

Reaction Diffusion models for biological pattern formation

Fahim Alam

Introduction

Alan Turing presented a revolutionary idea in 1952 that a combination of reaction and diffusion can cause spatial patterns. He also showed that the behavior of a complex system in which two substances interact with each other and diffuse at different diffusion rates, which is known as the reaction–diffusion (RD) system. Turing proved mathematically that such system can form some characteristic spatial-temporal patterns in the field.

If we consider the simplest 1-dimensional case, let $u(x, t)$ be the concentration of some chemical placed on the real line on x at time t . Then, the reaction-diffusion equation has the form:

$$\frac{\partial u}{\partial t} = D_u \frac{\partial^2 u}{\partial x^2} + f(u) \quad (1)$$

where D_u is a coefficient associated with the diffusive properties of u , and $f(u)$ is a function that describes how u grows or decays depending on its current state. In equation 1, the first term on the RHS is diffusion and the other term is reaction.

When we think of a “reaction”, the first thing that comes to our mind is probably that of a mad chemist mixing two chemicals together and causing a minor bang. But in the case of Equation (1), what is the single chemical (whose concentration is u) reacting with? In some sense, a one-dimensional reaction means that the chemical is reacting with zero and is either producing more of itself or decaying. A simple example of a decaying f is

$$f(u) = -u$$

and leads to formulate the well-known model of

$$\frac{du}{dt} = -u$$

which has many applications including radioactive decay, and protein degradation. It is imperative to know that here the term “reaction” is used lightly, so it is best to think of $f(u)$ as the function that defines how the concentration of u changes depending on its local value. Reactions in 2D are possibly more intuitive since they comprise two concentrations, say, $u(x, t)$ and $v(x, t)$; some examples are:

Chemical reactions: Imagine you have a beaker and you have two chemicals and you pour them in and they begin reacting.

Population dynamics: We have two possibilities. In a predator-prey example, the “reaction” is that whenever the predator and prey are close enough to each other the predator will eat the prey. In a competitive system, then they will not eat each other, but due to limited resources, the two populations will die off if their population density gets too high.

Now let’s talk about diffusion. Before the year 1800s, the term ‘diffusion’ was used in physics to define how particles of gases, liquids, and solids interact and interchange from areas of high concentration to low concentration without chemical amalgamation because of each particle’s kinetic energy. Adolf Fick described diffusion mathematically and arrived at this result using a macroscopic approach. In fact, the diffusion equation

$$\frac{\partial u}{\partial t} = D_u \frac{\partial^2 u}{\partial x^2}$$

is also known as Fick’s second law [Mehrer and Stolwijk, 2009]. In this project, however, we will cover a microscopic derivation of the diffusion equation that is closely related to Brownian motion. Brownian motion is coined after Robert Brown. He described “an unusual character in the motions of the elements of pollen in water”, and more prominently he specified that this motion is not due to the elements being alive but is instead of a mechanical nature. Albert Einstein, 50 years later, proposed a first approximation to Brownian motion from a physical perception. Einstein’s intellectual image of Brownian motion demonstrates the link to diffusion. He imagined a microscopic particle (e.g. one of Brown’s pollen elements) suspended in liquid. The pollen element is microscopic, but usually much larger than

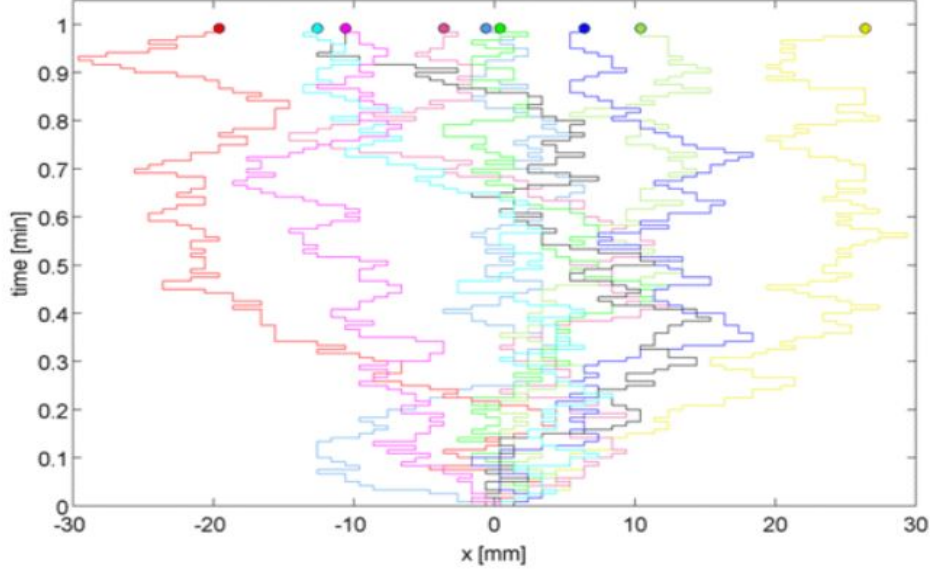


Figure 1: **Diffusing particles** This figure demonstrates the trail of 10 particles that were ongoing from the origin. At each time step of size $\Delta t = .01$, the particles will shift their directions by $dx = 1$. The simulation is run for $t = 1$ and the path of each particle is plotted in the particle's color.

the molecules in the fluid, so every time it gets “hit” by the fluid molecules, the particle will move a small amount or each hit. The hits come at random intervals and from all directions [Einstein, 1956][Nelson, 1967].

We consider a 1D mesh, where, at $x = 0, \pm h, \dots$, we define the concentration $u(x, t)$ as the predictable number of particles in the spot x at time t . Let us assume first that after some time Δt i.e $t = t + \Delta t$ each particle moved right or left with equal probability $\frac{p}{2}$ or stayed in the same place with probability $1 - p$. Then, the expected concentration at the next point is:

$$u(x, x + \Delta t) = \frac{p}{2}u(x - h, t) + \frac{p}{2}u(x + h, t) + (1 - p)u(x, t)$$

We now want to generalize from the random walk to 1D diffusion by taking a limit as $h \rightarrow 0$ and $\Delta t \rightarrow 0$. We subtract $u(x, t)$ from both sides to get,

$$\underbrace{u(x, x + \Delta t) - u(x, t)}_{\approx \Delta t \frac{\partial u}{\partial t}} = \frac{p}{2} \underbrace{[u(x - h, t) - 2u(x, t) + u(x + h, t)]}_{\approx h^2 \frac{\partial^2 u}{\partial x^2}}$$

Therefore,

$$\frac{\partial u}{\partial t} = D \frac{\partial^2 u}{\partial x^2}$$

where we have defined the diffusion constant to be

$$D = \frac{h^2}{2 \Delta t}$$

In Figure 1, we provide an example of the stochastic movement of $N = 10$ particles, that is, at each step in time, $dt = .01$, a random number generator is used to determine whether each of the particles moves left or right. We can compare with the exact solution of the diffusion equation, which is given by

$$u(x, t) = \frac{A}{\sqrt{4\pi Dt}} e^{-\frac{x^2}{4Dt}}$$

The microscopic random walk approximation will be similar to the analytical solution as is shown in Figure 2, where the above equation is plotted on top of the distribution of N balls that started at the origin, whose motion was Brownian, and whose final position was exhibited as a histogram.

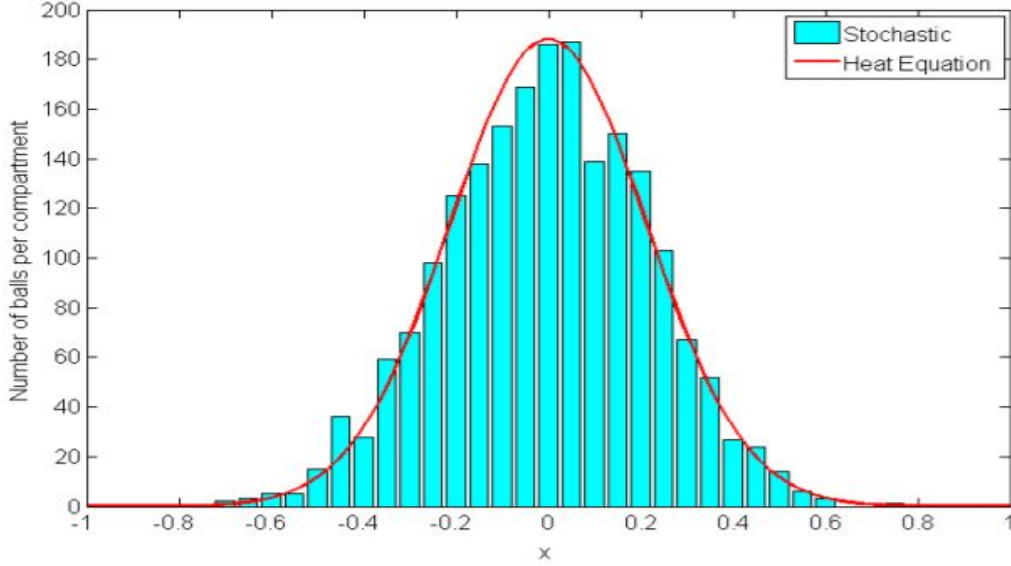


Figure 2: **Associating the heat equation and Brownian motion** This figure displays the solution to the diffusion equation, or the heat equation, in bloodshot. To obtain the teal histogram, 2000 balls with Brownian motion were simulated for 800-time steps. As a result, each bar signifies the number of balls whose final location was in that bin.

A combination of reaction and diffusion One of the key question arises while studying any mathematical models of natural phenomena is from where the mode came. So, we now set out to establish why reaction-diffusion models were proposed for pattern formation in the first place.

To understand why RD systems were proposed, we recall that all the mathematics behind pattern formation was advanced in the context of development. So, like all other key contributors, Turing were looking for the idea behind how all the organisms could arise from a single cell. It was suggested that chemical gradients throughout the embryo could be one mechanism through which spatial heterogeneity could be achieved. This chemical concentration profile can then influence gene transcription and drive cells to differentiate into different tissue types, which will eventually form the different organs in the body. The mechanism through which these gradients were set up, however, was not immediately apparent [Maini et al. (2012)]. The mechanism through which these gradients were set up, however, was not immediately apparent.

For a long time, diffusive models had been overlooked because they were assumed to be too slow to establish a stable chemical gradient but this altered in 1970 when Francis Crick modeled diffusion in a one-dimensional embryo and showed that diffusion is sufficiently fast in small domains. Crick's model was,

$$\frac{\partial U}{\partial t} = D \frac{\partial^2 U}{\partial x^2} \quad (2)$$

where U is the concentration of the chemical at position x and time t . Also, he set the boundary conditions on the 1D embryo of length L to be $U(0, t) = U_0$ and $U(L, t) = 0$.

Crick sought for a stable gradient (in time), so he set the left hand side of (2) equal to zero. This system has the form:

$$\frac{\partial^2 U}{\partial x^2} = 0$$

and its solution is a straight line.

Finally Crick calculated how much time it would take to reach this stable concentration gradient. From the definition of diffusion constant D , we can say, it has units $[length^2/time]$. Thus, the time it takes to set up the gradient is,

$$t = A \frac{(nl)^2}{D},$$

where t is time in seconds, n is the number of cells in the embryo, l is length of each cell in cm , D is the diffusion constant in $cm^2 s^{-1}$ and A is a numerical constant that is fit from the data. Assuming that the time it takes a real embryo to set up the chemical gradient is around 3 hours, Crick found that diffusion

would be fast enough if L was on the order of millimeters, which is the case in fruit flies, which is the animal model used to study this phenomena.

Not having the essential technology to determine the concentration gradients of any chemicals in the fruit fly embryos, Crick couldn't finish the work, he started. So, this was the range of his analysis. Nowadays, New imaging technologies have been developed that gives us access to measure the concentration of chemicals in embryos. One very important chemical called Bicoid, which determines what cells become part of which organ of the body (Little et al 2011).

This proposes that the diffusive model alone does not entirely clarify how chemical gradients are established in the embryo. Thus, models of Bicoid typically present a reaction term that defines how Bicoid is formed and how it reduces as it diffuses across the embryo. This model has the following form:

$$\frac{\partial U}{\partial t} = D \frac{\partial^2 U}{\partial x^2} - \frac{1}{\tau} U + \rho$$

where D is the diffusion constant, τ is the degradation rate, and ρ is the synthesis rate and both U and ρ is function of x and t . Avoiding synthesis rate, we get,

$$\frac{\partial U}{\partial t} = D \frac{\partial^2 U}{\partial x^2} - \frac{1}{\tau} U$$

which we can solve for a stable gradient analytically,

$$U(x, t) = U_0 e^{-\frac{x}{\lambda}}, \quad \lambda = \sqrt{D\tau}$$

This example confirms why sometimes reaction and diffusion are needed to make genuine biological models. Diffusion can model spatial phenomena, but often, like in the case of Bicoid, we have local reactions that can only be involved in the model with equations like the Reaction-Diffusion PDE in that mentioned equation.

Reaction-Diffusion equations and spatial domains So far it has been shown that diffusion is very effective in small distances how reaction and diffusion can work together to model experimental data. However, to truly comprehend pattern formation, it is essential to study the spatial properties of reaction-diffusion equations.

We consider the survival of a phytoplankton population in a body of water. Assume that the phytoplankton can only survive in waters with suitable conditions, and that these regions of water are bounded by bodies of water where the phytoplankton will die. We ask whether there exists a minimum water mass size where the phytoplankton population will survive?

We consider a very thin tube on which a mass of water has been stretched out and impose boundary conditions on the concentration of phytoplankton u such that any phytoplankton at the boundaries are automatically destroyed, and also that the concentration is constant at $t = 0$. That is, we have the following initial and boundary conditions:

$$u(0, t) = 0 = u(L, t)$$

$$u(x, 0) = u_0$$

Also, assume that the phytoplankton cannot swim so their movement is ruled by diffusion. Therefore, if the phytoplankton population does not grow or decrease, its concentration will be the solution to the diffusion equation which has the form:

$$\frac{\partial u}{\partial t} = D \frac{\partial^2 u}{\partial x^2}$$

However, since phytoplankton are living organisms, we add a reactive term that describes the population growth of the phytoplankton so that we now have,

$$\frac{\partial u}{\partial t} = D \frac{\partial^2 u}{\partial x^2} + Ku$$

where K is a growth constant.

Before we solve this using separation of variables, we can simplify our problem by scaling out the diffusion-less exponential growth,

$$u(x, t) = f(x, t) e^{Kt}$$

and substituting this to our new equation, , we find that f must satisfy the standard diffusion (or heat) equation of the previous part,

$$\frac{\partial f}{\partial t} = D \frac{\partial^2 f}{\partial x^2}$$

By the standard techniques of Fourier series, and using the boundary conditions of $u = 0$ at $x = 0, L$, we get that,

$$f = \sum_{n=1}^{\infty} B_n \sin\left(\frac{n\pi x}{L}\right) e^{-\frac{n^2 \pi^2 D}{L^2} t},$$

where B_n are the Fourier sine coefficients given by,

$$B_n = \frac{2}{L} \int_0^L u_0 \sin\left(\frac{n\pi x}{L}\right) dx,$$

for $n = 1, 2, \dots$, which are then computed for given initial concentration, u_0 . After some simple calculations we get,

$$u(x, t) = \sum_{n=1}^{\infty} B_n \sin\left(\frac{n\pi x}{L}\right) e^{(K - \frac{n^2 \pi^2 D}{L^2})t}$$

But what will be the steady state of the phytoplankton population? The key is to note that in the previous equation of $u(x, t)$ that because the Fourier coefficients are bounded and decreasing as $n \rightarrow \infty$, and the sinusoidals are well behaved, the long term behavior of the system will be controlled by the time term in that equation, $e^{(K - \frac{n^2 \pi^2 D}{L^2})t}$.

In particular, the argument, $K - \frac{n^2 \pi^2 D}{L^2}$, will determine whether the population of plankton will grow, stay the same or decay. In particular, if it is exactly zero, the population will be at equilibrium, if the argument is negative, the population will decay over time, and if it is positive, then the population will grow over time.

Moreover, if these conditions hold for the $n = 1$ mode, then the higher modes don't change the steady-state behavior. For $n = 1$, the bifurcation, or the point at which the behavior changes from decay to growth, is found at the length, L such that $K - \pi^2 \frac{D}{L^2} = 0$.

Therefore, we can get a critical length of the form:

$$L_c = \pi \sqrt{\frac{D}{K}}$$

In summary, we have found the critical length of the domain such that for $L = L_c$, the population stays constant, for $L > L_c$, the population increases and for $L < L_c$, the population will decay.

As a final note, observe that the critical length increases proportional to D but inversely proportional to K . This suggests that the steady-state behavior of the plankton population is determined by the relative strength of the diffusive and reactive terms in,

$$\frac{\partial u}{\partial t} = D \frac{\partial^2 u}{\partial x^2} + Ku.$$

When $L > L_c$ then the reactive term Ku will dominate the long-term behavior, but when $L < L_c$ the diffusive term $D \frac{\partial^2 u}{\partial x^2}$ dominates. When $L = L_c$ the diffusive and reactive forces balance each other equally.

Diffusion-driven instabilities in general

Consider the system of equations:

$$\frac{\partial u}{\partial t} = D_u \frac{\partial^2 u}{\partial x^2} + f(u, v) \tag{3}$$

$$\frac{\partial v}{\partial t} = D_v \frac{\partial^2 v}{\partial x^2} + g(u, v) \tag{4}$$

where D_u and D_v are diffusion constants, u and v are function of position and time and f, g describe how u and v interact.

We now introduce a couple of definitions:

Definition 1: Patterns are spatially heterogeneous solutions of u and v from the system of equations above.

Definition 2: A diffusion-driven instability, or Turing instability, occurs when a steady state, stable in

the absence of diffusion, becomes unstable when diffusion is present.

When will we get patterns? In the next section of the project we derive the conditions that are needed for a system to have Turing instabilities (i.e. to have patterns). Keep in mind that our goal is to have: Stability in the zero-diffusion case: If the chemicals do not diffuse, or they diffuse at the same rate, they will tend to go to a stable state, meaning that if we add small perturbations to a steady state, the system returns to equilibrium.

Instability with diffusion: When we add diffusion, then the stability of the reaction is shifted in such a way that we get that if we start at the steady state and perturb it slightly, the whole spatial structure will change (i.e. the system will be driven away from its steady state to form patterns).

Conditions for Turing Instabilities

In this section we will take the general equations (3 and 4) and analyze the conditions for Turing Instabilities to occur. The main goal in this section is to find what the system must satisfy to be stable without diffusion (time-independent) and to become unstable when the diffusion terms are added in (spatially heterogeneous). We assume a stationary uniform state (u_0, v_0) exists (i.e. $f(u_0, v_0) = g(u_0, v_0) = 0$). Let $u(x, t) = u_0 + \tilde{u}$ and $v(x, t) = v_0 + \tilde{v}$, where \tilde{u} and \tilde{v} are small. Note that when we do a Taylor Expansion about the fixed points, we get,

$$\begin{aligned} f(u, v) &= f(u_0, v_0) + \tilde{u} \frac{\partial f(u_0, v_0)}{\partial u} + \tilde{v} \frac{\partial f(u_0, v_0)}{\partial v} + \dots \\ g(u, v) &= g(u_0, v_0) + \tilde{u} \frac{\partial g(u_0, v_0)}{\partial u} + \tilde{v} \frac{\partial g(u_0, v_0)}{\partial v} + \dots \end{aligned}$$

so when we linearize Equations about (u_0, v_0)

$$\begin{aligned} \frac{\partial \tilde{u}}{\partial t} &= f_u + f_v + D_u \frac{\partial^2 \tilde{u}}{\partial x^2} + \dots \\ \frac{\partial \tilde{v}}{\partial t} &= g_u + g_v + D_v \frac{\partial^2 \tilde{v}}{\partial x^2} + \dots \end{aligned}$$

For simplicity we can rewrite this in matrix notation as,

$$\frac{\partial}{\partial t} \begin{Bmatrix} \tilde{u} \\ \tilde{v} \end{Bmatrix} = \left(D \frac{\partial^2}{\partial x^2} + J \right) \begin{Bmatrix} \tilde{u} \\ \tilde{v} \end{Bmatrix}$$

where

$$J = \begin{bmatrix} f_u & f_v \\ g_u & g_v \end{bmatrix}$$

and

$$D = \begin{bmatrix} D_u & 0 \\ 0 & D_v \end{bmatrix}$$

The diffusion-less linearized system looks like:

$$\left[\frac{\partial}{\partial t} \begin{Bmatrix} \tilde{u} \\ \tilde{v} \end{Bmatrix} \right] = \begin{bmatrix} f_u & f_v \\ g_u & g_v \end{bmatrix} \begin{Bmatrix} \tilde{u} \\ \tilde{v} \end{Bmatrix} \quad (5)$$

In seeking diffusion-driven instabilities (see Definition 2), we are thus looking for steady-state solutions which are asymptotically stable. This requires $Re(\lambda_{1,2}) < 0$ where $\lambda_{1,2}$ are the eigenvalues of J. We check at the following two conditions for the stability of (5):

$$\text{Trace of } J = f_u + g_v < 0 \text{ and Determinant of } J = f_u g_v - f_v g_u > 0$$

Now, according to Def. 1, patterns are time-independent and spatially heterogeneous solutions to Eq. (3) and (4). We assume that the solution is separable, so set:

$$\delta \tilde{u}(x, t) = A(t) e^{iqx}$$

and

$$\delta \tilde{v}(x, t) = B(t) e^{iqx}$$

where each q is the wave-number of a Fourier mode. Then, the diffusion terms become:

$$D_u \frac{\partial^2}{\partial x^2} A(t) e^{iqx} = -q^2 D_u A(t) e^{iqx}$$

$$D_v \frac{\partial^2}{\partial x^2} B(t) e^{iqx} = -q^2 D_v B(t) e^{iqx}$$

After we perturb the system by find that the Jacobian for this system is:

$$\frac{\partial}{\partial t} \begin{Bmatrix} \delta \tilde{u} \\ \delta \tilde{v} \end{Bmatrix} = \begin{bmatrix} f_u - q^2 D_u & f_v \\ g_u & g_v - q^2 D_v \end{bmatrix} \frac{\partial}{\partial t} \begin{Bmatrix} \delta \tilde{u} \\ \delta \tilde{v} \end{Bmatrix} \quad (6)$$

Equation (6) is stable when: $\text{Trace} = f_u + g_v - q^2(D_u + D_v) < 0$; and $\text{Determinant} = (f_u - q^2 D_u)(g_v - q^2 D_v) - f_v g_u > 0$. It can be easily showed that the first condition is holds true since $D_u, D_v \in \mathbb{R}^+$ and previously mentioned $f_u + g_v < 0$. Thus, if we want the system to become unstable we need the 2nd condition (determinant) to be false. We look for $q > q_{min}$, where q_{min} is the first mode that can cause an instability, i.e. satisfy,

$$H(q^2) = (f_u - q^2 D_u)(g_v - q^2 D_v) - f_v g_u < 0 \quad (7)$$

We notice that the equation (7) is a quadratic with respect to q^2 , so,

$$q_{min}^2 = \frac{D_u g_v + D_v f_u}{2 D_u D_v}$$

and if we look at where the determinant of the quadratic is positive, we find that:

$$D_u g_v + D_v f_u > 2 \sqrt{D_u D_v (f_u g_v - g_u f_v)}$$

This may seem a bit too abstract, so in the next section of the notes we will go through an Activator-Inhibitor model known as the Gierer-Meinhardt model.

The previous section derived the conditions that are needed for a Turing instability to exist. Now, let us step through an example in order to see how this works in practice.

Gierer-Meinhardt Model

The Gierer-Meinhardt model, a reaction diffusion system that describes an activator-inhibitor interaction. It is one of the equations that have been used to model morphogenesis and patterns in development. A slightly simplified version of the original Gierer-Meinhardt model [Gierer and Meinhardt, 1972] is,

$$\frac{\partial u}{\partial t} = \frac{u^2}{v} - bu + D_u \frac{\partial^2 v}{\partial x^2} \quad (8)$$

$$\frac{\partial v}{\partial t} = u^2 - v + D_v \frac{\partial^2 v}{\partial x^2} \quad (9)$$

where we will call u our “activator” and v our “inhibitor”, D_u and D_v are diffusion constants and b is the rate at which the activator u will naturally degrade.

Stability without Diffusion:

The diffusionless model looks like,

$$\begin{aligned} \frac{\partial u}{\partial t} &= \frac{u^2}{v} - bu \\ \frac{\partial v}{\partial t} &= u^2 - v \end{aligned}$$

We see that the steady state is given by $u_0 = \frac{1}{b}$ and $v_0 = u_0^2 = \frac{1}{b^2}$. Linearizing about the steady state (u_0, v_0) (i.e. by Taylor expanding about the steady state and ignoring higher order terms), we obtain

that the Jacobian is, $J = \begin{bmatrix} -b + \frac{2u}{v} & -\frac{u^2}{v^2} \\ 2u & -1 \end{bmatrix}$

Evaluating J at steady state (u_0, v_0) , we get the matrix, $J = \begin{bmatrix} b & -b^2 \\ \frac{2}{b} & -1 \end{bmatrix}$

We then check that it is stable recalling from the previous discussion that this means $\text{tr}(J) < 0$ and $\det(J) > 0$. Therefore, we require that $\text{tr}(J) = b < 1$ and $\det(J) = b > 0$. This constrains the value of the parameter b to $0 < b < 1$.

Instability with diffusion:

When we add diffusion to the system we want it to be unstable. The way we look at this is by starting at

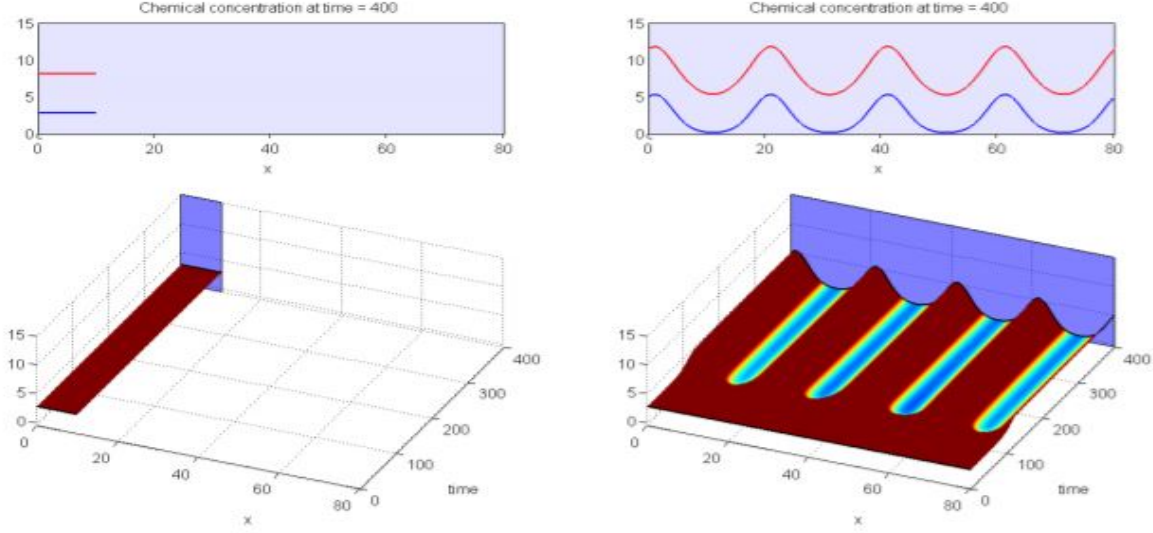


Figure 3: **Spatial dependence on patterns.** This figure shows two simulations of the Gierer-Meinhardt system with periodic boundary conditions. The only difference between the two simulations is the spatial domain, and it can be seen that whether or not the system develops spatial patterns depends on the domain .

the steady state and adding a small perturbation, and what we want is for these perturbations to grow over time.

Let $u(x, t) = u_0 + \tilde{u}$ and $v(x, t) = v_0 + \tilde{v}$ with \tilde{u} and \tilde{v} very small. Then, we look at the linearised system to study $\frac{\partial \tilde{u}}{\partial t}$ and $\frac{\partial \tilde{v}}{\partial t}$. The linearized system looks like,

$$\begin{aligned}\frac{\partial \tilde{u}}{\partial t} &= b\tilde{u} - b^2\tilde{v} + D_u \frac{\partial^2 \tilde{u}}{\partial x^2} \\ \frac{\partial \tilde{v}}{\partial t} &= \frac{2}{b}\tilde{u} - \tilde{v} + D_v \frac{\partial^2 \tilde{v}}{\partial x^2}\end{aligned}$$

The system can be solved by separation of variables as we saw in the previous discussion, so we look for solutions of the form,

$$\begin{bmatrix} \tilde{u} \\ \tilde{v} \end{bmatrix} = \begin{bmatrix} A(t)e^{iqx} \\ B(t)e^{iqx} \end{bmatrix}$$

where q are the Fourier modes.

The system becomes,

$$\frac{\partial}{\partial t} \begin{bmatrix} \delta \tilde{u} \\ \delta \tilde{v} \end{bmatrix} = \begin{bmatrix} b - q^2 D_u & -b^2 \\ \frac{2}{b} & -1 - q^2 D_v \end{bmatrix} \begin{bmatrix} \delta \tilde{u} \\ \delta \tilde{v} \end{bmatrix}$$

We want to find the eigenvalues $\lambda_{1,2}$ of the 2×2 matrix and we want them to be distinct, and at least one of $\text{Re}(\lambda_i) > 0$, $i = 1, 2$. We observe that $\text{tr}(J) = b - 1 - q^2(D_u + D_v)$ is always negative since $b < 1$ by our condition above, and D_u, D_v are both positive by definition, this condition holds true. In order for the system to become unstable, we need,

$$\det(J) = H(q^2) = (b - D_u q^2)(-1 - D_v q^2) + 2b < 0$$

Notice that the determinant is a quadratic function with respect to q^2 . In the figure above we can see a graph of H for different values of b between 0 and 0.35. We will not get patterns for small values of b , but we will get patterns once the quadratic crosses the x -axis (i.e. has real nonnegative roots). We will get two real roots for the quadratic when,

$$-bD_v + D_u > 2\sqrt{(D_u D_v)b}$$

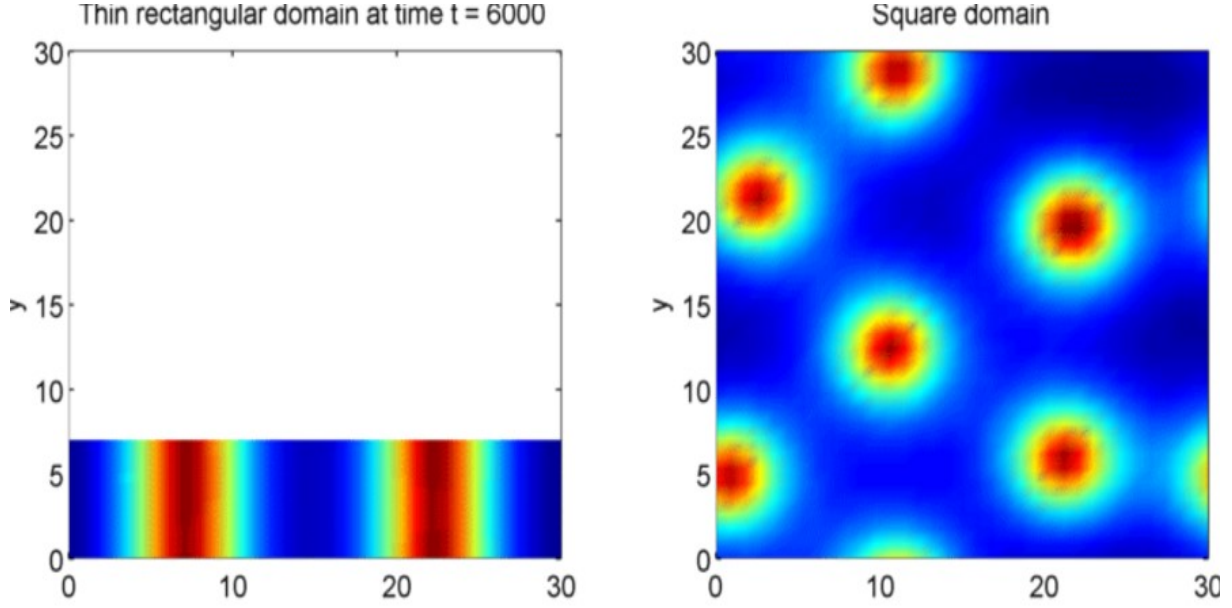


Figure 4: **2D Gierer-Meinhardt system.** This figure shows two simulations of a two-dimensional Gierer-Meinhardt system with periodic boundary conditions. The thin domain develops stripes and the square domain form spots.

Spatial Domain:

If we apply periodic boundary conditions over a domain $x \in [0, L]$, the separable solution will then be of the form

$$\sum_k A_k e^{\lambda(q^2)t} \cos qx$$

and over the allowed values of k i.e.

$$q = \frac{n\pi}{L}, n \in 1, 2, \dots$$

Since we want patterns to form, then the smallest allowed L has to be such that

$$q^2 = \frac{\pi^2}{L^2} > \frac{A + \sqrt{A^2 - B}}{2D_u D_v} = q_+^2$$

where $A = bD_v - D_u$, $B = 4bD_u D_v$ and q_+^2 is the bigger of the two solutions of $H(q^2)$. In other words, our critical length will be $L_c = \frac{\pi}{q_+}$. The dependence on the spatial domain is illustrated by Figure 3.

Pattern formation

Now it's time: Where do tigers get their stripes?

To answer that, we extend our analysis into two dimensions and revisit the idea of spatial dependence of patterns with the 2D Gierer-Meinhardt model on a thin domain and on a square domain.

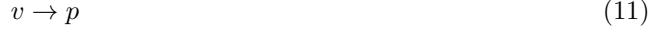
We keep all other parameters the same, but we change the width. As a result, we get stripes on a rectangular domain (because of the short edge, we get a pattern in one direction) and spots on a square domain (because we get a pattern from both directions). Previously we have shown that there was a least size for the Gierer-Meinhardt system to form patterns. Now from this we can conclude that various types of pattern can be formed by changing domains.

What connection can this have with animal coats? Murray ran simulations of reaction-diffusion models on cylindrical domains that tapered off at the ends (i.e. on a trapezoidal surface with periodic boundary conditions on the legs and zero-flux boundary conditions on the bases), and saw that you could get tails that were either entirely striped or that had spots that became stripes at the tip of the tail, similar to the markings observed on the tails of different felines ([Murray, 1988], 3.1 in [Murray, 1989]). This phenomenological model is exciting because it suggests that if coat patterns are due to the reaction between two (or more) chemical species, the same biological mechanism can result in different patterns (eg. fully striped genet tails and half-spotted half-striped jaguar tails) due to the different sizes of the

tails during development [Murray, 1981].

Beyond Turing:

Not all reaction-diffusion systems generate patterns through the same mechanism that was originally proposed by Alan Turing. If we do some small changes in the parameters other than the spatial domain, we get very different patterns. For example, we can talk about the Gray Scott equations, which stimulate an activator-substrate system; its mechanism can be showed as,



Our previous model has an activator and an inhibitor, but this model has the following system of equations which is interpreted from the chemical equations (above), where two chemicals u and v are reacting to produce v and at the same time v is transformed as a substrate called p .

$$\begin{aligned} \frac{\partial u}{\partial t} &= D_u \frac{\partial^2 u}{\partial x^2} - uv^2 + F \times (1 - u) \\ \frac{\partial v}{\partial t} &= D_v \frac{\partial^2 v}{\partial x^2} + uv^2 - (F + c)v \end{aligned}$$

where D_u, D_v are the diffusion constants as usual, and F, c are constants.

The system may seem very difficult but it can be easily translated if we look closely. Both equations of the system have three terms, we call the 1st term as diffusive term and the 2nd term as reaction rate but the interesting case is the last one. For 1st equation, the term $F \times (1 - u)$ is the refill term for u and F is the feed rate. For 2nd equation, the term $(F + c)v$ has a diminishing term v without which the concentration of chemical V could increase without limit and k is the rate at which the reaction $v \rightarrow p$ takes place.

Simulations of the Gray-Scott equations can lead to very different patterns using slightly different parameters (Figure 5). It is interesting to watch the structures unfold while varying the feed rates, removal rate, and diffusion rates - all of which can have dramatic consequences on the process. For instance, we set the feed rate 0.03 and 0.04, but we keep all other parameters same we get figure 5.¹

Note that the Gray-Scott equations lead to much more complicated dynamics than the Turing systems, and the patterns that you see are due to the nonlinear interactions between u and v .

Numerical solutions of reaction-diffusion equations

Numerical simulations are very useful to understand the behavior of reaction diffusion equations. This section will review some of the key numerical techniques that are used to simulate partial differential equations.

The heat equation:

Recall that the Heat equation (also the diffusion equation),

$$\frac{\partial u}{\partial t} - D_u \frac{\partial^2 u}{\partial x^2} = 0, \quad (12)$$

where u is temperature, and D_u is a constant that determines how fast heat spreads out. Before we go into the numerics let us step through the solution to the heat equation.

Imagine we have an one dimensional system with initial condition $u(x, 0) = u_0$ boundary conditions $u(x, t) = u(L, t) = 0$. We want to solve the PDE in Equation [12]. We assume that the solutions are separable, so,

$$u(x, t) = T(t)X(x)$$

We can substitute this solution into Equation [12] to get

$$T'(t)X(x) = D_u T(t)X''(x)$$

where the LHS is u_t and the RHS is u_{xx} . Rearranging terms we get,

$$\frac{T'(t)}{D_u T(t)} = \frac{X''(x)}{X(x)}$$

¹We have used a program called "Ready" to explore the model which can be downloaded from <https://github.com/GollyGang/ready/>



Figure 5: Simulation of GS model: where $D_A = 0.00002, D_B = 0.00001, k = 0.06, \text{time step}=1$

Note that the LHS (left hand side) is a function of time where the RHS (right hand side) is a function of position. In order for this equality to be satisfied for all x and t , we must have that they are both equal to a constant. We let,

$$\frac{T'(t)}{D_u T(t)} = \frac{X''(x)}{X(x)} = -\lambda^2, \lambda > 0.$$

Solving for each variable we get that ,

$$\begin{aligned} T(t) &= A e^{-\lambda^2 D_u t} \\ X(x) &= B \cos(\lambda x) + C \sin(\lambda x) \end{aligned}$$

where A is a positive real constant. We can apply our boundary conditions to find what B and C should be. Since the edges at $x = 0$ is clamped at zero ($u(0, t) = 0$), then $B = 0$. The system is also clamped at zero at $x = L$, and since $C \neq 0$, then $\sin(\lambda L) = 0$. This means that $\lambda_n = \frac{n\pi}{L}$, where $n \in \mathbb{Z}$. Note that (i) $n = 0$ will give a trivial solution, and (ii) $n \in \mathbb{Z}^-$ just makes all the coefficients negative, so we can just consider the positive values of n without loss of generality.

As a result, we get the following eigenfunctions,

$$u_n(x, t) = \sum_{n=1}^{\infty} A_n e^{-\lambda_n^2 D_u t} \sin(\lambda_n x)$$

is still a solution. We would like it then, if we could express u_0 as a sum of sine functions as shown in the above equation. This is true for most u_0 and it is the theory of Fourier Series. It can be shown that the Fourier sine coefficients are,

$$A_n = \frac{2}{L} \int_0^L u_0(x) \sin(\lambda_n x) dx$$

However, in general, it is not always easy to obtain solutions to PDE's in closed form. Instead, we turn to numerical simulations to Partial Differential equations.

Forward (explicit) method:

One of the difficulties when numerically simulating the heat equation is that (12) contains partial derivative in both time and space. We can approximate the partial derivatives of $u(x, t)$ in Eqn. (12) as follows:

$$\begin{aligned} \frac{\partial^2 u}{\partial x^2} &\approx \frac{u(x + \Delta x, t) - 2u(x, t) + u(x - \Delta x, t)}{\Delta x^2} \\ \frac{\partial u}{\partial t} &\approx \frac{u(x, t + \Delta t) - u(x, t)}{\Delta t} \end{aligned}$$

Let n be the index for the time steps, and m be the index for position. We'll also use $k = \Delta t$ and $h = \Delta x$, and write $u(m, n) = u_m^n$. Then, the heat equation can be solved numerically by using the following,

$$u_m^{n+1} = \frac{k}{h^2} u_{m-1}^n + \left(1 - \frac{2k}{h^2}\right) u_m^n + \frac{k}{h^2} u_{m+1}^n \quad (13)$$

Now, let us consider the behavior at the edges of the rod. Let us discretize our rod at M points, $u_1^n, u_2^n, \dots, u_{M-1}^n, u_M^n$. Notice that (13) will work at every position along a one-dimensional rod except for

the two edges (at u_1 and u_M), because there are no values for u_0 and u_{M+1} to approximate the centered finite difference. This requires us to add boundary conditions, and in this section we consider periodic boundary conditions.

This means that $u_1^n = u_m^n$, so it is convenient to rewrite (13) as a matrix operation,

$$\vec{u}^{n+1} = B\vec{u}^n \quad (14)$$

where \vec{u}^n are the values of u at time n for all values x_1, \dots, x_M , and

$$B = \begin{bmatrix} a & b & 0 & \cdots & b & 0 \\ b & a & b & \cdots & 0 & 0 \\ 0 & b & a & \ddots & & 0 \\ 0 & & \ddots & \ddots & \ddots & \vdots \\ \vdots & & & & b & a & b \\ 0 & b & \cdots & 0 & b & a \end{bmatrix}$$

where $a = 1 - \frac{2k}{h^2}$, $b = \frac{k}{h^2}$, at $B_{1,M-1} = B_{M,2} = b$ that satisfies the boundary conditions.

Backward (implicit) method:

The forward method does not guarantee stability. As a result, it is often convenient to use Implicit methods, which are stable, and which will allow you to take larger time steps, even though the ‘accuracy’ of the simulation will still depend on the size of the time step.// The idea is the same, but the algorithm is as follows,

$$u_m^n = -\frac{k}{h^2}u_{m-1}^{n+1} + \left(1 + \frac{2k}{h^2}\right)u_m^{n+1} - \frac{k}{h^2}u_{m+1}^{n+1} \quad (15)$$

We can write (15) as a product of matrices to get,

$$\vec{u}^{n+1} = B'\vec{u}^n \quad (16)$$

where B' has the same form as B in the previous case but with $a = 1 + \frac{2k}{h^2}$, $b = -\frac{k}{h^2}$. Then, at each step we need to solve Equation(16) for \vec{u}^n , so

$$\vec{u}^{n+1} = B'^{-1}\vec{u}^n \quad (17)$$

Adding in the reaction term

Let us now see how to update our value of u , when we are looking at a Reaction-Diffusion system like,

$$\frac{\partial u}{\partial t} = D \frac{\partial^2 u}{\partial x^2} + f(u)$$

Recall that if we just had,

$$\frac{\partial u}{\partial t} = f(u)$$

then we simulate it using the forward Euler method so,

$$\vec{u}^{n+1} = f(\vec{u}^n)k \quad (18)$$

where $k = \Delta t$.

Therefore, for the explicit method, we combine (14) and (18) to obtain that the update at each time step is,

$$\vec{u}^{n+1} = B\vec{u}^n + f(\vec{u}^n)k$$

If we use the implicit method for the diffusion, and the explicit method, then we need to solve

$$B'\vec{u}^{n+1} = \vec{u}^n + f(\vec{u}^n)k$$

, for \vec{u}^{n+1} . Thus, at each step we need to compute,

$$\vec{u}^{n+1} = B'^{-1}(\vec{u}^n + f(\vec{u}^n)k).$$

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