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TRADEOFFS IN ADAPTING BIOLOGICAL SYSTEMS

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Abstract

Biological systems must sense and adapt to changes in their environment. Molecular networks capable of such adaptation belong to two well-known classes, feedforward and feedback structures, but the fundamental limitations and tradeoffs of these two classes remain unknown. Here we study the advantages and limitations of the feedforward class using three-node circuits representative of these architectures. The feedforward model we investigate displays a tradeoff between the sensitivity of the response (its peak response) and its precision (its error in its return to steady-state). We suggest two ways in which this tradeoff can be alleviated: (1) by introducing a nonlinearity in the production of a specific node in the network, or (2) by adding a feedback loop to the input. We present analytical and numerical examples to support our findings.

1 Introduction

Often, organisms need to regulate their internal environment to adjust to external changes. For instance in yeast, the Hog pathway senses osmotic shock and regulates the release of glycerol to maintain constant turgor pressure [1]. In *E. coli*, the binding of a ligand to a membrane receptor initiates a motor response as well as feedback regulation to eventually shut off the response [2]. In mammals, light is sensed by the G-protein coupled receptor Rhodopsin which initiates visual signal transduction but also, through a delayed feedback loop, deactivates itself [3].

In each of these examples, sensing of a signal is regulated by a control system that maintains an internal variable at a setpoint. In the case of the Hog pathway, this homeostasis is essential for survival. In its absence, a cell would be unable to maintain shape and necessary ion concentration after changes in osmolytes in the environment. In the case of *E. coli* chemotaxis and mammalian neurons, this mechanism ensures that the cell can continue to process new information.

The focus of this paper is on biological systems that *adapt*, namely they respond to an environmental step stimulus by initiating a response and then return to approximately their pre-stimulus level. There are two broad classes of architectures that achieve adaptation, feedforward and feedback structures [4]. Here, we study simplified representatives of the feedforward class using circuits consisting of three molecular nodes that are modeled using plausible molecular interactions. We investigate the tradeoffs inherent in different molecular implementations of the interactions among the different molecules, focusing on the effects of adding an explicit feedback loop to the feedforward architecture.

The rest of this paper is organized as follows. Section 2.1 introduces the dynamical systems under study and defines the two key properties of systems that adapt, their