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## Mathematical and data-driven models of infectious disease spreading

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### Outline

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### **Epidemic Spreading**



Can we predict the evolution in real time of a disease outbreak?

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### What do we have?

• Susceptible-Infected-Susceptible (SIS)

$$\begin{array}{ccc} S+I & \xrightarrow{\lambda} & I+I \\ I & \xrightarrow{\mu} & S \end{array}$$

• Susceptible-Infected-Removed (SIR)

$$\begin{array}{ccc} S+I & \stackrel{\lambda}{\longrightarrow} & I+I \\ I & \stackrel{\mu}{\longrightarrow} & R \end{array}$$

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### Mean-field Approach: SIS

### **Homogeneous Case**

- (k): average number of contacts per unit time of an individual
- *ρ*: density of infected individuals

$$\dot{
ho}(t) = -\mu
ho(t) + \lambda\langle k
angle [1-
ho(t)]
ho(t)$$



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### Mean-field Approach: SIS

### Heterogeneous Case

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- k: actual number of contacts per unit time of an individual
- *ρ<sub>k</sub>*: density of infected individuals with degree k

• 
$$\dot{\rho_k}(t) = -\mu \rho_k(t) + \lambda k [1 - \rho_k(t)] \Theta(\rho(t))$$

• 
$$\Theta(\lambda) = \sum_{k} \frac{kP(k)\rho_k}{\sum_s sP(s)} = \frac{1}{\langle k \rangle} \sum_k kP(k)\rho_k$$

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### Mean-field Approach: SIS

### Heterogeneous Case

• At the stationary state:  $0 = -\mu \rho_k + \lambda k [1 - \rho_k] \Theta(\lambda)$ 

• Thus:  $\rho_k = \frac{\lambda k \Theta}{1 + \lambda k \Theta}$ 

• and 
$$\Theta(\lambda) = \frac{1}{\langle k \rangle} \sum_{k} k P(k) \frac{\lambda k \Theta}{1 + \lambda k \Theta} = F(\Theta)$$

- If  $\frac{dF(\Theta)}{d\Theta}|_{\Theta=0} > 1$ , a non-trivial solution exists.
- the previous inequality reduces to  $\frac{\lambda}{\langle k \rangle} \sum_k k^2 P(k) > 1$

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### Mean-field Approach: SIS

### **Heterogeneous Case**

• 
$$\lambda > \frac{\langle k \rangle}{\langle k^2 \rangle} \Rightarrow \lambda_c = \frac{\langle k \rangle}{\langle k^2 \rangle}$$
  
•  $\rho = \sum_k P(k) \rho_k$ 

$$\begin{cases} \rho = 0, & \text{if } \lambda < \lambda_c \\ \rho > 0 & \text{if } \lambda > \lambda_c \\ \text{with } \lambda_c = \frac{\langle k \rangle}{\langle k^2 \rangle} \end{cases}$$

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### What do the previous results tell us?

Both models show the same critical properties despite the many differences between them!

- The epidemic threshold is a function of the first two moments of the degree distribution  $P(k)\sim k^{-\gamma}$  as

$$\lambda_c = \frac{\langle k \rangle}{\langle k^2 \rangle},$$

\* that leads to the (already classical) result due to Pastor-Satorras and Vespignani for SF networks with 2  $<\gamma$   $\leq$  3:

$$\lambda_c \rightarrow 0$$
,

when  $N \to \infty$ .



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### Spreading of Sexually Transmitted Diseases

### Data.







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### Spreading of Sexually Transmitted Diseases

### Data.

**Table:** Statistical properties of sexual contact networks from national sex surveys. The exponents  $\gamma_F$  and  $\gamma_M$  are referred to the distribution of number of sexual partners cumulated in 12 months and in the respondent's lifetime.

survey	$\gamma_F$ (12 months)	$\gamma_M$ (12 months)	$\gamma_F$ (life)	$\gamma_M$ (life)
Sweden	$3.54 \pm 0.20$	$3.31\pm0.20$	$3.1 \pm 0.30$	$2.6\pm0.30$
U.K.	$3.10 \pm 0.08$	$2.48 \pm 0.05$	$3.09 \pm 0.20$	$2.46 \pm 0.10$
Zimbabwe	$2.51 \pm 0.40$	$3.07 \pm 0.20$	$2.48 \pm 0.15$	$2.67 \pm 0.18$
Burkina Faso	$3.9 \pm 0.2$	$2.9\pm0.1$	-	-

- No significant differences between 1-year and lifetime exponents.
- The most common case involves one exponent greater than 3 and the other between 2 and 3.

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### **Theoretical Modeling**<sup>1</sup>

Criss-Cross Model in Heterosexual Populations





 $\begin{array}{ccc} S^F + I^M & \stackrel{\nu_F}{\longrightarrow} & I^F + I^M, \\ S^M + I^F & \stackrel{\nu_M}{\longrightarrow} & I^M + I^F, \end{array}$ 

with

$$N_{M} = N_{F} \frac{\langle k \rangle_{F}}{\langle k \rangle_{M}}$$
$$\simeq N_{F} \left(\frac{\gamma_{M} - 2}{\gamma_{F} - 2}\right) \left(\frac{\gamma_{F} - 1}{\gamma_{M} - 1}\right)$$

<sup>1</sup> JGG, VL, YM, & EP, PNAS **105**, 1399 (2008)

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### **Theoretical Modeling**

Mean-field Equations

$$\frac{1}{\mu_F}\frac{di_k^F(t)}{dt} = -i_k^F(t) + \lambda_F k \left[1 - i_k^F(t)\right] \Theta_k^M(t),$$
$$\frac{1}{\mu_M}\frac{di_k^M(t)}{dt} = -i_k^M(t) + \lambda_M k \left[1 - i_k^M(t)\right] \Theta_k^F(t).$$

Threshold

$$\sqrt{\lambda_F \lambda_M} > \lambda_c^* = \sqrt{\frac{\langle k \rangle_F \langle k \rangle_M}{\langle k^2 \rangle_F \langle k^2 \rangle_M}}.$$

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Theoretical Modeling...

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$$\sqrt{\lambda_F \lambda_M} > \lambda_c^* = \sqrt{\frac{\langle k \rangle_F \langle k \rangle_M}{\langle k^2 \rangle_F \langle k^2 \rangle_M}}.$$

Threshold

$$\lambda_{c} = \frac{\langle k \rangle}{\langle k^{2} \rangle} = \frac{2 \langle k \rangle_{M} \langle k \rangle_{F}}{\langle k^{2} \rangle_{M} \langle k \rangle_{F} + \langle k^{2} \rangle_{F} \langle k \rangle_{M}}.$$

• When  $(\gamma_F, \gamma_M)$  are both > 3

$$\lambda_{c}^{*} = \frac{1}{k_{0}} \sqrt{\frac{(\gamma_{F} - 3)(\gamma_{M} - 3)}{(\gamma_{F} - 2)(\gamma_{M} - 2)}},$$
  
$$\lambda_{c} = \frac{2(\gamma_{F} - 3)(\gamma_{M} - 3)}{k_{0} [(\gamma_{F} - 2)(\gamma_{M} - 3) + (\gamma_{M} - 2)(\gamma_{F} - 3)]},$$

• Both are the same only when  $\gamma_F = \gamma_M$ .

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A quick note on Rumors When N is finite and for  $\gamma_F(\gamma_M) > 2$  and  $2 < \gamma_M(\gamma_F) < 3$ :

• Threshold (unipartite)

$$\lambda_c \sim N_M^{\frac{\gamma_M - 3}{\gamma_M - 1}}.$$

• To be compared with the new (bipartite) threshold. When evaluated for  $2 < \gamma_G < 3$  (G = F, M) and, e.g.,  $\gamma_F > \gamma_M$  yields

$$\lambda_{c}^{*} \sim N_{M}^{\frac{1}{2} \left( \frac{\gamma_{M}-3}{\gamma_{M}-1} + \frac{\gamma_{F}-3}{\gamma_{F}-1} \right)}.$$

• When e.g.  $\gamma_F > 3$ , the expression reduces to

$$\lambda_c^* \sim N_M^{\frac{\gamma_M - 3}{2(\gamma_M - 1)}}$$

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A quick note on Rumors Table: Scaling exponents,  $\alpha$  and  $\alpha^*$ , of the epidemic thresholds,  $\lambda_c \sim N_M^{-\alpha}$  and  $\lambda_c^* \sim N_M^{-\alpha^*}$ . The two situations considered (2 <  $\gamma_F$  < 3 and  $\gamma_F$  > 3) correspond to 2 <  $\gamma_M$  < 3.

Network	$\alpha^*$	$\alpha$
$2 < \gamma_F < 3$	$\frac{1}{2} \left( \frac{3 - \gamma_F}{\gamma_F - 1} + \frac{3 - \gamma_M}{\gamma_M - 1} \right)$	$\frac{3-\gamma_M}{\gamma_M-1}$
$\gamma_F > 3$	$\frac{1}{2}\left(\frac{3-\gamma_M}{\gamma_M-1}\right)$	$\frac{3-\gamma_M}{\gamma_M-1}$



Both models predict that the threshold is zero for infinite systems but, for finite populations, the effective epidemic threshold could be two times greater than that for the unipartite case. This is good news!

Finite-Size Corrections...

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### **Contact-based Disease Spreading**<sup>2</sup>



- Can we build a formalism for contact-based epidemic spreading?
- Can we do this at the individual level?

<sup>2</sup>SG, AA, JBH, SM & YM, EPL **89**, 38009 (2010)

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### General Formalism.

Contact-based Spreading...

 Consider the probability p<sub>i</sub>(t) that node i is infected at time t,

$$egin{array}{rcl} p_i(t+1) &=& (1-q_i(t))(1-p_i(t))+(1-\mu)p_i(t) \ && +\mu(1-q_i(t))p_i(t) \end{array}$$

 q<sub>i</sub>(t): probability of node i not being infected by any neighbor

$$q_i(t) = \prod_{j=1}^N (1 - \beta r_{ji} p_j(t))$$

#### where:

- (1 q<sub>i</sub>(t))(1 p<sub>i</sub>(t)): probability of a susceptible being infected by at least a neighbor.
   (1 μ)p<sub>i</sub>(t): probability of a susceptible not being recovered.
- µ(1 q<sub>i</sub>(t))p<sub>i</sub>(t): probability of a susceptible being recovered, but infected by at least a
   neighbor.

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- The previous equation corresponds to a family of possible models, parameterized by the contact probabilities  $r_{ij}$ .
- The general case is represented by  $\lambda_i$  random walkers leaving node *i* at each time step:

$$r_{ij} = 1 - \left(1 - rac{w_{ij}}{w_i}
ight)^{\lambda_i}$$

At the stationary state:

$$p_i = (1-q_i) + (1-\mu)p_iq_i$$

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A quick note on Rumors • When  $\beta \to \beta_c$ , the probabilities  $p_i \approx \epsilon_i$ , where  $0 \le \epsilon_i \ll 1$ :

$$q_i \approx 1 - \beta \sum_{j=1}^N r_{ji} \epsilon_j$$

• Neglecting second order terms in  $\epsilon$ 

$$\sum_{j=1}^{N} \left( r_{ji} - \frac{\mu}{\beta} \delta_{ji} \right) \epsilon_j = 0 \qquad \forall i = 1, \dots, N$$

• Non-trivial solutions exist if and only if  $\mu/\beta$  is an eigenvalue of the matrix  ${\bf R}$ 

$$\beta_c = \frac{\mu}{\Lambda_{\max}}$$

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• For random uncorrelated networks, the largest eigenvalue of the matrix **R** is  $\Lambda_{max} = \langle k^2 \rangle / \langle k \rangle$ .

Contact-based Spreading...

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Average fraction of infected individuals,  $\rho_1$  as a function of the spreading rate  $\beta$  for  $N = 10^4$ . The symbols correspond to MC simulations of the SIS model on top of random scale-free networks with  $\gamma=2.7$  (error bars are smaller than the size of the symbol) and the lines stand for the analytical solutions of our formalism (with  $\lambda = \infty$ ). We also represent in the inset a scatter plot for the probability that a node i (i = 1, ..., N) is infected using results of MC simulations (the y-axis) and the analytical solution (x-axis).



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Density of infected individuals  $\rho$  as a function of  $\beta$  for different values of  $\lambda$  in the air transportation network

- Critical points and  $\rho \beta$  phase diagrams' greatly change at varying  $\lambda$ .
- For small values of  $\lambda$  the disease prevalence is moderate.
- Large values of λ is akin to a RP.

Contact-based Spreading...

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### **Mesoscopic Equations.**

• Defining  $R_{\lambda}(x) = 1 - (1 - x)^{\lambda}$ , the generalized HMF equation reads

$$0 = -\mu\rho_{k} + \beta k(1 - \rho_{k}) \sum_{k'} P(k'|k) R_{\lambda}(k'^{-1}) \rho_{k'}$$
$$+ \mu\beta k\rho_{k} \sum_{k'} P(k'|k) R_{\lambda}(k'^{-1}) \rho_{k'}$$
$$+ \frac{1}{2}\beta^{2}k \sum_{k'} R_{\lambda}(k'^{-1})^{2} P(k'|k) \rho_{k'}^{2}$$
$$- \frac{1}{2}\beta^{2}k^{2} \left( \sum_{k'} R_{\lambda}(k'^{-1}) P(k'|k) \rho_{k'} \right)^{2}$$

• When 
$$\lambda = 1$$
,  $R_1(k^{-1}) = \frac{1}{k}$ ,  $\rightarrow CP$ .

• When  $\lambda \to \infty$ ,  $R_{\infty}(k^{-1}) = 1$ ,  $\to \mathsf{RP}$ .

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### **Contact-based Spreading.**



Worldwide infection probabilities using the ATN.

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### Metapopulation models.



Schematic representation of a metapopulation system.

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### Metapopulation models.

Global invasion threshold.

- If R<sub>0</sub> = β/μ > 1, an outbreak takes place. For metapopulation models, the relation holds for a subpopulation.
- However, due to mobility, there is a second threshold, known as global invasion threshold.
- Let D<sup>0</sup><sub>k</sub> be the number of diseased subpopulations of degree k at generation 0. We can study the evolution of this number using a tree-like approximation relating D<sup>n</sup><sub>k</sub> with D<sup>n-1</sup><sub>k</sub>.
- The total number of infected individuals circulating through the network after *n* 1 generations is:

$$\omega^{n-1} = \frac{\lambda \alpha}{\mu} \sum_{k'} D_{k'}^{n-1} N_{k'}$$

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### Metapopulation models.

The average number of infected individuals in the class of degree k during the evolution of the epidemic is  $\alpha N_k$ .

Each infected individual stays in the infectious state for an average time  $\mu^{-1}$ .

Then the number of infected people circulating through the network after n-1 generations is:

$$\omega^{n-1} = \frac{\lambda \alpha}{\mu} \sum_{k'} D_{k'}^{n-1} N_{k'}$$
(1)

Global invasion threshold.

The number of infected individuals that will pass through a subpopulation of degree k will be

$$\gamma_k^{n-1} = \frac{b_k}{b_{tot}} \omega^{n-1},\tag{2}$$

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where  $b_{tot}$  is the sum of all the betweenness of the nodes.

Global invasion threshold.

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### Metapopulation models.

For the  $n^{th}$  generation we have:

$$D_{k}^{n} = V_{k} \left( 1 - \frac{D_{k}^{n-1}}{V_{k}} \right) \left[ 1 - R_{0}^{-\gamma_{k}^{n-1}} \right],$$
(3)

where the second factor on the right is the probability that the subpopulation is not already seeded by infected individuals and the last is the probability that the new seeded subpopulation will experience an outbreak.

In the early time and for  $R_0 \sim 1$  we can approximate the last expression considering:

$$\frac{D_k^{n-1}}{V_k} \ll 1,\tag{4}$$

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and

$$1 - R_0^{-\gamma_k^{n-1}} \sim (R_0 - 1)\gamma_k^{n-1}, \tag{5}$$

obtaining:

$$D_k^n = (R_0 - 1) V_k \gamma_k^{n-1} = (R_0 - 1) \frac{\lambda \alpha}{\mu} V_k \frac{b_k}{b_{tot}} \sum_{k'} D_{k'}^{n-1} N_{k'}.$$
 (6)

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### Metapopulation models.

Considering at the equilibrium:

$$N_k = \frac{k}{\langle k \rangle} \bar{N},\tag{7}$$

where  $\bar{N} = \sum_{k} P(k) N_k$  is the average subpopulation size, we get:

$$D_k^n = (R_0 - 1) \frac{\lambda \alpha}{\mu} \bar{N} V_k \frac{b_k}{b_{tot}} \frac{1}{\langle k \rangle} \sum_{k'} D_{k'}^{n-1} k'.$$
(8)

Let us define now  $\Theta^n = \sum_k D_k^n k$ , then we have:

$$\Theta^{n} = (R_{0} - 1) \frac{\lambda \alpha}{\mu} \bar{N} \frac{\Theta^{n-1}}{\langle k \rangle} \sum_{k} V_{k} k \frac{b_{k}}{b_{tot}}.$$
(9)

Global invasion threshold.

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### Metapopulation models.

The last term needs can be further developed as:

$$\sum_{k} V_{k} k \frac{b_{k}}{b_{tot}} = \frac{V \sum_{k} P(k) k b_{k}}{V \sum_{k'} P(k') b_{k'}}.$$
 (10)

Global invasion threshold.

Considering now  $b_k \sim k^{\eta}$  one is left with:

$$\Theta^{n} = (R_{0} - 1) \frac{\lambda \alpha}{\mu} \bar{N} \frac{1}{\langle k \rangle} \frac{\langle k^{1+\eta} \rangle}{\langle k^{\eta} \rangle} \Theta^{n-1}.$$
(11)

We finally get the global invasion threshold as:

$$R^* = (R_0 - 1) \frac{\lambda \alpha}{\mu} \bar{N} \frac{1}{\langle k \rangle} \frac{\langle k^{1+\eta} \rangle}{\langle k^{\eta} \rangle}.$$
 (12)

We can write the threshold condition for the mobility rate:

$$\lambda \bar{N} \ge \frac{\langle k^{\eta} \rangle}{\langle k^{1+\eta} \rangle} \frac{\langle k \rangle \mu}{\alpha} (R_0 - 1)^{-1}.$$
 (13)

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### Metapopulation models.



Analytics versus numerics. Meloni et al., Nature Scientific Reports, 2011.

Global invasion threshold.

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### Metapopulation model with behavioral change.



Schematic representation of the model. Meloni et al., Nature Scientific Reports, 2011.

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### Metapopulation model with behavioral change.



Effects of the different mechanisms. Meloni et al., Nature Scientific Reports, 2011.

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Finite-Size Corrections

Contact-base Epidemic Spreading

Impact of Behavioral Changes

A quick note on Rumors

### Metapopulation model with behavioral change.





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### Metapopulation model with behavioral change.



Effects of the different mechanisms on an epidemic within the USA. Meloni et al., Nature Scientific Reports, 2011.

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### Epidemic-like processes: Rumors

# Rumor spreading is similar, but fundamentally different from disease spreading

- We are not constrained to model an actual process. Rumor algorithms can be freely designed depending on the application.
- The annihilation term makes the difference: it does not depend any more on a rate, but on the interactions between the different classes.
- There is no rumor threshold: always, a finite fraction of the population learn the rumor.
- Ignorants (1), Spreaders (S), Stiflers (R)

$$\begin{array}{ccc} I + S & \xrightarrow{\lambda} & I + I \\ S + S & \xrightarrow{\alpha} & R \\ S + R & \xrightarrow{\alpha} & R \end{array}$$

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### Homogeneous Case

$$\begin{aligned} \partial_t i &= -\lambda ki(t)s(t) \\ \partial_t s &= \lambda ki(t)s(t) - \alpha ks(t)[s(t) + r(t)] \\ \partial_t r &= \alpha ks(t)[s(t) + r(t)] \end{aligned}$$

• The solution in the infinite-time limit  $(s(\infty))$  is given by:

$$r_{\infty} = 1 - e^{-\beta r_{\infty}}$$

• which reduces to a condition that is always satisfied:

$$\frac{\lambda}{\alpha} > 0$$

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There is no rumor threshold!!! (NOTE: at first-order MF description)