Chapter 8

From discrete to continuum models

The differential equation models we have studied thus far typically view species as densities or concentrations that vary continuously with time and position (see Figure 8.1). We have mostly used phenomenological descriptions of *e.g.* rates and forms of growth, reactions / interactions and movement to model how population density or concentration evolves in time. However, it is very difficult to relate these phenomenological "population-level" functions to the behaviour of individuals – for example, cells, animals, people, and even molecules – within the population. In fact, in writing down a model one should ideally start with a hypothesis of how the individuals behave and use mathematical techniques (*e.g.* coarse graining) to derive how these behaviours manifest at the population level. This question of how to derive differential equation models from individual-level descriptions of behaviours is the subject of this chapter. Some of the approaches that we will use to derive continuum descriptions for the case studies are explored in more detail in the Part B course *Stochastic modelling of biological systems.*

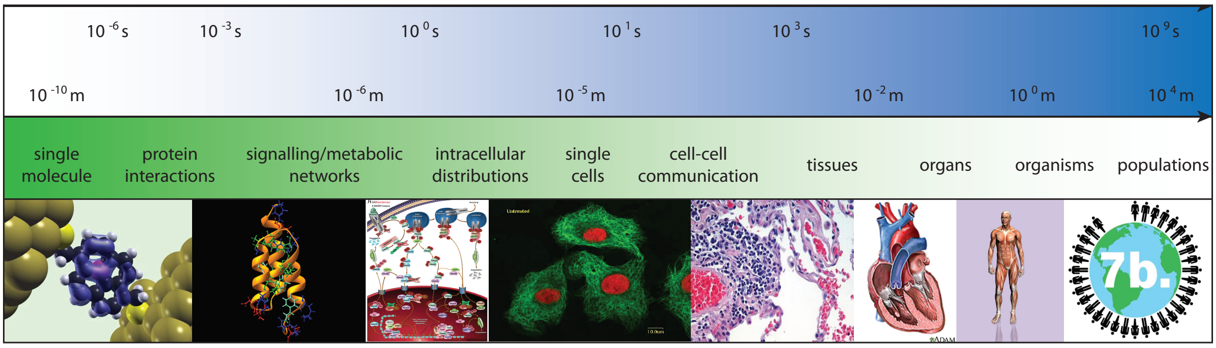

Figure 8.1: An illustration of the different spatial and temporal scales in biology.

8.1 Individual-based models for population growth

First, we will think about models for population growth, and show how to derive some of the population-level growth models that you might have seen in the Part A "Mathematical modelling in biology" course.

8.1.1 An exponential growth model

We will use the notation $p_n(t)$ to denote the probability that there are n individuals at time t, given N_0 individuals at time zero. We will assume that individuals proliferate (*i.e.* produce a daughter individual) at constant rate b, so that over a time interval of length $\mathrm{d}t$, the probability that an agent proliferates is $b\mathrm{d}t + \mathcal{O}(\mathrm{d}t^2)$. Then we can write the following discrete conservation equations

$$p_n(t+\mathrm{d}t) = (n-1)b\mathrm{d}t\, p_{n-1}(t) + (1-nb\mathrm{d}t)\, p_n(t), \quad n = N_0+1, N_0+2, \ldots, \tag{8.1}$$

and

$$p_{N_0}(t+\mathrm{d}t) = (1-N_0 b\mathrm{d}t)\, p_{N_0}(t), \tag{8.2}$$

Rearranging and dividing by $\mathrm{d}t$ gives

$$\frac{p_n(t+\mathrm{d}t) - p_n(t)}{\mathrm{d}t} = (n-1)b\, p_{n-1}(t) + nb\, p_n(t), \quad n = N_0+1, N_0+2, \ldots, \tag{8.3}$$

and

$$\frac{p_{N_0}(t+\mathrm{d}t) - p_{N_0}(t)}{\mathrm{d}t} = N_0 b\, p_{N_0}(t), \tag{8.4}$$

Taking the limit as $\mathrm{d}t \to 0$ gives

$$\frac{\mathrm{d}p_n(t)}{\mathrm{d}t} = (n-1)b\, p_{n-1}(t) + nb\, p_n(t), \quad n = N_0+1, N_0+2, \ldots, \tag{8.5}$$

and

$$\frac{\mathrm{d}p_{N_0}(t)}{\mathrm{d}t} = -N_0 b\, p_{N_0}(t), \tag{8.6}$$

with initial conditions

$$p_n(0) = \begin{cases} 1 & \text{for } n = N_0, \\ 0 & \text{for } n \neq N_0. \end{cases} \tag{8.7}$$

Note that we often call Equations (8.5)-(8.6) together the "master equation" — it is a continuous differential equation in time, t, but a discrete difference equation in n.

There are a number of ways we can use Equations (8.5)-(8.7) to gain insight into the dynamics of the system. We will briefly outline some of them below.

Evolution of the moments

To examine the mean behaviour of the system, we multiply Equations (8.5)-(8.6) by n and sum:

$$\begin{aligned}
\frac{\mathrm{d}}{\mathrm{d}t}\sum_{n=0}^{\infty} np_n(t) &= b\sum_{n=0}^{\infty} n(n-1)p_{n-1}(t) - b\sum_{n=0}^{\infty} n^2 p_n(t), && (8.8)\\
&= b\sum_{n=0}^{\infty} n(n+1)p_n(t) - b\sum_{n=0}^{\infty} n^2 p_n(t), && (8.9)\\
&= b\sum_{n=0}^{\infty} np_n(t), && (8.10)
\end{aligned}$$

where we have used $p_n(t) = 0$ for $n < N_0$, and shifted indices on the second line. Denote the mean agent number, $\langle n(t)\rangle = \sum_{n=0}^{\infty} np_n(t)$, as $M(t)$ we have

$$\frac{\mathrm{d}M}{\mathrm{d}t} = bM(t) \quad \Longrightarrow \quad M(t) = N_0 e^{bt}, \tag{8.11}$$

i.e. the population grows exponentially at rate b.

To evaluate the variance, we first derive an expression for the rate of change of $\langle n^2(t)\rangle = \sum_{n=0}^{\infty} n^2 p_n(t)$:

$$\begin{aligned}
\frac{\mathrm{d}}{\mathrm{d}t}\sum_{n=0}^{\infty} n^2 p_n(t) &= b\sum_{n=0}^{\infty} n^2(n-1)p_{n-1}(t) - b\sum_{n=0}^{\infty} n^3 p_n(t), && (8.12)\\
&= b\sum_{n=0}^{\infty} n(n+1)^2 p_n(t) - b\sum_{n=0}^{\infty} n^{p}_{n}(t), && (8.13)\\
&= b\sum_{n=0}^{\infty} (2n^2+n)p_n(t). && (8.14)
\end{aligned}$$

Using the fact that $V(t) = \langle n^2(t)\rangle - M(t)^2$, we have

$$\frac{\mathrm{d}}{\mathrm{d}t}V(t) = 2bV + bM \qquad \Longrightarrow \qquad V(t) = N_0\left(e^{bt}-1\right)e^{bt}. \tag{8.15}$$

Note. The expression for the mean population growth, Equation (8.11), is the consistent with the continuum model we would have assumed from writing population growth as the "reaction" A → 2A and using the Law of Mass Action. However, in general this will not be the case, as subsequent examples will show, and we will need to use some approximations to write down closed form equations for evolution of the mean number of individuals over time.

Generating functions

Another means to explore these types of models is the use of generating functions. We define the probability generating function $G : [-1,1] \times [0,\infty) \to \mathbb{R}$ by

$$G(s,t) = \sum_{n=0}^{\infty} p_n(t) s^n.$$

Recall that we can recover a number of useful statistics about the $p_n(t)$ by evaluating the generating function in different ways. For example, the coefficient of s^n is $p_n(t)$ and

$$\begin{aligned} M(t) &= \frac{\partial G}{\partial s}(1,t), & (8.16)\\ V(t) &= \frac{\partial^2 G}{\partial s^2}(1,t) + M(t) - M^2(t). & (8.17) \end{aligned}$$

To make progress, we multiply Equations (8.5)-(8.6) by s^n, sum over n and shift indices to give a partial differential equation for $G(s,t)$:

$$\begin{aligned} \frac{\partial G}{\partial t} &= \frac{\partial}{\partial t} \sum_{n=0}^{\infty} p_n(t) s^n \\ &= b\left[\sum_{n=0}^{\infty} (n-1) p_{n-1}(t) s^n - \sum_{n=0}^{\infty} n p_n(t) s^n\right] \\ &= b\left[\sum_{n=0}^{\infty} n p_n(t) s^{n+1} - \sum_{n=0}^{\infty} n p_n(t) s^n\right] \\ &= b\left[s^2 \sum_{n=0}^{\infty} n p_n(t) z^{n-1} - s \sum_{n=0}^{\infty} n p_n(t) s^{n-1}\right] \\ &= bs(s-1)\frac{\partial G}{\partial s}. \qquad (8.18) \end{aligned}$$

We then need to solve

$$\frac{\partial G}{\partial t} = bs(s-1)\frac{\partial G}{\partial s} \quad \text{with} \quad G(s,0) = s^{N_0}. \qquad (8.19)$$

The characteristic equations are

$$\frac{\mathrm{d}t}{\mathrm{d}\tau} = 1, \quad \frac{\mathrm{d}s}{\mathrm{d}\tau} = -bs(s-1), \quad \frac{\mathrm{d}G}{\mathrm{d}\tau} = 0, \qquad (8.20)$$

with

$$t(z,0) = 0, \quad s(z,0) = z, \quad G(z,0) = z^{N_0}, \qquad |z| \le 1. \qquad (8.21)$$

We can integrate the first and third of these to give

$$t(z,\tau) = \tau \qquad \text{and} \qquad G(z,\tau) = z^{N_0}. \tag{8.22}$$

We can use partial fractions to integrate the second: we have

$$-b\tau + B(z) = \int \left(\frac{1}{s-1} - \frac{1}{s}\right) \mathrm{d}s = \ln\left(\frac{s-1}{s}\right), \tag{8.23}$$

where

$$B(s) = \ln\left(\frac{s-1}{s}\right). \tag{8.24}$$

This gives

$$s = \frac{z}{z-(z-1)e^{b\tau}}, \tag{8.25}$$

and hence

$$G(s,t) = \left(\frac{s}{s-(s-1)e^{bt}}\right)^{N_0} = \left(\frac{se^{-bt}}{1-(1-e^{-bt})s}\right)^{N_0}. \tag{8.26}$$

Note that this formulation reveals that $G(s,t)$ is the probability generating function of a negative binomial distribution *i.e.* that the $p_n(t)$ are negative-binomial distributed, $p_n(t) \sim \mathrm{NB}(N,p)$ with parameters $p = e^{-bt}$ and $N = N_0$.

The mean is given by

$$M(t) = \left.\frac{\partial G}{\partial s}\right|_{s=1} = N_0 e^{bt}, \tag{8.27}$$

and the variance is

$$V(t) = \left.\frac{\partial^2 G}{\partial s^2}\right|_{s=1} + \left.\frac{\partial G}{\partial s}\right|_{s=1} - \left(\left.\frac{\partial G}{\partial s}\right|_{s=1}\right)^2 = N_0\left(e^{bt}-1\right)e^{bt}. \tag{8.28}$$

More generally, we can evaluate $p_n(t)$ (for any n) via differentiation of the result in Equation (8.26).

8.1.2 Models for stochastic logistic growth

We will now consider a population of individuals for which, when there are n individuals in the population, the probability a single individual is born over a time interval of length $\mathrm{d}t$ is $\lambda_n \mathrm{d}t + \mathcal{O}(\mathrm{d}t^2)$, and the probability that a single individual dies over a time interval of length $\mathrm{d}t$ is $\mu_n \mathrm{d}t + \mathcal{O}(\mathrm{d}t^2)$. We further assume that the probability that more than one individual is born or dies is $\mathcal{O}(\mathrm{d}t^2)$, and that there are initially N_0 individuals in the population.

Then we can write the following discrete conservation equations

$$p_n(t+\mathrm{d}t) = \lambda_{n-1}\mathrm{d}t\, p_{n-1}(t) + (1-\lambda_n\mathrm{d}t - \mu_n\mathrm{d}t)\, p_n(t) + \mu_{n+1}\mathrm{d}t\, p_{n+1}(t), \quad n = 0,1,2,\ldots, \tag{8.29}$$

with

$$p_{-1}(t) \equiv 0. \tag{8.30}$$

Note that from a biological perspective it is sensible to assume that $\mu_0 = 0$ so that there are no deaths when the population contains zero individuals.

Rearranging, dividing by dt and taking the limit as d$t \to 0$ gives

$$\frac{\mathrm{d}p_n(t)}{\mathrm{d}t} = \lambda_{n-1}p_{n-1}(t) - (\lambda_n + \mu_n)p_n(t) + \mu_{n+1}p_{n+1}(t), \quad n = 0,1,2,\ldots, \tag{8.31}$$

with

$$p_{-1}(t) \equiv 0, \tag{8.32}$$

and initial conditions

$$p_n(0) = \begin{cases} 1 & \text{for } n = N_0, \\ 0 & \text{for } n \neq N_0. \end{cases} \tag{8.33}$$

Evolution of the mean number of individuals

To examine the mean behaviour of the system, we multiply Equations (8.31) by n and sum:

$$\begin{aligned} \frac{\mathrm{d}}{\mathrm{d}t}\sum_{n=0}^{\infty} np_n(t) &= \sum_{n=0}^{\infty} n\lambda_{n-1}p_{n-1}(t) - \sum_{n=0}^{\infty} n(\lambda_n+\mu_n)p_n(t) + \sum_{n=0}^{\infty} n\mu_{n+1}p_{n+1}(t), \\ &= \sum_{n=0}^{\infty}(n+1)\lambda_n p_n(t) - \sum_{n=0}^{\infty} n(\lambda_n+\mu_n)p_n(t) + \sum_{n=0}^{\infty}(n-1)\mu_n p_n(t), \quad (8.34) \\ &= \sum_{n=0}^{\infty}\lambda_n p_n(t) - \sum_{n=0}^{\infty}\mu_n p_n(t). \quad (8.35) \end{aligned}$$

We now make the assumption that

$$\lambda_n = \begin{cases} b_1 n + b_2 n^2 & \text{for } n > 0, \\ 0 & \text{for } n = 0, \end{cases} \qquad \text{and} \qquad \mu_n = \begin{cases} d_1 n + d_2 n^2 & \text{for } n > 0, \\ 0 & \text{for } n = 0, \end{cases} \tag{8.36}$$

where b_1, b_2, d_1 and d_2 are non-negative constants. In this case, we have

$$\frac{\mathrm{d}M}{\mathrm{d}t} = (b_1 - d_1)M + (b_2 - d_2)\langle n^2\rangle, \tag{8.37}$$

where the second moment is defined as

$$\langle n^2 \rangle = \sum_{n=0}^{\infty} n^2 p_n(t). \tag{8.38}$$

Note that the presence of the $\langle n^2 \rangle$ term means that Equation (8.37) is not closed so we cannot immediately solve it to provide insight into how the mean number of individuals evolves over time. In order to make progress, we invoke a commonly used mean-field assumption of the form $\langle n^2 \rangle \approx M^2$ to write

$$\frac{\mathrm{d}M}{\mathrm{d}t} = (b_1 - d_1)M + (b_2 - d_2)M^2 = rM\left(1 - \frac{M}{K}\right), \tag{8.39}$$

where

$$r = b_1 - d_1 \qquad \text{and} \qquad K = \frac{b_1 - d_1}{d_2 - b_2}. \tag{8.40}$$

Hence, the mean number of individuals approximately evolves according to the logistic equation, and we can solve explicitly to find $M(t)$. However, note that there are four constants in the individual-level model, but only two in the deterministic model. Comparing the coefficients, we see that there are an infinite number of stochastic models that all give rise, approximately, to the same average behaviour.

Evolution of the second moment

Instead of closing at first order using the mean-field assumption, we can derive an expression for how the second moment evolves over time:

$$\begin{aligned}
\frac{\mathrm{d}}{\mathrm{d}t}\langle n^2 \rangle &= \frac{\mathrm{d}}{\mathrm{d}t}\sum_{n=0}^{\infty} n^2 p_n(t) \\
&= \sum_{n=0}^{\infty} n^2 \lambda_{n-1} p_{n-1}(t) - \sum_{n=0}^{\infty} n^2(\lambda_n + \mu_n) p_n(t) + \sum_{n=0}^{\infty} n^2 \mu_{n+1} p_{n+1}(t) \qquad (8.41) \\
&= \sum_{n=0}^{\infty} (n+1)^2 \lambda_n p_n(t) - \sum_{n=0}^{\infty} n^2(\lambda_n + \mu_n) p_n(t) + \sum_{n=0}^{\infty} (n-1)^2 \mu_n p_n(t) \\
&= \sum_{n=0}^{\infty} (2n+1) \lambda_n p_n(t) - \sum_{n=0}^{\infty} (2n-1) \mu_n p_n(t). \qquad (8.42)
\end{aligned}$$

For the specific choices of λ_n and μ_n we made above, we have

$$\frac{\mathrm{d}}{\mathrm{d}t}\langle n^2 \rangle = (b_1 + d_1)M + \left\{2(b_1 - d_1) + (b_2 + d_2)\right\}\langle n^2 \rangle + 2(b_2 - d_2)\langle n^3 \rangle. \tag{8.43}$$

We make two observations. First, there are distinct four parameter combinations in Equation (8.43): $b_1 - d_1$, $b_1 + d_1$, $b_2 - d_2$ and $b_2 + d_2$. This means that we could potentially use the variability in population numbers to differentiate between models that display the same averaged behaviour. Second, the variance increases as $b_1 + d_1$ and $b_2 + d_2$ are increased.

Finally, we remark that Equation (8.43) is, similarly to the equation for $M(t)$, not closed. To find an approximate solution we would need to make a further closure assumption to write $\langle n^3 \rangle$ in terms of M and $\langle n^2 \rangle$. This need for moment closure approximations in order to find closed form expressions for the mean and variance of the number of individuals arises whenever λ_n and/or μ_n are quadratic or higher order polynomials in n. The most appropriate closure assumption, for a general scenario, is still an open question.

8.2 Individual-based models for cell motility

In this section we will write down some simple models for the behaviour of motile cell populations, and learn how to coarse grain them to derive corresponding partial differential equation models for the evolution of cell density. For simplicity, we will assume that each cell undergoes a random walk on a lattice in one spatial dimension. However it is simple to extend all these models to two and three spatial dimensions.

8.2.1 A simple model of biased cell motility

We first consider single cell undergoing a random walk on one-dimensional lattice along the x-axis, where the lattice sites are all of width dx (see Figure 8.3). We let $p_n(t)$ now be the probability that the cell is in lattice site n at time t, with $p_n(0) = p_n^0$ *i.e.* the probability that the particle is initially at site n is p_n^0 for $n \in \mathbb{Z}$.

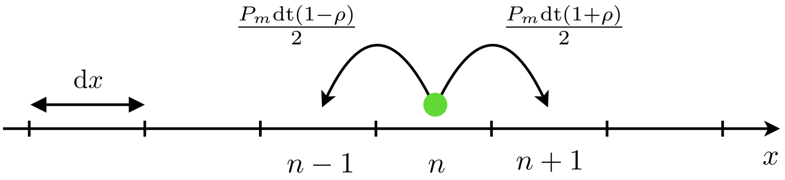

Figure 8.2: Illustration of the biased random walk in one dimension.

We assume that over a time step of length dt, the cell moves one lattice site to the right with constant probability $P_m(1+\rho)\mathrm{d}t/2$, or one lattice site to the left with constant probability $P_m(1-\rho)\mathrm{d}t/2$ (see Figure 8.3). Note that this equates to an overall movement rate of P_m (and probability of movement $P_m\mathrm{d}t$), with movements biased in the right-hand direction for $\rho > 0$.

We can write down a discrete conservation equation for the position of the cell at time $t + \mathrm{d}t$:

$$p_n(t+\mathrm{d}t) = \frac{1}{2}(1+\rho)P_m \mathrm{d}t\, p_{n-1}(t) - (1 - P_m \mathrm{d}t)\, p_n(t) + \frac{1}{2}(1-\rho)P_m \mathrm{d}t\, p_{n+1}(t). \tag{8.44}$$

If the size of the lattice is sufficiently small we can relate $p_n(t)$ to a continuous probability $p(x,t)$ by writing $p_n(t) = p(n\mathrm{d}x, t)$, and then rearrange Equation (8.44) to give

$$\frac{p(n\mathrm{d}x, t+\mathrm{d}t) - p(n\mathrm{d}x, t)}{\mathrm{d}t} = \frac{1}{2}(1+\rho)P_m\, p((n-1)\mathrm{d}x, t) - P_m p(n\mathrm{d}x, t) + \frac{1}{2}(1-\rho)P_m\, p((n+1)\mathrm{d}x, t) \tag{8.45}$$

We can then perform Taylor expansions in both $\mathrm{d}x$ and $\mathrm{d}t$ to give

$$\begin{aligned}\frac{\partial}{\partial t}p(n\mathrm{d}x, t) + \mathcal{O}(\mathrm{d}t) &= \left(\frac{1}{2}(1+\rho)P_m - P_m + \frac{1}{2}(1-\rho)P_m\right) p(n\mathrm{d}x, t)\\ &\quad + \left(-\frac{1}{2}(1+\rho)P_m + \frac{1}{2}(1-\rho)P_m\right)\mathrm{d}x \frac{\partial}{\partial x}p(n\mathrm{d}x, t)\\ &\quad + \left(\frac{1}{4}(1+\rho)P_m + \frac{1}{2}(1-\rho)P_m\right)\mathrm{d}x^2 \frac{\partial^2}{\partial x^2}p(n\mathrm{d}x, t) + \mathcal{O}(\mathrm{d}x^3).\end{aligned} \tag{8.46}$$

Simplifying, and taking the limit as $\mathrm{d}x$ and $\mathrm{d}t$ tend to zero, gives an advection-diffusion partial differential equation for the probability of the position of the cell:

$$\frac{\partial p}{\partial t} = D\frac{\partial^2 p}{\partial x^2} - v\frac{\partial p}{\partial x}, \tag{8.47}$$

where

$$D = \lim_{\mathrm{d}x \to 0} \frac{P_m \mathrm{d}x^2}{2} \qquad \text{and} \qquad v = \lim_{\mathrm{d}x \to 0} P_m \rho\, \mathrm{d}x. \tag{8.48}$$

The initial conditions are given as the continuous extension of the discrete initial condition: $p(x,0) = p^0(x)$.

We now make a number of remarks about the derivation.

- If $\rho = 0$ the the jumps are unbiased, and the position of the particle evolves according to the diffusion equation.
- We can verify that our results make sense by considering the units of the parameters D and v. In SI units we have:
  - the units of P_m are s^{-1} and those of $\mathrm{d}x$ are m, hence the units of D are $\mathrm{m}^2\mathrm{s}^{-1}$;
  - the units of P_m are s^{-1}, those of $\mathrm{d}x$ are m and ρ is non-dimensional, hence the units of v are ms^{-1}.

- The bias must scale with $\mathrm{d}x$ for a well-defined limit (since P_m scales like $1/\mathrm{d}x^2$).
- Equation (8.47) can also be used to describe the evolution of a population of non-interacting cells by suitable choice of initial condition.

There are many ways to extend the basic framework used above to take more biological detail into account. The key point is to include all the relevant (source and sink) terms when using the principle of mass balance to derive the discrete conservation equations. Other processes that could be included are:

- chemotaxis – here, the probabilities of moving left and right from site n will depend on the concentration of a diffusible chemoattractant in boxes $n \pm 1$ and box n;
- proliferation and death;
- competition for space.

We consider this idea of competition for space in the next section.

8.2.2 A model of biased cell motility that includes competition for space

We now consider a population of cells undergoing a random walk on one-dimensional lattice along the x-axis, where the lattice sites are all of width $\mathrm{d}x$. We assume that $\mathrm{d}x$ is approximately equal to one cell diameter, so that at most one cell can occupy any site on the lattice at any time.

We let $p(A_n, t)$ be the probability that a cell is in lattice site n at time t. The probability that the lattice site is empty is denoted $p(0_n, t)$ where $p(0_n, t) = 1 - p(A_n, t)$. We prescribe initial conditions of the form $p(A_n, 0) = p_n^0$ *i.e.* the probability that a cell is initially at site n is p_n^0 for $n \in \mathbb{Z}$.

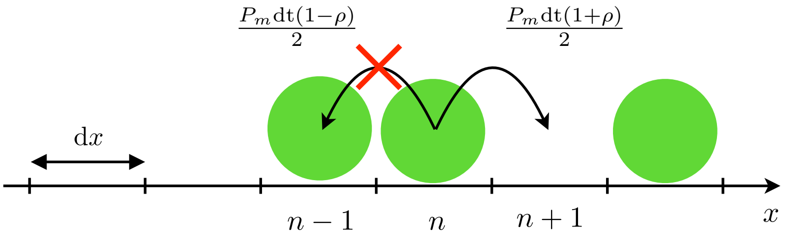

Figure 8.3: Illustration of the biased random walk with exclusion in one dimension. Note that if the cell at lattice site n attempts to jump left, the jump is aborted because there is already a cell in site $n-1$.

We assume that over a time step of length $\mathrm{d}t$, the cell attempts to move with probability $P_m \mathrm{d}t$. If the cell attempts to move, it will jump one lattice site to the right with constant probability

$(1+\rho)/2$, or one lattice site to the left with constant probability $(1-\rho)/2$, but the attempted move is successful only if the target site is vacant.

We can write down a discrete conservation equation for the change in occupancy probability of lattice site n over time step $[t, t+\mathrm{d}t)$:

$$\begin{aligned} p(A_n, t+\mathrm{d}t) - p(A_n, t) \;\; = \;\; & \frac{1}{2}(1+\rho)P_m \mathrm{d}t\, p(A_{n-1}, 0_n, t) - \frac{1}{2}(1-\rho)P_m \mathrm{d}t\, p(0_{n-1}, A_n, t) \\ & + \frac{1}{2}(1-\rho)P_m \mathrm{d}t\, p(0_n, A_{n+1}, t) - \frac{1}{2}(1+\rho)P_m \mathrm{d}t\, p(A_n, 0_{n+1}, t), \end{aligned} \tag{8.49}$$

where $p(A_n, 0_m)$ denotes the probability that site n is occupied and site m is vacant. To make progress in deriving a corresponding advection-diffusion partial differential equation, we write

$$\begin{aligned} p(A_n, t+\mathrm{d}t) - p(A_n, t) \;\; = \;\; & \frac{P_m}{2}\mathrm{d}t\Big[p(A_{n-1}, 0_n, t) - p(0_{n-1}, A_n, t)\Big] \\ & + \frac{P_m}{2}\mathrm{d}t\Big[p(0_n, A_{n+1}, t) - p(A_n, 0_{n+1}, t)\Big] \\ & + \frac{P_m}{2}\rho\, \mathrm{d}t\Big[p(A_{n-1}, 0_n, t) - p(0_{n-1}, A_n, t)\Big] \\ & - \frac{P_m}{2}\rho\, \mathrm{d}t\Big[p(0_n, A_{n+1}, t) - p(A_n, 0_{n+1}, t)\Big]. \end{aligned} \tag{8.50}$$

We now divide by $\mathrm{d}t$ and simplify the first two terms on the right-hand side using conservation statements of the form

$$p(A_n, A_m, t) + p(A_n, 0_m, t) = p(A_n, t), \tag{8.51}$$

to give

$$\frac{P_m}{2}\Big[p(A_{n-1}, t) - 2p(A_n, t) + p(A_{n+1}, t)\Big]. \tag{8.52}$$

In order to close the system of discrete conservation equations (for $n \in \mathbb{Z}$), so that the right-hand side contains only occupancy probabilities of single lattice sites (rather than pairs of neighbouring lattice sites), we make the assumption that the occupancy probabilities of neighbouring lattice sites are independent of one another *e.g.*

$$p(A_n, 0_{n\pm1}) = p(A_n)p(0_{n\pm1}). \tag{8.53}$$

This is known as a mean-field approximation, and it allows us to write

$$\begin{aligned}\frac{p(A_n, t+\mathrm{d}t) - p(A_n, t)}{\mathrm{d}t} &= \frac{P_m}{2}\Big[p(A_{n-1}, t) - 2p(A_n, t) + p(A_{n+1}, t)\Big] \\ &\quad + \frac{P_m}{2}\rho\Big\{\big[1 - p(A_n, t)\big]\big[p(A_{n-1}, t) - p(A_{n+1}, t)\big] \\ &\qquad + p(A_n, t)\Big[\big(1 - p(A_{n-1}, t)\big) - \big(1 - p(A_{n+1})\big)\Big]\Big\}. \quad (8.54)\end{aligned}$$

Similarly to the previous section, if the size of the lattice sites (and hence the cell diameter) are sufficiently small compared to the region occupied by the cell population, we can relate $p(A_n, t)$ to a continuous probability by writing (with plenty of abuse of notation!) $p(A_n, t) = p(n\mathrm{d}x, t)$ so that

$$\begin{aligned}\frac{p(n\mathrm{d}x, t+\mathrm{d}t) - p(n\mathrm{d}x, t)}{\mathrm{d}t} &= \frac{P_m}{2}\Big[p((n-1)\mathrm{d}x, t) - 2p(n\mathrm{d}x, t) + p((n+1)\mathrm{d}x, t)\Big] \quad (8.55) \\ &\quad + \frac{P_m}{2}\rho\Big\{\big[1 - p(n\mathrm{d}x, t)\big]\big[p((n-1)\mathrm{d}x, t) - p((n+1)\mathrm{d}x, t)\big] \\ &\qquad + p(n\mathrm{d}x, t)\Big[\big(1 - p((n-1)\mathrm{d}x, t)\big) - \big(1 - p((n+1)\mathrm{d}x)\big)\Big]\Big\}.\end{aligned}$$

We can then perform Taylor expansions in both dx and dt, and take the limit as dx and dt tend to zero, to give an advection-diffusion partial differential equation for the cell density:

$$\frac{\partial p}{\partial t} = D\frac{\partial^2 p}{\partial x^2} - v\frac{\partial}{\partial x}\big(p(1-p)\big), \qquad (8.56)$$

where

$$D = \lim_{\mathrm{d}x \to 0} \frac{P_m \mathrm{d}x^2}{2} \qquad \text{and} \qquad v = \lim_{\mathrm{d}x \to 0} P_m \rho \, \mathrm{d}x. \qquad (8.57)$$

Once again, the initial conditions are given as the continuous extension of the discrete initial condition: $p(x, 0) = p^0(x)$.

As in the non-excluding case if $\rho = 0$ then the jumps are unbiased and the position of the particle evolves according to the diffusion equation. However, if $\rho \neq 0$, then we note two differences. First, we need to use a moment closure approximation to derive a closed form partial differential equation describing evolution of the density over time. This means that Equation (8.56) does not exactly describe how the density evolves – in particular, we might expect discrepancies whenever there are correlations in lattice site occupancies, so that $p(A_n, A_m)$ is not well approximated by $p(A_n)p(A_m)$. We also note that the inclusion of a simple description of competition for space impacts the advection term, changing it from $v\partial p/\partial x$ to $v\partial p(1-p)/\partial x$.

Suggested reading

- H. G. Othmer, S. A. Dunbar and W. Alt (1988). Models of dispersal in biological systems. *J. Math. Biol.* 26:263–298.
- L. J. S. Allen (2010). *An introduction to stochastic processes with applications in biology.* Chapman and Hall/CRC; 2nd edition.
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