Abstract

I will discuss a new theoretical approach to information and decisions in signalling systems and relate this to new experimental results about the NF-kappaB signalling system. NF-kappaB is an exemplar system that controls inflammation and in different contexts has varying effects on cell death and cell division. It is activated by various stress stimuli, including inflammatory cytokines such as TNFalpha and IL-1beta and is regarded as one of the most important stress response pathways in the mammalian cell. In a variety of conditions it displays oscillatory dynamics when stimulated, with the transcription factor entering the nucleus in a pulsatile fashion with a period of roughly 100 minutes. It is commonly claimed that it is information processing hub, taking in signals about the infection and stress status of the tissue environment and as a consequence of the oscillations, transmitting higher amounts of information to the hundreds of genes it controls. My aim is to develop a conceptual and mathematical framework to enable a rigorous quantifiable discussion of information in this context in order to follow Francis Crick's counsel that it is better in biology to follow the flow of information than those of matter or energy. In my approach the value of the information in the signalling system is defined by how well it can be used to make the "correct decisions" when those "decisions" are made by molecular networks. As part of this I will introduce a new mathematical method for the analysis and simulation of large stochastic non-linear oscillating systems. This allows an analytic analysis of the stochastic relationship between input and response and shows that for tightly-coupled systems like those based on current models for signalling systems, clocks, and the cell cycle this relationship is highly constrained and non-generic.

Biography

Dr. David Rand’s earlier research work in nonlinear dynamics was distinguished by its breadth and the fact that he made lasting contributions not only to pure and applied dynamical systems, but also to theoretical physics, fluid dynamics, and ecology and epidemiology. His current work is on the interface between mathematics and systems biology where he has developed substantial collaborations with a number of leading experimental biologists in what are examples of the approach advocated for systems biology in areas such as inflammation, immunology, circadian biology, cancer, endocrinology, and gene regulation. In parallel, in collaboration with Bärbel Finkenstädt and others he has developed new statistical techniques and mathematical tools for the analysis of the sort of biological systems models and data found in these biological areas. He has extensive management and administrative experience (in particular as a head of Warwick’s Mathematics Institute and its Systems Biology Centre). His prizes and distinctions include the LMS Whitehead prize, the UK’s top prize for mathematicians under 40, and a prestigious EPSRC Senior Research Fellowship.