Information capacity in promoter models with multiple states

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Short Abstract — **To study how noise limits the reliability in cellular responses, we calculate the information capacity of a genetic element. So far most models have been limited to promoters with two internal states. We analyze how noise derived from a multi-state promoter model influences information transmission. We find that more states generally do not increase the capacity. However, specific architectures that can be linked to cooperative binding and promoter cycling do yield more information.**

I. Introduction

ADAPTAION to the current conditions and the proper development of an organism require cells to respond to external and internal signals. The precision with which this can be done is limited by the inherent noise of molecular processes. Information theory provides tools to quantitatively analyze the impact of noise on the reliability of signaling.

Apart from its well-established applications in neuroscience, information theory has also been used to describe certain aspects of cellular signaling [1-4]. On the one hand, it has been shown that the principle of optimizing positional information is relevant for development [5]. Another application is that it can be linked to fitness in changing environments. It is possible to compute a minimum of information about the current environment that an organism needs to posses to achieve a certain fitness [6].

Most models of stochastic gene expression work with only two promoter states. Some extensions to this model have been proposed but it remains unclear how the presence of further states influences information capacity. Here, we study the information capacity of more general models of gene expression. The central question is if and how more states can lead to an increased information capacity.

II. Methods

A. Promoter model

To calculate the information capacity of a genetic element, one needs its mean-noise relationship, or noise characteristic. We use a generalization of the thermodynamic model of gene regulation [7] to include general states (not necessarily with mechanistic interpretations). We model the promoter as a state transition diagram with multiple states. In a mechanistic interpretation, the states are certain molecular arrangements of the promoter (transcription factors, RNA polymerase, DNA) and the transition rates depend on the concentration of transcription factors and their binding and interaction energies. Assuming steady state and using the Langevin formalism, we get two additive noise sources: a switching term from the bursting behavior of the promoter and output noise from the birth-death process of mRNA production.

B. Input noise

In addition to the two sources of noise that directly follow from the promoter model, we also consider propagation of up-stream noise. One important interpretation of this noise term is the locally changing concentration of transcription factors caused by their diffusion [8].

C. Small noise approximation

To calculate the information capacity of the promoter, we use the small noise approximation. This means that for a fixed input, we assume the distribution of outputs to be Gaussian. An expression for the maximal mutual information can then be obtained analytically.

III. Results

We find that more internal states of the promoter generally do not improve the capacity of a genetic element to transmit information. However, for some cases where the input regulates more than one transition or we have more than one expressing state, the capacity can be enhanced. These models can be linked to promoters that allow for cooperative binding of transcription factors and promoters with cyclic behavior.

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