

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

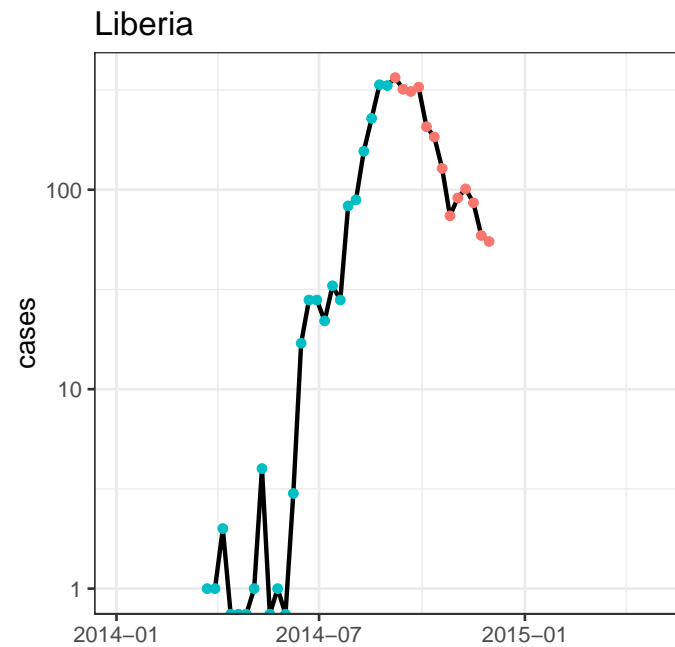
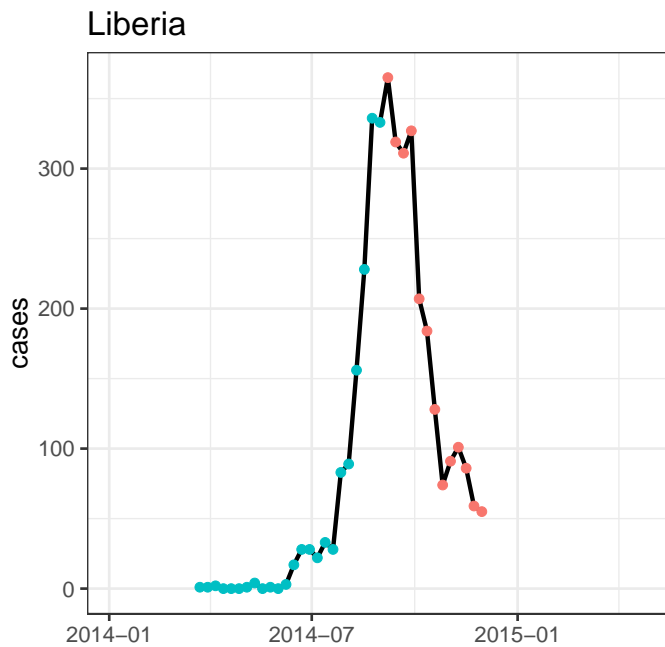
2 Rate of spread

- 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} .

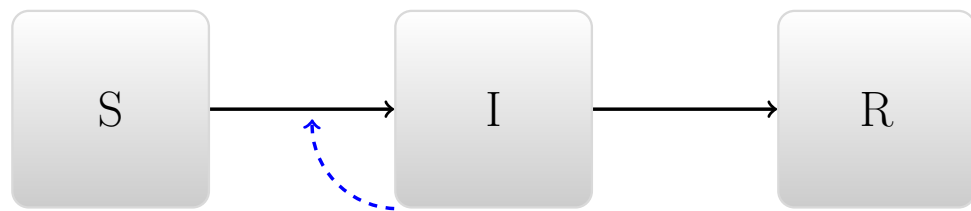
Example: the West African Ebola epidemic



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:

Quantities

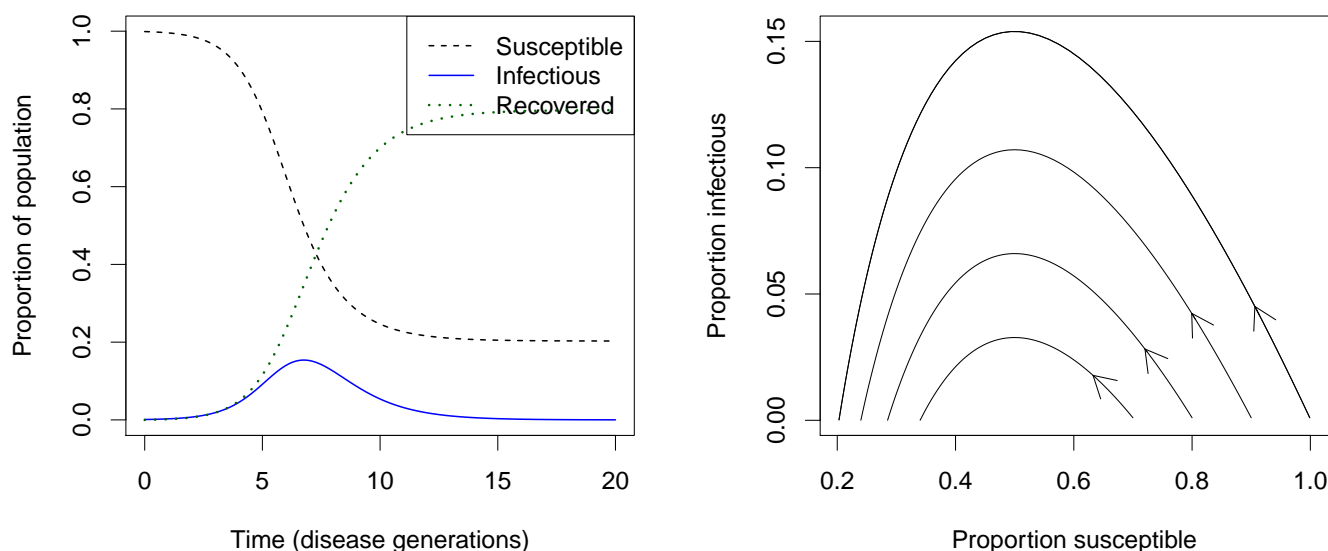
State variables

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

Parameters

- Susceptible people have **potentially effective** contacts at rate β (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 γ (units [1/time])
 - Total recovery rate is γI
 - 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 β (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

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?

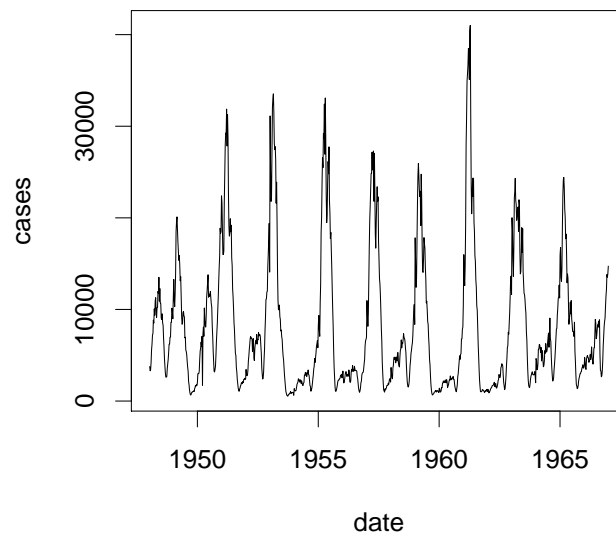
- Poll: What limits epidemics in our simple models?
 - Answer: Depletion of susceptibles
- Poll: What else limits epidemics in real life?
 - Answer: Interventions
 - Answer: Behaviour change
 - Answer: Heterogeneity (differences between hosts, locations, etc.)

4 Recurrent epidemic models

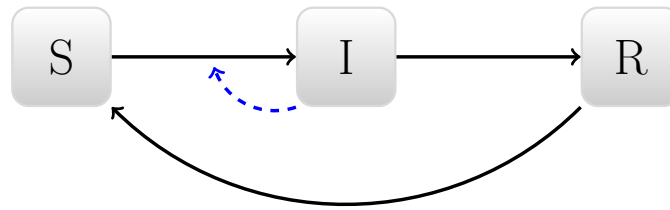
- Poll: If epidemics tend to burn out, why do we often see repeated epidemics?
 - Answer: People might lose immunity
 - Answer: Births and deaths; newborns are susceptible

Recurrent epidemics

Measles reports from England and Wales

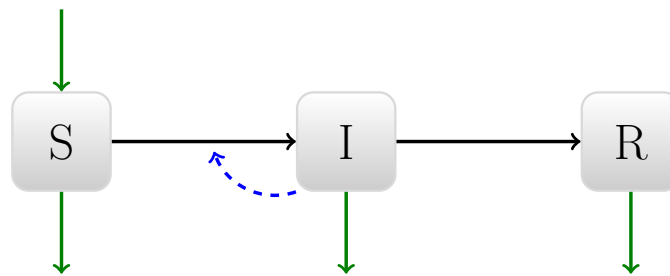


Closing the circle



- Answer: Loss of immunity

Closing the circle



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

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

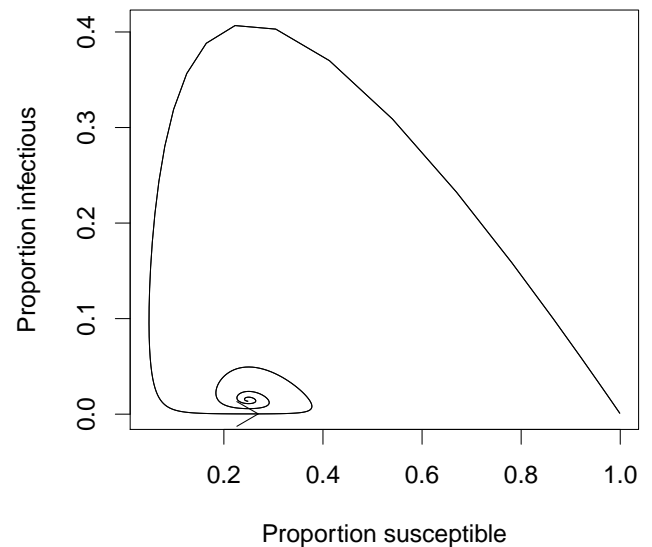
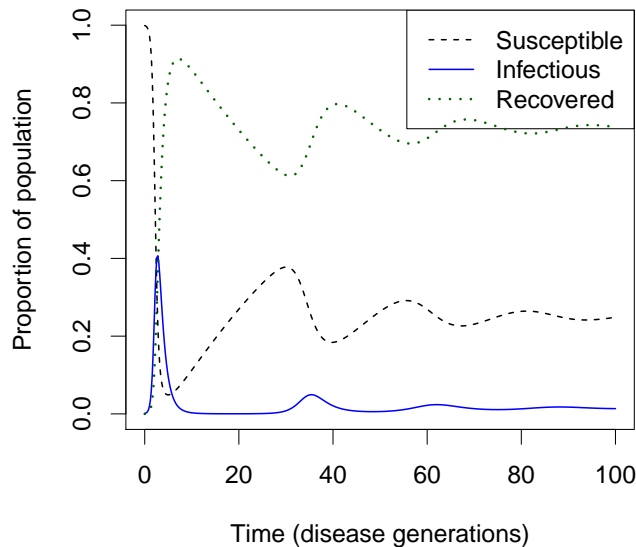
Reciprocal control

- 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 at equilibrium does not change
 - **Answer:** Fewer susceptibles removed by infection (some are removed by us)
 - **Answer:** Less disease
- 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

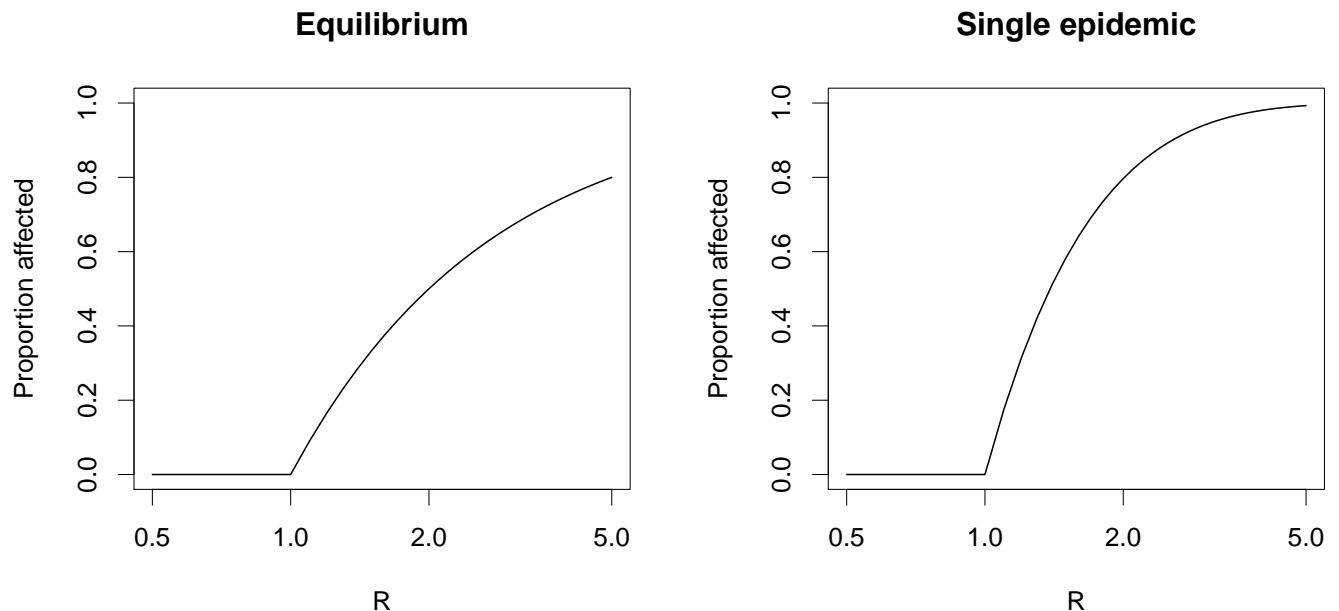
Persistent oscillations

- 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.
 - Poll: What proportion of the population should be vaccinated to eliminate polio?
 - **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