Problem Set 5

1. *Stability of a reaction diffusion system*.

Consider the following general reaction diffusion system

$$\frac{\partial u}{\partial t} = A_1 F(u,v) + D_1 \frac{\partial^2 u}{\partial x^2}$$
$$\frac{\partial v}{\partial t} = A_2 G(u,v) + D_2 \frac{\partial^2 v}{\partial x^2}$$

(4) *a*. Show that by choosing units properly this system can be rewritten as

$$\frac{\partial \bar{u}}{\partial \bar{t}} = \gamma F(u,v) + \frac{\partial^2 \bar{u}}{\partial \bar{x}^2} \equiv \gamma f(\bar{u},\bar{v}) + \frac{\partial^2 \bar{u}}{\partial \bar{x}^2}$$
$$\frac{\partial \bar{v}}{\partial \bar{t}} = \gamma G(u,v) + d\,\frac{\partial^2 \bar{v}}{\partial \bar{x}^2} \equiv \gamma g(\bar{u},\bar{v}) + d\,\frac{\partial^2 \bar{v}}{\partial \bar{x}^2}$$

From now on we will work with this system and we will drop the bars to simplify the notation. Assume $\gamma > 0$.

(4) *b*. Let's first consider some homogeneous solution $u(x,t) = u_0$ and $v(x,t) = v_0$. Write, in terms of the derivatives of the functions f and g, the conditions that will ensure the stability of this solution. From now on, assume that this solution is stable.

(4) *c*. As done in class, now consider inhomogeneous perturbations of the form

$$u(x,t) = u_0 + \delta u(t)\cos(x/\ell)$$
$$v(x,t) = v_0 + \delta v(t)\cos(x/\ell)$$

and, assuming $\delta u(t)$ and $\delta v(t)$ to be small, derive linear differential equations for $\delta u(t)$ and $\delta v(t)$.

(6) *d*. Show that in order for at least some of these perturbations to be unstable these conditions must hold:

$$d f_u + g_v > 0$$
$$(d f_u + g_v)^2 - 4d(f_u g_v - f_v g_u) > 0$$

where, for instance, f_u stands for the partial derivative of f with respect to u evaluated at (u_0, v_0). Show that these conditions along with the ones derived in part *b* imply that the signs of f_u and g_v must be different. Aditionally show that when we assume that $f_u > 0$ then $d > 1$.

(6) *e*. What are the possible interaction structures compatible with a system that presents this kind of instability? (*i.e.*, How does each variable affect itself and the other near the fixed point? Inhibiting or enhancing production?) Compare these structures with the local-activation-long-range-inhibition picture. What does the condition $d > 1$ represent in each case?

(7) *f*. Look up in the literature for two examples of pattern forming systems and compare the networks involved with the ones you derived in *e*.

2. *Turing patterns in 2D*.

We will consider the following dimensionless system restricted to a square region in 2D with a side of length L and periodic boundary conditions.

$$\frac{\partial u}{\partial t} = \gamma\left(a - u - \frac{\rho u v}{1 + u + K u^2}\right) + \nabla^2 u$$
$$\frac{\partial v}{\partial t} = \gamma\left(\alpha(b - v) - \frac{\rho u v}{1 + u + K u^2}\right) + d\nabla^2 v$$
where $\nabla^2 f = \frac{\partial^2 f}{\partial x^2} + \frac{\partial^2 f}{\partial y^2}$

We will work with the parameters $d = 10$, $a = 92$, $b = 64$, $\alpha = 1.5$, $\rho = 18.5$, $K = 0.1$ and we will try to study how the behavior changes as γ is varied.

(4) *a*. Show that by choosing length and time units properly a system in which the length of the square is L' can be thought as a system in which $L = 1$ but with a different value of γ. So, we can think that by changing γ we are effectively studying systems of different sizes.

(4) *b*. Compute the homogeneous stationary solutions u_0 and v_0 numerically.

(4) *c*. Show that for the given parameter values the system in unstable to some inhomogeneous perturbations.

(6) *d*. What are the unstable wave vectors or wave lengths? Your answer will depend on γ.

(6) *e*. Now we will study the system numerically using an explicit first order Euler scheme for approximating the solution of the partial differential equations. For pure diffusion this scheme involves discretizing

$$\frac{\partial u}{\partial t} = D\left(\frac{\partial^2 u}{\partial x^2} + \frac{\partial^2 u}{\partial y^2}\right) \text{ into}$$

$$\frac{u_{n+1,m_x,m_y} - u_{n,m_x,m_y}}{\Delta t} = D\left(\frac{u_{n,m_x+1,m_y} + u_{n,m_x-1,m_y} - 2u_{n,m_x,m_y}}{\Delta \ell^2} + \frac{u_{n,m_x,m_y+1} + u_{n,m_x,m_y-1} - 2u_{n,m_x,m_y}}{\Delta \ell^2}\right)$$

where we have set $u(n\Delta t, m_x\Delta\ell, m_y\Delta\ell) = u_{n,m_x,m_y}$. Propose a solution of the form $u_{n,m_x,m_y} = \xi^n e^{i(m_x k_x + m_y k_y)\Delta\ell}$ and compute ξ in terms of k_x, k_y, Δt and $\Delta\ell$. What condition on ξ will ensure that the method is numerically stable? Show that in order to get numerical stability you need

$$\Delta t < \frac{\Delta\ell^2}{4D}.$$

How would you generalize this condition to the case when you have two species with different diffusion coefficients?

(6) *f*. Simulate the system for different values of γ and study whether patterns form or not. You can start by trying γ = 0, 10, 100, 1000. Let the system evolve till you are convinced that it has

reached a stationary behavior. What kind of patterns do you get? Do you always get patterns? Why? Note: These simulations will take some time to run; plan ahead.

3. *Spatial oscillations in E. coli – Howard et al model*[1].

Consider the Howard model for the spatial oscillations of the proteins that control the positioning of the midcell division plane

$$\frac{\partial \rho_D}{\partial t} = -\frac{\sigma_1 \rho_D}{1+\sigma_1' \rho_e} + \sigma_2 \rho_e \rho_d + D_D \frac{\partial^2 \rho_D}{\partial x^2}$$

$$\frac{\partial \rho_d}{\partial t} = +\frac{\sigma_1 \rho_D}{1+\sigma_1' \rho_e} - \sigma_2 \rho_e \rho_d$$

$$\frac{\partial \rho_E}{\partial t} = +\frac{\sigma_4 \rho_e}{1+\sigma_4' \rho_D} - \sigma_3 \rho_D \rho_E + D_E \frac{\partial^2 \rho_E}{\partial x^2}$$

$$\frac{\partial \rho_e}{\partial t} = -\frac{\sigma_4 \rho_e}{1+\sigma_4' \rho_D} + \sigma_3 \rho_D \rho_E$$

In these equations ρ_D represents the linear number density of MinD in the cytoplasm, ρ_d the density of MinD bound to the membrane and ρ_E and ρ_e are the analogous quantities for MinE. We will consider this system in a finite 1D region of length L with no-flux boundary conditions on the end points, *i.e*. for every density ρ, at any given time, on the end points we have

$$\left.\frac{\partial \rho}{\partial x}\right|_{t,x=\text{end point}} = 0$$

We will use this set of parameters: $\sigma_1 = 20\ \mathrm{s}^{-1}$, $\sigma'_1 = 0.028\ \mu\mathrm{m}$, $\sigma_2 = 0.0063\ \mu\mathrm{m/s}$, $\sigma_3 = 0.04\ \mu\mathrm{m/s}$, $\sigma_4 = 0.8\ \mathrm{s}^{-1}$ and $\sigma'_4 = 0.027\ \mu\mathrm{m}$, $D_D = 0.28\ \mu\mathrm{m}^2/\mathrm{s}$, $D_E = 0.6\ \mu\mathrm{m}^2/\mathrm{s}$, $L = 2\ \mu\mathrm{m}$.

(3) *a*. Give a biological interpretation for every term in the equations.

(5) *b*. Show that the total amount of MinD and MinE are conserved quantities. We will consider the average densities of MinD and MinE, which equal these total conserved amounts divided by L, as two other parameters of the system; we will call them $\langle\rho_D\rangle$ and $\langle\rho_E\rangle$. They do not explicitly appear in the set of equations above, so, how do they enter the model? Based on the literature, give estimates for the order of magnitude of these two quantities.

(4) *c*. Under what conditions is the trivial solution $\rho_D = 0$, $\rho_d = \langle\rho_D\rangle$, $\rho_E = \langle\rho_E\rangle$, $\rho_e = 0$ unstable to homogeneous perturbations?

(5) *d*. Write a system of equations for computing the homogeneous steady state solutions and write some MATLAB code for computing nontrivial homogeneous steady state solutions numerically (when they exist). Plot the nontrivial stable homogeneous steady state relative density of MinD in the cytoplasm ($\equiv \rho_D / \langle\rho_D\rangle$) as a function of $\langle\rho_D\rangle$ and $\langle\rho_E\rangle$ in the range $\langle\rho_D\rangle \in [0, 2500]\ \mu\mathrm{m}^{-1}$, $\langle\rho_E\rangle \in [0, 150]\ \mu\mathrm{m}^{-1}$. You might find the MATLAB commands `surf`, `mesh`, `pcolor` or similar ones, useful for the plotting.

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[1] Phys. Rev. Lett. 87 (27), 278102 (2001).

(4) *e*. Set your coordinate system so that the endpoints of the region of interest are at $x = \pm L/2$ and consider an arbitrary small perturbation around the homogenous steady state of the form $\rho_i = \rho_{i,\mathrm{hss}} + \delta\rho_i \cos(kx)$. What are the possible values of k compatible with the boundary conditions of the problem? How does your answer change if you consider perturbations of the form $\rho_i = \rho_{i,\mathrm{hss}} + \delta\rho_i \sin(kx)$?[2]

(6) *f*. Write code that will compute the eigenvalues of the system when disturbed from equilibrium with a perturbation of wave vector k. Plot the real and imaginary part of the eigenvalues as a function of k for these two cases:
(i). $\langle\rho_D\rangle = 1000\ \mu\mathrm{m}^{-1}$; $\langle\rho_E\rangle = 75\ \mu\mathrm{m}^{-1}$.
(ii).$\langle\rho_D\rangle = 2000\ \mu\mathrm{m}^{-1}$; $\langle\rho_E\rangle = 125\ \mu\mathrm{m}^{-1}$.

(6) *g*. Divide the parameter space $\langle\rho_D\rangle \in [0, 2500]\ \mu\mathrm{m}^{-1}$, $\langle\rho_E\rangle \in [0, 150]\ \mu\mathrm{m}^{-1}$ in 100×100 points and for each combination of parameters decide whether the nontrivial homogeneous solution is stable or not against inhomogeneous perturbations. If it is unstable, is the imaginary part of the unstable eigenvalues zero? Use this information to construct a phase diagram in which you identify regions for which the system exhibits different qualitative behaviors.

(6) *h*. Write some code to simulate the system for some combinations of parameters in the distinct regions you found in *h*. How do you have to choose Δt in order to avoid numerical instabilities? Use inhomogeneous initial conditions in order to test the system against this kind of perturbations. For each simulation show space-time plots of $\rho_d / \langle\rho_D\rangle$ for a period of time of at least 200 s once a regular behavior is established. These simulations might take some time to run, so plan in advance!

[2] The subindex hss stands for homogenous steady state.