CALIFORNIA INSTITUTE OF TECHNOLOGY
BioEngineering

Bi 250

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Problem Set #7

Issued: 25 Feb 12
Due: 5 Mar 12

1. *Alon 8.3. Polynomial self-enhanced degradation.* Find the steady state concentration profile of a morphogen produced at x=0. The morphogen diffuses into a field of cells, with nonlinear self-enhanced degradation described by:

$$\frac{dM}{dt} = D\frac{d^2M}{dx^2} - \alpha M^n$$

When is patterning with this profile robust to the level of M at the boundary, M_o? *Hint:* Try a solution of the form $M(x) = a(x+b)^m$ and find the parameters a and b in terms of D, M_o, and α.

2. *Alon 8.4. Robust Timing.* A signaling protein X inhibits pathway Y. At time t=0, X production stops and its concentration decays due to degradation. The pathway Y is activated when X levels drop below a threshold T. The time at which Y is activated is t_Y. Our goal is to make t_Y as robust as possible to the initial level of X, $X(t=0) = X_o$. Note that all concentrations are spatially uniform in this problem.

   a) Implement a simulation for this pathway for a linear degradation of X,

$$\frac{dX}{dt} = -\alpha X.$$

   Plot the concentrations of proteins vs time for several initial conditions.

   b) Implement a simulation for this pathway for a self-enhanced degradation of X,

$$\frac{dX}{dt} = -\alpha X^n.$$

   Plot the concentrations of proteins vs time for several initial conditions.

   c) Compare the robustness of the time t_Y, at which Y is activated with respect to fluctuations in X_0. Which degradation mechanism is more robust to fluctuations in X_0. Explain.

   d) Explain why a robust timing mechanism requires a rapid decay of X at times close to t=0.

3. *Robustness of Morphogen Gradients. Based on Eldar, et al., Developmental Cell, 2003*

   Eldar et al. compare two models of Hedgehog signaling in "Self-Enhanced Ligand Degradation Underlies Robustness of Morphogen Gradients", 2003. By referring to figure 6 in this paper, compare the signaling profile for these two models. What needs to be added to the simplified Hedgehog model to get a graded signaling profile? Explain how the dynamics might be affected with different concentrations of molecules in both models.