

Lecture 1

Intro to Modeling

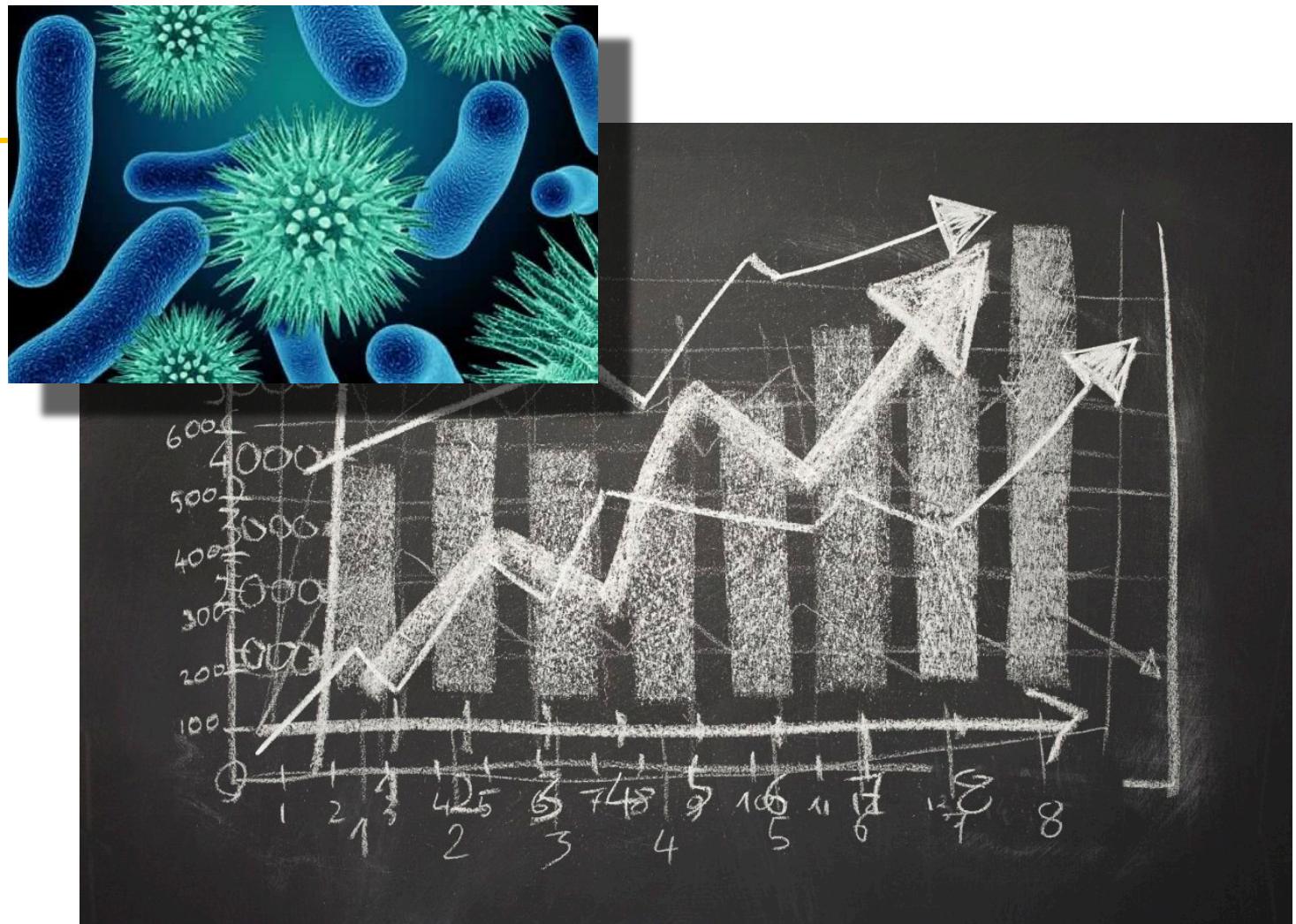
Micaela E. Martinez
WE ACT for Environmental Justice

slides in part adapted from Pej Rohani & John Drake's SISMID 2019 course materials

Modeling Infectious Diseases

Course Objectives:

- Modeling 101
- Basic Reproduction Ratio (R_0)
- Simple Epidemic Dynamics
- Vaccination & interventions
- Heterogeneity
- Modeling during a pandemic
- Informing models with data
- Deviations from the Basic Models

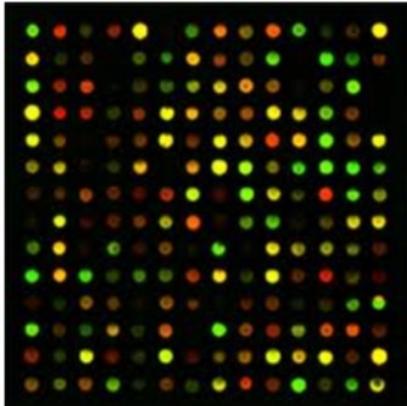


Many ways to study infectious diseases

Medicine



Genomics



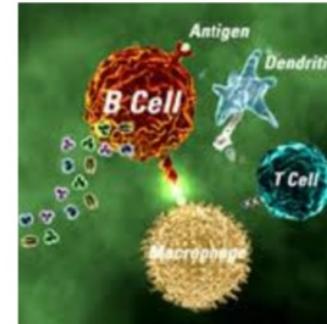
Microbiology



Many disciplines focus on infectious diseases from the:

- (1) individual level
- (2) within-host scale
- (3) microbe perspective

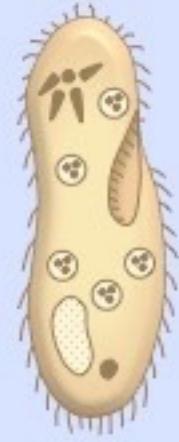
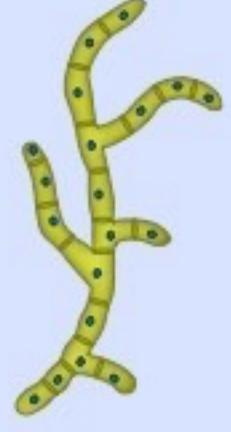
Immunology



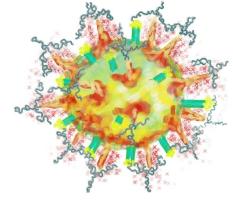
Vaccines & Drugs



Agents of infectious diseases

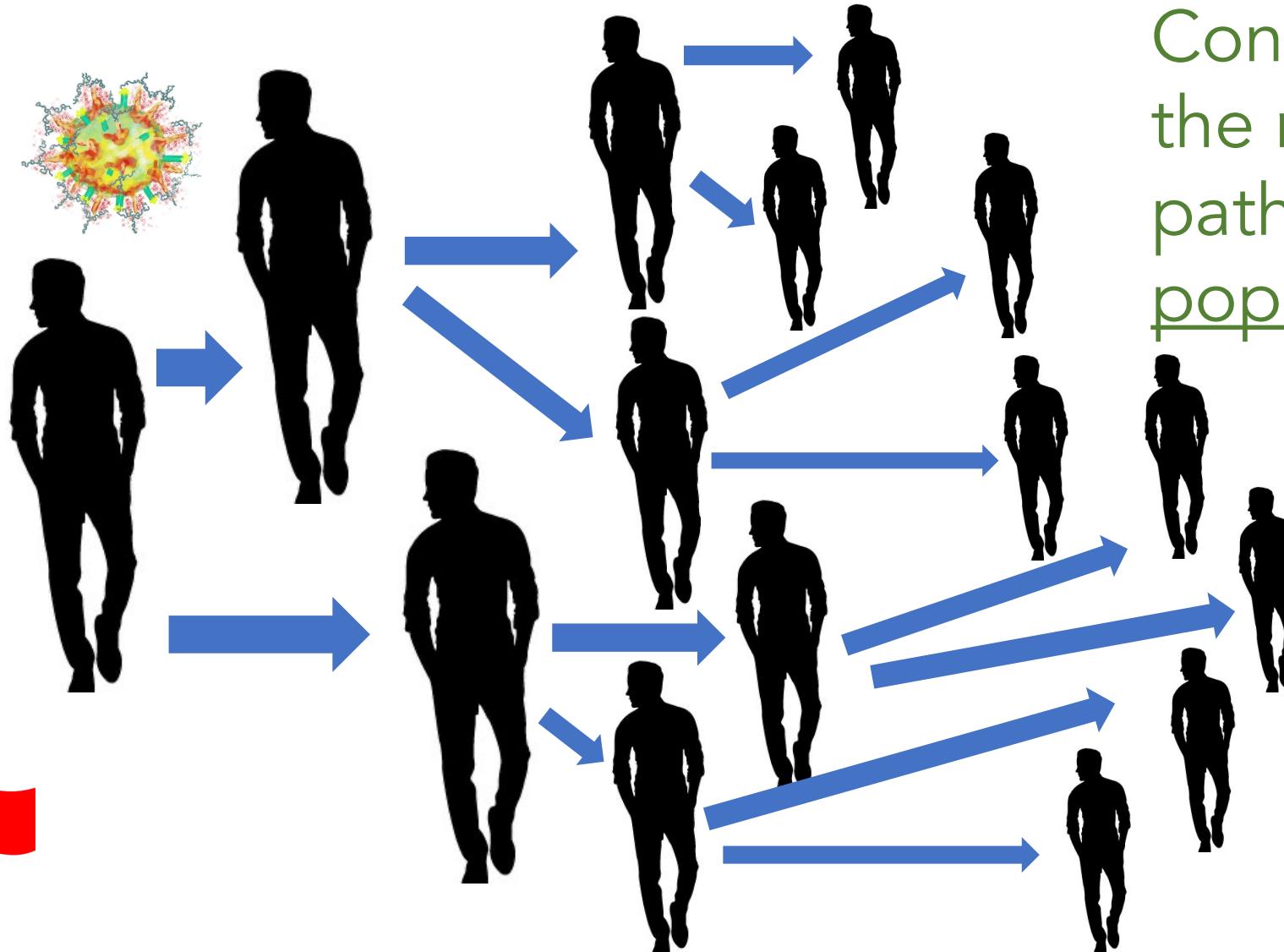
CELLULAR				ACELLULAR	
					
Parasites (e.g. helminthes) ⇒ Tapeworm	Protozoa (e.g. plasmodia) ⇒ Malaria	Fungi (e.g. tinea) ⇒ Athlete's foot	Prokaryote (i.e. bacteria) ⇒ Leprosy	Virus (e.g. HIV) ⇒ AIDS	Prion ⇒ CJD

Epidemiology & Disease Ecology focus on the population-level



Concept: We can track
the movement of
pathogens throughout
populations

Epidemiology & Disease Ecology focus on the population-level



Concept: We can track the movement of pathogens throughout populations

A transmission chain is the set of infection events that occur as a pathogen moves through a population.



The use of time series data

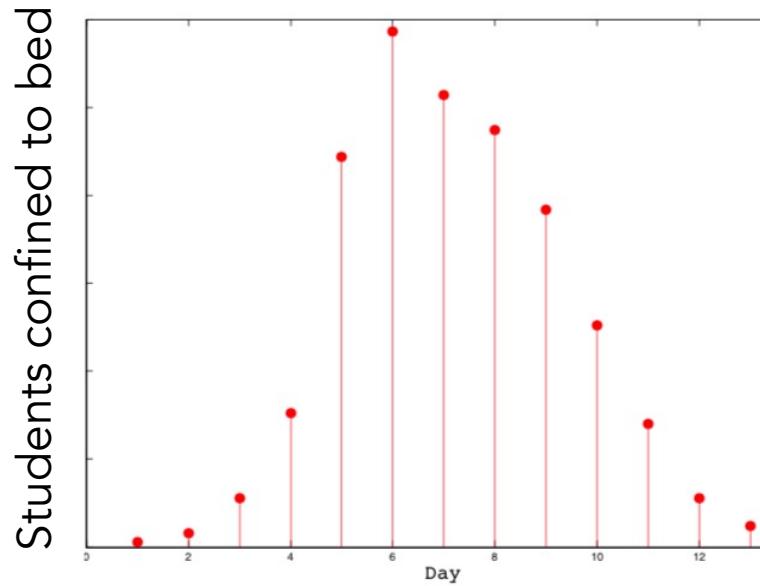


What pathogen is causing the illness?

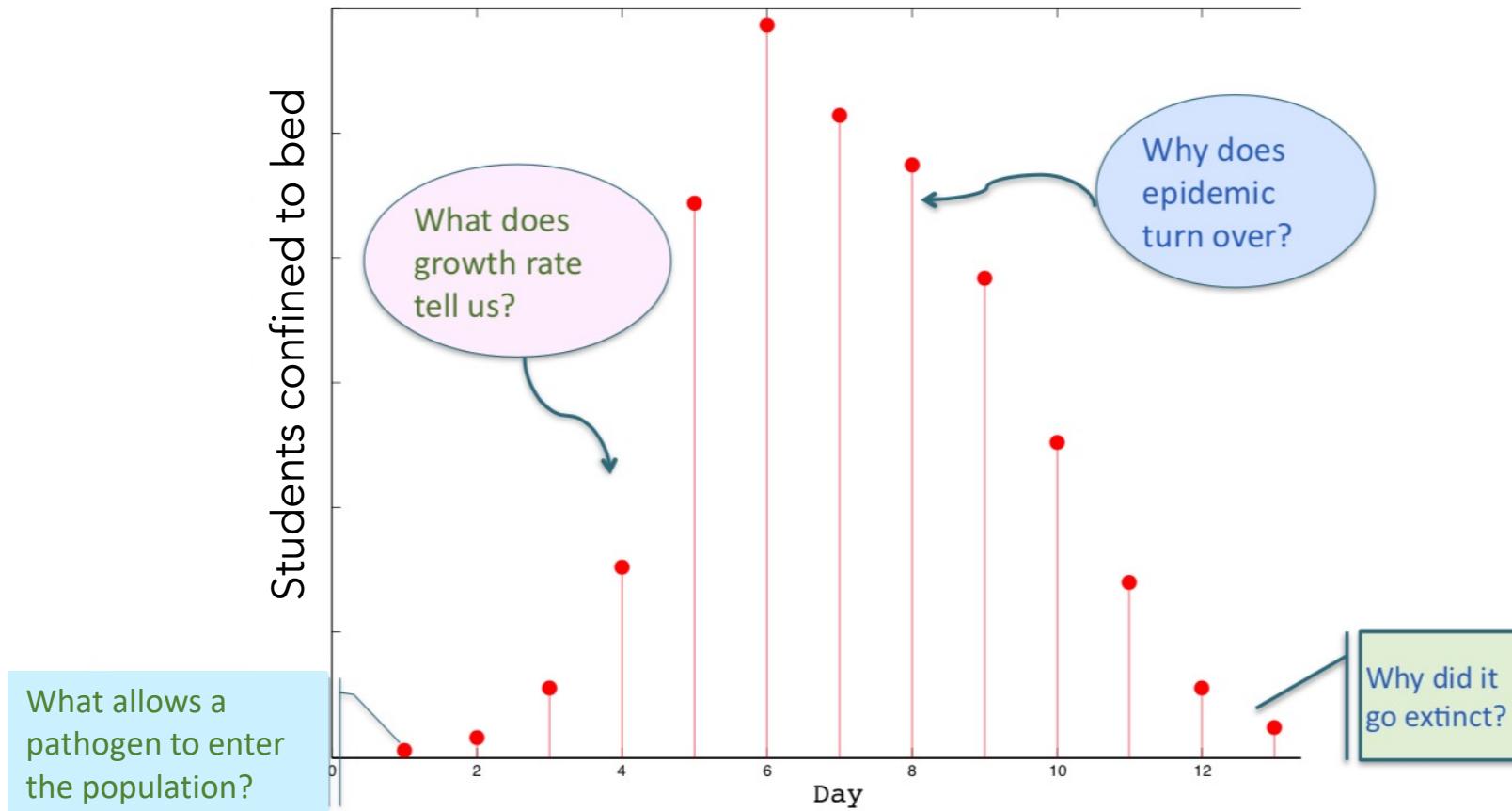
Is it a novel pathogen?

Is there a vaccine or treatment?

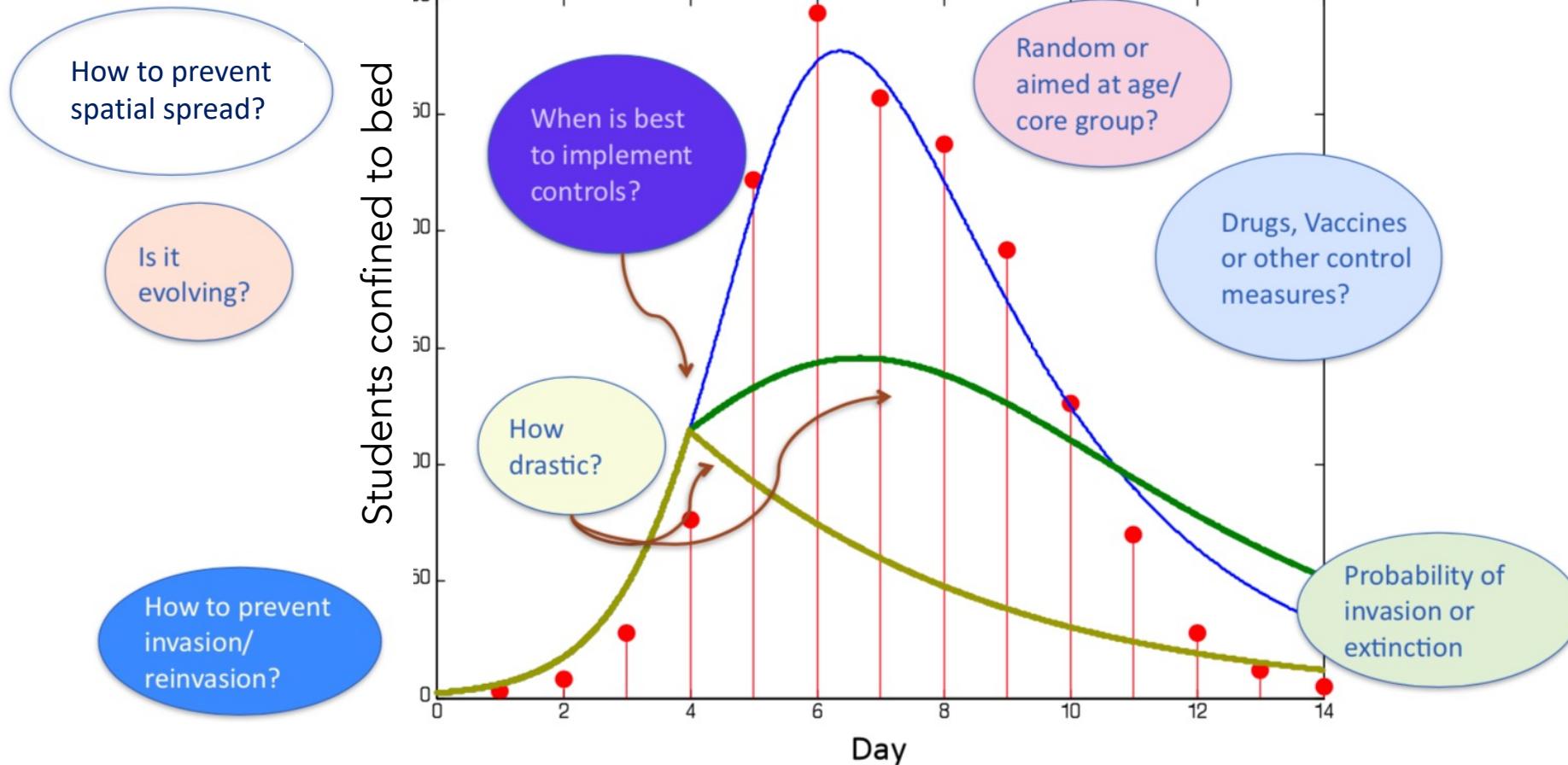
1978 outbreak in a British boarding school



Biological questions we can ask of time series

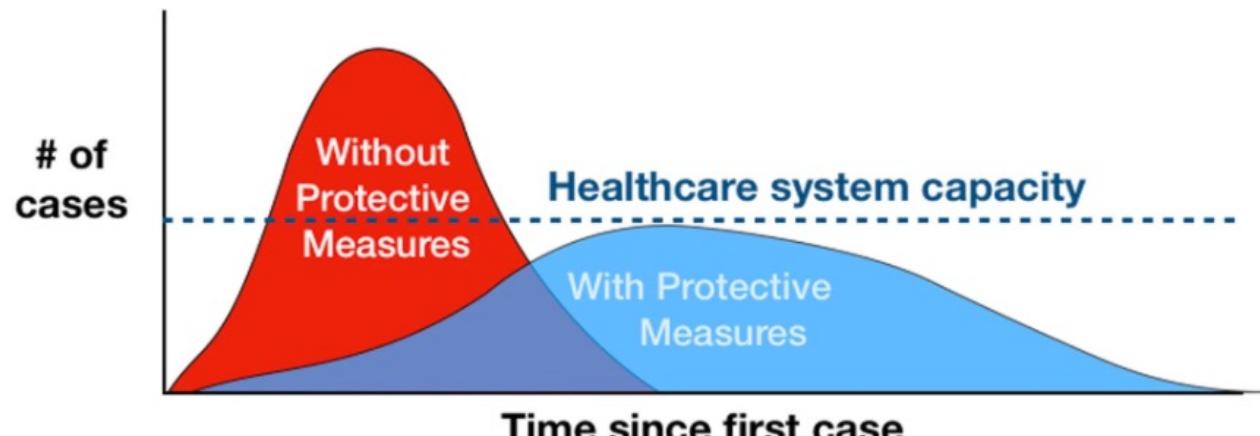


Questions about interventions we can ask of time series



Flattening the Coronavirus Curve

One chart explains why slowing the spread of the infection is nearly as important as stopping it.



Adapted from CDC / The Economist

The shape of the epidemic curve contains information about transmission

Different types of models:

A mathematical model is a set of equations that describe the mechanistic behavior of a system; such as a biological system, a physical system, a technology or social system.

A statistical model describes relationships between observed quantities and independent variables

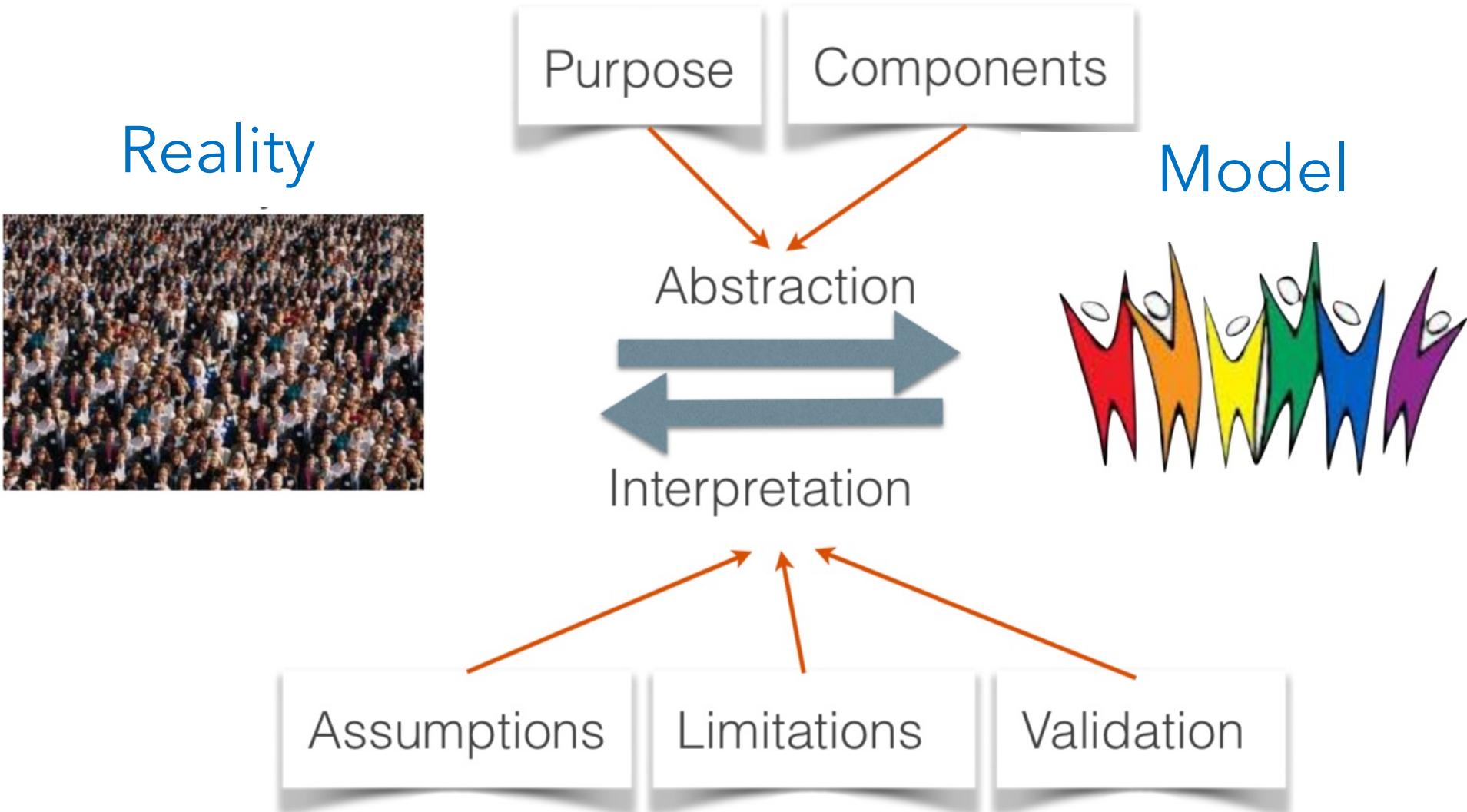
Developing a mathematical model is different from statistical analyses of data



What is a
model?



Mathematical models are abstractions of reality



- Choice of model depends crucially on focal question and available data
- Models are a tools and typically several types of models can be deployed for any given disease system
- Models are used principally for understanding nature or making projections under various scenarios



What is a
“*good*”
model?



Judging a Model...

Three fundamental features of models, often opposing forces:

Accuracy: ability to capture observed patterns (qualitative or quantitative) and make predictions

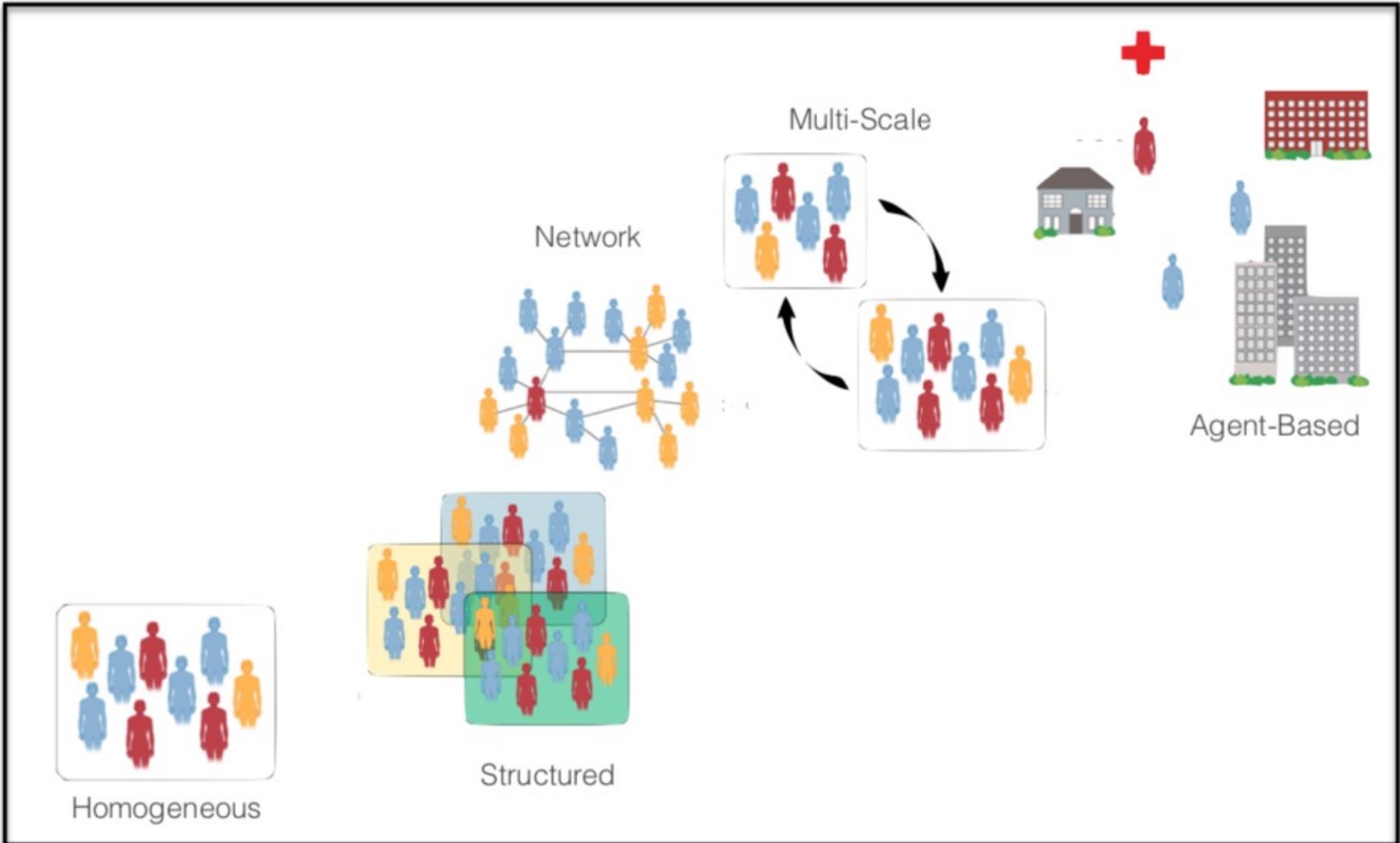
Transparency: Ability to understand model components. Decreases with model complexity

Flexibility: How easily the model can be adapted to new scenarios. Decreases with model complexity



What is a
“*good*”
model?

Realism & Complexity vs. Transparency & Flexibility



How do you implement a mathematical model?

Analytical Models

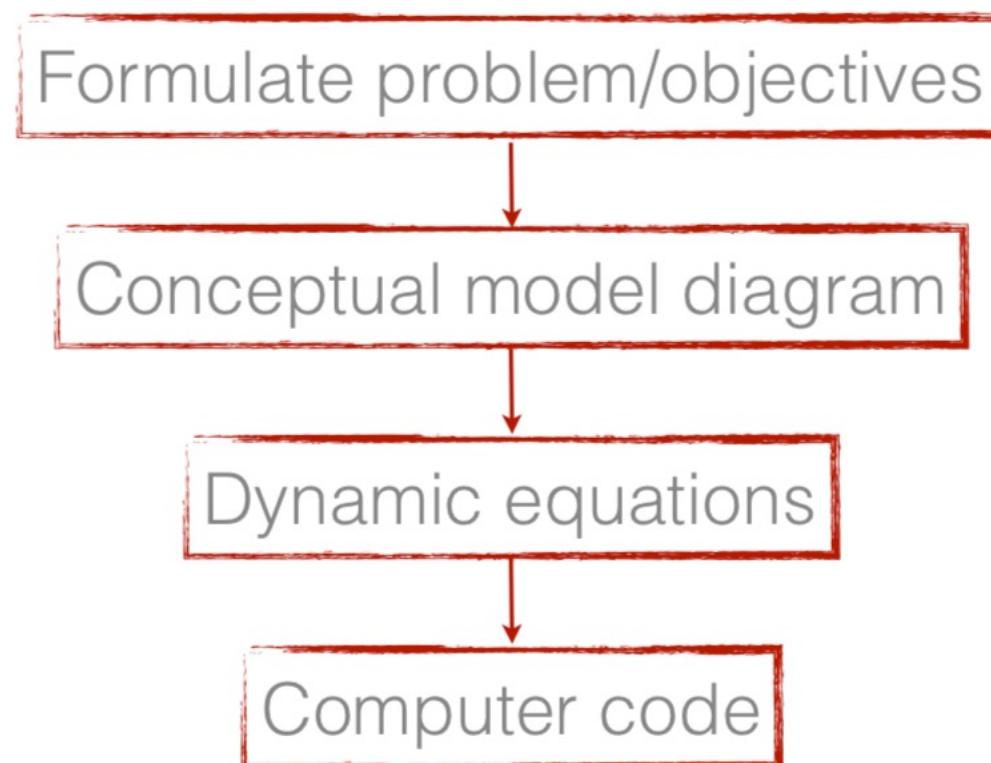
Concentrate on problems that can be expressed and analyzed fully using analytical approaches (*i.e., pure math*)

Computational Models

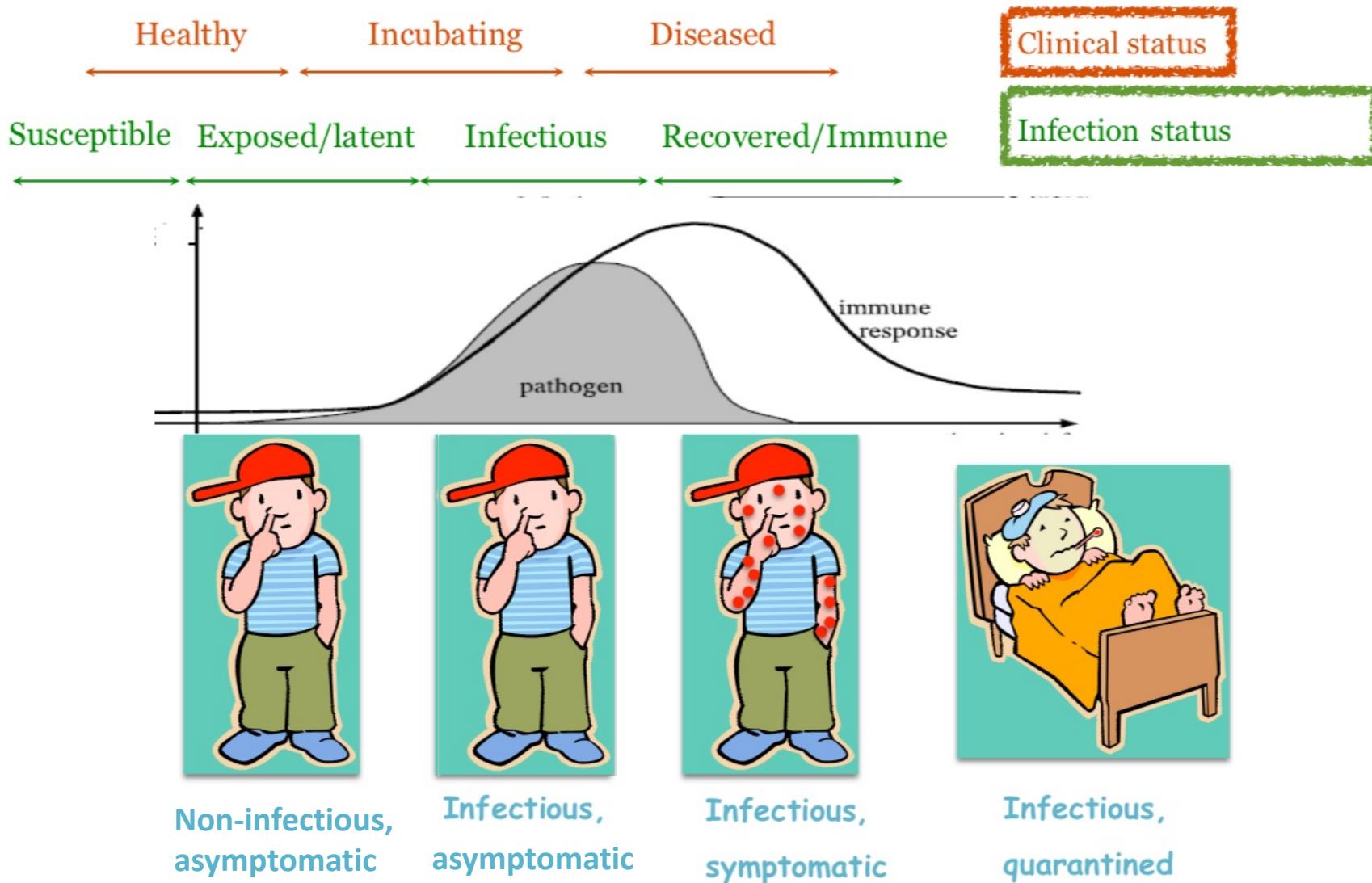
Construct an appropriate model for the system and use a combination computational methods for analysis and scenario analysis (*i.e., computer simulations*)



Steps in Developing a Model



Categories of Disease Status & Infection



Categories of Disease Status & Infection

Incubation period: Interval from infection to symptoms onset

Latent period: Interval from infection to becoming infectious

Symptoms onset is important for detecting infection; whereas, the onset of infectiousness is important for onward transmission

Simple Models

Pragmatic choice: categorize individuals in population according to their infection status:

- Susceptible (S)
- Infectious (I)
- Recovered/Immune (R)

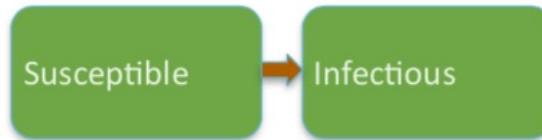
These are called **state variables**, they represent different states of the system that we are modeling



Simple Models

What model structure?

- Determined by pathogen biology



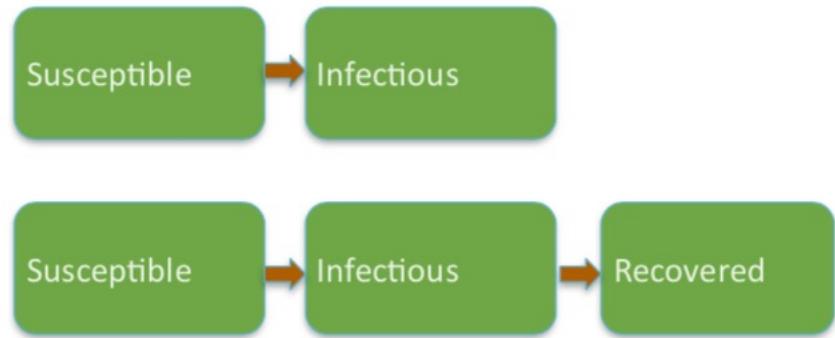
SI models can be used for fatal or chronic infections



Simple Models

What model structure?

- Determined by pathogen biology



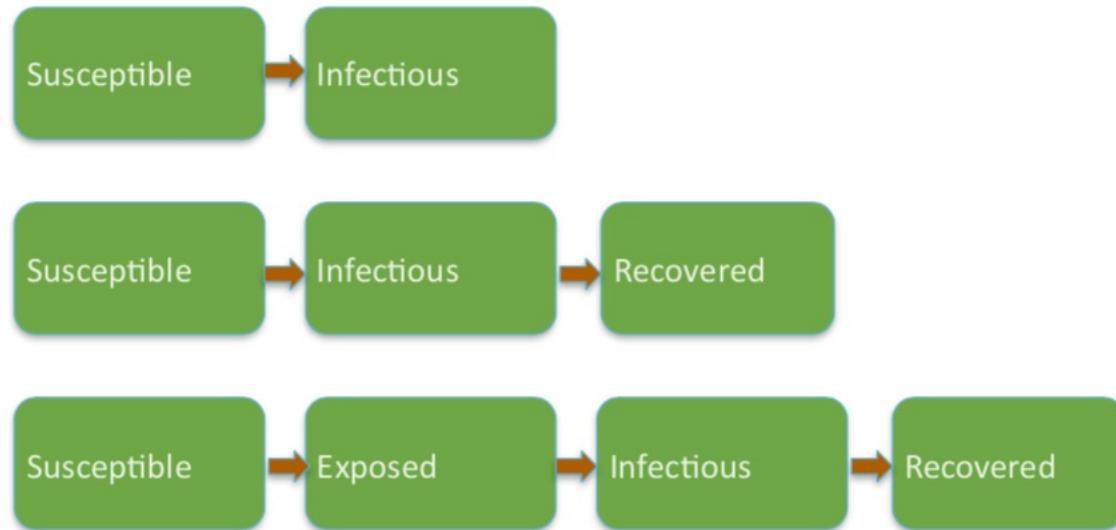
SIR models can be used for infections where there is recovery and immunity



Simple Models

What model structure?

- Determined by pathogen biology



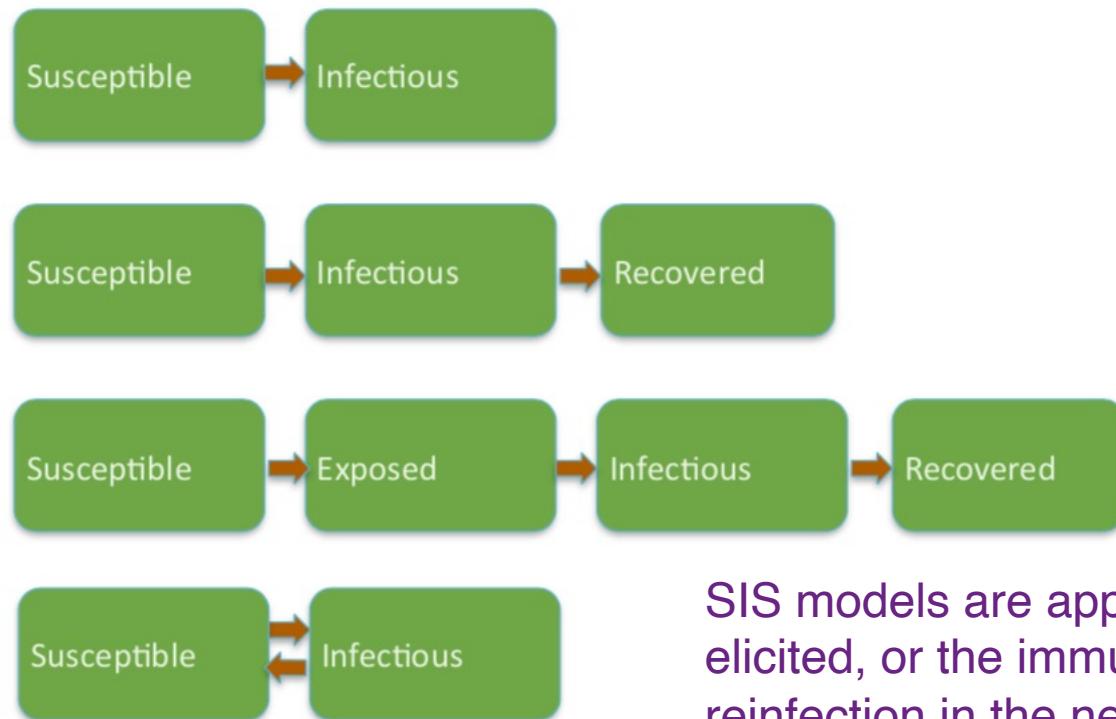
SEIR models can be used for infections where there is a non-negligible latent period when individuals are infected but not infectious. This can be a good category to have, for example for COVID-19, when considering testing and quarantine early on in infection.



Simple Models

What model structure?

- Determined by pathogen biology

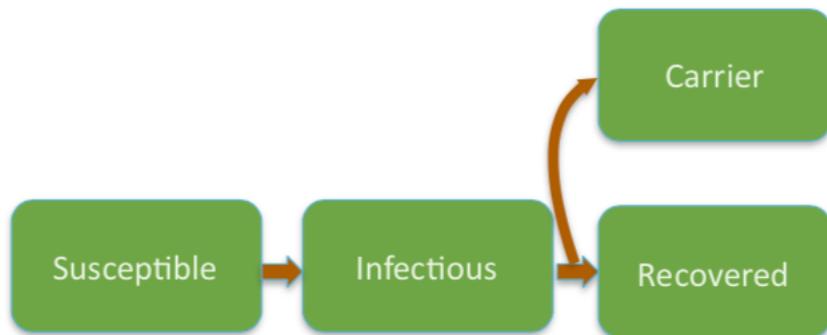


SIS models are appropriate when there is little immunity elicited, or the immunity elicited will not protect from reinfection in the near-future.

Simple Models

What model structure?

- Determined by pathogen biology



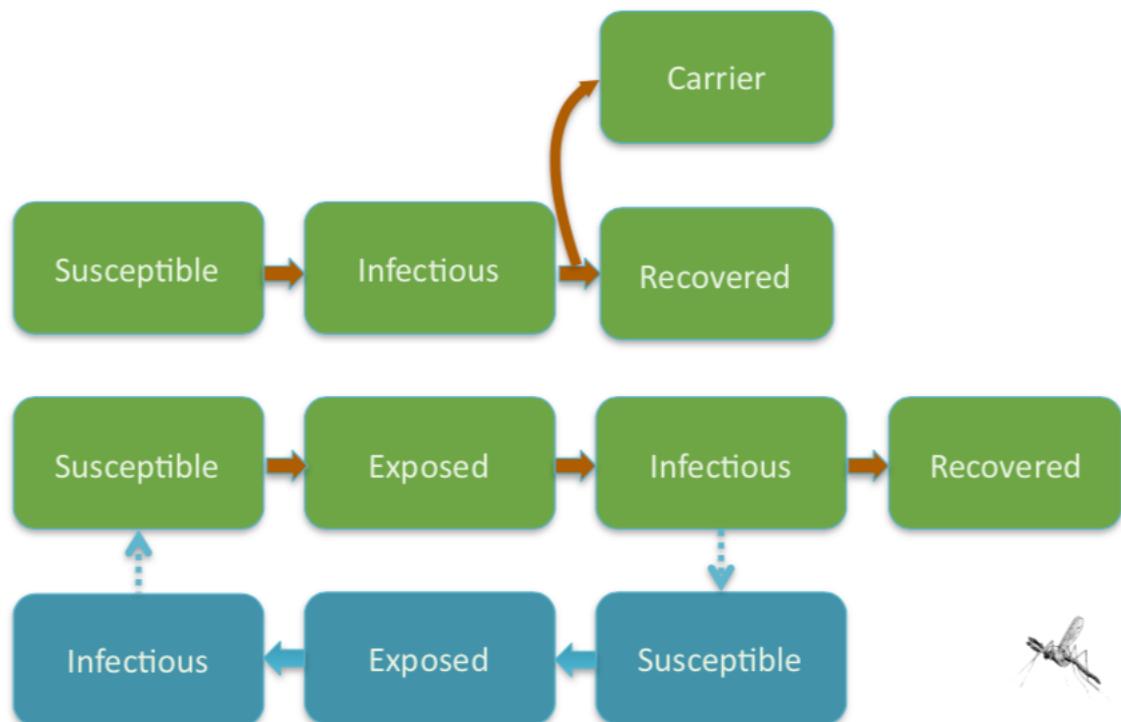
SIR – with carriers



Simple Models

What model structure?

- Determined by pathogen biology



SIR – with carriers

Vectored transmission



Simple Models

- **What model structure?**
- Depends on what do we know about the pathogen (eg, influenza)
 - It's directly transmitted (aerosol)
 - An acute infection
 - Lifelong immunity (to that strain)



Break

LECTURE 1 INTRO TO MODELING: CONTINUED

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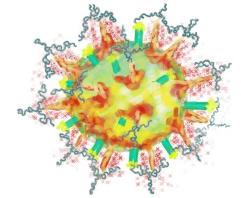
Transmission Recovery



State variables: Susceptible, Infectious, Recovered

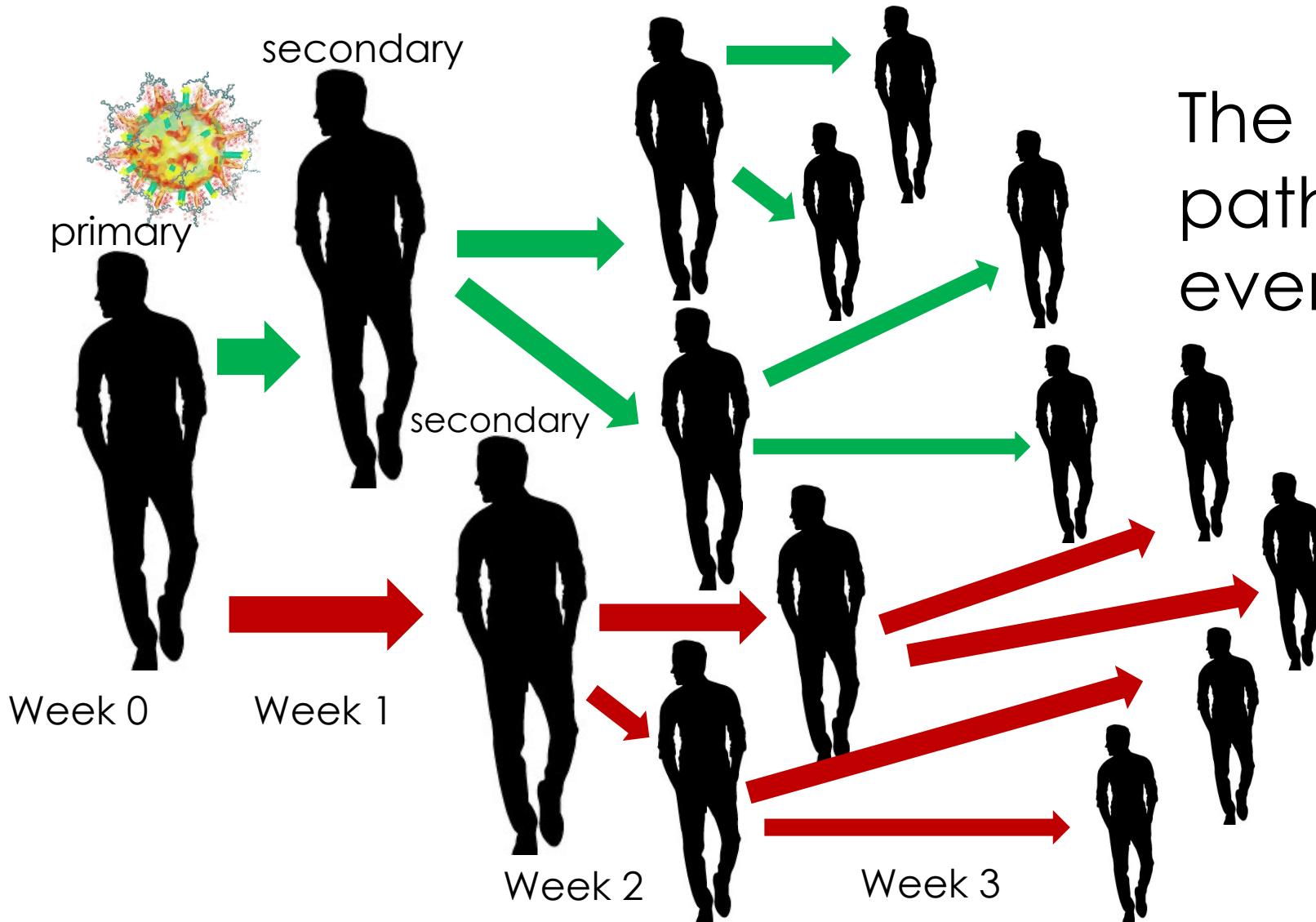
Parameters: Transmission rate, Recovery rate

Transmission Chain



Concept: The set of host-to-host pathogen transmission events

Transmission Chain



The set of host-to-host pathogen transmission events

Each individual infected two others

The Basic Reproductive Number

- **basic reproduction number, R_0 :** average number of infections caused by a typical infected individual in a population consisting only of susceptibles; if $R_0 > 1$, the infectious agent can start to spread.

infection	Geographic location	Time period	R_0
measles	England & Wales	1950-1968	16-18
measles	Kansas, USA	1918-1921	5-6
pertussis	Maryland, USA	1943	16-17
chicken pox	New Jersey, USA	1912-1921	7-8
mumps	Netherlands	1970-1980	11-14
rubella	West Germany	1970-1977	6-7
polio	USA	1955	5-6

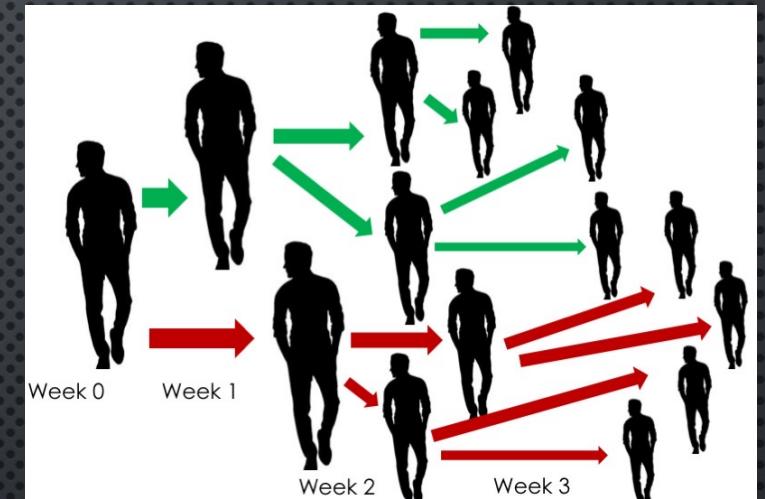
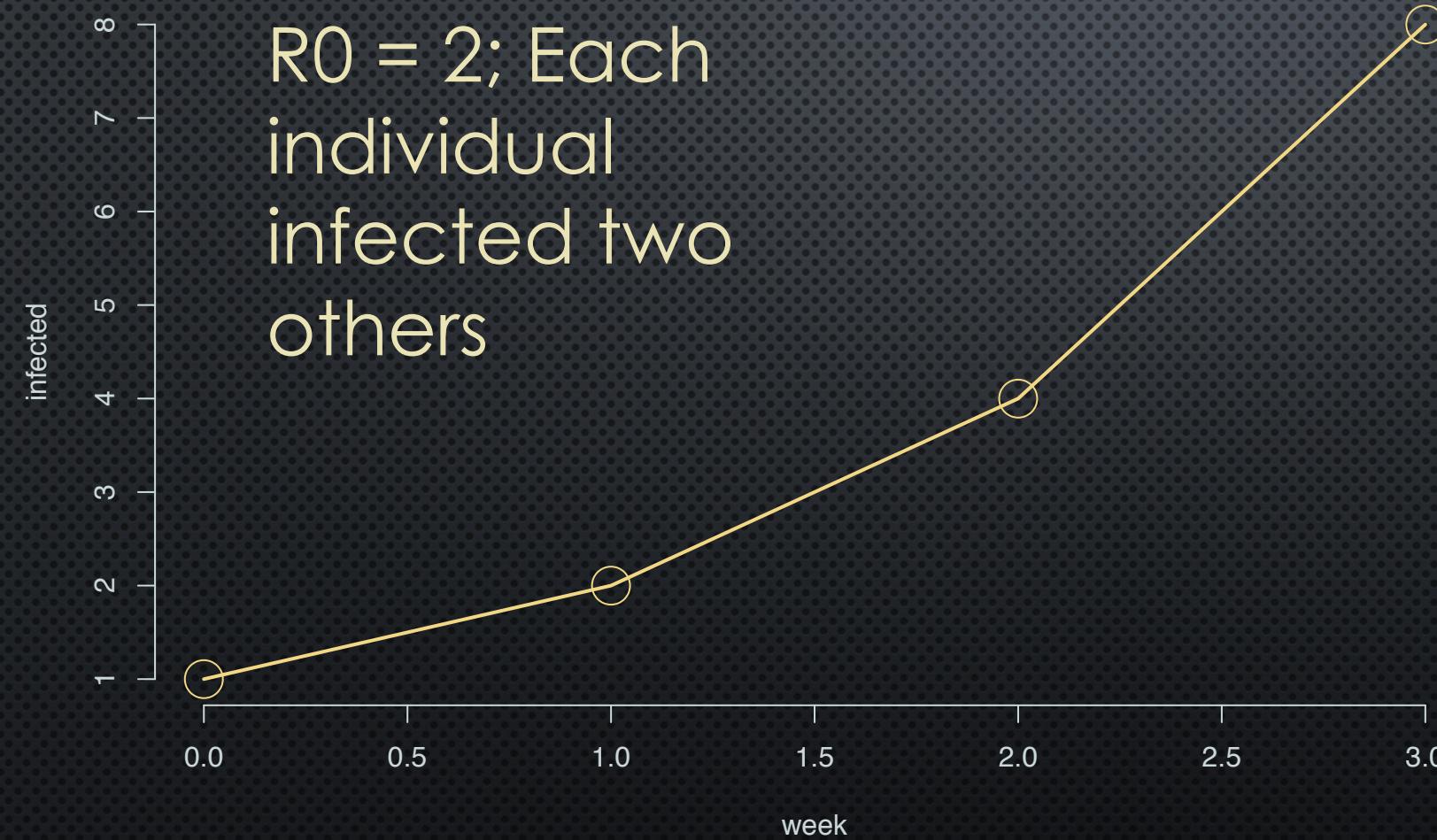
R_0 varies among:

1. diseases
2. populations
3. time periods

(Heesterbeek et al. 2015;
Anderson & May 1991)

Infections in the population

$R_0 = 2$; Each individual infected two others



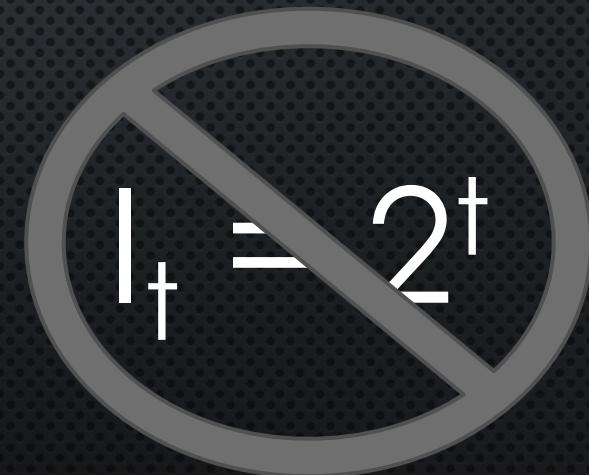
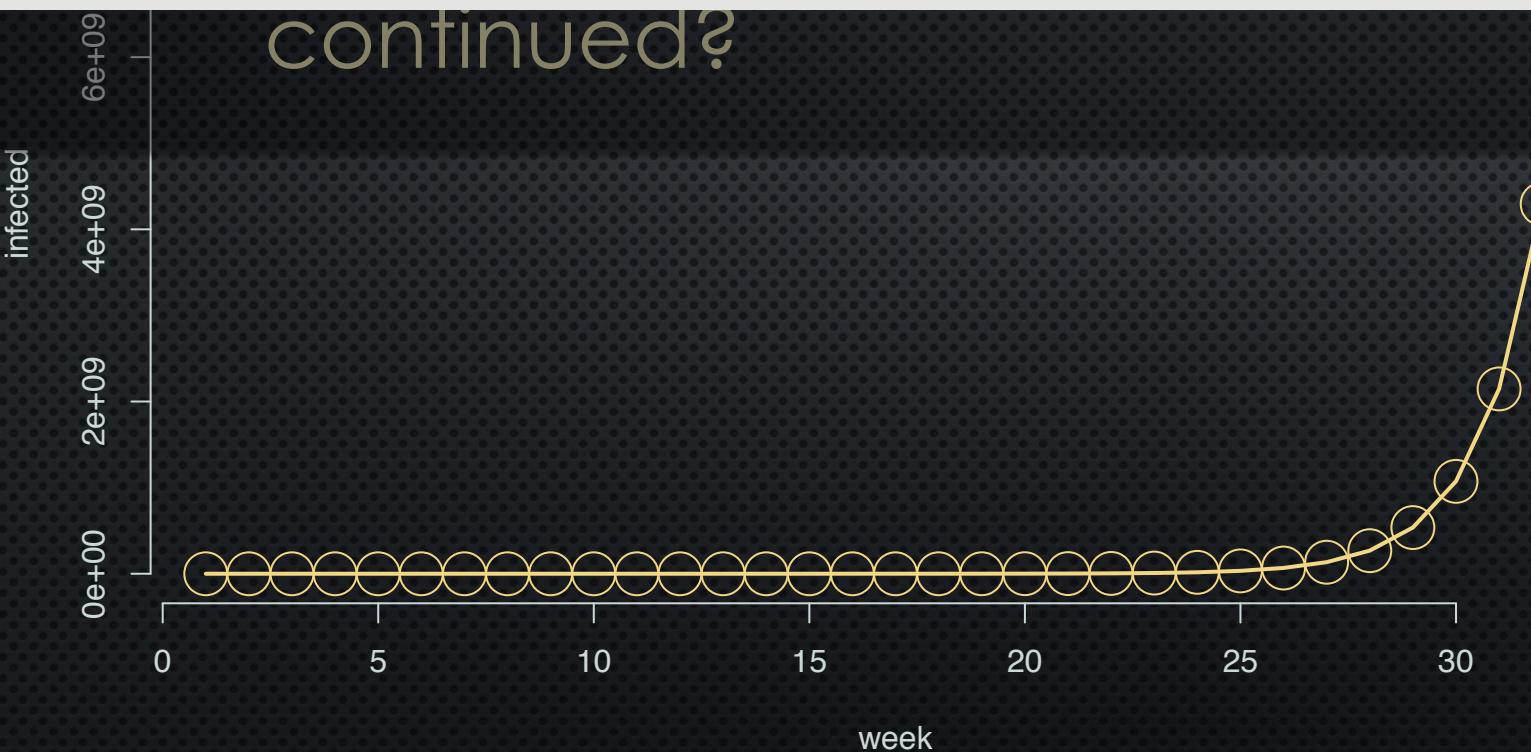
$$I_t = 2^t$$

Infections in the population

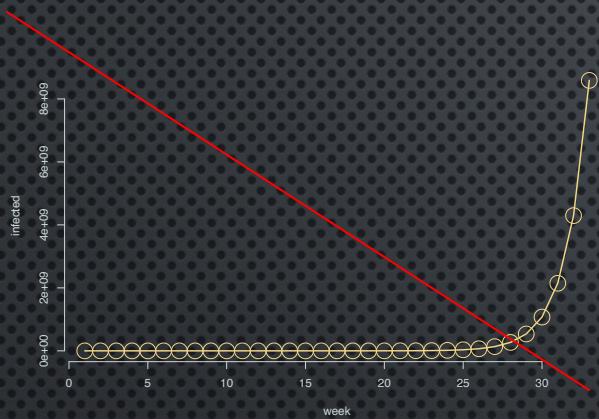
8 589 934 592

- **basic reproduction number, R_0 :** average number of infections caused by a typical infected individual in a population consisting only of susceptibles; if $R_0 > 1$, the infectious agent can start to spread.

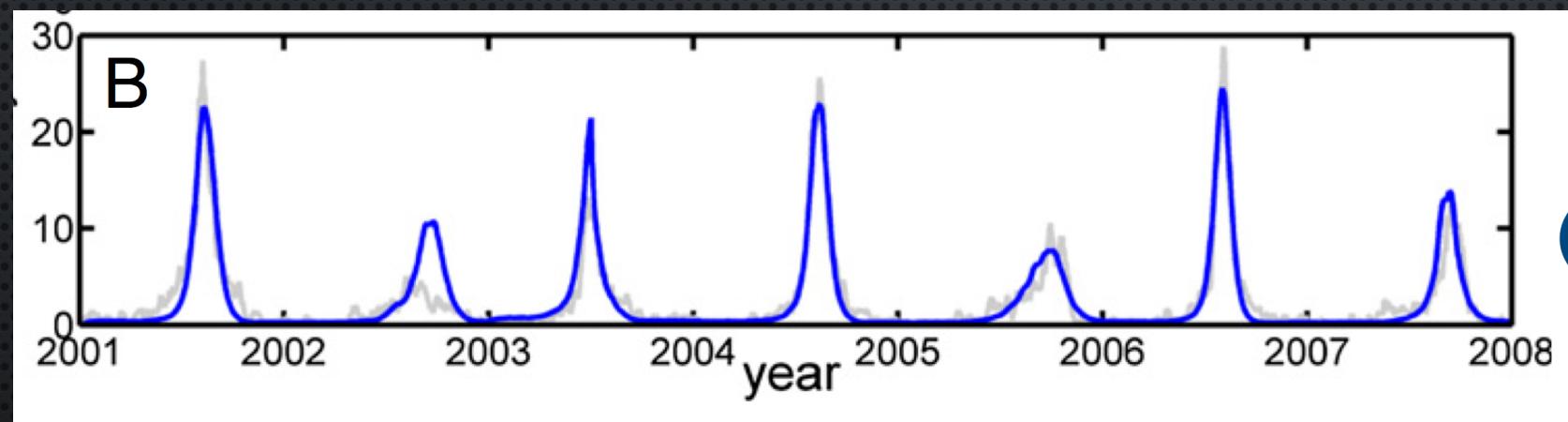
continued?



Structure of Epidemics



Influenza in Jerusalem



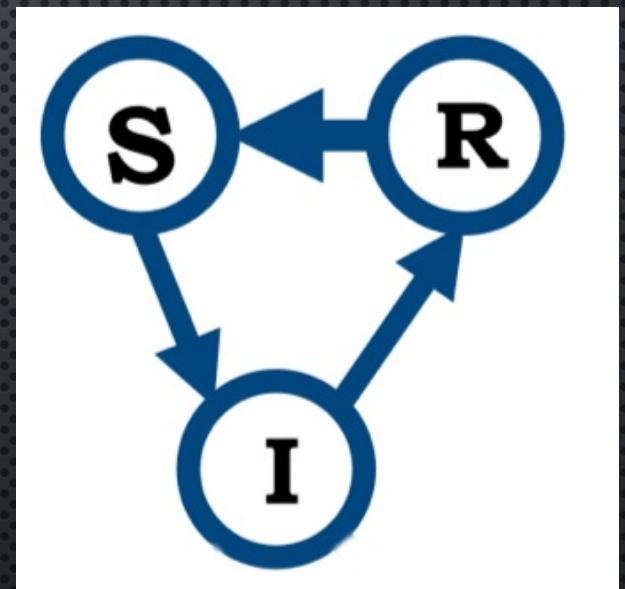
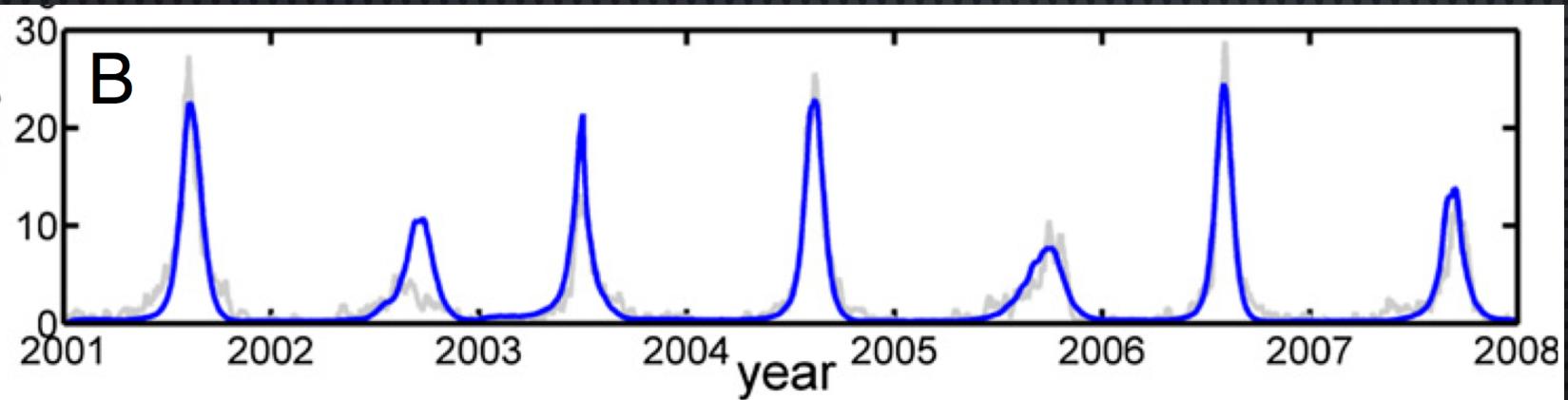
Features:

1. Exponential growth
2. Curtails (susceptible depletion and/or transmission decline)
3. Inter-epidemic period



Recurrent Epidemics

S: Susceptible
I: Infected
R: Recovered



Immunological Memory

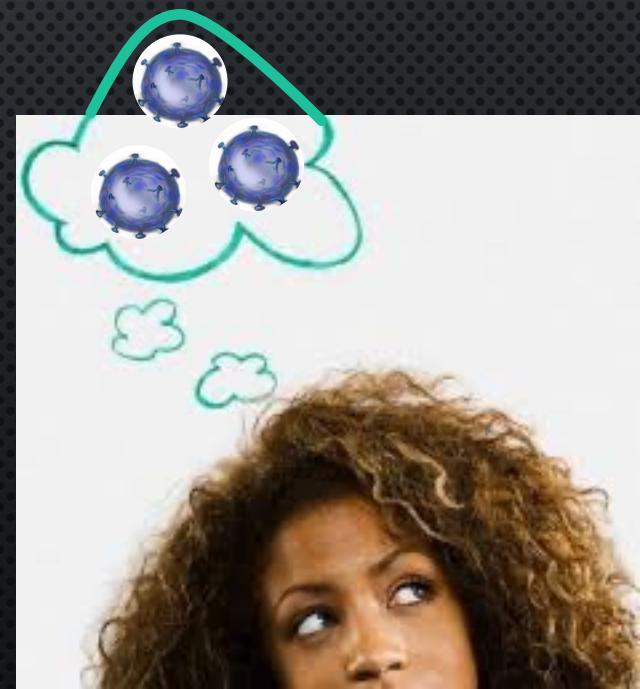
IMMUNOLOGICAL MEMORY REFERS TO THE ABILITY OF THE IMMUNE SYSTEM TO RESPOND MORE RAPIDLY AND EFFECTIVELY TO A PATHOGEN THAT HAS BEEN ENCOUNTERED PREVIOUSLY.

S: Susceptible

I: Infected

R: Recovered class
contains individuals with
immunological memory
(i.e., immunity, which is
pathogen-specific)

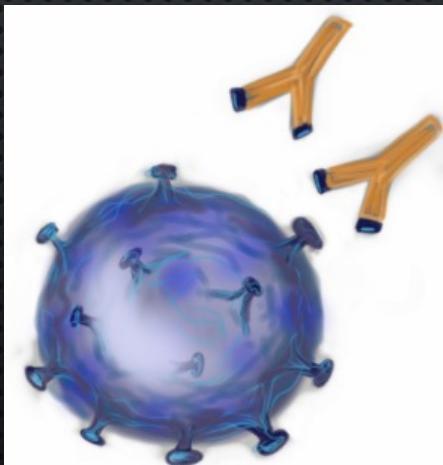
Immune
system
remembering
pathogens



Immunological Memory: Antibodies

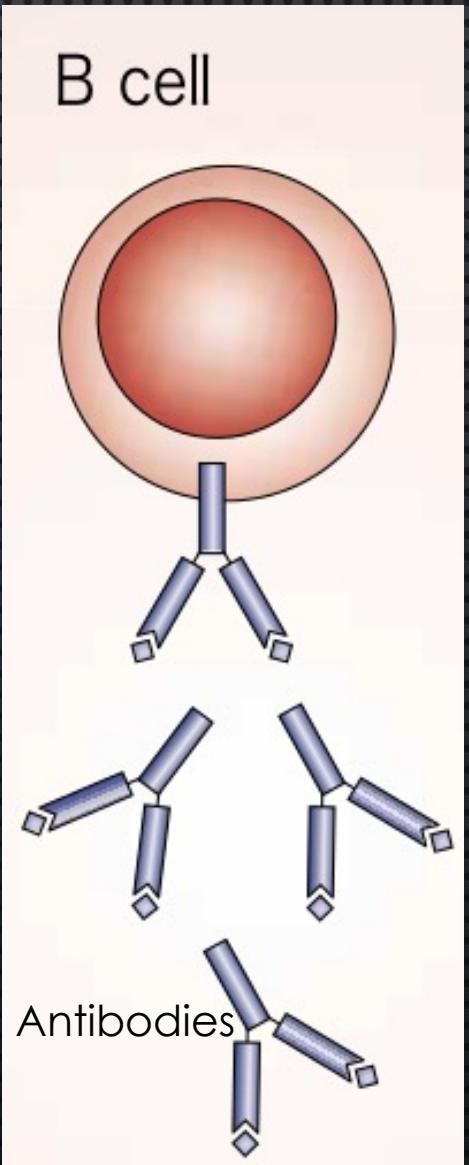
Antibodies are found in the fluid component of blood, or plasma, and in extracellular fluid

The simplest and most direct way in which **antibodies** can protect from pathogens is by binding to them and blocking their access to cells that they might infect or destroy. This is known as **neutralization**.



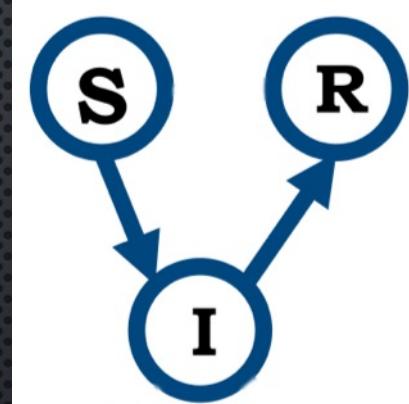
Antibodies

Virus to be neutralized



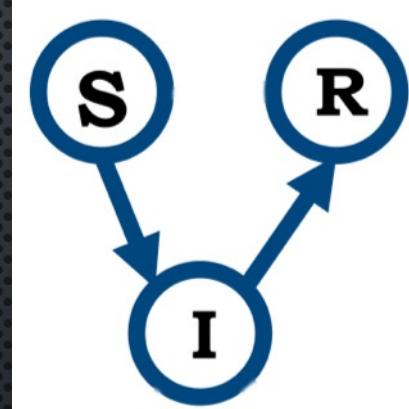
Susceptible-Infected-Recovered Models

Math



Susceptible-Infected-Recovered Models

- (1) Population size $N = S + I + R$
- (2) Change in susceptible over time $\frac{dS}{dt} = \mu N - \beta IS - \delta S$
- (3) Change in infected over time $\frac{dI}{dt} = \beta IS - \gamma I - \alpha I - \delta I$
- (4) Change in recovered over time $\frac{dR}{dt} = \gamma I - \delta R$



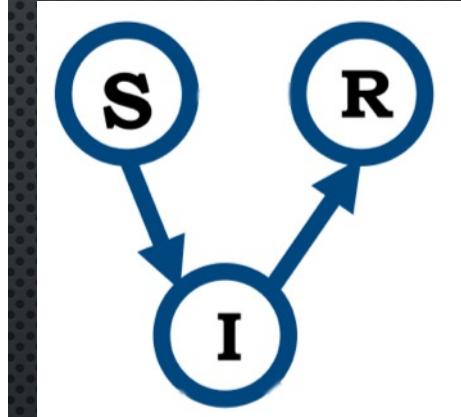
Susceptible-Infected-Recovered Models

- + individuals added to the class
- individuals leaving the class

(2) Change in susceptible over time

$$\frac{dS}{dt} = \mu N - \beta IS - \delta S$$

New infections
New births
Natural death



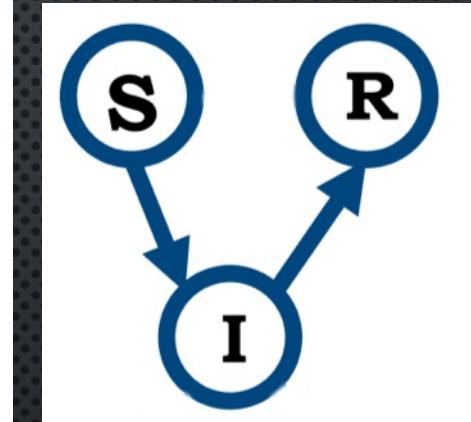
Susceptible-Infected-Recovered Models

- + individuals added to the class
- individuals leaving the class

(3)

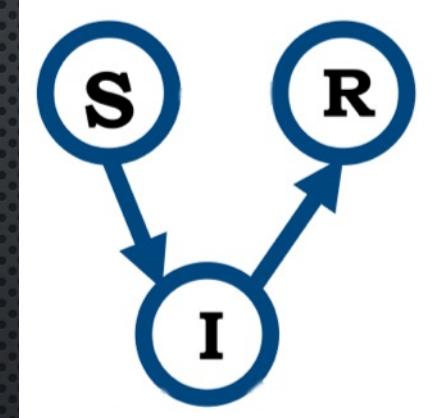
Change in infected over time

$$\frac{dI}{dt} = \beta IS - \frac{\text{New infections}}{\text{recovery}} - \frac{\text{Infection-induced mortality}}{\text{Natural death}}$$



Susceptible-Infected-Recovered Models

- + individuals added to the class
- individuals leaving the class



(4)

Change in recovered over time

$$\frac{dR}{dt} = \gamma I - \delta R$$

recovery
Natural
death

Growth of the Infected Class

$$\frac{dI}{dt} = \beta IS - \gamma I - \alpha I - \delta I$$

$$\frac{dI}{dt} = \underbrace{\beta SI}_{\text{Rate in}} - \underbrace{(\gamma + \alpha + \delta)I}_{\text{Rate out}}$$

Rate
in

Rate
out

Rate
in

Rate
out

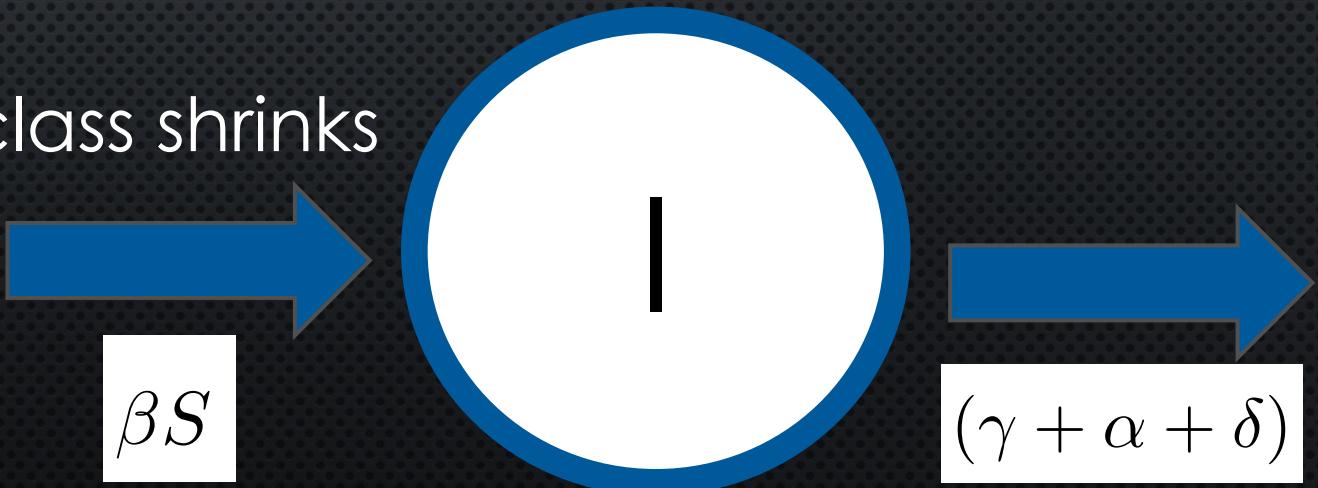


Change in Infected Class

Size of infected class remains constant

Infected class grows (rate in > rate out)

Infected class shrinks



Change in Infected Class

$$\beta S = (\gamma + \alpha + \delta)$$

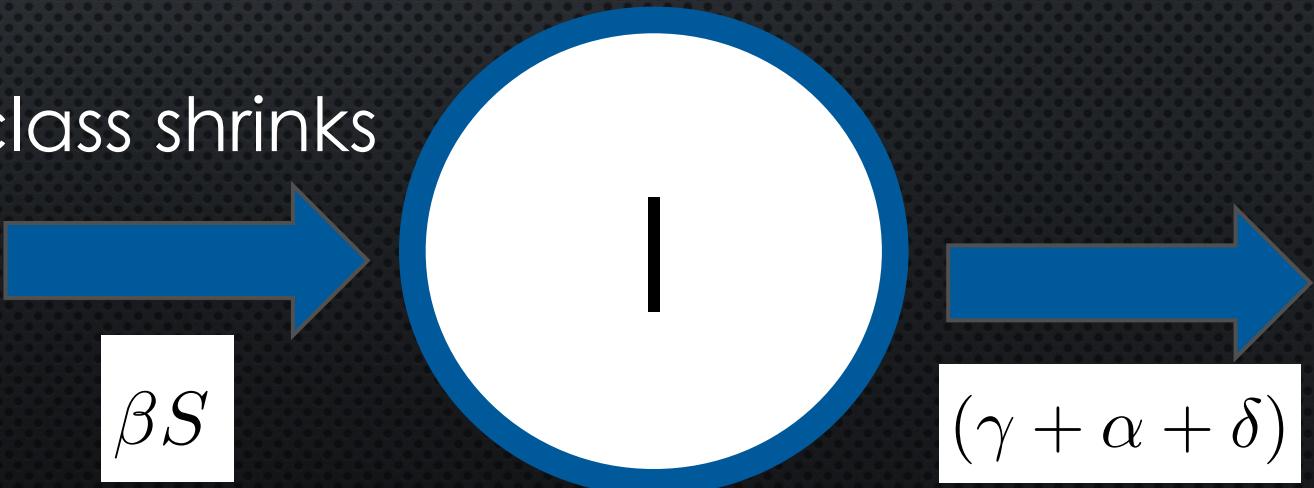
Size of infected class remains constant

$$\beta S > (\gamma + \alpha + \delta)$$

Infected class grows (rate in > rate out)

$$\beta S < (\gamma + \alpha + \delta)$$

Infected class shrinks



Calculating the Reproductive Ratio

$$\frac{\beta S}{(\gamma + \alpha + \delta)}$$

Called the reproductive ratio because it tells us how many new infections “reproduced” by each infected individual before they leave the infected class

If greater than 1, the infectious agent is successfully spreading and the infected class grows in size

