Tutorial: Network Dynamics and Cell Physiology

Length:
Two three-hour sessions, Sunday afternoon and Monday morning before the conference begins.

Leaders:
John J. Tyson  
University Distinguished Professor, Department Biological Sciences  
Director, Division of Systems Biology  
Virginia Tech  
Blacksburg VA 24061 USA  
Bela Novak  
Professor of Integrative Systems Biology  
Department of Biochemistry  
Oxford University  
Oxford UK

Rationale:
A major theme of the International Conference on Systems Biology will be mathematical models of the molecular regulatory networks that underlie cell signaling, cell differentiation, cell growth and division, cell stress responses, cancer cell development, and other aspects of cell physiology. Because we expect many ‘newcomers’ to be attending the conference, it seems appropriate to hold an introductory tutorial on mathematical modeling on Sunday afternoon and Monday morning before the conference begins. The tutorial will be taught by two pioneers of the field, Professors John Tyson and Bela Novak, who have worked together for 25 years on mathematical models of cell growth and division, who have published some of the foundational papers in the field, and who have written several highly cited tutorial papers on “network dynamics and cell physiology”. The tutorial will combine lecture-style instruction with hands-on problem solving and computer exercises. Participation will be first-come, first-served; maximum enrollment = 30.

Description:
Day 1 (Sunday afternoon, 3 hours): "Deterministic Models"  
In this session, we will teach participants how to build simple deterministic models (i.e., nonlinear ordinary differential equations) of molecular networks representing toggle switches and oscillators in the signaling networks of living cells. We will teach them some elementary ideas from dynamical systems theory (phase plane portraits, saddle-node bifurcations and Hopf bifurcations), and we will show them how to use a free software package, XPP-Aut, to carry out simulations and analysis of ODE models. Instruction will involve hands-on work with model-building and software utilization. We will also discuss how to interpret the results of models in terms of cellular decision-making (toggle switches) and time-keeping (oscillations). Major applications will be cell-cycle checkpoints and circadian rhythms.

Sources:  
Class handouts.  
Day 2 (Monday morning, 3 hours): "Stochastic Models"

In this session, we will teach participants how to build simple stochastic models of molecular regulatory networks in single cells. We will start with a straightforward ‘birth-death’ model of mRNA synthesis and degradation, and prove that the number of mRNA molecules per cell should follow a Poisson distribution. Then we will show participants how to simulate the process by Gillespie’s stochastic simulation algorithm (SSA), using XPP-Aut to do the calculations. Next, we will consider a transcription-translation model of gene expression (gene $\rightarrow$ mRNA $\rightarrow$ protein), deriving the expected distribution of protein molecules per cell, and simulating the system by SSA. Finally, we will develop a more complex model of a cell-cycle regulatory network and simulate its behavior by SSA. If time permits, we will consider approximate simulation methods, like the Langevin equation.

Sources:
Class handouts.

Other Personnel:
We will invite other people to assist with the tutorial, e.g., Jing Chen, Young Cao and Will Mather to assist with instruction, and grad students and postdocs to assist with active-learning projects. No stipends will be paid to instructors or assistants.