Electromagnetic-Induced Calcium Signal with Network Coding for Molecular Communications

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Abstract. Molecular communication (MC) has become a new communication technology between nano-scale devices due to its biocompatibility and low energy consumption. Calcium signaling gradually becomes a hot research topic as a typical case of molecular communication in biological cells, but the system performance of Ca^{2+} signal-based molecular communication is low because the intracellular Ca^{2+} concentration decays with time and space. In this work, we firstly introduce a hybrid communication scheme based on electromagnetic and molecular communication to investigate the mechanism of action of cytoplasmic calcium ions induced by alternating fields. Secondly, the Ca^{2+} signal is analyzed in a multimodal analysis using an external electromagnetic device that emits electromagnetic waves as a control wave to drive the transmitter. In addition, we propose a network coding scheme based on Ca^{2+} signal frequency and a high-efficiency communication system with XOR logic gates. The proposed network coding communication system reduces the number of information exchanges and has a higher communication efficiency compared to conventional communication.

Keywords: Molecular communication · Network Coding · Electromagnetic-induced · Calcium Oscillation

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1 Introduction

With the development of interdisciplinary fields such as synthetic biology and nanotechnology, the construction of a heterogeneous and ubiquitous Internet of nano-things (IoNTs) is becoming a reality in vivo. However, bio-nanomachines must overcome power and functional limitations to achieve a large number of complex biomedical applications, such as bio-detection and tissue repair [1]. Currently, it is difficult for nanolevel devices to wireless communication due to the size and energy consumption limitations of the device unit (e.g., antenna). To solve this challenge, a novel communication technology between nanoscale devices, i.e., molecular communication (MC) [2], is proposed.

Molecular communication, as an innovative communication technology, uses molecular or chemical signals as carriers to communicate between biological nanomachines [3]. Information molecules are small in size usually in the nanoscale and can be biological compounds or synthetic compounds such as proteins, nanoparticles, etc. The MC channels are water or gas environments where tiny molecules can freely pass. The transmitter encodes messages onto the molecules and releases them into the molecular communication channel. After the receiver detects the message molecule, the receiver reacts biochemically with the molecule to decode the message and perform the corresponding function [4]. The biocompatibility and low energy consumption of molecular communication are promising for applications in the human body, such as target detection, organ repair, etc [5].

Many works have now investigated calcium (Ca^{2+}) signaling as typical of MC in bio-cellular networks and have identified Ca^{2+} signaling as a potential physical mechanism to research [6]. Ca^{2+} signaling plays an significant role in a variety of physiological processes, including fertilization and prominence transfer [7], and it is important to understand its conduction process. From a biological point of view, Ca^{2+} signaling is prevalent in cells as intracellular second messenger. From a communication engineering point of view, the multimodal waveforms of calcium signals are suitable for information encoding and for transmitting information in biological cell networks [8]. Due to the intracellular Ca^{2+} concentration decays with time space, the system performance of MC based on Ca^{2+} signals is low. However, communication between nanomachines can be established by nanomechanical, acoustic, chemical, and electromagnetic (EM) communication methods, in addition to using molecular communication.

Molecular communication and electromagnetic communication are envisioned as the most promising paradigms in vivo, and a great deal of research has been conducted in both of them. MC is a novel biomimetic communication technology that offers the possibility of building IoNTs in vivo. However, existing MC methods exhibit slow and unstable properties in biological environments due to the decay and interactions of biochemical molecules, which limits their application. Therefore, many studies have considered combining molecular communication with other communication paradigms to enhance molecular communication performance. In addition, the communication efficiency of molecular communication systems is a problem to be solved. Although the communication distance can be extended by relay nodes, it will also the complexity of information transmission between nodes.

Many previous works have investigated the molecular communication of calcium signals. In [9], a model of Ca^{2+} oscillations inside biological cells is developed and combined with a biological perspective to describe Ca^{2+} signal generation. In [10], the mechanism of the effect of alternating current field on cytoplasmic calcium concentration was proposed, and the effect of electric field strength on Ca^{2+} signal was analyzed. [11] introduces a hybrid communication scheme based on electromagnetic nano-communication and molecular communication, and explores some open problems and challenges. In addition, many works have begun to investigate efficient molecular communication networks to build molecular computers of the future. In [12], an XOR gate is constructed using details of the interactions of certain types of two-reactant reaction diffusion. In [13], frequency coding based on Ca^{2+} signals is investigated and it is shown how noise degrades the performance of channel switching. [14] proposes the use of biological cells to develop logic gates that are implemented by controlling the intercellular Ca2+ signal through an external input signal.

In this work, we propose a hybrid communication scheme based on electromagnetic communication and molecular communication, and theoretically investigate the mechanism of action of cytoplasmic calcium ions induced by alternating fields. Then, we use an external electromagnetic device that emits electromagnetic waves as a control wave to drive the transmitter, oscillatory forces can be applied to each free electrolyte and affect changes in the biological cell. In addition, we introduce an MC network coding scheme based on Ca^{2+} signal frequencies to generate different Ca^{2+} signals for coding by an external electromagnetic device. The exchange of information between cells is then done efficiently using XOR logic gates as a way to improve communication efficiency with the aim of expanding and implementing more applications.

The rest of paper is presented below. Section 2 describes the Ca^{2+} signal generation mechanism for electromagnetic enablement, Sect. 3 describes Ca^{2+} signal-based network coding, and Sect. 4 summarizes the full paper and presents future related work.

2 Electromagnetic-Induced Ca^{2+} Signaling Mechanism

In this section, we describe the mechanism of Ca^{2+} signal oscillation induced by external electromagnetic devices. The mechanism consists of a phase of membrane potential change induced by electromagnetic potential coupling and a phase of potential-induced calcium signal oscillation, as shown in Fig. 1.

2.1 Electromagnetic-Induced Membrane Potential Change Phase

It has been shown that low-frequency electric and magnetic fields can influence the activity of biological cells, which is mainly caused by forced vibrations of all free ions by external oscillatory fields. The function of the biological cell and the internal electrochemical balance will be disrupted by the coherent vibration of this charge [15]. In addition, the free ions (Na, Ca^{2+}, etc.) present around the

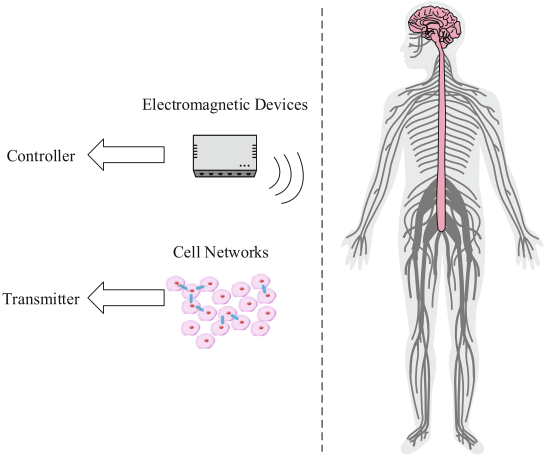


Fig. 1. System model.

cell membrane also play an essential role in the intercellular signaling process. Thus an oscillating external electric or magnetic field will apply an oscillating force for the free ions crossing the plasma membrane, and this force induces coherent forced vibrations that can be combined with the random motion of the ions [16].

The total potential difference in the cell membrane is caused by the movement of all available ions, which is facilitated by three different types of forces, as follows [15]:

$$m\frac{d^2l}{dt^2} - F_3 + F_1 = F_2 \tag{1}$$

$$F_1 = -m\omega^2 l \tag{2}$$

$$F_2 = E_m z q_e \sin(2\pi f t) \tag{3}$$

$$F_3 = -\lambda\frac{dl}{dt} \tag{4}$$

where F_1 is the restoring force generated by the electrochemical gradient, which is determined mainly by the ion mass m, the angular frequency of self-sustained oscillations ω and the distance travelled l by the ions. F_2 denotes the external force brought about by electromagnetism, where E_m is the electromagnetic intensity, f is the alternating frequency, z is the chemical valence of the ion, and $q_e = 1.6 * 10^{-19}C$. F_3 indicates the attenuation force and λ is the attenuation coefficient.

In addition, the cell membrane potential V_m is associated with the cell membrane thickness s, effector force F and charge q, i.e., the membrane potential can be expressed as:

$$V_m = F \cdot \frac{s}{q} \tag{5}$$

Here, we regard the influence of electromagnetism on SOC channels in cell membranes caused by a force.

$$F = \frac{1}{4\pi\varepsilon\varepsilon_0} \cdot \frac{q \cdot zq_e}{r^2} \tag{6}$$

where ε_0 and ε are the vacuum permittivity and relative permittivity, respectively. $q = 1.6 * q_e$, r indicates the distance between the free charge and the SOC channel. Therefore, it can be solved by the difference operation:

$$\partial V_m = \frac{1}{2\pi\varepsilon\varepsilon_0} \cdot \frac{q \cdot zq_e}{r^3} \partial r \tag{7}$$

Assuming $\partial x = \partial r$, i.e. the position of the ion is the initial origin, and the membrane potential can be expressed as:

$$\partial V_m = \frac{1}{2\pi\varepsilon\varepsilon_0} \cdot \frac{q \cdot zq_e}{r^3} \cdot \frac{s}{q} \cdot \frac{E_0 zq_e}{\lambda} \sin(2\pi v t)\partial \mathrm{t} \tag{8}$$

2.2 Potential-Induced Ca^{2+} Oscillation Phase

The cell undergoes an intracellular signaling cascade in response to an external stimulus. The intracellular calcium reservoir (ER) opens calcium channels and then Ca^{2+} begins to diffuse into the cytoplasm generating a large Ca^{2+} concentration gradient. However, excessive Ca^{2+} concentration may lead to apoptosis, so cells maintain Ca^{2+} concentration homeostasis through internal ion regulatory mechanisms. The constant oscillation of Ca^{2+} generates signals within the cell and transmits them to adjacent cells via intercellular channels. Here, we use a widely accepted Ca^{2+} oscillation model to describe the generation of Ca^{2+} signals [17]:

$$\frac{dx}{dt} = K_1 - K_2 + K_3 + n_1 y - n_2 x + I_G \tag{9}$$

$$\frac{dy}{dt} = K_2 - K_3 - n_1 y \tag{10}$$

where x denotes the cytoplasmic Ca^{2+} concentration, y is Ca^{2+} concentration in the internal calcium pool, K_1 indicates the influx of extracellular Ca^{2+} into the cell through different classes of channels. K_2 and K_3 for Ca^{2+} exchange between cytoplasm and internal stores. Here, K_1 is mainly composed of non-electromagnetic and electromagnetic induced components, which can be expressed as follows:

$$K_1 = w_1 + w_2(t) \tag{11}$$

$$C_m \frac{dV_m}{dt} = w_2(t) \tag{12}$$

where w_1 indicates a non-EM-induced increase in Ca^{2+}, i.e., a constant influx of Ca^{2+} stimuli into the cell interior. $w_2(t)$ is induced by electromagnetism leading to an increase in Ca^{2+} concentration, which is mainly associated with changes in the membrane potential V_m and C_m the capacitance of the membrane. The specific parameter settings for the two stages are shown in [10,15–17].

Figure 2 indicates that the Ca^{2+} signal shows different calcium waves with the electric field intensity, including pulsed calcium signal and sinusoidal calcium signal. Figure 3 demonstrates that the Ca^{2+} signal varies with alternating frequency and that the resulting sinusoidal calcium signal has a higher frequency (Fig. 3b). Simulation results show that it is feasible to use an external electromagnetic device as an input device to control Ca^{2+} signal generation. And the generated Ca^{2+} signals exhibit multimodal characteristics, i.e., pulsed calcium signals and sinusoidal calcium signals. Based on these findings, we generated Ca^{2+} signals of different frequencies by external electromagnetic devices and used Ca^{2+} signals for molecular coding to enhance intercellular communication efficiency.

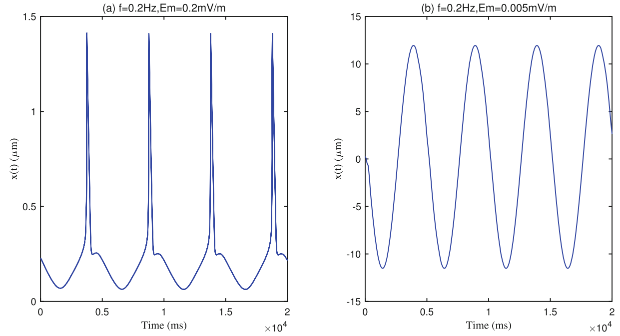


Fig. 2. Variation of Ca^{2+} waveform with electric field intensity.

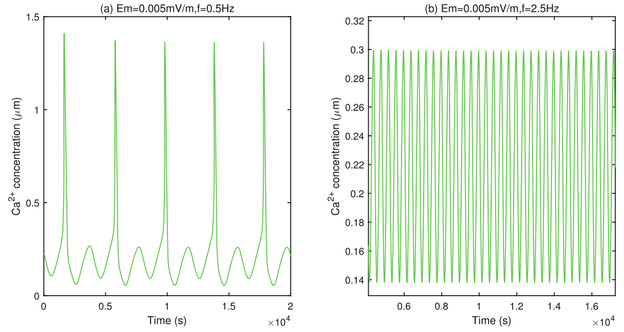


Fig. 3. Variation of Ca^{2+} waveform with alternating frequency.

3 Network Coding

In this section, we introduce a molecular communication network coding system based on multimodal Ca^{2+} signals and investigate the use of logic gates to achieve efficient communication between cells.

3.1 Intercellular Communication Model

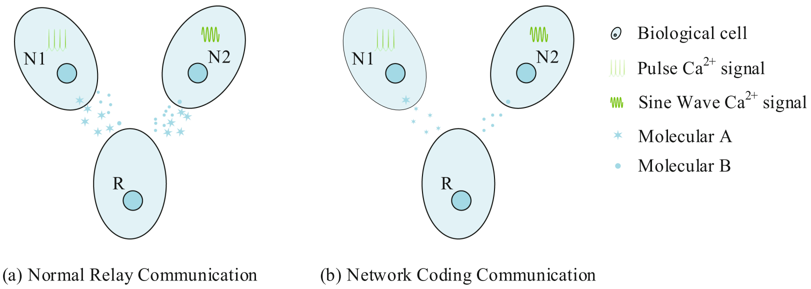
Logic gate circuits constructed by biological cells will enable a new molecular computing technology that can rely on Boolean logic gates for intercellular communication [18]. A logic circuit consisting of Boolean logic gates can be used to reconfigure the computation of metacell operations. A fundamental function of synthetic logic circuits is communication, including communication between cells or between groups of cells [14]. Therefore, constructing logic gate circuits in intercellular molecular communication network species can not only accomplish efficient communication but also enable reconfigurability of logic operations.

The Ca^{2+} signaling molecular communication system is a short-term intercellular communicatio that uses Ca^{2+} as signaling between cellular gap junctions. To improve the system communication efficiency, we propose a Ca^{2+} signaling network encoding mechanism to accomplish efficient communication between cells or between cell populations through the XOR gate. Figure 4 briefly illustrates the two communication modes between cells, including the traditional relay communication mode (Fig. 4a) and the network coded communication mode (Fig. 4b). The network model includes two communicating cells, N1 and N2, and a relay cell, R, and cells N1 and N2 can only communicate through the relay cell. Without the use of network coding, the information of exchange cells N1 and N2 needs to be transmitted four times, i.e., regular relay communication. The information exchange realized by network coding only needs to be transmitted 3 times, i.e. N1 to R for A and N2 to R for B, which has higher communication efficiency. The cell R passes the information molecule to both N1 and N2 after the logic gate operation, and N1 and N2 then perform the logic operation to complete the information exchange, i.e., network coded communication.

3.2 Intercellular Communication

In Sect. 3, the Ca^{2+} signals induced by external electromagnetic devices exhibit multimodal characteristics (i.e., pulsed calcium signals and sinusoidal calcium signals). Here, we consider coding using the Ca^{2+} waveform frequency, and the cell treats the pulsed Ca^{2+} signal as releasing the A molecule (bit “1”) and the sinusoidal Ca^{2+} signal as releasing the B molecule (bit “0”). This makes it possible to construct a combination of logic gates using Ca^{2+} frequency coding exactly to perform logic gate operations. It is assumed that every biological cell can have XOR logic gate and the cell can know the molecule it sends. In addition, we define the XOR logic gate operation rules:

$$A \oplus B = A \tag{13}$$



(a) Normal Relay Communication (b) Network Coding Communication

Fig. 4. Intercellular communication patterns.

$$B \oplus B = B \tag{14}$$

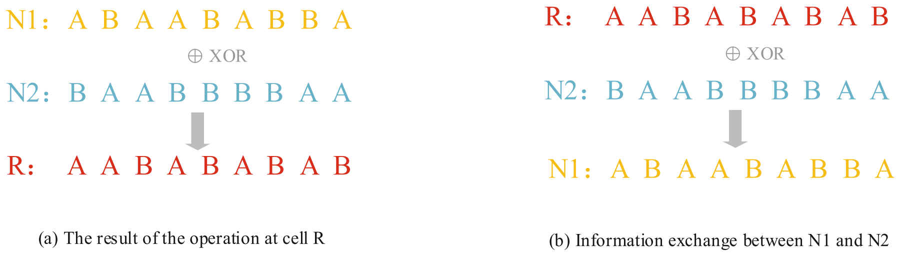
$$A \oplus A = B \tag{15}$$

The coding rules follow the difference as A and the same as B. The specific network code table is shown in Table I. After the relay cell R performs the heterogeneous operation and releases the information molecules to N1 and N2 for heterogeneous operation, N1 and N2 realize the intercellular communication.

Table 1. Molecular communication codes.

Bits transmitted(N1, N2)	N1 releases	N2 releases	Concentration of R	R releases
(0,0)	B	B	Low	B
(0,1)	B	A	High	A
(1,0)	A	B	High	A
(1,1)	A	A	Low	B

Figure 5 illustrates the process of intercellular communication based on the XOR gate. At first cells N1 and N2 use Ca^{2+} signaling generated by external electric fields to transmit molecular information chains. Relay cell R undergoes XOR operation after receiving the information chain from cells N1 and N2, as in Fig. 5a. The relay cell R then generates a new information link according to the molecular communication coding rules in Table 1 and simultaneously transmits it to the sending cell. After receiving the information transmitted by R, cells N1 and N2 perform XOR operations with their own information chains to complete the information exchange between cells, i.e., Fig. 5b. The proposed molecular communication coding system has better communication efficiency compared to conventional relay communication where four transmissions are required to complete the information exchange.



(a) The result of the operation at cell R

(b) Information exchange between N1 and N2

Fig. 5. Intercellular communication between N1 and N2.

4 Conclusion

In this paper, we introduce a hybrid molecular communication scheme based on alternating electric fields and propose the use of molecular communication codes to enhance intercellular communication efficiency. First, we theoretically investigated the alternating field-induced membrane potential changes in cells and explored the mechanism of potential-induced cytoplasmic calcium ion oscillations. In addition, a molecular communication coding system based on Ca^{2+} signal frequency was proposed using the multimodal characteristics of calcium signals induced by electric fields. We also demonstrate the rules of the molecular communication coding system, which is able to improve the efficiency of intercellular communication compared to the codeless communication mode.

In future work, we will continue to investigate the coding system for long-range communication between cell populations. We also consider the coding efficiency between coding rules, anti-interference and other issues, and combine with the actual biological cell network scenario to find a more efficient calcium signal molecular communication system through indepth research, aiming to build a real nano-Internet of things.

References

1. Bi, D., Almpanis, A., Noel, A., Deng, Y., Schober, R.: A survey of molecular communication in cell biology: establishing a new hierarchy for interdisciplinary applications. IEEE Commun. Surv. Tutorials **23**(3), 1494–1545 (2021). https://doi.org/10.1109/COMST.2021.3066117
2. Nakano, T., et al.: Random cell motion enhances the capacity of cell-cell communication. IEEE Trans. Molecular Biolog. Multi-Scale Commun. **5**(2), 158–162 (2019). https://doi.org/10.1109/TMBMC.2020.2983909
3. Barros, M.T., Dey, S.: Feed-forward and feedback control in astrocytes for Ca^{2+}-based molecular communications nanonetworks. IEEE/ACM Trans. Comput. Biol. Bioinform. **17**(4), 1174–1186 (2020). https://doi.org/10.1109/TCBB.2018.2887222

4. Atamiş, F.B., Işık, İ.: Analysis of the signal reception in mobile molecular communication system by using antenna. In: 2021 29th Signal Processing and Communications Applications Conference (SIU), pp. 1–4 (2021). https://doi.org/10.1109/SIU53274.2021.9477881
5. Okaie, Y.: Cluster formation by mobile molecular communication systems. IEEE Trans. Molecular Biological Multi-Scale Commun. **5**(2), 153–157 (2019). https://doi.org/10.1109/TMBMC.2020.2981662
6. Han, J.M., Periwal, V.: A mathematical model of calcium dynamics: obesity and mitochondria-associated ER membranes. PLoS Comput. Biol. **15**(8), e1006661 (2019)
7. He, P., Pi, B., Liu, Q.: Calcium signaling in mobile molecular communication networks: from a multimedia view. IEEE Access **7**, 164825–164834 (2019). https://doi.org/10.1109/ACCESS.2019.2953074
8. He, P., Su, M., Cui, Y., Wu, D., Wang, R.: Epidemic-like calcium signaling in mobile molecular communication networks. IEEE Trans. Nanobiosci. **21**(3), 425–438 (2022). https://doi.org/10.1109/TNB.2022.3155644
9. Barros, M.T.: Ca^{2+}-signaling-based molecular communication systems: design and future research directions. Nano Commun. Netw. **11**, 103–113 (2017)
10. MingYan, L., Kun, S., Xu, Z., et al.: Mechanism for alternating electric fields induced-effects on cytosolic calcium. Chin. Phys. Lett. **26**(1), 017102 (2009)
11. Yang, K., Bi, D., Deng, Y., et al.: A comprehensive survey on hybrid communication in context of molecular communication and terahertz communication for body-centric nanonetworks[J]. IEEE Trans. Molecular Biological Multi-Scale Commun. **6**(2), 107–133 (2020)
12. Adamatzky, A., Costello, B.D.L.: Experimental logical gates in a reaction-diffusion medium: the XOR gate and beyond. Phys. Rev. E **66**(4), 046112 (2002)
13. He, P., Nakano, T., Mao, Y., et al.: Stochastic channel switching of frequency-encoded signals in molecular communication networks. IEEE Commun. Lett. **22**(2), 332–335 (2017)
14. Barros, M.T., Doan, P., Kandhavelu, M., et al.: Engineering calcium signaling of astrocytes for neural-molecular computing logic gates. Sci. Rep. **11**(1), 1–10 (2021)
15. Panagopoulos, D.J., Karabarbounis, A., Margaritis, L.H.: Mechanism for action of electromagnetic fields on cells. Biochem. Biophys. Res. Commun. **298**(1), 95–102 (2002)
16. Barnes, F.S.: Interaction of DC and ELF electric fields with biological materials and systems. In: Polk, C., Postow, E. (eds.) CRC Handbook of Biological Effects of Electromagnetic Fields, pp. 27–96. CRC Press, Boca Raton, FL (1996)
17. Goldbeter, A., Dupont, G., Berridge, M.J.: Minimal model for signal-induced Ca^{2+} oscillations and for their frequency encoding through protein phosphorylation. Proc. Natl. Acad. Sci. **87**(4), 1461–1465 (1990)
18. Mao, C., LaBean, T.H., Reif, J.H., et al.: Logical computation using algorithmic self-assembly of DNA triple-crossover molecules. Nature **407**(6803), 493–496 (2000)