Differential Equation and Agent-Based Models in Epidemiology

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Outline

- Modeling problem
- Differential equation vs. agent-based models
- Differential equation models
- Differential equation model example
- Agent-based models
- Social networks
- Agent-based model example
- Conclusions

Problem

- Accurate modeling of the propagation of a disease epidemic
- Accurate models essential for mitigating bioterrorist attacks
- Accurate portrayal of the disease propagation necessary to formulate an effective response
- Larger problem of diffusion
  - Similar to many other social diffusive problems
  - Diffusion of ideas, rumors, financial panic, etc.
- Two main types of models of epidemics
  - Differential equation (DE)
  - Agent-based (AB)

Problem

- Goal is to determine best response to an epidemic
  - Mass vaccination
  - Targeted vaccination
  - Quarantine
- Focus on smallpox

Smallpox

- Acute, highly contagious viral disease
- 3 stages (or 4)
  - Incubation
  - Prodromal
  - Pox
- No consensus on parameters of disease model
- Eradicated in 1979 by World Health Organization campaign
  - Mass vaccination somewhat effective but did not entirely eradicate the disease
  - Traced vaccination strategy successfully eradicated the disease

Smallpox

- Concern that smallpox could be used in a terrorist attack
- U.S. government has stockpiled 300 million vaccines for smallpox
- 2002 CDC response
  - Based on previous W.H.O. successful scheme
  - Traced vaccination and quarantine of symptomatic smallpox cases
  - More massive vaccination if cases does not drop off after two or three generations
- Is this the best response?

Differential Equation vs. Agent-based Models

Differential Equation

- Highly aggregate
- Broad boundary
- Perfect mixing assumption
- Few number of parameters
- Computationally reasonable
- Continuous time

Agent-based

- Highly disaggregate
- Narrow boundary
- Heterogeneity in agent attributes
- Large number of parameters
- Computationally intensive
- Discrete time

Spectrum of Model Characteristics

- DE and AB models generally thought in terms of previous listed characteristics
- However, the models often contain characteristics of both
- Aggregation
  - Disaggregate DE models with many components
  - Aggregate AB models with agents representing multiple people
- DE models can "mimic" heterogeneity by setting parameters in a certain manner (e.g., transmission rate)
- DE/AB hybrid models possible

DE Models of Epidemics

- Usually highly aggregate
- Model large populations easily
- Often result in systems of nonlinear equations that must be solved numerically
- In general, most appropriate when a wide range of feedback is necessary
- In general, less ideal than AB when social interaction network important to model

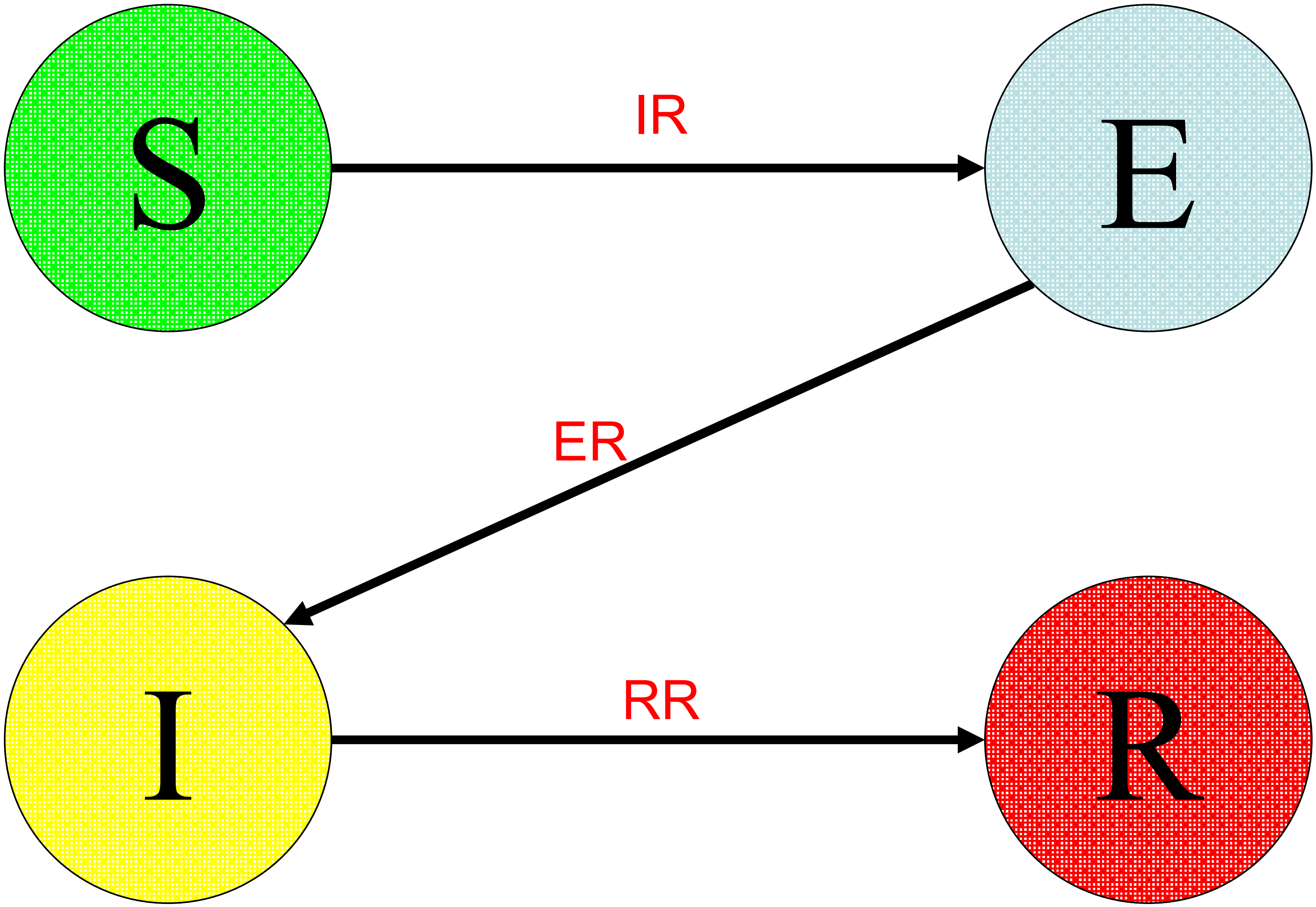
SEIR Model

- Simple, lumped nonlinear DE model
- All members belong to four basic states
- Several simplifying assumptions
  - Perfect mixing/homogeneity within each state
  - Mean field aggregation
  - …
- Applied to successfully model many diseases
- Additional states often included
  - More complex disease life-cycles
  - Add more heterogeity
  - Birth, death

States of SEIR Model

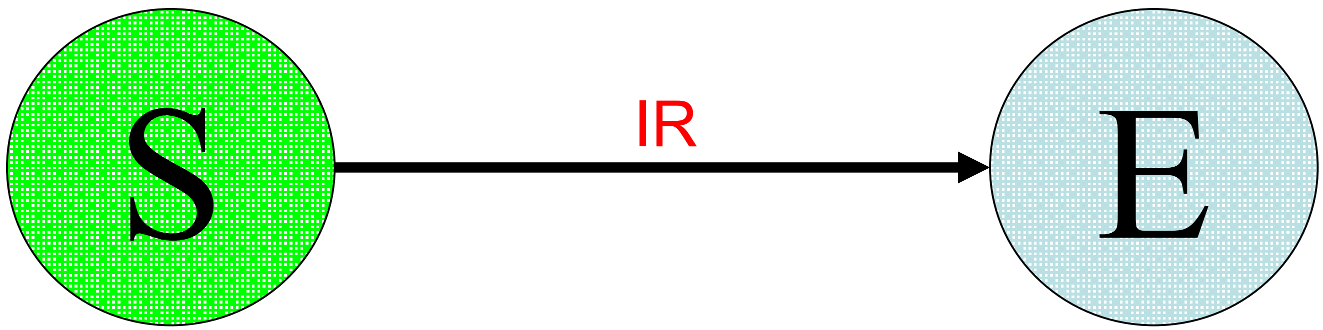
- Susceptible (S)
  - Unexposed portion of the population
  - Has not entered E, I, or R states
- Exposed (E)
  - Contagious
  - Not symptomatic
- Infected (I)
  - Contagious
  - Symptomatic
- Recovered/Dead (R)
  - Recovered assumed to have everlasting immunity

States of SEIR Model



Infection Rate (IR)

- Rate at which new cases of the disease are generated by contact with E and I

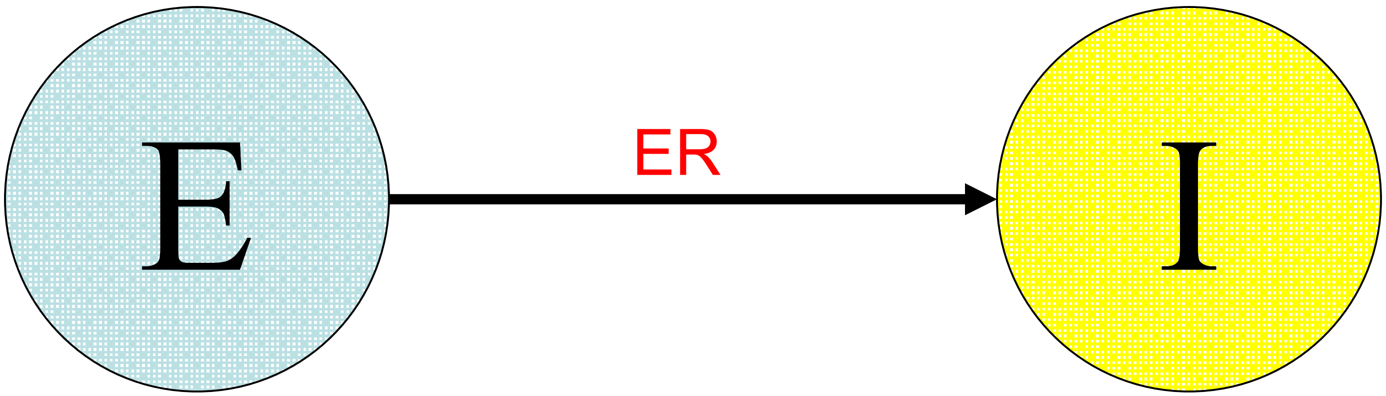


$$IR = \left(c_{ES} i_{ES} E + c_{IS} i_{IS} I\right) \frac{S}{N}$$

c_{ES} – contact frequency between E, S
i_{ES} – infectivity of state E
E – number of people in state E
N – population size

Emergence Rate (ER)

- Rate at which asymptomatic, exposed individuals become symptomatic



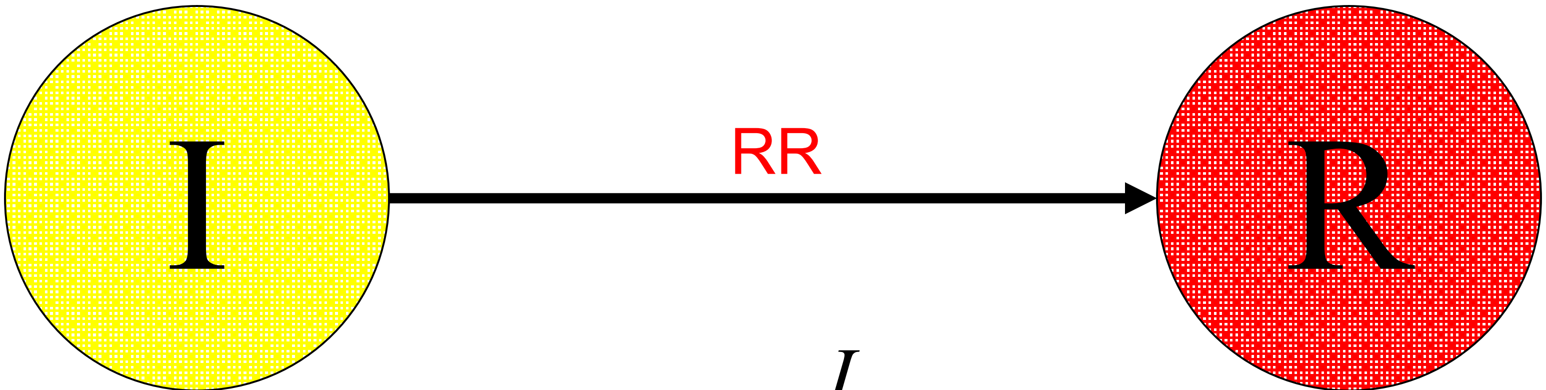
$$ER = \frac{E}{\varepsilon}$$

E – number of people in state E

ε – incubation time

Recovery Rate (RR)

- Rate at which symptomatic individuals recover or die

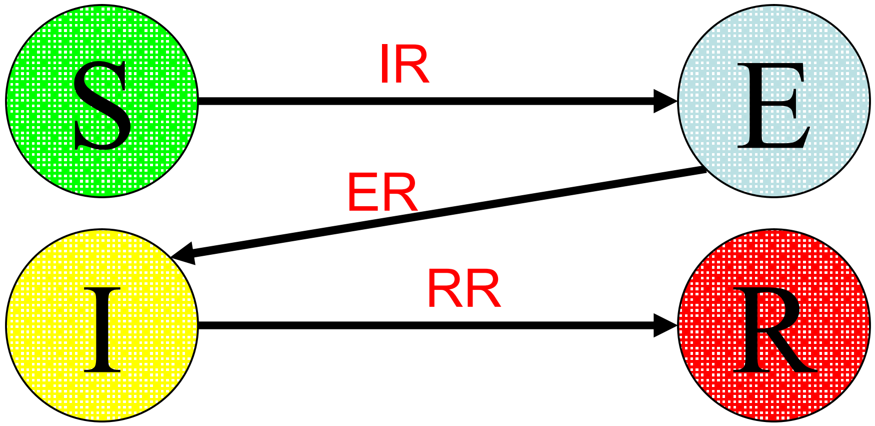


$$RR = \frac{I}{\delta}$$

I – number of people in state I

δ – duration of disease

SEIR: System of Differential Equations



$$\frac{dS}{dt} = -IR = -\left(c_{ES} i_{ES} E + c_{IS} i_{IS} I\right)\frac{S}{N}$$

$$\frac{dE}{dt} = IR - ER = \left(c_{ES} i_{ES} E + c_{IS} i_{IS} I\right)\frac{S}{N} - \frac{E}{\varepsilon}$$

$$\frac{dI}{dt} = ER - RR = \frac{E}{\varepsilon} - \frac{I}{\delta}$$

$$\frac{dR}{dt} = RR = \frac{I}{\delta}$$

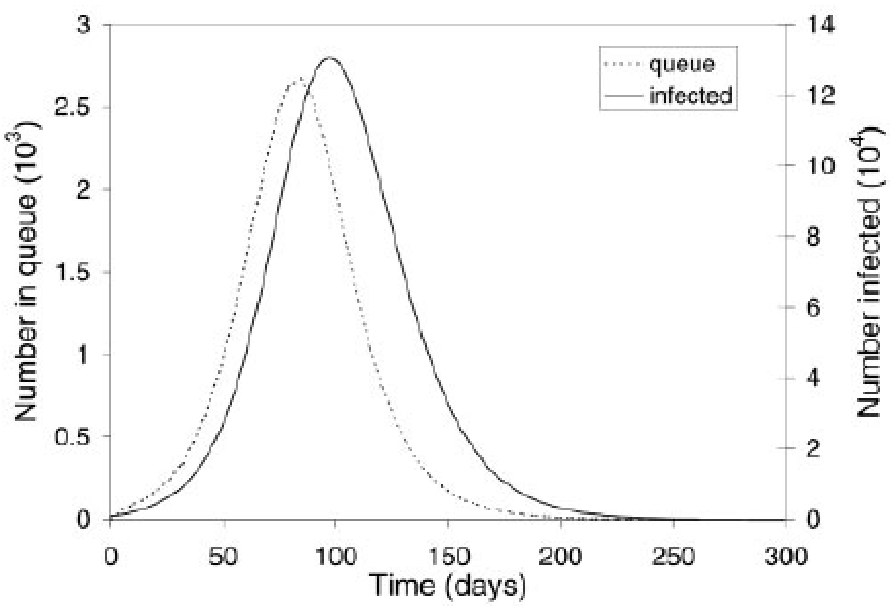
DE Model Example: Kaplan, et al.

- SEIRlike model by Kaplan, et al. (4 disease stages)
  - Asymptomatic, noninfectious, vaccine sensitive
  - Asymptomatic, noninfectious, vaccine insensitive
  - Asymptomatic, infectious
  - Symptomatic, isolated
- Modeled smallpox epidemic and response
  - Mass vaccination
  - Traced vaccination
- Additional States
  - Death
  - Queues, etc.

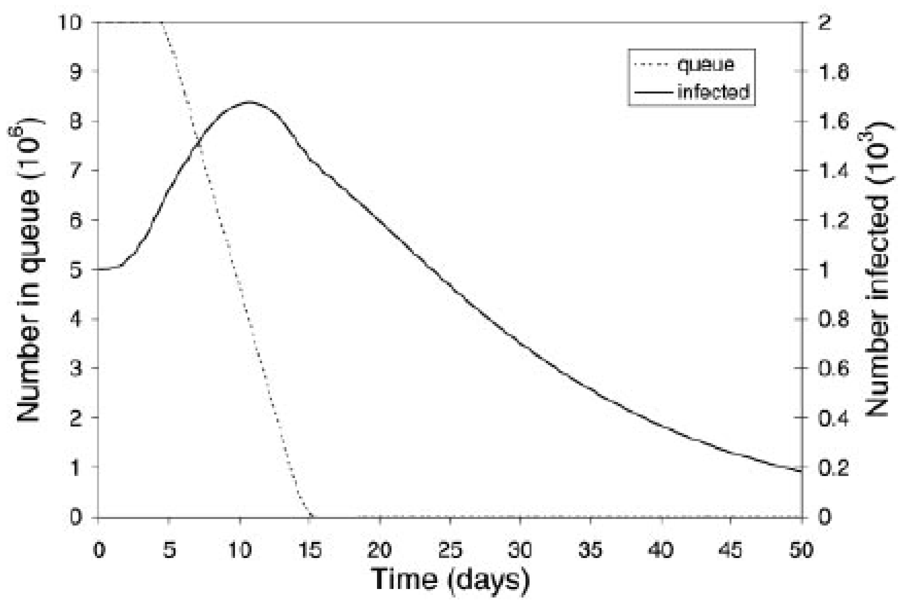
Kaplan, et al.: Perfect Mixing

- As with SEIR model, assumes perfect mixing within states
- Recognize not accurate model of population interaction
- Claim perfect mixing leads to larger epidemics than nonrandom mixing
- Argue control strategy needs to handle this worst case
- Strategies that work in worst case should work in best

Kaplan, et al.: Results

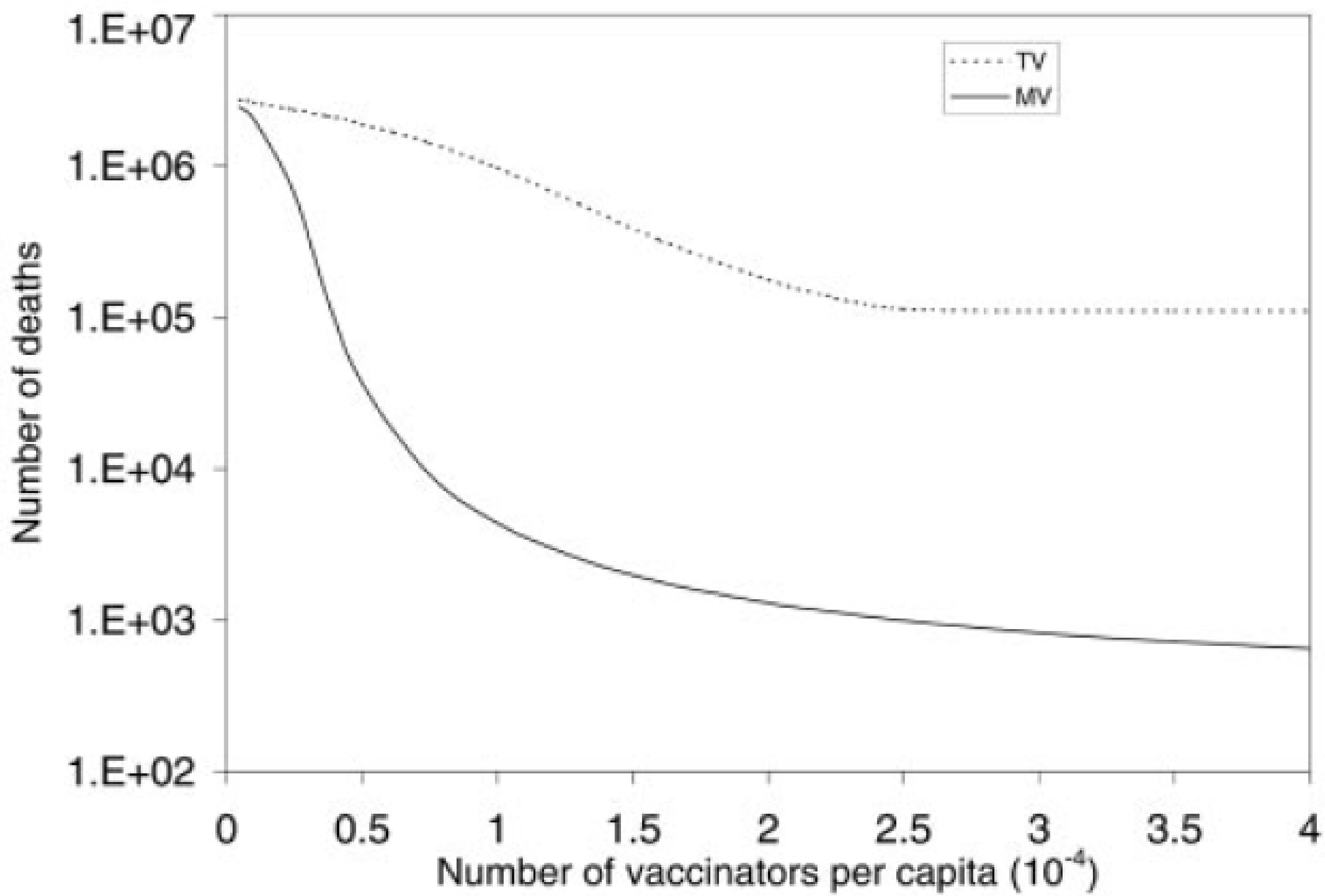


Targeted



Mass

Kaplan, et al.: Results



Kaplan, et al.: Conclusions

- Mass vaccination preferable to traced vaccination
  - Fewer deaths
  - Shorter life of epidemic
- CDC policy of traced vaccination, switching to mass vaccination when necessary costly
- CDC should use mass vaccination immediately as a response to smallpox attack in urban areas instead of traced vaccination

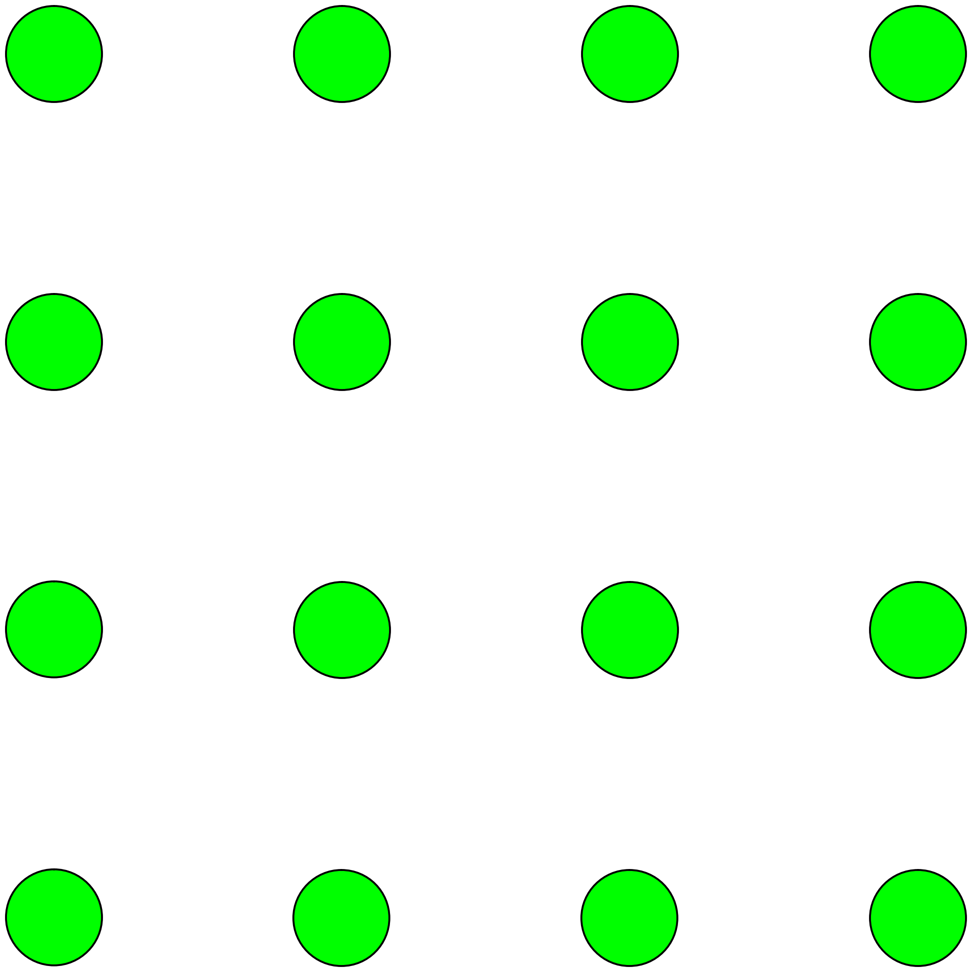
Agent-based Epidemic Models

- Usually highly disaggregate
- Expensive computationally
  - Hard to model large populations
  - Hard to do sensitivity analysis
- Many parameters obtained from distributions
- Most appropriate when epidemic depend greatly on heterogeneity and stochastic events
- More ideal than DE Models when social interaction network important
- Social networks extremely important to AB
  - Model people's interactions
  - Model flow of people through locations

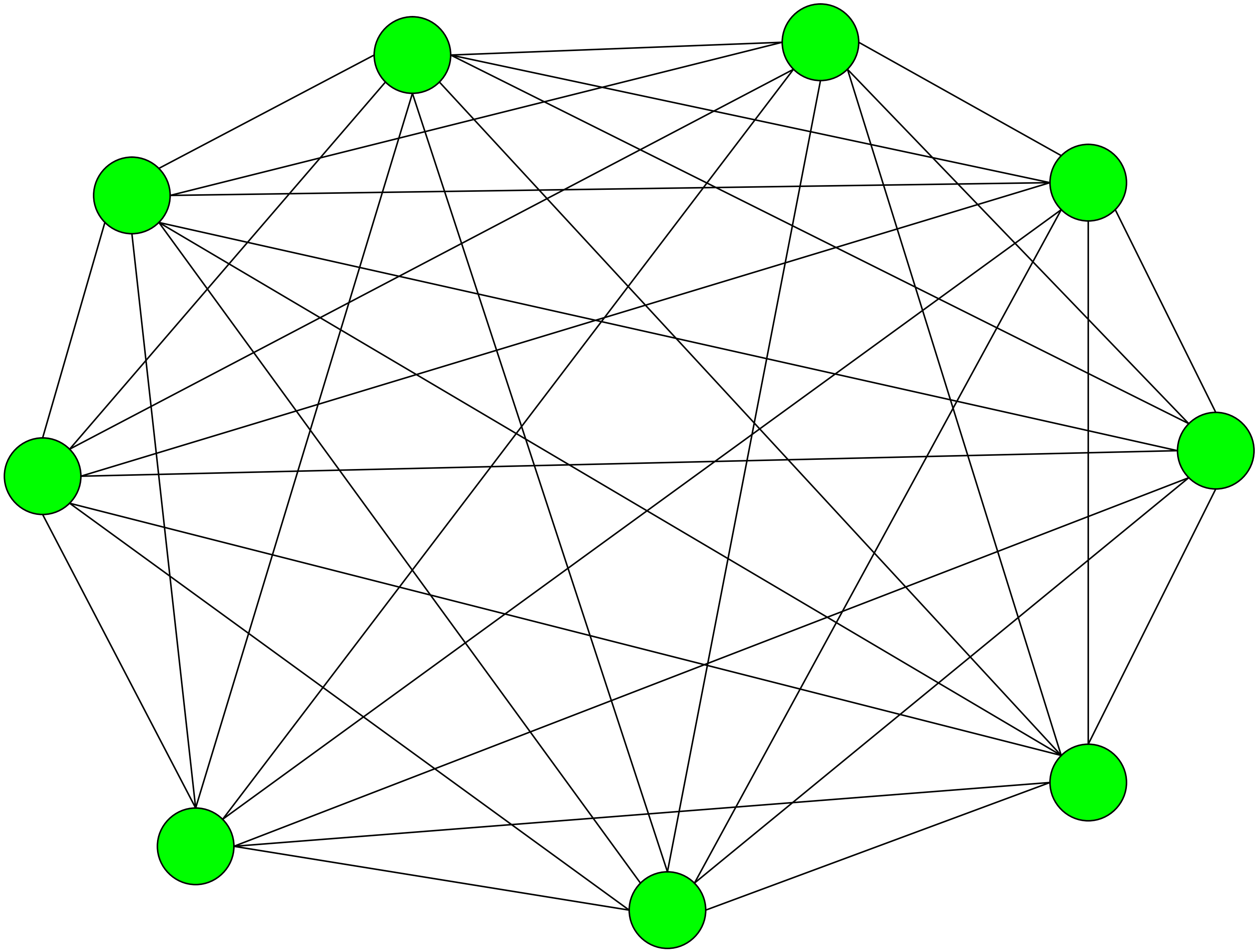
Basic Social Network Models

- Fully connected (Uniform)
  - Probability of interaction the same for any 2 pairs
- Random
  - Connections between individuals randomly chosen
- Lattice
  - Connections only through nearest neighbors
- Small-world
  - Most connections local, a few long-range
- Scale-free
  - Some nodes highly connected, most sparsely connected

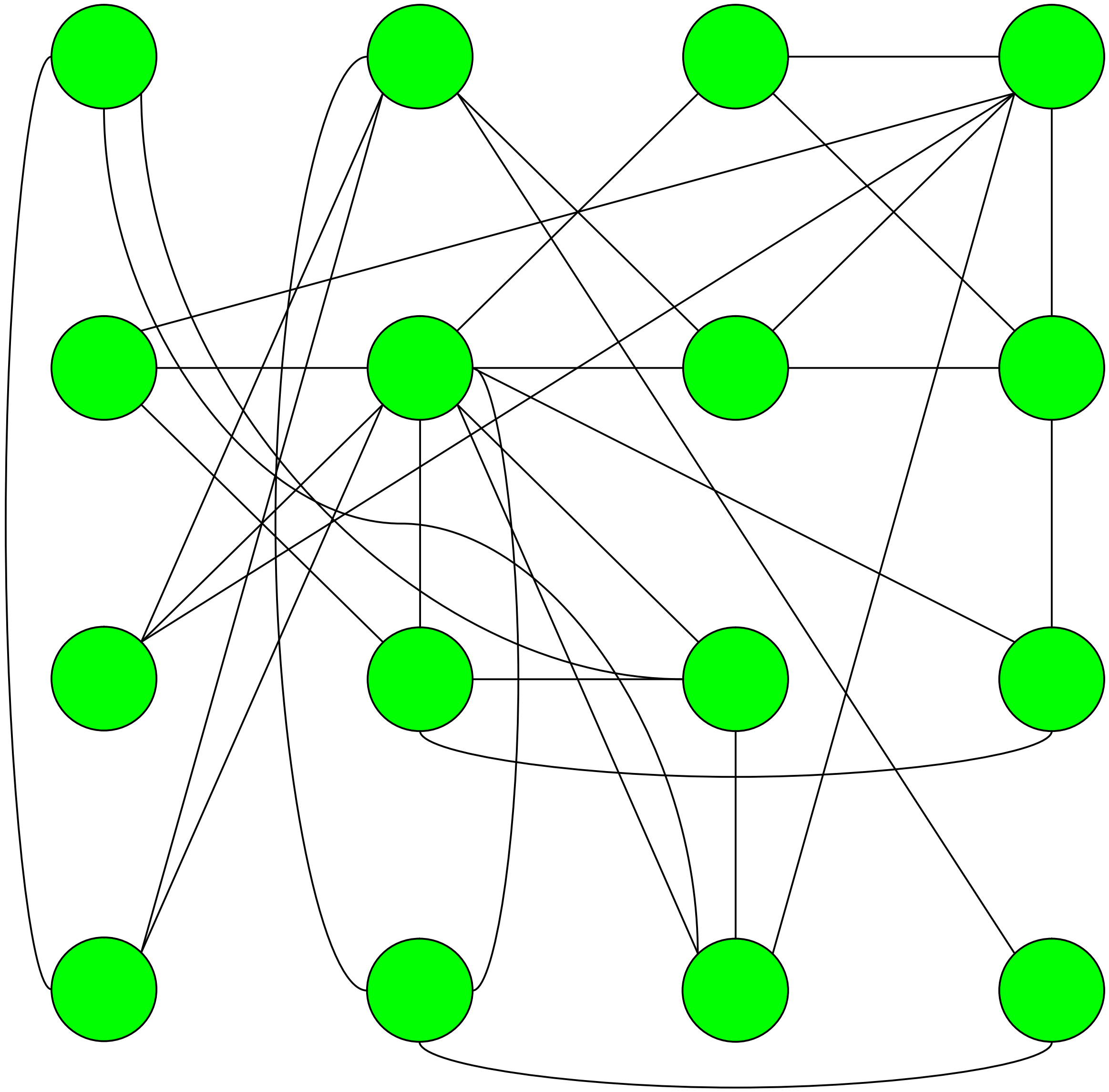
Networks



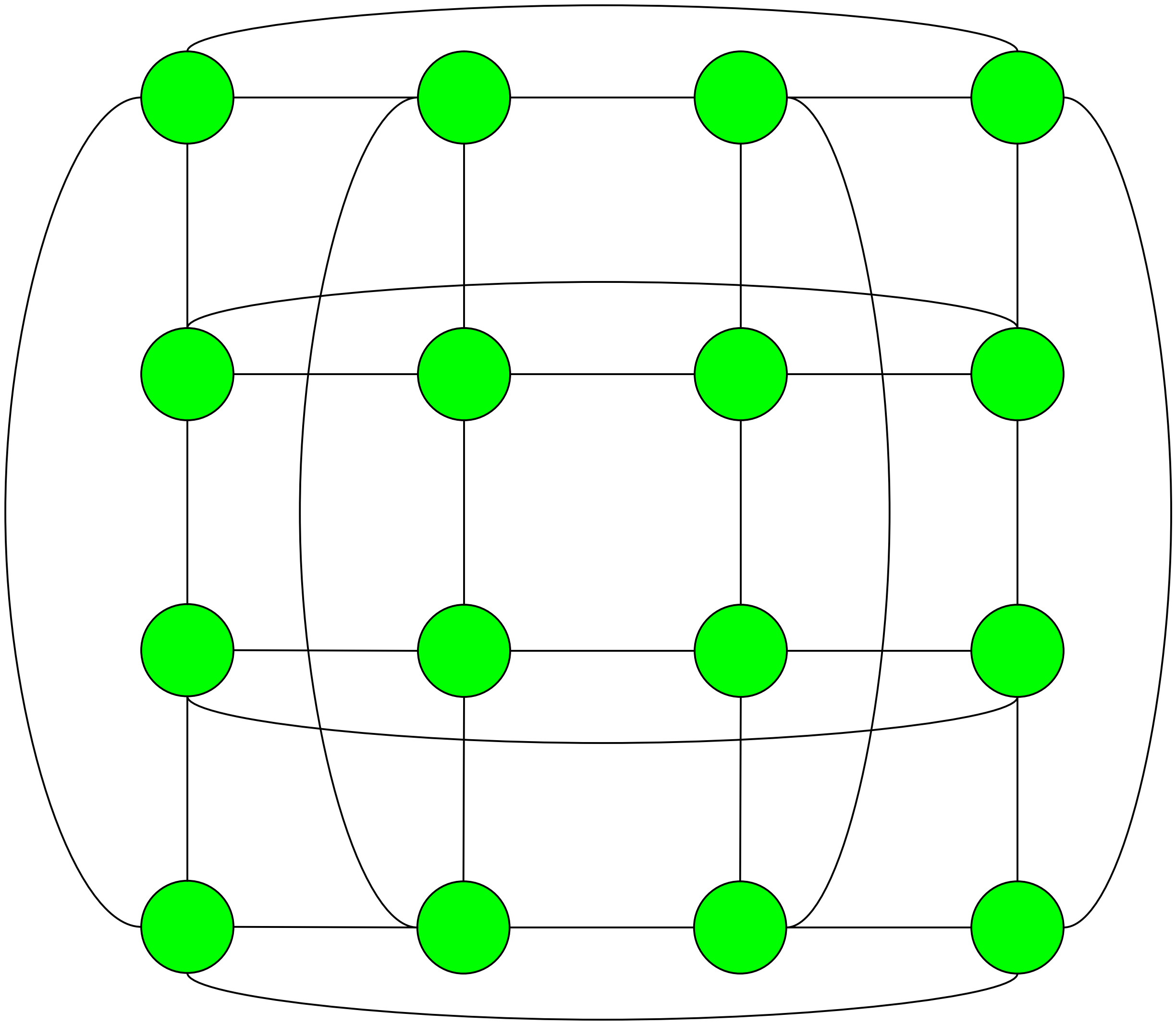
Fully Connected (Uniform)



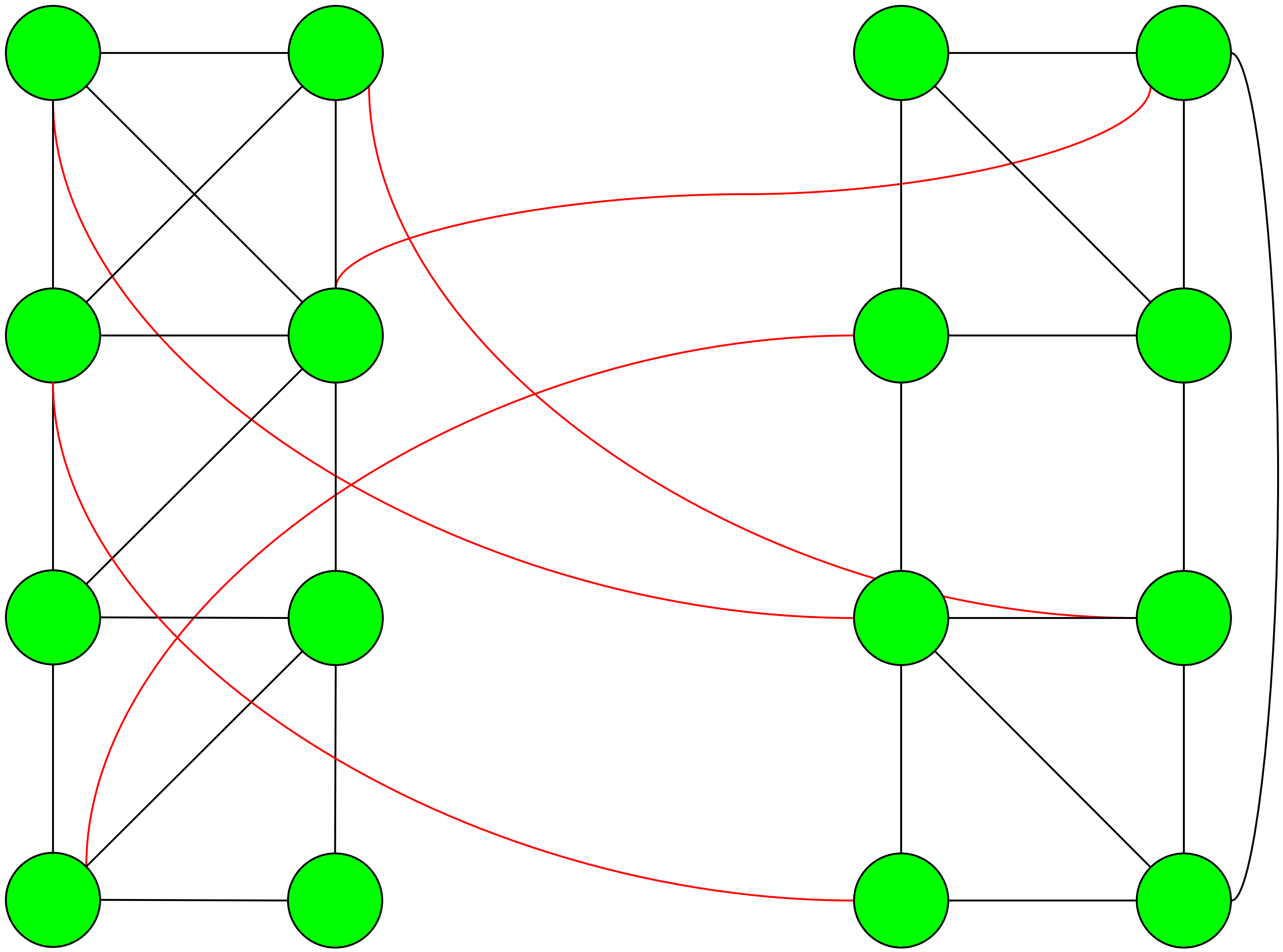
Random Network



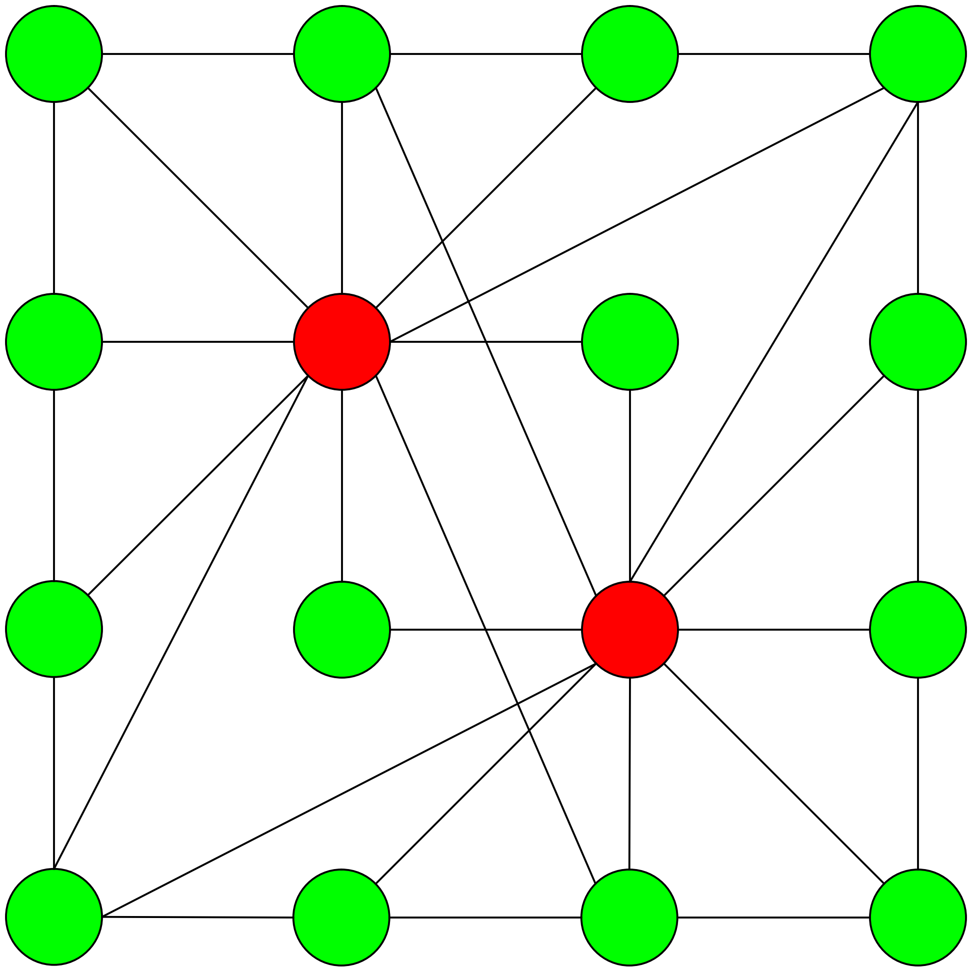
Lattice Network



Small-world Network



Scale-free Networks



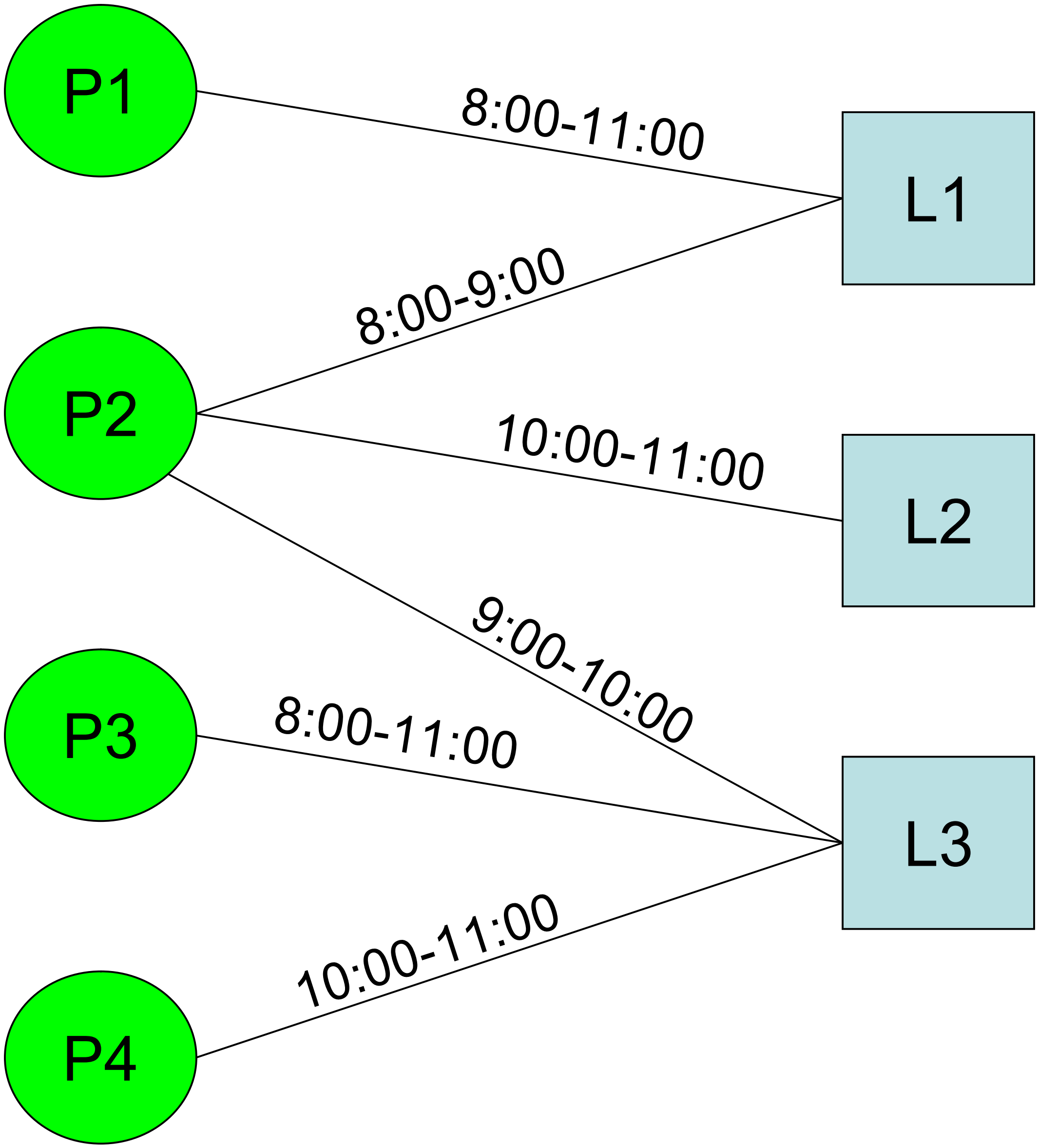
AB Example: EpiSims

- Agent-based model by Stephen Eubank, et al. (2004)
- Models smallpox epidemic in urban areas
- Utilizes realistic urban social network
  - Network data obtained from Los Alamos TRANSIMS
    - Realistic estimates of population mobility
    - Census, land-use data
    - Comprehensive data Portland, Oregon
  - Based on assumption that transportation infrastructure shapes population mobility

AB Example: EpiSims

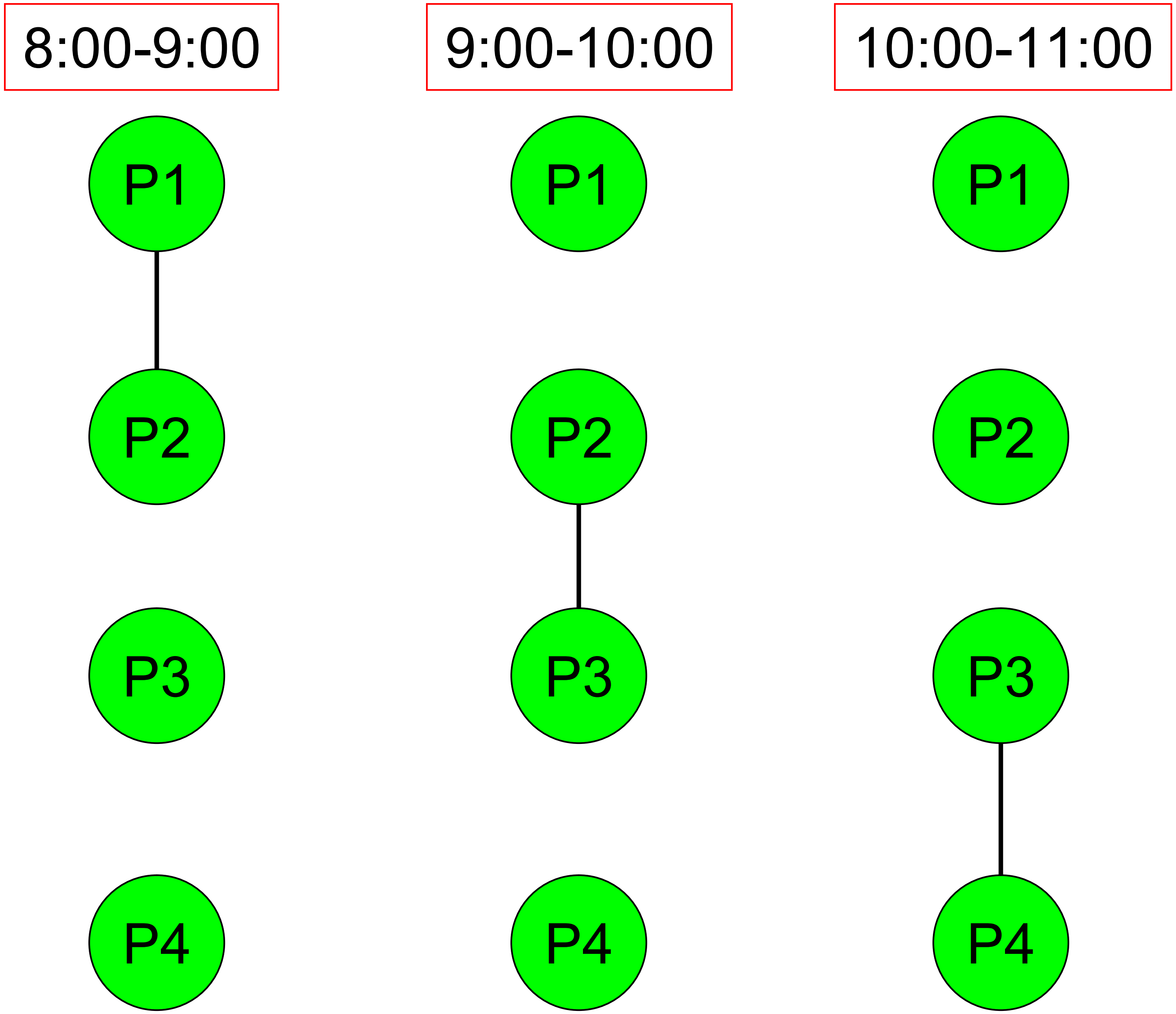
- TRANSIMS creates a representative artificial population based on census data
- TRANSIMS then generates a second-by-second list of the positions of the population
- EpiSims produces dynamic graphs for the social network from this data
- Bi-partite graphs with two types of vertices
  - People vertices
  - Location vertices

EpiSims: Bipartite Graph

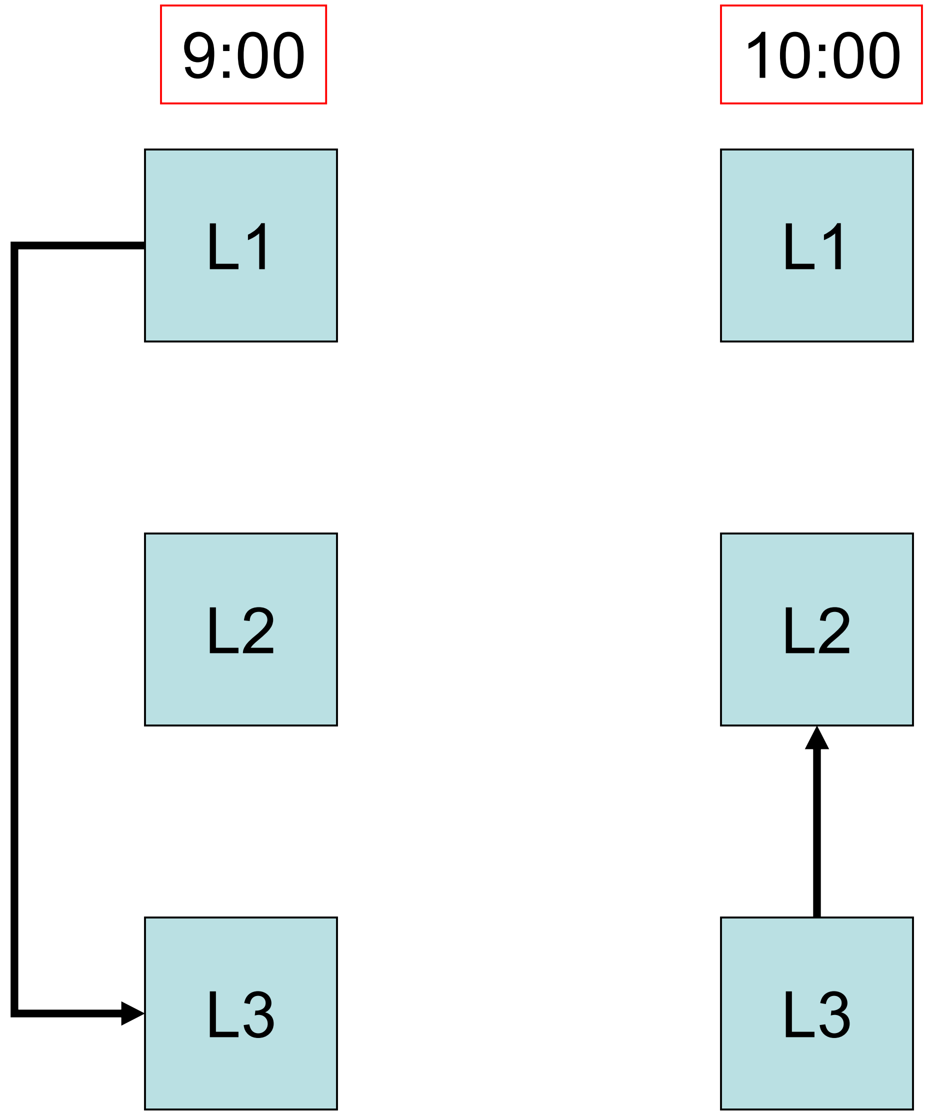


- Portland
- 1.5 million people vertices
- 180,00 location vertices

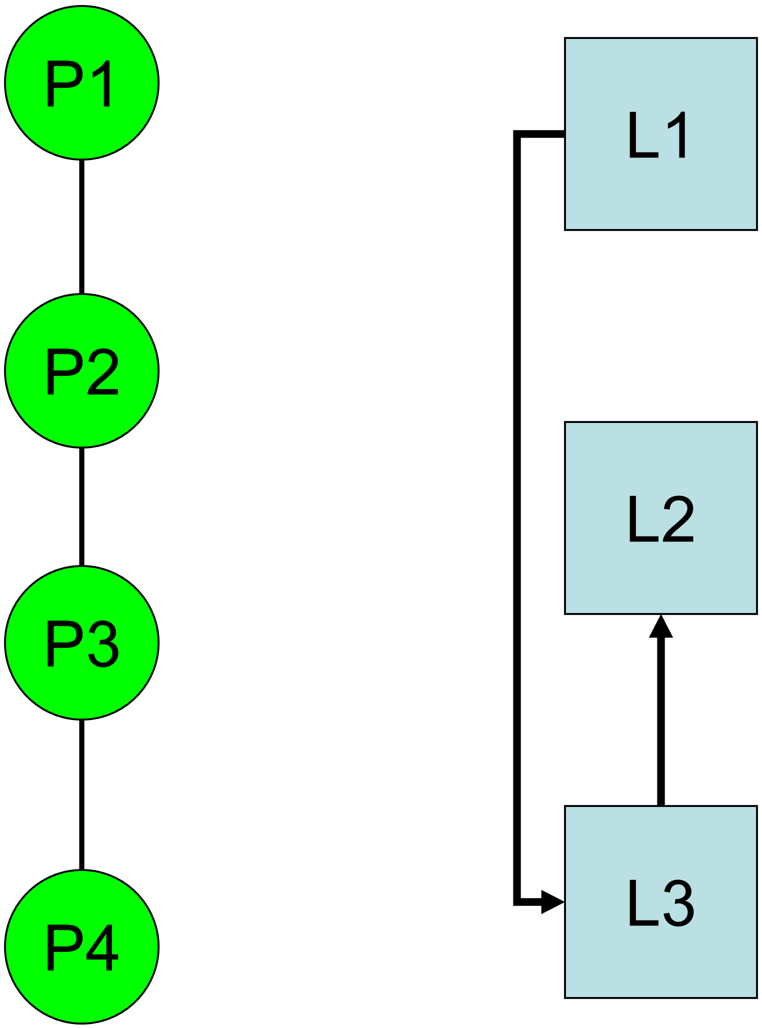
EpiSims: Population Contact Graphs



EpiSims: Travel Projection Graphs



EpiSims: Static Projections



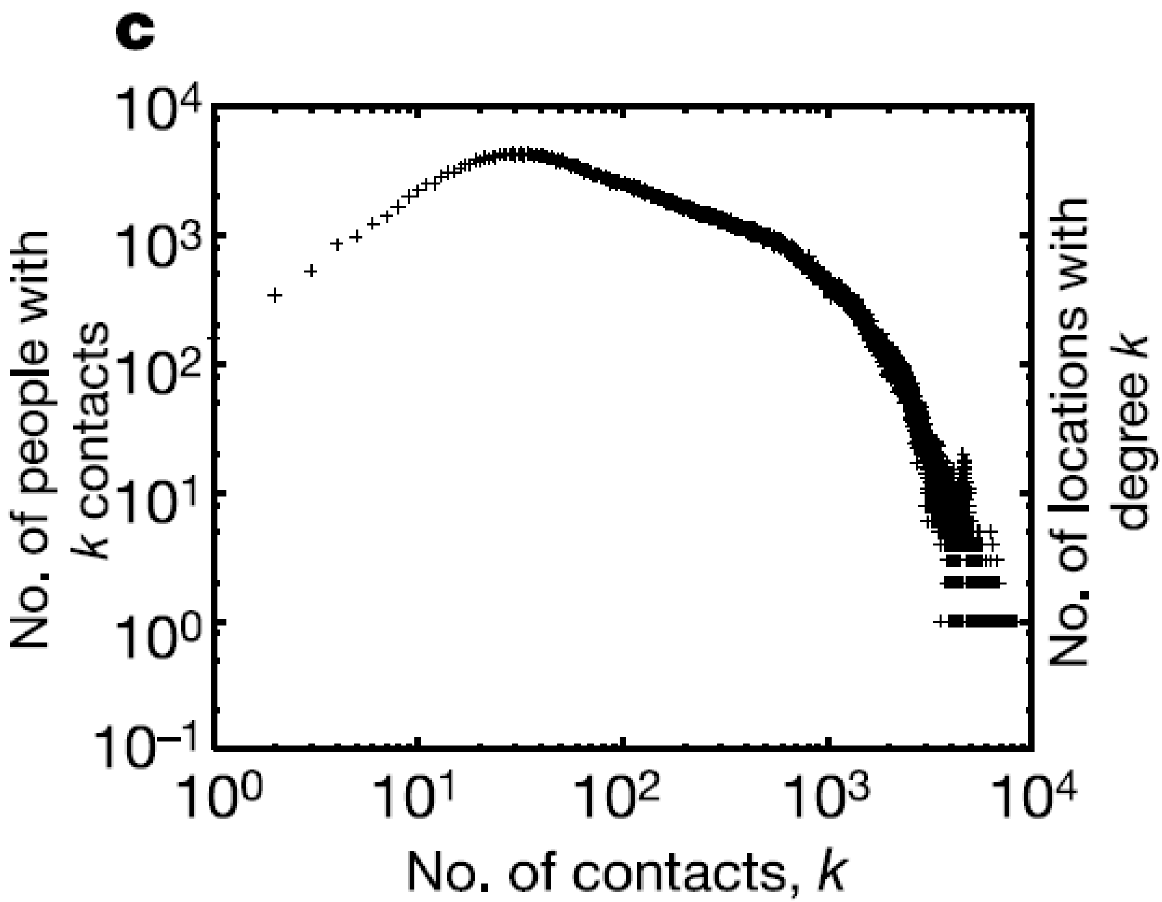
- Worst-case scenario

EpiSims: Graph Properties

- Analysis of social network graphs show several important properties
- Population contact graphs exhibit small-world like properties
  - Highly clustered, connected groups of people
  - A few long range "travelers"

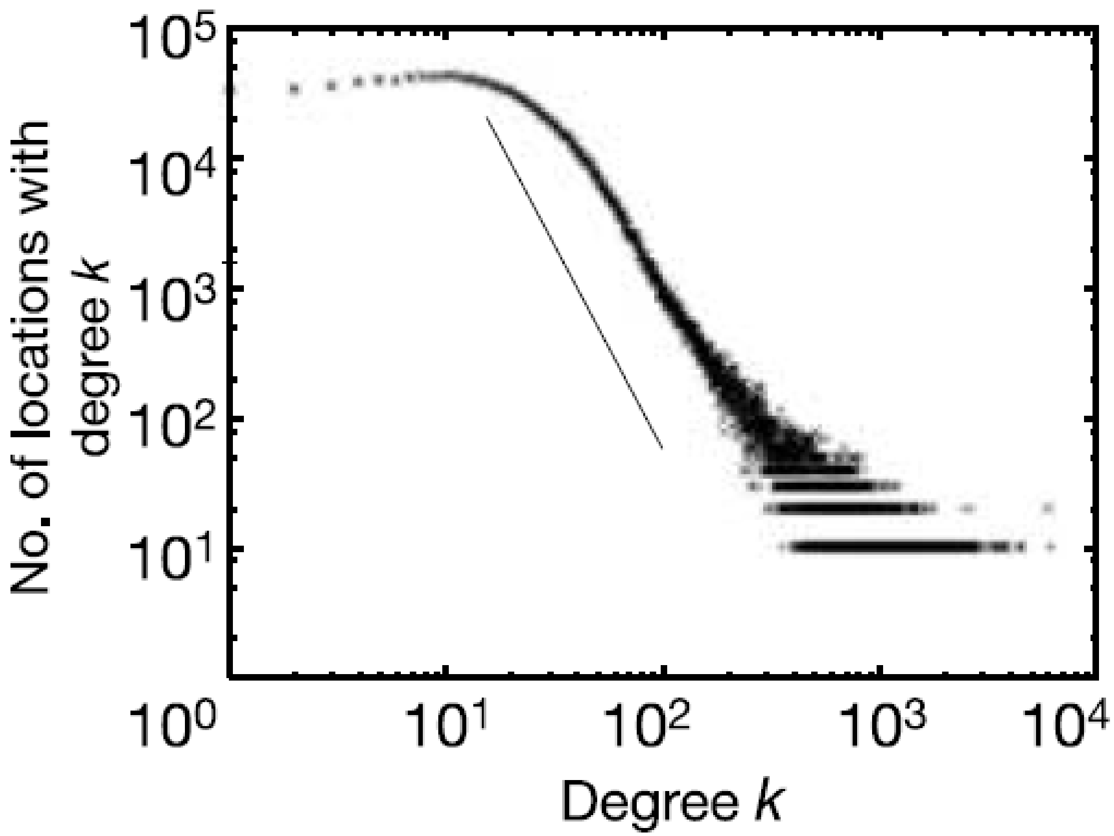
EpiSims: Graph Properties

- Population contact graph vertices are highly connected (not scale-free)



EpiSims: Graph Properties

- Location graph is scale-free
  - A few locations ("hubs") with many connections
  - Majority of locations have relatively few connections



EpiSims: Containment Strategies from Graphs

- The graph properties give intuition into effective containment strategies
  - Alternatives to mass vaccination
- Overall high connectivity of people contact graphs
  - Cannot target social people for vaccination
  - Would not reduce overall connectivity of graph
  - Would not greatly increase graph diameter

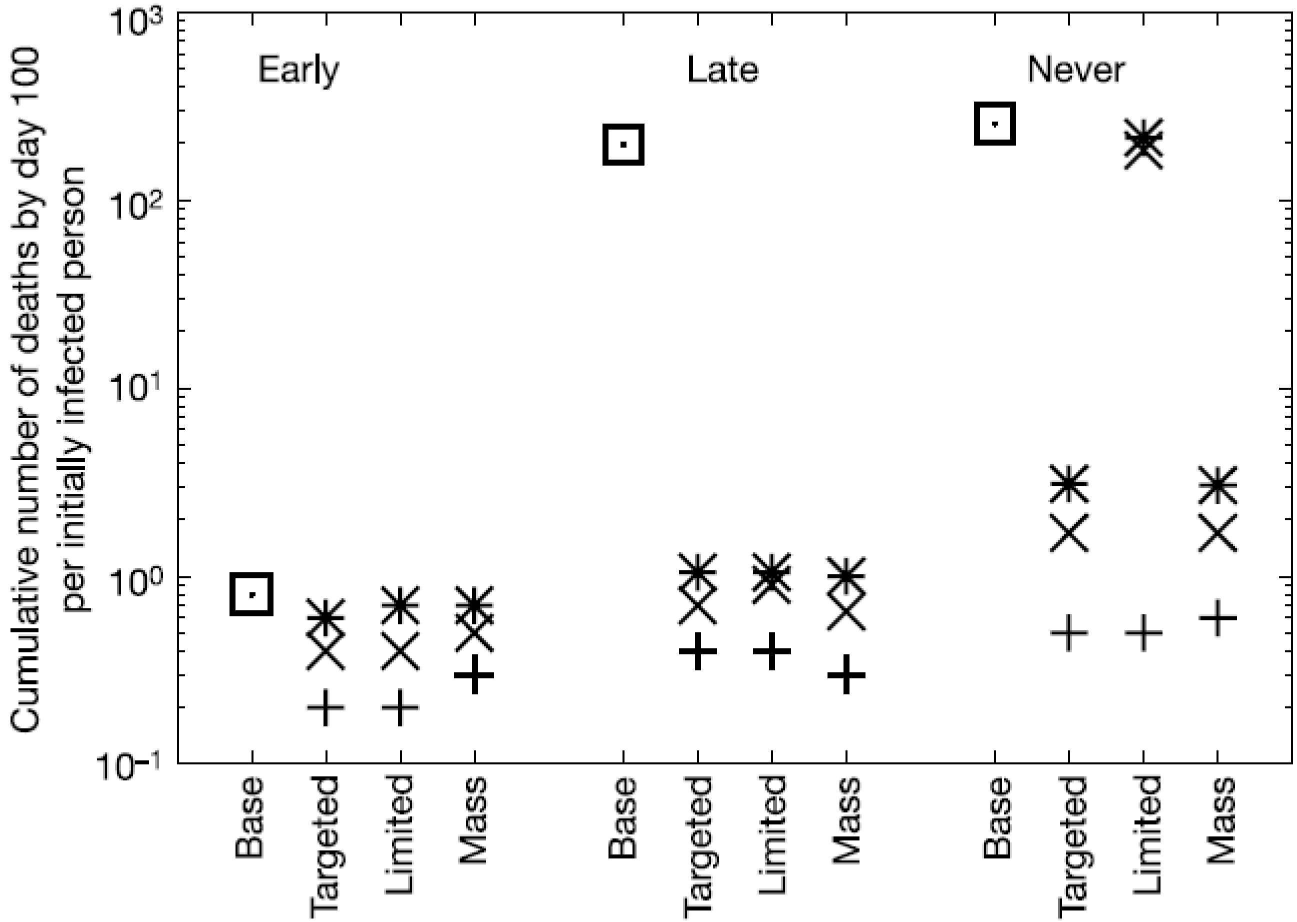
EpiSims: Containment Strategies from Graphs

- Small-world property of people contact graphs
  - Vaccinating long distance travelers crucial
  - Eliminates small-world property
  - Increases everybody's "degree of separation"
  - Slows spread of disease
- Scale-free property of location graphs
  - Closing "hubs" might be effective
  - Eubank, et al. argue maybe not
    - Showed did not greatly effect the largest connected component in people contact graph
    - Removed locations of over 100 degrees to see improvement
  - Perhaps still graph diameter would increase and epidemic slowed

EpiSims: Vaccination Strategies

- Compared four vaccination strategies
  - No vaccination
  - Mass vaccination
  - Targeted vaccination
    - Traced vaccination
    - Vaccination of "travelers"
  - Limited targeted vaccination
- Varied Response Time
  - 10-day delay
  - 7-day delay
  - 4-day delay
- Varied Withdrawal Time

EpiSims Results: Vaccination Strategies



* - 10 day delay

X - 7 day delay

\+ - 4 day delay

EpiSims: Discussion/Conclusions

- Early withdrawal most important
- Quick response time second most important
- Type of vaccination least important (assuming some vaccination)
- Targeted vaccination as effective as mass vaccination
- Limited targeted vaccination almost as effective as other two methods

Overall Conclusions

- Much is unknown about the spread of diseases such as smallpox
- Two different models (one DE, one AB) provide different conclusions about the best vaccination scheme
- Unclear which model is better
- Difficult to validate that we are actually modeling the spread of smallpox

Overall Conclusions

- AB model provides more insight into social interaction aspects and better intuition into potential containment strategies
- DE model is cheaper

Overall Conclusions

- So what vaccination strategy is better?
- Mass vaccination
  - Be safe and vaccinate everybody
  - Smallpox vaccination is somewhat dangerous
  - Can transmit virus to others
  - Vaccinating people unnecessarily is not a good idea
- Targeted vaccination
  - Better if effective
  - Risk losing control of epidemic

References

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