Economics of Epidemic Planning and Response

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Collaborators and Acknowledgments

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Epidemics and epidemiology in history

HISTORY OF INFECTIOUS DISEASES

500-1300	1300-1700	1700-1900	1900-2000	2000-Present
THE MIDDLE AGES	**THE RENAISSANCE**	**INDUSTRIAL AGE**	**20TH CENTURY**	**21ST CENTURY**
Nearly two-thirds of the European population were affected by the plague. Public health initiatives were developed to stop the spread of the disease.	Rebirth of thinking led to critical observations of disease outbreaks. Data was studied for the purpose of understanding health status.	Industrialization led to over crowding, poor sanitation and subsequent epidemics. Policy makers began addressing health problems and sanitation.	Discovery of Penicillin. Social reform shaped health and human services. Increased vaccination aided against childhood diseases.	Human Genome Project completed. New and emerging diseases: SARS, H1N1, Chikungunya. Tracking diseases through social media.

- 1918 Pandemic: 50 million deaths in 2 years (3-6% world pop) Every country and community was effected

- *Good news:* Pandemic of 1918 lethality is currently unlikely Governments better prepared and coordinated: e.g. SARS epidemic. But ..
- Planning & response to even a moderate outbreak is challenging: inadequate vaccines/anti-virals, unknown efficacy, hard logistics issues
- *Modern trends complicate planning:* increased travel, immuno-compromised populations, increased urbanization

Epidemic science in real-time

Editorial, Fineberg and Harvey, Science, May 2009: Epidemics Science in Real-Time

Five areas: (i) Pandemic risk, (ii) vulnerable populations, (iii) available interventions, (iv) implementation possibilities & (v) pitfalls, and public understanding.

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EDITORIAL

Epidemic Science in Real Time

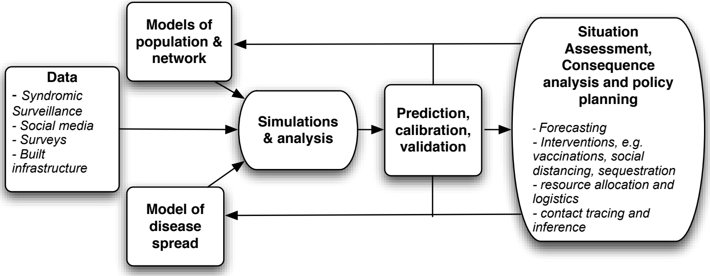
Modeling before an epidemic

(*i*) Determine the (non)medical interventions required, (*ii*) feasibility of containment, (*iii*) optimal size of stockpile, (*iv*) best use of pharmaceuticals once a pandemic begins

Modeling during an epidemic

(*i*) Quantifying transmission parameters, (*ii*) Interpreting real-time epidemiological trends, (*iii*) measuring antigenic shift and (*iv*) assessing impact of interventions.

Key elements of computational epidemiology

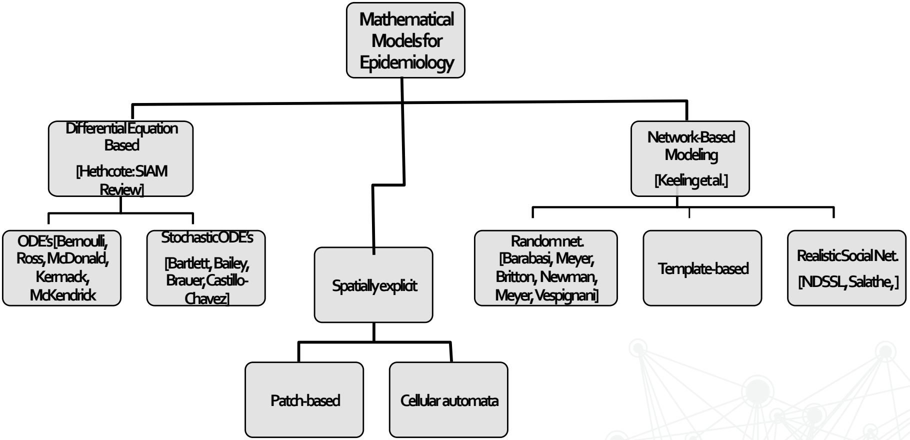


- Modeling, characterization and analysis:
  - Will there be a big outbreak? Has it peaked?
  - Mathematical models of disease spread and efficient simulation tools for analysis
- Prediction, calibration and validation:
  - Learn parameters of disease model, and individual effects
- Situational assessment and policy planning:
  - Interventions to control outbreak: Whom to vaccinate? Should we close schools,
  - Surveillance and parameter refinement, adaptive control

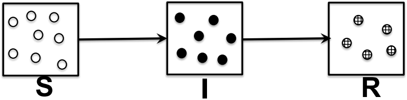
Outline

- Mathematical models for epidemic spread
- Intervention design as optimization problems
  - Social objective: designing interventions to minimize outbreak (centralized)
  - Social objective with limited compliance: group level interventions (partially centralized)
  - Individual level objective: game-theoretical interventions (decentralized)
  - Combining individual and social objectives: anti-viral distribution problem

Classifying formal models



Mass action compartmental Models



Assumption: complete mixing among population of size N

$$\frac{ds}{dt} = -\beta is$$
$$\frac{di}{dt} = \beta is - \gamma i$$
$$\frac{dr}{dt} = \gamma i$$

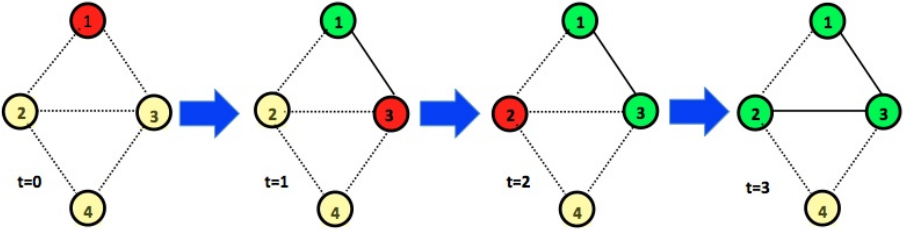
- Individuals in states *Susceptible* (S), *Infected* (I) or *Resistant/Recovered* (R).
- Epidemic characterized by *reproductive number* R_0
  - Large epidemic if $R_0 > 1$
  - Modeling epidemic = estimating R_0
  - Controlling epidemic: reducing R_0
- Limited use in large realistic populations
  - Does not capture heterogeneity in population
  - Extensions using compartmental models with mixing parameters, but becomes hard to analyze

Pros and cons of compartmental models

- Compartmental models have been immensely successful over the last 100 years – (*i*) workhorse of mathematical epidemiology, (*ii*) easy to extend and quick to build; (*iii*) good solvers exist, simple ones can be solved analytically; (*iv*) mathematical theory of ODEs is well developed
- SARS was estimated to have $R_0 \in [2.2, 3.6]$[1]
  - Though it spread across many countries, small number of infections
  - Estimates were based on infections in crowded hospital wards, where complete mixing assumption was reasonable
- Compartmental models lack agency and heterogeneity of contact structure
  - True complexity stems from interactions among many discrete actors
  - Each kind of interaction must be explicitly modeled
  - Refinement is difficult
- Human behavioral issues – Inhomogeneous compliance; changes in the face of crisis
- Harder to design implementable interventions.

[1] Lipsitch et al., *Science*, 2003; Riley et al., *Science*, 2003

Networked epidemiology: Discrete time SIR model on a network



Fixed point: $R = \{1, 2, 3\}$ and $S = \{4\}$

$$p(1,3)(1 - p(1,2))p(2,3)(1 - p(2,4))(1 - p(3,4))$$

- Each node is in states S (susceptible), I (infectious) or R (recovered)
- Time is discrete
- Each infected node u spreads the infection independently to each susceptible neighbor v with probability $p(u, v)$
- Infected node u recovers after 1 time step
- *Fixed point:* all nodes in states S or R

Dynamics of the SIR model: impact of network structure

- Phase transition for SIR model shown in many graph models: there exists a threshold p_t such that few infections if $p < p_t$ but large outbreak if $p > p_t$
- Technique: mainly extends branching process
- Clique on n nodes[2]: $p_t = 1/(n-1)$
- Lattice $\mathbb{Z}^d$: $p_t \rightarrow 1/(2d)$, as $d \rightarrow \infty$
- Random d-regular graphs: $p_t = 1/d$
- Not well understood in general graphs
  - Partial characterization in finite regular expander graphs with high girth[3]
  - Characterization in terms of the second moment[4]

[2] Erdős and Rényi, 1959
[3] Alon, Benjamini and Stacey, 2001
[4] Chung, Horn, Lu, 2009

Interventions as optimization problems

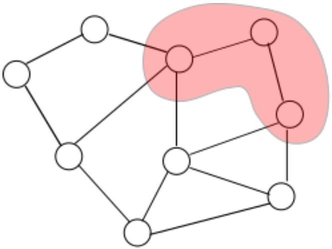
Given (maybe?)

- A social network $G(V, E)$
- Initial infected set A
- Budget B
- Stochastic model for disease spread

Objective(s)

- Choose $S \subseteq V$ to vaccinate so that $|S| \leq B$, and expected #infected nodes is minimized
- Other objectives
  - Reduce the epidemic duration
  - Reduce peak
  - Delay epidemic
- Individual compliance depends on their utilities

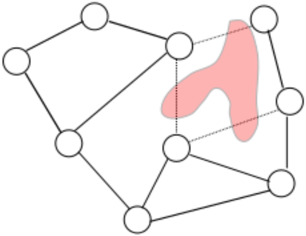
Interventions



Pharmaceutical interventions (PI)

- use of prophylactic vaccinations and anti-viral drugs
- modeled as node deletions

Interventions



Non Pharmaceutical interventions (NPI)

- Reducing contacts by social distancing, school or work place closure, or isolation.
- Modeled as edge deletions

Different kinds of issues in studying interventions as optimization problems

- Resource constraints, e.g., budget for vaccines to use
- Complex and multiple objective functions, e.g., expected outbreak size, peak size and duration
  - Need multi-criteria optimization
- Implementability and compliance
  - Interventions should be described succinctly
  - Individual vs social good
- Computationally very hard problems
  - Computing basic properties related to epidemics (e.g., probability that a node gets infected) is #P-hard in network models
  - Optimization problems NP-hard even for very simplistic settings (e.g., SI model or simple contagion)
  - Simplistic brute-force methods are unlikely to scale to realistic networks
  - Metaheuristics do not give any insights into how well they perform (relative to the best possible).

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Our approach

Formalize interventions in terms of network structure

Dynamics in the SIS model: preliminaries

- Nodes in Susceptible (S) or Infectious (I) states
- Each infected node spreads infection to each susceptible neighbor with rate β
- Each infected node becomes susceptible with rate δ
- $\rho(A)$: spectral radius of adjacency matrix A
- $T = \delta/\beta$
- Generalized isoperimetric constant: $\eta(G, m) = \inf_{S \subset V, |S| \leq m} \frac{|E(S,\bar{S})|}{|S|}$

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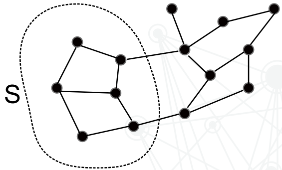
- Generalized isoperimetric constant: $\eta(G, m) = \inf_{S \subset V, |S| \leq m} \frac{|E(S, \bar{S})|}{|S|}$
- Spectral radius $\rho(A) = \max_x x^T Ax/x^x$
- Avg degree $\leq \rho(A) \leq \Delta(G)$, where $\Delta(G)$ is the maximum node degree



$\eta(G, 6) \leq 2/6$

Dynamics in the SIS model (informal) spectral characterization[7]

- $\rho(A)$: spectral radius of adjacency matrix A
- $T = \delta/\beta$
- Generalized isoperimetric constant: $\eta(G, m) = \inf_{S \subset V, |S| \leq m} \frac{E(S, \bar{S})}{|S|}$

- If $\rho(A) < T$: epidemic dies out "fast"
- If $\eta(m) > T$: epidemic lasts "long"

Similar implications but different assumptions, extended to SEIR models[5] [6]

[5] BA Prakash, D Chakrabarti, M Faloutsos, N Valler, C Faloutsos. *Knowledge and Information Systems*, 2012

[6] Y. Wang, D. Chakrabarti, C. Wang and C. Faloutsos, *ACM Transactions on Information and System Security*, 2008.

[7] A. Ganesh, L. Massoulie and D. Towsley, *IEEE INFOCOM*, 2005

Formally

Lemma (Sufficient condition for fast recovery)

Suppose $\rho(A) < T$. Then, the time to extinction τ satisfies

$$E[\tau] \leq \frac{\log n + 1}{1 - \rho(A)/T}$$

Lemma (Sufficient condition for lasting infection)

If $r = \frac{\delta}{\beta\eta(m)} < 1$, then the epidemic lasts for "long":

$$\Pr[\tau > r^{-m+1}/(2m)] \geq \frac{1-r}{e}(1 + O(r^m))$$

Implications for different network models

- Hypercube: $\rho(G) = \log_2 n$, and $\eta(m) = (1-a)\log_2 n$ for $m = n^a$
  - Fast die out if $\beta < \frac{1}{\log_2 n}$, slow die out if $\beta > \frac{1}{(1-a)\log_2 n}$
- Erdős-Rényi model: $\rho(G) = (1+o(1))np = (1+o(1))d$ and $\eta(m) = (1+o(1))(1-\alpha)d$ where $m/n \to \alpha$
  - Fast die out if $\beta < \frac{1}{(1+o(1))d}$, slow die out if $\beta > \frac{1}{(1+o(1))(1-\alpha)d}$
- Power law graphs (Chung-Lu model): assume degree distribution with power law exponent $\gamma > 2.5$
  - $E[\tau] = O(\log n)$ if $\beta < (1-u)/\sqrt{m}$ and $E[\tau]$ exponential if $\beta > m^\alpha/\sqrt{m}$ for some $u, \alpha \in (0,1)$ and $m = n^\lambda$, for $\lambda \in (0, \frac{1}{\gamma-1})$
- In general, gap between necessary and sufficient conditions for epidemic to last long

Controlling epidemics in the SIS model

- Reduce spectral radius below T to ensure the epidemic dies out fast.
- Spectral radius can be reduced by deleting nodes (vaccination) or edges (social distancing)

Spectral Radius Minimization (SRM) problem

- *Given*: graph G=(V, E), threshold T and cost $c(e)$ for edges
- *Objective*: choose cheapest set $E' \subseteq E$ of edges to delete, so that $\lambda_1(G[E - E']) \leq T$.

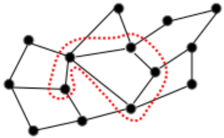
Similarly: node version

Reducing the spectral radius to control epidemic spread

- Interventions (node/edge deletion) to reduce spectral radius below given threshold
- NP-hard to approximate within a constant factor
- Heuristics based on components of the first eigenvector and degree: [Tong et al., 2012], [Van Mieghem et al., 2011]
- Node version: if G has a power law degree sequence with exponent $\beta > 2$ and $T^2 \leq cd_{max}$, then a high degree strategy gives an $O(T^{\beta-1})$ approximation.
- Node version: $\Theta(1)$ approximation by a high degree strategy in Chung-Lu random graphs with power law weights with exponent $\beta > 2$.

Some notation and properties

- A: adjacency matrix of G with eigenvalues $\lambda_1 \geq \lambda_2 \geq \ldots \lambda_n$
- Let $\mathcal{W}_k(G)$ denote the set of closed walks of length k
- Let $W_k(G) = |\mathcal{W}_k(G)|$
- Edge e “hits” walk w if $e \in w$.
- $n(e, G)$: #walks in $\mathcal{W}_k(G)$ containing edge e
- Let $E_{opt}(T)$ denote the optimum set of edges, whose deletion reduces the spectral radius below T
- $\sum_i \lambda_i^k = \sum_i A_{ii}^k = \sum_{w \in \mathcal{W}_k(G)} d(w)$, where $d(w)$ is the number of distinct nodes in walk w



An $O(\log^2 n)$-approximation algorithm

Algorithm GreedyWalk: Pick the smallest set of edges E' which hit at least $W_k(G) - nT^k$ walks, for even $k = c \log n$

- Initialize $E' \leftarrow \phi$
- Repeat while $W_k(G[E \setminus E']) \geq nT^k$:
  - Pick the $e \in E \setminus E'$ that maximizes $\frac{n(e, G[E \setminus E'])}{c(e)}$
  - $E' \leftarrow E' \cup \{e\}$

Lemma

We have $\lambda_1(G[E \setminus E']) \leq (1+\epsilon)T$, *and*
$c(E') = O(c(E_{\mathrm{OPT}}(T)) \log n \log \Delta/\epsilon)$ *for any* $\epsilon \in (0, 1)$.

Similar bound for node version

Proof: bounding spectral radius of residual graph

By construction: $W_k(G') \leqslant nT^k$, where $G' = G[E - E']$. Therefore,

$$\sum_{i=1}^{n} \lambda_i(G')^k = \sum_i A_{ii}^k = \sum_{w \in \mathcal{W}(G')} d(w) \le kW_k(G')$$

$$\Rightarrow \sum_{i=1}^{n} \lambda_i(G')^k \leqslant nkT^k$$

and therefore, $\lambda_1(G') \leqslant 2^{(\log n + \log k)/k} T$

$$\leqslant (1+\epsilon)T, \text{ for } k \geqslant \frac{2}{\epsilon} \log n.$$

Proof: bounding $c(E')$

- Let E_{HITOPT} be optimal solution for the partial covering instance: cheapest subset of edges that hits at least $W_k(G) - nT^k$ walks.
- Standard greedy analysis $\Rightarrow c(E') = O(c(E_{\text{HITOPT}}) \log H)$, where $H = $ #elements in covering instance.
- Elements= walks $\Rightarrow H = |W_k(G)| \leqslant n\Delta^k$
- By definition, $\lambda_1(G[E - E_{\mathrm{OPT}}(T)]) \leq T$. Therefore, $W_k(G[E - E_{\mathrm{OPT}}(T)]) \leq \sum_{i=1}^{n} \lambda_i(G[E - E_{\mathrm{OPT}}(T)])^k < nT^k$.
- $\Rightarrow c(E_{\text{HITOPT}}) \leq c(E_{\mathrm{OPT}}(T))$
- $c(E') = O(E_{\mathrm{OPT}}(T) \log n \log \Delta)$.

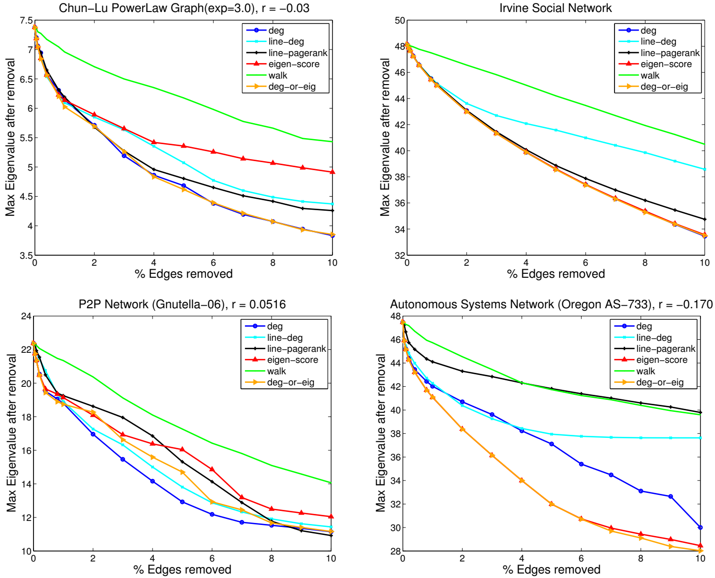
Improvement to $O(\log n)$ factor

- Partial coverage problem: primal-dual algorithm of [Gandhi et al., 2004] for selecting a minimum cost collection of sets that covers at least k elements, with $O(f)$-approximation, where f is the maximum number of sets containing any element
- Our set system:
  - Sets $\equiv$ edges, elements $\equiv$ walks in $\mathcal{W}_k$
  - $f = O(\log n)$, since walks have length $k = O(\log n)$
- Set system of size $n^{O(\log n)}$, so cannot apply primal-dual algorithm of [Gandhi et al., 2004] directly
  - Can do updates implicitly and get polynomial time $O(\log n)$-approximation
  - Results in $c(E') = O(c(E_{\mathrm{OPT}}(T)) \log n)$, $\lambda_1(G[E - E']) \leq (1 + \epsilon)T$
- Constant factor approximation by semidefinite programming based rounding.

Heuristics that work well

- Pick edges $e = (i, j)$ in decreasing order of $eigenscore(i, j) = x^1(i) \cdot x^1(j)$ [Tong et al., 2012], [Van Mieghem et al., 2011]
- Pick edges $e = (i, j)$ in decreasing order of $degscore(i, j) = d(i)d(j)$ [Van Mieghem et al., 2011]
- Hybrid rule: pick edge from either order whose removal causes the largest reduction in λ_1

Empirical analysis of different heuristics



Analysis of degree heuristic

Lemma

Let G be a power law graph with exponent $\beta > 2$, where β is a constant and let threshold T satisfy $T^2 \leqslant c\Delta$ for a constant $c < 1$. Then, the number of edges removed by the degree heuristic is $O(T^{\beta-2}|E_{\mathrm{OPT}}(T)|)$.

Lemma

Let $G(\mathbf{w})$ be a Chung-Lu random power law graph on n nodes with exponent $\beta > 2$ and $w(V)$ a constant. Let T be the threshold satisfying $\max_{i \in V} w_i > T^2$ and $T = \Omega(\log n)$. Then, the number of edges removed by the degree heuristic is $O\big((\log n)^{\beta-1}\big)|E_{\mathrm{OPT}}|$.

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Group level intervention

- Assume $V = V_1 \cup V_2 \cup \ldots V_k$
  - Each V_i might denote a demographic group
- If n_i vaccines are allocated to V_i, assume they are distributed randomly within the set

Group Node Immunization Problem

- Given: Graph $G(V, E)$, a partition $V = V_1 \ldots \cup V_k$, with vaccine cost C_i for each group i, budget B
- Select subset $S_i \subset V_i$, $i = 1, \ldots, k$, such that $\lambda_1(G[\cup_i V_i - S_i])$ is minimized.

GreedyWalk can be extended to group level

Algorithm GroupGreedyWalk

Algorithm $\textsc{GroupGreedyWalk}(G, B)$

1. Initialize $\mathbf{x} = \mathbf{0}$. Let $N = |\mathcal{W}(G, k)|$.
2. While $\sum_j x_j \leq B$
   1. Let i be the index that maximizes $\textsc{CountWalks}(G, \mathbf{x} + \mathbf{e}_i) - \textsc{CountWalks}(G, \mathbf{x})$.
   2. $\mathbf{x} = \mathbf{x} + \mathbf{e}_i$

Lemma

Let $\mathbf{x}^{opt}(B)$ be the optimum solution corresponding to budget B of edges removed. Let $\mathbf{x}^g$ be the allocation returned by $\textsc{GroupGreedyWalk}(G, c_1 B \log^2 n)$, for a constant c_1. Then, we have $\lambda_1(G(\mathbf{x}^g)) \leq c_2 T$ for a constant c_2.

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Epidemic containment game in the SIS model

- Let $\mathbf{a} = (a_1, a_2, ..., a_n)$ denotes the strategy profile with $a_x = 1$ denoting that node x is vaccinated
- Let $S = S(\mathbf{a}) = \{x \in V : a_x = 1\}$ denote the set of vaccinated nodes
- Cost for node v, given strategy vector $\mathbf{a}$:

$$\mathrm{cost}(v, \mathbf{a}) = \begin{cases} C, & \text{if } a_v = 1, \\ L, & \text{if } a_v = 0 \text{ and } \lambda_1(G[V - S(\mathbf{a})]) < T, \\ L_e, & \text{if } a_v = 0 \text{ and } \lambda_1(G[V - S(\mathbf{a})]) \geq T. \end{cases}$$

Nash equilibrium $\mathbf{a}$: if no node v has incentive to switch unilaterally, given that other players' strategies are fixed
Social cost $\mathrm{cost}(\mathbf{a}) = \sum_v \mathrm{cost}(v, \mathbf{a})$

Structure of Nash equilibria

- Assume $C = 1, L = 0, L_e > 1$
- The strategy corresponding to any *minimal* set S such that $\lambda_1(G[V - S]) < T$ is a NE.
- Finding the social optimum of an EC game is NP complete. Moreover, the cost of social optimum cannot be approximated within a factor of 1.3606 unless P=NP.

Results: price of anarchy

- Let G be a power law graph with exponent $\beta > 2$, where β is a constant and let $T^2 \leq c\Delta$ for a constant $c < 1$, where Δ is the maximum node degree. Then, the price of anarchy is $O\left(T^{2(\beta-1)}\right)$.
- Erdős-Rényi random graph model: if $G = G(n, p)$, for $p \geq \frac{c}{n}$, where c is a suitably large constant and $np \geq (1+\delta)T^2$ for any positive constant δ, the price of anarchy is almost surely $O\left(\frac{\log n}{np}\right)$.

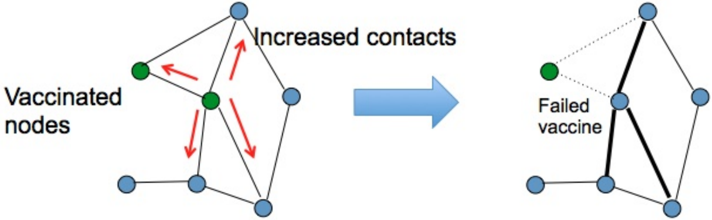
Results: price of anarchy

- Chung-Lu random graph model: given a weight sequence $\mathbf{w} = (w(v_1, V), w(v_2, V), ..., w(v_n, V))$ for nodes $v_i \in V$, the random graph $G(\mathbf{w})$ is constructed in the following manner:
  - add edge (v_j, v_k) with probability $\frac{w(v_j,V)w(v_k,V)}{\sum_{v_i \in V} w(v_i,V)}$

Theorem

Consider a Chung-Lu random power law graph $G(\mathbf{w})$ of n nodes and power law exponent $\beta > 2$. Suppose $w(V) = \sum_v w(v)/|V| = O(1)$ and $w_{\max} = \max_v\{w_v\} \geq (1+\delta)T^2 w(V)$ for some constant δ and $T = \Omega(log^2 n)$. The price of anarchy in $G(\mathbf{w})$ is $\theta(T^{2(\beta-1)})$ almost surely.

Effect of behavioral changes: coevolution



- Network coevolves with epidemic spread
  - People reduce contacts if there is an epidemic going on
  - Risky behavior: people increase contacts if they feel they are protected (e.g., after a vaccine)
- Model of risk behavior
  - Vaccines have limited efficacy
  - Individuals who are vaccinated increase their contact strengths with some probability

Effect of behavioral changes: coevolution

Lemma

For $G \in G(n, p)$ (the Erdös-Rényi model), there exist parameters p_f (vaccine failure probability) and p_r (the increased probability of contact due to risky behavior), such that the expected outbreak size is $o(n)$ for $p_v = 0, 1$, but is $\Theta(n)$ for some $p_v \in (0, 1)$.

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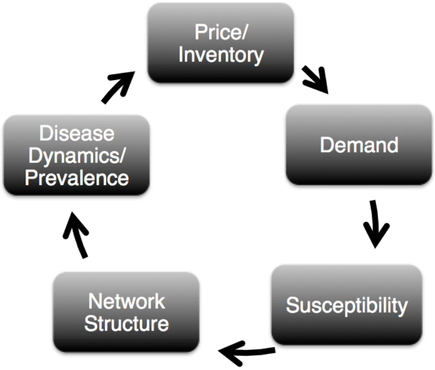
Combining social and individual incentives: anti-viral distribution problem

- Policy Problem: Is there an optimum strategy to partition the scarce AV doses between public stockpile administered through hospitals and private stockpile distributed using a market-mechanism
- Measures of Effectiveness: Number of infected, peak infections, cost of recovery, equitable allocation
- Additional issues: How do disease prevalence, individual behavior, network structure, disease dynamics and AV demand co-evolve?



Models of individual behaviors and adaptation

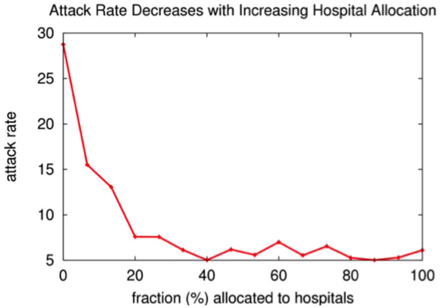
- Isolation based on Prevalence (fear contagion)
  - Entire household isolated when perceived prevalence > threshold
  - Compliance rate: 40%
- Economic Behavior: Demand elasticity based on Prevalence
  - Household demand: $D_{t,h} = \frac{B_{t,h}}{P_t}(1 - e^{-\beta x_t})$
  - Increases with disease prevalence x_t
  - Increases with household budget $B_{t,h}$, decreases with price P_t, and price is linear in remaining supply
  - β reflects risk aversion or prevalence elastic demand to AV.
- Disease Reporting and treatment
  - Anti-virals are administered to individuals who are symptomatic, report clinic and are correctly diagnosed.

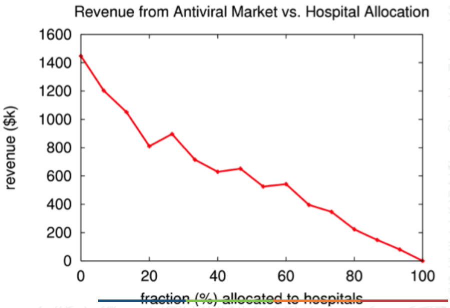
Organizational Behavioral models

- Hospitals
  - Total AV supply is 15K: allocated between hospitals and market
  - Hospitals: give to diagnosed as infected
- Markets
  - Market: sells to households according to demand and price
  - Markets provide A/Vs on a first come first serve basis (are not spatially sensitive in this version)
  - Assume a centralized market. Linear price curves (as a function of remaining A/V stock)

Results (I): both Private and Public Distribution are important

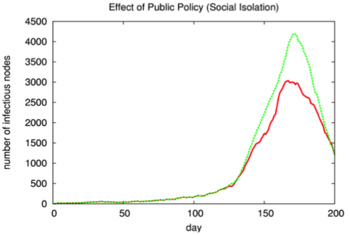
- Suggests optimal allocation strategy of AVs between public and private stockpile
  - Hospitals (public sector) should be given priority
  - If > threshold, the remaining stockpile be distributed via market.
  - Private stockpile useful for individuals who are infectious but not symptomatic
- Optimal split (40% to hospitals, 60% to the market) recovers the cost of antiviral manufacturing if the unit cost is below a bound.

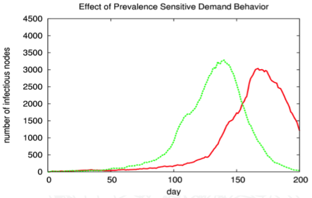




Results (II): Role of Behavioral Adaptations

- Both behavioral adaptation were critical in controlling the epidemic
  - Household isolation reduces the peak infection rate by 30%.
  - Prevalence based demand delays the peak infection rate by 30 days.





Natural behavior adaptation to an epidemic in conjunction with well established logistics (markets + public distribution) reduce and delay the peak infection rate

Conclusion

- Network based formulations for designing interventions
  - Tools from dynamical systems, spectral graph theory, approximation algorithms
- Novel challenges
  - Multiple and competing objectives
  - Logistical issues: how to distribute vaccines
  - Network not really known: realistic population and network models
  - Uncertainty: source, network, epidemic model parameters not known accurately
- Taking individual incentives into account
- Coevolution of disease with network

Thank You

Questions?