Mathematics 562  
Homework Assignment 2  
Due Tuesday Feb 22, 2016

Quasi-steady state approximation, Stability of a fixed point and its location on nullclines

Question 1:

1. The FitzHugh-Nagumo model is given by

\[
\begin{align*}
    x' &= f(x) - y, \quad (f(x) = I + x(x - \alpha)(1 - x), \quad 0 < \alpha < 1/2), \\
    y' &= \epsilon(kx - y), \quad (\epsilon, \ k > 0).
\end{align*}
\]

Consider the case \( I = 0. \)

(a) At the limit \( \epsilon \to \infty, \) use quasi-steady state approximation to study the behaviour of the system. Predict the long term behaviour of the system for different initial conditions for distinctive choices of \( k \) while \( \alpha \) is fixed.

(b) Write a .ode file that allows you to study the difference between the approximate system obtained in (a) and the original system for \( \epsilon = 1, 10, 100, 1000. \) (Use \( \alpha = 0.2 \) and \( k = 1, \) and initial condition \( x(0) = 1, \ y(0) = 0. \)) (Hint: Define the fast variable as a function of the slow one obtained in the quasi-steady state approximation as an aux variable in XPP. Then, plot it against the fast variable in the original system in comparison). Identify the difference between the two.

(c) If \( \alpha \) is a fixed parameter, find the value \( k = k_c \) at which a SN of steady state occurs (i.e., there is one s.s. for \( k > k_c \) and three for \( k < k_c. \))

(d) Sketch the nullclines of the system for \( k > k_c. \)

2. Now, consider the FitzHugh-Nagumo model for \( I \neq 0. \)

(a) Show that for \( k > f'((1 + \alpha)/3) > k_c, \) there is only one fixed point for changing values of \( I. \)

(b) Show that for \( k > f'((1 + \alpha)/3) > k_c, \) the determinant of \( J(x_s, y_s) \) is always positive.

(c) Show that for \( k > f'((1 + \alpha)/3) > k_c, \) \( f'(x_s) = \epsilon \) is a Hopf bifurcation which is only possible when \( 0 < \epsilon < f'((1 + \alpha)/3). \)

(d) Show that for \( k > f'((1 + \alpha)/3) > k_c, \) the steady state is unstable if \( f'(x_s) > \epsilon \) which is only possible when \( 0 < \epsilon < f'((1 + \alpha)/3). \)

(e) Verify the results in (a)-(d) using XPP.
Question 2:

Consider the following form of FitzHugh-Nagumo equation

\[
\begin{align*}
\dot{x} &= f(x) - y, \\
\dot{y} &= \epsilon(x + a),
\end{align*}
\]

where \( f(x) = x - x^3/3 \), \( \epsilon > 0 \) and \( a \) are parameters.

(a) Show that the steady state \((x_s, y_s) = (-a, f(-a))\) is stable if \( f'(x) < 0 \) at the fixed point. It is unstable if \( f'(-a) > 0 \). Show that \( f'(x) = 0 \) at \( x = \pm 1 \) which happens when \( a = \mp 1 \). Both are Hopf bifurcation points.

(b) Use XPP to demonstrate that for \( a \) values slightly larger than 1, the system is more excitable as the value of \( \epsilon \) decreases. The degree of excitability can be determined by the amplitude of the response of the system to stimuli that are above threshold.

(c) Use XPPAUT to draw the bifurcation diagrams against parameter \( a \) for three different values of \( \epsilon \): 1, 0.1, 0.01. Draw both the steady state and oscillatory branches of the solutions.

Question 3:

In the glycolytic oscillator model,

\[
\begin{align*}
\text{Hexoses} & \rightarrow \text{F6P} \rightarrow \text{FBP} \rightarrow \text{...} \rightarrow 2 \text{Pyruvate} \\
\text{ATP} & \rightarrow \text{ADP} \rightarrow 2 \text{ADP} \rightarrow 2 \text{ATP}
\end{align*}
\]

Letter \( S \) denotes the substrate of the reaction, \( P \) represents the product. We assume that the allosteric enzyme \( E \) has 2 identical subunits and that the enzyme in R (relaxed) state binds to \( S \) and \( P \) but not the T (tense) state. Monod-Wyman-Changeux model (Monod, J., Wyman, J, Changeux, J.P. On the nature of allosteric transitions: a plausible model. \textit{J Mol Biol.} 12:88-118, 1965) leads to the following system of ODEs
\[
\begin{align*}
\frac{ds}{d\tau} &= v - \phi(s, p), \\
\frac{dp}{d\tau} &= \epsilon^{-1}\phi(s, p) - p,
\end{align*}
\] (2)

where \( s = [S]/K_S, p = [P]/K_P, \tau = kt, v = V/(kK_S), \sigma = 2k[E]_T/(kK_S), \epsilon = K_P/K_S, \)
\( L = k_1/k_2 \) are all positive dimensionless.

Here are the assignments:

(a) The nullclines of this system are plotted in the figure given below. Show that the steady state is unstable only when it is located on the part of \( p' = 0 \) nullcline where the slope satisfies

\[
\left. \frac{ds}{dp} \right|_{p'=0} < -\epsilon.
\]

That is, it is unstable only when the slope is more negative than \(-\epsilon\).

(b) Explain why the specific functional form of \( \phi(s, p) \) is not important for the previous result to hold as long as it generates the \( N \)-shaped nullcline in the fast variable and the monotonic nullcline in the slow variable and that: \( \frac{\partial \phi}{\partial s} > 0 \) and \( \frac{\partial \phi}{\partial p} > 0 \) for all \( s, p > 0 \).