SFU SIMON FRASER UNIVERSITY

An introduction to epidemic modelling

made for EpiCoronaHack participants

by the MAGPIE research group

Why do we need math to fight infectious disease?

Two main goals:

1. **Understand disease dynamics** – what are the fundamental processes driving the spread of infection?
2. **Develop tools for forecasting and prediction** – what's going to happen next, as well as when, where and how?

We often ask questions such as:

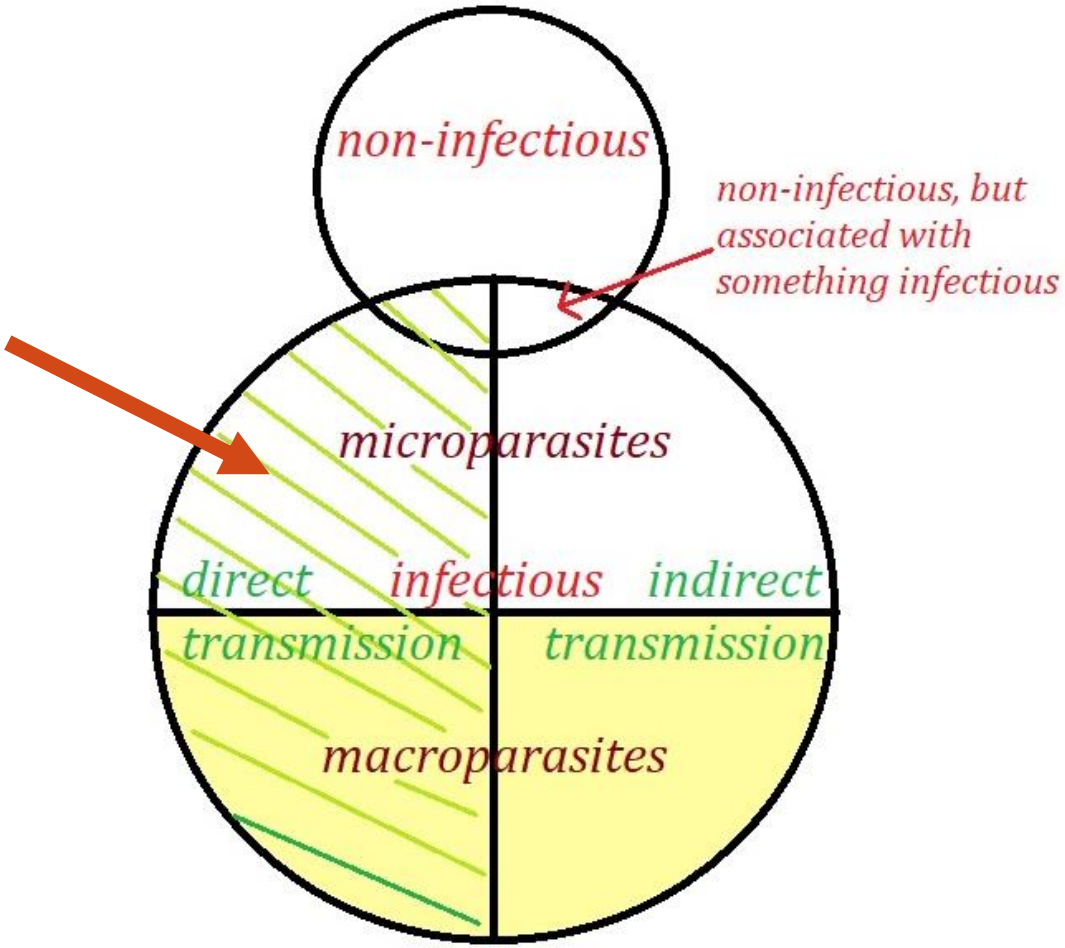
- How best can we control the spread of disease?
- How many people will get infected in an outbreak?
- What is the average length of time between getting infected and infecting others?
- On average, how many people will someone infect?
- What is the primary method of transmission?
- Should we quarantine infectives, and how?
- Could we eradicate the disease?

We can work with all types of infectious disease…

Hepatitis	Tuberculosis
Malaria	Cholera
Leprosy	HIV/AIDS
Influenza	Rabies
Measles	Dengue
Meningitis	Pneumonia
Rubella	Foot and Mouth disease
Ebola	Smallpox
Respiratory disease (colds)	and many more….

Not just human-human, but also between animals or vector borne diseases

A classification of diseases



Coronavirus
(mostly direct anyway)

Modelling Infectious Diseases In humans and animals
Matt J. Keeling and Pejman Rohani

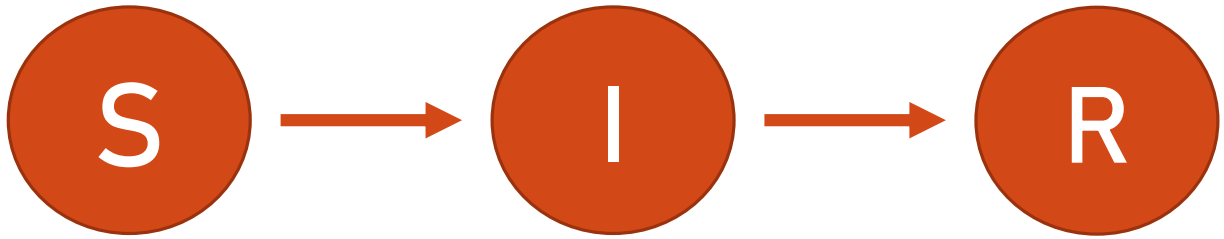
An example:

Polio eradication by the World Health Organisation

- The WHO began their campaign in 1988 – to eradicate Polio through vaccination campaigns, environmental monitoring and close evaluation of new cases.
- The Polio Global Eradication Initiative used mathematical modelling to identify the highest risk regions and also key factors leading to outbreaks
- Key measures now include regularly collecting sewage samples, and a focus on vaccination of young people
- In 2018, there were 33 diagnosed cases, compared to 350,000 in 1988

Compartmental models

We model the stages of a disease with compartmental models, such as the **SIR model**. Think of individuals flowing through these stages:



Susceptible

An uninfected individual, who may be infected by contact with anyone infectious

Infective

Someone who has been infected, and is now able to infect others

Removed

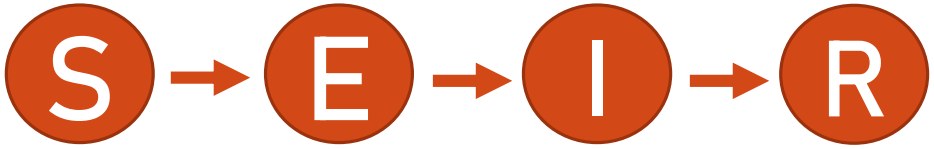
Someone who has recovered from the disease, and is now assumed to be immune

Compartmental models:

Lots of other compartmental models are used too e.g. …

Susceptible Infective Susceptible

Reinfection is possible here (recovered individuals do not have immunity)



Susceptible Exposed Infective Removed

In the exposed period, people are infected but not yet infectious (also known as a latent or incubation period)

Compartmental models

Our models must make approximations to reality, so that they are not too complex to work with. Often, we make assumptions such as:

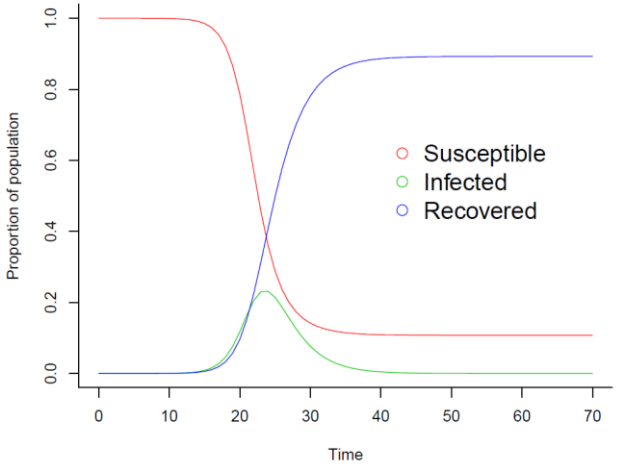
- Stable population size
- Stationary age distribution
- Homogeneous mixing of individuals -every individual has an equal chance of contacting any other individual
- No reinfection – recovered individuals have immunity or just realistically don't have time be infected again over the timescale of the outbreak

Some of these assumptions are more reasonable than others, and we have to develop more complex models when we think these assumptions are invalid.

Compartmental models

We want to describe the movement of individuals through these categories in time

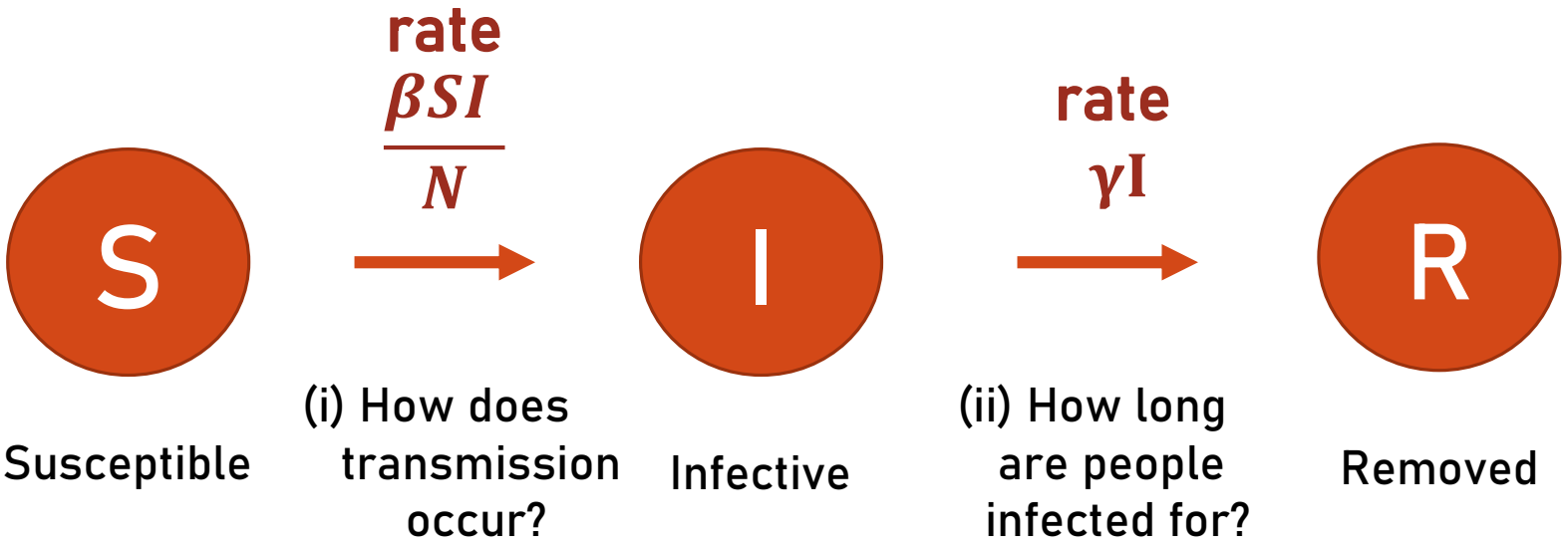
Functions S(t), I(t), R(t) will look something like:



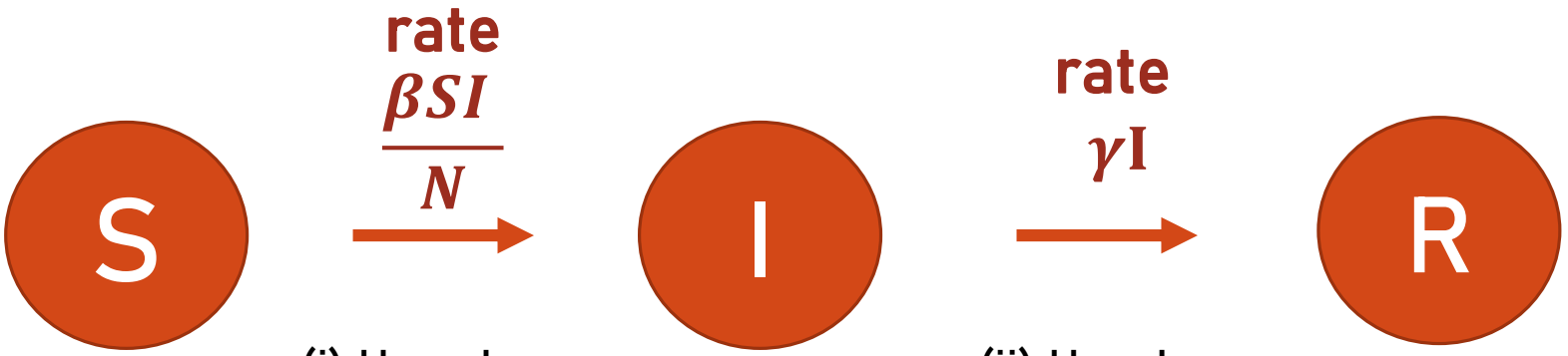
The exact shape of these curves will be determined by the level of disease infectivity and how quickly people recover.

Compartmental models: ODEs

We consider individuals as moving between compartments at the following rates:



Compartmental models: ODEs



β = infection rate
= (rate of contact between individuals)*(probability of transmission)

$\frac{\beta I}{N}$ is also known as the **force of infection** (for directly transmitting pathogens)

γ = removal/recovery rate
So,
$\frac{1}{\gamma}$ = average infectious period

Compartmental models: ODEs

We use ODEs to describe the movement of individuals between the compartments

$$\frac{dS}{dt} = -\frac{\beta SI}{N}$$

$$\frac{dI}{dt} = \frac{\beta SI}{N} - \gamma I$$

$$\frac{dR}{dt} = \gamma I$$

Compartmental models: ODEs

$$\frac{dS}{dt} = -\frac{\beta SI}{N}$$
$$\frac{dI}{dt} = \frac{\beta SI}{N} - \gamma I$$
$$\frac{dR}{dt} = \gamma I$$

However, in a closed population (known as the SIR model without demography), $S + I + R = N$, so we don't need the third equation.

Note: We sometimes think of S, I and R as the **proportions** of individuals in each category, and sometimes as the actual **number** in each category (in which case we scale by N, as here).

Compartmental models: ODEs

$$\frac{dS}{dt} = -\frac{\beta SI}{N}$$
$$\frac{dI}{dt} = \frac{\beta SI}{N} - \gamma I$$
$$\frac{dR}{dt} = \gamma I$$

Typical initial conditions are:

$$S(0) = N - 1$$
$$I(0) = 1$$
$$R(0) = 0$$

We assume that everyone is initially susceptible except for 1 initial infective.

Although this system of equations is very simple, we cannot obtain an exact analytical solution.

Compartmental models: ODEs

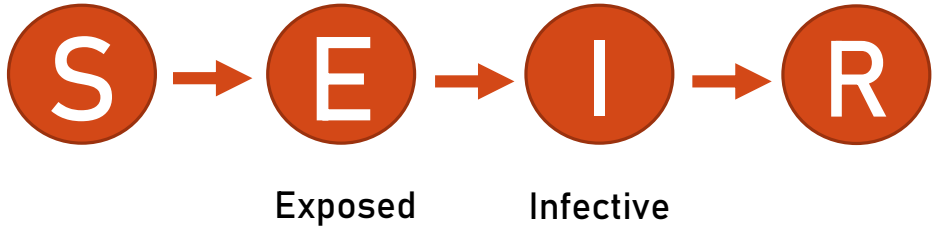
$$\frac{dS}{dt} = -\frac{\beta SI}{N}$$
$$\frac{dI}{dt} = \frac{\beta SI}{N} - \gamma I$$
$$\frac{dR}{dt} = \gamma I$$

This is known as the **deterministic** SIR model, since given a particular set of initial conditions we will always get the same model behaviour. It is also possible to write a **stochastic** SIR model, which introduces some randomness/noise to account for the randomness in real-life outbreaks

The general stochastic epidemic model

Stochastic compartmental models follow the same compartment structure, but describe individuals moving between compartments according to, in the case of the **general stochastic epidemic model**, Markovian (or other stochastic) processes. For example, the length of the infectious period is often assumed to be a random sample from an exponential distribution with rate γ (the same γ as in our ODEs). These lengths of time are independent and identically distributed for all individuals. Infection occurs according to 'infectious contacts' between infectives and susceptibles, which happen according to a Poisson process at rate β say (again, the same β as before).

SEIR models



SEIR models have mostly been used to model nCov-2019 so far, since it is believed to have an exposed/incubation period. The incubation period is defined as the length of time between a case being infected and becoming able to infect others. In practice, individuals are often assumed to become infective when they first show clinical symptoms, however this is not always the case.

In practice, the SEIR model has very similar behavior to the SIR model, but leads to a slower outbreak growth rate as individuals need to pass through the E class.

Within SIR, SEIR or any other compartmental models, we can also introduce sub-categories which allow for different behavior for e.g. age, workplace, health or any other factor we think may affect infectivity/susceptibility to the disease.

An important epidemic principle

Threshold parameter, R_0

Does an outbreak 'take off'?

$$\frac{dI}{dt} = I\left(\frac{\beta S}{N} - \gamma\right) < 0 \qquad \text{iff} \qquad \frac{S}{N} < \frac{\gamma}{\beta}$$

So, if the initial proportion of susceptibles $\frac{S(0)}{N} < \frac{\gamma}{\beta}$, the outbreak will fail to invade

We call $\frac{\beta}{\gamma}$ the basic reproductive ratio/basic reproduction number, R_0.

An important epidemic principle

Threshold parameter, R_0

$R_0 = \frac{\beta}{\gamma}$

= average number of secondary cases arising from an average primary case, in an entirely susceptible population

If $S(0) = N - 1$ (effectively, everyone is susceptible), we require $R_0 > 1$ for an outbreak to be expected to establish itself. If $R_0 < 1$, we can be sure the outbreak will die out.

An important epidemic principle

Threshold parameter, R_0

This is a widely used measure of the infectiousness of a disease, and can be compared between different diseases

Disease	R_0
Influenza	1-4 (different types)
Rabies (in dogs)	2.4
SARS	2-5
Chickenpox	10-12
Measles	16-18

An important epidemic principle

Threshold parameter, R_0

It is easy to misinterpret R_0 - remember that it represents the **average** number of secondary cases arising from an **average** primary case, in an **entirely susceptible population**

In reality, the number of secondary cases is often greatly reduced by

- Changes in behaviour – staying at home when ill reduces the number of people contacted
- Immunity – once many people are in the 'R' compartment, the chance of contacting a susceptible person greatly decreases

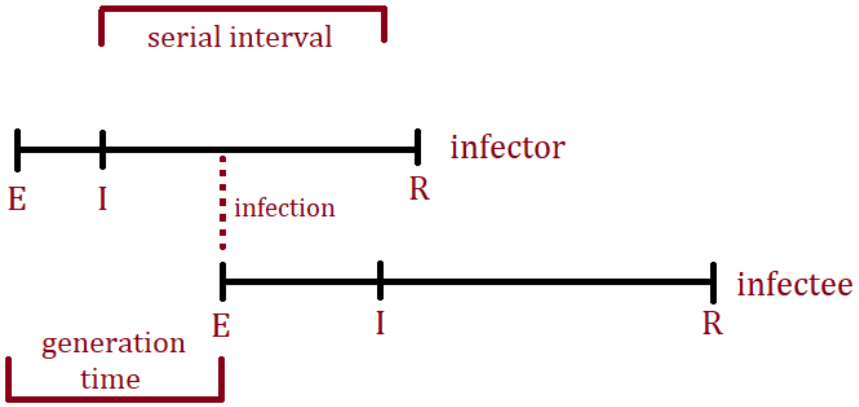
Effective reproduction number R_e

Because of these issues with interpreting R_0, we will often use the **effective reproduction number R_e** (sometimes written as simply R) instead. This is simply defined as:

$$R_e = R_0 * \mathrm{x}$$

where x is the fraction of the host population that is susceptible. The effective reproductive number is then the average number of secondary cases arising per primary case in a population made up of both susceptible and non-susceptible hosts. R_e will change over the course of an epidemic.

Generation time/ serial interval



Two final quantities of interest are the **generation time** and the **serial interval**. The generation time has origins in population biology, where it is defined as the average length of time between 2 generations of a population. Potentially confusingly, these 2 quantities are often defined as the same, and often differently!

For clarity here, we will define the serial interval as the time from onset of infectiousness in a primary case to onset of infectiousness in a secondary case infected by that primary case. (This accounts for incubation periods).

We define the generation time as the time from infection of a primary case to infection of a secondary case infected by that primary case. (In an SIR model with no incubation, the serial interval and the generation time are indeed then the same).

Generation times are often estimated by modelling outbreaks as branching processes (rather than using compartmental models), where branching events represent infection.