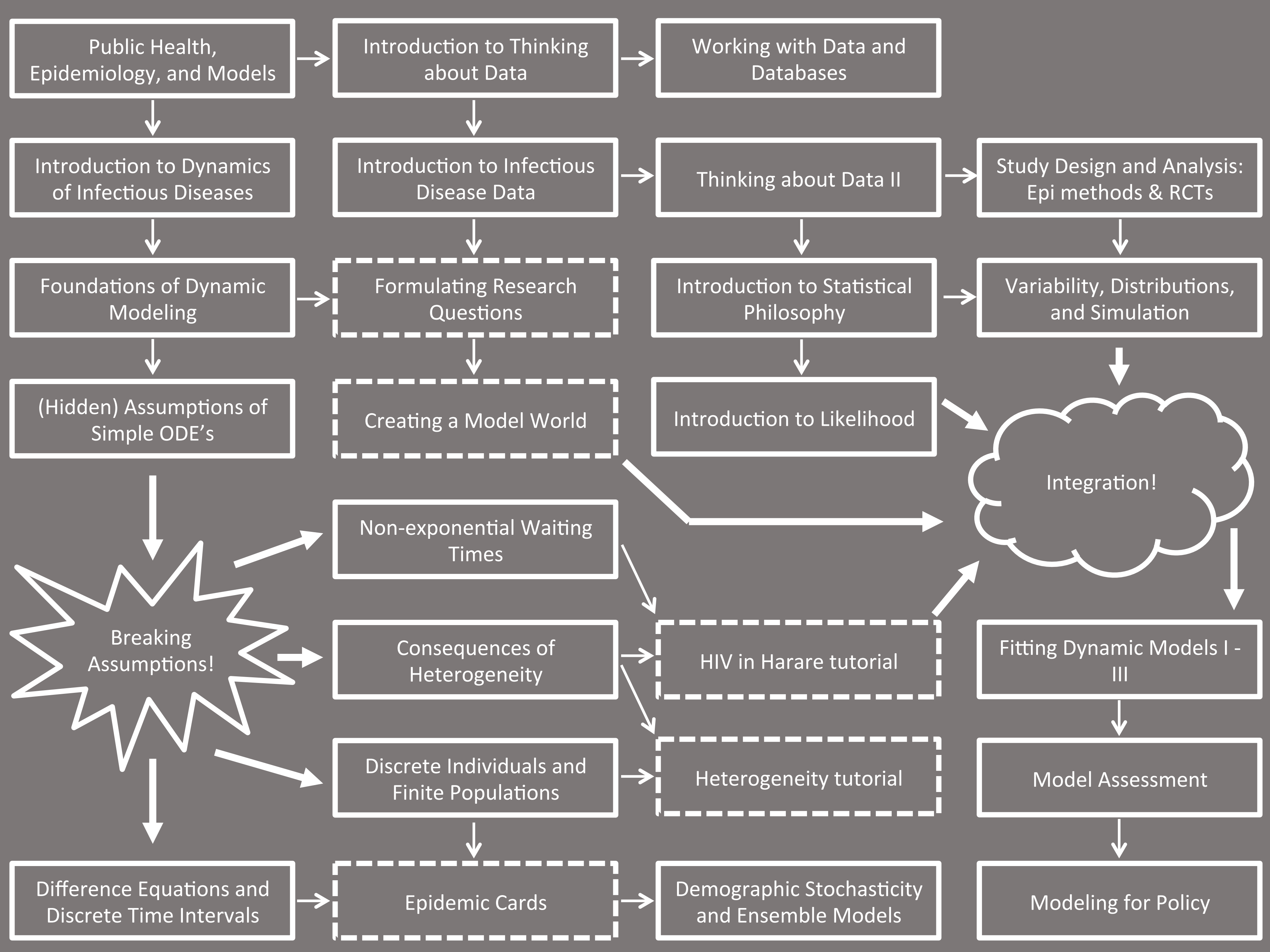
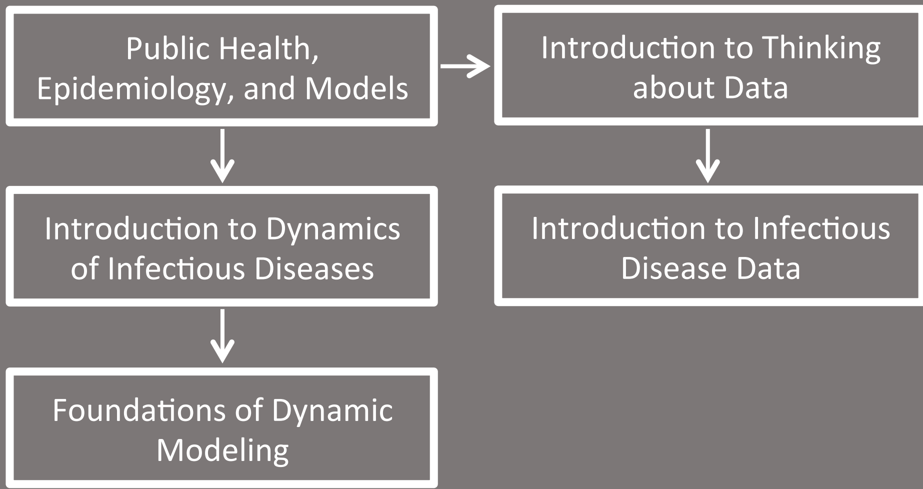

Public Health, Epidemiology, and Models
Introduction to Thinking about Data
Working with Data and Databases
Introduction to Dynamics of Infectious Diseases
Introduction to Infectious Disease Data
Thinking about Data II
Study Design and Analysis: Epi methods & RCTs
Foundations of Dynamic Modeling
Formulating Research Questions
Introduction to Statistical Philosophy
Variability, Distributions, and Simulation
(Hidden) Assumptions of Simple ODE's
Creating a Model World
Introduction to Likelihood
Integration!
Non-exponential Waiting Times
Breaking Assumptions!
Consequences of Heterogeneity
HIV in Harare tutorial
Fitting Dynamic Models I - III
Discrete Individuals and Finite Populations
Heterogeneity tutorial
Model Assessment
Difference Equations and Discrete Time Intervals
Epidemic Cards
Demographic Stochasticity and Ensemble Models
Modeling for Policy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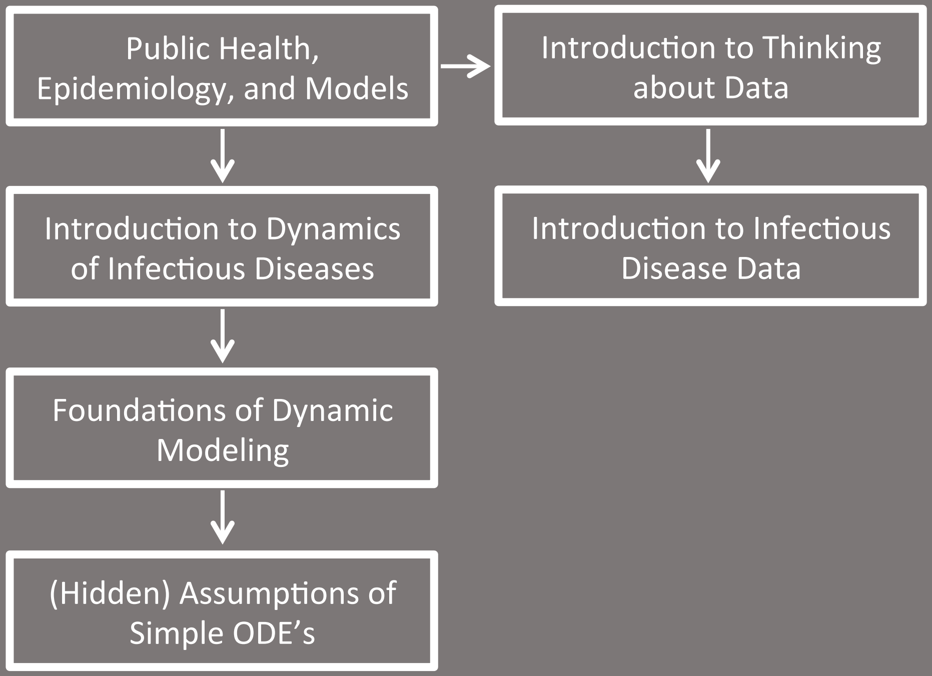
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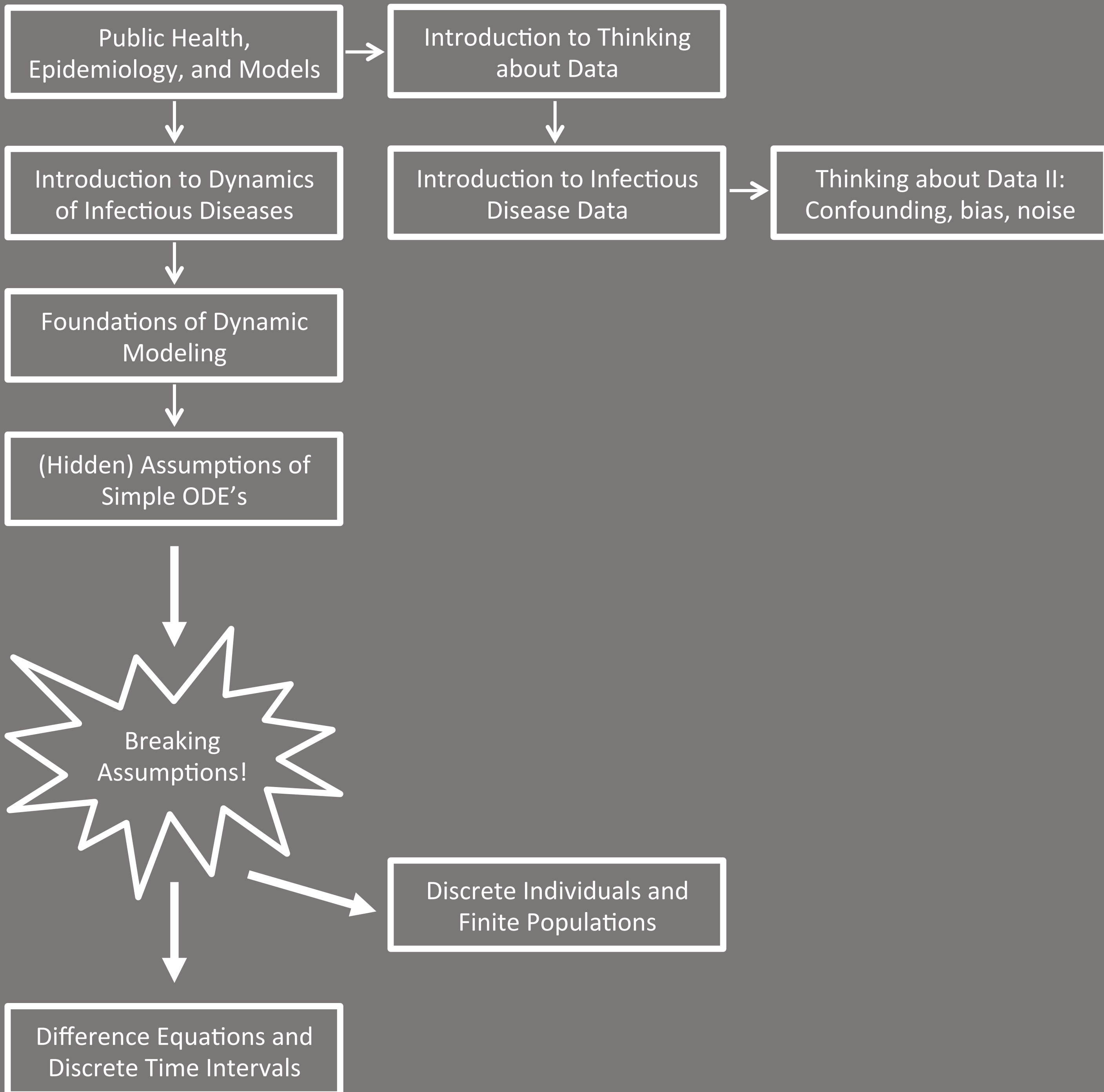
Public Health, Epidemiology, and Models
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(Hidden) Assumptions of Simple ODE's
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(Hidden) Assumptions of Simple ODE Models

Cara Brook
Department of Ecology and Evolutionary Biology
Princeton University

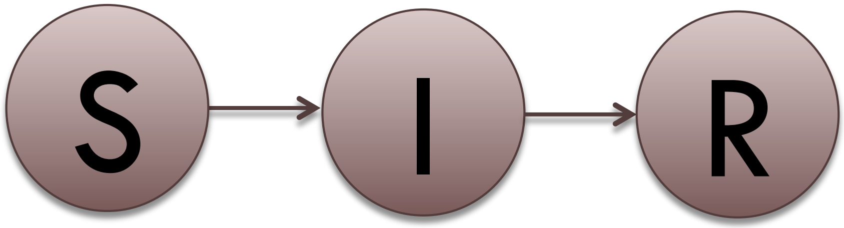
Juliet Pulliam, PhD
Department of Biology and Emerging Pathogens Institute
University of Florida

May 31, 2016

Meaningful Modeling of Epidemiological Data (MMED) clinic, ICI3D Program, AIMS - South Arica

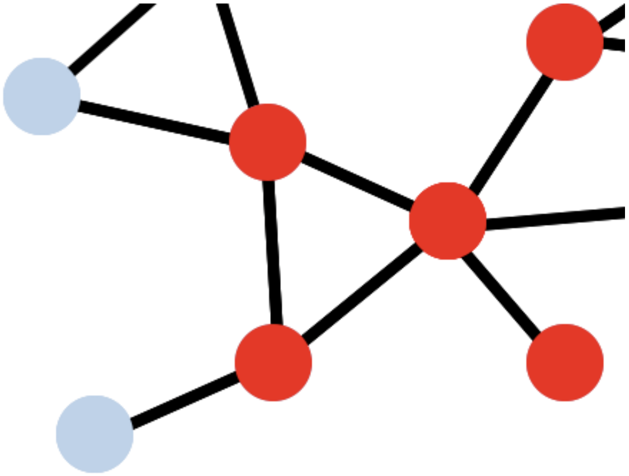
Model terminology

- Compartmental models



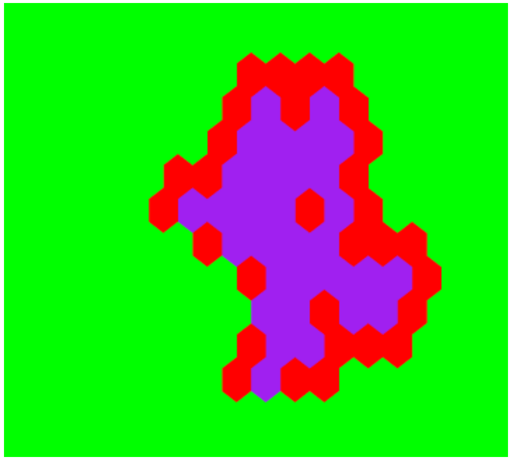
Model terminology

- Compartmental models
- Network models



Model terminology

- Compartmental models
- Network models
- Individual-based models



Model terminology

- Compartmental models
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- Continuous time
- Discrete time

- Deterministic
- Stochastic

Ordinary Differential Equations (ODEs)

- **Compartmental** models
- Network models
- Individual-based models

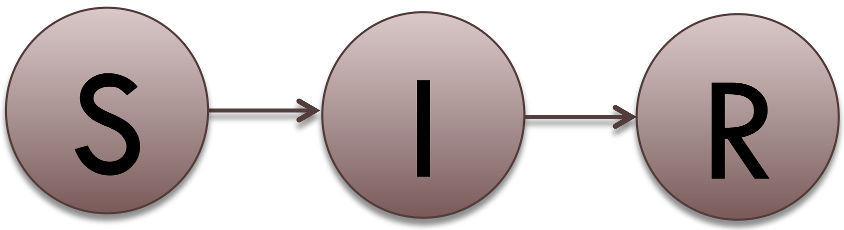
- **Continuous time**
- Discrete time

- **Continuous treatment of individuals**

- **Deterministic**
- Stochastic

Ordinary Differential Equations (ODEs)

- Describe change in **state variables** through time



Ordinary Differential Equations (ODEs)

- Describe change in **state variables** through time
  - ***deterministic*** *progression from set of* ***initial conditions***

Ordinary Differential Equations (ODEs)

- Describe change in **state variables** through time
  - ***deterministic*** *progression from 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

Ordinary Differential Equations (ODEs)

Characteristics:

A. Continuous treatment of individuals
B. Continuous treatment of time
C. Assumptions:
   1. large (infinite) populations
   2. well-mixed contacts
   3. homogeneous individuals
   4. exponential waiting times (memory-less)

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A. Continuous Treatment of Individuals

- appropriate for:
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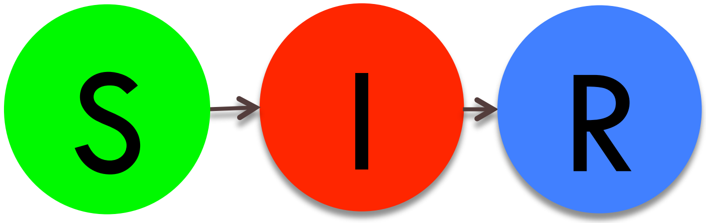
  - population densities



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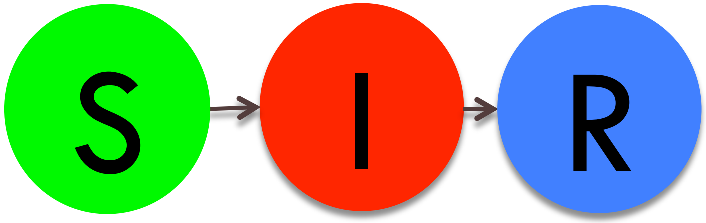

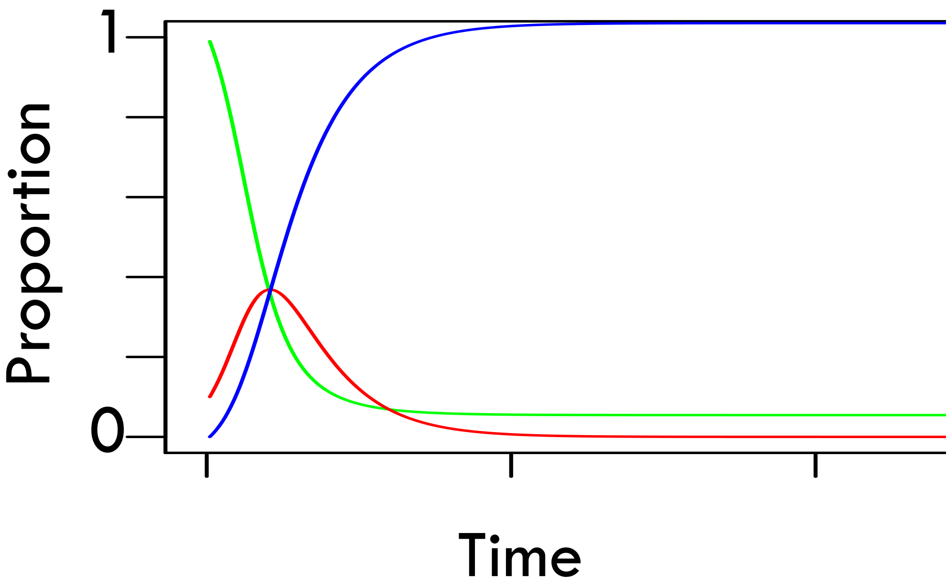

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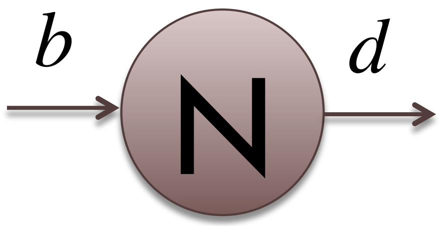

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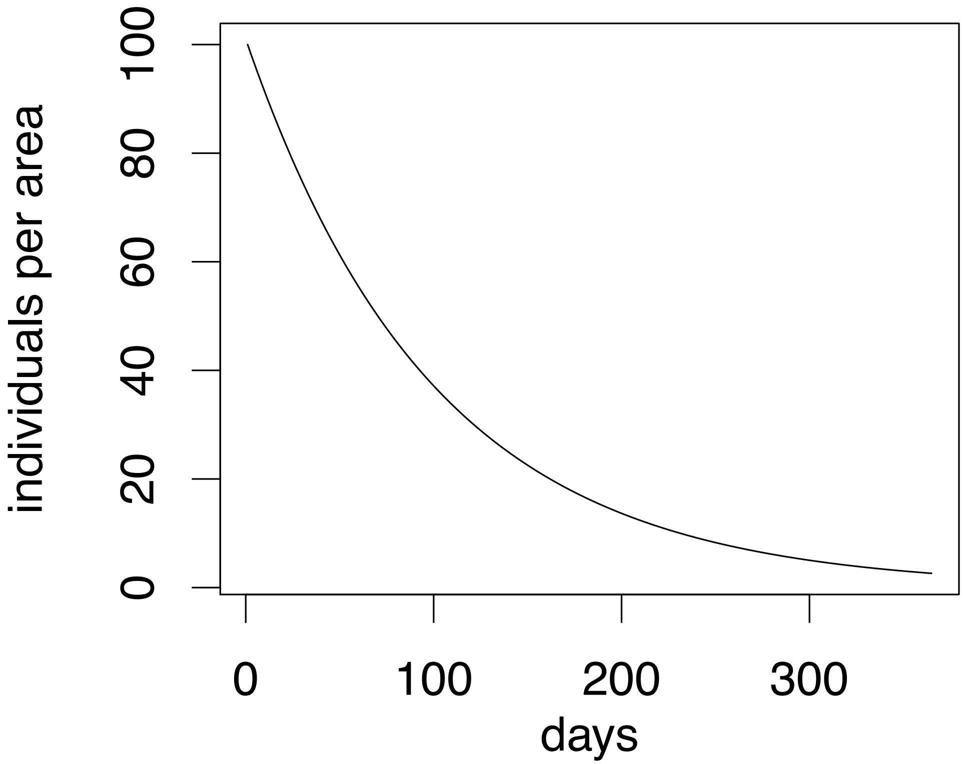

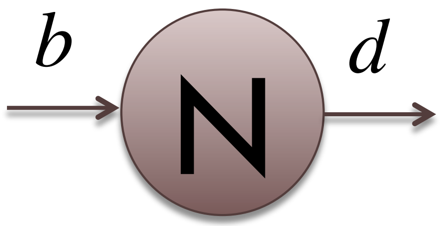

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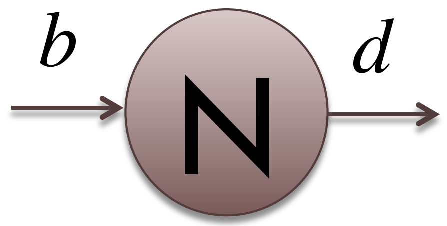

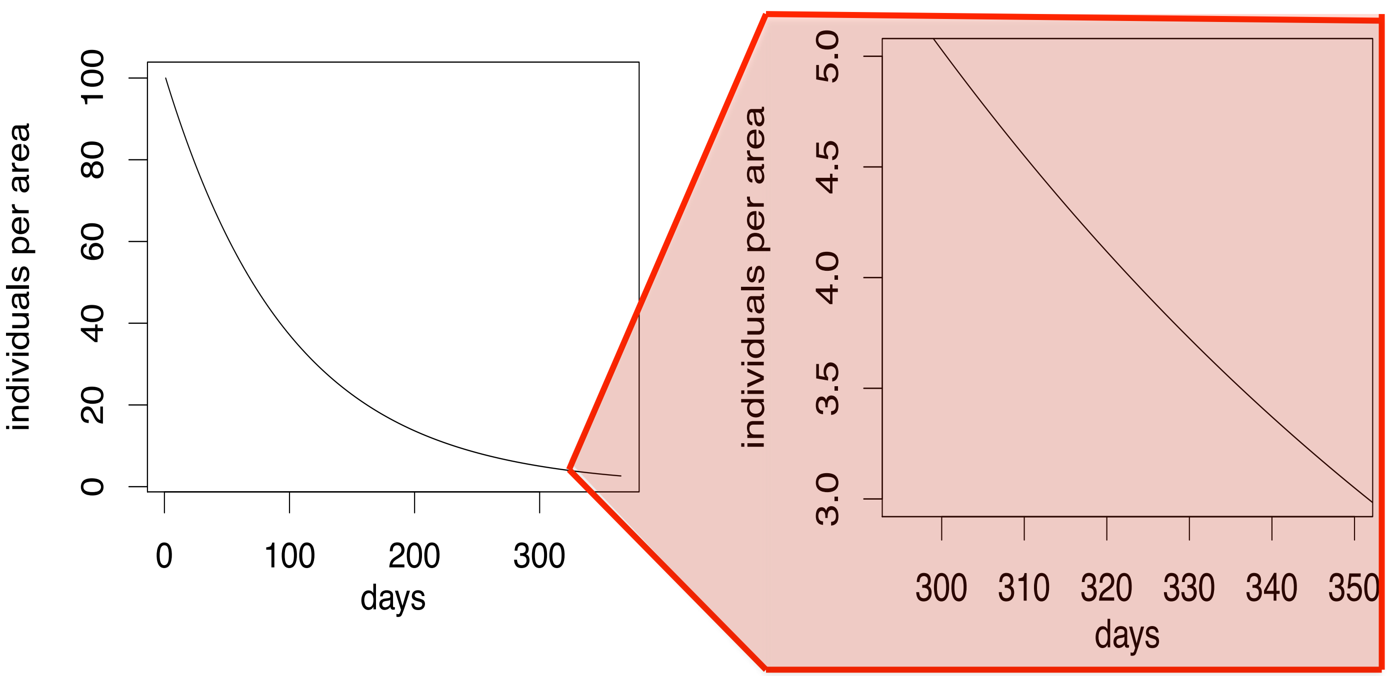

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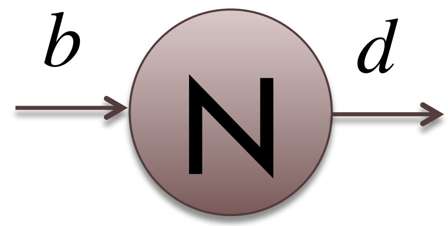

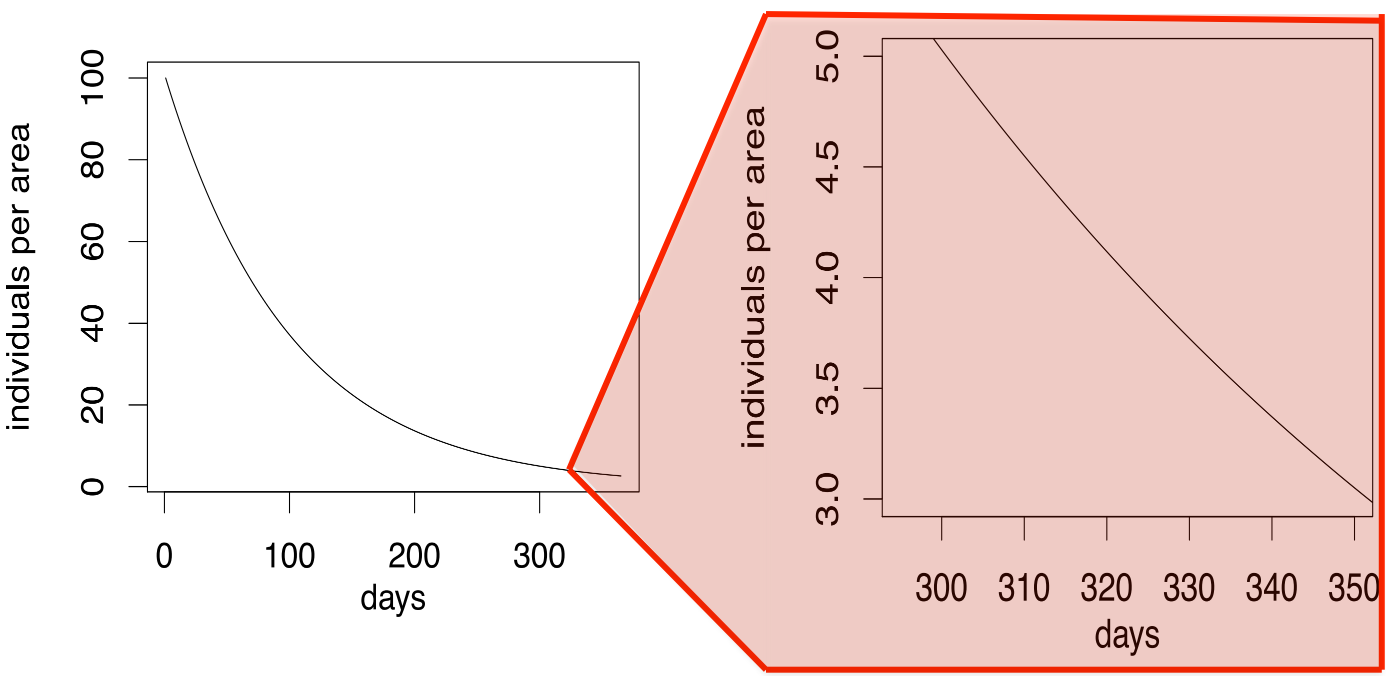


```
> tail(out)
time        N
360         2.759832
361         2.732372
362         2.705184
363         2.678267
364         2.651618
365         2.625234
```

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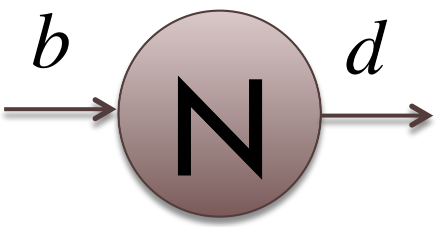
B. Continuous (v. Discrete) Treatment of Time

- Continuous treatment of time



$$\frac{dN}{dt} = bN - dN$$

- Treatment of time as discrete steps

$$\frac{\Delta N}{\Delta t} = bN - dN$$

- N = population size or density
- t = time
- Δ denotes "change in"
- b = ***per capita*** birth rate (units = time^{-1})
- b*N = total birth rate (units = indiv/time)
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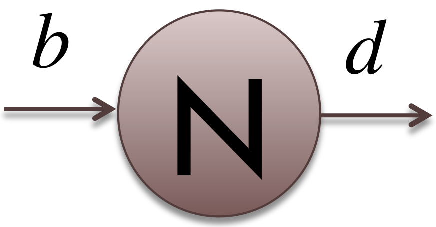

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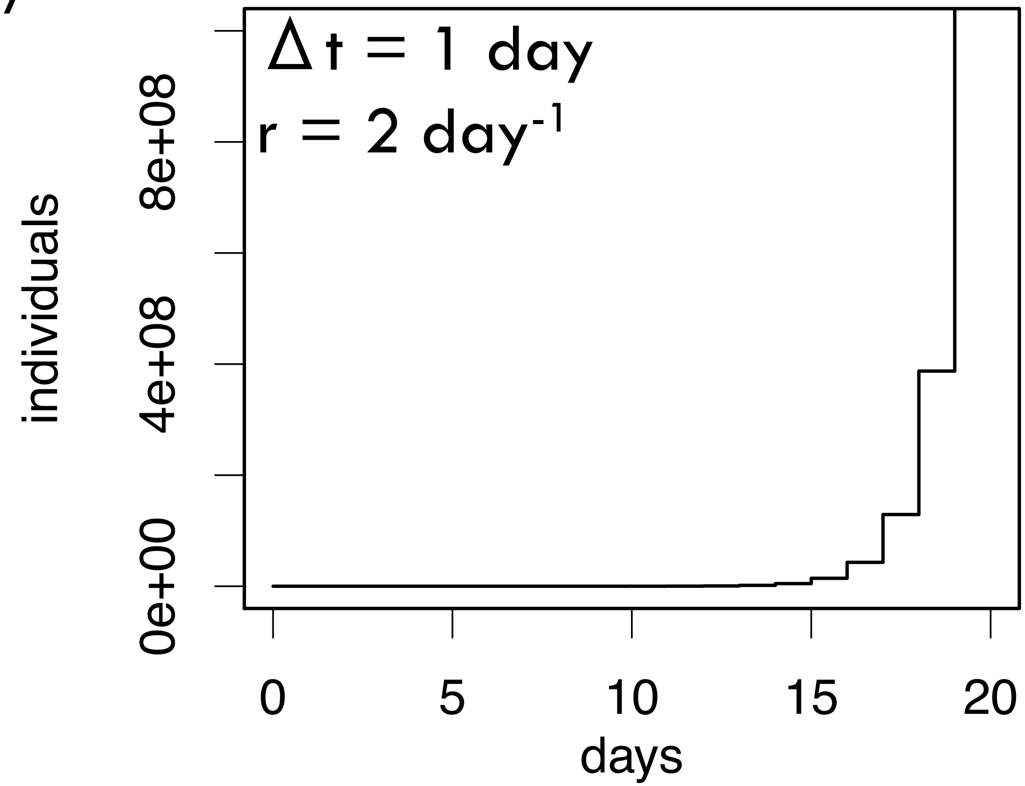
- **r is called the "intrinsic population growth rate"**
- r is like R0, but by convention, we think about it as *b-d* instead of *b/d*, so:
- **if r>0, N increases with time**
- **if r<0, N decreases with time**
- **if r=0, then N is constant**

B. Continuous (v. Discrete) Treatment of Time

- At r>0, population grows exponentially

$$\Delta N = r N \Delta t$$



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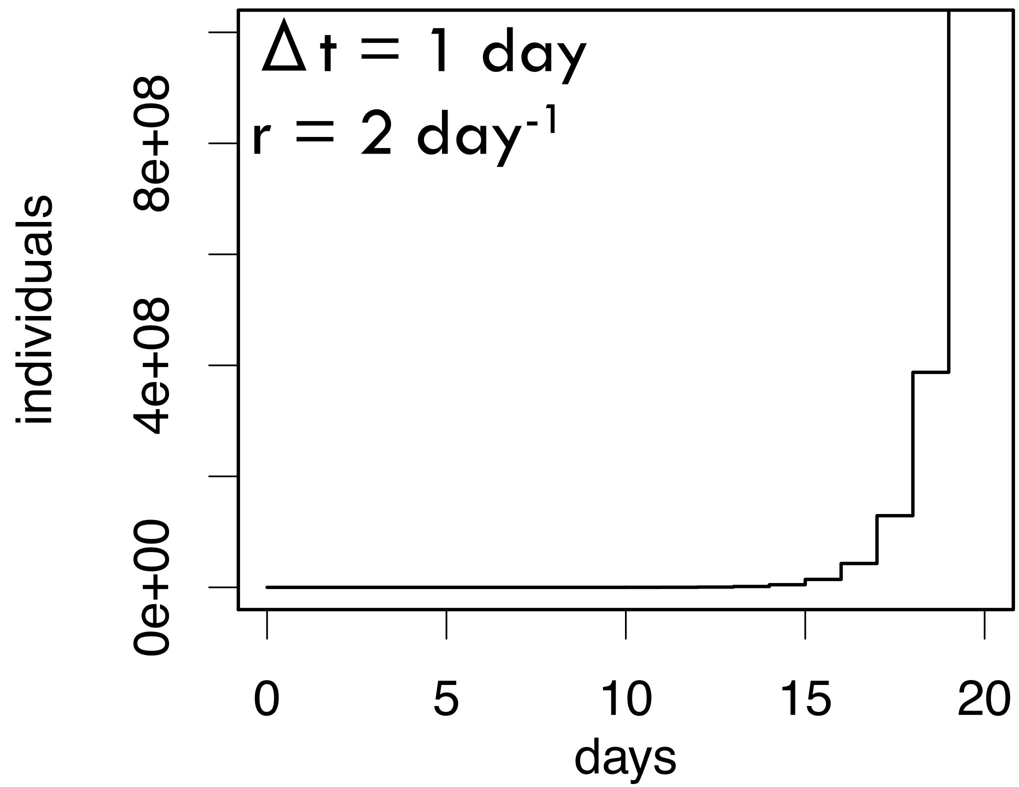

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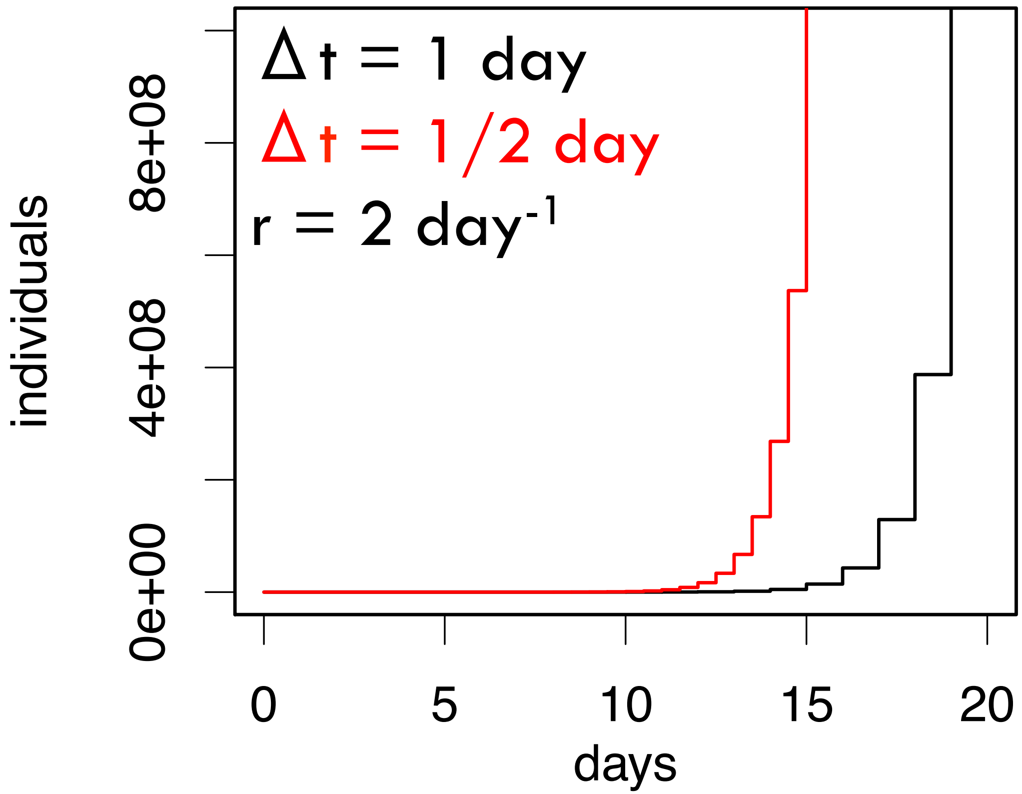
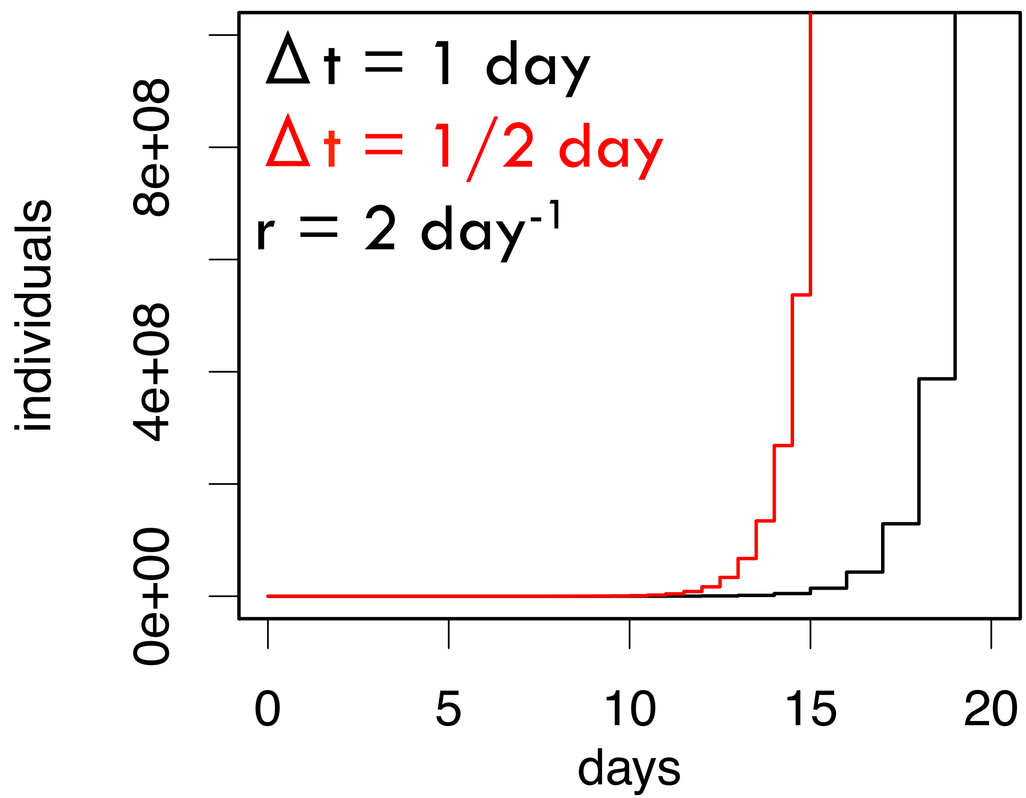


B. Continuous (v. Discrete) Treatment of Time

- At r>0, population grows exponentially
- But at smaller Δ t, exponential growth is faster. Why?
- **We can have equivalent per capita growth rates but higher population level growth!**

$$\Delta N = r N \Delta t$$



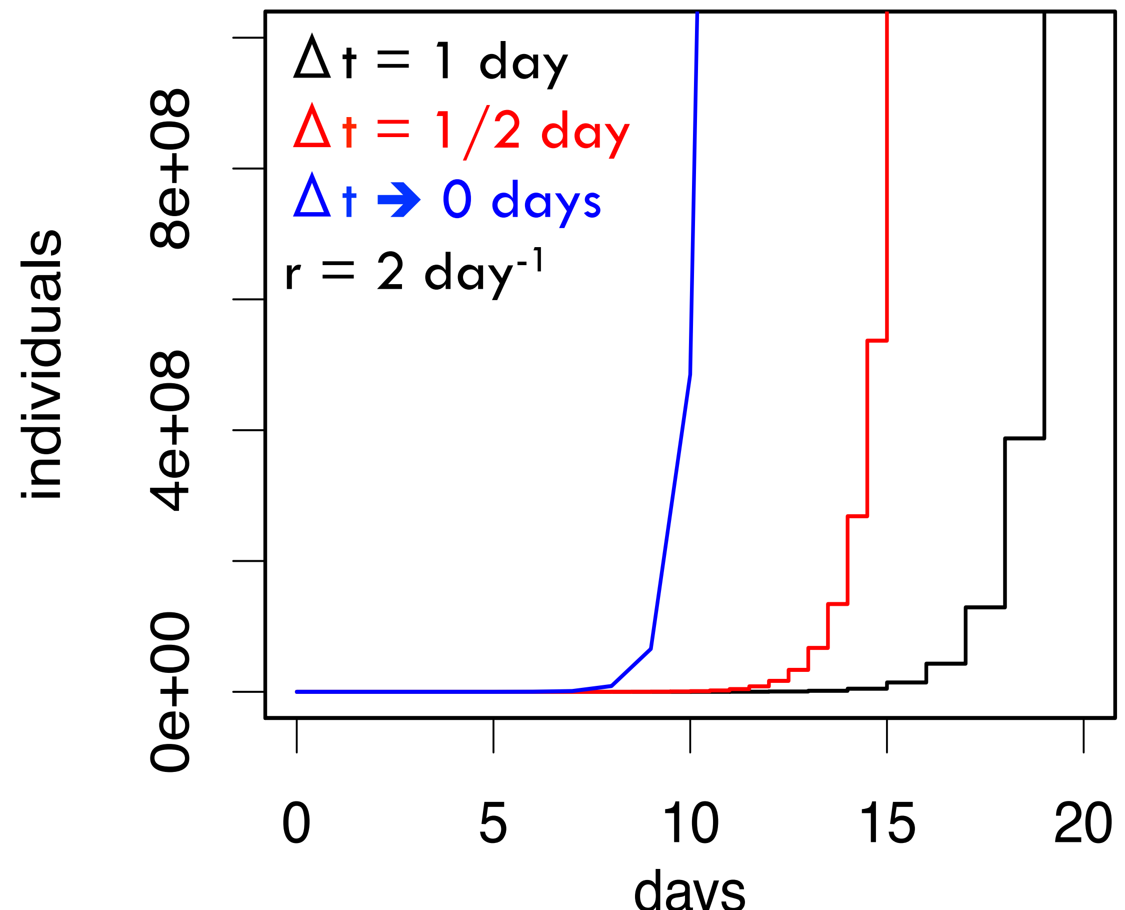
B. Continuous (v. Discrete) Treatment of Time

- Continuous time offers the smallest Δt of all:

$$\frac{dN}{dt} = \lim_{\Delta t \to 0} \frac{\Delta N}{\Delta t} \quad \Rightarrow \quad N_t = N_0 e^{rt}$$

B. Continuous (v. Discrete) Treatment of Time

$$N_t = N_0 e^{rt}$$



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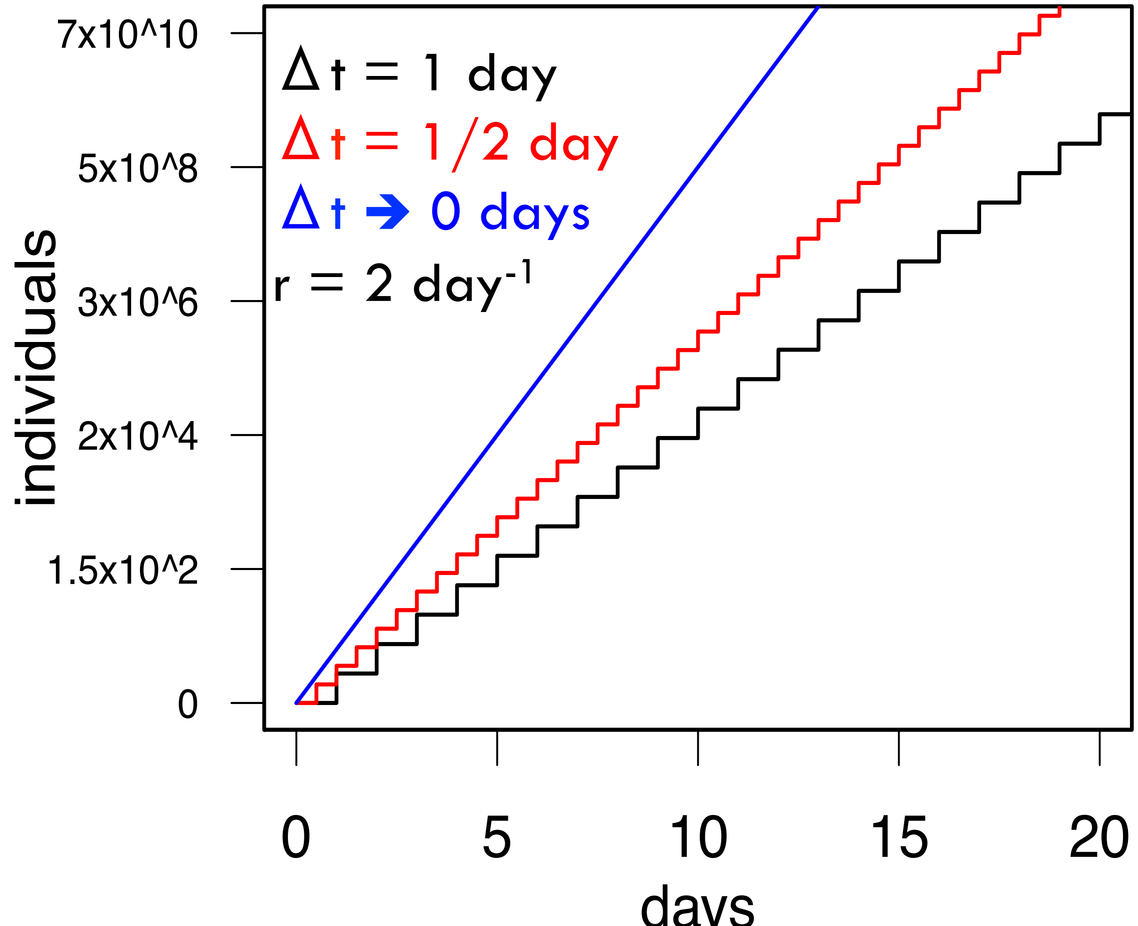

B. Continuous (v. Discrete) Treatment of Time

- Treatment of time affects population-level growth

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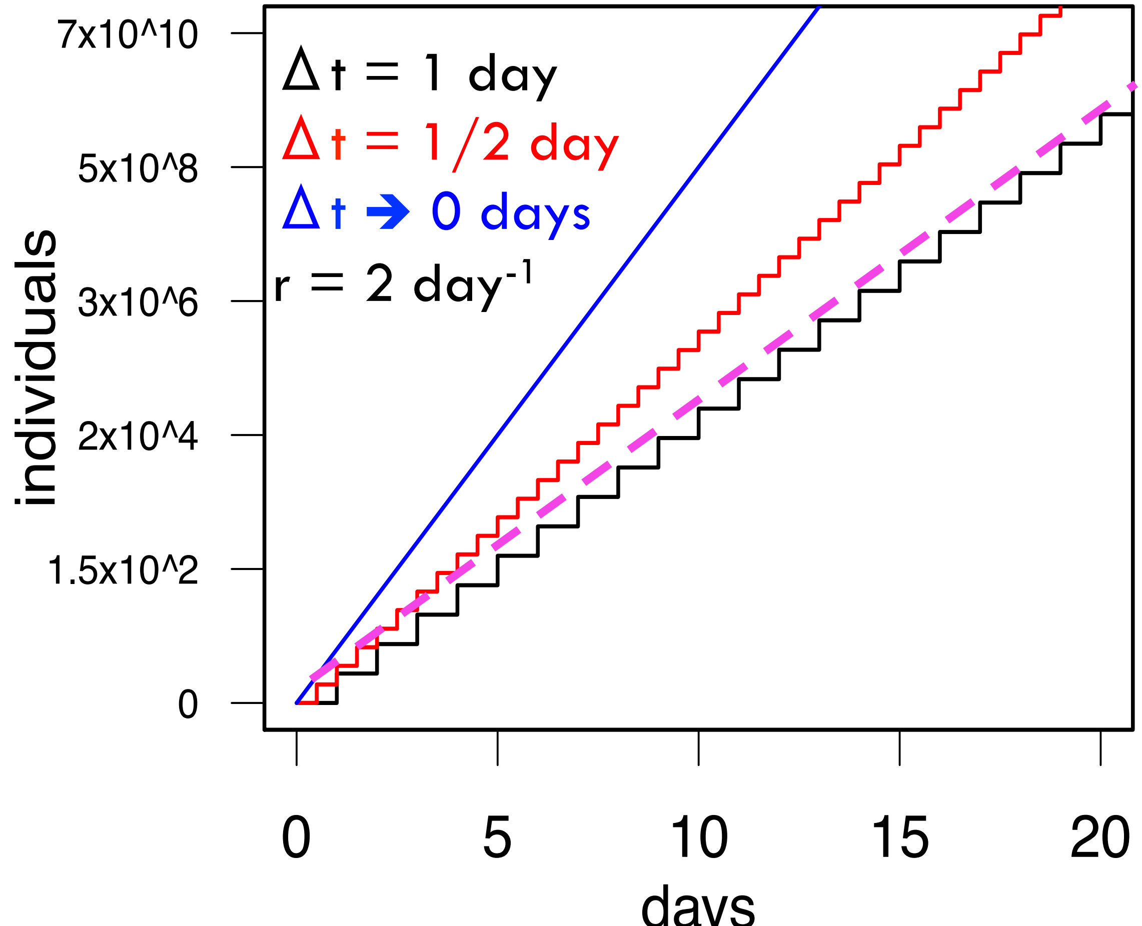

B. Continuous (v. Discrete) Treatment of Time

- Treatment of time affects population-level growth
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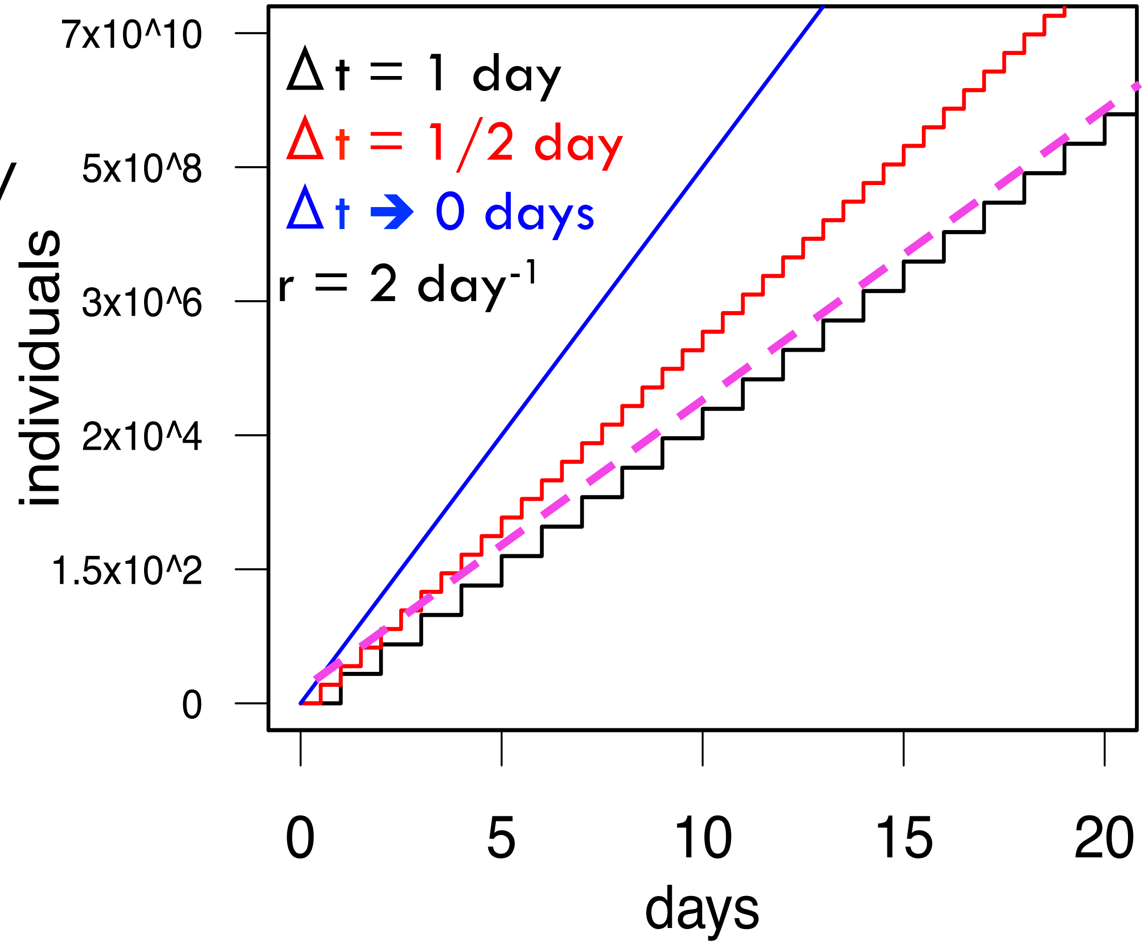

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- $\lambda = e^{r \Delta t}$

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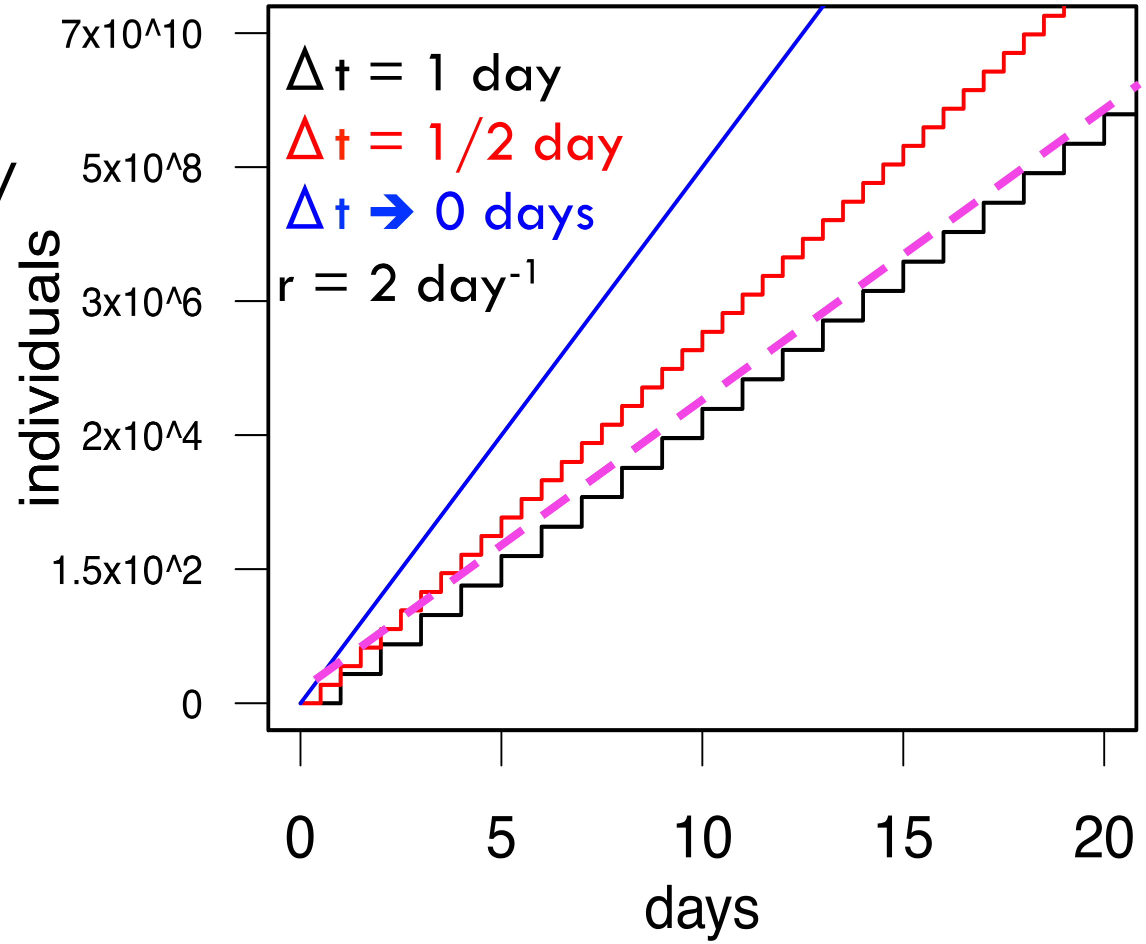
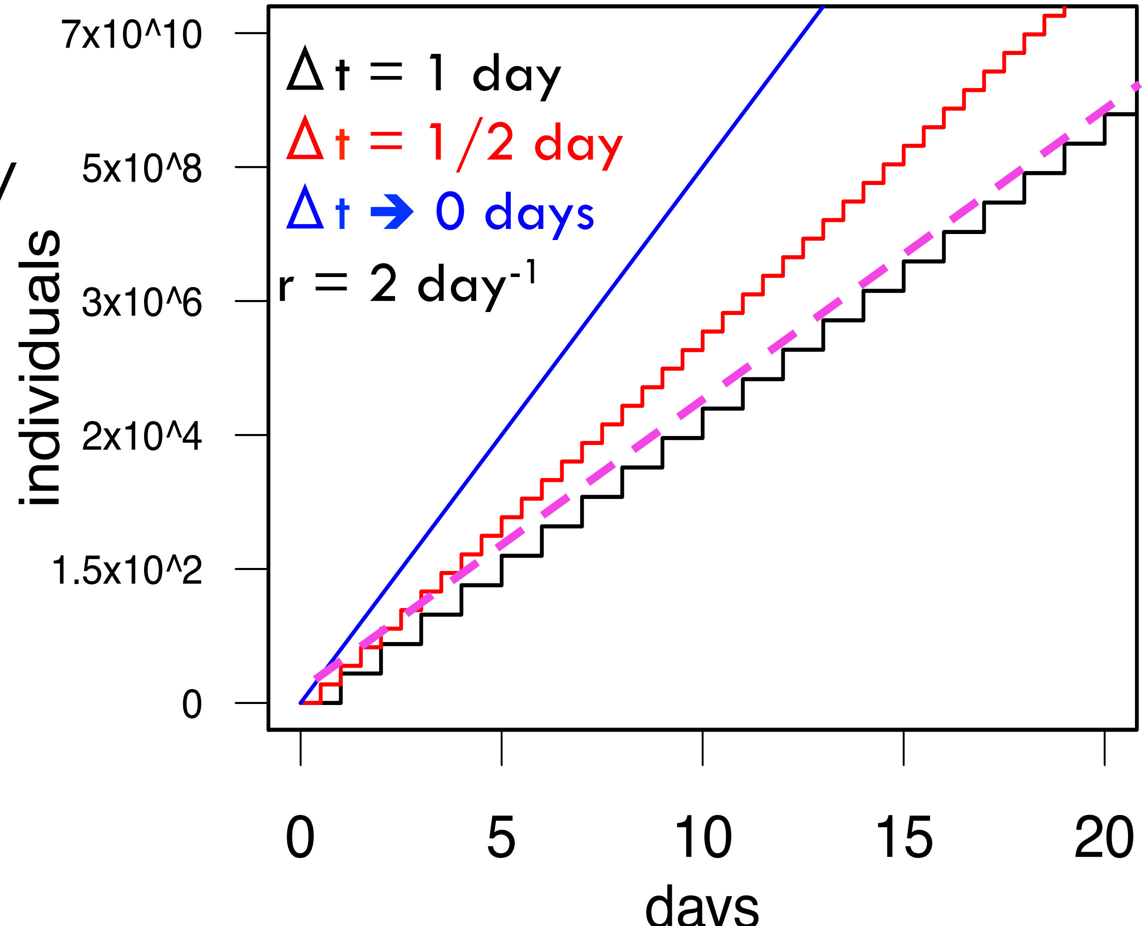


B. Continuous (v. Discrete) Treatment of Time

- Treatment of time affects population-level growth
- Must think carefully about parameters
- $\lambda = e^{r \Delta t}$
- **Sometimes, discrete time may be more appropriate than continuous!**

$$N_t = N_0 e^{rt}$$



Ordinary Differential Equations (ODEs)

Characteristics:

A. Continuous treatment of individuals
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C. **Assumptions:**
   1. **large (infinite) populations**
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Assumptions: (1) Large populations

$$S \xrightarrow{\frac{\beta SI}{N}} I \xrightarrow{\gamma I} R$$

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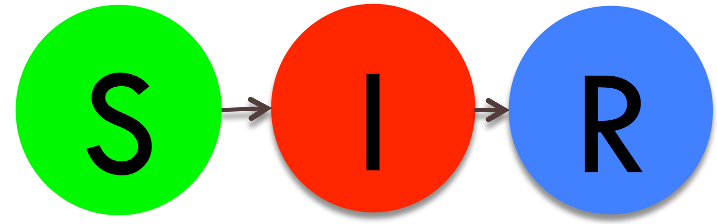
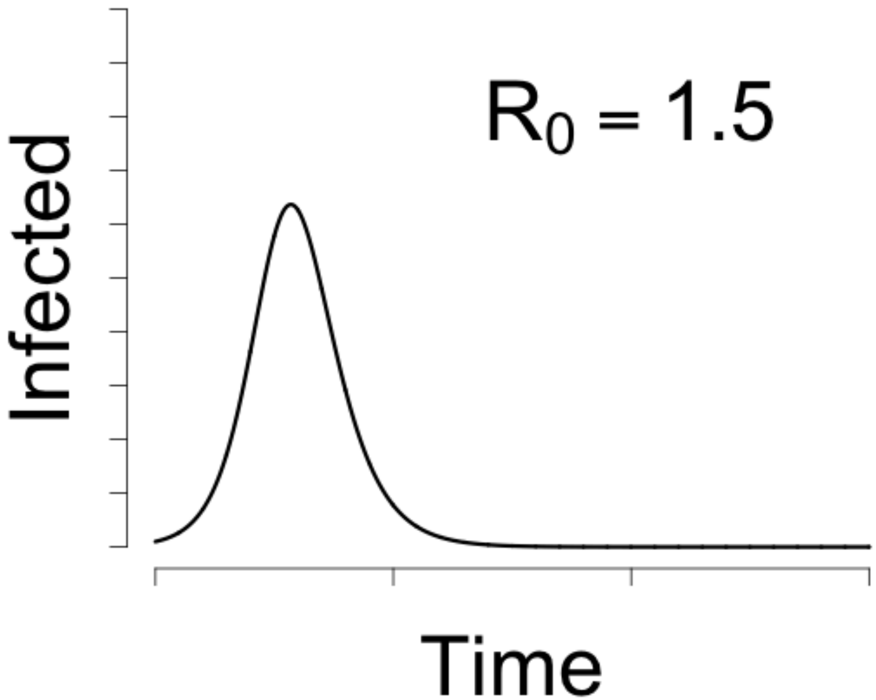
When *N* is large (infinite), **stochastic fadeout** and **demographic stochasticity** do not occur

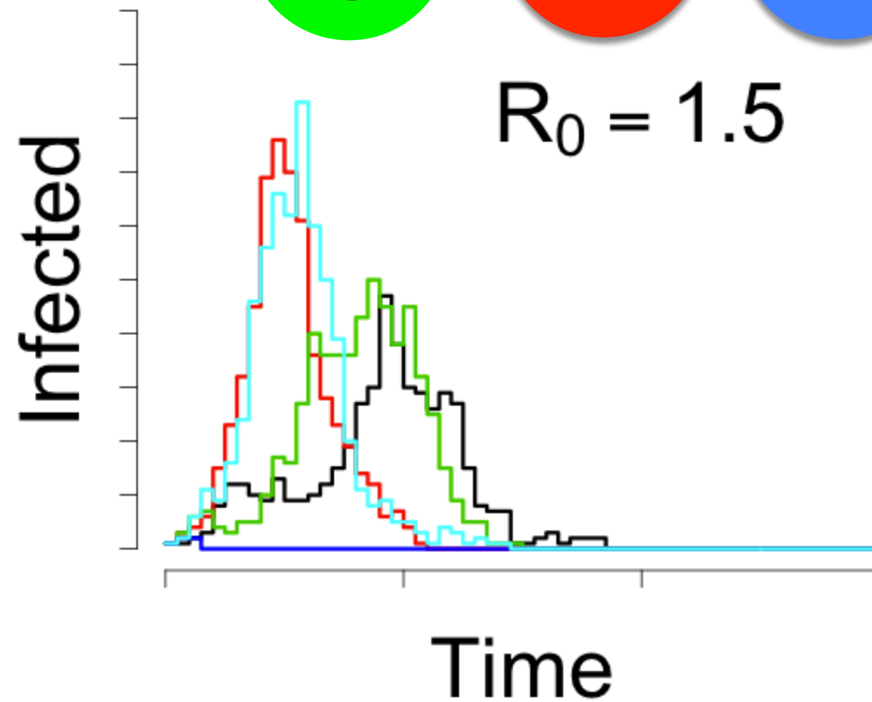
Assumptions: (1) Large populations

- average system behavior





ODE



Stochastic, discrete-time

Assumptions: (1) Large populations

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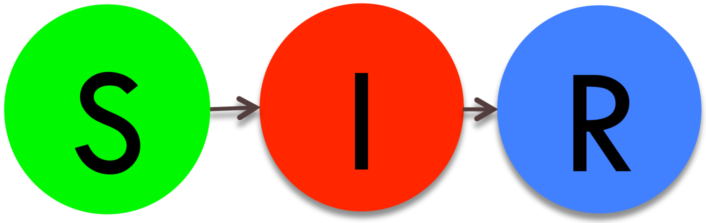
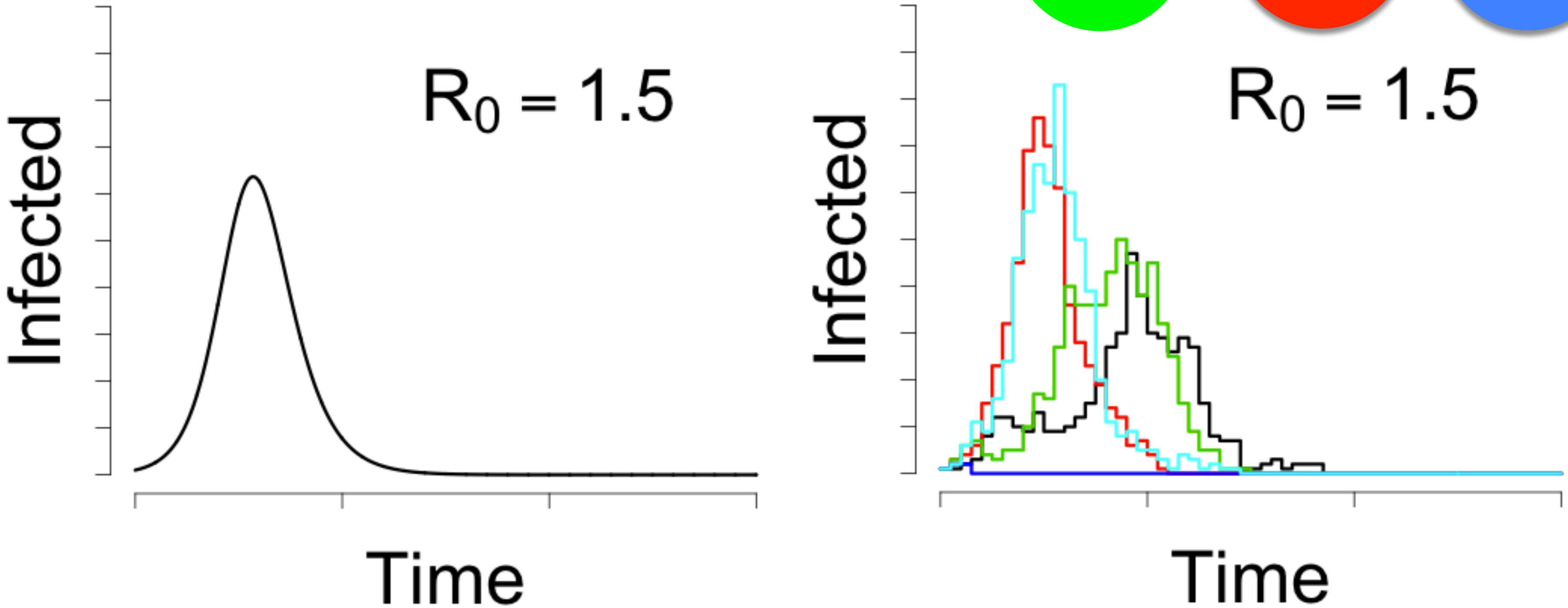
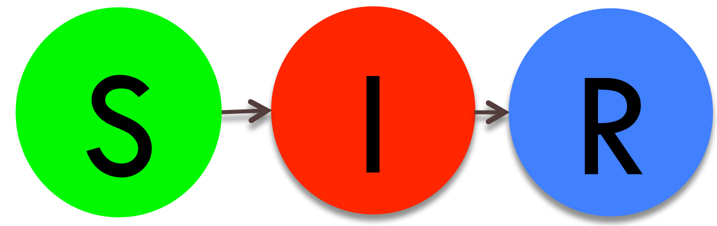


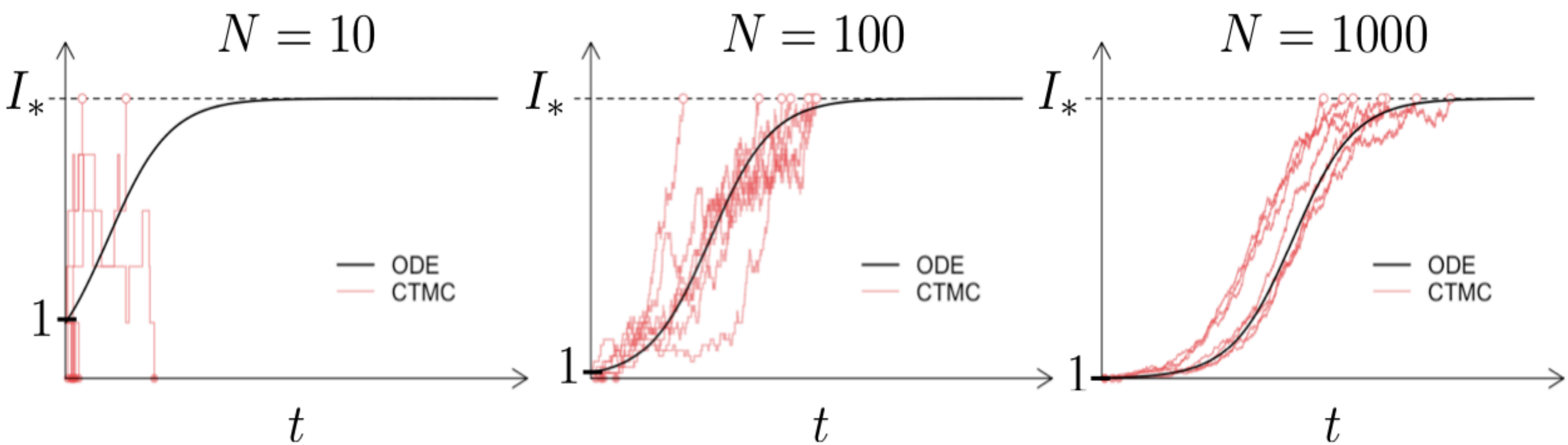


As the population size gets large, these curves begin to look more like the average behavior of the system (left)

Assumptions: (1) Large populations

- **average system behavior**





Continuous Time Markov Chain (CTMC)

Ordinary Differential Equation (ODE)

(Rebecca Borchering 2016)

Ordinary Differential Equations (ODEs)

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Assumptions: (2) well-mixed contacts

$$R_0 = \frac{\beta}{\gamma} = c * \rho * \left(\frac{1}{\gamma}\right)$$

- R_0 = basic reproduction number
  - number of new infections generated by 1 infectious individual in a completely susceptible population

Assumptions: (2) well-mixed contacts

$$R_0 = \frac{\beta}{\gamma} = c * \rho * \left(\frac{1}{\gamma}\right)$$

contact rate

(ODE assumes every infected equally likely to come in contact with every susceptible)

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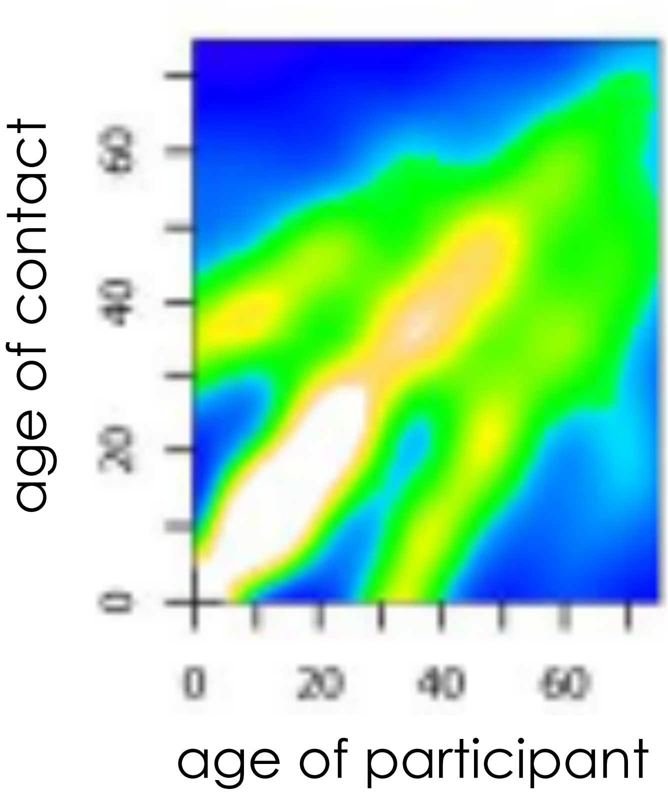
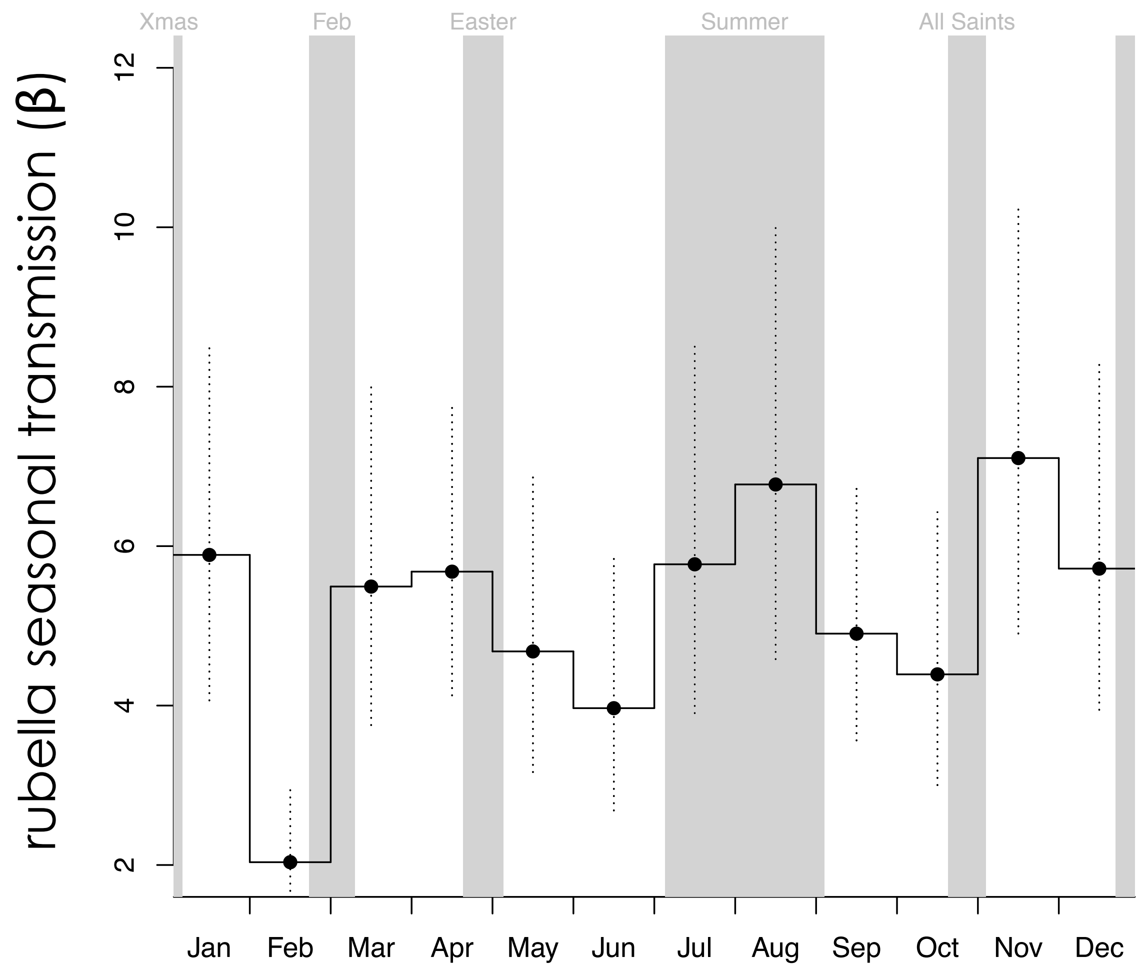
Assumptions: (2) well-mixed contacts

- Often not true!



(Mossong et al. 2008)



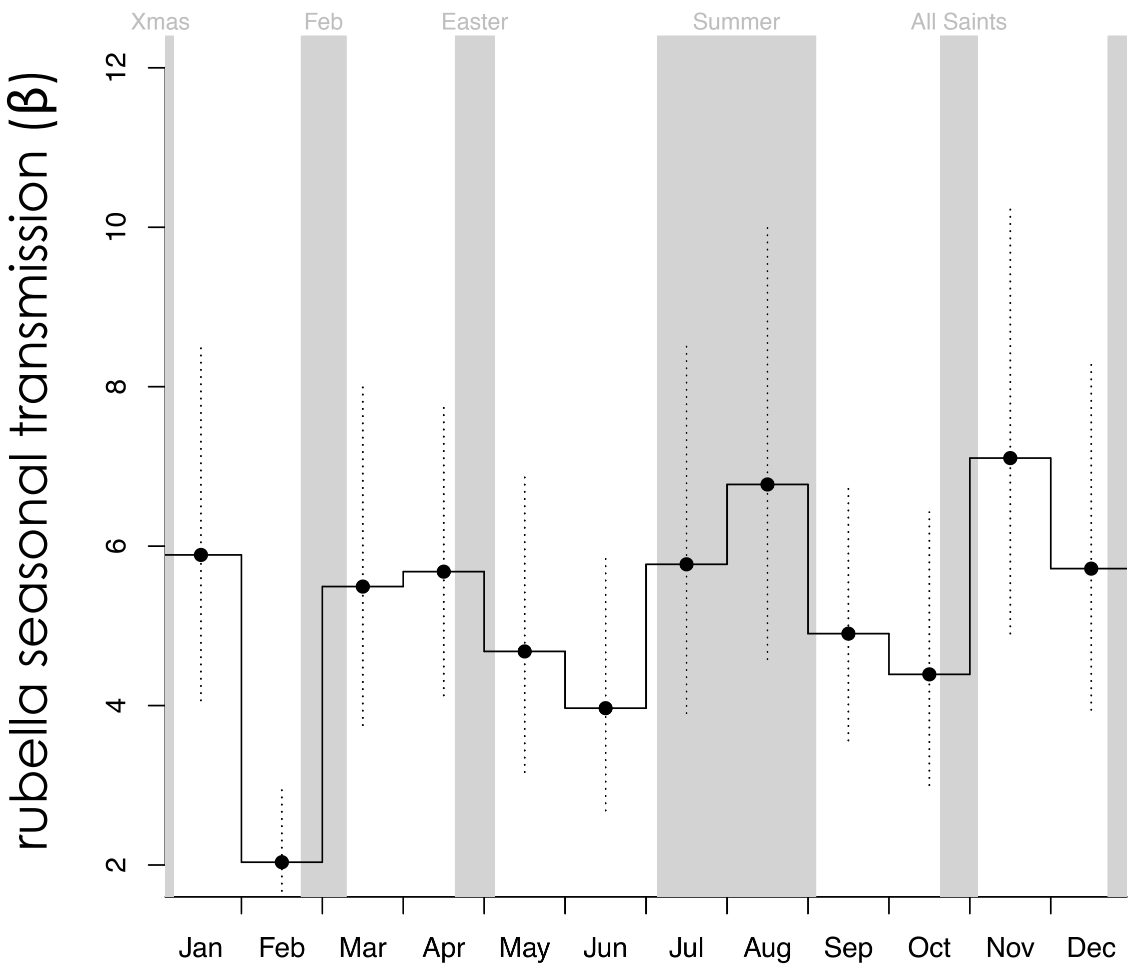
(Wesolowski*, Mensah*, Brook* et al. 2016)

Assumptions: (2) well-mixed contacts

$$R_0 = \frac{\beta}{\gamma}$$

If $(1/\gamma) = \Delta t$ for a discrete time model and we rescale time to the same units:

$\mathbf{R_0} = \beta\ \text{time-1} * \Delta t$



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Assumptions: (3) homogeneous individuals

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probability infection given contact

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Assumptions: (3) homogeneous individuals

- Also often not true!
- Heterogeneity in ρ
  - Immunocompromised individuals
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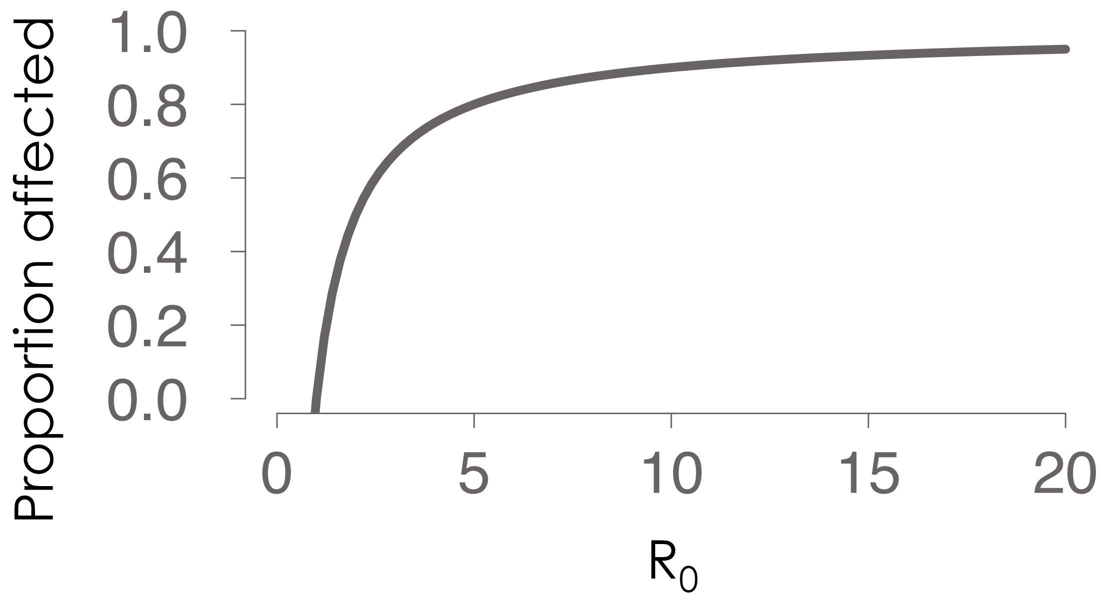

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- Also often not true!
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  - Immunocompromised individuals
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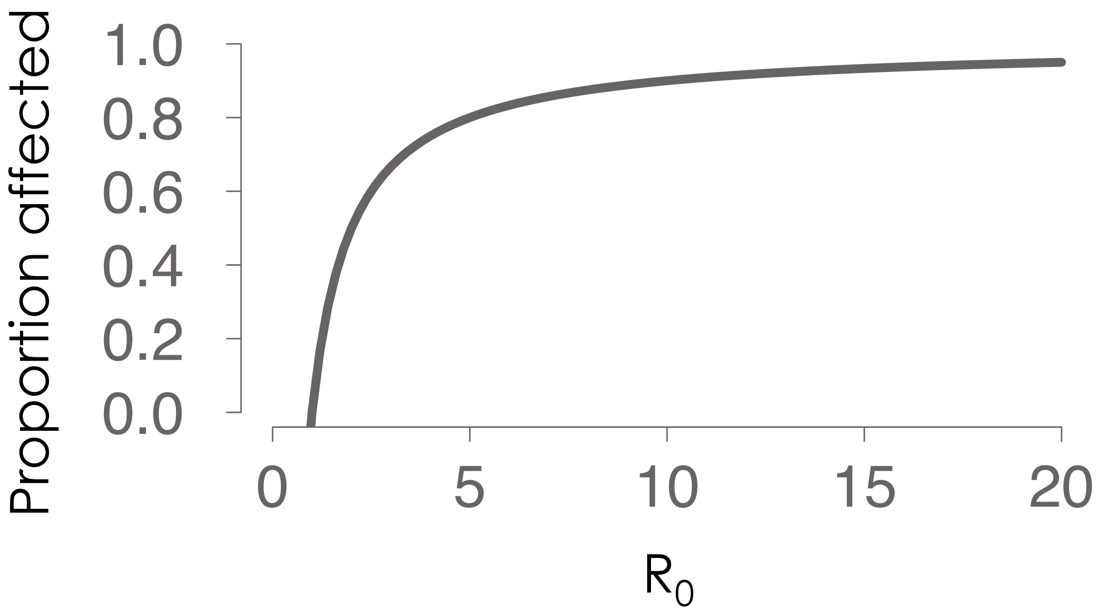
For a simple model, the population currently or previously infected at equilibrium = $1-1/R_0$

But heterogeneity alters this relationship!



Assumptions: (3) homogeneous individuals

- Also often not true!
- Heterogeneity in ρ
  - Immunocompromised individuals
  - Superspreaders
- Heterogeneity in other parameters
  - i.e. duration of infection

For a simple model, the population currently or previously infected at equilibrium = $1-1/R_0$

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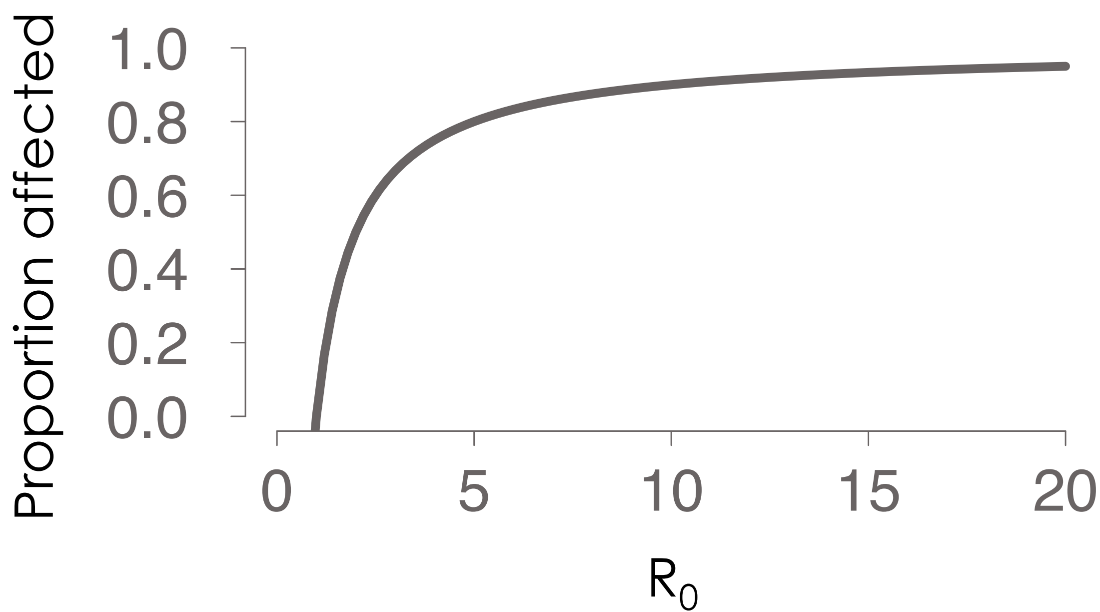
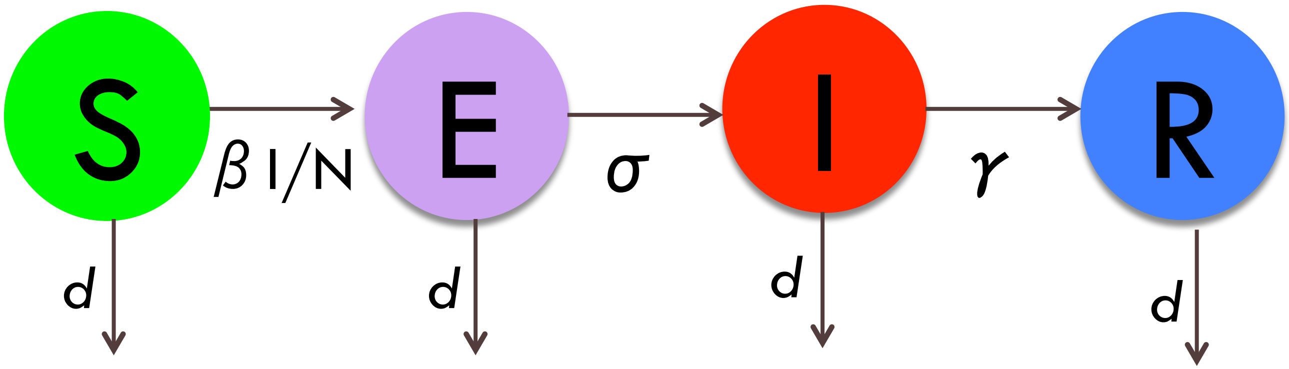


Ordinary Differential Equations (ODEs)

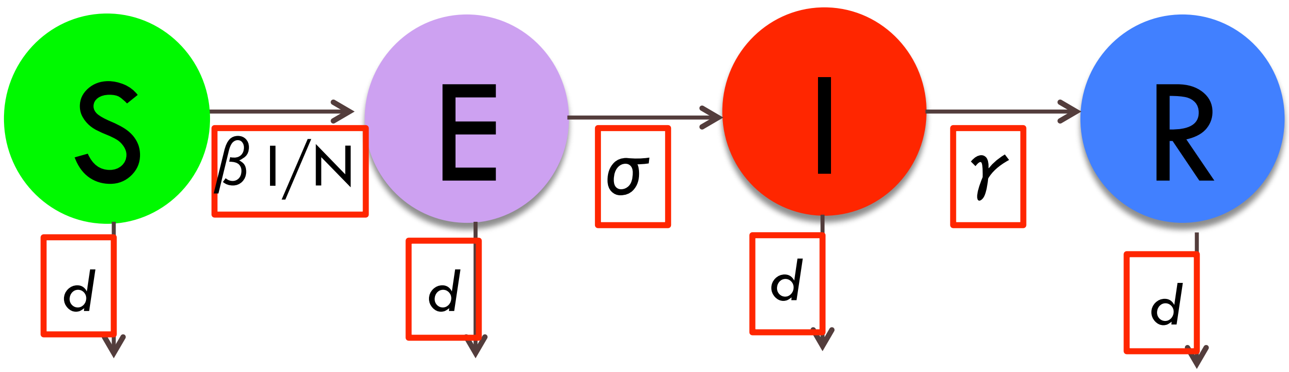
Characteristics:

A. Continuous treatment of individuals
B. Continuous treatment of time
C. **Assumptions:**
   1. large (infinite) populations
   2. well-mixed contacts
   3. homogeneous individuals
   4. **exponential waiting times (memory-less)**

Assumptions: (4) exponential waiting times

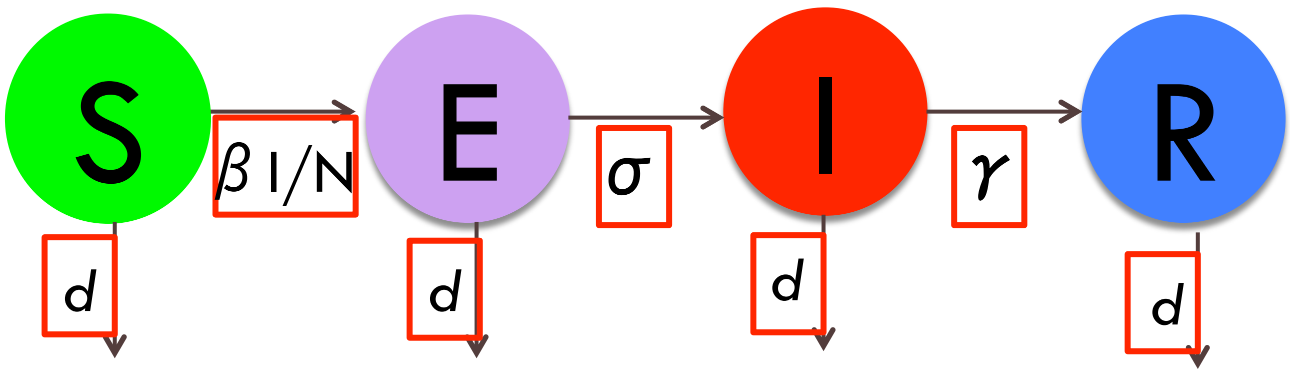


Assumptions: (4) exponential waiting times



- In a simple ODE, the 'waiting time' for these events to occur (**infection, incubation, recovery, death**) is **memoryless**, meaning the distribution of the waiting time at time t_{25} is the same as at t_0.

Assumptions: (4) exponential waiting times



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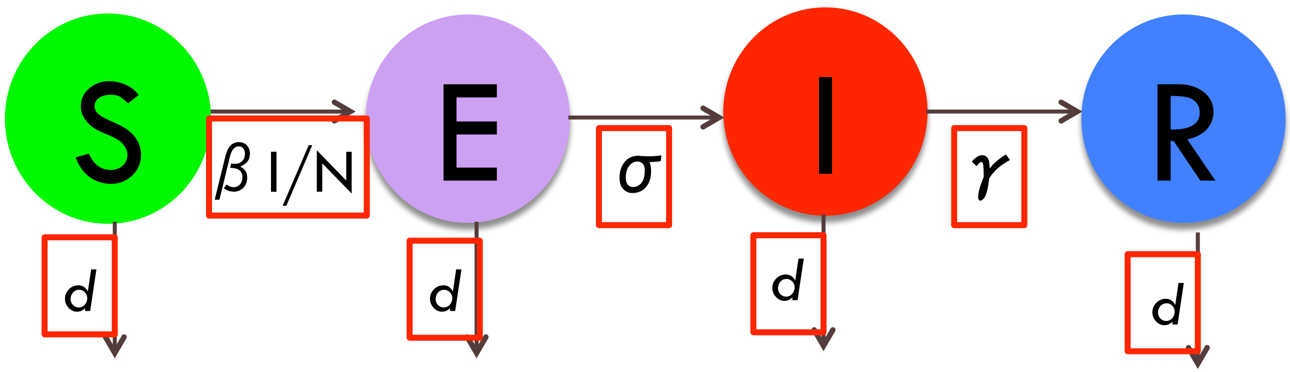
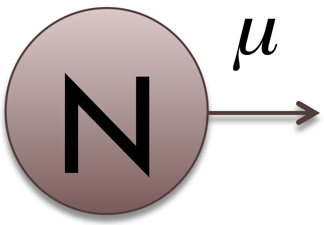


- In a simple ODE, the 'waiting time' for these events to occur (**infection, incubation, recovery, death**) is **memoryless**, meaning the distribution of the waiting time at time t_{25} is the same as at t_0.
- This means that your exit rate does not change, regardless of how long you've been in each box
- **This is often not true!**

Assumptions: (4) exponential waiting times

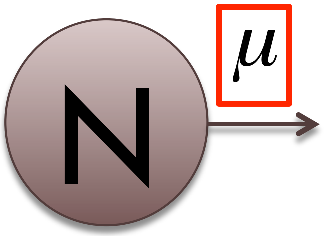
Exponential survival:



$$\frac{dN}{dt} = -\mu N$$

Assumptions: (4) exponential waiting times

Exponential survival:



$$\frac{dN}{dt} = -\mu N$$

- In a simple survival ODE, the ‘waiting time’ for death to occur is **memoryless**, meaning that the probability is no different at $t_{0,}$ $t_{25,}$ or t_{75}

Assumptions: (4) exponential waiting times

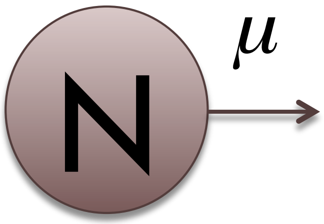
Exponential survival:

$$N_t = N_0 e^{-\mu t}$$

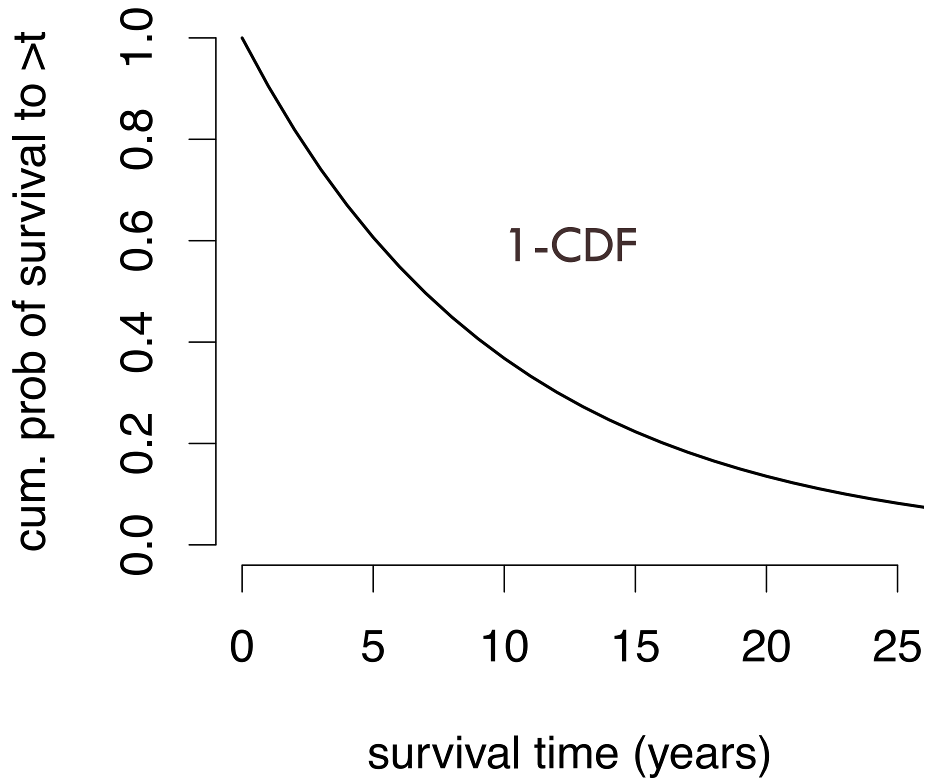
- In a simple survival ODE, the 'waiting time' for death to occur is **memoryless**, meaning that the probability is no different at t_0, t_{25}, or t_{75}

Assumptions: (4) exponential waiting times

Exponential survival:



$$\frac{N_t}{N_0} = e^{-\mu t}$$



- In a simple survival ODE, the 'waiting time' for death to occur is **memoryless**, meaning that the probability is no different at $t_{0,}$ $t_{25,}$ or t_{75}

Model terminology

- Compartmental models
- Network models
- Individual-based models

- Continuous time
- Discrete time

- Deterministic
- Stochastic

Ordinary Differential Equations (ODEs)

- **Compartmental** models
- Network models
- Individual-based models

- **Continuous time**
- Discrete time

- **Continuous treatment of individuals**

- **Deterministic**
- Stochastic

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