

Digital epidemiology

Lesson 6

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Mathematical modeling of epidemics

Modeling



abstraction,
conceptualization

reality

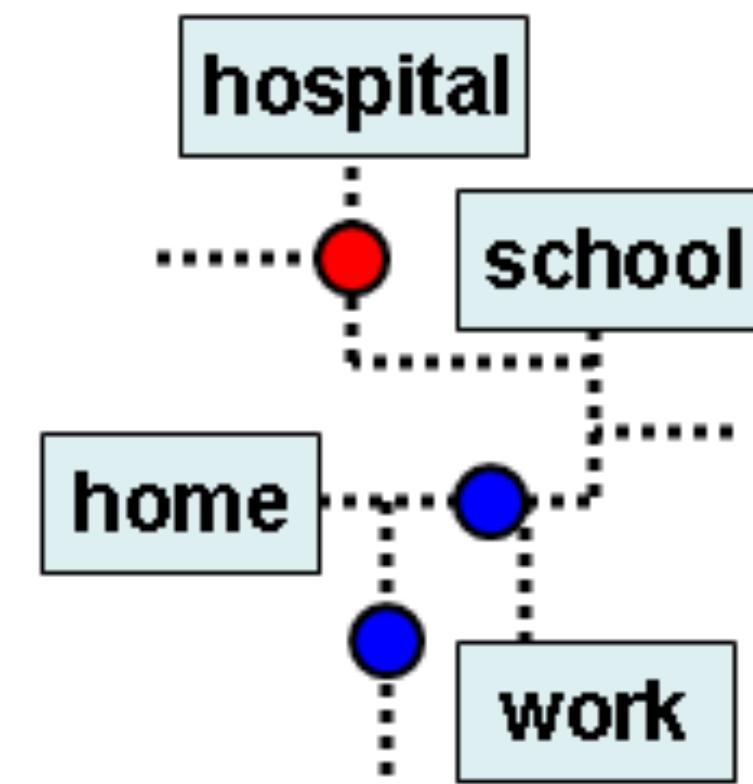
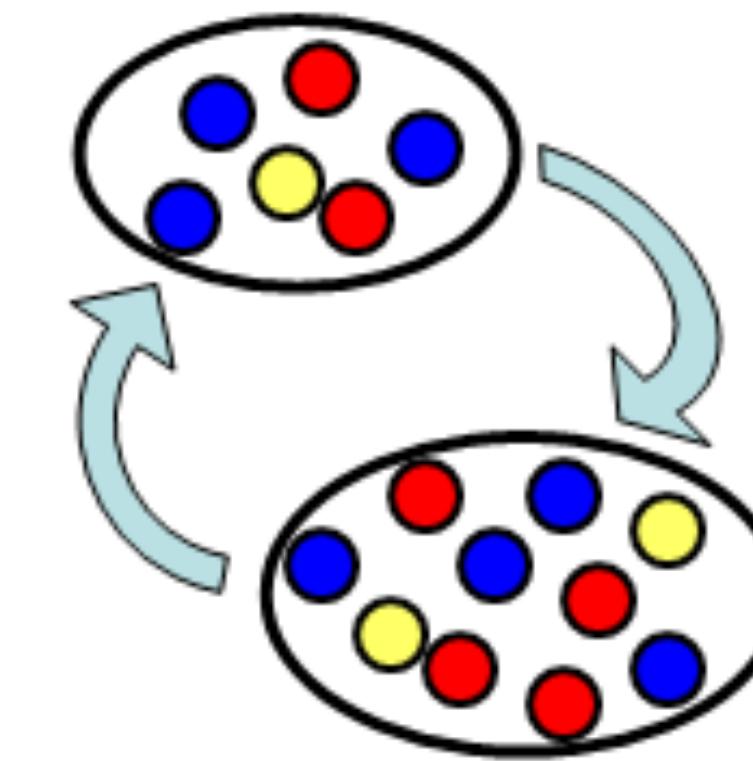
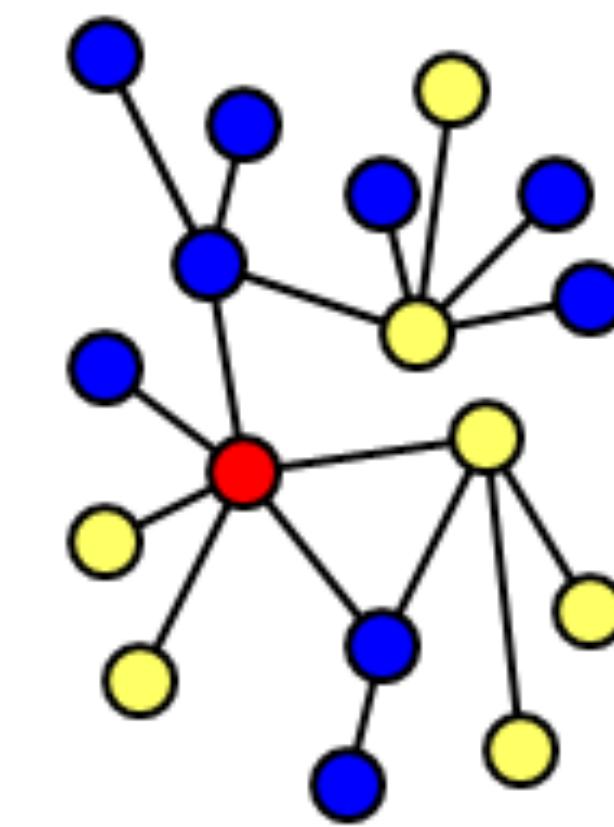
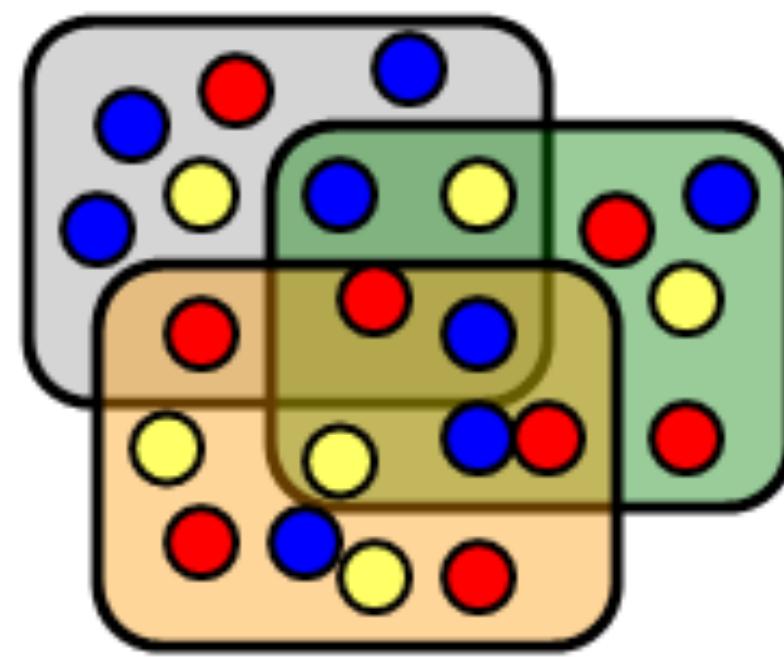
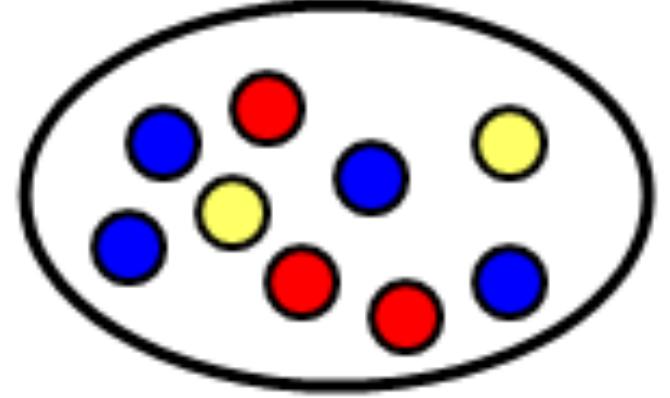


“

All models are wrong.
Some are useful.

-George E. P. Box

Models



**Homogeneous
mixing**

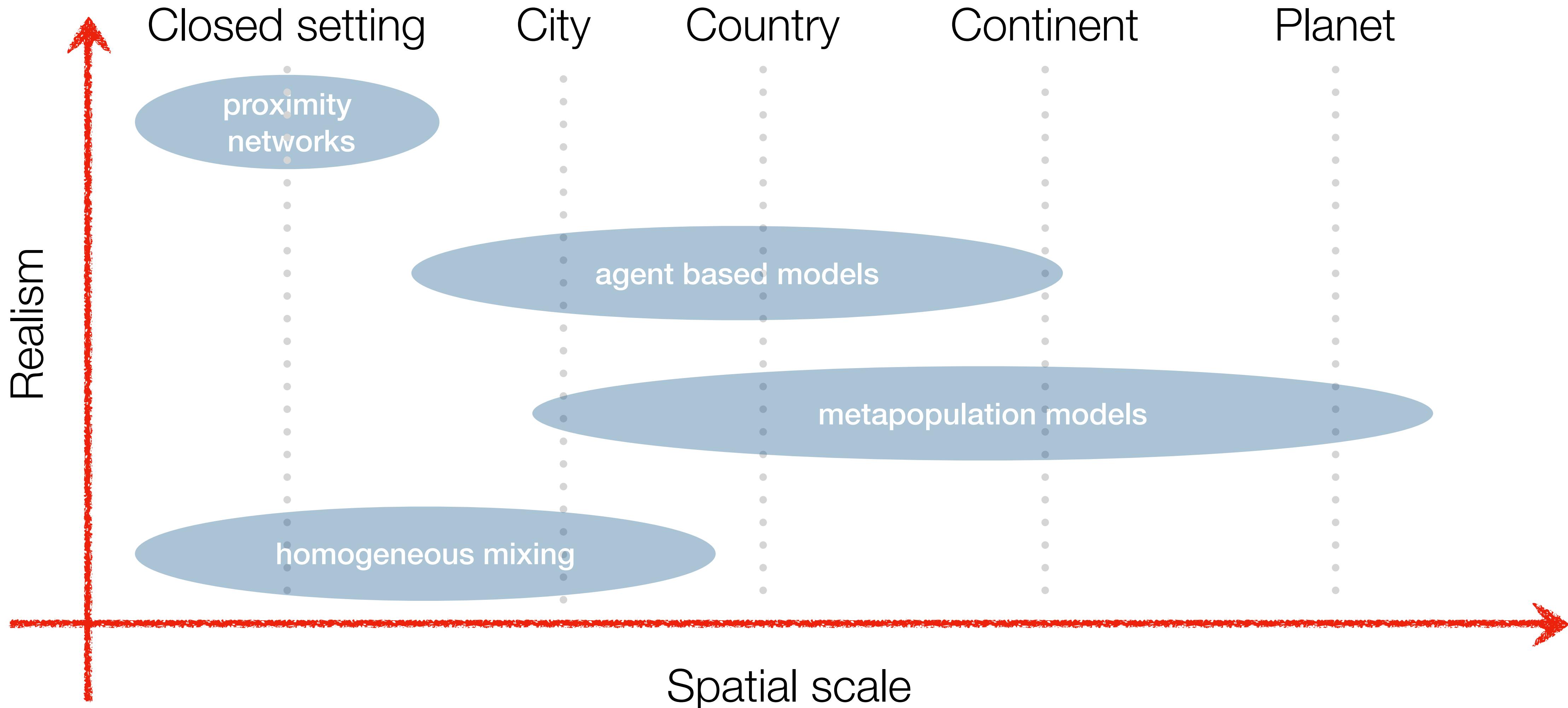
Social structure

**Contact network
models**

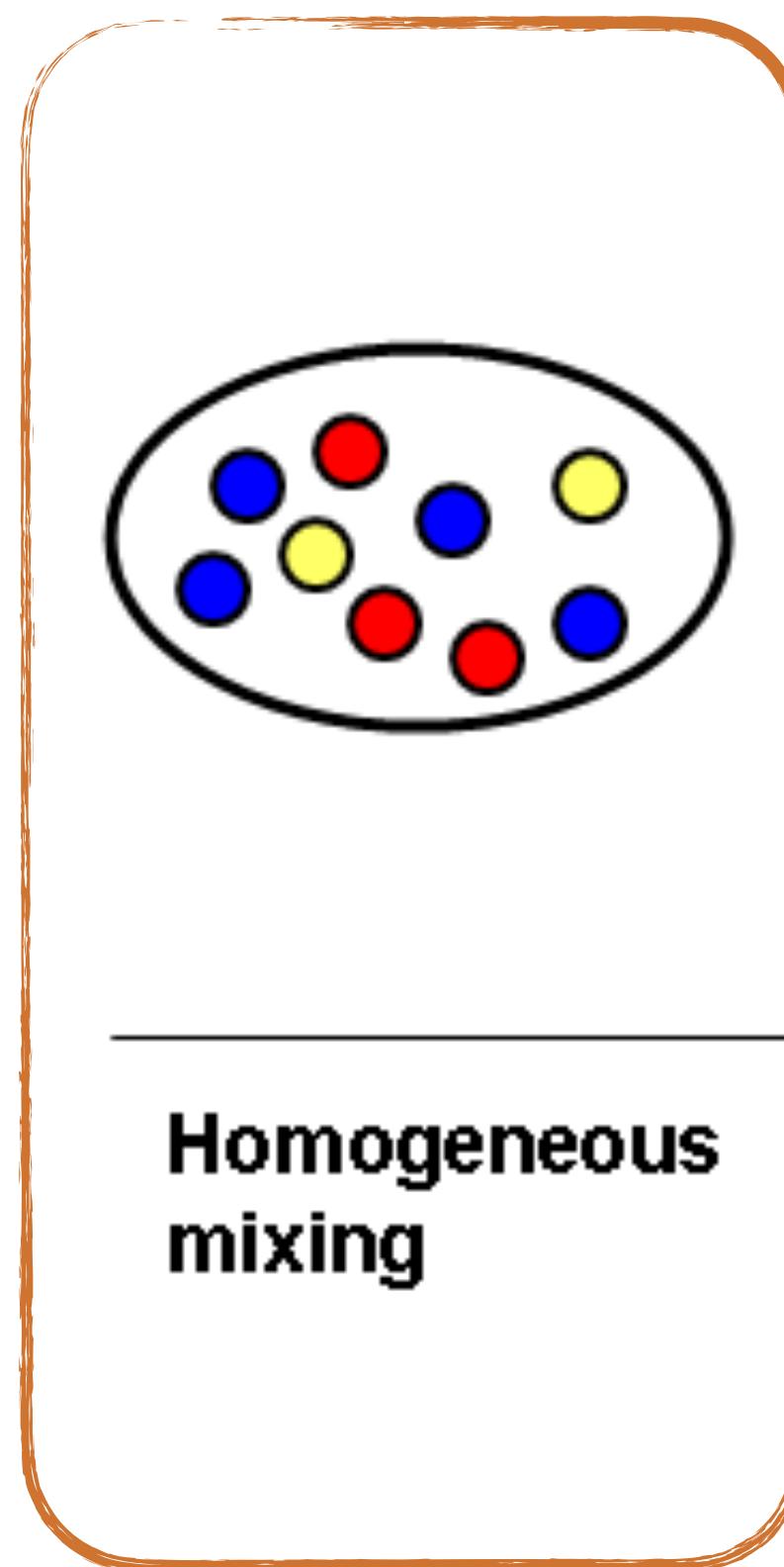
**Multi-scale
models**

**Agent Based
models**

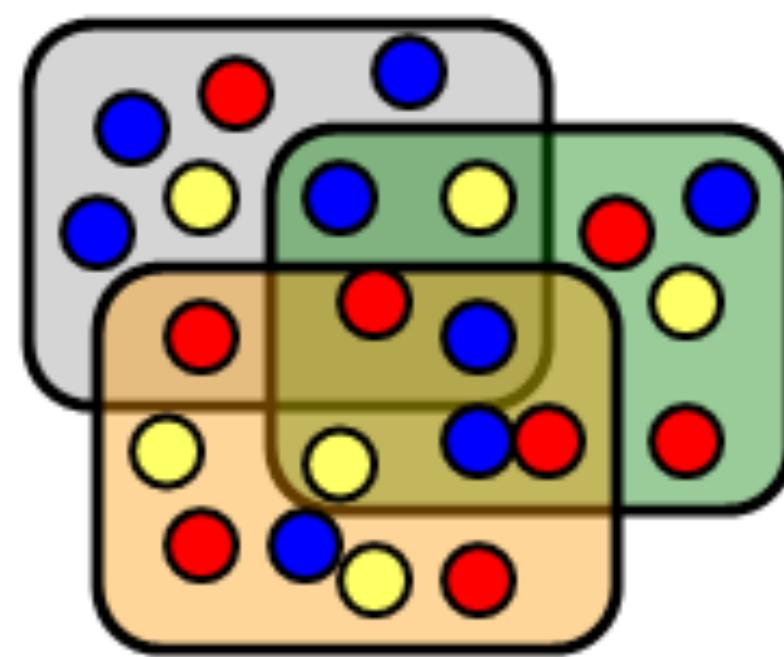
Spatial scales



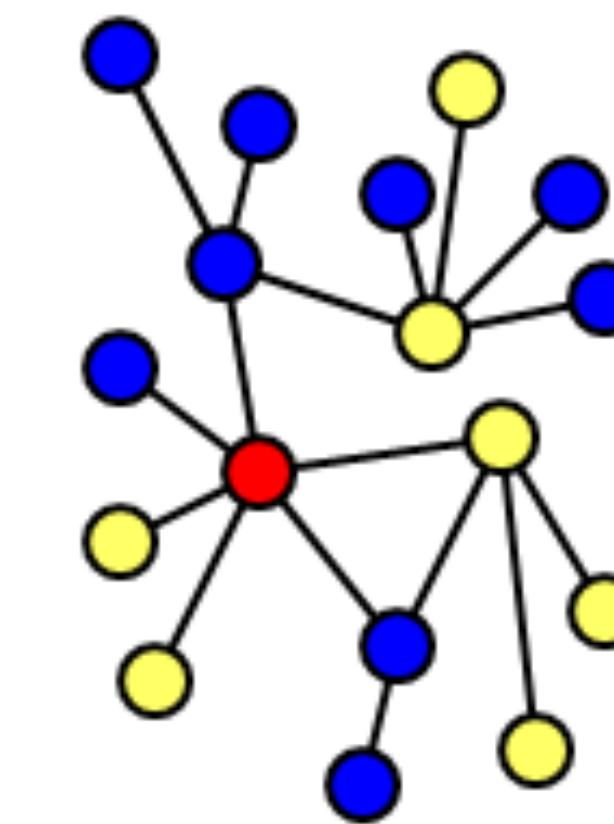
Models



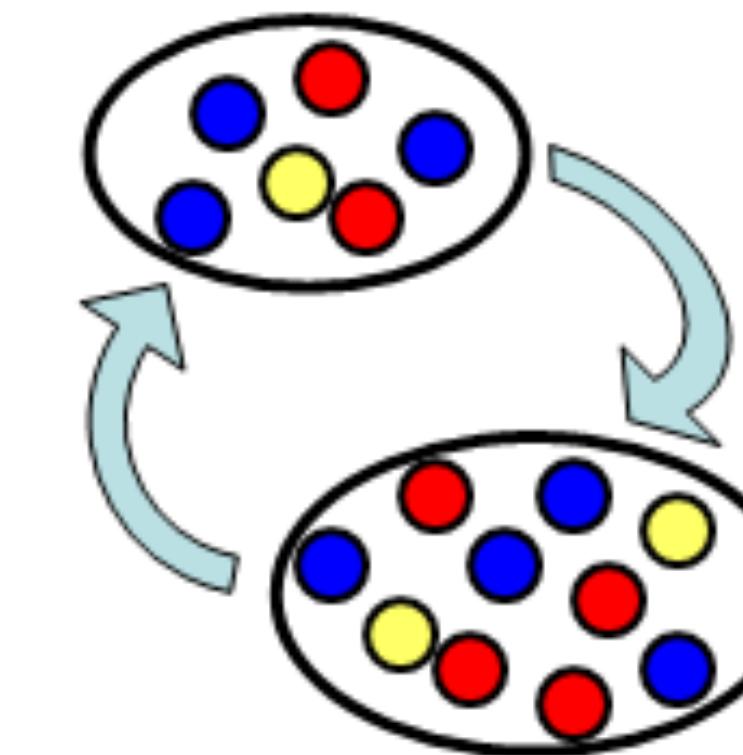
Homogeneous
mixing



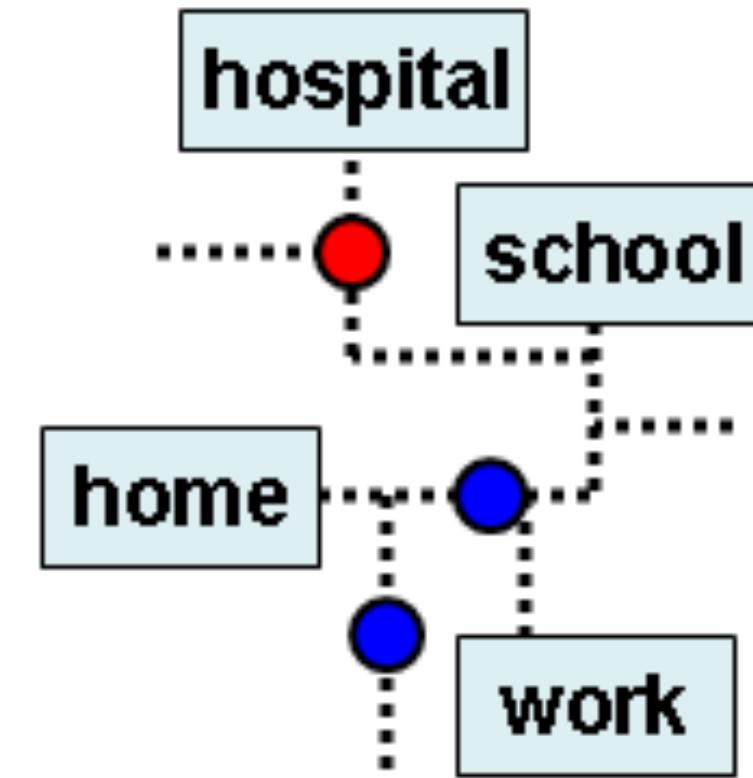
Social structure



Contact network
models

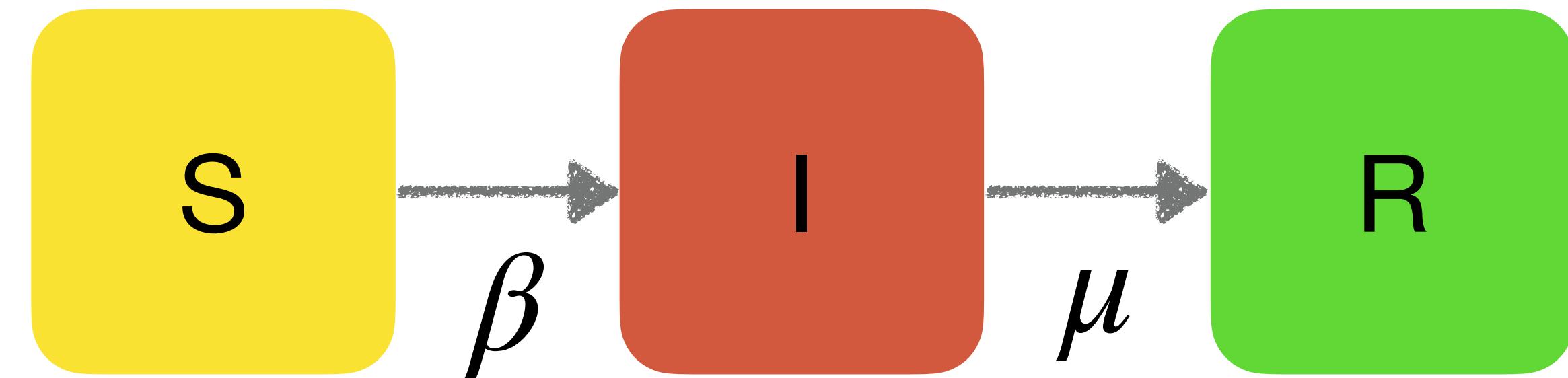


Multi-scale
models



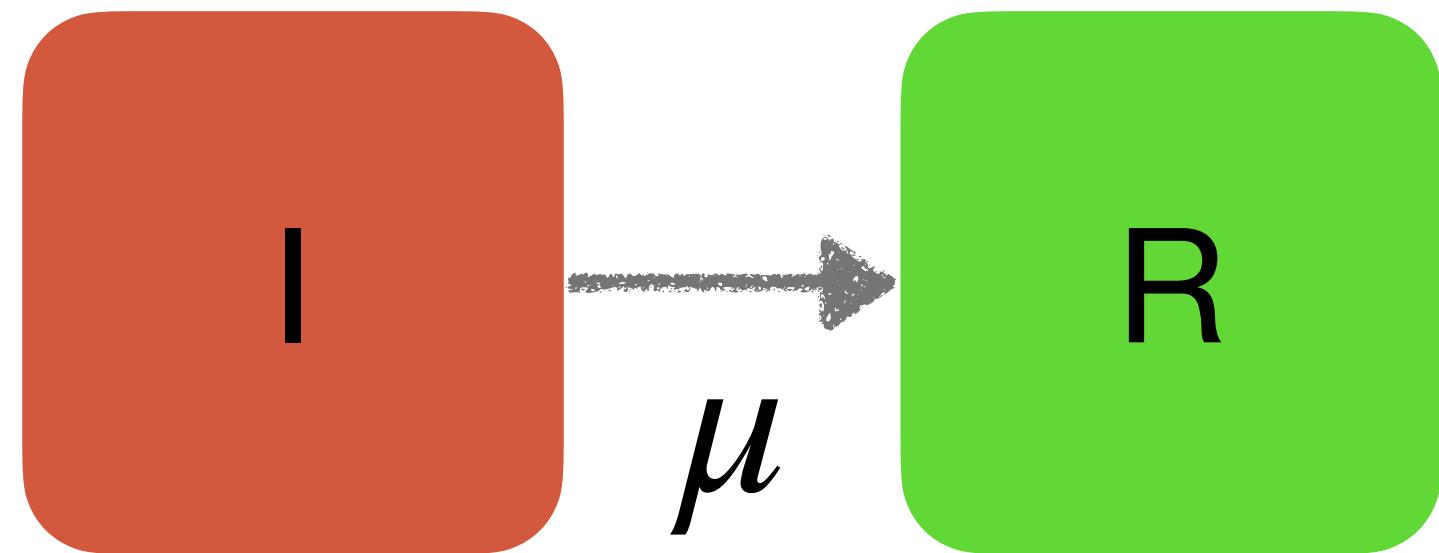
Agent Based
models

The SIR model



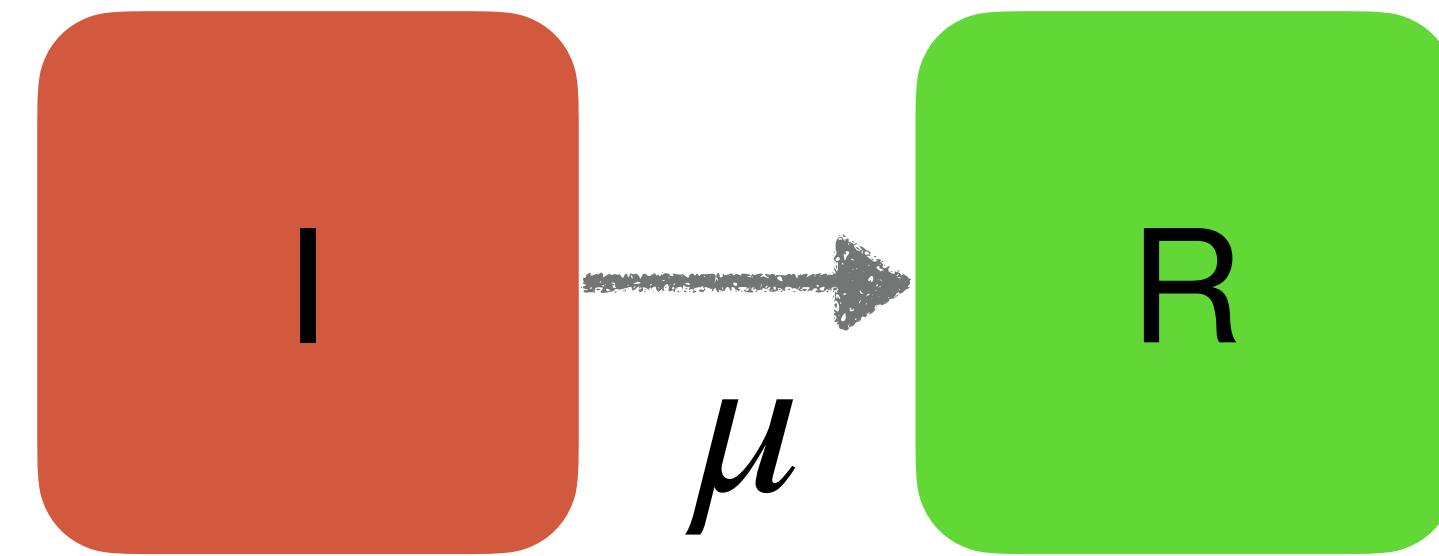
- Population is closed and constant (no demographics) $S + I + R = N$
- Population is “well mixed” (no heterogeneities)
- **Recovery** takes place at constant rate: μ
- **Transmission** rate is constant: β

Recovery transition



- The transition from I to R is **spontaneous**. It does not depend on other compartments.
- The model assumes a constant probability of recovery in the time unit, μ
- In a discrete-time formulation, the time an individual will spend on average in the infectious compartment, the **mean infectious period**, is then equal to μ^{-1} time steps.

Recovery transition



- In a continuous-time formulation, μ is a rate

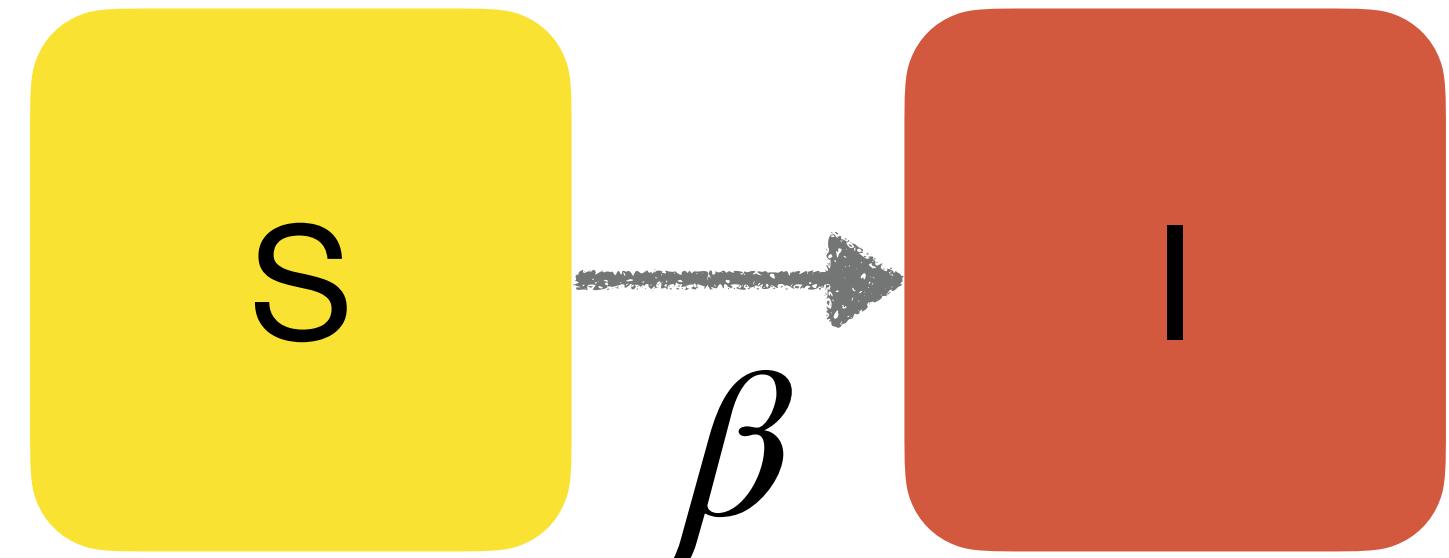
$$P_{inf}(\tau) = \mu e^{-\mu\tau}$$

Probability an individual spends τ in the infectious compartment

$$\langle \tau \rangle = \mu^{-1}$$

Average infectious period

Transmission



- **Homogeneous mixing:** individuals interact at random with each other.
- We define the *force of infection* as the probability that an individual S may contract the infection in a single time step

$$\lambda = \beta \frac{I}{N}$$

Transmission

$$\lambda = \beta \frac{I}{N}$$

frequency dependent

$$\beta = \hat{\beta} \kappa \longrightarrow \text{number of contacts}$$

transmission per contact

$$\Delta S = \lambda S = \beta \frac{SI}{N} \Delta t$$

Transmission

$$\lambda' = \beta'I$$

density dependent

$$\beta' = \hat{\beta}'k \longrightarrow \text{number of contacts}$$

transmission per contact

$$\Delta S = \lambda' S = \beta'I\Delta t$$

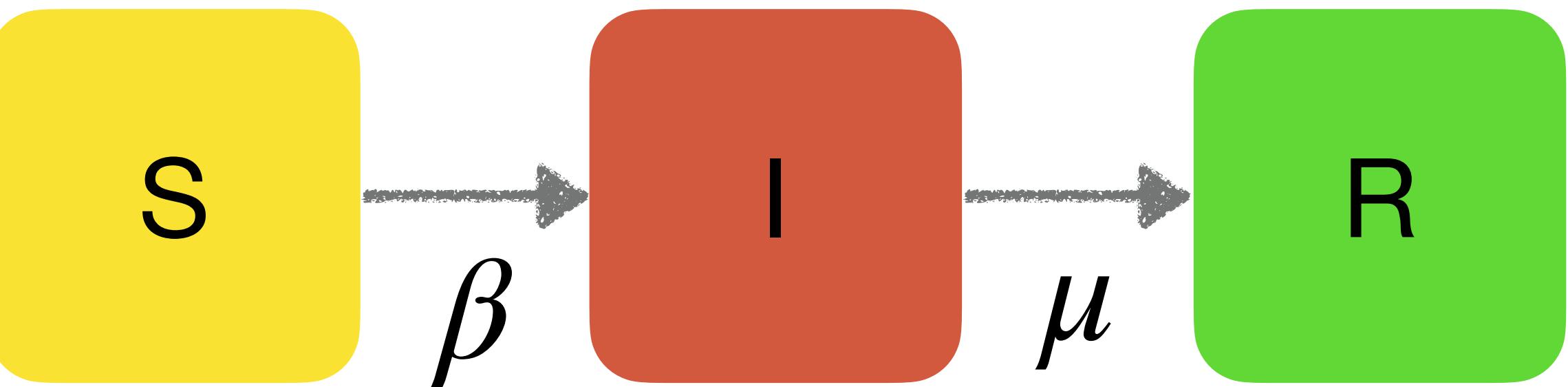
The SIR model

$$S(t + \Delta t) - S(t) = -\beta \frac{SI}{N} \Delta t$$

$$I(t + \Delta t) - I(t) = \beta \frac{SI}{N} \Delta t - \mu I \Delta t$$

frequency dependent

$$R(t + \Delta t) - R(t) = \mu I \Delta t$$



The SIR model

$$\left\{ \begin{array}{l} \frac{dS}{dt} = -\beta \frac{SI}{N} \\ \frac{dI}{dt} = \beta \frac{SI}{N} - \mu I \\ \frac{dR}{dt} = \mu I \end{array} \right.$$

- No closed solution
- We can solve the system in the **early stage approximation**
- Two fundamental results from the model:
 1. The **threshold phenomenon**
 2. The **asymptotic state**, i.e. why the epidemic dies out

Epidemic threshold

$$\left\{ \begin{array}{l} \frac{dS}{dt} = -\beta \frac{SI}{N} \\ \frac{dI}{dt} = \beta \frac{SI}{N} - \mu I \\ \frac{dR}{dt} = \mu I \end{array} \right.$$

Early stage approximation

$$\boxed{\begin{aligned} t &\rightarrow 0 \\ I(0) &\ll N \\ S(0) &\simeq N \end{aligned}}$$

Epidemic threshold

Early stage approximation

$$t \rightarrow 0$$

$$I(0) \ll N$$

$$S(0) \simeq N$$

$$\frac{dI}{dt} \simeq (\beta - \mu)I$$

$$\frac{dI}{I} \simeq (\beta - \mu)dt$$

Epidemic threshold

Early stage approximation

$$t \rightarrow 0$$

$$I(0) \ll N$$

$$S(0) \simeq N$$

$$I(t) \simeq I_0 e^{(\beta - \mu)t}$$

$$\beta - \mu > 0$$

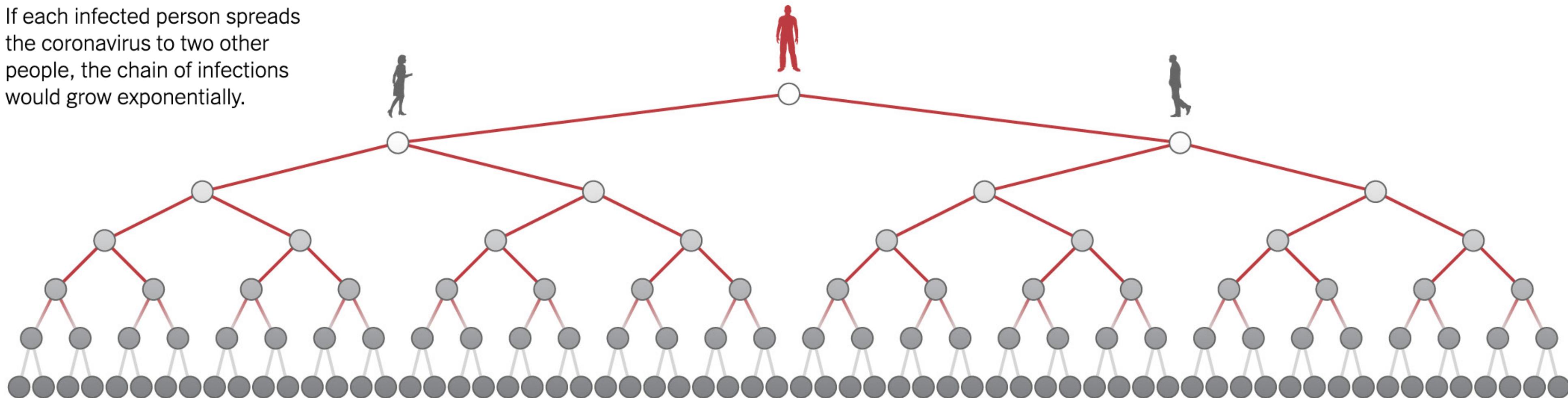
$$R_0 = \frac{\beta}{\mu} > 1$$

Epidemic threshold

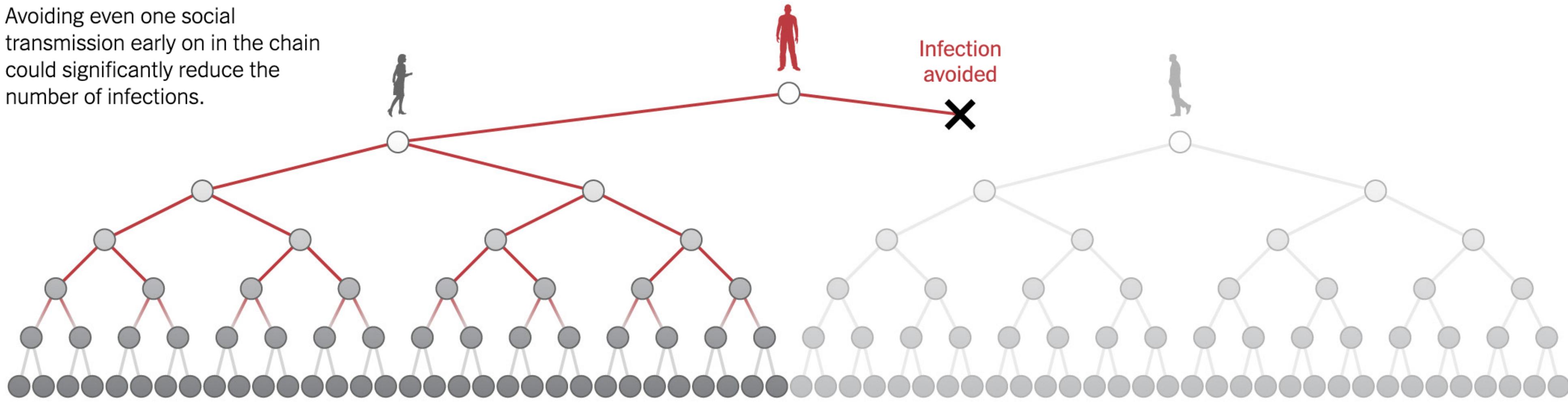
- The **basic reproductive number** is the average number of individuals that are infected by an infectious one during his infectious period, in a fully susceptible population.
- An epidemic outbreak **can occur only** if the basic reproductive number is **larger than 1**.

Epidemic threshold

If each infected person spreads the coronavirus to two other people, the chain of infections would grow exponentially.



Avoiding even one social transmission early on in the chain could significantly reduce the number of infections.



Epidemic threshold

TABLE 2.1.

Some Estimated Basic Reproductive Ratios.

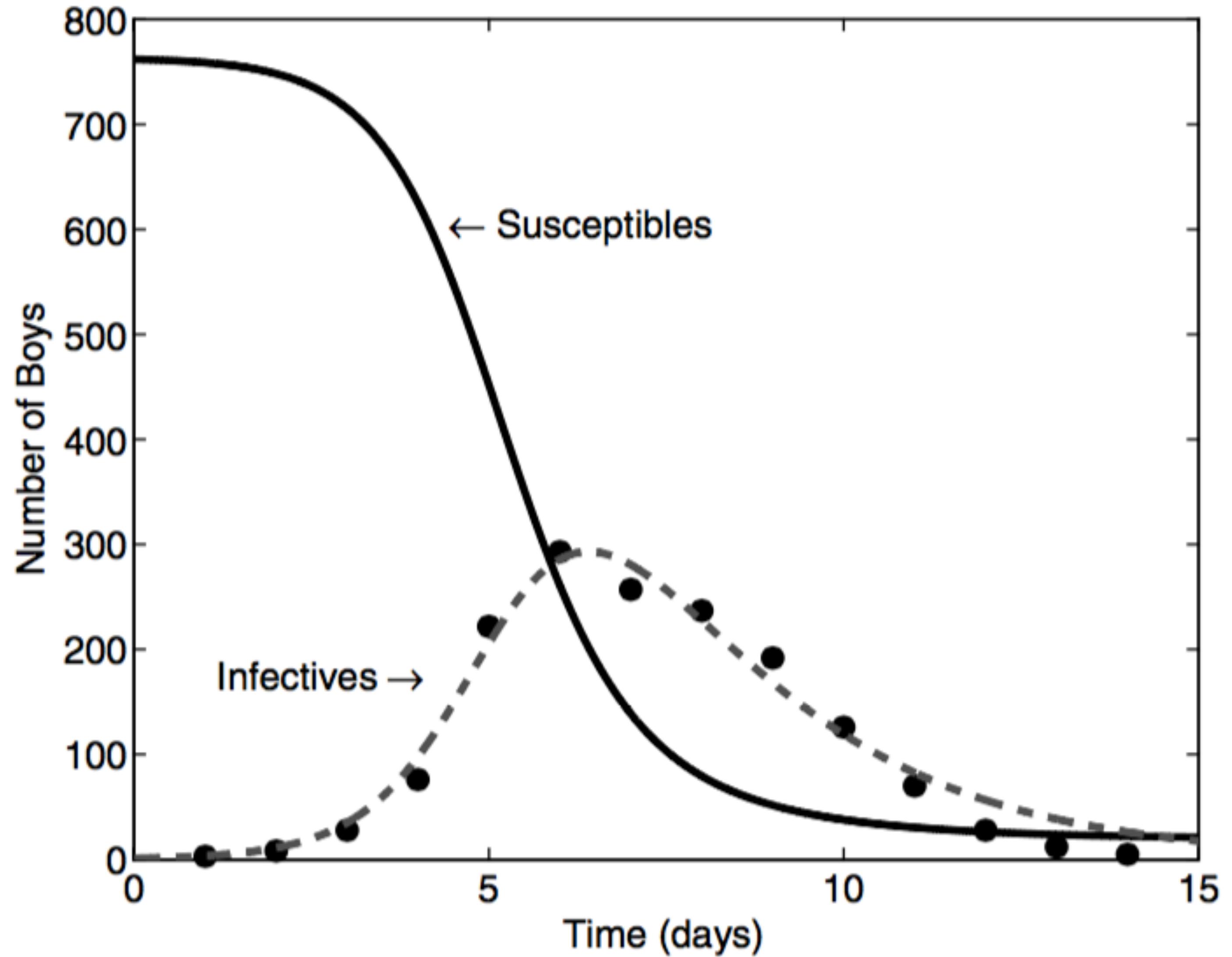
<i>Infectious Disease</i>	<i>Host</i>	<i>Estimated R_0</i>	<i>Reference</i>
FIV	Domestic Cats	1.1–1.5	Smith (2001)
Rabies	Dogs (Kenya)	2.44	Kitala et al. (2002)
Phocine Distemper	Seals	2–3	Swinton et al. (1998)
Tuberculosis	Cattle	2.6	Goodchild and Clifton-Hadley (2001)
Influenza	Humans	3–4	Murray (1989)
Foot-and-Mouth Disease	Livestock farms (UK)	3.5–4.5	Ferguson et al. (2001b)
Smallpox	Humans	3.5–6	Gani and Leach (2001)
Rubella	Humans (UK)	6–7	Anderson and May (1991)
Chickenpox	Humans (UK)	10–12	Anderson and May (1991)
Measles	Humans (UK)	16–18	Anderson and May (1982)
Whooping Cough	Humans (UK)	16–18	Anderson and May (1982)

SARS-CoV-2



SIR application

- Flu epidemic in a boarding school in England, 1978
(data from BMJ)
- Data can be fitted with SIR by ordinary least squares
- Estimated parameters:
 - $R_0 = 3.65$
 - infectious period = 2.2 days



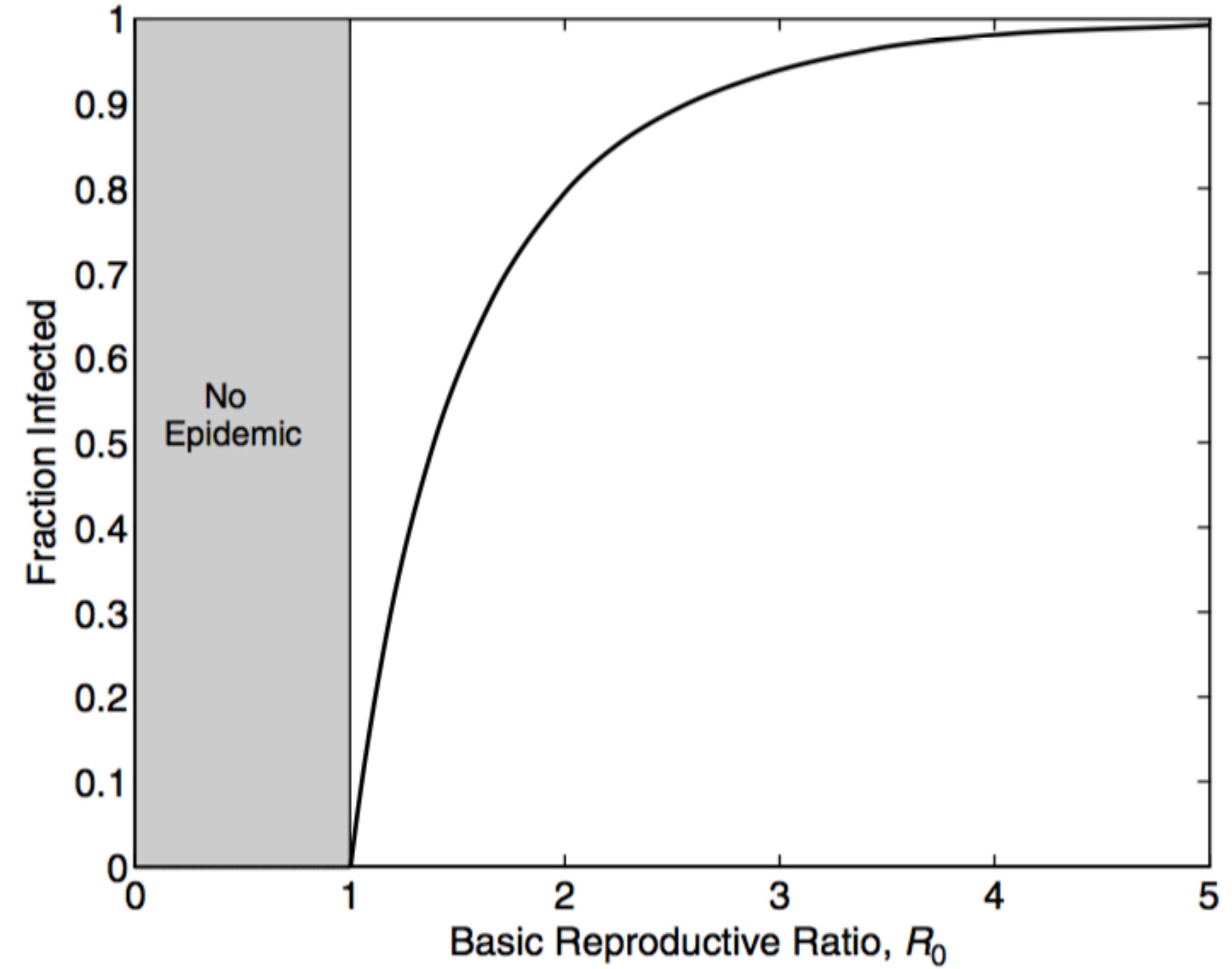
The asymptotic state

$$\left\{ \begin{array}{l} \frac{dS}{dt} = -\beta \frac{SI}{N} \\ \frac{dI}{dt} = \beta \frac{SI}{N} - \mu I \\ \frac{dR}{dt} = \mu I \end{array} \right.$$

$$\frac{dS}{dR} = -R_0 \frac{S}{N}$$

$$s(t) = s(0)e^{-R_0 r(t)}$$

The asymptotic state



$$r(\infty) = 1 - s(\infty) = 1 - s(0)e^{-R_0 r(\infty)}$$

$$1 - r(\infty) - s(0)e^{-R_0 r(\infty)} = 0$$

There is a non-zero solution for r if $R_0 > 1$.

The chain of transmission eventually breaks due to the decline in infectives, **not due to a complete lack of susceptibles**.

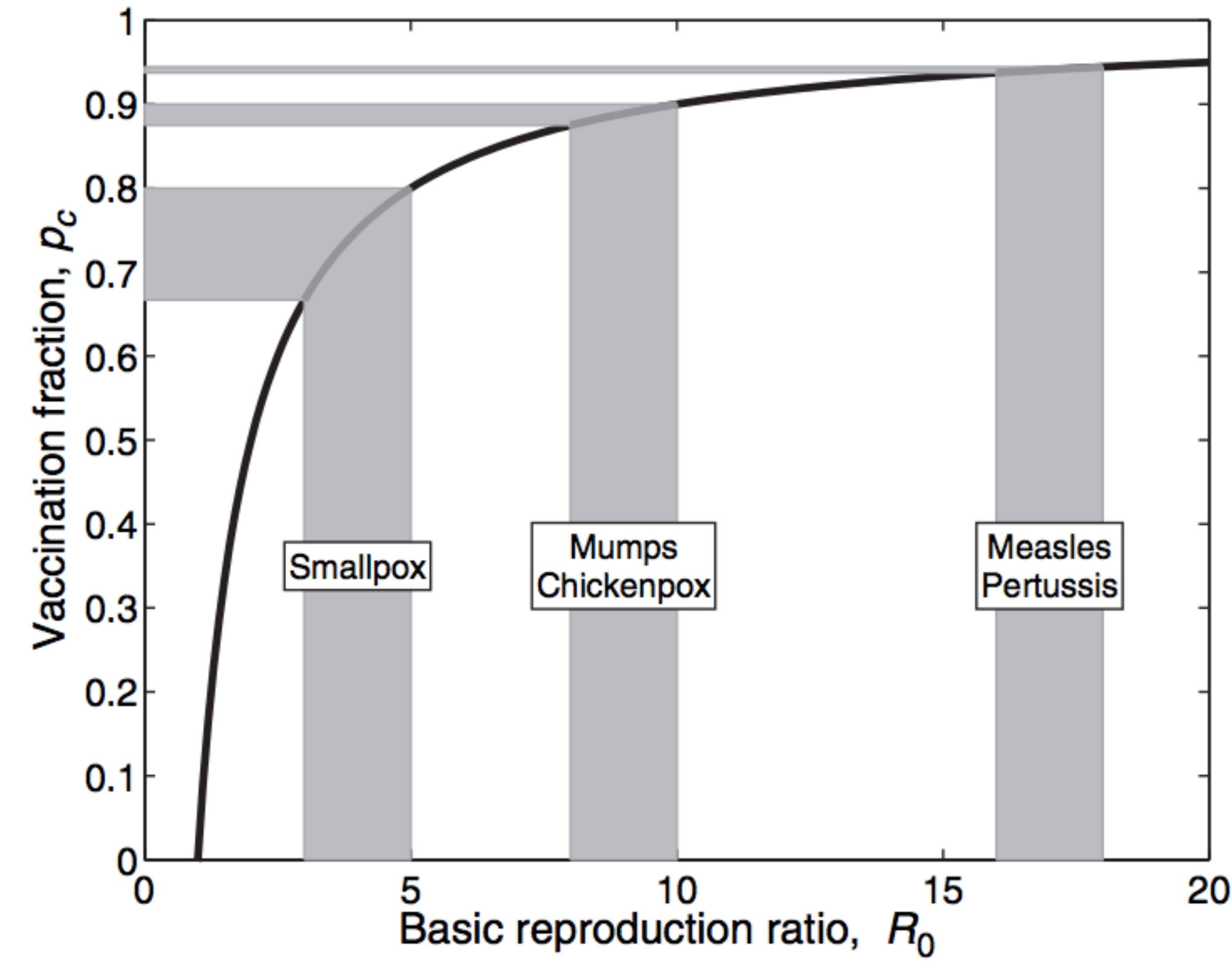
The herd immunity

- We can stop the epidemic by reducing the pool of susceptible through removal or **vaccination**.

$$\frac{dI}{dt} \simeq \beta(1 - f_V)I - \mu I$$

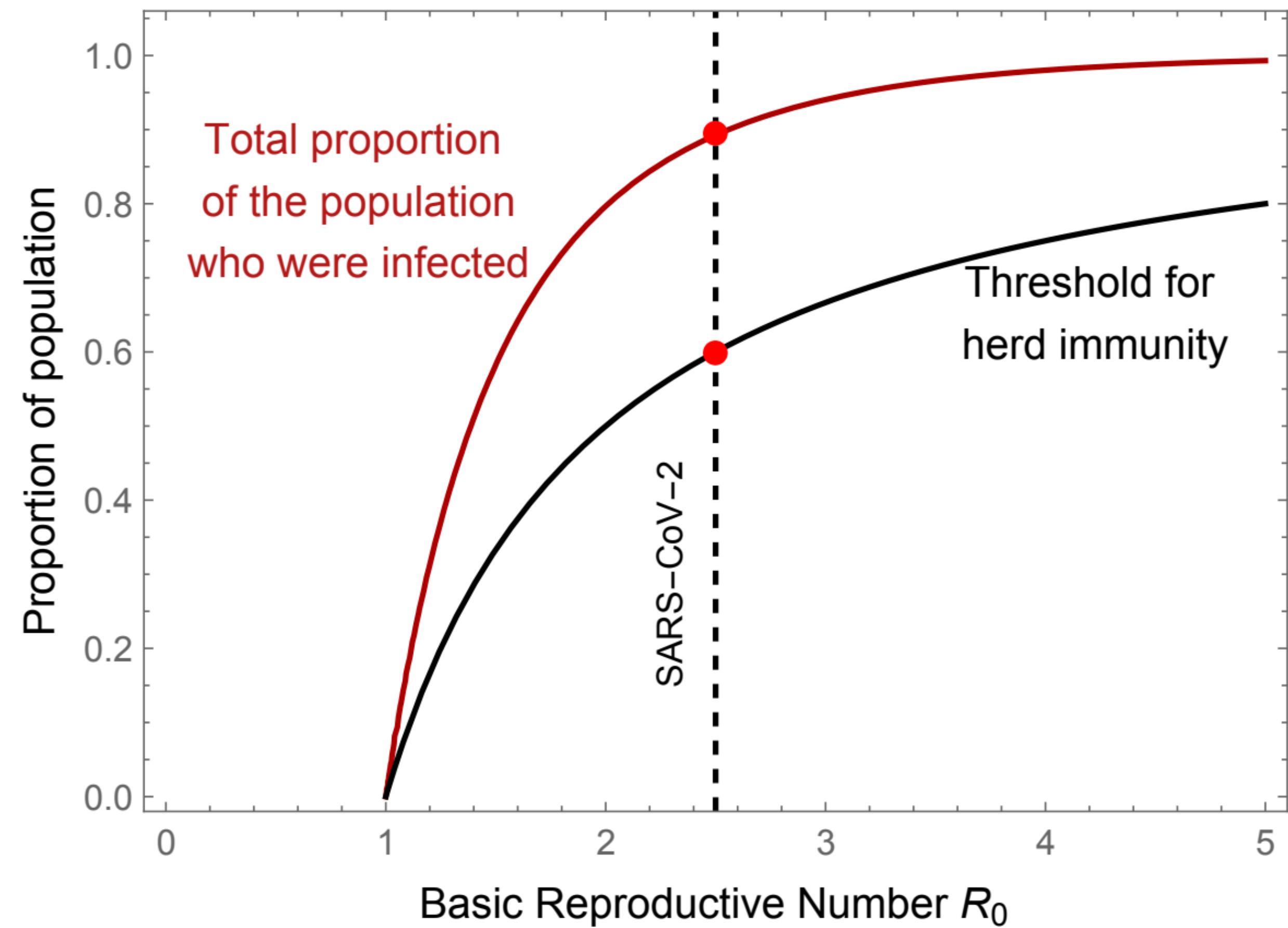
$$\frac{\beta}{\mu}(1 - f_V) > 1 \rightarrow f_{V,th} = 1 - \frac{1}{R_0}$$

The herd immunity

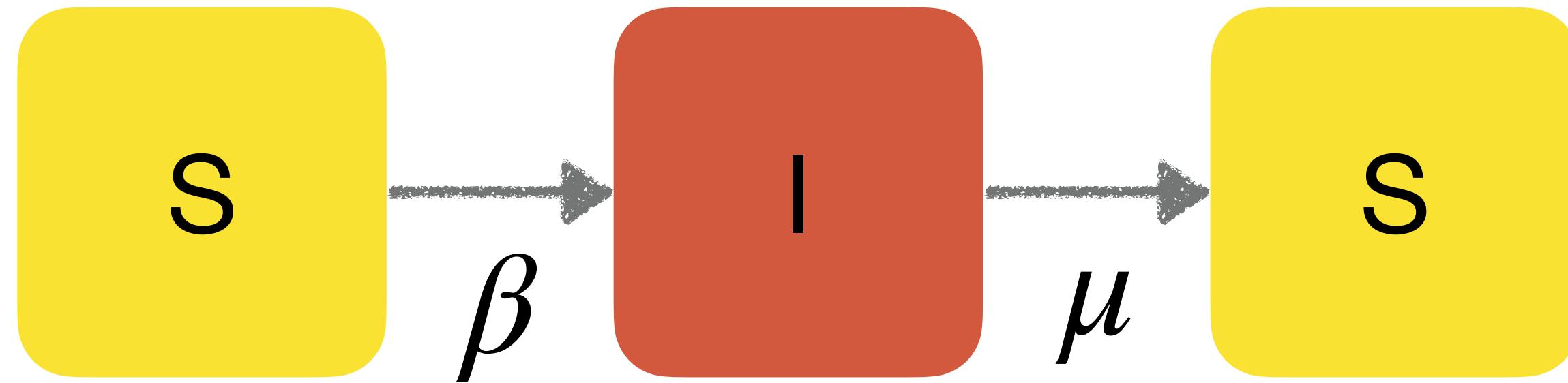


The overshoot

- What if we just let the epidemic spread through the population until we reach herd immunity?
There will be many more infections than the threshold.

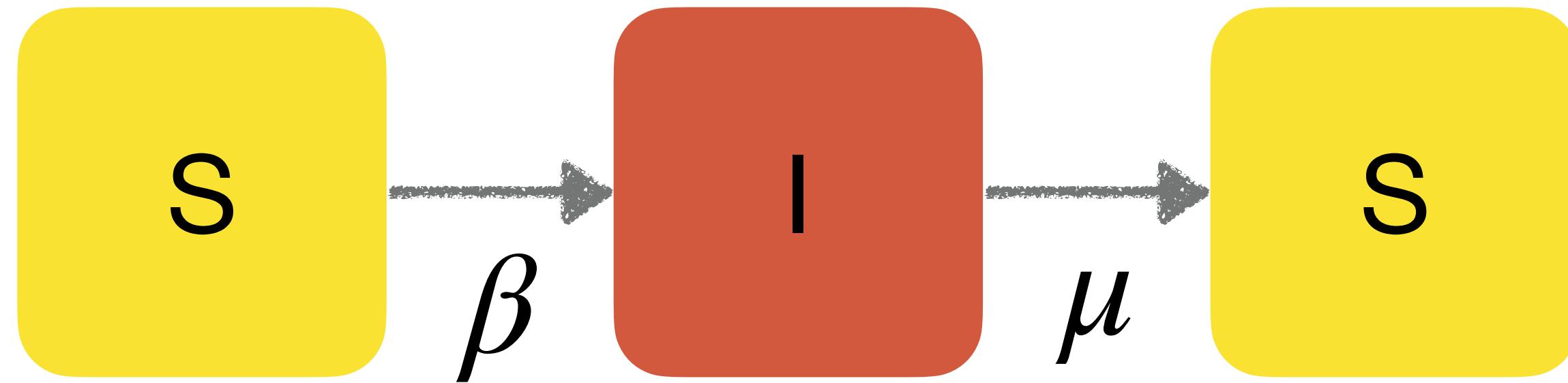


The SIS model



$$\left\{ \begin{array}{l} \frac{dS}{dt} = -\beta \frac{SI}{N} + \mu I \\ \frac{dI}{dt} = \beta \frac{SI}{N} - \mu I \end{array} \right. \quad S + I = N$$

The SIS model



$$\frac{dI}{dt} = (\beta - \mu)I - \frac{\beta}{N}I^2$$

$$\frac{\beta}{\mu} > 1 \Rightarrow \lim_{t \rightarrow +\infty} I(t) = \left(1 - \frac{\mu}{\beta}\right) N$$

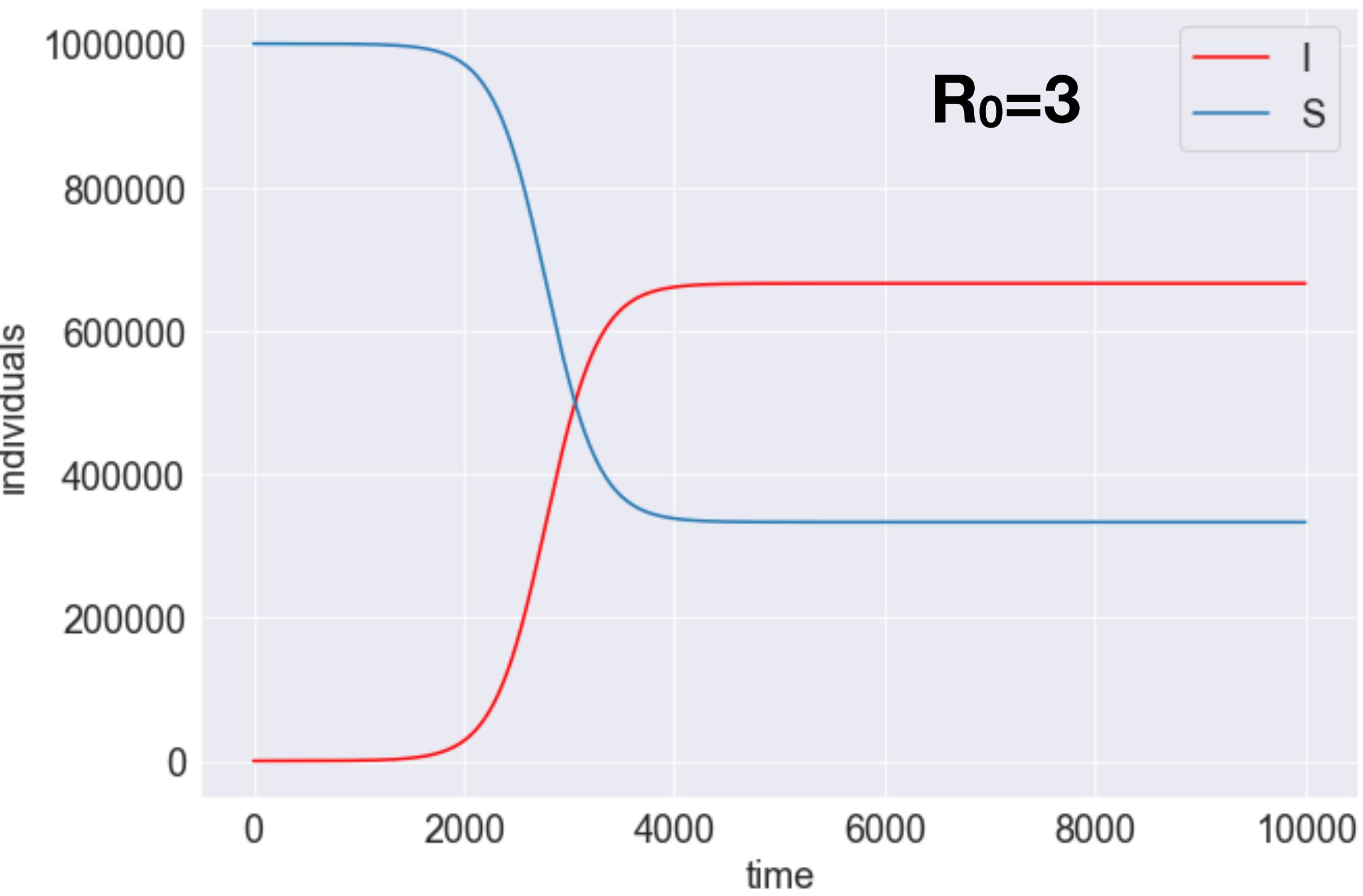
Logistic equation

Non-trivial equilibrium

The SIS model

- The disease persists as long as $R_0 > 1$
- The system reaches an endemic state, with:

$$I^* = \left(1 - \frac{1}{R_0}\right) N$$



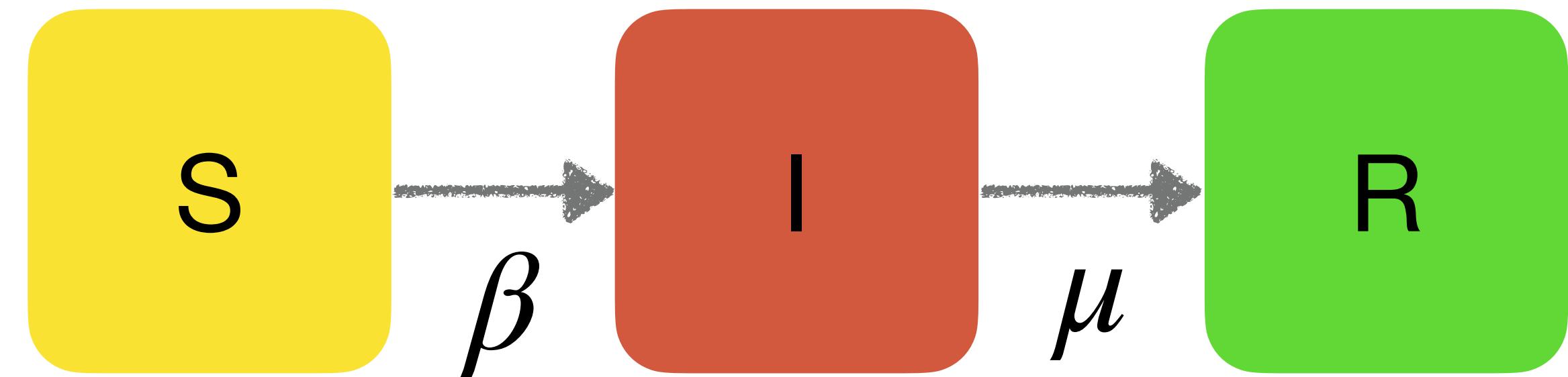
Deterministic vs stochastic models

- Deterministic models provide insights into the general behavior of the system (e.g. threshold effect)
- They represent a good way to study closed systems, and infer basic parameters
- They lack important details for realism:
 - **Stochasticity** (effects of chance)
 - The condition $R_0 > 1$ does not guarantee an outbreak to take off
 - **Discretization** (real epidemic variables are not continuous)

Stochastic numerical simulations

- Variables representing the compartments are discrete
- Transitions between compartments are simulated as random binomial or multinomial processes
- This is done through the use of **(pseudo) Random Number Generators**

Stochastic SIR model



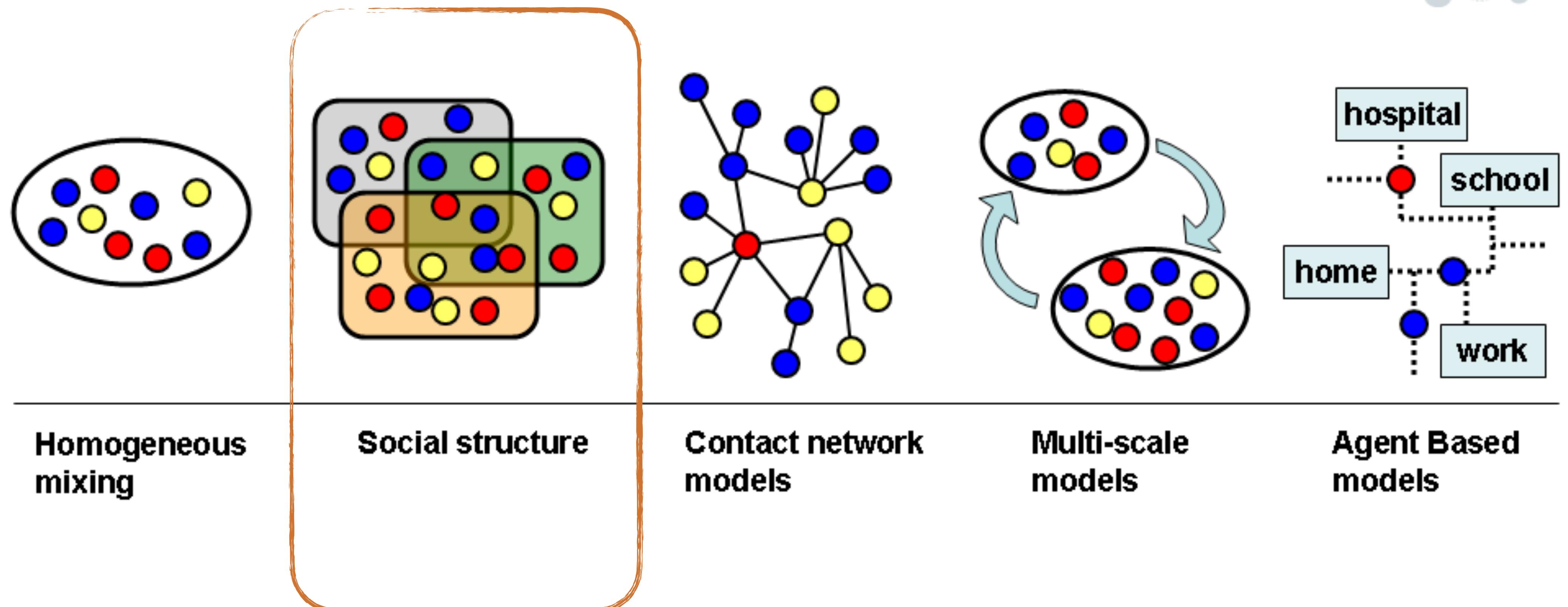
- infection and recovery are **random processes**, like flipping coins
 - probability of success: $\beta\Delta t I(t)/N$, $\mu\Delta t$
 - number of trials: $S(t)$, $I(t)$
 - number of successes: $\Delta S = \text{Binom}(S(t), \beta\Delta t I(t)/N)$,
- $$\Delta R = \text{Binom}(I(t), \mu\Delta t)$$

Stochastic SIR model

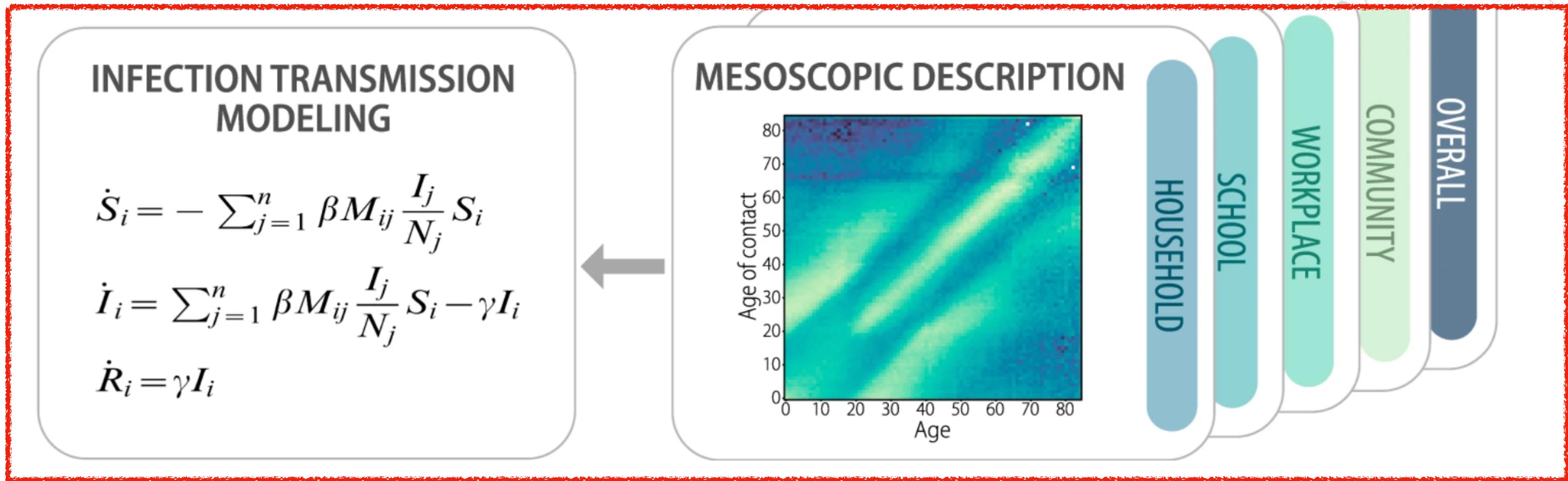
- Fundamental **differences** with respect to the deterministic SIR:
 - ★ each realization of the model is different (many simulations are required, sometimes millions)
 - ★ the outcome of a simulation **depends on the initial conditions**, I_0
 - ★ the value of R_0 determines the probability of an outbreak to occur

$$P_{outbreak} = 1 - \frac{1}{R_0^{I_0}}$$

Models



Age-structured models



- Compartments are structured into n age classes
- M_{ij} represents the average contact rate between individuals of age i and j

Contact matrices

- Contact matrices can be estimated in different ways
- Through **empirical surveys**, which are more accurate but require significant resources (Mossong et al. 2008).
- By the creation of **synthetic populations** (Fumanelli et al. 2012).

PLOS COMPUTATIONAL BIOLOGY

OPEN ACCESS PEER-REVIEWED

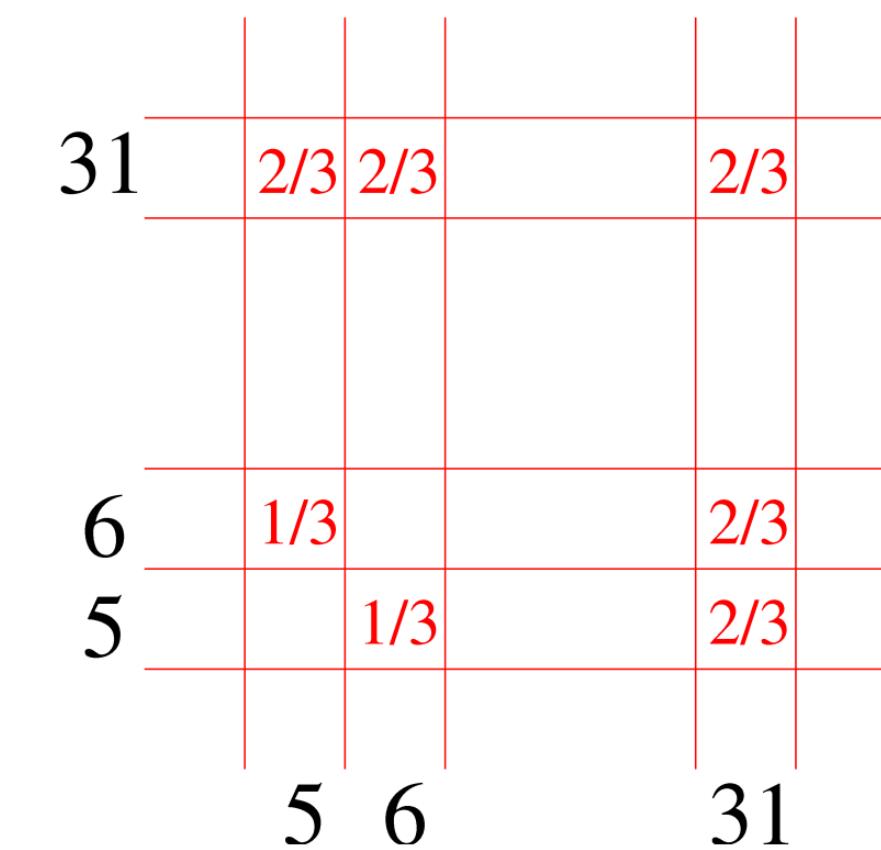
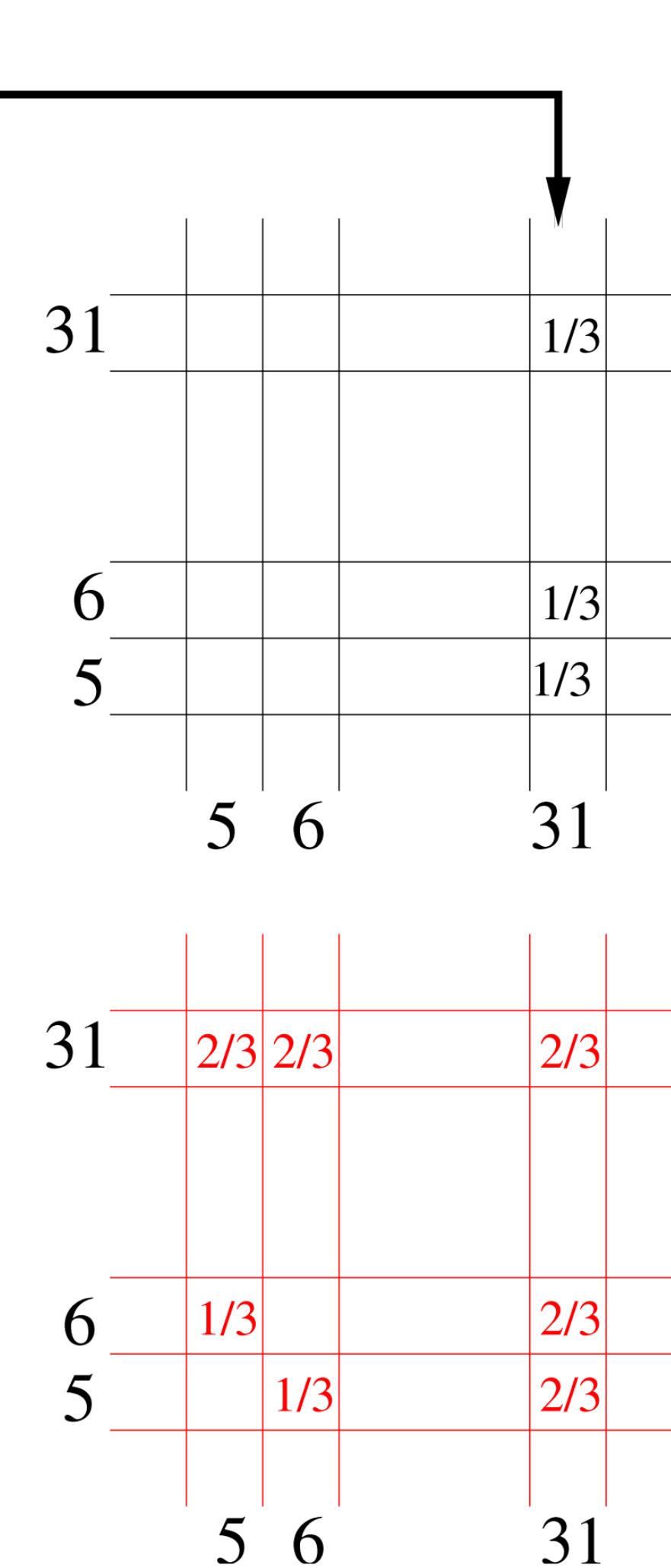
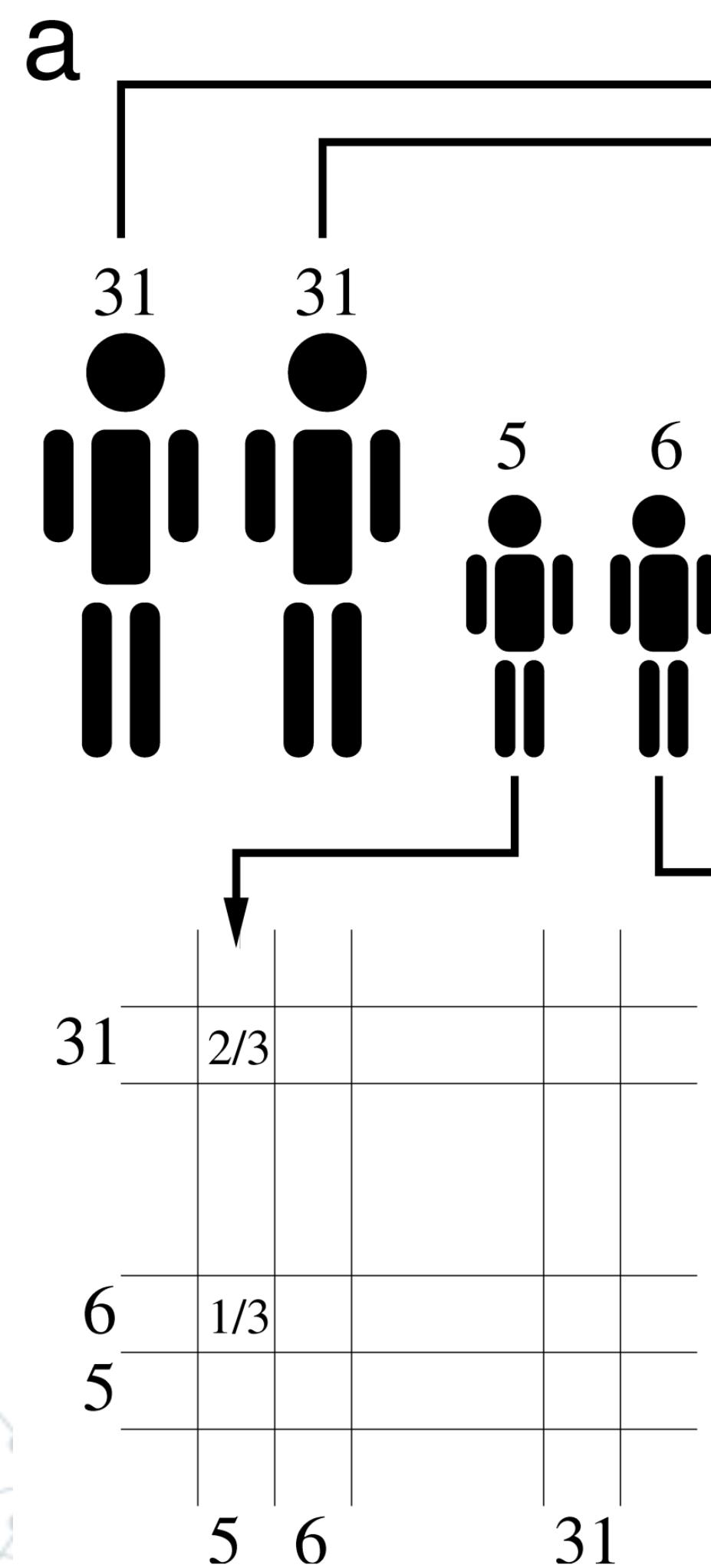
RESEARCH ARTICLE

Inferred the Structure of Social Contacts from Demographic Data in the Analysis of Infectious Diseases Spread

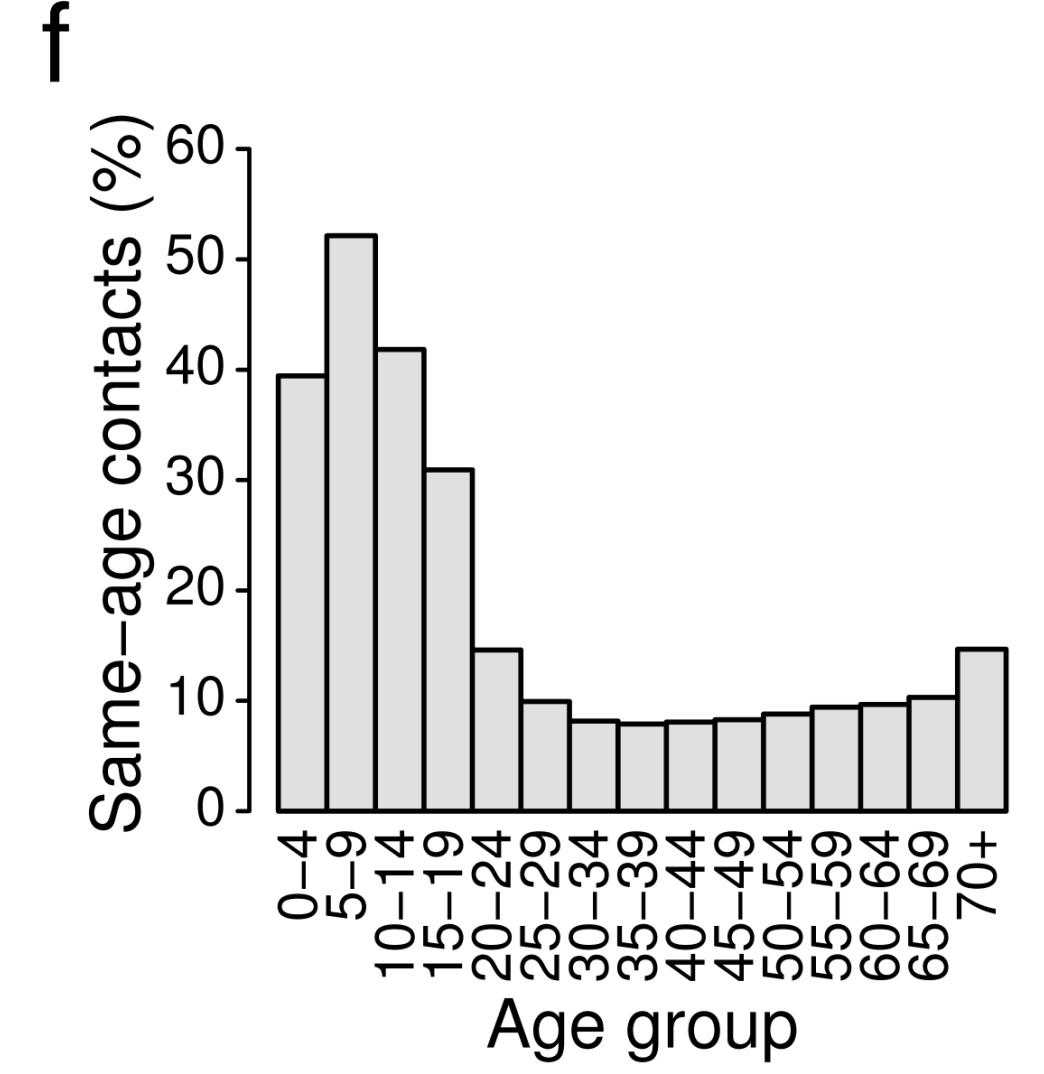
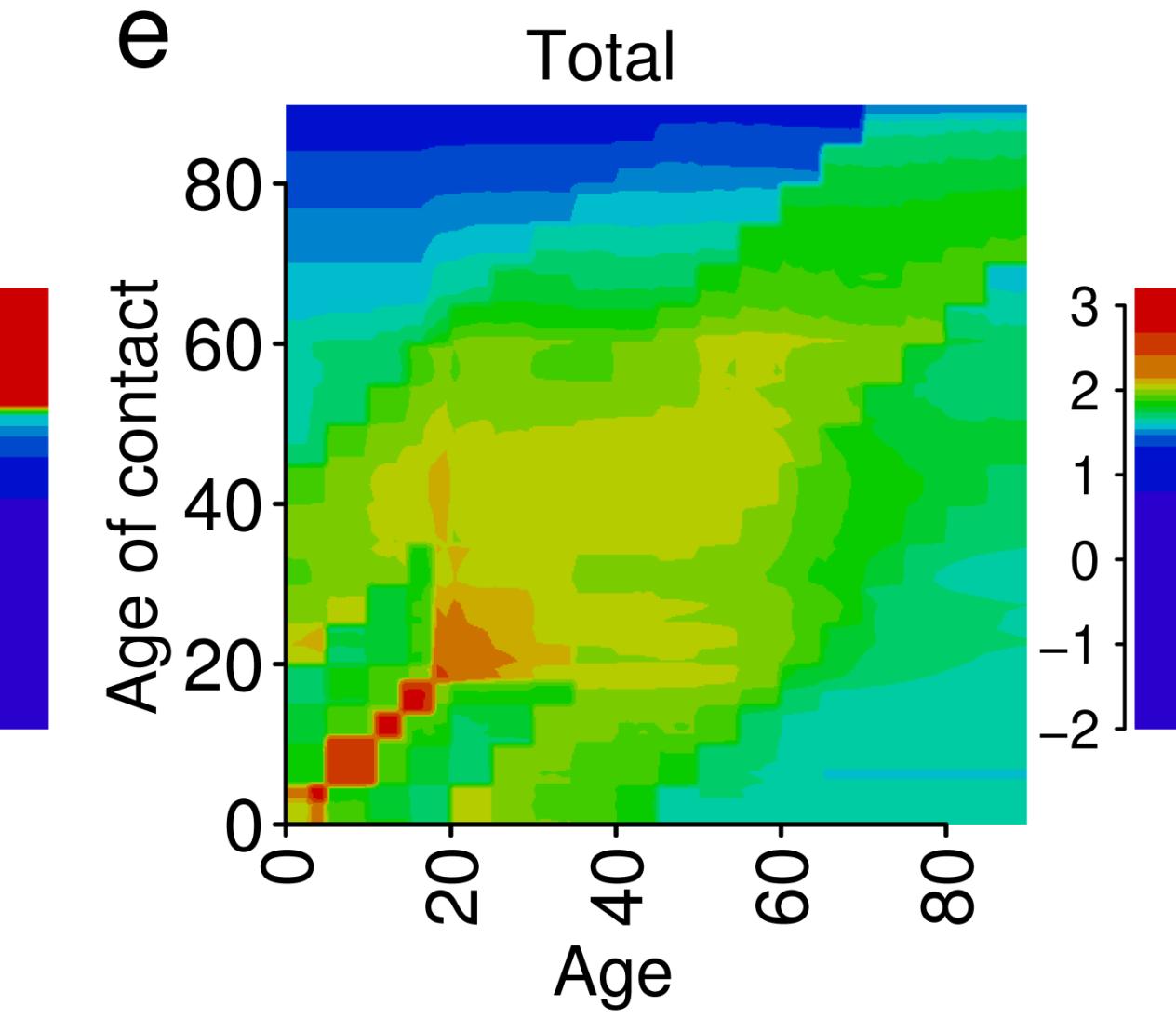
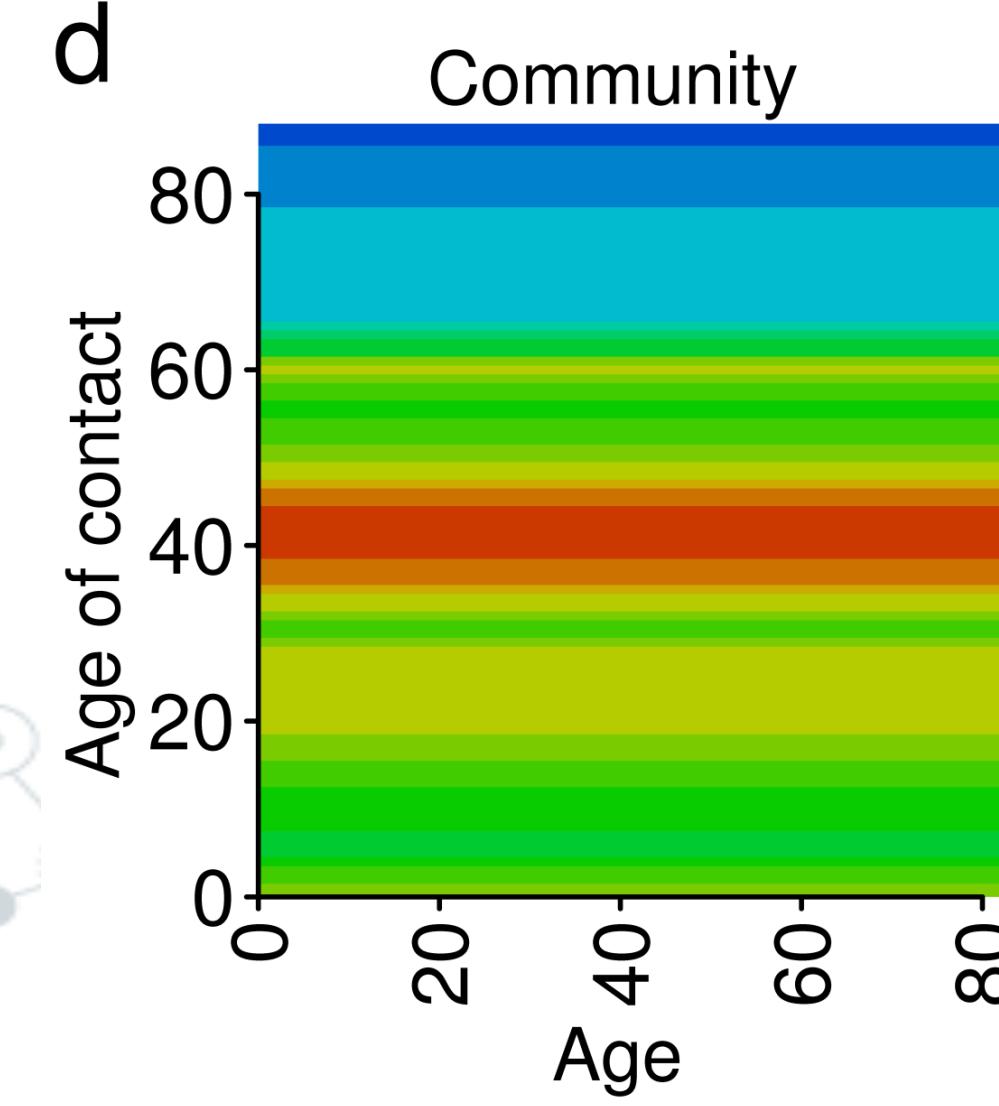
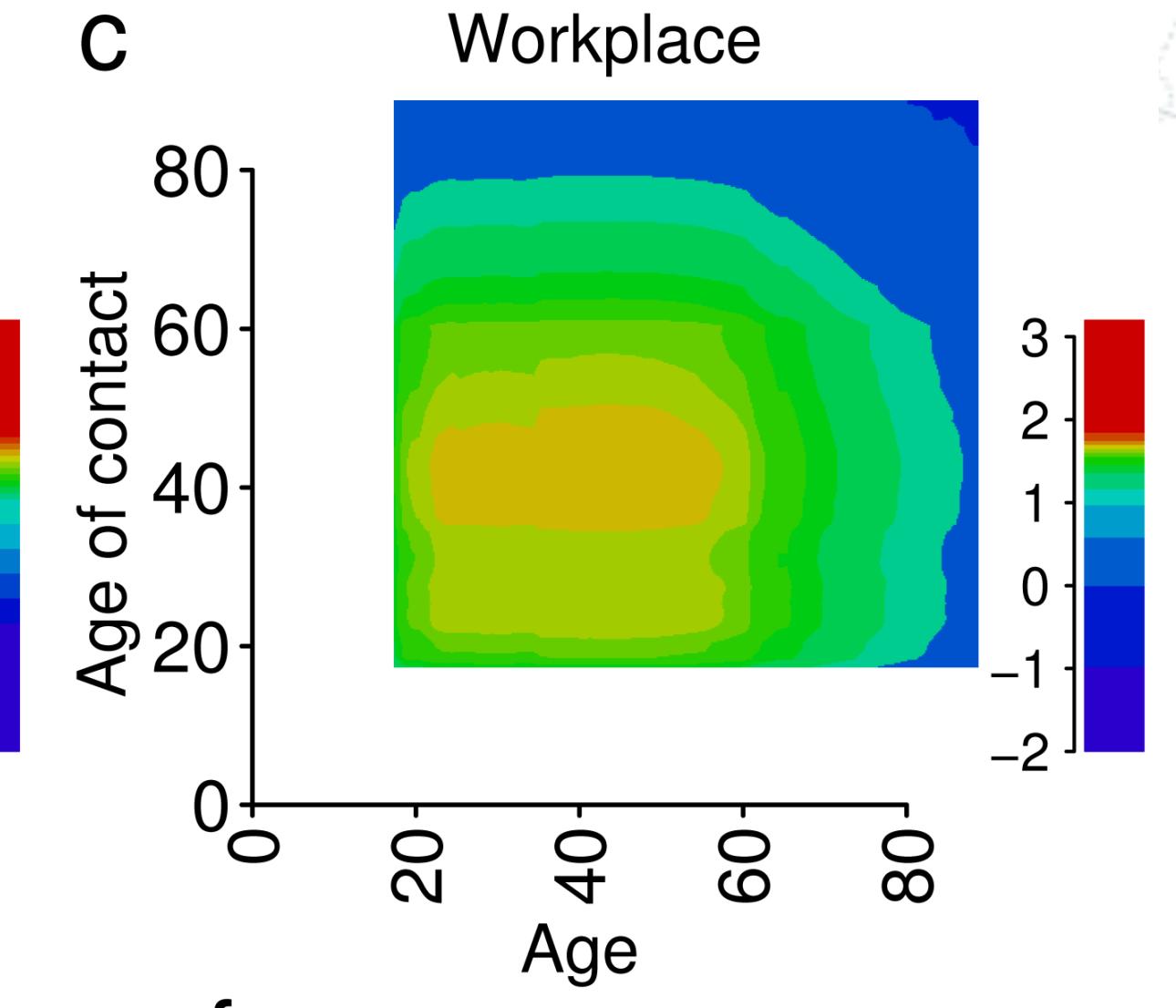
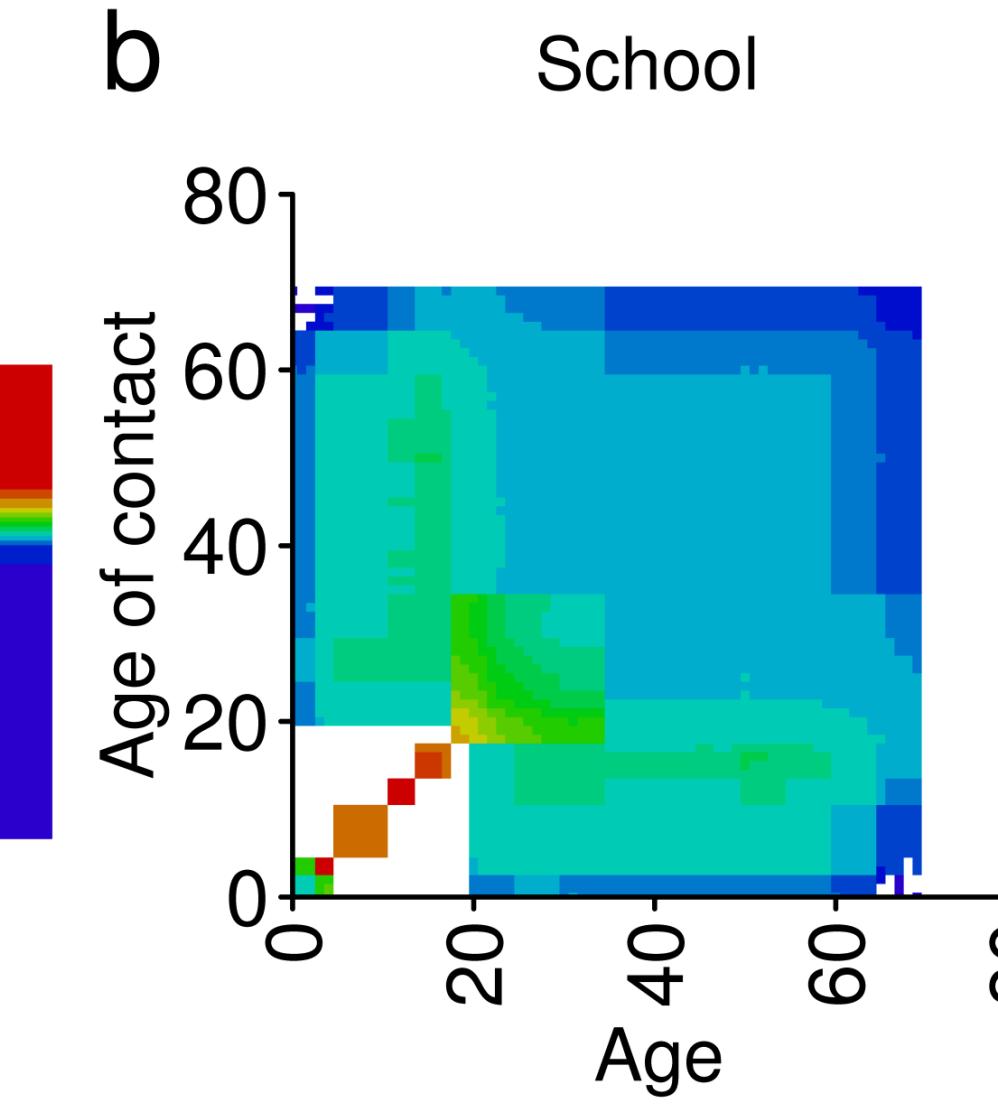
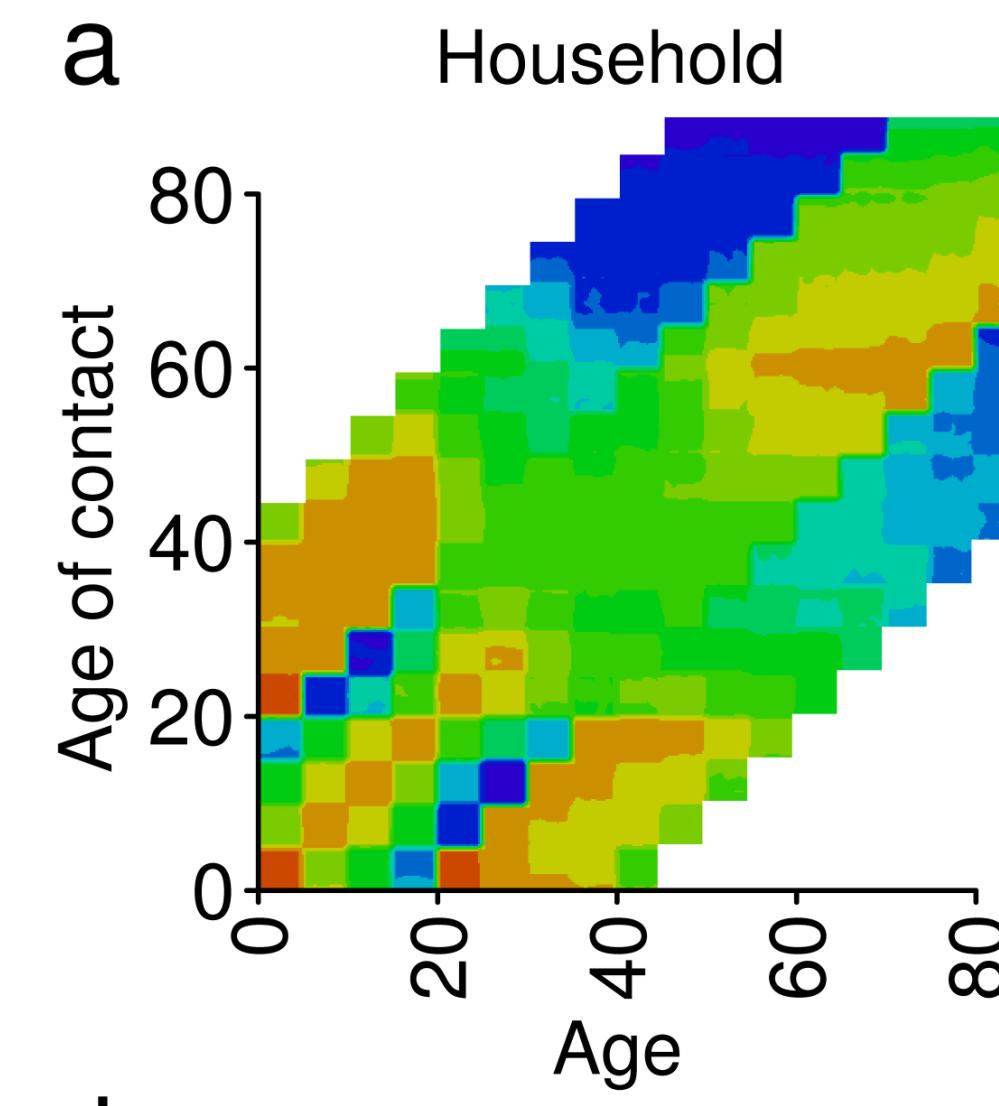
Laura Fumanelli , Marco Ajelli, Piero Manfredi, Alessandro Vespignani, Stefano Merler

Published: September 13, 2012 • <https://doi.org/10.1371/journal.pcbi.1002673>

Synthetic populations



Synthetic populations



Next generation matrix

- In the case of an age-structured epidemic model, what is the value of R_0 ?
- We can compute it using the so called “**next-generation matrix**” approach, first introduced by Diekmann *et al.* (1990).
- We will not go through a formal proof of the approach but in the case of a simple age-structured SIR model, it is quite intuitive.
- The **basic reproductive number** of the model corresponds to the largest of the absolute values of the eigenvalues of the contact matrix M (**the spectral radius**).

$$R_0 = \rho \left(\frac{\beta}{\mu} M \right)$$

Next... Coding