Gene Regulatory Networks

Resources:

1. week5_feedback_systems.ipynb: This notebook introduces the analysis of feedback systems using Python and describes the role of feedback in system design using simulations of mathematical models.

2. week6_system_analysis.ipynb: This notebook uses analytical and computational tools to discuss functions and utilities of different gene regulatory networks.

3. Python tutorials online: You are free to use any tutorials from the Internet on Numpy, Scipy, or any other Python package that you may use to solve the homework problems.

4. Submit your homework to GradeScope by downloading the jupyter notebook as a PDF. Go to Files -> Download as -> PDF. If that does not work, you can go to File -> Print Preview -> Ctrl + P (to print) -> Save as PDF.

Due date: 1st March on GradeScope.

Problem 1: Cascade Gene Regulation

(Adapted from [Alon] Problem 1.4) Cascades: Consider a cascade of three activators, $X \to Y \to Z$. Protein X is initially present in the cell in its inactive form. The input signal of X, u_X, appears at time $t = 0$. As a result, X rapidly becomes active and binds the promoter of gene Y, so that protein Y starts to be produced at rate β. When Y levels exceed a threshold K_y, gene Z begins to be transcribed. All proteins have the same degradation/dilution rate α.

(a) Write a mathematical model to model the cascade phenomena described above. You may model the system by describing the rate of change of protein concentrations.

(b) Simulate your model in (a) by choosing biologically relevant parameters. What is the concentration of protein Z as a function of time?

(c) Compute the response time of Z with respect to the time of addition of u_X? Discuss how you can improve the speed of the response of this system by changing parameters. To compare the response times for different parameter settings, normalize the steady-state to show a fair comparison of the response time.

(d) Assume that you have a repressor cascade instead of an activation cascade. How do your conclusions change for parts (a) - (c).

Problem 2: Eukaryotic Transcriptional Control

Read this short paper on eukaryotic transcriptional control:

Kornberg, Roger D. "Eukaryotic transcriptional control." Trends in biochemical sciences 24.12 (1999): M46-M49. URL

Write a one paragraph summary on key differences in transcriptional control in prokaryotes and the eukaryotes.

Problem 3: Autorepression Speeds Up Response

A paper published in 2002 showed that autorepression speeds up the response times of transcription networks in cells. We discussed the autorepression mechanisms in Week 4 and Week 5. In your simulations for HW 4, you could observe that the autorepression shows faster response when compared to unregulated gene expression. The goal of this problem is to use a similar mathematical model to analytically reason about the response time. Read the paper:

Rosenfeld, Nitzan, Michael B. Elowitz, and Uri Alon. "Negative autoregulation speeds the response times of transcription networks." Journal of molecular biology 323.5 (2002): 785-793. URL

Re-derive the expression of rise-time as shown in this paper to analytically comment about how autorepression can lead to faster response times.

Feedback:

Please submit the feedback form on Gradescope (if you haven't yet) and write here the number of hours you needed to finish this problem set.