Vancouver Workshop 1

1.1: Why modelling?

- Used for testing hypotheses, extrapolate beyond experiment, and finding relative effects
- Mechanistic modelling uses knowledge and observation to build models based on assumptions

CAUTION: All modelling must be interpreted in context of assumptions

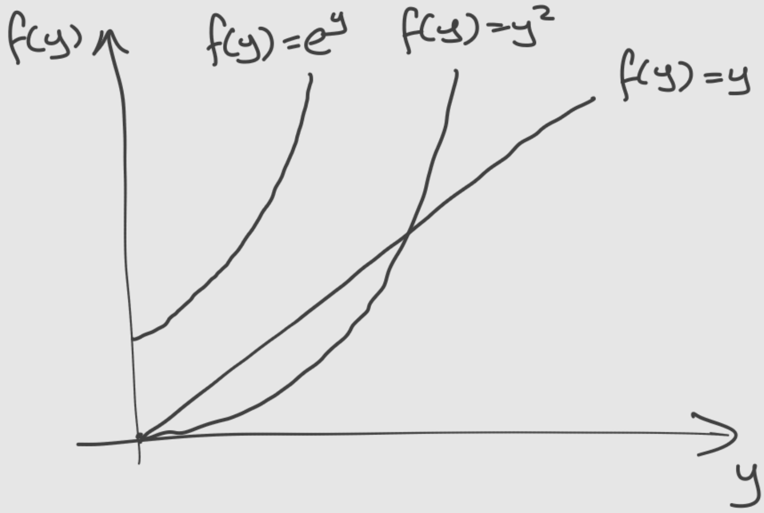
1.2: Mathematical foundations

Def$^{\underline{n}}$: Function

A function takes inputs (these will be numbers or variables) and changes them to something else. We write them as the following

$$\overbrace{f(y)}^{\text{Output}}$$

Function Input



$$\overbrace{g(\underbrace{y,t}_{\text{2 inputs}})}^{\text{output}}$$

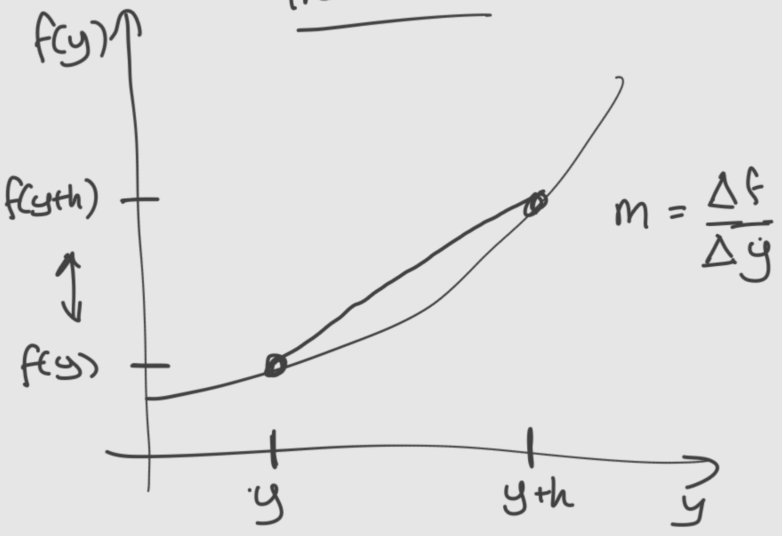
Function

Def$^{\underline{n}}$: Derivative

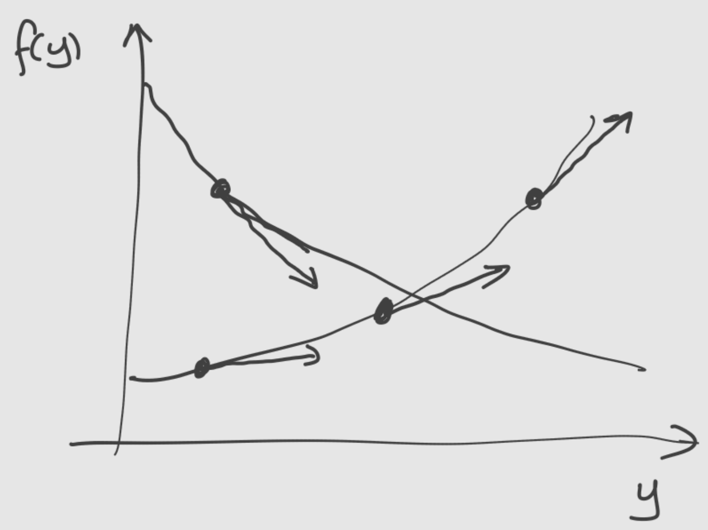
The derivative of a function f with respect to its input

y, denoted as $\frac{df}{dy}(y) = f'(y)$, is the gradient, or rate of change, of the function f at a position y.

Gradient



Derivative



$$\frac{df}{dy}(y) = \lim_{h \to 0} \left(\frac{f(y+h) - f(y)}{h} \right)$$

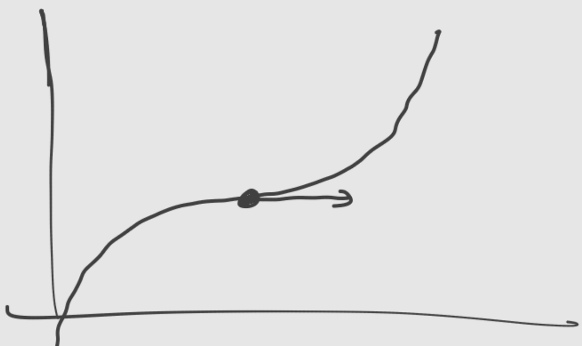
$$\boxed{M = \frac{f(y+h) - f(y)}{\underbrace{y+h-y}_{h}}}$$

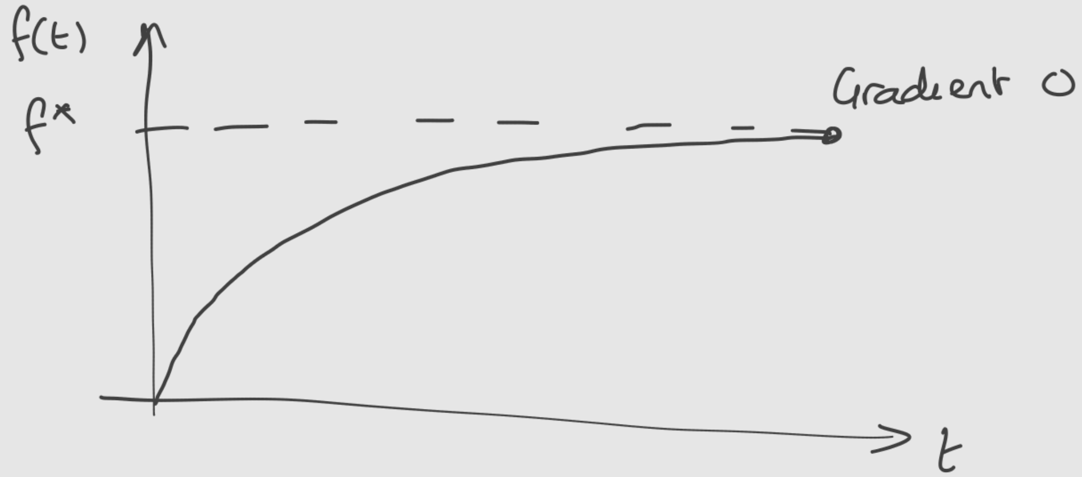
Def^n: State variable

State variable = dependent variable.

Def^n: Steady state / equilibrium

A value of a function where the derivative is 0.





1.2.2: Common modelling ideas

Occam's Razor

"If you have two competing explanations, the one with the fewest assumptions is likely correct".

I was taught KISS - Keep it simple stupid.

Law of Mass Action

The law of mass action says that the number of events caused by interaction with two types of species/agents/individuals is proportional to the product of the number of each.

e.g Infection through contact

S susceptible, I infected, # contacts $= SI$

Rates:

A rate tells us how fast something occurs. Alternatively, the inverse of a rate (rate r, inverse $1/r$) tells us the average length of time it takes for the event to occur.

$r = 0.5$ per year. $\rightarrow$ $\frac{1}{r} = 2$ years

1.3 : Mathematical Frameworks

1.3.1: Discrete vs continuous time

Discrete-time

Discrete time (DT) is useful for phenomena that change in generations. Suppose we want to measure the quantity of something labelled as X at a generation n, denoted as

$$X_n = (X(n))$$

We describe how one generation is generated from previous ones via a function f:

$$X_{n+1} = f(X_n, X_{n-1}, \ldots)$$

$$\underline{X_{n+1} = f(X_n)}, \qquad \underbrace{X_0}_{\text{Initial condition}} = x$$

These together form a difference equation (DE)

e.gs:
- Fibonacci numbers
- Beverton-Holt model

$\}$ (1.3.2)

Continuous time

For continuous time, $t > 0$, we again consider a quantity X at time t, denoted $X(t)$. Then we need an analogue for "the next generation" or a concept of "...

for the next generation", or a concept of "where we are going" $\rightarrow$ The derivative. (ordinary differential equations, ODEs)

$$\frac{dx}{dt}(t) = f(x(t)) \; ; \quad x(0) = x$$

$$x_{n+1} = f(x_n) \; ; \quad x_0 = x$$

e.g: • Exponential growth (1.3.3)
• Logistic growth (1.4.2)

1.3.2: Examples of DEs.

Fibonacci Numbers

Let F_n be the number of breeding pairs of rabbits in month n. Then

$$F_{n+1} = F_n + F_{n-1}$$
$$= f(F_n, F_{n-1}) \qquad F_0 = F_1 = 1$$

This has a solution

$$F_n = \frac{\varphi^n - (-\varphi)^{-n}}{\sqrt{5}}, \quad \varphi = \frac{1+\sqrt{5}}{2}.$$

Beverton-Holt model

A classical difference equation which has an equilibrium point called "environmental capacity"

$$x_{n+1} = f(x_n) = \frac{r x_n}{1 + x_n/M}. \qquad x_0 = x$$

This has a solution

$$X_n = \frac{M(r-1)x}{x + (M(r-1) - x)e^{-r}}$$

Environmental capacity is $R_0 = M(r-1)$

1.3.3: Exponential growth

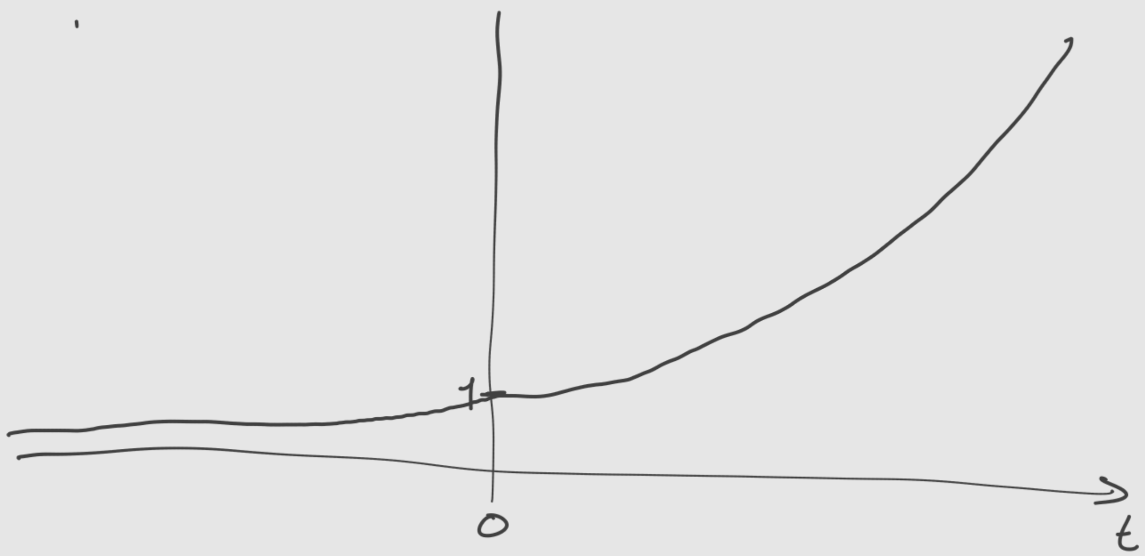
Consider a population denoted by X at a time $t>0$ that reproduces at a rate a, then

$$\frac{dX}{dt} = aX \quad , \qquad X(0) = x$$

This has a solution

$$X(t) = x\exp\{at\} = xe^{at}$$

A note on exp



This is exponential growth.

1.4: A one-dimensional example

1.4.1: An intro to assumptions

Biologically, suppose we want to investigate how the size of a population of sheep changes over time under only births and deaths.

We will make assumptions:

1) No host heterogeneity. All sheep are the same.
2) Births occur with a constant rate.
3) All sheep have the same expected life-span

We convert each of these into mathematical expressions

1) Label the population by N at continuous time t ($N(t)$)
2) Let the birth rate be b. Then the rate of change caused by births is an increase of $bN(t)$
3) Let $1/d$ be the average lifespan → death rate $= d$ and the rate of change caused by deaths is a decrease of $dN(t)$

Transfer diagram

Model:

$$\frac{dN}{dt} = bN - dN = \underbrace{(b-d)}_{a}N = aN$$

Solution

$$N(t) = N_0 \exp\{(b-d)t\}$$

If $b>d$, then $N(t) \to \infty$ as $t \to \infty$ ☹

1.4.2: Modifying a model

As with Occam's Razor, we have tried something simple, but it isn't working. → Increase complexity.

Revisit (2).

Instead of constant births, let births be density dependent.

We want, as the pop^n reaches some capacity, say K, births will decrease. Replace bN with $B(N)N$.

We want:

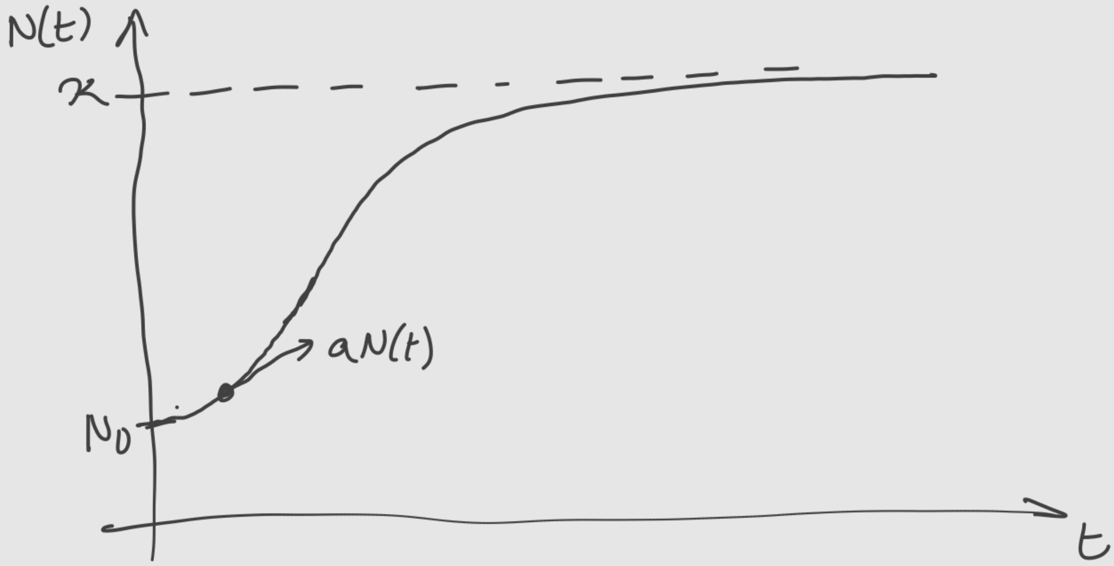
- If N is between 0 and K, $B(N)>0$
- If N is bigger than K, $B(N)<0$
- If N is K, $B(K)=0$

Simplest option, $B(N) = b\left(1-\frac{N}{K}\right)$

Incorporating into model

$$\begin{aligned}\frac{dN}{dt} &= B(N)N - dN \\ &= bN\left(1-\frac{N}{K}\right) - dN \\ &= aN\left(1-\frac{N}{\kappa}\right), \quad a = b-d, \quad \boxed{\kappa = \frac{K(b-d)}{b}}\end{aligned}$$

This is the <u>logistic equation</u>.



Solution:

$$N(t) = \frac{a\kappa N_0}{N_0 + (N_0 - a\kappa)e^{-at}}$$

$\beta_1 SI$ $\qquad\qquad$ $\beta_2 SI$

$\underbrace{(\beta_1 + \beta_2)}_{\beta} SI$ $\qquad\qquad$ $\beta S.$

X_n , $X(t)$

$n \rightarrow t_n = 0 + n\Delta t$

$$\left.\begin{aligned} M_{n+1} &= f(M_n, H_n) \\ H_{n+\frac{1}{2}} &= g(M_n, H_n) \\ H_{n+1} &= h(M_n, H_{n+1/2}, H_n) \end{aligned}\right\}$$

$$\frac{dM}{dt} = f(M, E, H)$$

$$\frac{dE}{dt} = g(M, E, H, t, T)$$

$$\frac{dH}{dt} = h(M, H)$$

$$N_{n+1} = b - dN_n$$

births generation

prob. of dying.

Vancouver workshop 2

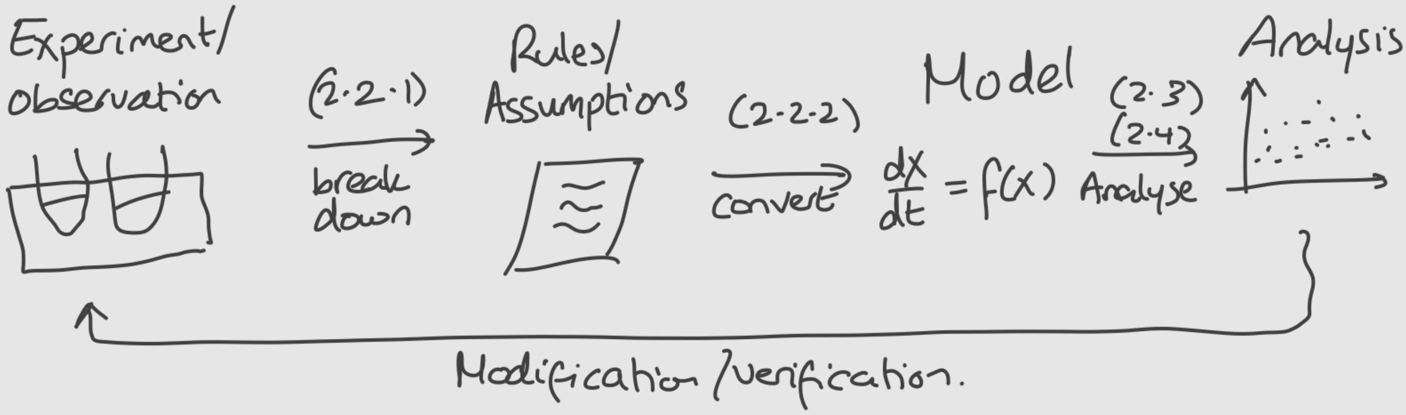
Mathematical assumptions and analysis

2.1 : Our example

"Consider a population of hosts which can be infected with a pathogen, which is only able to be transmitted through contact with infected individuals. The pathogen can be recovered from and can also cause death."

2.2 : Assumptions and mathematical formulation

We now go through the modelling process.



2.2.1 : From problem to assumption.

We break down the problem into small chunks.

1) contact w/ individuals ⟶ no vertical transmission ⟶ "all individuals are born susceptible to the pathogen"

2) Not described, but we introduce host (natural) mortality. This ensures turnover in population.

NOTE: These first two are not always necessary, especially if the modelling time frame is "small"

3) Pathogen recovery ⟶ include a recovery rate
we also need to assume at what happens on recovery.

- Become immune
- Temporary immunity

Require "immunity, recovered" state variable

• Temporary immunity

• Immediately susceptible

4) We have excess death → "virulence" term.

2.2.2 : From assumption to mathematics

STATE VARIABLES : $S(t)$ – Density (or number) of susceptible individuals at time $t>0$.

$I(t)$ – Density of infected individuals.

$N(t) = S(t) + I(t)$ – total density.

From now on, we will drop the (t).

1) All inds. born susceptible → increase in susceptible inds of $B(N)N$. Need to choose $B(N)$ [See (5)]

2) Background mortality – average lifespan of $1/d$ – death rate d → loss of susceptible and infected of dS or dI.

3) Recovery – time to recovery (on average) – $1/\gamma$ - recovery rate γ. Loss of γI from infected group and they appear in susceptible group

4) Excess mortality / virulence – rate α – loss of αI from I.

Extra assumptions

5) Choosing $B(N) = b\left(1-\frac{N}{K}\right)$ – b is maximum birth rate

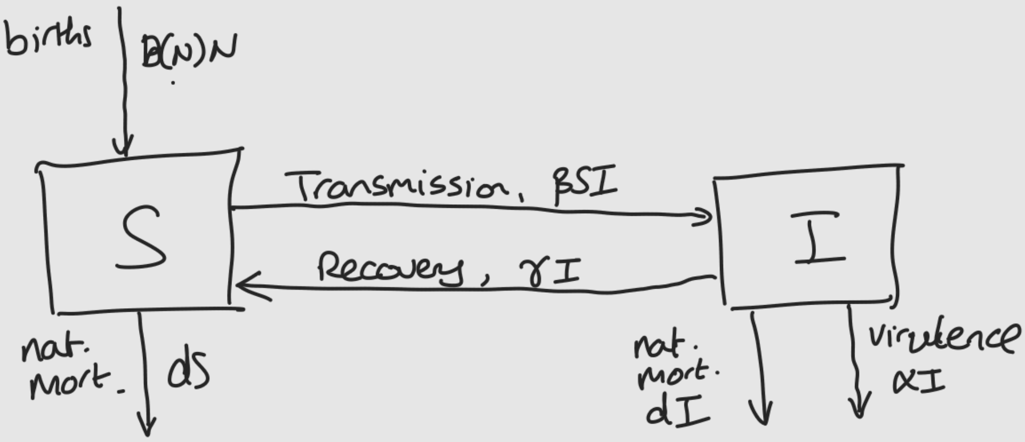
– K is environmental capacity.

6) Transmission – use the law of mass action

$S \longleftrightarrow I$ # of these is SI

Rate per infected individual of $\beta \rightarrow \beta S I$ transmission

<u>Transfer diagram</u>



2.<u>2.3</u>: Model formulation

$$\left.\begin{aligned} \frac{dS}{dt} &= B(N)N - dS \\ \frac{dI}{dt} &= -dI \end{aligned}\right\} \quad \begin{array}{l} \text{Assumptions} \\ (1) \,\&\, (2) \\ \text{Disease-free population} \end{array} \qquad (2.1)$$

From (2.1)

$$\left.\begin{aligned} \frac{dS}{dt} &= B(N)N - dS + \gamma I - \beta S I \\ \frac{dI}{dt} &= -dI - \gamma I - \alpha I + \beta S I \end{aligned}\right\}$$

<u>Tidying</u>:

$$\left.\begin{aligned} \frac{dS}{dt} &= bN\left(1 - \frac{N}{K}\right) - (d + \beta I)S + \gamma I \\ \frac{dI}{dt} &= \beta S I - (d + \gamma + \alpha) I \end{aligned}\right\} (2.2)$$

2.3: Analysis

Work with system (2.1).

We will look for steady states of (2.1). Solve for (S^*, I^*) such that the following hold simultaneously

$$0 = bN^*\left(1 - \frac{N^*}{K}\right) - dS^*$$

$$0 = -dI^*.$$

Since $d>0$ (finite lifespan), we must have $\underline{I^* = 0}$

With $I^*=0$ we simplify 1st equation

$$\underline{0} = b(S^*+I^*)\left(1 - \frac{S^*+I^*}{K}\right) - dS^*$$

$$\overset{(I^*=0)}{=} bS^*\left(1 - \frac{S^*}{K}\right) - dS^*$$

$$= S^*\left[b\left(1 - \frac{S^*}{K}\right) - d\right]$$

Either $S^* = 0 = I^* \rightsquigarrow (S^*, I^*) = (0,0)$ is a steady state

$\to$ extinction steady state

If $S^* \neq 0$

$$\Rightarrow b\left(1 - \frac{S^*}{K}\right) - d = 0$$

$$\rightsquigarrow S^* = \frac{K(b-d)}{b}$$

Second steady state $(S^*, I^*) = \left(\frac{K(b-d)}{b}, 0\right)$

Disease-free steady state.

Let $\frac{D}{N}$ be the prob of dying, d death rate (at a time T)

$$\frac{D}{N} = e^{-dT} \rightarrow d = \frac{-1}{T}\log\left(\frac{D}{N}\right)$$

Approximate Bayesian computation (ABC)