Cell-Cycle Process and Regulatory Power of Canalizing Genes Modeled by Context-Sensitive Probabilistic Boolean Networks

Ronaldo Fumio Hashimoto[1]

[1] Instituto de Matemática e Estatística da Universidade de São Paulo (IME-USP)

Abstract

A context-sensitive probabilistic Boolean network (cPBN) has been introduced in order to model biological systems. Essentially, a cPBN is a finite collection of Boolean Networks (BNs) with perturbation (each gene is allowed to randomly change its value at each instant time with a small perturbation probability). This modeling makes the resulting system behave as an ergodic Markov chain possessing a steady-state probability distribution. Switching a BN to another one corresponds to switching the wiring diagram of the network. In this way, taking the perspective that this switch corresponds to a change in context for the cell, this PBN model is called context-sensitive PBN. Under this model, we can investigate the cell-cycle process and the regulatory power of canalizing genes.

A complex molecular network is responsible for the cell-cycle process by which a cell grows and divides into two daughter cells. In order to model and understand the cell-cycle process, a considerable amount of attention has been paid to the budding yeast cell cycle regulation [1,2,3]. In particular, after an exhaustive literature investigation, Li et al. [1] modeled the yeast cell-cycle system under the Boolean network (BN) model and studied its dynamics and structural properties. Zhang et al. [2] extended Li's model including in it effects of stochasticity and noise. Trepode et al. [3] introduced a more sophisticated model called probabilistic genetic network (PGN) which uses negative feedbacks and genes interactions representations as stochastic processes in order to obtain a strong robustness in the presence of moderate noise and parameters fluctuations. In this talk, we will present some directions to model the cell cycle of the budding yeast using cPBNs.

A canalizing gene possesses a broad regulatory power, and its action sweeps across a such a wide swath of processes, that the full set of affected genes is not highly correlated under normal conditions. A set of predictor genes is said to be intrinsically multivariate predictive (IMP) for a target gene if all properly contained subsets of the predictor set are bad predictors of the target but the full predictor set predicts the target with great accuracy. The IMP concept can be applied to characterize the behavior of the gene DUSP1, which exhibits control over a central, process-integrating signaling pathway, thereby providing preliminary evidence that IMP can be used as a criterion for discovery of canalizing genes [4]. In this talk, we will indicate some directions to model IMP genes using cPBNs.

References

[1] F. Li, T. Long, Y. Lu, Q. Ouyang and C. Tang; The Yeast Cell-Cycle Network is Robustly Designed, Proceedings of the National Academy of Sciences Vol. 101, N. 14, 4781-4786, 2004.
[2] Y. Zhang, M. Quian, Q. Ouyang, M. Deng, F. Li and C. Tang; Stochastic Model of Yeast Cell-Cycle Network, Physica D 209, 35-39, 2006.
[3] N.W. Trepode, H.A. Armelin, M. Bittner, J. Barrera, M.D. Gubitoso and R.F. Hashimoto; A Robust Structural Model for Control of Cell-Cycle Progression Stabilized by Negative Feedbacks, EURASIP Journal on Bioinformatics and Systems Biology, Vol. 2007, Article ID 73109, 11 pages, 2007.
[4] D. Martins, U. Braga-Neto, R. F. Hashimoto, M. L. Bittner, E. R. Dougherty, Intrinsically Multivariate Predictive Genes, IEEE Journal of Selected Topics in Signal Processing, Vol. 2, No. 3, 424-439, June, 2008.