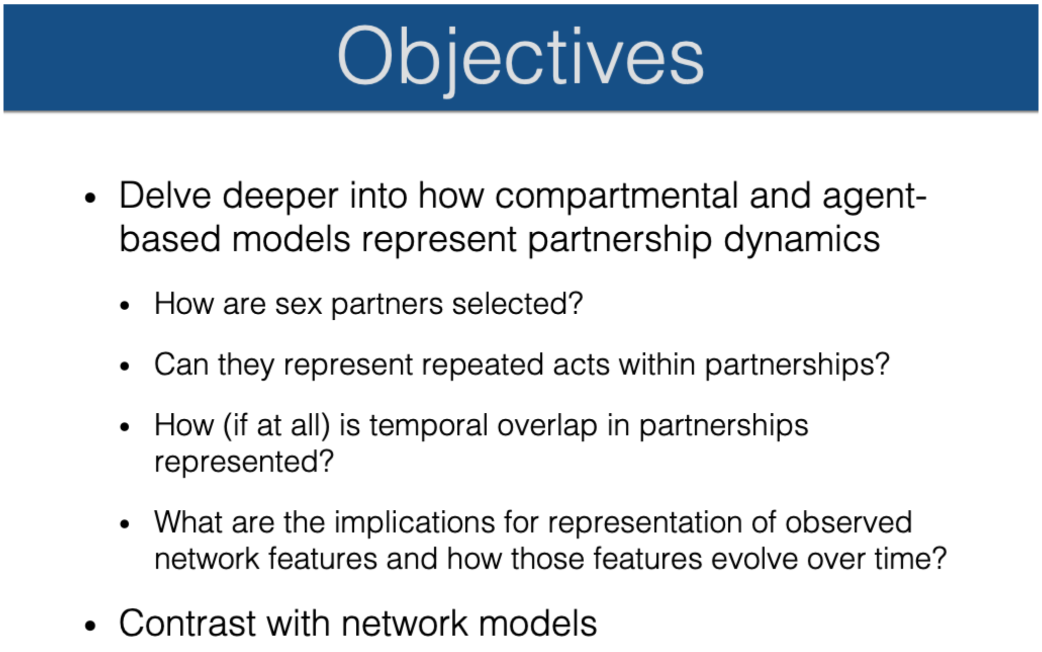
DAY 1 Homework

How are partnerships handled in different modeling frameworks?

NME WORKSHOP

Slides developed by Darcy Rao, PhD



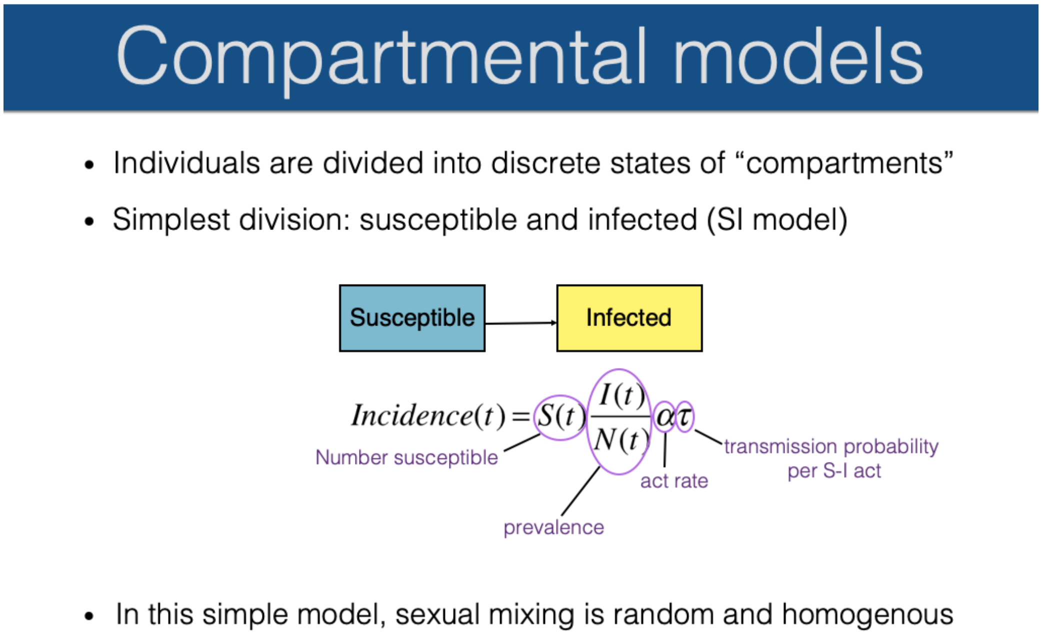
Objectives

- Delve deeper into how compartmental and agent-based models represent partnership dynamics
  - How are sex partners selected?
  - Can they represent repeated acts within partnerships?
  - How (if at all) is temporal overlap in partnerships represented?
  - What are the implications for representation of observed network features and how those features evolve over time?
- Contrast with network models

You've seen 3 modeling frameworks today - deterministic compartmental, agent-based or individual, and network models

A key distinction between them is how they handle partnerships, and how those partnerships fit into the larger network structure

In this presentation, we'll delve a bit deeper into how each of these model frameworks represent partnership dynamics



Compartmental models

- Individuals are divided into discrete states of “compartments”
- Simplest division: susceptible and infected (SI model)

$$Incidence(t) = S(t)\frac{I(t)}{N(t)}\alpha\tau$$

Number susceptible

prevalence

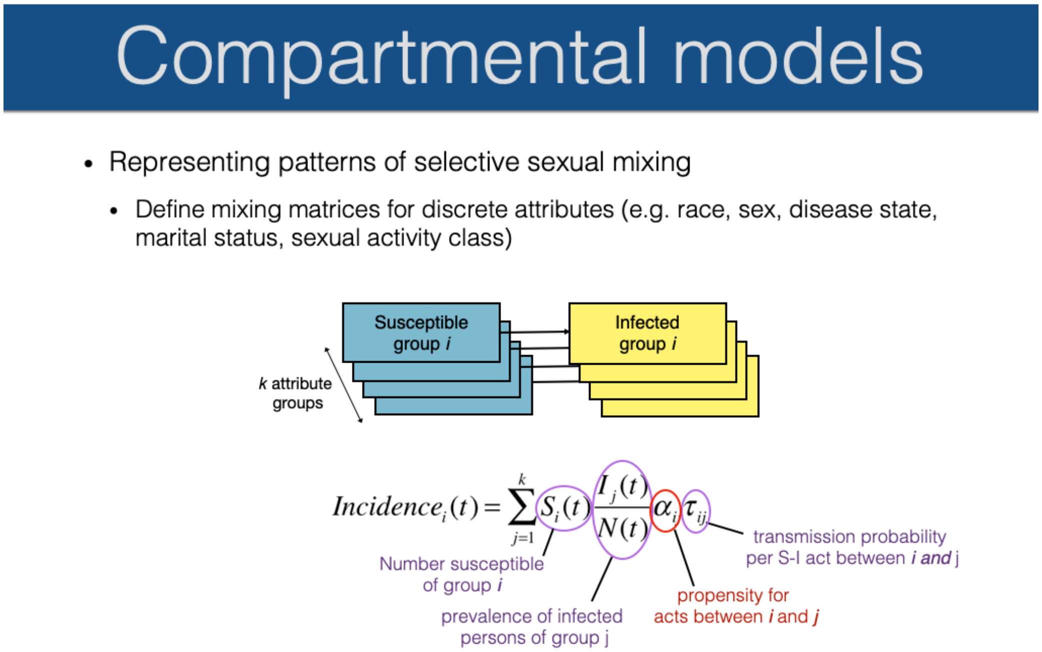
act rate

transmission probability per S-I act

- In this simple model, sexual mixing is random and homogenous

As you learned this morning, compartmental models divide the population into discrete compartments corresponding to disease states or population groups
The simplest division defines a susceptible and an infected compartment, within which individuals are assumed to be homoengous

In this model, sexual mixing is random and the probability of exposure to an infected individual is dependent on the proportion of the population that is infected



Compartmental models

- Representing patterns of selective sexual mixing
  - Define mixing matrices for discrete attributes (e.g. race, sex, disease state, marital status, sexual activity class)

$$Incidence_i(t) = \sum_{j=1}^{k} S_i(t) \frac{I_j(t)}{N(t)} \alpha_i \tau_{ij}$$

Number susceptible of group *i*

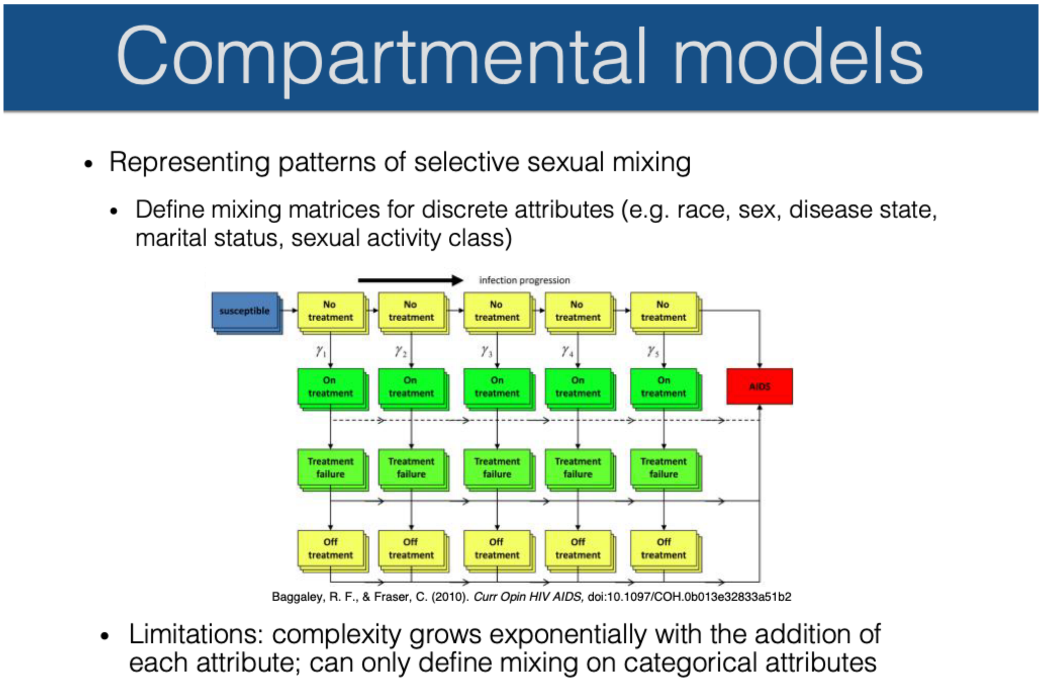
prevalence of infected persons of group j

propensity for acts between *i* and *j*

transmission probability per S-I act between *i and* j

Most compartmental models further divide the population into groups to represent heterogeneity in attributes.
With these divisions, differential patterns of sexual mixing can be defined for each combination of attributes

The probability of infection for a person in group *i* depends on the prevalence of infection in each group *j* with which they might mix and the propensity for acts between individuals of group i and j. In some models, the probability of transmission per SI act may vary depending on the attributes of the groups involved



Compartmental models

- Representing patterns of selective sexual mixing
  - Define mixing matrices for discrete attributes (e.g. race, sex, disease state, marital status, sexual activity class)

Baggaley, R. F., & Fraser, C. (2010). *Curr Opin HIV AIDS*, doi:10.1097/COH.0b013e32833a51b2

- Limitations: complexity grows exponentially with the addition of each attribute; can only define mixing on categorical attributes

The models you will see in the literature will typically divide the population based on several attributes, such as age and sexual risk group, represented by the layers in this example figure, and will divide the infected group into compartments to represent different stages of infection and treatment.

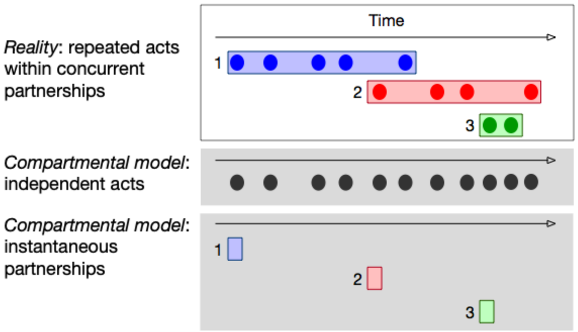
For each additional attribute added to the model, the complexity grows exponentially -

- mixing matrices need to be defined for each possible combination of attributes, and in this case, differing transmission probabilities would need to be defined depending on the stage of infection of the infected person.

Additionally, mixing can only be defined for categorical attributes or those that can be categorized into discrete compartments.

Compartmental models

- In the standard compartmental framework, sexual contact is modeled as independent acts or instantaneous partnerships

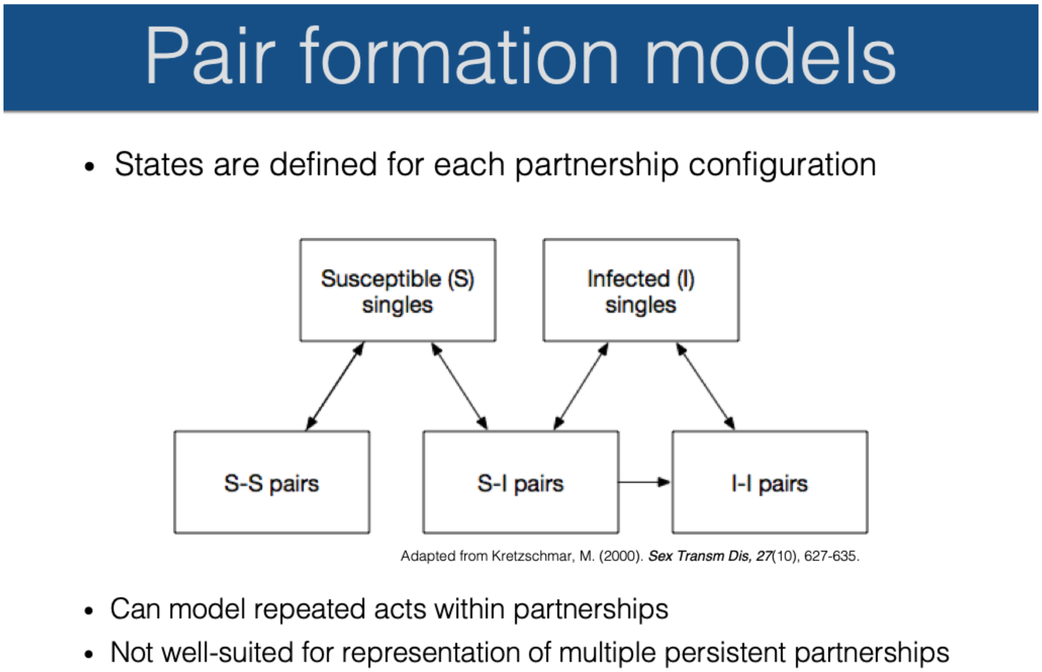


- Neither approach captures temporal overlap in partnerships (concurrency) or multiple acts within partnerships

Another limitation when it comes to representing partnership dynamics is that the standard compartmental model framework cannot represent partnerships with duration.
As we discussed this morning, sexual contact is typically either defined as a single sex act or as an instantaneous partnership

If in reality an individual has repeated acts within multiple concurrent partnerships, a compartmental model will either represent each of the acts as independent or will collapse each partnership to a single point in time.

As we learned in the last lecture, both approaches are limited in the ability to represent transmission potential and the reachable path of transmission



Pair formation models

- States are defined for each partnership configuration

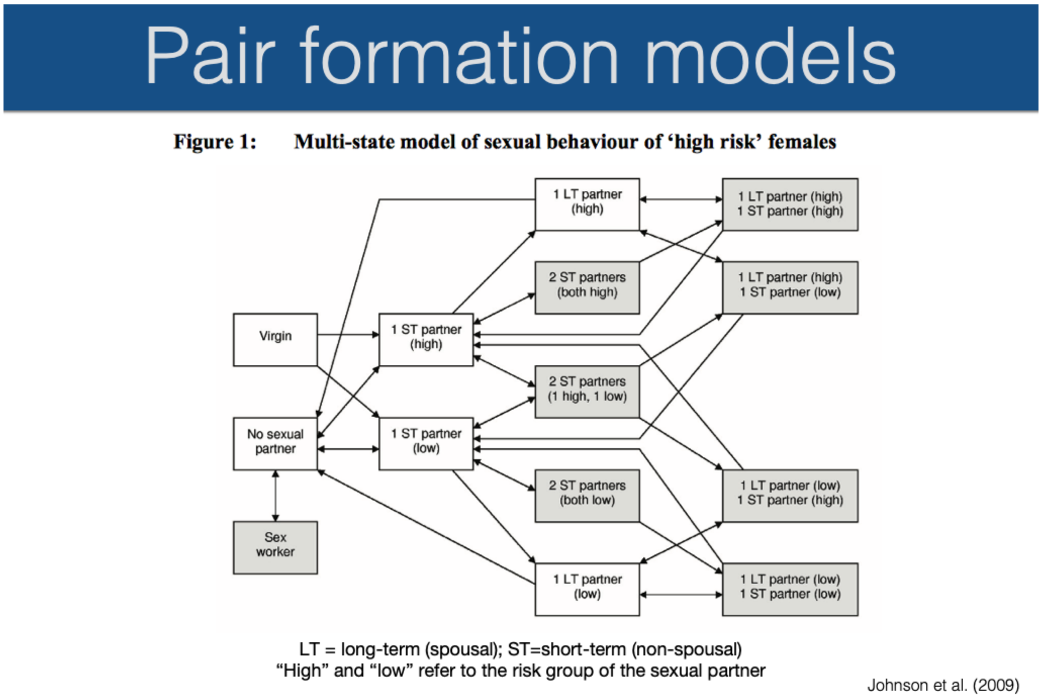
Adapted from Kretzschmar, M. (2000). *Sex Transm Dis, 27*(10), 627-635.

- Can model repeated acts within partnerships
- Not well-suited for representation of multiple persistent partnerships

An exception to this rule is pair formation models, which are an extension of compartmental models that can represent partnerships with duration

States are defined to represent groups of single individuals and different paired configurations, so people can remain in a partnership across time steps

While some pair formation models can represent concurrent partnerships, each additional partnership configuration requires defining new compartments and equations to describe patterns of mixing and transitions into and out of the various states.
As such, these models are not well suited to represent multiple concurrent partnerships with duration - most model up to one partnership with duration per person with the possibility of forming one-time concurrent partnerships



Pair formation models

Figure 1: Multi-state model of sexual behaviour of 'high risk' females

LT = long-term (spousal); ST=short-term (non-spousal)
"High" and "low" refer to the risk group of the sexual partner

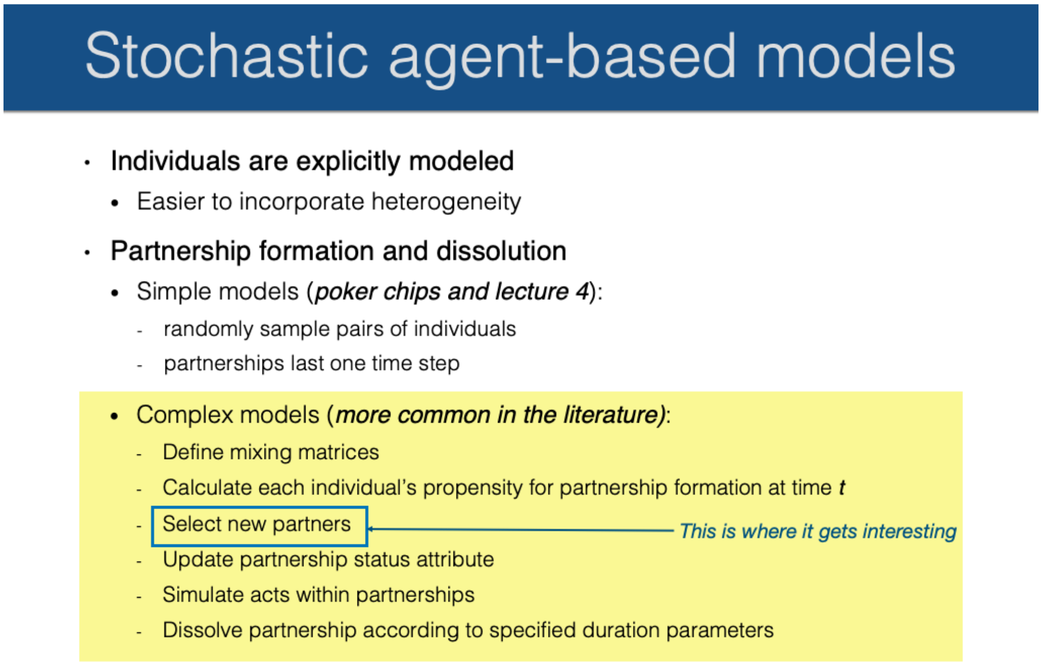
Johnson et al. (2009)

These models quickly become unwieldy, especially if the model is also stratified on attributes such as age or risk group

This is an example of a model in this vein that represents concurrent partnerships, shown in gray.
This model also defines two partnership types (short and long term) and high and low risk groups with differing propensity for concurrency.

Not represented in this diagram is that each state is further divided into 5-year age groups and six HIV states —> **1344 compartments!!**

(Note this is an example of a model that does allow for multiple persistent partnerships - short-term partners have an average duration of 6 months. Johnson refers to it as a "cohort component projection model", not a pair formation model… but it seems to have that structure)



Stochastic agent-based models

- Individuals are explicitly modeled
  - Easier to incorporate heterogeneity
- Partnership formation and dissolution
  - Simple models (*poker chips and lecture 4*):
    - randomly sample pairs of individuals
    - partnerships last one time step
  - Complex models (*more common in the literature)*:
    - Define mixing matrices
    - Calculate each individual's propensity for partnership formation at time *t*
    - Select new partners
    - Update partnership status attribute
    - Simulate acts within partnerships
    - Dissolve partnership according to specified duration parameters

This is where it gets interesting

Better suited to this task are stochastic agent-based, also referred to as stochastic individual models.

We saw some basic individual models with the poker chips, the examples we worked through in EpiModel Web, and the corresponding code to simulate such a model.

In the examples we worked through this morning, partnerships were formed by randomly sampling from the pool of available individuals, and we didn't track individual partnerships through time
But individual models you may see in the literature often represent much more complexity in partnership dynamics.

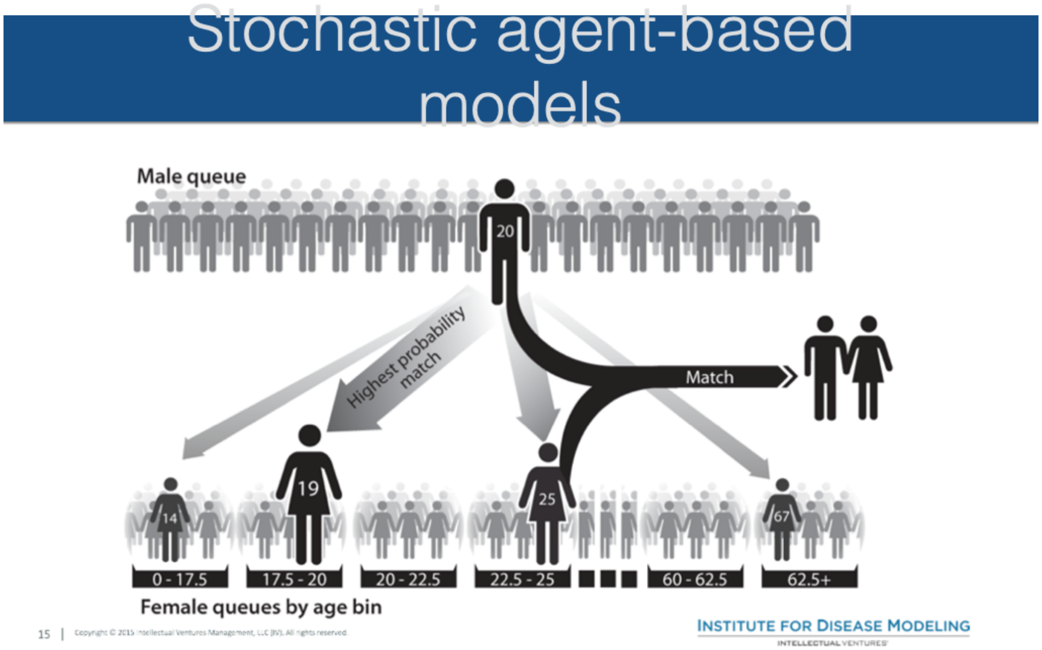
The process by which partnerships are formed and dissolved differs slightly from model to model, but many have the same basic structure:

- mixing matrices are defined to specify preferential section of partners according to attributes like age and risk group
- and in each time step the model calculates an individuals'

propensity for forming a new partnership
    - in some models, this is determined only by an individual’s current relationship status and propensity for having multiple overlapping partners.
    - In others, it is defined to additionally vary by age, HIV status, and stage of disease
- For individuals able to form new partnerships, a partner is selected in accordance with the mixing matrices
- The partner status of the individuals involved is updated
- and relationships dissolve according to rates specifying average duration

- Let’s dig a little deeper into how new partners are selected

Stochastic agent-based models



INSTITUTE FOR DISEASE MODELING
INTELLECTUAL VENTURES

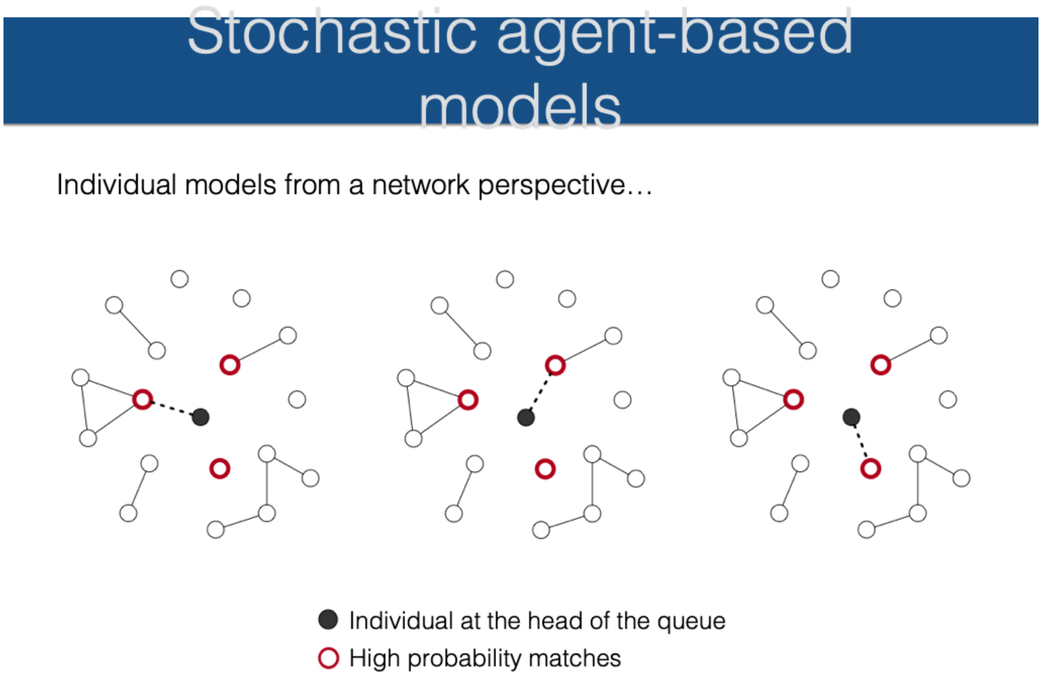
Daniel Klein, lecture in EPI 554 on October 15, 2015

This is a diagram for the Institute for Disease Modeling's EMOD-HIV model

In each time step, individuals are organized into a partnership queue, which determines the order in which they get to select partners

- For the individual at the head of the queue, a partner is selected from the pool of available matches according to who had been in the queue the longest

In this model, if no female is available in the selected age group, the male does not form a new partner and remains in the queue in the next time step



Stochastic agent-based models

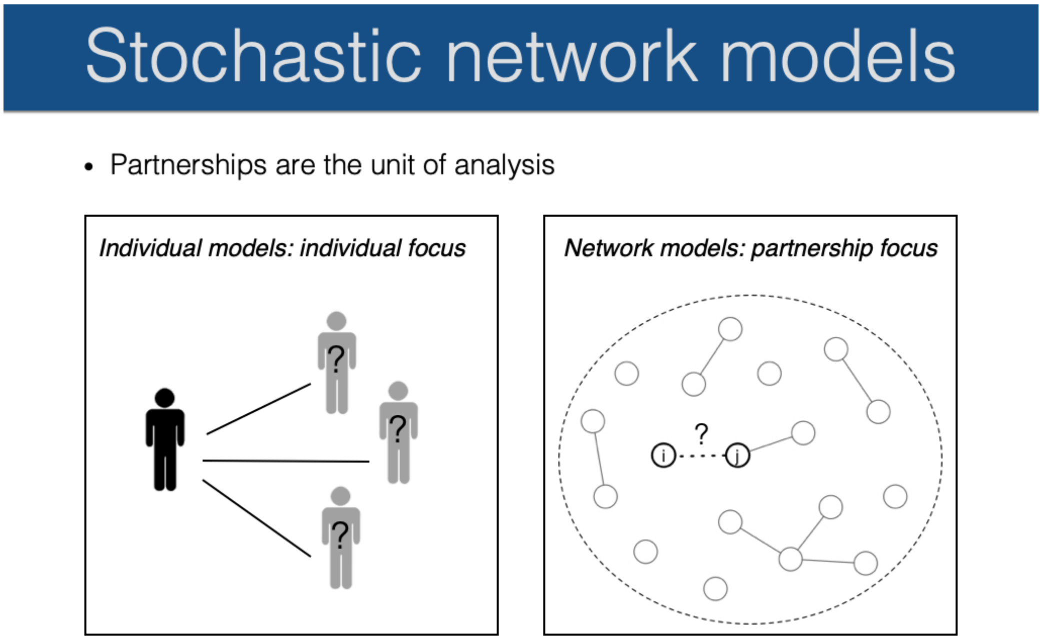
Individual models from a network perspective…

● Individual at the head of the queue
○ High probability matches

If we represent this process as a network graph, where the circles are individuals in the model and the lines represent existing partnerships.

- The solid black individual at the center is at the head of the partnership formation queue,
- and these red individuals are available for new partnerships and have been determined by the mixing algorithm to be high probability matches (i.e. they are in the selected age group)

- In an individual model framework, each of these three ties is equally likely …
- …But the implications for network structure and connectivity are different



Stochastic network models

- Partnerships are the unit of analysis

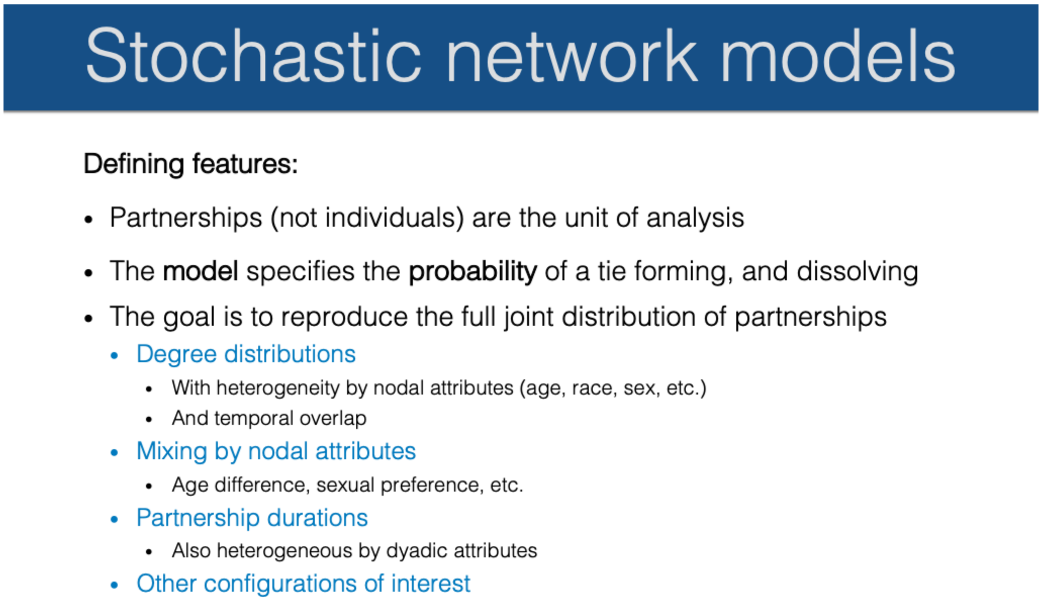
Individual models: individual focus

Network models: partnership focus

In contrast, network models are an extension of individual models where partnerships are the unit of analysis

- Individual models focus on the activity of individuals.
    - If an individual is set to make a tie, that tie will happen with someone if an acceptable partner can be found, and the main determinant of who the partner will be is who has been waiting longest

- In network models, the focus is on partnerships - whether or not a partnership forms depends on the presence and configuration of other ties and the characteristics of the individuals involved.



Stochastic network models

Defining features:

- Partnerships (not individuals) are the unit of analysis
- The **model** specifies the **probability** of a tie forming, and dissolving
- The goal is to reproduce the full joint distribution of partnerships
  - Degree distributions
    - With heterogeneity by nodal attributes (age, race, sex, etc.)
    - And temporal overlap
  - Mixing by nodal attributes
    - Age difference, sexual preference, etc.
  - Partnership durations
    - Also heterogeneous by dyadic attributes
  - Other configurations of interest

The key difference is the focus on partnerships.

- Network models rely on statistics that represent counts of ties

Because it is stochastic, it is a probability model

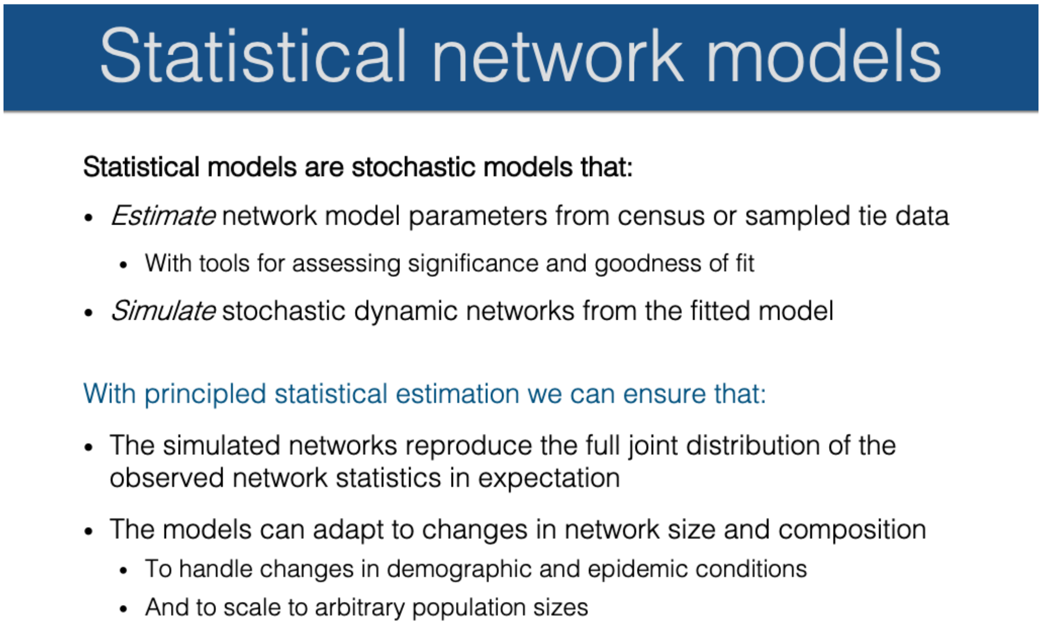
- And the probability of interest is the probability of a tie forming, or dissolving
- So there is an explicit equation that represents the model for tie formation, and another for tie dissolution

The model represents these probabilities as a function of the configurations that they produce

- Degree distributions
- Mixing patterns
- Duration distributions
- And other configurations (e.g. triads)

So, more common configurations will have higher probabilities

But … how do we know what those probabilities are? For that, we need data, and a way to estimate the model from data. That’s what a statistical model does.



Statistical network models

Statistical models are stochastic models that:

- *Estimate* network model parameters from census or sampled tie data
  - With tools for assessing significance and goodness of fit
- *Simulate* stochastic dynamic networks from the fitted model

With principled statistical estimation we can ensure that:

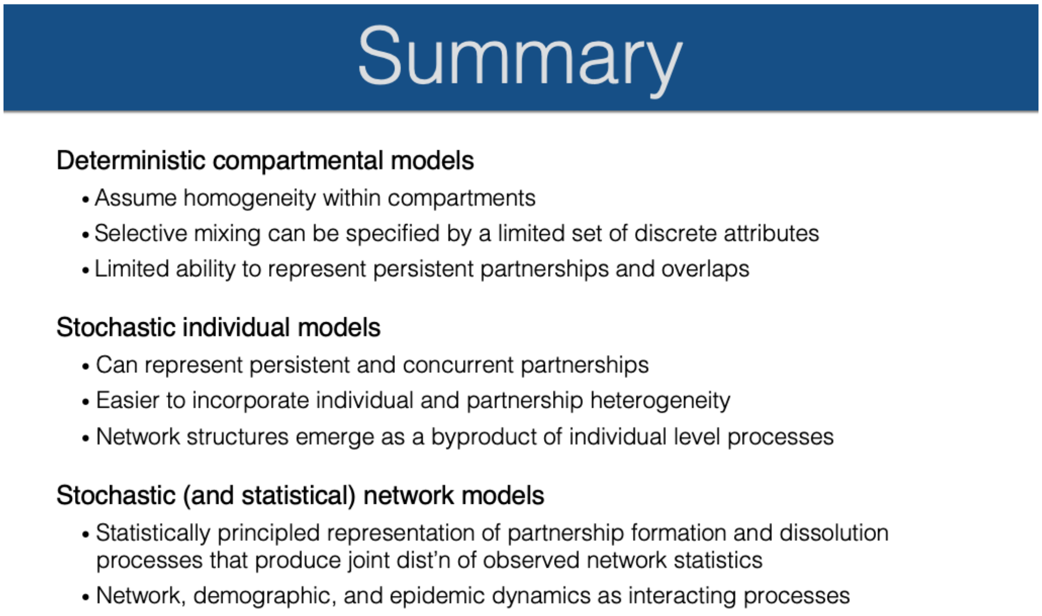
- The simulated networks reproduce the full joint distribution of the observed network statistics in expectation
- The models can adapt to changes in network size and composition
  - To handle changes in demographic and epidemic conditions
  - And to scale to arbitrary population sizes

These models are built around a principled statistical framework

- A single data point here is a partnership; the data set can be the full census of partnerships in a population, or a sample of partnerships
- Network statistics are calculated from observed data, including the joint distribution of ties broken down by nodal and dyadic attributes, the degree distribution, and partnership duration
- These network statistics are the “covariates” used to statistically estimate the model parameters (in a linear model y = a + bx, the covariate would be x and the parameter would be b.
- The fitted model can be used for simulation of stochastic dynamic networks

Together this provides a virtual laboratory for simulating epidemic processes over the simulated networks

- the simulations will preserve the joint distribution of the observed network statistics in expectation
- and allow them to evolve with changes in demographic and epidemic conditions



Summary

Deterministic compartmental models

- Assume homogeneity within compartments
- Selective mixing can be specified by a limited set of discrete attributes
- Limited ability to represent persistent partnerships and overlaps

Stochastic individual models

- Can represent persistent and concurrent partnerships
- Easier to incorporate individual and partnership heterogeneity
- Network structures emerge as a byproduct of individual level processes

Stochastic (and statistical) network models

- Statistically principled representation of partnership formation and dissolution processes that produce joint dist'n of observed network statistics
- Network, demographic, and epidemic dynamics as interacting processes

To summarize,

- In DCMS, everyone within a defined subgroup is assumed to be homogenous
    - patterns of sexual mixing can be defined by dividing the population by attributes, though the complexity grows exponentially with each added attribute and they have to be categorical
    - With the exception of pair models, partnerships are instantaneous, and even pair models have limited ability to represent dynamic network structures that result from persistent overlapping partnerships

- Individual models can track specific partnerships across time steps,
    - and some of these models allow for multiple persistent partnerships
    - as such, these models can represent a range of partnership configurations and macro-level network structures
    - But, in contrast to network models, these structures emerge

        as a byproduct of processes at the individual level, and the resulting network structure is somewhat arbitrary

- In network models, the focus is on partnerships and the dependent processes that influence tie formation and dissolution.
    - By using a statistical model for estimation and simulation, these models allow for simulation of complete, dynamic networks
    - And the network coefficients are automatically updated at each time step to account for shifts in demographic and epidemic conditions

Examples

- Deterministic compartmental models

  Johnson, L. F., Hallett, T. B., Rehle, T. M., & Dorrington, R. E. (2012). The effect of changes in condom usage and antiretroviral treatment coverage on human immunodeficiency virus incidence in South Africa: a model-based analysis. *J R Soc Interface, 9*(72), 1544-1554. doi:10.1098/rsif.2011.0826

  Cremin, I., McKinnon, L., Kimani, J., Cherutich, P., Gakii, G., Muriuki, F., . . . Hallett, T. B. (2017). PrEP for key populations in combination HIV prevention in Narobi: a mathematical modelling study. *Lancet HIV*. doi:10.1016/s2352-3018(17)30021-8

  Smith, J. A., Anderson, S. J., Harris, K. L., McGillen, J. B., Lee, E., Garnett, G. P., & Hallett, T. B. (2016). Maximising HIV prevention by balancing the opportunities of today with the promises of tomorrow: a modelling study. *Lancet HIV, 3*(7), e289-296. doi:10.1016/s2352-3018(16)30036-4

- Pair formation models

  Ferguson, N. M., & Garnett, G. P. (2000). More realistic models of sexually transmitted disease transmission dynamics: sexual partnership networks, pair models, and moment closure. *Sex Transm Dis, 27*(10), 600-609. Agent-based models

  Powers, K. A., Ghani, A. C., Miller, W. C., Hoffman, I. F., Pettifor, A. E., Kamanga, G., . . . Cohen, M. S. (2011). The role of acute and early HIV infection in the spread of HIV and implications for transmission prevention strategies in Lilongwe, Malawi: a modelling study. *Lancet, 378*(9787), 256-268. doi:10.1016/s0140-6736(11)60842-8

  Johnson, L., Dorrington, R., Bradshaw, D., Pillay-Van Wyk, V., & Rehle, T. (2009). Sexual behaviour patterns in South Africa and their association with the spread of HIV: insights from a mathematical model. *Demographic Research, 21*(11), 289-340.

- Stochastic agent-based models

  Bershteyn, A., Klein, D. J., & Eckhoff, P. A. (2016). Age-targeted HIV treatment and primary prevention as a ‘ring fence’ to efficiently interrupt the age patterns of transmission in generalized epidemic settings in South Africa. *International Health, 8*(4), 277-285. doi:10.1093/inthealth/ihw010

  Johnson, L. F., & Geffen, N. (2016). A Comparison of Two Mathematical Modeling Frameworks for Evaluating Sexually Transmitted Infection Epidemiology. *Sex Transm Dis, 43*(3), 139-146. doi:10.1097/olq.0000000000000412

- Stochastic network models

  Jenness, S. M., Goodreau, S. M., Morris, M., & Cassels, S. (2016). Effectiveness of combination packages for HIV-1 prevention in sub-Saharan Africa depends on partnership network structure: a mathematical modelling study. *Sex Transm Infect, 92*(8), 619-624. doi:10.1136/sextrans-2015-052476

  Jenness, S. M., Sharma, A., Goodreau, S. M., Rosenberg, E. S., Weiss, K. M., Hoover, K. W., . . . Sullivan, P. (2017). Individual HIV Risk versus Population Impact of Risk Compensation after HIV Preexposure Prophylaxis Initiation among Men Who Have Sex with Men. *PLoS One, 12*(1), e0169484. doi:10.1371/journal.pone.0169484

  Goodreau, S. M., Rosenberg, E. S., Jenness, S. M., Luisi, N., Stansfield, S. E., Millett, G. A., & Sullivan, P. S. (2017). Sources of racial disparities in HIV prevalence in men who have sex with men in Atlanta, GA, USA: a modelling study. *Lancet HIV, 4*(7), e311-e320. doi:10.1016/s2352-3018(17)30067-x