Modeling Yeast Cell Cycle Regulation

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The cell cycle regulation in the budding yeast Saccharomyces cerevisiae is one of the best studied biological systems. Many major players and their interactions have been identified by decades of work in genetics and biochemistry as well as by the more recent effort in high throughput genomics and proteomics. On the other hand, current information about the network is mostly qualitative-while there is a circuit diagram (although it may not be complete) of who regulates whom, there is little quantitative information (e.g. the kinetic constants) about the regulation. Here we construct a model of yeast cell-cycle regulation from the known circuit diagram using ordinary differential equations and focus our attention on the global dynamic property and structural stability of the system. We found that certain qualitative conclusions about the system's behavior are very robust to parameter choices. In particular, each checkpoint can be a global attractor-when a checkpoint is on all cell states evolve to the stationary state corresponding to the checkpoint arrest. Furthermore, there is a unique globally attracting trajectory for this dynamic system, which corresponds to the biological pathway of the cell cycle regulation. Substantial changes of certain parameters, especially when several parameters are changed simultaneously, can result in qualitative changes in the system's behavior. Typically, these not-so-robust parameters are associated with transitions between different cell-cycle phases and the corresponding abnormal behavior is often related to the arrest or bypass of a checkpoint. Our results reveal a robust picture of the yeast cell cycle regulation and the mechanisms under which the robustness can be compromised.