

MOLECULAR NETWORK MODELING AND DATA ANALYSIS

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Advances in analytical and computational technologies are driving the transition to a systems biology that deals with the integrated behavior of biomolecular networks. As the volume of biological activity data (mRNA, protein, metabolite concentrations and localization) is progressively growing, we need to develop the conceptual frameworks and computational tools that will allow us to manage the data and extract meaning from it. This process can be organized into a series of steps: 1) Prerequisite statistical assessment of data quality, precision and reproducibility 2) Grouping of data into categories - cluster analysis, pathway inference 3) Inference of causal relationships from state transition data - analysis of perturbation responses and time series, “reverse engineering” 4) Predictive modeling - continuous and discrete network models, prediction of temporal and spatial activity patterns, discovery of principles of network organization. We anticipate that a successful integration of experimental biology with advanced computational technologies will allow us to discover key biological control processes relevant to therapeutics and bioengineering.

Six papers were selected for publication. The paper by Akutsu *et al.* introduced a qualitative network model that lies between the boolean network model and the differential equation model. In this model, regulation rules are represented as qualitative rules which are embedded in a network and they present algorithms for inferring qualitative networks from time series data of gene expressions. A discrete circuit model is analyzed by Ideker *et al.* for inferring the underlying gene regulatory networks from data obtained by designed biological perturbations. A network inference method for producing all putative networks consistent with gene expression data is presented together with computational experiments. Simulation systems will play a key role in functional analysis and modeling. Kyoda *et al.* has designed and developed

a simulation system whose scope is over multi-cellular organisms for dealing with intra/extra-cellular molecular processes. The usefulness of this system is demonstrated with a model of *Drosophila*'s Smad signal transduction. It is very important to investigate the consistency of experimental observations and its underlying gene network model. Marnellos *et al.* made a work on examining the Delta-Notch lateral inhibitory patterning the emergence of ciliated cells in *Xenopus* and a connectionist gene-network model. It provides a quite convincing model for predictions. Considerable attentions are paid to Petri nets for describing gene regulations and molecular interactions. Matsuno *et al.* used the most recent model of Petri net called the hybrid Petri net model that allows both discrete and continuous elements. By employing the hybrid Petri net model, they provided an efficient strategy for describing gene regulatory networks and succeeded in simulating a part of gene regulatory network of λ phage. Zhang and Kim considered a mathematical model that can integrate many aspects of chemotaxis. Their mathematical framework characterizes the effect of receptor clustering on the sensitivity and dynamic range of biochemical signaling.