Assignment 4

BT5240 Computational Systems Biology | Jan - May 2022
Flux Balance Analysis & Dynamical Modelling

April 19, 2022

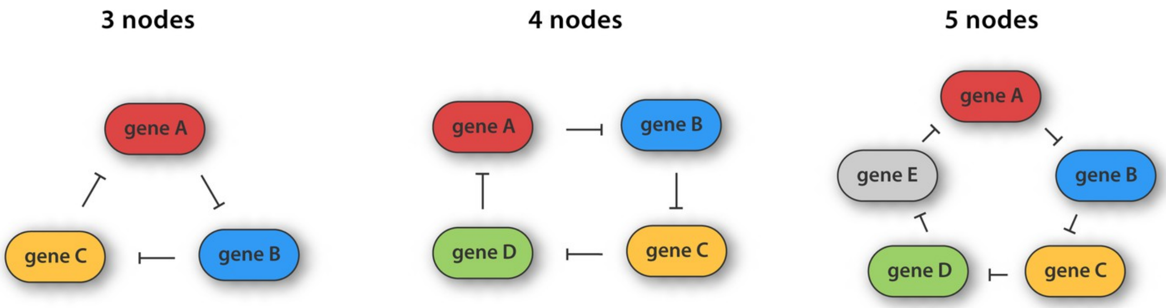
Due Date: 29th April, 2022
Maximum marks: 25

Academic Integrity: You are allowed to 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 will be 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 http://tinyurl.com/bt5240-submit
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: Boolean algebra (5 marks)
Consider a gene network containing three genes, a through c, which are transcribed to mRNA and further translated to the proteins A through C, synthesised by translation. The protein complex A-B activates the expression of gene c. The protein C represses the expression of genes a and b. Sketch the network and compute all the possible state transitions when all the genes are activated initially. Comment on the attractors observed in the network. (Hand Calculation - 5 marks)

Problem 2: Dynamical Modelling of Gene Regulation (15 marks)
Various network motifs are commonly seen in Gene Regulatory Networks. These motifs can exhibit robust behaviors under appropriate conditions. One such interesting behavior is oscillations. It is seen that repressilators can often show oscillations. Examples of repressilator motifs are shown below.



[Adopted from Rosier et al eLife 2015]

In this question, simulate the three-node repressilator using the equations given below.

$$\frac{dA}{dt} = g \cdot Hills^{-}(C) - k \cdot A \qquad Hills^{-}(M) = \frac{\lambda M^{n} + M_{0}^{n}}{M^{n} + M_{0}^{n}}$$

$$\frac{dB}{dt} = g \cdot Hills^{-}(A) - k \cdot B$$

$$\frac{dC}{dt} = g \cdot Hills^{-}(B) - k \cdot C$$

Parameter values	Initial conditions
$g = 50$	$A = 0.1$
$k = 0.05$	$B = 10$
$\lambda = 0.001$	$C = 0.1$
$M_0 = 10$	
$n = 2$	

a) Simulate the three node repressilator using the parameters given above for 1000 time points. What behaviour do you observe? Do you observe oscillations? If yes, is the amplitude sustained or decaying? Is the time period sustained or decaying? (7 marks)

b) Extend this to include four nodes. Modify the equations appropriately and simulate it for 1000 time points. What behaviour do you observe? Do you observe oscillations? If yes, is the amplitude sustained or decaying? Is the time period sustained or decaying? (4 marks)

c) Further extend this for five nodes. Modify the equations appropriately and simulate it for 5000 time points. What behaviour do you observe? Do you observe oscillations? If yes, is the amplitude sustained or decaying? Is the time period sustained or decaying? (4 marks)

Problem 3: Constraint-based modeling (FSEOF) (5 marks)

Identify at least five potential knockouts and five overexpression targets to produce ethanol from iMM904 (*S. cerevisiae*) using the concept of FSEOF (5 marks)