【Grant-in-Aid for Scientific Research (S)】

Theranostics via Autonomous and Decentralized Molecular Systems

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Project Information	Project Number : 25H00416 Keywords : Molecular robot, Nanopore, DNA computing, Liposome, Theranostics	Project Period (FY) : 2025-2029

Purpose and Background of the Research

●Outline of the Research

The role of materials has traditionally been defined by mechanical properties (e.g., strength and hardness) for structural integrity, workability, and chemical properties (e.g., heat resistance and corrosion resistance). For example, reinforced concrete, which combines steel and concrete, provides the necessary strength, workability, and durability, making it widely used in construction. However, conventional materials like concrete, steel, stone, wood, and metal lack information-processing capabilities.

In contrast, computers process information using the binary states of electron flow in semiconductors. They are composed of various components, such as arithmetic units and storage units, each made from different materials. Computation relies on electricity, and both input and output must be converted into formats that can be recognized by humans.

Some biological materials naturally process information. DNA, proteins, and glycans store and transmit data within living organisms. DNA encodes genetic information, proteins translate sequences into structures, and glycans store functional information. These molecules also serve as essential structural components.

DNA-based information processing is being explored in DNA computing. Traditional output methods include gel electrophoresis and fluorescent labeling. Our research group has developed a rapid, label-free electrical readout technique for detecting DNA molecules using a nanopore-based electrical single-molecule detection method. In particular, we have proposed the potential application of DNA molecules not only for performing computations but also for rapidly processing information on tumor marker expression patterns, enabling ultra-early cancer diagnosis.

Based on these findings, this study aims to construct a material that can autonomously process information using DNA molecules (Figure 1). For example, DNA molecules can be encapsulated within cell-sized liposomes (lipid vesicles), where they communicate with each other through artificial channels or nanopores embedded in the lipid membrane.

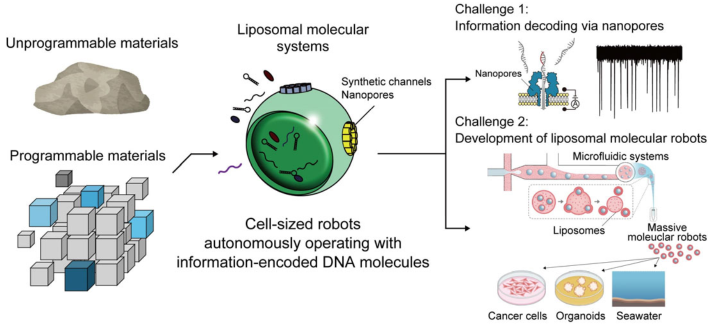

Figure 1. Autonomous distributed molecular system

The goal is to develop a cell-sized, autonomous, decentralized theranostic system. We aim to construct a micro-scale molecular robot capable of capturing tumor-related microRNAs and synthesizing antisense DNA drugs for tumor suppression. To achieve this, we are addressing challenges in fundamental technologies (electrochemistry, microfluidics) and scientific aspects (DNA design, reactions, nanopore proteins) (Figure 1).

●Research Organization

This research is a collaboration between the Tokyo University of Agriculture and Technology (Tokyo), the Japan Agency for Marine-Earth Science and Technology (Kanagawa), and the National Hospital Organization Disaster Medical Center (Tokyo), all located nearby for efficient experiments and sample exchange (Figure 2).

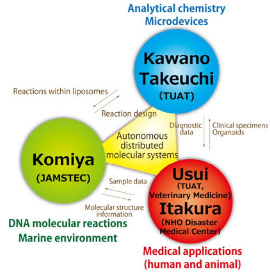

Figure 2. Research organization

Expected Research Achievements

The objective of this study is to materialize and systematize molecules that possess the capacity for information processing, with two primary objectives:

1) Constructing autonomous materials that process information using only molecules.

2) Developing autonomous and decentralized theranostic systems for diagnosis and treatment.

We aim to develop intelligent molecular systems that process environmental information using programmable molecules and embedded data, exploring their autonomous functions, applications, and underlying scientific principles.

To achieve this, we have established several subprojects:

1) Autonomous Molecular Information Processing Materials
- 1-1) Fabrication of cell-sized liposomes using microfluidic channels (Figure 3).
- 1-2) Construction of reaction systems inside liposomes.
- 1-3) Development of uptake and release mechanisms for external substances.
- 1-4) Creation of reaction environments using liquid marbles.
- 1-5) Testing functionality in biological and natural environments.

2) DNA Molecular Theranostics for Autonomous Diagnosis & Treatment
- 2-1) Development of DNA reactions for identifying cancer-derived miRNA patterns.
- 2-2) Evaluation and optimization using nanopore decoding (Figure 4).
- 2-3) Machine learning-based nanopore signal analysis.
- 2-4) Validation of diagnostic accuracy and therapeutic efficacy using human/animal samples.

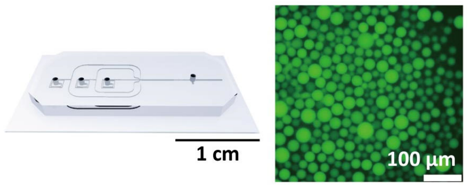

Figure 3. Fabrication of liposomes using microfluidic channels

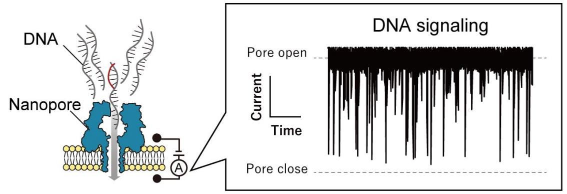

Figure 4. Nanopore decoding

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