BT612 Systems Biology

Total Marks: 60 | **End-semester Examination July-November 2023** | **Time: 3 hr.**

Instructions

1. *Preferably* write the answers following the order of questions
2. **You MUST SHOW ALL the calculation STEPS. MARK the FINAL answer clearly.**
3. Use standard mathematical notations/symbols only.
4. All graphs should be suitably labeled and axes clearly marked.
5. All question has equal mark.

Trick??

Q1. Some cell types in a tissue represent only a tiny portion of the total cell population, such as hematopoietic stem cells in the blood. Imagine that a particular cell type is present at a rate of 1 cell in 100000. If we are given a sample with 100000 cells, what is the probability of finding exactly 1 of these rare cells?

Check

Q2. Two copies of a gene G are in a cell, controlled by two homologous promoters – P1 and P2. The transcription rate of G under the control of P1 is $\lambda_1 = 0.25$ per minute. P2 is a stronger promoter. The transcription rate of G under P2 is $\lambda_2 = 1.75$ per minute. What is the probability that three copies of mRNA of G will be produced in the next two minutes?

Q3. In a coin toss experiment, the probability of getting a head is 0.4. Perform a simulation for 6 successive coin tosses and report the number of heads obtained. For simulation, use the following uniformly distributed random numbers U(0, 1) sequentially from left to right: 0.21, 0.38, 0.93, 0.07, 0.44, 0.11, 0.56, 0.55, 0.42, 0.31, 0.12, 0.03, 0.19, 0.69, 0.2

Q4. The PDF of a continuous random variable x is given:

$$f_X(x) = 2xe^{-x^2}\text{; here } x \geq 0$$

How will you generate random numbers that follow this distribution?

Q5. We are simulating a system of reactions as given below, using Gillespie's algorithm.

$2A + 2B \rightarrow 2C + 2D$, Mesoscopic rate constant = 0.01 per sec

$C + E \rightarrow 2F$, Mesoscopic rate constant = 0.02 per sec

$2D + 2A \rightarrow 2G$, Mesoscopic rate constant = 0.01 per sec

$2B \rightarrow H$, Mesoscopic rate constant = 0.04 per sec

One of these four reactions happened at t = 12 sec. That led to a change in the numbers of some of these molecules. The updated numbers of A, B, C, D, E, F, G, and H at t = 12 sec are 4, 4, 2, 2, 4, 0, 1, and 0 respectively. Calculate the average waiting time for the next reaction to happen in this system.

Q6. X is a continuous random variable, with the PDF: $f(x) = a + bx^2$ for $0 \leq x \leq 1$. If $E(x) = 3/5$, find a and b.

N feedback

Q7. The ODE-based model of a small regulatory molecular circuit is shown here. A steady state for this system is $x = y = 1$. A) What sort of network motif is this? B) Calculate the relationship between α and β that assures a stable periodic oscillation of x and y around the steady state.

$$\frac{dx}{dt}=1-xy^{\beta}\ ;\quad \frac{dy}{dt}=\alpha y\left(xy^{\beta-1}-1\right)\ ;\ x\geq 0\ ;\ y\geq 0\ ;\ \alpha>0\ ;\ \beta>1$$

Q8. The following system of ODE represents a small molecular circuit. The steady state of this system is $(x=2, y=1)$. A) Is this steady state stable? B) What type of phase portrait do you expect for this steady state? No need to draw a diagram. Only mention the type of phase portrait based on your calculations.

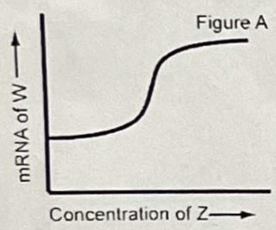
$$\frac{dx}{dt}=1-x\frac{y^2}{1+y^2}\ ;\quad \frac{dy}{dt}=\frac{x^2}{1+x^2}-y\frac{x^2}{1+x^2}$$

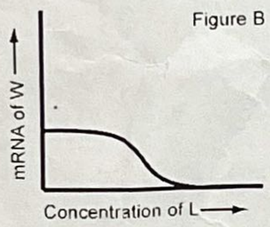
2 Feed forward

Q9. A) Which network motifs can act as adaptive motifs? Draw the generic structures of these motifs.

B) What are the differences between a coherent and an incoherent feed-forward motif? Explain with schematic representations of these two motifs.

Q10. Two signaling molecules Z and L independently control the expression of a protein W. We treated cells with different concentrations of Z, without any L, and measured the steady state level of mRNA of W. The data is shown in Figure A. A similar experiment was performed, where cells were treated with different concentrations of L, in the absence of Z. The data of this experiment is shown in Figure B. Create an ODE-based model to capture the dynamics of the protein W, under the control of these two signaling molecules. You have to write only the ODEs and give the reasoning behind your model. Clearly declare constants/parameters used in the ODEs.





Q11. For the following system of ODEs draw the phase plane plot with nullclines. Identify the steady state in this plot and mark it on the plot. Will this system show bifurcation if the values of α or β are varied? Explain your answer using the phase plot. Consider $x\geq 0$ and $y\geq 0$.

$$\frac{dx}{dt}=\alpha.\frac{1}{1+y}-x\ ;\quad \frac{dy}{dt}=\beta.\frac{1}{1+x}-y$$

Q12. The concentration of a protein in a cell is 25 μM. If the volume of the cell is 10^{-12} mL, calculate the number of copies of this protein in the cell.