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Emergence of Orchestrated and Dynamic Metabolism of Saccharomyces cerevisiae

Background/Objective

Microbial metabolism is a fundamental cellular process that involves many biochemical events and is distinguished by its emergent properties. While the molecular details of individual reactions have been increasingly elucidated, it is not well understood how these reactions are quantitatively orchestrated to produce collective cellular behaviors. Here we developed a coarse-grained, systems, and dynamic mathematical framework, which integrates metabolic reactions with signal transduction and gene regulation to dissect the emergent metabolic traits of *Saccharomyces cerevisiae*.

Approach

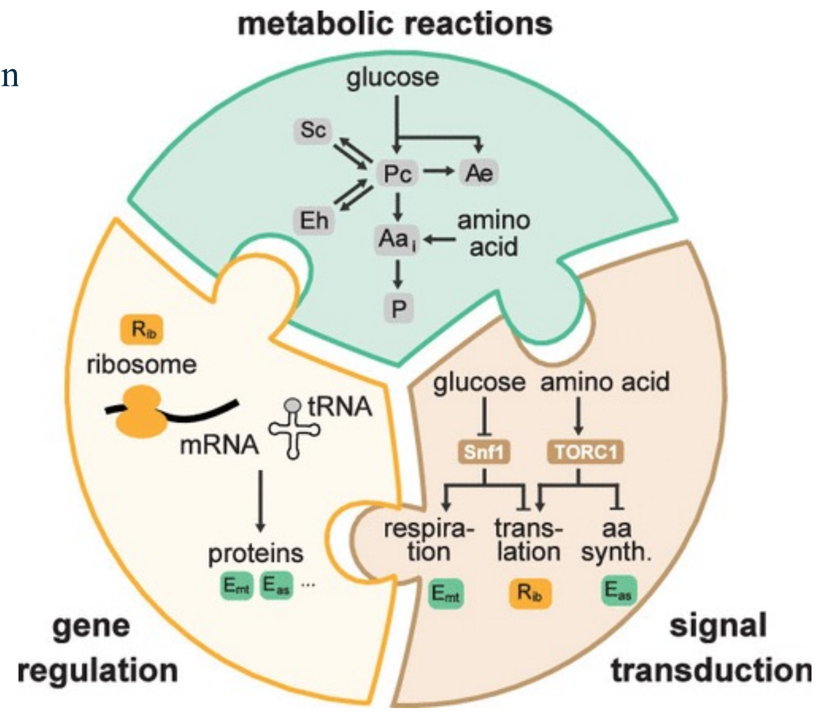
To manage the complexity of *S. cerevisiae* metabolism, we used a modular model design that decomposed the system into three parts: metabolic reactions, signaling, and gene regulation. Each module was coarse-grained and characterized individually before assembly into one integrated framework by connecting their inputs and outputs. We used it to examine the molecular-level coordination of carbon metabolism and the resultant collective cellular behaviors.

Results

The model mechanistically captures a set of characteristic cellular behaviors, including the Crabtree effect, diauxic shift, diauxic lag time, and differential growth under nutrient-altered environments. It also allows zooming in on specific pathways of interest for detailed metabolic profiles. It's course-grained scheme also makes it more adaptable to model other organisms, such as *Rhodotorula toruloides*, thereby reducing the efforts needed to gain insights.

Significance/Impacts

This study provides a systems-level mathematical framework for yeast metabolic behaviors, providing insights into yeast physiology and metabolic engineering.



Schematic illustration of *S. cerevisiae* metabolism, which involves the orchestration of metabolic, signaling, and gene regulation networks.

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