Control Seminar

Noise in Gene Regulatory Networks: Biological Role and Mathematical Analysis

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Abstract:

The cellular environment is abuzz with noise. Generated by random molecular events, cellular noise not only results in random fluctuations within individual cells but it is also a source of phenotypic variability among clonal cellular populations. In some instances fluctuations are suppressed downstream through an intricate dynamical network that acts to filter the noise. Yet in other instances, noise induced fluctuations are exploited to the cell's advantage. Intriguing mechanisms that rely on noise include stochastic switches, coherence resonance in oscillators, and stochastic focusing. While mathematical models of genetic networks often represents gene expression and regulation as deterministic processes with continuous variables, the stochastic nature of cellular noise necessitates an approach that models these variables as discrete and stochastic. In this framework, probability densities of the system states evolve according to a (usually infinite dimensional) Chemical Master Equation (CME). Until recently, sample trajectories have been computed almost exclusively with Kinetic Monte Carlo methods, such as Gillespie's Stochastic Simulation Algorithm. In this talk we present a new direct approach for computing the relevant statistics, which involves the projection of the solution of the CME onto finite subsets. We illustrate the algorithm underlying our Finite State Projection approach and introduce a variety of systems theory based modifications and enhancements that enable large reductions and increased efficiency with little to no loss in accuracy. Model reduction techniques based on linear perturbation theory allow for the systematic projection of multiple time scale dynamics onto a slowly varying manifold of much smaller dimension. The proposed projection approach is illustrated on few important models of genetic regulatory networks.