Coexistence Within Communicating Biological Systems

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***Abstract*—A key question for molecular communication systems operating nearby other biochemical processes is how to ensure coexistence. That is, how can a biochemical process maintain its function, while still allowing for reliable communication? In this paper, we consider the scenario where the information molecular production process and the biochemical process are part of the same biological system. In particular, we formalize a new design problem for this scenario and identify avenues of future work.**

I. Introduction

A key problem in molecular communication systems operating nearby other biological processes is coexistence [1], [2]. In the coexistence problem, both the reliability of the communication system and the function of the biological system must be ensured. In the case that steady-state concentrations of chemical species in a biological system are connected to function—as is the case in many biological systems with chemosensing mechanisms [3]—the impact of the communication system can be quantified by studying changes in the steady-state concentrations.

To resolve the coexistence problem, two clear strategies are either to use information molecules that do not impact steady-state concentrations [1] or to use a coding scheme that limits the change of the steady-state concentation [2]. As was noted in [2], these two coexistence strategies are analogous to interweaving and overlay, respectively, in cognitive radio [4]—a framework to develop communication strategies to ensure coexistence in wireless networks.

In cognitive radio, there is also a third strategy known as underlay. In the context of molecular communications, it was suggested in [2] that underlay corresponds to the situation where the communication strategy is coupled to other processes inside the biological system. Although not formalized, it was suggested that underlay arises in bacteria colonies exhibiting quorum sensing since communication is *built in* to DNA transcription, which also governs other processes in the cell [5].

In this paper, we propose a formalization of the underlay strategy in the context of a biological system communicating with another nano or microscale system via the emission of a small number of molecules. Our formalization is based on a change in perspective from [1], [2]: we view the coexistence constraint as arising from biochemical processes within the transmitting biological system. In other words, communication may be incorporated into existing biochemical processes. Using a simplified—but biologically inspired—model of the system, we establish communication constraints accounting for changes to the pre-existing biochemical processes. This leads to a new design problem for molecular communication systems able to account for the dynamics of realistic biochemical processes. We highlight that this work is an initial formalization of this problem that is readily generalizable to more sophisticated interactions between pre-existing biochemical processes and the information molecule production process.

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II. Model

Many biochemical processes—at least to a first approximation—can be modeled via chemical reaction systems. In general, such systems consist of a set of chemical species, $\mathcal{S}$, a set of reactions of the form $\mathbf{y} \to \mathbf{y}', \mathbf{y}, \mathbf{y}' \in \mathbb{Z}_{\geq 0}^{|\mathcal{S}|}$, denoted by $\mathcal{R}$, and a rate function k. Let $\mathbf{x}(t)$ be the vector consisting of the concentrations of each chemical species at time t. Under mass action kinetics, the chemical reaction system is governed by the system of ordinary differential equations

$$\dot{\mathbf{x}}(t) = \sum_{\mathbf{y} \to \mathbf{y}' \in \mathcal{R}} k_{\mathbf{y} \to \mathbf{y}'} \mathbf{x}(t)^{\mathbf{y}} (\mathbf{y}' - \mathbf{y}), \tag{1}$$

where $\mathbf{x}(t)^{\mathbf{y}} = x_1(t)^{y_1} x_2(t)^{y_2} \cdots$. If it exists, the *steady-state concentation* is defined as the solution to $\dot{\mathbf{x}}(t) = 0$.

In this paper, we model the internal dynamics of a biological system (e.g., a cell) by a chemical reaction system $(\mathcal{S}, \mathcal{R}, k)$ with mass-action kinetics and initial concentations $\mathbf{x}(0)$. In order for the biological system to communicate, we assume that a new biochemical process is also introduced into the biological system. The full system is illustrated in Fig. 1.

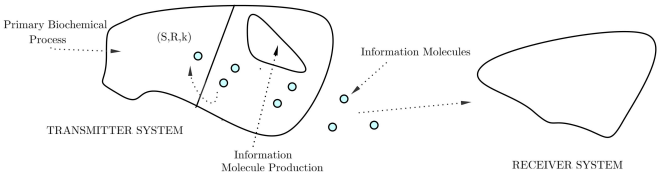

Fig. 1. A molecular communication system with a coupling between information molecule production and a primary biochemical process.

The role of this new process is to produce information molecules. In general, the information molecule production

will be coupled to the pre-existing biochemical processes. For example in bacteria exhibiting quorum sensing, the production of autoinducers (which play the role of information molecules) is part of the DNA transcription process.

As a first step to studying the coupling between communication and the pre-existing processes, we assume that the produced information molecules may react with chemical species in $\mathcal{S}$, which affects the initial conditions $\mathbf{x}(0)$. To preserve the steady-state concentrations of the reaction system $(\mathcal{S}, \mathcal{R}, k)$, a new communication constraint must be introduced.

Note that the quantity of information molecules produced in any given time period, denoted by X, is a random variable. This is due to the fact that modulation will lead to symbols corresponding to different numbers of information molecules, and also because the production process may be noisy. Following [2], we desire that the steady-state concentration of a given species following the production of the X information molecules, denoted by Y, in the biological system satisfies

$$|\mathbb{E}[Y|X=0] - \mathbb{E}[Y]| \leq \Delta. \tag{2}$$

Using the argument in [2, Theorem 1], this can be guaranteed by ensuring that distribution for the number of information molecules that remain in the biological system, Z, satisfies[1]

$$D(P_Z||P_{Z|X=0}) \leq \Delta. \tag{3}$$

It is now possible, by exploiting the connection to covert communications in [2], to establish fundamental limits of communication. Due to space constraints, we do not develop this in the present paper and instead focus on identifying the key design challenges for the underlay strategy.

III. Design Problem

In general, biomolecular control may be implemented either by adjusting initial concentrations of each chemical species, or adjusting reaction rates (or in a stochastic model, propensities) [6]. In this section, we therefore suppose that the biological system may be modified in order to adjust the initial concentrations $\mathbf{x}(0)$. The purpose of this modification is to mitigate the impact of the information molecular production process on the steady-state concentrations of the primary biochemical process.

Since the initial conditions $\mathbf{x}(0)$ for the biological system $(\mathcal{S}, \mathcal{R}, k)$ may be modified, it is in principle possible to allow for a larger perturbation by the information molecule production process. By allowing changes to the biological system, larger values of Δ in (3) are feasible, which increases the quantity of information that may be communicated in a given time period.

There are therefore two key questions:

1) Given an ability to modify the initial conditions for the biological system, $\mathbf{x}(0)$, what is the maximum value of Δ in (3)?
2) What physical (e.g., light) or chemical (e.g., inducers) mechanisms can be used in order to control the initial concentrations of the biological system?

In order to gain some insight into these questions, we focus on a simplified model of the regulation process in bacteria chemotaxis (or more generally robust adaptation) [3]. In particular, consider the following chemical reactions

$$\begin{aligned} \mathsf{A} + \mathsf{B} &\xrightarrow{\alpha} 2\mathsf{B} \\ \mathsf{B} &\xrightarrow{\beta} \mathsf{A}, \end{aligned} \tag{4}$$

where B corresponds to the species used to transmit information and A an activated protein, important for biological function. The concentrations[2] satisfy $[\mathsf{A}](t) + [\mathsf{B}](t) = \Theta,\ \forall t \geq 0$. At equilibrium,

$$\begin{aligned} [\mathsf{A}]_e &= \frac{\beta}{\alpha} \\ [\mathsf{B}]_e &= \Theta - \frac{\beta}{\alpha}, \end{aligned} \tag{5}$$

whenever a strictly positive equilibrium exists. When $\frac{\beta}{\alpha} > \Theta$, then $[\mathsf{A}]_e = \Theta$ and $[\mathsf{B}]_e = 0$. In our problem, Θ (stochastically) depends on the number of information molecules produced. Clearly, given a mechanism to adjust the initial concentration of A and B, new quantities of B introduced by the information molecule production process may be accounted for.

IV. Conclusions

For applications of molecular communications in the presence of biological systems, coexistence strategies provide a means of ensuring that both function and reliable communication are preserved. In this paper, we have explored the underlay strategy when the biological system and production processes for the information molecules lie within the same membrane. Unlike the strategies studied in [1], [2], the model allows for the pre-existing biochemical processes to be modified. This alternative perspective on the coexistence problem introduces new design problems. In the future, we intend to investigate solutions, particularly in the context of bacteria cultures exhibiting quorum sensing.

References

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[1] P_X denotes the probability distribution of the random variable X. $D(P_X||P_Y)$ denotes the Kullback-Leibler divergence between P_X and P_Y.

[2] In this paper, $[\mathsf{X}](t)$ denotes the concentration of a chemical species X at time t.