Assignment 4

BT5240 Computational Systems Biology | Jan - May 2025

Dynamic Modelling

April 3, 2025

Due Date: 20th April, 2025, 5:00 PM
Maximum Marks: 30

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.

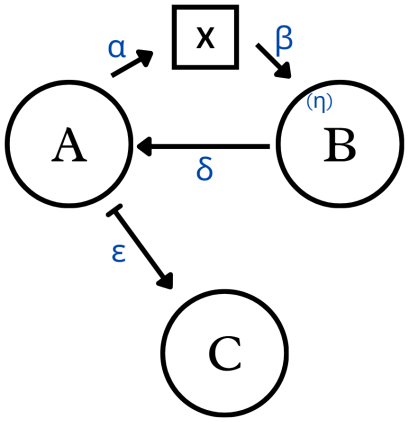
Submission: Since this is a computational assignment, we would also like to look at your codes. Submit your assignment as one zip file by uploading it at https://tinyurl.com/bt5240-submit. Your zip file should be named something like BTyyBxxx.zip based on your roll number. This zip file must contain 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.

Question 1: Dynamic Modeling - Interaction between bacterial species

Bacterial species interact with each other to bring about critical ecological functions. Consider a system of three bacterial species - A, B, and C with the following interactions:

- Species A and species B share a mutualistic relationship driven by the following interactions
    - Cross-feeding: Species A produces metabolite X, which is consumed by species B. Only a fraction of the consumed metabolite contributes to B's biomass.
    - Environmental mediation: Species B mediates the environment(by unknown mechanisms) and enhances the growth of A.
- C is a parasite that exploits A, reducing its population.

A diagram illustrating these interactions and their associated parameters is provided below:



a. Write down the differential equations that describe the population dynamics of this system. Clearly define and briefly explain the biological meaning of the key parameters in your equations. (5 marks)
   HINT: Include parameters for species' intrinsic growth, death rates, and interaction effects.
b. Numerically simulate the system dynamics for t = 5 hrs for the three different test cases given below. The parameter values(fixed values for all test cases) to be used are also given. Include your codes and plots.

Parameter	Species	Case 1	Case 2	Case 3
Growth Rate (g_biomass/hr)	A	0.2	0.65	0.3
	B	0.2	0.7	0.25
	C	0.2	0.1	0
Death Rate (g_biomass/hr)	A	0.1	0.02	0.05
	B	0.1	0.02	0.01
	C	0.1	0.01	5

Parameter	Value	Units
alpha	0.60	mmol/g_biomass/hr
beta	0.85	mmol/g_biomass/hr
delta	0.80	g_biomass/hr
epsilon	0.30	g_biomass/hr
eta	60%	
initial biomass for all species	5	g_biomass
initial metabolite conc	0	mmol

i. In all three cases, individually based on the plots, analyze the system's behavior - identify whether the system reaches a stable equilibrium, oscillations, or extinction for any species. (4 marks)
ii. Compare the three cases and comment briefly on any common trends or patterns you can observe. (2 marks)

c. Suppose a fourth bacterial species D, is introduced, which inhibits the growth of species C by 80%.
i. Modify the differential equations of the system to include D. (2 marks)
ii. Explain the effect of the new species on the system behavior and individual species population. (2 marks)

Question 2: Boolean Modeling - Tumor regulation network

Tumor growth is regulated by a set of key molecular players that determine whether a tumor cell undergoes **proliferation** or **apoptosis**. Among them, P53 (tumor suppressor), MDM2 (oncogene), MYC (oncogene), and RB (tumor suppressor) play crucial roles in deciding the cell fate. Consider a simple (hypothetical) regulatory network with P53, MYC, MDM2, and RB based on the following regulatory interactions:

- P53 is activated by MYC and activates apoptosis in the cell
- MDM2 inhibits the activity of P53 protein towards apoptosis
- MYC promotes cell proliferation but is inhibited by RB
- RB inhibits cell proliferation but is inactivated by MYC
- Cell fate is decided by the processes of apoptosis and cell proliferation based on the following rules
    - Apoptosis(A) if P53(t) and not MDM2(t)
    - Proliferation(P) if MYC(t) and not RB(t)

Questions:

a. Define the Boolean update rules governing the interactions of the given tumor regulatory network and illustrate them through a network diagram. (3 marks)

b. Identify the four regulators' biologically feasible and infeasible states and the cell fate based on the above interactions. Construct a truth table for all possible initial conditions. (3 marks)
   (NOTE: Represent their states using 1(on/active) and 0(off/inactive) and cell fate as A/P)

c. Simulate the boolean model over time for three different initial conditions. Does the system always reach a stable state, or does it exhibit oscillatory behavior? Interpret the biological significance of your findings. (5 marks)

d. Scientists want to test Drugs A, B, and C based on their current knowledge. They want to predict and simulate the regulatory network in the presence of each drug. Infer how each drug may affect the tumor growth. (4 marks)
    - Drug A: Inhibits MDM2
    - Drug B: Inhibits MYC
    - Drug C: Activates RB