

# Chapter 4

## Movement in space

Our view of the world is structured by time and space and, we believe, this reflects reality: to interact, entities have to be at the same position at the same time. So far we concentrated on changes in time, but now we are going to incorporate spatial position. In the present chapter we only consider independent particles (molecules, bacteria, ...) but in the next we shall incorporate interaction.

### 4.1 Flux

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The *density* of bacteria on an agar plate is, by definition, the number of bacteria per unit of area. Likewise, the *concentration* of a chemical substance in solution is the number of molecules per unit of volume. The density or concentration in a *point* is an idealisation, corresponding to the thought experiment of shrinking the area or volume to zero while focusing our attention on the point. We then write  $u = u(t, x)$  and consider  $u$  as a smooth function of time  $t$  and position  $x$ . Note that we need to integrate  $u(t, \cdot)$  over space to obtain an amount. If the total number is conserved, but the individual particles move,  $u(t, \cdot)$  changes with time. How? How does redistribution over space manifest itself in changes in density/concentration?

Let us first consider a one-dimensional space (one might think of a river) and deterministic motion with prescribed velocity  $c = c(x)$  (one might think of algae that float with the streaming water). The *flux* at  $x$  is the number of organisms that pass  $x$ , say from left to right, per unit of time. We denote the flux by  $J = J(t, x)$ . Clearly

$$J(t, x) = c(x)u(t, x), \quad (4.1.1)$$

as is indeed also suggested by the dimensional identity

$$\frac{\text{number}}{\text{time}} = \frac{\text{length}}{\text{time}} \cdot \frac{\text{number}}{\text{length}}. \quad (4.1.2)$$

Equally clearly,

$$\frac{d}{dt} \int_a^b u(t, x) dx = J(t, a) - J(t, b), \quad (4.1.3)$$

or, in words, if neither creation nor annihilation occurs, then the total number of organisms between  $a$  and  $b$  changes only by way of flux in at  $a$  and flux out at  $b$  (convince yourself that this terminology is appropriate when  $a < b$  and  $c > 0$  or when  $a > b$  and  $c < 0$ , but should be adjusted otherwise). According to the fundamental theorem of calculus,

$$J(t, b) - J(t, a) = \int_a^b \frac{\partial J}{\partial x}(t, \xi) d\xi. \quad (4.1.4)$$

Hence,

$$\int_a^b \left( \frac{\partial u}{\partial t}(t, \xi) + \frac{\partial J}{\partial x}(t, \xi) \right) d\xi = 0, \quad (4.1.5)$$

and as this holds for arbitrary  $a$  and  $b$ , the integrand must be zero (see Lemma of DuBois-Reymond (Lin and Segel, 1998)), and so in combination with (4.1.1) we arrive at the *conservation law*

$$\frac{\partial u}{\partial t} + \frac{\partial}{\partial x}(cu) = 0. \quad (4.1.6)$$

Two important variations on this theme are

- (i) in *higher space dimension* the flux  $J$  is a *vector* and the conservation law takes the form

$$\frac{\partial u}{\partial t} + \nabla \cdot J = 0, \quad (4.1.7)$$

with the *divergence* of the flux  $\nabla \cdot J$  defined by

$$\nabla \cdot J = \sum_{i=1}^n \frac{\partial J_i}{\partial x_i} \quad (4.1.8)$$

(more explanation below).

- (ii) The motion of pollen that the botanist Brown observed under his microscope was very irregular. So much so that it became the prototype for *random* motion. A phenomenological description takes *Fick's law*

$$J = -d\nabla u, \quad (4.1.9)$$

as the constitutive relation that links the flux  $J$  to the density  $u$  by requiring that  $J$  is proportional to the *gradient*  $\nabla u$ , with  $d$  a constant of proportionality called the *diffusion constant*, since when we substitute (4.1.9) into (4.1.7) we obtain the *diffusion equation*

$$\frac{\partial u}{\partial t} = d\Delta u, \quad (4.1.10)$$

where  $\Delta = \sum_{i=1}^n \frac{\partial^2}{\partial x_i^2}$  is the *Laplacian*. Note that  $d$  has dimension  $(\text{length})^2/\text{time}$ .

In the next subsection we shall provide various derivations that yield a quasi-mechanistic underpinning of Fick's Law. We conclude this subsection with a few observations on the notion of flux in higher dimensions.

Consider a point in two-space. If we want to talk about the traffic of particles in that point, we need to specify a direction. This we do by choosing a unit vector  $m$ . The flux  $J$  at the point is a vector such that, whatever choice of  $m$ , the number of particles crossing per unit of time a straight line  $L$  perpendicular to  $m$  in an interval of length  $h$  centred at the focus point equals

$$J \cdot m h + o(h) \quad \text{as } h \rightarrow 0.$$

For deterministic motion we have just as in the one-dimensional case that the flux is the product of the velocity, which is now a vector, and the density (so in particular, the traffic is maximal in the direction of the velocity and zero in the direction perpendicular to the velocity).

In the present context, the analogue of the fundamental theorem of calculus is the *Divergence Theorem*

$$\int_{\Omega} \nabla \cdot F dA = \int_{\partial\Omega} F \cdot n ds, \quad (4.1.11)$$

where  $n$  is the outward pointing unit vector (outward normal) perpendicular to the boundary  $\partial\Omega$  of the domain  $\Omega$ .

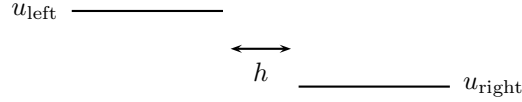


FIGURE 4.1.

In three dimensions, one replaces  $L$  by a plane and the interval of length  $h$  by a subset of this plane of area  $h$ . The Divergence Theorem now reads

$$\int_{\Omega} \nabla \cdot F \, dV = \int_{\partial\Omega} F \cdot n \, dS, \quad (4.1.12)$$

and is usually called *Gauss' Theorem*.

Note that if we substitute Fick's Law (4.1.9) into the identity of the Divergence or Gauss' Theorem, we obtain

$$\int_{\Omega} \Delta u = \int_{\partial\Omega} \frac{\partial u}{\partial n}. \quad (4.1.13)$$

## 4.2 Various ways to motivate Fick's Law

**Derivation 1** Consider one-dimensional space and suppose that at every point particles move at speed  $c$ , but half of them to the left and half to the right. Consider a point where the density jumps over a gap of length  $h$  from a constant density  $u_{\text{left}}$  to a constant density  $u_{\text{right}}$  (see Fig. 4.1). In a time interval of length  $\Delta t$  the net transport to the right equals

$$\frac{1}{2}(u_{\text{left}} - u_{\text{right}})c\Delta t.$$

So per unit of time  $\frac{1}{2}(u_{\text{left}} - u_{\text{right}})c$  is transported, which we write as

$$\frac{u_{\text{left}} - u_{\text{right}}}{h} \frac{1}{2}ch.$$

When we now take the limit  $h \rightarrow 0$  while assuming that

$$\frac{1}{2}hc \rightarrow d,$$

we obtain

$$\text{flux} = -d \frac{\partial u}{\partial x}.$$

The key point of this very debatable “derivation” is that it clearly shows that in the limit we should have  $c \rightarrow \infty$ . So, in a sense, we consider particles that move infinitely fast but never can make up their mind about the direction in which they go.

**Derivation 2** Imagine a particle moving on a one-dimensional lattice that we represent by  $\mathbb{Z}$ . We take time discrete and at every time step the particle moves to the left with probability  $\frac{1}{2}$  and to the right with probability  $\frac{1}{2}$ . If the particle is at position zero at time zero then the probability  $p_i(n)$  that it is at position  $i$  at time  $n$  is given explicitly by

$$p_i(n) = \begin{cases} \binom{n}{\frac{1}{2}(n+i)} \left(\frac{1}{2}\right)^n & \text{for } n+i \text{ even and } -n \leq i \leq n, \\ 0 & \text{otherwise.} \end{cases}$$

(Indeed, if the particle makes  $k$  steps to the right then it makes  $n - k$  steps to the left, and to end up at  $i$  we should have  $k - (n - k) = i$ . Hence  $k = \frac{1}{2}(n + i)$ . The probability that  $k$  out of  $n$  steps are to the right equals  $\binom{n}{k}(\frac{1}{2})^k(\frac{1}{2})^{n-k} = \binom{n}{k}(\frac{1}{2})^n$ .)

If we now take  $i = \frac{x}{\lambda}$  and  $n = \frac{t}{\tau}$ , let both  $\lambda$  and  $\tau$  approach zero but in such a way that  $\lambda^2/2\tau$  converges to  $d$ , then the binomial distribution converges to the normal distribution (see e.g. Section 7.3 in (Chung, 1974), or better still, verify this yourself)

$$p(t, x) = \frac{1}{2\sqrt{\pi dt}} e^{-\frac{x^2}{4dt}}.$$

This, as we shall see later on, is the fundamental solution of the one-dimensional diffusion equation. Note that one can interpret  $\lambda/\tau$  as the speed and that this speed grows beyond any bound.

Alternatively, we can shorten the distance between the lattice points as well as the time intervals between steps. Then, by performing a formal Taylor expansion for  $p$  we derive the diffusion equation directly from the random walk assumptions by taking a limit. The next derivation is essentially of this type, but considers right away both space and time as continuous variables.

Note once again that for independently moving particles we need not make a distinction between the density of many particles and the probability density for one particle.

**Derivation 3** We postulate that

$$u(t + \tau, x) = \int_{-\infty}^{\infty} u(t, x - y) \frac{1}{\varepsilon} \phi\left(\frac{y}{\varepsilon}\right) dy \quad (4.2.1)$$

for a function  $\phi$  satisfying  $\phi \geq 0$ ,  $\int_{-\infty}^{\infty} \phi(y) dy = 1$ , and  $\phi(-y) = \phi(y)$ . Then, in particular,  $\int_{-\infty}^{\infty} y\phi(y) dy = 0$ . The identity (4.2.1) states that between times  $t$  and  $t + \tau$  particles are moved over a distance  $y$  with probability density  $\frac{1}{\varepsilon}\phi\left(\frac{y}{\varepsilon}\right)$  and the symmetry guarantees that there is no preferred direction. A formal Taylor expansion yields

$$u(t + \tau, x) = u(t, x) + \tau \frac{\partial u}{\partial t}(t, x) + \dots, \quad (4.2.2)$$

$$u(t, x - y) = u(t, x) - y \frac{\partial u}{\partial x}(t, x) + \frac{1}{2} y^2 \frac{\partial^2 u}{\partial x^2}(t, x) + \dots. \quad (4.2.3)$$

Substituting these expressions in (4.2.1) we find

$$\tau \frac{\partial u}{\partial t}(t, x) = \frac{1}{2} \int_{-\infty}^{\infty} y^2 \frac{1}{\varepsilon} \phi\left(\frac{y}{\varepsilon}\right) y dy \frac{\partial^2 u}{\partial x^2}(t, x) + \dots, \quad (4.2.4)$$

$$= \frac{\varepsilon^2}{2} \int_{-\infty}^{\infty} z^2 \phi(z) dz \frac{\partial^2 u}{\partial x^2}(t, x) + \dots \quad (4.2.5)$$

If we now let both  $\tau$  and  $\varepsilon$  converge to zero but in such a manner that

$$\frac{\varepsilon^2}{2\tau} \int_{-\infty}^{\infty} z^2 \phi(z) dz \rightarrow d,$$

we arrive at

$$\frac{\partial u}{\partial t} = d \frac{\partial^2 u}{\partial x^2}. \quad (4.2.6)$$

**EXERCISE 4.2.1.** Let  $u(t, x)$  satisfy (4.2.6). Show that  $u$  as a function of  $t$  decreases where  $u$  as a function of  $x$  has a maximum, and that  $u$  as a function of  $t$  increases where  $u$  as a function of  $x$  has a minimum. Conclude that the diffusion equation has an equalising effect. Do you agree that this is already embodied in Fick's Law?

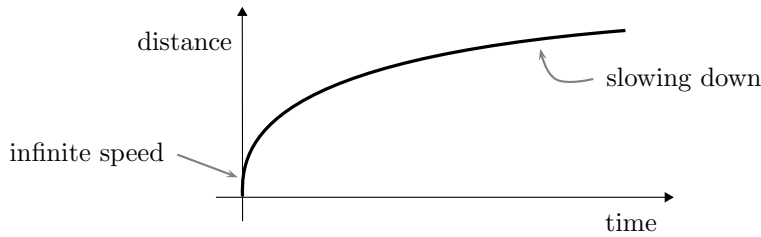


FIGURE 4.2.

### 4.3 Transport by diffusion

The two observations

- (1)  $\dim d = \frac{(\text{length})^2}{\text{time}}$ ,
- (2) the diffusion equation (4.2.6) is *invariant* under a scaling

$$t^* = \varepsilon^2 t, \quad x^* = \varepsilon x,$$

both motivate the following statements:

- the average distance over which diffusion transports particles in a given time interval of length  $t$  is proportional to  $\sqrt{dt}$
- the average time it takes to diffuse over a distance  $h$  is proportional to  $h^2/d$ .

Please contrast Figure 4.2 with the deterministic straight line distance = velocity · time. It appears that the efficiency of diffusion as a transport mechanism depends very much on the distance to be travelled! We need the circulatory blood system for active transport of, among other things, oxygen. But the very last bit of transport to the muscle tissue is by diffusion! See (Vogel, 1988, Chapter 8) for some general considerations.

### 4.4 How to measure the diffusion coefficient

A capillary tube is inserted into a suspension of bacteria of known concentration (see Fig. 4.3). After a prescribed period of time, the tube is extracted and the number of bacteria that have entered is counted. Assume that the bacteria can be described in terms of a concentration  $u$ , that they move randomly, that the concentration at the mouth of the tube is always a constant,  $u_0$  say, that there are no bacteria in the tube at the beginning of the experiment, and that the concentration in the tube varies only in the length direction and not in the radial direction. A mathematical formulation of these assumptions reads

$$\frac{\partial u}{\partial t} = d \frac{\partial^2 u}{\partial x^2} \quad 0 < x < \infty, \quad t > 0 \quad (4.4.1)$$

$$u(t, 0) = u_0 \quad t > 0 \quad (4.4.2)$$

$$u(0, x) = 0 \quad x > 0, \quad (4.4.3)$$

where  $x$  measures the distance down the (infinitely long, by debatable assumption) tube.

EXERCISE 4.4.1. Derive the expression

$$d = \frac{\pi N^2}{4u_0^2 A^2 T} \quad (4.4.4)$$

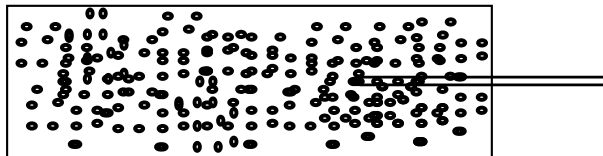


FIGURE 4.3.

where  $N$  denotes the number of bacteria in the tube at time  $T$  and  $A$  the cross-sectional area of the tube.

The way (4.4.4) is used is: for several choices of  $u_0$  and  $T$  the experiment is performed and  $N$  is determined. The right hand side is then computed and if, within reasonable accuracy, the value is the same for all  $u_0$ ,  $T$  and  $N$  combinations, then we have confidence in the model and, in addition, the value serves as an estimate for  $d$ . A typical value is  $0.2 \text{ cm}^2/\text{hr}$ .

Hints and remarks: take as a starting point the *fundamental solution*

$$\frac{1}{2\sqrt{\pi dt}} e^{-\frac{x^2}{4dt}},$$

which we will derive later on in Section 5.1. The fundamental solution serves as a building block: since the equation is linear, the *superposition principle* applies. The fundamental solution is the solution of the diffusion equation with initial data  $u_0(x) = \delta(x)$ , the Dirac delta function. For instance, if we replace this initial condition by the general condition  $u(0, x) = g(x)$ , for  $x \in \mathbb{R}$ , then

$$u(t, x) = \frac{1}{2\sqrt{\pi dt}} \int_{\mathbb{R}} e^{-\frac{(x-y)^2}{4dt}} g(y) dy.$$

To make this formula applicable to (4.4.3), we need the trick of extending the domain and the initial condition to  $(-\infty, \infty)$  in such a way that the boundary condition automatically holds (essentially this is based on symmetry). The right choice is

$$u(0, x) = 2u_0, \quad x < 0,$$

so that the value for  $x = 0$  is (for  $t = 0$ , but in fact also for  $t > 0$ ) exactly the average of the value to the left and the value on the right. You should now arrive at

$$\frac{u(t, x)}{u_0} = \frac{2}{\sqrt{\pi}} \int_{x/\sqrt{4dt}}^{\infty} e^{-\xi^2} d\xi. \quad (4.4.5)$$

To be clear: deriving (4.4.5) forms part of the Exercise! To derive (4.4.4), you may want to use integration by parts.

## 4.5 About sojourn times

Suppose particles enter a compartment at a rate  $F$ . Let  $N$  denote the total number of particles in the compartment. To find a relation between  $N$  and  $F$  we need to know how long particles stay in the compartment. We assume that this so-called sojourn time is a stochastic variable  $T$  with a continuous probability distribution.

EXERCISE 4.5.1. Assume that both  $F$  and  $N$  depend on time  $t$ . Explain in words the bookkeeping considerations underlying the identity.

$$N(t) = \int_0^{\infty} F(t - \sigma) P(T \geq \sigma) d\sigma. \quad (4.5.1)$$

EXERCISE 4.5.2. Now assume that both  $N$  and  $F$  are constant. Let  $f$  denote the probability density of  $T$ , so, in particular,

$$P(T \geq \sigma) = \int_{\sigma}^{\infty} f(s) ds, \quad \text{and} \quad \int_0^{\infty} f(s) ds = 1.$$

Let

$$\tau = \int_0^{\infty} \sigma f(\sigma) d\sigma$$

denote the mean of  $T$ . Show that  $N = F\tau$ . Are you surprised? Finally, reflect a moment on the possibility that  $\tau = \infty$ . How would you interpret the result  $N = F\tau$  in that case?

## 4.6 How long does it take?

Suppose particles are released at  $x = L$  and removed upon arrival at  $x = 0$ . We want to check that the rule of thumb formulated in Section 4.3 applies. To do so, we use a trick: we consider a steady situation with continuous release and removal rather than following an individual particle (the point being that in this manner we let the equation take care of the statistics; this works since we are satisfied with the average, the expected, time and do not aim to derive the full probability distribution).

EXERCISE 4.6.1. Why should we supplement the steady state equation

$$d \frac{\partial^2 u}{\partial x^2} = 0$$

with the *boundary conditions*

$$u(L) = u_0 \quad \text{and} \quad u(0) = 0.$$

Compute the steady particle density, i.e., find a function  $u$  that satisfies the equation as well as the boundary conditions. Express the influx  $J_{\text{in}}$ , i.e., the number of particles that enter at  $x = L$  per unit of time, in terms of  $u_0$ ,  $d$  and  $L$ . Next, compute the total number  $N$  of particles that are present.

How are  $J_{\text{in}}$  and  $N$  related (recall Section 4.2)? Compute the average sojourn time. Check in particular that it does not depend on  $u_0$  (did you already anticipate this?) and that it confirms nicely to the rule of thumb.

The efficiency of diffusion as a transport mechanism depends not only on size but also on *shape*, in particular on the dimension (1, 2 or 3) of the domain. We now want to demonstrate that it has advantages for a cell to arrange the chemical “factories” along a two-dimensional membrane (incidentally, recent findings indicate that a cell is partly an assembly-belt and that the traditional picture of a freely floating 3D chemical soup is fundamentally flawed). In this connection it is also good to realise that diffusion can only “work” if there is an excess of particles, as any one of them may go the wrong direction and/or take ages before reaching the target (if at all).

EXERCISE 4.6.2. Consider a *radially symmetric* two-dimensional setting. Show that the conservation equation takes the form

$$r \frac{\partial u}{\partial t} = - \frac{\partial}{\partial r} (rJ),$$

that Fick’s law amounts to

$$J = -d \frac{\partial u}{\partial r},$$

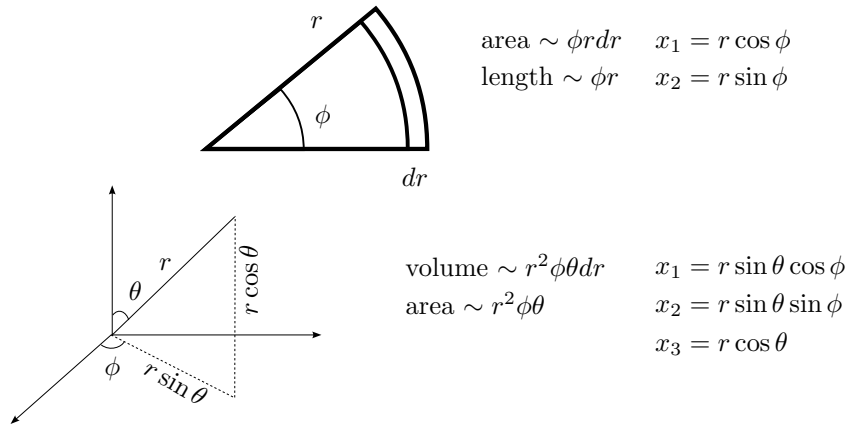


FIGURE 4.4.

and that accordingly the diffusion equation reads

$$\frac{\partial u}{\partial t} = \frac{1}{r} \frac{\partial}{\partial r} \left( dr \frac{\partial u}{\partial r} \right).$$

Next show that in three dimensions one obtains

$$\frac{\partial u}{\partial t} = \frac{1}{r^2} \frac{\partial}{\partial r} \left( dr^2 \frac{\partial u}{\partial r} \right).$$

For both these exercises, a hint: see Figure 4.4.

Now suppose the particle density is held at  $u_0 > 0$  on a circle/ball of radius  $L$  and at zero at a circle/ball of radius  $a < L$ . Derive that the average sojourn time is given by, respectively

$$\frac{1}{2d} \left\{ L^2 \left( \log \frac{L}{a} - \frac{1}{2} \right) + \frac{1}{2} a^2 \right\},$$

and

$$\frac{1}{ad} \left\{ \frac{1}{3} L^3 - \frac{a}{2} L^2 + \frac{1}{6} a^3 \right\}.$$

Reflect on the difference for large  $L$ .

As a final note along this theme, let us consider phytoplankton cells drifting in an ocean of depth  $L$ , undergoing random motion due to turbulent eddy diffusivity in the ocean's mixed layer, and about to be devoured by clams waiting at the ocean floor. How long does a phytoplankton cell drift on average? Does it drift long enough to be able to grow, absorb light and take up nutrients, and divide? Gravity is less of a problem than random motion by turbulent eddy diffusivity. The key observation: let  $T(x)$  be the *expected* time till absorption (i.e., until it is eaten by the big monster at the boundary). Then

$$T(x) = t + \int_{-\infty}^{\infty} \Phi(t, \xi - x) T(\xi) d\xi + \text{small correction}$$

for  $t$  small and  $x$  not very near to the boundary [This requires some additional explanation]. Differentiate with respect to  $t$ , and use that  $\Phi$  satisfies the diffusion equation to find

$$0 = 1 + d \int_{-\infty}^{\infty} \left( \Phi(t, \xi - x) \right)_{xx} T(\xi) d\xi + \dots$$



Integrate by parts twice and let  $t \rightarrow 0$  to find

$$0 = 1 + T''(x).$$

The boundary conditions are  $T(0) = 0$  (the monster!) and  $T'(L) = 0$  (no flux, reflecting). Then the explicit solution is given by

$$T(x) = -\frac{1}{2} \frac{x^2}{d} + \frac{L}{d}x = \frac{x}{d} \left( L - \frac{x}{2} \right) < 0,$$

$T$  reaches its maximum  $L^2/2d$  at  $x = L$ , and for  $x = L/2$  we have  $T = \frac{3L^2}{8d}$ . The vertical eddy diffusivity in the ocean's mixed layer is approximately  $10^{-4} \text{ m}^2\text{s}^{-1}$ , so if the ocean is about 10 meters deep, it takes about 4 days to reach the bottom and be devoured by the clams.

## 4.7 A remark on boundary conditions

The idea behind the boundary condition  $u(L) = u_0$  in Exercise 4.6.1 is that to the right of  $x = L$  there is a reservoir of particles which is held at a constant density. Alternatively, we might imagine a pumping device that somehow manages to generate a constant influx. In that case we should put as boundary conditions

$$d \frac{\partial u}{\partial x}(L) = \text{prescribed influx} \sim \frac{\text{number}}{\text{time}}$$

(note that, as we saw in Section 4.2, Derivation 1, the flux equals  $-d \frac{\partial u}{\partial x}$  if our orientation is from left to right; but the domain is to the left of  $x = L$ , i.e., the inward normal points to the left). One can redo Exercise 4.6.1 with the alternative boundary condition and arrive, of course, at the same answer.

If we model animals that can move freely in some domain  $\Omega$ , but cannot (for whatever reason) leave  $\Omega$ , we should put *no-flux boundary conditions*

$$\frac{\partial u}{\partial n} \Big|_{\partial\Omega} = 0.$$

These are also called (*zero-Neumann conditions*) and we omitted, as usual, the factor  $d$  since when we put zero at the right-hand side it has no influence (but be aware of this factor when the flux isn't required to reduce to zero!).  $\partial\Omega$  is called a *reflecting* boundary.

If  $u$  is the density of plants and the diffusion term is used to describe the dispersal of seeds, it may be that the complement of  $\Omega$  is simply unsuitable habitat in which no plant can grow. We may then impose (*zero-Dirichlet conditions*)

$$u \Big|_{\partial\Omega} = 0,$$

but should realise that such a form of heterogeneity of the world as a whole has a strong impact on pattern formation (we shall return to this point in the next chapter).

Mixed boundary conditions

$$\left[ -(1-\theta)d \frac{\partial u}{\partial n} + \theta u \right]_{\partial\Omega} = 0$$

are, from a mathematical point of view, a one-parameter family that forms a homotopy between no-flux and zero-Dirichlet and describe, from a biological point of view, a partially reflecting boundary to a completely hostile exterior. Their relevance in a biological modelling context is not clear at all.

In some diffusion problems arising in population genetics, the spatial variable  $x$  is actually a fraction of the population carrying a certain allele. In such problems  $d$  depends on  $x$  and declines to zero when  $x$  approaches the boundary points  $x = 0$

and  $x = 1$ . The classification of the mechanistic effect of the boundary is far more subtle in such a situation, see (Feller, 1952, 1954, 1955).

Boundary conditions should be chosen on the basis of modelling considerations, even though this is far less straightforward than one is tempted to believe. Much mathematical work on biology inspired equations is wasted for the simple reason that boundary conditions, in particular zero-Dirichlet conditions, are chosen out of habit and without a critical reflection on their meaning and effect.