Dynamical models of infectious-disease spread

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NCTS Infectious Disease Workshop
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Goals

- This lecture will:
  - discuss the basic concepts of dynamical modeling
  - explain why dynamical modeling is a key tool for understanding infectious disease
  - discuss and demonstrate simple dynamical models from the SIR model family
  - investigate some insights that can be gained from these models


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Outline

Dynamical modeling

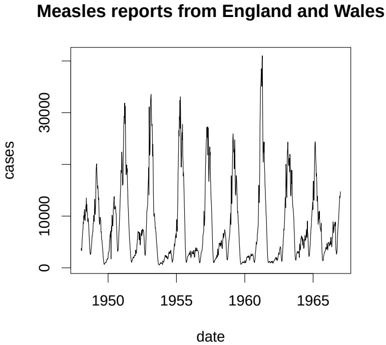
Modeling approaches

- Conceptual modeling
- Deterministic models
- Stochastic models
- Statistical fitting

Limitations

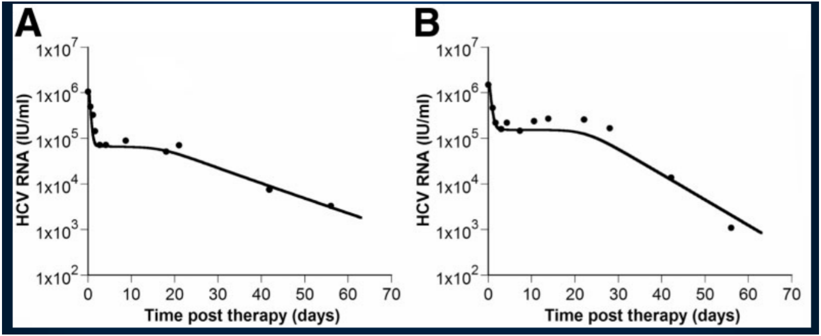
- Heterogeneity
- Behavioural changes

Dynamical modeling connects scales



- Start with rules about how things change in short time steps
  - Usually based on *individuals*
- Calculate results over longer time periods
  - Usually about *populations*
- Also known as "mechanistic" or "mathematical"

Example from yesterday



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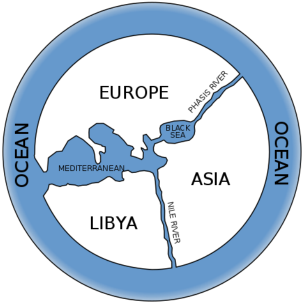
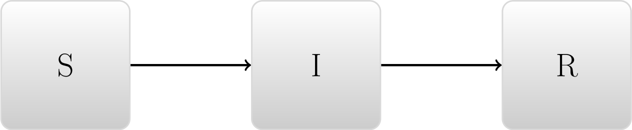
Model worlds

- A dynamical model is based on a model world
- The model world has *enough* assumptions to allow us to calculate dynamics
- The model world is *simpler* than the real world
- Essentially, all models are wrong, but some are useful. – Box and Draper (1987), *Empirical Model Building* ...



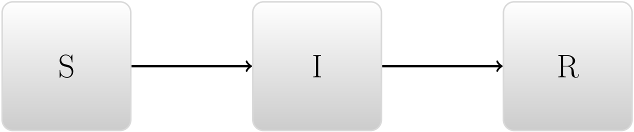
Simple models of disease spread

- Divide people into categories:

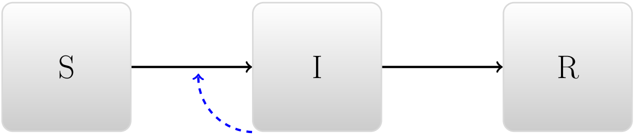


- Susceptible: can be infected
- Infectious: can infect others
- Recovered: cannot be infected

What determines transition rates?



What determines transition rates?



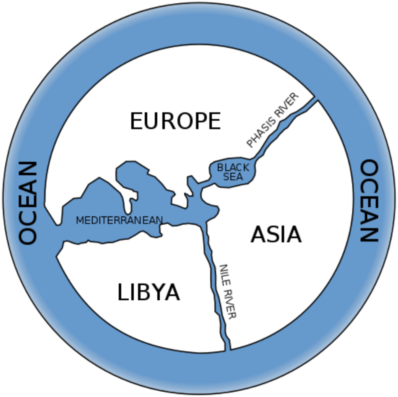
- People get better independently
- People get infected by infectious people

Outline

Outline

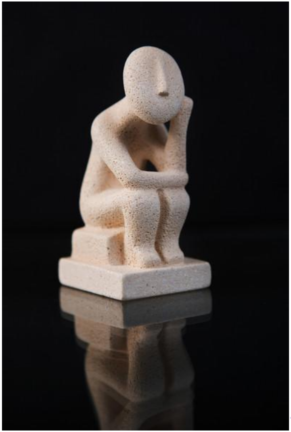
Conceptual modeling

$$\begin{tikzcd} \mathrm{S} \arrow[r] & \mathrm{I} \arrow[r] & \mathrm{R} \end{tikzcd}$$

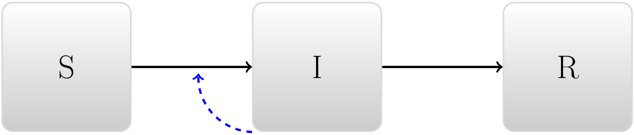


Conceptual modeling

$$S \longrightarrow I \longrightarrow R$$



Conceptual modeling



- What is the final result?
- How do disease levels change?
- When does disease increase, decrease?

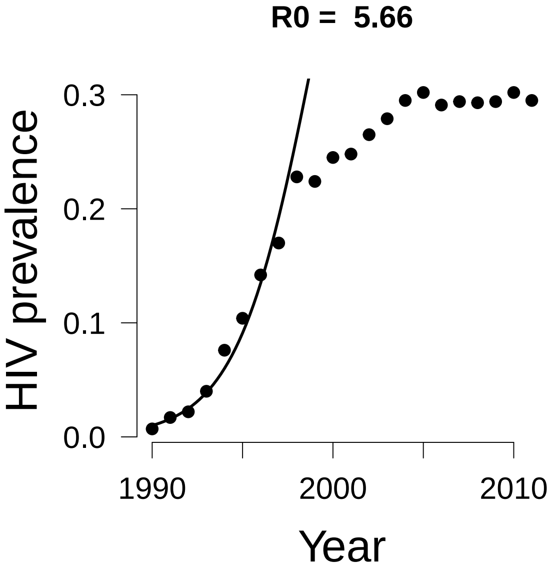
Result: change tends to be exponential

- The number of people recovering or becoming infected is *proportional* to the number infected
  - I infect three people, they each infect 3 people ...
  - How fast does disease grow?
    - Rate of exponential growth r
  - How quickly do we need to respond?

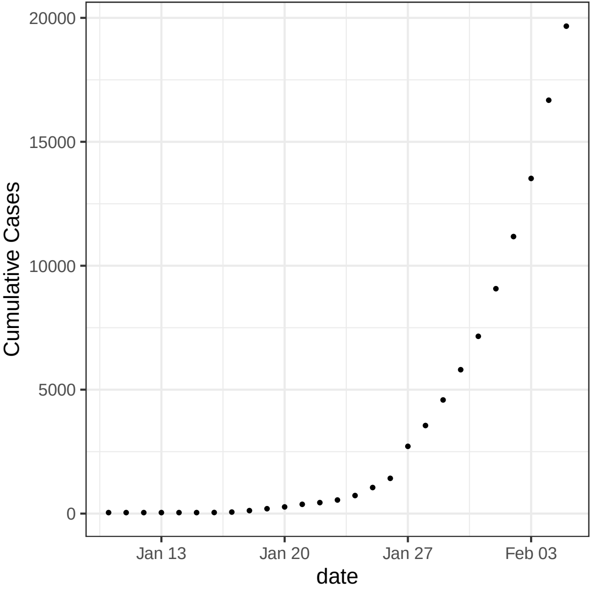
little r

- We measure epidemic *speed* using little r:
  - *Units*: $[1/\text{time}]$
  - Disease increases like e^{rt}
- Characteristic time scale is $C = 1/r$
  - COVID, $C \approx 1\text{month}$
  - HIV in SSA, $C \approx 18\text{month}$
  - Doubling time is $0.69C$
- Often focus on initial period (may also say r_0)

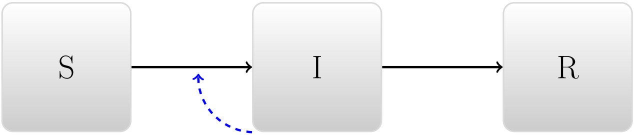
Exponential growth (HIV in Africa)



Exponential growth (COVID 2020)



Result: disease does not always spread

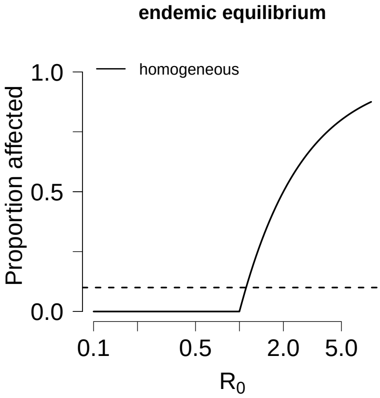


- If rate out of I is faster than the rate into I
- I $\to$ 0 and the outbreak stops

Concept: reproductive number

- $\mathcal{R}$ is the number of people who would be infected by an infectious individual
- $\mathcal{R} = \beta/\gamma = \beta D = (cp)D$
  - c: Contact Rate
  - p: Probability of transmission (infectivity)
  - D: Average duration of infection
- A disease can invade a population if and only if $\mathcal{R} > 1$.
- We say $\mathcal{R}_0$ for the initial period, or a fully susceptible population.

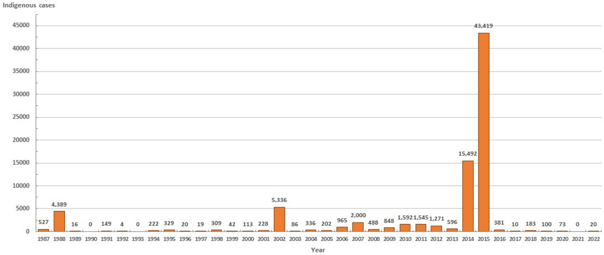
Yellow fever in Panama



Example: Dengue (Taiwan CDC) 登革熱

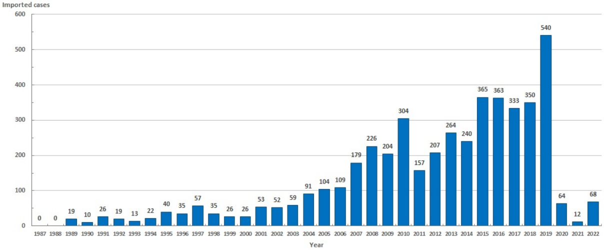
Indigenous cases

40,000

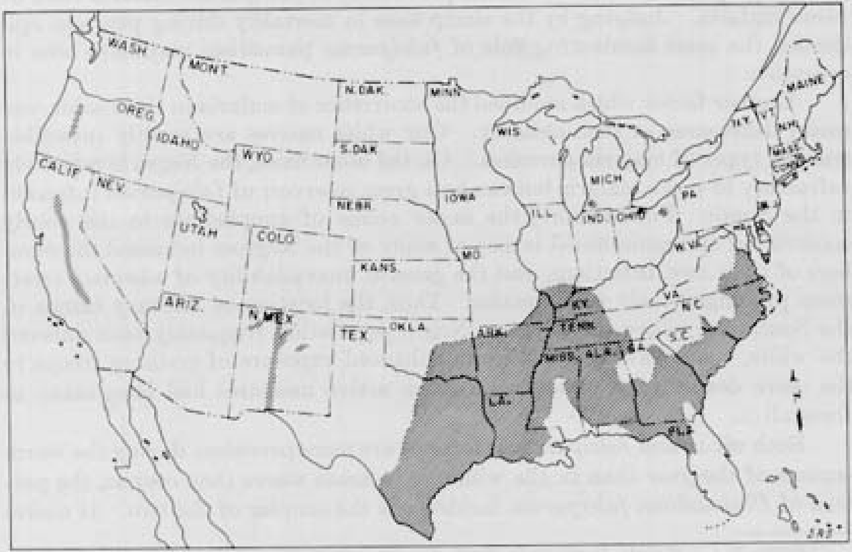


Imported cases

500

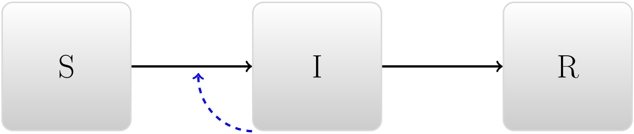


Example: Malaria in the US



MAP 4.—Areas of the continental United States believed to be malarious in 1934–35.

Result: not every one gets infected



- When S gets low, then I goes down and the outbreak stops
- There is not always a reason why you didn't get infected!
  - Remember the model world
  - Everyone in this model is assumed to be the same

Next steps

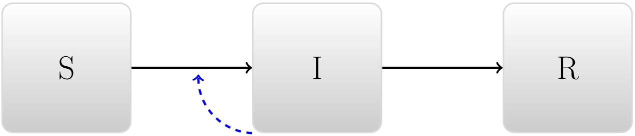
- We can *implement* the model and see what it's going to do
- This requires more assumptions, for example:
  - Time steps or continuous time?
  - Deterministic or stochastic?

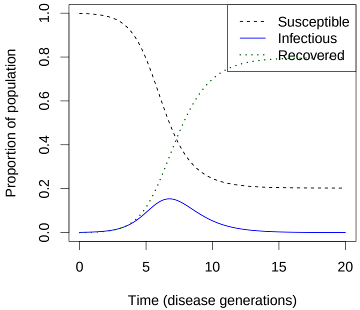
Outline

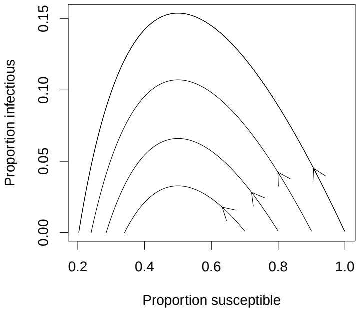
Deterministic models

- For a given set of assumptions, a deterministic model always predicts the same results
- In other words, our model world *determines* the outcome

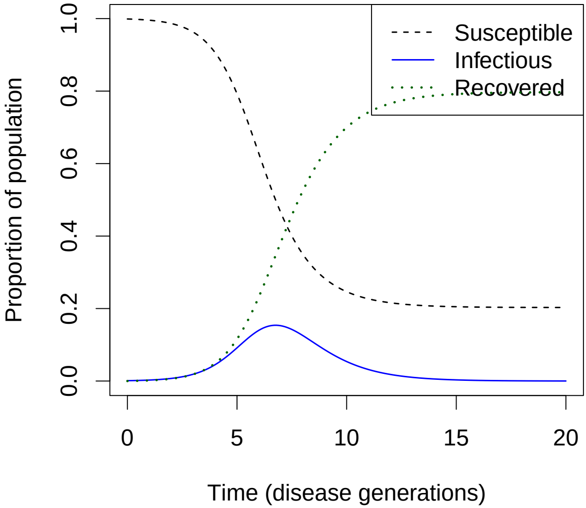
Simulations



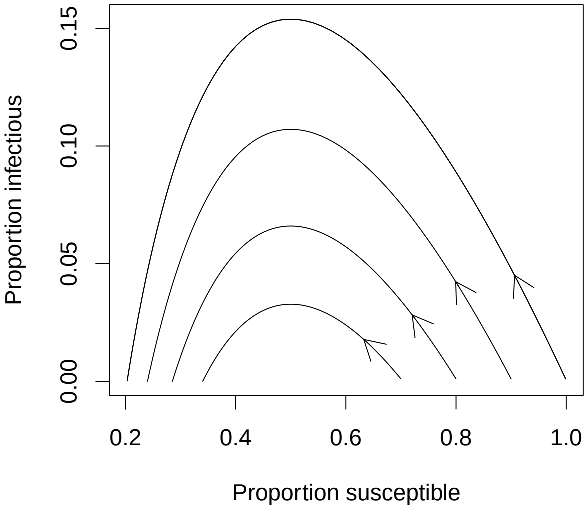




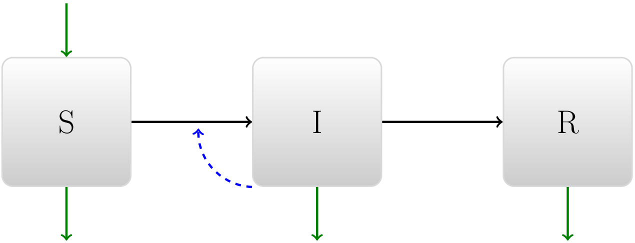
Simulations



Simulations



Closing the circle



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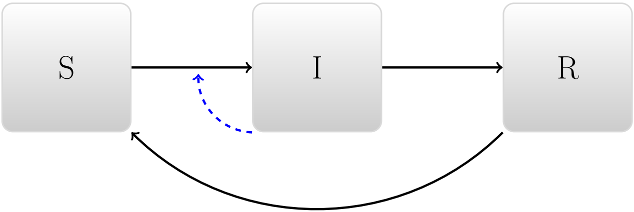
Closing the circle



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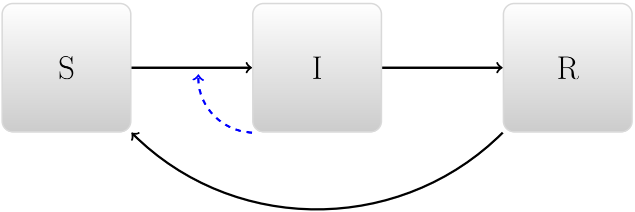
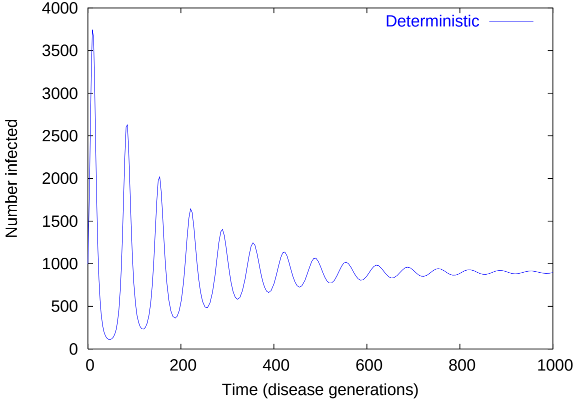
Processes and rates

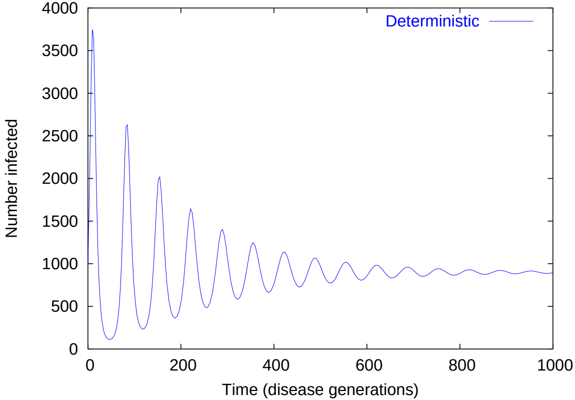


Event	**transition**	**rate**	**Effect** (S, I)
Infection	$S \to I$	$\beta SI/N$	$(-1, 1)$
Recovery	$I \to R$	γI	$(0, -1)$
Loss of immunity	$R \to S$	$\mu(N - S - I)$	$(1, 0)$

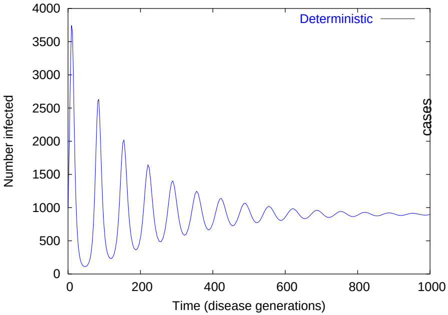
Result: Diseases tend to oscillate

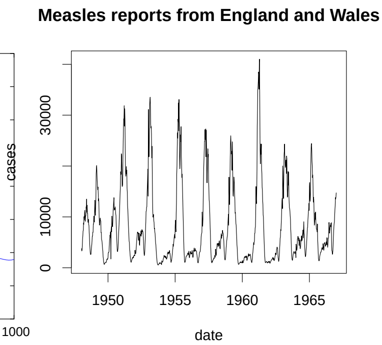


Result: Oscillations tend to be damped



What is missing from our model world?





What is missing from our model world?

- Almost everything! So what's important?
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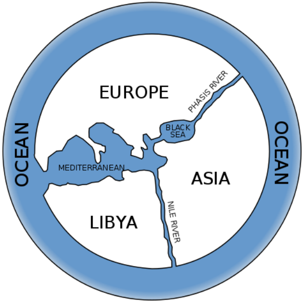
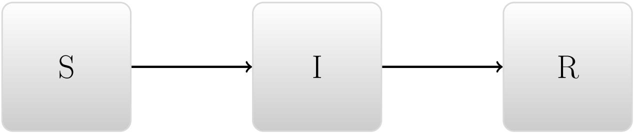


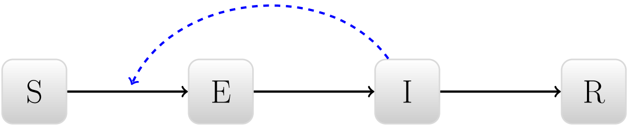
Example: Ebola transmission (埃博拉)

- How much Ebola spread occurs before vs. after death
- Highly context dependent
  - Funeral practices, disease knowledge
- *Weitz and Dushoff Scientific Reports 5:8751.*

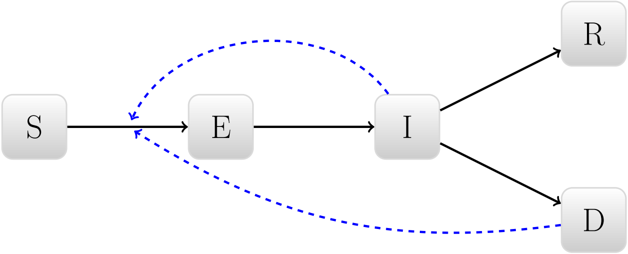
Simple disease model



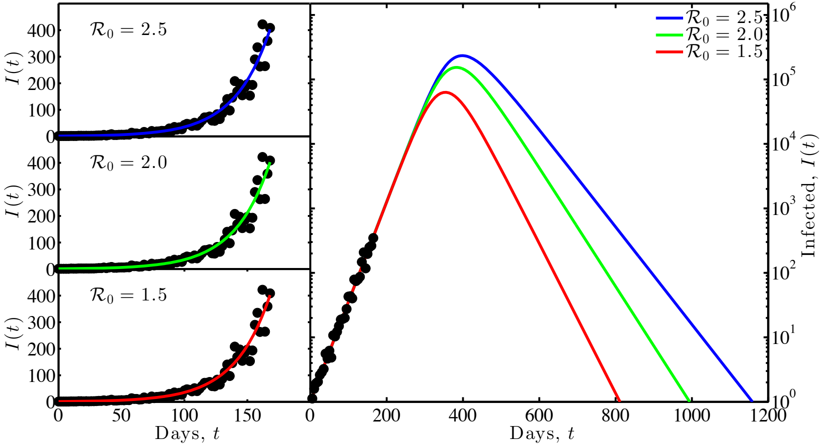
Model with latent period



Include post-death transmission



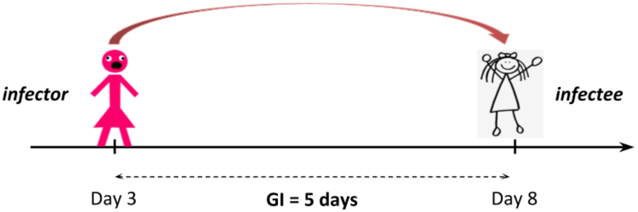
Result: generation interval links $r\mathcal{R}$



Definition

Generation Interval:

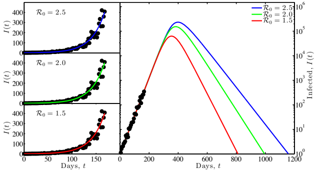
Interval between the time that an individual is infected by an infector and the time this infector was infected



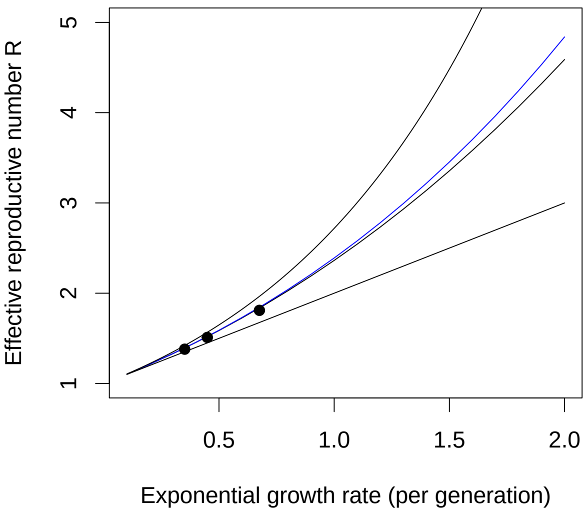
Result: generation interval links $r\mathcal{R}$

- Mechanistic view: If we know $\mathcal{R}$, faster generations mean faster spread (bigger r)

- Phenomenological view: If we know r, slower generations mean stronger spread (bigger $\mathcal{R}$)



Calculations



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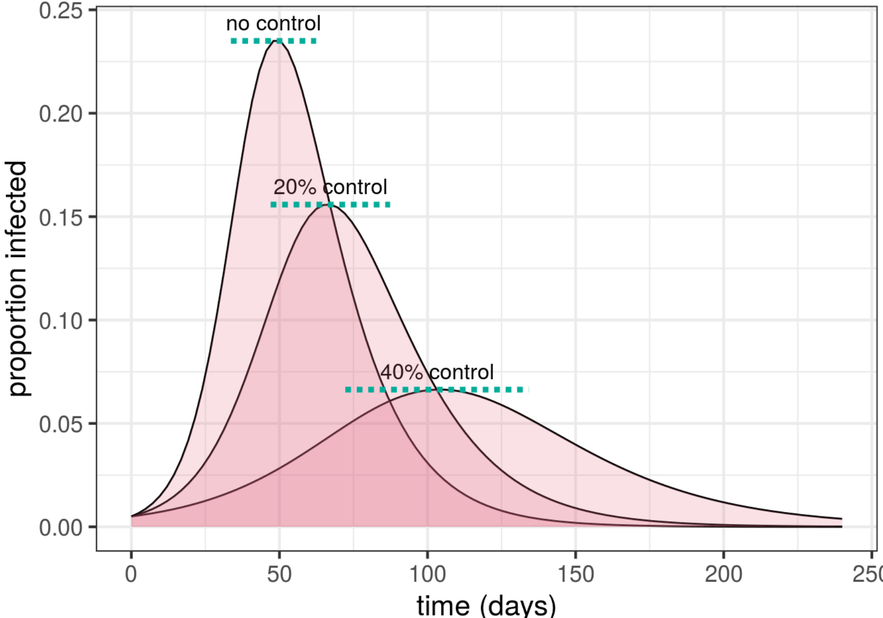
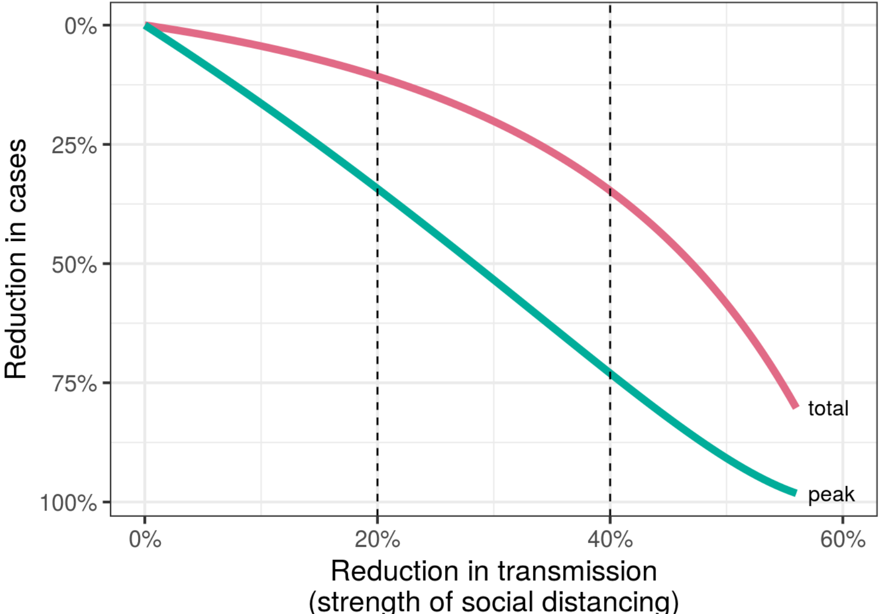
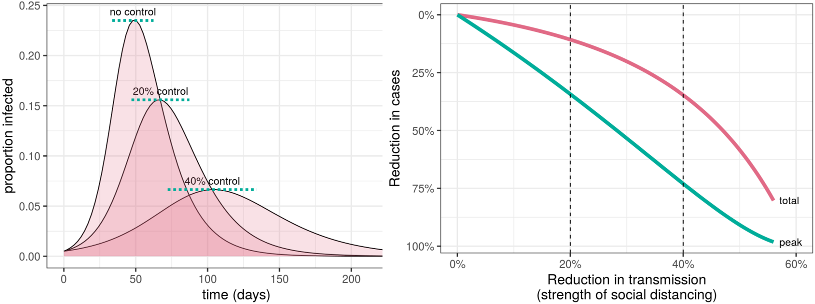
Example: COVID: flatten the curve



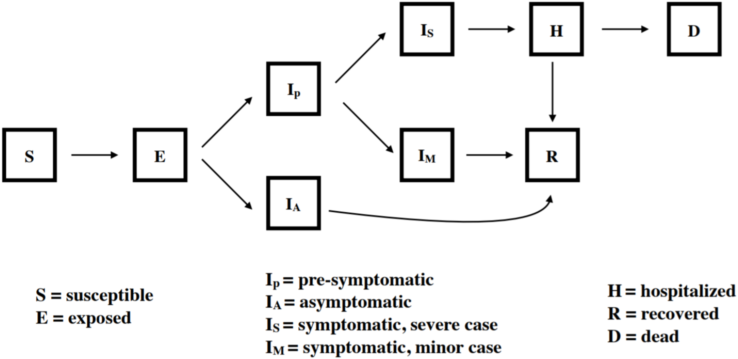
Example: COVID



Result: It is easier to reduce the peak than the total cases

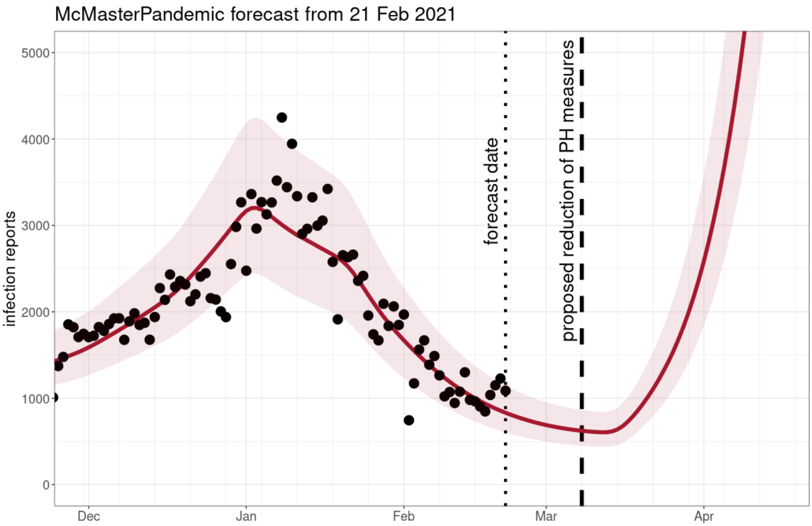


More box models

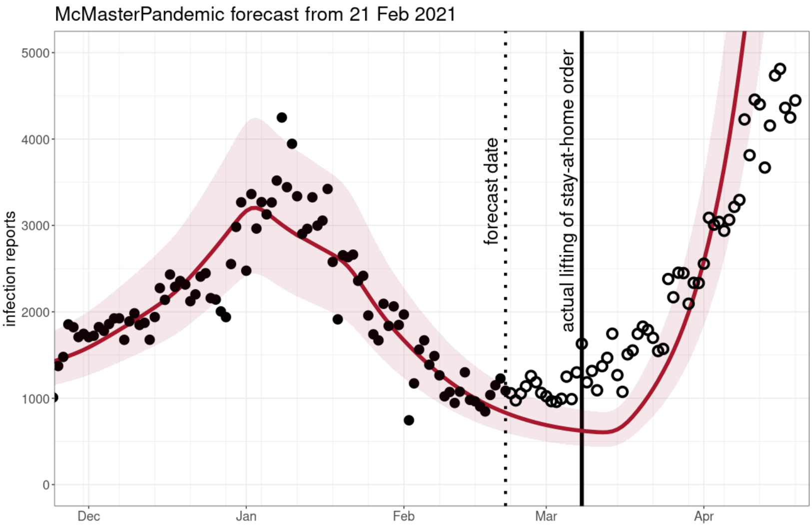


Childs et al., http://covid-measures.stanford.edu/

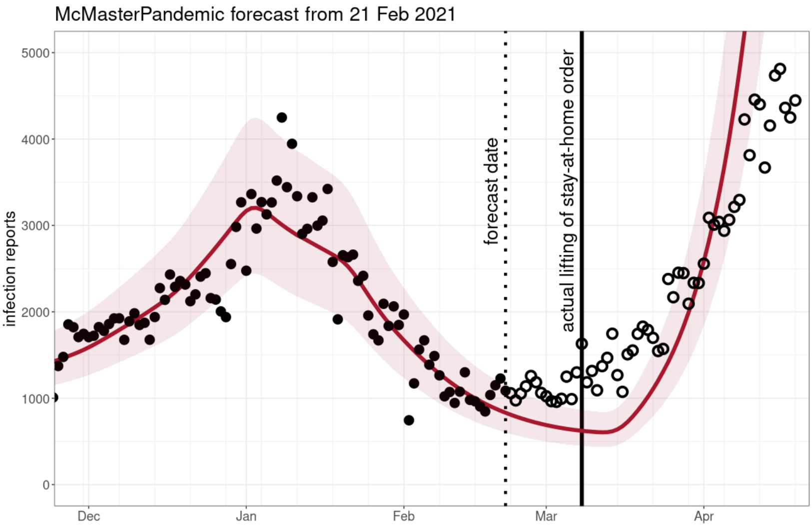
Example: COVID waves



Example: COVID waves

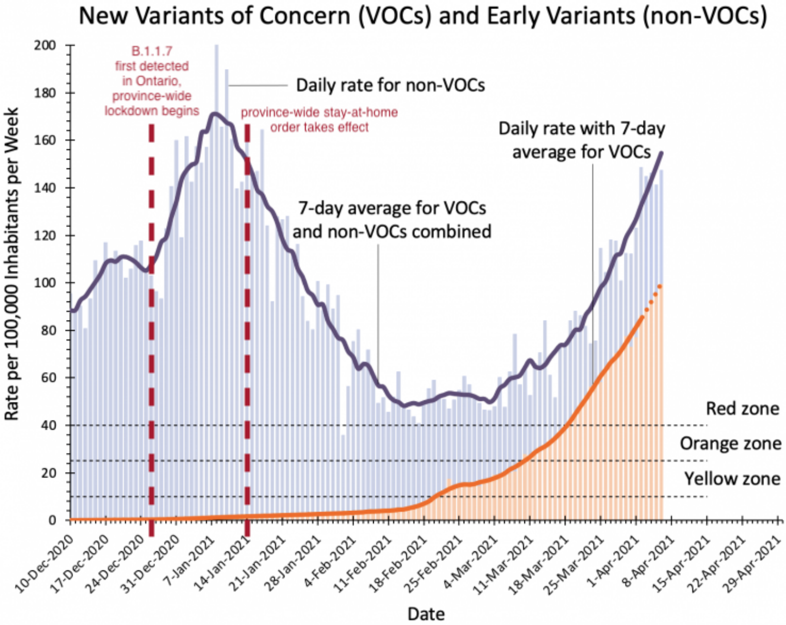


COVID waves



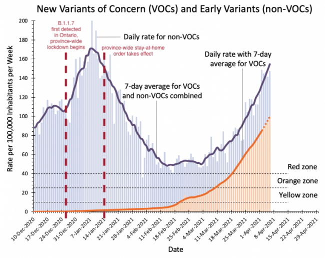
McMasterPandemic forecast from 21 Feb 2021
infection reports
5000
4000
3000
2000
1000
0
Dec
Jan
Feb
Mar
Apr
forecast date
actual lifting of stay-at-home order

Example: COVID waves



COVID waves

- alpha variant was increasing even though total was decreasing
- using a dynamical perspective allows us to project the effect of this



The daily rates of new variants of concern (VOCs) for the last 4 days are predicted.

Outline

Stochastic models

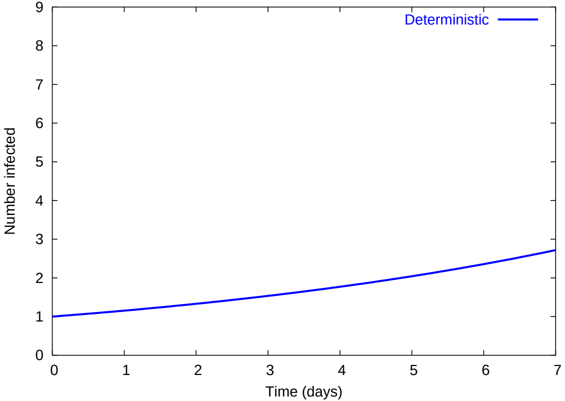
- For a given set of assumptions, a stochastic model predicts a variety of possible results
- In other words, there is room for randomness (stochasticity) inside our model world
  - We may think the world is really stochastic
  - Or simply that there are things we can't predict ...

Types of stochasticity

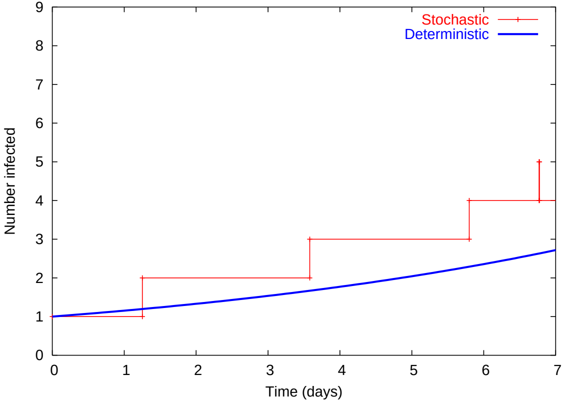
Event	**transition**	**rate**	**Effect** (S, I)
Infection	$S \to I$	$\beta SI/N$	$(-1, 1)$
Recovery	$I \to R$	γI	$(0, -1)$
Loss of immunity	$R \to S$	$\mu(N - S - I)$	$(1, 0)$

- We can add random changes to the rates
  - Contact rate (β), for example, may go up and down for reasons we can't predict
- We also get a stochastic model even by just treating individuals as individuals!

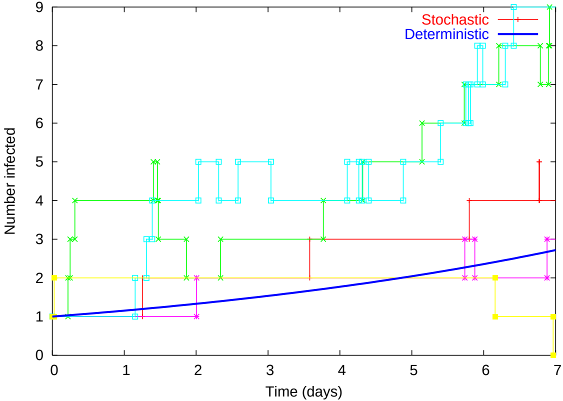
Deterministic spread



Demographic spread



Demographic spread



- Demographic refers to the *minimum* stochasticity corresponding to treating individuals as individuals

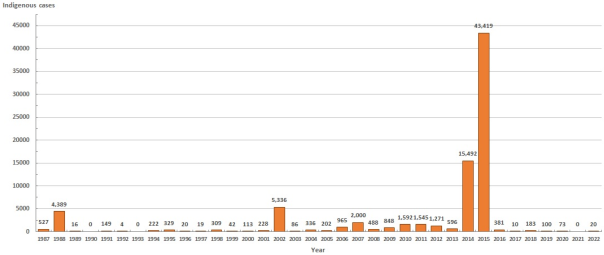
Result: outbreaks can die out at random

- In simple models, the probability of a single introduction going extinct at random is $1/\mathcal{R}$
- If an introduction does not lead to an outbreak, there's not always a reason

Result: Pattern of outbreak sizes is related to $\mathcal{R}$

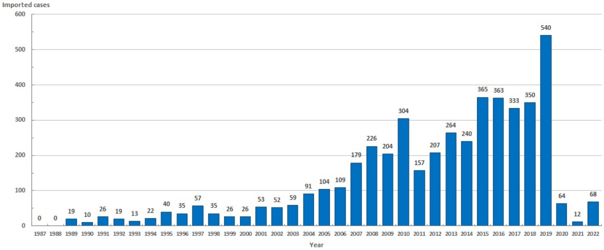
Indigenous cases

40,000

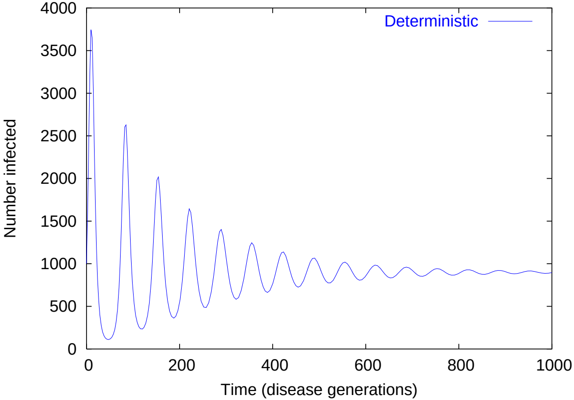


Imported cases

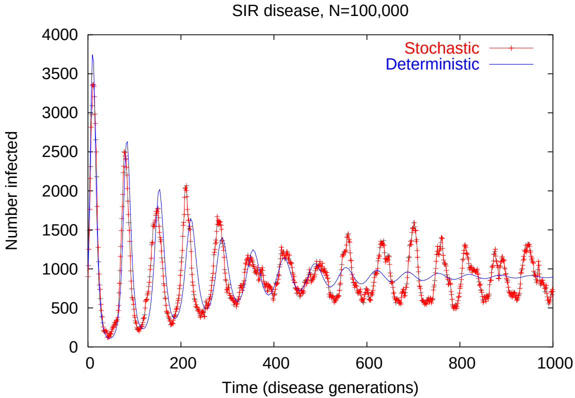
500



Result: stochasticity interacts with oscillations

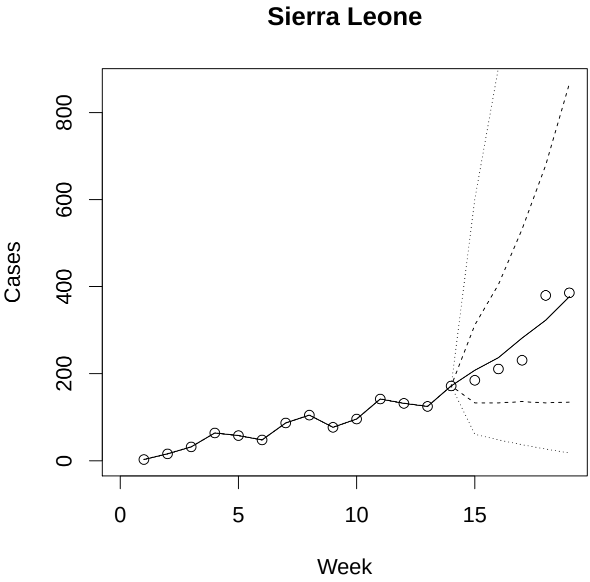


Result: stochasticity interacts with oscillations



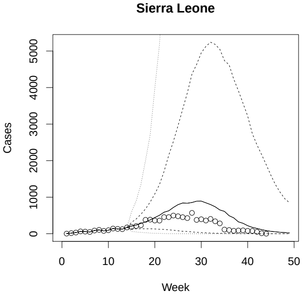
Outline

Statistical fitting



Statistical fitting

- How certain or uncertain are our projections?
- What else do we need to know?



Outline

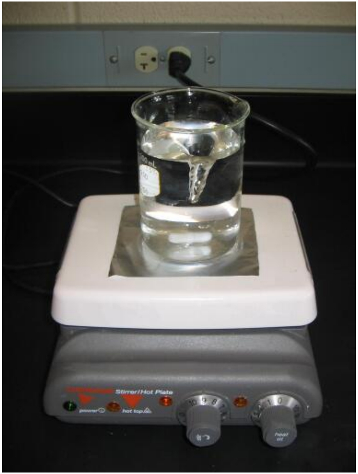
Dynamical modeling

Modeling approaches
- Conceptual modeling
- Deterministic models
- Stochastic models
- Statistical fitting

Limitations
- Heterogeneity
- Behavioural changes

Outline

Heterogeneity



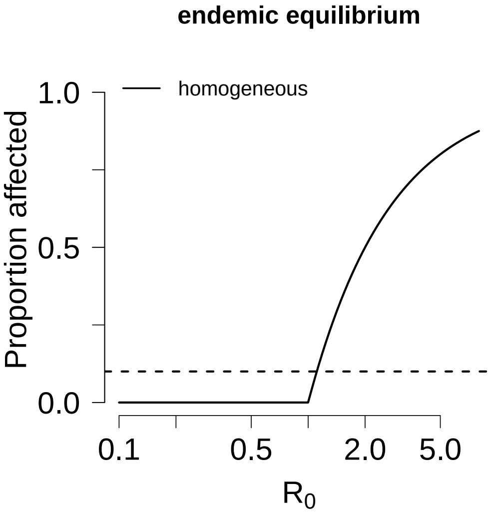
- Simple models treat the world like this cup
- People are all the same
- Perfectly mixed
- *Lots of people*
  - (for deterministic models)

Human heterogeneity

Human heterogeneity

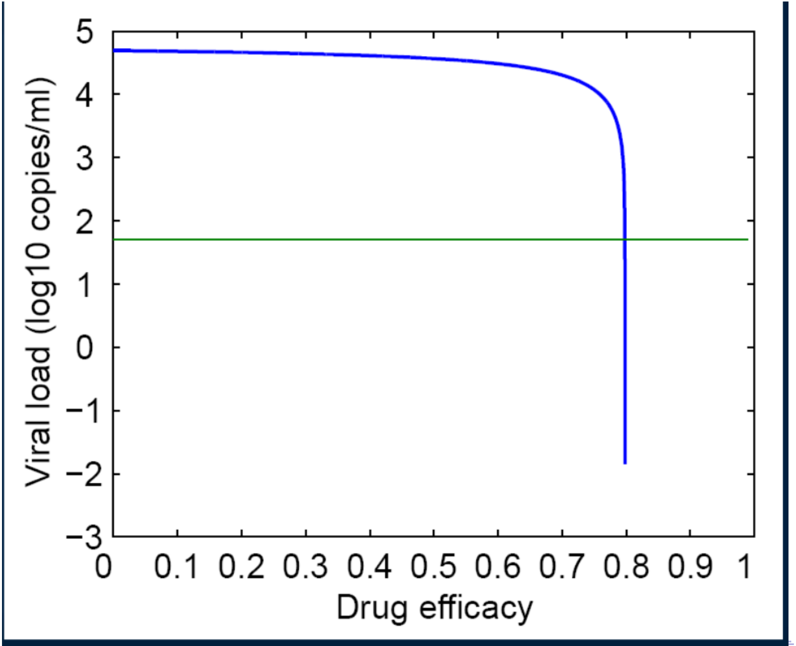
Human heterogeneity

Example: Gonorrhea



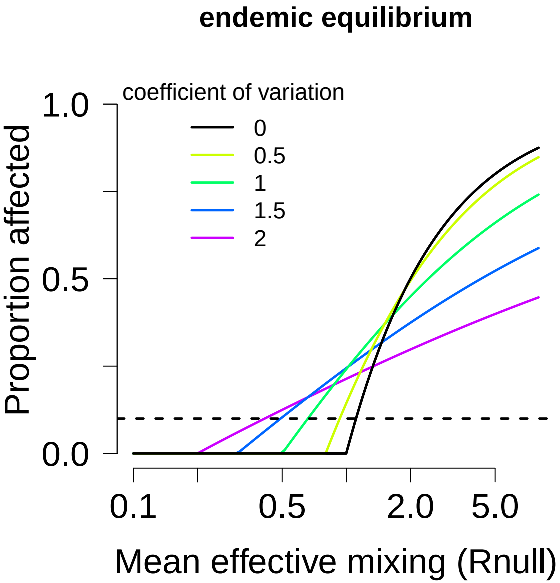
- Homogeneous model cannot explain global pattern
- What does this remind you of?

Fragility



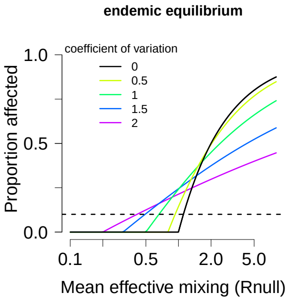
Viral load (log10 copies/ml)
5
4
3
2
1
0
−1
−2
−3
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1
Drug efficacy

Example: Gonorrhea



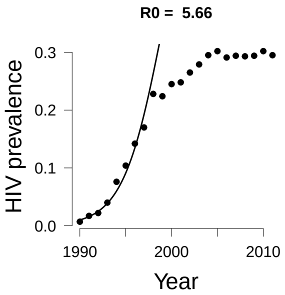
Result: heterogeneity makes incidence robust

- Disease levels are more resistant to change
- Higher when averaged transmission is low
- Lower when averaged transmission is high



Example: HIV

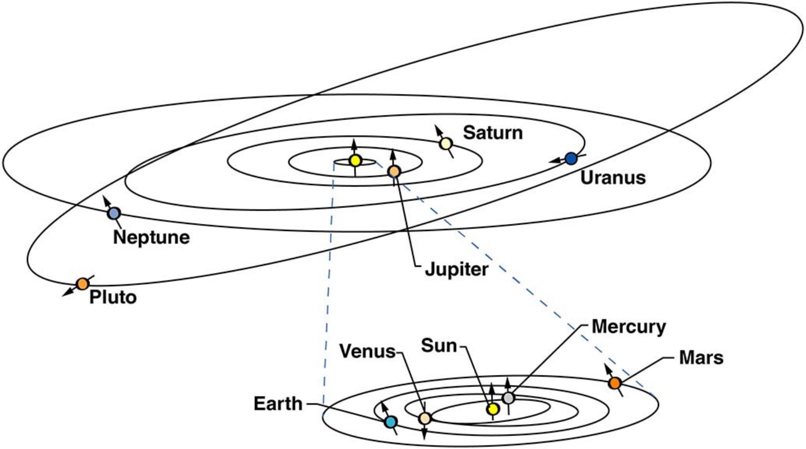
- If our model matches initial spread, it can't match later values
- What happened?
  - Heterogeneity (intrinsic)
  - Policy change (extrinsic)
  - Behaviour change (could model either way)



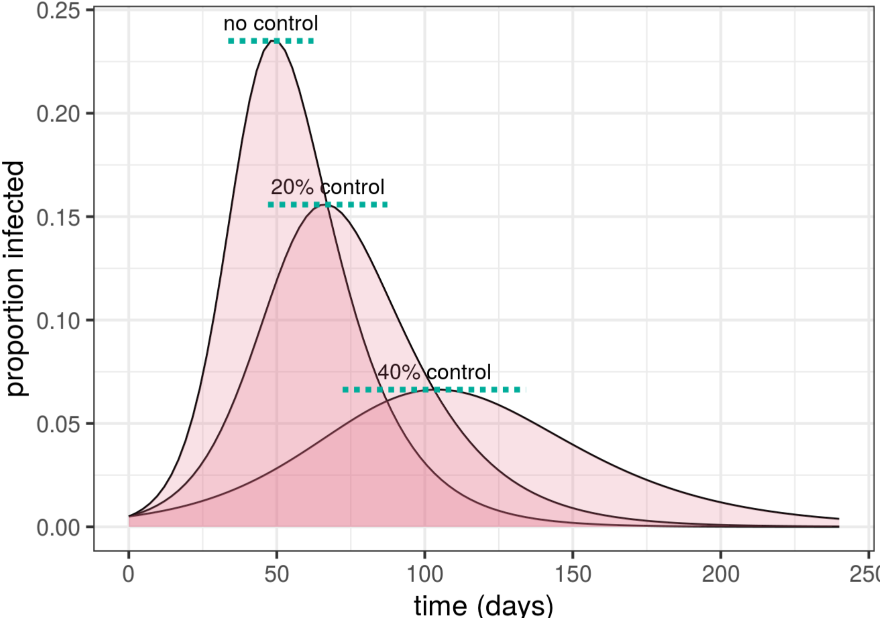
Outline

Behavioural changes

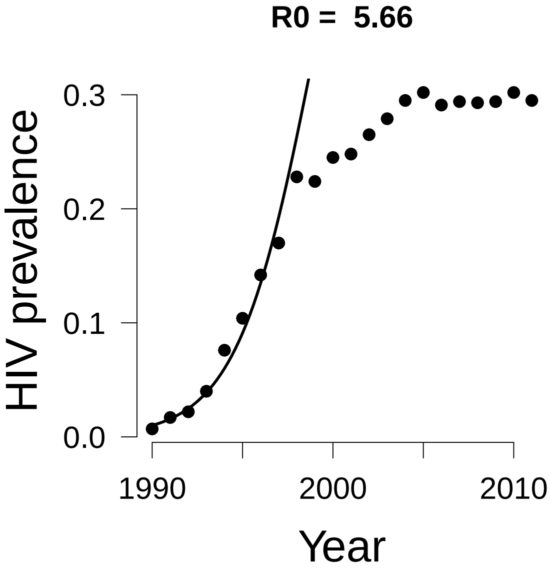
- I can calculate the motion of heavenly bodies, but not the madness of people. – Isaac Newton



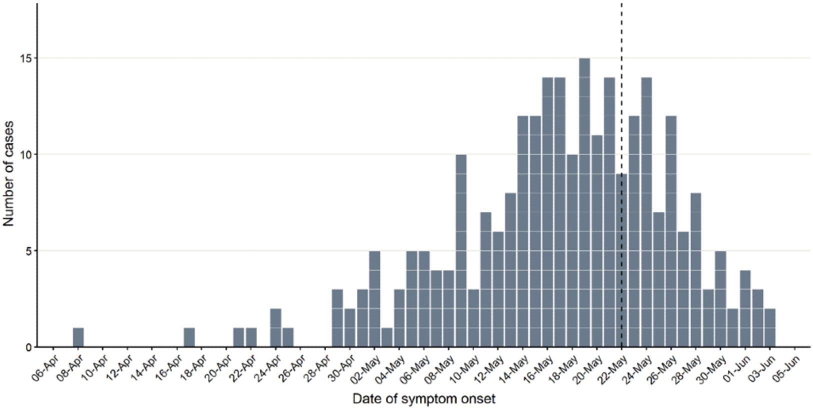
Example: COVID



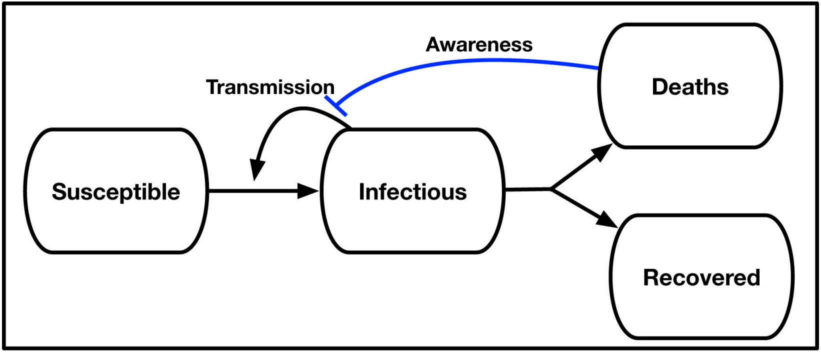
Example: HIV



Example: mpox (猴痘)



Example: COVID awareness



Weitz et al. `https://www.pnas.org/doi/10.1073/pnas.2009911117`

Summary

- Dynamical models are an essential tool to link scales
- Very simple models can provide useful insights
- More complex models can provide more detail, but also require more assumptions, and more choices
  - Statistical fitting can guide in interpretation
- We can evaluate assumptions
  - What was right, what was wrong?
  - What else do we need to know?

Current projects

- Rabies in African and Asia
- Mpox in Africa
- Respiratory infections in Canada
  - Merge COVID with "seasonal" infections to improve surveillance
  - Re-emerging diseases (measles)
- Other interests
  - HIV, TB and malaria

Rabies

- Important human mortality and economic burden
- Almost entirely vaccine preventable (if you vaccinate domestic dogs)

Educational outreach

- Workshops in Africa and Asia
- `www.ici3d.org`
- *National Center for Theoretical Sciences, Taiwan*

Thanks

- Organizers
- Collaborators
- Funders
- Audience