A Design of a Molecular Communication System for Nanomachines Using Molecular Motors

Michael Moore^{*}, Akihiro Enomoto^{*}, Tadashi Nakano^{*}, Ryota Egashira^{*}, Tatsuya Suda^{*} Atsushi Kayasuga⁺, Hiroaki Kojima⁺, Hitoshi Sakakibara⁺ and Kazuhiro Oiwa⁺.

^{*}Information and Computer Science, University of California, Irvine, CA, USA ⁺National Institute of Information and Communications Technology (NICT), Kobe, Japan

> ^{*}{mikemo, enomoto, tnakano, egashira, suda}@ics.uci.edu ⁺{kayasuga, sakaki, kojima, oiwa}@nict.go.jp

Abstract

Molecular communication is one solution for nano-scale communication between nanomachines. Nanomachines (e.g., biological molecules, artificial devices) represent small devices or components that perform computation, sensing, or actuation. Molecular communication provides a mechanism for one nanomachine to encode or decode information into molecules and to send information to another nanomachine. This paper describes a molecular motor communcation system in terms of a high level architecture for molecular communication. We also briefly discuss current and future work in molecular communcation.

1. Introduction

Molecular communication is one solution for nanoscale communication between nanomachines. Nanomachines (e.g., biological molecules, artificial devices) represent small devices or components that perform computation, sensing, or actuation. Molecular communication provides a mechanism for one nanomachine to encode or decode information into molecules and to send information to another nanomachine. Nanomachines already exist in the form of biological cells and the chemical processes within those cells. Current bionanotechnology has advanced to the point where engineering of biological systems (e.g., receptors, nano-scale reactions) is feasible, as demonstrated through modification of DNA to produce new cell functionality [8]. As bionanotechnology becomes more mature, study in communications can be applied toward the design of larger-scale nanomachine systems.

If multiple nanomachines communicate, they may cooperate and perform complex tasks. Medical research has been increasing the methods and complexity of ways of modifying living humans, such through medical implants. Molecular as communication may represent a more direct and precise mechanism for monitoring human health or directly interacting with biological cells (e.g. generating sensory or synaptic stimulus)[4]. Another area that communicating nanomachines may be useful is molecular computing. Researchers are currently attempting to create molecular logic gates (e.g., an inverter and a NAND gate) [6][7][8] and memory [5] using existing components from biological systems. Nanomachines implementing logic gates and memory may communicate through molecules (e.g., ions, proteins, DNA) and combine to perform more complex computing functionality.

1.1. Features of Molecular Communication

Applying molecular communications to these areas causes nanomachines and communications to take on several features.

Biocompatibility: Inserting nanomachines into a human body for medical applications requires nanomachines that are biologically friendly. Biological nanomachines can interface directly with natural processes that also function through receiving, interpreting, and releasing molecules. Thus it is not necessary to include harmful inorganic chemicals. Biological nanomachines may also be programmed to

be broken down after use to avoid procedures for removal or cleanup of devices (e.g. implanting of a temporary medical device that removes itself after one month).

Scale: Because of the size of nanomachines, it is difficult to control individual nanomachines. Individual nanomachines can be designed to affect and react to specific molecules, and thus molecular communication is a reasonable approach for communication between nanomachines. Also, bottom-up self assembly techniques based on biological systems may help to control and coordinate many nanomachines.

Information representation: Molecules represent information through chemical structure, sequence information, relative positioning, or concentration (e.g. protein, DNA, calcium propagation). Molecular information thus provides different methods for manipulating and interacting with information since operations performed are also non-binary and information can directly react to other information.

Probabilistic: Probability arises in the form of nanomachines probabilistically reacting to chemicals, unpredictable movement of molecules in the environment, and random breakdown of molecules over time. The probabilistic environment of nanomachines inherently affects the design of molecular communication systems. For example, cells use large numbers of molecules for communication so that failure of a few molecules does not impact communication.

Energy Efficiency: One beneficial feature of biological systems is the energy efficiency of chemical processes. Biological systems take advantage of probabilistic features to lower the energy necessary to react and communicate information. For example, myosin energy converts ATP to mechanical work with 90 percent efficiency.

Asynchronous: As a result of the delays in reactions and communication, biological systems have developed into asynchronous systems with a high degree of parallelism. Correct execution of functions often does not require a synchronizing clock, but rather relies on specialization of cells for specific tasks and maintaining of chemical concentrations. For example, metabolism of chemicals within a biological system is separated into organs that perform specific functions to maintain homeostasis. Communication between organs is achieved through the chemicals that are maintained. Section 2 discusses related biological communication systems. Section 3 describes a generic communication architecture based on observed biological systems. Section 4 describes a molecular communication system using molecular motors in terms of the generic communication architecture. Section 5 describes potential areas of future work in applying the generic communication architecture.

2. Molecular Communication in Biological Systems

Biological nanomachines exhibit a wide variety of mechanisms for exchanging information at the nano and micron scales. Some specific biological mechanisms include intracellular transport, intercellular communication, homeostasis, and bacterial conjugation. These mechanisms provide a basis for developing molecular communication. This paper focuses on applying molecular motor transport to molecular communication, and the observations in this section are of molecular motors.

In intracellular transport, communication within a biological cell is performed using molecules that are carried by molecular motors. A molecular motor is a protein or protein complex that transforms chemical energy (e.g., ATP hydrolysis) into mechanical work at the molecular scale. Eukaryotic cells use molecular motors (e.g., kinesin and dynein) to transport large molecules that do not diffuse well and to transport other large cell structures such as organelles and vesicles.

Since molecular motors walk internally along cytoskeletal tracks (e.g. acetylcholine is transported along the axon of a neuron), molecules move in the direction corresponding to the cytoskeletal track rather than the random Brownian motion of diffusion. For example, acetylcholine released at the axon of a neuron causes a response in the adjacent neuron with a receptor for acetylcholine [1]. The cytoskeletal track is most often composed of microtubules or actin filaments and is organized by a cell for various functionalities. Molecular motors can also control the directionality of transport by occurring in different ratios such as having more active kinesin motors that results in walking towards the plus end of a microtubule or more active dynein motors that results in walking towards the minus end of a microtubule.

There also exist a variety of proteins and processes that help construct these networks. γ -tubulin provides a starting point for growing microtubule filaments and MAPs (microtubule accessory proteins) help to stabilize and arrange multiple microtubules to form single cell-scale networks with a variety of functionalities (e.g. transport of molecules between the ER and Golgi, structural support of cells, adjusting of the cell shape in muscles, or dividing of a cell membrane during mitosis.)



Figure 1. Intracellular communication (vesicles transported by molecular motors)

3. Generic Communication Architecture from observed biological systems

As described in the previous section, molecular communication mechanisms already exist in the biological systems. These biological systems can be described relative to а generic molecular communication architecture that consists of system components and communication processes of a molecular communication. the In following subsections, we describe the system components and communication processes of molecular communication. Figure 2 in the section provides a schematic representation of the generic communication architecture.



Figure 2. Generic communication architecture

3.1. Assumption about the environment

The environment is space in which the information molecules propagate from the sender to the receiver. Our assumption is an environment where system components (e.g. biological proteins) correctly operate. The environment should be an aqueous environment with necessary molecules at biologically appropriate conditions (e.g., human body temperature).

3.2. System Components

Information molecule: In molecular communication, information can be described as a biological reaction at a receiver. Since a biological reaction is an interaction between molecules, a biological reaction can be caused by sending molecules. In molecular communication, the information molecule is the molecule which stores such reaction information.

Carrier molecule: In biological system, some molecules reach its destination by free diffusion, while others need a carrier (e.g., molecular motors in the previous section) to aid sending. The carrier molecule is the system component molecule which binds and facilitates transport of information molecules.

Sender and Receiver nanomachines: The sender nanomachine is the system component that encodes a sensed reaction onto information molecules and sends the information molecules into the environment. As described in section 2, in biological systems, information molecules which are sent by senders (e.g. ER) are caught by carrier molecules (e.g., molecular motors) and then transported to a receivers (e.g. Golgi).

The receiver nanomachine is the system component that detects the transported information molecules and decodes the information molecules to cause a desired biological reaction at an information sink.

Information source and sink: The information source (e.g., some events, chemical reaction) has information to send through a sender nanomachine to a receiver nanomachine. The information sink is the destination where the desired biological reaction is caused.

3.3. Network Topology

A nanomachine may only be able to communicate to a limited set of other nanomachines due to the range of molecule diffusion or movement within some space (e.g. diffusion along a microtubule). Network topology is the set of communication channels between each sender and receiver through which information molecules are transferred. The network topology represents possible paths for information molecules and may change dynamically for adaptation of communication.

3.4. Communication Processes

As we described earlier, the general communication architecture is between senders and receivers (illustrated in Figure 2). The following describes the five basic processes to perform a communication.

Encoding: Encoding is the process by which a sender nanomachine senses some information (e.g., biological reaction) inside or outside the nanomachine and translates the information into information molecules that the receiver can capture or detect. Information may be encoded in the specific molecules used, in a subcomponent of the molecule (e.g. subsequence of a DNA sequence) or in characteristics of the molecules. Information may also be encoded in the environment by, for example, the sender emitting molecules that modify the environment, and a receiver that detects the changes in the environment.

Sending: Sending is the process by which the sender emits the information molecule into the environment. A sender may emit molecules using peptide translation machinery. The endoplasmic reticulum (ER) contains machinery that translates DNA sequence information into peptide sequences. A peptide may include sequence information indicating that the peptides are to be encapsulated into a vesicle and the molecular motor machinery of the cell recognizes that the vesicle is to be transported. The peptide may be processed and be emitted directly outside of the cell using vesicle systems (e.g., the exocytosis of the peptide).

Propagating: Propagation is the process by which information molecules move through the environment from a sender to a receiver. Propagation may occur through simple passive propagation (e.g. Brownian motion) in which the information molecules do not actively use energy to move through the environment. An example of controlled propagation is molecular motors that walk over rail molecules to transport carrier molecules.

Receiving: Receiving is the process by which the receiver captures information molecules propagating in the environment. The receiver may contain a selective receptor (e.g. sensitive to calcium ions or specific peptides) to capture the information molecule. Another method of receiving is fusion of vesicles (observed in vesicle transport) containing information molecules into the membrane of receivers.

Decoding: Decoding is the process by which the receiver, after receiving information molecules,

decodes the received molecules into a reaction. The design of a reaction is dependent on the application. If biological cells are used as receivers, potential reactions include enzyme-mediated reactions or protein synthesis. For instance, to report a detected molecule, the receiver may express GFP (Green Fluorescent Protein) in response to the transmitted information molecule.

4. Molecular Communication Using Molecular Motors

As described in section 2, molecular motors (e.g. kinesin, dynein) transport materials (e.g. vesicle, mRNA) in eukaryotic cells along filaments called rail molecules (e.g. microtubules). To develop a molecular communication system, the system of molecular motors is used for controlled nanomachine communication (Figure 1 right). In this system, rail molecules (microtubules) are deployed between nanomachines, and molecular motors (kinesin) carry vesicles containing information molecules along the rail molecules from sender nanomachines to receiver nanomachines. The destination may be specified by a protein tag that binds to specific receptors on receiver nanomachines.

4.1. Assumption about the environment

Due to the difficulty in reengineering biological systems, the environment is assumed to have adequate numbers of molecules available to provide necessary communication components (e.g. rail molecules, molecular motors, information molecule). Since molecular motors are biological proteins, the entire system must operate at a controlled temperature of natural animal systems. Nanomachines are deployed in some application dependent manner, and the molecular motor communication system is self-organized in an application independent manner. The molecular communication process is activated in response to an assumed information source that is externally controlled (e.g. a sensor molecule becomes activated).

4.2. System Components

The system components of the generic single hop architecture in Section 3 have a corresponding component in the molecular motor system. The sender and receiver are however unspecified but must be capable of releasing and interpreting of information molecules (e.g. a biological cell that releases vesicles or a molecule that is released when an input condition occurs). Information molecules must be capable of binding to and releasing from a molecular motor which acts as the carrier molecule for transporting the information molecules. The environment contains rail molecules that guide the propagation of molecular motors and provides the necessary molecules (e.g. ATP) necessary to perform transport.



Figure 3. Molecular Communication Using Molecular Motors

4.3. Microtubule topology

The form of the microtubule topology determines in what direction molecular motors will move. In biological systems, the microtubule topology occurs within the confined volume of a biological cell and often exists in star-like and random mesh forms.

A star-like topology is centered at some location within the cell (e.g. a centrosome). A star topology may provide a mechanism for distributing molecules away from a single point to far away points (e.g. broadcasting molecules from a single source) or to gather molecules to a location within the cell (e.g. gathering molecules for analysis by a nanomachine).

A random mesh topology represents a distribution of microtubules that covers some volume. A mesh may provide a mechanism for evenly distributing molecules through random movement across the topology.

4.4. Molecular Communication Using Molecular Motors

As described in Section 3, the communication between nanomachines involves the following five processes

Encoding: Sender nanomachines encode information on information molecules (e.g., DNA, proteins,

peptides). For example, nanomachines encode information on sequences of peptides and inject the peptides into vesicles [1]. Vesicles can be loaded on molecular motors [2], and thus a variety of encoded molecules can be sent.

Sending: Sender nanomachines then emit the information molecules to molecular motors that move along rail molecules. Information molecules are then attached to and loaded on molecular motors.

Propagation: Propagation is performed through molecular motors that move along rail molecules from sender nanomachines to receiver nanomachines in a directed manner.

Receiving: Receiver nanomachines are assumed to retrieve carrier molecules from molecular motors using protein tags. When molecular motors approach to receiver nanomachines, carrier molecules such as vesicles[3] may be fused into receiver nanomachines.

Decoding: In decoding, receiver nanomachines invoke reactions in response to information molecules. For example, peptides (e.g. neurotransmitters) transported through molecular motors in a neuron cause receiver neurons to generate an action potential.

5. Future Work

This paper has focused primarily on sending information over a single hop; however, the following describes single hop and multiple hop communication mechanisms that are necessary to implement more complex nanomachine systems. Ideally, communication mechanisms are generic so that different nanomachine can operate with the same communication mechanism.

5.1. Single hop communication

Amplification: Amplification of information molecules is beneficial for converting nano-scale information into a macro-scale signal that can be read through existing communications (e.g. to amplify information molecules for sending over long-distance or for multicast to target nanomachines). Amplification requires large scale coordination among nanomachines to simultaneously perform the same function, to avoid generating too many information molecules and to removing information molecules after completion.

Feedback: Feedback is used in molecular communication systems to provide a method for the receiver nanomachine to respond to the sender of a communication. Feedback may apply in applications for querying a specific nanomachine for information (e.g. an embedded ID tag) or for requesting specific molecules (e.g. requesting molecules that provide a specific functionality).

Addressing: Addressing increases the functionality of single hop communication by allowing the sender nanomachine to determine which receiver nanomachines receive a communication. An address can be specified by sending a molecule that only the correct receiver can receive (e.g. send a drug that targets a type of cells) or addressing can be according to spatial or temporal information (e.g. send a drug along a specific link from the sender, so that only receivers in one direction receive the communication).

5.2. Multiple hop communication

Relay: Relay communication extends single hop communication through the addition of intermediate nanomachines that participate in communication between a sender and receiver. Intermediate nodes blindly transfer molecules extending the distance over which the communication is sent. The information may also be changed at each hop due to processing by nanomachines (e.g. decoding of information molecules by intermediate nanomachines).

Routing: Routing is related to addressing, however, the network is responsible for selecting the path through the environment since the sender may not be capable of directly sending to a receiver. To achieve routing, an intermediate nanomachine may have several methods of communication, and the intermediate nanomachine switches to the appropriate method to reach the receiver.

6. Conclusion

In this paper, we have described an architecture for describing the basic processes of molecular communication and have described initial designs for a molecular communication system that uses molecular motors to perform communication.

We are currently designing various molecular communication mechanisms. Current work on the molecular motor communication system described in this paper focuses on propagation aspects. Propagation by molecular motors is a significant factor when determining which molecular communication system to apply. We are currently investigating through experiments propagation of molecular motors and methods for forming a network of rail molecules in a self-organizing manner.

Acknowledgement

This research is supported by NICT (National Institute of Communication Technology, Japan), the NSF through grants ANI-0083074, ANI-9903427 and ANI-0508506, by DARPA through grant MDA972-99-1-0007, by AFOSR through grant MURI F49620-00-1-0330, and by grants from the California MICRO and CoRe programs, Hitachi, Hitachi America, Hitachi CRL, Hitachi SDL, DENSO IT Laboratory, Nippon Telegraph and Telephone (NTT), NTT Docomo, NS Solutions Corporation, Fujitsu and Novell.

References

[1] B. Alberts, A. Johnson, J. Lewis, M. Raff, K. Roberts, and P. Walter, "Molecular Biology of the Cell," Garland Science, 4th Bk&Cdr edition, 2002.

[2] S. M. Blockm, L. S. Goldstein, and B. J. Schnapp, "Bead Movement by Single Kinesin Molecules Studied with Optical Tweezers." Nature 348(6299), pp. 348-52, 1990.

Optical Tweezers," Nature 348(6299), pp. 348-52, 1990. [3] A. R. Cross, "Intracellular Transport," Encyclopedia of Life Science, Macmillan Reference Ltd, 1997.

[4] R. A. Freitas Jr., "Nanomedicine, Volume I: Basic Capabilities," Landes Bioscience, 1999.

[5] T. Head, M. Yamamura, and S. Gal, "Aqueous Computing -- Writing on Molecules," in the Proc. CEC'99, pp. 1006-10, 1999.

[6] C. Mao, T. H. Labean, J. H. Reif, and N. C. Seeman, "Logical Computation Using Algorithmic Self-assembly of DNA Triple-crossover Molecules," Nature 407, pp. 493-6, 2000.

[7] K. Sakamoto, H. Gouzu, K. Komiya, D. Kiga, S. Yokoyama, T. Yokomori, and M. Hagiya, "Molecular Computation by DNA Hairpin Formation," Science, 288 (2469), pp. 1223-26, 2000.

[8] R. Weiss, S. Basu, S. Hooshangi, A. Kalmbach, D. Karig, R. Mehreja, and I. Netravali, "Genetic Circuit Building Blocks for Cellular Computation, Communications, and Signal Processing," Natural Computing 2, pp. 47-84, 2003.