

# Optimization of metabolic networks in biotechnology applications

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## Overview

Optimization methods play a central role in systems biology studies as they can help in identifying key processes that can be experimentally changed so that specific biological goals can be attained. Given a metabolic network described by a general mass action (GMA) model, the goal of the optimization model presented here is to determine the appropriate changes in enzyme activities that maximize/minimize the synthesis rate of a metabolite of interest produced by the network assuming steady state conditions.

In particular, we present a model for the maximization of the ethanol production in the fermentation pathway of *Saccharomyces cerevisiae*. The input data for the problem includes: (1) the stoichiometry of the reactions involved in the production/consumption of each internal metabolite in the metabolic network; and (2) the value of the parameters of the power-law formalism representing the kinetics of each of these particular reactions at the basal state.

The problem is modeled as a mixed-integer nonlinear (MINLP) programming one. In this formulation, continuous variables are used to represent the concentrations of metabolites as well as the enzyme activities, whereas binary variables are employed to model whether a given enzyme is modified or not through genetic manipulation. The model has been implemented in GAMS and solved by the commercial packages DICOPT, SBB and Alpha-ECP.