Department of Biotechnology
Indian Institute of Technology Kharagpur
Mid-semester Examination, Spring Semester 2019-20

Subject: Introduction to Systems Biology
Time: 02 hours
Date – 19th February, 2020, AN (14:00 - 16:00h)

Subject No: BT60006
Full Marks: 30
Number of students: 64

Instruction: Answer ALL questions. ***Answer all the components of one question in one place. Answer precisely to the point. Make appropriate assumptions wherever necessary.***

Part-A

1. (a) Consider the set of following sequences from S1 to S8:

```
S1 MSGTRKEEWE
S2 MSGTRKEGWE
S3 MCGTRKEEWE
S4 MSGTRKEEWQ
S5 MCGTCKEEWE
S6 MNGTCKEEWE
S7 MSGTRKECWE
S8 MNGTCKEEQE
```

Calculate the pairwise distance matrix between the sequences from S1 to S8 and draw the genotype network by connecting only the sequences that are at distance one from each other. **[4]**

(b) With the help of a schematic diagram, explain negative, positive and reciprocal sign epistasis between two mutations M_1 and M_2 both of which have deleterious fitness effect. **[3]**

2. A transcription factor 'A' activates the expression of a protein 'B'. The production rate of 'B' is 100nM min^{-1} and the removal rate of 'B' is 0.5 h^{-1}. Calculate the steady state concentration of 'B' and its response time. **[1+1=2]**

3. Gene 'X' negatively autoregulates its own expression with production rate 500nM min^{-1} when its concentration is below 10μM but the production rate drops to zero when the concentration of X is above this value. Calculate the steady state and the response time of the system. Compare the response time of this circuit with that of a simple regulation circuit that also reaches the same steady state with production rate of 500nM min^{-1}.

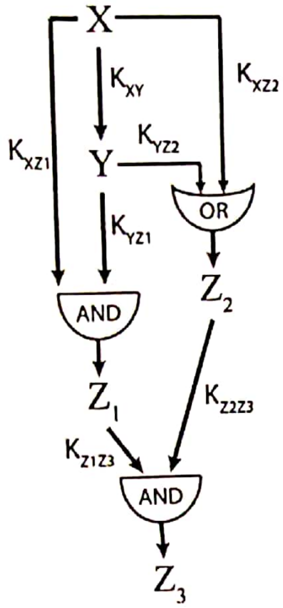
[2+1=3]

4. Gene X encodes a repressor that negatively regulates its own expression and also represses gene Y, which also negatively regulates its own expression. At time t=0, X begins to be produced at a rate 5nM min^{-1} starting from an initial concentration of X=0 and Y begins to produce at a rate of 6nM min^{-1} from initial concentration of Y=0. Schematically plot the dynamics of X and Y. What are the response times of X and Y? Assume repression thresholds 20nM and 12nM for action of X on its own promoter and on the Y promoter, respectively and 15nM for the action of Y on its own promoter. Also assume that all repression lead to zero production.

[2+2=4]

5. Consider a cascade of activators X→Y→Z. Protein X is initially present in the cell in its inactive form. The input signal of X, S_x, appears at time t=0 for a pulse of duration 'T', and then vanishes. What is the concentration of Y with respect to time? What is the minimal pulse duration needed for the activation of gene Z? The threshold for activation of Z by Y is K_{yz}. **[3]**

6.



Consider the gene regulation circuit as shown in the diagram with indicated activation thresholds and input functions. Assume that the signals for Y, Z_1, and Z_2 are present throughout.

(a) At t=0, the signal for X, S_x appears and leads to production of X and generates the active form X*. Draw the dynamics of the circuit.

(b) After a long time of being on, the signal S_x disappears. Draw the dynamics of the circuit.

Assume that $K_{xz1}<K_{xy}<K_{xz2}$, $K_{yz2}<K_{yz1}$ and $K_{z1z3}<K_{z2z3}$.

[5]

Part-B

7.

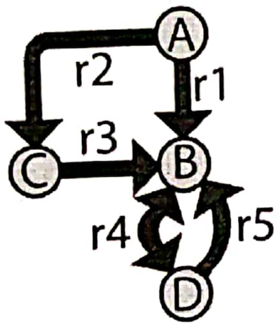


Figure 1.

Construct the stoichiometric matrix for the network shown in Figure 1. Assume all reactions are proceeding in the direction indicated by the arrow and are irreversible.

[2]

8. For the network below draw the corresponding metabolic reaction network map. For the same network write out the S matrix.

Name	Reaction
v1	A→ B
v2	2B→ C + byp
v3	2B + cof → D + byp
v4	D→ E + cof
v5	C + cof → D
v6	C → E
b1	Axt → A
b2	E → Ext
b3	byp → bypxt

[2+2=4]