

157. Ensemble modeling for increasing lipid production in *Yarrowia lipolytica*

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Project Goals: Use novel simulation methods not requiring a priori knowledge of enzyme parameters to identify possible in vivo genetic manipulations that will increase lipid production.

In metabolic engineering, the number of possible targets for genetic manipulation is prohibitively high for unguided experimental efforts. Thus, metabolic modeling is an important tool for the identification of the most promising targets for enzyme manipulation. Typical kinetic modeling is often an involved process requiring empirical determination of kinetic parameters. Ensemble modeling (EM) exploits network information, like network stoichiometry and reference steady state, to eliminate the need for determining kinetic parameters. Using a Monte Carlo approach, sufficient numbers of random parameter sets are chosen which satisfy these requirements. In EM, parameter sets aren't empirically determined. However, the network information constrains the parameter space to realistic behavior. Additionally, other data such as metabolomics or production yields can be used to further refine ensembles. Model construction for a large-scale model using EM is demonstrated here in *Yarrowia lipolytica*. Following model construction, identification of potential targets to increase fatty acid production is a straight-forward automated process. The methods demonstrated here are readily generalizable to other organisms with minimal information required.

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