Generalized Logical Network Model of Cell Cycle with Mitosis and Exit Control

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***Short Abstract* — The complexity of the genetic interactions underlying the mitotic cell cycle requires sophistication of representation beyond human intuition. Various mathematical models for cell cycling have been developed [3]. An example is the generic cell cycle model [2] which includes thirteen differential equations: six for the Cdk/cyclin complexes and seven for other regulators (Cdh1, CK1, TriB, preMPF, APCP, Cdc20A, Cdc20T). These models have reflected the most important biological phenomena that occur in the cell cycle,. however no existing mathematical models include both mitosis and cell cycle exit control, though the genes responsible for promoting cell cycle exit have been under heavy investigation [1].**

***Keywords* — Generalized Logical Network, Cell Cycle.**

During normal development, many cells will exit the cell cycle to become quiescent at the appropriate place and time. A failure to properly exit the cell cycle exit is believed to be a key molecular mechanism behind cancer. However, a complete and accurate mathematical model for cell cycle control incorporating the process of cell cycle exit is unavailable. Here we describe the construction of a generalized logical network to represent the qualitative behaviors in gene regulation of a complete cell cycle incorporating DNA Synthesis, Mitosis and the process of cell cycle exit. This is achieved by creating a GLN model and then developing algorithms to optimize the GLN model so that its dynamics are consistent with biological knowledge of cell cycle behaviors. This includes the triggering of cycle exit when certain exit signals are received at a given time point. Generalized logical networks [4], first studied in [5], is a family of dynamic models for representing biological systems. As a discrete-time and discrete-value dynamic system model, a GLN is represented by a directed graph with a generalized truth-table (gtt) attached to each node. Each abstract node represents information about a molecule, a cell, or a species. The gtt, generalizing the Boolean logic, allows a discrete variable to take more than two possible values and to reflect subtle but crucial changes, and encodes precisely the biological mechanisms that the nodes use to interact with each other.

Acknowledgements: This project is supported by an NIH U54 grant and an NSF CREST grant.

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The gtt H for a node X maps all possible combinations of values of parent nodes to values of X. A GLN is Kth-order if the value of any node involves parent values at most K time points back into history. The discrete nature of a GLN enables a unique modeling framework that provides a global view of dynamic system behaviors through state transitions, difficult within a continuous-value modeling framework such as ODE (Ordinary Differential Equations), and at the same time still captures complex nonlinear interaction patterns among nodes.

We have built an initial GLN model that incorporates additional cell cycle behaviors beyond those in current models such as the process of cell cycle exit.

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