論文内容の要旨

論文題目　Wet DNA nanodevices for molecular computing

（分子コンピューティングのためのウェットな DNA ナノデバイス）

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DNA nanodevices are nanometer-scale devices constructed with DNA molecules and their specific base-pairing reactions. The nanodevices attract attention due to realizability of molecular nanoscaffold, molecular communication, molecular information processing, and molecular computing. In this thesis, I described three types of novel DNA nanodevices: hairpin DNA memory, AND gate, and oscillator.

The hairpin DNA memory is a rewritable memory device using molecular addressing to store information represented by DNA sequences. The molecular addressing is realized by specific hybridization reactions between hairpin-like memory strands and linear data strands. The hybridization reactions are controlled by temperature changes of a reaction solution. The data is stored on the memory at a writing temperature, and it is erased from the memory by quick cooling from an erasing temperature. In this study, 50 times repetitions of selective/parallel writing and erasing were successfully achieved for two independent molecular addresses.

The AND gate is constructed with Reverse Transcription and TRanscription-based Autonomous Computing System (RTRACS), whose fundamental reaction is an RNA sequence conversion. In this study, numerical simulations of the AND gate were compared to *in vitro* experiments. Its model was described by simultaneous nonlinear differential equations based on Michaelis-Menten type enzymatic reactions and two-state model nucleic-acid hybridizations. The kinetic simulations demonstrated output RNA production rate reached the maximum rate as the reaction proceeded. As a result of analyzing the relationship between input RNA concentrations and output RNA production rate, the maximum rate of output production rose sharply at lower input concentrations and rose gradually at higher concentrations. The initial slope of output production rate was decreased at higher input concentrations. This was explained by back-hybridizations repressing intermediates production to generate the output RNA. The significance of this study is demonstration on a methodology to design a program of RTRACS described as a molecular reaction network as well as achievement on simulating the AND gate.

The oscillator was intended as a nanosystem to control other nanomechanical devices driven by nucleic-acid hybridizations. It was modeled after a circadian rhythm in life systems and was constructed based on an autonomous molecular computing system carrying out RNA sequence conversion. The oscillator was analyzed using a three-variable model and a detailed model. The sequence conversion reactions were treated as black boxes assumed to be Hill-type reactions in the three-variable model, and were described as reaction networks composed of nucleic-acid hybridization, RNA transcription, DNA extension, RNA degradation, and uracil-containing DNA degradation in the detailed model. The nucleic-acid hybridizations and the enzymatic reactions were assumed to be two-state model reactions and Michaelis-Menten type reactions, respectively. As a result of linear stability analysis for the two models, the system os-

cillated, converged or diverged depending on balance between RNA influx and RNA degradation into/from the system. The system became easy to oscillate as system cooperativity increased. In this study, the numerical simulation could supply a principle to construct the system in *in vitro*.

In the future, DNA nanodevices will be energetically applied to a variety of situations by combining with various nanodevices. In addition, the world of DNA nanodevices will spread by cooperating with other nanoscience or nanotechnology.