Homework 5_Gierer-Meinhardt
Modeling Biological Systems
Spring 2024

DUE: Monday, April 22, 2024, by midnight

You may consult with the TAs, but all scripts and answers must be your own. We will inspect the scripts and answers closely. Please do this on your own!!

The project is based loosely on the following paper
Gierer, A. and Meinhardt, H. (1972). A theory of biological pattern formation. Kybernetik 12, 30–39.

The Gierer-Meinhardt equations (Equations12a/12b or 15a/15b in the paper) are similar to the Turing equations:

$$\frac{\partial A}{\partial T} = k_a \frac{A^2}{H + H_0} - \omega_a A + \Sigma + D_a \frac{\partial^2 A}{\partial X^2} \qquad Eq. 1$$

$$\frac{\partial H}{\partial T} = k_h A^2 - \omega_h H + D_h \frac{\partial^2 H}{\partial X^2} \qquad Eq. 2$$

These equations "improve" the Turing equation by making it more physiological. For example, both activator (A) and inhibitor (H) are subject to degradation, the ω_a, ω_h terms, whereas in Turing only the inhibitor degraded. The activation of A and H are cooperative; this is important because it distinguishes the activation of A from its degradation. Another improvement is that H inhibits A through the denominator term. This prevents A and H becoming negative. H_0 is a small constant that prevents division by zero (I added this) and Σ is a small synthesis term for A. All the coefficients are ≥ 0 (from physical considerations).

Equations 1 and 2 have 6 free parameters (ignoring H_0 and Σ, which are small). We can reduce the number of free parameters to 2 by non-dimensionalizing the equations:

$$\frac{\partial a}{\partial t} = \frac{a^2}{h + h_0} - a + \sigma + D \frac{\partial^2 a}{\partial x^2} \qquad Eq. 3$$

$$\frac{\partial h}{\partial t} = \omega(a^2 - h) + \frac{\partial^2 h}{\partial x^2} \qquad Eq. 4$$

where $D = D_a/D_h$ is the ratio of the diffusion coefficients and $\omega = \omega_h/\omega_a$ is the ratio of the degradation rates. Note that four parameters have been removed my normalizing time, position, activator concentration and inhibitor concentration so there are really only 2 parameters, D and ω (we will take $h_0 \ll 1$ and $\sigma \ll 1$).

<u>Question 1</u> (1 point for graduate students, bonus for undergrads)
Non-dimensionalize Equations 1 and 2 to give Equations 3 and 4.
Hint. Substitute $T = \alpha t$, $X = \beta x$, $A = \chi a$, $H = \delta h$. The parameters $\alpha, \beta, \chi, \delta$ are "free parameters" that can be chosen at will to simplify the equation. First knock out ω_a. Then

D_h. Then k_a (to get the ratio χ/δ). Finally, force $a^2$and h to have the same prefactors in the inhibitor equation.

<u>Question 2</u>

(i) (2 points) Taking $h_0 \ll 0$ and $\sigma = 0$, find the nontrivial fixed points (i.e. $a \neq 0$ and $h \neq 0$) of Eq. 3 & 4 when there is no spatial gradient (i.e., the spatial derivatives are zero).

<u>Question 3</u>

(i) (2 points) For a sinusoidal spatial gradient $a = a_0 \sin kx$ and $h = h_0 \sin kx$ find the Jacobian matrix at the fixed point you found in Question 2 (assume $h_0 \ll 1$ and $\sigma \ll 1$). The Jacobian is

$$\mathbf{J} = \begin{pmatrix} \partial f/\partial a & \partial f/\partial h \\ \partial g/\partial a & \partial g/\partial h \end{pmatrix}$$

Note that this defines an equivalent Turing system.

(ii) (1 points) In the absence of a spatial gradient, what is the condition on ω for the fixed point to be stable?

(iii) (1 point) What is the interpretation of this condition on ω?

<u>Question 4</u> (1 point)

In the notes, we showed that at the critical point, where the linear Turing system starts oscillating, $\det\mathbf{J} = \mathbf{0}$ and $\det'\mathbf{J} = 0$ (where the prime is differentiation with respect to k^2). Using the condition $\det'\mathbf{J} = 0$ with the Jacobian above, find the relationship between the spatial frequency k and the parameters D and ω when the system first becomes unstable at the fixed point. Show that you recover the formula for the wavelength $L = 2\pi/k$ given on page 7 of the notes, noting that a from the notes is 1, $d = -\omega$, $\mu = D$ and $\nu = 1$.

<u>Question 5</u> (5 points)

Put the script folder in your MatLab folder. The program PS5_GM_equation.mlx has four trial pairs of parameters (D, ω), one in each section.
These correspond to the four different types of behavior.
(i) (1 point) A stable pattern for $(0.05, 2)$. What is the wavelength? How does the wavelength compare to your prediction in Question 4? What are some possible reasons for the discrepancy (Hint: see part (iv)).

(ii) (1 point) A homogenous steady state for $(0.4, 2)$. How do the steady state values of a and *h* compare to the predictions in Question 2? Why is there a discrepancy (I must admit that I don't understand why it is so large)?

(iii) (1 point) The third is a temporal oscillation for $(0.4, 1)$. Any idea where this is coming from?

(iv) (1 point) The fourth is trivial solution for $(0.4, 0.5)$. Check that the fixed point (0,0) (when $\sigma = 0$) is stable by evaluating the Jacobian at (0,0).

(iv) (2 points) Use the supplied MATLAB code to map out the “phase diagram” for oscillations of the non-dimensionalized Gierer-Meinhardt equation given in Question 1. Explore other pairs of parameters and determine the boundaries between the different behaviors. Keep your parameters between $(0.05, 0.05)$ and $(0.5,5)$, otherwise the results may be unpredictable. <u>Note:</u> for the purposes of the homework, you can change $tmax$ (the time the simulation is run for) up to 500, but don’t make it too long (I don’t want the problem to be unending, and I cannot guarantee that the long-time behavior is correct).

Please hand in a copy of the phase diagram with the points that you tried out (you don’t have to show them all). Plot D on the x-axis and ω on the y-axis. Use different behaviors color or symbols to distinguish the different behaviors. Draw lines (by hand) to indicate the different regions.

<u>Question 6</u>. (1 point for graduate students, bonus for undergrads)
(i) Get the approximate boundary between the stable uniform solution and the temporally oscillating and spatially uniform solution by setting $k^2 = 0$ in the determinant of the Jacobian and use the condition that a negative determinant leads to an unstable solution.

(ii) In your phase plot, you will see that there is a line that separates a stable spatial pattern from a stable uniform solution. As you cross the line (from right to left) the system becomes unstable. Calculate the equation for his line from the condition that the system becomes critical when $\det\mathbf{J} = \mathbf{0}$ and $\det'\mathbf{J} = 0$. This is a bit complicated, so start by using the formula for the spatial frequency squared (k^2) (Question 4) and substitute this into $\det\mathbf{J} = 0$ to get a relation between D and ω.