CALIFORNIA INSTITUTE OF TECHNOLOGY
Bioengineering and Biology

Bi 250b

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Winter 2011 Due: Jan 18

1. *Negative auto regulation.*

   In this problem, we consider two different models of a synthetic Lac repressor and compare features. The ODEs for the first model are:

$$\frac{d[LacI_m]}{dt} = \alpha_m - \delta_m[LacI_m]$$

$$\frac{d[LacI_p]}{dt} = p[LacI_m] - \delta_p[LacI_p]$$

   a) What do $[LacI_m]$ and $[LacI_p]$ represent? What do the parameters $\alpha_m, \alpha_p, \delta_m, \delta_p, p$ represent? What biological systems can these equations model?

   b) Estimate model parameters $\alpha_m, \alpha_p, \delta_m, \delta_p, p$ in *E. coli.* You can use the BioNumbers website at Harvard: http://bionumbers.hms.harvard.edu/ as reference. Include units.

   c) Run the program *lacOpenMain.m* in Matlab and plot concentrations of $[LacI_m]$ and $[LacI_p]$ as a function of time. What are the steady states for each species?
   The ODEs for the second model are:

$$\frac{d[LacI_m]}{dt} = \frac{\beta K}{K + [LacI_p]} - \delta_m[LacI_m]$$

$$\frac{d[LacI_p]}{dt} = p[LacI_m] - \delta_p[LacI_p]$$

   a) Describe the term $\frac{\beta K}{K+[LacI_p]}$ and the biological function it represents. Explain how this does this biological circuit differs from the first one.

   b) Run the program *lacClosedMain.m* in Matlab and plot concentrations of $[LacI_m]$ and $[LacI_p]$ as a function of time. What are the steady states for each species?

   c) What is the response time of $[LacI_p]$ for unregulated and regulated circuits? Define the response time as the time it takes to reach 90% of the steady state.

   d) Comment on differences between unregulated and regulated gene expression.

2. *Toggle switch.*

   Consider a positive transcriptional feedback loop composed of two negative interactions $X \dashv Y$ and $Y \dashv X$.

a) Run the program *toggle.m*. How does changing degradation and basal transcription rates change the steady state of the system?

b) Plot the vector field of the toggle program using *pplane8*, setting min x and min y values to 0 and max x and max y values to 4. This is a phase diagram for the toggle switch that includes steady states (equilibrium points). Describe the stability of the steady states observed.
(Note: To plot vector fields, download *pplane8* from *http://math.rice.edu/˜ dfield/#8.0* and add *pplane8.m* to your path as outlined in the Matlab tutorial.)

c) Run the program *toggle.m*. Plot the time response of X and Y using the following two initial conditions: (X=1,Y = 4) and (X=4, Y=1).

d) How do the responses change with initial conditions? Describe a situation where this type of interaction would be useful and give another example.

3. *Positive feedback loops*

Consider the following network $X \to Y$ and $X \to X$.

a) Plot the vector field using *pplane8*. How many steady states do you observe?

b) Describe the stability of the steady states.

c) Describe the relevance of having a positive feedback loop in a biological system.