional entrepreneurs play an important role, and the "district" dynamics derives from cumulation of technological infrastructure supporting a variety of product-value chains ("technological agglomeration").

Chapter 3 analyses how expectations and visions about nanotechnology are presented in the case of molecular machines. Two sets of texts were used: all publications referred to in an authoritative review article in *Nature Nanotechnology*, and all articles mentioning 'molecular machines'in the popular science magazine *New Scientist*. Presentation of results and articulation of visions were always combined, where the former is emphasized in the scientific articles and the latter in the articles in *New Scientist*.

In Chapter 4, the starting point is the need for open-ended roadmapping (in contrast to usual roadmapping) in new science and technology where the situation is rapidly evolving. The key step is to recognize emerging path dependencies and other emerging irreversibilities, including structuring effects of expectations. This allows identification of "endogenous futures", and on that basis, sketching multiple paths into the future. The case of lab-on-a-chip, with its close ties with the nanoworld, is used because of its "platform" characteristics – lab-on-a-chip can be used in many applications in diverse sectors. This is typical for many nanotechnologies.

In Chapter 5, I develop a (socio-technical) scenario technique that is an alternative to scenarios as visions of the future that are somewhat disconnected from the present, a fictive space to explore and assess the futures. The technique puts at its centre the transformation of the present into potential futures, not to assess the future world, but to explore the dynamics and interactions of socio-technical arrangements and their entanglements. Such scenarios allow the playing out of multiple options amidst an evolving socio-technical system. The empirical case for which an annotated scenario is presented explores possible governance effects of the present interest in, and move towards, responsible research and innovation of nanotechnology. The chapter further describes the conceptual underpinnings of the technique and the construction of the scenarios.

PART III Constructive Technology Assessment Activities and Insertion as a Method to Do So

The embedding of constructive technology assessment in ongoing developments of nanotechnology has two main components: moving about in the world of nanotechnology, inserting myself and CTA workshops into this world; and dedicated experiments in interaction ("bridging events") in the form of stakeholder workshops supported by sociotechnical scenarios about possible developments in the areas of nanotechnology which were at stake,

Insertion should be seen as a methodology in its own right, In Chapter 6, I discuss the nature of this methodology, and exemplify it by using my own experiences, presenting, diary-style, the successive "stretches" of interactions in the five-year period covered by my insertion in the nano-world. This also provides insights and methods to handle the challenges and opportunities of a CTA-analyst, tailoring and embedding CTA in ongoing activities. Insertion allows capturing entanglements in co-evolution as they occur, which is necessary for data collection about newly emerging S&T.

Eventually, five dedicated CTA experiments-in-interaction were done. They are reported in detail in the Appendices. In Chapter 7, I analyze how features of these experiments, from the starting conditions and the understanding of what was at stake in the domain, the workshop preparation, and the dynamics of interactions within the microcosm of a workshop contributed to the outcomes of the experiments in interaction.. Each workshop was a microcosm of the real world, realized by co-locating a variety of actors and providing support material on the socio-technical linkages and dynamics at play. The workshops functioned as microcosms, albeit with various specificities as a consequence of the eventual composition of the participants and positioning of the workshop.

The animation of the workshop and the preparatory material play a major role in providing a productive microcosm. One effect is the exploration of new pathways that may emerge due to nanotechnology, and which may not have been salient to some of the participating stakeholders, who have vested interests and some things already at stake. Another effect of the CTA experiments is that the workshops facilitate broadening of perspectives through enabling the articulation and exploration of linkages (and their dynamics) which are not regularly part of the enactor perspective, such as user demands, and issues of political and societal acceptability. Data on the process of broadening was captured through observation of mutual probing (of visions and positions) and issue articulation in the workshops. Different forms of probing can occur, and shape the outcomes of the CTA experiments

Chapter 8 starts by drawing out guidelines for doing empirical CTA (for newly emerging technologies) and for insertion. For empirical CTA, the steps are: studying the lay of the nano-land and diagnosing issues, participant composition and working with contingencies, developing socio-technical scenarios and the role of other support material, the dynamics and processes of interactions within workshops, and exploration of broadening enactment cycles of technology developers.

Then I consider co-evolution of nanotechnology and society which is the backdrop against which my CTA projects were shaped and performed. The experiences in the CTA projects also offered insights into the forcefields and dynamics of co-evolution. In Chapter 1, I indicated that there are already some elements of reflexive co-evolution. During my insertion (reported in Chapter 6) this was very visible, also in how my own moving about became part of larger developments, at first being constrained, but then being enabled by them in the sense that there was more acceptance. At the same time my activities also contributed to these larger developments by showing that something interesting and useful could be done with regard to reflexivity of co-evolution.

The question can be raised whether further arenas for bridging do emerge and are being taken up. Activities like nanodialogues, citizen's juries and developments of codes of conducts are definite indications of increasing entanglement of nanotechnology and society, even if they do not always lead to arenas for bridging. A further observation is how consideration of eventual impacts is on the agenda. The repeated occurrence and acceptance of the acronyms ELSA (Ethical, Legal, and Societal Aspects) and EHS (Environmental, Health, Safety) in discourse on, and governance of, nanotechnology research is an indication. This may become

important in the mobilisation of resources for research, and then lead to some alignment between societal concerns and allocation of resources.

CTA-agents find openings for their activities amidst these alignment and entanglements. They can thus orchestrate (as I have done) bridging events in various locations within the co-evolving socio-technical networks. These have become accepted in the nano-world, but the challenge of making their analysis and its representation recognizable and acceptable when interacting with their subjects remains.

APPENDICES Experiments in Interactions

The appendices present full details of the five CTA experiments in interactions. For each of the activities, I detail the starting conditions and the context in which it was orchestrated. The domain was and the various stakeholders were mapped. This understanding was translated into socio-technical scenarios and annotated versions of the scenarios are given, to show how they were constructed and how they build on ongoing developments and tensions. These are presented along with an abridged transcript of the interactions within the one-day workshop (an integral part of each CTA activity).

Topics explored were lab-on-a-chip for cell analysis, nanotechnology drug delivery options for gene therapy, molecular machines, deep-brain implants for neurological disorders and roles and responsibilities in the governance of nanotechnology.

Samenvatting

Al in zijn huidige vroege stadium van ontwikkeling is nanotechnologie aanleiding tot debatten, georganiseerde dialogen, promotie en protest. Belangrijk is het anticiperen op toekomstige technologische ontwikkeling, maatschappelijke impacts, en de co-evolutie van beide.

Nanwetenschappers en nanotechnologen (in het vervolg 'nanotechnologen' genoemd) spelen als 'enactors' van nanotechnologie een belnagrijke rol in dit vroege stadium van het ontwikkelingsproces. Ze ondervinden druk om bepaalde activiteiten te ondernemen waarvoor anticipatie nodig is. Er is druk om onderzoek te vertalen naar toepassingen van waarde voor de economie en de maatschappij (een verantwoordelijkheid om te innoveren); druk om strategisch te zijn, met name om anticiperende coördinatie-activiteiten te ondernemen, tot en met road mapping en het formuleren van strategische agenda's; druk om transparant te zijn en aandacht te schenken aan publieksinformatie, tot en met vroege ("upstream") interacties met publieken; en druk om zich bezig te houden met, en rekening te houden met ethische en maatschappelijke aspecten van technologie-ontwikkelingsactiviteiten. Dit laatste is gekoppeld aan de verschuiving in de richting van verantwoordelijk onderzoek en innovatie.

Dit is een vruchtbare bodem voor Constructief Technology Assessment (CTA), wat zich richt op analyse van sociotechnische dynamiek (tot en met inbedding in de maatschappij) en terugkoppeling van de analyses naar ontwerpprocessen van technologie en de ontwikkeling en maatschappelijke inbedding van nieuwe technologieën. Het idee van CTA werd voorgesteld midden jaren tachtig, maar bleef lange tijd alleen een belofte. ER was conceptuele ontwikkeling, met name een beter begrip van sociotechnische dynamiek en interventies daarin (van den Belt & Rip 1987, Rip, Misa and Schot 1995, Schot & Rip 1997, Rip & Schot 2002). Concrete CTA exercities werden echter maar beperkt gedaan.

Deze situatie veanderde toen het Nederlandse nano-onderzoek consortium NanoNed technology assessment (en maatschappelijke aspecten) van nanotechnologie opvoerde als een van zijn "flagship" programma's. Een belangrijk doel van dit programma was om CTA van een aantal gebieden van nanowetsnchap en nanotechnologie te doen en op deze manier de methodologie verder te ontwikkelen. Dit vormde het startpunt voor het onderzoek waarover dit proefschrift rapporteert. Het is een bijdrage aan het empirische programma van CTA, en brengt dus de empirische wending in CTA een stap verder.

Deel I: Nano "enactors" en hun rol in vorm geven van nanotechnologie en maatschappij

In Hoofdstuk 1 bespreek ik de veranderende relatie van technologie-ontwikkeling en maatschappij en hoe indicaties van deze verschuiving expliciet zichtbaar zijn in het opkomende gebied nanotechnologie. Ik identificeer activiteiten en processen die tonen dat ondanks dat ontwikkelingspaden van nanotechnologie tot op zekere hoogte beïnvloed worden door meer actores en op meer niveaus, de nanotechnologen zelf nog het meeste effect hebben.

Na een gerichte bespreking van de literatuur van technologie studies, innovatiestudies en technology assessment formuleer ik de drie componenten van mijn studie:

(1) Beter begrip van ontwikkelingen in de emergente nano-wereld (Deel II)
(2) Het inbedden van Constructief Technology Assessment in lopende ontwikkelingen van nanotechnologie (Deel III)
(3) De ervaringen met operationaliseren en het doen van Constructief Technology Assessment in en rond workshops (Appendices)

Deel II: Analyse van nanotechnologie en hulpmiddelen voor reflexieve anticipatie

In hoofdstuk 2 worden twee cases van een nano-district (een industrieel district waarin nanotechnologie bedrijvigheid de kern is) geanalyseerd, de Grenoble regio in Frankrijk, en de Nederlandse centra voor nanotechnologie (die ook verenigd waren in NanoNed). Institutionele entrepreneurs spelen een belangrijke rol, en de "district" dynamiek is een gevolg van cumulatie in technologische infrastructuur die verschillende produkt-waarde ketens ondersteunen ("technologische agglomeratie").

Hoofdstuk 3 analyseert hoe verwachtingen en visies over nanotechnologie naar voren gebracht worden in het geval van moleculaire machines. Twee sets of teksten werden gebruikt: alle publikaties waarnaar verwezen werd in een gezaghebbend review artikel in *Nature Nanotechnology*, en alle artikelen die 'molecular machines' noemden in het populair-wetenschappelijke tijdschrift *New Scientist*. Presentatie van resultaten en articuleren van visies werden steeds gecombineerd, waarbij het eerste nadruk krijgt in de wetenschappelijke artikelen en het tweede voorop staat in de *New Scientist*.

In hoodstuk 4 is het startpunt dat open-einde roadmapping (in plaats van de gebruikelijke roadmapping aanpak) nodig is voor nieuwe wetenschap en technologie waar de situatie in hoog tempo evolueert. De sleutel-stap is de herkenning van emergente pad-afhankelijkheden en andere emergente irreversibiliteiten, inclusief de structurerende effecten van verwachtingen. Op die

basis worden “endogene toekomsten” geïdentificeerd en kunnen meerdere paden van toekomstigeontwikkeling geschetst worden. De casus van lab-on-a-chip, met nauwe verbanden met de nano-wereld, wordt gebruikt vanwege zijn “platform” kenmerken – lab-on-a-chip kan ingezet worden voor vele toepassingen in diverse sectoren. Dit is typerende voor vele nanotechnologieën.
In hoofdstuk 5 ontwikkel ik een (sociotechnische) scenario techniek die een alternatief is voor scenario’s als visies op de toekomst zonder veel verband met het heden, fictieve ruimtes om toekomsten te exploreren en evalueren. De techniek stelt de transformatie van het heden naar mogelijke toekomsten centraal, niet om de toekomstige wereld te evalueren maar om de dynamiek en de interacties van sociotechnische arrangementen en hun verwikkelingen te exploreren. Het empirische domein waarvoor een geannoteerd scenario gegeven wordt is de mogelijke governance effecten van de huidige aandacht voor, en verschuiving naar, verantwoordelijk onderzoek en innovatie van nanotechnologie. Het hoofdstuk beschrijft ook de conceptuele onderbouwing van de techniek en de constructie van de scenario’s.

Deel III: Constructief Technology Assessment activiteiten en invoegen als een methode om dit te doen

Het inbedden van constructief technology assessment in voortgaande ontwikkelingen van nanotechnologie heeft twee componenten: verkeren in de nano-wereld en invoegen van mezelf zowel als CTA workshops in die wereld; en gerichte experimenten in interactie (“bridging events”) in de vorm van stakeholder workshops ondersteund door sociotechnische scenario’s about mogelijke ontwikkelingen in de domeinen van nanotechnologie die aan de orde waren.

Invoegen moet als een eigenstandige methodologie worden gezien. In hoofdstuk 6 bespreek ik de aard van deze methodologie, en gebruik mijn eigen ervaringen als voorbeeld door in dagboekstijl de vijf “stukken” interacties in de vijf jaar periode van mijn invoegen in de nano-wereld. Dit levert ook inzichten en methodes hoe de uitdagingen en kansen voor een CTA analyst in het passend maken en inbedden van CTA in voortgaande activiteiten te hanteren. Het invoegen maakt het mogelijk verwikkelingen in co-evolutie te zien terwijl ze optreden, wat noodzakelijk is voor data verzameling over nieuw opkomende wetenschap en technologie.

Uiteindelijk zijn vijf gerichte CTA experimenten-met-interactie gedaan. De gedetailleerde rapportages staan in de Appendices. In hoofdstuk 7 analyseer ik hoe kenmerken van deze experimenten, van de beginvoorwaarden, begrip van wat aan de orde was in het domein, de voorbereiding van de workshop en vervolgens de dynamiek van interacties in de “microcosmos” van de workshop bijdroegen aan de

resultaten en effecten. Elke workshop was een microcosmos, een verkleinde versie van de echte wereld, gecreëerd door verschillende soorten actores bij elkaar te brengen en ondersteunend materiaal over sociotechnische koppelingen en de dynamieken die speelden te leveren. De workshops functioneerden inderdaad als een microcosmos, zij het met allerlei bijzonderheden als gevolg van de uiteindelijke samenstelling van deelnemers en positionering van de workshop.

De "animatie", d.w.z. orkestratie en leiding, van de workshop en het voorbereidende materiaal spelen een voorname rol in het realiseren van een produktieve microcosmos. Eén effect is het exploreren van nieuwe ontwikkelingspaden die kunnen opkomen vanwege nanotechnologie en welke niet duidelijk waren voor sommige stakeholders met hun gevestigde belangen en bestaande inzetten. Een ander effect van de CTA experimenten is dat de workshops verbreding van perspectieven faciliteren, en wel door de articulatie en exploratie van verbanden (en hun dynamiek) mogelijk te maken die niet regulier deel zijn van het "enactor" perspectief, zoals gebruikersvraag en kwesties van politieke en maatschappelijke aanvaardbaarheid. Data over het proces van verbreding werden verzameld door observatie van wederzijds peilen van visies en posities, en van articulatie van kwesties gedurende de workshops. Verschillende vormen van peilen kunnen voorkomen en de uitkomsten van het CTA experiment beïnvloeden.

Hoofdstuk 8 begint met het formuleren van richtlijnen voor het doen van empirisch CTA (voor nieuw opkomende technologieën) en voor invoegen als een methodologie. De stappen voor empirisch CTA zijn: studie van hoe het nano-gebied er uitziet en diagnose van kwesties die spelen, samenstelling van deelnemers en het hoofd bieden aan contingenties, ontwikkelen van sociotechnische scenario's en de rol van ander ondersteunend materiaal, dynamiek van interactieprocessen in de workshops, en exploreren van verbreding van "enactment" activiteiten van technologie-ontwikkelaars.

Vervolgens richt ik me op co-evolutie van nanotechnologie en maatschappij, de achtergrond waartegen mijn CTA projecten vorm werden gegeven en uitgevoerd. De ervaringen in de CTA projecten leverden dan ook inzichten in de krachtenvelden en dynamiek van deze co-evolutie. In hoofdstuk 1 gaf ik aan dat er al elementen van reflexieve co-evolutie zijn. Tijdens de invoeging die ik pleegde (zoals geanalyseerd in hoofdstuk 6) was dit nadrukkelijk zichtbaar, ook in hoe mijn eigen verkeren in de nano-wereld onderdeel van bredere ontwikkelingen was: aanvankelijk ingeperkt door de "vreemdheid" van mijn inzet, maar op de duur verwelkomd, althans in de zin dat er meer acceptatie was. Tegelijkertijd droegen mijn activiteiten zelf bij aan de bredere onwtikkeling door te tonen dat het mogelijk

was iets interessants and nuttigs te doen op het punt van reflexiviteit van co-evolutie.

De vraag kan opgeworpen worden of er verdere arena's voor overbrugging opkomen and gebruikt worden. Activiteiten zoals nanodialogen, "citizen's juries" en het ontwikkelen van gerdagscodes zijn duidelijke indicaties van toenemende verwikkeldheid van nanotechnlogie en maatschappij, ook al leiden ze niet altijd tot arena's voor overbrugging. Een verdere observatie hoe de beschouwing van evetuele impacts op de agenda staat. Terugkerend voorkomen en acceptatie van de acroniemen ELSA (Ethical, Legal and Social Aspects) en RHS (Environmental, Health and Safety) in de discours over, en governance van nanotechnologie onderzoek is een indicatie. Dit kan belangrijk worden in het mobiliseren van hulpbronnen voor onderzoek en dan tot enige samenhang tussen maatschappelijke zorgen en allocatie van hulpbronnen leiden.

CTA "agents" vinden openingen voor hun activiteiten in en dankzij deze verwikkelingen en groeiende samenhangen. Ze kunen dus (zoals ik gedaan heb) "bridging events" orkestreren op verschillende locaties in de co-evoluerende sociotechnische netwerken. Dat is een geaccepteerd onderdeel van de nano-wereld geworden. Wat blijft is de uitdaging om hun analyse en hoe deze gepresenteerd wordt herkenbaar en accepteerbaar te maken in hun interacties met stakeholders.

Appendices: Experimenten in interacties

The appendices geven de details van de vijf CTA experimenten in interacties. Voor elk van de activiteiten geef ik aan wat de beginvoorwaarden waren en de context waarin de activiteit opgezet en vormgegeven werd. Het domein werd, en de verschillende stakeholders werden in kaart gebracht. Dit inzicht werd vertaald in sociotechnische scenario's. Geannoteerde versies van deze scenario's worden gegeven om te laten zien hoe ze geconstrueerd werden en hoe ze bouwen op voortgaande ontwikkelingen en spanningen. Daarnaast wordt een verkorte transcript gegeven van de interacties gedurende de eendaagse workshop (een integraal onderdeel van elke CTA activiteit).

Onderwerpen die op deze manier geëxploreerd werden waren lab-on-a-chip voor cel analyse, nanotechnologie-ondersteunde medicijn toediening opties voor geen therapie, moleculaire machines, diepe hersen-implanten voor neurologische afwijkingen, en rollen en verantwoordelijkheden in de governance van nanotechnologie.

Curriculum Vitae – Douglas K. R. Robinson

Prior to his PhD project in the TA-NanoNed (NL) programme, Douglas obtained his undergraduate and masters degree in Physics and Space S&T at the University of Leicester (UK) and the Universität Siegen (Germany) with two theses one on mathematical modelling magnetospheres of Jupiter and Saturn (the space radiation environment) related to the Cassini-Huygens Mission, the other focused on heavy ion beam cancer therapy for brain tumours. Alongside his first degree, Douglas worked for a 10-week placement as radiologist in Leicester Royal Infirmary and 8-weeks as Biophysicist at the Darmstadt Heavy Ion accelerator GSI (Gesellschaft für Schwerionenforschung GmbH). Following his 1st degree Douglas has conducted an experiment in zero-gravity as part of the European Space Agency Parabolic Flight Campaign 2002 with 60 periods of zero gravity during two flights.

His second degree (MSc) at the International Space University (ISU) in Strasbourg was an interdisciplinary study of the space sector, including knowledge management, innovation studies, business, economics, policy and law related to the space industry. His project covered space biomedicine and cosmonautics research in the former Soviet Union, which involved a 3-month placement at the cosmonaut training centre (Star City) and the Institute of Biomedical Problems (IMBP), Moscow, Russia, where in addition to his broad in scope study he also assisted researchers on a focussed experiment on support afferentation for the mitigation of muscle deterioration in long-term space flight. Following this, after a brief placement at the space SME Delta-Utec, evaluating thermal protection systems for re-entry vehicles, he joined three colleagues from ISU to form a start up company at the European Space Incubator located at ESA-ESTEC, the Netherlands.

He then took the decision to research technological innovation, governance and technology assessment, and embarked on the PhD research project which has been reported in this dissertation.

At the time of writing, Douglas works as a research scientist at the Centre de Gestion Scientifique, Ecole Nationale Supérieur des Mines de Paris, where he researches anticipatory coordination support tools with a view to the design and management of innovation pathways and the socio-technical systems which shape and are shaped by such pathways. He focuses in the main on early stage newly emerging technologies, such as nanotechnology, which is taken up in his other position as Technical Analyst at the Institute of Nanotechnology (UK) where he works on mapping nanotechnology research and innovation in the agrifood and healthcare sectors and R&D performance indicators in the FP7 NMP Scoreboard project.