CALIFORNIA INSTITUTE OF TECHNOLOGY
BioEngineering

BE 250C

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Problem Set #4

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1. In this problem we will compare the model with single methylation site vs. double methylation sites. The model with a single methylation site is given by:

$$\frac{d(X + X*)}{dt} = V_R R - \frac{V_B B X*}{K + X*}$$

where the *activity* is given by $A = X*$. The model with two methylation sites is given by

$$\frac{d(X_2 + X_2*)}{dt} = \frac{RV_R X_1}{X_1 + X_0} - BV_B X_2*$$

$$\frac{d(X_1 + X_1*)}{dt} = BV_B X_2 * + \frac{RV_R X_0}{X_1 + X_0} - \frac{RV_R X_1}{X_1 + X_0} - BV_B X_1*$$

$$\frac{dX_0}{dt} = -\frac{RV_R X_0}{X_0 + X_1} + BV_B X_1*$$

and the activity is given by $A = X_1 * + X_2*$. Let $K = 10, V_R R = 1, V_B B = 2$. Derive the parameter sensitivities of the activities ($\frac{dA}{dp_i}$) for both the single and double methylation models. Comment on which parameter each model is most robust and most sensitive to.

2. Consider a toy model of protein production:

$$\frac{dm}{dt} = f(p) - \gamma m$$

$$\frac{dp}{dt} = g(p) - \delta p$$

a) Assume that there is transcriptional self-regulation ($f(p) = \frac{\alpha}{K+p^n}$). We now know that the mRNA transcription process and thus we want to understand the sensitivity with respect to the mRNA transcription rate α_0. Compute the transfer function from α to p. Plot this transfer function for $\alpha = 0.002, \beta_0 = 0.1, \gamma = 0.005, \delta = 0.001, K = 0.002$. Compare it with the transfer function from α_0 to p without regulation ($f(p) = \alpha_0 = 0.001$). (Note: As a reminder on how to compute these transfer functions, see BFS chapter 3 page 3-11).

b) Now assume that there is no transcriptional regulation ($f(p) = \alpha_0$) but there is translational self-regulation such that $g(p) = \frac{\beta m}{K+p^n}$. Computer the transfer function from α_0 to p when $\beta = 0.2$. Compare again with the case with no regulation.

3. Consider a simple model of chemotaxis:

$$\frac{dX_m}{dt} = k_R R + k^f(L)X_m^* - k^r X_m$$

$$\frac{dX_m^*}{dt} = -k_B B^p \frac{X_m^*}{K_{X_m^*} + X*_m} - k^f(L)X_m^* + k^r X_m$$

where X_m is the concentration of methylated receptor complex, and X_m^* is the concentration of activated, methylated receptor complex. Ligand concentration enters into the equation through the rate $k^f(L)$. In this model, $CheR$ (R) and $CheB^P$ (B^P) concentrations are constant. (BFS, Section 5)

a) Pick parameter values such that $k_B B^p > k_R R$ and plot the dynamics, doubling the ligand concentration at time t=20. Compare to figure 5.12 in BFS.

b) Now assume that CheR no longer acts in saturation. Rederive the dynamics and plot. Comment on how this assumption affects adaptation.