LPA - WAVE PINNING HOMEWORK

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This HW is intended to give you familiarity with the application of the Local Perturbation Analysis (LPA) to reaction diffusion systems. We will consider a cell biology related system (see Mori, 2008 Biophys. J.). The system to be discussed is given by the following equations

$$\frac{du}{dt} = f(u,v) + D_u \triangle u \qquad \frac{dv}{dt} = -f(u,v) + D_v \triangle u \tag{0.1}$$

where

$$f(u,v) = \left(k_0 + \gamma \frac{u^n}{k^n + u^n} \right) v - \delta u. \tag{0.2}$$

This system is indicative of Rho-GTPase dynamics where u represents and active, slow diffusing form and v an inactive fast diffusing form. k_0 is a basal activation rate, n a Hill coefficient, and δ an inactivation rate. Use the following as a base parameter set

$$k_0 = .02, \quad \gamma = .1, \quad k = 1, \quad \delta = .1, \quad n = 4, \quad T = 2 \tag{0.3}$$

where T is the total CONSERVED concentration $u + v$.

Note that where bifurcation diagrams are produced, any bifurcation software package is sufficient. I have a few short videos regarding the use of Matcont on my website as well as included matlab codes for precisely this system.

(1) For the base parameter set, compute the well mixed steady state (u^s, v^s) (diffusion removed and only the kinetics considered). Is it stable or unstable?
(2) Using either Matcont or XPP (or another package), continue this equilibrium with respect to k_0. Is the well mixed system stable or bistable? (Hint, the two equations in (0.1) are degenerate and the linearized system will have a 0 eigenvalue due to linear dependence. Use conservation ($v = T - u$) to remove one of the equations eliminating this degeneracy.
(3) Raise and lower δ (inactivation rate) in increments and recompute the well mixed bifurcation diagram (steps 1,2 repeated). What do you notice?
(4) Vary γ as well. What do you notice?
(5) In the above variations, the well mixed system should exhibit bistability in some circumstances. What parameter variations lead to this behaviour? How can this be interpreted?
(6) Return to the base parameter set and fix v at its well mixed steady state. With v fixed, solve $f(u,v) = 0$ for u. How many solutions do you get?
(7) Write down the LPA system associated with (0.1). Recall, slow variables will have local and global forms while fast variables only have global forms.
(8) Perform a LPA as follows
    (a) First notice that the equations for u^g and v^g are degenerate. Use conservation to eliminate v^g and reduce the system to 2 equations.

Date: May 24, 2012.

(b) Verify that $u^l = u^s$, $u^g = u^s$ is a steady state of the reduced LPA system of ODE's. Note that this is just the situation where the local and global forms are the same and is representative of the well mixed steady state.

(c) Continue this equilibrium forward and backward with respect to k_0. What do you notice about the values of u^l, u^g on this branch? (Hint: Pay attention to eigenvalues to keep track of the stability of various branches.)

(d) Two branch points should appear. Switch branches and continue along the intersecting branch. What do you notice about the values of u^l, u^g on this branch?

(9) For the resulting bifurcation diagram, you should see one curve that is increasing with k_0 and another that forms a loop structure. Interpret these curves. How do the various curves correlate to the different states found in question 7?

(10) In which regions are the well mixed steady state unstable vs stable? Where can patterning occur?

(11) Perform similar parameter variations with δ and γ as above. What do you notice?

(12) EXTRA CREDIT: This analysis determines distinct pattern forming regimes. These can be verified through 1D simulation. Choose the domain length $L = 1$ along with $D_u = .01$ or .001, $D_v = .1$ and run simulations for various parameter values. This can be done with *pdepe* in matlab.

(13) EXTRA CREDIT: Change the Hill coefficient to $n = 3$ and perform a similar analysis. What changes? Are these changes meaningful in a biological sense? (This requires a good understanding of the underpinnings of the LPA and what the various branches in a LPA represent.)