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Introduction to modeling

*and*

A simple deterministic model  
application

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Mathematical Modeling of Infectious  
Diseases Symposium

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# Outline

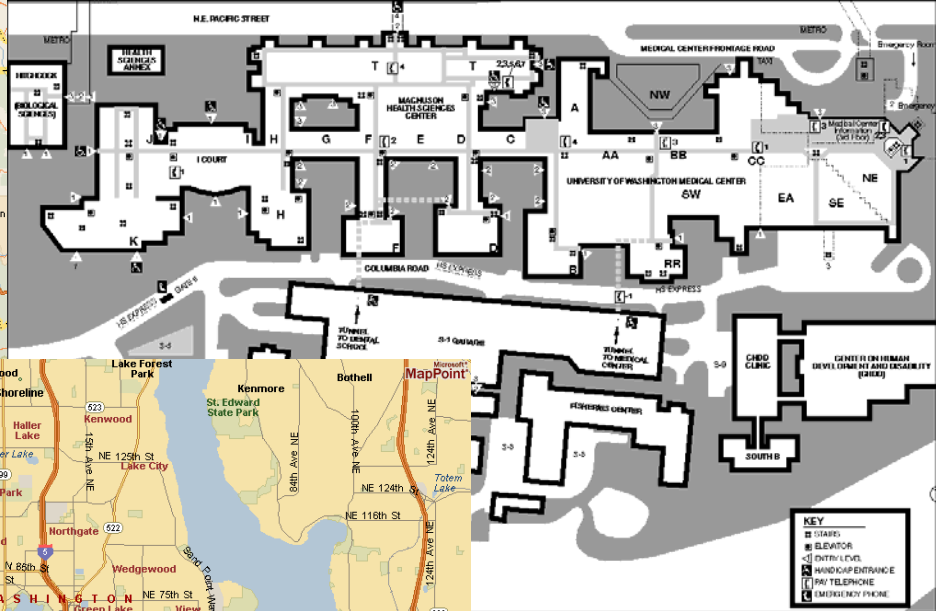
- Basic introduction to mathematical modeling of infectious diseases
  - Simple deterministic model
  - Application: Secondary HIV Transmission in Mozambique
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# Mathematical modeling of infectious disease

- Uses of models:
    - Predict population-level disease outcomes from individual-level behavior
    - Support clinical trial design
    - Model impacts from HIV interventions
    - Virtual laboratory for systematically testing components of model
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# Maps



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# Models must balance realism with generality

Like maps, models...

... are *abstractions*

... have *scale*

... must balance *realism* with *generality*

The kind of model you choose to use will depend on the question you want to answer.

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# Models have three basic components

- System definition – elements needed for persistence
    - Persons
    - Animals (potential reservoirs, or focus of interest)
    - Pathogens
    - Vectors (e.g., mosquitoes)
  
  - States – attributes of system elements
    - Persons/animals
      - Infection status (Susceptible, Infected...)
      - Demographics, Behavior
    - Pathogens (life cycle, interaction with host)
    - Vectors (life cycle)
  
  - Rates – movement between states
    - Deterministic
    - Stochastic
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# Transmission types

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## **Direct**

*Respiratory*  
*Fecal-oral*  
*Sexual*  
*Vertical*

## **Vector-borne**

*Mosquitoes*  
*Fleas*  
*Flies*  
*etc*

## **Vehicle-borne**

*Water-borne*  
*Food-borne*  
*Soil-borne*

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# Basic transmission dynamics – direct transmission

**Infected person**       $\longrightarrow$       **Susceptible person**

**Requires:**

**Infected person**

**Susceptible person**

**Contact between them**

**Transmission given contact**

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# Simple system: SIR model

## States

Susceptibles  
 $S(t)$

Infecteds  
 $I(t)$

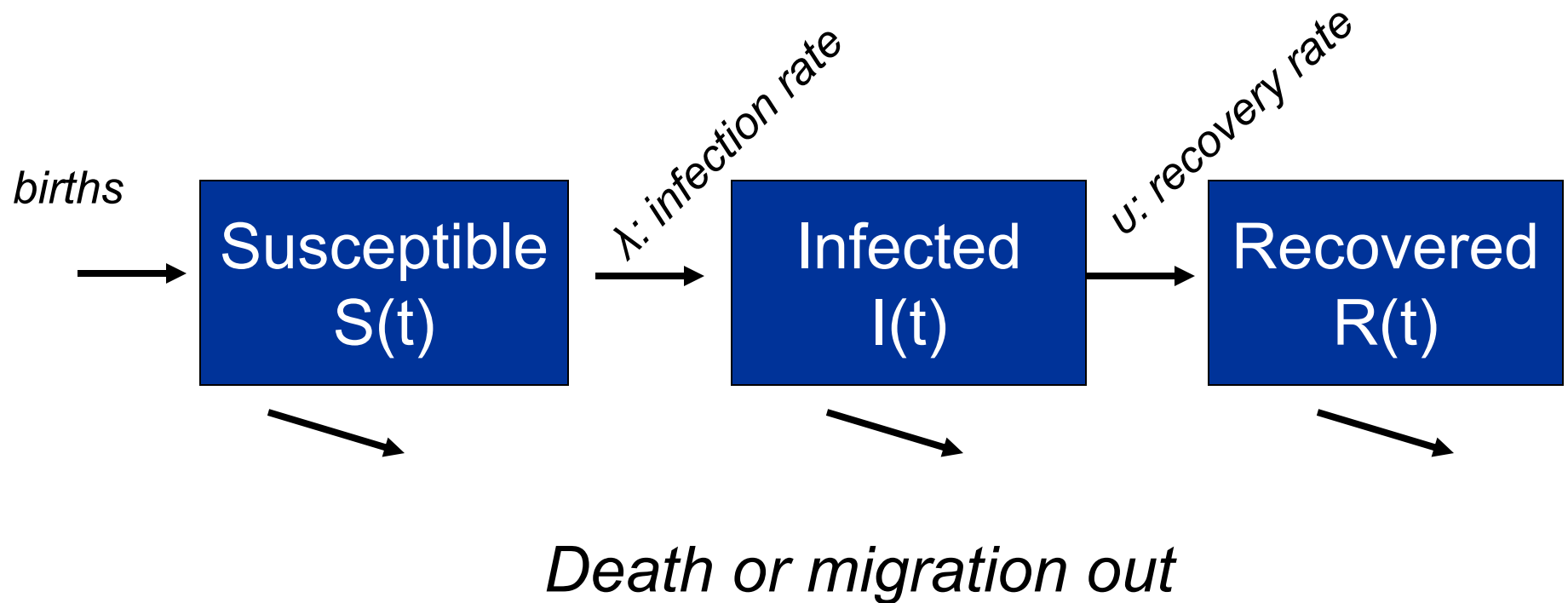
Recovereds  
 $R(t)$

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# Simple system: SIR model

## Rates



## Common notation

Model	Change in cases	Prevalence
I: Infecteds only	$\frac{dI(t)}{dt} = \lambda I(t)$	$I(t) = I(0)e^{\lambda t}$
SI : susceptibles & infecteds	$\frac{dI(t)}{dt} = \lambda S(t)I(t)$	$I(t) = \frac{I(0)N}{I(0) + [S(0)]e^{\lambda t}}$
SIR : add recovered/removed	$\frac{dI(t)}{dt} = \lambda S(t)I(t) - \nu I(t)$	No longer analytically tractable

susceptible (S), infected (I), and removed (R); N = total population size  
infection rate  $\lambda$ , death/recovery rate  $\nu$ , time t,

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# Models often classified by rates

- Transitions between states: **deterministic** or **stochastic**
    - **Deterministic models:** use an average *rate* of transition between states – everyone in the compartment given the same rate
    - **Stochastic models:** use the *probability* that an individual makes a transition between states – individuals draw from a probability distribution
  - Often has implications for **states** (careful!):
    - **Deterministic models:** usually built on group aggregates or macro-level states (i.e. compartments),
    - **Stochastic models:** usually built to reflect the micro-level states occupied by discrete individual persons.
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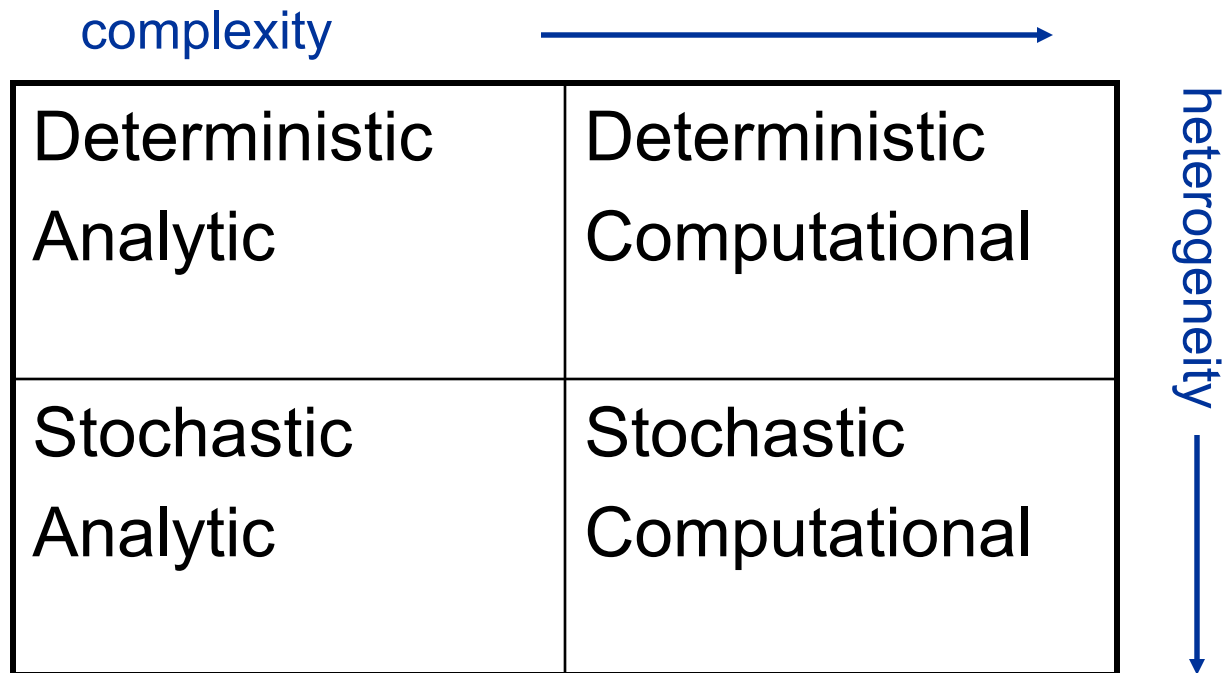
# Models can also be classified by how they are solved

- Dynamics over time can be solved **analytically** or **computationally**
    - Analytic, or “closed form” solutions isolate outcome on left-hand side of equation, determinants on the right
    - Computational, or numerical, solutions need to be used if the outcome is on both sides of the equation – ex: non-trivial feedback loops
      - This happens very quickly; most models with realistic heterogeneity need to be solved this way
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# Model classification

...in a simplified scheme...



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# Solutions may exist for other properties of the system

Even if closed form solutions are not available for the state variables

We may still be able to solve for qualitative properties. A classic example:

$$R_0 = \beta c D$$

The basic reproduction number of an infectious process

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# The basic and effective reproductive numbers

$R_0$  The Basic Reproductive Number - The number of new infections caused by one infection in an entirely susceptible population

$R_t$  The Effective Reproductive Number - The number of new infections caused by one infection at a given time

$$R_0 = \beta * c * D$$

Transmission probability per contact  $\beta$  ←

Contact rate  $c$  ←

Duration of infectiousness  $D$  ←

$$R_t = R_0 * S/N$$

Proportion of contacts susceptible  $S/N$  ←

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## Simple deterministic model for estimating secondary HIV transmissions

$$\frac{\partial I}{\partial t} = \lambda S(t)I(t)$$

$$\frac{\partial I}{\partial t} / I(t) = \lambda S(t)$$

= expected number of new  
infections per case

Will modify states of  $I(t)$  and force of infection  $\lambda$

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# Lets unpack the force of infection

$$\lambda_s = p * [1 - (1 - \mu * \beta_s)^a]$$

- This simple model looks complex!
  - Let's step through each piece
  - Then see why the expansion is useful
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$$\lambda_s = p * [1 - (1 - \mu * \beta_s)^a]$$

- $\beta$  = the probability of HIV transmission per sex act
  - $\beta_s$  is the probability by stage of disease (s)
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$$\lambda_s = p * [1 - (1 - \mu * \beta_s)^a ]$$

- $\mu$  = factors which increases or decreases the probability of HIV transmission
  - $\beta$  = the probability of HIV transmission per sex act
  - $\beta_s$  is the probability by stage of disease (s)
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$$\lambda_s = p * [1 - (1 - \mu * \beta_s)^a ]$$

- $(1 - \mu * \beta_s)$  = the probability that transmission \*does not\* occur
  - $\mu$  = factors which increases or decreases the probability of HIV transmission
  - $\beta$  = the probability of HIV transmission per sex act
  - $\beta_s$  is the probability by stage of disease (s)
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$$\lambda_s = p * [1 - (1 - \mu * \beta_s)^a ]$$

- $a$  = the number of sex acts in a typical partnership
  - $(1 - \mu * \beta_s)$  = the probability that transmission \*does not\* occur
  - $\mu$  = factors which increases or decreases the probability of HIV transmission
  - $\beta$  = the probability of HIV transmission per sex act
  - $\beta_s$  is the probability by stage of disease (s)
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$$\lambda_s = p * [1 - (1 - \mu * \beta_s)^a ]$$

- $(1 - \mu * \beta_s)^a$  is the probability that transmission does not occur during the partnership
  - $a$  = the number of sex acts in a typical partnership
  - $(1 - \mu * \beta_s)$  = the probability that transmission \*does not\* occur
  - $\mu$  = factors which increases or decreases the probability of HIV transmission
  - $\beta$  = the probability of HIV transmission per sex act
  - $\beta_s$  is the probability by stage of disease (s)
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$$\lambda_s = p * [1 - (1 - \mu * \beta_s)^a]$$

- $[1 - (1 - \mu * \beta_s)^a]$  is the probability that transmission does occur
  - Therefore,  $(1 - \mu * \beta_s)^a$  is the probability that transmission does not occur during the partnership
  - $a$  = the number of sex acts in a typical partnership
  - $(1 - \mu * \beta_s)$  = the probability that transmission \*does not\* occur
  - $\mu$  = factors which increases or decreases the probability of HIV transmission
  - $\beta$  = the probability of HIV transmission per sex act
  - $\beta_s$  is the probability by stage of disease (s)
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$$\lambda_s = p * [1 - (1 - \mu * \beta_s)^a]$$

- p is the number of partners in the last 3 months
  - $[1 - (1 - \mu * \beta_s)^a]$  is the probability that transmission does occur
  - Therefore,  $(1 - \mu * \beta_s)^a$  is the probability that transmission does not occur during the partnership
  - a = the number of sex acts in a typical partnership
  - $(1 - \mu * \beta_s)$  = the probability that transmission \*does not\* occur
  - $\mu$  = factors which increases or decreases the probability of HIV transmission
  - $\beta$  = the probability of HIV transmission per sex act
  - $\beta_s$  is the probability by stage of disease (s)
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$$\lambda_s = p * [1 - (1 - \mu * \beta_s)^a]$$

- $p * [1 - (1 - \mu * \beta_s)^a]$  is the number of partners infected (if susceptible)
  - $p$  is the number of partners in the last 3 months
  - $[1 - (1 - \mu * \beta_s)^a]$  is the probability that transmission does occur
  - Therefore,  $(1 - \mu * \beta_s)^a$  is the probability that transmission does not occur during the partnership
  - $a$  = the number of sex acts in a typical partnership
  - $(1 - \mu * \beta_s)$  = the probability that transmission \*does not\* occur
  - $\mu$  = factors which increases or decreases the probability of HIV transmission
  - $\beta$  = the probability of HIV transmission per sex act
  - $\beta_s$  is the probability by stage of disease (s)
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## The states of the model are

- the stage of respondent HIV infection,
  - characteristics of respondent and partner:
    - circumcision,
    - condom use,
    - antiretroviral treatment (ART),
    - and co-factor STDs,
  - the HIV status of the partner.
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# The rate of transmission depends on these states

- Many different types of respondents defined by these state variables
  - So there are many different rates
  - But for any given status, only one rate
  - So this is a deterministic model
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# Estimating Secondary Transmission Among HIV-positive Mozambicans Prior to HAART

## Objectives:

1. Estimate # of sexual partners who would acquire HIV from study population in past 3 months
2. Test how sensitive the findings are to the model inputs
3. Compare model outcomes with data collected after population initiated HAART (work in progress)

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# Study population

- Ego-centric data collection
    - 350 HIV+, HAART-naïve Mozambicans
    - 157 sexually active respondents (78 women, 79 men)
    - 191 sexual partners (all heterosexual)
  - Data on partnerships recalled over last 3 months
-

## Model inputs

$\beta$ : probability of transmission	0.0031 if late-stage 0.0007 if mid-stage
circumcision factor	(1 – 0.6) if male partner is circumcised 1 otherwise
condom use factor	(1 – 0.95*correct & consistent condom use)
HAART factor	(1 – 0.48*% adherence) if on HAART 1 otherwise
syphilis factor	7.5 if respondent syphilis 1 otherwise
HSV-2 factor	2.7 if respondent HSV-2 1 otherwise

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# Description of sample

- Serostatus of partners:
    - 55% HIV+, 18% HIV-, 27% HIV?
  - Unprotected sex acts occurred in 70% of partnerships
  - Average # of sex acts with partner over last 3 months:  
6.4
-

Parameters	Rate (100/year)	Reduction in transmission
Base model	4.00	
Correct and consistent condom use (27% base model prevalence)		
50%	2.87	0.28
75%	1.58	0.61
Syphilis (16.7% base model prevalence)		
8%	2.94	0.27
5%	2.56	0.36
HSV-2 (90% base model prevalence)		
45%	2.81	0.30
25%	2.28	0.43
Male circumcision (31% base model prevalence)		
50%	3.79	0.05
75%	3.52	0.12
Persons on HAART (base model is 0% adherent)		
95%	2.20	0.45
80%	2.49	0.38
Treatment only		
Syphilis & HSV2 (50%)	2.09	0.48
Syphilis & HSV2 (50%) & HAART (95%)	1.14	0.72

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## Effective epidemic potential?

Recall  $R_0 = \beta c D$ ,  $R_t = R_0 * S/N$

Assume  $D = 10$  years

$\beta c = 4$  infections per 100 person-years

= 0.04 transmission events per person per year

Then,  $R_t = 0.40$  \*and this is only sexually active HIV+ individuals\*

If all partners were HIV-:  $R_t = 1.6$

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# Pro's and con's to simple model

## Pros

- No need for fancy software – can use MS Excel
- Good for 1) simple pre/post comparisons, 2) sensitivity analysis of parameters, 3) predicted impacts from treatment and prevention interventions
- Simple back-of-envelope calculations for  $R_0$  given population behaviors
- Can use individual-level data or group-level

## Cons

- Assume multiplicative risk ratios
  - Model not bounded, but OK for small transmission probabilities
  - Not good for complex questions such as prediction of magnitude of epidemics
  - Others?
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# Last thoughts

- A model is only as good as its structure, assumptions & parameter estimates
  - Knowing a little bit about modeling takes the mystery away, and the reader can judge the quality of the model and outcomes for herself
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