[Invited Talk]

Photonic DNA Processors for Optical Communication between Nano and Macro World

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Abstract—For detailed observation and control of biomolecular events with optical means, we study a photonic DNA processor with optical communication between the nano- and macro-world. In this paper, we present our recent study of photonic DNA processors based on energy transfer at nanoscale and DNA structural changes: molecular logic operation, molecular encoding, and optical control of nanoscale signaling.

1. Introduction

Observation and manipulation of molecular events are important in the variety of fields including bioscience, medical science, healthcare, and so on. There is a demand for an efficient method to obtain biomolecular information and to control biomolecular behaviors in the molecular-scale region (nano-world) according to the external environment (macro-world). Due to remote accessibility, propagating light is a useful carrier of information for communication between the nano-world and the macro-world. However, the amount of information that can be transmitted is often restricted by light properties. Effective methods for optical communication between the nano- and the macro-world are required.

A promising approach for the nano-macro communication is to employ information processing systems at a nanoscale [1]. Nanoscale information processing provides encoding and decoding tasks at the molecular level. With these tasks, effective signal transfer can be achieved even if the capacity of the optical communication channels is restricted. For example, essential information can be extracted and encoded from the original information source at the nanoscale, and the coded signal can be transferred to the external environment through a band-limited communication path.

For the purpose, we are studying on photocic DNA processors based on photonics and DNA nanotechnology [2]. Figure 1 shows a schematic diagram of information flow in optical communication with photonic DNA processors. To send information in the nano-world, photonic DNA processors capture biomolecules, encode the biomolecular signals, and output the result as optical signals. In contrast, optical signals from the macro-world are received, decoded, and converted into molecular actions. To implement the photonic DNA processor, we use energy transfer-based signaling and DNA structural changes. Fluorescence resonance energy transfer (FRET) is a physical phenomenon in which excited energy is transferred from a donor dye to an acceptor dye via dipole-dipole interactions. FRET provides an important method for signal processing within a few nanometer region. Since the FRET efficiency depends on the fluorescent molecules and their separation distance,

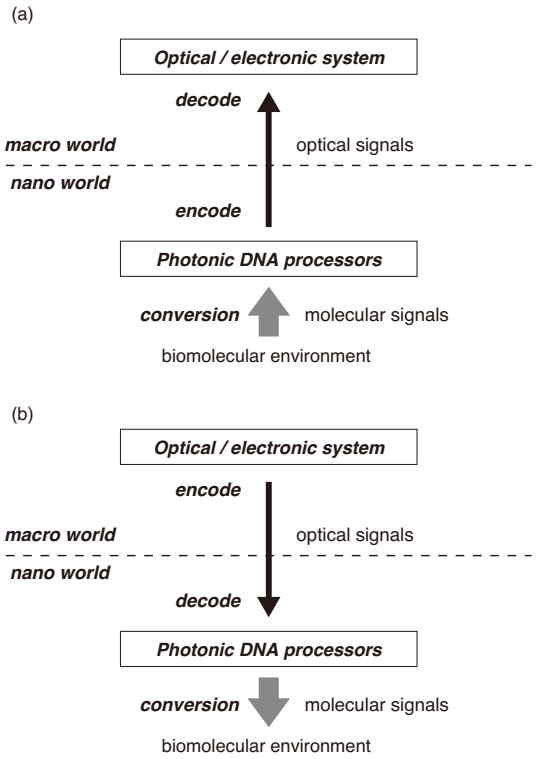

Figure 1: Optical communication between the nano- and macro-world by using photonic DNA processors. (a) Sending information related to bimolecular environment from photonic DNA processors. (b) Receiving instructions from the macro-world by phoronic DNA processors.

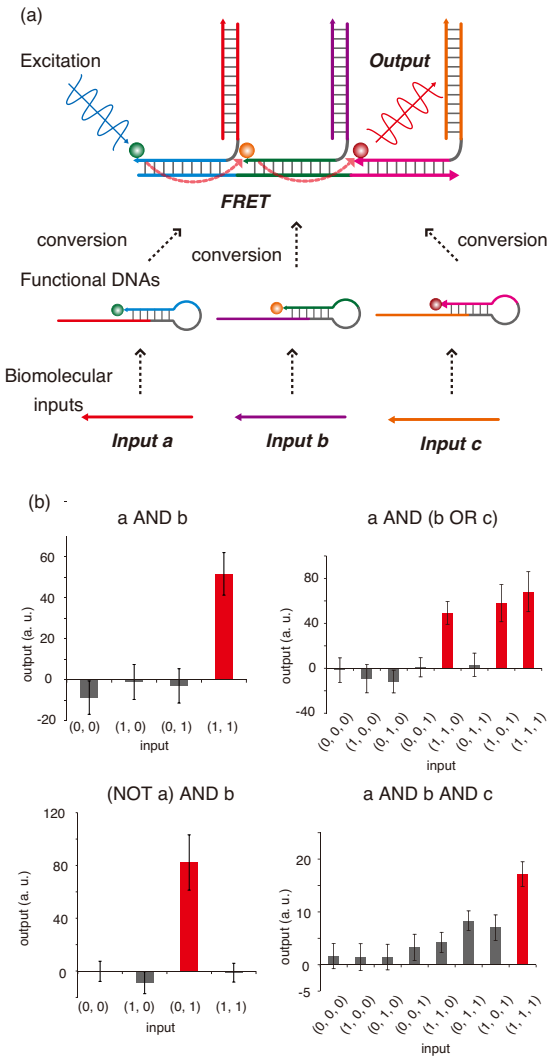

Figure 2: (a) Schematic diagram of DNA scaffold logic of three-input AND operation. (b) Fluorescence output for a AND b, (NOT a) AND b, a AND (b OR c), and a AND b AND c.

FRET signaling can be regulated by selection of fluorescent molecules and design of their positions. DNA structural changes are usable in precise control of fluorescent dyes. This paper presents recent progress in our study of photonic DNA processors: molecular logic operation, molecular color encoding, and optical control of FRET signaling.

2. Molecular logic operation: DNA scaffold logic

DNA scaffold logic is an example of molecular logic operations by FRET-based signal processing [3]. By the molecular logic operation, the essential signals are detected efficiently via fluorescent signals. Because FRET signaling are implemented in a few nanometer scale, this approach provides readout of bimolecular information from spaces much smaller than that determined by diffraction limit of light.

Figure 2 shows a schematic diagram of DNA scaffold logic. DNA scaffold logic accepts DNA inputs and produces fluorescent outputs representing the results of logical operations. A single strand DNA is prepared as a scaffold to construct a FRET path. Functional DNA strands make fluorescent molecules on or off the DNA scaffold according to existence of the DNA inputs. When the combination of DNA inputs satisfies a given logic condition, a complete signal path is formed on the DNA scaffold. The excited energy of the initiating molecule by light irradiation transfers to the reporting molecule through a FRET cascade. As a result, the reporting molecule is excited and fluorescence light emits as the output signal. On the other hand, when the DNA inputs do not satisfy the given logic condition, there is no complete FRET signal path and the reporting dye is not excited.

Experimentally, we verified the operation of a complete set of Boolean logic functions (AND, OR, NOT) and combinational logic operations using a FRET-signal cascade [3]. DNA scaffold logic executes operations in the conjugate normal form and any logic functions can be executed in principle. Although there are a lot of implementation methods for DNA based-logic operation, this approach has a unique advantage that consecutive reactions for executing a logic operation are not required for large-scale logic circuits. In DNA scaffold logic, DNA reactions are used for encoding the input signals into a FRET signaling path. Without complicated DNA reaction cascades, molecular information is converted logically into fluorescent output.

3. Molecular encoding: Biomolecule-to-fluroescenct-color encode system

Use of fluorescence is a possible approach for sending information from molecular environment. However, the number of usable fluorescent molecules restricts the amount of information that can be sent with fluorescence. An attractive alternative is to encode bimolecular signals into color codes, in which combinations of fluorescence wavelengths and intensity levels offer a large number of codes for representing biomolecular information. As an example, we have proposed a biomolecule-to-fluorescence-color (B/F) encode system that modulates the fluorescence signal using control of FRET [4]. By using a variety of fluorescent color codes, the B/F encode system makes it possible to generate enormous biomolecular codes without spatial coding.

Figure 3(a) shows the schematic diagram of a B/F encode system. The B/F encoder transduces a bimolecular signal to fluorescent one represented by fluorescent wavelengths and intensities. The fluorescent signal is modulated with structural changes of DNA strands. A biomolecular signal is obtained by specific bindings with DNA probes. The DNA structural changes are designed by the specificity

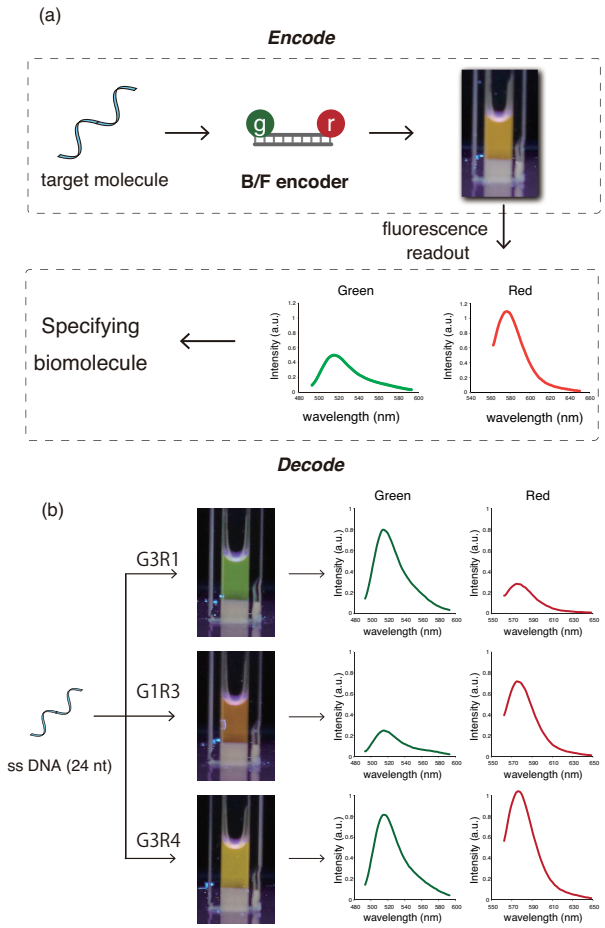

Figure 3: (a) Schematic diagram of biomolecule-to-fluorescence-color encode system. (b) Results of encoding a bimolecular signal into fluorescent color codes.

and predictability of Watson–Crick base pairing. The fluorescent molecules are manipulated according to the structural changes. Use of the FRET-efficiency change makes it possible to generate fluorescent color-codes depending on bimolecular signals. According to the decoding table, the bimolecular signals can be identified from the results of fluorescent measurement.

We demonstrated the behavior of a B/F encoder using two dyes and five intensity levels for readout of biomolecules [4]. Figure 3(b) shows examples of encoding a single stranded DNA into color codes. Amplification and encoding of biomolecular signals are carried out at a molecular level by manipulation of fluorescent dyes with DNA structural changes. The encoded molecular information can be decoded by analyzing the fluorescence spectra and intensities. The process is performed without enzymatic reactions or DNA microarrays, thus offering an inexpensive and convenient method of biomolecular detection. An exponential increase in the number of codes with additional fluorescence wavelengths makes it possible

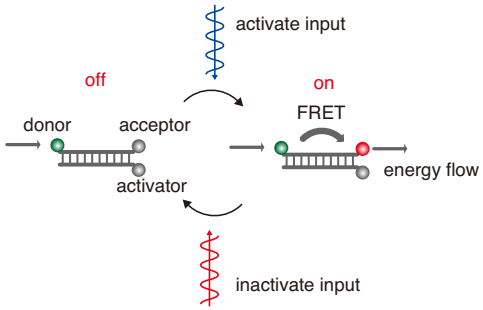

Figure 4: Schematic diagram of control of FRET signaling with optical inputs.

to enhance the B/F encoder. With further improvements, this technique will contribute to the realization of on-site biomolecular screening for clinical diagnosis and patient care.

4. Optical switching of nanoscale signaling

For manipulation of nanoscale information with light, optical signals should be decoded at a nanoscale. A method to expand optical signals to biomolecular information offers complicated control at a nanoscale. For the purpose, we investigate a method for control of FRET signaling with optical inputs [5]. An elemental device has been developed by using a photoactivatable fluorescent dye. The device consists of three functional fluorescent dyes, the donor, the acceptor, and the activator as shown in Fig. 4. The optical inputs change the state of the acceptor. Irradiation of the acceptor dye with the inactivating light switches the dye from the active fluorescent state to the nonfluorescent one. Upon excitation of the activator, the acceptor recovers the fluorescent state. The acceptor dye at the fluorescent state accepts the excited energy from the donor dye. According to the phtoregulated state of the acceptor, the FRET signaling is changed between the on-state and off-state.

We demonstrated experimentally that the FRET switch can modulate the energy flow and the modulation is operated repeatedly [5]. We are now investigating an implementation of a circuit consisting of multiple FRET switches. In the circuit, different activator–reporter pairs that act as photoswitchable pairs are prepared, and multiple switching points are introduced in the FRET signaling system. This FRET switching method is useful for optical programming in photonic DNA processors.

5. Conclusion

As an approach for communication between the nano- and macro-world via optical signals, information processing at a molecular level with photonic DNA processors was described. Molecular and optical nanoscale information pro-

cessing provides a novel method for observation and manipulation of molecular systems.

Acknowledgments

A part of this work was supported by a Grant-in-Aid for JSPS Fellows (No. 256027) from the Japan Society for the Promotion of Science (JSPS).

References

[1] Y. Ogura, T. Nishimura, H. Yamamoto, K. Yamamda, and J. Tanida, "Photonic DNA Nano-Processor: A Photonics-Based Approach to Molecular Processing Mediated by DNA," Nanophotonic Information Physics, chapter 4, 91–113 (2014).

[2] T. Nishimura, Y. Ogura, H. Yamamoto, K. Yamamda, and J. Tanida, "A photonic DNA processor: concept and implementation," SPIE NanoScience and Engineering, Proc. SPIE 8102, 810207 (2011).

[3] T. Nishimura, Y. Ogura, and J. Tanida, "Fluorescence resonance energy transfer-based molecular logic circuit using a DNA scaffold," Applied Physics Letters 101, 233703 (2012).

[4] T. Nishimura, Y. Ogura, K. Yamada, Yuko Ohno, and J. Tanida, "Amplification and modulation of fluorescent signals by using hybridization chain reactions for multiplexed sensing of biomolecules in a one-pot," Proc. SPIE 8954, Nanoscale Imaging, Sensing, and Actuation for Biomedical Applications XI, 89540P (2014).

[5] T. Nishimura, Y. Ogura, and J. Tanida, "A nanoscale set-reset flip-flop in fluorescence resonance energy transfer-based circuits," Applied Physics Express 6, 015201 (2013).