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Biotechnology Policy and Achievement 1980-88 [and Discussion]

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Biotechnology policy and achievement 1980–88

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Much progress has been made in line with the spirit of Spinks, but it is inevitable that perspectives have changed since 1980. At the research level, we know that much strategic work remains to be done before the full industrial benefits of biotechnology can be secured, even though there has been a gratifying improvement in academic–industrial liaison. The industrial progress and dissemination of biotechnology has been slower than Spinks implied, but we have a clear understanding of the importance of such contributors to the climate for investment as balanced regulation, training and public perception. The international dimension is important not only for the potential benefit of research and development programmes but also to monitor progress in the U.K. with respect to our competitors. Biotechnology now finds itself in a new framework of Government policy for innovation; there are new challenges in sustaining and adding to the impetus built up by the academic and industrial communities.

Introduction

Eight years may be a long time for science policy, but it is certainly a short time in getting a novel biotechnology product to the market. And if there is one central lesson in assessing the scene-setting reports and comment on biotechnology in the late 1970s, it is that their timescale was usually optimistic.

May I quote the first paragraph of the Spinks Report (Spinks 1980).

> We envisage biotechnology – the application of biological organisms, systems or processes to manufacturing and service industries – as creating wholly novel industries, with low fossil energy demands, which will be of key importance to the world economy in the next century. Over the next two decades, biotechnology will affect a wide range of activities such as food and animal feed production, provision of chemical feedstocks, alternative energy sources, waste recycling, pollution control, and medical and veterinary care. We are convinced that it will shortly be possible to use microbial and other cells to make a wide range of organic chemicals which either cannot at present be made economically on a large scale or, if they can be made, require extensive inputs of land, energy and capital plant for their production from feedstocks, such as oil, which will become more expensive.

I am sure that with the benefit of hindsight the Spinks Report would be quite different today. Insufficient attention was given to the transfer of science through technology into production. History shows that scientific breakthroughs usually take 25 years to come to fruition in the market place and the thrust of the report suggested that the mould had been broken and the benefits of gene cloning and other techniques would appear very rapidly.

It would be quite wrong, however, to seek to assess progress since Spinks just in terms of commercial impact. The sectors, such as diagnostics, where many products have been marketed are the exception. However, there are no grounds for disappointment that early and unrealistic predictions have not been realized. The state of development of biotechnology is best evaluated by the size, source and position of industrial investment and by the transfer of technology from the science base.

A review of 1980–88

The central concern of the Spinks Report was that the U.K. was in danger of missing significant opportunities. It is clear that the specific opportunities and rates of commercialization identified by Spinks were on the one hand too optimistic in expecting an impact in commodity chemicals and in the renewal of existing industry, and on the other hand too blinkered in that the focus on manufacturing industry obscured the agricultural opportunities. It is, nevertheless, important to try to assess progress in U.K. biotechnology in relation to developments overseas and to consider whether there is evidence of real opportunities being lost.

The information available to address this question is far from comprehensive. The OTA Report published in 1984 is of little relevance today. The comparison of the relative threats from Europe and Japan to the United States in the field was seriously flawed because of the much greater effort devoted by the consultants to Japan. It was a parallel of the story about a drunk searching for a coin he had dropped at night. A passer-by, finding him on his knees under a lamp post asked 'Where did you drop the coin?' The drunk replies 'Over the other side of the road, but it's dark over there so I am looking under the light.'

In my view, the research base and contacts built up by the large U.K. companies have been appropriate and well directed for a field in which commercial opportunities require careful appraisal and substantial resources to bring to fruition. The investment of major companies (ICI, Unilever) in both research and development and acquiring seed interests and in the intensifying pharmaceutical research by Glaxo, Wellcome and ICI is clear. The commitment to biotransformation as an alternative to chemical synthesis is signalled by the recent announcement of ICI's L-chloropropionic acid process.

The large number of bio-boutiques in the U.S.A. has often been contrasted with the U.K. position. Although this route to the market place is not so common here, we are well ahead of any other European country. Celltech is now profitable and still expanding. Their ability to raise over £40M for further investment in research and development and capital in the aftermath of the Stock Exchange crash in October 1987 is a clear indication of the perceived strength of the company. Porton International, British Biotechnology, Agricultural Genetics, Enzymatix and others show considerable promise for the future.

Collecting reliable data on R&D inputs is difficult when the boundaries of biotechnology are ill-defined and public expenditure is only part of the story. The large companies are often reticent about their research investment and some sources invariably exaggerate claims of activity in a sort of virility contest.

It is true that the U.K. has been less successful overall than the Netherlands in attracting inward investment in biotechnology, but the number of spinoffs is still relatively small compared with the resources of indigenous companies. The broad industrial picture is healthier in the U.K. than that in any other European country. I suggest that it is only in the United States, with its much greater resources, that the commercial prospects may be better and more broadly based.

Despite some retrenchment in academic research, Research Councils have declared a commitment to biotechnology and it is encouraging to see the prominence given to it in their corporate plans.

Spinks was quite firm on the need for improved coordination between Research Councils,

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but it is hard to point to significant progress. Indeed, there are recent signs that positions are hardening and rivalries intensifying. There are two central problems. First, cultural differences mean that the Councils differ greatly in the extent to which they are prepared to identify and back areas important for future wealth creation. Second, Councils with research institutes have less flexibility to devote resources to new managed programmes. These differences are accentuated when science policy emphasizes cross-sectoral collaboration with industry and when all Councils suffer from resource constraints. The Department of Trade and Industry (DTI) is keen to collaborate with all the Councils; the task would be easier with a spirit of tolerance and compromise between them.

Since the early days of the Science and Engineering Research Council (SERC) Biotechnology Directorate and the DTI Biotechnology Unit, both organizations have worked hard to ensure complementary programmes and a consistent approach to industry. The collaboration has been effective and plans are now being laid for even closer ties with common committees for programme strategy and evaluation.

The drawing together of the research base and industry has been a significant feature of the U.K. Government policy towards biotechnology. New modes of collaboration through research clubs and in managed co-sponsored programmes with industry have been much admired by officials in other European countries and in the Commission. There is a wide diversity of types of collaborative activity, fostered mainly by SERC and DTI. It is worth dwelling for a moment on three examples, because there is certainly room to expand activities of this sort and I should like to see other agencies adopting similar tactics.

At one level there are clubs to encourage technology transfer and to raise awareness of opportunities for collaboration. The Biotransformation Club is a good example; some 60 members, industrial and academic, pay a modest annual subscription for newsletters, technology awareness reports and attendance at meetings. Numerous specific collaborations have developed from this initiative. It is gratifying that a LINK programme in biotransformation, funded by SERC and DTI, has grown out of the Club to fund collaborative projects with clusters of companies at the fruitful interface of chemistry and biology.

Research clubs can be exemplified by the SERC activities in protein engineering. Here, companies and researchers came together to identify strategic areas of enabling research in protein engineering; SERC invited proposals from the university community and collaborated with companies in selecting a number for funding. A researcher in mid-career took on the task of encouraging the formation of an active community of interest in the subject.

My third example is the Plant Gene Toolkit, which seeks to establish sound practical procedures for introducing foreign genes into key crop plants. The project draws together work at two Agriculture and Food Research Council (AFRC) institutes and two universities. The researchers proposed an integrated programme of work to companies and DTI. Following expressions of interest, there needed to be detailed agreements on confidentiality, intellectual property and project management, because the research, although of high risk, was targeted towards significant commercial opportunities. Eleven companies, from multinationals to new research-based companies, stayed the lengthy course of negotiation to set up the collaboration that has seen the largest financial contribution (£1.5M) from industry to date.

The experience of breaking ground towards these collaborative projects has been hard won, but forms a good basis for more. Some anxieties remain. The academic community is concerned at the exclusivity of research clubs and what can be seen as a break from the tradition of peer

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review towards decisions in 'smoke-filled rooms'. In a broader perspective, it is plain that the projects in SERC clubs are subject to an extraordinary degree of review, both by academic peers and by co-sponsoring companies. And in projects in which companies are providing collectively at least 50% of the cost, it is clear that weight must be given to their views.

To get science policy right for biotechnology, we need to take account of its breadth. Research relevant to biotechnology is funded by four Research Councils and six Government Departments. Each Council has views on the appropriate balance between basic, strategic and applied research. Each Department decides priorities within its range of responsibilities. Spinks envisaged in inter-Departmental committee to direct national support of biotechnology research, but it is quite unrealistic to suppose that Departments will relinquish control over resources to that degree. What can be achieved is to establish programmes in areas of common interest with technical missions agreed between Research Councils and Departments and with means to disseminate the results throughout the programme.

The way ahead

I shall now look at the actions necessary to address the opportunities of biotechnology as we see them now. This symposium is concerned almost exclusively with research, as is quite correct for a technology that is still mainly close to the research base. We should not forget that for the research outputs to be successfully exploited we need a climate that encourages innovation and the transfer of technology through to the market place. The prime responsibility for exploitation must rest with industry, but there is a role for government. It is important that the public and private sectors work in harmony.

Current government policies are well suited to the development of biotechnology. The science base is being improved through selection and concentration. The support for interdisciplinary research centres (IRCs) should benefit biotechnology, allowing substantial interdisciplinary teams with good links into industry to be built up. The DTI policies are aimed at improving collaboration between companies and between industry and the science base. These policies are entirely appropriate for biotechnology at the present stage of development. After a slow start, the interest in the LINK initiative is increasing substantially. Programmes in eukaryotic genetic engineering, biotransformations, food processing, selective drug delivery and targeting relevant to biotechnology have already been approved and additional programmes in protein engineering, plant metabolism and biochemical engineering are in an advanced stage of preparation. LINK provides an excellent framework for collaboration between industry and the science base. Used effectively, we should increase the chances of U.K. research discoveries being translated into products and processes by U.K. companies. It is also an effective mechanism by which higher education institutions (HEIs) can increase their support from government and industry for targeted programmes.

Finance for industry is a matter primarily for the private sector. The U.K. is fortunate in having a well-developed venture capital market with ample resources for new and expanding businesses. The perceived gap for small start-up funds of the order of £100000 still needs attention. However, the DTI SMART Scheme has already helped some biotechnology companies and more awards under the second round of competition will be announced next month.

There is a good case for seeing the public perception of biotechnology as a key factor in the climate for investment. The term 'genetic engineering' is capable of much misinterpretation.

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A Channel 4 television programme contrived to connect transgenic microorganisms seamlessly with the invasion of the reproductive rights of women as an integrated attack on society as we know it. Some companies with considerable investment in applied microbiology are anxious not to be identified as biotechnology companies. Media reports are often distorted and alarmist. Given this perception there is an understandable hesitancy in investing in biotechnology.

Improving the public perception of a technology of such scope is no easy task and it is clear that an aggressive campaign of publicity could be counter-productive. More fruitful, I believe, would be the provision of material designed to set the new advances in context and to provide a background of balanced information against which the inevitable scare stories can be set. I would also urge a degree of caution in the announcement of research results in sensitive areas such as transgenic animals and agricultural biotechnology. I have no doubt that the research community is highly responsible and that the regulatory régime gives adequately balanced protection. But latent public concerns can be fuelled all too easily and it is in everyone's interest to encourage balanced and cautious presentations.

We should not forget that successful innovation depends also upon a regulatory régime balanced correctly between encouraging innovation and protecting the environment and the consumer. Biotechnology presents many problems in regulation that often cross boundaries between areas of Departmental responsibility. Led by the Health and Safety Executive, there is an admirable tradition of pragmatic, case-by-case development of regulation of industrial biotechnology in the U.K. Similarly, the Advisory Committee on Genetic Manipulation has provided wise counsel and is widely respected throughout U.K. industry. We need to preserve the approach in the regulation of agricultural biotechnology. There is evidence that the balance is not right in some European countries and consequently production is being transferred to Japan.

Many of the most significant opportunities in biotechnology involve the release into the environment of transgenic organisms, whether microorganisms, plants or animals. There is a draft European directive for the regulation of such releases, which contains many unsatisfactory features, not least among them the proposal that any member state may object to a proposed release in another member state, with the Commission as a court of appeal. The caution arises in part from powerful environmental lobbies but also from an understandable wish to know more about the risk entailed by such releases. There is a central need for authoritative methods and studies in risk assessment in this area, which would be in the interest of all parties. It is encouraging to note that there are moves towards coordination of the interests of Research Councils, Government Departments and industry in research of this sort. There is a need for earlier and better communication between the regulatory authorities, industry and the research base to facilitate regulations that protect society without imposing unnecessary burdens upon innovation.

Training is another central contribution to success in biotechnology. There is clear evidence in the research base and in industry of a shortage of highly trained staff. SERC has a promising record of attention to training in key strategic disciplines in biotechnology but more needs to be done by a wider range of agencies. The demographic trend will increase the competition for young, trained scientists and engineers and the re-training of staff in industry through specialist short courses will increase in importance and provide opportunities for HEIs for alternative sources of income. In information technology some companies have worked with polytechnics

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to develop courses to meet their requirements and biotechnology companies could follow this example.

International programmes in biotechnology are going to gain in importance. The Human Frontier Science Programme is focused on basic research, but has clear relevance for biotechnology.

The European Community has a great facility for coining good acronyms for programmes (BRIDGE, ECLAIR and FLAIR all contain elements of biotechnology) and increasing substantially the funds available for research. As the prime purpose of the Community R&D programmes is to make Europe more competitive, we must ensure that these programmes are well directed and concentrate on exploitable science. This has not always been the case in the past but we have been arguing, with some success, for larger, more industrially relevant projects in these programmes. The need now is for U.K. researchers to identify partners in Europe for significant collaborative projects. A head of steam has been built up behind a proposal for a Community-wide effort to sequence the yeast genome. Views on the value of the work proposed are mixed, but in the absence of competitive projects it is likely to go ahead. My message here is that the U.K. must devote more effort to influencing the programmes; our pre-eminence in the biosciences in Europe gives a good base from which to work. Positive and constructive proposals at an early stage in the formulation of programmes can be much more effective than criticism after the publication of a draft proposal.

There are strong signals emerging from Europe that expenditure on R&D by the Commission will grow substantially in the 1990s. Some resources will go into new programme areas, but also I expect there will be pressure for further increases in support of biotechnology. Some researchers might see this as an opportunity for additional funding and therefore very desirable, but if this means a shift of resources from the U.K. to Brussels, would they be equally happy?

I have made no forecasts about future commercial prospects for the U.K. This is a deliberate omission because these will be decided mainly by the effectiveness of U.K. companies in a free and competitive market. Government has a role in ensuring a favourable climate for enterprise, fair and evenhanded regulations and an adequate science base providing sufficient skilled people to develop and commercialize the technology, but it strongly resists picking winners or identifying commercial goals.

Conclusion

This symposium brings out admirably the breadth and strength of U.K. research in biotechnology; later papers describe exciting new developments. We owe the late Alf Spinks and his committee a considerable debt for their efforts in the late 1970s. Their report had a significant influence on the debate within Government and industry and I hope those that are left believe that most of their views have borne fruit. The collaboration between academe and industry has improved significantly but further progress depends on goodwill and a commitment to adapt programmes and share the benefits. As more commercial successes are demonstrated, based on basic science, this should encourage others to follow. Transferring technology from the research base to industry cannot be hurried and this is not the time to slacken the effort.

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Discussion

D. A. Rees (*Medical Research Council, London, U.K.*). Dr Coleman's assertion that 'research institutes have less flexibility when programmes are managed' is a surprising remark from a former manager at the National Physical Laboratory and Director of the Laboratory of the Government Chemist; it certainly wouldn't be echoed by Directors of MRC and AFRC establishments. Many major advances in this country that got biotechnology started here and abroad *did* start in the institutes of MRC and AFRC. We ought to be thinking how to make the best use of these magnificent resources and how to nurture the innovative cultures within them, rather than throwing all balls up in the air on the basis of a dubious theory that innovative research in biotechnology can be better managed through committees of general managers dispensing project grants.

The effectiveness of strategic research also depends crucially on making the right long-term commitments, on putting together multidisciplinary facilities and teams, and on looking after the resources and career development of scientists and technical staff, including the encouragement of full-time research by senior scientists. The institutes have very special structural advantages in setting up and managing such ventures.

R. F. Coleman. The Research Councils and institutes have an important role to play in both basic and strategic research. They are at their best in those areas in which there is a long-term requirement, particularly those requiring the maintenance of substantial facilities or specialized expertise. Many of the Research Council institutes have been very successful in this way.

There is, however, another side to the coin. As science and technology develop within a constant financial envelope we have to make room for new opportunities. It is much easier to switch resources on a project basis from one university group to another than to redirect the work of a research institute which is no longer of the highest priority.

It is question of balance between intra- and extramural research programmes. The larger the extramural programme, the more flexibility that is available. Furthermore, when it comes to biotechnology, and I stress technology rather than science, the views of industrialists and the market place are more important than the research scientists' in the institutes. Thus I believe that research managers covering the views of the whole community can sort out the relevant priorities and commission the appropriate research rather better than leaving it solely in the hands of a research institute.

M. Lex (*Biotechnology Directorate, SERC, Swindon, U.K.*). I would like to say a word in support of the SERC approach. The Biotechnology Directorate was charged by Council to relate all its research to the needs of industry. Recognizing the limitation on our budget, we have talked with industry about the road areas of fundamental research that would interest them. This has led to our Priority Sectors, Clubs and LINK programmes, etc. We have then used our resources in most cases as a lever to encourage companies to co-sponsor the programmes with us. As a result, over the six years 1982–87, companies have contributed £4.3M towards these

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programmes. This money has been spent on fundamental and pre-competitive research in the universities. Multidisciplinary groups are now working on coordinated programmes co-sponsored by the Directorate, their progress being closely followed by groups of British companies ready to exploit further the results, either in-house or via 1:1 contracts with the universities. This pooling of private and public resources in the support of academic research appears to be ideally suited to biotechnology. We believe it is the way ahead in times of Government financial stringency.

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