

Construction of a Kinetic Model for Yeast Lipid Metabolism

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Project Goals:

To construct a kinetic model to elucidate the metabolic and regulatory influences of sphingolipid metabolism in *Saccharomyces cerevisiae* on fatty acid pathways.

Abstract:

Kinetic models consisting of ordinary differential equations offer a comprehensive method to analyze and predict the dynamics of cellular metabolism. However, their use often poses a challenge due to uncertainties in parameter estimates and incomplete information on gene regulation processes. Here we develop a kinetic model of yeast lipid metabolism, specifically consisting of the pathways involved in sphingolipid metabolism and fatty acid synthesis and degradation. The model has been adapted from a previously published kinetic model (Savoglidis et al., 2016), and includes new pathways on fatty acid synthesis, as well as gene regulatory information wherever possible. A preliminary analysis of the parameter estimation process was used to highlight parameters with high uncertainty in estimated values. This can be used to aid in the design of perturbation experiments for further reducing the uncertainty in the model. Metabolic Control Analysis (MCA) was performed on the kinetic model to yield the pathway enzymes that exert strong influence on reaction fluxes and metabolite concentrations. Analysis of metabolic control can inform useful targets for metabolic engineering of target lipid overproduction.

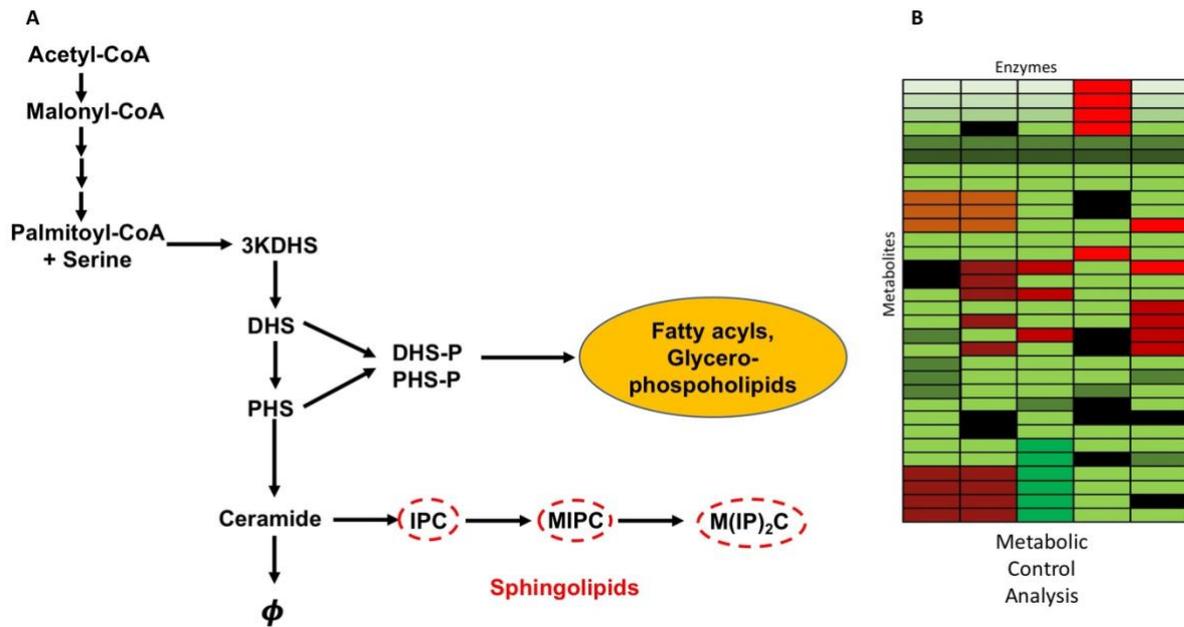


Figure 1. (A) Reaction map of sphingolipid metabolism depicting important compounds as well as pathways connecting sphingolipid intermediates to fatty acid and glycerophospholipid pathways. (B) Diagram illustrating the results of metabolic control analysis (MCA) as a heat map highlighting the enzymes that exert significant control over metabolites.

References:

Savoglidis, G., da Silveira Dos Santos, A. X., Riezman, I., Angelino, P., Riezman, H., Hatzimanikatis, V., 2016. A method for analysis and design of metabolism using metabolomics data and kinetic models: Application on lipidomics using a novel kinetic model of sphingolipid metabolism. *Metab Eng.* 37, 46-62.

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