Epidemic Processes

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Epidemic processes

Branching processes

Traditional epidemic modeling

Network-based epidemic modeling

Synchronization
Most systems studied from a network-based perspective are **dynamic**

Naturally 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 are phenomena prevalent in excess to the expected. Commonly used for contagious diseases due to biological pathogens. Examples include malaria, bubonic plague, AIDS, and influenza.

Biological issues are mixed with social ones. Spread patterns depend on:
- Pathogen e.g., contagiousness, severity, infectious period
- Network structures within the affected population

Quantitative epidemic modeling is 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.
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 \( G(V, E) \)

\[ \Rightarrow \text{Vertices } i \in V \text{ represent elements of the population} \]
\[ \Rightarrow \text{Edges } (i, j) \in E \text{ indicate contact between elements } i \text{ and } j \]

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.
The branching process (BP) is the simplest model for a contagion.

The BP model considers different waves, i.e., discrete-time instants.

- First wave: one infected 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. $p$.

The contact network can be naturally represented by a $k$-ary tree.
Relevant questions

- **Q**: What is the behavior of an epidemic under the BP model?
- Looking at sample paths of the BP, can have severe or mild diseases

- **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
  \[ \Rightarrow \text{Hence } R_0 = kp, \text{ independent of the particular individual} \]

**Theorem**

*Consider a branching process with parameters $k$ and $p$*

- (a) *If* $R_0 < 1$, *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*

- Interpret two basic kinds of public health measures to yield $R_0 < 1$
  \[ \Rightarrow \text{Reduce } k \text{ by quarantining people; and} \]
  \[ \Rightarrow \text{Reduce } p \text{ by encouraging better sanitary practices} \]
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

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

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

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

- Since \( R_0 < 1 \), it follows that \( \lim_{n \to \infty} \mathbb{E}[Y(n)] = 0 \)
Proof of a) (cont.)

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

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

- 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
- Can leverage standard machinery since $\{Y(n)\}_{n=0}^{\infty}$ is a Markov chain
Proof of b)

- Define the probability \( q_n = P(\text{disease survives after } n \text{ waves}) \)
- By Markovianity of the BP, for any node \( i \) in the first wave we have
  \[
P(\text{disease survives after } n - 1 \text{ more waves} \mid X_i(1) = 1) = q_{n-1}
  \]
- Since the root has \( k \) children, disease goes extinct by wave \( n \) w.p.
  \[
P(\text{disease extinct by wave } n) = 1 - q_n = (1 - pq_{n-1})^k
  \]
- Thus the 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 \( R_0 < 1 \), 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 \( y = x \)

\[ \Rightarrow \text{A solution } q^* \text{ exists in the open interval } (0, 1) \]
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 $R_0 < 1$ 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

- Dichotomy disappears, but $R_0$ still important for intuition
Modeling epidemics

Branching processes

Traditional epidemic modeling

Network-based epidemic modeling

Synchronization
Most used epidemic model is the susceptible-infected-removed (SIR) model.

Stochastic formulation of simplest case with no contact network.

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

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

The triple $\{N_S(t), N_I(t), N_R(t)\}_{t=0}^\infty$ is a continuous-time random process.

Still 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)
  - Infection: $S + I \rightarrow 2I$
  - Recovery: $I \rightarrow \emptyset$

- Susceptible individual infected by infective individual on chance encounter
  - $\beta =$ Rate of encounters between susceptible and infective
  - $S$ susceptibles and $I$ infectives $\Rightarrow \beta SI =$ rate of first reaction
- Each infective recovers (and is removed) at rate $\gamma$
  - Population of $I$ infectives $\Rightarrow \gamma I =$ rate of second reaction

- Model assumption: ‘homogenous mixing’ among population members
  - 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)
- The 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 \(\beta\):
    \[P\left( N_S(t + \delta t) = s - 1, N_I(t + \delta t) = i + 1 \mid N_S(t) = s, N_I(t) = i \right) \approx \beta s i \delta t\]
  - **Recovery** with rate \(\gamma\):
    \[P\left( N_S(t + \delta t) = s, N_I(t + \delta t) = i - 1 \mid N_S(t) = s, N_I(t) = i \right) \approx \gamma i \delta t\]
  - **Unchanged state**:
    \[P\left( N_S(t + \delta t) = s, N_I(t + \delta t) = i \mid N_S(t) = s, N_I(t) = i \right) \approx 1 - (\beta s + \gamma) i \delta t\]
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
  - Transitions from state \((s, i)\) after time \( T \sim \exp((\beta s + \gamma)i) \)
  - **Infection**: to state \((s - 1, i + 1)\) w.p. \( \beta si/[(\beta s + \gamma)i] \)
  - **Recovery**: to state \((s, i - 1)\) w.p. \( \gamma i/[(\beta s + \gamma)i] \)

- This formulation of the model facilitates the simulation of realizations

![Schematic characterization of an SIR process](image.png)
Transition-probability functions

- CTMC evolution given by matrix of transition-probability functions

\[ P_{s,i}(t) = P \left( N_S(t) = s, N_I(t) = i \mid N_S(t) = N, N_I(t) = 1 \right) \]

- Full description of the epidemic process under the SIR model

- Transition probability functions satisfy the differential equations

\[
\begin{align*}
\frac{\partial P_{N,1}(t)}{\partial t} &= - (\beta N + \gamma) P_{N,1}(t) \\
\frac{\partial P_{s,i}(t)}{\partial t} &= \beta (s + 1)(i - 1) P_{s+1,i-1}(t) - i(\beta s + \gamma) P_{s,i}(t) + \gamma (i + 1) P_{s,i+1}(t)
\end{align*}
\]

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

- These equations are known as the Kolmogorov forward equations

- Exact analytical solution possible, but its 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

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

- Interestingly, a threshold theorem holds as for the BP model [Whittle’55]

**Theorem**

*Consider a generic SIR model with infection rate $\beta$ and recovery rate $\gamma*

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

- 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 $\beta$ and $\gamma$ (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

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

▶ The 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 $\beta$ and $\gamma$ since they relate to time

▶ Can still use the method-of-moments to produce an estimate of $R_0$

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

Branching processes

Traditional epidemic modeling

Network-based epidemic modeling

Synchronization
Structured population models

- So far assumed ‘homogenous mixing’ among population members
  - All pairs of members equally likely to interact with one another
- Admittedly simple and poor approximation to reality for some diseases
- Increasingly interest has shifted towards structured population models
  - Assumed contact patterns take into account population structure
- Ex: structure derives from spatial proximity, social contact, demographics
- Structured population models introduce a non-trivial contact network $G$
- Homogeneous mixing assumption $\Leftrightarrow$ Complete graph $G \equiv K_{N_v}$
- Epidemic models on graphs study dynamic processes $X(t) = \{X_i(t)\}_{i \in V}$
Network-based SIR model

- Let $G(V, E)$ be the contact network for a population of $N_v$ elements.
- At time $t = 0$, one vertex is infected and the rest are susceptible.
- Susceptible individual 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 $\beta$.
- Each infective recovers (and is removed) at rate $\gamma$.
  - $\Rightarrow$ Time till recovery is exponentially distributed with parameter $\gamma$.
- Define the stochastic process $X(t) = \{X_i(t)\}_{i \in V}$, where
  
  $X_i(t) = \begin{cases} 
  0, & \text{if vertex } i \text{ is susceptible at time } t \\
  1, & \text{if vertex } i \text{ is infected at time } t \\
  2, & \text{if vertex } i \text{ is recovered at time } t
  \end{cases}$
The process $X(t)$ is a CTMC, with state vectors $x \in \{0, 1, 2\}^{N_v}$

When state transitions from $x$ to $x'$, a single vector entry changes

If entry $i$ changes, the instantaneous state transition probabilities are

$$P(X(t + \delta t) = x' \mid X(t) = x) \approx \begin{cases} \beta M_i(x) \delta t, & \text{if } x_i = 0 \text{ and } x'_i = 1 \\ \gamma \delta t, & \text{if } x_i = 1 \text{ and } x'_i = 2 \end{cases}$$

Defined $M_i(x)$ as the number of infective neighbors of vertex $i$, i.e.,

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

⇒ The contact network $G$ enters the model through $M_i(x), i \in V$

Given $X(t)$ 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

- The 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

⇒ Characteristic of the epidemic process are affected by the network
Reproductive number

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

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

- Probability that an infective transmits the infection before recovering
- Expected number of neighbors in $G$ of a single infective (early on)

- Ex: Erdös-Rényi where $G = \mathcal{G}_{N,v,p} \Rightarrow R_0 \approx \beta N_v p / (\beta + \gamma)$
- Ex: Power-law $\{f_d\}$ for which we can expect $\mathbb{E}[d^2] \gg \mathbb{E}[d]$
  \(\Rightarrow\) Increases $R_0$, easier for epidemics to occur than for $\mathcal{G}_{N,v,p}$
- Intuitive, suffices to infect a small number of high-degree vertices

Synchronization

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Synchronization
Immunity and reinfections

- **Q**: What if individuals can be infected multiple times?
- SIR epidemic falls short, models full immunity (or death) after infection
- **SIS model**: infectives recover at rate $\gamma$, but are susceptible again
  \[
  S \rightarrow I \rightarrow S \rightarrow I \rightarrow S \rightarrow \ldots
  \]
- **Ex**: Gonorrhea, no immunity acquired after infection
- **SIRS model**: infectives recover at rate $\gamma$, then immune for **limited time**
  \[
  S \rightarrow I \rightarrow R \rightarrow S \rightarrow I \rightarrow R \rightarrow S \rightarrow \ldots
  \]
- **Ex**: Syphilis, limited temporal immunity
Synchronization

- Epidemics of certain diseases tend to synchronize across a population
  - 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
- Recent research points 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
  - Coordination in timing of flare-ups across the whole network
  - Network-wide deficit in number and connectivity of susceptibles
- Large “drop” in the outbreak following the “peak” from earlier flare-ups
Temporary immunity can explain oscillations locally. Global effects?

Network rich in long-range ties to coordinate disease flare-ups globally

**Small-world contact networks**

- **Homophilous ties**: highly-clustered links forming local communities
- **Weak ties**: long-range links connecting distant parts of the network

Relevance of small-world properties to synchronization


Small-world contact networks leading to oscillation in epidemics

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

- Rigorous analysis of synchronization onset challenging, largely unexplored
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