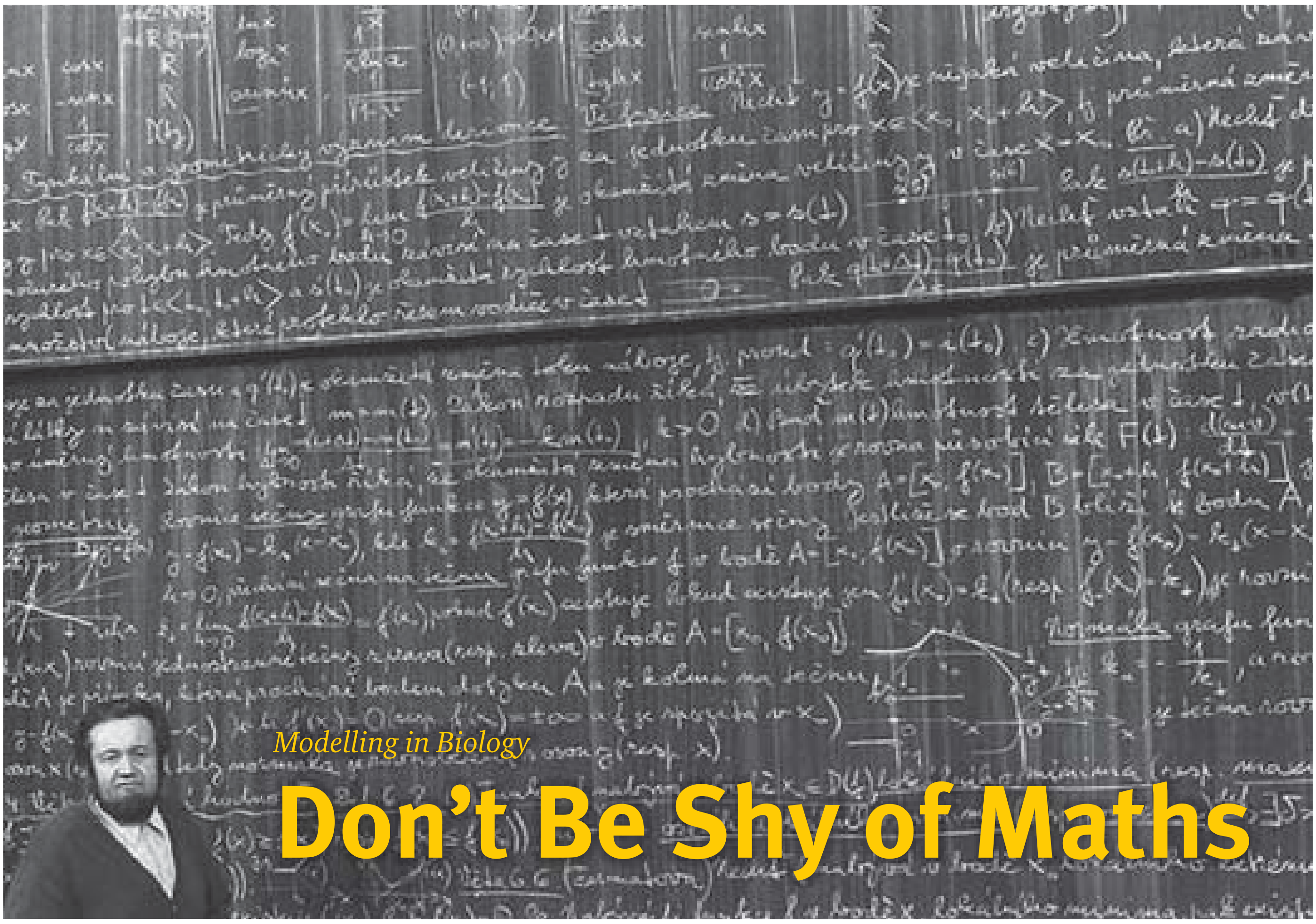

Modelling in Biology

Don’t Be Shy of Maths

It’s no longer possible to turn the explosively increasing datasets of modern research into biological insights without mathematical modelling. Fortunately, new software packages open this door to even the most entrenched mathophobe.

Biologists hate maths. Somehow we are more comfortable with our box-and-arrow pathways, with their intuitive feel of how causality flows from one molecule to the other, leading from cause to effect, stimulus to response.

However, times are rapidly changing. The explosive increase in the number and size of datasets generated by large-scale experiments, such as microarray, proteomics and metabolomics projects, is forcing a change in the way we model biological systems. Just how are we to turn these parts lists into insights into how cells, tissues and organs work? The human brain cannot cope with the complexity of the dynamic models needed to do this and so we are turning more and more to computer-operated mathematical models. Also it is not just large-scale pharmaceutical companies or dedicated math-biology labs that are doing this. New software packages are opening the door to the power of predictive modelling to even the most entrenched mathophobe.

Virtual man

Computer modelling does nothing more than scientists have always done down through the ages. They model systems using numbers and mathematical functions and look to see if the relationship between the inputs (stimuli) and the outputs (responses) match those of the real world. It is just that computers can handle much more complicated models than the poor human brain ever could.

Computerised biological models are growing, both in complexity and in predictive power. Massive models of metabolic and signalling networks are opening the way for rapid *in silico* design of new drugs. They can also test for their toxicity, at the same time reducing reliance upon the use of animal testing. A good model can save a lot of time and money.

Not without problems

Do they really work? Given the complexity of even a single cell and our ignorance of so much of what goes on in even the best-studied processes, can they really make useful predictions? Companies like Entelon think they can and they have the financial backing to prove it. Entelon is taking the power of predictive simulations seriously, developing huge bio-models of several human diseases. They harvest data from biomedical literature and assemble it into models called “virtual patients”, a term which gives some idea of the confidence they place in the models’ predictive power. Last month Entelon was granted a patent on a model of diabetes that is to be used to predict not only the system-wide effects of drugs, along with their optimal doses, but also to suggest the best paradigms for clinical trials.

Mathematical modelling in biology, however, is not without its problems. For a start, there is the issue of the quality of the data. Even the best model can be no better than the data it is built upon and this is particularly true for mechanistic models, in which every component has to be represented with some degree of accuracy. The problem is that there is a mismatch between the speed at which we can obtain certain data, such as protein expression levels or metabolite concentrations, and the time it takes to get other kinds of data, such as kinetic equilibrium constants. Plus it is often just these kinds of hard-to-get data that make all the difference to the predictive power of a mechanistic model.

Logical approaches

There are ways around this, however. Some labs have completely sidestepped this issue altogether, questioning even the need for such refinement of data. Last year, for instance, Julio Saez-Rodriguez and colleagues published a paper in *PLoS Computational Biology* in which they modelled the signalling network that controls activation of T-cells by T-cell receptors (*PLoS Comput. Biol. 3(8): e163*). Their model incorporated 94 nodes and 123 interactions and it accurately mimicked several of the published observations on this network. They then went on to test the predictive power of the model and found that it anticipated the con-