

Modeling and Analysis of Asynchronous Boolean Networks

Abstract of Thesis

During the past few years, there are significant progress in the area of systems biology for modeling genetic regulatory networks. Gene regulatory network (GRN) is a biochemically dynamical system for complex molecular interactions among genes, proteins, and small molecules, etc. that control various cellular functions and processes in a biological system. Mathematical and computational modeling of GRNs help to unambiguously describe the network structure and to infer predictions of the dynamical behavior of the cellular system in response to different perturbations or stimuli. In the past, different kinds of computational and mathematical models have been developed to investigate the behaviors of GRNs such as ordinary differential equation, Boolean network, probabilistic Boolean network, asynchronous Boolean network, etc. The differential equation model gives detailed quantitative description of the dynamics at the cost of computational complexity. Although the Boolean network is the simplest approach, it is not an appropriate model for real biological systems, because it assumes that all the genes/proteins in the GRN change their states synchronously. In asynchronous Boolean network (ABN), different nodes (genes) in the network update their state (expression level) at different time instances. However, the existing ABN models do not consider the actual delays among nodes and update the nodes without any biological validation. In real biological networks, time delay phenomena have significant impact on the dynamics of GRNs as different kinds of molecular interactions happen at different time scales, ranging from fractions of a second to multiple hours. Hence, it is essential to include different time delays corresponding to different regulatory interactions in modeling of genetic networks.

Considering the fact that true biological networks are time-continuous and follow asynchronous transitions between states, this dissertation introduces a continuous-time discrete-state ABN model considering the quantitative delays for transcription regulations in the genetic network. The proposed model is as simple as the Boolean network and provides the detailed temporal dynamics of gene networks as accurate as an ODE model. The research work focuses on the modeling of an ABN from biological pathways and transcriptional parameters, and the linear representation of the model using semi-tensor product of matrices approach.

Keywords: Gene regulatory network; asynchronous Boolean network; delays; network motifs; p53-signaling pathway; attractor; activation and inhibition; semi-tensor product; structure matrix.