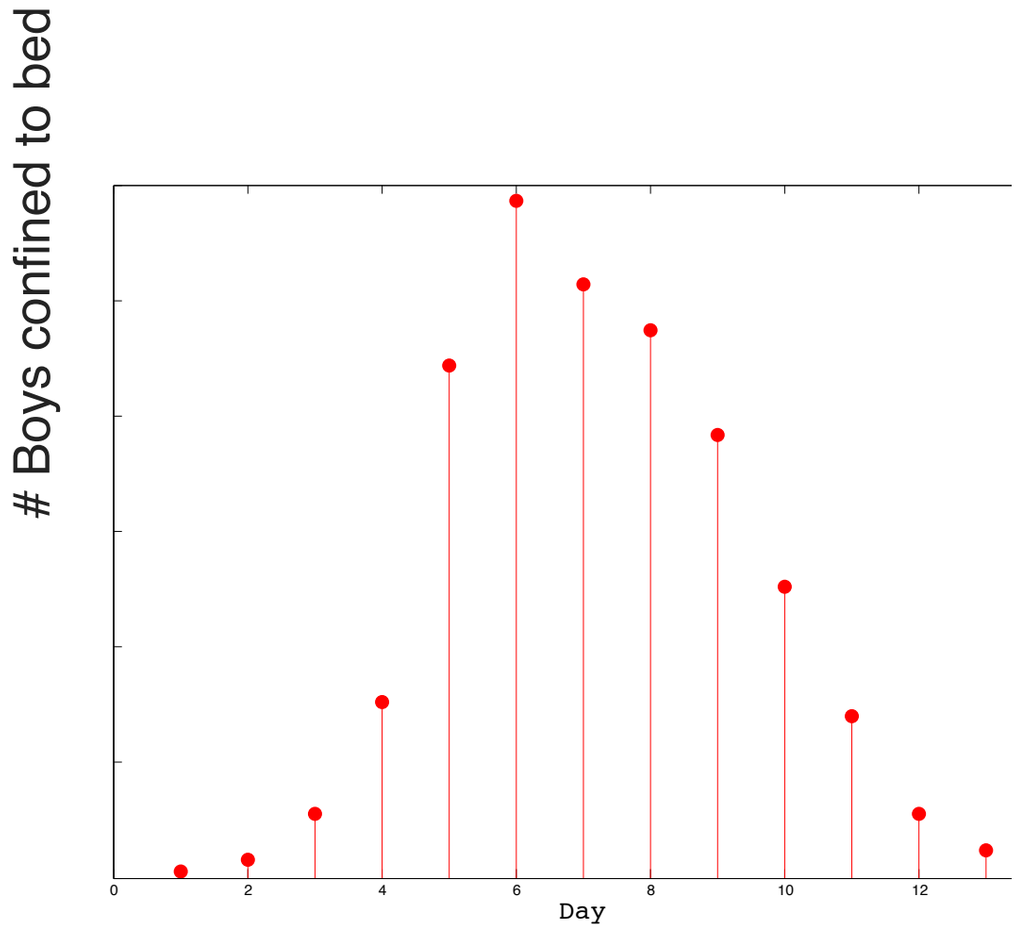
Modeling Infectious Diseases

- Pej Rohani & John Drake

- Odum School of Ecology
- University of Georgia

School outbreak

Boarding School, England
Jan 1978



Raises numerous questions:

- What is etiological agent?
- Is it novel?
- Is a vaccine available?

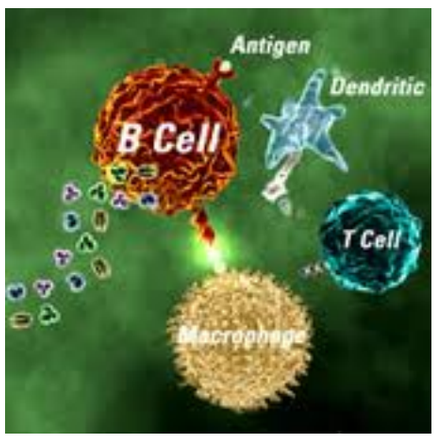
Multifaceted approach to understanding infectious diseases

Medicine

But these approaches don't address important questions at population level ...

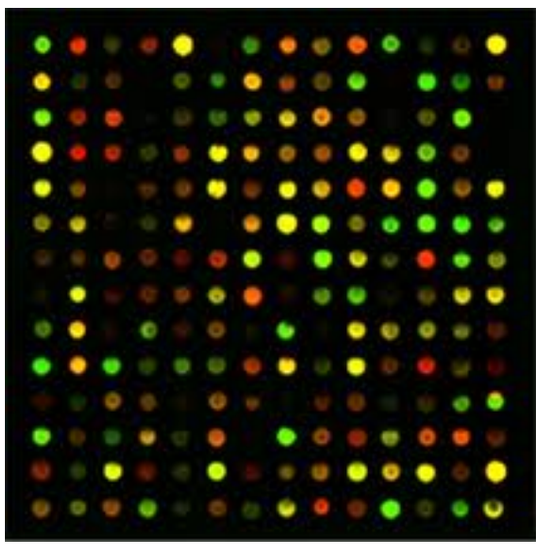
Microbiology

Immunology

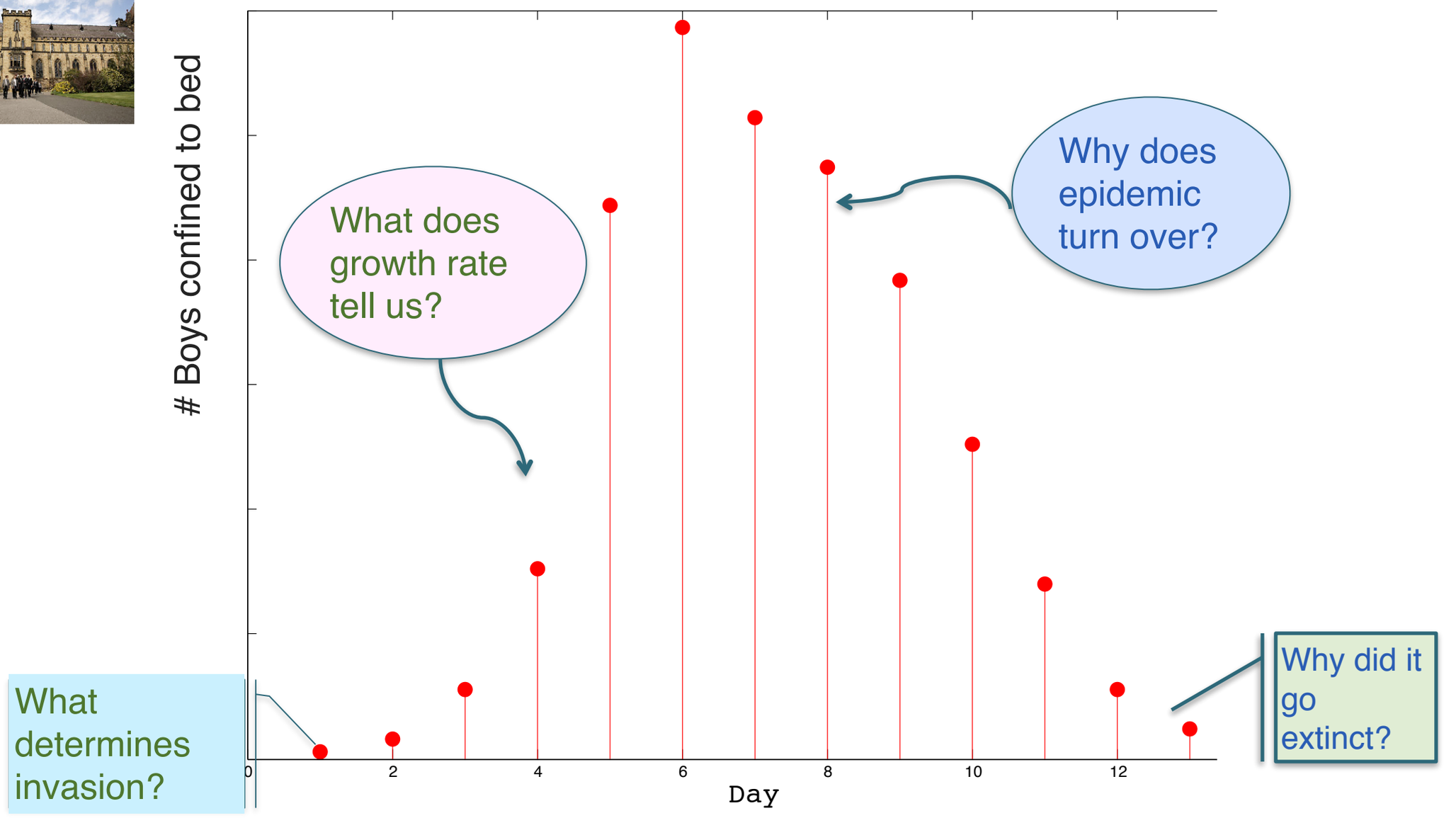


Vaccines & Drugs

Genomics



Modeling questions I. Basics

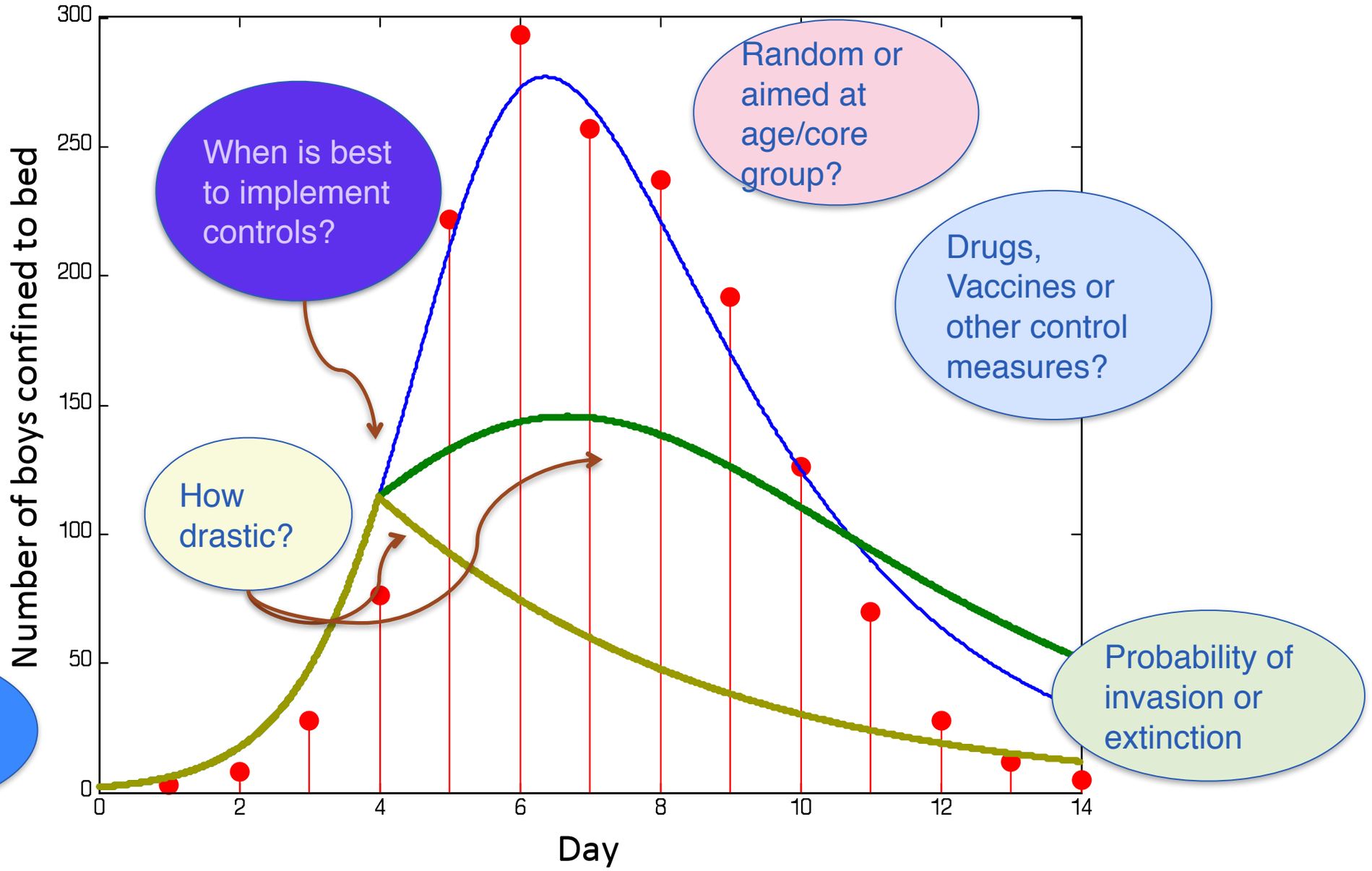


Modeling questions II. Control Implications

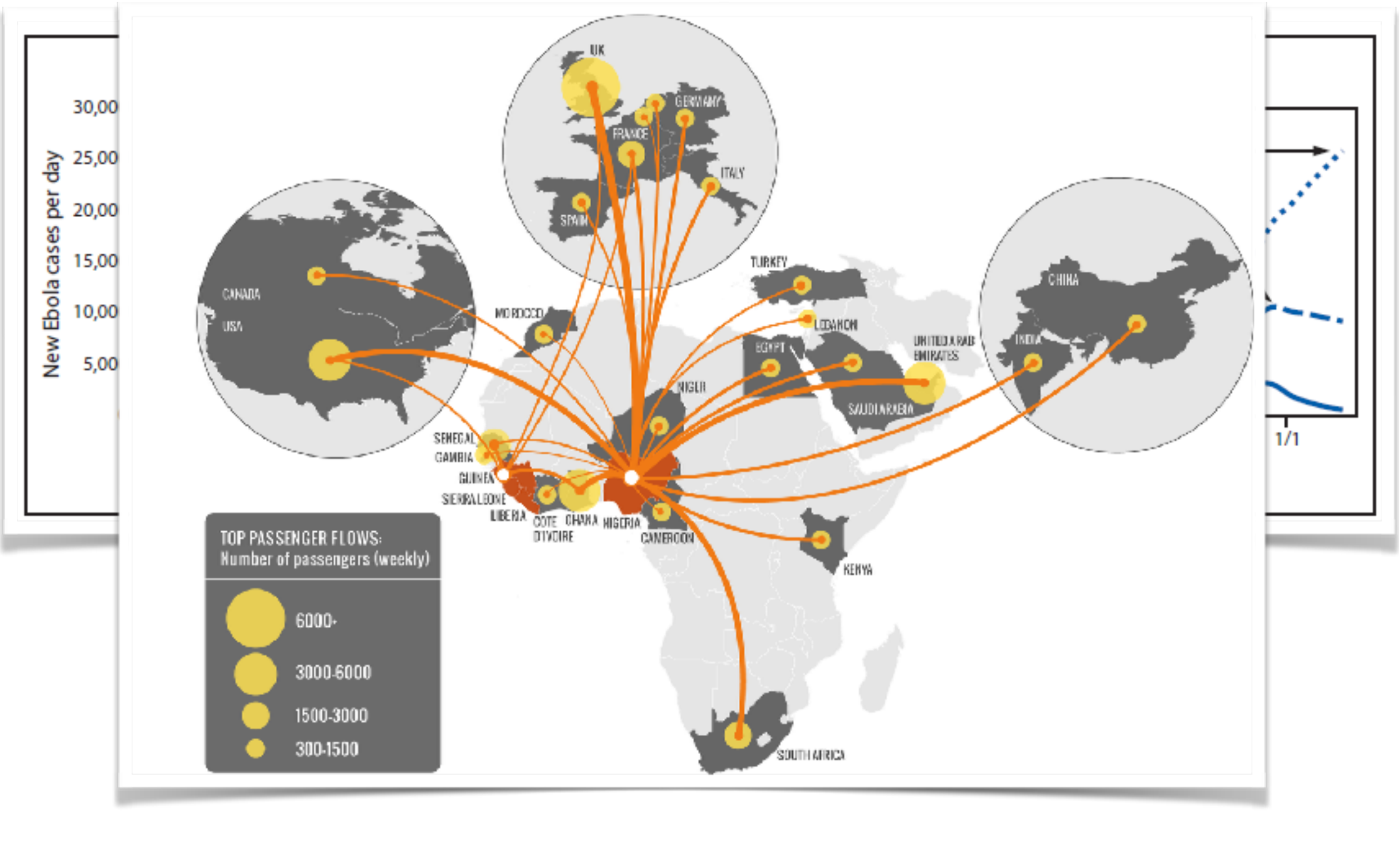
How to prevent spatial spread?

Is it evolving

How to prevent invasion/ reinvasion?



Emerging pathogens



What is a model?

- Different types of models:
  - A **mathematical/computational model** is an abstract model that uses mathematical language to describe behaviour of a system
  - A **Statistical model** attempts to describe relationships between observed quantities and independent variables

- Developing a mechanistic model is different from statistical analyses of data

Abstraction

Purpose

Components

Reality

Conceptualization

Abstraction

Interpretation

Assumptions

Limitations

Validation

What's a 'Good' Model?

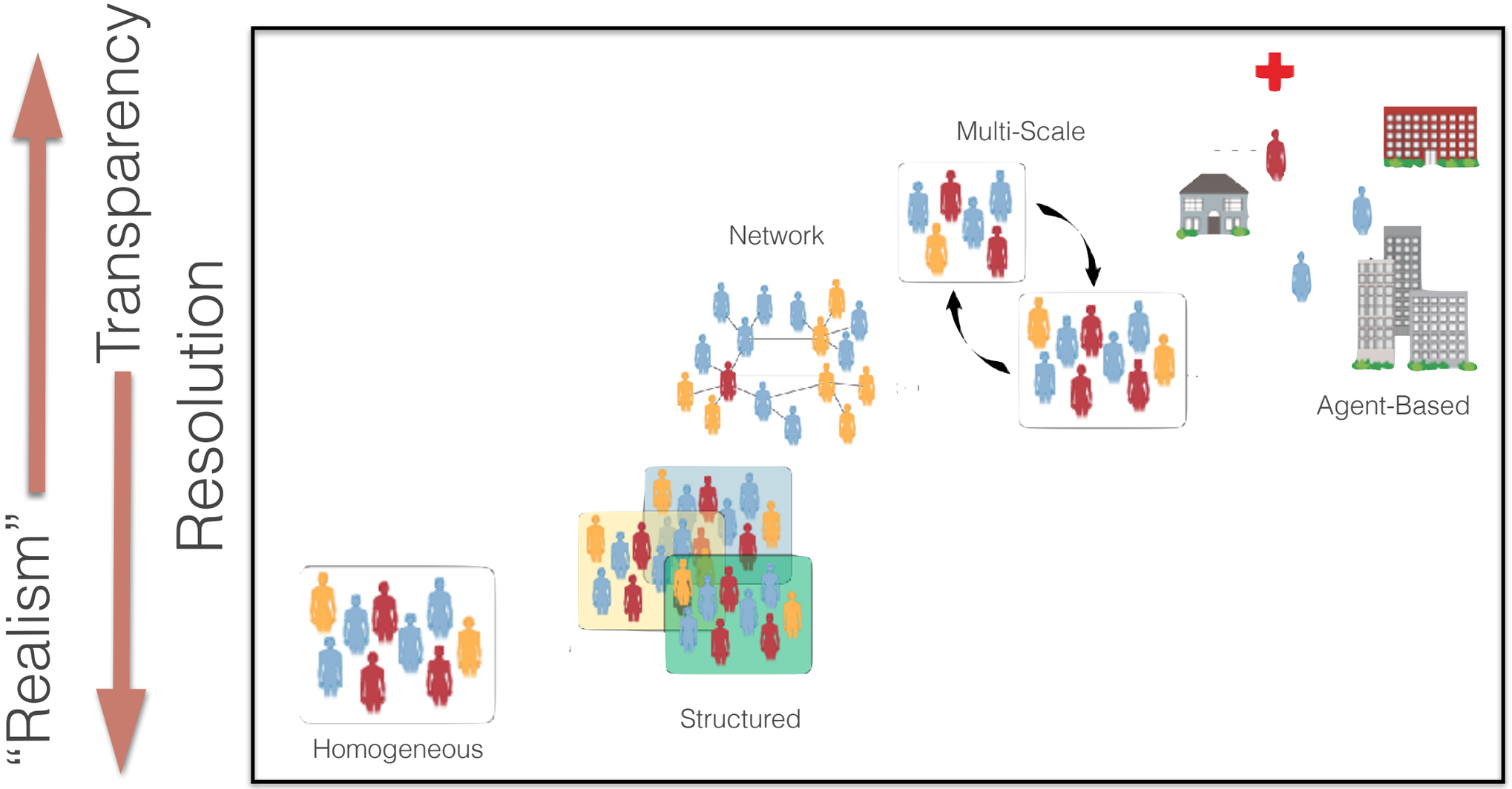
- Choice of model depends crucially on focal question and available data (hammer & chisel or pneumatic drill?)

- Use model principally for
  - understanding nature
  - making predictions

Judging a Model…

- Three fundamental features of models, often opposing forces:
  - **Accuracy**
    - Capture observed patterns (qualitative or quantitative?) and make predictions
    - Increases with model complexity
  - **Transparency**
    - Ability to understand model components
    - Decreases with model complexity
  - **Flexibility**
    - How easily can model be adapted to new scenarios?
    - Decreases with model complexity

Realism Vs Transparency



Solution tools

‘How’ do you Model?

Analytical Models

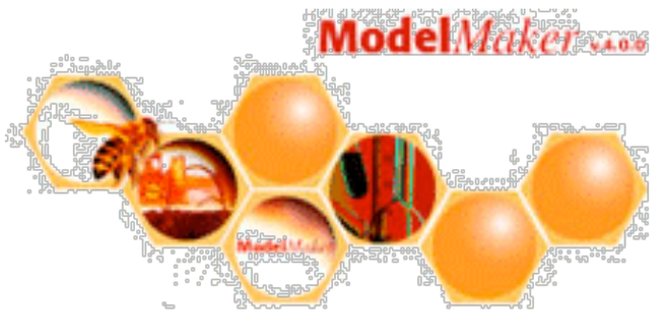
Concentrate on problems that can be expressed and analysed fully using analytical approaches

Problem-based Models

Construct most “appropriate” model and use whatever combination of methods for analysis and prediction

Ready-Made Software

ModelMaker



www.modelkinetix.com/modelmaker/modelmaker.html

Global simulators

Resource Materials

- Keeling & Rohani (2008)
- Vynnycky & White (2010)
- Anderson & May (1991)
- Otto & Day (2007)
- Diekmann et al. (2012)

Modelling Infectious Diseases

- **<u>Objective 1</u>:** Setting up simple models
  - Different transmission modes
    - Basic Reproduction Ratio (R_0), Simple Epidemics, Invasion threshold & extinction
  - Stability analysis

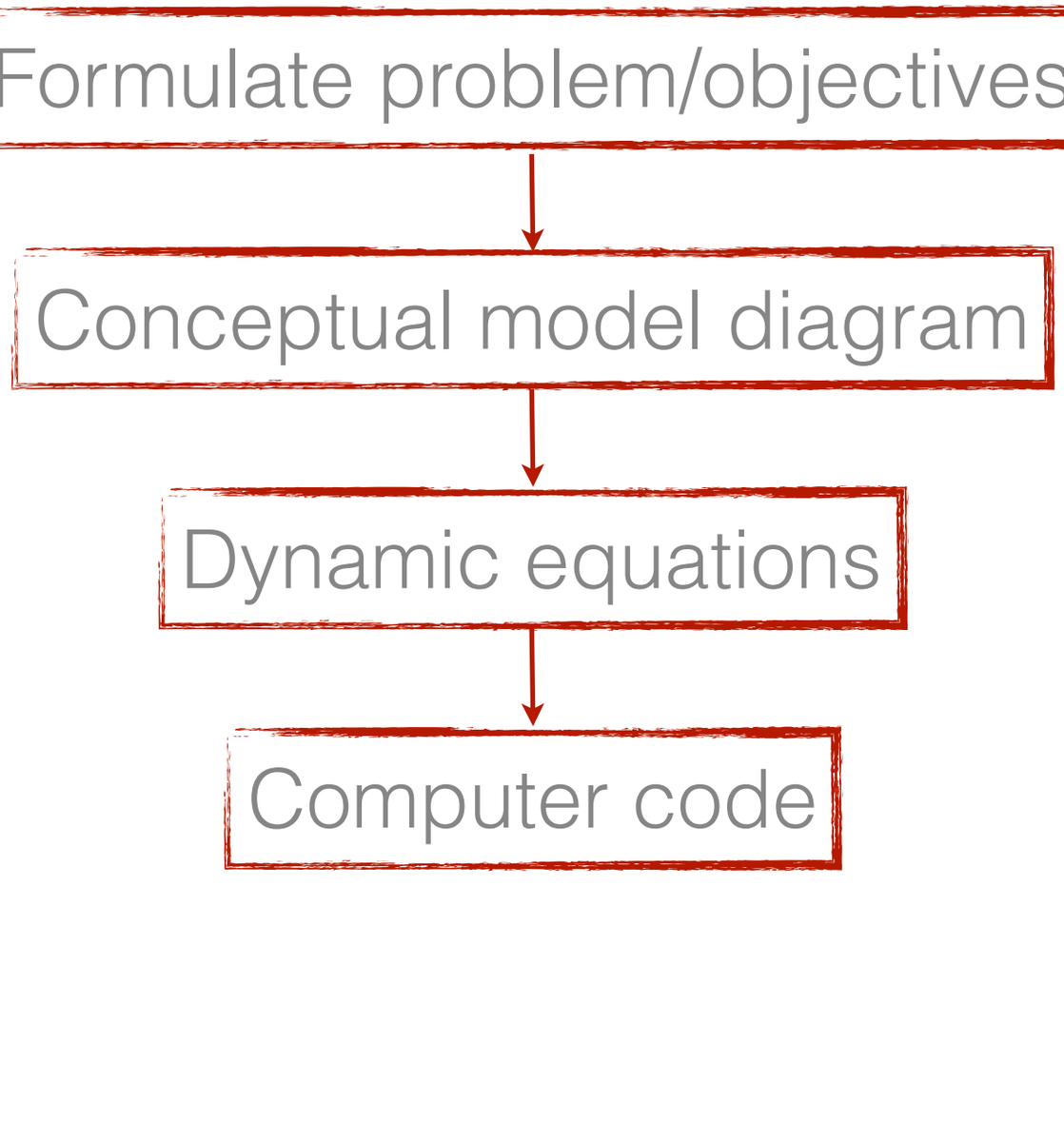
- **<u>Objective 2</u>:** Control
  - Infection management

- **<u>Objective 3</u>:** Statistical estimation
  - R_0 and other parameters

- **<u>Objective 4</u>:** Heterogeneities
  - Risk structure
  - Age-structured transmission
  - Realistic pathogenesis
  - Seasonality

- **<u>Objective 5</u>:** Sensitivity & Variability
  - Stochastic implementation
  - Parameter uncertainty

Steps in Developing a Model



The simplest models

- Let's develop a model for Boarding School influenza outbreak
- Some **important** choices need to be made at outset

1. **What do we want to keep track of?**
   - Amount of *virus* in population?
   - *Antibody titre* of everyone in population (school)?
   - *Cities* in which infected people have been found?

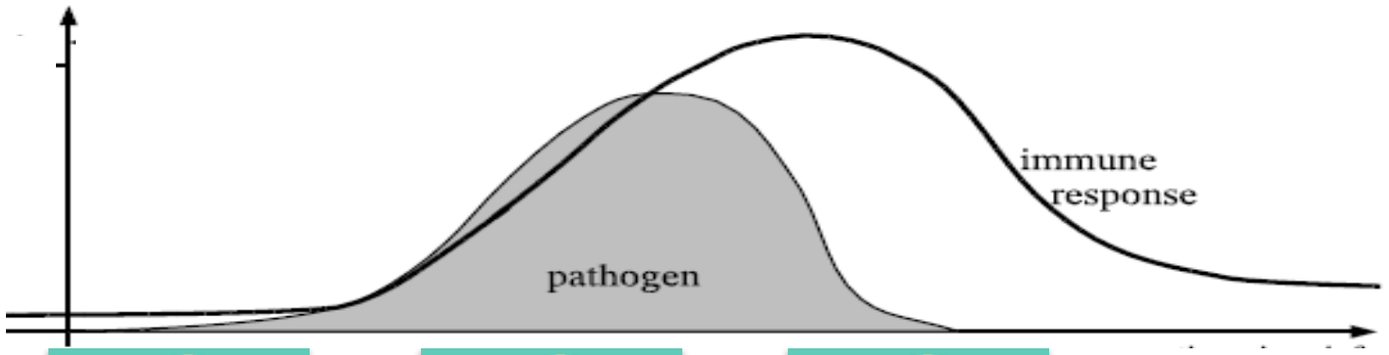
Categorising individuals

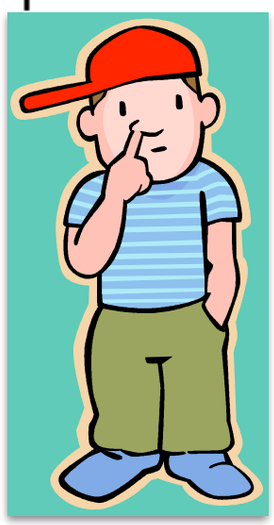
Healthy — Incubating — Diseased

Clinical status

Susceptible — Exposed/latent — Infectious — Recovered/Immune

Infection status





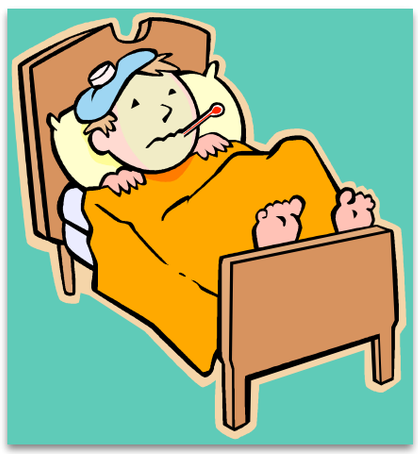
Incubating

Infectious,

latent

Infectious,

symptomatic



Infectious,

quarantined

The simplest models

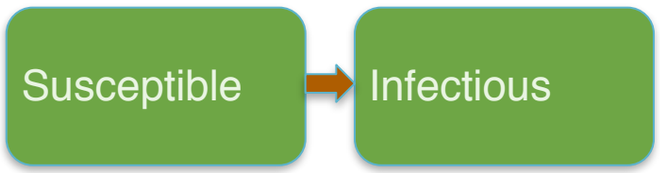
- Pragmatic choice: categorise individuals in population according to their infection status, eg:
  - Susceptible
  - Infectious
  - Recovered/Immune

These are our "system variables"

The simplest models

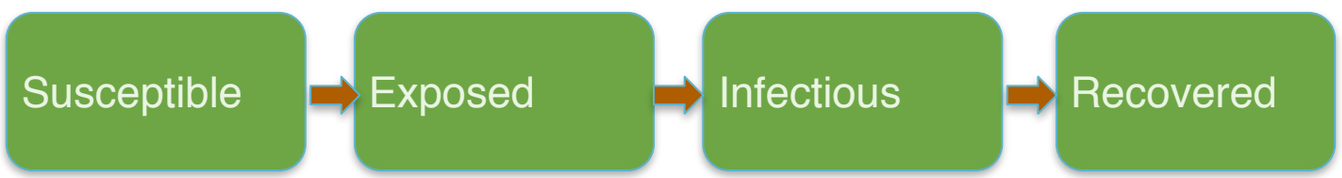
2. **What model structure?**

   -- Determined by pathogen biology

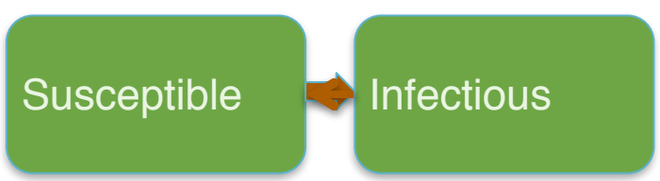


SI – signifies fatal infection

SIR – recovery after infection



SEIR – latency

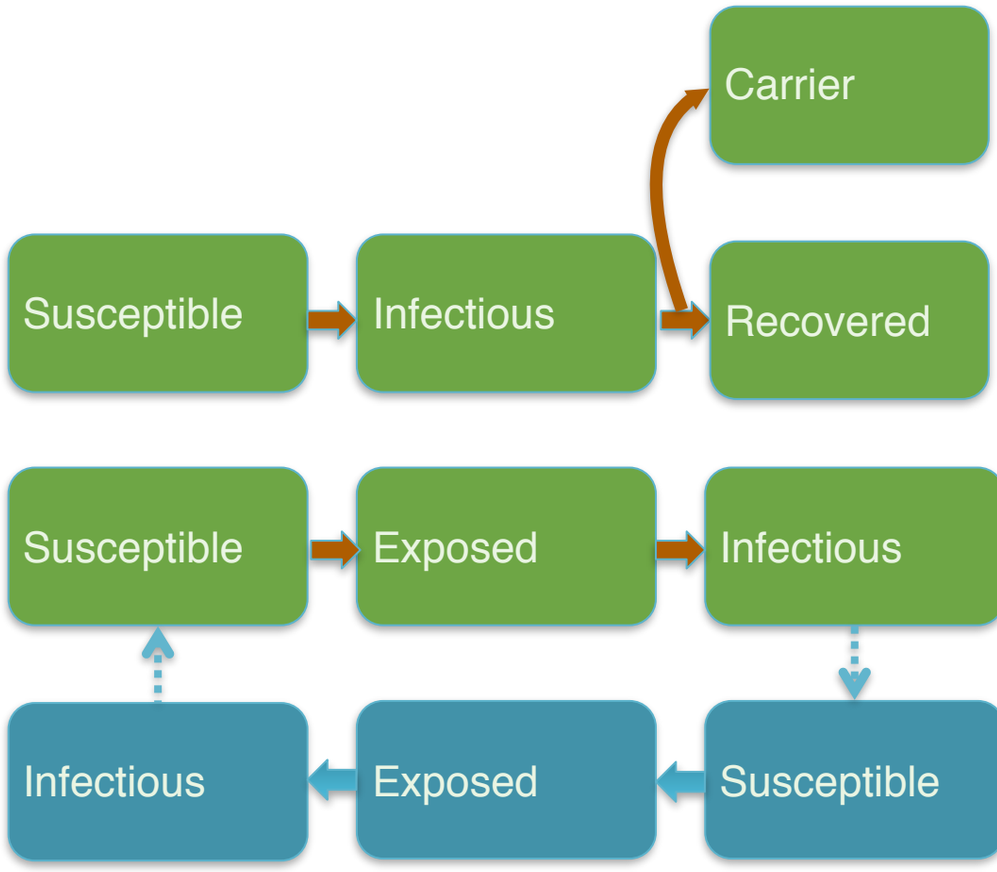


SIS – no immunity elicited

The simplest models

2. **What model structure?**

   -- Determined by pathogen biology



SIR – with carriers

Vectored transmission

The simplest 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)

The simplest models

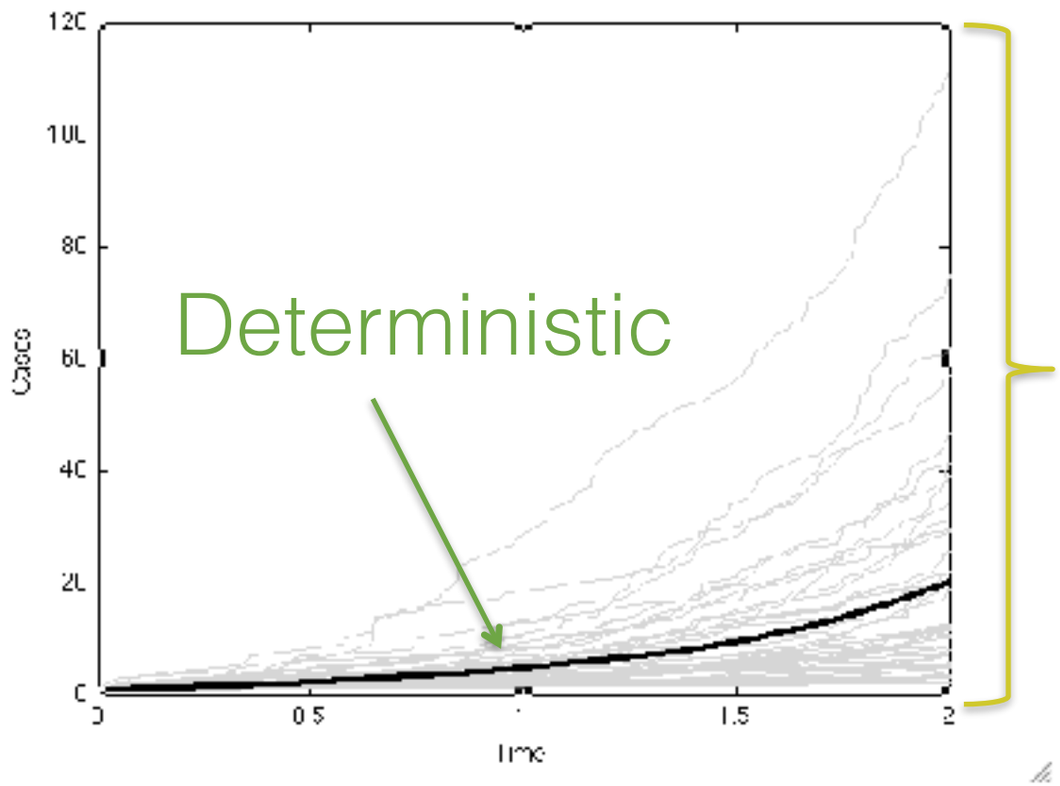
- Flow between classes/compartments determined by details of host population structure and pathogen biology

- Host population size
- Contact rates
- Pathogen infectivity

These are our "parameters"

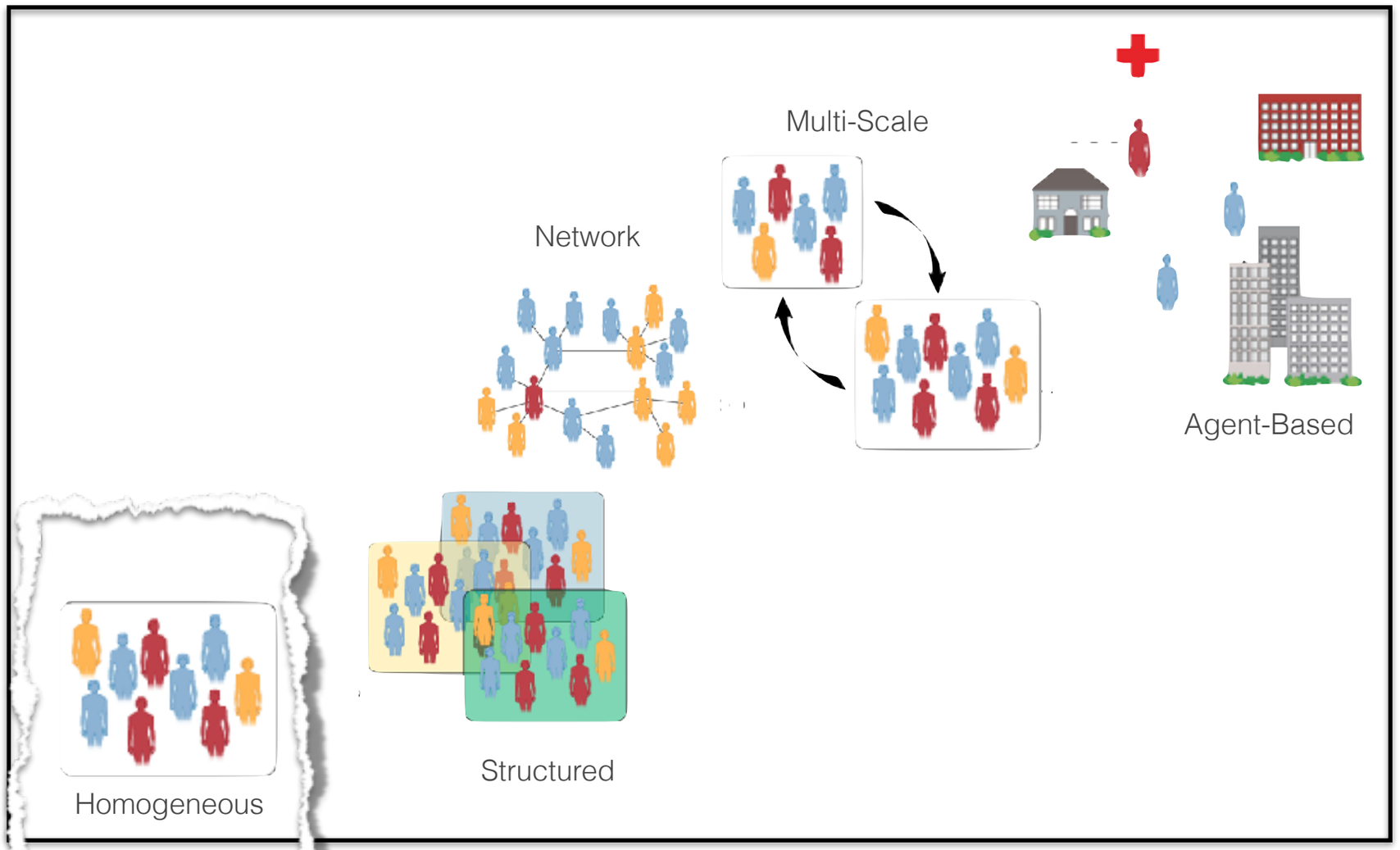
The simplest models

- **Deterministic or Stochastic?**



On average, stochastic simulations identical to deterministic predictions, though individual realizations may be quite different

Realism Vs Transparency



Solution tools

The simplest models

- We've settled on a deterministic SIR model – now what?
- How do we write down some equations to describe spread of 'flu in this population?
  - Assign each system variable a unique Roman letter, eg:
    - Susceptible, S (proportion) or X (number)
    - Infectious, I (proportion) or Y (number)
    - Recovered/Immune, R (proportion) or Z (number)
  - Assign parameters a unique (typically Greek) letter, eg:
    - Contact rate, κ
    - Pathogen infectivity, ν

Very important!

- NOTHING SPECIAL ABOUT MY CHOICE OF NOTATION – USE OF PARTICULAR LETTERS HIGHLY IDIOSYNCRATIC

- OTHER AUTHORS MAY USE DIFFERENT LETTERS TO DENOTE SAME VARIABLES OR PARAMETERS.

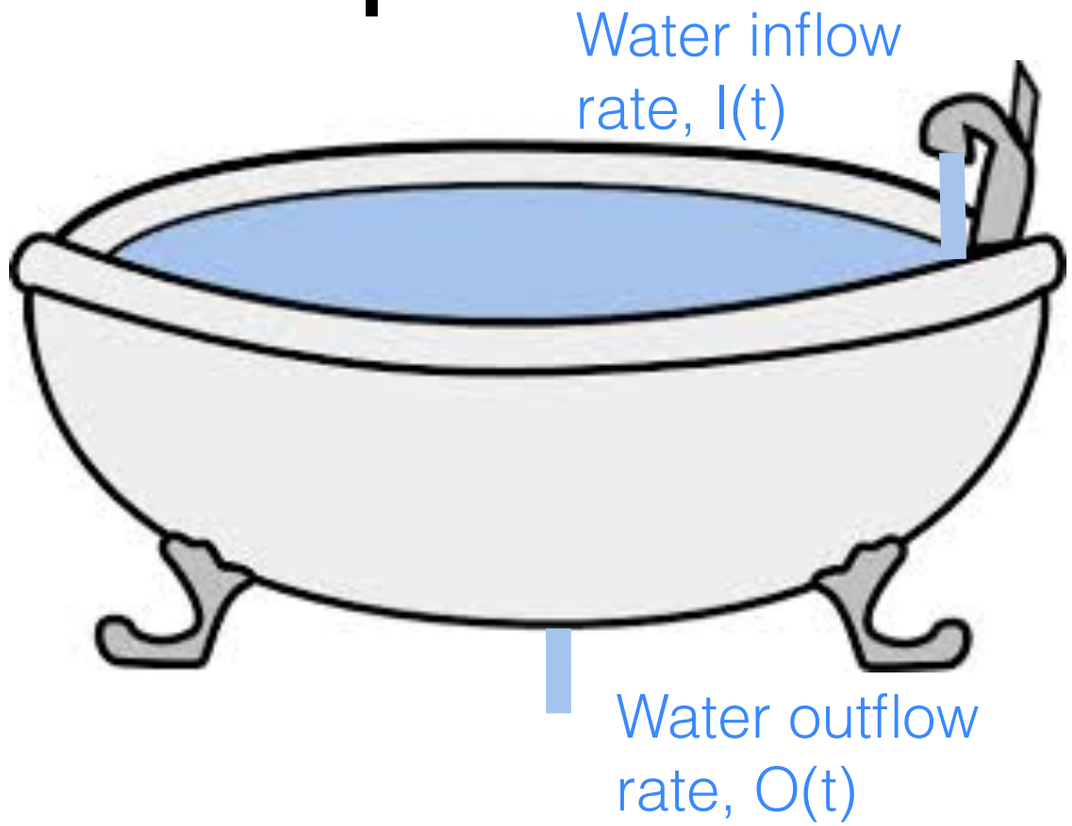
- YOU CANNOT AUTOMATICALLY ASSUME THAT β IN TWO DIFFERENT PAPERS MEANS THE SAME THING!

3. Model equations

Bath tub example

- Let W(t) be amount of water in bathtub (ml)

- Need a <u>dynamic equation</u> that tells us how W(t) will change through time



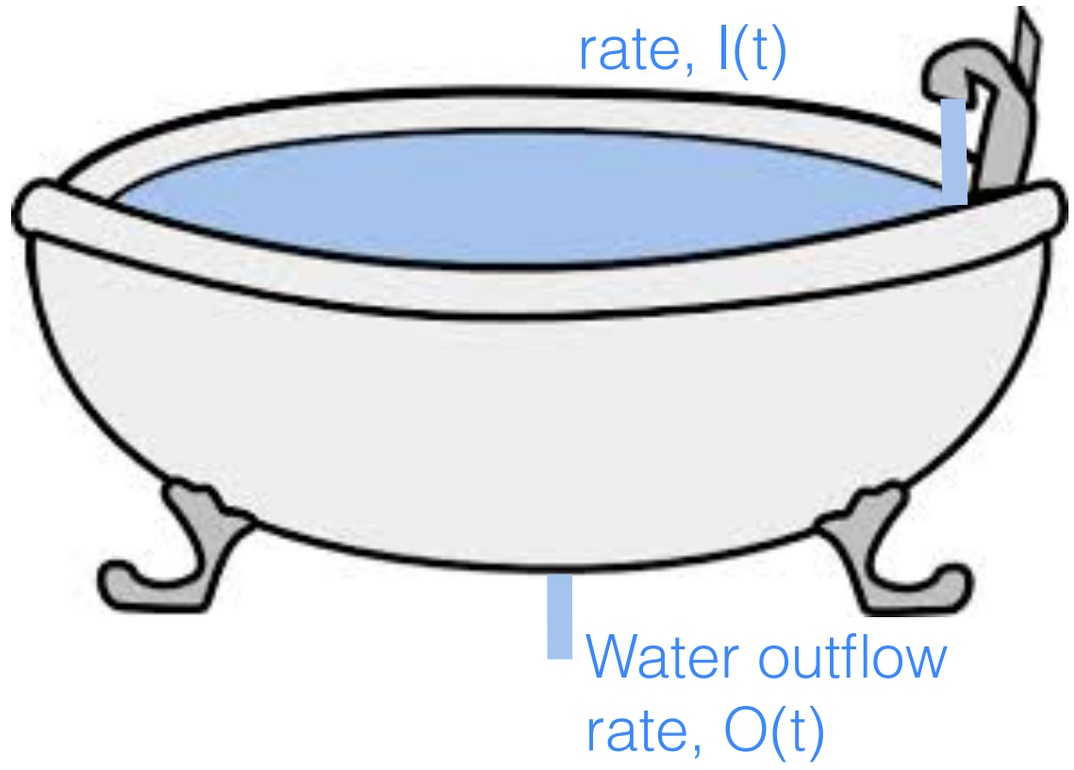
* Consider a small time interval, δt

* Then,

  W(t+ δt) = W(t) + Inflow rate × elapsed time - Outflow rate × elapsed time

Bath tub example

$$W(t+\delta t) = W(t) + I \times \delta t - O \times \delta t$$



* Rearrange

$$\frac{W(t+\delta t) - W(t)}{\delta t} = I - O$$

* Left hand side is a difference quotient for derivative of W with respect to time

* Let δt → 0

$$\frac{dW}{dt} = I - O$$

Many Linked bath tubs

= compartment models

Model equations

- If we knew X_t and Y_t, could we predict $X_{t+\delta t}$ and $Y_{t+\delta t}$, where δt is some (very short) time later?

$$X_{t+\delta t} = X_t - \text{Transmission}$$

$$Y_{t+\delta t} = Y_t + \text{Transmission}$$

- Transmission rate per susceptible $\propto$ Contacts x P(Infectious) x P(Transmission)

$$= \kappa \times \delta t \times \frac{Y_t}{N} \times \nu$$

$$= \kappa\nu \frac{Y_t}{N}$$

$$= \beta \frac{Y_t}{N}$$

Model equations

- If we knew X_t and Y_t, could we predict $X_{t+\delta t}$ and $Y_{t+\delta t}$, where δt is some (very short) time later?

$$X_{t+\delta t} = X_t - X_t (\beta\ \delta t)\ Y_t/N$$

$$Y_{t+\delta t} = Y_t + X_t (\beta\ \delta t)\ Y_t/N - \text{Recovery}$$

- Recovery assumed at constant rate, γ

Basic questions?

$\beta = \nu\kappa$

$$X_{t+\delta t} = X_t - (\beta\ \delta t)\ X_t\ Y_t/N$$

$$Y_{t+\delta t} = Y_t + (\beta\ \delta t)\ X_t\ Y_t/N - (\gamma\ \delta t)\ Y_t$$

$$Z_{t+\delta t} = Z_t + (\gamma\ \delta t)\ Y_t$$

- Average infectious period given by $1/\gamma$ [why?]

Mean life time calculation

Consider recovery of a single infectious individual: $I(t) = e^{-\gamma t}$

$$1 = \int_o^\infty ce^{-\gamma t}dt \quad = \frac{c}{\gamma}$$

Hence, probability density function is $\gamma e^{-\gamma t}$

$$\tau = \int_0^\infty t\gamma e^{-\gamma t}dt \; = \frac{1}{\gamma}$$

For a random variable x, with probability density function f(x), the mean is given by $\int_0^\infty xf(x)dx$

An ODE model

- Consider equation describing Susceptible dynamics

$$X_{t+\delta t} = X_t - (\beta\, \delta t)\, X_t\, Y_t/N$$

- Re-write as

$$X_{t+\delta t} - X_t = -(\beta\, \delta t)\, X_t\, Y_t/N$$

$$(X_{t+\delta t} - X_t)/\, \delta t = \beta\, X_t\, Y_t/N$$

By fundamental theorem of calculus, as $\delta t \rightarrow 0$,

$$dX/dt = -\beta\, X\, Y/N$$

An ODE SIR model

$$\frac{dX}{dt} = -\beta X \frac{Y}{N}$$

$$\frac{dY}{dt} = \beta X \frac{Y}{N} - \gamma Y$$

$$\frac{dZ}{dt} = \gamma Y$$

- By definition, X+Y+Z = N
- These equations describe rates of change in state variables
- Parameters β, γ represent instantaneous rates

An ODE SIR model

$$\frac{dX}{} \qquad Y$$

In my lectures (as in K&R 2008), variables X, Y & Z refer to the numbers of individuals in each class. Variables S, I, & R refer to the proportions of the population in each class

- These equations describe rates of change in state variables
- Parameters β, γ represent instantaneous rates

An ODE SIR model

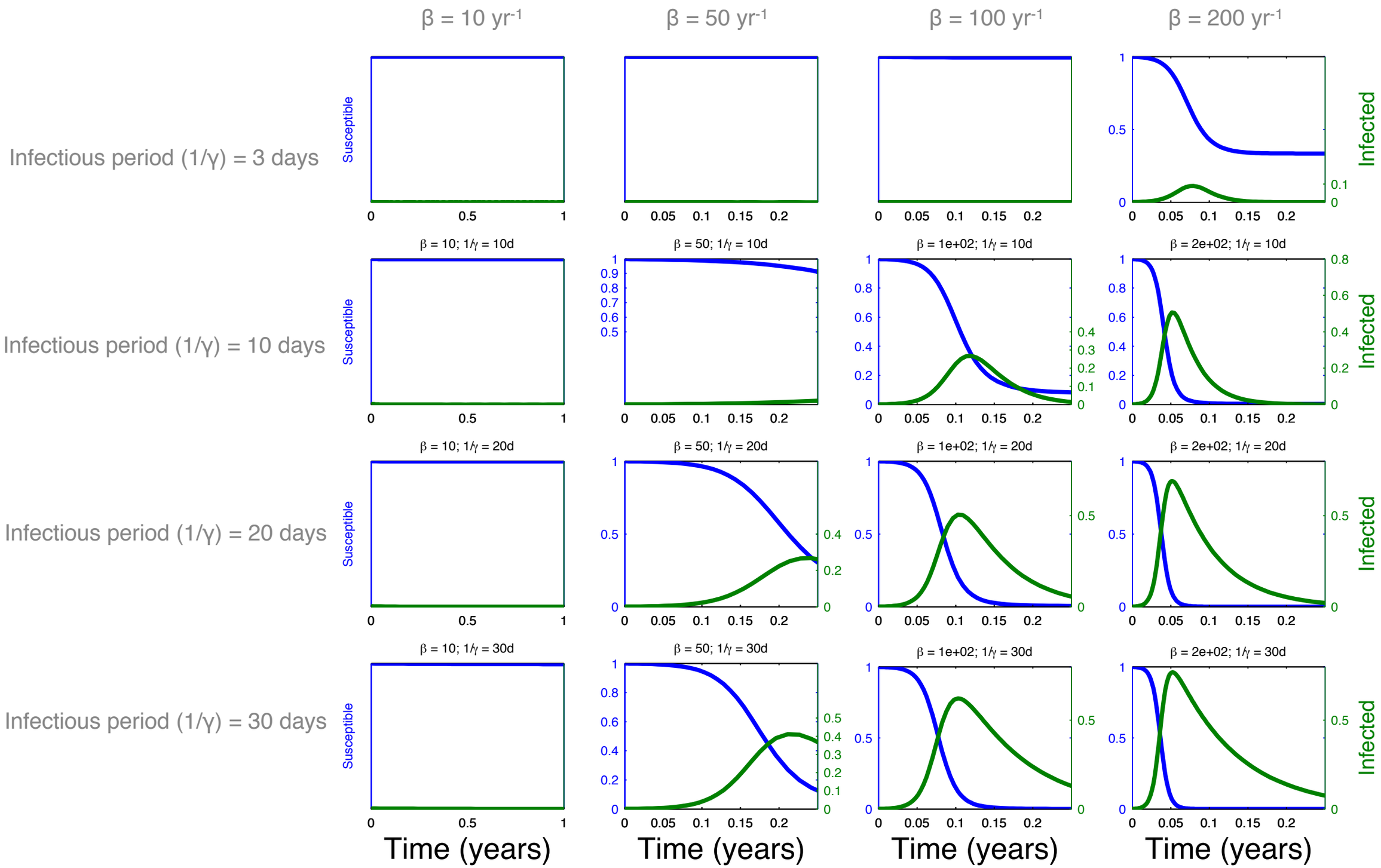
$$\frac{dX}{dt} = -\beta X \frac{Y}{N}$$

$$\frac{dY}{dt} = \beta X \frac{Y}{N} - \gamma Y$$

$$\frac{dZ}{dt} = \gamma Y$$

- Important to notice: transmission rate is assumed to depend on frequency of infecteds in population (Y/N). Hence, this is frequency-dependent transmission

Simulating epidemics



Model dynamics

- As parameters are varied, model predicts different outcomes

- Can we anticipate trajectories without resorting to numerical integration?

- Question: under what conditions will an infectious disease invade a system?

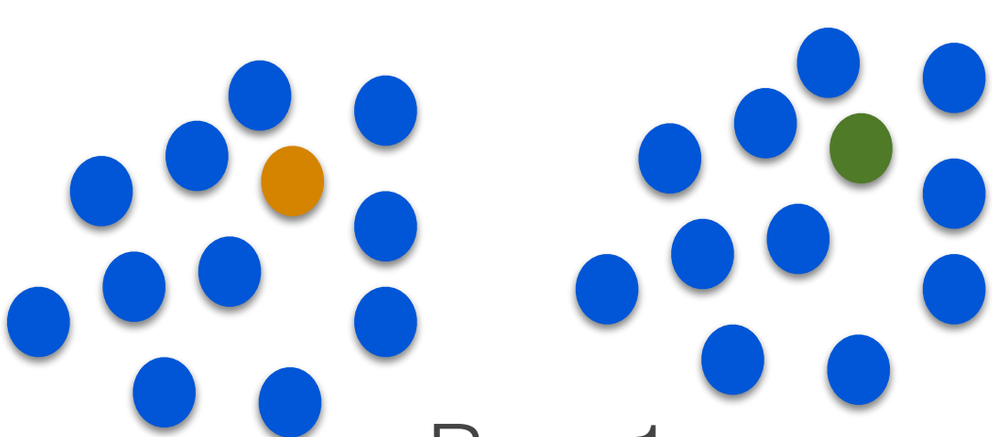
The Invasion Threshold

- When can an infectious disease invade a population?
- Initial conditions: $X(0) = N$, $Y(0) = 1$, $Z(0) = 0$
- Invasion only if $dY/dt > 0$
- ie, $\beta XY/N - \gamma Y > 0 \quad \Rightarrow Y(\beta X/N - \gamma) > 0$
  - If and only if $X/N > \gamma/\beta$
  - Since $X=N$, requires $1 > \gamma/\beta$
  - Or $\beta/\gamma > 1$

Kermack & McKendrick (1927)

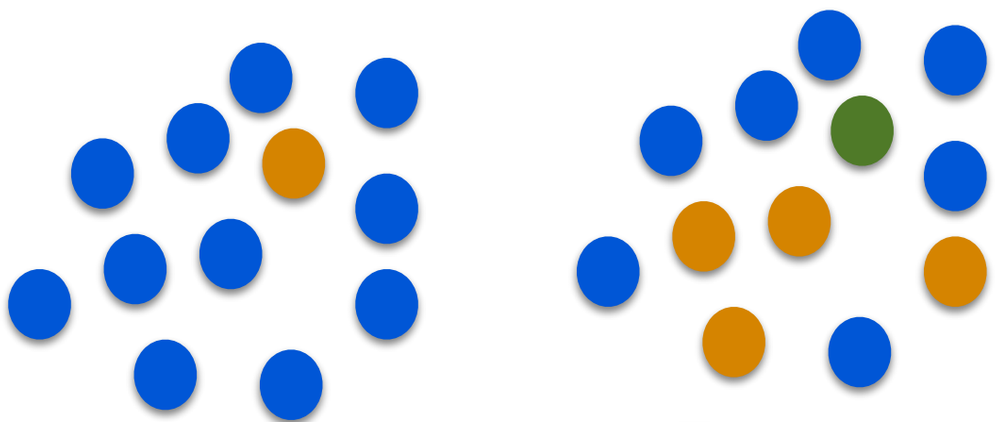
Basic Reproductive Ratio, R_0

- Ratio β/γ gives number of cases before infected individual recovers
- Universally referred to as R_0 or **Basic Reproductive Ratio**
- Definition: Number of secondary cases generated by a typical infected in an entirely susceptible population



$R_0 < 1$

No invasion



$R_0 = 4$

Successful invasion

R_0 and Model parameters