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Introduction to Computational Science

5. Stochasticity in SIR Models

Michael Lees – m.h.lees@uva.nl

1. Modelling Consideration (revist)
2. Stochastic SIR equations
3. Event Driven Approaches
4. Stochastic Extinction

5.1 Modelling Considerations (revisit)

Major decisions in designing a model

Even after compartmental framework is chosen, still need to decide:

- Discrete vs continuous time
- Discrete vs continuous state variables
- Deterministic vs stochastic
- Random mixing vs structured population
- Homogeneous vs heterogeneous
  - and which heterogeneities to include?

So far, continuous time, continuous state variables, deterministic, random mixing, homogeneous

Lets now add ***stochasticity*** and ***discrete state*** *variables*

Major decisions in designing a model

Ideally consider the question then make the right model to answer the question.

Coarse/Low Resolution ⟷ Detailed/individual/High Resolution

- Computationally Cheap
- Few parameters
- Relatively low data requirements
- Robust
- Easier to understand/reason
- Significant assumptions

- Computationally Expensive
- Many parameters
- Extremely high data requirements
- Can be brittle (impossible falsification)
- Understanding behaviour hard
- Significant flexibility, scenarios

Calder M et al. 2018 Computational modelling for decision-making: where, why, what, who and how.R. Soc. open sci.5: 172096. http://dx.doi.org/10.1098/rsos.172096

Deterministic vs stochastic models

Deterministic models

- Given model structure, parameter values, and initial conditions, there is no variation in output.

Stochastic models incorporate chance

- Stochastic effects are important when numbers are small, e.g. during invasion of a new disease
- Demographic stochasticity: variation arising because individual outcomes are not certain
- Environmental stochasticity: variation arising from fluctuations in the environment (i.e. factors not explicitly included in the model)

Is stochasticity important?

What is your model predicating?

- Predicting seasonal impact of flu/measles, provisioning for vaccines?

  Vs.

- Deciding upon lockdown/distancing measures for covid-19 or Ebola?

In the first case the number of infected is larger, in the second case small events can trigger outbreaks (by definition looking at early infection).

Stochasticity can arise from the disease variation in incubation, symptoms, etc. or <u>when we don't know much about the disease!</u>

"*In general, the role played by chance will be most important whenever the number of infectious individuals is relatively small, which can be when the population size is small, when an infectious disease has just invaded, when control measures are successfully applied, or during the trough phase of an epidemic cycle.*"

[Keeling & Rohani pg. 190]

Important classes of stochastic epidemic models

Monte Carlo simulation

- Any model can be made stochastic by using a pseudo-random number generator to “roll the dice” on whether events occur.

Branching process

- Model of invasion in a large susceptible population
- Allows flexibility in distribution of secondary infections but does not account for depletion of susceptibles.

Important classes of stochastic epidemic models

Chain binomial

- Model of an epidemic in a finite population.
- For each generation of transmission, calculates new infected individuals as a binomial random draw from the remaining susceptibles.

Diffusion

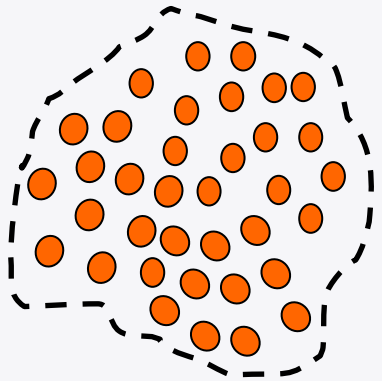
- Model of an endemic disease in a large population.
- Number of infectious individuals does a random walk around its equilibrium value → quasi-stationary distribution

Continuous vs discrete state variables

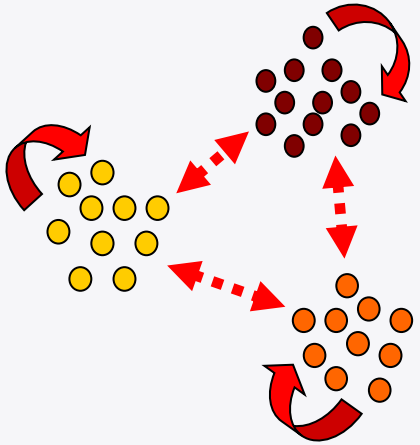
- Continuous state variables arise naturally in differential equation models.
  - Mathematically tractable, but biological interpretation is vague (sometimes called ‘density’ to avoid problem of fractional individuals).
  - Ignoring discreteness of individuals can yield artefactual model results.
  - Quasi-extinction threshold: assume that population goes extinct if continuous variable drops below a small value
- Discrete state variables arise naturally in many stochastic models, which treat individuals (and individual outcomes) explicitly.

Models for population structure

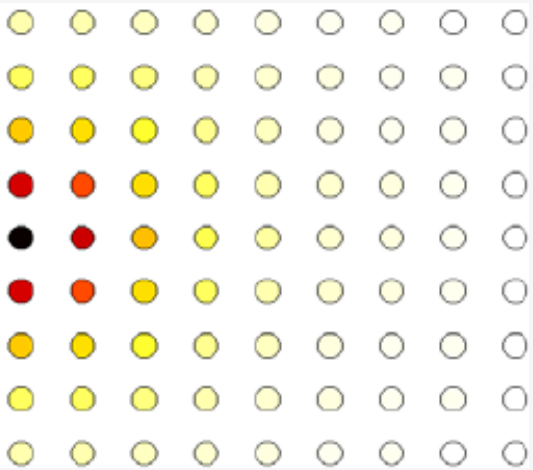
Random mixing



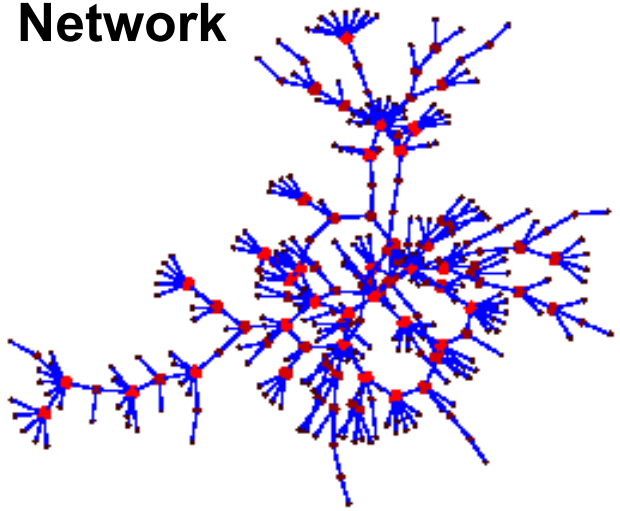
Multi-group



Spatial mixing



Network



Individual-based model

Population heterogeneities

- In real populations, almost everything is heterogeneous – no two individuals are completely alike.

- Which heterogeneities are important for the question at hand?
  - Mobility, age, underlying conditions, gender, etc.
- Do they affect epidemiological rates or mixing? Can parameters be estimated to describe their effect (**Nothing for free**)?
- Often modelled using multi-group models, but networks, ABMs, PDEs also useful.

5.2 Stochastic SIR equations

Stochastic Dynamics in modelling infectious diseases

- So far, our SIR models were completely deterministic
  - Given an initial condition, the dynamics is always the same
- Often not realistic for real epidemics
  - If it were possible to “re-run” a real-world epidemic, we would not expect to observe exactly the same people becoming infected at exactly the same times. Clearly, there is an important element of chance
- Role of chance important
  - For small population sizes
  - For small number of infectious
    - At the start of an invasion (will the disease actually spread?)
    - When control measures are applied (will the disease be eradicated?)
    - When the dynamics goes through a minimum (can the pathogen go extinct?)

Modelling the Chance Aspect

Three ways to introduce this into the model

1. Introduce chance directly in the population variables
   - Adding noise to the deterministic ODEs
2. Random parameter variation
   - Adding noise to values of the parameters in the deterministic ODEs
3. Individual-level, explicit modelling of random events
   - Discrete event modelling

Stochastic Simulations

- Different outcomes when starting from the same initial conditions
  - Multiple simulations are needed to determine the expected range of behavior (e.g. means and standard deviations)

- Requires use of Random Number Generators (RNGs)
  - In python, e.g. ‘numpy.random’ or ‘scipy.stats’.
  - Understand how seeds work, numpy.random vs. import random
  - Various algorithms: MersenneTwister, Wichmann-Hill, etc.

Random Variables

- Consider a Continuous Random Variable X

  X takes values in a continuous interval.

- Probability Density Function

  Given a continues random variable X. The probability that X lies in the interval [*a*,*b*] is $P(a \leq X \leq b) = \int_a^b f(x)dx$. $f(x)$ is the Probability Density Function (pdf) of X, with $f(x) > 0$ and $\int f(x)dx = 1$ (integrated over the full range of X).

- The Cumulative Distribution Function $F(x)$ *(cdf)*

  gives the probability that a random variable X assumes a value less then or equal to x, $F(x) = P(X \leq x)$, so $F(X) = \int_{-\infty}^{x} f(t)dt$.

- The expected value, or expectation of X
  - $E[X] = \int_{-\infty}^{\infty} xf(x)dx$
- The Variance of X
  - $V[X] = E[(X - E[X])^2] = E[X^2] - (E[X])^2$

SIR type models with stochasticity

- The number of susceptibles X, the number of infectious Y, and the number of recovered Z are now random variables.

- They have an underlying *pdf* which we don't (need to) know.

- We are now interested in their expected values, variances, and maybe covariances.
  - Remember, covariance between two random variables X and Y is $Cov[X, Y] = E[XY] - E[X]E[Y]$

Five key features in stochastic SIR type models

1. Variability between simulations
   - It is generally impossible to predetermine the precise disease prevalence at any given point in the future.
2. Variances and covariance
   - Stochastic processes lead to variance in the prevalence of disease.
   - Interaction between stochasticity and underlying deterministic nonlinear dynamics leads to negative covariance between number of susceptibles and infectious.
   - And because of that, the mean population level $(\overline{X}, \overline{Y})$ deviate from the deterministic equilibria.
3. Increased transients
   - Stochastic perturbations away from the endemic equilibrium are countered by the restorive forces of the endemic attractor, leading to transient like returns to the endemic equilibrium

Five key features in stochastic SIR type models

4. Stochastic Resonance
   - Stochastic perturbations can excite oscillations close to the natural frequency of the deterministic SIR dynamics. So, stochasticity can excite epidemic oscillations around the endemic state.

5. Extinctions
   - For integer-valued stochastic models, stochasticity can lead to extinctions (that is, the number of infectious individuals goes to zero due to fluctuations), even when $R_0 > 1$.
   - In closed populations, chance fluctuations will *always* in the long run lead to extinction of the disease.
   - Long term persistence only possible via import of the pathogen
   - Similar extinctions may occur during the early stage of invasion.

Types of Noise

Observational Noise

- For this approach, the underlying epidemic dynamics remain the standard deterministic differential equations, but there is assumed to be some uncertainty in the recorded data.

Process Noise

- A more intuitive and fundamentally different way to incorporate noise is to introduce it directly into the deterministic equations. As such, the dynamics at each point in time are subject to some random variability and this variability is propagated forward in time by the underlying equations. We are, therefore, concerned with the interplay between deterministic and stochastic forces—how they cancel out or amplify each other.

Adding Process Noise

Add noise to the equations

- e.g. in the transmission term, to reflect e.g. fluctuations in the number of contacts per unit time κ or fluctuations in the probability of disease transmission upon contact c.

Stochastic ODEs

- Very extended topic, we will hardly scratch the surface
- Consider $\frac{dx}{dt} = \zeta$ where ζ is Gaussian random variable with mean 0 and standard deviation 1.

- Solve with forward Euler,

$$x_{t+\delta t} = x_t + \delta t \frac{dx}{dt} = x_{t+\delta t} = x_t + \delta t \zeta = x_0 + \delta t \sum_{1}^{t/\delta t} \zeta$$

Adding Process Noise

$$x_{t+\delta t} = x_t + \delta t \frac{dx}{dt} = x_{t+\delta t} = x_t + \delta t \zeta = x_0 + \delta t \sum_{1}^{t/\delta t} \zeta$$

- Note, that for $\delta t \to 0$ the noise terms effectively cancel and the variance in x will be zero. This reflects the problem with adding noise terms to ODEs.
- Trick to resolve this is to scale noise with time step, $\xi = \frac{\zeta}{\sqrt{\delta t}}$ (diffusive scaling) and write $\frac{dx}{dt} = f\xi$.
- In this way, in the long run, the mean of x is zero, and the standard deviation grows like $f\sqrt{\delta t}$, so diffusive behaviour.

Process Noise

We first assume that the variables themselves fluctuate, to explore the impact of stochasticity on the dynamics.

1. First, we consider constant noise in the transmission term
   - We will observe variability, variance and covariance, stochastic resonance, and deviations of mean values from the deterministic equilibrium.

2. Next, we will look at properly scaled noise in all rates in the model
   - We will observe the interaction between population size and noise.

Process Noise in the SIR transmission term

$$\frac{dX}{dt} = \nu N - [\beta\, XY/N + f(X,Y)\xi] - \mu X$$

$$\frac{dY}{dt} = +[\beta\, XY/N + f(X,Y)\xi] - \gamma Y - \mu Y$$

$$\frac{dZ}{dt} = +\gamma Y - \mu Z$$

For generality, a function f (X, Y) is included to scale the randomness in response to the current variable sizes.

Constant noise $f(X,Y) = f$

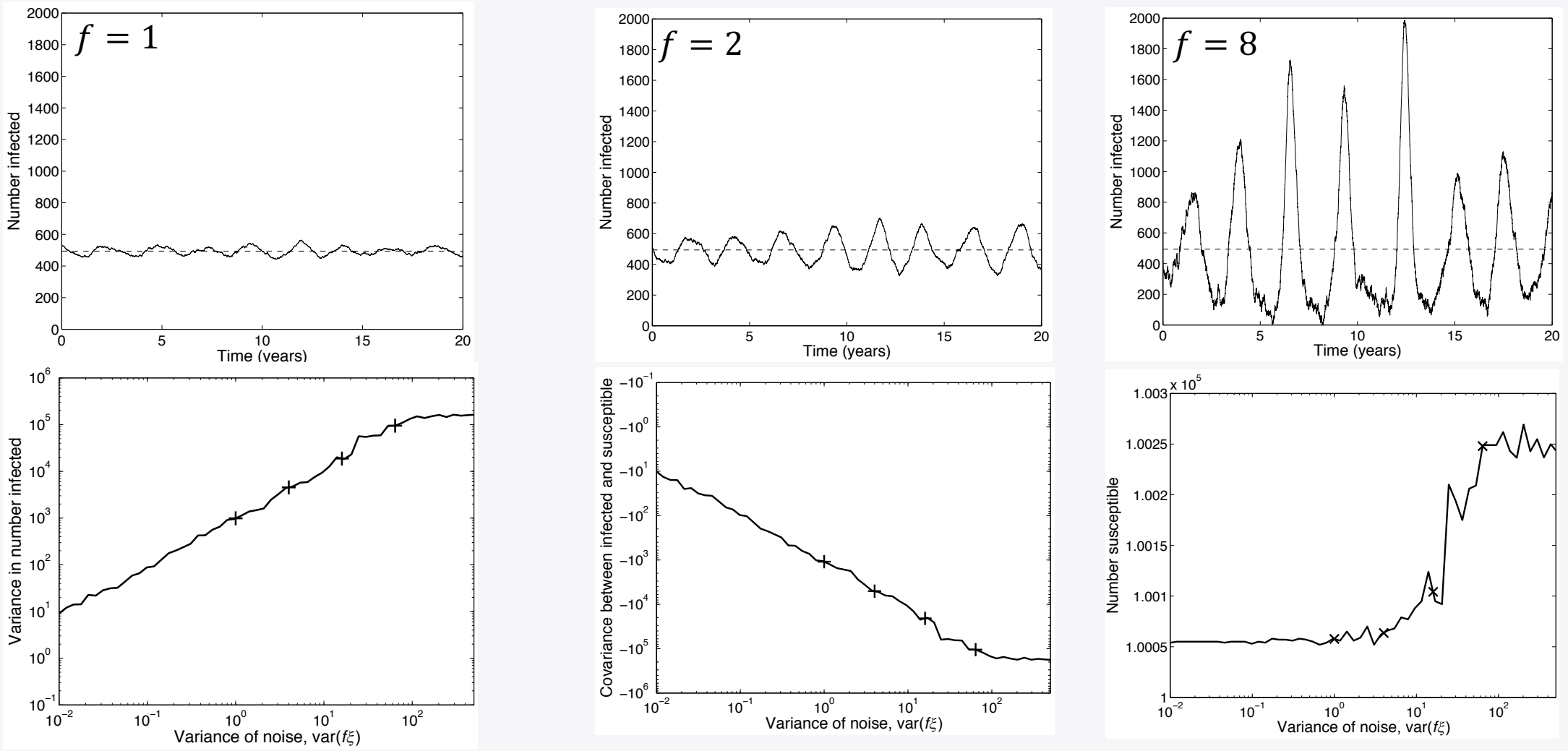


Figure 6.2 from Keeling and Rohani, The top row gives examples of the dynamics of the SIR model with births and deaths ($\mu = \nu = 0.02$ per year, $R_0 = 10$, $1/\gamma = 10$ days, $N = 10^6$). The amount of noise added to the transmission term increases from left to right ($f = 1, 2, \text{and } 8$). The deterministic equilibrium is depicted by the horizontal dashed line. The bottom row shows how the variance in the number of infected, the covariance between susceptible and infecteds, and the average number of suceptibles change with the variance of the noise. From biological considerations, if noise ever forced the number of infected individuals below zero, the number was reset to zero – this only occurs for the largest levels of noise. Dots on the right-hand graphs mark the values of f used to generate the left-hand graphs.

Scaled Noise

- In general, the amplitude of the noise terms $f(X, Y)$ scales with the population size.

- We have assumed that all the rates in the SIR model are due to Poisson processes, for which we know that the mean value equals the variance, leading to $f = \sqrt{\text{rate}}$.

- We can then generalise this to all rates in the SIR model

SIR with scaled noise terms

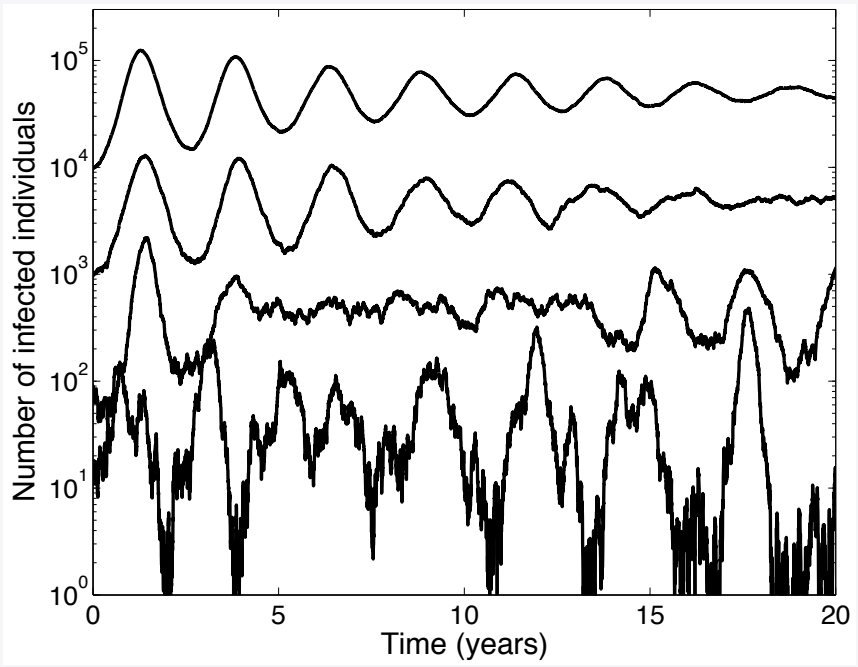
$$\frac{dX}{dt} = \left[\nu N + \sqrt{\nu N}\xi_1\right] - \left[\beta\, XY/N + \sqrt{\beta\, XY/N}\,\xi_2\right] - \left[\mu X + \sqrt{\mu X}\xi_3\right]$$

$$\frac{dY}{dt} = +\left[\beta\, XY/N + \sqrt{\beta\, XY/N}\,\xi_2\right] - \left[\gamma Y + \sqrt{\gamma Y}\xi_4\right] - \left[\mu Y + \sqrt{\mu Y}\xi_5\right]$$

$$\frac{dZ}{dt} = +\left[\gamma Y + \sqrt{\gamma Y}\xi_4\right] - \left[\mu Z + \sqrt{\mu Z}\xi_6\right]$$

- ξ_1 Birth rate noise
- ξ_2 Infection rate noise
- ξ_3 Susceptible death rate noise
- ξ_4 Recovery rate noise
- ξ_5 Infected death rate noise
- ξ_6 Recovered death rate noise

Dynamics of SIR with scaled noise



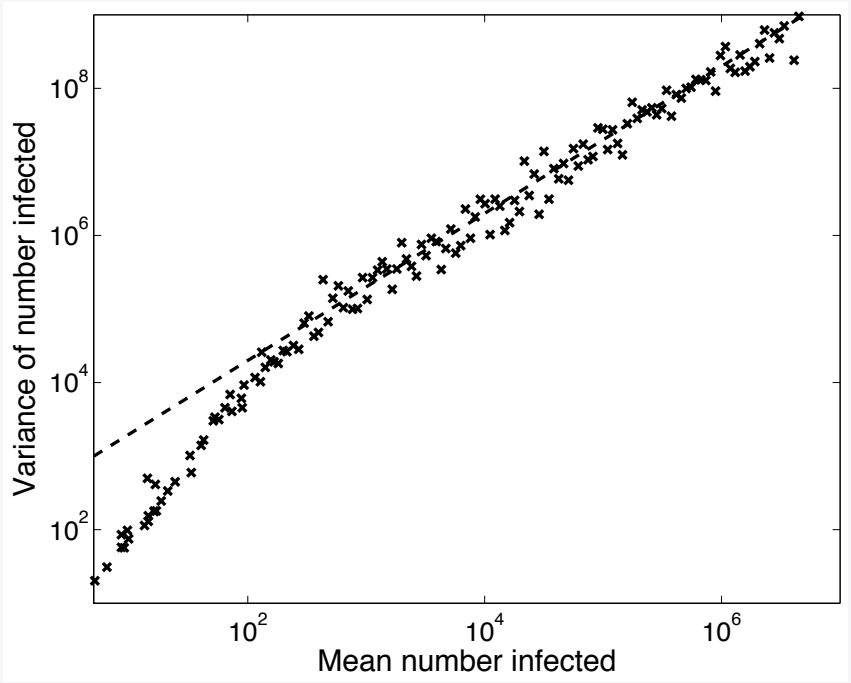


Figure 6.3 from Keeling and Rohani, The dynamics of SIR epidemics ($\mu = \nu = 5.5\times10^{-5}$ per day, $R_0 = 10$, $1/\gamma = 10$ days) with scaled noise. The left-hand graph shows how the expected oscillatory behavior becomes disrupted by noise in smaller populations, whereas large populations conform close to the deterministic ideal ($N = 10^5, 10^6, 10^7, 10^8$). The right-hand graph shows the mean-variance relationship for a range of population sizes, from 10,000 to 100 million. The dashed line represents $var = 100\times mean$, clearly showing how the scaling operates at larger populations.

Note that the standard deviation then scales as $sd = 10\times\sqrt{mean}$ and so $\frac{sd}{mean} = \frac{10}{\sqrt{mean}}$, so the relative noise contribution becomes larger for smaller populations.

Advantages & Disadvantages

1. Minor modification to existing equations – can use same techniques.
2. Clear correspondence between deterministic and stochastic equations is clear—as the noise terms are reduced to zero, we regain the deterministic dynamics.
3. The computational overheads associated with this form of stochastic model are small.

The stochastic equations suffer from one big drawback, they do not incorporate the discrete, individual nature of populations.

➔ Therefore not suitable if number of infected is small (e.g., initial infection)

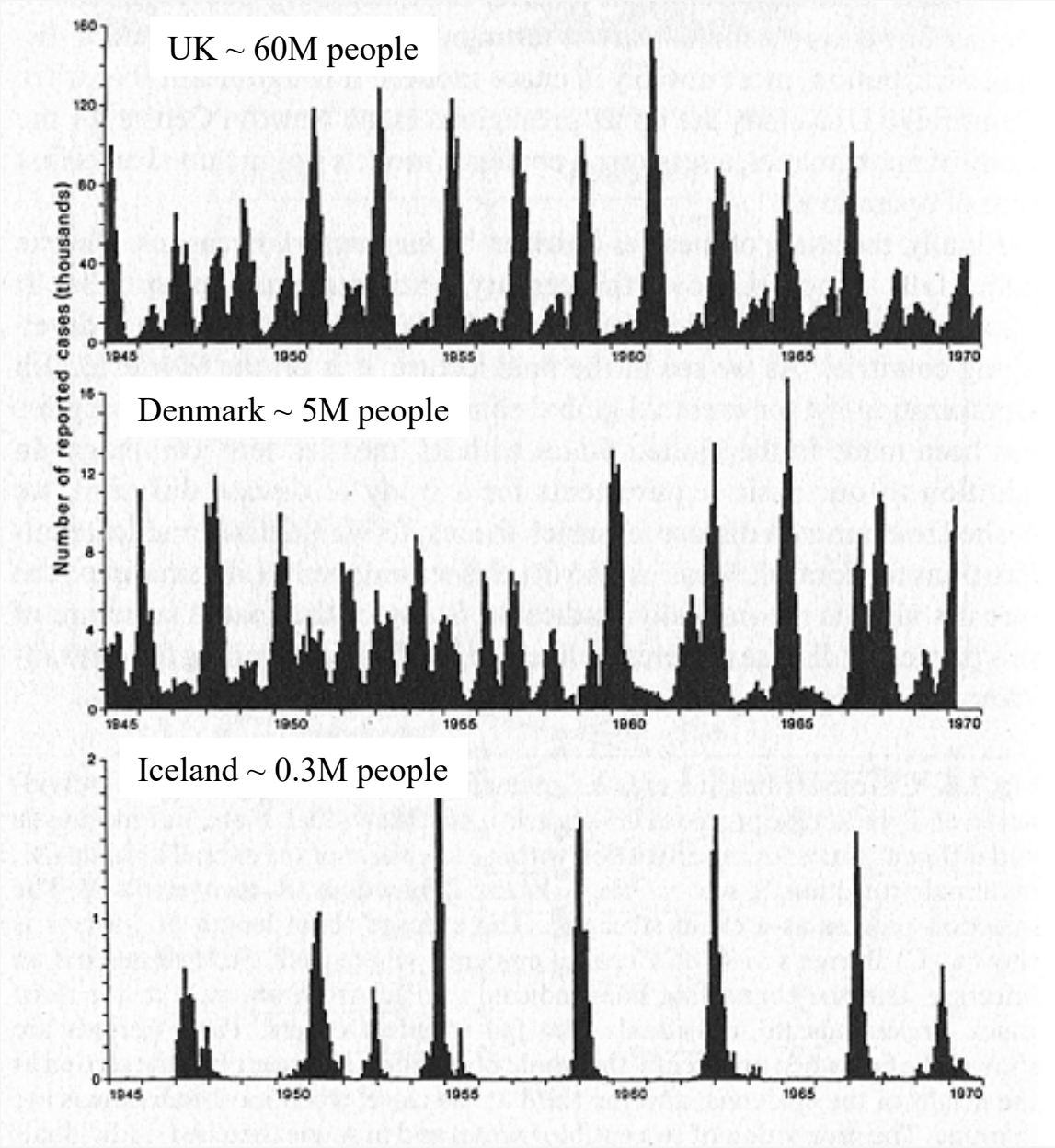
5.3 Event Driven Approaches

Look at some real data

Measles

- Note that measles dies out between major outbreaks in Iceland, but not in the UK or Denmark.

- What determines persistence of an acute infection?



Event Driven Approaches

- Lets now look at individual **events** that happen in spreading an infectious disease and apply ***discrete event simulations***.
- In SIR with demography, 6 **events**
  1. **Birth** $X \to X + 1$
  2. **Transmission** $Y \to Y + 1$ and $X \to X - 1$
  3. **Recovery** $Y \to Y - 1$ and $Z \to Z + 1$
  4. **Death**, three independent events, $X \to X - 1$, $Y \to Y - 1$, $Z \to Z - 1$
- Approach will be to schedule next events by drawing the time to the next event based on the rates.
- Remember that the underlying statistics are based on Poisson processes.

remember? The I → R transition

Probability of recovery is assumed constant?

- Too simple, in reality, to be estimated e.g. from clinical data

In a discrete time formulation

- Assume discrete time stepping, and time is numbered by the integer i.
- Define the recovery probability γ that an individual will recover at any time step
- The time an individual will spend on average in the infectious compartment, so the mean infectious period, is then equal to $1/\gamma$ time steps.
- The probability to not recover at any time step and stay in the Infected compartment is $1-\gamma$.
- The probability to recover at time i is then $p(i) = \gamma(1-\gamma)^{(i-1)}$
  - Note that ($\sum_{i=1}^{\infty} p(i) = 1$, so properly normalized)
- The average time to recovery therefore is $E[i] = \sum_{i=1}^{\infty} i\gamma(1-\gamma)^{(i-1)} = \frac{1}{\gamma}$.

remember? The I → R transition

- In a continuous-time formulation
  - assume recovery to be a Poisson process
  - γ now is a rate (probability per unit time)
  - The probability that an individual remains infected for a time τ follows an exponential distribution $\mathrm{p}(\tau) = \gamma e^{-\gamma\tau}$
  - Again, with an average infection time $\mathrm{E}[\tau] = \frac{1}{\gamma}$.
- In the discrete setting, per time step γY individuals move from the Infected to the Recovered compartment
  - with Y the total amount of infected individuals
- In the continuous setting, there is a rate γY individuals per time unit moving from the Infected to the Recovered compartment.

remember? Derivation of frequency dependent transmission term

- Assume homogeneous mixing between S and I compartments in the population
- Assume Susceptible individuals have on average κ contacts per unit time.
- A fraction $I = Y/N$ are contacts with infectious individuals.
- In a time interval $(t, t + \delta t)$ the average number of contacts with infectious individuals is $\kappa(Y/N)\delta t$
- Define c as the probability of successful disease transmission upon contact
- Probability that and individual escapes transmission following $\kappa(Y/N)\delta t$ contacts is $1 - \delta q = (1 - c)^{\kappa(Y/N)\delta t}$
- So, $\delta q = 1 - e^{\beta(Y/N)\delta t}$ with $\beta = -\kappa \ln(1 - c)$
- Taylor expand the exponential, divide by δt and take the limit $\delta t \to 0$ results in $\frac{dq}{dt} = \beta\, Y/N$, the transmission rate per individual.
- The final transmission term then becomes $\lambda = \beta\, XY/N$

The Poisson Process 1

Consider random arrival events

- Customers in a shop
- Susceptible being infected

Count the events with a counting function $N(t)$, the amount of events in a time interval $[0, t], t \geq 0$.

$N(t)$ is the observation of a random variable, which assumes values 0, 1, 2, …

Assume that the probability that an arrival occurs in $[t, t + \delta t]$ equals $\lambda \delta t$

The Poisson Process 2

- This arrival process, or counting process $\{N(t), t \geq 0\}$ is a Poisson process with mean rate λ if

  - Arrivals occur one at a time,
  - Arrivals are completely random; number of arrivals in an interval $[t, t + \delta t]$ depends only on interval length δt (so, e.g. no 'rush hours'),
  - No correlation exists between non-overlapping time intervals.

Rumor has it that the first use of the Poisson process was as a model of deaths from kicks of horses in the Prussian army...

(not true !!)

The Poisson distribution 1

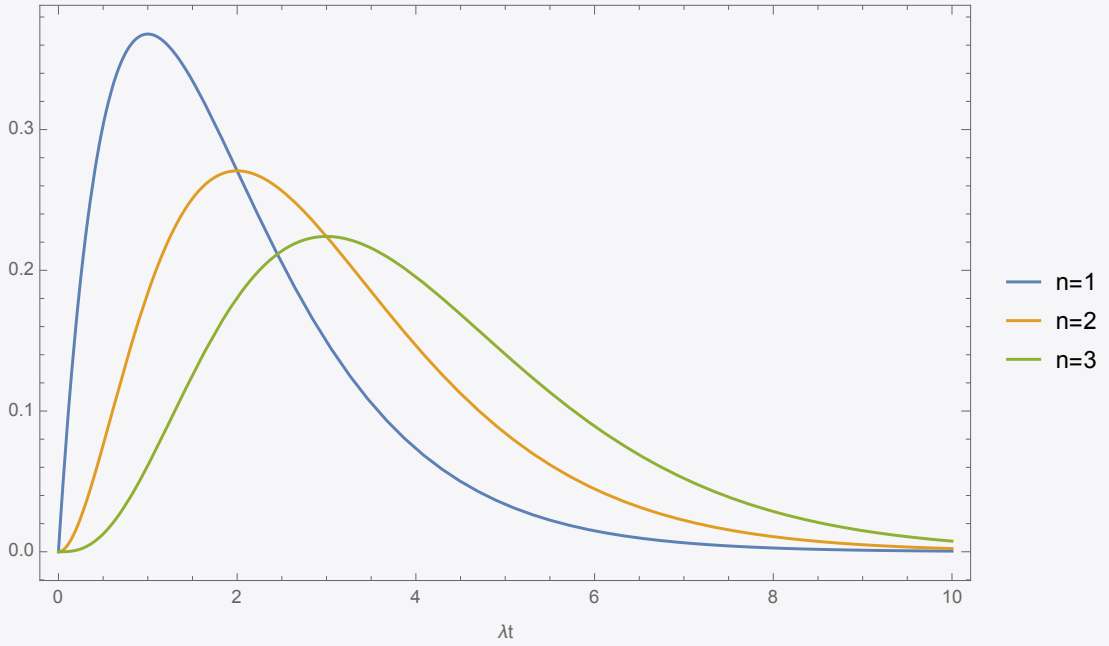
Consider the probability that $N(t) = n$

$$\mathrm{P}(N(t) = n) = p_n(t).$$

We will prove this follows the distribution:

$$p_n(t) = \frac{(\lambda t)^n e^{-\lambda t}}{n!}, t \geq 0, n = 0,1,2, \cdots$$

which is the famous
Poisson distribution.



Inter arrival times

Next, consider the actual times of arrival

let the first arrival be at $t = A_1$,

let the second arrival be at $t = A_1 + A_2$, etc.

A_1, A_2,... are successive inter arrival times. The inter arrival times are a continuous random variable.

We now seek the *pdf* of this random variable.

cdf of inter arrival times

Since the first arrival occurs after time t if and only if there are no arrivals in (0, t), we immediately conclude that

$$P(A_1 > t) = P(N(t) = 0) = e^{-\lambda t}$$

Thus, the probability that the first arrival will occur in (0, t) is then given by

$$P(A_1 < t) = 1 - e^{-\lambda t}$$

This is the *cdf* of the *pdf* that we are looking for.

cdf of exponential distribution

The *cdf* of the exponential distribution

$$F(x) = P(X \leq x) = \int_0^x \lambda e^{-\lambda x} dx = 1 - e^{-\lambda x}$$

This is exactly the *cdf* of the inter arrival times of a Poisson process with mean rate λ. Hence, A_1, and for that matter all inter arrival times, are exponentially distributed with mean $1/\lambda$.

A discrete event simulation - Gillespie's First Reaction Method

u is uniform random variable drawn from $[0,1]$.

How to generate exponential from uniform random number see [1]

1. Label all possible events $E_1, E_2 \cdots E_n$.
2. For each event determine the rate at which it occurs $R_1, R_2 \cdots R_n$.
3. For each event, m, calculate the time until it next occurs, $\delta_t = \frac{-1}{R_m}\ln(u)$
4. Find the event, p, that happens first (has smallest δ_t),
5. Update the time $t \to t + \delta_t$ and event p is executed
6. Return to step 2

This is called the Gillespie's First reaction method.

- Easy to implement
- But slow
- Note that in pure discrete event simulation systems you can do this smarter (see Stochastic Simulation course).
- Other variants of the Gillespie's method, see book.

[1] https://www.win.tue.nl/~marko/2WB05/lecture8.pdf

Rates

In SIR with demography, 6 events plus rates

1. Birth $X \to X + 1$ with rate μN
2. Transmission $Y \to Y + 1$ and $X \to X - 1$ with rate $\beta \frac{XY}{N}$.
3. Recovery $Y \to Y - 1$ and $Z \to Z + 1$ with rate γY
4. Death, three independent events,
    1. $X \to X - 1$ with rate μX,
    2. $Y \to Y - 1$ with rate μY,
    3. $Z \to Z - 1$ with rate μZ

5.4 Stochastic Extinction

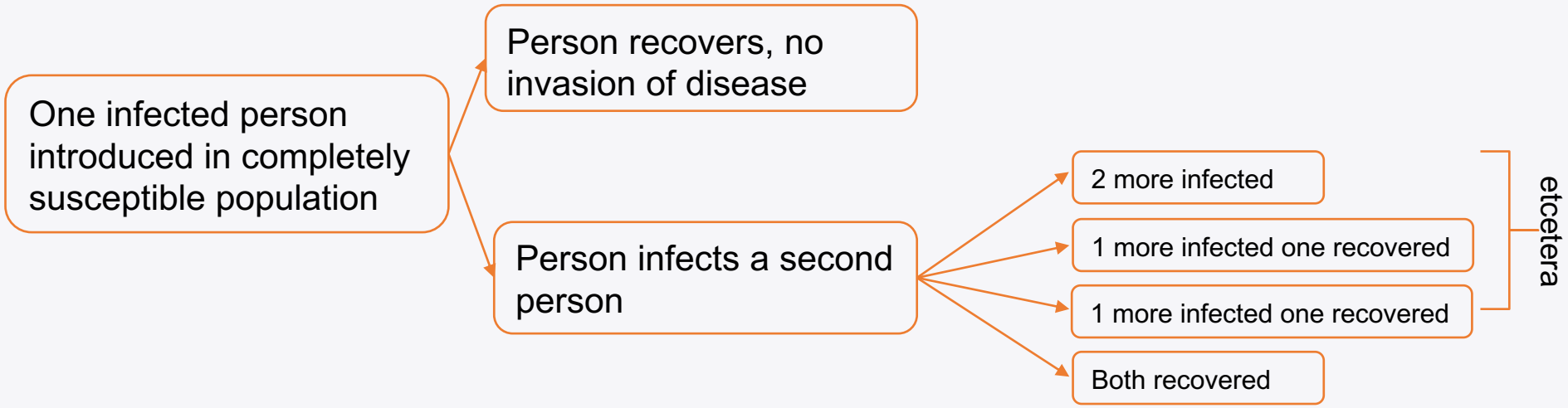
Stochastic Extinction

- When this event happens:

$$Y = 1 \rightarrow Y - 1 = 0$$

- This can happen most likely in
  - small populations
  - diseases that undergo large amplitude oscillations (e.g. due to seasonal forcing)
  - diseases with small R_0
- Also in case of invading disease
  - Chance that an invading infected individual **recovers before** passing the infection to a secondary case.

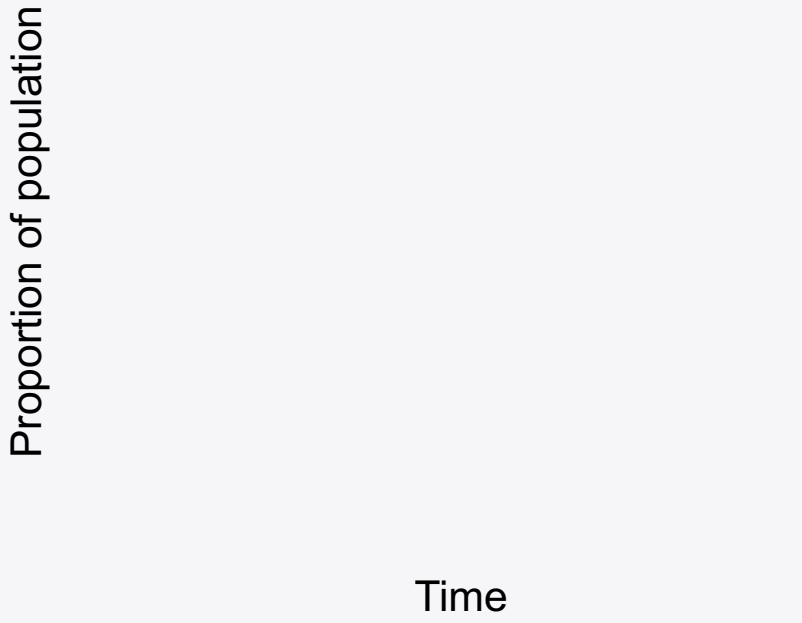
Branching processes in invasion



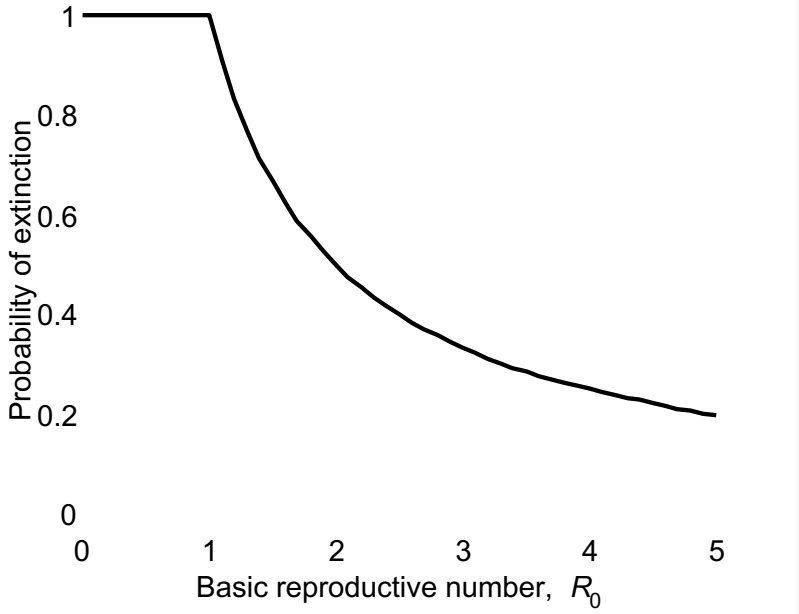
- Compute the probability that a disease goes extinct after introduction of one infected person, P_{ext}.
- Rate of recovery is γ (because $Y = 1$), and rate of infection is β (because $\beta \frac{XY}{N} = \beta \frac{N-1}{N} = \beta$ for large N)
- Following the branches we can write $P_{ext} = \frac{\gamma}{\beta+\gamma} + \frac{\beta}{\beta+\gamma} P_{ext}^2$
- So, we find, $P_{ext} = \frac{\gamma}{\beta} = \frac{1}{R_0}$

SIR output, stochastic effects

6 stochastic epidemics with $R_0 = 3$.



Probability of disease extinction following introduction of 1 case.



Stochasticity → risk of disease extinction when number of case is small,

even if $R_0 > 1$.

Branching processes in invasion

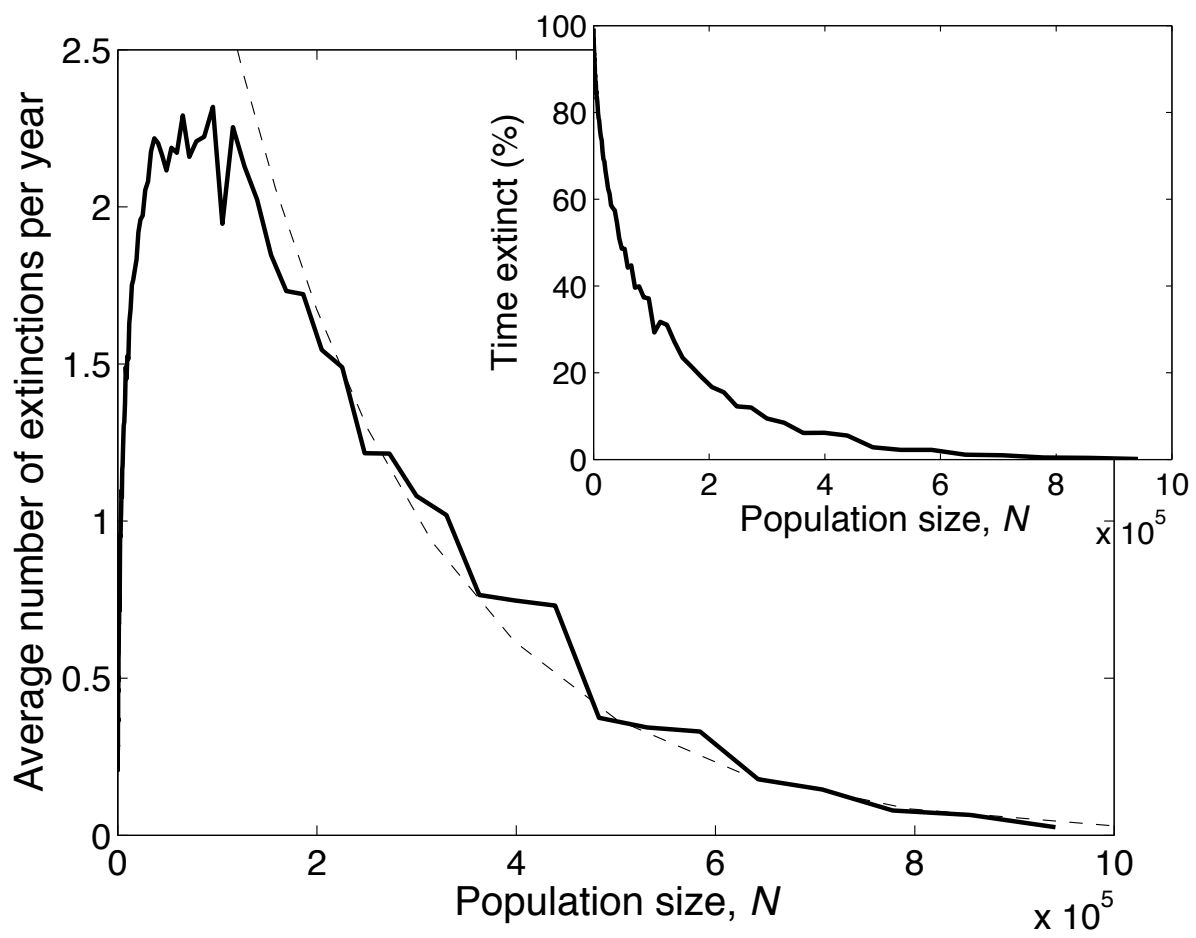
- Now if we would start with introducing n infected persons, and assume that the population already had some immunity $S = \frac{X}{N} < 1$ at the time of introduction
- The branching process analysis then leads to $P_{ext} = \frac{1}{R^n}$ where $R = R_0 S$ is the effective reproductive ratio at the time of introduction.

Imports

- Extinction of pathogen can be prevented by imports from the outside
  - By an infected person moving into the population, leading to an event $Y \to Y + 1$ with rate $\delta(N)$
    - If the population size should stay constant, the event would then also include $X \to X - 1$ or $Z \to Z - 1$ mimicking e.g. an emigration event.
  - By an infected person passing through the population, infecting a susceptible, and moving out again, leading to an event $X \to X - 1$ and $Y \to Y + 1$ with rate $\epsilon(N)X$
- These imports have been measured
  - For human populations, scale with the square root of the population size
    - For measles in England and Wales, rate of imports $\approx 5.5\times10^{-5}\sqrt{N}$
    - By a clever scaling argument (see book) this leads to

    $\delta(N) = 0.0625\mu(R_0 - 1)\sqrt{N}$

Rates of extinction



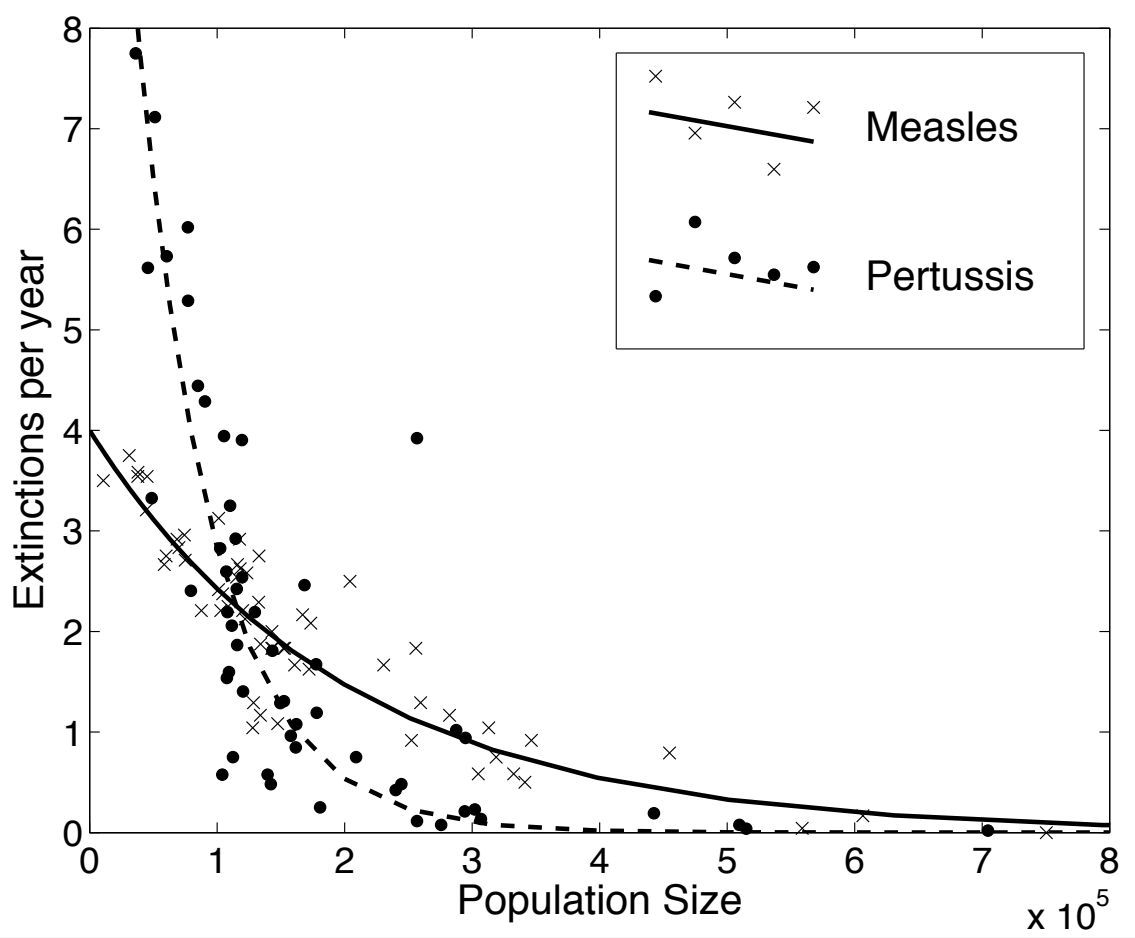
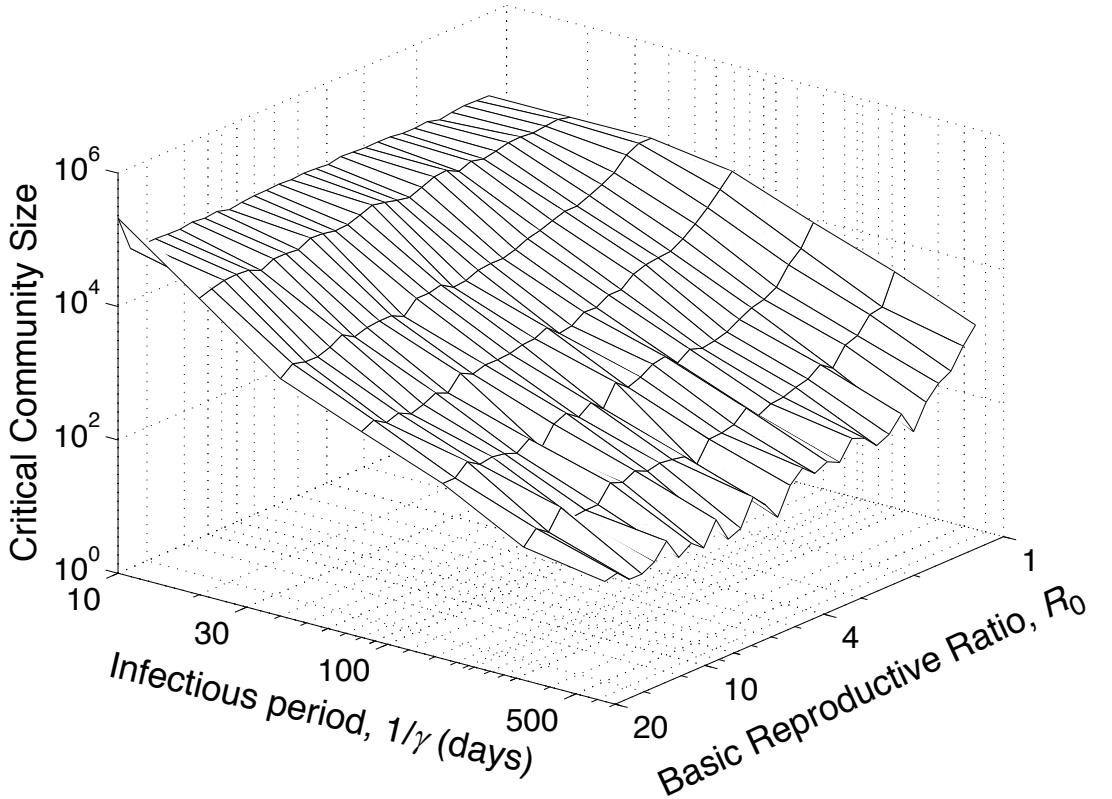


Figure 6.5 from Keeling and Rohani, The number of extinctions per year from a simple SIR stochastic model (left-hand graph) and from measles and pertussis (whooping cough) data in England and Wales before vaccination (right-hand graph). Exponential functions, $k \sim \exp(-\alpha N)$, are fitted to the point data. The inset graph in the left-hand figure shows how the amount of time the population is disease-free scales with the population size. ($\mu = \nu = 5.5 \times 10^{-5}$ per day, $R_0 = 10$, $1/\gamma = 10$ days, import rate $\delta = 0.02\sqrt{N}$ per year.

Critical Community Size

- Critical Community Size (CCS) is defined as the population size that does not suffer disease extinction
  - For measles, around 400,000



- The stochastic model does capture the CCS, but the actual number for e.g. measles is much higher than actually observed when including seasonality forcing.
- Greater heterogeneity in the model is needed.

Figure 6.6 from Keeling and Rohani, The CCS, approximated as the population size that experiences one extinction event per year, for the stochastic SIR model ($\mu = \nu = 0.02$ per year, import rate $\epsilon = 0.213\,(R_0 - 1)/\sqrt{N}$ per year. Results are from simulations of 100 years after transients

Persistence

How to measure persistence of a pathogen in stochastic models

- (give it a try in the lab course)

1. Extinctions with imports

   Count the number of extinctions per time unit

   - Corresponds to reality
   - Hard however to parametrize the import rate

2. Time to extinction

   Start simulation close to endemic equilibrium and then measure the average time until extinction

   - A.k.a. first passage time
   - No imports are needed, but does not correspond to biological reality

3. Conditional Extinctions

   Look at asymptotic rate of extinctions.

   - First start many populations, discard those that go extinct after a set period, and then study the asympotic extinctions in the remaining populations.