

Introduction to Infectious Disease Modelling

Clinic on the Meaningful Modeling of Epidemiological Data, 2015

African Institute for Mathematical Sciences

Muizenberg, South Africa

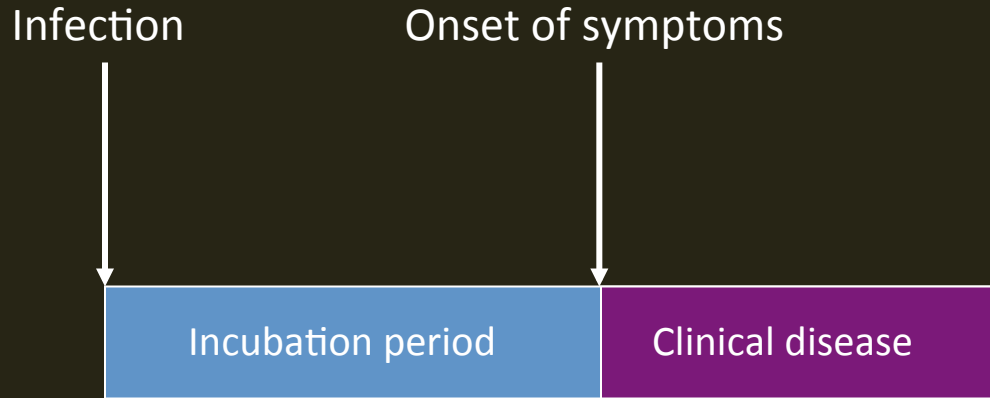
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Postdoctoral Fellow

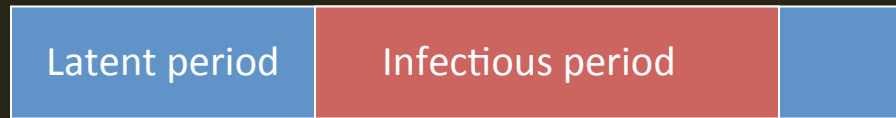
Center for Computational Biology & Bioinformatics

University of Texas at Austin

Natural History of Infection



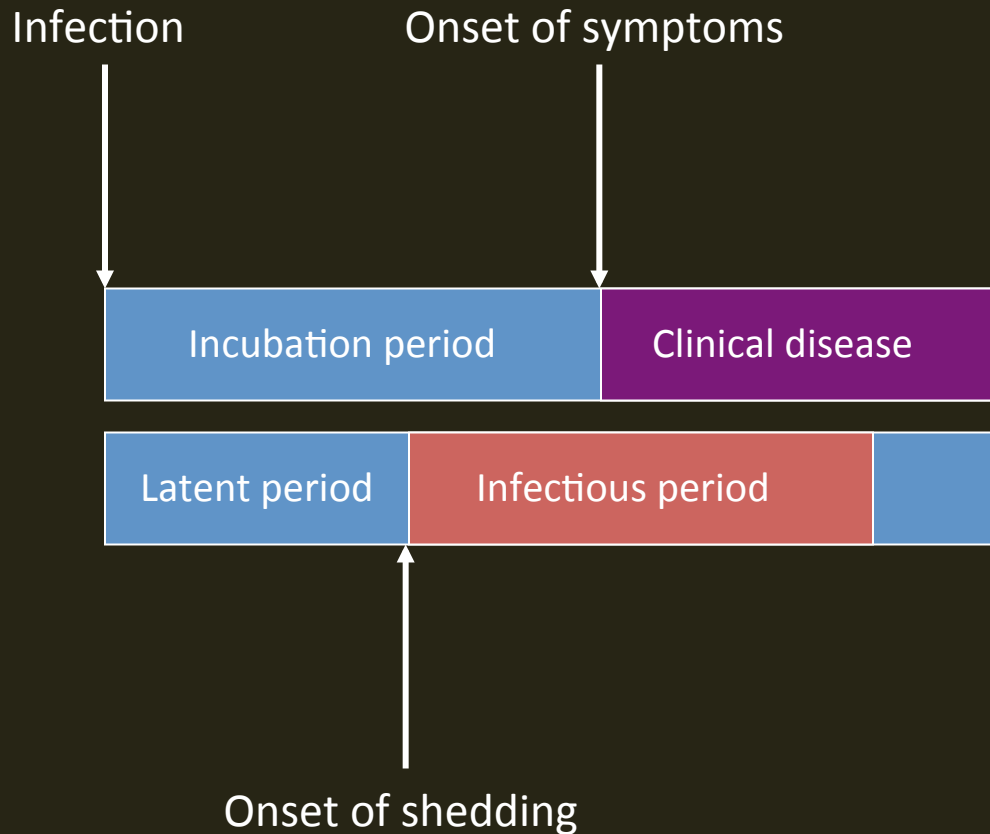
Natural History of Infection



Onset of shedding

Natural History of Infection

Let's start by talking about acute, immunizing diseases



Acute

Infection time course

<<<

host lifespan

Immunizing

infection → antibody production

prevents future infection

Examples

Whooping cough



Foodborne



Chicken pox



Measles



Smallpox

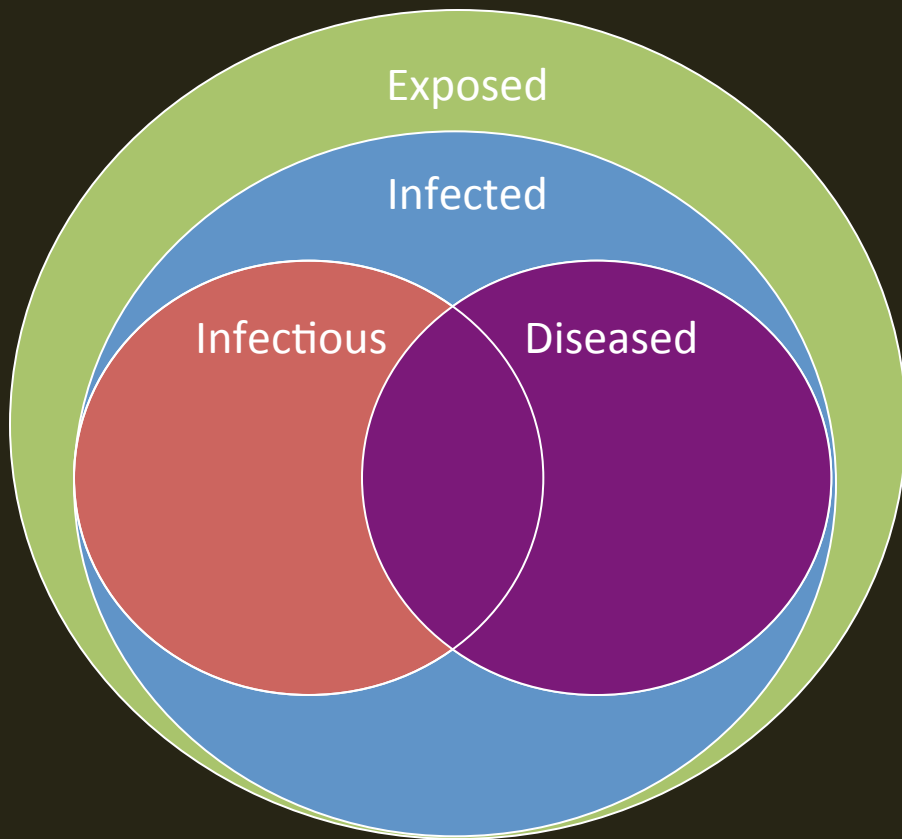


Natural History of Infection

Table 3.1 Incubation, latent and infectious periods (in days) for a variety of viral and bacterial infections. Data from Fenner and White (1970), Christie (1974), and Benenson (1975)

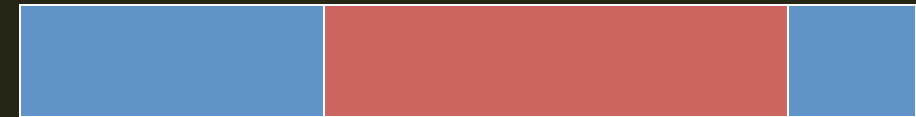
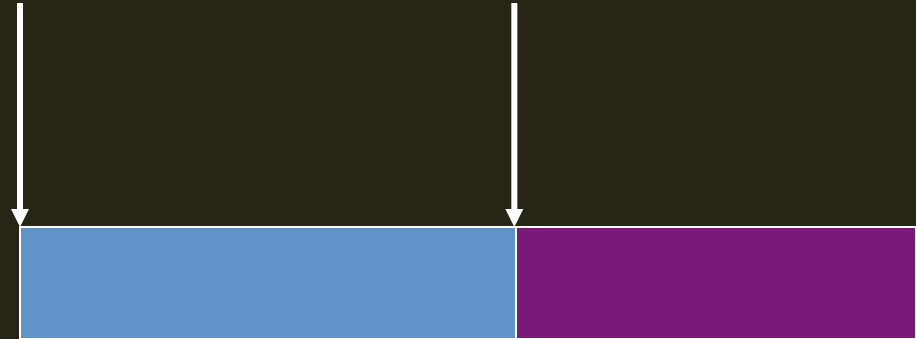
| Infectious disease | Incubation period | Latent period | Infectious period |
|----------------------------|-------------------|---------------|-------------------|
| Measles | 8–13 | 6–9 | 6–7 |
| Mumps | 12–26 | 12–18 | 4–8 |
| Whooping cough (pertussis) | 6–10 | 21–23 | 7–10 |
| Rubella | 14–21 | 7–14 | 11–12 |
| Diphtheria | 2–5 | 14–21 | 2–5 |
| Chicken pox | 13–17 | 8–12 | 10–11 |
| Hepatitis B | 30–80 | 13–17 | 19–22 |
| Poliomyelitis | 7–12 | 1–3 | 14–20 |
| Influenza | 1–3 | 1–3 | 2–3 |
| Smallpox | 10–15 | 8–11 | 2–3 |
| Scarlet fever | 2–3 | 1–2 | 14–21 |

Terminology



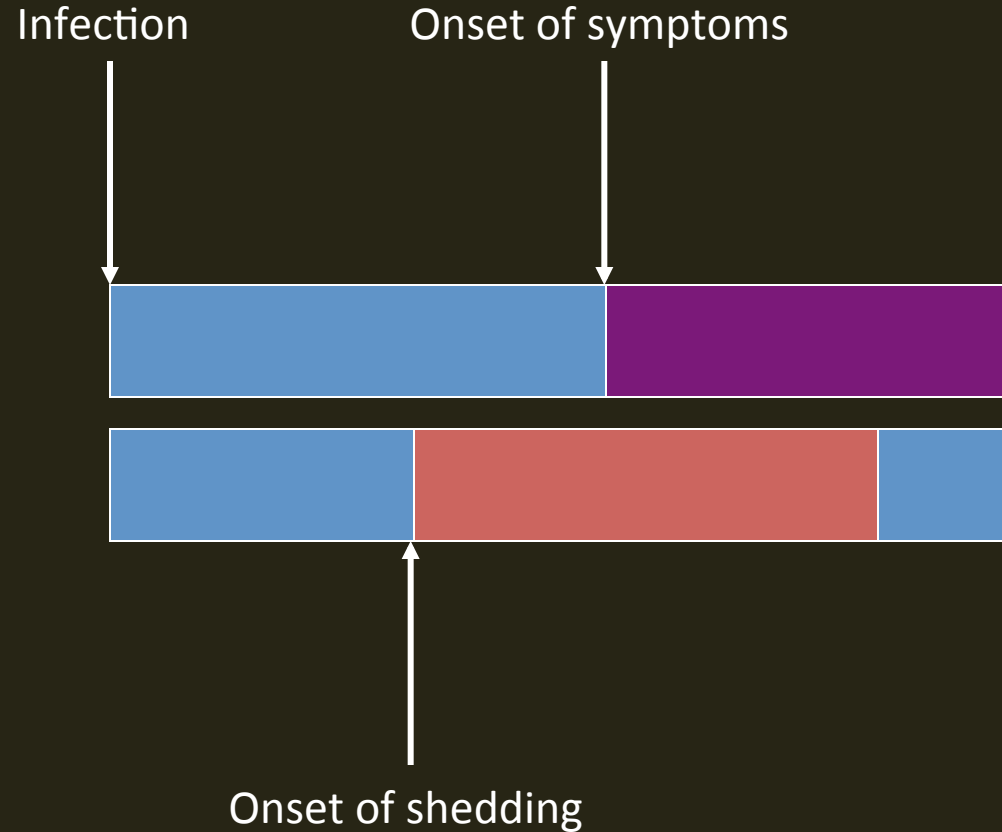
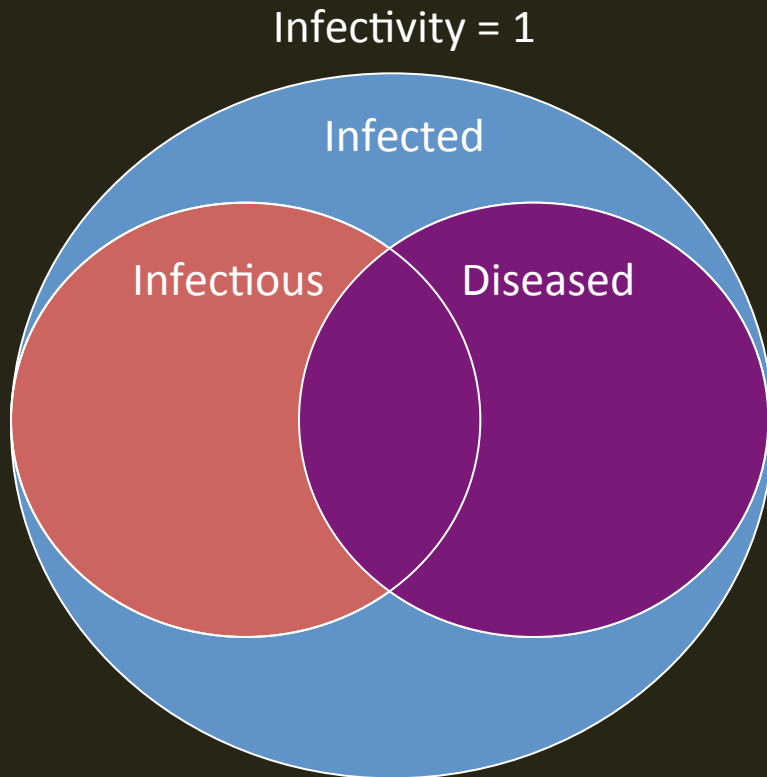
Infection

Onset of symptoms



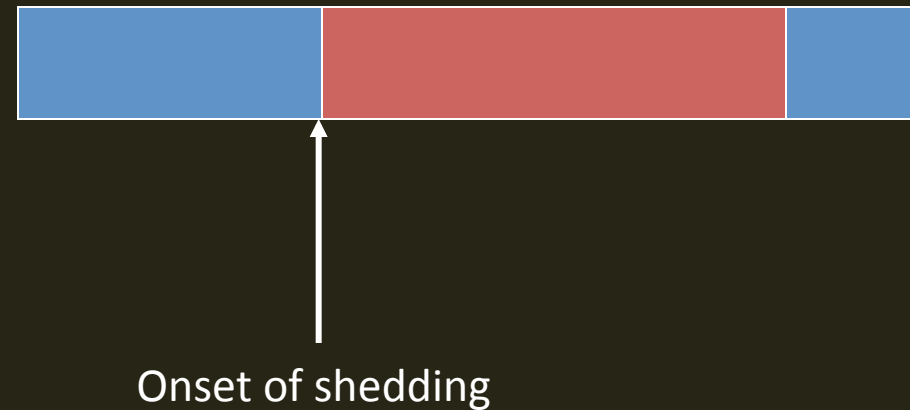
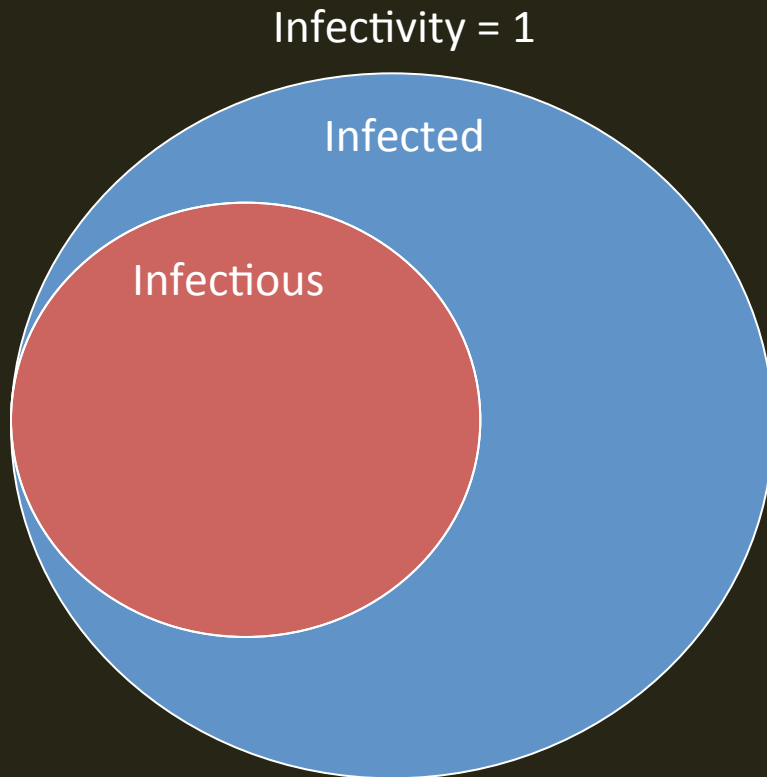
Onset of shedding

A **simple** view of the world



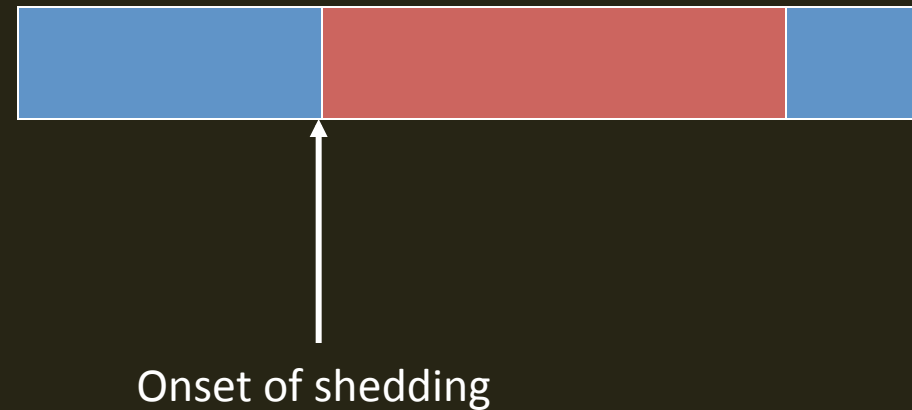
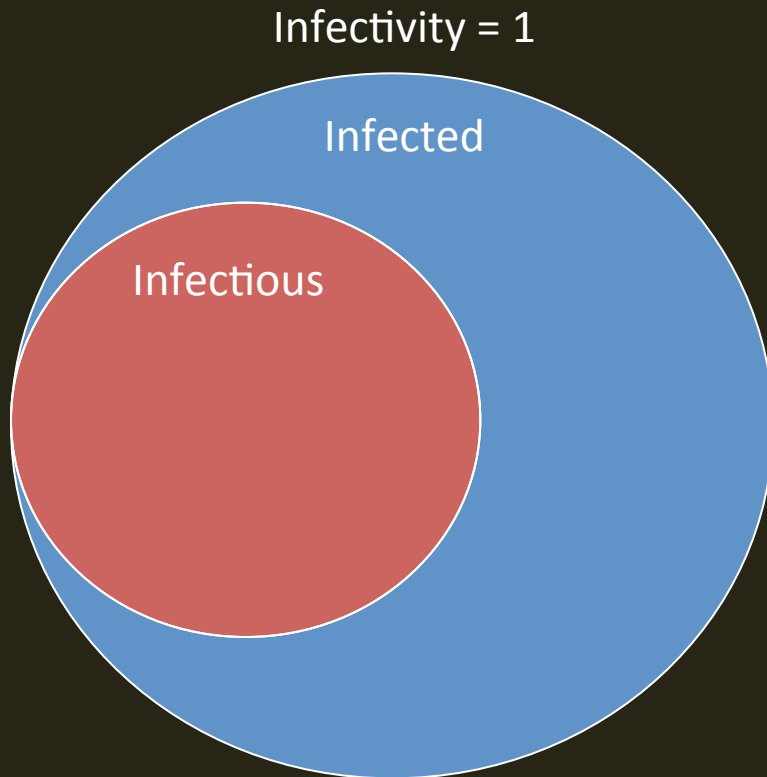
A simpler view of the world

Don't worry about symptoms and disease!



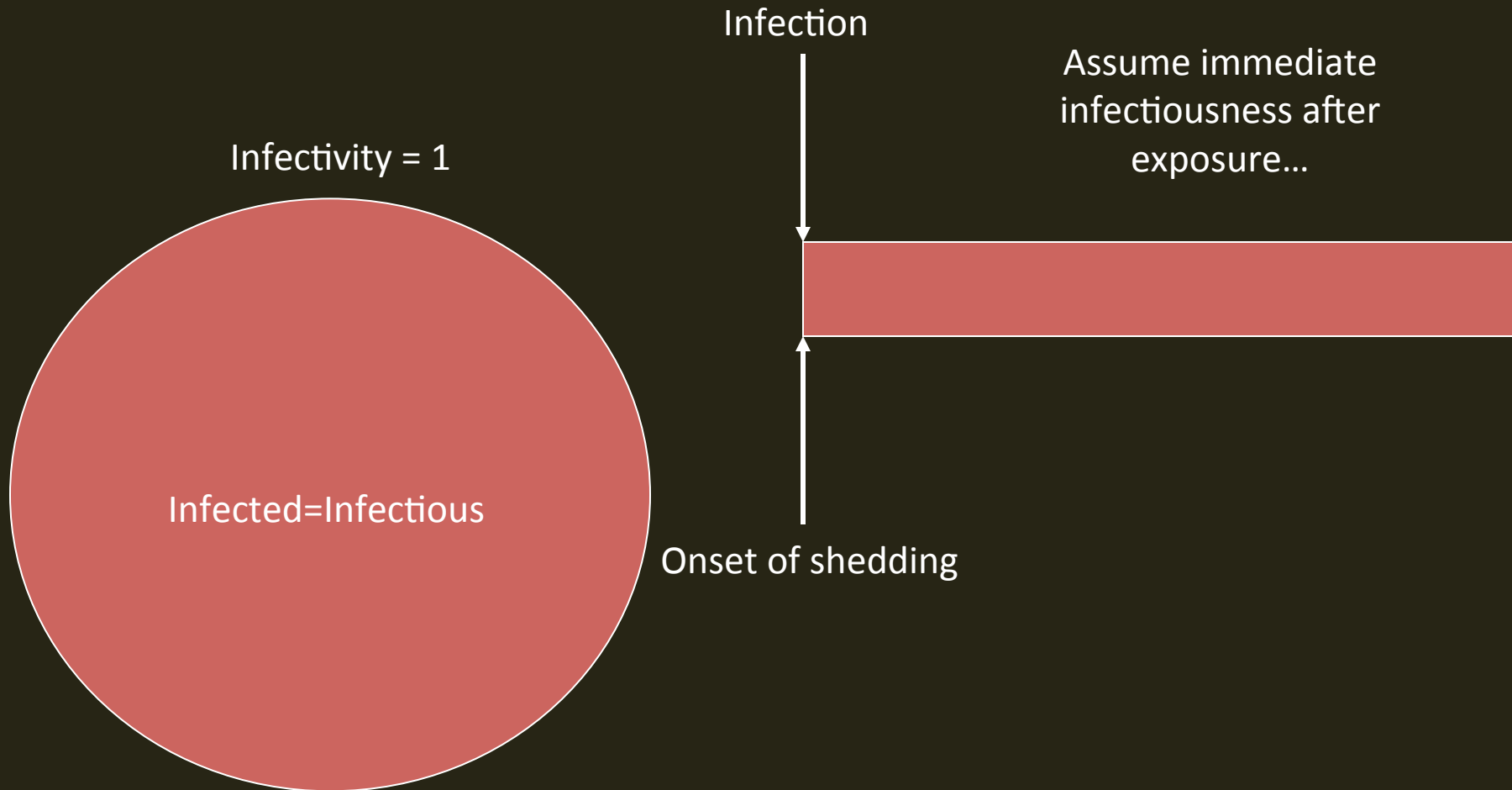
An **even simpler** view of the world

Don't worry about
symptoms and disease!



An extremely simple view of the world

Don't worry about symptoms and disease!



An **extremely simple** view of the world



An **extremely simple** view of the world



Susceptible



Infectious

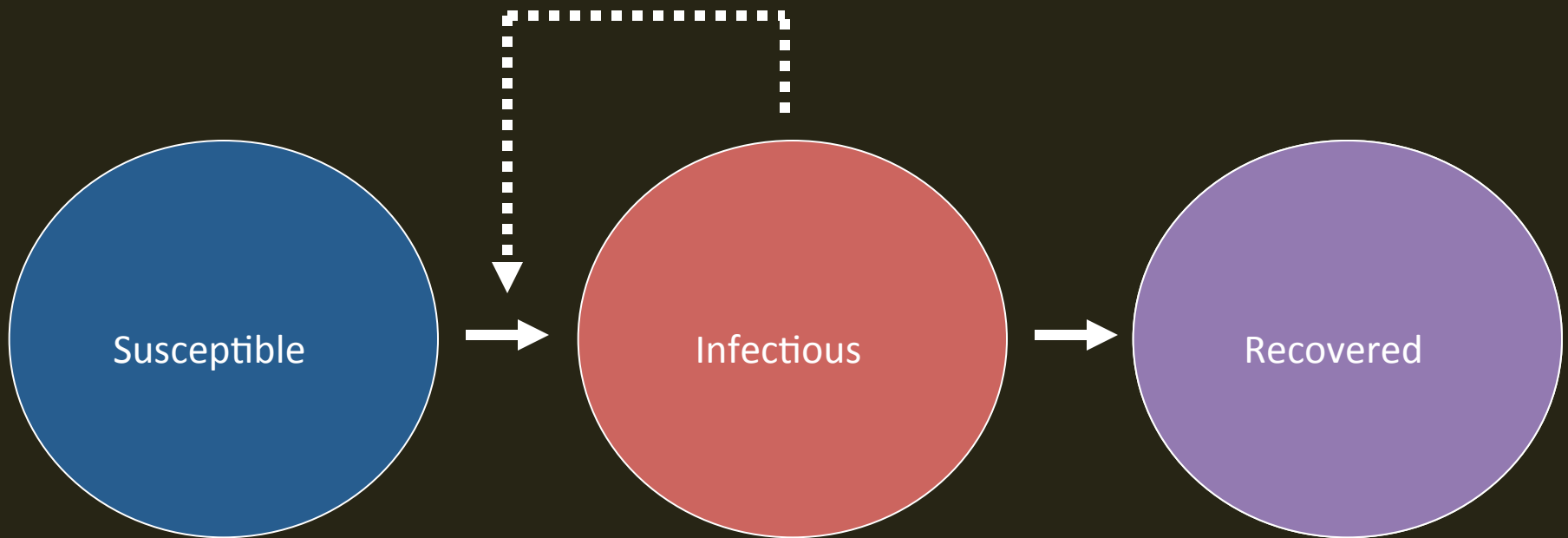


Recovered

An **extremely simple** view of the world

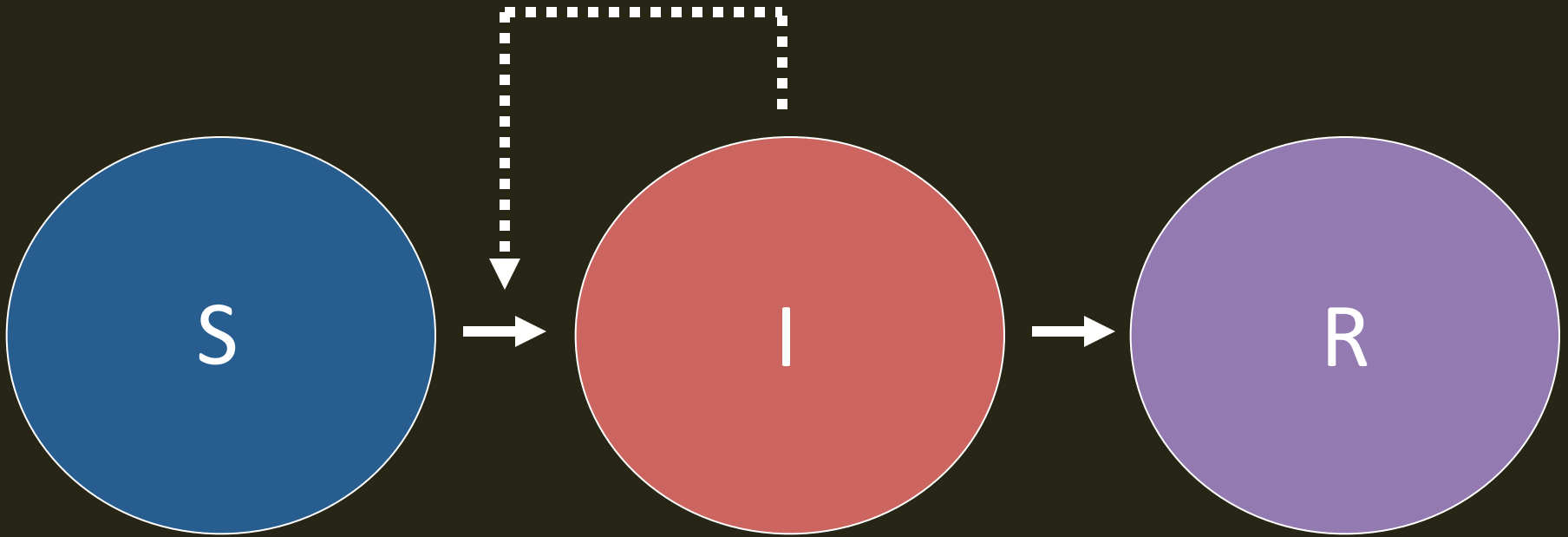


Health-related States

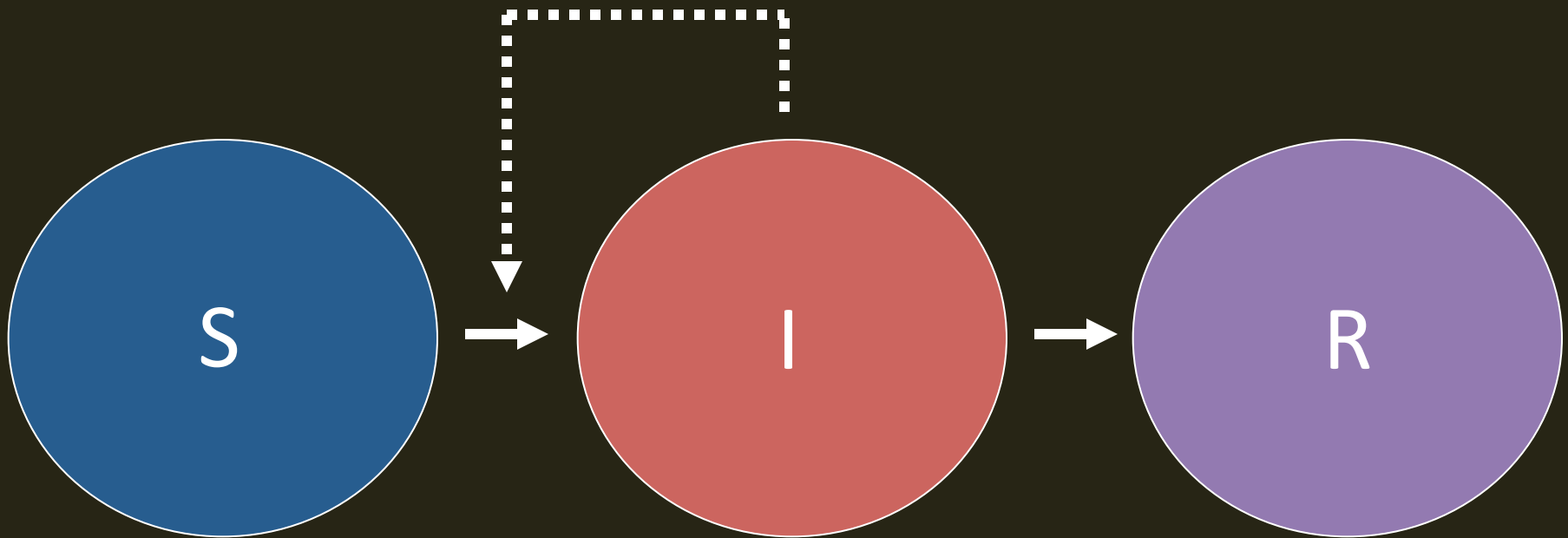


The rate at which susceptible individuals become infected depends on how many infectious people are in the population

State variables

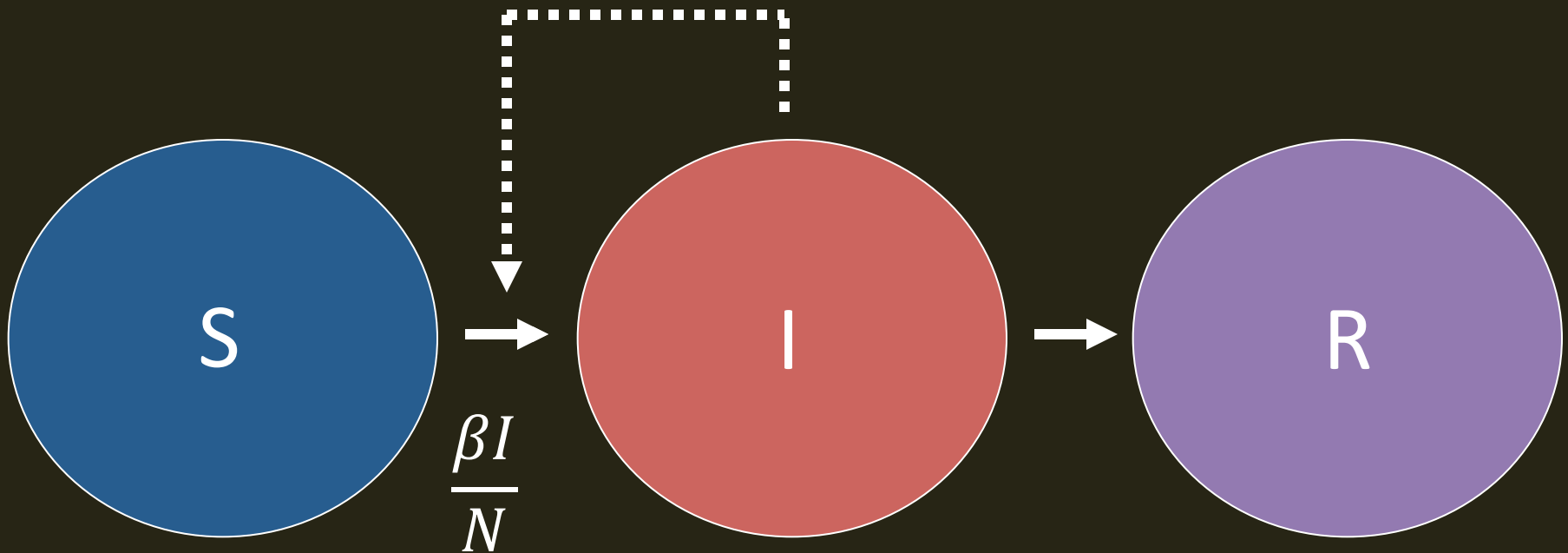


State variables



We can use ordinary differential equations to describe the rate at which individuals flow between states

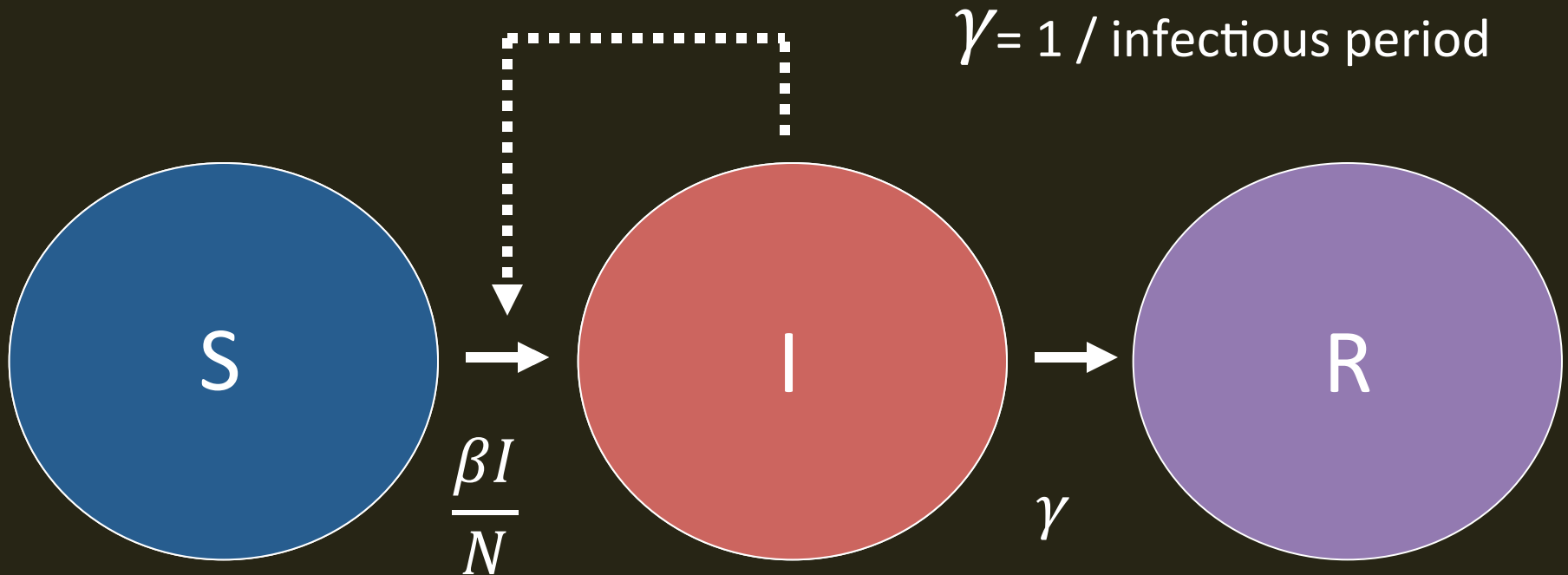
SIR Model



β = transmission coefficient
= per capita contact rate * infectivity
= per capita contact rate (infectivity = 1)

$\frac{I}{N}$ = proportion of contacts that are with an infectious individual

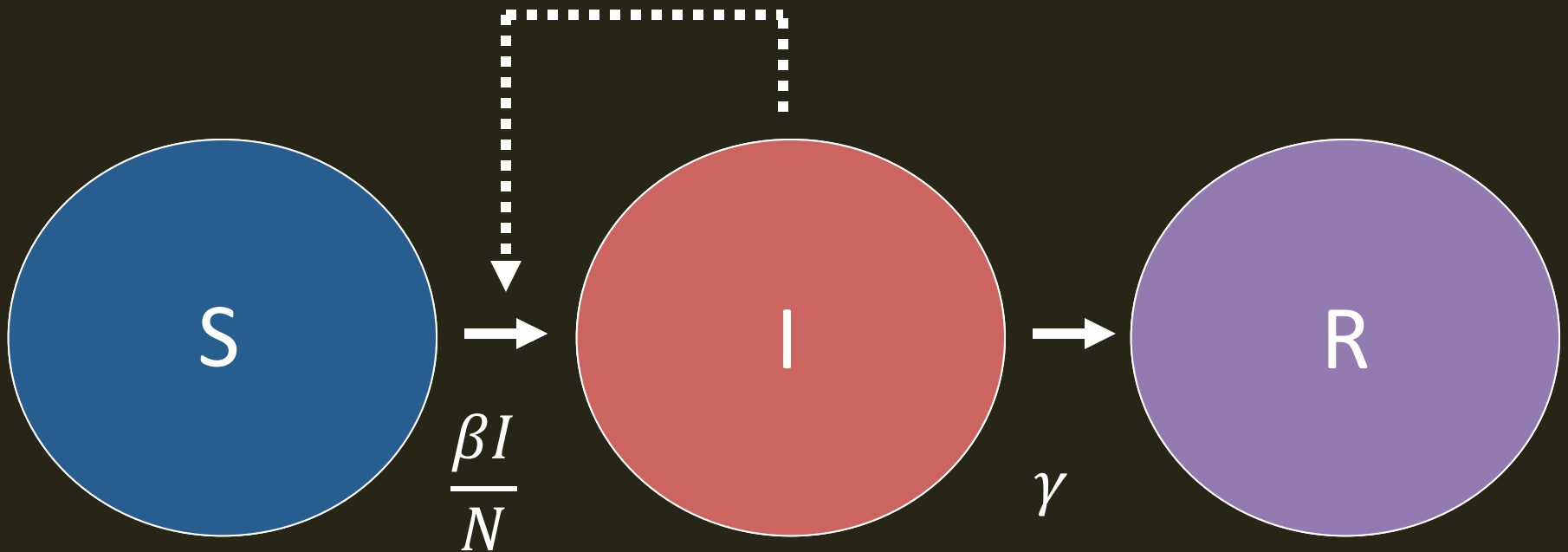
SIR Model



If infectious people recover at a rate of 0.2 / day,

the average time they spend infectious is $1 / 0.2 = 5$ days

SIR Model



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

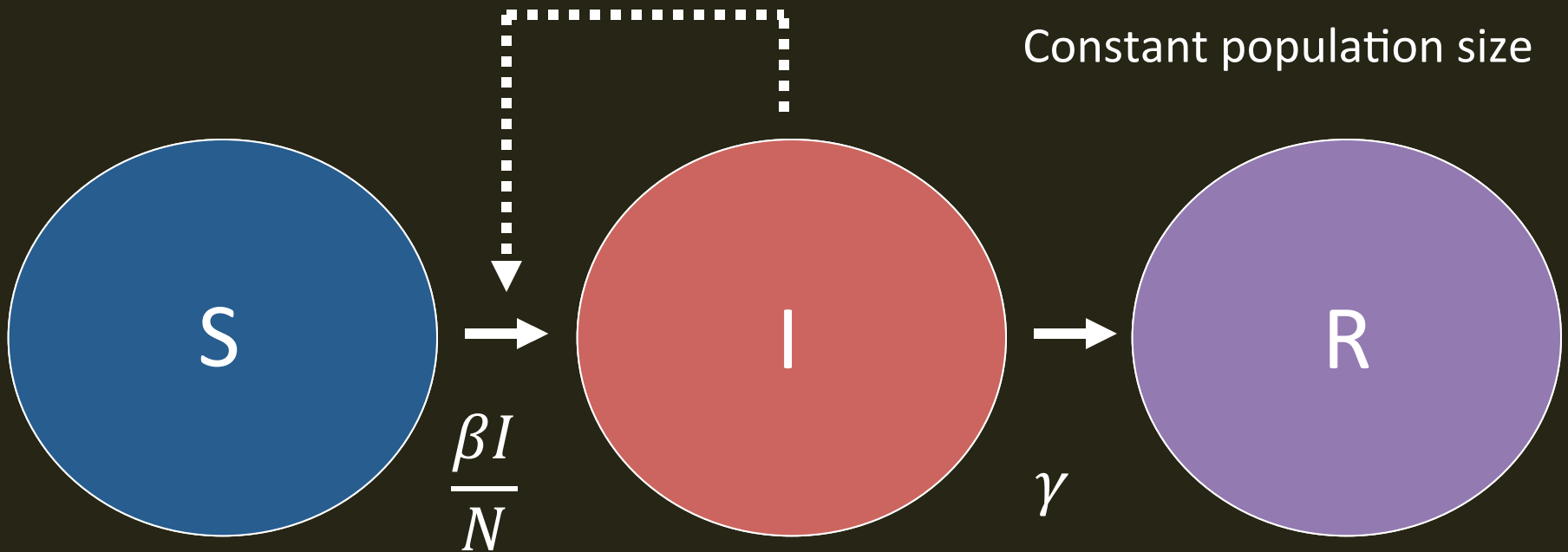
$$\frac{dI}{dt} = \frac{\beta SI}{N} - \gamma I$$

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

SIR Model

$$N = S + I + R$$

Constant population size



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

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

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

SIR Model

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

N population size

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

γ recovery rate

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

β transmission coefficient

SIR Model

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

$$R_0 =$$

infections produced by

1 infectious individual

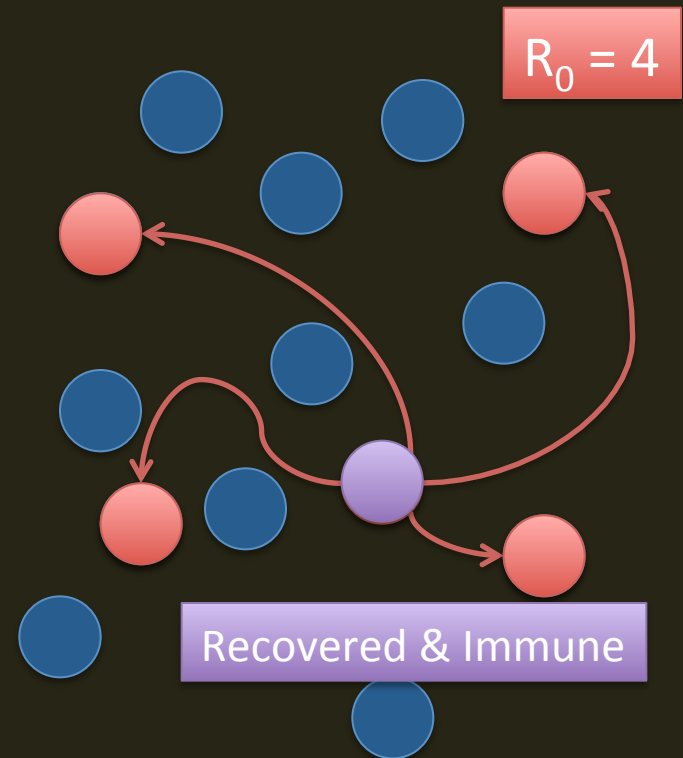
in a fully susceptible population.

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

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

R_0 : The Basic Reproductive Number

- Average # of secondary infections an infected host produces in a susceptible population.



SIR Model

$$R_0 =$$

$$\frac{\beta SI}{N}$$

$$\xrightarrow{N \text{ large}} \beta$$

Rate at which an infected individual produces new infections in a naïve population

X

1

Proportion of new infections that become infectious

X

$1/\gamma$

Average duration of infectiousness

SIR Model

$$R_0 = \frac{\beta}{\gamma}$$

$$R_0 =$$

Rate at which an infected individual produces new infections in a naïve population

X

Proportion of new infections that become infectious

X

Average duration of infectiousness

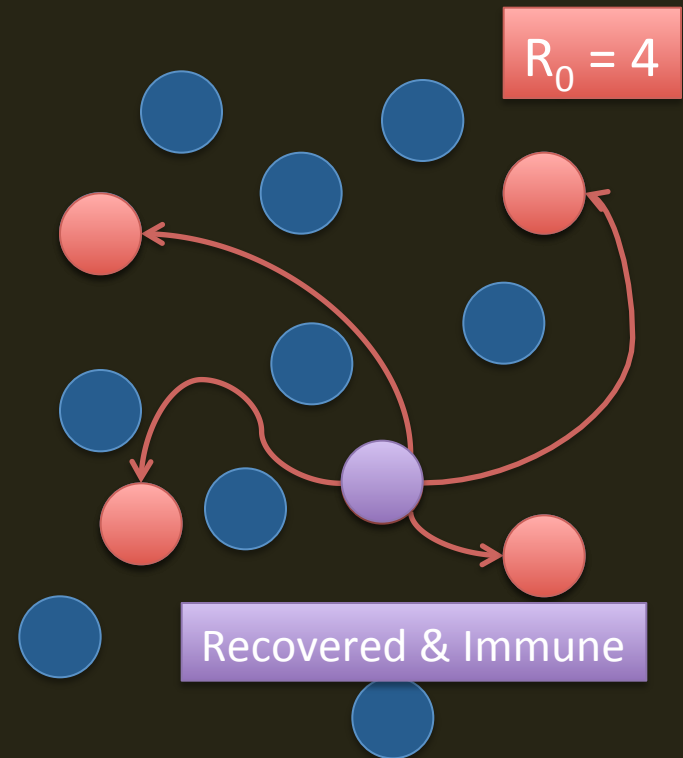
R_0 : The Basic Reproductive Number

- Average # of secondary infections an infected host produces in a susceptible population.

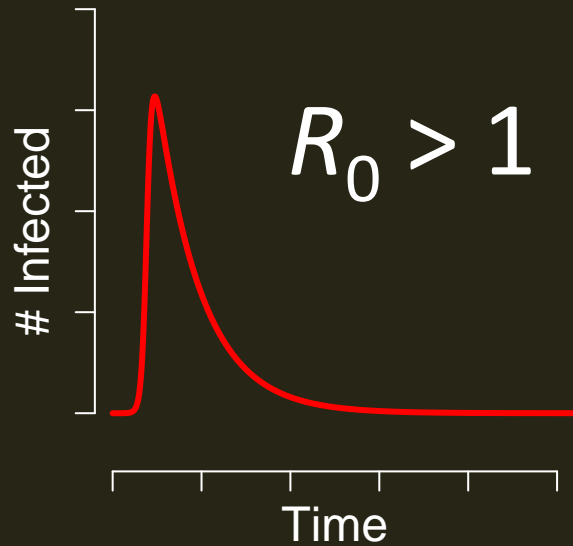
- Threshold criteria:

If $R_0 < 1$, disease dies out

If $R_0 > 1$, disease persists

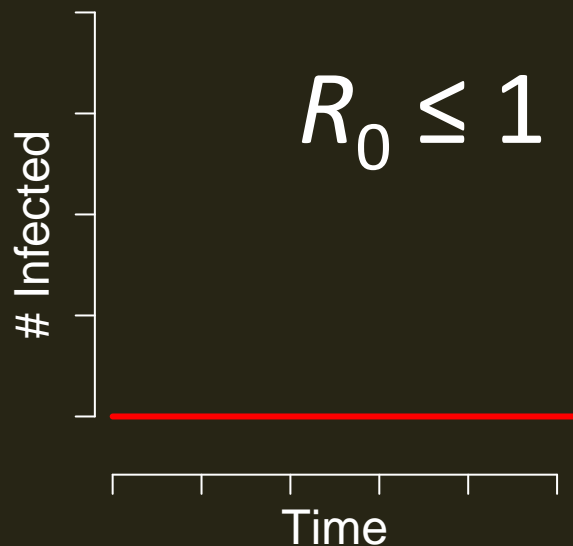


SIR Model: R_0 as a Threshold



$$R_0 = \frac{\beta}{\gamma}$$

Disease Introduction:



Epidemic occurs if $R_0 > 1$.

R_{eff} : Effective Reproductive Number

$$\frac{\beta S}{N}$$

Rate at which an infected individual produces new infections in a non-fully susceptible population

$$1$$

Proportion of new infections that become infectious

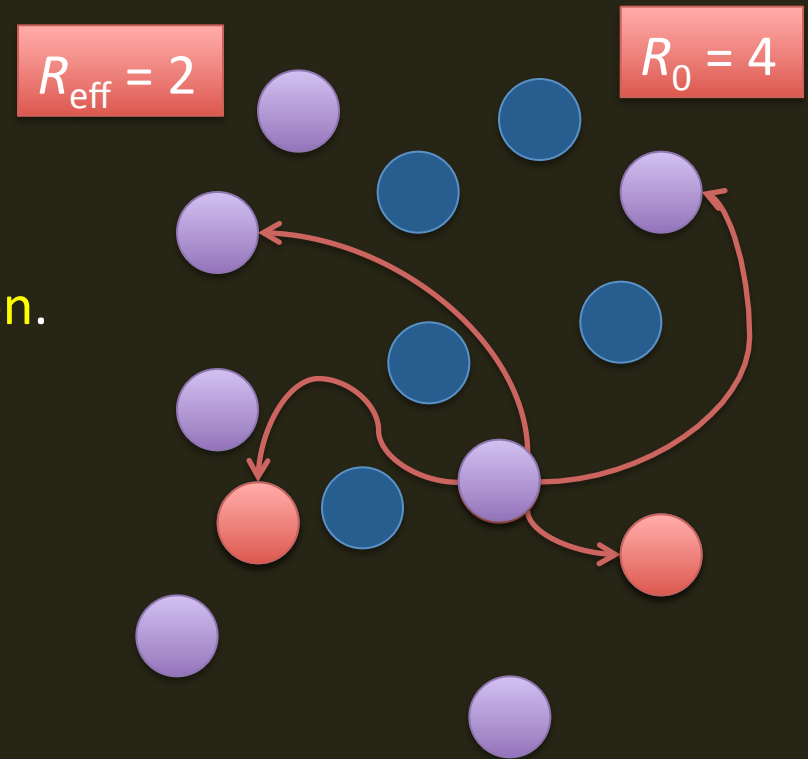
$$1/\gamma$$

Average duration of infectiousness

$$R_{eff} = R_0 \frac{S}{N}$$

R_{eff} : The Effective Reproductive Number

- The average # of secondary infections that an infected host produces in an **only partially susceptible population**.

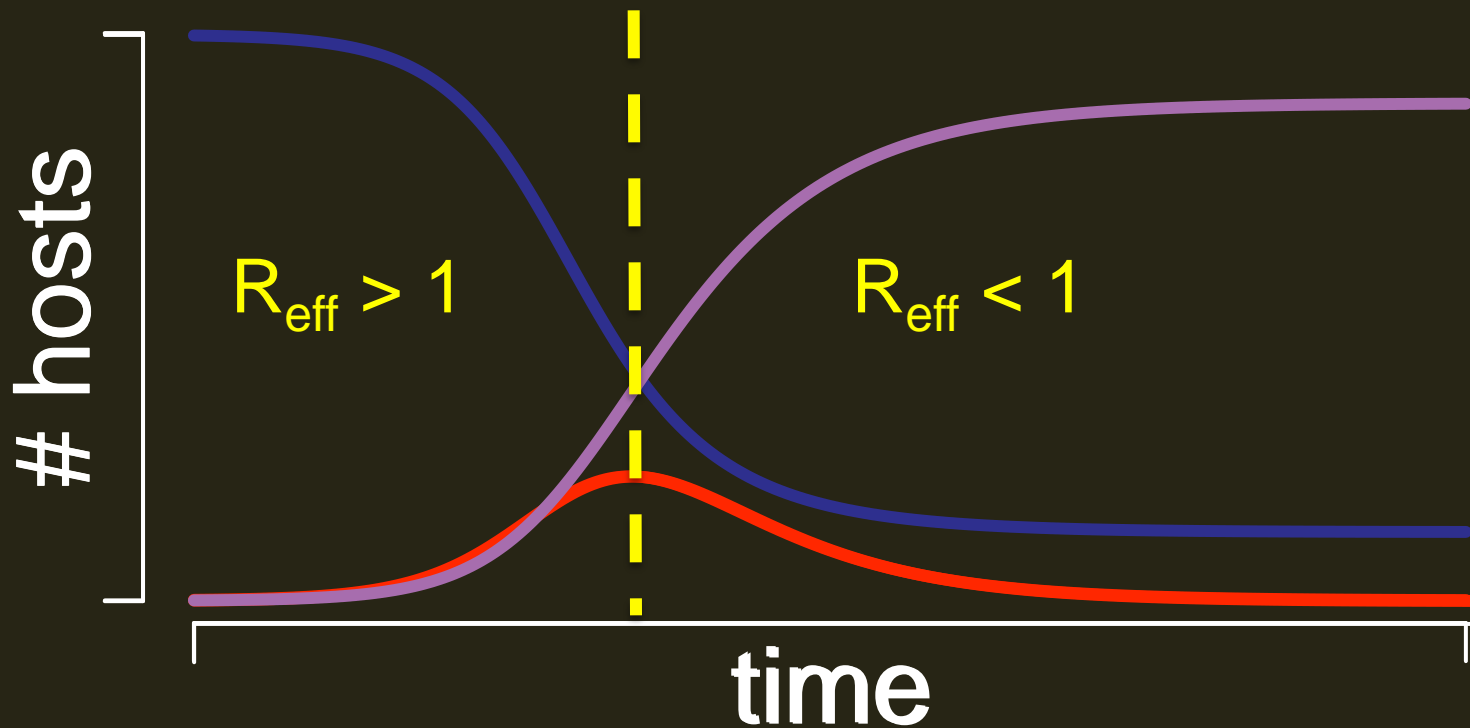


Example: 50% Recovered & Immune

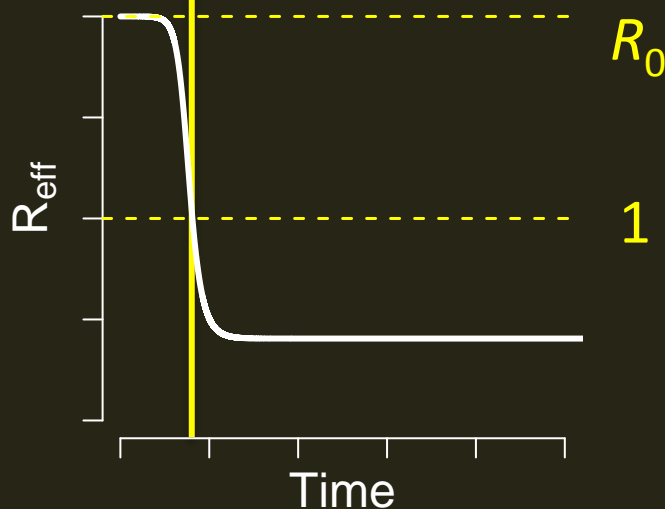
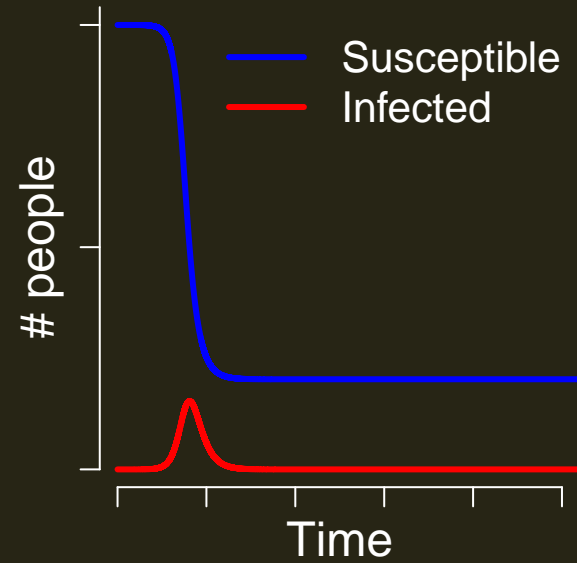
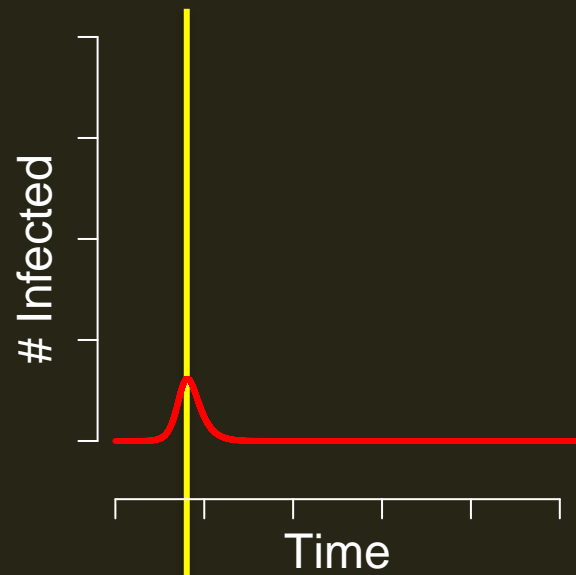
Why do epidemics peak?

Death or long-term immunity leads to exhaustion of susceptibles

— Infected Hosts



R_{eff} : The Effective Reproductive Number

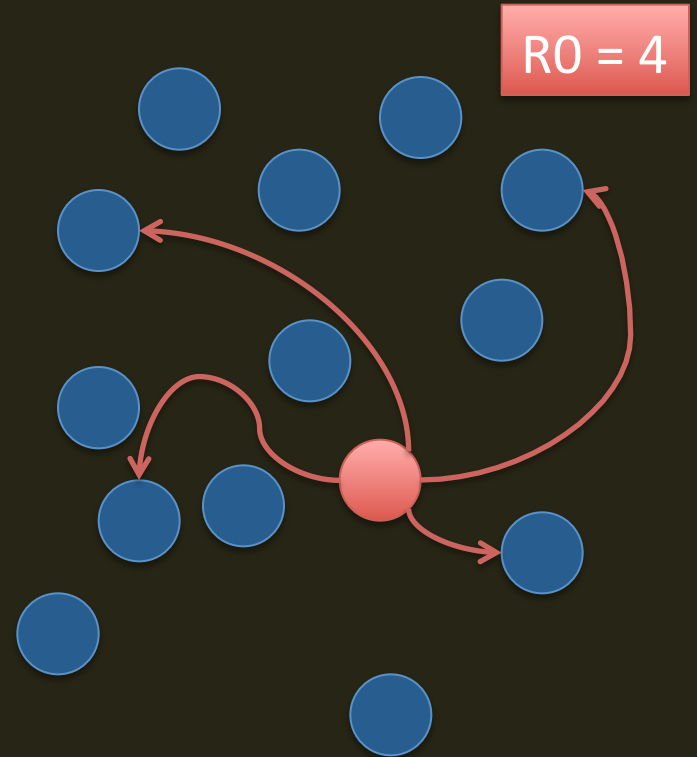


$$R_{\text{eff}}(t) = R_0 \frac{S(t)}{N}$$

$$R_{\text{eff}}(t) = \frac{\beta S(t)}{\gamma N}$$

Proportion to Vaccinate

- So what % of the population must be vaccinated to eliminate transmission in a population?



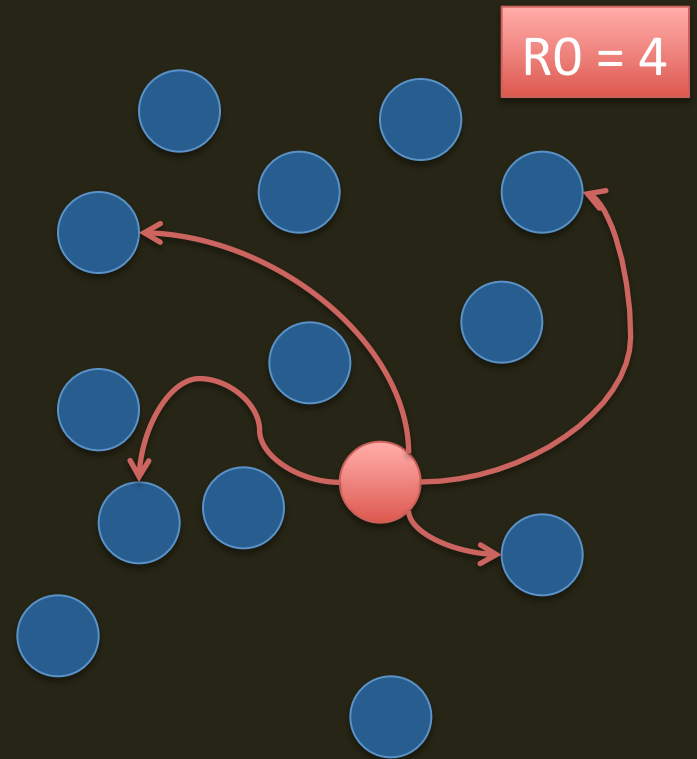
Proportion to Vaccinate

$$R_{eff} = R_0 \frac{S}{N}$$

For a disease to die out, $R_{eff} \leq 1$

$$R_0 \frac{S}{N} \leq 1$$

$$\frac{S}{N} \leq \frac{1}{R_0}$$



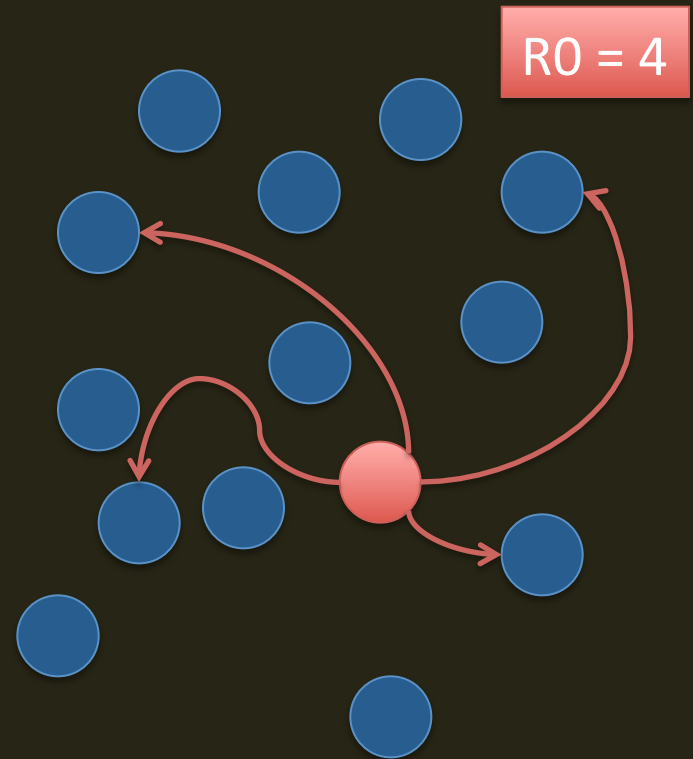
Proportion to Vaccinate

$$\frac{S}{N} \leq \frac{1}{R_0}$$

Proportion immune = $P_V =$
1 – proportion susceptible

$$P_V \geq 1 - \frac{1}{R_0}$$

$$P_V \geq \frac{R_0 - 1}{R_0}$$



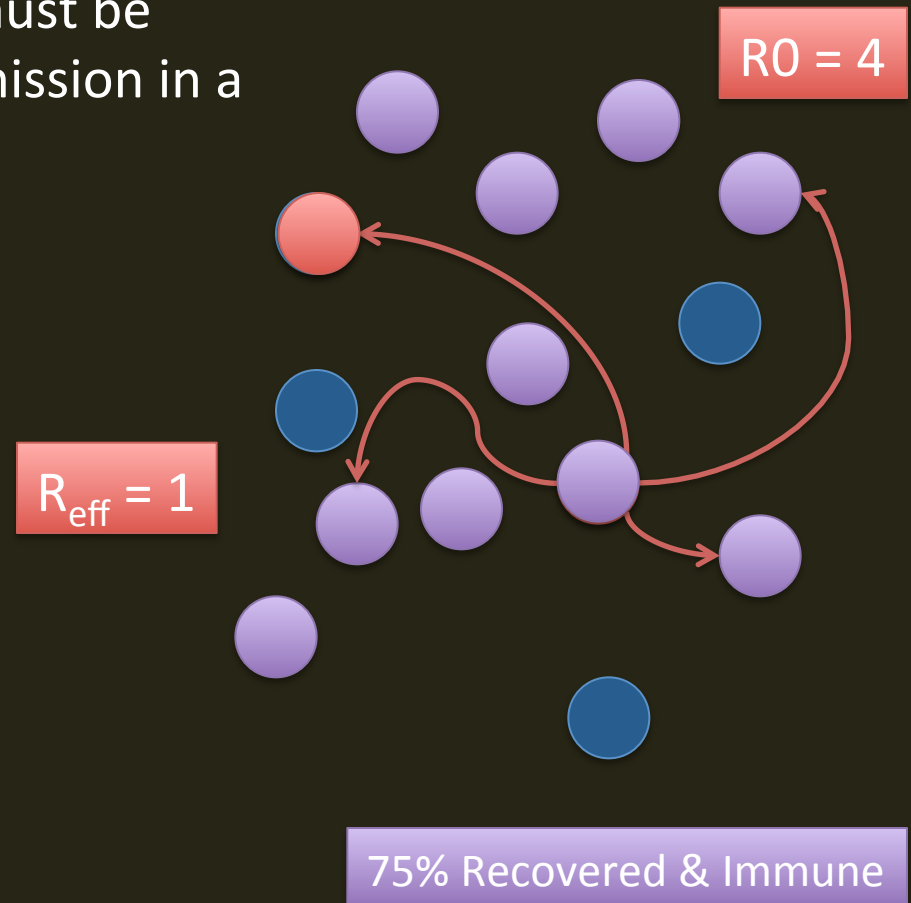
You don't have to vaccinate everyone to eliminate transmission!!!

Proportion to Vaccinate

- So what % of the population must be vaccinated to eliminate transmission in a population?

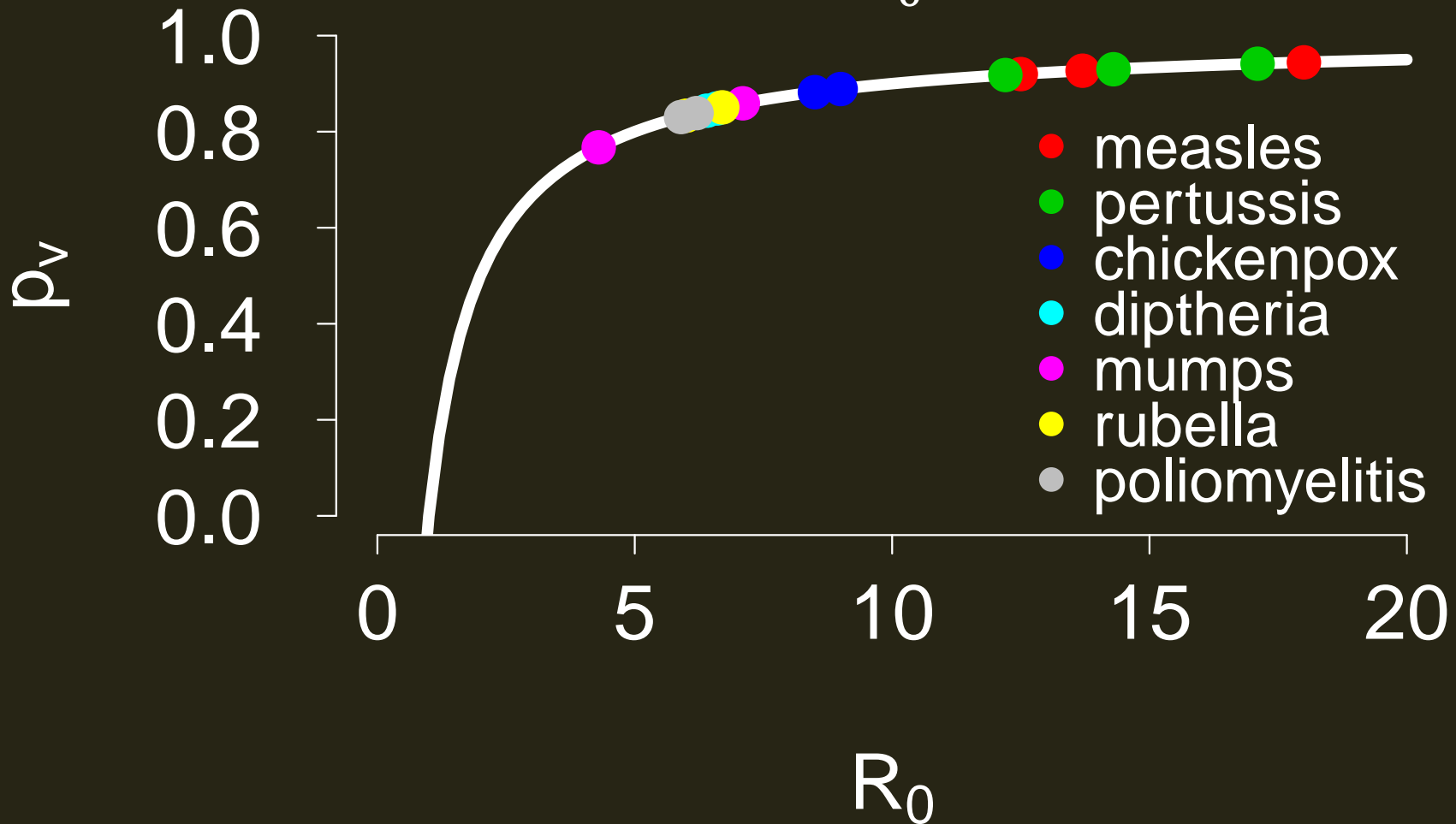
$$P_V \geq \frac{R_0 - 1}{R_0}$$

$$P_V \geq \frac{4 - 1}{4} = \frac{3}{4}$$

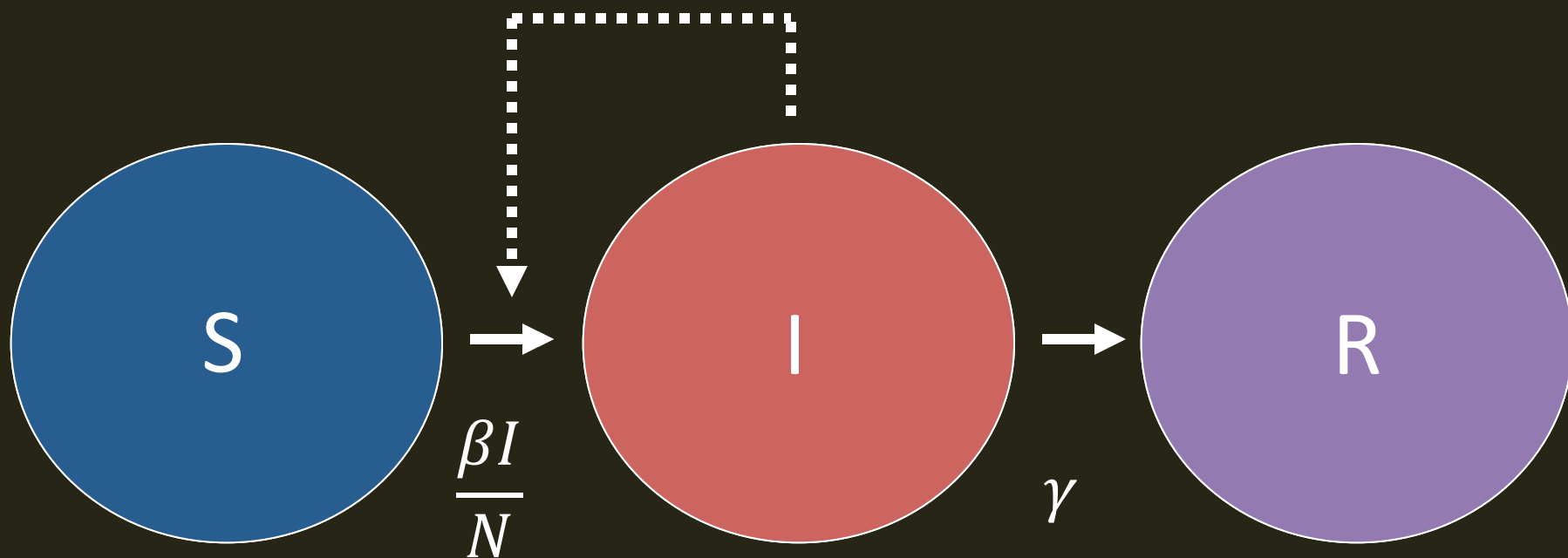


Elimination Thresholds

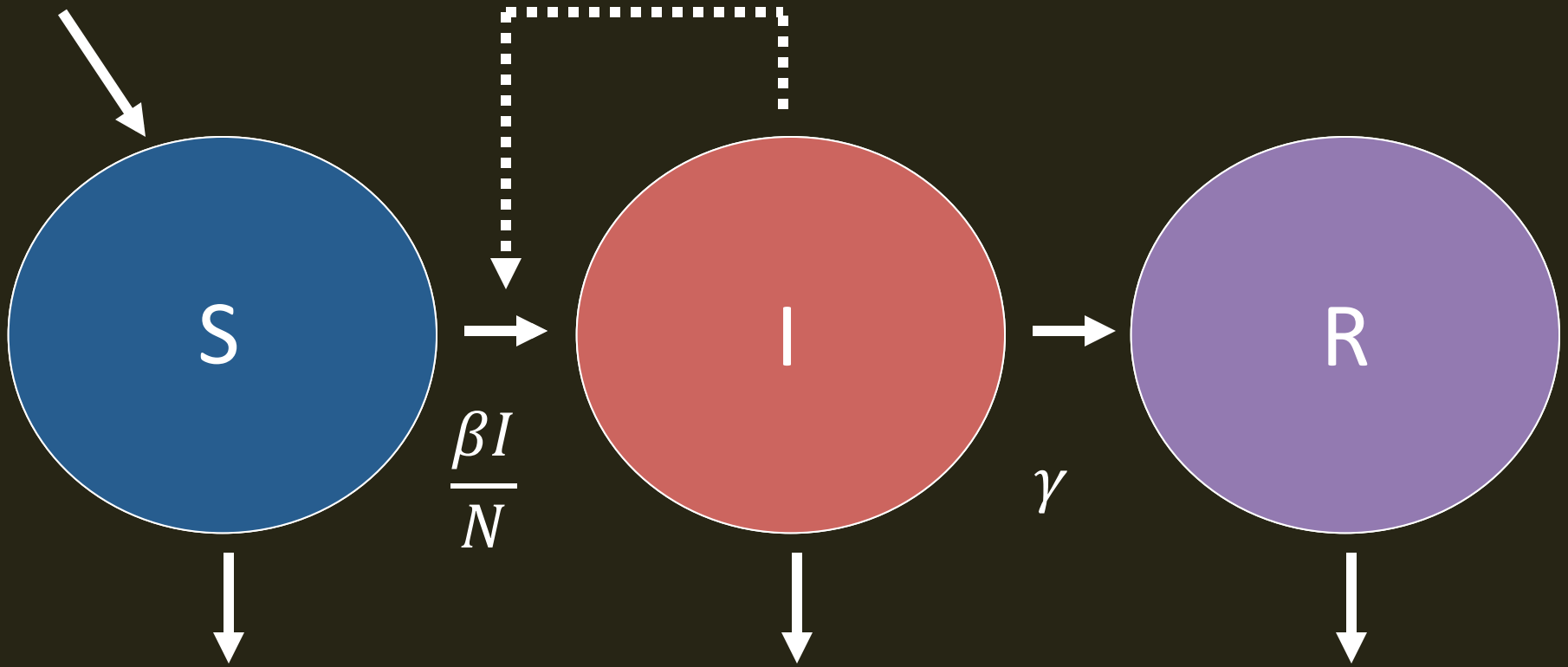
$$P_V = \frac{R_0 - 1}{R_0}$$



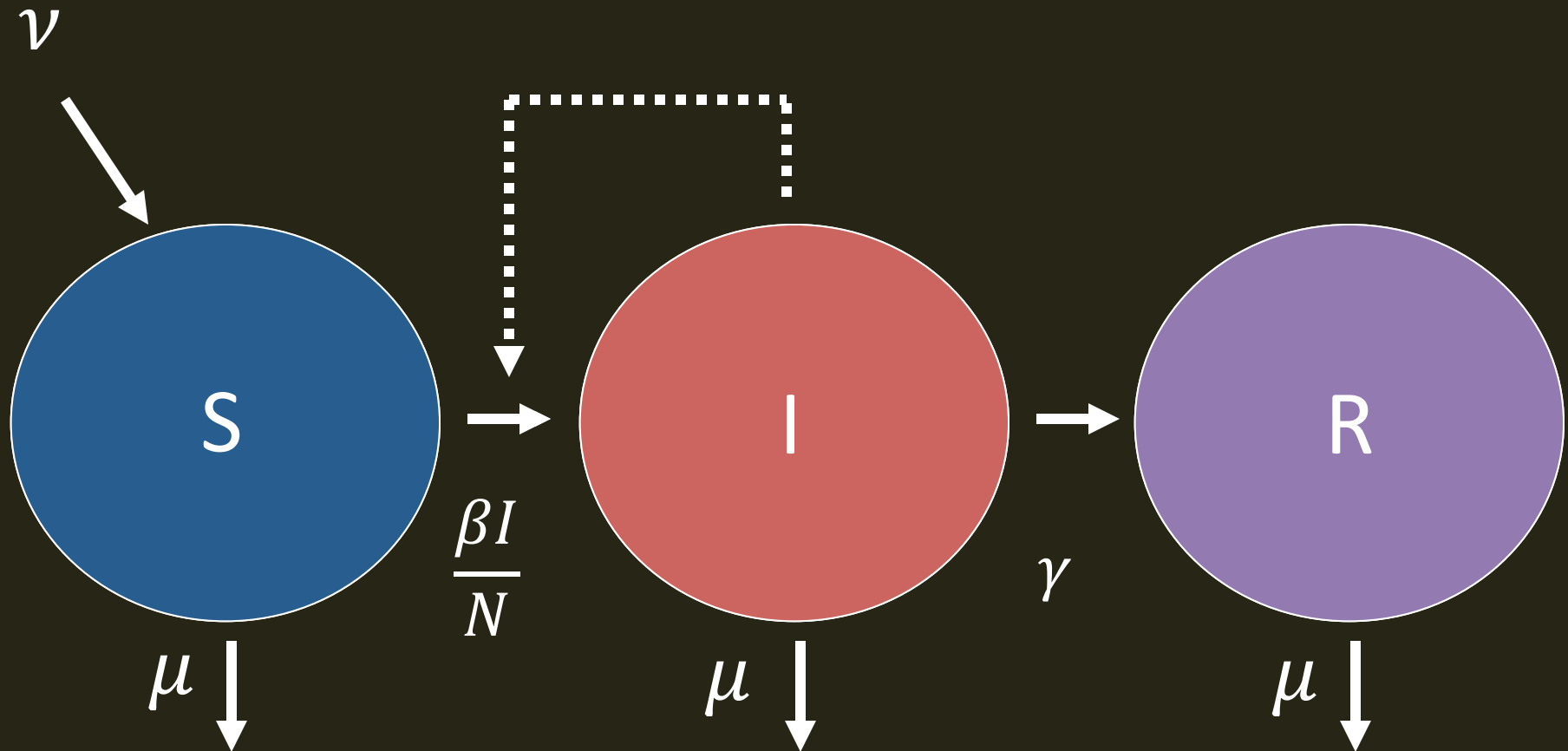
SIR Model



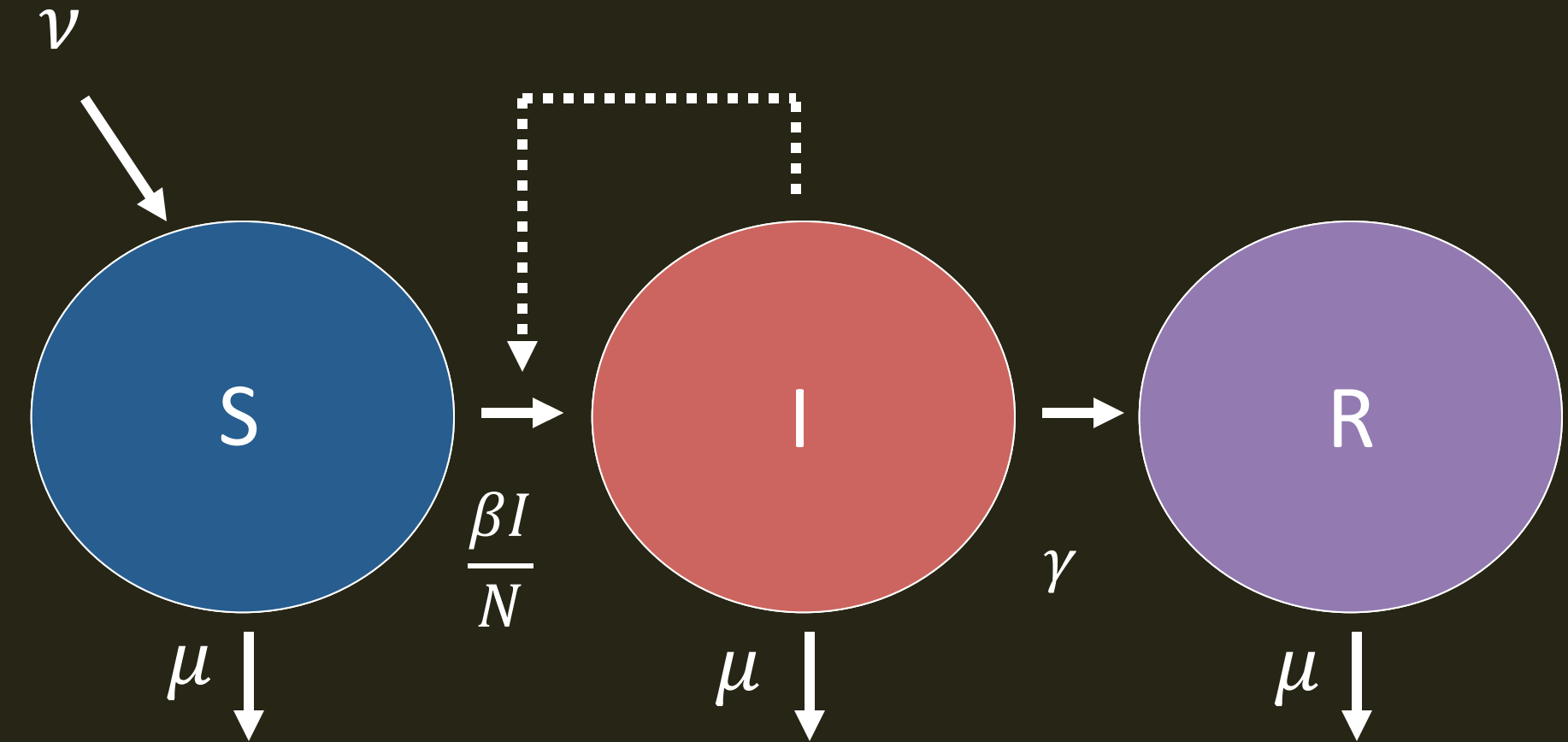
SIR Model with Birth & Death



SIR Model with Birth & Death



SIR Model with Birth & Death



$$\frac{dS}{dt} = \nu - \frac{\beta SI}{N} - \mu S$$

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

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

SIR Model with Birth & Death

$$\frac{dS}{dt} = \nu - \frac{\beta SI}{N} - \mu S$$

$$N = S + I + R$$

so

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

$$\frac{dN}{dt} = \nu - \mu N$$

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

SIR Model with Birth & Death

$$\frac{dS}{dt} = \nu - \frac{\beta SI}{N} - \mu S$$

$$N = S + I + R$$

so

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

$$\frac{dN}{dt} = \nu - \mu N$$

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

To assume constant population size,
births = deaths:

$$\nu = \mu N$$

SIR Model with Birth & Death

$$R_0 =$$

$$\frac{\beta SI}{N} \xrightarrow{N \text{ large}} \beta$$

Rate at which an infected individual produces new infections in a naïve population

X

1

Proportion of new infections that become infectious

1

X

$$\frac{1}{\gamma + \mu}$$

Average duration of infectiousness

SIR Model with Birth & Death

$$R_0 = \frac{\beta}{\gamma + \mu}$$

$$R_0 =$$

Rate at which an infected individual produces new infections in a naïve population

X

Proportion of new infections that become infectious

X

Average duration of infectiousness

SIR Model with Birth & Death

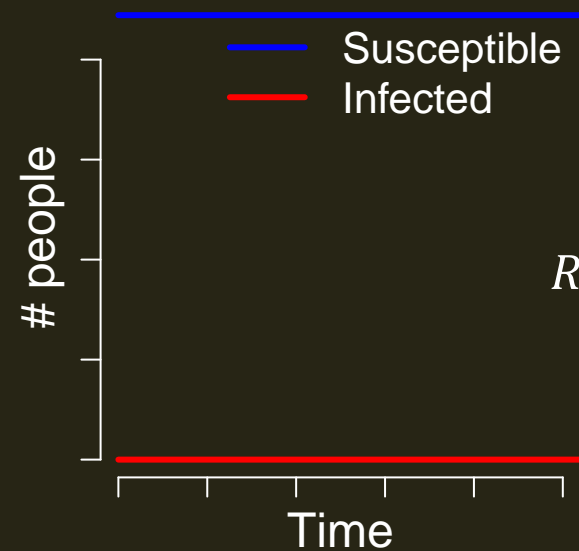
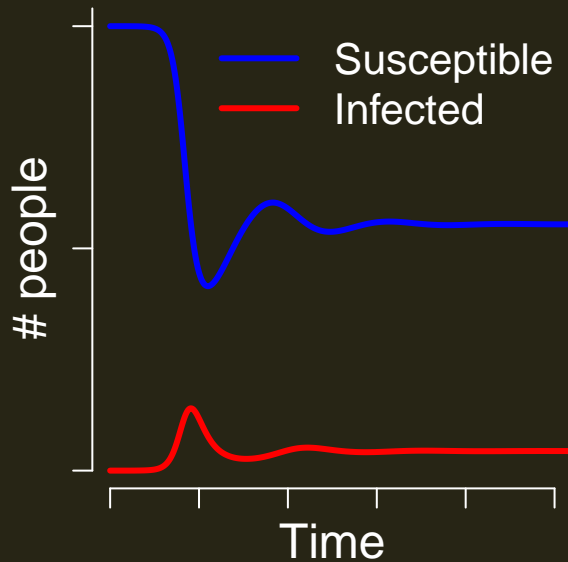
Dynamics upon introduction:

Epidemic if $R_0 > 1$

No epidemic if $R_0 \leq 1$

Endemic state

No endemic state



$$R_0 = \frac{\beta}{\gamma + \mu}$$

R_{eff} : Effective Reproductive Number

$$\frac{\beta S}{N}$$

Rate at which an infected individual produces new infections in a non-fully susceptible population

$$1$$

Proportion of new infections that become infectious

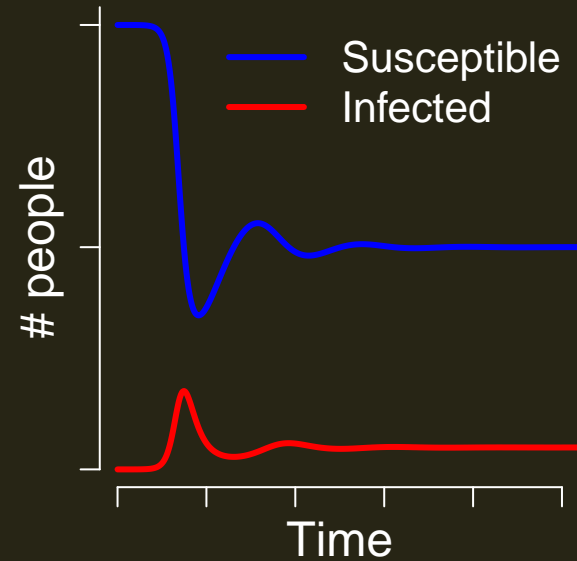
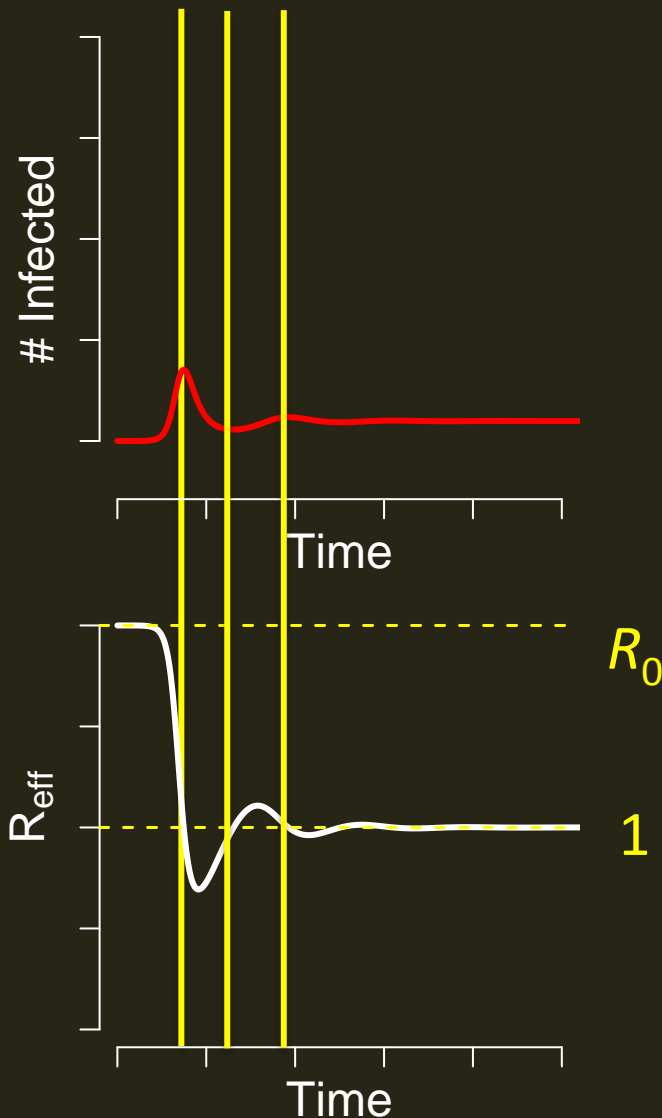
$$1$$

Average duration of infectiousness

$$\frac{1}{\gamma + \mu}$$

$$R_{eff} = R_0 \frac{S}{N}$$

R_{eff} : The Effective Reproductive Number

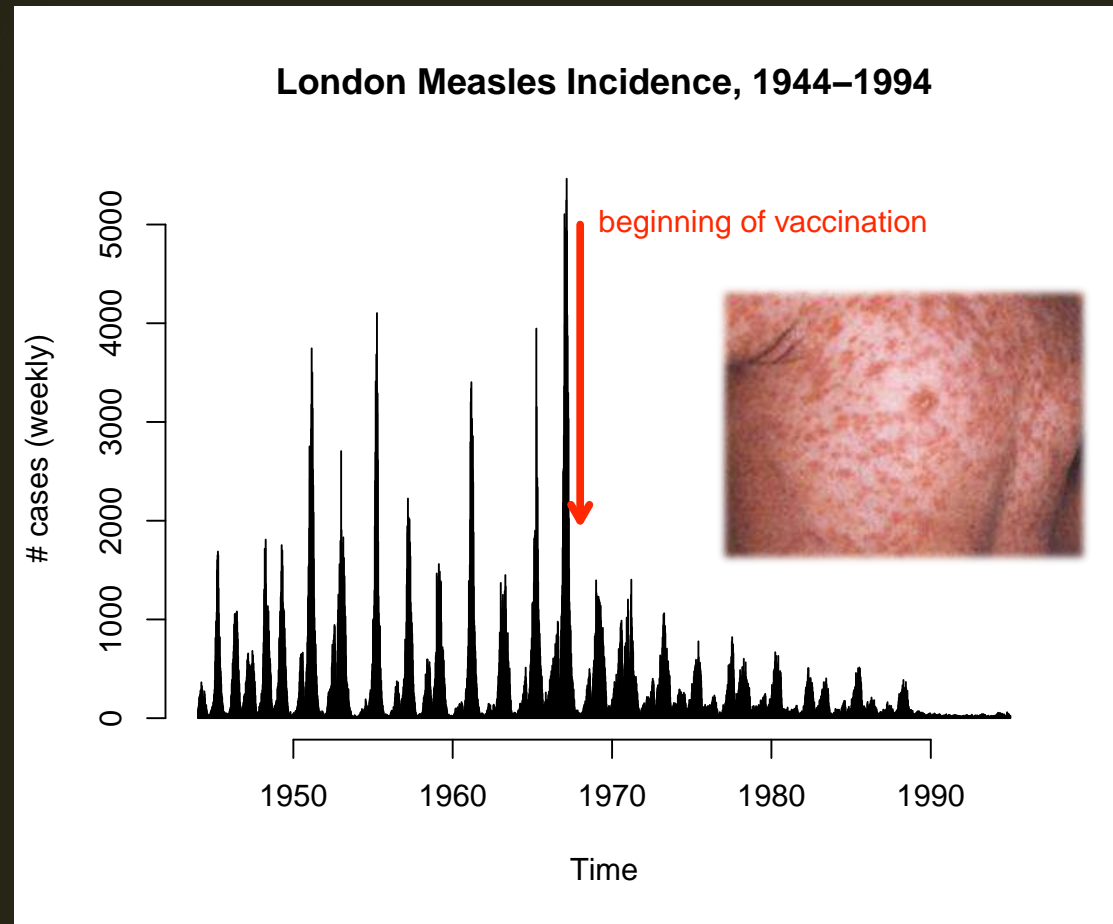


$$R_{\text{eff}}(t) = R_0 \frac{S(t)}{N}$$

$$R_{\text{eff}}(t) = \frac{\beta S(t)}{(\gamma + \mu)N}$$

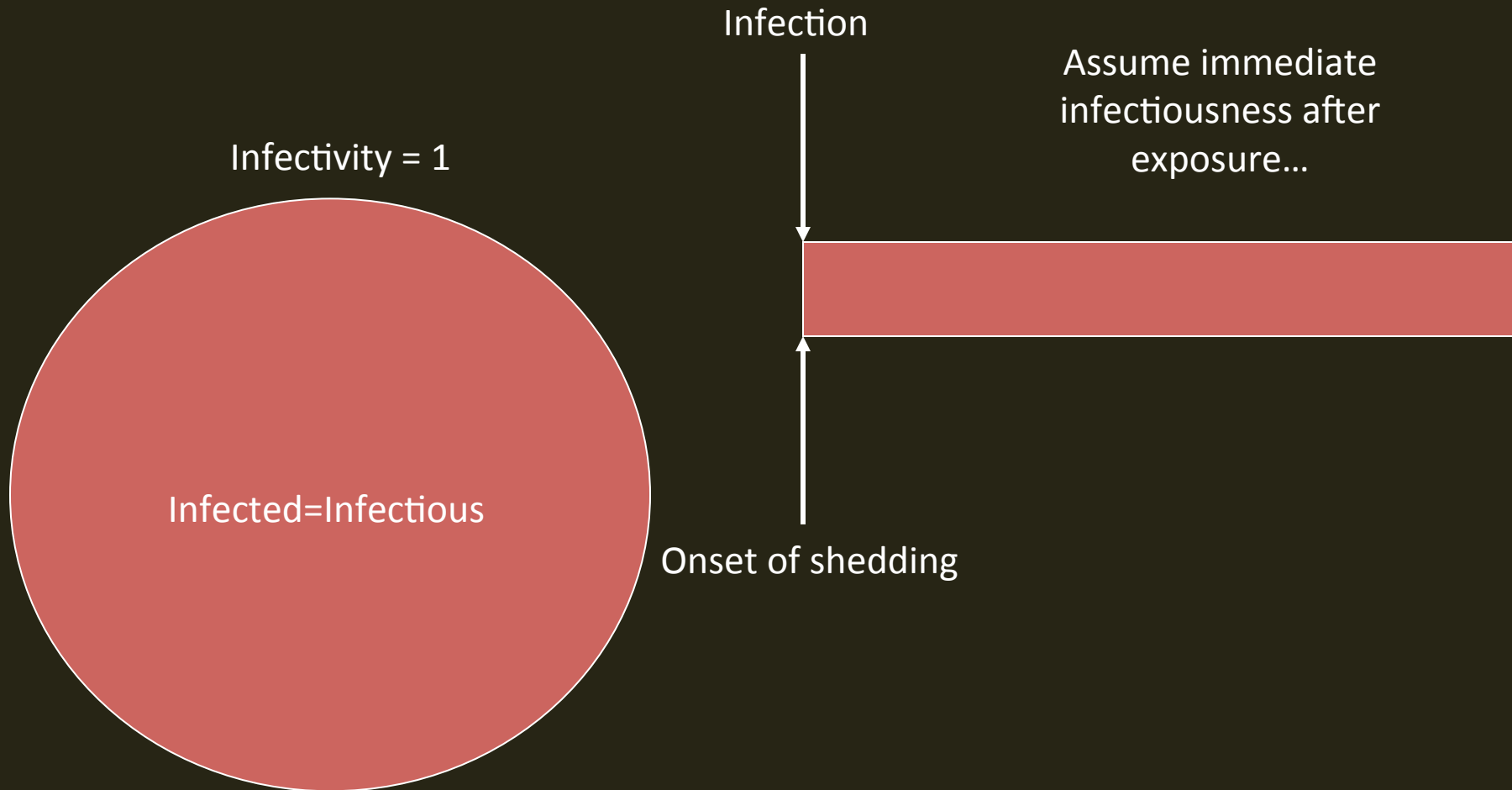
Why do recurrent epidemics happen?

- **Susceptibles exhausted** from an epidemic
- **Disease does not completely die out** (or is reintroduced).
- **Susceptibles replenished** through birth or loss of immunity, epidemic occurs.



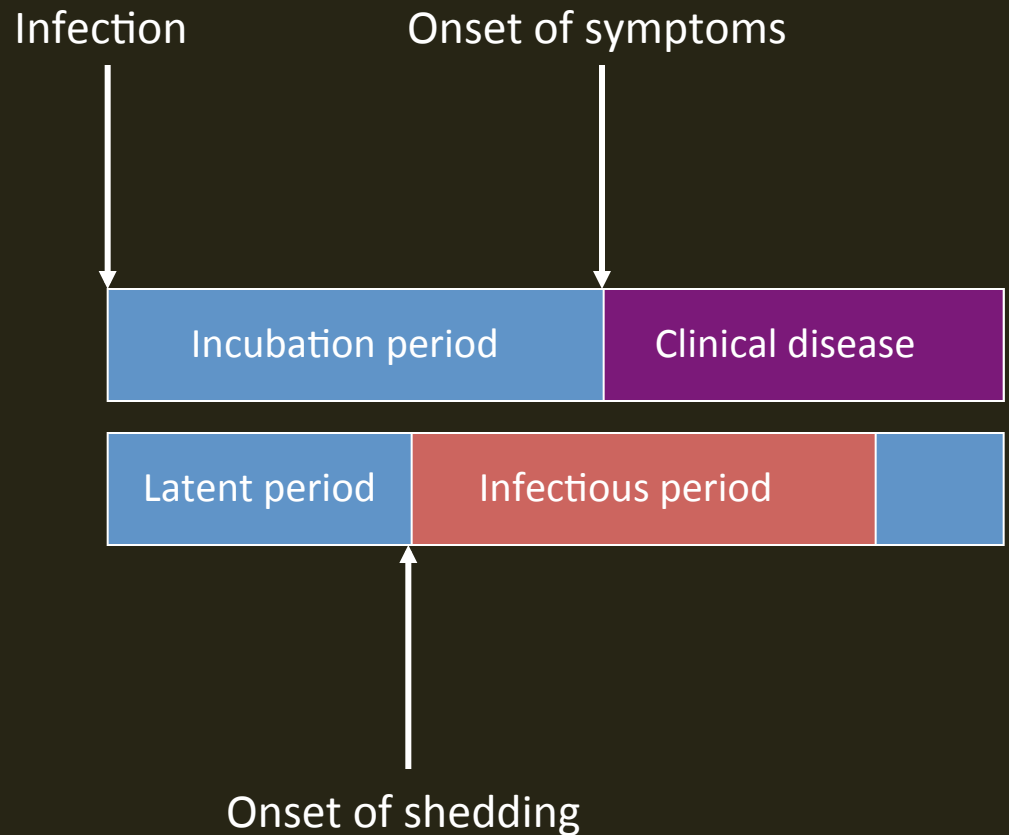
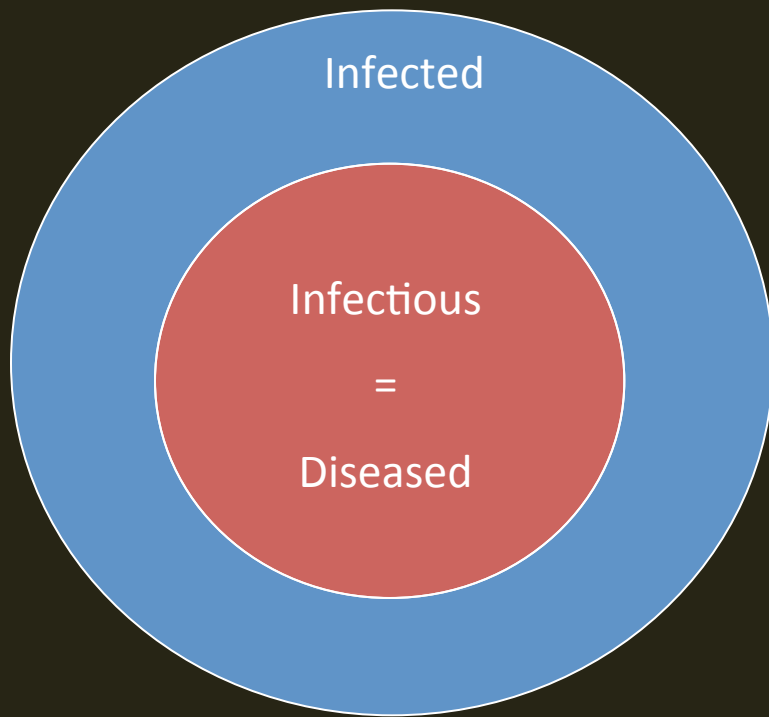
An extremely simple view of the world

Don't worry about symptoms and disease!



A slightly more realistic model

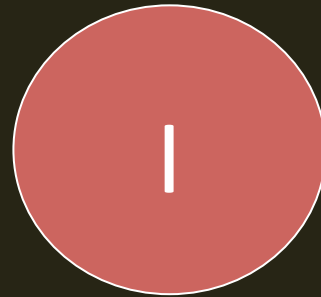
Infectivity = 1
(everyone exposed becomes infected)



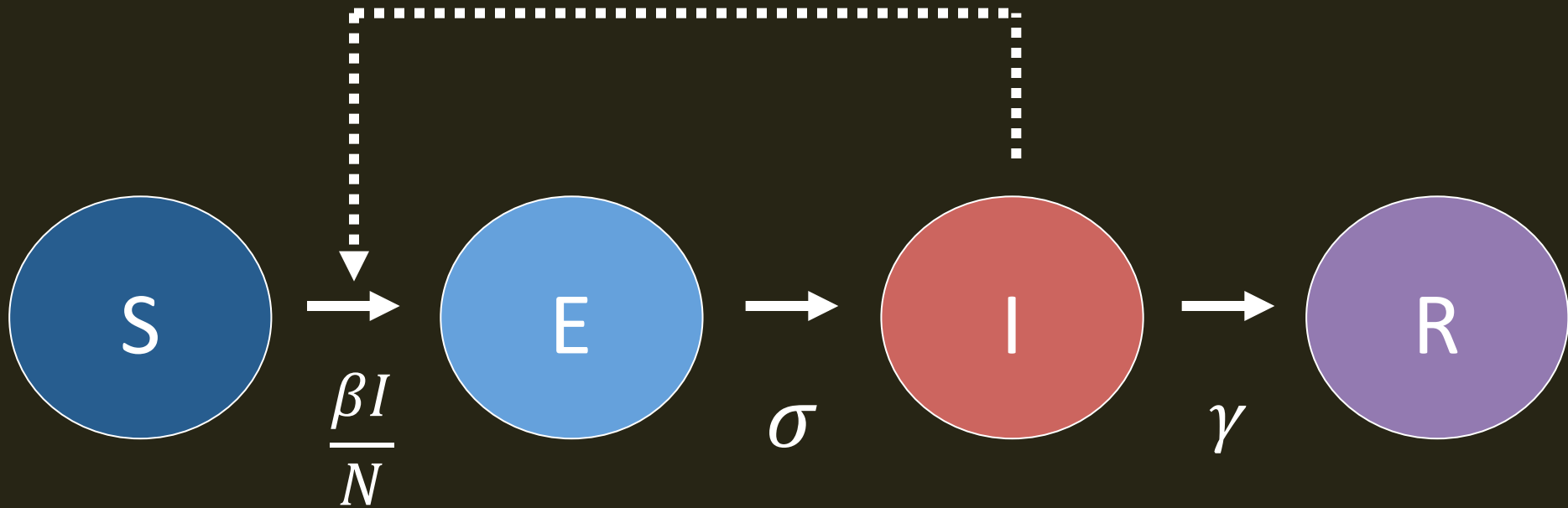
A slightly more realistic model



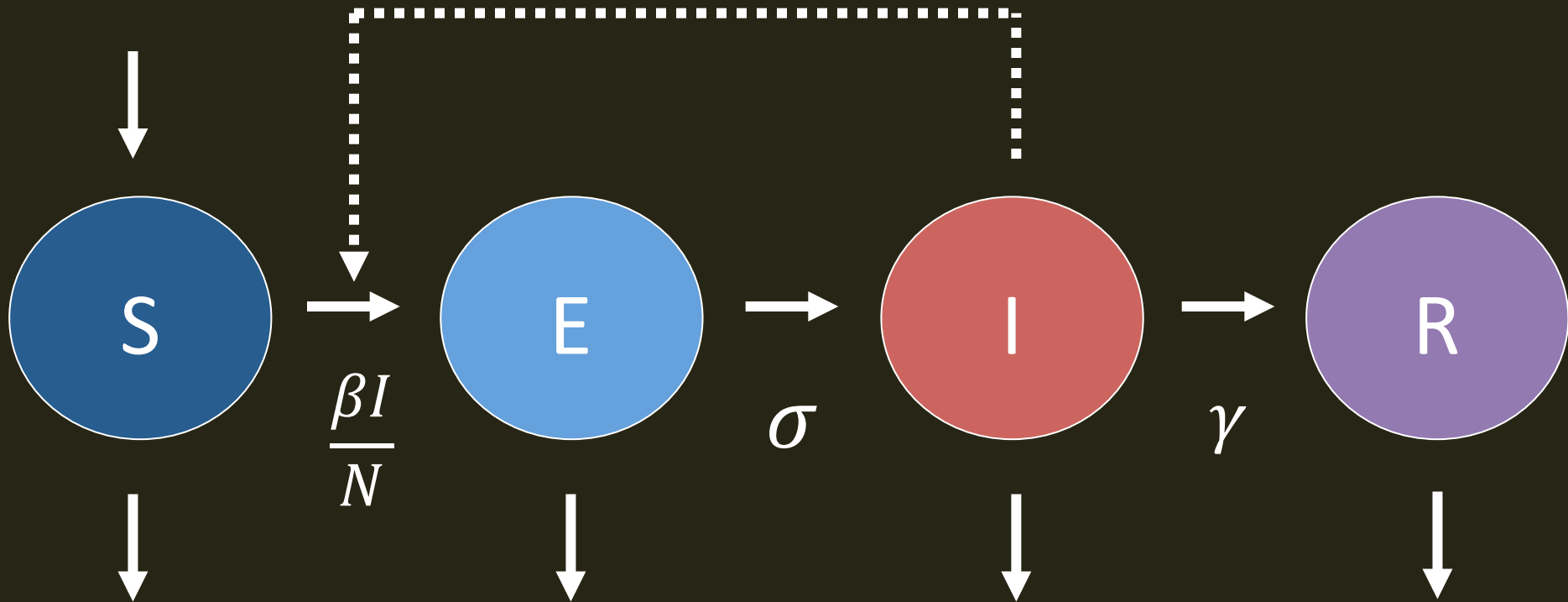
SEIR Model



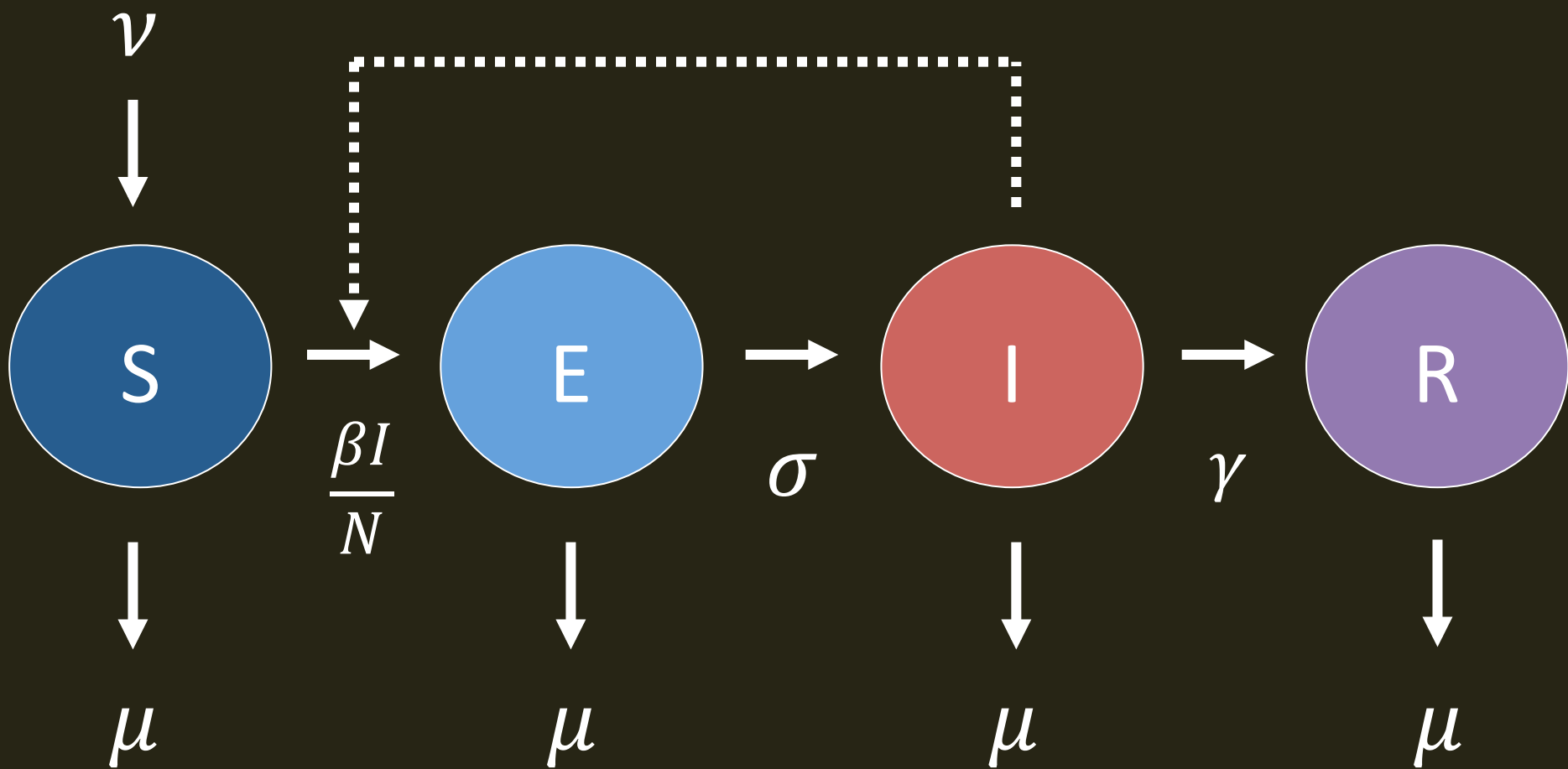
SEIR Model



SEIR Model



SEIR Model



SEIR Model

$$\frac{dS}{dt} = \nu - \frac{\beta SI}{N} - \mu S$$

 ν

birth rate

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

 μ

mortality rate

 σ

1 / latent period

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

 γ

1 / infectious period

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

 β

transmission coefficient

SEIR Model

$$\frac{dS}{dt} = \nu - \frac{\beta SI}{N} - \mu S$$

Assume constant
population size

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

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

$$\nu = \mu N$$

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

SEIR Model

$$\frac{dS}{dt} = \nu - \frac{\beta SI}{N} - \mu S$$

$$R_0 =$$

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

Rate at which an infected individual produces new infections in a naïve population

X

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

Proportion of new infections that become infectious

X

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

Average duration of infectiousness

SEIR Model

$$\frac{dS}{dt} = \nu - \frac{\beta SI}{N} - \mu S$$

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

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

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

$$R_0 = \beta \left(\frac{\sigma}{\mu + \sigma} \right) \left(\frac{1}{\mu + \gamma} \right)$$

SEIR Model

$$\frac{dS}{dt} = \nu - \frac{\beta SI}{N} - \mu S$$

Equilibria...

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

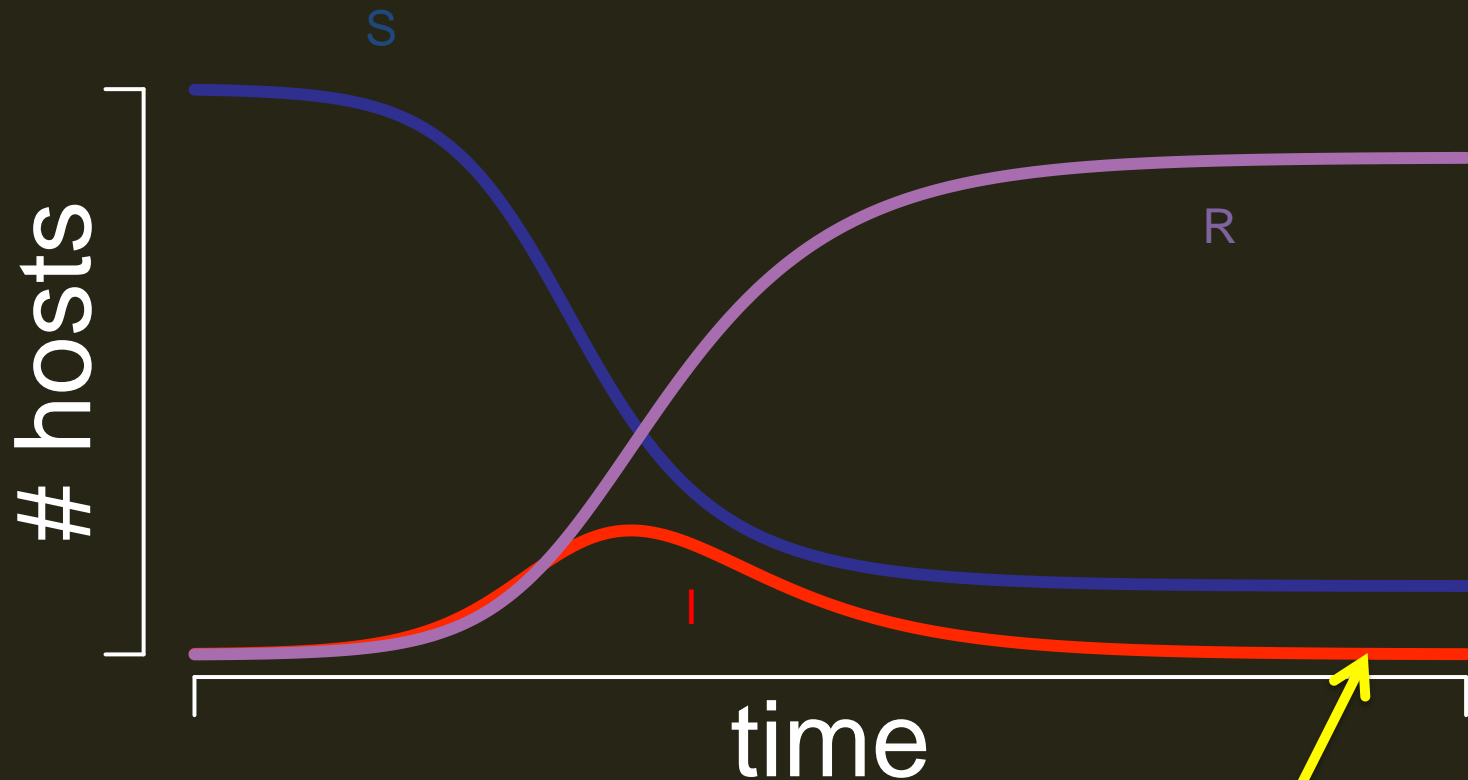
Disease free
equilibrium

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

Endemic equilibrium

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

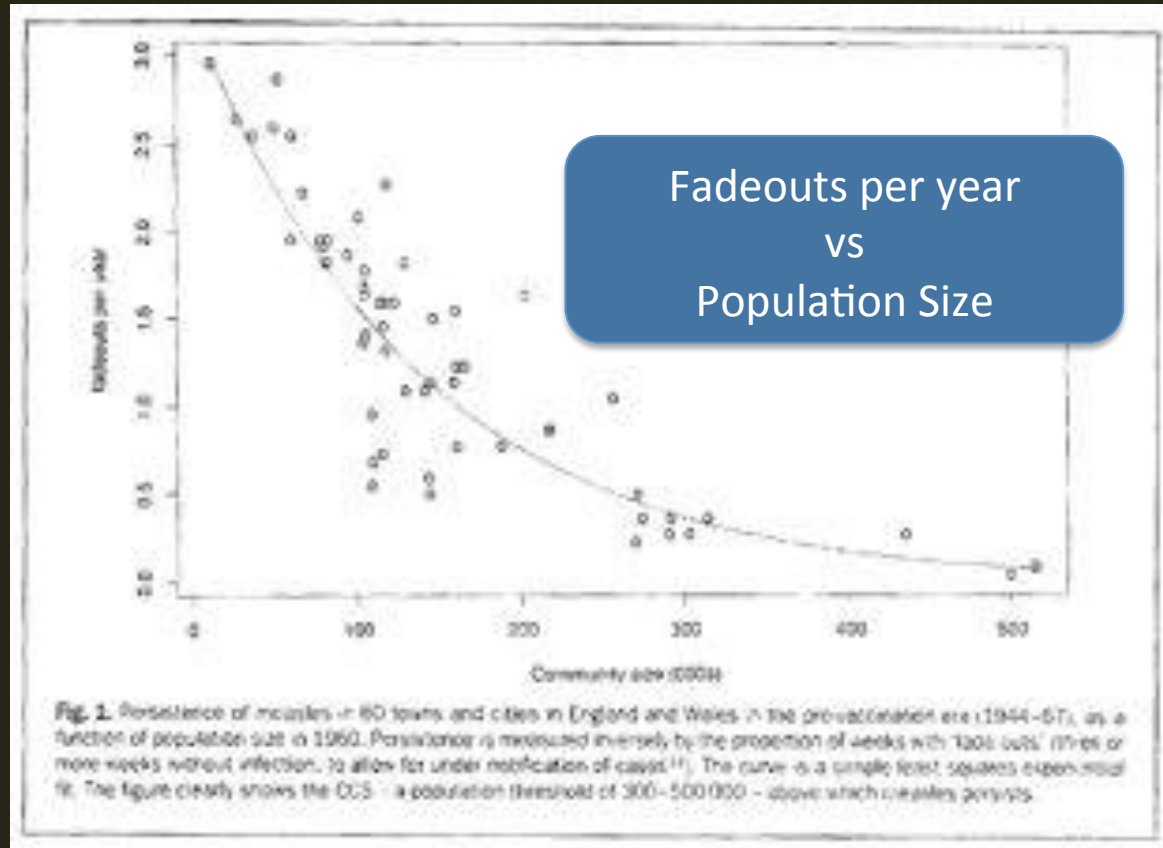
Back to the SIR: When does a disease fade out?



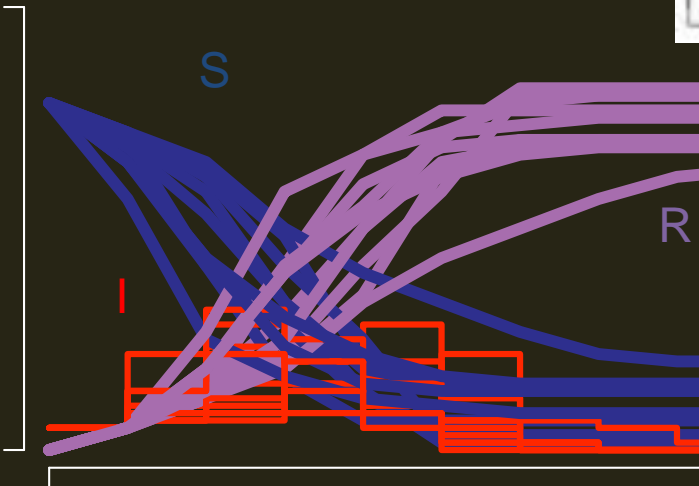
In simple “SIR” models of epidemics, # of infected hosts never goes to zero... What allows a fadeout?

Fadeouts do occur!

- **Critical Community Size**
The (\approx) threshold population size at which a disease can persist.

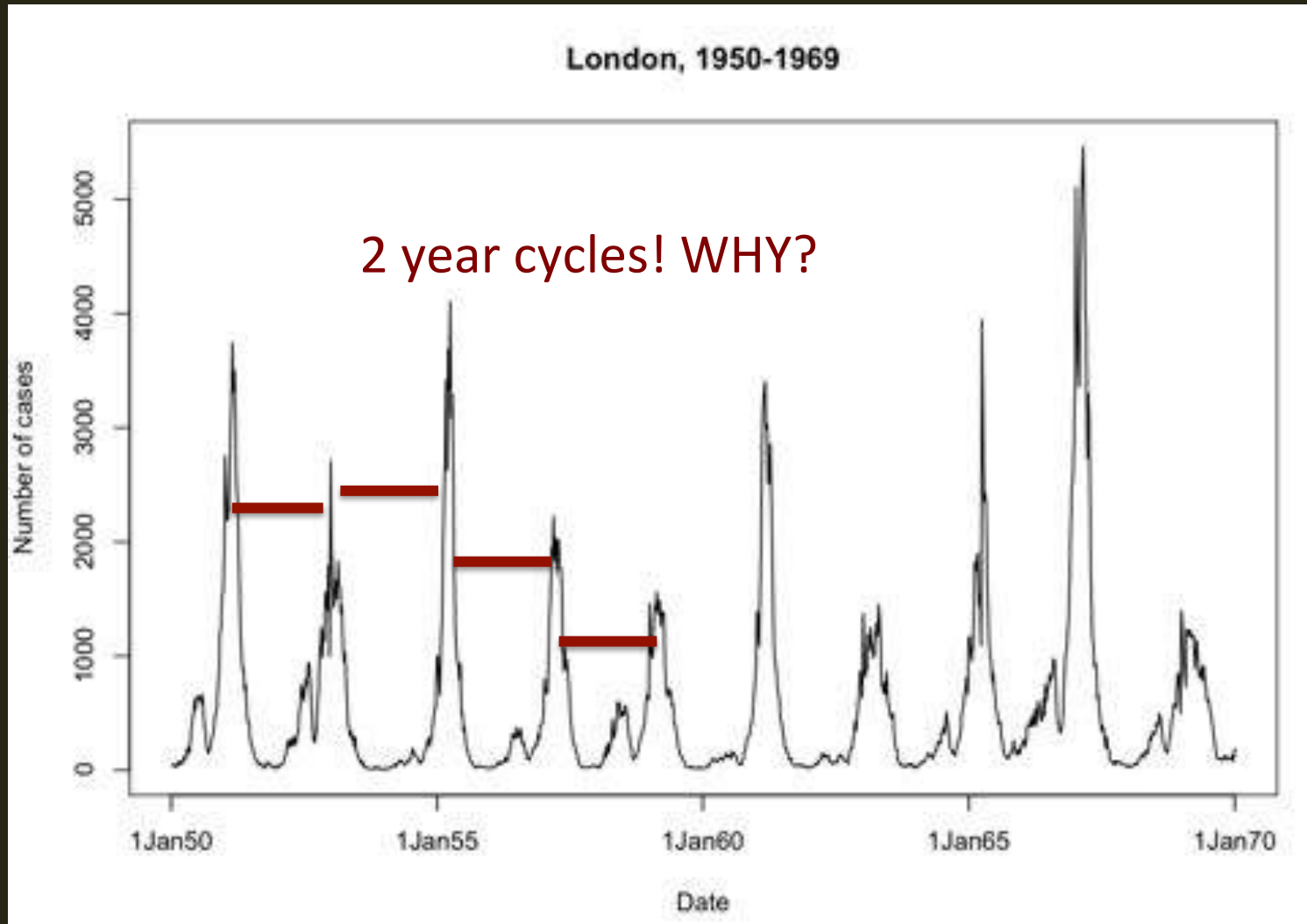


Grenfell and Harwood, 1997



- Stochasticity in epidemic troughs causes disease fadeout in small populations.

What accounts for epidemic cycles?



From: Earn et al. 2000 *Science*

Seasonal SEIR Model

$$\frac{dS}{dt} = \nu - \frac{\beta SI}{N} - \mu S$$

$$\nu = \mu N \quad \text{individuals/year}$$

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

$$\mu = 0.02 \quad \text{years}^{-1}$$

$$\sigma = 1/8 \quad \text{days}^{-1}$$

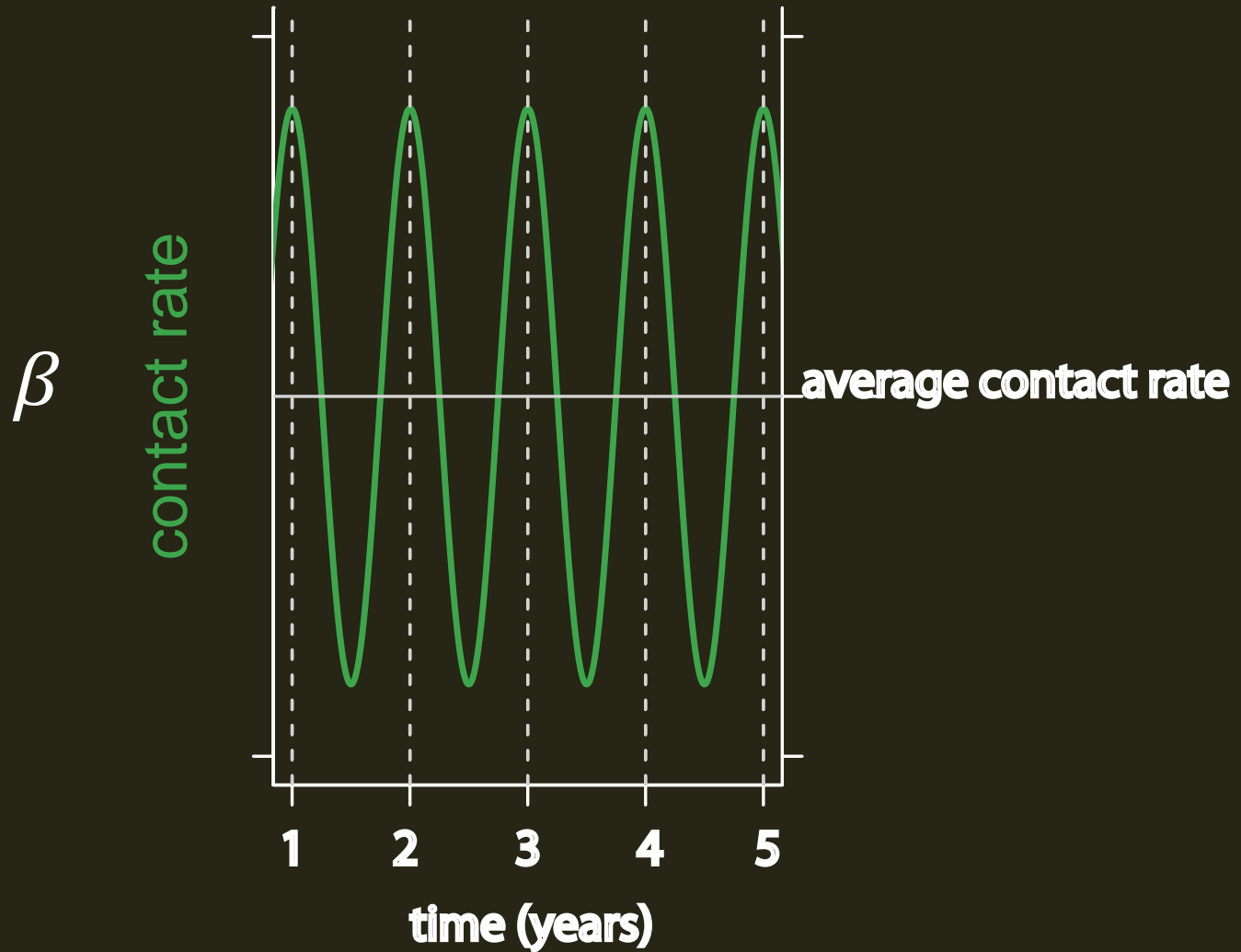
$$\frac{dI}{dt} = \sigma E - \gamma I - \mu I$$

$$\gamma = 1/5 \quad \text{days}^{-1}$$

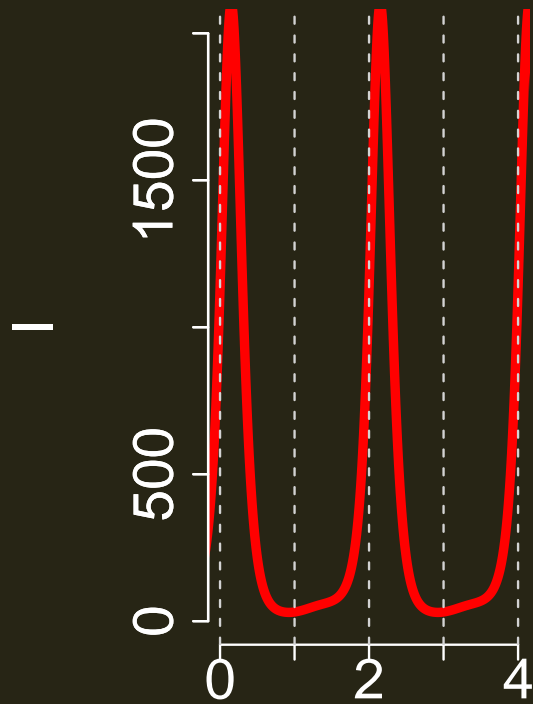
$$\frac{dR}{dt} = \gamma I - \mu R$$

$$\beta \quad \text{seasonal (school terms)}$$

Seasonal SEIR Model

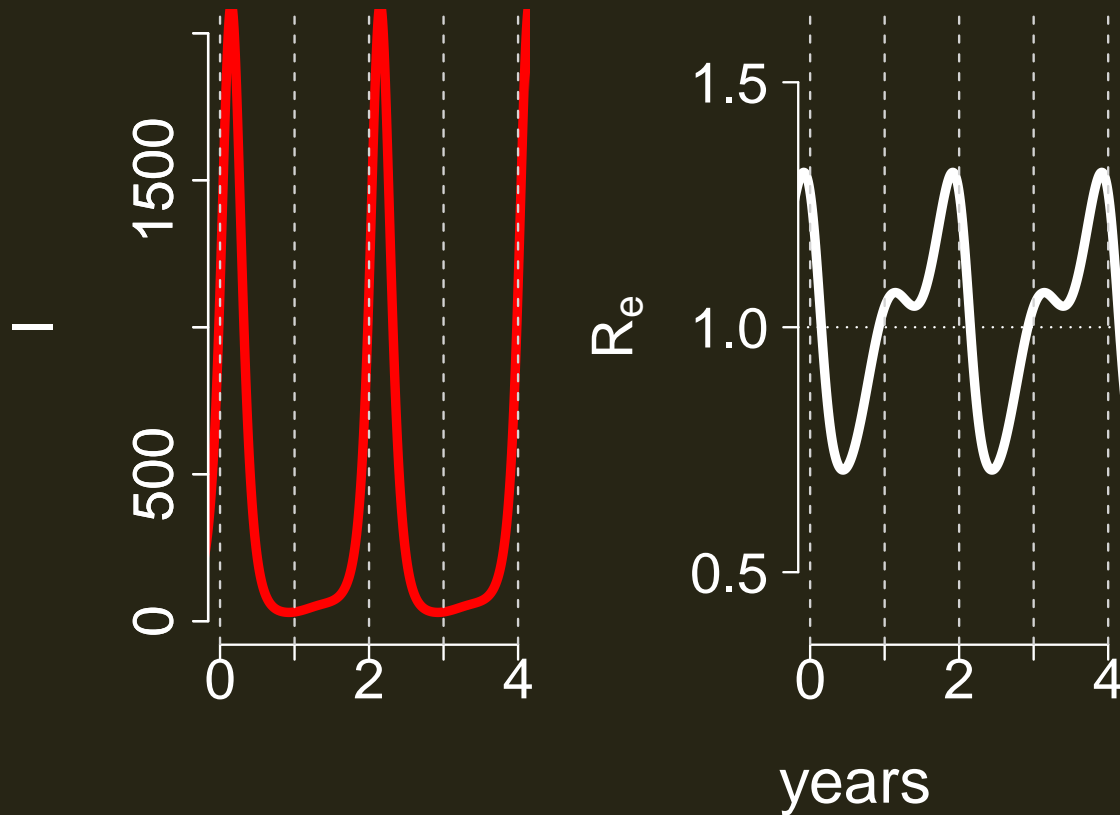


Susceptible Replenishment & Periodicity



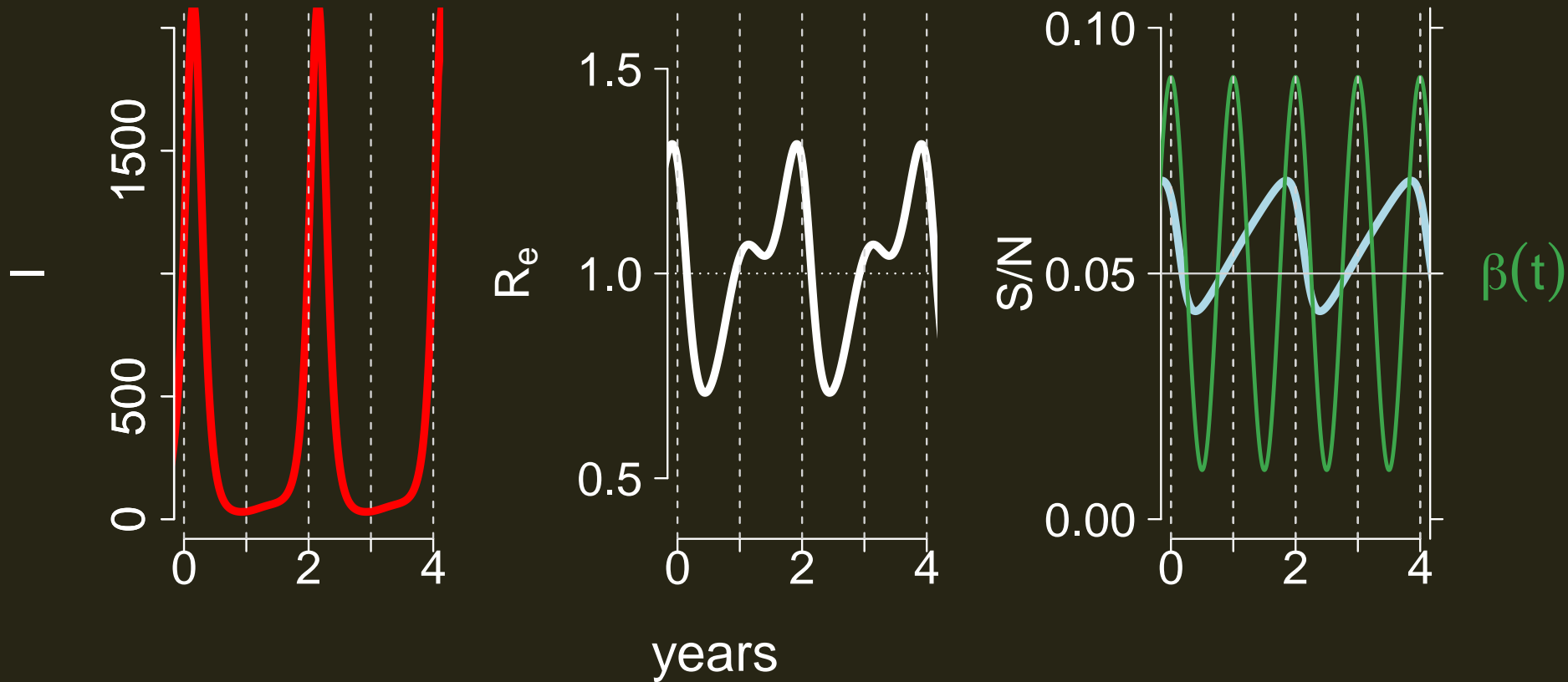
Life Expectancy of 40 years

Susceptible Replenishment & Periodicity



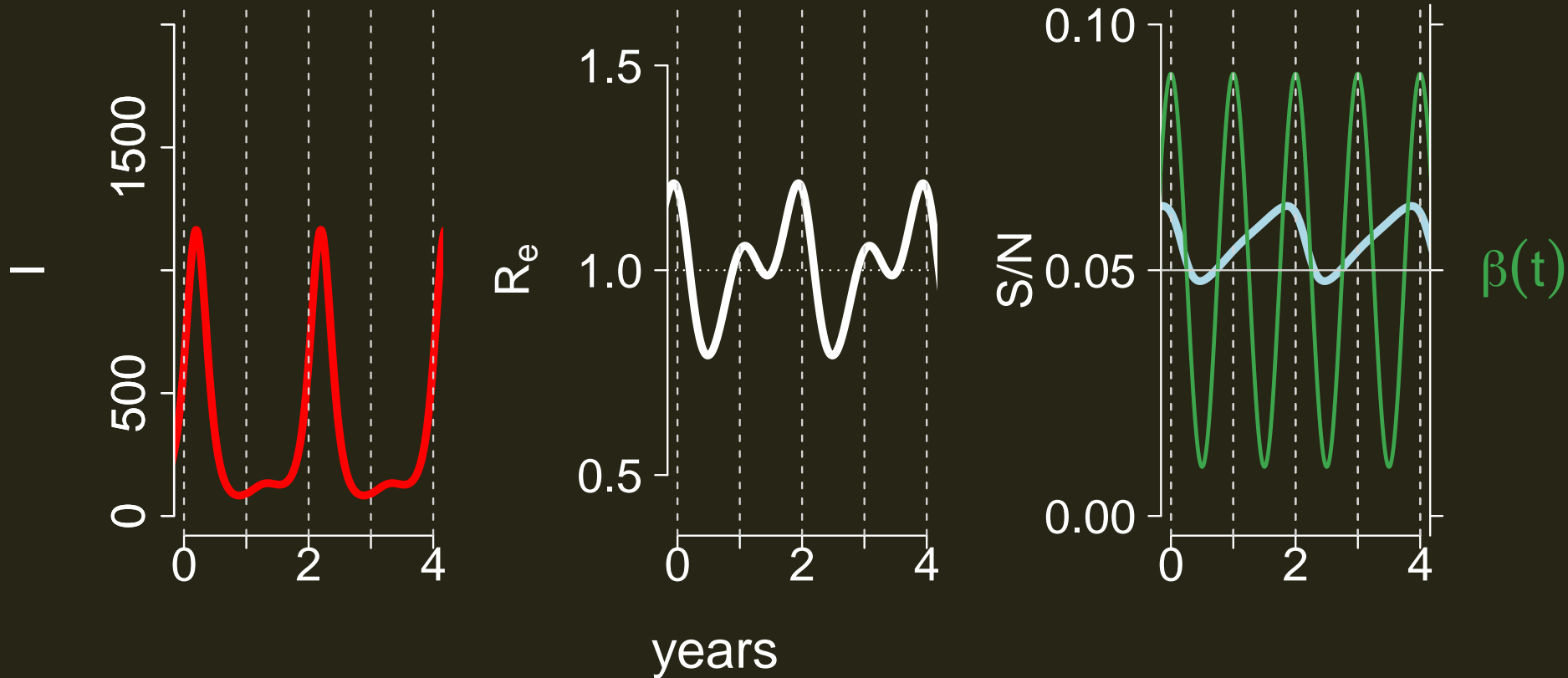
Life Expectancy of 40 years

Susceptible Replenishment & Periodicity



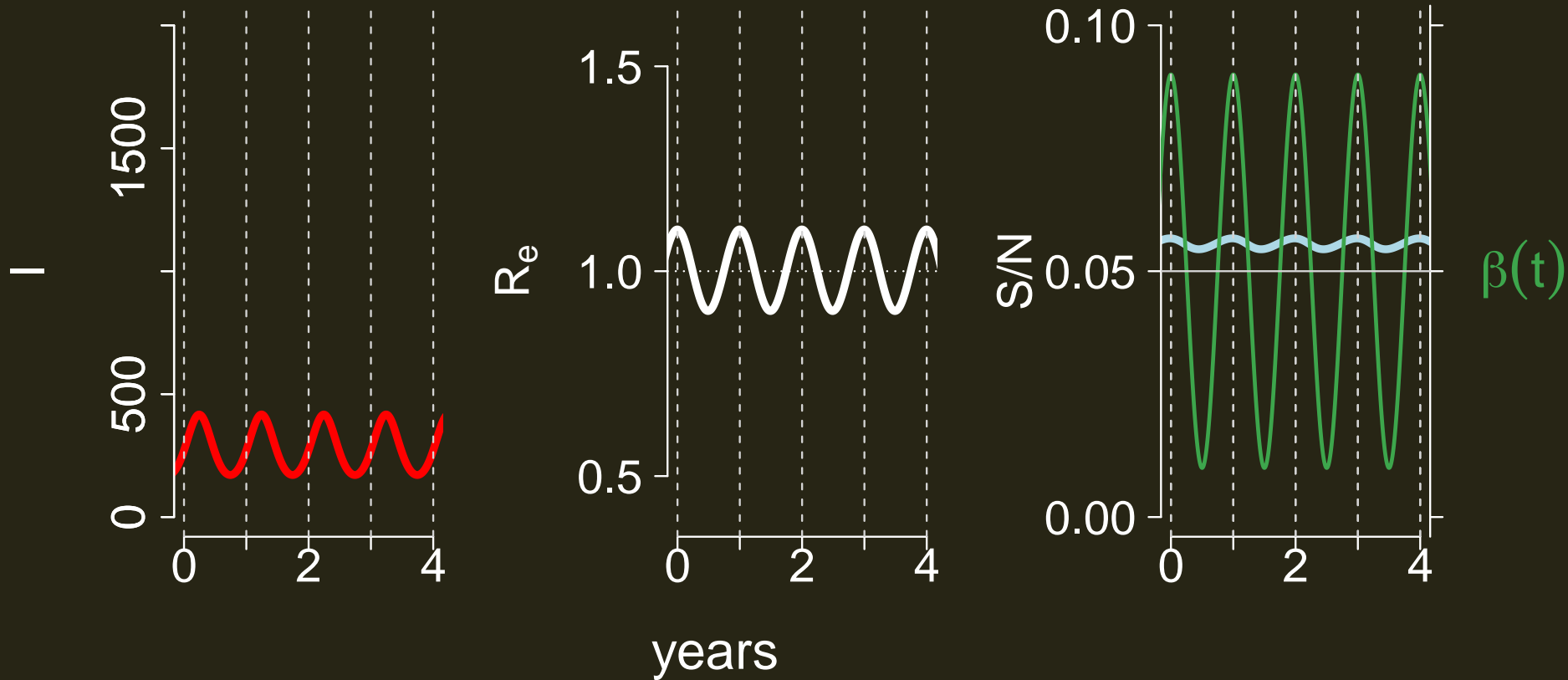
Life Expectancy of 40 years

Susceptible Replenishment & Periodicity



Life Expectancy of 50 years

Susceptible Replenishment & Periodicity



Life Expectancy of 60 years