379g Parameter Estimation in Yeast Fermentation

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Fermentation processes follow different metabolic pathways depending on the availability of nutrients in the media. Highly nutritive environments are characterized by a maximization of biomass production. On the other hand, lack of key nutrients in the environment leads to a significant reduction in the metabolic activity.

Flux balance analysis has shown to be a very effective tool to interpret and predict the metabolism of various microorganisms in continuous cultures when the set of available measurements is not sufficient to solve the fluxes within the cell. On the other hand, the different metabolic behaviors of batch cultures can be represented by an underdetermined stoichiometric model in which the different behaviors —and the rule for switching between them— are modeled as linear programs (LPs) embedded into a system of ordinary differential equations.

While the proposed representation has shown suitable for numerical simulation, the discontinuous nature of the model raises challenging issues for the optimization and parameter estimation of such models. Given the large-scale nature of the resulting model, mixed-integer nonlinear optimization is often not a plausible alternative. For this reason, we rely on recent advances in the formulation and solution of Mathematical Programs with Equilibrium Constraints (MPECs), which provide a sound framework in which the aforementioned challenges can be efficiently overcome.

The procedure is formulated as a NonLinear Program (NLP), where the LPs are transformed into a set of nonlinear constraints. However, some of these constraints violate standard regularity conditions, making the direct numerical solution very difficult. Hence, a barrier formulation is used to represent these constraints, and an iterative procedure is defined that allow solving the problem to the desired degree of convergence. Within the barrier approach, an exact penalty is used to enforce the complementarity constraints associated with the LPs. Modeling the complementarity conditions as an exact penalty, removes the degeneracy associated with the hard-constraint formulation.

After validating the model with experimental data, we consider the data reconciliation of rates obtained experimentally from the metabolism of *Saccharomyces cerevisiae*, using a metabolic model that consists of 37 reactions and 43 metabolites. With the methodology proposed, we are able to estimate efficiently the biomass composition of the system considered.