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Boolean modeling of cellular regulatory networks[1]

REKA ALBERT, Pennsylvania State University

Interaction between gene products forms the basis of essential processes like signal transduction, cell metabolism or embryonic development. Recent experimental advances helped uncover the structure of many cellular networks, creating a surge of interest in the dynamical description of gene regulation. Traditionally genetic and protein interactions are modeled by differential equations based on reaction kinetics, but these studies are greatly hampered by the sparsity of known kinetic detail. As an alternative, qualitative models assuming a small set of discrete states for gene products, or combinations of discrete and continuous dynamics, are gaining acceptance. Many results also suggest that the interaction topology plays a determining role in the dynamics of regulatory networks and there is significant robustness to changes in kinetic parameters. This presentation will focus on a Boolean model of the signal transduction network regulating drought response in plants. We integrate qualitative and indirect relationships into the simplest network consistent with all experimental observations, and express the regulation of network nodes as logical functions. Our model captures the regulation of more than forty identified network components, and accords well with previous experimental results at both the pathway and whole cell physiological level. We identify the dynamical repertoire of the network by varying process durations and initial conditions and by simulating gene disruptions, and find a remarkable robustness against a significant fraction of possible perturbations. Although qualitative, the model provides a ranking of disruptions and perturbations in the order of their severity. We experimentally test, and validate, the most surprising prediction. The success of this model illuminates the emergent (network-level) functional robustness of cellular regulatory networks.

[1]S. Li, S. M. Assmann, R. Albert, Predicting essential components of signal transduction networks: A dynamic model of guard cell abscisic acid signaling, PLoS Biology 4: e312 (2006).