

## In this issue

### Mathematical modelling in biology

Biology is primarily an experimental science. From the descriptive coarse-grained approach, it has turned itself into a molecular science through the advancements in physicochemical techniques. To complete the circle, the trend is now to put together the detailed molecular information for getting the holistic picture. Theoretical studies in biology have always gained from these transitions and evolved accordingly.

Theoretical biology, like a coin, has two faces – abstraction and reality. The approach to confront a biological problem depends on the face that one looks at. Since most workers in this field have made their forays from the physicochemical and mathematical sciences, the top-down approach is common in problem-solving. This approach, though considered essential for physical systems and involves detailed mathematical analysis and abstraction, has alienated many biologists who find it too abstract to relate with the biology of the problems. There are some who have made serious efforts to familiarize themselves with the intricacies of biological processes (which are generally complex) and have attempted a realistic bottom-up approach to problem-solving. A rigorous, detailed, process-based, mathematical description of the biological problem can give a realistic model which can give biologically-relevant results particularly suitable to the problem under study.

It would be unwise to denounce one approach for the other. Both have their own subtleties and qualities. Incorporation of realism in models makes them, most often, very complex, and the analyses are generally numerical. Such formulations have their inherent problems obvious to modellers. The abstract formalism

hinges on the understanding that biological systems use diverse ways (i.e. a variety of molecular mechanisms) to perform similar functions. In other words, a specific process is modelled using an abstract formalism (which may or may not have similarity with the underlying biological reactions) because the dynamic behaviour of the model is similar to the functional response of the process. In general these types of models are simpler and sometimes analytically tractable. Ideally one needs a formalism between the two extremes which can happen only with true exchange of information and collaboration between the theoreticians and experimentalists. Finally it is a biological problem that one aims to solve/understand in terms of biological knowledge. Theory helps in conceptualizing and putting the details in a coherent framework necessary for systematizing and prediction.

This collection of papers in the Special Section in 'Modelling in Biology' attempts to give a flavour of the different types of problems and approaches that are currently in use in the area of theoretical biology. It is by no means complete in either of the above-mentioned aspects. Few of the papers review the activities in a particular field and attempt to present a general framework of understanding. Some others deal with specific biological problems using a particular theoretical methodology. Some describe theoretical advancements in other areas of science that is being applied to biology effectively. There was no intention to cover all the fields of enquiry in biology, nor to touch all the methods of mathematical modelling. Prominent among those which have not been covered are molecular structure and sequence analyses, neural networks and neurobiology, and pattern formation and reaction-diffusion systems. There have been good review

articles on these areas in *Current Science* during the last few years.

Lee A. Segel (page 929) gives a personal account of his decade-long contribution in theoretical immunology. His paper deals with the integration of a large body of data into a theoretical framework involving the unifying principles of feedback. Based on his in-depth experience, the author has finally brought in the concepts of artificial intelligence to describe the immune system. In this thought-provoking review, Segel has attempted what is all theoreticians' dream – to tie up many diverse problems in immunology with a common thread.

Rhythms are widespread in biological systems and span time periods from milliseconds to years. In a synthetic approach, Albert Goldbeter (page 933) models a variety of oscillatory processes in cells which arise from very different molecular processes – from circadian rhythms in *Drosophila* to glycolytic oscillations in yeast. His work shows that the causative mechanism in the generation of cellular rhythms in widely different systems is the presence of positive and negative feedbacks. His models are realistic and based on molecular details of the processes, and yet his framework is general.

One field in biology that has had a long association with mathematical and statistical modelling is population genetics. Here complex statistical methods are used to analyse the gene frequency data in populations under a variety of models of intra- and inter-genic interactions. Swapan K. Nath and Partha P. Majumder (page 940) have modelled complex genetic disorders in humans by considering other causal factors which act as sources of complexity in the inheritance or transmission patterns of a disease in families. Though the models are general, the authors indicate particular genetic disorders and

causal factors where their treatment can be applied.

A long-standing debate in ecology has been the origin of variability in population abundance data. Some favour the hypothesis that the observed irregular oscillations are often manifestations of the inherent nonlinearity of the system. Others give arguments favouring homeostasis superimposed with environmental noise as the key source of the variability. Acknowledging the presence of both in nature, my paper (page 949) attempts to address the dichotomy by incorporating common ecological processes (e.g. migration) in the existing models.

Mathematical modelling in physiology has always had a special importance due to its relevance in medicine. Gita Subba Rao, J. S. Bajaj and J. Subba Rao (page 957) have analysed different forms of the disease diabetes mellitus with a realistic model that incorporates many relevant physiological processes in balancing the glucose and insulin levels in plasma. This model not only gives a better fit to clinical

data for different types of the disease; it also predicts, using different mathematical methods, the critical parameters which may have a greater role in developing therapeutic measures.

Genetic algorithm (GA) has been considered to be an important tool to study evolving complex systems, and problems in evolutionary biology are particularly suitable for it. Narayan Behera (page 968) has reviewed the use of GA to study one of the fascinating problems in evolution – phenotypic plasticity – an extraordinary example of genotype–environment interaction during development. The study shows that plastic alleles can not only improve the degree of adaptation of the population, it also speeds up the rate of evolution with the help of regulatory genes.

One development that has made deep impact in all sciences is the theory of chaos. Biological systems are both complex and nonlinear. Many a times the normal regular behaviour of a system is replaced by chaotic irregular functioning due to genetic or systemic changes

(diseased state). Avoiding or controlling such situations is a matter of important concern to theorists and experimentalists alike. Sudeshna Sinha (page 977) has reviewed the methods which have been developed to control chaos and their application as experimental tools in controlling cardiac and neuronal diseases.

Ph. de Reffye and F. Houllier (page 984) used a novel theoretical approach to model plant architecture based on the idea that plant functioning and structure are intimately related. They used computer graphics, morphological algorithms (fractals), formal grammar, theory of graphs and automata rules based on experimental data to generate three-dimensional virtual plants. With this synthesis of ecophysiological, morphological and mathematical knowledge, they have simulated the reaction of the plants to changing environments, and predicted the use of the knowledge for many agronomic and silvicultural applications by performing virtual experiments.

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