

Welcome To Math 463:
Introduction to Mathematical
Biology

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Introduction to Mathematical Biology
MWF 1:00-2:00, 3096 East Hall
<http://www.math.lsa.umich.edu/courses/463/>

Instructor: Dr. Trachette Jackson

Course Synopsis:

A variety of topics in population biology, physiology and in the biomedical sciences will be considered including single and competing species ecological models, enzyme reaction kinetics, biological oscillators, epidemiology, and infectious diseases. There will time set aside for group discussions and modeling projects related to the more interesting and advanced issues concerning the topics mentioned above. Approximately one class period each week will be held in the mathematics computer laboratory where numerical techniques for finding and visualizing solutions of differential and discrete systems will be discussed.

Text:

This course will follow closely the first several chapters of: *Mathematical Models in Biology*, Leah Edelstein-Keshet, 1988 supplemented by material from the current literature and lecture notes from the instructor.

Prerequisites:

A major focus of this course will be the derivation and analysis of discrete and differential equations which model specific biological and medical problems. In order to be successful in this course, it will be necessary to have completed the following mathematics courses or their equivalent: Math 217, 417, or 419 and Math 216, 286 or 316 or to have permission of the instructor.

Grading:

Grades will be based on the completion of a final project which will require an in class presentation as well as a substantial research paper (25%), two examinations (50%), and weekly (or biweekly) homework assignments and in class presentation of problems (25%). Note: There will also be numerical component to some of the homework assignments which will require the use of MATLAB or MAPLE.

- **HOMEWORK POLICY**
NO LATE homework will be accepted. All homework will be due at the BEGINNING of class.

What is Mathematical Modeling?

- A mathematical model is the formulation in mathematical terms of the assumptions believed to underlie a particular real-world problem
- Mathematical modeling is the process of deriving such a formulation

Why is it Worthwhile to Model Biological Systems

- To help reveal possible underlying mechanisms involved in a biological process
- To help interpret and reveal contradictions/incompleteness of data
- To help confirm/reject hypotheses
- To predict system performance under untested conditions
- To supply information about the values of experimentally inaccessible parameters
- To suggest new hypotheses and stimulate new experiments

What are some Limitations of Mathematical Models

- Not necessarily a ‘correct’ model
- Unrealistic models may fit data very well leading to erroneous conclusions
- Simple models are easy to manage, but complexity is often required
- Realistic simulations require a large number of hard to obtain parameters

Disclaimer

- Models are not explanations and can never alone provide a complete solution to a biological problem.

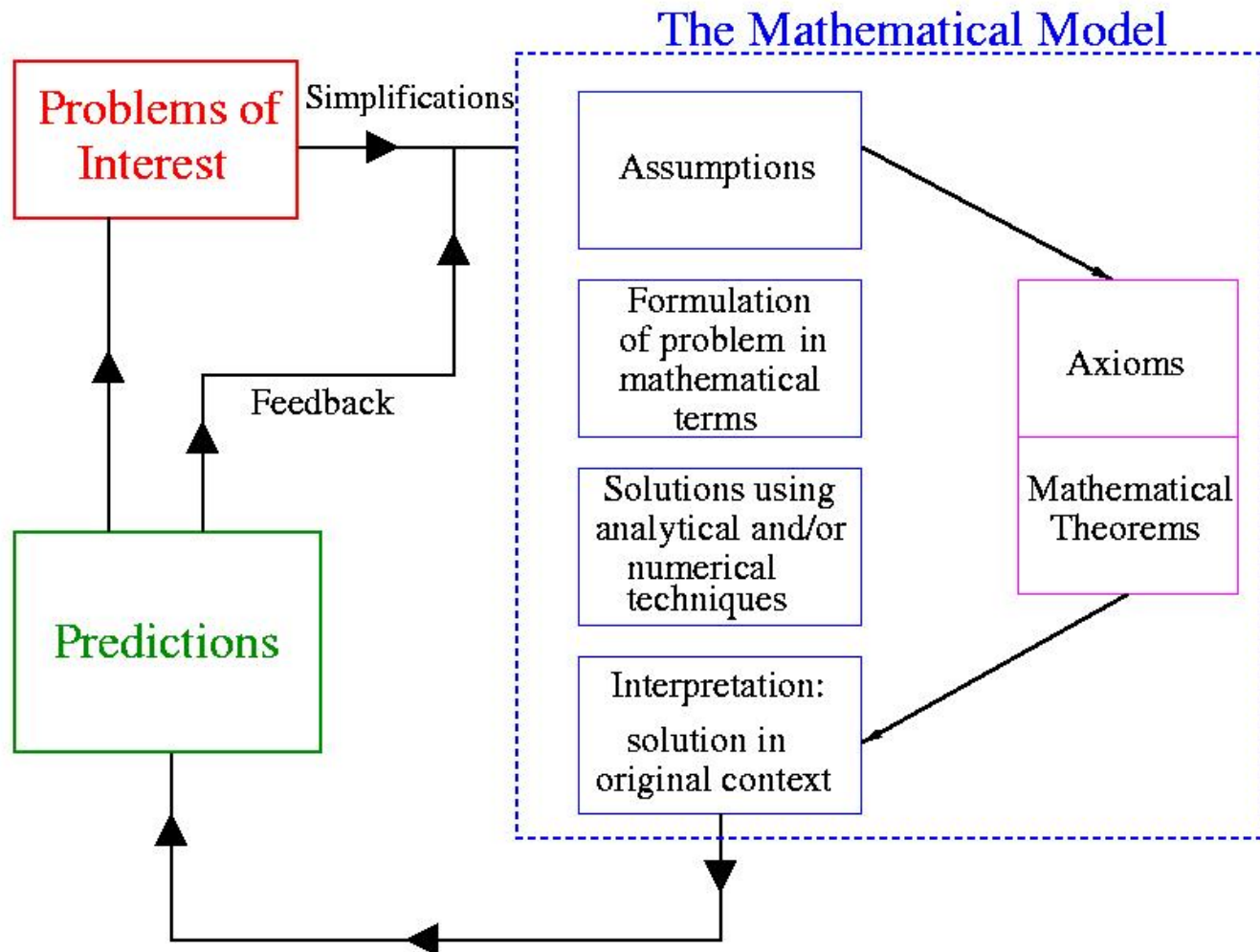
How Are Models Derived?

- Start with a problem of interest
- Make reasonable simplifying assumptions
- Translate the problem from words to mathematically/physically realistic statements of balance or conservation laws

What do you do with the model?

- Solutions—Analytical/Numerical
- Interpretation—What does the solution mean in terms of the original problem?
- Predictions—What does the model suggest will happen as parameters change?
- Validation—Are results consistent with experimental observations?

The Modeling Process

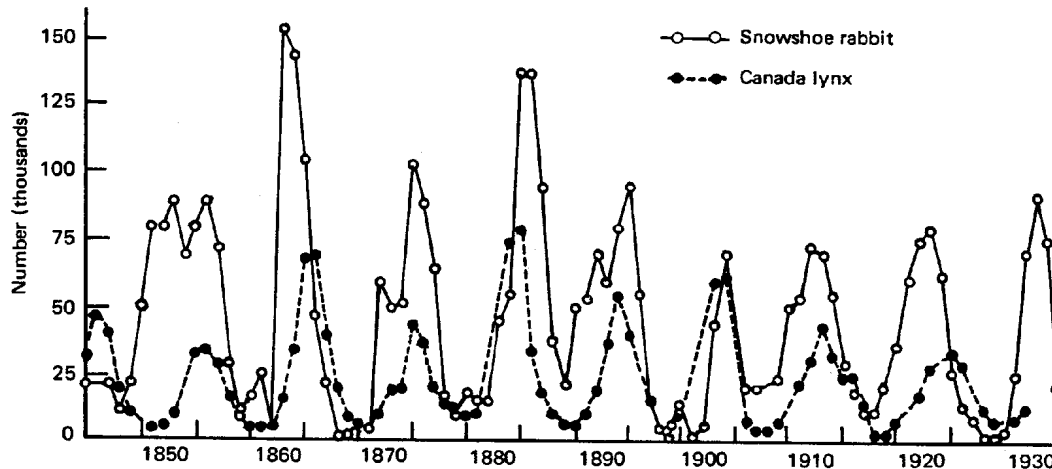


Modeling Has Made a Difference

Example 1: Population Ecology



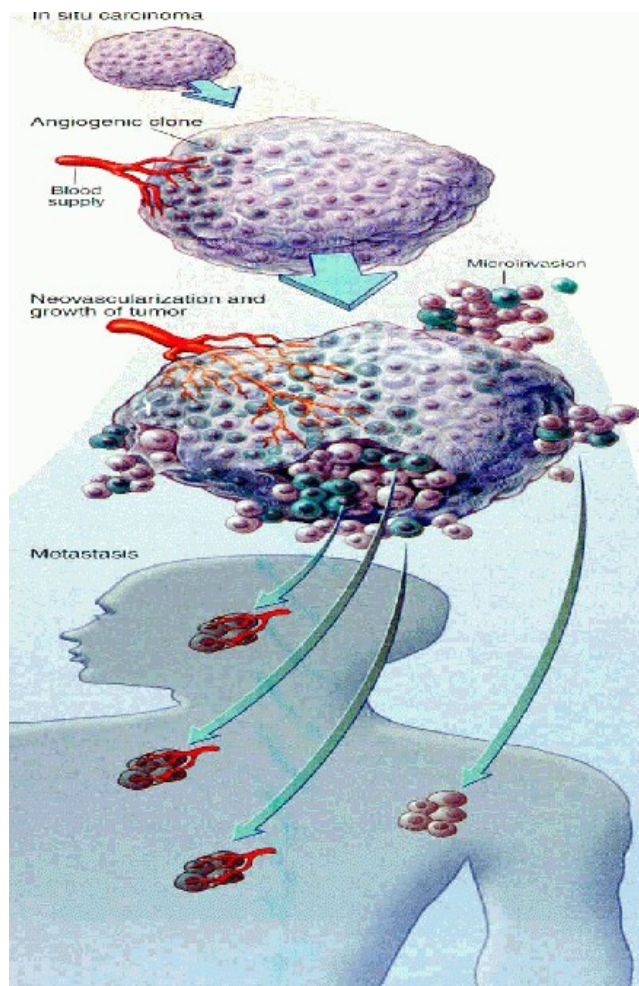
■ Canadian lynx and snowshoe rabbit



■ Predator-prey cycle was predicted by a mathematical model

Modeling Has Made A Difference

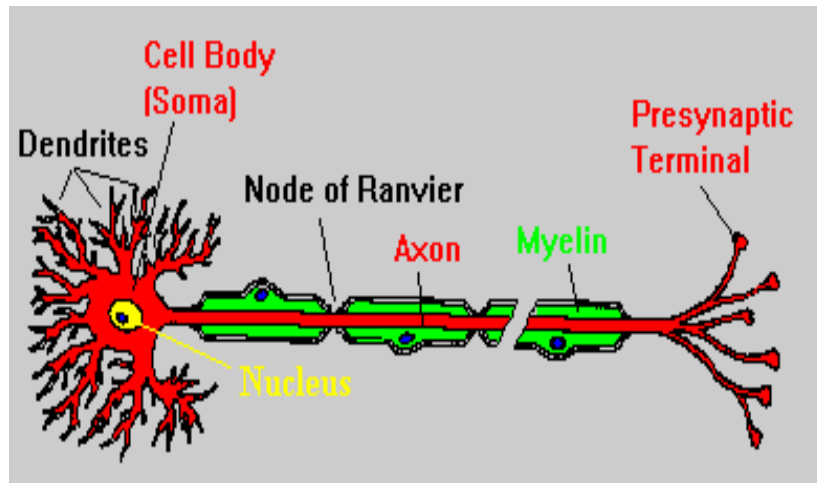
Example 2: Tumor Growth



- Mathematical models have been developed that describe tumor progression and help predict response to therapy.

Modeling Has Made a Difference

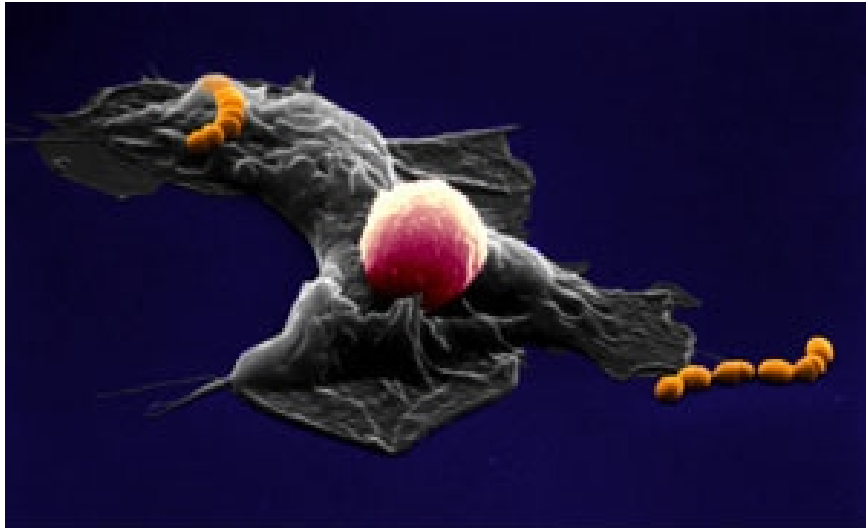
Example 3: Electrophysiology of the Cell



- In the 1950's Hodgkin and Huxley introduced the first model to designed to reproduce cell membrane action potentials
- They won a nobel prize for this work and sparked the a new field of mathematics—excitable systems

Modeling Has Made a Difference

Example 4: Microbiology/Immunology



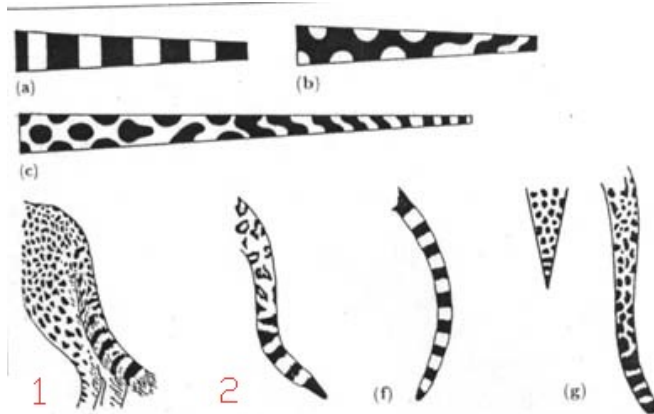
- How do immune cells find a bacterial target?
- Under what conditions can the immune system control a localized bacteria infection?
- If the immune system fails, how will the bacteria spread in the tissue?

Modeling Has Made a Difference

Example 5: Biological Pattern Formation



- How did the leopard get its spots?
- A single mechanism can predict all of these patterns



Course Goals

- Critical understanding of the use of differential equation methods in mathematical biology
- Exposure to specialized mathematical/computations techniques which are required to study ODEs that arise in mathematical biology
- By the end of this course you will be able to derive, interpret, solve, understand, discuss, and critique discrete and differential equation models of biological systems.

Discrete-Time Models

Lecture 1

When To Use Discrete-Time Models

Discrete models or *difference equations* are used to describe biological phenomena or events for which it is natural to regard time at fixed (discrete) intervals.

Examples:

- The size of an insect population in year i ;
- The proportion of individuals in a population carrying a particular gene in the i -th generation;
- The number of cells in a bacterial culture on day i ;
- The concentration of a toxic gas in the lung after the i -th breath;
- The concentration of drug in the blood after the i -th dose.

What does a model for such situations look like?

- Let x_n be the quantity of interest after n time steps.
- The model will be a rule, or set of rules, describing how x_n changes as time progresses.
- In particular, the model describes how x_{n+1} depends on x_n (and perhaps x_{n-1} , x_{n-2} , ...).
- In general:
$$x_{n+1} = f(x_n, x_{n-1}, x_{n-2}, \dots)$$
- For now, we will restrict our attention to:
$$x_{n+1} = f(x_n)$$

Terminology

The relation $x_{n+1} = f(x_n)$ is a difference equation; also called a recursion relation or a map.

Given a difference equation and an initial condition, we can calculate the iterates x_1, x_2, \dots , as follows:

$$x_1 = f(x_0)$$

$$x_2 = f(x_1)$$

$$x_3 = f(x_2)$$

.
.
.

The sequence $\{x_0, x_1, x_2, \dots\}$ is called an orbit.

Question

- Given the difference equation $x_{n+1} = f(x_n)$
can we make predictions about the
characteristics of its orbits?

Modeling Paradigm

- Future Value = Present Value + Change

$$x_{n+1} = x_n + \Delta x_n$$

- Goal of the modeling process is to find a reasonable approximation for Δx_n that reproduces a given set of data or an observed phenomena.

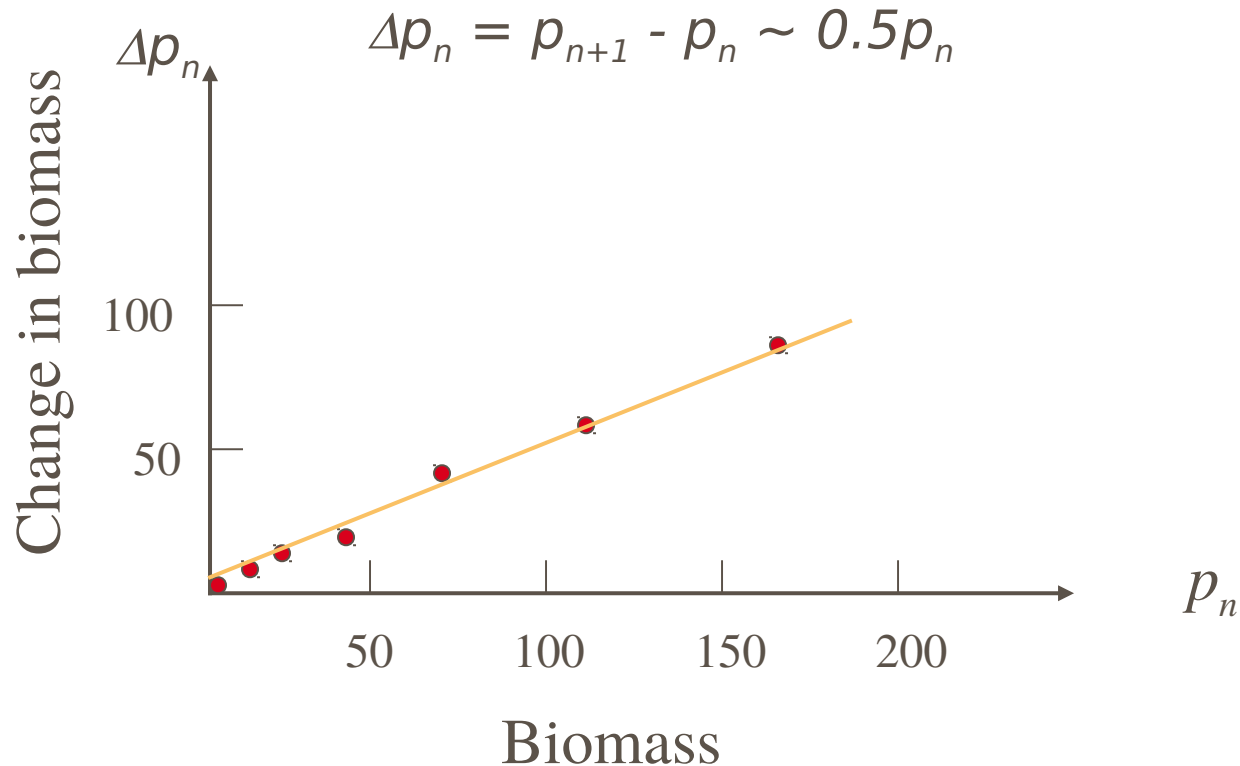
Example: Growth of a Yeast Culture

The following data was collected from an experiment measuring the growth of a yeast culture:

Time (hours)	Yeast biomass	Change in biomass
n	p_n	$\Delta p_n = p_{n+1} - p_n$
0	9.6	8.7
1	18.3	10.7
2	29.0	18.2
3	47.2	23.9
4	71.1	48.0
5	119.1	55.5
6	174.6	82.7
7	257.3	

Change in Population is Proportional to the Population

Change in biomass vs. biomass



Explosive Growth

- From the graph, we can estimate that $\Delta p_n = p_{n+1} - p_n \sim 0.5p_n$ and we obtain the model

$$p_{n+1} = p_n + 0.5p_n = 1.5p_n$$

The solution is:

$$p_{n+1} = 1.5(1.5p_{n-1}) = 1.5[1.5(1.5p_{n-2})] = \dots = (1.5)^{n+1} p_0$$

$$p_n = (1.5)^n p_0.$$

 This model predicts a population that increases forever.

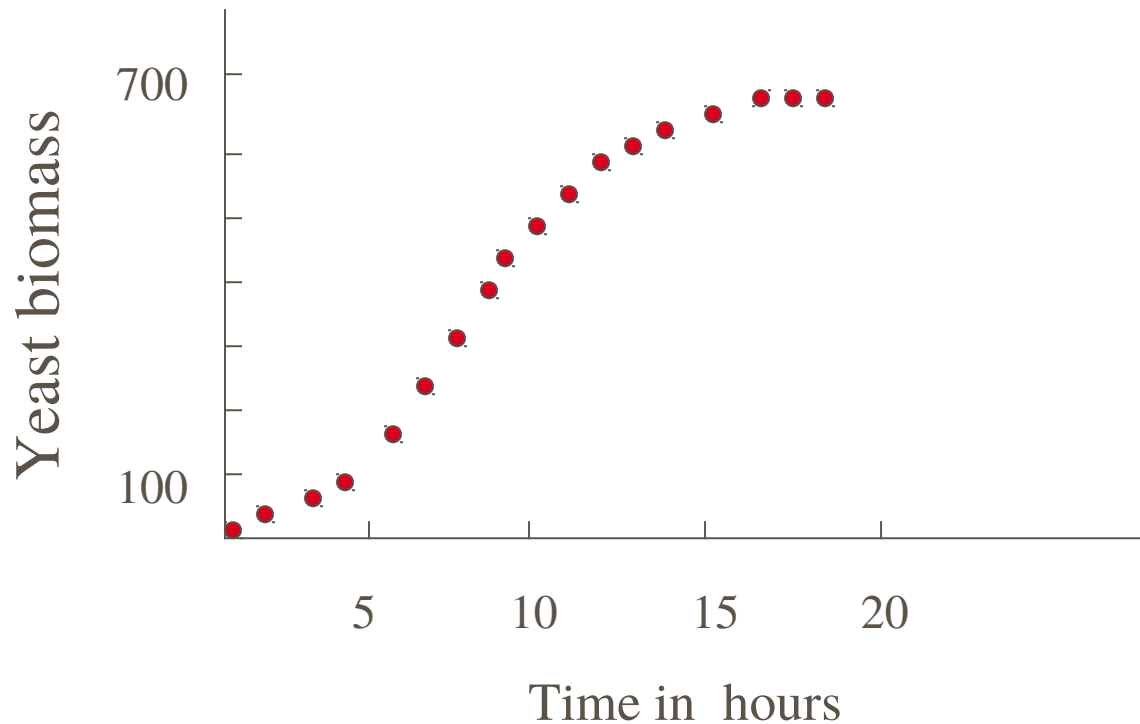
Clearly we should re-examine our data so that we can come up with a better model.

Example: Growth of a Yeast Culture

Revisited

Time (hours)	Yeast biomass	Change in biomass
n	p_n	$\Delta p_n = p_{n+1} - p_n$
0	9.6	8.7
1	18.3	10.7
2	29.0	18.2
3	47.2	23.9
4	71.1	48.0
5	119.1	55.5
6	174.6	82.7
7	257.3	93.4
8	350.7	90.3
9	441.0	72.3
10	513.3	46.4
11	559.7	35.1
12	594.8	34.6
13	629.4	11.5
14	640.8	10.3
15	651.1	4.8
16	655.9	3.7
17	659.6	2.2
18	661.8	

Yeast Biomass Approaches a Limiting Population Level



The limiting yeast biomass is approximately 665.

Refining Our Model

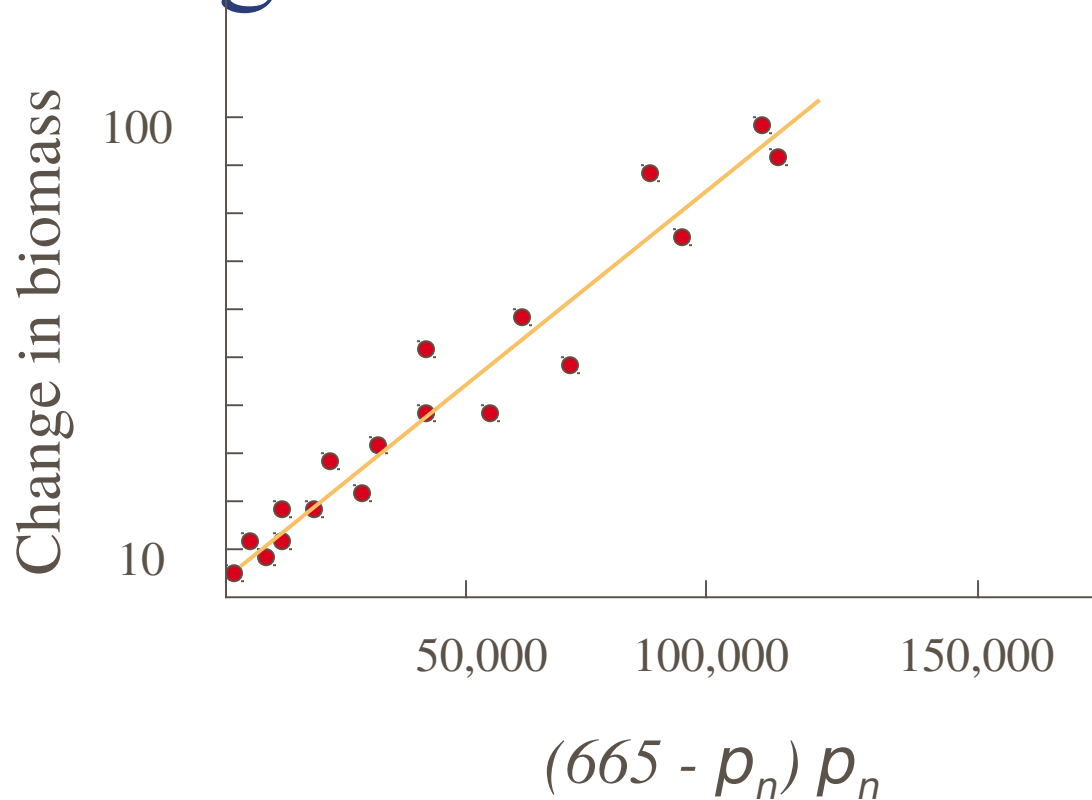
- Our original model: $\Delta p_n = 0.5p_n$ $p_{n+1} = 1.5p_n$
- Observation from data set: The change in biomass becomes smaller as the resources become more constrained, in particular, as p_n approaches 665.
- Our new model: $\Delta p_n = k(665 - p_n) p_n$
 $p_{n+1} = p_n + k(665 - p_n) p_n$



Testing the Model

- We have hypothesized $\Delta p_n = k(665 - p_n) p_n$ ie, the change in biomass is proportional to the product $(665 - p_n) p_n$ with constant of proportionality k .
- Let's plot Δp_n vs. $(665 - p_n) p_n$ to see if there is reasonable proportionality.
- If there is, we can use this plot to estimate k .

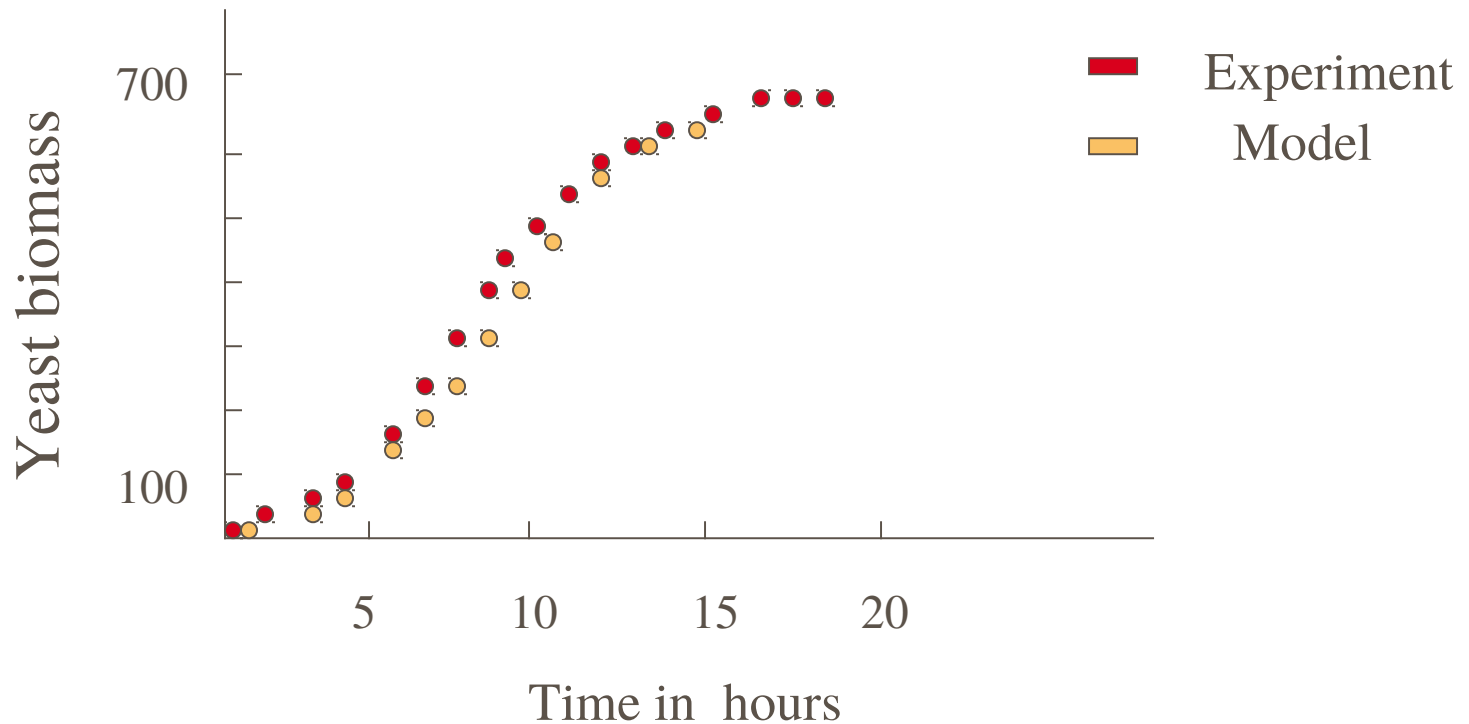
Testing the Model Continued



Our hypothesis seems reasonable, and the constant of Proportionality is $k \sim 0.00082$.

Comparing the Model to the Data

Our new model: $p_{n+1} = p_n + 0.00082(665 - p_n) p_n$



The Discrete Logistic Model

$$X_{n+1} = X_n + k(N - X_n) X_n$$

■ Interpretations

- Growth of an insect population in an environment with limited resources
 - X_n = number of individuals after n time steps (e.g. years)
 - N = max number that the environment can sustain
- Spread of infectious disease, like the flu, in a closed population
 - X_n = number of infectious individuals after n time steps (e.g. days)
 - N = population size

Two Models Examined So Far

- Model 1 (linear): Geometric Growth

- $x_{n+1} = x_n + kx_n \rightarrow$

- $x_{n+1} = rx_n$, where $r = 1+k$

- Model 2 (nonlinear): Logistic Growth

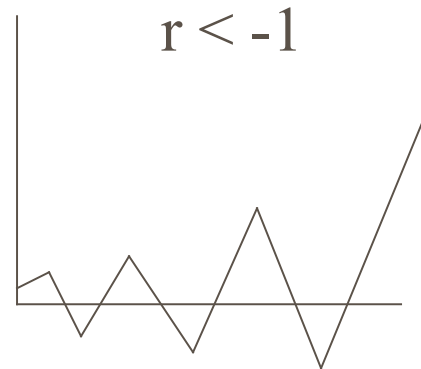
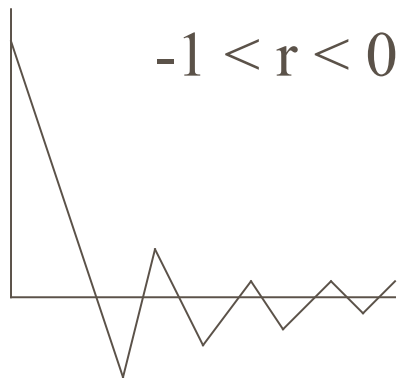
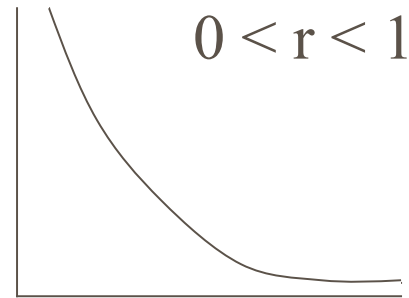
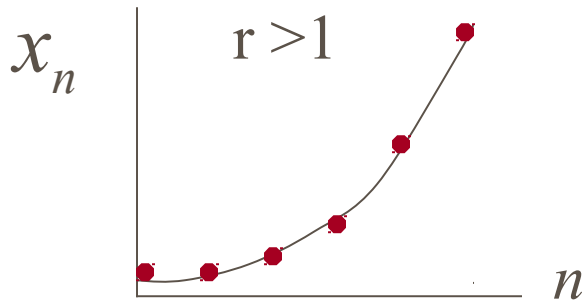
- $x_{n+1} = x_n + k(N - x_n) x_n \rightarrow$

- $x_{n+1} = rx_n(1 - x_n/K),$
where $r = 1+kN$ and $K = r/k$

Model 1: Geometric Growth

■ The Model: $x_{n+1} = rx_n$

■ The Solution: $x_n = x_0 r^n$



Model 2: Logistic Growth

- $x_{n+1} = rx_n(1-x_n/K)$
- There is no explicit solution
 - That is we cannot write down a formula for x_n as a function of n and the initial condition, x_0 .
- However, given values for r and K we can predict happens to x_n in the long run (very interesting behavior arises)
- But first we'll explore linear models in more detail

Friday

Meet in B735 Computer Lab

MATLAB Tutorial and Computer
Assignment #1