University of Dundee

MA42002

MA42002

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Introduction

Welcome to MA42002 Mathematical Biology II.

My name is Philip Murray and I am the module lead.

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Lecture notes

You can find lecture notes for the module on this page. If you would like a pdf this can be easily generated by clicking on the pdf link on the top left of the webpages. I will occasionally edit/update the notes as we proceed through lectures. If you spot any errors/typos/inconsistencies/omissions etc. please report an issue using the report an issue link on the right-hand side of the webpages.

Reading

Mathematical Biology II, James Dickson Murray (2003)

Python codes

I have provided Python codes for most of the figures in the html version of the notes (you can unfold code section by clicking 'Code'). Note that the Python code does not appear in the pdf.

Many of you have taken the Introduction to Programming module at Level 2 and have therefore some experience using Python. I strongly encourage you to use the provided codes as a tool to play around with numerical solutions of the various models that we will be working on. The codes should run as standalone Python codes.

Plan

Table 1: Projected delivery

Week	Chapter	Tutorial sheet	Class Test
1	1	1	—-
2	2	1	—-
3	3	2	—-
4	3	2	—-
5	4	3	Yes
6	4	4	—-
7	5	4	—-
8	5	5	—-
9	6	5	—-
10	6	6	Yes
11	7	6	—-

References

1 Conservation equations

1.1 Introduction

Many biological systems are spatio-temporal, i.e. concentrations of biochemicals, densities of cells etc. depend on spatial position as well time. To describe such cases we must *relax* a major assumption that was made in Mathematical Biology I (MA32009): spatial homogeneity. We now models biological system using partial differential equations.

A conservation equation is the most fundamental statement through which changes in the distribution of the density (or concentration, temperature) is described.

$$\begin{pmatrix} \text{rate of change} \\ \text{in the population density} \end{pmatrix} = (\text{spatial movement}) + \begin{pmatrix} \text{birth, growth, death,} \\ \text{production or degradation} \\ \text{due to chemical reactions} \end{pmatrix}$$

1.1.1 Notation

We will consider $x \in \mathbb{R}^n$, $t \in [0, \infty)$ and functions $c : \mathbb{R}^n \times [0, \infty) \to \mathbb{R}$, where $n = 1, 2, 3$. For example:

- $c(x, t)$ - the density of a population [number per volume] at position x and time t (at (x, t))
- $c(x, t)$ - the concentration of a substance (chemicals, particles) [mass per volume] at position x and time t (at (x, t))
- $c(x, t)$ - the temperature at (x, t).

1.2 Spatially homogeneous models

In this section, we neglect spatial movement and consider examples of growth/death and chemical reactions (i.e. revision from MA32009).

1.2.1 Population dynamics

1.2.1.1 Modelling the growth of bacteria in a petri dish (flask) containing nutrient medium

As an example let's consider a population of bacteria growing in a bounded domain (e.g. a petri dish).

Bacteria reproduce by undergoing successive cell divisions.

Let $N(t)$ represent bacterial density at time t (i.e. number of cells per volume).

Let K represent the *per capita* rate of reproduction. Over a period of time, Δt, $KN(t)\Delta t$ cells will be added. Hence

$$N(t+\Delta t) = \quad N(t) + \quad KN(t)\Delta t. \tag{1.1}$$

Assuming that N is differentiable, dividing Equation 1.1 by Δt and taking the limit as $\Delta t \to 0$

$$\frac{dN}{dt} = KN. \tag{1.2}$$

Depending on the biological context, the growth rate K may take several forms e.g.

- $K =$ constant
- $K = K(t)$ time-dependent
- $K = K(N(t))$ depends on bacterial density
- $K = K(c(t)) := \kappa c(t)$, (with $\kappa > 0$ a constant), which depends on the nutrient concentration $c(t)$ at time t.

1.2.1.2 Logistic growth via nutrient depletion

Suppose that the population growth rate depends on nutrient availability. Suppose also that nutrient levels are depleted by population growth.

Let $c(t)$ represent the nutrient concentration at time, t. Based on the above assumptions we derive

$$\begin{aligned} \frac{dN}{dt} &= K(c)N = \kappa cN, \\ \frac{dc}{dt} &= -\alpha \frac{dN}{dt} = -\alpha\kappa cN, \end{aligned} \tag{1.3}$$

where κ and $\alpha \in \mathfrak{R}$. Consider the initial conditions

$$N(0) = N_0 \quad \text{and} \quad c(0) = c_0.$$

Noting the conserved quantity

$$\alpha \frac{dN}{dt} + \frac{dc}{dt} = 0,$$

integration yields

$$c(t) = -\alpha N(t) + c(0) + \alpha N(0) = -\alpha N(t) + \beta, \tag{1.4}$$

where $\beta = c_0 + \alpha N_0$. Substituting for Equation 1.4 in Equation 1.3 we obtain the *logistic growth* equation

$$\frac{dN}{dt} = \kappa(\beta - \alpha N)N, \qquad N(0) = N_0 \quad , \tag{1.5}$$

where $K = K(N) = \kappa(\beta - \alpha N)$.

The last equation can be rewritten as

$$\frac{dN}{dt} = \rho N\,(1 - \frac{N}{B}) \qquad N(0) = N_0, \tag{1.6}$$

where $\rho = \kappa\beta$ is the *intrinsic growth rate* and $B = \frac{\beta}{\alpha}$ is the *carrying capacity*. The solution of Equation 1.6 is given by

$$N(t) = \frac{N_0 K}{N_0 + (B - N_0)e^{-\rho t}} \ .$$

1.2.1.3 Death/decay

In addition to growth, we may assume that cells die at rate d and the simple growth Equation 1.2 can be generalised to

$$\frac{dN}{dt} = KN - dN,$$

where d is the mortality (death) rate.

1.2.1.4 Competition

Consider a situation in which the *per capita* death rate increases at higher density. For example, suppose that

$$d = d_1 N,$$

i.e. the mortality (death) rate is proportional to the population density. This assumption might arise in a situation where individuals compete for food, habitat (i.e. space) or any limited resources. Hence we could obtain the nonlinear ODE

$$\frac{dN}{dt} = KN - d_1 N^2,$$

1.2.2 SIR Model

Consider a model of infectious disease in which a population is split into three compartments:

- susceptible
- infected
- recovered

Suppse that when susceptible and infected individuals interact, the susceptibles become infected. Suppose also that infected people only remain infectious for a limited time.

Let $S(t)$, $I(t)$ and $R(t)$ represent the population densities of susceptible, infected and recovered populations, respectively.

Consider the governing ODE

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

where r is the infection rate and a is the recovery rate.

1.2.3 Activator inhibitor kinetics

Consider a pair of interacting biochemical species, A and B. Suppose that both A and B are produced at a constant rate and that A undergoes linear degradation. Suppose also that A and B interact such that

$$2A + B \to 3A.$$

Applying the law of mass action

$$\begin{aligned}\frac{da}{dt} &= k_1 - k_2 a + k_3 a^2 b,\\ \frac{db}{dt} &= k_4 - k_3 a^2 b,\end{aligned}$$

where k_1 and k_4 are production rates, k_2 is a degradation rate and k_3 is the reaction rate for the A and B interaction.

1.3 Spatial movement

Consider a spatial domain V. A conservation equation can be written either in terms of the mass or number of particles of a species as follows:

$$\begin{pmatrix}\text{rate of change of}\\ \text{number of particles}\\ \text{per unit time}\end{pmatrix} = \begin{pmatrix}\text{rate of entry of}\\ \text{particles into } V\\ \text{per unit time}\end{pmatrix} - \begin{pmatrix}\text{rate of exit of}\\ \text{particles from } V\\ \text{per unit time}\end{pmatrix} + \begin{pmatrix}\text{rate of degradation}\\ \text{or creation of particles}\\ \text{in } V \text{ per unit time}\end{pmatrix}$$

1.3.1 One-dimensional conservation equations

Assume

- motion takes place in a one-dimensional domain (e.g. a long very thin tube)
- the tube has a constant cross-section area

Let x be the distance along the tube relative to an origin. We shall consider the interval $(x + \Delta x, t)$, for some $\Delta x > 0$, and a domain $V = (x, x + \Delta x) \times S$, where S is the cross-section of the tube with the constant area $A = |S|$.

- $c(x, t)$ - concentration of particles (number of particles per unit volume) at time, t, and position, x
- $J(x, t)$ - flux of particles per unit time and unit area (number of particles crossing a unit area in the positive x-direction per unit time)
- $f(x, t, c(x, t))$ - source/sink (number of particles created or destroyed per unit volume and unit time)

We consider S to be very small and $c(x, t)$ is assumed to be constant in S (independent of y and z). We also assume that c is continuously differentiable with respect to t.

The volume of V is $A\Delta x$ and number of particles in the volume is given by

$$\int_x^{x+\Delta x} c(\tilde{x}, t)\, d\tilde{x} A.$$

Then a conservation equation for the number of particles in the volume V is given by

$$\frac{\partial}{\partial t}\int_x^{x+\Delta x} c(\tilde{x}, t) A d\tilde{x} = J(x, t)\, A - J(x + \Delta x, t)\, A + \int_x^{x+\Delta x} f(\tilde{x}, t, c(\tilde{x}, t))\, A\, d\tilde{x}. \qquad (1.7)$$

i.e. the flux that changes the total population in V is that entering through the cross-section at x and leaving through the cross-section at $x + \Delta x$ (it is assumed that there no flux through

the external surface of the tube). Assuming c and f to be sufficiently smooth (continuous in x) and applying The Mean Value Theorem in Equation 1.7, we obtain

$$\frac{\partial}{\partial t}c(\xi,t)A\Delta x = J(x,t)\,A - J(x+\Delta x,t)\,A + f(\eta,t,c(\eta,t))\,A\Delta x, \qquad \xi,\eta\in(x,x+\Delta x). \tag{1.8}$$

Dividing Equation 1.7 by $A\,\Delta x$ yields

$$\frac{\partial}{\partial t}c(\xi,t) = -\frac{J(x+\Delta x,t)-J(x,t)}{\Delta x} + f(\eta,t,c(\eta,t)), \qquad \xi,\eta\in(x,x+\Delta x). \tag{1.9}$$

Assuming that J is differentiable with respect to x and taking the limit as $\Delta x\to 0$ (and using the definition of partial derivatives) we obtain a one-dimensional conservation (balance) equation:

$$\frac{\partial}{\partial t}c(x,t) = -\frac{\partial}{\partial x}J(x,t) + f(x,t,c(x,t)). \tag{1.10}$$

1.3.2 Conservation equations in $\mathbb{R}^n$

Let $V\subset\mathbb{R}^n$ be an arbitrary bounded domain (i.e. satisfying the conditions of the divergence theorem) and let S be the surface enclosing V, i.e $S=\partial V$.

- $c(x,t)$ – concentration of particles at $x\in V$ and $t>0$ (number of particles per unit volume)
- $J(x,t)$ – flux vector of particles across V (number of particles per unit area and per unit time entering or leaving through S (the boundary of V).
- $f(x,t,c(x,t))$ - source/sink term (number of particles created or destroyed per unit volume and per unit time)

Then the conservation equation reads

$$\frac{\partial}{\partial t}\int_V c(x,t)\,dx = -\int_S J(x,t)\cdot\mathbf{n}\,d\sigma + \int_V f(x,t,c)dx,$$

where $\mathbf{n}$ is the outward normal vector to S. The normal component of the flux J on S leads to a change of number of particles (of mass) in V. Applying the divergence theorem, i.e.

$$\int_S J\cdot\mathbf{n}\,d\sigma = \int_V \mathrm{div}J\,dx,$$

and using the fact that V is independent of time t we obtain

$$\int_V \Big(\frac{\partial}{\partial t}c(x,t) + \nabla\cdot J(x,t) - f(x,t,c)\Big)dx.$$

Since V can be chosen arbitrary we get the conservation equation in $\mathbb{R}^n$ (or a subdomain $\Omega\subset\mathbb{R}^n$)

$$\frac{\partial}{\partial t}c(x,t) = -\nabla \cdot J(x,t) + f(x,t,c), \quad x \in \mathbb{R}^n \text{ (or } x \in \Omega), \quad t > 0. \tag{1.11}$$

1.3.3 Types of flux terms

- Fickian Diffusion

  Diffusion is an important and ‘’metabolically cheap” transport mechanism in biological systems. It can be also viewed as the random motion of individual molecules.

  $$\mathbf{J} = -D\nabla c, \tag{1.12}$$

  where D is the diffusion coefficient. D depends on the size of the particles, the type of solvent, the temperature, ….

  Then applying Equation 1.12 in Equation 1.11 we obtain reaction-diffusion equation

  $$\frac{\partial}{\partial t}c = -\nabla \cdot (-D\nabla c(x,t)) + f(x,t,c) = \nabla \cdot (D\nabla c) + f(x,t,c), \quad x \in \mathbb{R}^n, \ t > 0. \tag{1.13}$$

  If D is a constant we can write

  $$\frac{\partial}{\partial t}c(x,t) = D\Delta c(x,t) + f(x,t,c), \quad x \in \mathbb{R}^n \text{ (or } x \in \Omega), \quad t > 0,$$

  where

  $$\Delta c = \sum_{j=1}^{n} \frac{\partial^2 c}{\partial x_j^2}.$$

- Nonlinear diffusion

  $$D = D(c), \qquad \text{e.g. } D(c) = D_0 c^m, \quad D_0 > 0,$$

  and

  $$\frac{\partial}{\partial t}c = D_0 \nabla \cdot (c^m \nabla c) + f(x,t,c), \quad x \in \mathbb{R}^n, \quad t > 0. \tag{1.14}$$

- Convection or advection

  $$J = \mathbf{v}c,$$

  where $\mathbf{v}$ is a velocity vector. Hence

  $$\frac{\partial}{\partial t}c(x,t) = -\nabla \cdot (\mathbf{v}(x,t)c(x,t)) + f(x,t,c), \quad x \in \mathbb{R}^n, \quad t > 0. \tag{1.15}$$

  If $\mathbf{v}$ is constant or $\nabla \cdot \mathbf{v} = 0$, then

  $$\frac{\partial}{\partial t}c = -\mathbf{v}\nabla c + f(x,t,c) \quad x \in \mathbb{R}^n, \quad t > 0.$$

- Taxis - directed movement in response to an external chemical or physical signal.
  - chemotaxis - movement directed by a chemical gradient
  - haptotaxis - movement directed by a gradient in density, adhesion

  In the presence of some chemoattractant $a(x,t)$ we have

$$\mathbf{J} = \chi(a) c \nabla a,$$

  where $\chi(a)$ is a 'model-specific' function of a defining the sensitivity to the signal, and the conservation equation reads

$$\frac{\partial}{\partial t} c(x,t) = -\nabla \cdot (\chi(a) c(x,t) \nabla a) + f(x,t,c), \quad x \in \mathbb{R}^n \quad t > 0. \tag{1.16}$$

1.3.4 Boundary conditions (B.C.)

- Infinite domain (e.g. $(-\infty, \infty)$, $\mathbb{R}^2$, $\mathbb{R}^3$):

the density is not influenced by the boundary

$$c(x,t) \to 0 \qquad \text{as} \qquad \|x\| \to \infty \quad \text{decay at infinity}$$

- Periodic B.C.

L-periodic function: $c(x,t) = c(x, t+L)$ for any x in the domain

Consider a domain $(0, L)$.

$$c(t,0) = c(t,L) \qquad \text{periodic boundary conditions}$$

- Dirichlet B.C.

density (concentration) is fixed at the boundary

In the 1-dim domain $(0, L)$

$$c(t,0) = c_1, \quad c(t,L) = c_2$$

can consider two reservoirs placed at the ends of the domain, that are held at constant densities (concentrations) c_1 and c_2, respectively.

For a domain $\Omega \subset \mathbb{R}^n$ we have

$$c(x,t) = c_D(x,t) \qquad x \in \partial\Omega, \ t \geq 0 \ .$$

- No-flux (homogeneous Neumann) B.C.

particles cannot escape from the domain

For a domain $\Omega \subset \mathbb{R}^n$

$$D\nabla c \cdot \mathbf{n} = 0 \quad \text{on} \quad \partial\Omega, \quad t > 0$$

In one-dimensional domain $(0, L)$

$$\frac{\partial c(x,t)}{\partial x} = 0 \quad \text{at} \quad x = 0 \text{ and } \quad x = L, \quad t > 0\ ,$$

- Non-homogeneous Neumann B.C.

For a domain $\Omega \subset \mathbb{R}^n$

$$D\nabla c \cdot \mathbf{n} = g(x,t) \quad \text{on} \quad \partial\Omega, \quad t > 0$$

with a given function g (g can also be a constant).

In one-dimensional domain $(0, L)$

$$D\frac{\partial c(x,t)}{\partial x} = g(x,t) \quad \text{at} \quad x = 0 \text{ and } \quad x = L, \quad t > 0\ ,$$

- Homogeneous Robin B.C.

$$D\nabla c(x,t) \cdot \mathbf{n} + kc(x,t) = 0 \quad \text{on} \quad \partial\Omega, \quad t > 0$$

with some constant $k \in \mathbb{R}$.

In one-dimensional domain $(0, L)$

$$D\frac{\partial c(x,t)}{\partial x} + kc(x,t) = 0 \quad \text{at} \quad x = 0 \text{ and } \quad x = L, \quad t > 0\ ,$$

- Non-homogeneous Robin B.C.

$$D\nabla c(x,t) \cdot \mathbf{n} + kc(x,t) = g(x,t) \quad \text{on} \quad \partial\Omega, \quad t > 0$$

with some constant $k \in \mathbb{R}$ and given function g (g can also be a constant).

In one-dimensional domain $(0, L)$

$$D\frac{\partial c(x,t)}{\partial x} + kc(x,t) = g(x,t) \quad \text{at} \quad x = 0 \text{ and } \quad x = L, \quad t > 0\ ,$$

Remark We can also have different types of boundary conditions at different parts of the boundary of the considered domain.

1.3.5 Initial conditions

For a conservation equation defined in a domain $\Omega \subset \mathbb{R}^n$, $n = 1, 2, 3$, additionally to boundary conditions we need to define an initial concentration, i.e. initial condition

$$c(0, x) = c_0(x), \qquad x \in \Omega \, .$$

1.3.6 Formulating a model

The models that we will consider will comprise one or more partial differential equations together with boundary and initial conditions. The right-hand side of the PDEs will be derived based upon assumptions about a particular biological system under study. We will consider exploratory numerical solutions and then study qualitative behaviours of the solutions using analyses familiar from MA32009 (e.g. steady state analysis, linear stability analysis).

We can have any combination of fluxes, depending on the biological system. For example, chemotaxis and diffusion

$$\frac{\partial}{\partial t} c = D\Delta c - \nabla \cdot (\chi(a) c \nabla a) + f(x, t, c), \quad x \in \mathbb{R}^n \quad t > 0, \tag{1.17}$$

which can be augmented by an equation for the (diffusible) chemoattractant a

$$\frac{\partial}{\partial t} a = D\nabla^2 a + g(x, t, a, c), \quad x \in \mathbb{R}^n \quad t > 0. \tag{1.18}$$

Equation 1.17 and Equation 1.18 form a system of equations, a so-called chemotaxis system.

Checklist

Depending on the problem under study, you will have to define and justify your use of the following:

1. Independent variables
2. Dependent variables
3. Domain of definition
4. Reaction kinetics
5. Fluxes
6. Initial conditions
7. Boundary conditions

1.3.7 Nondimensionalization

The variables and parameters in a biological or physical model have units:

- $\#\text{velocity} = \dfrac{\#\text{length}}{\#\text{time}}$
- $\#\text{concentration} = \dfrac{\text{num.moles}}{\#\text{volume}}$
- $\#\text{density} = \dfrac{\text{number of particles}}{\#\text{volume}}$
- $\#\text{diffusion coefficient} = \dfrac{\#\text{length}^2}{\#\text{time}}$
- $\#\text{source/sink (reaction term)} = \dfrac{\#\text{concentration (or density)}}{\#\text{time}}$
- $\#\text{flux} = \dfrac{\text{mass (number) of particles}}{\#\text{area} \times \#\text{time}}$

It is standard to non-dimensionalise a system of differential equations by scaling or non-dimensionalising both the dependent and independent variables in the model.

Part I

Single species

2 Linear reaction diffusion equations

We will now consider equations (and systems of such equations) of the general form:

$$\frac{\partial c}{\partial t} = D\nabla^2 c + f(c), \quad c \equiv c(\mathbf{x}, t), \;\; \mathbf{x} \in \mathbb{R}^n, \;\; t > 0.$$

Such an equation is known as a *reaction-diffusion equation*, being composed of a reaction term, $f(c)$, and a diffusion term, $D\nabla^2 c$. Reaction-diffusion equations have many applications in biological systems e.g. travelling waves of invasion, pattern formation, spread of infectious diseases. For most of the remainder of the course we will consider such systems in one-space dimension i.e. $x \in \mathbb{R}$.

Consider the one-dimensional reaction-diffusion equation with constant diffusion coefficient $D > 0$:

$$\frac{\partial c}{\partial t} = D\frac{\partial^2 c}{\partial x^2} + f(c), \quad x \in \mathbb{R}, \;\; t > 0. \tag{2.1}$$

2.1 One-dimensional diffusion equations

In order to provide some insight into the structure of solutions of reaction-diffusion equations, we make an initial simplifying assumption i.e. we assume $f(c) = 0$, and obtain the linear diffusion equation (or heat equation):

$$\frac{\partial c}{\partial t} = D\frac{\partial^2 c}{\partial x^2}, \quad x \in \mathbb{R}, \;\; t > 0. \tag{2.2}$$

This equation is used to model the evolution of the concentration of a chemical in a long thin tube, or the temperature of a long thin rod.

We assume that the solution is initialised to be non-zero at one point $x = 0$, i.e.

$$c(x_0, 0) = \delta_0(x) \qquad x \in \mathbb{R}, \tag{2.3}$$

where δ_0 is a *Dirac delta distribution* (Dirac measure) satisfying

$$\int_{-\infty}^{+\infty} \delta_0(x) = 1 \quad \text{and} \quad \int_{-\infty}^{+\infty} f(x)\delta_0(x) = f(0), \text{ for continuous } f.$$

2.1.1 Fundamental solution

It can be shown that the sequence of functions $\{\phi_\varepsilon(x)\}$ given by

$$\frac{1}{\varepsilon\sqrt{\pi}}e^{-\frac{x^2}{\varepsilon^2}}$$

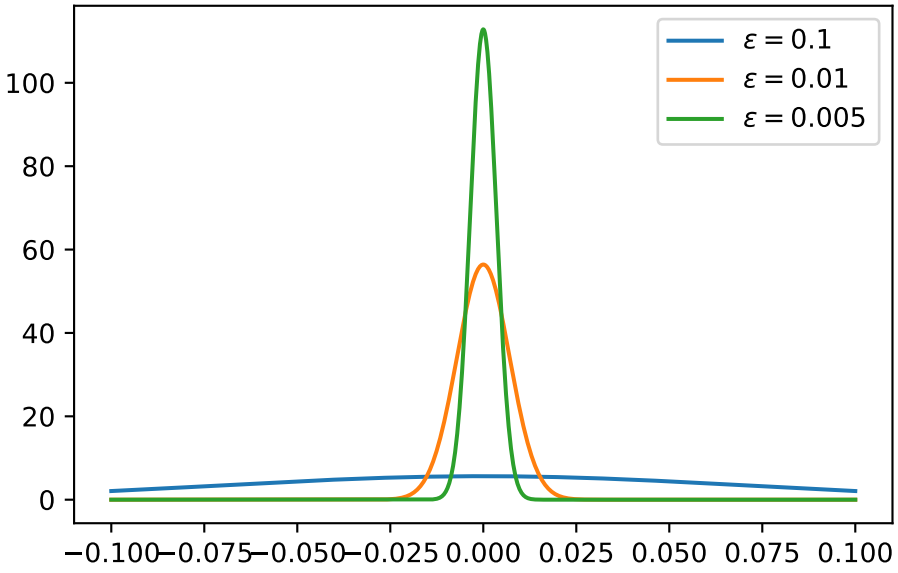

Figure 2.1: Approximation of Dirac delta function.

converges to $\delta_0(x)$ as $\varepsilon \to 0$ (in the sense of distributions or generalized functions).

Then for the diffusion Equation 2.2 with initial condition Equation 2.3, it can be shown that the explicit (analytic) solution is given by

$$c(x,t) = \frac{1}{\sqrt{4\pi Dt}} \exp\left(-\frac{x^2}{4Dt}\right). \tag{2.4}$$

This is known as the *fundamental* solution of the diffusion equation in $\mathbb{R}$.

We also have, for general initial condition $c(x,0) = c_0(x)$ for $x \in \mathbb{R}$:

$$c(x,t) = \int_{-\infty}^{+\infty} \frac{c_0(y)}{\sqrt{4\pi Dt}} \exp\left(-\frac{(x-y)^2}{4Dt}\right) dy.$$

This result can be generalized to $\mathbb{R}^n \times (0,\infty)$ where the fundamental solution has the form

$$c(x,t) = \frac{1}{(4\pi Dt)^{n/2}} \exp\left(-\frac{(x_1^2 + x_2^2 + ... + x_n^2)}{4Dt}\right).$$

2.1.2 Numerical solution

In Figure 2.3 we compute a numerical solution of the diffusion equation and compare it with the exact solution given by Equation 2.4.

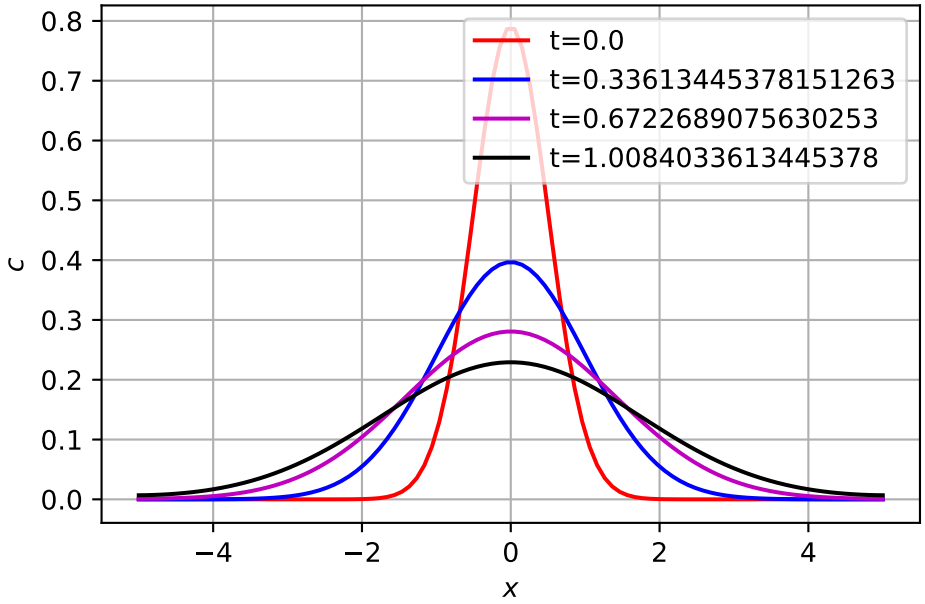

Figure 2.2: Numerical solution of diffusion equation.

2.1.3 Key properties of the (linear) diffusion equation (heat equation)

- The solution is infinitely smooth.
- The solution $c(x,t)$ stays positive for all $t > 0$ and $x \in \mathbb{R}$ if $c(x,0) > 0$ for $x \in \mathbb{R}$.
- The solution "propagates' ' with infinite speed i.e. for any $t > 0$, the solution is everywhere in $\mathbb{R}$.
- If we change the initial data $c(x,0)$ (continuously) then the solution also changes (continuously).

2.1.4 Diffusive transit time

We now demonstrate the connection between time and space in diffusion equations Consider particles of concentration $c(x,t)$ diffusing with constant diffusion D in a one-dimensional domain $(0,L)$, with a constant concentration at one boundary and removed by a sink at the other boundary. At steady-state, the equation governing the concentration is given by:

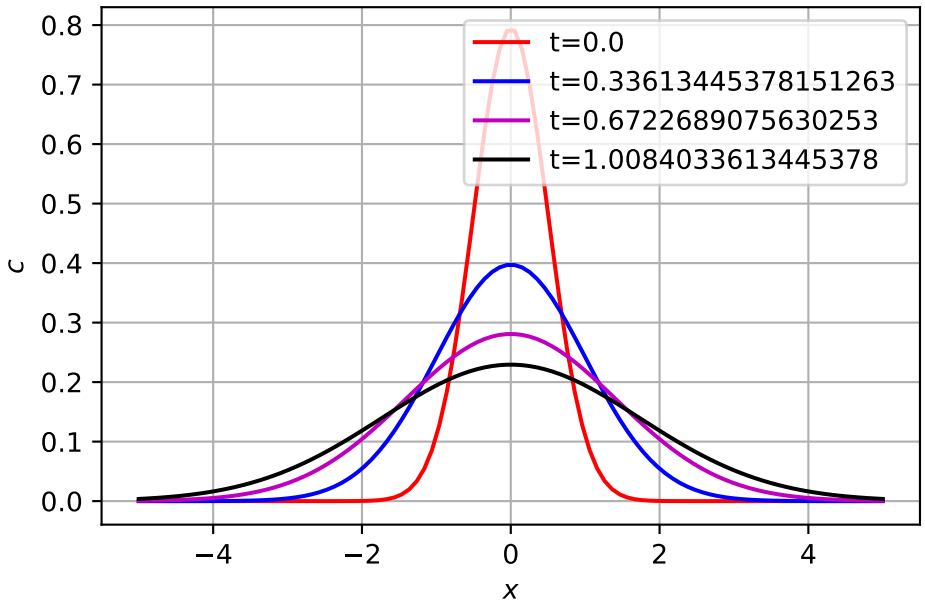

Figure 2.3: Exact solution of diffusion equation.

$$D\frac{d^2c}{dx^2} = 0 \quad \text{in } (0, L), \quad c(0) = C_0,\, c(L) = 0.$$

The solution (**Exercise**) is:

$$c(x) = C_0\left(1 - \frac{x}{L}\right).$$

Then the number of particles entering at $x = 0$ due to diffusive flux (Fickian diffusion) is:

$$J = -D\frac{dc}{dx} = D\frac{C_0}{L},$$

In the middle of the domain the particle concentration is

$$c(\frac{L}{2}) = \frac{C_0}{2}.$$

A typical particle speed is approximated by

$$\frac{J}{c} = \frac{D\frac{C_0}{L}}{\frac{C_0}{2}} = \frac{2D}{L}$$

Travelling at this speed, the average time it takes a particle to travel a distance, L, is

$$\tau = \frac{\text{distance}}{\text{speed}} = \frac{L^2}{2D.}$$

Hence the average distance through which diffusion transports a particle in a time τ is $L = \sqrt{2D\tau}$.

2.1.5 Diffusion as the limit of a random walk

Consider a *random walk* of particles in a one-dimensional domain. Let λ_L and λ_R represent hopping rates, such that the probability of a particle hopping distance Δx to the right in time Δt is

$$\lambda_R \Delta t.$$

Similarly, the probability of hopping a distance Δx to the left is

$$\lambda_L \Delta t.$$

In Figure 2.4 results from a simulation of 400 random walkers is presented. Each particle is initialised at the origin and can move one step left or right with equal probability at every time step of the simulation. As time evolves the particle density (histogram) disperses. The normalised particle density appears to be well described by the solution of the diffusion equation (see solid lines, Equation 2.4).

Let $c(x,t)$ represent the particle density at spatial location x and time t.

A conservation equation for c is given by

$$c(x,t+\Delta t) = c(x,t) + \lambda_R \Delta t c(x-\Delta x,t) - \lambda_R \Delta t c(x,t) + \lambda_L \Delta t c(x+\Delta x,t) - \lambda_L \Delta t c(x,t).$$

Applying a Taylor series expansion about (x,t) implies

$$c(x,t)+\frac{\partial c}{\partial t}\Delta t+\frac{1}{2}\frac{\partial^2 c}{\partial^2 t}(\Delta t)^2+h.o.t. = \lambda_R \Delta t\Big(c(x,t)-\frac{\partial c}{\partial x}\Delta x+\frac{1}{2}\frac{\partial^2 c}{\partial^2 x}(\Delta x)^2+h.o.t.\Big)+\lambda_L \Delta t\Big(c(x,t)+\frac{\partial c}{\partial x}\Delta x+\frac{1}{2}\frac{\partial^2 c}{\partial x^2}(\Delta$$

Upon cancellation

$$\frac{\partial c}{\partial t}\Delta t + \frac{1}{2}\frac{\partial^2 c}{\partial^2 t}(\Delta t)^2 + h.o.t. = \frac{\partial c}{\partial x}\Delta x \Delta t(\lambda_L - \lambda_R) + \frac{1}{2}\Delta t(\lambda_L + \lambda_R)\frac{\partial^2 c}{\partial x^2}(\Delta x)^2 + h.o.t.$$

Dividing by Δt gives

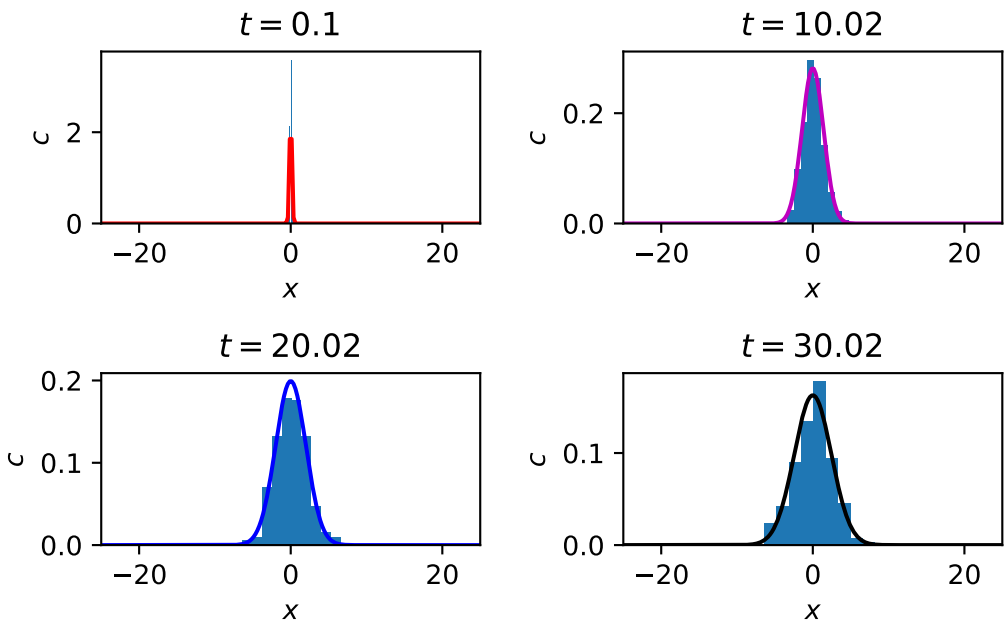

Figure 2.4: Numerical implementation of random walk

$$\frac{\partial c}{\partial t} + \frac{1}{2}\frac{\partial^2 c}{\partial^2 t}\Delta t + h.o.t. = \frac{\partial c}{\partial x}\Delta x(\lambda_L - \lambda_R) + \frac{1}{2}(\lambda_L + \lambda_R)\frac{\partial^2 c}{\partial x^2}(\Delta x)^2 + h.o.t.$$

Considering the symmetric case where the probability of hopping left and right are equal, i.e.

$$\lambda = \lambda_L = \lambda_R$$

yields

$$\frac{\partial c}{\partial t} + \frac{1}{2}\frac{\partial^2 c}{\partial^2 t}\Delta t + h.o.t. = \lambda\frac{\partial^2 c}{\partial^2 x}(\Delta x)^2 + h.o.t.$$

Considering the limit $\Delta t \to 0$ and $\Delta x \to 0$ such that

$$D = \lambda(\Delta x)^2$$

is finite yields the (one-dimensional) diffusion equation

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

Note that D has appropriate units (length^2/time) and that the probability of a particle hopping a distance Δx in time Δt is

$$\lambda \Delta t = \frac{D \Delta t}{\Delta x^2}.$$

This approach can be extended to consider other types of movement e.g. convection. For example, biasing hopping such that

$$\lambda_L - \lambda_R = \varepsilon,$$

yields a *reaction-diffusion-convection* equation (see tutorial).

Finally we note that there is a connection between diffusion and the normal distribution function.

Recall The normal distribution function in one-dimension with zero mean and variance σ^2 is given by

$$N(0, \sigma^2) \sim \frac{1}{\sqrt{2\pi\sigma^2}} \exp\left(-\frac{x^2}{2\sigma^2}\right).$$

Examining the formula for the fundamental solution of the diffusion Equation 2.4 in one-dimension, we see by inspection that the probability density function of the position of a particle performing a random walk in one-dimension starting at the origin is normally distributed with mean zero and variance

$$\sigma^2 = 2Dt.$$

2.2 Linear reaction-diffusion equations

Consider now the linear reaction term: $f(c) = \rho c$, so that Equation 2.1 takes the form

$$\frac{\partial c}{\partial t} = D\frac{\partial^2 c}{\partial x^2} + \rho\, c, \quad x \in \mathbb{R},\ t > 0, \tag{2.5}$$

where $\rho \in \mathbb{R}$ is a constant.

Once again we consider the initial condition to be concentrated at the origin:

$$c(0, x) = \delta_0(x). \tag{2.6}$$

2.2.1 Exact solution

By considering a *separation of variables* approach, i.e. making the *ansatz*

$$c(x,t) = w(t)\tilde{c}(t,x),$$

it can be shown (**Exercise**) that the explicit solution for the linear reaction-diffusion Equation 2.5 with initial condition Equation 2.6 is given by

$$c(t,x) = \frac{1}{\sqrt{4\pi Dt}} \exp\left(\rho t - \frac{x^2}{4Dt}\right).$$

In Figure 2.6 we compare numerical and exact solutions of Equation 2.5.

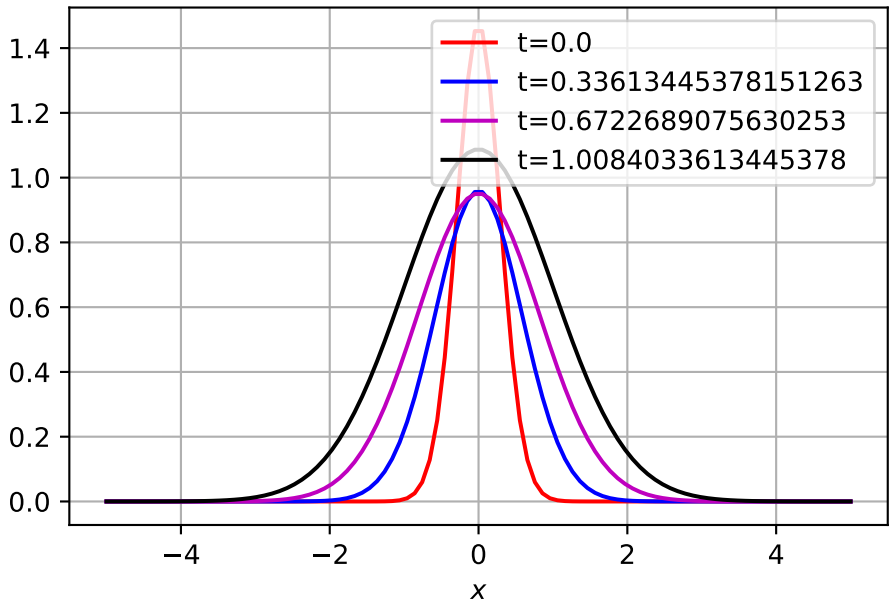

Figure 2.5: Numerical solution of linear reaction diffusion equation

2.2.2 Speed of a wave of invasion

Muskrats, which were introduced in 1905 in Bohemia, initially spread rapidly throughout Europe through a combination of random movement and proliferation (initially there were no predators and proliferation was rapid). A model for the initial spread can therefore be given by a two-dimensional diffusion equation combined with exponential growth and assuming that M individuals were released at the origin (i.e. in Bohemia). Letting $u(\mathbf{x},t)$, represent the density of muskrats, the evolution equation is

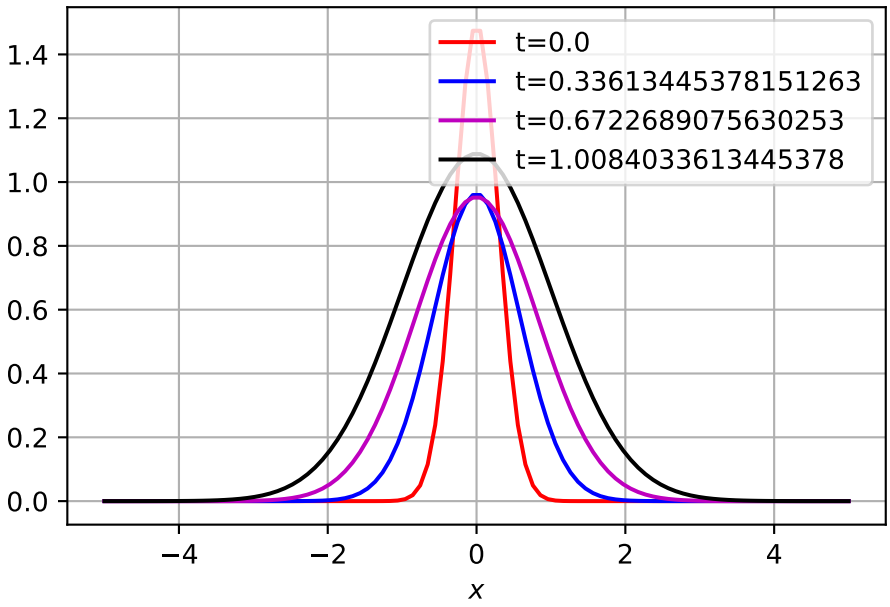

Figure 2.6: Exact solution of linear reaction diffusion equation

$$\frac{\partial u}{\partial t} = D\left(\frac{\partial^2 u}{\partial x_1^2} + \frac{\partial^2 u}{\partial x_2^2}\right) + \rho\, u, \quad \mathbf{x} = (x_1, x_2) \in \mathbb{R}^2,\ t > 0, \tag{2.7}$$

with initial condition

$$u(\mathbf{x}, 0) = M\delta_0(\mathbf{x}), \quad \mathbf{x} \in \mathbb{R}^2. \tag{2.8}$$

It can be shown that the solution of Equation 2.7 with initial conditions given by Equation 2.8 is:

$$u(\mathbf{x}, t) = \frac{M}{4\pi D t} \exp\left(\rho t - \frac{|\mathbf{x}|^2}{4Dt}\right) = \frac{M}{4\pi D t} \exp\left(\rho t - \frac{(x_1^2 + x_2^2)}{4Dt}\right).$$

Transforming to polar coordinates $x_1 = r\cos\varphi$, $x_2 = r\sin\varphi$ we obtain

$$u(\mathbf{x}, t) = \frac{M}{4\pi D t} \exp\left(\rho t - \frac{r^2}{4Dt}\right).$$

From the properties of the fundamental solution, the wave of invasion extends all the way to infinity for any $t > 0$. For practical purposes, we have to define the front of the wave.

Consider that there is some detection threshold for the muskrats i.e. some predetermined small value of the density u_1, say, such that any changes in density for $u < u_1$ cannot be detected.

Because of the symmetry of the problem, then the leading edge of the invading wave front of muskrats is the circle of radius $r = r_1(t)$ where $u = u_1$, i.e. from the explicit solution of Equation 2.7

$$u_1(\mathbf{x}, t) = \frac{M}{4\pi D t} \exp\left(\rho t - \frac{r_1^2}{4Dt}\right).$$

Rearranging and solving for r_1, using the fact that

$$\lim_{t\to\infty} \frac{\ln t}{t} = 0,$$

we obtain for large t that

$$r_1(t) \approx 2\sqrt{\rho D} t.$$

Hence, the speed of invasion of the leading edge of the muskrats is given by:

$$v = \frac{r_1(t)}{t} = 2\sqrt{\rho D}.$$

3 Travelling waves in nonlinear reaction diffusion equations

Travelling waves

A travelling wave is a solution of a PDE that has a constant profile (shape) and a constant propagation speed.
A travelling wave solution could take the form of:

- Travelling pulse: $u(x,t) \to a$, as $x \to \pm\infty$.
- Travelling front : $u(x,t) \to a$, as $x \to -\infty$, $u(x,t) \to b$, as $x \to +\infty$ and $a \neq b$ (this is what we see in Figure 3.1)
- Travelling train: $u(x,t)$ is a periodic function in x.

A travelling wave solution of a PDE can be written in the form $u(x,t) = W(z)$, where $z = x - vt$. We shall consider $v > 0$, which describes a wave moving from left to right.

3.1 Fisher's equation

We now consider the one-dimensional diffusion equation with a non-linear reaction term of "logistic growth", to give the nonlinear reaction-diffusion equation:

$$\frac{\partial u}{\partial t} = D\frac{\partial^2 u}{\partial x^2} + \rho u\left(1 - \frac{u}{K}\right), \qquad x \in \mathbb{R},\ t > 0, \tag{3.1}$$

with initial Condition

$$u(x,0) = u_0(x).$$

This is known as **the Fisher equation**, and was introduced by Fisher in 1937 ("The Wave of Advance of Advantageous Genes" (1937)).

We can non-dimensionalise Equation 3.1 by considering the scaling

$$t^* = \rho t, \quad x^* = \sqrt{\frac{\rho}{D}}x, \quad u^* = \frac{u}{K}.$$

Dropping the asteriks we obtain the non-dimensionalised Fisher equation (**Exercise**):

$$\frac{\partial u}{\partial t} = \frac{\partial^2 u}{\partial x^2} + u(1-u), \qquad x \in \mathbb{R},\ t > 0$$

with initial condition

$$u(x,0) = u_0(x). \tag{3.2}$$

3.1.1 Numerical solutions

In Figure 3.1 we have computed a numerical solution to Equation 3.2 together with no-flux boundary conditions. See Python code for further details. The key point to note is that the numerical solutions appear to be a *travelling wave*, at successive times the solution is translated along the x axis. At long times the solution tends to $u \sim 1$ (behind the wavefront). Ahead of the front, the solution is $u \sim 0$.

The numerical results motivate the following questions:

- Can we prove the existence of a travelling wave (e.g. the numerical solution *could* have a profile that varies on a very slow time scale)?
- How does the travelling depend on initial data?
- How does the wave speed relate to model parameters?
- How do the boundary conditions affect the wave propagation?

3.1.2 Spatially homogeneous solutions

Consider first the *spatially uniform (homogeneous)* solution of Equation 3.2

$$\frac{\partial u}{\partial t} = u(1-u), \qquad t > 0. \tag{3.3}$$

Steady states of Equation 3.3 are

$$u = u_1 = 1$$

and

$$u = u_2 = 0.$$

To analyse the stability we consider

$$f(u) = u(1-u) \quad \text{and} \quad \frac{df}{du}(u) = 1 - 2u.$$

Then

$$\frac{df}{du}(u_1) = -1 \quad \text{and} \quad \frac{df}{du}(u_2) = 1.$$

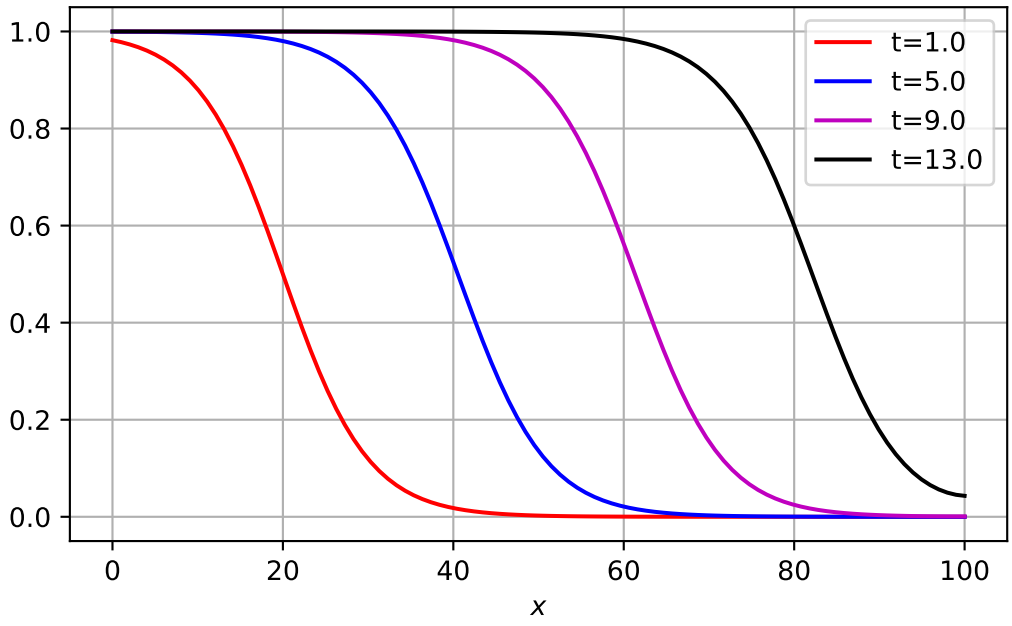

Figure 3.1: Numerical solution of Fisher's equation.

Thus $u_1 = 1$ is *stable* and $u_2 = 0$ is *unstable*.

This stability analysis suggests that for the spatially dependent situation we can have a travelling wave solution that connects the two steady states u_1 and u_2 i.e. a travelling front.

3.1.3 Travelling wave solutions

Consider the travelling wave *ansatz*

$$u(x,t) = W(z) = W(x - vt),$$

where v is a positive constant. Changing variables in Equation 3.2 and using

$$\begin{aligned}
\frac{\partial u}{\partial t} &= \frac{dW}{dz}\frac{\partial z}{\partial t} = -v\frac{dW}{dz}, \\
\frac{\partial u}{\partial x} &= \frac{dW}{dz}\frac{\partial z}{\partial x} = \frac{dW}{dz}, \\
\frac{\partial^2 u}{\partial x^2} &= \frac{d^2W}{dz^2}\left(\frac{\partial z}{\partial x}\right)^2 + \frac{dW}{dz}\frac{\partial^2 z}{\partial x^2} = \frac{d^2W}{dz^2},
\end{aligned}$$

we obtain a second order ordinary differential equation for W

$$\frac{d^2W}{dz^2} + v\frac{dW}{dz} + W(1-W) = 0. \tag{3.4}$$

Boundary conditions are chosen that represent solutions to the spatially homogeneous problem, i.e.

$$W(z) \to 1 \quad \text{as} \quad z \to -\infty, \quad W(z) \to 0 \quad \text{as} \quad z \to +\infty, \tag{3.5}$$

and

$$W(z) \in [0, 1]. \tag{3.6}$$

We can rewrite Equation 3.4 as a system of two first order ODEs

$$\begin{aligned} \frac{dW}{dz} &= P = F(W, P), \\ \frac{dP}{dz} &= -vP - W(1-W) = G(W, P). \end{aligned} \tag{3.7}$$

3.1.3.1 Numerical solutions

In Figure 3.2 we plot the numerical solution to equations Equation 3.7 for different values of the wave speed, v. Note that when the wave speed is too small the solution spirals in towards the origin. This solution cannot be valid as it implies that $u < 0$ for some z.

> What if a travelling wave solution does not exist?
>
> Note that some problems will not have a travelling wave solution. In this situation we might still make the travelling wave ansatz but this would usually result in a contradiction.

3.1.3.2 Steady state and linear stability analysis

The steady states of Equation 3.7 are $(W_1, P_1) = (0, 0)$ and $(W_2, P_2) = (1, 0)$.

The *Jacobian matrix* for Equation 3.7 is given by:

$$J(W, P) = \begin{pmatrix} \frac{\partial F}{\partial W} & \frac{\partial F}{\partial P} \\ \frac{\partial G}{\partial W} & \frac{\partial G}{\partial P} \end{pmatrix} = \begin{pmatrix} 0 & 1 \\ -1 + 2W & -v \end{pmatrix}.$$

At $(W_1, P_1) = (0, 0)$ the eigenvalues of $J(0, 0)$ are solutions of the characteristic polynomial

$$\det(J(0,0) - \lambda I) = \begin{vmatrix} -\lambda & 1 \\ -1 & -v - \lambda \end{vmatrix} = \lambda^2 + v\lambda + 1 = 0.$$

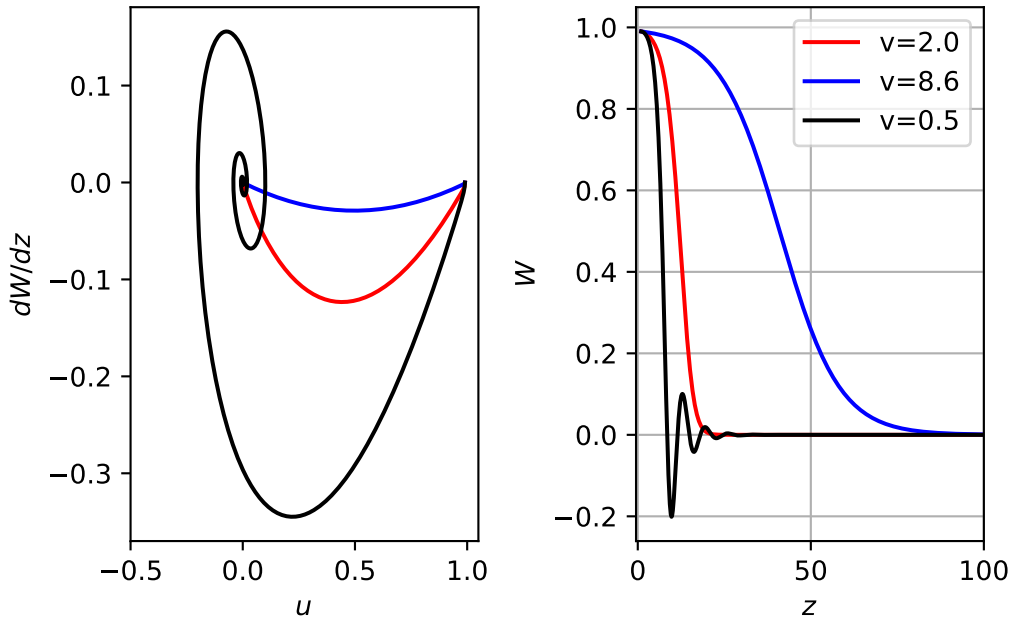

Figure 3.2: Numerical solution of Equation 3.7 with different values of wavespeed,v.

Thus

$$\lambda_1^{\pm} = \frac{1}{2}(-v \pm \sqrt{v^2 - 4})$$

and we have for $v > 0$ that $Re(\lambda_1^{\pm}) < 0$.

Therefore at $(0, 0)$ we have a

$$\begin{cases} \text{stable node if } \ v^2 \geq 4, \\ \text{stable focus if } \ v^2 \leq 4 \quad (\text{ complex eigenvalues}) \end{cases} \tag{3.8}$$

The eigenvectors are defined by

$$-\lambda W + P = 0.$$

Thus at $(W_1, P_1) = (0, 0)$ we have

$$\Phi_1 = \begin{pmatrix} W \\ \lambda_1^- W \end{pmatrix}, \quad \Phi_2 = \begin{pmatrix} W \\ \lambda_1^+ W \end{pmatrix}.$$

Consider that

$$\lambda_1^- \leq \lambda_1^+ < 0 \quad \text{and choose} \quad W = \pm 1.$$

At $(W_2, P_2) = (1, 0)$ the eigenvalues of $J(1, 0)$ are solutions of the characteristic polynomial

$$\det(J(1,0) - \lambda I) = \begin{vmatrix} -\lambda & 1 \\ 1 & -v - \lambda \end{vmatrix} = \lambda^2 + v\lambda - 1 = 0.$$

Thus

$$\lambda_2^{\pm} = \frac{1}{2}(-v \pm \sqrt{v^2 + 4})$$

and we have for $v > 0$ that $\lambda_2^- < 0 < \lambda_2^+$. Therefore $(1, 0)$ is a saddle.

At $(W_2, P_2) = (1, 0)$ we have

$$\Psi_1 = \begin{pmatrix} W \\ \lambda_2^- W \end{pmatrix}, \quad \Psi_2 = \begin{pmatrix} W \\ \lambda_2^+ W \end{pmatrix}.$$

Consider that

$$\lambda_2^- < 0 < \lambda_2^+ \quad \text{and choose} \quad W = \pm 1.$$

The eigenvectors are sketched in Figure 3.3.

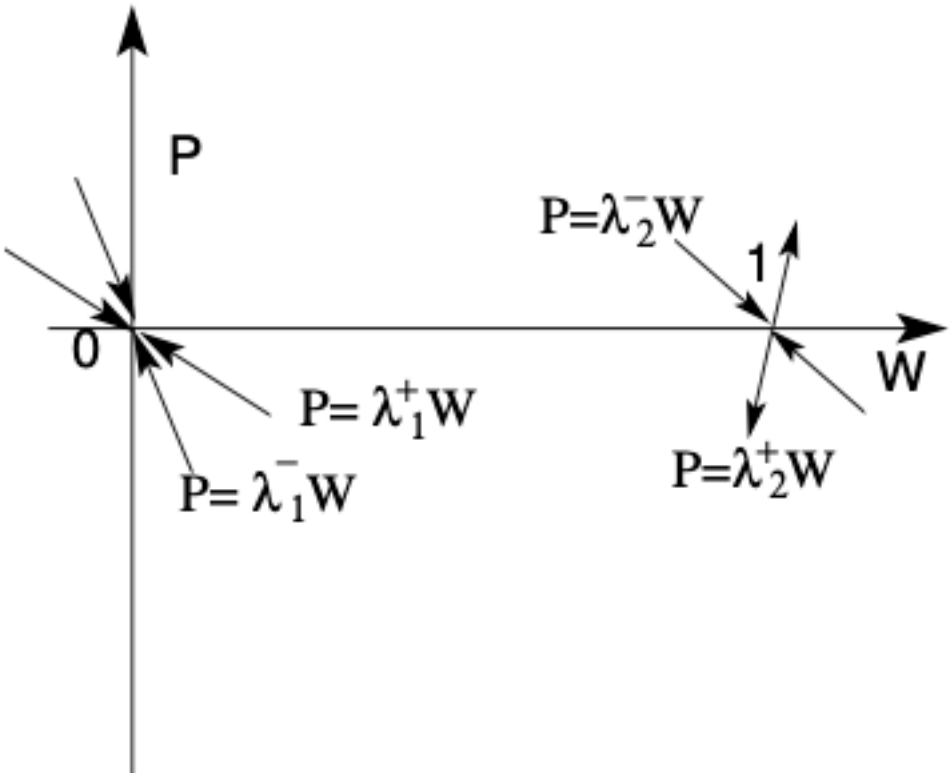

Figure 3.3: Schematic diagram of eigenvectors.

We seek a travelling wave solution that is represented by a trajectory that connects the unstable manifold of the saddle with the stable manifold at the origin.

Definition 3.1. The trajectory that connects two different points is called a heteroclinic connection. The trajectory that connects a point with itself is called a homoclinic connection.

3.1.3.3 Minimal wave speed

It can be shown that for $v < 2$ a heteroclinic connection between $(0, 0)$ and $(1, 0)$ exists, but in this situation the steady state $(0, 0)$ is a stable focus and corresponds to an oscillatory front (see numerical solution in Figure 3.2)

In the context of a model of a biological process W is the profile of a population density and $W \geq 0$. Hence, for $v < 2$ trajectories connecting $(0, 0)$ and $(1, 0)$ are not biologically realistic.

To avoid negative solutions we impose the condition that the origin cannot be a spiral. Considering Equation 3.8 we obtain the nondimensional minimal speed

$$v^*_{\min} = 2$$

for which we have a travelling wave front solution for Fisher's equation.

In the original dimensional variables we have:

$$z^* = x^* - v^* t^* = x\sqrt{\frac{\rho}{D}} - v^* t\rho, \quad \sqrt{\frac{D}{\rho}} z^* = x - \sqrt{D\rho}\, v^*\, t.$$

Thus for $z = x - vt$ we have

$$v = v^*\sqrt{D\rho},$$

and

$$v_{\min} = v^*_{\min}\sqrt{D\rho} = 2\sqrt{D\rho}.$$

3.1.3.4 The existence of a travelling wave solution

To show the existence of a travelling wave we will construct a **confined region** or **confined set** in $\mathbb{R}^2$, which contains both steady states such that, once inside this region solution trajectories cannot escape from it (also known as an **invariant region** or **invariant set**). If we can then show that there are no other steady states in the confined region and that the solution is not oscillatory, the only valid solution must be a heteroclinic trajectory that connects the unstable manifold (eigenvector) of one steady state with the stable manifold of another.

Consider

$$T = \{(W, P) : 0 \leq W \leq 1,\ P \leq 0,\ P \geq \mu W\}$$

for some $\mu < 0$.

Consider normal vectors at each boundary of T:

$$\text{at } P=0 \,:\, n_1 = \begin{pmatrix} 0 \\ -1 \end{pmatrix}, \quad \text{at } W=1 \,:\, n_2 = \begin{pmatrix} -1 \\ 0 \end{pmatrix}, \quad \text{at } P=\mu W \,:\, n_3 = \begin{pmatrix} -\mu \\ 1 \end{pmatrix}.$$

Consider the scalar product between normal vectors and the **flow vector**

$$\begin{pmatrix} \dfrac{dW}{dz} \\ \\ \dfrac{dP}{dz} \end{pmatrix},$$

of Equation 3.7.

At $P=0$

$$\begin{pmatrix} \dfrac{dW}{dz} \\ \\ \dfrac{dP}{dz} \end{pmatrix} \cdot n_1 = \begin{pmatrix} \dfrac{dW}{dz} \\ \\ \dfrac{dP}{dz} \end{pmatrix} \cdot \begin{pmatrix} 0 \\ -1 \end{pmatrix} = (vP + W(1-W))\Big|_{P=0} = W(1-W) \geq 0, \text{ for } W \in [0,1].$$

At $W=1$

$$\begin{pmatrix} \dfrac{dW}{dz} \\ \\ \dfrac{dP}{dz} \end{pmatrix} \cdot n_2 = \begin{pmatrix} \dfrac{dW}{dz} \\ \\ \dfrac{dP}{dz} \end{pmatrix} \cdot \begin{pmatrix} -1 \\ 0 \end{pmatrix} = -P \geq 0, \text{ since } P \leq 0.$$

At $P=\mu W$

$$\begin{aligned} \begin{pmatrix} \dfrac{dW}{dz} \\ \\ \dfrac{dP}{dz} \end{pmatrix} \cdot n_3 &= \begin{pmatrix} \dfrac{dW}{dz} \\ \\ \dfrac{dP}{dz} \end{pmatrix} \cdot \begin{pmatrix} -\mu \\ 1 \end{pmatrix} \\ &= (-\mu P - vP - W(1-W))\Big|_{P=\mu W} \\ &= -\mu^2 W - \mu v W - W(1-W) = -W(\mu^2 + \mu v + 1) + W^2. \end{aligned}$$

Thus

$$\begin{pmatrix} \dfrac{dW}{dz} \\ \\ \dfrac{dP}{dz} \end{pmatrix} \cdot n_3 \geq 0,$$

if

$$\mu^2 + \mu v + 1 \leq 0.$$

The last inequality is satisfied if we have real roots of the equation $\mu^2 + \mu v + 1 = 0$. We have that

$$\mu_{1,2} = \frac{-v \pm \sqrt{v^2 - 4}}{2}$$

are real if $v^2 \geq 4$.

Thus, since $v > 0$, for $v \geq 2$ and any

$$\mu \in \left[\frac{-v - \sqrt{v^2 - 4}}{2}, \frac{-v + \sqrt{v^2 - 4}}{2} \right]$$

we have

$$\begin{pmatrix} \dfrac{dW}{dz} \\ \\ \dfrac{dP}{dz} \end{pmatrix} \cdot n_3 \geq 0 \qquad \text{at} \quad P = \mu W.$$

Therefore we have shown that at the boundaries of T the flow vector points in to the region T and any trajectory approaching the boundaries from inside of T will return to T without crossing any of the boundaries of T. Thus we have constructed an invariant (trapping) triangular region containing the steady states $(0, 0)$ and $(1, 0)$.

If we can show that there no other steady states or periodic solutions of the system Equation 3.7, then a trajectory that leaves $(1, 0)$ must approach $(0, 0)$.

Theorem 3.1. *Bendixson's Negative Criterion, Dulac's Negative Criterion*

If there exists a function $\varphi(W, P)$, with $\varphi \in C^1(\mathbb{R}^2)$, such that

$$\frac{\partial(\varphi F)}{\partial W} + \frac{\partial(\varphi G)}{\partial P},$$

has the same sign $(\neq 0)$ almost everywhere in a simply connected region (region without holes), then the system

$$\begin{aligned} \frac{dW}{dz} &= F(W, P) \ , \\ \frac{dP}{dz} &= G(W, P), \end{aligned}$$

has no periodic solutions in this region.

We can apply Theorem 3.1 to our situation taking $\varphi(W,P)=1$. Then using Equation 3.7 we have

$$\frac{\partial(\varphi F)}{\partial W}+\frac{\partial(\varphi G)}{\partial P}=-v<0\,.$$

Thus we have no periodic solutions and also only two steady states $(0,0)$ and $(1,0)$ in the confined (invariant) simply-connected region T. Therefore the trajectory that leaves $(1,0)$ will approach $(0,0)$.

We have therefore shown that for any $v\geq 2$ there exist a heteroclinic trajectory $P(W)$ connecting $(0,0)$ and $(1,0)$.

Thus for any wave speed v satisfying $v\geq 2$, we have the existence of travelling wave front $u(x,t)=W(x-vt)$ of Fisher's equation Equation 3.2.

3.1.3.5 Sign of the wave speed

Consider Equation 3.4 together with boundary condition

$$W(z\to-\infty)=1\quad W(z\to\infty)=0.$$

Multiply Equation 3.4 by $\dfrac{dW}{dz}$ and integrate over $(-\infty,+\infty)$:

$$\int_{-\infty}^{+\infty}\frac{d^2W}{dz^2}\frac{dW}{dz}\,dz+v\int_{-\infty}^{+\infty}\left|\frac{dW}{dz}\right|^2dz+\int_{-\infty}^{+\infty}W(1-W)\frac{dW}{dz}\,dz=0.$$

Then

$$\frac{1}{2}\int_{-\infty}^{+\infty}\frac{d}{dz}\left(\left|\frac{dW}{dz}\right|^2\right)dz+v\int_{-\infty}^{+\infty}\left|\frac{dW}{dz}\right|^2dz+\int_{W(-\infty)}^{W(+\infty)}W(1-W)\,dW=0.$$

and since $W(z)\to 1$ as $z\to-\infty$ and $W(z)\to 0$ as $z\to+\infty$ we obtain

$$\frac{1}{2}\left(\left|\frac{dW(+\infty)}{dz}\right|^2-\left|\frac{dW(-\infty)}{dz}\right|^2\right)+v\int_{-\infty}^{+\infty}\left|\frac{dW}{dz}\right|^2dz+\int_{1}^{0}W(1-W)\,dW=0.$$

The fact that W is constant at $\pm\infty$ implies that

$$\left.\frac{dW}{dz}\right|_{z=-\infty}=\left.\frac{dW}{dz}\right|_{z=+\infty}=0.$$

Thus we have

$$v\int_{-\infty}^{+\infty}\left|\frac{dW}{dz}\right|^2dz=\int_0^1W(1-W)dW=\frac{1}{6}$$

and

$$v = \frac{\frac{1}{6}}{\int_{-\infty}^{+\infty} \left|\frac{dW}{dz}\right|^2 dz}.$$

Thus the wave speed must be positive and the wave therefore travels in the positive direction along the x axis.

In contrast, if we were to swap the boundary conditions such that

$$W(z \to -\infty) = 0 \quad W(z \to \infty) = 1,$$

the wavespeed would be negative and the wave would travel in the negative direction along the x axis.

3.1.3.6 Initial conditions

One final key question is: For which initial conditions $u(x, 0) = u_0(x)$ does the solution evolve to a travelling wave solution?

If we start with a travelling wave shape initial condition, i.e. $u_0(x) = W(z)|_{t=0} = W(x)$, then this simply propagates as a travelling wave. However if $u_0(x) \neq W(x)$, then it is not immediately obvious how the solution will evolve. This problem was considered by Kolmogorov et al. Kolmogorov, Petrovsky, and Piskunov (1937), who showed that for any initial data satisfying

$$u_0(x) \geq 0, \qquad \text{with} \quad u_0(x) = \begin{cases} 1 \text{ if } x \leq x_1, \\ 0 \text{ if } x \geq x_2, \end{cases}$$

where $x_1 < x_2$ and u_0 is continuous in $[x_1, x_2]$, the solution of Fisher's Equation 3.2 evolves to a travelling wave with minimal speed

$$v_{\min} = 2\sqrt{\rho D}$$

and

$$u(t, x) \to 1 \quad \text{as} \quad x \to -\infty, \quad u(t, x) \to 0 \quad \text{and} \quad x \to +\infty.$$

3.2 Bistable equation

We now consider a reaction-diffusion equation of the form

$$\frac{\partial u}{\partial t} = \frac{\partial^2 u}{\partial x^2} + f(u), \qquad x \in \mathbb{R},\ t > 0, \tag{3.9}$$

with initial condition

$$u(x,0) = u_0(x), \qquad x \in \mathbb{R}.$$

We impose the condition that f has three roots, such that

$$f(0) = f(a) = f(1) = 0, \quad \text{with} \quad 0 < a < 1.$$

There are therefore three spatially uniform steady states $u_1 = 0$, $u_2 = a$, $u_3 = 1$.

We also impose that

$$f'(0) < 0, \quad f'(a) > 0 \quad \text{and} f'(1) < 0$$

Hence the spatially homogeneous steady states $u_1 = 0$ and $u_3 = 1$ are stable and $u_2 = a$ is unstable.

An example of such a function (Figure 3.4) is

$$f = u(u-a)(1-u),$$

which arises in the study of nerve action potentials along nerve fibres and other problems in *excitable media* (Keener and Sneyd (2009)).

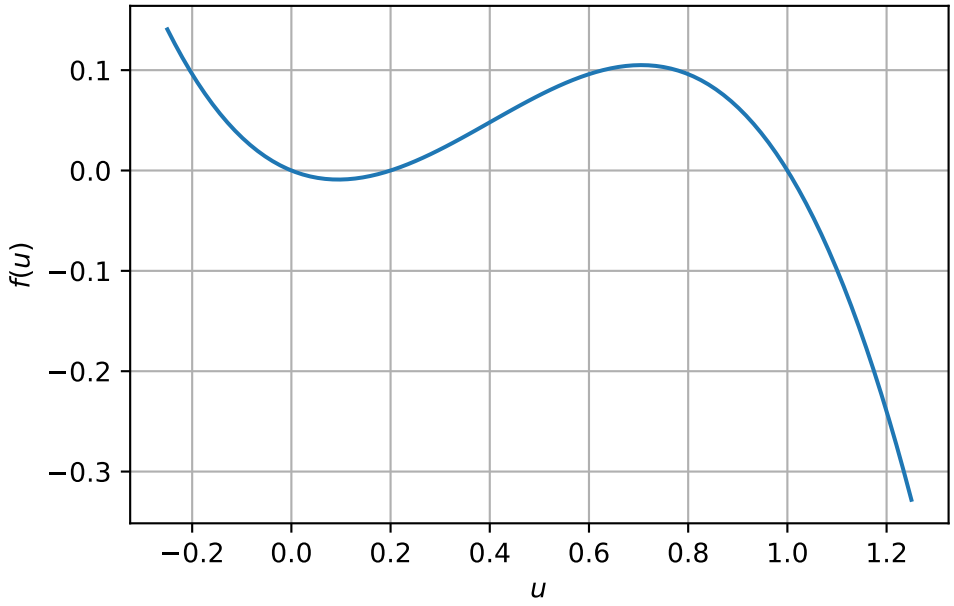

Figure 3.4: A plot of f(u) against u. Note location of roots. ”

3.2.1 Numerical solution

In Figure Figure 3.5 we plot a numerical solution of Equation 3.9. Note the emergence of a travelling wave solution.

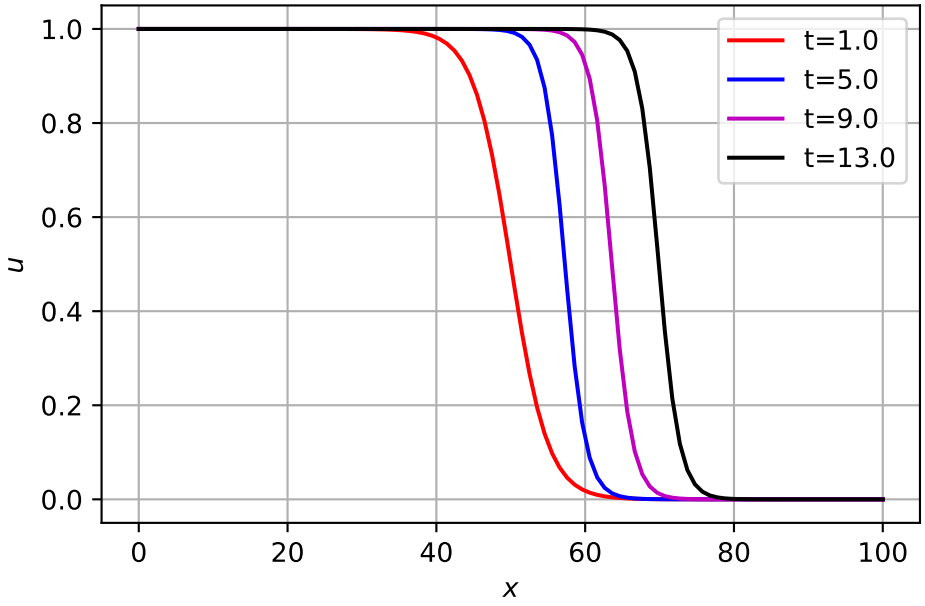

Figure 3.5: Travelling waves in a numerical solution of bistable PDE.

3.2.2 Travelling wave ansatz

In a similar manner to Section 3.1.3, we look for a travelling wave solution of the form $u(x,t) = W(z)$ with $z = x - vt$, yielding

$$\frac{d^2W}{dz^2} + v\frac{dW}{dz} + f(W) = 0, \ . \tag{3.10}$$

We can rewrite Equation 3.10 as asystem of two 1st order ODEs

$$\begin{aligned} \frac{dW}{dz} &= P = F(W,P), \\ \frac{dP}{dz} &= -vP - f(W) = G(W,P), \end{aligned} \tag{3.11}$$

3.2.2.1 Linear stability of the steady states

The steady states of Equation 3.11 are

$$(W_1, P_1) = (0, 0), \quad (W_2, P_2) = (a, 0), \quad (W_3, P_3) = (1, 0).$$

The Jacobian matrix is given by

$$J(W, P) = \begin{pmatrix} \frac{\partial F}{\partial W} & \frac{\partial F}{\partial P} \\ \frac{\partial G}{\partial W} & \frac{\partial G}{\partial P} \end{pmatrix} = \begin{pmatrix} 0 & 1 \\ -f'(W) & -v \end{pmatrix}$$

At steady states (W_j, P_j), the eigenvalues of $J(W_j, P_j)$ are solutions of the characteristic polynomial

$$\det(J(W_j, P_j) - \lambda I) = \begin{vmatrix} -\lambda & 1 \\ -f'(W_j) & -v - \lambda \end{vmatrix} = \lambda^2 + v\lambda + f'(W_j) = 0.$$

Therefore:

$$\lambda_j^{\pm} = \frac{-v \pm \sqrt{v^2 - 4f'(W_j)}}{2}.$$

At $(W_1, P_1) = (0, 0)$ since $f'(0) < 0$ we obtain

$$\lambda_1^- < 0 < \lambda_1^+.$$

Hence (0,0) is a saddle point.

At $(W_2, P_2) = (a, 0)$ since $f'(a) > 0$ we obtain

$$(a, 0) - \begin{cases} \text{focus} & \text{if } v^2 < 4f'(a) \text{ and is stable if } v > 0, \text{ unstable if } v < 0, \\ \text{node} & \text{if } v^2 \geq 4f'(a) \text{ and is stable if } v > 0, \text{ unstable if } v < 0, \\ \text{centre} & \text{if } v = 0\ . \end{cases}$$

At $(W_3, P_3) = (1, 0)$ since $f'(1) < 0$ we obtain

$$\lambda_3^- < 0 < \lambda_3^+$$

and it is a saddle point.

Eigenvectors are given by

$$P = \lambda W$$

and at each steady state we have two eigenvectors

$$\Psi_j^{\pm} = \begin{pmatrix} W \\ \lambda_j^{\pm} W \end{pmatrix}, \qquad j = 1, 2, 3.$$

See Figure 3.6 for a sketch of the phase plane in the cases $v > 0$ and $v = 0$.

The stable and unstable manifolds are dependent on v. We wish to show that for some v the unstable manifold leaving one saddle point coincides with the stable manifold entering the other saddle point, i.e. we can choose a value for the wave speed v such that a heteroclinic connection between $(1, 0)$ and $(0, 0)$ is obtained. We shall use a "shooting argument" to prove this.

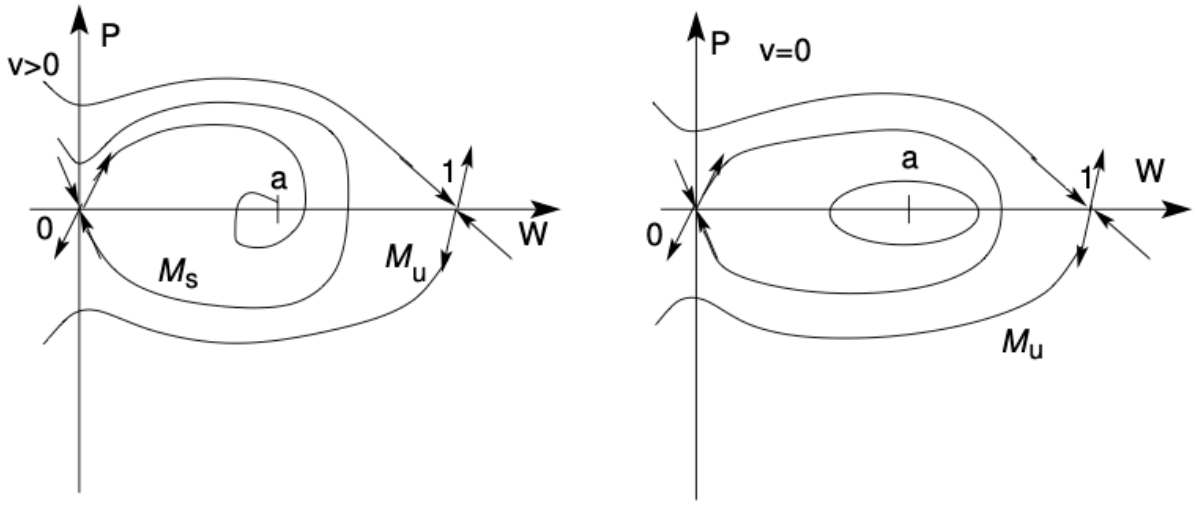

Figure 3.6: Schematic diagram of eigenvectors.

3.2.2.2 Relation between sign of v and sign of $\int_0^1 f(u)\,du$

Using similar arguments to Section 3.1.3.5

$$v = \frac{\int_0^1 f(W)\,dW}{\int_{-\infty}^{+\infty} \left|\frac{dW}{dz}\right|^2 dz}.$$

Since $\int_{-\infty}^{+\infty} \left|\frac{dW}{dz}\right|^2 dz > 0$ we can conclude that

$$\int_0^1 f(u)\,du > 0 \quad \Longrightarrow \quad v > 0, \quad \int_0^1 f(u)\,du = 0 \quad \Longrightarrow \quad v = 0, \quad \int_0^1 f(u)\,du < 0 \quad \Longrightarrow \quad v < 0.$$

Thus the direction of travel of the propagating front depends on the parameter a.

3.2.2.3 Numerical shooting method

In Figure 3.7 we plot numerical solutions to equation Equation 3.11. These results suggest that there are potentially different wavefront solutions connecting steady states.

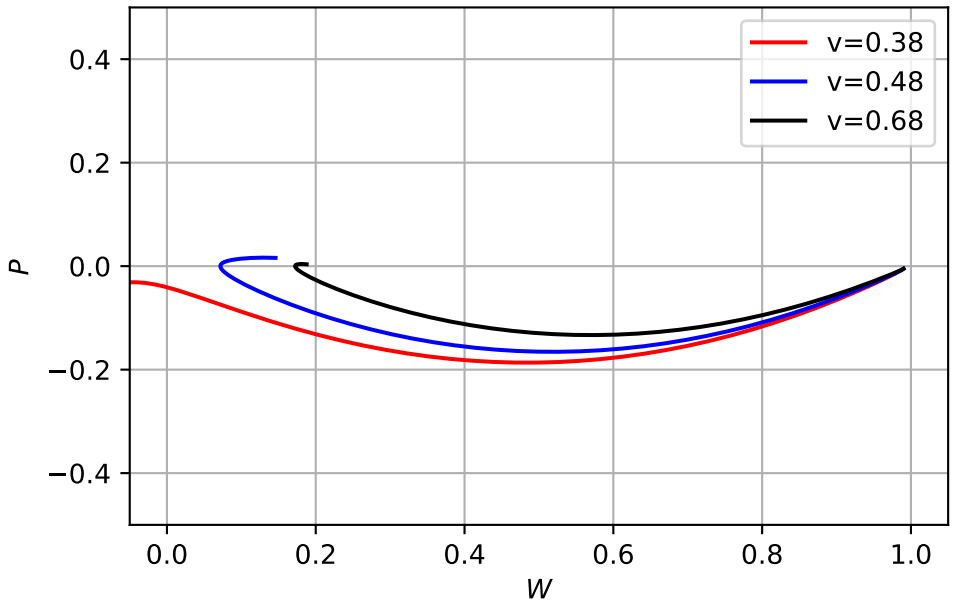

Figure 3.7: Using a shooting method to investigate travelling wave solutions. Continuity arguments suggest that there exists a travelling wave solution with v int he interval [0.38,0.48] such that a heteroclinic trajecotry connects (1,0) and (0,0).

3.2.2.4 The shooting method proof of a heteroclinic connection

Let's assume that

$$\int_0^1 f(u)\,du > 0.$$

Suppose that $v = 0$. An explicit expression for the trajectory is found by multiplying Equation 3.10 by P and integrating over z. Hence

$$\frac{P^2}{2} + \int_0^W f(u)du = 0.$$

If this trajectory reached $W = 1$ then

$$\frac{P^2}{2}\Big|_\infty + \int_0^1 f(u)du = 0.$$

The boundary condition

$$\frac{P^2}{2}\Big|_\infty = 0,$$

necessary for a travelling wave solution, therefore would imply that

$$\int_0^1 f(u)du = 0.$$

This contradicts the assumption

$$\int_0^1 f(u)du > 0. \tag{3.12}$$

Moreover, such a trajectory intersects the $W = 0$ axis for some $P < 0$. An intersection on the $P = 0$ axis would again imply (**czerobreakingcond?**).

Now suppose that v is large. The aim in this case is to show that solutions leaving (1,0) must intersect the $P = 0$ axis for some $W > 0$.

1. The stable eigenvector at (0,0) is
$$P = \lambda\_W.$$
Note that $\lambda_- < v$.

2. A solution trajectory must satisfy
$$\frac{dP}{dW} = \frac{-vP - f(W)}{P} = -v - \frac{f(W)}{P}$$

3. Consider the line $P = -\sigma W$ with $\sigma > 0$. On this line
$$\frac{dP}{dW} = -v + \frac{1}{\sigma}(W - a)(1 - W) < -v + \frac{K}{\sigma}$$
for some K that can be identified (exercise).

4. Hence for large enough v dP/dW can be made arbitrarily negative and the condition
$$\frac{dP}{dW} < -\sigma \tag{3.13}$$
can be satisfied.

5. This result implies that a trajectory leaving (1,0) with sufficiently large v cannot intersect (0,0). If it did it would have to intersect the line $P = \sigma W$. This is not possible given Equation 3.13 and that W is decreasing.

Hence a trajectory approaching $(0, 0)$ with sufficiently large v is bounded below by the line $P = -\sigma W$. Such a trajectory must intersect the $P = 0$ axis for some $W > 0$.

Finally, we have shown that * trajectories with $v = 0$ intersect the line $W = 0$ for $P < 0$ * trajectories with large v intersect the line $P = 0$ for some $W > 0$.

As solution trajectories depend continuously on parameters, there must exist some value of v for which a trajectory intersects (0,0). Hence a heteroclinic trajectory exists.

We can repeat the analysis for

$$\int_0^1 f(u)\,du < 0$$

and obtain a travelling wave solution with $v_0 < 0$.

If

$$\int_0^1 f(u)\,du = 0,$$

then we have a standing wave with $v = 0$, since the calculations for P_0 and P_1 implies $P_0 = P_1$ and there exists a heteroclinic orbit between $(1, 0)$ and $(0, 0)$ in the phase space.

Note: There exists a unique travelling wave velocity v for which we have a travelling wave solution for bistable Equation 3.9.

3.3 References

Part II

Multi species

4 Lotka Voltera model

Consider a predator-prey system (modified Lotka-Voltera equations) with diffusion of both the prey and the predator species. Suppose that the reaction kinetics are given by:

- prey undergoes logistic growth in the absence of predator.
- the predation rate is proportional to the amount of predator
- predator growth rate is proportional to the amount of prey
- predator undergoes natural degradation

Let $u(x,t)$ and $n(x,t)$ represent the density of the prey and predator, respectively. The governing equations are:

$$\begin{aligned} \frac{\partial u}{\partial t} &= \rho\, u\left(1-\frac{u}{K}\right) - \alpha\, u\, n + D_u \Delta u, \\ \frac{\partial n}{\partial t} &= \beta\, u\, n - \gamma\, n + D_n \Delta n, \end{aligned} \tag{4.1}$$

where ρ is the prey linear growth rate, K is the prey carrying capacity, β is predator growth rate per unit prey, α is the prey removal rate per unit predator, γ is predator natural death rate, D_u is diffusion coefficient of the prey and D_n is the diffusion coefficient for the predator.

We will consider one spatial dimension such that $x \in \mathbb{R}$ and $t > 0$.

THe boundary conditions are assumed to be Dirichlet (i.e. the values of u and n are prescribed).

4.1 Nondimensionalization

Consider the scaling

$$x^* = x\sqrt{\frac{\rho}{D_n}}, \qquad t^* = \rho, t, \quad u^* = \frac{u}{K}, \quad n^* = n\frac{\alpha}{\rho}.$$

Upon dropping the asteriked notation, Equation 4.1 transform to

$$\begin{cases} \dfrac{\partial u}{\partial t} = u(1-u-n) + D\dfrac{\partial^2 u}{\partial x^2} \;=\; f(u,n) + D\dfrac{\partial^2 u}{\partial x^2} & x \in \mathbb{R}, t > 0\,, \\ \dfrac{\partial n}{\partial t} = a\, n(u-b) + \dfrac{\partial^2 n}{\partial x^2} \;=\; g(u,n) + \dfrac{\partial^2 n}{\partial x^2} & x \in \mathbb{R}, t > 0, \end{cases} \tag{4.2}$$

where

$$D = \frac{D_u}{D_n}, \quad a = \frac{\beta K}{\rho}, \quad b = \frac{\gamma}{K\beta}.$$

4.2 Numerical solutions

In Figure 4.1 we plot numerical solution of Equation 4.2. No flux boundary conditions are imposed at $x = 0$ and $x = 150$.

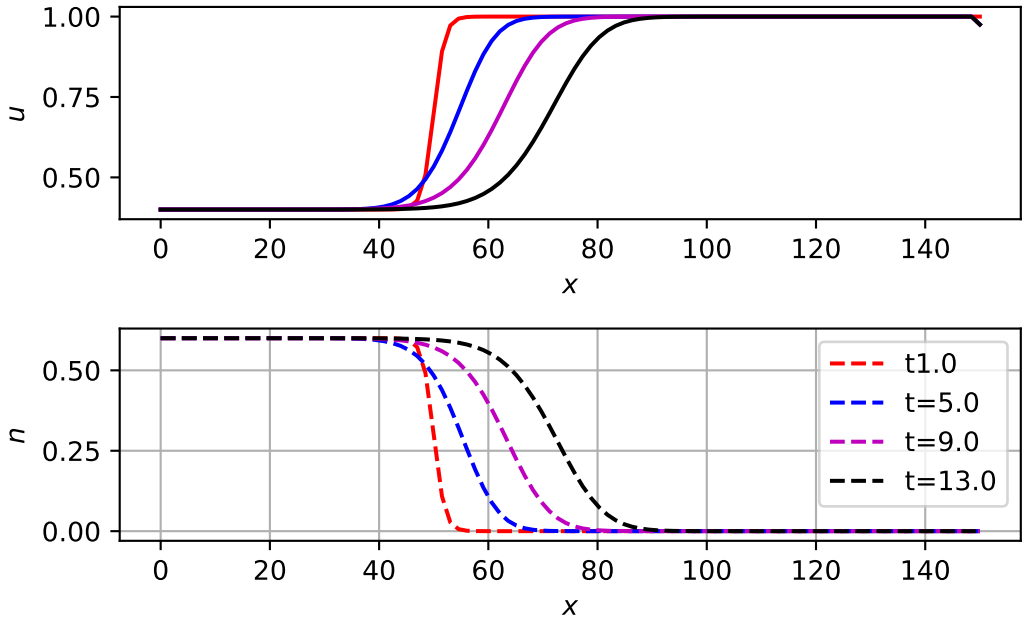

Figure 4.1: Numerical solution of LV model. a=0.2. b=0.4.

4.3 Spatially homogeneous steady states

We firstly consider spatially homogeneous steady states, i.e.

$$f(u, n) = 0, \quad g(u, n) = 0.$$

Thus

$$u(1 - u - n) = 0, \quad u = 0, \quad u + n = 1,$$
$$an(u - b) = 0, \quad n = 0, \quad u = b.$$

Thus the steady states are

$$(u_1^*, n_1^*) = (0, 0), \quad (u_2^*, n_2^*) = (1, 0), \quad (u_3^*, n_3^*) = (b, 1 - b),\ 0 \leq b < 1.$$

4.4 Stability of steady states to spatially homogeneous perturbations

The Jacobian matrix is

$$J(u_j^*, n_j^*) = \begin{pmatrix} 1-2u-n & -u \\ an & a(u-b) \end{pmatrix}_{(u_j^*, n_j^*)}, \quad j = 1, 2, 3.$$

At the steady state

$$(u_1^*, n_1^*) = (0, 0)$$

the characteristic equation is

$$\det(J(0,0) - \lambda I) = -(1-\lambda)(\lambda + ab) = 0.$$

The eigenvalues are

$$\lambda_1^+ = 1, \quad \lambda_1^- = -ab < 0.$$

Thus $(0, 0)$ is a saddle point.

At the steady state

$$(u_2^*, n_2^*) = (1, 0)$$

the characteristic equation is

$$\det(J(1,0) - \lambda I) = -(1+\lambda)(a(1-b) - \lambda) = 0.$$

The eigenvalues are

$$\lambda_2^- = -1, \quad \lambda_2^+ = a(1-b) > 0 \ \text{ for } \ 0 \le b < 1.$$

Thus $(1, 0)$ is a saddle point.

At the steady state

$$(u_3^*, n_3^*) = (b, 1-b)$$

the characteristic equation is

$$\det(J(b, 1-b) - \lambda I) = \lambda^2 + b\lambda + ab(1-b) = 0.$$

If

$$4ab(1-b) \leq b^2 \implies \lambda_3^{\pm} < 0,$$

$(b, 1-b)$ is a stable node.

If

$$4ab(1-b) > b^2 \qquad \implies \Re(\lambda_3 \pm) < 0, \Im(\lambda_3^{\pm}) \neq 0,$$

$(b, 1-b)$ is a stable focus (spiral).

For $b > 0$, $1 - b > 0$ spiral oscillations are biologically realistic so long $u > 0$ and $n > 0$.

4.5 Existence of travelling wave profiles connection $(1, 0)$ and $(b, 1-b)$

Condider the travelling wave *ansatz*

$$\begin{aligned} u(t,x) &= W(x+vt) = W(z), \quad v > 0, \\ n(t,x) &= N(x+vt) = N(z), \quad v > 0. \end{aligned}$$

We consider boundary conditions that connect $(1, 0)$ to $(b, 1-b)$, i.e.

$$\begin{aligned} u(t,x) &\to 1 \text{ as } x \to -\infty, & W(z) &\to 1 \text{ as } z \to -\infty, \\ u(t,x) &\to b \text{ as } x \to +\infty, & W(z) &\to b \text{ as } z \to +\infty, \\ n(t,x) &\to 0 \text{ as } x \to -\infty, & N(z) &\to 0 \text{ as } z \to -\infty, \\ n(t,x) &\to 1-b \text{ as } x \to +\infty, & N(z) &\to 1-b \text{ as } z \to +\infty. \end{aligned}$$

Equation 4.2 transforms to

$$\begin{aligned} v\frac{dW}{dz} &= D\frac{d^2W}{dz^2} + W(1-W-N), \\ v\frac{dN}{dz} &= \frac{d^2N}{dz^2} + aN(W-b), \end{aligned}$$

with boundary conditions given by

$$\begin{aligned} &W(z) \to 1 \text{ as } z \to -\infty, \quad W(z) \to b \text{ as } z \to +\infty, \\ &N(z) \to 0 \text{ as } z \to -\infty, \quad N(z) \to 1-b \text{ as } z \to +\infty. \end{aligned} \tag{4.3}$$

Upon making the assumption that the prey moves much more slowly than the predator species, i.e.

$$D = \frac{D_u}{D_n} \ll 1,$$

Equation 4.3 simplify to

$$\begin{aligned} v\frac{dW}{dz} &= W(1-W-N), \\ v\frac{dN}{dz} &= \frac{d^2N}{dz^2} + aN(W-b). \end{aligned} \tag{4.4}$$

We can rewrite Equation 4.4 as a system of first order ODEs:

$$\begin{aligned} \frac{dW}{dz} &= \frac{1}{v}W(1-W-N) = F(W,N,P), \\ \frac{dN}{dz} &= P = G(W,N,P), \\ \frac{dP}{dz} &= vP - aN(W-b) = R(W,N,P). \end{aligned} \tag{4.5}$$

The steady states of Equation 4.5 are

$$\begin{aligned} (W_1^*, N_1^*, P_1^*) &= (0,0,0), \\ (W_2^*, N_2^*, P_2^*) &= (1,0,0), \\ (W_3^*, N_3^*, P_3^*) &= (b, 1-b, 0). \end{aligned}$$

The Jacobian matrix is

$$J(W,N,P) = \begin{pmatrix} \frac{1}{v} - \frac{2W}{v} - \frac{N}{v} & -\frac{W}{v} & 0 \\ 0 & 0 & 1 \\ -aN & a(b-W) & v \end{pmatrix}.$$

At

$$(W_1^*, N_1^*, P_1^*) = (0,0,0)$$

we have

$$\det(J(0,0,0) - \lambda I) = \left(\frac{1}{v} - \lambda\right)(\lambda^2 - \lambda v - ab) = 0$$

and

$$\lambda_1^1 = \frac{1}{v} > 0, \quad \lambda_2^{\pm} = \frac{v \pm \sqrt{v^2 + 4ab}}{2}.$$

Thus $(0,0,0)$ is a saddle point with a 2-dim unstable manifold.

At $(W_2^*, N_2^*, P_2^*) = (1,0,0)$ we have

$$\det(J(1,0,0) - \lambda I) = \left(-\frac{1}{v} - \lambda\right)(\lambda^2 - \lambda v + a(1-b)) = 0,$$

and

$$\lambda_1^1 = -\frac{1}{v} < 0, \quad \lambda_2^{\pm} = \frac{v \pm \sqrt{v^2 - 4a(1-b)}}{2}.$$

Since

$$0 \leq b < 1 and 4(1-b) > 0,$$

- If $v^2 \geq 4a(1-b)$, (1,0,0) is a saddle with 2-dim unstable manifold.\
- If $v^2 < 4a(1-b)$ (1,0,0)is an unstable focus

Thus for a travelling wave with $W \geq 0$ and $N \geq 0$ to exist we require

$$v^2 \geq 4a(1-b)$$

and obtain a minimal wave speed

$$v_{\min} = 2\sqrt{a(1-b)} \quad \text{with} \quad 0 \leq b < 1.$$

At

$$(W_3^*, N_3^*, P_3^*) = (b, 1-b, 0)$$

we have

$$\det(J(b, 1-b, 0) - \lambda I) = \lambda^3 - \lambda^2(v - \frac{b}{v}) - \lambda b - \frac{1}{v}ab(1-b) = p(\lambda) = 0.$$

It can be shown that the extrema of $p(\lambda)$ are independent of the parameter a.

To identify extrema, we compute

$$p'(\lambda) = 3\lambda^2 - 2\lambda\left(v - \frac{b}{v}\right) - b = 0$$

and find that

$$\lambda_{m,M} = \frac{1}{3}\left[\left(v - \frac{b}{v}\right) \pm \sqrt{\left(v - \frac{b}{v}\right)^2 + 3b}\right].$$

If $a = 0$, the eigenvalues are

$$\lambda_3^1 = 0, \quad \lambda_3^{\pm} = \frac{1}{2}\left(v - \frac{b}{v} \pm \sqrt{\left(v - \frac{b}{v}\right)^2 + 4b}\right).$$

Thus there exists a critical value $a^* > 0$ such that for $a \in (0, a^*)$, we obtain two real negative eigenvalues and one positive real eigenvalue. Hence $(b, 1-b, 0)$ is a saddle with 2-dim stable manifold and 1-dim unstable manifold

For $a > a^*$, we obtain a pair of complex conjugate eigenvalues with negative real part and one real positive eigenvalue corresponding to 1-dim unstable manifold.

This can be easily seen from a sketch of the cubic equation:

$$p(\lambda) = \lambda^3 - \lambda^2(v - \frac{b}{v}) - \lambda b - \frac{1}{v}ab(1-b).$$

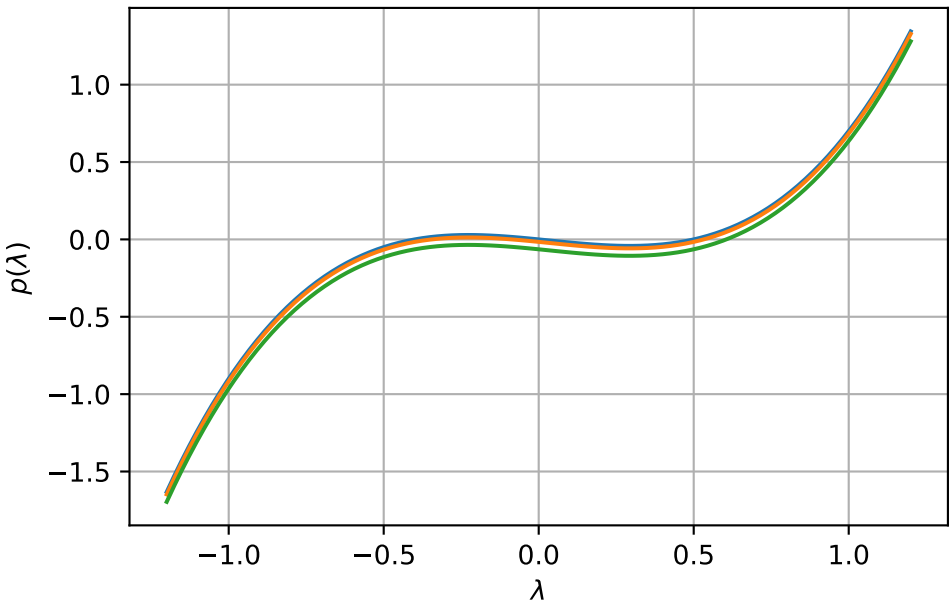

Figure 4.2: Plot of cubic.

Thus we have a possible heteroclinic connection between $(1,0,0)$ and $(b,1-b,0)$, i.e. between 2-dim unstable manifold at $(1,0,0)$ and 2-dim stable manifold at $(b,1-b,0)$, and therefore an existence of a travelling wave front solution for Equation 4.2 with

$$\begin{aligned} &u(x,t) \to 1 \ \text{ as } x \to -\infty, \quad u(x,t) \to b \ \text{ as } x \to +\infty, \\ &n(x,t) \to 0 \ \text{ as } x \to -\infty, \quad n(x,t) \to 1-b \ \text{ as } x \to +\infty. \end{aligned}$$

4.6 Exercise

Use Python code to numerically investigate dependence of travelling wave solution on the parameter a.

5 Aggregation via chemotaxis

Dictyostelium discoideum (Dicty) is a slime-mold that is widely studied experimentally as a model organism. The individual amoebae that constitute a slime-mold exhibit a range of phenomena also observed in mammalian cells e.g. differentiation, proliferation, migration.

Under nutirent starvation conditions, Dicty cells undergo complex collective behaviours. Individual amoebae secrete a diffusible chemical, cyclic AMP or cAMP. The amoebae respond chemotactically to cAMP and begin to migrate towards regions of high cAMP concentration via *chemotaxis*. As they migrate they generate a range of intricate patterns including *spiral waves* and *streaming* aggregation patterns (e.g. Figure 5.1).

The movie below depicts slime mold aggregation. https://www.youtube.com/watch?v=bkVhLJLG7ug Note the aggregation between 0:35 and 0.48.

In Figure 5.1 we can see stills-shot images of spiral patterns. This spirals are dynamic as can be seen in this movie. https://www.youtube.com/watch?v=OX5Yiz38fgY See spiral pattern at around 0:36.

Figure 5.1: Spiral wave patterns underly Dictystelium aggregation. Image from Durston (2013).

- can we simulate/model the mechanisms regulate that give rise to cellular aggregation?
- how do features of patterns that form (e.g. pattern wavelength, speepd of aggregation) depend on individual cell properties?

5.1 Model derivation

We consider a model for Dicty aggregation through the secretion of and chemotactic response to cAMP. We denote by $n(\mathbf{x}, t)$ the density of amoebae and $a(\mathbf{x}, t)$ the concentration of cAMP. The general conservation equation for the amoebae can be written:

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

where $f(n, a)$ models any reaction terms for the amoebae e.g. proliferation, and the flux is given by

$$\mathbf{J} = \mathbf{J}_{diffusion} + \mathbf{J}_{chemotaxis}.$$

Assuming Fickian diffusion and the general chemotactic flux stated earlier (Section 1.1), the general *reaction-diffusion-chemotaxis* model for the amoebae responding to cAMP is given by:

$$\begin{aligned}\frac{\partial n}{\partial t} &= \underbrace{D_n \nabla^2 n}_{diffusion} - \underbrace{\nabla \cdot (\chi(a) n \nabla a)}_{chemotaxis} + f(n, a),\\ \frac{\partial a}{\partial t} &= D_a \nabla^2 a + g(n, a),\end{aligned}$$

where we have assumed Fickian diffusion for the cAMP and $g(a, n)$ represents the kinetics i.e. source/sink terms, of cAMP.

One simple model has the following assumptiond:

$$f(n, a) = 0, \quad g(n, a) = \mu n - \delta a, \quad \chi(a) = \chi_0$$

i.e.

- there are no kinetics for the amoebae - they simply move randomly via diffusion and undergo chemotaxis in response to cAMP;
- proliferation is neglected; - this is a reasonable assumption given the timescales involved, since they amoebae move on a faster timescale than they proliferate;
- the amoebae are assumed to produce cAMP in proportion to their density, which means the more amoebae there are, the more cAMP (a reasonable first approximation);
- the chemotactic function is taken to be a constant, again a reasonable first approximation;
- $D_a > D_n$ since chemicals diffuse faster than cells move randomly.

Under such assumptions we obtain the model equation

$$\begin{aligned}\frac{\partial n}{\partial t} &= D_n \nabla^2 n - \chi_0 \nabla \cdot (n \nabla a),\\ \frac{\partial a}{\partial t} &= D_a \nabla^2 a + \mu n - \delta a,\end{aligned}$$

which becomes, upon considering a 1-dimensional domain $[0, L]$,

$$\begin{aligned} \frac{\partial n}{\partial t} &= D_n \frac{\partial^2 n}{\partial x^2} - \chi_0 \frac{\partial}{\partial x}\left(n \frac{\partial a}{\partial x}\right), \\ \frac{\partial a}{\partial t} &= D_a \frac{\partial^2 a}{\partial x^2} + \mu n - \delta a, \end{aligned} \qquad (\dagger) \qquad (5.1)$$

with zero flux boundary conditions:

$$\begin{aligned} D_a \frac{\partial a}{\partial x} &= 0, \quad x = 0, L, \\ D_n \frac{\partial n}{\partial x} - \chi_0 n \frac{\partial a}{\partial x} &= 0, \quad x = 0, L. \end{aligned}$$

These reduce to:

$$\frac{\partial a}{\partial x} = \frac{\partial n}{\partial x} = 0, \quad x = 0, L.$$

5.2 Numerical solutions

In Figure 5.2 we plot numerical solution of Equation 5.1 together with no-flux boundary condition. The initial data are uniformly sampled. Note the emergence of periodic spatial structure in both variables. These correspond to peaks and troughs of cell density. The cells produce chemoattractant, a, and the this induces a chemtactic flux up the gradient in a. Hence more cells move towards regions where a is high, more chemoattractant is produced in this region etc.

- What is the long-time behaviour of these solutions
- For which parameters do we expect to see pattern formation?
- How does spatial pattern depend on the initial data?

5.3 Spatially Homogeneous Steady States

Define the total number of cells, N,

$$N = \int_0^L n(x, t) dx$$

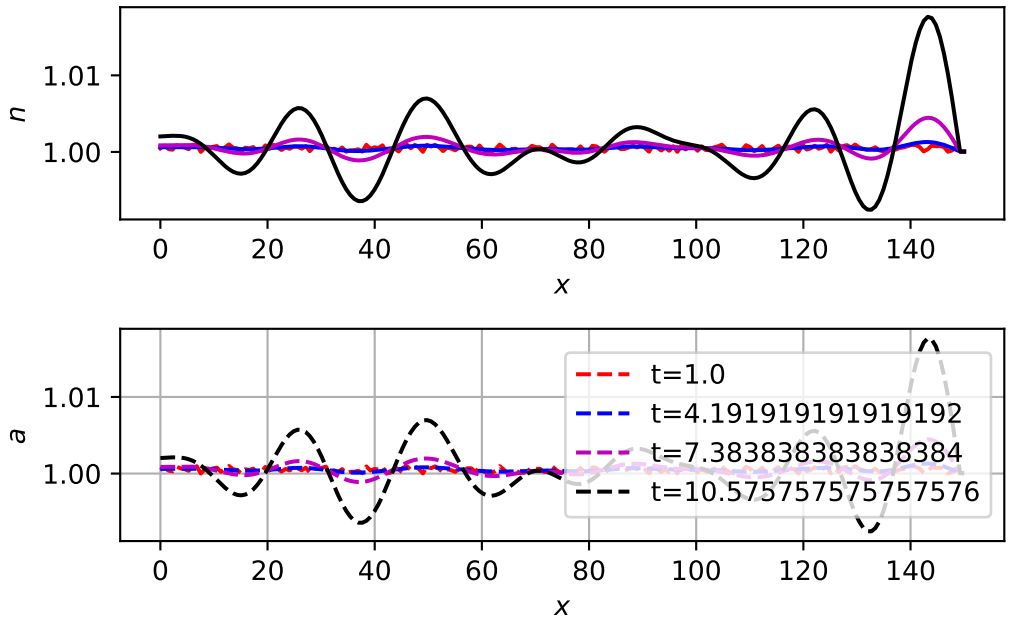

Figure 5.2: Numerical solution of bacterial chemtaxis model.

Upon differentiation with respect to time

$$\frac{dN}{dt} = \int_0^L \frac{\partial n(x,t)}{\partial t} dx \quad = \int_0^L D_n \frac{\partial^2 n}{\partial x^2} - \chi_0 \frac{\partial}{\partial x}\left(n \frac{\partial a}{\partial x}\right) dx.$$

Upon integration of the right-hand side w.r.t. x, subsequent application of the no-flux boundary condition implies

$$\frac{dN}{dt} = 0.$$

Hence the total number of cells in the domain is fixed by the initial data. For a spatially homogeneoud solutions, th4 cells must be uniformly distributed in space, i.e.

$$n^* = N/L$$

Additionaly, the spatially homogeneous steady state solution (n^*, a^*) satisfies:

$$a^* = \frac{\mu}{\delta} n^*.$$

We now undertake a linear stability analysis to determine whether this is stable or unstable. If the above spatially homogeneous steady state is unstable, this will indicate that aggregation patterns may arise in the system.

5.4 Stability Analysis

In a similar manner to previous stability analyses, we consider small perturbations around the spatially homogeneous steady state (n^*, a^*), i.e.

$$n(x,t) = n^* + \tilde{n}(x,t), \quad a(x,t) = a^* + \tilde{a}(x,t)$$

where $\tilde{n}(x,t)$ and $\tilde{a}(x,t)$ are "small" so that higher order terms can be neglected.

NOTE Unlike previous stability analysis, these perturbations are both *time* and *space* dependent.

Substituting the above perturbations into equations (†), we neglect higher order terms and retain only linear terms. This is largely straightforward, but we provide some detail for the linearization of the chemotactic term i.e.

$$\frac{\partial}{\partial x}\left[(n^* + \tilde{n})\frac{\partial}{\partial x}(a^* + \tilde{a})\right] = \frac{\partial}{\partial x}\left[(n^* + \tilde{n})\frac{\partial \tilde{a}}{\partial x}\right] \approx n^* \frac{\partial^2 \tilde{a}}{\partial x^2}.$$

The fully linearized system is then given by:

$$\begin{aligned} \frac{\partial \tilde{n}}{\partial t} &= D_n \frac{\partial^2 \tilde{n}}{\partial x^2} - \chi_0 n^* \frac{\partial^2 \tilde{a}}{\partial x^2} \\ \frac{\partial \tilde{a}}{\partial t} &= D_a \frac{\partial^2 \tilde{a}}{\partial x^2} + \mu \tilde{n} - \delta \tilde{a}. \end{aligned} \tag{5.2}$$

Although the above equations are linear, an explicit solution is non-trivial and we are required to make a further "separation of variables" *ansatz*. We seek solutions of the form

$$\tilde{n}(t,x) = u(t)\phi_1(x)$$

and

$$\tilde{a}(t,x) = v(t)\phi_2(x)$$

Upon substitution

$$\begin{aligned} \frac{\partial u}{\partial t}\phi_1 &= D_n u \frac{\partial^2 \phi_1}{\partial x^2} - \chi_0 n^* v \frac{\partial^2 \phi_1}{\partial x^2} \\ \frac{\partial v}{\partial t}\phi_2 &= D_a v \frac{\partial^2 \phi_2}{\partial x^2} + \mu u\, \phi_1 - \delta v\, \phi_2, \end{aligned}$$

with boundary conditions

$$u\frac{\partial \phi_1}{\partial x} = 0, \quad v\frac{\partial \phi_2}{\partial x} = 0 \quad \text{for } x = 0,\ x = L.$$

We assume that

$$\phi_1 = \phi_2 = \phi,$$

where ϕ is the solution of the elliptic problem

$$\begin{aligned} \frac{d^2\phi}{dx^2} &= -k^2\phi \quad \text{in } (0, L), \\ \frac{d\phi}{dx} &= 0 \qquad\quad \text{for } x = 0,\ x = L. \end{aligned}$$

We can compute that solution of the equation for ϕ are of the form

$$\phi(x) = A\cos(kx) + B\sin(kx).$$

Since ϕ satisfied zero Neumann boundary conditions we have that

$$\phi(x) = A\cos(kx),$$

where A is an arbitrary constanr, and

$$k = \frac{m\pi}{L}, \quad m \in \mathbb{N}.$$

Then we have

$$\begin{aligned} \frac{\partial u}{\partial t}\phi &= -k^2 D_n u\phi + \chi_0 n^* k^2\, v\,\phi, \\ \frac{\partial v}{\partial t}\phi &= -k^2 D_a\, v\phi + \mu u\,\phi - \delta v\,\phi, \end{aligned}$$

and since ϕ is not identically zero on $(0, L)$ we obtain a system of linear ODEs for $(u(t), v(t))$

$$\begin{aligned} \frac{\partial u}{\partial t} &= -k^2 D_n u + \chi_0 n^* k^2\, v, \\ \frac{\partial v}{\partial t} &= -k^2 D_a\, v + \mu u - \delta v. \end{aligned}$$

We know that solutions of linear ODEs have the form

$$u(t) = C_1 e^{\lambda t} \quad \text{and} \quad v(t) = C_2 e^{\lambda t}$$

for some constant C_1, C_2 and λ are eigenvalues of the corresponding matrix.

Thus we obtain

$$\begin{aligned} \lambda C_1 &= -D_n k^2 C_1 + \chi_0 n^* k^2 C_2, \\ \lambda C_2 &= -D_a k^2 C_2 + \mu C_1 - \delta C_2, \end{aligned}$$

which can be written

$$\begin{pmatrix} -D_n k^2 - \lambda & \chi_0 n^* k^2 \\ \mu & -D_a k^2 - \delta - \lambda \end{pmatrix} \begin{pmatrix} C_1 \\ C_2 \end{pmatrix} = \mathbf{0}.$$

Remark Notice that we obtained that $\tilde{n}$ and $\tilde{a}$ are of the form

$$\tilde{n}(x,t) = C_1 e^{\lambda t} e^{ikx}, \quad \tilde{a}(x,t) = C_2 e^{\lambda t} e^{ikx}.$$

For a non-trivial solution (for non-trivial perturbations $\tilde{n}$, $\tilde{a}$), i.e. $C_1 \neq 0$ and $C_2 \neq 0$, the determinant of the above matrix must be zero, and this leads to the following quadratic equation to be solved for λ:

$$\lambda^2 + \left(D_n k^2 + D_a k^2 + \delta\right)\lambda + D_n k^2 \left(D_a k^2 + \delta\right) - \mu\chi_0 n^* k^2 = 0.$$

This is of the form

$$\lambda^2 + \alpha\lambda + \beta = 0,$$

and so has roots:

$$\lambda = \frac{-\alpha \pm \sqrt{\alpha^2 - 4\beta}}{2}.$$

NOTE This has two *real* roots, since

$$\alpha^2 - 4\beta > 0$$

(see Exercise/Tutorial).

For stability, we require both roots to be negative. Since both roots are real, this leads to:

$$\lambda < 0 \Leftrightarrow \alpha > 0 \quad \text{and} \quad \beta > 0.$$

Now

$$\alpha = D_n k^2 + D_a k^2 + \delta > 0,$$

and so for stability, we require $\beta > 0$ i.e.

$$\begin{aligned} D_n k^2 \left(D_a k^2 + \delta\right) - \mu\chi_0 n^* k^2 > 0 \\ \Rightarrow \mu\chi_0 n^* < D_n \left(D_a k^2 + \delta\right) \end{aligned}$$

Hence, we will have instability when this condition is not satisfied i.e.

$$\mu\chi_0 n^* > D_n \left(D_a k^2 + \delta\right).$$

The precise value of k^2 can be determined from the zero-flux boundary conditions i.e.

$$k = \frac{m\pi}{L}, \quad m = 1, 2, ...$$

if we look for non-constant ϕ.

Hence, we will have instability whenever

$$\mu\chi_0 n^* > D_n \left(D_a \frac{m^2\pi^2}{L^2} + \delta \right), \quad m = 1, 2, ...$$

It can be shown (see Exercise/Tutorial), that $\lambda(k^2)$ (or $\lambda(m^2)$) is monotonic decreasing and hence the fastest growing mode is $m = 1$ i.e. we have an instability as long as

$$\mu\chi_0 n^* > D_n \left(\frac{D_a\pi^2}{L^2} + \delta \right).$$

In general, from the above inequality, we can say that there is a likelihood of instability (amoebae aggregation) if:

- D_a, D_n and δ are all "small' '
- L is "large' '
- χ_0, μ, n^* are "large' '

Considering all other parameters to be fixed, in theory the above result states that it is possible to find a large enough value for the chemotactic coefficient χ_0 to satisfy the instability condition i.e. chemotaxis induces instability and leads to aggregation of the amoebae.

5.5 Exercise

From the results we have obtained we deduce that:

- chemotaxis has a destabilizing effect
- diffusion has a stabilizing effect on spatially homogeneous solutions

If this is true then one might expect the numerical results presented in Figure 5.2 to have spatially homogeneous solutions if the diffusion coefficient is made sufficiently large. * Can you test this by running the code for larger values of the parameter D? * Alternatively, what happens if you make the chemotactic coefficient χ_0 smaller? * what kind of aggregation patterns do you see if the system is solved in two spatial dimensions?

However, there is one type of system where diffusion also has a destabilizing effect…

6 Diffusion driven instability

6.1 Spatial Pattern Formation via Reaction-Diffusion

6.1.1 Pattern in Developmental Biology

Embryology or developmental biology is that part of biology which is concerned with the formation, growth and development of the embryo from fertilization until birth. From the very moment of conception the embryo undergoes a process of dynamic change, brought about largely by cells responding to various chemical signalling cues e.g. migration, differentiation, proliferation.

https://www.youtube.com/watch?v=SEejivHRIbE

Many of the processes occurring at this early stage are vital for the successful subsequent development of the embryo and also lay down basic structures (e.g. somites) that form the foundation of major body structures later on (e.g. the vertebrae of the spine)

https://www.youtube.com/watch?v=kYZt5ygmaTA

> **i** Professor Lewis Wolpert
>
> *It is not birth, marriage, or death, but gastrulation which is truly the most important time in your life.*

A fundamental question is: how do robust pattern emerge during embryo development?

In the Turing pre-pattern theory, chemicals, or morphogens, react together and, if certain conditions concerning their reaction kinetics and diffusion rates are satisfied (to be derived in the next section), then a *pre-pattern* of varying chemical concentrations is set up in the spatial domain. This means that throughout the spatial domain, the concentration levels of the chemicals will vary i.e. there will be a *heterogeneous* distribution of chemical concentrations which is known as a pre-pattern. Any cells in the domain which subsequently encounter these varying levels of morphogens will then respond by, for example, proliferating differentially throughout the domain. In this way, the domain will then contain a spatially heterogeneous distribution of cell densities (i.e. a cellular pattern) which have responded to the morphogen pre-pattern. This pre-pattern theory was first proposed by Alan Turing (of Enigma Code fame) in his seminal 1952 paper, *The chemical basis of morphogenesis* Turing (1990).

In the mechano-chemical theory, cells interact with their surroundings and by exerting forces perturb their local environment. The combination of cell migration/proliferation and cell-generated forces is sufficient in certain circumstances to create a spatially heterogeneous distribution of cell densities i.e. the pattern is generated *simultaneously* with the cell migration/proliferation. This alternative pattern formation theory was proposed by Murray and Oster James D. Murray and Oster (1984) and is particularly appropriate for patterns generated in early embryogenesis by *mesenchymal cells* such as fibroblasts.

6.2 Reaction-diffusion (Turing) Pre-pattern Mechanisms

We now consider our general (dimensional) reaction-diffusion model for two chemicals or morphogens with concentrations $A(\mathbf{x}, t)$ and $B(\mathbf{x}, t)$ which react together and diffuse in some spatial domain:

$$\frac{\partial A}{\partial t} = F(A, B) + D_A \nabla^2 A,$$
$$\frac{\partial B}{\partial t} = G(A, B) + D_B \nabla^2 B,$$

where $F(A, B)$ and $G(A, B)$ describe the reaction kinetics between the two morphogens and $D_A, D_B > 0$ are the diffusion coefficients. Turing's theory (Turing, 1952) *The chemical basis of morphogenesis* proposed that it was the diffusion of the substances A, B which led to the evolution of a spatially heterogeneous solution to arise i.e. a spatial pattern. This has given rise to the phrase *diffusion-driven instability*. This was a rather revolutionary and counter-intuitive proposal, since, as we have seen, diffusion normally has the opposite tendency i.e. to smooth or average out spatial heterogeneities, and to give rise to spatially homogeneous solutions.

Various forms can be considered for the kinetic functions F and G. However, we will focus mainly on three specific classes as follows:

6.2.1 Schnackenberg kinetics

$$F(A, B) = k_1 - k_2 A + k_3 A^2 B, \quad G(A, B) = k_4 - k_3 A^2 B$$

k_1, k_2, k_3, $k_4 > 0$. The term $k_3 A^2 B$ is *autocatalytic*, since the species A upregulates its own production.

6.2.2 Gierer and Meinhardt kinetics

Gierer and Meinhardt "A Theory of Biological Pattern Formation" (1972) developed a model that describes activator-inhibitor kinetics. The total reaction rates are

$$F(A,B) = k_1 - k_2 A + \frac{k_3 A^2}{B}, \quad G(A,B) = k_4 A^2 - k_5 B$$

where k_1, k_2, k_3, k_4, $k_5 > 0$. The term $k_3 A^2/B$ is **autocatalytic**.

6.2.3 Thomas kinetics

Thomas developed a model of substrate inhibition in which

$$\begin{aligned} F(A,B) &= k_1 - k_2 A - H(A,B), \\ G(A,B) &= k_4 A^2 - k_4 B - H(A,B), \\ H(A,B) &= \frac{k_5 AB}{k_6 + k_7 + k_8 A^2}. \end{aligned}$$

with $k_i > 0$. In the original paper of Thomas (1975), A represents the concentration of oxygen (substrate) and B the concentration of uricase (enzyme). Substrate inhibition is evident in the term $k_8 A^2$.

6.3 Non-dimensionalisation

Before proceeding further, it is prudent to non-dimensionalise each of the above systems.

6.3.1 Schnakenberg

We illustrate this process for the Schnakenberg kinetics. Using the scaling

$$u = A\left(\frac{k_3}{k_2}\right)^{1/2}, \quad v = B\left(\frac{k_3}{k_2}\right)^{1/2}, \quad t^* = \frac{D_A t}{L^2}, \quad x^* = \frac{x}{L},$$

where L is a typical length scale, the dimensionless reaction-diffusion system with Schnakenberg kinetics becomes (upon dropping the $*$ for notational convenience):

$$\begin{aligned}\frac{\partial u}{\partial t} &= \gamma(a - u + u^2 v) + \nabla^2 u = \gamma f(u,v) + \nabla^2 u,\\ \frac{\partial v}{\partial t} &= \gamma(b - u^2 v) + d\nabla^2 v = \gamma g(u,w) + d\nabla^2 v,\end{aligned} \tag{6.1}$$

where

$$d = \frac{D_B}{D_A}, \quad a = \frac{k_1}{k_2}\left(\frac{k_3}{k_2}\right)^{1/2}, \quad b = \frac{k_4}{k_2}\left(\frac{k_3}{k_2}\right)^{1/2}, \quad \gamma = \frac{L^2 k_2}{D_A}.$$

6.3.2 Gierer and Meinhardt

The Gierer-Meinhardt kinetics can be non-dimensionalised as follows:

$$f(u,v) = a - bu + \frac{u^2}{v}, g(u,v) \quad = u^2 - v,$$

where a and b are positive parameters (Exercise/Tutorial).

6.3.3 Thomas

The Thomas kinetics can be non-dimensionalised as follows:

$$\begin{aligned}f(u,v) &= a - u - h(u,v),\\ g(u,v) &= \alpha(b - v) - h(u,v),\\ h(u,v) &= \frac{\rho u v}{1 + u + K u^2},\end{aligned}$$

where a , b, α, ρ , K are positive parameters (see Exercise/Tutorial).

6.3.4 General

Any reaction-diffusion system can be non-dimensionalised and scaled following the above procedure to take the general form:

$$\begin{aligned}\frac{\partial u}{\partial t} &= \gamma f(u,v) + \nabla^2 u,\\ \frac{\partial v}{\partial t} &= \gamma g(u,w) + d\nabla^2 v,\end{aligned}$$

where the parameter d is the ratio of the diffusion coefficients and the parameter γ can be interpreted in any one of the following ways:

- $\gamma^{1/2}$ is proportional to the *linear size* of the spatial domain in one-dimension. In two-dimensions, γ is proportional to the area.
- γ represents the relative strength of the reaction terms – an increase in γ may represent an increase in the activity of some rate-limiting step in the reaction sequence.
- An increase in γ is equivalent to a decrease in the diffusion coefficient, d.

Note that in the case where the parameter $d > 1$, this means that the original diffusion coefficients are not equal. Specifically, in the case of the Gierer-Meinhardt activator-inhibitor system, $d > 1$ implies that the inhibitor *diffuses more quickly* than the activator [$d > 1 \Rightarrow D_B > D_A$]. The spatial implications of this are shown in Figure 6.1 – the inhibitor diffuses a greater distance than the activator, giving rise to what is known as *local activation, long-range inhibition.*

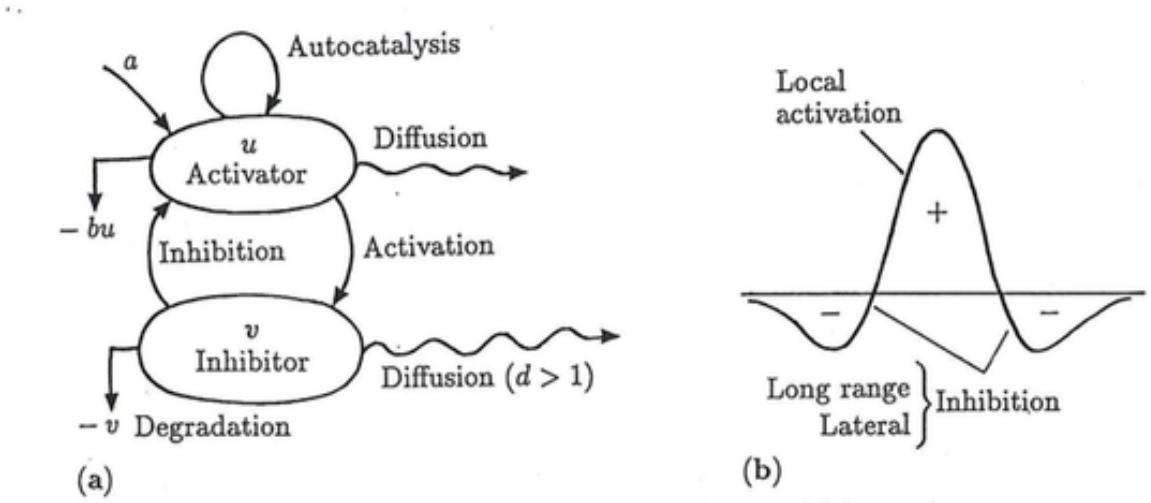

Figure 6.1: Schematic diagram of activator inhibitor

6.4 Numerical solution

In Figure 6.3 we consider a numerical solution of the Schnackenberg model on a 2D square domain with no-flux boundary conditions.

6.5 General conditions for diffusion-driven instability

Let $\Omega \subset R^n$ be a domain with smooth (sufficiently regular) boundary $\partial\Omega$, with outward unit normal $\mathbf{n}$. Our general, non-dimensional reaction-diffusion system is then:

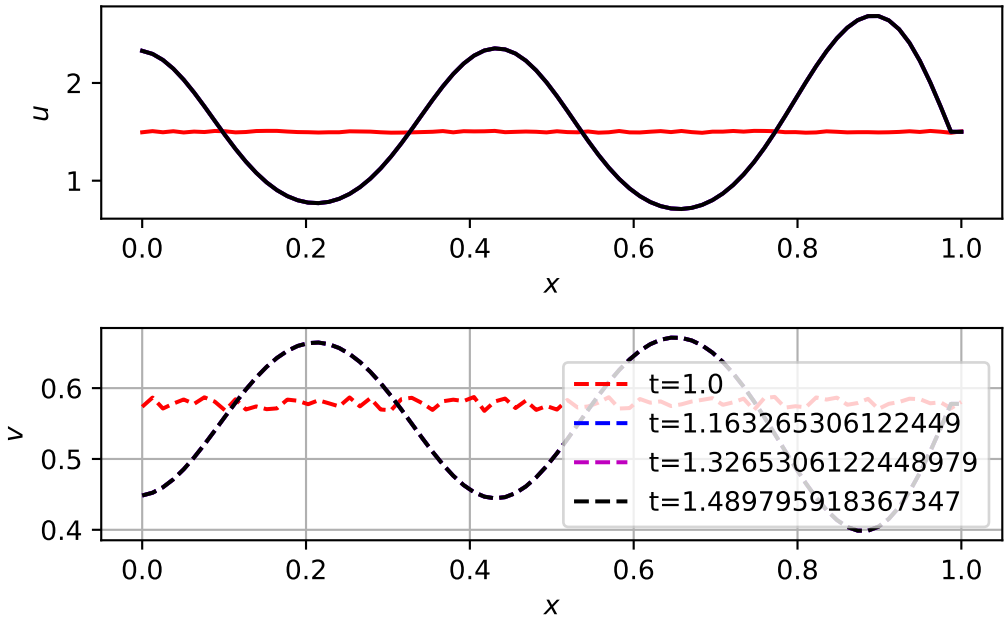

Figure 6.2: DDI with Schnackenberg kinetics.

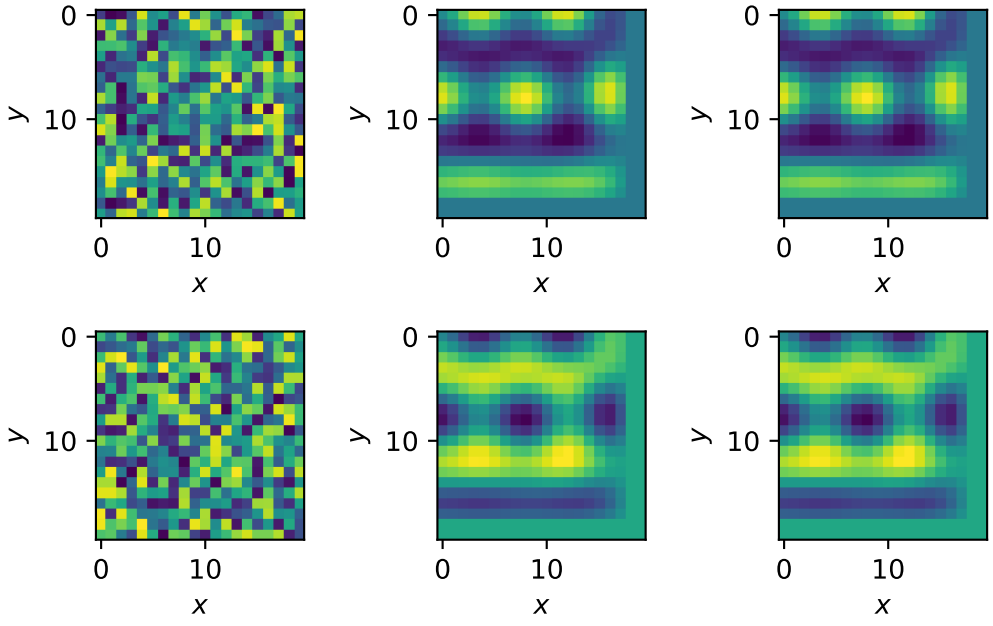

Figure 6.3: DDI with Schnackenberg kinetics in 2D

$$\begin{aligned}\frac{\partial u}{\partial t} &= \gamma\, f(u,v) + \nabla^2 u, \qquad x \in \Omega, \quad t > 0,\\ \frac{\partial v}{\partial t} &= \gamma\, g(u,v) + d\nabla^2 v, \qquad x \in \Omega, \quad t > 0,\end{aligned} \tag{6.2}$$

together with boundary and initial conditions

$$\begin{aligned}&\nabla u \cdot \mathbf{n} = 0, \qquad \nabla v \cdot \mathbf{n} = 0, \qquad x \in \partial\Omega, \quad t > 0,\\ &u(x,0) = u_0(x), \qquad v(x,0) = v_0(x), \qquad x \in \Omega\,.\end{aligned} \tag{6.3}$$

A *spatially homogeneous steady-state* of Equation 6.2 and Equation 6.3 satisfies

$$f(u,v) = 0, \qquad g(u,v) = 0$$

and we denote it by (u_0, v_0).

6.5.1 Stability of spatially homogeneous steady states to spatially homogeneous perturbations

Before we consider the effect of diffusion in Equation 6.2 and Equation 6.3, we first explore the stability of the spatially homogeneous steady state.

Consider the following perturbations to the steady state (u_0, v_0):

$$u(x,t) = u_0 + \tilde{u}(t), \quad v(x,t) = v_0 + \tilde{v}(t), \qquad \|\tilde{u}(t)\| \ll 1, \quad \|\tilde{v}(t)\| \ll 1.$$

Upon substitution into Equation 6.2

$$\begin{aligned}\frac{d\tilde{u}}{dt} &= \gamma\, f(u_0 + \tilde{u}, v_0 + \tilde{v}),\\ \frac{d\tilde{v}}{dt} &= \gamma\, g(u_0 + \tilde{u}, v_0 + \tilde{v}).\end{aligned} \tag{6.4}$$

Taylor expansion of f and g about (u_0, v_0) yields the linearised system

$$\begin{pmatrix}\tilde{u}_t\\ \tilde{v}_t\end{pmatrix} = \gamma J \begin{pmatrix}\tilde{u}\\ \tilde{v}\end{pmatrix}, \tag{6.5}$$

where

$$J = J(u_0, v_0) = \begin{pmatrix}f_u & f_v\\ g_u & g_v\end{pmatrix}_{(u_0, v_0)}.$$

The general solution of Equation 6.5 is

$$\begin{pmatrix}\tilde{u}(t)\\ \tilde{v}(t)\end{pmatrix} = C_1\phi_1 e^{\lambda_1 t} + C_2\phi_2 e^{\lambda_2 t},$$

where C_1, C_2 are arbitrary constants, λ_1, λ_2 are the eigenvalues of γJ, i.e. solutions of the characteristic equation

$$\det(\gamma J - \lambda I) = 0,$$

and ϕ_1, ϕ_2 are corresponding eigenvectors. It is easily seen that

$$\lambda_{1,2} = \frac{\gamma}{2}\left(\mathrm{tr}(J) \pm \sqrt{\mathrm{tr}(J)^2 - 4\det(J)}\right),$$

and thus a spatially homogeneous steady state (u_0, v_0) is *stable* to spatially homogeneous perturbations if

$$\mathrm{Re}(\lambda_{1,2}) < 0,$$

i.e. if

$$\begin{aligned}\mathrm{tr}(J) &= f_u + g_v < 0,\\ \det(J) &= f_u g_v - f_v g_u > 0.\end{aligned} \tag{6.6}$$

We shall be interested only in such parameter values for which conditions Equation 6.6 are satisfied (i.e. the spatially homogeneous steady state is linearly stable in the absence of diffusion).

6.5.2 Stability of spatially homogeneous steady states to spatially heterogeneous perturbations

We now consider perturbations about the spatially homogeneous steady state that are spatially dependent, i.e.

$$u(x,t) = u_0 + \tilde{u}(x,t), \quad v(x,t) = v_0 + \tilde{v}(x,t), \qquad \|\tilde{u}(x,t)\| \ll 1, \quad \|\tilde{v}(x,t)\| \ll 1.$$

Upon substitution in Equation 6.2 and Taylor expanding f and g about (u_0, v_0) yields the linearised problem

$$\begin{aligned}\frac{\partial \tilde{u}(x,t)}{\partial t} &= \gamma\left(f_u\tilde{u}(x,t) + f_v\tilde{v}(x,t)\right) + \nabla^2\tilde{u}(x,t), \quad x \in \Omega,\ t > 0,\\ \frac{\partial \tilde{v}(x,t)}{\partial t} &= \gamma\left(g_u\tilde{u}(x,t) + g_v\tilde{v}(x,t)\right) + d\nabla^2\tilde{v}(x,t) \quad x \in \Omega, t > 0,\end{aligned} \tag{6.7}$$

with boundary conditions

$$\mathbf{n} \cdot \nabla \tilde{u}(x,t) = 0, \qquad \mathbf{n} \cdot \nabla \tilde{v}(x,t) = 0, \qquad x \in \partial\Omega,\ t > 0. \tag{6.8}$$

Defining

$$V(x,t) = \begin{pmatrix} \tilde{u}(x,t) \\ \tilde{v}(x,t) \end{pmatrix}$$

we rewrite Equation 6.7 as

$$\frac{\partial}{\partial t} V(x,t) = \gamma J V(x,t) + D\nabla^2 V(x,t),$$

where

$$D = \begin{pmatrix} 1 & 0 \\ 0 & d \end{pmatrix}.$$

We shall consider a separation of variables approach, i.e.

$$V(x,t) = \begin{pmatrix} \bar{u}(t)\varphi_1(x) \\ \bar{v}(t)\varphi_2(x) \end{pmatrix},$$

and obtain

$$\begin{aligned} \frac{d\bar{u}(t)}{dt}\varphi_1(x) &= \gamma\ (f_u \bar{u}(t)\varphi_1(x) + f_v \bar{v}(t)\varphi_2(x)) + \bar{u}(t)\nabla^2\varphi_1(x), \quad x \in \Omega,\ t > 0, \\ \frac{d\bar{v}(t)}{dt}\varphi_2(x) &= \gamma\ (g_u \bar{u}(t)\varphi_1(x) + g_v \bar{v}(t)\varphi_2(x)) + d\bar{v}(t)\nabla^2\varphi_2(x), \quad x \in \Omega,\ t > 0, \end{aligned} \tag{6.9}$$

with boundary conditions

$$\mathbf{n} \cdot \nabla \varphi_1(x) = 0, \qquad \mathbf{n} \cdot \nabla \varphi_2(x) = 0, \qquad x \in \partial\Omega,\ t > 0. \tag{6.10}$$

It is assumed that

$$\bar{u}(t) \not\equiv 0 \quad \text{and} \quad \bar{v}(t) \not\equiv 0$$

for $t > 0$.

Lemma 6.1. *Consider the spatial eigenvalue problem for the Laplacian ∇^2 with zero-Neumann boundary conditions, i.e.*

$$\begin{aligned} \nabla^2\psi(x) &= -k^2\psi(x), \qquad x \in \Omega, \\ \mathbf{n}\cdot\nabla\psi(x) &= 0, \qquad x \in \partial\Omega. \end{aligned} \tag{6.11}$$

For a bounded domain Ω there exists a discrete set of eigenvalues

$$0 \le k_1^2 < k_2^2 \le k_3^2 \le \ldots \le k_j^2 \le \ldots,$$

with

$$j \in \mathbb{N}, \quad \textit{and} \quad k_j^2 \to \infty \quad \textit{as} \quad j \to \infty.$$

*Moreover, the eigenfunctions $\{\psi_k(x)\}$ form an **orthogonal set** of basis functions of the corresponding functional space (i.e. $L^2(\Omega)$, $H^1(\Omega)$).*

Thus we can look for the spatial component of the solution of Equation 6.9 as follows:

$$\varphi(x) = \begin{pmatrix} \varphi_1(x) \\ \varphi_2(x) \end{pmatrix} = \sum_k C_k\psi_k(x), \qquad C_k = \begin{pmatrix} C_k^1 \\ C_k^2 \end{pmatrix} \in \mathbb{R}^2$$

and

$$V(x,t) = \sum_k \hat{V}_k(t)\psi_k(x), \qquad \text{where} \quad \hat{V}_k(t) = \begin{pmatrix} C_k^1\ \bar{u}(t) \\ C_k^2\ \bar{v}(t) \end{pmatrix}. \tag{6.12}$$

Since

$$\nabla^2\psi_k(x) = -k^2\psi_k(x)$$

we obtain

$$D\nabla^2 V(x,t) = D\nabla^2\left[\sum_k \hat{V}_k(t)\psi_k(x)\right] = \sum_k D\hat{V}_k(t)\nabla^2\psi_k(x) = -\sum_k k^2 D\hat{V}_k(t)\psi_k(x).$$

Hence

$$\sum_k \frac{d}{dt}\hat{V}_k(t)\psi_k(x) = \sum_k \gamma J\hat{V}_k(t)\psi_k(x) - \sum_k k^2 D\hat{V}_k(t)\psi_k(x).$$

Since $\{\psi_k(x)\}$ is a orthogonal basis we obtain that

$$\frac{d}{dt}\hat{V}_k(t)\psi_k(x) = \gamma J\hat{V}_k(t)\psi_k(x) - k^2 D\hat{V}_k(t)\psi_k(x),$$

for each k. Finally, since

$$\psi_k(x) \not\equiv 0$$

in Ω this implies for each k a system of ODEs:

$$\frac{d}{dt}\hat{V}_k(t) = (\gamma J - k^2 D)\,\hat{V}_k(t) \quad = \tilde{J}\hat{V}_k(t), \tag{6.13}$$

where $\tilde{J}$ is the "modified" Jacobian:

$$\tilde{J} = \begin{pmatrix} \gamma f_u - k^2 & \gamma f_v \\ \gamma g_u & \gamma g_v - dk^2 \end{pmatrix}.$$

Now solutions of Equation 6.13 are of the form

$$\hat{V}_k(t) = e^{\lambda t} P_k$$

with $P_k \in \mathbb{R}^2$, where, since $P_k \neq 0$ (looking for nontrivial solutions), we find that λ are the eigenvalues of $\tilde{J}$, i.e. solutions of the characteristic equation

$$\det(\tilde{J} - \lambda I) = \det(\gamma J - k^2 D - \lambda I) = 0. \tag{6.14}$$

Evaluating the above determinant, we arrive at the equation:

$$\lambda^2 + [k^2(1+d) - \gamma(f_u + g_v)]\lambda + h(k^2) = 0, \tag{6.15}$$

where

$$h(k^2) = dk^4 - \gamma(df_u + g_v)k^2 + \gamma^2|J|. \tag{6.16}$$

NOTE: From Equation 6.14, Equation 6.15 we can recover the characteristic equation for the spatially homogeneous perturbation when $k = 0$, i.e.

$$\tilde{J}\Big|_{k=0} = (\gamma J - k^2 D)\Big|_{k=0} = \gamma J.$$

Thus the steady state (u_0, v_0) is *unstable* to spatially heterogeneous perturbations iff

$$\mathrm{Re}(\lambda_1) > 0 \quad \text{and/or} \quad \mathrm{Re}(\lambda_2) > 0,$$

where $\lambda_{1,2}$ are solutions of Equation 6.14, Equation 6.15.

Now for

$$\mathrm{Re}(\lambda_1) > 0 \quad \text{and/or} \quad \mathrm{Re}(\lambda_2) > 0$$

to be satisfied we require

$$\mathrm{tr}(\tilde{J}) > 0 \quad \text{or} \quad \det(\tilde{J}) < 0.$$

Consider first $tr(\tilde{J})$. We have

$$\mathrm{tr}(\tilde{J}) = \gamma(f_u + g_v) - k^2(1+d) < 0,$$

since $\gamma > 0$ and

$$f_u + g_v < 0$$

by the stability condition for the spatially homogeneous perturbation Equation 6.6. Thus instability to the spatially heterogeneous perturbation *can only occur* if

$$\det(\tilde{J}) < 0$$

and so we require:

$$\det(\tilde{J}) = h(k^2) = dk^4 - \gamma(d\, f_u + g_v)k^2 + \gamma^2 \det(J) < 0.$$

From the spatially homogeneous stability conditions Equation 6.6 we have $\det(J) > 0$. Thus $h(k^2) < 0$ is possible only if

$$df_u + g_v > 0. \tag{6.17}$$

However, once again, due to Equation 6.6, we have $f_u + g_v < 0$, and so we can conclude that $d \neq 1$ and f_u and g_v must have *opposite signs*.

Condition Equation 6.17 is *necessary but not sufficient* to ensure $h(k^2) < 0$. In order to guarantee that $h(k^2) < 0$, the minimum value h_{min} must be negative. Differentiating Equation 6.16 w.r.t. k^2, we find that:

$$k_m^2 = \gamma \frac{df_u + g_v}{2d} \quad \Rightarrow \quad h_{min} = \gamma^2 \left[|J| - \frac{(df_u + g_v)^2}{4d} \right]. \tag{6.18}$$

Thus the condition that $h(k^2) < 0$ for some k^2 is:

$$\frac{(df_u + g_v)^2}{4d} > |J|.$$

The transition from stability to instability i.e. *bifurcation*, occurs when $h_{min} = 0$. From Equation 6.18, this means at bifurcation we have

$$|J| = \frac{(df_u + g_v)^2}{4d}. \tag{6.19}$$

For a fixed set of kinetics parameters, this means that we have a *critical diffusion coefficient* $d_c(>1)$, which, after re-arranging Equation 6.19, is the appropriate root of

$$q(d_c) = d_c^2 f_u^2 + 2(2f_v g_u - f_u g_v)d_c + g_v^2 = 0. \tag{6.20}$$

Finally, we note that using Equation 6.18, Equation 6.19, the *critical wave number* can be written:

$$k_c^2 = \gamma \frac{(d_c f_u + g_v)}{2d_c} = \gamma \left[\frac{|J|}{d_c}\right]^{1/2} = \gamma \left[\frac{f_u g_v - f_v g_u}{d_c}\right]^{1/2}. \tag{6.21}$$

Figure 6.5 (a) shows a schematic diagram of the (quadratic) function $h(k^2)$ for three different values of the diffusion coefficient d:

- $d < d_c,\ h(k^2) > 0$, and there is no pattern;
- $d = d_c,\ h_{min} = 0$, critical case;
- $d > d_c,\ h(k^2) < 0$, and there is pattern.

Hence we can see from Equation 6.15 that whenever $h(k^2) < 0$ the curve $\lambda(k^2)$ is positive for the same range of wavenumbers that make $h(k^2)$ negative. The range of unstable wavenumbers

$$k_1^2 < k^2 < k_2^2$$

can be found from the roots of Equation 6.16, $h(k^2) = 0$:

$$\begin{aligned} k_1^2 &= \gamma \frac{(df_u + g_v) - \left\{(df_u + g_v)^2 - 4d|J|\right\}^{1/2}}{2d} < k^2 \\ &< \gamma \frac{(df_u + g_v) + \left\{(df_u + g_v)^2 - 4d|J|\right\}^{1/2}}{2d} = k_2^2 \end{aligned} \tag{6.22}$$

Figure 6.5 (b) shows a schematic diagram of $\mathrm{Re}\lambda(k^2)$ for three different values of the diffusion coefficient d:

- \$d < d_c, ; $\mathrm{Re}\lambda(k^2) < 0$, k^2 \$, and there is no pattern;
- $d = d_c,\ k_c^2 = 0$, critical case;

The expression $\lambda = \lambda(k^2)$ is known as the *dispersion relation* and the plot of $\mathrm{Re}\lambda$ against k^2 is known as the *dispersion curve*.

From the previous analysis, within the unstable range of wavenumbers (k_1^2, k_2^2), $\mathrm{Re}\lambda(k^2) > 0$ has a *maximum value* at wavenumber k_m^2 given by Equation 6.18 when $d > d_c$. This implies that there is a *fastest growing mode* in the solution Equation 6.12 of our linearised system Equation 6.9.

Recalling Equation 6.12,

$$V(x,t) = \sum_k C_k e^{\lambda(k^2)t}\,\psi_k(x),$$

and noting the above analysis, this implies that as $t \to \infty$ the dominant contributions in the above sum are those for which $\mathrm{Re}\lambda(k^2) > 0$, since all other modes will tend to zero exponentially fast as $t \to \infty$. Thus, for large t, the solution is effectively given by:

$$V(x,t) \approx \sum_{k_1}^{k_2} C_k e^{\lambda(k^2)t}\,\psi_k(x)\ .$$

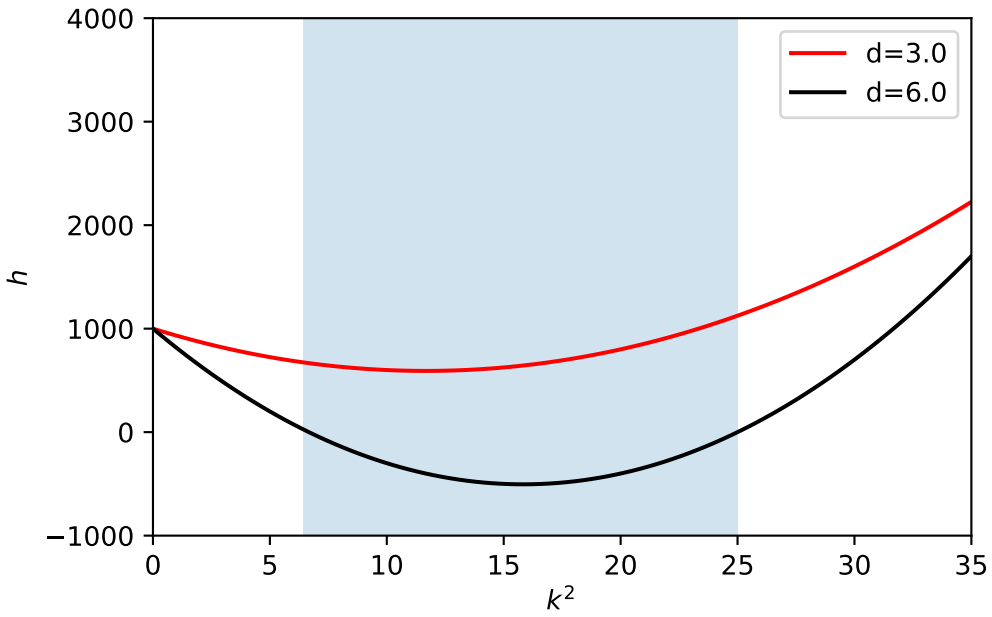

Figure 6.4: A plot of $h(k^2)$ plotted against k^2. Shaded region denotes unstable wave numbers in case of largets d.

NOTE

All the previous calculations concern a *linear stability analysis* carried out about a spatially homogeneous steady state of the system Equation 6.2. This linear theory indicates that for $d > d_c$ there exists a finite number of *linearly unstable* spatial eigenfunctions which grow exponentially as $t \to \infty$. However, this linear theory holds only when we are close to the steady state i.e. it only holds for small perturbations. In the full *nonlinear system* the exponentially growing (unbounded) modes will eventually be bounded by the nonlinear terms and so bounded, stable spatial patterns characterised by the corresponding wavenumbers will be formed.

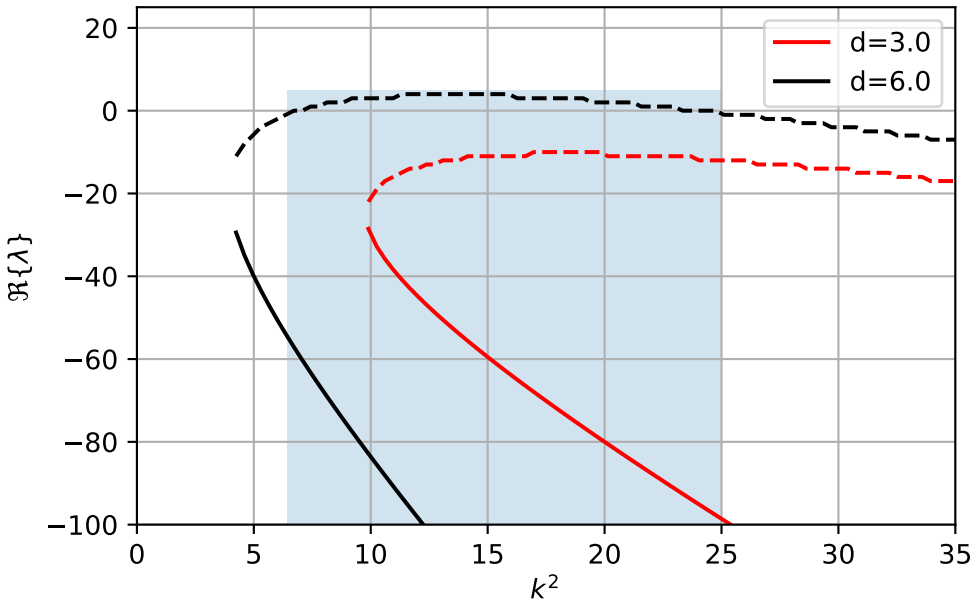

Figure 6.5: The real part of the eigenvalue plotted against k^2.

Summary

We have obtained conditions for the generation of spatial patterns via systems of reaction-diffusion equations of the general form Equation 6.2. Such systems involve *two chemicals or morphogens* reacting and diffusing together to generate a chemical pre-pattern that underlies a subsequent cellular pattern. The four conditions are as follows:

$$\begin{aligned} f_u + g_v &< 0, \\ f_u g_v - f_v g_u &> 0, \\ d f_u + g_v &> 0, \\ (d f_u + g_v)^2 - 4d(f_u g_v - f_v g_u)^2 &< 0, \end{aligned}$$

with all partial derivatives being evaluated at the spatially homogeneous steady state (u_0, v_0).

From the first and third conditions, $d \neq 1$ and f_u and g_v must be of different signs. For each of the reaction kinetics mentioned here (Schnakenberg, Gierer-Meinhardt, Thomas), we have that $f_u > 0, g_v < 0$ and so this implies that $d > 1$.

If the conditions Equation 6.23 are satisfied, then there is a range of unstable wavenumbers given by Equation 6.22 which give rise to a spatial pattern. The spatial patterns which initially grow are those spatial eigenfunctions $\psi_k(x)$ whose wavenumbers k are such that $k_1 < k < k_2$.

In most biological systems, the kinetic parameters and diffusion coefficients are fixed. This means that the only variable parameter in the system is γ which as we have seen is related to the size of the domain under consideration. This has implications when considering patterns on finite domains, as will be seen in the next section.

6.6 Exercises

Demonstrate that the derived results are consistent with numerical solutions. Some predictions to test:

- No patterning when diffusion coefficients are equal
- How does spatial pattern formation change as you try values of parameters a and b?
- Can you correlate the observation of pattern to the conditions for DDI being satisfied?
- what about different kinetics (e.g. Gierer-Meinhardt, Thomas models)?

6.7 References

7 Infectious disease

Mathematical modelling of infectious diseases can help to understand complex (nonlinear) interactions, to design vaccination strategies, predict further outbreaks of diseases, how many individual will be affected.

During the Covid-19 pandemic variants of the SIR ODE model were used to study disease transmission. One limitation of the SIR model is that it assumes a well-mixed population. In reality, infectious disease transmission is a spatio-tempral process.

7.1 Generalising the SIR model

Assumptions

- Total population is constant: the duration of the epidemic is short compared to the lifetime of its hosts, so we can neglect birth and disease-unrelated death
- Consider a disease which, after recovery, confers immunity (and/or death if lethal)
- Simple diffusion for spatial distribution of population

Consider consider three categories of population

- S – susceptibles - can be infected
- I – infectives - have the disease and can transmit to susceptibles
- R – recovered (removed) - have had the disease and are no longer infective.

Progress through the disease

$$S \longrightarrow I \longrightarrow R$$

Model assumptions

- The gain in the infectives class is at the rate proportional to the number of infectives I and susceptibles S, i.e. $r\ I\ S$, ; $r > 0$.
- The susceptibles are lost at the same rate, i.r. $r\ I\ S$
- The rate of removal of infectives to the recovered class R is proportional to the number of invfectives, i.e. $a\ I$, ; $a > 0$.

$1/a$ measures the time spent in the infectious state.

- The incubation period is short enough to be negligible: susceptibles are directly infected after coming into contact with the disease (with infectives).

Then a simple SIR model reads (in a long thin domain or in 3-dim domain with solutions in a form of planar fronts)

$$\begin{aligned}
\frac{\partial S}{\partial t} &= -rSI + D_S \frac{\partial^2 S}{\partial x^2}\,, \quad x \in \mathbb{R}, t > 0\,,\\
\frac{\partial I}{\partial t} &= rSI - aI + D_I \frac{\partial^2 I}{\partial x^2}\,, \quad x \in \mathbb{R},\ t > 0\,,\\
\frac{\partial R}{\partial t} &= aI + D_R \frac{\partial^2 R}{\partial x^2}\,, \quad x \in \mathbb{R},\ t > 0\\
S(0,x) &= S_0(x), \qquad I(0,x) = I_0(x), \quad R(0,x) = R_0(x), \qquad x \in \mathbb{R}\,,
\end{aligned} \tag{7.1}$$

where

- $a > 0$ – removal or death rate
- $r > 0$ – transmission or infection rate
- $D_S > 0$, ; $D_I > 0$, ; $D_R > 0$ – diffusion coefficients

We assume that $S_0(x) \geq 0$, $I_0(x) \geq 0$, $R_0(x) \geq 0$ for $x \in \mathbb{R}$ and obtain that solutions of Equation 7.1 are nonnegative, i.e.

$$S(t,x) \geq 0, \quad I(t,x) \geq 0, \quad R(t,x) \geq 0, \quad x \in \mathbb{R}, \quad t > 0\,.$$

To analyse the model Equation 7.1 it is sufficient to consider the first two equations, since R is completely determined by I and does not influence the dynamics of S and I.

Considering the non-dimensionalisation

$$I^* = \frac{I}{\bar{S}_0}, \quad S^* = \frac{S}{\bar{S}_0}, \quad x^* = \left(\frac{r\bar{S}_0}{D_I}\right)^{1/2} x, \quad t^* = r\bar{S}_0 t$$

we obtain (after dropping '$*$')

$$\begin{aligned}
\frac{\partial S}{\partial t} &= -SI + d\frac{\partial^2 S}{\partial x^2}\,, && x \in \mathbb{R},\ t > 0\,,\\
\frac{\partial I}{\partial t} &= SI - \mu I + \frac{\partial^2 I}{\partial x^2}\,, && x \in \mathbb{R},\ t > 0\,,\\
S(0,x) &= \frac{S_0(x)}{\bar{S}_0}, \qquad I(0,x) = \frac{I_0(x)}{\bar{S}_0}, && x \in \mathbb{R}\,,
\end{aligned}$$

where $\bar{S}_0$ is a representative population density and $\mu = a/r\bar{S}_0$.

We would like to investigate the spatial spread of an epidemic wave of infectives into a uniform susceptibles population $S_0(x) = \bar{S}_0$. We would like to determine conditions for existence of an epidemic wave and propagation speed.

We shall assume first that $D_S = D_I$, i.e. $d = 1$. Consider travelling wave solutions

$$S(t,x) = s(z), \quad I(t,x) = i(z), \quad z = x - vt, \quad v > 0$$

and obtain following ODEs for s and i

$$\begin{aligned} s'' + vs' - is &= 0 \,, \\ i'' + vi' + is - \mu i &= 0 \,. \end{aligned} \tag{7.2}$$

We would like to analyse the existence of a travelling wave from for S and travelling wave pulse for I. We assume that the infection comes into susceptible population from the left.

Therefore we consider the following boundary conditions for the travelling wave solutions

$$\begin{aligned} s(z) &\to 1 \quad z \to +\infty, \quad & i(z) &\to 0 \quad z \to +\infty \,, \\ s(z) &\to \sigma \quad z \to -\infty, \quad & i(z) &\to 0 \quad z \to -\infty \,, \\ s'(z) &\to 0 \quad z \to \pm\infty, \quad & i'(z) &\to 0 \quad z \to \pm\infty \,, \end{aligned} \tag{7.3}$$

where $0 \le \sigma < 1$.

The steady states of Equation 7.2 are given by

$$is = 0, \quad i(s-\mu) = 0 \quad \Longrightarrow \quad i = 0, \quad s = \text{const.}$$

Considering boundary conditions Equation 7.3 we obtain two steady states

$$(s_0, i_0) = (1, 0), \qquad (s_0, i_0) = (\sigma, 0)$$

Hence we would like to have a heteroclinic connection between $(\sigma, 0)$ and $(1, 0)$.

The necessary condition for existence of travelling wave solutions satisfying Equation 7.2 and Equation 7.3 is

$$v \ge 2\sqrt{1-\mu} \quad \text{and} \quad 0 \le \mu < 1 \,. \tag{7.4}$$

In terms of original parameters we have

$$\mu = \frac{a}{rS_0} < 1.$$

This is the necessary threshold conditions for the propagation of an epidemic wave pulse. The condition Equation 7.4 determine also the non-dimensionalised minimal wave speed

$$v^*_{\min} = 2\sqrt{1-\mu}$$

In dimensional terms we obtain

$$z^* = x^* - v^* t^* = \left(\frac{rS_0}{D_I}\right)^{1/} x - v^* r S_0 t = \left(\frac{rS_0}{D_I}\right)^{1/} (x - vt) = \left(\frac{rS_0}{D_I}\right)^{1/} z$$

and

$$v = \sqrt{rS_0 D_I} v^* \quad v_{\min} = 2\sqrt{rS_0 D_I}\sqrt{1-\mu} = 2\sqrt{rS_0 D_I}\sqrt{1-\frac{a}{rS_0}}$$

We can analyse the behaviour of travelling wave solutions as $z \to +\infty$.

Linearised equation for the second equation in Equation 7.2 near $s = 1$, $i = 0$, i.e. as $z \to +\infty$ reads

$$i'' + vi' + i - \mu i = 0 \, .$$

Thus

$$i(z) \sim \exp\left(\frac{1}{2}\left[-v \pm \sqrt{v^2 - 4(1-\mu)}\right] z\right) \quad \text{as } z \to +\infty \, . \tag{7.5}$$

We can also show that the travelling wave solution $s(z)$ can not have a local maximum, since for $s'(z) = 0$ first equation in Equation 7.2 implies

$$s''(z) = is > 0,$$

which implies a local minimum. So $s(z)$ is monotone increasing.

Considering linearisation of the first equation in Equation 7.2 near $s = 1$, $i = 0$, i.e. as $z \to +\infty$, we obtain with $s(z) = 1 - \tilde{s}(z)$

$$\tilde{s}'' + v\tilde{s}' - i = 0 \, .$$

The using Equation 7.5 we can conclude that

$$\tilde{s}(z) \sim \exp\left(\frac{1}{2}\left[-v \pm \sqrt{v^2 - 4(1-\mu)}\right] z\right) \quad \text{as } z \to +\infty \, . \tag{7.6}$$

and

$$s(z) \sim 1 - C\exp\left(\frac{1}{2}\left[-v \pm \sqrt{v^2 - 4(1-\mu)}\right] z\right) \quad \text{as } z \to +\infty \, . \tag{7.7}$$

7.2 Spatial spread of rabies among foxes

Spread of rabies is due primary to the migration of infected foxes. We assume the heathy foxes are territorial and do not travel very far, whereas rabid foxes wander over large distances.

Thus we assume that $D_S \ll D_I$ and $d = D_S/D_I \approx 0$.

$$\begin{aligned} &\frac{\partial S}{\partial t} = -SI \ , && x \in \mathbb{R},\ t > 0 \ , \\ &\frac{\partial I}{\partial t} = SI - \mu I + \frac{\partial^2 I}{\partial x^2} \ , && x \in \mathbb{R},\ t > 0 \ , \\ &S(0,x) = 1, \qquad I(0,x) = \frac{I_0}{S_0}, && x \in \mathbb{R} \ , \end{aligned} \tag{7.8}$$

We shall look for travelling wave solutions of Equation 7.8: travelling wave front for S and travelling wave pulse for I. Considering

$$S(t,x) = s(z), \quad I(t,x) = i(z), \quad z = x - vt, \quad v > 0$$

and obtain following ODEs for s and i

$$\begin{aligned} &vs' = is \ , \\ &i'' + vi' + is - \mu i = 0 \end{aligned} \tag{7.9}$$

and corresponding boundary conditions

$$\begin{aligned} s(z) &\to 1 \quad z \to +\infty, \qquad i(z) \to 0 \quad z \to +\infty \ , \\ s(z) &\to \sigma \quad z \to -\infty, \qquad i(z) \to 0 \quad z \to -\infty \ , \\ s'(z) &\to 0 \quad z \to \pm\infty, \qquad i'(z) \to 0 \quad z \to \pm\infty \ , \end{aligned} \tag{7.10}$$

where $0 \le \sigma < 1$.

As before, the steady states of Equation 7.9 are given by

$$is = 0, \quad i(s - \mu) = 0 \quad \Longrightarrow \quad i = 0, \quad s = \text{const} \ .$$

Considering boundary conditions Equation 7.10 we obtain two steady states

$$(s_0, i_0) = (1, 0), \qquad (s_0, i_0) = (\sigma, 0) \ .$$

Linearising equations Equation 7.9 about the steady state $(1, 0)$ and requiring that i is non-negative we obtain, as for Equation 7.2, the necessary conditions for existence of travelling wave solutions satisfying Equation 7.9 and Equation 7.10 :

$$v \ge 2\sqrt{1 - \mu} \quad \text{and} \quad 0 \le \mu < 1 \ .$$

We can determine the relation between density of susceptibles left behind the infection pulse and the model parameters.

Using first equation in Equation 7.9 in the second implies

$$i'' + vi' + vs' - \mu i = 0 \, . \tag{7.11}$$

Integrating with respect to z yields

$$i' + vi + vs - \mu \int i \, dz = K = const \, . \tag{7.12}$$

Consider now ageing the first equation in Equation 7.9

$$i = v\frac{s'}{s}, \qquad s \neq 0$$

and obtain from Equation 7.12

$$i' + vi + vs - v\mu \int \frac{s'}{s} \, dz = K = const \, .$$

or

$$i' + vi + vs - v\mu \ln(s) = K \, . \tag{7.13}$$

Using now in Equation 7.13 boundary conditions as $z \to +\infty$, from Equation 7.10, we can determine constant K:

$$v = K \, .$$

Thus we have

$$i' + vi + v(s - \mu \ln(s) - 1) = 0 \, . \tag{7.14}$$

Using now in Equation 7.14 boundary conditions as $z \to -\infty$, see Equation 7.10, gives

$$v(\sigma - \mu \ln(\sigma) - 1) = 0 \, .$$

and

$$\frac{\sigma - 1}{\ln(\sigma)} = \mu \, . \tag{7.15}$$

We obtain that the number of susceptibles is defined independently of the wave speed and the smaller μ corresponds to smaller σ (i.e. fever susceptibles survive infection wave). Thus μ measures how sever the epidemic is.

Considering the critical value for $\mu = 1$, which in dimensional terms means

$$\frac{a}{rS_0} = 1,$$

we can conclude that there exists no wave of infection

- if S_0 is too low - density of foxes is too low in order to spread the disease,

- or if removal rate is too large - high death rate and the infection is too virulent
- or if infection rate r is too small - the disease is too

7.3 Generalisation of simple SIR model

We developed a simple model for the passage of a wave of infection, however data of a spread of rabies in continental Europe looks quite different, i.e. comprises oscillations behind the wave front. It is likely that birth-death processes, not included in the simple model, impact dynamics of susceptibles and invectives.

We generalised the simple model by considering growth of susceptibles population in a logistic manner

$$\begin{aligned} &\frac{\partial S}{\partial t} = -rSI + BS\left(1 - \frac{S}{S_0}\right) , && x \in \mathbb{R},\ t > 0 , \\ &\frac{\partial I}{\partial t} = rSI - aI + D_I \frac{\partial^2 I}{\partial x^2} , && x \in \mathbb{R},\ t > 0 , \\ &S(0,x) = S_0, \qquad I(0,x) = I_0, && x \in \mathbb{R} , \end{aligned} \tag{7.16}$$

where B is the intrinsic growth rate and S_0 is the carrying capacity.

We can non-dimensionalize Equation 7.16 as before and obtain

$$\begin{aligned} &\frac{\partial S}{\partial t} = -SI + bS\,(1 - S) , && x \in \mathbb{R},\ t > 0 , \\ &\frac{\partial I}{\partial t} = SI - \mu\, I + \frac{\partial^2 I}{\partial x^2} , && x \in \mathbb{R},\ t > 0 , \\ &S(0,x) = 1, \qquad I(0,x) = I_0/S_0, && x \in \mathbb{R}, \end{aligned} \tag{7.17}$$

where

$$b = \frac{B}{rS_0}.$$

Spatially homogeneous steady states of Equation 7.17 are $(S_1^*, I_1^*) = (1, 0)$ and $(S_1^*, I_1^*) = (\mu, b(1-\mu))$.

To analyse the existence of travelling wave solutions we write equations for $s(z)$ and $i(z)$, where $s(z) = S(t,x)$, $i(z) = I(t,x)$ with $z = x - vt$

$$\begin{aligned} -vs' &= -is + bs(1-s) , \\ -vi' &= is - \mu i + i'' \end{aligned}$$

{eq-sir_tw_growth} and by introducing new variable $w = i'$ obtain

$$\begin{aligned} s' &= \frac{1}{v} i\, s - \frac{b}{v}\, s(1-s)\ , \\ i' &= w, \\ w' &= -vw - i(s-\mu)\ . \end{aligned} \tag{7.18}$$

The system Equation 7.18 has two stationary solutions

$$(s_1^*, i_1^*, w_1^*) = (1, 0, 0)$$

and

$$(s_2^*, i_2^*, w_2^*) = (\mu, b(1-\mu), 0)$$

. Considering linearisation of Equation 7.18 and computing eigenvalues of the Jabocian matrix

$$J(s,i,w) = \begin{pmatrix} \frac{i}{v} - \frac{b}{v} + \frac{2bs}{v} & \frac{s}{v} & 0 \\ 0 & 0 & 1 \\ -i & \mu - s & -v \end{pmatrix}$$

evaluated at the steady states we obtain that

$$(s_1^*, i_1^*, w_1^*) = (1, 0, 0)$$

is a saddle point and

$$(s_2^*, i_2^*, w_2^*) = (\mu, b(1-\mu), 0)$$

is a stable node for $\mu < \mu^*$ and a stable spiral (focus) for $\mu > \mu^*$, with some threshold value μ^*.

Thus we can show that a travelling wave solution exists which connects two steady states $(1, 0)$ and

$$(\mu, b(1-\mu))$$

and there exists a threshold $\mu = \mu^*$ such that for

$$1 > \mu > \mu^*$$

the approach to

$$(\mu, b(1-\mu))$$

is oscillatory, whereas for

$$0 < \mu < \mu^*$$

it is monotonic.

Part III

Appendices

8 Numerical methods in Python

8.1

Python has been installed on most computers on campus and you can access it via AppsAnywhere. The icon is located on your desktop. From AppsAnywhere, please select Anaconda 3.

However, you can also use your own personal computer. If you decide to do so, you will need to install Python on it. Python is free and works on Windows, Mac OS X and Linux.

It is strongly recommended that you download and install Anaconda. Install might take 5-15 minutes. Then reboot your computer.

If install has

Once you have installed Anaconda you can open Spyder. This will provide you with an editor to run python codes.

Install a development environment (for writing and unnirn gscripts). I use Visual studio Code.

Install the VS Code Python extension

Copy and paste the code below and save as DemoPythonCode.py.

```
4
```

You should see the answer 4 printed out on the terminal.

You will likely now need to install some libraries

8.2 Python libraries

- matplotlib
- numpp
- scipy

8.3 Single PDEs

8.3.1 MOL

8.3.2 Spatial discretisation

8.3.3 odeint

8.3.4 implementing boundary conditions

8.3.5 Identifying parameters

8.4 Systems of PDEs

9 Linear stability analysis of a system of nonlinear ODES

Consider a system of ODEs

$$\frac{du}{dt} = f(u) \quad \text{with} \quad u \in \mathbb{R}^m \quad \text{and} \quad t \in \mathbb{R}.$$

As an example consider $m = 2$:

$$\begin{cases} \dfrac{du_1}{dt} = F(u_1, u_2), \\ \dfrac{du_2}{dt} = G(u_1, u_2) \end{cases} \tag{9.1}$$

$(u_1, u_2) = (u_1^*, u_2^*)$ is the steady state of the system Equation 9.1, i.e.

$$\frac{du_1}{dt} = 0$$

and

$$\frac{du_2}{dt} = 0$$

.

To determine the behaviour of the solution near a steady state we consider

$$u_1(t) = u_1^* + \bar{u}_1(t), \quad u_2(t) = u_2^* + \bar{u}_2(t)$$

$$\begin{cases} \dfrac{d(u_1^* + \bar{u}_1)}{dt} = F(u_1^* + u_1, u_2^* + \bar{u}_2), \\ \dfrac{d(u_2^* + \bar{u}_2)}{dt} = G(u_1^* + u_1, u_2^* + \bar{u}_2) \end{cases} \tag{9.2}$$

Then using the fact that (u_1^*, u_2^*) is a steady state and applying Taylor series expansion about (u_1^*, u_2^*) and assuming that

$$\sup_t |\bar{u}_1(t)| \ll 1, \sup_t |\bar{u}_2(t)| \ll 1$$

(small perturbations of the steady state) we have

$$\begin{cases} \dfrac{d\bar{u}_1}{dt} = F(u_1^*, u_2^*) + \dfrac{\partial F}{\partial u_1}(u_1^*, u_2^*)\,\bar{u}_1 + \dfrac{\partial F}{\partial u_2}(u_1^*, u_2^*)\,\bar{u}_2 + O(|\bar{u}_1|^2, |\bar{u}_2|^2), \\ \dfrac{d\bar{u}_2}{dt} = G(u_1^*, u_2^*) + \dfrac{\partial G}{\partial u_1}(u_1^*, u_2^*)\,\bar{u}_1 + \dfrac{\partial G}{\partial u_2}(u_1^*, u_2^*)\,\bar{u}_2 + O(|\bar{u}_1|^2, |\bar{u}_2|^2) \end{cases} \tag{9.3}$$

Thus since (u_1^*, u_2^*) is a steady state, i.e. $F(u_1^*, u_2^*) = 0$ and $G(u_1^*, u_2^*) = 0$ (ignoring negligibly small higher order terms) we obtain system of linearised equations

$$\begin{pmatrix} \dfrac{d\bar{u}_1}{dt} \\ \dfrac{d\bar{u}_2}{dt} \end{pmatrix} = J(u_1^*, u_2^*) \begin{pmatrix} \bar{u}_1 \\ \bar{u}_2 \end{pmatrix} \tag{9.4}$$

where the Jacobian matrix $J(u_1^*, u_2^*)$ is defined as

$$J(u_1^*, u_2^*) = \begin{pmatrix} \dfrac{\partial F(u_1^*, u_2^*)}{\partial u_1} & \dfrac{\partial F(u_1^*, u_2^*)}{\partial u_2} \\ \dfrac{\partial G(u_1^*, u_2^*)}{\partial u_1} & \dfrac{\partial G(u_1^*, u_2^*)}{\partial u_2} \end{pmatrix}$$

Therefore the behaviour of the nonlinear system Equation 9.1 near the steady state (u_1^*, u_2^*) is determined by solutions of system of linear ODEs Equation 9.4.

Since Equation 9.4 is linear we can write the general solution of (**eqsystem_ode14?**)

$$\begin{pmatrix} \bar{u}_1 \\ \bar{u}_2 \end{pmatrix} = e^{\lambda_1 t} \begin{pmatrix} \phi_1 \\ \phi_2 \end{pmatrix} + e^{\lambda_2 t} \begin{pmatrix} \psi_1 \\ \psi_2 \end{pmatrix} \tag{9.5}$$

where λ_1 and λ_2 are eigenvalues of Jacobian matrix $J(u_1^*, u_2^*)$ and

$$\phi = \begin{pmatrix} \phi_1 \\ \phi_2 \end{pmatrix} \quad \text{and} \quad \psi = \begin{pmatrix} \psi_1 \\ \psi_2 \end{pmatrix}$$

are corresponding eigenvectors.

Denote

$$\bar{u} = \begin{pmatrix} \bar{u}_1 \\ \bar{u}_2 \end{pmatrix}$$

.

If both $\lambda_{1,2} \neq 0$ then the stability of the steady state (u_1^*, u_2^*) is determined by the real part of the eigenvalues $\lambda_{1,2}$.

- If either $\mathcal{R}e(\lambda_1) > 0$ or $\mathcal{R}e(\lambda_2) > 0$ then
  $|\bar{u}(t)| \to +\infty$ as $t \to +\infty$ and (u_1^*, u_2^*) is unstable.

- If $\mathcal{R}e(\lambda_1) < 0$ and $\mathcal{R}e(\lambda_2) < 0$ then $|\bar{u}(t)| \to 0$ as $t \to +\infty$ and (u_1^*, u_2^*) is stable.
- If $\lambda_1 = 0$ or $\lambda_2 = 0$ we have to consider higher order terms.

Denote $\beta = \mathrm{tr}(J(u_1^*, u_2^*))$ and $\gamma = \det(J(u_1^*, u_2^*))$. Then the characteristic (eigenvalue) equation for $J(u_1^*, u_2^*)$ is

$$\lambda^2 - \beta\lambda + \gamma = 0\ , \quad \lambda_{1,2} = \frac{\beta \pm \sqrt{\beta^2 - 4\gamma}}{2}.$$

Then

- If $\gamma < 0$ we have two real eigenvalues with different signs, i.e. $\lambda_1 < 0 < \lambda_2$. Thus (u_1^*, u_2^*) is a **saddle**.
- If $\gamma > 0$ and $\beta^2 \geq 4\gamma$ we have two real eigenvalues with the same sign. Thus (u_1^*, u_2^*) is a **node**.
  - if $\beta > 0$ then $\lambda_2 > \lambda_1 > 0$ and (u_1^*, u_2^*) is an **unstable node**.
  - if $\beta < 0$ then $\lambda_1 < \lambda_2 < 0$ and (u_1^*, u_2^*) is a **stable node**.
- If $\gamma > 0$ and $\beta^2 < 4\gamma$ we have two complex conjugate eigenvalues. Thus (u_1^*, u_2^*) is a **focus (spiral)**.
  - if $\beta > 0$ then $\mathcal{R}e(\lambda_{1,2}) > 0$ and (u_1^*, u_2^*) is an **unstable focus**
  - if $\beta < 0$ then $\mathcal{R}e(\lambda_{1,2}) < 0$ and (u_1^*, u_2^*) is a **stable focus**.
  - If $\beta = 0$ then for linear system we have a **centre**, but in general we have no information on the behaviour of the nonlinear system near the steady state (u_1^*, u_2^*).

** Insert figure phase plane **

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