MA42002

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Preface

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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. This leads us to describe biological system using partial differential equations.

1.2 Notation

Throughout this course, we will study $\{$*partial differential equation models*$\}$ *of biological systems and as such 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:*

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

1.3 Derivation of conservation equations

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

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

1.3.1 Spatially homogeneous model

In this introductory first section, we neglect spatial movement and consider examples of growth/death and chemical reactions.

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

Bacteria are found to reproduce by undergoing successive cell divisions.

Denote by $N(t)$ - bacterial density observed at time t [number of cells per volume].

Over a period of one unit time a single bacterial cell divides, then its daughter cells divide, and so forth, leading to a total of K new bacterial cells.

Define K - rate of reproduction per unit time, $K > 0$, and

$$\begin{array}{cccc} N(t+\Delta t) = & N(t) + & KN(t)\Delta t & \\ \text{density at time } t+\Delta t & \text{density at time } t & \text{increase in density due to reproduction during the time interval } \Delta t & \end{array} \tag{1.1}$$

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

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

*{eq-n_2} The growth rate K can 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 i.e. K depends on the available resources*

1.3.1.2 Logistic growth via depleting nutrient source

We denote by α the units of nutrients consumed during the production of one unit of population increment (Note: the quantity $Y = 1/\alpha$ is called the yield) and obtain

$$\begin{aligned} \frac{dN}{dt} &= K(c)N = \kappa c N, \\ \frac{dc}{dt} &= -\alpha \frac{dN}{dt} = -\alpha\kappa c N, \end{aligned} \tag{1.2}$$

with initial conditions

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

We can determine the nutrient concentration by integrating the second of Equation 1.2 with respect to time and obtaining

$$c(t) = -\alpha N(t) + c(0) + \alpha N(0) = -\alpha N(t) + \beta, \tag{1.3}$$

where $\beta = c_0 + \alpha N_0$. *Using Equation 1.3 in Equation 1.2 we obtain the* logistic growth *equation*

$$\frac{dN}{dt} = \kappa(\beta - \alpha N)N, \qquad N(0) = N_0 \tag{1.4}$$

Here we have $K = K(N) = \kappa(\beta - \alpha N)$.

The last equation can be rewritten as

$$\frac{dN}{dt} = \rho N\,(1 - \frac{N}{B}) \qquad N(0) = N_0, \tag{1.5}$$

where $\rho = \kappa\beta$ *is the* {intrinsic growth rate} and $B = \frac{\beta}{\alpha}$ is the {*carrying capacity*}. *The solution of* ***?@eq-n__5*** *is given by*

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

1.3.1.3 Death/decay

In addition to growth, we may assume that cells die at rate d *and the simple growth* ***?@eq-n__2*** *can be generalised to*

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

where d *is the mortality (death) rate.*

1.3.1.4 Competition

The fact that individuals compete for food, habitat (i.e. space) or any limited resources, means that an increase in the net mortality of the population may be observed under crowded conditions

$$\frac{dN}{dt} = KN - d_1N^2,$$

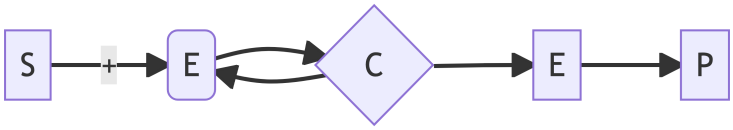
where $d = d_1N$ *is the mortality (death) rate and is proportional to the population density.*

1.3.1.5 Chemical reactions

Basic enzyme reactions

Most biochemical reactions involve proteins called {enzymes} which act as catalysts of chemical reactions. Enzymes react selectively on specific compounds called {*substrates*}.

A substrate S *reacts, in a* {reversible reaction}, with an enzyme E to form a **complex** SE or C, which in turn is converted into a product P. This may be described as follows:



where k_{-1}, k_1 and k_2 are rate constants (> 0) determining the rate of the reaction i.e. how fast the reaction proceeds.

The law of mass action states that the rate of a reaction is proportional to the product of the concentrations of the reactants. (Note: The law of mass action is only an approximation, but it is a very good one for dilute solutions of the chemical concerned.)

We denote the concentrations $ [;]$ as follows:

$$s = [S], \quad e = [E], \quad c = [SE], \quad p = [P]$$

and obtain

$$\begin{aligned}
\frac{ds}{dt} &= -k_1 es + k_{-1} c, & s(0) &= s_0, \\
\frac{de}{dt} &= -k_1 es + k_{-1} c + k_2 c, & e(0) &= e_0, \\
\frac{dc}{dt} &= k_1 es - k_{-1} c - k_2 c, & c(0) &= 0, \\
\frac{dp}{dt} &= k_2 c, & p(0) &= p_0.
\end{aligned}$$

A study of this system is given in Homework 1.

1.3.2 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:

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

1.3.2.1 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 $(x, x+\Delta x)$, 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 $A = |S|$.

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

We consider S to be very small and $c(t, x)$ 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 is given by

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

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

$$\frac{\partial}{\partial t} \int_x^{x+\Delta x} c(t, \tilde{x}) A d\tilde{x} = J(t, x)\, A - J(t, x + \Delta x)\, A + \int_x^{x+\Delta x} f(t, \tilde{x}, c(t, \tilde{x}))\, A\, d\tilde{x}. \tag{1.6}$$

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 1.6, we obtain

$$\frac{\partial}{\partial t} c(t, \xi) A \Delta x = J(t, x)\, A - J(t, x + \Delta x)\, A + f(t, \eta, c(t, \eta))\, A \Delta x, \qquad \xi, \eta \in (x, x + \Delta x). \tag{1.7}$$

Dividing Equation 1.6 by $A\,\Delta x$ yields

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

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:

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

1.3.2.2 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 $S = \partial V$.

- $c(t, x)$ – concentration of particles at $x \in V$ and $t > 0$ (number of particles per unit volume)
- $J(t, x)$ – 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).
- $f(t, x, c(t, x))$ - source/sink term (number of particles created or destroyed per unit volume and per unit time)

Then the conservation equation reads

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

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

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

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

$$\frac{\partial}{\partial t}c(t,x) = -\nabla\cdot J(t,x) + f(t,x,c), \quad x \in \mathbb{R}^n \text{ (or } x \in \Omega), \quad t > 0. \tag{1.10}$$

1.3.2.3 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.

  $$\mathbf{J} = -D\nabla c, \tag{1.11}$$

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

Then applying Equation 1.11 in Equation 1.10 we obtain reaction-diffusion equation

$$\frac{\partial}{\partial t}c = -\nabla \cdot (-D\nabla c(t,x)) + f(t,x,c) = \nabla \cdot (D\nabla c) + f(t,x,c), \quad x \in \mathbb{R}^n,\ t > 0. \quad (1.12)$$

If D is a constant we can write

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

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

  $$\frac{\partial}{\partial t}c = D_0 \nabla \cdot (c^m \nabla c) + f(t,x,c), \quad x \in \mathbb{R}^n, \quad t > 0. \quad (1.13)$$

- Convection or Advection

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

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

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

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

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

- 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 $a(t,x)$ 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

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

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

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

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

$$\frac{\partial}{\partial t}a = D\nabla^2 a + g(t,x,a,c), \quad x \in \mathbb{R}^n \quad t > 0. \tag{1.17}$$

Equation 1.16 and Equation 1.17 form a system of equations, a so-called chemotaxis system.

1.3.3 Boundary conditions (B.C.)

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

the density is not influenced by the boundary

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

- Periodic B.C.

L-periodic function: $c(t,x) = c(t,x+L)$ 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

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

- 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 $(0, L)$

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

- Non-homogeneous Neumann B.C.

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

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

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

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

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

- Homogeneous Robin B.C.

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

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

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

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

- Non-homogeneous Robin B.C.

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

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

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

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

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

1.3.4 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

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

1.3.5 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 willbe dervied 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).

1.3.6 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-dimensionalize a system of differential equations by scaling or non-dimensionalizing 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 $D > 0$:

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

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):

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

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 initial condition for our species c is located in one point $x = 0$ i.e.

$$c(x_0, 0) = \delta_0(x) \qquad x \in \mathbb{R}, \tag{2.2}$$

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

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

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

Then for the diffusion Equation 2.1 with initial condition Equation 2.2, it can be shown that the explicit (analytic) solution is given by

$$c(t,x) = \frac{1}{\sqrt{4\pi Dt}} \exp\left(-\frac{x^2}{4Dt}\right). \tag{2.3}$$

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 $x \in \mathbb{R}$:

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

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

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).

```
import numpy as np
from scipy.integrate import odeint
import matplotlib.pyplot as plt

T=10
L=10

N_x=100
N_t=120

t=np.linspace(0,T,N_t)
x=np.linspace(0,L,N_x)-L/2


D=1.5
epsilon=0.1

u_0=1/(epsilon*np.sqrt(np.pi))*np.exp(-x**2/epsilon**2)

dx=L/(N_x-1)
dt=T/(N_t-1)


def diffusionPDErhs(u,t):
    N_x=len(u)
    f=np.zeros_like(u)
    for i in range(1,N_x-1):

      f[i]=D/dx**2*(u[i-1]-2*u[i]+u[i+1])


    i=0
    f[i]=D/dx**2*(-u[i]+u[i+1])
    i=N_x-1

    f[i]=D/dx**2*(u[i-1]-u[i])
    return f

sol=odeint(diffusionPDErhs,u_0,t)



[x_mesh,t_mesh]=np.meshgrid(x,t)

c_exact=1/np.sqrt(4*np.pi*D*t_mesh)*np.exp(-x_mesh**2/(4*D*t_mesh))

fig,ax=plt.subplots()
ax.plot(x, sol[1,:], 'r')
ax.plot(x, sol[4,:], 'b')
ax.plot(x, sol[8,:], 'm')
ax.plot(x, sol[12,:], 'k')
plt.legend(['t'+ str(t[0]),'t='+ str(t[4]),'t='+ str(t[8]),'t='+ str(t[12])])
plt.xlabel('$x$')
```

2.1.4 Diffusive transit time

We now demonstrate the connection between time and space in diffusion equations. Consider a domain $V \subset \mathbb{R}^n$, $n = 1, 2, 3.$, and particles that are entering V and are being removed from V. Define

N - total number of particles in V

F - total number of particles entering V per unit time

λ - average removal rate of particles from V

$\tau = \frac{1}{\lambda}$ - transit time or average time of residency in V

Regardless of spatial variations, we can make the following general statement regarding the total number of particles in V, where we assume a constant entry rate F and a constant removal rate λ at some sink in V:

$$\frac{dN}{dt} = \text{entry rate} - \text{removal rate} = F - \lambda N.$$

At steady state ($dN/dt = 0$) we obtain

$$Missingcontenthere.Checknotes!$$

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:

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

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:

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

and the total number of particles is given by:

$$N = \int_0^L c(x)\, dx = \frac{1}{2}LC_0.$$

If we assume a cross-section of unit area at $x = 0$, then

$$F = \text{flux} \times \text{area} = J \times 1 = D\frac{C_0}{L}$$

and

$$\tau = \frac{N}{F} = \frac{C_0 L}{2}\frac{L}{DC_0} = \frac{1}{2}\frac{L^2}{D}.$$

Thus the average time it takes a particle to diffuse a distance, L, is

$$\tau = \frac{L^2}{2D}$$

or viewed another way, 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 the **random walk** of particles in a one-dimensional domain. Suppose that the particles move randomly a distance, Δx, every time step, Δt. Assume that the particles move left with probability λ_L and right with probability λ_R.

In Figure Figure 2.3 a simulation of 400 random walking particles 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 (solid lines, Equation 2.3).

```
import numpy as np
from scipy.integrate import odeint
import matplotlib.pyplot as plt
import random

N_particles=400

L=50
N_x=200

T=500
N_t=25000
D=0.1

dt=T/N_t
```

```
move_probability=D*dt/dx**2

x=np.linspace(0,L,N_x)-L/2
t=np.linspace(dt,T,N_t)

particle_positions=np.zeros((N_t,N_particles),dtype=float)

# loop over time
for i in range(1,N_t):
  # loop over particles
  for j in range(N_particles):

    r=random.random()
    # move particle j right
    new_particle_position=particle_positions[i-1,j]
    if r<move_probability:
      new_particle_position+=dx
    # move particle j left
    elif r<2*move_probability:
      new_particle_position-=dx
    particle_positions[i,j]=new_particle_position


[x_mesh,t_mesh]=np.meshgrid(x,t)
c_exact=1/np.sqrt(4*np.pi*D*t_mesh)*np.exp(-x_mesh**2/(4*D*t_mesh))


fig,ax=plt.subplots(2,2)
ax[0,0].hist(particle_positions[5,:],density=True)
ax[0,0].plot(x, c_exact[5,:], 'r')
ax[0,0].set_title('$t=$'+str(t[5]))

ax[0,1].hist(particle_positions[500,:],density=True)
ax[0,1].plot(x, c_exact[500,:], 'm')
ax[0,1].set_title('$t=$'+str(t[500]))

ax[1,0].hist(particle_positions[1000,:],density=True)
ax[1,0].plot(x, c_exact[1000,:], 'b')
ax[1,0].set_title('$t=$'+str(t[1000]))

ax[1,1].hist(particle_positions[1500,:],density=True)
```

```
ax[1,1].plot(x, c_exact[1500,:], 'k')
ax[1,1].set_title('$t=$'+str(t[1500]))

ax[0,0].set_xlim([-L/2,L/2])
ax[0,1].set_xlim([-L/2,L/2])
ax[1,0].set_xlim([-L/2,L/2])
ax[1,1].set_xlim([-L/2,L/2])
plt.xlabel('$x$')
plt.grid()
plt.show()
```

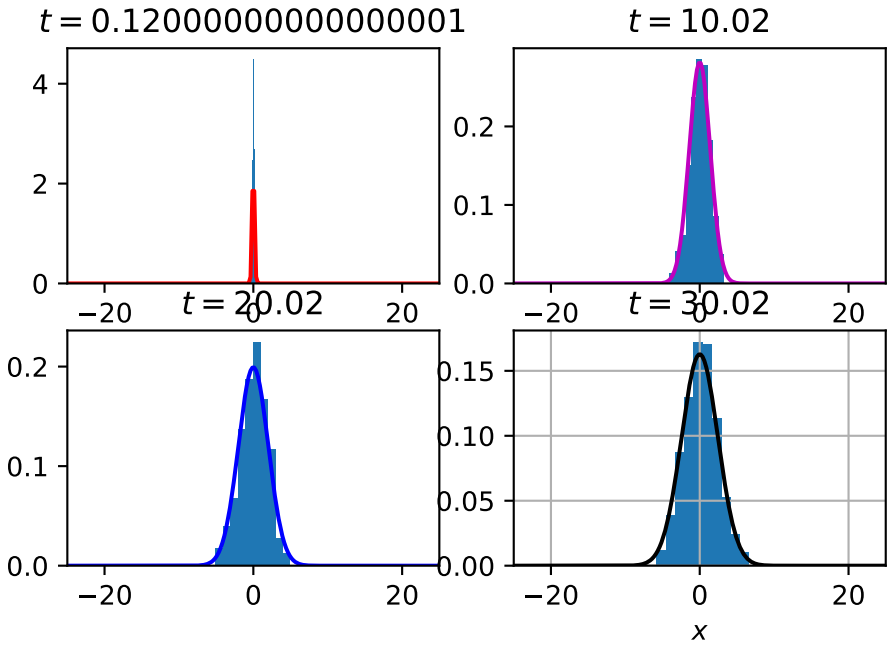


Figure 2.3: Numerical implementation of random walk

Concider the concentration of particles $c(x,t)$ at spatial location x and time t, (or more precisely, the probability density function of the position of a particle performing a random walk) we have:

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

If we assume that $\lambda_R + \lambda_L = 1$ then

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

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

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

Using $\lambda_R+\lambda_L=1$ and assuming $\lambda_L=\lambda_R=\frac{1}{2}$ we obtain

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

Dividing by Δt gives

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

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

$$\frac{(\Delta x)^2}{2\Delta t}\to D,$$

yields the (one-dimensional) diffusion equation

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

This approach can be extended to consider other types of movement e.g. convection. For example, if we assume that

$$\lambda_R+\lambda_L=1,$$

and

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

the motion of the particles is biased and we may derive an appropriate **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 @#eq-fund_sol.

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

Examining the formula for the fundamental solution of the diffusion Equation 2.3 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 our reaction-diffusion equation is:

$$\frac{\partial c}{\partial t} = D\frac{\partial^2 c}{\partial x^2} + \rho\, c, \quad x \in \mathbb{R},\ t > 0, \tag{2.4}$$

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

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

$$c(0, x) = \delta_0(x). \tag{2.5}$$

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 2.4 with initial condition Equation 2.5 is given by

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

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). Considering the density of muskrats $u(\mathbf{x}, t)$, the equation is

```
import numpy as np
from scipy.integrate import odeint
import matplotlib.pyplot as plt

T=10
L=10

N_x=100
N_t=120


t=np.linspace(0,T,N_t)
x=np.linspace(0,L,N_x)-L/2

D=0.5
rho=1.0
epsilon=0.1

u_0=1/(epsilon*np.sqrt(np.pi))*np.exp(-x**2/epsilon**2)

dx=L/(N_x-1)

dt=T/(N_t-1)


def logisticPDErhs(u,t):
    N_x=len(u)
    f=np.zeros_like(u)
    for i in range(1,N_x-1):
      f[i]=D/dx**2*(u[i-1]-2*u[i]+u[i+1])


    i=0

    f[i]=D/dx**2*(-u[i]+u[i+1])
    i=N_x-1

    f[i]=D/dx**2*(u[i-1]-u[i])

    reac=rho*u
    f=f+reac
    return f

sol=odeint(logisticPDErhs,u_0,t)


[x_mesh,t_mesh]=np.meshgrid(x,t)

c_exact=1/np.sqrt(4*np.pi*D*t_mesh)*np.exp(rho*t_mesh-x_mesh**2/(4*D*t_mesh))

fig,ax=plt.subplots()
ax.plot(x, sol[1,:], 'r')
ax.plot(x, sol[4,:], 'b')
```

$$\frac{\partial u}{\partial t} = D\left(\frac{\partial^2 u}{\partial x_1^2} + \frac{\partial^2 u}{\partial x_2^2}\right) + \rho\, u, \quad \mathbf{x} = (x_1, x_2) \in \mathbb{R}^2,\ t > 0, \tag{2.6}$$

$$u(\mathbf{x}, 0) = M\delta_0(\mathbf{x}), \quad \mathbf{x} \in \mathbb{R}^2. \tag{2.7}$$

The solution of Equation 2.6 with initial conditions Equation 2.7 is equal to:

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

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 if $t > 0$. Thus, for practical purposes, somehow 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 2.6,

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

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 Non linear reaction diffusion equations

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 to investigate the speed of an advantageous (mutant) gene in a population "The Wave of Advance of Advantageous Genes" (1937).

We can non-dimensionalize 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-dimensionalized 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 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 $u \sim 0$.

- Can we prove this is a travelling wave (e.g. the solution could be dynamic on a very slow time scale that is not captured by the numeircal solution)?

- Can we derived a form for the travelling wave profile?
- Will we see a travelling wave for any initial data?
- How does the wave speed relate to model parameters?

```
import numpy as np
from scipy.integrate import odeint
import matplotlib.pyplot as plt

T=100
L=100

N_x=100
N_t=100

t=np.linspace(1,T,N_t)
x=np.linspace(0,L,N_x)


u_0=0.5*(1+np.tanh(-0.1*(x-20)))

dx=L/(N_x-1)
dt=T/(N_t-1)


def logisticPDErhs(u,t):
    N_x=len(u)
    f=np.zeros_like(u)
    for i in range(1,N_x-1):
      f[i]=1/dx**2*(u[i-1]-2*u[i]+u[i+1])+u[i]*(1-u[i])


    i=0
    f[i]=1/dx**2*(-u[i]+u[i+1])+u[i]*(1-u[i])
    i=N_x-1

    f[i]=1/dx**2*(u[i-1]-u[i])+u[i]*(1-u[i])
    return f

sol=odeint(logisticPDErhs,u_0,t)

plt.plot(x, sol[0,:], 'r')
plt.plot(x, sol[4,:], 'b')
```

```
plt.plot(x, sol[8,:], 'm')
plt.plot(x, sol[12,:], 'k')
plt.legend(['t'+ str(t[0]),'t='+ str(t[4]),'t='+ str(t[8]),'t='+ str(t[12])])
plt.xlabel('$x$')
plt.grid()
plt.show()
```

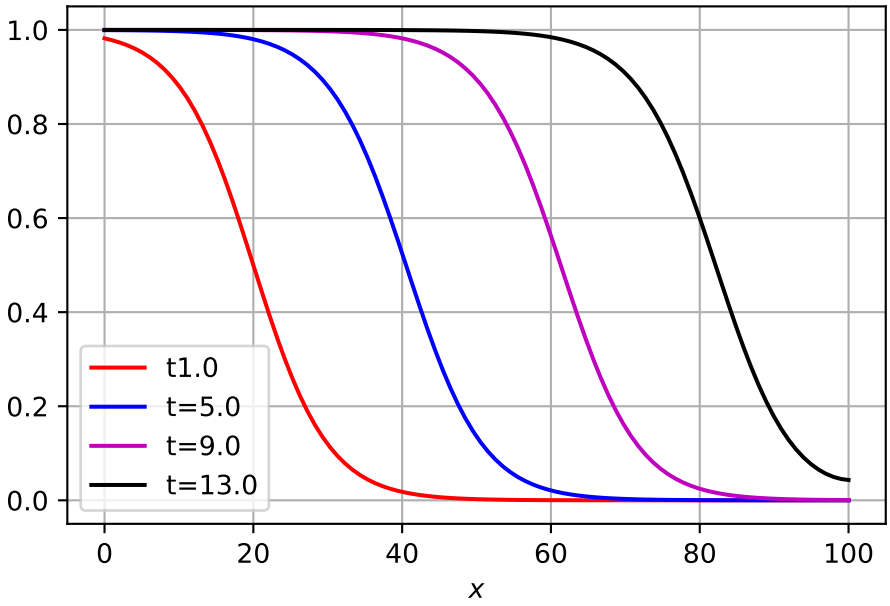


Figure 3.1: Numerical solution of logistic PDE

3.2 Travelling waves

It is known that the Fisher Equation 3.2 exhibits what are known as **travelling wave solutions**.

Definition 3.1. A travelling wave is a solution of a partial differential equation with a constant profile (shape) and a constant propagation speed.

3.2.1 Types of travelling waves

- Travelling pulse: $u(x,t) \to a$, as $x \to \pm\infty$.

- Travelling front : $u(x,t) \to a$, as $x \to -\infty$, $u(t,x) \to b$, 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.

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

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

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.

Considering the travelling wave **ansatz**

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

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

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

where

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

and

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

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

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

3.2.2 Numerical solutions

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

Note that some problem will not have a travelling wave solution. In this situation we could still make the travelling wave ansatz but this would usually result in a contradiction. In such a case this tells us that a travelling wave solution is not possible.

```
import numpy as np
from scipy.integrate import odeint
import matplotlib.pyplot as plt

T=300

a=0.2
N_z=5000

z=np.linspace(1,T,N_z)

u_0=[0.99,-0.0001]

c_1=2.0
c_2=8.6
c_3=0.5

def fisherTrWaveODErhs(u, t, c):
    f=np.zeros_like(u)
    reaction=u[0]*(1-u[0])
```

```
    f[0]=u[1]
    f[1]=-c*u[1]-reaction
    return f

sol=odeint(fisherTrWaveODErhs,u_0,z, args=(c_1,))
sol2=odeint(fisherTrWaveODErhs,u_0,z, args=(c_2,))
sol3=odeint(fisherTrWaveODErhs,u_0,z, args=(c_3,))

fig, ax = plt.subplots(1,2)
ax[0].plot(sol[:,0],sol[:,1], 'r')
ax[0].plot(sol2[:,0],sol2[:,1], 'b')
ax[0].plot(sol3[:,0],sol3[:,1], 'k')
ax[0].set_xlim([-0.5, 1.05])
ax[0].set_xlabel('$u$')
ax[0].set_ylabel('$du/dz$')

ax[1].plot(z,sol[:,0], 'r')
ax[1].plot(z,sol2[:,0], 'b')
ax[1].plot(z,sol3[:,0], 'k')
ax[1].set_xlim([-0.5, 100])

ax[1].set_xlabel('$z$')
ax[1].set_ylabel('$u$')
plt.legend(['c='+str(c_1),'c='+str(c_2), 'c='+str(c_3)])
plt.grid()
plt.show()
```

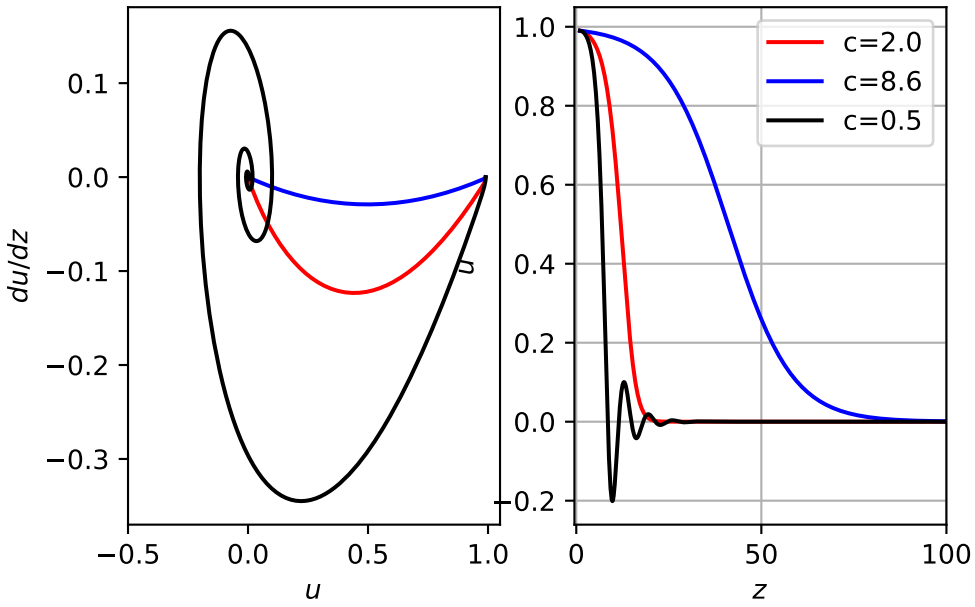


Figure 3.2: Proposed numerical solution of Equation 3.7 with prospective values of wavespeed c.

3.2.3 Steady state analysis

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

Using

$$\frac{dP}{dW} = \frac{dP}{dz}\frac{dz}{dW} = \frac{\frac{dP}{dz}}{\frac{dW}{dz}}$$

and Equation 3.7 we can write an equation for $P = P(W)$:

$$\frac{dP}{dW} = -v - \frac{W(1-W)}{P}, \tag{3.8}$$

together with

$$P(0) = 0, \quad P(1) = 0, \tag{3.9}$$

and

$$P(W) < 0 \quad \text{or} \quad W \in (0, 1). \tag{3.10}$$

The condition Equation 3.10 is given by the form of travelling front, which we would like to show that it exists

Lemma 3.1. *For every solution of Equation 3.4 satisfying Equation 3.5 and Equation 3.6 we have that* $\dfrac{dW(z)}{dz} < 0$ *for all finite* z*, i.e.*

$$P(W) < 0 \quad \text{for} \quad W \in (0,1).$$

Thus in phase-plane we shall look for a trajectory connecting $(W_1, P_1) = (0,0)$ and $(W_2, P_2) = (1,0)$ and $P < 0$.

3.2.4 Connection between sign of P and sign of speed v

Consider equation Equation 3.8. Multiplying it by P and integrating over W from 0 to 1, we obtain

$$\int_0^1 \frac{dP}{dW} P(W)\, dW = -v \int_0^1 P(W) dW - \int_0^1 W(1-W) dW.$$

Using conditions Equation 3.9 we have

$$\int_0^1 \frac{dP}{dW} P\, dW = \frac{1}{2} \int \frac{d}{dW}(P^2) dW = \frac{1}{2}\left(P^2(1) - P^2(0)\right) = 0,$$

and

$$v \int_0^1 P(W) dW = -\int_0^1 W(1-W) dW < 0, \qquad \text{since} \int_0^1 W(1-W) dW > 0.$$

Thus for $v > 0$ we have $P = W' < 0$ and for $v < 0$ we have $P = W' > 0$.

Note: $u(x,t) = W(z)$, where $z = x - vt$ with $v < 0$ and $\frac{dW}{dz} > 0$ will also be a travelling wave for the Fisher Equation 3.2, i.e. a travelling wave front moving to the left.

Note: Instead of $z = x - vt$ we can also consider $z = x + vt$. The sign of v determines the direction of movement: If $z = x - vt$ for $v > 0$ we have travelling wave moving to the right and for $v < 0$ we have travelling wave moving to the left.

If $z = x + vt$ for $v > 0$ we have travelling wave moving to the left and for $v < 0$ we have travelling wave moving to the right.

3.2.5 Stability of steady states

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

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

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 $(0, 0)$

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

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.

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 $(W_2, P_2) = (1, 0)$ 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 the figure below.

Insert eigenvector picture here

Definition 3.2. 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.

3.2.6 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.

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.

Thus we obtain the minimal speed $v^*_{\min} = 2$ (non-dimensionalized) 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

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

3.2.6.1 The existence of a confined region

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**).

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

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

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 $(1,0)$.

Theorem 3.2. *For $P(W)$ satisfying Equation 3.8, Equation 3.9 and $P(W) < 0$ for $W \in (0,1)$, there exists a solution $W(z)$ of Equation 3.4 satisfying Equation 3.5 and Equation 3.6.*

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.

3.2.7 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

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

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

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

3.3 Travelling waves in bistable equations

Consider now the reaction-diffusion equation:

$$\frac{\partial u}{\partial t} = \frac{\partial^2 u}{\partial x^2} + f(u) \qquad x \in \mathbb{R},\ t > 0, \tag{3.11}$$

with initial condition

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

where $f(0) = f(a) = f(1) = 0$ and $0 < a < 1$. There are three spatially uniform steady states $u_1 = 0$, $u_2 = a$, $u_3 = 1$.

The stability of the steady states is given by the sign of $f'(u_j)$ for $j = 1, 2, 3$.

If we have that $f'(0) < 0$, $f'(a) > 0$ and $f'(1) < 0$ then $u_1 = 0$ and $u_3 = 1$ are stable steady states and $u_2 = a$ is an unstable steady state of Equation 3.11.

An example of such a function is f 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**.

The existence of two stable steady states gives rise to the name "bistable equation''.

3.4 Numerical solutions

```
import numpy as np
from scipy.integrate import odeint
import matplotlib.pyplot as plt

T=100
L=100

a=0.2

N_x=100
N_t=100

t=np.linspace(1,T,N_t)
x=np.linspace(0,L,N_x)


u_0=6*0.5*(1+np.tanh(-1*(x-50)))*0.5*(1+np.tanh(1*(x-50)))
u_0=0.5*(1+np.tanh(-1*0.2*(x-50)))

dx=L/(N_x-1)
dt=T/(N_t-1)

fig, ax = plt.subplots(1)
u_samp=np.linspace(0,1,100)
reac=u_samp*(u_samp-a)*(1-u_samp)
ax.plot(u_samp,reac)
plt.show()


def bistablePDErhs(u,t):
    N_x=len(u)
    f=np.zeros_like(u)
    for i in range(1,N_x-1):
      f[i]=1/dx**2*(u[i-1]-2*u[i]+u[i+1])
    i=0
    f[i]=1/dx**2*(-u[i]+u[i+1])
    i=N_x-1

    f[i]=1/dx**2*(u[i-1]-u[i])

    reaction=u*(u-a)*(1-u)
    f= f+reaction
    return f

sol=odeint(bistablePDErhs,u_0,t)

plt.plot(x, sol[0,:], 'r')
plt.plot(x, sol[15,:], 'b')
plt.plot(x, sol[30,:], 'm')
plt.plot(x, sol[45,:], 'k')
plt.legend(['t'+ str(t[0]),'t='+ str(t[4]),'t='+ str(t[8]),'t='+ str(t[12])])
```

3.5 General assumptions on f

- $f(0) = f(a) = f(1) = 0$,
- $f(u) < 0$ in $(0, a)$, $\quad f(u) > 0$ in $(a, 1)$
- $f'(0) < 0, \quad f'(1) < 0$

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

$$\frac{d^2W}{dz^2} + v\frac{dW}{dz} + f(W) = 0, \ . \tag{3.12}$$

We can rewrite Equation 3.12 as asystem of two 1st order ODEs

$$\begin{aligned} \frac{dW}{dz} &= P = F(W,P), \\ \frac{dP}{dz} &= -vP - f(W) = G(W,P), \end{aligned} \tag{3.13}$$

3.5.1 Stability of the steady states

The steady states of Equation 3.13 are $(W_1, P_1) = (0,0)$, $(W_2, P_2) = (a,0)$, $(W_3, P_3) = (1,0)$.

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 \$ _1^{-} <0< _1^{+} \$ and it 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 $ _3^{-} <0< _3^{+} $ and it is a saddle point. \

Eigenvectors are given by

$$P = \lambda W$$

and at each steady state we have two eigenvectors

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

As we vary the wave speed v, the stable and unstable manifolds move and 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.

** Insert fig3 here**

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

Consider Equation 3.12, multiply it by $\dfrac{dW}{dz}$ and integrate over $(-\infty, +\infty)$:

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

Then

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

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

$$\frac{1}{2}\left(\left|\frac{dW(+\infty)}{dz}\right|^2 - \left|\frac{dW(-\infty)}{dz}\right|^2\right) + v\int_{-\infty}^{+\infty} \left|\frac{dW}{dz}\right|^2 dz + \int_1^0 f(W)\,dW = 0.$$

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

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

Thus we have

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

and

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

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

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

3.5.3 The shooting method proof of a heteroclinic connection

3.5.3.1 Numerical shooting method

```
import numpy as np
from scipy.integrate import odeint
import matplotlib.pyplot as plt

T=300

a=0.2
N_z=5000

z=np.linspace(1,T,N_z)

u_0=[0.99,-0.0001]

c_1=2.0
c_2=0.6
c_3=0.425
```

```
def bistableTrWaveODErhs(u, t, c):
    f=np.zeros_like(u)
    reaction=u[0]*(u[0]-a)*(1-u[0])

    f[0]=u[1]
    f[1]=-c*u[1]-reaction
    return f

sol=odeint(bistableTrWaveODErhs,u_0,z, args=(c_1,))
sol2=odeint(bistableTrWaveODErhs,u_0,z, args=(c_2,))
sol3=odeint(bistableTrWaveODErhs,u_0,z, args=(c_3,))

fig, ax = plt.subplots(1)
plt.plot(sol[:,0],sol[:,1], 'r')
plt.plot(sol2[:,0],sol2[:,1], 'b')
plt.plot(sol3[:,0],sol3[:,1], 'k')
ax.set_xlim([-0.05, 1.05])

plt.xlabel('$u$')
plt.ylabel('$du/dz$')
plt.legend(['c='+str(c_1),'c='+str(c_2), 'c='+str(c_3)])
plt.grid()
plt.show()
```

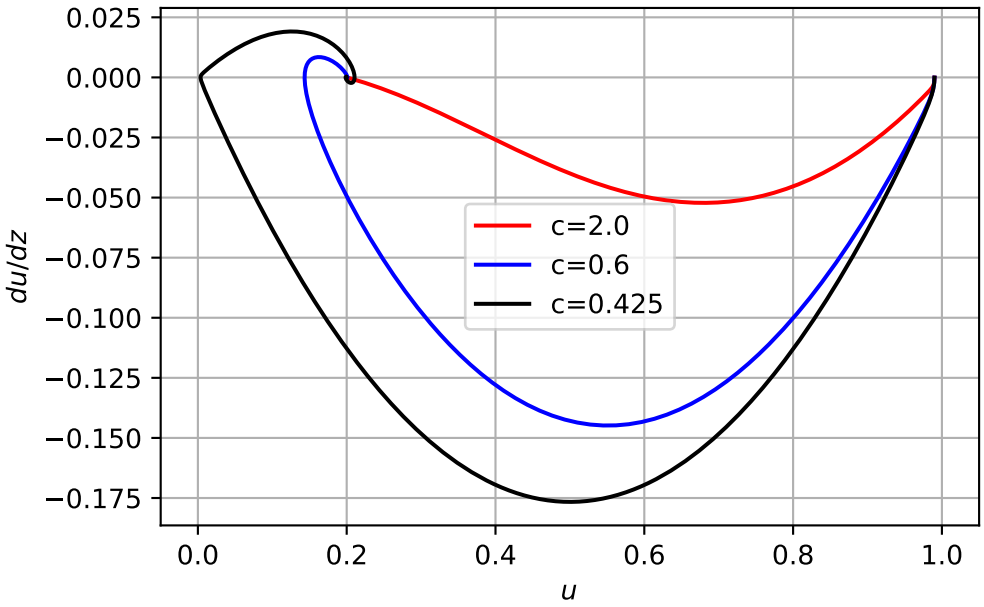


Figure 3.5: Numerical solution of bistable PDE

Assume

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

i.e. $v > 0$.

- Consider first $v = 0$.

  From the equations in Equation 3.13 and the assumptions on the function f we have

  – If $W \in (0, a)$

    Using the fact that $f(W) < 0$ for $W \in (0, a)$ and $P < 0$ and $v = 0$ we have

$$\begin{cases} \dfrac{dW}{dz} = P < 0, \\ \dfrac{dP}{dz} = -f(W) > 0 \end{cases} \qquad \rightarrow \quad \frac{dP}{dW} < 0$$

    Thus the trajectory enters $(0, 0)$ with

$$\frac{dP}{dW} < 0,$$

    along the stable manifold $M_s^{(0,0)}$ and intersects the line $\{W = a\}$ at the point (a, P_0).

– If $W \in (a,1)$

Using the fact that $f(W) > 0$ for $W \in (a,1)$ and $P < 0$ and $v = 0$ we have

$$\begin{cases} \dfrac{dW}{dz} = P < 0, \\ \dfrac{dP}{dz} = -f(W) < 0 \end{cases} \qquad \rightarrow \quad \frac{dP}{dW} > 0$$

Thus the trajectory leaves $(1,0)$ with

$$\frac{dP}{dW} > 0$$

along the unstable manifold $M_u^{(1,0)}$ and intersects the line $\{W = a\}$ at the point (a, P_1).

** Insert fig1 here **

Now we shall compare P_0 and P_1. For this we consider again equation Equation 3.12, multiply by $\dfrac{dW}{dz}$ and integrate first over $(-\infty, z^*)$ and then over $(z^*, +\infty)$, where $z^* \in (-\infty, +\infty)$ such that $W(z^*) = a$. Then since $v = 0$ we have first

$$\int_{-\infty}^{z^*} \frac{d^2W}{dz^2}\frac{dW}{dz}\,dz + \int_{-\infty}^{z^*} f(W)\frac{dW}{dz}\,dz = 0.$$

and

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

Since $W(-\infty) = 1$ we are moving along the unstable manifold $M_u^{(1,0)}$ and

$$\frac{dW(z^*)}{dz} = P(z^* + 0) = P_1.$$

Thus using that $\dfrac{dW}{dz}\Big|_{z=-\infty} = 0$ we obtain

$$\frac{1}{2}P_1^2 + \int_1^a f(W)dW = 0 \quad \Longrightarrow \quad P_1^2 = 2\int_a^1 f(W)dW$$

Integration over $(z^*, +\infty)$ implies

$$\int_{z^*}^{+\infty} \frac{d^2W}{dz^2}\frac{dW}{dz}\,dz + \int_{z^*}^{+\infty} f(W)\frac{dW}{dz}\,dz = 0.$$

and

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

Since $W(+\infty) = 0$ we are moving along the stable manifold $M_s^{(0,0)}$ and $\dfrac{dW(z^*)}{dz} = P(z^* - 0) = P_0$. Thus using that $\dfrac{dW}{dz}\Big|_{z=+\infty} = 0$ we obtain

$$-\frac{1}{2}P_0^2 + \int_a^0 f(W)dW = 0 \quad \Longrightarrow \quad P_0^2 = -2\int_0^a f(W)dW \ .$$

Since

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

we obtain

$$P_1^2 - P_0^2 = 2\int_0^1 f(W)\,dW > 0 \quad \Longrightarrow \quad P_1^2 > P_0^2$$

Then since $P < 0$ we have

$$P_1 < P_0 \ .$$

- Consider $v > 0$ large.

From the equations in Equation 3.13 and the assumptions on the function f we have

`* If $W \in (0,a)$`

Using the fact that $f(W) < 0$ for $W \in (0, a)$, $P < 0$ and $v > 0$ we have

$$\begin{cases} \dfrac{dW}{dz} & = P < 0, \\ \dfrac{dP}{dz} & = -vP - f(W) > 0 \end{cases} \quad \Longrightarrow \quad \frac{dP}{dW} < 0$$

Thus $P(W)$ is always decreasing for $W \in (0, a)$. * If $W \in (a, 1)$

Using the fact that $f(W) > 0$ for $W \in (a, 1)$, $P < 0$ and $v > 0$ we have

$$\frac{dW}{dz} = P < 0,$$

$$\left\{ \frac{dP}{dz} = -vP - f(W) < 0 \quad \text{for small } |P| \text{ and } \frac{dP}{dz} = -vP - f(W) > 0 \quad \text{for large } |P|. \right.$$

Thus

$$\begin{cases} \dfrac{dP}{dW} > 0 & \text{for small } |P|, \\ \dfrac{dP}{dW} < 0 & \text{for large } |P| \ . \end{cases}$$

Therefore if $v > 0$ large we have that $P(W)$ is monotone increasing for small $|P|$ and monotone decreasing for large $|P|$.

** Insert fig2 here **

Thus since for $v = 0$ we have $P_1 < P_0$ and for $v > 0$ we have that $P(W)$ is monotone decreasing for large $|P|$, due to the continuity of the phase trajectories with respect to the velocity v we obtain that there exists a travelling wave speed $v_0 > 0$ such that $P_0 = P_1$ and we have a heteroclinic connection between $(1, 0)$ and $(0, 0)$ in the phase plane. Hence for $v = v_0$ there exists a travelling wave front solution for the bistable Equation 3.11.

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 3.11.

Part II

Multi species

4 Lotka Voltera model

Consider the predator-prey system (modified Lotka-Voltera equations) with diffusion of both the prey and the predator species:

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

where

- u – density of the prey,
- n – density of the predator,
- ρ – growth rate of the prey,
- K – carrying capacity,
- βu – growth rate of the predator,
- α – rate at which the predator eats the prey,
- γ – death rate of the predator,
- D_u – diffusion coefficient of the prey
- D_n - diffusion coefficient for the predator .

4.1 Nondimensionalization

Consider the scaling

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

in one dimension. Upon dropping the asteriked notation

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

where

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

4.2 Numerical solutions

```
import numpy as np
from scipy.integrate import odeint
import matplotlib.pyplot as plt

T=100
L=150

a=0.2
b=0.4
D_u=0.10

N_x=100
N_t=100

t=np.linspace(1,T,N_t)
x=np.linspace(0,L,N_x)

u_0=b+(1-b)*0.5*(1+np.tanh(1*0.5*(x-50)))
n_0=(1-b)*0.5*(1+np.tanh(-1*0.5*(x-50)))

u_0=np.concatenate((u_0,n_0))

dx=L/(N_x-1)
dt=T/(N_t-1)

def LVPDErhs(sol,t):

    N_x=int(np.ceil(len(sol)/2))

    u=sol[0:N_x]
    n=sol[N_x:2*N_x]



    f_u=np.zeros_like(u)
    f_n=np.zeros_like(u)

    for i in range(1,N_x-2):
      f_u[i]=D_u/dx**2*(u[i-1]-2*u[i]+u[i+1])
```

```
    i=0
    f_u[i]=D_u/dx**2*(-u[i]+u[i+1])
    i=N_x-1
    f_u[i]=D_u/dx**2*(u[i-1]-u[i])

    for i in range(1,N_x-2):
      f_n[i]=1/dx**2*(n[i-1]-2*n[i]+n[i+1])
    i=0
    f_n[i]=1/dx**2*(-n[i]+n[i+1])
    i=N_x-1
    f_n[i]=1/dx**2*(n[i-1]-n[i])

    reaction_u=u*(1-u-n)
    reaction_n=a*n*(u-b)

    f_u=f_u+reaction_u
    f_n=f_n+reaction_n

    f= np.concatenate((f_u, f_n))
    return f

sol=odeint(LVPDErhs,u_0,t)

u=sol[:,0:N_x]
n=sol[:,N_x:2*N_x]

print(np.shape((u)))

fig, ax = plt.subplots(2,1)

ax[0].plot(x,u[0,:],'r')
ax[0].plot(x,u[16,:],'b')
ax[0].plot(x,u[32,:],'m')
ax[0].plot(x,u[48,:],'k')
ax[0].set_xlabel('$x$')
ax[0].set_ylabel('$u$')

ax[1].plot(x, n[0,:],'r--')
ax[1].plot(x, n[16,:],'b--')
ax[1].plot(x, n[32,:],'m--')
ax[1].plot(x, n[48,:],'k--')
```

```
ax[1].set_xlabel('$x$')
ax[1].set_ylabel('$n$')

plt.legend(['t'+ str(t[0]),'t='+ str(t[4]),'t='+ str(t[8]),'t='+ str(t[12])])
plt.xlabel('$x$')
plt.grid()
plt.show()
```

```
(100, 100)
```

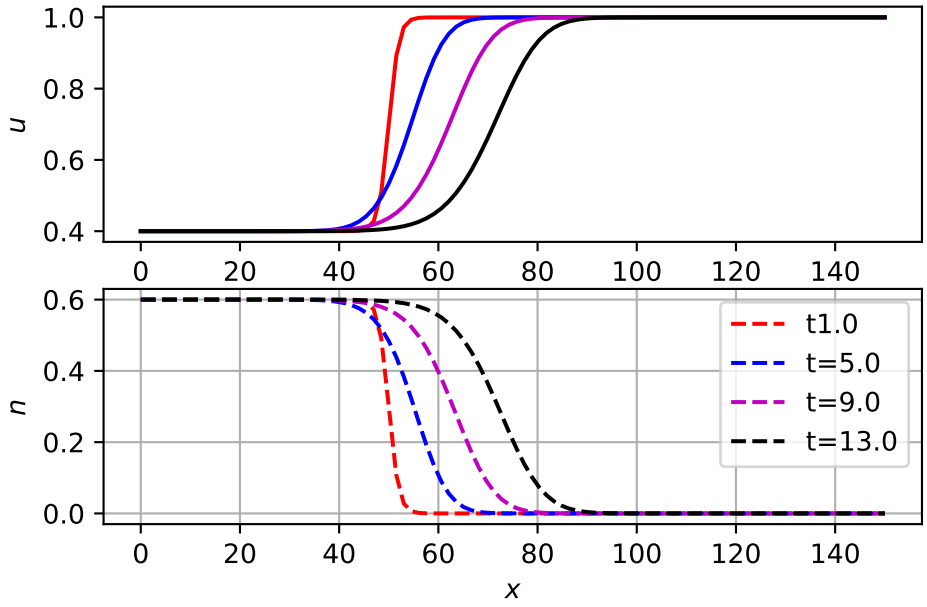


Figure 4.1: Numerical solution of LV model

4.3 Spatially homogeneous steady states

We have for spatially homogeneous steady states

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

Thus

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

Thus steady states are

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

Stability of steady states to spatially homogeneous perturbations

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

For

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

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

and

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

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

For

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

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

and

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

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

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

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

and

$$\text{If } \ 4ab(1-b) \le b^2 \qquad \lambda_3^{\pm} < 0 \quad \text{stable node}$$

$$\text{If } \ 4ab(1-b) > b^2 \qquad Re(\lambda_3 \pm) < 0,\ Im(\lambda_3^{\pm}) \ne 0 \quad \text{stable focus (spiral)},$$

for $b > 0,\ 1-b > 0$ spiral oscillations are biologically realistic as long $u > 0,\ n > 0$.

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

Consider travelling wave solutions

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

and

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

The system Equation 4.2 becomes

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

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

We shall suppose that the prey species moves much more slowly than the predator species, i.e.

$$D = D_u/D_n \ll 1$$

and simplify Equation 4.3 as

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

We can rewrite Equation 4.4 as a system of 1st order ODEs:

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

Steady states of Equation 4.4 are

$$(W_1^*, N_1^*, P_1^*) = (0,0,0), \quad (W_2^*, N_2^*, P_2^*) = (1,0,0), \quad (W_3^*, N_3^*, P_3^*) = (b, 1-b, 0).$$

Stability of steady states

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

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

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

Thus 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

For a travelling wave with $W \geq 0$ and $N \geq 0$ to exist we requite $v^2 \geq 4a(1-b)$ 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

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

To analyse $p(\lambda)$ we observe that local min and max of $p(\lambda)$ are independent of a:

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

and

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

If $a = 0$ then we have eigenvalues

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

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

- for $a > a^*$ we will have 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:

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

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

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

5 Aggregation via Chemotaxis

Dictyostelium discoideum is a slime-mold. It is widely studied experimentally since the individual amoebae that constitute the slime-mold exhibit a range of phenomena also observed in developmental biology by cells e.g. differentiation, proliferation, migration. During one particular stage of its life-cycle the single-cell amoebae become starved of food and begin to 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. Examples of such patterns can be seen in **?@fig-dicty_spiral**.

See also this link to a fascinating Youtube movie of slime mold aggregation. Note the aggregation between 0:35 and 0.48.

In **?@fig-dicty_spiral** we can see stills-shot images of spiral patterns. This spirals are dynamic as can be seen in this movie. See spiral pattern at around 0:36.

- 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 the aggregation of *Dictyostelium discoideum* 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, 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 assumption 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, when considering a 1-dimensional domain $[0, L]$:

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

with zero flux boundary conditions:

$$D_a \frac{\partial a}{\partial x} = 0, \quad x = 0, L,$$
$$D_n \frac{\partial n}{\partial x} - \chi_0 n \frac{\partial a}{\partial x} = 0, \quad x = 0, L,$$

which in this case reduce to:

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

5.2 Numerical solutions

In Figure 5.1 we plot numerical solution of @#eq-chemotaxis1d 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?

```
import numpy as np
from scipy.integrate import odeint
import matplotlib.pyplot as plt
import random


T=80
L=150

mu=1.2
```

```
delta=0.1
D_n=2.50
D_a=2.5
chi_0=1.4

N_x=200
N_t=100

t=np.linspace(1,T,N_t)
x=np.linspace(0,L,N_x)

u_0=np.ones_like(x)+0.01*np.random.uniform(low=0.0, high=0.1, size=(N_x,))
n_0=np.ones_like(x)

u_0=np.concatenate((u_0,n_0))

dx=L/(N_x-1)
dt=T/(N_t-1)

def LVPDErhs(sol,t):

    N_x=int(np.ceil(len(sol)/2))

    n=sol[0:N_x]
    a=sol[N_x:2*N_x]



    f_n=np.zeros_like(n)
    f_a=np.zeros_like(n)

    for i in range(1,N_x-2):
      f_n[i]=D_n/dx**2*(n[i-1]-2*n[i]+n[i+1]) - chi_0*n[i]*1/dx**2*(a[i-1]-2*a[i]+a[i+1])-

    i=0
    f_n[i]=D_n/dx**2*(-n[i]+n[i+1]) - chi_0*n[i]*1/(2*dx)**2*(-a[i]+a[i+1])-chi_0/(2*dx)**

    i=N_x-1
    f_n[i]=D_n/dx**2*(n[i-1]-n[i])- chi_0*n[i]*1/(2*dx)**2*(a[i-1]-a[i])-chi_0/(2*dx)**2*(
```

```
    for i in range(1,N_x-2):
      f_a[i]=D_a/dx**2*(a[i-1]-2*a[i]+a[i+1])
    i=0
    f_a[i]=D_a/dx**2*(-a[i]+a[i+1])
    i=N_x-1
    f_a[i]=D_a/dx**2*(a[i-1]-a[i])

    reaction_n=0
    reaction_a=mu*n-delta*a

    f_n=f_n+reaction_n
    f_a=f_a+reaction_a

    f= np.concatenate((f_n, f_a))
    return f

sol=odeint(LVPDErhs,u_0,t)

n=sol[:,0:N_x]
a=sol[:,0:N_x]

fig, ax = plt.subplots(2,1)

ax[0].plot(x,n[0,:],'r')
ax[0].plot(x,n[16,:],'b')
ax[0].plot(x,n[32,:],'m')
ax[0].plot(x,n[48,:],'k')
ax[0].set_xlabel('$x$')
ax[0].set_ylabel('$n$')

ax[1].plot(x, a[0,:],'r--')
ax[1].plot(x, a[16,:],'b--')
ax[1].plot(x, a[32,:],'m--')
ax[1].plot(x, a[48,:],'k--')
ax[1].set_xlabel('$x$')
ax[1].set_ylabel('$a$')

plt.legend(['t'+ str(t[0]),'t='+ str(t[4]),'t='+ str(t[8]),'t='+ str(t[12])])
plt.xlabel('$x$')
plt.grid()
plt.show()
```

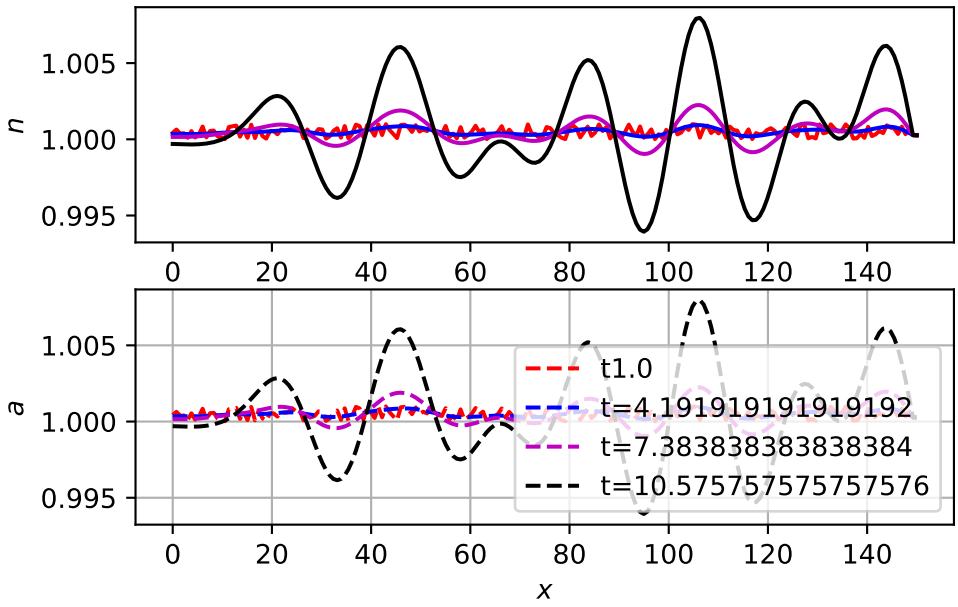


Figure 5.1: Numerical solution of bacterial chemtaxis model

5.3 Spatially Homogeneous Steady States

The spatially homogeneous steady state (n^*, a^*) satisfies:

$$\mu n^* = \delta a^*$$

and 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 *ansatz*. We use the"separation of variables " approach where

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

and

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

$$\begin{aligned} &\frac{\partial u}{\partial t}\phi_1 = D_n u\frac{\partial^2 \phi_1}{\partial x^2} - \chi_0 n^* v\frac{\partial^2 \phi_1}{\partial x^2} \\ &\frac{v}{\partial t}\phi_2 = D_a v\frac{\partial^2 \phi_2}{\partial x^2} + \mu u\,\phi_1 - \delta v\,\phi_2, \\ &u\frac{\partial \phi_1}{\partial x} = 0, \quad v\frac{\partial \phi_2}{\partial x} = 0 \quad \text{for } x=0,\ x=L. \end{aligned}$$

We assume that

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

where ϕ_1 is the solution of the elliptic problem

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

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 $\phi(x) = A\cos(kx)$, with an arbitrary const A, and $k = \dfrac{m\pi}{L}$, ; $m \in \mathbb{N}$.

Then we have

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

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

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

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

$$\lambda C_1 = -D_n k^2 C_1 + \chi_0 n^* k^2 C_2,$$
$$\lambda C_2 = -D_a k^2 C_2 + \mu C_1 - \delta C_2,$$

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 5.1 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 chemotaxic 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 Mechanisms

** Insert human embryogenesis image **

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. Figure **??** shows some of the major changes in embryonic development which occur up to a few weeks after fertilization. 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) cf. Professor Lewis Wolpert: '*It is not birth, marriage, or death, but gastrulation which is truly the most important time in your life.*'

There are two main theories which describe how pattern arises during embryogenesis - one is the **Turing pre-pattern theory**, the other is the **mechano-chemical** theory. 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). This was developed in more detailed manner by Alfred Gierer and Hans Meinhardt in another ground-breaking paper in 1972, *A theory of biological pattern formation* "A Theory of Biological Pattern Formation" (1972), where they introduced the concept of activating chemicals and inhibiting chemicals.

J.D. Murray then applied the theory as an explanation for the generation of patterns observed on animal coats J. Murray (1981).

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 J. 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 is involved in its own production. https://en.wikipedia.org/wiki/Autocatalysis

6.2.2 Activator-inhibitor kinetics cf. Gierer-Meinhardt system; Gierer & Meinhardt, 1972

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

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

6.2.3 Substrate-inhibition system (Thomas, 1975)

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

$$H(A,B) = \frac{k_5 AB}{k_6 + k_7 + k_8 A^2} \ ,$$

$k_i > 0$. 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-dimensionalization

Before proceeding with our analysis, it is prudent to non-dimensionalize each of the above systems. 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 $*$):

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

where

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

The Gierer-Meinhardt and Thomas kinetics can be non-dimensionalized as follows:

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

and

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

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

Any reaction-diffusion system can be non-dimensionalized and scaled following the above procedure to take the following 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 from the dimensional system 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 **??** – the inhibitor diffuses a greater distance than the activator, giving rise to what is known as *local activation, long-range inhibition.*

** Insert activator_inhibitor here **

6.4 Numerical solution

In Figure Figure 6.1 we plot numerical solutions of Equation 6.1 with no flux boundary conditions.

In this numerical solution the initial condition are the spatially homogeneous steady state perturbed by uniformly sampled noise. As time evolves a spatial pattern emerges. The main

idea from a biological perspeftive is that an unpatterned region of an embryo could undergo chemical reactions, with the result being a patterned chemcial field.

SOme question that might arise:

- How does pattern formation depend on model parameters?
- How does pattern formation depend on domain size?
- How does the pattern wavelength depend on model parameters?
- How does the pattern depend on the initial conditions?
- How can we numerically solve the reaction diffusion PDEs?

```
import numpy as np
from scipy.integrate import odeint
from scipy.integrate import solve_ivp

import matplotlib.pyplot as plt
import random

T=3
L=1

gamma=650.0
a=0.2
b=1.3
d=30.0

N_x=80
N_t=50

t=np.linspace(1,T,N_t)
x=np.linspace(0,L,N_x)

u_0=(a+b)*np.ones_like(x)+0.01*np.random.uniform(low=-1.0, high=1.0, size=(N_x,))
v_0=b*(1/(a+b)**2)*np.ones_like(x)+0.01*np.random.uniform(low=-1.0, high=1.0, size=(N_x,))

u_0=np.concatenate((u_0,v_0))

dx=L/(N_x-1)
dt=T/(N_t-1)

def ShcnackPDErhs(sol,t):

    N_x=int(np.ceil(len(sol)/2))
```

```
    u=sol[0:N_x]
    v=sol[N_x:]

    f_u=np.zeros_like(u)
    f_v=np.zeros_like(u)

    for i in range(1,N_x-2):
      f_u[i]=1/dx**2*(u[i-1]-2*u[i]+u[i+1])

    i=0
    f_u[i]=1/dx**2*(-u[i]+u[i+1])

    i=N_x-1
    f_u[i]=1/dx**2*(u[i-1]-u[i])


    for i in range(1,N_x-2):
      f_v[i]=d/dx**2*(v[i-1]-2*v[i]+v[i+1])
    i=0
    f_v[i]=d/dx**2*(-v[i]+v[i+1])
    i=N_x-1
    f_v[i]=d/dx**2*(v[i-1]-v[i])

    reaction_u=gamma*(a-u+(u**2)*v)
    reaction_v=gamma*(b-(u**2)*v)

    f_u=f_u+reaction_u
    f_v=f_v+reaction_v

    f= np.concatenate((f_u,f_v))
    return f

sol=odeint(ShcnackPDErhs,u_0,t)
#soln = solve_ivp(ShcnackPDErhs,(0, T), u_0, method='Radau')

u=sol[:,0:N_x]
v=sol[:,N_x:]

fig, ax = plt.subplots(2,1)

ax[0].plot(x,u[0,:],'r')
```

```
ax[0].plot(x,u[16,:],'b')
ax[0].plot(x,u[32,:],'m')
ax[0].plot(x,u[48,:],'k')
ax[0].set_xlabel('$x$')
ax[0].set_ylabel('$u$')

ax[1].plot(x, v[0,:],'r--')
ax[1].plot(x, v[16,:],'b--')
ax[1].plot(x, v[32,:],'m--')
ax[1].plot(x, v[48,:],'k--')
ax[1].set_xlabel('$x$')
ax[1].set_ylabel('$v$')

plt.legend(['t'+ str(t[0]),'t='+ str(t[4]),'t='+ str(t[8]),'t='+ str(t[12])])
plt.xlabel('$x$')
plt.grid()
plt.show()
```

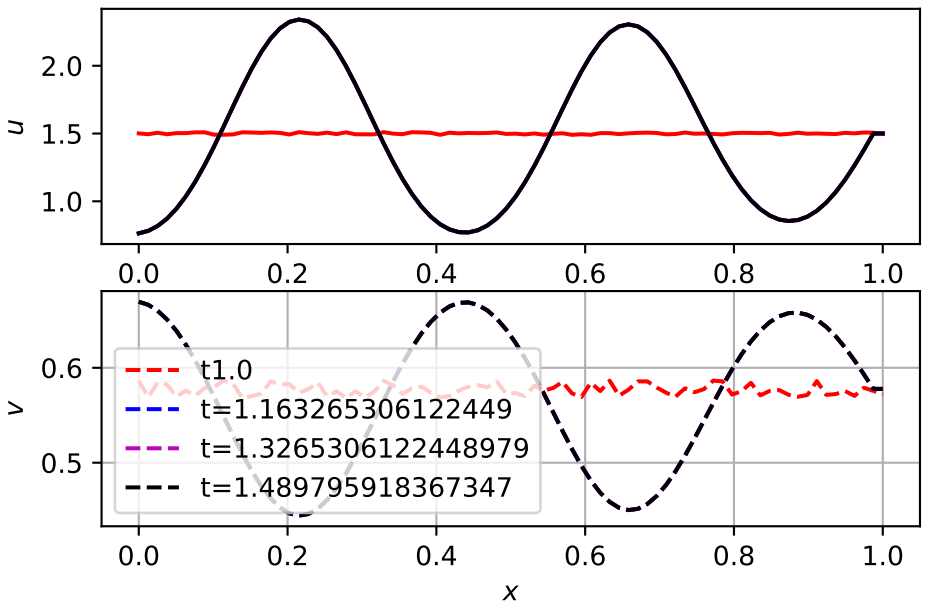


Figure 6.1: DDI with Schnackenberg kinetics

In Figure Figure 6.2 we consider a numerical solution of the Schnackenberg model on a 2D square domain with no-flux boundary conditions. Note

```
import numpy as np
from scipy.integrate import odeint
from scipy.integrate import solve_ivp

import matplotlib.pyplot as plt
import random

T=5
L=1

gamma=650.0
a=0.2
b=1.3
d=25.0

N_x=20
N_t=30

t=np.linspace(1,T,N_t)
x=np.linspace(0,L,N_x)
y=np.linspace(0,L,N_x)

[x,y]=np.meshgrid(x,y)

u_0=(a+b)*np.ones_like(x)+0.01*np.random.uniform(low=-1.0, high=1.0, size=(N_x,N_x))
v_0=b*(1/(a+b)**2)*np.ones_like(x)+0.01*np.random.uniform(low=-1.0, high=1.0, size=(N_x,N_

u_0=np.concatenate((np.ravel(u_0),np.ravel(v_0)))

dx=L/(N_x-1)
dt=T/(N_t-1)



def ShcnackPDErhs2d(sol,t):

    num_nodes=int(np.ceil(len(sol)/2))

    u=sol[0:num_nodes]
    v=sol[num_nodes:]
```

```
u=np.reshape(u,(N_x,N_x))
v=np.reshape(v,(N_x,N_x))

f_u=np.zeros_like(u)
f_v=np.zeros_like(u)



for i in range(1,N_x-2):
  for j in range(1,N_x-2):
    f_u[i,j]=1/dx**2*(u[i-1,j]-4*u[i,j]+u[i+1,j]+u[i,j+1]+u[i,j-1])
    f_v[i,j]=d/dx**2*(v[i-1,j]-4*v[i,j]+v[i+1,j]+v[i,j+1]+v[i,j-1])

i=0
for j in range(1,N_x-2):
  f_u[i,j]=1/dx**2*(-3*u[i,j]+u[i+1,j]+u[i,j+1]+u[i,j-1])
  f_v[i,j]=d/dx**2*(-3*v[i,j]+v[i+1,j]+v[i,j+1]+v[i,j-1])

i=N_x-1
for j in range(1,N_x-2):
  f_u[i,j]=1/dx**2*(u[i-1,j]-3*u[i,j]+u[i,j+1]+u[i,j-1])
  f_v[i,j]=d/dx**2*(v[i-1,j]-3*v[i,j]+v[i,j+1]+v[i,j-1])

j=0
for i in range(1,N_x-2):
    f_u[i,j]=1/dx**2*(u[i-1,j]-3*u[i,j]+u[i+1,j]+u[i,j+1])
    f_v[i,j]=d/dx**2*(v[i-1,j]-3*v[i,j]+v[i+1,j]+v[i,j+1])

j =N_x-1
for i in range(1,N_x-2):
    f_u[i,j]=1/dx**2*(u[i-1,j]-3*u[i,j]+u[i+1,j]+u[i,j-1])
    f_v[i,j]=d/dx**2*(v[i-1,j]-3*v[i,j]+v[i+1,j]+v[i,j-1])

i=0
j=0
f_u[i,j]=1/dx**2*(-2*u[i,j]+u[i+1,j]+u[i,j+1])
f_v[i,j]=d/dx**2*(-2*v[i,j]+v[i+1,j]+v[i,j+1])

i=0
j=N_x-1
f_u[i,j]=1/dx**2*(-2*u[i,j]+u[i+1,j]+u[i,j-1])
```

```
    f_v[i,j]=d/dx**2*(-2*v[i,j]+v[i+1,j]+v[i,j-1])

    i=N_x-1
    j=0

    f_u[i,j]=1/dx**2*(u[i-1,j]-2*u[i,j]+u[i,j+1])
    f_v[i,j]=d/dx**2*(v[i-1,j]-2*v[i,j]+v[i,j+1])

    i=N_x-1
    j=N_x-1


    f_u[i,j]=1/dx**2*(-2*u[i,j]+u[i-1,j]+u[i,j-1])
    f_v[i,j]=d/dx**2*(-2*v[i,j]+v[i-1,j]+v[i,j-1])


    reaction_u=gamma*(a-u+(u**2)*v)
    reaction_v=gamma*(b-(u**2)*v)

    f_u=f_u+reaction_u
    f_v=f_v+reaction_v



    f= np.concatenate((np.ravel(f_u),np.ravel(f_v)))
    return f

sol=odeint(ShcnackPDErhs2d,u_0,t)
#soln = solve_ivp(ShcnackPDErhs,(0, T), u_0, method='Radau')


u_0=sol[0,0:N_x**2]
v_0=sol[0,N_x**2:]
u_0=np.reshape(u_0,(N_x,N_x))
v_0=np.reshape(v_0,(N_x,N_x))

u_m=sol[20,0:N_x**2]
v_m=sol[20,N_x**2:]
u_m=np.reshape(u_m,(N_x,N_x))
v_m=np.reshape(v_m,(N_x,N_x))
```

```
u=sol[-1,0:N_x**2]
v=sol[-1,N_x**2:]
u=np.reshape(u,(N_x,N_x))
v=np.reshape(v,(N_x,N_x))

fig, ax = plt.subplots(2,3)
ax[0,0].imshow(u_0)
ax[1,0].imshow(v_0)
ax[0,1].imshow(u_m)
ax[1,1].imshow(v_m)
ax[0,2].imshow(u)
ax[1,2].imshow(v)

'''
ax[0].plot(x,u[0,:],'r')
ax[0].plot(x,u[16,:],'b')
ax[0].plot(x,u[32,:],'m')
ax[0].plot(x,u[48,:],'k')
ax[0].set_xlabel('$x$')
ax[0].set_ylabel('$u$')

ax[1].plot(x, v[0,:],'r--')
ax[1].plot(x, v[16,:],'b--')
ax[1].plot(x, v[32,:],'m--')
ax[1].plot(x, v[48,:],'k--')
ax[1].set_xlabel('$x$')
ax[1].set_ylabel('$v$')
'''

plt.xlabel('$x$')
plt.show()
```

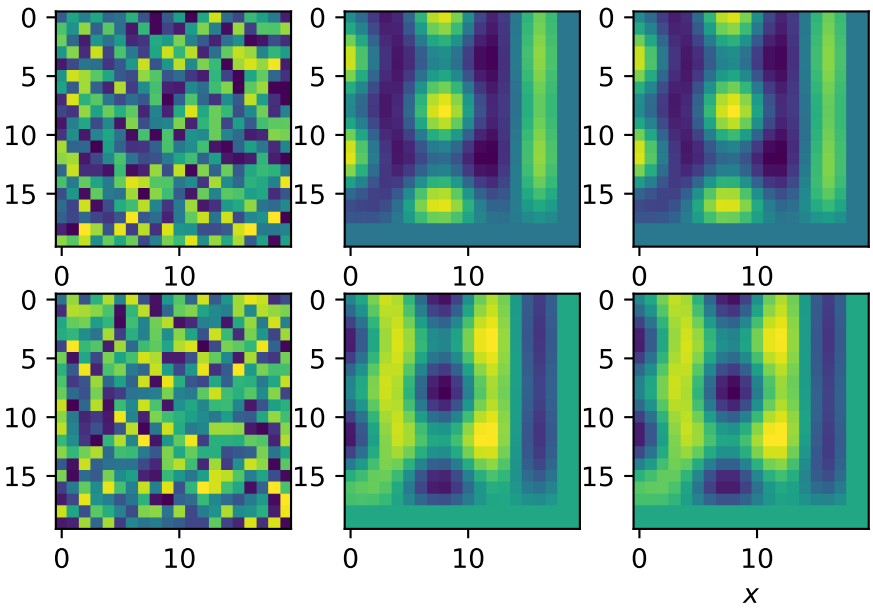


Figure 6.2: DDI with Schnackenberg kinetics in 2D

6.5 Linear Stability Analysis and Evolution of Spatial Pattern: General Conditions for Diffusion-driven Instability

Let $\Omega \subset \mathbb{R}^n$ 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:

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

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

A **spatially homogeneous steady-state** of the system Equation 6.2 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 the spatial terms in the system (i.e. diffusion), we first of all explore the stability of the underlying spatially homogeneous steady state, defined previously.

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

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

Substitute these into Equation 6.2

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

and using a Taylor expansion of f and g about (u_0, v_0) we obtain 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 the above system of linear ODEs 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 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

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

Conditions Equation 6.6 provide restrictions on the parameters in the model equations Equation 6.2. We shall be interested only in such parameter values for which conditions Equation 6.6 are satisfied.

6.5.2 Stability of spatially homogeneous steady states to spatially heterogeneous: spatially dependent, perturbations

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

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

Once again substitute into Equation 6.2 and apply a Taylor expansion about (u_0, v_0) to f and g to obtain the linearised problem

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

Defining

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

we can 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

$$\begin{aligned}
\frac{d\bar{u}(t)}{dt}\varphi_1(x) &= \gamma\ (f_u\bar{u}(t)\varphi_1(x) + f_v\bar{v}(t)\varphi_2(x)) + \bar{u}(t)\nabla^2\varphi_1(x), \quad x\in\Omega,\ t>0,\\
\frac{d\bar{v}(t)}{dt}\varphi_2(x) &= \gamma\ (g_u\bar{u}(t)\varphi_1(x) + g_v\bar{v}(t)\varphi_2(x)) + d\bar{v}(t)\nabla^2\varphi_2(x), \quad x\in\Omega,\ t>0,\\
&\mathbf{n}\cdot\nabla\varphi_1(x) = 0, \qquad \mathbf{n}\cdot\nabla\varphi_2(x) = 0, \qquad x\in\partial\Omega,\ t>0
\end{aligned} \tag{6.8}$$

with

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

for $t>0$.

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

$$\begin{aligned}
\nabla^2\psi(x) &= -k^2\psi(x), \qquad x\in\Omega,\\
\mathbf{n}\cdot\nabla\psi(x) &= 0, \qquad x\in\partial\Omega\ .
\end{aligned} \tag{6.9}$$

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 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

$$V(x,t) = \sum_k \hat{V}_k(t)\psi_k(x), \qquad \text{where} \quad \hat{V}_k(t) = \begin{pmatrix}C_k^1\ \bar{u}(t)\\ C_k^2\ \bar{v}(t)\end{pmatrix}. \tag{6.10}$$

Then since $\nabla^2\psi_k(x) = -k^2\psi_k(x)$ we obtain

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

and 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:

$$\frac{d}{dt}\hat{V}_k(t) = (\gamma J - k^2 D)\,\hat{V}_k(t) \quad = \tilde{J}\hat{V}_k(t), \tag{6.11}$$

where $\tilde{J}$ is a "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 6.11 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

$$\det(\tilde{J} - \lambda I) = \det(\gamma J - k^2 D - \lambda I) = 0. \tag{6.12}$$

Evaluating the above determinant, we arrive at the equation:

$$\lambda^2 + [k^2(1+d) - \gamma(f_u + g_v)]\lambda + h(k^2) = 0, \tag{6.13}$$

where

$$h(k^2) = dk^4 - \gamma(df_u + g_v)k^2 + \gamma^2|J|. \tag{6.14}$$

NOTE: From Equation 6.12, Equation 6.13 we can recover the characteristic equation for the spatially homogeneous perturbation when $k = 0$, i.e.

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

```
import numpy as np
import matplotlib.pyplot as plt

# genera
k_sq=np.linspace(0,25,100)


gamma=10
d_1=0.02
d_2=3
d_3=6


f_u=0.2
g_v=-0.5
term1=d*f_u+g_v
J=1.0 # positive determinant



def Computeh(k_sq,d):
  h=d*k_sq**2-gamma*(term1)*k_sq+ gamma**2*J
  return h

def SolveReLambda(k_sq,d):
   # a lam^2 + b * lam +c
    a=1
    b= k_sq*(1+d)-gamma*(f_u+g_v)
    c= Computeh(k_sq,d)

    lambda_m= (-b-np.sqrt(b**2-4*a*c))/(2*a)
    lambda_p= (-b+np.sqrt(b**2-4*a*c))//(2*a)
    return lambda_m,lambda_p

def TestDDIconditions(d):

    cond_1=f_u+g_v
    cond_2 = J
    cond_3 = d*f_u+g_v
    cond_4 = (d*f_u+g_v)**2-4*d*J


    cond_true=np.zeros((4,1),dtype=bool)
    cond_true[0]=(cond_1<0)
    cond_true[1]= (cond_2>0)
    cond_true[2]= (cond_3>0)
    cond_true[3]=(cond_4<0)


    return cond_true
```

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 6.12, Equation 6.13.

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

$$df_u + g_v > 0. \tag{6.15}$$

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 6.15 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 6.14 w.r.t. k^2, we find that:

$$k_m^2 = \gamma\frac{df_u + g_v}{2d} \quad \Rightarrow \quad h_{min} = \gamma^2\left[|J| - \frac{(df_u + g_v)^2}{4d}\right]. \tag{6.16}$$

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 6.16, this means at bifurcation we have

$$|J| = \frac{(df_u + g_v)^2}{4d}. \tag{6.17}$$

For a fixed set of kinetics parameters, this means that we have a **critical diffusion coefficient** d_c (> 1), which, after re-arranging Equation 6.17, is the appropriate root of

$$q(d_c) = d_c^2 f_u^2 + 2(2f_v g_u - f_u g_v)d_c + g_v^2 = 0. \tag{6.18}$$

Finally, we note that using Equation 6.16, Equation 6.17, the **critical wave number** can be written:

$$k_c^2 = \gamma \frac{(d_c f_u + g_v)}{2d_c} = \gamma \left[\frac{|J|}{d_c}\right]^{1/2} = \gamma \left[\frac{f_u g_v - f_v g_u}{d_c}\right]^{1/2}. \tag{6.19}$$

Figure 6.4 (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 6.13 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 6.14, $h(k^2) = 0$:

$$\begin{aligned} k_1^2 &= \gamma \frac{(df_u + g_v) - \left\{(df_u + g_v)^2 - 4d|J|\right\}^{1/2}}{2d} < k^2 \\ &< \gamma \frac{(df_u + g_v) + \left\{(df_u + g_v)^2 - 4d|J|\right\}^{1/2}}{2d} = k_2^2 \end{aligned} \tag{6.20}$$

Figure 6.4 (b) shows a schematic diagram of $\mathrm{Re}\lambda(k^2)$ for three different values of the diffusion coefficient d: * \$d < d_c, ; $\mathrm{Re}\lambda(k^2) < 0,\ k\hat{}2\ \$$, 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 6.16 when $d > d_c$. This implies

that there is a **fastest growing mode** in the solution Equation 6.10 of our linearised system Equation 6.8.

Recalling Equation 6.10,

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

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

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

%The critical value of $d = d_c$ at which the bifurcation to instability occurs is defined by $h_{\min} = 0$, i.e. such value of d at which $h(k^2) = 0$ has a double root.

** include figure dispersion **

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.

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 6.21 are satisfied, then there is a range of unstable wavenumbers given by Equation 6.20 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

Part III

Appendices

7 Numerical methods in Python

7.1 Python libraries

- matplotlib
- numpp
- scipy

7.2 Single PDEs

7.2.1 MOL

7.2.2 Spatial discretisation

7.2.3 odeint

7.2.4 implementing boundary conditions

7.2.5 Identifying parameters

7.3 Systems of PDEs

8 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 $m = 2$:

$$\begin{cases} \dfrac{du_1}{dt} = F(u_1, u_2), \\ \dfrac{du_2}{dt} = G(u_1, u_2) \end{cases} \tag{8.1}$$

$(u_1, u_2) = (u_1^*, u_2^*)$ is the steady state of the system Equation 8.1, 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

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

$$\begin{cases} \dfrac{d(u_1^* + \bar{u}_1)}{dt} = F(u_1^* + u_1, u_2^* + \bar{u}_2), \\ \dfrac{d(u_2^* + \bar{u}_2)}{dt} = G(u_1^* + u_1, u_2^* + \bar{u}_2) \end{cases} \tag{8.2}$$

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

$$\begin{cases} \dfrac{d\bar{u}_1}{dt} = F(u_1^*, u_2^*) + \dfrac{\partial F}{\partial u_1}(u_1^*, u_2^*)\,\bar{u}_1 + \dfrac{\partial F}{\partial u_2}(u_1^*, u_2^*)\,\bar{u}_2 + O(|\bar{u}_1|^2, |\bar{u}_2|^2), \\ \dfrac{d\bar{u}_2}{dt} = G(u_1^*, u_2^*) + \dfrac{\partial G}{\partial u_1}(u_1^*, u_2^*)\,\bar{u}_1 + \dfrac{\partial G}{\partial u_2}(u_1^*, u_2^*)\,\bar{u}_2 + O(|\bar{u}_1|^2, |\bar{u}_2|^2) \end{cases} \tag{8.3}$$

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

$$\begin{pmatrix} \dfrac{d\bar{u}_1}{dt} \\ \dfrac{d\bar{u}_2}{dt} \end{pmatrix} = J(u_1^*, u_2^*) \begin{pmatrix} \bar{u}_1 \\ \bar{u}_2 \end{pmatrix} \tag{8.4}$$

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 8.1 near the steady state (u_1^*, u_2^*) is determined by solutions of system of linear ODEs Equation 8.4.

Since Equation 8.4 is linear we can write the general solution of (**eqsystem_ode14?**)

$$\begin{pmatrix} \bar{u}_1 \\ \bar{u}_2 \end{pmatrix} = e^{\lambda_1 t} \begin{pmatrix} \phi_1 \\ \phi_2 \end{pmatrix} + e^{\lambda_2 t} \begin{pmatrix} \psi_1 \\ \psi_2 \end{pmatrix} \tag{8.5}$$

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 $\beta = \text{tr}(J(u_1^*, u_2^*))$ 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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