

## UNIT 8: Infectious disease

### 1 Introduction

#### Infectious disease

- Extremely common
- Huge impacts on ecological interactions
- A form of exploitation, but doesn't fit well into our previous modeling framework
  - How many people are there?
  - How many influenza viruses are there?
  - How do they find each other?

#### Disease agents

- Poll: Name an infectious agent that causes disease in humans.
- Disease agents vary tremendously:
  - Most **viruses** have just a handful of genes that allow them to hijack a cell and get it to make virus copies
    - \* **Answer:** influenza virus, Ebola virus, HIV, measles
  - **Bacteria** are independent, free-living cells with hundreds or thousands of chemical pathways
    - \* **Answer:** Tuberculosis, anthrax, pertussis
  - **Eukaryotic** pathogens are nucleated cells who are more closely related to you than they are to bacteria
    - \* **Answer:** Malaria, various worms

#### Microparasites

- For infections with small pathogens (viruses and bacteria), we don't attempt to count pathogens, but instead divide disease into stages
  - Latently infected
  - Productively infected
  - Recovered

## Microparasite models

- We model microparasites by counting the number of hosts in various **states**:
  - **Susceptible** individuals can become infected
  - **Infectious** individuals are infected and can infect others
  - **Resistant** individuals are not infected and cannot become infected
- More complicated models might include other states, such as latently infected hosts who are infected with the pathogen but cannot yet infect others

## Models as tools

- Models are the tools that we use to connect scales:
  - individuals to populations
  - single actions to trends through time

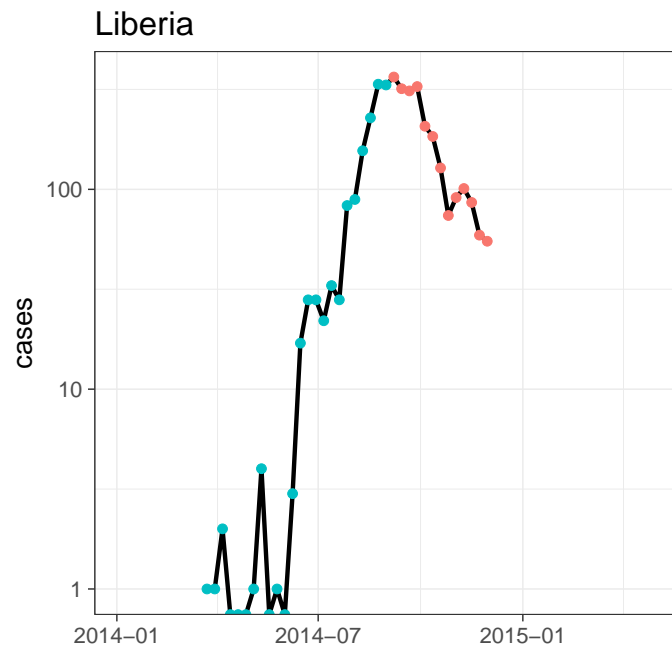
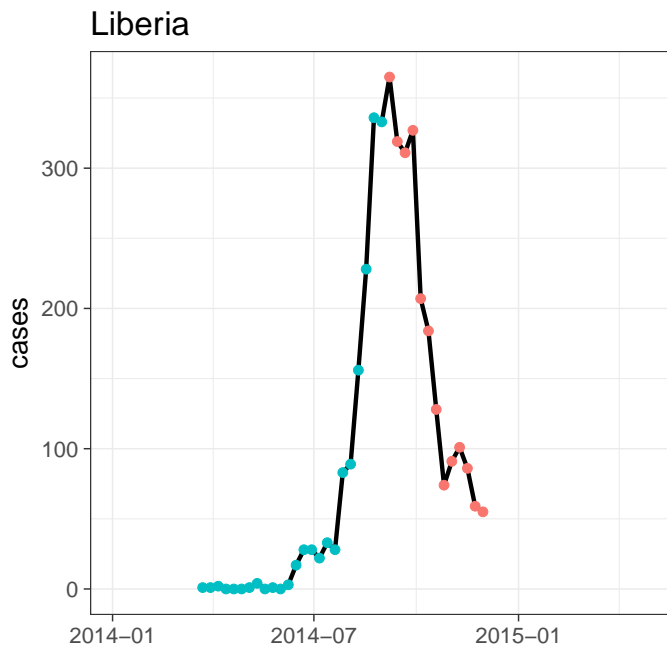
## 2 Rate of spread

- Poll: For many diseases, especially new diseases, we can *observe* and *estimate*  $r$ .
  - **Answer**: Instantaneous rate of increase (per capita)
    - \* **Answer**: Units of  $1/t$
    - \* **Answer**: Gives the exponential rate of spread
- Poll: Want to know what factors contribute to that, and how it relates to  $\mathcal{R}$ .
  - **Answer**: number of new cases per case
  - **Answer**: Unitless

## Basic reproductive number

- People in the disease field love to talk specifically about  $\mathcal{R}_0$
- But they don't always mean the same thing when they say  $\mathcal{R}_0$ :
  - Actual value of  $\mathcal{R}$  before an epidemic
  - Hypothetical value assuming no immunity
  - Hypothetical value assuming no immunity and no control efforts whatsoever
- Often easier to talk simply about  $\mathcal{R}$ .

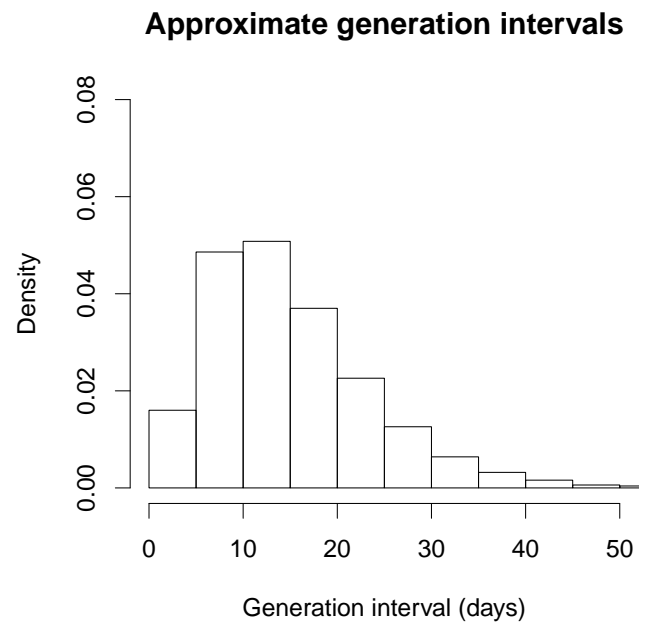
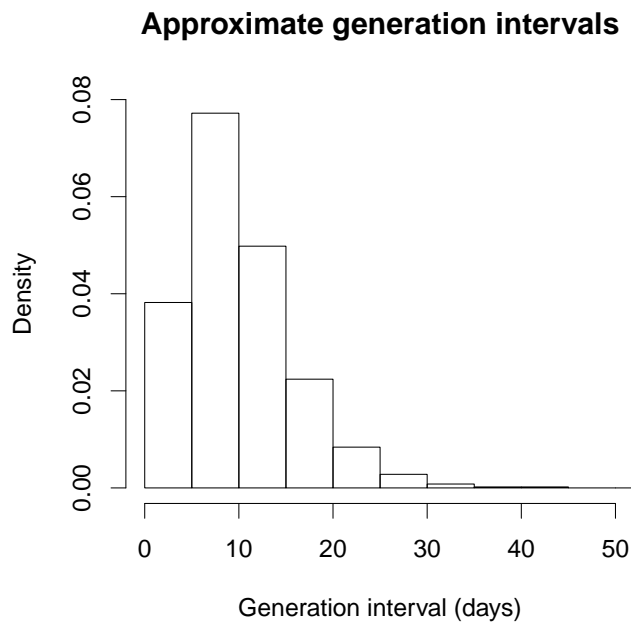
## Example: the West African Ebola epidemic



### Generation intervals

- Researchers try to estimate the *proportion* of transmission that happens for different **ages of infection**
- How long from the time you are *infected* to the time you *infect someone else*?
- Analogous to a life table
- The effective generation time  $\hat{G}$  has units of time

### Generation intervals



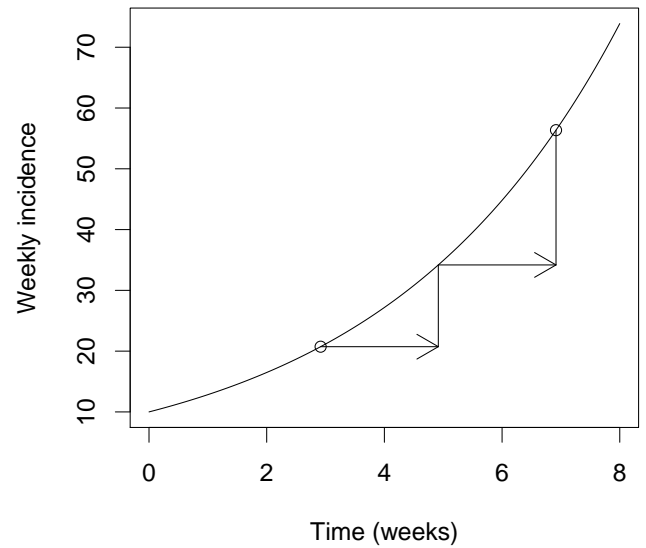
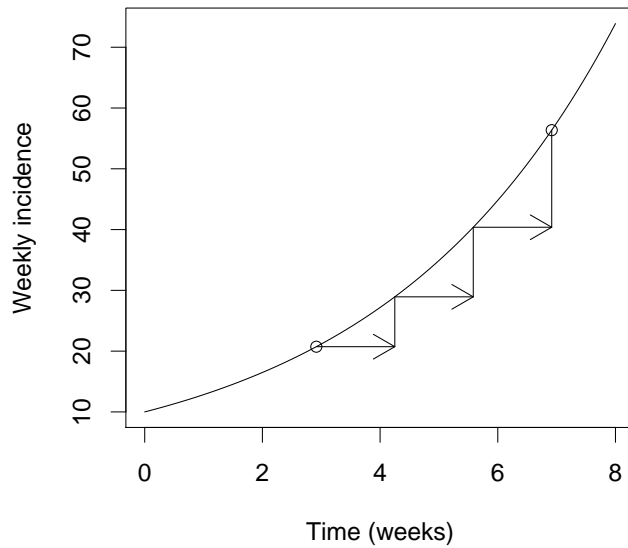
## Speed and risk

- Which is more dangerous, a fast disease, or a slow disease?
  - How are we measuring speed?
  - How are we measuring danger?
  - *What do we already know?*

## Generation time and risk

- If we know  $\mathcal{R}$ , what does the generation time tell us about  $r$ ?
  - **Answer:** The faster the generations (small  $\hat{G}$ ), the faster the exponential growth (large  $r$ )
- If we know  $r$ , what does the generation time tell us about  $\mathcal{R}$ ?
  - **Answer:** The faster the generations (small  $\hat{G}$ ), the the *smaller* the strength of the epidemic (small reproductive number  $\mathcal{R}$ )
- $\mathcal{R} = \exp(r\hat{G})$

## Generation time and risk



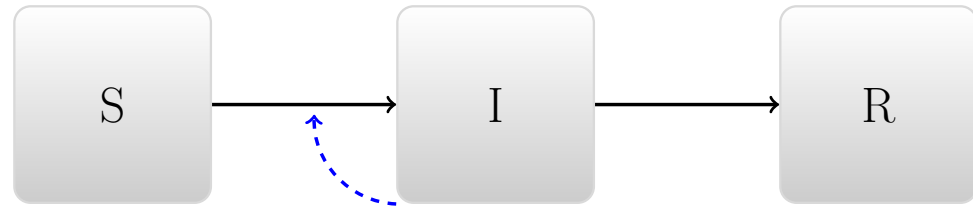
## Generation time and risk

- $\mathcal{R} = \exp(r\hat{G})$
- An intuitive view:
  - Epidemic speed = Generation strength  $\times$  Generation speed
  - Comment: Mathematically:  $r = \log(\mathcal{R}) * (1/\hat{G})$
- If we know generation speed, then a faster epidemic speed means:
  - **Answer**: More strength required (greater  $\mathcal{R}$ )
- If we know epidemic speed, a faster generation speed means
  - **Answer**: Less strength required (smaller  $\mathcal{R}$ )

## 3 Single-epidemic model

- Susceptible  $\rightarrow$  Infectious  $\rightarrow$  Recovered
- We also use  $N$  to mean the total population

## Transition rates



- What factors govern movement through the boxes?
  - People get better independently
  - People get infected by infectious people

## Conceptual modeling

- Poll: What happens in the long term if we introduce an infectious individual?
  - Answer: The *may be* an **epidemic** – an outbreak of disease
  - Answer: Disease burns out
  - Answer: Everyone winds up either recovered or susceptible
  - Answer: Not everyone gets infected!

## Interpreting

- Why might there not be an epidemic?
  - Answer: If the disease can't spread well enough in the population
    - \* Answer: Could depend on season, or immunity ...
  - Answer: Demographic stochasticity: if we only start with one individual, we expect an element of chance
- Why doesn't everyone get infected?
  - Answer postponed:

## Implementing the model

- The simplest way to implement this conceptual model is with differential equations:

$$\begin{array}{l} - \\ - \\ - \\ - \end{array} \quad \begin{array}{l} \frac{dS}{dt} = -\beta \frac{SI}{N} \\ \frac{dI}{dt} = \beta \frac{SI}{N} - \gamma I \\ \frac{dR}{dt} = \gamma I \\ N = S + I + R \end{array}$$

## Quantities

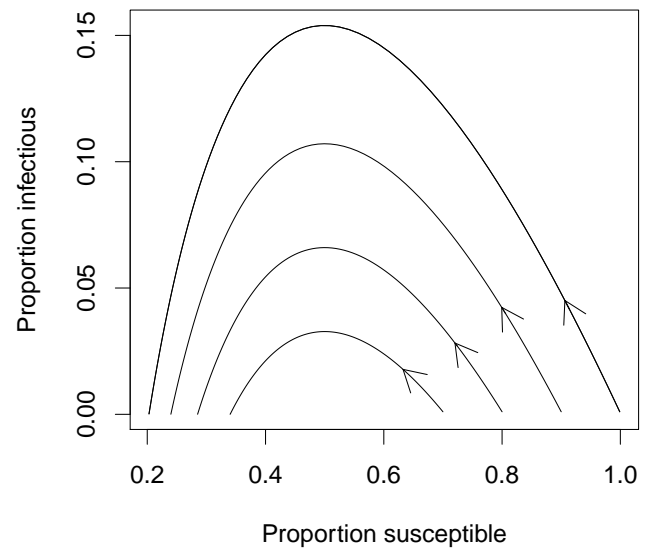
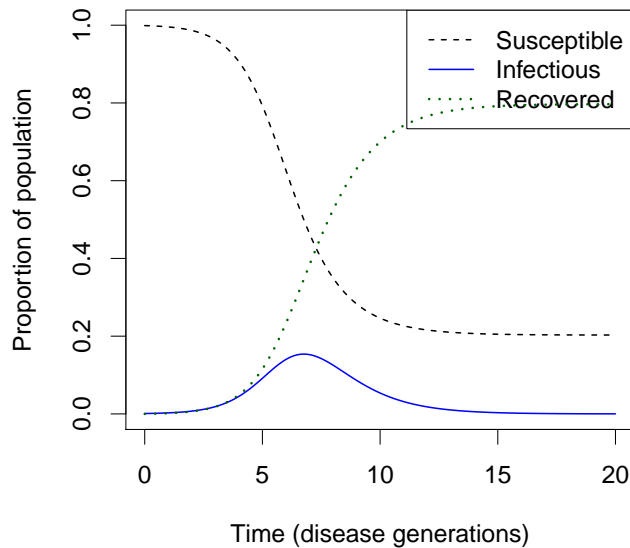
State variables

- $S, I, R, N$ : [people] or [people/ha]

Parameters

- Susceptible people have **potentially effective** contacts at rate  $\beta$  (units [1/time])
  - These are contacts that would lead to infection if the person contacted is infectious
  - Total infection rate is  $\beta I/N$ , because  $I/N$  is the proportion of the population infectious
- Infectious people recover at *per capita* rate  $\gamma$  (units [1/time])
  - Total recovery rate is  $\gamma I$
  - Mean time infectious is  $D = 1/\gamma$  (units [time])

## Simulating the model



## Basic reproductive number

- Poll: What *unitless* parameter can you make from the model above?
  - **Answer:**  $\mathcal{R}_0 = \beta D = \beta/\gamma$  is the **basic reproductive number**
  - **Answer:** The *potential* number of infections caused by an average infectious individual
    - \* **Answer:** That is: the number they would cause on average if everyone else were susceptible
  - **Answer:** The product of the rate  $\beta$  (units  $[1/t]$ ) and the duration  $D$  ( $[t]$ )

## Basic reproductive number implications

- Poll: What happens early in the epidemic if  $\mathcal{R}_0 > 1$ ?
  - **Answer:** Number of infected individuals grows exponentially
- What happens early in the epidemic if  $\mathcal{R}_0 < 1$ ?
  - **Answer:** Number of infected individuals does not grow (disease cannot invade)

## Effective reproductive number

- The effective reproductive number gives the number of new infections per infectious individual in a partially susceptible population:
  - **Answer:**  $\mathcal{R}_e = \mathcal{R}_0 S/N$
- Is the disease increasing or decreasing?



- **Answer:** It will increase when  $\mathcal{R}_e > 1$  (more than one case per case)
- **Answer:** This happens when  $S/N > 1/\mathcal{R}_0$
- Why doesn't everyone get infected?
  - **Answer:** When susceptibles are low enough  $\mathcal{R}_e < 1$
  - **Answer:** When  $\mathcal{R}_e < 1$ , the disease dies out on its own (less than one case per case)

### 3.1 Epidemic size

- In this model, the epidemic always burns out
  - No source of new susceptibles
- Epidemic size is determined by:
  - **Answer:**  $\mathcal{R}_0$ – larger  $\mathcal{R}_0$  leads to a bigger epidemic
  - **Answer:** The number of susceptibles at the beginning of the epidemic
    - \* **Answer:** More susceptibles leads to a bigger epidemic
    - \* **Answer:** ...and *fewer* susceptibles at the end
  - **Answer:** The number of infected individuals at the beginning of the epidemic
    - \* **Answer:** Usually relatively small (and a relatively small effect)

### Overshoot

- Why does more susceptibles at the beginning mean fewer susceptibles at the end?
  - **Answer:** More susceptibles  $\implies$
  - **Answer:** Faster initial growth  $\implies$
  - **Answer:** Bigger epidemic  $\implies$
  - **Answer:** More infections at peak (same number of susceptibles)  $\implies$
  - **Answer:** More generations needed for disease to fade out  $\implies$
  - **Answer:** More infections after peak ...

### Ebola example

- In September, the US CDC predicted “as many as” 1.5 million Ebola cases in Liberia by January
- In fact, their model predicted many *more* cases than that by April
- What happened?

## What limits epidemics?

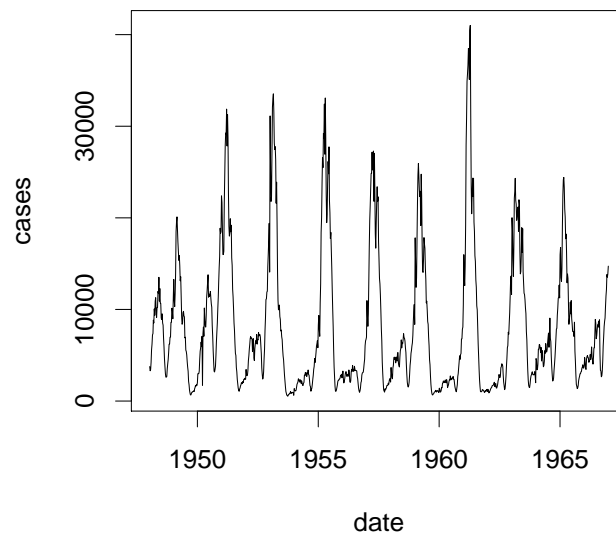
- Poll: What limits epidemics in our simple models?
  - Answer: Depletion of susceptibles
- Poll: What else limits epidemics in real life?
  - Answer: Interventions
  - Answer: Behaviour change
  - Answer: Heterogeneity (differences between hosts, locations, etc.)

## 4 Recurrent epidemic models

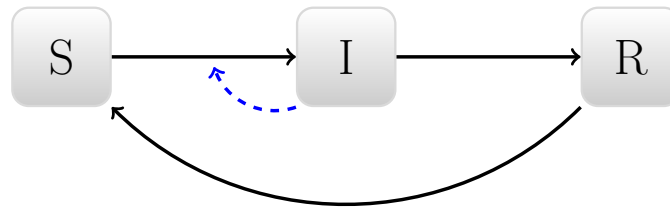
- Poll: If epidemics tend to burn out, why do we often see repeated epidemics?
  - Answer: People might lose immunity
  - Answer: Births and deaths; newborns are susceptible

### Recurrent epidemics

**Measles reports from England and Wales**

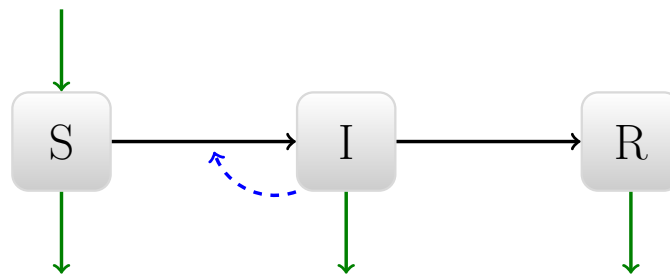


Closing the circle



- Answer: Loss of immunity

Closing the circle



- Answer: Births and deaths
  - Answer: Effect on dynamics is similar to loss of immunity

Births and deaths

•

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

•

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

- 

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

- We often assume  $b = d$ 
  - $\implies$  population is constant

## 4.1 Dynamics

### Equilibrium

- At equilibrium, we know that  $\mathcal{R}_e = 1$ 
  - One case per case
  - Number of susceptibles at equilibrium determined by the number required to keep infection in balance
    - \*  $S/N = 1/\mathcal{R}_0$
- What does this remind you of?
  - **Answer:** Reciprocal control!
- Number of infectious individuals determined by number required to keep susceptibles in balance.
- As susceptibles go up, what happens?
  - Per capita replenishment goes down
  - Infections required goes down

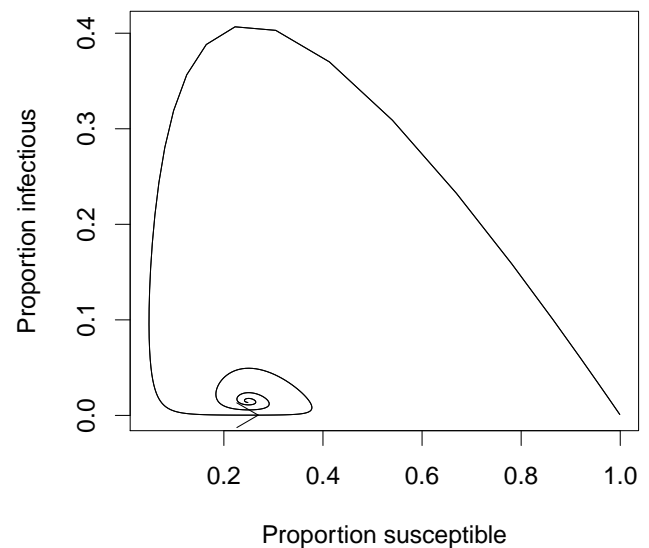
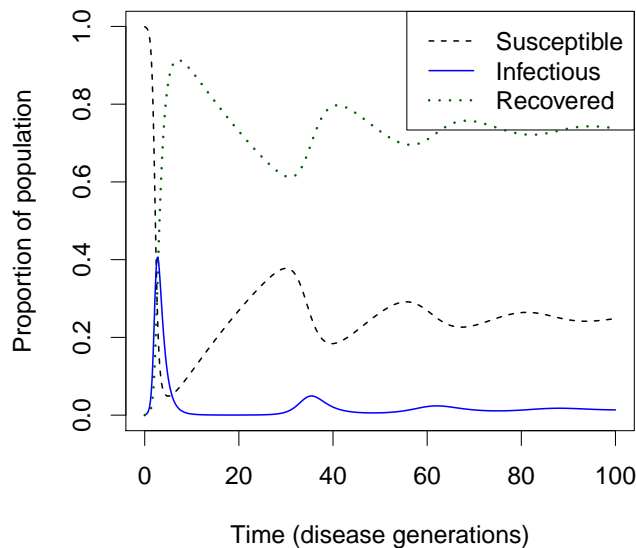
### Reciprocal control

- What happens to *equilibrium* if we protect susceptibles (move them to  $R$  class)?
  - **Answer:** Equation for  $dI/dt$  does not change
  - **Answer:** Number of susceptibles does not change
  - **Answer:** Fewer susceptibles need to be removed by infection (some are removed by us)
  - **Answer:** Number of infectious individuals goes down
- What else could happen?
  - **Answer:** If we remove susceptibles fast enough, infection could go extinct
  - **Answer:** If we keep increasing the rate ...
    - \* **Answer:** Number of susceptibles goes down

## Reciprocal control

- Poll: What happens if we remove infectious individuals at a constant rate (find them and cure them or isolate them)?
  - Answer: We need more susceptibles to balance  $dI/dt$
  - Answer: If we have more susceptibles, then per capita replenishment goes down
    - \* Answer: So the number of infectious individuals required for balance goes down
  - Answer: If we remove infectious individuals fast enough, the infection could go extinct

## Tendency to oscillate



## Tendency to oscillate

- “Closed-loop” SIR models (ie., with births or loss of immunity):
  - Tend to oscillate
  - Oscillations tend to be damped
    - \* System reaches an **endemic** equilibrium – disease persists

## Source of oscillations

- Similar to predator-prey systems
- What happens if we start with too many susceptibles?
  - Answer: There will be a big epidemic

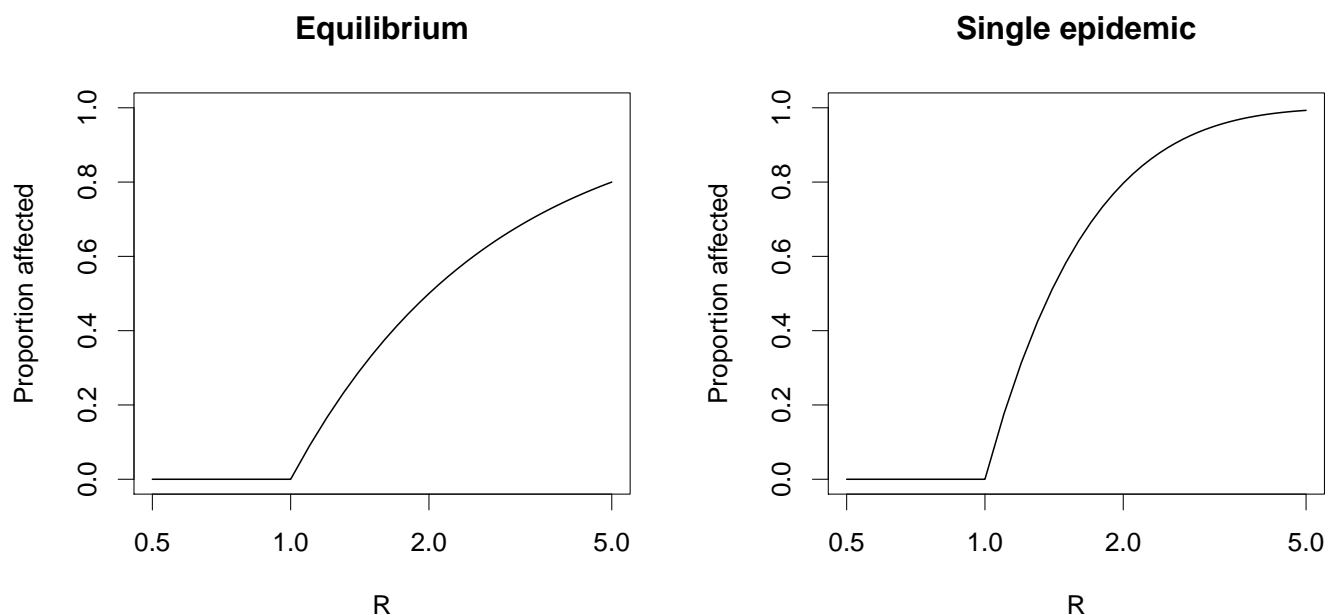
- **Answer:** ...then a very low number of susceptibles
- **Answer:** ...then a very low level of disease
- **Answer:** ...then an increase in the number of susceptibles

## Persistent oscillations

- Poll: If oscillations tend to be damped in simple models, why do they persist in real life?
  - **Answer:** Weather
    - \* **Answer:** Seasonality
    - \* **Answer:** Environmental stochasticity
  - **Answer:** School terms
  - **Answer:** Demographic stochasticity
  - **Answer:** Changes in Behaviour
    - \* **Answer:** People are more careful when disease levels are high

## 5 Reproductive numbers and risk

- At equilibrium, the proportion of people who are susceptible to disease should be approximately  $S/N = 1/\mathcal{R}_0$
- Proportion “affected” (infectious or immune) should be approximately  $V/N = 1 - 1/\mathcal{R}_0$
- If you have a single, fast epidemic, the size is also predicted by  $\mathcal{R}_0$ .



## Examples

- Ronald Ross predicted 100 years ago that reducing mosquito densities by a factor of 5 or so would *eliminate* malaria
- Gradual disappearance of polio, typhoid, etc., without risk factors going to zero
- Eradication of smallpox!

## Threshold for elimination

- What proportion of the population should be vaccinated to eliminate a disease?
  - **Answer:** Transmission should be reduced by a factor of  $\mathcal{R}$ , so at least fraction  $1 - 1/\mathcal{R}$  should be vaccinated

## Examples:

- Polio has an  $\mathcal{R}_0$  of about 5.
  - **Answer:** At least  $1 - 1/5 = 80\%$
- Measles has an  $\mathcal{R}_0$  of about 20. What proportion of the population should be vaccinated to eliminate measles?
  - **Answer:** At least  $1 - 1/20 = 95\%$
- If gonorrhea has an  $\mathcal{R}_0$  of about 2, what proportion of unprotected sexual encounters should be protected to eliminate gonorrhea?
  - **Answer:** At least  $1 - 1/2 = 50\%$

## Persistence of infectious disease

- Why have infectious diseases persisted?
  - The pathogens *evolve*
  - Human populations are **heterogeneous**
    - \* People differ in: nutrition, exposure, access to care
  - Information and misinformation
    - \* Vaccine scares, trust in health care in general

## Heterogeneity and persistence

- Heterogeneity *increases*  $\mathcal{R}_0$ 
  - When disease is rare, it is concentrated in the most vulnerable populations
    - \* Cases per case is high
    - \* Elimination is harder
- Marginal populations
  - Heterogeneity could make it easier to concentrate on the most vulnerable populations and eliminate disease
  - Humans rarely do this, however: the populations that need the most support typically have the least access