

Problem Set 4
Due in class

Assigned: 10.21.04
Due: 11.16.04

1. *Waiting times for chemical reactions.*

We showed in class that, for a chemical reaction occurring at rate r , the distribution of waiting times τ between reaction events is given by:

$$\wp(\tau)d\tau = re^{-r\tau}d\tau \quad (1)$$

- (5) a. By integrating over time, verify that the distribution is normalized.
- (5) b. Suppose u is a random variable with some distribution $\wp(u)$, and $\theta(u)$ is a function of u . Then the probability that θ lies between $\theta(u)$ and $\theta(u+du)$ is the same as the probability that u lies between u and $u+du$. This gives us a recipe for calculating the distribution $\wp(\theta)$:

$$\wp(\theta)d\theta = \wp(u)du \quad \Rightarrow \quad \wp(\theta) = \wp(u) \left| \frac{du}{d\theta} \right|.$$

Assuming u is uniformly distributed between 0 and 1, show that the number

$$\theta(u) = \frac{1}{r} \ln \left(\frac{1}{u} \right)$$

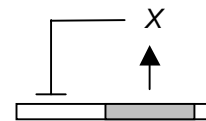
is distributed precisely as required by Eq. 1.

2. *Stochastic simulation of an autoregulatory system.*

In scheme (1), the protein X is expressed constitutively, while in scheme (2), X represses its own synthesis. In a deterministic setting, the concentration of X would evolve according to:

$$(1) \quad \frac{dx}{dt} = A - \gamma x \quad (2) \quad \frac{dx}{dt} = \frac{B}{1 + Kx} - \gamma x.$$

Scheme (2)



For the remainder of this problem, use $\gamma = 1$.

- (5) a. Suggest a plausible biochemical origin for the hyperbolic repression term in scheme (2).
- (10) b. If we measure volume in units of cell size, then concentrations are equivalent to molecule numbers. The accompanying MATLAB code implements a discrete stochastic simulation. Fill in the required lines to model scheme (1). For both $A = 10$ and $A = 100$, verify that the variance and mean of the steady state distribution are consistent with Poisson statistics. Print out histograms of final x values in each case, as well as a copy of your code.
- (15) c. For scheme (2), set $K = 1/100$, and choose B so that $\langle x \rangle \sim 100$ in steady state. Modify the MATLAB code to model scheme (2). Use the simulation to show that the variance of the autoregulated system is lower than that of the constitutive system with the same mean. Print out the final histogram as well as a copy of your code.

2. Stability of a reaction-diffusion system.

In class we discussed the following example of a reaction-diffusion system (equation (128) in the syllabus):

$$\frac{\partial A}{\partial \tau} = 1 + R \frac{A^2}{I} - A + \frac{\partial^2 A}{\partial s^2}$$

$$\frac{\partial I}{\partial \tau} = Q(A^2 - I) + P \frac{\partial^2 I}{\partial s^2}$$

where

$$P = \frac{D_i}{D_a}; Q = \frac{\gamma_i}{\gamma_a}; R = \frac{k_a \gamma_i}{r_a k_i}.$$

In the question below you may assume $R \gg 1$.

- (5) a. Describe in words what this assumption means.
- (10) b. Let's introduce a new parameter $U \equiv Q/P$. Give an interpretation for \sqrt{U} .

As shown in the syllabus, inhomogeneous perturbations can have the following form:

$$A'(s, \tau) = \hat{A}(\tau) \cos\left(\frac{s}{\ell}\right)$$

$$I'(s, \tau) = \hat{I}(\tau) \cos\left(\frac{s}{\ell}\right)$$

where A' and I' are the variations of the activator and inhibitor concentrations around the homogeneous solution. There exists a critical value U_c such that, for $U > U_c$, the homogeneous solution is always stable, independent of the perturbation wavelength ℓ . However for $U < U_c$, stability depends on the value of the wavelength ℓ .

- (10) c. Demonstrate that, in order for the homogeneous solution to be stable against all inhomogeneous perturbations, U should be larger than $U_c \approx 0.17$.
- (15) d. Plot U versus ℓ and indicate the regions of parameter space for the homogeneous solution is stable against inhomogeneous perturbations.
- (10) e. If U is tuned just below U_c , the homogeneous solution is stable for most wavelengths. However, perturbations close to a critical wavelength ℓ_c will blow up. Show that the critical wavelength $\ell_c \approx 1.55$.