Exploratory Research on Molecular Communication between Nanomachines

Tatsuya Suda, Michael Moore, Tadashi Nakano, Ryota Egashira and Akihiro Enomoto

Donald Bren School of Information and Computer Sciences

University of California, Irvine

CA, 92697, USA

{suda, mikemo, tnakano, egashira, enomoto}@ics.uci.edu

ABSTRACT

This paper describes the possibility of molecular communication as a solution for communication between nanomachines. Nanomachines are artificial or biological nano-scale devices that perform simple computation, sensing, or actuation. Existing communication technologies cannot be applied to nano-scale communication between nanomachines due to difficulty of scaling down and energy inefficiency of existing technologies. Molecular communication applies the communication mechanisms existing in biological cells to provide a mechanism for nanomachines to communicate over a short distance (adjacent nanomachines to tens of micrometers) by sending and receiving molecules as a communication carrier. Communicating nanomachines can spur the creation of entirely new applications such as communication among the computation gates of a molecular computer. This paper presents the framework of the molecular communication.

Categories and Subject Descriptors

C.2.1 [Network Architecture and Design]: Network communications; J.2 [Physical Sciences and Engineering] Chemistry and engineering; J.3. [Life and Medical Sciences]: Biology and genetics

General Terms

Design

Keywords

Bionanotechnology, nanomachine communication

1. INTRODUCTION

This paper describes *molecular communication* [9, 12] as a solution for nano-scale communication between nanomachines. Molecular communication allows nanomachines to communicate over a short-range through sending and receiving carrier molecules. It is one solution for nano-scale communication

Permission to make digital or hard copies of all or part of this work for personal or classroom use is granted without fee provided that copies are not made or distributed for profit or commercial advantage and that copies bear this notice and the full citation on the first page. To copy otherwise, or republish, to post on servers or to redistribute to lists, requires prior specific permission and/or a fee.

Genetic and Evolutionary Computation Conference (GECCO)'05, June 25-29, 2005, Washington, DC, USA. Copyright 2005 ACM 1-58113-000-0/00/0004...\$5.00 between nanomachines.

Nanomachines, both those found in biological systems and artificially created, represent small devices or components that are capable of performing only very simple tasks of computation, sensing, or actuation (e.g., detection of molecules, generation of motion, or performing chemical reactions) because of their limited size and limited complexity. Some examples of nanomachines in biological systems include molecular motors [11] that produce motion or a receptor [13] that reacts to specific molecules. Examples of artificial nanomachines include nanomachines synthesized using NEMS (Nanoelectro- mechanical Systems) technology from organic and/or artificial components at the submicron dimension [7, 14, 15].

If multiple nanomachines communicate, they may cooperate and perform complex tasks such as nano-scale computing. Researchers are currently attempting to create nano-scale logic gates (e.g., an inverter and a NAND gate) [3, 17] and memory [8] using existing components from biological systems. If nanomachines implementing logic gates and memory communicate, by for instance, using signal molecules (e.g., ions, proteins, DNA) in an aqueous environment, they can perform more complex computing functionality (e.g., a full adder).

In this paper, we present a new concept of molecular communication and describe a first attempt to design a framework for describing such communication systems. Molecular communication is based on the observation that existing biological systems use molecules as communication carriers. For instance, in a biological cell, molecular motors transport molecules along with rail molecules; between cells, biological cells coordinate activity using calcium signaling. We believe that with the advancement of current research in synthetic biology [2, 4, 10, 16, 17] and in bio-nanotechnologies [5, 6], it may become relatively easy in the near future to adapt existing components from biological systems (e.g., receptors, nano-scale reactions, communication molecules) to design a framework for molecular communication between nanomachines.

Section 2 discusses molecular communication in biological systems. Section 3 describes our initial designs for describing molecule communication, and Section 4 briefly introduces the current status of our molecular communication research.

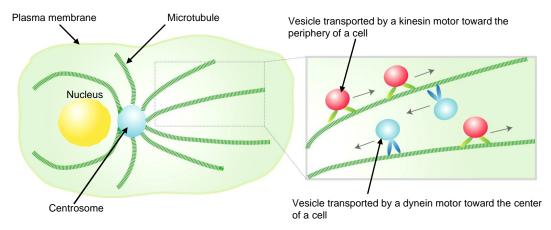


Figure 1: Vesicle transport by molecular motors

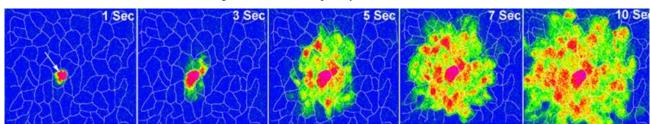


Figure 2: Calcium signaling among biological cells

2. OBSERVATION OF BIOLOGICAL COMMUNICATION SYSTEMS

Biological nanomachines exhibit a wide variety of mechanisms for exchanging information at the nano and micron scales. Some example biological mechanisms include intracellular and intercellular communication mechanisms.

In intracellular communication, communication occurs between components within a single biological cell (Figure 1). For example, the component of the cell transfers molecules (e.g., vesicles containing acetylcholine) carried by molecular motors. A molecular motor is a protein or protein complex that transforms chemical energy (e.g., ATP hydrolysis) to change the position or structure of the molecular motor. Within some eukaryotic cells, molecular motors (e.g., kinesins and dyneins) transport molecules and organelles internally along cytoskeletal tracks. For example, acetylcholine is transported within a neuron along the axon and released, causing a response in the adjacent neurons that have a receptor for acetylcholine [1].

In intercellular communication, communication can occur through cell-cell channels called gap junctions. Gap junctions allow connected cells to share small molecules such as Ca^{2+} (calcium ions) and inositol 1,4,5-trisphosphate (IP₃) and therefore, enable coordinated actions among adjacent cells in response to extracellular signals. For example, ciliated airway epithelial cells communicate with each other through the diffusion of IP₃ via gap junctions (Figure 2). A stimulated cell first increases the intracellular IP₃ concentration that results in the release of Ca^{2+} from the intracellular calcium store. IP₃ diffuses through gap junctions to adjacent cells, resulting in the release of Ca^{2+} from intracellular stores in each of the adjacent cells. Diffusion of IP₃

continues and thus propagating calcium waves over a number of cells.

3. MOLECULAR COMMUNICATION

As described in the previous section, nano-scale or micron scale communication mechanisms already exist in the biological systems. In creating molecular communication systems, we use existing biological nano-scale communication mechanisms (e.g. intracellular, intercellular communication mechanisms of exchanging molecules) and communication components (e.g. molecular motors, cells with receptors).

One of the advantages of using biological systems (e.g., molecular motors to transport molecules, or communication among cells) is that they can address the difficulties of nano-scale communication that the current electrical and optical wave based communication systems may encounter. Biological communication mechanisms have already been naturally selected for functioning at the nano-scale. With the current research emphasis on bottom up approach and self-assembly techniques to create nano materials, it may become relatively easy in the near future to use and adapt existing components from biological systems (e.g., receptors, nano-scale reactions, communication molecules).

Another advantage of using biological systems is that the usage of biological components increases the compatibility of molecular communication with applications that are sensitive to artificial materials (e.g. require ecological breakdown).

Another advantage of using biological systems is energy efficiency. Existing biological systems use highly energy-efficient processes. For example, myosin energy converts ATP to mechanical work with 90 percent efficiency. A single molecular reaction may represent multiple computations, and consumes a

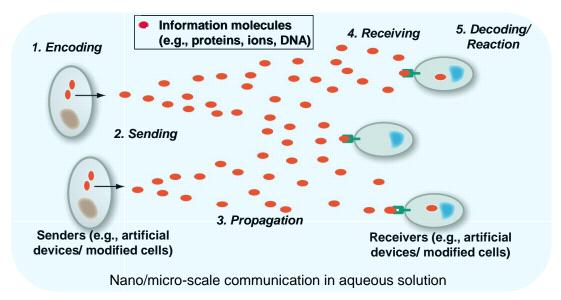


Figure 3: Communication processes in molecular communication

relatively small amount of power (e.g. 10,000 times less than a micro electronic transistor). Thus, non-electrical nanotechnology may be able to provide more energy efficiency per computation component, and thus may be able to perform more computation with less energy and heat dissipation than existing electrical components. For the range of communication, molecular communications may be transmitted over longer ranges while still using the same amount of power and without loss of information.

In the following, we explain system components and communication processes in molecular communication required to achieve communication between nanomachines.

3.1 SYSTEM COMPONENTS

The generic molecular communication system consists of communication *carrier molecules* (i.e., molecules such as proteins or ions) that carry the information to be transmitted, *sender nanomachines* that transmit the carrier molecules, *receiver nanomachines* that receive carrier molecules, and the environment in which the carrier molecules propagate from the sender to the receiver.

The sender and receiver nanomachines may be biological cells that use peptides, ions, or phosphates such as inositol-triphosphate as carrier molecules (e.g. cells that communicate through calcium ions). The sender stores carrier molecules and releases the carrier molecules according to some event (e.g. high concentration of a specific external signal molecule). For instance, calcium ions may be pumped into a sender cell from the external environment and stored in the endoplasmic reticulum of a sender cell. A sender may then release the stored calcium when a ligand binds to a receptor of a sender cell. The receiver includes calcium sensitive components to detect increased calcium concentration and reacts to the increased calcium concentration. For example, calcium ions bind to receptors of the receiver, resulting in neuron action potential or a cellular immune response such as inflammation.

The carrier molecules propagate from the sender to the receiver in the environment. The environment of molecular communication may be an aqueous medium with various ions and molecules dissolved in solution (e.g. a saline solution with 0.85% NaCl), similar to the environment of communication in the biological systems described in section 2.

3.2 COMMUNICATION PROCESSES

The communication processes of molecular communication include encoding, sending, propagation, receiving, and decoding (Figure 3).

Encoding is the process by which a sender translates information into carrier 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 is the process by which the sender emits the carrier molecule into the environment. For example, a sender may emit ligands toward membrane receptors of nearby cells, which results in the generation of calcium waves that propagate from cell to cell. Another example of sending is the sender emitting carrier molecules using peptide translation machinery. In this case, the carrier molecule may be a peptide sequence that is encapsulated into a vesicle, transported by molecular motor machinery of the cell from the endoplasmic reticulum (site of vesicle encapsulation) to the cellular membrane (site of vesicle exocytosis), and emitted outside of the sender cell using vesicle exocytosis.

Propagation is the process by which carrier 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 carrier molecules do not actively use energy to move through the environment. Propagation may also be controlled by constraining the volume of the environment in which carrier molecules can move. For example, in propagation through gap junctions, propagation is limited to inside the cell and the gap junction and thus molecules do not propagate in arbitrary directions. Another example of controlled propagation is

molecular motors that walk over rail molecules to transport carrier molecules.

Receiving is the process by which the receiver captures carrier molecules propagating in the environment. The receiver may contain a selective receptor (e.g. sensitive to calcium ions or specific peptides) to capture the carrier molecule. The receiver may contain gap junctions that allow molecules (e.g. calcium ions) to flow into the cell without using receptors. Another option for receiving is to use fusion of vesicles (observed in vesicle transport) containing carrier molecules into the membrane of receivers.

Decoding is the process by which the receiver, after receiving carrier 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 signal.

4. CURRENT STATUS

We are currently designing possible molecular communication systems by choosing and combining appropriate system components and mechanisms from the biological systems. Two of the molecular communication systems being designed are briefly described in the following.

Molecular communication using molecular motors: As illustrated in Figure 1, molecular motors (e.g. kinesin, myosin, dynein) are used to transport materials (e.g. vesicles) within a cell. A designed molecular communication system uses this mechanism to transport carrier molecules from a sender nanomachine to a receiver nanomachine. In this type of molecular communication, rail molecules are first deployed between nanomachines and molecular motors walk along the rail molecules in order for nanomachines to exchange carrier molecules. We are currently investigating through experiments how to form a network of rail molecules in a self-organizing manner.

Molecular communication using calcium signaling: One type of intercellular communication found in biological systems is through gap junctions as illustrated in Figure 2. Gap junctions found in biological cells allow small molecules such as ions and second messengers to be shared among neighboring cells, and thus enable coordinated actions (e.g., synchronized contraction of the heart muscle). A molecular communication system being designed is based on a network of cells interconnected via gap junctions. Such a network may provide a shared medium for a sender nanomachine to transmit information to multiple receiver nanomachines. This is analogous to computer networks that consist of networking devices attached to a shared medium providing the broadcast capability for a single sender to transmit data to multiple receivers. Novel functionalities such as signal switching and signal aggregation can be achieved in such a network by controlling the permeability of gap junctions. We are currently investigating the feasibility of this type of molecular communication through experiments using a cell culture.

Acknowledgements

This research was supported by the NSF through grants ANI-0083074 and ANI-9903427, 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, Novell, Nippon Telegraph and Telephone (NTT), NTT DoCoMo, Fujitsu, NS Solutions Corporation, DENSO IT Laboratory, and NICT. The authors would like to thank Prof. Scott Boitano, at the Department of Physiology, University of Arizona, Health Sciences Center for kindly offering Figure 3 of calcium signaling among ciliated epithelial cells.

5. REFERENCES

- 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] M. B. Elowttz and S. Leibler, "A synthetic oscillatory network of transcriptional regulators," Nature 403, 335 – 338, Jan. 2000.
- [3] J. E. Dueber, B. J. Yeh, R. P. Bhattacharyya, and W. A. Lim, "Rewiring cell signaling: the logic and plasticity of eukaryotic protein circuitry," Current Opinion in Structural Biology 14, 690-699, 2004.
- [4] D. Endy and R. Brent, "Modeling cellular behavior," Nature 409, 391-395, 2001.
- [5] H. Hess, C. Matzke, R. Doot, J. Clemmens, G. Bachand, B. Bunker, and V. Vogel, "Molecular shuttles operating undercover: A new photolithographic approach for the fabrication of structured surfaces supporting directed motility," Nano Letters, 3, 1651-1655, 2003.
- [6] Y. Hiratsuka, T. Tada, K. Oiwa, T. Kanayama, and T. Q. Uyeda., "Controlling the direction of kinesin-driven microtubule movements along microlithographic tracks," Biophysics Journal, 81 1555-1561, 2001.
- [7] P. Holliger and H. R. Hoogenboom, "Artificial Antibodies and Enzymes: Mimicking Nature and Beyond," Trends Biotechnol 13(1), pp. 7-9, 1995.
- [8] T. Head, M. Yamamura, and S. Gal, "Aqueous Computing: Wiriting on Molecules." in the Proc. Proc. the Congress on Evolutionary Computation, 1999.
- [9] S. Hiyama, Y. Moritani, T. Suda, R. Egashira, A. Enomoto, M. Moore and T. Nakano, "Molecular Communication", in Proc. of the 2005 NSTI Nanotechnology Conference, May 2005.
- [10] H. Kobayashi, M. Kærn, M. Araki, K. Chung, T. S. Gardner, C. R. Cantor, and J. J. Collins, "Programmable cells: Interfacing natural and engineered gene networks," Proceedings of the National Academy of Sciences, vol. 101, no. 22, pages 8414-8419, June 2004.
- [11] K. Kinosita, K. Adachi, and H. Itoh, "Rotation of F1-ATPASE: How an ATP-Driven Molecular Machine May Work," Annual Review of Biophysics and Biomolecular Structure, Vol. 33, pp. 245-268, 2004.
- [12] T. Nakano, T. Suda, M. Moore, R. Egashira. A. Enomoto, and K. Arima, "Molecular Communication for Nanomachines Using Intercellular Calcium Signaling," in Proc. of the IEEE NANO 2005, July 2005.

- [13] T. Pawson and P. Nash, "Protein-protein Interactions Define Specificity in Signal Transduction," Vol. 14, No. 9, pp. 1027-1047, 2000.
- [14] J. A. Pelesko and D. H. Bernstein, "Modeling MEMS and NEMS," CRC Press, 2002.
- [15] M. L. Roukes, "Nanoelectromechanical Systems," Tech. Digest of the 2000 Solid State Sensor and Actuator Workshop, 2000.
- [16] L. You, R. S. Cox 3rd, R. Weiss, F. H. Arnold, "Programmed population control by cell-cell communication and regulated killing," Nature 428 868-871, 2004.
- [17] 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.