Chapter 6

Pattern formation

Examples of spatial pattern and structure can be seen just about everywhere in the natural world, and there are many outstanding questions about how these patterns are generated and maintained in a such robust and reproducible manner. We will focus attention on a class of reaction-diffusion models that generate patterns via what is known as a diffusion-driven instability. We will explore how to analyse the models to determine necessary conditions for a diffusion-driven instability, and how to predict the kinds of patterns that can form.

6.1 Diffusion-driven instability

We will consider a system that consists of two diffusible species, which diffuse and react according to the following coupled partial differential equations

$$\frac{\partial u}{\partial t} = D_u \nabla^2 u + f(u,v), \tag{6.1}$$

$$\frac{\partial v}{\partial t} = D_v \nabla^2 v + g(u,v), \tag{6.2}$$

for $\boldsymbol{x} \in \Omega$, $t \in [0,\infty)$ and Ω bounded. The initial conditions are

$$u(\boldsymbol{x},0) = u_0(\boldsymbol{x}), \quad v(\boldsymbol{x},0) = v_0(\boldsymbol{x}), \tag{6.3}$$

and the boundary conditions are either Dirichlet, *i.e.*

$$u = u_B, \quad v = v_B, \quad \boldsymbol{x} \in \partial\Omega, \tag{6.4}$$

or homogeneous Neumann, *i.e.*

$$\boldsymbol{n} \cdot \nabla u = 0, \quad \boldsymbol{n} \cdot \nabla v = 0, \quad \boldsymbol{x} \in \partial\Omega, \tag{6.5}$$

where $\boldsymbol{n}$ is the outward pointing normal on $\partial\Omega$.

We will be interested in analysing the pattern forming potential of this system where we define a pattern to be a stable, time-independent, spatially heterogeneous solution of Equations (6.1)–(6.2). In particular, we will be interested in patterns formed through a diffusion-driven instability.

Definition. A *diffusion-driven instability*, also referred to as a *Turing instability*, occurs when a spatially uniform steady state that is stable in the absence of diffusion becomes unstable when diffusion is present.

Note. Diffusion-driven instabilities can drive pattern formation in chemical systems and there is significant, but not necessarily conclusive, evidence that they can drive pattern formation in a variety of biological systems. A key point is that this mechanism can drive the system from close to a homogeneous steady state to a state with spatial pattern and structure. The fact that diffusion is responsible for this is initially quite surprising. Diffusion, in isolation, disperses a pattern; yet diffusion, combined with kinetic terms, can often drive a system towards a state with spatial structure.

6.1.1 Linear analysis

We wish to understand when a diffusion-driven instability occurs. We have

$$\frac{\partial}{\partial t}\begin{pmatrix} u \\ v \end{pmatrix} = \begin{pmatrix} D_u & 0 \\ 0 & D_v \end{pmatrix} \nabla^2 \begin{pmatrix} u \\ v \end{pmatrix} + \begin{pmatrix} f(u,v) \\ g(u,v) \end{pmatrix}, \tag{6.6}$$

for $\boldsymbol{x} \in \Omega$, $t \in [0, \infty)$, with

$$\boldsymbol{n}.\nabla u = 0 = \boldsymbol{n}.\nabla v, \quad \boldsymbol{x} \in \partial\Omega. \tag{6.7}$$

Using vector and matrix notation we define

$$\boldsymbol{u} = \begin{pmatrix} u \\ v \end{pmatrix}, \quad \boldsymbol{F}(\boldsymbol{u}) = \begin{pmatrix} f(u,v) \\ g(u,v) \end{pmatrix}, \quad \boldsymbol{D} = \begin{pmatrix} D_u & 0 \\ 0 & D_v \end{pmatrix}, \tag{6.8}$$

and write the problem with homogeneous Neumann boundary conditions as

$$\frac{\partial \boldsymbol{u}}{\partial t} = \boldsymbol{D}\nabla^2 \boldsymbol{u} + \boldsymbol{F}(\boldsymbol{u}), \quad \boldsymbol{x} \in \Omega, \; t \in [0, \infty), \tag{6.9}$$

with

$$\boldsymbol{n} \cdot \nabla \boldsymbol{u} = 0, \quad \boldsymbol{x} \in \partial\Omega. \tag{6.10}$$

Let $\boldsymbol{u}_s$ be a steady state of the system *i.e.* such that $\boldsymbol{F}(\boldsymbol{u}_s) = \boldsymbol{0}$. Implicit in this definition is the assumption that $\boldsymbol{u}_s$ is a constant vector.

Let $\boldsymbol{w} = \boldsymbol{u} - \boldsymbol{u}_s$ with $|\boldsymbol{w}| \ll 1$. Then we have

$$\frac{\partial \boldsymbol{w}}{\partial t} = \boldsymbol{D}\nabla^2 \boldsymbol{w} + \boldsymbol{F}(\boldsymbol{u}_s) + \boldsymbol{J}\boldsymbol{w} + \text{higher order terms}, \tag{6.11}$$

where

$$\boldsymbol{J} = \left.\begin{pmatrix} \frac{\partial f}{\partial u} & \frac{\partial f}{\partial v} \\ \frac{\partial g}{\partial u} & \frac{\partial g}{\partial v} \end{pmatrix}\right|_{\boldsymbol{u}=\boldsymbol{u}_s}, \tag{6.12}$$

is the Jacobian of $\boldsymbol{F}$ evaluated at the spatially uniform steady state, $\boldsymbol{u} = \boldsymbol{u}_s$. Note that $\boldsymbol{J}$ is a *constant* matrix.

Neglecting higher order terms in $|\boldsymbol{w}|$, we have

$$\frac{\partial \boldsymbol{w}}{\partial t} = \boldsymbol{D}\nabla^2 \boldsymbol{w} + \boldsymbol{J}\boldsymbol{w}, \quad \boldsymbol{x} \in \Omega \quad \text{and} \quad \boldsymbol{n} \cdot \nabla \boldsymbol{w} = 0, \quad \boldsymbol{x} \in \partial\Omega. \tag{6.13}$$

This is a linear equation and so we look for a solution in the form of a linear sum of separable solutions. To do this, we must first consider a general separable solution given by

$$\boldsymbol{w}(\boldsymbol{x}, t) = A(t)\boldsymbol{p}(\boldsymbol{x}), \tag{6.14}$$

where $A(t)$ is a scalar function of time. Substituting from Equation (6.14) into Equation (6.13) yields

$$\frac{1}{A}\frac{\mathrm{d}A}{\mathrm{d}t}\boldsymbol{p} = \boldsymbol{D}\nabla^2 \boldsymbol{p} + \boldsymbol{J}\boldsymbol{p}. \tag{6.15}$$

Clearly to proceed, with $\boldsymbol{p}$ dependent on $\boldsymbol{x}$ only, we require $\dot{A}/A$ to be time independent. It must also be independent of $\boldsymbol{x}$ as A is a function of time only. Thus $\dot{A}/A$ is constant.

We take $\dot{A} = \lambda A$, where λ is an, as yet, undetermined constant. Thus

$$A = A_0 \exp(\lambda t), \tag{6.16}$$

for $A_0 \neq 0$ constant. Hence we require that our separable solution is such that

$$\lambda \boldsymbol{p} - \boldsymbol{J}\boldsymbol{p} - \boldsymbol{D}\nabla^2 \boldsymbol{p} = 0. \tag{6.17}$$

Suppose $\boldsymbol{p}$ satisfies the equation

$$\nabla^2 \boldsymbol{p} + k^2 \boldsymbol{p} = 0, \quad \boldsymbol{x} \in \Omega \quad \text{and} \quad \boldsymbol{n} \cdot \nabla \boldsymbol{p} = 0, \quad \boldsymbol{x} \in \partial\Omega, \tag{6.18}$$

where $k \in \mathbb{R}$. This is motivated by the fact in one-dimensional on a bounded domain, we have $p'' + k^2 p = 0$; the solutions are trigonometric functions which means one immediately has a Fourier series when writing the sum of separable solutions.

Then we have

$$\left[\lambda \boldsymbol{I} - \boldsymbol{J} + \boldsymbol{D} k^2\right] \boldsymbol{p} = 0, \tag{6.19}$$

with $|\boldsymbol{p}|$ not identically zero. Hence, for a solution to exist we must have

$$\det\left[\lambda \boldsymbol{I} - \boldsymbol{J} + k^2 \boldsymbol{D}\right] = 0. \tag{6.20}$$

This can be rewritten as

$$\det \begin{pmatrix} \lambda - f_u + D_u k^2 & -f_v \\ -g_u & \lambda - g_v + D_v k^2 \end{pmatrix} = 0, \tag{6.21}$$

where the partial derivatives are evaluated at the spatially uniform steady state, $\boldsymbol{u}_s$. Expanding gives the following quadratic in λ

$$\lambda^2 + \left[(D_u + D_v)k^2 - (f_u + g_v)\right] \lambda + h(k^2) = 0, \tag{6.22}$$

where

$$h(k^2) = D_u D_v k^4 - (D_v f_u + D_u g_v)k^2 + (f_u g_v - g_u f_v). \tag{6.23}$$

Note 1. Fixing model parameters and functions (*i.e.* fixing D_u, D_v, f, g), we have an equation which gives λ as a function of k^2.

Note 2. For any k^2 such that Equation (6.18) possesses a solution, denoted $\boldsymbol{p}_k(\boldsymbol{x})$ below, we can find a $\lambda = \lambda(k^2)$ and, hence, a general separable solution of the form

$$A_0 e^{\lambda(k^2)t} \boldsymbol{p}_k(\boldsymbol{x}). \tag{6.24}$$

The most general solution formed by the sum of separable solutions is therefore

$$\sum_{k^2} A_0(k^2) e^{\lambda(k^2)t} \boldsymbol{p}_k(\boldsymbol{x}), \tag{6.25}$$

if there are countable k^2 for which Equation (6.18) possesses a solution. Otherwise the general solution formed by the sum of separable solutions is of the form

$$\int A_0(k^2)e^{\lambda(k^2)t}\boldsymbol{p}_{k^2}(\boldsymbol{x})\,\mathrm{d}k^2, \tag{6.26}$$

where k^2 is the integration variable.

Unstable points

If, for any k^2 such that Equation (6.18) possesses a solution, we find $\Re e(\lambda(k^2)) > 0$ then:

- $\boldsymbol{u}_s$ is (linearly) unstable and perturbations from the stationary state will grow;
- while the perturbations are small, the linear analysis remains valid. The perturbations grow until the linear analysis is invalid and the full non-linear dynamics comes into play;
- a small perturbation from the steady state develops into a growing spatially heterogeneous solution, which subsequently seeds spatially heterogeneous behaviour of the full non-linear model;
- a spatially heterogeneous pattern can emerge from the system from a starting point which is homogeneous to a very good approximation.

Stable points

If, for all k^2 such that Equation (6.18) possesses a solution, we find $\Re e(\lambda(k^2)) < 0$ then:

- $\boldsymbol{u}_s$ is (linearly) stable and perturbations from the stationary state do not grow;
- patterning will not emerge from perturbing the homogeneous steady state solution $\boldsymbol{u}_s$;
- the solution will decay back to the homogeneous solution.

Note. Strictly, this conclusion requires completeness of the separable solutions. This can be readily shown in one dimension on bounded domains (solutions of $p'' + k^2p = 0$ on bounded domains with Neumann conditions are trigonometric functions and completeness is inherited from the completeness of Fourier series). Even if completeness of the separable solutions is not clear, numerical simulations of the full equations are highly indicative and do not, for the models typically encountered, contradict the results of the linear analysis. With enough effort and neglecting any biological constraints on model parameters and functions, one may well be able to find $D_u,\ D_v,\ f,\ g$ where there is such a discrepancy, but that is not the point of biological modelling.

6.2 Detailed study of the conditions for a Turing instability

For a Turing instability we require the homogeneous steady state to be **stable without diffusion** and **unstable with diffusion**. Here we analyse the requirements for each of these conditions to be satisfied. Note that, in the following analysis, all partial derivatives f_u, f_v, g_u and g_v are evaluated at the steady state, $\boldsymbol{u}_s$.

6.2.1 Stability without diffusion

First, we require that in the absence of diffusion the system is stable. This is equivalent to

$$\Re e(\lambda(0)) < 0, \tag{6.27}$$

for *all* solutions of $\lambda(0)$, as setting $k^2 = 0$ removes the diffusion terms in Equation (6.20) and the preceding equations.

We have that $\lambda(0)$ satisfies

$$\lambda(0)^2 - [f_u + g_v]\,\lambda(0) + [f_u g_v - f_v g_u] = 0, \tag{6.28}$$

with roots

$$\lambda(0)_\pm = \frac{(f_u + g_v) \pm \sqrt{(f_u + g_v)^2 - 4(f_u g_v - f_v g_u)}}{2}. \tag{6.29}$$

Insisting that $\Re e(\lambda(0)) < 0$ gives the conditions

$$f_u + g_v < 0, \tag{6.30}$$

$$f_u g_v - f_v g_u > 0. \tag{6.31}$$

6.2.2 Instability with diffusion

Now consider the effects of diffusion. In addition to $\Re e(\lambda(0)) < 0$, we must show, for diffusion-driven instability, that there exists $k^2 \neq 0$ such that

$$\Re e(\lambda(k^2)) > 0, \tag{6.32}$$

so that diffusion does indeed drive an instability.

We have that $\lambda(k^2)$ satisfies

$$\lambda^2 + \left[(D_u + D_v)k^2 - (f_u + g_v)\right]\lambda + h(k^2) = 0, \tag{6.33}$$

where

$$h(k^2) = D_u D_v k^4 - (D_v f_u + D_u g_v)k^2 + (f_u g_v - g_u f_v), \tag{6.34}$$

and

$$\alpha = (f_u + g_v) - (D_u + D_v)k^2 < 0. \tag{6.35}$$

Thus $\Re e(\lambda(k^2)) > 0$ requires that

$$\Re e\left(\alpha \pm \sqrt{\alpha^2 - 4h(k^2)}\right) > 0 \quad \Longrightarrow \quad h(k^2) < 0. \tag{6.36}$$

Hence we must find k^2 such that

$$h(k^2) = D_u D_v k^4 - (D_v f_u + D_u g_v)k^2 + (f_u g_v - g_u f_v) < 0, \tag{6.37}$$

so that we have $k^2 \in [k_-^2, k_+^2]$ where $h(k_\pm^2) = 0$. Figure 6.1 shows a plot of a caricature $h(k^2)$.

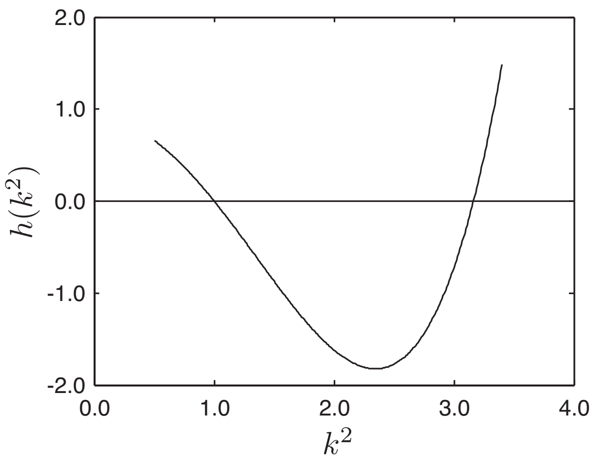


Figure 6.1: A plot of a caricature $h(k^2)$.

We conclude that we have instability whenever

$$k^2 \in \left[\frac{A - \sqrt{A^2 - B}}{2D_u D_v}, \frac{A + \sqrt{A^2 - B}}{2D_u D_v}\right] = \left[k_-^2, k_+^2\right], \tag{6.38}$$

where

$$A = D_v f_u + D_u g_v \quad \text{and} \quad B = 4D_u D_v(f_u g_v - g_u f_v) > 0, \tag{6.39}$$

and there exists a solution of the following equation

$$\nabla^2 \boldsymbol{p} + k^2 \boldsymbol{p} = 0, \quad \boldsymbol{x} \in \Omega \quad \text{and} \quad \boldsymbol{n} \cdot \nabla \boldsymbol{p} = 0. \quad \boldsymbol{x} \in \partial\Omega, \tag{6.40}$$

for k^2 in the above range.

Insisting that k is real and non-zero (we have considered the $k = 0$ case above) we have

$$A > 0 \quad \text{and} \quad A^2 - B > 0, \tag{6.41}$$

which gives us that when $\Re e(\lambda(k^2)) > 0$, the following conditions hold:

$$D_v f_u + D_u g_v \quad > \quad 0, \tag{6.42}$$

$$D_v f_u + D_u g_v \quad > \quad 2\sqrt{D_u D_v (f_u g_v - f_v g_u)}. \tag{6.43}$$

6.2.3 Summary

We have found that diffusion-driven instability can occur when conditions stated in Equations (6.30), (6.31), (6.42) and (6.43) hold. Then the instability is driven by separable solutions which solve Equation (6.18) with k^2 in the range stated in Equation (6.38).

Key point 1. Note that the constraints in Equations (6.30) and (6.42) immediately give us that $D_u \neq D_v$. Thus one cannot have a diffusion-driven instability with *identical* diffusion coefficients.

Key point 2. From the constraints in Equations (6.30), (6.31) and (6.42) the signs of the partial derivatives f_u, g_v must be such that $\boldsymbol{J}$ takes the form

$$\boldsymbol{J} = \begin{pmatrix} + & + \\ - & - \end{pmatrix} \quad \text{or} \quad \begin{pmatrix} + & - \\ + & - \end{pmatrix} \quad \text{or} \quad \begin{pmatrix} - & - \\ + & + \end{pmatrix} \quad \text{or} \quad \begin{pmatrix} - & + \\ - & + \end{pmatrix}. \tag{6.44}$$

Key point 3. A Turing instability typically occurs via *long-range inhibition and short-range activation.* In more detail, suppose

$$\boldsymbol{J} = \begin{pmatrix} + & - \\ + & - \end{pmatrix}. \tag{6.45}$$

Then we have $f_u > 0$ and $g_v < 0$ by the signs of $\boldsymbol{J}$. In this case $D_v f_u + D_u g_v > 0 \Longrightarrow D_v > D_u$. Hence the activator has a lower diffusion coefficient and spreads less quickly than the inhibitor.

6.2.4 The threshold of a Turing instability

The threshold of a Turing instability is defined such that Equation (6.23), *i.e.*

$$D_u D_v k^4 - (D_v f_u + D_u g_v)k^2 + (f_u g_v - g_u f_v) = 0,$$

has a single root, which we will denote k_c^2. This requirement is satisfied when

$$A^2 = B \quad i.e. \quad (D_v f_u + D_u g_v)^2 = 4D_u D_v(f_u g_v - g_u f_v) > 0, \tag{6.46}$$

whereupon

$$k_c^2 = \frac{A}{2D_u D_v} = \frac{D_v f_u + D_u g_v}{2D_u D_v}. \tag{6.47}$$

Strictly one also requires that a solution exists for

$$\nabla^2 \mathbf{p} + k^2 \boldsymbol{p} = 0, \quad \boldsymbol{x} \in \Omega \quad \text{and} \quad \boldsymbol{n} \cdot \nabla \boldsymbol{p} = 0, \quad \boldsymbol{x} \in \partial\Omega, \tag{6.48}$$

when $k^2 = k_c^2$. However, the above value of k_c^2 is typically an excellent approximation.

6.3 Extended example 1

Consider the one-dimensional case

$$\frac{\partial u}{\partial t} = D_u \frac{\partial^2 u}{\partial x^2} + f(u,v), \tag{6.49}$$

$$\frac{\partial v}{\partial t} = D_v \frac{\partial^2 v}{\partial x^2} + g(u,v), \tag{6.50}$$

for $x \in [0, L]$, $t \in [0, \infty)$ and zero flux boundary conditions at $x = 0$ and $x = L$.

The analogue of

$$\nabla^2 \boldsymbol{p} + k^2 \boldsymbol{p} = 0, \quad \boldsymbol{x} \in \Omega \quad \text{and} \quad \boldsymbol{n} \cdot \nabla \boldsymbol{p} = 0, \quad \boldsymbol{x} \in \partial\Omega, \tag{6.51}$$

is

$$\frac{\mathrm{d}^2 p}{\mathrm{d}x^2} + k^2 p = 0, \quad x \in (0, L) \quad \text{and} \quad p'(0) = p'(L) = 0, \tag{6.52}$$

which gives us that

$$p_k(x) = A_k \cos(kx), \quad k = \frac{n\pi}{L}, \quad n \in \{1, 2, \ldots\}, \tag{6.53}$$

where A_k is k-dependent in general but independent of x and t.

Thus the separable solution is of the form

$$\sum_k A_k e^{\lambda(k^2)t} \cos(kx), \tag{6.54}$$

where the sum is over the allowed values of k *i.e.*

$$k = \frac{n\pi}{L}, \quad n \in \{1, 2, \ldots\}. \tag{6.55}$$

Figure 6.2 shows example patterns formed using the Gierer-Meinhardt model [4].

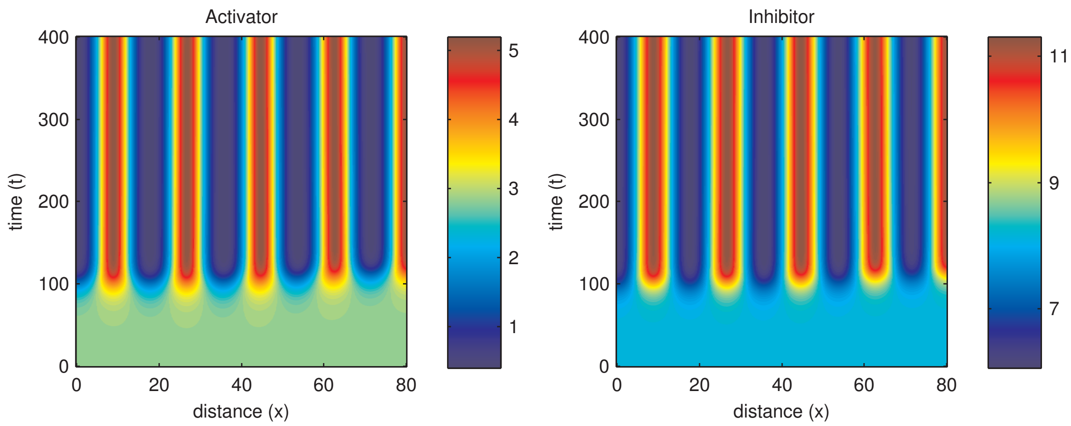


Figure 6.2: Numerical simulation of the Gierer-Meinhardt model for pattern formation.

6.3.1 The influence of domain size

If the smallest allowed value of $k^2 = \pi^2/L^2$ is such that

$$k^2 = \frac{\pi^2}{L^2} > \frac{A + \sqrt{A^2 - B}}{2D_u D_v} = k_+^2, \tag{6.56}$$

then we cannot have a Turing instability.

Thus for very small domains there is *no* pattern formation via a Turing mechanism. However, if one slowly increases the size of the domain, then L increases and the above constraint eventually breaks down and the homogeneous steady state destabilises leading to spatial heterogeneity. This phenomenon has been observed in chemical systems. It is regularly hypothesised to be present in biological systems (*e.g.* animal coat markings, fish markings, the interaction of gene products at a cellular level, the formation of ecological patchiness) though the evidence is not conclusive at the current time.

6.4 Extended example 2

Consider the two-dimensional case with spatial coordinates $\boldsymbol{x} = (x, y)^T$, $x \in [0, L_x]$, $y \in [0, L_y]$, and zero flux boundary conditions. We find that the allowed values of k^2 are

$$k^2_{m,n} = \left[\frac{m^2\pi^2}{L_x^2} + \frac{n^2\pi^2}{L_y^2}\right], \tag{6.57}$$

with

$$p_{m,n}(\boldsymbol{x}) = A_{m,n} \cos\left(\frac{m\pi x}{L_x}\right) \cos\left(\frac{n\pi y}{L_y}\right), \quad n, m \in \{0, 1, 2, \ldots\}, \tag{6.58}$$

excluding the case where n, m are both zero.

Suppose the domain is long and thin, $L_y \ll L_x$. We may have a Turing instability if

$$k^2_{m,n} = \left[\frac{m^2\pi^2}{L_x^2} + \frac{n^2\pi^2}{L_y^2}\right] \in \left[k^2_-, k^2_+\right] \quad \text{where} \quad h(k^2_\pm) = 0. \tag{6.59}$$

For L_y sufficiently small, this requires $n = 0$ and therefore no spatial variation in the y direction. This means that the seed for pattern formation predicted by the linear analysis is a separable solution which is "stripes"; this typically invokes a striped pattern once the non-linear dynamics sets in.

On the other hand, for a large rectangular domain, $L_x \sim L_y$ sufficiently large, it is clear that a Turing instability can be initiated with n, $m > 0$. This means that the seed for pattern formation predicted by the linear analysis is a separable solution which is "spots". This typically invokes a spotted pattern once the non-linear dynamics sets in.

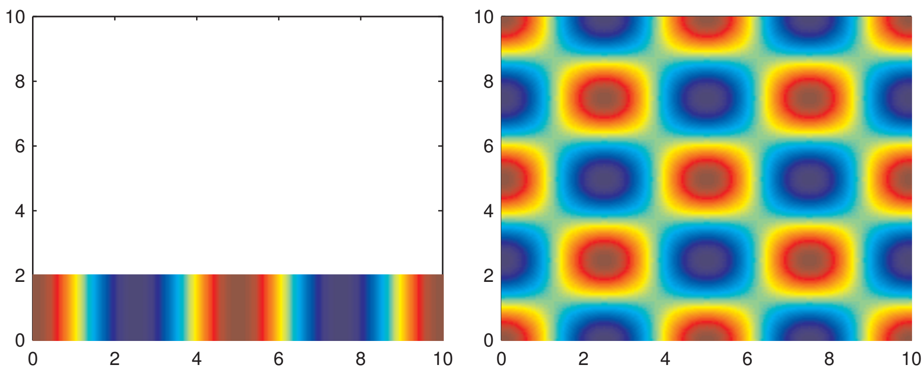
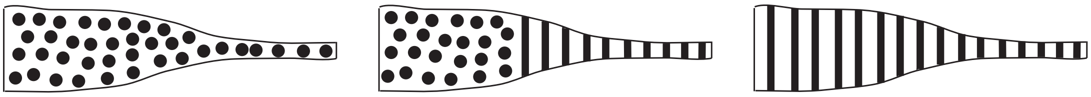


Figure 6.3: Changes in patterning as the domain shape changes.

Figure 6.3 shows how domain size may affect the patterns formed. On the left-hand side the domain is long and thin and only a striped pattern results, whilst the on the right-hand side the domain is large enough to admit patterning in both directions.

Suppose we have a domain which changes its aspect ratio from long and wide to long and thin. Then we have the following possibilities:



This leads to an interesting prediction, in the context of animal coat markings, that if patterning is indeed driven by a diffusion-driven instability, then one should not expect to see an animal with a striped body and a spotted tail.

Figure 6.4: Animal coat markings which are consistent with the predictions of pattern formation by a Turing instability.

Common observation is consistent with such a prediction (see Figure 6.4) but one should not expect universal laws in the realms of biology as one does in physics (see Figure 6.5). More generally, this analysis has applications in modelling numerous chemical and biochemical reactions, in vibrating plate theory, and studies of patchiness in ecology and modelling gene interactions.

Figure 6.5: Animal coat markings which are inconsistent with the predictions of pattern formation by a Turing instability.

Suggested reading.

- J. D. Murray, *Mathematical Biology, Volume II* – Chapters 2 and 3.
- N. F. Britton, *Essential Mathematical Biology* – Chapter 7.