Finite State Projection Solutions to the CME Arising in Gene Regulatory Networks

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***Short Abstract* — Because rare but important regulatory molecules can cause a great amount of intrinsic noise within a cell, stochasticity is of crucial importance in the analysis of gene regulatory problems. Such systems are frequently modeled with jump Markov processes, whose probability distributions evolve according to the Chemical Master Equation (CME). In this poster we will present recent Finite State Projection (FSP) based approaches to solving the CME.**

***Keywords* — Chemical Master Equation, Stochastic Gene Regulatory Networks, Model Reduction, Markov Processes.**

I. Purpose

The cellular environment is abuzz with noise due to random events that govern the motion of cellular constituents. Intriguing examples of mechanisms that rely on noise include stochastic switches, coherence resonance in oscillators, and stochastic focusing for the amplification of signals [1]. Given the importance of noise induced stochastic fluctuations in the cell, quantitative modeling and analysis of these fluctuations is of paramount importance for the understanding and synthesis of biological networks.

The topic of this presentation is the mathematical modeling and analysis of discrete stochastic chemically reacting systems, with an eye on applications to gene regulatory networks. Essentially, for an N species chemical reaction, the infinite dimensional Chemical Master Equation (CME) [2] is the ordinary differential equation that describes the evolution of probability measure along an N-dimensional non-negative integer lattice.

Although we will review a few recent Kinetic Monte Carlo approaches to generate sample trajectories of the CME [3-5], this presentation will focus primarily on Finite State Projection (FSP) based approaches to solving the CME. We will give an intuitive understanding of our original FSP approach [6], and we will illustrate the power of the FSP approach to (1) provide approximations to the CME with strict accuracy guarantees; and (2) enable *exact* computations of certain important quantities such as switch rates.

We will intuitively describe four systems theory based modifications and enhancements that enable large reductions and increased efficiency of the FSP with little or no loss in accuracy. The first reduction separates the system into slow and fast partitions and then utilizes perturbation theory to average over fast dynamics and project the system to its slow manifold [7,8]. The second scheme utilizes the linearity and time invariance properties of the CME to solve the FSP problem with an equivalent sequence of smaller dimensional systems over short time intervals [9]. The third reduction scheme recognizes that one often does not require the full solution to the CME. Instead one may specify an output quantity (switch rate, population expectation, etc...) and obtain an equivalent minimal realization of the system [10]. The fourth reduction scheme for the FSP solves the CME not on its full integer lattice but on much coarser grid of interpolation points [11].

Each of these reduction schemes will be illustrated and compared on two biological examples. The first example is a stochastic model of Gardner's genetic toggle switch [12] and the second is a toy model of the heat shock mechanism in *E. coli.*

Acknowledgements: This material is based upon work supported by the National Science Foundation under Grant NSF-ITR CCF-0326576 and the Institute for Collaborative Biotechnologies through Grant DAAD19-03-D-0004 from the U.S. Army Research Office.

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