A Design Process for Molecular Communication Systems Based on Biological Circuits in Cells

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***Abstract*—While theoretical studies on communication systems based on the exchange of molecules, *i.e.*, Molecular Communication (MC), are opening up a novel domain of applications for the telecom and networking fields, practical technologies to implement these systems are currently understudied. In particular, the engineering of biological cells and their behavior through synthetic biology is a very promising avenue for MC research, where the MC capabilities of cells could be harnessed and manipulated to realize the aforementioned systems. This technical abstract explores this research direction through the definition of a design process derived from recent work on the characterization of MC systems with a single transmitter cell and receiver cell, and their enhancement through digital channel coding techniques realized with biological circuits.**

***Index Terms*—Molecular Communication; Synthetic Biology; Mutual Information; Stochastic Simulation; Channel Coding; Genetic Circuit.**

I. Introduction

Molecular communication (MC) is an emerging engineering area directly inspired by natural communication among cells in biology, where information is encoded into and decoded from molecules [1]. Although MC has been envisioned at the forefront of novel bio-hybrid pervasive sensing, actuation, and computing systems, *i.e.*, the Internet of Bio-Nano Things [2], there is currently a gap between communication theoretical results and deployable technologies based on which MC systems can be designed and implemented.

Recent progresses in synthetic biology are providing new tools for the design, construction, and control of new biological parts and processes. The engineering of synthetic biological circuits through genetic code manipulation has enabled the programming of specifically designed functions to be executed by cells [3]. Amongst diverse synthetic biology implementations, engineered cell-to-cell communication systems have been experimentally demonstrated, where controlled exchange of information molecules is implemented through biological circuits that include genetic programs [4].

In this technical abstract, we present a method to compute the theoretical performance of an engineered cell-to-cell communication system, based on the stochastic simulation of biochemical reactions, which is utilized to understand the potential of an existing synthetic biology design, in terms of mutual information. Then, based on the technology of biological circuit engineering from synthetic biology, we review a digital coding scheme working entirely in the biochemical domain, designed to enhance the performance of this system.

II. Theoretical Performance of Engineered Cell-to-cell Molecular Communication

In the most general form of engineered cell-to-cell MC system [5], an information source releases a message $\overline{X}_{source}$ in the environment where the cells live. This message is then processed by the transmitter cell/s through a series of chained chemical reactions, which transduce the source message into time-varying concentrations of molecules of different species $X_i(t)$, $i = 1, \ldots, S_{tx}$, with the final effect of shaping (*e.g.*, filtering, amplification) the concentration signal of transmitted molecules $X_{tx}(t)$ ($= X_{S_{tx}}(t)$ at the transmitter). This concentration signal propagates to the receiver cell/s through free diffusion in the extracellular environment as $X_{rx}(t)$ ($= X_{S_{tx}}(t)$ at the receiver), where it is processed by another series of chained chemical reactions $X_j(t)$, $j = S_{tx}+1, \ldots, S_{tx}+S_{rx}$ into a destination message $\overline{X}_{dest}$ that is acquired by the information destination. The nature of the source message and the destination message are in general different, and depend on the particular design of engineered cell-to-cell communication system. To estimate the theoretical performance of such a system, we make the following assumptions. i) The concentration of all the aforementioned molecule species is considered homogeneous at any time instant inside the cells. ii) The membranes of the transmitter and receiver cells separate the intracellular space from the extracellular space, and are permeable only by the transmitted and received molecules (small molecules). iii) The noise in the system is generated by the stochastic behavior of the chemical reactions and the diffusion process. The chemical reaction noise can be expressed according to the Chemical Langevin Equation (CLE) approximation, as we did in [5], which results in a stochastic model equivalent to the integral of a non-stationary Gaussian process with increments correlated through the time evolution of the aforementioned species $X_i(t)$, $i = 1, \ldots, S_{tx}+S_{rx}$. The stochastic model of diffusion process noise can be approximated as a Poisson probability mass function (pmf) [6], with variance and expected value changing over time. If we assume a digital communication system as described in Sec. III, and we consider the expected value of the number of molecules $E[N_{rx}(t_d)]$ at the so called

pulse delay $t_d = r_{rx}^2/(6D)$, where r_{rx} is the distance between transmitter and receiver and D is the diffusion coefficient, the number of received molecules $N_{rx}(t)$ can be approximated as a Poisson variable with distribution conditioned to the transmitted bit 0 or 1, where N_0 (or N_1) is the average number of received molecules associated with bit 0 (or 1).

To characterize the information exchange performance of an engineered cell-to-cell communication system through the Mutual Information (MI) parameter from information theory, *i.e.*, $I(\overline{X}_{source}; \overline{X}_{dest}) = H(\overline{X}_{dest}) - H(\overline{X}_{dest}|\overline{X}_{source})$, we adopt a computational approach based on the stochastic simulation algorithm (SSA) methodology [7] for simulating the time evolution of the engineered cell-to-cell communication system affected by noise. We estimate the MI by collecting and analyzing data according to the procedure in [8], with the main difference that here we are based on a computational model rather than expensive wet lab experiments, which does not pose stringent constraints on the size of the data set that can be collected. As detailed in [5], to compute the MI formula, the sample distributions of the destination message, $P_{\overline{X}_{dest}}(x_{dest})$ and the conditional probability density $P_{\overline{X}_{dest}|\overline{X}_{source}}(x_{dest}|x_{source})$ are obtained from histograms, which are built by dividing the range of output message values $X_{dest,i}$ in N uniform spaced bins of width $w_{\overline{X}_{dest}}$ and $w_{\overline{X}_{dest}|\overline{X}_{source}}$, respectively. By stemming from this analysis, one can formulate an optimization problem to estimate the information Capacity (C), which should also take into account an optimal sampling of the input messages.

III. Enhancement of Cell-to-cell Molecular Communication through Channel Coding Design

Our study in [5] provides the basis for the design and realization of digital MC systems based on engineered cells. Our next design step consists in the implementation of encoders and decoders for error correcting codes using tools from synthetic biology. From the decoding perspective, soft decision allows to achieve a better performance than hard decision decoding because it uses unquantized information in the process of decision making.

As an example in [9] we focused on soft decoding of the single parity check (SPC) code. This code is able to detect a single error but it does not correct any error. The $(n, n{-}1)$ SPC code is defined by the set of all the n-tuples with even number of ones, so the sum of all the entries of any code word is zero. The code rate is $r = 1{-}1/n$. In [9] the case $n = 3$ is considered so that the resulting codewords is $[u_1, u_2, u_p]$, where $u_p = u_1 \oplus u_2$ is the parity check bit given by the modulo-2 sum of u_1 and u_2, *i.e.*, the first and second transmitted information bits.

Let y_i be the received concentration associated to the ith transmitted bit u_i. According to the channel model defined in Sec. II, the conditioned log-likelihood ratio (LLR) used to implement the soft decoding of information bits is [10]

$$L(y_i|u_i) = y_i V \log\left(\frac{N_0}{N_1}\right) - (N_0 - N_1). \tag{1}$$

Following [11], the likelihood of the first and second information bits is computed as

$$L(\hat{u}_{1/2}) = L(y_{1/2}|u_{1/2}) + \big(L(y_{2/1}|u_{2/1}) \boxplus L(y_p|u_p)\big) \tag{2}$$

where $\boxplus$ indicates the box-plus operation

$$a \boxplus b = 2\mathrm{atanh}\left(\tanh\left(\frac{a}{2}\right) \cdot \tanh\left(\frac{b}{2}\right)\right). \tag{3}$$

In [9], [12] we implemented the encoding of the SPC code and its soft decoding based on biological circuits. In particular, the analog computing functionalities of biological circuits are exploited to compute the LLRs of the transmitted sequence of encoded bits, as defined by the formula in (2) to compute the (analog) likelihood of the first and second information bits of the code.

IV. Conclusion

We have explored a novel design process to realize MC systems starting from engineered cell-to-cell communications based on synthetic biology. In particular, we have summarized the main steps to computationally estimate their mutual information and apply channel coding to enhance the performance, based on biological circuit design.

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