Lecture 1
Intro to Modeling

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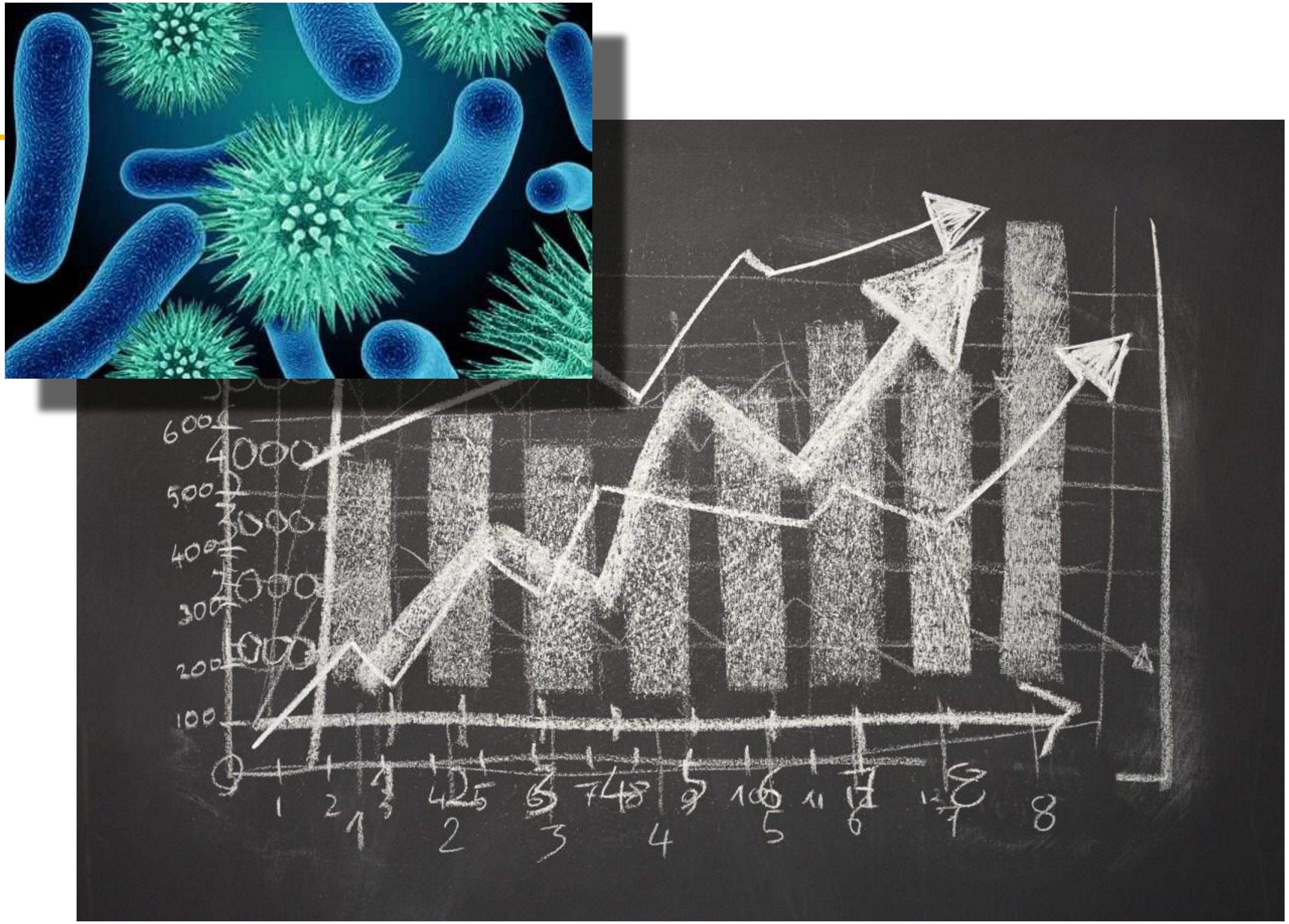
slides in part adapted from Pej Rohani & John Drake's SISMID 2019 course materials

Modeling Infectious Diseases



Course Objectives:

- Modeling 101
- Basic Reproduction Ratio (R0)
- Simple Epidemic Dynamics
- Vaccination & interventions
- Heterogeneity
- Modeling during a pandemic
- Informing models with data
- Stochasticity and uncertainty

Many ways to study infectious diseases

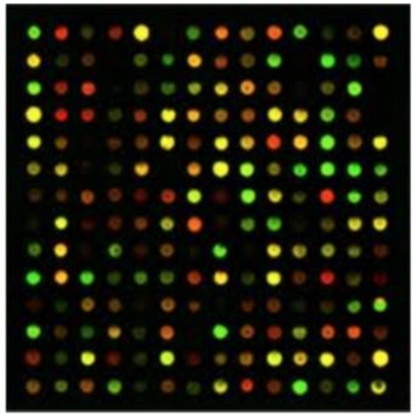
Some disciplines focus on infectious diseases from the:

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

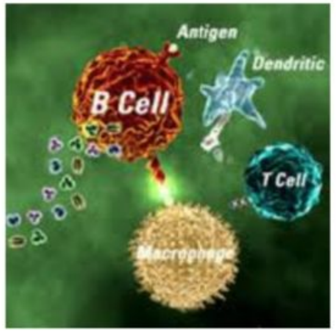
Medicine

Microbiology

Genomics

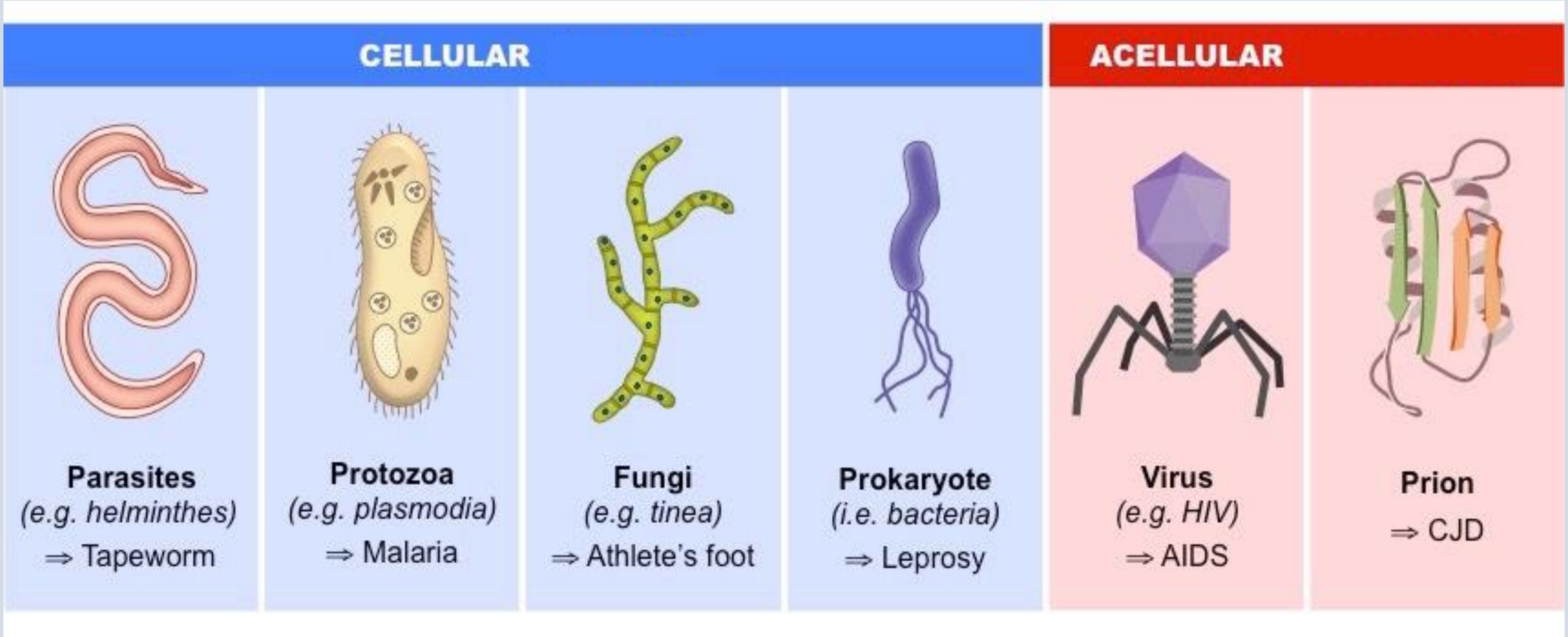


Immunology

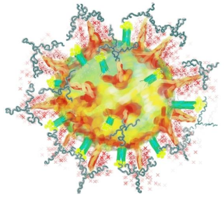


Vaccines & Drugs

Agents of infectious diseases

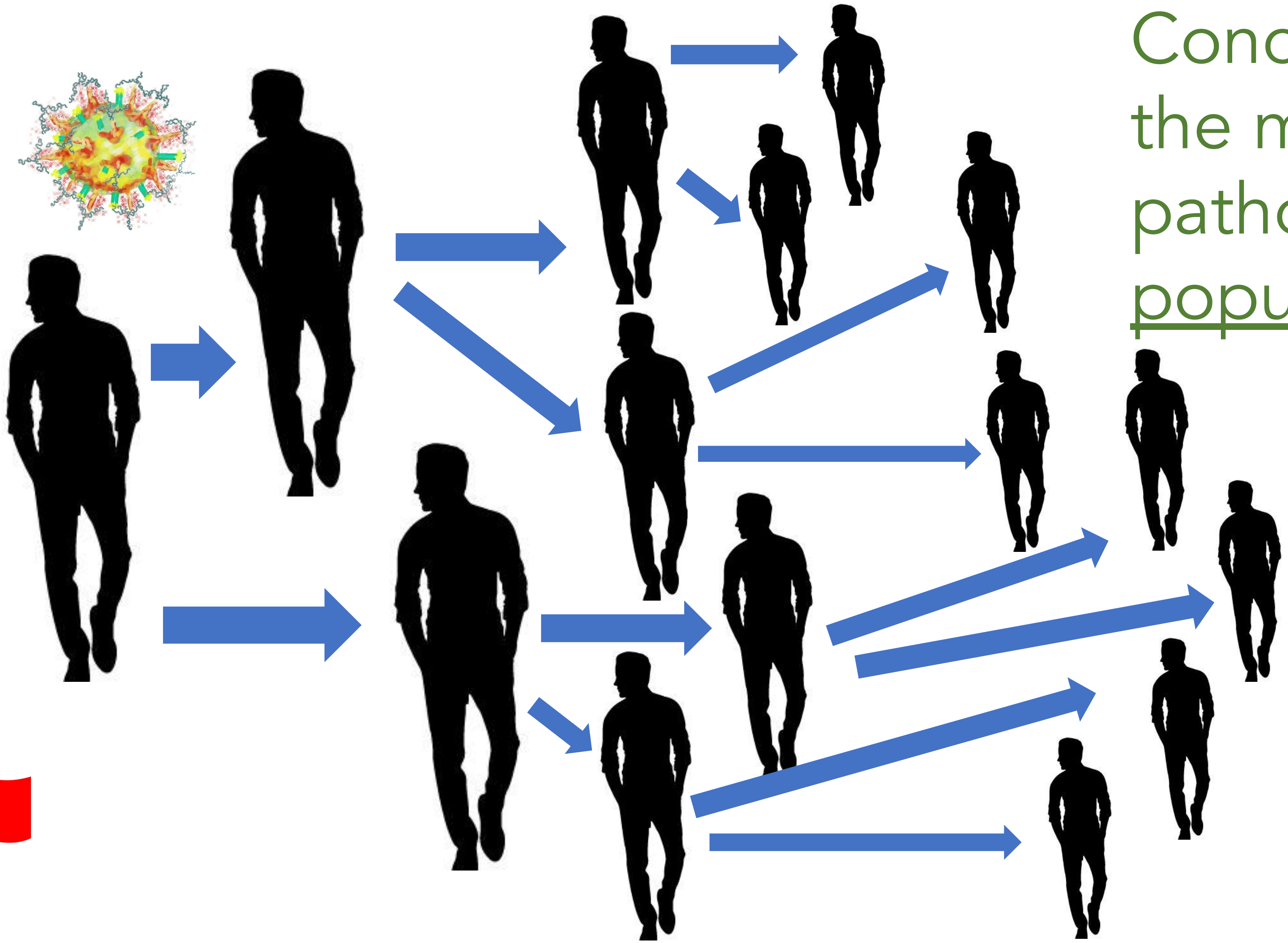


Epidemiology & Disease Ecology focus on the population-level



Concept: We can track the movement of pathogens throughout populations

Epidemiology & Disease Ecology focus on the population-level

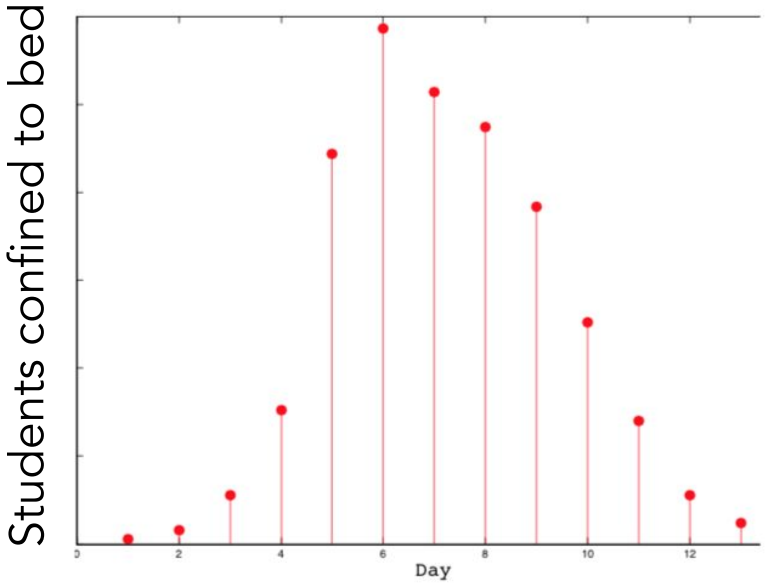


Concept: We can track the movement of pathogens throughout <u>populations</u>

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

The use of time series data

1978 outbreak in a British boarding school

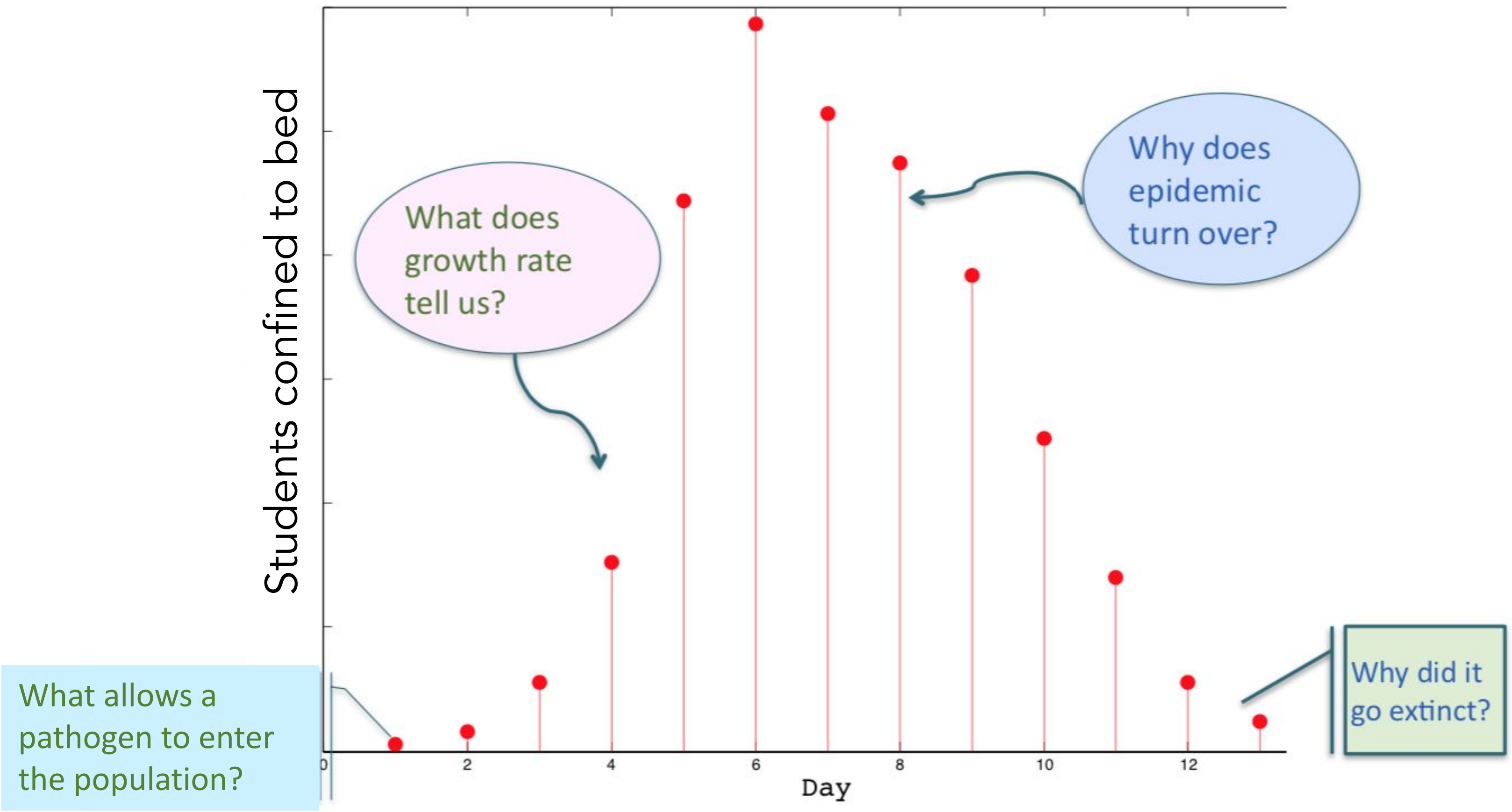


What pathogen is causing the illness?

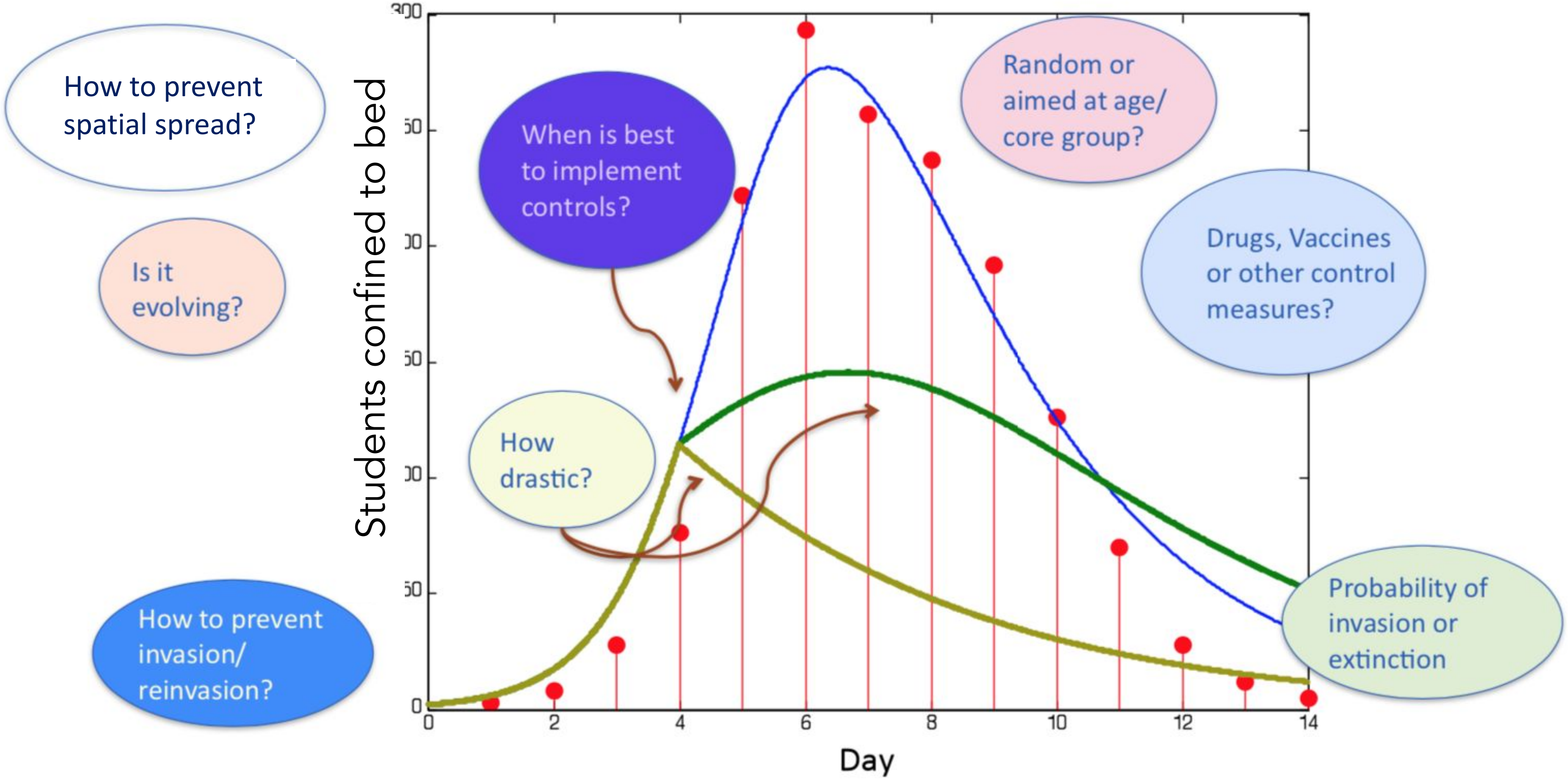
Is it a novel pathogen?

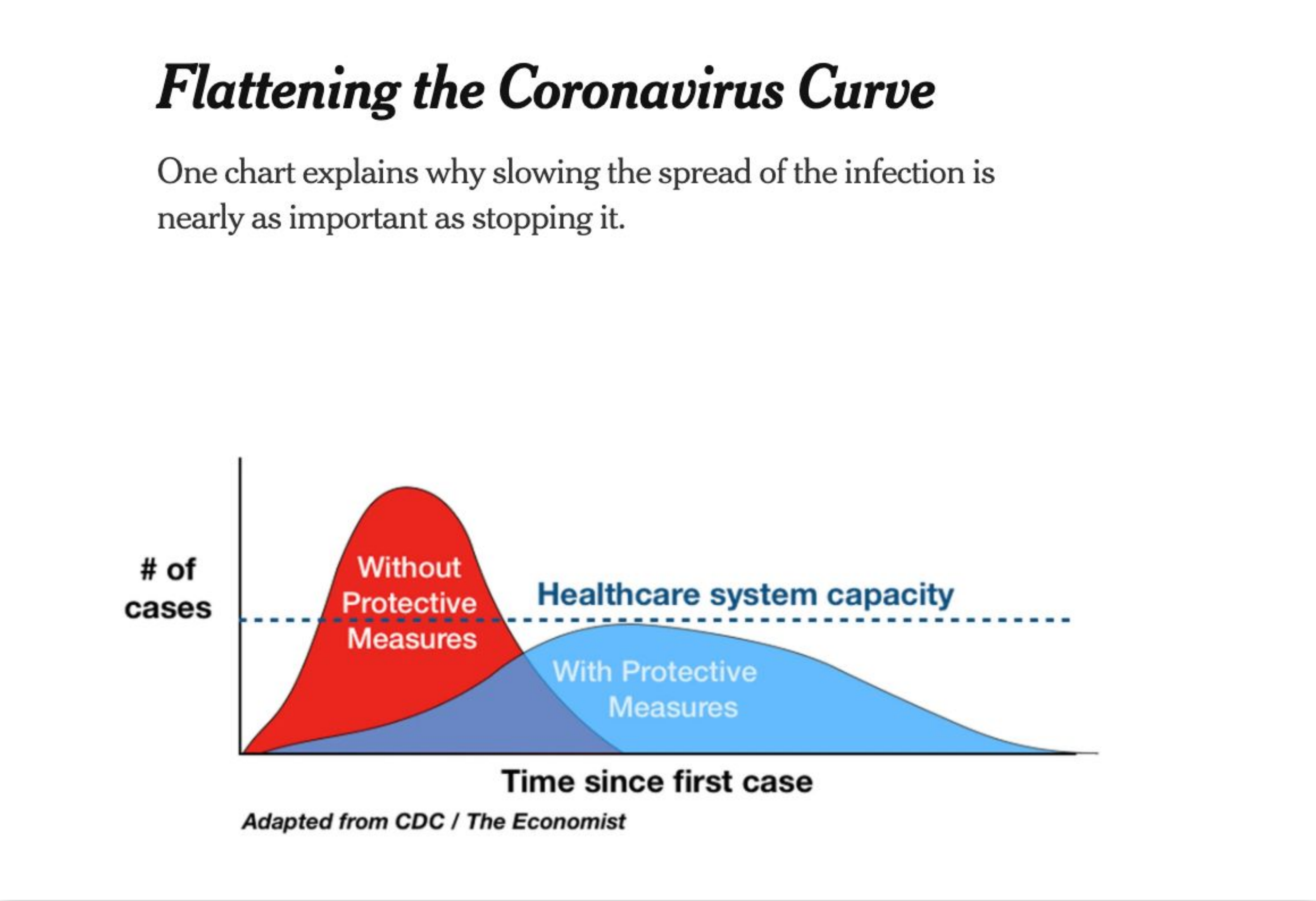
Is there a vaccine or treatment?

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.

The shape of the epidemic curve contains information about transmission

What is a model?

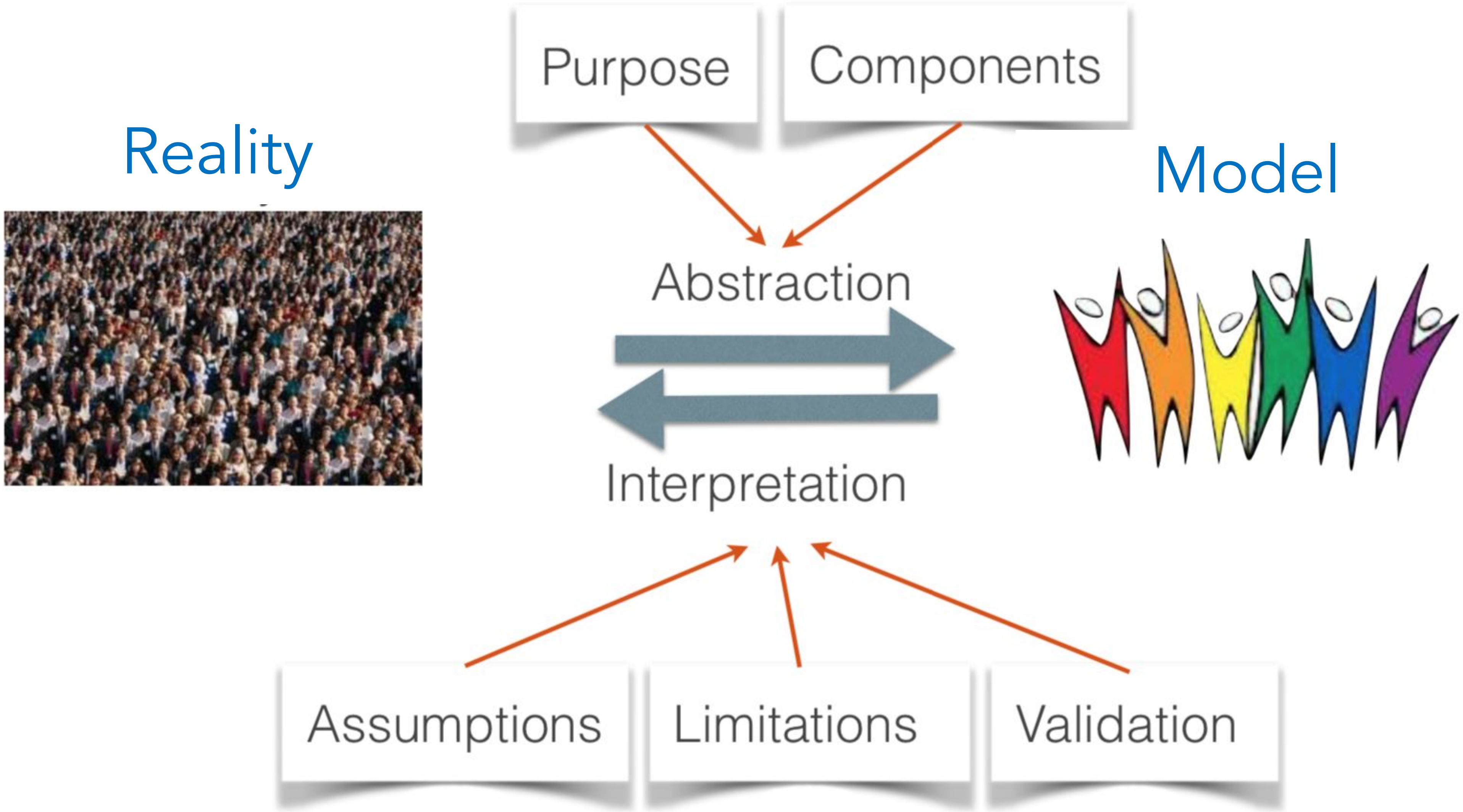
Different types of models:

A **mathematical model** is a set of equations that describe 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

Mathematical models are abstractions of reality



What is a *"good"* model?

- 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

Judging a Model...

Three fundamental features of models, often opposing forces:

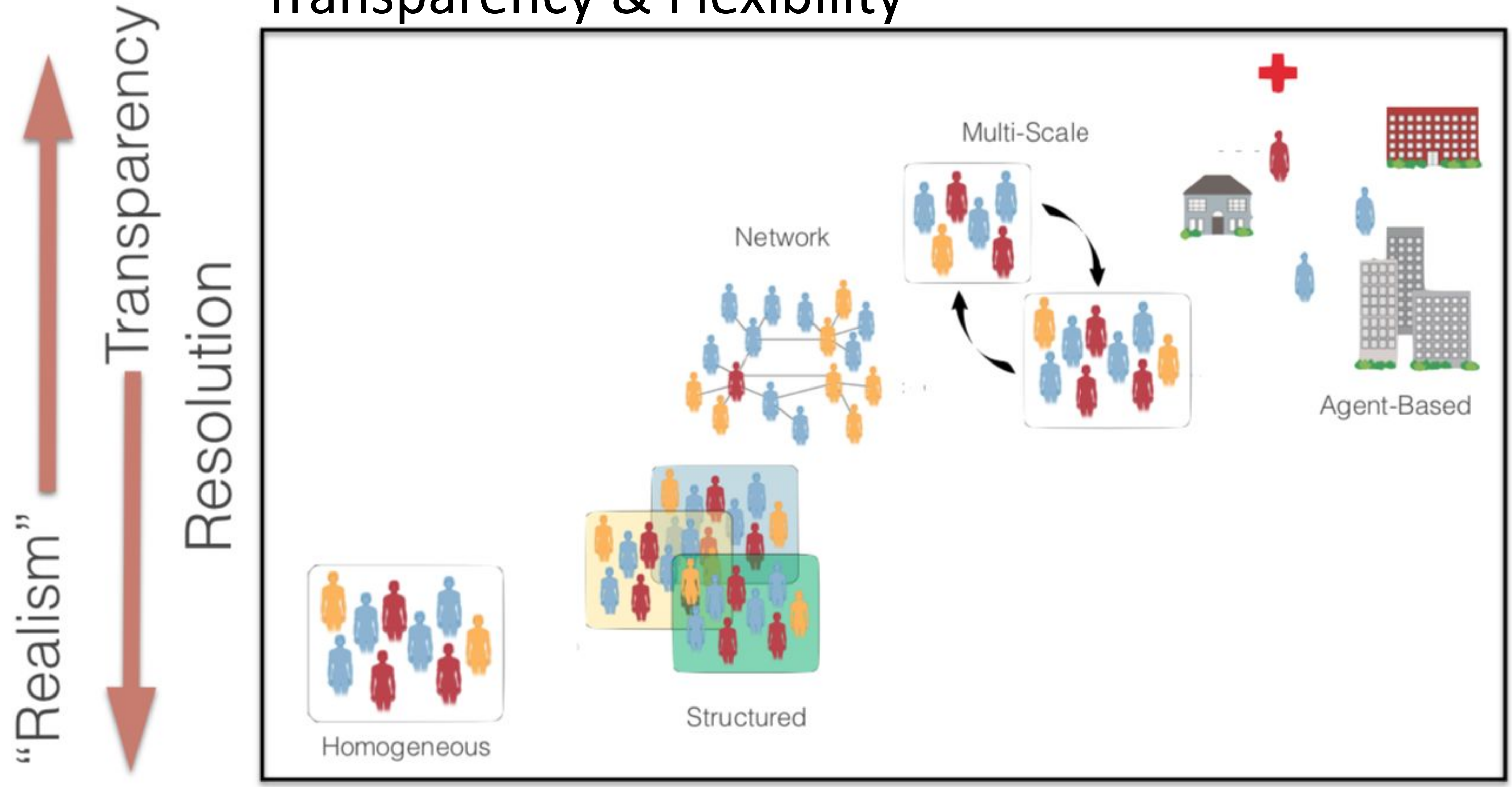
Accuracy: ability to capture observed patterns (qualitative or quantitative) and make predictions

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

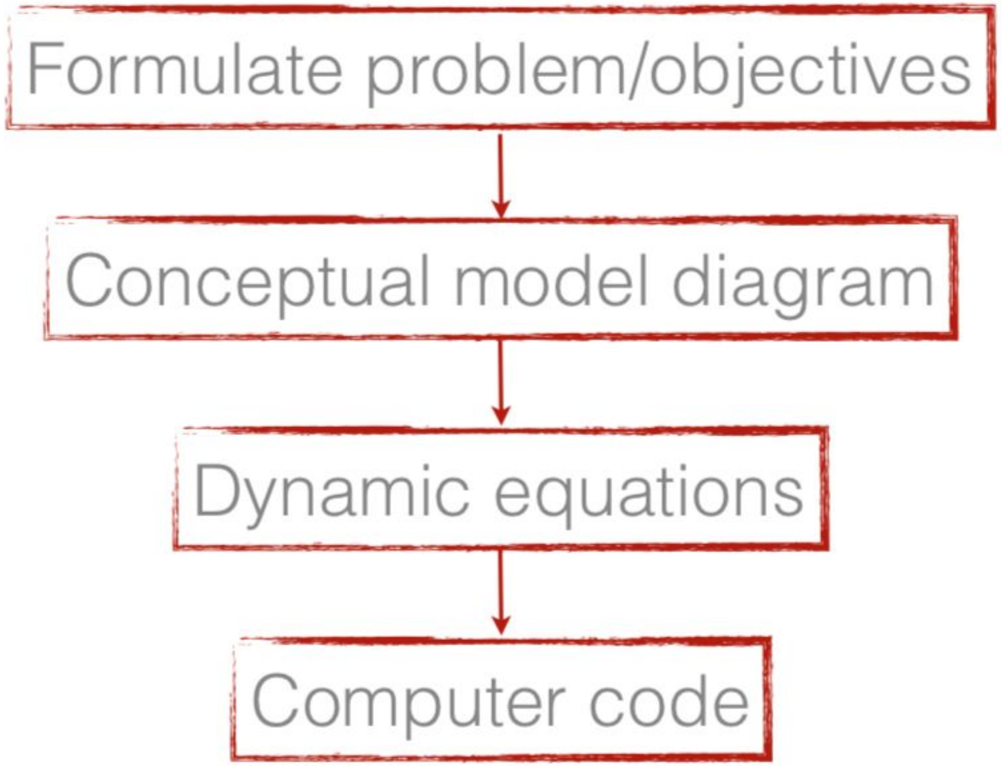


How do you implement a mathematical model?

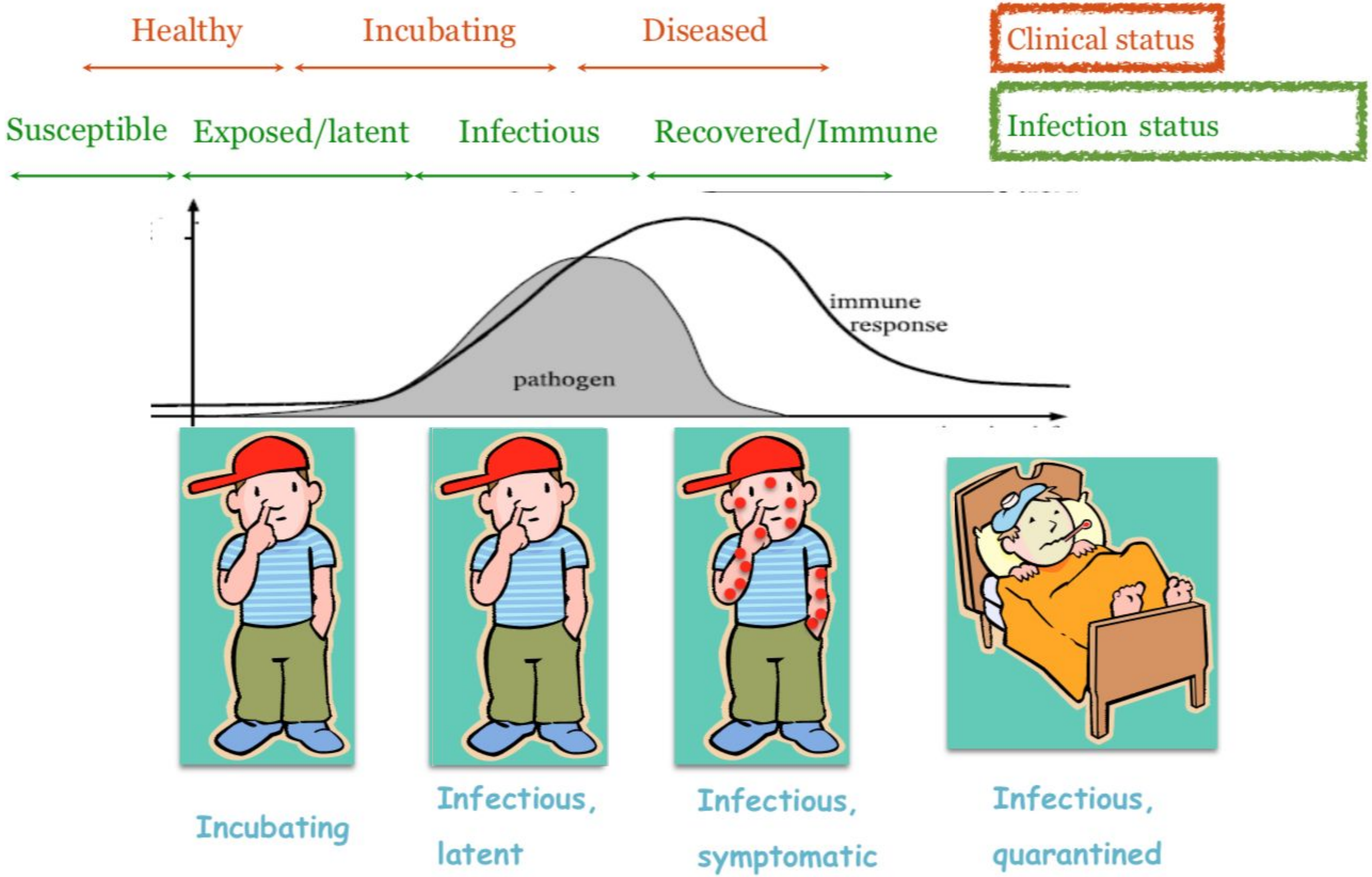
Analytical Models
Concentrate on problems that can be expressed and analyzed fully using analytical approaches (*i.e., pure math*)

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



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?

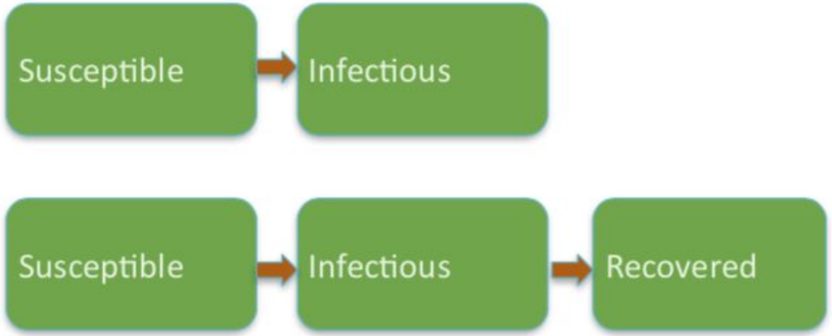
-- Determined by pathogen biology

SI models can be used for fatal or chronic infections

Simple Models

What model structure?

-- Determined by pathogen biology

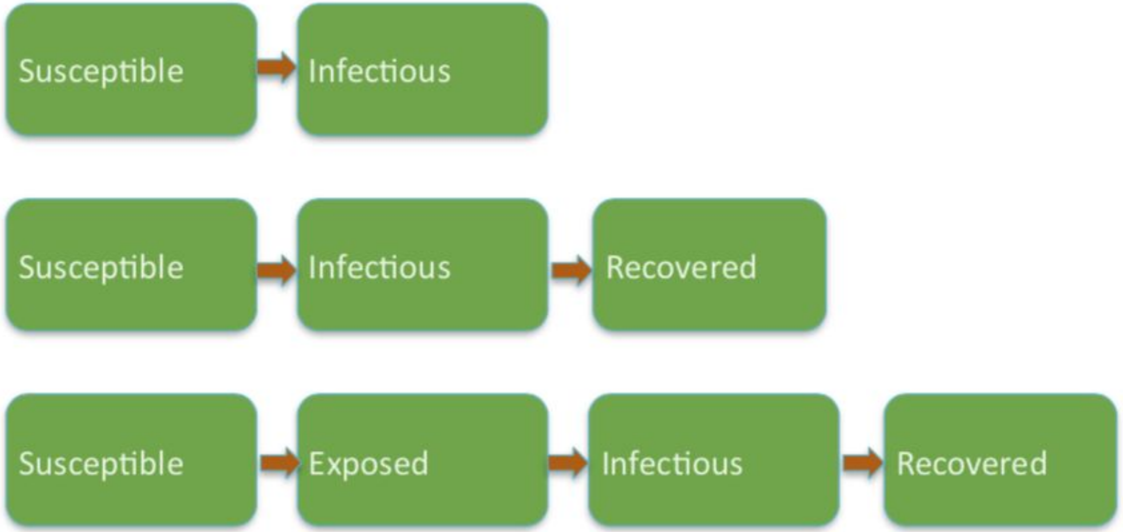


SIR models can be used for infections where there is recovery and immunity

Simple Models

What model structure?

-- Determined by pathogen biology

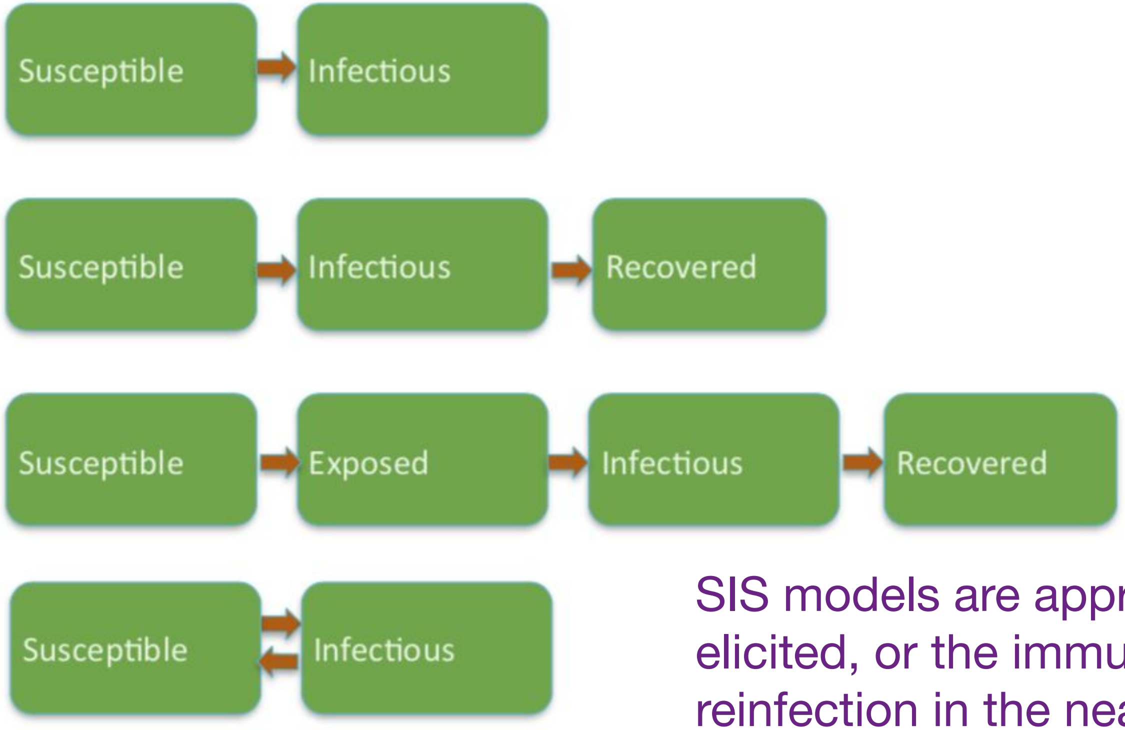


SEIR models can be used for infections where there is a non-negligible latent period when individuals are infected but not infectious. This can be a good category to have, for example for COVID-19, when considering testing and quarantine early on in infection.

Simple Models

What model structure?

-- Determined by pathogen biology

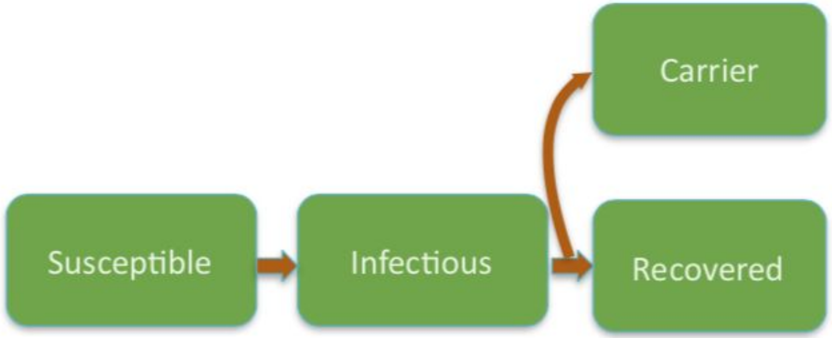


SIS models are appropriate when there is little immunity elicited, or the immunity elicited will not protect from reinfection in the near-future.

Simple Models

What model structure?

-- Determined by pathogen biology

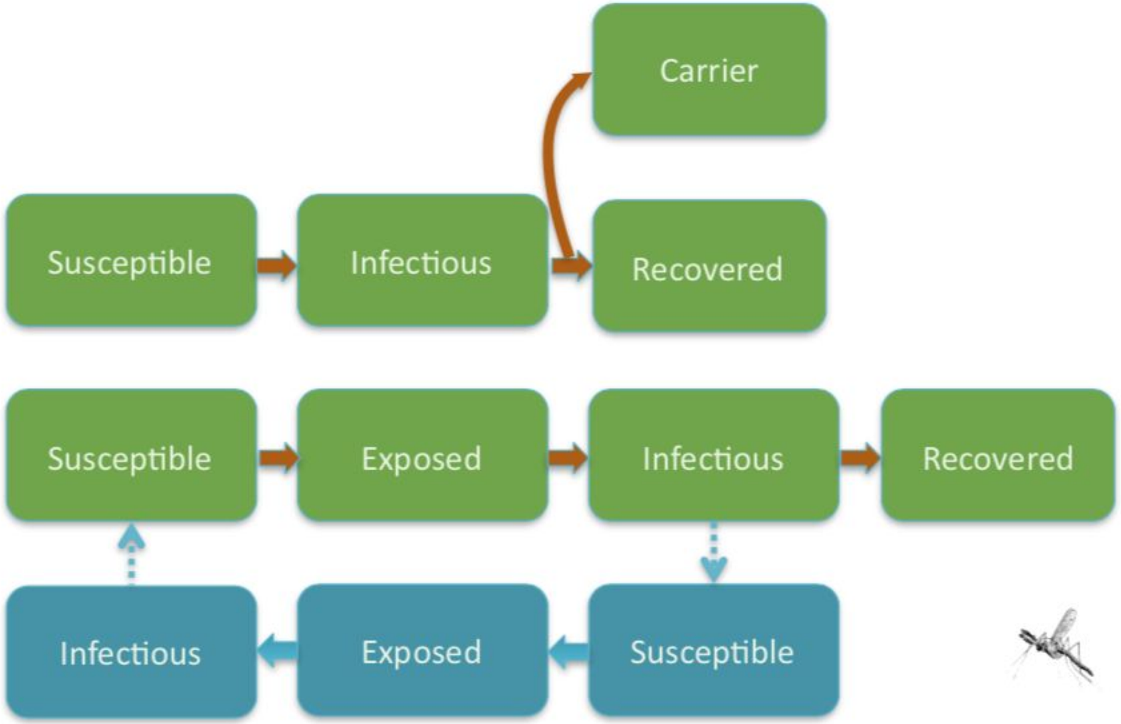


SIR – with carriers

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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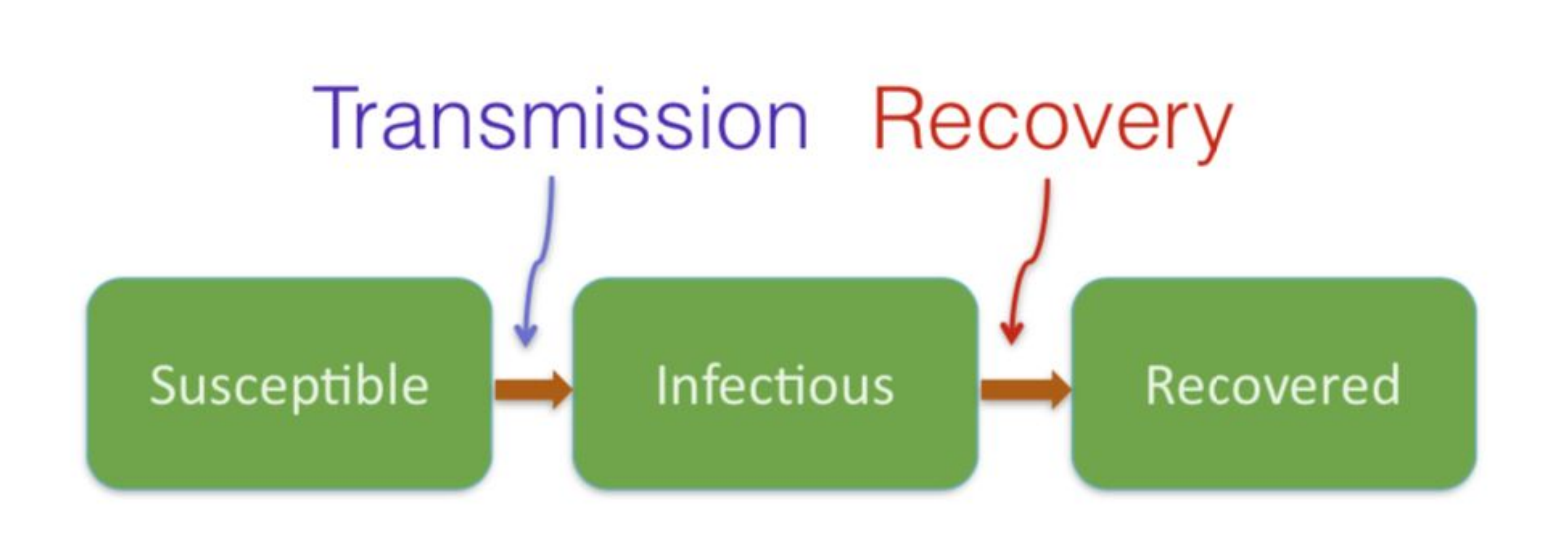
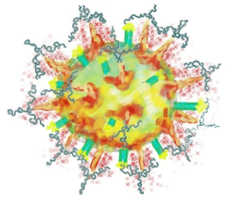
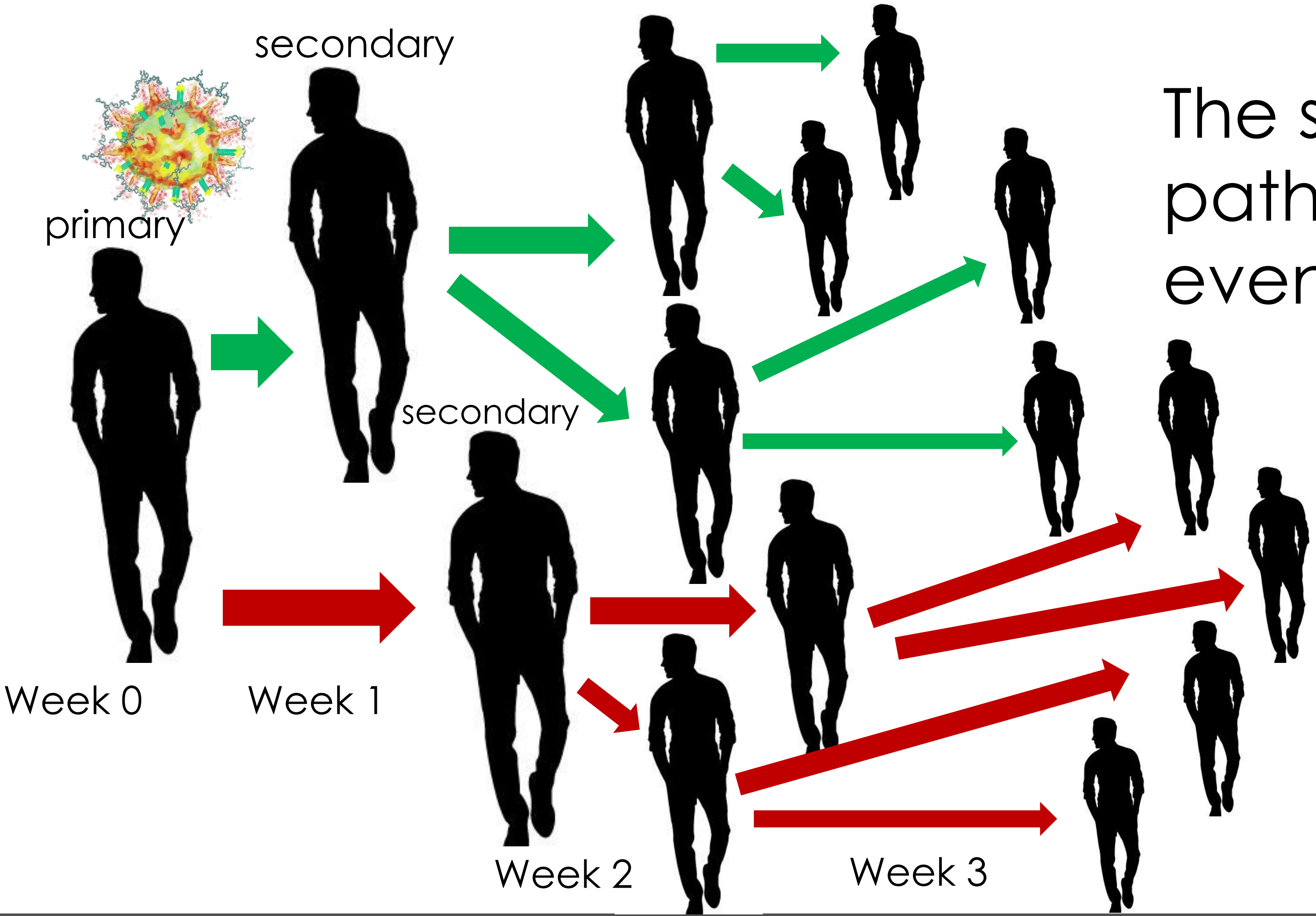

Transmission
Recovery
Susceptible
Infectious
Recovered

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.

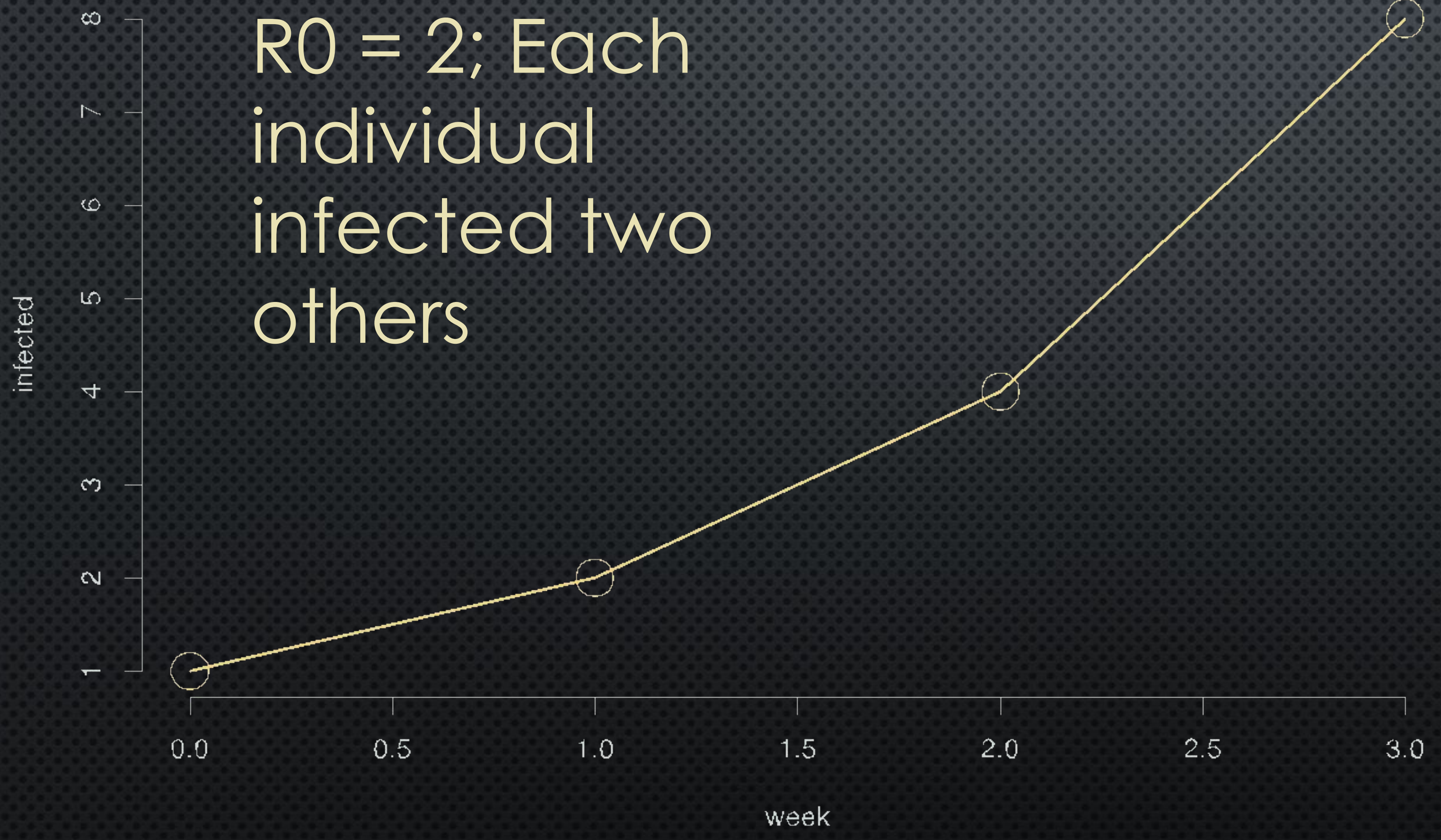
infection	Geographic location	Time period	R0
measles	England & Wales	1950-1968	16-18
measles	Kansas, USA	1918-1921	5-6
pertussis	Maryland, USA	1943	16-17
chicken pox	New Jersey, USA	1912-1921	7-8
mumps	Netherlands	1970-1980	11-14
rubella	West Germany	1970-1977	6-7
polio	USA	1955	5-6

R0 varies among:

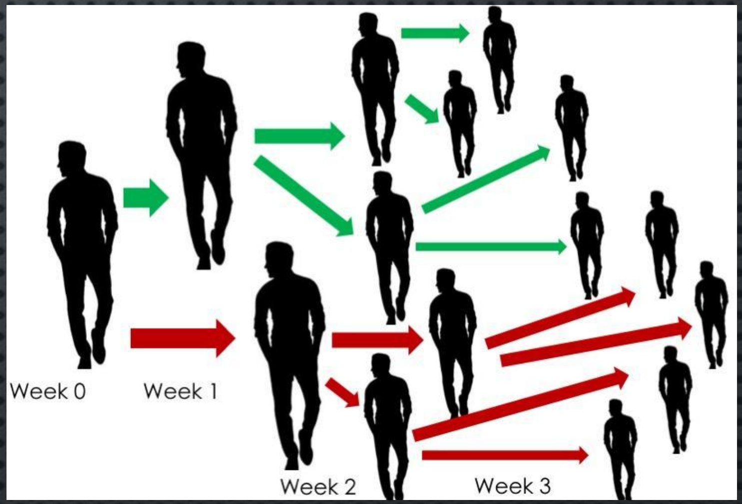
1. diseases
2. populations
3. time periods

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

Infections in the population



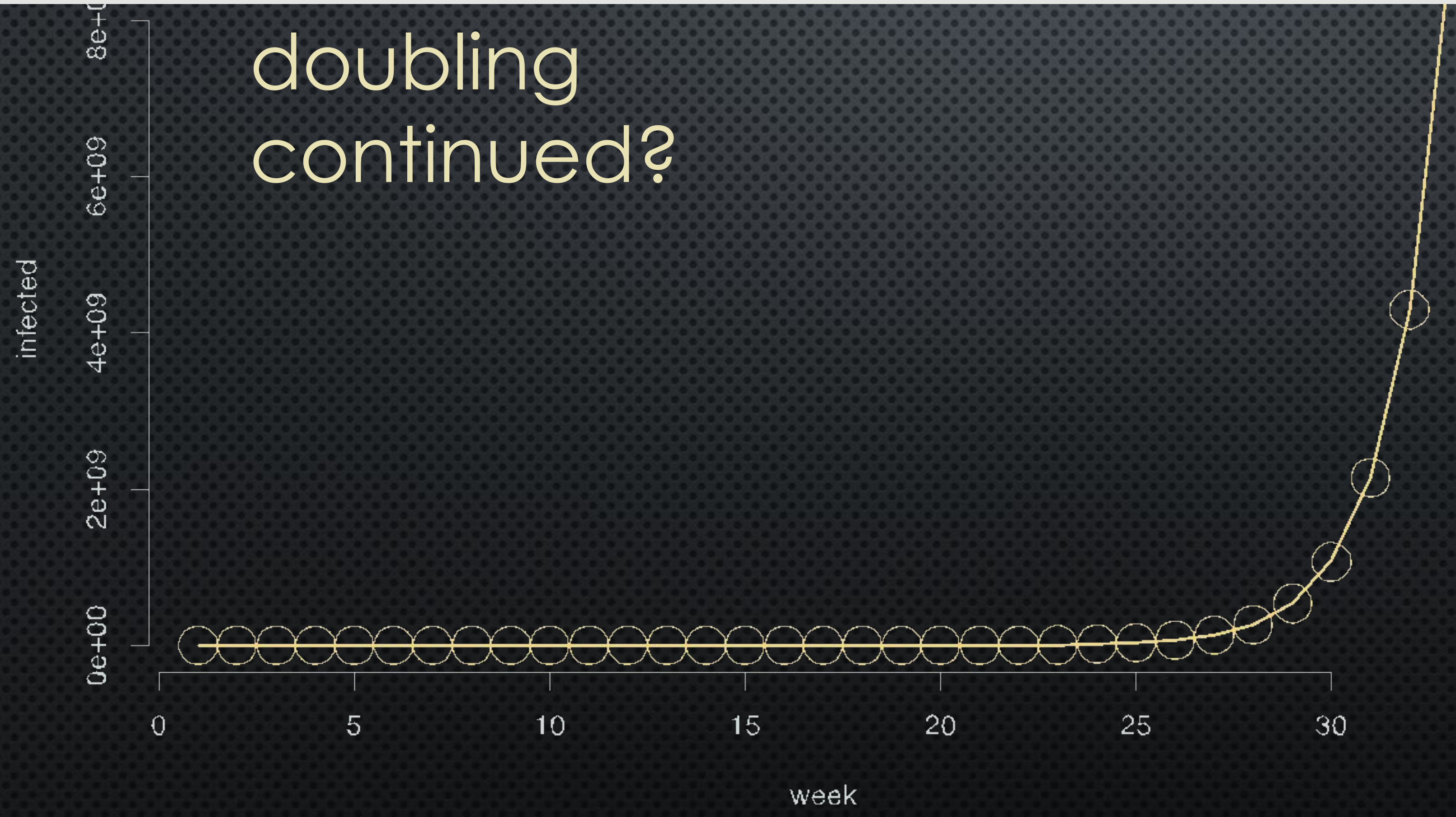
R0 = 2; Each individual infected two others



$$I_t = 2^t$$

Infections in the population

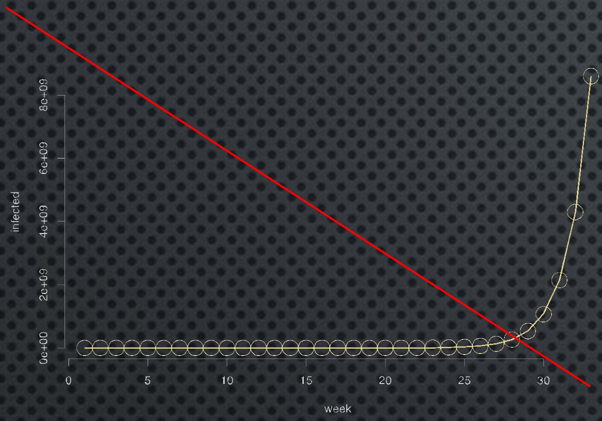
• **basic reproduction number, R_0**: average number of infections caused by a typical infected individual in a population consisting only of susceptibles; if $R_0 > 1$, the infectious agent can start to spread.



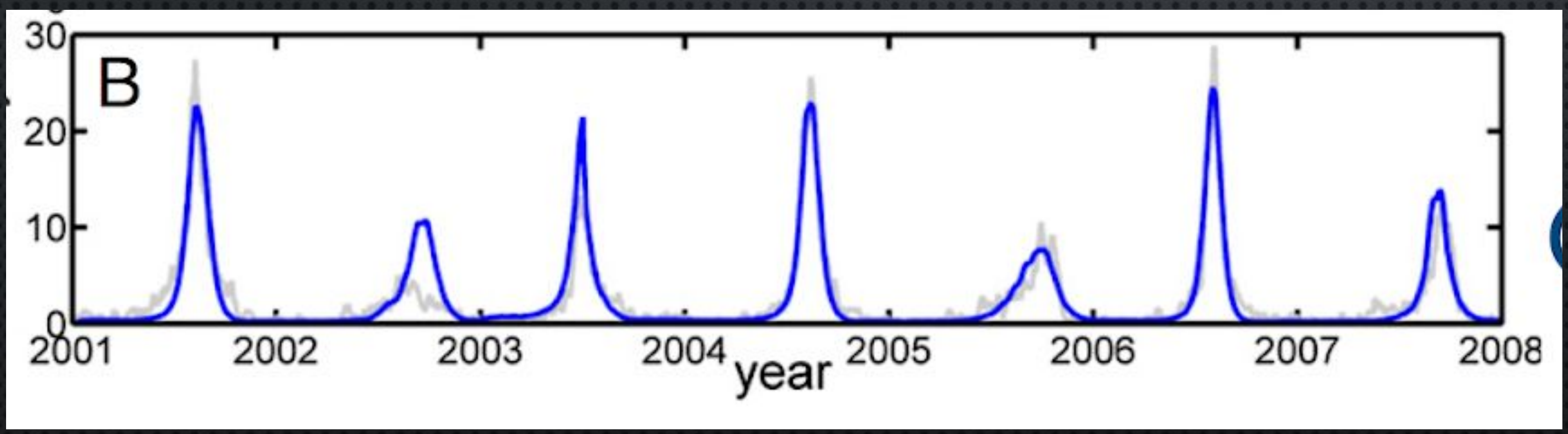
> world pop

$I_t = 2^t$

Structure of Epidemics

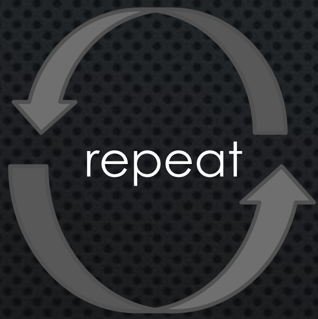


Influenza in Jerusalem



Features:

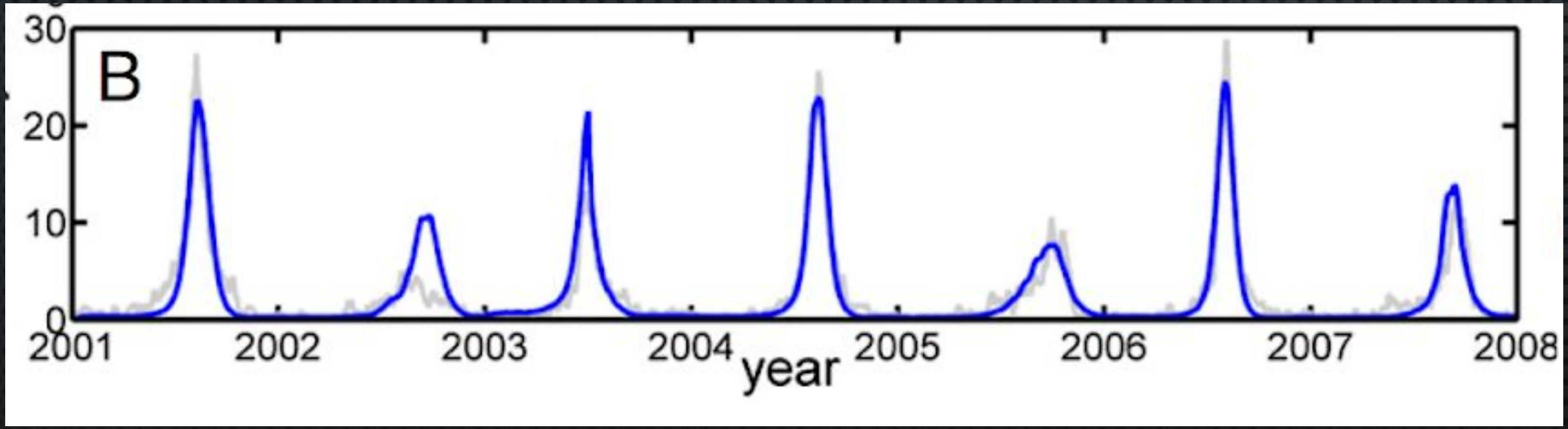
1. Exponential growth
2. Curtails (susceptible depletion and/or transmission decline)
3. Inter-epidemic period

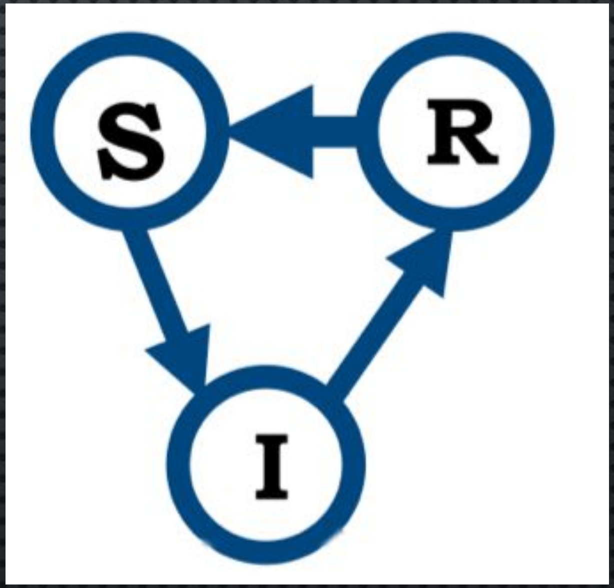


(Axelsen et al., 2014)

Recurrent Epidemics

S: Susceptible
I: Infected
R: Recovered





(Axelsen et al., 2014; Heesterbeek at al. 2015)

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
<u>R: Recovered class contains individuals with immunological memory</u>

Immune system remembering pathogens

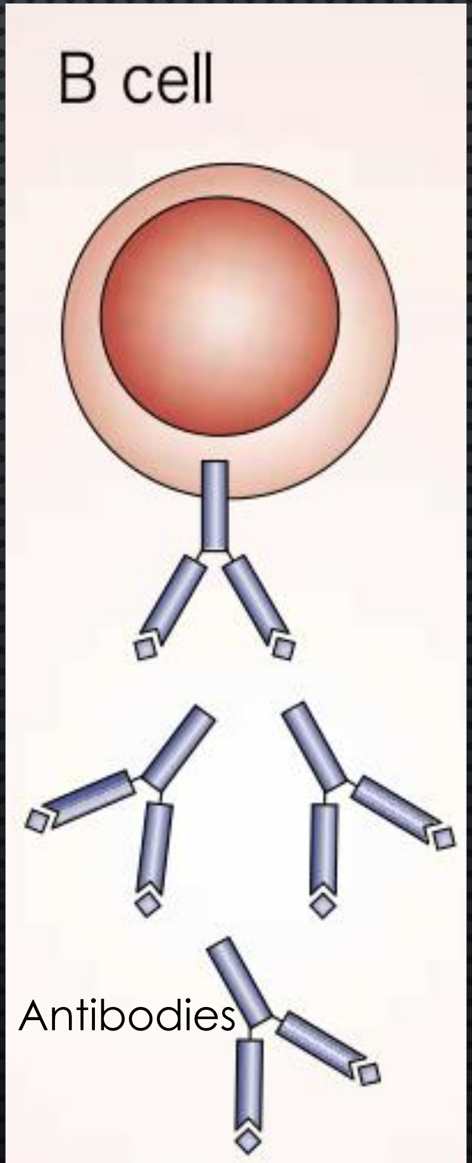
Immunological Memory: Antibodies

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

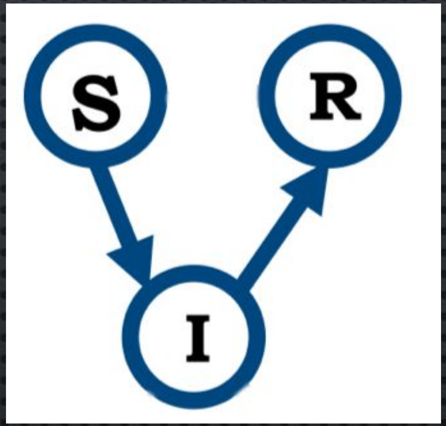
Virus to be neutralized



Immunobiology, 5th edition

Susceptible-Infected-Recovered Models

Math



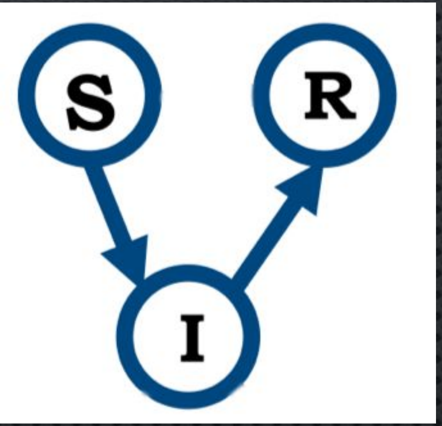
Susceptible-Infected-Recovered Models

(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

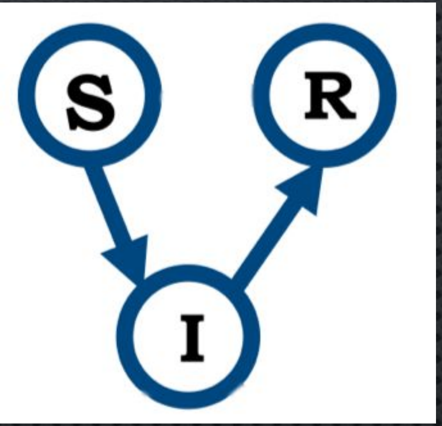
(2) Change in susceptible over time

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

New infections

New births

Natural death



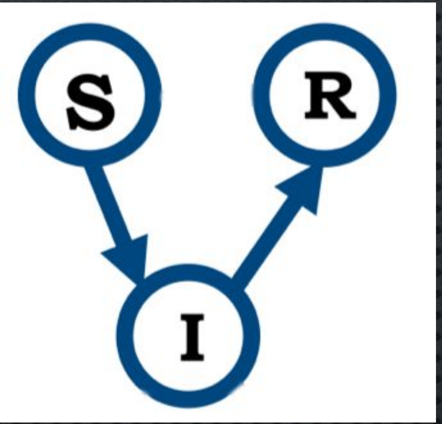
Susceptible-Infected-Recovered Models

+ individuals added to the class
- individuals leaving the class

(3) Change in infected over time

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

New infections (βIS); recovery (γI); Infection-induced mortality (αI); Natural death (δI)



Susceptible-Infected-Recovered Models

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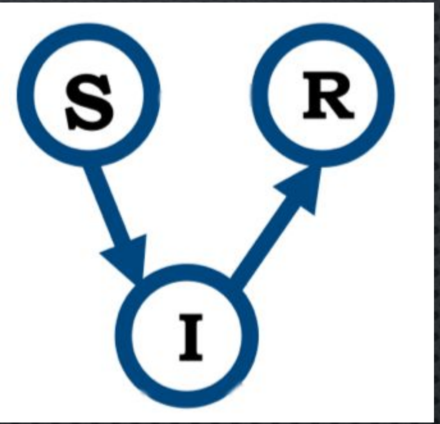


Natural death

(4) Change in recovered over time

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

recovery

Growth of the Infected Class

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

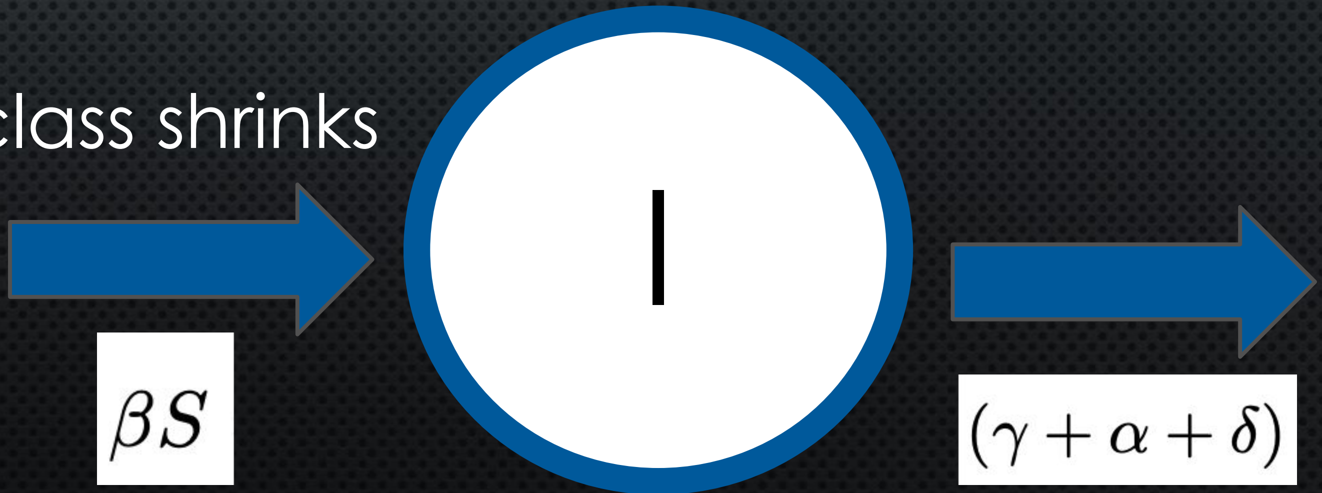
$$\frac{dI}{dt} = \underbrace{\beta SI}_{\text{Rate in}} - \underbrace{(\gamma + \alpha + \delta)}_{\text{Rate out}} I$$

Change in Infected Class

Size of infected class remains constant

Infected class grows (rate in > rate out)

Infected class shrinks



Change in Infected Class

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

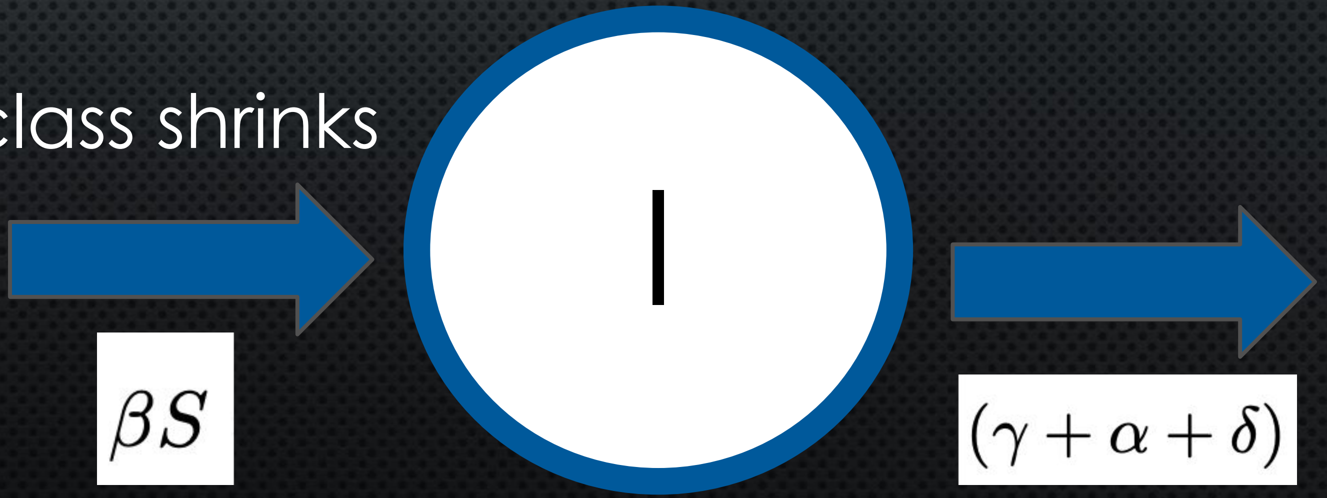
Size of infected class remains constant

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

Infected class grows (rate in > rate out)

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

Infected class shrinks



Calculating the Reproductive Ratio

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

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

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