Bioinformatics Center
- Pathway Engineering -

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Scope of Research

This laborabory develops research on computational knowledge discovery, e.g. inference of pathway information from gene expression profile data, and simulation system for cells and organisms through the biopathway simulation of gene regulatory networks, signaling pathways, metabolic pathways, and physical simulations, etc. With this approach, the functions of genes and systems of genes will be analyzed and predicted.

Research Activities (Year 2002)

Presentations

Estimation of genetic networks and functional structures between genes by using Bayesian networks and nonparametric regression, Imoto S, Goto T, Miyano S, Pacific Symposium on Biocomputing 2002, Hawaii, USA, Jan 3 - 7, 2002.

Inferring, modeling and simulating biopathway, Miyano S, Journee Ouvertes Biologie Informatique Mathematique 2002 (JOBIM 2002), St. Malo, France, 10 - 12 June, 2002.

Genomic Object Net in JAVA (Ver.1.0): a general platform for biopathway modeling and simulation, Miyano S, The Fourth Biopathway Consortium Meeting, Edmonton, Canada, 1 - 2 August, 2002.

Bayesian network and nonparametric heteroscedastic regression for nonlinear modeling of genetic network, Imoto S, Kim S, Goto T, Aburatani, S (Kyushu U), Tashiro K (Kyushu U), Kuhara S (Kyushu U), Miyano S, The First IEEE Computer Society Bioinformatics Conference, Stanford, USA, 15 - 17 August, 2002.

Inferring gene regulatory networks from time-ordered gene expression data using differential equations, de Hoon MJL, Imoto S, Miyano S, The 5th International Conference on Discovery Science, Luebeck, Germany, 24 - 26 November, 2002.

A string pattern regression algorithm and its application to pattern discovery in long intron, Bannai H, Inenaga S (Kyushu U), Shinohara A (Kyushu U), Takeda M (Kyushu U), Miyano S, The Thirteenth International Conference on Genome Informatics, Tokyo, Japan, 16 - 18 December, 2002.

Grants

Miyano S, Genome-Wide Analysis of Genes Related to Disease Susceptibility and Drug Responsiveness, Research for Future Programs by Japan Society for the Promotion of Science, 1 April 2000 - 31 March 2004.

Miyano S, Mathematical Foundations of Computational Knowledge Discovery from cDNA Microarray Data, Grant-in-Aid for Scientific Research (B)(1), 1 April 2000 - 31 March 2003.

Computational Challenges in Systems Biology.

Systems biology can be explored by development of computational tools and capabilities which enable us to understand complex biological systems. Scientific contributions are strongly anticipated to produce practical benefits such as biomedical applications, solutions for environmental problems, etc. For this purpose, gene networks will play a central role in systems biology and computational challenges to inferring, modeling and simulating biological systems are receiving more attentions.

Advances in measurement technology have enabled genome-wide biological data production. Fig. 1 shows some aspects of data and computational topics towards understanding of biological systems. Our challenge in this scope is comprised of two approaches.

The first is "how to create gene network information". For this direction, we have developed three kinds of computational methods for inferring gene networks from gene expression profile data obtained from various perturbations such as gene disruptions, shocks, etc. We developed a method which can analyze the continuous data and automatically detect linear and even nonlinear relationships between genes. We employed nonparametric regression for capturing nonlinear relationships between genes and derive a new criterion called BNRC (Bayesian Network and Nonlinear Regression) for choosing the network in general situations. We also extended this method to Bayesian network and nonparametric heteroscedastic regression that can cope with variances in microarrays.

The second is "how to model and simulate gene networks". Obviously, an important challenge is a creation of a platform with which biological scientists can comfortably model and simulate dynamic causal interactions and processes in the cell such as gene regulations, metabolic pathways, and signal transduction cascades. For this direction, we have developed a software tool Genomic Object Net (GON) (http://www.genomicobject.net/) for biopathway modeling and simulation (Fig. 2). We also have developed a tool which transforms biopathway models in KEGG and BioCyc to the GON XML files. Especially, all metabolic pathway models in KEGG are now ready for re-modeling and simulation with GON (Fig. 3). This tool can also be extended to cope with another biopathway databases.

Systems biology has a chance to create a new paradigm for drug target selection by employing computational modeling of gene networks. As an application of these efforts, we have recently succeeded in discovering an antifungal medicine target gene by analyzing gene networks constructed with our methods from cDNA microarray gene expression profile data of S. cerevisiae based on gene disruptions and drug doses.

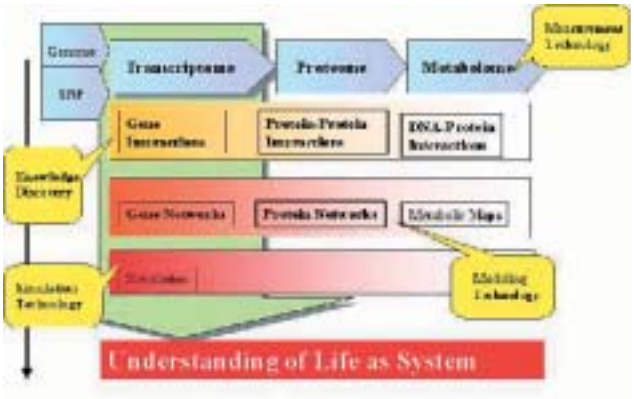

Fig. 1: Genome-wide data and computational issues towards understanding of life.

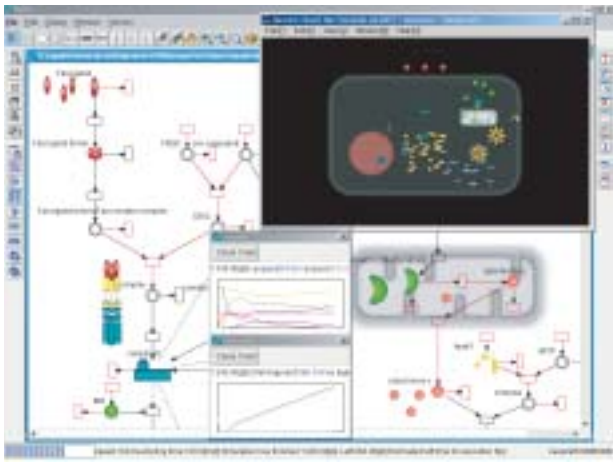

Fig. 2: Modeling and simulation of Fas ligand induced apoptosis pathway with Genomic Object Net.

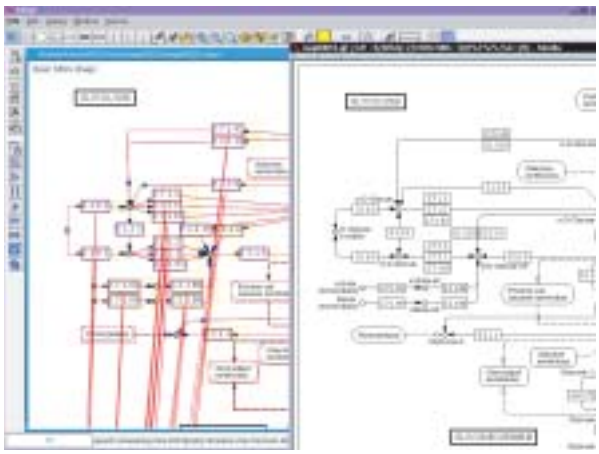

Fig. 3: A biopathway view of KEGG (right window) and its corresponding GON biopathway view (left window) that is simulatable with GON.