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The modern synthesis

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For a quick "101"

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And then

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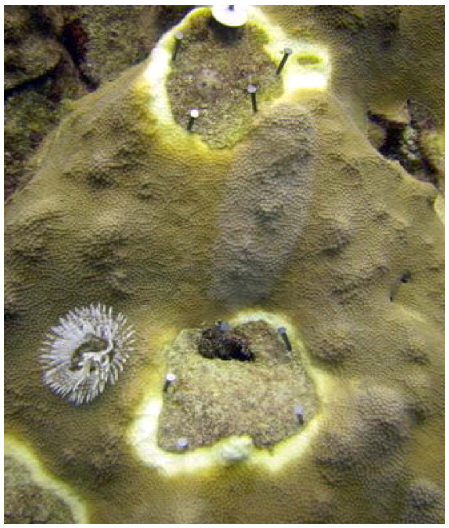
Computational Sustainability Seminar: Epidemic models

Stephen P. Ellner, Ecology and Evolutionary Biology, Cornell University

spe2@cornell.edu



J. Mao-Jones, K.B. Ritchie, L.E. Jones, S.P. Ellner. 2010. How microbial community composition regulates coral disease transmission (PloS Biology, in press).

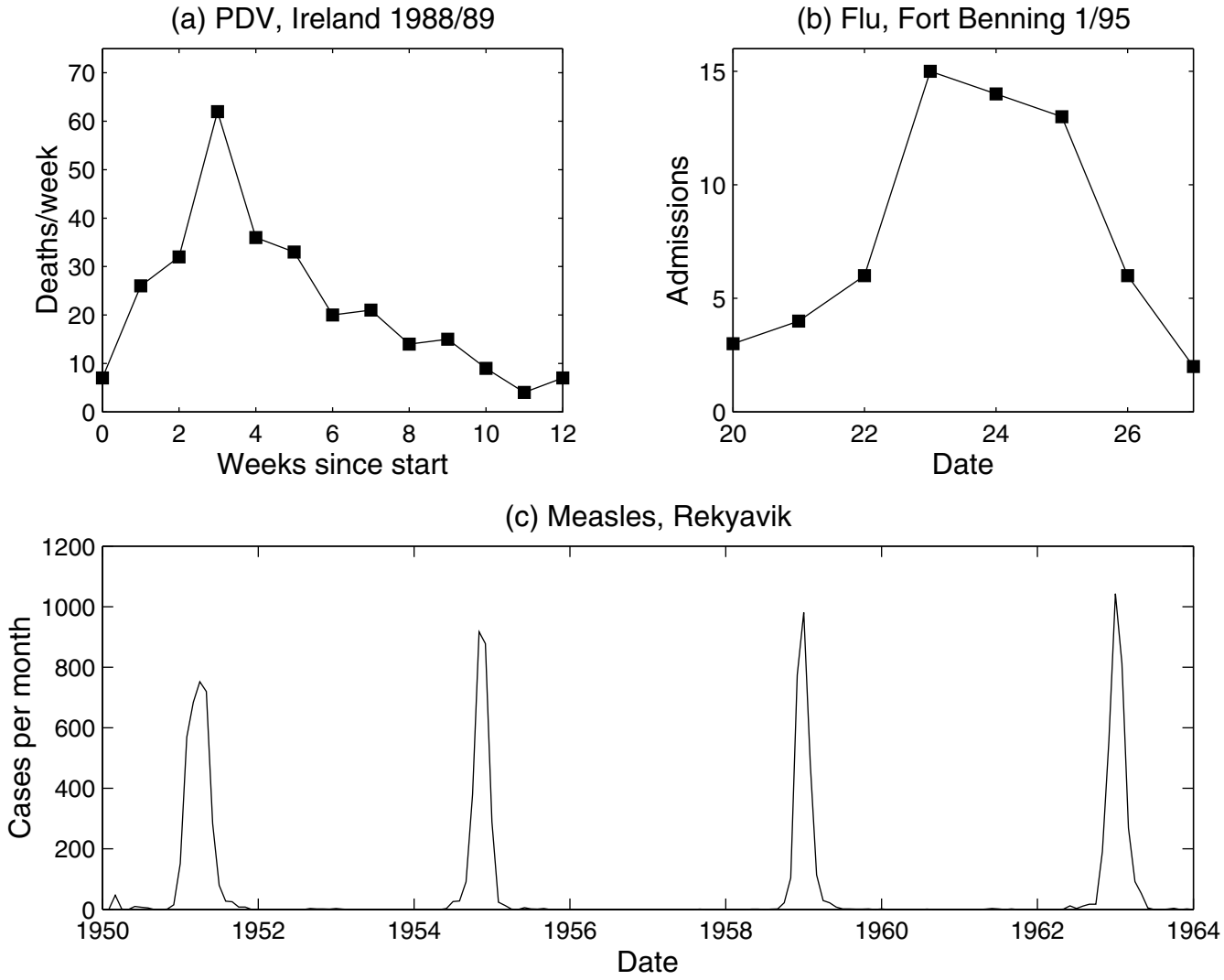
J. Bruno, S.P. Ellner, I. Vu, K.Kim, C.D. Harvell. Impacts of aspergillus on sea fan coral demography: modelling a moving target (Ecological Monographs, in review).

S.P. Ellner, L.E. Jones, L.D. Mydlarz, C.D. Harvell. 2007. Within-host disease ecology in the sea fan Gorgonia ventalina: modeling the spatial immunodynamics of a coral-pathogen interaction. American Naturalist 170, E143 − E161.

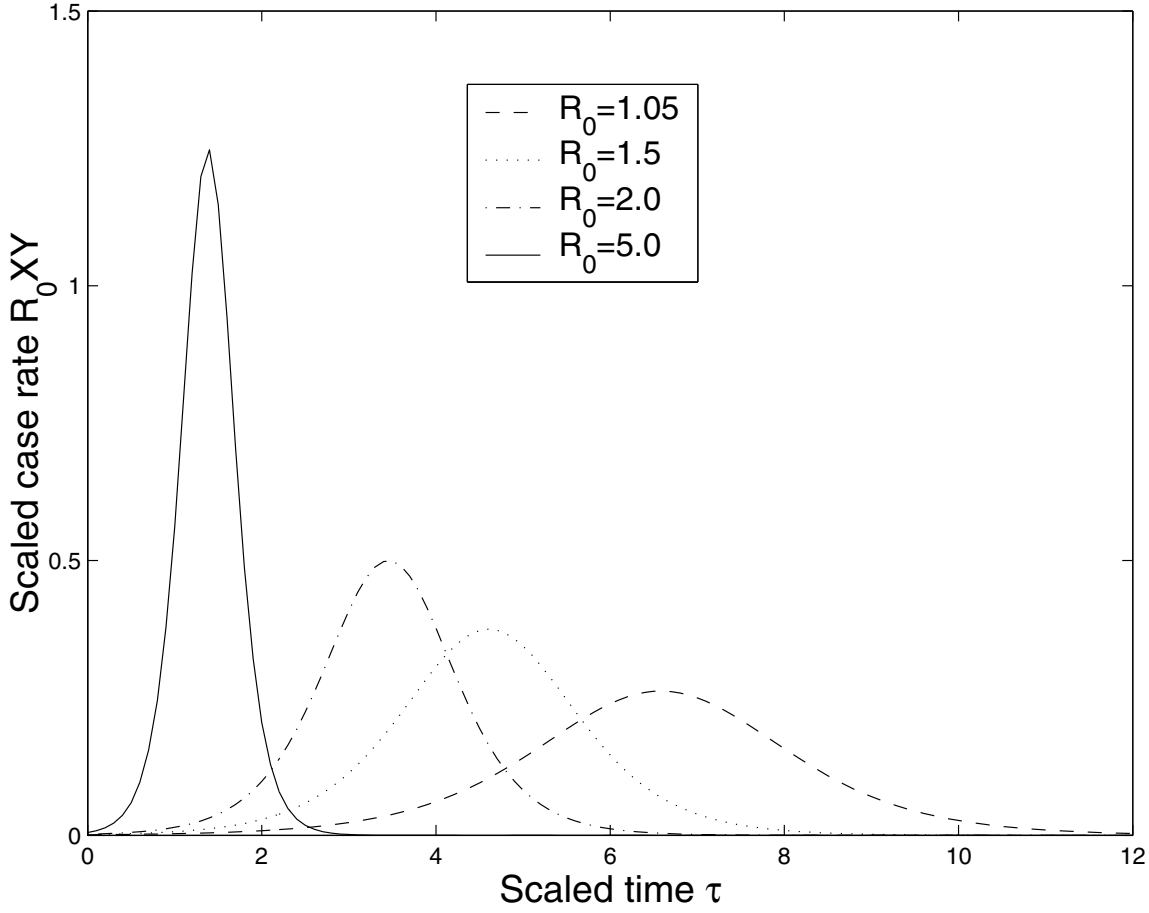
Sir Ronald Ross (1857-1932). Nobel Prize in Medicine (1902) for determining the life cycle of the malaria parasite and the role of mosquitos in malaria transmission.

DR. RONALD ROSS, C.B., THE HERO OF THE MOSQUITO THEORY OF MALARIA.

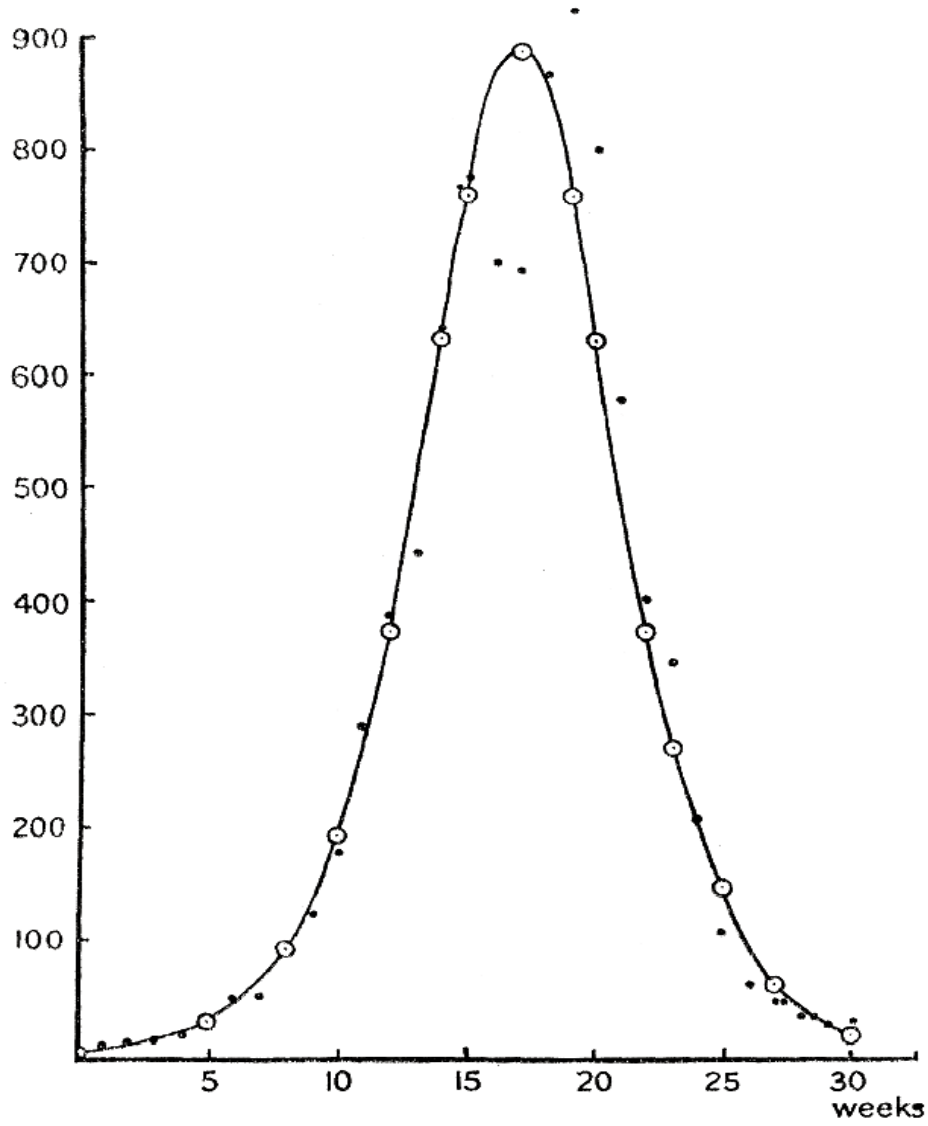
Examples of epidemic curves



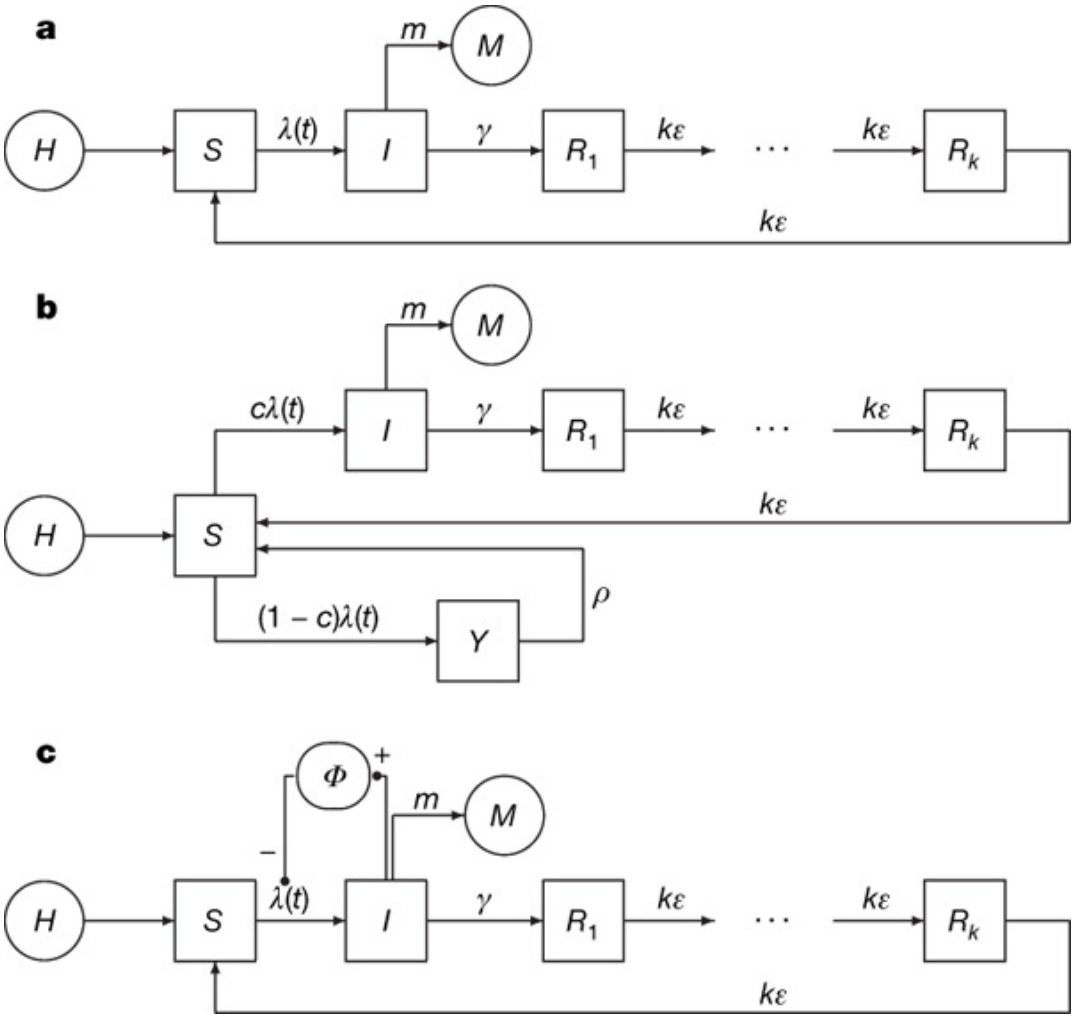
Epidemic curves in Kermack-McKendrick model for disease without recovery.



Deaths per week from plague in the island of Mumbai, December 17, 1905 to July 21, 1906 (from Kermack and McKendrick 1927)



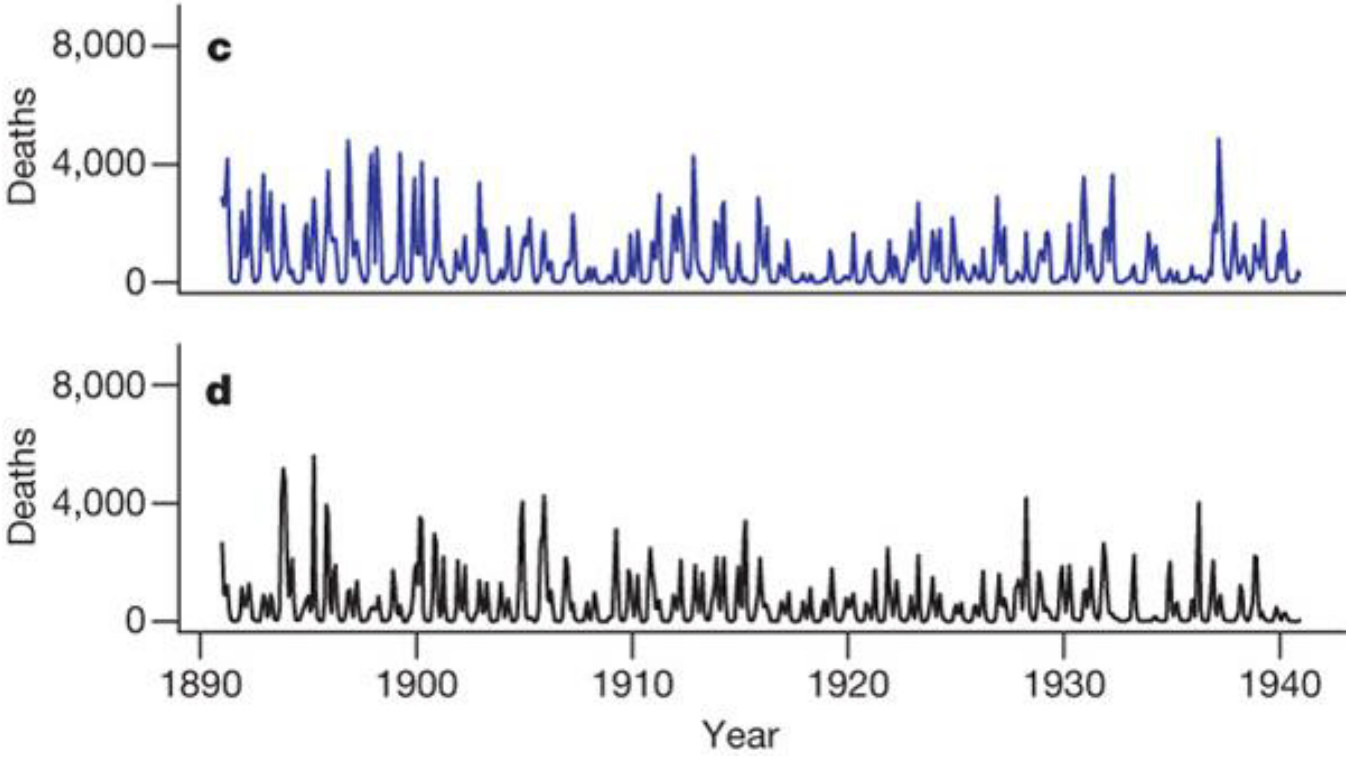
Aaron A. King, Edward L. Ionides, Mercedes Pascual, Menno J. Bouma. 2008. Inapparent infections and cholera dynamics. Nature 454, 877-880.



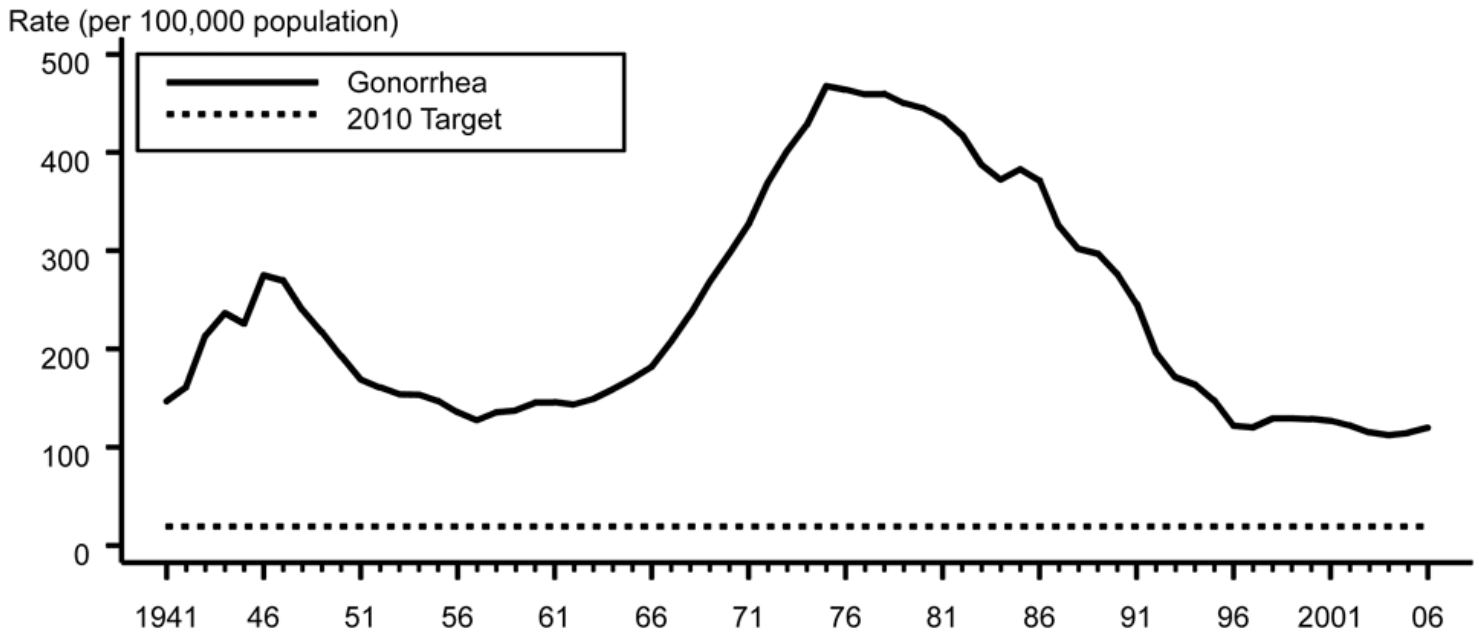
(a) SIRS model
(b) Two-path model (inapparent (Y) and serious (I) infections)
(c) Environmental-phage model
Force of infection $\lambda(t)$ includes human-to-human transmission and an environmental reservoir.

Aaron A. King, Edward L. Ionides, Mercedes Pascual, Menno J. Bouma. 2008. Inapparent infections and cholera dynamics. Nature 454, 877-880.

Simulated and actual cholera deaths



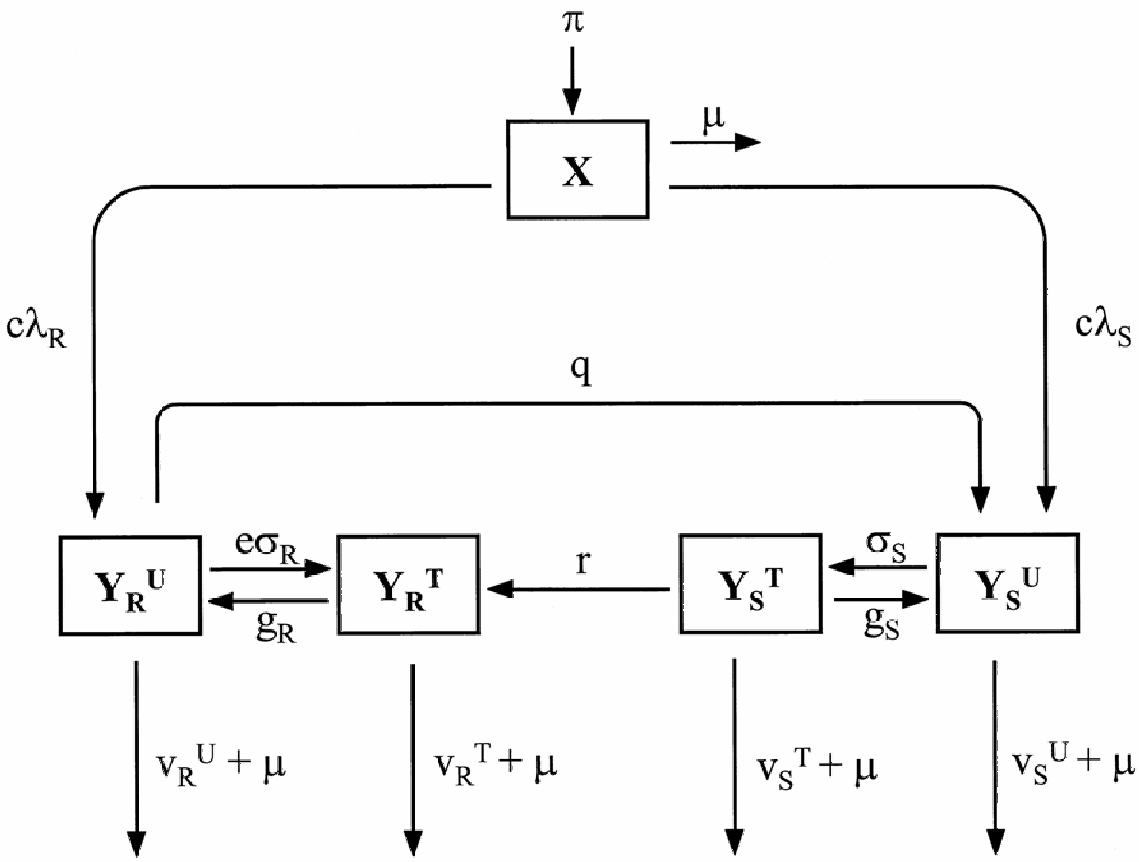
Gonorrhea rate (cases per 100,000 population) in the US.
Source: CDC 2006 Sexually Transmitted Diseases Surveillance Report, at
`www.cdc.gov/std/stats/toc2006.htm`.



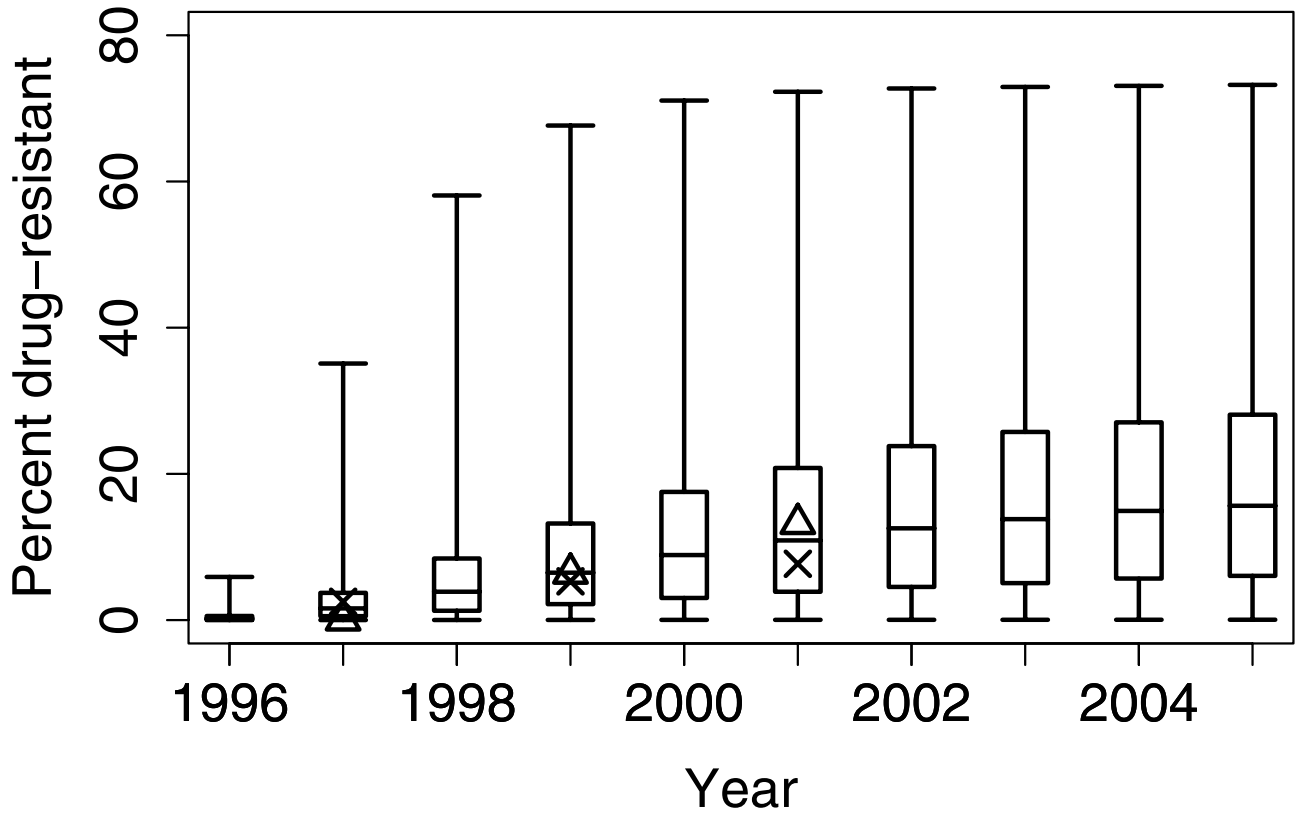
Blower et al. (2000) model for emergence of ARV-resistant HIV

X =Susceptible

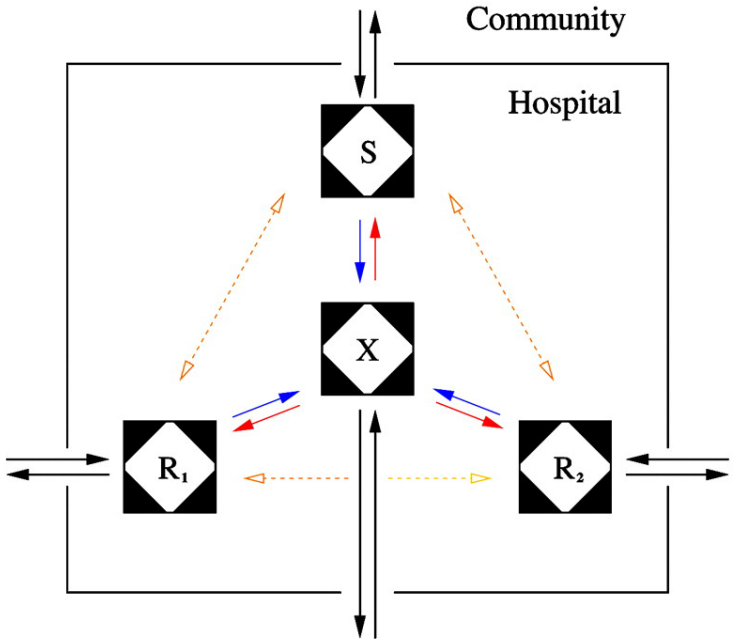
Y =infected: **T**reated or **U**ntreated, **S**usceptible or **R**esistant Strain



Model predictions versus empirical data (243 newly infected individuals in San Francisco with no prior exposure to ARV drugs). Redrawn from Blower et al. (2003)
Boxes enclose interquartile range of model simulations with bar at the median
Triangles: estimated fraction resistant to non-nucleoside reverse transcriptase inhibitor
Crosses: estimated resistance to protease inhibitor



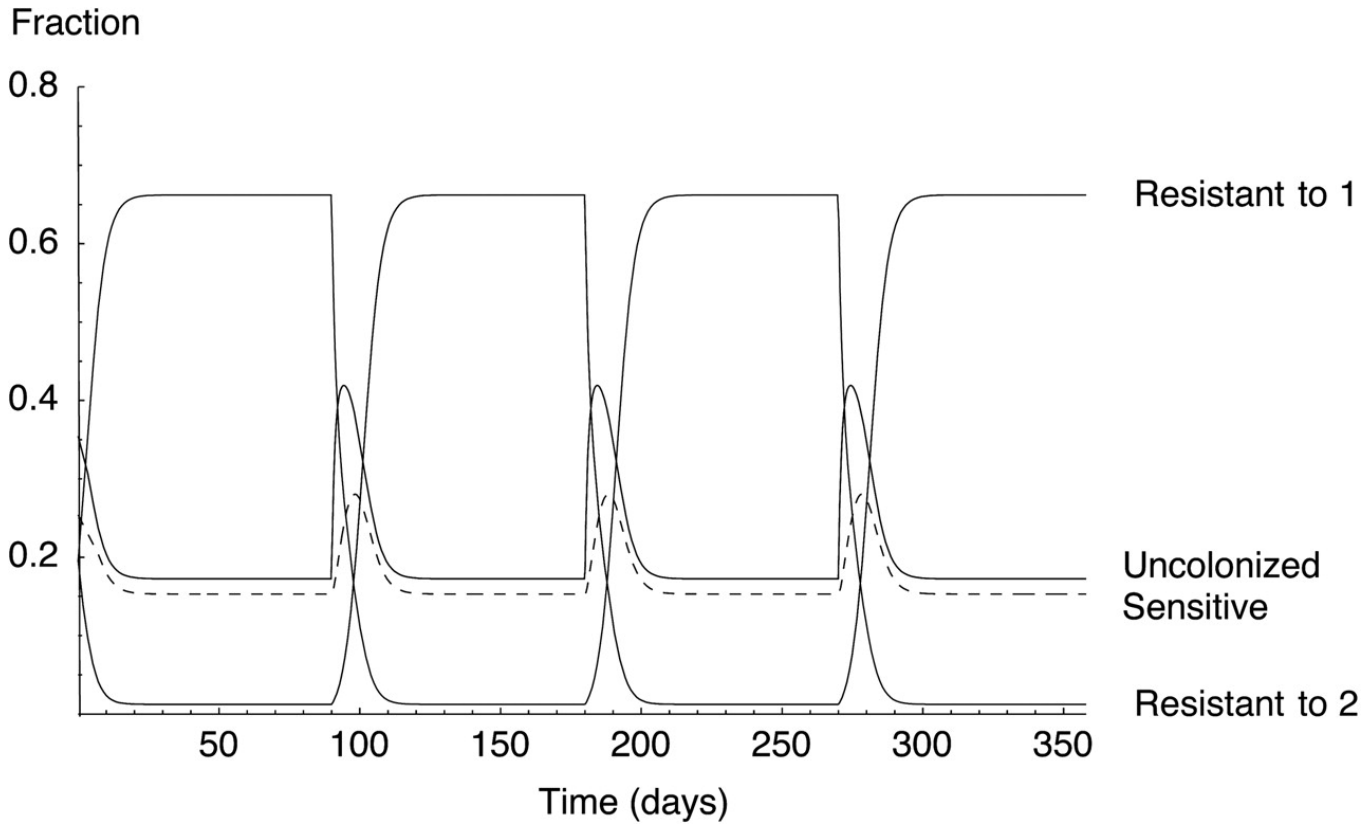
C. T. Bergstrom, M. Lo, and M. Lipsitch. 2003. Ecological theory suggests that antimicrobial cycling will not reduce antimicrobial resistance in hospitals. PNAS 101: 13285-13290.



$$
\begin{aligned}
dS/dt &= (m - S)\,\mu - (\tau_1 + \tau_2 + \gamma)\,S + \beta\,S\,X + \sigma\,\beta\,(c_1 R_1 + c_2 R_2)\,S \\
dR_1/dt &= (m_1 - R_1)\,\mu - (\tau_2 + \gamma)\,R_1 + \beta\,(1 - c_1)\,R_1\,X - \sigma\beta\Big(c_1\,S + (c_1 - c_2)\,R_2\Big)\,R_1 \\
dR_2/dt &= (m_2 - R_2)\,\mu - (\tau_1 + \gamma)\,R_2 + \beta\,(1 - c_2)\,R_2\,X - \sigma\beta\Big(c_2\,S + (c_2 - c_1)\,R_1\Big)\,R_2 \\
dX/dt &= (1 - m - m_1 - m_2 - X)\,\mu + (\tau_1 + \tau_2 + \gamma)\,S + (\tau_2 + \gamma)\,R_1 + (\tau_1 + \gamma)\,R_2 \\
&\quad -\beta\,X\,\Big(S + (1 - c_1)R_1 + (1 - c_2)R_2\Big)
\end{aligned}
$$

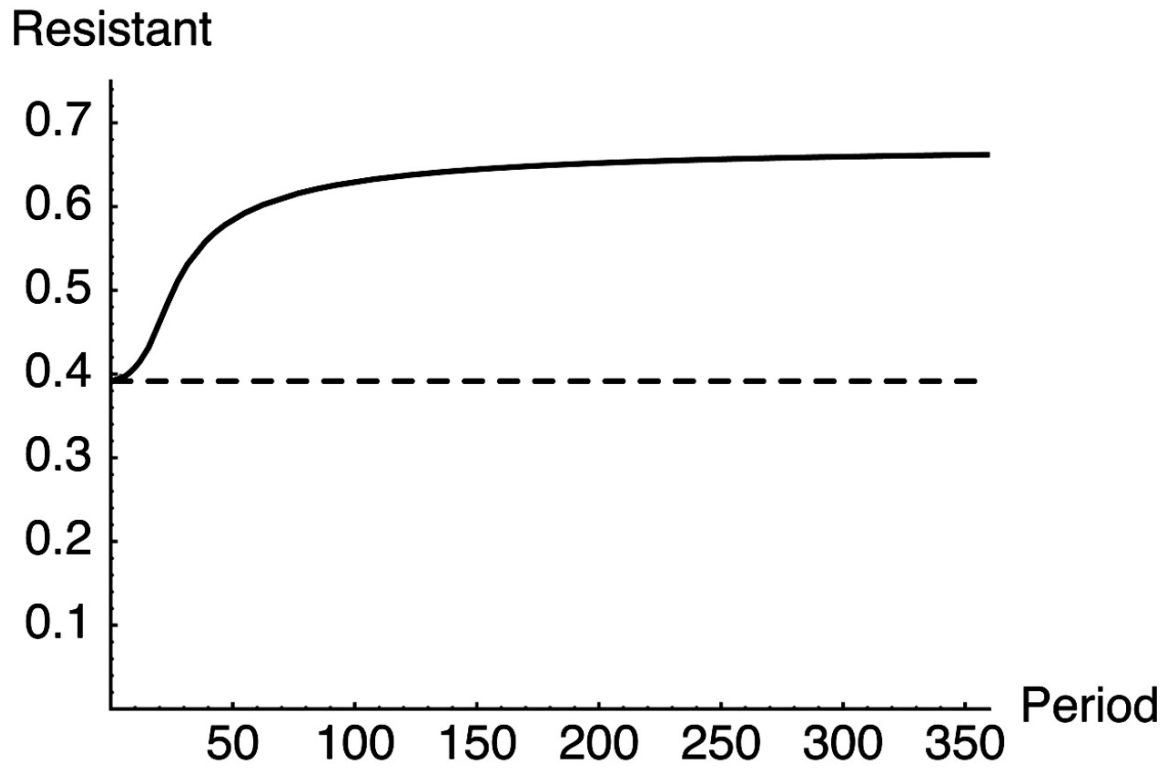
X=No infection, S=Infected w/Susceptible strain, R_i=Infected w/drug i-Resistant strain. Red=infection, yellow=supercolonization, blue=clearance, black=influx and efflux.

C. T. Bergstrom, M. Lo, and M. Lipsitch. 2003. Ecological theory suggests that antimicrobial cycling will not reduce antimicrobial resistance in hospitals. PNAS 101: 13285-13290.



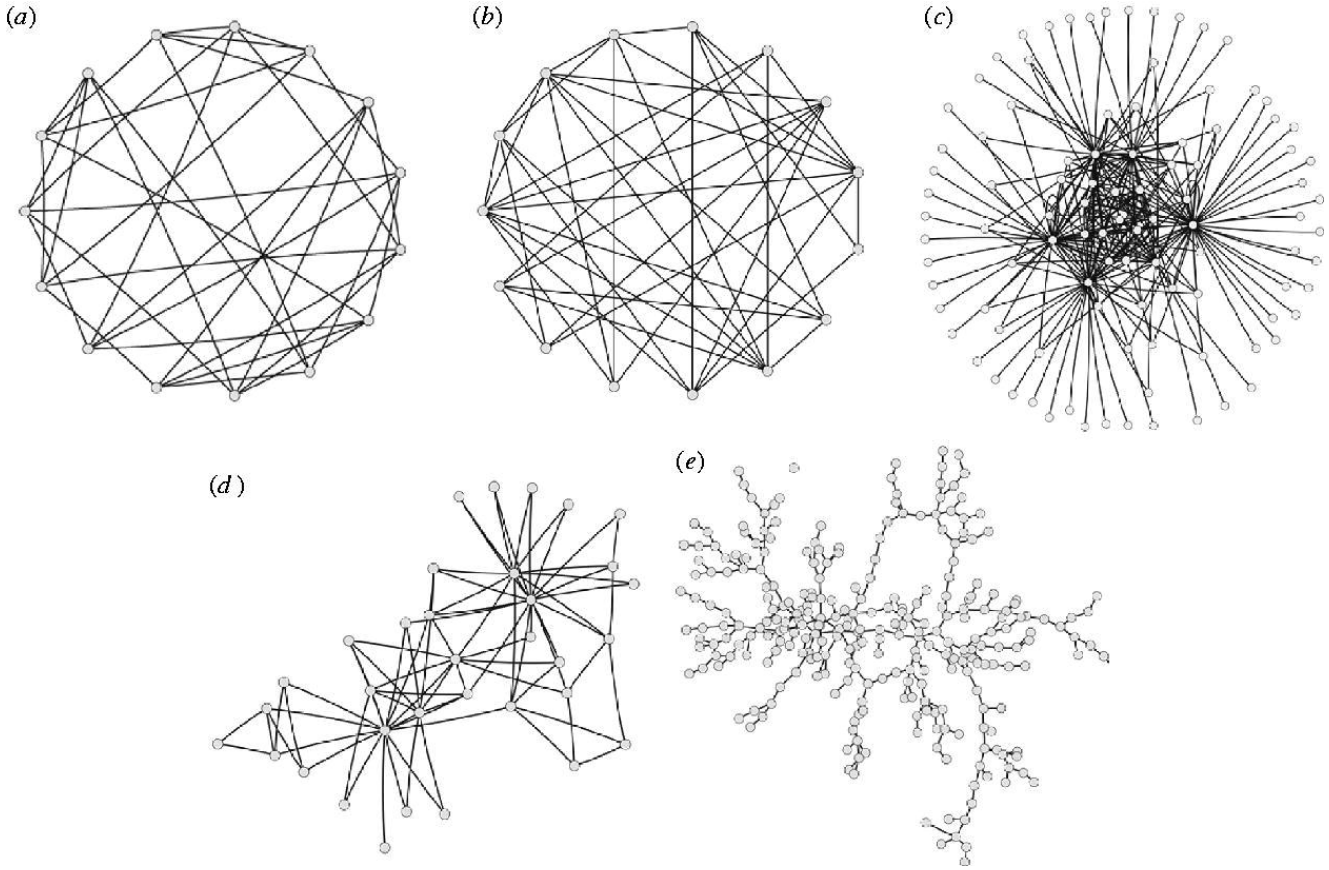
Strain frequencies over time for cycling with drug switch every 90 days and 80% compliance. Parameter values: $\beta = 1, c = 0, Y = 0.03, m = 0.7, m_1 = .05, m_2 = .05, \tau_1 + \tau_2 = 0.5, \mu = 0.1, \sigma = 0.25$.

C. T. Bergstrom, M. Lo, and M. Lipsitch. 2003. Ecological theory suggests that antimicrobial cycling will not reduce antimicrobial resistance in hospitals. PNAS 101: 13285 - 13290.

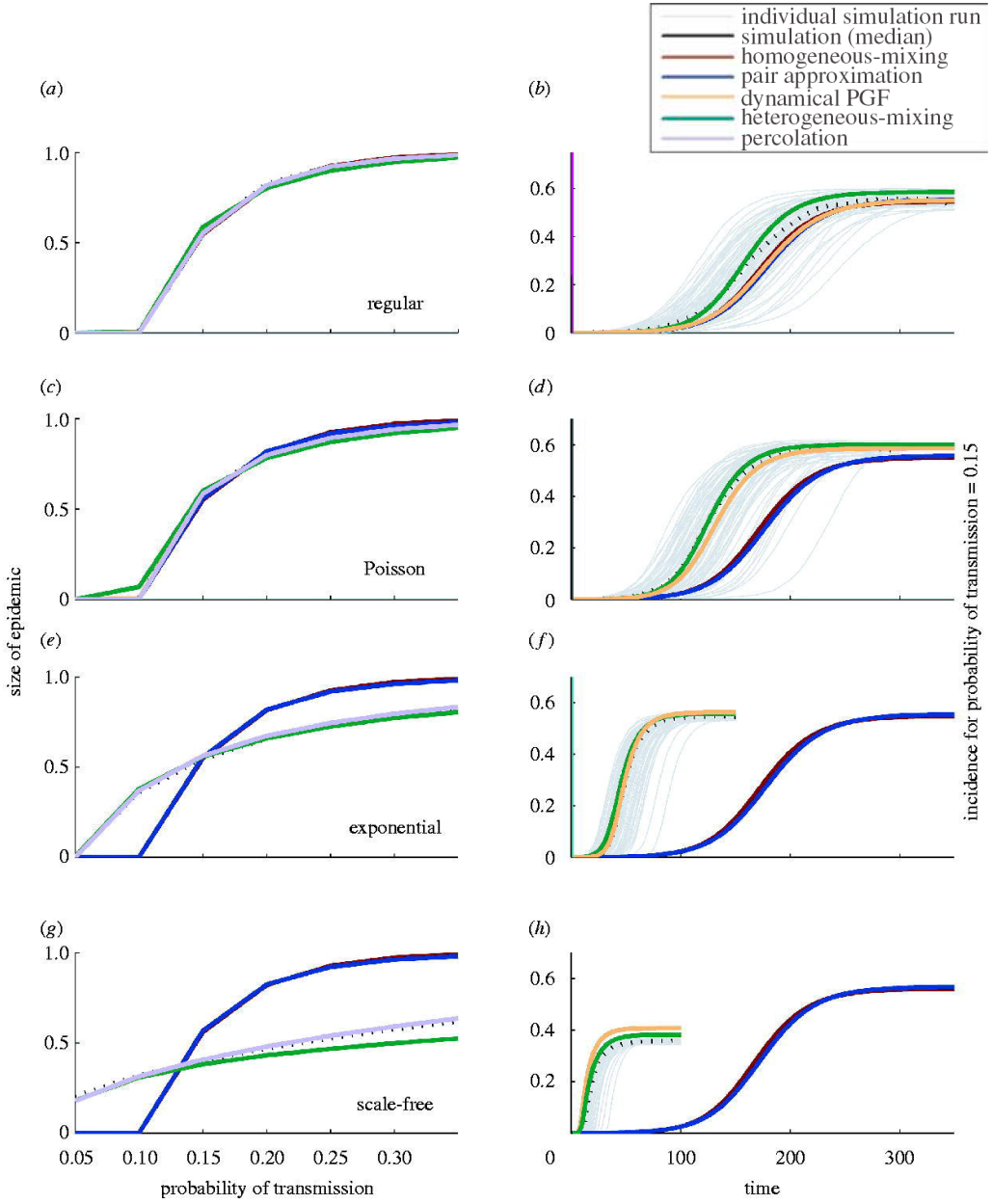


Average total resistance as a function of cycle period, calculated numerically. Solid lines, average total fraction of patients colonized with resistant bacteria under cycling; dashed lines, total fraction of patients colonized with resistant bacteria under a 50-50 mixing regime.

S. Bansal, B.T. Grenfell, L.A. Meyers. 2007. When individual behaviour matters: homogeneous and network models in epidemiology Journal of The Royal Society Interface 4(6): 879 - 891.



(a) Regular random network with 15 nodes and mean=5, (b) Poisson random graph with 15 nodes and mean=5, (c) Scale-free random graph with 100 nodes and mean=5, (d) Zachary Karate Club contact network (Zachary 1977) with 34 nodes and mean=5 and (e) the sexual network for adolescents in a Midwestern US town, with 287 nodes and mean=2. These networks do not contain spatial information; layouts were chosen to facilitate visual comparisons.



From Bansal et al. (2007). Comparison of homogeneous-mixing and network models on random networks. Networks have 10000 nodes and mean degree of 10. (b,d,f,h) Grey lines, individual simulation runs; dotted black line, median of simulation runs. The network-based models are pair approximation (Keeling 1999), percolation (Newman 2002), heterogeneous mixing (Moreno et al. 2002) and dynamical PGF (Volz in press). In (a,c), all curves overlap. In (b), curves for homogeneous-mixing, pair approximation and dynamical PGF overlap. In (d-h), curves for homogeneous-mixing and pair approximation overlap. In (e,g), curves for dynamical PGF and percolation completely overlap. Percolation does not provide dynamical predictions and is thus not graphed in (b), (d), (f) or (h).

Agent-based SIS model

Deterministic ODE model:

$$\begin{aligned} dS/dt &= -\beta(t)SI + \gamma I \\ dI/dt &= \beta(t)SI - \gamma I \end{aligned} \tag{1}$$

Stochastic agent-based model:

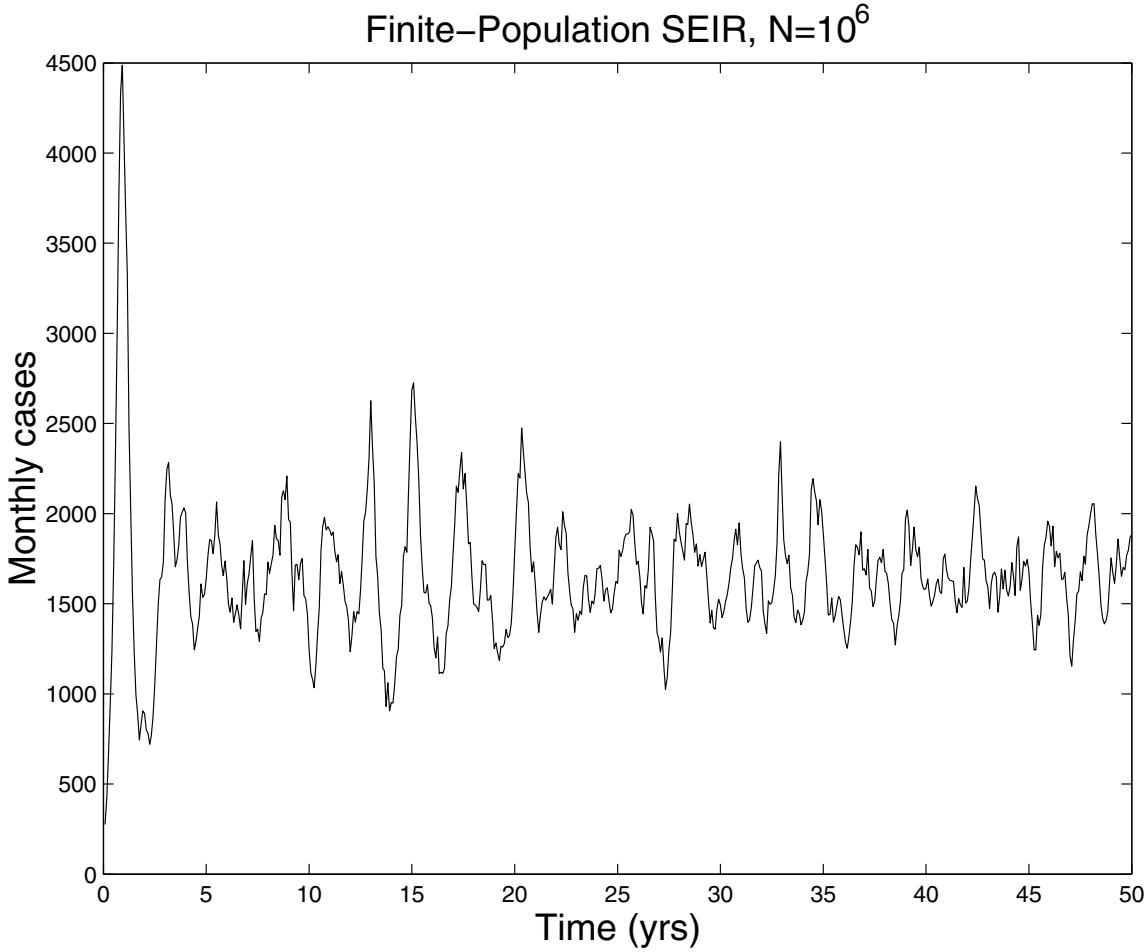
Discretize time into short increments $0, \tau, 2\tau, 3\tau, \cdots$.

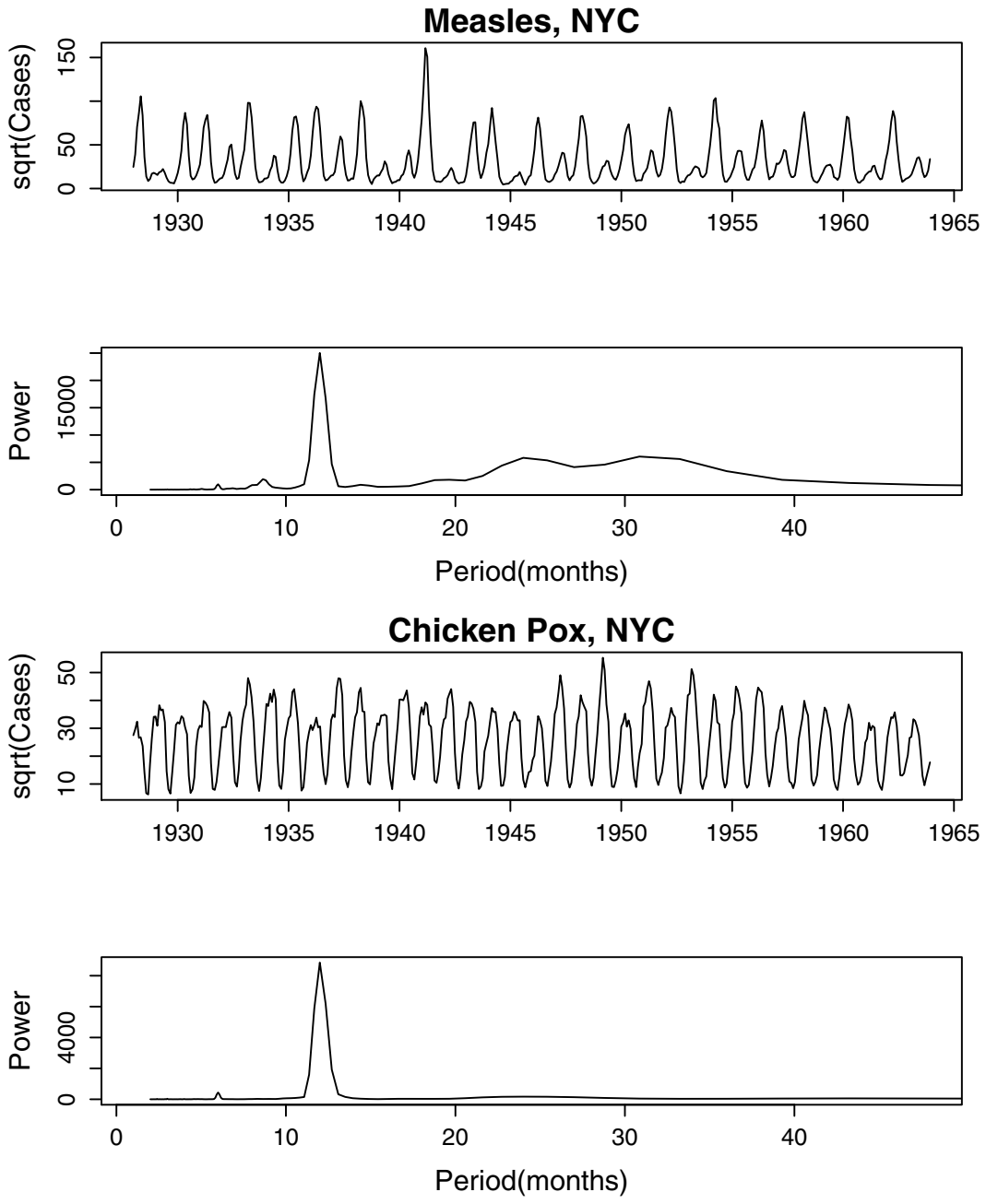
To get from time $t = n\tau$ to time $(n+1)\tau$, see who changes state:

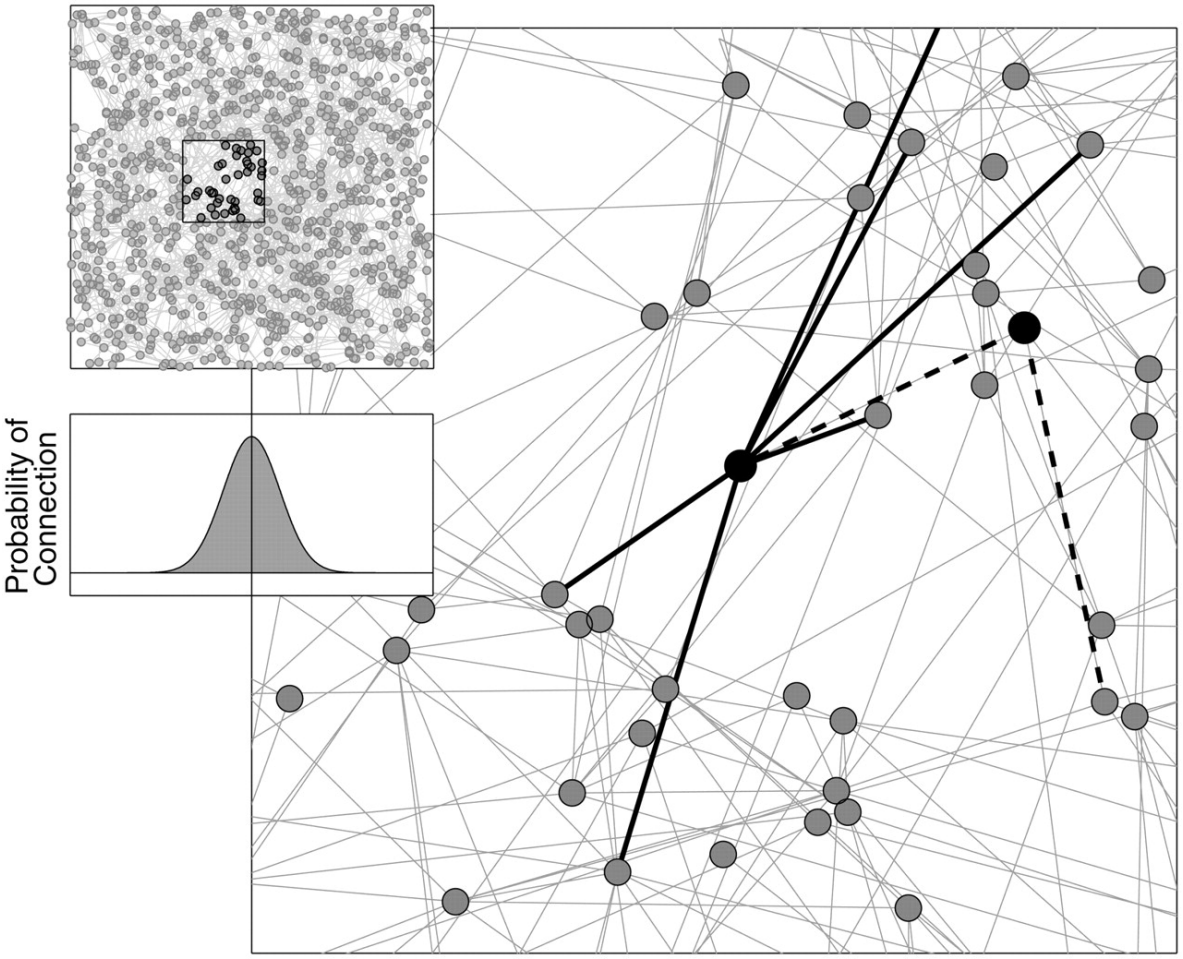
- each individual in S at time t tosses a coin with P(Heads)=$\beta(t)I(t)\tau$
- each individual in I at time t tosses a coin with P(Heads)=$\gamma\tau$
- each individual who got Heads moves to the other compartment, giving new state variables $S(t+\tau), I(t+\tau)$

Exact (continuous-time) simulation also possible, by *Gillespie algorithm*

Finite-population SEIR model with parameters for pre-vaccination measles in a city of 1 million, without seasonal variation



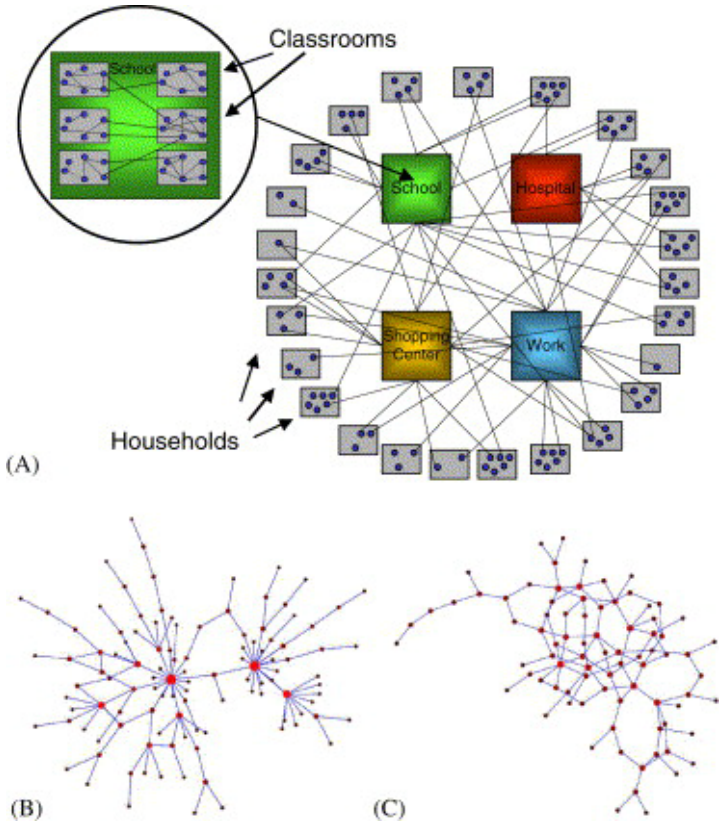

Measles, NYC
sqrt(Cases)
0
50
150
1930
1935
1940
1945
1950
1955
1960
1965
Power
0
15000
0
10
20
30
40
Period(months)
Chicken Pox, NYC
sqrt(Cases)
10
30
50
1930
1935
1940
1945
1950
1955
1960
1965
Power
0
4000
0
10
20
30
40
Period(months)



An example of the full contact network (Upper Inset) and a magnified section (main graph). Individuals are placed at random at an average density of one per unit area. The probability kernel determining the connection of two nodes (shown at the same scale as the full network in the Lower Inset) is the sum of a localized Gaussian (whose height and breadth may be specified) and a fixed probability representing global connections.

L.A. Meyers, B. Pourbohloul, M.E.J. Newman, D.M. Skowronski, R. C. Brunham. 2005. Network theory and SARS: predicting outbreak diversity. Journal of Theoretical Biology 232: 71 81.

Schemata of: (A) urban, (B) power law, and (C) Poisson networks.



Epstein JM, Goedecke DM, Yu F, Morris RJ, Wagener DK, et al. 2007 Controlling Pandemic Flu: The Value of International Air Travel Restrictions. PLoS ONE 2(5): e401.

Table S1 – Parameters and Values for the Model that Do Not Vary over Time

No.	Parameter Name	Description	Type	Default Value
2	nCities	Total number of cities in the model	integer	155
3	initExposedCity	Index # of the city initially exposed to the disease	integer	53
4	initExposedNumber	Number of individuals initially exposed to the disease	integer	100
15	alpha	Fraction of population that is initially susceptible	real	1
16	beta	Fraction of newly infectious persons reported to the health registry	real	0.3
17	R0	Basic reproduction number of virus	real	1.7
18	tau1	Maximum day of the Exposed period	integer	1
19	tau2	Maximum day of the Infectious period	integer	7
20	deathRate	Fraction of infected persons who die	real	0
21	interveneSequentially	Controls whether interventions are sequential or simultaneous	Boolean	true
22	interventionThreshold	Threshold of newly Infectious at which to apply interventions	real	1000
23	restrictTravel	Controls whether travel intervention is applied	Boolean	true
24	restrictionLevel	Fraction by which to restrict travel	real	0.90
25	quarantine	Controls whether quarantine is applied	Boolean	false
26	quarantineFraction	Fraction of Infectious who may be quarantined before recovery	real	0.5
27	vaccinateOneTime	Controls whether one-time vaccination occurs	Boolean	true
28	vaccinationFractionOneTime	Fraction of susceptibles to be vaccinated when one-time vaccination occurs	real	0.1
29	vaccinateDaily	Controls whether daily vaccination occurs	Boolean	false
30	vaccinationFractionDaily	Fraction of Susceptibles to be vaccinated daily	real	0.001
31	randomTravel	Controls whether travel is random	Boolean	true
32	randomContact	Controls whether number of infectious SI contacts is random	Boolean	true
34	minSF	Minimum value of seasonal scale factor	real	0.1
35	maxSF	Maximum value of seasonal scale factor	real	1.0
36	minLatN	Northern boundary of equatorial zone	real	23.5 °
37	maxLatN	Northern boundary of increasing northern seasonality	real	66.5 °
38	minLatS	Southern boundary of equatorial zone	real	- 23.5 °
39	maxLatS	Southern boundary of increasing southern seasonality	real	- 66.5 °

Partial list of parameters for a VORTEX model.

Required (all models)	
Age at first breeding α	males & females
Mating system	
Maximum longevity	
Mean % of adults breeding each year	males & females
Variance in % breeding each year	males & females
Maximum litter size M	
Litter size distribution	$a_j, j = 0, 1, \cdots M$
Annual mortality	$p_x, x = 0, 1, \cdots, p$, males & females
Magnitude of environmental variability	in survival, in fecundity
Correlation of environmental variability between survival and fecundity	
% inbreeding depression due to recessive lethal alleles	
Optional	
Frequency of catastrophes	
Effect of catastrophes	On survival, on reproduction
Number of populations	
Which sexes disperse?	
Which ages disperse?	
Survival during dispersal	
% of individuals dispersing	
Effects of population density	On survival, fecundity, dispersal,

Advantages of network and other agent-based models

1. Easy to model individual differences in
   - Spatial location
   - Disease parameters (susceptibility, infectivity, duration)
   - Which (and how many) individuals are regularly and persistently "linked"
   - Behavioral "rules"
2. Easy to model stochasticity (individual "coin-tossing")
3. Individuals often can be observed directly: go straight from data to a model based on observed *rules*, rather than *rates* resulting from the rules.

Disadvantages (=research projects)

1. Realism $\Rightarrow$ model can only be studied computationally. We can see what the model does, but it's hard to know why: what are the (analogs of) equilibria, eigenvalues/vectors, low-dimensional attracting surfaces?
2. *Lots* of assumptions and parameters to estimate.
3. What is $\dfrac{\partial R_0}{\partial \text{rule}}$? How to know which assumptions/parameters determine important predictions?
4. How can a model be simplified for better understanding, while preserving its essential properties?

Without answers to 3. and 4., 2. becomes a big problem: you have to make up a whole lot.