HW 3: Synthetic transcriptional circuits.

(Dated: October 13, 2010)

1. COMBINATORIAL GENE REGULATION.

The Lac promoter in the Lac operon is regulated both by a transcriptional repressor and a transcriptional activator. Build a mathematical for the production and degradation of the lac mRNA as a function of the repressor and activator concentrations. The general form of the equation for the mRNA is

$$\dot{m} = \alpha_m \frac{g_{on}}{g_{tot}} - \gamma_m m. \tag{1}$$

You thus need to express g_{on}/g_{tot} as a function of repressor and activator concentration. Assume that gene expression is on only in the case where the activator is bound but not the repressor. In all other cases, gene expression is off. Compare the following two situations:

1. Binding of the repressor and activator is independent of one another (like in the lac operon). This is the case we started to discuss in class.
2. Binding sites for the activator and repressor overlap and binding of the two proteins is mutually exclusive.

2.STABILITY OF THE BISTABLE SWITCH.

In class, we introduced the following model for a genetic bistable switch:

$$\dot{P}_1 = \frac{\alpha}{1 + P_2^n/K} - \gamma P_1, \tag{2}$$

$$\dot{P}_2 = \frac{\alpha}{1 + P_1^n/K} - \gamma P_2. \tag{3}$$

To derive theses equations we assumed that mRNA dynamics are fast relative to protein dynamics and that degradation and production rates are the same for both proteins and mRNAs. Assume $n = 1$, find the equilibrium point(s) and then calculate the Jacobian at those points. Based on the eigenvalue of the Jacobian are the equilibria stable? Is the system bistable?

3. MODELING A TRANSCRIPTIONAL OSCILLATOR.

Simulate the repressilator, a transcriptional synthetic oscillator.

- Use the equations and parameters given in the original paper by Elowitz (A synthetic oscillatory network of transcriptional regulators, Michael B. Elowitz and Stanislas Leibler, Nature 403, p.335 (2000), see class web page).
- Now assume that the mRNA dynamics are fast relative to the protein dynamics (i.e in steady state). Use this assumption to eliminate the mRNA and obtain a reduced model (three equations) that only explicitly contains the protein dynamics. Simulate this model with the same parameters as before. What do you observe?