

Using Boolean Networks to Model Post-transcriptional Regulation in Gene Regulatory Networks

A. Benso, S. Di Carlo, G. Politano, A. Savino, H. ur Rehman

In Gene Regulatory Networks research there is a considerable lack of techniques and tools to understand these networks from a System Biology point of view. The typical biological approach is to reconstruct a particular network from expression patterns, then try to validate its dynamics by simulation, use simulation to analyze its reactions to some perturbations, and finally go back “in vitro” to validate the simulation results. Nevertheless, when the goal is to understand the high-level, general mechanisms that allow these networks to work or to be stable under mild perturbations, this type of approach has shown very strong limitations. In this work we want to better understand the role of miRNA as a stabilizing mechanism in gene regulatory networks.

Boolean networks have been recently used to better understand the structural and dynamical properties of regulatory networks. Attractors and ergodic sets have been easily correlated with many of the typical biological cell behaviors (cancer, differentiation, pluripotential, ...). The most widely used model are nevertheless very simple, and work under too strict constraints.

We are defining an enhanced model based on Boolean Networks but also able to take into account post-transcriptional regulation and possibly be extended to other regulatory mechanisms (e.g. ceRNA) that have been already proven crucial in vivo.

The final goal is to try to understand if the wide number of miRNA targets constitutes a structural network-stability mechanism used to make the network immune to „regulatory“ noise. To achieve this result we evolve the modified Boolean networks for high or low sensitivity to perturbations, and then analyze the resulting networks to understand if specific structural patterns containing miRNA-like post-transcriptional regulatory elements can be correlated with the network stability.