From START to FINISH: Computational Analysis of Cell Cycle Control in Budding Yeast

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***Short Abstract* — In the cell division cycle of budding yeast, START refers to a set of tightly linked events that prepare a cell for budding and DNA replication, and FINISH denotes the interrelated events by which the cell exits from mitosis and divides into mother and daughter cells. Based on recent progress made by molecular biologists in characterizing the genes and proteins that control START and FINISH, we crafted a new mathematical model of cell cycle progression in yeast.**

***Keywords* — Cell Cycle, Budding Yeast.**

The cell division cycle is the ordered sequence of events by which a cell replicates its genome and segregates the replicated chromosomes to two daughter cells during mitosis. In budding yeast, *Saccharomyces cerevisiae*, START refers to a set of tightly linked events that prepare the cell for budding and a new round of DNA replication and FINISH denotes the interrelated events by which the cell exits from mitosis and divides into mother and daughter cells. Based on the noteworthy progress made by molecular cell biologists in characterizing the genes and proteins that control cell cycle progression in budding yeast, we have built a comprehensive mathematical model of the molecular mechanisms underlying START and FINISH. For this mathematical model, we use a new modeling framework in which all reactions are classified into three basic types: protein synthesis and degradation ($\rightarrow C \rightarrow$), phosphorylation and de-phosphorylation ($C \leftrightarrow CP$), and binding to activator or inhibitor partners ($C+A \leftrightarrow C{:}A$).

Results: The model successfully explains the observed phenotypes of 263 mutant yeast strains and can be used to predict the phenotypes of novel combinations of mutant alleles. The credibility of these predictions has been assessed by distinguishing between fragile predictions (which are sensitive to values of adjustable parameters) and robust predictions (which depend on the regulatory network itself rather than specific parameter values).

Conclusions: Our comprehensive model of the molecular events controlling cell cycle progression in budding yeast has both explanatory and predictive power. Future experimental tests of fragile predictions will be useful to constrain adjustable parameters of the model, and future tests of robust predictions will either confirm the underlying molecular mechanism or provide new insights into how the cell division cycle is regulated.

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