Abstract of Presentation

Presentation Title:

Computational Strategy for Systems Biology and Drug Target Pathway Discovery

Abstract : We developed a series of computational methods based on Bayesian networks and nonparametric regression for mining gene networks from microarray gene expression data. These computational methods for computing gene networks were applied for searching drug target pathways. For a given drug, our strategy assumes two kinds of microarray gene expression data: One is time-course gene expression data for the drug responses. The other is a set of gene expression data obtained by knock-downs of several hundreds of carefully selected genes (one knock-down for each microarray measurement). We prepared more than 350 novel gene knock-downs for HUVEC by using siRNA and some time-course drug response gene expression data. From these data, we computed gene networks of 1000 genes by intensively using the supercomputer system at our Human Genome Center of University of Tokyo. We show how we can explore these computed networks for analyzing dynamic features of the networks and for searching drug target genes and hubs in the networks. We also developed a software tool Cell Illustrator (CI) which aims at analyzing and simulating complex dynamic causal interactions and processes such as metabolic pathways, signal transduction cascades, gene regulations. Simultaneously, we have been developing an XML format Cell System Markup Language CSML (http://www.csml.org/) for describing biological systems with dynamics and ontology (Cell System Ontology). In 2008, we released a Java web start software Cell Illustrator Online 4.0 (CIO) (http://cionline.hgc.jp/) combined with CSML databases including TRANSPATH that has more sophisticated GUI functions including automatic pathway layout algorithms using ontology information. Furthermore, we have developed a super-computer based computational method for automatic parameter estimation of dynamic models by using a technolgy called "*data assimilation*" which "blends" simulation models and observational data "rationally". This technology will be a strong computational strategy with which we can estimate personalized models from general biological models by using individual measurement data.