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Biomolecular sensing with *in-situ* computation by photonic DNA computing

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1. Introduction

Optical methodologies for sensing, imaging, or controlling biomolecules have been revealing mechanisms of various biological activities. Because many molecules work with interactions at a time in a biological system, it is necessary to deal with diverse molecules simultaneously or to manipulate much information on the molecules for effective analysis or control. Multi-channel fluorescence imaging is a good example to satisfy the demand. *In-situ* computation on molecules is another promising strategy because it offers, for example, encoding a set of information into a simplified code to support efficient sensing or imaging. It also enables to make physical or chemical reactions depending on the status of the target molecules at the positions where they exist. We are studying on photonic DNA computing, which is helpful to achieve *in-situ* computation on biomolecules based on DNA and photonics technologies. In this report, we present some implementing methods of photonic DNA computing for biomolecular sensing.

2. Photonic DNA computing

Photonic DNA computing is a natural computing concept for processing information associated with biomolecules at a nanoscale. DNA is employed as an information carrier interacting with surrounding molecules, and light is utilized to transfer information between macroscale devices and nanoscale materials. Based on this system structure, nanoscale computing is realized using propagating light, although the spatial resolution of the light itself is restricted by the diffraction limit. Use of light provides many advantages including capabilities in location-dependent, adaptive, and temporal computation. These features suggest that photonic DNA computing has potential for offering advanced biomolecular sensing.

3. Implementing methods

We have developed DNA scaffold logic as a computing scheme [1]. In this scheme, a logic operation for a set of input molecules is executed, and the result is transmitted as a fluorescence signal. The logic operations are realized by arrangement of fluorescence molecules on a DNA scaffold depending on the status of input molecules and fluorescence resonance energy transfer (FRET) between the fluorescence molecules. When and only when a set of input variables satisfies a given logical formula, a FRET path from the first fluorescence molecule (donor) and the reporting one (the last accepter) is made completely, and a high FRET signal is transmitted. Experimental results show that AND, OR, NOT operations are executed successfully. The method provides sensing with arbitrary *in-situ* biomolecular logic operations between multiple kinds of DNAs.

Capability in changing logic formulas executed flexibly on request is important to perform different operations with the same hardware. To achieve this functionality, we constructed a photo-switchable FRET structure by using a photoactivatable fluorescence molecule to switch FRET routes [2]. When a photoactivatable fluorescence molecule placed within a FRET route is activated, the FRET occurs along the route; on the other hand, when it is inactivated, the energy transfer stops there and energy does not reach at the end of the route. By combining multiple photo-switchable FRET structures with sharing a single donor and by controlling activation of the individual FRET structures, an energy transfer route can be selected from the potential routes relating to the individual FRET structures and then an intended logic operation is executed. We demonstrated that two logic operations were switched repeatedly and correct results were obtained with following temporal variation in a set of input molecules. With a single computing instrument, sensing with various logic operations is achievable.

A unique advantage of sensing with *in-situ* computation is that physical of chemical reactions can be induced by following the status of the sensed molecules in the environment. For example, release of a DNA strand is usable to regulate the behavior of a biomolecular system. A single-stranded DNA can be released from a double-stranded DNA by increasing temperature. We investigated release of a DNA strand via photothermal effect of a black hole quencher (BHQ) because it is effective to increase temperature in a small volume (within a molecule). We constructed such a system for regulating a toehold-mediated reaction by direct excitation of the BHQs and confirmed it experimentally.

4. Conclusions

Photonic DNA computing is a promising approach to achieve biomolecular sensing with *in-situ* logic operation. Sensing, computing, and actuating functions can be integrated into nanoscale hardware by combining implementing methods we demonstrated, and the integrated system is expected to provide advanced biomolecular sensing useful for life science.

References

[1] T. Nishimura, *et al*., Appl. Phys. Lett., **101** (2012) 233703.
[2] R. Fujii, *et al*., Opt. Rev., **22** (2015) 316.