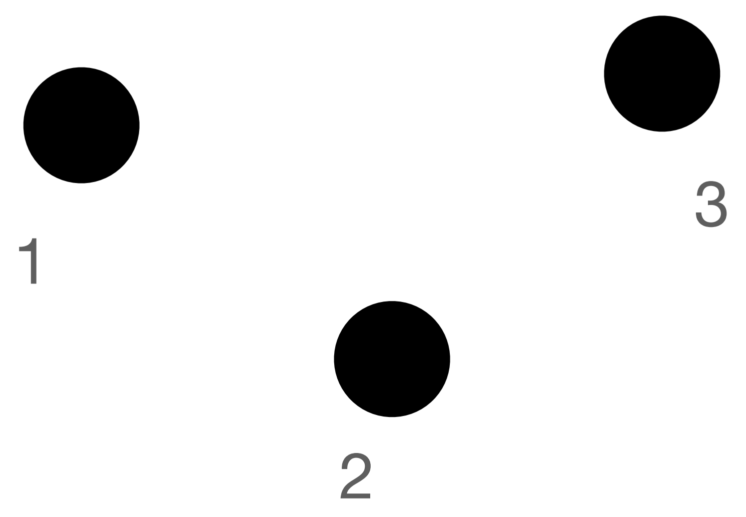
Infectious-disease models: Types and theory

Ben F. Maier // Summer School "Modellierung schwerer Infektionskrankheiten" // 2022-09-13

Infectious disease modeling
Or: Sophisticated counting

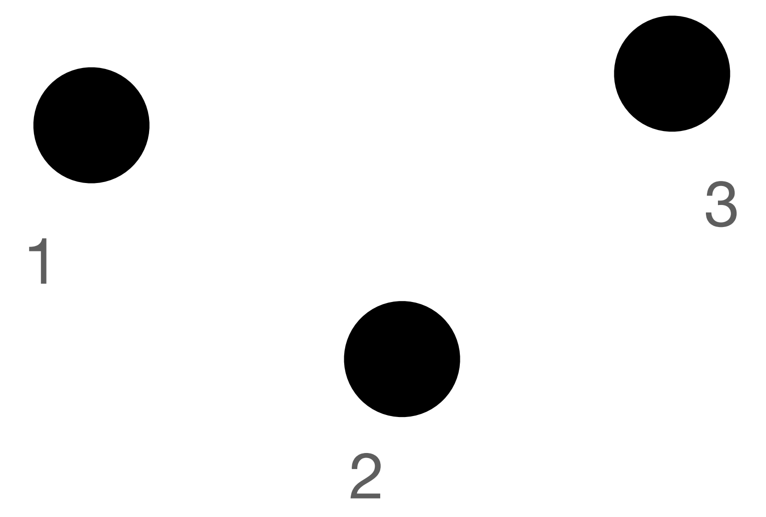
- At the center of attention: individuals



Infectious disease modeling

Or: Sophisticated counting

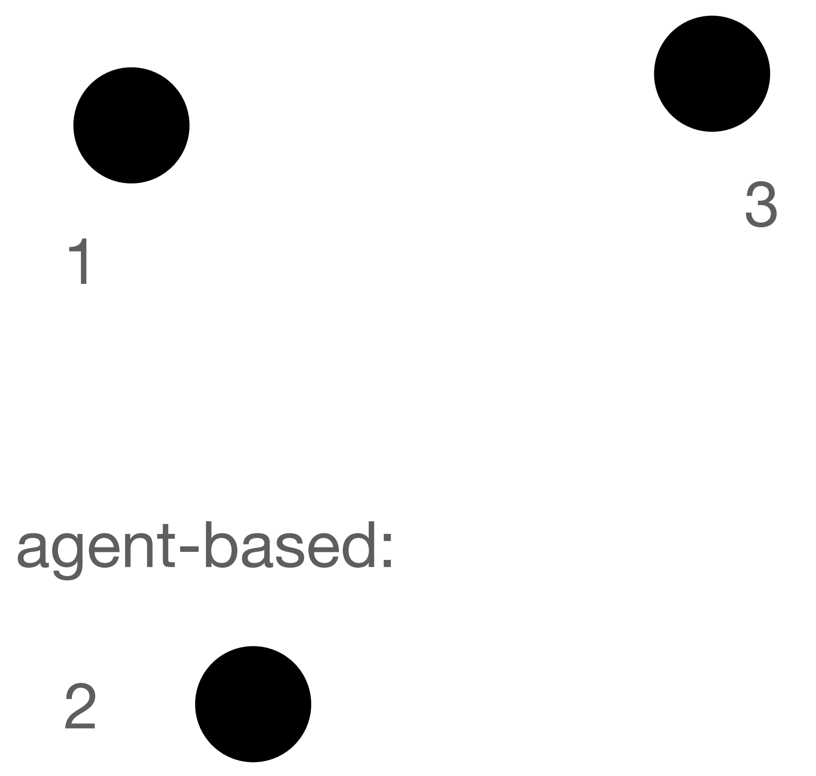
- At the center of attention: individuals
- individuals can be in certain states
    - infected with disease X
    - hospitalized with disease X
    - between 14 and 37 years old
    - smoker
    - living in Hanover



Infectious disease modeling

Or: Sophisticated counting

- At the center of attention:
  individuals
- individuals can be in certain states
  - infected with disease X
  - hospitalized with disease X
  - between 14 and 37 years old
  - smoker
  - living in Hanover



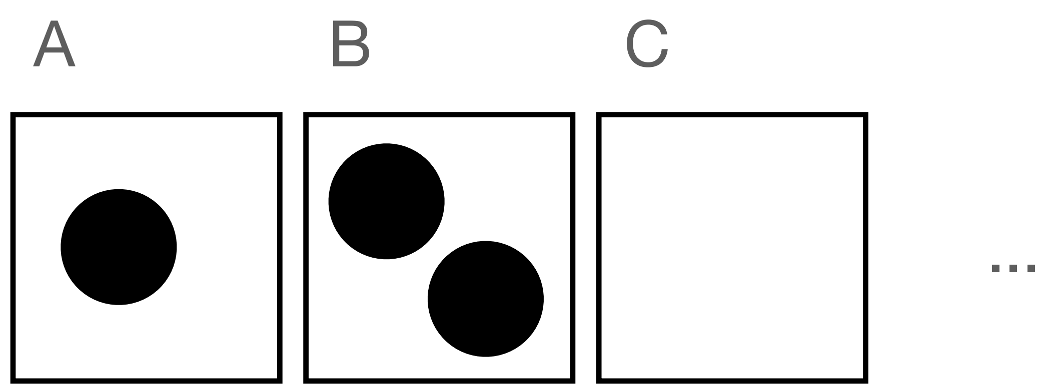
[
infected,
hospitalized,
age_group_14_37,
smoker_yes,
hanover
]

Infectious disease modeling
Or: Sophisticated counting

- At the center of attention: individuals
- individuals can be in certain states
    - infected with disease X
    - hospitalized with disease X
    - between 14 and 37 years old
    - smoker
    - living in Hanover

compartmentalized view:

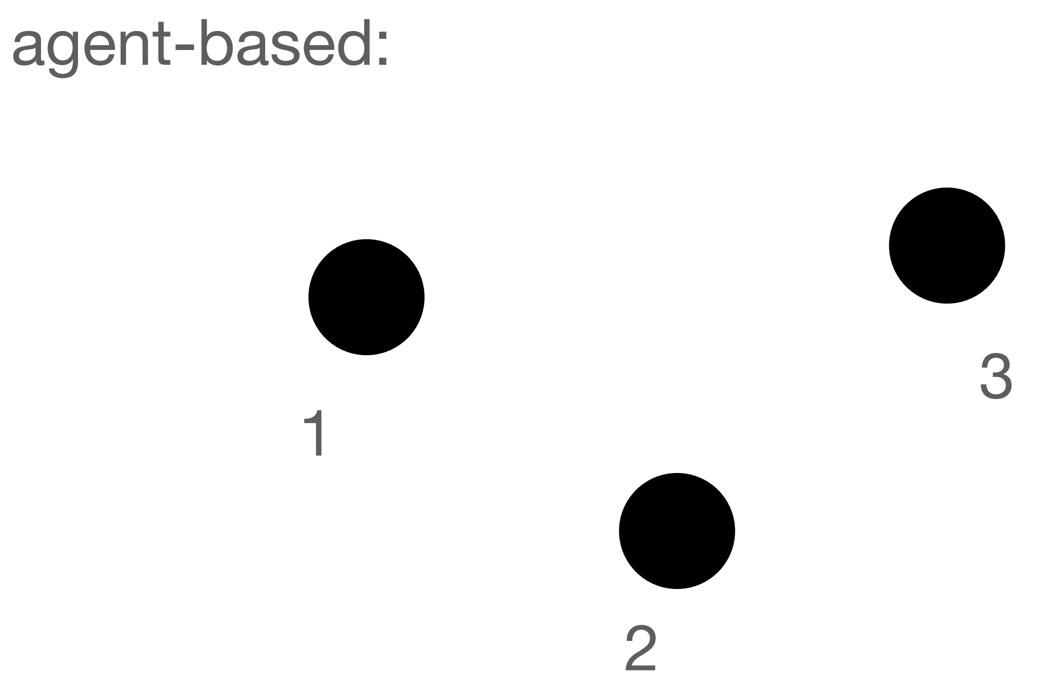
Count of individuals in compartment A ([
    infected,
    hospitalized,
    age_group_14_37,
    smoker_yes,
    hanover
]) = 1

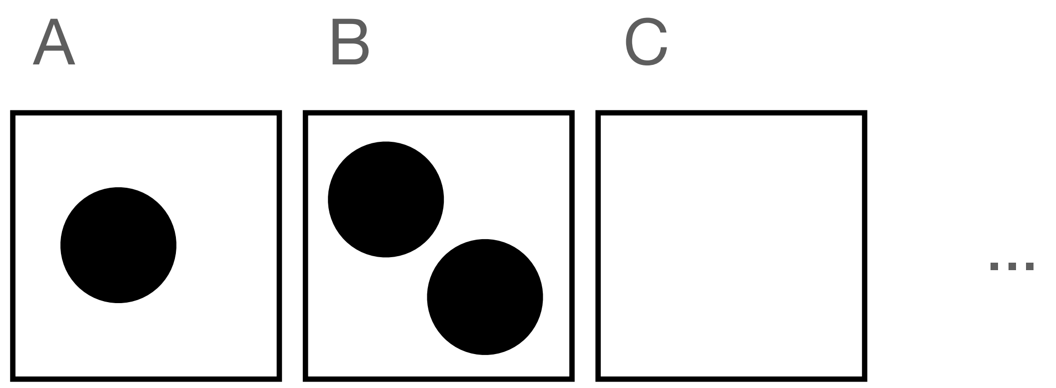


Infectious disease modeling

Or: Sophisticated counting

- At the center of attention: individuals
- individuals can be in contact
  - agent-based: explicitly
  - compartmentalized: implicitly (-> well-mixed)



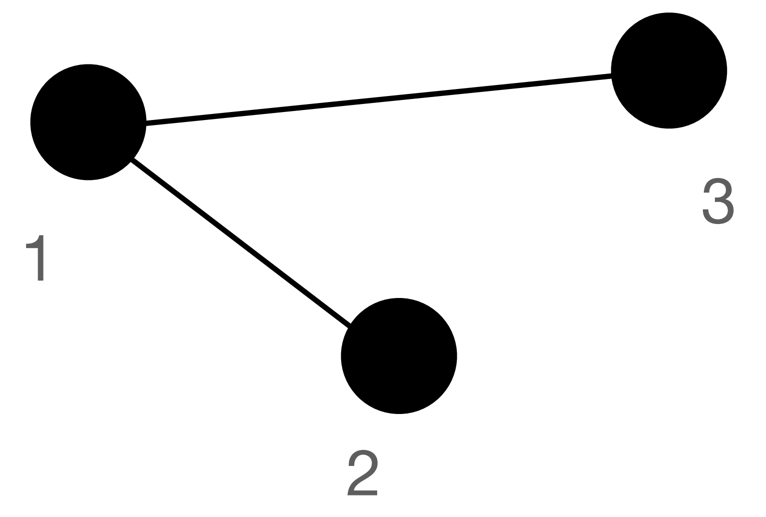


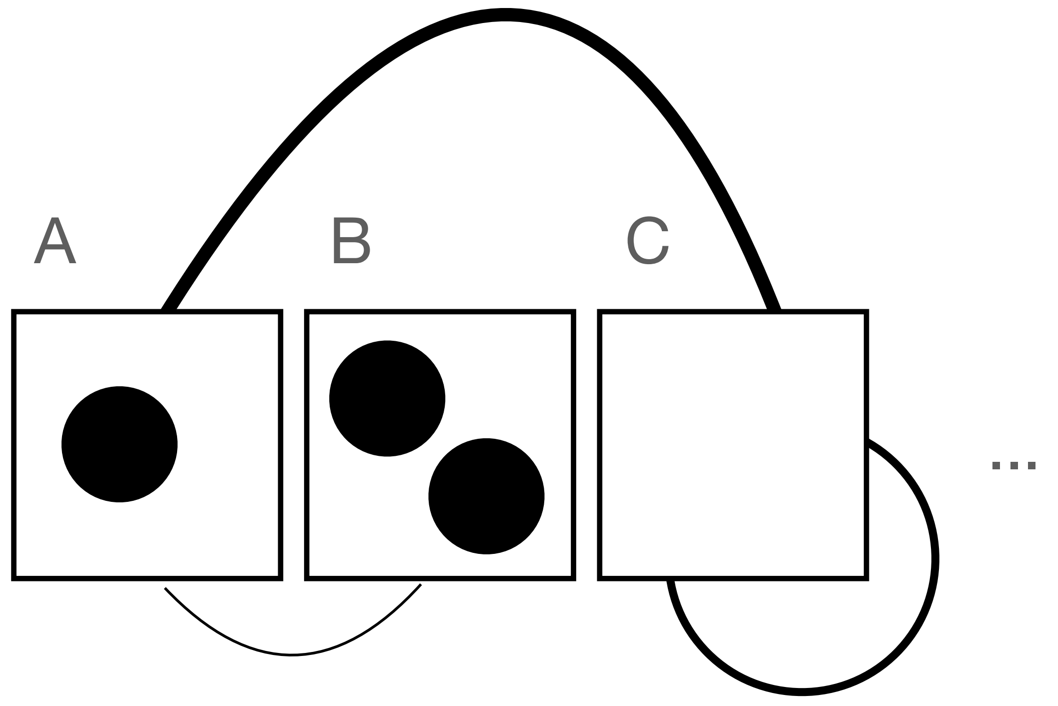
Infectious disease modeling

Or: Sophisticated counting

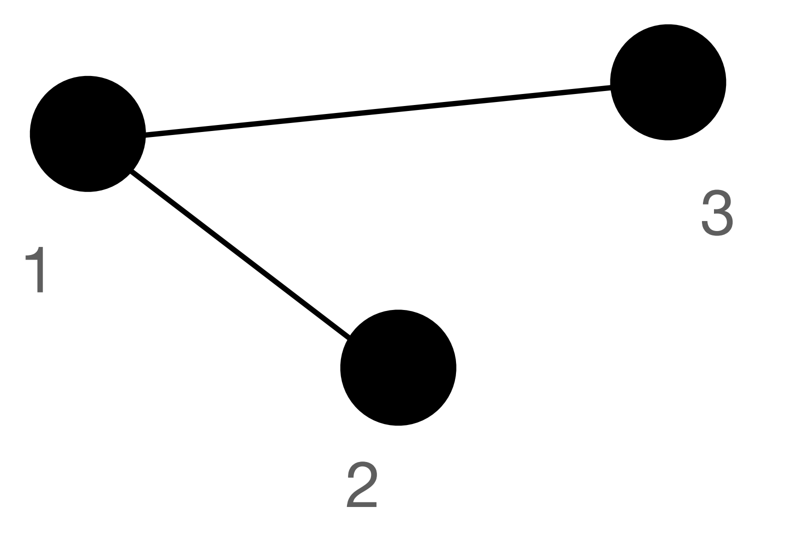
- At the center of attention: individuals
- individuals can be in contact
  - agent-based: explicitly
  - compartmentalized: implicitly (-> well-mixed)

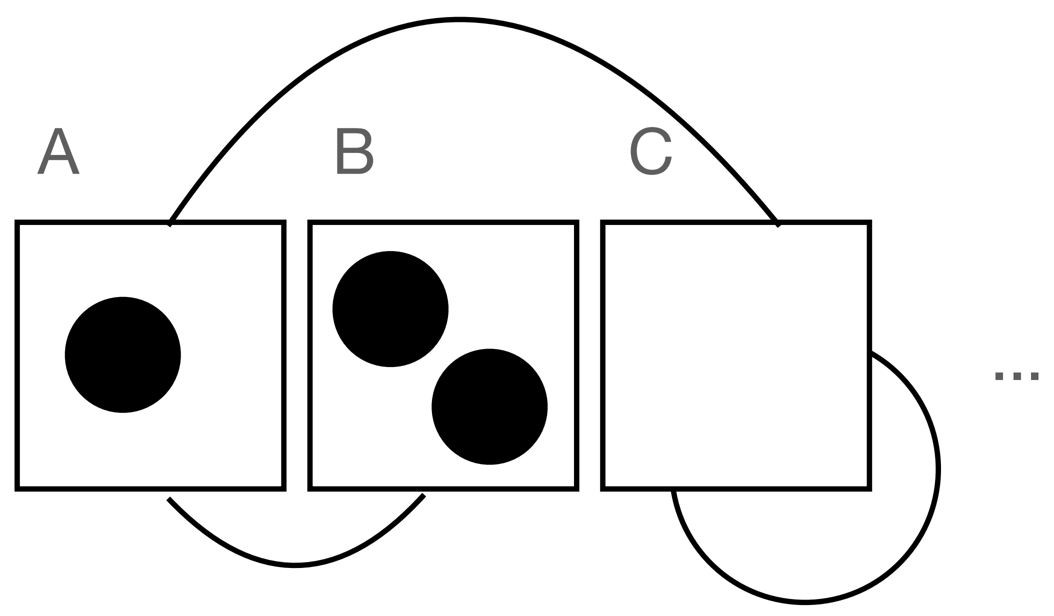
agent-based:





Bottom-up vs. Top-down





Agent-Based

*usually

- individuality is center of the formulation
- stochastic
- formulation as temporal contact networks and/or continuous in space

Compartmentalized

*usually

- Markovian (dependent on current state only)
  -> individuality non-existent or washed away (e.g. contact history)
- deterministic
- formulation as ODEs

ordinary differential equations

Blackboard

Agent-based stochastic perspective

- The Poisson process
- indiv. being in state "A" ≡ "alive"

$$A \longrightarrow \emptyset$$

- death: spontaneous reaction
- Poisson process

1. time step dt
   only 1 event

2. $P(\text{"event happens"}) \propto dt$
   ~~P("event~~
   $= \lambda dt$
   rate

3. The process is Markovian (only current state of system)

$\bullet A$ $t=0$ $P_0(dt)$? prob that A is still alive

zero events

$$P_1(dt) = \lambda dt$$

$$P_0(dt) = 1 - P_1(dt)$$
$$= 1 - \lambda dt$$

let dt pass

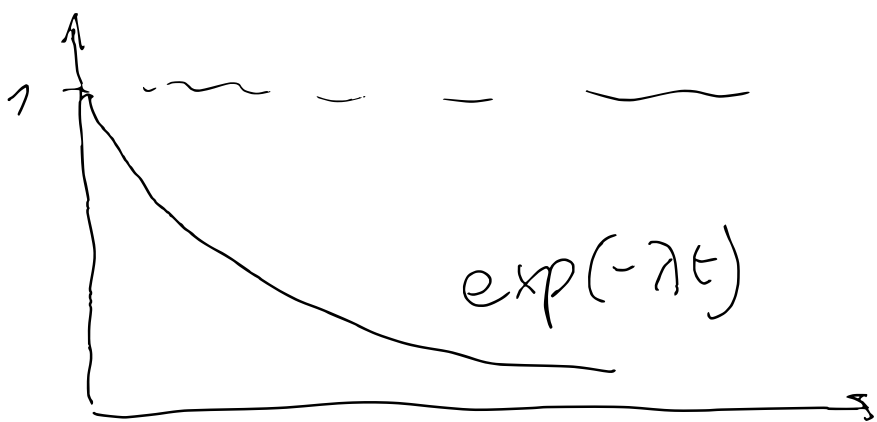
$$P_0(t+dt) = P_0(t) \times P_0(dt)$$
$$= P_0(t) \times (1 - \lambda dt)$$
$$= P_0(t) - P_0(t)\lambda dt$$

$$(P_0(t+dt) - P_0(t))/dt = -\lambda P_0(t) \quad | \lim_{dt \to 0}$$

$$\frac{dP_0}{dt} = -\lambda P_0 \qquad P_0 = e^{-\lambda t}$$

P("no dying event up and incl. time t") =

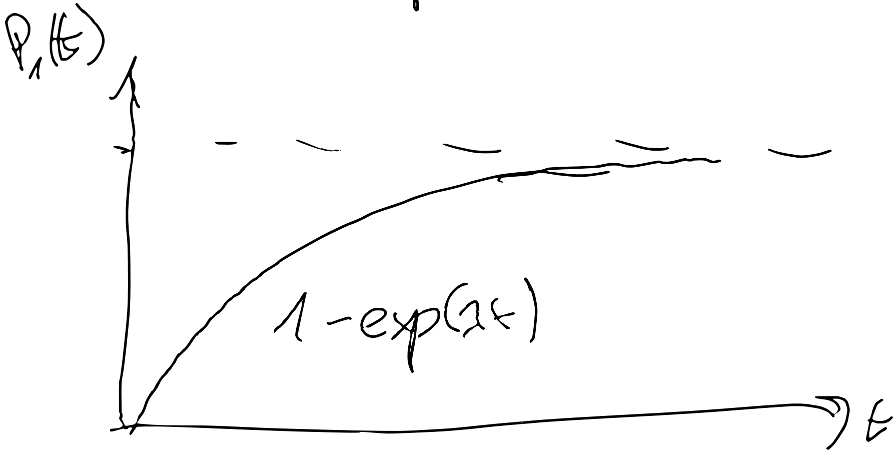
$= P(\text{"no event}, t) = \exp(-\lambda t)$



$P(\text{"at least one event happened"}) =$

$1 - P_0(t)$

$= 1 - \exp(-\lambda t) = P_1(t)$



$$p_{death}(\tau) = \frac{\partial}{\partial t} P_1(t) \Big|_{t=\tau} = \boxed{\lambda e^{-\lambda \tau}}$$

Definition

Given transition

$$X \xrightarrow{\lambda} Y$$

waiting time distribution

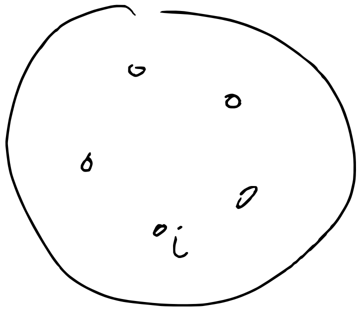
is

$$p(\tau) = \lambda \exp(-\lambda \tau)$$

$$\langle \tau \rangle = \frac{1}{\lambda}$$

ODEs

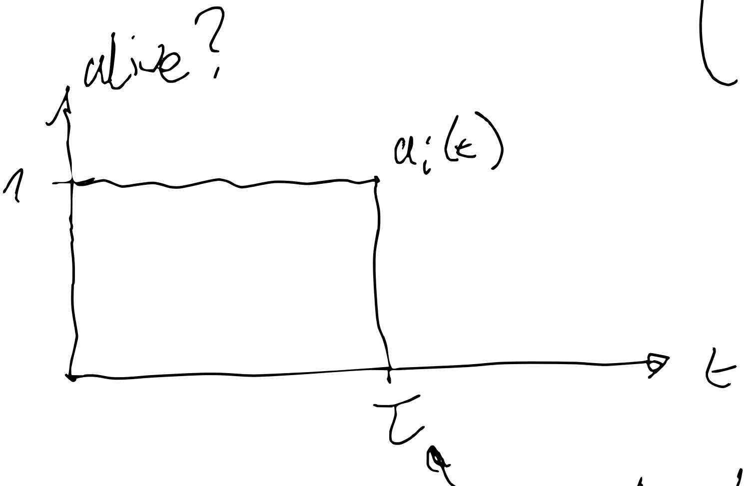
$\longrightarrow$



$t=0$

$N=5$

$$a_i(t) = \begin{cases} 1 & \text{if } i \text{ is alive} \\ 0 & \text{if it isn't} \end{cases}$$



$$\langle a_i(t) \rangle = 1 \times P_{0,i}(t) + 0 \times (1 - P_{0,i}(t))$$
$$= P_{0,i}(t) \implies$$

number of alive individuals $\langle A \rangle$ avg over many realizations

is given

$$A(t) = \sum_{i=1}^{N} a_i(t) \quad \Big| \langle \cdot \rangle$$

$$\langle A(t) \rangle = \sum_{i=1}^{N} \langle a_i(t) \rangle = \sum_{i=1}^{N} P_{0,i}(t) \quad \Big| \frac{d}{dt}$$

$$= \sum_{i=1}^{N} -\lambda P_{0,i} \qquad \frac{d}{dt} P_{0,i} = -\lambda P_{0,i}$$

$$\frac{d\langle A \rangle}{dt} = -\lambda \langle A \rangle$$

"dead"

$$A \xrightarrow{\lambda} B$$

$$\frac{dA}{dt} + \frac{dB}{dt} = 0$$

$$A + B = \text{const}$$

$$\boxed{\frac{dA}{dt} = -\lambda A}$$

$$\boxed{\frac{dB}{dt} = +\lambda A}$$

the time spent in

A is exponentially distributed

$$p(\tau) = \lambda e^{-\lambda t}$$

$$\boxed{\langle \tau \rangle = \frac{1}{\lambda}}$$

$$\begin{tikzcd}
 & B \\
A \arrow[ur, "\lambda"] \arrow[dr, "\mu"'] & \\
 & C
\end{tikzcd}$$

example

$$\begin{tikzcd}
 & R \\
I \arrow[ur, "\lambda"] \arrow[dr, "K"'] & \\
 & X
\end{tikzcd}$$

average time spent infec.

$\tau_I = \frac{1}{\lambda}$

avg time until isol.

$\tau_X = \frac{1}{K}$

$\lambda + K$

$\Rightarrow \tau_{eff,I} = \frac{1}{\lambda + K}$

a single I individual

I for how long will I stay in its state?

$$P(\text{"still in I state"}, t) = P(\text{"no event"}, t)$$

$$= P(\text{"no rec. event"}, t) \times P(\text{"no isol. even"}, t)$$

$$= e^{-\lambda t} \times e^{-\kappa t}$$

$$P(\text{"not I anymore"}) = 1 - P(\text{"still in I"})$$

$$= 1 - e^{-(\lambda+\kappa)t}$$

$$\Big| \frac{d}{dt}$$

$$\boxed{p_I(\tau) = (\lambda+\kappa)\, e^{-(\lambda+\kappa)t}}$$

Which happens first

$$P_R(\tau_R) = \lambda e^{-\lambda\tau} \leftarrow$$

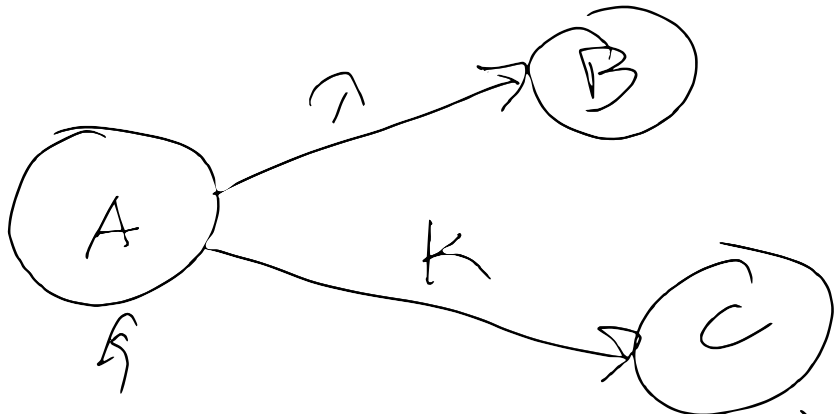
$$P_X(\tau_X) = \kappa e^{-\kappa\tau} \leftarrow$$

$$\underline{P}(\text{"rec first"}) = P(\tau_R < \tau_X) = \int_0^\infty d\tau_X \, P_X(\tau_X) \int_0^{\tau_X} P_R(\tau_R)$$

$$= \int_0^\infty d\tau_X \, \kappa e^{-\kappa\tau_X} \int_0^{\tau_X} d\tau_R \, \lambda e^{-\lambda\tau_R}$$

$$= 1 - \kappa \underbrace{\int_0^\infty e^{-(\kappa+\lambda)\tau_X}}_{=\frac{1}{\kappa+\lambda}} = 1 - \frac{\kappa}{\kappa+\lambda}$$

$$= \frac{\lambda}{\lambda+\kappa}$$



$$p_A(\tau) = (\lambda + K)\, e^{-(\lambda+K)t}$$

$$P_\lambda = \frac{\lambda}{\lambda + K}$$

1 alive
0 dead

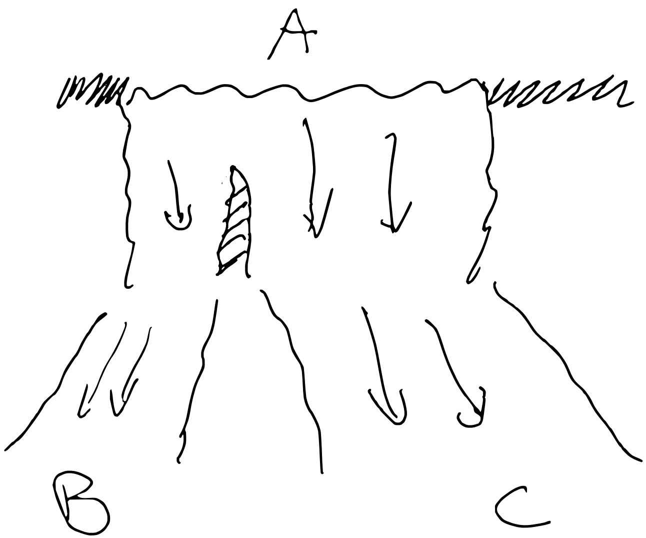
$$\langle A(t)\rangle = \sum_{i=1}^{N} \langle a_i(t)\rangle$$

$$\boxed{\frac{d\langle A\rangle}{dt} = -\lambda \langle A\rangle - K\langle A\rangle}$$

$$\frac{dB}{dt} = +\lambda A$$

$$\left(\frac{dA}{dt} = -\lambda A - kA \right)$$

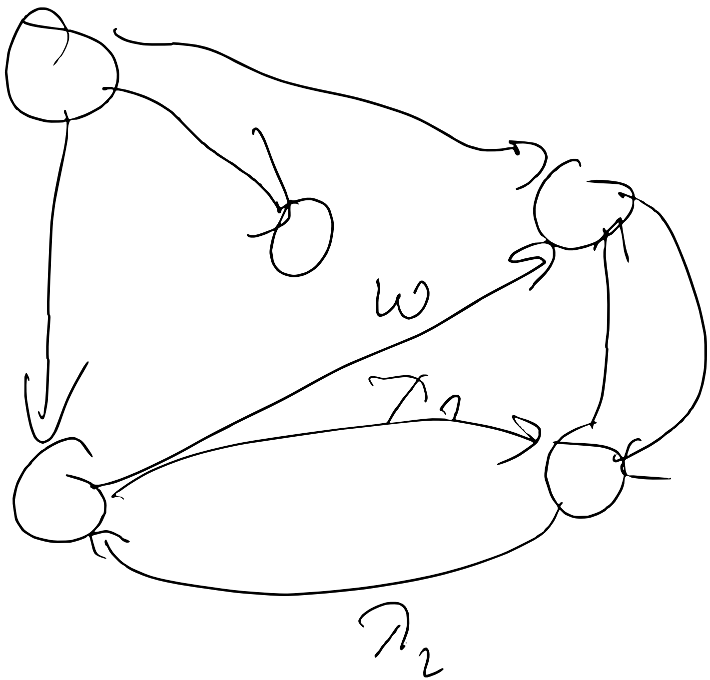
$$\frac{dC}{dt} = +kA$$



$$\frac{dA}{dt} = -\text{outflux}_A$$

$$\frac{dB}{dt} = P_{\text{ending up in B}} \times \text{outflux}\,A$$

$$\frac{dC}{dt} = P_{\text{ending up in C}} \times \text{outflux}\,A$$

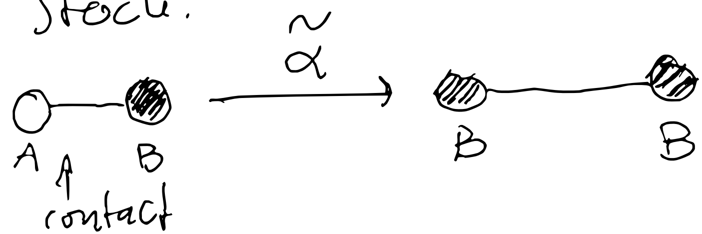


$$\frac{dx_i}{dt} = f(x_i)$$

$$\Rightarrow \frac{d\vec{x}}{dt} = \hat{A}\vec{x} + \vec{b}$$

auto-catalytic process

Stock:



when event takes place

$$\Delta A = -1$$
$$\Delta B = +1$$

$$[AB] \xrightarrow{\tilde{\alpha}} [BB]$$

if there's A A-indiv,
B B-indiv. $\Rightarrow$ #pairs = $A \times B$

contact $\hat{=}$ if A and B are "near enough"

number of ex. pairs =

$$= A \times B \times \underbrace{\frac{\delta V}{V}}$$

= prob. that an A-B-pair "shares space"

= prob. that an A-B-pair "in contact"

$$= \frac{\text{number of all contacts betw. agents}}{\text{number of all possible contacts}}$$

N agents

$\frac{1}{2} N \times (N-1)$

every agent to have k_0 contacts

$\frac{1}{2} N \times k_0$

$$p = \frac{\frac{1}{2} N k_0}{\frac{1}{2} N(N-1)} = \frac{k_0}{N-1} \Longrightarrow$$

#actual A-B pairs $= A \times B \times \frac{k_0}{N-1}$

number of B ind.

$$= A \times k_0 \times \frac{B}{N-1}$$

number of A agents

number of contacts this agent has

prob. that a contact is infected (B-state)

A

B

$$\boxed{\Lambda \simeq A \times B \times \frac{k_0}{N-1} \times \tilde{\alpha}}$$

How do we go to the ODE picture?

Poisson process

- Prop for 1 such ev. happening in dt is $P_1(dt) = \Lambda\, dt$
- Bernoulli variable

$$\Theta = \begin{cases} 1 & \text{happened in } dt \ (P_1) \\ 0 & \end{cases}$$

$$\langle \Theta \rangle = P_1(dt)$$

$$\Delta A = -1$$

$$\Delta B = +1$$

$$A(t+dt) = A(t) + \Delta A \times \Theta(dt)$$

whether or not the event has taken place

number of A after dt

number of A before dt

change of A through the event

$\Rightarrow \langle \cdot \rangle$

$$\langle A(t+dt)\rangle - \langle A(t)\rangle = \Delta A \, P_1(dt)$$

$$= \Delta A \, \Lambda \, dt$$

$$= -1 \times A \times k_0 \times \tilde{\alpha} \times \frac{B}{N-1} \, dt$$

$\lim_{dt \to 0}$

$$\frac{d\langle A\rangle}{dt} = -\tilde{\alpha} k_0 \times \langle A \times \frac{B}{N-1}\rangle$$

$\Rightarrow$

$$\frac{d\langle B\rangle}{dt} = + \text{———} \;\;''\;\; \text{———}$$

$$\frac{dA}{dt} = -\phi A \Rightarrow \phi = \underbrace{\tilde{\alpha} \times k_0}_{\alpha} \times \frac{B}{N-1}$$

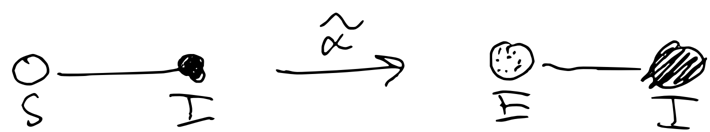
$$= -\alpha A \frac{B}{N\cancel{-1}} \qquad N \gg 1$$

$$= -\alpha A \frac{B}{N}$$

$A \to S$ (susceptible)

$B \to I$ (inf

$$\frac{dS}{dt} = -\alpha S \frac{I}{N}$$

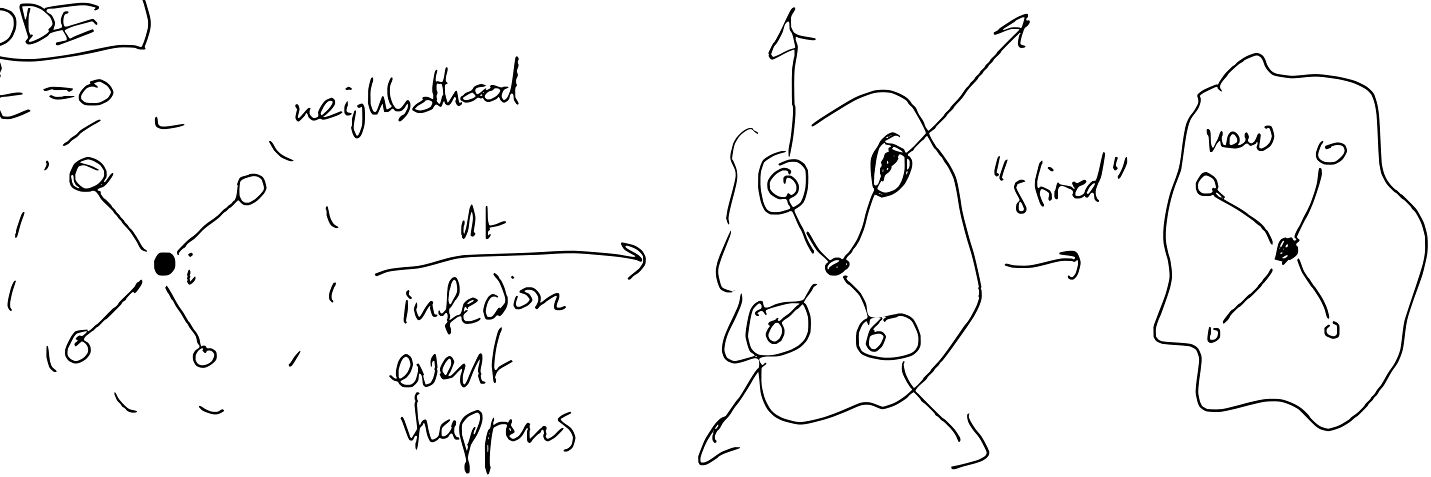


assumption

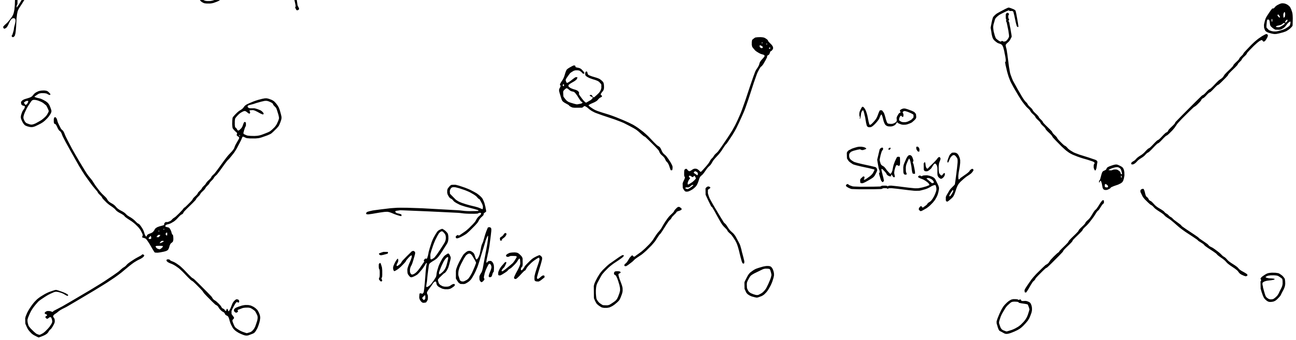
$$\langle AB \rangle = \langle A \rangle \langle B \rangle$$

$\boxed{\text{ODE}}$

$t=0$



time-scale of mixing $\gg$ time-scale of any other process quenched



$S \to I \to R$

$$\frac{dS}{dt} = -\alpha S I$$

$$\frac{dI}{dt} = +\alpha S I - \beta I$$

$$\frac{dR}{dt} = +\beta I$$

in the beginning

$S \simeq 1$

$$\frac{dI}{dt} = \alpha I - \beta I = \lambda I$$

$$\lambda = \alpha - \beta$$

$$\rightarrow \quad I = I_0 \exp(\lambda t)$$

$R_0 > 1 \quad \alpha \gg \beta \Rightarrow \lambda > 0 \Rightarrow$ exp. growth

$R_0 < 1 \quad \alpha \ll \beta \Rightarrow \lambda < 0 \Rightarrow$ exp decay

$$I = I_0 \exp\left(\beta\left(\frac{\alpha}{\beta} - 1\right)t\right)$$

$$\boxed{R_0 = \frac{\alpha}{\beta}}$$ basic repr. number

$$A \xrightarrow{\alpha} A + A$$

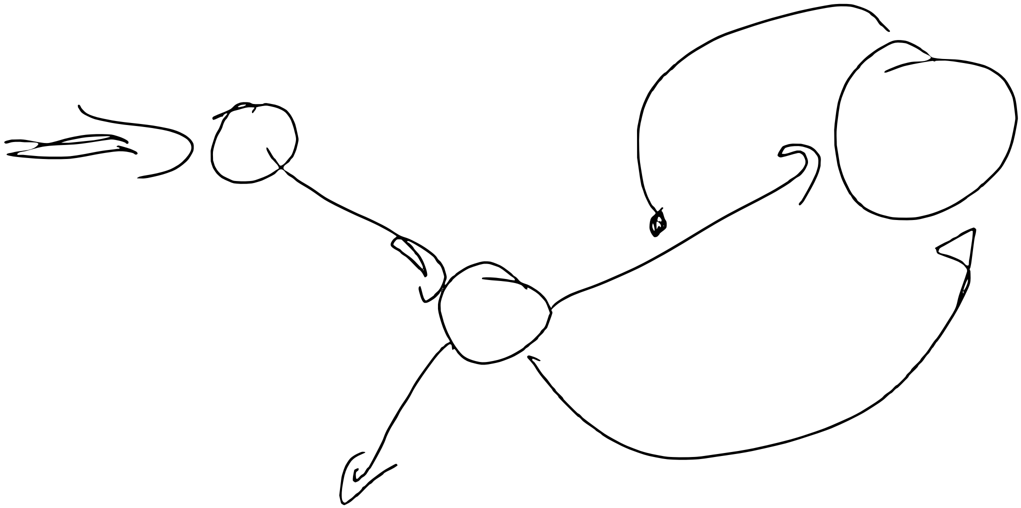
$$\Rightarrow \quad \cancel{A} \qquad \Omega(\tau) \propto \alpha\tau$$

$$\Rightarrow \quad p(\tau) = \beta \exp(-\beta\tau)$$

$$\Rightarrow \langle \tau \rangle$$

$$\langle \Omega \rangle = \alpha \langle \tau \rangle$$

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



$$\frac{d}{dt} y_i = \sum_{j<k} \alpha_{ijk}^{(f)} y_j y_k + \sum_j \beta_{ij} y_j + \gamma_i$$

N might be
in this term

$$Y_i \Rightarrow \{S, I, R\}$$

$$Y_i \Rightarrow \{S_1, S_2, \ldots E_1, E_2\}$$

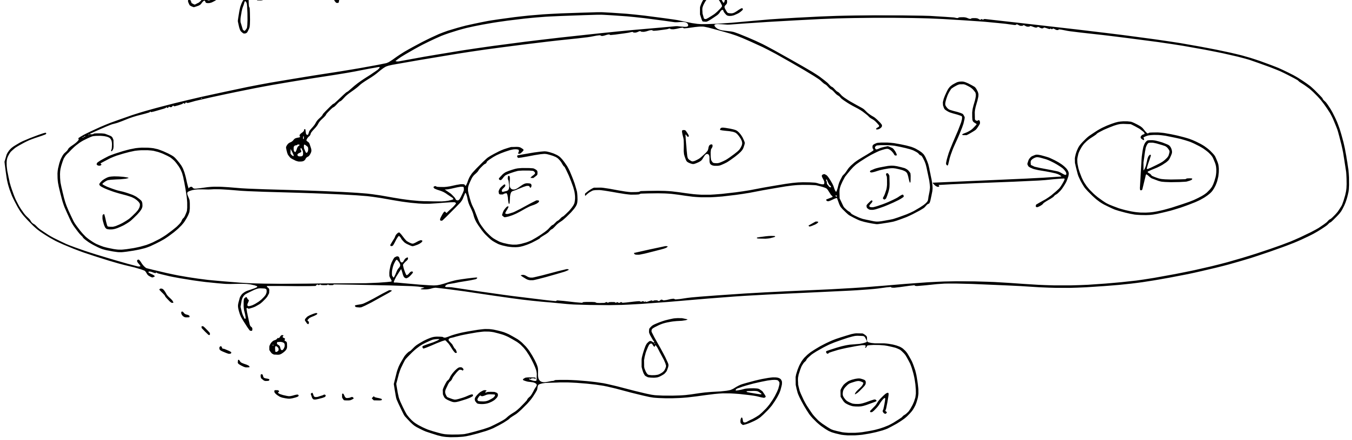
$$Y_i \Rightarrow \{S_{1,a}, \ldots S_{5,b}\}$$

any combination of $(\ldots\ldots) \Rightarrow i$

$$\frac{dY_i}{dt}$$

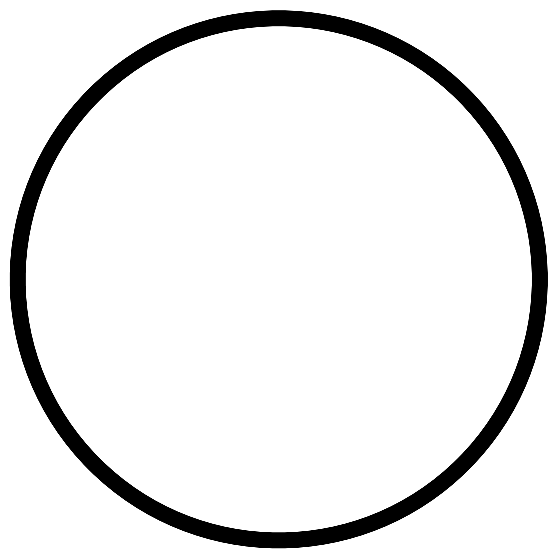
$$\sum_{i=1}^{M} \frac{dY_i}{dt} = 0 \Rightarrow \sum Y_i = \text{const.}$$

$\Rightarrow$ agents are in a mix of states

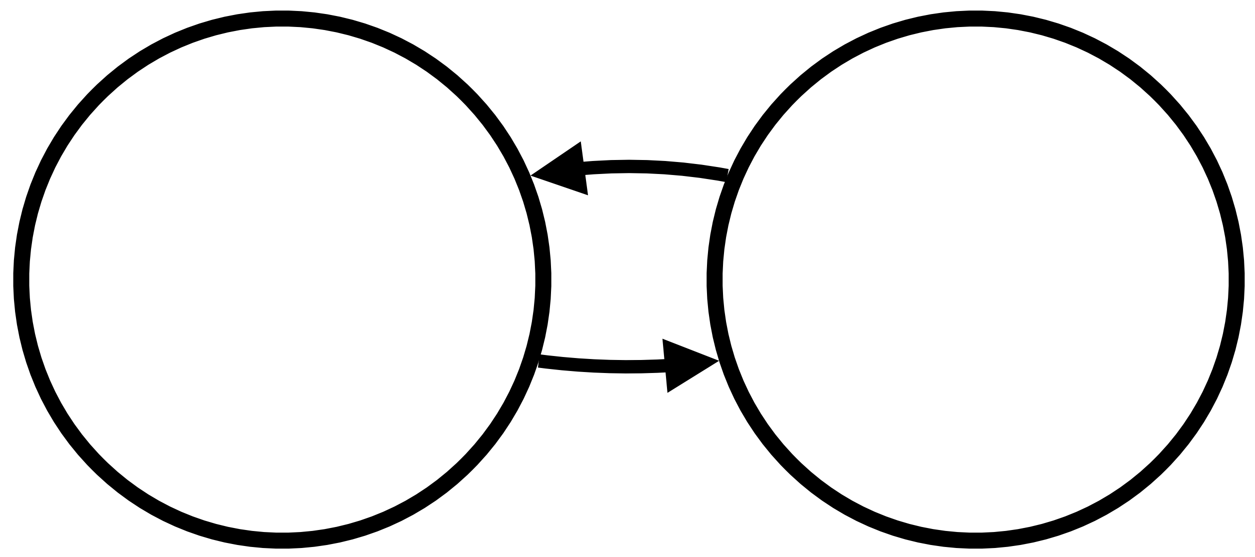


“The SIR model is unrealistic:
Spread is spatial and age-dependent”

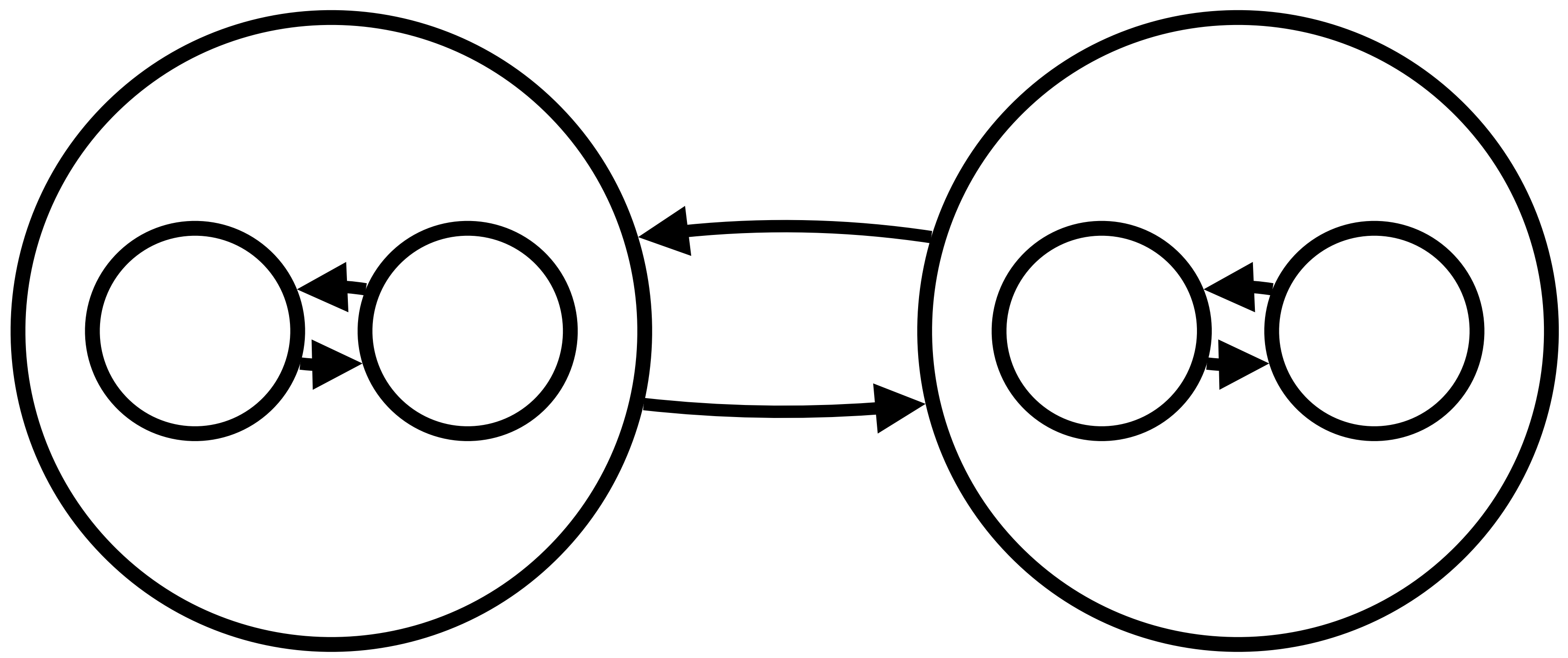
Multi-Scale Analyses



Spread in
Single Population



Spread between
Populations

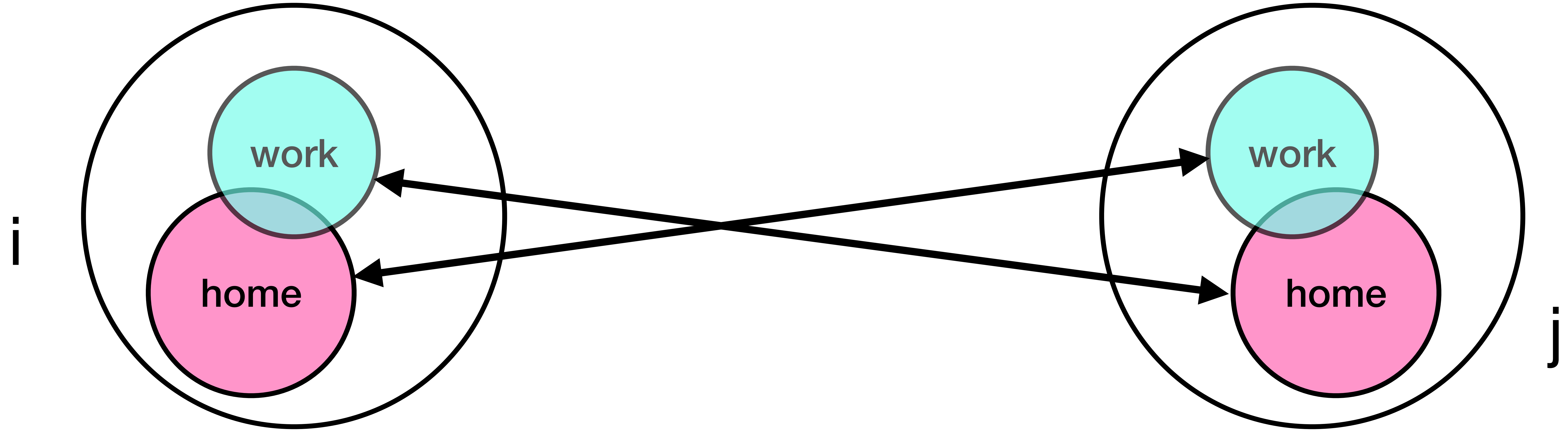


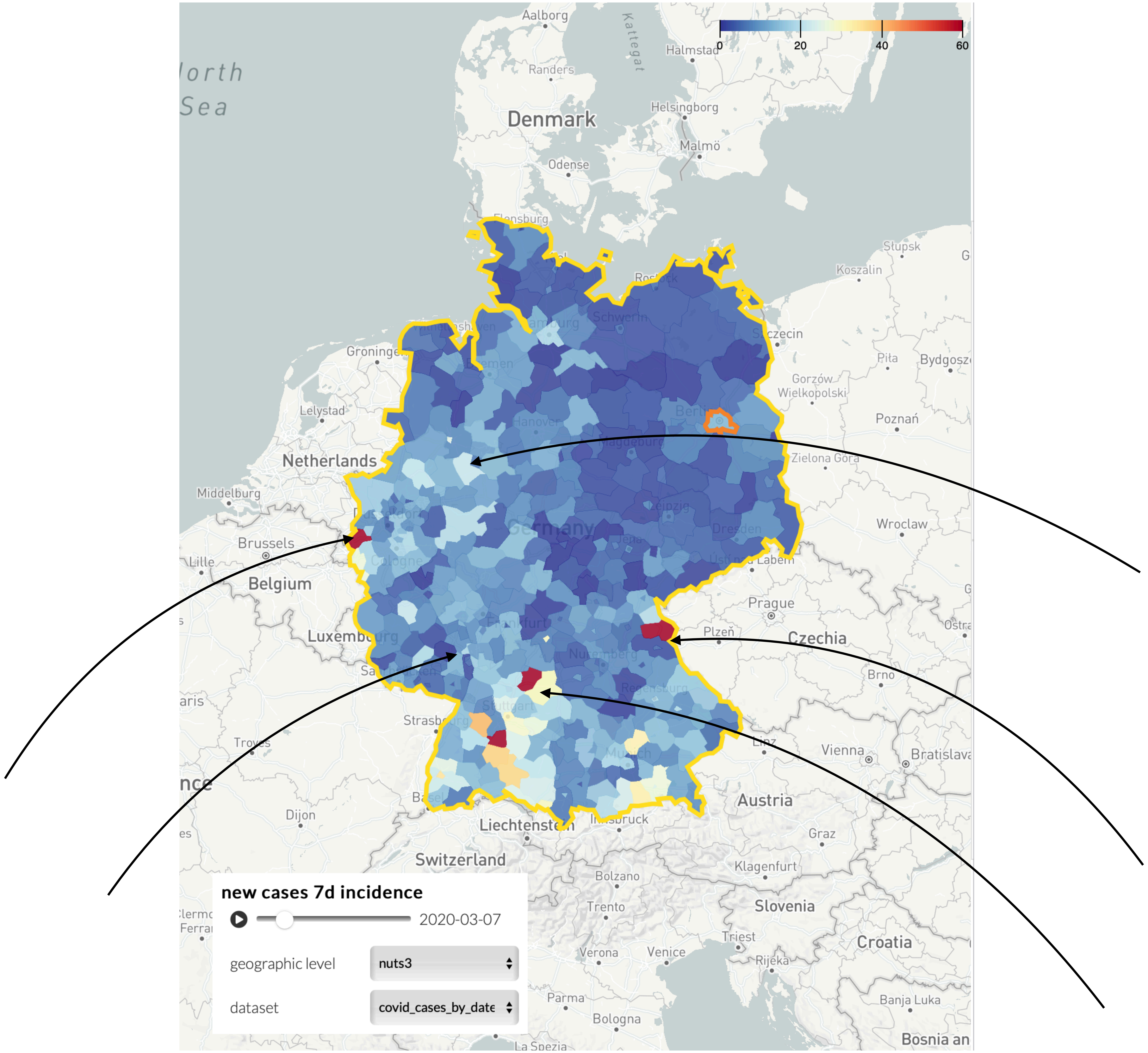
Diffusive Spread between
Regions of Populations

Spread in Commuter Models

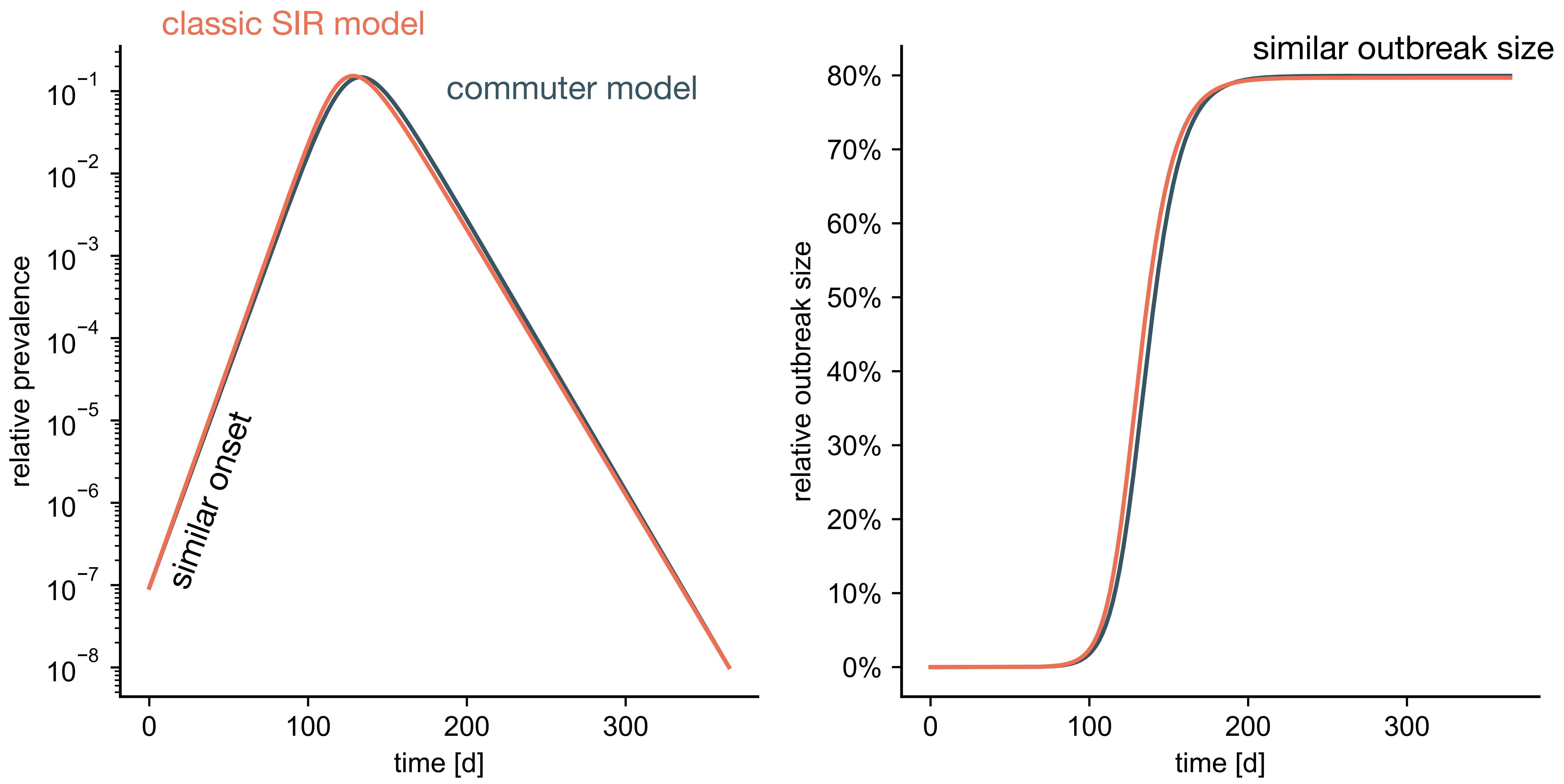
$$\frac{\mathrm{d}S_{ji}}{\mathrm{d}t} = -S_{ji}\left(\lambda_i^{\mathrm{home}} + \lambda_j^{\mathrm{work}}\right) = -S_{ji}\left(\frac{\beta}{2}\frac{\sum_k^m I_{ki}}{\sum_k^m N_{ki}^{(\mathrm{pop})}} + \frac{\beta}{2}\frac{\sum_k^m I_{jk}}{\sum_k^m N_{jk}^{(\mathrm{pop})}}\right),$$

- individuals living in i and working in j
- can get infected by individuals living in i
- can get infected by individuals working in j





0
20
40
60
new cases 7d incidence
2020-03-07
geographic level
nuts3
dataset
covid_cases_by_date
Denmark
Netherlands
Belgium
Czechia
Austria
Switzerland
Slovenia
Croatia



classic SIR model
commuter model
similar onset
relative prevalence
10^{-1}
10^{-2}
10^{-3}
10^{-4}
10^{-5}
10^{-6}
10^{-7}
10^{-8}
0
100
200
300
time [d]
similar outbreak size
relative outbreak size
80%
70%
60%
50%
40%
30%
20%
10%
0%
0
100
200
300
time [d]

Multi-Scale Analyses

$$\frac{dS}{dt} = -\eta SI$$
$$\frac{dI}{dt} = +\eta SI - \rho I$$
$$\frac{dR}{dt} = +\rho I$$

$$\frac{\mathrm{d}S_{ji}}{\mathrm{d}t} = -S_{ji}\left(\lambda_i^{\mathrm{home}} + \lambda_j^{\mathrm{work}}\right) = -S_{ji}\left(\frac{\beta}{2}\frac{\sum_k^m I_{ki}}{\sum_k^m N_{ki}^{(\mathrm{pop})}} + \frac{\beta}{2}\frac{\sum_k^m I_{jk}}{\sum_k^m N_{jk}^{(\mathrm{pop})}}\right),$$

$$\begin{aligned}
\partial_t I_n &= \alpha S_n I_n / N_n - \beta I_n + \sum_{m \neq n} (w_{nm} I_m - w_{mn} I_n) \\
\partial_t S_n &= -\alpha S_n I_n / N_n + \sum_{m \neq n} (w_{nm} S_m - w_{mn} S_n) \\
\partial_t R_n &= \beta I_n + \sum_{m \neq n} (w_{nm} R_m - w_{mn} R_n)
\end{aligned}$$

General Model

$$\frac{d}{dt}Y_i = \sum_{j,k} \alpha_{ijk}(t, Y_1, Y_2, \ldots)Y_jY_k/N + \sum_j \beta_{ij}(t, Y_1, Y_2, \ldots \})Y_j$$

transmission transition

linearized around disease-free state

$$\partial_t Y = (T + \Sigma)Y$$

infected states

transmission matrix in disease-free state

transmission matrix in disease-free state

General Model

$$\partial_t Y = (T + \Sigma) Y$$

basic reproduction number

$$\boxed{R_0 = \eta/\rho}$$

General Model

$$\partial_t Y = (T + \Sigma)Y$$

basic reproduction number

$$\boxed{R_0 = \eta/\rho}$$

next-generation matrix

$$\hat{R} = -T\Sigma^{-1}$$

General Model

basic reproduction number

$$\boxed{R_0 = \eta/\rho}$$

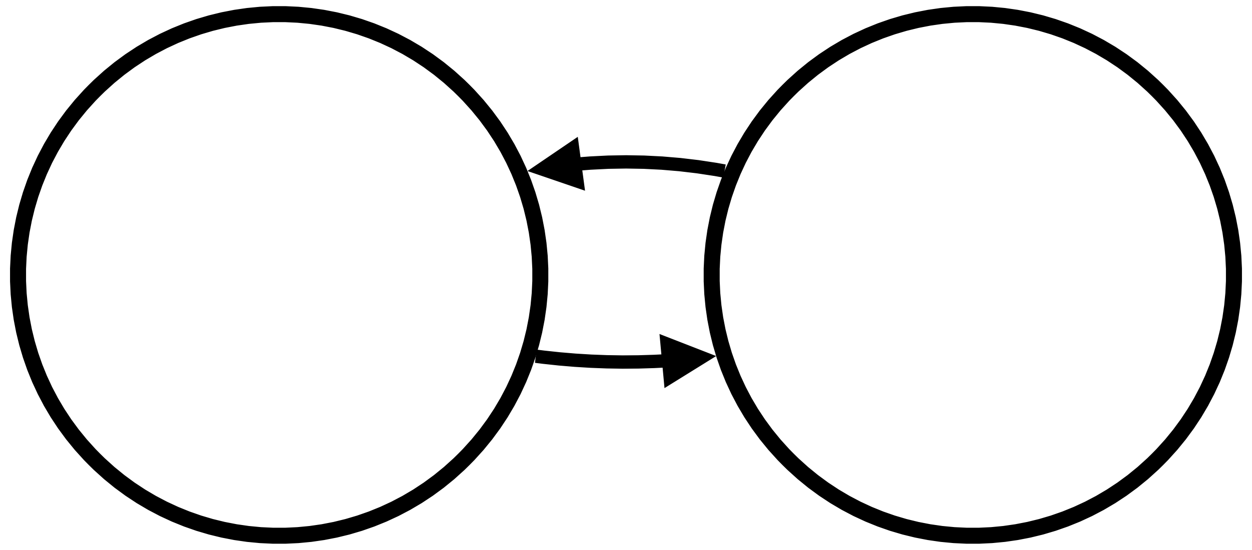
$$\partial_t Y = (T + \Sigma)Y$$

next-generation matrix

$$\hat{R} = -T\Sigma^{-1}$$

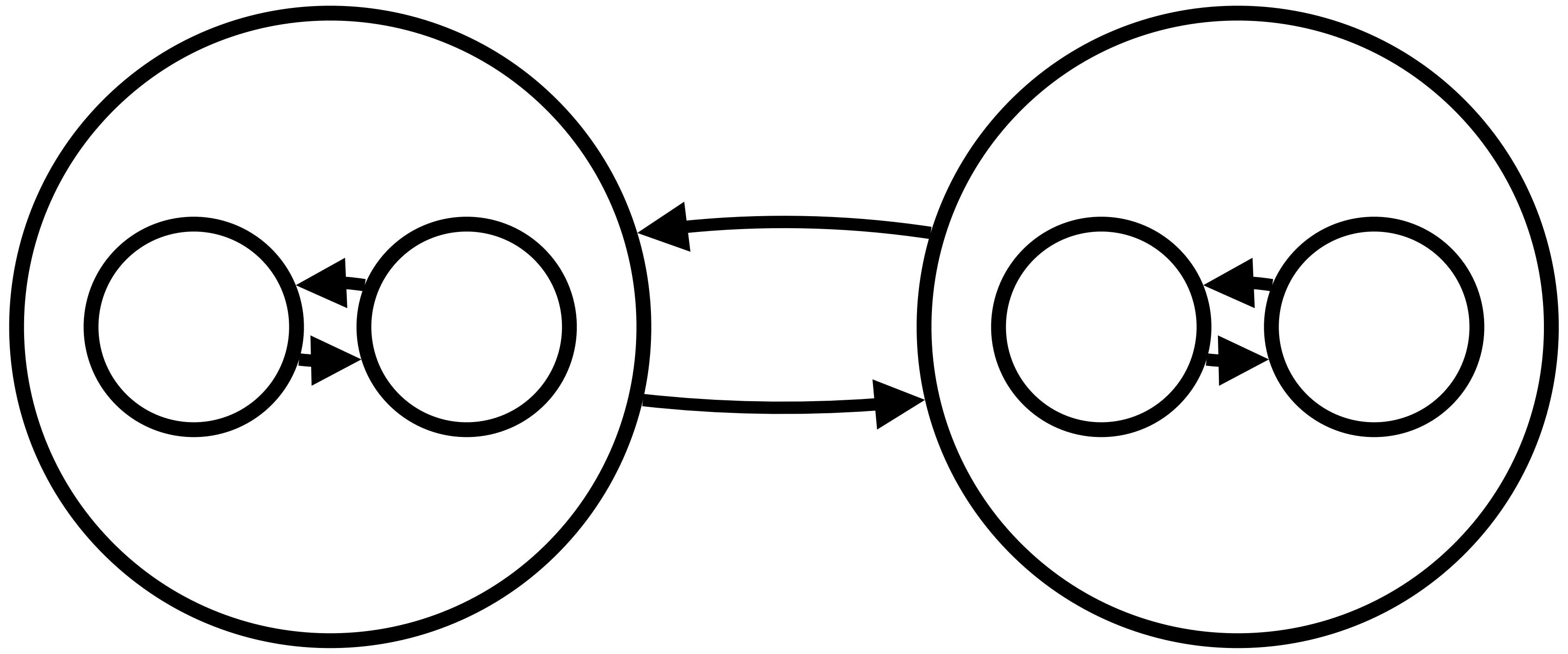
$$R_0 = \text{spectral radius}(\hat{R})$$

if unmitigated, system will always approach eigenvector of $\hat{R}$



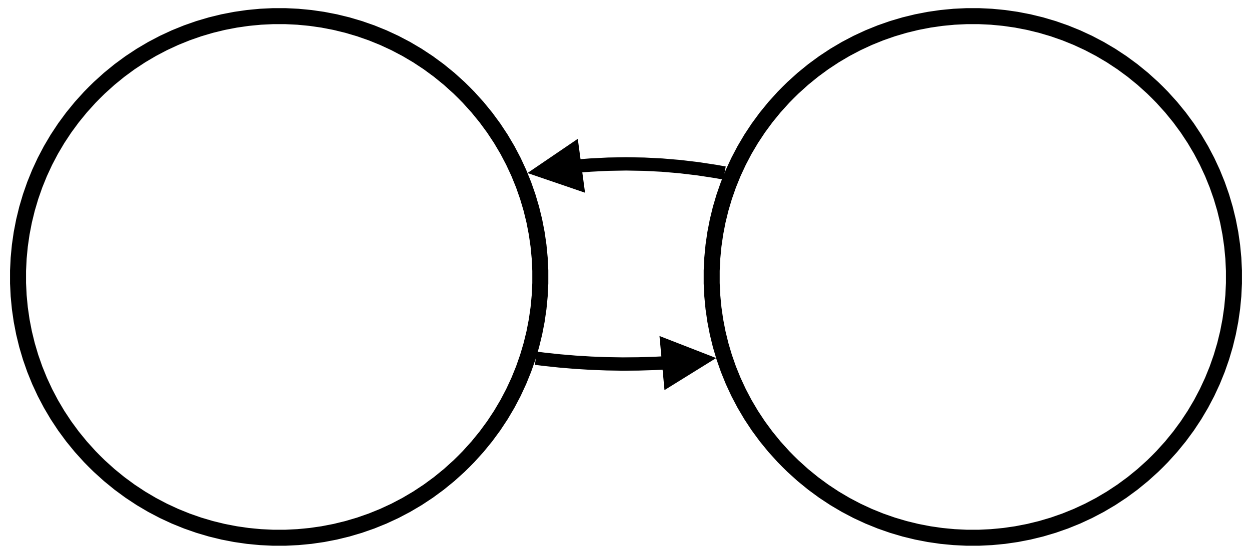
Spread between
Populations

compute eigenvectors of next-generation matrix

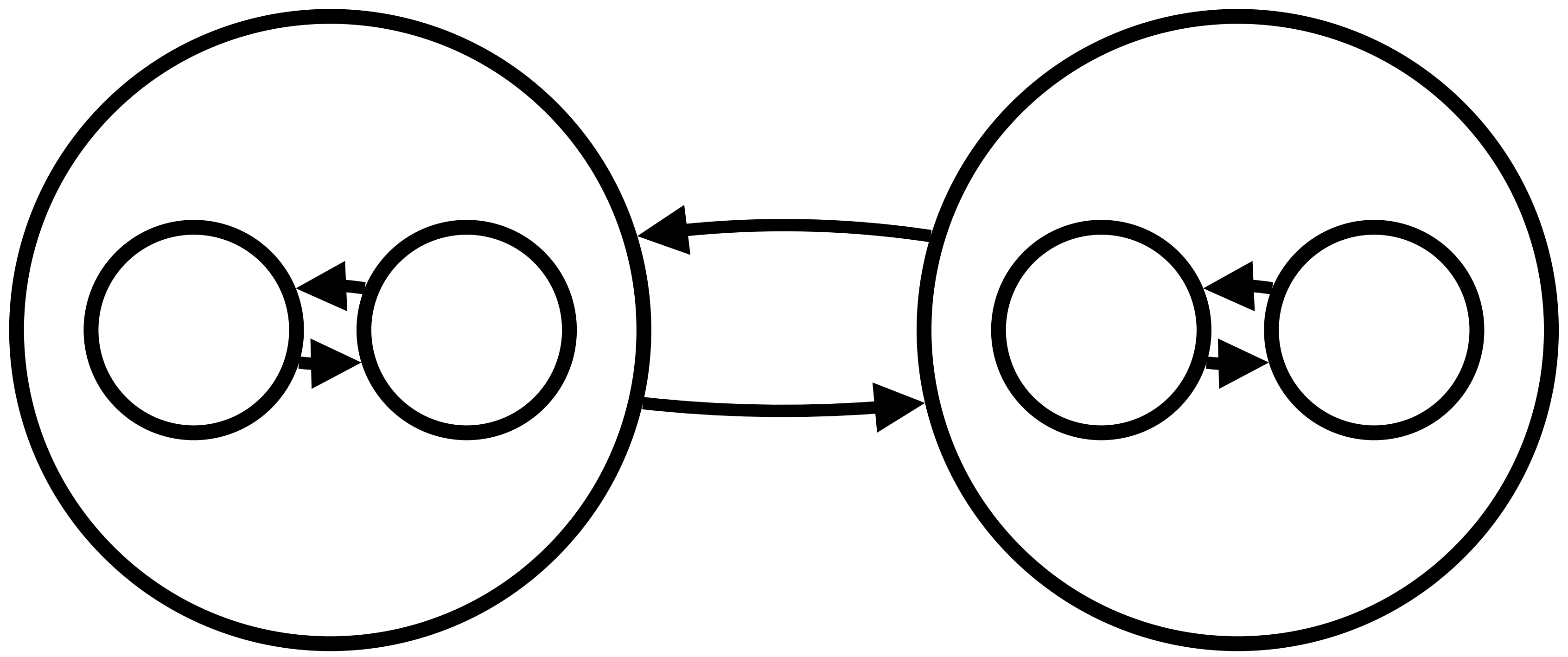


Diffusive Spread between
Regions of Populations

compute eigenvectors of next-generation matrix



Spread between
Populations



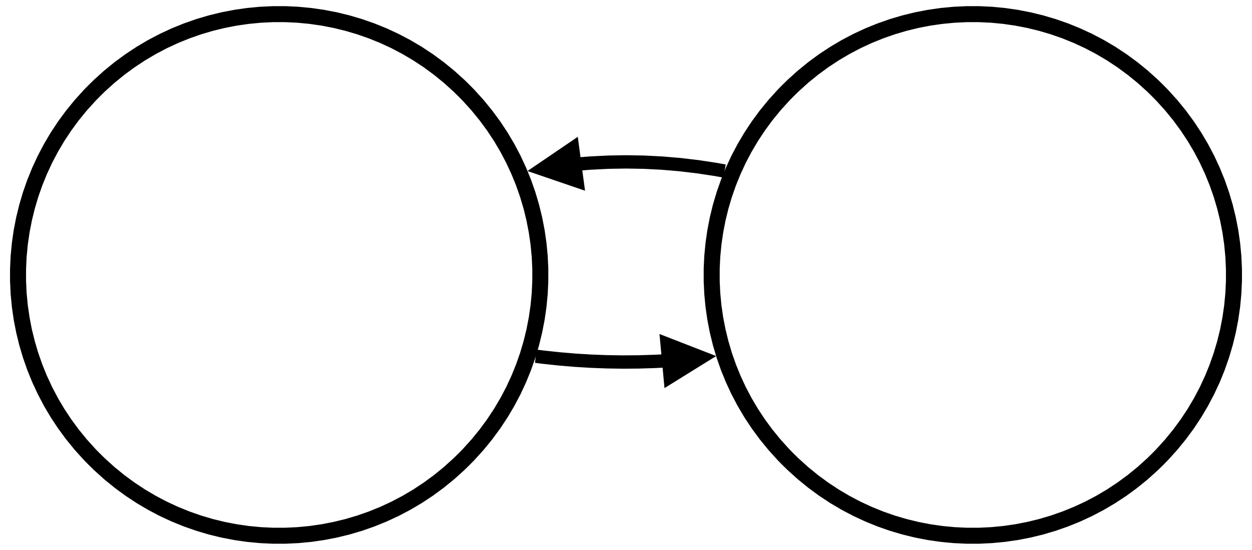
Diffusive Spread between
Regions of Populations

compute eigenvectors of next-generation matrix

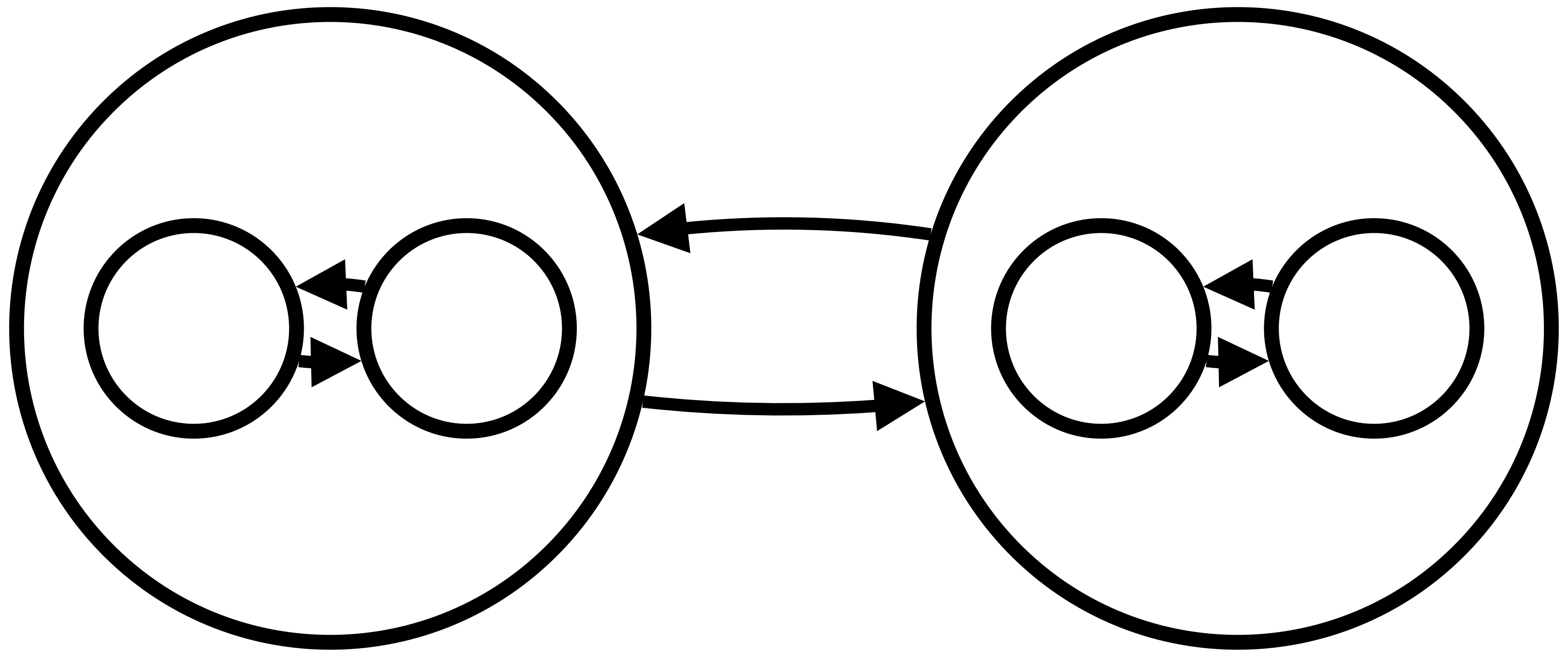
initiate simulation with outbreak in direction of eigenvector

compute eigenvectors of next-generation matrix

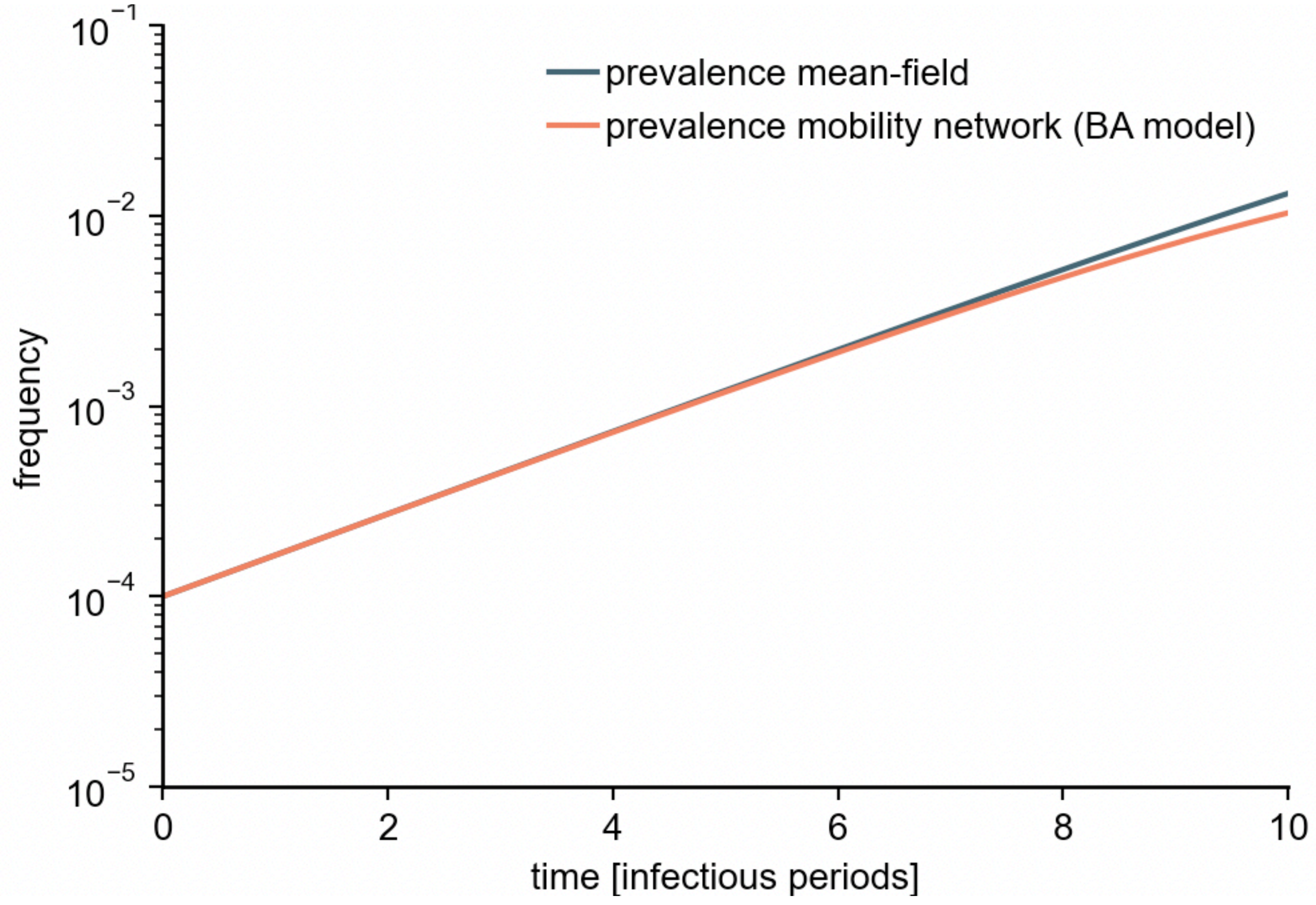
initiate simulation with outbreak in direction of eigenvector

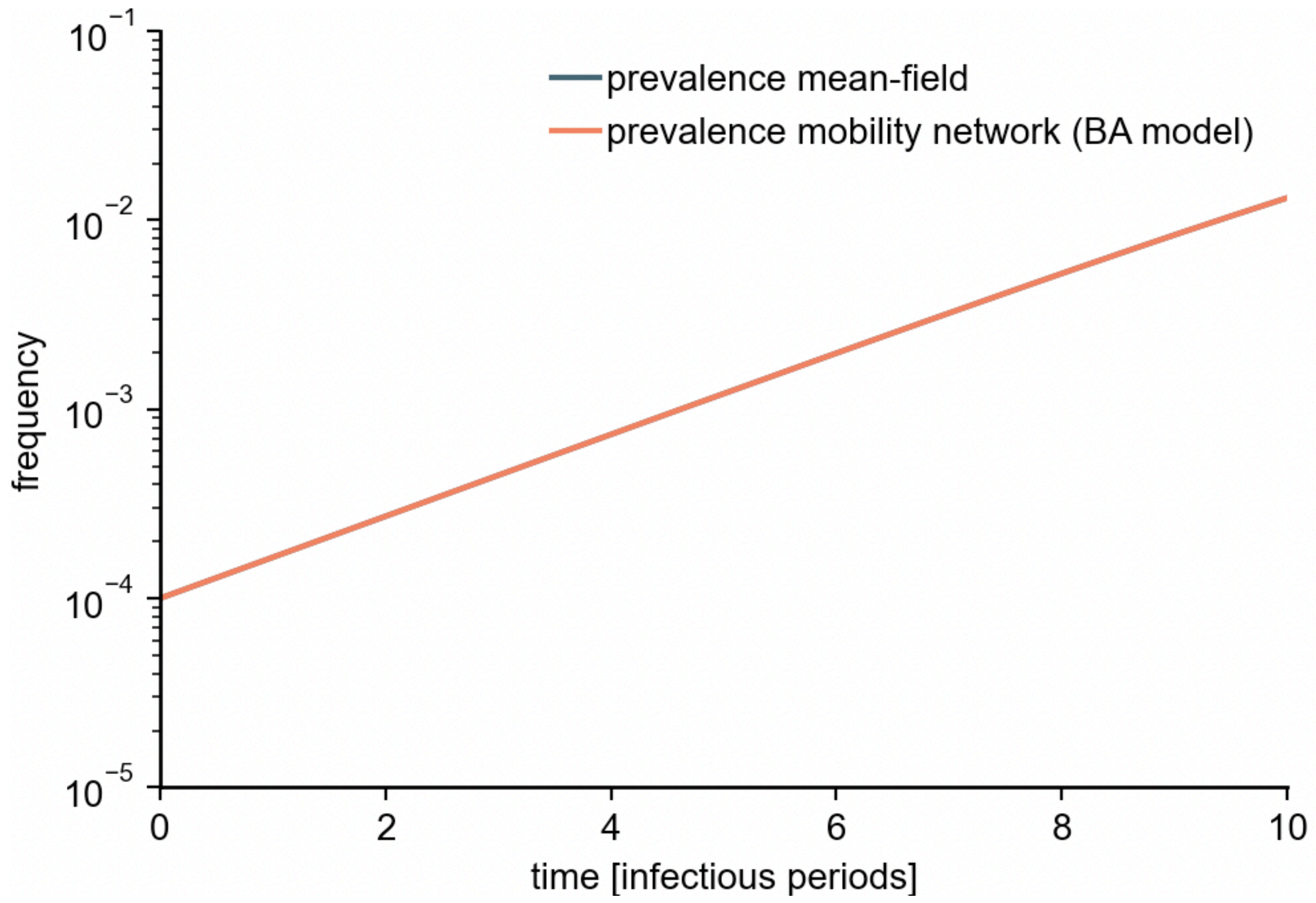


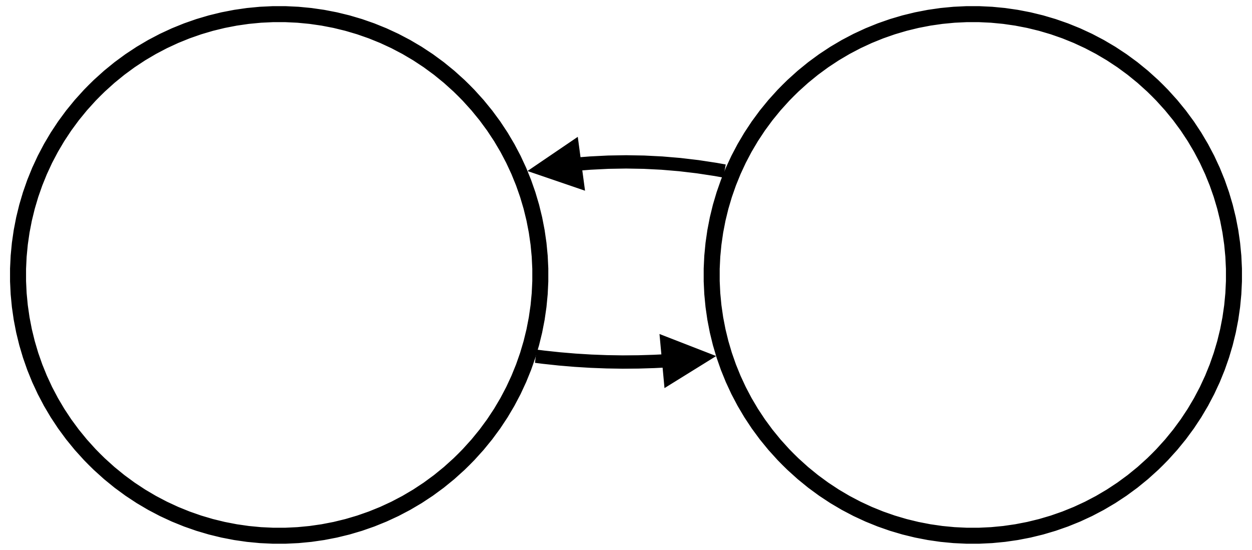
Spread between
Populations



Diffusive Spread between
Regions of Populations

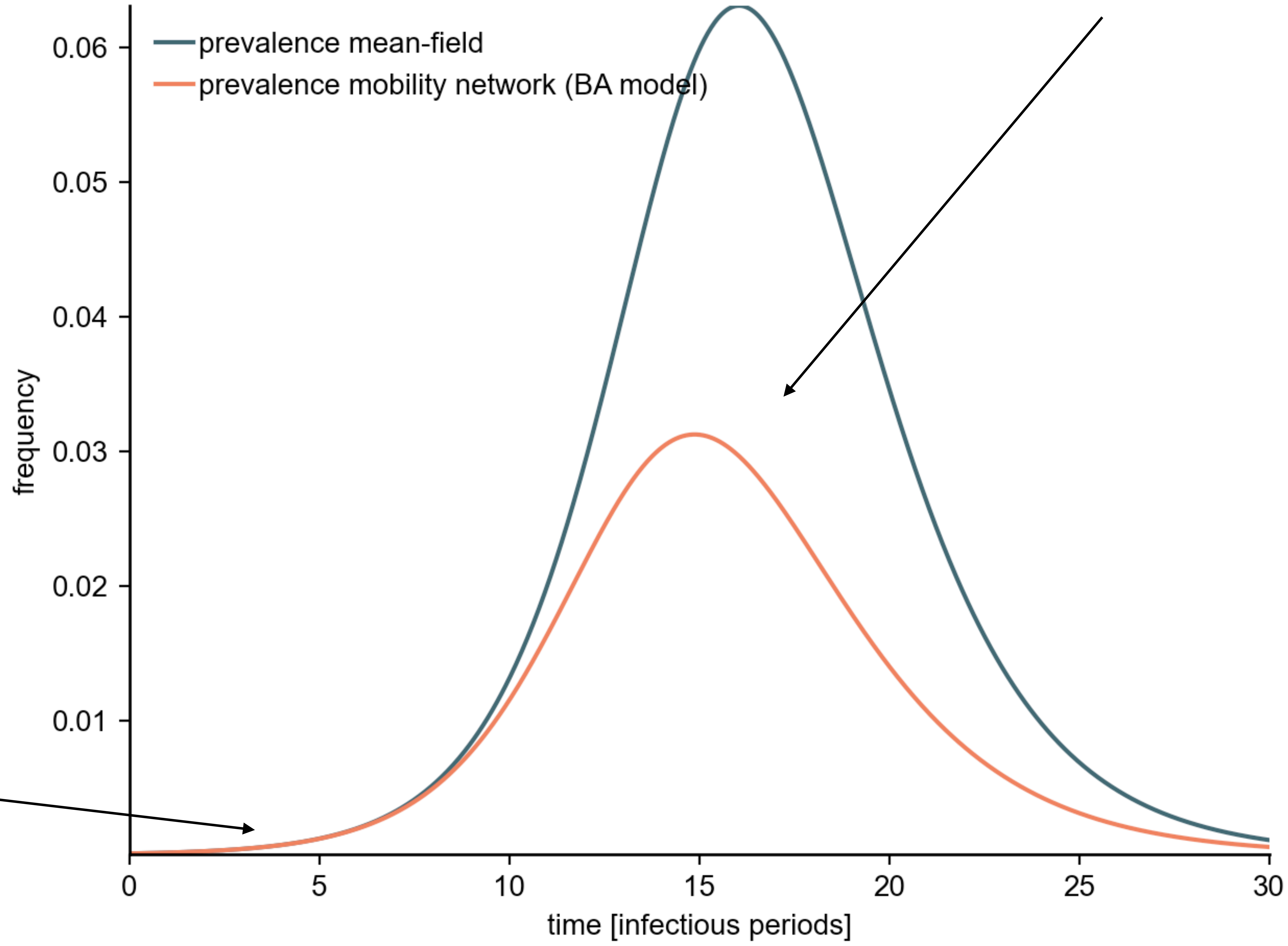






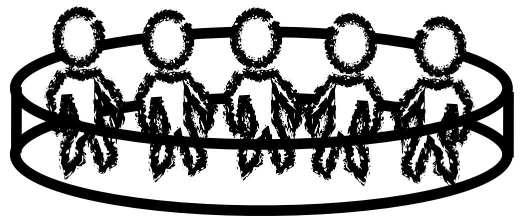
Spread between
Populations

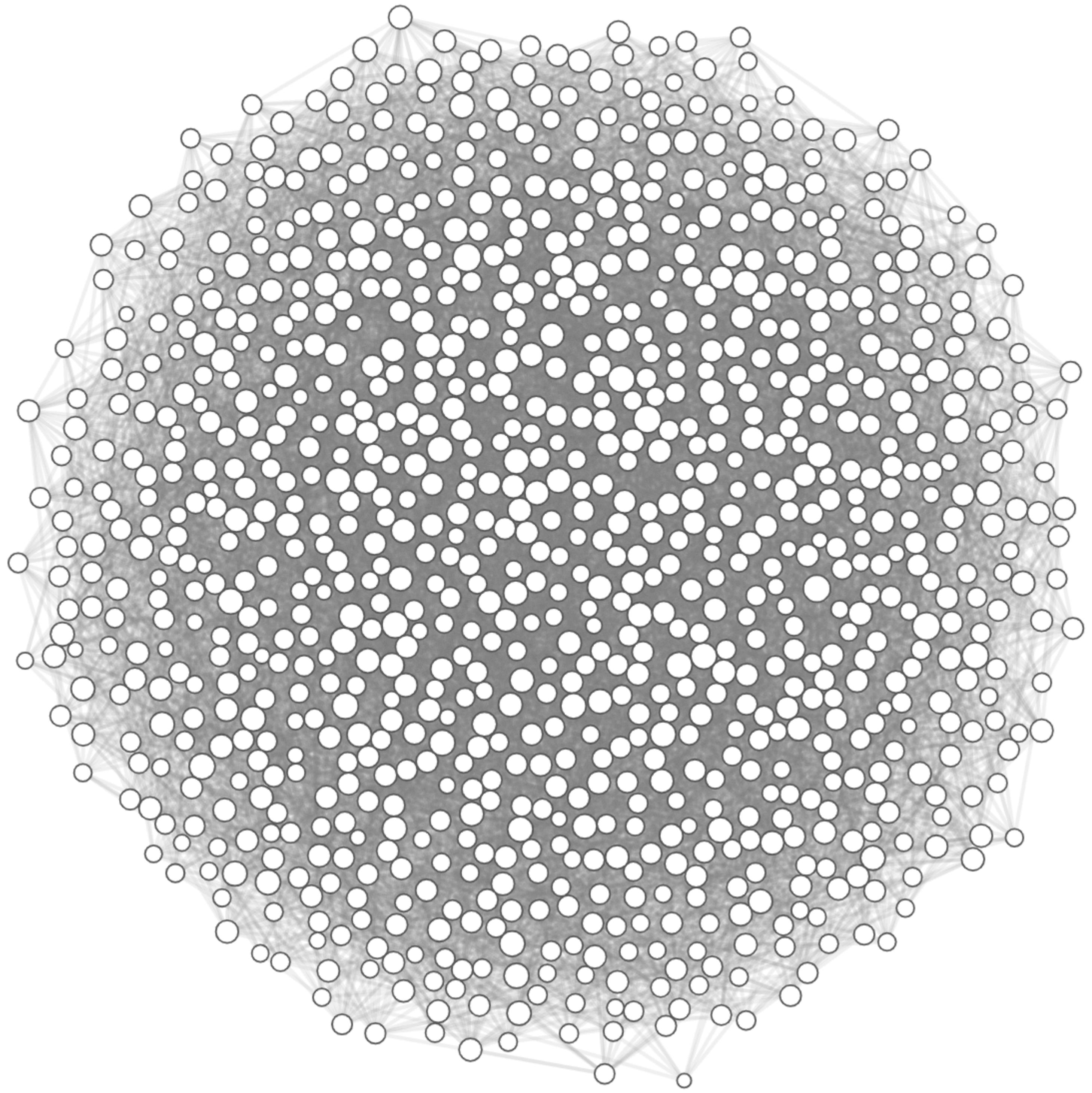
outcome different



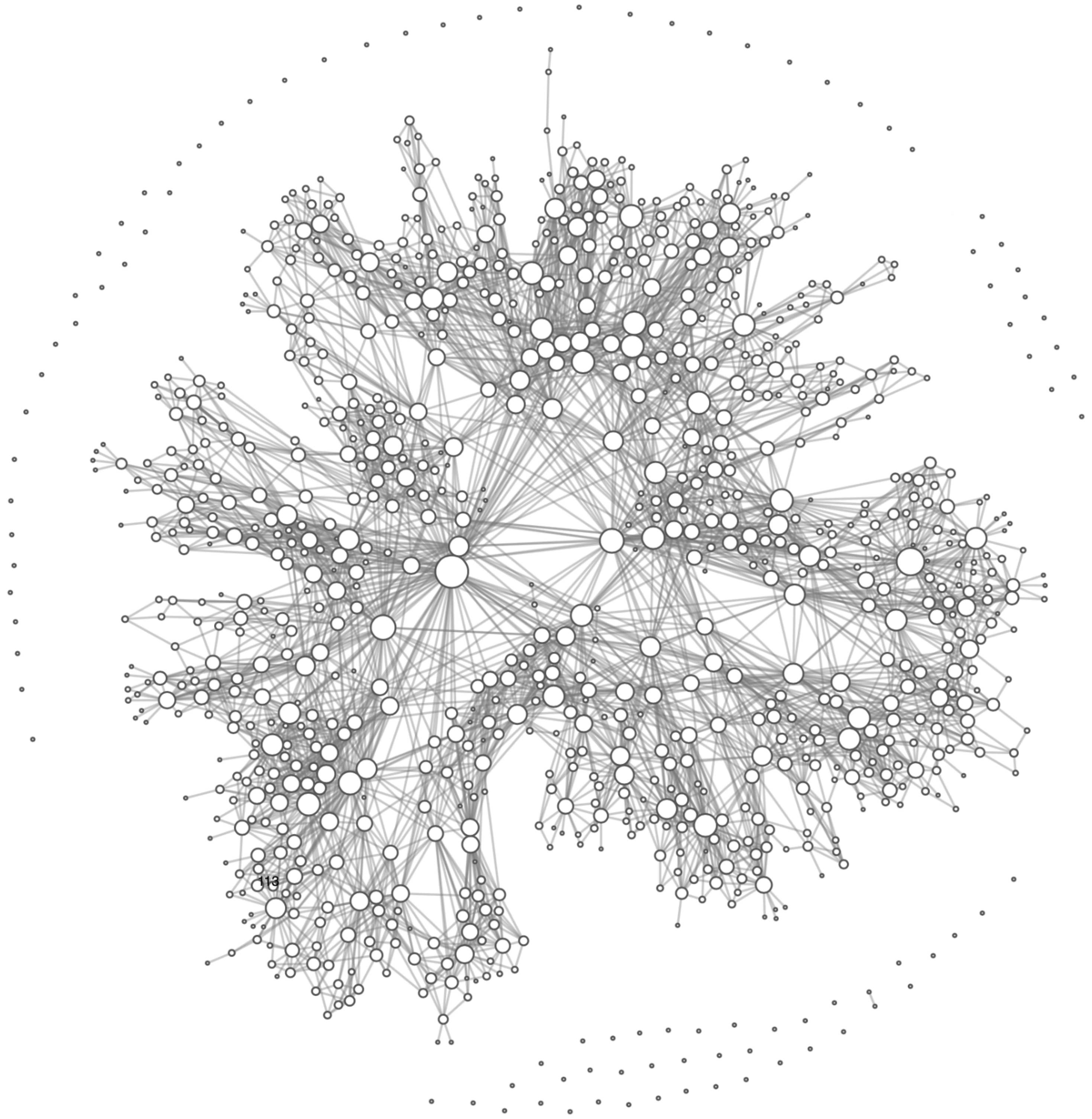
onset equal

“Agent-based is always better because it increases realism”





- non-local
- small-world
- homogeneous contact behavior



- locally-clustered
- small-world
- heterogeneous contact behavior

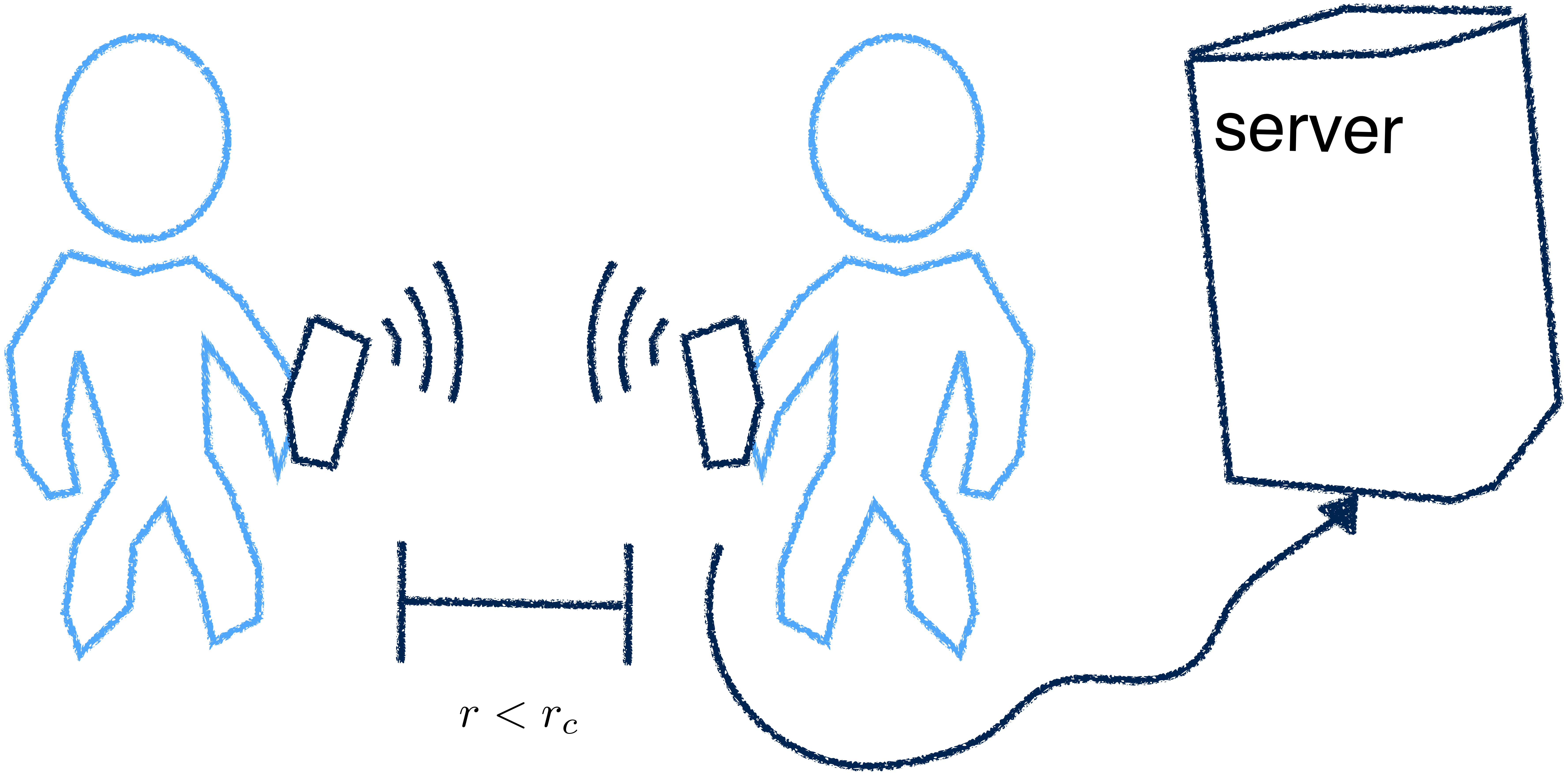
Comment on this paper

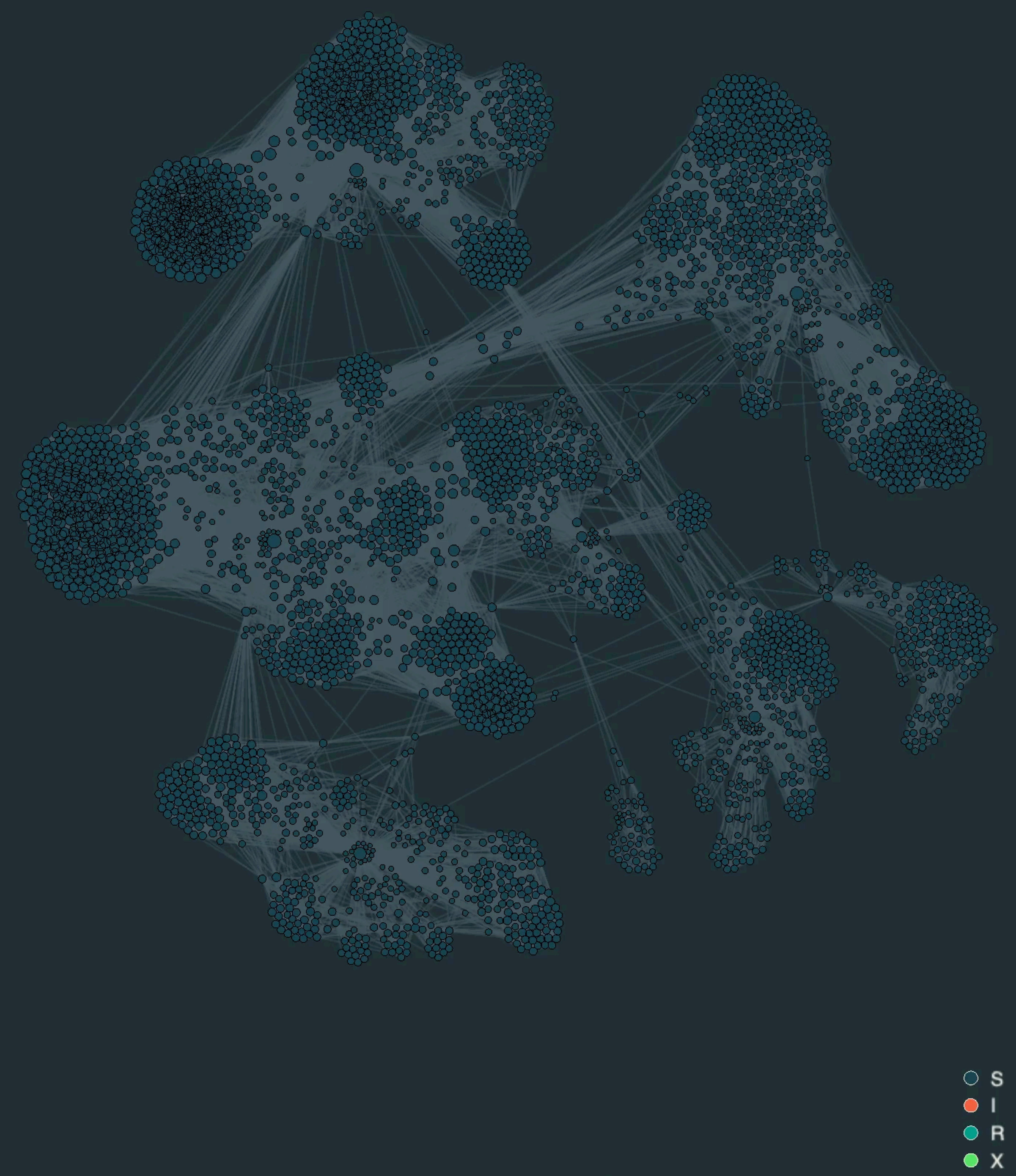
Digital contact tracing contributes little to COVID-19 outbreak containment

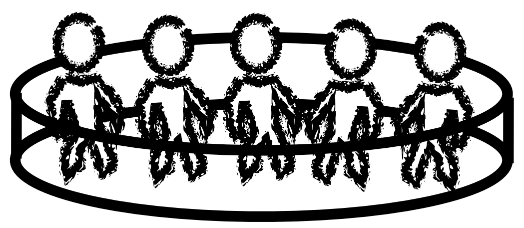
A. Burdinski, D. Brockmann, B. F. Maier

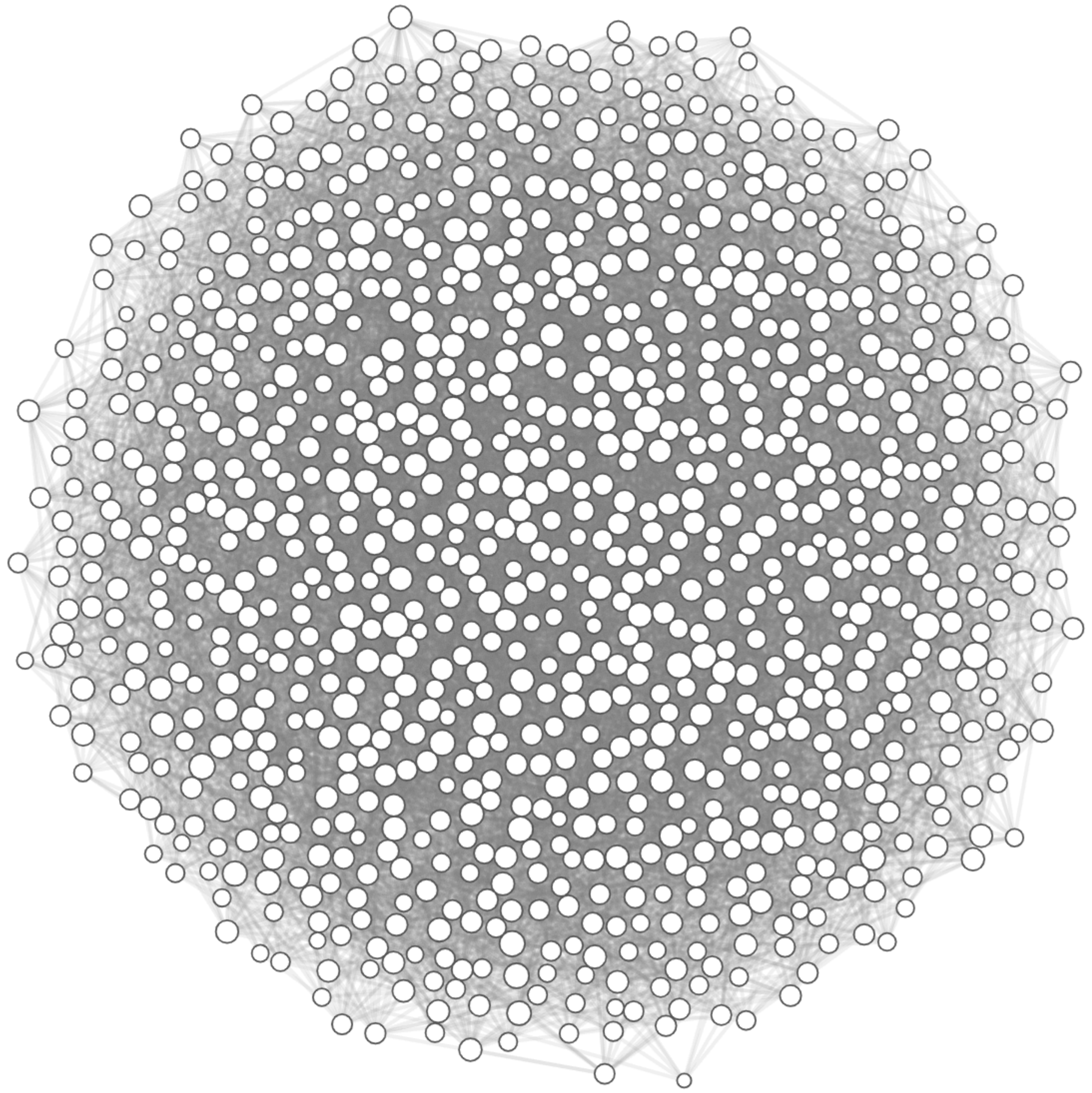
doi: https://doi.org/10.1101/2021.06.21.21259258

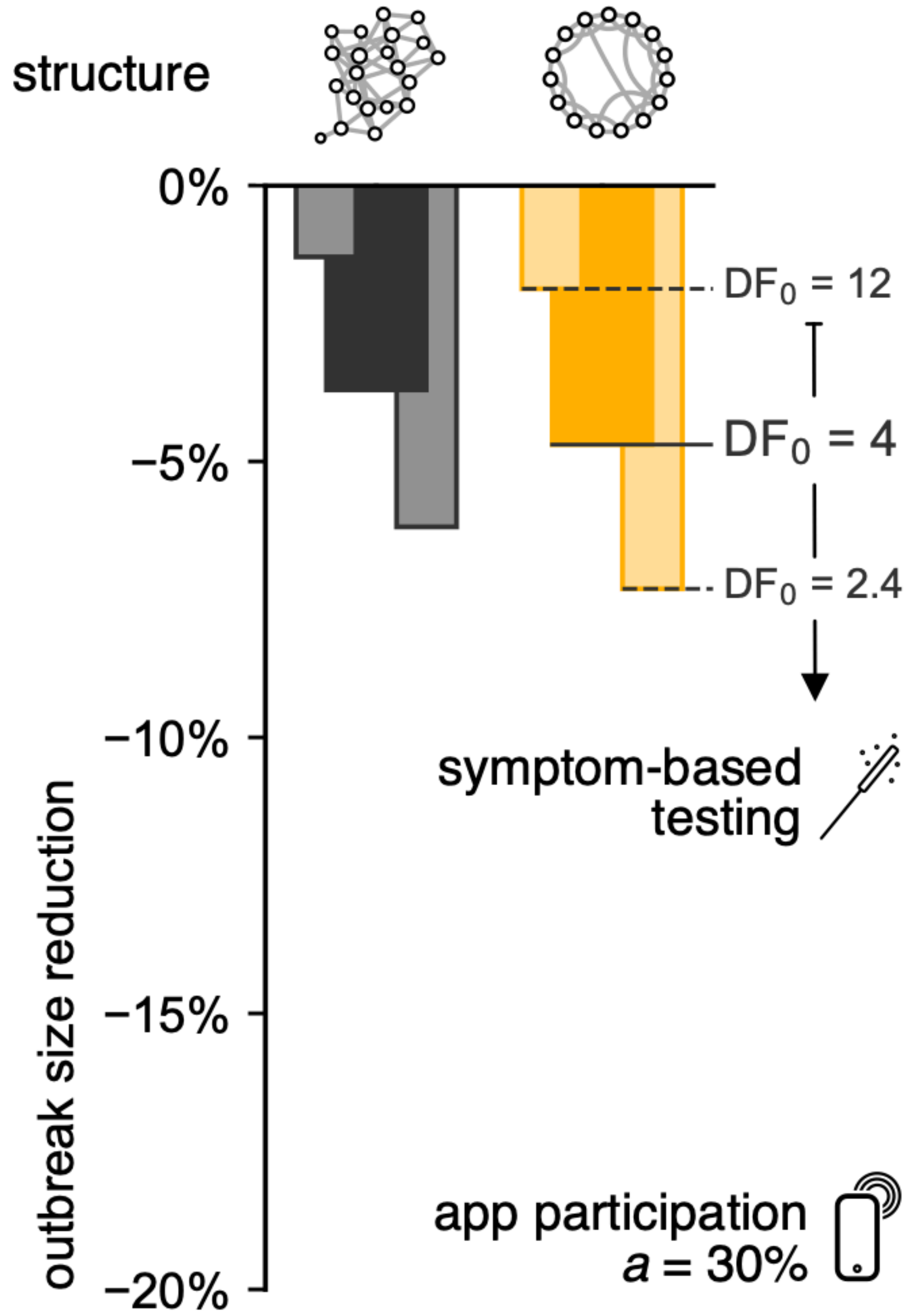
Angelique
Burdinski

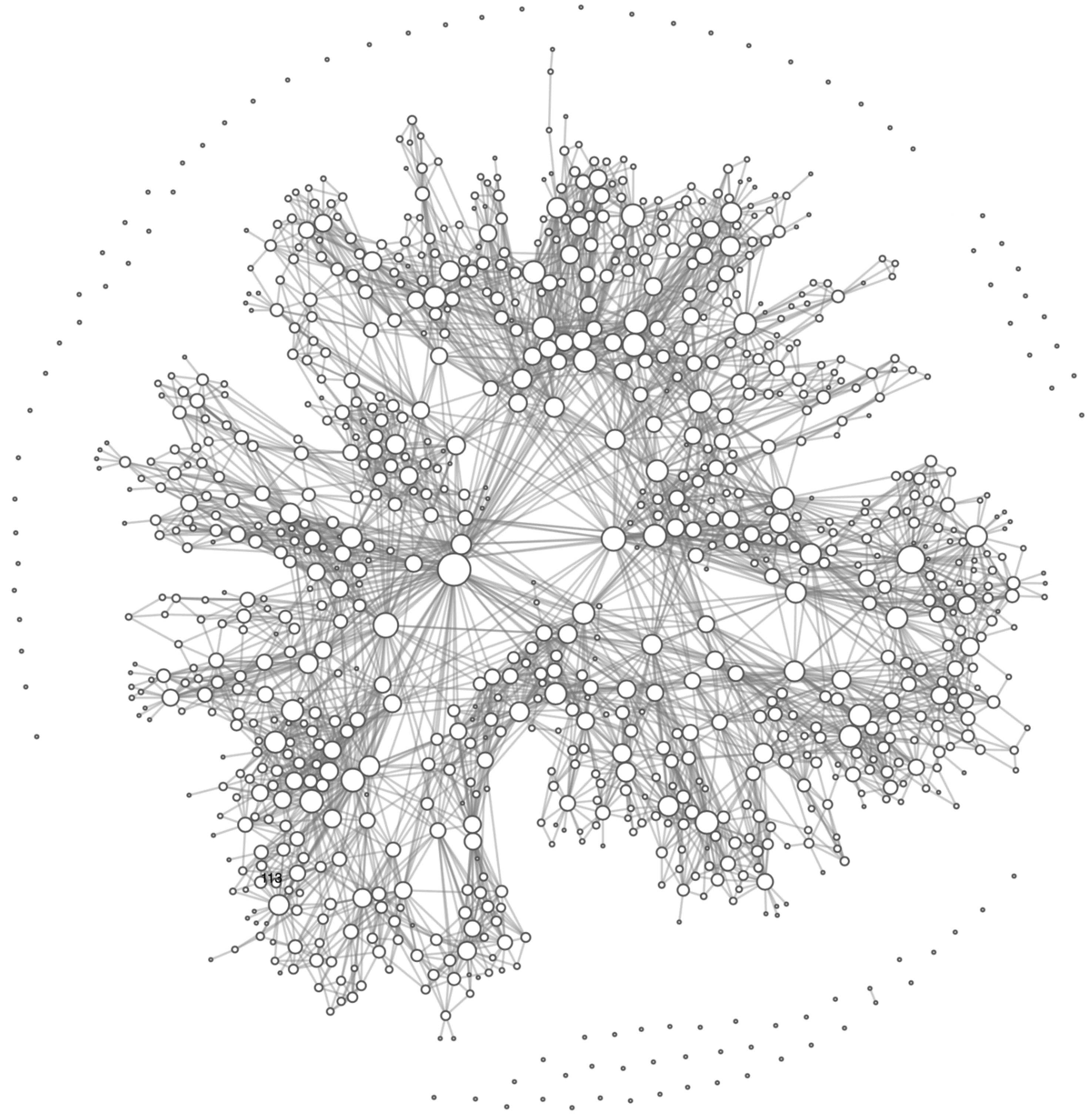

server
$r < r_c$


S
I
R
X









- non-local
- small-world
- homogeneous contact behavior

- locally-clustered
- small-world
- heterogeneous contact behavior