Session 1: Why use mathematical models?

Primer for Mathematical Modelling for Biologists
EASTBIO Foundation Masterclasses

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Overview

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- What can mathematical models be used for?
- Why use a mathematical model?
- How do you design and build a mathematical model?
- What are the different types of mathematical model?

What is mathematical modelling?

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Simply, using mathematical concepts to describe a (biological) system.

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Note, a model may be used for more than one of these objectives.

What areas are models being applied within?

- Ecology

interacting species (*e.g.*, predation), animal migration, conservation, population control, etc.

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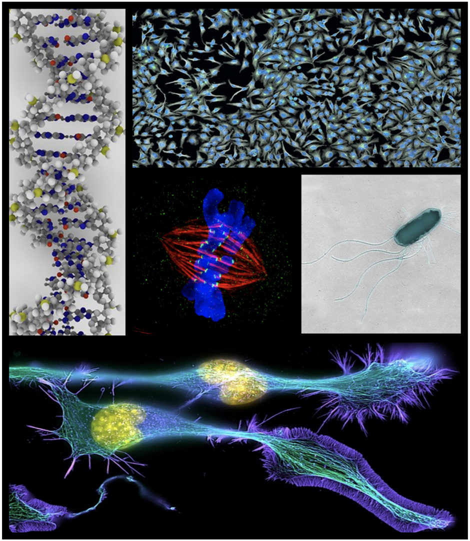
- Cell biology



cell structure, cell division, cell migration, cell mechanics, mutation etc.

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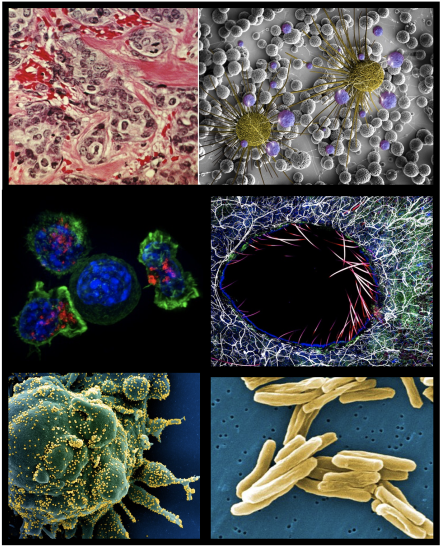
- Ecology
- Cell biology
- Within-host disease progression and treatment



cancer, immunology, wound healing, viral dynamics, bacterial dynamics etc.

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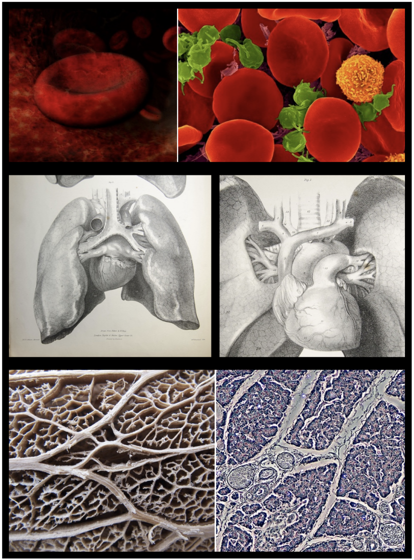
- Within-host disease progression and treatment
- Human biology



blood flow, airways, oxygen dynamics, nutrient dynamics, vasculature etc.

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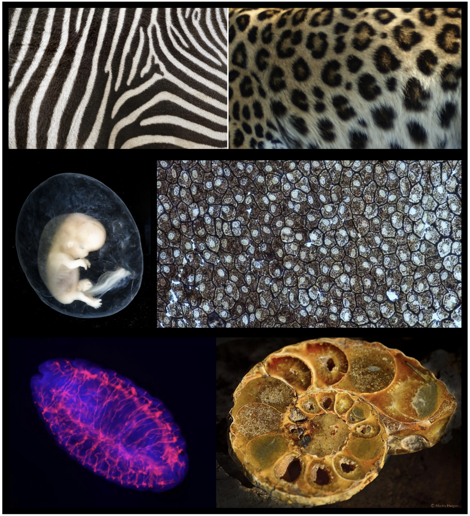
- Cell biology
- Within-host disease progression and treatment
- Human biology
- Growth and development



pattern formation, embryogenesis, gene regulation etc.

- Ecology
- Cell biology
- Within-host disease progression and treatment
- Human biology
- Growth and development
- Human behaviours

population growth, disease spread (*e.g.* COVID-19), vaccination protocols, emergency exit plans etc.

Why use a mathematical model?

Why mathematical modelling in biology?

Biological systems are complex - we can use math models to 'zoom in' on different aspects of the system.

Benefits and limitations of models

" This model will be a simplification and an idealisation and consequently a falsification. It is hoped that the features retained for discussion are those of greatest importance in the present state of knowledge"

- Alan Turing, 'The chemical basis of morphogenesis', 1952.

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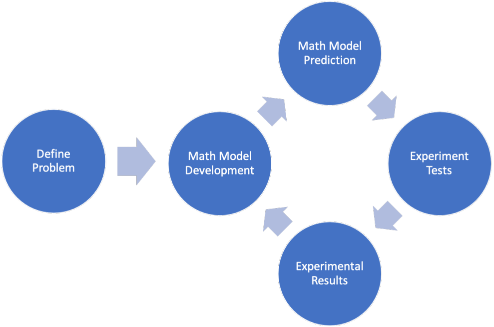
– Cannot capture all biological mechanisms
– Understanding of the biological system and data (or rough estimates) required
– Complexity and lack of data can lead to multiple assumptions

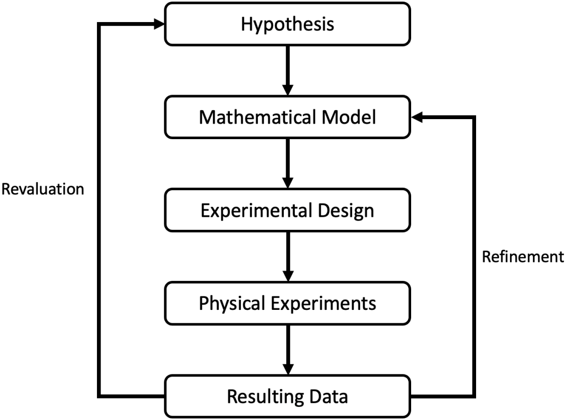
Collaborative approach

One way to overcome limitations of both experimental and mathematical models is to use a combined approach.



Collaborative approach

Another more detailed approach,



How do you design and build a mathematical model?

How do you design and build a mathematical model?

1. Define the problem
   - What are you trying to measure/predict?
   - What specifically do you want to know?

How do you design and build a mathematical model?

1. Define the problem
2. Make (informed) assumptions
   - From previous research what can you remove/omit?
   - What are the key parts of the system?
   - Properties of the system (*e.g.*, *in vivo*, *in vitro*)

How do you design and build a mathematical model?

1. Define the problem
2. Make (informed) assumptions
3. Define variables
   - What are your inputs and outputs?
   - What parameters are there (variables that are constant over time)?
   - What are the units of the components and parameters in the model?

How do you design and build a mathematical model?

1. Define the problem
2. Make (informed) assumptions
3. Define variables
4. Build model
   - Are there any existing models that are similar?
   - More than one approach may work
   - Availability of data may impact the type of model used
   - We will look at modelling approaches later

How do you design and build a mathematical model?

1. Define the problem
2. Make (informed) assumptions
3. Define variables
4. Build model
5. Analyse results/output
   - Does your result make sense in regards to the available data and historical data
   - Does your model work as expected?
   - Is the result consistent each time you run the model?
   - What parameters are most important? (Sensitivity analysis)
   - Are your results qualitative and/or quantitative?

How do you design and build a mathematical model?

1. Define the problem
2. Make (informed) assumptions
3. Define variables
4. Build model
5. Analyse results/output
6. Modify, extend and/or refine the model
   - Did you omit things in step 2 that can now be added
   - Is new data available?

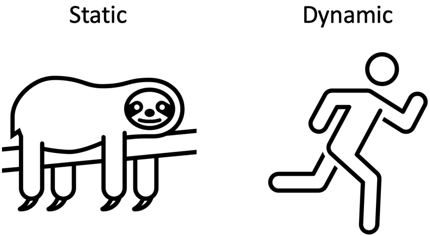
Methods of mathematical modelling

Useful terms

- Function - a relation or expression involving one or more variables.
- *e.g.*, $f(t,x)$ - f is a function dependent on time t and spatial coordinates x.
- *e.g.*, $f(t,x)$ - is the output value of f at time t at position x
- *e.g.*, $f(0,x)$ - is the output value of f at time 0

Useful terms

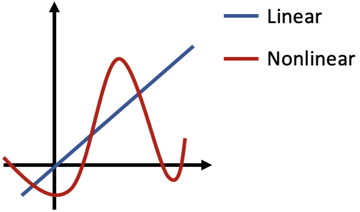
- Static - A static (or steady-state) model calculates the system in equilibrium. The system doesn't change in time (or space).
- Dynamic - A dynamic model accounts for time-dependent changes in the state of the system.



Useful terms

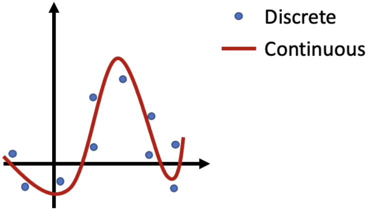
- Linear - A mathematical function that can be graphically represented as a straight line.

- Nonlinear - A mathematical function that **cannot** be graphically represented as a straight line.



Useful terms

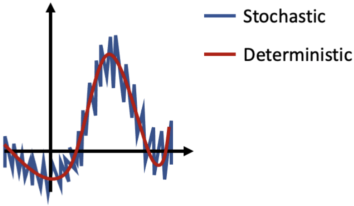
- Discrete - A discrete function allows the x-values to be only certain points in the interval
- Continuous - A continuous function allows the x-values to be any points in the interval



Useful terms

- Deterministic - A system in which no randomness is involved in the development of future states of the system. A deterministic model will thus always produce the same output from a given starting condition or initial state.

- Stochastic - A system in which some level of randomness is involved in the development of future states of the system. A stochastic model can produce varying output from the same given starting condition or initial state.



Useful terms

- Derivative - The rate of change of a function with respect to a variable.

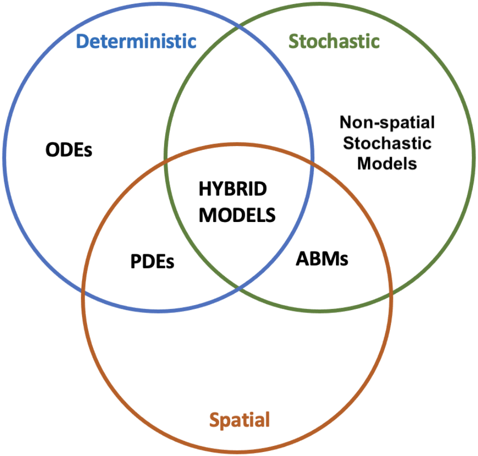
e.g., Velocity (speed and direction of an object) is defined as the derivative of position, x, with respect to time:

$$v = \frac{dx}{dt}$$

Acceleration is defined as the second derivative of position, x, with respect to time:

$$a = \frac{dv}{dt} = \frac{d^2x}{dt}$$

Models types we will consider



Note, these are just the ones we shall consider today. Other types of model exist.

ODEs

Ordinary differential equations (ODEs)

- continuous equations, deterministic
- contain one or more functions of **one** independent variable and the derivatives of those functions.
- track the change in a function with respect to the independent variable.
- useful for intracellular level dynamics, small (spatial) scale dynamics.

1st order:

$$\frac{df(t)}{dt} = g(f,t), \quad \frac{df(x)}{dx} = g(f,x).$$

2nd order:

$$\frac{d^2f(t)}{dt^2} + \frac{df(t)}{dt} = g(f,t), \quad \frac{d^2f(x)}{dx^2} + \frac{df(x)}{dx} = g(f,x).$$

PDEs

Partial differential equations (PDEs)

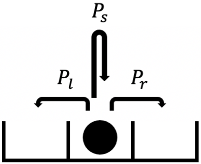
- continuous equations, deterministic
- contain one or more functions of **several** independent variables and the derivatives of those functions.
- track the change in a function with respect to the independent variables.
- useful for tissue level dynamics, whole populations.

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

$$\frac{\partial f(t,x,y)}{\partial t} = \frac{\partial^2 f(t,x,y)}{\partial x^2} + \frac{\partial^2 f(t,x,y)}{\partial y^2} + g(f,t,x,y)$$

Agent based models (also known as Individual based models)

- discrete models, generally stochastic.
- consider each particle/cell individually.
- agents react and interact according to a set of rules.
- can be based on a grid and can be probability based.
- useful for single cell, cellular level dynamics.



Hybrid Models

Hybrid or multiscale models may use multiple types of model within them, *e.g.*,

- ODEs to describe intracellular processes (mutation, activation, pathways)
- ABM to describe stochastic cell interactions (movement, adhesion)
- PDEs to describe continuous processes (oxygen, nutrients, chemicals)

Summary

Overview

- A mathematical model is description of a process or system using mathematical concepts.
- Mathematical models can be used for a wide variety of biological applications.
- Mathematical models can be beneficial when used in conjunction with experimental data.
- Model design and building is dependent on previous understanding and the available data.

Questions?