1. **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.

\[
\frac{\partial u}{\partial t} = \gamma \left( a - u - \frac{\rho u v}{1 + u + Ku^2} \right) + \nabla^2 u
\]

\[
\frac{\partial v}{\partial t} = \gamma \left( \alpha (b - v) - \frac{\rho u v}{1 + u + Ku^2} \right) + d \nabla^2 v
\]

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 $\gamma$ is varied.

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

(5) b. Compute the homogeneous stationary solutions $u_0$ and $v_0$ numerically.

(5) c. Show that for the given parameter values the system is unstable to some inhomogeneous perturbations.

(5) d. What are the unstable wave vectors or wave lengths? Your answer will depend on $\gamma$.

(5) e. Now we will study the system numerically. In order to do this you can use the attached MATLAB code `ps5_1.m` (and the routine `laplacian2dperiodic.m`), which implements an explicit first order Euler scheme for solving the partial differential equations. For pure diffusion this scheme involves discretizing

\[
\frac{\partial u}{\partial t} = D \left( \frac{\partial^2 u}{\partial x^2} + \frac{\partial^2 u}{\partial y^2} \right)
\]

\[
\frac{u_{n+1,m,m} - u_{n,m,m}}{\Delta t} = D \left( \frac{u_{n,m+1,m} + u_{n,m-1,m} - 2u_{n,m,m}}{\Delta \ell^2} + \frac{u_{n,m,m+1} + u_{n,m,m-1} - 2u_{n,m,m}}{\Delta \ell^2} \right)
\]

where we have set $u(n\Delta t, m_\Delta \ell, m_\Delta \ell) = u_{n,m,m}$. Propose a solution of the form $u_{n,m,m} = \xi \exp(k_x m \Delta \ell + k_y m \Delta \ell)$ and compute $\xi$ in terms of $k_x$, $k_y$, $\Delta t$ and $\Delta \ell$. What condition on $\xi$ 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?

(5) f. Simulate the system for different values of $\gamma$ and study whether patterns form or not. You can start by trying $\gamma = 0, 10, 100, 1000$. 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.

(0) **g. CHALLENGE:** What is the symmetry of the patterns that you get? Why do you get that type of symmetry?

2. **Spatial oscillations in E. coli – Howard et al model**.

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

\[
\frac{\partial \rho_D}{\partial t} = -\frac{\sigma_1 \rho_D}{1 + \sigma_1 \rho} + \sigma_2 \rho_c \rho_d + D_D \frac{\partial^2 \rho_D}{\partial x^2}
\]

\[
\frac{\partial \rho_d}{\partial t} = +\frac{\sigma_3 \rho_D}{1 + \sigma_1 \rho} - \sigma_2 \rho_c \rho_d
\]

\[
\frac{\partial \rho_E}{\partial t} = +\frac{\sigma_4 \rho_c}{1 + \sigma_4 \rho} - \sigma_3 \rho_D \rho_E + D_E \frac{\partial^2 \rho_E}{\partial x^2}
\]

\[
\frac{\partial \rho_e}{\partial t} = -\frac{\sigma_4 \rho_c}{1 + \sigma_4 \rho} + \sigma_3 \rho_D \rho_E
\]

In these equations \(\rho_D\) represents the linear number density of MinD in the cytoplasm, \(\rho_d\) the density of MinD bound to the membrane and \(\rho_E\) and \(\rho_e\) 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 \(\rho\), at any given time, on the end points we have

\[
\frac{\partial \rho}{\partial x} \bigg|_{x \text{ end point}} = 0
\]

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

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

(4) **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?

(4) **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 \(\langle \rho_D \rangle \in [0, 2500] \text{ \mu m}^{-1}\).

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\[ \langle \rho_D \rangle \in [0, 150] \ \mu \text{m}^{-1} \]. You might find the MATLAB commands `surf`, `mesh`, `pcolor` or similar ones, useful for the plotting.

(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 \( \rho_i = \rho_{i, \text{hss}} + \delta \rho_i \cos(kx) \). 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 \( \rho_i = \rho_{i, \text{hss}} + \delta \rho_i \sin(kx) \)?

(10) f. Write a MATLAB 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). \( \langle \rho_D \rangle = 1000 \ \mu \text{m}^{-1}; \langle \rho_E \rangle = 75 \ \mu \text{m}^{-1} \).
(ii). \( \langle \rho_D \rangle = 2000 \ \mu \text{m}^{-1}; \langle \rho_E \rangle = 125 \ \mu \text{m}^{-1} \).

(10) g. Divide the parameter space \( \langle \rho_D \rangle \in [0, 2500] \ \mu \text{m}^{-1}, \langle \rho_E \rangle \in [0, 150] \ \mu \text{m}^{-1} \) 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 zero or not? Use this information to construct a phase diagram in which you identify regions for which the system exhibits different qualitative behaviors.

(5) h. Modify the accompanying MATLAB code `ps5_2.m` to simulate the system for some combinations of parameters in the distinct regions you found in h. How do you have to choose \( \Delta t \) 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 \( \rho_a / \langle \rho_D \rangle \) 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!

3. **Gradient sensing.**

The concentration distribution along the surface of a cell in a linear chemical gradient has the general form \( c(\theta) = c_0 + c_1 \cos(\theta) \), with the angle \( \theta \) measured from the cell’s leading edge. We will calculate how a cell might respond to such a stimulus, based on the receptor activation-inactivation model of Levchenko and Iglesias.

This model assumes that two biochemical species, \( A \) and \( I \), are produced in the cell membrane at rates linearly proportional to the extracellular signal concentration \( c(\theta) \). The levels of these chemicals are “read out” by a receptor R whose steady state concentration is given by \( r_{\text{ss}} = a / i \) (where lower case letters represent normalized concentrations). Both \( A \) and \( I \) undergo first-order decay, and both diffuse along the membrane. The equations describing this system are:

\[
\begin{align*}
\frac{\partial a}{\partial t} &= \gamma_a (c(\theta) - a) + D_a \frac{\partial^2 a}{\partial \theta^2} \\
\frac{\partial i}{\partial t} &= \gamma_i (c(\theta) - i) + D_i \frac{\partial^2 i}{\partial \theta^2}
\end{align*}
\]

\(^2\) The subindex hss stands for homogenous steady state.

\(^3\) Biophys J. 82, 50-63 (2002).
(5)  a.  First assume a uniform concentration situation: $c(\theta) = c_0$. In this case, $a$ and $i$ will be independent of $\theta$. Calculate the steady state values of $a$, $i$, and $r_{ss} = a / i$. Now suddenly double the signal concentration to $2c_0$. Calculate the time evolutions $a(t)$ and $i(t)$. For $\gamma_a = 5$ and $\gamma_i = 1$, plot $r(t) = a(t) / i(t)$. Is the system perfectly adapting?

(8)  b.  Now assume a linear concentration gradient $c(\theta) = c_0 + c_1 \cos(\theta)$. Guess a solution of the form $a(\theta, t) = c_0 + \beta_a(t) \cos(\theta)$, $i(\theta, t) = c_0 + \beta_i(t) \cos(\theta)$, substitute these guesses into the dynamical equations and calculate the steady state values of $\beta_a$ and $\beta_i$. Also write down an expression for $r_{ss}(\theta)$.

(7)  c.  Suppose that $A$ diffuses slowly, while $I$ diffuses fast, i.e., take $D_a/\gamma_a << 1$ and $D_i/\gamma_i >> 1$. What is $r_{ss}(\theta)$ in this limit?

(5)  d.  These calculations show that the system is perfectly adapting in uniform concentrations, but polarized in a concentration gradient, matching experimental observations. Explain in words how this behavior comes about.