Information Transfer through Calcium Signaling

Tadashi Nakano[1] and Jian-Qin Liu[2]

[1] Frontier Research Base for Global Young Researchers
Graduate School of Engineering
Osaka University, Japan
tnakano@wakate.frc.eng.osaka-u.ac.jp
[2] Kobe Advanced ICT Research Center
National Institute of Information and Communications Technology, Japan
liu@nict.go.jp

Abstract. In this paper, we discuss information transfer through calcium signaling, one form of molecular communication that is ubiquitously used in natural biological systems and that is potentially useful to design synthetic biological systems. We use a mathematical model to describe a molecular communication system in which a transmitter communicates information with the receiver over a calcium signaling channel. Mutual information between transmitter and receiver is then used to calculate the amount of information transfer from the transmitter to the receiver. An example simulation result is provided to illustrate how we measure the amount of information transferred over a calcium signaling channel. Our approach may further develop an understanding of design principles of biological systems as well as help design synthetic biological systems.

Keywords: molecular communication, calcium signaling, channel capacity.

1 Introduction

Molecule-based communication or *molecular communication* plays a key role in regulating numerous biochemical processes and cellular functions in biological systems as well as in synthetic biological systems [1][2][3].

In molecular communication, information is encoded to and decoded from molecules, rather than electrons or electromagnetic waves. Figure 1 schematically describes the basic form of molecular communication in which molecules are used as a carrier of information. The transmitter and receiver are the two communicating molecular machines, (e.g., molecules, cells, organs.) The signal molecules are transmitted by a sender(s) of communication, propagated passively or actively through a communication channel, and received by the recipient(s) of communication. A communication channel contains various noise sources such as thermal noise and other molecules that may chemically react to signal molecules, which significantly influence how signal molecules propagate in the channel.

One form of molecular communication is calcium signaling that is found in virtually all biological cells. Calcium signaling in biological cells is used to regulate a number of cellular processes from death to growth. Figure 2 shows an example of calcium signaling observed among Human Epithelial Cells (HeLa cells) expressing

A. Schmid et al. (Eds.): Nano-Net 2009, LNICST 20, pp. 29–33, 2009.

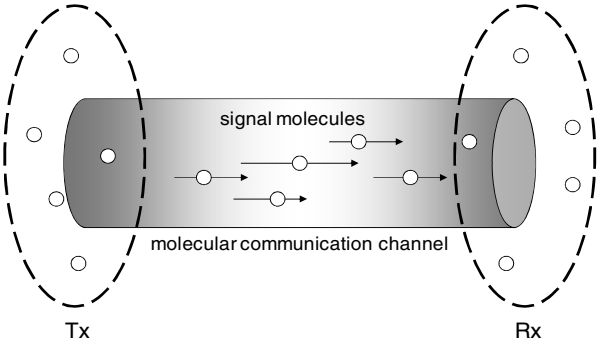

Fig. 1. Molecular communication

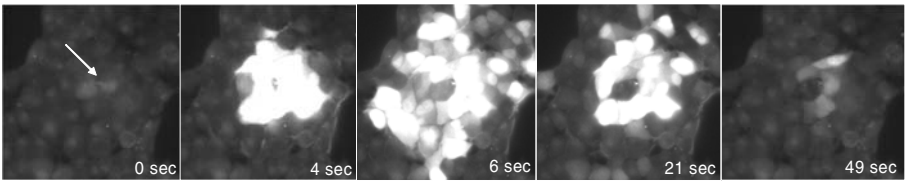

Fig. 2. Calcium signaling in HeLa cells expressing gap junction channels

gap junction channels. The series of images in Figure 2 demonstrate that a mechanically stimulated cell (indicated by the arrow at 0 sec) generates signal molecules including calcium ions that propagate cell-to-cell.

Calcium signaling itself has been intensively studied in cell biology experimentally. It has been also long studied in mathematical biology and a number of mathematical models have been developed. However, its information aspects are not satisfactorily investigated. From an information theory view point, there are a set of interesting questions to ask – for example, "how many bits of information can cells communicate through calcium signaling (information transfer capacity)?", "how the information transfer capacity can be maximized?", and "what is the impact of noise on the information transfer capacity and how the noise can be optimally filtered out in such a noisy environment like the cellular environment?".

Motivated by the information theoretic view point, we propose in this paper to apply information theoretic criteria to evaluate the capacity of calcium signaling. We develop an information communication model and present preliminary simulation results to illustrate how we measure the amount of information transfer over a calcium signaling channel.

There are a few research efforts in the literature addressing information transfer capacity of molecular communication channels [4][5][6]. In [4], Eckford quantified the capacity of a molecular communication channel, in which signal molecules propagate from transmitter to receiver based on Brownian motion. Atakan and Akan have also modeled a free-diffusion media considering various environmental factors that affect the channel capacity [5]. In [6] Moore et al. modeled an active-transport based molecular communication channel, in which signal molecules actively propagate using

molecular motors over molecular rails. In this paper, we focus on a calcium signaling channel that has not been studied previously.

2 Information Communication Model

Our communication system consists of the transmitter, channel and receiver in accordance with the generic model shown in Figure 1. Given the limited space available in this paper, the following description on our model is inevitably selective and is focused on information theoretic modeling aspects.

- The transmitter represents a calcium release channel (or a cluster of calcium release channels). The transmitter has two states $x = \{x_0, x_1\}$. When $x=x_1$, the transmitter is in the transmission mode releasing calcium signals at a constant rate. When $x=x_0$, the transmitter is not releasing calcium signals.
- The calcium signaling channel is a cytosolic medium that propagates calcium signals and that is capable of amplifying calcium signals through calcium induced calcium release (CICR). The calcium dynamics on the channel (i.e., how calcium signals propagate and get amplified) is described using a set of ordinary differential equations as in [7].
- The receiver is a calcium sensitive protein that is activated (e.g., phosphorylated) by Ca^{2+} signals. The receiver has two states $y = \{y_0, y_1\}$. State y_0 represents that the receiver is inactive while state y_1 active. The activation of an inactive receiver occurs at the rate dependent on the cytosolic calcium concentration and it is based on a Hill slope. The inactivation of an active receiver is at a constant rate.

To quantify the information transfer capacity of calcium signaling channels, we introduce two probabilities $p(x)$ and $p(y)$ which respectively represent the probability that the transmitter is in state $x = \{x_0, x_1\}$ and the probability that the receiver is in state $y = \{y_0, y_1\}$. $p(y|x)$ then refers to the conditional probability that the receiver is in state y under the condition that the transmitter is in state x. Now, using the common formula of mutual information, the amount of information transfer from transmitter to receiver can be quantified as follows:

$$\begin{aligned} I(X;Y) &= \sum_{y\epsilon Y}\sum_{x\epsilon X} p(x,y)\left(log_2\frac{p(x,y)}{p(x)p(y)}\right) \\ &= \sum_{y\epsilon Y}\sum_{x\epsilon X} p(x)p(y|x)\left(log_2\frac{p(y|x)}{p(y)}\right) \end{aligned} \quad (1)$$

The channel capacity is then defined as

$$C = max\ I(X;Y) \quad (2)$$

In our simulation, $I(X; Y)$ is calculated assuming that the transmitter's states are randomly set in the following manner. The transmitter is initially in state x_0. Every T second the transmitter alternates the state from one state to the other, and remains in the same state for the duration of T. Each simulation is run for the duration of $2n \times T$. Thus, a total time period that the transmitter is in state x_0 is equal to the total time period in state x_1, and it is $n \times T$. Therefore, $p(x=x_0) = p(x=x_1) = 0.5$. From each

simulation run, the following probabilities are obtained: $p(y=y_0)$, $p(y=y_1)$, $p(y=y_0|x=x_0)$, $p(y=y_1|x=x_0)$, $p(y=y_0|x=x_1)$, $p(y=y_1|x=x_1)$ and $I(X; Y)$ is calculated based on Eq. (1).

3 Simulation Results

Figure 3 shows an example simulation setup and numerical results (T=30 seconds and n=3 in the figure). Figure 3A illustrates a simulated one-dimensional space in which a transmitter is positioned at a single place and receivers are distributed uniformly over the space. Figure 3B shows $p(x=x_1)$, the probability that the transmitter is transmitting calcium signals. Figure 3C shows the cytosolic calcium concentration, denoted as $[Ca^{2+}]_i$ (μM), and $p(y=x_1)$, the probability that the receiver is in active form, measured at five different positions 0 to 4 as shown in Figure 3A. The five graphs in Figure 3C together illustrate how the calcium dynamics at each position is affected by the transmitter signals, and how receivers are activated by the calcium dynamics.

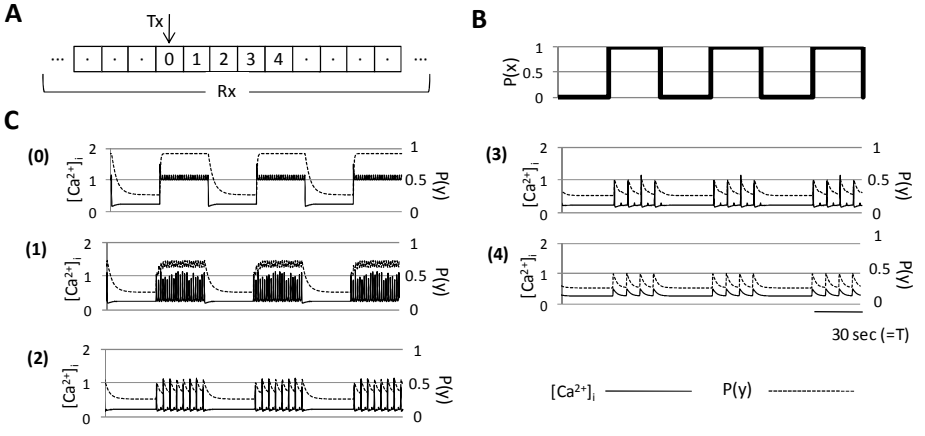

Fig. 3. Simulation Results

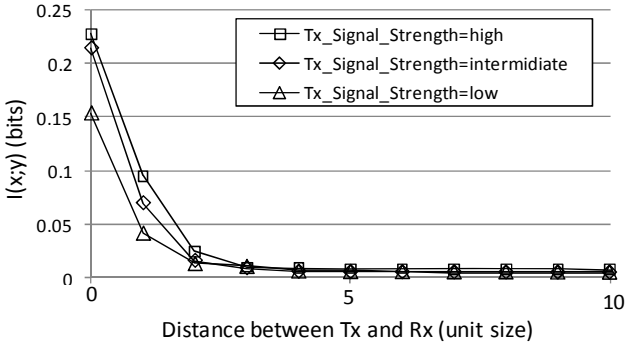

Fig. 4. Mutual information as a function of distance between transmitter and receiver

Figure 4 shows mutual information between the transmitter and receivers at each position measured using Eq. (1). Three graphs are obtained from three sets of simulations using particular strengths of transmitter signals; low, intermediate and high (the calcium release rate constant is linearly increased from low, intermediate to high). As shown in the figure, the amount of information that the transmitter can transfer to a receiver decreases sharply as the distance to the receiver increases. In addition, increasing the signal strength does not increase the amount of information that distant receivers receive. The simulation results may indicate an optimal design of biological systems in terms of bits – e.g., optimal placement and distribution of transmitters and receivers to maximize the amount of information to be transferred under some constraints such as the number of transmitters/receivers that can be synthesized and maintained, the amount of energy that can be used to generate transmitter signals, and the cell size/volume.

The simulation results shown here are just illustrative to demonstrate how we investigate the information transfer over a calcium signaling channel. We are currently performing parameter optimization to identify conditions to maximize the mutual information, and more results will be obtained and published in an upcoming paper.

Acknowledgement

Part of this research has been carried out at the Frontier Research Base for Global Young Researchers, Osaka University, through the program Promotion of Environmental Improvement to Enhance Young Researchers' Independence, the special coordination funds for promoting science and technology, Japan ministry of education, culture, sports, science and technology.

References

1. Weiss, R., Basu, S., Hooshangi, S., Kalmbach, A., Karig, D., Mehreja, R., Netravali, I.: Genetic circuit building blocks for cellular computation, communications, and signal processing. Natural Computing 2, 47–84 (2003)
2. Nakano, T., Hsu, Y.H., Tang, W.C., Suda, T., Lin, D., Koujin, T., Haraguchi, T., Hiraoka, Y.: Microplatform for intercellular communication. In: Third Annual IEEE International Conference on Nano/Micro Engineered and Molecular Systems (January 2008)
3. Hiyama, S., Inoue, T., Shima, T., Moritani, Y., Suda, T., Sutoh, K.: Autonomous loading, transport, and unloading of specified cargoes by using DNA hybridization and biological motor-based motility. Small 4(4), 410–415 (2008)
4. Eckford, A.: Achievable information rates for molecular communication with distinct molecules. In: Workshop on Computing and Communications from Biological Systems: Theory and Applications (2007)
5. Atakan, B., Akan, O.B.: An information theoretical approach for molecular communication. In: 2nd International Conference on Bio-Inspired Models of Network, Information, and Computing Systems (2007)
6. Moore, M., Oiwa, K., Suda, T.: Molecular communication: modeling noise effects on information rate (in press)
7. Nakano, T., Suda, T., Koujin, T., Haraguchi, T., Hiraoka, Y.: Molecular communication through gap junction channels. In: Priami, C., Dressler, F., Akan, O.B., Ngom, A. (eds.) Transactions on Computational Systems Biology X. LNCS (LNBI), vol. 5410, pp. 81–99. Springer, Heidelberg (2008)