Engineering Multi-signal Systems for Complex Pattern Formation

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Abstract

Biological pattern formation networks orchestrate complex processes of constituent cells, often through the use of multiple intercellular signals. The forward engineering of such multi-signal systems in synthetic biology has a number of important applications including biosensing, tissue engineering, and biomaterial fabrication. In addition, such synthetic systems provide a testing ground for quantitatively studying the fundamental principles governing similar natural genetic networks. However, an initial requirement for engineering multi-signal networks is the characterization and tuning of various properties of the signaling systems, including crosstalk, receiver response strength, and sensitivity. We characterize crosstalk interactions for synthetic receivers built from components of the Las and Rhl quorum sensing systems from Pseudomonas aeruginosa*. Next, we present results from genetic constructs designed to amplify weak transcriptional responses to signaling molecules. We then discuss results from directed evolution of receptor proteins to optimize receiver sensitivity. These methods of engineering synthetic constructs with desired response strengths and sensitivities to external signals have a number of important applications in their own right, such as the development of biosensors for detection of trace amounts of toxins. In addition to the experimental results that show how signaling constructs can be optimized for such applications, we present simulations for two example pattern formation systems that can be constructed from these tuned components.*