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Author(s)	鈴木, 龍司
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Description	Supervisor:小長谷 明彦, 知識科学研究科, 修士

A Petri Net System applied to Biochemical Reaction Networks

Ryuji Suzuki

School of Knowledge Science,
Japan Advanced Institute of Science and Technology
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Information about genes and proteins is gathered in large amounts due to the quick increase in computer power and the development of improved analytic techniques and experiments.

This information should not be considered in isolation, but rather as part of a larger system. Hence, a synthetic approach is required to verify whether or not the whole system can be reconstructed from the combination of those parts.

In this context, recent researches investigate the application of graph theory to describe the parts and their interaction. The theory thus developed provides a common methodological framework that can be applied at various abstraction levels (e.g., from a molecular reaction pathway to a full ecosystem represented as a network of individuals). This makes it possible to understand the life phenomenon at various levels.

In this dissertation, we use Petri nets to model these networks. More specifically, we present models built using an extension of Petri nets adapted to the situation, and simulations based on those models.

The variant of Petri nets used in this research is based on “hybrid Petri net,” which allows both discrete and continuous values for tokens as well as arc weights. It extends hybrid Petri nets to allow the amount of token moved to be

parameterized by external values, such as general chemical reaction kinetics or enzyme reaction kinetics. It further extends hybrid Petri nets to allow the simulation of a system with spatial information. We call the resulting Petri net a “positional hybrid Petri net.”

In this dissertation, we use positional hybrid Petri nets to model and simulate the cell cycle control system, which is one of the well-known biochemical reaction pathways. Since this pathway involves no positional information, we repeat the process with the pattern formation in drosophila embryogenesis, another pathway which does. We came to the following conclusions based on our results.

- Our method yields more accurate results than other existing methods, and we have been able to verify its actual superiority.
- MPF is a gene that promotes M-phase, the protein that triggers cell division. According to cell cycle simulation, we could observe the periodic activity of MPF and hence could effectively reproduce the cell cycle. We could influence the activity cycle of MPF by changing the expression of Cdc25B phosphatase, which is consistent with experimental observations.
- Our simulation of the pattern formation in drosophila embryogenesis successfully confirmed the formation of the striped patterns of even-skipped, one of the pair-rule genes. The simulation was made out of a networks of genes, and its initial conditions were determined by the distribution of bicoid and nanos, two maternal genes.
- On the one hand, the simulation of the cell cycle control system is a numerical computation model which uses enzyme reaction kinetics. On the other hand, the simulation of the pattern formation in drosophila embryogenesis consists of a set of if-then rules with a behavior akin to cell automata. Being able to reconcile so different models within the same framework speaks in favor of the validity of our approach.