
Modelling global epidemics: theory and simulations

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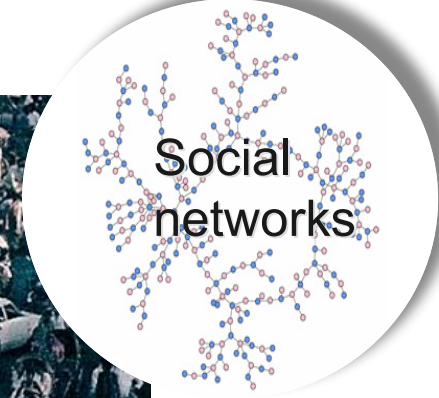
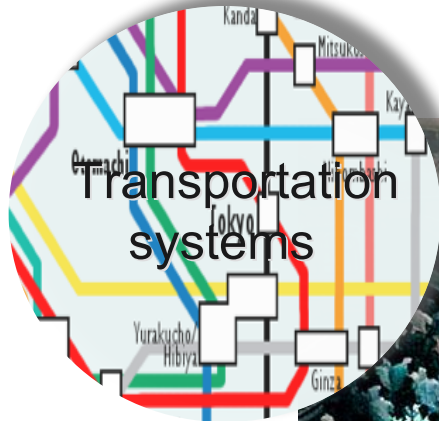


Manchester meeting
Modelling complex systems (21-23 june 2010)

Outline

- Introduction
- Metapopulation model: applications
 - SARS
 - Testing strategies
- Metapopulation model: theory
 - Pandemic threshold
- Discussion and perspectives

Epidemiology: an interdisciplinary field



Epidemiology and statistical physics

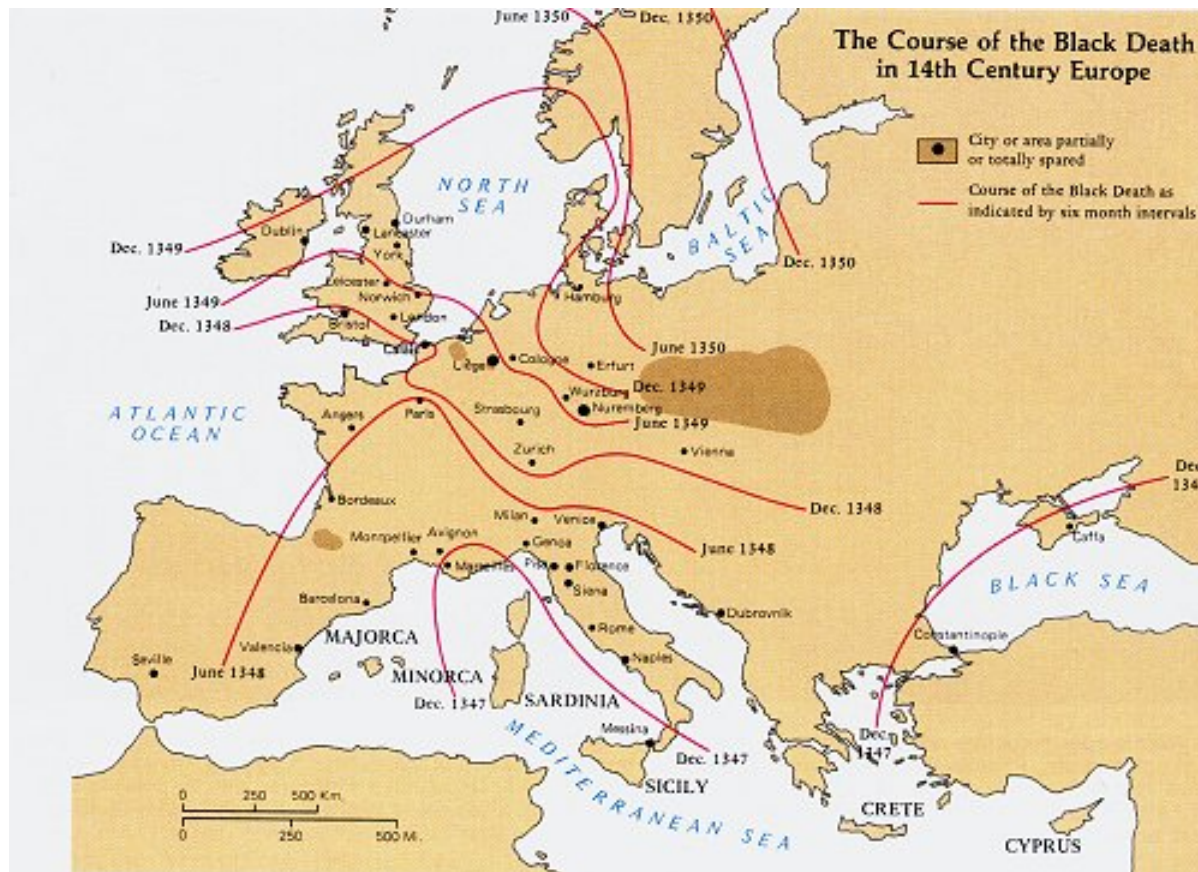
- Microscopic level (bacteria, viruses): compartments
 - Understanding and killing off new viruses
 - Quest for new vaccines and medicines

statistical physics

- Macroscopic level (communities, species)
 - Integrating biology, movements and interactions
 - Vaccination campaigns and immunization strategies

Pandemic spread modeling: past and current

- Human movements and disease spread

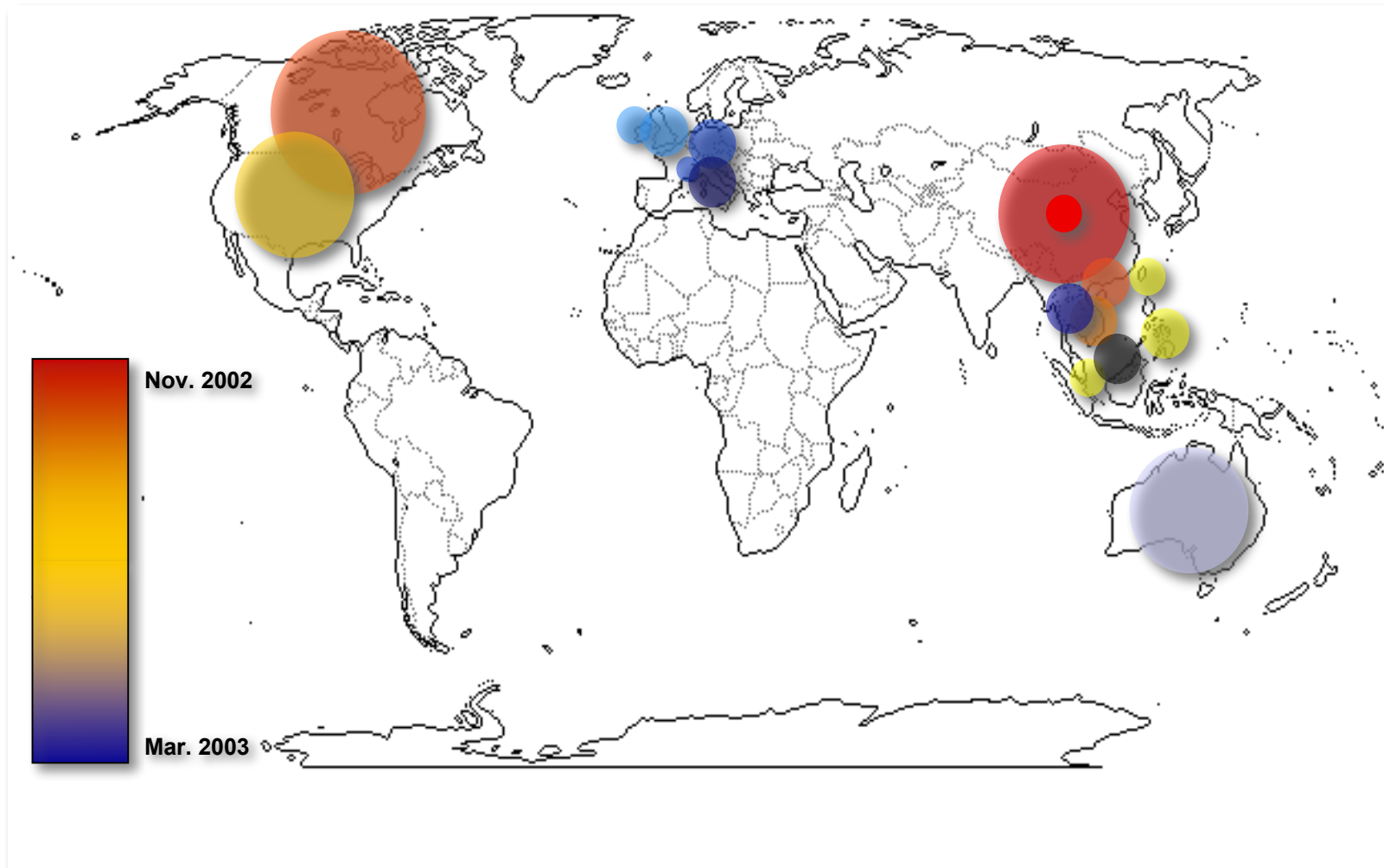


**Black death (14th)
Spatial diffusion
Model:**

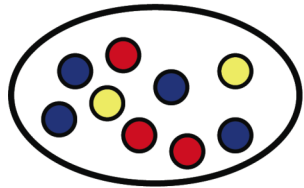
$$V \approx 140 \text{ miles/year}$$

Pandemic spread modeling: past and current

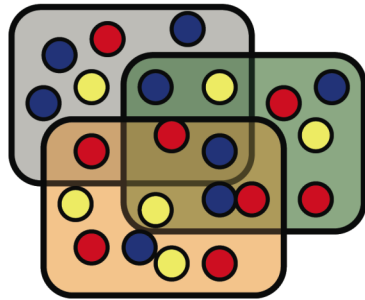
- Complex movement patterns: different means, different scales (SARS): Importance of transportation networks (air travel)



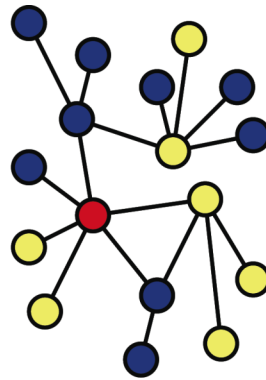
Modeling in Epidemiology: parameters, realism, simplicity, ...



Homogeneous mixing

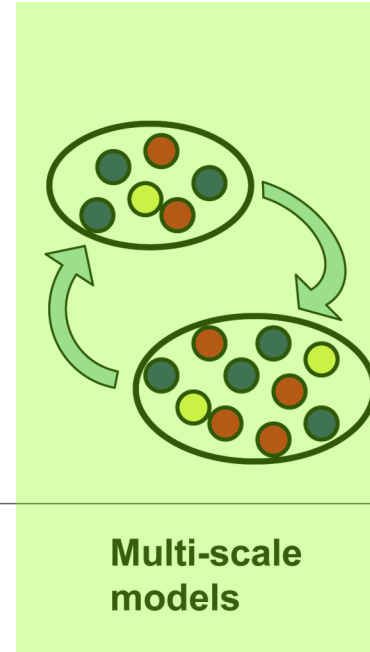


Social structure



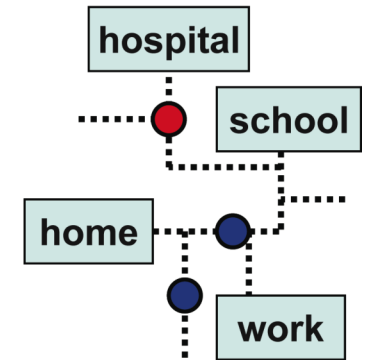
Contact network models

Social network



Multi-scale models

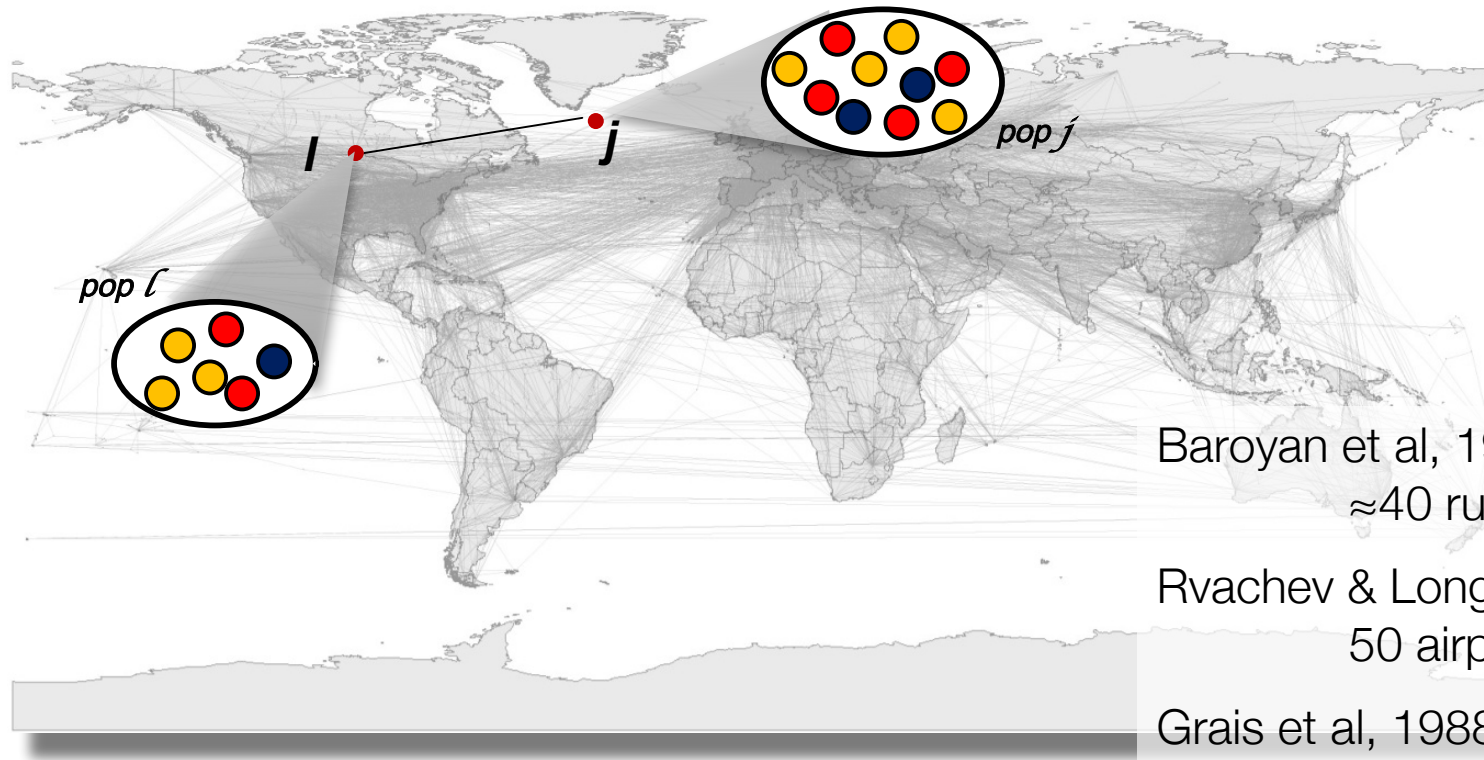
Pandemic modelling (metapopulation)



Agent Based models

Intra urban spread

Metapopulation model



Baroyan et al, 1969:
≈40 russian cities

Rvachev & Longini, 1985:
50 airports worldwide

Grais et al, 1988:
150 airports in the US

Hufnagel et al, 2004:
500 top airports
worldwide

Colizza et al, 2006:
>99% of the total traffic

One population: Simple models of epidemics

Stochastic model:

- SIS model: $S \xrightarrow{\lambda} I \xrightarrow{\mu} S$
- SIR model: $S \xrightarrow{\lambda} I \xrightarrow{\mu} R$
- SI model: $S \xrightarrow{\lambda} I$

λ : proba. per unit time of transmitting the infection

μ : proba. per unit time of recovering

One population: Simple models of epidemics

Stochastic model:

- SIS or SIR model (mean-field):

$$\partial_t I = \lambda S \frac{I}{N} - \mu I$$

λ : proba. per unit time of transmitting the infection

μ : proba. per unit time of recovering

One population: diffusion effect

Modeling: SIR with spatial diffusion $i(x,t)$:

$$\frac{\partial i}{\partial t} = \lambda s i - \mu i + D \nabla^2 i$$

where: λ = transmission coefficient (fleas->rats->humans)

μ = 1/average infectious period

S_0 = population density, D = diffusion coefficient

$$V = 2(\lambda S_0 D)^{1/2} \left[1 - \frac{\mu}{\lambda S_0} \right]^{1/2}$$

$\sim 100 - 200$ miles/year

Metapopulation model (mean-field)

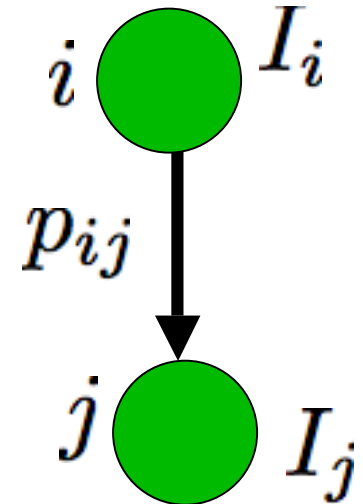
Reaction-diffusion models
FKPP equation

- Rvachev Longini (1985)

$$\partial_t I_i(t) = K_i[I_i(t)] + \Omega_i(t)$$

Inner city term
(one population
homogeneous mixing)

Travel term
(network)



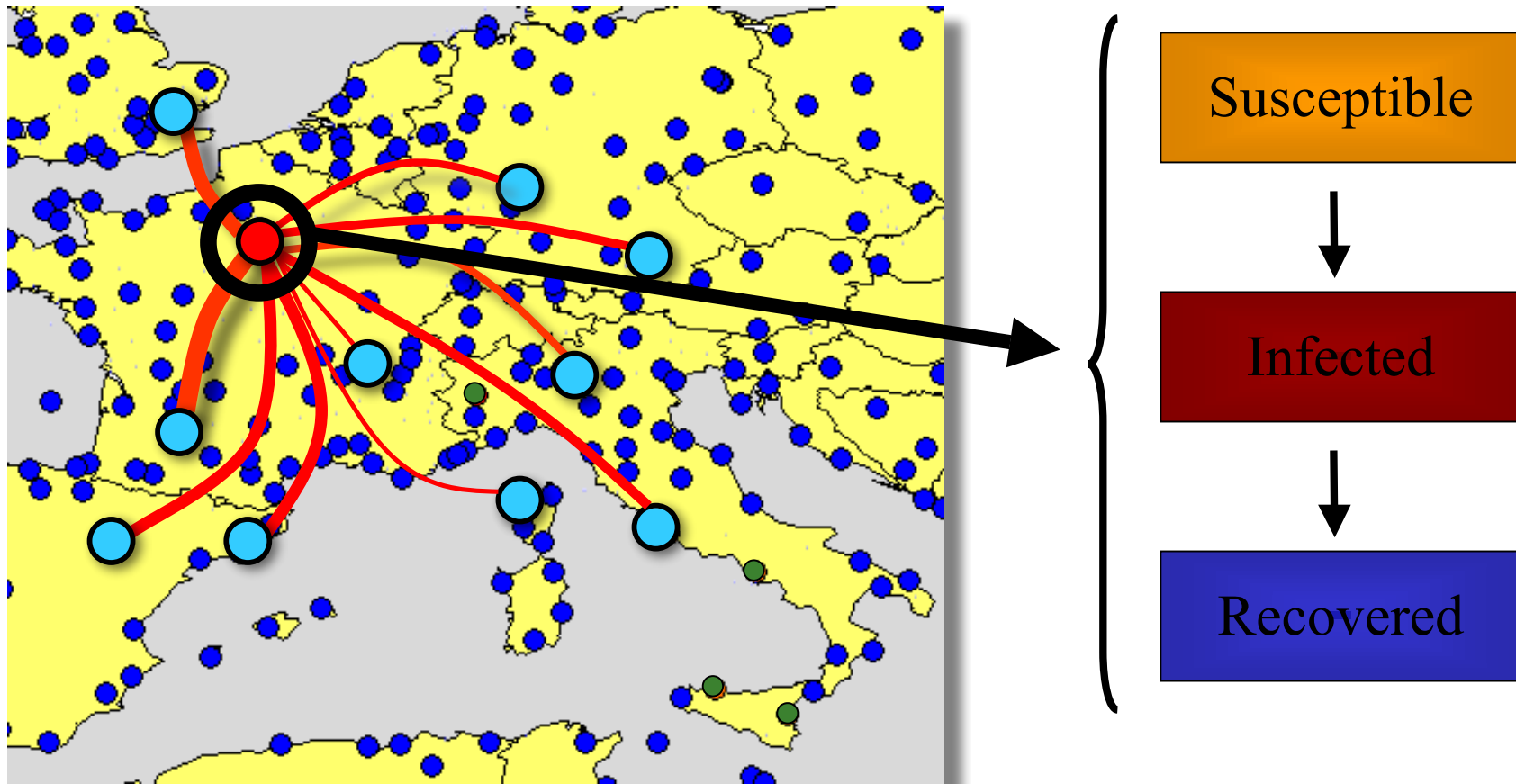
- Transport operator (mean-field):

$$\Omega_i(t) = \sum_{j \in \Gamma_i} p_{ji} I_j(t) - p_{ij} I_i(t)$$

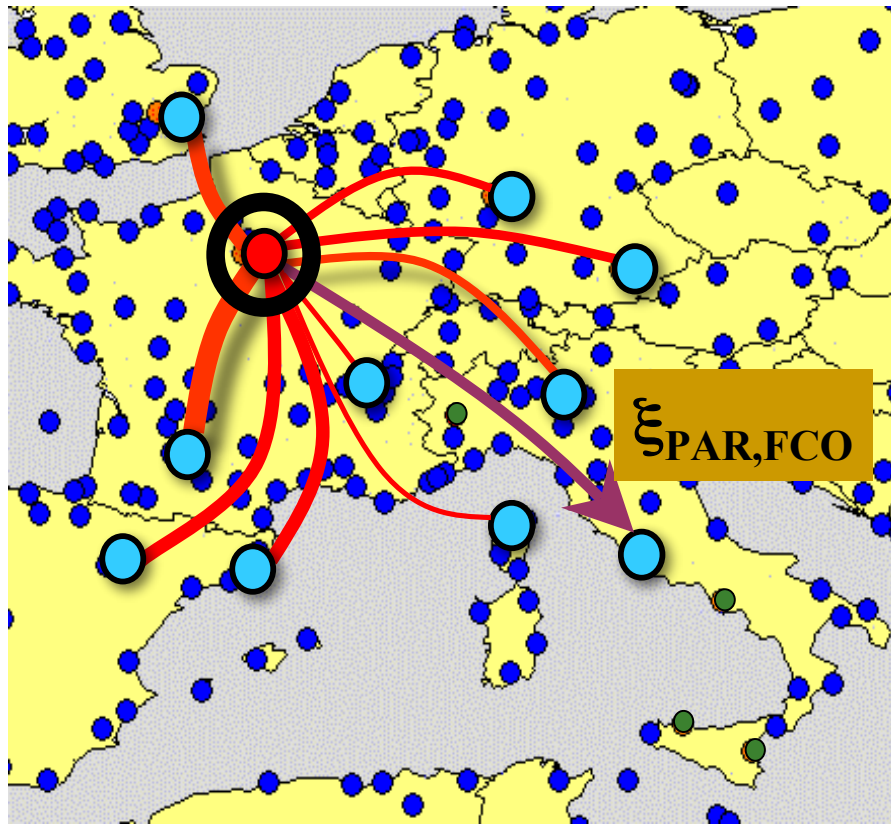
Flahault & Valleron (1985); Hufnagel et al, PNAS 2004, Colizza, Barrat, Barthelemy, Vespignani PNAS 2006, BMB, 2006. Theory: Colizza & Vespignani, Gautreau & al, ...

Stochastic model

compartmental model + air transportation data



Metapopulation model



Travel probability
from *PAR* to *FCO*:

$$p_{PAR,FCO} = \frac{\xi_{PAR,FCO}}{N_{PAR}} \delta t$$

$\xi_{PAR,FCO}$ # passengers
from *PAR* to *FCO*
(input data)

Metapopulation model (mean-field)

- Reaction-diffusion models
 - Reaction at each node $S + I \rightarrow 2I$
 - Diffusion

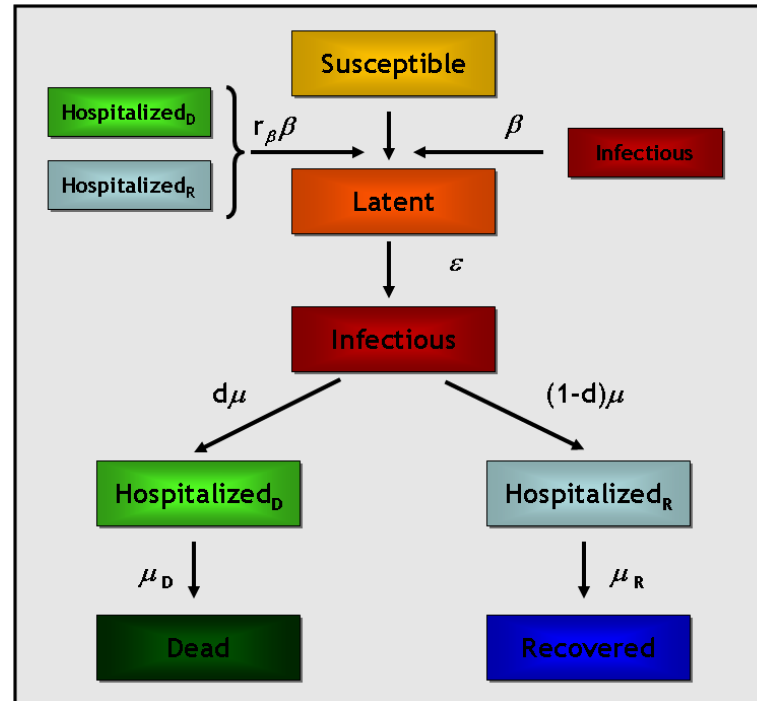
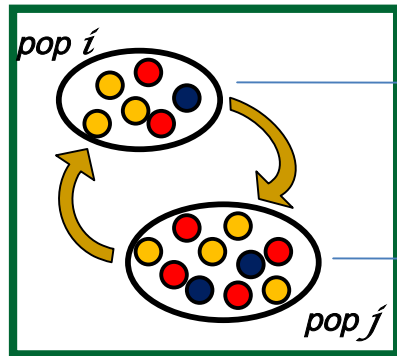
- FKPP equation (continuous limit, $d=1$)

$$\partial_t h(t) = \gamma h(1 - h) + D \nabla^2 h$$

Metapopulation model: Applications

- Testing against historical examples
 - SARS (2003)
- Testing strategies
 - Antivirals: cooperative versus egoistic strategies
 - Travel restrictions

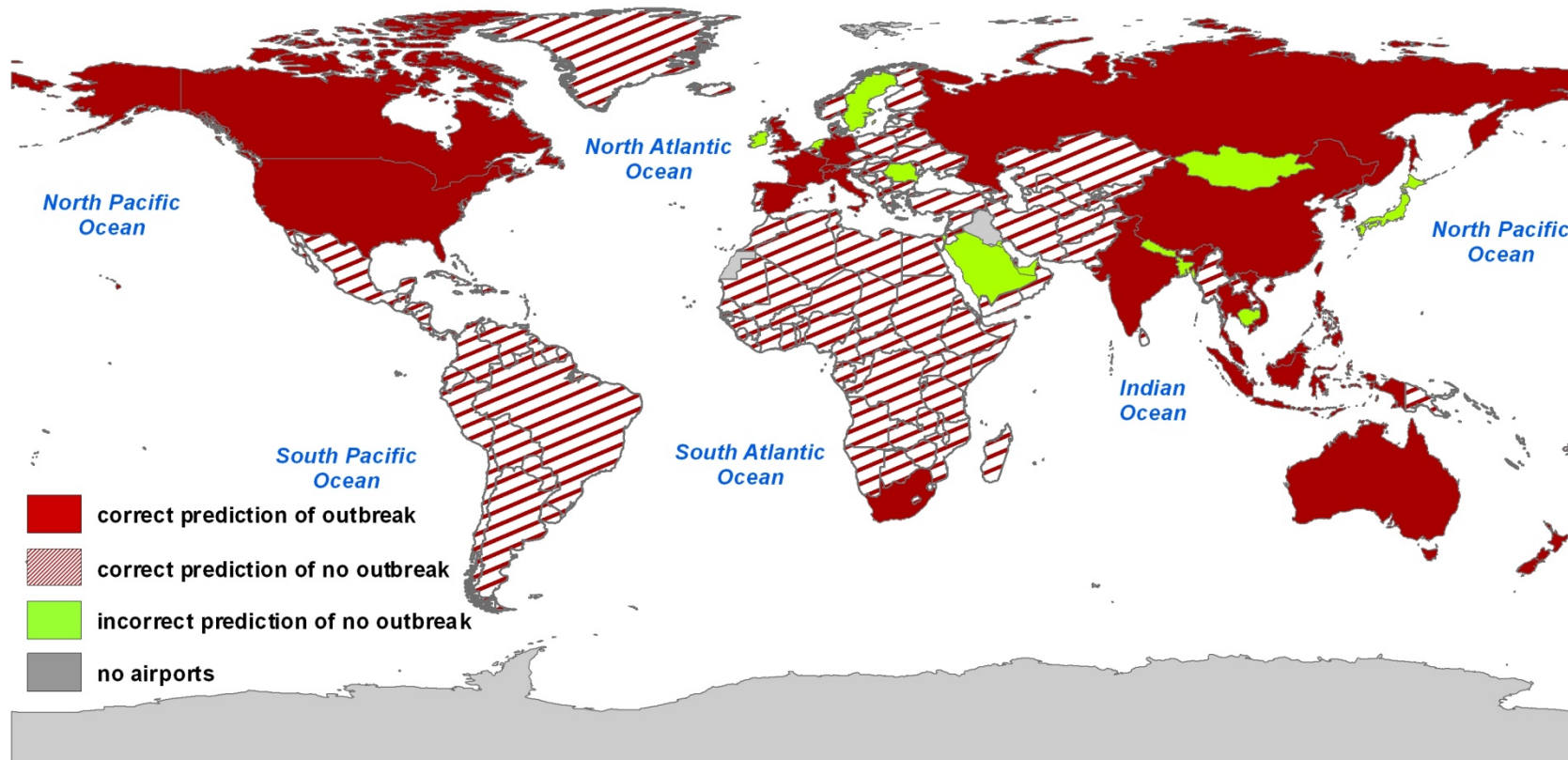
Application: SARS



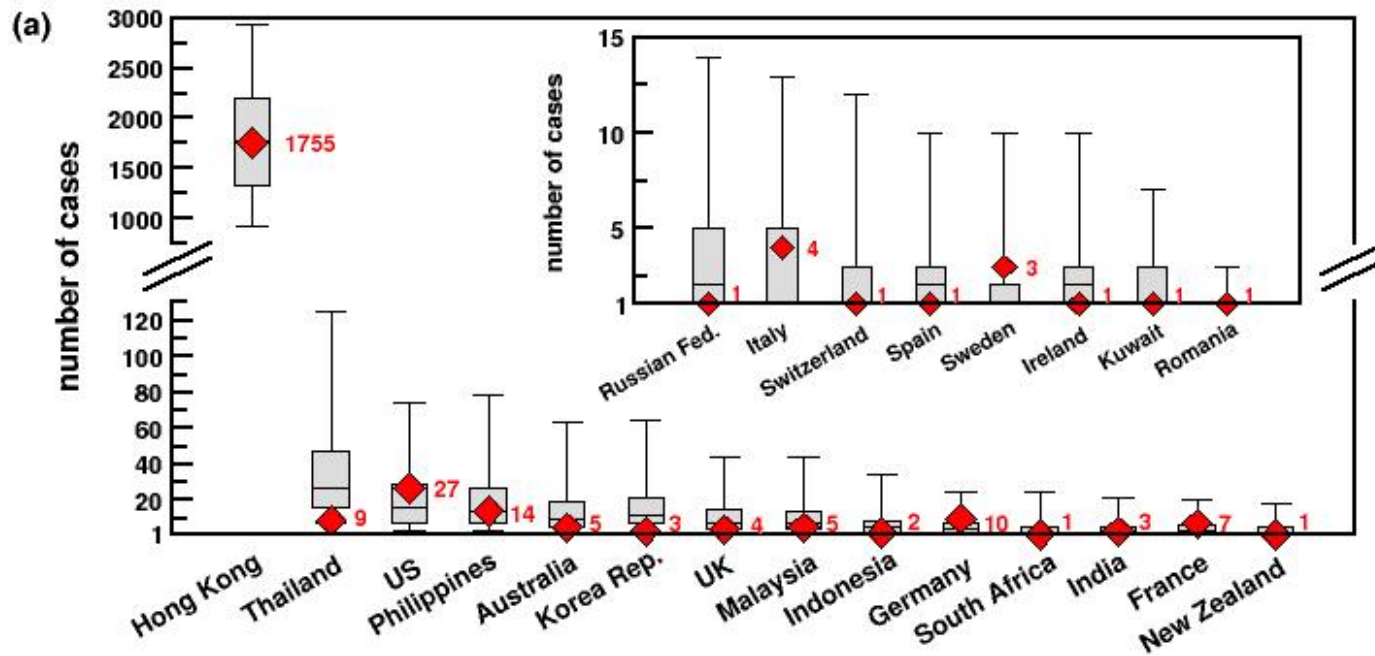
- refined compartmentalization
- parameter estimation: clinical data + local fit
- geotemporal initial conditions: available empirical data
- modeling intervention measures: standard effective modeling

SARS: predictions

Comparison forecasts/empirical data July 11, 2003



SARS: predictions (2)



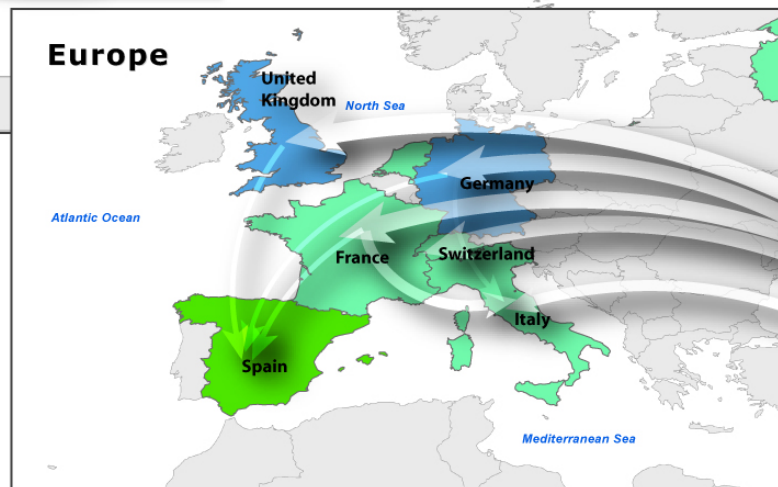
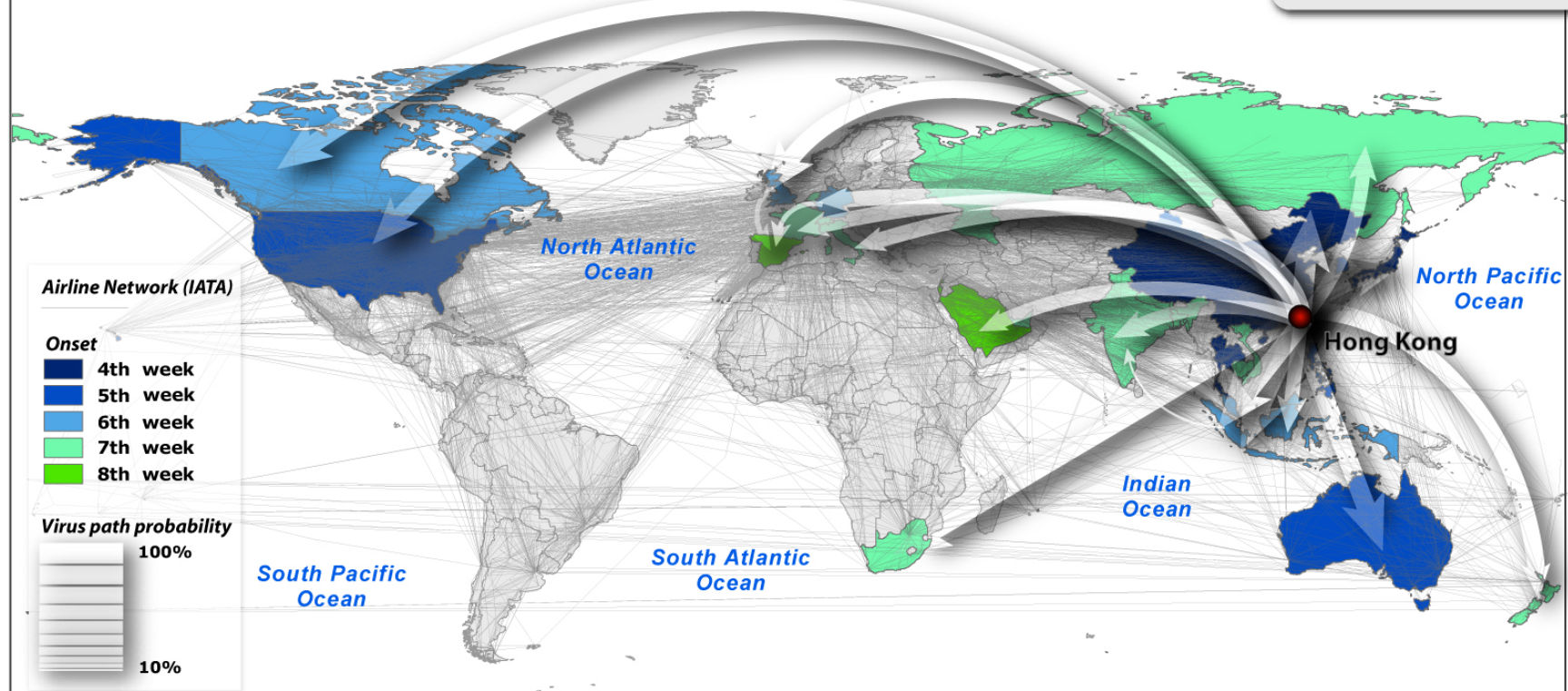
More from SARS - Epidemic pathways

- For every infected country:

where is the epidemic coming from ?

- Redo the simulation for many disorder realizations
(same initial conditions)
- Monitor the occurrence of the paths
(source-infected country)

SARS - Epidemic Pathways



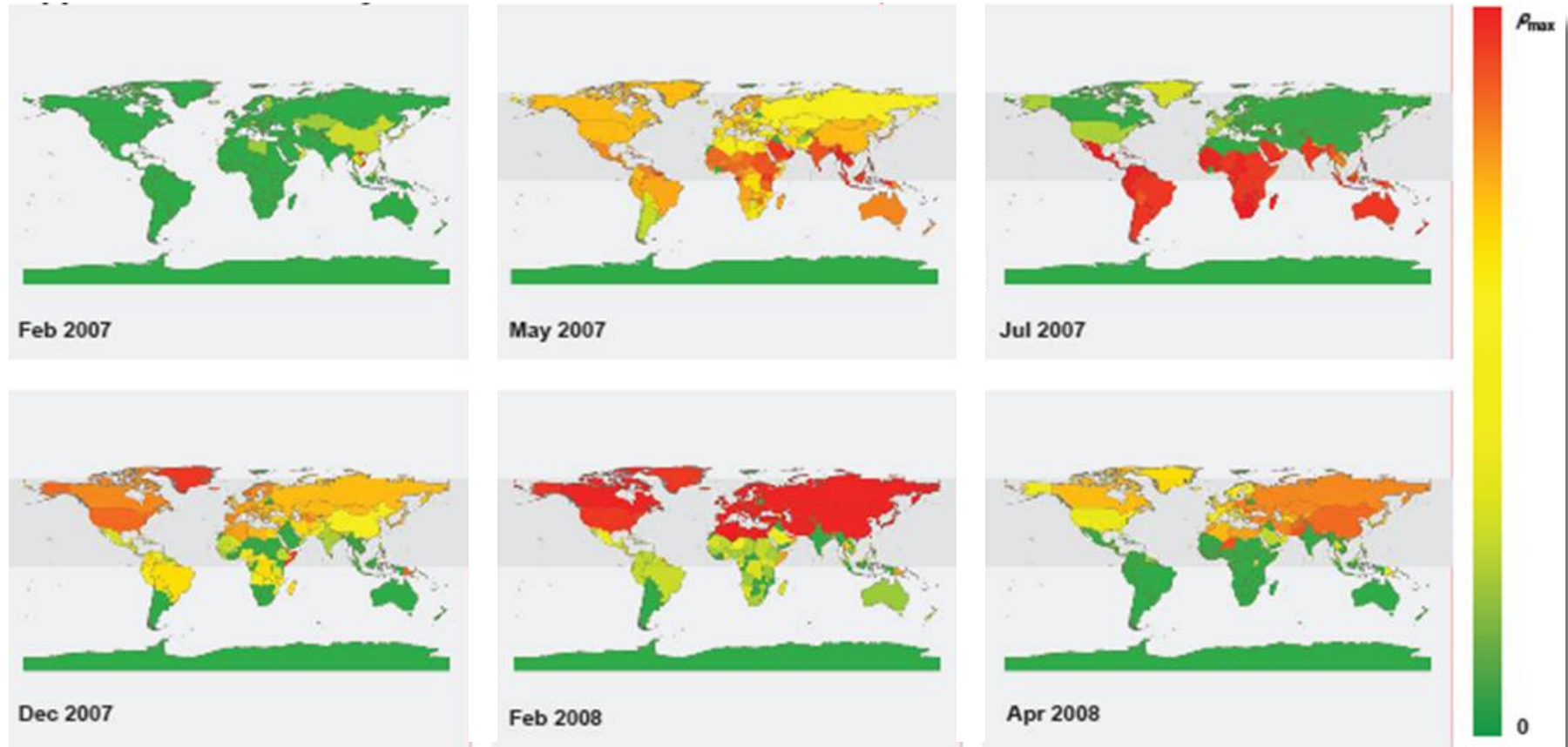
SARS- what did we learn ?

- Metapopulation model, no tunable parameter:
good agreement with WHO data !
- Existence of pathways:
confirms the possibility of epidemic forecasting !
Useful information for control strategies

Application of the metapopulation model: effect of antivirals

- Threat:Flu
- Question: use of antivirals
 - Best strategy for the countries ?
- Model:
 - Etiology of the disease (compartments)
 - Metapopulation+Transportation mode (air travel)

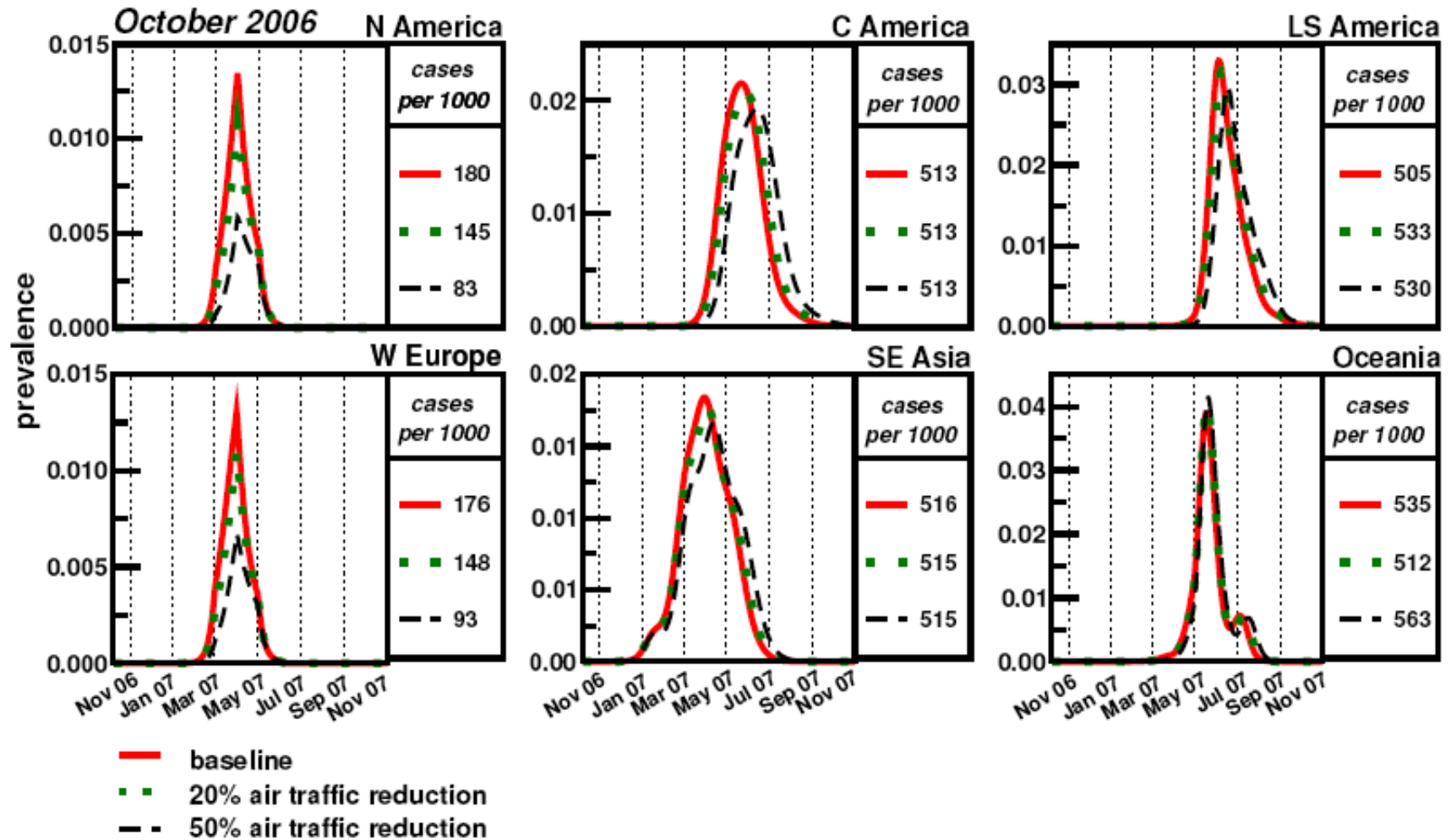
Predictions: pandemic flu



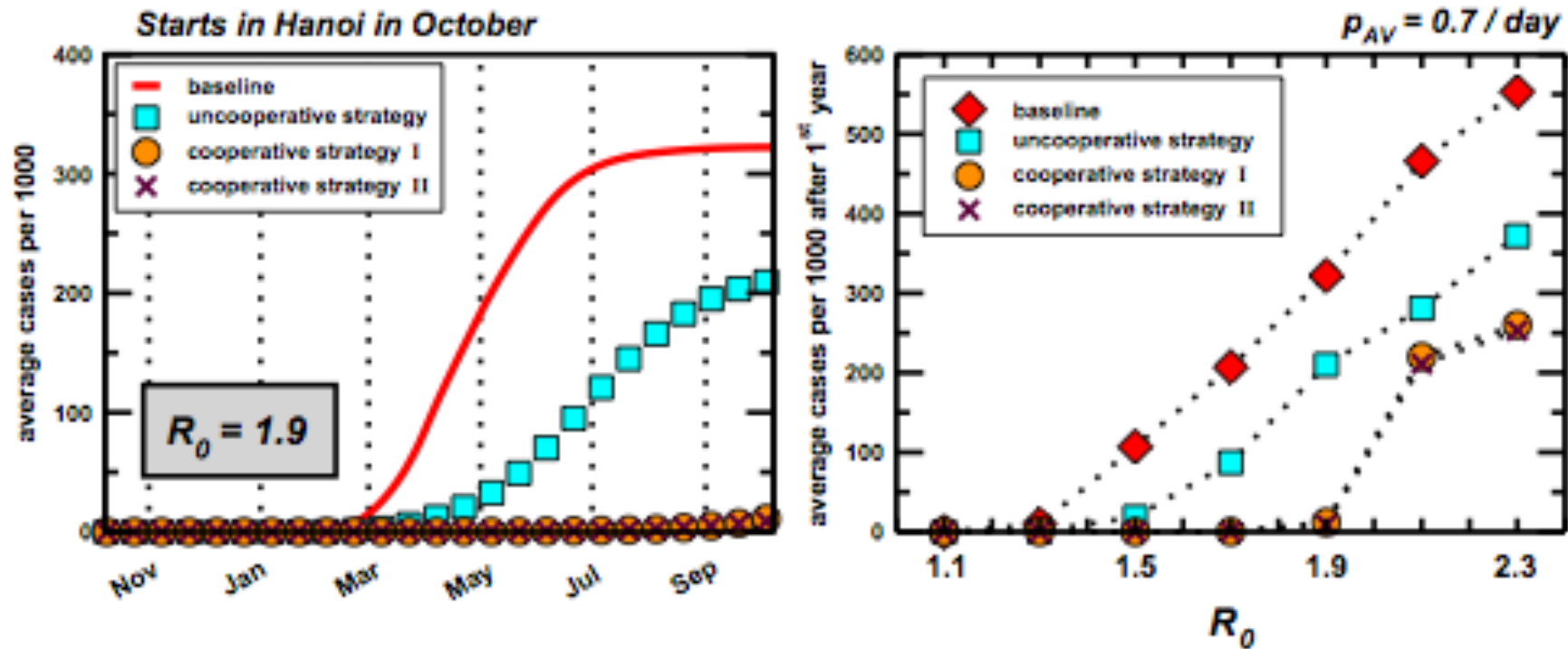
Effect of antivirals

- Comparison of strategies
 - Baseline: reference point (no antivirals)
 - Travel restrictions
 - “Uncooperative”: each country stockpiles AV
 - “Cooperative”: each country gives 10% (20%) of its own stock

Travel limitations....



Effect of antivirals: Strategy comparison



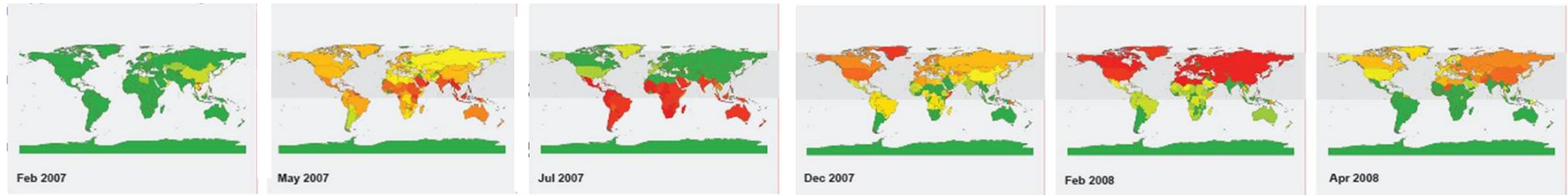
Best strategy: Cooperative !

Metapopulation model: theory

- Theoretical questions
 - Effect of heterogeneity on the predictability
 - Arrival time ?
 - Epidemic threshold ? At what conditions can a disease become a pandemic ?

Predictability

One outbreak realization:



Another outbreak realization ? Effect of noise ?

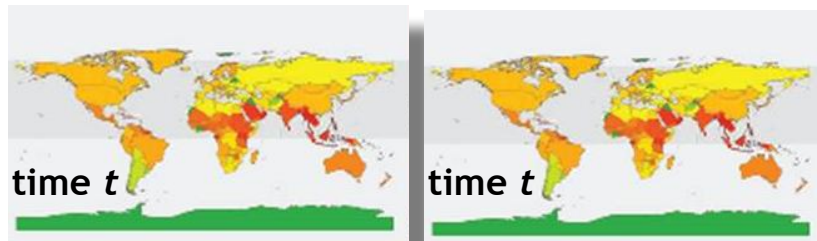


Overlap measure

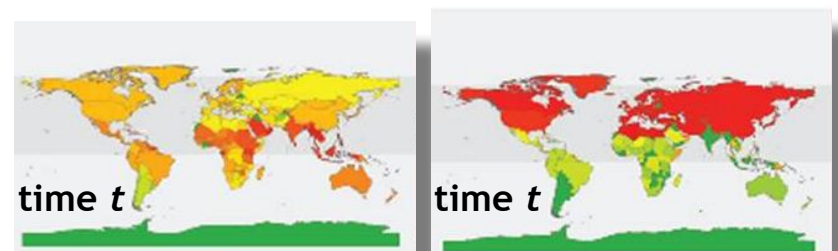
Similarity between 2 outbreak realizations:

$$\Theta(t)$$

Overlap function

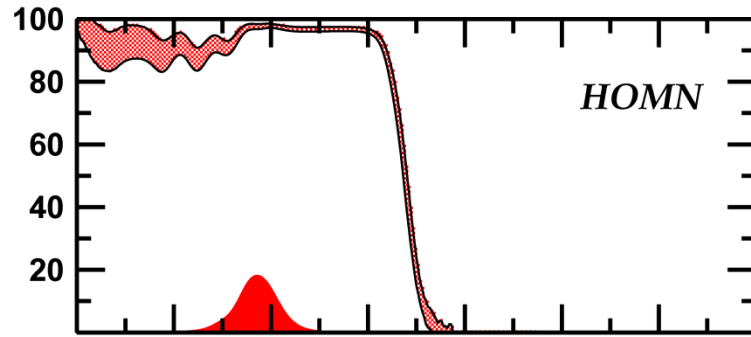


$$\Theta(t) = 1$$

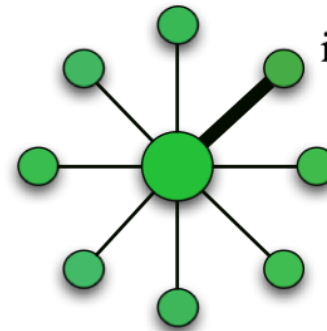
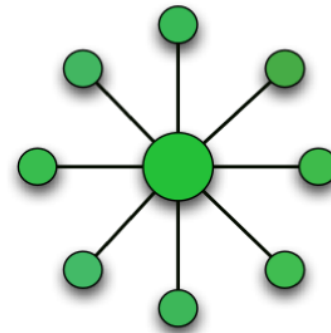


$$\Theta(t) < 1$$

Predictability

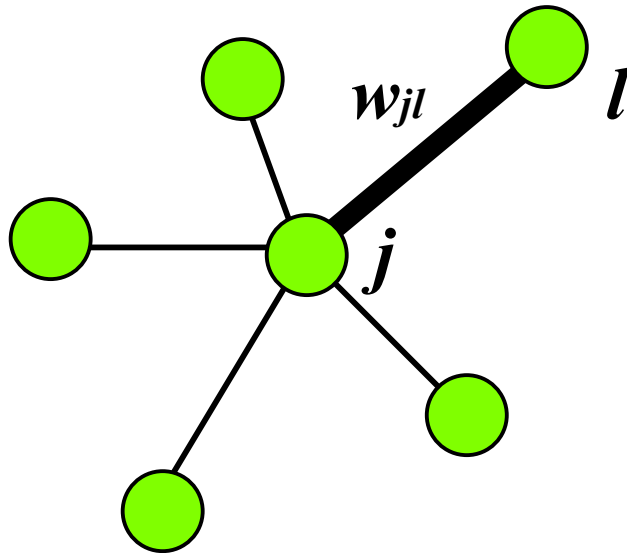


no degree fluctuations
no weight fluctuations



Predictability

- Effect of heterogeneity:



- degree heterogeneity:
decreases predictability

- Weight heterogeneity:
increases predictability !

Good news: Existence of preferred channels !

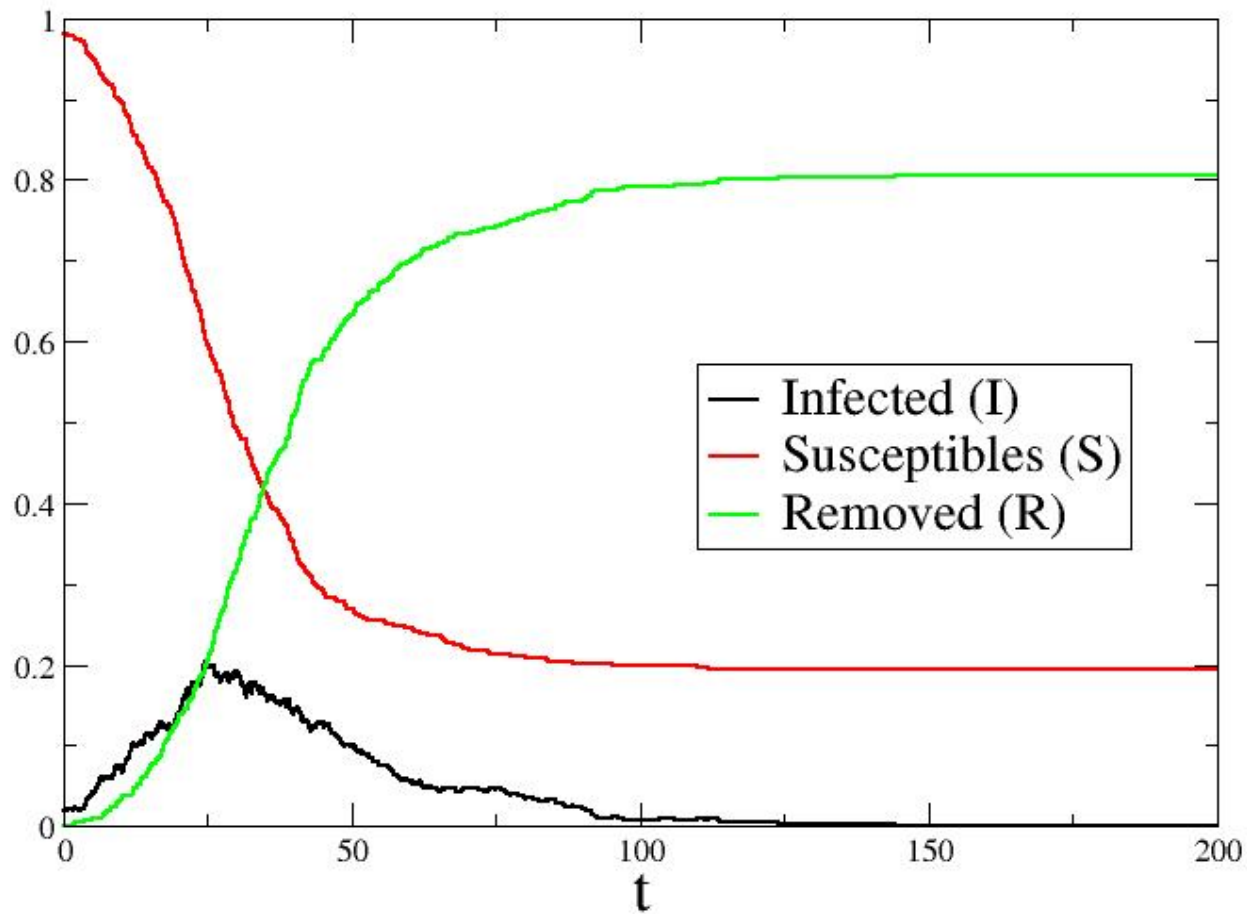
Epidemic forecast, risk analysis of **containment strategies**

Pandemic threshold

Once a city is infected:

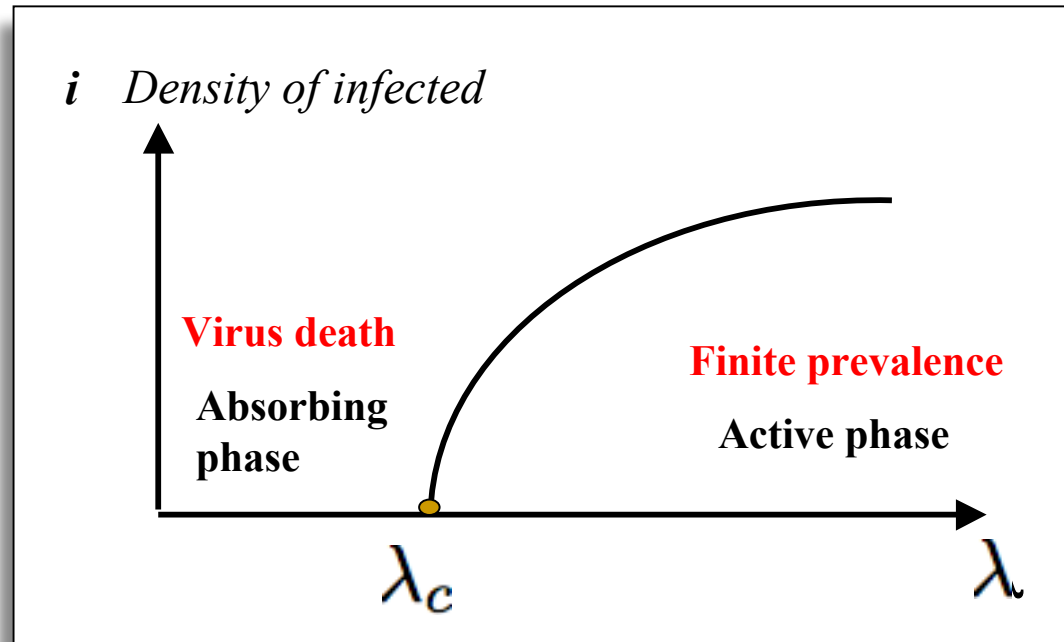
- what is the condition for non-extinction in the city ?
($R_0 > 1$)
- will it spread to other cities ?
- will it invade the whole world ?
- can we express a condition of the form $R^* > 1$?

One population: SIR (stochastic version)



One population: main results

Epidemic Threshold λ_c (SIR, SIS,...)



- **Epidemic threshold = critical point**
- **Prevalence i = order parameter**

Basic reproductive number:

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

One population: main results

Probability of extinction (stochastic version):

$$p_{ext} = \begin{cases} 1 & \text{if } R_0 < 1 \\ \frac{1}{R_0^{I_0}} & \text{if } R_0 > 1 \end{cases}$$

I_0 Number of infected individuals at $t=0$

Many populations connected through a network

Assumptions:

- Cities with the same population N
- p : probability per unit time for any individual to jump from one node to one of its neighbor

Many populations connected though a network

Assumptions (cont'd): Uncorrelated, complex network:

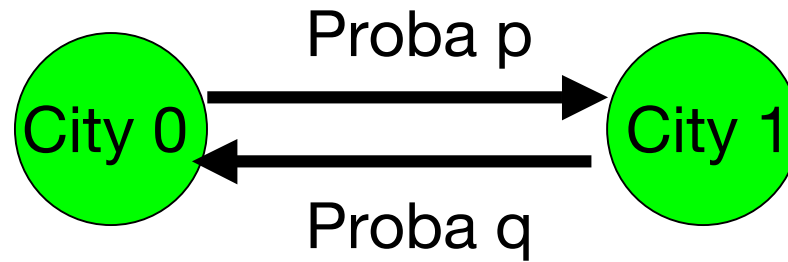
- Degree distribution $P(k)$, moments $\langle k \rangle$, $\langle k^2 \rangle$

- Percolation threshold: $p_c \simeq \frac{\langle k \rangle}{\langle k^2 \rangle}$ for $\langle k^2 \rangle \gg 1$

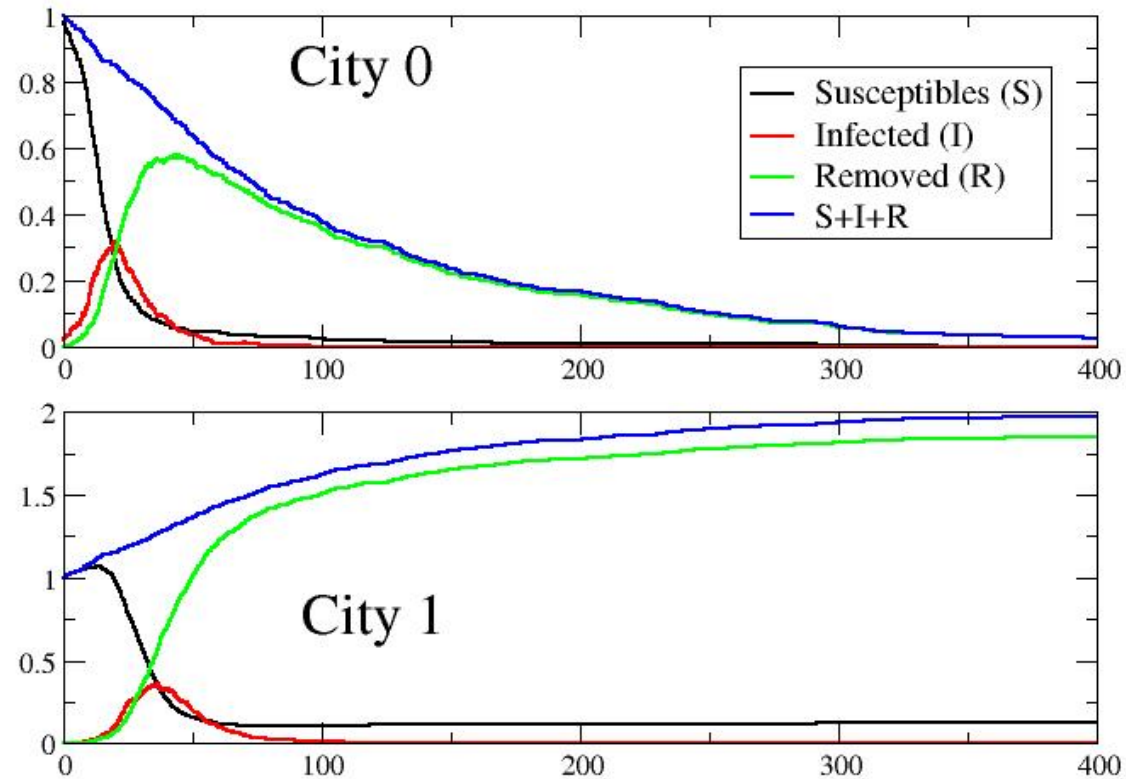
- Scale-free networks:

$$\frac{\langle k^2 \rangle}{\langle k \rangle} \gg 1$$

Building block: two cities



$p=0.01, q=0$
 $R_0=2$



Building block: two cities

- Arrival time probability in city 1 of an infected individual:

$$\begin{aligned} P(t_1 = t)dt &= \left[1 - (1 - pdt)^{I_0(t)} \right] \prod_{\tau=0}^{t-1} (1 - pdt)^{I_0(\tau)} \\ &= pdt I_0(t) e^{-p \int_0^t I_0(\tau) d\tau} \end{aligned}$$

- Cumulative:

$$P(t_1 > t) = e^{-p \int_0^t I_0(\tau) d\tau}$$

Condition for a network

- Condition for a pandemic spread:

$$P(t_1 < \infty) = 1 - e^{-p \int_0^\infty I_0(\tau) d\tau} > p_c$$

- Explicitly (SIR):

$$\frac{pN}{\mu} \frac{\langle k^2 \rangle}{\langle k \rangle} \frac{R_0 - 1}{R_0} > 1$$

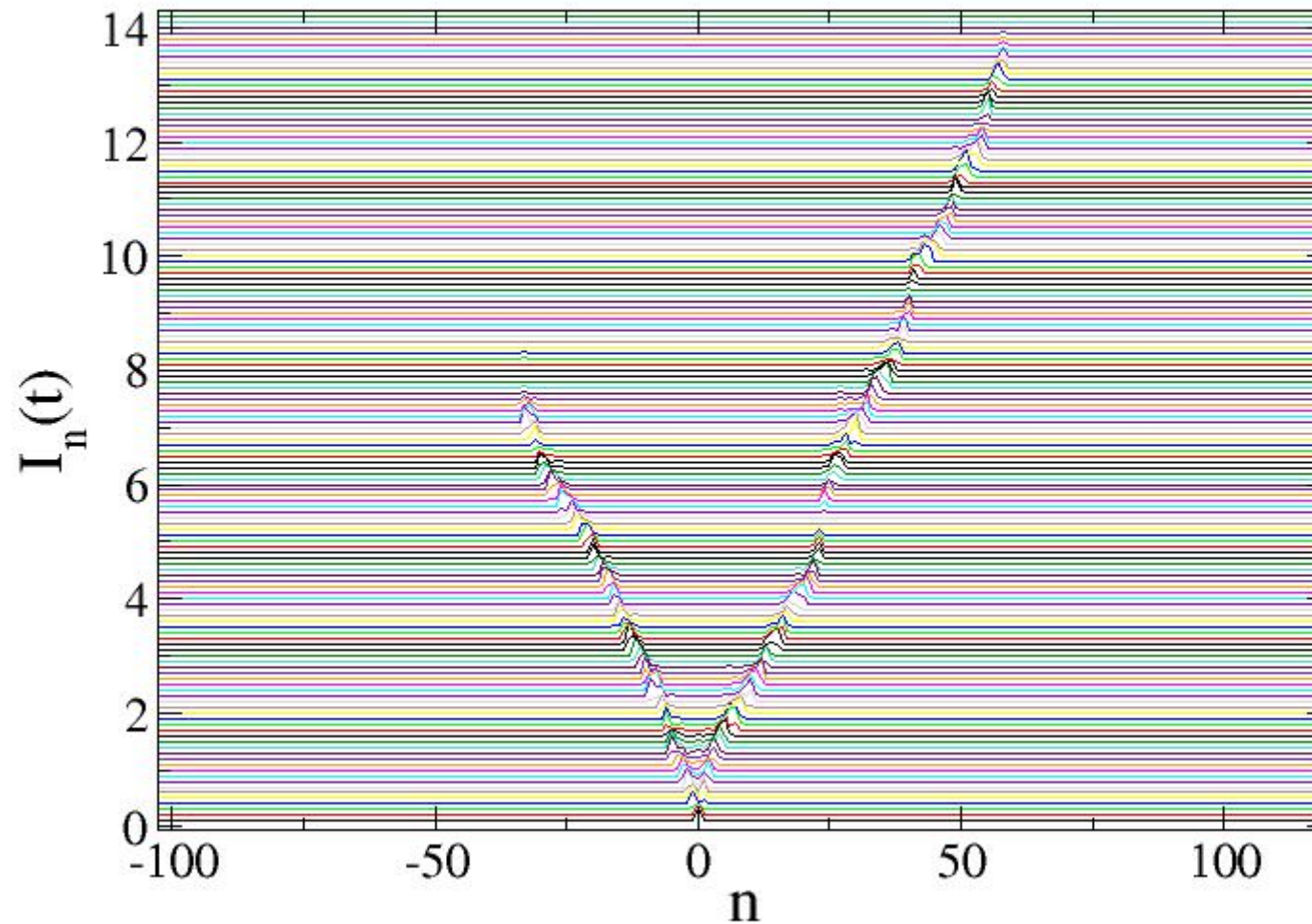
Consequences (1)

$$\frac{pN}{\mu} \frac{\langle k^2 \rangle}{\langle k \rangle} \frac{R_0 - 1}{R_0} > 1$$

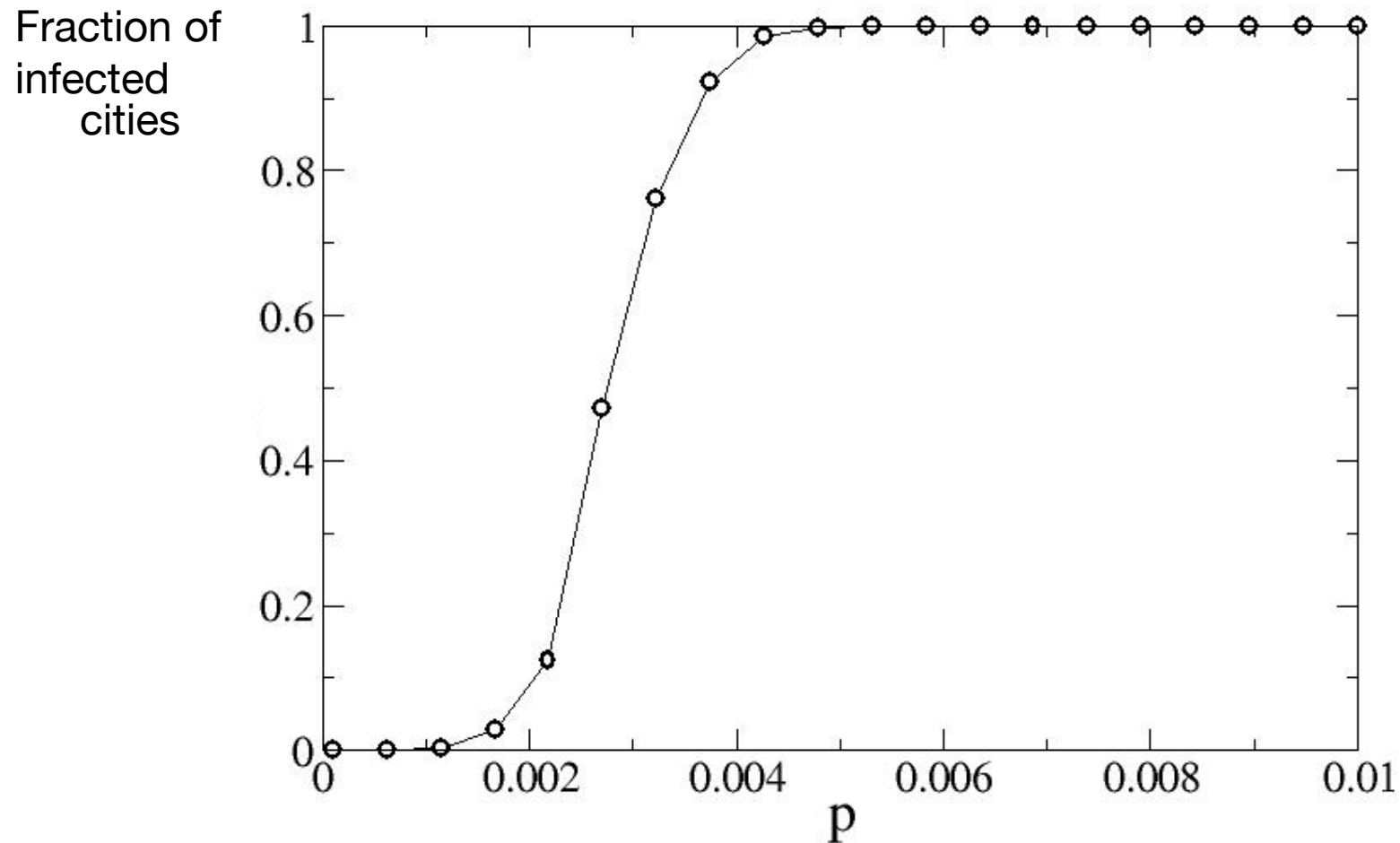
- Scale-free network: $\frac{\langle k^2 \rangle}{\langle k \rangle} \gg 1$
⇒ Travel restrictions inefficient !
- In agreement with a simple mean-field argument
[Colizza & Vespignani, PRL (2007)]

Consequences (2)

- $d=1: p_c=1 \Rightarrow$ finite cluster $\xi \sim (1-p)^{-1}$



Consequences (3)



- $d=2$ and Bethe lattice: $p_c < 1$

Conclusions

- Metapopulation model
 - Works for modeling pandemic spread
 - Mostly numerical results, many theoretical problems (reaction-diffusion on networks)
 - Existence of a “pandemic threshold” connected to percolation

Perspectives

- Population and travel probabilities (broadly) distributed: effect on the pandemic threshold ?

- Challenges of modern epidemiology:
 - Smaller scales ? (urban area)

 - Human mobility and city structure: statistical characterization ? Models ?

Collaborators (metapopulation model)

- Numerical studies on the metapopulation model
 - A. Barrat (CPT, Marseille)
 - V. Colizza (ISI, Turin)
 - A.-J. Valleron (Inserm, Paris)
 - A. Vespignani (IU, Bloomington)
- Theoretical analysis of the metapopulation model
 - C. Godrèche (IPhT, CEA)
 - J.-M. Luck (IPhT, CEA)

Thank you.
