BM2053 Mathematical Models & Systems Biology

Problem Set 4

Instructions

1. You are not supposed to submit the solutions to these questions.
2. To get the most out of these, solve all the problems on your own.

Questions

1. Write down a Python program to solve the diffusion equation with different boundary conditions. Explore the role of the choice of values of Δt and Δx on the solution.

2. Consider diffusion of a small molecule in a one-dimensional domain between $x = 0$ and $x = 8$ μm. We denote the concentration of the molecule by $\phi(x,t)$. The initial concentration of the molecule in the domain is given by

$$\phi(x,0) = 0.25 + 0.1\left(1 - \frac{x}{8}\right)\sin\left(\frac{\pi x}{8}\right)\mu\text{M}.$$

and the diffusivity of the domain is also not fixed and is given by

$$D(x) = D_0 + \epsilon x$$

where $D_0 = 10^{-7}$ m^2/s, and $\epsilon = 10^{-5}$ m/s. The boundary conditions are given by $\phi(0,t) = 0.25\ \mu$M and $\dfrac{\partial \phi}{\partial x}(8,t) = 0\ \mu\text{M/m}$. Numerically estimate the concentration profile at $t = 12$ hours.

3. Consider a one-dimensional ecosystem where two species reside- one predator and one prey. Within this 1D domain, the predator moves in a diffusive manner and consumes the prey. Derive a mathematical model for this two-species system. List down all the assumptions.

4. (From Uri Alon book) The regulator Y in coherent FFLs in transcription networks is often negatively autoregulated. How does this affect the dynamics of the circuit, assuming that it has an ANDN input function at the Z promoter? How does it affect the delay times? The Y regulator in an OR gate coherent FFL is often positively autoregulated. How does this affect the dynamics of the circuit? How does it affect the delay times? Explore these questions by
   (a) sketching the curves for protein levels as function of time
   (b) by numerically solving the equations

5. (From Uri Alon book) The four-node diamond pattern occurs when X regulates Y and Z, and both Y and Z regulate gene W.
   (a) How does the mean number of diamonds scale with network size in random ER networks?
   (b) What are the distinct types of sign combinations of the diamond (where each arrow is either activation or repression)? How many of these are coherent?
   (c) Consider a diamond with four activation arrows. Assign activation thresholds to all arrows. Analyze the dynamics of W following a step of S for both AND and OR logic at the W promoter. Are there sign-sensitive delays?

6. Toggle switches can show tristability, in which there are three stable states. Tristability can occur when the autoregulation of X and Y is strong and cooperative enough. Consider a toggle switch in which the inhibition function of X by Y is

$$f(y) = \frac{1}{1 + \left(\dfrac{y}{k_1}\right)}$$

and the autoregulation function is sigmoidal

$$g(x) = \alpha_0 + \alpha_1 \frac{\left(\dfrac{x}{k_2}\right)^2}{1 + \left(\dfrac{x}{k_2}\right)^2}$$

and the inhibition and autoregulation functions combine multiplicatively (resembling an `AND` gate). The interaction functions for Y are the same as for X (symmetric circuit).

   (a) Write the equations for this circuit.
   (b) Sketch the nullclines. How many intersection points can they have for different choices of parameters?
   (c) Is symmetry essential for tristability? If not, sketch non- symmetric nullclines with tristability.

7. Analyze the GRNs we have seen in the class under the limit $n \to \infty$.

8. In class, we have seen how `AND` and `OR` operations work at the promoter of a gene in GRNs. Using these, can you design a gene regulatory circuit that can perform `XOR` operation?

9. Consider the `ON` (when protein is expressed) and `OFF` (when it is not) states of genes as information in the form of binary digits (or 'bits'). Can you design a gene regulatory circuit that can function as an 'adder' of two binary digits?