Abstract

The systems biological view on microorganisms using genome scale metabolic models enables inference on physiological capacities which can be used for biotechnological purposes e.g. to increase the yield of a certain desired product or decrease unwanted byproduct formation. Furthermore metabolic models give hints on essential genes which are useful for metabolic engineering.

In the course of this thesis, genome scale metabolic models of five biotechnologically-relevant *Escherichia coli* strains - MG1655, W3110, HMS174, RV308 and BL21(DE3)- were corrected, refined and extended. In parallel, each of the strains was subjected to batch cultivations, whereas substrate consumption rates and biomass formation were measured. These values in turn were used as input parameters for model simulation. Furthermore, knock out simulations were performed in order to find genes, which are essential to only one of the strains despite high homology of the genome.

Depending on the strain roughly 50 genes were added to the network reconstructions, equaling an extension of the gene lists of 3 %, encoding for around 30 new reactions. Furthermore incorrect predictions regarding gene essentiality was corrected. Using these improved models, a strain-specific essentiality of RV308 for, *folD*, a gene involved in folate metabolism, was found. Batch cultivations on minimal medium supplemented with glucose yielded similar growth rates for strains MG1655, W3110 and BL21(DE3), whereas HMS174 grew roughly 20 % slower and RV308 grew significantly faster (22 %). As substrate uptake rates were the only input parameters or model simulation, simulated growth rates were more than twice as high as the experimental ones.

Future focus should therefore be put on a more extensive analysis of cultivation (by-)products to have additional input parameters at hand. Additionally, strain-specific differences in the biomass composition should be investigated in order to fundamentally improve in silico predictions.

Keywords: Genome scale metabolic models, *Escherichia coli cultivation*, Knock out simulation