targets then it will make the whole process of screening almost irrelevant. It will enable you to go straight to the molecules that are of interest without the hard work in-between, but it still needs validating.

Advances in HTS and increased compound availability have resulted in the generation of huge amounts of data. Which data-mining methods do you think could prove to be a leader?

We use a variety of tools to go through activity data and we put a lot of effort into the recursive partitioning technology to try to cluster activity and structure relationships. In terms of handling of data, we use IDBS ActivityBase, along with other packages. Spotfire is getting increasing good press as a visualization package.

Where do you think HTS will be in ten years' time?

HTS will either be a non-issue and everything will be done computationally or we could be in effectively the same position as now; supplying a pipeline of molecules to the rest of the drug discovery process, but conceivably 10–100-fold more efficiently. Another development could be, I think, the concept of personal HTS. The delivery of substantial screening power to an individual in a target-oriented environment is, to me, a very feasible new trend. In the same way as computing made the transfer from monolith to the desktop PC, so screening is getting smaller, cheaper and simpler and its target market will become much wider. The same trend has already happened with other analytical equipment.

Who do you think has the most innovative products/ideas in the HTS field?

In terms of miniaturization, Evotec has a lot of skill in readout technologies. For ultimate long-term gain, companies such as Caliper with the LapChip technology probably represent the new wave of technology but it requires a fair amount of work on their part to turn that into the reality of HTS screening. Aurora also has good readout technologies. Perkin-Ellmer has good imaging and readout technologies. The key direction in terms of HTS is certainly miniaturization, and good liquid-handling and detection technologies are vital to make progress. The Irori Nano-Kan system for library synthesis is also very elegant and clever technology.

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Has your company seen any success so far with leads generated from HTS programmes?

Yes. Candidate drugs that had their origins in HTS are being progressed.

Now that some drugs selected through HTS programmes have finally started to reach clinical trials, do you feel that HTS will eventually deliver all that was anticipated at the beginning?

In the early days of HTS, there was an ill-conceived view that HTS would deliver leads or even candidate drugs ready for development. This incorrect view has led to some dissatisfaction with the apparent 'success' of HTS. However, it is now recognised that HTS is only one part of the drug discovery process. HTS provides compounds that are active against targets of interest. The best active compounds must be selected and refined to produce leads that can then be optimized to give candidates for development as drugs. In this context, HTS complements activities such as structure-based design and traditional medicinal chemistry. When considered in its proper context, HTS can and does deliver value to drug discovery activities.

Do you think the benefits of HTS do/will equal the level of financial input required?

It is possible, even easy, to waste a huge amount of money on HTS and its associated technologies. If technologies are chosen and implemented wisely, then HTS will deliver in line with the level of financial investment. It needs teamwork, commitment and a non-parochial attitude or the likelihood of success is diminished.

How do you see the future for miniaturization? Do you ever see the 1536-well plate becoming the most commonly used density?

Possibly. 384-well plates are now established as a commonly used format, although 96-well densities are still used. There are extra challenges in moving to 1536-well plates but they can be solved. The question really is related to whether moving to 1536-well plates is cost-effective and provides real benefit. I suspect there will be a fragmentation with different formats being used for different purposes so it might be that there will be no 'universal' format in the way that 96-well plates once were.

Do you think we should go towards further miniaturization, even past 3456-well plate densities?

Possibly, but not in plates. I think that plates become increasingly troublesome as the well size gets smaller. Physics and chemistry will limit the degree of miniaturization that can be achieved in a robust, reliable and cost-effective manner in plates. Miniaturization will continue for certain applications but it is unlikely to be in plates with open wells.

Do you think companies are being selective enough about which compounds are being screened?
No. As we learn more about structure–activity relationships, the targets we are interested in, and as we have efficient methods for supplying compound subsets to screens, we will become more selective. The days of HTS as we now know it are numbered.

Do you outsource any of your screening?
Not significantly. Screening is such a key part of our drug discovery activities that we prefer to keep most of it in-house. I think a successful outsourcing collaboration requires commitment on both sides to make it work: trust, teamwork and shared goals.

How do you think the human genome sequence information will impact on HTS?
The conventional wisdom is that it will deliver more targets. However, I think it is more likely to help us to better understand diseases and associated targets. It will probably help us to be more selective and to home in on the best targets. It might reduce the need for HTS in favour of a more considered approach.

What do you think will be the impact of informatics and computational chemistry on the direction of screening in drug discovery?
They will result in us being able to screen selected subsets of compounds against targets that we understand better using methods with a much higher degree of sophistication than is the current practice. Eventually, it will lead to the re-emergence of rational design as a viable component of *de novo* lead identification.

Advances in HTS and increased compound availability have resulted in the generation of huge amounts of data. Which data-mining methods do you think could prove to be a leader?
I don't know. Actually, I don't believe there will necessarily be one leader. We will need a range of approaches matched to the job in hand. It is similar to the mistaken belief that HTS, in isolation, would revolutionize drug discovery. We need powerful databases, query tools and visualization approaches together with people who know what data to store and what questions to ask.

Where do you think HTS will be in ten years' time?
We probably won't be doing HTS as we understand it today for the reasons discussed above.

Who do you think has the most innovative products/ideas in the HTS field?
The microplate in its various versions (starting with 96 wells) has been hugely influential and has resulted in the development of a vast range of instruments and automation. The parallel processing and the equipment developed to enable this has been crucial. However, ineffective, unreliable and inappropriate automation has probably been one of the most counter-productive developments in HTS. I anticipate that the most important developments will probably turn out to be the imaging instrumentation and the effective application of informatics, although the latter area still has some way to go.

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Has your company seen any success so far with leads generated from HTS programmes?
There has been substantial success with running HTS programmes in 96- and 384-well plates for several years now in Novartis.

Now that some drugs selected through HTS programmes have finally started to reach clinical trials, do you feel that HTS will eventually deliver all that was anticipated at the beginning?
For sure, HTS is playing and will play a major role in the current and future drug discovery process. The expectations throughput the industry are very high but, in most organizations, the screeners and the drug design people are working closely together. It is this combination between random screening and the rational approaches that are generating real added value in drug discovery.

Do you think the benefits of HTS do/will equal the level of financial input required?
The field of HTS technology is very dynamic and will not stop after a certain technology has been established. Therefore, there will always be a lot of pre-investment in screening technology. However, the strategy between different companies varies. Whereas some companies are trend-setters in establishing new screening technology in collaboration with innovative biotech firms, others wait until a certain technique has a proven track record before they get involved.

How do you see the future for miniaturization? Do you ever see