Modeling, Monitoring and Control of Bioprocesses

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The purpose of this research area is to develop novel model, monitoring and control strategies for bioprocess optimization. The models constructed are based on dynamical balances to the main state variables of the processes and parameter estimation has been performed using algorithms like Simulated Annealing and Evolutionary Algorithms.

Optimal experimental design strategies have also been applied for yield coefficients estimation in *E. coli* fed-batch fermentation models. The feeding profiles are designed by optimisation of a scalar function based on the Fischer Information Matrix. Those optimal conditions have been implemented experimentally and a closer approximation between simulated and experimental data has been obtained.

The constructed models have been applied both for designing optimal operation conditions and deriving advanced control strategies. Moreover, the deduction of software sensors has been performed, aiming at estimating non-measured state variables from the available on-line fermentation data. A software sensor for the estimation of biomass concentration in *E. coli* fed-batch fermentation was derived and implemented experimentally, allowing to estimate this state variable from exhaust gas measurements.

Besides the direct use of macroscopic dynamic models, the integration of genomic information for deducing control strategies is being pursued. The purpose is to derive advanced monitoring and control strategies from genome-scale metabolic and regulatory models for application in the fed-batch fermentation process of *E. coli*. For that aim, existing genome-scale stoichiometric models with inclusion of regulatory phenomena are being used and accurate model reduction and simplification performed using several approaches, like lumping of reactions from linear metabolic pathways, model-order reduction by using sensitivity analysis tools, and elimination of the dynamics of the some processes based on their time scales. Simultaneously, the metabolic behaviour of the organism is being studied *in silico* and monitoring strategies will be proposed that allow identifying different metabolic or physiological states for use in online process control.

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