Introduction to Dynamic Modeling of Infectious Diseases

Clinic on the Meaningful Modeling of Epidemiological Data, June 2023

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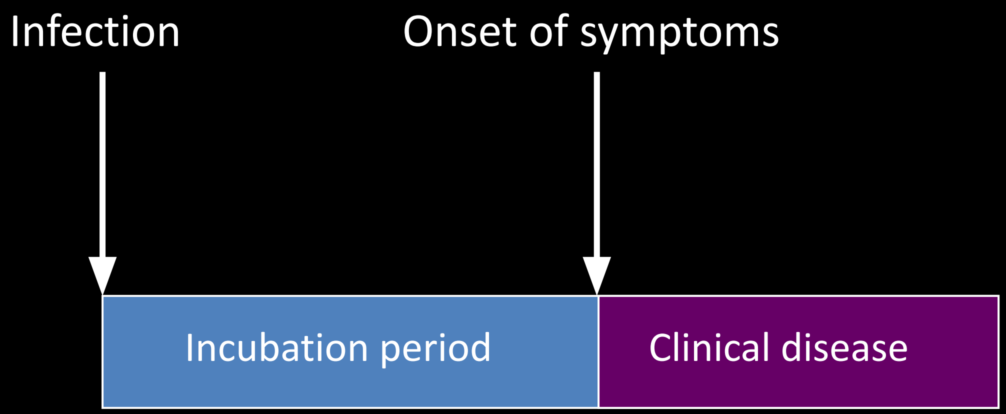
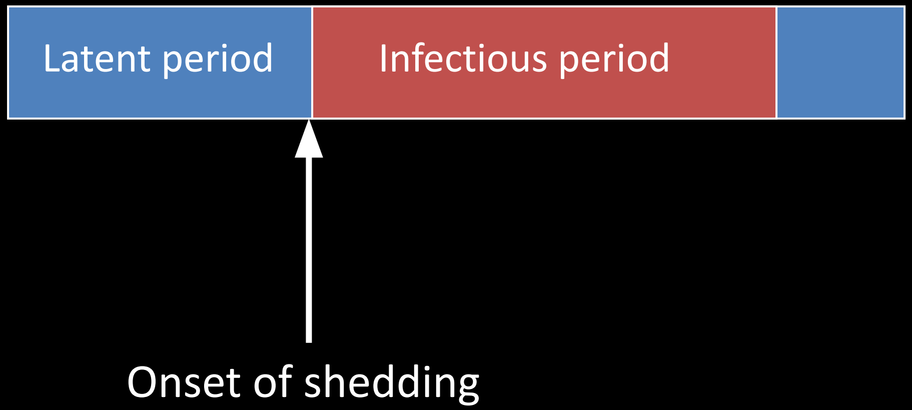
Goals

- Understand the natural history of infection
- Explains SIR model formulation
- Define the basic reproduction number (R_0)
- Calculate vaccinated proportion needed for pathogen elimination
- Explain the effect of demography on epidemics

Natural History of Infection

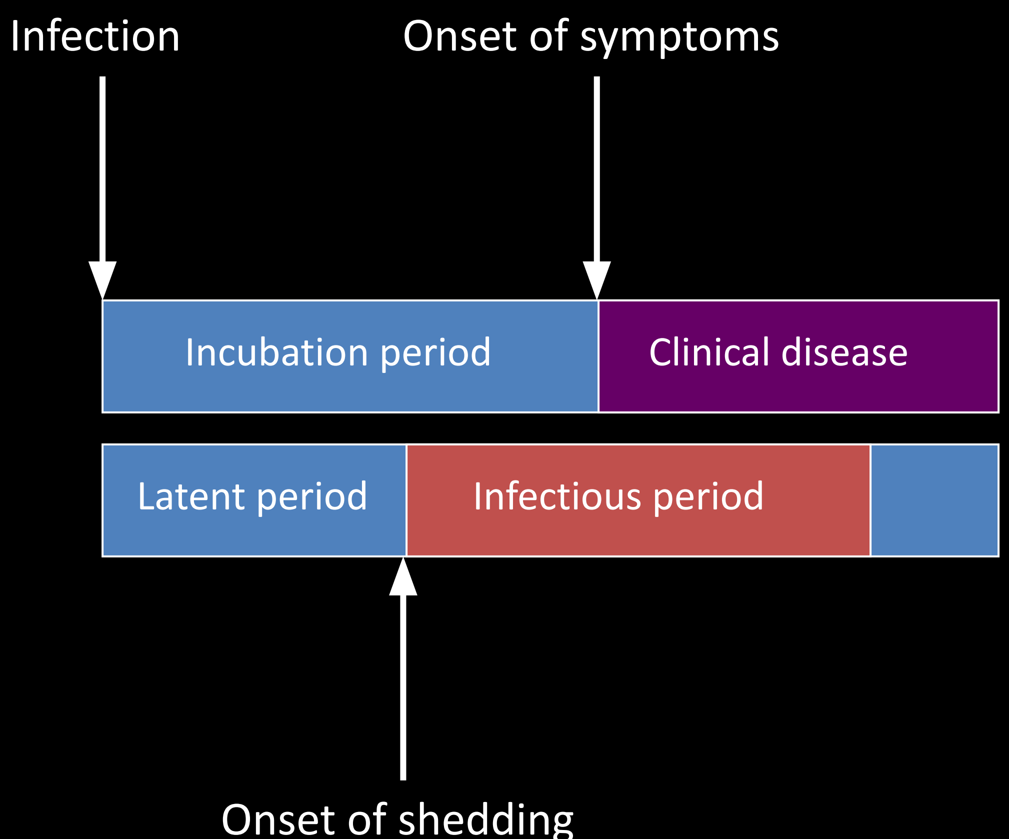


Natural History of Infection



Natural History of Infection

Let’s start by talking about acute, immunizing diseases



<u>Acute</u>

Infection time course

<<

Host lifespan

<u>Immunizing</u>

Infection □ antibody production

prevents future infection

Examples

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

Anderson and May (1982) Science

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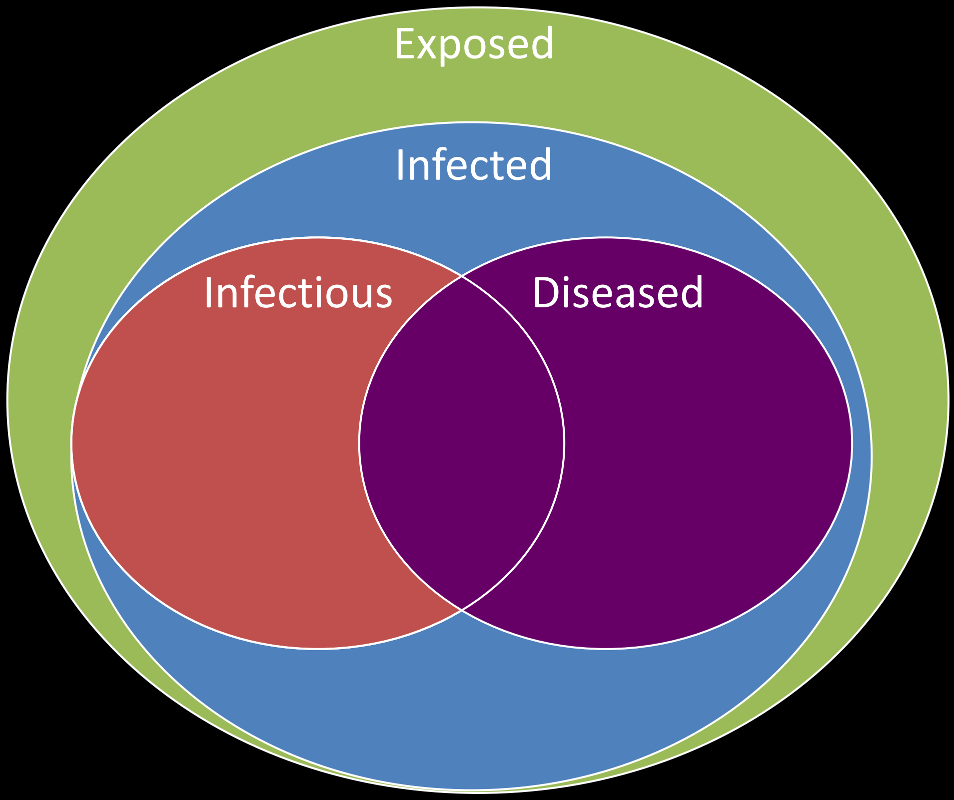
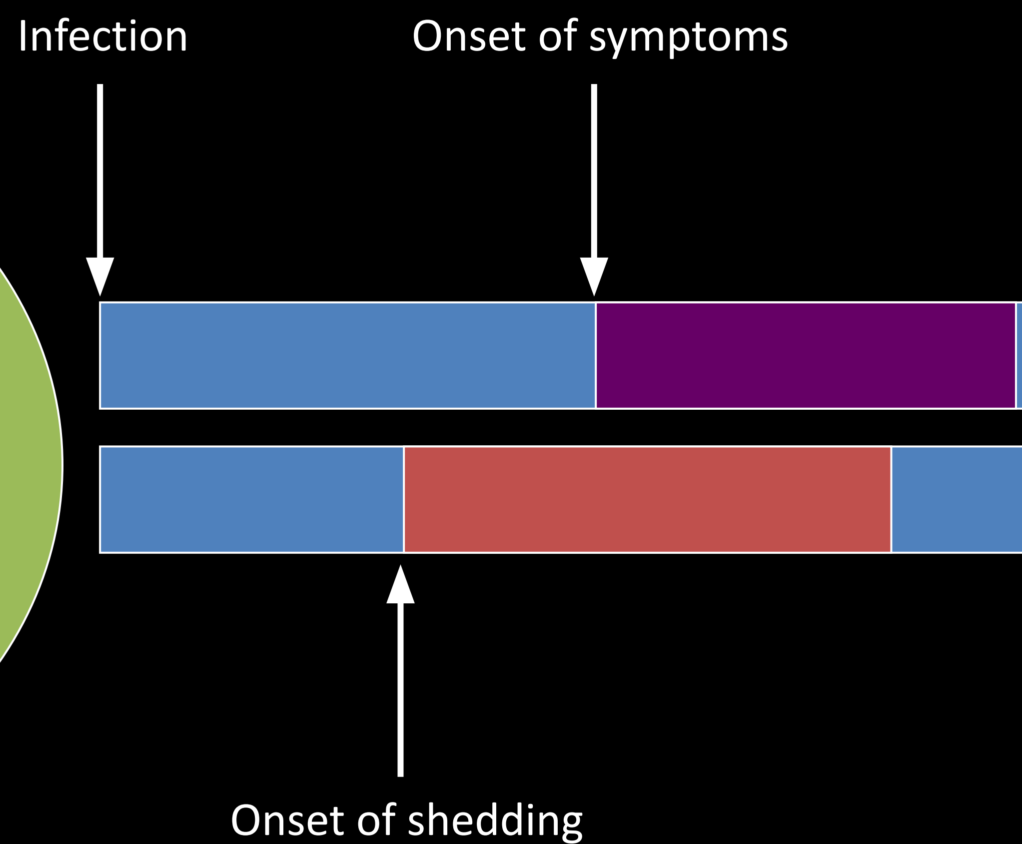
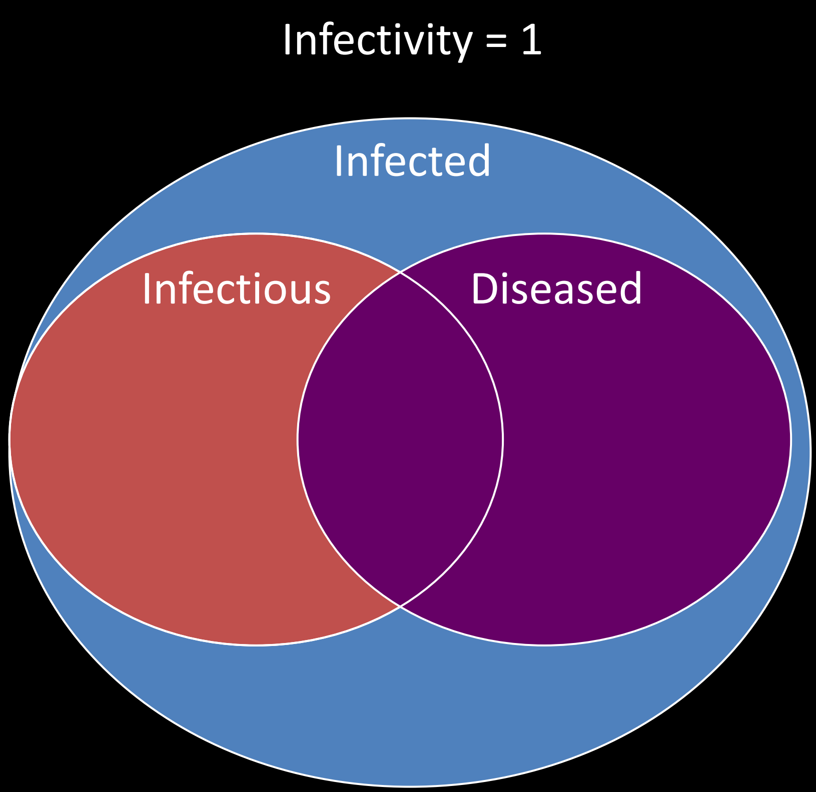
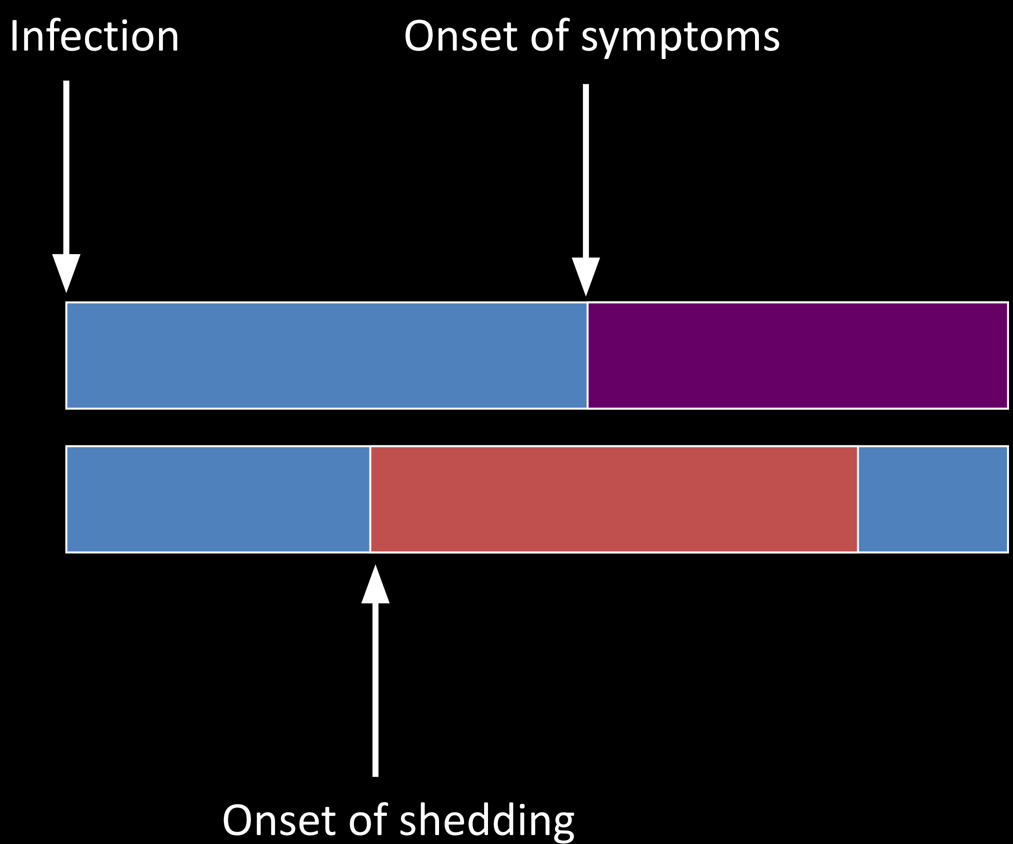
Terminology





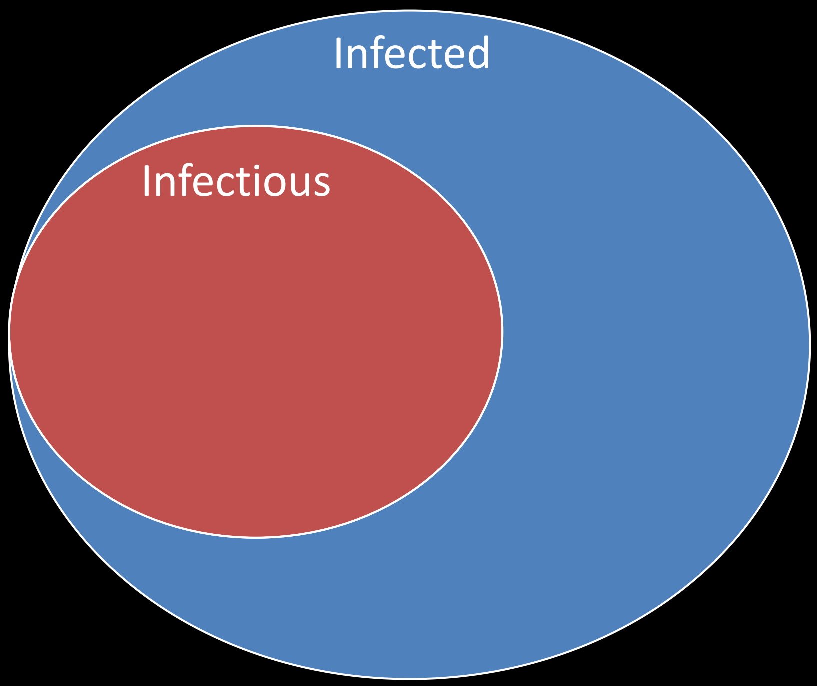
A simple view of the world



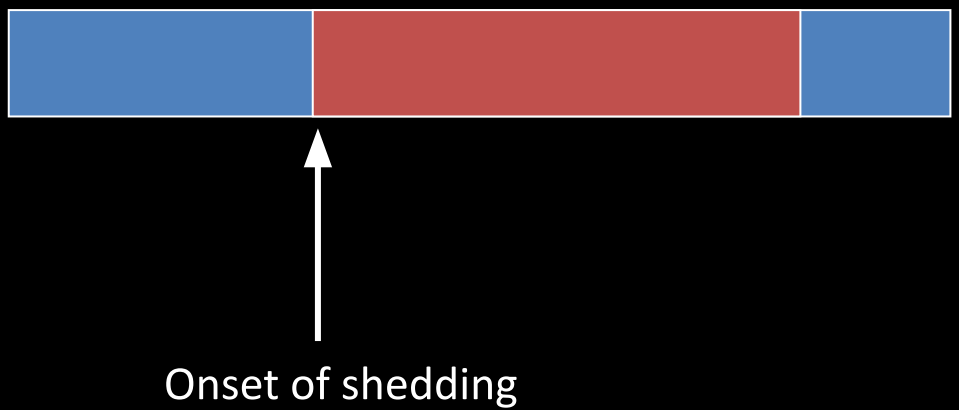


A simpler view of the world

Infectivity = 1



Don’t worry about symptoms and disease!



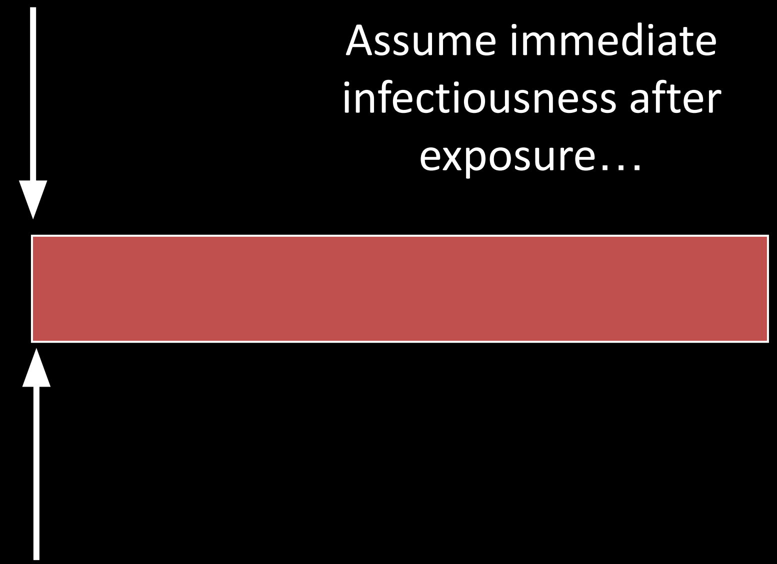
An extremely simple view of the world

Don't worry about symptoms and disease!

Infectivity = 1

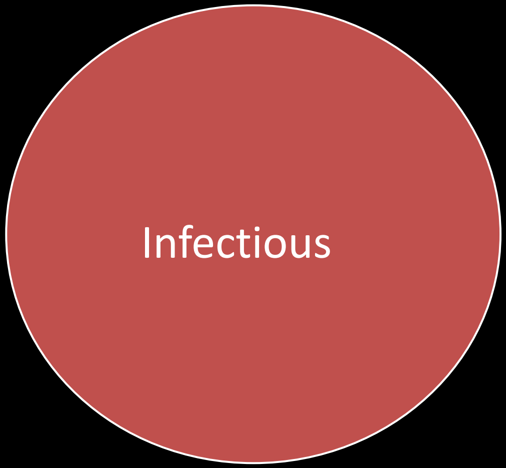
Infection

Assume immediate infectiousness after exposure…



Onset of shedding

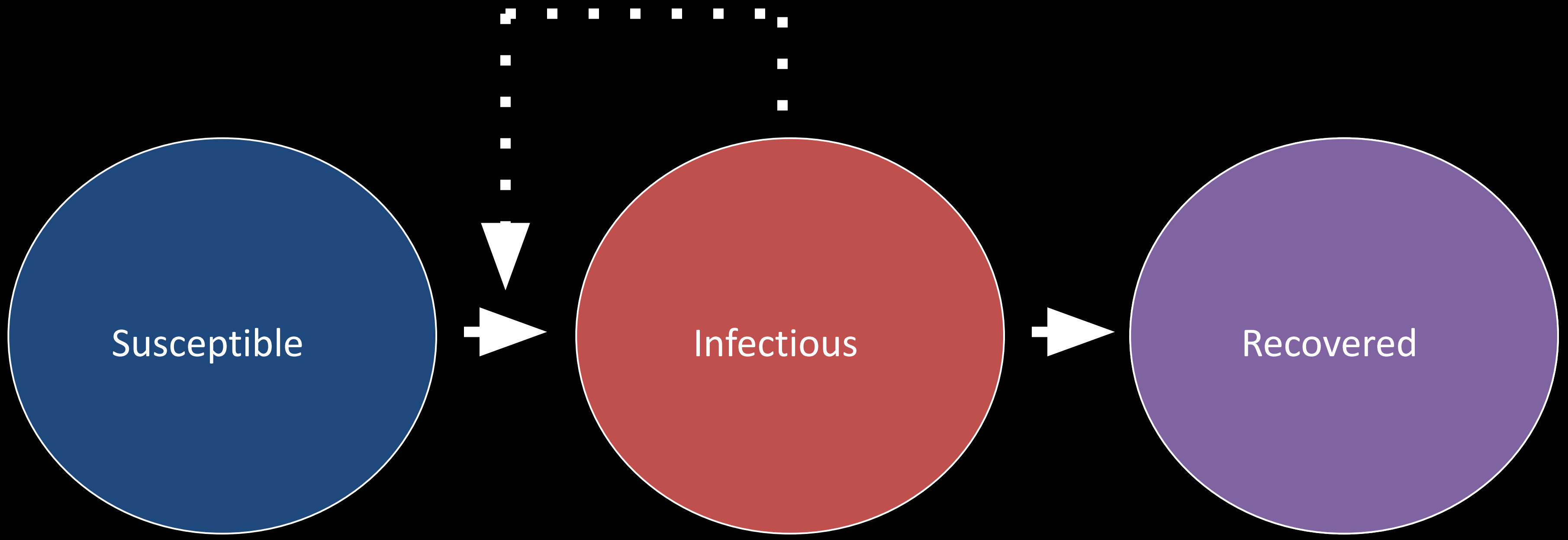
An extremely simple view of the world



An extremely simple view of the world

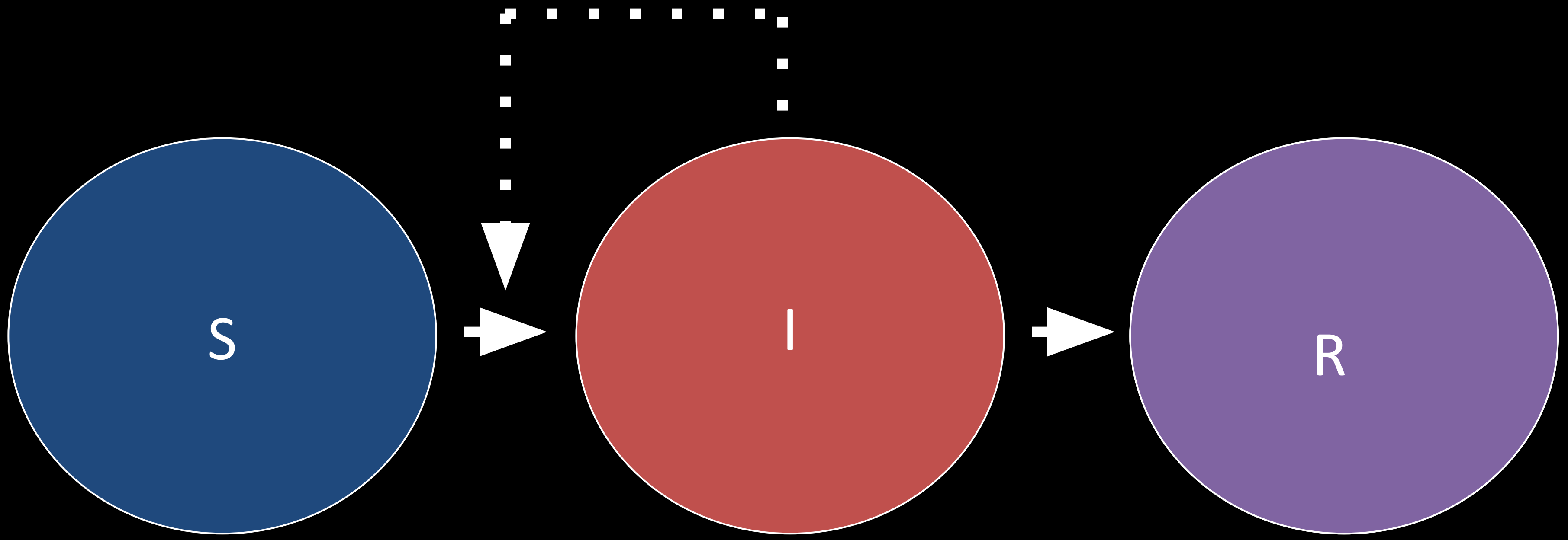
An extremely simple view of the world

Health-related States



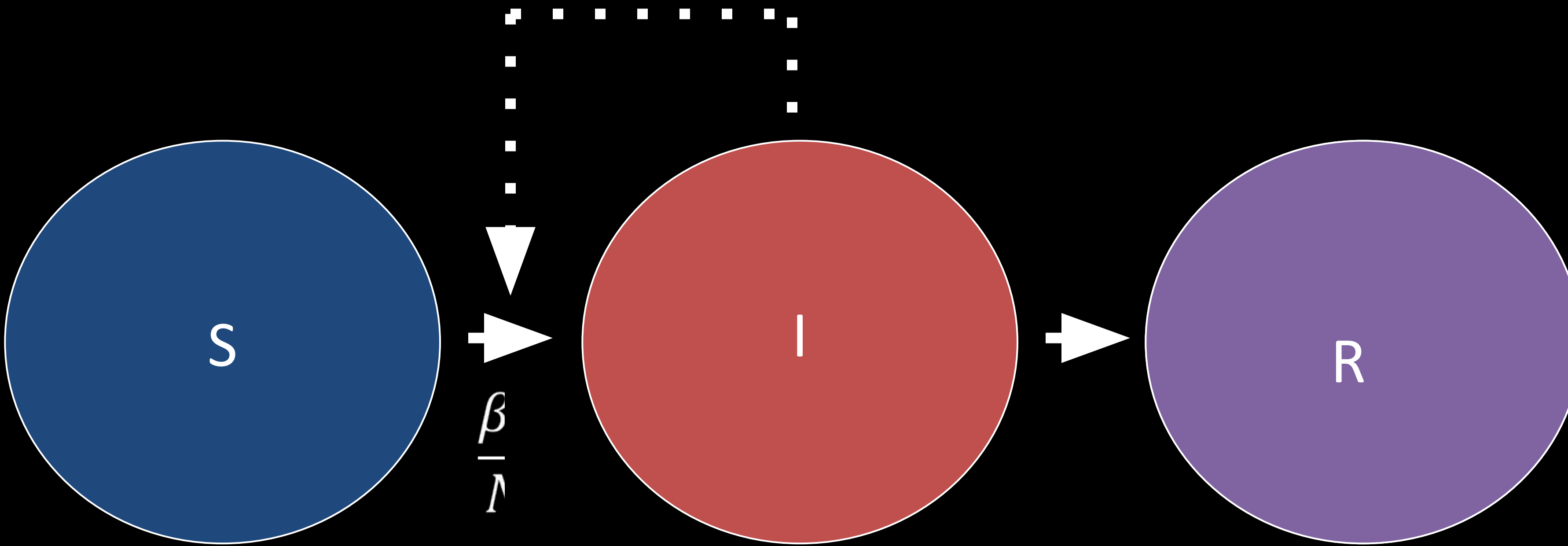
The rate at which susceptible individuals become infected depends on how many infectious people are in the population

State variables



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

SIR Model



β = transmission coefficient

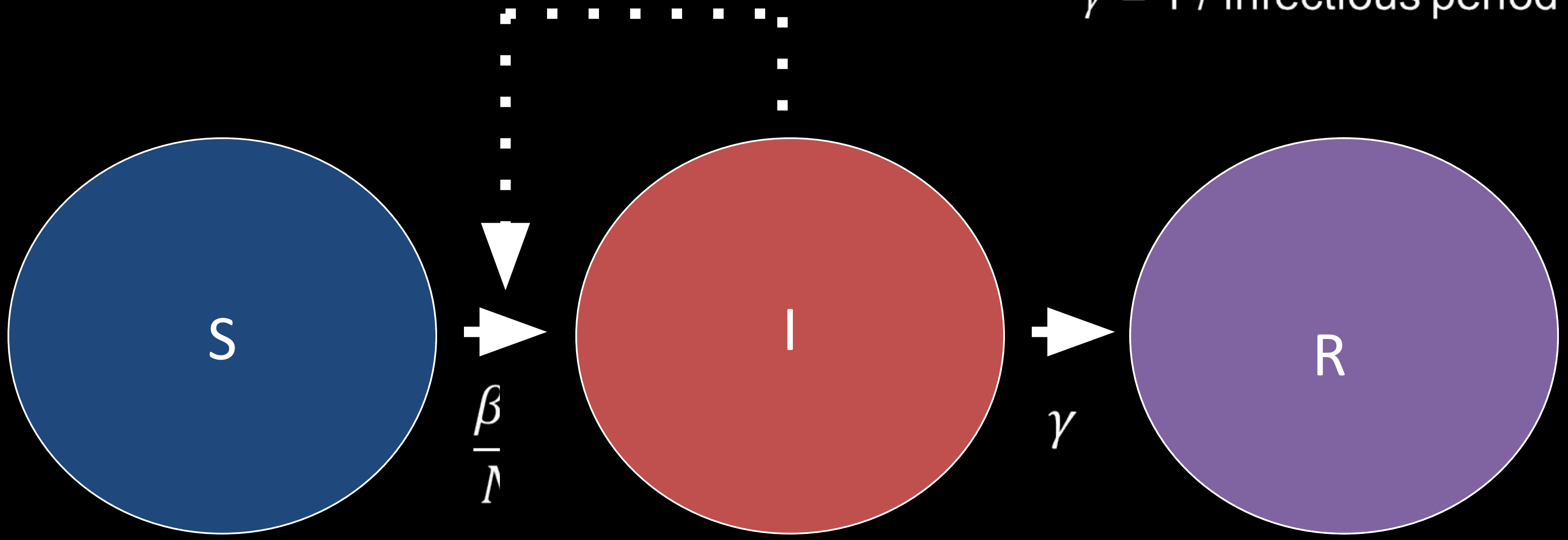
= per capita contact rate * infectivity

= per capita contact rate (infectivity = 1)

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

SIR Model

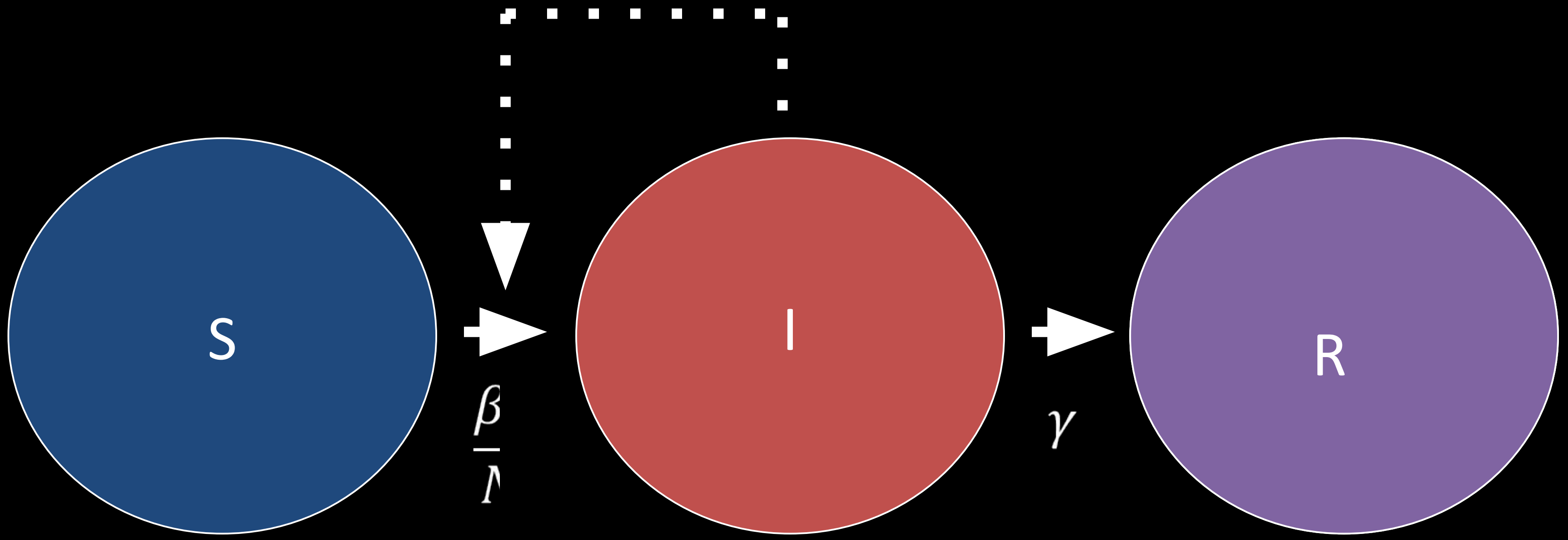
γ = 1 / infectious period



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

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

SIR Model



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

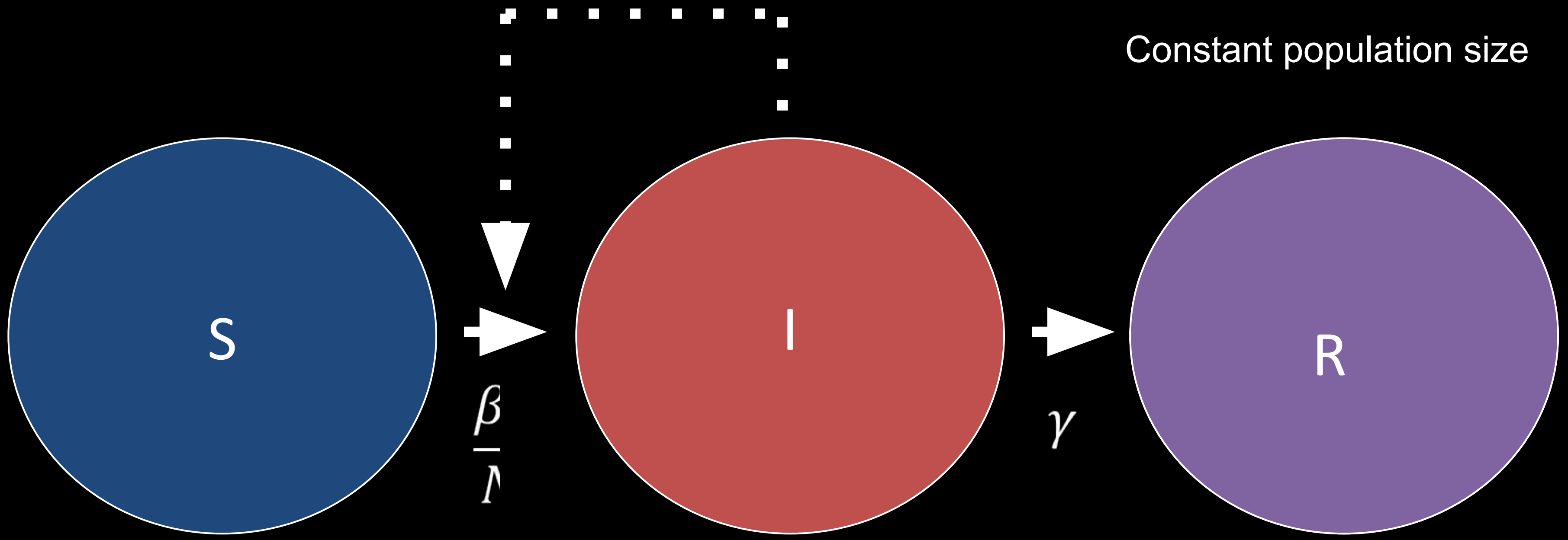
$$\frac{dI}{dt} = \frac{\beta SI}{N} - \gamma I$$

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

SIR Model

$$N = S + I + R$$

Constant population size



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SIR Model

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

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

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

N population size

γ recovery rate

β transmission coefficient

SIR Model

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

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

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

$$R_0 =$$

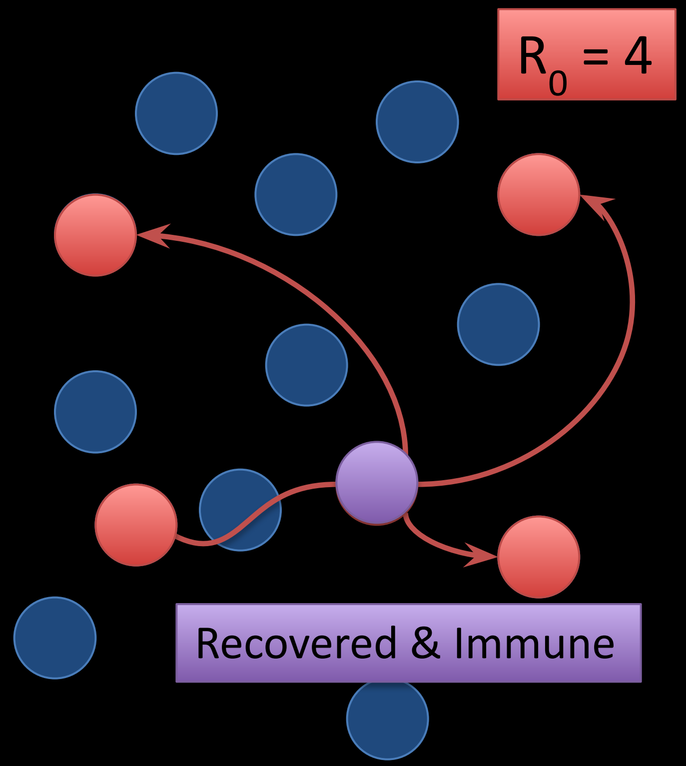
infections produced by

1 infectious individual

in a fully susceptible population.

R_0: The Basic Reproductive Number

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



SIR Model

$$\frac{\beta S I}{N} \xrightarrow{\text{N large}} \beta$$

$$R_0 =$$

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

X

$$1$$

Proportion of infections that become infectious

X

$$\frac{1}{\gamma}$$

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 infections that become infectious

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R_0: The Basic Reproductive Number

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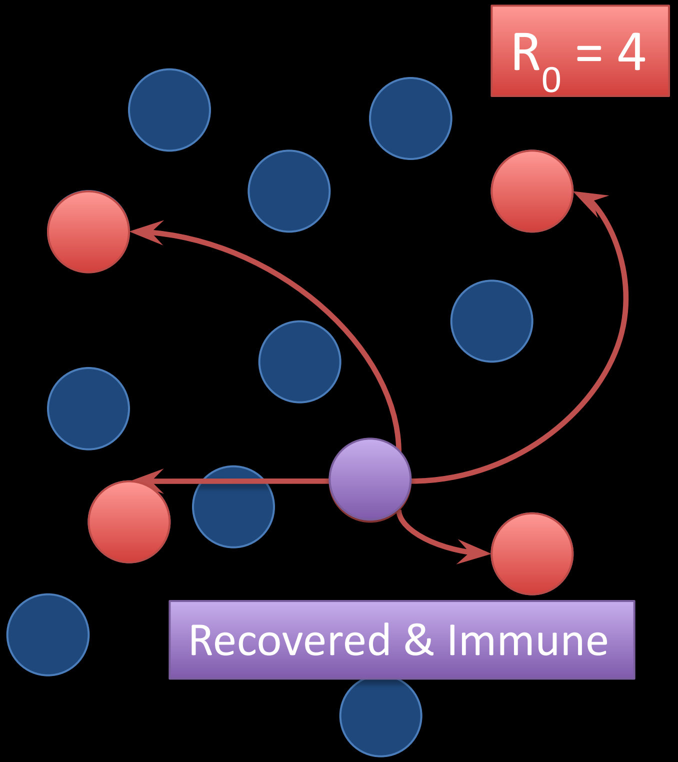
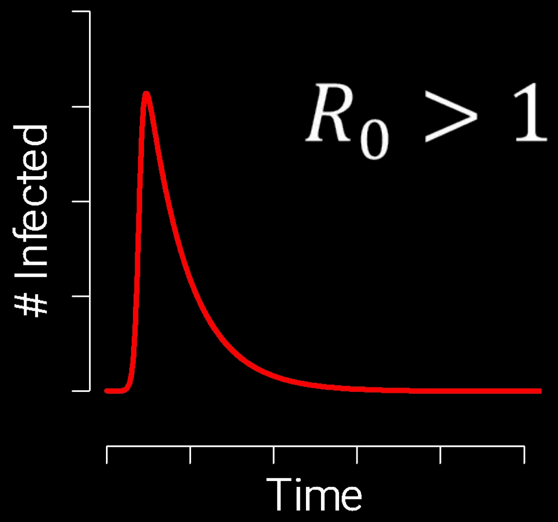
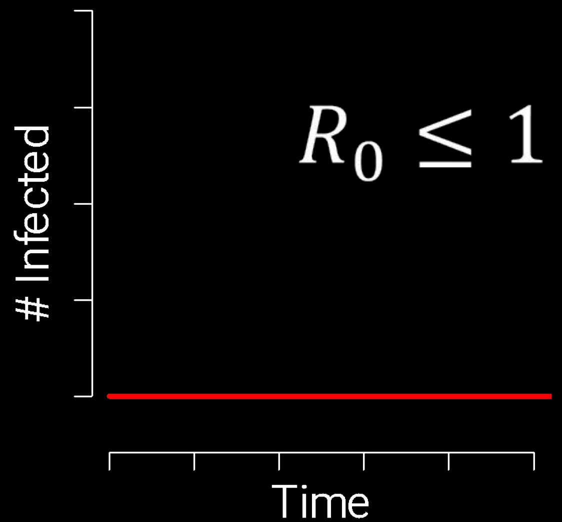


SIR Model: R_0 as a Threshold





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

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 partially susceptible population

X

1 Proportion of new infections that become infectious

X

$\frac{1}{\gamma}$ Average duration of infectiousness

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

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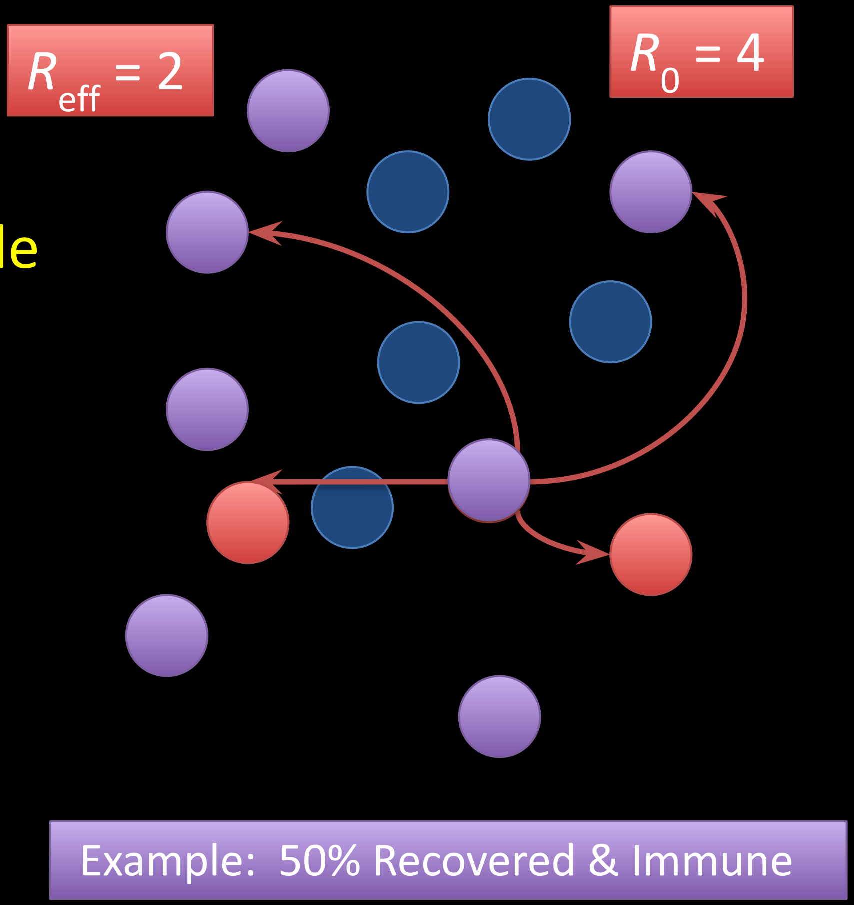
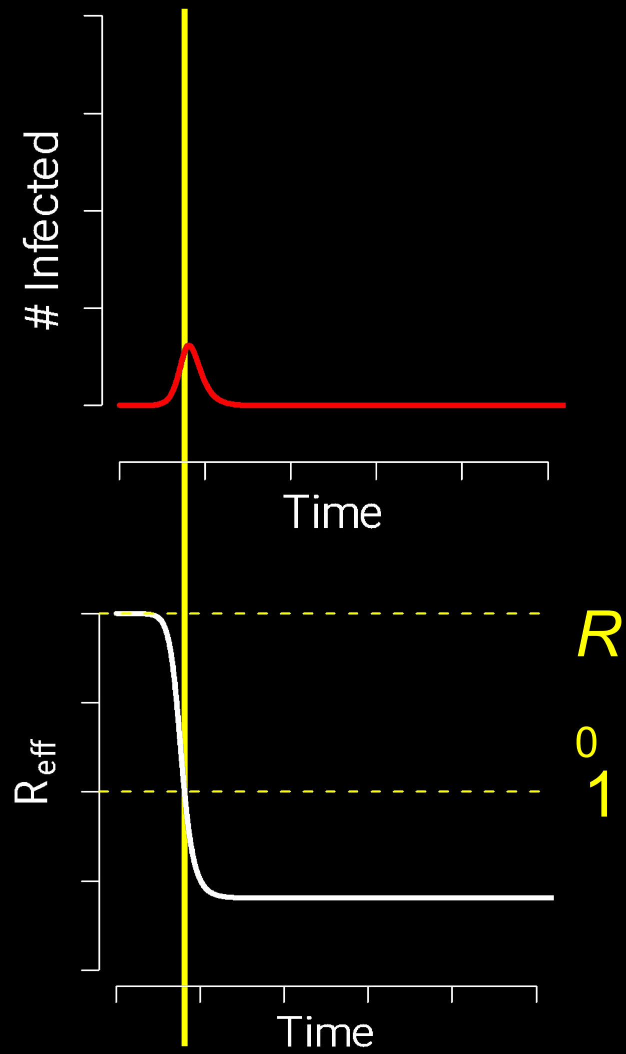
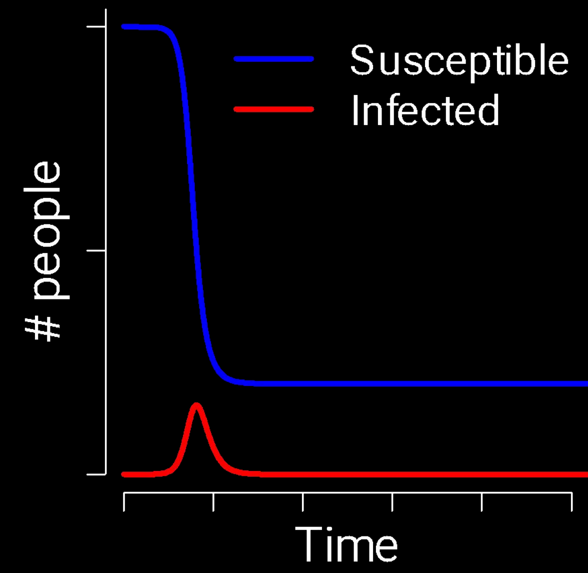
R_{eff}: The Effective Reproductive Number

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



R_{eff}: The Effective Reproductive Number



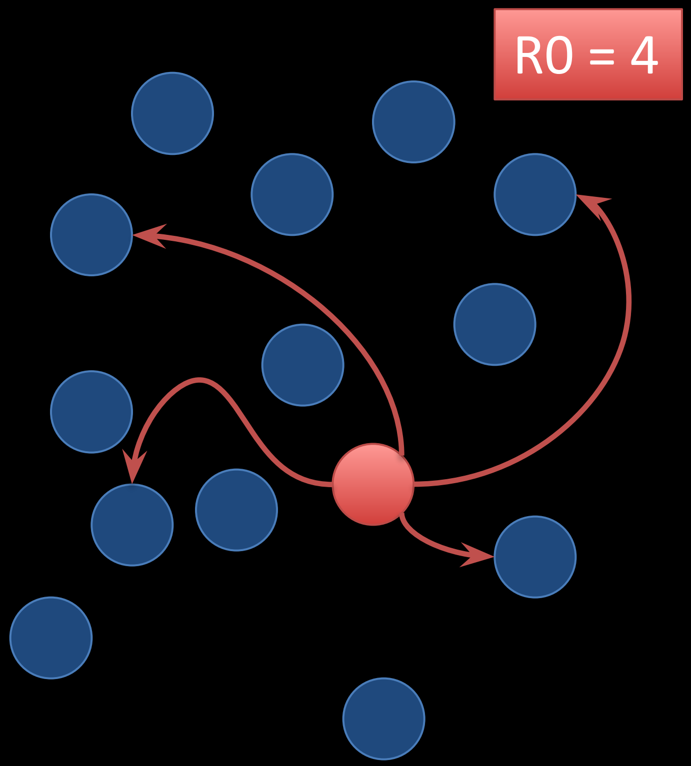


$$R_{eff}(t) = R_0 \frac{S(t)}{N}$$

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

Proportion to Vaccinate

- So what proportion of the population must be vaccinated to prevent an epidemic?



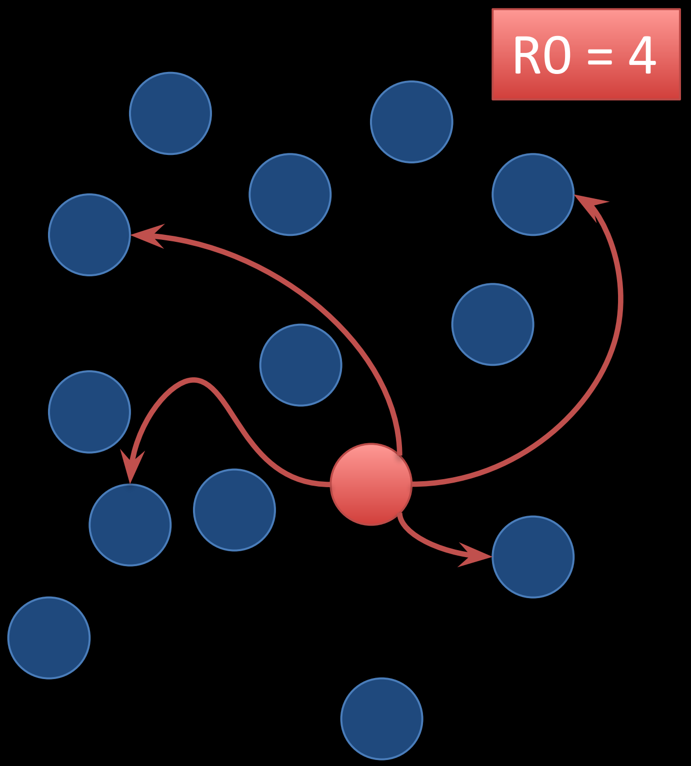
Proportion to Vaccinate

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

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

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

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



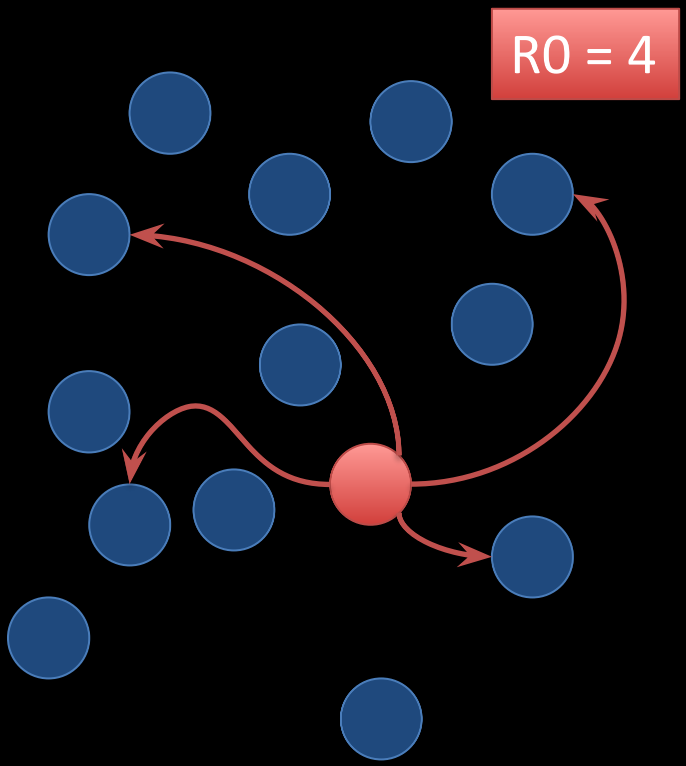
Proportion to Vaccinate

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

Proportion immune = P_V = 1- proportion

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

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



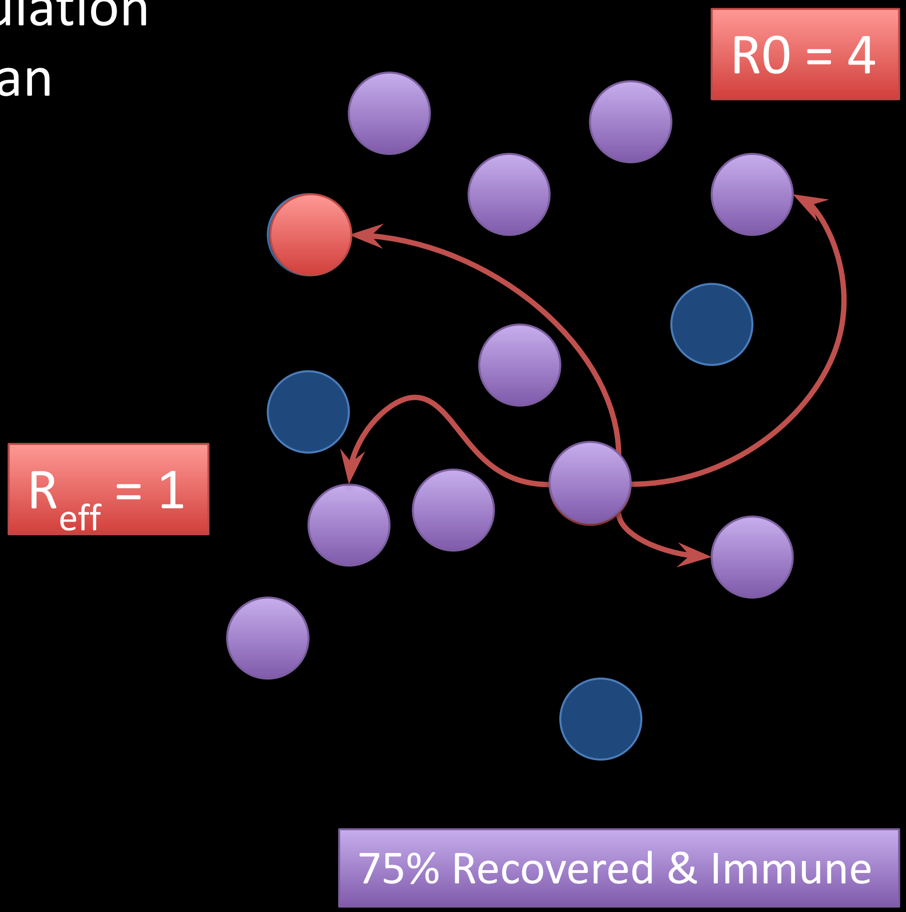
You don't have to vaccinate everyone to prevent an epidemic!!!

Proportion to Vaccinate

- So what proportion of the population must be vaccinated to prevent an epidemic?

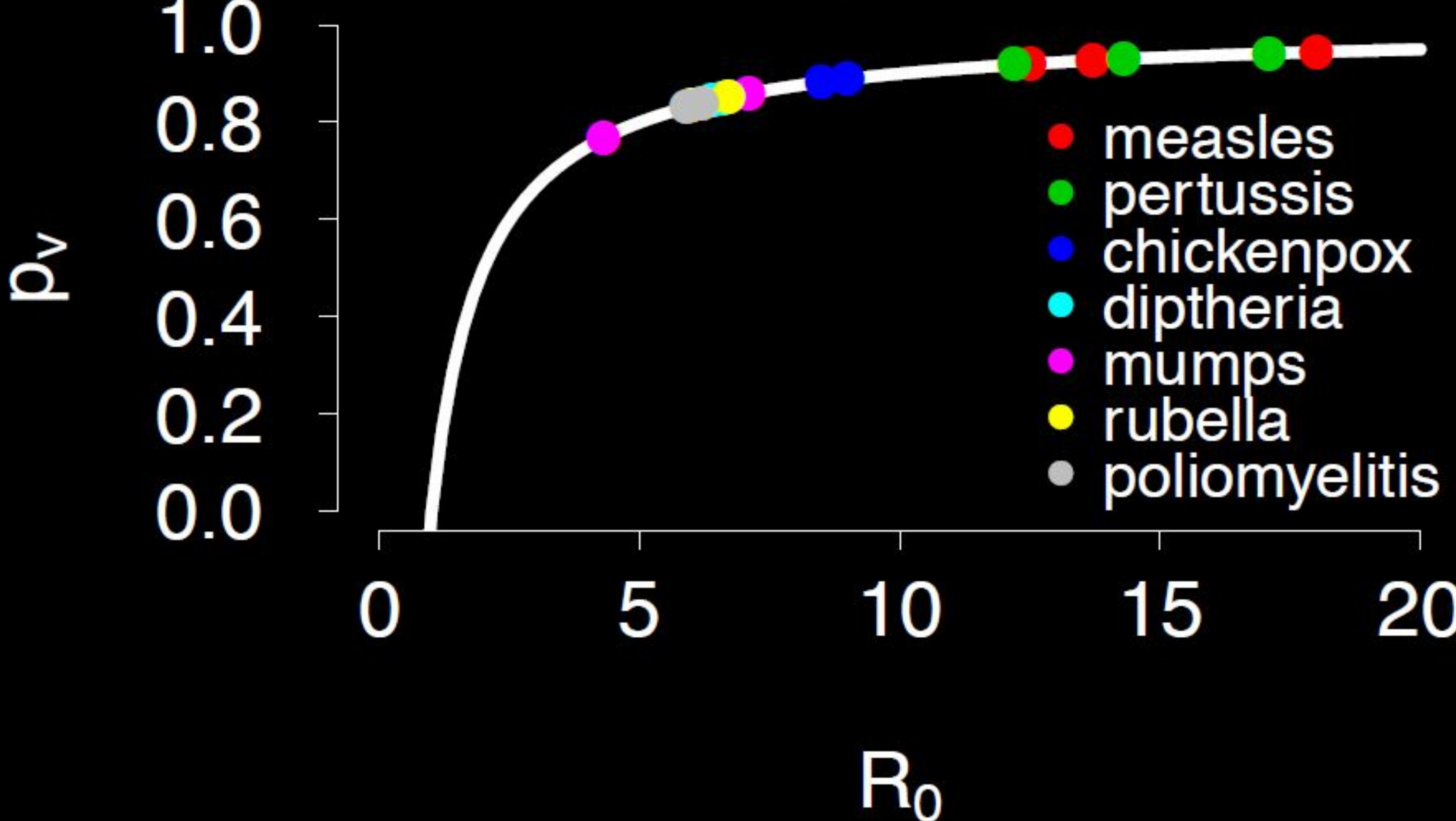
$$P_V \geq \frac{R_0 - 1}{R_0}$$

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

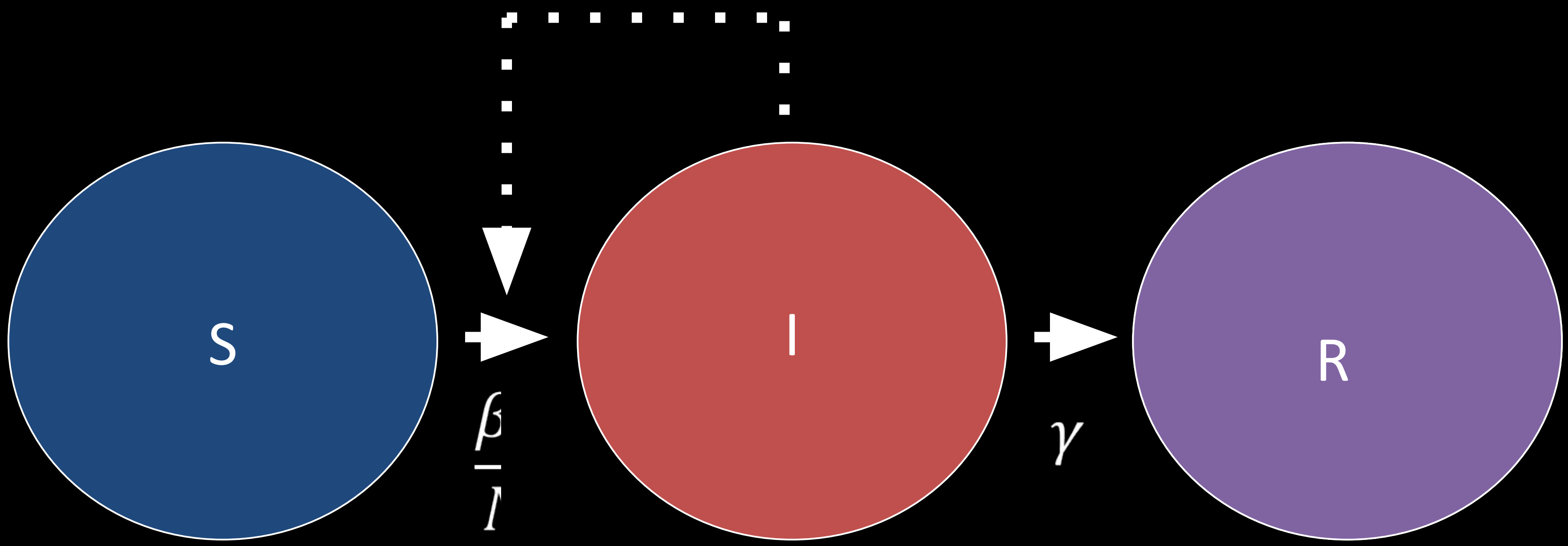


Elimination Thresholds

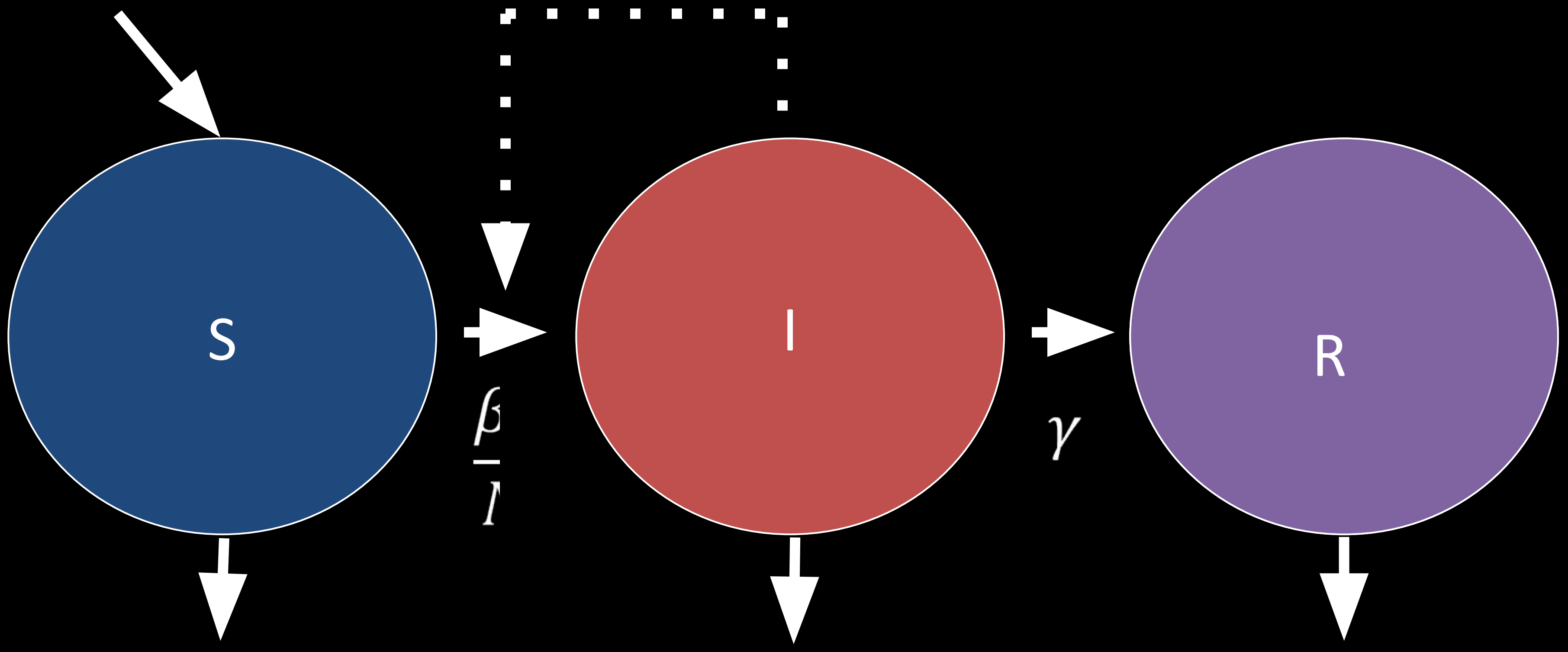
$$P_V = \frac{R_0 - 1}{R_0}$$



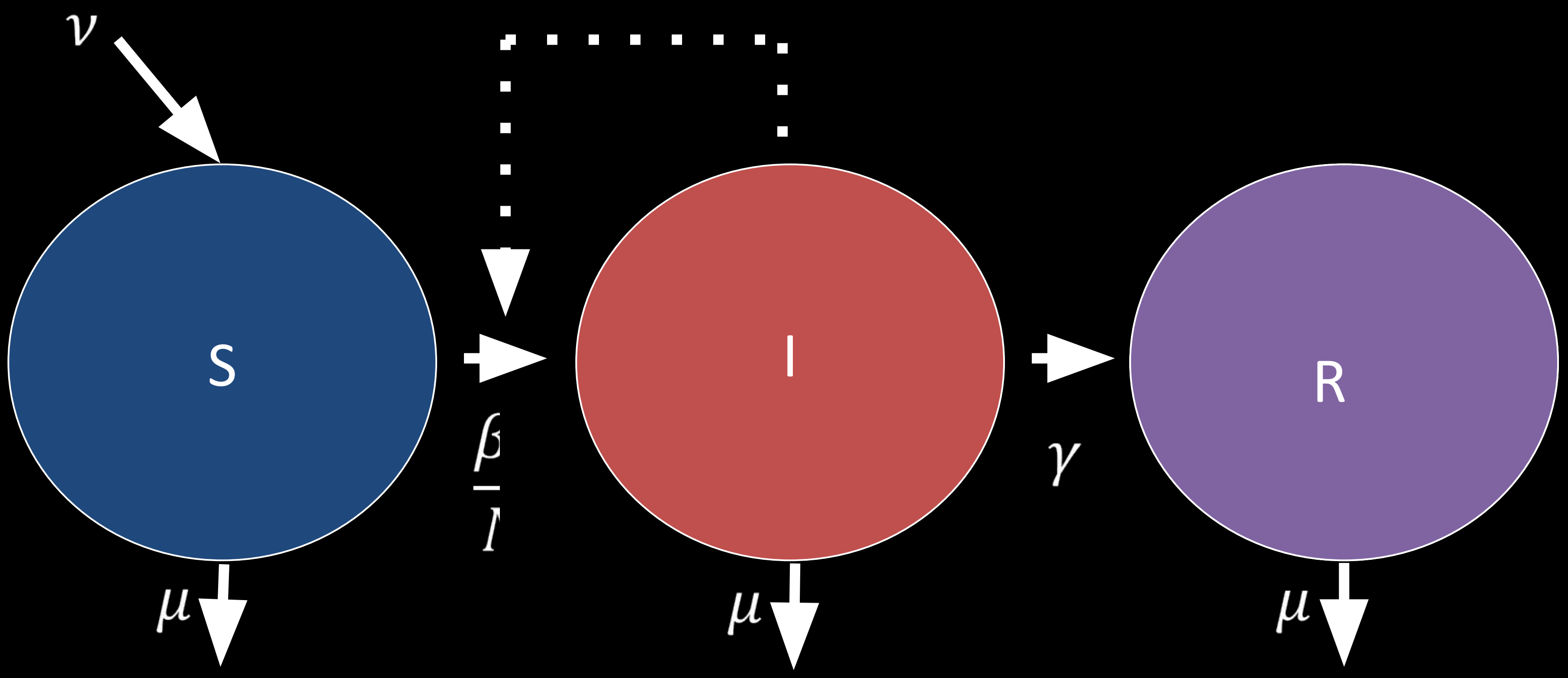
SIR Model



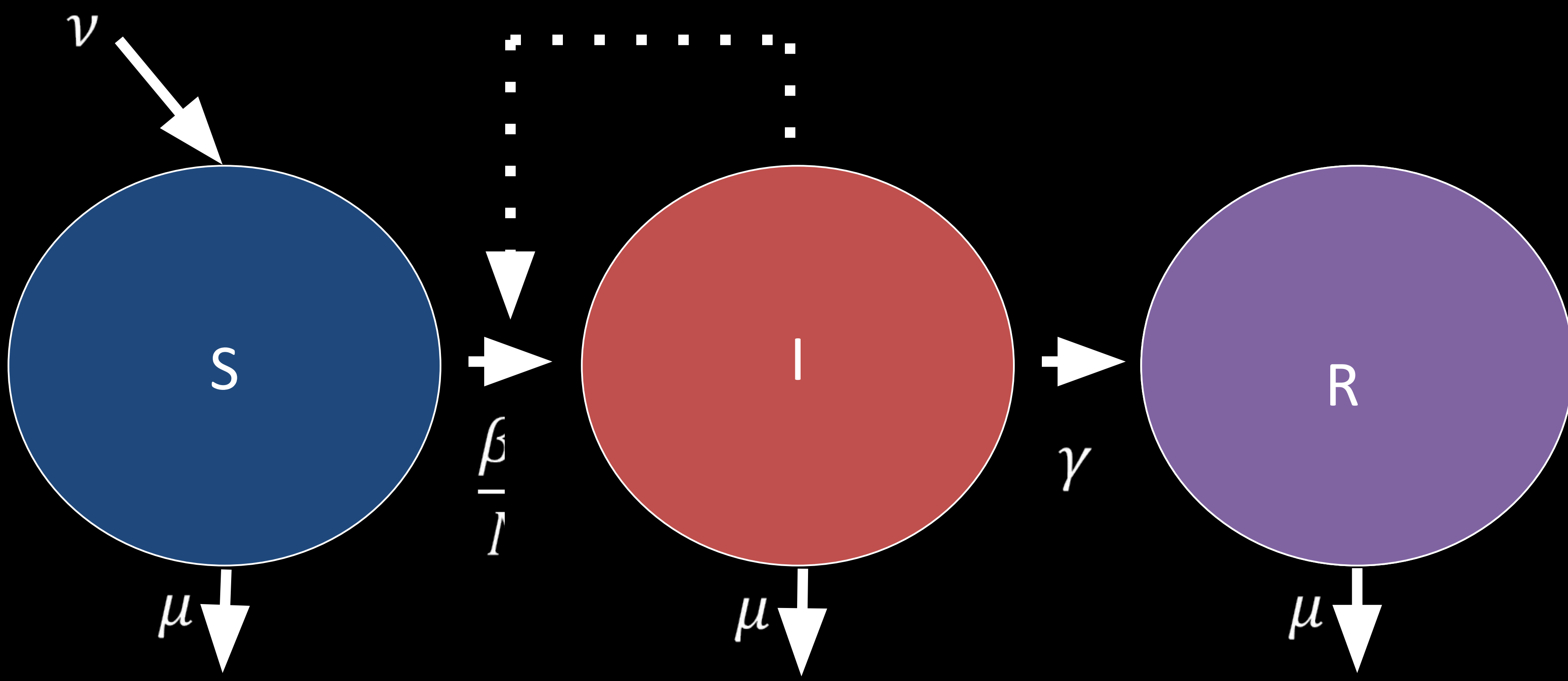
SIR Model with Birth & Death



SIR Model with Birth & Death



SIR Model with Birth & Death



$$\frac{dS}{dt} = \nu - \frac{\beta SI}{N} - \mu S \qquad \frac{dI}{dt} = \frac{\beta SI}{N} - \gamma I - \mu I \qquad \frac{dR}{dt} = \gamma I - \mu R$$

SIR Model with Birth & Death

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

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

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

$$N = S + I + R$$

so

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

SIR Model with Birth & Death

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

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

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

$$N = S + I + R$$

so

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

To assume constant population size, births = deaths:

$$\nu = \mu N$$

SIR Model with Birth & Death

$$R_0 =$$

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

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

X

$$1$$

Proportion of new infections that become infectious

X

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

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 infections that become infectious

X

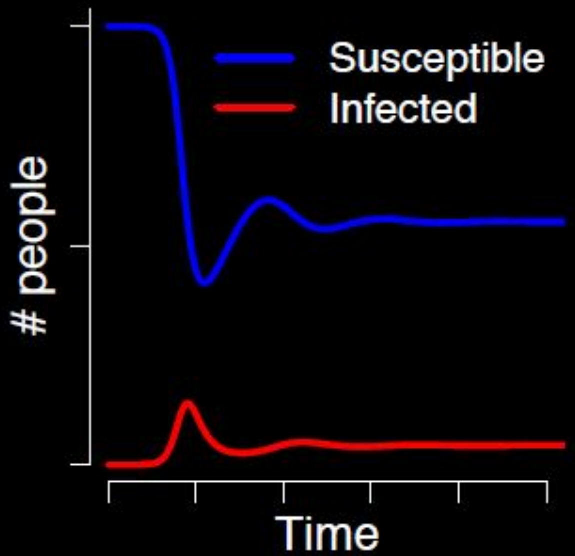
Average duration of infectiousness

SIR Model with Birth & Death

Dynamics upon introduction:

Epidemic if $R_0 > 1$

Endemic state



No epidemic if $R_0 \leq 1$

No endemic state

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

ICI3D

R_{eff}: Effective Reproductive Number

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

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

X

$$1$$

Proportion of new infections that become infectious

X

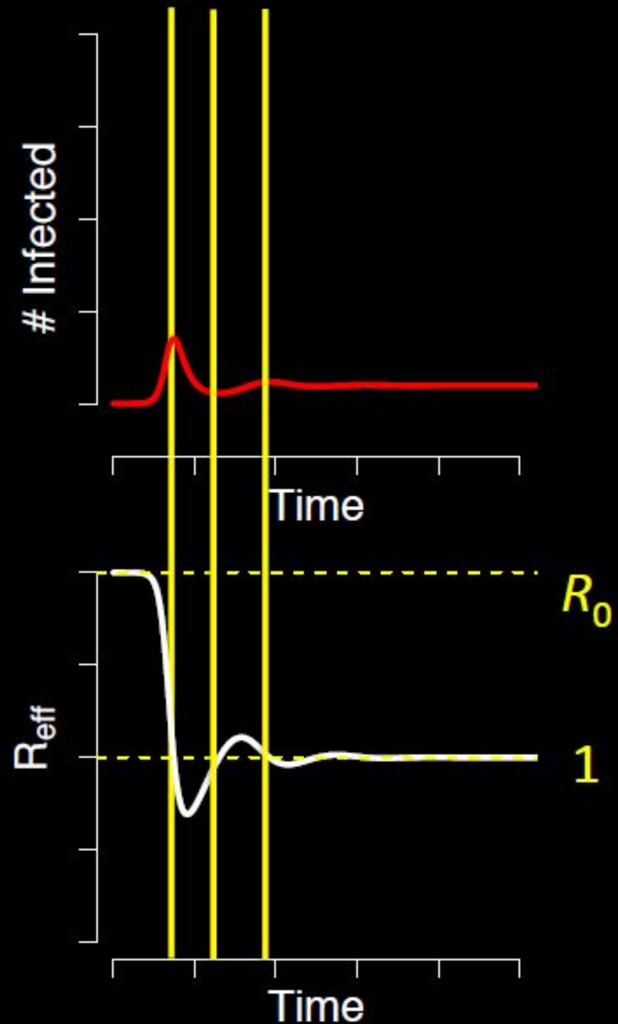
$$\frac{1}{\gamma + \mu}$$

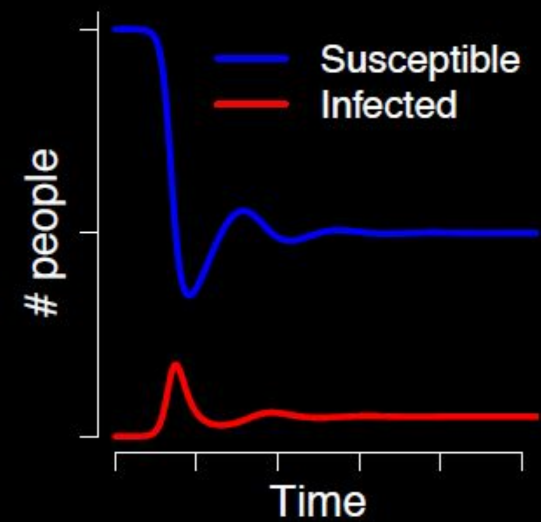
Average duration of infectiousness

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

ICI3D

R_{eff}: Effective Reproductive Number



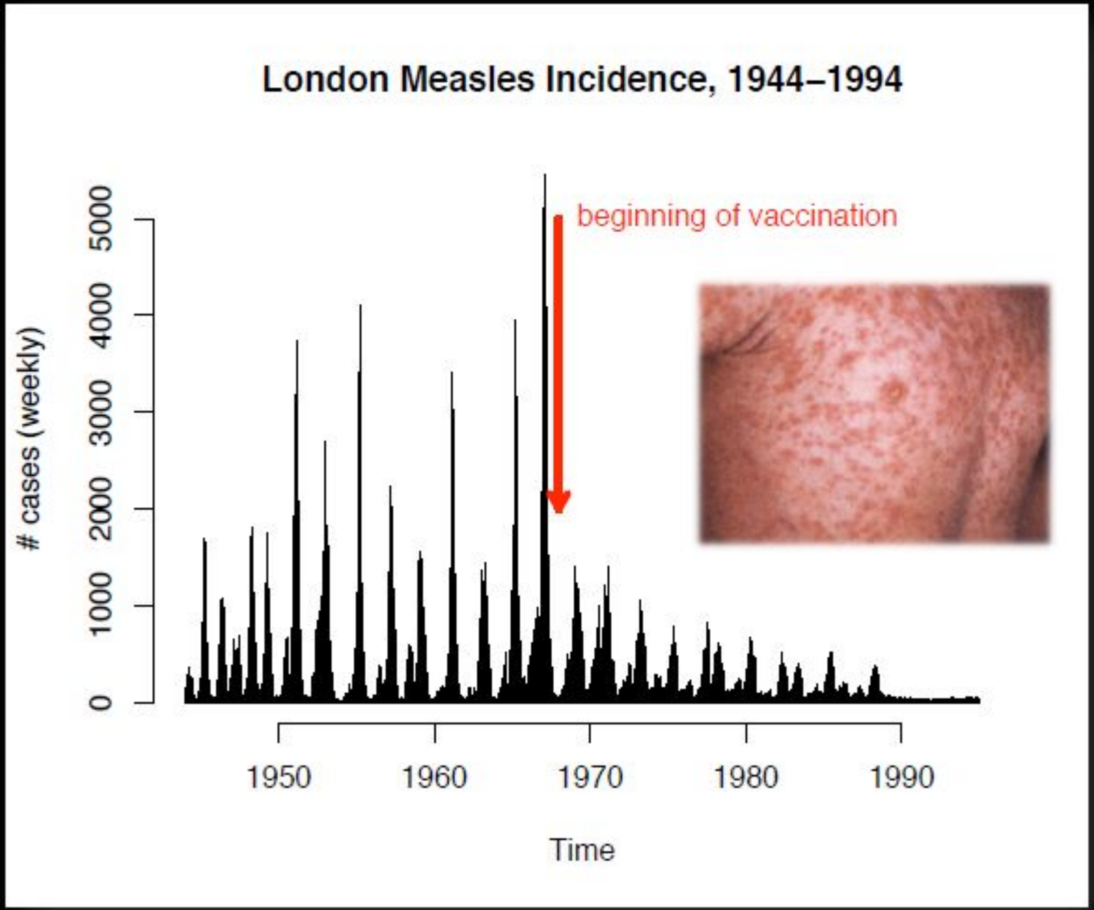


$$R_{eff}(t) = R_0 \frac{S(t)}{N}$$

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

Why do recurrent epidemics happen?

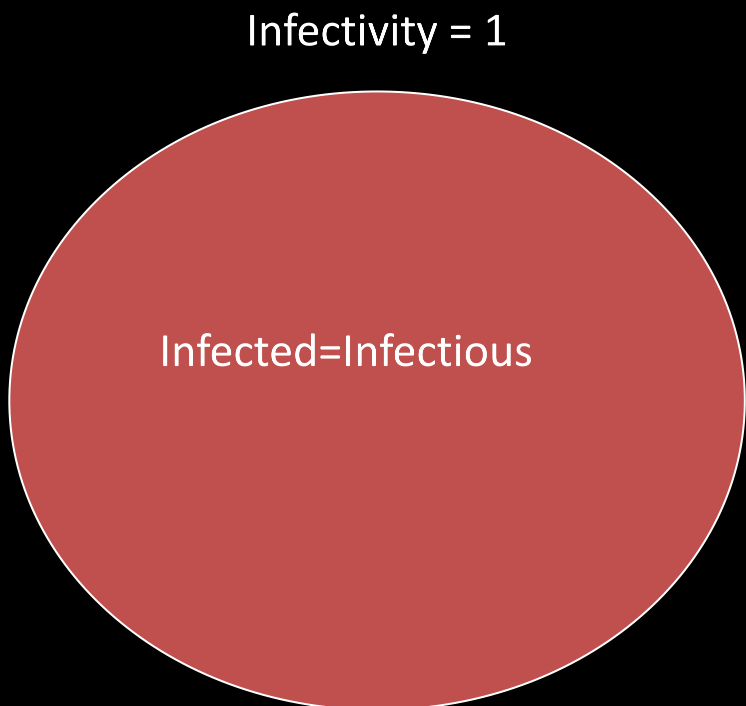
- Susceptibles exhausted from an epidemic
- Disease does not completely die out (or is reintroduced).
- Susceptibles replenished through birth or loss of immunity, epidemic occurs.



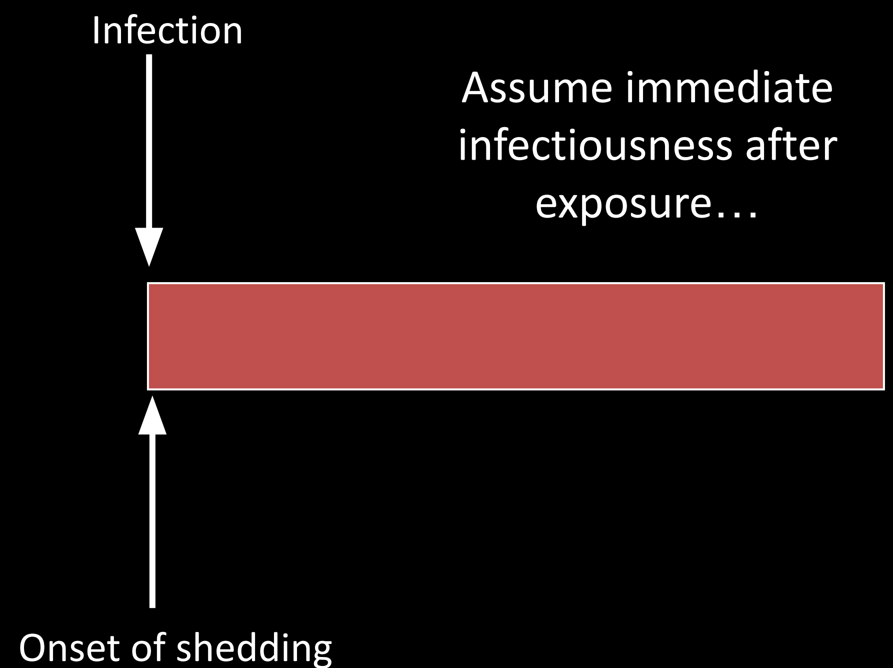
ICI3D

An extremely simple view of the world

Don't worry about symptoms and disease!



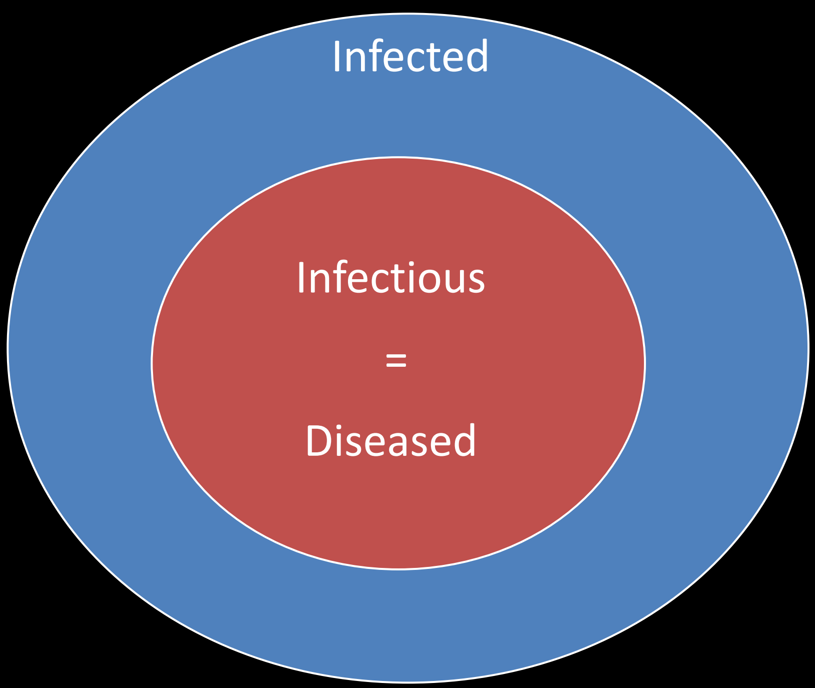
Assume immediate infectiousness after exposure…

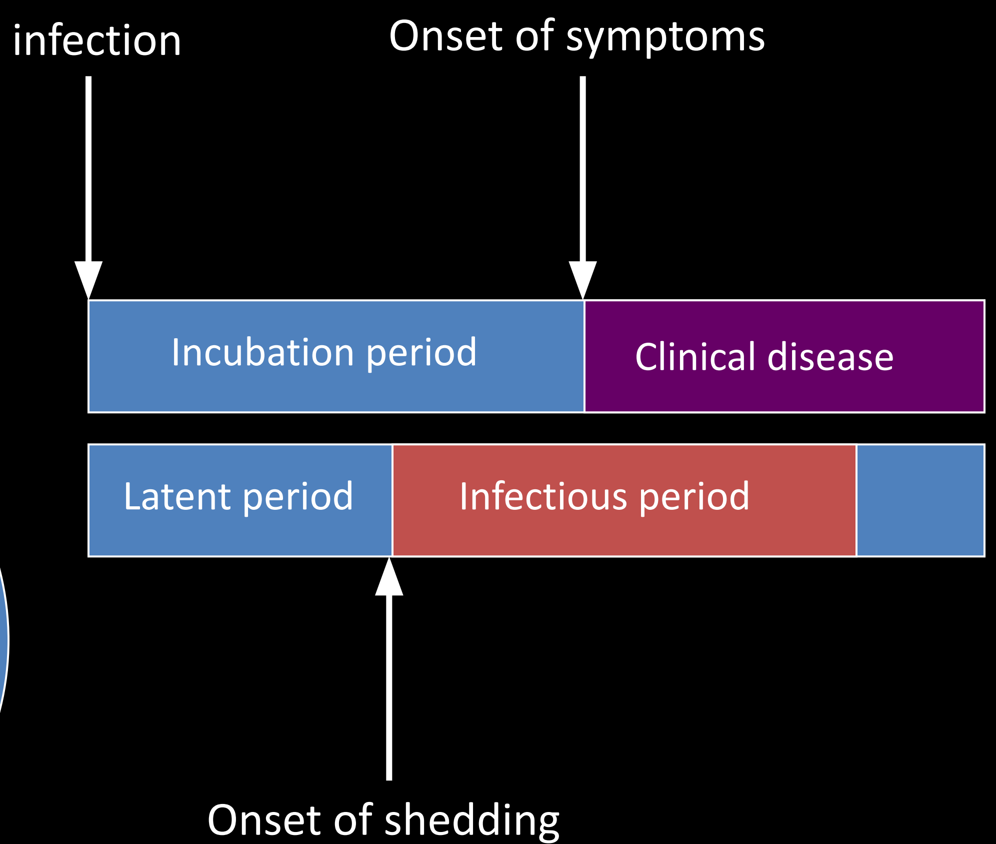


A slightly more realistic model

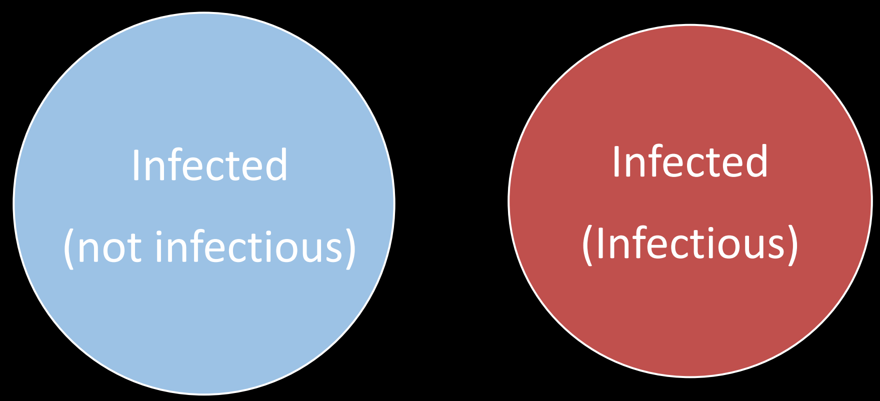
Infectivity = 1

(everyone exposed becomes infected)



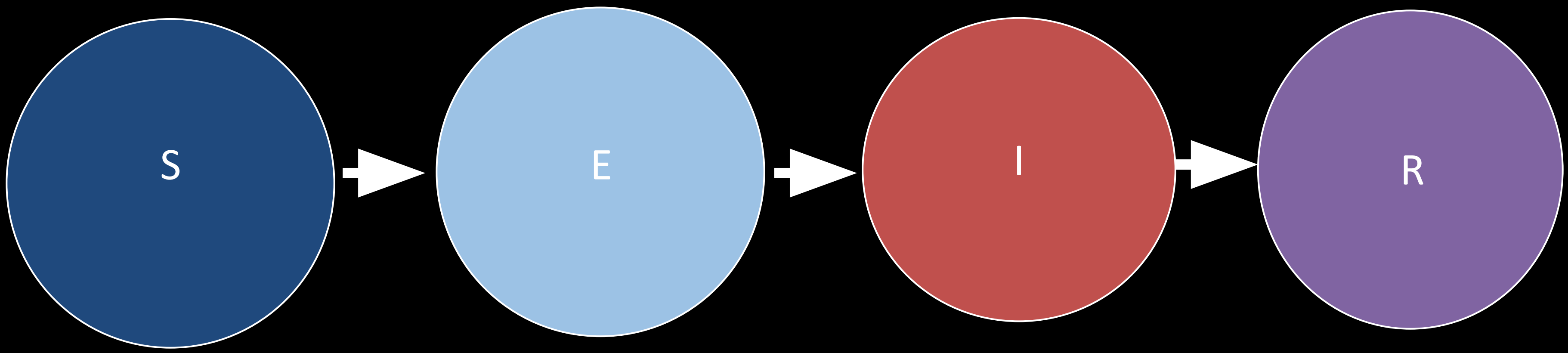


A slightly more realistic model

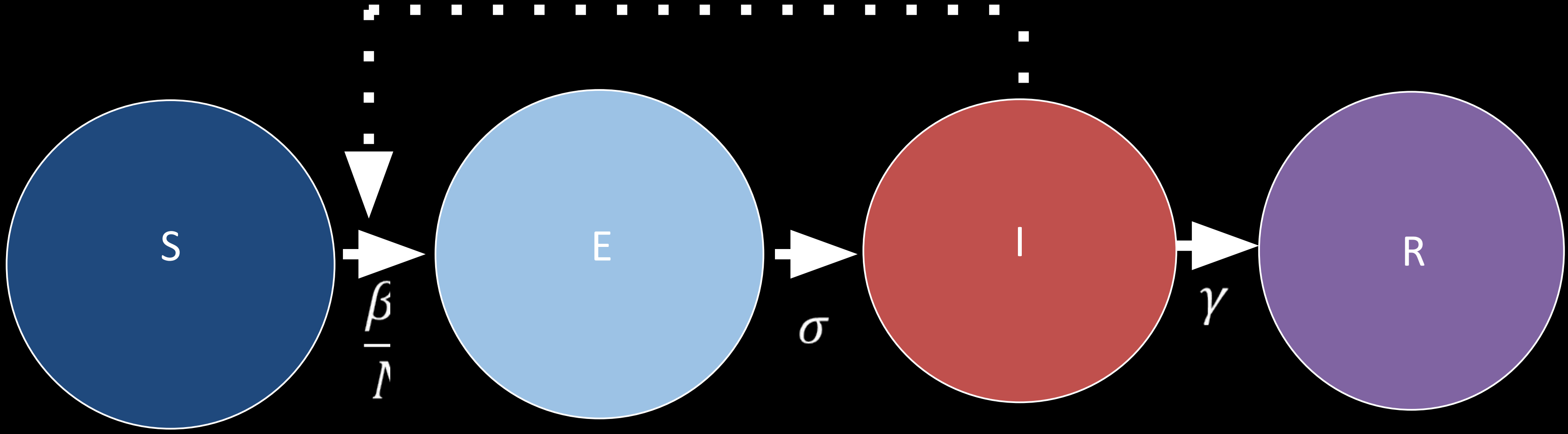


A slightly more realistic model

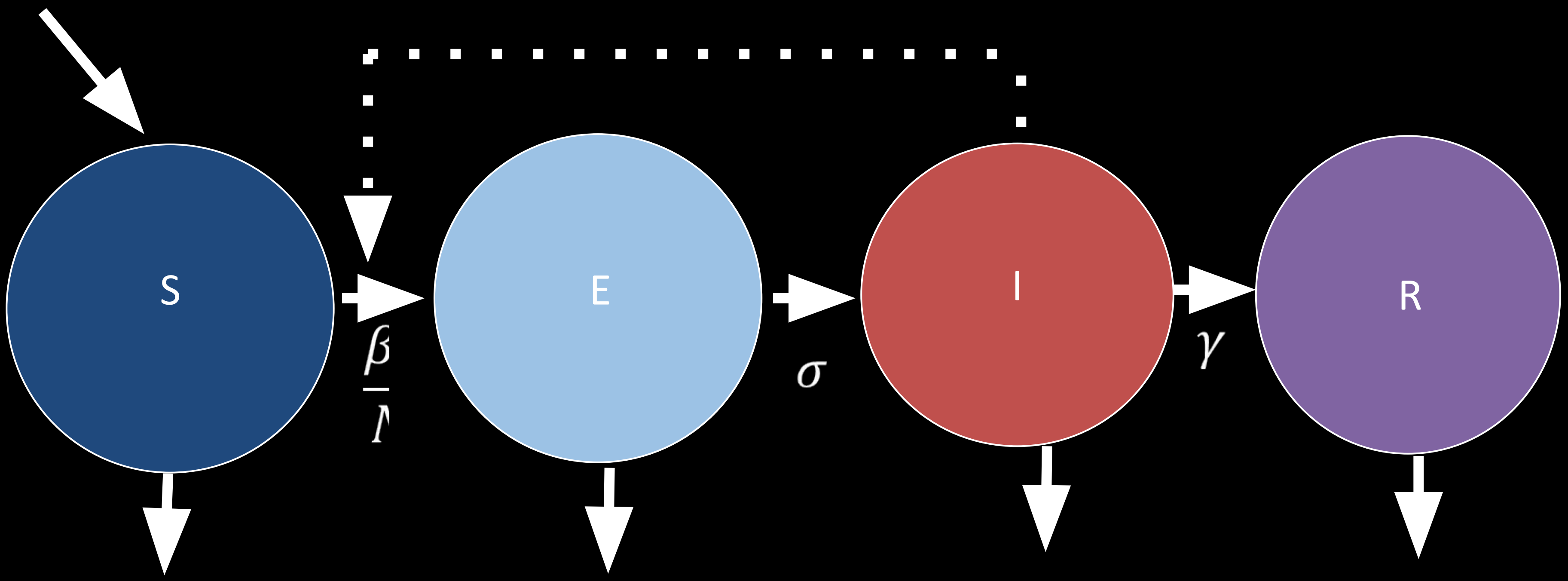
SEIR Model



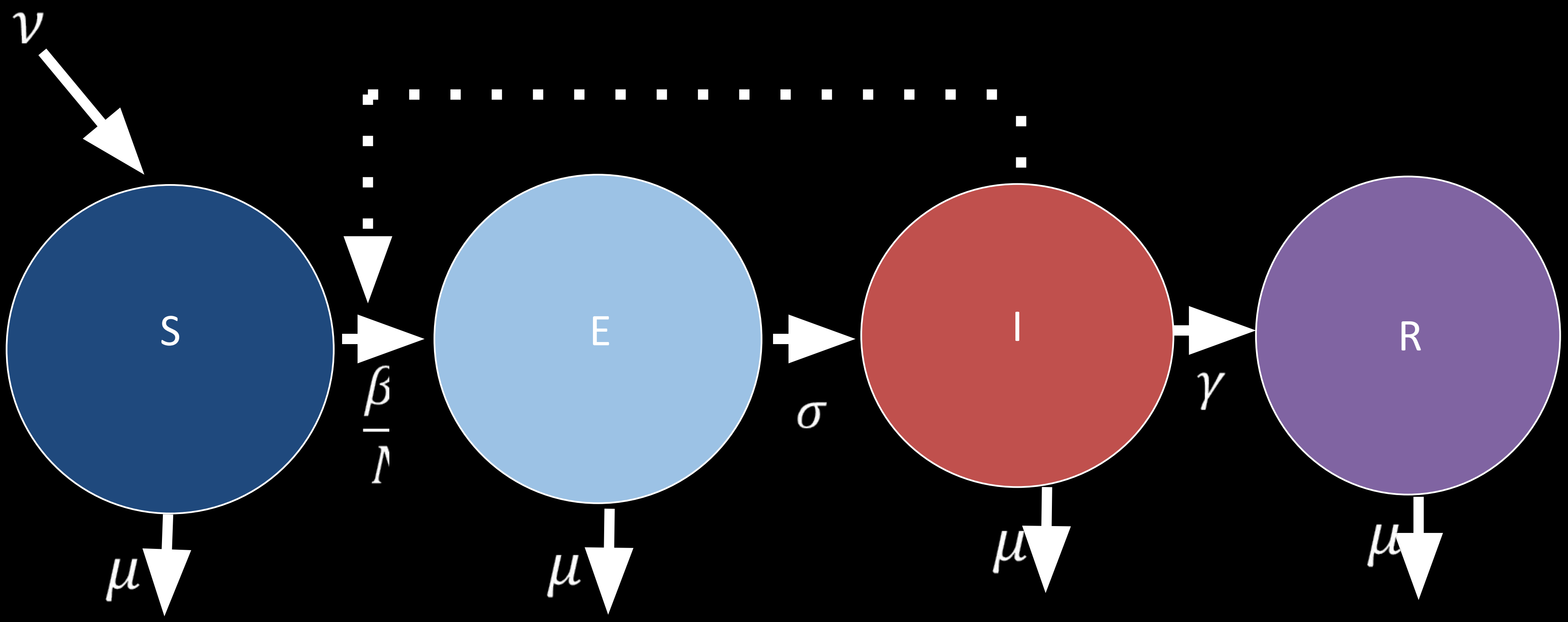
SEIR Model



SEIR Model



An extremely simple view of the world



SEIR Model

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

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

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

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

ν	birth rate
μ	mortality rate
σ	1/latent period
γ	1/ infectious period
β	transmission coefficient

SEIR Model

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

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

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

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

Assume constant population size

$$\nu = \mu N$$

SEIR Model

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

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

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

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

$R_0 =$

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

SEIR Model

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

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

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

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

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

SEIR Model

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

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

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

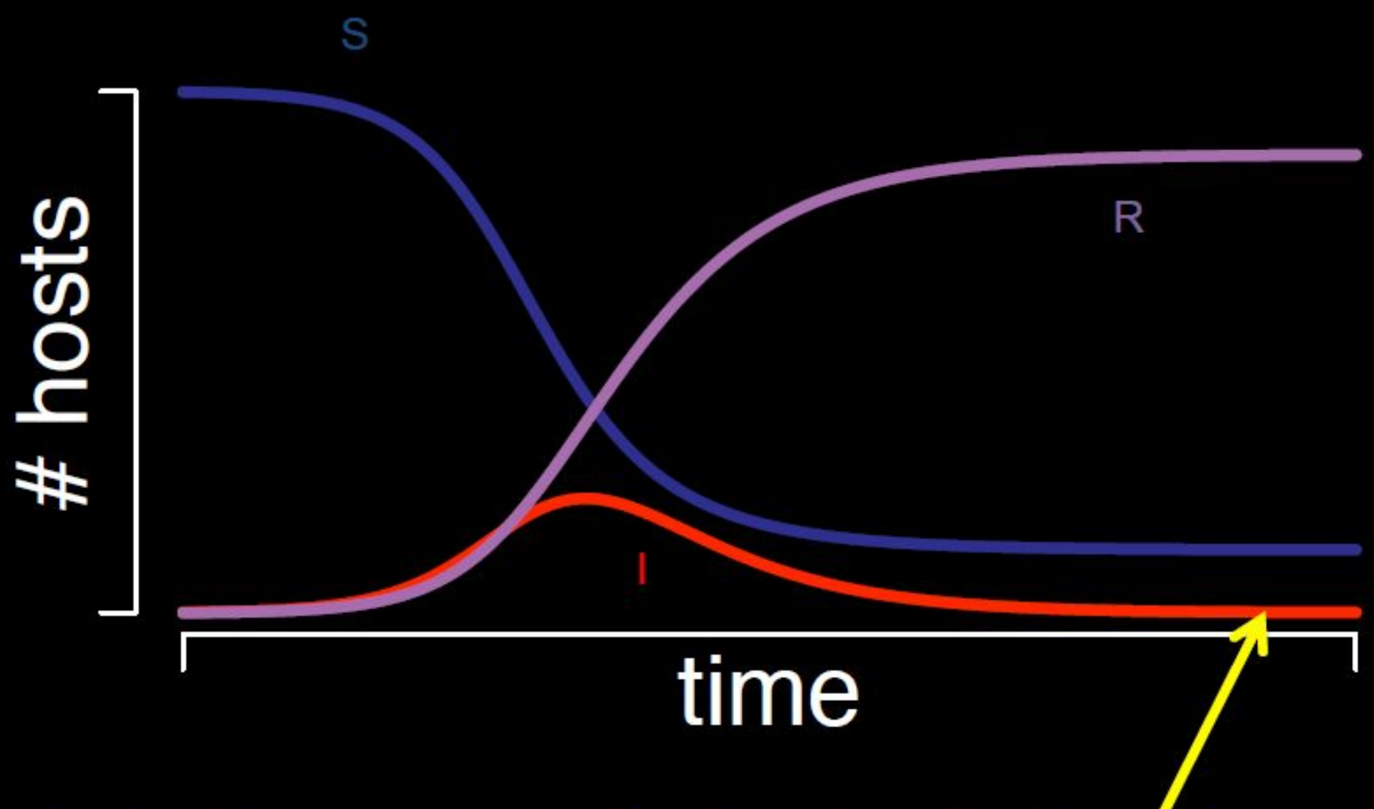
$$\frac{dR}{dt} = \gamma I - \mu R$$

Equilibria…

Disease free equilibrium

Endemic equilibrium

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 (≈) threshold population size at which a disease can persist.

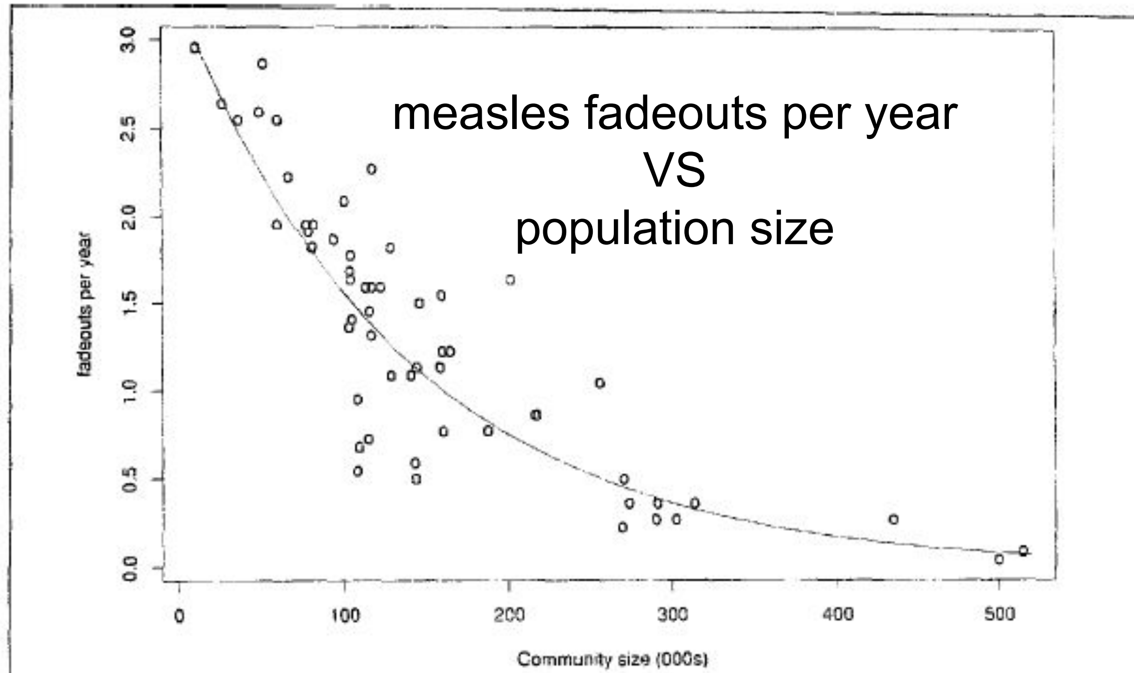
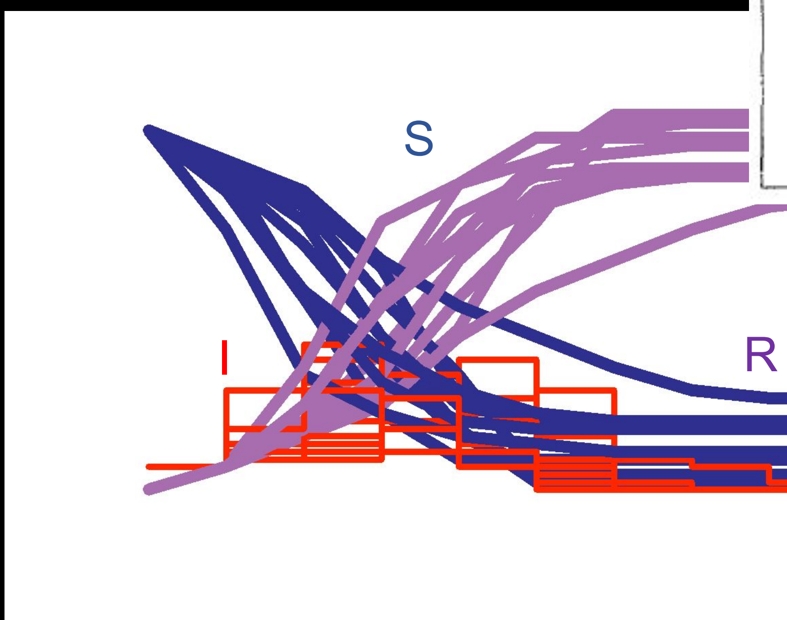


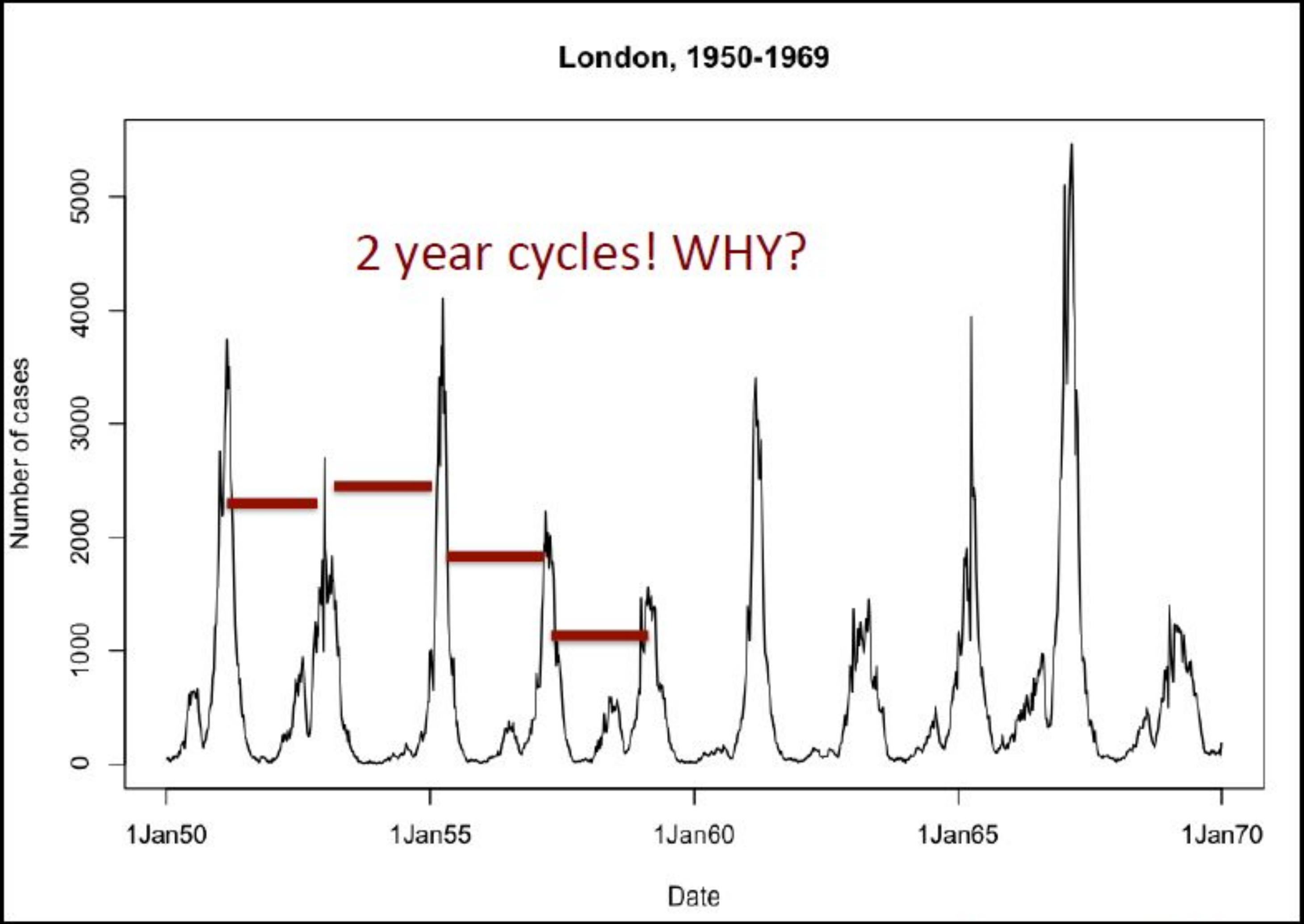
Fig. 1. Persistence of measles in 60 towns and cities in England and Wales in the pre-vaccination era (1944–67), as a function of population size in 1960. Persistence is measured inversely by the proportion of weeks with 'fade-outs' (three or more weeks without infection, to allow for under-notification of cases[34]). The curve is a simple least squares exponential fit. The figure clearly shows the CCS – a population threshold of 300–500 000 – above which measles persists.

Grenfell and Harwood, 1997



Stochasticity in epidemic troughs causes disease fadeout in small populations.

What accounts for epidemic cycles?



Earn et al. 2000 *Science*

Seasonal SEIR Model

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

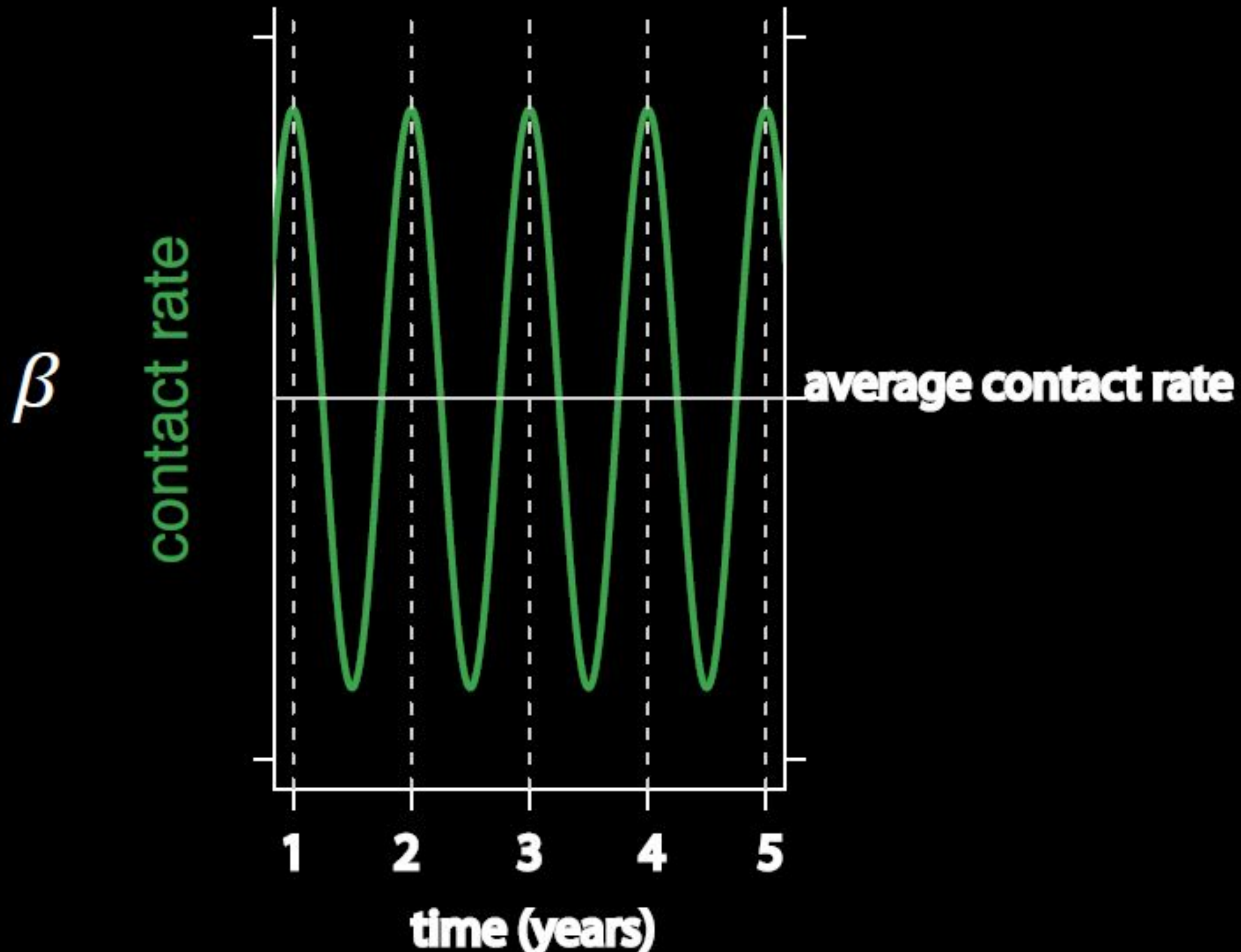
$$\frac{dE}{dt} = \frac{\beta SI}{N} - \sigma E - \mu E$$

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

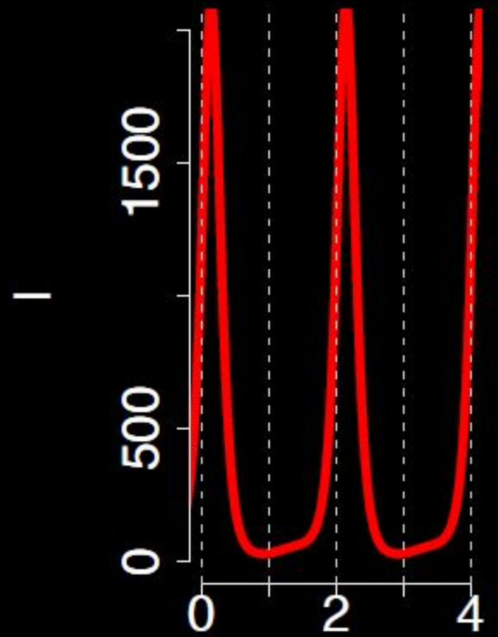
$$\frac{dR}{dt} = \gamma I - \mu R$$

$\nu = \mu N$	individuals/year
$\mu = 0.02$	years^{-1}
$\sigma = 1/8$	days^{-1}
$\gamma = 1/5$	days^{-1}
β	Seasonal (school terms)

Seasonal SEIR Model

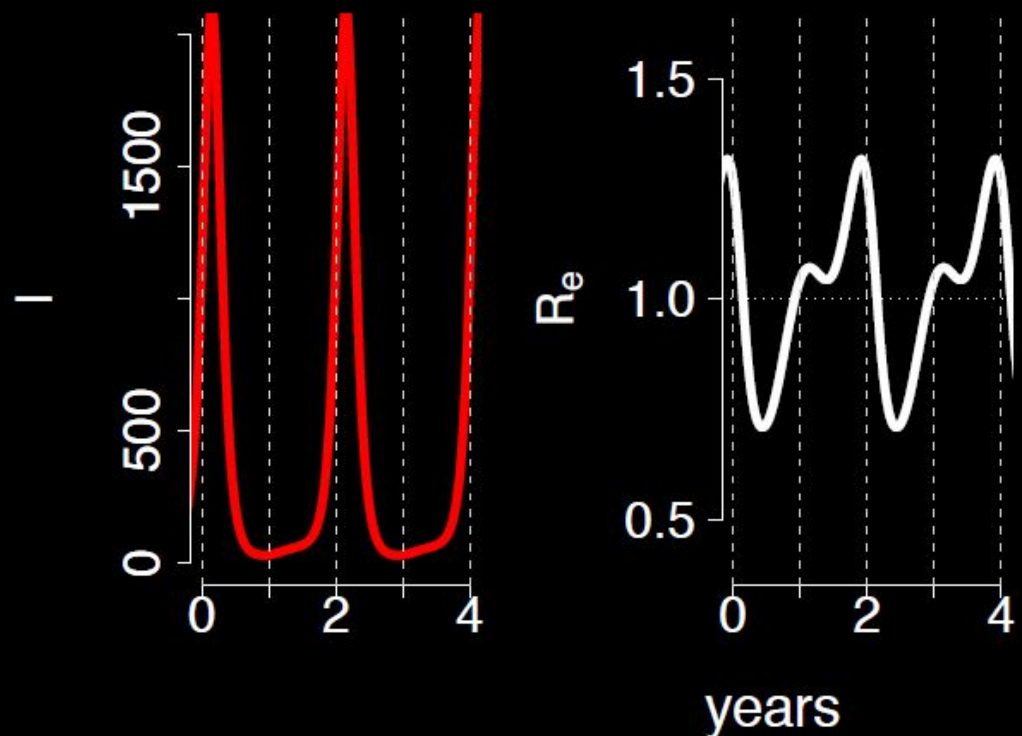


Susceptible Replenishment & Periodicity



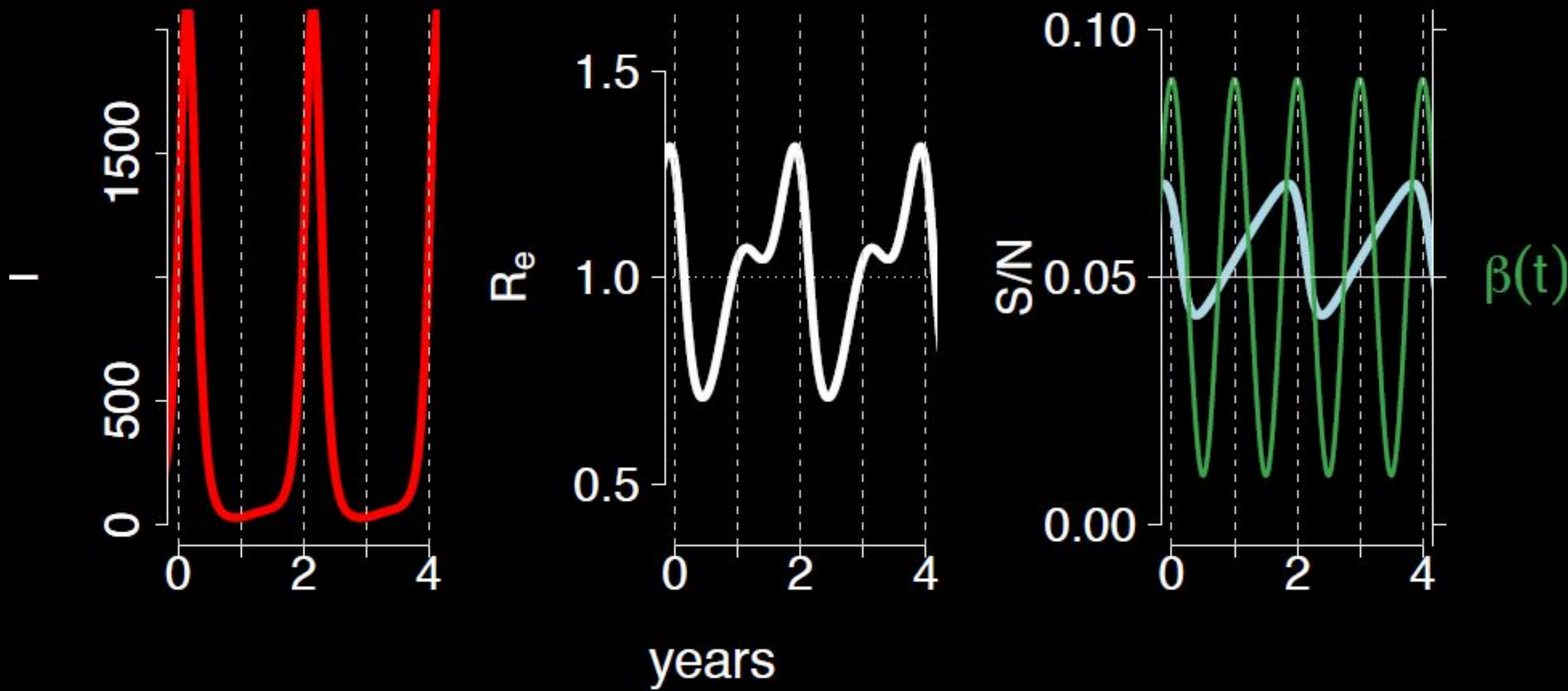
Life Expectancy of 40 years

Susceptible Replenishment & Periodicity



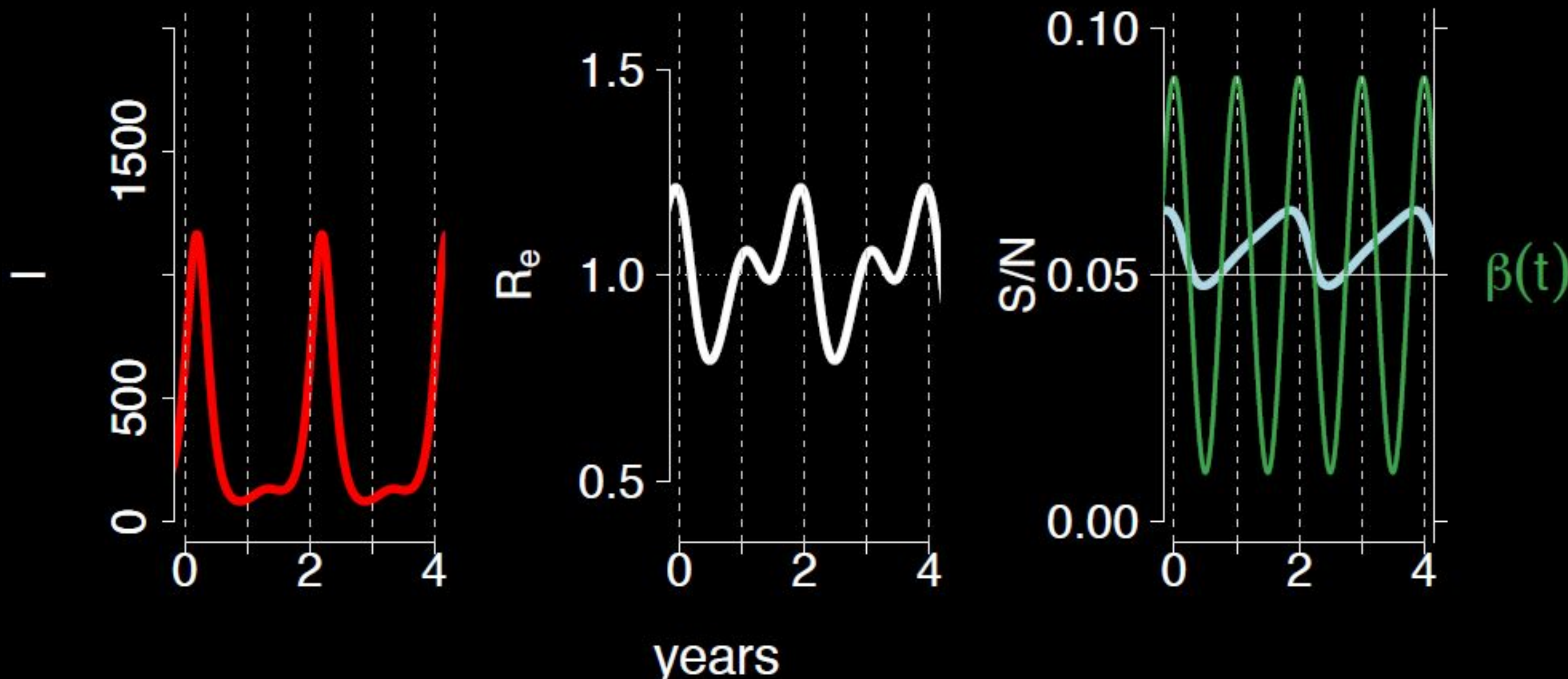
Life Expectancy of 40 years

Susceptible Replenishment & Periodicity



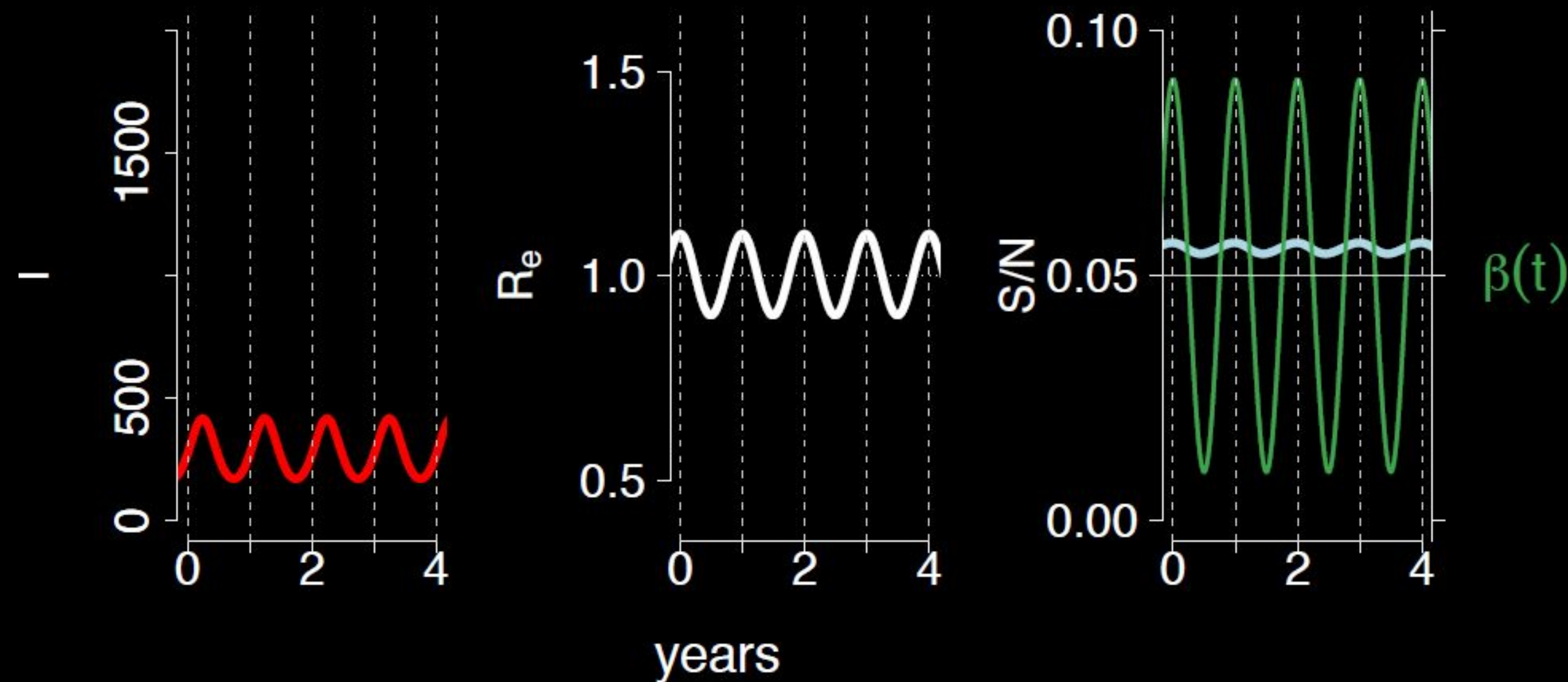
Life Expectancy of 40 years

Susceptible Replenishment & Periodicity



Life Expectancy of 50 years

Susceptible Replenishment & Periodicity



Life Expectancy of 60 years

Summary

- Latent/infectious periods drive epidemic time scale
- $R_0 = 1$ is the threshold for invasion
- $(R_0 - 1)/R_0$ is the proportion to vaccinate for elimination
- Periodicity is driven by the interaction between susceptible replenishment and seasonal contact

Bellan SE and Pulliam JRC. "Introduction to Infectious Disease Dynamics" Clinic on the Meaningful Modeling of Epidemiological Data. DOI:10.6084/m9.figshare.5043139.

For further information or modifiable slides please contact figshare@ici3d.org.

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