

## Introduction to network epidemiology

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#### Outline

-modeling an epidemic
-epidemics on networks
-epidemics in space
-interacting epidemics
-computer simulations

#### Outline

#### -modeling an epidemic

-epidemics on networks

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#### Western Africa ebola outbreak, 2014



#### 28 646 cases 11 323 death

#### UNPRECEDENTED SIZ

The current outbreak dwarfs the largest historical outbreaks in Africa, which were rural and relatively easy to control. Ebola has now spread to dense urban areas, where control is harder to achieve.







## Western Africa ebola outbreak, 2014



#### quantitative description



```
3000
        Mathematical description of the
   2500
        essential mechanisms underling the
        epidemic spread
   2000
Number of cases
        -disease progress within an
   1500
        individual
   1000
        -contagion
        -human contacts and behaviour
   500
```



[Keeling & Rohani, Modeling Infectious Diseases (2008)]

3000 contagion directly transmitted 2500 - airborne - physical contact 2000 (hand shake) Number of cases - sexual contact 1500 NON directly transmitted - vector-borne - food-born 1000 - fomites 500 0 A-16 ×20 ×3ª 1436 014-38 A.06 A.08 1432 A.OA ×`^°

week

[Keeling & Rohani, Modeling Infectious Diseases (2008)]

2014-40



week

[Keeling & Rohani, Modeling Infectious Diseases (2008)]





k contacts  $\beta$  transmission per contact

[Kermack & McKendrick Proc Roy Soc A 1927, Keeling & Rohani, Modeling Infectious Diseases (2008)]



$$d_t S(t) = -k\beta \frac{I(t)}{N} S(t)$$
$$d_t I(t) = k\beta \frac{I(t)}{N} S(t) - \mu I(t)$$

$$d_t R(t) = \mu I(t)$$

$$S(t) + I(t) + R(t) = N$$

[Kermack & McKendrick Proc Roy Soc A 1927, Keeling & Rohani, Modeling Infectious Diseases (2008)]

$$d_t S(t) = -k\beta \frac{I(t)}{N} S(t)^{-N}$$
$$d_t I(t) = k\beta \frac{I(t)}{N} S(t) - \mu I(t)$$

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

 $d_t R(t) = \mu I(t)$ 





# basic reproductive ratio $k\beta - \mu > 0$ Exponential growth $\frac{k\beta}{\mu} > 1$ $R_0$

average number of individuals infected by an infected individual during her/his infectious period in a fully susceptible population.

#### basic reproductive ratio

$$k\beta - \mu > 0$$
 — Exponential growth

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

outbreak	R <sub>0</sub>	Ref
H1N1 pandemic (2009)	1.2 - 2.0	[Fraser et al. Science 2009]
Zika (2015)	2.6 - 4.0	[Kucharski et al. PLoS Negl Trop Dis 2016]
smallpox	3.5 - 6.0	[Gani et al. Nature 2001]
Measles	16 - 18	[Anderson & May et al. Science 1982]





Projected 1.4 million cases by January 20, 2015

[Meltzer, MMWR Suppl., 65 2016]

## epidemic forecast

Projected 1.4 million cases by January 20, 2015

[Meltzer, MMWR Suppl., 65 2016]

- disregarding contact structure yields a larger number of cases
- prediction based on the hypothesis of nointerventions







 $N = S(t) + I(t) + R(t) + V \rightarrow S(t) = N - I(t) - R(t) - V$ 



$$d_t I(t) = k\beta \frac{I(t)}{N} \left(S(t) - V\right) - \mu I(t)$$
$$d_t I(t) = k\beta \frac{I(t)}{N} \left(1 - v\right) - \mu I(t)$$
$$v = \frac{V}{N}$$

 $N = S(t) + I(t) + R(t) + V \rightarrow S(t) = N - I(t) - R(t) - V$ 



$$d_t I(t) = k\beta \frac{I(t)}{N} \left( S(t) - V \right) - \mu I(t)$$
  

$$d_t I(t) = k\beta \frac{I(t)}{N} \left( 1 - v \right) - \mu I(t)$$
  

$$v = \frac{V}{N}$$
  

$$I(t) = e^{[\beta(1-v) - \mu]t}$$
  

$$R_{\text{eff}} = R_0(1-v)$$

$$v_c = \frac{R_0 - 1}{R_0}$$





#### agent based





homogeneous mixing

## epidemic containment

**ring vaccination:** the contacts and contacts of contacts of each index case are identified and vaccinated

#### <u>agent based model for Pujehun</u> <u>district of Sierra Leone</u>

- creation of a synthetic population
- individual spatial distribution
- demography
- household compositions
- link among households as typical in rural Africa



## epidemic containment

**ring vaccination:** the contacts and contacts of contacts of each index case are identified and vaccinated

#### <u>agent based model for Pujehun</u> <u>district of Sierra Leone</u>

- creation of a synthetic population
- individual spatial distribution
- demography
- household compositions
- link among households as typical in rural Africa
- 2 days identify the contacts and obtain consent and administer vaccine
- 4 days to develop immunity





agent based





population structure



homogeneous mixing

#### compartmental models

**complex disease unfolding**: the population is divided in classes according to diseases stages



#### compartmental models

**complex disease unfolding**: the population is divided in classes according to diseases stages



#### compartmental models

**complex population structure**: further division in classes based on host characteristic of epidemiological relevance





different contacts rates within/across age classes  $\rightarrow$  different infections rates

## social contacts by age

University, UK ~ 100 participant [Edmund et al Pro R Soc Lond B (1997)]

8 countries in Europe ~ 7000 participants [Mossong et al PLoS Med (2008)]

## All contacts



#### conclusion

- simple models can be useful
- key concepts: epidemic threshold and  $R_{\rm 0}$
- agent based models: 🧼 most realistic, allow the exploration of possible intervention scenarios, 😞 data & computational intensive
- in some cases complex compartmental models can be a good compromise

#### Outline

-modeling an epidemic

#### -epidemics on networks

-epidemics in space

-interacting epidemics

-computer simulations
### key ingredient: human to human contacts



relatives; colleagues; partners; random encounters (public transports, ...)



### early network data



#### HIV spread

[Auerbach, et al the American Journal of medicine 76, 487 1984]



### network properties

- small world
- high clustering
- heterogeneous contact behaviours
- presence of communities
- degree-degree correlations

# network properties: heterogeneous connectivity

#### Swedish survey with 2810 respondents

#partners in the last year





$$P(k) \propto k^{-\alpha}, \ \alpha \simeq 2.3$$
$$2 < \alpha < 3 \Rightarrow \langle k^2 \rangle \to \infty$$

#### power law distribution

-variance is big

-existence of hubs

### modelling epidemic on networks





[Pastor-Satorras & Vespignani PRL 2001, review :Pastor Satorras et al. Rev Mod Phys 2015]



what is the probability that a node with degree k is linked to an infected node of whatever degree k'?





force of infection =  $\beta k \sum_{k'} P(k'|k) I_{k'}$ 

$$P(k'|k) = k' \frac{P(k')}{\langle k \rangle}$$

If I make a connection at random I will do it more likely with someone that is very social (more stubs)



force of infection= m(k')



 $\frac{dI_k}{dt} = -\mu I_k(t) + S_k(t)\beta k \sum_{k'} k' \frac{p(k')}{\langle k \rangle} I_{k'}$ 

$$\frac{dI_{k}}{dt} = -\mu I_{k}(t) + S_{k}(t)\beta k \sum_{k'} k' \frac{p(k')}{\langle k \rangle} I_{k'}$$
...
Exponential growth  $\beta \frac{\langle k^{2} \rangle}{\langle k \rangle} - (\mu + \beta) \langle k \rangle$ 

#### vanishing epidemic threshold in the infinite size limit!

 $P_c - \langle k^2 \rangle$ 

[Pastor-Satorras & Vespignani PRL 2001, review :Pastor Satorras et al. Rev Mod Phys 2015]

#### heterogeneity favours epidemic spreading



[Pastor-Satorras & Vespignani PRL 2001, review :Pastor Satorras et al. Rev Mod Phys 2015]

# immunisation in heterogeneous networks

imagining of immunising a fraction g of individuals

$$\beta \left(1-\mathbf{g}\right) \leq \beta_c$$

immunisation threshold  $g_c = 1$ 

random immunisation is totally ineffective



targeted immunisation is extremely effective

[Pastor-Satorras & Vespignani, PRE 65, 036104 (2002)] [Dezso & Barabasi cond-mat/0107420; Havlin et al. preprint (2002)]

# immunisation in heterogeneous networks

my friend has more friends than me ...

$$\kappa_{\mathrm{nn},i} = \frac{1}{k_i} \sum_{j \in \mathcal{V}(i)} k_j \quad \text{average nearest neighbour degree}$$

$$\kappa_{\mathrm{nn},i} = \sum_{k'} k' P(k'|k_i) = \sum_{k'} \frac{k'^2 P(k')}{\langle k \rangle}$$

$$P(k'|k) = k' \frac{P(k')}{\langle k \rangle}$$

$$\kappa_{\mathrm{nn},i} = \frac{\langle k^2 \rangle}{\langle k \rangle}$$

\'''/

# immunisation in heterogeneous networks

my friend has more friends than me ...

$$\kappa_{\mathrm{nn},i} = \frac{\langle k^2 \rangle}{\langle k \rangle}$$

choose a person at random, immunise one of his friends

#### friends also as sensor to monitor an outbreak

[Cohen et la PRL 2003; Christakis & Fowler PLoS ONE 2010]

### network properties

- small world
- high clustering
- heterogeneous contact behaviours
- presence of communities
- degree-degree correlations



#### accounting for the whole network knowledge





#### Markov chain Prob(*i* is infectious, *j* is infectious) = $p_i p_j$ $p_i(t+1) = 1 - [1 - (1 - \mu)p_i(t)] \Pi_j [1 - \beta A_{ji}p_j(t)]$



#### Markov chain

 $\operatorname{Prob}(i \text{ is infectious}, j \text{ is infectious}) = p_i p_j$ 

$$p_i(t+1) = 1 - \left[1 - (1-\mu)p_i(t)\right] \Pi_j \left[1 - \beta A_{ji}p_j(t)\right]$$

prob *i* is not infectious prob *i* does not get infected from before



#### Markov chain

 $\operatorname{Prob}(i \text{ is infectious}, j \text{ is infectious}) = p_i p_j$ 

$$p_i(t+1) = 1 - [1 - (1 - \mu)p_i(t)] \Pi_j [1 - \beta A_{ji}p_j(t)]$$

linearize

$$p(t+1) = (1 - \mu + \beta A^{\dagger})p(t) + \mathcal{O}(||p(t)||^2)$$



$$p(t+1) = (1 - \mu + \beta A^{\dagger})p(t) + \mathcal{O}(||p(t)||^2)$$
$$\left(\frac{\beta}{\mu}\right)_{\text{critical}} = \frac{1}{\rho[A]} \quad \substack{\text{spectral radius} \\ (\text{largest eigenvalue})}$$

### quenched vs. heterogeneous

#### quenched mean field approximation

heterogeneous mean field approximation

[Castellano, Pastor-Satorras PRL 2010]

exact structure of the network

-fully account for network
information
-comparison with null models for
assessing relevant properties
-test possible interventions

[Wang et al. SRDS 2003; Gómez et al. 2010]

coarse graining statistical properties

-simple transparent formula -analytical understanding of immunisation processes -full network information not available in many cases

[Pastor-Satorras & Vespignani PRL 2001, Pastor Satorras et al. Rev Mod Phys 2015]



#### recent network data





#### internet mediated prostitution

sexual contacts between 6,624 escorts and 10,106 sex buyers extracted from an online community [LEC. Rocha, et al, PNAS 2009]



#### recent network data

#### face-to-face contacts

#### **RFID technology**





schools - workplaces - hospitals - museums - conferences households - rural Africa

[Salathé et al. Proc Natl Acad Sci 2010; **Sociopatterns.org** - Stehlé et al. BMC Medicine 2011; Kiti et al. EPJ Data Science 2016; Ozella et al. PLoS ONE 2018; **iBird** - Obadia et al. PLoS Comp Bio 2015]

#### recent network data



bovine displacement among farms

[Bajardi, PLoS ONE (2011)]

in the 90's generative network models

# generative network models

#### in the 90's generative network models

preferential attachment model: rich gets richer



- $m_0$  initial nodes
- each time step: a new node enters with *m* stubs
- probability it connects with a node with degree  $k_i$ :  $\Pi(k_i) = \frac{k_i}{\sum_i k_i}$

 $\frac{2m^2}{k^3}$ 

degree distribution in the stationary limit: P(k)

# generative network models

#### in the 90's generative network models

preferential attachment model: rich gets richer



the model explains the topology of the network **but** the network dynamics is decoupled from the dynamical process unfolding on the top of the network

time scale separation not applicable in many cases



[LEC. Rocha, et al, PNAS 2009]

Nowadays temporal network models

#### Nowadays **temporal network models** activity driven model [Perra et al, Sci Rep 2012]

- activity potential  $x_i$  : number of activation in a  $\Delta t$
- F(x) : distribution of the activity potential
- a node activates with rata  $\,a_i=\eta x_i$  and forms m connections



### activity driven model

#### Nowadays temporal network models activity driven model [Perra et al, Sci Rep 2012]

heterogenous topology in the aggregated network, over a window T, result from a heterogeneous activity potential



#### activity driven model

#### Nowadays **temporal network models** activity driven model [Perra et al, Sci Rep 2012]

activity potential affects spreading and the epidemic threshold

spreading dynamics  

$$I_{a}^{t+\Delta t} = -\mu \Delta t I_{a}^{t} + I_{a}^{t} + \lambda m \left(N_{a}^{t} - I_{a}^{t}\right) \int da' \frac{I_{a'}^{t} a' \Delta t}{N}$$

epidemic threshold  

$$\frac{\beta}{\mu} > \frac{2\langle a \rangle}{\langle a \rangle + \sqrt{\langle a^2 \rangle}}$$
### temporal network properties Nowadays temporal network models

- activation rate
- turn over
- inter-contact time
- memory

# account for the full temporal dimension



#### 

### infection propagator approach

 $S \xrightarrow{\lambda} \blacksquare \xrightarrow{\mu} S$ 



[Scholtes et al Nature Com 2015]

[Valdano et al PRX 2015]



#### NT x NT supra-adjacency matrix



### infection propagator approach

threshold on temporal network STATIC network

epi threshold  $\rho[\mathbf{M}(\lambda_{thr},\mu)] = 1$ 

dim = NT [Powell, arXiv, 2011] dim = N

$$\rho[\mathbf{P}(\lambda_{thr},\mu)] = 1$$

$$\mathbf{P} = (1-\mu + \lambda A_1)(1-\mu + \lambda A_2) \cdots (1-\mu + \lambda A_T)$$
[Lentz et al, PRL 2013]
infection
infe

### conclusion

- Network topology affect spreading
- Degree heterogeneity lower the epidemic threshold
- heterogenous mean field approach vs. quenched mean field approach
- network temporal dimension and interplay with spreading process
- activity driven vs. infectious propagator approach

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### Western Africa ebola outbreak, 2014



### Western Africa ebola outbreak, 2014



### black death,14th century



### H1N1 influenza pandemic, 2009



H1N1 influenza pandemic, 2009

### mobility network data

air traveling

data collected by the International Air Trasport Association

[Hufnagel et al. PNAS 2004; Colizza et al. PLoS Med 2007; Balcan et al. PNAS 2009]



### mobility network data

**commuting data** census data of different countries [Balcan, Colizza et al. PNAS (2009)]



### mobility network data



#### local mobility

mobile phone data

[Gonzalez et al, Nature (2008)]

### mobility network properties

... heterogeneous!



traffic heterogeneity





## metapopulation models: a compromise



## metapopulation models: a compromise



# metapopulation models: a compromise



local populations:

- discrete entities in space: patches
- Interaction between populations : coupling, flows

### metapopulation models



<sup>[</sup>Hanski, I. & Gaggiotti, Elsevier, Academic Press, 2004]

### SIR metapopulation models



global 
$$S(t) = S_1(t) + S_2(t) + S_3(t) + \dots + S_V(t) = \sum_i S_i(t)$$
  
variables  
 $I(t) = I_1(t) + I_2(t) + I_3(t) + \dots + I_V(t) = \sum_i I_i(t)$   
 $R(t) = R_1(t) + R_2(t) + R_3(t) + \dots + R_V(t) = \sum_i R_i(t)$   
 $N(t) = N_1(t) + N_2(t) + N_3(t) + \dots + N_V(t) = \sum_i N_i(t)$ 

### SIR metapopulation models

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







probability for an individual in *i* to travel from *i* to *j*?  $p_{ij} = \frac{W_{ij}}{N_i}$  for all compartments



average number of individuals in compartment X in *i* traveling from *i* to *j*?  $\langle T_{ij}^X \rangle = p_{ij} X_i(t) = \frac{W_{ij}}{N_i} X_i(t)$ 

### SIR metapopulation models

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

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

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

$$\Omega_i^X = \sum_j \left(\frac{w_{ji}}{N_j}X_j - \frac{w_{ij}}{N_i}X_i\frac{1}{j}\right)$$

\* global invasion threshold
 \* spatial propagation & predictability

### global invasion threshold



which are the condition for a local outbreak to spread at global proportion?

### global invasion threshold



#### coarse graining

following the spread from one subpopulation to another

mapping the spreading dynamics among subpopulation into the spreading on a network

### global invasion threshold



- Invasion dynamics at the subpopulation level
- branching process approximation

D<sup>n</sup>: diseased subpopulations at generation n

## invasion threshold: homogeneous system



p~ traveling probability along each link  $\langle k \rangle$  # connection of each subpopulation

total # infectious individuals sent from i to j during the local outbreak

 $\lambda_{ij} = \frac{pR_{\infty}}{\mu}$ 

probability of early extinction  $P_{
m ext}$ 

$$_{\rm t} = \left(\frac{1}{R_0}\right)^{\lambda_{ij}}$$

$$D^{n} = (\langle k \rangle - 1) \left( 1 - P_{\text{ext}} \right) \left( 1 - \sum_{m=0}^{n-1} \frac{D^{n}}{V} \right) D^{n-1}$$

[Colizza & Vespignani, PRL 2007, JTB 2008]

# invasion threshold: homogeneous system

$$D^{n} = \left(\langle k \rangle - 1\right) \left(1 - P_{\text{ext}}\right) \left(1 - \sum_{m=0}^{n-1} \frac{D^{n}}{V}\right) D^{n-1}$$

$$R_* = \left(\langle k \rangle - 1\right) \left(1 - P_{\text{ext}}\right)$$

[Colizza & Vespignani, PRL 2007, JTB 2008]

# invasion threshold: heterogeneous system



$$D_{k}^{n} = \sum_{k'} D_{k'}^{n-1} \left( \frac{k'-1}{P(k \mid k')} \left( 1 - \sum_{m=0}^{n-1} \frac{D_{k}^{m}}{V_{k}} \right) \left( 1 - P_{\text{ext}}(\lambda_{k'k}) \right)$$

[Colizza & Vespignani, PRL 2007, JTB 2008]

# invasion threshold: heterogeneous system



[Colizza & Vespignani, PRL 2007, JTB 2008]

## invasion threshold: increasingly realistic models



commuting and recurrent mobility patterns: beyond the markovian assumption [Balcan & Vespignani Nat Phys 2011, Belik et al PRX 2011]

heterogeneous travel duration [Poletto et al Sci Rep 2012]

heterogeneity in travel frequency: children are more social but travel less [Apolloni et al BMC Inf Dis 2013]

behavioural response to the presence of a disease [Meloni et al Sci Rep 2011]

\* global invasion threshold
 \* spatial propagation & predictability

### 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*:

$$P\left(t_{\text{seeding}} = t \, dt\right) = \prod_{s=1}^{t-1} (1-p)^{I(s \, dt)} \times \left[1 - (1-p)^{I(t \, dt)}\right]$$
$$\downarrow p \to 0$$

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



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

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

$$P(t_{\text{seeding}} = t) = pe^{at}e^{-pae^{at}}$$
Gumbel distribution
$$\langle t_{\text{seeding}} \rangle \simeq \frac{1}{a}\ln(pa)$$

## spatial propagation: travel restrictions



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

p rescaled of a factor ~lpha

$$\Delta \langle t_{\text{seeding}} \rangle = -\frac{1}{a} \ln(\alpha)$$

[Gautreau et al JTB 2008; Bajardi et al PLoS ONE 2011; Hollingsworth et al Nature Med 2006; Scalia Tomba et al Math Biosci 2008]



# how did restriction in mobility affect spreading?

TRAVEL BAN &

**BORDER CLOSURE** 

FLIGHT

**AFFECTED** 

AREA

**SUPPRESSION** 

[Poletto, Eurosurveillance 2014]



### how did restriction in mobility affect spreading?



ated	iravei-related measurokuthorities) Companies	Starting date of intervention*	Target alea	Additional details <sup>to</sup>
paression	Three European airlines	From 6 Aug 2014 to 18 Aug 2014	Liberia Sierra Leone	See SI
	7wo Asian airlines	From 6 Aug 2014 to 14 Aug 2014	Guines Kenya	See SI
	Six African airtines	From 6 Aug 2014 to 16 Aug 2014	Guinez Liberiz Niperia Sierra Leone	See Si
n and/or csure	Glana	1 Aug 2016	Liberiz Nigeria Sierra Leone	Bas of all flights from the affected countries
	Zambia	8 Aug 2014	Liberia Nigeria Sierra Leone	Bar onentry for chizens of the target countries
	Mauritania	33 Aug 20:4	Liberia Nigeria Sierra Leone	Bar on entry far citizens of the target courtries
	Chad	11 Aug 20:4	Liberia Sierra Leone	Ban of all flights
	Cote D'Ivoire	13 Aug 20:4	Nigeria	Ban of all flights, dosare af land borders
	Nigeria	13 Aug 20:4	Guinea Liberia Sierra Leone	Bas of all flights from the affected countries
	Botiwana	14 Aug 2014	Guinea Liberia Sierra Leone	Banned travellets from affected countries
	Equatorial Guinea	15 Aug 20:4	Guinea Liberia Sierra Leone	Suspended the issuance of visas
	Gambia	15 Aug 2014	Guinea Liberia Sierra Leone	Ban of all flights
	Kenya	16 Aug 2014	Guinea Liberia Sierra Leone	Ban of all flights
	Cape Verde Islands	19 Aug 2014	Guinea Liberia Sierra Leone	Eorder closure
	South Africa	21 Aug 2014	Guinea Liberia Sierra Leone	Bar on entry far citizens of targe: countries
	Cameroon	21 Aug 2014	Guinea Literia Sierra Leone	Eorder closure
	Senegal	21 Aug 2014	Guines Liberis Sierra Leone	Closure of land borders
	Rwanda	24 Aug 2014	Guinea Liberia Sierra Leone	Eorder closure
	Gabos	26 Aug 2014	Guinea Literia Sierra Leone	Eorder closure
	Naniba	26 Aug 2014	Guines Liberis Sierra Leone	Eorder closure
	Guinea Bissau	Before 26 Aug 2014	Guinea Liberia Sierra Leone	Ban of all flights, dosure of land borders
	Тэдо	Before 26 Aug 20:4	Guinea Literia	Ban of all flights

SI: supplementary information.

Depending on the information available, this can be either the date of intervention or the date of the bulletin/news.

<sup>1</sup> Gosure of land korcers is for all travellers irrespective of citizership.

Border closure is generally for citizens of the larget countries and travellers coming from the affected area, with the exception of nationals of the destination sountry.

he list is obtained from publicly available sources extracted from the search ("ebola" AND "travel") on Twitter on a September 2014. Additional searches of news published on the Internet were performed to confirm and complement the initial list. More detailed information and references are provided in the supplementary information" available at http://www.mobs-lab.org/ebola-eurosarvesp.html

The list is obtained from publicly available sources extracted from the search (= bola = AND = traver) on initier on 1 september 2014. Additional searches of news published on the Internet were performed to confirm and complement the initial list. More detailed information and references are provided in the supplementary information\* available at http://www.mobs-lab.org/ebola-eurosurvsup.html

#### overall reduction with Western Africa = ~60%

Bepending on the information available, this can be either the date of intervention or the date of the bulletin/new

#### [Poletto et al, Eurosurveillance 2014]

# how did restriction in mobility affect spreading?

**30**c

11d

27d

66%

41%

22d

AFFECTED

DELAY

TRAVEL

REDUCTION

AREA

**0d** 

42%

[Poletto et al, Eurosurveillance 2014]

8%

**EBOLA** 

2014

2d

10%

## spatial propagation: effective distance among two nodes

effective distance along the link

 $\ln(p_{ij})$ 

[Gautreau et al JTB 2008; Brockmann, Helbing, Science 2013]

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

CDG

## spatial propagation: effective distance among two nodes

effective distance along the link

 $\ln(p_{ij})$ 

[Gautreau et al JTB 2008; 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]

# middle east respiratory syndrome 2012-2015



# International spread follows simple rules



#### modelling worldwide spread of epidemics



52 major cities: spread of 1968 - 1969 H3N2 pandemic from Hong Kong

[Rvachev, Longini, Math. Biosci. 1985]





~ 3000 - 4000 cities: spread of SARS, 2009 H1N1 pandemic, MERS, Ebola, hypothetical pandemic scenarios

[Hufnagel et al. PNAS 2004; Colizza et al. PLoS Med 2007; Balcan et al. PNAS 2009; Poletto et al. Eurosurveillance 2014; Gomes et al. PLoS Curr 2014]

## GLEaM: GLobal Epidemic and Mobility model



### GLEaM: demography and mobility



#### Population Distribution

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



#### 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: epidemic model



[www.gleamviz.org Balcan et al. PNAS 2009]



[www.gleamviz.org Balcan et al. BMC Med 2009]



[www.gleamviz.org Balcan et al. BMC Med 2009]



[Poletto et al. Eurosurveillance 2014; Poletto et al. Epidemics 2016; also: Cauchemez, et al. Lancet Infect Dis 2014; Balcan et al. BMC Med 2009, Fraser et al. Nature 2009] international propagation driven by the epidemic in the source area

exploit knowledge of the international propagation to **infer** the spread in the source area



[www.gleamviz.org Balcan et al. BMC Med 2009]



[www.gleamviz.org Balcan et al. BMC Med 2009]

#### conclusion

- metapopulation model simple enough to allow for mathematical understanding
- yet enough accurate to allow for realistic description of outbreaks
- international travel: highly populated patched connected by relatively small mobility fluxes
- out from this regime modelling spatial spread more complicated & lack of data

#### Outline

-modeling an epidemic
-epidemics on networks
-epidemics in space
-interacting epidemics

-computer simulations





Host

hospital

agent based

home

school

work

### multistrain & influenza



Source: European Centre for Disease Prevention and Control (ECDC) 2009 Reproduced and adapted (2009) with permission of Dr Masato Tashiro, Director, Center for Influenza Virus Research, National Institute of Infectious Diseases (NIID), Japan.



- 3 circulating subtypes + continuous mutation
- ~ billion cases annually (~3-5 million severe illness)
- ~300,000-500,000 deaths
- vaccine effectiveness: 23% (in 2014-15) 47% (in 2015-16)

### can we increase the impact of vaccination?

[http://www.cdc.gov/flu/professionals/vaccination/effectiveness-studies.htm]

#### multistrain & pneumococcal disease



[Weinberger et al. the Lancet 2011]

#### HIV & TB





risk of TB ~16-27
 times greater in
 people living with HIV

- 10.4 million cases of TB disease globally,
1.2 million [11%] among HIV patient

#### multi strain: fundamental questions

### cooperation EPIDEMIOLOGICAL IMPACT competition dominance/co-dominance COEXISTENCE

#### a simple model with 2 strains



- $\xi > 1$  cooperative
- $\xi < 1$  competitive

#### competitive diseases: winner takes it all!



$$A_{ij}~$$
 adjacency matrix  $\rho\left[A\right]~$  spectral radius

#### $\rho[A]\beta/\mu$ strength of the strain

[Prakash et al, Proceedings of the 21 WWW 2012]

#### competitive diseases: winner takes it all!



#### cooperative diseases



[Cai et al Nature Phys 11 936 2015; Chen et al New J Phys 19 103041 2017]

#### cooperative diseases



[Cai et al Nature Phys 11 936 2015; Chen et al New J Phys 19 103041 2017]

#### cooperative diseases

strain

strain

 $\xi > 1$ 

suscep

- abrupt phase transitions

 $\mu$ 

- hysteresis: epidemic threshold is different from the eradication threshold
- the behaviour depends on the network topology



[Cai et al Nature Phys 11 936 2015; Chen et al New J Phys 19 103041 2017]

#### interacting diseases: general framework





TABLE I. Definition of model parameters.

Parameter	Dynamical meaning
λ <sub>1</sub>	Baseline infectiousness of disease 1
λ <sub>2</sub>	Baseline infectiousness of disease 2
$\mu_1$	Baseline recovery rate of disease 1
$\mu_2$	Baseline recovery rate of disease 2
$\beta_1^a$	Variation of disease 1 infectiousness due to the fact that the susceptible individual exposed to disease 1 is infected with disease 2
$\beta_2^a$	Variation of disease 2 infectiousness due to the fact that the susceptible individual exposed to disease 2 is infected with disease 1
$\beta_1^b$	Variation of disease 1 infectiousness due to the fact that the spreader is also infected with disease 2
$\beta_2^b$	Variation of disease 2 infectiousness due to the fact that the spreader is also infected with disease 1
η <sub>1</sub>	Variation of disease 1 recovery rate for individuals also infected with disease 2
η <sub>2</sub>	Variation of disease 2 recovery rate for individuals also infected with disease 1

- heterogeneous mean-field approximation
- network underlying spreading is disease-specific
- accounting for a wide array of possible interaction
- second disease introduced at a certain time
- both SIS & SIS and SIR & SIR

[Sanz et al PRX 4, 04100 2014]

#### interacting diseases: general framework



[Sanz et al PRX 4, 04100 2014]

#### competing diseases in space

- SIR
- same  $R_0$
- different infectious period  $\rightarrow$   $\tau_s > \tau_f$
- full cross-immunity



#### competing diseases in space

- SIR
- same  $R_0$
- different infectious period  $\rightarrow$   $\tau_s > \tau_f$
- full cross-immunity





- the 2 strains originate from different patches
- stochastic simulations of the outbreak

## role of p on dominance/co-dominance?


[Poletto et al. PLoS Comp Bio 2013]

## scale of individuals



## scale of subpopulations



$$R_* = \left(\langle k \rangle - 1\right) \left[ 1 - \left(\frac{1}{R_0}\right)^{\frac{pR_\infty}{\mu}} \right]$$

 $R_*$  increasing function of  $\mu^{-1}$   $\square > R_*^s > R_*^f$  $R_{st}$  increasing function of ho

#### <u>large p:</u>

 $R_*^s$  and  $R_*^f >> 1$ fast strain reaches more rapidly new subpopulations

### <u>small p:</u>





allow for different  $R_0$ 

→ when does mobility matters?



exponential growth in homogenous mixing  $G = \mu (R_0 - 1)$ 

percolation capability  $R_{st}$ 

# conclusion

- interaction between pathogens critical for the epidemic outcome
- the interaction dynamics is critically affected by the structure of the host population, e.g. contact behaviour and mobility

# Outline

-modeling an epidemic
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-epidemics in space
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-computer simulations

# software: <u>GLEaMviz.org</u>

input



## **GLEAM Server + GLEAMviz Client**

**<u>GLEAM Server:</u>** uses GLEAM as the engine to perform the simulations on highperformance computers

**<u>GLEAMviz Client:</u>** desktop application to interact with tGLEAM Server through a visual interface



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HINI Hano	26/10/08 MR geodata v2	multi-run	complete.	complete		
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# software: <u>GLEaMviz.org</u>



# **GLEAM Server + GLEAMviz Client**

**GLEAM Server:** uses GLEAM as the engine to perform the simulations on high-performance computers

**<u>GLEAMviz Client:</u>** desktop application to interact with tGLEAM Server through a visual interface



# python package: epidemic threshold (? Features Business Explore Marketplace Pricing Search



## infection propagator approach for temporal networks

[Valdano et al PRX 2015]



No description, website, or topics provided.

@41 commits	2 branches	⊘ 0 releases	1 contributor	
Branch: stools = New pull request			Find file	Clone or download *
Eugenio Valdano and Eugenio Valdano	repare networkx		Latest co	nimit bacagaa on 16 Apr
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	1	update license and readme		3 years ago
F) MANIFEST.in	t	irst commit		2 years ago
README.md		sython/python	a year ago	
E requirements.txt		assuming cython	a year ago	
(=) setup.py	1	assuming cython	a year ago	
lei test_system.py		readma updated 2 years		

### https://github.com/eugenio-valdano/threshold

# python package: spreading dynamics on networks

github.com/springer-math/ Mathematics-of-Epidemics-on-Networks

epidemicsonnetworks.readthedocs.io/ en/latest/index.html

Mathematics of Epidemics on Networks' by Kiss, Miller, and Simon



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# data: <u>sociopatterns.org</u>

follow us on builter

## SocioPatterns

Close proximity interaction data collected with RFID tags in different settings

#### WELCOME

SocioPatterns is an interdisciplinary research collaboration formed in 2006 that adopts a datadriven methodology to study social dynamics and human activity.

Since 2008, we have collected longitudinal data on the physical proximity and face-to-face contacts of individuals in numerous real-world environments, covering widely varying contexts across several countries: schools, museums, hospitals, etc. We use the data to study human behaviour and to develop agent-based models for the transmission of infectious diseases.

We make most of the collected data freety available to the scientific community.

#### FEATURED: INFECTIOUS SOCIOPATTERNS POSTER



Left: One of the sixty-rine daily diagrams of contact activity, Right: Thumbhail of the poster with the complete visualization and accompanying text.

We have created a visualization of sixty-nine days of face-to-face contact activity among more that 30,000 persons based on data collected during the INFECTIOUS: STAY AWAY exhibition in the Science Gallery in Dublin, Ireland. This visualization is published in our gallery as a poster that can be freaty downloaded.

READ MORE ....

#### COLLABORATION MEMBERS

SocioPatterns is a collaboration between researchers and developers from the following institutions and companies:

- + ISI Foundation Turin, Italy
- > CNRS Centre de Physique Théorique Marseille, France
- » Bitmenufactory Cambridge, UK

#### NEWS

NEWS

#### New paper in Nature Communications

PRESS | DATA

We have published a new paper in Neture Communications. In this paper, we consider the issue of how to correctly inform numerical models of the propagation of infectious diseases when only partial information on the contacts of individuals is available, due to population sampling.

Indeed, the coverage of the population in many measures of detailed contact networks is incomplete, and this yields a systematic underestimation of epidemic risk if the data is used without precaution. Here, we introduce a method to compensate for this systematic bias. and obtain accurate evaluations of epidemic risk using incomplete data. To this aim, we have developed an algorithm that effectively fills in the gaps of the empirical data with a realistic picture of the missing contact network. Although the obtained surrogate contacts are different from the actual missing contacts, using them in the simulation of an influenzalike process gives an accurate estimation of what would have been obtained on using complete data. It is therefore possible to have a good estimation of the epidemic risk, even if a substantial fraction of the contacts are missing from the empirical data.



# SIR on network: pseudo-code

- $A_{ij}$  Adjacency matrix
  - $\boldsymbol{n}$  number of nodes
  - $\beta\,$  transmission probability per link & per time step
- One variable=one individuals

**Vector** =  $(a_1, a_2, a_3, \dots, a_n)$ 

For instance Tim=  $a_3$ 

- We assign possible states to each value of each variable
  - a<sub>i</sub> =0 => susceptible
  - a<sub>i</sub> =1 => infected
  - a<sub>i</sub>= 2 => removed

# SIR on network: pseudo-code

- $A_{ij}$  Adjacency matrix
  - n number of nodes
  - $\beta$  transmission probability per link & per time step
- Do i=1, n
  - If  $a_i(t)=1$  with probability  $\mu \implies a_i(t+1)=2$
  - If a<sub>i</sub>(t)=0 then
  - Do j=1, n

    - If  $A_{ij}=1$  and  $a_j(t)=1$  With proability  $\beta \implies a_i(t+1)=1$
  - End do
- End do

Repeat over time step until a<sub>i</sub> is only 0 or 2

At each time step measure the quantities of infected etc.





# thank you!

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