Dynamics of complex biological systems 1.
Introduction: What is the origin of cell diversity?

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One of the largest problems in modern biology is many examples of large networks providing information on the interaction between biomolecules. It is believed that the dynamics of molecular activities based on such networks are the origin of biological functions. For example, diversity of cell states has been understood as the diversity of steady states of gene activities based on such networks. However, the dynamics resulting from, and encoded in, such complex network systems are not understood sufficiently.

In this talk, I give some introductions to network systems in biology, and mathematical methods for studying dynamical behaviors based on the networks. I introduce a simple model of ODE systems for dynamics of molecular activities. Using the framework, I determined the expected numbers of steady states observed in a randomly generated network. The obtained results contradict the previously accepted belief. The expected number of steady states in a random network is shown to be very small, independent of the number of genes, and that of linkages. These results imply that neither gene number nor linkage number is the direct driving force for the diversity of cell types.

Further Reading

1. Mochizuki A. *et al.* (2005) *J. theor. Biol.* **236**, 291-310.

Dynamics of complex biological systems 2.
Observe/Control of nonlinear systems based on network structures

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Modern biology provides many networks describing regulations between bio-molecules. It is widely believed that dynamics of molecular activities based on such regulatory networks are the origin of biological functions. In this study we present a mathematical theory to provide an important aspect of dynamics from information of regulatory linkages alone. We show that "feedback vertex set" (FVS) of a regulatory network is a set of "determining nodes" of dynamics [1]. It assures that i) any long-term dynamical behavior of whole system, such as steady states, periodic oscillations or quasi-periodic oscillations, can be identified by measurements of a subset of molecules in the network, and that ii) the subset is determined from the regulatory linkage alone. The theory also claims that iii) dynamical behavior of whole system can be switched from one attractor to others just by controlling dynamics of FVS. We applied our theory to a real biological network to verify our prediction by collaborating with experimental biologists. We analyzed a regulatory network of ascidian embryo including 90 genes, and responsible for cell differentiation in the early development. We identified five genes in minimum FVS of the network. The exhaustive artificial activation/inhibition of five genes showed that the system could be controlled totally just by controlling activities of five genes in FVS.

Further Reading

[1] Mochizuki, A., Fiedler, B. et al. *J. Theor. Biol.*, **335**, 130-146.
[2] Kobayashi, K., Maeda, K., Tokuoka, M., Mochizuki, A. and Satou, Y. In Review.