The *Discussion Forum* provides a medium for airing your views on any issues related to the pharmaceutical industry and obtaining feedback and discussion on these views from others in the field. You can discuss issues that get you hot under the collar, practical problems at the bench, recently published literature, or just something bizarre or humorous that you wish to share. Publication of letters in this section is subject to editorial discretion and company-promotional letters will be rejected immediately. Furthermore, the views provided are those of the authors and are not intended to represent the views of the companies they work for. Moreover, these views do not reflect those of Elsevier, *Drug Discovery Today* or its editorial team. Please submit all letters to Dr Rebecca Lawrence, News & Features Editor, *Drug Discovery Today*, e-mail: Rebecca.Lawrence@current-trends.com

Communication networks: key to success of new technologies ▼

Numerous scientific technology waves – computer-aided drug design, combinatorial chemistry, HTS – have swept through drug research in the past years. Invariably, at some point following each wave, some observers comment that once again a particular technology has failed in its promise to be the answer to the problem of the industry's innovation gap. However, comparison with other effective innovation environments suggest that such judgements are premature: most, if not all, of these applications could still prove to be important contributors to innovation once they are effectively linked into a dynamic data transmission and communication pipeline in the discovery organization.

Noted high-innovation periods such as the Renaissance and, much more recently, the Internet, share the characteristics of intensified and freer flow of ideas and dialog[1]. Relative to the previous situation – whether the plaza of the Italian city-state or the Web – increased participation in the innovation space by a wider diversity of persons led to an explosion in creativity. Fundamental to productive exchange in these innovation spaces is that ideas and thought models are challenged: breakthrough happens not because new ideas are developed but because old ideas are confronted and escaped[2].

In modern communication system space, Yochai Benkler (New York University, NY, USA) defines three layers that comprise a 'communication system': the physical layer (the wires that connect), the logical layer (the system that controls who gets access, or what gets to run where), and the content layer (the data or ideas that flow). In this context, the chemistry and biology high-throughput technologies and their output have too often remained silos in the organization's physical and human resource layers. The transfer of their data value through the wider organizational communication pipeline has often been abbreviated. Too often, before the layer for broader access is completed (or even built, in some cases) a newer, more powerful form of some base hardware technology looms, keeping energies focussed on re-assessment of the base technology decision. In the early days of molecular visualization and analysis, for example, constant assessment of successive hardware engine operating systems and graphics boards left both the customers and the suppliers exhausted and distracted. (One hardware vendor took visible pride in being the creator of constant chaos.) As J. Fraser Glickman suggested in a previous commentary on optimizing screening technology in this section[3], the lure of technology power is often such that the point of diminishing returns is crossed and, invariably, this over-attention comes at the cost of under-attention to benefit-extending communication layers.

Paralleling the concern about over-attention to hardware technology, some observers point to unnecessary overload in the amount of data currently being generated. Their argument is that the data activity churn is simply building a bigger haystack rather than bettering the chances of finding the needle in the haystack. Their observation is probably correct in part. However, this imbalance will likely be adjusted as more detailed experimentation and assessment methods evolve. For example, molecular diversity pre-analysis and structure and property methodologies quickly offered improvements in efficiency from more random combinatorial chemistry approaches. Further scientific refinement will continue to pinpoint those pattern markers and methods that can be applied earlier in the research cycle to select data points relevant to the project at hand.

For many research organizations, the basic problem seems to be the disorganization of historical data, often scattered in private databases on individual desktops and in different formats. Can the industry's current IT catch-up moves help address the innovation gap? Studies have underscored that architectural competence – the ability to integrate knowledge into a company – is positively associated with research productivity, especially when collaborative processes are also adopted in parallel[4]. New data handling and drill down methods are offering 'pattern breaking' ways of organizing and interpreting the information, a key requirement for creativity to occur. Can informed domain tools keyed to

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encourage precise and powerful probing of data relationships matter? One potentially relevant example is the Challenger spacecraft, where project engineers failed to spot what the data could have told them about the link between launch pad ambient temperature and O-ring erosion[5].

Targeted methodologies and promising models for the fusion of experiments and informatics are emerging. Also emerging is a newly enriched scientific commons with a multi-disciplinary vernacular. Related enterprise data communication and analysis systems are taking shape. Only when these communication networks are in place to facilitate data-enriched dialog does it seem fair to judge whether the scientific technology platforms have been part of the problem or part of the solution.

References

1 Lessig, L. (2001) *Commons*, Draft 2.0
2 Tushman, M. and O'Reilly III, C. (1997) *Winning Through Innovation: A Practical Guide to Leading Organizaional Change and Renewal*, Harvard Business School Press
3 Glickman, J.F. (2001) Optimizing screening technology: how much to invest? *Drug Discov. Today* 6, 73–74
4 Henderson, R. and Cockburn, I. (1994) Measuring competence? Exploring firm effects in drug discovery. *Strategic Manag. J.* 15 (Winter Special Issue), 63–84
5 Tufte, E.R. (1997) Visual and statistical thinking: displays of evidence for making decisions. In *Innovations: Images and Quantities, Evidence and Narrative*, Chapt. 2, pp. 39–53, Graphics Press

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More microwave reactors required ▼

Microwave energy was first shown to accelerate organic reactions in the 1980s. There were, however, major concerns with the use of this technology as there was a lack of available systems with adequate temperature control, and there were risks associated with the use of flammable organic solvents. As time moved on, safe microwave heating equipment was brought onto the market that enabled both accurate temperature and pressure control, as well as convenient monitoring of reactions. As a consequence, the total number of articles appearing in the literature describing rapid chemical synthesis promoted by microwave irradiation has grown from ~200 in 1995 to ~1000 in 2001. Excellent reviews have been also published on microwave-assisted chemistry[1].

Pharmaceutical companies are under pressure to speed-up their drug discovery programmes and to drive down the cost of discovering new medicines. We are aware of the interest that has been generated from combinatorial and high-throughput chemistry as a potential means of speeding up the drug discovery process. These techniques have been embraced widely by the pharmaceutical industry, but there is room for further increases in the speed with which we carry out drug discovery. The use of microwave energy to accelerate organic transformations is one route to increasing efficiency.

The majority of microwave-promoted organic synthesis has been performed in multi-mode domestic ovens. For safety reasons, the use of microwave reactors designed for organic chemistry is strongly recommended. One drawback of the present design of safe ovens is that the reaction size is more or less fixed at a relatively small volume.

There have been several procedures using microwave-assisted chemistry for the production of compounds of relevance to medicinal chemistry. One example used microwave irradiation to achieve rapid alkylation of a range of piperidines and piperazines to generate a library using parallel synthesis[2]. This library was screened in a herpes simplex virus-1 (HSV-1) helicase ATPase assay and confirmed hits were identified.

This is just one example where the advantages of parallel synthesis have been combined with the reaction acceleration possible with microwave-promoted organic synthesis. This synergy has tremendous potential for the future in impacting on the generation of compound libraries for biological screening. One area which will need addressing is to ensure microwave-assisted chemistry does not suffer from limitations of throughput, if library sizes running into many thousands of individual compounds is a goal.

There are other reaction types that have proven suitable for microwave acceleration but have not, to date, been exploited in the context of library production. Many other reactions have potential for automated medicinal and combinatorial chemistry, traditionally performed with long reaction times, and might be dramatically accelerated by microwave heating. Carbonylative reactions are one example.

It is unfortunate that only a few modern microwave reactors designed for safe automated synthesis are currently available. It is up to end-users to demonstrate an increased desire to use such equipment. In doing so, this will ensure the commercial production of single-mode cavity based synthesizers, satisfying the requirements of academia and the pharmaceutical industry.

References

1 Larhed, M. and Hallberg, A. (2001) Microwave-assisted high-speed chemistry: a new technique in drug discovery. *Drug Discov. Today* 6, 406–416
2 Selway, C.N. and Terrett, N.K. (1996) Parallel-compound synthesis: methodology for accelerating drug discovery. *Bioorg. Med. Chem. Lett.* 4, 645–654

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