Computation in Transcriptional Regulatory Networks

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***Short Abstract** –* **The transcriptional regulatory machinery of a gene can be viewed as a computational device, with transcription factor concentrations as inputs and expression level as the output. This view begs the question: What kinds of computations are possible? We show that different parameterizations of simple chemical kinetic models of transcriptional regulation are able to approximate all four standard arithmetic operations (addition, subtraction, multiplication and division), various equality and inequality operations, as well as more exotic functions such as the square root, other fractional powers, and even the posterior probability distribution for two-class Bayesian discrimination problems. We also demonstrate the such genes can be combined into networks to perform yet more sophisticated operations.**

Keywords – **transcriptional regulation, chemical kinetics, computation, Bayesian discrimination**

I. Background

Experimental characterization of transcriptional regulatory networks is providing us with an ever-more-detailed picture of how gene expression is regulated [10,13,14]. In face of the growing complexity of this knowledge, many researchers have turned to computational metaphors for summarizing gene function [7,11]. Taking seriously the view of genes as computational devices raises the question of what kinds of computations are possible? Logical descriptions of gene function are common in biology textbooks [2] and in mathematical-biological analyses of gene networks (e.g., [1,12]). Theoretical models of gene regulation are capable of implementing arbitrary logical rules [3,5,6,9]. However, the detailed experimental studies of transcriptional regulatory networks cited above reveal a behavior far richer than simple logical responses.

II. Results

We have analyzed the computational capabilities of simple chemical-kinetic models of transcription regulation [4]. We find that by appropriately setting the parameters of the model, genes can be designed that approximate various arithmetic functions: addition, subtraction, multiplication, division, fractional powers, and testing for various equalities and inequalities. Such genes can also be combined into networks to perform more sophisticated functions. In particular, we describe a network capable of tracking the mean and standard deviation of a time-varying signal and flagging statistically significant deviations. In related work, we show that even a single gene is capable of approximating the posterior probability function in a two-class Bayesian discrimination problem [8]. These results highlight the possibility of sophisticated and/or probabilistic computations embedded in genetic networks—a possibility not implausible given that single cells are constantly bombarded by stochastic signals which they must interpret and to which they must respond. Finally we consider the inverse two-class discrimination problem—the problem of determining what probabilistic discrimination problem a gene is solving, if any, based on its response surface. We use this approach to construct plausible interpretations of the complex response surface of the lac operon. Our observations are important for the interpretation of naturally occurring networks and imply new possibilities for the design of synthetic networks.

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*Joint work with Peter Swain, Eric Libby and Sean Cory