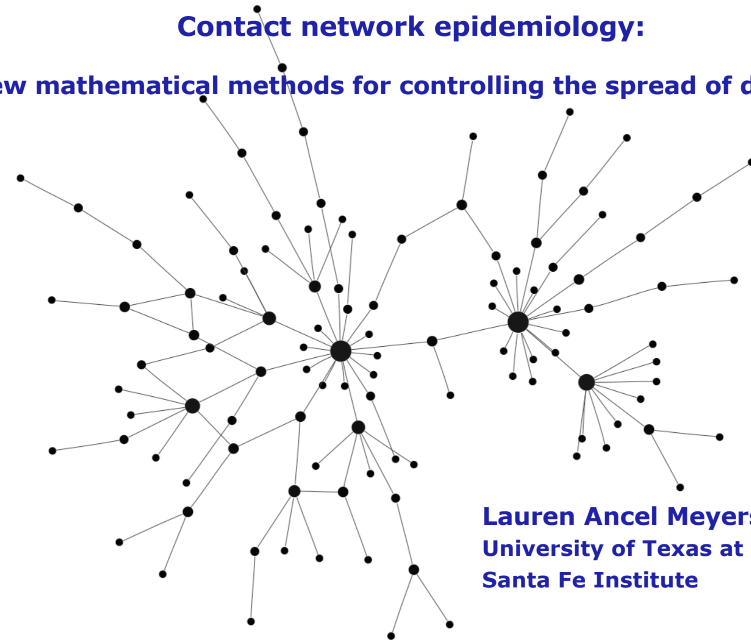
Contact network epidemiology:

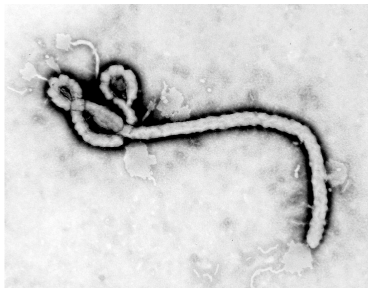
New mathematical methods for controlling the spread of diseases



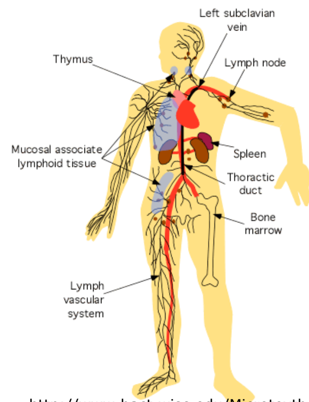
Lauren Ancel Meyers
University of Texas at Austin
Santa Fe Institute

By any definition …
a very <u>complex system</u>

Multiple levels of structure

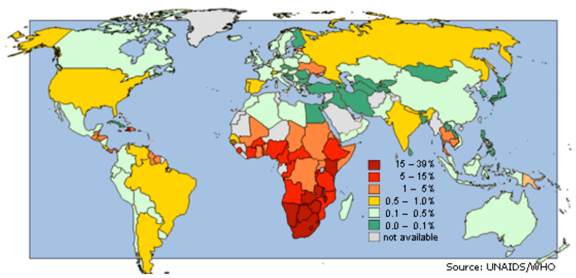


chamorrobible.org/gpw/gpw-20050430.htm



http://www.bact.wisc.edu/Microtextbook

People's Daily Online



By any definition …
a very <u>complex system</u>

Multiple levels of structure

Emergence

CDC's *Emerging Infectious Diseases*

Pathogen	Prior host	Year reported
Ebola virus	Bats (?)	1977
Escherichia coli O157:H7	Cattle	1982
Borrelia burgdorferi	Rodents (?)	1982
HIV-1	Chimpanzees	1983
HIV-2	Primates	1986
vCJD	Cattle	1996
H5N1 influenza A virus	Chickens	1997
SARS coronavirus	Palm civets (?)	2003

Woolhouse (2006) *Microbe*

By any definition …
a very complex system

Multiple levels of structure

Emergence

From single viral particles, immune cells, hosts …

come epidemiological dynamics

Feedback

Pathogen spreads and evolves

Induce immunity and public health responses

(shapes its own environment)

Pathogen spreads and evolves

…

Today and tomorrow…

I. Infectious diseases

II. Brief history of mathematical epidemiology

III. Contact network epidemiology

IV. Who gets the flu shot?

V. Very new methods

VI. Challenges

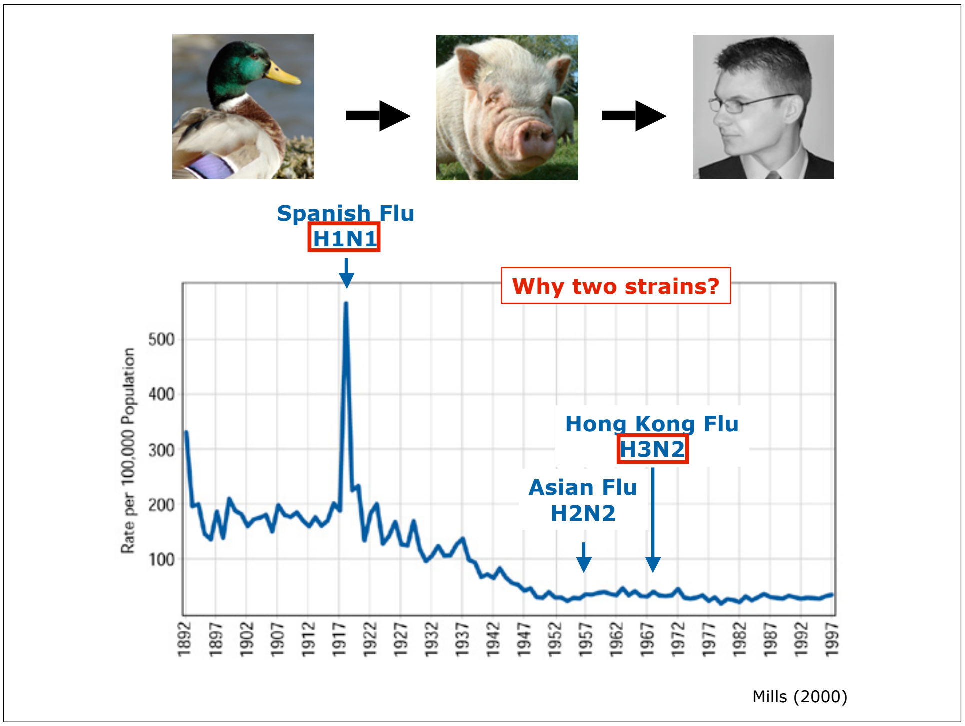
Modes of transmission

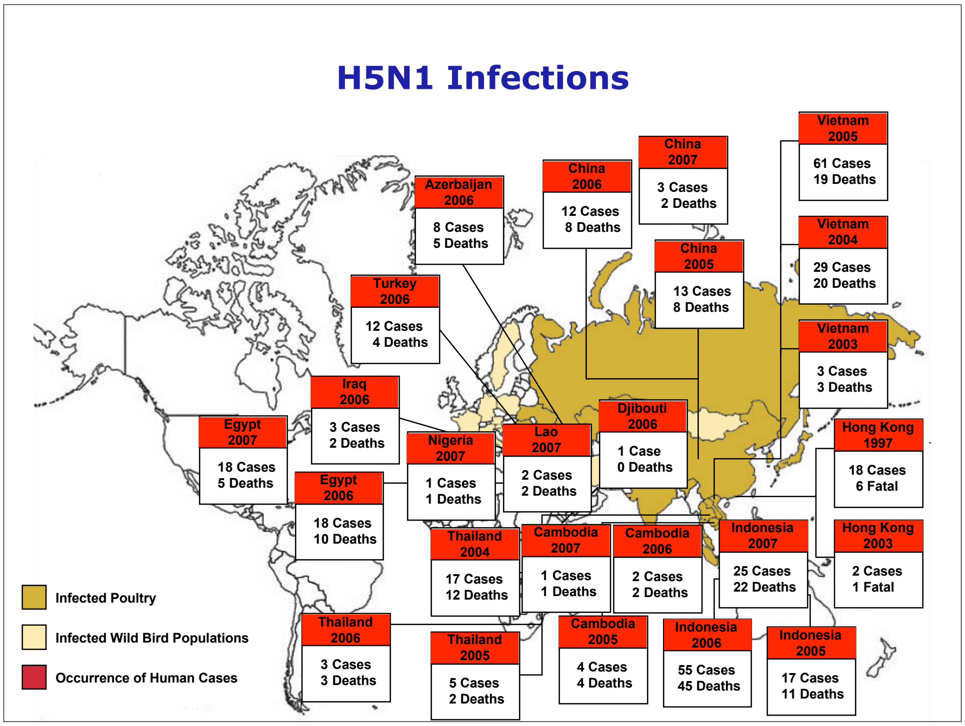
Vector-borne (fleas)

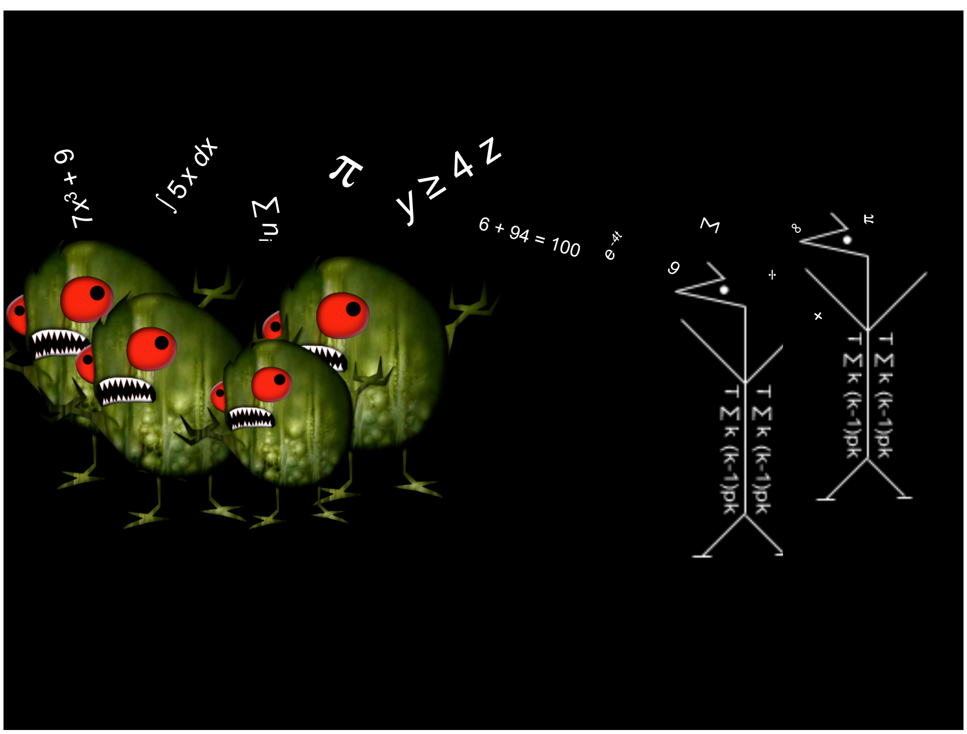
Water-borne

Contact

Sex/Needles


Spanish Flu
H1N1
Why two strains?
Hong Kong Flu
H3N2
Asian Flu
H2N2
Rate per 100,000 Population
500
400
300
200
100
1892
1897
1902
1907
1912
1917
1922
1927
1932
1937
1942
1947
1952
1957
1962
1967
1972
1977
1982
1987
1992
1997
Mills (2000)


H5N1 Infections
Vietnam 2005
61 Cases 19 Deaths
Vietnam 2004
29 Cases 20 Deaths
Vietnam 2003
3 Cases 3 Deaths
China 2007
3 Cases 2 Deaths
China 2006
12 Cases 8 Deaths
China 2005
13 Cases 8 Deaths
Azerbaijan 2006
8 Cases 5 Deaths
Turkey 2006
12 Cases 4 Deaths
Iraq 2006
3 Cases 2 Deaths
Egypt 2007
18 Cases 5 Deaths
Egypt 2006
18 Cases 10 Deaths
Nigeria 2007
1 Cases 1 Deaths
Lao 2007
2 Cases 2 Deaths
Djibouti 2006
1 Case 0 Deaths
Hong Kong 1997
18 Cases 6 Fatal
Hong Kong 2003
2 Cases 1 Fatal
Thailand 2004
17 Cases 12 Deaths
Cambodia 2007
1 Cases 1 Deaths
Cambodia 2006
2 Cases 2 Deaths
Indonesia 2007
25 Cases 22 Deaths
Thailand 2006
3 Cases 3 Deaths
Thailand 2005
5 Cases 2 Deaths
Cambodia 2005
4 Cases 4 Deaths
Indonesia 2006
55 Cases 45 Deaths
Indonesia 2005
17 Cases 11 Deaths
Infected Poultry
Infected Wild Bird Populations
Occurrence of Human Cases


6 + 94 = 100
Σ k (k-1)pk

"I simply wish that, in a matter which so closely concerns the wellbeing of the human race, no decision shall be made without all the knowledge which a little analysis and calculation can provide"

Daniel Bernoulli 1760

Smallpox in the 18th century …

3/4 of all people had been infected

Typically caught in first 5 years of life

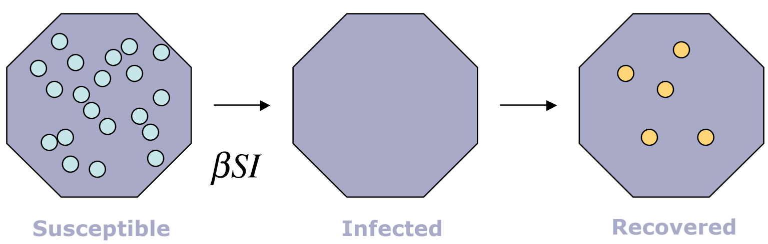
Killed 20-30% of individuals infected

1/10 of all mortality due to smallpox

Variolation

The 20th century …

Compartmental models

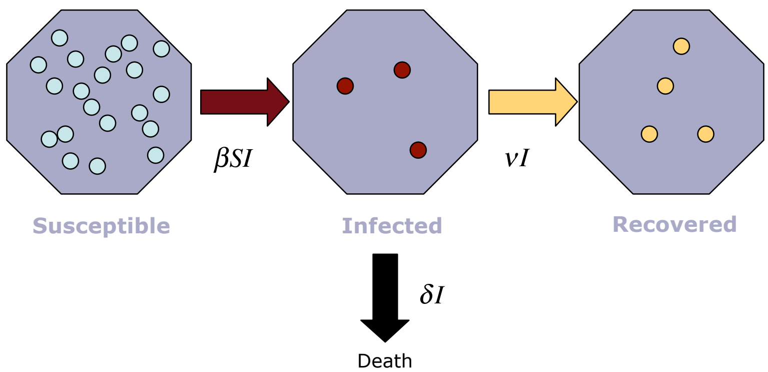


Mass action assumption

Kermack and McKendrick 1927

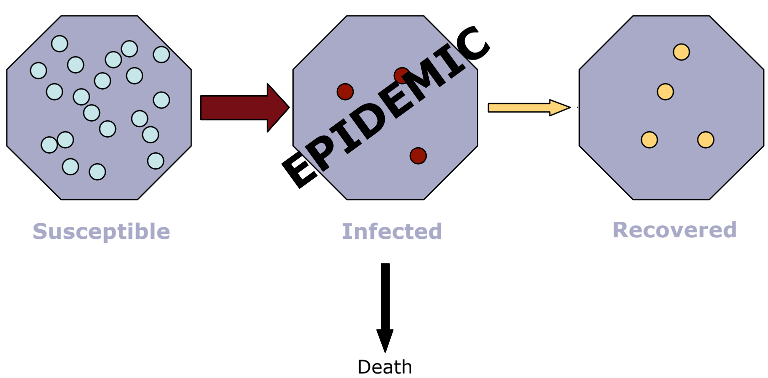
Will an outbreak lead to an epidemic?

$$\frac{\text{Infection rate}}{\text{Mortality + Recovery}} = \frac{\beta S}{\nu + \delta}$$



Reproductive ratio of the disease

$$R_0 = \frac{\text{Infection rate}}{\text{Mortality + Recovery}} > 1$$



Reproductive ratio of the disease

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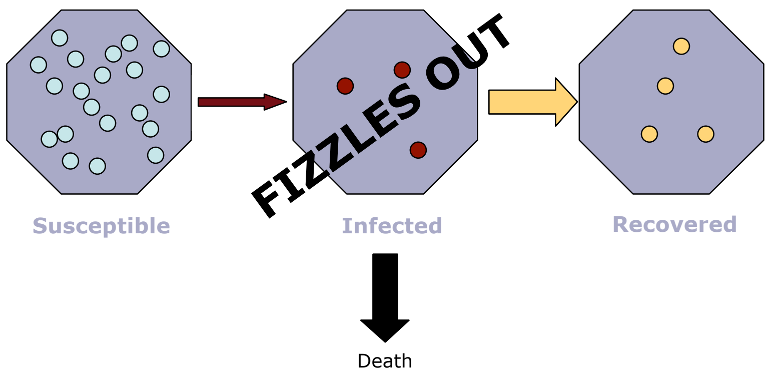
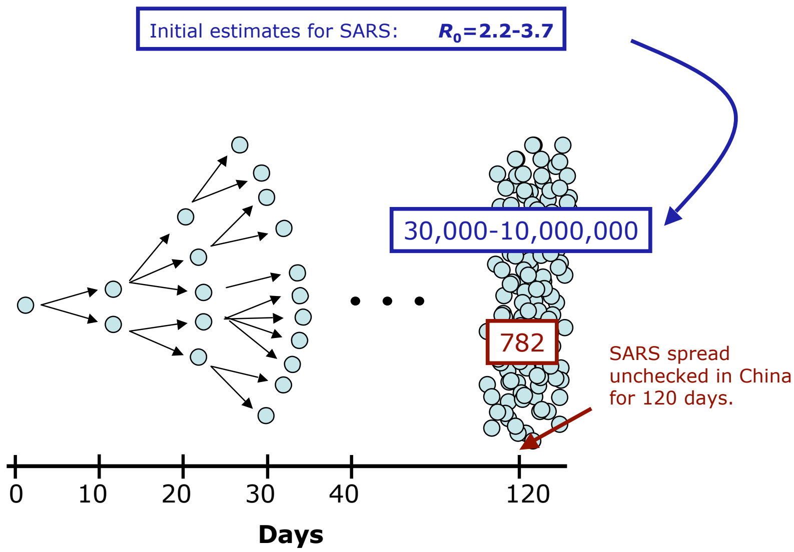


Herd immunity

$$R_0 = \frac{\text{Infection rate}}{\text{Mortality + Recovery}} = \frac{\beta S}{\nu + \delta} < 1$$

Disease	R_0	Vaccination minimum
Measles	5-18	90-95%
Chicken pox	7-12	85-90%
Polio	5-7	82-87%
Smallpox	1.5-20+	70-80%
SARS	2.2-3.7	?

SARS and R_0

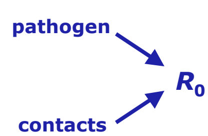


What's wrong with these estimates?

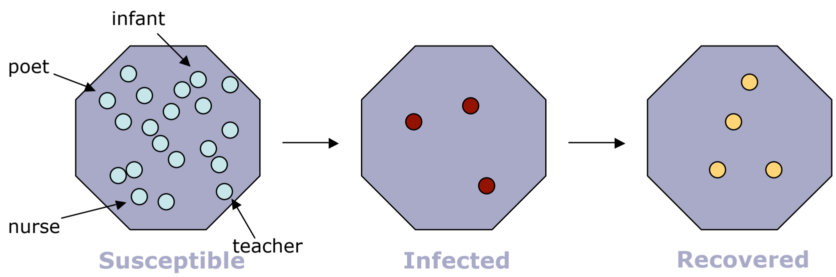
They are based on data from **hospitals** and **crowded apartment buildings** where people have **unusually high rates of contact** with each other.

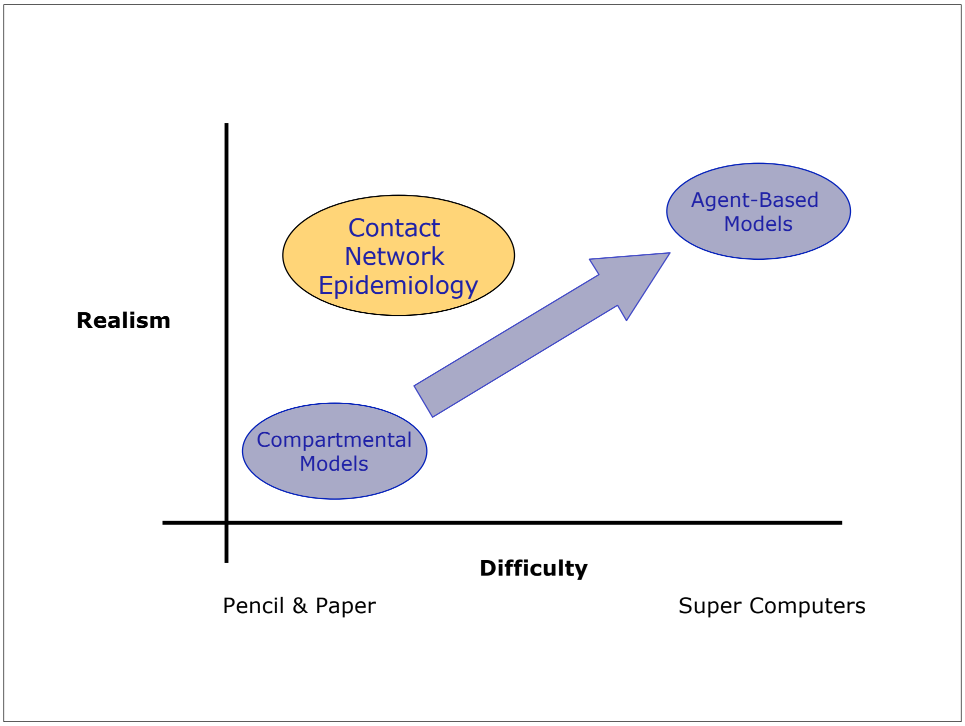
Transmission efficiency, incubation period, etc. will be approximately the same everywhere

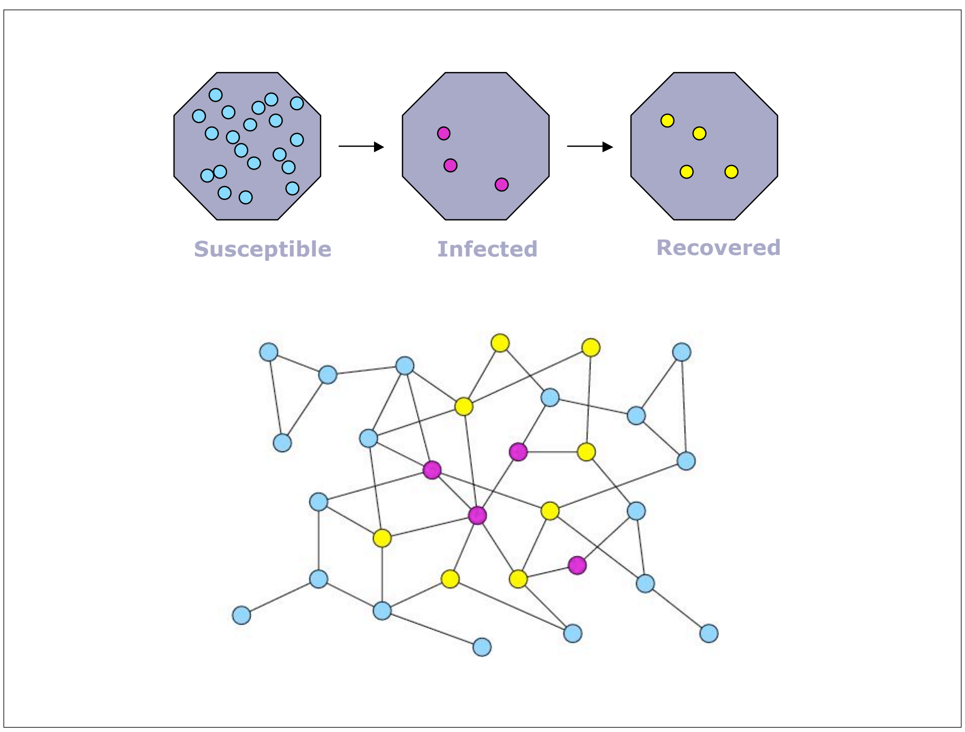
Contact patterns can vary **enormously**.



What's missing in traditional models?

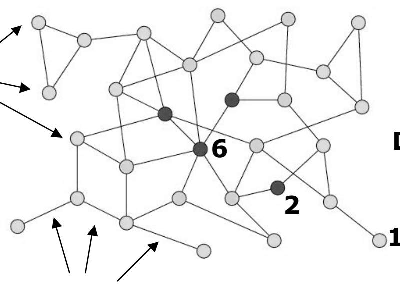



Realism
Contact
Network
Epidemiology
Agent-Based
Models
Compartmental
Models
Difficulty
Pencil & Paper
Super Computers


Susceptible
Infected
Recovered

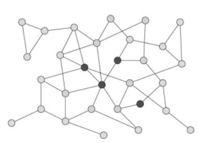
Terminology

Vertex / Node: People or places that can become infected

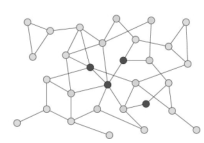


Degree: The number of edges coming out of a vertex

Edges: contacts that can lead to disease transmission



Contact Network Epidemiology



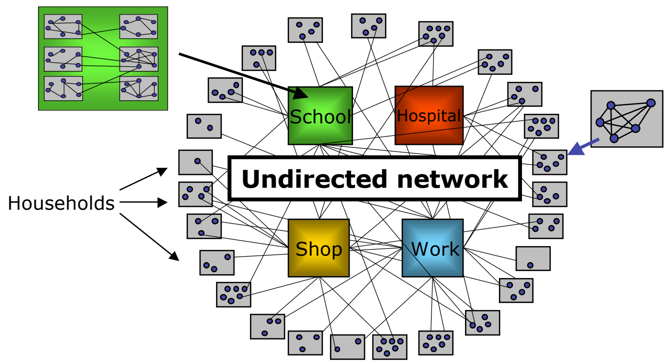
Three step process

1. Build a realistic contact network
2. Predict the spread of disease through the network
3. Quantify the impact of intervention

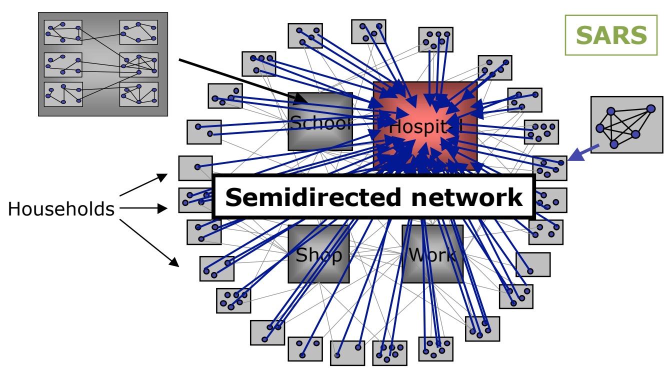
I. Building realistic networks

globe, **country**, state, **metropolitan area**, community, **hospital**, nursing home, **school**, military facility, **prison**, cruise ship, …

Vancouver, British Columbia



I. Building realistic networks



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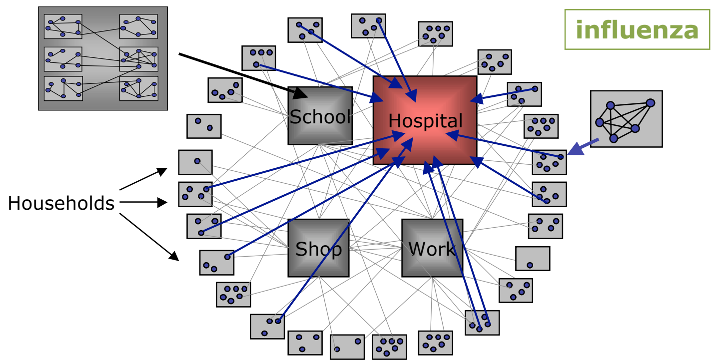
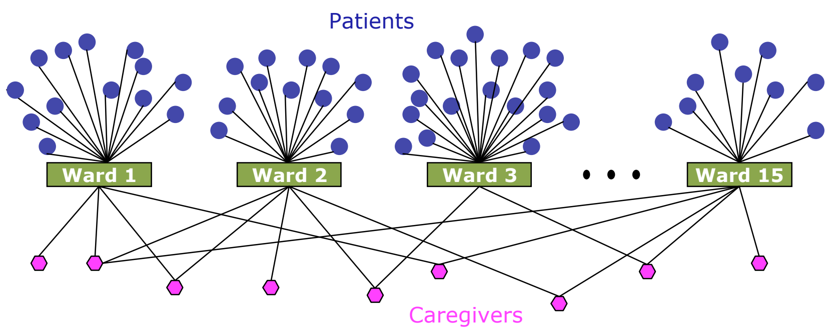


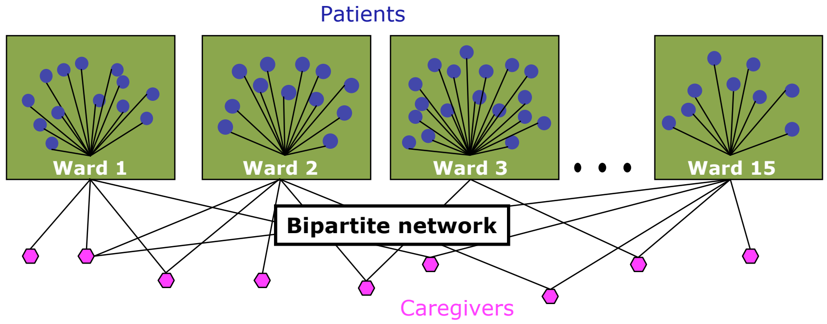
I. Building realistic networks

Evansville psychiatric institution

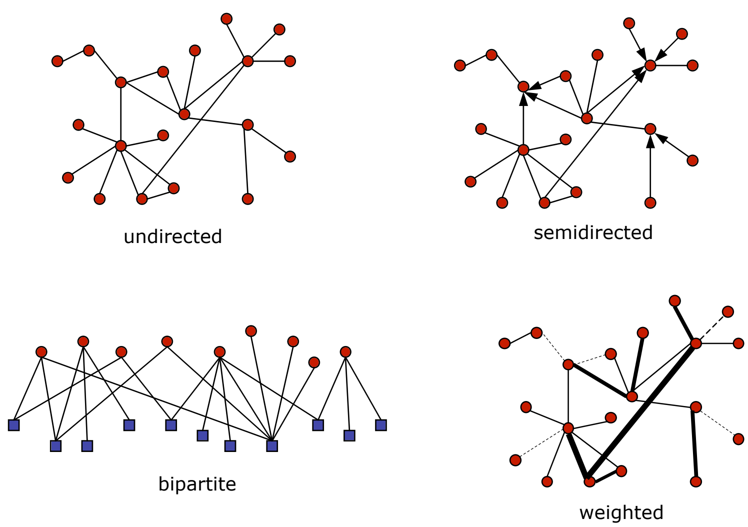


I. Building realistic networks

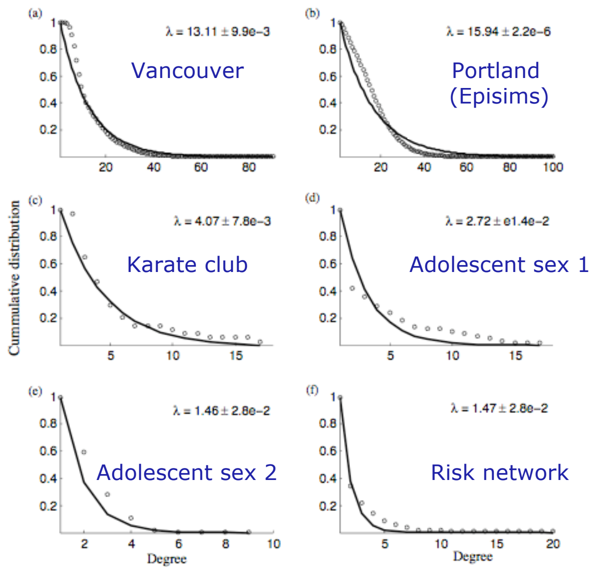
Evansville psychiatric institution



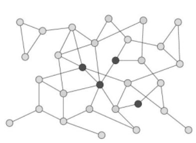
I. Building realistic networks



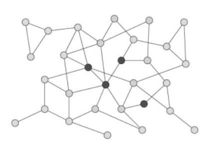
I. Realistic networks: Is everything scale-free?



Bansal, S., L.A. Meyers (2007) *Interface*



What do we do with these networks?



Three step process

1. Build a realistic contact network
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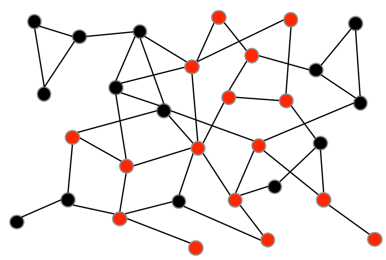
II. Predicting epidemics: The idea



Percolation theory

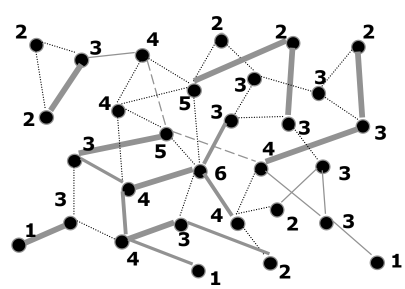
Grassberger, P. (1983) *Mathematical Biosciences*. 63: 157-172.
Newman, M.E.J. (2002) *Physical Review E*. 66: 016128.

II. Predicting epidemics: The math

The Two Basic Ingredients

1. Degree distribution: The frequency of each degree in the population

Degree	Frequency
1	3/30 = 0.1
2	7/30 = 0.23
3	11/30 = .37
4	6/30 = 0.2
5	2/30 = 0.07
6	1/30 = 0.03



2. Transmissibility: The probability that an infected individual will transmit the disease to another individual on the opposite side of an edge.

II. Predicting epidemics: The math

Probability generating functions

$$G_0(x) = \sum_{k=0}^{\infty} p_k x^k$$

the probability that a randomly selected vertex has degree k

You can recover the probabilities from the pgf

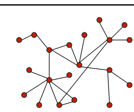
$$p_k = \frac{1}{k!} \frac{d^k G_0}{d x^k}\bigg|_{x=0}$$

The mean:

$$\langle k \rangle = \sum_{k=0}^{\infty} k p_k = G_0'(1)$$

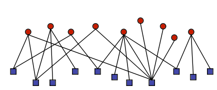
II. Predicting epidemics: The math

$$G_0(x) = \sum_{k=0}^{\infty} p_k x^k$$

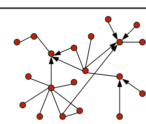


$$F_0(x) = \sum_{k=0}^{\infty} p_k x^k$$

$$G_0(x) = \sum_{k=0}^{\infty} q_k x^k$$

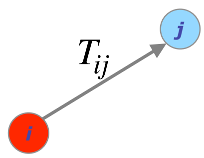


$$G_0(x, y; u) = \sum_{k=0}^{\infty} p_{jkm} x^j y^k u^m$$



II. Predicting epidemics: The math

Simplifying transmissibility



Average transmissibility

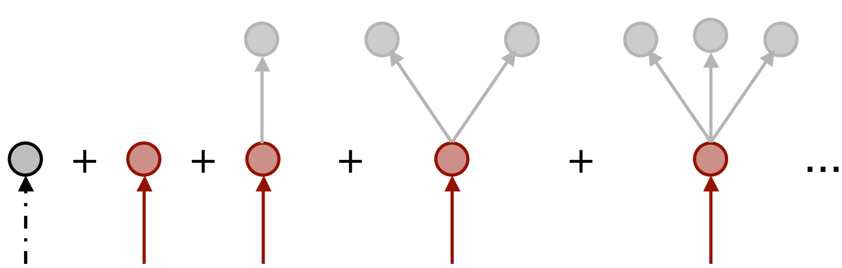
$$T = \langle T_{ij} \rangle$$

II. Predicting epidemics: The math

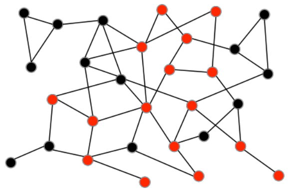
Percolation Threshold

There is a level of contagion below which there will be only small-finite sized outbreaks and above which large-scale epidemics are possible.

Below the threshold



II. Predicting epidemics: The math



Mean outbreak size:

$$\langle s \rangle = 1 + \frac{T\sum kp_k}{1 - T\left(\frac{\sum k(k-1)p_k}{\sum kp_k}\right)}$$

Degree distribution

Average transmissibility

II. Predicting epidemics: The math

Epidemic threshold:

$$T_c = \left(\frac{\sum kp_k}{\sum k(k-1)p_k}\right)$$

Degree distribution

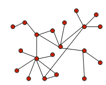
Critical transmissibility

$T < T_c$
Small outbreaks only

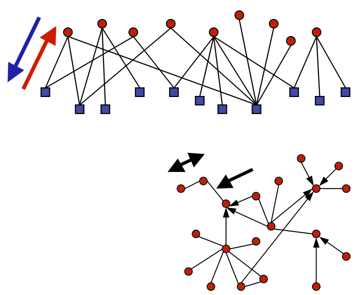
$T > T_c$
An epidemic is probable

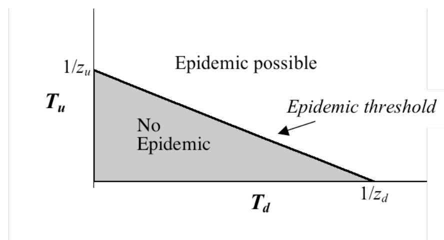
II. Predicting epidemics: The math

Epidemic threshold:



$$T_c = \left(\frac{\sum k p_k}{\sum k(k-1) p_k} \right)$$





Meyers, L.A., M.E.J. Newman, B. Pourbohloul (2006) *Journal of Theoretical Biology*

II. Predicting epidemics: The math

Percolation Threshold

There is a level of contagion below which there will be only small-finite sized outbreaks and above which large-scale epidemics are possible.

Above the threshold

The probability that an outbreak will spark and epidemic is equal to the size of the giant component.

We cannot calculate this directly.

Instead we use generating functions to calculate:

S = 1 - Prob{random introduction causes small outbreak only}

II. Predicting epidemics: Other quantities

$T_c = \left(\frac{\sum kp_k}{\sum k(k-1)p_k}\right)$

Epidemic threshold

Size of a small outbreak

Probability and size of a large epidemic

Who gets infected?

Does it matter who gets sick first?

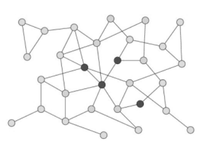
These quantities for a variety of networks

Disease dynamics

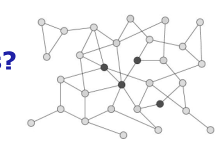
Dynamic networks

$\langle s \rangle = 1 + \frac{T\sum kp_k}{1 - T\left(\frac{\sum k(k-1)p_k}{\sum kp_k}\right)}$

$P_e = 1 - \sum_{jkm} p_{jkm}(1+(\alpha-1)T)^k(1-(\beta-1)T)^m$



What do we do with these networks?



Three step process

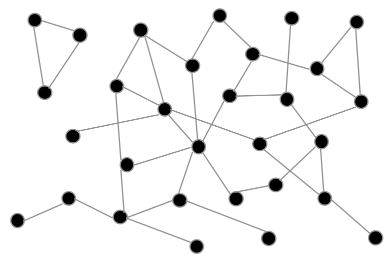
1. Build a realistic contact network
2. Predict the spread of disease through the network
3. Quantify the impact of intervention

III. Assessing control strategies

Three categories of intervention

Contact reducing interventions
Quarantine, cohorting, travel restrictions, etc.

Degree	Old	New
1	0.10	0.23
2	0.23	0.23
3	0.37	0.43
4	0.20	0.03
5	0.07	0.07
6	0.03	0



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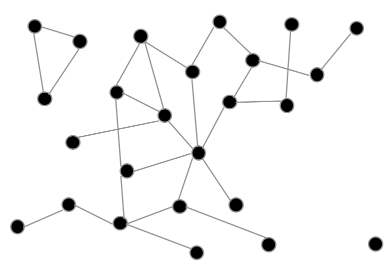
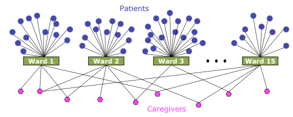


Vaccination
Targeted, general, ring, etc.

Degree	Old	New
1	0.23	0.26
2	0.23	0.30
3	0.43	0.30
4	0.03	0.09
5	0.07	0.04
6	0	0

Transmission reducing interventions
Face masks, hand washing, etc.

III. Disease control in health care settings



Candidate strategies for control of mycoplasma pneumonia:

- respiratory precautions
- cohorting symptomatic cases
- antibiotic prophylaxis of asymptomatic individuals

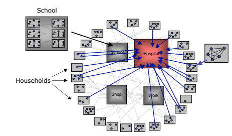
The best strategy … None of the above!

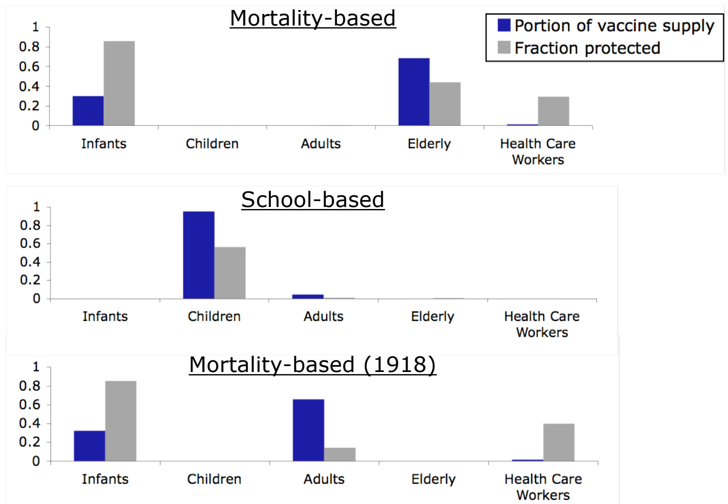
At the first sign of an outbreak, limit caregiver interactions.

Meyers, L.A., M.E.J. Newman, M. Martin and S. Schrag (2003) *Emerging Infectious Diseases*

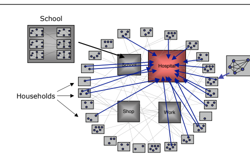
III. Evaluating Flu Vaccination Programs

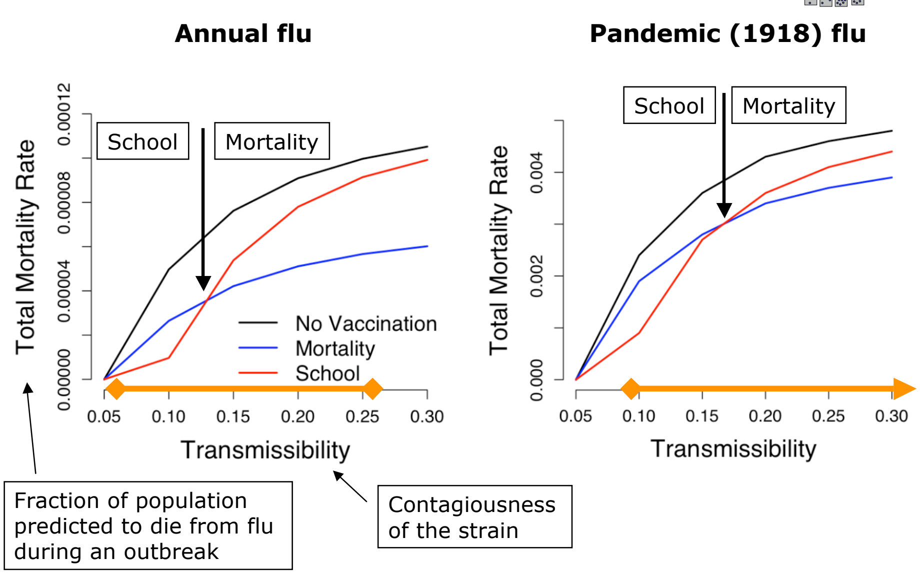
III. Evaluating Flu Vaccination Programs





III. Evaluating Flu Vaccination Programs





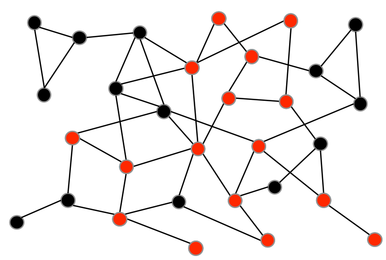
III. Evaluating Flu Vaccination Programs

What should the CDC and other health agencies do?

- If the contagiousness of the strain is known, select the best strategy
- If not, target high-risk groups
- If vaccination is delayed or flu is introduced multiple times into the population, target high-risk groups

Bansal, S., B. Pourbohloul, L.A. Meyers (2006) *PLoS Medicine*

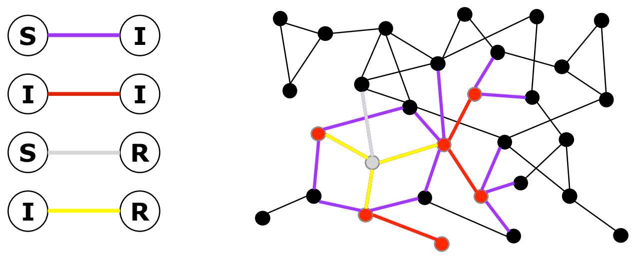
Predicting epidemics: A new framework



Network SIR Models

Volz, E (*in press*) *Journal of Mathematical Biology*
Volz, E. and L.A. Meyers (*in review*)

Predicting epidemics: A new framework



Track edge states

Include recovery parameter

The network SIR model: Static network

transmission rate

$$\dot{\theta} = -rp_I\theta$$

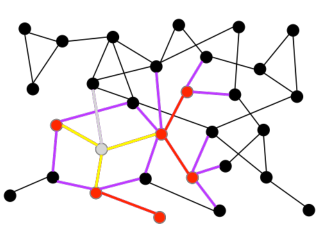
$$\dot{p}_S = rp_S p_I\left(1-\theta g''(\theta)/g'(\theta)\right)$$

$$\dot{p}_I = rp_S p_I\, g''(\theta)/g'(\theta) - p_I\left(1-p_I\right)r - p_I\mu$$

network pgf *recovery rate*

Fraction of degree one nodes which are still susceptible

Fraction of susceptibles' contacts that are infectious



$$\frac{\text{Purple}}{\text{black + purple + gray}}$$

The network SIR model: Static network

transmission rate

- $\dot{\theta} = -rp_I\theta$
- $\dot{p}_S = rp_S p_I \left(1 - \theta g''(\theta)/g'(\theta)\right)$
- $\dot{p}_I = rp_S p_I\, g''(\theta)/g'(\theta) - p_I\left(1 - p_I\right)r - p_I\mu$

network pgf *recovery rate*

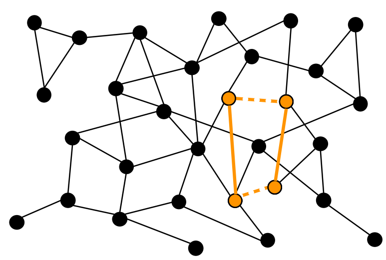
Fraction of degree one nodes which are still susceptible

Fraction of susceptibles' contacts that are infectious

Fraction of infecteds' contacts that are still susceptible

Prevalence: $S_t = g\left(\theta_t\right) = \sum_k p_k \theta_t^k$

The network SIR model: Dynamic network



Neighbor exchange model

Total number of contacts per person remains constant

The network SIR model: Dynamic network

neighbor exchange rate

$$\dot{\theta} = -rp_I\theta$$
$$\dot{p}_S = rp_S p_I\left(1-\theta g''(\theta)/g'(\theta)\right) + \rho\left(g'(\theta)/g'(1) - p_S\right)$$
$$\dot{p}_I = rp_S p_I\, g''(\theta)/g'(\theta) - p_I\left(1-p_I\right)r - p_I\mu + \rho\left(M_I - p_I\right)$$
$$\dot{M}_I = -\mu M_I + rp_I\left(\theta^2 g''(\theta) + \theta g'(\theta)\right)/g'(1)$$

Fraction of all edges that have at least one infected end

Prevalence: $S_t = g(\theta_t) = \sum_k p_k \theta_t^k$

A continuum of models

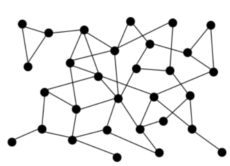
neighbor exchange rate

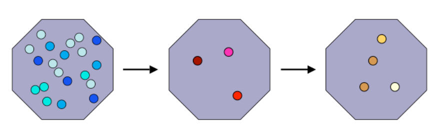
$$\dot{\theta} = -rp_I\theta$$
$$\dot{p}_S = rp_S p_I\left(1-\theta g''(\theta)/g'(\theta)\right) + \rho\left(g'(\theta)/g'(1) - p_S\right)$$
$$\dot{p}_I = rp_S p_I\, g''(\theta)/g'(\theta) - p_I\left(1-p_I\right)r - p_I\mu + \rho\left(M_I - p_I\right)$$
$$\dot{M}_I = -\mu M_I + rp_I\left(\theta^2 g''(\theta) + \theta g'(\theta)\right)/g'(1)$$

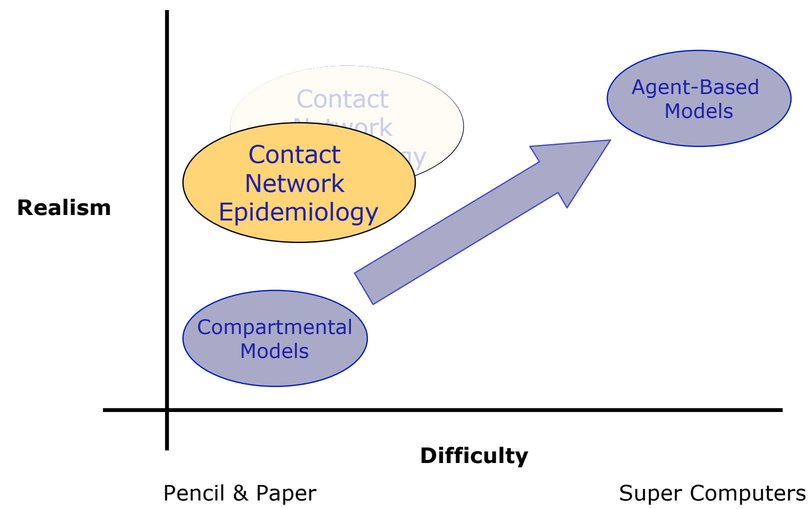
← ρ →

$\rho = 0$
Static network model
(final state = bond percolation)

$\rho = \infty$
Fully-mixed model
(compartmental with heterogeneity)







Challenges

Beyond static semi-random graphs

Dynamic contacts, clustering, modularity, assortativity, …

Host heterogeneity

Susceptibility, disease progression, transmission rates, …

Disease-induced behavioral changes

Pathogen evolution

SIRS dynamics

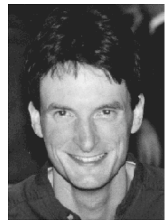
Applications …

Diverse diseases, sociological controls, …

Babak Pourbohloul
British Columbia CDC

Shweta Bansal
Meyers Lab
University of Texas

Erik Volz
University of Texas



Mark Newman
University of Michigan

CDC

NSF

UBC Centre for Disease Control

CIHR IRSC

James S. McDonnell Foundation

SANTA FE INSTITUTE
Celebrating 20 years of Complexity Science