ABSTRACT

Title: FROM THE GENOME SEQUENCE TO MODELING OF BIOLOGICAL FUNCTIONS: METABOLISM, GROWTH AND CELL CYCLE

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Abstract content:
As the first sequenced eukaryote (1996), *Saccharomyces cerevisiae* is a vital model for understanding conserved cellular mechanisms in higher organisms [1] because fundamental processes—such as metabolism, cell growth, and the cell cycle—are highly conserved between budding yeast and higher eukaryotes. The *S. cerevisiae* genome sequence catalyzed the shift from classical single-gene genetics to modern functional genomics and systems biology.
Whole-cell modeling is an advanced computational systems biology approach that aims to simulate the comprehensive physiological, biochemical, and biophysical processes of an entire living cell within a single unified mathematical framework. By integrating diverse, heterogeneous datasets across multiple networks, these multiscale models transition biology from a descriptive science to a highly quantitative discipline [2].
While traditional whole-cell computational modeling relies on bottom-up aggregation of individual gene products, we developed a low-resolution, top-down multiscale approach.
This low-granularity framework integrates metabolism, cell mass growth, and cell cycle progression to efficiently simulate yeast populations and provide a scaffold for molecularly detailed models [3].
Our model predicts that cells with constitutive respiration fail to modulate size in response to growth conditions—a finding we experimentally validated using glycolysis and glucose-transport mutants. The model can be used as a scaffold for plugging-in models of increasing granularity, potentially allowing for a molecular description of one or more biological functions, improving the predictions from the cellular to the molecular level. We will exemplify this concept by showing data regarding the G1/S transition [3] and the ribosome assembly pathway [4]. Finally, we are extending the model to transient conditions, such as an ethanol-to-glucose shift-up. Incorporating In summary, this hybrid multiscale approach provides a robust framework for predicting cell phenotypes under diverse genetic and environmental conditions.
[1] Goffeau A, Barrell BG, Bussey H, et al. Life with 6000 genes. Science. 1996;274(5287):546-567.

[2] Carrera J, Covert MW. Why Build Whole-Cell Models?. Trends Cell Biol. 2015;25(12):719-722.
[3] Vanoni M, Palumbo P, Papa F, et al. A modular model integrating metabolism, growth, and cell cycle predicts that fermentation is required to modulate cell size in yeast populations. PLoS Comput Biol. 2025;21(7):e1013296.
[4] Conditions for exponential growth in a ribosome biosynthesis model across multiple scales, Federico Papa, Arianna Di Bernardo, Stefano Busti, Marco Vanoni, Pasquale Palumbo, IEEE Control Systems Letters (L-CSS)