Diffusion in Networks and Infectious Disease Epidemics

Erik M Volz
Department of Epidemiology
University of Michigan– Ann Arbor

June 24, 2010

Introduction

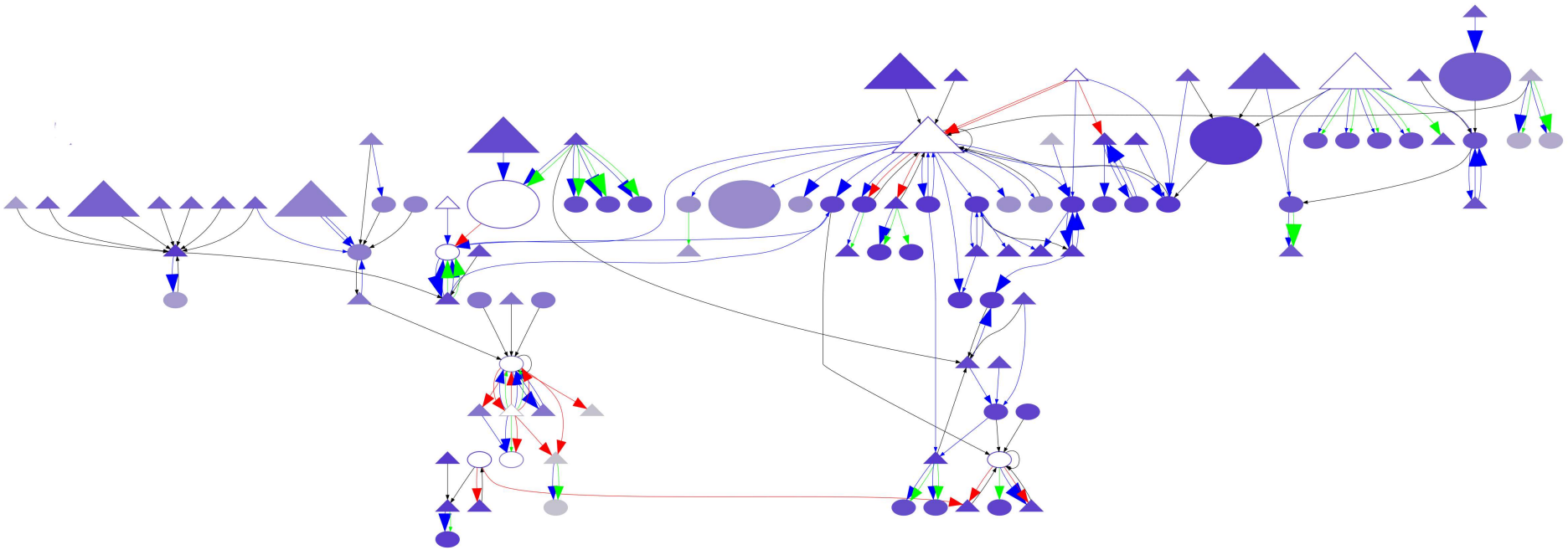
▷ Introduction
Main challenges
Quick history of mathematical models for epidemics in networks
Quick history: pair approximations & moment closure
Quick history: Rate equations
Probability Generating Functions (PGFs)
Static properties of epidemics
Can you include ... in your network model?
Transitivity and Clustering
Application to HIV
Conclusion

How do epidemics spread through networks ? We consider simple transmission dynamics and increasingly complicated generalizations of configuration model graphs.

- Simple transmission dynamics
  - Nodes can be susceptible, infectious, or recovered
  - Transmit to neighbors in the network at a constant rate and recover at a constant rate
- Complex population structure
  - Consider dynamics in ensembles of random graphs
  - Multiple edge types, node types, and simple edge rearrangement

The sort of data I work with ...

- small n, but detailed information for nodes and edges



Main challenges

Introduction
▷ Main challenges
Quick history of mathematical models for epidemics in networks
Quick history: pair approximations & moment closure
Quick history: Rate equations
Probability Generating Functions (PGFs)
Static properties of epidemics
Can you include ... in your network model?
Transitivity and Clustering
Application to HIV
Conclusion

Why is this a hard modeling problem ? Classic approach makes use of the *mass action* assumption

$$\dot{S} \propto SI$$

- Heterogeneous nodes
  - Degree (eg heavy-tailed or scale-free distributions)
  - Correlated partnerships (transitivity, assortativity, spatial structure etc)
- Extended duration partnerships $\longrightarrow$ autocorrelated contacts
- Network might be changing at the same time that the epidemic is spreading

Quick history of mathematical models for epidemics in networks

Introduction
Main challenges
Quick history of mathematical models for epidemics in networks
Quick history: pair approximations & moment closure
Quick history: Rate equations
Probability Generating Functions (PGFs)
Static properties of epidemics
Can you include ... in your network model?
Transitivity and Clustering
Application to HIV
Conclusion

- Pair approximation / moment closure (Altman, Bauch, Eames, Keeling et al.)
- Rate equations (Vespignani, Pastor Satorras, Ball & Neal, Lindquist, Ma, van den Driessche, Willeboordse et al.)
- Bond percolation (Newman, Watts, Strogatz, Callaway, Pourbohloul, Meyers, Bansal, Funk et al.)

Quick history: pair approximations & moment closure

Introduction
Main challenges
Quick history of mathematical models for epidemics in networks
Quick history: pair approximations & moment closure
Quick history: Rate equations
Probability Generating Functions (PGFs)
Static properties of epidemics
Can you include ... in your network model?
Transitivity and Clustering
Application to HIV
Conclusion

- Main idea: $\dot{S} = -\beta[SI]$.

$$[\dot{S}I] = \beta\left([SSI] - [ISI] - [SI]\right) - \gamma[SI] \qquad (1)$$

- The simplifying assumption: Moment closure– $[SSI] \approx [SS][SI]/[S], [ISI] \approx [SI]^2/[S]$
- Pros/Cons: Very flexible framework; can handle many network topologies. But very high-dimensional; the number of equations required grows as k_{max}^2

Quick history: Rate equations

Introduction
Main challenges
Quick history of mathematical models for epidemics in networks
Quick history: pair approximations & moment closure
Quick history: Rate equations
Probability Generating Functions (PGFs)
Static properties of epidemics
Can you include ... in your network model?
Transitivity and Clustering
Application to HIV
Conclusion

- Main idea: $\frac{\mathrm{d}}{\mathrm{d}t} s_k \propto -\beta \nu k s_k$
- The simplifying assumption: $\nu(t) = \sum_k q_k x_k(t)$
- Pros/Cons: Very good approximation early in the epidemic; but for some networks it is a very bad approximation late in the epidemic

Probability Generating Functions (PGFs)

Introduction
Main challenges
Quick history of mathematical models for epidemics in networks
Quick history: pair approximations & moment closure
Quick history: Rate equations
Probability Generating
▷ Functions (PGFs)
Static properties of epidemics
Can you include ... in your network model?
Transitivity and Clustering
Application to HIV
Conclusion

$$g(x) = p_0 + p_1 x + p_2 x^2 + p_3 x^3 + \cdots$$

A generating function is a clothesline on which we hang up a sequence of numbers for display.
–Herbert Wilf

- Poisson: $g(x) = e^{z(x-1)}$
- Negative binomial: $g(x) = (p/(1-(1-p)x))^r$

Static properties of epidemics

Introduction
Main challenges
Quick history of mathematical models for epidemics in networks
Quick history: pair approximations & moment closure
Quick history: Rate equations
Probability Generating Functions (PGFs)
Static properties of epidemics
Can you include ... in your network model?
Transitivity and Clustering
Application to HIV
Conclusion

Bond percolation solutions for static properties of epidemics in configuration model (CM) networks.

- $FS = 1 - g(u), u = g_1(u)$
- $R_0 = \tau g''(1)/g'(1)$
- Many extensions
  - Multi-partite, semi-directed, approximations for clustering, heterogeneous susceptibility and infectiousness
- Bond percolation only calculates static properties
- Bond percolation can't handle simultaneous epidemic and population dynamics
  - Partner rearrangement / *serosorting*
  - Adaptive vaccination strategies

Introduction
Can you include ... in your network model?
Can you include arbitrary degree distributions ?
Can you include temporary partnerships ?
Can you include multiple partnerships types ?
Can you include multiple stages of infection ?
Can you include the dynamics of preferential attachment ?
Transitivity and Clustering
Application to HIV
Conclusion

Can you include ... in your network model?

Can you include arbitrary degree distributions ?

Introduction
Can you include ... in your network model?
Can you include arbitrary degree distributions ?
Can you include temporary partnerships ?
Can you include multiple partnerships types ?
Can you include multiple stages of infection ?
Can you include the dynamics of preferential attachment ?
Transitivity and Clustering
Application to HIV
Conclusion

- Many sexual networks have been shown to feature heavy tailed distributions in the number of partners
- Pair approximation methods struggle with these scenarios, since the number of dynamic variables grows quadratically with the number of degree classes
- PGFs simplify the problem substantially
  - Provides a link between the number of susceptible individuals and a potentially infinite number of degree classes

Dynamic PGFs

Introduction
Can you include ... in your network model?
Can you include arbitrary degree distributions ?
Can you include temporary partnerships ?
Can you include multiple partnerships types ?
Can you include multiple stages of infection ?
Can you include the dynamics of preferential attachment ?
Transitivity and Clustering
Application to HIV
Conclusion

Based on the idea that
$S_k =$ the probability that a degree k node remains susceptible is S_1^k

$$S = g(S_1) = p_0 + p_1 S_1 + p_2 S_1^2 + p_3 S_1^3 + \cdots$$

- Dummy variable S_1 will be a dynamic variable
- Differential equation for S_1
- Edge-based rather than node-based quantities

Dynamic PGF derivations

Introduction

Can you include ... in your network model?

Can you include arbitrary degree distributions ?

Can you include temporary partnerships ?

Can you include multiple partnerships types ?

Can you include multiple stages of infection ?

Can you include the dynamics of preferential attachment ?

Transitivity and Clustering

Application to HIV

Conclusion

Hazard is proportional to degree

$$\lambda_k \propto k$$

$$S_k = e^{\int -\lambda_k(t)dt} = \left(e^{\int -\lambda_1(t)dt}\right)^k$$

$$\Rightarrow S_k = S_1^k$$

$$S = p_1 S_1 + p_2 S_2 + p_3 S_3 + \dots$$

$$S = p_1 S_1 + p_2 S_1^2 + p_3 S_1^3 + \dots$$

$$S = g(S_1)$$

We propose

$$\lambda_k = \beta k \frac{M_{SI}}{M_S} \qquad \neq \beta k \frac{M_I}{M}$$

Dynamic PGF derivations

$$\frac{\mathrm{d}}{\mathrm{d}t}S_1 = \frac{\mathrm{d}}{\mathrm{d}t}\theta = -\beta\frac{M_{SI}}{M_S}\theta$$

Dynamics of M_{SI} require careful accounting of how edges are rearranged following a transmission event

$$\frac{\mathrm{d}}{\mathrm{d}t}M_{SI} = -(\beta+\gamma)M_{SI} + (-\dot{S})\delta_S\left(M_{SS} - M_{SI}\right)/M_S$$

Derived variables:

- $M_S = \sum_k k p_k \theta^k = \theta g'(\theta)$
- M_{SI}/M_S is the probability that an edge connected to a susceptible leads to an infected
- $-\dot{S}$ rate of transmissions
- $\delta_S = \theta g''(\theta)/g'(\theta)$ is the average excess degree of a susceptible node

How many equations ?

Introduction
Can you include ... in your network model?
Can you include arbitrary degree distributions ?
Can you include temporary partnerships ?
Can you include multiple partnerships types ?
Can you include multiple stages of infection ?
Can you include the dynamics of preferential attachment ?
Transitivity and Clustering
Application to HIV
Conclusion

- Recent Joel Miller (arXiv:0909.4485) showed that that this system can be reduced to a single ODE

$$\dot{\theta} = -\beta\theta + \gamma(1-\theta) + \beta\frac{g'(\theta)}{g'(1)}$$

ie SIR in a population with unlimited heterogeneity can be modeled with a single ODE...

Can you include temporary partnerships ?

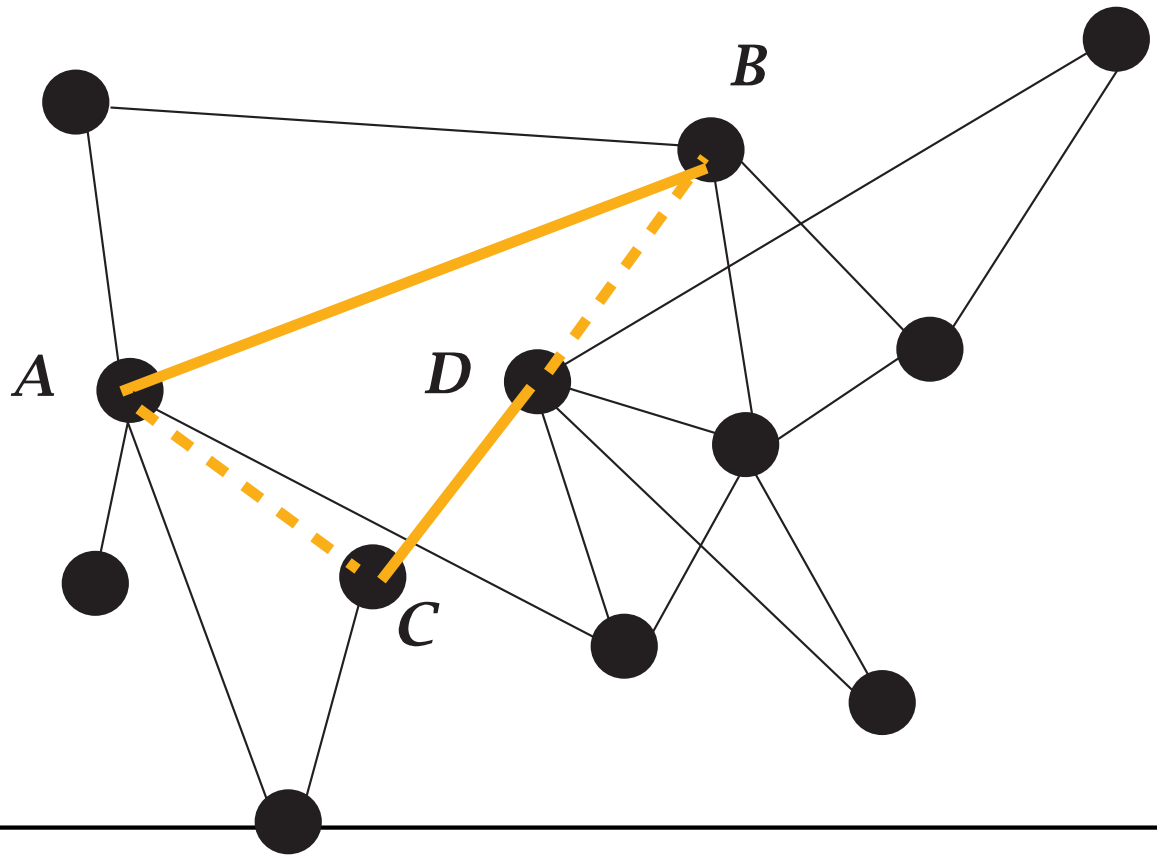
Introduction
Can you include ... in your network model?
Can you include arbitrary degree distributions ?
Can you include temporary partnerships ?
Can you include multiple partnerships types ?
Can you include multiple stages of infection ?
Can you include the dynamics of preferential attachment ?
Transitivity and Clustering
Application to HIV
Conclusion

- What if the network is changing at the same time that the epidemic is spreading ?
- Might be important for diseases with very long infectious period
- Or for diseases that are spread by very casual contacts of short duration

Extensions to dynamic PGFs

1. NE model: Partnerships are temporary– terminated and created at a constant rate, and every node has a number of concurrent partnerships

Mixing term: $\rho\left(M_S M_I/M - M_{SI}\right)$



The reproduction number in dynamic nets

Introduction

Can you include ... in your network model?

Can you include arbitrary degree distributions ?

Can you include temporary partnerships ?

Can you include multiple partnerships types ?

Can you include multiple stages of infection ?

Can you include the dynamics of preferential attachment ?

Transitivity and Clustering

Application to HIV

Conclusion

$$R_0 = \frac{\tau(\beta+\rho)}{\gamma}\frac{g''(1)}{g'(1)} + \frac{\rho\tau}{\gamma}$$

$$\tau^* = \frac{\beta}{\beta+\gamma+\rho} = \frac{\gamma g'(1)}{g''(1)(\gamma+\rho)+\rho g'(1)}$$

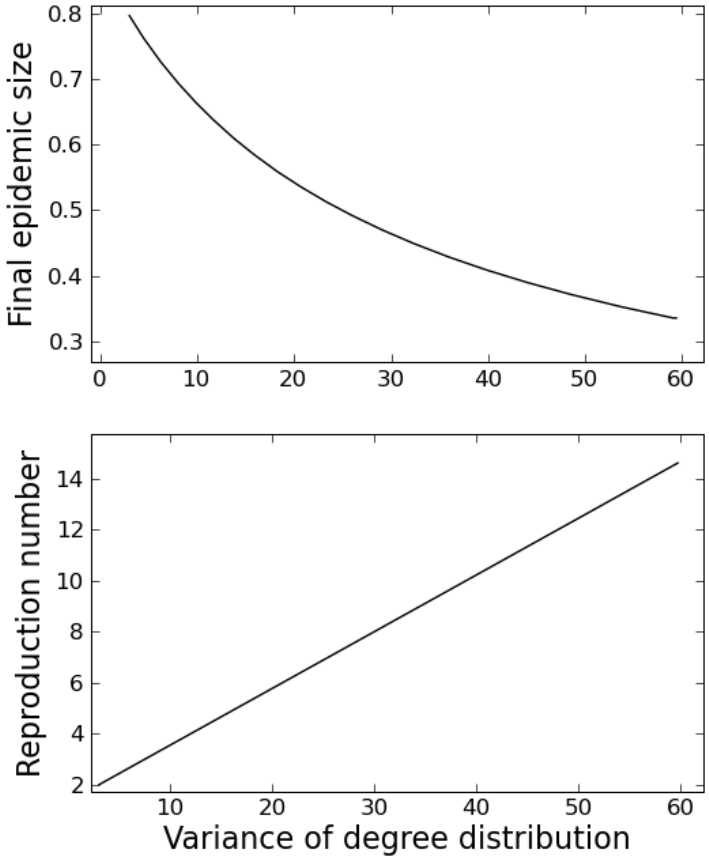
$$\beta^* = \frac{\gamma(\gamma+\rho)g'(1)}{g''(1)(\gamma+\rho)+(\rho-\gamma)g'(1)}$$

$$\rho^* = \frac{\gamma(\beta+\gamma)g'(1)-\beta\gamma g''(1)}{\beta g''(1)+g'(1)(\beta-\gamma)}$$

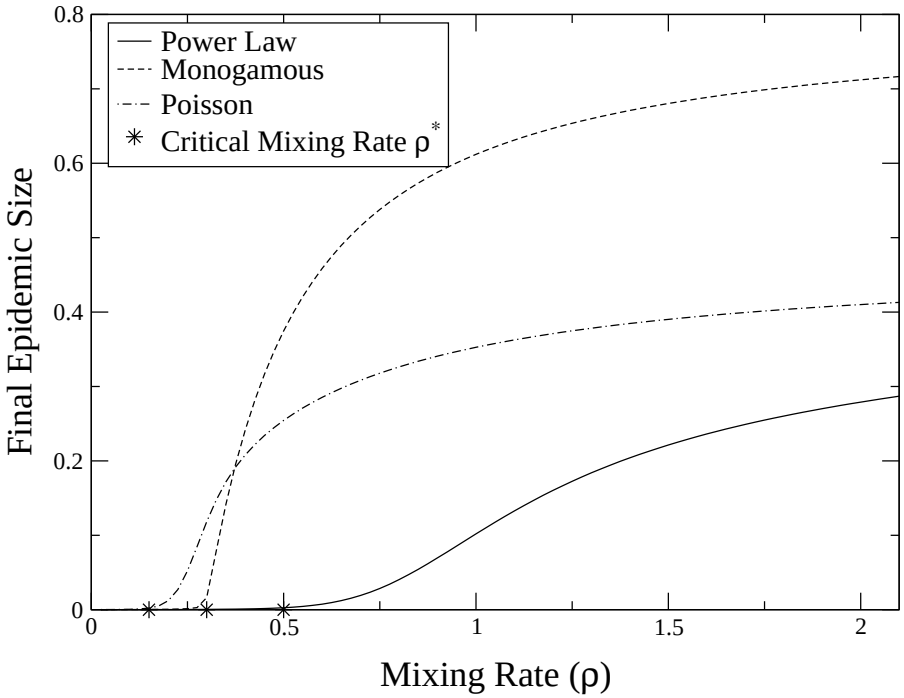
Rules of thumb– variance of the DD

Introduction
Can you include ... in your network model?
Can you include arbitrary degree distributions ?
Can you include temporary partnerships ?
Can you include multiple partnerships types ?
Can you include multiple stages of infection ?
Can you include the dynamics of preferential attachment ?
Transitivity and Clustering
Application to HIV
Conclusion

- Heterogeneity in the number of partners
  - increases R_0
  - *usually* decreases final size
  - increases the initial rate of epidemic spread
  - decreases threshold levels of transmissibility.



Rules of thumb– duration of partnerships



- Increasing the rate of partnership turnover
  - increases R_0
  - increases final size
  - increases the initial rate of epidemic spread
  - decreases threshold levels of transmissibility.

NE model– special cases

Introduction

Can you include ... in your network model?

Can you include arbitrary degree distributions ?

Can you include temporary partnerships ?

Can you include multiple partnerships types ?

Can you include multiple stages of infection ?

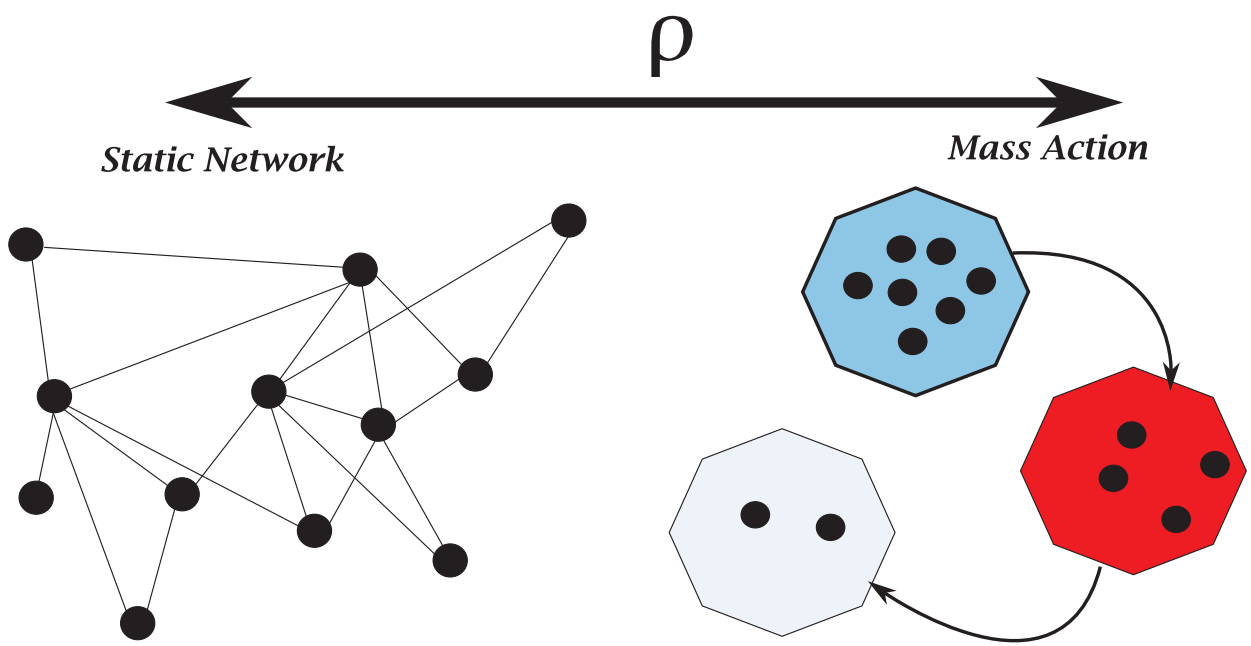
Can you include the dynamics of preferential attachment ?

Transitivity and Clustering

Application to HIV

Conclusion

- NE model is related to a number of standard models that are often used for STIs
- Serial monogamy: $g(x) = x$
- if $g(x) = x$ and $\rho \to \infty$ then we retrieve the standard mass-action SIR model. $\dot{S} = -\beta SI, \dot{I} = \beta SI - \gamma I$



NE model– special cases; rate equations revisited

- In the limit $\rho \to \infty$, reduces to a mass action model

$$M_{SI} \to M_S \frac{M_I}{M}, \quad \dot{\theta} \to -\theta\beta \frac{M_I}{M} = -\theta\beta \sum_k q_k I_k$$

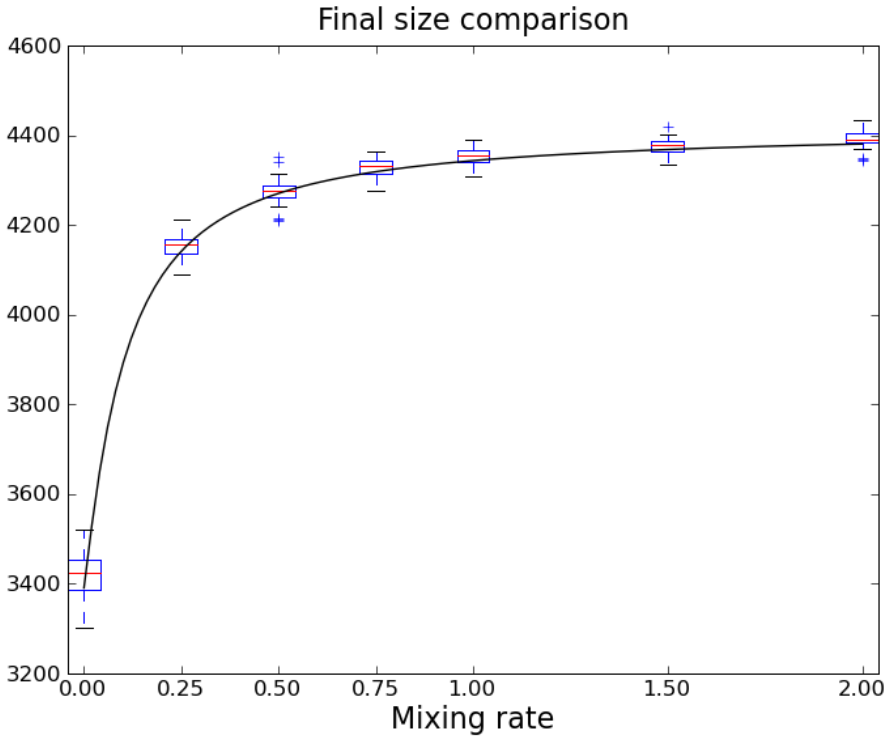
- "What, if anything, do the rate equations correspond to ?"
  - The rate equations exactly correspond to a dynamic network in the limit of large mixing rate.
- This also indicates when the rate equations will be most biased. The difference between $R_0(\rho = 0)$ and $\lim_{\rho\to\infty} R_0$ is greatest when
  - small $\langle k \rangle$ and large β/γ.

Other extensions: What if concurrent degree is not constant?

Introduction
Can you include ... in your network model?
Can you include arbitrary degree distributions ?
Can you include temporary partnerships ?
Can you include multiple partnerships types ?
Can you include multiple stages of infection ?
Can you include the dynamics of preferential attachment ?
Transitivity and Clustering
Application to HIV
Conclusion

- The neighbor-exchange keeps the number of concurrent partners; what if the network dynamics are more realistic ?
- Alternative model: Each node has a unique *preferred* degree k; nodes accumulate new partners at a rate $k\rho$, and each edge was terminated at constant rate ρ
  - The degree at any time is described by a Markov integer jump process
  - The time average degree of a node would be the preferred value– k
  - The degree at a random time would be a Poisson random variable with mean k
- How good an approximation is the NE model to a scenario where the degree is not constant ?
- Is there an exact solution ?

Dynamic nets with non-constant degree sequence



- Poisson DD (2.5), $\beta = 2\gamma$.
- Simulations based on $N = 5000$
- 5 initial infections
- $\beta = 2\gamma$
- ρ from zero to 20γ

Dynamic nets with non-constant degree sequence

Introduction

Can you include ... in your network model?

Can you include arbitrary degree distributions ?

Can you include temporary partnerships ?

Can you include multiple partnerships types ?

Can you include multiple stages of infection ?

Can you include the dynamics of preferential attachment ?

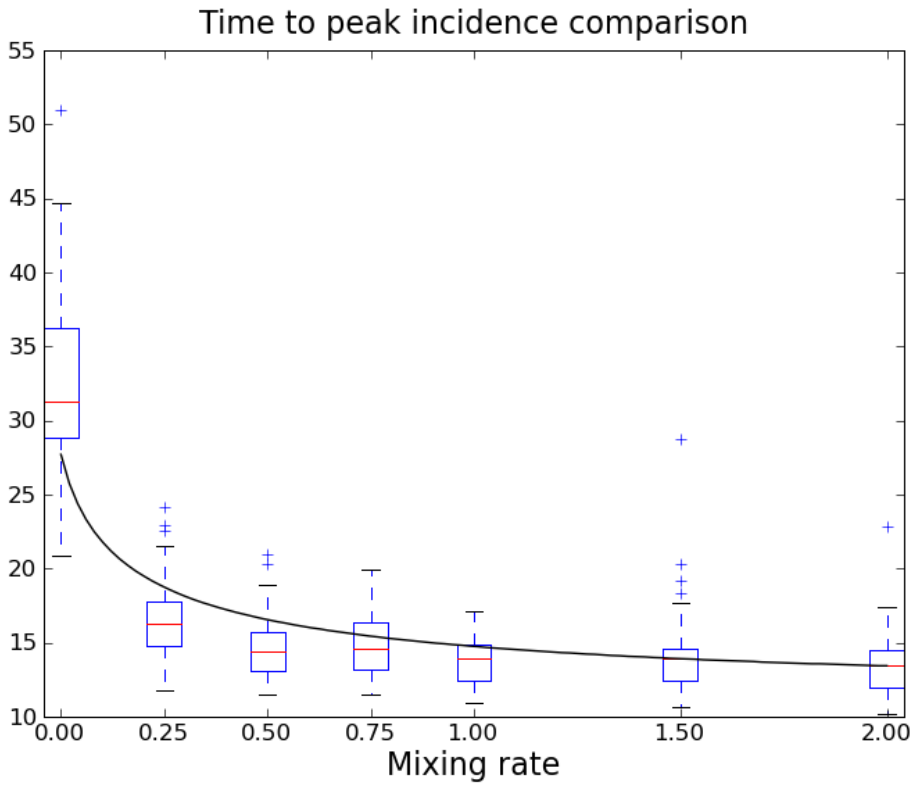
Transitivity and Clustering

Application to HIV

Conclusion

- We define time to peak incidence (TTP) as

$$TTP = \text{argmax}(-\dot{S}(t)) = \text{argmax}(\beta M_{SI}(t))$$

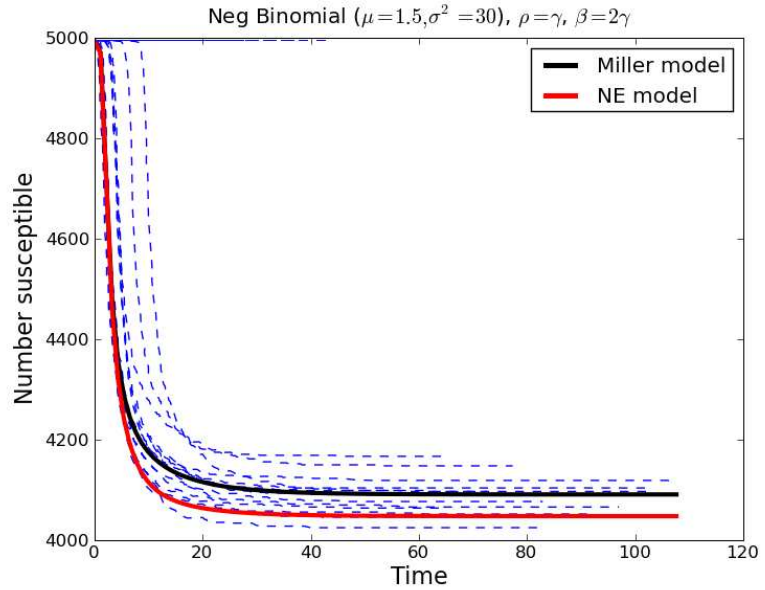


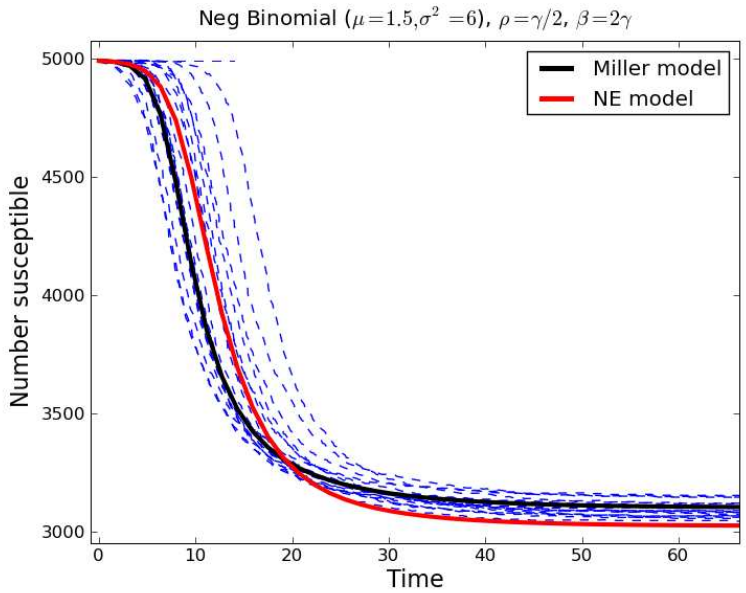
Exact soln's for SIR in nets with non-constant deg. sequence

- Exact solution recently developed by Joel Miller

$$\dot{\theta} = -\beta \Phi_I$$

$$\dot{\Phi}_I = \beta \Phi_I \frac{\Psi_2(\theta)}{\Psi_1(1)} + \rho \Pi_I - \Phi_I(\rho + \beta + \gamma)$$





Can you include multiple partnerships types ?

Introduction
Can you include ... in your network model?
Can you include arbitrary degree distributions ?
Can you include temporary partnerships ?
Can you include multiple partnerships types ?
Can you include multiple stages of infection ?
Can you include the dynamics of preferential attachment ?
Transitivity and Clustering
Application to HIV
Conclusion

What if there are multiple types of risk contact and each type has it's own transmission rates and typical duration ?

$$g(\vec{x}) = \sum_{\vec{d} \in \mathbb{Z}_+^m} P(\vec{d}) \prod x_i^{d_i}$$

$$\dot{M}_{SI}^{(i)} = -M_{SI}^{(i)}(\beta_I^{(i)} + \gamma_I) + \rho(M_S^{(i)} \frac{M_I^{(i)}}{g^{(i)}(1)} - M_{SI}^{(i)}) + \frac{M_{SS}^{(i)} - M_{SI}^{(i)}}{M_S^{(i)}} \sum_j T_j \delta(i,j)$$

- This makes it possible to merge static network models and mass action models; eg partner type i may have $\rho = 0$, while type j may have $\rho = \infty$.

Can you include multiple stages of infection ?

Introduction

Can you include ... in your network model?

Can you include arbitrary degree distributions ?

Can you include temporary partnerships ?

Can you include multiple partnerships types ?

▷ Can you include multiple stages of infection ?

Can you include the dynamics of preferential attachment ?

Transitivity and Clustering

Application to HIV

Conclusion

What if transmission rates are non uniform over the infectious period ?

What if the infectious period is poorly approximated by the exponential distribution ?

In the case of HIV, we are interested in models which have at least two infectious periods: $S \rightarrow$acute infection $\rightarrow$ chronic infection

$$\dot{\theta}^{(i)} = -\beta_I^{(i)}\theta^{(i)}\frac{M_{SI}^{(i)}}{M_S^{(i)}} - \beta_J^{(i)}\theta^{(i)}\frac{M_{SJ}^{(i)}}{M_S^{(i)}}$$

$$\dot{M}_{SJ}^{(i)} = -M_{SJ}^{(i)}(\beta_J^{(i)} + \gamma_J) + M_{SI}^{(i)}\gamma_I - \frac{M_{SJ}^{(i)}}{M_S^{(i)}}\sum_j T_j\delta(i,j)$$

Can you include the dynamics of preferential attachment ?

Introduction
Can you include ... in your network model?
Can you include arbitrary degree distributions ?
Can you include temporary partnerships ?
Can you include multiple partnerships types ?
Can you include multiple stages of infection ?
Can you include the dynamics of preferential attachment ?
Transitivity and Clustering
Application to HIV
Conclusion

What if susceptible individuals preferentially attached to other susceptibles to limit exposure to the disease (*Serosorting*)?

- In Atlanta/Urban seropositives were 2.2× more likely to contact another seropositive.
  - Partnerships between susceptibles and infecteds decay at constant rate; replaced by partnerships between susceptibles and between infecteds.
  - Sorting term : $-\mu M_{SI}$

Introduction
Can you include ... in your network model?
Transitivity and Clustering
Can you include transitivity (clustering) of partnerships?
Clustering and final epidemic size
Comparison of FS predictions
Application to HIV
Conclusion

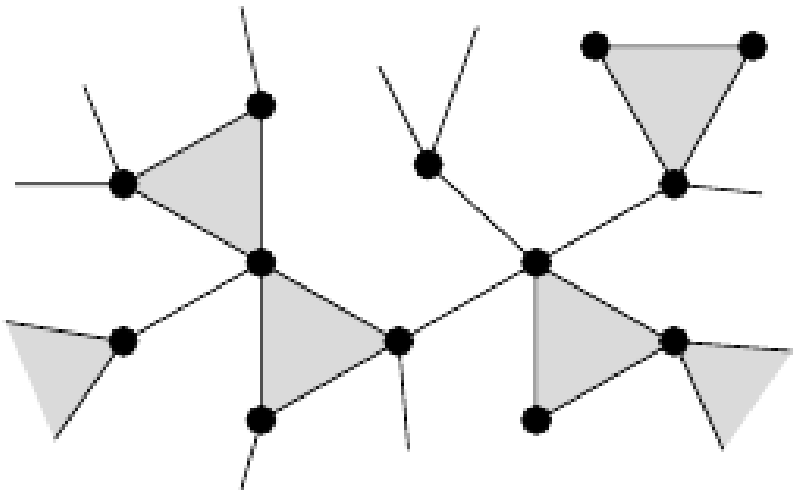
Transitivity and Clustering

Can you include transitivity (clustering) of partnerships?

- Bond percolation theory was recently developed by M Newman and J Miller for CM networks with clustering

$$g(x,y) = \sum_{s,t=0}^{\infty} p_{st} x^s y^t$$

- p_{st} is the probability that a random node is connected to s edges and t 3-cliques



Dynamic PGF model with clustering

Introduction
Can you include ... in your network model?
Transitivity and Clustering
Can you include transitivity (clustering) of partnerships?
Clustering and final epidemic size
Comparison of FS predictions
Application to HIV
Conclusion

- Recently extended this theory to continuous-time SIR dynamics with dynamic PGFs (arXiv:1006.0970)
- Works by introducing variables for the number of three cliques that have i susceptible and j infected

$$n_{30}, n_{21}, n_{20}, n_{12}, n_{11}$$

- This model has 9 equations; can clearly be generalized to CM nets with larger clique sizes;
- The number of equations required for clique size m is $r_m := \binom{m+1}{2} + 3$

Dynamic PGF model with clustering

Our solution is:

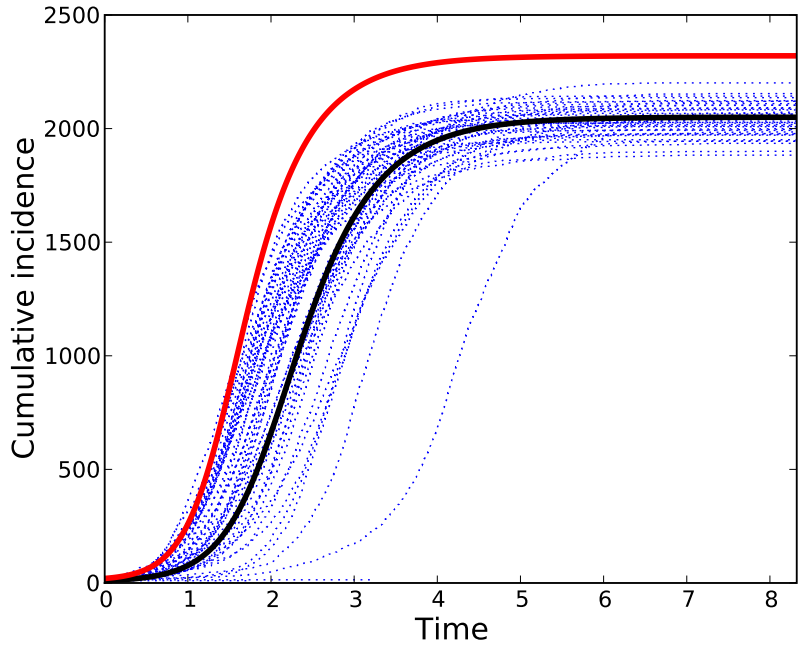
$$\begin{aligned}
\dot{\theta}_l &= -\theta_2 T_2 / M_S \\
\dot{\theta}_t &= -\theta_3 T_3 / \hat{M}_S \\
\dot{M}_{SS} &= -2\frac{M_{SS}}{M_S}\left(T_2\delta_{ll} + T_3\delta_{tl}\right). \\
\dot{n}_{21} &= -(2\beta+\gamma)n_{21} \\
&\quad + \left(T_3\delta_{tt} + T_2\delta_{lt}\right)\left(\frac{3n_{30}}{\hat{M}_S} - \frac{2n_{21}}{\hat{M}_S}\right).
\end{aligned}$$

where we use the derived variables:

$$\begin{aligned}
T_2 &= \beta M_{SI}, \\
T_3 &= \beta(2n_{21} + 2n_{12} + n_{11}), \\
\delta_{ll} &= \theta_2 g_q^{(x)}(1,1), \\
\delta_{lt} &= \theta_3 g_q^{(y)}(1,1), \\
\delta_{tt} &= \theta_3 g_r^{(y)}(1,1), \\
\delta_{tl} &= \theta_2 g_r^{(y)}(1,1).
\end{aligned}$$

Clustering and final epidemic size

- Clustering can noticeably impact the timescale and final size of the epidemic
- This example based on a NB degree distribution
- $N = 5000, I(0) = 10, p_t = 0.9, \beta = 1,$ and $\gamma = 1$.
- For comparison, a trajectory with $p_t = 0$ is shown in red.



The House-Keeling clustering model

Introduction
Can you include ... in your network model?
Transitivity and Clustering
Can you include transitivity (clustering) of partnerships?
Clustering and final epidemic size
Comparison of FS predictions
Application to HIV
Conclusion

Recently House & Keeling (to appear in J Roy Soc Interface) investigated the connection between dyn pgf models and pair approximation.

$$\dot{\theta} = -\theta\beta[SI]/M_S$$

$$[SSI] \approx [SS][SI]\frac{G''(\theta)}{N(G'(\theta))^2}\left((1-\phi) + \phi G'(1)\frac{[SI]}{\theta G'(\theta) M_I}\right).$$

We will often compare our results to the HK model; *but not a fair comparison*

The HK model is premised on a different mechanism for introducing clustering; each possible 3-clique exists with indep. probability ϕ

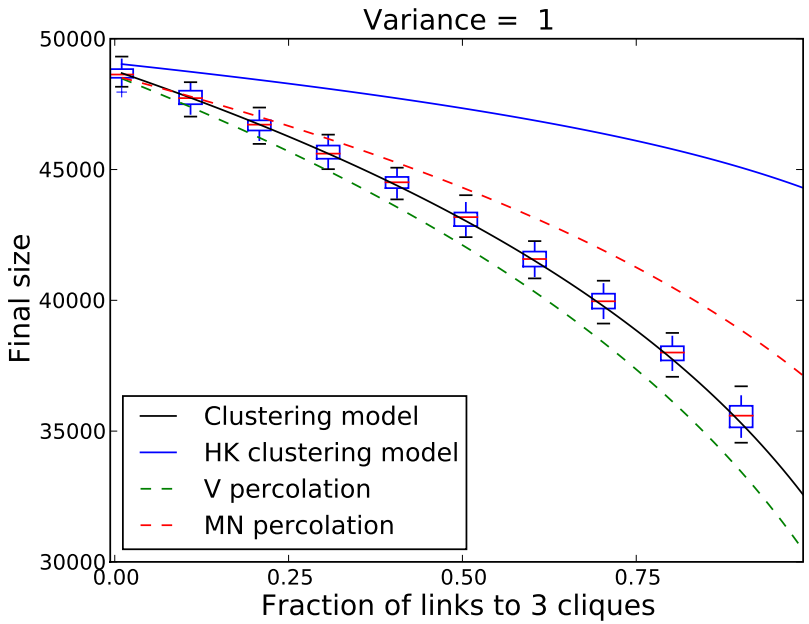
MN percolation is potentially biased

Introduction
Can you include ... in your network model?
Transitivity and Clustering
Can you include transitivity (clustering) of partnerships?
Clustering and final epidemic size
Comparison of FS predictions
Application to HIV
Conclusion

- The MN percolation is based on the assumption that transmissibility per edge is constant
- This assumption is false when the infectious period is not constant (eg if an exponential rv)– $\tau = 1 - e^{-\beta t}$
- Bias of BP final size is negligible when $\phi = 0$ (Kenah & Robins, Durrett)
  - although R_0 and epidemic thresholds may be substantially biased even when $\phi = 0$
- We find that when $\phi > 0$ and the infectious period is not constant, the MN percolation solution for final size is biased
- Recently F. Ball et al. presented bond percolations for final size in clustered networks that correctly take variable infectious periods into account (Math. Biosciences 2009)

Comparison of FS predictions

- NB degree distribution
- The boxplots illustrate the 90% confidence interval from 50 stochastic simulations on networks with 5000 nodes.
- $\beta = \gamma = 1$, and both the mean and variance of the degree distribution is 2.
- The proposed clustering model correctly predicts final size
- MN percolation and the HK model always over estimate final size



Why does MN percolation over-estimate ?

Introduction
Can you include ... in your network model?
Transitivity and Clustering
Can you include transitivity (clustering) of partnerships?
Clustering and final epidemic size
Comparison of FS predictions
Application to HIV
Conclusion

MN percolation is premised on calculating the number of secondary infecteds– R– following a single introduction in a 3-clique

- one secondary infection: $\bar{\alpha}_1 := 2\bar{\tau}(1-\bar{\tau})^2$,
- two secondary infections: $\bar{\alpha}_2 := \bar{\tau}^2 + 2\bar{\tau}^2(1-\bar{\tau})$.

$\bar{R} = 2\bar{\alpha_2} + \bar{\alpha}_1$

Why does MN percolation over-estimate ?

Introduction
Can you include ... in your network model?
Transitivity and Clustering
Can you include transitivity (clustering) of partnerships?
Clustering and final epidemic size
Comparison of FS predictions
Application to HIV
Conclusion

Probabilities depend on infectious period of the initial case.

- One secondary infection:

$$\begin{aligned}\alpha_1 &:= \int_0^\infty \gamma e^{-\gamma t}\left(2(1-e^{-\beta t})e^{-\beta t}(1-\bar{\tau})\right)\mathrm{d}t \\ &= 2(1-\bar{\tau})^2 - 2\frac{\gamma}{2\beta+\gamma}(1-\bar{\tau})\end{aligned}$$

- Two secondary infections:

$$\begin{aligned}\alpha_2 &:= \int_0^\infty \gamma e^{-\gamma t}\left((1-e^{-\beta t})^2 + 2(1-e^{-\beta t})e^{-\beta t}\bar{\tau}\right)\mathrm{d}t \\ &= 1 + (1-2\bar{\tau})\frac{\gamma}{2\beta+\gamma} + 2(1-\bar{\tau})(\bar{\tau}-1)\end{aligned}$$

Given $R = 2\alpha_2 + \alpha_1$, it is straightforward to show $R < \bar{R}$

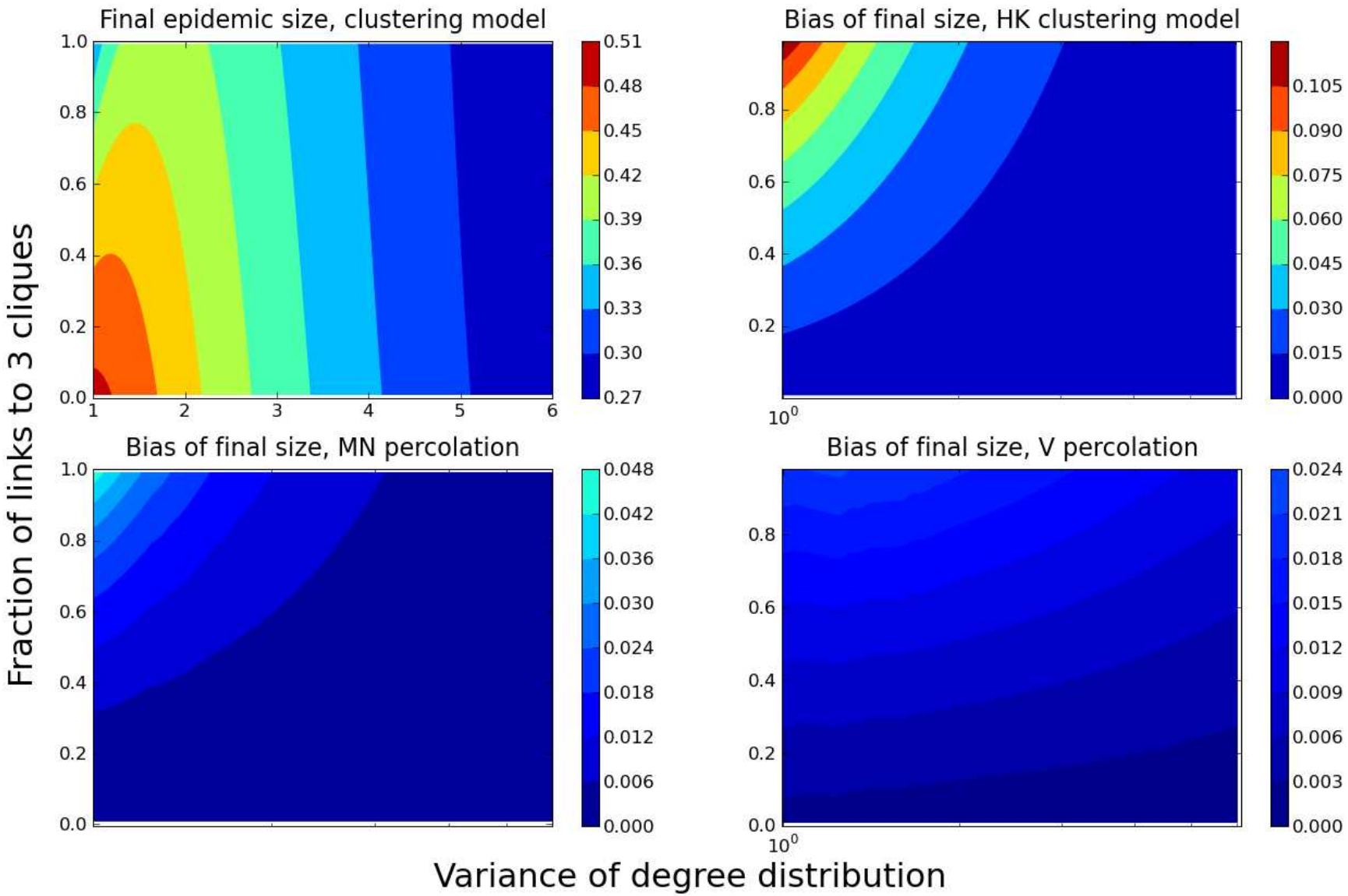
final size = $f(\phi, \sigma^2)$

- Goal is to elucidate the interaction of σ^2 and ϕ in determining epidemic size and timescale
- We choose DD to interpolate over a range of σ^2 while holding $\langle k \rangle$ and ϕ constant
- Edges (clustered or not) occur in pairs

$$g_{nb}(x; r, p) = \left(\frac{p}{1 - (1-p)x} \right)^r .$$

$$g(x, y) = g_{nb}((1 - p_t)x^2 + p_t y).$$

Characterization of final size

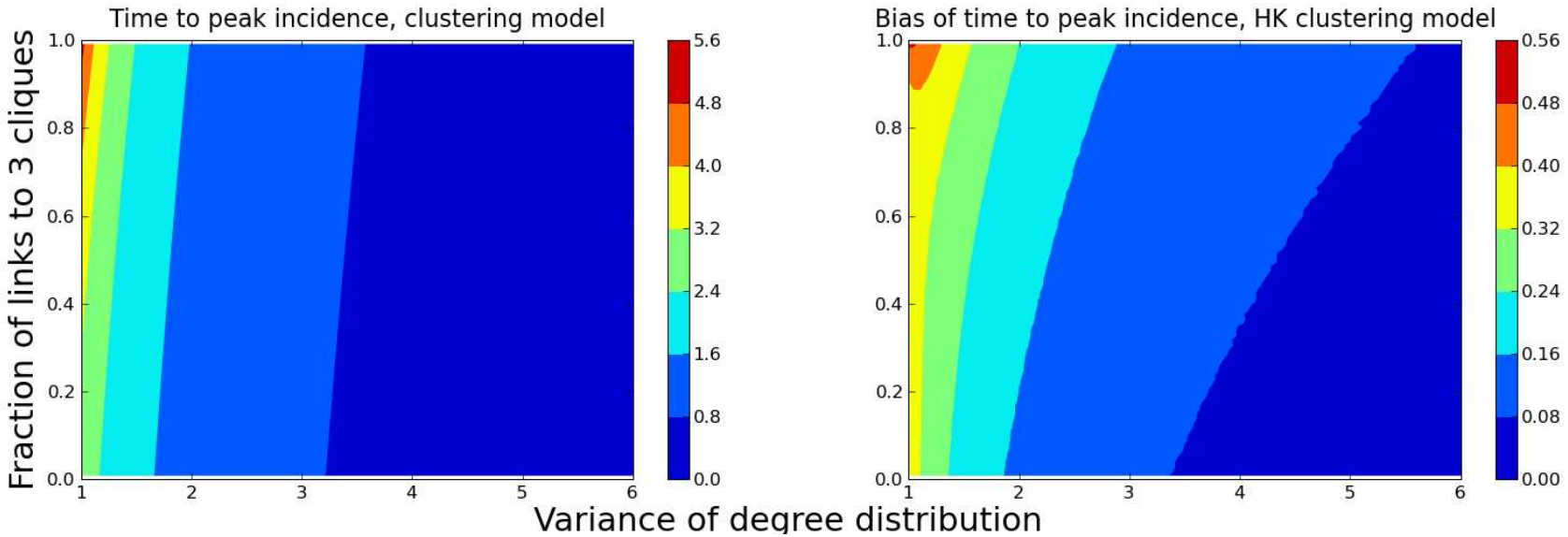


Variance of the DD and clustering

Introduction
Can you include ... in your network model?
Transitivity and Clustering
Can you include transitivity (clustering) of partnerships?
Clustering and final epidemic size
Comparison of FS predictions
Application to HIV
Conclusion

- Clustering always decreases final size
- Standard theory predicts that R_0 is strictly increasing with the variance of the DD
- Conversely, the final epidemic size is *usually* decreasing with variance (holding mean constant)
- Clustering attenuates this relationship (eg FS may increase or decrease with variance)

Characterization of timescale

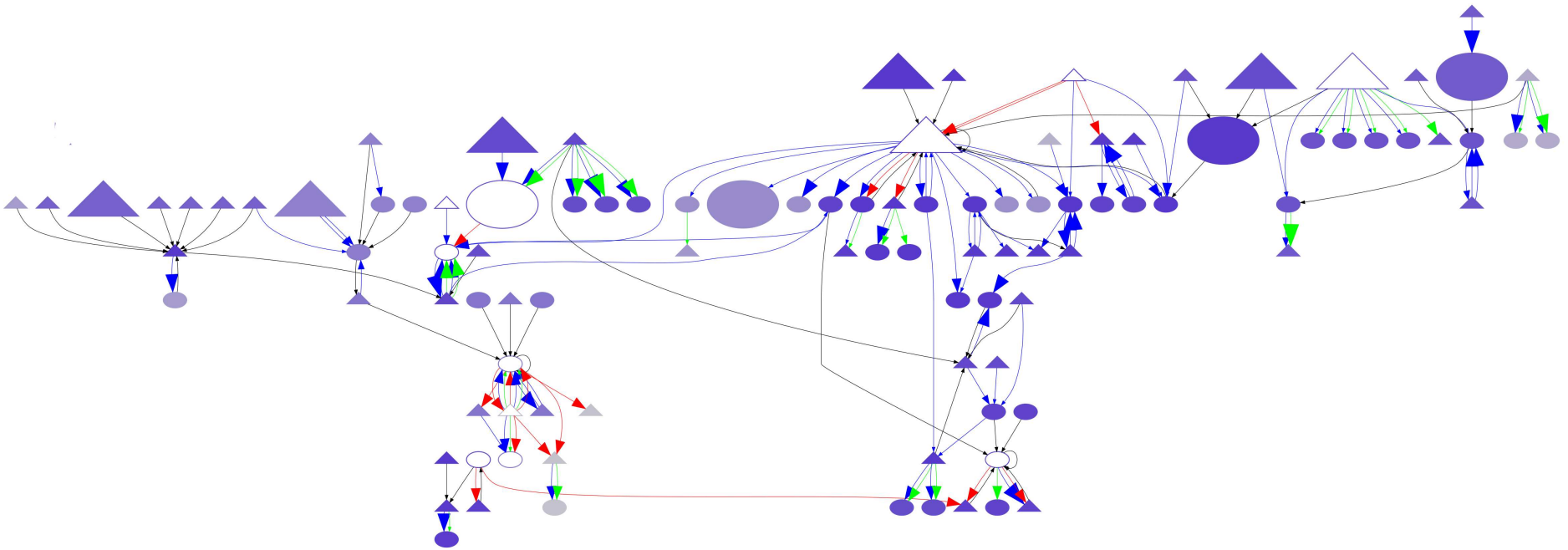


$\beta = \gamma = 1.$

Introduction
Can you include ... in your network model?
Transitivity and Clustering
Application to HIV
Atlanta/Urban
Compartmentalization
Degree distributions
Parameter priors
Computational experiments
Predicted epidemic prevalence
Fraction of transmissions made by each risk category
Why are IDUs important ?
IDUs are central
Estimating serosorting rates in dynamic networks
Conclusion

Application to HIV

Atlanta/Urban



- Atlanta, GA; 225 "at-risk" individuals; HIV Prevalence = 13.3% ; chain-link design
- How can this behavioral data be used to accurately project epidemic dynamics?
- Can our models not only reproduce the observed prevalence, but also the pattern of infection?

Compartmentalization

Introduction
Can you include ... in your network model?
Transitivity and Clustering
Application to HIV
Atlanta/Urban
▷ Compartmentalization
Degree distributions
Parameter priors
Computational experiments
Predicted epidemic prevalence
Fraction of transmissions made by each risk category
Why are IDUs important ?
IDUs are central
Estimating serosorting rates in dynamic networks
Conclusion

Three ways to compartmentalize a SIR model

1. Contact types (sex, drugs, aerosols etc.)
2. Node types (age, gender, race etc.)
3. Stages of infection (Incubating, Latent, Acute, Chronic, In-treatment etc.)

Realistic modeling of HIV requires particular attention to contact-type & and stages of infection.

- 3 Contact types: MSM (anal sex), IDU, Heterosexual (vaginal sex)
  - $\theta \Rightarrow \theta_A, \theta_I, \theta_V$
- 4 stages: Susceptible, Acute, Chronic, and Recovered
  - $$M_{SI} \Rightarrow M_{SI1,A}, M_{SI1,I}, M_{SI1,V}, M_{SI2,A}, M_{SI2,I}, M_{SI2,V}$$

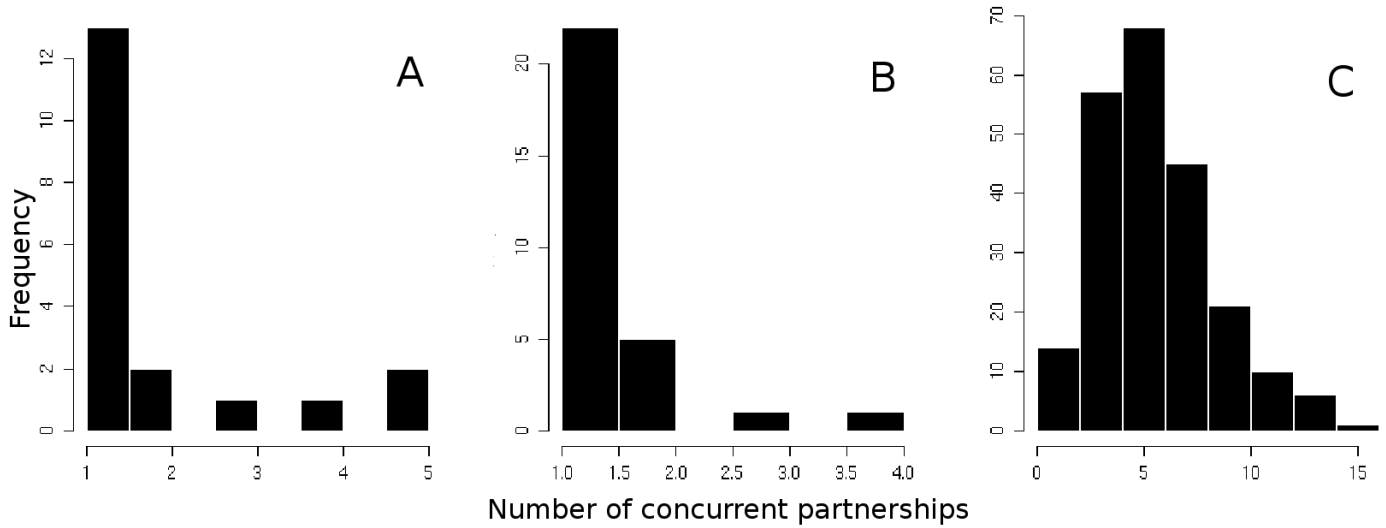
Compartmentalization necessarily leads to more complex equations.

$$\frac{d}{dt}M_{SI1,A} = -(r_{1,A} + \mu_1)M_{SI1,A}$$
$$+\text{Mixing Term} + \text{Sorting Term}$$
$$+(-\dot{S}_{I1,A})(\delta_{I1,A}(S) - \delta_{I1,A}(I1, A)/M_A$$
$$+(-\dot{S}_{I2,A})(\delta_{I2,A}(S) - \delta_{I2,A}(I1, A))/M_A$$
$$+(-\dot{S}_{I1,I})(\delta_{I1,I}(S) - \delta_{I1,A}(I1, I)/M_I$$
$$+(-\dot{S}_{I2,I})(\delta_{I2,I}(S) - \delta_{I2,A}(I1, I))/M_I$$
$$+(-\dot{S}_{I1,V})(\delta_{I1,V}(S) - \delta_{I1,A}(I1, V)/M_V$$
$$+(-\dot{S}_{I2,V})(\delta_{I2,V}(S) - \delta_{I2,A}(I1, V))/M_V$$

$$\frac{d}{dt}\theta_A = -\theta_A r_{2,A} M_{SI2,A}/M_{S,A} + r_{1,A} M_{SI1,A}/M_{S,A}$$

Degree distributions

$$g(x_A, x_I, x_V) = \sum_{ego \in \mathcal{S}} w(ego) x_A^{d_A(ego)} x_I^{d_I(ego)} x_V^{d_V(ego)} / \sum_{ego \in \mathcal{S}} w(ego)$$



Anal: Exponential, 0.127; IDU: Exponential, 0.118; Vag: Poisson, 5.08

Parameter priors

- Acute⇒ Chronic: Once per 90 days
- Chronic⇒ Recovered: Once per 10 years
- Contact rates: 116 MSM, 112 IDU, 111 Heterosexual per thousand per day
- Mixing rates: 3.1 MSM, 1.1 IDU, 1.8 Heterosexual per thousand per day
- Transmission probabilities
  - MSM. Leynaert et al., American Journal of Epidemiology, 148, 1, 1998. n = 499
    - Acute: 18.3%
    - Chronic: 1.4%
  - IDU. Kaplan et al., Interfaces 23, 1993
    - Acute: 8.8 %
    - Chronic: 0.67%
  - Heterosexual. Leynaert et al.
    - Acute: 0.92%
    - Chronic: 0.07%

Computational experiments

Introduction
Can you include ... in your network model?
Transitivity and Clustering
Application to HIV
Atlanta/Urban
Compartmentalization
Degree distributions
Parameter priors
▷ Computational experiments
Predicted epidemic prevalence
Fraction of transmissions made by each risk category
Why are IDUs important ?
IDUs are central
Estimating serosorting rates in dynamic networks
Conclusion

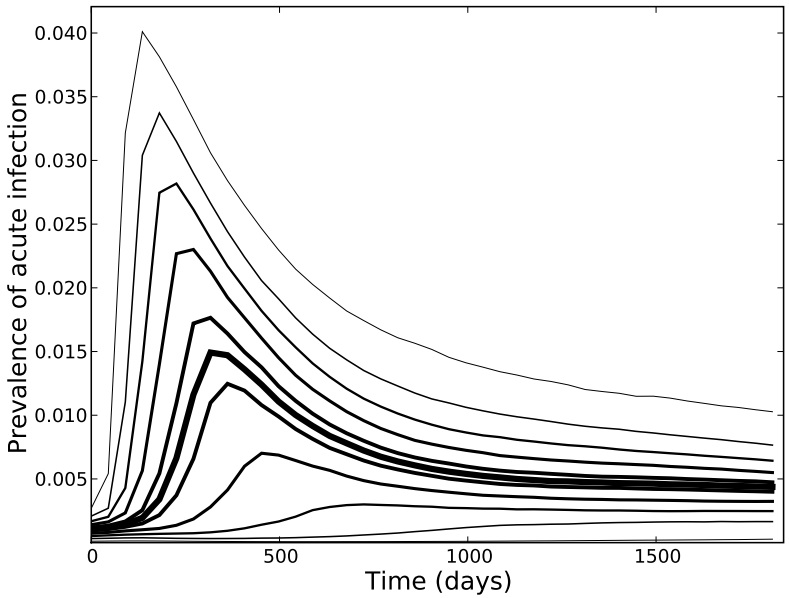
1. Draw a set of parameters from prior distribution
2. Integrate MT NE HIV model
3. Repeat

Parm	Mean	SD
T_{A1}	0.183	0.083
T_{A2}	0.014	0.0102
T_{I1}	0.088	0.088
T_{I2}	0.0067	0.0067
T_{V1}	0.0092	.0013
T_{V2}	0.0007	0.0001

$\epsilon \sim \text{Norm}(10^{-3}, 10^{-4})$

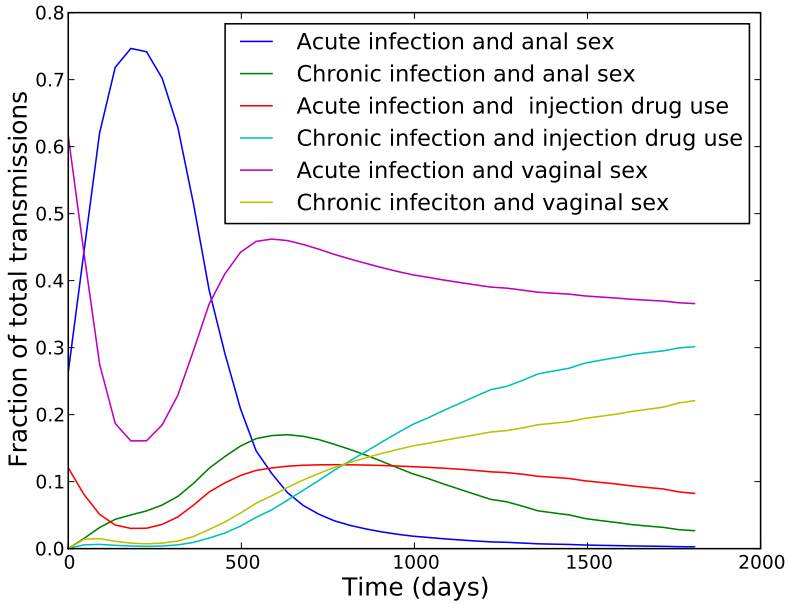
Sorting rate = Mixing rate $\times(0, 1/4, 1/2, 1, 2)$

Predicted epidemic prevalence



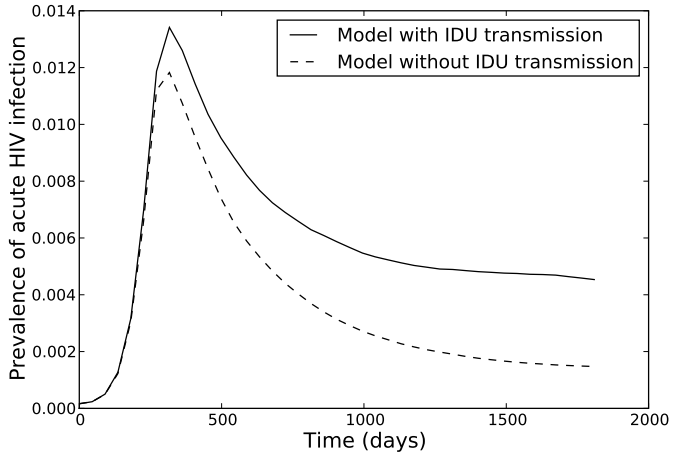
Predicted prevalence of acute HIV infection over five years. The thickest line shows the median prevalence from 4000 model runs at a given time point. Each trajectory is based on a distinct set of parameters draw independently from the set of prior distributions. The thinnest lines show 90% confidence intervals. Intermediate lines show quantiles in increments of 10%.

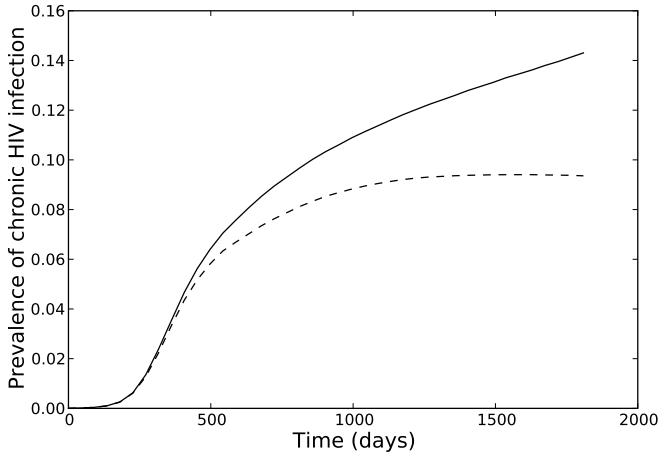
Fraction of transmissions made by each risk category

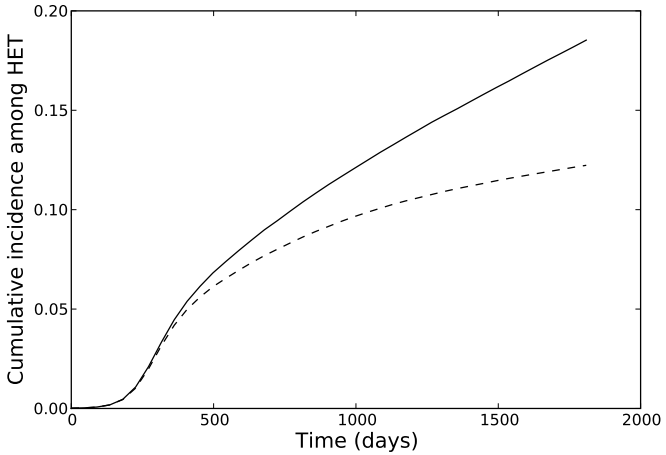


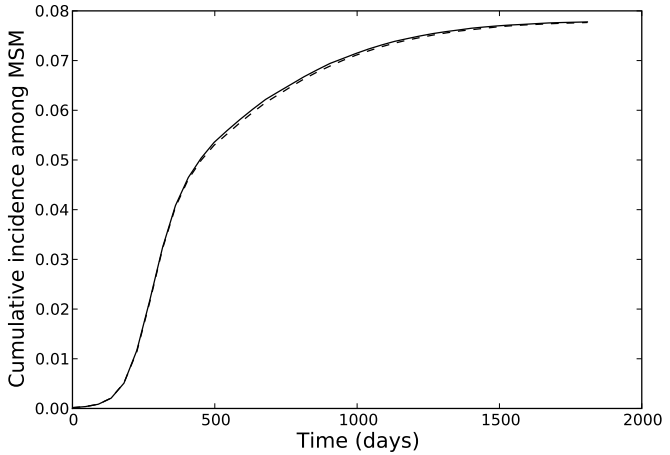
The predicted fraction of transmission events that are due to anal sex, vaginal sex, and injection drug use over five years. These fractions are further categorized by whether transmission was committed by an acute or chronically infected individual.

Why are IDUs important ?









Why are IDUs important ?

Introduction
Can you include ... in your network model?
Transitivity and Clustering
Application to HIV
Atlanta/Urban
Compartmentalization
Degree distributions
Parameter priors
Computational experiments
Predicted epidemic prevalence
Fraction of transmissions made by each risk category
▷ Why are IDUs important ?
IDUs are central
Estimating serosorting rates in dynamic networks
Conclusion

- Prevalence of acute and chronic infections (top) and cumulative infections (bottom) over five years.
- Cumulative infections are sub-categorized by primary risk factor: vaginal sex (HET) bottom left and anal-sex (MSM) bottom right.
- Trajectories are shown both for the standard model (solid line) and a hypothetical model in which all transmissions via injection drug use are removed (dashed line).

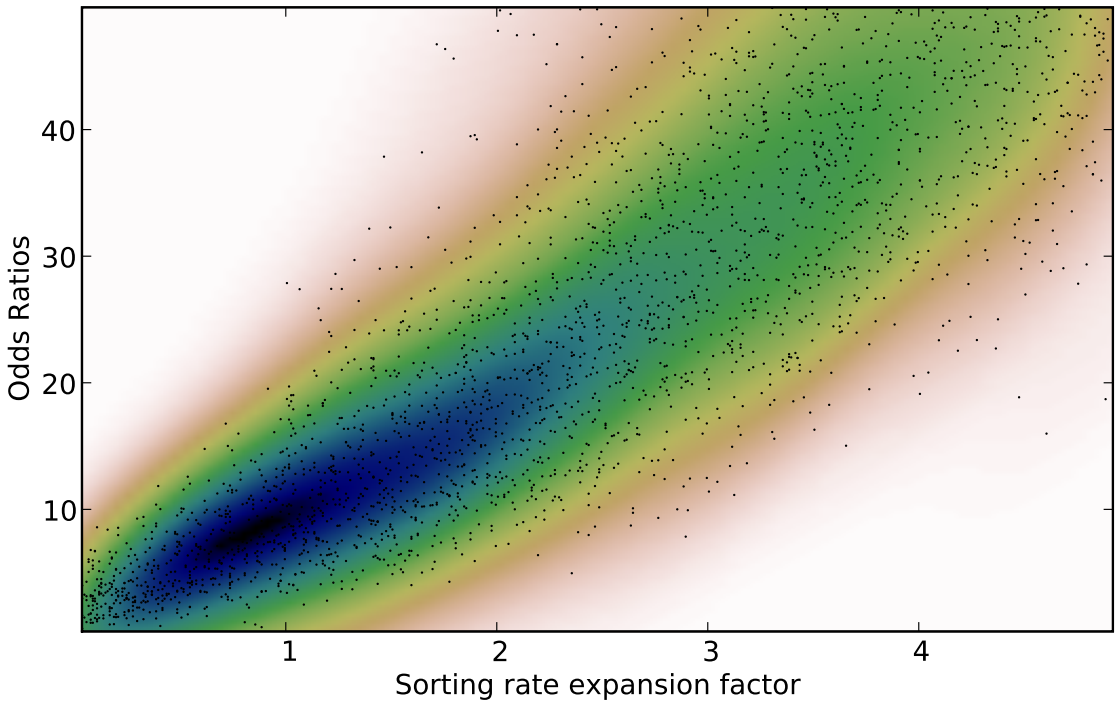
IDUs are central

Introduction
Can you include ... in your network model?
Transitivity and Clustering
Application to HIV
Atlanta/Urban
Compartmentalization
Degree distributions
Parameter priors
Computational experiments
Predicted epidemic prevalence
Fraction of transmissions made by each risk category
Why are IDUs important ?
▷ IDUs are central
Estimating serosorting rates in dynamic networks
Conclusion

- Betweenness centrality is a measure of how many shortest paths between pairs of individuals route through a particular individual
- Individuals in the Atlanta Urban network with at least one IDU contact have an average betweenness centrality of 0.0058 while non-IDUs have an average betweenness centrality of 0.0024.

Estimating serosorting rates in dynamic networks

The odds of having an infected partner given that the node is susceptible versus the ratio of the sorting rate to the neighbor exchange rate.



Introduction
Can you include ... in your network model?
Transitivity and Clustering
Application to HIV
▷ Conclusion
Thanks

Conclusion

What else can you include in the network model ?

Introduction
Can you include ... in your network model?
Transitivity and Clustering
Application to HIV
Conclusion
Thanks

- Growing networks with birth and death (C Kamp,arXiv:0912.4189)
- J Miller & E Volz in progress:
  - Networks with directed edges
  - or, a mixture of directed and undirected edges
  - "Dormant" edges
  - Seasonal effects (periodic transmission rates)
  - Heterogeneity of infectiousness and susceptibility
  - Vaccination both before and during an epidemic
  - Co-circulating epidemics conferring immunity

What is difficult or impossible to include in the network model?

Introduction
Can you include ... in your network model?
Transitivity and Clustering
Application to HIV
Conclusion
Thanks

Dynamic PGFS don't work whenever λ_k is not proportional to k

- ☐ Recovery to a susceptible state
- ☐ Contact tracing
- ☐ Co-circulating epidemics with partial immunity
- ☐ Behavioral adaptation in response to infected neighbors
- ☐ Spatial structure (eg lattices)

Thanks

Introduction
Can you include ... in your network model?
Transitivity and Clustering
Application to HIV
Conclusion
▷ Thanks

- Lauren Ancel Meyers, Dept of Integrative Biol., University of Texas–Austin
- Alison Galvani, Dept of Epid., Yale
- Joel Miller, Dept of Epid., Harvard
- Simon Frost, Dept of Vet Med, Cambridge
- Richard Rothenberg, School of Med, Georgia State University