Modelling global epidemics: theory and simulations

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Outline

- Introduction
- Metapopulation model: applications
  - SARS
  - Testing strategies
- Metapopulation model: theory
  - Pandemic threshold
- Discussion and perspectives
Epidemiology: an interdisciplinary field

Transportation systems

Social networks

Urbanism

Biology, virology
Epidemiology and statistical physics

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

- 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, ...

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Social network  Pandemic modelling (metapopulation)  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:

\[
S \xrightarrow{\lambda} I
\]

\(\lambda\): proba. per unit time of transmitting the infection

\(\mu\): proba. per unit time of recovering
One population: Simple models of epidemics

Stochastic model:

- SIS or SIR model (mean-field):

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

\( \lambda \): proba. per unit time of transmitting the infection
\( \mu \): proba. per unit time of recovering
Modeling: SIR with spatial diffusion $i(x,t)$:

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

where: $\lambda$ = transmission coefficient (fleas->rats->humans)
$\mu$=1/average infectious period
$S_0$=population density, $D$=diffusion coefficient

$$V = 2(\lambda S_0 D)^{1/2} \left[1 - \frac{\mu}{\lambda S_0}\right]^{1/2} \sim 100 - 200 \text{ miles/year}$$
**Metapopulation model**  
(mean-field)

- 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):

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


**Reaction-diffusion models**  
FKPP equation
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

- Correct prediction of outbreak
- Correct prediction of no outbreak
- Incorrect prediction of no outbreak
- No airports

North Pacific Ocean
North Atlantic Ocean
South Pacific Ocean
South Atlantic Ocean
Indian Ocean
North Pacific Ocean
SARS: predictions (2)

Colizza, Barrat, Barthelemy & Vespignani, bmc med (2007)
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- 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:

\[
\Theta(t) = \begin{cases} 
1 & \text{if } t = t_1 \\
< 1 & \text{else}
\end{cases}
\]
Predictability

no degree fluctuations
no weight fluctuations

+ degree heterogeneity

+ weight heterogeneity

Colizza, Barrat, Barthelemy & Vespignani, PNAS (2006)
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 $\lambda_c$ (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):

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

\[ I_0 \quad \text{Number of infected individuals at } t=0 \]
Many populations connected though 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:

$$pc \simeq \frac{\langle k \rangle}{\langle k^2 \rangle} \quad \text{for} \quad \langle k^2 \rangle \gg 1$$

- Scale-free networks:

$$\frac{\langle k^2 \rangle}{\langle k \rangle} \gg 1$$
Building block: two cities

City 0 \rightarrow \text{Proba } p \rightarrow \text{City 1}

City 0 \leftarrow \text{Proba } q \leftarrow \text{City 1}

\begin{align*}
p &= 0.01, \quad q = 0 \\
R_0 &= 2
\end{align*}
Building block: two cities

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

\[
P(t_1 = t) dt = \left[1 - (1 - p dt)^{I_0(t)}\right] \prod_{\tau = 0}^{t-1} (1 - p dt)^{I_0(\tau)}
\]

\[= p dt I_0(t) e^{-p \int_0^t I_0(\tau) d\tau}\]

- Cumulative:

\[P(t_1 > t) = e^{-p \int_0^t I_0(\tau) d\tau}\]
Condition for a network

- Condition for a pandemic spread:

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

- Explicitely (SIR):

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

Barthelemy, Godreche, Luck (2010)
Consequences (1)

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

- Scale-free network: \( \frac{\langle k^2 \rangle}{\langle k \rangle} \gg 1 \)
  \( \Rightarrow \) 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 $\xi \sim (1 - p)^{-1}$
- $d=2$ 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.