Quantitative prediction of *Basfia succiniciproducens* metabolic potential for succinic acid and 1,4-butanediol production with constraint-based models

Zsolt Bodor¹, Hunor Bartos², Katalin Bodor^{2,3}, Márta Both-Fodor²,
Csongor Orbán Kálmán¹, Szabolcs Lányi^{1,4}, Ildikó Miklóssy¹
¹Sapientia Hungarian University of Transylvania, Department of Bioengineering,
Miercurea Ciuc, Romania, bodorzsolt@uni.sapientia.ro
²University of Pécs, Fac. Science, Hungary; ³ Heineken Romania, Miercurea Ciuc, Romania
⁴Politehnica University of Bucharest, Fac. Applied Chemistry & Materials Science, Romania

Biology has become from a data-poor to a data-rich environment, since various "omics" datasets are available. The utilization of these data is a stringent need as long as the complex interactions taking place inside a cell cannot be analysed and understand by the reductionist approach. The need for systems analysis in biology and systems biology has become a rapidly growing field and it is widely used to cope with the challenges we are facing due to metabolic engineering. Hence, mathematical models known as genome-scale metabolic models (GEMs) are created in order to analyse complex biological systems and incorporate all the genomic, proteomic and metabolic data available into these models. Modern biological models need to meet new sets of criteria, the most important are: organism-specific, data-driven, environment-specific, easily scalable or gene-protein-reaction association. GEMs can be used for example to analyse the metabolic potential of a cell or an organism to predict metabolic fluxes or redesign the metabolism, to create industrially important strains, capable of producing various natural and non-natural metabolites which can represent the base of the bio-based industry. The most widely used metabolic models are for well known organisms such as Escherichia coli or Saccharomyces cerevisiae, however it is mandatory to in silico analyse the metabolic potential of less known but with huge potential organisms like B. succiniciproducens. The extending concept of bio-based economy is based on the bioconversion of renewable feedstocks to value added chemicals such as succinic acid or 1,4-butanediol (BDO). Using in silico models we can generate novel, testable and very often quantitative predictions of cellular behavior, reducing the time and wet experiments cost. B. succiniciproducens has been recently isolated as a novel producer for succinic acid and possibly for BDO, important platform chemicals, from various renewable carbon sources. The purpose of this study was to investigate the production potential of the host organism using mathematical models and optimize the production potential in silico. In order to address BDO production potential formerly designed biosynthetic pathways were tested under different environmental and genetic conditions. To the best our best knowledge, this is the first attempt to analyse in detail the host strain metabolic network and the impact of different factors on succinic acid and BDO production using a systems biology approach.