Epidemic Processes

Gonzalo Mateos
Dept. of ECE and Goergen Institute for Data Science
University of Rochester
gmateosb@ece.rochester.edu
http://www.ece.rochester.edu/~gmateosb/

April 25, 2019

Epidemic processes

Branching processes

Traditional epidemic modeling

Network-based epidemic modeling

Synchronization

Dynamic network processes

- Most systems studied from a network-based perspective are dynamic
  $\Rightarrow$ Most processes on network graphs are dynamic processes

Example

- Cascade of failures in the electrical power grid
- Diffusion of knowledge and spread of rumors
- Spread of a virus among a population of humans or computers
- Synchronization of behavior as neurons fire in the brain
- Interactions of species such as prey-predator dynamics

- Dynamic process on a network graph is $\{X_i(t)\}_{i \in V}$ for $t \in \mathbb{N}$ or $\mathbb{R}_+$
  - Both deterministic and stochastic models commonly adopted
  - Ex: differential equations or time-indexed random (Markov) processes

Epidemics

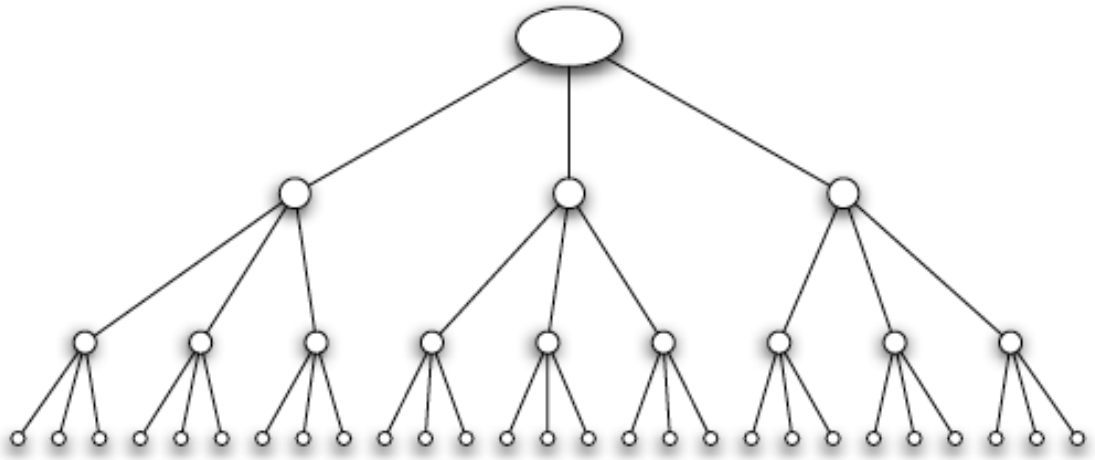
- Epidemics are phenomena prevalent in excess to the expected
  - Encountered with contagious diseases due to biological pathogens
  - Ex: malaria, bubonic plague, AIDS, influenza
- Biological issues mixed with social ones. Spread patterns depend on:
  - $\Rightarrow$ Pathogen e.g., contagiousness, severity, infectious period
  - $\Rightarrow$ Network structures within the affected population
- Quantitative epidemic modeling concerned with three basic issues:
  - (i) Understanding the mechanisms by which epidemics spread;
  - (ii) Predicting the future course of epidemics; and
  - (iii) Gaining the ability to control the spread of epidemics

Contact networks

- **Def:** In a contact network the people (vertices) are connected if they come into contact so that the disease can spread among them
- Natural to represent this structure as a network graph $G(V, E)$
  - $\Rightarrow$ Vertices $i \in V$ represent elements of the population
  - $\Rightarrow$ Edges $(i, j) \in E$ indicate contact between elements i and j
- Contact does not indicate actual infection, only the possibility of it
- Topology of the contact network varies depending on the disease
  - Dense when highly contagious e.g., airborne transmission via coughs
  - Sparser connectivity in e.g., sexually transmitted diseases
- Often difficult to measure the structure of contact networks

Branching processes

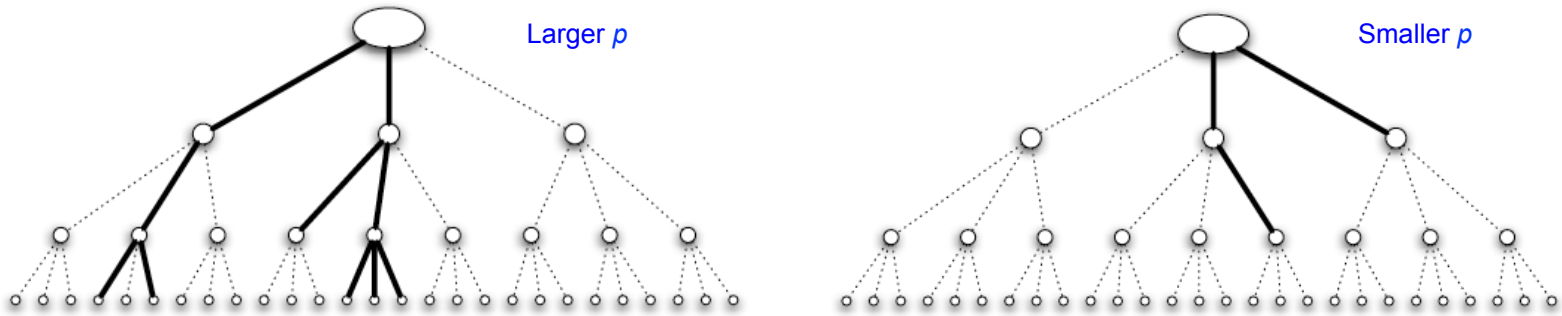
- The branching process (BP) is the simplest model for a contagion
- BP model considers different waves, i.e., discrete-time instants
  - First wave: one infective enters the population, meets k other friends
  - Wave n: each person of wave $n-1$ meets k different new friends
- Suppose the disease is transmitted to friends independently w.p. p
- Contact network naturally represented by a k-ary tree ($k = 3$ below)



Relevant questions

- Q: What is the behavior of an epidemic under the BP model?

  $\Rightarrow$ From sample paths of the BP, can have severe or mild diseases



- Interesting questions we can answer under this simple model
  - Q1: Does the epidemic eventually die out?
  - Q2: Is the infected number of individuals infinite?
  - Q3: If it dies out, how long does it take until it goes extinct?

- Dichotomy: the epidemic dies out for finite n or goes on forever

Reproductive number

- **Def:** The reproductive number R_0 is the expected number of new infected cases with the disease caused by a single individual
- **BP:** number of infected friends of each individual is a Bino(k, p) RV
  $\Rightarrow R_0 = kp$, independent of the particular individual

Theorem

Consider a branching process with parameters k and p

a) *If $R_0 \leq 1$, the disease dies out after finite number of waves w.p. 1*

b) *If $R_0 > 1$, w.p. $q^* > 0$ the disease persists for infinitely many waves*

- Two basic kinds of public health measures to yield $R_0 < 1$
  $\Rightarrow$ Reduce k by quarantining people; and
  $\Rightarrow$ Reduce p by encouraging better sanitary practices

Proof of a)

- Easier if we consider the number of infected individuals. Define:
  - $Y(n)$ as the number of infected individuals at wave n
  - J_n as the number of individuals in wave n, i.e., $J_n = k^n$
  - $X_i(n) = \mathbb{I}\{i \text{ is infected}\}$, for $i = 1, \ldots, J_n$
- Based on the definitions, it follows that $Y(n) = \sum_{i=1}^{J_n} X_i(n)$. Hence

$$\mathbb{E}[Y(n)] = \sum_{i=1}^{J_n} \mathbb{E}[X_i(n)] = \sum_{i=1}^{J_n} \mathrm{P}(i \text{ is infected})$$

- Wave n node infected if all ancestors infected: $\mathrm{P}(i \text{ is infected}) = p^n$

$$\Rightarrow \mathbb{E}[Y(n)] = \sum_{i=1}^{J_n} \mathrm{P}(i \text{ is infected}) = k^n p^n = R_0^n$$

- For $R_0 < 1$ it follows that $\lim_{n \to \infty} \mathbb{E}[Y(n)] = 0$ (study $R_0 = 1$ later)

Proof of a) (cont.)

- Recall that for a nonnegative RV X with $\mathbb{E}[X] < \infty$, constant $a > 0$
  $\Rightarrow$ Markov's inequality states $\rightarrow$ $\mathrm{P}(X \geq a) \leq \frac{\mathbb{E}[X]}{a}$
- Application of Markov's inequality to $Y(n)$ with $a = 1$ yields

$$\mathrm{P}(Y(n) \geq 1) \leq \mathbb{E}[Y(n)] \rightarrow 0 \text{ as } n \rightarrow \infty$$

□

- Let Y be the total number of infected individuals. What is $\mathbb{E}[Y]$?

$$\mathbb{E}[Y] = \sum_{n=0}^{\infty} \mathbb{E}[Y(n)] = \sum_{n=0}^{\infty} R_0^n = \frac{1}{1 - R_0}$$

- Calculating the expected duration of the disease is more involved
  $\Rightarrow$ Leverage standard tools since $\{Y(n)\}_{n=0}^{\infty}$ is a Markov chain

Proof of b)

- Define the probability $q_n = \mathrm{P}\,(\text{disease survives after } n \text{ waves})$
- By Markovianity of the BP, for any node i in the first wave we have

$$\mathrm{P}\left(\text{disease survives after } n-1 \text{ more waves} \,\middle|\, X_i(1) = 1\right) = q_{n-1}$$

- Since the root has k children, disease goes extinct by wave n w.p.

$$\mathrm{P}\,(\text{disease extinct by wave } n) = 1 - q_n = (1 - pq_{n-1})^k$$

$\Rightarrow$ Recursion $q_n = 1 - (1 - pq_{n-1})^k$ holds for $n = 0, 1, \ldots$

- Claim regarding the recursion's fixed point q^* as $n \to \infty$, i.e.,

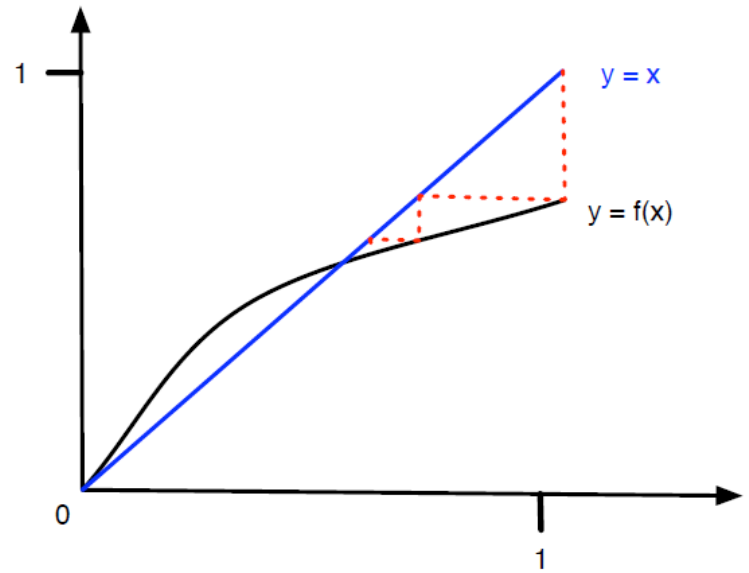
$$q^* = 1 - (1 - pq^*)^k$$

$\Rightarrow$ If $R_0 \leq 1$, then the only solution in $[0, 1]$ is $q^* = 0$

$\Rightarrow$ If $R_0 > 1$, there is also a nonzero solution in $[0, 1]$

Proof of b) (cont.)

- To establish the claim, define $f(x) = 1 - (1 - px)^k$. Properties:
  - $f(x)$ is increasing and continuous
  - $f(x)$ is differentiable with $f'(x) = R_0(1 - px)^{k-1}$
  - $f(0) = 0$, $f(1) < 1$ and $f'(0) = R_0$



- If $R_0 > 1$ then $f'(0) > 1$ and $y = f(x)$ intersects the line $y = x$

  $\Rightarrow$ A solution q^* exists in the open interval $(0, 1)$ $\square$

Closing remarks on BP model

- Simple BP model suffices to capture basic effects of the epidemic
- The spread of the disease depends on both
  - Properties of the pathogen via p
  - Properties of the contact network via k
- Dichotomous behavior depending on the reproductive number R_0
  - When $R_0 \leq 1$ the disease is not able to replenish itself
  - When $R_0 > 1$ the outbreak is constantly trending upward
- 'Knife-edge' behavior around $R_0 = 1$ implies high sensitivity
  - Even when $R_0 > 1$, the probability q^* of persistence is less than one
  - Ultracontagious diseases can 'get unlucky' and die out early on
- Up next: more general models applicable to any contact network

  $\Rightarrow$ Reproductive number R_0 still important for intuition

Modeling epidemics

Branching processes

Traditional epidemic modeling

Network-based epidemic modeling

Synchronization

SIR model

- Most used epidemic model is the susceptible-infected-removed (SIR) model
- Stochastic formulation of simplest case with no contact network
  $\Rightarrow$ Will extend later for the case of arbitrary graph $G(V, E)$
- Consider a closed population of $N + 1$ elements. At any time $t \in \mathbb{R}_+$
  - $N_S(t)$ elements are susceptible to infection (called 'susceptibles')
  - $N_I(t)$ elements are infected (called 'infectives')
  - $N_R(t)$ elements are recovered and immune (or 'removed')
- Given $N_S(t)$ and $N_I(t)$, can determine $N_R(t)$ due to the constraint

$$N_S(t) + N_I(t) + N_R(t) = N + 1$$

  $\Rightarrow \{N_S(t), N_I(t), N_R(t)\}_{t=0}^{\infty}$ is a continuous-time random process
  $\Rightarrow$ Need to specify the probabilistic law for their evolution

A simple epidemic model

- Populations of $N_S(t) = S$ susceptibles and $N_I(t) = I$ infectives
- Two possible reactions (events)

$$\Rightarrow \text{Infection:} \quad S + I \rightarrow 2I$$
$$\Rightarrow \text{Recovery:} \quad I \rightarrow \emptyset$$

- Susceptible infected by infective on chance encounter
  - $\Rightarrow \beta =$ Rate of encounters between susceptible and infective
  - $\Rightarrow S$ susceptibles and I infectives $\Rightarrow \beta SI =$ rate of first reaction
- Each infective recovers (and is removed) at rate γ
  - $\Rightarrow$ Population of I infectives $\Rightarrow \gamma I =$ rate of second reaction
- Model assumption: 'homogenous mixing' among population members
  - $\Rightarrow$ All pairs of members equally likely to interact with one another

State transition probabilities

- Consider the bivariate state $[N_S(t), N_I(t)]^\top$ ($N_R(t)$ uniquely defined)

  $\Rightarrow$ Process starts with one infective and N susceptibles, i.e.,

$$N_I(0) = 1,\ N_S(0) = N,\ \text{and}\ N_R(0) = 0$$

- Process evolves according to instantaneous transition probabilities

  Infection with rate β:

$$\mathrm{P}\left(N_S(t+\delta t) = s-1, N_I(t+\delta t) = i+1 \,\middle|\, N_S(t) = s, N_I(t) = i\right) \approx \beta s i \delta t$$

  Recovery with rate γ:

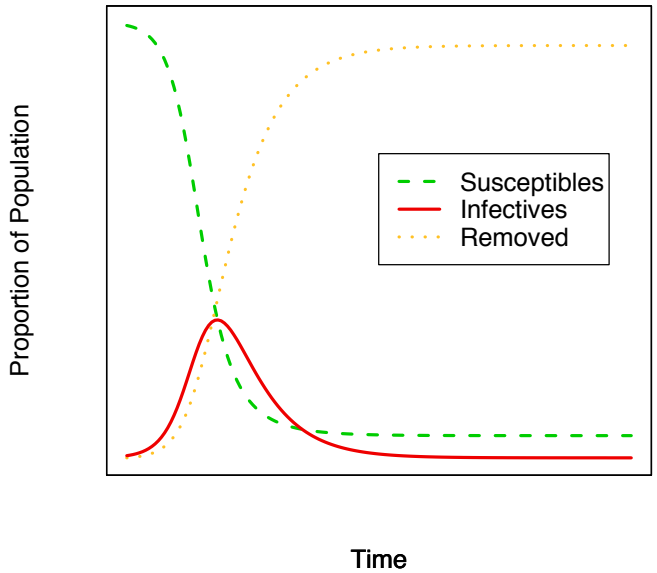
$$\mathrm{P}\left(N_S(t+\delta t) = s, N_I(t+\delta t) = i-1 \,\middle|\, N_S(t) = s, N_I(t) = i\right) \approx \gamma i \delta t$$

  Unchanged state:

$$\mathrm{P}\left(N_S(t+\delta t) = s, N_I(t+\delta t) = i \,\middle|\, N_S(t) = s, N_I(t) = i\right) \approx 1-(\beta s+\gamma) i \delta t$$

Continuous-time Markov chain

- Process $\{N_S(t), N_I(t)\}_{t=0}^{\infty}$ is a continuous-time Markov chain (CTMC)
- Equivalently implies that given $N_I(t) = i, N_S(t) = s$, then the CTMC
  - $\Rightarrow$ Transitions from state (s, i) after time $T \sim \exp((\beta s + \gamma) i)$
  - $\Rightarrow$ Infection: to state $(s-1, i+1)$ w.p. $\beta si/[(\beta s + \gamma) i]$
  - $\Rightarrow$ Recovery: to state $(s, i-1)$ w.p. $\gamma i/[(\beta s + \gamma) i]$
- This formulation of the model facilitates the simulation of realizations



Transition-probability functions

- CTMC evolution given by matrix of transition-probability functions

$$P_{s,i}(t) = \mathrm{P}\left(N_S(t) = s, N_I(t) = i \,\middle|\, N_S(0) = N, N_I(0) = 1\right)$$

  $\Rightarrow$ Full description of the epidemic process under the SIR model

- Transition probability functions satisfy the differential equations

$$\frac{\partial P_{N,1}(t)}{\partial t} = -(\beta N + \gamma) P_{N,1}(t)$$

$$\frac{\partial P_{s,i}(t)}{\partial t} = \beta(s+1)(i-1) P_{s+1,i-1}(t) - i(\beta s + \gamma) P_{s,i}(t) + \gamma(i+1) P_{s,i+1}(t)$$

  - Initial conditions $P_{N,1}(0) = 1$ and $P_{s,i}(0) = 0$ for all $(s,i) \neq (N,1)$

- These are known as the Kolmogorov forward equations

  $\Rightarrow$ Exact analytical solution possible, but form is quite complicated

Reproductive number of the general SIR model

- Can still derive basic results without explicit formulas for $P_{s,i}(t)$
- For the general epidemic SIR model, the reproductive number is

$$R_0 = \frac{N\beta}{\gamma}$$

$\Rightarrow$ Threshold theorem holds as for the BP model [Whittle'55]

Theorem
Consider a generic SIR model with infection rate β and recovery rate γ

a) *If $R_0 = N\beta/\gamma \leq 1$, the disease dies out after finite time*
b) *If $R_0 = N\beta/\gamma > 1$, an epidemic occurs w.p. $q^* = 1 - \frac{1}{R_0}$*

- Again, threshold theorems useful to design epidemic control procedures

  Ex: reduce R_0 to less than unity via vaccination, education, quarantine

Inference of model parameters

- In practice, quantities β and γ (hence R_0) are unknown. Estimates?
- If $\{N_S(t), N_I(t)\}_{t=0}^{\tau}$ observed in $(0, \tau)$, ML rate estimates given by

$$\hat{\beta} = \frac{N - N_S(\tau)}{(1/N)\int_0^\tau N_S(t)N_I(t)dt} \quad \textit{and} \quad \hat{\gamma} = \frac{N_R(\tau)}{\int_0^\tau N_I(t)dt}$$

  $\Rightarrow$ ML estimate of R_0 then follows as $\hat{R}_0 = N\hat{\beta}/\hat{\gamma}$

- Unfortunately, rarely are such complete measurements available
- Often only the final state of the epidemic is observed, i.e., $N_R(\tau)$

  $\Rightarrow$ Impossible to estimate β and γ since they relate to time

- Can still use the method-of-moments to estimate R_0

$$\hat{R}_0 \approx \frac{-\log(1 - N_R(\tau)/N)}{N_R(\tau)/N}$$

Incorporating the contact network

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Synchronization

Structured population models

- So far assumed 'homogenous mixing' among population members
  $\Rightarrow$ All pairs of members equally likely to interact with one another
- Admittedly simple and poor approximation to reality for some diseases
- Interest has shifted towards structured population models (SPM)
  $\Rightarrow$ Assumed contact patterns take into account population structure

  Ex: structure derives from spatial proximity, social contact, demographics
- SPM introduce a non-trivial contact network G
  $\Rightarrow$ Homogeneous mixing assumption $\Leftrightarrow$ Complete graph $G \equiv K_{N_v}$
- Epidemic models on graphs study dynamic processes $\mathbf{X}(t) = \{X_i(t)\}_{i \in V}$

Network-based SIR model

- Let $G(V, E)$ be the contact network for a population of N_v elements
  - $\Rightarrow$ At $t = 0$, one vertex is infected and the rest are susceptible
- Susceptible infected by **infective neighbor** on chance encounter
  - $\Rightarrow$ Infective has infectious contacts independently with each neighbor
  - $\Rightarrow$ Time till contact is exponentially distributed with parameter β
- Each infective recovers (and is removed) at rate γ
  - $\Rightarrow$ Time till recovery is exponentially distributed with parameter γ
- Define the stochastic process $\mathbf{X}(t) = \{X_i(t)\}_{i \in V}$, where

$$X_i(t) = \begin{cases} 0, & \text{if vertex } i \text{ is susceptible at time } t \\ 1, & \text{if vertex } i \text{ is infected at time } t \\ 2, & \text{if vertex } i \text{ is recovered at time } t \end{cases}$$

State transition probabilities

- The process $\mathbf{X}(t)$ is a CTMC, with state vectors $\mathbf{x} \in \{0, 1, 2\}^{N_v}$
- When state transitions from $\mathbf{x}$ to $\mathbf{x}'$, a single vector entry changes

  $\Rightarrow$ If entry i changes, instantaneous transition probabilities are

$$\mathrm{P}\left(\mathbf{X}(t+\delta t) = \mathbf{x}' \,\middle|\, \mathbf{X}(t) = \mathbf{x}\right) \approx \begin{cases} \beta M_i(\mathbf{x})\delta t, & \text{if } x_i = 0 \text{ and } x_i' = 1 \\ \gamma \delta t, & \text{if } x_i = 1 \text{ and } x_i' = 2 \\ 1 - [\beta M_i(\mathbf{x}) + \gamma]\delta t, & \text{if } x_i = 2 \text{ and } x_i' = 2 \end{cases}$$

- Defined $M_i(\mathbf{x})$ as the number of infective neighbors of vertex i, i.e.,

$$M_i(\mathbf{x}) := |\{j : (i,j) \in E, x_j = 1\}|$$

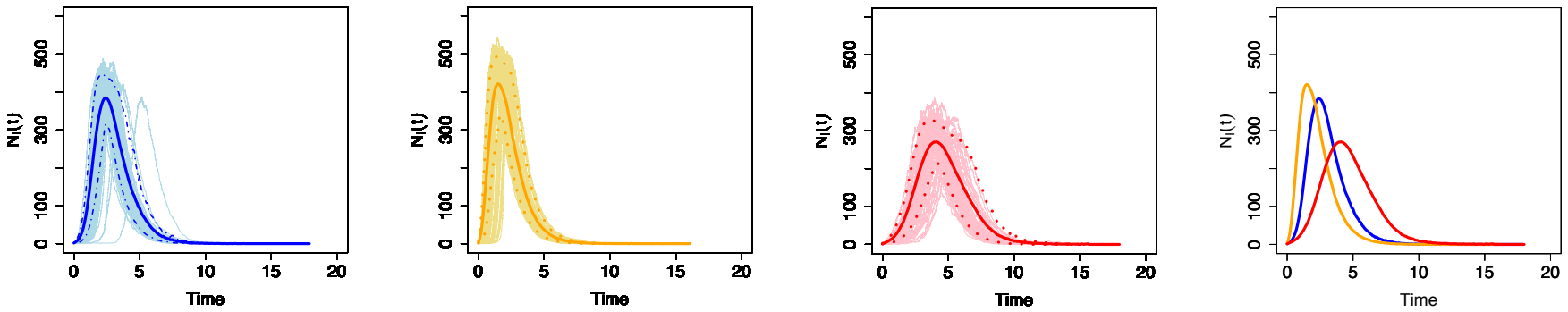
  $\Rightarrow$ Contact network G enters the model through $M_i(\mathbf{x})$, $i \in V$

- Given $\mathbf{X}(t)$ can define the processes $\{N_S(t), N_I(t), N_R(t)\}$ by counting

  Ex: number of susceptibles $N_S(t) = \sum_{i=1}^{N_v} \mathbb{I}\{X_i(t) = 0\}$

Effect of the contact network

- Simulated the CTMC for contact networks with $N_v = 1000$ and $\bar{d} \approx 10$
  - Erdös-Rényi (blue), Barabási-Albert (yellow), Watts-Strogatz (red)
  - Plot 100 sample paths of $N_I(t)$ and the average over 1000 epidemics



- Curves $\mathbb{E}[N_I(t)]$ have the same general form as when $G = K_{N_v}$
- Different rates of growth and decay, effective duration of the epidemic

  $\Rightarrow$ Characeristics of the epidemic process are affected by the network

Reproductive number

- Suppose G drawn from $\mathcal{G}$ with fixed degree distribution $\{f_d\}$
  - $\Rightarrow$ Reproductive number for the SIR model can be shown to equal

$$R_0 = \frac{\beta}{\beta + \gamma}\left(\frac{\mathbb{E}\left[d^2\right]}{\mathbb{E}\left[d\right]} - 1\right)$$

  - Probability that an infective transmits the disease before recovering
  - Expected number of neighbors in G of a single infective (early on)
- Ex: Erdös-Rényi where $\mathcal{G} = \mathcal{G}_{N_v,p} \Rightarrow R_0 \approx \beta N_v p/(\beta + \gamma)$
- Ex: Power-law $\{f_d\}$ for which we can expect $\mathbb{E}\left[d^2\right] \gg \mathbb{E}\left[d\right]$
  - $\Rightarrow$ Increases R_0, easier for epidemics to occur than for $\mathcal{G}_{N_v,p}$
  - $\Rightarrow$ Suffices to infect a small number of high-degree vertices
- H. Anderson and T. Britton, *Stochastic Epidemic Models and Their Statistical Analysis.* Springer, 2000.

Synchronization

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Synchronization

Immunity and reinfections

- Q: What if individuals can be infected multiple times?
  $\Rightarrow$ SIR model falls short, assumes immunity (or death) after infection
- **SIS model:** infectives recover at rate γ, but are susceptible again

$$S \to I \to S \to I \to S \to \dots$$

  Ex: Gonorrhea, no immunity acquired after infection

- **SIRS model:** infectives recover at rate γ, then immune for limited time
  $\Rightarrow$ Immunity time exponentially distributed with parameter δ
  $\Rightarrow$ Recovered individual susceptible again and can be reinfected

$$S \to I \to R \to S \to I \to R \to S \to \dots$$

- Ex: Syphilis, limited temporal immunity

Synchronization

- Epidemics of certain diseases tend to synchronize across a population
  $\Rightarrow$ Strong oscillations in the number of infectives over time

  Ex: Such 'life cycle' effects are well known for measles and syphilis
- Traditionally, cycles attributed to large-scale societal changes
  $\Rightarrow$ Recently to contagion dynamics and network structure
- Can use simple e.g., SIRS models to produce such cyclic effects

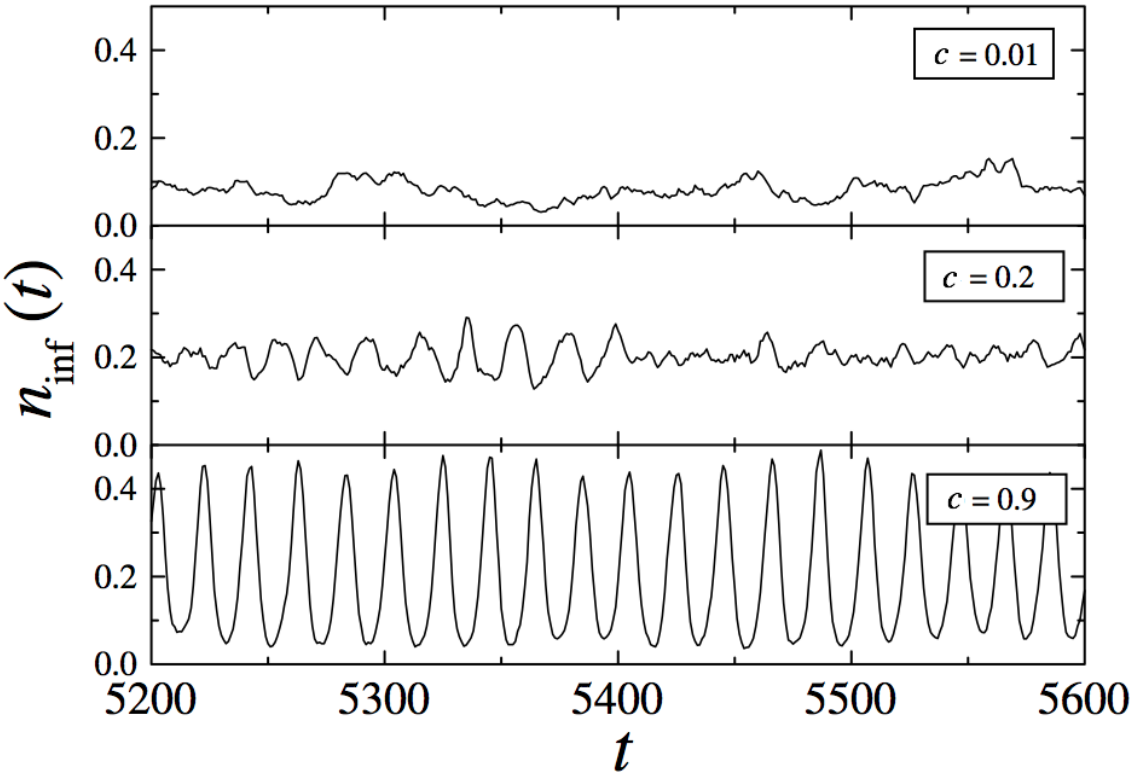
  Key ingredients: temporary immunity combined with long-range links
  $\Rightarrow$ Coordination in timing of flare-ups across the whole network
  $\Rightarrow$ Network-wide deficit in number and connectivity of susceptibles
- Large "drop" in the outbreak following the "peak" from earlier flare-ups

Small-world contact networks

- Temporary immunity can explain oscillations locally. Global effects?
- Small-world contact networks
  - $\Rightarrow$ Homophilous ties: highly-clustered links forming local communities
  - $\Rightarrow$ Weak ties: long-range links connecting distant parts of the network
- Network rich in long-range ties to coordinate disease flare-ups globally
- Relevance of small-world properties to synchronization
- D. J. Watts and S. H. Strogatz "Collective dynamics of 'small-world' networks," *Nature,* vol. 393, pp. 440-442, 1998
- Small-world contact networks leading to oscillation in epidemics
- M. Kuperman and G. Abramson, "Small world effect in an epidemiological model," *Physical Rev. Letters,* vol. 86, no. 13, pp. 2909-2912, 2012

SIRS model and weak ties

- SIRS behavior different depending on fraction c of long-range weak ties



- Complex dynamics emerge from simple contagion and network models

  $\Rightarrow$ Rigorous analysis of synchronization onset challenging

Glossary

- Dynamic network process
- Epidemic
- Contact network
- Branching process
- Reproductive number
- Threshold theorems
- 'Knife-edge' behavior
- SIR model
- Susceptibles
- Infectives
- Removed
- Homogeneous mixing
- Continuous-time Markov chain
- Continuous-time Markov chain
- Transition-probability function
- Kolmogorov forward equations
- Structured population models
- Reinfection
- SIS model
- SIRS model
- Temporary immunity
- Synchronization
- Oscillations
- Long-range weak ties
- Small-world network