EEB C119B / C219B:
Mathematical and computational modeling in ecology

What can models do? What can we do with models?

(Five models for HIV dynamics)

and

Formulating a model – decisions you will have to make.

Prof. Jamie Lloyd-Smith

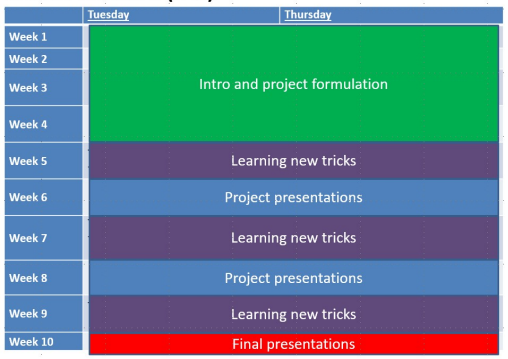
Logistics

- Continue meeting in this class until we decide otherwise
- Complete Ana's survey about discussion sections ASAP
  - https://acrgomez.github.io/EEBC119B_C219B/

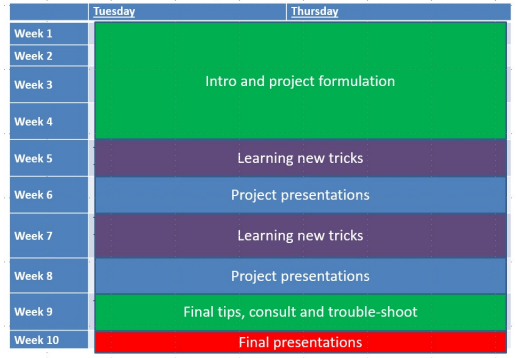
- Maddi and Gaurav leading a free Software Carpentry workshop on scientific computing, Jan 18-19
  - Must register to attend!
  - https://ucla-hacky-hours.gitlab.io/2020-01-18-SWC/

Time to vote:

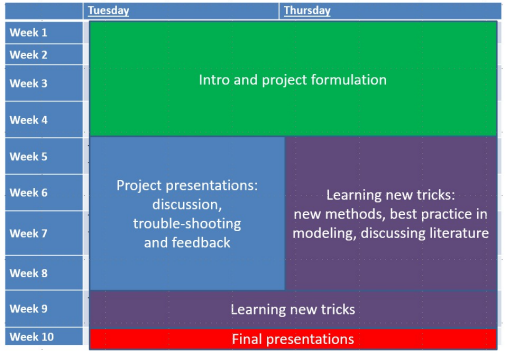
Course schedule (v1a)



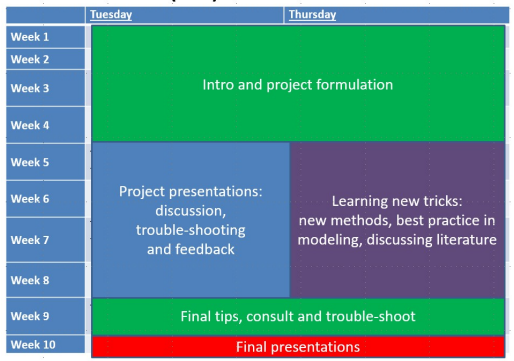
Course schedule (v1b)



Course schedule (v2a)



Course schedule (v2b)



Either way, you will present your project work twice in weeks 5-8, and briefly present a paper once in weeks 5-9.

Why bother with modelling?

(Ellner & Guckenheimer 2006)

1. Scientific understanding
   - Can processes A and B account for pattern C?
   - Which processes match the data best?
   - What other patterns might we expect?
2. Using our scientific understanding to manage the world
   - Optimizing interventions, harvesting, etc
3. Experiments are small, the world is big
   - Large-scale implications of small-scale data collection (!!)
4. There are experiments you would rather not do
   - Model analysis is better than guesswork
5. The curse of dimensionality
   - Model-guided fieldwork or experimentation

Types of models (Ellner & Guckenheimer 2006)

Practical Models	Theoretical Models
Main goals are management, design, and prediction	Main goals are theoretical understanding and theory development
Numerical accuracy is desirable, even at the expense of simplicity	Numerical accuracy is not essential; the model should be as simple as possible
Processes and details can be ignored only if they are numerically unimportant	Processes and details can be ignored if they are conceptually irrelevant to the theoretical issues
Assumptions are quantitative representations of system processes	Assumptions may be qualitative representations of hypotheses about the system, adopted conditionally in order to work out their consequences
System and question specific	Applies to a range of similar systems

Theoretical models are also called ‘toy models’, ‘strategic models’ or ‘conceptual models’.

Why do we model infectious diseases?

Following Heesterbeek & Roberts (1995)

1. Gain insight into mechanisms influencing disease spread, and link individual scale 'clinical' knowledge with population-scale patterns.
2. Focus thinking: model formulation forces clear statement of assumptions, hypotheses.
3. Derive new insights and hypotheses from mathematical analysis or simulation.
4. Establish relative importance of different processes and parameters, to focus research or management effort.
5. Thought experiments and "what if" questions, since real experiments are often logistically or ethically impossible.
6. Explore management options.

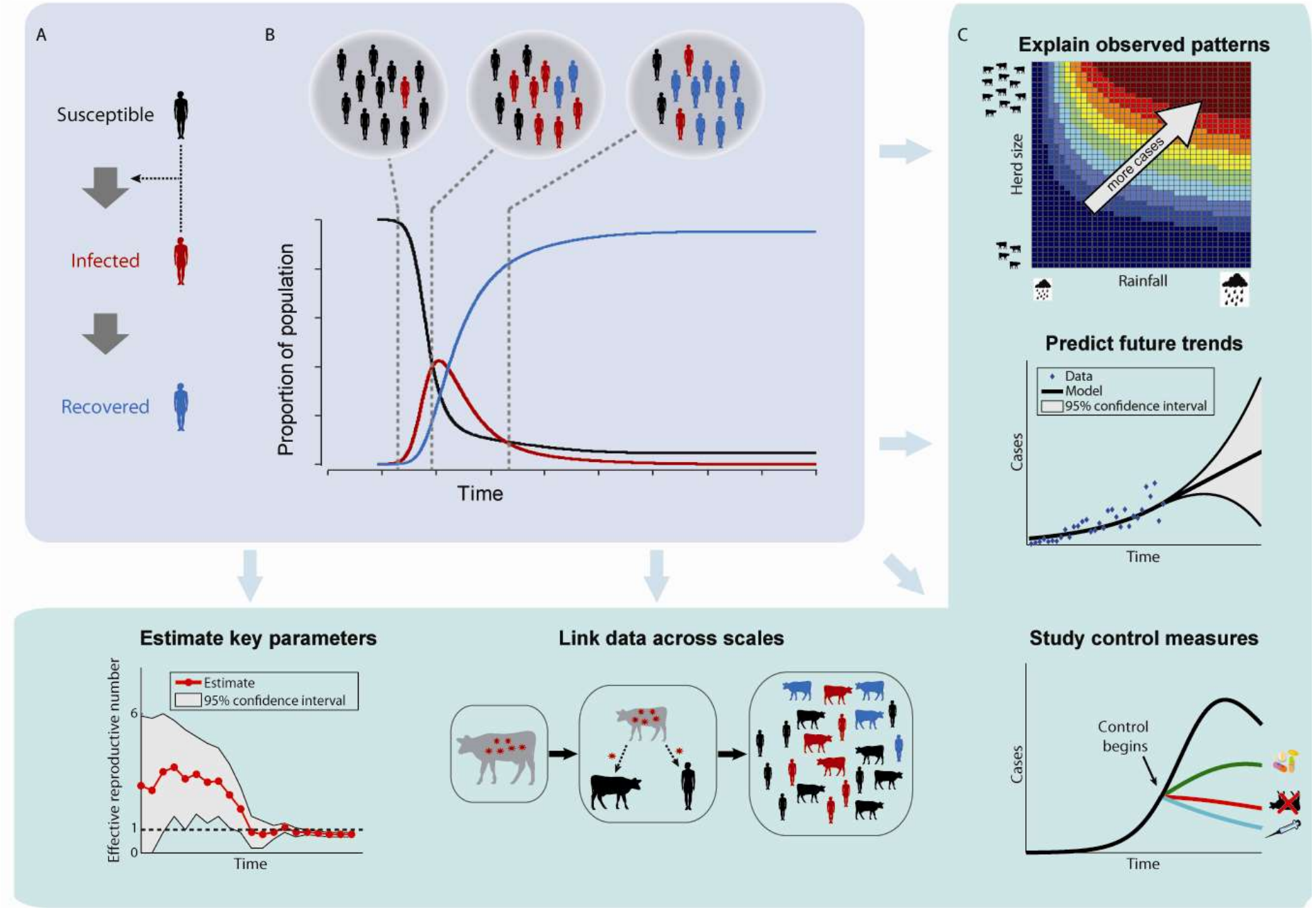
*Note the absence of prediction. Models are highly simplified representations of very complex systems, and parameter values are difficult to estimate. → quantitative predictions are very difficult.

Though in last decade, model-based forecasting has become a hot field.

Types of models (JLS, this morning…)

- Proof-of-concept toy models
  - “Could this pattern be explained by these mechanisms?”
- Theoretical analyses of specific questions
  - “Here’s how we think this system works, what are the consequences for XX?”
- Models to integrate knowledge across disciplines or scales
  - “If temperature impacts tree growth of species AA like XX, and species AA and BB compete like YY, then forest composition will change like ZZ under climate change…”
- Models as frameworks to extract insights from data
  - “What is the likelihood of these observations given our hypotheses about data-generating mechanisms?”
- Models for explicit prediction
  - “If this model represents the system accurately, what will happen under this future scenario…?”

Modeling the population dynamics of epidemics



Approaches to including models in your work

Models can play various roles in scientific studies.

Published papers can:

- present a model to address a question, and analyze it
- center on one question, and use several overlapping/complementary models to address it
- present a model analysis, with a bit of data that demonstrates relevance to real world
- present empirical work, with a modeling analysis added to generalize or interpret the findings.
- present empirical work/data, and use model to analyze or draw more insights from it.

Any of these, or many other models, are suitable modeling projects for this course.

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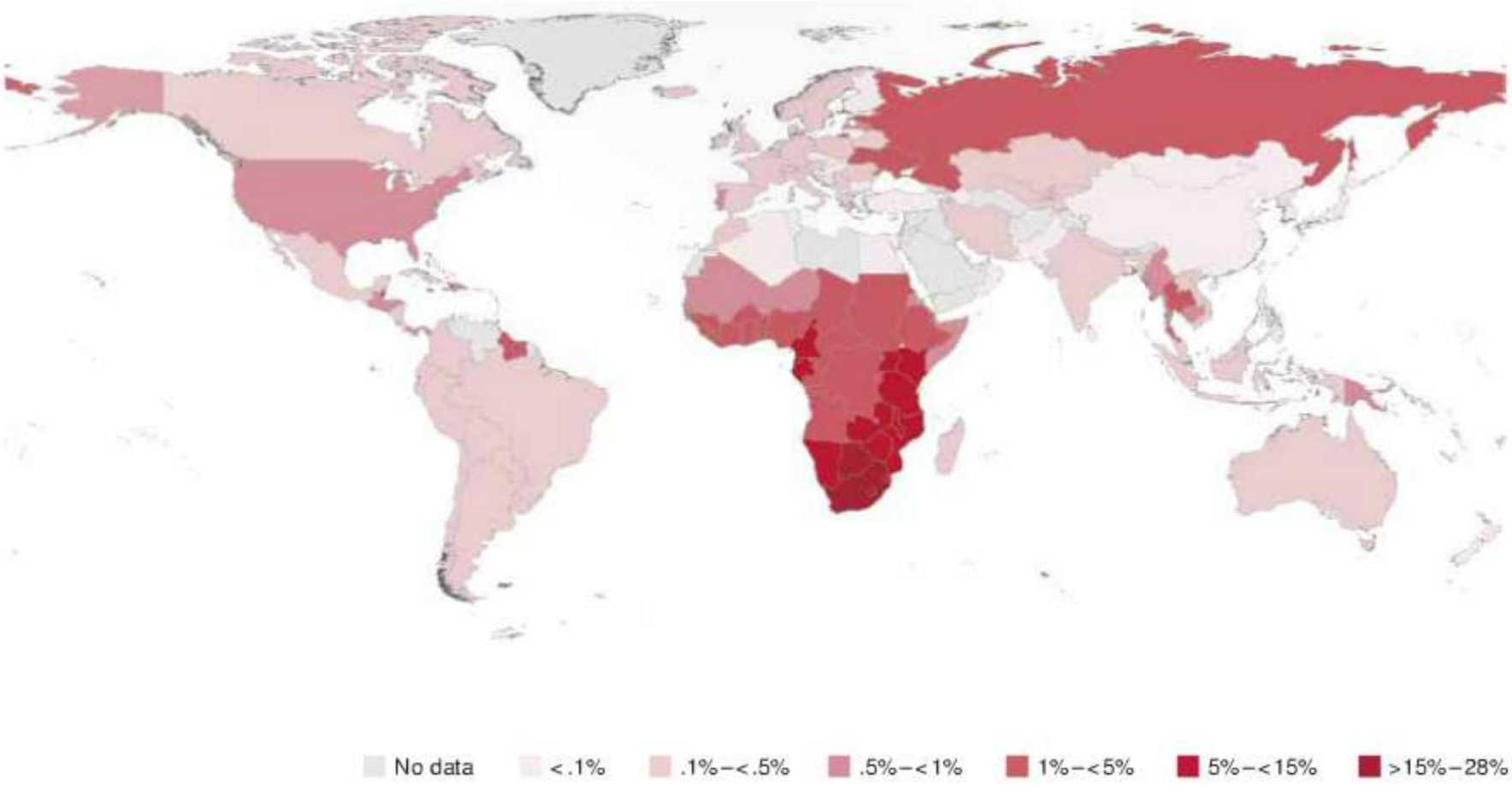
Five models for HIV dynamics

Prof. Jamie Lloyd-Smith

Global prevalence of HIV, 2012



Source: UNAIDS.

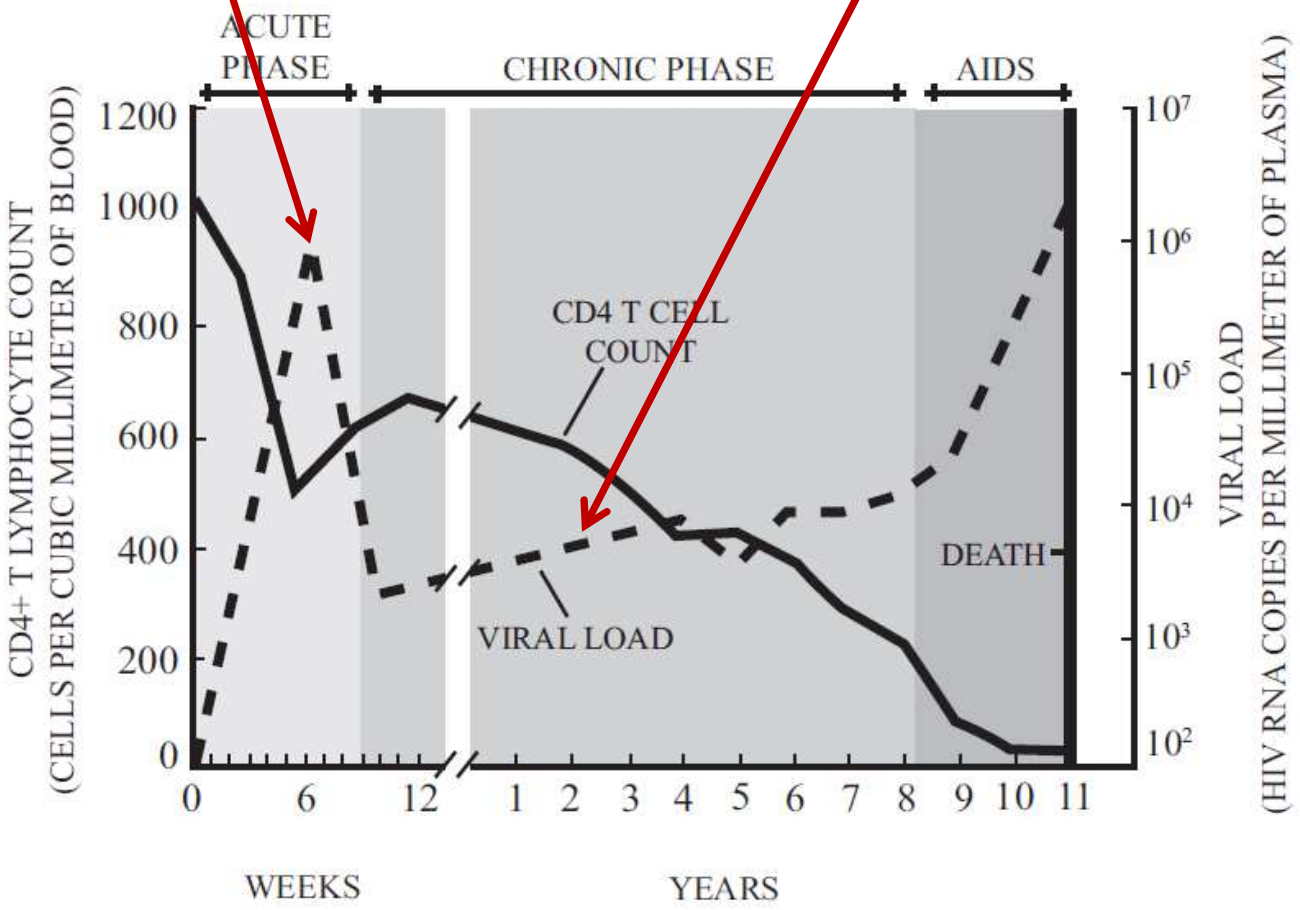
World Health Organization

UNAIDS

HIV progression within an infected person

What causes this peak?
(why does viral load go down?)

What's going on during this long flat period?



Model 1. Why does viral load peak?

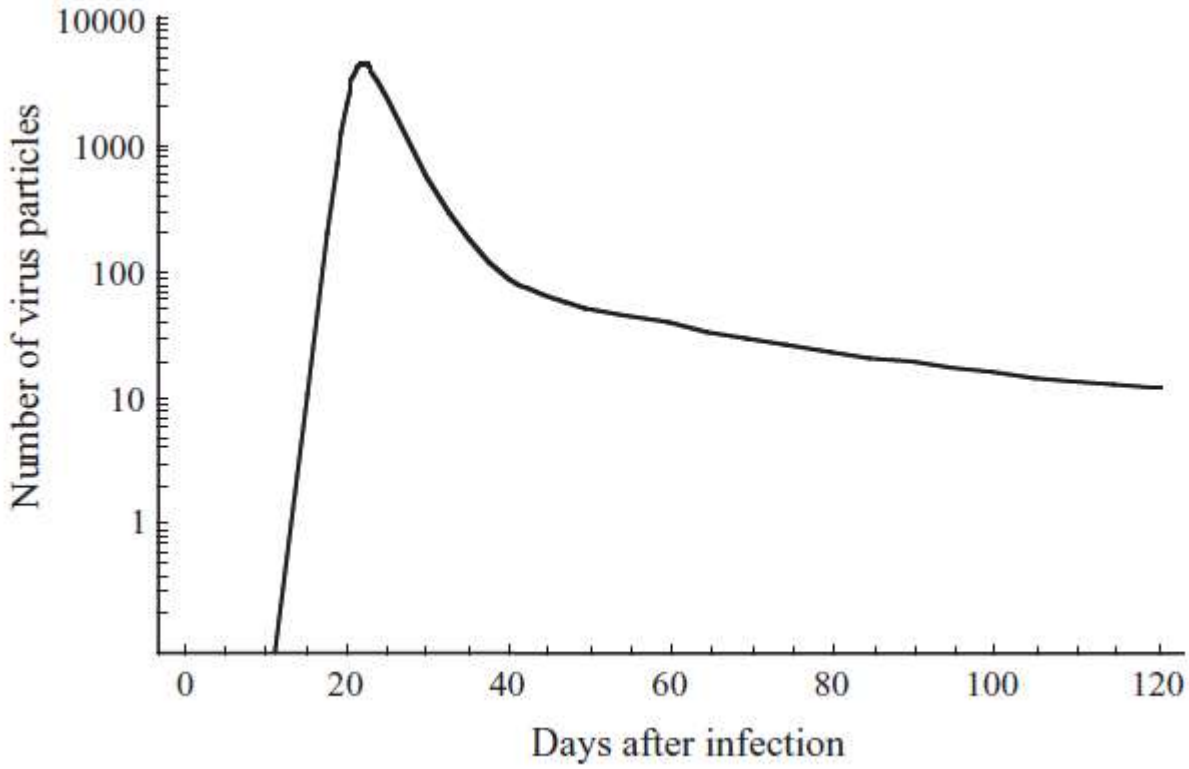
Important question when HIV was first discovered.

Obvious answer: immune system learns to recognize virus and fight it off.

Alternative idea: maybe the virus runs out of CD4 cells to infect?

Phillips (1996) made a model tracking the number of uninfected and infected CD4 cells – essentially an “epidemic” of infection within an individual host.

Model 1. Why does viral load peak?



Showed that you can get a viral load peak due only to the depletion of CD4 cells – no need to invoke immune response.

(Principle of parsimony)

Model 2. What's happening during "set-point" phase

Viral load is ~ constant for 8-10 years.

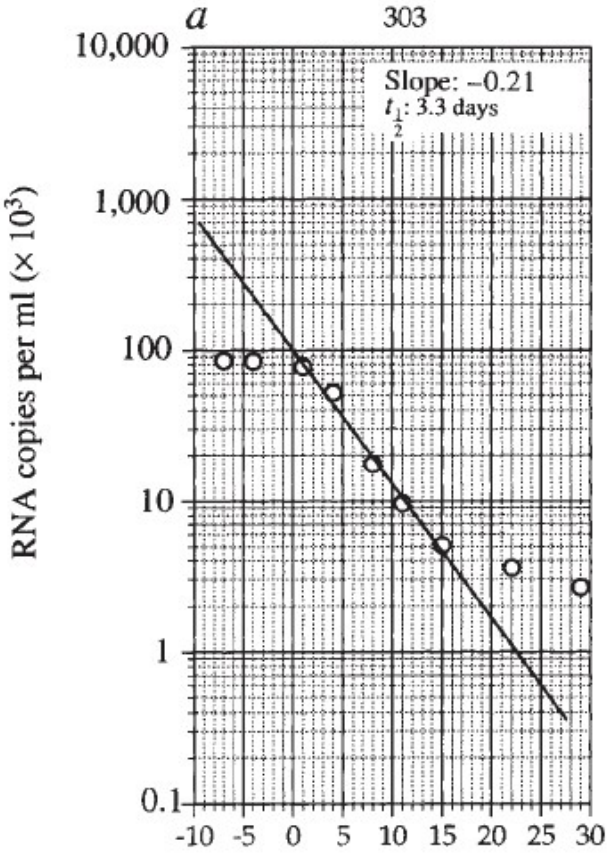
Obvious explanation: Looks like not much is happening. Maybe virus-infected cells live a long time, turn over very slowly.

Ho et al (1995) did experiments where they treated HIV patients with an antiviral drug and measured changes in viral load afterward.

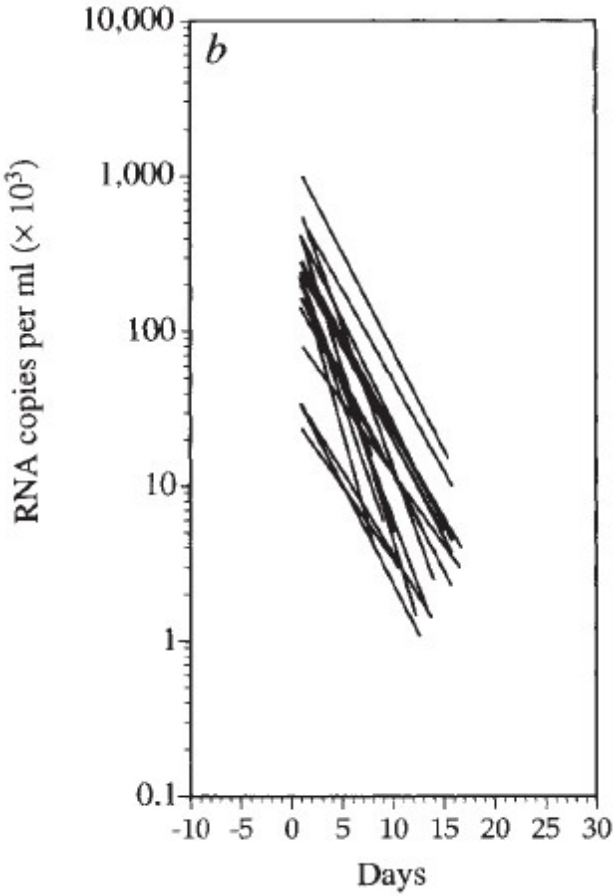
Used simple population models to extract the "death rate" of viruses from these data.

Model 2. What's happening during "set-point" phase

One patient



20 patients



Showed that viruses are turning over rapidly all the time.

~ 1 billion new viruses produced every day during set-point period.

→ Big implications for viral evolution (and hence drug resistance).

Model 3. How will antiretroviral drugs impact the HIV epidemic?

In the late 1990s, effective antiretroviral drugs were developed.

Used in combination “drug cocktails”, they were effective at decreasing the viral load of HIV patients and extending survival.

Looked great, but two concerns:

1) “behavioral disinhibition”: people might be less afraid of the disease, and more likely to engage in risky behaviors
2) HIV might evolve resistance to the new drugs.

Model 3. How will antiretroviral drugs impact the HIV epidemic?

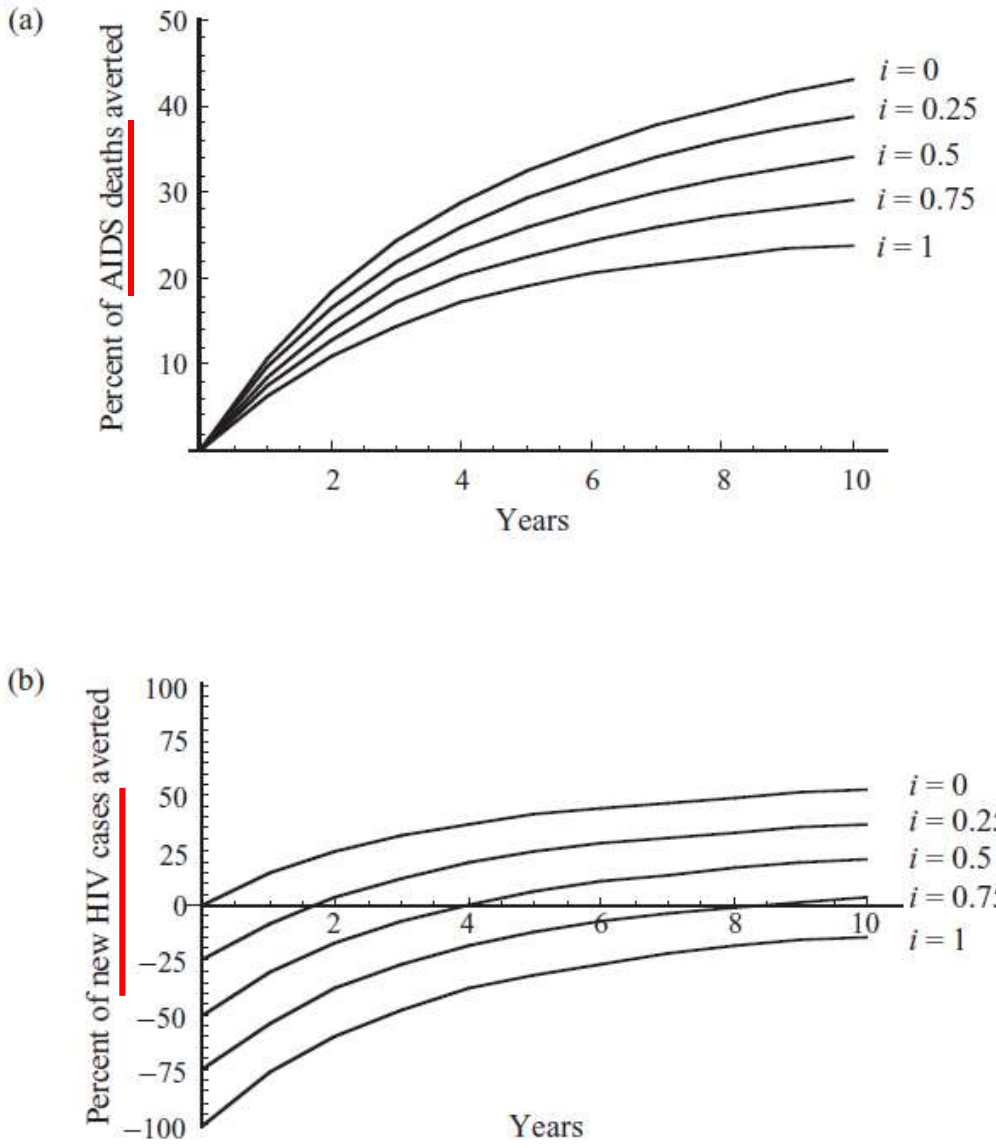
Blower et al (2000) built a model to predict how drug therapy might affect the # of new cases and # of deaths from HIV.

- Model included population dynamics of infection with drug-sensitive strain or drug-resistant strain.
- Also included evolution of resistance, and possibility that people might increase their risk behavior.
- Tailored model to data from San Francisco gay community.
- Emphasized **uncertainty**: many parameters not well known (or 'future' parameters that haven't happened yet).

Model 3. How will antiretroviral drugs impact the HIV epidemic?

Parameter *i* measures the increase in risky behavior due to disinhibition.

Its value strongly influences the impact of antiviral drugs on the HIV epidemic – it can even make the epidemic worse!



Model 4. Estimating the rate of new infections, and who is at risk.

Preventing HIV spread requires knowing who is most at risk.

But studies to determine risk are very costly and time-consuming.

With limited data in the early part of the epidemic, can we learn who is at risk from information about who is currently infected?

Williams et al (2001) modeled changes in HIV status of women in a rural district in South Africa.

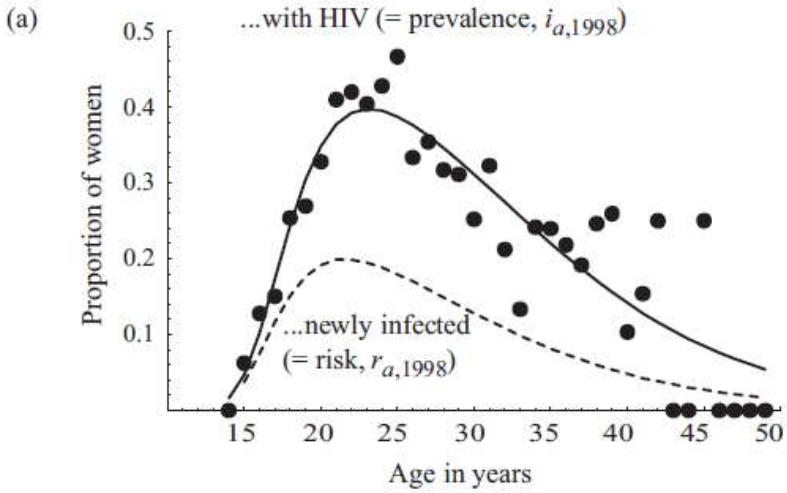
- worked with available data to answer question now, instead of waiting for perfect data
- Used data about current situation to infer what processes gave rise to it – looking backward not forward.

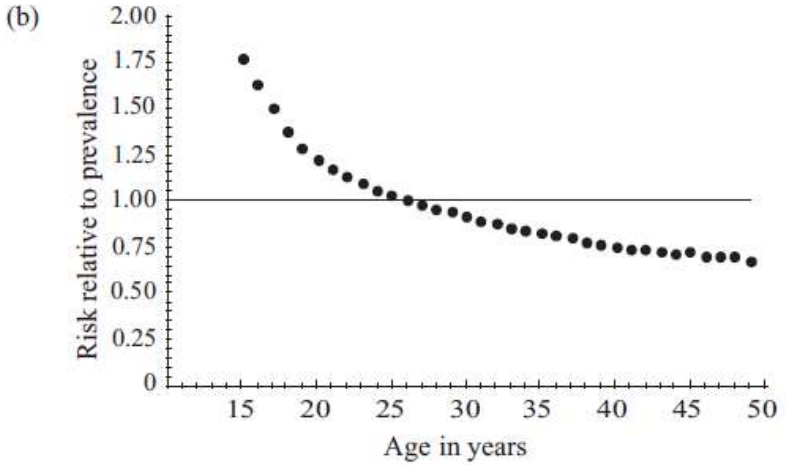
Model 4. Estimating the rate of new infections, and who is at risk.

Current prevalence-vs-age pattern (in 1998) quite similar to the risk-vs-age pattern

→ HIV is still invading population

But current prevalence data don't directly indicate who is at greatest risk of infection.





Model 5. Projecting the possible impact of adult male circumcision on the HIV epidemic.

Randomized clinical trials published in 2005 and 2006 showed that circumcision protects men against infection with HIV.

- risk of infection for circumcised men is approximately 60% lower than for uncircumcised men.

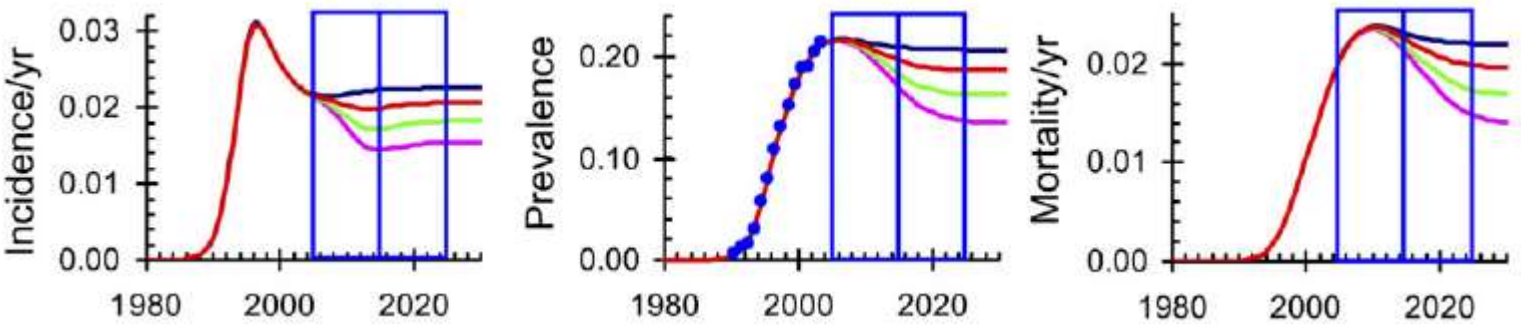
→ Circumcision is acting almost like a vaccine – what impact could it have on the whole epidemic?

Williams et al (2006) modeled the HIV epidemics in many countries of sub-Saharan Africa, and estimated the possible benefit of rolling out voluntary medical circumcision programs.

The Potential Impact of Male Circumcision on HIV in Sub-Saharan Africa

Brian G. Williams[1*], James O. Lloyd-Smith[2,3], Eleanor Gouws[4], Catherine Hankins[4], Wayne M. Getz[2], John Hargrove[5], Isabelle de Zoysa[6], Christopher Dye[1], Bertran Auvert[7,8,9]

PLoS Medicine | www.plosmedicine.org 1032 July 2006 | Volume 3 | Issue 7 | e262



What if…

- all men became circumcised by 2015?
- Circumcision reduces female-to-male transmission by 32%, 60% or 72%.
- Blue line shows epidemic in the absence of any intervention.

Further reading

Read summaries of the first four models in Chapter 1 of *A Biologist's Guide to Mathematical Modelling* (BGMM).

Available free online: http://press.princeton.edu/chapters/s8458.pdf

Read summaries of how models 1 and 3 were formulated in Boxes 2.4 and 2.5 of BGMM.

Original articles

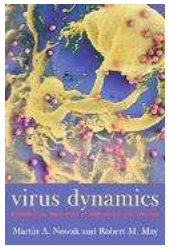
Model 1: Phillips (1996) *Science* 271: 497-499.

Model 2: Ho et al. (1995) *Nature* 373: 123-126.

Model 3: Blower et al. (2000) *Science* 271: 650-654.

Model 4: Williams et al. (2001) *Statistics in Medicine* 20: 2003-2016.

Model 5: Williams et al. (2006) *PLoS Medicine* 3:e262
http://www.plosmedicine.org/article/info:doi/10.1371/journal.pmed.0030262



Further info on modeling viruses within hosts:
Virus dynamics by Nowak & May (Oxford, 2000)

Examples of past project topics – conservation

Global Warming May Lead Emperor Penguin Population to Extinction

The Golden Eagle Population in Denali National Park and how it is Affected by Lead Poisoning

The Effects of Forest Conversion to Oil Palm and Agroforest: Implications for the Future of the Sumatran Orangutan (*Pongo abelii*)

Sustainable harvesting pink salmon in Alaska

Hunting and the Allee Effect in the red panda (*Ailurus fulgens*)

Modeling the proposed wildlife corridor for bobcats (*Lynx rufus*) in the Santa Monica Mountains

The Use of Marine Protection Areas to Support Long Term Sustainability of Red Snapper Populations

Examples of past project topics – epidemics

Understanding the effects of quarantine rate and time of quarantine initiation using SIR model

Prevention of outbreaks of yellow fever in the Democratic Republic of Congo

The Impact of Sheep Populations by the Schmallenberg Virus: Predictive Analysis using SIR Modeling

The Effect of Temperature on the Transmission of Lyme Disease

Modeling disease dynamics of tuberculosis in badgers

Examples of past project topics – other

Nutrients Drive Trophic Disequilibrium and Carbon Sequestration in Subtropical Gyres

The Role of Reactive Oxygen Species in Breast Cancer: A Modeling Approach to Nitric Oxide-Mediated Treatments

Drug Resistant Mutations of Tuberculosis

Examining the Impact of Alternate Prey on Predator-Prey Dynamics

Evaluating the relationship between insect survivorship and spatial heterogeneity in temperature

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Formulating a model – decisions you will have to make.

Prof. Jamie Lloyd-Smith

Formulating a model

- Think about your system, and what question you would like to address.
    - You should be able to express your question in one sentence, in plain English.
- What are the essential elements of the system, needed to:
    - Provide a minimal representation of the key processes
    - Address your question (what model outcomes will you use?)
- Brainstorm: what state variables *could* you use?

  what processes can affect these system states?

  what are characteristics of individuals in your system?

  how will you handle time, chance, population structure?
- Distill: what are the most important processes and characteristics? What is essential to address your question?

Start as simple as possible! Then think about how you would formulate and analyze your model. Repeat as needed.

“All models are wrong, but some are useful.”

George Box

“Everything should be made as simple as possible, but not simpler.”

Albert Einstein

Major decisions in designing a model

Pick appropriate state variables for system and questions!

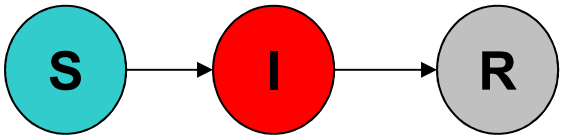
… and define the relations between them.

Can be creative with choice of state variables -- it doesn't always have to be population size.

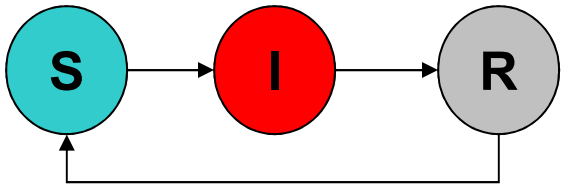
Other examples:

- number of farms infected with a virus
- proportion of nesting sites occupied by breeding birds
- forage quality on a habitat patch
- number of individuals in different states of appetite (hungry, full, in-between)
- *… almost any quantity that changes through time*

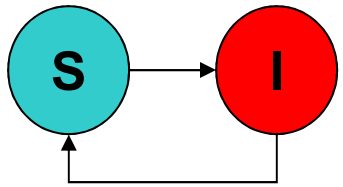
Adapt model framework to biology and to your problem!



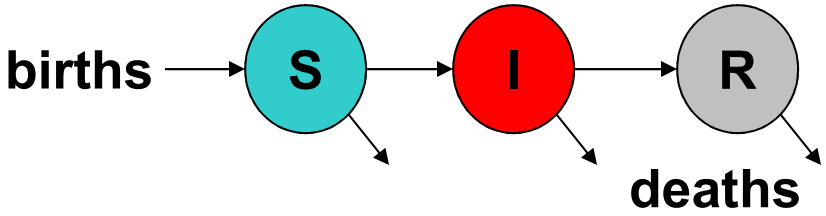
SIR

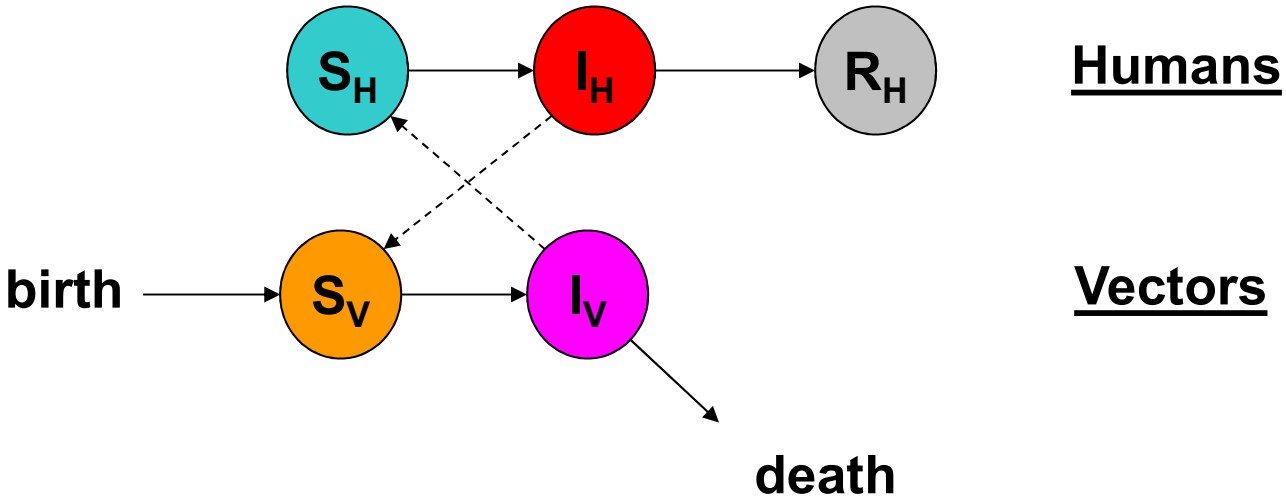


SIRS



SIS





Major decisions in designing a model

Even after compartmental framework is chosen, still need to decide:

- Discrete vs continuous time
- Discrete vs continuous state variables
- Deterministic vs stochastic
- Homogeneous vs heterogeneous

  (and which heterogeneities to include?)
- Well-mixed vs structured population

Let the biology and your questions guide these decisions.

Continuous vs discrete time

Continuous-time models (ODEs, PDEs)

$$\frac{dN}{dt} = \lambda N$$

- Well suited for mathematical analysis
- Real events occur in continuous time
- Allow arbitrary flexibility in durations and residence times

Discrete-time models

$$N(t+1) = \lambda N(t)$$

- Can match natural timescale of system, e.g. generation time or length of a season
- Data often recorded in discrete time intervals
- Easy to code (simple loop) and intuitive
- Note: can yield unexpected behaviour which may or may not be biologically relevant (e.g. chaos).

Continuous vs discrete state variables

Continuous state variables arise naturally in differential equation models.

- Mathematically tractable, but biological interpretation is vague (sometimes called 'density' to avoid problem of fractional individuals).
- Ignoring discreteness of individuals can yield artefactual model results (e.g. the "atto-fox" problem).
- Quasi-extinction threshold: assume that population goes extinct if continuous variable drops below a small value

Discrete state variables arise naturally in many stochastic models, which treat individuals (and individual outcomes) explicitly.

Deterministic vs stochastic models

Deterministic models

- Given model structure, parameter values, and initial conditions, there is no variation in output.

Stochastic models incorporate chance.

- Stochastic effects are important when numbers are small, e.g. during invasion or near extinction
- *Demographic stochasticity*: variation arising because individual outcomes are not certain
- *Environmental stochasticity*: variation arising from fluctuations in the environment (i.e. factors not explicitly included in the model)
- Can use analytic "stochastic process" models or Monte Carlo simulations

Model taxonomy

	CONTINUOUS TREATMENT OF INDIVIDUALS (averages, proportions, or population densities)	DISCRETE TREATMENT OF INDIVIDUALS
DETERMINISTIC	CONTINUOUS TIME • Ordinary differential equations • Partial differential equations DISCRETE TIME • Difference equations	
STOCHASTIC	CONTINUOUS TIME • Stochastic differential equations DISCRETE TIME • Stochastic difference equations	CONTINUOUS TIME • Gillespie algorithm DISCRETE TIME • Binomial chain type models

Credit: Juliet Pulliam, U of Florida

Population heterogeneities

In real populations, almost everything is heterogeneous – no two individuals are completely alike.

Which heterogeneities are important for the question at hand?

(age, size, competitive ability, etc)

Do they affect demographic rates or interactions?

Can parameters be estimated to describe their effect?

Heterogeneity and structure – what's the difference?

Tough to define, but *roughly…*

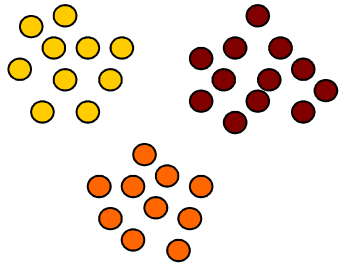
Heterogeneity describes differences among individuals or groups in a population.

Population structure describes deviations from random mixing in a population, due to spatial or social factors.

The language can get confusing:

- models that include heterogeneity in host age are called "age-structured".
- models that include spatial structure where model parameters differ through space are called "spatially heterogeneous".

Modelling heterogeneity



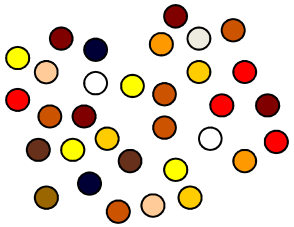
Group-level heterogeneity and multi-group models

Break population into sub-groups, each of which is homogeneous.

(often assume that all groups mix randomly)

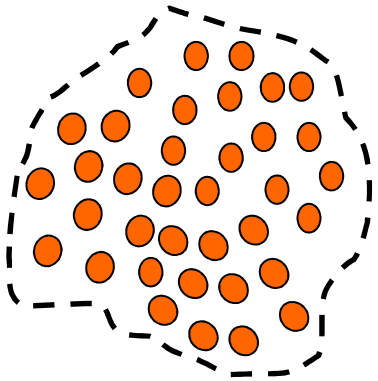
Individual-level heterogeneity

Allow continuous variation among individuals.

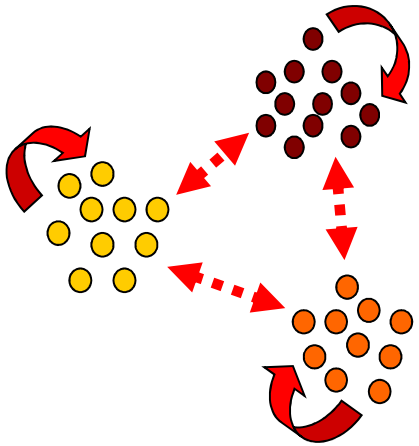


Models for population structure

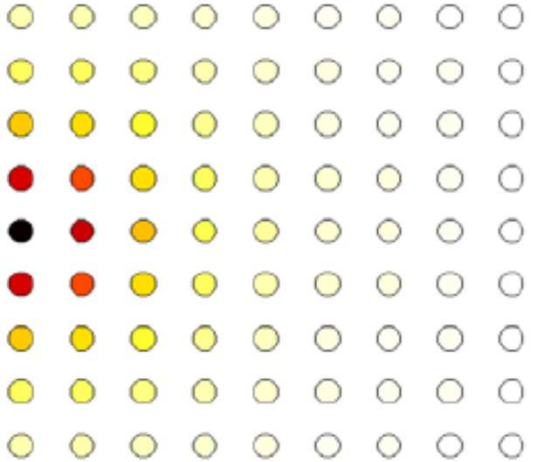
Random mixing



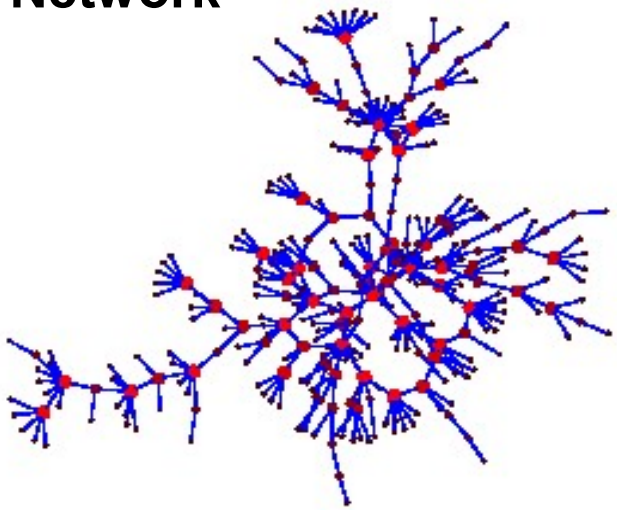
Multi-group



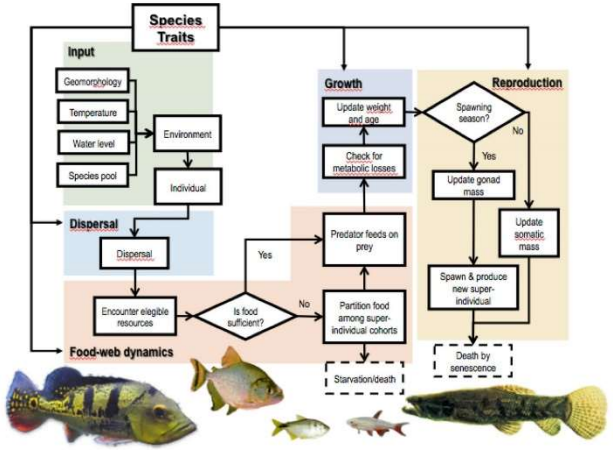
Spatial mixing



Network



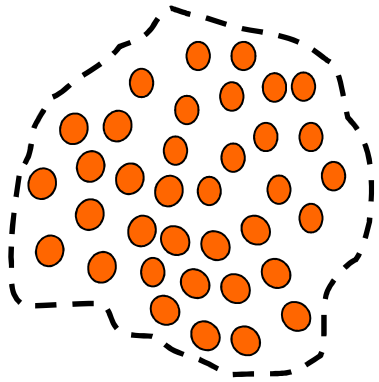
Individual-based model



Models for population structure

Random mixing

or mean-field

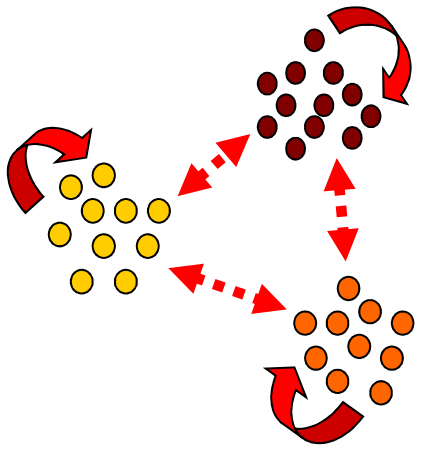


- Treat entire population as one unit.
- Every individual in population has equal probability of interacting with any other individual.
- Mathematically simple – “mass action” formulations borrowed from chemistry – but often biologically unrealistic.

Models for population structure

Multi-group

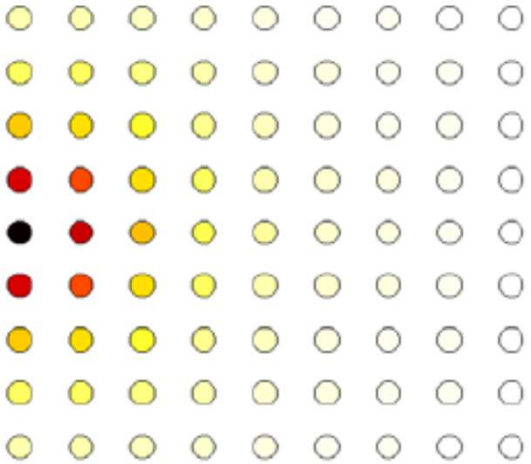
or metapopulation

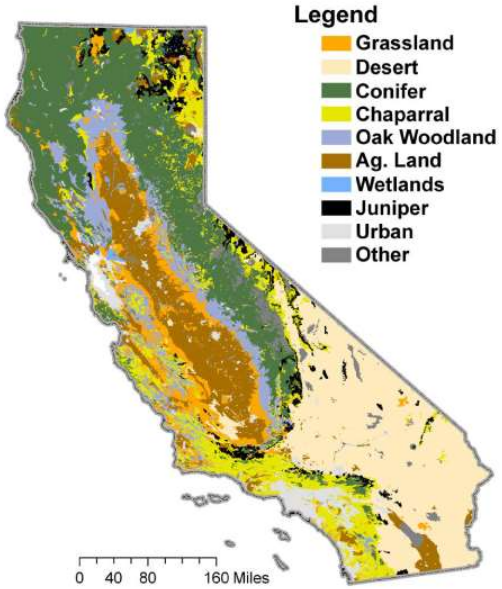


- Divides population into multiple discrete groupings, based on spatial or social differences.
  - in ecological setting, can think of groups as the sub-populations occupying different habitat patches
  - or can be social groupings, e.g. for animals living in herds or packs
- Usually assume that most processes take place within groups, then need to model movements between patches explicitly.

Models for population structure

Spatial mixing

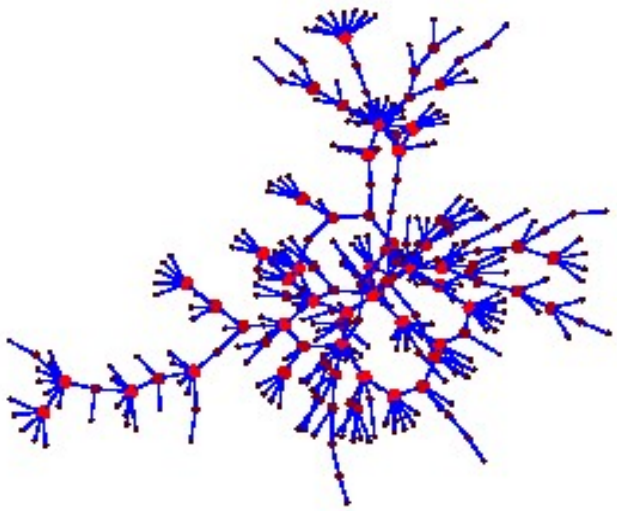




- Used when explicit spatial processes (mixing, movement, range expansion, habitat gradients, etc) are of interest.
- Can model many ways:
  - continuous space models (e.g. reaction-diffusion or contact kernel)
  - individuals as points on a lattice (e.g. cellular automaton)
  - patch models (metapopulation with spatial mixing)

Models for population structure

Social network

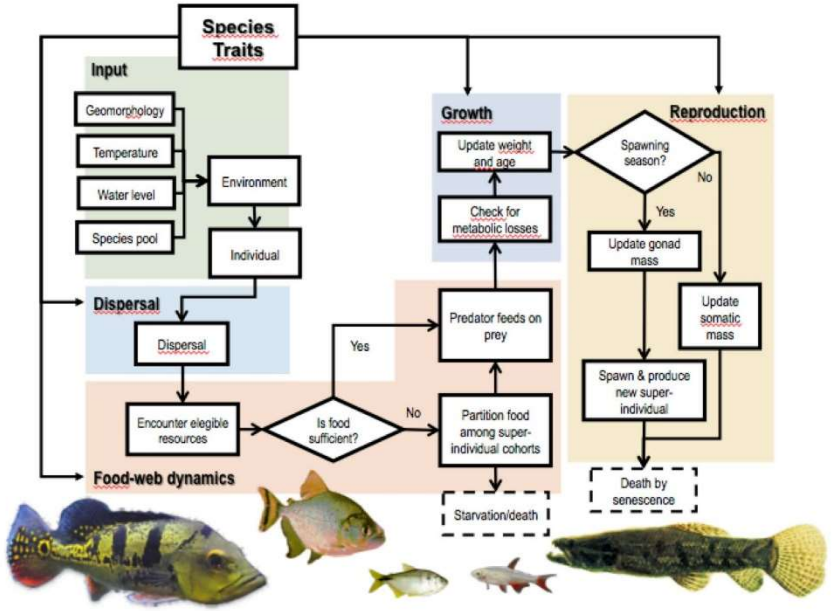


- Precise representation of contact structure within a population
- “Nodes” are individuals and “edges” are contacts
- Important decisions: Binary vs weighted? Undirected vs directed?
  Static vs dynamic?
- Basic network statistics include degree distribution (number of edges per node) and clustering coefficient (How many of my friends are friends with each other?)
- Powerful tools of discrete mathematics can be applied.

Models for population structure

Individual-based model (IBM)

or microsimulation model



- The most flexible framework.
- Every individual in the model carries its own attributes (age, sex, location, risk behaviour, etc etc)
- Can represent arbitrarily complex systems (= realistic?) and ask detailed questions, but difficult to estimate parameters and to analyze model output; also difficult for others to replicate the model.

Next week: discussion of project ideas

- Identify your system of interest
- Identify your research question
- Think about how to formulate a model to address your question

  (see handout.)

- In class, we will discuss your project ideas in small groups, to help refine your thinking for the project proposals.