DOI: http://dx.doi.org/10.7551/978-0-262-31709-2-ch031

Construction of a remote-controlled supramolecular micro-crawler

Daiki Komatsu[1], Kei Fujiwara[1], and Shin-ichiro M. Nomura[1]

[1]Tohoku University, 6-6-01 Aramaki Aza-Aoba, Aobaku, Sendai 980-8579, Japan
komatsu@molbot.mech.tohoku.ac.jp, nomura@molbot.mech.tohoku.ac.jp

Abstract

We aimed to develop a micro-robot that can crawl on contact surfaces in biological environments. The prototype chassis of this micro-bot consists of a lipid membrane that encapsulates and bonds micro-sized magnetic particles. By applying a rotating magnetic field, we hope to obtain a micro-crawler robot. In this report, we describe our observations of the rotational movement of liposomes (10–60 μm in diameter) encapsulating magnetic particles following manipulation of an external magnetic field using a neodymium magnet. Since this robot actively makes contact with the external environment, it will be possible to salvage some important molecule from the contact surface. It is expected that development of this system will lead to the development of new diagnostic and treatment systems.

Introduction

Since the dawn of history, numerous functional molecules have been discovered and synthesized by scientists. System integration of such molecular devices can facilitate the construction of human-controllable molecular machines. Designing and controlling nano- and micro-meter-sized chemical systems is considered one of the most effective means of examining the invisible small world. Recently, molecular self-organization has been gaining increasing interest with a view to creating higher-order chemical systems at the single-molecule level. This represents a crucial step in the development of the new research field of "Molecular Robotics" [1]. For prototyping a molecular robot, compartmentalization in a homogeneous aqueous solution is an essential requirement. One of the key materials in this regard is a supramolecular structure called the "liposome." Liposomes consist of a closed phospholipid bilayer membrane and behave as hydrophilic capsules. These lipid vesicles have the property of excellent biocompatibility, are capable of holding various solutions, have readily modified surfaces, and can potentially be prepared in large amounts. Since their discovery, many applications, including carriers of drugs, have been studied.

The liposome "capsule" is essentially floating in a solution. By encapsulating magnetic particles within liposomes, active drug delivery to target tissues could be realized by controlling the external magnetic field. In this regard, studies of the positional control of liposomes in blood vessels using MRI apparatus have been reported [2]. Local accumulation of liposomes in the fluid environment and the control of drug release by applying external stimuli using a high-temperature superconducting bulk magnet have also been performed [3]. However, such floating particles are unable to detect surface molecular information. Nevertheless, we have noted that investigations of the interactions between solutions and living surfaces is important for an understand of living systems.

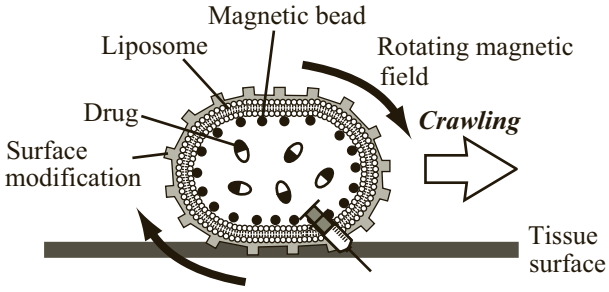

Figure 1: Schematic image of supramolecular micro-crawler.

To this end, we have attempted to construct a crawler-type micro-molecular robot (supramolecular micro-crawler; Figure 1). The liposomes of this crawler consist of lipid and adhered-encapsulated magnetic micro-particles. This multicomponent structure is expected to function on tissue in the body environment, for example, via vascular flow, by crawling induced by external rotating magnetic field.

We believe that these types of robots will not only have the ability of remotely controllable drug delivery in three dimensional motion, but will also be able to determine normal or abnormal areas of tissue by sensing the surface molecules through interaction with the cellular-contact surface. We also anticipate the construction of new diagnostic and therapeutic systems, such as the robot described here, and that these will be applied to the treatment of malignant tissue through making a diagnosis of living tissue as a result of rolling on the tissue surface.

In this paper, we present the results of the rotational motion of liposome-encapsulated magnetic beads generated by applying an external magnetic field to construct the micro-robot described above.

Experiments

We adopted the water-in-oil (W/O) emulsion method to prepare the liposomes (Figure 2) [4]. The composition of the buffer solution used was as follows: 10 mM HEPES-KOH, 2.6 mM $Mg(OAc)_2$, with 20 mM potassium glutamate (pH 7.6). A lipid mixture of 1,2-dioleoyl-sn-glycero-3-phosphoethonolamine-n-(biotinyl) (sodium salt) (biotinyl DOPE), 1,2-dipalmitoyl-sn-glycero-3-phosphocholine

(DPPC), and cholesterol (at molar ratio of 1:1:1) was dissolved in liquid paraffin.

The lipid solution was mixed with the buffer containing 150 mM sucrose, 350 mM glucose and streptavidin magnetic particles (inner solution). This mixture was vortexed for 60 s to form a W/O emulsion. The emulsion was then gently placed on top of the buffer containing 500 mM glucose (outer solution) in a tube. The sample tube was centrifuged and the emulsion was then passed through an oil/water interface

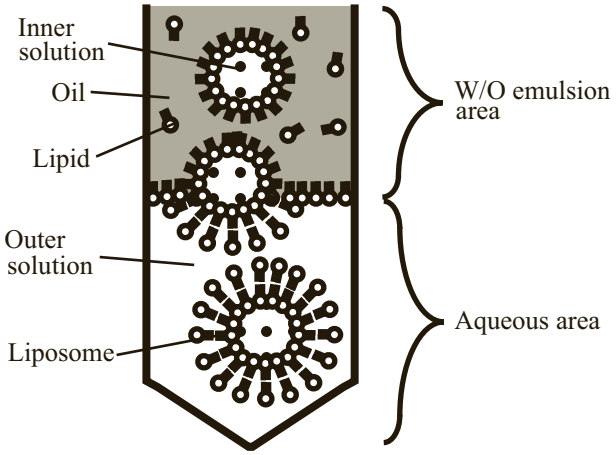

Figure 2: The W/O emulsion method for liposome formation.

saturated with lipids to form a bilayer structure. The procedure is a slightly modified version of that previously described by Nishijima et al. [5].

The top-most W/O emulsion was removed and the liposomes (maximum diameter of approximately 60 μm) encapsulating magnetic beads were collected by micropipette. The liposomes thus obtained were clearly observable under a phase-contrast microscope (IX-71; Olympus). On the microscope stage, we attempted to observe the rotational movement of liposomes containing the magnetic particles by applying an external magnetic field. The rotational magnetic field was generated using a round-type neodymium magnet (φ 11 mm × 3 mm). Sample solution containing liposomes was placed in a hole in a silicone sheet on a slide glass, and covered with a cover glass. The magnet was placed next to the prepared slide on the microscope stage.

Results and Discussion

The rotating magnetic field was generated in two different ways: (A) by moving the neodymium magnet around the samples, and (B) by rotating the magnet near the samples. The results for each method are shown in Figure 3A and B, respectively. It was possible to perform rotational movement using both methods. The rotational cycle was not fast and limited to ~0.3 Hz. Share resistance between the double-layer of the liposome membrane, and viscosity of the buffer solution should be affected. We then attempted to place the suitable chemical structure onto the liposome surface. The results of this investigation will be discussed in the conference.

In this study, we controlled liposome movement by applying a magnetic field to liposomes encapsulating magnetic particles for the construction of a supramolecular micro-crawler, which will be used to develop new diagnostic and treatment systems, and we succeeded in obtaining rotational motion of the our designed liposomes using two different rotational magnetic fields. We are currently examining the crawling motion of liposomes on surfaces. For this purpose, we will modify the surface properties of the

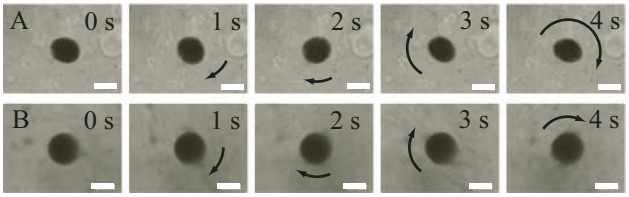

Figure 3: Rotational behaviors of a liposome using two different methods. Scale bars are 20 μm.

liposomes and the contact surface (e.g., molecular modification and charge), and conduct experiments in static and fluid environments. In addition, we are constructing a device that will be used to rotate the liposomes. We also aim to collect target molecules consisting of fluorescent molecules using a micro-robot prepared from liposomes.

Acknowledgements

We would like to thank Prof. S. Murata and S. Hamada for their insightful comments. This work was supported by JSPS KAKENHI (grant numbers 24104004, 22220001 and 23.3718).

References

[1] Murata, S., Konagaya, A., Kobayashi, S., Saito, H. and Hagiya, M. (2013). Molecular Robotics: A New Paradigm for Artifacts. *New Generation Computing*, 31:27-45.

[2] Martel, S. (2012). Magnets steer medical microbots through blood vessels. *IEEE Spectrum*, 49(10):48-53.

[3] Nakagawa, K., Mishima, F., Akiyama, Y. and Nishijima, S. (2012). Study on Magnetic Drug Delivery System Using HTS Bulk Magnet. *IEEE Transactions on Applied Superconductivity*, 23(3): 4903804.

[4] Pautot, S., Frisken, J. B. and Weitz, D. A. (2003). Engineering asymmetric vesicles. *Proceedings of the National Academy of Sciences of the United States of America*, 100(19): 10718-10721.

[5] Nishijima, K., Hosoi, T., Sunami, T., Toyota, T., Fujinami, M., Oguma, K., Matsuura, T., Suzuki, H. and Yomo, T. (2009). Population Analysis of Structural Properties of Giant Liposomes by Flow Cytometry. *Langmuir*, 25(18): 10439-10443.