Part II Mathematical Biology Lent Term 2012

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These lecture notes, plus matlab programs, examples sheets and any other extra material will be made available at http://www.damtp.cam.ac.uk/user/phh/mathbio.html.

1 Introduction

1.1 Preamble

Biology is the study of living organisms. Mathematical biology is a term used to describe the application of mathematical analysis to give enhanced understanding of biological systems.

The aim in mathematical biology is to use a quantitative mathematical framework to answer real biological questions and to make predictions about real biological phenomena (following the successful application of mathematics over the last 500 years or so to answer questions about the physical world).

In study of the physical world mathematics has naturally been part of the scientific method.

1. **MODEL**: proposed set of rules as to how system works, naturally expressed in terms of mathematical equations
2. **PREDICTIONS**: solve equations to predict behaviour of system in some range of cases
3. **COMPARISON WITH OBSERVATIONS** (perhaps using mathematical tools to make the comparison as precise as possible)
4. **REFINE OR REJECT MODEL**

The use of this approach in biology, with the exploitation of mathematics having a prominent role has rapidly increased over the last 50 years or so. Part of this increase is stimulated by the increasing amount of quantitative information on biological systems. Part of it is allowed by the increasing range of tools, analytical and computational, available to mathematicians.

Note that in the above, whether applied to the physical world or the biological world, formulating a model and then making refinements to it does not follow simply from a cycle of mathematical calculations. Physical or biological understanding is required to make sensible choices about what to include in a model and what to omit.

One important difference between study of the physical world and study of the biological world is that in the former there are a small number of simple overarching equations, such as Newton's Second Law, Maxwell's equations, the Schrödinger equations, which can be used as building blocks and from which much else follows. In biological systems these simple overarching equations are missing.

One line of argument that has been pursued successfully in the study of physical systems and is also applicable to some biological systems is the idea that systems are composed of large number of individual members each interacting with their environment in some way (e.g. individual molecules in a cell, individual cells in an organism, individual organisms in a population).

One approach (A) to studying such systems is to consider average or large-scale quantities via a 'bulk' formalism which is expressed in terms of (deterministic) ordinary differential equations or partial differential equations.

Another (B) is to recognise differences between individual elements and the importance of individual events, perhaps using models that are explicitly probabilistic. (The detail of a sequence of interactions may be less important than overall statistical details of that sequence of interactions.)

In this course we consider mostly approach (A), but include some of approach (B).

[Next part of lecture is primarily motivational, showing some examples of interesting and important biological systems where application of mathematics has proved to be, or might prove to be, a significant aid to understanding.]

1.2 Simple quantitative approaches

One early quantitative approaches in biology was the study of *allometric scaling*. Allometry considers the relation of shape to size. Allometric scaling is non-isometric, i.e. the proportions of an organism change according to its size.

Example: The scaling of W, resting metabolic rate (e.g. some measure of resting oxygen consumption) with body mass M.

It is observed that $\log W$ varies linearly with $\log M$, but what is the constant of proportionality?

A simple model might be that $W \propto N$, with N the number of cells in the organism, and similarly that $M \propto N$. (This assumes that the nature of individual cells, is independent of the size of the organism.) This implies that $W \propto M$.

However the chemical reactions that convert food and oxygen together into useable energy have efficiency less than 1, implying heat production within the organism. Another possible assumption is that cells operate within the same range of temperatures independently of the size of the organism and hence that the core temperature of organisms is independent of size. The temperature of the organism is proportional to rate of heat generation divided by surface area and hence to W divided by surface area. Therefore if R is the size of the organism it must be that $W \propto R^2$. But $M \propto R^3$ and hence $W \propto M^{2/3}$.

Actually what is observed is that $W \propto M^{3/4}$ ('Kleiber's Law') suggesting that shape changes with size so that $M \propto (\text{surface area})^{4/3}$ rather than $M \propto (\text{surface area})^{3/2}$. (Shape becomes more complex as size increases.)

This implies that W/M decreases as M increases, so the rate of working of individual cells is smaller for larger organisms. Perhaps this is why larger organisms are longer lived.

[Detailed discussions of this topic are given in the books by D'Arcy Thompson (1992, 'On Growth and Form', Cambridge University Press, Abridged edition by John Tyler Bonner) and Schmidt-Nielsen (1984, 'Scaling: Why is Animal Size so Important?' Cambridge University Press). For a recent critical discussion of Kleiber's Law see Glazier (2007, Biological Reviews of the Cambridge Philosophical Society, 80, 611-662).]

Example: Implications for flight

Assume that muscle mass $\propto M$ and therefore that power available $\propto M$.

How much power is required for flight? The power is required to overcome drag and a

basic principle of aerodynamics is that lift and drag are in proportion with the ratio being a number C_L.

Drag $\propto \rho S U^2$ where ρ is air density, S is surface area and S is speed.

Lift $\propto Mg$ where g is gravitational acceleration.

Power required = Drag$\times U$ = Drag$^{3/2}\times(\rho S)^{-1/2} \propto C_L^{-3/2}(Mg)^{3/2}\times(\rho S)^{-1/2} \propto M^{3/2}S^{-1/2}$.

If we assume that $S \propto M^{2/3}$ then Power required $\propto M^{7/6}$ which increases more rapidly than M. Therefore the required power increases with M faster than the available power.

This is consistent with the observation that, on Earth at least, there are no flying birds with $M \gtrsim 12$kg.

2 Deterministic systems without spatial structure

The main topic in this section will be models for populations, based on ordinary differential equations (for systems that are continuous functions of time) and difference equations (for systems with discrete generations). (The equations will be deterministic but reality is stochastic.)

We will start with simple models and add complexity. (More complexity in principle implies more realism, but are all ingredients represented with certainty?) Models are often most useful in identifying what is important and what is not. We will generally be interested in qualitative features, e.g. is there any equilibrium population? is it stable? if it is not stable then what happens?

2.1 One species models

2.1.1 Continuous time variation

(i) The simplest possible model

Species (people, rabbits, flies, bacteria) which feed all the time, without synchronised generations. Alternatively there may be large numbers of individuals so that the number of births or deaths in some interesting time interval is a small fraction of the total.

Let $x(t)$ be population size as a function of time t. Assume that the number of offspring produced per individual (or per female for fixed sex ratio) per unit time is a constant $a > 0$. Similarly assume that the death rate (number of deaths per unit time per individual) is a constant $b > 0$.

$$x(t+\delta t) - x(t) = ax\delta t - bx\delta t$$

Divide by δt and take the limit as $\delta t \to 0$.

$$\frac{dx}{dt} = (a-b)x = rx$$

where $r = a - b$.

Solution is $x(t) = x_0 e^{rt}$, where $x(0) = x_0$, so the population grows indefinitely if $r = a - b > 0$ and decays to zero (implying extinction) if $r < 0$.

This behaviour (and therefore this model) is not very interesting. What needs to be added?

(ii) Does discrete time help?

Let x_n be the population in generation n. Assume that individuals reproduce by factor α and then die. Hence $x_{n+1} = \alpha x_n$ and $x_n = \alpha^n x_0$. Again alternatives are indefinite growth (if $\alpha > 1$) and extinction (if $\alpha < 1$).

(iii) Birth and death rates depending on population size

This gives more interesting behaviour. Consider

$$\frac{dx}{dt} = f(x) \tag{1}$$

e.g. $f(x) = \alpha x(x_e - x)$ (the *logistic equation*). $f(x) < 0$ for $x > x_e$ ('death wins') and $f(x) > 0$ for $0 < x < x_e$ ('birth wins'). Rescale variables, $\tilde{x} = x/x_e$, $\tilde{\alpha} = \alpha \tilde{x}_e$.

$$\frac{d\tilde{x}}{dt} = \tilde{\alpha}\tilde{x}(1-\tilde{x}).$$

Now drop ˜s.

Solve the above:

$$\frac{1}{x(1-x)}\frac{dx}{dt} = \alpha = \left(\frac{1}{x} + \frac{1}{1-x}\right)\frac{dx}{dt} = \frac{d}{dt}\log\left(\frac{x}{1-x}\right).$$

Hence

$$\frac{x}{(1-x)} = \frac{x_0 e^{\alpha t}}{(1-x_0)}$$

and

$$x = \frac{x_0 e^{\alpha t}}{(1-x_0) + x_0 e^{\alpha t}}.$$

Note that $x \to 1$ as $t \to \infty$ (from above if $x_0 > 1$ and from below if $x_0 < 1$. There is a non-zero equilibrium, achieved for all initial conditions (and therefore stable). Another equilibrium is $x = 0$, by the above this is unstable.

More generally if

$$\frac{dx}{dt} = f(x)$$

where $f(x_i^*) = 0$ for $i = 1, \ldots, N$, then x_i^* is a steady state for each i.

The stability of each possible steady state can be determined by linearisation:

$$x = x_i^* + y, \qquad f(x) \simeq f(x_i^*) + y f'(x_i^*) + O(y^2) \simeq y f'(x_i^*)$$

hence

$$\frac{dy}{dt} \simeq f'(x_i^*) y \quad \text{and} \quad y(t) \simeq y(0)\exp(f'(x_i^*)t).$$

$y(t)$ grows if $f'(x_i^*) > 0$ (*unstable*) and $y(t)$ decays if $f'(x_i^*) < 0$ (*stable*).

(iv) Delay models

Previously considered models have had the birth and death rate depend only on the instantaneous population size. In reality there may be effects of time to reach maturity, finite gestation time, etc. These may be incorporated by allowing dependence on previous values of x, e.g. as a simple extension of the model considered in (iii),

$$\frac{dx}{dt} = \alpha x(t)\left\{1 - \int_{-\infty}^{t} W(t-s)x(s)\,ds\right\}$$

where the function $W(.)$ is known as a *history kernel*.

A very simple choice might be $W(s) = \delta(s - T)$, where $T > 0$ is a constant and $\delta(.)$ is the Dirac delta function. Then

$$\frac{dx}{dt} = \alpha x(t)\{1 - x(t-T)\}, \tag{2}$$

i.e. birth rate minus death rate depends both on the instantaneous population $x(t)$ and the population $x(t-T)$ evaluated T before the current time.

Is there a steady state? Certainly $x(t) = 1$ for all time is a possible steady state as it was for the case $T = 0$ studied in (iii).

Now we ask whether this steady state is stable. We write $x(t) = 1 + y(t)$ where y is assumed small, and ask whether $y(t)$ remains small, or grows without bound.

Substitute $x(t) = 1 + y(t)$ into (2) and retain only terms that are $O(1)$ or $O(y)$.

$$\frac{d}{dt}(1+y) = \frac{dy}{dt} = \alpha(1+y(t)) \times (1-1-y(t-T)) \simeq -\alpha y(t-T).$$

Note that the $O(1)$ terms cancel, as they must, if we are considered departures from a self-consistent steady state.

The number of individual parameters may be reduced by writing $\tau = \alpha t$, then

$$\frac{dy}{d\tau} = -y(\tau - \alpha T).$$

Seek a solution of the form $y(\tau) = \Delta e^{s\tau}$, as you have in stability analysis of steady solutions of conventional differential equations, and substitute into the equation, implying

$$s\Delta e^{s\tau} = -\Delta e^{s(\tau - \alpha T)}$$

and hence that

$$s = -e^{-s\alpha T}.$$

Note that the assumed form of the solution worked – we are left with an equation for the unknown constant s and all dependence on τ has disappeared.

If all roots of this equation have negative real parts, then $y \to 0$ as $t \to \infty$ and perturbations away from the steady state decay, so the steady state is stable. On the other hand if there are any roots with positive real parts, most initial conditions for y will lead to exponential growth and therefore the steady state is unstable.

First consider whether this equation has any real roots, by noting that such roots correspond to the intersection of the graph of $se^{s\alpha T}$ with -1. $se^{s\alpha T}$ has a single turning point, a minimum, when $s = -(\alpha T)^{-1}$ and $se^{s\alpha T} = -(\alpha T e)^{-1}$.

Therefore there are real roots if $\alpha T < e^{-1}$ and otherwise no real roots. Furthermore when there are real roots they are both negative, since $se^{s\alpha T}$ is negative only when s is negative, so these real roots do not imply instability.

To determine whether there is stability or instability we need to consider possible complex roots. We write $s = \sigma + i\omega$, where σ and ω are both real and substitute into the equation, separating real and imaginary parts to give,

$$\sigma = -e^{-\alpha T\sigma}\cos(\alpha T\omega)$$

$$\omega = e^{-\alpha T\sigma}\sin(\alpha T\omega).$$

Note that this in turn implies that

$$\sigma^2 + \omega^2 = e^{-2\alpha T\sigma},$$

$$\omega = -\sigma\tan(\alpha T\omega).$$

Now consider the implications of $\sigma > 0$. The second equation implies that $\tan(\alpha T\omega)$ has a different sign to ω, and hence that $\alpha T|\omega| > \frac{1}{2}\pi$. The first equation implies that $|\omega| < 1$. Therefore $\alpha T > \alpha T|\omega| > \frac{1}{2}\pi$. It follows that for $0 < \alpha T < \frac{1}{2}\pi$ there are no roots with $\sigma > 0$.

Therefore we ask at what value of αT does a root with $\sigma > 0$ actually first appear? ($\alpha T > \pi/2$ is necessary for instability but is it sufficient?) The 'marginal' case is when $\sigma = 0$. Then, from the above, $\cos(\omega\alpha T) = 0$ and $\omega = \sin(\omega\alpha T)$. Without loss of generality we may take $\omega > 0$ (since the equations are invariant under the transformation $\omega \leftrightarrow -\omega$). It follows that $\omega = \pi/2\alpha T$ or $5\pi/2\alpha T$ or $9\pi/2\alpha T$, etc, and hence $\alpha T = \pi/2$ or $5\pi/2$ or $9\pi/2$ etc. Therefore a root with $\sigma > 0$ first appears (as αT increases from 0) when $\alpha T = \pi/2$.

In summary we have deduced that for $0 < \alpha T < \pi/2$ the steady state is stable, but that for $\alpha T > \pi/2$ the steady state is unstable.

We might also distinguish between $0 < \alpha T < e^{-1}$ when the slowest decay of disturbances from the steady state corresponds to real s, i.e. monotonic expoential decay, and $e^{-1} < \alpha T < \pi/2$ when the decay of disturbances from the steady state corresponds to complex s, i.e. exponentially decaying oscillations.

At the marginal case $\alpha T = \pi/2$ the root with $\sigma = 0$ has $\omega = 1$. This suggests (but does not prove) that for αT just greater than $\pi/2$ the evolution may take the form of oscillations with frequency close to 1 (in τ) and hence frequency $\alpha = \pi/2T$ in t. Numerical solution (e.g. MATLAB program `delay-differential logistic model`) shows that when $\alpha T > \pi/2$ the solution $x(t)$ shows finite-amplitude oscillations.

A more general conclusion is that for sufficiently large T equations of the form (2) may generate oscillatory behaviour. In the biological context this means that a population under external conditions that are kept steady in time may exhibit oscillations.

May (1973, 'Stability and Complexity in Model Ecosystems', Princeton University Press) suggested (2) as a model for the observed behaviour in experiments (where the supply of food was carefully regulated) of Australian sheep blowfly. This was further discussed by Gurney et al (1980, Nature, 287, 17-21) who showed that many aspects of the observed behaviour could be explained by a model

$$\frac{dx}{dt} = R(x(t - t_D)) - kx(t)$$

where $x(t)$ is the number of adult blowflies, the $R(.)$ term represents recruitment into the adult population of larvae from eggs produced time t_D earlier and the $-kx(t)$ term represents death at a fixed rate k (per individual). The function $R(.)$ is taken to have a single maximum, e.g. $R(x) = Px\exp(-x/x_0)$, representing the fact that the rate of production of eggs becomes small when the population is large.

Delay-differential equations in physiology

In respiration the amount of air V inhaled in one breath at time t depends on the concentration C of carbon dioxide in the blood in the lungs at some earlier time $t - T$, with T constant. T might be the time delay between oxygenation of blood in the lungs and monitoring by chemoreceptors in the brainstem.

$V(C)$ is usually assumed to be a 'sigmoidal' function (i.e. its graph has an 'S' shape). A simple representation is the Hill function

$$V(C) = \frac{V_{max}C^m}{a^m + C^m}$$

where V_{max} and a are constants.

The rate of change of C is equal to rate of production minus rate of destruction, which can be represented simply as

$$\begin{aligned}\frac{dC}{dt} &= p - bC(t)V(t) \\ &= p - bC(t)V_{max}\frac{\{C(t-T)\}^m}{a^m + \{C(t-T)\}^m}\end{aligned}$$

where p and b are also constants. Note that the rate of destruction of carbon dioxide in the blood is assumed to be proportional to the current concentration and to the volume of air inhaled in one breath.

It is good practice to nondimensionalise (to reduce as far as possible the number of independent parameters appearing in the equation), here by writing $\tilde{x} = C/a$, $\tilde{t} = pt/a$, $\tilde{T} = pT/a$, $\alpha = abV_{\max}/p$ and $\tilde{V} = V/V_{max}$ to give

$$\frac{d\tilde{x}}{d\tilde{t}} = 1 - \alpha\tilde{x}(\tilde{t})\frac{\tilde{x}(\tilde{t}-\tilde{T})^m}{1+\tilde{x}(t-T)^m} = 1 - \alpha\tilde{x}(\tilde{t})v(\tilde{x}(\tilde{t}-\tilde{T}))$$

where the function $v(.)$ is defined by the last equality. We now, for convenience, drop the ˜s (i.e. $\tilde{x} \to x$, etc).

The above equation has a possible steady state (corresponding to regular breathing) with $x(t) = x_s$ for all t if $1/x_s = \alpha v(x_s)$. Since $v(x)$ is monotonically increasing it follows that

for every α there is always one possible value of x_s.

The form of $v(.)$ is determined by physiological factors. Abnormal physiology maybe problematic. There is a breathing abnormality, the 'Cheyne Stokes phenomenon' when breathing waxes and wanes. Periods of active breathing, lasting for a minute or so, are interrupted by periods of weak breathing ('apnea').

We might anticipate that if the model equation above exhibits this sort of behaviour, it corresponds to a situation when the steady state $x = x_s$ is unstable. The stability in the model system is controlled by the form of the function $v(.)$.

To investigate the stability of the steady state write $x(t) = x_s + y(t)$, substitute into the delay-differential equation and retain only linear terms in y. This gives

$$\frac{dy}{dt} \simeq 1 - \alpha x_s v(x_s) - \alpha v(x_s) y(t) - \alpha x_s v'(x_s) y(t-T) = -\alpha v(x_s) y(t) - \alpha x_s v'(x_s) y(t-T)$$

with the two terms $1 - \alpha x_s v(x_s)$ cancelling because of the steady state condition.

Then try the solution $y(t) = y_0 e^{st}$ where the constant s is to be determined. Substituting into the equation gives

$$s y_0 e^{st} = -\alpha v(x_s) y_0 e^{st} - \alpha x_s v'(x_s) y_0 e^{s(t-T)}$$

and hence

$$\begin{aligned} s &= -\alpha v(x_s) - \alpha x_s v'(x_s) e^{-sT} \\ &= -A - Be^{-sT} \end{aligned}$$

where the constants A and B are both positive.

As before, seek complex roots of the form $s = \sigma + i\omega$. Substitute into the above to give:

$$\begin{aligned} \sigma &= -A - Be^{-\sigma T} \cos \omega T \\ \omega &= Be^{-\sigma T} \sin \omega T \end{aligned}$$

Note first that $\{(\sigma + A)^2 + \omega^2\}^{1/2} = Be^{-\sigma T}$, hence $Be^{-\sigma T} > |\sigma + A|$. If $\sigma > 0$ then $B > Be^{-\sigma T} > |\sigma + A| > A$. Therefore if $B < A$ there are no roots with $\sigma > 0$. Following the approach in the previous example this suggests that we consider B increasing from 0, or from A, and determine at what value of B instability first occurs. In particular we seek the smallest value of B for which $\sigma = 0$.

If $\sigma = 0$ then

$$\begin{aligned} A &= -B \cos \omega T \\ \omega &= B \sin \omega T \end{aligned}$$

so $A^2 + \omega^2 = B^2$ and $\omega = -A \tan \omega T$.

Without loss of generality we may take $\omega > 0$ (since the equations are invariant under the transformation $\omega \leftrightarrow -\omega$). Also it is convenient to consider ωT rather than ω. The equation $\omega T = -AT \tan \omega T$ has a root $g(AT)$ in $\pi/2 < \omega T < \pi$, another in $3\pi/2 < \omega T < 2\pi$, another in $5\pi/2 < \omega T < 2\pi$, etc.

But note that $\omega = B \sin \omega T$ can be satisfied only by the first, third, etc of these. Note

also that since $B^2 = A^2 + \omega^2$ it is the minimum possible value of ωT, i.e. the first root $g(AT)$, that is of interest.

We deduce that the transition from stability to instability takes place at $B = \{A^2 + g(AT)^2/T^2\}^{1/2}$. The function $g(AT)$ is such that $g(AT) \to \frac{1}{2}\pi^+$ as $AT \to 0$ and $g(AT) \to \pi^-$ as $AT \to \infty$.

Note, in particular, that $B < \{A^2 + \pi^2/4T^2\}^{1/2}$ implies stability and $B > \{A^2 + \pi^2/T^2\}^{1/2}$ implies instability.

[Note also that in the limit $A \to 0^+$ the transition value of $B \to (\pi/2T)^+$ consistent with the first stability analysis for steady states of (2).]

Recall that $A = \alpha v(x_s)$ and $B = \alpha x_s v'(x_s)$. Instability requires that $B > A$, therefore that $x_x v'(x_s) > v(x_s)$. In the case that $v(x) = x^m/1 + x^m$ it is straightforward to show that this criterion can be satisfied only if $m > 1$.

Numerical solution (e.g. MATLAB program `Cheyne-Stokes delay-differential model`) verifies that the steady state solution becomes unstable when αT or, alternatively, m are increased sufficiently, consistent with the above analysis.

(v) Populations with age distributions

The birth and death rates of most animals depend on their ages.

Let $n(a, t)$ be the number of individuals (more precisely, reproducing individuals) of age a at time t. The total population is therefore $N(t) = \int_0^\infty n(a, t)\, da$.

Let the birth rate to individuals aged a be $b(a)$ and the death rate of individuals aged a be $\mu(a)$.

Typical forms for humans might be:

Now consider the change in the number of individuals, aged a at time t, between time t

and time $t + \delta t$ due to death.

$$n(a + \delta t, t + \delta t) = n(a, t) - \mu(a)n(a, t)\delta t.$$

Note that there are no births at age a if $a > 0$, also that if there are no deaths at age a then individuals simply age by δt.

Estimate $n(a + \delta t, t + \delta t)$ using partial derivatives.

$$n(a + \delta t, t + \delta t) - n(a, t) \simeq \frac{\partial n}{\partial a}\delta t + \frac{\partial n}{\partial t}\delta t = -\mu(a)n(a, t)\delta t.$$

Hence deduce the partial differential equation (for $a > 0$).

$$\frac{\partial n}{\partial t} + \frac{\partial n}{\partial a} = -\mu(a)n(a, t). \tag{3}$$

Note that the combination of partial derivatives on the left-hand side suggests a wave equation (recall IB Methods).

If $\mu = 0$ then the population just ages: $n(a, t) = g(a - t)$ for some function $g(.)$.

The partial differential equation (3) requires initial and boundary conditions.

$$n(a, 0) = n_0(a) \qquad \text{given initial distribution.} \tag{4}$$

$$n(0, t) = \int_0^\infty b(a)n(a, t)\, da \qquad \text{newborns.} \tag{5}$$

To justify this boundary condition note that the number of individuals born in time δt is approximately $n(0, t)\delta t$ and equal to the total birth rate times δt.

An alternative derivation of the newborns condition is to consider the rate of change of the total population $N(t)$. dN/dt = total rate of birth − total rate of death, i.e.

$$\frac{dN}{dt} = \frac{d}{dt}\int_0^\infty n(a,t)\,da = \int_0^\infty b(a)\,n(a,t)\,da - \int_0^\infty \mu(a)\,n(a,t)\,da.$$

Hence

$$\int_0^\infty \left(\frac{\partial n}{\partial t} + \mu n\right) = \int_0^\infty b(a)n(a,t)\,da$$

but from (3)

$$\int_0^\infty \left(\frac{\partial n}{\partial t} + \mu n\right) da = -\int_0^\infty \frac{\partial n}{\partial a}\,da = n(0,t)$$

implying that $n(0,t) = \int_0^\infty b(a)\,n(a,t)\,da$. (We have assumed that $n(a,t) \to 0$ as $a \to \infty$.)

How does the population vary? (3) may be solved by the method of characteristics or by transforming into a simple wave equation as follows.

Write $n(a,t) = \hat{n}(a,t)\exp(-\nu(a)$ where $\nu(a) = \int_0^a \mu(a')\,da'$, so that $d\nu/da = \mu(a)$. Substitute into (3)

$$\frac{\partial n}{\partial a} + \frac{\partial n}{\partial t} = \left(\frac{\partial \hat{n}}{\partial a} + \frac{\partial \hat{n}}{\partial t}\right)\exp(-\nu(a)) - \frac{d\nu}{da}\hat{n}(a,t) = -\mu(a)\hat{n}(a,t)\exp(-\nu(a))$$

Hence

$$\frac{\partial \hat{n}}{\partial a} + \frac{\partial \hat{n}}{\partial t} = 0$$

with solution $\hat{n}(a,t) = g(a-t)$ and hence

$$n(a,t) = \exp(-\nu(a))g(a-t), \tag{6}$$

with the function $g(.)$ to be determined.

Part of the information about $g(.)$ comes from the initial condition $n(a,0) = n_0(a)$ (for $a > 0$). Hence $g(a) = n_0(a)\exp(\nu(a))$ for $a > 0$.

Substituting for $g(.)$ in (6) determines the solution $n(a,t)$ for $a > t$. To determine the solution for $a < t$ requires use of the newborns condition.

$$n(0,t) = \exp(-\nu(0))g(-t) = g(-t) = \int_0^\infty b(a)n(a,t)\,da.$$

Now split the last integral into two parts $0 < a < t$ and $a > t$, noting that we already have an explicit form for the solution in $a > t$.

$$n(0,t) = g(-t) = \int_0^t b(a)\exp(-\nu(a))g(a-t)\,da + \int_t^\infty b(a)n_0(a)\exp(\nu(a-t) - \nu(a))\,da.$$

This is an integral equation for $g(.)$, with $g(-t)$ being given in terms of an integral of $g(s)$ over the range $-t < s < 0$.

The last expression for the rate of birth $n(0,t)$ can be written symbolically as

$$n(0,t) = \int_0^t H(a)n(0,t-a)\,da + B_0(t)$$

where the first part represents offspring of individuals born after time 0 and the second part represents offspring of individuals present in the population at time 0.

At large times we might expect the second part to be very small (or, in many models, zero) since 'old' individuals are unlikely to reproduce. If the second part can be neglected a useful approach is to try a 'normal mode' solution of the form $n(a,t) = r(a)e^{\gamma t}$ for some constant γ.

Substituting in (3) gives

$$(\gamma r(a) + \frac{dr}{da})e^{\gamma t} = -\mu(a)r(a)e^{\gamma t}$$

and hence that

$$r(a) = r(0)\exp\left(-\gamma a - \int_0^a \mu(s)\,ds\right) = r(0)\exp\left(-\gamma a - \nu(a)\right).$$

Now substitute into the newborns condition (5)

$$r(0)e^{\gamma t} = \int_0^\infty b(a)r(a)e^{\gamma t}\,da = \int_0^\infty b(a)r(0)e^{\gamma t}\exp\left(-\gamma a - \nu(a)\right)\,da,$$

hence

$$1 = \int_0^\infty b(a)\exp\left(-\gamma a - \nu(a)\right)\,da = \phi(\gamma)$$

where the second equality defines $\phi(.)$. This equation determines γ.

Note that $\phi(.)$ is a decreasing function, with $\phi(\gamma) \to \infty$ as $\gamma \to -\infty$ and $\phi(\gamma) \to 0$ as $\gamma \to \infty$ (for sensible choices of $b(.)$ and $\mu(.)$)

Thus the sign of γ is determined by $\phi(0) = \int_0^\infty b(a)\exp(-\nu(a))\,da$.

If $\phi(0) > 1$ then $\gamma > 0$ and there is growth.

If $\phi(0) < 1$ then $\gamma < 0$ and there is decay.

$\phi(0)$ can be interpreted as the average number of offspring of an individual.

As for the 'simplest possible model' discussed in (i) above the possible outcomes here are either exponential growth ($\gamma > 1$) or extinction ($\gamma < 1$). Introducing age structure does not give other possible outcomes.

Final remark: The 'normal mode' solution $n(a,t) = r(a)e^{\gamma t}$ is found to be the asymptotic large-t solution for any initial conditions.

2.1.2 Discrete-time systems

(i) The discrete-time logistic equation

We consider a discrete-time version of the logistic equation (1). The discrete-time equation takes the form

$$x_{n+1} = f(x_n) = \alpha x_n(1 - x_n) \tag{7}$$

expressing (for example) the number x_{n+1} of individuals in generation $n+1$ as a function of the number x_n in generation n.

For $x_{n+1} \geq 0$ we need $0 \leq x_n \leq 1$ and (hence) $0 \leq \alpha \leq 4$.

An equilibrium solution has $x_{n+1} = x_n = x_*$ say, with

$$x_* = \alpha x_*(1 - x_*)$$

hence $x_* = 0$ or $x_* = 1 - 1/\alpha$ (the latter only if $\alpha \geq 1$).

To investigate the stability of this equilibrium we write $x_n = x_* + \delta_n$. Hence

$$x_* + \delta_{n+1} = f(x_* + \delta_n) = f(x_*) + \delta_n f'(x_*) + O(\delta_n^2).$$

Neglecting quadratic terms

$$\delta_{n+1} = \delta_n f'(x_*)$$

implying that the equilibrium is stable if $|f'(x_*)| < 1$ and unstable if $|f'(x_*)| > 1$.

For the specific example $f(x) = \alpha x(1 - x)$

$$\begin{aligned} f'(x_*) = \alpha(1 - 2x_*) &= \alpha \quad (x_* = 0) \\ &= \alpha(2/\alpha - 1) = 2 - \alpha \quad (x_* = 1 - 1/\alpha). \end{aligned}$$

For $0 < \alpha < 1$ $x_* = 0$ is the only steady state and it is stable.

For $1 < \alpha$ $x_* = 0$ is unstable. $x_* = 1 - 1/\alpha$ is a second possible steady state, which is stable if $1 < \alpha < 3$ and unstable if $\alpha > 3$.

Note change in behaviour at $\alpha = 2$. For $1 < \alpha < 2$ $f'(x_*) > 0$ and the approach to x_* is monotonic. For $2 < \alpha < 3$ $f'(x_*) < 0$ and the approach to x_* is oscillatory.

Graphical analysis via a 'cobweb' diagram

A plot of $f(x)$ as a function of x can be exploited as a plot of x_{n+1} as a function of x_n.

$0 < \alpha < 1$

$1 < \alpha < 2$

$2 < \alpha < 3$

Use expanded view to contrast $\alpha < 3$ ($|f'(x_*)| < 1$) with $\alpha > 3$ ($|f'(x_*)| > 1$).

For $\alpha > 3$ the two possible steady states $x_* = 0$ and $x_* = 1 - 1/\alpha$ are unstable, but the solution stays within $(0, 1)$. What happens?

Consider the second iteration

$$x_{n+2} = \alpha x_{n+1}(1 - x_{n+1}) = \alpha^2 * x_n(1 - x_n)(1 - \alpha x_n(1 - x_n)) = f_2(x_n)$$

What are the fixed points of f_2? If x_* is a fixed point then

$$x_* - \alpha^2 x_*(1 - x_*)(1 - \alpha x_*(1 - x_*)) = 0.$$

Note that $f_2 = f \circ f$ (f composed with itself), hence 0 and $1 - 1/\alpha$ are fixed points, implying factorization

$$x_*(1 - \alpha x + \alpha x_*)(1 + \alpha - \alpha(1 + \alpha)x_* + \alpha^2 x_*^2) = 0.$$

Last factor implies the two roots

$$x_* = \frac{1}{2\alpha^2}\left\{\alpha(1 + \alpha) \pm \sqrt{\alpha^2(\alpha + 1)(\alpha - 3)}\right\} = \frac{1 + \alpha}{2\alpha} \pm \frac{\sqrt{(\alpha + 1)(\alpha - 3)}}{2\alpha}.$$

These roots are real for $\alpha \geq 3$ and both equal to $2/3$ at $\alpha = 3$. The implication is that as α increases through 3 the stable fixed point of f at $2/3$ splits into a stable period-2 orbit (corresponding to two fixed points of f_2).

Bifurcation diagram

There is bifurcation from period-2 to period-4 at $\alpha = 1 + \sqrt{6} \simeq 3.45$ and there are an infinite number of such 'period-doubling' bifurcations by $\alpha = \alpha_\infty \simeq 3.5699$. As α increases beyond α_∞ there are regions of 'chaos' (i.e. aperiodic behaviour) separated by narrow windows of periodicity.

Numerical solution (e.g. MATLAB program `Cobweb diagram for the logistic map`) demonstrates the above behaviour.

The phenomenon of deterministic chaos was rediscovered (after Poincaré) by Lorenz (in meteorology) and by May (in discrete-time behaviour of populations).

Note that the behaviour of the discrete-time system (7) is much richer than that of the previously considered continuous-time system (1), but the relation between the two is weak – there is no general implication that discrete-time systems are more interesting that continuous-time systems.

(ii) Higher-order discrete-time systems

(a) A discrete-time model of respiration (Recall earlier discussion of Cheyne-Stokes phenomenon.)

Volume in breath $n+1$ is function of CO_2 concentration after breath $n-l$.

$$V_{n+1} = f(C_{n-l}) = \alpha C_{n-l}$$

with the function $f(.)$ being taken as linear for simplicity, implying the last equality, with α a positive constant.

Mass balance equation states that the difference in total amount of CO_2 in the lung between breath n and breath $n+1$ is the amount produced by the body minus the amount lost in one breath

$$\begin{aligned} KC_{n+1} - KC_n &= M - \beta V_{n+1} \\ KC_{n+1} - KC_n &= M - \alpha\beta C_{n-l} \end{aligned}$$

with K, M and β constant.

There is a steady state solution with $C_n = C_*$ for all n, with $C_* = M/\alpha\beta$.

Investigate stability by writing $C_n = C_* + \delta_n$, hence

$$\delta_{n+1} = \delta_n - \frac{\alpha\beta}{K}\delta_{n-l}.$$

If $l = 0$ then

$$\delta_{n+1} = \delta_n(1 - \frac{\alpha\beta}{K})$$

implying stability only if $\alpha\beta/K < 2$.

If $l = 1$ then

$$\delta_{n+1} = \delta_n - \frac{\alpha\beta}{K}\delta_{n-1},$$

hence $\delta_n = A_1 p_1^n + A_2 p_2^n$ with A_1 and A_2 constant and p_1 and p_2 the roots of

$$p^2 - p + \frac{\alpha\beta}{K} = 0$$

hence

$$p = \frac{1}{2} \pm \sqrt{\frac{1}{4} - \frac{\alpha\beta}{K}}.$$

For $\alpha\beta/K < 1/4$, $0 < p_1, p_2 < 1$. Stable. Fluctuations decay without oscillation.

For $1/4 < \alpha\beta/K < 1$, p_1 and p_2 are complex with $|p_1| = |p_2| < 1$. Stable. Fluctuations decay with oscillation.

For $1 < \alpha\beta/K$, p_1 and p_2 are complex with $|p_1| = |p_2| > 1$. Unstable. Fluctuations increase in size with oscillation.

Note that going from $l = 0$ to $l = 1$ reduces the threshold value of $\alpha\beta/K$ required for instability, i.e. delay increases the tendency for instability. (Consider the case $l = 2$ as an exercise. The threshold value of $\alpha\beta/K$ is then $\frac{1}{2}(\sqrt{5} - 1) < 1$.)

For f linear the above are exact solutions. For f nonlinear we expect the unstable cases to exhibit limit cycles or chaos.

(b) Linear population model with more than one generation

Consider poppies which live for one year and produce seeds which may germinate after 1 year, or 2 years, or not at all.

Let x_n be the number of germinating poppies in year n and s_n be the number of seeds produced by these poppies, say γ per plant. (In a more complex model γ might be a stochastic variable.)

Suppose that a fraction σ of the 1-year-old seeds germinate in year 1 and a fraction τ of the 2-year-old seeds germinate in year 2.

At the beginning of year n let there be $s_n^{(1)}$ 1-year-old seeds and $s_n^{(2)}$ 2-year-old seeds.

$$x_n = \sigma s_n^{(1)} + \tau s_n^{(2)}$$

$$s_n^{(1)} = \gamma x_{n-1} \quad \text{(number of seeds produced in year } n-1\text{)}$$

$$\begin{aligned} s_n^{(2)} &= (1-\sigma) s_{n-1}^{(1)} \quad \text{(fraction of 1-year-old seeds in year } n-1 \text{ which did not germinate)} \\ &= (1-\sigma)\gamma x_{n-2}. \end{aligned}$$

Hence

$$x_n = \sigma\gamma x_{n-1} + \tau(1-\sigma)\gamma x_{n-2}.$$

This has solutions of the form $x_n = A_1 p_1^n + A_2 p_2^n$ with A_1 and A_2 constants and p_1 and p_2 the roots of

$$p^2 - \sigma\gamma p - \tau(1-\sigma) = 0,$$

i.e.

$$p = \frac{\sigma\gamma}{2} \pm \frac{1}{2}\sqrt{\sigma^2\gamma^2 + 4\gamma\gamma(1-\sigma)}.$$

Note that both roots are real and that we can choose $p_2 < 0 < p_1$ with $|p_1| > |p_2|$. This implies that whilst x_n can vary monotonically initially, eventually the p_1^n term dominates and there is either monotonic increase (unbounded growth) and monotonic decrease (extinction). The boundary between the two is when $p_1 = 1$, i.e. 1 is a root, i.e.

$$\sigma\gamma + \tau(1-\sigma)\gamma = 1.$$

Hence $\sigma\gamma + \tau(1-\sigma)\gamma < 1$ implies extinction and $\sigma\gamma + \tau(1-\sigma)\gamma > 1$ implies unbounded growth.

A more interesting model might have

$$x_n = N(\sigma\gamma x_{n-1} + \tau(1-\sigma)\gamma x_{n-2})$$

where $N'(0) = 1$ and $N(s) \to N_m$ as $s \to \infty$ so that the number of individuals is limited.

There is a steady state with $x_n = x_*$, where $x_* = N(\{\sigma\gamma + \tau(1-\sigma)\gamma\}x_*)$. $x_* = 0$ is always a root, and there is a non-zero root if $\sigma\gamma + \tau(1-\sigma)\gamma > 1$. Stability is governed by the equation

$$\delta_n = N'(x_*)\{\sigma\gamma\delta_{n-1} + \tau(1-\sigma)\gamma\delta_{n-2}\}$$

The previous analysis applies, except that γ is replaced by $N'(x_*)\gamma$.

2.2 Multi-species models

(i) Enzyme reactions

These provide a chemical example.

We consider the Michaelis-Menten reaction. A substrate S reacts with a small amount of enzyme E to form a complex C. C breaks down to form a product P, releasing E. (Rates of reaction with E present are much faster than those without, so other reaction pathways may be ignored.)

$$\mathrm{E} + \mathrm{S} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \mathrm{C}$$

$$\mathrm{C} \xrightarrow{k_2} \mathrm{E} + \mathrm{P}$$

A back reaction in the second reaction is possible in principle, but is so slow as to be negligible.

Represent the progress of these reactions by a system of ordinary differential equations. (s represents the concentration of S, etc.) k_1, k_{-1}, k_2 are rate constants.

$$\frac{ds}{dt} = -k_1 es + k_{-1} c \tag{8}$$

$$\frac{de}{dt} = -k_1 es + (k_{-1} + k_2) c \tag{9}$$

$$\frac{dc}{dt} = k_1 es - (k_{-1} + k_2) c \tag{10}$$

$$\frac{dp}{dt} = k_2 c \tag{11}$$

(Note these equations assume that the chemical species are well-mixed.)

Consider $s(0) = s_0$, $e(0) = e_0 \ll s_0$, $c(0) = 0$, $p(0) = 0$ as initial conditions.

We seek to calculate the rate of production of P, i.e. $R = dp/dt$.

Simplifying features are that (11) is uncoupled and that (9 + (9) implies

$$\frac{d}{dt}(c + e) = 0.$$

(The reaction swaps between C and E, with the combination being conserved.)

Hence $c + e = e_0$.

Eliminate e and the system reduces to

$$\frac{ds}{dt} = -k_1(e_0 - c)s + k_1 c$$

$$\frac{dc}{dt} = k_1(e_0 - c)s - (k_{-1} + k_2)c$$

with initial conditions $s(0) = s_0$ and $c(0) = 0$.

Rescale variables to reduce the number of independent constants:

$$\tau = k_1 e_0 t \qquad s = s_0 u(\tau) \qquad c = e_0 v(\tau).$$

implying

$$s_0 k_1 e_0 \frac{du}{d\tau} = -k_1 e_0 s_0 (1 - v)u + k_{-1} e_0 v$$

$$e_0 k_1 e_0 \frac{dv}{d\tau} = k_1 e_0 s_0 (1 - v)u - (k_{-1} + k_2) e_0 v$$

and hence

$$\frac{du}{d\tau} = -(1 - v)u + \frac{k_{-1}}{k_1 s_0} v = -u + v(u + \mu - \lambda)$$

$$\frac{e_0}{s_0}\frac{dv}{d\tau} = \epsilon \frac{dv}{d\tau} = (1 - v)u - \frac{k_{-1} + k_2}{k_1 s_0} v = u - (u + \mu)v$$

where

$$\mu = \frac{k_{-1} + k_2}{k_1 s_0} \qquad \lambda = \frac{k_2}{k_1 s_0} \qquad \epsilon = \frac{e_0}{s_0} \ll 1.$$

Initial conditions are $u(0) = 1$ and $v(0) = 0$.

These equations are simple to integrate numerically, but can we make analytical progress?

$\epsilon \ll 1$ suggests omitting the $\epsilon dv/d\tau$ term, but this reduces the order of the equations, so not all the initial conditions can be satisfied.

Trying this anyway implies that $u - (u + \mu)v = 0$, hence $v = u/(\mu + u)$.

Substituting this expression into that for $du/d\tau$ gives

$$\frac{du}{d\tau} \simeq -u + v(u + \mu - \lambda) = -u + u - \frac{\lambda u}{u + \mu} = -\frac{\lambda u}{u + \mu}.$$

Integrating gives $u + \mu \log u \simeq -\lambda\tau + A$.

Applying the inital condition $u(0) = 1$ implies $A = 1$, hence $u + \mu \simeq\simeq 1 - \lambda\tau$.

Now consider

$$R = \frac{dp}{dt} = k_2 c = k_2 e_0 v(\tau) \simeq \frac{k_2 e_0 u(\tau)}{\mu + u(\tau)} = \frac{k_2 e_0 s}{\mu s_0 + s}$$

This expression for R in terms of s follows as a consequence of (10) being close to equilibrium.

Rearranging gives

$$\frac{1}{R} = \frac{\mu s_0 + s}{k_2 e_0 s} = \frac{\mu s_0}{k_2 e_0}\frac{1}{s} + \frac{1}{k_2} e_0.$$

The graph of $1/R$ against $1/s$ is therefore linear, with gradient $\mu s_0/k_2 e_0$ and intersecting the $1/s$ axis at $-1/\mu s_0$.

Plotting $1/R$ against $1/s$ is a technique used to analyse experimental results ('Lineweaver-Burk' plot) and may be used to deduce the constants $\mu s_0 = (k_{-1} + k_2)/k_1$ and $k_2 e_0$.

Note that in the above approach we have ignored the initial condition $v(0) = 0$. (In our solution $v(0) = u(0)/u(0) + \mu = 1/1 + \mu \neq 0$.)

Numerical solution (e.g. MATLAB program `Michaelis-Menten differential equations`) shows that in practice there is a rapid adjustment, on a time that is $O(\epsilon)$ from an arbitrary initial condition to the quasi-steady solution $v = u/u + \mu$.

The important property demonstrated in this example is the separation of timescales. The natural timescale for s is $(k_1 e)^{-1}$. The natural timescale for e (and hence c) is $(k_1 s)^{-1}$. But typically $e \ll s$, so the timescale for s is much larger than the timescale for e (and c).

(ii) Predator-prey systems

$N(t)$ is prey, $P(t)$ is predators.

Prey grow if there are no predators and decline if there are many predators. Predators decline if there are no prey.

The simplest relevant model is

$$\frac{dN}{dt} = N(a - bP)$$
$$\frac{dP}{dt} = P(cN - d)$$

with a, b, c and d all positive constants.

These are the Lotka-Volterra equations (e.g. recall IA Differential Equations). (In reality there will be more complex effects including randomness.)

There is a rescaling of N (replaced by u), P (replaced by v) and t which replaces the above by

$$\frac{du}{dt} = u(1 - v)$$
$$\frac{dv}{dt} = -\alpha v(1 - u).$$

(*Exercise:* find the rescaling.) Note that this leaves a single parameter α.

We can analyse the above equations by considering the nullclines $du/dt = 0$ and $dv/dt = 0$.

There are two steady states $(u, v) = (0, 0)$ and $(u, v) = (1, 1)$. Denote either by (u_*, v_*).

Now consider stability of these steady states, writing $u = u_* + \xi$ and $v = v_* + \eta$.

Consider the general case

$$\frac{du}{dt} = f(u, v)$$
$$\frac{dv}{dt} = g(u, v)$$

such that $f(u_*, v_*) = g(u_*, v_*) = 0$.

Then

$$\frac{d\xi}{dt} = f(u_*, v_*) + \xi f_u|_* + \eta f_v|_* + \dots$$
$$\frac{d\eta}{dt} = g(u_*, v_*) + \xi g_u|_* + \eta g_v|_* + \dots$$

where $|_*$ denotes evaluation at (u_*, v_*) (and will subsequently be omitted).

Seek solutions of the form $\xi = \xi_0 e^{pt}$, $\eta = \eta_0 e^{pt}$, where ξ_0, η_0 and p are constants. Then

$$p\begin{pmatrix}\xi_0\\ \eta_0\end{pmatrix} = \begin{pmatrix}f_u & f_v\\ g_u & g_v\end{pmatrix}\begin{pmatrix}\xi_0\\ \eta_0\end{pmatrix} = J_*\begin{pmatrix}\xi_0\\ \eta_0\end{pmatrix}$$

where J_* is the Jacobian $\partial(f,g)/\partial(u,v)$ evaluated at (u_*, v_*).

The possible values for p, are the two eigenvalues p_1 and p_2 of J_*. If either or both of $\mathrm{Re}(p_1) > 0$ and $\mathrm{Re}(p_2) > 0$ then the steady state (u_*, v_*) is unstable. If $\mathrm{Re}(p_1) \le 0$ and $\mathrm{Re}(p_2) \le 0$ and one is equal to zero then the the steady state (u_*, v_*) is neutrally stable.

$$(p - f_u)(p - g_v) - f_v g_u = 0$$

and hence

$$p = \tfrac{1}{2}\mathrm{Tr}J_* \pm \tfrac{1}{2}\sqrt{(\mathrm{Tr}J)^2 - 4\det J_*}$$

Stability requires $\mathrm{Tr}J_* < 0$ and $\det J_* > 0$. Instability requires either $\det J_* < 0$ (saddle point) or $\mathrm{Tr}J_* > 0$, $\det J_* > 0$ (unstable focus or unstable node).

Return to example: $f(u,v) = u(1-v)$, $g(u,v) = -\alpha v(1-u)$

$$J = \begin{pmatrix}1-v & -u\\ \alpha v & -\alpha(1-u)\end{pmatrix} = \begin{pmatrix}1 & 0\\ 0 & -\alpha\end{pmatrix} \quad \text{at } (0,0)$$
$$= \begin{pmatrix}0 & -1\\ \alpha & 0\end{pmatrix} \quad \text{at } (1,1)$$

Hence $(0,0)$ is unstable (saddle) and $(1,1)$ is neutrally stable (centre, eigenvalues are $\pm i\sqrt{\alpha}$).

Note that this system can be integrated. Eliminate t to give

$$\frac{du}{dv} = -\frac{u(1-v)}{\alpha v(1-u)},$$

hence

$$\alpha(1-u)\frac{du}{u} = -(1-v)\frac{dv}{v},$$

implying that $\alpha \log u - \alpha u + \log v - v = H(u, v)$ is constant. Solution curves are contours of $H(u, v)$ and in particular form closed curves around $(1, 1)$.

This system is unusual – the existence of many possible finite-amplitude oscillations, each corresponding to a different contour of $H(u, v)$ is a property that is unlikely to be robust to small changes in the system.

Nonetheless, according this model, the populations of prey and predators display oscillations. Note that the prey leads the predator – the prey population grows, then the predator population grows, then the prey population decays, then the predator population decays, etc.

One interesting observed example of oscillations in natural systems is in the populations of lynx and hares in Canada in the late 19th century. However it has been pointed out that in this case the oscillation in lynx population seem to lead the oscillation in the hare population, suggesting that the lynx are the prey for the hares! A possible resolution of this difficulty is to include the effect of fur traders.

Consider a modest perturbation to this system, e.g.

$$\frac{du}{dt} = u(1 - v) - \epsilon_1 u^2$$

$$\frac{dv}{dt} = -\alpha v(1 - u) - \epsilon_2 \alpha v^2.$$

This is a logistic-equation representation of the inhibition of growth of population when the population is large, due to competition for resources.

The fixed points (u_*, v_*) are $(0, 0)$ or (u_0, v_0), where u_0 and v_0 satisfy

$$1 - v_0 = \epsilon_1 u_0$$

$$1 - u_0 = \epsilon_2 v_0.$$

The Jacobian evaluated at (u_0, v_0) is

$$J = \begin{pmatrix} 1 - v_0 - 2\epsilon_1 u_0 & -u_0 \\ \alpha v_0 & -\alpha(1-u_0) - 2\epsilon_2 \alpha v_0 \end{pmatrix} = \begin{pmatrix} -\epsilon_1 u_0 & -u_0 \\ \alpha v_0 & -\alpha\epsilon_2 v_0. \end{pmatrix}$$

Hence

$$\begin{aligned} \det J &= \alpha u_0 v_0 (1 + \epsilon_1 \epsilon_2) > 0, \\ \mathrm{Tr} J &= -\epsilon_1 u_0 - \alpha \epsilon_2 v_0 < 0, \end{aligned}$$

implying complex conjugate p_1 and p_2 with negative real parts, a stable focus.

Another perturbation is to add logistic growth and harvesting of prey, but not predators:

$$\frac{du}{dt} = u(1-v) - \epsilon u^2 - f$$

$$\frac{dv}{dt} = -\alpha v(1-u)$$

One fixed point has $v = 0$ and u the positive root of $u - \epsilon u^2 - f =$, i.e. a perturbation to $(0, 0)$.

The second fixed point has $u = u_0 = 1$ and $v = v_0 = 1 - \epsilon - f$, i.e. a perturbation to $(1, 1)$. Note that the effect of harvesting is to reduce the predators, but not the prey!

In this case the Jacobian evaluated at (u_0, v_0) is

$$J = \begin{pmatrix} 1 - v_0 - 2\epsilon u_0 & -u_0 \\ \alpha v_0 & -\alpha(1-u_0) \end{pmatrix} = \begin{pmatrix} f - \epsilon & -1 \\ \alpha(1-\epsilon-f) & 0. \end{pmatrix}$$

implying

$$\begin{aligned} \det J &= \alpha(1 - \epsilon - f) = \alpha v_0 > 0, \\ \mathrm{Tr} J &= f - \epsilon, \end{aligned}$$

so (u_0, v_0) is a stable focus if $f < \epsilon$ and an unstable focus if $f > \epsilon$.

A different system to predator-prey is one where there is competition between two species. The simplest relevant model is

$$\frac{dN}{dt} = N(a - bP)$$
$$\frac{dP}{dt} = P(d - cN)$$

with a, b, c and d all positive constants. (The right-hand side of the second equation has changed in sign from predator-prey.) As before rescale to give

$$\frac{du}{dt} = f(u, v) = u(1 - v)$$
$$\frac{dv}{dt} = \alpha v(1 - u),$$

with $\alpha > 0$.

$(0, 0)$ and $(1, 1)$ remain as steady states.

The Jacobian is

$$J = \begin{pmatrix} 1 - v & -u \\ -\alpha v & \alpha(1 - u) \end{pmatrix} = \begin{pmatrix} 1 & 0 \\ 0 & \alpha \end{pmatrix} \quad \text{at } (0, 0)$$
$$= \begin{pmatrix} 0 & -1 \\ -\alpha & 0 \end{pmatrix} \quad \text{at } (1, 1)$$

Hence $(0, 0)$ is an unstable note and $(1, 1)$ is a saddle point ($\mathrm{Tr}J = 0$, $\det J < 0$). In this case one species always wins out over the other, with the winning species depending on initial conditions.

(iii) Infectious diseases

There is a long history of modelling infectious diseases, e.g. measles (Anderson and May 1986), rabies, AIDS, SARS, bird flu.

The simplest standard model is the SIR model.

The total population N is divided into

- 'susceptible' S
- 'infected' I
- 'removed' R (either recovered or dead).

A particular example (e.g. measles) is when the 'removed' are immune and cannot be re-infected.

I increases at a rate proportional to the rate at which I meet S and decreases as Is recover or die.

Schematic representation is

$$\mathrm{S} + \mathrm{I} \xrightarrow{r} \mathrm{I} \xrightarrow{a} \mathrm{R}.$$

The evolution is governed by the equations

$$\begin{aligned} \frac{dI}{dt} &= rIS - aI \\ \frac{dS}{dt} &= -rIS \\ \frac{dR}{dt} &= aI. \end{aligned}$$

Note that $S + I + R = N =$ constant.

The question of interest for this system is whether, given the parameters a and r and the initial conditions $S = S_0$, $I = I_0$ and $R = 0$, there will be an epidemic (I increasing from its initial value) or not (I decreasing from its initial value).

Note that $N = I_0 + S_0$ and $dS/dt \leq 0$.

Then $dI/dt = (rS - a)I \leq (rS_0 - a)I$.

So I can increase only if $rS_0 > a$, i.e. $S_0 > a/r = \rho$. This is the condition for an epidemic to begin.

For an explicit solution note that

$$\frac{dI}{dS} = -1 + \frac{\rho}{S}$$

implying

$$I = \rho \log S - S + I_0 + S_0 - \rho \log S_0 = I_0 + S_0 - S + \rho \log(S/S_0).$$

Note that for all initial conditions $I \to 0$, $S \to S_\infty > 0$. Consequently $R \to N_0 - S(\infty)$. Note that the disease out from lack of infectives, not from lack of susceptibles.

$S(\infty)$ is the ultimate number who have never been infected, with $S(\infty)$ satisfying the equation $S(\infty) - \rho \log(S(\infty)/S_0) = N_0$.

The model described above can be modified, e.g. to include different age classes, non-zero incubation time, different pathways (e.g. recovered $\xrightarrow{r}$ susceptible – see Q9 on Example Sheet 1), and different classes (e.g. carriers).

2.3 Systems exhibiting nonlinear oscillations

Nonlinear oscillations are an interesting mathematial behaviour relevant to many biological phenomena, e.g. respiration, populations and chemical reactions.

(i) More realistic predator-prey models

Consider a more general model that that considered previously. so that the number of prey N satisfies the equation

$$\frac{dN}{dt} = NF(N,P) = N\{r(1 - \frac{N}{K}) - PR(N)\}$$

where P is the number of predators and r and K are constants.

Some possible forms for $NR(N)$:

For the Lotka-Volterra equations $NR(N)$ increases without bound. Other choices of $R(N)$ such that $NR(N)$ saturates as N becomes large represent the fact that when prey is abundant there is limited predator capability to reduce their numbers.

We consider $R(N) = k/(N + D)$, where k and D are constants, so that

$$\frac{dN}{dt} = N\{r(1 - \frac{N}{K}) - \frac{kP}{N + D}\}.$$

A different possible form for the predator growth equation is

$$\frac{dP}{dt} = sP(1 - \frac{hP}{N}).$$

This is of logistic form, but the transition value of P between growth and decay is proportional to N. This transition value (N/h in this case) is sometimes called the *carrying capacity.*

As usual, rescale to decrease as far as possible the number of independent parameters.

$$\tau = rt \qquad u(\tau) = \frac{N(t)}{K} \qquad v(\tau) = \frac{hP(t)}{K}$$

$$\alpha = \frac{k}{hr} \qquad \beta = \frac{s}{r} \qquad \delta = \frac{D}{k}$$

The rescaled equations are then

$$\begin{aligned} \frac{du}{d\tau} &= f(u, v) = u(1 - u) - \frac{\alpha uv}{u + \delta} \\ \frac{dv}{d\tau} &= g(u, v) = \beta v(1 - \frac{v}{u}). \end{aligned}$$

Nullclines in $u > 0$, $v > 0$ are $\alpha v = (1-u)(u+\delta)$ and $u = v$.

Steady states are (i) $(0,0)$, (ii) $(1,0)$ and (iii) (u_0, u_0) where $u_0 = \frac{1}{2}\{(1-\delta-\alpha) + \sqrt{(1-\delta-\alpha)^2 + 4\delta}$ is the positive root of $\alpha u_0 = \delta + (1-\delta)u_0 - u_0^2$.

Stability is determined by the Jacobian J:

$$J = \begin{pmatrix} 1 - 2u - \frac{\alpha\delta v}{(u+\delta)^2} & -\frac{\alpha u}{u+\delta} \\ \frac{\beta v^2}{u^2} & \beta - \frac{2\beta v}{u} \end{pmatrix}$$

At $(0,0)$

$$\mathrm{Tr}J = 1 + \beta(1 - \frac{2v}{u}) \qquad \det J = \beta(1 - \frac{2v}{u})$$

hence either $\det J < 0$ or $\det J > 0$, $\mathrm{Tr}J > 0$, hence unstable.

At $(1,0)$

$$\mathrm{Tr}J = \beta - 1 \qquad \det J = -\beta$$

hence $\det J < 0$, hence unstable.

At (u_0, u_0)

$$\mathrm{Tr}J = 1 - \beta - 2u_0 - \frac{\alpha\delta u_0}{(u_0+\delta)^2} \qquad \det J = u_0\beta(1 + \frac{\alpha}{(u_0+\delta)^2})$$

$\det J > 0$ (note that the quadratic equation satisfied by u_0 has been used in simplifying the expression for $\det J$) so there is stability if $\mathrm{Tr}J < 0$ and instability if $\mathrm{Tr}J > 0$. In the latter case, since $\det J > 0$ the unstable steady state is either an unstable focus or an unstable node.

In the case where (u_0, u_0) is stable, trajectories converge on this point. What happens if (u_0, u_0) is unstable (in which case all three possible steady states are unstable)? The trajectories then converge to a *limit cycle*, i.e. the limiting trajectory is a closed curve. This may be proved using the Poincaré-Bendixson Theorem which states that for an autonomous two-dimensional dynamical system, i.e. a system of the form $du/dt = f(u,v)$, $dv/dt = g(u,v)$, where 'autonomous' denotes that f and g are not explicitly dependent on time t, then if there is a domain $\mathcal{D}$ such that (a) $\mathcal{D}$ contains no fixed points and (b) all trajectories on the boundary of $\mathcal{D}$ enter $\mathcal{D}$ then $\mathcal{D}$ contains at least one stable limit cycle.

To apply the Poincaré-Bendixson theorem to our system we choose $\mathcal{D}$ as a region surrounding, but not including, the point (u_0, u_0).

The shape of the small excluded region around (u_0, u_0) has to be chosen carefully, e.g. if (u_0, u_0) is a unstable focus then the excluded region could be a small ellipse of appropriate shape. (Note that it is important that (u_0, u_0) is not a saddle point.)

The shape of the external boundary of $\mathcal{D}$ can be chosen as lines of constant x or constant y, except for the part of the boundary close to the v-axis and above the $du/d\tau = 0$ nullcline. For this part it is useful to note that, for c constant and u small,

$$\frac{d}{d\tau}(u - cv) \simeq \frac{c\beta v^2}{u} + u(1 - \frac{\alpha v}{\delta}) > 0 \quad \text{if } v^2 > \frac{u^2}{c\beta}(\frac{\alpha v}{\delta} - 1).$$

If u is small then a small positive c will ensure that this condition is statisfied.

We conclude that there is a stable limit cycle in $\mathcal{D}$ provided that (u_0, u_0) is unstable, i.e. if $\mathrm{Tr}J > 0$, i.e. if

$$\beta < \frac{\alpha u_0^2}{(u_0 + \delta)^2} - u_0$$

Further insight follows by considering how the quantity on the right-hand side of the above inequality, $B(\alpha, \delta)$, say, varies with δ for fixed α, remembering that δ is the positive root of $\alpha u_0 = \delta + (1 - \delta)u_0 - u_0^2$ (so only two of α, δ and u_0 are independent).

As $\delta \to 0^+$ then $u_0 \to 1 - \alpha$ and $B(\alpha, \delta) \to 2\alpha - 1$. As $\delta \to \infty$ then $u_0 \to 1 - \alpha/\delta \simeq 1$ and $B(\alpha, \delta) \to -1 + \alpha/\delta^2 \simeq -1$.

The condition for $B(\alpha, \delta) = 0$ is that $\delta^2 + 2(1 + \alpha)\delta + 1 - 2\alpha = 0$. This has one positive root for δ if $\alpha > \frac{1}{2}$ and no positive roots if $\alpha < \frac{1}{2}$.

It follows that if $\alpha < \frac{1}{2}$ then $B(\alpha, \delta) < 0$ for all δ, therefore (u_0, u_0) is stable and there is no limit cycle for any choice of β. If $\alpha > \frac{1}{2}$ then $\delta > \sqrt{\alpha^2 = 4\alpha} - 1 - \alpha$ implies that $B(\alpha, \delta) < 0$, so again no limit cycle behaviour is possible for any choice of β. But if $\alpha > \frac{1}{2}$ and $\delta < \sqrt{\alpha^2 + 4\alpha} - 1 - \alpha$ then there is limit cycle behaviour for $0 \leq \beta < B(\alpha, \delta)$.

For numerical solution of the above equations see the MATLAB program `More general predator-prey equations`.

(ii) Excitable systems

Examples are: nerve impulses (the membrane electric potential must exceed a critical value before a signal is fired), heart muscle, plankton blooms.

We consider the Fitzhugh-Nagumo model, which is a simplified version of the Hodgkin-Huxley model for initiation and propagation of nerve impulses. There are two variables $u(t)$, related to the membrane potential, and $v(t)$, related to everything else (e.g. ions) which tend to bring the system back to its quiet state. In this analysis spatial variation is ignored. Note that all variables have been suitably scaled to simplify the equations.

$$\begin{aligned} \frac{du}{dt} &= c(v + u - \tfrac{1}{3}u^3 + z(t)) = f(u, v; z) \\ \frac{dv}{dt} &= -(\frac{u - a + bv}{c}) = g(u, v), \end{aligned}$$

where $1 - \frac{2}{3}b < a < 1$, $0 < b < 1$ and $b < c^2$ (and we will take $c \gg 1$). The $z(t)$ appearing in the first equation is a forcing term.

First consider $z = 0$. Then the nullclines are

$$\begin{aligned} v &= \tfrac{1}{3}u^3 - u \qquad (\frac{du}{dt} = 0) \\ v &= \frac{a - u}{b} \qquad (\frac{dv}{dt} = 0). \end{aligned}$$

Exercise: Verify that the quoted inequalities imply that there is one fixed point (u_*, v_*) and it is to the right of the minimum of the $du/dt = 0$ nullcline (i.e. $u_* > 1$).

To determine the stability of the fixed point consider the Jacobian J evaluated at (u_*, v_*):

$$J = \begin{pmatrix} c(1-u_*)^2 & c \\ -\frac{1}{c} & -\frac{b}{c} \end{pmatrix}.$$

$\mathrm{Tr}J = c(1-u_*^2) - b/c < 0$ if $u_* > 1$. (Since $c \gg 1$ the 'if' is almost an 'only if'.)

$\det J = -b(1-u_*^2) + 1 > 0$ since $b < 1$.

Hence (u_*, v_*) is stable.

Now consider a sudden excitation $(z = 0) \to (z = -V_0)$ (with $V_0 > 0$). The effect is that the $du/dt = 0$ nullcline moves upwards by an amount V_0. If before the excitation the system is at the fixed point (u_*, v_*) then what happens next?

$c \gg 1$ implies that changes in u are rapid relative to changes in v. If the system is away from the $du/dt = 0$ nullcline then it adjusts rapidly to 'find' it.

If $V_0 - \frac{2}{3} < (a - u_*)/b$ then the system simply moves quickly to the new steady state.

If $V_0 - \frac{2}{3} > (a - u_*)/b$ then the trajectory does not intersect the du/dt nullcline in $u > 1$ and continues to move in the negative u direction until it intersects the nullcline in $u < 0$ (actuallly $u < -1$). It then has $dv/dt > 0$ and moves rightwards along the nullcline to the maximum at $u = -1$, when it jumps to intersect the $du/dt = 0$ nullcline in $u > 1$. It now has $dv/dt < 0$ and moves leftward along the nullcline.

If V_0 is not too large then a stable fixed point persists and the system simply moves to this. If V_0 is larger then the fixed point becomes unstable and the system follows a limit cycle. (Consider how to use the Poincareé-Bendixson theorem to prove that the limit

cycle exists.) If V_0 is increased further then eventually the fixed point enters $u < -1$ and becomes stable, so the system converges to this.

The limit cycle is divided into two slow ('refractory') phases when $v \simeq \frac{1}{3}u^3 - u + V_0$ and two fast phases in which u changes rapidly and v is almost constant. The period of the limit cycle is dominated by the two slow phases, the first as (u, v) changes from $(-2, V_0 - \frac{2}{3})$ to $(-1, V_0 + \frac{2}{3})$ (P_1 to P_2) and the second as (u, v) changes from $(2, V_0 + \frac{2}{3})$ to $(1, V_0 - \frac{2}{3})$ (P_1' to P_2').

The time from P_1 to P_2 is estimated by

$$\int_{P_1}^{P_2} \frac{c}{a - u - bv}\, dv = c \int_{-2}^{-1} \frac{u^2 - 1}{a - u - b(\frac{1}{3}u^3 - u - V_0)}\, du$$

and similarly the time from P_1' to P_2' is estimated by

$$\int_{P_1'}^{P_2'} \frac{c}{a - u - bv}\, dv = c \int_{1}^{2} \frac{u^2 - 1)}{a - u - b(\frac{1}{3}u^3 - u - V_0)}\, du.$$

Adding the two integrals gives an estimate for the period as $cF(a, b, V_0)$ where $F(a, b, V_0)$ is determined by explicit evaluation of the integrals.

For numerical solution of the above system see the MATLAB program `Fitzhugh-Nagumo models`.

3 Stochastic models

Stochastic models are relevant to many biological systems, e.g. populations, epidemics, cell growth, random walks of organisms.

The primary example that we shall consider is populations, but the last part of this section is relevant to random walks in space, which will be important in §4.

Populations consist of discrete individuals and individual births or deaths are quasi-random events, which occur with a certain probability in a given time, not at a specified (deterministic) rate. This implies that population evolution cannot be predicted precisely, rather that the probability of a particular evolution can be given.

This section considers the probabilistic dynamics of populations and other systems, including estimates of fluctuations as well as evolution of the mean.

There are two important aspects of this.

1. An observation of a single realisation of an evolving system needs to be interpreted correctly. This is not the same as the evolution of the mean of many such systems.

2. Stochastic models and the corresponding deterministic models may have different behaviour, e.g. there may be a non-zero probability of extinction where the deterministic prediction is a non-zero steady state population.

In general differences between stochastic and the corresponding deterministic systems will be most significant in small systems, e.g. an epidemic in a small population, evolution of a chemical system with a relatively small number of molecules.

3.1 Discrete birth and death processes

We consider time-continuous Markov processes where the probability of a transition depends only on the current state, not on details on previous transitions or states.

(i) birth processes

Consider a very simple system that jumps at some random time from the starting state A to a second state B.

$P(A,t)$ is the probability of being in state A at time t.

$$\begin{aligned} P(A,t+\delta t) &= P(\text{ no jump in interval } (t,t+\delta)|\text{in state } A \text{ at time } t) \times P(A,t) \\ &= \{1 - P(\text{ jump in interval } (t,t+\delta)|\text{in state } A \text{ at time } t)\} \times P(A,t). \end{aligned}$$

Hence, taking the limit as $\delta t \to 0$,

$$\frac{\partial P(A,t)}{\partial t} = -\frac{\lim_{\delta t \to 0}\{P(\text{ jump in interval } (t,t+\delta)|\text{in state } A \text{ at time } t)\}}{\delta t} \times P(A,t)$$

The first factor on the right-hand side is the transition probability per unit time, which is the natural characterization of the system.

The simplest possible case is when the transition probability per unit time is a constant λ, say. Then

$$\frac{\partial P(A,t)}{\partial t} = -\lambda P(A,t).$$

Assume that $P(A,0) = 1$, then $P(A,t) = e^{-\lambda t}$ and hence $P(B,t) = 1 - e^{-\lambda t}$ since $P(A,t) + P(B,t) = 1$.

$P(\text{jump has occured by } t) = P(B,t) = 1 - e^{-\lambda t}$. This is the distribution function of the time T_J of the jump, hence the probability density function of T_J is $\partial P(B,t)/\partial t = \lambda e^{-\lambda t}$.

It follows that

$$\begin{aligned} \langle T_J \rangle &= \int_0^\infty t\lambda e^{-\lambda t}\, dt = \frac{1}{\lambda} \\ \text{var}(T_J) &= \int_0^\infty t^2\lambda e^{-\lambda t}\, dt - \frac{1}{\lambda^2} = \frac{1}{\lambda^2} \\ \sigma(T_J) &= \frac{1}{\lambda}. \end{aligned}$$

Note that fluctuations are important in this system (the standard deviation is as large as the mean).

An example of a more complicated system is one with states $\{0, 1, 2, \ldots, n, \ldots\}$ where the probability per unit time of a jump from state n to state $n+1$ is λ.

$$0 \xrightarrow{\lambda} 1 \xrightarrow{\lambda} 2 \xrightarrow{\lambda} 3 \xrightarrow{\lambda} 4 \ldots \xrightarrow{\lambda} n \xrightarrow{\lambda} \ldots$$

$P(n,t)$ is the probability of being in state n at time t.

Assume initial conditions $P(0,0) = 1$ and $P(n,0) = 0$ for $n \geq 1$.

As before consider $P(n, t+\delta t)$ for $n \geq 1$

$$\begin{aligned} P(n,t+\delta t) &= P(\text{no jump in } (t,t+\delta t) | \text{in state } n \text{ at } t) \\ &\quad + P(\text{jump in } (t,t+\delta t) | \text{in state } n-1 \text{ at } t) \\ &\quad + P(\text{2 jumps in } (t,t+\delta t) | \text{in state } n-2 \text{ at } t) + \ldots \\ &\simeq \lambda\delta t P(n-1,t) + (1-\lambda\delta t)P(n,t) + O(\delta t^2) \end{aligned}$$

Hence

$$\frac{\partial P(n,t)}{\partial t} = \lambda\{P(n-1,t) - P(n,t)\} \qquad (n \geq 1) \tag{12}$$

The above may also be considered to hold for $n = 0$ if we impose $P(-1,t) = 0$.

This is a probability balance equation or *master equation*, taking the form of a differential equation in t and a difference equation in n.

There are range of techniques available to solve this equation, one being to use a generating function (recall IA Probability). Define

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

There is a boundary condition on ϕ implied by the normalisation condition on the $P(n,t)$

$$\phi(1,t) = \sum_{n=0}^{\infty} P(n,t) = 1$$

and the initial condition implies

$$\phi(s,0) = P(0,0) = 1.$$

The following are useful general properties of ϕ.

$$\begin{aligned}
P(n,t) &= \frac{1}{n!}\left(\frac{\partial}{\partial s}\right)^n \phi(s,t)|_{s=0} \\
\langle n\rangle &= \sum_{n=0}^{\infty} nP(n,t) = \frac{\partial \phi}{\partial s}|_{s=1} \\
\langle n^2\rangle &= \sum_{n=0}^{\infty} n^2 P(n,t) = \sum_{n=0}^{\infty} n(n-1)P(n,t) + \sum_{n=0}^{\infty} nP(n,t) = \frac{\partial^2 \phi}{\partial s^2}|_{s=1} + \frac{\partial \phi}{\partial s}|_{s=1} \\
\sigma^2 &= \langle n^2\rangle - \langle n\rangle^2 = \frac{\partial^2 \phi}{\partial s^2}|_{s=1} + \frac{\partial \phi}{\partial s}|_{s=1} - \left(\frac{\partial \phi}{\partial s}|_{s=1}\right)^2
\end{aligned}$$

Using (12) we may deduce an equation for ϕ as follows.

$$\begin{aligned}
\frac{\partial \phi}{\partial t} &= \sum_{n=0}^{\infty} s^n \frac{\partial P(n,t)}{\partial t} = \lambda \sum_{n=0}^{\infty} s^n \{P(n-1,t) - P(n,t)\} \\
&= \lambda\{s\sum_{n=0}^{\infty} s^{n-1}P(n-1,t) - \sum_{n=0}^{\infty} s^n P(n,t)\} = \lambda(s-1)\phi
\end{aligned}$$

where the last step has used $P(-1,t) = 0$.

Hence

$$\phi(s,t) = \phi(s,0)e^{\lambda(s-1)t} = e^{\lambda(s-1)t} = \sum_{n=0}^{\infty} \frac{(\lambda t)^n}{n!} e^{-\lambda t} s^n.$$

.

It follows that $P(n,t) = e^{-\lambda t}(\lambda t)^n/n!$ which is a Poisson distribution with properties

$$\begin{aligned}
\langle n\rangle &= \frac{\partial \phi}{\partial s}|_{s=1} = \lambda t e^{\lambda(s-1)t}|_{s=1} = \lambda t \\
\langle n^2\rangle &= \frac{\partial^2 \phi}{\partial s^2}|_{s=1} + \frac{\partial \phi}{\partial s}|_{s=1} = \lambda^2 t^2 + \lambda t \\
\sigma^2 &= \langle n^2\rangle - \langle n\rangle^2 = \lambda t.
\end{aligned}$$

Note that $\sigma/\langle n\rangle = (\lambda t)^{-1/2} \to 0$ as $t \to \infty$, so fluctuations become (relatively) less important for large t.

The corresponding deterministic system would be described by $dN/dt = \lambda$ with $N(0) = 0$, so in this case the evolution of $\langle n \rangle$ matches N, i.e. the mean of the stochastic system follows the evolution of the deterministic system, and the effect of stochasticity is simply to introduce fluctuations about the mean.

(ii) birth and death processes

Extend the Poisson process defined above, by adding a probability of death per unit time and per member of population β.

$$n-1 \underset{\beta n}{\overset{\lambda}{\rightleftarrows}} n \underset{\beta(n+1)}{\overset{\lambda}{\rightleftarrows}} n+1$$

If the above applies for $n \geq 1$ then strictly speaking it is a birth + death + immigration process, since the population can increase even when $n = 0$.

The corresponding master equation is

$$\frac{\partial P(n,t)}{\partial t} = \lambda\{P(n-1,t) - P(n,t)\} + \beta\{(n+1)P(n+1,t) - nP(n,t)\}$$

(where as previously we can regard this equation as holding for all $n \geq 0$ providing we take $P(-1,t) = 0$).

It is useful to use the generating function $\phi(s,t)$ defined previously. Then

$$\begin{aligned} \frac{\partial \phi}{\partial t} &= \sum_{n=0}^{\infty} s^n \frac{\partial P(n,t)}{\partial t} = \sum_{n=0}^{\infty} \lambda\{P(n-1,t) - P(n,t)\}s^n + \beta\{(n+1)P(n+1,t) - nP(n,t)\}s^n \\ &= \lambda(s-1)\phi + \beta(1-s)\frac{\partial \phi}{\partial s} = (s-1)(\lambda\phi - \beta\frac{\partial \phi}{\partial s}). \end{aligned}$$

Apply the initial condition $\phi(s,0) = 1$ (corresponding to $n = 0$ at $t = 0$).

The partial differential equation for ϕ could be solved by transforming to a wave equation (recall IB Methods), but instead seek a solution of the form $\phi(s,t) = \exp\{(s-1)f(t)\}$ with $f(0) = 0$. Note that the constraint $\phi(1,t)$ is satisfied by construction. Substituting into the partial differential equation gives

$$(s-1)f'(t) = (s-1)(\lambda - \beta f(t)),$$

hence $f(t) = \lambda(1 - e^{-\beta t})/\beta$ and

$$\phi(s,t) = \exp\{(s-1)\frac{\lambda}{\beta}(1 - e^{-\beta t})\}.$$

It is straightforward to show that $\langle n\rangle = \lambda(1-e^{-\beta t})/\beta$, $\langle n(n-1)\rangle = \lambda^2(1-e^{-\beta t})^2/\beta^2$ and hence that $\mathrm{var}(n) = \langle n\rangle$, for all t.

As $t \to \infty$ we have $\phi(s,t) \to \exp\{(s-1)\lambda/\beta\}$, so the system tends to a steady stage probability distribution $P(n)$ with

$$P(n) = e^{-\lambda/\beta}\left(\frac{\lambda}{\beta}\right)^n \frac{1}{n!}$$

which is a Poisson distribution with mean λ/β. (Note that this could also have been deduced by solving the steady-state limit of the partial differential equation for ϕ.)

A generalisation of the above is where birth results in M new individuals, hence

$$\frac{\partial P(n,t)}{\partial t} = \lambda\{P(n-M,t) - P(n,t)\} + \beta\{(n+1)P(n+1,t) - nP(n,t)\}.$$

The corresponding equation for the generating function $\phi(s,t)$ is

$$\frac{\partial \phi}{\partial t} = \lambda(s^M - 1)\phi + \beta(1-s)\frac{\partial \phi}{\partial s}.$$

In the steady state this implies

$$\frac{\partial \phi}{\partial s} = \frac{\lambda}{\beta}\frac{(s^M-1)}{s-1}\phi$$

which can be solved subject to the boundary condition $\phi = 1$ at $s = 1$.

Even though in this case there is a relatively simple expression for the steady-state form of ϕ, the corresponding expression for the time evolving form will be complicated. Cases where closed form expression for ϕ, either the complete time evolution or in the steady state, are relatively few. Therefore it is worth considering other approaches to analysing the system.

One is to construct evolution equations for $\langle n\rangle$ and for higher moments. This is done as follows for the case above.

$$\begin{aligned}
\frac{d\langle n\rangle}{dt} &= \sum_{n=0}^{\infty} n\frac{\partial P(n,t)}{\partial t} = \lambda\sum_{n=0}^{\infty} n\{P(n-M,t) - P(n,t)\} + \beta\sum_{n=0}^{\infty} n\{(n+1)P(n+1,t) - nP(n,t)\} \\
&= \lambda\sum_{n=0}^{\infty}\{(n-M)P(n-M,t) - nP(n,t) + MP(n-M,t)\} \\
&\quad +\beta\sum_{n=0}^{\infty}\{n(n+1)P(n+1,t) - n(n-1)P(n,t) - nP(n,t)\} \\
&= \lambda\langle n\rangle - \lambda\langle n\rangle + M + \beta\langle n(n-1)\rangle - \beta\langle n(n-1)\rangle - \beta\langle n\rangle \\
&= M - \beta\langle n\rangle.
\end{aligned}$$

The approach in this calculation has been to rearrange to give terms that cancel when summed. The calculation has also relied on the fact that $P(r,t) = 0$ for $r < 0$.

The result is a self-contained differential equation for $\langle n \rangle$ which may be solved to give

$$\langle n \rangle = \frac{\lambda M}{\beta}(1 - e^{-\beta t})$$

assuming that $\langle n \rangle = 0$ when $t = 0$. (An alternative initial condition simply adds a constant.)

In same way an evolution equation for $\langle n^2 \rangle$ can be constructed as

$$\begin{aligned}
\frac{d\langle n^2 \rangle}{dt} &= \sum_{n=0}^{\infty} n^2 \frac{\partial P(n,t)}{\partial t} = \lambda \sum_{n=0}^{\infty} n^2 \{P(n-M,t) - P(n,t)\} \\
&\quad + \beta \sum_{n=0}^{\infty} n^2 \{(n+1)P(n+1,t) - nP(n,t)\} \\
&= \lambda(\langle (n+M)^2 \rangle - \langle n^2 \rangle) + \beta(\langle (n-1)^2 n \rangle - \langle n^3 \rangle) \\
&= \lambda M^2 + (2M\lambda + \beta)\langle n \rangle - 2\beta \langle n^2 \rangle.
\end{aligned}$$

This may be solved, exploiting the previously obtained expression for $\langle n \rangle$, to give $\langle n^2 \rangle$ as a function of t.

In the example above, the equations for $\langle n \rangle$ and the equation for $\langle n^2 \rangle$ are both closed, i.e. neither equation relies on knowledge of higher-order moments. In general this does not hold and the equation for $d\langle n^p \rangle / dt$ depends on $\langle n^q \rangle$ where $q > p$ (e.g. see Q2 on Example Sheet 2). Solution is therefore possible only by making some kind of approximation which estimates higher-order moments in terms of lower-order moments.

It is also the case in the example above that the evolution of $\langle n \rangle$ is as would be expected from the corresponding deterministic system $dN/dt = M\lambda - \beta N$. Therefore, again, the effect of stochasticity in this system is simply to introduce fluctuations about the mean, rather than to affect the evolution of the mean itself. This does not hold in general.

(iii) extinction

The existence of a steady state probability distribution in the above examples depends crucially on the inclusion of immigration. If there is no immigration, i.e. the jump from $n = 0$ to $n = 1$ is not allowed then the behaviour of the system is changed and there is the possibility of extinction.

Consider the system

$$n-1 \underset{d(n)}{\overset{b(n-1)}{\rightleftarrows}} n \underset{d(n+1)}{\overset{b(n)}{\rightleftarrows}} n+1$$

so that $b(n)$ is the rate of birth in state n and $d(n)$ is the rate of death in state n. The possibility of extinction is allowed by taking $b(0) = 0$.

Let $P_e(m)$ be the probability of extinction if the initial population is m. Then, conditioning on the first step, it follows that

$$\begin{aligned} P_e(m) &= \{\text{probability that first jump is } m \to m-1\} \times P_e(m-1) \\ &\quad + \{\text{probability that first jump is } m \to m+1\} \times P_e(m+1) \\ &= \frac{d(m)}{b(m)+d(m)} P_e(m-1) + \frac{b(m)}{b(m)+d(m)} P_e(m+1). \end{aligned}$$

Rearranging the above gives

$$\{P_e(m+1) - P_e(m)\} = \frac{d(m)}{b(m)} \{P_e(m) - P_e(m-1)\}$$

and hence

$$P_e(m+1) - P_e(m) = S_m \{P_e(1) - P_e(0)\} = S_m \{P_e(1) - 1\}$$

where

$$S_m = \prod_{l=1}^{m} \frac{d(l)}{b(l)}.$$

Therefore

$$P_e(m+1) = \left(\sum_{l=1}^{m} S_l \right) \{P_e(1) - 1\} + P_e(1).$$

If $\sum_{l=1}^{m} S_l$ diverges as $m \to \infty$ then, since $P_e(m+1) \leq 1$, it must be the case that $P_e(1) = 1$ and hence $P_e(n) = 1$ for all $n \geq 0$. Extinction is therefore inevitable.

Note in particular that in any resource limited population we expect $d(l) > b(l)$ for large l, implying that S_l does not tend to zero, hence that $\sum_{l=1}^{m} S_l$ diverges, hence extinction is inevitable. (This holds in particular for the examples considered in the previous section if there is no immigration.)

A similar calculation gives $T_e(m)$, the time to extinction from state m.

The evolution of a birth-death system without immigration and with a logistic type of representation of birth and death is simulated by the MATLAB program `logistic birth-death model`.

The stochasticity in the above systems comes from the probabilistic nature of individual birth and death events. Another important source of stochasticity is *environmental stochasticity* – where for example the birth and death rates $b(n)$ and $d(n)$ may themselves be random variables sampled from an appropriate distribution.

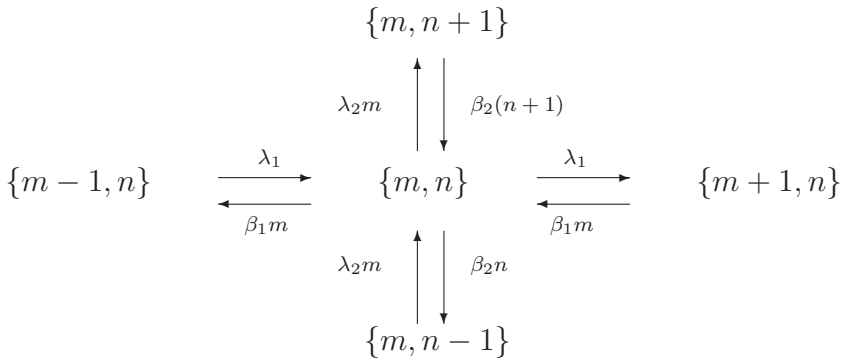
(iv) Multivariate master equations

Consider a system where two random variables interact, e.g. predator-prey, or population plus environment.

Two interacting populations of m wildebeest and n flies.

Birth rate of wildebeest is λ_1 and death rate is $\beta_1 m$.

Birthrate of flies is $\lambda_2 m$ (depends on wildebeest) and death rate is $\beta_2 n$ (depends on flies).



$$\frac{\partial P(m,n,t)}{\partial t} = \lambda_1\{P(m-1,n,t) - P(m,n,t)\} + \beta_1\{(m+1)P(m+1,n,t) - mP(m,n,t)\}$$
$$+\lambda_2 m\{P(m,n-1,t) - P(m,n,t)\} + \beta_2\{(n+1)P(m,n+1,t) - nP(m,n,t)\}$$

Now use the method of (ii) above to consider the rate of change of various moments.

$$\frac{d\langle m\rangle}{dt} = \lambda_1 - \beta_1\langle m\rangle$$

as before (since there is no effect of n on the evolution of m.

$$\frac{d\langle n\rangle}{dt} = \sum_{m,n} \lambda_1 n\{P(m-1,n,t) - P(m,n,t)\} + \beta_1 n\{(m+1)P(m+1,n,t) - mP(m,n,t)\}$$
$$+\lambda_2 mn\{P(m,n-1,t) - P(m,n,t)\} + \beta_2\{n(n+1)P(m,n+1,t) - n^2P(m,n,t)\}$$
$$= \lambda_1\langle n\rangle - \lambda_1\langle n\rangle + \beta_1\langle nm\rangle - \beta_1\langle nm\rangle + \lambda_2\langle m(n+1)\rangle - \lambda_2\langle mn\rangle + \beta_2\langle n(n-1)\rangle - \beta_2\langle n^2\rangle$$
$$= \lambda_2\langle m\rangle - \beta_2\langle n\rangle,$$

so $\langle n\rangle = \lambda_2\langle m\rangle/\beta_2$ in the steady state.

Similarly it can be shown that

$$\frac{d\langle n^2\rangle}{dt} = \lambda_2(2\langle mn\rangle + \langle m\rangle) + \beta_2(\langle n\rangle - 2\langle n^2\rangle)$$

(fluctuations in n depend on correlations between m and n)

$$\frac{d\langle mn\rangle}{dt} = 2\lambda_2\langle m^2\rangle + \lambda_1\langle n\rangle - (\beta_1+\beta_2)\langle mn\rangle.$$

Hence in the steady state:

$$\begin{aligned}\langle n^2\rangle &= \tfrac{1}{2}\langle n\rangle + \frac{\lambda_2}{\beta_2}(\langle mn\rangle + \tfrac{1}{2}\langle m\rangle)\\ &= \langle n\rangle + \frac{\lambda_2}{\beta_2}\langle mn\rangle.\end{aligned}$$

$$\begin{aligned}\mathrm{var}(n) &= \langle n\rangle + \frac{\lambda_2}{\beta_2}\langle mn\rangle - \langle n\rangle^2\\ &= \langle n\rangle + \frac{\lambda_2}{\beta_2}\{\langle mn\rangle - \langle m\rangle\langle n\rangle\}.\end{aligned}$$

The first term on the right-hand side represents intrinsic variability in n (present in the system without m) and the second term is extrinsic (fluctuations in n induced by fluctuations in m).

3.2 The Fokker-Planck equation

The Fokker-Planck equation is the continuous limit of the master equation.

(i) Single variable case

Consider a general one-variable master equation

$$\frac{\partial P}{\partial t} = \sum_{r=-\infty}^{\infty} W(x-r,r)P(x-r,t) - P(x,t)\sum_{r=-\infty}^{\infty} W(x,r)$$

where $W(x,r)$ is the probability per unit time of a jump from x to $x+r$. Note that we have used x as the variable describing the state of the system. In the master equation above x is allowed to take integer values.

We now regard $P(x,t)$ and $W(x,r)$ as smooth functions of the continuous variable x and expand them as Taylor series, retaining terms up to quadratic, so that

$$W(x-r,r)P(x-r,t) \simeq W(x,r)P(x,t) - \frac{\partial}{\partial x}\{rW(x,r)P(x,t)\} + \tfrac{1}{2}\frac{\partial^2}{\partial x^2}\{r^2W(x,r)P(x,t)\}.$$

Hence regarding x as a continuous variable, we deduce the *Fokker-Planck equation*

$$\frac{\partial}{\partial t}P(x,t) = -\frac{\partial}{\partial x}\{a_1(x)P(x,t)\} + \tfrac{1}{2}\frac{\partial^2}{\partial x^2}\{a_2(x)P(x,t)\},$$

where

$$\begin{aligned} a_1(x) &= \sum_{r=-\infty}^{\infty} rW(x,r) \\ a_2(x) &= \sum_{r=-\infty}^{\infty} r^2W(x,r) > 0. \end{aligned}$$

Note that we need to assume that $W(x,r)$ decreases sufficiently rapidly with $|r|$ that the above series converge.

The Fokker-Planck equation is a partial differential equation, rather than a mixed differential-difference equation and may therefore provide a convenient route to finding approximate soluations to the master equation.

The Fokker-Planck equation has the form of an 'advection-diffusion' equation (e.g. Part II Fluids). $a_1(x)$ represents a drift velocity in the x-direction leading to a displacement of the probability density function. $a_2(x) > 0$ represents a diffusivity, leading to the broadening of the probability density function.

The Fokker-Planck equation can be used to deduce the evolution of moments such as $\langle x\rangle$ and $\langle x^2\rangle$. (Motivated by the birth-death process where x is the number of individuals in the population, we assume that x is positive, but we might need to vary this assumption in other examples, e.g. a random walk in space.)

$$\begin{aligned} \frac{d}{dt}\langle x\rangle &= \int_0^\infty x\frac{\partial}{\partial t}P(x,t)\,dx \\ &= \int_0^\infty -x\frac{\partial}{\partial x}\{a_1(x)P(x,t)\} + \tfrac{1}{2}x\frac{\partial^2}{\partial x^2}\{a_2(x)P(x,t)\}\,dx \\ &= \int_0^\infty \big[\frac{\partial}{\partial x}\{-xa_1(x)P(x,t)\} + a_1(x)P(x,t) \\ &\quad +\tfrac{1}{2}\frac{\partial}{\partial x}\{x\frac{\partial}{\partial x}\{a_2(x)P(x,t)\}\} - \tfrac{1}{2}\frac{\partial}{\partial x}\{a_2(x)P(x,t)\}\big]\,dx \\ &= \langle a_1(x)\rangle \end{aligned}$$

where the integrals of terms of the form $(\partial/\partial x)(.)$ are assumed to vanish under appropriate boundary conditions. (For example, it might be assumed that $P(x,t) \to 0$ as $x \to \infty$.)

Using similar reasoning it follows that

$$\begin{aligned}\frac{d}{dt}\langle x^2\rangle &= \langle 2xa_1(x)\rangle + \langle a_2(x)\rangle \\ \frac{d}{dt}\mathrm{var}(x) &= \langle 2xa_1(x)\rangle - 2\langle x\rangle\langle a_1(x)\rangle + \langle a_2(x)\rangle = 2\mathrm{cov}(x, a_1(x)) + \langle a_2(x)\rangle,\end{aligned}$$

where $\mathrm{cov}(.,.)$ denotes the covariance of two variables.

As an example consider the birth-death process discussed previously. Here $W(x,1) = \lambda$, $W(x,-1) = \beta x$ and $W(x,r) = 0$ for $|r| \geq 2$.

Then $a_1(x) = \lambda - \beta x$ (the mean jump per unit time) and $a_2(x) = \lambda + \beta x$ (the mean square jump per unit time).

The corresponding Fokker-Planck equation is

$$\frac{\partial}{\partial t}P(x,t) = -\frac{\partial}{\partial x}\{(\lambda - \beta x)P(x,t)\} + \tfrac{1}{2}\frac{\partial^2}{\partial x^2}\{(\lambda + \beta x)P(x,t)\}$$

Then

$$\frac{d}{dt}\langle x\rangle = \langle a_1(x)\rangle = \lambda - \beta\langle x\rangle.$$

Hence if $\langle x\rangle = 0$ at t then

$$\langle x\rangle = \frac{\lambda}{\beta}(1 - e^{-\beta t}) \to \frac{\lambda}{\beta} \qquad \text{as } t \to \infty.$$

Note that this as precisely as predicted by solution of the master equation (assuming the same initial condition).

Correspondingly

$$\frac{d}{dt}\langle x^2\rangle = \langle 2xa_1(x)\rangle + \langle a_2(x)\rangle = \langle 2x(\lambda - \beta x)\rangle + \langle \lambda + \beta x\rangle = \lambda + (2\lambda + \beta)\langle x\rangle - 2\beta\langle x^2\rangle$$

and

$$\frac{d}{dt}\mathrm{var}(x) = \lambda + (2\lambda + \beta)\langle x\rangle - 2\beta\langle x^2\rangle - 2\lambda\langle x\rangle - 2\beta\langle x\rangle^2 = \lambda + \beta\langle x\rangle - 2\beta\mathrm{var}(x).$$

Using the expression for $\langle x\rangle$ and applying the initial condition $\mathrm{var}(x) = 0$ at $t = 0$ it follows that

$$\mathrm{var}(x) = \frac{\lambda}{\beta}(1 - e^{-\beta t}).$$

Again this is exactly as predicted by solution of the master equation, i.e. the Fokker-Planck equation predicts the first two moments exactly in this case.

But there are differences between the predictions of the master equation and of the Fokker-Planck equation for higher moments. For example the Fokker-Planck equation predicts

$$\langle x^3 \rangle = \lambda^3 t^3 + 3\lambda^2 t^2,$$

whereas the master equation predicts

$$\langle n^3 \rangle = \lambda^3 t^3 + 3\lambda^2 t^2 + \lambda t,$$

though note that these are in agreement for large t (in the sense that the ratio between them tends to 1). These differences are to be expected given the neglect of higher-order terms in the Taylor series in going from the master equation to the Fokker-Planck equation.

Even with the simple forms of $a_1(x)$ and $a_2(x)$ in the above example it is not possible to solve the Fokker-Planck equation in closed form. Therefore it is useful to seek approximate solutions.

A potentially useful approximation in the steady state is that the factor $a_2(x)$ (which varies with x) may be replaced by $a_2(\langle x \rangle)$ (which is constant).

For the example above, in the steady state $\langle x \rangle = \lambda/\beta$, hence $a_2(x) = 2\lambda$ and the corresponding approximate form of the steady state Fokker-Planck equation is

$$-\frac{\partial}{\partial x}\{(\lambda - \beta x)P(x)\} + \tfrac{1}{2}\frac{\partial^2}{\partial x^2}\{2\lambda P(x)\} = 0$$

(note that the t dependence of P has been suppressed). Integrating once implies

$$-(\lambda - \beta x)P(x) + \frac{\partial}{\partial x}\{\lambda P(x)\} = C$$

where C is a constant. The boundary condition $P \to 0$ as $x \to \infty$ implies that that $C = 0$. Integrating again gives

$$P(x) = A \exp(-\frac{\beta}{2\lambda}(x - \frac{\lambda}{\beta})^2),$$

i.e. a Gaussian distribution restricted to $x > 0$, where the constant A is determined by the normalisation condition $\int_0^\infty P\,dx = 1$. Note that $P(0) = A\exp(-\lambda/2\beta)$ so if $\lambda \gg \beta$ then the normalisation condition is very closely approximated by $\int_{-\infty}^{\infty} P\,dx = 1$ and hence $A = (\beta/2\pi\lambda)^{1/2}$.

The mean of the Gaussian distribution is λ/β and the variance is also λ/β consistent with previous expressions.

Note that in deriving this approximate solution we have neglected the variation of $a_2(x)$ away from its value 2λ at $x = \lambda/\beta$. Noting that the standard deviation is $(\lambda/\beta)^{1/2}$ this may be justified provided that $\beta(\lambda/\beta)^{1/2} \ll \lambda$ i.e. if $\lambda/\beta \gg 1$.

Finally, recall that in most birth-death problems without immigration there is no steady probability distribution (or rather the steady distribution is concentrated at zero population). However if the time for extinction is typically large, then it may be useful to consider a quasi-steady distribution (e.g. the distribution conditioned on the fact that extinction has not yet occurred) and approximate steady-state solutions to the Fokker-Planck equation may be useful.

(ii) Generalisation to the multivariate case

We now consider the state of the system at time t to be described by a vector $\mathbf{x}$ where the components of $\mathbf{x}$ are integers. The master equation for $P(\mathbf{x}, t)$ is

$$\frac{\partial}{\partial t}P(\mathbf{x},t) = \sum_{\mathbf{r}} W(\mathbf{x}-\mathbf{r},\mathbf{r})P(\mathbf{x}-\mathbf{r},t) - \sum_{\mathbf{r}} W(\mathbf{x},\mathbf{r})P(\mathbf{x},t)$$

where by analogy with the single variable case $W(\mathbf{x}, \mathbf{r})$ is the probability per unit time of a jump from $\mathbf{x}$ to $\mathbf{x} + \mathbf{r}$ and the summation is over all possible jumps $\mathbf{r}$.

We now exploit Taylor's theorem for functions of several variables, which implies that

$$f(\mathbf{x}-\mathbf{r}) \simeq f(\mathbf{x}) - \sum_i r_i \frac{\partial f}{\partial x_i}(\mathbf{x}) + \tfrac{1}{2}\sum_{i,j} r_i r_j \frac{\partial^2 f}{\partial x_i \partial x_j}(\mathbf{x})$$

where the subscripts denote individual components of vector quantities.

Hence, making the above approximation,

$$\begin{aligned}\frac{\partial}{\partial t}P(\mathbf{x},t) &= -\sum_i \frac{\partial}{\partial x_i}\{P(\mathbf{x},t)\sum_{\mathbf{r}} r_i W(\mathbf{x},\mathbf{r})\} + \tfrac{1}{2}\sum_{i,j}\frac{\partial^2}{\partial x_i \partial x_j}\{P(\mathbf{x},t)\sum_{\mathbf{r}} r_i r_j W(\mathbf{x},\mathbf{r})\} \\ &= -\sum_i \frac{\partial}{\partial x_i}\{A_i(\mathbf{x})P(\mathbf{x},t)\} + \tfrac{1}{2}\sum_{i,j}\frac{\partial^2}{\partial x_i \partial x_j}\{B_{ij}(\mathbf{x})P(\mathbf{x},t)\}\end{aligned}$$

where the vector $A_i(\mathbf{x})$ and the $n \times n$ symmetric positive-semidefinite matrix $B_{ij}(\mathbf{x})$ are defined by the second equality and we now regard the variable $\mathbf{x}$ as continuously varying.

The above equation can be written more compactly if we use the summation convention as

$$\frac{\partial}{\partial t}P(\mathbf{x},t) = -\frac{\partial}{\partial x_i}\{A_i(\mathbf{x})P(\mathbf{x},t)\} + \tfrac{1}{2}\frac{\partial^2}{\partial x_i \partial x_j}\{B_{ij}(\mathbf{x})P(\mathbf{x},t)\}.$$

As for the one-variable case, we can obtain information directly from the Fokker-Planck equation about moments.

$$\begin{aligned}\frac{d}{dt}\langle x_k\rangle &= \int -x_k\frac{\partial}{\partial x_i}(A_iP)+\tfrac{1}{2}x_k\frac{\partial^2}{\partial x_i\partial x_j}(B_{ij}P)\,dV(\mathbf{x})\\ &= \int -\frac{\partial}{\partial x_i}(x_kA_iP)+\tfrac{1}{2}\frac{\partial}{\partial x_i}\{x_k\frac{\partial}{\partial x_j}(B_{ij}P)\\ &\qquad -\tfrac{1}{2}\delta_{ik}\frac{\partial}{\partial x_j}(B_{ij}P)+A_kP\,dV(\mathbf{x})\\ &= \langle A_k(\mathbf{x})\rangle\end{aligned}$$

where the integral is taken over all of $\mathbf{x}$-space and, again, integrals of terms of the form $(\partial/\partial x_l)(.)$ are assumed to vanish under appropriate boundary conditions.

Similarly,

$$\begin{aligned}\frac{d}{dt}\langle x_kx_l\rangle &= \int -x_kx_l\frac{\partial}{\partial x_i}(A_iP)+\tfrac{1}{2}x_kx_l\frac{\partial^2}{\partial x_i\partial x_j}(B_{ij}P)\,dV(\mathbf{x})\\ &= \int -\frac{\partial}{\partial x_i}(x_kx_lA_iP)+\tfrac{1}{2}\frac{\partial}{\partial x_i}\{x_kx_l\frac{\partial}{\partial x_j}(B_{ij}P)\}\\ &\qquad -\tfrac{1}{2}(x_l\delta_{ik}+x_k\delta_{il})\frac{\partial}{\partial x_j}(B_{ij}P)+(x_lA_k+x_kA_l)P\,dV(\mathbf{x})\\ &= \int -\frac{\partial}{\partial x_i}(x_kx_lA_iP)+\tfrac{1}{2}\frac{\partial}{\partial x_i}\{x_kx_l\frac{\partial}{\partial x_j}(B_{ij}P)\\ &\qquad -\tfrac{1}{2}\frac{\partial}{\partial x_j}\{(x_l\delta_{ik}+x_k\delta_{il})B_{ij}P\}+(x_lA_k+x_kA_l+B_{kl})P\,dV(\mathbf{x})\\ &= \langle x_lA_k+x_kA_l+B_{kl}\rangle.\end{aligned}$$

It follows from the two results above, using the symmetry of B_{kl} that

$$\frac{d}{dt}\mathrm{cov}(x_k,x_l)=\mathrm{cov}(x_k,A_l)+\mathrm{cov}(x_l,A_k)+\langle B_{kl}\rangle.$$

Now consider the case of small fluctuations about equilibrium already studied for a one variable system. We approximate $A_k(\mathbf{x})$ as a linear function of $\mathbf{x}$, $A_{kl}(\mathbf{x})\simeq a_{kl}(x_l-\langle x_l\rangle)$, where a_{kl} is constant, and B_{kl} as constant, $B_{kl}(\mathbf{x})\simeq B_{kl}(\langle\mathbf{x}\rangle)=b_{kl}$.

Then writing $C_{kl}=\mathrm{cov}(x_k,x_l)$ and substituting the above approximations in the equation for dC_{kl}/dt it follows that

$$\frac{d}{dt}C_{kl}=a_{km}C_{lm}+a_{lm}C_{km}+b_{kl}$$

or in matrix form

$$\frac{d}{dt}\mathbf{C} = \mathbf{AC} + \mathbf{CA}^T + \mathbf{B}.$$

This is an equation describing small fluctuations about equilibrium. (It is a version of the 'fluctuation-dissipation' relation.) The steady state form $\mathbf{AC} + \mathbf{CA}^T + \mathbf{B} = 0$ is a *Lyapunov equation* which appears in other contexts such as control theory.

To recap, what we have here is a procedure for estimating fluctuations about equilibrium for a general jump process. The first step is to derive a Fokker-Planck equation from the master equation. The second step is to derive expressions for mean and covariance, which in turn depend on estimates of the functions appearing in the Fokker-Planck equation. These estimates may be approximated by assuming that fluctuations are small.

3.3 Random walks, diffusion and Brownian motion

In §4 we will consider systems with spatial variations, so that communication between different spatial locations becomes important. This communication occurs in part through random processes, e.g. random motion of molecules or organisms.

Consider a simple 1-dimensional random walk, e.g. as considered in IA Probability.

Assume the starting position is the origin and that jumps occur at discrete time intervals τ. The jump is either to the left (-1) or to the right (+1), with equal probability of $\frac{1}{2}$ for each.

The discrete-time master equation for the probability $P(n,t)$ that the system is in state n at time t is

$$P(n,t+\tau) = P(n,t) + \tfrac{1}{2}\{P(n+1,t) + P(n-1,t) - 2P(n,t)\}.$$

Note that at this stage t takes the discrete values $0, \tau, 2\tau, 3\tau, \ldots, m\tau, \ldots$.

Now assume that τ is small, so that $P(n,t)$ can be regarded as function of the continuous variable t. It follows from the above (approximating $P(n,t+\tau)$ by a Taylor series in the second argument), that

$$\frac{\partial P(n,t)}{\partial t} = \frac{1}{2\tau}\{P(n+1,t) + P(n-1,t) - 2P(n,t)\}.$$

This is a continuous time master equation.

(Exercise: Check that the important property $(d/dt)\sum_n P(n,t) = 0$ is satisfied by the above equation.)

From this continuous time master equation we may also derive equations for $d\langle n\rangle/dt$ and $d\langle n^2\rangle/dt$.

$$\begin{aligned}\frac{d\langle n\rangle}{dt} &= \sum_n n\frac{\partial P(n,t)}{\partial t} = \frac{1}{2\tau}\sum_n\{nP(n+1,t) + nP(n-1,t) - 2nP(n,t)\} \\ &= \frac{1}{2\tau}\{\langle n-1\rangle + \langle n+1\rangle - 2\langle n\rangle = 0.\end{aligned}$$

Hence $\langle n\rangle$ is constant.

$$\begin{aligned}\frac{d\langle n^2\rangle}{dt} &= \sum_n n^2\frac{\partial P(n,t)}{\partial t} = \frac{1}{2\tau}\sum_n\{n^2P(n+1,t) + n^2P(n-1,t) - 2n^2P(n,t)\} \\ &= \frac{1}{2\tau}\{\langle(n-1)^2\rangle + \langle(n+1)^2\rangle - 2\langle n^2\rangle = \frac{1}{2\tau}\times 2 = \frac{1}{\tau}.\end{aligned}$$

Hence, if $\langle n\rangle = 0$ and $\langle n^2\rangle = 0$ at time $t = 0$, then $\langle n\rangle = 0$ for all t, $\langle n^2\rangle = \mathrm{var}(n) = t/\tau$ and $\sigma = (t/\tau)^{1/2}$. (Recall that τ is the time between jumps.)

We may also introduce an adjustable jump length by defining the variable $x = n\delta$, where δ is constant. Then $\langle x^2\rangle = \mathrm{var}(x) = \delta^2 t/\tau$.

If we now regard x as a continuous variable then the continuous time master equation reduces to a Fokker-Planck equation

$$\begin{aligned}\frac{\partial P(x,t)}{\partial t} &= \frac{1}{2\tau}\{P(x+\delta,t) + P(x-\delta,t) + -2P(x,t)\} \\ &\simeq \frac{(\delta-\delta)}{2\tau}\frac{\partial P(x,t)}{\partial x} + \frac{1}{2\tau}(\tfrac{1}{2}\delta^2 + \tfrac{1}{2}\delta^2)\frac{\partial^2 P(x,t)}{\partial x^2} \\ &= \frac{\delta^2}{2\tau}\frac{\partial^2 P(x,t)}{\partial x^2} = D\frac{\partial^2 P(x,t)}{\partial x^2},\end{aligned}$$

where $D = \delta^2/2\tau$ is the diffusivity resulting from a random walk with steps of size δ at time intervals τ.

In the above $P(x,t)$ is the probability density function of a single particle undergoing a random walk.

We can reinterpret $P(x,t)$ as the local concentration of particles in a large ensemble, with each particle undergoing an independent random walk.

$P(x,t)$ may then represent the concentration of pollutant molecules in a gas, or of solute molecules in a liquid, or of small particles † subject to bombardment by molecules in a liquid or of individual organisms in an unintelligent population. [† is the classical example of Brownian motion, observed by Robert Brown (1773-1858), Scottish botanist.]

Note that diffusivity D may be interpreted as

$$D = \frac{\delta^2}{2\tau} = \tfrac{1}{2}\left(\frac{\delta}{\tau}\right)^2 \times \tau = \tfrac{1}{2}\text{velocity fluctuation}^2 \times \text{correlation time for velocity fluctuations}$$

For a particle of mass m in a viscous liquid, thermodynamics suggests that $m\langle v^2\rangle = k_B T$ where, $\langle v^2\rangle$ is mean squared velocity, k_B is Boltzmann's constant and T is temperature.

Response of particle to a fluctuating force is related to the response to a steady applied force. The latter implies that

$$\tau = \frac{\text{mass} \times \text{terminal velocity}}{\text{weight}} = \frac{m}{6\pi\mu a},$$

where μ is viscosity and a is radius.

Hence

$$D = \frac{k_B T}{m} = \frac{k_B T \tau}{6\pi\mu a}.$$

This is the Stokes-Einstein relation.

For a solute molecule $a \sim 2\times 10^{-10}$m, hence

$$D = \frac{1.4\times 10^{-23}\times 270}{20\times 2\times 10^{-10}\times 10^{-3}} \sim 10^{-9}\text{m}^2\text{s}^{-1}.$$

For a bacterium $a \sim 2\times 10^{-10}$m, hence

$$D = \frac{1.4\times 10^{-23}\times 270}{20\times 2\times 10^{-6}\times 10^{-3}} \sim 10^{-13}\text{m}^2\text{s}^{-1}.$$

Note that the time scale $T \sim l^2/D$ for diffusion increases rapidly with distance l.

For a solute molecule diffusing across the width of a bacterium ($l \sim 10^{-6}$m), $T \sim 10^{-12}\text{m}^2$ / $10^{-9}\text{m}^2\text{s}^{-1} \sim 10^{-3}$s.

For a solute molecule diffusing across the width of an algal cell ($l \sim 10^{-1}$m), $T \sim 10^{-2}\text{m}^2$ / $10^{-9}\text{m}^2\text{s}^{-1} \sim 10^{7}$s.

(Bacteria can therefore rely on diffusion, but larger organisms cannot.)

4 Continuous systems with spatial structure

4.1 Transport equation and diffusion

We consider transport of 'stuff' in a domain $\mathcal{D}$ ('stuff' can be chemical pollutant, heat, organisms, etc).

Let $C(\mathbf{x}, t)$ be concentration of stuff per unit volume. Consider a fixed volume $\mathcal{V}$, a subset of $\mathcal{D}$, with bounding surface $\mathcal{S}$. Then the rate of increase of the total amount of stuff in $\mathcal{V}$ [(i)] is equal to the net rate of creation of stuff inside $\mathcal{V}$ ($F(\mathbf{x}, t)$ per unit volume) [(ii)] minus the rate at which stuff leaves $\mathcal{V}$ across the surface $\mathcal{S}$ (equal to the integral over $\mathcal{S}$ of the normal component of the flux $\mathbf{J}(\mathbf{x}, t)$ per unit area) [(iii)].

$$\underset{\text{(i)}}{\frac{d}{dt}\int_{\mathcal{V}} C\, dV} \;=\; \underset{\text{(ii)}}{\int_{\mathcal{V}} F(\mathbf{x}, t)\, dV} - \underset{\text{(iii)}}{\int_{\mathcal{S}} \mathbf{J}.\mathbf{n}\, dS}.$$

Now note that d/dt can be taken inside the integral (i) (because $\mathcal{V}$ is fixed) and that the divergence theorem can be used to convert the surface integral (iii) into a volume integral, to give

$$\int_{\mathcal{V}} \{\frac{\partial C}{\partial t} + \nabla.\mathbf{J} - F\}\, dV = 0.$$

Since this equation holds for any choice of the fixed volume $\mathcal{V}$ the integrand must vanish, hence

$$\frac{\partial C}{\partial t} + \nabla.\mathbf{J} = F.$$

This is the local expression of the contributions of transport and in-situ (net) creation to the rate of change of C.

What is the flux $\mathbf{J}$?

(1) If the background medium is a moving fluid, then stuff is carried along in the fluid. If the fluid velocity is $\mathbf{u}(\mathbf{x}, t)$ then the corresponding flux is

$$\mathbf{J}_u = C\mathbf{u} \qquad \text{advective flux.}$$

(2) If stuff is moving relative to the fluid (or moving in a background medium at rest) e.g. swimming, flying, sedimenting at velocity $\mathbf{v}(\mathbf{x}, t)$ then there is a flux

$$\mathbf{J}_v = C\mathbf{v} \qquad \text{non-advective flux.}$$

(3) In addition to (1) or (2) there is diffusion implying a flux

$$\mathbf{J}_D = -D\nabla C \qquad \text{diffusive flux (Fick's law, with diffusivity } D.).$$

The form of Fick's law may be motivated by considering diffusion as a consequence of random motion, as represented by the Fokker-Planck equation and then noting that the Fokker-Planck equation includes a probability flux that is in part proportional to $\nabla P(\mathbf{x}, t)$.

Combining the fluxes (1), (2) and (3) we have

$$\frac{\partial C}{\partial t} + \nabla.(C\mathbf{u} + C\mathbf{v} - D\nabla C) = F. \tag{13}$$

In the case when diffusion is the only transport process ($\mathbf{u} = \mathbf{v} = \mathbf{0}$) and there is no creation (or destruction) ($F = 0$) then this reduces to the diffusion equation

$$\frac{\partial C}{\partial t} = \nabla.(D\nabla C). \tag{14}$$

Note that this is a slight generalisation, to allow D to be non-constant, of the form you may have encountered previously, e.g. in IB Methods.

Note that partial differential equations of the above form need initial conditions, e.g. $C(\mathbf{x}, 0) = C_0(\mathbf{x})$, and boundary conditions, perhaps specifying C or the normal component of $\mathbf{J}$ on the boundary.

4.2 Solutions to the diffusion equation

(i) Steady diffusion with constant diffusivity

($\mathbf{u} = \mathbf{v} = \mathbf{0}$, $F = 0$.) (14) reduces to

$$\nabla^2 C = 0,$$

i.e. Laplace's equation (recall IB Methods). To specify a unique solution boundary conditions are required everywhere on the boundary of the domain of interest.

Example (a) 1-dimensional system, e.g. tube $0 \leq x \leq L$. Impose boundary conditions $C(0) = C_0$ and $C(L) = C_1$. (These are 'conducting' boundary conditions – the concentration C is maintained at a fixed value at the boundaries. This is a standard boundary condition when C is temperature.)

1-dimensional form of $\nabla^2 C = 0$ is $d^2C/dx^2 = 0$, hence fitting boundary conditions,

$$C(x) = C_0 + (C_1 - C_0)\frac{x}{L}$$

$$\text{Diffusive Flux in } x\text{-direction} \quad J = -DC_x = -\frac{D(C_1 - C_0)}{L}.$$

Flux is independent of x, required since $\nabla.\mathbf{J} = \partial J/\partial x = 0$.

Example (b) 3-dimensional system, e.g. hot sphere, $C = C_1$ on $|\mathbf{x}| = a$ and $C \to C_0$ as $|\mathbf{x}| \to \infty$, with C representing temperature.

$\nabla^2 C = 0$ with no angular dependence implied by boundary conditions, hence seek solution $C(r)$ with

$$\frac{1}{r^2}\frac{d}{dr}(r^2\frac{dC}{dr}) = 0$$

hence

$$r^2\frac{dC}{dr} = A$$

where A is constant, hence

$$C(r) = -\frac{A}{r} + B = C_0 + \frac{(C_1 - C_0)a}{r}$$

where B is constant and then A and B have been determined from the boundary conditions.

Rate of loss of heat from sphere is $4\pi a^2 \times (-DdC/dr|_{r=a}) = 4\pi aD(C_1 - C_0)$. (Note that $4\pi r^2 J_r$, with J_r radial component of flux, is constant.)

Example (c) plane geometry, e.g. rectangle $(0,0)$, $(a,0)$, (a,b), $(0,b)$ with $C = C_0$ on three sides, $C = C_1$ on side $(a,0),(a,b)$.

$$\nabla^2 C = 0 \quad \text{in } 0 < x < a,\ 0 < y < b.$$

Write $C = C_0 + \tilde{C}$, then $\nabla^2\tilde{C} = 0$ in $0 < x < a$, $0 < y < b$, with $\tilde{C} = 0$ on all boundaries except $\tilde{C} = (C_1 - C_0)$ on side $(a,0),(a,b)$.

Apply separation of variables technique. Consider solutions of the form $X(x)Y(y)$. $\nabla^2\{X(x)Y(y)\} = 0$ implies $X''(x)Y(y) + X(x)Y''(y) = 0$, hence

$$\frac{X''(x)}{X(x)} = \frac{Y''(y)}{Y(y)} = -\lambda^2$$

where λ is constant. Second equality follows because first expression is a function of x alone and second is a function of y alone. Consider solutions for $Y(y)$ that match boundary condition $\tilde{C}(x,0) = \tilde{C}(x,b) = 0$, implying $\lambda = n\pi/b$ where n is integer and $Y(y)\sin(n\pi y/b)$. Corresponding solution for $X(x)$ matching $\tilde{C}(0,y) = 0$ is $X(x) =$

$\alpha_n \sinh(n\pi x/b)$, where α_n is constant. Superposing all possible solutions and multiplying by suitable constants gives

$$C(x,y) = C_0 + (C_1 - C_0)\sum_{n=1}^{\infty} \alpha_n \sinh(\frac{n\pi x}{b}) \sin(\frac{n\pi y}{b}).$$

Now we choose the α_n so that the above fits the boundary condition on $x = a$, requiring

$$\sum_{n=1}^{\infty} \alpha_n \sinh(\frac{n\pi a}{b}) \sin(\frac{n\pi y}{b}) = 1$$

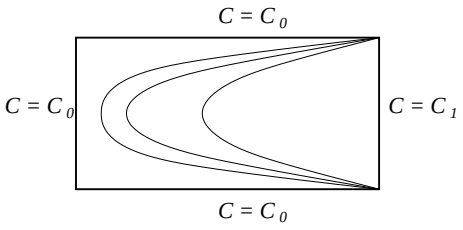
for all y.

Multiplying by $\sin(n\pi y/b)$ and integrating from $y = 0$ to $y = b$ implies

$$b\frac{1 - \cos m\pi}{m\pi} = \tfrac{1}{2} b\alpha_m \sinh(\frac{m\pi a}{b}).$$

Hence $\alpha_m = 2/\{m\pi \sinh(m\pi a/b)\}$ (m odd) and $\alpha_m = 0$ (m even) and

$$C(x,y) = C_0 + (C_1 - C_0) \sum_{n=1,\, n \text{ odd}}^{\infty} \frac{2}{n\pi \sinh(n\pi a/b)} \sinh(\frac{n\pi x}{b}) \sin(\frac{n\pi y}{b}).$$



(ii) Unsteady diffusion

Consider $C_t = C_{xx}$. If C is localised near $x = 0$ at $t = 0$ how does it evolve with time?

Apply boundary conditions $C \to 0$ as $|\mathbf{x}| \to \infty$ to above.

Consider total amount of stuff $\int_{-\infty}^{\infty} C\, dx = S$.

$$\frac{dS}{dt} = \int_{-\infty}^{\infty} \frac{\partial C}{\partial t}\, dx = \int_{-\infty}^{\infty} DC_{xx}\, dx = [DC_x]_{-\infty}^{\infty} = 0.$$

Hence S is constant.

Suppose length scale of initial concentration distribution is l_0.

Dimensional quantities appearing in the problem are S, l_0, x, t, D.

Corresponding dimensions are CL, L, L, T, L^2/T, where L is length, T is time and C has dimensions of concentration.

The only quantity containing dimensions of concentration is S, therefore $C(x,t) = S/\text{length} \times$ function of dimensionless variables.

Two dimensionless variables are $l_0/(Dt)^{1/2}$ and $x/(Dt)^{1/2}$. (All other dimensionless combinations of the variables can be expressed as functions of these two.) Therefore, without loss of generality,

$$C(x,t) = \frac{S}{(Dt)^{1/2}} \times \Phi(\frac{l_0}{(Dt)^{1/2}}, \frac{x}{(Dt)^{1/2}}).$$

We know that solutions of the diffusion equation spread in x with time, and therefore expect the initial length scale l_0 to have less and less effect as t increases. This suggests

$$C(x,t) = \frac{S}{(Dt)^{1/2}} F(\frac{x}{(Dt)^{1/2}}) = \frac{S}{(Dt)^{1/2}} F(\xi),$$

where ξ is defined by the second equality.

Now determine F by requiring that the above satisfies $C_t = DC_{xx}$.

$$C_t = -\frac{D}{2}\frac{S}{(Dt)^{3/2}} F(\xi) - \frac{D}{2}\frac{S}{(Dt)^{1/2}}\frac{x}{(Dt)^{3/2}} F'(\xi).$$

$$C_x = \frac{S}{Dt} F'(\xi), \qquad C_{xx} = \frac{S}{(Dt)^{3/2}} F''(\xi).$$

Hence

$$-\tfrac{1}{2}F - \tfrac{1}{2}\xi F' = F''.$$

Note that the left-hand side is $-\frac{1}{2}(\xi F)'$ and integrate to give $F' = -\frac{1}{2}\xi F$ where the constant of integration has been deduced to be zero from the boundary conditions.

Integrating again gives $F = A\exp(-\frac{1}{4}\xi^2)$.

The constraint $\int_{-\infty}^{\infty} C(x,t)\,dx$ implies that $\int_{-\infty}^{\infty} F\,d\xi = 1$, hence $A = 1/2\sqrt{\pi}$ and

$$C(x,t) = \frac{S}{2(\pi Dt)^{1/2}} \exp(-\frac{x^2}{4Dt}).$$

This is a *similarity solution.* Its x scale changes with time, but after scaling, its overall shape stays the same. (It has *self similar* form.)

We may calculate the moments of C, according to this similarity solution. $\int_{\infty}^{\infty} C\,dx = S$,

$\int_\infty^\infty xC\,dx = S$, $\int_\infty^\infty x^2 C\,dx = 2SDt$, etc. (Compare with previous results on solutions of the Fokker-Planck equation.)

Note that in the limit $t \to 0^+$, $\int_\infty^\infty C\,dx = S$, but $C(x,t) \to 0$ for all $|x| > 0$. Therefore $C(x,t) \to S\delta(x)$ (Dirac delta function).

The above similarity solution is therefore a Green's function for the initial-value problem for the diffusion equation and can be used to construct solutions with more general initial conditions, e.g. if $C = C_0(x)$ at $t = 0$ then

$$C(x,t) = \frac{1}{2(\pi Dt)^{1/2}} \int_{-\infty}^{\infty} C_0(x') \exp(-\frac{(x-x')^2}{4Dt})\,dx'.$$

We could take a more abstract approach to finding a similarity solution to $C_t = C_{xx}$, without using dimensional analysis.

Try $C(x,t) = t^\alpha G(x/t^\beta)$.

Then

$$C_t = \alpha t^{\alpha-1} G(\frac{x}{t^\beta}) - \beta t^{\alpha-\beta-1} G'(\frac{x}{t^\beta}).$$

$$C_{xx} = t^{\alpha-2\beta} G''(\frac{x}{t^\beta}).$$

Hence writing $\xi = x/t^\beta$

$$t^{\alpha-1}\{\alpha G(\xi) - \beta\xi G'(\xi)\} = Dt^{\alpha-2\beta} G''(\xi).$$

This equation balances only if $\beta = \frac{1}{2}$. But α remains undetermined.

α is determined by global conditions, e.g. if $\int_{-\infty}^{\infty} C\,dx$ is constant then $t^{\alpha+\beta}$ is constant, hence $\alpha = -\beta = -\frac{1}{2}$. (This is precisely what we determined earlier by dimensional analysis.) But a different global condition may be applied, e.g. if $\lim_{x\to\pm\infty} C$ is constant then $\alpha = 0$ and G satisfies the equation

$$-\tfrac{1}{2}\xi G'(\xi) = DG''(\xi).$$

Integration implies

$$G(\xi) = A\int_0^\xi \exp(-\tfrac{1}{4}\frac{s^2}{D})\,ds + B$$

where A and B are constants.

A useful choice of A and B is

$$G(\xi) = \frac{1}{\sqrt{\pi D}} \int_0^\xi \exp(-\tfrac{1}{4}\frac{s^2}{D})\,ds = 1 - \operatorname{erfc}(\frac{\xi}{2\sqrt{D}}).$$

where erfc(.) is the complementary error function. In this case $G(\xi) \to \pm 1$ as $\xi \to \pm\infty$. The corresponding form for $C(x,t)$ is

$$C(x,t) = 1 - \text{ erfc}(\frac{x}{2\sqrt{Dt}}).$$

As $t \to 0^+$ $C(x,t) \to 1$ for $x > 0$ and $C(x,t) \to -1$ for $x < 0$. The solution represents the adjustment under diffusion from an initial condition which is a sharp front between two regions in which C is constant.

Consider the rate of change of the total amount of stuff in the region $x > 0$.

$$\frac{d}{dt}\left[\int_0^\infty C(x,t)\,dx\right] = \int_0^\infty \frac{\partial C}{\partial t}\,dx = \int_0^\infty DC_{xx}\,dx = D[C_x]_0^\infty = -DC_x|_0$$

where the last step follows from the boundary condition $C_x \to 0$ as $x \to \infty$. (Verify from the similarity solution.) This is simply a statement that the rate of change of the total amount of stuff in $x > 0$ is equal to the diffusive flux (in the positive x direction) across $x = 0$. $-DC_x|_0$ may then be evaluated from the similarity solution to deduce that

$$\frac{d}{dt}\left[\int_0^\infty C(x,t)\,dx\right] = -D \times \frac{1}{\sqrt{\pi D}}\frac{\partial}{\partial x}\int_0^{x/t^{1/2}} \exp(-\tfrac{1}{4}\frac{s^2}{D})\,ds|_{x=0} = -\sqrt{\frac{D}{\pi t}}.$$

There are corresponding similarity solutions to the diffusion equation $C_t = D\nabla^2 C$ in higher dimensions. An expression of the form $C(\mathbf{x},t) = t^\alpha G(|\mathbf{x}|/t^\beta)$ can satisfy the equation if $\beta = \frac{1}{2}$, as in one dimension. The constant α is again determined by some other piece of information, perhaps associated with the initial conditions and/or boundary conditions. For example, if the total amount of stuff $\int C\,dV(\mathbf{x})$ (where $dV(\mathbf{x})$ is area in two dimensions and volume in three dimensions) is set by the initial condition and stays constant according to the boundary conditions, then $\alpha + \beta N = \alpha + \frac{1}{2}N = 0$, where N is the number of dimensions, and hence $\alpha = -\frac{1}{2}N$.

(iii) Semi infinite domain with oscillating end condition

Solve $C_t = DC_{xx}$ with $C(x,t) = C_1$ as $x \to \infty$ and $C(0,t) = C_0 \cos\omega t + C_1$. C_0, C_1 and ω are constants.

Seek an oscillatory solution ignoring any initial transients.

$$C = C_1 + C_0 \mathrm{Re}\{e^{i\omega t} f(x)\}$$

for some complex $f(x)$, with $f(0) = 1$ and $f(x) - \to 0$ as $x \to \infty$.

Substituting the above expression for $f(x)$ into the diffusion equation implies that$f(x)$ satisfies

$$i\omega f = Df''(x)$$

hence $f(x) = A_+ e^{\lambda x} + A_- e^{-\lambda x}$, where $\lambda^2 D = i\omega$. Take $\lambda = (1+i)(\omega/2D)^{1/2}$, then only the $e^{-\lambda x}$ part of the solution can satisfy the boundary condition as $x \to 0$ and hence

$$\begin{aligned} C &= C_1 + C_0 \mathrm{Re}\{\exp(i\omega t - (1+i)(\frac{\omega}{2D})^{1/2} x)\}, \\ &= C_1 + C_0 \exp(-(\frac{\omega}{2D})^{1/2} x) \cos(\omega t - (\frac{\omega}{2D})^{1/2} x) \end{aligned}$$

The exponential factor in the expression multiplying C_0 implies a decay scale $(2D/\omega)^{1/2}$. The argument of cos implies an oscillating structure in x which propagates in the positive x direction at speed $(2D\omega)^{1/2}$

If C is to represent chemical concentration $C_0 < C_1$ ensures that $C(x,t)$ is non-negative everywhere.

(iv) Initial value problem for finite domain

Consider $C_t = DC_{xx}$ with boundary conditions $C(0,t) = 0$ and $C(L,t) = C_0$ and initial condition $C(x,0) = f(x)$ where $f(0) = 0$ and $f(L) = C_0$ (for compatibility with the boundary conditions).

The steady solution that matches the boundary conditions is $C = C_0 x/L$. Therefore seek

a time-dependent solution of the form

$$C(x,t) = \frac{C_0 x}{L} + C_1(x,t)$$

satisfying $(C_1)_t = D(C_1)_{xx}$. $C_1(0,t) = 0$, $C_1(L,t) = 0$, $C_1(x,0) = f(x) - C_0 x/L$.

As in case (ii) separation of variables can be used to generate an appropriate solution. Here relevant solutions are of the form $T(t)X(x)$ with $T'(t)/T(t) = X''(x)/X(x) = -\lambda^2$, with λ constant. Possible values of λ^2 are eigenvalues for the problem $X''(x) = -\lambda^2 X(x)$ with $X(x)$ satisfying the boundary conditions, $X(0) = X(L) = 0$ in this case. (Refer back to IB Methods for details.)

The resulting expression for $C_1(x,t)$ is

$$C_1(x,t) = \sum_{n=1}^{\infty} A_n \sin(\frac{n\pi x}{L}) \exp(-\frac{n^2\pi^2 Dt}{L^2})$$

with the A_n following from the initial condition, which requires

$$\sum_{n=1}^{\infty} A_n \sin(\frac{n\pi x}{L}) = f_1(x), \quad \text{hence} \quad A_n = \frac{2}{L^2}\int_0^L f_1(x)\sin(\frac{n\pi x}{L})\,dx$$

.

Note that the slowest decaying part of the series solution for $C_1(x,t)$ is the term with $n = 1$ and therefore at large times the solution for $C(x,t)$ may be approximated by

$$C(x,t) \simeq \frac{C_0 x}{L} + A_1 \sin(\frac{\pi x}{L}) e^{-D\pi^2 t/L^2}.$$

The general principle here is that there is a slowest decaying pattern corresponds to the 'gravest mode' in the system – i.e. the largest scale pattern that fits the boundary conditions.

In the above we have considered *conducting* boundary conditions with C imposed on the boundary. When considering the diffusion of chemical species *insulating* boundary conditions, with $\mathbf{n}.\nabla C = 0$ on the boundary ($\mathbf{n}$ is the unit normal) are usually more

relevant. In the one dimensional case above this would correspond to $C_x =$ at $x = 0$ and $x = L$ and the corresponding 'gravest mode' would be $\cos(\pi x/L)$. But note that $C = constant$ also satisfies the boundary conditions and at large times the solution will take the form of a non-zero constant set by the initial conditions, since under these boundary conditions the total amount of C in the system stays constant, with a slowest decaying part proportional to $\cos(\pi x/L)$.

All the above can be generalise to more complicated geometries in higher dimensions. The allowable λs are then such that $-\lambda^2$ is an eigenvalue of the ∇^2 operator subject to the appropriate boundary conditions (conducting or insulating).

4.3 Advection, diffusion, reaction-diffusion

Recall the general form of the transport equation (13) $C_t + \nabla.(\mathbf{u}C + \mathbf{v}C - D\nabla C) = F$. We have so far considered only the effect of diffusion and have set $\mathbf{u} = \mathbf{v} = \mathbf{0}$ and $F = 0$. We now relax these restrictions.

(i) Advection

($\mathbf{u} \neq \mathbf{0}$, $\mathbf{v} = 0$, $F = 0$.) Example problem: uniform flow past a source of some chemical, e.g. a point source or a boundary source. We consider the case of a point source S_0 at the origin in 2-dimensions, assume the uniform flow $\mathbf{u} = \mathbf{U} = (U, 0)$, where $U > 0$, and consider the steady-state distribution.

The concentration C in the steady state satisfies, at all points except the origin (where the source is located)

$$U\frac{\partial C}{\partial x} = D\nabla^2 C$$

and we seek solutions such that $C \to 0$ as $|\mathbf{x}| \to \infty$, i.e. the concentration becomes small far away from the source.

We may take account of the effect of the source by considering the flux integrated over a large rectangle $\mathcal{R}$ containing the origin. The outward flux across this rectangle must be equal to the source strength S_0, i.e.

$$\int_{\mathcal{R}} (C\mathbf{U} - D\nabla C).\mathbf{n}\, dS = S_0$$

Note that we have assumed that C decays at large distances from the source, but clearly this decay cannot be such that all terms in the above integral vanish for $\mathcal{R}$ large enough. It turns out that the diffusive flux contribution becomes smaller and smaller as $\mathcal{R}$ increases

in size, but there is a finite contribution from the advective flux terms downstream of the source. (C reduces more rapidly upstream of the source than downstream, because of the effect of advection.) The implication is that

$$\int_{-\infty}^{\infty} C\, dy = S_0.$$

for large positive x. Also for large positive x the rate of variation in the x direction is much smaller than the rate of variation in the y direction, i.e. $\partial/\partial x \ll \partial/\partial y$, and therefore the transport equation may be approximated by

$$U\frac{\partial C}{\partial x} \simeq D\frac{\partial^2 C}{\partial y^2}.$$

This leaves us with the same equation and the same integral constraint as for the 1-dimensional diffusion equation considered in (ii) above, except that t has been replaced by x/U, x has been replaced by y and S has been replaced by S_0/U. Therefore the solution is

$$C(x,y) = \frac{S_0}{2(\pi DxU)^{1/2}} \exp(-\frac{Uy^2}{4Dx})$$

Note that the y scale implied by this solution is $(Dx/U)^{1/2} \ll x$ (x is large) so the assumption $\partial/\partial x \ll \partial/\partial y$ made earlier is self-consistent.

Another important length scale is D/U, this is the scale on which advection and diffusion balance and is an estimate of the distance upstream of the source that the chemical penetrates. (The upstream penetration is limited by the oncoming flow.)

[The assumptions leading to the approximate solution above might seem difficult to follow. In fact it may be shown that there is a solution of the form $C = \exp(Ux/D)g(r)$, where $(rg')' = U^2 rg/4D^2$, with $g' \to -S_0/(2\pi r)$ as $r \to 0+$ and $g \to 0$ as $r \to \infty$. All of the properties mentioned above may be verified directly from this solution.]

(ii) Nonlinear diffusion

($\mathbf{u} = \mathbf{v} = \mathbf{0}$, $F = 0$, D depends on C.) This is motivated by models of insect dispersal, where observations, some under controlled laboratory conditions, suggest that diffusivity increases with C, perhaps because population pressure encourages increased travel, e.g. to seek food.

We consider the specific example $D = kC$ where k is constant. Then the transport equation becomes

$$\frac{\partial C}{\partial t} = k\frac{\partial}{\partial x}(C\frac{\partial C}{\partial x}).$$

Suppose that there is a finite amount of C at time $t = 0$, confined to some small region about $x = 0$. As in previous cases, it follows from the transport equation that $\int_{-\infty}^{\infty} C\,dx$ is constant in time, and equal to S, say, with S determined by the initial conditions.

Again we use dimensional analysis and (following the example in (ii) of the similarity solution for constant diffusivity) seek a solution that is independent of any initial length scale l_0.

Dimensional quantities appearing in the problem are S, x, t, k.

Corresponding dimensions are CL, L, T, L^2/TC, where L is length, T is time and C has dimensions of concentration.

The only dimensionless group that can be formed from the above is Skt/x^3. Therefore try a similarity solution of the form

$$C(x,t) = \frac{S}{(Skt)^{1/3}}F(\frac{x}{(Skt)^{1/3}}) = \frac{S}{(Skt)^{1/3}}F(\xi)$$

where the second equality defines ξ. Given that the concentration is localised near the origin at $t = 0$ we expect that $F \to 0$ as $|\xi| \to \infty$. Note that the prefactor has to be of the form S/length scale for dimensional consistency and the choice of the length scale as $(Skt)^{1/3}$ allows the integral constraint to be satisfied, provided that $\int_{-\infty}^{\infty} F(\xi)\,d\xi = 1$.

Substituting the possible similarity solution into the equation it follows that

$$-\tfrac{1}{3}(\frac{S^2}{kt^4})^{1/3}F - \tfrac{1}{3}(\frac{S^2}{kt})^{1/3}\frac{x}{(Skt^4)^{1/3}}F_\xi = \frac{k}{(Skt)^{2/3}}\frac{S}{(Skt)^{1/3}}\frac{S}{(Skt)^{1/3}}(FF_\xi)_\xi,$$

hence

$$-\tfrac{1}{3}F - \tfrac{1}{3}\xi F_\xi = -\tfrac{1}{3}(\xi F)_\xi = (FF_\xi)_\xi.$$

Integrating once and setting the integration constant to be zero, given the boundary condition that $F \to 0$ as $|\xi| \to 0$, it follows that $-\frac{1}{3}\xi F = FF_\xi$, hence that $F_\xi = -\frac{1}{3}\xi$ and

hence that $F = A - \frac{1}{6}\xi^2$ where A is constant. This solution cannot hold for all ξ since it cannot satisfy the boundary condition. It will also will not be positive for large $|\xi|$, whereas we expect that an initial condition with $C \geq 0$ for all x at $t = 0$ will imply that $C \geq 0$ for all x for all $t > 0$. A possible resolution of this dilemma is to take

$$\begin{aligned} F &= A - \tfrac{1}{6}\xi^3 \qquad \text{for } 0 \leq |\xi| \leq (6A)^{1/2} \\ F &= 0 \qquad\quad \text{for } |\xi| > (6A)^{1/2}. \end{aligned}$$

The integral constraint then becomes

$$\int_{-\infty}^{\infty} F(\xi)\, d\xi = \int_{-(6A)^{1/2}}^{(6A)^{1/2}} (A - \tfrac{1}{6}\xi^2)\, d\xi = (96A^3/9)^{1/2} = 1.$$

Hence $A = (3/32)^{1/3}$, $(6A)^{1/2} = (9/2)^{1/3}$ and $F(\xi) = (3/32)^{1/3}(1 - (2/9)^{2/3}\xi^2)$ for $|\xi| \leq (9/2)^{1/3}$, with $F(\xi) = 0$ otherwise.

This solution implies that $C(x,t)$ is non-zero only for $|x| \leq (9Skt/2)^{1/3}$. The region of non-zero concentration is strictly finite and expands as $t^{1/3}$. The magnitude of the maximum concentration decays as $t^{-1/3}$.

Contrast the case with constant diffusivity where for $t > 0$ the concentration is non-zero at all x, but decays at large x and the width of the region of largest concentrations increases as $t^{1/2}$.

Note that the similarity solution could have been deduced simply by assuming $C(x,t) = t^{\alpha}F(x/t^{\beta})$, as demonstrated for the constant diffusivity case.

A generalisation of the nonlinear diffusion equation considered above is that $C_t = (kC^m C_x)_x$. There is a similarity solution of the form $t^{-\beta(m)}G(x/t^{\beta(m)}$ where $\beta(m) = 1/(m+2)$. The solution is non-zero only in a finite region if $m > 0$. Further investigation is left as an exercise. See also the `nonlinear diffusion` MATLAB program available on the course website.

(iii) Reaction-diffusion equations

($\mathbf{u} = \mathbf{v} = \mathbf{0}$, $F \neq 0$, D constant.) We consider $C_t = D\nabla^2 C + F(C)$ describing the evolution of a single chemical or biological species. (In general we would want to consider interacting species and C would become a vector and $F(C)$ a vector function of a vector.)

The simplest possible choice for $F(C)$ is $F(C) = -\alpha C$ where α is constant. Even this simple choice has biological relevance, e.g. as a model of parasitic worms in sheep, where the larvae are excreted, disperse across a field and are then eaten.

In 1 dimension the equation is $C_t = DC_{xx} - \alpha C$. Put $C = e^{-\alpha t} f(x,t)$, then $f_t = Df_{xx}$ and for a localised initial distribution of C and hence of f, we may use the similarity solution already derived for this equation, hence

$$C(x,t) = \frac{S}{(4\pi Dt)^{1/2}} \exp(-\alpha t - \frac{x^2}{4Dt}).$$

This solution implies that if $\alpha > 0$, i.e. local death wins out over local birth, the population dies out everywhere.

If $\alpha < 0$, i.e. local birth wins out over local death, then the above solution implies that the population eventually increases without bound everywhere. But note that the growth becomes significant only when $-\alpha t > x^2/(4Dt)$, i.e. when $|x| < 2(-\alpha D)^{1/2} t$. The effect of an initially localised disturbance propagates at speed $(-\alpha D)^{1/2}$ which is a sort of 'reactive-diffusive' speed of propagation.

We will now introduce nonlinearity into $F(C)$ to give more interesting possible behaviour. Note that if $F(C_0) = 0$ then $C = C_0$ is a possible spatially uniform steady state. To investigate the stability of this steady state write $C(x,t) = C_0 + \tilde{C}(x,t)$, hence

$$\tilde{C}_t = D\tilde{C}_{xx} + F(C_0 + \tilde{C}) - F(C_0) \simeq D\tilde{C}_{xx} + F'(C_0)\tilde{C}.$$

where the second equality follows by neglecting quadratic and higher terms in $\tilde{C}$. It follows from the analysis presented above that $\tilde{C}$ grows if $F'(C_0) > 0$ and that $\tilde{C}$ decays if $F'(C_0) < 0$. In other words the steady state is unstable if $F'(C_0) > 0$ and stable if $F'(C_0) < 0$.

These ideas are developed further in the following sections. A key question will be – if a reaction-diffusion system has a spatially steady state that is stable to spatially uniform disturbances can it be unstable to spatially varying disturbances? The answer is yes in some cases and this provides a possible mechanism for the spontaneous emergence of spatial patterns in reaction-diffusion and similar systems.

(iv) Propagating waves: the Fisher equation

This equation, first studied by R.A. Fisher in the 1930s in studying the propagation of a gene in a population, is a special form of the reaction-diffusion equation for a single species where the reaction equation has logistic form. With suitable scaling of the space, time and concentration variables the equation may be written as

$$u_t = u_{xx} + u(1-u).$$

$u = 0$ and $u = 1$ are two possible equilibrium solutions, the former is unstable and the latter is stable.

We consider the evolution of a disturbance, initially localized near $x = 0$, to the unstable state $u = 0$. Locally we might expect the disturbance to grow and approach the equilibrum value $u = 1$. (The unbounded growth predicted by the linear stability analysis is modified when u is large enough that the $-u^2$ term is important.) We might also expect the growth in u excited by the localised initial condition to propagate in x.

We seek a solution that describes the propagation of the disturbance into a region where $u = 0$ initially, with $u = 1$ as a final state behind the propagating disturbance. We assume that the propagating disturbance has a shape that does not vary in time, i.e.

$$u(x,t) = f(x - \gamma t) = f(\xi)$$

with $\gamma > 0$ (propagation in the positive x direction), $f(\xi) \to 0$ as $\xi \to \infty$ ($u = 0$ ahead of the propagating disturbance) and $f(\xi) \to 1$ as $\xi \to -\infty$ ($u = 1$ behind the propagating disturbance). (There will be a corresponding solution representing a wave propagating in the negative x-direction.) Substituting into the Fisher equation implies that

$$-\gamma f' = f'' + f(1-f).$$

We also require $f \geq 0$ for all ξ, motivated by the expectation that the solution of a reaction-diffusion equation will be non-negative for all t if it is non-negative initially.

There are several different approaches to analysing this equation and we consider three (a), (b) and (c).

(a) phase-plane analysis

Write the equation for f as $f' = g$ and $g' = -\gamma g - f(1-f)$ and consider solution curves in the (f, g)-plane.

There are fixed points at $(f, g) = (0, 0)$ and $(f, g) = (1, 0)$.

At $(f, g) = (0, 0)$ the Jacobian J is given by

$$J = \begin{pmatrix} 0 & 1 \\ -1 & -\gamma \end{pmatrix}$$

and it follows that $(0, 0)$ is a stable node if $\gamma \geq 2$ and a stable focus if $\gamma < 2$.

At $(f, g) = (1, 0)$ the Jacobian J is given by

$$J = \begin{pmatrix} 0 & 1 \\ 1 & -\gamma \end{pmatrix}$$

and it follows that $(1, 0)$ is a saddle point.

The solution of interest leaves the saddle point $(1, 0)$ along one of the unstable directions and tends to the point $(0, 0)$ at large times. If $\gamma \geq 2$ the trajectory leaving the saddle point $(1, 0)$ can tend to the stable node at $(0, 0)$ without entering $f < 0$. If $\gamma < 2$ on the other hand then the presence of a stable focus at $(0, 0)$ implies that the trajectory cannot approach $(0, 0)$ without entering the region $f < 0$. But this is not acceptable for the reasons given above, therefore we must require that $\gamma \geq 2$.

(b) far-field solution

For f small (required for large ξ) the equation for f is a second-order linear differential equation with constant coefficients, therefore consider the approximate solution $f(\xi) \simeq e^{-a\xi}$, with $a > 0$. (Note we do not allow complex ξ since this would imply negative values of f.) Substituting into the differential equation implies $\gamma a = a^2 + 1$, hence

$$\gamma = a + \frac{1}{a} \geq 2 \qquad \text{for } a \text{ real and positive.}$$

Again this implies that that minimum wave speed γ is 2, achieved for $a = 1$ It also suggests that the speed of the leading edge of a propagating disturbance is controlled by the far-field behaviour in the initial condition.

Now consider a solution made up of a part $e^{-a\xi}$ associated with an initial condition $u(x, 0) \sim e^{-ax}$ for large x and another part $e^{-\xi}$ propagating with the minimum wave

speed, which might be excited, for example, by nonlinear behaviour at finite x. Which of these dominates in the far field depends on the relative sizes of

$$\exp\{-a(x-(a+\frac{1}{a})t)\} \qquad \text{versus} \qquad \exp\{-(x-2t)\}.$$

The first term dominates at large x if $a<1$, but not if $a>1$.

(a) and (b) above provide some useful insight. There is a rigorous result due to Kolmogorov that if the initial condition $u(x,0)$ has 'compact support' (i.e. there is a finite L such that $u(x,0)=0$ if $|x|\geq L$) then the leading edge of the disturbance propagates with speed 2.

Numerical solution of the Fisher equation is demonstrated by the MATLAB program `Fisher equation` available on the course website.

(c) mechanical analogy

A third method of analysis is to rewrite $-\gamma f' = f'' + f(1-f)$ as

$$f'' = -\gamma f' - f(1-f) = -\gamma f' - \frac{dV}{df} = -\gamma f' - \frac{d}{df}(\tfrac{1}{2}f^2 - \tfrac{1}{3}f^3)$$

where $V(f)$ is defined by the second equality and then to note that this is the equation for a particle of unit mass moving in a potential V and experiencing linear friction with coefficient γ. The potential is a maximum at $f=1$ and a minimum at $f=0$. Note that the maximum of V corresponds to a stable state, and the minimum to an unstable state, according to the chemical evolution equations.

We seek a solution where the particle leaves the maximum of V at $f=1$ in the distant past and tends to the minimum of V at $f=0$. There is such a solution for all positive γ, but if γ is small, i.e. the friction is weak, then the particle oscillates about $f=0$, which violates the requirement that $f\geq 0$. γ must be large enough to ensure a monotonic

approach to $f = 0$, and must therefore be equal to or greater than the value $\gamma = 2$ required for critical dampling.

Therefore once again we deduce that $\gamma \geq 2$.

Bistable analogue of the Fisher equation: Now consider a modification to the Fisher equation

$$u_t = u_{xx} - u(u-r)(u-1).$$

where $0 < r < 1$. The logistic term $u(1-u)$ has been replaced by $-u(u-r)(u-1)$. This is a *bistable system*. The possible steady states are $u = 0$, $u = r$ and $u = 1$ and, by previous analysis, $u = 0$ and $u = 1$ are stable and $u = r$ is unstable. There are therefore two stable spatially uniform equilibrium states, $u = 0$ everywhere and $u = 1$ everywhere, and a natural question is what happens when part of the domain has $u = 0$ and part has $u = 1$?

We seek a solution representing the transition between $u = 1$ for large negative x and $u = 0$ for large positive x. Following the analysis of the Fisher equation we try

$$u(x,t) = f(x - \gamma t) = f(\xi),$$

where $f(\xi) \to 1$ as $\xi \to -\infty$ and $f(\xi) \to 0$ as $\xi \to \infty$. f is required to satisfy the equation

$$f'' = -\gamma f' + f(f-r)(f-1) = -\gamma f' - \frac{dV}{df} = -\gamma f' - \frac{d}{df}(-\tfrac{1}{2}rf^2 + \tfrac{1}{3}(r+1)f^3 - \tfrac{1}{4}f^4).$$

In this case V has a maxima at $f = 0$ and at $f = 1$ and a minimum at $f = r$. We have defined V such that $V(0) = 0$, then $V(1) = (1-2r)/12$. Thus $V(0) < V(1)$ if $r < \frac{1}{2}$ and $V(0) > V(1)$ if $r > \frac{1}{2}$.

We seek a solution where the particle leaves the maximum of V at $f = 1$ and arrives at the maximum of V at $f = 0$. If $V(1) > V(0)$ (i.e. if $r < \frac{1}{2}$) then this is possible for some

positive value of γ – the value that ensures that the particle loses just enough energy to come to a halt at the 'top' of the maximum of V at $f = 0$.

Thus we deduce that if $r < \frac{1}{2}$ the transition region between $u = 1$ and $u = 0$ propagates in the positive x-direction – at any point u eventually tends to 1.

On the other hand if $r > \frac{1}{2}$ then $V(1) < V(0)$. The particle can only move from $f = 1$ to $f = 0$ if it gains energy and this is possible only if $\gamma < 0$. Again γ has to take a particular value, for each r, that brings the particle to rest at the maximum of V at $f = 0$ as $\xi \to \infty$.

Thus if $r > \frac{1}{2}$ the transition region between $u = 1$ and $u = 0$ propagates in the negative x-direction – at any point u eventually tends to 0.

$r = \frac{1}{2}$ is a special case. Then $V(0) = V(1)$ and the particle can start at $f = 1$ and finish at $f = 0$ without losing energy, i.e. $\gamma = 0$. In this case there is a steady solution for u with $u \to 1$ as $x \to -\infty$ and $u \to 0$ as $x \to \infty$. The solution can be found by taking $u_t = 0$, hence $u_{xx} - u(u - r)(u - 1) = 0$. Multiplying by u_x and gives

$$u_x u_{xx} - u_x u(u - r)(u - 1) = \frac{d}{du}(\tfrac{1}{2}u_x^2 - \tfrac{1}{4}u^2(1 - u)^2) = 0.$$

Integrating and applying the boundary condition $u \to 0$ as $x \to \infty$ gives that $\frac{1}{2}u_x^2 - \frac{1}{4}u^2(1 - u)^2 = 0$, hence, taking the negative square root $u_x = -u(1 - u)/\sqrt{2}$. This equation may be integrated, applying the boundary condition as $x \to -\infty$ to give

$$u = \frac{e^{x/\sqrt{2}}}{1 + e^{x/\sqrt{2}}} = \tfrac{1}{2}(1 - \tanh(\frac{x}{2\sqrt{2}})).$$

Numerical solution of the above equation is demonstrated by the MATLAB program `Bistable reaction-diffusion equation` available on the course website.

(v) Chemotaxis

Taxis is the tendency of organisms to move in a particular direction in response to external stimuli, e.g. gravity ('gravitaxis'), light ('phototaxis') or chemicals ('chemotaxis'). In chemotaxis bacteria may swim up or down the gradient of a chemical (e.g. towards food, away from toxins or the chemical signals of competitors).

We consider a model system where n is the concentration of organisms or cells and c is the concentration of the chemoattractant (the chemical species towards which the organisms are attracted).

We generalise the transport equation considered previously to a multi-species system, taking $\mathbf{u} = 0$ (background medium at rest), but for the organisms $\mathbf{v} \neq 0$ (swimming).

The transport equation for the organisms is

$$\frac{\partial n}{\partial t} + \nabla.(\mathbf{J}_v + \mathbf{J}_D) = F(n, c).$$

We take $\mathbf{J}_D = -D_n \nabla n$ representing the random motion of the organisms, with D_n a positive constant.

We take $\mathbf{J}_v = n\mathbf{v} = n\chi(c)\nabla c$ representing the systematic tendency of the organisms to swim up the gradient of c (if the 'chemotactic factor' $\chi(c) > 0$) or down the the gradient of c (if the 'chemotactic factor' $\chi(c) < 0$).

In the following example we take $\chi(c)$ to be a positive constant and the birth/death term $F(n, c)$ to be zero.

The equation for c is also very important. Here we take

$$\frac{\partial c}{\partial t} = D_c \nabla^2 c + \alpha n - \beta c$$

with D_c, α and β positive constants. The αn term represents the production of the chemoattractant c by the organisms themselves. The $-\beta c$ term represents the chemical decay of c.

The above model is the Keller-Segel model (Keller and Segel, 1970, Journal of Theoretical Biology) of chemotaxis for the organism *Dictyostelium discoideum* which moves up the gradient of a chemical secreted by itself.

Note that the two diffusivities D_c and D_n need not be the same and we expect $D_c > D_n$ recalling earlier discussion of the dependency of diffusivity on size. Molecules of c are smaller than cells of n.

Again the key question is, can a spatially uniform steady state that is stable to spatially uniform disturbances be unstable to spatially nonuniform disturbances.

A possible steady state of the above system is $n = n_0$ and $c = c_0$, where n_0 and c_0 are constants, such that $\alpha n_0 = \beta c_0$.

Now disturb the steady state so that $n = n_0 + \tilde{n}(\mathbf{x}, t)$ and $c = c_0 + \tilde{c}(\mathbf{x}, t)$. Substituting into the equations for n and c and linearizing gives

$$\begin{aligned} \frac{\partial \tilde{n}}{\partial t} &= D_n \nabla^2 \tilde{n} - n_0 \chi \nabla^2 \tilde{c} \\ \frac{\partial \tilde{c}}{\partial t} &= D_c \nabla^2 \tilde{c} + \alpha \tilde{n} - \beta \tilde{c} \end{aligned}$$

Note that there are no functions of $\mathbf{x}$ (or t) in the coefficients of this equation and it may therefore be analysed by seeking solutions of the form

$$\begin{aligned} \tilde{n} &= \mathrm{Re}(\hat{n}(\mathbf{k},t)e^{i\mathbf{k}.\mathbf{x}}) \\ \tilde{c} &= \mathrm{Re}(\hat{c}(\mathbf{k},t)e^{i\mathbf{k}.\mathbf{x}}). \end{aligned}$$

An arbitrary initial condition may be considered by taking a superposition of these solutions. (Recall Fourier Transforms, Fourier Series, etc.)

Substituting into the equations for $\tilde{n}$ and $\tilde{c}$ gives

$$\begin{aligned} \frac{\partial \hat{n}}{\partial t} &= -D_n k^2 \hat{n} + n_0 \chi k^2 \hat{c} \\ \frac{\partial \hat{c}}{\partial t} &= -D_c k^2 \hat{c} + \alpha \hat{n} - \beta \hat{c}. \end{aligned}$$

where $k = |\mathbf{k}|$.

Now seek solutions proportional to $e^{\sigma t}$ where σ is constant.

$$\begin{aligned} (\sigma + D_n k^2)\hat{n} &= n_0 \chi k^2 \hat{c} \\ (\sigma + D_c k^2 + \beta)\hat{c} &= \alpha \hat{n}. \end{aligned}$$

Hence

$$(\sigma + D_n k^2)(\sigma + D_c k^2 + \beta) = \alpha n_0 \chi k^2$$

which is a quadratic equation for σ. If both roots have zero or negative real parts then disturbances stay the same amplitude or decay. If one or both roots have positive real parts then disturbances grow.

(i) Note that the form of the quadratic equation implies that the sum of the roots is negative. This implies that a transition from real part positive to real part negative cannot take place when there are complex roots. If there is such a transition then one root must be equal to zero.

(ii) Note that for large k both roots are negative (e.g. consider the standard formula for the roots in this limit). Therefore if there is a value of k where there is a root with positive real part then there must be a larger value of k where one root is zero.

The condition for a root $\sigma = 0$ is that

$$D_n k^2 (D_c k^2 + \beta) = \alpha n_0 \chi k^2$$

implying that $k^2 = 0$ or $k^2 = \alpha n_0/(D_n D_c) - \beta/D_c$.

Taken with (i) and (ii) above this implies that if $\alpha n_0 > \beta D_n$ then at least one root for σ has a positive real part for $0 < k^2 < \alpha n_0/(D_n D_c) - \beta/D_c = k_c^2$ (defining k_c). The system is unstable to disturbances with wavenumber $\mathbf{k}$ such that $0 < |\mathbf{k}| < k_c$.

On the other hand if $\alpha n_0 < \beta D_n$ then for $k^2 > 0$ there is no root for σ with a positive real part. (Note that $k^2 < 0$ is not of interest.) In this case an arbitrary initial condition will stay constant (note that $\sigma = 0$ for $k = 0$) or decay. The system is stable.

In the unstable case an arbitrary initial condition will contain components with $k < k_c$ and these will grow exponentially in time. Since $\sigma = 0$ for $k = 0$ and $\sigma = 0$ for $k = k_c$ there is an intermediate wavenumber k_m ($0 < k_m < k_c$) for which the growth rate is a maximum. At large times the part of the disturbance with this value of k will dominate – this is a scale that is preferentially selected by the system.

(vi) Turing instabilities and chemical pattern formation

Chemotaxis provides a mechanism in a two-component system (organisms plus chemoattractant) for instability of a spatially uniform steady state. But the chemotaxis considered is active upgradient transport and the potential for instability might not seem too surprising.

Can instability occur without active upgradient transport, i.e. with only downgradient transport? It turns out yes if the system is multicomponent and the diffusivities of different components are sufficently different. This was first demonstrated by Turing in a paper "The chemical basis of morphogenesis" published in 1951.

Consider the reacting chemical species with concentrations $u(\mathbf{x}, t)$ and $v(\mathbf{x}, t)$ described by the equations

$$\begin{aligned} \frac{\partial u}{\partial t} &= f(u, v) + D_1 \nabla^2 u \\ \frac{\partial v}{\partial t} &= g(u, v) + D_2 \nabla^2 v \end{aligned}$$

A spatially uniform steady state $u(\mathbf{x}, t) = u_0$ $v(\mathbf{x}, t) = v_0$, with u_0 and v_0 constants, is possible if $f(u_0, v_0) = 0$ and $g(u_0, v_0) = 0$.

The stability of this steady state to spatially uniform disturbances is determined by the eigenvalues of the Jacobian

$$J = \begin{pmatrix} f_u & f_v \\ g_u & g_v \end{pmatrix}$$

where the partial derivatives are evaluated at (u_0, v_0). There is stability if $\mathrm{Tr}J = f_u + g_v < 0$ and $\det J = f_u g_v - f_v g_u > 0$. We assume that these conditions hold.

Now we analyse the stability of the steady state to spatially varying disturbances by taking $u(\mathbf{x}, t) = u_0 + \tilde{u}(\mathbf{x}, t)$ and $v(\mathbf{x}, t) = v_0 + \tilde{v}(\mathbf{x}, t)$. The equations for $\tilde{u}$ and $\tilde{v}$ are

$$\begin{aligned} \frac{\partial \tilde{u}}{\partial t} &= f_u \tilde{u} + f_v \tilde{v} + D_1 \nabla^2 \tilde{u} \\ \frac{\partial \tilde{v}}{\partial t} &= g_u \tilde{u} + g_v \tilde{v} + D_2 \nabla^2 \tilde{v}. \end{aligned}$$

(Again the partial derivatives f_u, f_v, g_u, g_v are evaluated at (u_0, v_0)).

We assume an unbounded domain and, in the previous study of chemotaxis, consider disturbances of the form $\tilde{u}, \tilde{v} \propto e^{i\mathbf{k}.\mathbf{x}}$, where the constant wavenumber vector $\mathbf{k}$ can be chosen freely. This allows the terms $\nabla^2 \tilde{u}$ and and $\nabla^2 \tilde{v}$ to be replaced by, respectively, $-k^2 \tilde{u}$ and $-k^2 \tilde{v}$, where $k = |\mathbf{k}|$. The equations above then become ordinary differential equations, with constant coefficients, for $\tilde{u}$ and $\tilde{v}$ as functions of t.

These differential equations have solutions with $\tilde{u}, \tilde{v} \propto e^{\sigma t}$, where possible values of the constant σ are roots of the quadratic equation

$$(\sigma + D_1 k^2 - f_u)(\sigma + D_2 k^2 - g_v) = f_v g_u.$$

which may be rewritten as

$$\sigma^2 + \sigma(D_1 k^2 + D_2 k^2 - f_u - g_v) + D_1 D_2 k^4 - D_1 k^2 g_v - D_2 k^2 f_u + f_u g_v - f_v g_u = 0.$$

There is instability if one of the roots σ_1 and σ_2 has a positive real part. (Without loss of generality assume that $\mathrm{Re}(\sigma_1) \geq \mathrm{Re}(\sigma_2)$.) Expressions for the two roots are given by the standard formula, but are algebraically complicated. To understand the stability properties it is better to consider the following:

(a) Standard properties of quadratic equations imply that $\sigma_1 + \sigma_2 = f_u + g_v - D_1 k^2 - D_2 k^2$. Since $f_u + g_v < 0$ (previous assumption) it follows that $\sigma_1 + \sigma_2 < 0$. Therefore if the roots σ_1 and σ_2 are complex their real part must be negative. It follows that if σ_1 has a positive real part it must be real, the other root σ_2 must be real and negative and the product $\sigma_1 \sigma_2$ must be negative. Therefore $D_1 D_2 k^4 - D_1 k^2 g_v - D_2 k^2 f_u + f_u g_v - f_v g_u < 0$. But $D_1 D_2 k^4 > 0$ and $f_u g_v - f_v g_u > 0$ (the latter by assumption). Therefore $D_1 g_v + D_2 f_u > 0$ is a necessary condition for instability. Note that this can be true only if $D_1 \neq D_2$, since $f_u + g_v < 0$

(b) The above quadratic has roots with negative real part when $k = 0$ (follows from stability to spatially uniform disturbances) and as $k \to \infty$ (in this limit the roots tend to $-D_1k^2$ and $-D_2k^2$). Therefore if there is instability it occurs for $0 < k_-^2 < k^2 < k_+^2 < \infty$.

Now consider the wavenumbers k_- and k_+ where there is a transition from stability to instability. (a) implies that $\sigma_1 = 0$ at $k = k_-$ and $k = k_+$, i.e. for these k

$$h(k^2) = D_1D_2k^4 - D_1k^2g_v - D_2k^2f_u + f_ug_v - f_vg_u = 0$$

where $h(k^2)$ is defined by the first equality. This equation has positive roots for k^2 only if $D_1g_v + D_2f_u > 0$ (the necessary condition for instability established in (a)) and has real positive roots for k^2 if and only if $D_1g_v + D_2f_u > 0$ and $(D_1g_v + D_2f_u)^2 > 4D_1D_2(f_ug_v - f_vg_u)$.

It follows that the necessary and sufficient condition for instability is $D_1g_v + D_2f_u > 2\sqrt{D_1D_2}\sqrt{f_ug_v - f_vg_u}$.

As in the chemotaxis example, we expect that the growth rate $\mathrm{Re}(\sigma_1)$ will be a maximum for some $k = k_m$ say with $k_- < k_m < k_+$. In principle we can calculate the value of k_m from the expressions for σ_1 and σ_2 as roots of the quadratic equation given above, but the algebra is complicated. It is useful to consider the special case where the condition for instability is just satisfied, i.e. $D_1g_v + D_2f_u$ is just greater than $2\sqrt{D_1D_2}\sqrt{f_ug_v - f_vg_u}$. Then the three wavenumbers k_-, k_m and k_+ are all approximately equal,

$$k_- \simeq k_m \simeq k_+ \simeq \frac{1}{2D_1D_2}(D_1g_v + D_2f_u) \simeq \frac{\sqrt{f_ug_v - f_vg_u}}{\sqrt{D_1D_2}}.$$

The lengthscale selected by the instability is therefore

$$\frac{2\pi}{k_m} = \frac{2\pi(D_1D_2)^{1/4}}{(f_ug_v - f_vg_u)^{1/4}}.$$

The instability is allowed by the differences in the two diffusivities D_1 and D_2. Suppose that $D_2 > D_1$. Then the requirement $D_1 g_v + D_2 f_u > 0$ implies $f_u > 0$ and $g_v < 0$.

For k small (e.g. the spatially uniform case) the coupling between the two reactions is important and gives stability, even though the term $f_u \tilde{u}$ on the right-hand side of the equation for $\partial\tilde{u}/\partial t$ is potentially destabilising. For k large diffusion dissipates disturbances in both $\tilde{u}$ and $\tilde{v}$. For intermediate k diffusion tends to dissipate $\tilde{v}$, the chemical coupling between $\tilde{u}$ and $\tilde{v}$ is weaker and hence the $f_u\tilde{u}$ term can destabilize the system.

Effect of geometry: In the above analysis we have considered disturbances with spatial structure of the form $e^{i\mathbf{k}.\mathbf{x}}$. In a finite domain we would have to consider disturbances with the spatial structure of eigenvalues of ∇^2, subject to appropriate boundary conditions, e.g. $\mathbf{n}.\nabla() = 0$ for insulating boundary conditions. The size of the domain will set a lower bound on k^2, equal to k_0^2, say. If $k_0^2 > k_+^2$ (with the latter as defined above) then no instability will be possible. If $k_0^2 < k_+^2$ then instability will be possible and the spatial pattern that arises will correspond to the eigenfunction of $-\nabla^2$ with value closest to $\max\{k_m^2, k_0^2\}$. If there are several such eigenfunctions then a family of patterns may be possible.

Turing instability provides a potential mechanism for formation of patterns, e.g. patterns of animal coats. (See Chapter 15 of 1st edition of Murray's book for more detail on this.) The hypothesis is that the a chemical pattern is laid down by Turing instability in the embryo stage and then this chemical pattern manifests as a colouring pattern at a later stage of development. The possibility of a family of patterns for given geometry and chemical parameters means that individuals of the same species may exhibit colouring patterns that are different in detail, as is observed. (But there are still arguments over the extent to which patterns are controlled by physico-chemical processes, such as Turing instability, versus genetic coding.)

In mammals the coat patterns seem to be laid down in the embryonic stage and not to change subsequently (except to expand in size). In fish on the other hand, patterning changes as the fish grows. The paper by Kondo and Asai (Nature, 1995) reports evolving patterns on the skin of the marine angelfish *Pomacanthus* and shows that the evolution of the patterns agrees well with a reactive-diffusive model. More recent papers, e.g. Nakamasu et al (PNAS, 2009), Inaba et al (Science, 2012), investigate molecular interactions between different pigment cells, which are nonlocal in nature and suggest generalisations of the reaction-diffusion model.

Example: Autocatalytic chemical reactions (taken from Murray, 1st Edition, §14.2).

$$\begin{aligned}\frac{\partial U}{\partial t} &= k_1 - k_2 U + k_3 U^2 V + d_1 \nabla^2 U \\ \frac{\partial V}{\partial t} &= k_4 - k_3 U^2 V + d_2 \nabla^2 V,\end{aligned}$$

with k_1, k_2, k_3 and k_4 all > 0.

Rescale: find P, Q, R and S such that if $\partial/\partial t \to P\partial/\partial\tau$, $U \to Qu$, $V \to Rv$ and $\nabla \to S\nabla$, to give

$$\begin{aligned}\frac{\partial u}{\partial \tau} &= a - u + u^2 v + \nabla^2 u = f(u,v) \\ \frac{\partial v}{\partial \tau} &= b - u^2 v + d\nabla^2 v = g(u,v),\end{aligned}$$

where $d = d_1/d_2 > 1$, say, and $a > 0$, $b > 0$.

Fixed point at (u_0, v_0), $u_0^2 v_0 = b$, so $u_0 = a + b$, $v_0 = b/(a+b)^2$.

Evaluate Jacobian J at (u_0, v_0)

$$J = \begin{pmatrix} -1 + 2u_0 v_0 & u_0^2 \\ -2u_0 v_0^2 & -u_0^2 \end{pmatrix},$$

so $\mathrm{Tr}J = -1 - u_0^2 + 2u_0 v_0$, $\det J = u_0^2 > 0$. Therefore stable if

$$\mathrm{Tr}J = \frac{1}{a+b}[b - a - (a+b)^3] < 0,$$

i.e. if $b - a < (a+b)^3$.

We previously showed that a necessary condition for Turing instability is that $df_u + g_v > 0$, i.e. $d(b-a) > (b+a)^3$ and that a sufficient condition is that $df_u + g_v > 2\sqrt{d}\sqrt{f_u g_v - f_v g_u}$, i.e. that

$$d\frac{b-a}{(b+a)^2} - 2\sqrt{d} - (b+a) > 0.$$

Under what conditions is the system stable to spatially uniform disturbances, but unstable to Turing instability? Write $b - a = X$ and $b + a = Y$. The above two criteria imply $X < Y^3$ and $dX - 2\sqrt{d}Y^2 - Y^3 > 0$. Hence

$$dY^3 > dX > 2\sqrt{d}Y^2 + Y^3$$

and therefore $Y > 2\sqrt{d}/(d-1)$.

But also $X < Y$, since $a > 0$. Therefore $dY > 2\sqrt{d}Y^2 + Y^3$, hence, from the previous result, $d > 2\sqrt{d}Y + Y^2 > 4d^2/(d-1)^2$ and hence $d > 3 + 2\sqrt{2} = (1+\sqrt{2})^2$. This is the condition on d for there to be Turing instability of a state that is stable to spatially uniform disturbances, for some value of a and b.