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Comparative Study of Two Saccharomyces cerevisiae Strains with Kinetic Models at Genome-Scale

Background/Objective

To build kinetic models of yeasts, we measure flux rates of a reference strain and select genetically perturbed variations. Unlike stoichiometric models that are mostly invariant to the specific strain, it is unclear if kinetic models for different strains of the same species have similar or significantly different parameters. This affects their applicability and prediction limits. We built and examined two large-scale kinetic models for two strains of *Saccharomyces cerevisiae,* CEN.PK 113-7D and growth-deficient BY474, to determine these effects.

Approach

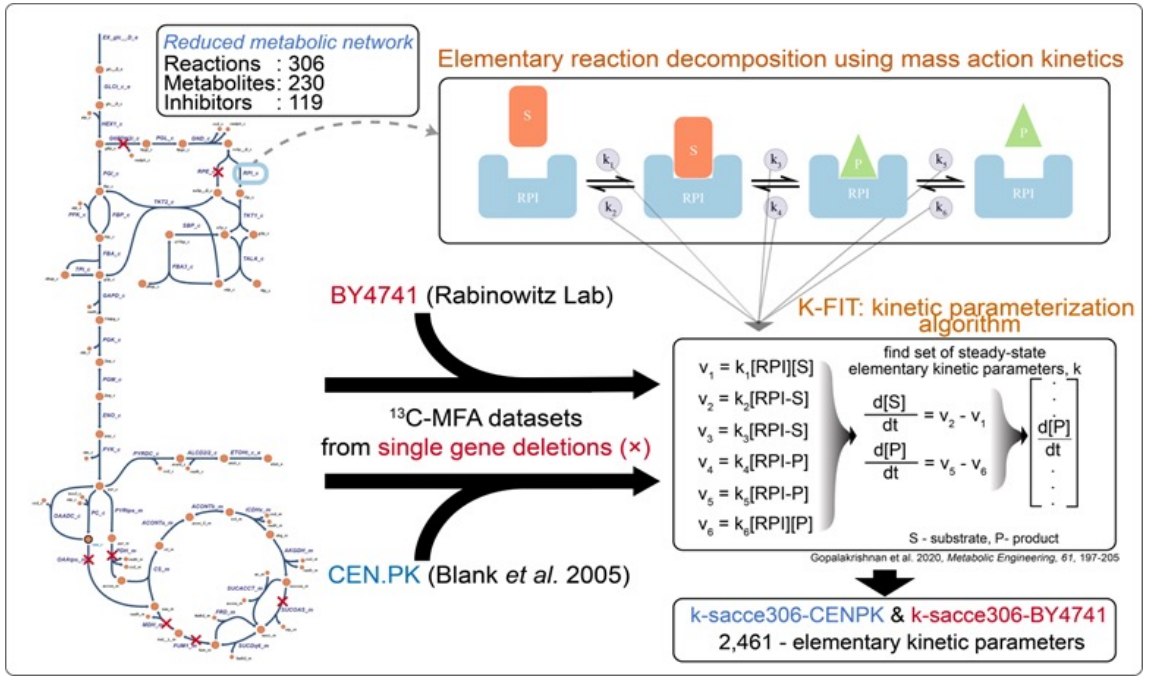
Measured flux rates of a reference strain along with select genetically perturbed variations and performed ^{13}C-multi-flux analysis (MFA) on *S. cerevisiae* BY4741 plus eight single-gene deletion mutants.

Results

- ^{13}C-MFA data revealed adaptation through localized responses in the BY4741 single-gene deletion variants.
- Lumping specific reactions reduced parameterization time.
- Although kinetic models cannot be readily used across strains as stoichiometric models, they can capture species-specific information through the kinetic parameterization process.

Significance/Impacts

Parameterized kinetic models can help determine targets for enzyme perturbation (i.e., knockouts or over/under-expression) to maximize a production target and inform process design.



Kinetic parameterization workflow for *S. cerevisiae*.

Hu, M., Dinh, H.V., Shen, Y., Suthers, P.F., Foster, C., Call, C., Ye, X., Fatma, Z., Zhao, H., Rabinowitz, J.D., Maranas, C.D. 2023. "Comparative Study of Two *Saccharomyces cerevisiae* Strains with Kinetic Models at Genome-Scale." *Metabolic Engineering* 76: 1-17. DOI: 10.1016/j.ymben.2023.01.001.