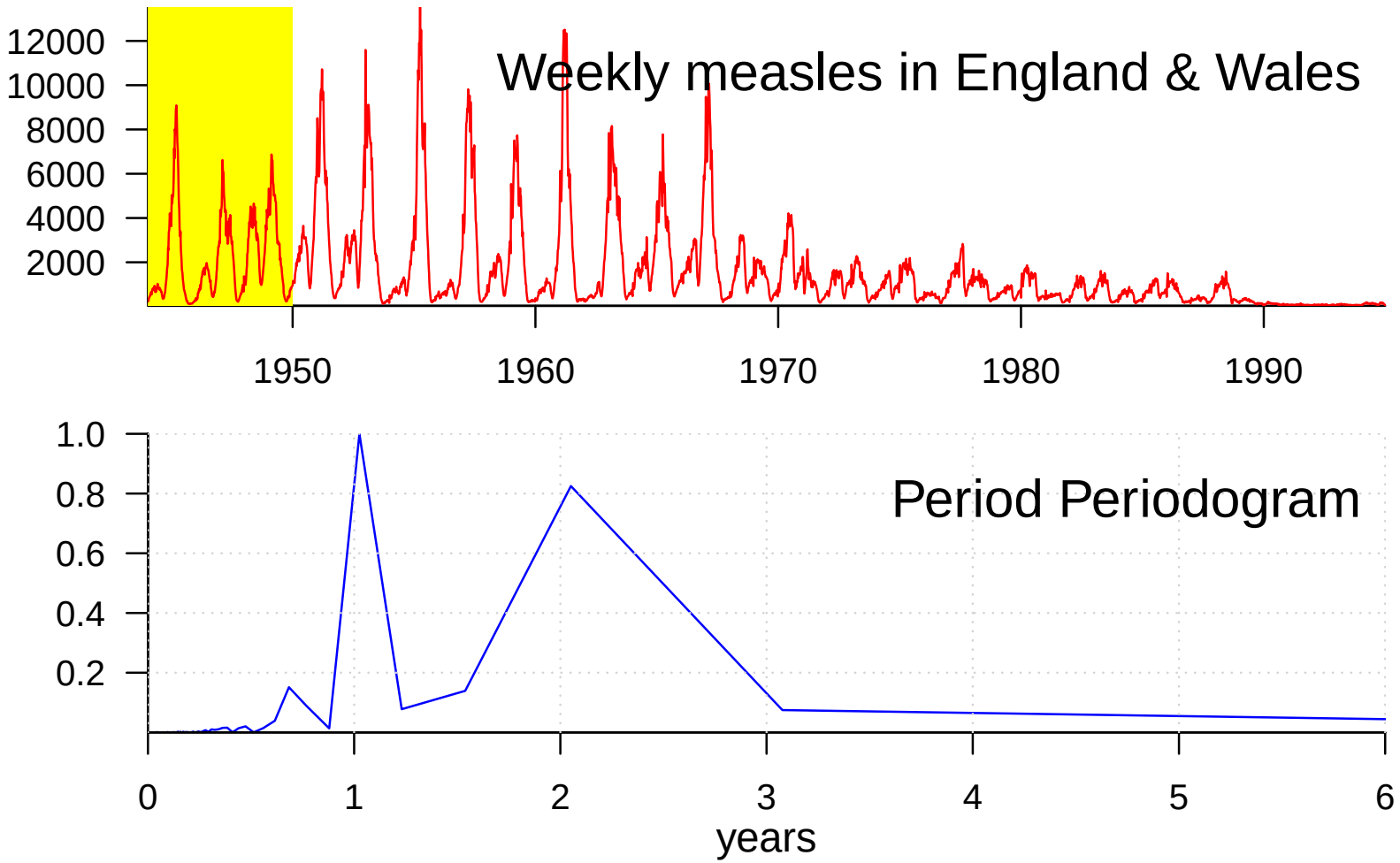
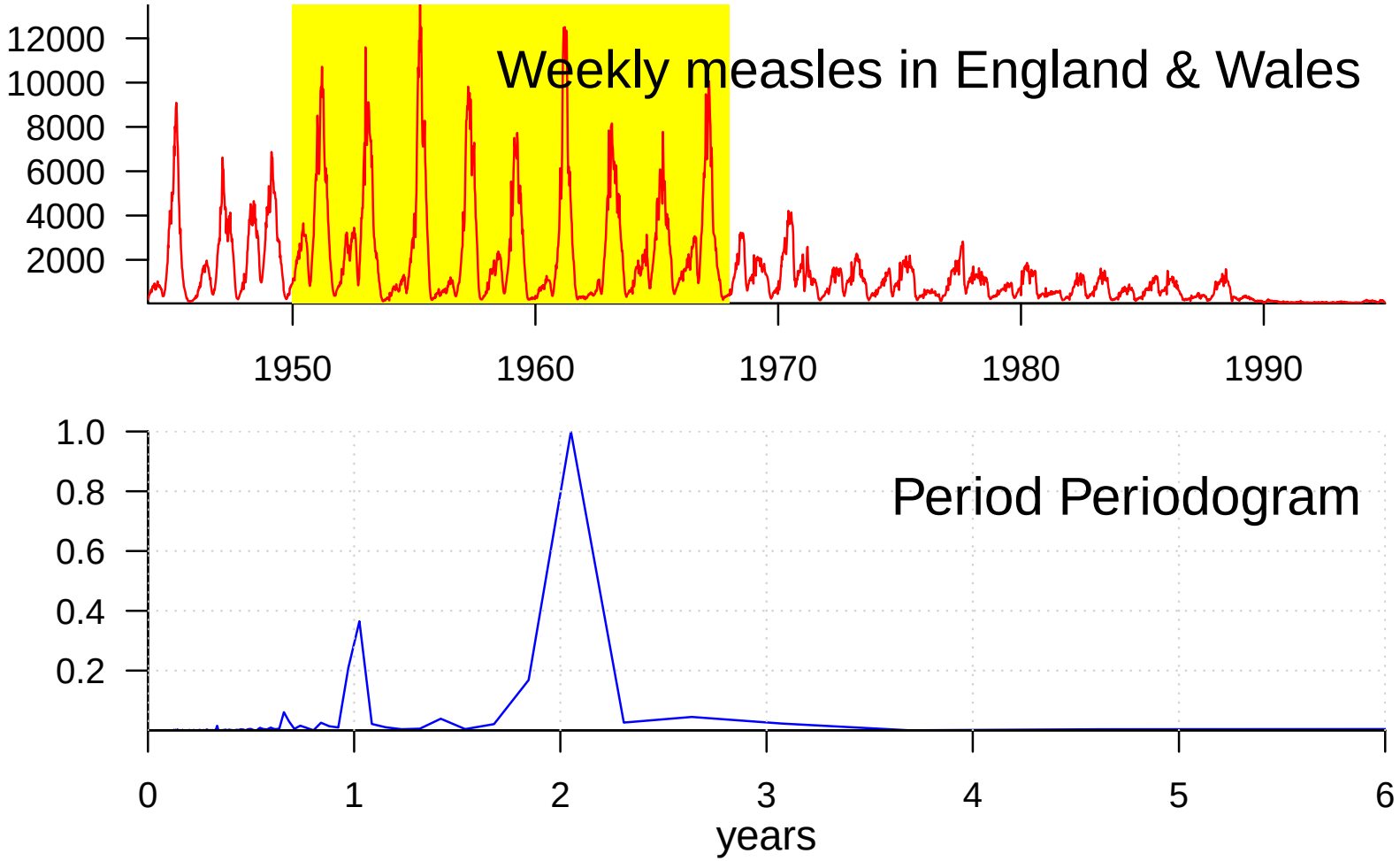
13 Mechanistic Modelling of Recurrent Epidemics

Mechanistic Modelling of Recurrent Epidemics

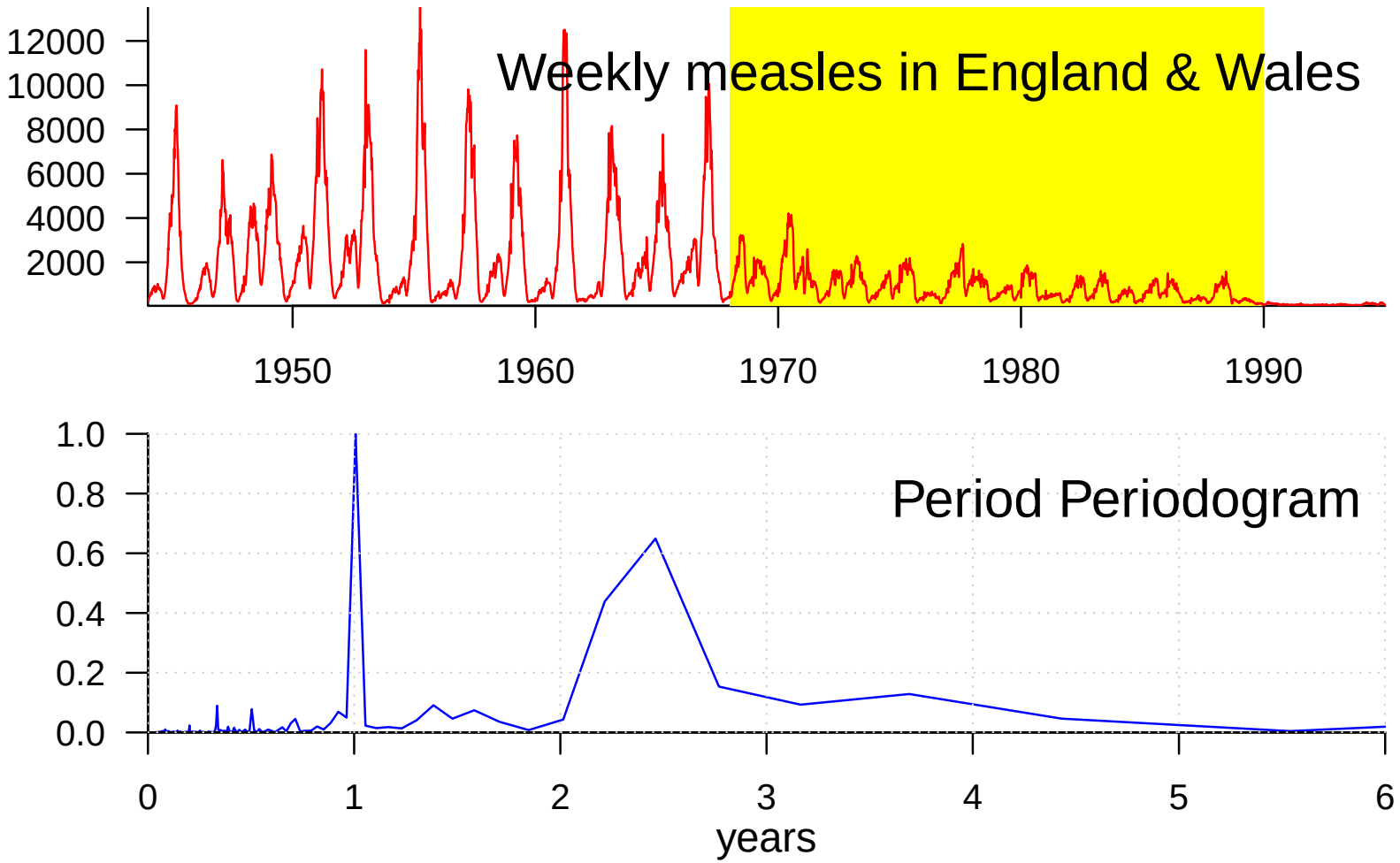
What causes changes in frequency content over time?



What causes changes in frequency content over time?

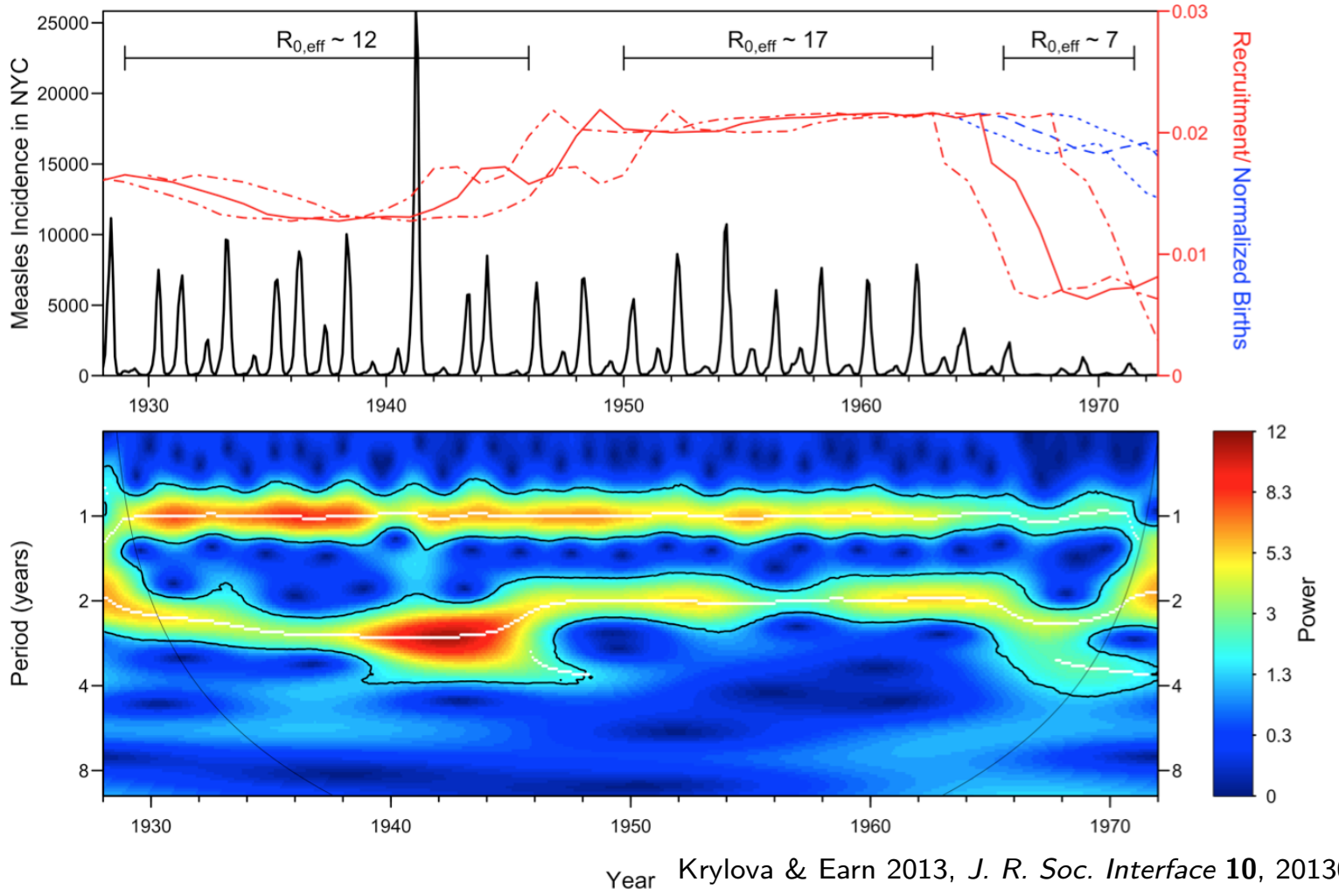


What causes changes in frequency content over time?



What causes changes in frequency content over time?

Measles in New York City

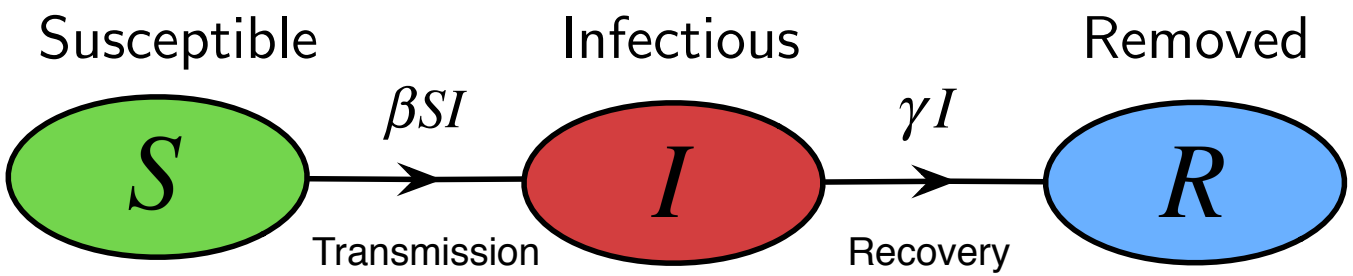


Krylova & Earn 2013, *J. R. Soc. Interface* **10**, 20130098

Mechanistic Epidemic Modelling: Principles

- Consider the biological mechanisms involved in disease transmission and spread
- Model mechanisms and infer their effects
- Start as simple as possible!
- Rule out simple models by comparing results with observed time series of incidence or mortality
- Add complexity one step at a time, so key mechanisms can be identified
- Ideally converge on simplest possible model that can explain observed patterns

The SIR model: Flow Chart and Parameters



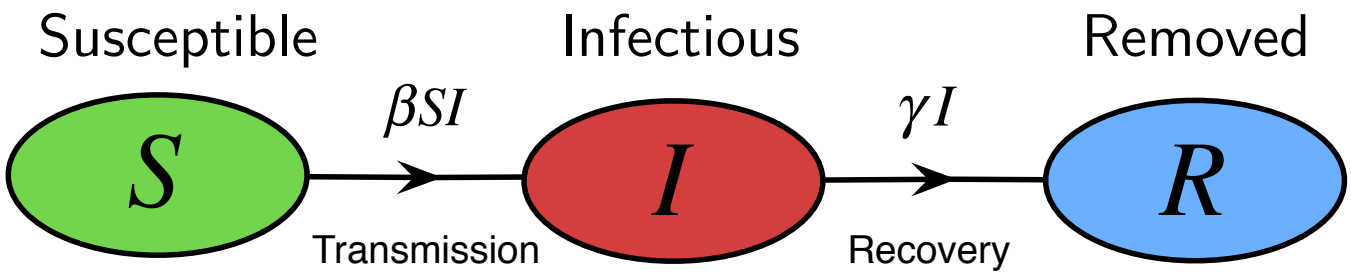
$$\frac{dS}{dt} = -\beta SI$$

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

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

- **Parameters:**
  - Transmission rate β
  - Recovery rate γ (or Removal rate)

The SIR model: Derived Parameters



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

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

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

- **Derived Parameters:**
  - Initial growth rate $\beta - \gamma$
  - Mean infectious period $\frac{1}{\gamma}$
  - Basic Reproduction Number

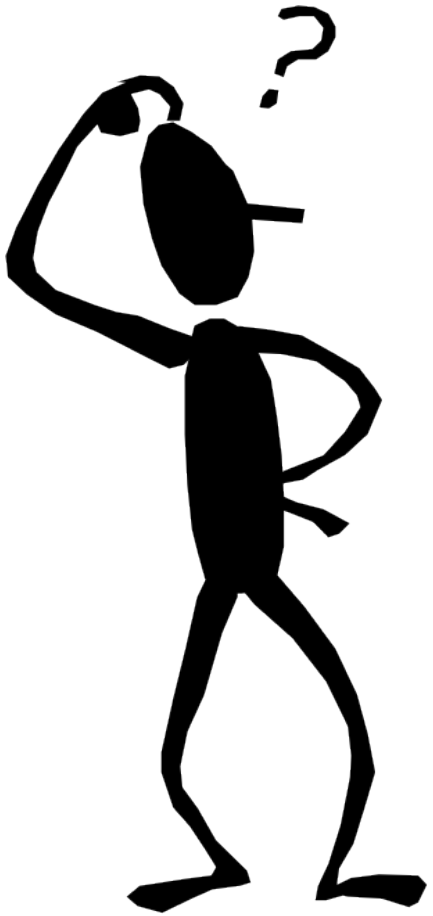
$$\mathcal{R}_0 = \frac{\beta}{\gamma}$$

Basic SIR Model: Important Results

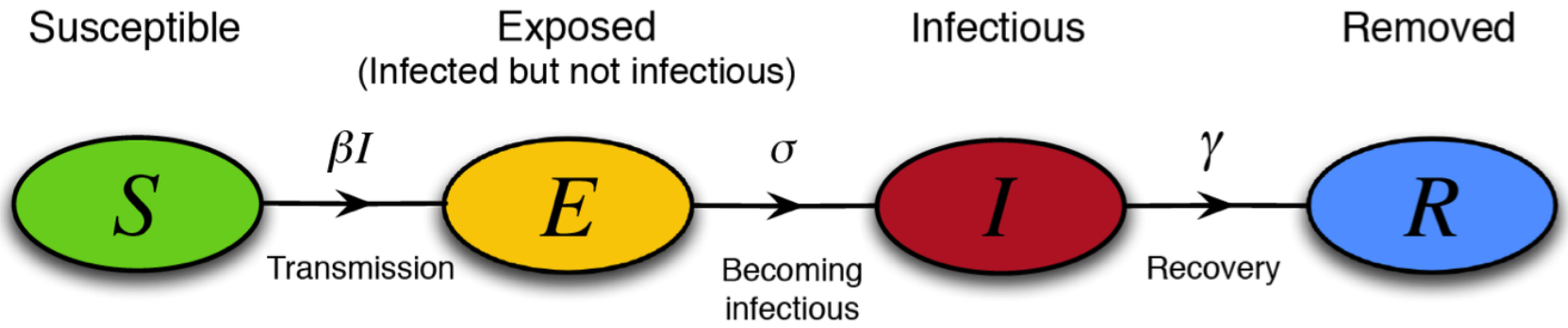
- Epidemic occurs if and only if $\mathcal{R}_0 > 1$
- Exact solution for phase portrait
- Single epidemic, then disease disappears
- Exact formula for final size as a function of $\mathcal{R}_0$

- Cannot explain diseases that persist
- Cannot explain recurrent cycles of epidemics

What are we missing?

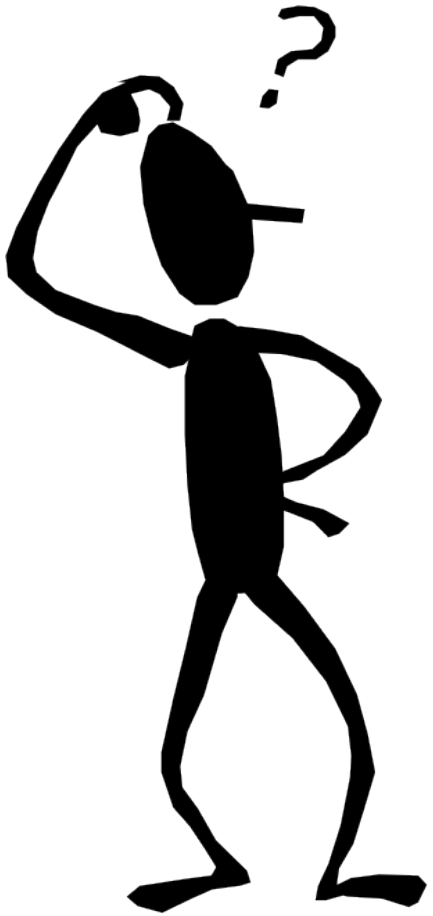


SEIR Model: flow chart

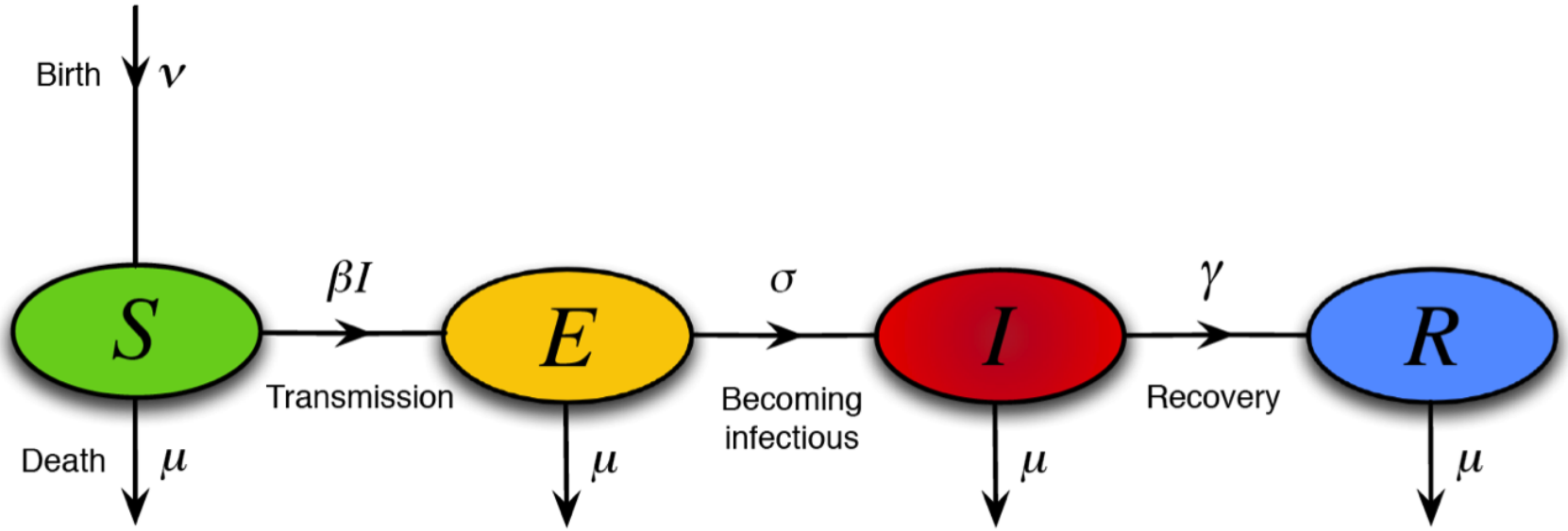


- Introduces only one new parameter (σ)
- Mean latent period ($1/\sigma$) can often be estimated
- But... effect of inclusion of exposed class usually small

What are we still missing?



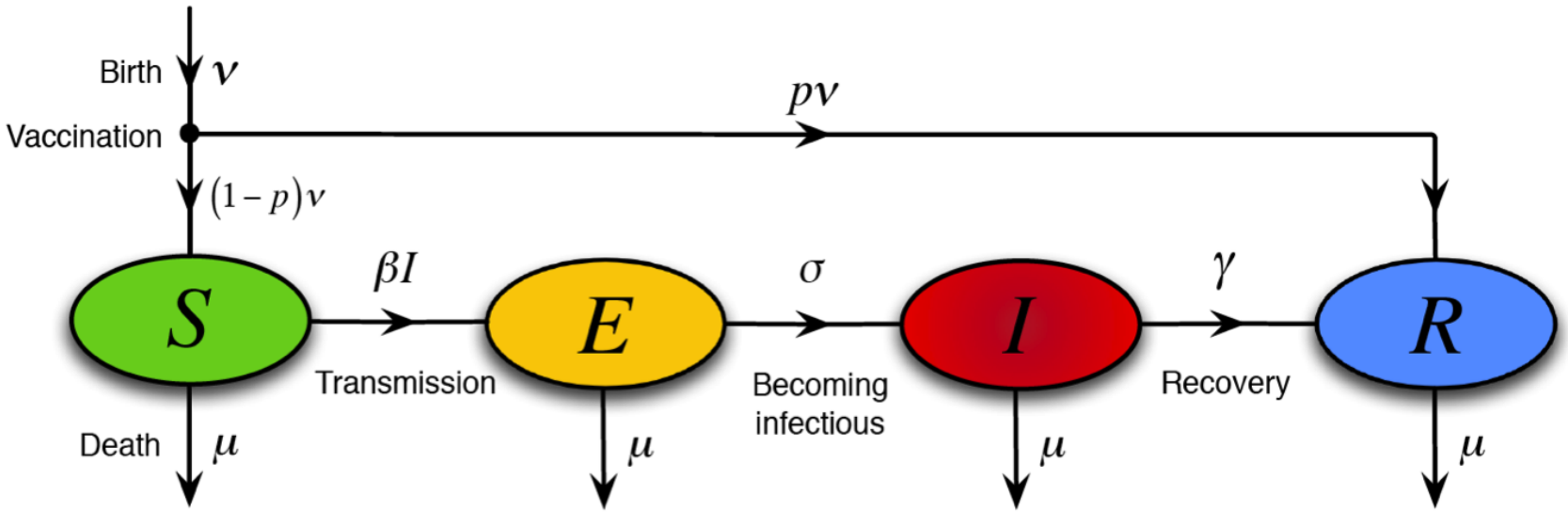
SEIR Model with vital dynamics: flow chart



New Parameters:

- Birth rate (ν for natality)
- Death rate (μ for mortality)
- Mean latent period ($1/\sigma$)

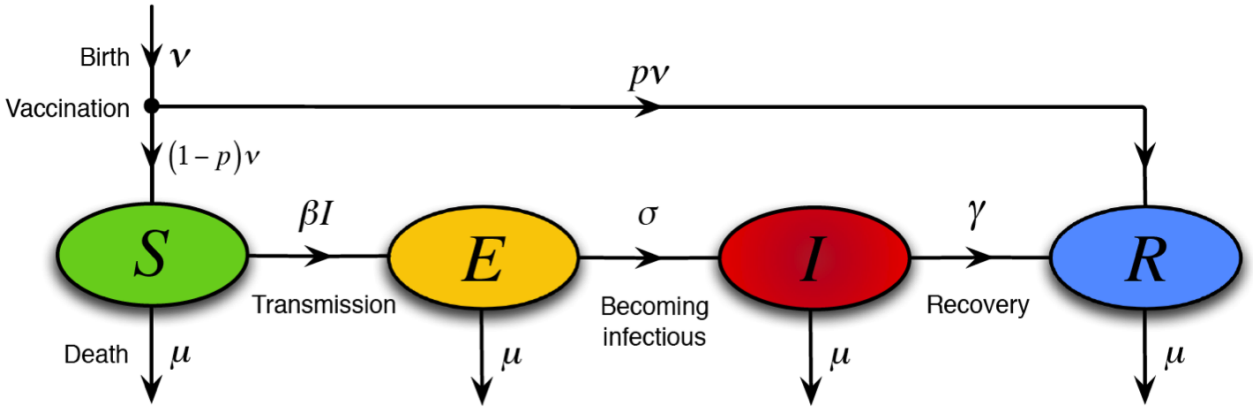
SEIR with vital dynamics and vaccination: flow chart



New Parameters:

- Birth rate (ν for natality)
- Death rate (μ for mortality)
- Mean latent period ($1/\sigma$)
- Proportion vaccinated (p)

SEIR with vital dynamics and vaccination: Equations



$$\frac{dS}{dt} = \nu(1-p) - \beta SI - \mu S$$

$$\frac{dE}{dt} = \beta SI - \sigma E - \mu E$$

$$\frac{dI}{dt} = \sigma E - \gamma I - \mu I$$

$$\frac{dR}{dt} = \nu p + \gamma I - \mu R$$

- Birth rate (ν for natality)
- Death rate (μ for mortality)
- Proportion vaccinated (p)
- Transmission rate (β)
- Mean latent period ($1/\sigma$)
- Mean infectious period ($1/\gamma$)

McMaster University

Mathematics and Statistics

$$\int_M d\omega = \int_{\partial M} \omega$$

Mathematics 4MB3/6MB3 Mathematical Biology

Instructor: David Earn

Lecture 13
Mechanistic Modelling of Recurrent Epidemics
Monday 5 February 2018

Announcements

- **Assignment 2:** Due TODAY!
  Do the Group contribution survey TODAY.
- **Assignment 3:** Will be posted tonight or tomorrow.
  Due Monday 26 February 2018, 11:30am.
- **Midterm test:**
  - *Date:* Thursday 8 March 2018
  - *Time:* 7:00pm to 9:00pm
  - *Location:* BSB-B154

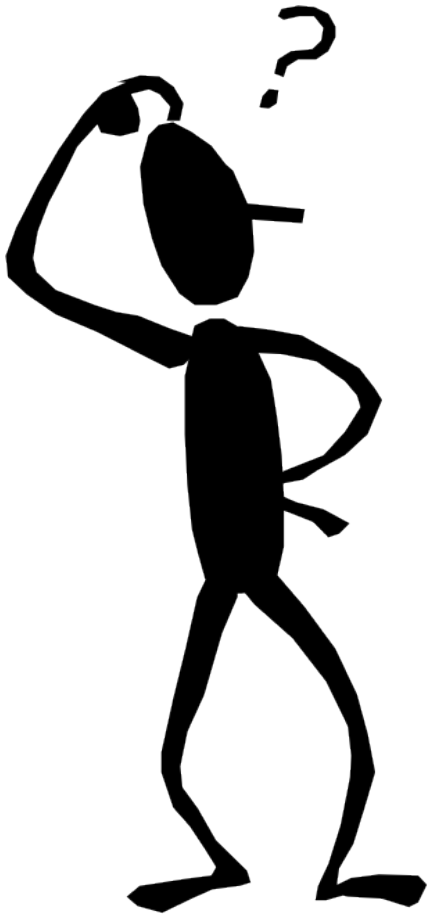
SEIR with vital dynamics and vaccination: Analysis

- $\mathcal{R}_0$?
  - Biological derivation: (assuming $\nu = \mu$ and $p = 0$)
    $\mathcal{R}_0 = \beta \times \frac{\sigma}{\sigma+\mu} \times \frac{1}{\gamma+\mu} \quad \simeq \frac{\beta}{\gamma} \quad \because \frac{1}{\mu} \gg \max\left(\frac{1}{\sigma}, \frac{1}{\gamma}\right)$
  - Mathematical derivation:
    $\mathcal{R}_0 = 1$ is stability boundary
- Final size ? Not well defined (because of continuous source of new susceptibles).
- Equilibria ?
  - Disease Free Equilibrium (DFE)
  - Endemic Equilibrium (EE)
  - That's all folks.
- Periodic solutions ? No.
- What else ? Chaos?

SEIR with vital dynamics and vaccination: Results

- $\exists$ Endemic Equilibrium $\iff \mathcal{R}_0(1-p) > 1$
  - EE is GAS in this case.
  - DFE is GAS otherwise.
- Eradication $\iff p > 1 - \frac{1}{\mathcal{R}_0}$ (herd immunity)
  - Smallpox: $\mathcal{R}_0 \sim 4 \implies p_{\text{crit}} \sim 75\%$
  - Measles: $\mathcal{R}_0 \sim 20 \implies p_{\text{crit}} \sim 95\%$
- Explains persistence of diseases (via births)
- No periodic solutions $\overset{?}{\implies}$ no recurrent epidemics
- GAS equilibrium $\implies$ no periodic solutions and no chaos
- Equilibrium approached by *damped oscillations* $\implies$ recurrent epidemics
- But observed epidemic patterns show *undamped* oscillations. . .

What are we STILL missing?



Demographic Stochasticity

- Differential equations describe the expected behaviour in the limit that the population size goes to infinity
- How do dynamics differ in finite populations?
- Re-cast the SEIR model as a stochastic process (Continuous time Markov process)
- Proving anything about stochastic epidemic models is difficult, but we can easily simulate them and learn a lot
- Standard algorithm for creating realizations of a stochastic epidemic model attributed to Daniel T. Gillespie

Gillespie 1976, *J. Comp. Phys.* **22**, 403–434

  - Rather than rates of change of compartment sizes consider event rates for transitions between disease states
  - Finite number of individuals
  - Assume event rates depend only on current state of population

Gillespie Algorithm

- Let a_1, a_2, ..., be the rates at which the various processes occur, *e.g.*,
  - a_1 = birth rate,
  - a_2 = rate of going from susceptible to exposed,
  - a_3 = the rate of going from infectious to removed (recovering),
  - *etc.*
- Let a_0 be the overall event rate, *i.e.*, $a_0 = \sum_i a_i$ (so average time between events $= 1/a_0$).
- Assume time spent in any state is exponentially distributed (transitions between states are "Poisson processes")
- $\therefore$ Probability next event occurs in $(t, t+dt)$ is $a_0 e^{-a_0 t} dt$
- Let $u = 1 - e^{-a_0 t}$. Then $u \in [0,1]$ and $du = a_0 e^{-a_0 t} dt$ $\implies$ u is uniformly distributed in $[0,1]$.
- $\therefore$ Get time t to next event by sampling u from uniform distribution in $[0,1]$ and setting $t = \frac{1}{a_0} \ln \frac{1}{1-u}$.

Gillespie Algorithm continued

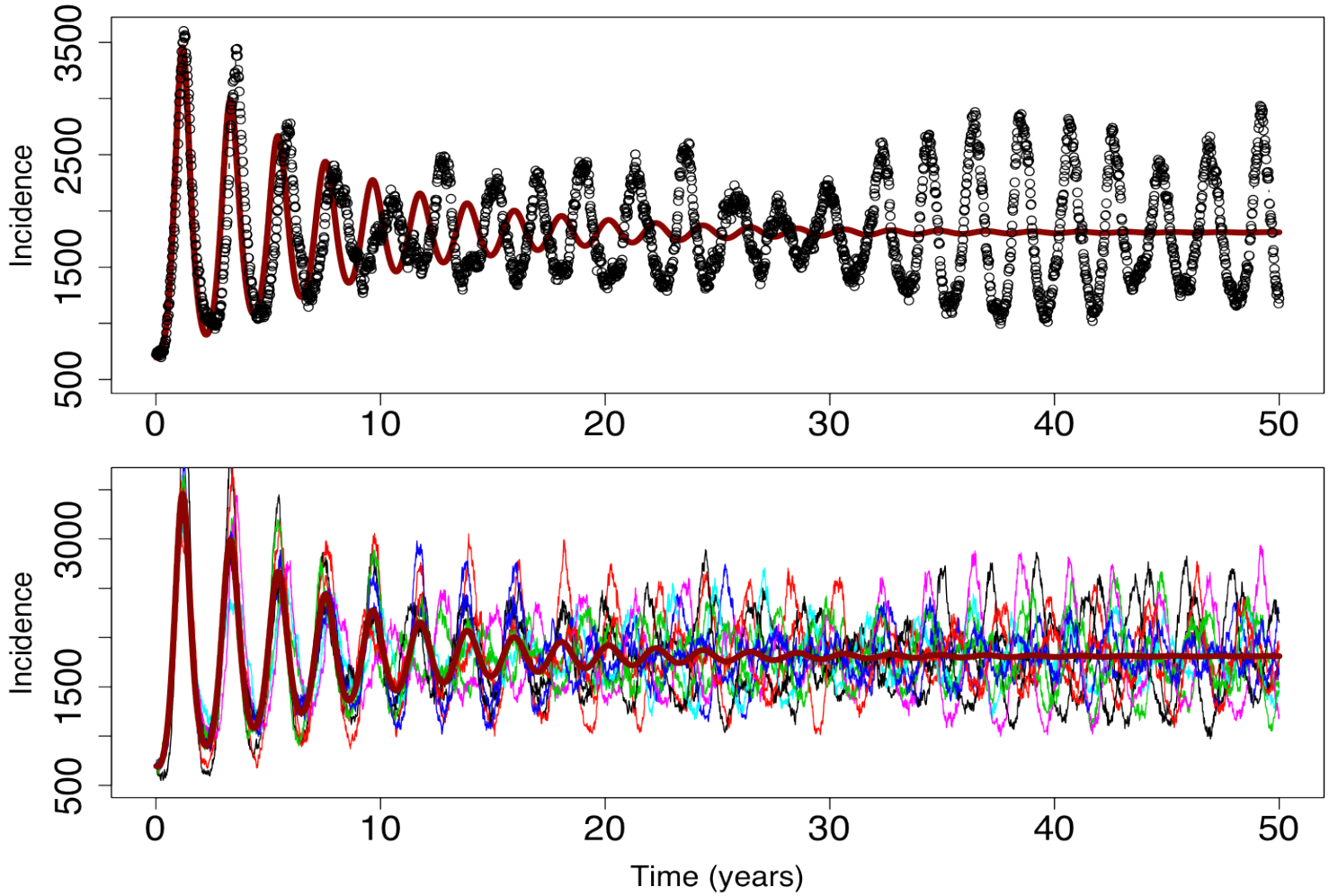
- We now know the time t of the next event, but we must still determine what type of event occurs at time t.
- Probability of event of type i is $\dfrac{a_i}{a_0}$
- $\therefore$ Can easily determine type of event by sampling a point from a uniform distribution on $[0, a_0]$:
  - Event is type i if the uniform deviate lies in the ith interval in the following list:

$$[0, a_1),\ [a_1, a_1 + a_2),\ \ldots,\ [a_1 + \cdots + a_{i-1}, a_1 + \cdots + a_i),\ \ldots$$

- How do realizations of this process differ from the solution of the deterministic (differential equation) model?

Gillespie Simulations: Results for Measles Parameters

$\mathcal{R}_0 = 17$, $T_{\rm lat} = 8$ days, $T_{\rm inf} = 5$ days, $\nu = \mu = 0.02$/year, $N = 5,000,000$



Earn 2009, *IAS/Park City Mathematics Series* **14**, 151–186

Effects of Demographic Stochasticity

- Sustains transient behaviour (oscillations do not damp out) (Bartlett 1950's)
- Explains undamped oscillations at a single period
- But, unable to explain changes in interepidemic period, or irregularity

What are we **STILL** missing?