Transmission in finite populations

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Day 2

Training Session on Mathematical Modeling of Infectious Disease Dynamics, CCD, icddr,b

Differential equations (ODE's)

- Assumptions
  - large (infinite) populations
  - well-mixed contacts
  - exponential waiting times (memory-less)

- Continuous treatment of individuals; appropriate for:
  - average system behavior
  - population proportions
  - population densities

Differential equations (ODE's)

- Equations describe the change in state variables through time
  - *deterministic progression from a set of initial conditions*

- Good for:
  - understanding periodicity in long time series for large populations
  - understanding effects of vaccination and birth rates on persistence and periodicity

Model terminology

- Deterministic
- Stochastic

- Continuous time
- Discrete time

- Compartmental models
- Network models
- Individual-based models

Model taxonomy

	Integer individuals Discrete treatment of individuals	Continuous approximation Continuous treatment of individuals (averages, proportions, or population densities)
Stochastic	CONTINUOUS TIME • Gillespie algorithm ← DISCRETE TIME • Binomial chain type models	CONTINUOUS TIME • Stochastic differential equations
Deterministic		CONTINUOUS TIME • Ordinary differential equations • Partial differential equations DISCRETE TIME • Difference equations • Reed-Frost type models

The Gillespie algorithm

- Provides an analogue to a system of differential equations that treats individuals as discrete entities
  - finite, countable populations
  - well-mixed contacts
  - exponential waiting times (memory-less)
  - noise (stochasticity) is introduced by the discrete nature of individuals
- Event-driven simulation
- Computationally slow
  - especially for large populations

The Gillespie algorithm

ODE model

$$\frac{dS}{dt} = -\frac{\beta S I}{N}$$
$$\frac{dI}{dt} = \frac{\beta S I}{N} - \gamma I$$
$$\frac{dR}{dt} = \gamma I$$

Two event types:

TRANSMISSION

$$(S, I, R) \rightarrow (S-1, I+1, R) \quad \text{at rate} \quad \frac{\beta S I}{N}$$

RECOVERY

$$(S, I, R) \rightarrow (S, I-1, R+1) \quad \text{at rate} \quad \gamma I$$

The Gillespie algorithm

Two event types:

TRANSMISSION

$$(S, I, R) \rightarrow (S-1, I+1, R) \quad \text{at rate} \quad \frac{\beta SI}{N} = \lambda_1$$

RECOVERY

$$(S, I, R) \rightarrow (S, I-1, R+1) \quad \text{at rate} \quad \gamma I = \lambda_2$$

Time to the next event: $\tau \sim \text{Exp}\left(\lambda = \sum_i \lambda_i\right)$

Probability the event is type i: $p_i = \frac{\lambda_i}{\sum_i \lambda_i}$

The Gillespie algorithm

```
while (I > 0 and time < MAXTIME)
        Calculate rates
        Determine time to next event
        Determine event type
        Update state variables
        Update time
end
```

The Gillespie algorithm

TRANSMISSION

$$(S, I, R) \rightarrow (S-1, I+1, R) \quad \text{at rate} \quad \frac{\beta S I}{N}$$

RECOVERY

$$(S, I, R) \rightarrow (S, I-1, R+1) \quad \text{at rate} \quad \gamma I$$

$$\frac{dS}{dt} = -\frac{\beta S I}{N}$$

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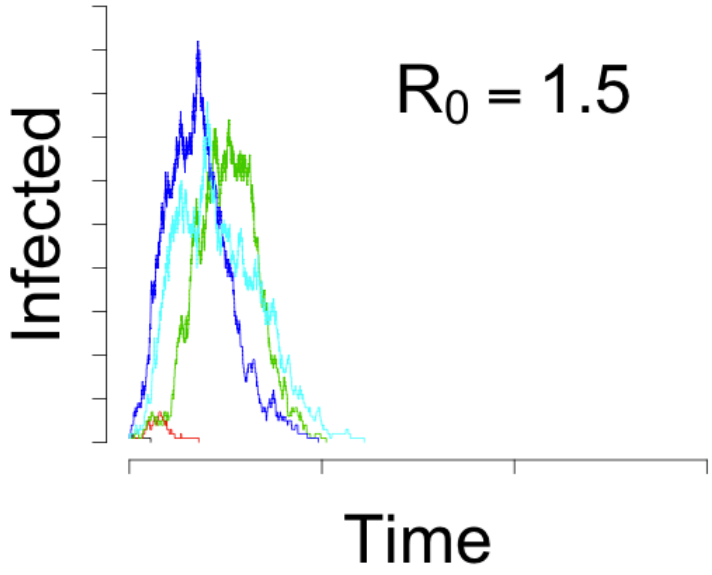

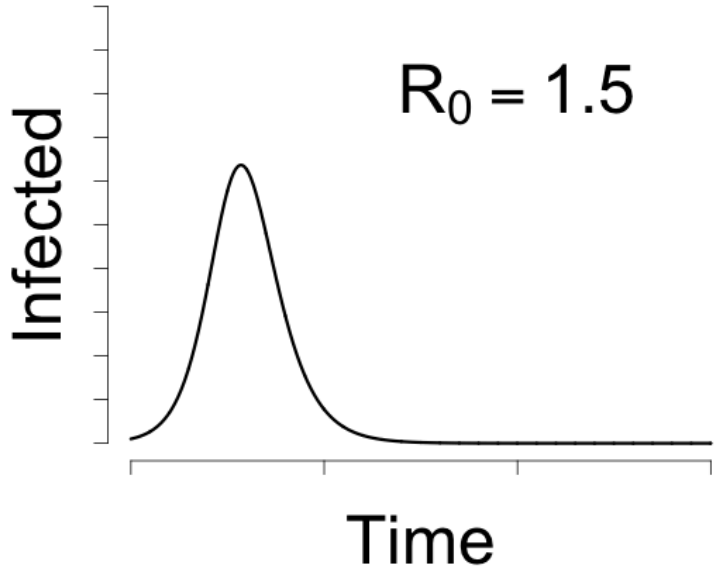

The Gillespie algorithm

- Gillespie, DT (1977) Exact stochastic simulation of coupled chemical reactions. J Phys Chem 81: 2340–2361.

- Example:
  - http://yushan.mcmaster.ca/theobio/mmed/index.php/Gillespie

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The Reed-Frost model

The infection is spread directly from infected individuals to others by a certain kind of contact (adequate contact) and in no other way.

Any non-immune individual in the group, after such contact with an infectious person in a given period, will develop the infection and will be infectious to others only within the following time period, after which he is wholly immune.

Each individual has a fixed probability of coming into adequate contact with any other specified individual in the group within one time interval, and this probability is the same for every member of the group.

The individuals are wholly segregated from others outside the group.

These conditions remain constant during the epidemic.

Abbey, H (1952) An examination of the Reed-Frost theory of epidemics. Hum Biol 24: 201-233. [As quoted in Fine, PEM (1977) Am J Epi 106(2): 87-100.]

The Reed-Frost model

- Time unit is roughly time from infection to end of infectiousness
- Generations of cases do not overlap
- If $p = 1 - q$ is the probability of any two individuals coming into "adequate contact" during a time unit, $1 - q^{C_t}$ is the probability a susceptible individual becomes infected during a time unit, so the expected number of cases in the next time unit is

$$C_{t+1} = S_t(1 - q^{C_t})$$

The Reed-Frost model

- The full set of equations describing the deterministic population update is:

$$C_{t+1} = S_t(1 - q^{C_t})$$

$$S_{t+1} = S_t - C_{t+1}$$

$$R_{t+1} = R_t + C_t$$

- If N=S+C+R is the total population size, the basic reproductive number for this model is

$$R_0 = (N-1)(1-q)$$

The Reed-Frost model

$$C_{t+1} = S_t(1 - q^{C_t})$$

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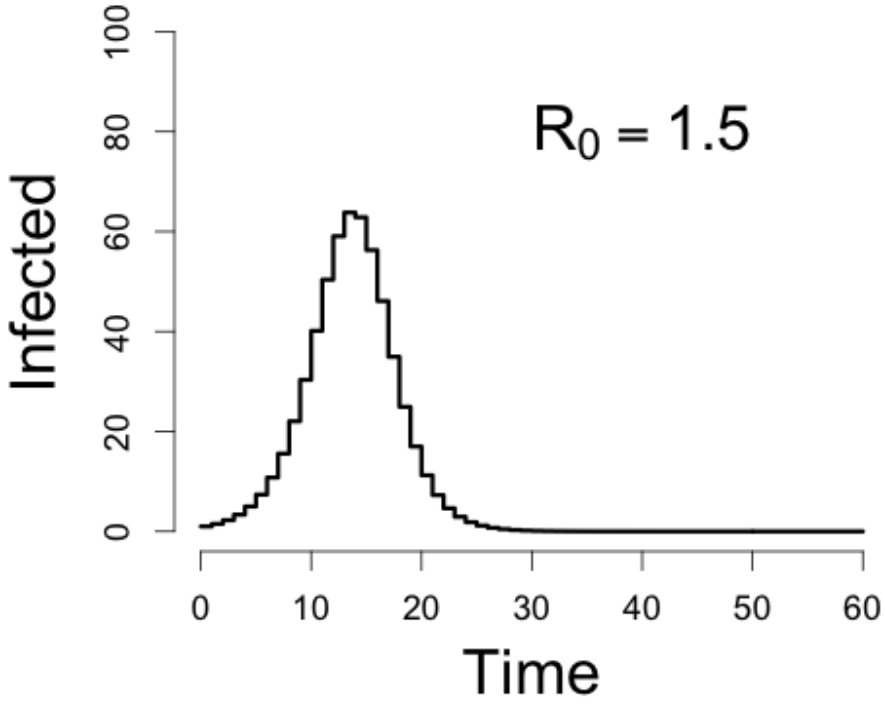

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The stochastic R-F model

- The stochastic formulation of the Reed-Frost model is a type of chain binomial model with non-overlapping generations

$$P\left(C_{t+1} = x\right) = \binom{S_t}{x} (1 - q^{C_t})^x \, (q^{C_t})^{S_t - x}$$

$$S_{t+1} = S_t - C_{t+1}$$

$$R_{t+1} = R_t + C_t$$

- For small populations (eg, households), final size distributions can be calculated

The stochastic R-F model

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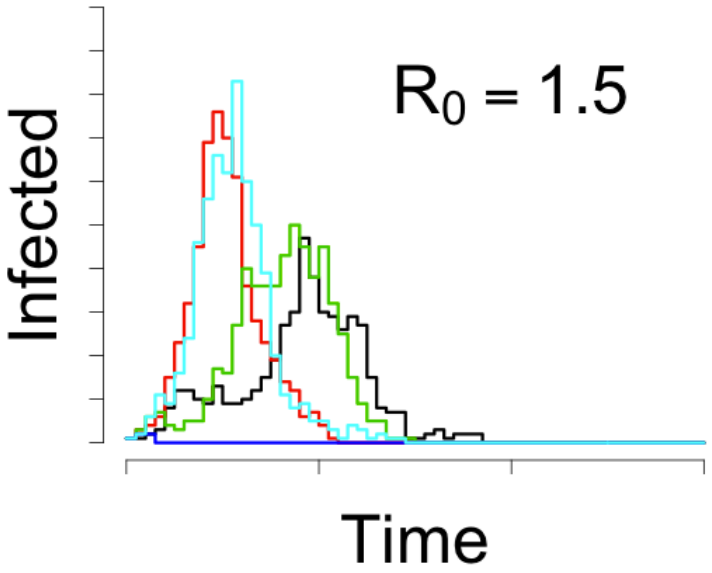

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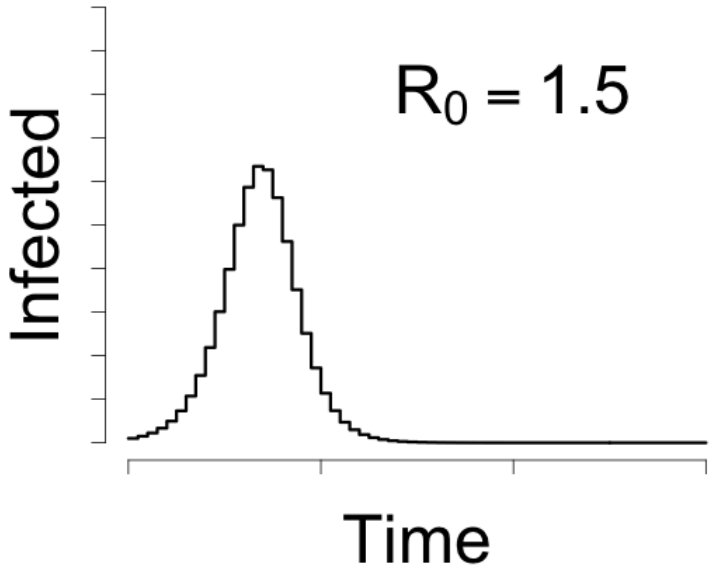

Chain binomial models

- Chain binomial models can also be formulated based on the same parameters we used in the ODE models and with overlapping generations
- As before, instantaneous hazard of infection for a individual susceptible individual is $\frac{\beta I}{N}$
- For a susceptible at time t, the probability of infection by time $t + \Delta t$ is

$$p = 1 - e^{-\frac{\beta I}{N}\Delta t}$$

Chain binomial models

- Similarly, for an infectious individual at time t, the probability of recovery by time $t + \Delta t$ is

$$r = 1 - e^{-\gamma \Delta t}$$

- The stochastic population update can then be described as

$$S_{t+\Delta t} = S_{t+\Delta t} - X$$

$$I_{t+\Delta t} = I_{t+\Delta t} + X - Y$$

$$R_{t+\Delta t} = R_{t+\Delta t} + Y$$

where $P(X = x) = \binom{S_t}{x} p^x (1-p)^{S_t - x}$

and

$$P(Y = y) = \binom{I_t}{y} r^y (1-r)^{I_t - y}$$

Chain binomial models

- For this model, if D is the average duration of infection, the basic reproductive number is:

$$R_0 = (N-1)\left(1 - e^{-\frac{\beta}{N}D}\right)$$

- Non-generation-based chain binomial models can be adapted to include many variations on the natural history of infection
- Discrete-time simulation of chain binomials is far more computationally efficient than event-driven simulation in continuous time

Chain binomial simulation

```
while (I > 0 and time < MAXTIME)
        Calculate transition probabilities
        Determine number of transitions for each type
        Update state variables
        Update time
end
```

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Proposed Topics

- **Day 1:** Infectious disease terminology and simple ODE models
- **Day 2:** Model taxonomy and transmission in finite populations
- Day 3: Contact networks and consequences of heterogeneity (?)
- Day 4: Matching models with data (?)
- Day 5: Case study – TBD (?)