Behavioral variability in the bacterial chemotaxis system arising from component localization

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***Short Abstract* — We perform a noise analysis of a simple push-pull network, accounting for the localization of substrate to a small fraction of the total cell volume. We find that this scheme can produce significantly higher levels of intracellular signaling noise than well-mixed models. We apply these results to the bacterial chemotaxis system and study its effect on information transmission, chemotactic performance and network robustness. These results may inform the study of a wide range of systems for which signaling noise could produce behaviorally significant effects.**

I. Introduction

PUSH-PULL systems are ubiquitous in biology: networks ranging from simple chemosensory systems to complex metabolic pathways employ this basic motif of a substrate modified by antagonistic enzymes. The signal amplification properties of these networks have been the focus of previous studies, including the seminal work of Goldbeter and Koshland [1] and more recent work considering the effects of diffusion and localization of the network components, *e.g.* [2]. A recent analysis of signaling noise in push-pull networks with well-mixed components was given in [3] as part of a study of behavioral variability in the *Escherichia coli* chemotaxis system. We extend this analysis to consider localization of the modifiable substrate to a small fraction of the total cell volume, and find that this model explains the magnitude of spontaneous fluctuations observed in the chemotaxis network [4]. Within the context of this model system, we consider the costs and benefits of these large fluctuations for signaling fidelity and chemotactic performance. This analysis is relevant to a large class of systems featuring push-pull architectures and should inform the study of other systems for which behavioral variability may have positive consequences for the organism's survival.

II. Methods

A. Models

Component localization may be modeled simply by splitting the cell volume into compartments with fixed levels of substrate, but between which the mobile enzymes are freely exchanged. We construct a simple analytic model by utilizing activity-dependent, Michaelis-Menten kinetics to describe the enzyme-substrate reactions within each compartment. For the specific case of bacterial chemotaxis, we present a more detailed model incorporating prior knowledge of the chemoreceptor substrate (*i.e.*, clustering [5], dose response measurements [6], enzyme tethering [7]) and including a flagellar motor [8] as output. The performance of these model cells is studied *in silico* using a novel stochastic simulation platform.

B. Performance metrics

The performance of the signaling network is evaluated based on its ability to transmit information [9] in addition to practical metrics such as the ability of the cell to explore space and to find and consume chemoattractants. Additional requirements, such as the robustness of network performance to variations in the levels of the constituent enzymes, are also considered.

III. Results

In contrast to previous models, we find that this scheme produces a high level of signaling noise while maintaining a steady state output relatively robust to variation in the levels of the adaptation enzymes, consistent with measurements of the bacterial chemotaxis system. Also for this model system, we find that the noise level may be tuned over two orders of magnitude, with significant effects on the cells' ability to explore space, but with relatively minor effect on the network's information throughput.

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