Next generation systems biology

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The biological network team focuses on how to model and analyze biological networks which are abstract and representing molecular and genetic relationships in living cells. Such networks are not real 'net' like a fishnet or wire gauze. These are domino fall chains of enzymatic reactions, cascade chains of phosphorylations, expression regulations among genes, etc. , and are not only strait forward pathways, but also complex networks which often contain loops and branches.

Most known biological networks should be metabolic pathways such as glycolysis that have been studied for seventy years. Many kinds of metabolic pathways can be found in textbooks. Many descriptions are also available for signal transduction pathways or phosphorylation networks as well as metabolic pathways. In addition, DNA micro-array technology which has been established in the last decade of the last century makes possible to infer regulatory relationship among genes including transcription networks. Abstract structures of many biological networks have been revealed today.

Systems biology is the research field about modeling and analysis of biological networks. It's expected that epoch-making knowledge are derived by the research for new drugs or further understanding of life phenomena, however, astonishing outcomes are not so much as expected. We consider that it should be due to a shortage of usefulness in medical applications.

Thus, we focus on quantitative models and single cell analysis to make a breakthrough in Systems biology and drug discovery.

Qualitative models have been well studied especially to analyze DNA micro-array data, and often applied to medical observation data which contains noise or error whose levels are too high to analyze with quantitative models. Outputs of qualitative models are generally binary, 1 or 0, which are interpreted as expressing or not, effective or not, active or not, and so on. Although advanced qualitative models, such as bayesian networks, can model probabilities, quantitative models are better to analyze `how much' or `how long'.

We are currently developing an analysis procedure for a multi-well living cell analyzer, as a part of a national project of Japan. The system consists of an image analysis method to recognize every cell in a image captured by the equipment, cell tracker for cells on time lapse images to produce time series data of gene expressions or molecular activities, and a network analysis method to reveal a quantitative network structures (activities of molecules and relationships between molecules). Our short goal is to make it possible to find which part of a signal transduction pathway is activated by a drug candidate compound from time lapse images of cell responses to the compound.

Since CBRC is a purely dry laboratory, we collaborate with a wet lab in the University of Tokyo. The wet lab runs the equipment and carries out experiments based on discussions with us about target cell types, interesting pathways and compounds, etc. Although discussions between mathematicians and biologists sometimes might be a waste of time by mutual incomprehension, our collaboration has been going well by complementing each other. Sound collaborations are fundamental to developing cutting-edge technology today.

Drug discovery is one of the most intense and stiff competition around the world (especially with EU and US) since it is also a patent competition. Of cause, on the other hand, it is very important that faster developing saves more patients. Our mission has significant meanings for our country and also for the world.