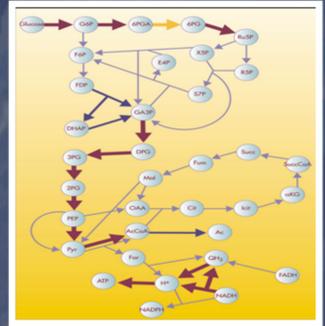


Central Metabolism of *Escherichia coli* in Stationery State: Flux Balance Analysis and Gene Expression Data Comparison

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http://www.csm.ornl.gov/Internships/rams_06/abstracts/k_walker.pdf

Abstract

Although *Escherichia coli* (*E. coli*) central metabolism has been studied for several decades, changes in metabolic fluxes imposed by sustained restriction of bacterial growth are poorly understood. This research project focused on modeling of the central metabolism of *E. coli* in the conditions of exponential growth and in the stationary state by the flux balance analysis and on . The modeling results were compared with the experimental data that characterize gene expression in these bacterial states. The obtained results will be used to identify limitations of the developed models and to reveal changes in the metabolic fluxes of *E. coli* in the stationary state. SimPheny software has been used to implement the tasks.

Background

- Poor understanding of metabolic changes underlying bacterial response to growth impairment
- Use of metabolic network modeling to reveal cellular mechanisms underlying bacterial response to growth impairment
- Flux Balance Analysis (FBA) of metabolic behavior based on linear programming
- Optimization of bacterial biomass by adjustment of metabolic fluxes
- SimPheny software for FBA-based metabolic modeling of the organism

Methodology

- Use Central Metabolism of *E. coli* as a simplified metabolic model of organism
- Apply single optimizations (maximization and minimization) in SimPheny software for aerobic and anaerobic growth conditions on glucose to simulate exponential and stationary state growth
- Compare simulation results with gene expression data of *E. coli* grown under same conditions (data location: Gene Expression Omnibus, GSE4375, accession numbers 4375 and 4376)

Results

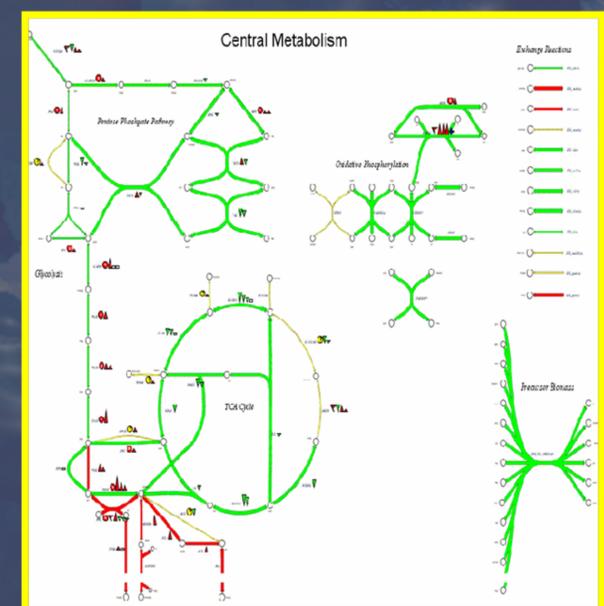
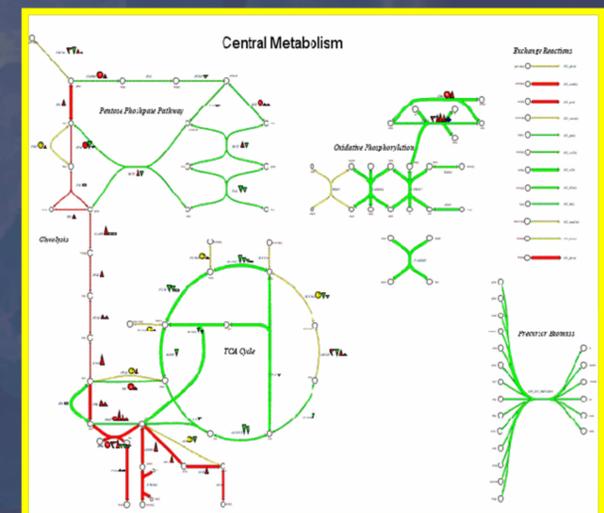


Figure 2: Central Metabolism of *E. coli* in conditions of exponential (a) and stationary state (b) anaerobic growth on glucose. Simulated metabolic fluxes (reactions on maps) and gene expressions (spikes near reactions) as log ratios vs. exponential aerobic growth on glucose. Green indicates enzyme down-regulation and red indicates enzyme up-regulation.

Conclusions

- Consistency of simulation of exponential growth on glucose under anaerobic conditions with experimental data
- Significant down-regulation of TCA cycle and up-regulation of glycolytic branch of Central Metabolism
- Experimentally observed increased activity of glycolytic enzymes and pentose phosphate pathway enzymes in stationary state growth
- Inability of simulation to capture these metabolic changes
- Possible reasons for disagreement: independence of biomass, used as objective function in simulation, on growth conditions of *E. coli*

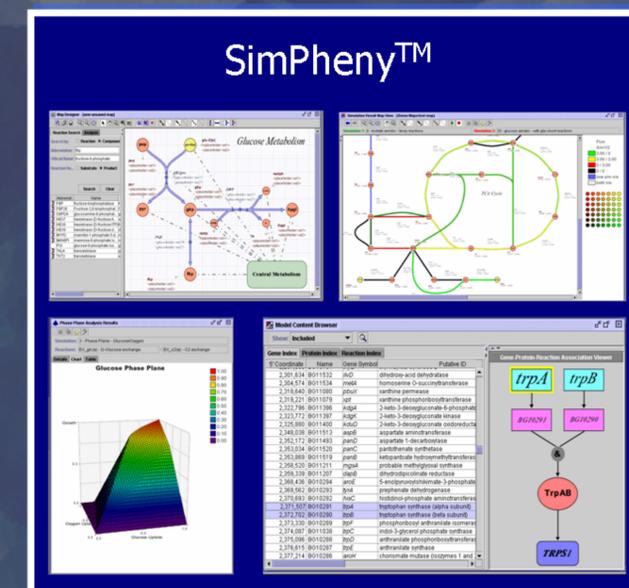


Figure 1: SimPheny software.

Future Research

- Improve simulation results in stationary state
- Modify objective function by introducing changes in biomass components specific for conditions of growth impairment