

## 6.581/20.482J Problem Set #4

**Due: 5 PM Friday 4/14/06**

### Problem 1

The following model was proposed by Griffith (1971) to describe the positive autoregulation of a gene. In the model, a particular gene codes for an mRNA species  $y$ . The mRNA is then translated to form a protein transcription factor  $x$ . The transcription factor must dimerize so it can go on to bind to the gene's promoter region and enhance the transcription of  $y$ . To simplify the model, the authors have made a few assumptions. First, the rate of transcription for the unbound DNA is assumed to be zero. Second, the binding of transcription factor is assumed to be much faster than the rate of transcription or translation, so transcription factor binding is modeled as a second order equilibrium binding. Third and finally, all other reactions are assumed to be first order. The resulting model is given by the equations 1 and 2:

$$\dot{x} = \gamma_y^x y - \gamma_x^0 x \quad (1)$$

$$\dot{y} = \gamma_{x_2}^y \frac{Kx^2}{1 + Kx^2} - \gamma_y^0 y \quad (2)$$

Here the  $\gamma_{ij}$ 's are rate coefficients and  $K$  is a binding parameter giving a total of five parameters.

We are interested in understanding the dynamics of this system. In particular, we would like to identify the fixed points in the system and then to characterize them as stable or unstable.

1. Solve analytically for the fixed points of this model  $(x^*, y^*)$ . A fixed point is a point where:

$$\begin{pmatrix} \dot{x} \\ \dot{y} \end{pmatrix}_{(x^*, y^*)} = \begin{pmatrix} 0 \\ 0 \end{pmatrix} \quad (3)$$

How many fixed points are there? Does this number depend on the values of the parameters? If so, give the criteria for the number of fixed points.

2. We discussed in class a sufficient criterion for a fixed point to be stable. What is the criterion? Apply this criterion to the model and find the stability of the fixed points in terms of the parameters. You do not have to solve for the eigenvalues explicitly, an implicit solution is acceptable. *Hint: write down the linearized model around the fixed point*

$$\delta \dot{x} = V(x^*) + J_{x^*} \delta x \quad (4)$$

*What is the value of  $V(x^*)$ ?*

3. We have provided an implementation of Newton's method `newton.m`. You will need to fill in the missing lines of the algorithm. For the case,  $\gamma_y^x = \gamma_x^0 = \gamma_{x_2}^y = \gamma_y^0 = 1$  and  $K = 1$ , use Newton's methods to solve for the fixed points numerically. How many fixed points are there? How do your results compare to the analytical solution? Are these fixed points stable?
4. Confirm your answers from Part 3 using the provided simulation code `integrate.m`. *Hint, start your simulation near each one of the fixed points and plot  $x$  vs  $y$ .*
5. Repeat parts 3 and 4 for the case  $\gamma_y^x = \gamma_x^0 = \gamma_{x_2}^y = \gamma_y^0 = 1$  and  $K = 4$ .
6. Repeat parts 3 and 4 for the case  $\gamma_y^x = \gamma_x^0 = \gamma_{x_2}^y = \gamma_y^0 = 1$  and  $K = 6$ .

## Problem 2

In this problem, we give you a model of the bacteriophage lambda lysis lysogeny decision. The model is in the canonical form we discussed in class:

$$\dot{\mathbf{x}} = \mathbf{V}(\mathbf{x}) = A^{(1)}\mathbf{x} + A^{(2)}\mathbf{x} \otimes \mathbf{x} + B^{(1)}\mathbf{u} + B^{(2)}\mathbf{u} \otimes \mathbf{x} \quad (5)$$

1. The file `lambda.m` contains the relevant matrices but leaves blank the lines specifying  $V$  (the time derivative of  $\mathbf{x}$  and  $J$  (the Jacobean of  $V$ ). What is the general form for  $J$ ? Fill in the missing lines of `lambda.m`.
2. Using the filled in `lambda.m` and the Newton's method implementation from Problem 1, find the fixed points of the model. Are these fixed points stable? *Hint: you should try the points suggested in the `lambda.m` file.*
3. How might this pattern of stable, and unstable fixed points help to describe the biology of lambda phage infection?