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Mathematical Modeling of Nutrient Signaling and Growth in Saccharomyces cerevisiae

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Mathematical Modeling of Nutrient Signaling and Growth in Saccharomyces cerevisiae

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The regulation of cell growth and division has long been considered a central problem in cell biology, and much work has been done, both theoretically and experimentally, towards expanding our understanding of the processes of cell division and cell size sensing [1]. However, there has been almost no systematic investigation of the molecular mechanisms that regulate cell growth pathways in response to fluctuating nutrient environments [2]. Due to the complex nature of the regulatory networks governing cell growth, mathematical modeling is an appropriate tool to investigate the dynamic responses of these pathways to various perturbations.

Here, we propose an ODE-based dynamical model of the regulatory mechanism governing growth in the budding yeast *S. cerevisiae*. The model is composed of key molecular regulators from the nutrient sensing and signaling pathways in yeast that ultimately modulate overall protein synthesis in the cell, in turn affecting cellular growth rate. By incorporating into this model the diverse nutritional contexts in which experiments are carried out, we aim to systematically explore the space of nutrient-sensitive phenotypes in the budding yeast. To this end, we demonstrate that our model correctly predicts the nutrient-dependent phenotypes of a number of genetic and chemical perturbations studied in the literature. In the future, we plan on integrating this model of nutrient signaling with the comprehensive model of the yeast cell cycle [3], with the goal of refining the phenotypic predictions made by the cell cycle model.

References

- [1] Jennifer C Ewald. How yeast coordinates metabolism, growth and division. Current Opinion in Microbiology, 45(nil):1–7, 2018.
- [2] Michaela Conrad, Joep Schothorst, Harish Nag Kankipati, Griet Van Zeebroeck, Marta Rubio-Texeira, and Johan M Thevelein. Nutrient sensing and signaling in the yeast *Saccharomyces cerevisiae*. *FEMS microbiology reviews*, 38(2):254–299, 2014.
- [3] Pavel Kraikivski, Katherine C Chen, Teeraphan Laomettachit, TM Murali, and John J Tyson. From start to finish: computational analysis of cell cycle control in budding yeast. *npj Systems Biology and Applications*, 1:15016, 2015.