Mathematical Biology

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Preface

The course “Mathematical Modeling” has a dual purpose: on one hand, to introduce students to some basic mathematical models in various areas of biology (demography, ecology, infectious diseases, enzyme reactions, physiology, molecular networks); on the other hand, to provide fundamental knowledge in the analysis and numerical simulation of ordinary and partial differential equations.

Specifically, the first part of the course is dedicated to modeling using ordinary differential equations and introduces various analytical techniques (linearization, equilibria and their stability, bifurcation, regular and singular perturbations).

- Overview of ordinary differential equations (ODEs): Solution of linear equations; equilibria and linearized stability; phase plane, limit cycles; numerical schemes for solving ODEs.
- One- or two-dimensional models in demography, ecology, epidemiology, and immunology. Non-dimensionalization of variables and parameters.
- Slow-fast systems, enzyme reaction models and their simplification using perturbative methods.
- Bifurcation of equilibria and application to predator-prey systems and molecular networks. Simplified models of important biological phenomena, such as the cell cycle and glucose-insulin oscillations.
- Excitable systems: Hodgkin-Huxley equations (overview) and FitzHugh-Nagumo equations.
- Parameter estimation for differential models.

In the second part, partial differential equation models and some techniques for constructing or approximating solutions will be studied. Additionally, some of the most interesting phenomena of reaction-diffusion equations (traveling wave solutions, Turing mechanism) will be presented in a biological context (morphogenesis).

- Dynamical systems on networks. Examples in epidemiology.
- Introduction to partial differential equations (PDEs): Solutions by separation of variables. Fourier series. The heat equation and Brownian motion. Eigenfunctions of the Laplacian. Numerical approximation.
- Skellam and Fisher equations: Waveform solutions; stationary solutions of the boundary value problem.

- Stability of stationary solutions of reaction-diffusion systems and Turing's mechanism for morphogenesis. Conditions for its validity and examples. Chemotaxis: The Keller-Segel model.

Part I

Lectures

1 Bathtub model

1.1 The bathtub model

The models of Newtonian physics are made of differential equations built starting from the second law of the dynamics. The structure of the models discussed here is instead simpler; they are based on the "balance equation of the bathtub": if $Q(t)$ is the quantity of a substance in the bathtub we have

$$\frac{\mathrm{d}Q}{\mathrm{d}t} = Q'(t) = I(t) - O(t),$$

where

- $I(t)$ is the *input rate* (quantity that enters per unit time)
- $Q(t)$ is the *output rate* (quantity that leaves per unit time).

To be more precise, the assumption is that, if $I_{(t,t+\Delta t)}$ is the quantity that enters in the interval $(t, t+\Delta t)$, we have $I_{(t,t+\Delta t)} = I(t)\Delta t + o(\Delta t)$, where $o(\Delta t)$ is a higher order infinitesimal than Δt. Hence:

$$I(t) = \lim_{\Delta t \to 0} \frac{I_{(t,t+\Delta t)}}{\Delta t}.$$

The input rate $I(t)$ is like an instantaneous velocity: the quantity entered in a given time, when that time becomes very small. Hence $I(t)$ is measured in $[C][t^{-1}]$ units where $[C]$ represents the concentration of the quantity Q. Similarly for the exit rate $O(t)$.

Let us start from a very simple example. Assume $I(t) = \Lambda$ constant input flux; $O(t) = \gamma Q(t)$, i.e. exit flux is proportional to the quantity present at the moment; the proportionality constant γ is often called the *exit rate* and has the dimension $[t^{-1}]$, the inverse of time. From these assumptions we get:

$$Q'(t) = \Lambda - \gamma Q(t), \tag{1.1}$$

supplemented with some *initial condition*

$$Q(0) = Q_0.$$

The solution is:

$$Q(t) = e^{-\gamma t} Q_0 + \frac{\Lambda}{\gamma}\left(1 - e^{-\gamma t}\right).$$

Exercise

Solve Equation 1.1 with the method you prefer.

Exercise

Solve Equation 1.1 with the general formula for linear ODEs, by first defining the matrix exponential (here, just a scalar function).

Note that if $\Lambda = 0$ (no input), the solution is simply

$$Q(t) = Q_0 e^{-\gamma t}.$$

This means that the survival time of a molecule initially present follows the exponential distribution:

$$\mathbb{P}[\text{a molecule present at time 0 is present at time } t > 0] = \frac{Q(t)}{Q_0} = e^{-\gamma t}.$$

From the properties of the exponential distribution, we obtain that the mean survival time $\mathbb{E}[T] = 1/\gamma$; hence the exit rate γ can be interpreted as the inverse of the mean survival time.

To be more precise, let us define a continuous random variable T, which measures the lifetime of a particle present in the bathtub. Then, the cumulative distribution $F(t)$ of T is given by

$$\begin{aligned} F(t) &= \mathbb{P}[T \leq t] \\ &= 1 - \mathbb{P}[T > t] \\ &= 1 - \mathbb{P}[\text{a molecule present at time 0 is present at time } t > 0] \\ &= 1 - e^{-\gamma t}. \end{aligned}$$

So, we indeed have an exponential distribution. The probability density function is:

$$f(t) = F'(t) = \gamma e^{-\gamma t},$$

and the expectation is:

$$\mathbb{E}[T] = \int_0^\infty t f(t) \mathrm{d}t = \frac{1}{\gamma}.$$

Exercise

Compute the above integral explicitly.

1.2 Malthus equation

The metaphor of the bathtub can be used to model the dynamics of a population. Neglecting all differences among individuals (due to age, sex, genetic,...) we can represent a population through its size $N(t)$; this will increase through inputs due to births and outputs due to deaths (if immigration and emigration are not considered). Hence

$$N'(t) = B(t) - D(t),$$

where $B(t)$ = births and $D(t)$ = deaths.

Malthus model assumes

- within a (short) time period of length Δt, each individual gives, on average, birth to $\beta \Delta t$ new individuals; hence $B(t) = \beta N(t)$;
- within the same time period Δt, each individual has probability $\mu \Delta t$ of dying; hence $D(t) = \mu N(t)$.

We get the following equation

$$N'(t) = \beta N(t) - \mu N(t) = (\beta - \mu) N(t),$$

that represents the *Malthus model*. The parameter β is known as *fertility rate*, while μ is the *mortality rate*. Finally,

$$r = \beta - \mu$$

is the (instantaneous) *growth rate* and is also called *Malthus parameter* or *biological potential* of the population.

With the initial condition

$$N(0) = N_0,$$

the evolution of the population is completely determined. In fact, the solution is

$$N(t) = N_0 e^{rt},$$

and we see that the population will go to extinction or will grow without limits if $r < 0$ or $r > 0$, respectively. If instead $r = 0$, the population size is constant (births and deaths compensate.)

```python
import numpy as np
import matplotlib.pyplot as plt
import seaborn as sns

sns.set_theme("notebook", style="whitegrid")
t = np.linspace(0,1,100)

plt.plot(t,np.exp(1*t),label='r > 0')
plt.plot(t,np.exp(-1*t),label='r < 0')
plt.plot(t,np.exp(0*t),label='r = 0')
plt.grid()
plt.legend()
plt.xlabel('Time')
plt.ylabel('Population')
plt.show()
```

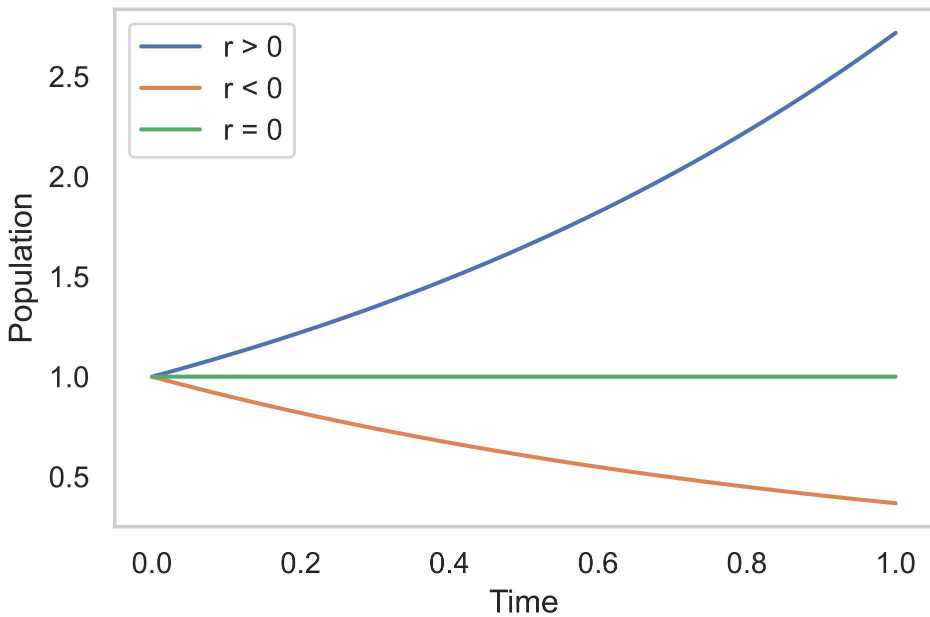

Figure 1.1: Example of solutions of Malthus equation