# 主 論 文 の 要 約

論文題目　Molecular Recognition and Aggregation Control of Distributed DNA Nanorobots (分散 DNA ナノロボット群の分子認識と凝集制御)

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## 論 文 内 容 の 要 約

Nanorobot's development has an enormous potential for many applications, particularly for biomedical field. This potential is principally due to the prospect of nanorobot ability to detect and to reach specific areas inside the body and then deliver a drug, thereby considerably reducing invasive procedures in therapeutics. However, how these microscopic particles can detect the cause of disease and how to multi robots will collaborate with each other to protect or make a cluster in the infected area are challenging.

Recently, DNA nanorobotics able to analyze the biological environment and diagnosis of a disease using decision system that integrated with sensor for the detection of any small molecule. However, classifying biomolecules require complex molecular computation processes that are not permissible for DNA nanorobots. Based on this issue, we introduce a parallel decision-making system for disease detection and classification based on the fact that DNA computing along with biomolecular systems can be subjected to massively parallel processing. We designed and programmed a DNA strand displacement reaction to implement rule-based classifiers from a binary tree classification as a decision-making system. In our framework for molecular robot development, the system components of molecular robots and simple classifier rules were used to alleviate the computational burden. The design consists of a basic model that generates rule-based classifier gates in several binary tree and cancer

classifications based on micro (mi)RNA expression. Simulation results showed that detection and classification were rapid using this system. Moreover, experiments using the synthetic miRNA hsa-miR-21 demonstrated that our model could be a feasible decision-making system for drug delivery.

Additionally we investigate an alternative double-stranded probe (dsProbe) system as detection platform that employs a similarity-based classifiers in DNA strand displacement reactions. We formulate label propagation based on DNA toehold domain as classifier, where a node propagates to neighboring nodes according to their proximity. We observe mismatch attributes of DNA strand sequences to recognize the effect of this model. The attributes are position, length and location number of mismatches. We carry out simulation using Nupack software and also experimental investigation.

Moreover, there is an important problem related to the degradation of DNA nanorobots in vivo environment before using as drug delivery system. Several studies reported that compact DNA nanostructures relative stability for a short time (a few hours) when against DNA nucleases. An alternative solution for this problem is aggregation of distributed DNA nanorobot using dynamic assembly and disassembly, which will make possibility increasing resistance of DNA nanorobot from biodegradation. According this issue, we present the multicomponent assembly and disassembly processes involving DNA strand displacement to construct molecular robots. The framework for development of molecular robots designates the components as parts of the robot. Molecular recognition is used to control the reversible processes of assembly and disassembly of multiple components. The molecular recognition system identifies not only a single-strand DNA but also a microribonucleic acid as molecular stimuli to control the processes. The processes were demonstrated by gel electrophoresis, fluorescence assays, and atomic force microscopy.

Furthermore, the aggregation control of distributed DNA nanorobots using molecular recognition are investigated to mimic the collective behavior of virus. A DNA nanorobot in hexagonal, square and triangle shape are fabricated by using DNA origami method. On this study, virus behavior were tried to mimic by using dynamic aggregation using DNA strand displacement. Several experiment were conducted to show the advantages and optimized the proposed method. These result will contribute the distributed behavior of DNA Nanorobots to protect DNA nanorobot from degradation.

In conclusion, we succeed on developing a decision system that conceivable for molecular recognition to a target cell. Moreover, by employing molecular recognition, the aggregation of distributed DNA nanorobot was realized using glue gate method.