Part II — Mathematical Biology

Based on lectures by R. Adhikari

Notes taken by Joseph Tedds using Dexter Chua's header and Gilles Castel's snippets.

Lent 2020

Introduction to the role of mathematics in biology

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Systems without spatial structure: deterministic systems

Examples: population dynamics, epidemiology, chemical reactions, physiological systems. Continuous and discrete population dynamics governed by deterministic ordinary differential equations or difference equations. Single population models: the logistic model and bifurcation to chaos; systems with time delay; age-structured populations. Two-species models: predator-prey interactions, competition, enzyme kinetics, infectious diseases. Phase-plane analysis, null-clines and stability of equilibrium. Systems exhibiting nonlinear oscillations: limit cycles; excitable systems. [9]

Stochastic systems

Discrete stochastic models of birth and death processes. Master equations and Fokker-Planck equations. The continuum limit and the importance of fluctuations. Comparison of deterministic and stochastic models, including implications for extinction/invasion. Simple random walk and derivation of the diffusion equation. [6]

Systems with spatial structure: diffusion and reaction-diffusion systems

The general transport equation. Fundamental solutions for steady and unsteady diffusion. Models with density-dependent diffusion. Fischer-Kolmogorov equation: propagation of reaction-diffusion waves. Chemotaxis and the growth of chemotactic instability. General conditions for diffusion-driven (Turing) instability: linear stability analysis and evolution of spatial pattern. [8]

Contents

0 Introduction

0.1 What is mathematical biology?

In this course we will attempt to quantitatively understand some aspects of the behaviour of biological systems.
Biological system:

$$\underset{1\mathrm{A}^0}{\text{atoms}} \to \underset{10\mathrm{A}^0}{\text{molecules}} \to \underset{100\ -\ 1000\ \mathrm{A}^0}{\text{biomolecules}} \to \underset{\mu\mathrm{m}}{\text{tissue}} \to \underset{\mathrm{cm}}{\text{organs}} \to \underset{\mathrm{m}}{\text{organism}} \to \underset{\mathrm{km}}{\text{populations}} \to \underset{\text{global}}{\text{ecosystem.}}$$

- Hierarchies: Each level consists of parts, but the whole is more than the sum of its parts.
- Emergence: New functional properties obtained from hierarchies "more is different": P.W. Anderson
- Complexity: Reductionism, of thinking of a biological system as a clockwork of parts, is spectacularly unsuccessful.
- Contingency: Unlike physical / chemical systems, biological systems have a degree of autonomy; therefore behaviour is contingent.

0.2 Comparison with mathematisation in other disciplines

Physics; Chemistry; Biology; Psychology; Sociology

These go from left to right in order of increasing complexity, contingency and right to left in order of decreasing quantifiability.
Physics: there are natural "laws", which have succinct mathematical expressions

Example.
- Classical mechanics - $F = ma$ (Newton)
- Quantum mechanics - $H\psi = E\psi$ (Schrodinger)
- Electrodynamics - $\nabla \cdot E = \rho$ (Maxwell)

In contrast, there are no laws in biology. The only real law is that of evolution by natural selection (Darwin). Physical laws are predictive. Evolution is retrospective, it can only rationalise past sequences of events, not predict future ones.

0.3 How do we model systems in biology?

- We first focus on a hierarchy, for example biomolecules / populations and empirically observe process that lead to change.
- Abstract this process in terms of variables suitable to the hierarchy.
- Changes can occur in both space and time; these are the independent variables of description.
- Changes can be deterministic (same each time we observe) or contingent (different, statistical observations), therefore probabilistic.

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1.1 Single population models

$x(t)$ is the population size as a function of time t. Construct a model for the change in $x(t)$. $x(t+\delta t) = x(t) + bx\delta t - dx\delta t$ $b, d > 0$ with b, d modelling births and deaths respectively. Rearrange and let $\delta t \to 0$ to obtain

$$\frac{\mathrm{d}x}{\mathrm{d}t} = (b-d)\cdot x = r\cdot x.$$

Which we know has solution $x(t) = e^{rt}x(0)$. If $r > 0$, explosive growth as $t \to \infty$, if $r < 0$ we have extinction as $t \to \infty$. Malthusian catastrophe: population explosion! Adding competition to the Malthusian model

$$\frac{\mathrm{d}x}{\mathrm{d}t} = b(x) - d(x).$$

For simple competition we say $b(x) = B\cdot x$ (linear birth), $d(x) = D\cdot x^2$ (quadratic death).

$$\frac{\mathrm{d}x}{\mathrm{d}t} = (B - Dx)x.$$

The asymptote, $t \to \infty$ is it possible that $\frac{\mathrm{d}x}{\mathrm{d}t} = 0$? i.e. a stationary population. Yes, this is possible when $x = 0$ or $X = \frac{B}{D}$. Dynamical systems $\to$ *fixed point*; $\frac{\mathrm{d}x}{\mathrm{d}t} = f(x)$; $\frac{\mathrm{d}x}{\mathrm{d}t} = 0$ so at $x = x^*, f(x^*) = 0$.
Non-dimensionalistion:

$$\frac{\mathrm{d}x}{\mathrm{d}t} = B\left(1 - \frac{D}{B}x\right)x = B(1 - \frac{x}{x^*})x.$$

With our fixed point $x^* = \frac{B}{D}$. If we divide through by x^* and B,

$$\frac{\mathrm{d}}{\mathrm{d}Bt}\left(\frac{x}{x^*}\right) B\left(1 - \frac{x}{x^*}\right)\left(\frac{x}{x^*}\right).$$

So under the change of parameters $t \to Bt, x \to \frac{x}{x^*}$ we obtain the logistic equation

$$\frac{\mathrm{d}x}{\mathrm{d}t} = (1-x)x.$$

$\tilde{x} = \frac{x}{x^*}$ is the population size relative to stationary population. $\tilde{t} = Bt$ is time measured in units of birth rate. Non-dimensionalised equations are better suited for mathematical analysis. Undoing the temporal scaling,

$$\frac{\mathrm{d}x}{\mathrm{d}t} = \alpha(1-x)x \quad \alpha = B.$$

If we separate the variables we obtain the solution $\log\left|\frac{x}{1-x}\right| = \alpha t + C$. Our initial condition is $x(0) = x_0, 0 \le x_0 \le 1$. Our solution is

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

For $t \to \infty, x \to 1$, for any x_0 in $0 < x_0 \le 1$. The point $x = 1$ is stable and the point $x = 0$ is unstable. Stability is an important qualitative feature of fixed points.

Remark. We will emphasize qualitative analysis aspects and geometric ideas.

1.2 Stability of fixed points of an ODE

$$\frac{\mathrm{d}x}{\mathrm{d}t} = f(x).$$

Assume $f(x^*) = 0$ (a fixed point). Perturb the solution around x^*: set $x(t) = x^* + \epsilon(t)$

$$f(x) = f(x^*) + \frac{\partial f}{\partial x}\Big|_{x=x^*} \cdot \epsilon + \frac{1}{2}\frac{\partial^2 f}{\partial x^2}\Big|_{x=x^*} \cdot \epsilon^2 \cdots .$$

$$\frac{\mathrm{d}x}{\mathrm{d}t} = \frac{\mathrm{d}}{\mathrm{d}t}(x^* + \epsilon) = \frac{\mathrm{d}\epsilon}{\mathrm{d}t}.$$

Combining these equations we find $\frac{\mathrm{d}\epsilon}{\mathrm{d}t} = J\epsilon$, $J = \frac{\partial f}{\partial x}\Big|_{x=x^*}$ the Jacobian. Hence $\epsilon(t) = e^{Jt}\epsilon(0)$. This means that $\epsilon(t)$ grows if $J > 0$ i.e. unstable and shrinks if $J < 0$ i.e. stable.

1.3 Stability of the logistic model

$$f(x) = \alpha(x - x^2), \quad J(x) = \alpha(1 - 2x);.$$

We see $J(0) = \alpha$ hence unstable and $J(1) = -\alpha$ hence stable.

1.4 More complicated models

$$\frac{\mathrm{d}x}{\mathrm{d}t} = f(x) = f_1(x) + f_2(x) + \cdots + f_N(x).$$

Where $f_i(x)$ is some abstraction of an empirically observed process.

1.5 Limitations: cannot model certain processes

i is an index for a partition of the domain (into squares). $x_i(t)$ is the population on the ith domain. $x(t) = \sum x_i(t)$ the aggregate population. We cannot model migrations: $x_i \to x_i + \Delta_{ij}$; Δ_{ij} is the transfer from $i \to j$. Population sum of i, j is

$$\underbrace{x_i + x_j}_{\text{before}} \quad (x_i + \Delta_{ij}) + (x_j - \Delta_{ij}) = \underbrace{x_i + x_j}_{\text{after}}.$$

1.6 Population models with delay

$$\frac{\mathrm{d}x}{\mathrm{d}t} = f(x) \dot{)} ODE \to \frac{\mathrm{d}x}{\mathrm{d}t} = f(x(t), x(t-T)).$$

T is a delay, $T > 0$. We call the second equation a Delay differential equation. Recall, the Malthusian model $\frac{\mathrm{d}x}{\mathrm{d}t} = b \cdot x - d \cdot x$. This ignores the gestation period for the individual to reach reproductive age, say T. Taking this into account gives

$$\frac{\mathrm{d}x}{\mathrm{d}t} = b \cdot x(t-T) - dx(t).$$

Since death is independent of gestation it does not depend on T.

Remark. Chemical reactions are another example of delay models.

$$A \underbrace{\to I_1 \to I_2 \cdots \to I_n}_{\text{chemical intermediates}} \to B.$$

The rate of change of B, forgetting intermediates; naively might say

$$\frac{\mathrm{d}B}{\mathrm{d}t} = f(A).$$

This ignores the times of intermediate formation. Taking into account this time, $\frac{\mathrm{d}B}{\mathrm{d}t} = f(A, A(t-T))$.

1.7 Solution of Malthusian model with delay

The model has 3 parameters, b, d, T ; $T = 0$ is the Malthus model. Since the equation is linear, we assume an exponential solution i.e. $x(t) = x_0 e^{St}$. Substitute trial solution into delay equation to get

$$Sx_0 e^{St} = -dx_0 e^{St} + bx_0 e^{S(t-T)}.$$

$S = -d + be^{-ST}$ our characteristic equation. For $T = 0, S = b - d = r$ our solution is $x = x_0 e^{rt}$ (as before)