

11. Reaction Diffusion, Chemotaxis, and Nonlocal Mechanisms

11.1 Simple Random Walk and Derivation of the Diffusion Equation

In an assemblage of particles, for example, cells, bacteria, chemicals, animals and so on, each particle usually moves around in a random way. The particles spread out as a result of this irregular individual particle's motion. When this microscopic irregular movement results in some macroscopic or gross regular motion of the group we can think of it as a *diffusion* process. Of course there may be interaction between particles, for example, or the environment may give some bias in which case the gross movement is not simple diffusion. To get the macroscopic behaviour from a knowledge of the individual microscopic behaviour is much too hard so we derive a continuum model equation for the global behaviour in terms of a particle density or concentration. It is instructive to start with a random process which we look at probabilistically in an elementary way, and then derive a deterministic model.

For simplicity we consider initially only one-dimensional motion and the simplest random walk process. The generalisation to higher dimensions is then intuitively clear from the one-dimensional equation.

Suppose a particle moves randomly backward and forward along a line in fixed steps Δx that are taken in a fixed time Δt . If the motion is unbiased then it is equally probable that the particle takes a step to the right or left. After time $N \Delta t$ the particle can be anywhere from $-N \Delta x$ to $N \Delta x$ if we take the starting point of the particle as the origin. The spatial distribution is clearly not going to be uniform if we release a group of particles about $x = 0$ since the probability of a particle reaching $x = N \Delta x$ after N steps is very small compared with that for x nearer $x = 0$.

We want the probability $p(m, n)$ that a particle reaches a point m space steps to the right (that is, to $x = m \Delta x$) after n time-steps (that is, after a time $n \Delta t$). Let us suppose that to reach $m \Delta x$ it has moved a steps to the right and b to the left. Then

$$m = a - b, \quad a + b = n \quad \Rightarrow \quad a = \frac{n + m}{2}, \quad b = n - a.$$

The number of possible paths that a particle can reach this point $x = m \Delta x$ is

$$\frac{n!}{a!b!} = \frac{n!}{a!(n-a)!} C_a^n,$$

where C_a^n is the binomial coefficient defined, for example, by

$$(x + y)^n = \sum_{a=0}^n C_a^n x^{n-a} y^a.$$

The total number of possible n -step paths is 2^n and so the probability $p(m, n)$ (the favorable possibilities/total possibilities) is

$$p(m, n) = \frac{1}{2^n} \frac{n!}{a!(n-a)!}, \quad a = \frac{n+m}{2}, \quad (11.1)$$

$n + m$ is even.

Note that

$$\sum_{m=-n}^n p(m, n) = 1,$$

as it must since the sum of all probabilities must equal 1. It is clear mathematically since

$$\sum_{m=-n}^n p(m, n) = \sum_{a=0}^n C_a^n \left(\frac{1}{2}\right)^{n-a} \left(\frac{1}{2}\right)^a = \left(\frac{1}{2} + \frac{1}{2}\right)^n = 1,$$

$p(m, n)$ is the *binomial distribution*.

If we now let n be large so that $n \pm m$ are also large we have, asymptotically,

$$n! \sim (2\pi n)^{1/2} n^n e^{-n}, \quad n \gg 1, \quad (11.2)$$

which is Stirling's formula. This is derived by noting that

$$n! = \Gamma(n+1) = \int_0^\infty e^{-t} t^n dt,$$

where Γ is the gamma function, and using Laplace's method for the asymptotic approximation for such integrals for n large (see, for example, Murray's 1984 elementary book *Asymptotic Analysis*). Using (11.2) in (11.1) we get, after a little algebra, the *normal or Gaussian probability distribution*

$$p(m, n) \sim \left(\frac{2}{\pi n}\right)^{1/2} e^{-m^2/(2n)}, \quad m \gg 1, \quad n \gg 1. \quad (11.3)$$

m and n need not be very large for (11.3) to be an accurate approximation to (11.1). For example, with $n = 8$ and $m = 6$, (11.3) is within 5% of the exact value from (11.1);

with $n = 10$ and $m = 4$ it is accurate to within 1%. In fact for all practical purposes we can use (11.3) for $n > 6$. Asymptotic approximations can often be remarkably accurate over a wider range than might be imagined.

Now set

$$m \Delta x = x, \quad n \Delta t = t,$$

where x and t are the continuous space and time variables. If we anticipate letting $m \rightarrow \infty, n \rightarrow \infty, \Delta x \rightarrow 0, \Delta t \rightarrow 0$ so that x and t are finite, then it is not appropriate to have $p(m, n)$ as the quantity of interest since this probability must tend to zero: the number of points on the line tends to ∞ as $\Delta x \rightarrow 0$. The relevant dependent variable is more appropriately $u = p/(2 \Delta x)$: $2u \Delta x$ is the probability of finding a particle in the interval $(x, x + \Delta x)$ at time t . From (11.3) with $m = x/\Delta x, n = t/\Delta t$,

$$\frac{p\left(\frac{x}{\Delta x}, \frac{t}{\Delta t}\right)}{2 \Delta x} \sim \left\{ \frac{\Delta t}{2\pi t (\Delta x)^2} \right\}^{1/2} \exp \left\{ -\frac{x^2}{2t (\Delta x)^2} \right\}.$$

If we assume

$$\lim_{\substack{\Delta x \rightarrow 0 \\ \Delta t \rightarrow 0}} \frac{(\Delta x)^2}{2 \Delta t} = D \neq 0$$

the last equation gives

$$u(x, t) = \lim_{\substack{\Delta x \rightarrow 0 \\ \Delta t \rightarrow 0}} \frac{p\left(\frac{x}{\Delta x}, \frac{t}{\Delta t}\right)}{2 \Delta x} = \left(\frac{1}{4\pi Dt} \right)^{1/2} e^{-x^2/(4Dt)}. \quad (11.4)$$

D is the *diffusion coefficient* or *diffusivity* of the particles; note that it has dimensions (length)²/(time). It is a measure of how efficiently the particles disperse from a high to a low density. For example, in blood, haemoglobin molecules have a diffusion coefficient of the order of $10^{-7} \text{ cm}^2 \text{ sec}^{-1}$ while that for oxygen in blood is of the order of $10^{-5} \text{ cm}^2 \text{ sec}^{-1}$.

Let us now relate this result to the classical approach to diffusion, namely, *Fickian diffusion*. This says that the flux, J , of material, which can be cells, amount of chemical, number of animals and so on, is proportional to the gradient of the concentration of the material. That is, in one dimension

$$J \propto -\frac{\partial c}{\partial x} \quad \Rightarrow \quad J = -D \frac{\partial c}{\partial x}, \quad (11.5)$$

where $c(x, t)$ is the concentration of the species and D is its diffusivity. The minus sign simply indicates that diffusion transports matter from a high to a low concentration.

We now write a general conservation equation which says that the rate of change of the amount of material in a region is equal to the rate of flow across the boundary plus any that is created within the boundary. If the region is $x_0 < x < x_1$ and no material is created,

$$\frac{\partial}{\partial t} \int_{x_0}^{x_1} c(x, t) dx = J(x_0, t) - J(x_1, t). \quad (11.6)$$

If we take $x_1 = x_0 + \Delta x$, take the limit as $\Delta x \rightarrow 0$ and use (11.5) we get the *classical diffusion equation* in one dimension, namely,

$$\frac{\partial c}{\partial t} = -\frac{\partial J}{\partial x} = \frac{\partial(D \frac{\partial c}{\partial x})}{\partial x}, \quad (11.7)$$

which, if D is constant, becomes

$$\frac{\partial c}{\partial t} = D \frac{\partial^2 c}{\partial x^2}. \quad (11.8)$$

If we release an amount Q of particles per unit area at $x = 0$ at $t = 0$, that is,

$$c(x, 0) = Q\delta(x), \quad (11.9)$$

where $\delta(x)$ is the Dirac delta function, then the solution of (11.8) is (see, for example, Crank's 1975 book)

$$c(x, t) = \frac{Q}{2(\pi Dt)^{1/2}} e^{-x^2/(4Dt)}, \quad t > 0 \quad (11.10)$$

which, with $Q = 1$, is the same result as (11.4), obtained from a random walk approach when the step and time sizes are small compared with x and t . Figure 11.1 qualitatively illustrates the concentration $c(x, t)$ from (11.10) as a function of x for various times.

This way of relating the diffusion equation to the random walk approach essentially uses circumstantial evidence. We now derive it by extending the random walk approach and start with $p(x, t)$, from (11.4), as the probability that a particle released at $x = 0$ at

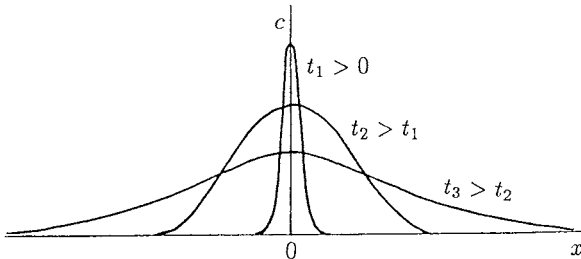


Figure 11.1. Schematic particle concentration distribution arising from Q particles released at $x = 0$ at $t = 0$ and diffusing according to the diffusion equation (11.8).

$t = 0$ reaches x in time t . At time $t - \Delta t$ the particle was at $x - \Delta x$ or $x + \Delta x$. Thus, if α and β are the probabilities that a particle will move to the right or left

$$p(x, t) = \alpha p(x - \Delta x, t - \Delta t) + \beta p(x + \Delta x, t - \Delta t), \quad \alpha + \beta = 1. \quad (11.11)$$

If there is no bias in the random walk, that is, it is isotropic, $\alpha = 1/2 = \beta$. Expanding the right-hand side of (11.11) in a Taylor series we get

$$\frac{\partial p}{\partial t} = \left[\frac{(\Delta x)^2}{2 \Delta t} \right] \frac{\partial^2 p}{\partial x^2} + \left(\frac{\Delta t}{2} \right) \frac{\partial^2 p}{\partial t^2} + \dots$$

If we now let $\Delta x \rightarrow 0$ and $\Delta t \rightarrow 0$ such that, as before

$$\lim_{\substack{\Delta x \rightarrow 0 \\ \Delta t \rightarrow 0}} \frac{(\Delta x)^2}{2 \Delta t} = D$$

we get

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

If the total number of released particles is Q , then the concentration of particles $c(x, t) = Qp(x, t)$ and the last equation becomes (11.8).

The random walk derivation is still not completely satisfactory since it relies on Δx and Δt tending to zero in a rather specific way so that D exists. A better and more sophisticated way is to derive it from the Fokker–Planck equations using a probability density function with a Markov process; that is, a process at time t depending only on the state at time $t - \Delta t$; in other words a one-generation time-dependency. See, for example, Skellam (1973) or the excellent book by Okubo (1980). The latter gives some justification to the limiting process used above. The review article by Okubo (1986) also discusses the derivation of various diffusion equations.

11.2 Reaction Diffusion Equations

Consider now diffusion in three space dimensions. Let S be an arbitrary surface enclosing a volume V . The general conservation equation says that the rate of change of the amount of material in V is equal to the rate of flow of material across S into V plus the material created in V . Thus

$$\frac{\partial}{\partial t} \int_V c(\mathbf{x}, t) dv = - \int_S \mathbf{J} \cdot \mathbf{ds} + \int_V f dv, \quad (11.12)$$

where \mathbf{J} is the flux of material and f , which represents the source of material, may be a function of c , \mathbf{x} and t . Applying the divergence theorem to the surface integral and

assuming $c(\mathbf{x}, t)$ is continuous, the last equation becomes

$$\int_V \left[\frac{\partial c}{\partial t} + \nabla \cdot \mathbf{J} - f(c, \mathbf{x}, t) \right] dv = 0. \quad (11.13)$$

Since the volume V is arbitrary the integrand must be zero and so the *conservation equation* for c is

$$\frac{\partial c}{\partial t} + \nabla \cdot \mathbf{J} = f(c, \mathbf{x}, t). \quad (11.14)$$

This equation holds for a general flux transport \mathbf{J} , whether by diffusion or some other process.

If classical diffusion is the process then the generalisation of (11.5), for example, is

$$\mathbf{J} = -D\nabla c \quad (11.15)$$

and (11.14) becomes

$$\frac{\partial c}{\partial t} = f + \nabla \cdot (D\nabla c), \quad (11.16)$$

where D may be a function of \mathbf{x} and c and f a function of c , \mathbf{x} and t . Situations where D is space-dependent are arising in more and more modelling situations of biomedical importance from diffusion of genetically engineered organisms in heterogeneous environments to the effect of white and grey matter in the growth and spread of brain tumours.

The source term f in an ecological context, for example, could represent the birth-death process and c the population density, n . With logistic population growth $f = rn(1 - n/K)$, where r is the linear reproduction rate and K the carrying capacity of the environment. The resulting equation with D constant is

$$\frac{\partial n}{\partial t} = rn \left(1 - \frac{n}{K} \right) + D\nabla^2 n, \quad (11.17)$$

now known as the *Fisher-Kolmogoroff equation* after Fisher (1937) who proposed the one-dimensional version as a model for the spread of an advantageous gene in a population and Kolmogoroff et al. (1937) who studied the equation in depth and obtained some of the basic analytical results. This is an equation we study in detail later in Chapter 13.

If we further generalise (11.16) to the situation in which there are, for example, several interacting species or chemicals we then have a vector $u_i(\mathbf{x}, t)$, $i = 1, \dots, m$ of densities or concentrations each diffusing with its own diffusion coefficient D_i and interacting according to the vector source term \mathbf{f} . Then (11.16) becomes

$$\frac{\partial \mathbf{u}}{\partial t} = \mathbf{f} + \nabla \cdot (D\nabla \mathbf{u}), \quad (11.18)$$

where now D is a matrix of the diffusivities which, if there is no cross diffusion among the species, is simply a diagonal matrix. In (11.18) $\nabla \mathbf{u}$ is a tensor so $\nabla \cdot D\nabla \mathbf{u}$ is a vector.

Cross-diffusion does not arise often in genuinely practical models: one example where it will be described is in Chapter 1, Volume II, Section 1.2. Cross-diffusion systems can pose interesting mathematical problems particularly regarding their well-posedness. Equation (11.18) is referred to as a *reaction diffusion* system. Such a mechanism was proposed as a model for the chemical basis of morphogenesis by Turing (1952) in one of the most important papers in theoretical biology this century. Such systems have been widely studied since about 1970. We shall mainly be concerned with reaction diffusion systems when D is diagonal and constant and \mathbf{f} is a function only of \mathbf{u} . Further generalisation can include, in the case of population models, for example, integral terms in \mathbf{f} which reflect the population history. In some cancer models involving mutating cancer cells—the situation which obtains with brain (glioblastoma) tumours and others—there are cross-diffusion terms and unequal diagonal terms in the diffusion matrix. The mathematical generalisations seem endless. For most practical models of real world situations it is premature, to say the least, to spend too much time on sophisticated generalisations¹ before the simpler versions have been shown to be inadequate when compared with experiment or observation.

It is appropriate to mention briefly, at this stage, an important area in physiology associated with reaction diffusion equations which we do not discuss further in this book, namely, facilitated diffusion. The accepted models closely mimic the experimental situations and involve biochemical reaction kinetics, such as oxygen combined reversibly with haemoglobin and myoglobin; the latter is crucially important in muscle. Myoglobin is less efficient than haemoglobin as a facilitator. The subject has been studied in depth experimentally by Wittenberg (see 1970 for a review) and Wittenberg et al. (1975) and their colleagues and in the case of proton facilitation by proteins by Gros et al. (1976, 1984). Without facilitated diffusion muscle tissue, for example, could not survive as heuristically shown theoretically by Wyman (1966). This is an area which is essentially understood as a consequence of the intimate union of mathematical models with experiment. The theory of oxygen facilitation was given by Wyman (1966), Murray (1971, 1974) and, in the case of carbon monoxide by Murray and Wyman (1971). For facilitation to be effective there must be a zone of reaction equilibrium within the tissue which implies that nonequilibrium boundary layers exist near the surface (Murray 1971, Mitchell and Murray 1973, Rubinow and Dembo 1977). The conditions for existence of the equilibrium zone provide an explanation of why haemoglobin is a better facilitator of oxygen than myoglobin and why carbon monoxide is not facilitated by myoglobin. The whole phenomenon of facilitated diffusion also plays a crucial role in carbon monoxide poisoning and the difficulties of getting rid of the carbon monoxide (Britton and Murray 1977).

The theory of proton facilitation is a much more complex phenomena since Gros et al. (1976, 1984; see these papers for earlier references) showed experimentally that it involves rotational diffusion by a form of haemoglobin and other proteins: the proton causes the haemoglobin molecule to rotate thereby increasing the overall diffusion across tissue containing haemoglobin molecules. A mathematical theory of rotational diffusion, which is very much more complicated, has been given by Murray and Smith (1986).

¹As de Tocqueville remarked, there is no point in generalising since God knows all the special cases.

11.3 Models for Animal Dispersal

Diffusion models form a reasonable basis for studying insect and animal dispersal and invasion; this and other aspects of animal population models are discussed in detail, for example, by Okubo (1980, 1986), Shigesada (1980) and Lewis (1997). Dispersal of interacting species is discussed by Shigesada et al. (1979) and of competing species by Shigesada and Roughgarden (1982). Kareiva (1983) has shown that many species appear to disperse according to a reaction diffusion model with a constant diffusion coefficient. He gives actual values for the diffusion coefficients which he obtained from experiments on a variety of insect species. Kot et al. (1996) studied dispersal of organisms in general and importantly incorporated real data (see also Kot 2001). A common feature of insect populations is their discrete time population growth. As would be expected intuitively this can have a major effect on their spatial dispersal. The model equations involve the coupling of discrete time with continuous space, a topic investigated by Kot (1992) and Neubert et al. (1995). The book of articles edited by Tilman and Kareiva (1998) is a useful sourcebook for the role of space in this general area. The articles address, for example, the question of persistence of endangered species, biodiversity, disease dynamics, multi-species competition and so on. The books by Renshaw (1991) and Williamson (1996) are other very good texts for the study of species invasion phenomena: these books have numerous examples. The excellent, more mathematical and modelling oriented, book by Shigesada and Kawasaki (1997) discusses biological invasions of mammals, birds, insects and plants in various forms, of which diffusion is just one mechanism. For anyone seriously interested in modelling these phenomena these books are required reading.

One extension of the classical diffusion model which is of particular relevance to insect dispersal is when there is an increase in diffusion due to population pressure. One such model has the diffusion coefficient, or rather the flux \mathbf{J} , depending on the population density n such that D increases with n ; that is,

$$\mathbf{J} = -D(n)\nabla n, \quad \frac{dD}{dn} > 0. \quad (11.19)$$

A typical form for $D(n)$ is $D_0(n/n_0)^m$, where $m > 0$ and D_0 and n_0 are positive constants. The dispersal equation for n without any growth term is then

$$\frac{\partial n}{\partial t} = D_0 \nabla \cdot \left[\left(\frac{n}{n_0} \right)^m \nabla n \right].$$

In one dimension

$$\frac{\partial n}{\partial t} = D_0 \frac{\partial}{\partial x} \left[\left(\frac{n}{n_0} \right)^m \frac{\partial n}{\partial x} \right], \quad (11.20)$$

which has an exact analytical solution of the form

$$n(x, t) = \frac{n_0}{\lambda(t)} \left[1 - \left\{ \frac{x}{r_0 \lambda(t)} \right\}^2 \right]^{1/m}, \quad |x| \leq r_0 \lambda(t) \quad (11.21)$$

$$= 0, \quad |x| > r_0 \lambda(t),$$

where

$$\lambda(t) = \left(\frac{t}{t_0} \right)^{1/(2+m)}, \quad r_0 = \frac{Q \Gamma(\frac{1}{m} + \frac{3}{2})}{\{\pi^{1/2} n_0 \Gamma(\frac{1}{m} + 1)\}}, \quad (11.22)$$

$$t_0 = \frac{r_0^2 m}{2D_0(m+2)},$$

where Γ is the gamma function and Q is the initial number of insects released at the origin. It is straightforward to check that (11.21) is a solution of (11.20) for all r_0 . The evaluation of r_0 comes from requiring the integral of n over all x to be equal to Q . (In another context (11.20) is known as the *porous media equation*.) The population is identically zero for $x > r_0 \lambda(t)$. This solution is fundamentally different from that when $m = 0$, namely, (11.10). The difference is due to the fact that $D(0) = 0$. The solution represents a kind of wave with the front at $x = x_f = r_0 \lambda(t)$. The derivative of n is discontinuous here. The wave ‘front,’ which we define here as the point where $n = 0$, propagates with a speed $dx_f/dt = r_0 d\lambda/dt$, which, from (11.22), decreases with time for all m . The solution for n is illustrated schematically in Figure 11.2. The dispersal patterns for grasshoppers exhibit a similar behaviour to this model (Aikman and Hewitt 1972). Without any source term the population n , from (11.21), tends to zero as $t \rightarrow \infty$. Shigesada (1980) proposed such a model for animal dispersal in which she took the linear diffusion dependence $D(n) \propto n$; see also Shigesada and Kawasaki (1997).

The equivalent plane radially symmetric problem with Q insects released at $r = 0$ at $t = 0$ satisfies the equation

$$\frac{\partial n}{\partial t} = \left(\frac{D_0}{r} \right) \frac{\partial}{\partial r} \left[r \left(\frac{n}{n_0} \right)^m \frac{\partial n}{\partial r} \right] \quad (11.23)$$

with solution

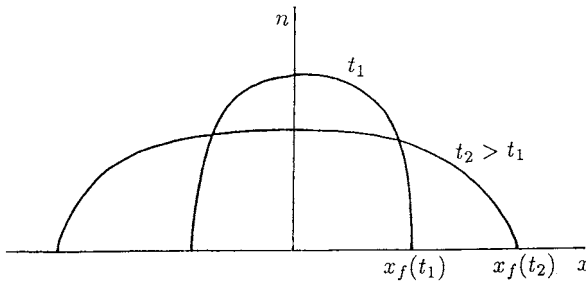


Figure 11.2. Schematic solution, from (11.21), of equation (11.20) as a function of x at different times t . Note the discontinuous derivative at the wavefront $x_f(t) = r_0 \lambda(t)$.

$$\begin{aligned}
 n(r, t) &= \frac{n_0}{\lambda^2(t)} \left[1 - \left\{ \frac{r}{r_0 \lambda(t)} \right\}^2 \right]^{1/m}, & r \leq r_0 \lambda(t) \\
 &= 0, & r > r_0 \lambda(t) \\
 \lambda(t) &= \left(\frac{t}{t_0} \right)^{1/2(m+1)}, & t_0 = \frac{r_0^2 m}{4D_0(m+1)}, \\
 r_0^2 &= \frac{Q}{\pi n_0} \left(1 + \frac{1}{m} \right).
 \end{aligned}
 \tag{11.24}$$

As $m \rightarrow 0$, that is, $D(n) \rightarrow D_0$, the solutions (11.21) and (11.24) tend to the usual constant diffusion solutions: (11.10), for example, in the case of (11.21). To show this involves some algebra and use of the exponential definition $\exp[s] = \lim_{m \rightarrow 0} (1 + ms)^{1/m}$.

Insects at low population densities frequently tend to aggregate. One model (in one dimension) which reflects this has the flux

$$J = Un - D(n) \frac{\partial n}{\partial x},$$

where U is a transport velocity. For example, if the centre of attraction is the origin and the velocity of attraction is constant, Shigesada et al. (1979) take $U = -U_0 \text{sgn}(x)$ and the resulting dispersal equation becomes

$$\frac{\partial n}{\partial t} = U_0 \frac{\partial}{\partial x} [n \text{sgn}(x)] + D_0 \frac{\partial}{\partial x} \left[\left(\frac{n}{n_0} \right)^m \frac{\partial n}{\partial x} \right],
 \tag{11.25}$$

which is not trivial to solve. We can, however, get some idea of the solution behaviour for parts of the domain.

Suppose Q is again the initial flux of insects released at $x = 0$. We expect that gradients in n near $x = 0$ for $t \approx 0$ are large and so, in this region, the convection term is small compared with the diffusion term, in which case the solution is approximately given by (11.21). On the other hand after a long time we expect the population to reach some steady, spatially inhomogeneous state where convection and diffusion effects balance. Then the solution is approximated by (11.25) with $\partial n / \partial t = 0$. Integrating this steady state equation twice using the conditions $n \rightarrow 0, \partial n / \partial x \rightarrow 0$ as $|x| \rightarrow \infty$ we get the steady state spatial distribution

$$\begin{aligned}
 \lim_{t \rightarrow \infty} n(x, t) \rightarrow n(x) &= n_0 \left(1 - \frac{mU_0|x|}{D_0} \right)^{1/m}, & |x| \leq \frac{D_0}{mU_0} \\
 &= 0, & |x| > \frac{D_0}{mU_0}.
 \end{aligned}
 \tag{11.26}$$

The derivation of this is left as an exercise. The solution (11.26) shows that the dispersal is *finite* in x . The form obtained when $m = 1/2$ is similar to the population distribution observed by Okubo and Chiang (1974) for a special type of mosquito swarm (see

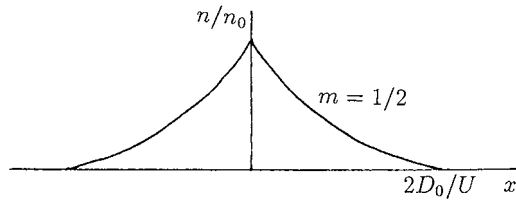


Figure 11.3. Schematic form of the steady state insect population distribution from (11.26), for insects which tend to aggregate at low densities according to (11.25).

Okubo 1980, Fig. 9.6). Figure 11.3 schematically illustrates the steady state insect population.

Insect dispersal is a very important subject which is still not well understood. The above model is a simple one but even so it gives some pointers as to possible insect dispersal behaviour. If there is a population growth/death term we simply include it on the right-hand side of (11.25) (Exercises 3 and 4). In these the insect population dies out as expected, since there is no birth, only death, but what is interesting is that the insects move only a finite distance from the origin.

The use of diffusion models for animal and insect dispersal is increasing and has been applied to a variety of practical situations; the books by Okubo (1980) and Shigesada and Kawasaki (1997) give numerous examples. The review by Okubo (1986) discusses various models and specifically addresses animal grouping, insect swarms and flocking. Mogilner and Edelstein-Keshet (1999) discuss models for swarming based on nonlocal interactions. Their models incorporate long range attraction and repulsion. They show that the swarm has a constant interior density and sharp edges (in other words it looks like a swarm) if the density-dependence in the repulsion term is of a higher order than in the attraction term. Chapter 14, Volume II is specifically concerned with wolf dispersal and territory formation as well as wolf–deer (the wolves' principal prey) survival. There, among other things, we consider a more realistic form of the term for the centre's attraction (which for the wolves is the summer den) which does not give rise to a gradient discontinuity as in Figure 11.3.

11.4 Chemotaxis

A large number of insects and animals (including humans) rely on an acute sense of smell for conveying information between members of the species. Chemicals which are involved in this process are called *pheromones*. For example, the female silk moth *Bombyx mori* exudes a pheromone, called bombykol, as a sex attractant for the male, which has a remarkably efficient antenna filter to measure the bombykol concentration, and it moves in the direction of increasing concentration. The modelling problem here is a fascinating and formidable one involving fluid mechanics and filtration theory on quite different scales at the same time (Murray 1977). The acute sense of smell of many deep sea fish is particularly important for communication and predation. Other than for territorial demarcation one of the simplest and important exploitations of pheromone release is the directed movement it can generate in a population. Here we model this

chemically directed movement, which is called *chemotaxis*, which, unlike diffusion, directs the motion *up* a concentration gradient.

It is not only in animal and insect ecology that chemotaxis is important. It can be equally crucial in biological processes where there are numerous examples. For example, when a bacterial infection invades the body it may be attacked by movement of cells towards the source as a result of chemotaxis. Convincing evidence suggests that leukocyte cells in the blood move towards a region of bacterial inflammation, to counter it, by moving up a chemical gradient caused by the infection (see, for example, Lauffenburger and Keller 1979, Tranquillo and Lauffenburger 1986, 1988 and Alt and Lauffenburger 1987). We discuss bacterial chemotaxis and some of its remarkable consequences in some detail in Chapter 5, Volume II.

A widely studied chemotactic phenomenon is that exhibited by the slime mould *Dictyostelium discoideum* where single-cell amoebae move towards regions of relatively high concentrations of a chemical called cyclic-AMP which is produced by the amoebae themselves. Interesting wavelike movement and spatial patterning are observed experimentally; see Chapter 1, Volume II. A discussion of the phenomenon and some of the early mathematical models which have been proposed together with some analysis are given, for example, in the book by Segel (1984). The kinetics involved have been modelled by several authors. As more was found out about the biological system the models necessarily changed. More complex and more biologically realistic models have been proposed by Martiel and Goldbeter (1987), Goldbeter (1996) and Monk and Othmer (1989). These new models all exhibit oscillatory behaviour. Spiro et al. (1997) presented a model of excitation and adaptation in bacterial chemotaxis in wider biological contexts. They incorporated detailed biochemical data into their model which they then used to shed light on the actual experimental process.

Most mathematical models for spatial patterning in *Dictyostelium discoideum* are based on continuum models for the chemoattractants and the cells. Dallon and Othmer (1997) developed an interesting new model in which the cells are considered as discrete entities with the chemoattractant concentrations continuous. The results agree well with many of the extant experimental results. With their model they were able to investigate the effects of different cell movement rules on aggregation patterns and wave motion, including the origin of the ubiquitous spiral waves. We discuss wave propagation, including spiral waves, in some detail in Chapter 13, and Chapter 1, Volume II. Chemotaxis is being found to be important in an increasing range of situations. The model equations are extremely rich in unexpected phenomena several of which we describe later in this volume and in Volume II.

Let us suppose that the presence of a gradient in an attractant, $a(\mathbf{x}, t)$, gives rise to a movement, of the cells say, up the gradient. The flux of cells will increase with the number of cells, $n(\mathbf{x}, t)$, present. Thus we may reasonably take as the chemotactic flux

$$\mathbf{J} = n\chi(a)\nabla a, \quad (11.27)$$

where $\chi(a)$ is a function of the attractant concentration. In the general conservation equation for $n(\mathbf{x}, t)$, namely,

$$\frac{\partial n}{\partial t} + \nabla \cdot \mathbf{J} = f(n),$$

where $f(n)$ represents the growth term for the cells, the flux

$$\mathbf{J} = \mathbf{J}_{\text{diffusion}} + \mathbf{J}_{\text{chemotaxis}},$$

where the diffusion contribution is from (11.15) with the chemotaxis flux from (11.27). Thus a basic *reaction-diffusion-chemotaxis equation* is

$$\frac{\partial n}{\partial t} = f(n) - \nabla \cdot n\chi(a)\nabla a + \nabla \cdot D\nabla n, \tag{11.28}$$

where D is the diffusion coefficient of the cells.

Since the attractant $a(\mathbf{x}, t)$ is a chemical it also diffuses and is produced, by the amoebae, for example, so we need a further equation for $a(\mathbf{x}, t)$. Typically

$$\frac{\partial a}{\partial t} = g(a, n) + \nabla \cdot D_a \nabla a, \tag{11.29}$$

where D_a is the diffusion coefficient of a and $g(a, n)$ is the kinetics/source term, which may depend on n and a . Normally we would expect $D_a > D$. If several species or cell types all respond to the attractant the governing equation for the species vector is an obvious generalisation of (11.28) to a vector form with $\chi(a)$ probably different for each species. In Chapter 5, Volume II we shall show how crucial are the forms of $f(n)$, $g(a, n)$ and $\chi(a)$ in determining the specific patterns that are formed.

In the seminal model of Keller and Segel (1971) for slime mould, $g(a, n) = hn - ka$, where h, k are positive constants. Here hn represents the spontaneous production of the attractant and is proportional to the number of amoebae n , while $-ka$ represents decay of attractant activity; that is, there is an exponential decay if the attractant is not produced by the cells.

One simple version of the model has $f(n) = 0$; that is, the amoebae production rate is negligible. This is the case during the pattern formation phase in the mould’s life cycle. The chemotactic term $\chi(a)$ is taken to be a positive constant χ_0 . The form of this term has to be determined from experiment; see Chapter 5, Volume II. With constant diffusion coefficients, together with the above linear form for $g(a, n)$, the model in one space dimension becomes the nonlinear system

$$\begin{aligned} \frac{\partial n}{\partial t} &= D \frac{\partial^2 n}{\partial x^2} - \chi_0 \frac{\partial}{\partial x} \left(n \frac{\partial a}{\partial x} \right), \\ \frac{\partial a}{\partial t} &= hn - ka + D_a \frac{\partial^2 a}{\partial x^2}, \end{aligned} \tag{11.30}$$

which we study in Chapter 1, Volume II. There we consider n to be a bacterial population and a the food which it consumes.

Other forms have been proposed for the chemotactic factor $\chi(a)$. For example,

$$\chi(a) = \frac{\chi_0}{a}, \quad \chi(a) = \frac{\chi_0 K}{(K + a)^2}, \quad \chi_0 > 0, \quad K > 0 \tag{11.31}$$

which are known respectively as the log law and receptor law. In these, as a decreases the chemotactic effect increases. In Chapter 5, Volume II we discuss the specific bacteria *Salmonella* and *E. coli* and give the forms for experimentally derived $f(n)$, $g(a, n)$ and $\chi(a)$ and so on in (11.28) and (11.29).

There are various ways to define a practical measurable *chemotaxis index*, I , which reflects the strength of the chemoattractant. Let us look at one example, and to be specific consider the planar movement of a cell, say, towards a source of chemoattractant at position x_s . Suppose the cell starts at x_A and the source is distance D_1 away. In the absence of chemotaxis the cell's movement is purely random and the mean distance, D_2 say, that the cell moves in a given time T in the direction of x_s is zero. In the presence of chemotaxis the random movement is modified so that there is a general tendency for the cell to move towards the chemoattractant source and over the same time T , $D_2 > 0$. We can define the index $I = D_2/D_1$: the larger I the stronger the chemotaxis. Tranquillo and Lauffenburger (1988) have analysed the detailed chemosensory movement of leukocyte cells with a view to determining its chemotaxis parameters. Woodward et al. (1995), Tyson (1996), Murray et al. (1998) and Tyson et al. (1998, 1999) give values, obtained from experiment, for the chemotaxis parameters for *Salmonella* and *E. coli*.

The movement of certain cells can be influenced by the presence of applied electric fields and the cells tend to move in a direction parallel to the applied field. This is called *galvanotaxis*. The strength of galvanotaxis can be defined in a similar way to chemotaxis. If V is an electric potential the galvanotaxis flux \mathbf{J} of cells can reasonably be taken as proportional to $nG(V)\nabla V$ where G may be a function of the applied voltage V .

Before leaving this topic, note the difference in sign in (11.28) and (11.30) in the diffusion and chemotaxis terms. Each has a Laplacian contribution. Whereas diffusion is generally a stabilising force, chemotaxis is generally *destabilising*, like a kind of negative diffusion. At this stage, therefore, it is reasonable to suppose that the balance between stabilising and destabilising forces in the model system (11.30) could result in some steady state spatial patterns in n and a , or in some unsteady wavelike spatially heterogeneous structure. That is, nonuniform spatial patterns in the cell density appear; see Chapters 1 and Chapter 5 in Volume II. On the other hand if the chemotactic effect is sufficiently strong there could be a possibility of solution blow-up. This in fact can happen: see, for example, the paper by Jäger and Luckhaus (1992), and other references given there, on explosion of solutions of model equations with chemotaxis.

11.5 Nonlocal Effects and Long Range Diffusion

The classical approach to diffusion, which we have used above, is strictly only applicable to dilute systems, that is, where the concentrations c , or densities n , are small. Its applicability in practice is much wider than this of course, and use of the Fickian form (11.15) for the diffusional flux, namely, $\mathbf{J} = -D\nabla c$, or $\mathbf{J} = -D(n)\nabla c$ from (11.19) in which the diffusion is dependent on n , is sufficient for many, if not most, practical modelling purposes. What these forms in effect imply, is that diffusion is a *local* or *short range* effect. We can see this if we consider the Laplacian operator $\nabla^2 n$ in the simple diffusion equation $\partial n/\partial t = D\nabla^2 n$. The Laplacian averages the neighbouring densities and formally (see, for example, Hopf 1948, Morse and Feshbach 1953)

$$\nabla^2 n \propto \frac{\langle n(\mathbf{x}, t) \rangle - n(\mathbf{x}, t)}{R^2}, \quad \text{as } R \rightarrow 0, \quad (11.32)$$

where $\langle n \rangle$ is the average density in a sphere of radius R about \mathbf{x} ; that is,

$$n_{av} = \langle n(\mathbf{x}, t) \rangle \equiv \left[\frac{3}{4\pi R^3} \right] \int_V n(\mathbf{x} + \mathbf{r}, t) \, d\mathbf{r}, \quad (11.33)$$

where V is the sphere of radius R . This interpretation of the Laplacian was first suggested by James Clerk Maxwell in 1871 (see Maxwell 1952, which is a compilation of some of his papers).

Because the radius $R \rightarrow 0$ we can expand $n(\mathbf{x} + \mathbf{r}, t)$ in a Taylor series about \mathbf{x} for small \mathbf{r} , namely,

$$n(\mathbf{x} + \mathbf{r}, t) = n(\mathbf{x}, t) + (\mathbf{r} \cdot \nabla)n + \frac{1}{2}(\mathbf{r} \cdot \nabla)^2 n + \dots$$

and substitute it into the integral in (11.33) for n_{av} to get

$$n_{av} = \left[\frac{3}{4\pi R^3} \right] \int_V \left[n(\mathbf{x}, t) + (\mathbf{r} \cdot \nabla)n + \frac{1}{2}(\mathbf{r} \cdot \nabla)^2 n + \dots \right] d\mathbf{r}.$$

Because of the symmetry the second integral is zero. If we neglect all terms $O(r^3)$ and higher in the integrand, integration gives

$$\begin{aligned} n_{av} &= \left(\frac{3}{4\pi R^3} \right) \left[n(\mathbf{x}, t) \int_V d\mathbf{r} + \nabla^2 n(\mathbf{x}, t) \int_V \frac{r^2}{2} d\mathbf{r} \right] \\ &= n(\mathbf{x}, t) + \frac{3}{10} R^2 \nabla^2 n(\mathbf{x}, t). \end{aligned} \quad (11.34)$$

If we now substitute this into the expression (11.32) we see that the proportionality factor is $10/3$.

In many biological areas, such as embryological development, the densities of cells involved are not small and a local or short range diffusive flux proportional to the gradient is not sufficiently accurate. When we discuss the mechanical theory of biological pattern formation in Chapter 6, Volume II we shall show how, in certain circumstances, it is intuitively reasonable, perhaps necessary, to include long range effects.

Instead of simply taking $\mathbf{J} \propto \nabla n$ we now consider

$$\mathbf{J} = \underset{r \in N(\mathbf{x})}{G} [\nabla n(\mathbf{x} + \mathbf{r}, t)], \quad (11.35)$$

where $N(\mathbf{x})$ is some neighbourhood of the point \mathbf{x} over which effects are noticed at \mathbf{x} , and G is some functional of the gradient. From symmetry arguments and assumptions of isotropy in the medium we are modelling, be it concentration or density, it can be shown that the first correction to the simple linear ∇n for the flux \mathbf{J} is a $\nabla(\nabla^2 n)$ term. The resulting form for the flux in (11.35) is then

$$\mathbf{J} = -D_1 \nabla n + \nabla D_2 (\nabla^2 n), \quad (11.36)$$

where $D_1 > 0$ and D_2 are constants. D_2 is a measure of the long range effects and in general is smaller in magnitude than D_1 . This approach is due to Othmer (1969), who goes into the formulation, derivation and form of the general functional G in detail. We give different motivations for the long range D_2 -term below and in Section 11.6.

If we now take the flux \mathbf{J} as given by (11.36) and use it in the conservation equation ((11.14) with $f \equiv 0$) we get

$$\frac{\partial n}{\partial t} = -\nabla \cdot \mathbf{J} = \nabla \cdot D_1 \nabla n - \nabla \cdot \nabla (D_2 \nabla^2 n). \quad (11.37)$$

In this form, using (11.32), we can see that whereas the first term represents an average of nearest neighbours, the second—the *biharmonic term*—is a contribution from the *average of nearest averages*.

The biharmonic term is stabilising if $D_2 > 0$, or destabilising if $D_2 < 0$. We can see this if we look for solutions of (11.37) in the form

$$n(\mathbf{x}, t) \propto \exp[\sigma t + i\mathbf{k} \cdot \mathbf{x}], \quad k = |\mathbf{k}| \quad (11.38)$$

which represents a wavelike solution with wave vector \mathbf{k} (and so has a wavelength $2\pi/k$) and σ is to be determined. Since (11.37) is a linear equation we can use this last solution to obtain the solution to the general initial value problem using an appropriate Fourier series or integral technique. Substitution of (11.38) into equation (11.37) gives what is called the *dispersion relation* for σ in terms of the wavenumber \mathbf{k} as

$$\sigma = -D_1 k^2 - D_2 k^4. \quad (11.39)$$

The growth or decay of the solution is determined by $\exp[\sigma t]$ in (11.38). Dispersion relations are very important in many different contexts. We discuss some of these in detail in Chapter 2, Volume II in particular. With σ as a function of k , the solution (11.38) shows the time behaviour of each wave, that is, for each k . In fact on substituting (11.39) into the solution (11.38) we see that

$$n(\mathbf{x}, t) \propto \exp[-(D_1 k^2 + D_2 k^4)t + i\mathbf{k} \cdot \mathbf{x}]$$

so, for large enough wavenumbers k , $k^2 > D_1/|D_2|$ in fact, we always have

$$n(x, t) \rightarrow \begin{cases} 0 \\ \infty \end{cases} \quad \text{as } t \rightarrow \infty \quad \text{if } D_2 \begin{cases} > 0 \\ < 0 \end{cases}. \quad (11.40)$$

In classical Fickian diffusion $D_2 \equiv 0$ and $n \rightarrow 0$ as $t \rightarrow \infty$ for all k . From (11.40) we see that if $D_2 > 0$ the biharmonic contribution (that is, the long range diffusion effect) to the diffusion process is stabilising, while it is destabilising if $D_2 < 0$.

Another important concept and approach to modelling long range effects uses an integral equation formulation. (This approach provides a useful unifying concept we

shall come back to later in Volume II when we consider a specific class of models for the generation of steady state spatial patterns; see Chapter 12, Volume II.) Here the rate of change of n at position x at time t depends on the influence of neighbouring n at all other positions x' . Such a model, in one space dimension, for example, is represented mathematically by

$$\frac{\partial n}{\partial t} = f(n) + \int_{-\infty}^{\infty} w(x - x')n(x', t) dx', \quad (11.41)$$

where $w(x - x')$ is the *kernel function* which quantifies the effect the neighbouring $n(x', t)$ has on $n(x, t)$. The form here assumes that the influence depends only on the distance from x to x' . The function $f(n)$ is the usual source or kinetics term—the same as we included in the reaction diffusion mechanisms (11.17) and (11.18); in the case of the application to neuronal cells, it is referred to as the firing rate as we discuss below and later in this volume. We assume, reasonably, that the influence of neighbours tends to zero for $|x - x'|$ large and that this influence is spatially symmetric; that is,

$$w \rightarrow 0 \quad \text{as} \quad |x - x'| \rightarrow \infty, \quad w(x - x') = w(x' - x). \quad (11.42)$$

Such a model (11.41) directly incorporates long range effects through the kernel: if w tends to zero quickly, for example, like $\exp[-(x - x')^2/s]$ where $0 < s \ll 1$, then the long range effects are weak, whereas if $s \gg 1$ they are strong.

To determine the spatiotemporal properties of the solutions of (11.41) the kernel w has to be specified. This involves modelling the specific biological phenomenon under consideration. Suppose we have neural cells which are cells which can fire spontaneously; here n represents the cells' firing rate. Then $f(n)$ represents the autonomous spatially independent firing rate, and, in the absence of any neighbouring cells' influence, the firing rate simply evolves to a stable steady state, determined by the zeros of $f(n)$. The mathematics is exactly the same as we discussed in Chapter 1. For example, if $f(n)$ is as in Figure 11.4(a) the rate evolves to the single steady state firing rate n_1 . If $f(n)$ is as in Figure 11.4(b) then there is a threshold firing rate above which n goes to a nonzero steady state and below which it goes to extinction.

If we now incorporate spatial effects we must include the influence of neighbouring cells; that is, we must prescribe the kernel function w . Suppose we assume that the cells are subjected to both excitatory and inhibitory inputs from neighbouring cells, with the strongest excitatory signals coming from the cells themselves. That is, if a cell is in a

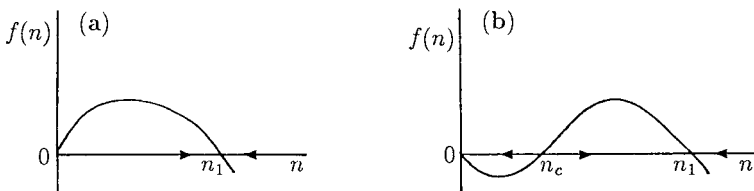


Figure 11.4. (a) Typical firing rate function $f(n)$ with a single nonzero steady state: $n \rightarrow n_1$ in the absence of spatial effects. (b) A typical multi-steady state firing function. If $n < n_c$, a critical firing rate, then $n \rightarrow 0$, that is, extinction. If $n > n_c$ then $n \rightarrow n_1$.

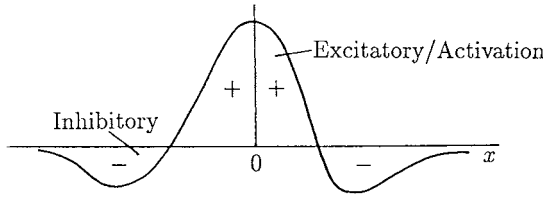


Figure 11.5. Typical excitatory–inhibitory kernel w for spatial influence of neighbours in the model (11.41).

high firing state n tends to increase; it is like autocatalysis. A kernel which incorporates such behaviour is illustrated in Figure 11.5.

We can relate this integral equation approach to the long range diffusion approximation which gave (11.37). Let

$$y = x - x' \quad \Rightarrow \quad \int_{-\infty}^{\infty} w(x - x')n(x', t) dx' = \int_{-\infty}^{\infty} w(y)n(x - y, t) dy.$$

If we now expand $n(x - y)$ about x as a Taylor series, as we did for the integral in (11.33),

$$\begin{aligned} \int_{-\infty}^{\infty} w(x - x')n(x', t) dx' &= \int_{-\infty}^{\infty} w(y) \left[n(x, t) - y \frac{\partial n(x, t)}{\partial x} + \frac{y^2}{2} \frac{\partial^2 n(x, t)}{\partial x^2} \right. \\ &\quad \left. - \frac{y^3}{3!} \frac{\partial^3 n(x, t)}{\partial x^3} + \frac{y^4}{4!} \frac{\partial^4 n(x, t)}{\partial x^4} - \dots \right] dy. \end{aligned} \tag{11.43}$$

Because of the assumed symmetry of the kernel $w(y)$,

$$\int_{-\infty}^{\infty} y^{2m+1}w(y) dy = 0, \quad m = 0, 1, 2, \dots \tag{11.44}$$

If we now define the *moments* w_m of the kernel $w(y)$ by

$$w_{2m} = \frac{1}{(2m)!} \int_{-\infty}^{\infty} y^{2m}w(y) dy, \quad m = 0, 1, 2, \dots \tag{11.45}$$

equation (11.41) becomes

$$\frac{\partial n}{\partial t} = f(n) + w_0n + w_2 \frac{\partial^2 n}{\partial x^2} + w_4 \frac{\partial^4 n}{\partial x^4} + \dots \tag{11.46}$$

Higher moments of typical kernels get progressively smaller; this is intuitively clear from (11.45). If we truncate the series in (11.46) at the 4th moment we get an approximate model equation with a biharmonic $\partial^4 n / \partial x^4$ contribution comparable to that in (11.37).

The solution behaviour of (11.41) depends crucially on the signs of the kernel moments and hence on the detailed form of the kernel, one typical form of which is shown qualitatively in Figure 11.5. For example, if $w_2 < 0$ the ‘short range diffusion’ term is destabilising, and if $w_4 < 0$ the ‘long range diffusion’ is stabilising (cf.(11.39)).

This integral equation approach is in many ways a much more satisfactory way to incorporate long range effects since it reflects, in a more descriptive way, what is going on biologically. As we have said above we shall discuss such models in depth in Chapter 12, Volume II which is about neural models which generate spatial patterns.

11.6 Cell Potential and Energy Approach to Diffusion and Long Range Effects

We now discuss an alternative approach to motivate the higher-order, long range diffusion terms. To be specific, in the following we have cell population densities in mind and for pedagogical reasons give the derivation of the classical (Fickian) diffusion before considering the more general case. The treatment here follows that given by Cohen and Murray (1981).

In general phenomenological terms if there is a gradient in a potential μ it can drive a flux \mathbf{J} which, classically, is proportional to $\nabla\mu$. We can, still in classical terms, think of the potential as the work done in changing the state by a small amount or, in other words, the variational derivative of an energy. Let $n(\mathbf{x}, t)$ be the cell density. We associate with a spatial distribution of cells, an energy density $e(n)$, that is, an internal energy per unit volume of an evolving spatial pattern so that the total energy $E[n]$ in a volume V is given by

$$E[n] = \int_V e(n) \, d\mathbf{x}. \quad (11.47)$$

The change in energy δE , that is, the work done in changing states by an amount δn , is the variational derivative $\delta E/\delta n$, which defines a potential $\mu(n)$. So

$$\mu(n) = \frac{\delta E}{\delta n} = e'(n). \quad (11.48)$$

The gradient of the potential μ produces a flux \mathbf{J} ; that is, the flux \mathbf{J} is proportional to $\nabla\mu$ and so

$$\mathbf{J} = -D\nabla\mu(n), \quad (11.49)$$

where D is the proportionality parameter, which in this derivation may depend on \mathbf{x} , t and n . The continuity equation for n becomes

$$\frac{\partial n}{\partial t} = -\nabla \cdot \mathbf{J} = \nabla \cdot [D\nabla\mu(n)] = \nabla \cdot [De''(n)\nabla n] \quad (11.50)$$

on using (11.48) for $\mu(n)$, and so

$$\frac{\partial n}{\partial t} = \nabla \cdot [D^*(n)\nabla n], \quad (11.51)$$

where

$$D^*(n) = De''(n). \quad (11.52)$$

In the simple classical diffusion situation with constant diffusion, the internal energy density is the usual quadratic with $e(n) = n^2/2$. With this, $\mu(n) = n$ and (11.51) becomes the usual diffusion equation $\partial n/\partial t = D\nabla^2 n$, with $D^* = D$, the constant diffusion coefficient. If D is a function of \mathbf{x} , t and n , the derivation is the same and the resulting conservation equation for n is then

$$\frac{\partial n}{\partial t} = \nabla \cdot [D^*(\mathbf{x}, t, n)\nabla n]. \quad (11.53)$$

Here n can be a vector of cell species.

This derivation assumes that the energy density $e(n)$ depends only on the density n . If the cells are sensitive to the environment other than in their immediate neighbourhood, it is reasonable to suppose that the energy required to maintain a spatial heterogeneity depends on neighbouring gradients in the cell density. It is the spatial heterogeneity which is ultimately of importance in biological pattern formation.

We take a more realistic energy functional, which is chosen so as to be invariant under reflections ($x_i \rightarrow -x_i$) and rotations ($x_i \rightarrow x_j$), as

$$E[n] = \int_V [e(n) + k_1 \nabla^2 n + k_2 (\nabla n)^2 + \dots] \mathbf{dx}, \quad (11.54)$$

where the k s may be functions of n . Using Green's theorem

$$\int_V k_1 \nabla^2 n \mathbf{dx} + \int_V \nabla k_1 \cdot \nabla n \mathbf{dx} = \int_S k_1 \frac{\partial n}{\partial N} \mathbf{ds},$$

where \mathbf{N} is the outward pointing normal to the surface S which encloses V and where we let k_1 depend on n so that $\nabla k_1 = k'_1(n)\nabla n$. From the last equation

$$\int_V k_1 \nabla^2 n \mathbf{dx} = - \int_V k'_1(n)(\nabla n)^2 \mathbf{dx} + \int_S k_1 \frac{\partial n}{\partial N} \mathbf{ds}. \quad (11.55)$$

We are not concerned with effects at the external boundary, so we can choose the bounding surface S such that $\partial n/\partial N = 0$ on S , that is, zero flux at the boundary. So (11.54) for the energy functional in a spatially heterogeneous situation becomes

$$E[n] = \int_V \left[e(n) + \frac{k}{2} (\nabla n)^2 + \dots \right] \mathbf{dx},$$

$$\frac{k}{2} = -k'_1(n) + k_2. \tag{11.56}$$

Here $e(n)$ is the energy density in a spatially homogeneous situation with the other terms representing the energy density (or ‘gradient’ density) which depends on the neighbouring spatial density variations.

We now carry out exactly the same steps that we took in going from (11.48) to (11.53). The potential μ is obtained from the energy functional (11.56) as

$$\mu = \mu(n, \nabla n) = \frac{\delta E[n]}{\delta n} = -k\nabla^2 n + e'(n), \tag{11.57}$$

using the calculus of variations to evaluate $\delta E[n]/\delta n$ and where we have taken k to be a constant. The flux \mathbf{J} is now given by

$$\mathbf{J} = -D^*\nabla\mu(n, \nabla n).$$

The generalised diffusion equation is then

$$\begin{aligned} \frac{\partial n}{\partial t} &= -\nabla \cdot \mathbf{J} = \nabla \cdot (D^*\nabla\mu), \\ &= D^*\nabla^2[-\nabla^2 n + e'(n)], \\ &= -kD^*\nabla^4 n + D^*\nabla \cdot [e''(n)\nabla n]. \end{aligned} \tag{11.58}$$

Here we have taken D^* , as well as k , to be constant.

A basic assumption about $e(n)$ is that it can involve only even powers of n since the energy density cannot depend on the sign of n . The Landau–Ginzburg free energy form (see, for example, Cahn and Hilliard 1958, 1959, Cahn 1959 and Huberman 1976) has

$$e(n) = \frac{an^2}{2} + \frac{bn^4}{4},$$

which on substituting into (11.58) gives

$$\frac{\partial n}{\partial t} = -D^*k\nabla^4 n + D^*a\nabla^2 n + D^*b\nabla^2 n^3.$$

If we now write

$$D_1 = D^*a, \quad D_2 = D^*k, \quad D_3 = D^*b,$$

the generalised diffusion equation (11.58) becomes

$$\frac{\partial n}{\partial t} = D_1\nabla^2 n - D_2\nabla^4 n + D_3\nabla^2 n^3. \tag{11.59}$$

Note the appearance of the extra nonlinear term involving D_3 . If the energy $e(n)$ only involves the usual quadratic in n^2 , $b = 0$ and (11.59) is exactly the same as (11.37) in

Section 11.4. If we now include a reaction or dynamics term $f(n)$ in (11.59) we get the generalised reaction diffusion equation equivalent to (11.14). With the one space dimensional scalar version of (11.59) and a logistic growth form for $f(n)$, Cohen and Murray (1981) have shown that the equation can exhibit steady state spatially inhomogeneous solutions. Lara-Ochoa (1984) analysed their model in a two-dimensional setting and showed that it reflects certain morphogenetic aspects of multicellular systems formed by motile cells.

Exercises

- 1 Let $p(x, t)$ be the probability that an organism initially at $x = 0$ is at x after a time t . In a random walk there is a slight bias to the right; that is, the probabilities of moving to the right and left, α and β , are such that $\alpha - \beta = \varepsilon > 0$, where $0 < \varepsilon \ll 1$. Show that the diffusion equation for the concentration $c(x, t) = Qp(x, t)$, where Q particles are released at the origin at $t = 0$, is

$$\frac{\partial c}{\partial t} + V \frac{\partial c}{\partial x} = D \frac{\partial^2 c}{\partial x^2},$$

where V and D are constants which you should define.

- 2 In a one-dimensional domain suppose insects are attracted to the origin $x = 0$ and are convected there by a constant velocity V . If the population pressure is approximated by a density-dependent diffusion coefficient $D(n) = D_0(n/n_0)^m$, where n is the population density and D_0 , n_0 and m are positive constants, show that the model equation for dispersal, in the absence of any population growth, is

$$\frac{\partial n}{\partial t} = -\frac{\partial J}{\partial x} = \frac{\partial}{\partial x} [V \operatorname{sgn}(x)n] + D_0 \frac{\partial}{\partial x} \left[\left(\frac{n}{n_0} \right)^m \frac{\partial n}{\partial x} \right].$$

Show that if $n \rightarrow 0$, $\partial n / \partial x \rightarrow 0$ as $|x| \rightarrow \infty$ a spatially inhomogeneous steady state population density exists and can be represented by

$$\begin{aligned} n(x) &= n_0 \left(1 - \frac{mV|x|}{D_0} \right)^{1/m}, & \text{if } |x| \leq \frac{D_0}{mV} \\ &= 0, & \text{if } |x| > \frac{D_0}{mV}. \end{aligned}$$

- 3 The larvae of the parasitic worm (*Trichostrongylus retortaeformis*) hatch from eggs in sheep and rabbit excreta. The larvae disperse randomly on the grass and are consequently eaten by sheep and rabbits. In the intestines the cycle starts again. Consider the one-dimensional problem in which the larvae disperse with constant diffusion and have a mortality proportional to the population. Show that n satisfies

$$\frac{\partial n}{\partial t} = D \frac{\partial^2 n}{\partial x^2} - \mu n, \quad D > 0, \quad \mu > 0,$$

where n is the larvae population. Find the population distribution at any x and t arising from N_0 larvae being released at $x = 0$ at $t = 0$. Show that as $t \rightarrow \infty$ the population dies out.

If the larvae lay eggs at a rate proportional to the population of the larvae, that is,

$$\frac{\partial E}{\partial t} = \lambda n, \quad \lambda > 0,$$

where $E(x, t)$ is the egg population density, show that in the limit as $t \rightarrow \infty$ a nonzero spatial distribution of eggs persists. [The result for $E(x, t)$ is an integral from which the asymptotic approximation can be found using Laplace's method (see, for example, Murray's 1984 *Asymptotic Analysis*): the result gives $E(x, t) \sim O(\exp[-(\mu/D)^{1/2}|x|])$ as $t \rightarrow \infty$.]

- 4 Consider the density-dependent diffusion model for insect dispersal which includes a linear death process which results in the following equation for the population $n(x, t)$,

$$\frac{\partial n}{\partial t} = D_0 \frac{\partial}{\partial x} \left[\left(\frac{n}{n_0} \right)^m \frac{\partial n}{\partial x} \right] - \mu n, \quad D_0 > 0, \quad \mu > 0.$$

If Q insects are released at $x = 0$ at $t = 0$, that is, $n(x, 0) = Q\delta(x)$, show, using appropriate transformations in n and t , that the equation can be reduced to an equivalent equation with $\mu = 0$. Hence show that the population wavefront reaches a finite distance x_{\max} from $x = 0$ as $t \rightarrow \infty$, where

$$x_{\max} = \frac{r_0}{(\mu m \tau_0)^{1/(m+2)}},$$

where

$$r_0 = \frac{Q\Gamma(\frac{1}{m} + \frac{3}{2})}{\pi^{1/2}n_0\Gamma(\frac{1}{m} + 1)}, \quad \tau_0 = \frac{r_0^2 m}{2D_0(m + 2)},$$

where Γ is the Gamma function.