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EDITORIAL

Technology-driven science

The physicist Freeman Dyson is reported to have remarked that 'scientific revolutions are more often driven by new tools than new concepts'. This sentiment must seem like heresy to the many, who have a glamorous view of science as an enterprise, driven by an urge to understand natural phenomena, with periodic revolutionary upsurges when new concepts and insights appear to form in the minds of the most gifted practitioners of science. The quantum revolution in the early part of the last century and the dramatic upheaval in structural molecular biology in the 1950s, appear as marvellous examples of the way in which science progresses. Technology is seen as a fall out of science; the transistor, the laser and the integrated chip are corollaries of the spectacular march of fundamental physics; an extraordinary spectrum of pharmaceuticals and materials, molecular diagnostics and vaccines appear to be the consequences of over a century of unimpeded progress in chemistry and biology. Useful technology clearly follows major scientific developments. But, can technology drive science, as Dyson implies? Are there branches of science where technological developments direct the path of inquiry; where the motivations for research are shaped by the tools available?

Modern biology inevitably springs to mind as a discipline, where the march of technology has changed the face of biological research. In his characteristically acerbic style, the molecular biologist, Sydney Brenner reflected on the issue of 'hunters and gatherers': 'I was taught in the pre-genomic era to be a hunter. I learnt how to identify the wild beasts and how to go out, hunt them down and kill then. We are now, however, being urged to be gatherers, to collect everything lying about and put it into storehouses. Someday, it is assumed someone will come and sort through the storehouses, discard the junk and keep the rare finds. The only difficulty is how to recognize them'. (*The Scientist*, 2002, **16**, 14). Brenner targets here the genomics programs, which seek to sequence as many genomes as possible, cataloguing the data, with no immediate questions in mind. Rather than 'hunt' in the traditional manner for disease genes, the new approaches involve sifting through reams of sequence data which have been 'gathered', in the hope that subsequent analysis will reveal the genes of interest. Brenner's heart appears to lie with the 'hunters', practitioners of classical 'hypothesis-driven science'; his ire directed at the 'gatherers', votaries of the rapidly advancing area of technology-driven science.

Biology has been transformed over the past twenty years by an array of powerful technologies, most notably the techniques to manipulate, clone, amplify and sequence DNA. Indeed, *Time* magazine was probably not guilty of its customary hyperbole, when it described the new DNA technologies as 'the most awesome and powerful skill acquired by man since the splitting of the atom'. Max Perutz describes Fred Sanger's pathbreaking work on DNA sequencing, thus: 'Sanger did not work *à la* Popper by formulating hypotheses and then performing experiments to test them by falsification. Instead he invented new chemical methods capable of solving problems that no one else had even approached, since it was believed they would defy solution. He did not measure his discoveries against existing paradigms, because they opened new worlds where no paradigms existed'. (Max Perutz in a review of P. B. Medawar's *Advice to a Young Scientist*). Sanger and indeed all the great analytical and synthetic chemists over the ages have worked in a manner that defies a Popperian classification; their science clearly not hypothesis-driven, but nevertheless wonderfully creative and inventive. Perutz adds: 'The process of invention is imaginative, but so far as I know no philosopher has thought it worthwhile to analyse it, because the mind's creative process is impenetrable'. DNA sequencing has come a long way from Sanger's original laboratory methods; it is, today, an immensely powerful technology. Indeed, in the sequencing centre that bears Sanger's name, array upon array of marvellous machines churn out genome sequence data that are automatically stored in banks of computers. The 'gatherers' are at work here and in many superbly organized facilities across the world. As genome after genome succumbs to the relentless onslaught of organized sequencing, the science of biology stands at the crossroads. Will the 'gatherers' transform into 'hunters'? Or will a new breed of hunters evolve, who like hyenas will emerge from the shadows to rip out the most succulent parts of fallen genomes. There is already some evidence for the emergence of a new species; bioinformaticists, who hope to sift through the mass of genome sequence data, to reveal the foundations on which biology's future advance will rest.

The study of genome sequences is not the only area where technology holds sway in biology. The developing science of genomics has two distinct components; functional genomics which aims to bridge the gap between genotype and phenotype and structural genomics, which promises to determine the three-dimensional structure of all the protein products, that result from the translation of information encoded in genes. Protein structures, in turn, may reveal the nature of their functions, providing another path towards understanding the control and flow of information in biology. Central to the area of functional genomics are powerful, automated methods for analysing simultaneously the expression of hundreds of genes, based on micro-array technologies. Structural genomics is fuelled by high throughput X-ray crystallography, with synchrotron beamlines and robotic crystallization procedures providing some of the tools which will hasten the process of structure determination; an activity that has traditionally been slow and laborious. High-field NMR spectroscopy with its monstrously expensive instrumentation is also being recruited to the task of determining protein structures, albeit limited by molecular size, but offers the advantage of bypassing the uncertainties of crystal growth. With biology awash in data, computers and computer scientists have become central to the field, a development largely unanticipated even thirty years ago. The new biology has been described as 'discovery science', requiring 'large-scale facilities for genome-wide analyses, including DNA sequencing, gene expression measurements and proteomics'. (Aebersold, R., Hood, L. E. and Watts, J. D., *Nature Biotechnol.*, 2000, **18**, 359). 'Discovery science' appears to be a term that finds favour in industry, promising as it does the prospect of new and patentable discoveries. Hypothesis-driven science, in comparison, seems a curiously inefficient, esoteric, academic exercise.

As the tide of technology-driven science rises, particularly in biology, we need to consider mechanisms for the support and conduct of research in areas, which depend heavily on the use of expensive and sophisticated equipment and, sometimes on alarmingly expensive consumable reagents. Not too long ago, biology laboratories in our institutions housed little by way of expensive equipment. Today, the demands of biology outstrip most other sciences. With growing awareness of new technologies, funding organizations in India face a new problem; requests for acquisition of extremely sophisticated research tools, by institutions with limited capacity to maintain and use such equipment. A new breed of scientists is beginning to emerge, 'the acquirers', whose sole aim, sometimes, seems to be the acquisition of sophisticated technology, which is often neither used nor maintained. Abetted by agents for companies which market the new technological tools of biology, institutions are being driven to purchase expensive equipment, which they do not always require. The 'acquirers' also betray a technical innocence, which can be quite disconcerting; they seriously believe that once the technology is in place, good science will follow. The alarming shortage of scientists and expert technicians in India, who are trained and comfortable with the cutting edge technologies of biology, must be addressed, if we are to effectively exploit the explosive development of new techniques. Acquiring instrumentation alone may hardly be adequate.

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