論文の内容の要旨

論文題目 Simulation and Automatic Design of Nucleic Acid Reaction System (核酸分子反応系のシミュレーションおよび自動設計に関する研究)

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I propose an efficient simulation technique for analyzing biological reactions and an automatic design method for developing artificial reactions, both of which are targeted to systems mainly composed of nucleic acids.

DNA that is one type of nucleic acids is utilized as a genetic information carrier in biology, while RNA that is the other type of nucleic acids has a biological functionality because of its reactivity. For better understanding of biological reaction, it is inevitable to analyze such nucleic acid reaction systems in detail by using computer simulations. Analyzing nucleic acid reaction systems in detail is difficult by using conventional simulation models that deal with small number of variables from a phenomenological point of view. To simulate the systems in detail by enumerating all possible structures of nucleic acids, however, is also difficult because of the combinatorial explosion of the number of structures. One technique to prevent such combinatorial explosion is to use the model reduction by assuming the independence of reactions. Because concrete nucleic acid re- action systems do not satisfy the assumption in general, the model reduction cannot directly be applied to the systems.

As another background of this research, numbers of artificial reactions making use of the chemical property of nucleic acid have been developed, which is expected to have applications such as drug delivery. Because every interaction of molecules in a system has to be taken into account, designing such device driven by chemical reaction of nucleic acids and enzymatic reaction is not easy for human. One approach to overcome the difficulty is to combine a simple building block or assemble basic chemical reaction like computer programming. Conventionally proposed design methods of artificial nucleic acid reaction systems, however, do not take advantage of complex structures because they are based on models that restrict the structure of nucleic acids. Because human trial and error of programming is required, it is still not easy to design a system where human have to think of huge combination of nucleic acids.

The goal of this research is proposing a simulation model with small restriction of the structure of nucleic acids, efficient simulation technique to prevent combinatorial explosion, and automatic design method of artificial reaction systems. In particular, I define nucleic acid reaction system as a graph rewriting system that has small restriction and can numerically simulate the systems based on chemical kinetics. To prevent the combinatorial explosion of the number of structures, I propose a model reduction that focuses on a local structure, which is applied to simulate concrete nucleic acid reaction systems (hybridization chain reaction and RNA interference). By the abstraction focusing on a local structure, it is possible to ignore the combinatorial explosion caused by represent- ing whole structure because the structure is represented by a set of local structures. To minimize the trial and error by human design, I propose an automatic design method using such simulation techniques and develop reaction systems such as logic gates and automaton, which can be implemented by actual nucleic acids. For the automatic design method, I define fitness functions of target systems and implement heuristic algorithm for the combinatorial optimization that can maximize the fitness value. Evaluation of this research is based on the discussion of the accuracy of the model reduction and the verification of the designed systems by actual chemical experiments. By this research, detail analysis of huge nucleic acid reaction systems and the development of artificial reaction systems that are nontrivial for human are expected.