Systems Biology for the development of microbial cell factories

Rocha, Isabel (1); Lourenço, Anália (1); Rocha, Miguel (2); Ferreira, Eugénio C. (1)

1: IBB - Institute for Biotechnology and Bioengineering, Centre of Biological Engineering, Universidade do Minho, Campus de Gualtar, 4710-057 Braga, Portugal;
2: Department of Informatics / CCTC, University of Minho, Campus de Gualtar, 4710-057 Braga, Portugal

E-mail: ecferreira@deb.uminho.pt

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Abstract

In recent years, with advances in Systems Biology, there has been an increasing trend towards using mathematical and computational tools for the in silico design of enhanced microbial strains, and it is expected that such strategies will become more efficient as more robust and reliable mathematical models describing the function of cell factories become available. The derivation of strategies for increasing the productivity of microbial cell factories by applying a Systems Biology perspective is being pursued at Bio-Process Systems Engineering group (BioPSEg).

The development of more reliable and standardized microbial models allows the improvement of model predictions and therefore makes possible the application of simulation and optimization algorithms for the design of rational metabolic engineering strategies. In that context, we have been focusing our research on generation of better mathematical models of microbial metabolism, applying Bioinformatics tools like Data Mining and Biological Text Mining.

Current projects include the reconstruction of the metabolic network of *Kluyveromyces lactis*, *Streptococcus pneumonia*, *Enterococcus* spp and improvement of existing models for *Escherichia coli* and *Helicobacter pylori*. For that aim, relevant data sources are identified and data integration strategies are defined for collecting and integrating available genomic and functional information for each organism. Model curation and validation are the subsequent steps in the iterative process of model building.

A new open-source, user-friendly, and modular tool, Optflux, is being introduced to support in silico metabolic engineering. It uses stoichiometric metabolic genome-scale models allowing the set of fluxes in the organism's metabolism to be determined, given a set of environmental constraints. The optimization tasks, i.e., the identification of metabolic engineering targets (the best set of gene modifications given an industrial goal), can be performed with Evolutionary Algorithms, Simulated Annealing and Local Search methods.