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Design of self-organizing microtubule networks for molecular communication

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ABSTRACT

In this paper, we investigated approaches to form a self-organizing microtubule network. Microtubules are protein filaments naturally occurring in the aqueous environment of cells. A microtubule network connects multiple nano- or micro-scale objects (i.e., nanomachines). In the paper, we propose two approaches to form an *in vitro* microtubule network in a self-organizing manner. The first approach utilizes polymerization and depolymerization of microtubules. The second approach utilizes molecular motors to reorganize a microtubule network. In addition, we conducted preliminary *in vitro* experiments to investigate the feasibility of the proposed approaches. In the preliminary experiments, we observed that a few sender and receiver nanomachines were interconnected with the first approach, and that distinct topologies of microtubules were reorganized with the second approach.

1. Introduction

1.1. Molecular communication system

Molecular communication is a possible solution for nanomachines to communicate with other nanomachines, where the communication is performed by transmitting molecules representing information. Nanomachines are natural or artificially synthesized assemblies and are made of biological molecules that perform limited computation [25], sensing [5], or actuation [31] by using chemical reactions. Molecular communication allows multiple nanomachines to cooperate and achieve complex functions that cannot be accomplished by a single nanomachine. In generic molecular communication, sender nanomachines encode a message (e.g., DNA code) onto biological molecules (e.g., mRNA), rather than encoding onto electrons, electromagnetic or acoustic waves.

The sender nanomachines transmit information encoded molecules (referred to as "information molecules") into the environment. These information molecules are then transported through the environment to the location of the receiver nanomachines with a certain probability. The receiver nanomachines then decode the message from the information molecules (e.g., Ribosome reads genetic instruction from mRNA and synthesizes a protein).

Through communication at such a scale, creation of entirely new applications which require cooperation of multiple nanomachines can be performed. Such applications may include distributed nanomachine computing [8], human health monitoring [15], bionano structure fabrication [28], programmable lab-on-a-chip [30], and biosensors [9].

Biological systems (e.g., biological cells) use several forms of molecular communication to exchange information. For example, biological systems have developed active and passive transport methods to transport information molecules [1] for molecular communication. In passive transport, information molecules move by random

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thermal motion without using chemical energy. Statistically, passive diffusion leads to molecule flow following a concentration gradient. In active transport, a transport nanomachine moves information molecules using chemical energy such as adenosine 5′-diphosphate (ATP). The direction of the movement is independent of a concentration gradient. An example of transport nanomachines in a biological cell is a kinesin. Kinesin, a type of protein motor, moves along a microtubule unidirectionally according to the polarity of the microtubule. A microtubule is a polar protein filament (i.e., one side is called a plus end and the other side is called a minus end) with a diameter of 25 nm. Both passive and active transport are essential methods to exchange information by transporting information molecules in biological systems.

This paper proposes a molecular communication system that employs molecular motors (i.e., employs active transport) as illustrated in Fig. 1. In the proposed system, microtubules form a network as information pathways between sender and receiver nanomachines. Through the microtubule network, molecular motors (e.g., kinesin) are the information carriers that transport information molecules along the microtubules from a sender nanomachine to a receiver nanomachine. An example process of information transfer is by allowing the sender nanomachine to encode information into a sequence of peptides, where this peptide is then injected into a vesicle [26]. During the transportation process between the nanomachines, the vesicles isolate the information molecules from the environment [24]. A receiver nanomachine would then have receptors that bind to the vesicle and allow the peptide information to be retrieved. Therefore, the molecular motors would transport the vesicles to dock with the receiver nanomachine [27,10]. A receiver nanomachine decodes information by reacting with information molecules and then performs application specific chemical reactions.

The environment may provide the molecules (e.g. ATP) necessary for molecular motors to perform active transport. The velocity of the transport for an information molecule depends on the type, number and location of molecular motors attached to the information molecule. Cai et al. reported that individual Kinesin-1 motors *in vivo* travel with an average velocity of 0.78 ± 0.11 μm/s [4]. The proposed system is beneficial when the sender and receiver nanomachines are bound on a surface a certain distance apart, and need to communicate. While the proposed solution provides active transport, there are certain limitations in the application of such networks (e.g. in an *in vitro* environment). The most suitable application of this type of network is in microfluidic applications or artificial environments.

One of the challenges in developing the proposed system is the ability to create microtubule networks that correctly interconnect specific nanomachines. The simplest case is when there is only a single microtubule that interconnects the nanomachines. However, interconnection in the case of multiple microtubules is more complicated. This complexity is worse when information molecules have multiple molecular motors, where these molecular motors can bind multiple nearby microtubules and form a molecular motor complex (e.g., motors that crosslink two microtubules). The crosslinked microtubules can still be used as an information pathway for molecular motors. However, all the microtubules in the crosslinked microtubules should be oriented in the same direction so that all the molecular motors can move along the crosslinked microtubules in the same direction from a sender nanomachine to a receiver nanomachine. If the microtubules are not in the same direction, motors may pull in opposite directions and cause the information molecule to move in an unpredictable manner or not move at all. This paper explores and proposes a method to correctly form a microtubule network which orients crosslinked microtubules to match the intended direction.

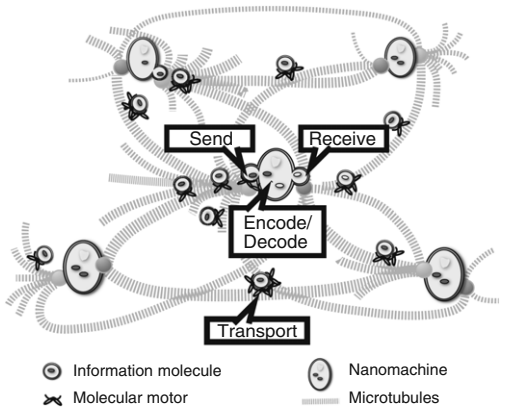

Fig. 1. The proposed molecular communication system employing molecular motors and microtubules. The nanomachines in this figure act as both sender nanomachines and receiver nanomachines.

Another challenge for the proposed system is to form a microtubule network in a self-organizing manner. Self organization is preferable since there are a large number of molecules in a nano- or micro-scale environment and human-level control molecule positioning is not feasible. A self-organizing microtubule network can provide coarse-grained control in deploying microtubules in the network. On the other hand, self-organizing microtubules are dynamically adaptive to the local details and changes in the environment or system. This paper explores and also proposes a method to form a microtubule network in a self-organizing manner.

1.2. Proposed work

This paper proposes two approaches in forming a self-organizing microtubule network. The first proposed approach aims to have the microtubules interconnect sender and receiver nanomachines in a self-organizing manner. This will be realized through the use of polymerization and depolymerization of microtubules inspired by the dynamic instability behaviors that are inherent in microtubules. In this first approach, sender and receiver nanomachines bind to microtubule seeds and microtubule binding sites, respectively. Microtubules seeds that are bound to a nanomachine perform dynamic instability (i.e., random elongation and shrinkage) to find and connect to another nanomachine that has corresponding microtubule binding sites.