Hamilton Institute

Systems Analysis of Cellular Networks Under Uncertainty

Professor Joerg Stelling
Dept. of Biosystems Science & Engineering
ETH Zurich, Switzerland

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Abstract:
For complex cellular networks, limited mechanistic knowledge,conflicting hypotheses, and relatively scarce experimental data hamper the development of mathematical models as systems analysis tools. The talk focuses on two approaches for dealing with this combination of complexity and uncertainty. They combine theory development and applications to specific biological examples.

Firstly, network reaction stoichiometries are relatively well-characterized and therefore suitable starting points for pathway analysis. It allows one to investigate the space of a (metabolic) network's feasible states. Applications are becoming possible for genome-scale networks, and they range from investigating the effects of network perturbations to predicting cellular control features. Moreover, recent theory extensions connect the approach to systems dynamics, for instance, to identify key mechanisms in cellular decision processes.

Secondly, and more mechanistically, we propose to cast hypotheses into a library of dynamic mathematical models, evaluate these against experimental observations, and design pivotal experiments to discriminate between alternatives. For TOR signaling in yeast, this strategy identified key control mechanisms that are quantitatively consistent with all available experimental data, and systematic extension of the approach to larger networks is a current challenge. Overall, the importance of network structures seems to outweigh the fine tuning of parameters. Structure-oriented analysis of biological systems, thus, provides challenging theory problems as well as broad perspectives for uncovering the organization and functionality of cellular networks.

Venue: Seminar Room, Hamilton Institute, Rye Hall, NUI Maynooth

Time: **3.00 - 4.00pm** (followed by tea/coffee)

Travel directions are available at www.hamilton.ie

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