Stochastic models for the spread of infection

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sto·chas·tic  (st -k s t k)

adj.
1. Of, relating to, or characterized by conjecture; conjectural.

2. Statistics
   a. Involving or containing a random variable or variables: stochastic calculus.
   b. Involving chance or probability: a stochastic stimulation.

[Greek stokhastikos, from stokhast s, diviner, from stokhazesthai, to guess at, from stokhos, aim, goal; see stegh- in Indo-European roots.]
Basic elements of the stochastic model

• System elements
  – Persons/animals, pathogens, vectors

• States
  – e.g., properties of persons
    • S, I, R or other indicators of infection status
    • Demographic attributes
    • Activity levels
    • Additional heterogeneity

• Rates
  – Movement from one state to another: Probabilistic
Deterministic vs. stochastic models

Simplest example: Epidemic growth in a very large population

- States: only I is tracked, population has an infinite number of susceptibles
- Rates: only $\lambda$, the force of infection

<table>
<thead>
<tr>
<th></th>
<th>Deterministic</th>
<th>Stochastic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incidence</td>
<td>$\frac{\partial I}{\partial t} = \lambda I$</td>
<td>$p(\Delta I_t = x</td>
</tr>
<tr>
<td>Prevalence</td>
<td>$I_t = I_0 e^{\lambda t}$</td>
<td>$\int_{t=0}^{T} \Delta I_t , dt$</td>
</tr>
</tbody>
</table>
What does this stochastic model mean?

\[ p(\Delta I_t = x \mid I_t) \] Depends on the model you choose for \( p(\bullet) \)

Example: Poisson – simple constant rate of new events

\[ p(\Delta I_t = x \mid I_t) = \frac{\mu^x e^{-\mu}}{x!} \]

mean: \( E(\Delta I_t) = \mu \)

variance: \( Var(\Delta I_t) = \mu \)

\[ \mu = \lambda I_t \Delta t \]

note that \( \frac{\mu}{\Delta t} = \lambda I \) the expected number of new cases in an interval

is the deterministic model prediction
Example: simple R code for this model

```r
n <- 70         # the number of time steps
delta.t <- 0.01  # step size. Total time on n*delta.t
lambda <- 5     # rate per unit time
p <- rep(0,n)   # to store the prevalence
i <- rep(0,n)   # to store the incidence
p[1] <- 1       # initial prevalence

# set up a plot
plot(x=delta.t*(1:n),y=1:n, ylim=c(1,20), type="n", xlab="time", ylab="number of infections")

# step through time
for(k in 1:(n-1)){
    i[k] <- rpois(n=1,lambda=lambda*p[k]*delta.t)
    p[k+1] <- p[k]+i[k]
    points(x=delta.t*k,y=p[k+1],pch=19,cex=0.2,col=2)
}

# plot the exponential deterministic model
lines(x=delta.t*(1:n), y=exp(lambda*delta.t*(0:(n-1))), col=2)
```

This, and the rest of the code, is in the simPoisson.r file on the symposium website
Is the stochastic-deterministic relation simple?

• Will the stochastic mean ever equal the deterministic mean?
  – Yes, but only for the linear model
  – The variance of the empirical stochastic mean depends on the number of repetitions

• Can you represent variation in deterministic simulations?
  – Sensitivity analysis shows how outcomes depend on parameters
  – Parameter uncertainty can be incorporated via Bayesian methods
  – But true stochastic variation can not be represented.

• Will stochastic variation always be the same?
  – No, can specify many different distributions with the same mean
  – Process may have the same mean, but different variance
    • Negative binomial
    • Geometric
    • Many other possibilities
Focus: The influence of partnerships on epidemics

• Two fundamental questions in epidemic modeling
  – Epidemic thresholds ($R_0$ or not $R_0$, that is the question)
  – Prevalence disparities

• Will examine how partnerships affect both
Epidemic thresholds

Most basic question: can transmission be sustained in a population?

- Depends on $E(\text{transmissions})$ from the first infected case: $R_0$
  - There is a threshold at $R_0 = 1$
  - Under (many) simplifying assumptions, $R_0 = \beta c D$

- The threshold means that epidemic potential is highly nonlinear
- Also means that small changes can have large impacts
The simplifying assumptions for $R_0 = \beta c D$

- Look at the dimensional analysis:

$$\beta c D = \frac{\text{transmission}}{\text{contact}} \times \frac{\text{contacts}}{\text{time}} \times \text{time}$$

  - Implies every contact is independent – i.e., no partnerships
  - Might work for vector, water, and airborne infections (malaria, cholera and flu)
  - But not for sexually transmitted infections, as contact is often with the same person

- Can we represent partnerships in the expression for $R_0$?

$$\tau p D = \frac{\text{transmission}}{\text{partnership}} \times \frac{\text{partnerships}}{\text{time}} \times \text{time}$$

... where $\tau = 1 - (1-\beta)^c$
First: $\beta$ influences transmission *within* partnerships

As in Susie Cassel’s model, the probability of transmission within a partnership is a function of both $\beta$ and $c$:

$$1 - (1-\beta)^c$$
Second: small changes in p can have threshold impacts

<table>
<thead>
<tr>
<th>Number of Partners</th>
<th>Largest components</th>
<th>Bicomponents in red</th>
<th>In largest component:</th>
<th>In largest bicomponent:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>2%</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>10%</td>
<td>1%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>41%</td>
<td>5%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>64%</td>
<td>15%</td>
</tr>
</tbody>
</table>

Source: Morris, Goodreau and Moody 2007
Implication: don’t need core groups or “superspreaders” to create generalized epidemics

- High degree hubs
  - Core groups and scale free networks build in this kind of connectivity
  - A small number of extremely active persons, with many sequential partners in a short period

- Low degree linking
  - Concurrent partnerships build connectivity this way
  - Not many partners, maybe one on the side, so partnership intervals overlap, and sequence no longer protects

Both of these configurations have the same number of persons and partnerships
  - The same average contact rate, but a different distribution
  - Very different prevention implications (targeting, and relational context)
Third: The sequencing of partners is critical

The difference between serial monogamy and concurrent partnerships

Same contact rate (5/yr), but the timing and sequence of partnerships is different

Not just a matter of reducing the interval between partnerships to 0…
Why concurrency matters

1. Removes the protection of sequence

   Backward path: New chain of infection
   Forward path: Less time lost locked in partnership

2. Larger components in the network

   ... this is why the woman with one partner gets infected
Implication:
Concurrent may explain disparities in HIV/STI

% of Men reporting concurrent partners

<table>
<thead>
<tr>
<th>Observation interval</th>
<th>Uganda</th>
<th>US: NHB</th>
<th>US: Other races</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cross-section</td>
<td>14.1</td>
<td>8.5</td>
<td>3.5</td>
</tr>
<tr>
<td>In last 1mo</td>
<td>15.2</td>
<td>15.3</td>
<td>5.6</td>
</tr>
<tr>
<td>In last 2mo</td>
<td>20.0</td>
<td>20.2</td>
<td>8.0</td>
</tr>
<tr>
<td>In last 6mo</td>
<td>21.4</td>
<td>22.7</td>
<td>10.0</td>
</tr>
<tr>
<td>Year</td>
<td>26.9</td>
<td>25.2</td>
<td>12.2</td>
</tr>
</tbody>
</table>

*NHB Non-Hispanic Black

US NHB concurrency is similar to Uganda, though a bit lower in the cross-section.
Network hypothesis for persistent disparities in HIV/STI:

Monogamy retards spread in this group, so prevalence stays low.

Concurrency amplifies spread in this group, so prevalence rises.

Assortative mixing reduces spread between groups, so a prevalence differential can be sustained over time.

Examples: Sub-Saharan Africa vs. other countries, Racial disparities in US.
Example: Explaining racial disparities in HIV/STI in US

• Stochastic model for network dynamics
  – Tie formation
  – Tie dissolution

• Data from National Longitudinal Survey of Adolescent Health

• Simulation of epidemic potential
  – Comparing concurrency pattern observed in the data
  – To a monogamous population with the same number of partnerships
Data source: Add Health

- National Longitudinal Survey of Adolescent Health

  Cohort of 20,000 respondents, with 3 waves of data
  Wave 3 from 2000-1 contains data on 18-25 year olds:

<table>
<thead>
<tr>
<th>Biomarkers</th>
<th>Local sexual network data</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gonorrhea</td>
<td>Partners in last 5 years</td>
</tr>
<tr>
<td>Trichomoniasis</td>
<td>Age, race, sex of each partner</td>
</tr>
<tr>
<td>Chlamydia</td>
<td>Dates of 1st &amp; last sex (duration)</td>
</tr>
<tr>
<td>HIV</td>
<td>Current status of partnerships</td>
</tr>
</tbody>
</table>
Add Health STI prevalence ratios: non-Hispanic Black to White

<table>
<thead>
<tr>
<th>STI:</th>
<th>Prevalence Ratio</th>
<th>Add Health</th>
<th>CDC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chlamydia</td>
<td></td>
<td>6.5</td>
<td>6.5</td>
</tr>
<tr>
<td>(Miller et al., STD 2005)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gonorrhea</td>
<td></td>
<td>21.8</td>
<td>23.6</td>
</tr>
<tr>
<td>(Miller et al., JAMA 2004)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trich.</td>
<td></td>
<td>5.9</td>
<td>*</td>
</tr>
<tr>
<td>(Miller et al., JAMA 2004)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HIV</td>
<td></td>
<td>22.4</td>
<td>20</td>
</tr>
<tr>
<td>(Morris et al., AJPH 2006)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Add Health Data: Concurrency

These are the “momentary degree distributions” that measure concurrency.

About 4% of whites report concurrent partners, with little difference between sexes.

About 12% of black male and 7% of black females do.

The means for non-isolates are:

1.06, 1.08 for WF WM
1.12, 1.26 for BF BM
Add Health Data: Mixing patterns by race

As with US adults, mixing is strongly assortative.

<table>
<thead>
<tr>
<th>Men's reports</th>
<th>White</th>
<th>Black</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>White</td>
<td>85.4</td>
<td>1.7</td>
<td>12.9</td>
</tr>
<tr>
<td>Black</td>
<td>12.7</td>
<td>77.5</td>
<td>9.7</td>
</tr>
<tr>
<td>Other</td>
<td>26.7</td>
<td>4.3</td>
<td>69.0</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Women's reports</th>
<th>White</th>
<th>Black</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>White</td>
<td>81.7</td>
<td>5.4</td>
<td>12.9</td>
</tr>
<tr>
<td>Black</td>
<td>3.3</td>
<td>89.6</td>
<td>7.1</td>
</tr>
<tr>
<td>Other</td>
<td>19.0</td>
<td>8.6</td>
<td>72.4</td>
</tr>
</tbody>
</table>
Add Health Data: Partnership length

### Means and Medians for Survival Time

<table>
<thead>
<tr>
<th>Race</th>
<th>Estimate</th>
<th>Std. Error</th>
<th>Lower Bound</th>
<th>Upper Bound</th>
<th>Estimate</th>
<th>Std. Error</th>
<th>Lower Bound</th>
<th>Upper Bound</th>
</tr>
</thead>
<tbody>
<tr>
<td>White non-Hispanic</td>
<td>27.040</td>
<td>.373</td>
<td>26.309</td>
<td>27.771</td>
<td>8.000</td>
<td>.220</td>
<td>7.569</td>
<td>8.431</td>
</tr>
<tr>
<td>Black non-Hispanic</td>
<td>30.878</td>
<td>.611</td>
<td>29.681</td>
<td>32.076</td>
<td>12.000</td>
<td>.435</td>
<td>11.147</td>
<td>12.853</td>
</tr>
<tr>
<td>Hispanic</td>
<td>34.542</td>
<td>.817</td>
<td>32.940</td>
<td>36.145</td>
<td>12.000</td>
<td>.613</td>
<td>10.798</td>
<td>13.202</td>
</tr>
<tr>
<td>Asian</td>
<td>30.410</td>
<td>1.228</td>
<td>28.004</td>
<td>32.815</td>
<td>8.000</td>
<td>.723</td>
<td>6.583</td>
<td>9.417</td>
</tr>
<tr>
<td>Other</td>
<td>26.400</td>
<td>2.239</td>
<td>22.011</td>
<td>30.789</td>
<td>8.000</td>
<td>1.537</td>
<td>4.988</td>
<td>11.012</td>
</tr>
</tbody>
</table>

*a.* Estimation is limited to the largest survival time if it is censored.

![Log Survival Function](image-url)
Focus: modeling the probability of forming a partnership

$$\text{logit}(p(x_{ij} = 1 | X^c)) = \theta + \theta_1 \delta(x_1) + \theta_2 \delta(x_2) + ... + \theta_n \delta(x_n)$$

where: $\delta(x) = \text{vector of network change statistics}$

$\theta = \text{vector of model parameters}$

A “change statistic” is the change in the count of a network configuration if a specific dyad state $x_{ij}$ is toggled {0 to 1, or 1 to 0}. For example:
- Number of ties
- Number of nodes with degree 2
- Number of partnerships between persons in the same demographic group
A stochastic simulation to show the impact of concurrency

- Primary focus: the reachable path of infection
- We get this by setting $\beta = 1$.
  - Guarantees all partners of infected nodes will be infected
  - So all transmission is determined by the contact network, partnership duration and sequence

- 10,000 node network, with 2 races, and 10 initial infection seeds
- Simulated over 10 years, no vital dynamics

- Match all of the target Add Health statistics
- Compare to a monogamous population with the same # of partnerships
Basic simulation code

Setup

- Estimate ERGM model for partnership network on Add Health
- Simulate a network with the ERGM estimates
- Seed 10 nodes with infection

Dynamic simulation:

- Transmission step
  - For each discordant pair, transmit infection (since $\beta=1$)
- Pair dissolution step
  - Evaluate all pairs, dissolve with probability = $1/\text{Duration}$
- Pair formation step
  - Draw two nodes, form pair with probability governed by ERGM
  - Repeat until target number of pairs is reached
- Repeat
Basic results

After 10 years (and over many different simulation runs)

• The mean number of cumulative partners for this population is 3-4.
  – 94% have 6 or fewer
  – The maximum observed is 12-15

• The cumulative connected component includes almost everyone
  – Only 97 of the 10,000 nodes are not connected

• But the maximum infection path reaches only 3% to 7% of the population
  – This is the protective effect of partnership duration and sequence
This level of concurrency doubles epidemic potential

Reachable Path ($\beta=1$) by comparison ($\beta=0.01$)
Concurrency is responsible for half of all infections

<table>
<thead>
<tr>
<th></th>
<th>Fraction of transmissions through dyads that are</th>
</tr>
</thead>
<tbody>
<tr>
<td>Monogamous</td>
<td>48.5 %</td>
</tr>
<tr>
<td>Concurrent</td>
<td>51.5 %</td>
</tr>
<tr>
<td>Backward chains</td>
<td>19.5</td>
</tr>
<tr>
<td>Forward acceleration</td>
<td>30.5</td>
</tr>
<tr>
<td>left censored</td>
<td>1.4</td>
</tr>
</tbody>
</table>

Though only about 5% of dyads are concurrent at any time
At the individual level, concurrency increases the likelihood of transmission, not infection.

![Graph 1: Probability of Infection by cumulative degree and concurrency](image1)

![Graph 2: Probability of Transmitting by cumulative degree and concurrency](image2)
Concurrency reduces the time to transmission by about 1/3

\[
\text{Time from infection to first secondary transmission}
\]

- **Concurrency**
- **Monogamy**

Days

0 200 400 600 800
Concurrency increases the racial disparity

Concurrent runs

Final Seroprevalence by Race, Sex, and Network

Observed levels of concurrency

- double the epidemic potential among whites.
- triple the epidemic potential among Blacks
Summary

- **The link between individual behavior and population transmission dynamics is mediated by networks**
  - Partnerships play a larger role than generally recognized
  - Per contact transmission probability reduction operate within partnerships

- **Stochastic models provide detailed control of network simulation**
  - Do you need this level of control? It depends on the system.

- **Concurrency may be a major determinant of HIV/STI transmission**
  - Uganda recognized this years ago, and developed an effective prevention message around “zero grazing”
  - The “B” in ABC
  - A small change may be enough to bring the HIV epidemic under control
The future of HIV is already happening in Uganda

And it is a hopeful future.
Prevalence declines are in fact happening throughout Sub Saharan Africa

Data from UNAIDS 2006 report: 13 countries have prevalence declines
Median decline is 50%
Predates circumcision, and drugs
Acknowledgments

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  – R01 HD41877
  – R01 DA012831

• The center grants that supported the research environment
  – Population centers at Penn State and the University of Washington (NICHD)
  – Center for AIDS Research at UW (NIAID)

• And the data used in this presentation:
  – The National Longitudinal Survey of Adolescent Health (JR Udry, PI, NICHD)
Readings and resources

Introduction to epidemic modeling (compares deterministic and stochastic approaches)


General review of networks and HIV


Tools for network estimation/simulation: statnet

• http://statnetproject.org/
• the statnet program produced the network movie in the application section of the talk