

# LIFE DATA EPIDEMIOLOGY

*lect. 3: application of metapopulation models*

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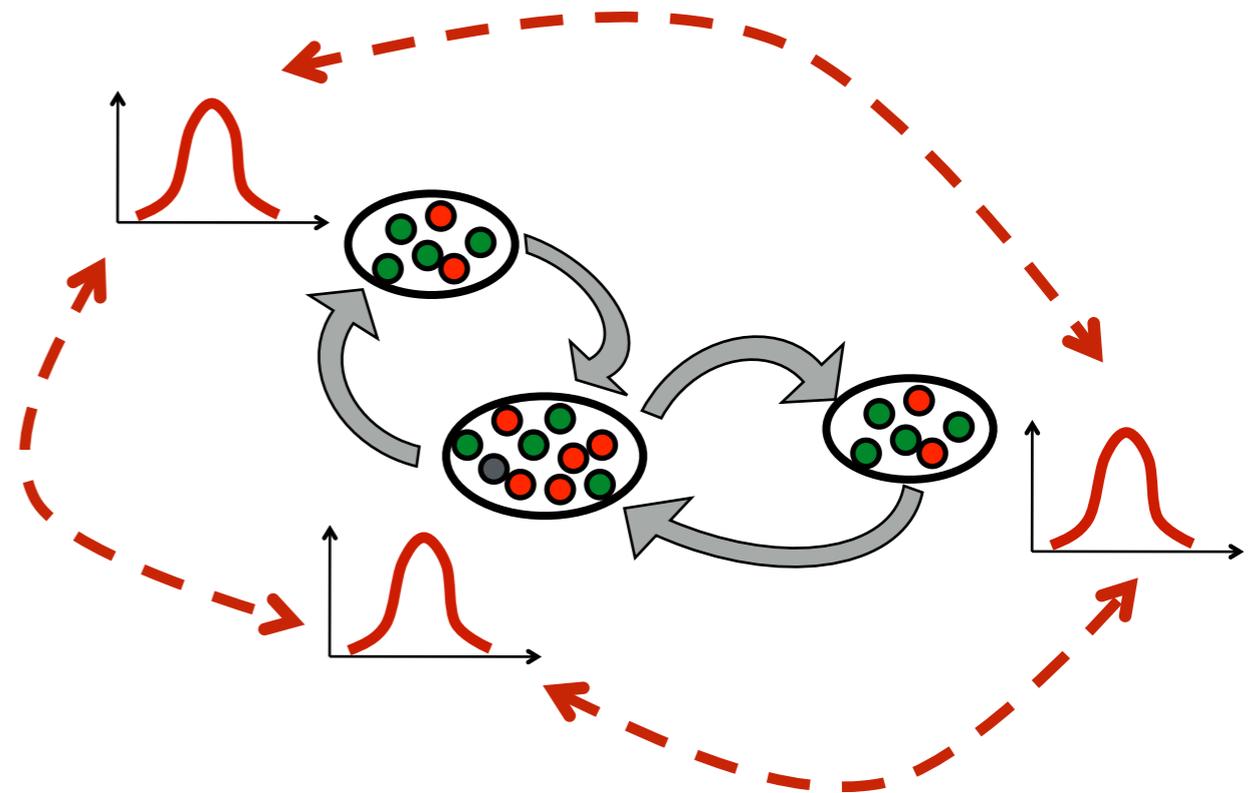
# SIR metapopulation model: markovian mobility

$$\frac{dS_i}{dt} = -\beta \frac{I_i(t)S_i(t)}{N_i} + \Omega_i^S$$

$$\frac{dI_i}{dt} = \beta \frac{I_i(t)S_i(t)}{N_i} - \mu I_i(t) + \Omega_i^I$$

$$\frac{dR_i}{dt} = \mu I_i(t) + \Omega_i^R$$

$$\Omega_i^X = \sum_j \frac{w_{ji}}{N_j} X_j - \frac{w_{ij}}{N_i} X_i$$



# SIR metapopulation model: markovian mobility

What can I do with that?

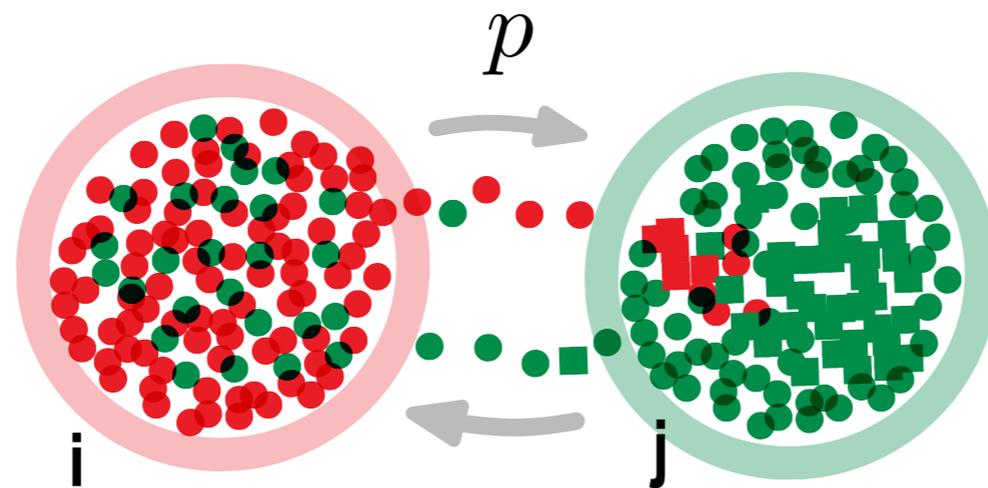
- analytical understanding
  - **spatial propagation & predictability**
  - global invasion threshold
- computer simulations

# spatial propagation

Dynamics of spatial spread above the epidemic threshold

An epidemic starts in a given city  $i$  how does it spread to  $j, h$ , etc.?

**seeding time (o arrival time),  $t_{\text{seeding}}$** : time of arrival of the first case in patch  $j$



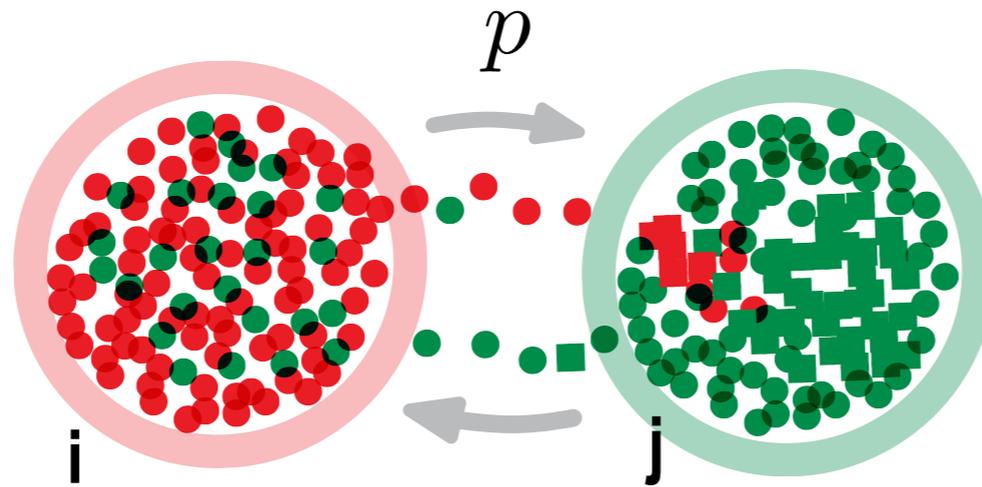
$p$  traveling probability from  $i$  to  $j$

$I(t)$  infectious in  $i$

probability that an infectious arrives in  $j$  at time  $t$ :

$$\left[ 1 - (1 - p)^{I(t) dt} \right]$$

# spatial propagation



probability that an infectious arrives in  $j$  at time  $t$ :  $\left[ 1 - (1 - p)^{I(t dt)} \right]$

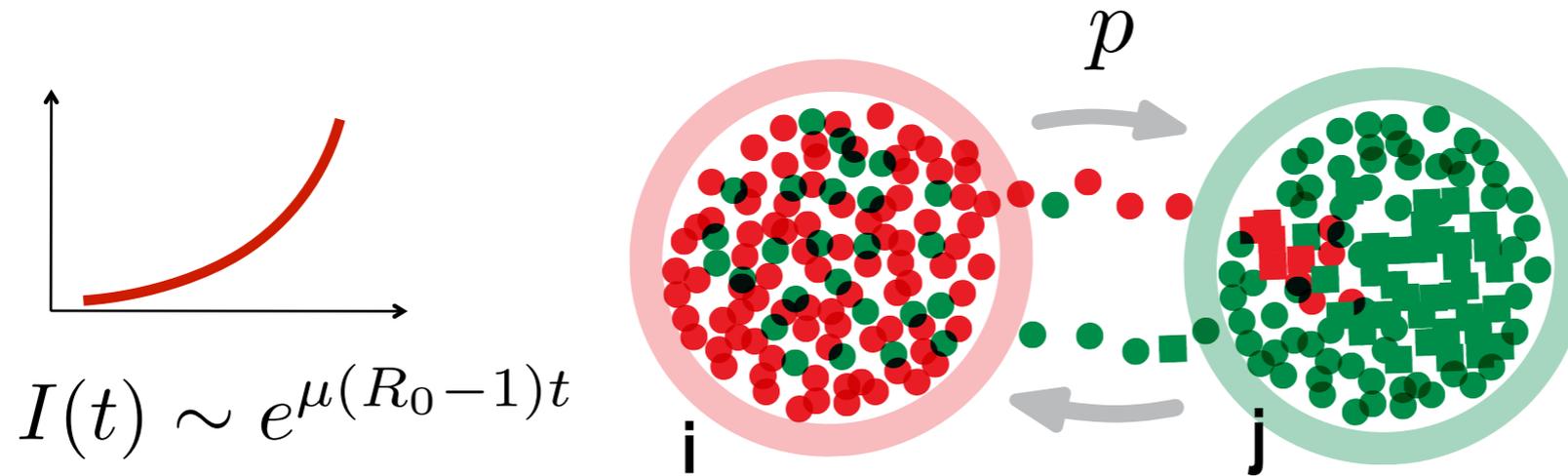
probability that the **first** infectious arrives in  $j$  at time  $t$ :

$$P(t_{\text{seeding}} = t dt) = \prod_{s=1}^{t-1} (1 - p)^{I(s dt)} \times \left[ 1 - (1 - p)^{I(t dt)} \right]$$

↓  $p \rightarrow 0$

$$P(t_{\text{seeding}} = t) = p I(t) e^{-p \int_0^t I(s) ds}$$

# spatial propagation



$$I(t) \sim e^{\mu(R_0-1)t}$$

$$P(t_{\text{seeding}} = t) = p I(t) e^{-p \int_0^t I(s) ds}$$

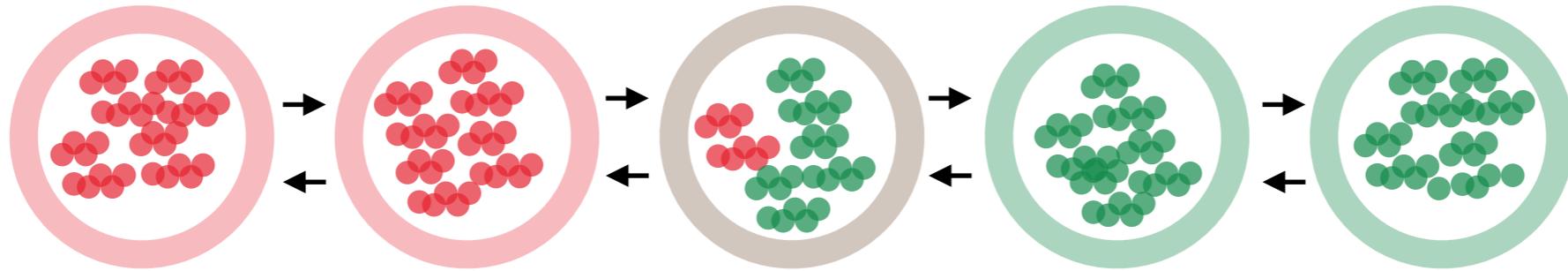
$$a = \mu(R_0 - 1)$$

$$P(t_{\text{seeding}} = t) = p e^{at} e^{-p a e^{at}}$$

**Gumbel distribution**

$$\langle t_{\text{seeding}} \rangle \simeq \frac{1}{a} \ln(p a)$$

# spatial propagation



**chain of identical cities (population  $N$  traveling weight  $p$ ):**

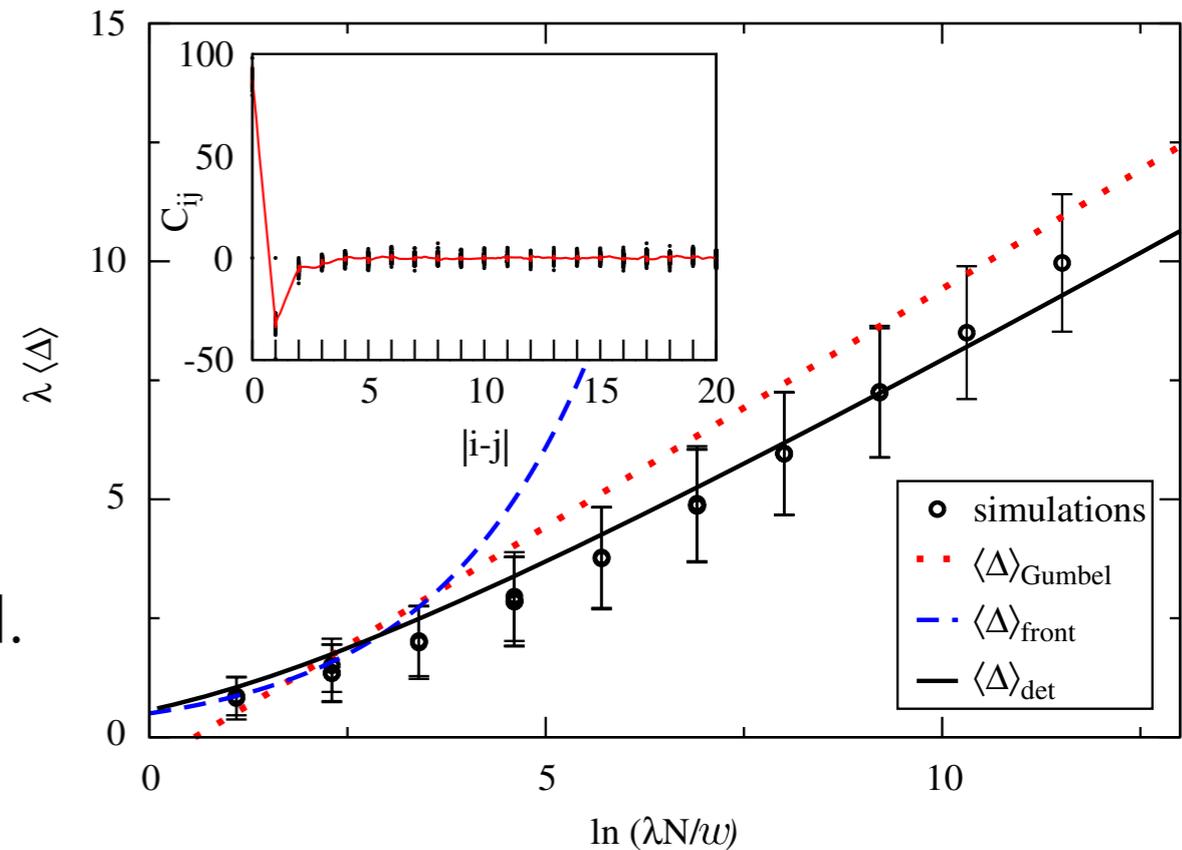
$$\langle t_{\text{seeding},i} \rangle - \langle t_{\text{seeding},i-1} \rangle = \Delta_i$$

$$\langle t_{\text{seeding},n} \rangle = \sum_{i=1}^n \Delta_i$$

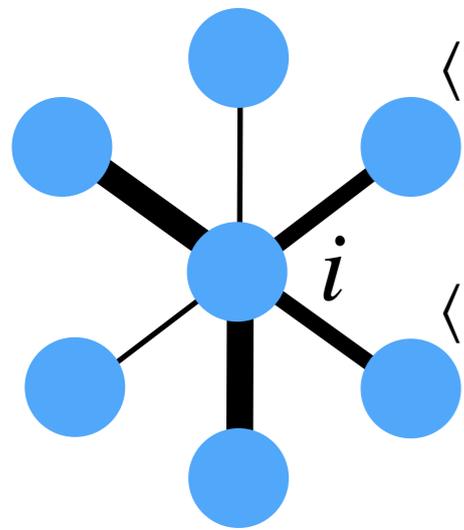
$\Delta_i$  are correlated and not identically distributed.

$$\text{Dimensional analysis: } a\Delta = F \left[ \frac{p}{a} \right]$$

The simple approximation  $\langle \Delta \rangle = \langle t_{\text{seeding},1} \rangle$  is not so bad!



# spatial propagation: spreading pathways



$$\langle t_{\text{seeding}, j} \rangle \simeq \frac{1}{a} \ln(p_{ij}a)$$

$$\langle t_{\text{seeding}, h} \rangle \simeq \frac{1}{a} \ln(p_{ih}a)$$

effective distance  
between  $i$  and  $j$

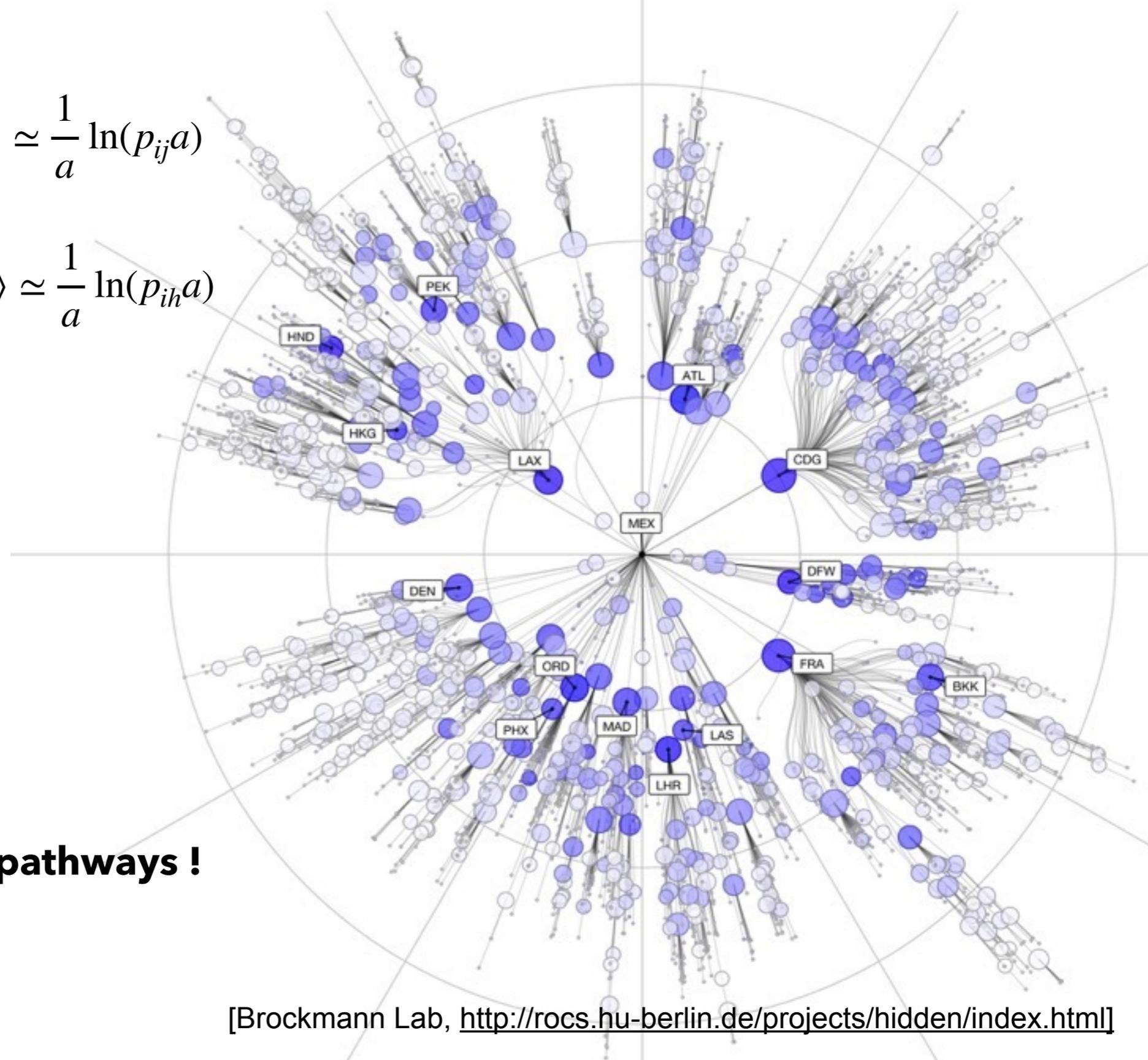
$$\ln(p_{ij})$$

[Brockmann, Helbing, Science  
2013]

**good news: existence of pathways !**

risk assessment analysis, ...

[Colizza, et al PNAS (2006)]

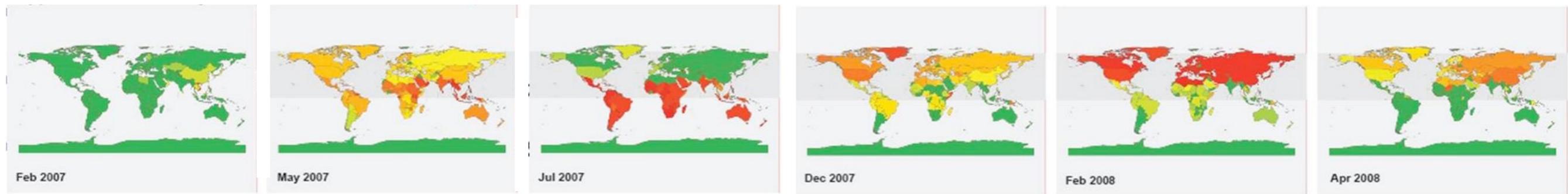


[Brockmann Lab, <http://rocs.hu-berlin.de/projects/hidden/index.html>]

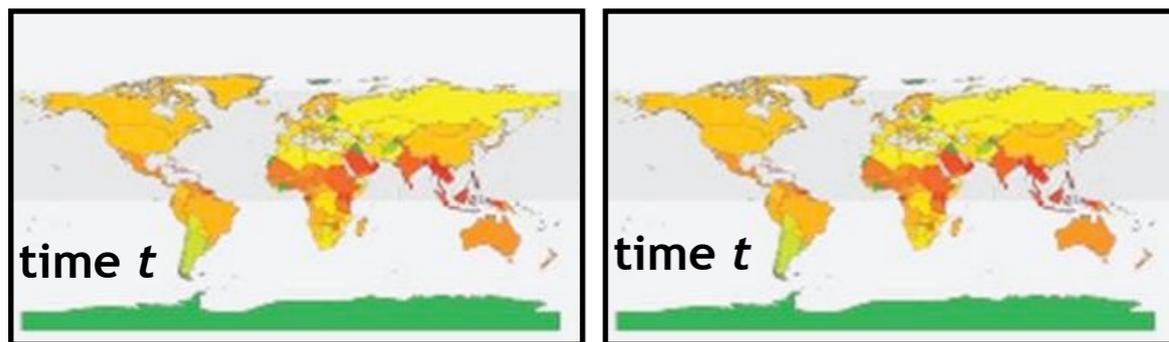
# spatial propagation: spreading pathways

numerical simulation of a global outbreak

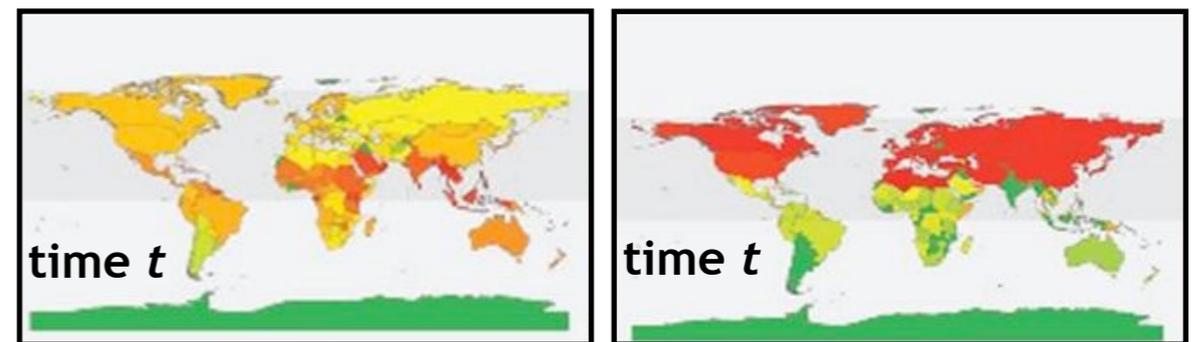
1 stochastic simulation:



similarity between 2 outbreak realizations: overlap function  $\Theta(t)$

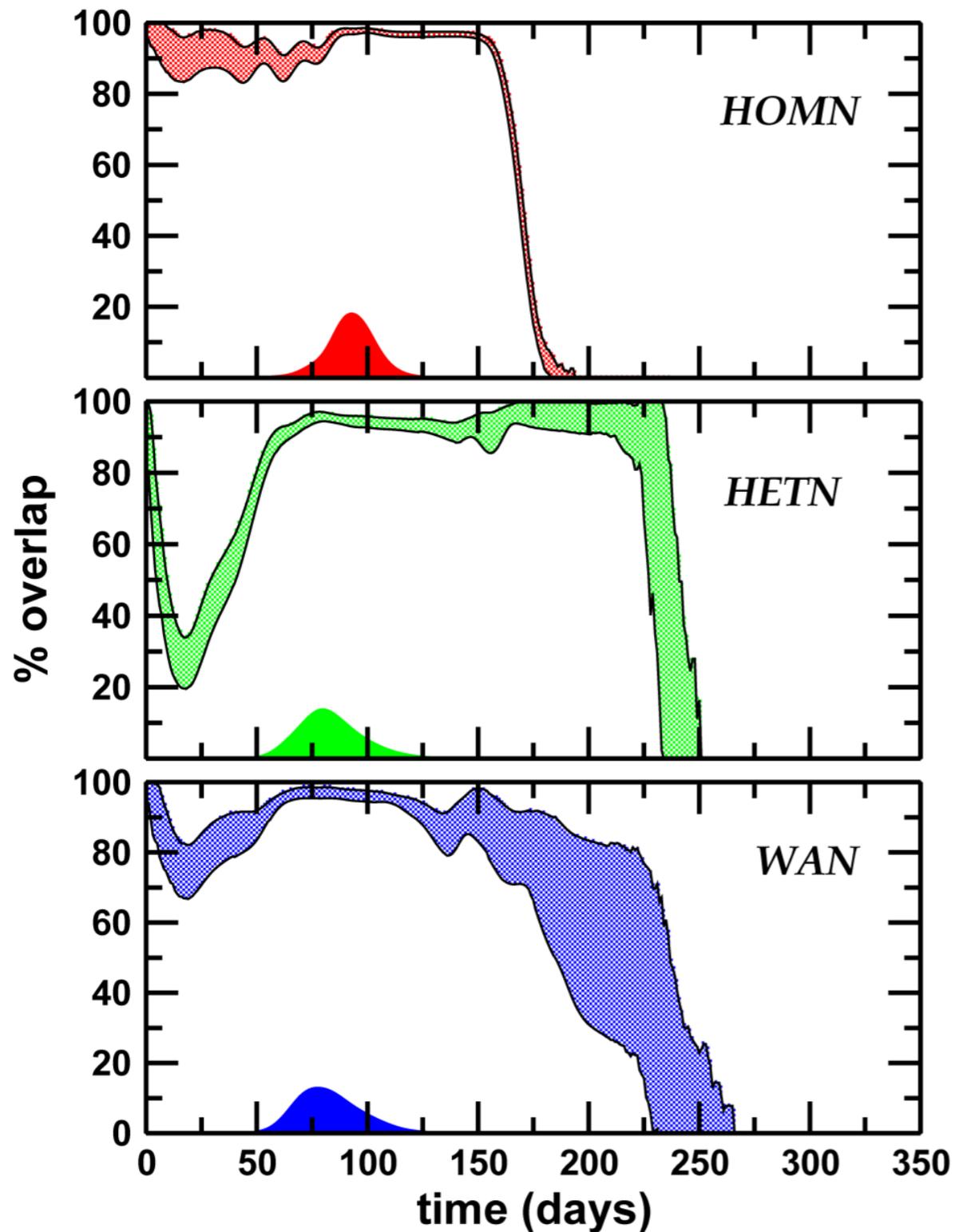


$$\Theta(t) = 1$$



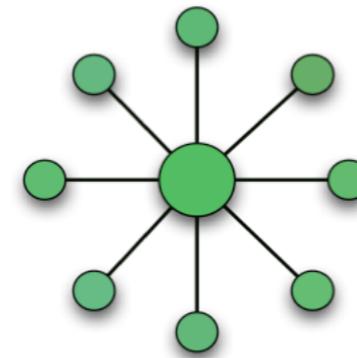
$$\Theta(t) < 1$$

# spatial propagation: spreading pathways



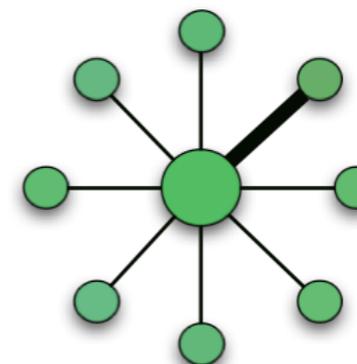
no degree fluctuations  
no weight fluctuations

+ degree  
heterogeneity



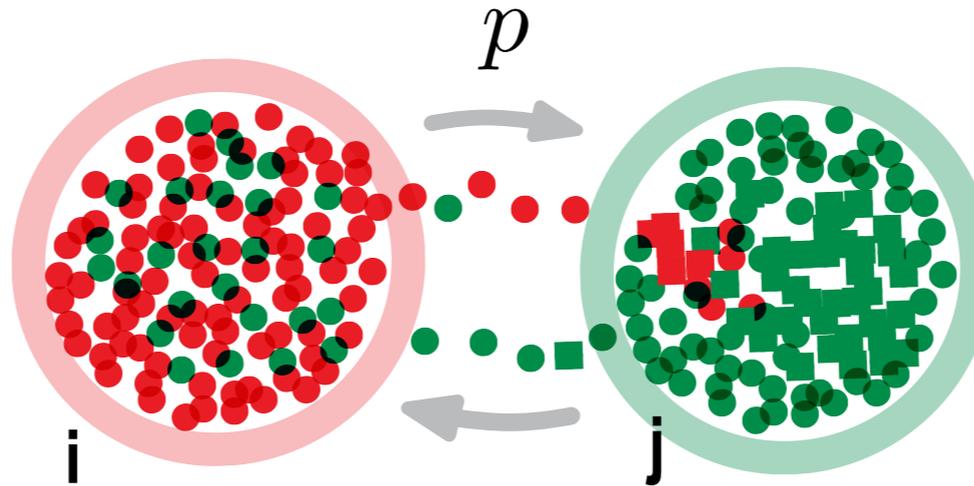
- **degree  
heterogeneity:**  
decreases  
predictability

+ weight  
heterogeneity



- **weight  
heterogeneity:**  
increases  
predictability

# spatial propagation: travel restrictions



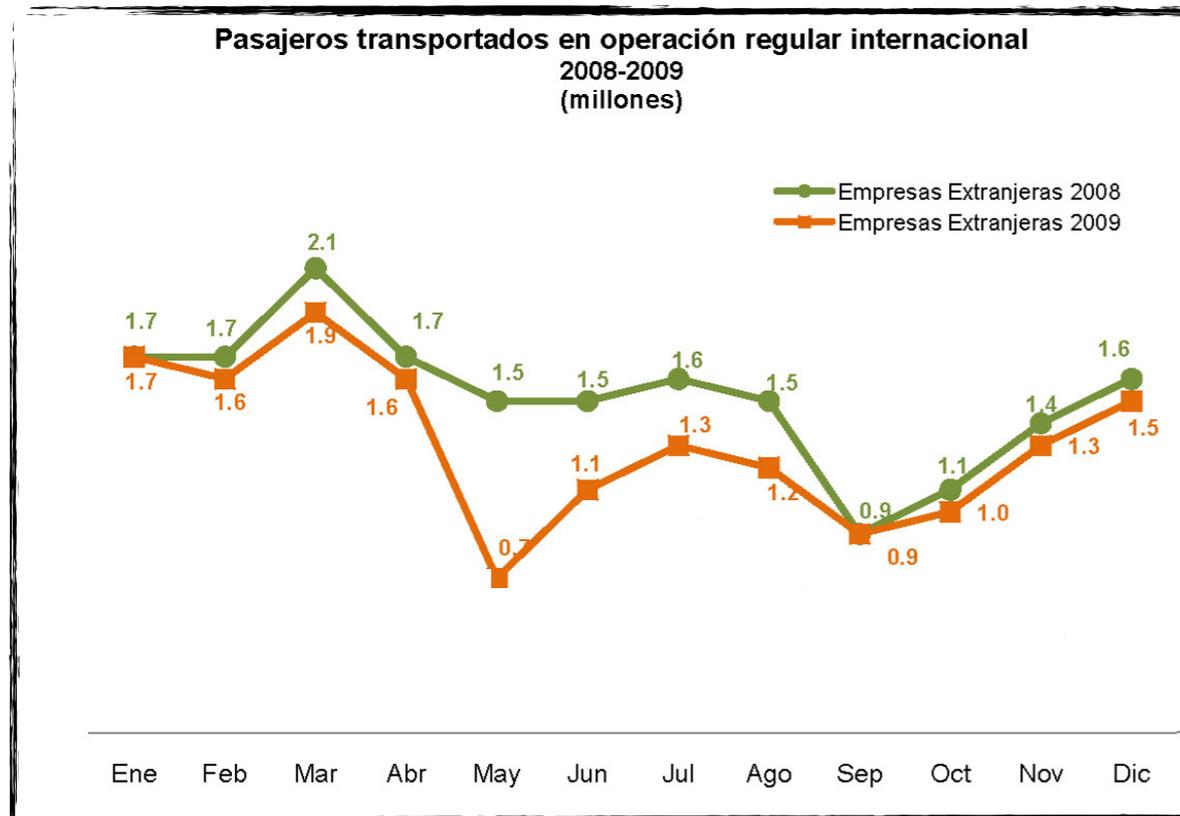
**I reduce the traffic with the epidemic origin: is it effecting in containing or delaying the propagation?**

I rescale the traveling probability of a factor  $\omega$

$$\langle t_{\text{seeding, T.R.}} \rangle \simeq \frac{1}{a} \ln(\omega pa)$$

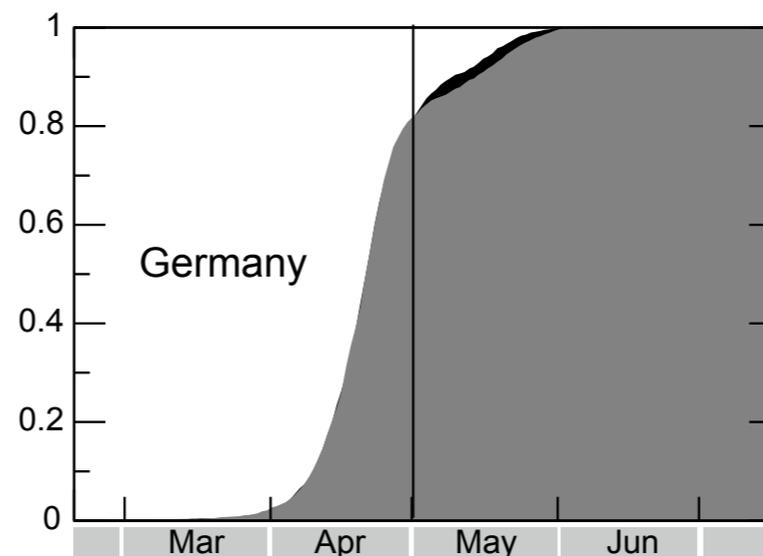
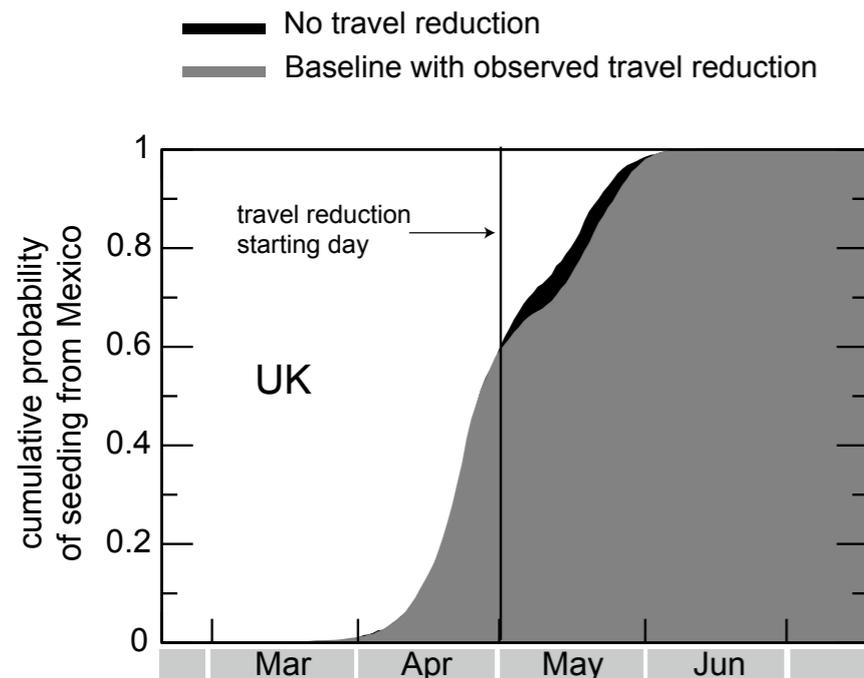
$$\begin{aligned} \langle t_{\text{seeding, T.R.}} \rangle - \langle t_{\text{seeding}} \rangle &\simeq \frac{1}{a} \ln(\omega pa) - \frac{1}{a} \ln(pa) \\ &= \frac{1}{a} \ln(\omega) + \frac{1}{a} \ln(pa) - \frac{1}{a} \ln(pa) \\ &= \frac{1}{a} \ln(\omega) \end{aligned}$$

# spatial propagation: travel restrictions



## H1N1 pandemic 2009

- drop of 40% in the air-travel to/from Mexico
- simulations with a global spreading model for influenza show negligible delay



[Bajardi et al, PLoS ONE 2011]

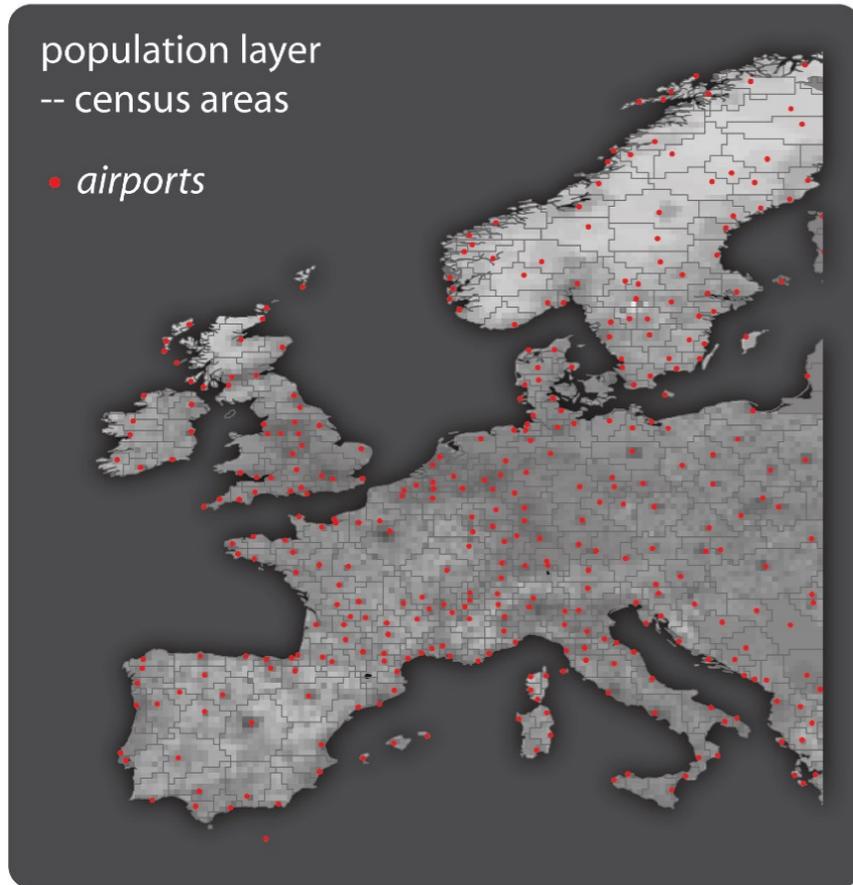
# SIR metapopulation model: markovian mobility

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  - spatial propagation & predictability
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- **computer simulations**



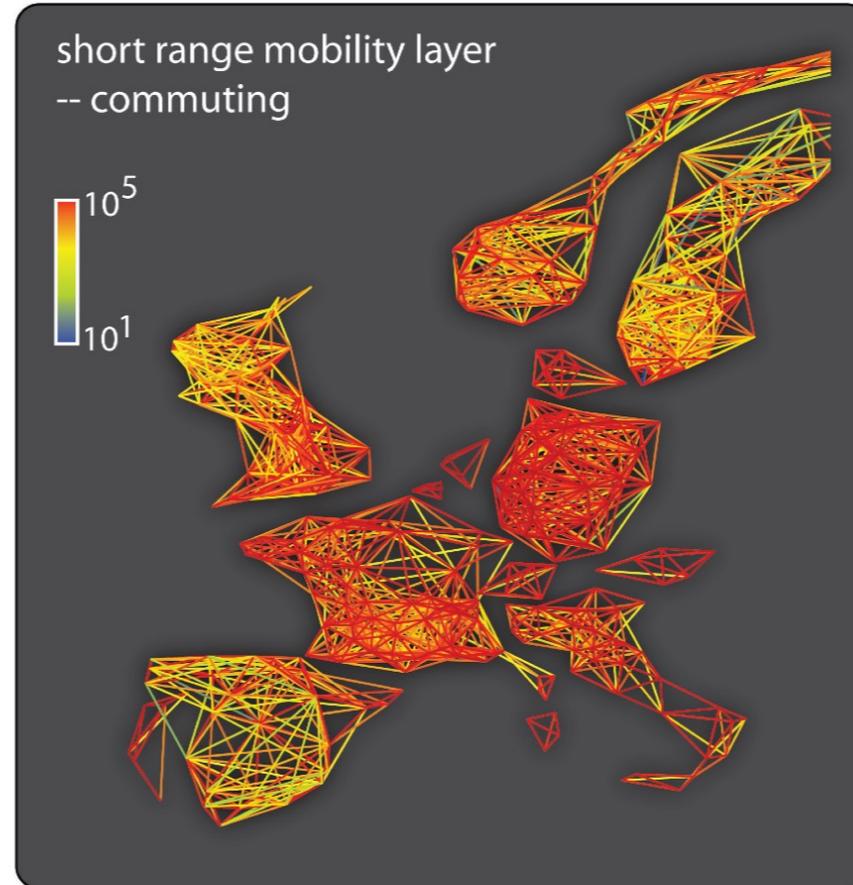
# GLEaM: Global epidemic and mobility model



## Population Distribution

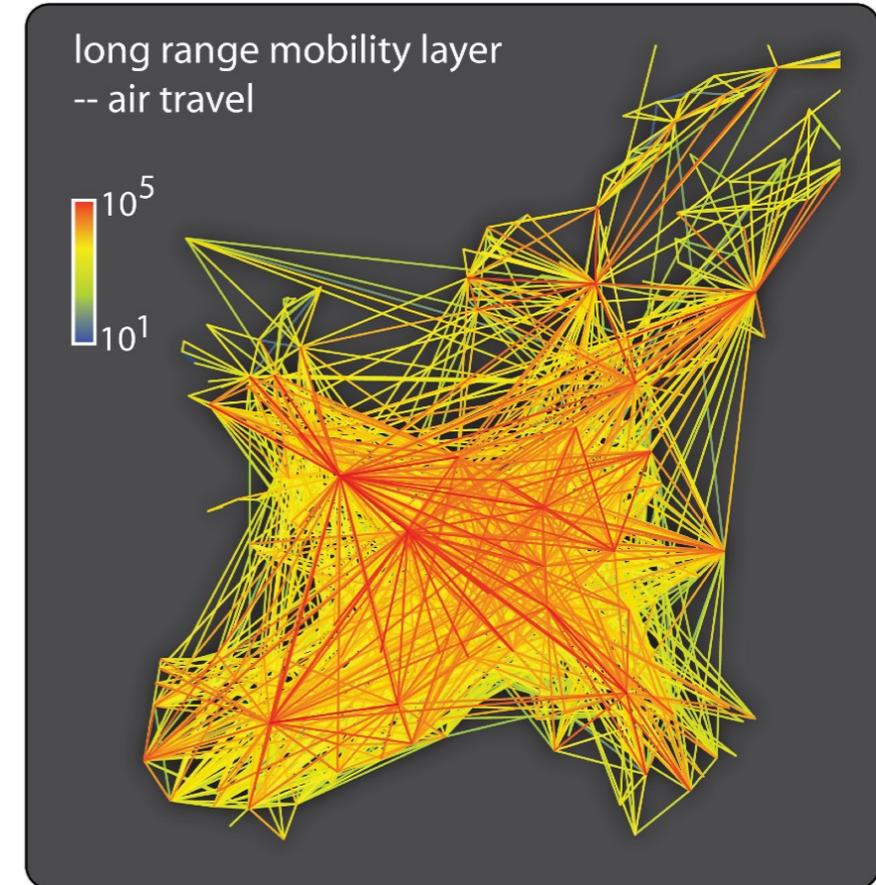
- resolution 15'x15' arc
- data source: SEDAC (Columbia University)
- tessellation: geographical census areas

[Balcan, Colizza et al. PNAS (2009)]



## Commuting Network

- census data for >40 countries in 5 continents
- different admin levels
- change of resolution scale: from admin boundaries to geo census areas

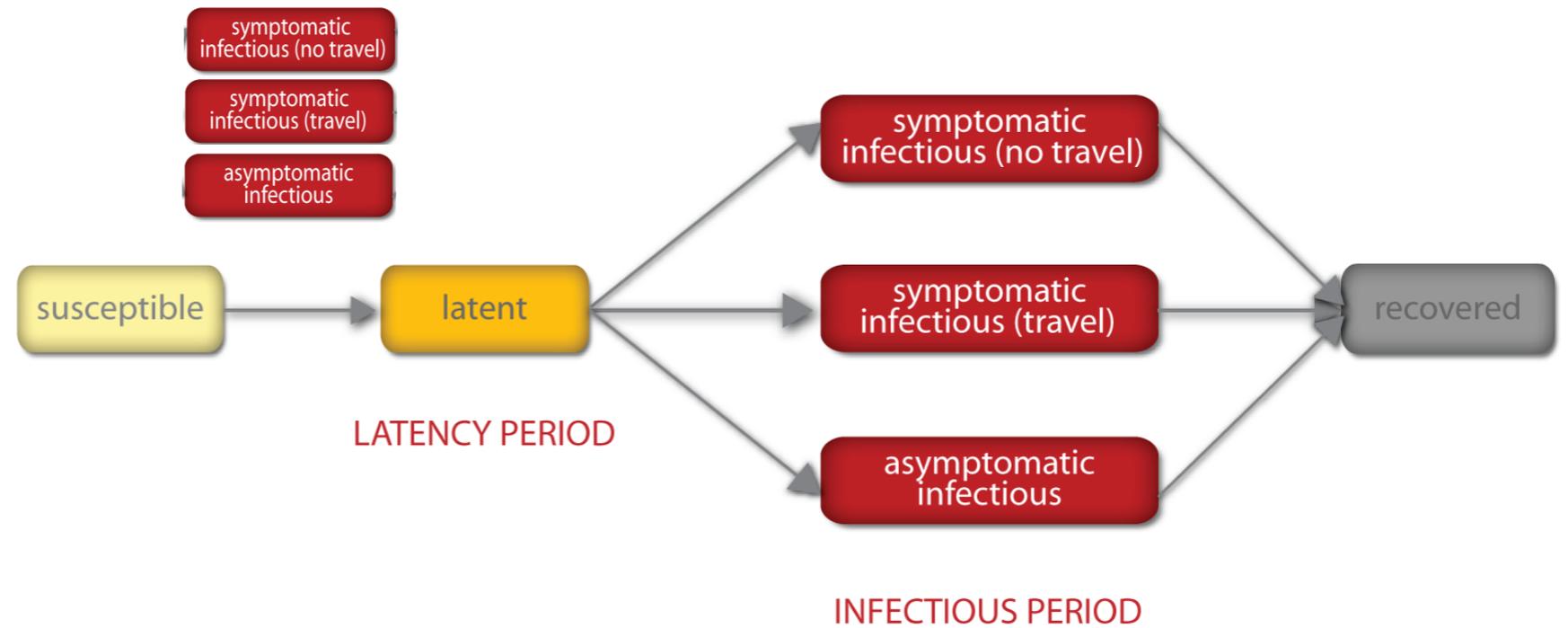


## World Airport Network

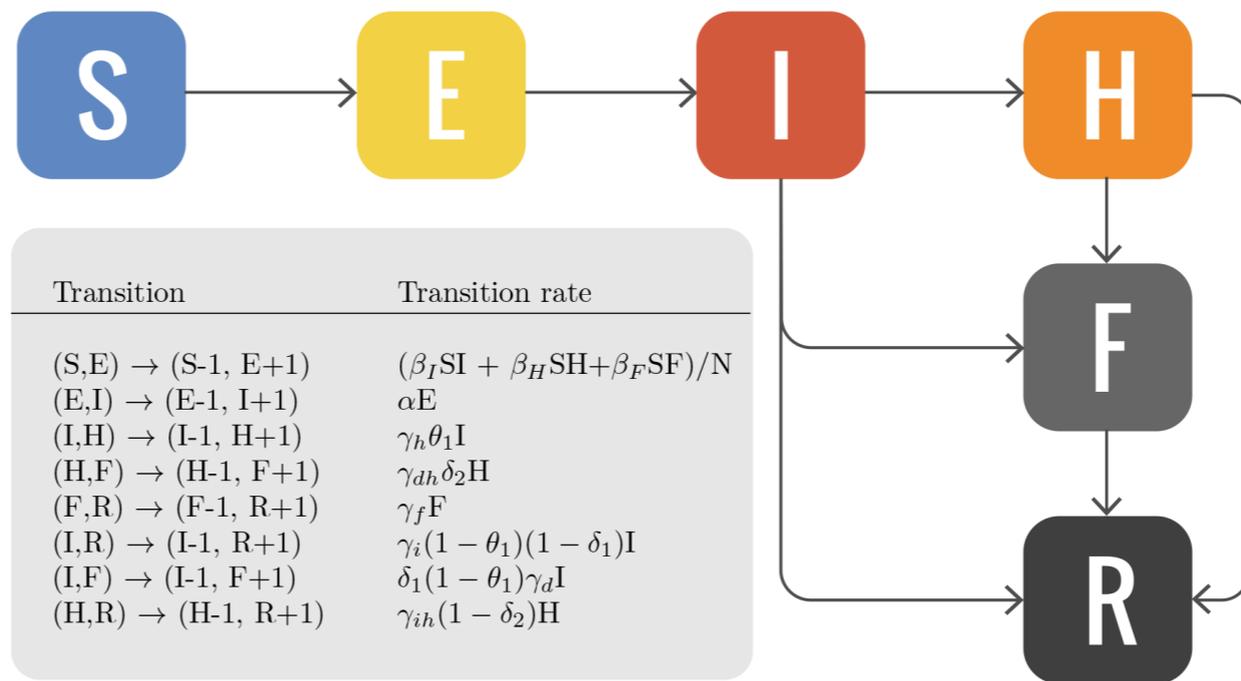
- 3362 airports in 220 countries
- 16842 connections with travel flows
- more than 99 % of the global commercial traffic
- data source: IATA, OAG

# GLEaM: Global epidemic and mobility model

## H1N1 pandemic:



## Ebola:



# SIR metapopulation model in a different regime: commuting

The Markovian assumption works well as long as

- travels are not frequent, i.e. traveling rate negligible with respect to the epidemic time scales  $p_{ij} \ll \mu$
- we want to model the short term dynamics of an epidemic

Situations for which this holds in first approximation:

- air-travel and acute infections. E.g. for flu: traveling rate =  $10^{-3}$  days<sup>-1</sup> vs. recovery rate  $> 0.1$  days<sup>-1</sup>)
- early spread of a flu pandemic. It does not work well if I want to model the long term continuous circulation

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- early spread of a flu pandemic. It does not work well if I want to model the long term continuous circulation

# SIIR metapopulation model in a different regime: commuting

In general treating mathematically the interplay between mobility and transmission is very difficult. The problem can be solved in **time scale separation**:

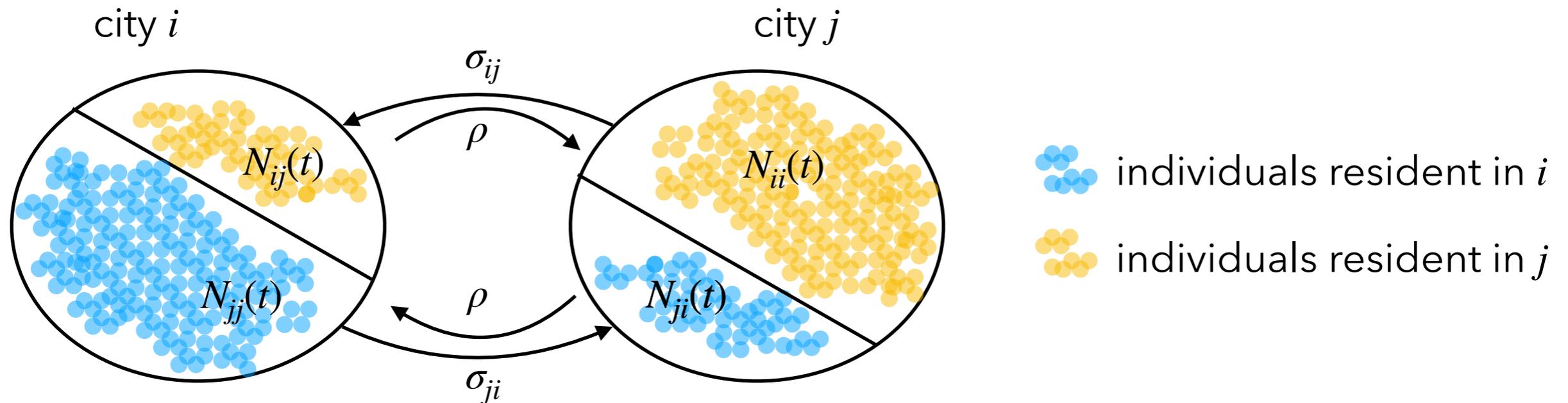
either

the epidemic unfolds faster than mobility (air-travel and flu: traveling rate =  $10^{-3}$  days $^{-1}$  vs. recovery rate  $> \sim 0.1$  days $^{-1}$ )

or

mobility faster than the epidemic (air-travel and flu: traveling rate =  $10^{-3}$  days $^{-1}$  vs. recovery rate =  $\sim 0.5$  days $^{-1}$ )

# SIR metapopulation model with memory



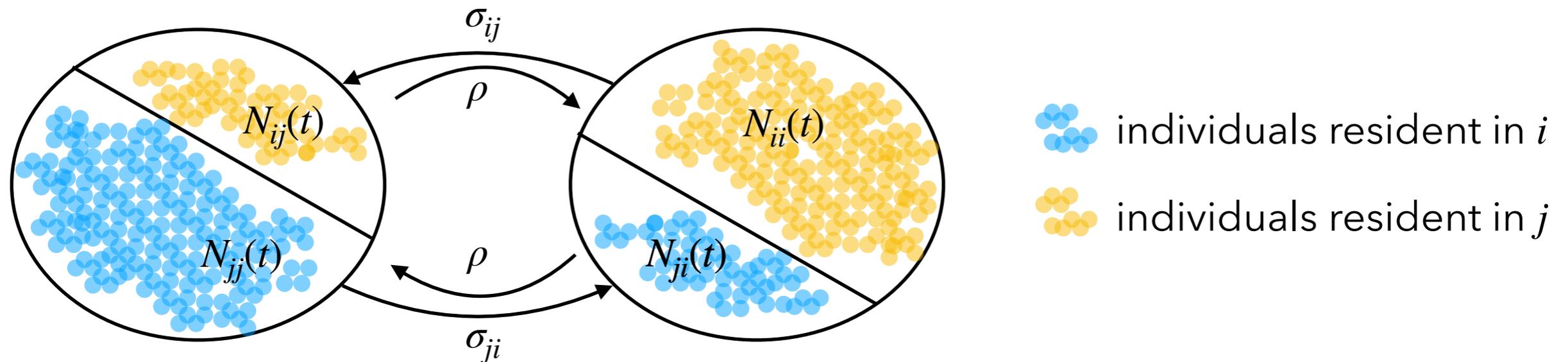
$\sigma_{ij}$  leaving rate, fraction of commuters

$\rho$  returning rate ( $\rho^{-1} = \tau \sim 8h$ )

$N_i = N_{ii}(t) + \sum_j N_{ij}(t)$  resident in *i*, constant

$N_{ij}(t)$  individuals resident in *i* and traveling to *j*

# SIR metapopulation model with memory



$\sigma_{ij}$  leaving rate, fraction of commuters

$\rho$  returning rate ( $\rho^{-1} = \tau \sim 8h$ )

$$N_i = N_{ii}(t) + \sum_j N_{ij}(t)$$

$$\partial_t N_{ii} = - \sum_j \sigma_{ij} N_{ii}(t) + \rho \sum_j N_{ij}(t)$$

$$\partial_t N_{ij} = \sum_j \sigma_{ij} N_{ii}(t) - \rho N_{ij}(t)$$

# SIR metapopulation model with memory

## solution

$$\partial_t N_{ii}(t) + (\rho + \sigma_i) N_{ii}(t) = N_i \rho$$

$$N_{ii}(t) = e^{-(\sigma_i + \rho)t} \left( C_{ii} + N_i \rho \int_0^t e^{(\sigma_i + \rho)s} ds \right)$$

$$N_{ii}(t) = \frac{N_i}{1 + \sigma_i/\rho} + \left( N_{ii}(0) - \frac{N_i}{1 + \sigma_i/\rho} \right) e^{-\rho(1 + \sigma_i/\rho)t}$$

$$N_{ij}(t) = \frac{\sigma_{ij} N_i / \rho}{1 + \sigma_i / \rho} - \frac{\sigma_{ij}}{\sigma_i} \left( N_{ii}(0) - \frac{N_i}{1 + \sigma_i / \rho} \right) e^{-\rho(1 + \sigma_i / \rho)t} +$$

$$+ \left[ N_{ij}(0) - \frac{\sigma_{ij} N_i / \rho}{1 + \sigma_i / \rho} - \frac{\sigma_{ij}}{\sigma_i} \left( N_{ii}(0) - \frac{N_i}{1 + \sigma_i / \rho} \right) \right] e^{-\rho t}$$

## differential equations

$$\partial_t N_{ii} = - \sum_j \sigma_{ij} N_{ii}(t) + \rho \sum_j N_{ij}(t)$$

$$\partial_t N_{ij} = \sum_j \sigma_{ij} N_{ii}(t) - \rho N_{ij}(t)$$

$$N_i = N_{ii}(t) + \sum_j N_{ij}(t)$$

$$\sigma_i = \sum_j \sigma_{ij}$$

# SIR metapopulation model with memory

## solution

$$N_{ii}(t) = \frac{N_i}{1 + \sigma_i/\rho} + \left( N_{ii}(0) - \frac{N_i}{1 + \sigma_i/\rho} \right) e^{-\rho(1+\sigma_i/\rho)t}$$

$$N_{ij}(t) = \frac{\sigma_{ij}N_i/\rho}{1 + \sigma_i/\rho} - \frac{\sigma_{ij}}{\sigma_i} \left( N_{ii}(0) - \frac{N_i}{1 + \sigma_i/\rho} \right) e^{-\rho(1+\sigma_i/\rho)t} + \left[ N_{ij}(0) - \frac{\sigma_{ij}N_i/\rho}{1 + \sigma_i/\rho} - \frac{\sigma_{ij}}{\sigma_i} \left( N_{ii}(0) - \frac{N_i}{1 + \sigma_i/\rho} \right) \right] e^{-\rho t}$$

time of relaxation to the equilibrium dominated by  $[\rho(1 + \sigma_i/\rho)]^{-1} \sim \rho^{-1} = \tau$ , since  $\rho \gg \sigma_i$

## Equilibrium solutions:

$$N_{ii}(t) = \frac{N_i}{1 + \sigma_i/\rho} \quad N_{ij}(t) = \frac{\sigma_{ij}N_i/\rho}{1 + \sigma_i/\rho}$$

## differential equations

$$\begin{aligned} \partial_t N_{ii} &= - \sum_j \sigma_{ij} N_{ii}(t) + \rho \sum_j N_{ij}(t) \\ \partial_t N_{ij} &= \sum_j \sigma_{ij} N_{ii}(t) - \rho N_{ij}(t) \end{aligned}$$

$$N_i = N_{ii}(t) + \sum_j N_{ij}(t)$$

$$\sigma_i = \sum_j \sigma_{ij}$$

# SIR metapopulation model with memory

## Equilibrium solutions:

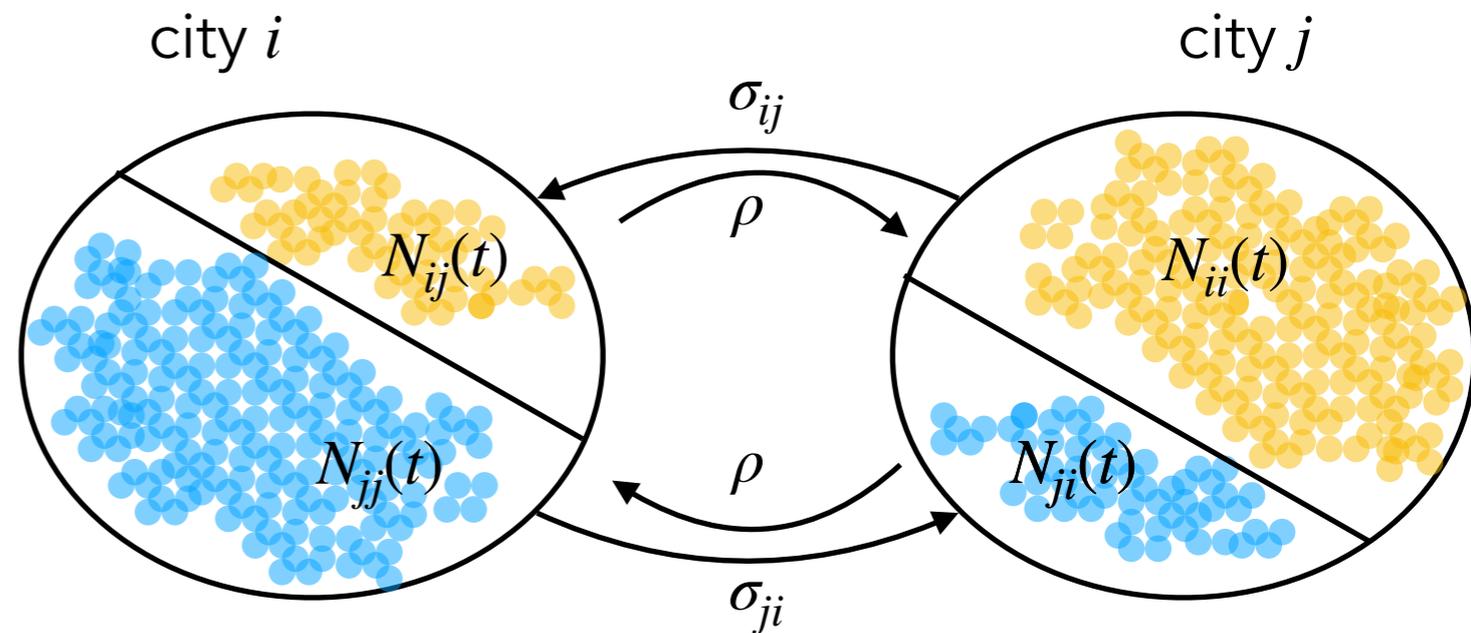
$$N_{ii}(t) = \frac{N_i}{1 + \sigma_i/\rho} \quad N_{ij}(t) = \frac{\sigma_{ij}N_i/\rho}{1 + \sigma_i/\rho}$$

## People resident in $i$

$$N_i = N_{ii}(t) + \sum_j N_{ij}(t)$$

## People present in $i$

$$N_i^* = N_{ii} + \sum_j N_{ji} = \frac{N_i}{1 - \sigma_i/\rho} + \sum_j \frac{N_j \sigma_{ji}/\rho}{1 - \sigma_j/\rho}$$



-  individuals resident in  $i$
-  individuals resident in  $j$

# SIR metapopulation model with memory

## Equilibrium solutions:

$$N_{ii}(t) = \frac{N_i}{1 + \sigma_i/\rho} \quad N_{ij}(t) = \frac{\sigma_{ij}N_i/\rho}{1 + \sigma_i/\rho}$$

$$N_i = N_{ii}(t) + \sum_j N_{ij}(t)$$

$$N_i^* = \frac{N_i}{1 - \sigma_i/\rho} + \sum_j \frac{N_j \sigma_{ji}/\rho}{1 - \sigma_j/\rho}$$

$\sigma_i/\rho$  quantify the ratio of time spent outside and in the residence population

## Simple limit cases:

$\sigma_i \rightarrow 0 \Rightarrow N_{ii}(t) \rightarrow N_i; N_{ij}(t) \rightarrow 0; N_i^* \rightarrow N_i$  people rarely leave their residence thus the population of non traveling approaches the population of resident

$\rho \rightarrow \infty \Rightarrow N_{ii}(t) \rightarrow N_i; N_{ij}(t) \rightarrow 0; N_i^* \rightarrow N_i$  people return home immediately thus the population of non traveling approaches the population of resident

$\rho \rightarrow 0 \Rightarrow N_{ii}(t) \rightarrow 0; N_{ij}(t) \rightarrow \frac{\sigma_{ij}}{\sigma_i} N_i; N_i^* \rightarrow \sum_j \frac{\sigma_{ji}}{\sigma_j} N_j$  migration: people never get

back and the population of resident in  $i$  is distributed among the neighbouring destinations  $j$

# SIR metapopulation model with memory

## Time scale separation

time of relaxation to the equilibrium dominated by  
 $[\rho(1 + \sigma_i/\rho)]^{-1} \sim \rho^{-1} = \tau$ , since  $\rho \gg \sigma_i$

commuting:  $\tau \sim 8h$

duration of an acute infection (e.g. flu):  $\mu^{-1} \simeq [1 - 3]$  days

transmission dynamics slower than mobility: we can assume that compartments occupations numbers is at the equilibrium with respect to mobility dynamics

$$X_{ii}^{[m]} = \frac{X_i^{[m]}}{1 + \sigma_i/\rho} \quad X_{ij}^{[m]} = \frac{\sigma_{ij}X_i^{[m]}/\rho}{1 + \sigma_i/\rho} \quad X^{[m]} = S, I, R$$

# SIR metapopulation model with memory

## Time scale separation

force of infection:

$$\partial_t I = \lambda S(t) - \mu I(t), \quad \lambda = \beta \frac{I(t)}{N(t)}$$

$$\begin{aligned}\partial_t S &= -\beta \frac{I(t)}{N_i(t)} S(t) \\ \partial_t I &= \beta \frac{I(t)}{N_i(t)} S(t) - \mu I(t) \\ \partial_t R &= \mu I(t)\end{aligned}$$

instead of explicitly modelling mobility, I directly compute the effect of the other patches on the risk of infection, i.e. I break down the force of infection in its contributions. **How many infectious individuals a susceptible person resident in  $i$  is exposed to?**

# SIR metapopulation model with memory

## Time scale separation

instead of explicitly modelling mobility, I directly compute the effect of the other patches on the risk of infection, i.e. I break down the force of infection in its contributions. **How many infectious individuals a susceptible person resident in  $i$  is exposed to?**

$S_i$  distributed among patch  $i$  and all possible destinations  $j$  in proportion

$$\left\{ \frac{1}{1 + \sigma_i/\rho}, \dots, \frac{\sigma_{ij}/\rho}{1 + \sigma_i/\rho}, \dots \right\}$$

$$\lambda_i = \frac{\lambda_{ii}}{1 + \sigma_i/\rho} + \sum_j \frac{\lambda_{ij}\sigma_{ij}/\rho}{1 + \sigma_i/\rho}$$

# SIR metapopulation model with commuting

$$\lambda_i = \frac{\lambda_{ii}}{1 + \sigma_i/\rho} + \sum_j \frac{\lambda_{ij}\sigma_{ij}/\rho}{1 + \sigma_i/\rho}$$

$$\lambda_{ii} = \frac{\beta_i}{N_i^*} \left[ I_{ii} + \sum_j I_{ji} \right] \quad \lambda_{ii} = \frac{\beta_i}{N_i^*} \left[ \frac{I_i}{1 - \sigma_i/\rho} + \sum_j \frac{I_j\sigma_{ji}/\rho}{1 - \sigma_j/\rho} \right]$$

$$\lambda_{ij} = \frac{\beta_j}{N_j^*} \left[ I_{jj} + \sum_l I_{lj} \right] \quad \lambda_{ij} = \frac{\beta_j}{N_j^*} \left[ \frac{I_j}{1 - \sigma_j/\rho} + \sum_l \frac{I_l\sigma_{li}/\rho}{1 - \sigma_l/\rho} \right]$$

$$N_i^* = \frac{N_i}{1 - \sigma_i/\rho} + \sum_j \frac{N_j\sigma_{ji}/\rho}{1 - \sigma_j/\rho}$$

# SIR metapopulation model with commuting

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$$N_i^* = \frac{N_i}{1 - \sigma_i/\rho} + \sum_j \frac{N_j\sigma_{ji}/\rho}{1 - \sigma_j/\rho}$$

understanding the relative role of mobility and infection parameters on the epidemic dynamics

mathematical expressions to speed up computer simulations