

A Course in Mathematical Biology

*Quantitative Modelling with Mathematical and Computational
Methods*

G. de Vries T. Hillen M. Lewis J. Müller

B. Schönfish

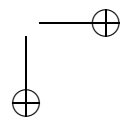
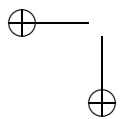
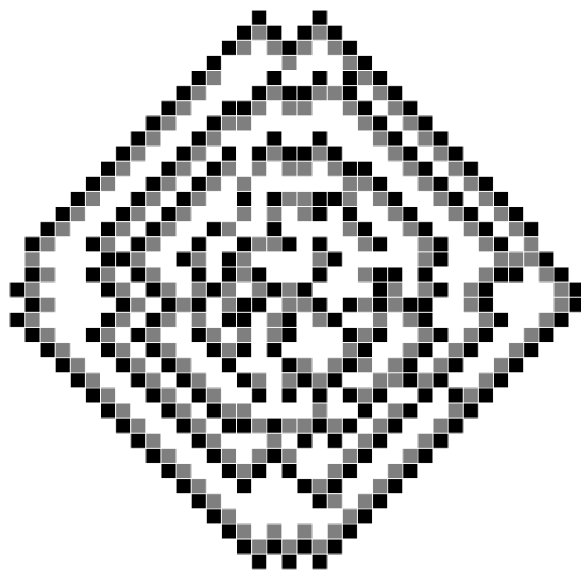




Figure 4.3. There is exactly one value $\bar{\lambda}$ such that equation (4.10) is satisfied.

Theorem 4.2.

If $\bar{\lambda} < 0$, then $u(t, a) \rightarrow 0$ as $t \rightarrow \infty$.

If $\bar{\lambda} > 0$, then $u(t, a) \rightarrow \infty$ as $t \rightarrow \infty$.

For each solution $u(t, a)$ the function $u(t, a)g_0^{-1}e^{-\lambda t}$ converges to $w(a)$ as $t \rightarrow \infty$ for each age a .

4.3 Reaction-Diffusion Equations

Another very important class of partial differential equations are *reaction-diffusion equations*, for which the independent variables are time, t , and space, x . Reaction-diffusion equations are used whenever the spatial spread of a population or chemical species is of importance. Reaction-diffusion models have their limitations and there are more advanced models (such as correlated random walks or transport equations), but it is always a good idea to start with a reaction-diffusion model for spatial spread. This has successfully been done in epidemic models, for pattern formation, for predator-prey systems, and in signal transport, to name a few areas. A good overview is given in Murray [112] and in Britton [24].

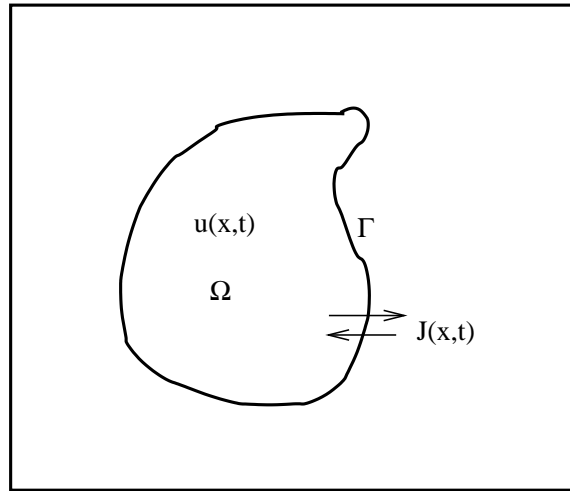


Figure 4.4. Sketch of a test volume Ω with boundary Γ , population density $u(x,t)$, and flux $J(x,t)$ through the boundary.

4.3.1 Derivation of Reaction-Diffusion Equations

Assume a population with density $u(x,t)$ is living and moving in a container. To describe movement, we introduce another dependent quantity, the particle flux, $J(x,t) \in \mathbb{R}^n$. At each location x and at each time t , the flux $J(x,t)$ is a vector which points in the general direction of movement at that location. Its magnitude, $|J(x,t)|$, is proportional to the amount of particles which flow in that direction per unit time. Specifically, the flux J plays the role of the heat flux in heat transport, or a concentration flux for a chemical reactor, and so on.

We consider a test volume Ω with boundary Γ and we balance the fluxes inward and outward on Ω through Γ (see Figure 4.4). In words,

Change of u in Ω = flux through Γ + change due to birth, death, interactions.

Written in mathematical relations, this means

$$\frac{d}{dt} \int_{\Omega} u(x,t) dV = - \int_{\Gamma} J(x,t) dS + \int_{\Omega} f(u(x,t)) dV,$$

where dV denotes integration in the whole space \mathbb{R}^n and dS denotes surface integration in dimension \mathbb{R}^{n-1} .

We use the Divergence Theorem

$$\int_{\Gamma} J(x,t) dS = \int_{\Omega} \text{div} J(x,t) dV,$$

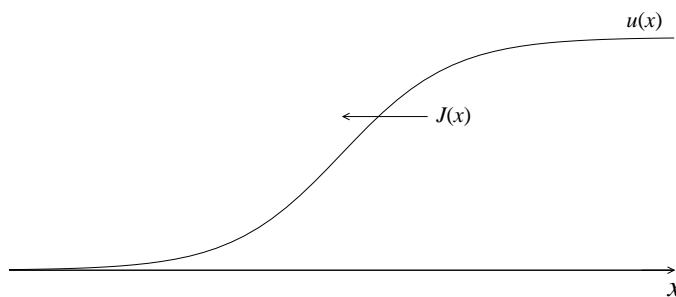


Figure 4.5. Schematic of Fick's second law. A positive gradient of u gives rise to a negative flux J .

and we get

$$\int_{\Omega} \left(\frac{d}{dt}u - f(u) + \operatorname{div}J \right) dV = 0.$$

The above relation is satisfied in each test volume Ω . Then (if the measure dV is not degenerate) it follows that

$$\frac{d}{dt}u - f(u) + \operatorname{div}J = 0. \tag{4.11}$$

Next, we need an expression of the flux in terms of the population distribution. As for chemical reactions, we use Fick's second law¹

$$J = -D\nabla u. \tag{4.12}$$

We assume that the flux J is proportional to the negative gradient of the particle distribution. In Figure 4.5, we show a positive gradient of u ($\frac{\partial}{\partial x}u(x, t) > 0$). The flux points to the left, leading to equilibrate high and low levels of u . If we combine the balance law (4.11) with Fick's law (4.12), we get a *reaction-diffusion equation*,

$$\frac{d}{dt}u = D\Delta u + f(u), \tag{4.13}$$

where the Laplacian Δu is defined as

$$\Delta u(x, t) = \frac{\partial^2}{\partial x_1^2}u(x, t) + \dots + \frac{\partial^2}{\partial x_n^2}u(x, t), \quad x = (x_1, \dots, x_n) \in \mathbb{R}^n.$$

If $f = 0$, then equation (4.13) is simply the *diffusion equation* or *heat equation*.

¹

In the interpretation of heat transport, this law is known as *Fourier's law*.

4.3.2 The Fundamental Solution

The fundamental solution is a particular solution of the diffusion equation ((4.13) with $f = 0$), that can be used to find other solutions by convolution (see, for example, Britton [24]). Moreover, this solution shows many of the common properties of solutions of reaction-diffusion equations in general.

The *fundamental solution* appears for a particle which starts at the origin 0. In terms of random walks on a grid (see Chapter 5), it is straightforward to start with a particle at 0. In the continuous case, however, we use a δ -distribution $\delta_0(x)$. The δ -distribution is not a function in the classical sense. It is defined by its action on smooth functions. If $f(x)$ is a smooth function, then $\delta_0(x)$ is the one and only object which satisfies

$$\int_{\mathbb{R}} \delta_0(x)f(x)dx = f(0)$$

and

$$\int_{\mathbb{R}} \delta_0(x)dx = 1.$$

To get an idea about the shape of $\delta_0(x)$ keep in mind that

$$\delta_0(x) = \begin{cases} +\infty & \text{for } x = 0, \\ 0 & \text{for } x \neq 0, \end{cases} \tag{4.14}$$

which is, however, not a valid definition of $\delta_0(x)$.

The δ -distribution is the prototype of a class of functions which are called *distributions* (we refer to Friedlander [53] for further details on distributions). For now, it is sufficient to understand the properties as described above, and consider the *initial-value problem* for a particle which diffuses in one dimension and starts with certainty at 0:

$$g_t = Dg_{xx}, \quad g(x, 0) = \delta_0(x). \tag{4.15}$$

The *fundamental solution* (in one dimension) (see Exercise 4.5.2) is

$$g(x, t) = \frac{1}{2\sqrt{\pi Dt}} e^{-\frac{x^2}{4Dt}}. \tag{4.16}$$

In Figure 4.6, we show this solution for time steps $t = 0$, $t = t_1 > 0$, $t = t_2 > t_1$, and $D = 1$. Although the initial condition is not continuous, the solution (4.16) is continuous for all $t > 0$. In fact, it is infinitely often continuously differentiable, a property which is known as the *regularizing* property of the diffusion equation.

At $t = 0$, we have $\delta_0(x) = 0$ for all $x \neq 0$. However, as soon as $t > 0$, we have $g(x, t) > 0$ for all $x \in \mathbb{R}$. There is a minimal chance to find the particle very far from its starting point. The diffusion equation allows for infinitely fast propagation.

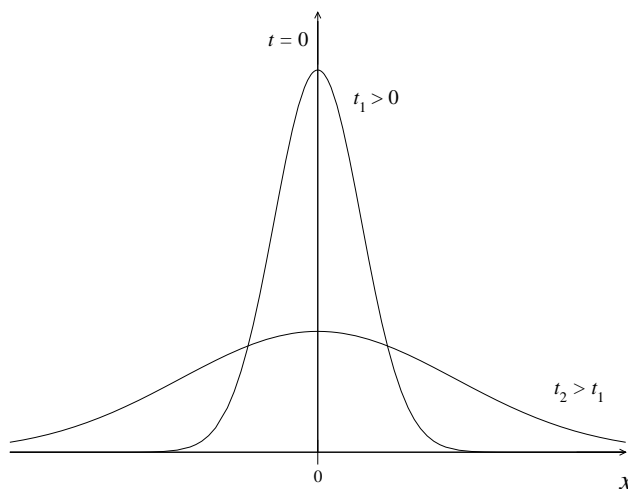


Figure 4.6. Solutions of the diffusion equation (4.15) for three time values, $t = 0$, $t = t_1 > 0$, and $t = t_2 > t_1$.

If we study the diffusion equation with a general initial condition,

$$u_t = Du_{xx}, \quad u(x, 0) = f(x), \tag{4.17}$$

then the solution can be found by convolution with g :

$$u(x, t) = (f * g(\cdot, t))(x),$$

where the convolution integral is given by

$$\begin{aligned} (f * g(\cdot, t))(x) &= \int_{-\infty}^{\infty} f(y) g(x - y, t) dy \\ &= \frac{1}{2\sqrt{\pi Dt}} \int_{-\infty}^{\infty} f(y) e^{-\frac{(x-y)^2}{4Dt}} dy. \end{aligned} \tag{4.18}$$

4.3.3 Critical Patch Size

Reaction-diffusion equations are used to estimate the size of a habitat that can support a population. In general, it is not possible to establish a stable surviving population on an island that is too small. For pests, like the spruce budworm (see Murray [110]), information about the critical patch size can be used to determine how to split a woodland into small enough patches so as to prevent the budworms from settling in.

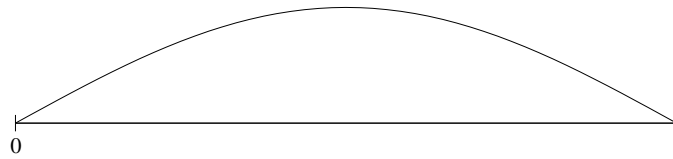


Figure 4.7. A typical solution of (4.19) with homogeneous Dirichlet boundary conditions (island-conditions).

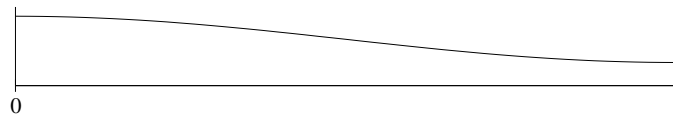


Figure 4.8. A typical solution of (4.19) with homogeneous Neumann boundary conditions (box-conditions).

To illustrate the use of reaction-diffusion equations in this context, we use Fisher’s equation, which shows all necessary features. Fisher [49] proposed the following model for the spread of an advantageous gene in a population:

$$u_t = Du_{xx} + \mu u(1 - u), \tag{4.19}$$

where $u(x, t)$ is the density of the gene in the population at time t and location x . The term $\mu u(1 - u)$ is already familiar to us: it is Verhulst’s law of growth with saturation. Fisher’s equation applies also for population growth of randomly moving individuals. We will study this equation on a one-dimensional patch of size l , $I = [0, l]$.

A partial differential equation on a bounded interval needs boundary conditions. Here we are guided by the application, and we discuss the most common possibilities.

The case of an island as a patch has already been mentioned. Appropriate *island boundary conditions* are

$$u(0, t) = 0, \quad u(l, t) = 0. \tag{4.20}$$

These are also called *homogeneous Dirichlet boundary conditions* (see Figure 4.7). We can also study a valley or a box, or a patch with sealing walls. Then no individual can leave the patch. Appropriate *box boundary conditions* are

$$u_x(0, t) = 0, \quad u_x(l, t) = 0, \tag{4.21}$$

which are sometimes called *homogeneous Neumann boundary conditions* (see Figure 4.8). Obviously, combinations of island and box boundary conditions can occur if, for example, the patch is bounded by a wall on the one side and by water on the other. We could also include some semi-permeable walls such that only a fraction of the population can leave the domain, etc. We restrict our attention to the first two cases given above. Note that we need *one set* of boundary conditions, either (4.20) or (4.21), but not both at the same time.

The question we are investigating is:

How large must an island or box be to support a population?

It has been shown in research articles (see for example Britton [24]) that it is equivalent to ask when the trivial solution $u(x, t) = 0$ is unstable. If $u(x, t) \equiv 0$ would be stable, then each solution (near 0) would converge to 0, and the population would die out. Hence, $u(x, t) \equiv 0$ has to be unstable to allow for a surviving population. We are not introducing the notion of *stable* or *unstable* for partial differential equations here, but we can use them in the same way as for ordinary differential equations (see Chapter 3).

For Fisher's equation (4.19), the following questions are equivalent (Grindrod [66]).

- (i) *How large must an island or box be to support a population?*
- (ii) *What is the critical domain length l^* such that $u \equiv 0$ is stable for $l < l^*$ and unstable for $l > l^*$?*
- (iii) *What is the critical domain length l^* such that a non-trivial stationary solution (steady state) exists for $l > l^*$?*

We investigate (iii):

A steady state satisfies $u_t = 0$, hence

$$u_{xx} = -\frac{\mu}{D}u(1 - u). \tag{4.22}$$

We are looking for solutions $u(x) \neq 0$ which satisfy the correct boundary conditions, and we will use phase plane analysis from Chapter 3 to study (4.22). With a new variable, $v := u_x$, we obtain the system

$$\begin{aligned} u_x &= v, \\ v_x &= -\frac{\mu}{D}u(1 - u), \end{aligned} \tag{4.23}$$

with Dirichlet boundary conditions (4.20)

$$u(0) = 0, \quad u(l) = 0,$$

or with Neumann boundary conditions (4.21)

$$v(0) = 0, \quad v(l) = 0.$$

The key to studying equation (4.23) is to understand x as a "time" variable and to consider

$$\begin{aligned} u' &= v \\ v' &= -\frac{\mu}{D}u(1 - u) \end{aligned} \tag{4.24}$$

as a 2×2 system of ordinary differential equations. The equilibria of (4.24) are

$$P_1 = (0, 0), \quad P_2 = (1, 0).$$

The Jacobian of (4.24) is

$$Df(u, v) = \begin{pmatrix} 0 & 1 \\ 2\frac{\mu}{D}u - \frac{\mu}{D} & 0 \end{pmatrix}.$$

The linearization of (4.24) at P_1 is

$$Df(0, 0) = \begin{pmatrix} 0 & 1 \\ -\frac{\mu}{D} & 0 \end{pmatrix},$$

which has purely imaginary eigenvalues $\lambda_{1/2} = \pm i\sqrt{\frac{\mu}{D}}$. Hence, $(0, 0)$ is a center.

At P_2 , we find

$$Df(1, 0) = \begin{pmatrix} 0 & 1 \\ \frac{\mu}{D} & 0 \end{pmatrix},$$

with eigenvalues $\lambda_{1/2} = \pm \frac{\mu}{D}$. Hence, $(1, 0)$ is a saddle.

Since $(1, 0)$ is a saddle for the linearization, it is also a saddle for the full, nonlinear system (4.24). This follows from the Hartman-Grobman Theorem (see Theorem 3.6). Unfortunately, the Hartman-Grobman Theorem does not apply to the center case. We cannot decide yet, whether $(0, 0)$ is a stable spiral, an unstable spiral, or indeed a center for the nonlinear system (4.24).

We can obtain the missing information from a *Hamiltonian function*, which is a function $H(u, v)$ that satisfies

$$\frac{\partial H}{\partial v} = u' \quad \text{and} \quad \frac{\partial H}{\partial u} = -v'. \tag{4.25}$$

For solutions $(u(x), v(x))$ of (4.24), we get via the chain rule

$$\frac{d}{dx}H(u(x), v(x)) = \frac{\partial H}{\partial u} \cdot u' + \frac{\partial H}{\partial v} \cdot v' = -v'u' + u'v' = 0. \tag{4.26}$$

For (4.24) we can write down the Hamilton function explicitly

$$H(u, v) = \frac{1}{2}v^2 + \frac{\mu}{D}\frac{u^2}{2} - \frac{\mu}{D}\frac{u^3}{3}.$$

Remember that we understand x as time, hence from (4.26), it follows that the value of H does not change along solution curves $(u(x), v(x))$.

In Figure 4.9, we show H as a function of (u, v) . Since H does not change along solution curves, the solution curves must follow the level lines of H . Since we have a Hamiltonian function, it follows that each bounded solution is either

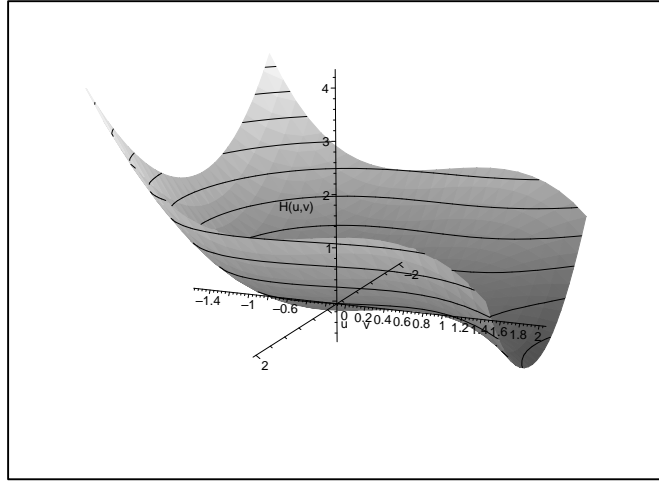


Figure 4.9. *Hamiltonian function $H(u, v)$ and level curves.*

1. an equilibrium point,
2. a connection of equilibrium points, or
3. a closed orbit.

This implies that the steady state $(0, 0)$ is a center. We now have enough information to sketch the phase portrait of (4.24) in Figure 4.10. Although the phase portrait includes regions of $u < 0$, we consider only solutions which satisfy $u \geq 0$. Since $u(x)$ is a population density, it cannot be negative. We refer to the region $u < 0$ as *not biologically relevant*.

To find relevant solutions, we have to consider the boundary conditions. In the notion of the “time” x , a Dirichlet solution is a solution that starts at 0 ($u(0) = 0$), and it connects to $u(l) = 0$, where $u \geq 0$ all the time. Curve a) in Figure 4.10 shows one such solution. Solutions to Neumann boundary conditions connect $v(0) = 0$ with $v(l) = 0$. A typical solution is indicated by curve b) in Figure 4.10. Of course, this solution is not biologically relevant. The only relevant solutions for the Neumann case are $u \equiv 0$ and $u \equiv 1$.

Hence for a box, we can already answer our original question. *A box of any size supports a population up to the carrying capacity (which is 1 in this case). The corresponding solution is $u(x, t) \equiv 1$.*

What is the minimal length for the Dirichlet problem? Let’s take a closer look at the Dirichlet solutions. Each solution has a unique u -axis intersection \bar{u} (see Figure 4.11). As $\bar{u} \rightarrow 1$, the solution approaches the saddle point. Very close to the saddle point, it takes longer and longer to move forward. Hence, $l \rightarrow \infty$ for $\bar{u} \rightarrow 1$.

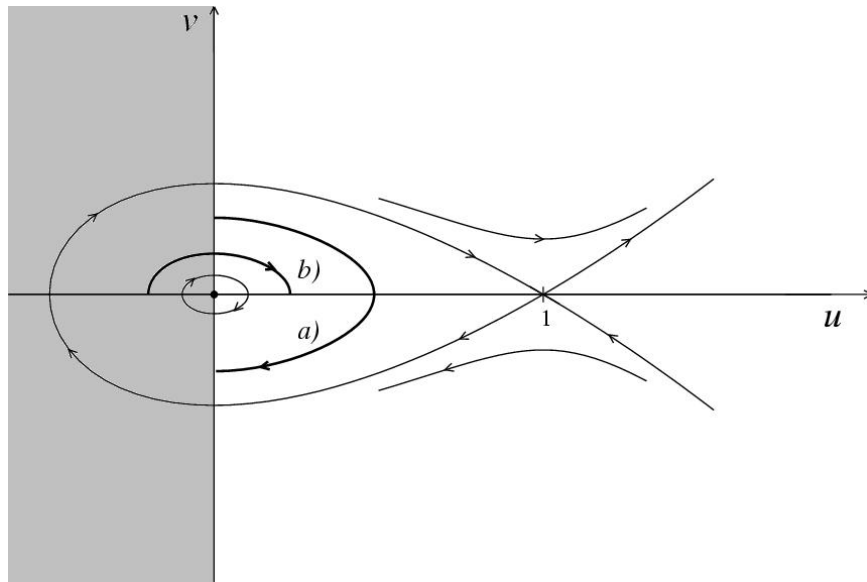


Figure 4.10. Phase portrait of system (4.24). The curve a) shows a solution which satisfies homogeneous Dirichlet boundary conditions, whereas b) is a solution with homogeneous Neumann boundary conditions. The grey area is not biologically relevant because $u < 0$.

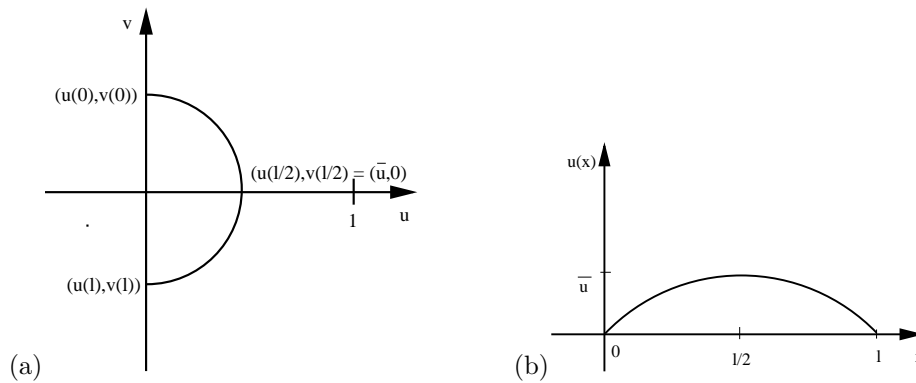


Figure 4.11. (a) For each possible Dirichlet solution there is a unique u -axis intersection \bar{u} . (b) The same Dirichlet solution shown as a function of x

One could guess that $l \rightarrow 0$ for $\bar{u} \rightarrow 0$, but this is false. For $\bar{u} \rightarrow 0$, we enter the range close to $(0, 0)$, where the linearization describes the behaviour of the solutions. Remember that $(0, 0)$ is a center with eigenvalues $\lambda_{1/2} = \pm i\sqrt{\frac{E}{D}}$. Hence the general solution near $(0, 0)$ is given as $(u(x), v(x))^T = (c_1 \cos(\sqrt{\frac{E}{D}}x), c_2 \sin(\sqrt{\frac{E}{D}}x))^T$.

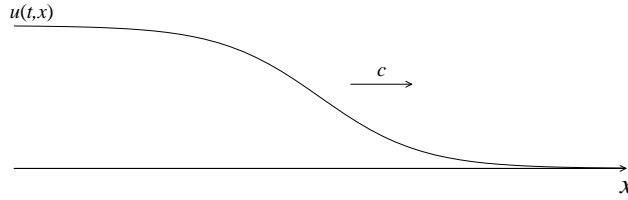


Figure 4.12. A typical invasion travelling wave.

A Dirichlet solution corresponds to a half circle starting at $(u(0), v(0)) = (0, c_2)$ and ending at $(u(l), v(l)) = (0, -c_2)$, which gives $\sqrt{\frac{\mu}{D}}l = \pi$, hence $l = \pi\sqrt{\frac{D}{\mu}}$. In the limit $\bar{u} \rightarrow 0$, we get a critical patch size of $l^* = \pi\sqrt{\frac{D}{\mu}}$.

If $l > l^*$, we get a population distribution of the form shown in Figure 4.7 and Figure 4.11 (b). If $l < l^*$, the patch cannot support the population. Note that the case $l = l^*$ cannot be decided by linear analysis. If $l = l^*$, one of the eigenvalues of the homogeneous solution equals zero, hence $(0, 0)$ is not hyperbolic and the Hartman-Grobman theorem cannot be applied. For $l = l^*$, the full nonlinear problem needs to be solved.

Now we are able to solve the problem for the island boundary conditions as well: *An island can support a population if its length l satisfies $l > l^* = \pi\sqrt{\frac{D}{\mu}}$. If $l < l^*$ each initial population will die out.*

4.3.4 Travelling Waves

Another important problem in spatial ecology is if and how species can invade new habitats. Our method for studying this is to look for travelling wave solutions of a reaction-diffusion equation. To illustrate this, we again study Fisher's equation,

$$u_t = Du_{xx} + \mu u(1 - u), \tag{4.27}$$

but now on the whole line \mathbb{R} . We seek solutions which describe the invasion of the population into a new habitat. In particular, we seek solutions $u(x, t)$ that have the form shown in Figure 4.12, and then move with constant speed c . A solution of this type can be expressed as

$$u(x, t) = \phi(x - ct).$$

For $c > 0$, the function $\phi(x - ct)$ is the function $\phi(x)$ shifted to the right by ct , see Figure 4.13. The parameter c is the *wave speed*, the new variable, $z := x - ct$, is called the *wave variable*, and the function $\phi(z)$ is called the *wave profile*.

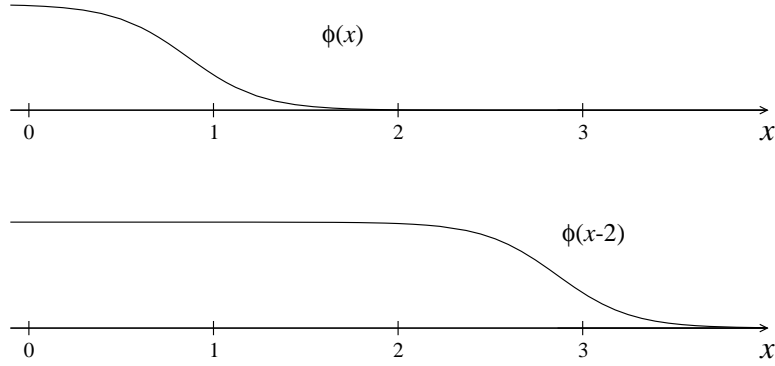


Figure 4.13. The profile $\phi(x)$ from the top figure is shifted by 2 to the right (bottom).

We make the *travelling wave ansatz*

$$u(x, t) = \phi(x - ct), \quad \phi(-\infty) = 1, \quad \phi(+\infty) = 0, \quad (4.28)$$

where instead of boundary conditions, we now have conditions at $\pm\infty$. For $x \rightarrow -\infty$, the population has already grown to its carrying capacity (1 in this case), and for $x \rightarrow +\infty$, the population has not arrived yet.

From (4.28), we obtain

$$\frac{\partial}{\partial t} u(x, t) = -c\phi', \quad \frac{\partial^2}{\partial x^2} u(x, t) = \phi'',$$

and (4.27) reduces to the following ordinary differential equation for $\phi(z)$

$$-c\phi' = D\phi'' + \mu\phi(1 - \phi). \quad (4.29)$$

As in the previous section, we introduce a new variable, $\psi := \phi'$, and write (4.29) as a 2×2 system

$$\begin{aligned} \phi' &= \psi, \\ \psi' &= -\frac{c}{D}\psi - \frac{\mu}{D}\phi(1 - \phi). \end{aligned} \quad (4.30)$$

The equilibria of (4.30) are $P_1 = (0, 0)$ and $P_2 = (1, 0)$. Using the linearization, we find that the point $P_1 = (0, 0)$ is stable for $c > 0$. It is a stable spiral for $c < 2\sqrt{D\mu}$, and a stable node for $c > 2\sqrt{D\mu}$. The point $P_2 = (1, 0)$ is always a saddle.

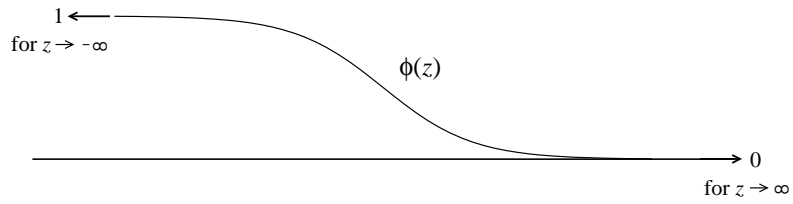


Figure 4.14. *The travelling wave as a function of the wave variable z .*

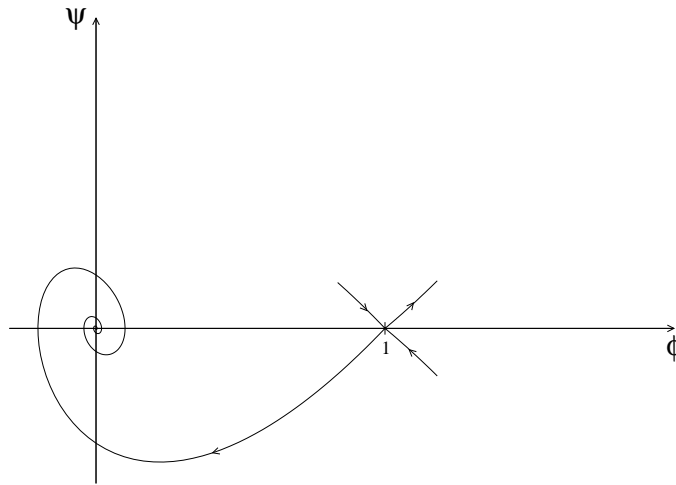


Figure 4.15. *Heteroclinic connection from the saddle at $(1, 0)$ to the stable spiral at $(0, 0)$. Here $\mu = D = 1$ and $c < 2$. There is no non-negative travelling wave.*

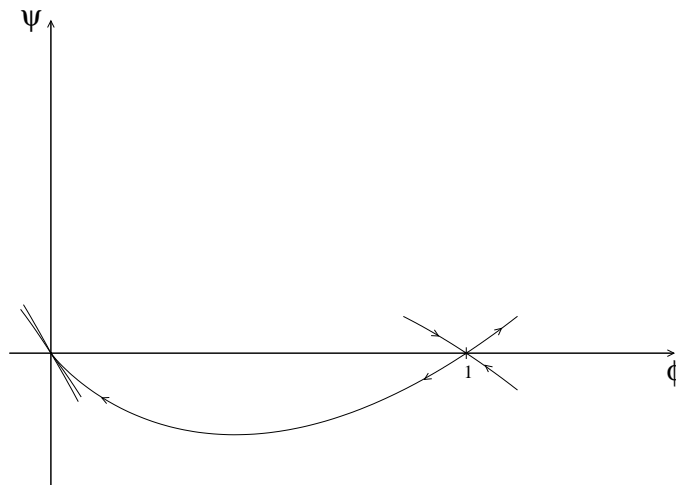


Figure 4.16. *Heteroclinic connection from the saddle at $(1, 0)$ to the stable node at $(0, 0)$. Here $\mu = D = 1$, $c > 2$. There exists a non-negative travelling wave.*

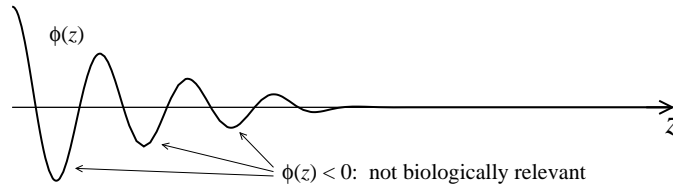


Figure 4.17. Oscillations of the leading edge of the wave from Figure 4.15.

As for the critical patch size, we interpret x as a time variable. Recall that the boundary conditions for the wave profile are $\phi(-\infty) = 1$ and $\phi(+\infty) = 0$. Moreover, from the form of ϕ as shown in Figure 4.14, it is clear that $\psi(-\infty) = \psi(+\infty) = 0$. Hence, in the phase portrait of system (4.30), we have to find a connection from the saddle $(1, 0)$ to the stable point $(0, 0)$. We show these connections for $c < 2\sqrt{D\mu}$ in Figure 4.15, and for $c > 2\sqrt{D\mu}$ in Figure 4.16 b).

The function ϕ is the profile of the population density; hence it has to be nonnegative. Thus solutions for $c < 2\sqrt{D\mu}$ are not biologically relevant. They correspond to an oscillating front (see Figure 4.17). We obtain that the minimal speed c^* for which a wavefront solution exists, is given by $c^* = 2\sqrt{D\mu}$ (here we argued graphically; a proof can be found in Källén *et al.* [88]).

General Fisher equation

The above result on minimal wave speed of travelling fronts can be generalized to general Fisher equations

$$u_t = Du_{xx} + f(u),$$

where $f(u)$ has a shape similar to $\mu u (1 - \frac{u}{K})$. The exact conditions on f are: there is a $K > 0$ such that

$$\begin{aligned} f(0) &= 0, & f(K) &= 0, \\ f(u) &> 0, & \text{for all } 0 < u < K, \\ f'(0) &> 0, & f'(K) &< 0. \end{aligned}$$

Moreover, if we assume that $f(u)$ satisfies the subtangential condition,

$$f'(0)u > f(u), \quad \text{for all } 0 < u < \infty,$$

then the minimal wave speed is

$$c^* = 2\sqrt{Df'(0)}.$$

The Linear Conjecture

As we saw in the previous sections, the minimal wave speed c^* is exactly that value where $(0, 0)$ changes from spiral into node. If we consider the travelling wave solution close to $(0, 0)$, then the behaviour is described by the linearization around $(0, 0)$. The Jacobian of (4.30) at $(0, 0)$ is

$$Df(0, 0) = \begin{pmatrix} 0 & 1 \\ -\frac{\mu}{D} & -\frac{c}{D} \end{pmatrix},$$

which has trace $-c/D$ and determinant μ/D . Hence, $(0, 0)$ is a node if and only if

$$c^2 - 4D\mu > 0,$$

or $c > 2\sqrt{D\mu}$. The eigenvalues then are given by

$$\lambda_{1/2} = -\frac{c}{2D} \pm \frac{1}{2}\sqrt{\frac{c^2}{D^2} - 4\frac{\mu}{D}},$$

and for $c^* = 2\sqrt{D\mu}$, we have an eigenvalue of multiplicity 2:

$$\lambda_1 = \lambda_2 = -\frac{c^*}{2D}.$$

The solution near $(0, 0)$ behaves like $e^{-\frac{c^*}{2D}x}$ for $x \rightarrow \infty$. Hence, $-\frac{c^*}{2D}$ is the decay rate at the wave front.

Indeed, in many cases, it is enough to measure the decay rate of the profile for large x to get a good approximation for the minimal wave speed c^* . This is known as *linear conjecture*.

4.4 Further Reading

There are a number of introductory textbooks on partial differential equations (PDE), such as the books by Haberman [68], and Keane [89]. The contents of these and similar books has been developed in the context of applications in engineering and physics. Most of the material deals with separation and series solutions (see also Exercise 4.5.6). Although these methods are very important, they do not play a major role in applications to biological systems. For PDE's in mathematical biology, a more modern approach is used, which is based on dynamical system theory and nonlinear dynamics. For example, the material in Section 4.3.3 cannot be found in any of the classical introductory textbooks, although it can be understood easily with a basic background in ordinary differential equations.

The text of Webb [150] is an introductory text and also a standard reference for age structured population models. The material from Section 4.2 is based on Webb. For reaction-diffusion equations (including the Fisher equation), a standard reference is Murray [112]. A very good introduction to critical domain size and traveling waves can be found in Britton [24]. The traveling wave problem also is discussed in detail in Grindrod [66].

The material on critical domain size and on travelling waves is also covered in the introductory biomath textbooks which are mentioned in Appendix A "Further Reading"; Britton [25], Jones and Sleeman [86], and Taubes [145].

Pattern formation, *Turing* instabilities, and *activator-inhibitor* systems have not been discussed in the present course. We refer to the aforementioned texts of Murray, Britton, or Grindrod. Okubo and Levine [119] give a detailed overview of the manifold applications of reaction-diffusion and reaction-advection-diffusion equations to biological problems (advection refers to directed movement).

Two more recent books on reaction-diffusion and related models applied to population dynamics are by Thieme [146] and Cantrell and Cosner [33]. Both texts give a comprehensive treatment of the underlying theory of dynamical systems, bifurcations and functional analysis. Thieme's book deals with stage-structured population models, and Cantrell and Cosner study questions about *permanence* and *persistence* in spatially nonhomogeneous ecological systems.

To obtain a good basic knowledge of the theory of PDE and their mathematical properties we recommend the following textbooks: Evans [47], McOwen [106], and Renardy and Rogers [127]. These texts are pure PDE courses and they do not feature biological applications. They are appropriate for an beginning graduate student, and they are not too easy. To properly derive a solution theory for PDE's one has to introduce appropriate function spaces and one needs some functional analytical tools.