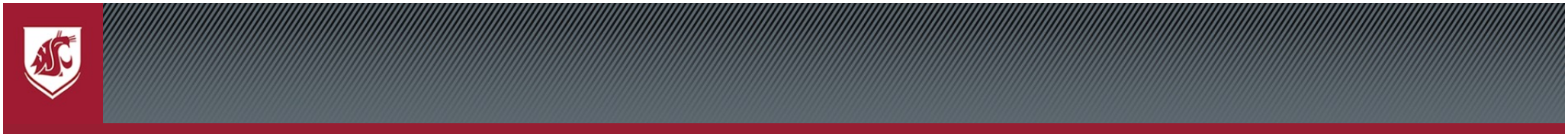
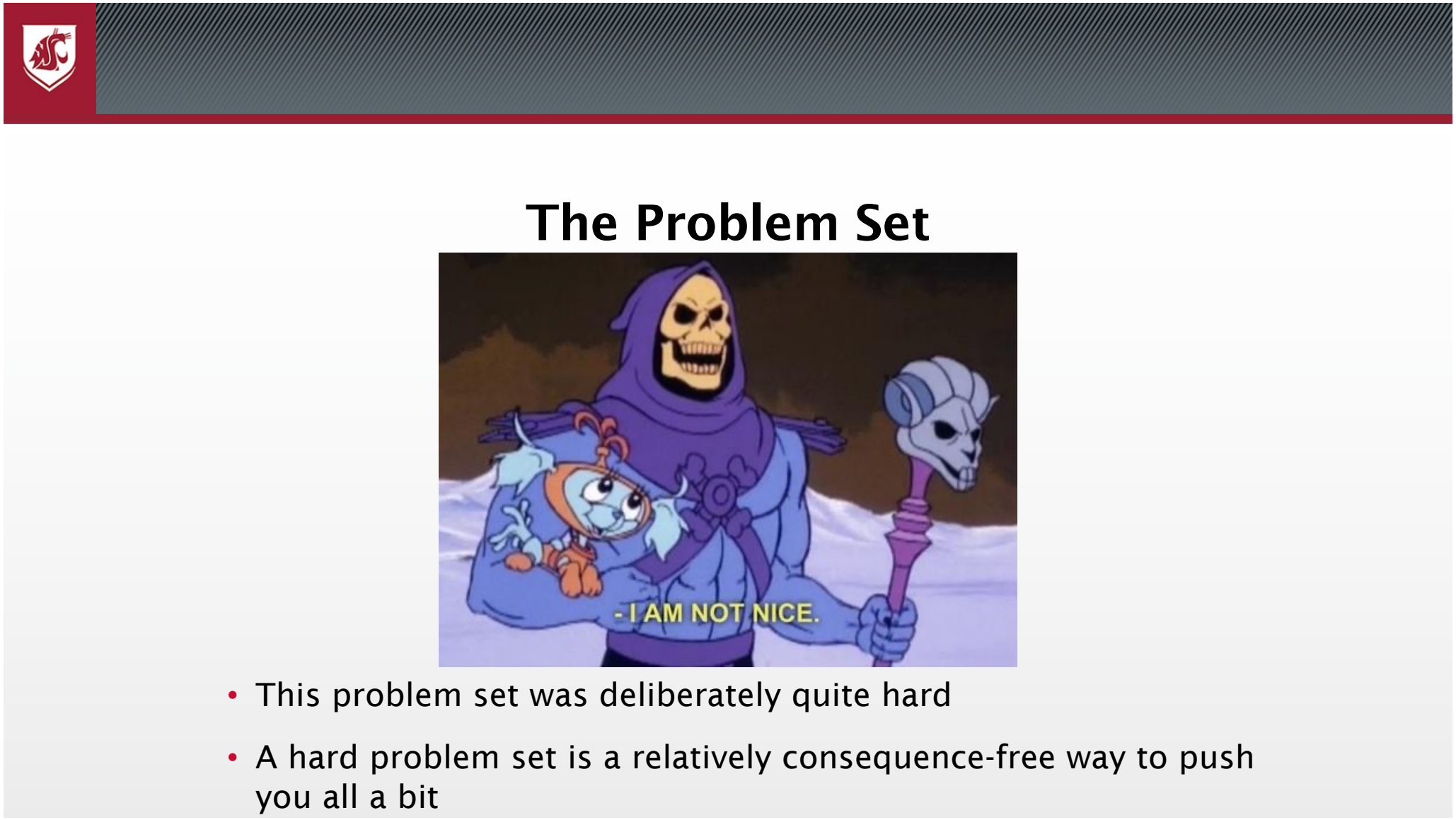
Deterministic Compartmental Models



Questions from Last Class?



The Problem Set

- This problem set was deliberately quite hard
- A hard problem set is a relatively consequence-free way to push you all a bit

Some Notes

- For those of you who have not read the books/watched the series, yes, people die *a lot*
- Yes, how you approached this was left intentionally ambiguous – outside of classwork, rare is the academic problem phrased as "Use logistic regression to estimate…"
- Pretty much everything we've covered so far was *a* valid approach to thinking about this problem

Some Musings

- When do you start counting – Book 1, or Book 0?
  - Is "had to survive to get to Book 1 in order to be introduced in Book 1" immortal person-time?
    - Philosophically, you could argue it is, practically, as it's applied uniformly, it probably doesn't matter
    - More than that, is "Had to survive to the book you were introduced in" immortal person time?
- When do you censor?
  - Do we administratively censor everyone at Book 5?
    - What does this assume?

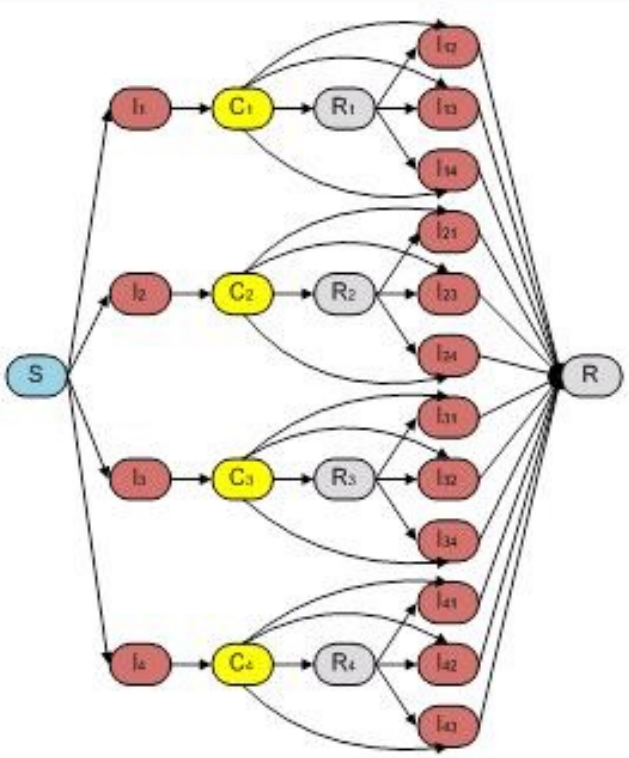
More Musings!

- Many of you tried both propensity score and traditional regression approaches and got very similar answers
- Why might this be?

Compartmental Models

- By far the most commonly used model in mathematical epidemiology
- Often called “SIR” models (a reference to the most common model)
- Based on the grouping of the population into particular states (compartments), usually health related
- Movement between compartments (also called *variables*) are governed by equations made up of *parameters*

Arbitrary Complexity and Variety



Types of Compartmental Models

- Discrete vs. Continuous
- Deterministic vs. Stochastic

Discrete vs. Continuous

- Discrete
  - Time is in single, separate chunks
  - Day 1, Day 2, Day 3…
- Continuous
  - Time is…continuous
  - Day 1, Day 1.0000001, Day 1.0000002…
  - Technically the above is still discrete
- No “right” form of modeling time
- Many human processes are discrete
- Most compartmental models are done in continuous time
  - This is largely a by-product of the difficult of proving things about difference equations (which we’ll talk about in a moment)

Stochastic vs. Deterministic

- Stochastic
  - Another word for random
  - Things happen with a *probability*
- Deterministic
  - Known, predictable rates
- There is 10% chance all of you will leave this lecture vs. 1/10th of the people here will leave
- For large populations, these will be approximately the same
- For small populations, these can be *wildly* different

How These Are Implemented

- Discrete, Deterministic
  - Difference Equations ($S_{t+1} = S_t$)
- Continuous, Deterministic
  - Differential Equations (dS/dt = S)
- All Stochastic
  - Various simulation algorithms
  - Most common: Gillespie's Direct Method
    - Quasi-continuous, has discrete event times but in very small time steps
  - We'll talk about this in future lectures

Compartmental Model Strengths

- Remarkably powerful – major insights like herd immunity, critical vaccination thresholds, etc. come from compartmental models
- Easy to compose, easy to implement
- Analytically tractable
  - You can prove things about them
- Very high reproducibility
- Low requirement for computation power
- Relatively low requirement for data
  - Technically can be data free

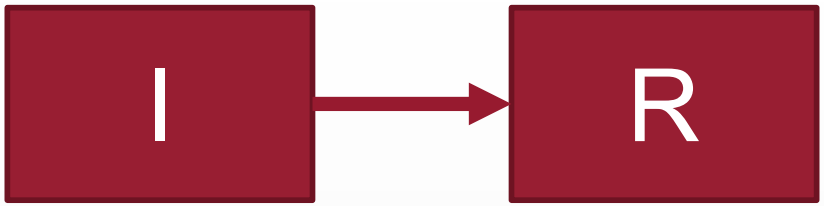
Compartmental Model Weaknesses

- Random mixing (aka Mass Action)
  - No patterns for how people interact
  - This is basically *always* untrue, but may or may not matter
- Everyone in a compartment is the same as everyone else in that compartment
- No "memory" of an individual's experience
- Building highly heterogeneous populations becomes very complex very quickly

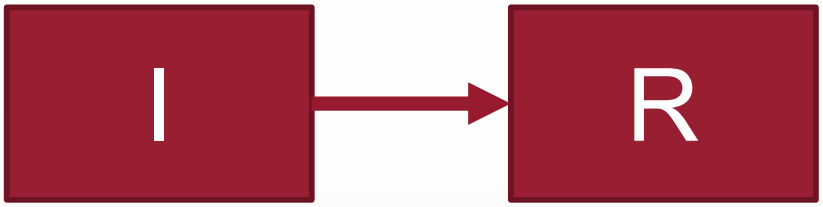
Compartmental Models: Reading and Writing

- Basic compartmental models are fairly straightforward to build
- Don't treat equations as a black box

- Returning to the SIR model, each variable is a letter (S, I and R)
- Parameters are often lower-case Greek letters
- Each compartment needs a variable, each arrow needs at least one parameter



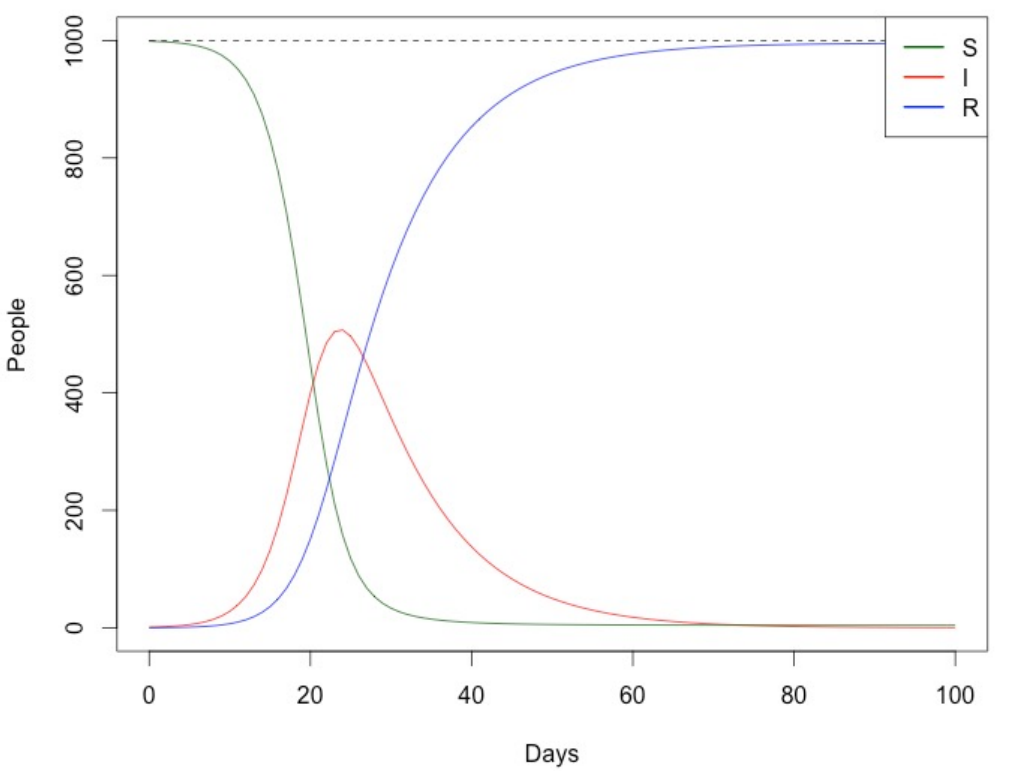
- Create an equation for each variable
  - For example, I
  - Left side: dI/dt
    - "The derivative of *I* with respect to *t*"
    - The change seen in *I* with an infinitesimally small change in time *t*
  - Right side: How things enter and leave a compartment
    - Going from I to R
    - Individuals leave *I* at a rate γ
    - $-\gamma I$
  - $dI/dt = -\gamma I$



- Link equations together
- We have γ people leave I per unit time
  - They need to go somewhere
  - Add γ people to R
- We now have two equations:
  - $dI/dt = -\gamma I$
  - $dR/dt = \gamma I$
- Everything is balanced
  - People go in, people go out

- S to I is a little harder
- Rather than a fixed rate, this is based on the people currently in I
- Dependent happenings
- β is a contact rate – takes into account the number of contacts someone has per unit time and the probability an S + I contact results in successful infection
- $dS/dt = -\beta SI$ Now we need to rebalance I
- $dI/dt = \beta SI - \gamma I$
- $dR/dt = \gamma I$

Numerical Integration



R_0 and Thresholds

- Analytical results tell us about the behavior of a system for *all possible* parameters
- Where will an epidemic not occur?
- $dI/dt \leq 0$
- Trivially: $\beta = 0$
- Other thresholds exist
- R_0 is the most common
  - Average number of cases caused by a single infective individual in an entirely susceptible population
  - If $R_0 < 1$, no epidemic occurs

Calculating R_0

- Lots of ways to calculate R_0
- Will vary for each model
- Again, a little beyond this course
- For an SIR model, $R_0 = \beta/\gamma$
- Other thresholds are related to R_0, like the critical vaccination threshold, which is $1 - 1/R_0$
- Alternatives:
  - R_E: Effective reproductive number (current vs. naïve population)
  - R_t: Varies over time

Where Do Parameters Come From

- Can be obtained from data
  - Leave one or two parameters (usually beta) unknown, use the value that best fits the data
- Estimates from the literature for some/all parameters
  - Good for established systems with good observational studies
  - Problem for novel diseases
- Guess
  - Expert opinion, “Delphi Method”
  - Monte Carlo sensitivity analysis

Fitting Models to Data

- *Lots* of ways to do this
  - Least Squares
  - Maximum Likelihood
  - Markov Chain Monte Carlo
  - Approximate Bayesian Computation
- Active area of research, will depend on your data, question, model, expertise, etc.
- Often referred to as ”Validating”
  - I hate this term
  - In this context, “Valid” does *not* mean right
    - That a model *can* fit the data does not mean it is the best or only means of doing so

Building a Model – A Worked Example

Basic Questions

- What is the question or system you want to model?
- Why does it need to be modeled?
- What kind of model does it need?
- How fast do you need an answer?
- "I want to study the effect of incarceration policy on neighborhood resilience. I think there is a lot of indirect effects and feedback loops that exist. I'd like to model fairly sophisticated behavior, and people's interactions with the environment, so I think I need an agent-based approach."
- "I want to make an agent-based model of tuberculosis."

Assemble a Team

- Modeling is inherently a team science endeavor
- Look for potential collaborators:
  - Clinical colleagues
  - Science of behavior/decision-making
    - Psychology, Anthropology, Economics
  - Biology/Ecology
    - Many of these models are also heavily used in those fields
  - Computer Science
  - Mathematics

Wildlife Example

- Question about toxoplasmosis
  - Caveat: I am not an expert on toxoplasmosis. Not even a little. Remember the last slide?
- Horizontal transmission believed not to occur in predators on Svalbard Island
- There are also no cats
- Believed to be sustained by periodic introductions from seabirds
  - Predator eats bird, vertical transmission in predators
- How often would the disease need to be re-introduced to sustain levels of toxo on the island?

Initial Thoughts

- Do we have any data on the levels of toxo on Svalbard?
  - Yes! Dr. Clearly Madeup has done an extensive prevalence survey
- Why do we care?
  - Validating or putting bounds on an interesting ecological theory
  - Maybe we can intervene in seabirds?
- Compartmental models seem like a reasonable first pass

First, we need some birds

B

- Birds arrive on the island at a rate α
  - dB/dt = α
  - This will result in infinite birds given time
  - Lets make it so birds arrive at rate α but are less likely to stay as the island grows more crowded, up to a carrying capacity κ_B
  - dB/dt = $\alpha(1 - \frac{B}{\kappa_B})$
  - We now have a population of birds that will grow until they hit carrying capacity
  - Birds also die, at a natural rate γ_B
  - dB/dt = $\alpha\left(1 - \frac{B}{\kappa_B}\right) - \gamma_B B$

Now, things to eat the birds…

B S

- Very similar dynamics to the birds – predators are born and they die. Birth rate μ will depend on the number of predators
  - $dS/dt = \mu S\left(1 - \frac{S}{\kappa_S}\right) - \gamma_S S$
- Predators S opportunistically prey on birds
  - This is often modeled by Predator-Prey interactions resulting in new predators
  - $dS/dt = \mu S\left(1 - \frac{S}{\kappa_S}\right) + \delta BS\left(1 - \frac{S}{\kappa_S}\right) - \gamma_S S$
  - $dB/dt = \alpha\left(1 - \frac{B}{\kappa_B}\right) - \gamma_B B - \tau BS$

But sometimes birds have parasites…

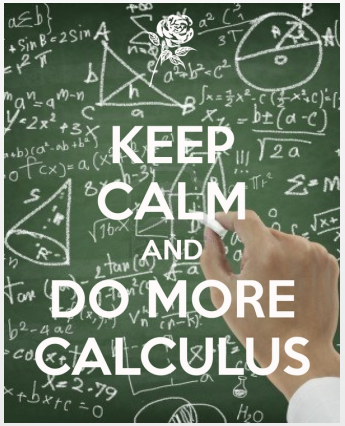
B S I

- Sometimes, the eating of a bird should result not in a new *S* predator, but in an *I* predator (representing maternal predation of an infected animal and subsequent vertical transmission)
- Lets call the prevalence of infection in birds θ and the probability of vertical transmission from an infected mother β.
  - dI/dt $= \mu I\left(1-\frac{S+I}{\kappa_S}\right)\beta + [\delta BS\left(1-\frac{S}{\kappa_S}\right)\beta\theta] - \gamma_S$I
- Why keep θ and β separate?
  - We might be able to intervene on one or the other
  - Could also simplify, but I find this less intuitive

This does things to the other populations

B S I

- Birds can be eaten by S or I
- Carrying capacity is now based on S + I
- Births from I mothers can result in S offspring



$$dS/dt = \mu S\left(1-\frac{S+I}{\kappa_S}\right)+\mu I(1-\beta)\left(1-\frac{S+I}{\kappa_S}\right)+\delta BI\left(1-\frac{S+I}{\kappa_S}\right)(1-\beta)+[\delta BS\left(1-\frac{S+I}{\kappa_S}\right)(1-\beta\theta)]-\gamma_S S$$

$$dI/dt = \mu I\beta\left(1-\frac{S+I}{\kappa_S}\right)+\left[\delta BS\left(1-\frac{S+I}{\kappa_S}\right)\beta\theta\right]+\delta BI\left(1-\frac{S+I}{\kappa_S}\right)\beta-\gamma_S I$$

$$dB/dt = \alpha\left(1-\frac{B}{\kappa_B}\right)-\gamma_B B-\tau BS-\tau BI$$

Back to the research question

- What level of α and β (the number of birds coming and the prevalence of toxo in birds) does it take for the population of I to match observed data?
  - Many simulations over many values of those two parameters
- Are the numbers reasonable?
  - If so, this theory is supported
  - If not, there may be something else going on
- Are there other parameters we might adjust to trigger local extinction of toxo? Can these be maintained even if α and β remain constant?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More Complexity!

- Note there's no behavioral differences between S and I predators
- Nor is there a survival difference, an impact on mortality, etc.
- What about more than one predator species? Or bird species?
- What about modeling more than one life stage for the predators? Perhaps susceptibility or hunting behavior differs by age?
- What about predation of infected predators by other predators?
- Currently treating Svalbard as a single, featureless island. Surely there are local populations that don't necessarily interact? Or groups of predators which rely more or less heavily on bird predation?

Key Takeaways

- Always be thinking about the problem you want to answer
- Don't get carried away with extraneous detail
- Seek out help – there's lots of people in lots of departments that do this
- Equations aren't nearly as scary as they look initially
  - Unpack them piece by piece
  - If something is subtracted, where does it turn up?