Assignment 3

BT5240 Computational Systems Biology | Jan - May 2025

Metabolic Modelling

March 8, 2025

Due Date: 18th March 2025, 5:00 PM
Maximum Marks: 50

Academic Integrity: You can discuss the problems verbally with your friends, but copying or looking at codes (either from your friend or the Web) is not permitted. Transgressions are easy to find and will be reported to the "Sub-committee for the Discipline and Welfare of Students" and dealt with very strictly. Mention any collaboration (discussions only!) in your solutions.

Submission: Since this is a computational assignment, we would also like to look at your codes. Submit your assignment as one zip file by uploading it at https://tinyurl.com/sysbiohw3. Your zip file should be named something like BTyyBxxx.zip, based on your roll number. This zip file must contain a single neatly typeset PDF of your solutions (named BTyyBxxx.pdf), including well-annotated plots and figures of legible font size, as well as the codes used for each of the problems in a separate folder code with proper annotations.

Problem 1: Knockout and overexpression targets to improve 2,3-butanediol production in *Geobacillus icigianus*

Geobacillus icigianus, a thermophilic bacterium, shows great potential as a bacterial platform for various biotechnological uses, particularly in producing 2,3-butanediol, a vital commodity chemical. Download the model from the attached link *Geobacillus icigianus*.

i) Simulate the model on the condition where the oxygen is uptaken at a rate of 0.03125 mmol gDCW-1 h-1
ii) *Geobacillus icigianus* grows on glucose with an uptake rate of 16 mmol gDCW-1 h-1, which is known to grow on other carbon sources. Simulate the model for growth using L-arabinose and then D-xylose as carbon sources. Report which source is a better carbon source.
iii) Identify the overexpression and gene knockout targets to improve the 2,3-butanediol production (bioengineering objective) while maximising the biomass objective.

Problem 2: Identify common targets between two dangerous pathogens.

★ *Mycobacterium tuberculosis* has been wreaking havoc on human populations for millennia. Dedicated effort is put in each day to reduce this burden on humanity. Your job is to aid in this effort by harnessing metabolic modelling to identify metabolic and genetic targets to arrest the notorious 'Robber of Youth'.

i) Download the model 'iNJ661' from the Bigg Models database (choose the format based on your systems' compatibility, use .xml if possible). Check the model components. In your opinion, how does the number of genes affect the number of metabolites and reactions? (Use E.coli core as a reference).

ii) Conduct an auxotrophic analysis on the model:

a. Identify the key carbon, nitrogen, and mineral sources it needs for survival.
b. Which of these sources (in each category) is best for growth?
c. Do you see any combined effects? (Check any 2 combinations of C, N sources and test how the growth varies).

iii) Identify essential genes in the model. What genes can we target to stop its growth? Note down the biological role that any one of these genes plays.

★ Humanity's woes have not ended yet! New threats emerge every day! *Acinetobacter baumanii* is a nosocomial pathogen that is on the rise. Can we use our newfound knowledge of lung pathogens to kill two microscopic birds with one GEM?

iv) Download the model 'iCN718' from the Bigg Models database. Any updates on your genes to metabolite/reactions relationship theory?
Identify common essential genes between this model and the TB model. Any surprises? Genes you didn't expect to see as common? Reason as to why any one gene would be commonly essential.