

## MASTER'S THESIS

### Study of fluctuations in gene regulation circuits with memory

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*Date of Award:*  
2012

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**Study of Fluctuations  
in Gene Regulation Circuits  
with Memory**

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A thesis submitted in partial fulfillment of the requirements

for the degree of

Master of Philosophy

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Hong Kong Baptist University

January 2012

# Abstract

The small number and transient activity of molecules involved in gene expression can lead to significant fluctuations in intracellular mRNA and protein concentrations. There have been numerous recent studies devoted to the consequences of such noise in observed cell-to-cell phenotypic differences in an isogenic population. Previously, stochastic models are developed to explore the fluctuation behavior in the copy number of key proteins, as characterized by their probability distribution. Theoretical treatments usually start from the master equation that describes the time evolution of the distribution function. However, this approach encounters unavoidable difficulties in the more general case of non-Markovian processes, i.e., stochastic processes with memory. In this thesis, we study a protein synthesis process using a birth-and-death model that incorporates multiple transformation steps in a single reaction. The non-Markovian feature of the model has to do with a non-Poisson distribution of the lifetime of the molecule in this combined reaction step. A modified Gillespie algorithm is implemented to perform simulations of the non-Markovian process. We characterize the fluctuations of the protein copy number by the Fano factor and the autocorrelation function. The presence of a feedback loop in the model introduces oscillations in the autocorrelation function. We find that, as the number of steps within the birth process increases, the amplitude of the oscillation increases. The same is true when the number of reaction steps in death process. We study how the correlation time of the oscillation grows and give some explanations on the underlying mechanism. Our results contribute to a better understanding of the effect of multiple steps in gene expression circuits with autoregulation.

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