

In this issue

Biotechnology: Using genes and proteins

Biotechnology is a vast, rapidly evolving discipline which seeks to exploit the advances in biological and physical sciences to develop practical application of science in fields like medicine and agriculture. The special section in this issue focuses on some selected aspects of biotechnology. Werner Arber defines (page 826) an overview of the field of functional genomics, charting its history over the past century. While the dawn of the 20th century saw the birth of modern genetics, the dawn of the 21st century marks the onset of genomics, particularly human genomics. Arber emphasizes, at several points in his essay, that identification of specific genetic information may lead to biotechnological applications.

Two papers on genomics explain the experimental methodology in microarray analysis and its use in analysing the rice genome. DNA microarray analysis, reviewed by H. P. Saluz *et al.* (page 829), is a 'state-of-the-art' technology being developed to profile the expression of the information content of an entire genome. The authors specifically discuss the differentially expressed genes found in several cell lines that could be easily detected using microarray technology. Such experimentation applied to diverse organisms and their hosts may lead to design of prophylactics and therapeutics based on the functional genomics. The paper on rice genomics by Takuji Sasaki (page 834) focuses on the genomics of a plant that provides staple diet for about half of the world population, tracing the history of the field from the beginning of restriction fragment length polymorphism (RFLP) studies leading up to the detailed mapping of quantitative trait loci (QTL) that are interactive associations of multi-gene complexes.

Knowledge of complete genome and the profiling of gene expression will hasten our efforts to introduce beneficial genes into the rice plants directly.

Proteomics is an approach that complements the genomic studies in the array of tools in the hands of a biotechnologist. E. J. Hayduk and coworkers (page 840) review the techniques available to study proteomics of an organism. To study the assortment of all expressed proteins in a sample, i.e. in a proteome, two-dimensional gel electrophoresis is used to separate the mixture of proteins followed by characterization using mass spectrometry. In addition, newer protein-chip technologies are making rapid headway. Computational biology is another important component of the emerging areas of modern biotechnology.

Marvin Edelman and co-workers present two papers on *in silico* docking algorithms. Such procedures serve a two-fold purpose – a molecular biologist interested in the structure–function relationship uses them for understanding intermolecular interactions like ligand–receptor, protein–protein or protein–DNA. These studies lead to sharpening of mechanistic understanding of molecular stereochemistry that is important for biological processes. Biotechnologists might apply similar tools for understanding antibody–antigen interactions to develop better vaccines, or they might utilize similar methodologies to design inhibitors that block specific enzymes in a metabolic pathway that could work as a therapeutic; they might also design specific ligands that could block signalling through specific membrane-bound receptors that could work as an anti-growth factor or an anti-mitogenic activity.

Specifically, Edelman *et al.* in their first paper (page 845) describe the various computer-based methods

available for docking a ligand molecule onto a protein. These methodologies would be useful for *de novo* drug design, once the target protein is known. The database for small molecules with known three-dimensional structures could be screened to fit into the putative binding site on the target protein. The various search algorithms, including simulated annealing, genetic algorithms and screening functions, specially the knowledge-based scoring functions, are discussed. The authors believe that future development in the field would call for better scoring functions.

In the following paper (page 857), Edelman *et al.* describe the docking procedure to analyse binding of the peptide toxin, tentoxin, a naturally occurring tetrapeptide to chloroplast ATP synthase as a test case. F_0 – F_1 -ATPase, or the ATP synthase, is a key enzyme important for formation of ATP from ADP and inorganic phosphate in bacteria, mitochondria and chloroplasts. The authors describe the intriguing effect of tentoxin, binding to chloroplast ATPase, that can be an inhibitor of ATP hydrolysis at low concentration and a stimulator of ATP hydrolysis at higher concentration. The modelling of the binding could be done with the docking software LIGIN, treating the ligand and the protein molecules as rigid bodies, and three putative cavities on the protein molecule surface are identified.

Malaria

On page 818 of this issue, Ramya *et al.* describe the strategies developed by the malarial parasite, *P. falciparum*, to sneak through the defences of the human host. They primarily focus on the uniqueness of the biosynthetic pathways in the protozoa contrasting with the human, and discuss the possibilities of deve-

loping prophylactic and therapeutics for malaria.

Studies of the route of transmission in the pathogenesis and epidemiology of malaria, suggest several points of intervention to eradicate the disease. Chemotherapy is increasingly limited by the emerging drug resistance in the parasite although this remains the only viable strategy against malaria. Prevention (immunoprophylaxis) may be achieved through vaccination – and trials are underway. Elimination of mosquito vectors, particularly using larvicides, is an attractive approach. The impediment to success has been poor public hygiene, and the developing resistance of the mosquitoes against insecticides. To prevent mosquito bite, use of bed-net, specially permethrin-coated bed-net, and DEET insect repellent on exposed skin has been advised (www.cdc.gov).

A novel, recent approach attempts to generate transgenic anopheline mosquitoes that are incapable of transmitting the parasite (Ito, J. *et al.*, *Nature*, 2002, **417**, 452–455).

In addition to therapy, and prevention by interfering with the mosquito vectors, immunoprophylaxis and anti-malarial vaccines are among the possibilities in the future. A 20-mer peptide that mimics a part of the merozoite surface protein, interfering with the binding of the receptor to the membrane, has been discussed as a potential immunoprophylactic (*Angew. Chem., Intl. Ed. Engl.*, 2001, **40**, 4654–4657). Understanding of structural and functional genomics of *Plasmodium* and the mosquito vectors will open many more avenues for combating malaria. The recent reporting of sequences of the genomes of *Plasmodium falciparum* and the anopheline mosquito mark the beginning of a new phase of malaria research.

Somatic embryogenesis

The use of bamboos is widespread in rural India. Household items, implements, furniture and decorations made using parts of bamboo plants are the

source of living for a large section of the rural folk. Bamboo 'rods' are used in making scaffoldings for rural homes, the leaves are used as fodder, and some bamboos are good for making various types of flutes. Multiple uses to support rural economy have made the bamboo plant a natural choice for social forestation programmes.

Cultivation of bamboo is limited by various factors. The large demand for strong, adult stems has stimulated the development of alternative artificial methods for rapid growth. Savita Godbole *et al.* (**page 885**) describe the somatic embryogenesis technique using the bamboo species, *Dendrocalamus hamiltonii*. This work demonstrates the use of nodal explants from adult, mature bamboo plants to generate plantlets suitable for growth under greenhouse conditions, employing rapid and reproducible techniques.

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