PIMS

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Short Summary

1 From random walk to diffusion

Stepping stone model or walk on a grid $\mathbb{Z}$ in discrete time

$$u_i^{(\nu+1)} = \frac{1}{2}\left(u_{i-1}^{(\nu)} + u_{i+1}^{(\nu)}\right). \tag{1.1}$$

Write as

$$u_i^{(\nu+1)} - u_i^{(\nu)} = \frac{1}{2}\left(u_{i-1}^{(\nu)} - 2u_i^{(\nu)} + u_{i+1}^{(\nu)}\right). \tag{1.2}$$

Write as difference quotients

$$\frac{u_i^{(\nu+1)} - u_i^{(\nu)}}{k} = \frac{1}{2}\frac{h^2}{k}\frac{u_{i-1}^{(\nu)} - 2u_i^{(\nu)} + u_{i+1}^{(\nu)}}{h^2}. \tag{1.3}$$

Embed the grid $h\mathbb{Z} \times k\mathbb{Z}_+$ in the x,t-plane. Assume

$$\frac{h^2}{k} \to D > 0. \tag{1.4}$$

Get diffusion equation

$$u_t = \frac{1}{2}Du_{xx}. \tag{1.5}$$

This is the stochastic view. In the numerical or analytic view one assumes

$$\frac{h^2}{2k} \to D \tag{1.6}$$

and arrives at

$$u_t = Du_{xx}. \tag{1.7}$$

2 de Moivre-Laplace

The transition from a difference equation to a differential equation is closely related to the transition from a random walk on a grid to a random walk (Brownian motion) on the line and also to the transition from the binomial distribution $B_{n,p}$ to a normal distribution $N(\mu, \sigma^2)$ (the convergence theorem is named after de Moivre and Laplace). Recall that also this transition requires special scaling $\mu = np$, $\sigma^2 = np(1-p)$. Hence the density of the normal distribution and the fundamental solution for the diffusion equation are almost the same, the fundamental solution is (in 1D)

$$u(t,x) = \frac{1}{\sqrt{4\pi t}} e^{-x^2/(4Dt)}. \tag{2.1}$$

3 Density and probability

Consider a particle performing Brownian motion on the real line starting at $x = 0$. The probability density $u(t,x)$ evolves according to the equation

$$u_t = \frac{1}{2} D u_{xx} \tag{3.1}$$

Then

$$\int_a^b u(t,x)dx$$

is the probability that the particle is in the interval $[a,b]$ at time t.

On the other hand look at the probability $U(t,x)$ that the particle is in $(-\infty, x)$ at time t. This function is given by

$$U(t,x) = \int_{-\infty}^{x} u(t,y)dy$$

It satisfies the equation

$$U_t = \frac{1}{2} D U_{xx} \tag{3.2}$$

Hence we have the same equation for two very different functions, a density and a probability.

4 Heat equation

Think of heat conduction in a homogeneous rod parameterized by a variable $x \in \mathbb{R}$. Let $u(t,x)$ be the temperature at time t at position x. One can

consider a "short" piece of the rod and look at the heat balance in that piece and the heat flow through the ends and derive the equation

$$u_t = \frac{k}{c\rho} u_{xx} \tag{4.1}$$

where k is heat conductivity, ρ is density and c is specific heat. Hence one arrives again at the diffusion equation with

$$D = \frac{k}{c\rho}. \tag{4.2}$$

5 Several dimensions

Here our question is: What is u_{xx} is several space dimensions?

Let $x = (x_1, \ldots, x_n)^T$. Let $u : \mathbb{R}^n \to \mathbb{R}$, i.e., $u(x) = u(x_1, \ldots, x_n)$. Then u_x is a row vector. If we use the scalar product then to u_x corresponds a unique column vector which is simply (for the standard scalar product) u_x^T. This vector is called the gradient of u,

$$\operatorname{grad} u = u_x^T. \tag{5.1}$$

Let v be any vector field, $v : \mathbb{R}^n \to \mathbb{R}^n$. The we can form the derivative v_x (which is a matrix, often called the Jacobian matrix). The divergence of v is defined as the trace of the derivative

$$\operatorname{div} v = \operatorname{tr} v_x. \tag{5.2}$$

In the special case of $v = \operatorname{grad} u$ the Jacobian becomes the Hessian u_{xx} (which is a symmetric matrix for smooth u). In this case we define

$$\Delta u = \operatorname{div} \operatorname{grad} u. \tag{5.3}$$

The operators grad and div are both linear, and so is Δ. This operator is called the Laplacian. The trace is the only linear functional on matrices (up to factors) which is invariant under similarity transforms. That is the reason why the Laplacian is the only meaningful generalization of the second derivative which is invariant under translations and rotations of the coordinate frame.

In coordinates the Laplacian becomes

$$\Delta u = u_{x_1 x_1} + u_{x_2 x_2} + \ldots + u_{x_n x_n}. \tag{5.4}$$

Because we take the trace, only the terms $u_{x_i x_i}$ show up and not any mixed derivative.

The gradient grad takes us from scalars to vectors while the divergence div takes us from vectors to scalars. Physicists use ∇ ("nabla") for both operators and often write $\nabla^2 = \Delta$. This is fine as long as one knows whether one applies ∇ to a scalar or to a vector.

So the diffusion equation in several dimensions assumes the form

$$u_t = D\Delta u. \tag{5.5}$$

6 Conservation laws

An equation

$$u_t + \operatorname{div} v = 0 \tag{6.1}$$

connecting a function u to a vector field v is called a conservation law. The idea is that matter distributed according to the density u is moving along the trajectories defined by the vector field v. This equation has to be supplemented by a constitutive law which connects the vector field to the density u,

$$v = \mathcal{F}(u)$$

where $\mathcal{F}$ can be almost everything.

One particular choice is

$$v = -D\operatorname{grad} u \tag{6.2}$$

saying that the flow is proportional to the negative gradient. If we replace v in the first equation by the second equation we get the diffusion equation

$$u_t = \operatorname{div} D\operatorname{grad} u \tag{6.3}$$

These ideas were developed by Fourier in his treatise of 1822. In 1855 Fick found that Fourier's ideas about heat conduction could be as well used to describe diffusion of particles. In this context the equation (6.2) is called the first Fickian law and (6.3) is called the second Fickian law.

7 Advantages and disadvantages

Because the Laplacian is the only second order operator which is invariant under the orthogonal group, it appears "everywhere" in mathematics

and physics (see Laplace equation, heat equation, diffusion equation, wave equation, real and imaginary part of a complex analytic function, vibrating membrane etc. etc.). Hence we have lots and lots of tools to study the diffusion equation. Therefore the diffusion equation is the most used model for biological spread.

On the other hand it has some deficiencies.
1) According to this model some particles move arbitrarily fast (although just a small fraction). The scaling with h^2/k helps understand why this is so. Explain this argument in detail! Think of walking on the grid in discrete time steps, toss a coin to decide whether going right or left, for $k \to 0$ we have any number of decisions in a finite time interval $[0, T]$.
2) The heat equation does not "know" that there an absolute zero temperature.
3) According to the model the gradient can be instantaneously observed.
4) According to the diffusion model particles have no impulse, inertia, or memory.
5) Many biological objects, e.g., many bacteria, perform more complicated "walks".

Therefore we look for more sophisticated models.

8 Cattaneo approach

Consider again a conservation law

$$u_t + \operatorname{div} v = 0$$

with some constitutive equation connecting v to u. As we have seen, one choice is $v = -D\operatorname{grad} u$. This choice is based on the idea that a particle can "observe" a gradient instantaneously. Cattaneo 1948 had the idea to introduce some time constant into the constitutive equation.

$$\begin{aligned} u_t + \operatorname{div} v &= 0 \\ \tau v + D\operatorname{grad} u + v &= 0 \end{aligned} \tag{8.1}$$

This system can be carried into a damped wave equation by what we now call Kac' trick: Assume a smooth solution. Get

$$\begin{aligned} \tau u_{tt} + \tau \operatorname{div} v_t &= 0 \\ -\tau \operatorname{div} v_t - \operatorname{div}(D\operatorname{grad} u) - \operatorname{div} v &= 0 \\ u_t + \operatorname{div} v &= 0 \end{aligned}$$

Add and get the equation

$$\tau u_{tt} + u_t = \operatorname{div}(D\operatorname{grad} u) \tag{8.2}$$

This is a damped wave equation.

For $\tau \to 0$ we obtain (formally) the diffusion equation

$$u_t = \nabla(D\nabla u). \tag{8.3}$$

The Kac trick has carried us from a Cattaneo system to a damped wave equation. In this transition some solutions get lost. Assume we have a constant vector field $\bar{v}$ with $\operatorname{div} \bar{v} =$. Then the solution $u = 0$, $\bar{v}\exp\{-t/\tau\}$ of the system is carried into the zero solution of the damped wave equation. In biological (or physical) terms: vector fields with zero mass are carried into zero.

The diffusion equation is a parabolic equation. It does not have characteristics, initial data become quickly smoothed. The damped wave equation is a hyperbolic equation. It has characteristics along which information is transported. Initial data are smoothed only in the limit of very long times. Nevertheless the diffusion equation and the damped wave equation have much in common, in particular with respect to existence of compact global attractors if reaction terms are added.

9 Transport operator

Again a conservation law with a constitutive equation

$$\begin{aligned} u_t + \operatorname{div} v &= 0 \\ v &= su \end{aligned}$$

with s being a constant vector. The expression su is indeed a vector field, although a very special one. The Jacobian is the rank one operator su_x (s is a column vector and u_x is a row vector). The divergence is $\operatorname{div}(su) = u_x s = s \cdot u_x$. Hence the system leads to the single equation

$$u_t + s \cdot u_x = 0 \tag{9.1}$$

This equation is called the transport equation.

Consider an initial data $u_0(x, s)$. The solution is

$$u(t, x, s) = u_0(x - st, s). \tag{9.2}$$

For given s, this function is a simple wave.

According to this model a particle travels on a straight line. In order to have a realistic model, we need to introduce turning.

10 Turning operator

A turning operator is defined as

$$(Tu)(x,s) = -u(x,s) + \int_V K(s,\tilde{s})u(x,\tilde{s})d\tilde{s} \tag{10.1}$$

where V is the set of admissible velocities. The kernel K has the properties $K(s,\tilde{s}) \geq 0$, $\int_V K(s,\tilde{s})ds = 1$. Then the transport equation becomes

$$u_t + s \cdot \nabla_x u = \mu(Tu). \tag{10.2}$$

Example: Pearson walk

$$V = \{s : |s| = \gamma\}$$

$$u_t + s \cdot \nabla_x u = -\mu u + \frac{\mu}{|V|}\int_V u(t,x,\tilde{s})d\tilde{s} \tag{10.3}$$

An appropriate model for bacteria that run and tumble. The system preserves positivity and total mass.

The underlying process has been designed by Pearson. He called it a random walk. This walk describes rather nicely what some bacteria seem do do. They go on a straight line with exponential holding line, stop, and choose a new direction by choosing a vector from the unit sphere according to the uniform distribution.

11 Correlated random walk

Particles move back and forth on the real line with constant speed $\gamma > 0$, then stop with a rate μ and choose a direction, with probability 1/2 for each direction (this is the Pearson walk in one space dimension)

$$\begin{aligned} u_t^+ + \gamma u_x^+ &= -\mu u^+ + \frac{\mu}{2}(u^+ + u^-) \\ u_t^- - \gamma u_x^- &= -\mu u^- + \frac{\mu}{2}(u^+ + u^-) \end{aligned} \tag{11.1}$$

or

$$\begin{aligned} u_t^+ + \gamma u_x^+ &= \frac{\mu}{2}(u^- - u^+) \\ u_t^- - \gamma u_x^- &= \frac{\mu}{2}(u^+ - u^-) \end{aligned} \tag{11.2}$$

The stopping rate is μ, and $\mu/2$ is the turning rate. Introduce the total mass and the probability flow

$$u = u^+ + u^-, \quad v = \gamma(u^+ - u^-) \tag{11.3}$$

and get a Cattaneo system

$$\begin{aligned} u_t + v_x &= = 0 \\ \frac{1}{\mu} v_t + \frac{\gamma^2}{\mu} u_x + v &= 0. \end{aligned} \tag{11.4}$$

Kac' trick leads to the damped wave equation.

$$\frac{1}{\mu} u_{tt} + u_t = \frac{\gamma^2}{\mu} u_{xx}. \tag{11.5}$$

The one-dimensional damped wave equation is also called a telegraph equation.

12 Boundary conditions

Diffusion equation

$$u_t = D u_{xx} \tag{12.1}$$

on a bounded interval $[0, l]$, Need boundary conditions. Several choices. For example at $x = l$.
1) $u(t, l) = \phi(t)$ Dirichlet
2) $u_x(t, l) = \psi(t)$ Neumann
3) $u_x(t, x) = -cu(t, l)$ Robin
Notice that at $x = l$ the derivative u_x is the derivative in the direction of the outer normal vector while at $x = 0$ we have the opposite sign. This fact needs some attention if we want the "correct" sign in boundary conditions depending on the flux.

For the correlated random walk system

$$\begin{aligned} u_t^+ + \gamma u_x^+ &= \frac{\mu}{2}(u^- - u^+) \\ u_t^- - \gamma u_x^- &= \frac{\mu}{2}(u^+ - u^-) \end{aligned} \tag{12.2}$$

we can prescribe boundary conditions only at ingoing characteristics. A Dirichlet condition assumes the form

$$\begin{aligned} u^+(t, 0) &= \phi^+(t) \\ u^-(t, l) &= \phi^-(t). \end{aligned} \tag{12.3}$$

A no-flux Neumann condition at both ends assumes the form

$$u^+(t, 0) = u^-(t, 0), \quad u^-(t, l) = u^+(t, l). \tag{12.4}$$

13 Integral operators

A migration equation is something like a generalization of a diffusion equation where the Laplacian has been replaced by a non-local operator

$$u_t(t,x) = d\left(\int_{\mathbb{R}^n} k(x-y)u(t,y)dy - u(t,x)\right), \tag{13.1}$$

$k \geq 0$, $k(Uz) = k(z)$ for $U^TU = I$, $\int_{\mathbb{R}^n} k(z)dz = 1$. We try to get a diffusion approximation. Write the equation as

$$\begin{aligned} u_t(t,x) &= d\left(\int_{\mathbb{R}^n} k(z)u(t,x+z)dz - u(t,x)\right) \\ &= d\left(\int_{\mathbb{R}^n} k(z)(u(t,x) + u_x(t,x)z + \frac{1}{2}z^T u_{xx}(t,x)z + o(|z|))dz - u(t,x)\right) \end{aligned}$$

Now

$$\int k(z)z^T u_{xx} z dz = \int k(z) \sum_{ij} u_{x_i x_j} z_i z_j dz$$

and

$$\int k(z)z_i z_j dz = \begin{cases} 0 & i \neq j \\ \int k(z)z_i^2 dz & i = j \end{cases}$$

and, because of the symmetry,

$$\int k(z)z_i^2 dz = \int k(x)z_1^2 dz$$

Hence

$$\int k(z)z^T u_{xx} z dz = \int k(z)z_1^2 dz \Delta u.$$

Arrive at

$$u_t = D\Delta u \tag{13.2}$$

with

$$D = \frac{1}{2}\int_{\mathbb{R}^n} k(z)z_1^2 dz \tag{13.3}$$

Of course we assume that $\int k(z)z_1^2 dz$ exists. Examples

$$e^{-z\cdot z}, \quad e^{-|z|}.$$

14 Reactions

Reactions are modeled by systems of ordinary differential equations

$$\dot{u} = f(u) \tag{14.1}$$

where $f : \mathbb{R}^n \to \mathbb{R}^n$, in coordinates

$$\dot{u}_i = f_i(u_1, u_2, \ldots, u_n)$$

Example: $m = 1$,

$$\dot{u} = f(u) = b(u)u - d(u)u$$

with a decreasing birth rate and an increasing death rate.

We observe that for $m = 1$ all solutions are monotone: strictly increasing, strictly decreasing, or constant.

This property is very useful in looking at scalar reaction diffusion equations.

In several dimensions $m > 1$ we do not have such monotonicity property. But there is another tool, the principle of positively invariant sets.

Let $M \subset \mathbb{R}^m$ be a bounded domain with a smooth boundary. Then at every boundary point $u \in \partial M$ we have a unique outer normal unit vector $\nu(u)$. We call the domain M positively invariant with respect to the flow of (14.1) if

$$\nu(u) \cdot f(u) \leq 0 \tag{14.2}$$

holds for all $u \in \partial M$. Indeed, this property is equivalent with the following:

If $u(0) \in M$ and $t \geq 0$ then $u(t) \in M$.

This observation can be extended, with some care, to domains M with a non-smooth boundary, e.g., polygons in the plane $\mathbb{R}^2$.

The method of positively invariant sets is somewhat more flexible than the method of Lyapunov functions. Of course, the level sets of a Lyapunov function are positively invariant sets.

15 Reaction and diffusion

Modeling transport or diffusion and reaction by the same model makes sense only if these processes run on comparable time scales. Otherwise one could just model spread at reaction equilibrium or a reaction in a well stirred setting.

Now if these processes run on comparable time scales then we have the reaction equation

$$\dot{u} = f(u)$$

and the diffusion equation

$$u_t = D\Delta u.$$

How do we unite these? Take the view of a splitting method. Define a time horizon $T > 0$ and choose a large natural number N and then define a step size $h = 1/N$. Next apply diffusion and reaction in an alternating fashion in intervals of length h, altogether N intervals for diffusion and N intervals for reaction (running up to total time $2T$). Letting N going to infinity we see that the only reasonable model system is obtained by adding the two actions. So we arrive at the reaction diffusion equation

$$u_t = D\Delta u + f(u) \tag{15.1}$$

With respect to this scalar equation we make the following observations.

Comparison of initial data:
$u(0,x) \leq v(0,x) \Rightarrow u(t,x) \leq v(t,x)$ for $t > 0$.

Hair trigger effect: If in addition $u(0,x) \not\equiv v(0,x)$ then $u(t,x) < v(t,x)$ for $t > 0$.

Comparison of right hand side:
Suppose $u_t = D\Delta u + f(u)$ and $v_t = D\Delta v + g(v)$ with initial data $u(0,x) = v(0,x)$. Further assume that

$$f(w) \leq g(w) \quad \text{for all} \quad w \in \mathbb{R}.$$

Then $u(t,x) \leq v(t,x)$ for $t > 0$ and all x.

16 The case of several species

Consider a reaction diffusion system for several species. So $x \in \mathbb{R}^n$ and $u \in \mathbb{R}^m$. For getting a geometric intuition it will be helpful to think of $m = 2$ species in an $n = 1$ dimensional domain.

Again we think of a positively invariant domain $M \subset \mathbb{R}^m$ for the ordinary differential equation $\dot{u} = f(u)$.

Consider the set of continuous bounded functions $u : \mathbb{R}^n \to \mathbb{R}^m$ which take their values in M, i.e., the set

$$\mathcal{M} = \{u \in C_b(\mathbb{R}^n) : u(x) \in M \quad \text{for all} \quad x \in \mathbb{R}^n\}. \tag{16.1}$$

It is evident that this set is positively invariant under the flow of the ordinary differential equation parameterized by x

$$u_t(t,x) = f(u(t,x)).$$

So we may conjecture that the set $\mathcal{M}$ is also positively invariant under the flow of the reaction diffusion equation

$$u_t = D\Delta u + f(u)$$

(all species with the same diffusion rate).

But this conjecture is wrong. It is true, however, if M is a convex set.

Positive Invariance Let the set M be convex. Assume the initial data $u(0,x)$ assume all its values in M. Then for $t > 0$ the solution $u(t,x)$ assumes all its values in M.

Next suppose that the the diffusion rates for the different species are all distinct. Then even a convex st M will not do. In this case the result is true if the set M is a parallelepiped with axes parallel to the coordinate axes,

$$M = \{x : a_i \le x_i \le b_i,\ i = 1, \dots, m\}.$$

Remember the counterexample with $u_t = Du_{xx}$, $D = \text{diag } (2,1)$ and $u_1(0,x) = u_2(0,x) = \exp\{-x^2\}$.

17 Reaction and correlated random walk

We want to incorporate reaction term $f(u)$ into a correlated random walk model. A naive way to do that would be

$$\begin{aligned} u_t^+ + \gamma u_x^+ &= \frac{\mu}{2}(u^- - u^+) + \frac{1}{2}f(u) \\ u_t^- - \gamma u_x^- &= \frac{\mu}{2}(u^+ - u^-) + \frac{1}{2}f(u). \end{aligned}$$

This "symmetric" model then leads to a Cattaneo system

$$\begin{aligned} u_t + v_x &= f(u) \\ v_t + \gamma^2 + \mu v &= 0 \end{aligned} \tag{17.1}$$

and then via Kac' trick to the damped wave equation

$$\frac{1}{\mu} + (1 - \frac{1}{\mu}f'(u))u_t = \frac{\gamma^2}{\mu}u_{xx} + f(u) \tag{17.2}$$

and finally to the reaction diffusion equation

$$u_t = Du_{xx} + f(u) \tag{17.3}$$

with $D = \gamma^2/\mu$.

Notice that the damping term is really "damping" if $f'(u) < \mu$.

This looks good from a mathematical point of view but not as a biological model, as can be seen if one takes $f(u) = au(1 - u/K)$.

So we better write the reaction term in the form of a birth-death balance

$$\dot{u} = f(u) = b(u)u - d(u)u$$

and treat birth and death differently and appropriately. Then we get the system

$$\begin{aligned} u_t^+ + \gamma u_x^+ &= \frac{\mu}{2}(u^- - u^+) + \frac{1}{2}b(u)u - d(u)u^+ \\ u_t^- - \gamma u_x^- &= \frac{\mu}{2}(u^+ - u^-) + \frac{1}{2}b(u)u - d(u)u^- \end{aligned}$$

From this system we get again a Cattaneo system for u and v

$$\begin{aligned} u_t + v_x &= f(u) \\ v_t + \gamma^2 u_x + \mu v + d(u)v &= 0. \end{aligned} \tag{17.4}$$

If we try to get to a damped wave equation we fail unless d is a constant. If d is a constant then we get the following

$$\begin{aligned} u_{tt} + v_{xt} &= f'(u)u_t \\ -v_{tx} - \gamma^2 u_{xx} - \mu v_x - dv_x &= 0 \\ (\mu + d)u_t + (\mu + d)v_x &= (\mu + d)f(u) \end{aligned}$$

Adding these equations gives

$$u_{tt} + (\mu + d - f'(u))u_t = \gamma^2 u_{xx} + (\mu + d)f(u) \tag{17.5}$$

Eventually we arrive at the diffusion equation

$$u_t = \frac{\gamma^2}{\mu + d}u_{xx} + f(u). \tag{17.6}$$

It is really interesting (and deserves further attention) that the death rate enters the diffusion coefficient.

18 Cattaneo and transport with reaction

Since for $n \geq 2$ we do not have a stochastic interpretation of the Cattaneo system, there is no way to imitate the modeling approach of the previous section with separate birth and death terms. We can only consider the symmetric system

$$\begin{aligned} u_t + \operatorname{div} &= f(u) \\ \tau v_t + D\operatorname{grad} u + v &= 0. \end{aligned} \tag{18.1}$$

However, for the transport model, such splitting is possible which will lead to

$$u_t + s \cdot \nabla_x u = \mu(Tu)(x,s) + \frac{1}{|V|} b(\bar{u})\bar{u} - d(\bar{u})u \tag{18.2}$$

where

$$\bar{u} = \bar{u}(t,x) = \int_V u(t,x,s)ds. \tag{18.3}$$

19 Traveling fronts

Model problem

$$u_t = Du_{xx} + f(u)$$

where f is a smooth function with $f(0) = f(1) = 0$, $f'(0) > 0$, $f'(1) < 0$, $f(u) > 0$ for $0 < u < 1$.

I) Initial data

$$u(0,x) = \begin{cases} 1 & x > 1 \\ 0 & x \leq 1 \end{cases}$$

The "splitting view" (alternating diffusion and reaction) suggests that the solution will develop into a front with asymptotically constant shape which moves with asymptotically constant speed.

If this were true then we expect that there is a similarity solution

$$u(t,x) = \phi(x - ct)$$

where $0 < \phi(x) < 1$ and $\phi(-\infty) = 1$, $\phi(+\infty) = 0$.

Then the profile ϕ satisfies the second order equation

$$-c\phi' = D\phi'' + f(\phi)$$

which can be written as a first order system

$$\begin{aligned} \dot{u} &= v \\ D\dot{v} &= -cv - f(u). \end{aligned} \tag{19.1}$$

This system has the stationary points $(u, v) = (0, 0)$ and $(1, 0)$. It can be seen that $(1, 0)$ is a saddle point for all values of $c > 0$ with the unstable manifold pointing into the direction $u < 1$, $v < 0$. We see that this unstable manifold is the only candidate for a trajectory describing the profile of a traveling front.

We further see that the point $(0, 0)$ is a focus is $c \in (0, c_*)$, where

$$c_* = 2\sqrt{Df'(0)}. \tag{19.2}$$

Hence there cannot be traveling fronts for $c < c_*$ which are meaningful solutions to the partial differential equation.

We follow the unstable manifold of the saddle for positive t and we find that it either ends up at the point $(0, 0)$ while staying in the range $0 < u < 1$ or it leaves that range and u becomes negative.

We further see that for large c the first case occurs, and this is true, if for one c then also for all larger c. Such argument shows that the set of all possible speeds is an upper half-line. A further argument shows that the half-line is closed. Hence the speeds of traveling fronts form a half-line $[c_0, \infty)$ with $c_0 \geq c_*$.

It is easy to see that

$$c_* \leq c_0 \leq 2\sqrt{D \sup_{0<u\leq 1} f(u)/u}\,. \tag{19.3}$$

Hence the "subtangential" condition

$$f(u) \leq f'(0)u \tag{19.4}$$

implies $c_0 = c_*$.

Follows a paragraph on spread numbers not included here.

20 Example: *Azospirillum*

The bacterium *Azospirillum brasilense* performs a rather peculiar random walk. Whereas many bacteria have a bundle of flagellae and run forward or tumble, depending on in which direction the flagella rotate, A.b. has a single

flagellum and runs forward (flagellum in front) or backward (flagellum behind) on essentially a straight line. The direction of the forward/backward motion changes only slowly. It is not quite clear how (and why) the bacterium keeps direction, some connection to the magnetic field of the earth has been suggested.

Alex Mogilner has modeled the walk of the bacterium by a correlated walk system in one dimension. Here we try to describe the movements of *A.b.* by a combination of a Goldstein-Kac random walk on a line and Brownian motion for the change of direction. For this system we derive an approximation in the form of a diffusion equation ("we" is KPH and Kevin Flores from ASU).

Let $\gamma > 0$ be the constant speed of the bacterium and let μ^+ be the rate at which the bacterium switches from forward motion to backward motion, and let μ^- be the rate of the reverse transition. The case $\mu^+ = \mu^-$ is called the symmetric case.

Let $u^+(t, x, s)$ be the density of bacteria at the space point x with direction s which travel forward and let $u^-(t, x, s)$ be the density of those which travel backward. We propose the following system of two coupled scalar partial differential equations.

$$\begin{aligned} u_t^+ + \gamma s \cdot \nabla_x u^+ &= \mu_- u^- - \mu_+ u^+ + d\Delta_s u^+ \\ u_t^- - \gamma s \cdot \nabla_x u^- &= \mu_+ u^+ - \mu_- u^- + d\Delta_s u^-. \end{aligned} \tag{20.1}$$

On the left hand side of each equation we have a transport operator which describes movement on a directed straight line with direction s. On the right hand side we have first the non-symmetric turning operator and then the diffusion operator for diffusion on the sphere of directions.

Define total particle density $u(t, x, s)$ and the "net flow" $v(t, x, s)$ as

$$u = u^+ + u^-, \quad v = u^+ - u^-. \tag{20.2}$$

In the symmetric case we have $\nu = 0$. These functions satisfy the system

$$\begin{aligned} u_t + \gamma s \cdot \nabla_x v &= d\Delta_s u \\ v_t + \gamma s \cdot \nabla_x u &= -\nu u - \mu v + d\Delta_s v \end{aligned} \tag{20.3}$$

where the new parameters μ and ν are given by

$$\mu = \mu^+ + \mu^-, \quad \nu = \mu^+ - \mu^-. \tag{20.4}$$

We find that this system can be approximated by

$$u_t = D\Delta_n u, \quad n = 2, 3. \tag{20.5}$$

Proposition: For large γ^2, μ, ν, and d, all of the same order of magnitude, the transport equation (20.3) can be approximated by the diffusion equation (20.5) with the diffusion coefficient

$$\begin{aligned} D_2 &= \frac{\gamma^2}{2(\mu+d)}\left(1+\frac{\nu^2}{\mu d}\right). \\ D_3 &= \frac{\gamma^2}{3(2d+\mu)}\left(1+\frac{\nu^2}{2d\mu}\right) \end{aligned} \tag{20.6}$$

The diffusion coefficient consists of two parts. The first part is caused by the symmetric part of the random walk on the line and the diffusion with rate d, the second part is caused by the asymmetry ν of the random walk. Of course it does not depend on the sign of ν. The two turning rates μ and d enter in a completely symmetric fashion, although with different weights.

21 Interlude: Michaelis-Menten kinetics

This section has been inserted after Leah Keshet introduced M-M kinetics. The Michaelis-Menten function has the form

$$x \mapsto \frac{ax}{b+x} = y.$$

The unknown parameters a and b are usually estimated in the sense of the least squares method by minimizing the functional

$$F(a,b) = \sum_{i=1}^{n} p_i \left(\frac{ax_i}{b+x_i} - y_i\right)^2 \tag{21.1}$$

in the range $a > 0$, $b > 0$.

The Michaelis-Menten function can also be fitted to data by solving the linear problem of minimizing

$$G(a,b) = \sum_{i=1}^{n} p_i \left(ax_i - (b+x_i)y_i\right)^2 \tag{21.2}$$

instead of the nonlinear problem (21.1). In general the linear problem yields immediately a unique solution. Similar difficulties as before arise because the solution may not be positive. In general the LSE solutions of (21.1) and (21.2) are not the same.

Corollary Let the data satisfy

$$x_1 \le x_2 \le \cdots \le x_n, \quad x_1 < x_n, \tag{21.3}$$

$$y_1 \le y_2 \le \cdots \le y_n, \quad y_1 < y_n, \tag{21.4}$$

and

$$\frac{y_1}{x_1} \ge \frac{y_2}{x_2} \ge \cdots \ge \frac{y_n}{x_n}, \quad \frac{y_1}{x_1} > \frac{y_n}{x_n}. \tag{21.5}$$

Then there is a global minimum $(a^\star, b^\star)$ with $a^\star > 0$, $b^\star > 0$.
Then the solution of the linear least squares problem (minimizing the function G) is positive.

This corollary is a special case of theorems that allow some deviations from the strict hypothesis of the corollary. That is to say the theorems allow for "outliers" in the data.

Theorem 1: Assume the data satisfy the inequalities

$$\sum_i p_i \left(\sum_i p_i x_i y_i \right)^2 \le \sum_i p_i x_i^2 \left(\sum_i p_i y_i \right)^2, \tag{21.6}$$

$$\sum_i p_i \sum_i p_i \frac{y_i}{x_i} < \sum_i p_i \frac{1}{x_i} \sum_i p_i y_i, \tag{21.7}$$

Then the function F has a global minimum $(a^\star, b^\star)$ with $a^\star > 0$, $b^\star > 0$.

Theorem 2: If the data satisfy the inequalities

$$\sum_i p_i x_i^2 \sum_i p_i x_i y_i^2 < \sum_i p_i x_i y_i \sum_i p_i x_i^2 y_i \tag{21.8}$$

and

$$\sum_i p_i x_i y_i \sum_i p_i x_i y_i^2 < \sum_i p_i x_i^2 y_i \sum_i p_i y_i^2 \tag{21.9}$$

then the solution $(a^\sharp, b^\sharp)$ of the least squares problem (21.2) is unique and positive.

See also the Linweaver-Burke approach to the problem.

22 Ecology

Most ecological models are systems of ordinary differential equations $\dot{u} = f(u)$ where u is a vector of species densities u_i. The right hand side f contains typically mass action terms and saturation terms and thus is made up from rational functions. In most cases the system is written in such a way that preservation of positivity is obvious,

$$\dot{u} = Uf(u), \quad U = (u_i \delta_{ij}),$$

but global existence or boundedness may present real problems in some cases.

A very special class of models are Lotka-Volterra equations

$$\dot{u} = U(Au - b) \quad \text{or} \quad \dot{u} = UAu - Bu, \quad B + (b_i \delta_{ij}) \tag{22.1}$$

where the growth rate is a linear function of the densities. Of course the Verhulst equation

$$\dot{u} = au(1 - \frac{u}{K})$$

fits into this class but also the simplest predator prey model

$$\begin{aligned} \dot{u}_1 &= au_1(1 - \frac{u_1}{K}) - bu_1u_2 \\ \dot{u}_2 &= cu_1u_2 - du_2 \end{aligned} \tag{22.2}$$

and the competition model (see below).

Another class of models are based on a game theoretic approach. If n types or policies play against each other and payoff for i in an encounter with j is a_{ij}, and if payoff is converted into offspring then one arrives at the equation

$$\dot{u} = UAu - u^T Au\, u. \tag{22.3}$$

Mathematically, the Lotka-Volterra systems for n species and game dynamics equations for $n + 1$ species are essentially equivalent. If the matrix A is symmetric, then the equation becomes Fisher's equation from population genetics for n alleles at an autosomal locus, and the quantity

$$V(u) = u^T Au$$

(the mean fitness) becomes a Lyapunov function (non-decreasing).

Lotka-Volterra equations have a number of strange properties. For example, if $\det A \neq 0$, there can be at most one stationary point in the interior

of $\mathbb{R}^n_+$. In general, these equations are poorly understood in dimensions greater than 2.

As an example of an ecological model which is not Lotka-Volterra consider the well-known MacArthur-Rosenzweig system

$$\begin{aligned} \dot{u} &= au(1-\frac{u}{K}) - \frac{buv}{1+mu} \\ \dot{v} &= c\left(\frac{u}{1+mu} - \frac{B}{1+mB}\right)v. \end{aligned} \tag{22.4}$$

If $0 < B < K$ then there is a coexistence point. This point is locally asymptotically stable if

$$\frac{1}{2}(K - \frac{1}{m}) < B < K$$

and unstable otherwise. If

$$0 < B < \frac{1}{2}(K - \frac{1}{m})$$

then the coexistence point is unstable and there is a unique limit cycle. Thus, if B is decreased from K through the critical value, then the system undergoes a Hopf bifurcation. This bifurcation is always forward, and the resulting limit cycle is locally stable.

By contrast, look at the FitzHugh-Nagumo system from neurobiology

$$\begin{aligned} \dot{u} &= u(1-u)(u-\alpha) + I \\ \dot{v} &= u - \nu v \end{aligned} \tag{22.5}$$

with $\delta, \nu > 0$ and $0 < \alpha < 1$. If I is running from $-\infty$ to $+\infty$ then there are two Hopf bifurcations. These two bifurcations are always in the same direction (as a result of the symmetry of the cubic). They may be forward or backward depending on the parameters.

Now we try a quick proof for a compact global attractor for the MacArthur-Rosenzweig model. We look at non-negative solutions. We find immediately

$$\dot{u} \leq au, \quad \dot{v} \leq \frac{c}{m}v$$

which gives at most exponential growth and hence global existence.

Next observe that we have (check this !!)

$$au(1-\frac{u}{K}) \leq aK - au$$

and hence

$$\begin{aligned}(u+\frac{b}{c}v)^{\cdot} &= au(1-\frac{u}{K})-\frac{bB}{1+mB}v\\ &\leq aK-au-\frac{cB}{1+mB}(\frac{b}{c}v)\\ &\leq aK-\delta(u+\frac{b}{c}v)\end{aligned}$$

with

$$\delta=\min(a,\frac{cB}{1+mB}).$$

Hence for every $\epsilon>0$ and every trajectory there is a $\bar{t}$ such that

$$(u+\frac{b}{c}v)(t)\leq\frac{aK}{\delta}+\epsilon$$

for $t\geq\bar{t}$.

The particular difficulty of this model lies in the fact that v is a factor in the right hand side of the second equation. Hence it does not help to get an upper bound on ( ) in the second equation because such bound is necessarily positive.

Of course, the expression $u+(b/c)v$ can be seen as a kind of Lyapunov function.

In general it can be said that there is no coherent mathematical theory for predator-prey models, food chains, food webs. Many examples have been treated separately. Of course, in many cases, one can use a graph argument (who feeds on whom) and get successive estimates first on the primary species and finally to the top predators. But already the example above shows that a bound on u (for example K) would not be sufficient to get v bounded.

The situation is different for cooperative and competitive models.

23 Epidemic spread

The simplest model of Kermack-McKendrick type for a constant population is

$$\begin{aligned}\dot{S} &= -\beta SI\\ \dot{I} &= \beta SI-\alpha I\\ \dot{R} &= \alpha I.\end{aligned}\tag{23.1}$$

The population size $P = S + I + R$ will be normalized to $P = 1$. We are interested in the trajectory starting at $(S, I, R) = (1-, 0+, 0)$. If the basic reproduction number

$$R_0 = \frac{\beta}{\alpha} \tag{23.2}$$

satisfies $R_0 > 1$ then this trajectory exists, along the trajectory $S(t)$ decreases and $I(t)$ first increases, then decreases, and $R(t)$ increases all the time. There is a positive number S_∞ of remaining susceptible.

We call the function βSI the incidence and the function I the prevalence of the disease. The number

$$\int_{-\infty}^{\infty} \beta SI dt = 1 - S_\infty$$

is the total size of the epidemic, and the number

$$\int_{-\infty}^{\infty} I dt$$

is the total cost (total number of sick days).

The nonlinearity βSI is called mass action incidence law. It makes sense only for a constant population. Otherwise we should use what is today called "standard incidence law",

$$\begin{aligned} \dot{S} &= -\frac{\beta}{P} SI \\ \dot{I} &= \frac{\beta}{P} SI - \alpha I \\ \dot{R} &= \alpha I. \end{aligned} \tag{23.3}$$

If we include demography into this model, with birth rate b and death rate μ, and differential mortality (disease related mortality) then the model assumes the form

$$\begin{aligned} \dot{S} &= bP - \mu S - \frac{\beta}{P} SI \\ \dot{I} &= \frac{\beta}{P} SI - \alpha I - \mu I - \delta I \\ \dot{R} &= \alpha I - \mu R. \end{aligned} \tag{23.4}$$

This is a homogeneous system of differential equations. In order to compute the basic reproduction number correctly, one must take into the washout rate due to net population change,

$$R_0^{\text{homog}} = \frac{\beta}{\alpha + \mu + \delta + (b - \mu)} \tag{23.5}$$

We see that the basic reproduction number *decreases* with increasing differential mortality. This observation is in agreement with the statement that "a well-adapted parasite does not kill its host".

The concept of differential mortality is fine for diseases where infected live and are active for an extended period. But there are other diseases where infected are infectious for a short period, then go to hospital and either recover or die. For such diseases one introduces, following Daniel Bernoulli, the concept of case fatality c which is the probability to die after getting infected.

The corresponding model reads

$$\begin{aligned} \dot{S} &= bP - \mu S - \frac{\beta}{P} SI \\ \dot{I} &= \frac{\beta}{P} SI - \mu I - \gamma I \\ \dot{R} &= \gamma(1-c)I - \mu R. \end{aligned} \tag{23.6}$$

We underline that δ is a rate and c is a probability. Hence $\delta \in (0, \infty)$ and $c \in [0, 1]$.

For the case fatality model the basic reproduction number is

$$R_0^{\text{homog}} = \frac{\beta}{\mu + \gamma + (b - \mu)}. \tag{23.7}$$

Notice that this expression is *independent* of c.

The Kermack-McKendrick model is structurally unstable (every model with a continuum of stationary points is) and hence small changes in the vector field may produce dramatic changes in the dynamics.

First look at the situation of a small reservoir (like a disease reservoir in domestic animals). We model this source of infection by a (small in comparison to β) number κ and get the model

$$\begin{aligned} \dot{S} &= -\beta SI - \kappa S \\ \dot{I} &= \beta SI + \kappa S - \alpha I \\ \dot{R} &= \alpha I. \end{aligned} \tag{23.8}$$

We look at the simplified system

$$\begin{aligned} \dot{S} &= -\beta SI - \kappa S \\ \dot{I} &= \beta SI + \kappa S - \alpha I. \end{aligned} \tag{23.9}$$

Now $(S, I) = (0, 0)$ is the only stationary point. The trajectory of interest passes through $(1, 0)$ with positive speed since $(1, 0)$ is not a stationary point.

Along the trajectory S is decreasing to 0, and I is first increasing and then also decreases to 0. It seems that the basic reproduction number has no meaning in this model.

A small rate of loss of immunity also changes the model, but in a quite different manner,

$$\begin{aligned} \dot{S} &= -\beta SI + \sigma R \\ \dot{I} &= \beta SI - \alpha I \\ \dot{R} &= \alpha I - \sigma R. \end{aligned} \tag{23.10}$$

The essential part of this model can also be written

$$\begin{aligned} \dot{S} &= -\beta SI + \sigma(1 - S - I) \\ \dot{I} &= \beta SI - \alpha I. \end{aligned} \tag{23.11}$$

There is another stationary point which is near $(0, 0)$ if σ is small. This point is feasible if $R_0 > 1$. The trajectory of interest first follows the same path as with $\sigma = 0$ but near $(S, I) = (S_\infty, 0)$ it makes a sharp bend and returns to the new stationary point. Some mathematicians call this phenomenon a "duck bifurcation".

Spread in space has been modeled in essentially two very different ways.

I) Contact distribution.

$$\begin{aligned} S_t &= -\beta S\bar{I} \\ I_t &= \beta S\bar{I} - \alpha I \\ R_t &= \alpha I \end{aligned} \tag{23.12}$$

with

$$\bar{I}(x) = \int_{-\infty}^{\infty} k(x - y)I(y)dy$$

The kernel k is non-negative and normalized by $\int k(z)dz = 1$. The kernel is called the contact distribution.

With a diffusion approximation we arrive at the equation

$$\begin{aligned} S_t &= -\beta S(I + \sigma I_{xx}) \\ I_t &= \beta S(I + \sigma I_{xx}) - \alpha I \\ R_t &= \alpha I. \end{aligned} \tag{23.13}$$

Models of such type have first been studied by David Kendall.

II) Migration model

$$\begin{aligned} S_t &= -\beta SI + d_S(\int k_S S dy - S) \\ I_t &= \beta SI - \alpha I + d_I(\int k_I I dy - I) \\ R_t &= \alpha I + d_R(\int k_R R dy - R). \end{aligned} \tag{23.14}$$

Again by diffusion approximation we get

$$\begin{aligned} S_t &= -\beta SI + D_S S_{xx} \\ I_t &= \beta SI - \alpha I + D_I I_{xx} \\ R_t &= \alpha I + D_R R_{xx} \end{aligned} \tag{23.15}$$

In order to compare the two approaches we consider the SIS case for both models.

The contact model becomes

$$\begin{aligned} S_t &= -\beta S(I + \sigma I_{xx}) + \alpha I \\ I_t &= \beta S(I + \sigma I_{xx}) - \alpha I \end{aligned} \tag{23.16}$$

and thus

$$I_t = \beta(1 - I)(I + \sigma I_{xx}) - \alpha I \tag{23.17}$$

The diffusion model becomes

$$\begin{aligned} S_t &= -\beta SI + \alpha I + DS_{xx} \\ I_t &= \beta SI - \alpha I + DS_{xx} \end{aligned} \tag{23.18}$$

and thus

$$I_t = \beta(1 - I)I - \alpha I + DI_{xx} \tag{23.19}$$

Notice that this equation is essentially the Verhulst equation with diffusion.

We get the wave speed simply by linearizing at the leading edge (this argument can be made rigorous).
$c_0 = 2\sqrt{(\beta - \alpha)\beta\sigma}$ for the contact model.
$c_0 = 2\sqrt{(\beta - \alpha)D}$ for the diffusion model.

The contact model and the diffusion model describe different scenarios. In the contact model each individual "sits" at some location and meets

other people at other locations with probability of contact decreasing with distance. The diffusion model is based on the idea that people move around and get into contact with other people. Of course this model does not imply that every person has home base to which he/she will eventually return.

The question is whether these are just two similar but different models or whether there is some connection. One connection can be made by designing a larger model for two types of stochastically moving people, those which move in their neighborhood and those who travel far. Then the two models before can be obtained as limiting cases.

24 Coupled phases

On all levels of biological organization we find quiescent phases although these may occur with different names. Genes may be suppressed, tumor cells quiescent, nerve cells at rest, animals hibernating or just inactive. Although these phenomena are quite diverse and can in no way cast into the same modeling framework, there are some common general features. There is an active phase and a quiescent phase and there is are transition laws which govern the exit to the quiescent phase and reentrance into the active phase.

It is useful to look at the general problem of coupling two phases. We shall explain in terms of a population of particles. We assume that the phases are described by two state vectors $v, w \in \mathbb{R}^n$ and that the actions during these phases are described by two ordinary differential equations

$$\begin{aligned} \dot{v} &= f(v) \\ \dot{w} &= g(w). \end{aligned} \tag{24.1}$$

By seasonal switching we understand a process where the total population switches between the dynamics f and g. Fix a step-size $h = 1$, choose $h_1, h_2 > 0$ with $h_1 + h_2 = 1$, and assume that f and g act in an alternating fashion. Then we get a non-autonomous system

$$\dot{u} = \chi(t)f(u) + (1 - \chi(t))g(u) \tag{24.2}$$

where $\chi(t)$ is periodic with period h and is given by

$$\chi(t) = \begin{cases} 1 & \text{if } N < t < N + h_1 \\ 0 & \text{if } N + h_1 < t < N + 1 \end{cases}$$

with N integer.

This strict on-off regime can be generalized to include sinusoidal switching and general oscillator switching by choosing χ as an arbitrary 1-periodic function with $\chi(t) \in [0,1]$.

Then we can choose a parameter $\delta > 0$ and change the period by considering the equation

$$\dot{u}_\delta = \chi(\frac{t}{\delta}) f(u_\delta) + (1 - \chi(\frac{t}{\delta})) g(u_\delta) \tag{24.3}$$

For $\delta \to 0$ we get the limiting equation

$$\dot{u} = \rho f(u) + (1-\rho) g(u) \tag{24.4}$$

where

$$\rho = \int_0^1 \chi(t) dt \tag{24.5}$$

If we fix an initial data $u_\delta(0) = \tilde{u}$ then we have uniform convergence on compact time intervals.

Having a quiescent phase, $g \equiv 0$, amounts to a scaling of time.

Now assume a situation where individual particles switch between phases according to Poisson processes with certain rates. Then we have a system

$$\begin{aligned} \dot{v} &= f(v) - pv + qw \\ \dot{w} &= g(w) + pv - qw \end{aligned} \tag{24.6}$$

with positive p, q. Then $u = v + w$ is the vector of total particle populations and the flows $z = pv - qw$. These satisfy the equations

$$\begin{aligned} \dot{u} &= f(\rho u + \tau z) + g((1-\rho)u - \tau z) \\ \tau \dot{z} &= \rho_2 f(\rho u + \tau z) - \rho g((1-\rho)u - \tau z) - z \end{aligned} \tag{24.7}$$

where

$$\rho = \frac{q}{p+q}, \quad \tau = \frac{1}{p+q}.$$

For $\tau \to 0$ we find the limiting equation

$$\dot{u} = f(\rho u) + g((1-\rho)u). \tag{24.8}$$

Notice that this time the factors are within the arguments of f, g.

If the different species have different rates then the system becomes

$$\begin{aligned} \dot{v} &= f(v) - Pv + Qw \\ \dot{w} &= g(w) + Pv - Qw \end{aligned} \tag{24.9}$$

with positive diagonal matrices P, Q.

25 Quiescent phases

Now we look at the special case of a quiescent phase. Then we compare the differential equation

$$\dot{u} = f(u) \tag{25.1}$$

to the system

$$\begin{aligned} \dot{v} &= f(v) - Pv + Qw \\ \dot{w} &= Pv - Qw \end{aligned} \tag{25.2}$$

This system in $\mathbb{R}^{2n}$ can be carried into a second order system in $\mathbb{R}^n$ in the following way: differentiate the first equation by t, add the two equations and multiply by Q. Then add. This gives

$$\begin{aligned} \ddot{v} - f'(v)\dot{v} + P\dot{v} &= Q\dot{w} \\ Q\dot{v} + Q\dot{w} &= Qf(v) \end{aligned}$$

and then

$$\ddot{v} - f'(v)\dot{v} + (P+Q)\dot{v} = Qf(v) \tag{25.3}$$

or

$$(P+Q)^{-1}(\ddot{v} - f'(v))\dot{v} + \dot{v} = (P+Q)^{-1}Qf(v) \tag{25.4}$$

This is the desired second order system. Now we let P, Q go to infinity, i.e., we look at this system as a singular perturbation problem by replacing P by P/ϵ and Q by Q/ϵ.

$$\frac{1}{\epsilon}(P+Q)^{-1}(\ddot{v} - f'(v))\dot{v} + \dot{v} = (P+Q)^{-1}Qf(v) \tag{25.5}$$

For $\epsilon \to 0$ we get the limiting equation

$$\dot{v} = (P+Q)^{-1}Qf(v). \tag{25.6}$$

Notice that the factor is a diagonal matrix with elements $q_i/(q_i + p_i)$.

25.1 Stationary points

From a biological point of view we want to know how the dynamics of a system is changed by introducing a quiescent phase. Suppose we have some insight into the dynamics of the system (25.1). These questions are also interesting from a mathematical point of view but some of them are surprisingly difficult. On the other hand we have some detailed results on

stationary points and some preliminary view on how periodic orbits are affected.

Suppose $\bar{u}$ is a stationary point of the system (25.1), i.e., $f(\bar{u}) = 0$. Then

$$(\bar{v}, \bar{w}) = (\bar{u},\, Q^{-1}P\bar{u}) \tag{25.7}$$

is a stationary point of (24.9).

Let $A = f'(\bar{u})$ be the Jacobian matrix of (25.1) at the stationary point. Then the Jacobian matrix of (24.9) is given by

$$B = \begin{pmatrix} A - P & Q \\ P & -Q \end{pmatrix}. \tag{25.8}$$

The eigenvalue problem of the matrix B is equivalent to that of the matrix pencil

$$\lambda^2 I + \lambda(P + Q - A) - AQ. \tag{25.9}$$

25.2 Equal rates

In the case equal rates we have $P = pI$, $Q = qI$. One can use the spectral mapping theorem. If μ is an eigenvalue of the matrix A then there are two eigenvalues λ_1 and λ_2, ordered by $\operatorname{Re}\lambda_2 \leq \operatorname{Re}\lambda_1$ which can be obtained from the equation

$$\lambda^2 + \lambda(p + q - \mu) - \mu q = 0. \tag{25.10}$$

This is a very simple quadratic equation. In principle the two solutions can be represented by an explicit formula. The problem is that μ is a complex number. The following can be shown. Always $\operatorname{Re}\lambda_2 < 0$. Hence λ_2 does not affect stability. Stability is governed by the eigenvalue λ_1.

Now there are three quite distinct cases.
If $\mu = 0$ then $\lambda_1 = 0$.
If μ is real then λ_1 is located between μ and 0. Hence, with respect to real eigenvalues, quiescence does not change stability.
If μ is complex (with non-vanishing imaginary part) then, generally speaking, for eigenvalues with positive real parts the real parts are decreased by introducing quiescence and may eventually become negative. This effect is most prominent for eigenvalues with large imaginary parts, i.e., high frequency oscillations are damped.

25.3 Periodic orbits

Numerical simulation of standard biological systems like the MacArthur-Rosenzweig model (Holling type II predator response) but also analytic results on highly symmetric systems show limit cycles of the system (25.1)

undergo some systematic changes if quiescent phases are introduced. From the local stability analysis at a stationary point it is evident that introducing a quiescent phase works against Hopf bifurcations. Suppose we have a system depending on some parameter α which undergoes a Hopf bifurcation. A stationary state is stable for $\alpha < 0$ and unstable for $\alpha > 0$ in such a way that a pair of eigenvalues crosses the imaginary axis at $\alpha = 0$. The stability suggest that by introducing a quiescent phase the Hopf bifurcation is shifted to some parameter value $\alpha > 0$. This is what indeed happens in concrete examples.

But such examples give even more insight. If, like in the MacArthur Rosenzweig model, we have a limit cycle in two dimensions then in the extended system we have either no limit cycle at all or again a limit cycle, this time in dimension four.

In numerical experiments, this four-dimensional limit cycle can be visualized in several ways. One way is to present the total population sizes for Prey and predator. This projection onto a two-dimensional plane provides at every moment the total population. But in this projection the effect of a quiescent phase is not easily recognized because the position of the (projection of) the stationary point is shifted. It is easier to project to the v-plane and also to the w-plane. Then one sees that the "size" of the projected limit cycle in the v-plane is smaller than the limit cycle in the system without quiescence and gets ever smaller if the rates are increased. Eventually the limit cycle may contact to the stationary point.

Here "size" is used as a phenomenological description. For the typical egg-shaped limit cycles of predator prey models area and circumference and diameter all shrink. It is interesting to observe that at the same time the projection onto the w-plane gets larger.

26 Rates depending on density

Some bacteria go quiescent (become spores) if conditions are unfavorable. Let v, w denote active and quiescent bacteria and s a substrate. Assume that the rate of going quiescent is increasing with decreasing substrate concentration. Assume further that substrate uptake is fast in comparison to reproduction and making spores. Then we have a system

$$\begin{aligned} \dot{v} &= F(s,v) - P(s)v + qw - \mu v \\ \epsilon\dot{s} &= -sv + r \\ \dot{w} &= P(s)v - qw \end{aligned} \tag{26.1}$$

Consider the limiting case $\epsilon \to 0$. Then $s = r/v$. Then define

$$p(v) = P(\frac{r}{v})v, \quad f(v) = F(r/v, v) - \mu v$$

Hence we arrive at the system

$$\begin{aligned} \dot{v} &= f(v) - p(v) + qw - \mu v \\ \dot{w} &= p(v) - qw \end{aligned} \tag{26.2}$$

Apply the trick

$$\begin{aligned} \ddot{v} &= f'(v)\dot{v} - (p(v))^{\cdot} + q\dot{w} \\ q\dot{v} + q\dot{w} &= qf(w) \end{aligned}$$

and get

$$\frac{\ddot{v} - f'(v)\dot{v}}{q + p'(v)} + \dot{v} = \frac{q}{q + p'(v)} f(v) \tag{26.3}$$

So in the limit we get, if $p'(v) > 0$,

$$\dot{v} = \frac{q}{q + p'(v)} f(v) \tag{26.4}$$

Stationary points are "the same". How is stability affected? If $\bar{v}$ is a stationary value, $f(\bar{v}) = 0$, then the derivative is

$$q \frac{f'(\bar{v})}{q + p(v)}$$

Hence the sign does not change but the absolute value gets smaller.

27 Example: Paradox of enrichment

The system with quiescent phases reads

$$\begin{aligned} \dot{u} &= au(1 - \frac{u}{K}) - b\frac{uv}{1 + mu} - p_1 u + q_1 w \\ \dot{v} &= c\left(\frac{u}{1 + mu} - \frac{B}{1 + mB}\right) v - p_2 v + q_2 z \\ \dot{w} &= p_1 u - q_1 w \\ \dot{z} &= p_2 v - q_2 z \end{aligned} \tag{27.1}$$

It can be shown (Lydia Bilinsky and KPH) that the introduction of quiescence enlarges the stability domain. Whereas for the system with quiescence stability is determined by $\delta = \det > 0$ and $\tau = \mathrm{tr} < 0$ for the extended system the stability boundary is shifted, for given δ, to positive values of τ.

28 Spread in space

Think of a particle that moves in space according to Brownian motion and with exponential holding time and then stops and stays on the spot again with exponential holding time. The probability density for such a particle is governed by the degenerate parabolic system

$$\begin{aligned} v_t &= \Delta v - pv + qw \\ w_t &= pv - qw \end{aligned} \tag{28.1}$$

Here we use the same idea as in (ref). Differentiate the first equation with respect to t. Add both equations and multiply by q.

$$\begin{aligned} v_{tt} - \Delta v_t + pv_t &= qw_t \\ qv_t + qw_t &= q\Delta u \end{aligned}$$

Add the latter two equations to get

$$v_{tt} - \Delta v_t + (p+q)v_t = q\Delta v = 0 \tag{28.2}$$

Define

$$\tau = \frac{1}{p+q}, \quad D = \frac{q}{p+q} \tag{28.3}$$

Finally we get the equation

$$\tau(v_{tt} - \Delta v_t) + v_t = D\Delta v \tag{28.4}$$

This equation is still parabolic although it *looks* like a wave equation. Indeed, in an engineering view of a vibrating membrane the term v_{tt} is an inertia term, the term v_t is proportional damping and $-\Delta v_t$ is a viscous damping term. Finally $D\Delta v$ is the membrane tension. We want to know how quiescence effects the decay to equilibrium. With this goal in mind we try separation of variables

$$v(t,x) = \phi(x)\psi(t)$$

and arrive at

$$\frac{\ddot{\psi}}{\psi} - \frac{\phi''}{\phi}\frac{\dot{\psi}}{\psi} + \frac{\dot{\psi}}{\psi} = D\frac{\phi''}{\phi}$$

Now the usual argument tells we should have

$$\dot{\phi}(x) = \mu\phi(x), \quad \ddot{\psi}(t) = \lambda\psi(t)$$

where μ and λ are coupled by

$$\tau(\lambda^2 - \mu\lambda) + \lambda = D\mu \tag{28.5}$$

This is essentially the equation (ref). So if we look at the equation in some finite interval $[0, l]$ and at a particular Fourier mode, say

$$\phi(x) = \cos\frac{k\pi x}{l}, \quad \mu = -\frac{k^2\pi^2}{l^2}$$

then we find that there are two real eigenvalues $\lambda_2 < \lambda_1$ and further, that $-\mu < \lambda_1 < 0$.

This result says that for the system with quiescence convergence to equilibrium is slower as compared to Brownian motion. If we think of periodic or no-flux boundary conditions then the essential quantity is the difference of the two decay rates

$$\mu = -\frac{\pi^2}{l^2} \quad \text{and} \quad \lambda = \frac{1}{2}(\mu - \frac{1}{\tau}) + \sqrt{(\mu - \frac{1}{\tau})^2 - \frac{4}{\tau}D\mu}$$

29 Spread and reaction

The standard model for spread and reaction is a reaction diffusion equation. For the present exposition we restrict to the scalar case

$$u_t = D\Delta u + f(u). \tag{29.1}$$

To this equation we can relate coupled systems and quiescent phases in several ways. We can assume that the dynamics of the reaction diffusion equation is coupled to a quiescent phase. Then we arrive at the system

$$\begin{aligned} v_t &= D\Delta v + f(v) - pv + qw \\ w_t &= pv - qw \end{aligned} \tag{29.2}$$

Or we can assume that population dynamics and spread occur in coupled compartments. Hence we can think of a population that is subject to standard population dynamics in a sedentary compartment and individuals make random excursions. In that case we can assume that migrating individuals are subject to some mortality. Then we get the system

$$\begin{aligned} v_t &= D\Delta v - dv - pv + qw \\ w_t &= f(w) + pv - qw \end{aligned} \tag{29.3}$$

30 Modeling locust swarms

Grunbaum, Keshet, Watmough 1998 have investigated whether locust swarms can be model by a variety of systems the simplest of which has the general form

$$\begin{aligned} v_t &= Dv_{xx} - dv_x - g(v,w) \\ w_t &= g(v,w) \end{aligned} \tag{30.1}$$

We see that this system is a system with quiescent phase. The variable v describes swarming locusts and the variable w sedentary locusts. Motion is described by diffusion with rate D and convection driven by wind with rat d.

The question whether such system has stable traveling pulse solutions. A traveling wave ansatz leads to

$$\begin{aligned} -c\dot{v} &= D\ddot{v} - d\dot{v} - g(v,w) \\ -c\dot{w} &= g(v,w) \end{aligned} \tag{30.2}$$

We add the two equations and get

$$-c\dot{v} - c\dot{w} = D\ddot{v} - d\dot{v}$$

and integrate

$$-cv - cw = D\dot{v} - dv - \kappa$$

with an integration constant κ. So we have a two-dimensional system

$$\begin{aligned} \dot{v} &= \frac{1}{D}(-cv - cw + dv + \kappa) \\ \dot{w} &= -\frac{1}{c}g(v,w) \end{aligned} \tag{30.3}$$

Interesting "objects" are stationary points, periodic orbits, heteroclinic orbits, homoclinic orbits. Homoclinic orbits correspond to pulse solutions of the desired types. Of course for special choices of the parameter functions such solutions exist. Perhaps their stability can be investigated by using the methods of John Evans' work on nerve pulses.

31 Age structure

We consider the following system of Gurtin-MacCamy type

$$\frac{\partial u(t,a)}{\partial t} + \frac{\partial u(t,a)}{\partial a} + \mu(a, W(t))u(t,a) = 0$$

$$
\begin{aligned}
u(t,0) &= \int_0^\infty b(a,W(t))u(t,a)da \\
W(t) &= \int_0^\infty \rho(a)u(t,a)da
\end{aligned} \tag{31.1}
$$

where W is the weighted population size.

We assume that the coefficients are piece-wise constant functions of a. We even allow that some of these functions have delta peaks. In general it does make sense to study a hyperbolic system with delta peaks in the coefficients but in the case of the Gurtin-MacCamy system these coefficients can be justified if the system is reformulated in terms of renewal equations. We assume a single jump or peak at the age $a = \tau$ where τ can be seen as the length of the maturation period. Hence the coefficients are

$$
\begin{aligned}
\mu(a) &= \mu_0(W) + (\mu_1(W) - \mu_0(W))H_\tau(a) \\
b(a) &= b_1(W)H_\tau(a) + b_2(W)\delta_\tau(a) \\
\rho(a) &= \begin{cases} \alpha & a < \tau \\ \beta & a \geq \tau \end{cases}
\end{aligned} \tag{31.2}
$$

where $\delta_\tau(a)$ is the delta peak at $a = \tau$ and $H_\tau(a)$ is the Heaviside function, $H_\tau(a) = 0$ for $a < \tau$ and $H_\tau(a) = 1$ for $a \geq \tau$. Hence the mortality jumps from μ_0 to μ_1; the fertility jumps from 0 to b_1 with a delta peak at $a = \tau$.

Now introduce the variables

$$
V(t) = \int_0^\tau u(t,a)da, \quad U(t) = \int_\tau^\infty u(t,a)da \tag{31.3}
$$

which represent the total juvenile population and the total adult population.

Suppose $u(t,a)$ is a solution of the system (31.1) with coefficients (31.2). For $0 < t < \tau$ the variables V and U satisfy a *non-autonomous system of ordinary differential equations* whereby the coefficients depend on the history, i.e., on the values of the initial data $u(0,a) = u_0(a)$ in the interval $0 \leq a \leq \tau$. For $t > \tau$ the variables U and V satisfy an *autonomous system of neutral delay differential equations*

$$
\begin{aligned}
\dot{V}(t) &= b_1(W(t))U(t) - \mu_0(W(t))V(t) \\
&\quad +(b_2(W(t)) - 1)[b_1(W(t))U(t) \\
&\quad +b_2(W(t))\{\dot{U}(t-\tau) + \mu_1(W(t-\tau))U(t-\tau)\}] \\
&\quad \times \exp\{-\int_0^\tau \mu_0(W(t-\tau+\sigma))d\sigma\} \\
\dot{U}(t) &= [b_1(W(t-\tau))U(t-\tau)
\end{aligned}
$$

$$
\begin{aligned}
& +b_2(W(t-\tau))\{\dot{U}(t-\tau)+\mu_1(W(t-\tau))U(t-\tau)\}] \\
& \times \exp\{-\int_0^\tau \mu_0(W(t-\tau+\sigma))d\sigma\} - \mu_1(W(t))U(t) \\
W(t) &= \alpha V(t) + \beta U(t). \qquad (31.4)
\end{aligned}
$$

Here we neglect the initial phase. We assume that the population has evolved at least for a time interval of length τ such that (31.4) applies.

Suppose that W depends only on the adult population, i.e., $\alpha = 0$, $\beta = 1$. Then the system (31.4) decomposes and the equation for U does not depend on V. We get a scalar neutral differential delay equation

$$
\begin{aligned}
\dot{U}(t) &= [b_1(U(t-\tau))U(t-\tau) \\
& +b_2(U(t-\tau))\{\dot{U}(t-\tau)+\mu_1(U(t-\tau))U(t-\tau)\}] \\
& \times \exp\{-\int_0^\tau \mu_0(U(t-\tau+\sigma))d\sigma\} - \mu_1(U(t))U(t) \qquad (31.5)
\end{aligned}
$$

with a point delay and a (nonlinear) distributed delay. The distributed delay describes the effect of the size of the adult population on juvenile mortality. Of course cannibalism is known in some fish and reptile species but for most invertebrate and even vertebrate species such effect does not exist. The system becomes much simpler if μ_0 is a constant.

32 The blowfly equation

Assume that μ_0 is a constant and that $b_2 \equiv 0$. Then the equation (31.5) reduces to

$$
\dot{u}(t) = b_1(u(t-\tau))u(t-\tau)e^{-\mu_0\tau} - \mu_1(u(t))u(t). \qquad (32.1)
$$

This is the blowfly equation with $b(u) = b_1(u)e^{-\mu_0\tau}$ and $\mu(u) = \mu_1(u)$. This formula has a very natural interpretation. Adults produce offspring with a birth rate b_1 but this offspring enters the adult population only after time τ and with a discount factor $e^{-\mu_0\tau}$ which accounts for juvenile mortality.

Hence we can state: The blowfly equation is the reduction of the Gurtin-MacCamy system for the special case where the juvenile mortality is a constant and the adult mortality and the adult fertility depend only on the adult population density.

33 Neutral delay equations

Now consider the equation (31.5) with constant μ_0 and general b_2. We get a neutral delay differential equation

$$\begin{aligned}\dot{U}(t) &= [b_1(U(t-\tau))U(t-\tau) \\ &\quad +b_2(U(t-\tau))\{\dot{U}(t-\tau)+\mu_1(U(t-\tau))U(t-\tau)\}]e^{-\mu_0\tau} \\ &\quad -\mu_1(U(t))U(t). \end{aligned} \tag{33.1}$$

So far our approach has shown three things: There is a large class of neutral delay equations which can be seen as population models. This class does not contain some equations which have been previously seen as population delay equations. This class is still special within the set of all nonlinear neutral delay equations.

Now consider a particular solution of (33.1) and define

$$Z(t) = \dot{U}(t) + \mu_1(U(t))U(t). \tag{33.2}$$

With the variable Z we can rewrite the neutral equation as a system

$$\begin{aligned}\dot{U}(t) &= Z(t) - \mu_1(U(t))U(t) \\ Z(t) &= [b_1(U(t-\tau))U(t-\tau) + b_2(U(t-\tau))Z(t-\tau)]e^{-\mu_0\tau}. \end{aligned} \tag{33.3}$$

The variable Z can be interpreted as the number of entries per time into the adult class. Hence the first equation of (33.3), which is an ordinary differential equation, says that surviving juveniles enter the adult class and then die with death rate $\mu_1(U)$. The second equation is essentially a shift map which yields new values for Z in terms of the history of U and Z. This system is perhaps the most transparent formulation of the neutral equation in biological terms and also well suited for numerical simulations.

34 Mentioned in passing:

Turing stability, in connection with reaction-diffusion and with quiescent phases.

Routh-Hurwitz criterion: An important tool for stability analysis!

Proteasome modeling: An example where differential equations and stochastic processes do not work. Try google "PAProC".

Exercise on boundary value problems for diffusion equation and damped wave equation.

Lamprey swimming as an example of a chain of coupled oscillators.

FitzHugh Nagumo system for space-clamp experiment (excitation), dendritic input (release of spikes), as a parabolic system (traveling spikes).

Recent invaders and non-invaders (Emerald ash-borer, Longhorn beetle, goutweed)

etc. etc.