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Tracking life science research

The availability of computerized databases has made the analysis of research output easier and more quantitative. Publication statistics are very popular amongst scientists, reminding us at least, in the season of children and their fascination for cricket statistics. What is not commonly appreciated is that the statistics of publications can be dangerously misleading, if the limitations of the underlying database are not well understood. Classification of journals into a specific discipline is very difficult nowadays. For instance, medical research databases include many journals dealing exclusively with basic biology and biochemistry. Important papers on magnetic resonance imaging may appear in physics or chemistry journals, which do not find a place in the roster of medically oriented publications. Nevertheless, many sub-databases exist which can be used for reasonably reliable mapping of scientific output.

Arunachalam (page 1191) uses the BIOISIS Biological Abstracts database (1992–94) for mapping 'Life Science' research in India. The subject is important since funding agencies have been consciously supporting research in this area since the early 1980s. A major problem of course is to define what constitutes 'life sciences'. The indexing procedure of the BIOISIS database allows 'biologically' oriented papers from a wide variety of 'non life science' journals to be included. The database is fairly large and allows many interesting conclusions to be drawn.

One inevitable feature of these analyses is that they remind us that the fraction of papers from India published in highly visible ('high impact') journals is small. This is a well-known and widely discussed fact. Arunachalam’s paper is full of many nuggets of information, which can be interpreted in different ways. He also makes some conclusions which may stir debate. For instance, he says 'What should be of concern to policy makers and funding agencies is that even scientists from better-known institutions publish a large number of papers in journals not indexed in SCI'. Most of these 'non-SCI' journals originate in India, leading to the uncomfortable question whether these journals and the papers they publish serve a useful role at all. Should the SCI be the overriding determinant of publishing practices? Arunachalam draws some perceptive conclusions. He identifies two distinct clusters of institutions: one 'working on classical biology and agriculture' which 'concentrate on certain sub-fields and publish often in journals of low impact and another smaller cluster of institutions working on new biology publish part of their papers in high impact journals'. The author points out that 'at the moment there seems to be very little overlap between the interests of the two clusters'.

Ribosome mediated folding

Christian Anfinsen is credited with the idea that the information necessary for folding protein structures is entirely encoded in the sequence of amino acids that make up the polypeptide chain. The efficient refolding of many proteins in vitro supports the idea that proteins do not need the assistance of other cellular components to acquire native three-dimensional structure. The discovery of cellular proteins, molecular chaperones, which assist folding in cells (and in many cases, folding in test tubes) was a major advance in biochemistry. The first crystal structures of chaperones quickly provided clues to their functioning, leading to models where their role is essentially passive, providing a nascent polypeptide chain a sequestered environment, preventing non-productive protein aggregation. The first report that ribosomal components can promote protein folding came from the work of Chanchal Das Gupta at the University of Calcutta. This observation has major implications for cellular processes since the ribosomes are indeed the site of polypeptide synthesis.

On page 1235 Chakrabarti et al. examine the structure of a model protein, horseradish peroxidase (HRP), during ribosome mediated folding. Their results provide 'evidence of direct physical association between the ribosome particle and denatured HRP during refolding'.

P. Balaram

Tuberculosis

Tuberculosis is known as 'King of diseases' today – although the adjective itself is a kind of oxymoron! No disease should ever be referred to as a King. If the population with low purchasing power is affected by a particular disease, it does not draw attention of the multinational drug companies. Tuberculosis was thought to be one such disease even in recent past. However, the scenario has changed; now the most affluent nations are alarmed with the increase in the number of tuberculous patients. The worst fear has come true. The bacteria appears to be extremely smart to evade the action of drugs like isoniazide and rifampicin. Thus, there is a renewed vigour to search for new drugs or new metabolic pathways which are affected due to mycobacterial infection.

The mechanism of action of the drug rifampicin has very well been worked out. It acts on the β-subunit of bacterial RNA polymerase, thereby inhibiting the transcription process. All the rifampicin-resistant mutants always have altered rpoB gene, which codes for the β-subunit of RNA polymerase. However, some bacterial strains with low resistance to rifampicin have been found with no alteration in the β-subunit, indicating thereby other cellular components which are responsible for drug resistance.

Geetha Ramachandran et al. (page 1231) have now discovered that drug-resistant tuberculosis strains show elevated level of cytochrome P-450 in comparison to that of sensitive strain. Cytochrome P-450 constitutes the most powerful oxidizing enzymes and is involved in the biotransformation of a wide variety of drugs and is found in liver microsomes. The authors have been able to assay cytochrome P-450 spectrophotometrically and have shown that its level is significantly higher in the rifampicin-resistant strain of M. tuberculosis and in its other variants. It is then responsible for quick degradation of the drug rendering it ineffective. The question which remains unanswered is whether there are inhibitors of cytochrome P-450 which will competitively leave out the drugs from metabolizing in a mixed assay system. Any new angle towards efficient handling of tuberculosis infection always appears to be a welcome change.

D. Chatterji