

Models of dispersal in biological systems

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Abstract. In order to provide a general framework within which the dispersal of cells or organisms can be studied, we introduce two stochastic processes that model the major modes of dispersal that are observed in nature. In the first type of movement, which we call the position jump or kangaroo process, the process comprises a sequence of alternating pauses and jumps. The duration of a pause is governed by a waiting time distribution, and the direction and distance traveled during a jump is fixed by the kernel of an integral operator that governs the spatial redistribution. Under certain assumptions concerning the existence of limits as the mean step size goes to zero and the frequency of stepping goes to infinity the process is governed by a diffusion equation, but other partial differential equations may result under different assumptions. The second major type of movement leads to what we call a velocity jump process. In this case the motion consists of a sequence of “runs” separated by reorientations, during which a new velocity is chosen. We show that under certain assumptions this process leads to a damped wave equation called the telegrapher’s equation. We derive explicit expressions for the mean squared displacement and other experimentally observable quantities. Several generalizations, including the incorporation of a resting time between movements, are also studied. The available data on the motion of cells and other organisms is reviewed, and it is shown how the analysis of such data within the framework provided here can be carried out.

Key words: Dispersal — Cell movement — Random walks — Stochastic processes

1. Introduction

Many theoretical analyses of the dispersal of cells or organisms are based on the hypothesis that the movement of the dispersing species can be described as a

* Supported in part by NIH Grant #GM 29123 and by NSF Grant #DMS-8301840

** Supported in part by NSF Grant #DMS-8301840

*** Supported in part by the DFG Heisenberg Program

random walk in which there is no correlation between steps. In an appropriate continuum limit the probability that an individual will be found at a given point in space at a fixed time satisfies a diffusion equation without drift. As we shall see, this process is the simplest example of what we call the space jump process. In order to motivate the generalizations that are introduced in the following sections, we discuss the standard approach to this process and to the simplest example of a velocity jump process in this section. A more comprehensive discussion of the use of diffusion processes in modeling spatial dispersal in ecology is given in Okubo (1980) and in Levin (1986).

Consider a one-dimensional uniform lattice, and suppose that there is no directional bias in the movement, by which is meant that the probabilities of a step in either direction are the same. The probability that a walker beginning at the origin is at site m after N steps is given by

$$p(m, N) = \frac{1}{2^N} \binom{N}{\frac{N-m}{2}}$$

where $\binom{\cdot}{\cdot}$ is the binomial coefficient, which is understood to be zero if $(N-m)/2$ is not an integer (Chandrasekhar (1943), Feller (1968)). For large N and $m \ll N$ an application of Stirling's approximation leads to

$$p(m, N) \sim \sqrt{\frac{2}{\pi N}} e^{-m^2/2N}.$$

Let $x = m\Delta$ and $N = \lambda t$, where Δ is the lattice spacing and λ is the rate at which steps are taken, and let

$$P(x, t) dx \equiv p\left(\frac{x}{\Delta}, \lambda t\right) \frac{dx}{2\Delta}.$$

Then

$$P(x, t) dx = \frac{1}{\sqrt{2\pi\lambda\Delta^2 t}} e^{-x^2/2\lambda\Delta^2 t} dx,$$

and if we let $\lambda \rightarrow \infty$ and $\Delta \rightarrow 0$, while holding $\lambda\Delta^2 = \text{constant} \equiv 2D$, then

$$P(x, t) = \frac{1}{\sqrt{4\pi Dt}} e^{-x^2/4Dt}. \quad (1)$$

Thus P is the fundamental solution of the diffusion equation, i.e. the solution of

$$\begin{aligned} \frac{\partial P}{\partial t} &= D \frac{\partial^2 P}{\partial x^2} \quad \text{for } x \in \mathbb{R}, t \in \mathbb{R}^+ \\ P(x, 0) &= \delta(x) \end{aligned} \quad (2)$$

where $\delta(x)$ is the Dirac distribution. The corresponding stochastic process is variously called a diffusion process without drift, Brownian motion, or a Wiener process. The most accessible statistic of such a process from an experimental

standpoint is the mean squared displacement

$$\langle x^2 \rangle = \int_{-\infty}^{+\infty} x^2 P(x, t) dx = 2Dt. \quad (3)$$

The analogous two dimensional diffusion problem is

$$\frac{\partial P}{\partial t} = D \left(\frac{\partial^2 P}{\partial x^2} + \frac{\partial^2 P}{\partial y^2} \right) \quad \text{for } (x, y) \in R^2, t \in R^+ \quad (4)$$

$$P(x, y, 0) = \delta(x)\delta(y)$$

and the solution is

$$P(x, y, t) = \frac{1}{4\pi Dt} e^{-(x^2+y^2)/4Dt}.$$

The formula for the mean squared displacement in the plane is $\langle r^2 \rangle = 4Dt$.

Since $P(x, t) > 0$ for $t > 0$ and any $x \in R$, a diffusion process predicts a non-zero probability for arbitrarily large displacements at arbitrarily small times, and in this sense the underlying propagation speed is infinite. However, it has long been known that equations such as (3) are best regarded as asymptotic approximations, valid for large time, of equations that more accurately describe the correlations in movement that can be detected when the process is observed on a sufficiently short time scale (Einstein (1905), Fürth (1920)). There are theoretical predictions that such correlation effects could be important in multicomponent reacting systems (Othmer (1969), Othmer (1976)), but to date there is no convincing evidence that such correlations are important on the time scales that characterize transport in condensed reacting media of the type usually studied by physical chemists and engineers.

However, dispersal of cells and large organisms occurs on entirely different time scales and often involves mechanisms that may introduce correlations in movements. For instance, there are various types of "taxes", there can be density dependence in the fluxes (Shigesada (1980)), avoidance phenomena, etc. (cf. Okubo (1980)). Furthermore, within the last 15 years several experimental studies have demonstrated the existence of significant correlations in the motions of several different types of cells. Gail and Boone (1970) showed that mouse fibroblasts exhibit persistence in their direction of motion when they are observed over successive time intervals of 2.5 h or less, but that this correlation is not observed over longer time intervals. In a similar vein, when the bacterium *E. coli* moves in an isotropic medium the successive turns are uncorrelated and independent of the step length, and the distribution of turn angles is symmetric about zero. In the presence of a gradient of a chemotactic substance the length of the steps increases when motion is up the gradient (Berg (1975, 1983)), i.e. some measure of persistence is increased. More recently Hall (1977) has studied the motion of *Dictyostelium discoideum* amoeba and detected correlations in the angle of turn between successive steps, but no correlation in the lengths of successive steps. Similar findings have been reported by Hall and Peterson (1979) for human granulocytes, by Dunn (1983) for chick heart fibroblasts, and by Kareiva and Shigesada (1983) for cabbage butterflies. The foregoing studies provide one of the motivations for our analysis of models other than the simplest diffusion model

for the description of biological transport. We shall discuss the results of these studies in more detail later.

A very simple model for a correlated random walk in one dimension was first analyzed by Goldstein (1951), and later by Kac (1974), McKean (1967) and Segel (1978). Suppose that a particle moves along the x -axis at a constant speed s , but that at random instants of time it reverses direction. Suppose that this "velocity-reversing" process is a Poisson process with intensity λ , i.e. the rate of reversal per unit time is λ . Let $p^+(x, t)$ be the probability density of particles that are at (x, t) and are moving to the right, and let $p^-(x, t)$ be the probability density of particles that are at (x, t) and are moving to the left. Then $p^\pm(x, t)$ satisfy the equations

$$\begin{aligned}\frac{\partial p^+}{\partial t} + s \frac{\partial p^+}{\partial x} &= -\lambda p^+ + \lambda p^- \\ \frac{\partial p^-}{\partial t} - s \frac{\partial p^-}{\partial x} &= \lambda p^+ - \lambda p^-\end{aligned}\tag{5}$$

The probability that a particle is at (x, t) is $p(x, t) \equiv p^+(x, t) + p^-(x, t)$, and the probability flux is $j \equiv s(p^+ - p^-)$. These satisfy the equations

$$\begin{aligned}\frac{\partial p}{\partial t} + \frac{\partial j}{\partial x} &= 0 \\ \frac{\partial j}{\partial t} + 2\lambda j &= -s^2 \frac{\partial p}{\partial x}\end{aligned}\tag{6}$$

and the initial conditions $p(x, 0) = p_0(x)$, $j(x, 0) = j_0(x)$, where p_0 and j_0 are determined from the initial distribution of p^+ and p^- . The system (6) is equivalent to the second-order equation

$$\frac{\partial^2 p}{\partial t^2} + 2\lambda \frac{\partial p}{\partial t} = s^2 \frac{\partial^2 p}{\partial x^2}\tag{7}$$

with initial conditions $p(x, 0) = p_0(x)$, $\partial p / \partial t(x, 0) = -\partial j_0 / \partial x(x)$. Equation (7) is called the telegrapher's equation and the underlying stochastic process will be called the telegraph process. A nonlinear version of this equation that incorporates birth and death is studied in Dunbar and Othmer (1986) and Dunbar (1987).

Since (7) is a hyperbolic equation signals cannot propagate faster than s , which is the underlying particle speed. Thus the telegraph process obviates one objection to the diffusion process. The mean squared displacement can be obtained from (7) by multiplying by x^2 and integrating over R . If $p(x, t)$ and its first two x derivatives tend to zero as $|x| \rightarrow \infty$, the right-hand side can be integrated by parts and one finds that

$$\frac{d^2 \langle x^2 \rangle}{dt^2} + 2\lambda \frac{d \langle x^2 \rangle}{dt} = 2s^2.$$

If we assume that $p(x, 0) = \delta(x)$ and $\partial p / \partial t(x, 0) = 0$, then the appropriate initial conditions for this equation are $\langle x^2(0) \rangle = d/dt \langle x^2(0) \rangle = 0$, and therefore

$$\langle x^2(t) \rangle = \frac{s^2}{\lambda} \left\{ t - \frac{1}{2\lambda} (1 - e^{-2\lambda t}) \right\}.\tag{8}$$

For small t , $\langle x^2(t) \rangle \sim s^2 t^2$, which is characteristic of a wave propagation process, and for large t , $\langle x^2(t) \rangle \sim s^2 t / \lambda$, which is characteristic of a diffusion process with diffusion coefficient $D = s^2 / 2\lambda$. To relate this result to the diffusion coefficient obtained earlier, note that in a Poisson process of intensity λ the mean time between events is $1/\lambda$. Thus the average distance traveled between reversals is $\Delta = s/\lambda$, and therefore

$$D = \frac{s^2}{2\lambda} = \frac{\lambda \Delta^2}{2}. \tag{9}$$

This is the same expression for D given earlier, and thus the “diffusion limit” of the telegraph process consists in letting $\lambda \rightarrow \infty$ and $s \rightarrow \infty$ while maintaining s^2/λ constant. The analog of (8) for a certain discrete-time correlated random walk in two space dimensions is given in Skellam (1973).

Further insight into the diffusion limit of the telegraph process can be gained from the integrated form of the second equation in (6), which reads

$$j(x, t) = e^{-2\lambda t} j(x, 0) - s^2 \int_0^t e^{-2\lambda(t-\tau)} \frac{\partial p}{\partial x}(x, \tau) d\tau. \tag{10}$$

It is easy to prove that

$$\lim_{\lambda \rightarrow \infty} 2\lambda \int_0^t e^{-2\lambda(t-\tau)} \frac{\partial p}{\partial x}(x, \tau) d\tau = \frac{\partial p}{\partial x}(x, t),$$

and therefore in the diffusion limit (10) reduces to

$$j(x, \tau) = -D \frac{\partial p}{\partial x}(x, \tau)$$

where D is given by (9). This gives one form of Fick’s law, and when this is used in the first equation of (6) one again obtains the diffusion equation. Thus the diffusion limit of the telegraph process can be viewed as a limit in which the probability flux relaxes instantaneously to the relationship given by Fick’s law. That is, inertial effects are negligible in this limit (cf. Othmer (1976)).

Since (7) is linear it can be solved explicitly. One finds that the solution for the initial conditions $p(x, 0) = \delta(x)$, $\partial p / \partial x(x, 0) = 0$ is given by (Morse and Feshbach (1953))

$$p(x, t) = \begin{cases} \frac{e^{-\lambda t}}{2} \left\{ \delta(x-st) + \delta(x+st) + \frac{\lambda}{s} \left[I_0(\Lambda) + \frac{\lambda t}{\Lambda} I_1(\Lambda) \right] \right\} & \text{for } |x| < st \\ 0 & \text{for } |x| \geq st \end{cases} \tag{11}$$

where $\Lambda = \lambda \sqrt{t^2 - x^2/s^2}$ and I_0 and I_1 are the modified Bessel functions. The Bessel functions have the asymptotic expansions (Abramowitz and Stegun (1965))

$$I_0 \sim \frac{e^x}{\sqrt{2\pi x}} + \mathcal{O}(1/x)$$

$$I_1 \sim \frac{e^x}{\sqrt{2\pi x}} + \mathcal{O}(1/x)$$

for $x \rightarrow \infty$, and it follows that

$$p(x, t) \sim \frac{1}{\sqrt{4\pi Dt}} e^{-x^2/4Dt} + e^{-\lambda t} \mathcal{O}(\xi^2)$$

for $\xi \equiv x^2/(st)^2$. Therefore, far from the boundaries $|x| = st$ of the forward light cone the solution reduces as $t \rightarrow \infty$ to the solution of the diffusion equation, as expected.

The diffusion and telegraph process are examples of what we shall call position jump or kangaroo processes and velocity jump processes, respectively. Both processes will be described in greater generality later. Kangaroos and grasshoppers provide the most amusing examples of movement via the first type of process, while the examples from cellular movement discussed earlier are best described as velocity jump processes. While the diffusion equation and the telegrapher's equation serve as useful tools for analyzing experimental data, it should be recognized that experimental data usually provides only a few spatial moments of the underlying stochastic process, and therefore the underlying process cannot be uniquely identified. Thus it is of interest and possibly of experimental value to identify general classes of processes that lead to the same observables, such as the mean squared displacement. This is one of the major objectives here.

In the following section we present a general formulation of position jump processes, based on an arbitrary waiting time distribution for the interval between jumps and a spatially homogeneous process for the direction and length of the jumps. We derive the time dependence of the first few spatial moments for some typical choices of the functions. We also show how some of the standard partial differential equations can be obtained from our integral equation formulation.

In Sect. 3 we present a general formulation of the velocity jump process in n -space for $n = 1, 2, 3$. In Sect. 4 we discuss several generalizations of the cases treated in Sects. 2 and 3, and in Sect. 5 we show how our approach can be used in analyzing data.

2. The position jump or kangaroo process

2.1. Derivation of the model

Consider a random jump process on R^n in which the particle executes a sequence of jumps of negligible duration, and suppose that the waiting times between successive jumps are independent and identically distributed. That is, if the jumps occur at T_0, T_1, \dots then the increments $T_i - T_{i-1}$ are identically and independently distributed, and therefore the jump process is a semi-Markov process (Feller (1968), Karlin and Taylor (1975)). Let \mathcal{T} be the waiting time between jumps and let $\phi(t)$ be the density for the waiting time distribution. \mathcal{T} is experimentally observable, and in principle $\phi(t)$ can be determined from experimental observations (cf. Sect. 5). If a jump has occurred at $t = 0$ then

$$\phi(t) = \Pr\{t < \mathcal{T} \leq t + dt\}.$$

The cumulative distribution function for the waiting times is

$$\Phi(t) = \int_0^t \phi(s) ds = \Pr\{\mathcal{T} \leq t\}$$

and the complementary cumulative distribution function is

$$\hat{\Phi}(t) = \int_t^{\infty} \phi(s) ds = 1 - \Phi(t) = \Pr\{\mathcal{T} \geq t\}.$$

For example, if the jumps are governed by a Poisson process then $\Phi(t) = 1 - e^{-\lambda t}$ and $\phi(t) = \lambda e^{-\lambda t}$. This is the only smooth distribution for which the jump process is Markovian (Feller (1968), p. 458).

Next we must specify how jumpers are redistributed in space, given that a jump occurs. For simplicity we shall assume that the spatial redistribution that occurs at jumps is independent of the waiting time distribution. Thus the probability of a transition from \mathbf{y} to \mathbf{x} at time t will simply be the product of $\Phi(t)$ times the function that gives the probability of the jump from \mathbf{y} to \mathbf{x} . This assumption of statistical independence between the event of deciding to jump and the event of deciding where to jump may clearly be too restrictive for some systems, for the direction and length of a jump may very well depend on the time elapsed since the last jump. Our formulation of the velocity jump process will incorporate some types of directional persistence, but for now we shall, in effect, assume that we have infinitely energetic jumpers that have no recollection of their previous location.

Let $T(\mathbf{x}, \mathbf{y})$ be the probability density function for a jump from \mathbf{y} to \mathbf{x} . That is, if $X(t)$ is a random variable giving the jumper's position at time t , then given that a jump occurs at T_i ,

$$T(\mathbf{x}, \mathbf{y}) d\mathbf{x} = \Pr\{\mathbf{x} \leq X(T_i^+) \leq \mathbf{x} + d\mathbf{x} | X(T_i^-) = \mathbf{y}\}, \quad (12)$$

where the superscripts \pm denote limits from the right and left, respectively. This definition allows for the possibility that the underlying medium is spatially nonhomogeneous and nonisotropic, in which case the transition probability depends on \mathbf{x} and \mathbf{y} separately. In the case of a homogeneous and isotropic medium $T(\mathbf{x}, \mathbf{y}) = \tilde{T}(\mathbf{x} - \mathbf{y})$, where \tilde{T} gives the absolute (unconditioned) probability of a jump of length $\mathbf{x} - \mathbf{y}$.

One of the purposes of the analysis is to show how the functions $\phi(t)$ and $T(\mathbf{x}, \mathbf{y})$ can be related to experimentally observable quantities. The statistics most accessible from observations are the various moments of the displacement and their dependence on t . To relate these to ϕ and T we must derive an evolution equation for the density function $P(\mathbf{x}, t|0)$, which is defined so that $P(\mathbf{x}, t|0) d\mathbf{x}$ is the probability that the position of a jumper which begins at the origin at time $t=0$ lies in the interval $(\mathbf{x}, \mathbf{x} + d\mathbf{x})$ at time t . We shall derive this equation via equations for some auxiliary quantities.

Let $Q_k(\mathbf{x}, t)$ be the conditional probability that a jumper which begins at $\mathbf{x} = 0$ at $t=0$ takes its k th step at t^- and lands in the interval $(\mathbf{x}, \mathbf{x} + d\mathbf{x})$. Then for $\mathbf{x} > 0$, $t > 0$, Q_k satisfies the first-order difference equation

$$Q_{k+1}(\mathbf{x}, t) = \int_0^t \int_{R^n} \phi(t - \tau) T(\mathbf{x}, \mathbf{y}) Q_k(\mathbf{y}, \tau) dy d\tau.$$

Summing this over k we obtain the density function for arriving in the interval $(\mathbf{x}, \mathbf{x} + d\mathbf{x})$ at time t^- after any number of steps. Thus we obtain the Volterra

integral equation

$$Q(\mathbf{x}, t) = \sum_{k=0}^{\infty} Q_k(\mathbf{x}, t) = Q_0(\mathbf{x}, t) + \int_0^t \int_{R^n} \phi(t-\tau) T(\mathbf{x}, \mathbf{y}) Q(\mathbf{y}, \tau) d\mathbf{y} d\tau \quad (13)$$

and this must satisfy the initial condition

$$Q(\mathbf{x}, 0) = \delta(\mathbf{x}).$$

Consequently (13) becomes

$$Q(\mathbf{x}, t) = \delta(\mathbf{x})\delta(t) + \int_0^t \int_{R^n} \phi(t-\tau) T(\mathbf{x}, \mathbf{y}) Q(\mathbf{y}, \tau) d\mathbf{y} d\tau.$$

The probability density function $P(\mathbf{x}, t|0)$ for the conditional probability that $X(t)$ lies in $(\mathbf{x}, \mathbf{x} + d\mathbf{x})$ at time t can be computed as the product of the probability of arriving in this interval at some time $\tau < t$, multiplied by the probability that no transition occurs in the remaining time $t - \tau$. Thus

$$\begin{aligned} P(\mathbf{x}, t|0) &= \int_0^t \hat{\Phi}(t-\tau) Q(\mathbf{x}, \tau) d\tau \\ &= \int_0^t \hat{\Phi}(t-\tau) \left\{ \delta(\mathbf{x})\delta(\tau) + \int_0^\tau \int_{R^n} \phi(\tau-s) T(\mathbf{x}, \mathbf{y}) Q(\mathbf{y}, s) d\mathbf{y} ds \right\} d\tau \\ &= \hat{\Phi}(t)\delta(\mathbf{x}) + \int_0^t \int_{R^n} \left(\int_s^t \hat{\Phi}(t-\tau)\phi(\tau-s) d\tau \right) T(\mathbf{x}, \mathbf{y}) Q(\mathbf{y}, s) d\mathbf{y} ds. \end{aligned} \quad (14)$$

On the other hand, it follows from (14) that

$$\begin{aligned} &\int_0^t \int_{R^n} \phi(t-\tau) T(\mathbf{x}, \mathbf{y}) P(\mathbf{y}, \tau|0) d\mathbf{y} d\tau \\ &= \int_0^t \int_{R^n} \int_0^\tau \phi(t-\tau)\hat{\Phi}(\tau-s) T(\mathbf{x}, \mathbf{y}) Q(\mathbf{y}, s) d\mathbf{y} ds d\tau \\ &= \int_0^t \int_{R^n} \left(\int_s^t \hat{\Phi}(\tau-s)\phi(t-\tau) d\tau \right) T(\mathbf{x}, \mathbf{y}) Q(\mathbf{y}, s) d\mathbf{y} ds. \end{aligned}$$

It is easy to show that

$$\int_s^t \hat{\Phi}(t-\tau)\phi(\tau-s) d\tau = \int_s^t \phi(t-\tau)\hat{\Phi}(\tau-s) d\tau$$

by setting $u = t - s$, $z = \tau - s$, and observing that the resulting integrals have the same Laplace transforms. Thus $P(\mathbf{x}, t|0)$ satisfies the following renewal equation:

$$P(\mathbf{x}, t|0) = \hat{\Phi}(t)\delta(\mathbf{x}) + \int_0^t \int_{R^n} \phi(t-\tau) T(\mathbf{x}, \mathbf{y}) P(\mathbf{y}, \tau|0) d\mathbf{y} d\tau. \quad (15)$$

If the initial distribution is given by $F(\mathbf{x})$ then

$$n(\mathbf{x}, t) \equiv \int_{R^n} P(\mathbf{x}, t|\mathbf{x}_0) F(\mathbf{x}_0) d\mathbf{x}_0$$

can be regarded as the number density of identical non-interacting jumpers at \mathbf{x} at time t . Clearly $n(\mathbf{x}, t)$ satisfies

$$n(\mathbf{x}, t) = \hat{\Phi}(t)F(\mathbf{x}) + \int_0^t \int_{R^n} \phi(t-\tau)T(\mathbf{x}, \mathbf{y})n(\mathbf{y}, \tau) d\mathbf{y} d\tau. \quad (16)$$

In order that the total number of jumpers be conserved in the jump process it is necessary that

$$N(t) = \int_{R^n} n(\mathbf{x}, t) d\mathbf{x} = N_0 \equiv \int_{R^n} F(\mathbf{x}) d\mathbf{x}$$

i.e. that

$$\hat{\Phi}(t)N_0 + \int_0^t \int_{R^n} \int_{R^n} \phi(t-\tau)T(\mathbf{x}, \mathbf{y})n(\mathbf{y}, \tau) d\mathbf{y} d\tau d\mathbf{x} = N_0.$$

We assume that $T \in L^1(R^n \times R^n)$, and therefore the \mathbf{x} and \mathbf{y} integrations can be interchanged by Fubini's theorem. It follows that the necessary and sufficient condition for conservation of jumpers is that

$$\int_{R^n} T(\mathbf{x}, \mathbf{y}) d\mathbf{x} = 1.$$

Hereafter we assume that Φ and T have the proper normalizations and sufficient regularity that the indicated operations make sense.

Special choices of ϕ and T lead to some of the standard random jump problems treated in the literature. For instance, if $\phi(t) = \delta(t-t_0)$ then $\Phi(t) = H(t_0-t)$, where $H(\cdot)$ is the Heaviside function, and (15) reduces to

$$P(\mathbf{x}, t|0) = H(t_0-t)\delta(\mathbf{x}) + [1-H(t_0-t)] \int_{R^n} T(\mathbf{x}, \mathbf{y})P(\mathbf{y}, t-t_0|0) d\mathbf{y}.$$

This is the governing equation for a discrete time, continuous space process in which jumps occur at intervals of t_0 . If in addition the support of T is concentrated on the points of a lattice $Z^n \subset R^n$, then

$$P(\mathbf{x}_i, t|0) = H(t_0-t)\delta_{i0} + [1-H(t_0-t)] \sum_j T_{ij}P(\mathbf{x}_j, t-t_0|0),$$

where δ_{i0} is the Kronecker delta, and \mathbf{x}_i is a lattice point. This can be written in the more conventional Chapman-Kolmogorov form as follows:

$$P_{i0}(n+1) = \sum_j T_{ij}P_{j0}(n), \quad n \geq 1.$$

Clearly the underlying process is Markovian for this ϕ .

2.2. Analysis of moments

As we remarked earlier, one of our purposes is to relate ϕ and T to the experimental observations. The statistics most accessible from observations are the various moments of the displacement, in particular their dependence on t .

We shall compute these moments from (15), and for illustrative purposes we assume that the medium is one-dimensional and spatially homogeneous. Define

$$\begin{aligned}\langle x^n(t) \rangle &= \int_{-\infty}^{+\infty} x^n P(x, t|0) dx \\ &= \int_{-\infty}^{+\infty} \int_0^t \int_{-\infty}^{+\infty} x^n \tilde{T}(x-y) \phi(t-\tau) P(y, \tau|0) dy d\tau dx.\end{aligned}\quad (17)$$

Let

$$m_k = \int_{-\infty}^{+\infty} x^k \tilde{T}(x) dx$$

be the k th moment of \tilde{T} about zero. Then (17) can be written

$$\langle x^n(t) \rangle = \int_0^t \sum_{k=0}^n \binom{n}{k} m_k \phi(t-\tau) \langle x^{n-k}(\tau) \rangle d\tau.\quad (18)$$

It follows that all the moments of $x(t)$ can be gotten by solving a sequence of linear integral equations of convolution type.

Let

$$X_k(s) = \mathcal{L}\{\langle x^k(t) \rangle\} \equiv \int_0^{\infty} e^{-s\tau} \langle x^k(\tau) \rangle d\tau$$

be the Laplace transform of the k th moment, and let $\bar{\phi}(s) = \mathcal{L}\{\phi(t)\}$. Then one finds that

$$X_1(s) = \frac{m_1}{s} \frac{\bar{\phi}(s)}{1 - \bar{\phi}(s)}\quad (19)$$

$$X_2(s) = \left(2m_1 X_1(s) + \frac{m_2}{s}\right) \frac{\bar{\phi}(s)}{1 - \bar{\phi}(s)}.$$

If the first moment of \tilde{T} vanishes then these simplify to

$$X_1(s) = 0\quad (20)$$

$$X_2(s) = \frac{m_2}{s} \frac{\bar{\phi}(s)}{1 - \bar{\phi}(s)}.$$

The asymptotic behavior of the moments can be gotten by applying limit theorems for Laplace transforms (Widder (1946)), but we shall merely illustrate the dependence of X_2 on t for two particular choices of ϕ . Firstly, suppose that $m_1 = 0$ and that

$$\phi(t) = \lambda e^{-\lambda t}\quad (21)$$

which is the density function for an exponential waiting time distribution. Then $\bar{\phi}(s) = \lambda/(s + \lambda)$ and it follows that

$$\langle x^2(t) \rangle = m_2 \int_0^t \mathcal{L}^{-1}\left(\frac{\lambda}{s}\right) d\tau = m_2 \lambda t.\quad (22)$$

Secondly, if we choose

$$\phi(t) = \lambda^2 t e^{-\lambda t}\quad (23)$$

which is the density function for a gamma waiting time distribution with parameters $(2, \lambda)$, then

$$\bar{\phi}(s) = \frac{\lambda^2}{(s + \lambda)^2}.$$

One finds that

$$\langle x^2(t) \rangle = m_2 \int_0^t \mathcal{L}^{-1} \left(\frac{\lambda^2}{s(s + 2\lambda)} \right) d\tau = \frac{m_2 \lambda}{2} \left\{ t - \frac{1}{2\lambda} (1 - e^{-2\lambda t}) \right\}, \quad (24)$$

which is shown in Fig. 1.

It is clear from the analysis given in the Introduction that (22) predicts the same mean squared displacement as a diffusion process with diffusion coefficient $D = m_2 \lambda / 2$. Similarly (23) leads to the same mean squared displacement as the telegraph process. Of course neither fact proves that the processes defined by (21) and (23) are diffusion and telegraph processes, respectively, but an experimentalist who can reliably measure only the first two moments of the displacement could not distinguish them from these processes. It is noteworthy that this conclusion holds under the reasonable hypothesis that the first two moments of T are finite, without any condition on the higher moments.

2.3. Diffusion limits for the exponential waiting time distribution

The results given by (22) and (24) raise the question as to whether, for some choice of T , the corresponding integral equations are equivalent to the diffusion and telegraph equations, respectively, in an appropriate limit. Consider first the choice $\phi(t) = \lambda e^{-\lambda t}$ which leads to (22). After differentiating (15) and rearranging one finds that

$$\frac{\partial P}{\partial t} = -\lambda P + \lambda \int_R \tilde{T}(x - y) P(y, t) dy \quad (25)$$

where here and hereafter we suppress the conditioning argument in P . If

$$\tilde{T}(x - y) = \frac{1}{2} [\delta(x - y - \Delta) + \delta(x - y + \Delta)] \quad (26)$$

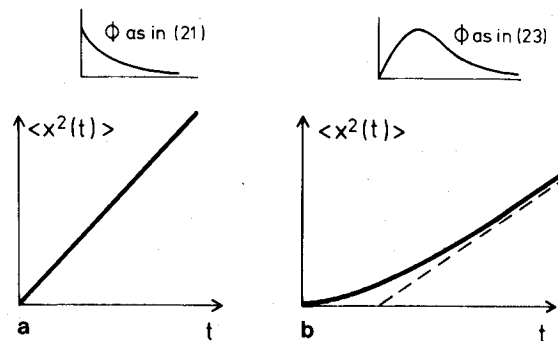


Fig. 1. Theoretical curves of the mean-squared displacement sketched for the position jump process with exponential (a) and gamma waiting time distribution (b)

then

$$\frac{\partial P}{\partial t} = \frac{\lambda}{2} [P(x + \Delta, t) - 2P(x, t) + P(x - \Delta, t)].$$

The right-hand side can be written

$$\frac{\lambda \Delta^2}{2} \left[\frac{\partial^2 P}{\partial x^2} + \mathcal{O}(\Delta^2) \right],$$

and therefore, in the diffusion limit ($\lambda \rightarrow \infty$, $\Delta \rightarrow 0$, $\lambda \Delta^2 = \text{constant}$) we obtain

$$\frac{\partial P}{\partial t} = D \frac{\partial^2 P}{\partial x^2}, \quad (27)$$

provided that the higher-order derivatives included in $\mathcal{O}(\Delta^2)$ are bounded.

In fact, a similar result holds in any dimension. Let

$$\tilde{T}(x-y) = \frac{\delta(x-y-\Delta)}{\Delta^{n-1} \omega_n}$$

where ω_n is the surface measure of the unit sphere in R^n . For this choice of \tilde{T} one finds that

$$\frac{\partial P}{\partial t} = \lambda [\bar{P}(x, \Delta, t) - P(x, t)]$$

where \bar{P} is the average of P over the surface of a sphere of radius Δ centered at x . By expanding P about x and performing the indicated average one finds that in the diffusion limit

$$\frac{\partial P}{\partial t} = D \nabla^2 P, \quad (28)$$

provided that P varies smoothly, i.e. provided that all higher-order derivatives are bounded. Here $D \equiv \lambda \Delta^2 / 2n$ is the diffusion coefficient in n dimensions.

A similar conclusion holds for much more general kernels \tilde{T} . Suppose that \tilde{T} has the form

$$\tilde{T}(x-y) = \frac{1}{\Delta} T_0\left(\frac{x-y}{\Delta}, \Delta\right).$$

Then

$$\frac{\partial P}{\partial t} = \lambda \left(\Delta \int_R T_0(r, \Delta) r dr \right) \frac{\partial P}{\partial x} + \lambda \left(\frac{\Delta^2}{2} \int_R T_0(r, \Delta) r^2 dr \right) \frac{\partial^2 P}{\partial x^2} + \mathcal{O}(\Delta^3). \quad (29)$$

It follows that if the first moment of T_0 is $\mathcal{O}(\Delta)$ for $\Delta \rightarrow 0$, if the second moment of T_0 tends to a constant, and if all higher moments are bounded, then in the diffusion limit ($\lambda \rightarrow \infty$, $\Delta \rightarrow 0$, $\lambda \Delta^2 = \text{constant}$) we obtain a diffusion equation with drift. The diffusion coefficient is given by

$$D = \lambda \frac{\Delta^2}{2} \lim_{\Delta \rightarrow 0} \int_R T_0(r, \Delta) r^2 dr \quad (30)$$

and the drift coefficient is given by

$$\beta = \lambda \frac{\Delta^2}{2} \lim_{\Delta \rightarrow 0} \int_R \frac{T_0(r, \Delta)}{\Delta} r dr. \tag{31}$$

If the kernel is symmetric then the drift coefficient vanishes. The reader can check that the foregoing conditions are satisfied for the kernel

$$\tilde{T}(x-y) = \frac{1}{2\sqrt{2\pi\sigma^2}} \{e^{-(x-y-\Delta)^2/2\sigma^2} + e^{-(x-y+\Delta)^2/2\sigma^2}\}$$

provided that $\sigma/\Delta \sim \mathcal{O}(1)$ as $\Delta \rightarrow 0$.

The situation is quite different when $\phi(t) = \lambda^2 t e^{-\lambda t}$. In this case the analog of (25) is

$$\frac{\partial^2 P}{\partial t^2} + 2\lambda \frac{\partial P}{\partial t} = -\lambda^2 P + \lambda^2 \int_R \tilde{T}(x-y) P(y, t) dy, \tag{32}$$

which is homogeneous in λt . Thus it is clear that there is no scaling of time in which the second-order time derivative can be neglected for $\lambda \rightarrow \infty$, irrespective of the choice of \tilde{T} . Thus there is no possibility of letting $\lambda \rightarrow \infty$ in such a way that the resulting equation is the telegrapher's equation on time intervals of the form $[t_0, \infty)$. Of course the choice given at (26) for $T(x, y)$ will produce a finite difference approximation to $\partial^2/\partial x^2$ on the right-hand side of (32) for any finite t_0 , but the higher-order spatial derivative terms cannot be removed by taking the limit $\lambda \rightarrow \infty$ in such a way that the telegrapher's equation remains.

3. Velocity jump processes

The prototypical organisms whose motion can be described as a velocity jump process are the flagellated bacteria, the best studied of which is *E. coli*. To search for food or escape an unfavorable environment, *E. coli* alternates two basic behavioral modes, a more or less linear motion called a run, and a highly erratic motion called tumbling, the purpose of which is to reorient the cell (cf. Fig. 2). Run times are typically much longer than the time spent tumbling, and when bacteria move in a favorable direction (i.e. either in the direction of foodstuffs

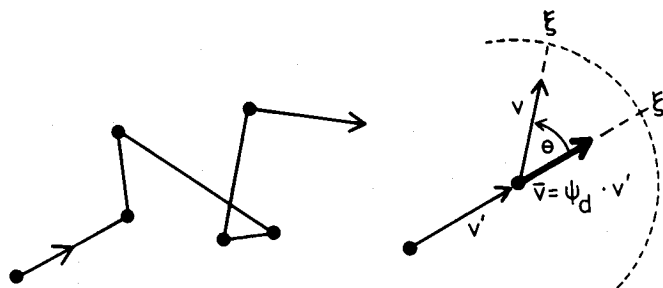


Fig. 2. Schematic drawing of a velocity jump process, during which a new moving direction $= v/\|v\|$ is chosen according to a turn angle distribution as in Fig. 4a for example. See text for details

or away from harmful substances) the run times are increased further. During a run the bacteria move at approximately constant speed in the most recently chosen direction. New directions are generated during tumbles, and when bacteria move in an unfavorable direction the run length decreases and the relative frequency of tumbling increases. The distribution of new directions is not uniform on the unit sphere, but has a bias in the direction of the preceding run. The effect of alternating these two modes of behavior, and in particular, of increasing the run length when moving in a favorable direction, is that a bacterium executes a three-dimensional random walk with drift in a favorable direction when observed on a sufficiently long time scale (Koshland (1980), Berg (1983)).

3.1. Derivation of the model

Our approach to velocity jump processes will be a direct generalization of the earlier derivation of the telegrapher's equation. Thus we shall work directly with the differential equation form of the conservation equation for a phase space density function that depends only on the position, velocity and time. The development is, except for some differences related to conserved quantities, the same as that which leads to the Boltzmann equation and its related moment equations in the kinetic theory of gases (cf. Resibois and DeLeener (1977)). In some circumstances it is desirable to incorporate internal variables in the distribution function in order to describe the effect of the internal state on parameters such as the run length. Such generalizations have been treated in Alt (1980).

Let $p(\mathbf{x}, \mathbf{v}, t)$ be the density function for individuals in a $2n$ -dimensional phase space with coordinates (\mathbf{x}, \mathbf{v}) , where $\mathbf{x} \in \mathbb{R}^n$ is the position of an individual, and $\mathbf{v} \in \mathbb{R}^n$ is its velocity. Then $p(\mathbf{x}, \mathbf{v}, t) d\mathbf{x} d\mathbf{v}$ is the number density of individuals with position between \mathbf{x} and $\mathbf{x} + d\mathbf{x}$ and velocity between \mathbf{v} and $\mathbf{v} + d\mathbf{v}$, and

$$n(\mathbf{x}, t) = \int p(\mathbf{x}, \mathbf{v}, t) d\mathbf{v}$$

is the number density of individuals at \mathbf{x} , whatever their velocity. The evolution of p is governed by the partial differential equation

$$\frac{\partial p}{\partial t} + \nabla_{\mathbf{x}} \cdot \mathbf{v} p + \nabla_{\mathbf{v}} \cdot \mathbf{F} p = \mathcal{R}, \quad (33)$$

where \mathbf{F} denotes the external force acting on the individuals and \mathcal{R} is the rate of change of p due to reaction, random choice of velocity, etc. For the present we assume that $\mathbf{F} \equiv 0$ and that only two processes contribute to the changes on the right-hand side of (33), namely, a birth/death process and a process that generates random velocity changes. We assume that the former is independent of the velocity and that it can be written

$$\left(\frac{\partial p}{\partial t} \right)_{\text{bd}} = kr(n)p \quad (34)$$

where k is a constant. We suppose that the random velocity changes are the result of a Poisson process of intensity λ , where λ may depend upon other variables. Thus λ^{-1} is a mean run length time between the random choices of

direction. The net rate at which individuals enter the phase-space volume at (\mathbf{x}, \mathbf{v}) is given by

$$\left(\frac{\partial p}{\partial t}\right)_{sp} = -\lambda p + \lambda \int T(\mathbf{v}, \mathbf{v}') p(\mathbf{x}, \mathbf{v}', t) d\mathbf{v}' \quad (35)$$

where “sp” denotes the change due to the stochastic process. Clearly this equation is the velocity-space analog of (25). The kernel $T(\mathbf{v}, \mathbf{v}')$ gives the probability of a change in velocity from \mathbf{v}' to \mathbf{v} , given that a reorientation occurs, and therefore $T(\mathbf{v}, \mathbf{v}')$ is non-negative and normalized so that

$$\int T(\mathbf{v}, \mathbf{v}') d\mathbf{v} = 1.$$

This normalization condition merely expresses the fact that no individuals are lost during the process of changing velocity. At present we assume that $T(\mathbf{v}, \mathbf{v}')$ is independent of the time between jumps.

In light of the foregoing assumptions, (33) becomes

$$\frac{\partial p}{\partial t} + \nabla_{\mathbf{x}} \cdot \mathbf{v} p = -\lambda p + \lambda \int T(\mathbf{v}, \mathbf{v}') p(\mathbf{x}, \mathbf{v}', t) d\mathbf{v}' + kr(n)p. \quad (36)$$

For most purposes one does not need the distribution p , but only its first few velocity moments. The first two are the number density $n(\mathbf{x}, t)$ introduced previously, and the average velocity $\mathbf{u}(\mathbf{x}, t)$, which is defined by

$$n(\mathbf{x}, t)\mathbf{u}(\mathbf{x}, t) \equiv \int p(\mathbf{x}, \mathbf{v}, t)\mathbf{v} d\mathbf{v}. \quad (37)$$

If we integrate (36) over \mathbf{v} we find that

$$\frac{\partial n}{\partial t} + \nabla_{\mathbf{x}} \cdot n\mathbf{u} = R(n) \quad (38)$$

where $R(n) \equiv knr(n)$. Similarly, multiplying by \mathbf{v} and integrating over \mathbf{v} gives

$$\frac{\partial(n\mathbf{u})}{\partial t} + \nabla \cdot \int p\mathbf{v}\mathbf{v} d\mathbf{v} = \lambda \int T(\mathbf{v}, \mathbf{v}')\mathbf{v} p(\mathbf{x}, \mathbf{v}', t) d\mathbf{v}' d\mathbf{v} - \lambda n\mathbf{u} + knr(n). \quad (39)$$

3.2. Analysis of some special cases

In one space dimension we define

$$T(\mathbf{v}, \mathbf{v}') = \delta(\mathbf{v} + \mathbf{v}')$$

and thus demand that individuals change direction each time a choice is made. This is consistent with the scheme that led to the telegrapher's equation in Sect. 1, but not for instance, with the random choice of direction made at each tumble in bacterial motion.

When the speed is constant $\mathbf{v} = \pm s$ and $n\mathbf{u} = s(p^+ - p^-)$, where $p^\pm \equiv p(\mathbf{x}, \pm s, t)$. Furthermore

$$\nabla \cdot \int p\mathbf{v}\mathbf{v} d\mathbf{v} = s^2 \frac{\partial n}{\partial x} = s^2 \frac{\partial}{\partial x} (p^+ + p^-).$$

For the foregoing choice of T the integral term in (39) reduces to $-\lambda s(p^+ - p^-)$, and thus in the absence of reaction (38) and (39) reduce to

$$\begin{aligned} \frac{\partial}{\partial t}(p^+ + p^-) + s \frac{\partial}{\partial x}(p^+ - p^-) &= 0 \\ s \frac{\partial}{\partial t}(p^+ - p^-) + s^2 \frac{\partial}{\partial x}(p^+ + p^-) &= -2\lambda s(p^+ - p^-). \end{aligned}$$

These are just the equations given at (6), written in a slightly different form.

In higher space dimensions Eqs. (38) and (39) do not specify n and \mathbf{u} as they stand, for they involve the second \mathbf{v} moment of p and the as yet unspecified kernel $T(\mathbf{v}, \mathbf{v}')$. Some further simplifying assumptions are necessary, and to describe some that are biologically meaningful we shall first introduce the notion of persistence.

Let $\mathbf{v} = s\xi$ where $s = \|\mathbf{v}\|$ is the speed (the Euclidean norm of \mathbf{v}) and $\xi = \mathbf{v}/\|\mathbf{v}\|$ is the direction of \mathbf{v} . For a fixed \mathbf{v}' , the average velocity $\bar{\mathbf{v}}$ after reorientation is defined by

$$\bar{\mathbf{v}} = \int T(\mathbf{v}, \mathbf{v}') \mathbf{v} \, d\mathbf{v} = \int T(\mathbf{v}, \mathbf{v}') \xi s^n \, ds \, d\omega_n$$

where $d\omega_n$ is the surface measure on the unit sphere S_0^{n-1} centered at the origin in R^n . While the average speed

$$\bar{s} = \int T(\mathbf{v}, \mathbf{v}') \|\mathbf{v}\| \, d\mathbf{v} = \int T(\mathbf{v}, \mathbf{v}') s^n \, ds \, d\omega_n$$

is always positive (since $T \geq 0$ and T is not concentrated at $\mathbf{v} = \mathbf{0}$), the average velocity vector may vanish, and $\|\bar{\mathbf{v}}\| \leq \bar{s}$, see Fig. 2. The angle between $\bar{\mathbf{v}}/\bar{s}$ and $\xi' = \mathbf{v}'/s'$ provides a measure of the tendency of the motion to persist in any given direction ξ' . Therefore we define the *index of directional persistence* as

$$\psi_d \equiv \frac{\bar{\mathbf{v}} \cdot \mathbf{v}'}{\bar{s}s'} \quad (40)$$

where $\psi_d \in [-1, +1]$. Of particular interest is the case in which the speed does not change with reorientation and the turning probability depends only on the cone angle θ between \mathbf{v}' and \mathbf{v} , which is given by

$$\theta(\mathbf{v}, \mathbf{v}') \equiv \arccos \frac{\mathbf{v} \cdot \mathbf{v}'}{ss'},$$

where $\theta \in [0, \pi]$. Then $T(\mathbf{v}, \mathbf{v}')$ has the form

$$T(\mathbf{v}, \mathbf{v}') = \frac{\delta(s-s')}{s^{n-1}} h(\theta(\mathbf{v}, \mathbf{v}')) \quad (41)$$

for any $n \geq 2$. The distribution h is normalized so that

$$2 \int_0^\pi h(\theta) \, d\theta = 1$$

for $n = 2$ and

$$2\pi \int_0^\pi h(\theta) \sin \theta d\theta = 1$$

for $n = 3$.

Given a velocity \mathbf{v}' , the average velocity after reorientation can be resolved into a component along \mathbf{v}' and a component \mathbf{v}'_\perp orthogonal to \mathbf{v}' . Since the probability of choosing a given direction depends only on θ for the foregoing T , it follows that $\mathbf{v}'_\perp = 0$. Furthermore, in this case ψ_d in (40) is independent of \mathbf{v}' and

$$\bar{\mathbf{v}} = \psi_d \mathbf{v}', \tag{42}$$

where the *persistence index* or *mean cosine* is given by

$$\psi_d = \begin{cases} 2 \int_0^\pi h(\theta) \cos \theta d\theta & \text{for } n = 2 \\ 2\pi \int_0^\pi h(\theta) \cos \theta \sin \theta d\theta & \text{for } n = 3 \end{cases} \tag{43}$$

(cf. Patlak (1953)). Some specific examples of interest in Sect. 5 will help to illustrate this. For the simple case of uniform random selection of direction on the unit circle, $h(\theta) = 1/(2\pi)$ and $\psi_d = 0$. For the circular normal distribution (Johnson and Kotz (1970)) with pole $\theta_0 = 0$, we have $h(\theta) = [2\pi I_0(k)]^{-1} \exp(k \cos \theta)$, where I_0 is the Bessel function of order zero of imaginary argument. For this distribution one finds that $\psi_d = I_1(k)/I_0(k)$ (Abramowitz and Stegun (1965), Eq. 9.6.19). For $k = 0$ we have uniform random selection of direction, while as $k \rightarrow \infty$ the new direction of motion tends to be the same as the previous direction, and $\psi_d \rightarrow 1$. From observations of the two-dimensional locomotion of *Dictyostelium* amoeba, the data from Hall (1977) yield $\psi_d \approx 0.7$ whereas the three-dimensional bacterial random walk data in Berg and Brown (1972) show $\psi_d \approx 0.33$ (cf. Berg (1983)).

It is also possible to derive simple equations for the *mean squared displacement* of individuals which begin at the origin at $t = 0$. Let

$$\mathcal{D}^2(t) \equiv \langle \|\mathbf{x}(t)\|^2 \rangle \equiv \int \|\mathbf{x}\|^2 p(\mathbf{x}, \mathbf{v}, t) d\mathbf{x} d\mathbf{v} / \int p(\mathbf{x}, \mathbf{v}, t) d\mathbf{x} d\mathbf{v} \tag{44}$$

be the mean squared displacement, and let

$$\mathcal{S}^m(t) \equiv \langle s^m \rangle \equiv \int s^m p(\mathbf{x}, \mathbf{v}, t) d\mathbf{x} d\mathbf{v} / \int p(\mathbf{x}, \mathbf{v}, t) d\mathbf{x} d\mathbf{v}$$

be the m th moment of the speed distribution. If N_0 individuals are released at $\mathbf{x} = 0$ at $t = 0$ then $n(\mathbf{x}, 0) = N_0 \delta(\mathbf{x})$ and $(n\mathbf{u})(\mathbf{x}, 0) = 0$. We shall assume that there is no birth/death term in (36), (38) and (39) until stated otherwise, and as a result

$$\int p(\mathbf{x}, \mathbf{v}, t) d\mathbf{x} d\mathbf{v} \equiv N_0.$$

To obtain a differential equation for $\mathcal{D}^2(t)$, multiply (36) by $\|\mathbf{x}\|^2$ and integrate over \mathbf{x} and \mathbf{v} . Under the assumption that terms of the form $\iint \mathbf{x}_i^2 v_j p \, d\mathbf{x} \, d\mathbf{v}$ vanish at infinity we obtain the equation

$$\frac{d}{dt} \mathcal{D}^2(t) = \frac{2}{N_0} \int (\mathbf{x} \cdot \mathbf{v}) p(\mathbf{x}, \mathbf{v}, t) \, d\mathbf{x} \, d\mathbf{v} \equiv 2\mathcal{B}(t). \quad (45)$$

By multiplying (36) by $\mathbf{x} \cdot \mathbf{v}$ and integrating we obtain the following equation for $\mathcal{B}(t)$:

$$\frac{d}{dt} \mathcal{B}(t) = \frac{-1}{N_0} \int (\mathbf{x} \cdot \mathbf{v}) \nabla_{\mathbf{x}} \cdot (\mathbf{v} p) \, d\mathbf{x} \, d\mathbf{v} - \lambda \mathcal{B}(t) + \frac{\lambda}{N_0} \int (\mathbf{x} \cdot \bar{\mathbf{v}}) p(\mathbf{x}, \mathbf{v}', t) \, d\mathbf{v}' \, d\mathbf{x}. \quad (46)$$

In cases where the relation (42) holds, the last term is simply $\lambda \psi_d \mathcal{B}(t)$.

Suppose that this is the case, and that terms of the form

$$\iint (x_i v_j v_k) p(\mathbf{x}, \mathbf{v}, t) \, d\mathbf{x} \, d\mathbf{v}$$

vanish at infinity; then (46) reduces to

$$\frac{d\mathcal{B}}{dt} + \lambda(1 - \psi_d) \mathcal{B} = \mathcal{S}^2 \quad (47)$$

where \mathcal{S}^2 , the second moment of the speed distribution, is a constant. Therefore integration of (47), subject to $\mathcal{B}(0) = 0$, and of (45) subject to $\mathcal{D}^2(0) = 0$, yields

$$\mathcal{B}(t) = \begin{cases} \frac{\mathcal{S}^2}{\lambda(1 - \psi_d)} [1 - e^{-\lambda(1 - \psi_d)t}] & \text{for } \psi_d \neq 1 \\ \mathcal{S}^2 t & \text{for } \psi_d = 1 \end{cases} \quad (48)$$

and

$$\mathcal{D}^2(t) = \begin{cases} \frac{2\mathcal{S}^2}{\lambda(1 - \psi_d)} \left[t - \frac{1}{\lambda(1 - \psi_d)} (1 - e^{-\lambda(1 - \psi_d)t}) \right] & \text{for } \psi_d \neq 1 \\ \mathcal{S}^2 t^2 & \text{for } \psi_d = 1. \end{cases} \quad (49)$$

The quantity $\lambda_0 = \lambda(1 - \psi_d)$ is a modified turning frequency associated with the reorientation kernel $T(\mathbf{v}, \mathbf{v}')$, and the inverse

$$P = 1/\lambda_0$$

is a characteristic run time that incorporates the effect of persistence. This is called a ‘‘persistence time’’ by Dunn (1983). The ‘‘motility’’ or diffusion coefficient is defined as

$$D = \mathcal{S}^2 P/n$$

in a space of dimension n . In terms of D the first equation in (49) reads

$$\mathcal{D}^2(t) = 2nD \left[t - \frac{1}{\lambda_0} (1 - e^{-\lambda_0 t}) \right] \quad (50)$$

(cf. Fig. 3a). To reduce this to the result obtained in Sect. 1, note that when a individual reverses direction at every step $\psi_d = -1$, and therefore $\lambda_0 = 2\lambda$. Consequently (50) is equivalent to (8) in the one-dimensional case.

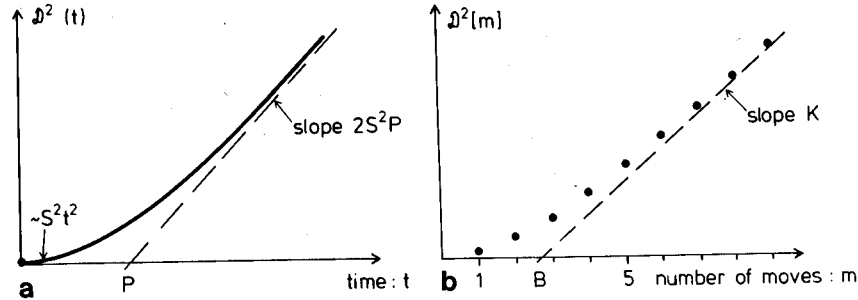


Fig. 3. A sketch of the theoretical values of the mean squared displacement **a** versus time t , according to Eq. (50) and **b** versus the number of consecutive moves m according to Eq. (51). See also Hall (1977), Fig. 7

However, while formula (50) measures the mean squared displacement $\mathcal{D}^2(t)$ for continuous times, most analyses are based on a discrete recording of the displacement data. The first and most frequently used approach consists in sampling the organism's location at equally spaced time instances, connecting these points by straight lines and computing from this "artificial random walk model" a discretized version of formula (50). This has been elaborated by Lovely and Dahlquist (1975), and has been applied in various experimental situations, e.g. to fibroblasts by Gail and Boone (1970), to crawling caterpillars by Kareiva and Shigesada (1983) (see Fig. 3 in their paper), and to white blood cells by Gruler and Bültman (1984). However this approach does not rely on the microscopic structure of the actual random paths, but rather, it arbitrarily chooses fixed observation intervals, which then define an artificial, approximating path. Dunn (1983) defined certain derived parameters (the speed and the persistence time) as limits in which the observation time goes to zero, which makes them independent of the choice of the interval length (see also Lackie (1986, Sect. 7)). It is obvious that this method applies mainly to random walks with fluctuating path curvature (cf. Tranquillo and Lauffenburger (1987)).

In another approach an attempt is made to identify (almost) straight moves in the observed paths and to sample the organisms location only at the *turning times*. From the resulting run length and turn angle distribution Hall (1977) derived the discrete analog of (50). For $n=2$ and $|\psi_d| < 1$, the mean squared displacement after m consecutive moves is given by

$$\mathcal{D}^2[m] = K(m - B(1 - \psi_d^m)) \quad (51)$$

which is plotted in Fig. 3b. Here ψ_d is the directional persistence index as in (43), and the "persistence number" B as well as the asymptotic slope K can be given explicitly in terms of ψ_d and the ratio $\langle r \rangle^2 / \langle r^2 \rangle$, which is computed from the distribution of run lengths r .

The advantage of the discrete formula (51) is that it holds independently of the possible resting periods at the turning points (see Sect. 4) and also of the speed distribution. It has, for example, been used to model ovipositing (or nectar-feeding) butterflies by a correlated random walk (see Fig. 2 of Kareiva and Shigesada (1983)).

The apparent disadvantage in comparison to the continuous formula (50) is that evaluation of the experimental data for $\mathcal{D}^2[m]$ requires the experimenter to follow the individual tracks, whereas $\mathcal{D}^2(t)$ can be measured as the squared displacement of individuals at fixed time t , averaged over the population sample.

4. Generalizations of the simplest cases

The simplest position-jump processes are based on constant waiting time distributions for the jump process and spatially-homogeneous redistribution kernels. This suggests two immediate types of generalizations, one in which the waiting time distribution is time and/or density dependent, and the other in which the redistribution kernel depends on the local density, a local average of the density, or is non-homogeneous by virtue of its dependence on some specified, nonconstant field. Here we shall briefly discuss a special class of processes with nonconstant waiting time distributions.

Suppose that the waiting time distribution of a position jump process is exponential with an intensity λ that depends on n and t . In this case it is easy to see that

$$\Phi(n, t) \equiv \Pr[\mathcal{T} \leq t] = 1 - \exp\left(-\int_0^t \lambda(n(\mathbf{x}, s), s) ds\right),$$

and therefore

$$\phi(n, t) \equiv \frac{d}{dt} \Phi(n, t) = \lambda(n(\mathbf{x}, t), t) \exp\left(-\int_0^t \lambda(n(\mathbf{x}, s), s) ds\right).$$

Equation (16) now reads

$$\begin{aligned} n(\mathbf{x}, t) = & \exp\left(-\int_0^t \lambda(n(\mathbf{x}, s), s) ds\right) F(\mathbf{x}) \\ & + \int_0^t \int_R \lambda(n(\mathbf{x}, t-\tau), t-\tau) \\ & \times \exp\left(-\int_0^{t-\tau} \lambda(n(\mathbf{x}, s), s) ds\right) T(\mathbf{x}, \mathbf{y}) n(\mathbf{y}, \tau) dy d\tau. \end{aligned}$$

Such a formulation should be capable of describing a variety of density-dependent aggregation or dispersal phenomena. For the latter one would expect that $\lambda(n, \cdot)$ is an increasing function of n , so that the mean waiting time between jumps becomes a decreasing function of the density. Conversely, density-dependent aggregation could be modeled by making λ a decreasing function of n , in which case the waiting time between jumps increases with the density. In either case one expects that λ has the form

$$\lambda = \lambda_0 + \lambda_1(n, t)$$

where the residual intensity λ_0 is non-vanishing. Some one-dimensional examples of this type of generalization have been reviewed by Aronson (1985). Shigesada (1980) has derived an explicit formula for the mean squared displacement for a diffusion process with the density-dependent diffusion coefficient $D = \beta n(\mathbf{x}, t)$, but one cannot expect to obtain such explicit formulas in general.

4.1. *Random walks with a resting phase*

A number of generalizations of the simple velocity jump process are also possible. Firstly, as is suggested by the notation used in (35), there is no necessity that the random process generating the velocity changes be a Poisson process. Whatever the underlying process, one simply has to compute $(\partial p / \partial t)_{sp}$ for that process, but of course if it is not Markovian the right-hand side of (35) will involve an integral over time. Secondly, we can include a resting time in the reorientation or tumbling phase, in order to more accurately describe for example the motion of foraging birds (Smith (1974)) and of certain species of bacteria (see Greenberg and Canale-Parola (1977)). The following analysis of this phenomenon is set in the bacterial context, but the results are applicable in other systems as well.

When a resting phase is incorporated, the total population is divided into two subpopulations, one consisting of the moving bacteria and the other comprising the resting bacteria. As before, let $p = p(\mathbf{x}, \mathbf{v}, t)$ be the density of bacteria at (\mathbf{x}, \mathbf{v}) , and let $r = r(\mathbf{x}, \mathbf{v}, \tau, t)$ be the density of bacteria in the resting phase, defined so that $r = r(\mathbf{x}, \mathbf{v}, \tau, t) d\mathbf{x} d\mathbf{v} d\tau$ is the number of bacteria with position between \mathbf{x} and $\mathbf{x} + d\mathbf{x}$, whose most recent non-zero velocity lies between \mathbf{v} and $\mathbf{v} + d\mathbf{v}$, and whose rest time lies between τ and $\tau + d\tau$. We assume as before that there are no external forces on the bacteria, and that the loss of bacteria from a given (\mathbf{x}, \mathbf{v}) point in position-velocity space is governed by a Poisson process of intensity λ . Now however the change is not to a non-zero velocity, but rather into the resting phase. Bacteria leave the resting phase at random times and choose a new velocity. The random exits from the resting phase are supposed to be governed by a Poisson process of intensity μ , and the new choice of velocity depends on the time spent in the resting phase as follows:

$$\mathbf{T}(\mathbf{v}, \mathbf{v}', \tau) = e^{-\gamma\tau} \mathbf{T}(\mathbf{v}, \mathbf{v}') + (1 - e^{-\gamma\tau}) g(\|\mathbf{v}\|). \tag{52}$$

Here $\mathbf{T}(\mathbf{v}, \mathbf{v}')$ is a velocity kernel of the type given at (41), and the speed distribution $g(s)$ is such that $g(0) = 0$ and

$$\omega_n \int_0^\infty g(s) s^{n-1} ds = 1. \tag{53}$$

The factor $\omega_n = 2\pi^{n/2} / \Gamma(n/2)$ is the surface area of the unit sphere in R^n . Thus the probability of choosing a random direction with speed $g(s)$ increases with the resting time, and any directional persistence embodied in the kernel $\mathbf{T}(\mathbf{v}, \mathbf{v}')$ is exponentially fading in the resting time.

In the absence of birth/death terms, the governing equations for p and r are

$$\frac{\partial p}{\partial t} + \mathbf{v} \cdot \nabla_{\mathbf{x}} p = -\lambda p + \mu \int_{R^n} \int_0^\infty \mathbf{T}(\mathbf{v}, \mathbf{v}', \tau) r(\mathbf{x}, \mathbf{v}', \tau, t) d\tau d\mathbf{v}' \tag{54}$$

and

$$\frac{\partial r}{\partial t} + \frac{\partial r}{\partial \tau} = -\mu r \tag{55}$$

with the initial condition on r having the renewal form

$$r(\mathbf{x}, \mathbf{v}, 0, t) = \lambda p(\mathbf{x}, \mathbf{v}, t). \tag{56}$$

If we define

$$N_p(t) \equiv \int_{R^n} \int_{R^n} p(\mathbf{x}, \mathbf{v}, t) d\mathbf{v} d\mathbf{x}$$

and

$$N_r(t) \equiv \int_0^\infty \int_{R^n} \int_{R^n} r(\mathbf{x}, \mathbf{v}, \tau, t) d\mathbf{v} d\mathbf{x} d\tau,$$

then, since the total number of particles are conserved in the absence of a birth/death process, $N_p(t)$ and $N_r(t)$ must satisfy

$$N_p(t) + N_r(t) = N_0.$$

It is easy to see that the solution of (55) and (56) is given by $r(\mathbf{x}, \mathbf{v}, \tau, t) = \lambda e^{-\mu\tau} p(\mathbf{x}, \mathbf{v}, t - \tau)$, and it is convenient to introduce the following notation for the two moments

$$r_0(\mathbf{x}, \mathbf{v}, t) \equiv \int_0^\infty r(\mathbf{x}, \mathbf{v}, \tau, t) d\tau$$

and

$$r_1(\mathbf{x}, \mathbf{v}, t) \equiv \int_0^\infty e^{-\gamma\tau} r(\mathbf{x}, \mathbf{v}, \tau, t) d\tau.$$

The governing equation for p can now be written

$$\begin{aligned} \frac{\partial p}{\partial t} + \mathbf{v} \cdot \nabla_{\mathbf{x}} p = & -\lambda p + \mu \int_{R^n} T(\mathbf{v}, \mathbf{v}') r_1(\mathbf{x}, \mathbf{v}', t) d\mathbf{v}' \\ & + \mu g(\|\mathbf{v}\|) \int_{R^n} (r_0(\mathbf{x}, \mathbf{v}', t) - r_1(\mathbf{x}, \mathbf{v}', t)) d\mathbf{v}'. \end{aligned} \quad (57)$$

As before, we define the mean squared displacement in \mathbf{x} of moving bacteria as

$$\mathcal{D}_p^2 = \int_{R^n} \int_{R^n} \|\mathbf{x}\|^2 p(\mathbf{x}, \mathbf{v}, t) d\mathbf{v} d\mathbf{x} / N_p(t),$$

and of resting bacteria as

$$\mathcal{D}_r^2 = \int_{R^n} \int_{R^n} \|\mathbf{x}\|^2 r_0(\mathbf{x}, \mathbf{v}, t) d\mathbf{v} d\mathbf{x} / N_r(t).$$

Furthermore, we define the corresponding second-order moments

$$\mathcal{B}_p = \int_{R^n} \int_{R^n} (\mathbf{x} \cdot \mathbf{v}) p(\mathbf{x}, \mathbf{v}, t) d\mathbf{v} d\mathbf{x} / N_p(t)$$

and

$$\mathcal{B}_r = \int_{R^n} \int_{R^n} (\mathbf{x} \cdot \mathbf{v}) r_1(\mathbf{x}, \mathbf{v}, t) d\mathbf{v} d\mathbf{x} / N_r(t).$$

These satisfy the following system of ordinary differential equations

$$\frac{d\mathcal{D}_p^2 N_p}{dt} = 2\mathcal{B}_p N_p - \lambda \mathcal{D}_p^2 N_p + \mu \mathcal{D}_r^2 N_r \tag{58}$$

$$\frac{d\mathcal{D}_r^2 N_r}{dt} = \lambda \mathcal{D}_p^2 N_p - \mu \mathcal{D}_r^2 N_r \tag{59}$$

$$\frac{d\mathcal{B}_p N_p}{dt} = \mathcal{S}_p^2 N_p - \lambda \mathcal{B}_p N_p + \mu \psi_d \mathcal{B}_r N_r \tag{60}$$

$$\frac{d\mathcal{B}_r N_r}{dt} = \lambda \mathcal{B}_p N_p - (\mu + \gamma) \mathcal{B}_r N_r \tag{61}$$

This system is not closed, for the second moments \mathcal{S}_p^2 and \mathcal{S}_r^2 of the speed distribution, which are defined as

$$\mathcal{S}_p^2 = \int_{R^n} \int_{R^n} s^2 p(\mathbf{x}, \mathbf{v}, t) d\mathbf{v} d\mathbf{x} / N_p(t)$$

and

$$\mathcal{S}_r^2 = \int_{R^n} \int_{R^n} s^2 r_1(\mathbf{x}, \mathbf{v}, t) d\mathbf{v} d\mathbf{x} / N_r(t),$$

are time-dependent, in contrast to the case analyzed in Sect. 3. One finds that

$$\begin{aligned} \frac{d\mathcal{S}_p^2 N_p}{dt} &= -\lambda \mathcal{S}_p^2 N_p + \mu S_r^2 N_r + \mu s_0^2 (N_r - R_1) \\ \frac{d\mathcal{S}_r^2 N_r}{dt} &= \lambda \mathcal{S}_p^2 N_p - (\mu + \gamma) \mathcal{S}_r^2 N_r \\ \frac{dN_r}{dt} &= \lambda N_p - \mu N_r \\ \frac{dR_1}{dt} &= \lambda N_p - (\mu + \gamma) R_1 \end{aligned} \tag{62}$$

where

$$s_0^2 \equiv \omega_n \int_0^\infty g(s) s^{n+1} ds$$

and

$$R_1 \equiv \int_{R^n} \int_{R^n} r_1(\mathbf{x}, \mathbf{v}, t) d\mathbf{v} d\mathbf{x}.$$

Since these equations are linear in $\mathcal{S}_p^2 N_p$, etc., they can be solved explicitly and the results can be used in (58)-(61). However, if λ and μ are large the solution

quickly relaxes to the steady-state solution, which is given by

$$\begin{aligned} N_r &= \frac{\lambda N_0}{\lambda + \mu} \\ N_p &= \frac{\mu N_0}{\lambda + \mu} \\ R_1 &= \frac{\lambda \mu N_0}{(\mu + \lambda)(\mu + \gamma)} \\ \mathcal{S}_p^2 &= s_0^2 \\ \mathcal{S}_r^2 &= \frac{\mu}{\mu + \gamma} s_0^2. \end{aligned} \quad (63)$$

Moreover, if we assume that initially the cells are released at the origin $\mathbf{x} = 0$, then $\mathcal{D}_p^2(0) = \mathcal{D}_r^2(0) = 0$, and if they have no preferential direction of motion then $\mathcal{B}_p(0) = \mathcal{B}_r(0) = 0$. If in addition the initial distribution between moving and nonmoving cells is the steady-state distribution given by (63), then (63) holds for all time and the mean squared speed

$$\mathcal{S}_p^2 = s_0^2 \quad (64)$$

is a constant. With these assumptions we obtain from (58) and (59) the usual formula

$$\frac{d\mathcal{D}^2}{dt} = 2\mathcal{B}N_p/N_0 \quad (65)$$

for the weighted mean squared displacement

$$\mathcal{D}^2(t) = \frac{\mathcal{D}_p^2(t)N_p + \mathcal{D}_r^2(t)N_r}{N_0}.$$

The quantity $\mathcal{B} \equiv \mathcal{B}_p$ satisfies the following second order equation, which is derived from (60), (61)

$$\frac{d^2\mathcal{B}}{dt^2} + (\lambda + \mu + \gamma) \frac{d\mathcal{B}}{dt} + \lambda(\mu(1 - \psi_d) + \gamma)\mathcal{B} = (\mu + \gamma)s_0^2. \quad (66)$$

It should be noted that in the limit $\mu \rightarrow \infty$, in which case the mean resting time $1/\mu$ tends to zero, Eq. (66) formally reduces to Eq. (47) with $\mathcal{S}^2 = s_0^2$. The solution of (66) and the solution of the reduced equation agree to within terms of $O(1/\mu)$, except in a neighborhood of $t = 0$.

This suggests the following definition of a modified turning frequency

$$\lambda_0 = \lambda \frac{\mu(1 - \psi_d) + \gamma}{\mu + \gamma}, \quad (67)$$

and if we solve (66) subject to $\mathcal{B}_r(0) = \mathcal{B}_p(0) = 0$ we obtain

$$\mathcal{B}(t) = \frac{s_0^2}{\lambda_0} \left\{ 1 - \frac{\lambda_+ - \lambda_0}{\lambda_+ - \lambda_-} e^{-\lambda_- t} + \frac{\lambda_- - \lambda_0}{\lambda_+ - \lambda_-} e^{-\lambda_+ t} \right\}, \quad (68)$$

where λ_{\pm} are given by

$$\lambda_{\pm} = \frac{\lambda + \mu + \gamma}{2} \left[1 \pm \sqrt{1 - 4\lambda \frac{(1 - \psi_d)\mu + \gamma}{(\lambda + \mu + \gamma)^2}} \right]. \quad (69)$$

Note that $\lambda_+ \sim \mu$ and $\lambda_- \rightarrow \lambda_0$ in the limit $\mu \rightarrow \infty$. The solution of (65) subject to the initial condition $\mathcal{D}^2(0) = 0$ gives a relation for the mean squared displacement, namely

$$\mathcal{D}^2(t) = \frac{2s_0^2}{\lambda_0} \frac{\mu}{\lambda + \mu} \left\{ t + \frac{1}{\lambda_-} \frac{\lambda_+ - \lambda_0}{\lambda_+ - \lambda_-} (e^{-\lambda_- t} - 1) - \frac{1}{\lambda_+} \frac{\lambda_- - \lambda_0}{\lambda_+ - \lambda_-} (e^{-\lambda_+ t} - 1) \right\}. \quad (70)$$

As we saw in Sect. 1, the first term in (70) arises in a diffusion process. It can be shown that λ_{\pm} are both real and therefore the foregoing generalization deviates from this by two exponentially decreasing terms with the relaxation times

$$P_{\pm} = \frac{1}{\lambda_{\pm}}.$$

A plot of the relation in (70) similar to Fig. 3a has an asymptote whose intercept with the t -axis is the persistence time

$$P = \frac{\lambda_+ + \lambda_- - \lambda_0}{\lambda_+ \lambda_-}.$$

4.2. Random walks in external fields

A third generalization of the simplest velocity jump process arises when λ and/or $T(\mathbf{v}, \mathbf{v}')$ in (35) are allowed to depend on the mean density or other specified fields. An example of such a field is given by the gradient of a chemotactic substance, and this problem has been studied by Alt (1980). The case in which the turning frequency λ depends on the direction of motion was analyzed by Nossal and Weiss (1974), who derived asymptotic expressions for the mean location and the variance. This was generalized to include a bias of T by Nossal (1976). In the remainder of this section we shall analyze a model for the two-dimensional motion of slime mold cells or leukocytes in a constant chemotactic gradient directed along the positive x_1 axis of the plane, under the assumption that the gradient only influences the turn angle distribution T . Our objective is to derive expressions for the mean location and related quantities that are valid for all time.

We begin with the velocity jump process studied in Sect. 3, and suppose that both the speed s and the turning frequency λ are constant. The appropriate density function is now $p(\mathbf{x}, \phi, t)$, where ϕ is the angle between the direction of motion and the positive x_1 axis. The direction of travel is $\xi = (\cos \phi, \sin \phi)$. We further suppose that there is no birth or death of cells, and that the gradient of the chemotactic substance affects the probability of turning but does not give rise to any persistent bias to the motion by polarization of the motile machinery. Under these assumptions the evolution equation (36) for p reduces to

$$\frac{\partial p}{\partial t} + s\xi \cdot \nabla_{\mathbf{x}} p = -\lambda p + \lambda \int T(\phi, \phi') p(\mathbf{x}, \phi', t) d\phi'. \quad (71)$$

We assume that the turn angle distribution T is the sum of a symmetric probability distribution h as in Sect. 3 and a bias term $k(\phi)$ that results from the gradient of the chemotactic substance. Since the gradient is directed along the x_1 axis, we assume that the bias term takes its maximum at $\phi = 0$, and that it is symmetric about $\phi = 0$. Thus we have

$$T(\phi, \phi') = h(\phi - \phi') + k(\phi)$$

where $T \geq 0$ for all (ϕ, ϕ') and h and k are normalized as follows

$$\begin{aligned} \int_0^{2\pi} h(\theta) d\theta &= 1 \\ \int_0^{2\pi} k(\phi) d\phi &= 0. \end{aligned} \quad (72)$$

Typical examples of h and k are shown in Fig. 4.

The statistics of interest are the mean location of cells $\mathcal{X}(t)$, their mean squared displacement $\mathcal{D}^2(t)$, and their mean velocity $\mathcal{V}(t)$, which are defined as follows

$$\begin{aligned} \mathcal{X}(t) &= \int_{R^2} \int_0^{2\pi} \mathbf{x} p(\mathbf{x}, \phi, t) d\phi d\mathbf{x} / N_0, \\ \mathcal{D}^2(t) &= \int_{R^2} \int_0^{2\pi} \|\mathbf{x}\|^2 p(\mathbf{x}, \phi, t) d\phi d\mathbf{x} / N_0 \\ \mathcal{V}(t) &= s \int_{R^2} \int_0^{2\pi} \boldsymbol{\xi} p(\mathbf{x}, \phi, t) d\phi d\mathbf{x} / N_0. \end{aligned} \quad (73)$$

In addition, we introduce the auxiliary function

$$\mathcal{B}(t) = \int_{R^2} \int_0^{2\pi} (\mathbf{x} \cdot \boldsymbol{\xi}) p(\mathbf{x}, \phi, t) d\phi d\mathbf{x} / N_0$$

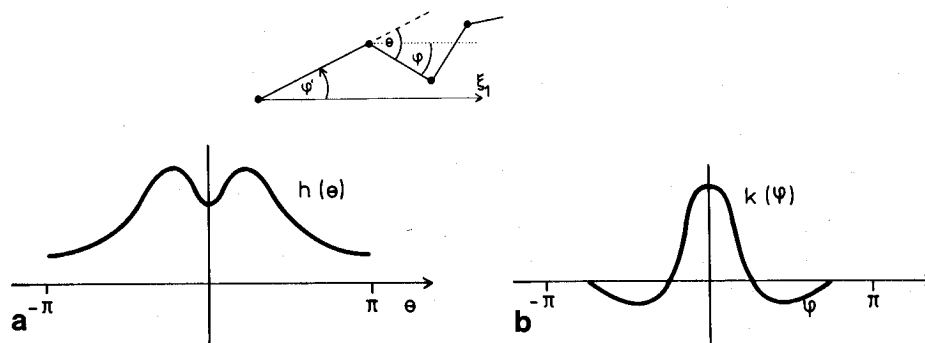


Fig. 4. Typical graphs **a** of a symmetric turn angle distribution $h(\theta)$ for $\theta = \phi - \phi'$, see inset and **b** of a symmetric bias distribution $k(\phi)$ in the gradient direction ξ . Experimental data like those for moving leukocytes given in Nossal (1983), Fig. 2 could be represented by superpositions $h(\theta) + k(\phi' + \theta)$ for a certain range of ϕ'

and define the *taxis coefficient*

$$\chi \equiv \int_0^{2\pi} k(\phi) \cos \phi \, d\phi.$$

We assume that $\chi < 1 - \psi_d$, where ψ_d is the persistence index defined in Eq. (43).

As before, we can derive differential equations for the evolution of the various statistics. An easy calculation shows that

$$\frac{d\mathcal{X}}{dt} = \mathcal{V} \tag{74}$$

$$\frac{d\mathcal{V}}{dt} = -\lambda_0 \mathcal{V} + \lambda \chi s \xi_1 \tag{75}$$

$$\frac{d\mathcal{D}^2}{dt} = 2s\mathcal{B} \tag{76}$$

$$\frac{d\mathcal{B}}{dt} = s - \lambda_0 \mathcal{B} + \lambda \chi x_1 \tag{77}$$

where $\xi_1 \equiv (1, 0)$. The solution of (74) and (75) subject to zero initial data is

$$\mathcal{X}(t) = s \frac{\chi}{1 - \psi_d} \left(t - \frac{1}{\lambda_0} (1 - e^{-\lambda_0 t}) \right) \xi_1$$

$$\mathcal{V}(t) = s \frac{\chi}{1 - \psi_d} (1 - e^{-\lambda_0 t}) \xi_1$$

where $\lambda_0 = \lambda(1 - \psi_d)$ as before (cf. Fig. 5a). Thus the mean velocity of cell movement is parallel to the direction of the chemotactic gradient and approaches the value

$$\mathcal{V}_\infty = s \frac{\chi}{1 - \psi_d} \xi_1$$

as t tends to infinity. The quantity

$$CI \equiv \frac{\chi}{1 - \psi_d}, \tag{78}$$

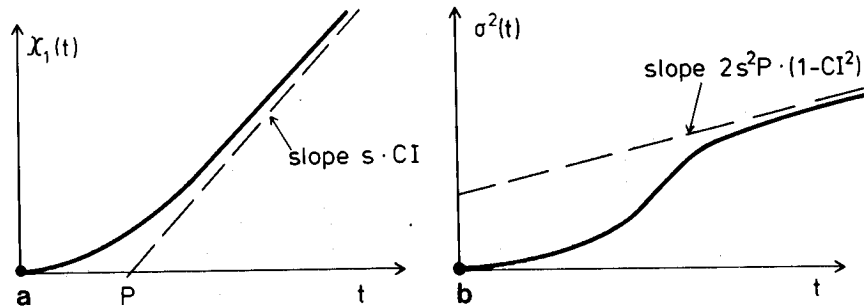


Fig. 5. Typical plots **a** of the mean displacement \mathcal{X}_1 in the gradient direction ξ_1 , and **b** of the mean squared deviation $\sigma^2(t)$. Notice that in **b** the intercept $M = 2s^2P(\frac{5}{2}CI^2 - 1)$ is positive provided the chemotaxis index CI is near 1. The asymptotic slope is decreased by the factor $(1 - CI^2)$ when compared to the unbiased random walk in Fig. 3a

which is called the *chemotactic index*, measures the net effect of the bias due to the chemotactic gradient on the motion in the direction ξ_1 . More precisely, the quotient of the expected displacement \mathcal{X}_1 in the direction ξ_1 and the total length $s \cdot t$ of the path is given by

$$\frac{\mathcal{X}_1}{s \cdot t} = CI \left(1 - \frac{1}{\lambda_0 t} (1 - e^{-\lambda_0 t}) \right),$$

which is sometimes called the “chemotropism index”.

A measure of the fluctuations of the cell path around the expected value is provided by the *mean squared deviation*, which is defined as follows

$$\begin{aligned} \sigma^2(t) &= \int_{\mathbb{R}^2} \int_0^{2\pi} \|\mathbf{x} - \mathcal{X}(t)\|^2 p(\mathbf{x}, \phi, t) d\phi d\mathbf{x} / N_0 \\ &= \mathcal{D}^2(t) - \|\mathcal{X}(t)\|^2. \end{aligned} \quad (79)$$

One finds that σ^2 satisfies the differential equation

$$\frac{d\sigma^2}{dt} = 2(s\mathcal{B} - \mathcal{X} \cdot \mathcal{V}). \quad (80)$$

Let $2b$ denote the right-hand side of (80); then b is the solution of

$$\frac{db}{dt} + \lambda_0 b = s^2(1 - CI^2(1 - e^{-\lambda_0 t})^2).$$

These lead to the following representation for the mean squared deviation:

$$\begin{aligned} \sigma^2 &= \frac{2s^2}{\lambda_0} \left((1 - CI^2)t - 2CI^2 t e^{-\lambda_0 t} + \frac{(2CI^2 - 1)}{\lambda_0} (1 - e^{-\lambda_0 t}) \right. \\ &\quad \left. + \frac{CI^2}{2\lambda_0} (1 - e^{-\lambda_0 t})^2 \right). \end{aligned} \quad (81)$$

As t tends to infinity this tends to

$$\sigma^2 \sim \frac{2s^2}{\lambda_0} \left((1 - CI^2)t + \frac{1}{\lambda_0} (\frac{1}{2}CI^2 - 1) \right).$$

The dependence of $\sigma^2(t)$ on t is shown in Fig. 5b.

From experimental recordings of the position of cells released at the origin at $t=0$ one can easily obtain values of $\mathcal{X}_1(t)$ and $\sigma^2(t)$ at a sequence of times (cf. Gruler and Bültman (1984)). Comparison with the theoretical functions that are graphed in Fig. 5 would enable one to determine the speed s , the persistence time P , and the chemotactic index CI . On the other hand, evaluation of the piecewise linear random paths of cells gives distributions for the speed, the run length and the turn angles, from which the mean speed s , the mean run length L and values of ψ_d and χ can be estimated (Keller and Zimmerman (1985)). The validity of the proposed model could then be tested by checking the identities

$$\frac{L}{s} = \frac{1}{\lambda} = (1 - \psi_d)P$$

and

$$\chi = (1 - \psi_d)CI.$$

5. Applications of the models to biological dispersal

In this section we consider examples of dispersal of cells, insects and mammals. These laboratory and field examples on a variety of biological scales provide both qualitative and quantitative support for the models of dispersal in the previous sections. In addition, the theoretical results from the models aid interpretation of the data from those examples.

We briefly describe each experimental or field study, and discuss why simple models of dispersal are inappropriate. Then we describe how to model the situation with the equations presented in this paper. In order to apply the models to systems that have been studied experimentally, one must estimate the redistribution functions and parameters in the models from the experimental data. We are not able to check all of the relevant formulas for the model of each particular dispersal example. This is often because the necessary data has not been collected. Nevertheless, we hope that the models together with the examples will suggest new experimental and data gathering approaches. Furthermore, a careful discussion of the modeling approaches can rule out wrong models and misleading interpretations.

5.1. Examples of cell dispersal

Using the same model as Hall (1977) for slime mold amoebae, Hall and Peterson (1979) studied the motion of leukocytes (human granulocytes) in a homogeneous medium. Hall and Peterson (1979) have shown that the movements of human granulocytes on a two dimensional medium can be characterized as a persistent or correlated random walk. Considering their moving paths on a glass surface as piecewise straight lines (deviations of half a cell diameter are allowed) they measured the step length and turn angle distributions (Figs. 2, 3 in their paper) from which they determined a persistence index as defined in (43) of

$$\psi_d \approx 0.3. \quad (82)$$

However, the time distributions for displacement are not available for their analysis.

Gruler and Bültman (1984) present plots of the mean squared displacement of leukocytes versus time (Fig. 6) and also a plot of the degree of orientation of paths (Fig. 7). They try to fit the latter data by an exponential function

$$P_1(t) \approx e^{-t/\tau_M}, \quad \text{with } \tau_M = 74 \text{ sec.} \quad (83)$$

In the terminology of Sect. 3, the mean orientation of a cell at time t compared to its initial moving direction becomes (after normalization to the positive x -axis)

$$P_1(t) = \iint \cos \xi p(x, v, t) dv dx \quad (84)$$

with

$$P_1(0) = 1. \quad (85)$$

Since $P_1(t)$ satisfies the differential equation

$$\frac{dP_1(t)}{dt} + \lambda(1 - \psi_d)P_1 = 0, \quad (86)$$

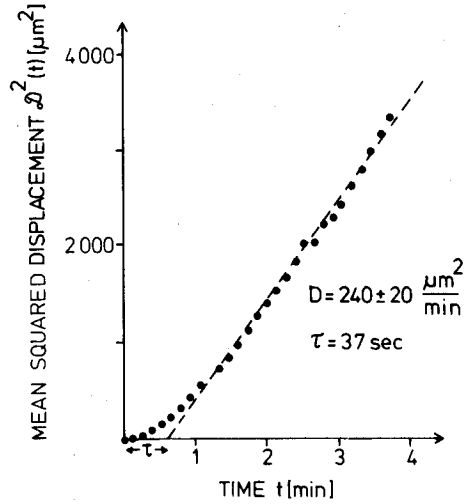


Fig. 6. Experimental values of the mean squared displacement of leukocytes as obtained by Gruler and Bültman (1984), Fig. 5

which is analogous to (47), we obtain from (85) and (86) the theoretical expression

$$P_1(t) = e^{-\lambda_0 t}$$

wherein $\lambda_0 = \lambda(1 - \psi_d)$. Comparison with (83) shows that the persistence time

$$P = \lambda_0^{-1} \approx \tau_M = 1.23 \text{ min}$$

is indeed the characteristic time to maintain an initial directionality. Using (82), we can estimate the turning frequency

$$\lambda = \frac{\lambda_0}{1 - \psi_d} \approx \frac{1}{0.7 \cdot 1.23} \text{ min}^{-1} = \frac{1}{0.86} \text{ min}^{-1},$$

which gives a mean run time of $\lambda^{-1} \approx 52 \text{ sec}$. This is consistent with representative paths as shown, for example, in Fig. 7a.

According to our theoretical formula (50), the mean squared displacement is given by

$$\mathcal{D}^2(t) = 4D[t - P(1 - e^{-t/P})] \tag{87}$$

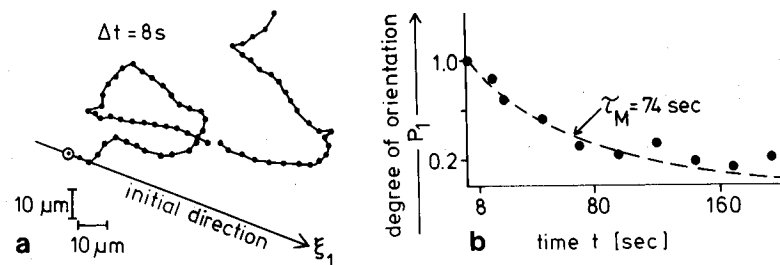


Fig. 7. Experiments showing persistence of direction in the random migration of leukocytes, from Gruler and Bültman (1984): a path of one cell with initial moving direction ξ_1 , cf. Fig. 7 in their paper. b Averaged values of the cosine deviation $P_1(t)$ versus time t for various cells and various starting points in their paths, cf. Fig. 8 there

with persistence time P and diffusion constant $D = \mathcal{S}^2 P/2$. Taking the experimental values for the mean squared displacement in Fig. 6 and assuming the above persistence time of $P \approx 1.23$ min, we estimate from the resulting asymptotic slope a value of $D \approx 350 \mu\text{m}^2/\text{min}$ in contrast to their value of $D \approx 240$. From this we obtain a mean squared speed of about

$$\mathcal{S}^2 = 2D/P \approx 560 (\mu\text{m}/\text{min})^2.$$

On the other hand, the asymptotic relation $\mathcal{D}^2(t) \approx \mathcal{S}^2 t^2$ for small t fits the experimental data using the value

$$\mathcal{S}^2 \approx 525 (\mu\text{m}/\text{min})^2.$$

The difference between these is well within the error in the data.

This brief analysis shows that the assumed random walk model for leukocyte movement is consistent with the data obtained thus far. More rigorous evaluation of displacement data and fitting to the whole theoretical curve (87) could further validate our modeling approach.

Noble and Levine (1986), and Boyarsky (1975), analyzed polymorphonuclear leukocytes moving in both the presence and absence of *E. coli*. They also analyzed lymphocyte movement in the presence of tumor cells. Their theoretical analysis was in terms of the stationary distribution of a discrete state space and continuous time Markov process. This is what we have called here a velocity jump process where the velocity redistribution function is discretized to a single speed and four turn angles representing the four movement states of the cells. Their analysis shows that the velocity redistribution kernel is nonuniform in the presence of taxis inducing agents such as *E. coli* or tumor cells.

Moreover they found that in the absence of taxis the leukocytes spend a considerable amount of time in a reorientation phase without visible translocation. Within the framework of Sect. 4.1, the Poisson intensities for the moving and resting phase can be estimated from their data by $\lambda \approx 0.5 \text{ min}^{-1}$ and $\mu \approx 0.2 \text{ min}^{-1}$. This means that the average time fraction spent by the cells on moving is $\mu/(\mu + \lambda) \approx 1/3$.

The turn angle distribution measured by Noble and Levine is nearly uniform, thus in our model equation (52) we should choose $\gamma = \infty$. Then, in this limit, Eqs. (67) and (69) yield $\lambda_0 = \lambda$ as well as $\lambda_- = \lambda$ and $\lambda_+ = \infty$. Finally from (70) we obtain the mean squared displacement

$$\mathcal{D}^2(t) = \frac{2S_0^2}{\lambda} \frac{\mu}{\mu + \lambda} \left(t - \frac{1}{\lambda} (1 - e^{-\lambda t}) \right)$$

which, compared to the standard expression (50) for nonresting random walks, is just reduced by the constant factor $\mu/(\mu + \lambda)$ measuring the proportion of moving time.

5.2. Examples of dispersal in some ecological systems

Kareiva (1983) made a survey of the data from mark and recapture field experiments on 12 species of herbivorous insects. In this study he estimates the diffusion coefficient from the data by using the equivalent of Eq. (4) from Sect. 1. Then, using the estimated value of D , he compared the observed distributions with the

bivariate normal distribution which is the solution of the two dimensional diffusion equation. The analogous one dimensional equation and its solution are discussed in the introduction as Eqs. (1) and (2). For 8 of the 12 species surveyed, he finds good agreement of the experimental data with the predicted values. From this he concludes that, at least in spatially homogeneous environments with uniform environmental conditions such as weather etc., the diffusion approximation is reasonable. The data from these studies may also be consistent with the space jump and velocity jump models of biological dispersal. This is because the space jump processes lead to the diffusion equation in certain limits, as was shown in Sect. 2.3. A space jump process with an exponential waiting time between jumps also leads to the expression for mean squared displacement in Eq. (22), which is formally identical to the expression in Eq. (3) from the diffusion equation. As mentioned in Sect. 2, the space jump process with exponential waiting time between jumps cannot be distinguished from a diffusion process by the measurement of mean squared displacement alone. Statistical comparison of the observed distributions with the predicted distributions as done in Kareiva's survey should help distinguish these possibilities. Furthermore, as stressed in Sect. 3, on long enough time scales the predicted mean squared displacement for the velocity jump process is asymptotically the same as the mean squared displacement for the diffusion approximation of various position jump processes. Since the measurements used in Kareiva's study were made on the order of days, it is possible that the insect movement is actually a jump process observed on a time scale too long to notice the effects of correlations between steps.

One of the main reasons for organisms to disperse is to search for food. In a homogeneous environment with sparse distribution of discrete nutrient spots this foraging search is mostly random. At about the same time as Berg and Brown (1972) were tracking the random walk of bacteria in 3-dimensional space, Smith (1974) obtained extensive records of thrushes hopping on a 2-dimensional meadow. The typical behavior is a sequence of more or less regular hops determining an almost straight move, which is followed by a longer pause used by the birds for pecking and scanning their surroundings. The resulting time distributions of pause and move durations have been evaluated (see Fig. 8a), and they show that the mean move duration d_m is about 1/10 of the mean pause duration d_p :

$$d_p = 4.8 \text{ sec} \gg 0.56 \text{ sec} = d_m.$$

Thus the time spent for moving can be neglected and one would try to model the random search of thrushes by a simple position jump process as in Sect. 2. The pause duration or waiting time duration in Fig. 8a resembles a gamma distribution, as in (23), with mean

$$\frac{2}{\lambda} = d_p \approx 4.8 \text{ sec},$$

which would give a value $\lambda \approx 0.4$ (1/sec).

Smith (1974) also measured the distribution of jump lengths, from which one might try to obtain radially symmetric redistribution kernels $T(\mathbf{x}, \mathbf{y}) = \tilde{T}(\|\mathbf{x} - \mathbf{y}\|)$. However, our position jump model assumes independence of the direction of successive steps, but this is not the case for Smith's data, as the turn angle distribution between successive moving directions shows (see Fig. 8b).

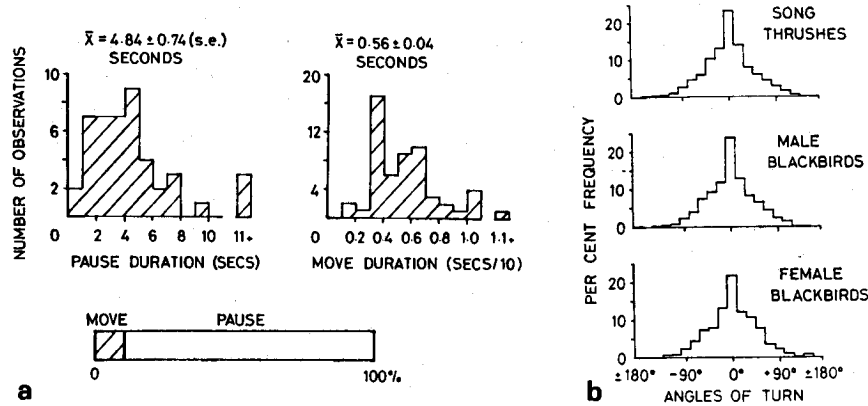


Fig. 8. Data on random searching of hopping birds from Smith (1974). **a** Histograms of move and pause durations measured from single frame cine film analysis. The *single horizontal bar* expresses the mean move duration as a percentage of the total mean move-plus-pause duration. See Fig. 7 in Smith (1974) **b** Frequency histograms of turn angles for three groups of thrushes (see Fig. 11 there)

Therefore, we have to revise the foregoing approach of a position jump process and go back to a general random walk model with pauses as described in Sect. 4.1. If we assume for simplicity that the move and pause durations are exponentially distributed, we would obtain

$$\mu = 1/d_p \approx 0.2 \text{ sec}^{-1}$$

and

$$\lambda = 1/d_m \approx 1.8 \text{ sec}^{-1}.$$

The mean squared speed s_0^2 may be determined from Fig. 8a, while the persistence index ψ_d can be calculated from the turn angle distribution $h(\theta)$ given in Fig. 8b using the definitions given in (43) and (52):

$$\psi_d = 2 \int_0^\pi \left[\left(1 + \frac{\gamma}{\mu} \right) h(\theta) - \frac{\gamma}{\mu} \frac{1}{2\pi} \right] \cos \theta \, d\theta.$$

Since $\lambda \gg \mu$ we could formally proceed to the limit $\lambda \rightarrow \infty$ in Eqs. (69) and (70). This gives $\lambda_+ = \lambda$, $\lambda_- = (1 - \psi_d)\mu + \gamma$, and the mean squared displacement formula

$$\mathcal{D}^2(t) = \frac{2s_0^2}{\lambda^2} \frac{\mu(\mu + \gamma)}{\lambda_-} \left(t - \frac{1}{\lambda_-} (1 - e^{-\lambda_+ t}) \right).$$

This means that we obtain the usual expression for a dispersal process again, which in the limit $\lambda \rightarrow \infty$ of vanishingly small moving periods and large speed $s_0^2 \rightarrow \infty$ describes a jump process with mean squared jump length $m_2 = s_0^2/\lambda^2 \sim O(1)$ as in Sect. 2.2, but now with correlations between subsequent jump directions. A general theory for these processes will be given elsewhere.

All parameters in the above formula are known except the decay parameter γ . Since the papers of Smith (1974) do not contain any displacement measurements, a final estimation of this physiological constant γ cannot be performed. Also, we should remark that further investigations are necessary before an assumption like (52) can be justified.

Although the mean squared displacement formula could not be checked for the thrush data, this example nevertheless shows that a careful discussion of the possible modeling approaches can rule out wrong models and misleading interpretations, as mentioned before. Moreover, it should encourage experimentalists to collect both data on the mean squared displacement of the population and data on the movements of individuals.

In another study, Siniff and Jessen (1969) collected data by radio telemetry about the movements of mammals within their home range. The movements of the mammals are a sequence of runs, followed a pause or rest of varying duration, then another run in a different direction with a possibly different speed. They obtained distributions of travel speeds for adult and juvenile foxes of both sexes and also for hares. Although the precise nature of the distribution was dependent on age, sex and species, the speed distributions all appeared to be of the form of a gamma probability distribution. Siniff and Jessen also measured the turning angle distributions of these species. They found that the turning angle distribution was unimodal and symmetric for the foxes and bimodal for the hares. If we assume that the distributions for speed and turning angle are independent, then we could do the parameter estimation as was done for the leukocytes to get a velocity redistribution kernel $T(\mathbf{v}, \mathbf{v}')$ of the type considered in Sect. 3.

Siniff and Jessen also measured the distribution of the duration of the moves and the duration of the rest periods. These distributions both appear to be of the form of an exponential distribution since they decline rapidly from an initial maximum value. Again we could assume independence of the random variables representing these two durations (which is probably not valid since one would presume that longer rests might follow longer movements), and we could use the approach given in Sect. 4.1.

Another possibility is to combine the data for the duration of movement distribution with the speed and angle data of the velocity redistribution kernel to get a two dimensional displacement distribution of the kind considered in Eq. (12). As was already mentioned, the waiting time distribution between jumps appears to be exponential as in the special case treated in Eq. (20). Then one would arrive at the model given in Eq. (15) with the exponential waiting time between jumps substituted for ϕ .

Because Siniff and Jessen only present the data for individual animals there is not sufficient data to actually estimate the parameters of the functions required to specify the models. Nevertheless the data presented suggests that the space jump and velocity jump process are an appropriate framework for modeling of the movements of these animals. The study of Siniff and Jessen points up one of the difficulties of ecological modeling, since all of the distributions are dependent not only on species but also upon age and sex within the species. For a complete model one should consider these effects and also consider the boundary effects caused by natural barriers such as lakes, mountains, forests, grasslands, and animal territoriality.

Several other studies on a variety of scales suggest that space jump or velocity jump processes may be appropriate models for biological dispersal. For instance, Jones (1977) and Kareiva and Shigesada (1983) characterized the flight sequences of cabbage butterflies as a persistent or correlated random walk. In this case the

turning angle distribution was unimodal and symmetric about 0° on the unit circle. Henderson and Renshaw (1980) describe a spatial stochastic process modeling the root growth of the *Sitka* spruce. A two dimensional random walk-like stochastic process described there has step lengths which are identically distributed gamma random variables, and the step angle change is given by a wrapped normal variable.

However, we should mention that for many other examples of cell or animal locomotion the foregoing idealizations cannot be justified, as, e.g. in the curved or helical movement of sperms or gametes (cf. Alt et al. (1985)). In these types of dispersal continuous fluctuations in the changes of moving direction seem to be the major component determining the final random displacement. It remains a question, whether the translocations of migrating cells, such as leukocytes or tissue cells always show structural piecewise straight components with expressed reorientation phases, as we assumed, or whether continuous fluctuations are dominant, as it is supposed for example in recent simulation studies (Tranquillo and Lauffenburger (1987)).

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