Evaluation of Metabolic Engineering Strategies for Production of a Large Panel of Chemicals

Anne Sofie Lærke Hansen

DTU Systems Biology, Technical University of Denmark
DTU Novo Nordisk Foundation Center for Biosustainability, Technical University of Denmark

INTRODUCTION

Microorganisms such as bacteria and fungi possess metabolic pathways that are essential to society – both now and in a future biobased society. Industrial biotechnology offers sustainable alternatives on how to produce bulk and speciality chemicals from renewable resources in contrast to today where the global chemical market is driven by petroleum feedstocks and synthetic chemistry.

Motivated by the possibilities that modern genome editing offers, metabolic engineers currently try to shift away from conventional practices of metabolic intuition, selection and random mutagenesis towards more rational engineering of microorganisms to turn them into high-yielding sustainable cell factories. In addition to adopting data driven approaches, mathematical models will play an essential part in this process.

APPROACH

A genome-scale metabolic model summarizes and enables mathematical representation of the metabolism of an organism. Constraint-based modeling of genome-scale metabolism represents a powerful modeling framework, as it enables prediction of heterologous pathways from a universe of known bio-transformations and metabolic processes, estimation of maximum theoretical yields, and recommendations of suitable production hosts and media.

In this project biochemical pathways to a large set of chemicals has been predicted using the software CAMEO[1] for the two common cell factories, the fungi *Saccharomyces cerevisiae* (baker's yeast) and the bacteria *Escherichia coli*.

The performance of the pathways has been/will be assessed from different perspectives:

- What are the maximum theoretical yields?
- Are the predicted pathways biologically thermodynamically feasible?
- How does the patent landscape look like and is there freedom to operate?

The project aims toward creating a scored and sorted list of chemicals that have a high potential of being sustainably produced, thus allowing metabolic engineers around the world to make informed decisions about which products to target.

[1] "Computer-Aided Metabolic Engineering and Optimization" developed at the Novo Nordisk Foundation Center for Biosustainability