Towards Stochastic Models of Epidemics
(and a recap of 1st day lessons learned)

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Atlanta GA, USA
This Workshop’s Central Objective:

**Helping you integrate computational models of living systems into your research and classes**

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**The Inspiration:**
**Mathematical Basics of Epidemics**
**Monday morning**
**What We Did Right, Wrong & What’s Next**

**The Setup:**
**Deterministic Models**
**Monday afternoon**

**For the Win:**
**Stochastic Models**
**Tuesday morning**

**The Future:**
**From Models to Interactive Communication**
**Tuesday afternoon**
**Network science and Covid-19**
### MONDAY, MAY 17

<table>
<thead>
<tr>
<th>Time</th>
<th>Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>8:45</td>
<td>Welcome to the Workshop – Prof. Joshua Weitz, School of Biological Sciences, Georgia Tech &amp; Prof. James C. Gumbart, School of Physics, Georgia Tech</td>
</tr>
<tr>
<td>9:00</td>
<td>Plenary Lecture – Core principles behind infection and disease spread – Prof. Sarah Cobey, Department of Ecology &amp; Evolution, University of Chicago</td>
</tr>
<tr>
<td>10:00</td>
<td>Q&amp;A</td>
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<tr>
<td>10:15</td>
<td>Break</td>
</tr>
<tr>
<td>10:30</td>
<td>Track 1: Introduction to programming</td>
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<td></td>
<td>Track 2: Journal club discussion for more advanced programmers</td>
</tr>
<tr>
<td>12:00</td>
<td>Lunch Break</td>
</tr>
<tr>
<td>13:00</td>
<td>Hands-on Modeling Epidemics I: Deterministic Models</td>
</tr>
<tr>
<td>15:00</td>
<td>Wrap-up day 1</td>
</tr>
</tbody>
</table>

### TUESDAY, MAY 18

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<thead>
<tr>
<th>Time</th>
<th>Activity</th>
</tr>
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<tbody>
<tr>
<td>9:00</td>
<td>Lecture: Stochastic Modeling of Epidemics – Prof. Joshua Weitz, School of Biological Sciences, Georgia Tech</td>
</tr>
<tr>
<td>10:00</td>
<td>Q&amp;A</td>
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<tr>
<td>10:15</td>
<td>Break</td>
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<tr>
<td>10:30</td>
<td>Hands-on Modeling Epidemics II: Stochastic Models</td>
</tr>
<tr>
<td>12:00</td>
<td>Lunch Break</td>
</tr>
<tr>
<td>13:00</td>
<td>Introduction to Dashboards – Applied Bioinformatics Laboratory (ABIL)</td>
</tr>
<tr>
<td>13:30</td>
<td>Hands-on Dashboard Implementation: Epidemic dynamics</td>
</tr>
<tr>
<td>15:00</td>
<td>Survey (Lottery among all participants)</td>
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<tr>
<td>15:15</td>
<td>Break</td>
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<tr>
<td>15:30</td>
<td>Plenary Lecture – Prof. Sam Scarpino, Network Science Institute, Northeastern University</td>
</tr>
<tr>
<td>16:30</td>
<td>Prize announcement of survey lottery</td>
</tr>
<tr>
<td>16:45</td>
<td>Closing thoughts</td>
</tr>
<tr>
<td>17:00</td>
<td>Workshop closes</td>
</tr>
</tbody>
</table>
What’s going to happen next?

A lecture bridging the gap between deterministic and stochastic model of epidemics.

Then a short break.

Then, break-out rooms where our team of QBioS + guest instructors will guide the hands-on modeling activities.

Yesterday, AM: Basics in coding/journal club.
Yesterday, PM: Deterministic epi models.
Today, AM: Stochastic models of epidemics.

Each group is working in one language (Matlab, Python or R).

The guides are in pdf-s so you should read, think, type in code, learn from (purposeful) mistakes, build your own epidemic models, and discover new insights along the way.

After lunch: from dashboards (w/ABiL) to network models (w/Sam Scarpino)
Morning Talk

Part 1 – Epidemic Modeling
the basics of SIR models

Part 2 – Principles of Outbreaks
strength, speed, and size

Part 3 - Variability and Epidemics
core concepts underlying stochasticity trajectories
Morning Talk

Part 1 – Epidemic Modeling
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Part 3 - Variability and Epidemics
core concepts underlying stochasticity trajectories
Modeling interactions depends on space
Modeling interactions depends on space

Non-spatial

Discrete space
Modeling interactions depends on space

Non-spatial

Discrete space

Continuous Space

Merler et al. BMC Medicine 2013
Modeling interactions depends on space

Non-spatial
ODEs

Discrete space
Network models

Continuous Space
PDE + Networks

Merler et al. BMC Medicine 2013
Modeling interactions depends on space

Non-spatial
ODEs

Discrete space
Network models

Continuous Space
PDE + Networks

More complicated models fit data better but are harder to parametrize and analyze

Merler et al. BMC Medicine 2013
SIR model: susceptible-infected-recovered
SIR model: susceptible-infected-recovered

How do we take these processes and turn them into a mathematical model?
SIR model: susceptible-infected-recovered

\[ S(t + 1) = S(t) - \ldots \]
\[ I(t + 1) = I(t) + \ldots - \ldots \]
\[ R(t + 1) = R(t) + \ldots \]

The biology view, part I
SIR model: susceptible-infected-recovered

\[
S(t + 1) = S(t) - \text{infections}
\]

\[
I(t + 1) = I(t) + \text{infections} - \text{recovery}
\]

\[
R(t + 1) = R(t) + \text{recovery}
\]

The biology view, part 2
SIR model: susceptible-infected-recovered

How do we go about turning these words “infections” and “recovery” into equations?

\[ S(t + 1) = S(t) - \text{infections} \]
\[ I(t + 1) = I(t) + \text{infections} - \text{recovery} \]
\[ R(t + 1) = R(t) + \text{recovery} \]
SIR model: susceptible-infected-recovered

\[
S(t + 1) = S(t) - \text{infections} \\
I(t + 1) = I(t) + \text{infections} - \text{recovery} \\
R(t + 1) = R(t) + \text{recovery}
\]
SIR model: susceptible-infected-recovered

\[
S(t+1) = S(t) - \underbrace{\cdots}_{\text{infections}}
\]

\[
I(t+1) = I(t) + \underbrace{\cdots}_{\text{infections}} - \gamma I
\]

\[
R(t+1) = R(t) + \gamma I
\]

Here, \( \gamma = \frac{1}{T_I} \) is a recovery rate.
**SIR model: susceptible-infected-recovered**

The SIR model describes the spread of infectious diseases in a population. The model categorizes individuals into three groups:

- **Susceptible (S)**: Individuals who can be infected.
- **Infected (I)**: Individuals who are carrying the disease and can infect others.
- **Recovered (R)**: Individuals who have recovered from the infection and are no longer infectious.

The model equations are given by:

- Susceptible cases:
  \[ S(t+1) = S(t) - \Delta S \]
- Infectious cases:
  \[ I(t+1) = I(t) + \Delta I - \gamma I \]
- Recovered cases:
  \[ R(t+1) = R(t) + \gamma I \]

Where:
- \( S(t) \), \( I(t) \), and \( R(t) \) represent the number of susceptible, infected, and recovered individuals at time \( t \), respectively.
- \( \beta \) is the infection rate.
- \( T_I \) is the incubation period.
- \( \gamma \) is the recovery rate.
SIR model: susceptible-infected-recovered

\[ S(t+1) = S(t) - \beta SI \]
\[ I(t+1) = I(t) + \beta SI - \gamma I \]
\[ R(t+1) = R(t) + \gamma I \]

Here $\beta$ is a transmission rate.
SIR model: susceptible-infected-recovered

Biology view to
Quantitative modeling view
Time is not just 0, 1, 2, …

Instead: consider smaller intervals
of time – “dt” (not 1 day, or even 1 hr, but minutes, seconds, etc.)

\[
S(t + dt) = S(t) - \beta SI \ dt \\
I(t + dt) = I(t) + \beta SI \ dt - \gamma I \ dt \\
R(t + dt) = R(t) + \gamma I \ dt
\]
**SIR model: susceptible-infected-recovered**

**Biology view to**
**Quantitative modeling view**

Time is not just 0, 1, 2, …

Instead: consider smaller intervals of time – “dt” (not 1 day, or even 1 hr, but minutes, seconds, etc.)

\[
\begin{align*}
\frac{S(t + dt) - S(t)}{dt} &= -\beta SI \\
\frac{I(t + dt) - I(t)}{dt} &= \beta SI - \gamma I \\
\frac{R(t + dt) - R(t)}{dt} &= \gamma I
\end{align*}
\]
The “SIR” model of disease transmission is a nonlinear, set of coupled, ordinary differential equations.

\[
\begin{align*}
\frac{dS}{dt} &= - \beta SI \\
\frac{dI}{dt} &= \beta SI - \gamma I \\
\frac{dR}{dt} &= \gamma I
\end{align*}
\]
Morning Talk

Part 1 – Epidemic Modeling
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strength, speed, and size

Part 3 - Variability and Epidemics
core concepts underlying stochasticity trajectories
Basic reproductive number, “R0”
Equal to the average number of new infections per sick person
Indirectly measured

Source: NY Times, Feb 7, 2020
Fatality rate (directly measured)

Early Question Motivating Work: How certain should we be about estimates of the strength – R0 – of a disease at the outset of an outbreak?

Basic reproductive number, “R0”
Equal to the average number of new infections per sick person
Indirectly measured

Source: NY Times, Feb 7, 2020
\[ R_0 = 1.5 \]

\[ I(t) \]

Days, \( t \)

Infected, \( I(t) \)

\[ R_0 = 2.0 \]

\[ R_0 = 2.5 \]
$R_0 = 1.5$

$R_0 = 2.0$

$\text{Days, } t$

$I(t)$
\( R_0 = 2.5 \)

\( R_0 = 2.0 \)

\( R_0 = 1.5 \)
$R_0 = 2.5$

$R_0 = 2.0$

$R_0 = 1.5$
The diagrams illustrate the progression of infections $I(t)$ over time $t$ for different values of the basic reproduction number $R_0$. The three scenarios shown are for $R_0 = 1.5$, $R_0 = 2.0$, and $R_0 = 2.5$. The charts depict the number of infected individuals as a function of time, with $R_0$ reflecting the average number of secondary infections produced by a single infected individual in a fully susceptible population. The graphs demonstrate how varying $R_0$ affects the spread and peak of infections, highlighting the importance of understanding $R_0$ in epidemiology.
Tentative conclusion: Many values of $R_0$ can be compatible with the same observed rate of increase in cases – even if projected outbreak sizes are different.
**Population “Classes”**

*S* – The number of susceptible individuals

*I* – The number of infectious individuals

*R* – The number of “removed” individuals (through recovery or, possibly, death)

**Mechanisms**

**Infection:** Requiring contact between a *S* and a *I* individual at rate $\beta$.

**Recovery:** After a period of infectiousness of average duration $T_I$. 
Starting with the SIR model...

\[
\frac{dS}{dt} = - \beta SI
\]

\[
\frac{dI}{dt} = \beta SI - \gamma I
\]

\[
\frac{dR}{dt} = \gamma I
\]

But approximate at the outset, when population is almost entirely susceptible, i.e., \(S \sim 1\)

\[
\frac{dI}{dt} = I (\beta - \gamma)
\]
Starting with the SIR model...

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\]

But approximate at the outset, when population is almost entirely susceptible, i.e., \( S \sim 1 \)

\[
\frac{dI}{dt} = I (\beta - \gamma)
\]

which yields

\[
\frac{dI}{dt} = \gamma I \left( \frac{\beta}{\gamma} - 1 \right)
\]
The expected number of cases, initially changes like:

\[ \dot{I} = \frac{I}{T_I} (R_0 - 1) \]
The expected number of cases, initially changes like:

\[ \dot{I} = \frac{I}{T_I} (R_0 - 1) \]

where

- \( R_0 \) is the Basic Reproductive Number,
- \( \beta \) is the rate of infections per time,
- \( T_I \) is the infectious period.

\[ R_0 \equiv \beta \times T_I \]
The expected number of cases, initially changes like:

\[
\dot{I} = \frac{I}{T_I} (R_0 - 1)
\]

where

\[ R_0 \equiv \beta \times T_I \]

such that

- Disease spreads whenever the average number of new cases exceeds unity, i.e: \( R_0 > 1 \)
- The increase is exponential
### Estimating, $R_0$, for 2019-nCoV

<table>
<thead>
<tr>
<th>Study</th>
<th>Basic reproductive number $R_0$</th>
<th>Authors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study 1</td>
<td>1.5–3.5</td>
<td>Bedford <em>et al.</em> [4]</td>
</tr>
<tr>
<td>Study 2</td>
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<td>Imai <em>et al.</em> [5]</td>
</tr>
<tr>
<td>Study 3</td>
<td>2.92 (95% CI: 2.28–3.67)</td>
<td>Liu <em>et al.</em> [6]</td>
</tr>
<tr>
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<td>Read <em>et al.</em> [8]</td>
</tr>
<tr>
<td>Study 5</td>
<td>2.2 (90% CI: 1.4–3.8)</td>
<td>Riou and Althaus [10]</td>
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<tr>
<td>Study 6</td>
<td>5.47 (95% CI: 4.16–7.10)+</td>
<td>Zhao <em>et al.</em> [9]</td>
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<tr>
<td>Study 7</td>
<td>2.0–3.1</td>
<td>Majumder and Mandl [7]</td>
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### Many model choices:
Branching process
SEIR model (like SIR but with an asymptomatic class)
Exponential growth…
Estimating, $R_0$, for 2019-nCoV

<table>
<thead>
<tr>
<th>Study</th>
<th>Basic reproductive number $R_0$</th>
<th>Mean generation interval $\bar{G}$ (days)</th>
<th>Generation-interval dispersion $\kappa$</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study 1</td>
<td>1.5–3.5</td>
<td>10</td>
<td>1</td>
<td>Bedford et al. [4]</td>
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<tr>
<td>Study 2</td>
<td>2.5 (1.5–3.5)*</td>
<td>8.4</td>
<td>unspecified†</td>
<td>Imai et al. [5]</td>
</tr>
<tr>
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<td>8.4</td>
<td>0.2</td>
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<td>7–14</td>
<td>0.5</td>
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<td>6–10</td>
<td>0</td>
<td>Majumder and Mandl [7]</td>
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</table>

Many model choices & latent assumptions:
Branching process
SEIR model (like SIR but with an asymptomatic class)
Exponential growth…

The brief answer is that speed and strength are linked (see Park et al, JRSI 2020 for more).
**Question:** consider data on an epidemic in which \( r = 1/4 \) weeks where

- Disease 1: \( T_I = 1 \) week
- Disease 2: \( T_I = 4 \) weeks

Which disease has the higher \( R_0 \)?
**Question:** consider data on an epidemic in which $r = 1/4$ weeks where
   Disease 1: $T_I = 1$ week
   Disease 2: $T_I = 4$ weeks
Which disease has the higher $R_0$?

**Answer:** Disease 2

**Algebra:**

$R_0 = 1 + T_I r$

Disease 1: $R_0 = 1.25$

Disease 2: $R_0 = 2$
Question: consider data on an epidemic in which \( r = 1/4 \) weeks where
- Disease 1: \( T_I = 1 \) week
- Disease 2: \( T_I = 4 \) weeks
Which disease has the higher \( R_0 \)?

Answer: Disease 2

Algebra: \( R_0 = 1 + T_I r \)
- Disease 1: \( R_0 = 1.25 \)
- Disease 2: \( R_0 = 2 \)

Intuition:
Disease 1 takes 4 infectious periods to “double” the case count.
Disease 2 takes only 1 infectious period to “double” the case count.
Hence, disease 2 has a higher average number of secondary infections per average infectious period (the definition of \( R_0 \)).
The implicit link between speed and strength

Shorter generation intervals

Reproduction number: 1.4

Longer generation intervals

Reproduction number: 1.65

Weekly incidence

Time (weeks)

A practical generation-interval-based approach to inferring the strength of epidemics from their speed

Sang Woo Park, David Champredon, Joshua S. Weitz, Jonathan Dunhoff
This link helps sort through putatively large $R_0$ claims (assumptions matter!)

A

![Serial interval graph]

B

![Density graph with Median $R_0 = 5.7$]
Roles of generation-interval distributions in shaping relative epidemic strength, speed, and control of new SARS-CoV-2 variants

Sang Woo Park¹,* Benjamin M. Bolker²,3,4 Sebastian Funk⁵,6 C. Jessica E. Metcalf¹,7 Joshua S. Weitz⁸,9 Bryan T. Grenfell¹,7,10 Jonathan Dushoff²,3,4

Generation interval assumptions also shape how we interpret the strength of variants as they spread and compete with ‘wild type’ strains.

medRxiv: 10.1101/2021.05.03.21256545v1
What Happens After the Outbreak Lifts Off?

Expectations from Continuous Theory

- Cases increase exponentially
- Eventually, the epidemic reaches a ‘peak’
- This peak corresponds to the onset of ‘herd immunity’
- Then, cases decline
- But, not everyone gets sick.

The peak and total size depend on “R0” (in theory).
Starting with the SIR model...

\[
\frac{dS}{dt} = - \beta SI
\]

\[
\frac{dI}{dt} = \beta SI - \gamma I
\]

\[
\frac{dR}{dt} = \gamma I
\]

What is the critical value of susceptibles when \( dI/dt = 0 \)?

\[
\frac{dI}{dt} = I(S\beta - \gamma) = 0
\]
SIR Model – Herd Immunity
Depend on Basic Reproductive Number, $R_0$

Starting with the SIR model...

\[
\frac{dS}{dt} = -\beta SI \\
\frac{dI}{dt} = \beta SI - \gamma I \\
\frac{dR}{dt} = \gamma I
\]

What is the critical value of susceptibles when $dI/dt = 0$?

\[
\frac{dI}{dt} = I (S\beta - \gamma) = 0
\]

which yields

\[
S_{herd} = \frac{1}{R_0} \quad \text{Total infected}_{herd} = 1 - \frac{1}{R_0}
\]
SIR Model – Herd Immunity Depend on Basic Reproductive Number, $R_0$

$R_0=3$

Herd Immunity when $2/3$ are infected

$$S_{herd} = \frac{1}{R_0}$$

Total infected $_{herd} = 1 - \frac{1}{R_0}$
SIR Model – Herd Immunity
Depend on Basic Reproductive Number, $R_0$

<table>
<thead>
<tr>
<th>$R_0$</th>
<th>Herd Immunity</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>$1/2$</td>
</tr>
<tr>
<td>3</td>
<td>$2/3$ (COVID-19)</td>
</tr>
<tr>
<td>4</td>
<td>$3/4$</td>
</tr>
<tr>
<td>5</td>
<td>$4/5$</td>
</tr>
<tr>
<td>6</td>
<td>$5/6$</td>
</tr>
<tr>
<td>etc.</td>
<td></td>
</tr>
</tbody>
</table>

But people still get sick even at herd immunity (which is effectively a ‘replacement’ level for infections).

& networks, mobility, behavior and other heterogeneities matter.

Herd Immunity when 2/3 are infected

$$S_{herd} = \frac{1}{R_0}$$

Total infected$_{herd} = 1 - \frac{1}{R_0}$
So What Did You All Do Yesterday?
## Challenge Problems: Basic Epidemics

### Challenge problem: Outbreak Criteria

Complete the simulation code below for the spread of an infectious disease beginning with 1 individual out of 10000 and estimate the value of $R_0$. Do you expect the disease to spread or not? Then, change the value of $p$ to 0.01 – will the disease spread, why or why not?

```matlab
% main data goes here
pars.c = 20; % Contacts per unit time (e.g., days)
pars.p = 0.025; % Probability of infectious contact
pars.beta = ... % Transmission rate
pars.gamma = 1/4; % Recovery rate (days^-1)
pars.basR0 = ... % Basic reproduction number
pars.N = 10000;
pars.I0 = 1;
pars.S0 = pars.N-pars.I0;

% Run the model
[t,y]=ode45(@(t,y,pars)sir_model(t,y,pars),[0 100],[pars.S0 pars.I0 0]/pars.N,[],pars);

% Plot the results
tmph=plot(t,y);
set(tmph,'linewidth',3);
xlabel('Time (days)');
ylabel('Population fraction');
tmph = legend('Susceptible','Infectious','Recovered');
legend('boxoff');
```

### Solutions to Challenge Problem: Outbreak Criteria

The missing components are shown below.

```matlab
pars.beta = pars.c*pars.p; % Transmission rate
pars.basR0 = pars.beta/pars.gamma; % Transmission rate * transmission period
```

These parameters describe an outbreak for the SIR model given $R_0 = 2$, $\beta = 0.5$ days$^{-1}$, $\gamma = 0.25$ days$^{-1}$. As a result, the simulation of the outbreak looks as follows:

In this case, the outbreak occurs because $R_0 > 1$. However, when $p = 0.01$ then $\beta = 0.2$ and $R_0 = 0.8$ which is less than 1. A simulation (results not shown) leads to the recovery of infectious individuals without a net increase in the number of cases.
Challenge Problems: Strength/Size

Challenge problem: Strength-Size Relationships in Phase Space
First, fix the value of the recovery rate to $\gamma = 0.25$, then modulate the transmission rate from $\beta = 0.25$ to $\beta = 2.5$. Assume that initially, 80% of the population is susceptible, one individual is infected, and the remainder of the population is recovered. In this case, does the disease always spread? Why or why not? In addition, find the outbreak size and show how it relates to $R_{eff}$ – the effective reproduction number given the initial susceptible population.

Solutions to Challenge problem: Strength-Size Relationships in Phase Space
The effective reproduction number $R_{eff} = \frac{\beta S_0}{\gamma}$ which ranges from 0.8 to 8 in this case. Hence, even though $\beta > \gamma$, there will not be an outbreak until $\beta > \gamma / S_0$ or $\beta_c = 5/16 = 0.3125$. This is apparent in the plots below (left-phase space; right-relationship between final size and $\beta$). As noted in the right plot, the ratio of $\beta / \gamma$ must exceed 1/0.8 or 1.25 for the outbreak to initiate.
Challenge Problem: From Outbreaks to Endemics

The SIR model, with rapid loss of immunity can be written in terms of an SI model:

\[
\frac{dS}{dt} = SI + I
\]

\[
\frac{dI}{dt} = SI - I
\]

Because those that recover are immediately susceptible, there is a new long-term possibility: an endemic disease state where 

\[
S^* = \frac{1}{R_0} \quad \text{and} \quad I^* = \frac{R_0 - 1}{R_0}
\]

Hence, the 'SI' model can be coded as follows:

```matlab
function dydt = si_model(t,y,pars)
    S = y(1);
    I = y(2);
    dSdt = -pars.beta*S*I+pars.gamma*I;
    dIdt = pars.beta*S*I-pars.gamma*I;
    dydt = [dSdt; dIdt];
end
```

As should be apparent, there is only an endemic state with 

\[
I^* > 0 \quad \text{when} \quad R_0 > 1.
\]

Challenge problem: From Epidemic Outbreaks to Endemics

Using \( \beta = 0.3 \) and \( \gamma = 0.25 \text{ days}^{-1} \) show the convergence of the dynamics to an endemic state, i.e., from an outbreak to endemicity. And then compare and contrast this with dynamics in which immunity is permanent. For these parameters, simulate the dynamics over a 1 year = 365 days period.

Solutions to Challenge problem: From Epidemic Outbreaks to Endemics

The contrast between the SIR model and the SI model can be seen in the plots below of the contrasting outcomes. In both cases there is an outbreak. However, with \( R_0 = 1.2 \), we expect 83.3% of the population to be susceptible at equilibrium, and therefore 16.7% to be infected – precisely as observed.
Morning Talk

Part 1 – Epidemic Modeling
the basics of SIR models

Part 2 – Principles of Outbreaks
strength, speed, and size

Part 3 - Variability and Epidemics
core concepts underlying stochasticity trajectories
Process noise arises from discrete interactions
Process noise arises from discrete interactions

*sniffle

vs.

*snore
Process noise arises from discrete interactions

*sneeze*

all the time at rate $\beta$

discrete times following

$$P(t) = \beta e^{-\beta t}$$
Process noise arises from discrete interactions.

Process noise is a large factor when populations are small.

\[ P(t) = \beta e^{-\beta t} \]

*sneeze* all the time at rate \( \beta \) vs. discrete times following.
Process noise arises from discrete interactions
Here’s an example of the processes for a “SEIR” model:

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<tr>
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<td>$r_1 = \beta \frac{S}{N}$</td>
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<tr>
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<td>$E \rightarrow I$</td>
<td>$r_2 = \sigma E$</td>
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<td>End of infectiousness (survival)</td>
<td>$I \rightarrow R$</td>
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But this is just one of the possible trajectories measured in terms of one state variable…

The full state includes the number of individuals in the $S$ ($E$), $I$, $R$, $D$ … classes
Ebola virus disease (EVD):

*Zaire ebolavirus*
- Causative agent of the current outbreak is *Zaire ebolavirus*, of the family Filoviridae.
- ssRNA enveloped virus, ~19,000 bp in length

**Outbreaks**
- >30 years of documented outbreaks, largely in Central Africa
- These outbreaks begin with infections arising from a zoonotic reservoir (e.g., bats, monkeys).

**Effects**
- Infected individuals are symptom-free for ~11 days
- ~50%-70% of infected individuals die
- Secondary transmission via body fluids, both pre- and post-death
In practice, the actual number of cases, though significant and striking, were well below predictions.

Data from Caitlin Rivers: https://github.com/cmrivers/ebola
An epidemic is a single stochastic trajectory driven by process noise

Sources of error: Observation noise (extrinsic)
Parameter uncertainty/variance (extrinsic)
Process noise (intrinsic)

Observed:
\[ \tilde{I}(t) = 56.0 \exp\left(\frac{t}{22.1}\right) \]
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Theory:
\[ \tilde{I}(t) = 56.0 \exp\left(\frac{t}{26}\right) \]
Instead of best fits, consider “Compatible Epidemic Trajectories” or “ComETs” (Taylor et al, JTB 2016)
How to do this on your own:
Gillespie algorithm for simulating stochastic outbreaks

1. Determine rates of events in the system, e.g. for SIR:
   a) Transmission \((S_{t-1}, I_{t+1}, R_{t})\)  \([\text{rate} \sim \frac{\beta S_t I_t}{N}]\)
   b) Recovery \((S_{t}, I_{t-1}, R_{t+1})\) \([\text{rate} \sim \gamma I_t ]\)
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2. Add up the total rate

3. Determine the exponentially distributed waiting time

4. Decide on which event happened at time \(t+\tau\)

5. Update the system state \((S_{t+\tau}, I_{t+\tau}, R_{t+\tau})\)

6. Go to step 1 and repeat

That’s it!

But… why are the waiting times exponential?
Consider events with rate $\lambda$ (probability per unit time). What is the probability of waiting a length of time $\tau$ before the event occurs?
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$$
1 - \lambda dt
$$

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such that...

$$P(\tau; \lambda)d\tau = e^{-\lambda \tau} \lambda d\tau$$
The stochastic lab breaks down the simple ‘SIR’ model into two processes, infection and recovery, each with a rate.

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Adding up these rates given you the total rate of events and then the event $i$ is chosen with probability $r_i/\Sigma r_i$. You can decide to extend this to arbitrary complexity (SEIR, age structure, etc.).

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If your code works, then your stochastic and deterministic models should converge (but keep in mind that a stochastic outbreak is not inevitable, even when \( R0 > 1 \)).
What Is the Chance That The Disease will Spread when R0 > 1

In a deterministic model, the answer is: 100%

But, not so in a stochastic model.

Recall: probability of event “i” is $r_i / \sum R_i$.

At start, rates are transmission $\beta$ and recovery $\gamma$

So, what is the probability transmission of single infectious individual occurs before recovery?
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In a stochastic model, chance plays a role (more so near \( R_0 \sim 1 \))
Closing Thoughts for the Morning

Part 1 – Epidemic Modeling
SIR model describes disease transmission in terms of mechanisms of infection and recovery.

Part 2 – Principles of Outbreaks
Epidemics can be described in terms of strength, speed, and size
- Strength – $R_0$
- Speed – $r$
- Size – herd immunity/final size
- (Also dispersion + more…)

Part 3 – Variability and Epidemics
Not every outbreak is the same, many sources of variation, particularly near the outset when individual trajectories matter more or in ‘small’ outbreak scenarios (school, facility, etc.).
What’s going to happen next?

A lecture bridging the gap between deterministic and stochastic model of epidemics.

Then a short break.

Then, break-out rooms where our team of QBioS + guest instructors will guide the hands-on modeling activities.


Each group is working in one language (Matlab, Python or R).

The guides are in pdf-s so you should read, think, type in code, learn from (purposeful) mistakes, build your own epidemic models, and discover new insights along the way.

After lunch: from dashboards (w/ABiL) to network models (w/Sam Scarpino)

workshop2021.qbios.gatech.edu
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Yesterday, AM: Basics in coding/journal club.
Yesterday, PM: Deterministic epi models.
Today, AM: Stochastic models of epidemics.
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After lunch: from dashboards (w/ABiL) to network models (w/Sam Scarpino).

And remember...

You can do it!

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Students from the first five cohorts (with a few friends of the program – Drs. Beckett, Demory, Taylor, Harris, and Lucia-Sanz) will be today’s instructors.

Many thanks to Dr. Jessica Irons and Audra Davidson for their assistance with workshop coordination, development, and logistics.