

CALIFORNIA INSTITUTE OF TECHNOLOGY  
Bioengineering

**BE 150**

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Winter 2012

**Problem Set #5**

Issued: 8 Feb 2012  
Due: 15 Feb 2012

1. For this problem, we return to our standard model of transcription and transcription process with probabilistic creation and degradation of discrete mRNA and protein molecules. The *propensity functions* for each reaction are as follows:
  - Probability of transcribing 1 mRNA molecule:  $0.2dt$
  - Probability of degrading 1 mRNA molecule:  $0.5dt$  and is proportional to the number of mRNA molecules.
  - Probability of translating 1 protein:  $5dt$  and is proportional to the number of mRNA molecules.
  - Probability of degrading 1 protein molecule:  $0.5dt$  and is proportional to the number of protein molecules.
  - $dt$  is the time step chosen for your simulation. Here we choose  $dt = 0.05$ .
  - (a) Simulate the stochastic system above until time  $T = 100$ . Plot the resulting number of mRNA and protein over time.
  - (b) Now assume that the proteins are degraded much more slowly than mRNA and the propensity function of protein degradation is now  $0.05dt$ . To maintain similar protein levels, the translation probability is now  $0.5dt$  (and still proportional to the number of mRNA molecules). Simulate this system as above. What difference do you see in protein level? Comment on the effect of protein degradation rates on noise.
2. Compare a simple model of negative autoregulation with one without autoregulation:

$$\frac{dX}{dt} = \beta_0 - \gamma X$$

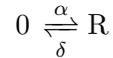
and

$$\frac{dX}{dt} = \frac{\beta}{1 + \frac{X}{K}} - \gamma X$$

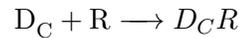
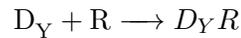
- (a) Assume that the basal transcription rates  $\beta$  and  $\beta_0$  vary between cells, following a Gaussian distribution with  $\frac{\sigma^2}{\langle X \rangle} = 0.1$ . Simulate time courses of both models for 100 different "cells" using the following parameters:  $\beta = 2, \beta_0 = 1, \gamma = 1, K = 0.5$ . Plot the nonregulated and autoregulated systems in two separate plots. Comment on the variation you see in the time courses.
- (b) Calculate the deterministic steady state for both models above. How does variation in the basal transcription rate  $\beta$  or  $\beta_0$  enter into the steady state and relate it to what you see in part (a).

3. *Intrinsic and extrinsic noise (based on Elowitz, et al. Stochastic Gene Expression in a Single Cell, Science, 2002.)* Consider a model for stochastic gene expression in a single cell.

Production and degradation of RNA polymerase:



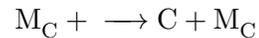
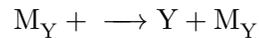
Binding of RNA polymerase to YFP and CFP



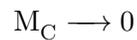
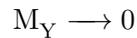
Transcription of YFP and CFP



Translation of YFP and CFP



Degradation of YFP and CFP mRNA



Degradation of YFP and CFP protein



- Assume that the RNA polymerase levels are constant. What do you expect to be the dominant form of noise observed (intrinsic or extrinsic)?
- Assume that the RNA polymerase levels are noisy. How does this change affect intrinsic and extrinsic noise?
- Plot intrinsic and extrinsic noise as a function of  $\alpha$  and  $\delta$ , (with  $\alpha = \delta$ ), does this match your intuition from (a) and (b)?