Abduction and asylum in the lives of transcription factors.

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Short Abstract — **Genomic studies verify that there are many nonfunctional transcription factor binding sites along a genome. Although these "decoy" sites compete with the promoter region for binding of transcription factors, they may also protect these proteins from degradation. We show that in the limit of perfect protection, where bound transcription factors are never degraded, the competitive effect of nonfunctional binding sites is completely canceled out by the stability gained from reduced degradation. We explore the cases of homogenous and heterogeneous binding affinity and show the effects that decoy binding sites have on reducing noise in steady state and increasing relaxation time to reach steady state.**

***Keywords*— auto-regulation, noise, stochastic gene expression, non-functional binding site.**

I. Introduction

When modeling gene networks, attempting to account for the entire cellular environment—composed of, among other things, DNA and regulatory proteins—is a practically impossible task. One complication is the fact that transcription factor binding affinity is not exclusive to promoter regulatory regions. It has been shown that in *E. coli*, nonspecific transcription factor/DNA binding plays a significant role in gene regulation [1]. In eukaryotes, short transcription factor binding motifs and long genomes ensure that there can be staggering numbers of decoy sites [2]. This so called non-functional binding has obvious kinetic implications for the identification of the target site [3], and slightly less obvious consequences for regulatory process of protein degradation.

Proteolysis is an important component of cellular regulation in eukaryotes and eubacteria. Recent studies exploring the question of whether active degradation can occur when a transcription factor is bound to DNA suggest the answer is context dependent. "Kamikaze activators" such as VP16 in *S. cerevisiae* are degraded during transcription initiation [5]. On the other hand, transcription factors such as p53 [6] and MyoD [7] have been shown to be immune to degradtion when bound to DNA. Because situations exhibiting both binding vulnerability and binding protection exist, we investigate both scenarios in the context of an auto-regulated gene surrounded by a variable number of nonfunctional transcription factor binding sites.

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II. Results

We use mass action equations for deterministic results and numerically solve the master equation for stochastic and out of equilibrium results.

A. Binding stability cancels out binding competition

If bound degradation is allowed, decoy binding sites impose a load on gene regulation because they sequester transcription factors. If bound degradation is forbidden, the addition of decoy binding sites has no *net* effect on the regulation of a gene in steady state.

B. Noise reduction

The addition of protective decoy sites allows the steady state occupancy of the promoter to approach the level that would be predicted by deterministic modeling and the noise in the distribution of transcription factor copy numbers to approach Poisson noise.

C. Relaxation to equilibrium

The addition of protective decoy sites increases the time that it takes for an auto-regulatory gene network to reach steady state. This effect is analyzed for sets of decoy sites with homogeneous and heterogeneous binding affinity.

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