Dynamical Systems in Biological Engineering: Slides for Chapter on Partial Equations

Eduardo D. Sontag

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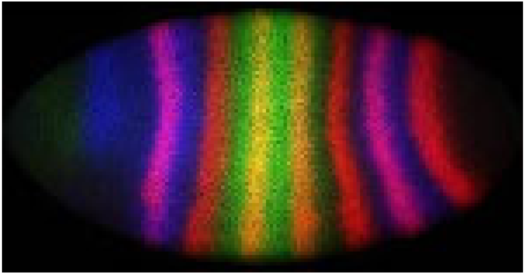
Contents

Space dependence

until now only functions of time (concentrations, populations)
from now on, consider functions that also depend on *space*

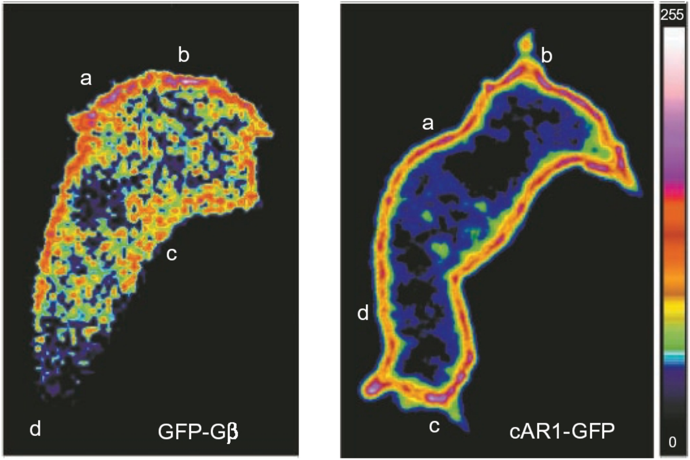
e.g. morphogen concentration as function of space and time



Drosophila embryo stained for protein products of
giant (blue), *eve* (red), and *Kruppel*
(other colors indicate areas where two or all genes are expressed)

Another example

or study space-dependence of a particular protein in a single cell gradients of two G-proteins in response to chemoattractant binding to receptors in surface of *Dictyostelium discoideum* amoebas



The key conservation equation

$x =$ space variable (here scalar for simplicity, but could be 2d, 3d)

$t =$ time variable

$c(x,t)$ *density* at time t, position x, so:

$\int_R c(x,t)\,dx =$ total amount of particle (or # individuals, mass of proteins of certain type, etc.) in region R of space

key formula:

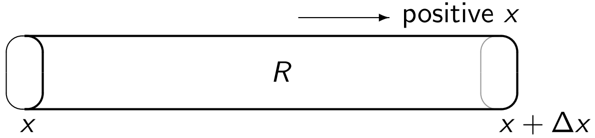
$$\boxed{\frac{\partial c}{\partial t} + \frac{\partial J}{\partial x} \;=\; \sigma}$$

$J(t,x) =$ *flux* at $x =$ # particles crossing ($\rightarrow$) per unit time

$\sigma(t,x) =$ rate of change of c due to *"local reactions"*

(among chemicals, individuals, bacteria, ... as ODE case if no J)

Follows from "conservation" or "balance" principle



- $J_{\text{in}} \;=\; \int_t^{t+\Delta t} J(x,\tau)\,d\tau$
- $J_{\text{out}} \;=\; \int_t^{t+\Delta t} J(x+\Delta x,\tau)\,d\tau$
- net formation (elimination): $\Sigma \;=\; \int_t^{t+\Delta t}\int_x^{x+\Delta x} \sigma(\xi,\tau)\,d\xi d\tau$
- starting amount: $C_t \;=\; \int_x^{x+\Delta x} c(\xi,t)\,d\xi$
- ending amount: $C_{t+\Delta t} \;=\; \int_x^{x+\Delta x} c(\xi,t+\Delta t)\,d\xi$

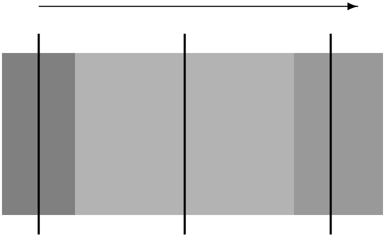
total change must balance: $C_{t+\Delta t} - C_t \;=\; \Delta C \;=\; J_{\text{in}} - J_{\text{out}} + \Sigma$

let $\Delta t \to 0$, $\Delta x \to 0$, use FTC $\rightsquigarrow \frac{\partial c}{\partial t} = -\,\frac{\partial J}{\partial x} + \sigma$

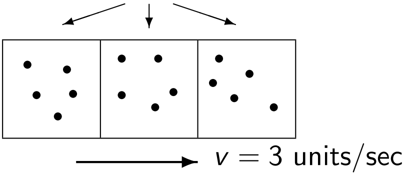
next: two special types of fluxes

Transport (convection, advection) equation

flux is due to transport: e.g. luggage transporting tape, wind carrying particles, water carrying dissolved substance, etc.



large flux small flux medium flux



imagine counter "clicks" when particle passes right endpoint

total flux in one second is $5 \times 3 = c\,v$

flux $J(x,t) \;=\; c(x,t)\,v(x,t)$: local concentration $\times$ velocity

Equation

$$\boxed{J(x,t) \;=\; c(x,t)\, v(x,t)}$$

since $\frac{\partial c}{\partial t} + \frac{\partial J}{\partial x} = \sigma$, we obtain the *transport equation*:

$$\boxed{\frac{\partial c}{\partial t} \;+\; \frac{\partial (cv)}{\partial x} \;=\; \sigma}$$

special case: constant velocity $v(x,t) \equiv v$:

$$\boxed{\frac{\partial c}{\partial t} \;+\; v\frac{\partial c}{\partial x} \;=\; \sigma}$$

more generally, in any dimension:

$$\boxed{\frac{\partial c}{\partial t} \;+\; \operatorname{div}(cv) \;=\; \sigma}$$

Soln for const velocity, exponential growth/decay

special case in which the reaction is linear: $\sigma = \lambda c$
decay or growth proportional to population (at given time & place)

$$\frac{\partial c}{\partial t} + v\frac{\partial c}{\partial x} \;=\; \lambda c$$

($\lambda > 0$ growth, $\lambda < 0$ decay)

Theorem: general solution is

$$c(x,t) \;=\; e^{\lambda t} f(x - vt)$$

for some (unspecified) differentiable single-variable function f

$c(x,0) = f(x)$ is "initial condition" in time, could use to find f

note these all satisfy PDE:

$$\Big[\lambda e^{\lambda t} f(x - vt) - v e^{\lambda t} f'(x - vt)\Big] + v e^{\lambda t} f'(x - vt) \;=\; \lambda\, e^{\lambda t} f(x - vt)$$

Showing is general solution

first special case $v = 0$:

for each fixed x*, we have an ODE*: $\frac{\partial c}{\partial t} = \lambda c$

which for each x has unique soln $c(x,t) = e^{\lambda t} c(x,0) = e^{\lambda t} f(x)$

key step: reduce the general case to this case:
given solution $c(x,t)$, introduce new variable $z = x - vt$
consider auxiliary function $\alpha(z,t) := c(z + vt, t)$
now use the PDE $v\frac{\partial c}{\partial x} = \lambda c - \frac{\partial c}{\partial t}$ to get:

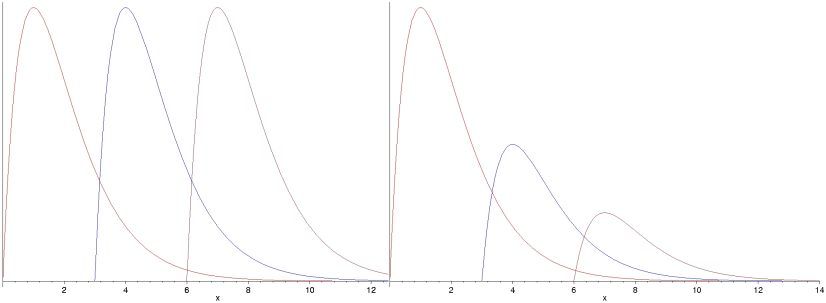
$$\frac{\partial \alpha}{\partial t}(z,t) = \left[\lambda c - \frac{\partial c}{\partial t}\right] + \frac{\partial c}{\partial t} = \lambda\, c(z + vt, t) = \lambda \alpha(z,t)\,.$$

so reduced to case $v = 0$ for α, so $\alpha(z,t) = e^{\lambda t}\alpha(z,0)$

$$\Rightarrow\ c(x,t) = \alpha(x - vt, t) = e^{\lambda t}\alpha(x - vt, 0) = e^{\lambda t} f(x - vt)$$

solutions *"travel"* [with decay or growth depending on sign λ]

E.g. ($v = 3$; $\lambda = 0$ and $\lambda < 0$ respectively; $t = 0, 1, 2$)



Example

A population, with density $c(x,t)$ (in one dimension), is being transported with velocity $v = 7$.

There is no additional growth or decay; just pure transport.

The initial density is $c(x,0) = \dfrac{1}{1+x^2}$.

Give a formula for $c(x,t)$.

Answer: in general, $c(x,t) = f(x - 7t)$,

and the initial condition says $f(x) = c(x,0) = \dfrac{1}{1+x^2}$

Therefore, $c(x,t) = f(x - 7t) = \dfrac{1}{1+(x-7t)^2}$.

Example

A population, with density $c(x,t)$ (in one dimension), is being transported with velocity $v=1$.

There is no additional growth or decay; just pure transport.

At time $t=1$, the density is $c(x,1)=x^2$.

Give a formula for $c(x,t)$.

Answer: in general, $c(x,t) = f(x-t)$;

we know $f(x-1) = c(x,1) = x^2$

which is the same as $f(u) = (u+1)^2$ (substitute $u = x-1$)

therefore, $c(x,t) = f(x-t) = (x+1-t)^2$

Example

A population, with density $c(x,t)$ (in one dimension), is being transported with velocity $v=3$,

at same time, the bacteria reproduce at a rate $2c$ ($\sigma = 2c$, $\lambda = 2$)

At time $t = 1$, the density is $c(x,1)=x^2$.

Give a formula for $c(x,t)$.

Answer: in general, $c(x,t) = e^{2t} f(x-3t)$;

we know $x^2 = c(x,1) = e^2 f(x-3) =$

which is the same as $f(u) = e^{-2}(u+3)^2$

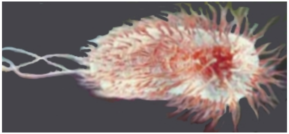
therefore,

$$c(x,t) \ = \ e^{2t-2}(x-3t+3)^2$$

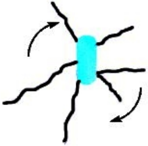
Chemotaxis

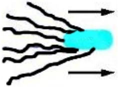
movement in response to chemoattractants/repellants
such as nutrients and poisons, respectively

best-studied example of chemotaxis involves *E. coli* bacteria
single-celled organisms, about 2 μm long, w/ flagella for movement



"tumble mode": flagella turn clockwise and reorientation occurs
"run": turn counterclockwise, form bundle that propels

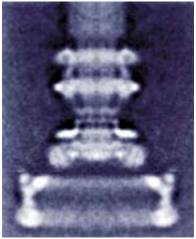


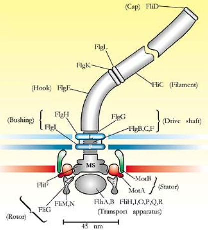


Chemotaxis, ctd

well-understood molecular mechanism senses *gradient* of nutrient
runs in increasing direction, tumbles every so often

runs are biased, drifting about 30 deg/s due to viscous drag and





Flux induced from external gradient

"potential" $V = V(x)$ quantifies concentration of chemical (or friends, or foes) at location x

want: model behavior in which population is toward V larger

assume that individuals move in the direction in which $V(x)$ increases the fastest when taking a small step
then (see next slide) velocity proportional to $\nabla V(x)$,

with factor $\chi(V(x))$ that may depend on $V(x)$

assume χ constant for simplicity, but often $\exists$ maximum speed, or high concentrations of $V(x)$ may be unfavorable

Problems:

1. give model so $\chi(V(x))$ is increasing in $V(x)$, but is bounded
2. give model so high concentrations of $V(x)$ are unfavorable

Recall from multivariate calculus

$V(x + \Delta x) - V(x)$ maximized in the direction of its gradient

proof: we need to find a direction, i.e., unit vector "u", so that $V(x + hu) - V(x)$ is maximized, for any small stepsize h

we take a linearization (Taylor expansion) for $h > 0$ small:

$$V(x + hu) - V(x) \;=\; [\nabla V(x) \cdot u]\, h \,+\, o(h)\,.$$

so formula for average change in V when taking a small step:

$$\frac{1}{h}\Delta V \;=\; \nabla V(x) \cdot u + O(h) \;\approx\; \nabla V(x) \cdot u$$

and thus max value when vector u is picked in direction of ∇V

so indeed the direction of movement given by gradient of V

Chemotaxis equation

as in general, flux $=$ density$\times$velocity, we conclude:

$$J(x,t) \;=\; \chi(V(x))\, c(x,t)\, \nabla V(x)$$

so, in case χ constant (only for simplicity):

$$\boxed{\frac{\partial c}{\partial t} = -\,\mathrm{div}\,(\chi\, c\, \nabla V)} \text{ or, equivalently: } \boxed{\frac{\partial c}{\partial t} \;+\; \mathrm{div}\,(\chi\, c\, \nabla V) = 0}$$

and in particular, in the special case of dimension one:

$$\boxed{\frac{\partial c}{\partial t} \;=\; -\;\frac{\partial\,(\chi\, c\, V')}{\partial x}} \quad \text{or, equivalently:} \quad \boxed{\frac{\partial c}{\partial t} \;+\; \frac{\partial\,(\chi\, c\, V')}{\partial x} \;=\; 0}$$

and therefore, using the product rule for x-derivatives:

$$\frac{\partial c}{\partial t} \;=\; -\chi \frac{\partial c}{\partial x} V' - \chi c V''$$

one can superimpose reactions and other effects; fluxes add up

Example

air flows (on a plane) Northward at 3 m/s, carrying bacteria.
there is a food source as well, placed at $x = 1, y = 0$,
which attracts according to the following potential:

$$V(x,y) = \frac{1}{(x-1)^2 + y^2 + 1}$$

(take $\alpha = 1$ and appropriate units)

$$\frac{\partial V}{\partial x} = -\frac{2\,x - 2}{((x-1)^2 + y^2 + 1)^2} \quad \text{and} \quad \frac{\partial V}{\partial y} = -2\,\frac{y}{((x-1)^2 + y^2 + 1)^2}\,.$$

the differential equation is, then:

$$\frac{\partial c}{\partial t} \;=\; -\mathrm{div}\,(c\nabla V) - \mathrm{div}\,(\begin{pmatrix} 0 \\ 3 \end{pmatrix} c) \;=\; -\frac{\partial (c\frac{\partial V}{\partial x})}{\partial x} - \frac{\partial (c\frac{\partial V}{\partial y})}{\partial y} - 3\frac{\partial c}{\partial y}$$

or, expanding:

$$\frac{\partial c}{\partial t} \;=\; \frac{\partial c}{\partial x}\,\frac{(2\,x-2)}{N^2} - 2\,c\,\frac{(2\,x-2)^2}{N^3} + 4\,\frac{c}{N^2} + 2\,\frac{\partial c}{\partial y}\,\frac{y}{N^2} - 8\,c\,\frac{y^2}{N^3} - 3\,\frac{\partial c}{\partial y}$$

where we wrote $N = (x-1)^2 + y^2 + 1$

Another flux example: Diffusion

diffusion is movement from higher to lower concentration regions:

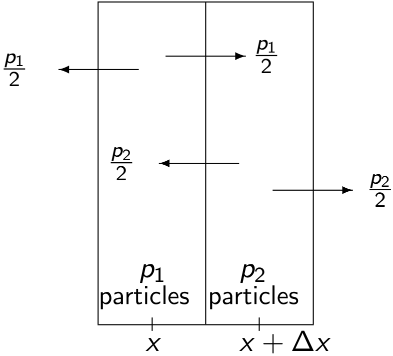
$$\boxed{J(x,t) \ \propto \ -D\, c_x(x,t)} \quad (D > 0 \text{ is "diffusion coefficient"})$$

(in 2 and 3d: $\propto -\nabla c(x,t)$; "Fick's Law")

movement of particles in solution ("thermal motion")

due to environment (e.g. molecules of solvent) "kicking" (Einstein)
(diffusion across membranes, random population movements, ...)

Intuition



in small Δt, particles jump right or left, equal probs

half of the p_1 particles in left half move right;
other half move left

similarly for p_2 in right
(assume jumps big enough, particles exit respective box)

net number of particles (counting rightward as positive) through segment proportional to $\frac{p_1}{2} - \frac{p_2}{2}$,

proportional roughly to $c(x,t) - c(x + \Delta x, t)$, and in turn to $-\frac{\partial c}{\partial x}$

[argument not really correct: what is velocity of particles?]

Diffusion (heat) equation

from $\dfrac{\partial c}{\partial t} + \dfrac{\partial J}{\partial x} \; = \; \sigma$ and $J(x,t) = -D\, c_x(x,t)$ get:

$$\boxed{\frac{\partial c}{\partial t} \; = \; D\,\frac{\partial^2 c}{\partial x^2} + \sigma}$$

("reaction-diffusion" equation, just diffusion if $\sigma = 0$)

in 2d and 3d, $J = -D\nabla c(x,t)$ and $\frac{\partial c}{\partial t} = -\mathrm{div}\, J \rightsquigarrow$

$$\frac{\partial c}{\partial t} \; = \; D\nabla^2 c$$

where $\nabla^2 = \frac{\partial^2 c}{\partial x_1^2} + \frac{\partial^2 c}{\partial x_2^2} + \frac{\partial^2 c}{\partial x_3^2}$ "Laplacian" (often "Δ")

[notation ∇^2: divergence can be thought of as "dot product by ∇"]
so "$\nabla \cdot (\nabla c)$" is written as $\nabla^2 c$]

Point source initial condition

if pure diffusion, and space is $\mathbb{R}$,

one has following "point-source" Gaussian formula:

$$p_0(x,t) = \frac{C}{\sqrt{4\pi Dt}} \exp\left(-\frac{x^2}{4Dt}\right)$$

is a solution in dimension 1

Problem: verify by substitution

(a similar formula holds in higher dimensions)

A simple reaction-diffusion equation

consider:

$$\frac{\partial c}{\partial t} \;=\; D\nabla^2 c + \alpha c$$

on the entire space (no boundary conditions)

population which is diffusing and also reproducing at some rate α

reaction is $dc/dt = \alpha c$, taking place in addition to diffusion

we may use an integrating factor trick in order to reduce it to a pure diffusion equation, entirely analogous to what is done for solving the transport equation with a similar added reaction

introduce the new dependent variable $p(x,t) := e^{-\alpha t} c(x,t)$

then (homework problem), p satisfies the pure diffusion equation:

$$\frac{\partial p}{\partial t} \;=\; D\nabla^2 p$$

A simple reaction-diffusion equation, ctd

as solution for p is Gaussian, conclude:

$$c(x,t) \;=\; \frac{C}{\sqrt{4\pi Dt}} \exp\left(\alpha t - \frac{x^2}{4Dt}\right)$$

equipopulation contours $c =$ constant have $x \approx \beta t$ for large t,
where β is some positive constant.
(homework problem)

noteworthy because, in contrast to the population dispersing a distance proportional to $\sqrt{t}$ (as with pure diffusion),
distance is, instead, proportional to t (which is $\gg \sqrt{t}$ for large t)

intuition: reproduction increases the gradient ("populated" area has even larger population) and hence flux

Spread under this model

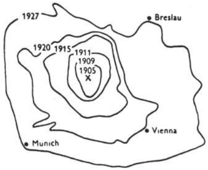
muskrats: large aquatic rodents originated in North America

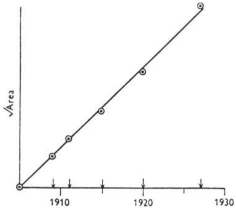
accidental escape near Prague, diffusion with exponential growth

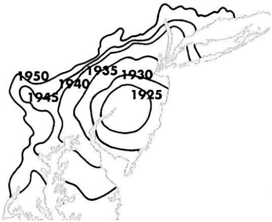
below: equipopulation contours, plot $\sqrt{}$(area of spread) vs time

($\sqrt{}$(area) would be $\propto$ dist, if circular equipopulation contours)

note: match to the prediction of a linear dependence on time







last figure is spread of Japanese beetles in Eastern US

Boundary Conditions

- fixed values at end points of finite domain $[0, L]$:

$$c(0, t) = c_0 \quad c(L, t) = c_L$$

- "no flux" at end points:

$$J(0, t) = J(L, t) = 0$$

which for diffusion is:

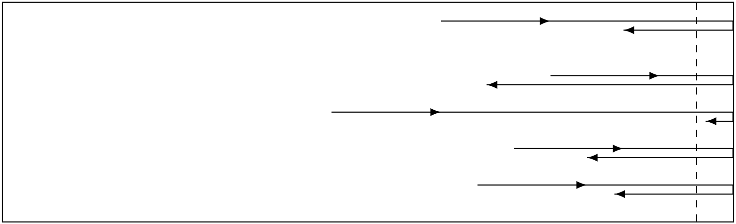
$$c_x(0, t) = c_x(L, t) = 0$$

or mixed, e.g. fixed value ("Dirichlet") at 0, no flux ("Neumann") at L

Intuition for no-flux

particles "bounce" at a "wall"

imagine a narrow strip (of width ε) about the wall
for $\varepsilon \ll 1$, most particles bounce back far into region, so the flux at $x = L - \varepsilon$ is ≈ 0.



Steady-state solutions of (reaction-)diffusion equations

(skipping sections on separation of variables and Gaussian solution)

at "steady state", $c_t = 0$ so get (Laplace equation if $\sigma = 0$):

$$\boxed{D\,\frac{\partial^2 c}{\partial x^2} + \sigma = 0}$$

subject to equality or no-flux boundary conditions

we now solve a few examples

in one space dimension, end up with 2nd order ODE on x for $c(x)$

(drop "t")

Fixed boundary values, pure diffusion

$$c(a,t) \equiv c_S \quad \boxed{\quad c_t = Dc_{xx} \quad} \quad c(L,t) \equiv c_0$$

$$x = a \qquad\qquad\qquad\qquad x = L$$

steady-state problem: find $c(x)$ s.e. satisfying the following ODE and boundary conditions:

$$Dc_{xx} \;=\; 0\,, \quad c(a) = c_S\,,\; c(L) = c_0$$

easy: $c(x)$ is linear, and fitting the boundary conditions gives the following unique solution:

$$c(x) \;=\; c_S \,+\, (c_0 - c_S)\,\frac{x-a}{L-a}$$

notice that then flux $= -Dc_x = -\dfrac{D}{L-a}(c_0 - c_S) = \dfrac{D}{L-a}(c_s - c_0)$

(side remark, not covered)

if $c_0 < c_S$, then $J > 0$
"Ohm's law for diffusion across a membrane"
when we think of R as a cell membrane:

$$c_S - c_0 = J \frac{L-a}{D}$$

entirely analogous to Ohm's law in electricity $V = IR$
interpret the potential difference V as the difference between inside and outside concentrations, the flux as current I, and the resistance of the circuit as the length divided by the diffusion coefficient
(faster diffusion or shorter length results in less "resistance")

A reaction-diffusion steady state example

bacteria move randomly, but also reproduces/dies with rate λc

from $\frac{\partial c}{\partial t} = D\frac{\partial^2 c}{\partial x^2} + \sigma$ get (assuming $D = 1$ for simplicity):

$$\boxed{\frac{\partial c}{\partial t} \;=\; \frac{\partial^2 c}{\partial x^2} + \lambda c}$$

what are possible steady state sols on interval $[0, \pi]$, with $c(0){=}c(\pi){=}0$?
(think of open tube, outside concentration =zero); need to solve:

$$c'' + \lambda c = 0\,, \quad c(0) = c(\pi) = 0$$

if $\lambda = 0$, then $c'' = 0$, $c(0) = c(\pi) = 0 \Rightarrow c \equiv 0$
if $\lambda < 0$, $c = ae^{\mu x} + be^{-\mu x}$, where $\mu := \sqrt{-\lambda}$,
so using two boundary conditions, $a + b = ae^{\mu\pi} + be^{-\mu\pi} = 0$, or:

$$\begin{pmatrix} 1 & 1 \\ e^{\mu\pi} & e^{-\mu\pi} \end{pmatrix} \begin{pmatrix} a \\ b \end{pmatrix} \;=\; 0\,.$$

since $\quad \det \begin{pmatrix} 1 & 1 \\ e^{\mu\pi} & e^{-\mu\pi} \end{pmatrix} = e^{-\mu\pi} - e^{\mu\pi} = e^{-\mu\pi}(1 - e^{2\mu\pi}) \neq 0\,,$

we obtain $a = b = 0$, so again $c \equiv 0$ (summary: $\lambda \leq 0 \Rightarrow c \equiv 0$)

A reaction-diffusion steady state example, ctd

if $\lambda \geq 0$, let $k := \sqrt{\lambda}$, so

$$c'' + k^2 c = 0 \;\Rightarrow\; c(x) = a \sin kx + b \cos kx$$

and $c(0) = c(\pi) = 0$ implies that $b = 0$ and that k must be a nonzero integer, so

$$c(x) = a \sin kx$$

for some constant a

in conclusion, in order to have a nonzero solution, we must have that λ^2 is an integer

(in fact, since c represents a density of a population, this solution only makes sense if $k = 1$, since otherwise $c(x)$ takes negative values in the interval $[0, \pi]$)

A variation as homework problem

suppose $c(x,t)$ is the density of a bacterial population undergoing random motions (diffusion), and living in a one-dimensional tube with endpoints at $x = 0$ and $x = \pi/2$
the bacteria reproduce with rate $\lambda c = c/4$
the tube is closed at $x = 0$ and open at $x = \pi/2$
and the outside density of bacteria is $c = 10$
taking $D = 1$ for simplicity:

1. Write down the appropriate equation, including boundary conditions.
2. Find a solution of the form $c(x) = aX(x)$, where X is a trigonometric function

A diffusion/chemotaxis model

now extend model so that flux is sum of two components

1. "random motion" (diffusion), and
2. "chemotaxis" (movement in direction of V_x)

think of V as denoting nutrient availability
want to move in direction of improving conditions
(i.e., V increasing)
no reproduction or loss in this model ($\sigma = 0$); so:

$$J \;=\; -D\frac{\partial c}{\partial x} + \alpha\, c\, V_x$$

where second term is simply transport term proportional to cv
and velocity is V_x

$$\frac{\partial c}{\partial t} \;=\; -J_x \;=\; -\,\frac{\partial}{\partial x}\left(-D\frac{\partial c}{\partial x} + \alpha\, c\, V_x\right)$$

Steady states for diffusion/chemotaxis model

assume no flux boundary conditions on one-dimensional interval $[0, L]$:

$$J(0,t) = J(L,t) = 0 \quad \forall\, t$$

set $\frac{\partial c}{\partial t} = -\frac{\partial J}{\partial x} = 0$, and view c as a function of x alone
using primes for $\frac{d}{dx}$, gives:

$$J = \alpha\, c\, V' - Dc' \;=\; J_0 \quad \text{(some constant)}$$

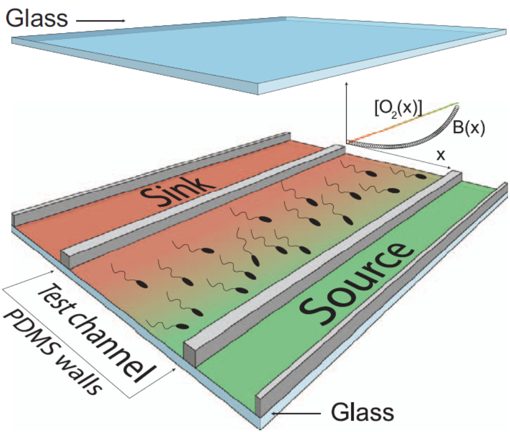
Since $J_0 = 0$ (because J vanishes at the endpoints), we have that $(\ln c)' = c'/c = (\alpha V/D)'$, and therefore

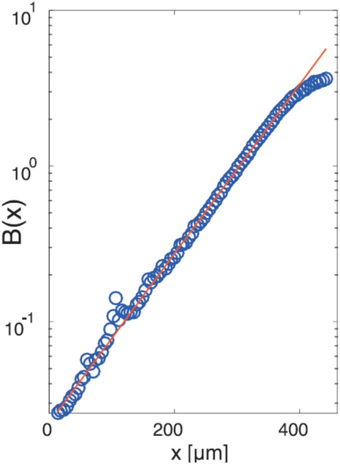
$$c \;=\; k\, \exp(\alpha V/D) \qquad \text{for some constant } k$$

so steady state c proportional to exponential of nutrient concentration
e.g.: steady-state nutrient, 0 at $x = 0$ and 1 at $x = L$, then
$V(x) = x/L$ so $c(x) = ke^{x/L}$ (assuming for simplicity $D = 1$, $\alpha = 1$)

Example (for aero-taxis in B. Sutilis)

note exponential steady-state distribution (log scale)





Menolascina, Rusconi, Fernandez, Smriga, Aminzare, Sontag, Stocker, Logarithmic sensing in Bacillus subtilis aerotaxis, Systems Biology and Applications, 2017

Simple problem

Consider a diffusion/chemotaxis model on a one-dimensional interval $[0,1]$. Suppose that there is a nutrient which is at diffusive steady state, and has values $V(0)=0$ and $V(1)=1$, just as in the example done in the notes. However now we do not assume zero-flux boundary conditions for the chemotactic bacterium, and instead assume a Dirichlet problem: there are fixed values at the endpoints, which we take for simplicity as $c(0)=0$, $c(1)=10$. Take $\alpha=D=1$. Solve for $c(x)$.

Hint: Your solution will have the form $c(x)=a(b+ce^x)$ for some constants a,b,c which you will compute, but **do not solve the problem by using this hint.** Instead, proceed systematically solving

$$\frac{\partial}{\partial x}\left(-D\frac{\partial c}{\partial x}\,+\,\alpha\,c\,V_x\right)=0$$

(you cannot use the trick of saying that the flux is zero, in this case). You will end up solving a linear second-order ODE with two boundary conditions. (First find general solutions, then fit conditions.) Note that $V(x)=x$.

Probabilistic Interpretation [will probably not cover]

population of indistinguishable particles (bacteria, etc.)
undergoing random motion
track *each individual particle*
(assumed small enough, they don't collide with each other)
think of huge number of one-particle experiments,
estimate distribution of positions $x(t)$ by averaging over runs
instead of just performing one big experiment with many particles
at once and measuring population density
prob of a single particle ending up, at time t, in a given region R
proportional to how many particles there are in R,
i.e. to Prob(particle in R) $\propto C(R,t) = \int_R c(x,t)\,dx$.
normalize to $C = 1$: Prob(particle in R) $= \int_R c(x,t)\,dx$
$c(x,t) =$ *probability density* of random variable giving position of
particle at time t (*random walk*)

Probabilistic Interpretation (ctd)

standard deviation $\sigma(t)$ proportional to $\sqrt{t}$
(rough estimate on approximate distance traveled)
average displacement of a diffusing particle is proportional to $\sqrt{t}$.
i.e. *traveling average distance L requires time* L^2
diffusion is simple and energetically relatively "cheap":
no need for building machinery for locomotion, etc.,
no loss due to conversion to mechanical energy (cellular motors and muscles)
at small scales, diffusion very efficient (L^2 is tiny for small L)
good fast method for nutrients and signals carried *short* distances
but not for long distances (L^2 huge if L is large)
e.g.: particle travels by diffusion covering 10^{-6}m ($= 1\mu$m) in 10^{-3} seconds (a typical order of magnitude in a cell),
how much time is required to travel 1 meter?
Answer: $x^2 = 2Dt \Rightarrow$ solve $(10^{-6})^2 = 2D10^{-3} \Rightarrow D = 10^{-9}/2$
So, $1 = 10^{-9}t$ means that $t = 10^9$ seconds, i.e. about 27 years!
not feasible in large organisms $\rightsquigarrow$ circulatory systems, cell motors ...

More on Random Walks

discrete analog: particle can move left or right
with a unit displacement and equal probability, independent steps
position after t steps?
e.e. 4 steps histogram:

ending	possible sequences	count	
-4	$-1-1-1-1$	1	x
-2	$-1-1-1+1, -1-1+1-1, \ldots$	4	xxxx
0	$-1-1+1+1, -1+1+1-1, \ldots$	6	xxxxxx
2	$1+1+1-1, 1+1-1+1, \ldots$	4	xxxx
4	$1+1+1+1$	1	x

Central Limit Theorem $\Rightarrow$ distribution (as $t \to \infty$) tends to be normal, with variance:

$$\sigma^2(t) = E(X_1 + \ldots + X_t)^2 = \sum\sum EX_iX_j = \sum EX_i^2 = \sigma^2 t$$

(since the steps are independent, $EX_iX_j = 0$ for $i \neq j$)
we see then that $\sigma(t)$ is proportional to $\sqrt{t}$
Brownian motion theory: similar analysis for continuous walks

Traveling waves in reaction-diffusion systems

interesting: r-d systems may exhibit traveling-wave behavior (examples in species competition, etc.)

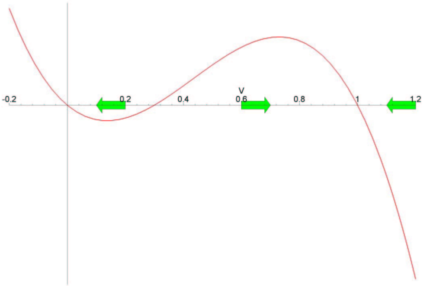
surprising: diffusion times scale like the $\sqrt{(\text{distance})}$, not linearly

simple example:

$$\frac{\partial V}{\partial t} = \frac{\partial^2 V}{\partial x^2} + f(V)$$

where f is a function that has zeroes at $0, \alpha, 1$, $\alpha < 1/2$, and satisfies:

$$f'(0) < 0, \;\; f'(1) < 0, \;\; f'(\alpha) > 0$$

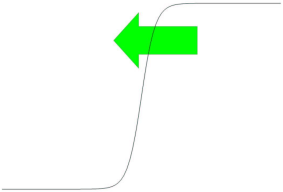


Traveling waves, ctd

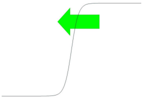
note differential equation $dV/dt = f(V)$ by itself, without diffusion, would be a bistable system

another classical example: Fisher equation, used in genetics to model the spread in a population of a given allele

interest in solutions that look like a "traveling front" moving to the left (we could also ask about right-moving solutions, of course)



Formalization



look for $V(x,t)$ such that, for some "waveform" U that "travels" at some speed c, V can be written as a translation of U by ct:

$$V(x,t) = U(x+ct)$$

so need these four conditions to hold:

$$V(-\infty,t) = 0\,,\ V(+\infty,t) = 1\,,\ V_x(-\infty,t) = 0\,,\ V_x(+\infty,t) = 0$$

key remark: PDE for V induces ODE for the waveform U
these boundary conditions constrain what U and speed c can be

Find conditions

to get an equation for U, plug-in $V(x,t) = U(x+ct)$ into $V_t = V_{xx} + f(V)$, obtaining:

$$cU' \ = \ U'' + f(U)$$

where "$'$" indicates derivative with respect to the argument of U,

which we write as ξ

$V(-\infty,t) = 0,\ V(+\infty,t) = 1,\ V_x(-\infty,t) = 0,\ V_x(+\infty,t) = 0$ translate into:

$$U(-\infty) = 0\,,\ U(+\infty) = 1\,,\ U'(-\infty) = 0\,,\ U'(+\infty) = 0$$

since U satisfies a second order ODE, may introduce $W = U'$ and see U as the first coordinate in a system of system of 2 ODE's

2D system

$$\begin{aligned} U' &= W \\ W' &= -f(U) + cW \end{aligned}$$

steady states: $W = 0$ and $f(U) = 0 \Rightarrow (0,0)$ and $(1,0)$
Jacobian is:

$$J = \begin{pmatrix} 0 & 1 \\ -f' & c \end{pmatrix}$$

has det $f' < 0$ at steady states, so they are both saddles
conditions on U translate into the requirements that:

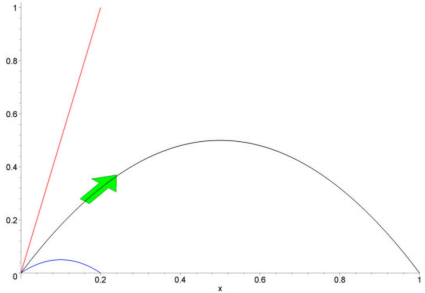
$$(U,W) \to (0,0) \text{ as } \xi \to -\infty \text{ and } (U,W) \to (1,0) \text{ as } \xi \to \infty$$

for $U(\xi)$ and its derivative, seen as solution of system of ODE's (note that "ξ" is now "time")

Heteroclinic connections

i.e. need to show the existence of an "heteroclinic connection" between these two saddles

one first proves that, for $c \approx 0$ and $c \gg 1$, there result trajectories that "undershoot" or "overshoot" the desired connection, so, by a continuity argument (similar to the intermediate value theorem), there is some value c for which the connection exactly happens details given in many mathematical biology books



Special case

$$f(V) = -A^2 V(V-\alpha)(V-1)$$

since U will satisfy $U' = 0$ when $U = 0, 1$,
we *guess* the functional relation:

$$U'(\xi) \ = \ BU(\xi)\,(1 - U(\xi))$$

(we are looking for a U satisfying $0 \leq U \leq 1$, so $1 - U \geq 0$)
write "ξ" for the argument of U, so not confuse with x.
we substitute $U' = BU(1-U)$ and also (follows from this)

$$U'' = B^2 U(1-U)(1-2U)$$

into the differential equation:

$$cU' = U'' + A^2 U(U-\alpha)(U-1)$$

and then cancel $U(U-1)$, leading to (homework problem):

$$B^2(2U-1) + cB - A^2(U-\alpha) \ = \ 0$$

Special case, ctd

as U is not constant (because $U(-\infty) = 0$ and $U(+\infty) = 1$), this means we can compare coefficients of U in this expression, and conclude: $2B^2 - A^2 = 0$ and $-B^2 + cB + \alpha A^2 = 0$, so:

$$B = A/\sqrt{2}\,, \quad c = \frac{(1-2\alpha)A}{\sqrt{2}}$$

substituting back into the ODE for U, we have:

$$U' \;=\; BU(1-U) \;=\; \frac{A}{\sqrt{2}}U(1-U)$$

which is an ODE that now does not involve the unknown B

solve this ODE by separation of variables and partial fractions, using for example $U(0) = 1/2$ as an initial condition, getting:

$$U(\xi) \;=\; \frac{1}{2}\left[1 + \tanh\left(\frac{A}{2\sqrt{2}}\xi\right)\right]$$

finally, since $V(x,t) = U(x+ct)$, we conclude that:

$$V(x,t) \;=\; \frac{1}{2}\left[1 + \tanh\left(\frac{A}{2\sqrt{2}}\,(x+ct)\right)\right]$$

Special case, ctd

where $c = \frac{(1-2\alpha)A}{\sqrt{2}}$

observe that the speed c was uniquely determined

it will be larger if $\alpha \approx 0$, or if the reaction is stronger (larger A)

this is not surprising! (why?)