Introduction to Biological Physics

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Exercise 2.

1. *Identifying network motifs*: Download the transcription network of E.coli from the course site, and write a program that counts the number of : self-loops $(x \to x)$, mutual regulation $(x \to y, y \to x)$, fan-outs $(x \to y, x \to z)$, and cascades $(x \to y, y \to z)$. Use your preferred language/platform (e.g. Matlab, python, R, Mathematica). Note: the network is presented in the file as three columns of number, the first is the index of the origin of the arrow, and the second is the target of the arrow, and the third is the sign of the arrow (which you can ignore for this exercise). The network is also available at http://www.weizmann.ac.il/mcb/UriAlon/sites/mcb.UriAlon/files/uploads/CollectionsOfComplexNetwroks/1aorinter_st.txt.

2. Write a program that generates a random network with the same number of nodes and arrows as the real network. (Optional: make a random network with the same degree distribution as the real network, meaning that each node has the same number of outgoing and incoming arrows as it does in the real network). Generate enough random networks (~10^3) in order to calculate the mean and std for each circuit of question 1. Which of these subgraphs is a network motif?

3. *Auto-repression with Hill input function*. What is the dynamics X(t) and response time for a repressor that cooperatively represses its own promoter (described by a Hill-function with Hill coefficient n)

$$\frac{dX}{dt} = \frac{\beta}{1 + (X/K)^n} - \alpha X$$

   To solve this equation, use the approximation of strong auto-repression, that is $(X/K)^n \gg 1$. (Hint: try changing X to a new variable $u = X^{n+1}$)
   a. Calculate the response time. How much faster is the response than in non-auto-regulated circuits for n=1,2, and 3?
   b. Calculate the steady state of X for the exact system and the approximate one for n=1, and compare.
   c. Solves the differential equation numerically using the initial conditions $X(t = 0) = 10,\ K = 1,$ $\beta = 1,\ \alpha = 1$ and $n = 1,2,3$. (use your preferred software/platform). Plot on the same graphs the analytical solution.
   d. Explain why the analytical solution seems accurate at early times but less accurate at late times (Hint: the solution used is an approximation).

4. When the DNA of *E coli* is damaged, for example by UV radiation, a sensor protein binds the damaged DNA, and rapidly cleaves (degrades) a transcriptional repressor called LexA. LexA represses genes for DNA repair such as uvrA (these genes are called the SOS repair system). LexA also represses its own gene.
   a. Sketch this gene regulation network.
   b. Sketch the dynamics of DNA damage, LexA and uvrA as a function of time after a pulse of UV light in which DNA is damaged. Assume that cleavage of LexA is rapid (seconds), and repair of the DNA damage by the repair genes takes about an hour. Once DNA is repaired, LexA is no longer cleaved.
   c. How would the dynamics change if LexA did not repress its own promoter? Why is the negative auto-regulation of LexA useful?
   d. One of the SOS genes makes a protein that stops the cell from dividing. Why does this make sense?