UNDERGRADUATE MATHEMATICS FOR

THE LIFE SCIENCES

MODELS
PROCESSES
AND
DIRECTIONS

Glenn Ledder, Jenna P. Carpenter, Timothy D. Comar

EDITORS

Undergraduate Mathematics for the Life Sciences

Models, Processes, and Directions

Undergraduate Mathematics for the Life Sciences

Models, Processes, and Directions

Edited by

Glenn Ledder
University of Nebraska-Lincoln

Jenna P. Carpenter
Louisiana Tech University

and

Timothy D. Comar
Benedictine University

The MAA Notes Series, started in 1982, addresses a broad range of topics and themes of interest to all who are involved with undergraduate mathematics. The volumes in this series are readable, informative, and useful, and help the mathematical community keep up with developments of importance to mathematics.

MAA Notes

Foreword: Looking Backward and Moving Forward in Undergraduate Life Science Quantitative Education

It is a pleasure to read the contributions in this book, particularly since the importance of mathematics in biology has only slowly been realized over the past several decades by the biological research and education community. When I organized a Quantitative Sciences Curriculum for the Life Sciences Students workshop in 1992 for leading practitioners of mathematical biology, there were few mathematics courses designed specifically for life science students and many bench biologists were unconvinced of a need for quantitative education. Although I did not know it at the time, several of the issues addressed in the 1992 and later workshops I organized had been the subject of the Cullowhee Conference on Training in Biomathematics held in 1961 at Western Carolina University in Cullowhee, North Carolina, and attended by many leading mathematical biologists. Issues addressed at the Cullowhee Conference still reverberate today, including: "To what extent should mathematical courses given to biologists be different from those given to mathematicians?" (H.D. Landahl) and "Traditional biology courses lay far too much emphasis on the direct acquisition of information. Insufficient attention is given to the interpretation of facts or to the drawing of conclusions from observation and experience." (J. G. Skellam).

So have we learned anything in the fifty years since the Cullowhee Conference? This volume is a testament to a resounding YES! Many model programs have been developed, curricular material has been assembled, biologists are more attuned to the utility of quantitative approaches, and education research provides guidance on what works – learning not training, research participation not canned labs, active learning and peer collaboration not listening to lectures. We have moved beyond anecdotes to the science of science education. The diversity of models and processes described in this book provides evidence of the need for alternative approaches to assist our students to become "fearless biologists" in utilizing quantitative concepts and skills so that they can not only assimilate, but also participate in modern biology.

Integrating quantitative perspectives throughout the undergraduate life science curriculum, a goal emphasized in the 1992 Workshop, is still a work in progress. The host of reports since that time, including *BIO2010* and *Vision and Change in Undergraduate Biology Education*, all emphasize the benefits of an integrative, multi-disciplinary view of modern biology with quantitative concepts and skills being a central component. This book provides evidence that there is institutional variation in successful methods to ensure that exposure to quantitative topics for life science students is not isolated in a few mathematics and statistics courses but are an integral part of the modern biologists' tool-box. The developers of the examples presented here are to be lauded for their willingness to take an integrative view of undergraduate biology education. The funding agencies that assisted them are to be encouraged by the progress to date and urged to continue to support successful ventures in quantitative education for all our students.

Louis J. Gross
National Institute for Mathematical and Biological Synthesis
University of Tennessee, Knoxville

Foreword: An Invitation to BIO SIGMAA

Although the history of mathematics and computation in biology began a long time ago, the history of this volume begins with the formation of BIO SIGMAA. In January of 2006, Carl Cowan and Michael Pearson spoke with me about the SIGMAAs of the MAA at the Joint Mathematics Meetings in San Antonio. Carl was President of the MAA at the time and saw mathematical biology as an important growing area in mathematics and one that might benefit from the SIGMAA program of the MAA. I had helped run several successful MAA PREP workshops related to mathematical and computational biology and I suppose that put me on Carl's list. I am also tall, which makes me easy to track down in a crowded room.

Over the next few days, we spent time talking with other people we thought might be interested in being a part of the SIGMAA. There was a great deal of support from people both more and less experienced than I. Somehow I found myself organizing the effort, but I was really just collating the ideas of others. I finished the first draft of the charter in April 2006 and after feedback, it was completed by July. In August 2006, BIO SIGMAA became the tenth SIGMAA.

Since biology can hardly be called a single field of study, mathematical and computational biology can be no less diverse. It was important from the beginning to be as inclusive as possible, welcoming all areas of biology and all approaches to understanding them. At the time the SIGMAA formed, there were several organizations promoting research in mathematical and computational biology, but the connection to educational practices and undergraduate research needed a broader platform and a bigger voice. BIO SIGMAA was created to strengthen the ties between research and education and to provide a venue for sharing ideas.

From 2006 to now, many people have put in a great deal of effort into BIO SIGMAA and it has grown in both numbers and maturity. This volume gives readers a taste of current educational practices in mathematical and computational biology. It represents approaches taken or proposed in different areas of biology, different approaches to the study of biology, and the relationship of these practices with different aspects of education.

There are many other ideas that did not fit into this volume and I feel sure new ideas will be motivated by those that did. I encourage everyone to share those ideas at an upcoming BIO SIGMAA event.

Eric Marland, founding board member of BIO SIGMAA
Department of Mathematical Sciences
Appalachian State University

Contents

Preface

This volume contains twenty-six articles on mathematics pedagogy for life science students, representing twenty-two institutions from large research universities to community colleges. While many of the articles discuss projects designed to fit a particular niche at a particular institution, each emphasizes lessons learned that could be applied elsewhere. The articles are sorted into three themes, Models, Processes, and Directions, as described in the General Introduction that follows the table of contents, and in the editorial introductions to the three parts. Curricular development in mathematics for biology is occurring at a variety of levels, including advanced undergraduate courses, interdisciplinary courses, alternatives to the standard calculus sequence, and complete curricula. Articles in the Models and Processes sections focus on curriculum projects on one of these levels. The division of the articles into two groups was motivated by the observation, made by many of the authors, that successful innovation in mathematics pedagogy for biology requires more than a good pedagogical idea. Several excellent projects have failed to become established because they could not attract sufficient enrollment or have fallen into disuse because they could not be institutionalized. We wanted to present them as outstanding models while addressing the reasons for their failure.

For the most part, articles in the Models section focus on the details of a curricular model, while articles in the Processes section focus on the issues involved in implementation. Some articles were written as a pair, one in each section, while others address both themes and were placed in whichever section seemed most appropriate; the connections are noted in the general introduction and the editorial introductions. Articles in the Directions section propose changes in emphasis and topic selection. We hoped to have articles on assessment of curricular projects as well, but we were unable to find any assessment results that we thought were sufficiently robust and exemplary to warrant inclusion as separate articles. A few of the articles contain assessment results, but there is clearly a need for assessment of curriculum projects that is only beginning to be met.

Each article begins with a brief summary of the institution and the students involved in the project; where possible, each indicates additional information accessible on the web. Other web resources can be found through the BIO SIGMAA and Bioquest web sites.

Many of the curriculum projects discussed in this volume started as responses to the publication in 2003 of the BIO2010 report of the National Academies. The report recommended improvements in the quantitative education of research biologists. It received some criticism from a small number of biologists who believed (incorrectly, in my opinion) that it was aimed primarily at medical research, but it was largely endorsed by biologists and thoroughly embraced by mathematics educators. "All" that remained was to implement its recommendations.

The Mathematics Association of America (MAA) published *Math and BIO2010*, edited by Lynn Arthur Steen, in 2005. It consists primarily of essays with suggestions for mathematics curriculum reform, but has very few concrete examples of successful programs. Simultaneously, a growing number of mathematics faculties began addressing problems of curriculum reform for their own institutions, and some textbooks from these projects were published in the first few years after *BIO2010*.

Mathematics curriculum development for biology expanded in 2006 with two developments. The first was that the planners for the Joint Mathematics Meetings (JMM) of 2007 found themselves with three distinct proposals for contributed paper sessions on mathematics education for biology. Two were consolidated, resulting in two distinct sessions. One was organized by Elton Graves of Rose-Hulman Institute of Technology; I organized the other with Jack Bookman, James Fulton, and Yajun Yang. The second development was the founding of the Biology Special Interest Group of the MAA (BIO SIGMAA) by Eric Marland of Appalachian State University. I was among the people invited by Eric to help form the group. I suggested that BIO SIGMAA's first action should be to sponsor my contributed paper session, which resulted in my selection as the first Program Director of BIO SIGMAA.

The mathematics-for-biology sessions at JMM 2007 were a great success. My session had so many contributors that it had to be broken into three parts. Though some parts were scheduled at undesirable times, the talks were well attended, with audiences ranging in size from twenty participants to more than fifty. The mathematics-for-biology sessions also caught the interest of people involved in publishing. Shortly after JMM 2007, I received offers for publications from *PRIMUS*[1] editor Brian Winkel and MAA Notes editor Steve Maurer. After discussions with the other JMM contributors, we arrived at a plan—I would edit a *PRIMUS* issue on ideas of small scope that could be implemented within the context of an individual course, and Jenna Carpenter and Tim Comar would join me in editing an MAA Notes volume on projects at the course and curriculum levels. The *PRIMUS* issue, published in January 2008, consisted of invited papers based on talks in my JMM session.

Jenna, Tim, and I planned this volume with help from Eric Marland. It was Eric who suggested that we should look for articles that would describe curricular models, discuss the curriculum change process, and suggest directions for the future. This led to the structuring of the volume in parts devoted to models, processes, and directions.

Some of the contributions for this volume were solicited from leaders in mathematics education for biology, but we also wanted to cast a wide net. We used the BIO SIGMAA listserv to send out a call for papers. This brought us a large number of proposals for articles, resulting in the twenty-six papers in this volume. The papers offer the reader a wealth of accumulated experience.

It appears likely that mathematics curriculum development for biology students will affect an increasing number of educational institutions. However, it is difficult to move from a good idea to an accepted course or curriculum. Models that meet the needs of one institution may not work for others. New courses or curricula need to be tested and refined at their own institution. For this reason, each article begins with a summary of the facts about the program and the institution. To the reader who is struggling with mathematics curriculum development for biology students, these articles offer an opportunity to make use of the experiences of those who have already faced the same challenges.

My co-editors and I want to acknowledge the valuable assistance of Steve Maurer and the team of reviewers that read through the articles. They had a lot of work to do with the first draft, owing to the lack of experience of the volume editors, but their critiques resulted in extensive changes for the better. While this volume has taken a long time to reach print— because of the large number of people and revisions involved—the extra time has allowed many articles to discuss how the projects changed over time. We hope that the information presented in this volume will inspire a new generation of successful curriculum models.

Glenn Ledder
November, 2012

---

[1] *Problems, Resources, and Issues in Mathematics Undergraduate Studies*

General Introduction

The mathematics curriculum as we know it grew out of the mathematical needs of physical science. We start with a full course in calculus, which requires three semesters at most institutions. This is followed by courses in linear algebra, differential equations, and calculus-based probability and statistics in some order. The latter subjects are the ones with the broadest applications in biology, along with several discrete topics that do not occupy a place in the physics-based mathematics curriculum. Biological applications in these courses have been rare until recently, but many authors are now incorporating biological examples. There are some books in these traditional areas for life science students, but there is no consensus mathematics curriculum for life science.

The standard biology curriculum includes very little mathematics, in spite of the development, beginning in the 1920s, of several important mathematical models for biology. The typical curriculum for biology majors includes just one course in calculus and one in non-calculus-based statistics, and anything beyond two courses is rare.

The result of the gap between the extensive mathematics background that is beneficial to biologists and the minimal mathematics background biology students acquire in their courses is an undergraduate education in biology with very little quantitative content. Mathematics could be incorporated into biology courses such as genetics and ecology, but this is difficult unless the biologist who teaches the course can count on students with the necessary mathematics background.

The obvious answer, from a mathematician's point of view, is for biology students to take the full calculus sequence followed by courses in linear algebra, differential equations, and probability with statistics. There are two problems with this answer. First, the courses contain almost no biology, being designed for the physical or social sciences. This could be fixed without a major curriculum change. More serious is the problem of fitting these courses into a biology student's program. As it is, all biology students are essentially double majors, with enough courses in mathematics, physics, and chemistry to encompass a major in general science, along with the major in biology. The addition of four more mathematics courses is impractical, even for biology students who have the interest and aptitude.

In this volume, authors from a variety of institutions address some of the problems involved in reforming mathematics curricula for biology students. The problems are sorted into three themes. We begin by examining curriculum Models. It is straightforward for mathematicians to generate curriculum ideas for the training of mathematicians, but it is more difficult to generate curriculum ideas for the training of biologists. A number of curriculum models have been introduced at various institutions, and a selection of them comprise the Models section. The second theme is Processes. Suppose we have created an outstanding course that clearly meets the needs of its students. This course amounts to nothing unless it is institutionalized in both the biology department, as a curricular requirement, and in the mathematics department, as a course that will be staffed even after the creator of the course is no longer on the faculty. The final theme is Directions. Here we look to the future, with each paper laying out a case for pedagogical developments that the authors would like to see.

There is some overlap between the Models and Processes themes. All of the Processes papers refer to some model, although its role is sometimes peripheral. Many of the Models papers mention process issues as well. Some contributors, such as Kubatko and Nance of Ohio State University, have pieces in both parts. Other papers were placed in whichever part seemed to be the better fit, but for some this was almost arbitrary. The papers by MacLean, Lee and Boyd, and Joplin et al combine almost equal doses of model and process; the first two appear in the Processes part and the last one in the Models part.

I
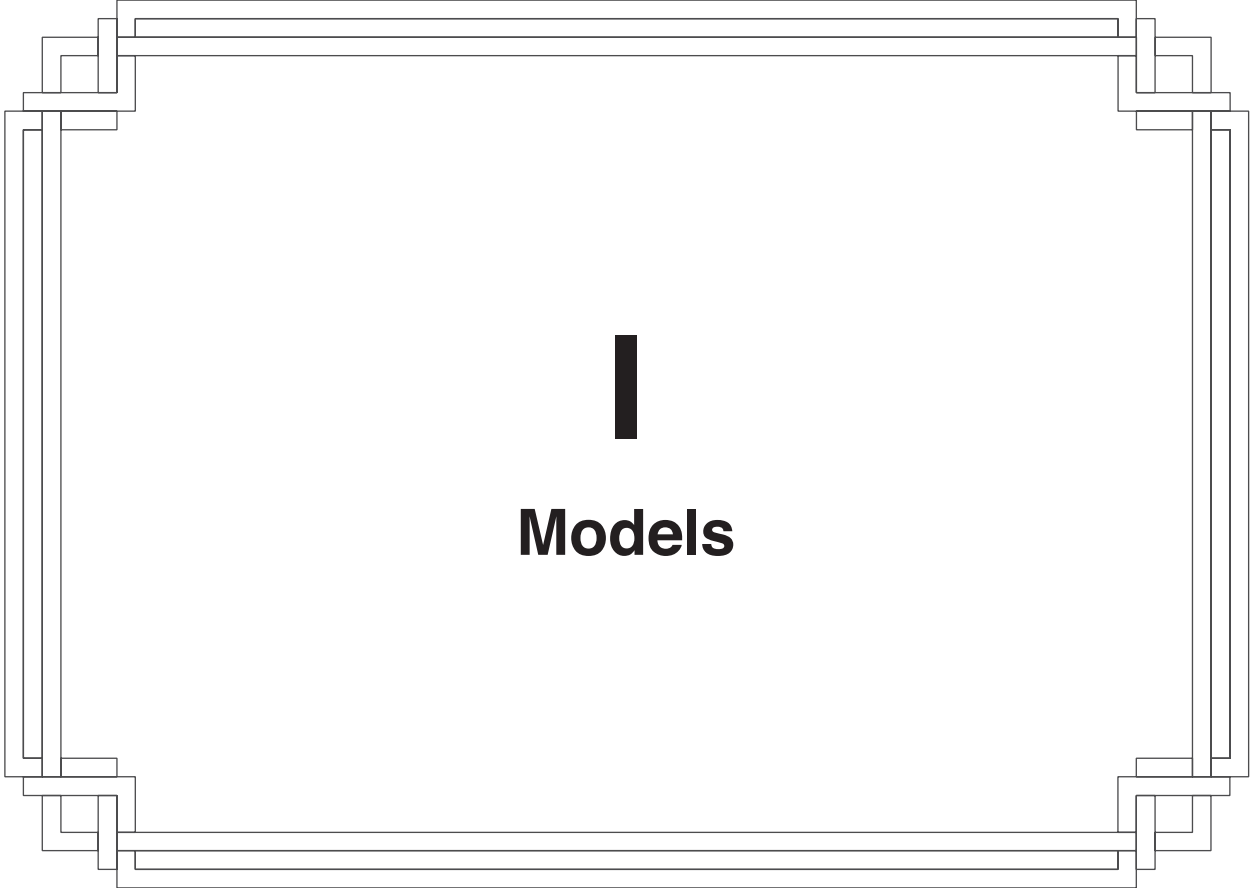
Models

Introduction

One reason for the diversity of curriculum ideas for biology is that there are only a small number of slots, perhaps only two or three, available in the packed curriculum of biology majors. A second reason is the lack of uniformity in the biology curriculum that the mathematics curriculum is supposed to support. Physicists are generally in agreement about what constitutes introductory learning in physics, which has led to a mathematics curriculum that varies little among institutions, with no issues more serious than the order of linear algebra and differential equations. Biologists, in contrast, have not yet reached a consensus on what constitutes introductory learning in biology. Accordingly, there is no single mathematics curriculum for biology that can be applied in all institutions.

In the past decade, a number of approaches to the problem of replacing the standard calculus sequence with something more appropriate for biologists have been made by mathematicians, with connections to various areas of biology. This broad issue of mathematics curricula for lower-division biology students is addressed in eight of the thirteen papers in the Modeling section, which fall into three classes.

The simplest approach, as seen in the first three papers, is to modify the courses that biology students are already taking, but to leave them compatible with the standard sequence so that students can move between the traditional physics-based and alternative biology-based courses. These three papers are arranged in order of increasing scope. We begin with a paper by Jerry Uhl and Judy Holdener that describes a one-semester biocalculus course at the University of Illinois that grew out of Jerry's well-known Calculus with Mathematica project and features significant use of a computer algebra system. Next is a paper by Tim Comar that describes the two-semester biocalculus sequence at Benedictine University. The courses incorporate dynamical systems and biology applications into the standard calculus sequence and also use computer laboratory projects. This group concludes with a paper by Laura Kubatko and colleagues that describes a two-quarter sequence of biology-oriented calculus courses, along with a one-quarter biology-oriented statistics course, at the Ohio State University. This group of papers offers a variety of options for modifying the standard curriculum.

A second approach, also represented by three papers, is to create a biology-based curriculum that does not try to be compatible with the standard curriculum. We can gain flexibility by diverging from the standard curriculum at the beginning, but at the cost of immediate tracking of students. The three papers in this group illustrate the variety that is made possible by abandoning the requirement of compatibility with standard courses. We have arranged these papers in order of decreasing seniority, beginning with a paper by Fred Adler that describes the one-year mathematics-for-biology curriculum he created at the University of Utah in the early 1990s. The Utah curriculum focuses on dynamical systems and probability/statistics, packaged to be accessible to students who have not previously taken a calculus course. Calculus topics are developed as needed. Next is a paper by several faculty at Macalester College that describes their Applied Calculus and Statistical Modeling sequence. Do not be misled by the word "Applied." Whereas the title Applied Calculus normally is used for the brief treatments designed for business students and often foisted on biology students, the Macalester Applied Calculus course is designed for students who have already had some exposure to calculus. It begins with a treatment of functions and differential calculus and concludes with material on differential equations and linear algebra. The Statistical Modeling course offers a calculus-based curriculum designed around statistical problems in biology. In the final paper of this group, Lester Caudill describes the Scientific Calculus sequence and a biomedical modeling course at the University of Richmond. The first semester in the Scientific Calculus sequence adds modeling, regression, and multivariable optimization to a first-semester calculus core, while the second semester focuses on probability, Taylor series, and dynamical systems. The third course focuses on modeling and dynamical systems. Having a third course makes it possible for the Richmond curriculum to retain more topics from

standard calculus than the other projects in this group. Readers interested in full-year freshman curricula will also want to look at the article by Lou Gross in the Processes section of this volume.

Recently, there has been some interest in the intermediate strategy of a standard-curriculum-compatible one-semester calculus course followed by a terminal one-semester course designed for biology students. This approach offers more flexibility than the first approach without the immediate tracking of the second. In the first paper of this group, I describe the Mathematical Methods for Biology and Medicine course that I created at the University of Nebraska. It begins with basics of mathematical modeling, with a focus on working with parameters and fitting data to models, before turning to probability distributions and concluding with dynamical systems. In the second paper of this group, Claudia Neuhauser describes a course at the University of Minnesota called Modeling Nature and the Nature of Modeling. This course focuses on discrete and continuous dynamical systems before turning to some partial differential equation models and stochastic processes, with an emphasis on computer modeling in Excel and Matlab.

The remaining papers in the Models section concern projects that fill specific niches identified at their institutions. Each is highly interdisciplinary and taught by a team that includes life science and mathematics faculty. Many include student research. Three focus on topics that do not normally appear in the mathematics curriculum and one encompasses basic biology as well as basic mathematics. They are examples of creative curriculum development in mathematical biology.

The papers by Rohan Attele and Dan Hrozencik of Chicago State University and by Glenn Ledder, Brigitte Tenhumberg, and Travis Adams of the University of Nebraska describe two approaches to designing a course based more on research than on specific content. Attele and Hrozencik describe a sophomore-level course in which students learn computational linear algebra and matrix population models before studying molecular evolution and phylogenetic trees. Students work in interdisciplinary teams on a research problem in population demographics. Ledder, Tenhumberg, and Adams describe a pre-college or freshman-level course centered on a research project in theoretical ecology. The students collect data on rates of aphid birth, growth, and death, which they use to parameterize a matrix model of aphid population growth. Another experiment collects population data used to test the predictions of the model. The lecture portion of the course supplements the laboratory portion by teaching students the methods and concepts needed for modeling and data analysis.

The next paper, by Raina Robeva, Robin Davies, and Michael Johnson, describes a Biomathematics course taught at Sweet Briar College by a team of one mathematician and one biologist to mathematics and biology majors who have taken courses in calculus, statistics, and general biology. The course employs mathematical methods to treat problems chosen for their biological content. These include Boolean network analysis, a topic that is nicely described in a paper by Martins, Vera-Licona, and Laubenbacher that appears in the Directions section of this volume.

In the next paper of the Models section, Steven Deckelman describes the bioinformatics program of the mathematics department at the University of Wisconsin-Stout. It is built from courses in computer science, biology, chemistry, and mathematics, and features a capstone course called Mathematical and Computational Foundations of Bioinformatics.

The final paper in the Models section describes an integrated year-long freshman sequence at East Tennessee State University that is equivalent to one statistics course, one calculus course, and three biology courses. The reader interested in interdisciplinary courses should also look at the paper by Mark MacLean in the Processes section.

The thirteen papers in the Models section do not provide a comprehensive listing of curriculum projects in mathematics for biology students, but they do contain a rich variety of projects that represent solutions to pedagogical problems that are partly general and partly dependent on the institutional setting. Readers who do not find a model here that they can adapt to their institution will at least find elements to incorporate into their own innovative model. Three additional papers in the Processes section (one by Lee and Boyd, one by Ardis and Subramanian, and one by Hom, Leaver, and Wilson) also contain significant descriptions of curriculum models.

1

BioCalc at Illinois

J. Jerry Uhl
Department of Mathematics, University of Illinois-Urbana

Judy Holdener[1]
Department of Mathematics, Kenyon College

Name of Institution	University of Illinois-Urbana
Size	28000 undergraduates and 9000 graduate students
Institution Type	large state university with PhD program
Student Demographic	recent high school graduates with high potential and interests in mathematics and/or biology
Department Structure	Mathematics and Biology are individual departments in the College of Arts and Sciences

Abstract

BioCalc is a Mathematica-driven calculus course for life science students. It has been taught at the University of Illinois since the fall of 1993. In this article we describe how the course came to be, how it is structured, and how it differs from other calculus courses. We also provide a sample of the electronic notebooks used in the course. Finally, we report on some of BioCalc's successes.

1.1   Course Structure

- Weeks per term: 15-week semester
- Classes per week/type/length: One or two 1-hour lecture periods
- Labs per week/length: Three or four 1-hour laboratory periods

---

[1] holdenerj@kenyon.edu

- Average class size: Sections are capped at 20.
- Enrollment requirements: First-year students in the biological sciences. Students cannot enroll unless they are life science majors.
- Faculty/dept per class, TAs: Typically taught by a graduate TA in mathematics or sometimes a faculty member. There is also one undergraduate class assistant.
- Next course: Life science majors must take two of Calculus I, Calculus II, and Statistics, so some continue on to Calculus II.
- Website: http://www-cm.math.uiuc.edu/

1.2   Introduction

In the late 1980s at Illinois, our Illinois-Ohio State group developed a Mathematica-based calculus course now offered at Illinois. By the early 1990s, the Mathematica-based calculus sequence *Calculus & Mathematica* (C&M) (Uhl et al., 2006) had been class-tested and revised. In this revision, we decided to place heavy emphasis on life science models because our vision of calculus had become that it is the study and measurement of growth. This led the way to an emphasis on teaching calculus with life science models. After all, what grows? Animals, populations, and epidemics do. As our course evolved, we could see that many students from a variety of fields, including engineering, identified better with the life science models than they did with the physics examples that are typically used in a calculus course. At that point a fortuitous event occurred . . .

Professor Sandra Lazarowitz of the School of Life Sciences at Illinois called one of us and said that the standard calculus course was not connecting with the life science students, who were not interested in computing the work done by a force or the position of a projectile. The engineering emphasis in calculus sent the signal that it had little to do with their future careers in the biological sciences. As evidence of the disconnect, Professor Lazarowitz said that approximately 60% of the life science majors enrolled in the traditional Calculus I course were receiving a grade of C or lower in the course. It is a common misconception that life science students are weak in mathematics. We told her we were working on a calculus course that might be better suited for her life science students.

In the fall of 1993, two Calculus & Mathematica sections were reserved for life science students. The pilot sections were small (approximately 16 students each) and were taught by graduate teaching assistants Judy Holdener and Bill Hammock in a computer lab located within the Life Sciences building.[2] The ACT scores of the students suggested that they would be at risk in traditional calculus, and many of the students had a high degree of math phobia. Despite these disadvantages, the students flourished in the experimental C&M sections. Professor Lazarowitz, who was also the Director of the Howard Hughes Program for Undergraduate Education in the Life Sciences at Illinois, happily reported "first year life science students [in Calculus & Mathematica sections] are studying mathematical models normally reserved for senior math majors, and student responses have been enthusiastic." She was encouraged by the success rate, reporting that life science students who would likely have dropped a traditional offering of calculus were able to earn As with the new approach. As a result of the success of the pilot sections, the Department of Mathematics and the School of Life Sciences entered into an agreement to call the course "BioCalc" and to make it a permanent offering for life science students.

After seventeen years, life science students continue to flourish in BioCalc. Using university records, staff at the Howard Hughes Medical Institute assessed the course in April of 2001 and cited the following conclusions in their report on the course (Fahrbach et al., 2001):

- The BioCalc course is equally attractive to life sciences students required to take Math 120 (the standard calculus course at Illinois). No life sciences option is over- or underrepresented.
- BioCalc students are as well prepared for Math 130 (the second calculus course in the standardsequence) as non-BioCalc students, as judged by the grade obtained in Math 130.

---

[2] This lab was funded by the Howard Hughes Medical Institute (HHMI).

- BioCalc students are roughly twice as likely to take an additional math course than non-BioCalc students.
- BioCalc students (80.4%) are slightly more likely to remain in a biological science major than non-BioCalc students (76.7%).
- CalcPrime successfully prepares for BioCalc those students who do not place into Math 120.[3]

1.3   The Differences between BioCalc and the Standard Calculus Course

So what is it that makes BioCalc so different from the traditional offering of calculus? Here are some differences:

Greater emphasis on applications and life science models in particular.

One of the biggest reasons for the success of BioCalc is its emphasis on life science models that reveal the relevance of calculus and reinforce the meaning of the derivative. There are exercises examining the decay of cocaine in the blood, models describing the spread of a disease, and data analyses investigating the correlation between cigarette smoking and lung cancer. Students examine data relating to the U.S. and world populations, the U.S. national debt, and the number of a space shuttle's O-ring failures. They compute the optimal speed of a salmon swimming up a river, and they model the growth rates of an animal's height and weight over time. (See the next section.) In BioCalc, life science students get enough experience to see for themselves that calculus plays a role in their lives and in their planned careers. One BioCalc student put it this way: "What we learned applies in our classes and in our lives."

Greater emphasis on visualization.

The authors of the electronic notebooks used in BioCalc have gone to great lengths to help the student learn visually. The "textbook" is a sequence of interactive electronic notebooks that introduce new ideas using graphic examples and geometric interpretations. By working through the notebooks, students experience mathematics at their own pace by seeing it happen and making it happen. The graphics offered by Mathematica allow students to create the mental images necessary to understand calculus—images that students won't always be able to create for themselves.

Less emphasis on mathematical language and proof but more emphasis on conceptual explanation.

Students in introductory calculus sometimes find the language of mathematics (i.e., the symbols and technical terminology) to be impenetrable, but among life science students the language barrier tends to be endemic. BioCalc circumvents the problem by using graphics and applications as the entry points for new material. Formal definitions and notation are introduced only after students internalize the ideas. Because most introductory calculus students will not choose careers involving the writing of mathematical proofs, BioCalc places a lesser emphasis on the writing of formal proofs and a greater emphasis on the use of calculus as a tool for solving problems.

Greater emphasis on writing and communication.

Although BioCalc places less emphasis on the writing of formal proofs, it places on a greater emphasis on writing. The electronic notebooks include numerous exercises that require students to describe what they see on the computer screen and to analyze what is happening. The students use their own words, and the writing solidifies their understanding of the material.

Studying the comprehensive group of models offered by BioCalc is possible only because of the computational and graphical power offered by Mathematica. Students regard Mathematica as a professional tool, and they are delighted to use it because most of them arrived in BioCalc knowing their hand computation skills were not at the level required for success in a standard calculus course.

---

[3] CalcPrime is a three-week transitional summer program for entering students at Illinois who underperform on the placement exam for MATH 120. CalcPrime students have lower Math ACT scores than other BioCalc students, and they are more likely to be non-Caucasian-American.

1.4   The Format of BioCalc

So how are the BioCalc lessons structured and what exactly do students do in and out of class? The "textbook" is electronic, consisting of a series of interactive Mathematica notebooks, and students learn calculus by working through tutorial problems, experimenting with built-in Mathematica routines, and explaining graphical and computational output. Each lesson follows the same format, with four components:

- The *Basics* section introduces the fundamental ideas in the lesson by presenting problems and explanations, often visual in nature. Students are encouraged to experiment with the problems by changing functions and numbers and rerunning the Mathematica code. Many of the problems prompt students to make conjectures about the patterns they observe in the computer output.

- The *Tutorial* section, like the *Basics* section, presents problems for the student, but the focus is on techniques and applications that relate to the ideas presented in the *Basics* section.

- The *Give it a Try* section is the heart of the course, providing a list of problems to be solved and submitted (electronically) by the student. Like the *Tutorial* section, problems are often application-based, incorporating models from the life sciences. Information needed to solve the problems is found in the *Basics* and *Tutorial* sections.

- The *Literacy Sheets* present problems to be worked out with paper and pencil. This section is completed after the student has already completed the electronic portions of the lesson.

Although the format may vary with the instructor, most BioCalc lessons are conducted in a computer lab. On a typical lab day, students work through the electronic notebooks at their own pace, asking questions of the instructor as needed. On every third or fourth session, the class meets in a standard classroom for a traditional chalkboard discussion. Students are graded on the electronic work they complete (in the *Give it a Try* section of the lesson) and the written work they do on the *Literacy Sheets*. Exams generally have both a written component and a computer component.

1.5   BioCalc Sampler

In this final section, we reveal the flavor of BioCalc's electronic lessons by examining BioCalc's coverage of the chain rule. The chain rule is often associated with hand computation in calculus, but BioCalc students learn it in parallel with constructing height and weight functions to model the growth of animals over time. We will illustrate below, starting with the first mention of the chain rule. (Incidentally, BioCalc does *not* allow students to rely on the computer for the computation of derivatives, among other things. A basic literacy is expected of the students.)

In introducing the chain rule, the *Basics* section starts by encouraging students to look for patterns in the derivatives of compositions of functions. What follows is taken directly from the electronic notebook covering the differentiation rules. Mathematica syntax is in bold (the code has not been executed).

- - - -
B.2) The chain rule: D[f[g[x]],x]=(f$'$)[g[x]] (g$'$)[x]

Let's check out the derivative of the composition of two functions.
Here is the derivative of Sin[x^2]:

Clear[f,x];
f[x_]=Sin[x^2]; (f$'$)[x]

Or

D[Sin[x^2], x]

This catches your eye because the derivative of Sin[x] is Cos[x] and the derivative of x^2 is 2x. It seems that the derivative of Sin[x^2] is manufactured from the derivative of Sin[x] and the derivative of x^2. Here is the derivative of (x^2+ Sin[x])^8:

D[(xˆ2+Sin[x])ˆ8, x]

This catches your eye because the derivative of xˆ8 is 8 xˆ7 and the derivative of xˆ2+ Sin[x] is 2x+Cos[x]. It seems that the derivative of (xˆ2+ Sin[x])ˆ8 is manufactured from the derivative of xˆ8, the derivative of Sin[x], and the derivative of xˆ2. Here is the derivative of f[g[x]]:

Clear[f,g]; D[f[g[x]],x]

Very interesting and of undeniable importance. This formula, which says that the derivative of h[x]=f[g[x]] is h′[x]=f′[g[x]] g′[x], is called the chain rule. Do a check:

Clear[f,g,x];
D[f[g[x]], x]==f′[g[x]]g′[x]

The chain rule tells you how to build the derivative of f[g[x]] from the derivatives of f[x] and g[x]. Here is the chain rule in action:
If h[x]=Sin[xˆ2], then h′[x]=Cos[xˆ2] 2 x in accordance with:

D[Sin[xˆ2], x]

And if h[x]=(xˆ2+ Sin[x])ˆ8, then h′[x]=(8 (xˆ2+ Sin[x]))ˆ7 (2 x+ Cos[x]) in accordance with:

D[(xˆ2+Sin[x])ˆ8, x]

B.2.a) Give an explanation of why the derivative of f[g[x]] is f′[g[x]] g′[x].

Answer: Put h[x]=f[g[x]].
Recall that h[x] grows h′[x] times as fast as x.
But
  ➜ f[g[x]] grows f′[g[x]] times as fast as g[x]
  ➜ g[x] grows g′[x] times as fast as x.
As a result, f[g[x]] grows f′[g[x]] g′[x] times as fast as x.
This explains why the instantaneous growth rate of f[g[x]] is f′[g[x]] g′[x].
In other words, the derivative of f[g[x]] with respect to x is f′[g[x]] g′[x].
This rule is called the chain rule, and it is important.

- - - -

After presenting this explanation of the chain rule, the *Basics* section continues with more examples, presenting the derivatives of $\sin(5x)$, $\sin(x^4)$, $(g(x))^3$, $f(x^3 y^2)$ (with respect to y), and $(e^x - x^2)^7$.

Later in the *Tutorial* section, the students examine the effects of scaling on surface area and volume and use the chain rule to explain why the instantaneous percentage growth rate of the weight of a Bernese Mountain Dog is three times the instantaneous percentage growth rate of the height. In the excerpt of the electronic textbook that follows, the only Mathematica output included are the plots. The rest of the output is excluded for the sake of space.

- - - -

T.3) Linear dimension: length, area, volume and weight

The volume measurement, V[r], and the surface area measurement, S[r], of a sphere of radius r are given by
    V[r]=(4 \[Pi] rˆ3)/3
    S[r]=4 \[Pi] rˆ2.
This says that V[r] is proportional to rˆ3 and S[r] is proportional to rˆ2.
For other three-dimensional objects, the formulas for volume and surface area are not so easy to come by, but the idea of proportionality survives. Here is the idea: A linear dimension of a given solid or shape is any length between specified locations on the solid. The radius of a sphere or the radius of a circle is a linear dimension. The total length of a solid, the total width, and the total height of a solid are examples of linear dimensions. The diameter of the finger loop on a coffee cup is a linear dimension of the cup.

Next take a given shape for a solid. If it stays the same but the linear dimensions change, then it is still true that the volume is proportional to the cube of any linear dimension and it is still true that the surface area is proportional to the square of any linear dimension.

Here is a shape in the x-y plane and the same shape with its linear dimensions increased by a factor of 3:
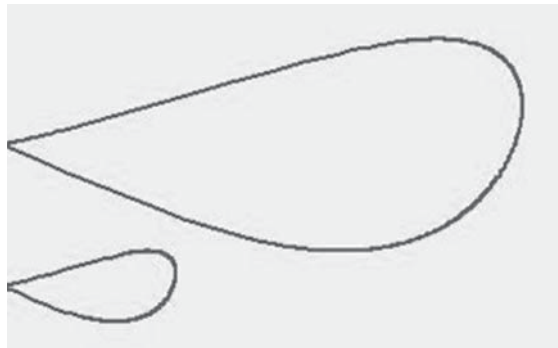
T.3.a) How does the area measurement of the larger blob above compare to the area measurement of the smaller blob?

Answer: Both are the same shape, but the linear dimensions of the larger blob are three times the linear dimensions of the smaller blob. The upshot: The area measurement of the larger blob is 3ˆ2=9 times the area of the smaller blob.

T.3.b) The idea of linear dimension leads to some intriguing biological implications. A giant mouse with linear dimension ten times larger than the usual mouse would not be viable because the volume of its body would be larger than the volume of the usual mouse by a factor of 10ˆ3, but the surface area of some of its critical supporting organs like lungs, intestines and skin would be larger only by a factor of 10ˆ2. That big mouse would be hungry and out of breath at all times! Similarly, there will never be a 12-foot-tall basketball player at Indiana or even at Duke. The approximate size of an adult mammal is dictated by its shape! The same common sense applies to buildings and other structures. An architect or engineer does not design a 200-foot-tall building by taking a design for a 20-foot-tall building and multiplying all the linear dimensions by 10. Now it's time for a calculation.

A crystal grows in such a way that all the linear dimensions increase by 25%. How do the new surface area and new volume compare to the old surface area and volume?

Answer:

Clear[newsurfacearea,oldsurfacearea];
newsurfacearea = 1.25ˆ2 oldsurfacearea

An increase of the linear dimensions by 25% increases the surface area by about 56%.
The percentage increase in volume is:

Clear[newvolume,oldvolume];
newvolume = 1.25ˆ3 oldvolume

An increase of the linear dimensions by 25% increases the volume by about 95%.

T.3.c.i) Calculus & Mathematica thanks Ruth Reynolds, owner of Pioneer Bernese Mountain Dog Kennel in Greenwood, Florida, for the data used in this problem.

Dogs and other animals grow so that a linear dimension of their bodies is given by what a lot of folks call a logistic function (b c eˆ(a t))/(b - c + c eˆ(a t)) , where t measures time in years elapsed since the birth of the animal. A good linear dimension for a dog is the height of the dog's body at the dog's shoulders:

Clear[height,a,b,c,t];
height[t_]=(b c Eˆ(a t))/(b-c+c Eˆ(a t))

To see what the parameters a, b, and c mean, look at:

height[0]

This tells you that c measures the dog's height at birth. The global scale of height[t]=(b c eˆ(a t))/(b - c + c eˆ(a t)) is
(b c eˆ(a t) eˆ(a t))/c=b. This tells you that b measures the dog's mature height. For a typically magnificent Bernese
Mountain Dog, as owned by the actor Robert Redford, b=24 inches and c=4.5 inches; so for the Bernese Mountain
Dog, height[t] is:

b=24.0;
c=4.5;
height[t]

The parameter a is related to how fast the dog grows. At one year, a typical Bernese Mountain Dog has achieved
about 95% of its mature height. This gives you an equation to solve to get a:

equation=height[1]==0.95 (24.0)

Solve[equation,a]

Now you've got the height function for the typical Bernese Mountain Dog:

a=4.41078;
height[t]

Here's a plot:

heightplot = Plot[{height[t],b,c},{t,0,2},PlotStyle-
>{{Thickness[0.01]},{Brown},{Brown}},PlotRange->All,AxesLabel-
>{"t","height[t]"}]
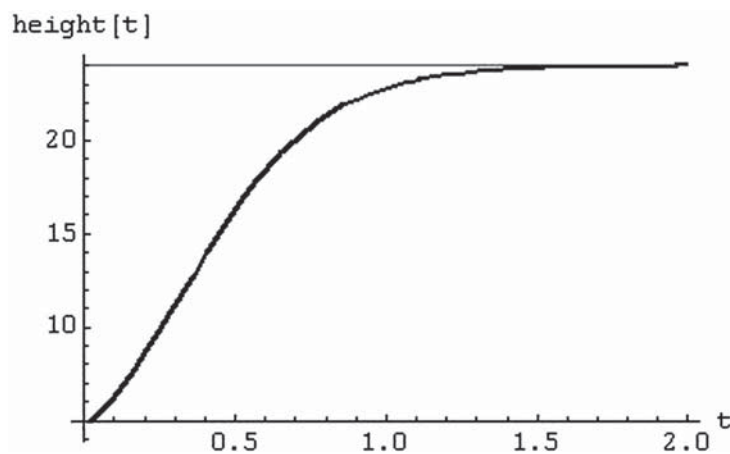
Looks OK.

Given that the typical mature Bernese Mountain Dog as described above weighs 85 pounds, give an approximate
plot of the dog's weight as a function of time for the first three years and give a critique of the plot.

Answer: If you assume the dog maintains the same shape throughout the growing process, then you can say:
  ➔ weight[t] is proportional to the volume of the dog's body at time t and
  ➔ the volume of the dog's body at time t is proportional to height[t]ˆ3. So
    weight[t] = k (height[t])ˆ3 =k ((b c eˆ(a t))/(b - c + c eˆ(a t)))ˆ3.
The global scale of weight[t] is k ((b c eˆ(a t))/(c eˆ(a t)))ˆ3=k bˆ3. For the typical Bernese Mountain Dog under
study here, k is given by:

Solve[85==bˆ3 k,k]

The weight of the typical Bernese Mountain Dog under study here t years after her birth is:

Clear[weight];
weight[t_] = 0.00614873 height[t]^3

Here comes a plot:

weightplot = Plot[{weight[t],85},{t,0,2},PlotStyle-
>{{Thickness[0.01]},{Brown},{Brown}},PlotRange->All,AxesLabel-
>{"t","weight[t]"}]
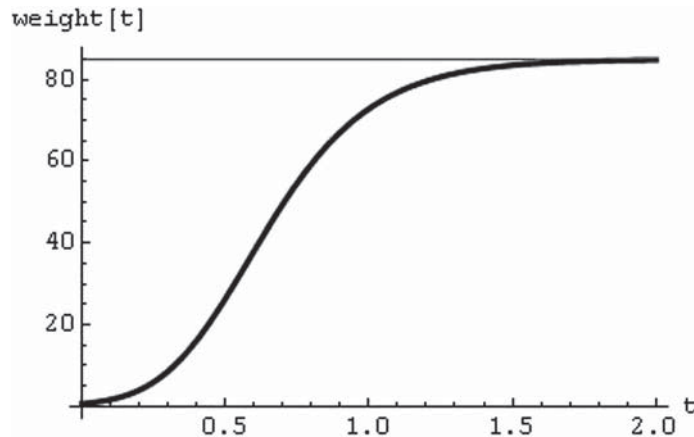
See the height plot and the weight plot side by side:

Show[GraphicsArray[{heightplot,weightplot}]]
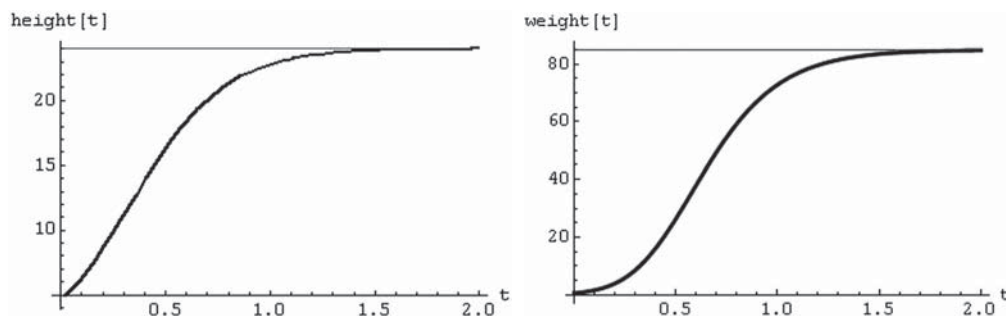
Somewhat interesting.

Now comes the bad news: The dogs do not maintain the same shape throughout their growing years; they maintain only approximately the same shape as they grow.

The upshot: The weight plot should be regarded only as an approximation of the true story. One way to check it is to see what it predicts the birth weight of a Bernese Mountain Dog pup is:

weight[0]

In ounces:

weight[0] 16

Not bad. The typical birth weight of a Bernese Mountain Dog pup is 14 to 20 ounces. The approximation above is off, but not by very much.

T.3.c.ii) Here are plots of the instantaneous growth rates of the weight and height of the Bernese Mountain Dog.

Plot[{(weight′)[t],(height′[t]},{t,0,2},PlotStyle->{Thickness[0.01],Red},AxesLabel-
>{"t","Instantaneous growth rates"}]

Instantaneous growth rates
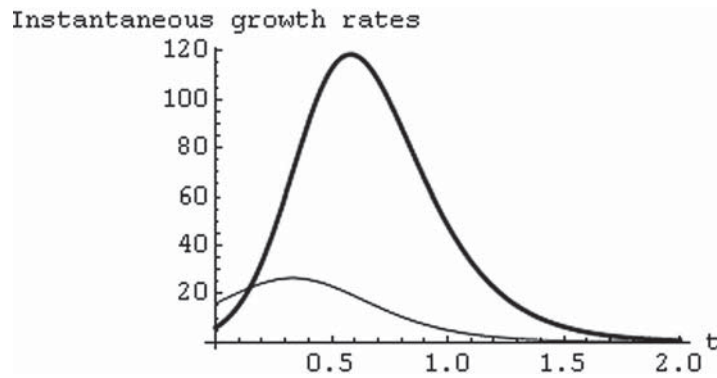
The height spurt happens before the weight spurt. This tells you that leggy adolescent animals are probably mathematical facts rather than anecdotal observations. Maybe someday someone will discover the mathematics of pimples.

Now look at plots of the instantaneous percentage growth rates of the weight and height of the Bernese Mountain Dog.

Plot[{(100 (weight′ [t])/weight[t],(100 (height′[t])/height[t]},{t,0,2},PlotRange->All,PlotStyle->{Thickness[0.01],Red},AxesLabel->{"t","Instantaneous percentage growth rates"}]

Instantaneous percentage growth rates
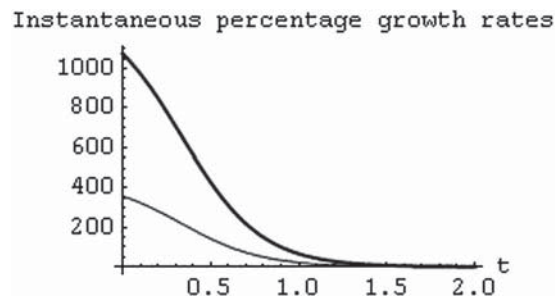
This plot looks a little suspicious.
It makes the strong suggestion that the instantaneous percentage growth rate of the weight is three times the instantaneous percentage growth rate of the height.
Is this an accident?

Answer: Get off it. In mathematics, there are no accidents.

Remember
    weight[t]=k height[t]^3.
So by the chain rule
    weight′[t]=3 k height[t]^2 height′[t].
Consequently, the instantaneous percentage growth rate of the weight is given by
    100 (weight′ [t]/weight[t]
    = 100 (3 k height[t]^2 (height′ [t])/(k height[t]^3)
    = 3 100 (height′ [t]/height[t]
    = 3 (instantaneous percentage growth rate of the height).
The upshot: No matter what the height function is, the instantaneous percentage growth rate of the weight is three times the instantaneous percentage growth rate of the height.

A new piece of biological insight brought to you by the chain rule.
- - - -

In the *Give it a Try* section following the *Tutorial*, students are required to perform a similar analysis to model the height and weight functions of Haflinger horses. Using these functions they determine whether or not a Haflinger horse grows up before it grows out. Finally, the students are asked to do a similar analysis on themselves. As the students discover, they can produce their own height and weight functions knowing just four numbers: their height at birth, their height at maturity, the percent of mature height achieved at a given age, and their weight at maturity.

The final section of the lesson, the *Literacy Sheets*, consists of a list of problems to be completed by hand. The section starts with a list of twenty-five derivatives, eighteen of which require an application of the chain rule—sometimes in tandem with some other rule, like the product rule, quotient rule, or power rule. Other problems addressing the chain rule are conceptual, as illustrated by these two problems:

> If Jenny does trig identities A times faster than Sam and Sam does trig identities B times faster than Cal, then Jenny does trig identities AB times faster than Cal. How is this little story related to the chain rule?

> If $f(x) = \sin(g(x))$, then $f'(x) = \cos(g(x))g'(x)$. How do you know this is correct?

As already mentioned, students in BioCalc are asked to write explanations throughout the course.

1.6   Interested in Using the BioCalc Materials?

Because self-paced Mathematica notebooks (like the one outlined above) drive the BioCalc course, the course must be taught in a computer-equipped classroom. However, the necessary infrastructure is minimal. Computers need only to be capable of running Mathematica (see http://www.wolfram.com/support/).

To learn more about BioCalc and other Mathematica-driven courses offered at Illinois, see http://www-cm.math .uiuc.edu/. The reader interested in accessing the BioCalc materials should contact the NetMath Project Director at netmathinfo@cm.math.uiuc.edu.

In Memoriam: J. Jerry Uhl (1940–2010)
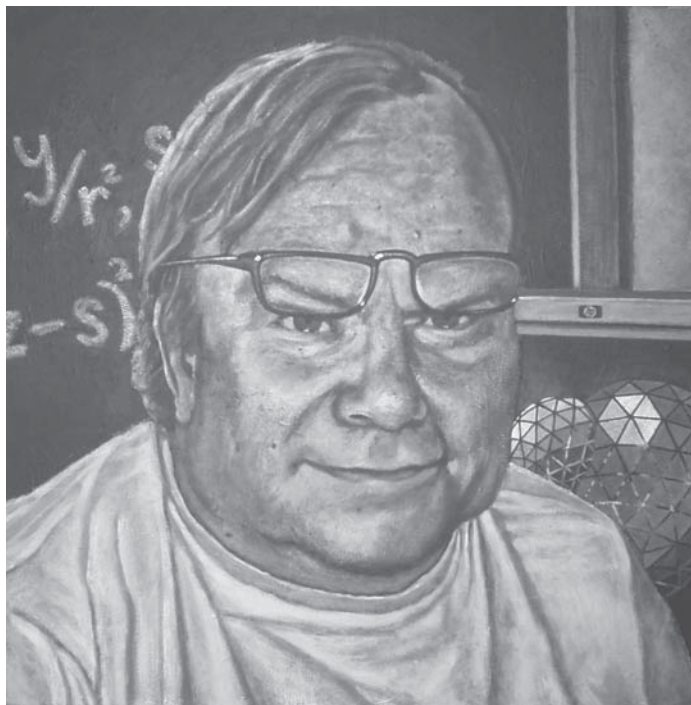
 "Jerry"—painted by Judy Holdener in 2005. In the painting, Jerry is seated in front of his computer. The computer-generated surface represents Jerry's belief that visualization plays a significant role in students' understanding of mathematics.

A few words from the second author: Jerry passed away during the final revisions of this article. A beloved professor, mentor, and friend, he played a significant role in my development as a teacher. Besides revealing the importance of student-centered learning, he taught me to take risks in my teaching, and he continues to inspire me to be a transformational force for my students. I will miss his humor, his playfulness, his passion, and the mischievous and outspoken way in which he responded to bureaucratic nonsense.

References

Fahrbach, S., C. Washburn, and N. Lowery, 2001: *The Impact of BioCalc on Life Sciences Undergraduates at UIUC*, a report prepared for the Howard Hughes Medical Institute, 13 pp., University of Illinois\Kenyon College.

Uhl, J.J., W. Davis, and H. Porta, 2006: *Calculus & Mathematica* at UIUC, [available online at http://www-cm.math.uiuc.edu/].

2

Biocalculus at Benedictine University

Timothy D. Comar[1]

Department of Mathematics, Benedictine University

Name of Institution	Benedictine University
Size	3500 undergraduate students, 8900 students in total
Institution Type	mid-sized university primarily devoted to undergraduate education with some graduate and professional programs
Student Demographic	recent high school graduates and community college transfers with interest in pursuing medical careers
Department Structure	Mathematics and Biology are individual departments in the College of Science

Abstract

This paper describes the biocalculus course sequence at Benedictine University. Benedictine University offers a two-semester biocalculus course sequence that integrates calculus-based mathematics, biological models, and computational software. In addition to the biocalculus courses, all first semester calculus students at Benedictine University take a computer laboratory course, which includes several biological applications. The paper concludes with a discussion of the success of the courses and of the challenges still facing them. This article is unique in that it describes a rigorous, introductory mathematical biology course sequence that can be implemented at small to mid-sized institutions in which only a limited number of sections of calculus are offered each year.

2.1 Course Structure

- Weeks per term: 15 weeks
- Classes per week/type/length: Biocalculus I: 4 50 minute lecture periods per week; Biocalculus II: 3 50 minute lecture periods per week

---

[1] tcomar@ben.edu

- Labs per week/length: Calculus with Analytics I Lab/Biocalculus II Lab: 1 2 hour period per week
- Average class size: Biocalculus I: about 15 students in each of two sections; Biocalculus II/Biocalculus II Lab: 5–10 students in one section; Calculus with Analytics Lab: up to 20 students
- Enrollment requirements: Biocalculus I: placement exam; Biocalculus II: a grade of C in Biocalculus I or Calculus with Analytics I
- Faculty/dept per class, TAs: One mathematics structure per class; same instructor for Biocalculus II and Biocalculus II Lab
- Next course: Biocalculus II/Biocalculus II Lab follows Biocalculus I. Students may take Calculus with Analytics III group or Mathematics Research after Biocalculus II.

2.2   Introduction

Benedictine University is private, primarily undergraduate institution located in the western suburbs of Chicago. Of the 3500 students enrolled as traditional undergraduates, over 500 are majoring in the biological and health sciences. Benedictine University has a reputation for involving undergraduate science and mathematics majors in research and regularly sends graduates to professional and graduate programs. The biocalculus course sequence at Benedictine was developed in response to the *Bio 2010* report (National Research Council 2003) to increase the mathematical and quantitative training for future researchers in the biological sciences and to provide a relevant calculus experience for biology students. There is also a recent push at Benedictine University for students to engage in interdisciplinary research involving mathematics and biology. The course sequence is now the required mathematics sequence for students in the research oriented Biochemistry/Molecular Biology (BMB) major, which was recently revamped in accordance with *Bio 2010* recommendations.

The course design was affected by the needs and nature of the student body and the Department of Mathematics' ability to staff calculus courses and laboratories. We have considered students who will take only a single semester of calculus, students who need a year of calculus-level mathematics, and students who intend to take more mathematics courses. When the courses were designed, trigonometry was the required mathematics course for biology and health science majors. We also have students who have been admitted into a dual acceptance program with a local pharmacy school. These students spend only two years at Benedictine University and have room for only one semester of calculus. Because of students who will only take one semester of calculus, it is important that the first semester biocalculus course include biological models and biologically-oriented computer laboratory projects.

We realize that majors in the biological sciences may not have the credit hours available to take additional mathematics courses beyond a year of calculus as undergraduates. We have chosen mathematical topics that enable students to develop a foundation in calculus and to be able to use mathematical and computational techniques to analyze biological mathematical models represented by systems of difference equations or differential equations by the end of the second course. On the other hand, it is necessary at our institution to keep the biocalculus sequence and the traditional calculus sequence at the same level of rigor so that students can switch tracks for their second course and so that all students would be prepared to succeed in a traditional third semester calculus course.

Another significant and unique aspect of first semester calculus at Benedictine University is that all students in the traditional first semester calculus course and the first semester biocalculus course must enroll in a common laboratory course, Calculus with Analytics I Laboratory (hereafter, Lab I). The course schedule is flexible so that it can be used for mixed classes of students from both versions of first-semester calculus. The course also lets us assess and compare performance between students in Biocalculus I and the traditional Calculus with Analytics I (hereafter, Calculus I).

Biocalculus I was first offered in Fall 2003, and Biocalculus II was first taught in Spring 2005. Enrollment levels initially ranged from ten to sixteen students in Biocalculus I and from five to six students in Biocalculus II. Currently, there are two sections of Biocalculus I offered each fall with average enrollment of about fifteen students, and the spring section of Biocalculus II has enrollment of about ten students. For comparison, each fall semester there are two sections of Calculus I with class size of about thirty students. Biocalculus I is open to all students who place into first semester calculus and is recommended for those majoring in the BMB program, biology, or the health sciences.

Lab I was first offered in Spring 2005, with its first mixed class of Biocalculus I and Calculus I students in Fall 2005. Multiple sections of Lab I with at most twenty students per section have been scheduled to accommodate the students in both calculus courses. We also offer two sections of a year-long integrated calculus and precalculus course sequence, Introduction to Calculus and Applications of Calculus, each year, with approximately sixty students per year divided into two sections. Each term, we also offer one section each of traditional second and third semester calculus courses. The biocalculus course sequence and accompanying laboratory courses are:

Course	Hours
Biocalculus I	4 credit hours
Calculus with Analytics I Laboratory	1 credit hour, 2 contact hours
Biocalculus II	3 credit hours
Biocalculus II Laboratory	1 credit hour, 2 contact hours

Table 1. Biocalculus and Laboratory Courses

The reader may find detailed syllabi and laboratory projects at the author's website:
http://www1.ben.edu/faculty/tcomar/index.htm

2.3   Description of the Courses

The philosophy behind the pedagogy of our biocalculus courses is the balance of mathematical content, rigor, and reasoning, biologically oriented examples and modeling applications driven by the use of real data where possible, and the use of computational tools to investigate biological and mathematical phenomena. Our presentation is infused with the Rule of Four popularized by the calculus reform movement. (The Rule of Four is the presentation of mathematical content symbolically, numerically, geometrically, and verbally.) Emphasis on the multiple representations of quantitative information is important for science students because they are more likely to work with data presented numerically or graphically in their science courses. Those who pursue avenues in which symbolic mathematical representations are relevant will have the skills to translate between verbal descriptions of phenomena and their expressions in mathematical notation.

2.3.1   Biocalculus I and Calculus with Analytics I Laboratory

We now describe in greater detail the Biocalculus I course and its connection with the common laboratory course. The syllabus, listed in Table 2 for Biocalculus I, was developed to meet the needs of our students and to accommodate the institutional considerations described above. At first glance, the course may seem not much different from a traditional first semester calculus course. This is significant because a similar syllabus can be implemented for a course to run concurrently with traditional calculus courses (as is done at Benedictine University) or can replace the traditional first semester calculus course without impacting the second semester of traditional calculus (as is done at Macalaster College (Bressoud 2004)). Table 2 includes some topics generally not found in the traditional first semester of calculus. An obvious question is how to adjust the content of the traditional material to accommodate the additions. Part of our solution was to move several topics, listed in Table 3, to the concurrent lab course. Other topics need to be streamlined. For example, limits of sequences are addressed thoroughly, including a discussion of formal definitions, before discussing limits of functions of real variables. When introducing the latter, we point out similarities between the two collections of limit laws and have already established a context in which we can efficiently present the formal ϵ-δ definition of a limit. Related rates are present, de-emphasized. Less time is spent on optimization application problems because other applications occur throughout the course.

The most important addition to the syllabus in Biocalculus I is difference equations. There are several advantages to studying these in a first semester calculus course. From the biological perspective, students can begin to understand some basic discrete population models without significant mathematical or biological background. Students learn how to represent discrete population models symbolically, how to implement them in Excel and Maple, and how to study their dynamics. From the mathematical perspective, there are significant pedagogical benefits. If difference equations are introduced before limits of functions of a real variable, students can learn about sequences early. Convergence

Review of functions
Nonlinear scales and allometry
Introduction to probability
First order difference equations, sequences, and population models
Limits and continuity of functions of a real variable
Differentiation
Applications of differentiation (including stability of difference equations)
The definite integral and Riemann sums
Antidifferentiation
The fundamental theorem of calculus
Basic applications of integration
Integration by substitution

Table 2. Topics for Biocalculus I

of sequences follows naturally from how students observe limits numerically and geometrically: they can observe to what number a sequence of numbers converges by looking at a table of values or a graph. Formal definitions of limits of sequences can then be introduced. Locally stable equilibria can be interpreted as values to which a sequence can converge. The limit of a function of a real variable can then be built on the limit in the discrete case. To help motivate the definition of the derivative, we can think of differences of successive terms as difference quotients having a unit difference between successive input values. Such differences provide a discrete approximation to the derivative. As the difference between successive input values decreases to zero, the derivative results. The criterion for local stability of a first order difference equation provides a nice application of differentiation, as it follows from using a tangent line approximation to linearize the difference equation. The stability result is a nice analog to the stability result for first order differential equations.

Conic sections
Parameter curves
Curve sketching
Numerical integration

Table 3. Calculus Topics in Calculus with Analytics I Laboratory

One of the themes discussed at the Biology CRAFTY Curriculum Foundations Project was that "Creating and analyzing computer simulations of biological systems provides a link between biological understanding and mathematical theory" (Dilts and Salem 2004). Additionally, the *Bio 2010* report asserts the importance for biologists of being able to use computers as tools: "Computer use is a fact of life of all modern life scientists. Exposure during the early years of their undergraduate careers will help life science students use current computer methods and learn how to exploit emerging computer technologies as they arise" (National Research Council 2003). These needs are met in the common laboratory course, Lab I (Comar and Townsley 2006) and through additional computational activities and projects in the Biocalculus I course.

The laboratory course, Lab I, is required of all students enrolled in either Calculus I or Biocalculus I. It helps to keep both first semester calculus courses at the same level and pace while providing time for content not covered in the lecture course and to explore additional applications, including biological applications. Students are introduced to the computer algebra system (CAS), Maple, as a calculating and graphing tool to analyze problems. (Maple is used throughout the calculus sequence at Benedictine University.) An important feature of the laboratory course is its collaborative nature. Students from the first semester calculus courses work together, enabling them to share their expertise to solve problems together, corresponding to the collaborative nature of academic research environments and industry. As much scientific research is done at the intersection of disciplines and as biological research is becoming increasingly computational and quantitative, it is important that science and mathematics students learn to communicate with each other. The lab experience offers biology majors and mathematics majors an opportunity

to work together and develop a common language. Currently, three of the weekly projects in the course investigate biological models (see Table 4).

Data fitting, nonlinear scales, allometric relationship between tree height and diameter

Stability of first order difference equations and cobwebbing using a discrete population model

Introduction to differential equations: slope fields, phase line diagrams, and Euler's method using the logistic model

Table 4. Biologically-oriented Projects in Calculus with Analytics I Laboratory

One of the goals of the biocalculus course sequence is to examine a wide array of biological problems using different computational platforms. The platform choice for a particular model depends on the ease of implemention and the applicability to future course or research work. Maple and Excel are used in Biocalculus I. The latest version of Maple is user-friendly and is appropriate for calculus courses. Moreover, activities can be developed in Maple so that the students are not burdened with programming and notational complexities. Maple is one of the leading commercially available computer algebra systems; those who pursue research are likely to encounter it or a similar computer algebra system for symbolic computation. We frequently use Excel for difference equation models because it is easy and convenient to implement recursion. Excel is ubiquitous and popular among biologists, so the students are likely to encounter it after their calculus course experience.

Biocalculus I students work on several computational activities throughout the term. Each explores at least one biological model and analyzes the effects of varying model parameters. The first project uses Maple to study a drug dosage model that, from the mathematical perspective, enables the students to analyze discontinuous functions with parameters. Another activity is a curve fitting problem in which the students fit a logistic curve to data measuring the length of a growing bean leaf over time. Students learn to implement discrete population models using difference equations in Excel and Maple. Both allow students to plot time series and cobweb diagrams and see the effects of varying parameters. Maple is nice for showing animated diagrams that step through the cobweb process one stage at a time and for creating bifurcation diagrams. Another activity analyzes a simple difference equation model for natural selection and in Excel.

Although the computer laboratory activities provide deeper investigation of biological models and introduce students to useful software programs, they take up a significant amount of class time, and more must be allotted to discussion. Incorporation of these activities promotes breadth over depth; diminishing or eliminating less crucial topics is necessary to allow for appropriate treatment of these time-consuming activities. The computer activities are integrated throughout the course during class time and through assignments. The course includes six or seven group homework assignments, two in-class exams, and a final exam, each of which has computer components.

2.3.2 Biocalculus II and Biocalculus II Laboratory

Unlike the first semester course, Biocalculus II deviates substantially from a traditional second semester calculus course. It is a hybrid of a second semester calculus course and an introductory course in mathematical biology. Its goal is to use calculus, related mathematical tools, and computational software to develop an understanding of biological mathematical models using difference equations, differential equations, matrix models, systems of difference equations, systems of differential equations, and the basics of probability. The course asks students to use mathematical and computational tools to investigate complex biological systems as a scientist. This approach is different from that of traditional mathematics courses, where the focus is simply on the mathematics. Topics have been chosen to achieve two distinct objectives (see Table 5). One objective reflects our understanding that students in this course may not be able to take another mathematics course. We present enough mathematical topics and provide experience analyzing biological models so that students are equipped to succeed in quantitative science courses and research experiences. The second objective is to ensure that students who complete the second semester of biocalculus will have developed sufficient mathematical maturity and background to succeed in a traditional third semester calculus course. Several former Biocalculus II students have successfully continued with Calculus III and additional mathematics courses.

Review of Biocalculus I and integration by substitution

Integration techniques: integration by parts, simple partial fractions, use of tables and computer algebra systems
    (Optional)

Indeterminate forms, L'Hôpital's rule, and improper integrals

Continuous probability distribution functions

Application of integration to volume calculations

First order differential equations with stability and bifurcations

Analytic geometry: vectors and equations of lines and planes

Matrix algebra: matrix properties and operations, including the determinant, the trace, eigenvalues and eigenvectors

functions of several variables

Limits of functions of several variables

Partial derivatives

Differentiability of real-valued and vector-valued functions of several variables, linearization

Nonlinear systems of difference equations

Linear and nonlinear systems of differential equations

Table 5. Biocalculus II Topics

Even though the Biocalculus II and the Biocalculus II Lab courses are separate courses, they are taught by the same instructor and comprise an integrated experience. Like the common lab course for first semester calculus students, the Biocalculus II Lab course is a one-credit hour course that meets for a two-hour session once a week. This provides five contact hours each week, as compared to the four hour weekly lecture time in the traditional second semester calculus course. We schedule projects throughout the term. They are biological and require work outside of class. The list of project titles is in Table 6. To help prepare students for research activities, an extended project has become the capstone of the course. The students read a research paper in mathematical biology, implement the model using an appropriate computation platform, and prepare written and oral reports about the model and their implementation. The workload for Biocalculus II also includes four group homework assignments, two in-class exams, a final exam in the lecture course, and a group final exam in the laboratory course.

Taylor polynomial approximations

Improper integrals and life tables

Stability of single ordinary differential equations, bifurcations, logistic model with harvesting

The Leslie matrix model for age-structured populations

Systems of nonlinear difference equations: host-parasitoid models

Systems of linear differential equations

Systems of nonlinear differential equations I: competition and predator prey models

Systems of nonlinear differential equations II: the Fitzhugh-Nugamo model

Table 6. Biocalculus II Lab Projects

2.4   Discussion

2.4.1   Successes

The biocalculus courses at Benedictine University have proven to be a success. First semester biocalculus and traditional calculus students perform comparably on calculus skills and in the laboratory course (Comar 2008); hence the two courses are taught at the same level of rigor and provide the same calculus skills. Other success are the integration of biological content into the common laboratory course and the success of students in succeeding courses and research experiences. Most importantly, the courses are now established in the curriculum.

We have two assessments that measure the performance of students in both first semester calculus courses, which enable us to ensure that students who successfully complete either course have demonstrated proficiency in a common

core of calculus concepts and skills and will be able to succeed in either second semester calculus course. The first assessment tool is a set of common final exam problems. The second is the common laboratory course, which provides a unique opportunity to compare first semester calculus students. Assessments in the laboratory course included the weekly laboratory activities, a written component of the final exam covering the calculus content specific to the lab course, and a collaborative component of the final exam testing modeling, problem solving, and use of a computer algebra system. Our data confirm comparable success rates (Comar 2008). Two conclusions are that students can switch between traditional calculus and biocalculus tracks and that students who complete Biocalculus I have the same fundamental calculus skills as those in the traditional Calculus with Analytics I course. This supports the biocalculus course as an alternative to the traditional first semester calculus course.

Students who have taken both biocalculus courses have had successful research experiences and have worked on projects at the intersection of mathematics and biology. These are key goals of the biocalculus courses, so the biocalculus course sequence is working. Even though the biocalculus sequence may be a terminal experience for most students, several have taken additional mathematics courses. Ten of the twenty-nine students who have completed Biocalculus II have registered for Calculus III. Eight of these earned grades of C or better, 1 student earned a D, and 1 student withdrew early in the term for personal reasons. Three of these eight students have become mathematics minors and three have added mathematics as a major. Five of the twenty-nine have participated in our Summer Science Research Program. Several others have pursued research activities during the academic year. (Research is required of all BMB majors.) One successful Biocalculus II student completed an integrated biology and mathematics project for the major research project in Benedictine University's Scholar's Program, which is the honors program at the university. Another able student has been hired to work with mathematics and biology faculty as a research assistant on a biocalculus textbook project. Several other biocalculus students who completed only Biocalculus I have participated in the Summer Science Research Program and have completed research projects as undergraduates. All students who have taken Calculus II following Biocalculus I have been successful, including two who became mathematics majors and one who completed a minor in mathematics.

The most important success of the biocalculus courses is that the courses have been institutionalized. Before the biocalculus courses were created, trigonometry was the only mathematics requirement for biology majors. Now, one semester of calculus is required for Bachelor's of Science biology majors and two semesters are required for the BMB majors. Biocalculus I is the recommended course for the first group and Biocalculus II with the lab is required for the second. This has contributed to the increase in enrollment in the courses and has enabled the university to offer two sections of Biocalculus I each fall. Instructors other than the course designer have been able to teach the courses successfully

2.4.2   Challenges

Recruitment into the biocalculus courses remains a challenge. There is a false perception that they are significantly more difficult than the traditional calculus courses. Moreover, some parents have felt more comfortable placing their freshmen children in a course called "Calculus" than "Biocalculus" because they are more familiar with the word "Calculus." Hence a significant number of biology and pre-med students still register for Calculus I. Freshman advisors are working with the Department of Mathematics to encourage students majoring in BMB, biology, and health sciences to take Biocalculus I. Biocalculus II consistently has a lower enrollment than Biocalculus I because fewer students are required to take the second calculus course than the first. Moreover, not all students who complete Biocalculus I are interested in the research orientation of course.

Acknowledgments

References

Bressoud, D.M., 2004: The changing face of calculus: first- and second-semester calculus as college courses. *Focus*, **24**, No. 8, 14–16.

Comar, T.D., 2008: Integration of Biology into Calculus Courses. *PRIMUS*, **18**, 47–70.

Comar, T.D., and L. Townsley, 2006: A common calculus laboratory course for traditional calculus and biocalculus students. *Proceedings of the 18th ICTCM*, Pearson Addison Wesley, Boston, MA.

Dilts, J., and A. Salem, 2004: Biology: CRAFTY Curriculum Foundation Project, Macalester College, November 2–5, 2000. *Curriculum Foundations Project: Voices of the Partner Disciplines*, S. Ganter and W. Barker, Eds., The Mathematical Association of America, 15–18.

Edelstein-Keshet, L., 2005: Adapting mathematics to the new biology. *Math & Bio 2010: Linking Undergraduate Disciplines*, L. A. Steen, Ed., The Mathematical Association of America, 63–73.

National Research Council, 2003: *Bio 2010: Transforming Undergraduate Education for Future Research Biologists*, National Academies Press, Washington, DC.

3

Implementation of First Year Biomath Courses at the Ohio State University

Laura Kubatko[1]

Departments of Statistics and of Evolution, Ecology, and Organismal Biology,
The Ohio State University

Janet Best[2], Tony Nance[3], and Yuan Lou[4]
Department of Mathematics, The Ohio State University

Name of Institution	The Ohio State University
Size	about 38,000 undergraduate students
Institution Type	large state university with PhD program
Student Demographic	recent high school graduates with interests in mathematics, statistics, and/or biology
Departments and Program Structures	Six departments (Mathematics, Statistics, and four biology), plus the biology major administered by the Center for Life Sciences Education, all inside the College of Arts and Sciences
Web Pages	http://www.stat.osu.edu/~lkubatko/CAUSEwebinar http://rumba.biosci.ohio-state.edu

Abstract

With approximately 38,000 undergraduates on the main campus in Columbus, Ohio, The Ohio State University (OSU) is one of the largest schools in the nation, providing a significant challenge in the creation of a BioMathematics curriculum that will adequately serve the needs of this undergraduate population. In this article, we describe our initial steps toward this goal, namely, the development and implementation of several first-year BioMath courses for students majoring in the Biological Sciences at OSU.

---

[1] kubatko.2@osu.edu
[2] best.82@osu.edu
[3] nance.1@osu.edu
[4] lou.8@osu.edu

3.1   Structure of Courses

- Weeks per term: 10 weeks (will convert to semesters in 2012)
- Classes per week/type/length: three 48-min lectures, two 48-min recitations
- Average class size: Calc I = up to 120; Calc II = up to 60; Stats = up to 40
- Enrollment requirements: Calc = standard; Stats = Calc II prerequisite
- Faculty per class, TAs: each course has 1 faculty and 2, 1, 1 TA respectively

3.2   Introduction

The Ohio State University (OSU) is one of the largest schools in the nation, with over 50,000 students on the main campus in Columbus, Ohio, approximately 38,000 of whom are undergraduates. The administrative structure of the University consists of eighteen distinct colleges, with a total of 167 undergraduate majors. The four biological science departments, housed within the College of the Arts and Sciences, serve approximately 2,300 undergraduates who obtain one of eight majors. Also, OSU houses the NSF-funded Mathematical Biosciences Institute (MBI), which provides a link between the mathematical and biological sciences.

In collaboration with the biological science departments at OSU, the Departments of Mathematics and of Statistics have developed courses to provide a quantitative foundation for the training received by undergraduates majoring in biological sciences (see accompanying article in this volume for details about the development of these courses). The courses include a two-quarter sequence in calculus and a one-quarter course in statistics. The calculus courses are taken by freshmen who have placed into calculus and who plan to obtain one of the eight biological science majors, and are structured so that students who complete them are prepared to continue with the more traditional Calculus III course offered by the Mathematics Department. Two sections of the calculus sequence have been offered in every academic year since 2006–07, serving approximately 160 students each year. The course in statistics is intended to serve as a follow-up elective course; students are recruited primarily from the calculus sequence, although any student who has completed two quarters of any calculus can enroll. The statistics course has been offered in the Spring quarter every year since 2007, with approximately forty students per section.

In this article, we describe each of these courses in detail. The next section describes the structure of each course, the material covered, and projects and class activities included. The Discussion section includes reflection on what aspects of the courses worked well and what needs improvement. We then discuss some more advanced courses that have recently been added to our BioMath curriculum. We conclude with a discussion of our long-term vision for the BioMath curriculum at OSU.

3.3   Description of First Year BioMath Courses at OSU

OSU followed the quarter system rather than the semester system until the Fall 2012 semester, with an academic year thus consisted of three 10-week quarters (Fall, Winter, and Spring) with a week of final examinations following each. Quarter courses generally comprised 3–5 credit hours of instruction per week, and often consisted of a mixture of lecture and laboratory sections. Each of the BioMath courses we developed was offered for 5 credit hours, with three 50-minute lectures taught by a full-time faculty member and two 50-minute laboratory sessions taught by Graduate Teaching Assistants (GTAs) per week. The lecture sessions were often large (ranging from 40 to 100 students), while the laboratory sessions generally had no more than 30 students. Laboratory sessions were devoted to hands-on activities and problem-solving, while lectures covered the introduction and discussion of new concepts. We now describe these courses in detail.

3.3.1   Calculus I and II for the Life Sciences

Both calculus courses were taught from the text *Calculus for Biology and Medicine* by Claudia Neuhauser (2003). The Calculus I course covered the first five chapters of the text, including sequences and difference equations (2 weeks), limits and continuity (2 weeks), and differentiation and applications (6 weeks). The Calculus II course covered

material in Chapters 6, 7, and 8: basic integration (2 weeks), advanced integration techniques (6 weeks), and differential equations (2 weeks). Course grades were based on weekly homework and quizzes, a project, two midterm examinations, and a comprehensive final examination.

An innovative aspect of the courses was the inclusion of group projects. During the first offering of Calculus I, ten projects were designed by the instructors and GTAs. In subsequent quarters, projects have been developed and supervised by post-doctoral researchers associated with the MBI. Each quarter, several post-docs developed projects and gave a lecture advertising their projects to the students; students then selected one of the projects to study in a group of three to five students. The post-docs arranged two additional class meetings to work with the students, who were also expected to spend time working on their own outside of class. Each project contained several questions to be addressed, and each student was required to write the solution to at least one of the questions. The group was responsible for combining the solutions to the questions to form a cohesive written report for the project as a whole. This has the advantage of giving students experience in writing in a research-like setting. The group reports contributed the equivalent of two homework assignments to each student's grade in the course. Here are examples of the projects.

Tumor Growth and Treatment. Differential equations can be used to model tumor growth. A tumor cell divides, generating two daughter cells with unlimited ability to reproduce. Initial rapid growth supported by abundant nutrients such as oxygen and glucose is followed by slower growth as the population size increases. Injecting anti-cancer drugs that kill a fraction of tumor cells per unit time may reduce the size of the tumor cell population. The project involves studying the differential equations to find the best strategy for reducing tumor size.

Analyzing Cartilage Health. In an osmotic loading experiment, chondrons (cartilage cells with encapsulating pericellular matrix, PCM) are extracted from cartilage and placed in different external concentrations of sodium chloride in water. Depending on the concentration of the sodium chloride, the chondron will either swell or shrink. We look at how the volume of the PCM changes with respect to the different external concentrations of sodium chloride in water.

Fisheries Management. Humans catch fish for a variety of reasons, such as for food or for sport. While these purposes may have merit, it is important to realize that there is not an unlimited number of fish in the sea. The National Marine Fisheries Service was formed by the U.S. government to manage marine resources in the U.S. In order to do their job, their scientific research teams use many tools, including mathematical models. In this project we explore a hypothetical fishery model for a sea bass population within an enclosure.

The material given to the students consisted of an expanded verbal description followed by the formulation of a mathematical model for the situation. The students were then asked to solve a series of problems using the model and to interpret their results. Also, the students were provided with information concerning expectations from the groups, both for functioning of the group as a whole and for individual interactions of each student with the group. The principal mathematical tool for the Calculus I projects is the derivative; differential equations, when they occur, are accompanied by solutions that the students must verify.

In the Calculus II projects, the main tools are derivatives and integrals, and many involve solving some ordinary differential equations. Example projects are:

Brain Waves with Noise. An EEG (electroencephalogram) machine measures local field potentials in the brain by recording from electrodes placed on a patient's scalp. These potentials represent an electrical signal from a large number of brain cells called neurons. Monitoring the EEG recording is useful in assessing brain activity and in diagnosing conditions such as epilepsy, sleep disorders, and coma. This project examines brain wave power when the signal is noisy.

Grass Management. A modern method to raise cattle consists of preventing cows from grazing in a field until the grass has reached an optimal height. When the grass is too short, it cannot recover well from being cropped. Older grass grows more slowly, may become senescent, and is less tasty to cows. In this project we examine grass growth and its optimal management.

Drug Absorption. Understanding therapeutic and adverse drug reactions is important in the treatment of many diseases, particularly cancer. Two models for drug absorption and toxicity are examined to compare injected drug therapies with a polymer delivery system.

3.3.2   Statistics for the Life Sciences

This course, intended as an optional course to follow the calculus sequence, was taught from *The Analysis of Biological Data* by M. C. Whitlock and D. Schluter (2009). Material was selected from Chapters 1 through 17, with additional materials provided by the instructor that built on the students' knowledge of calculus (the text does not assume Calculus). Topics included descriptive statistics and graphical methods (1 week), probability, including Bayes Theorem (1 week), discrete distributions and the analysis of categorical data (2.5 weeks), one- and two-sample inference for means and variances (2.5 weeks), experimental design (1 week), and correlation and regression (1.5 weeks).

As in the calculus sequence, assessment was based on weekly homework and in-class examinations. The lectures were in the traditional style, though activities were incorporated into a few of the sessions. The recitation sessions were divided between problem-solving sessions and activity sessions. In the activity sessions, students used the StatCrunch software (StatCrunch, 2012) to analyze biological data sets after being given an introduction to the biological setting. Results of their analyses were brought into the lecture sessions and used as examples for subsequent topics in many cases, creating continuity between the recitation sessions and the lectures. A short lab manual for the course can be found at http://www.stat.osu.edu/~lkubatko/CAUSEwebinar.

Examples of the data sets included in the course and with the topics they illustrate are:

Fisher's Iris Data. A well-known data set studied by R. A. Fisher includes measurements on characteristics of three species of irises, including sepal length, sepal width, petal length, and petal width (Anderson, 1935; Fisher, 1936). These data were used in several ways. When the normal distribution was introduced, students used it to explore the distribution of characteristics in the recitation session using the StatCrunch software. They examined histograms and normal probability plots for the data when all three species are grouped together and for each species separately. The data is later used in lecture to motivate hypothesis testing by asking whether the mean sepal width differs between pairs of species. After an example is worked in lecture, the ideas are reinforced in recitation by carrying out hypothesis tests using the StatCrunch software.

Population Frequencies of Human Chemokine Receptor Gene Variants. A genetic variant of the human chemokine receptor gene appears to provide strong resistance to HIV infection. This variant is found in all European populations with varying frequency. Lucotte and Mercier (1998) studied a sample of 2,522 people throughout Europe to determine their genotypes, and found an overall allele frequency for the gene variant of approximately 9%. In the recitation session, students are given this information as background to the problem (with some added discussion about what is a genotype). They then compute the expected frequency of this gene variant in various European subpopulations, and compare them to the observed data of Lucotte and Mercier (1998). Although hypothesis testing has not yet been formally introduced, the students compute quantities similar to p-values by examining the probability of observing the data given in the paper if the variant gene frequency actually is 9%. This example is used to motivate hypothesis testing later in the lecture sessions.

Old-Growth Forest Data. This data set consists of an extensive survey of an old-growth beech-maple forest carried out at the James H. Barrow Field Station (owned and maintained by Hiram College in northeastern Ohio) during the summer of 1993 by Laura Kubatko. The goal of the data collection was to assess the diversity and distribution of tree species in the forest. The data were collected by subdividing the forest into 50m × 50m plots. Within each of sixty-seven plots, four 10m × 10m sub-plots were randomly selected to be surveyed. All tree species occurring within the sub-plots were counted and recorded. The diameter at breast height (dbh) was measured for any tree larger than 3.0 cm dbh. An interesting feature of this data set is that the forest can be divided into four distinct areas that vary in composition of species and size-class distributions due to various external stresses (e.g., chestnut blight and an area affected by a tornado in the early 1970s) and physical characteristics (west-facing slopes).

These data are used in the course to give students experience with examining and comparing distributions. When discussing summary statistics and graphical displays, students are asked to use the StatCrunch software to find graphical displays for the counts of the number of trees of each species in various areas of the forest and for the distribution of

trees among size classes (based on dbh). Later, the data are used to compare areas of the forest using hypothesis tests and confidence intervals.

3.4 Discussion

3.4.1 Successes

Feedback from the courses has been positive. Students seemed motivated and interested in what was taught, and many commented on its usefulness to them in their future careers. The current cohort of students in the courses is generally well-prepared for this level of mathematics. As we look to expand the offerings to include a broader group of students, our approaches may need to be adjusted to accommodate differing levels of preparation among our students.

The class structure (three lectures and two recitations per week) worked well for several reasons. One is that it divides our potentially large (40–100 student) lecture sections into smaller groups, so that students can receive more individual attention. This allows for activities (such as the calculus group projects) and computer exercises (such as analysis of real data using StatCrunch in the statistics course) to be included. Another advantage of this format is that the GTAs were able to get experience teaching students from the biosciences. The GTAs were involved in developing course materials for the recitation sessions, and were therefore able to learn how to communicate with this group of students. Since the GTAs are the next generation of instructors in biomath, the early exposure to such courses with the guidance of a faculty mentor is very valuable. Although the GTAs were not given special training in preparation for teaching the courses, we worked to ensure that they were interested in teaching in this setting. All GTAs were carefully mentored throughout the quarter.

Another positive feature was the inclusion of the MBI post-docs in the calculus sequence through the development and mentoring of the student projects. The exposure of the undergraduate students to a variety of research areas in BioMathematics and the interaction with the BioMathematics community at OSU is beneficial in creating an interest in and appreciation for interdisciplinary work. Several of us have had discussions with students interested in pursuing undergraduate research projects in these areas, and we expect such interactions to continue to increase over time.

3.4.2 Challenges

One challenge in designing and implementing the courses was that of finding textbooks with an appropriate mix of biological motivation and mathematical rigor. We were happy with the Neuhauser text used in the calculus sequence in that it was easy to teach from, as it is similar to a traditional calculus text but infused with biological examples. However, other books (e.g., Adler 2004) that are more oriented toward biology-driven mathematics than calculus per se are also appealing. An important point to consider is that some students in these courses may decide to continue in the traditional mathematics curriculum, and thus the courses need to prepare them to do so.

It was also difficult to select the topics, both biological and mathematical, that should be covered in the courses. The topic coverage in both the calculus and the statistics courses was similar to what would be covered in traditional courses, though the time spent on them varied somewhat. On the biological side, the students consisted largely of freshmen who, while mathematically prepared for the courses, were just beginning their study of biology. Thus we often had to teach a fair amount of the biology underlying our examples, as well as the mathematics, which could be a bit overwhelming for the students (and for us!) at times. In the future, particularly as we convert our courses to the semester system, we hope to work more closely with faculty in the biological sciences to understand the freshmen biology curriculum better, which will allow us to use examples that utilize biological concepts to which the students have been exposed, and to gain a further appreciation for which mathematical and statistical topics will be most relevant for students in their future study and careers.

A final challenge is recruiting students to take the elective courses (statistics and the courses described in the next section) following the calculus sequence. Because the students are freshmen, they are also taking laboratory courses in biology and chemistry, which is a substantial academic load in the first year. It may be more convenient for students to return to mathematics courses in their second or third year, when they have more flexibility in their scheduling, and we therefore expect these courses to grow.

3.4.3   BioMath Courses at OSU Beyond the First Year

In addition to the first-year courses, we have developed two additional courses to enhance student interest in mathematical biology at OSU. The first is an undergraduate seminar that has been developed as a result of our recently-funded NSF UBM grant for undergraduate research in mathematical biology at OSU. As part of our program, called RUMBA (Research for Undergraduates: adventures in Mathematical Biology and its Applications—see http://rumba.biosci. ohio-state.edu for more information), the seminar course is offered in each academic term. It meets for one hour each week and consists of talks or discussions led by PIs for the program and speakers from within the OSU BioMath community. The outside speakers have included faculty in Mathematics, Statistics, and Biological Sciences, Visiting Scholars at the MBI, and MBI post-docs. The seminar enrolls approximately fifteen undergraduates at all academic ranks (freshmen to senior) and a variety of majors (mathematics, biology, environmental science, pre-medicine, etc.). Student evaluations have been very positive, and we feel that the course is succeeding in its goal of increasing interest in and awareness of the field of mathematical biology.

The second new course is titled Introduction to Mathematical Biology and was taught for the first time during the 2009–2010 academic year. The topics included population dynamics (logistic growth model and Lotka-Volterra predator-prey model), epidemiological modeling, competition, neuronal dynamics, and enzyme kinetics. We expect that this course will be offered every year. We have also added a mathematical biology track within the math major. All of these recent efforts build on our earlier curriculum development to strengthen the undergraduate BioMath program at OSU.

3.4.4   Future BioMath Curriculum Development at OSU

Our most recent efforts in BioMath curriculum development at OSU are focused on converting our courses to the semester system which will take effect at the start of the 2012–13 academic year. Our goal is to refine them to meet the needs of broader groups in the biological sciences and the university as a whole. At present, our calculus sequence accommodates a maximum of 160 students per year, which is just a fraction of entering students planning to major in biological sciences. Students majoring in health science fields may also benefit from taking these courses rather than the traditional calculus sequence.

One reason for our success has been the presence of a group of faculty working in mathematical biology who interact with both the mathematical/statistical and biological communities at OSU. This has been facilitated by the MBI, several recent joint hires between departments (including such department as Mathematics; Statistics; Evolution, Ecology, and Organismal Biology; and Molecular Genetics), and several hires of faculty within the Mathematics Department who work in mathematical biology. As we continue to assemble a community of interdisciplinary researchers, we hope to build our curriculum further. Two areas of growth that have been discussed are the development of courses that enable students in one field to obtain a major or minor in the other, and the development of interdisciplinary degree programs, such as the BioMath concentration. The recent addition of our RUMBA program has enabled us to establish an interdisciplinary research program for undergraduates at OSU, and has thus facilitated the continued enhancement and expansion of our curriculum development.

Overall, we view our mission as helping undergraduate life science majors learn to think in a quantitative manner, whether for modeling biological phenomena or analyzing experimental data. With this goal in mind, we have enjoyed meeting the challenges of cross-department collaboration on curriculum development in a large university, and we look forward to continuing our progress.

Acknowledgments

References

Adler, F.A., 2004: *Modeling the Dynamics of Life: Calculus and Probability for Life Scientists*, 2nd ed. Brooks/Cole.

Anderson, E., 1935: The irises of the Gaspe peninsula. *Bulletin of the American Iris Society*, **59**, 2–5.

Fisher, R.A., 1936: The use of multiple measurements in taxonomic problems. *Annals of Eugenics*, **7**, 179–188.

Lucotte, G. and G. Mercier, 1998: Distributions of the CCR5 gene 32 bp deletion in Europe. *J. Acquir. Imm. Def. Hum. Retrov.*, **19**, 174–177.

Neuhauser, C., 2003: *Calculus for Biology and Medicine*. 2nd ed. Pearson/Prentice Hall.

StatCrunch, cited 2012: StatCrunch: Data Analysis on the Web. [Available online at http://www.statcrunch.com/.]

Whitlock, M.C., and D. Shluter, 2009: *The Analysis of Biological Data*. Roberts.

4

Teaching Calculus, Probability, and Statistics to Undergraduate Life Science Majors: A Unified Approach

Frederick R. Adler[*]
University of Utah

Institution	University of Utah
Size	about 20,000 students
Institution Type	Large comprehensive state university offering bachelors through doctoral degrees
Student Demographic	Biology majors (recommended in lieu of the standard first two semesters of calculus, but taken only by a minority due mainly to scheduling constraints).
Department Structure	Mathematics and Biology are separate departments in the College of Science.

Abstract

The Department of Mathematics at the University of Utah has developed an integrated modeling, calculus, and probability course for life science majors that emphasizes the central role of dynamics in biological thinking, including statistical analysis. The course and associated textbook use the themes of growth, diffusion, and selection throughout, and we describe how diffusion is presented in several contexts. Although the University of Utah has a large group of faculty and students in mathematical biology, we discuss the challenges of serving all biology majors, integrating the course with the biology and mathematics curriculum, and motivating mathematically underprepared students.

[*] adler@math.utah.edu

4.1   Course Structure

- Weeks per term: Two semesters, about 30 weeks
- Classes per week: Three 1-hour lectures
- Labs per week: One 1-hour lab
- Average class size: 25–50 students
- Enrollment requirements: For freshman, students should have passed college algebra and trigonometry, or have Math SAT score of at least 630, Math ACT score of at least 28, or AP Calculus AB score of at least 3
- Faculty/dept per class, TAs: One math instructor with one graduate student TA to handle the computer labs
- Next course: The purpose of this course is to prepare students for the quantitative aspects of the biology curriculum
- Current website: `http://www.math.utah.edu/~borisyuk/OLD_TEACHING/1170_Fall12/`
- Archived website: `http://www.math.utah.edu/~adler/oldcourses/math1170_2008/`

4.2   Scope and Goals

In 1990, the University of Utah received a grant from the Howard Hughes Medical Institute; among the goals of the proposal was the development of a new calculus course and associated textbook for life science majors. The University of Utah had, and still has, a one-year mathematics requirement for biology majors. To this end, I was hired as a new faculty member into a joint position in the Departments of Mathematics and Biology to develop the course.

I was given one semester for preparation, and had a committee of experts in biology and mathematics to help with planning. The goal was to create a course that could serve the quantitative needs of the large majority of life science majors, but without closing off the option of taking additional mathematics courses.

After surveying the biology faculty, we found that modeling and statistics were the two most important topics (along with the basics of being able to read a graph effectively and other remedial skills). The course was designed to emphasize these elements by covering three areas under the quarter system then in effect:

1. Discrete-time dynamical systems
2. Differential equations
3. Probability and statistics

Within these broad headings, united by their focus on modeling, the fundamental ideas of functions, differentiation, and integration were to be seamlessly intertwined.

We chose to take a conventional approach toward teaching in two ways. First, the course would build from simple basic principles toward more complex ideas (rather than confronting students with realistic data to analyze right from the start). Second, much of the learning would be done in a traditional classroom setting, but supplemented with an additional hour each week in the computer lab.

Because no textbook then existed that matched this model and built from biological principles, I began to draft what became *Modeling the Dynamics of Life: Calculus and Probability for Life Scientists* (Adler, 1998; Adler, 2005).

The biological themes were simple and chosen so that they could be revisited in multiple contexts: growth, diffusion and selection. The goal was to develop materials that would focus on understanding the modeling process, with as much (or as little) attention on the mechanics of algebraic calculation as was necessary to achieve this goal.

The section on probability and statistics was to tie the work on deterministic models together with data analysis using the basic models of probability theory (the binomial, Poisson, exponential and normal distributions). Through computer experimentation, students were to see how the probabilistic nature of population growth, selection, and diffusion make patterns difficult to see without the proper tools, namely a combination of basic understanding and statistical insight.

4.3   Course Content

The course begins with a four-week section that introduces modeling by using discrete-time dynamical systems, building or renewing students' familiarity and facility with linear, exponential, and trigonometric functions and their

graphs. Starting with the classic model of exponential growth, we derive a linear diffusion model of gas exchange in the lungs, and a non-linear model that shows how a selectively-favored allele spreads through a population. Students use graphical methods, such as cobwebbing, to visualize and understand dynamics.

The central portion of the first semester introduces derivatives and some of their applications. After learning the meaning of the derivative, its graphical interpretation, and computation rules for biologically important functions, students use the derivative to analyze stability of equilibria of discrete-time dynamical systems. Other applications include optimization, using the derivative to understand graphs of complex functions, and using the tangent line and Taylor polynomials to approximate functions. If time permits, we tie together approximation and discrete dynamics by developing Newton's method for numerical solution of nonlinear equations.

The first semester concludes with an introduction to integration, starting with the antiderivative as the way to solve simple pure-time differential equations, where the rate of change depends only on time. Riemann sums and the interpretation of integrals as areas are delayed, and emphasize the importance of the fundamental theorem of calculus in linking definite and indefinite integrals. The principal methods of integration are covered, although in less detail than in a standard calculus course.

The second semester begins with autonomous differential equations and shows how they parallel discrete-time dynamical systems. The phase-line diagram, like cobwebbing for discrete-time dynamical systems, provides graphical understanding. The parallel with discrete-time dynamics continues with the application of the derivative to analyze stability, and the parallel with pure-time differential equations continues with their solution using separation of variables. The phase plane forms the culmination of the deterministic portion of the course, emphasizing the interplay between modeling and analysis in the dynamics of a neuron as described by the Fitzhugh-Nagumo equations.

The remainder of the second semester, 10–12 weeks, is devoted to probability and statistics, with an emphasis on modeling in data interpretation. The first section develops the concepts of probability, focusing on conditional probability and independence, and includes the visual display of probabilistic information. The second section introduces probability distributions through their derivation from discrete-time dynamical systems (the binomial and geometric distributions) and from differential equations (the Poisson and exponential distributions). This section concludes with the central limit theorem (presented without proof) and the normal distribution, along with the difficult concept of the probability density function and its link with the fundamental theorem of calculus.

The course concludes with an introduction to statistics designed to tie together the key ideas of modeling and calculus. Maximum likelihood forms the backbone, showing how maximization methods can be applied to data when interpreted in terms of probability distributions. Although necessarily brief, the key ideas of classical statistics, such as confidence limits and hypothesis testing, are introduced with their application to linear regression, analysis of variance, and contingency tables.

4.4 An Extended Example: Diffusion

The course treats diffusion in several ways. In the first chapter, before the introduction of calculus, students develop a discrete-time model of gas exchange in the lungs,

$$c_{t+1} = (1-q)c_t + \gamma q,$$

where c_t is the concentration of some inert gas as a function of the fraction of air exchanged, q, and the ambient concentration γ. The students derive this from first principles (keeping track of air volumes), and then as a weighted average. This allows students to develop more realistic equations for a gas, like oxygen or carbon dioxide, that is used or created in the lung with each breath. After the development of the derivative, students use stability analysis to show that the lung will indeed approach the ambient concentration, and to study the effects of non-linearities.

The second portion of the course, on differential equations, introduces both Newton's law of cooling and the formally identical law for chemical diffusion between two containers in continuous time,

$$\frac{dC}{dt} = \beta(\Gamma - C),$$

where β is rate of chemical exchange and Γ is the ambient concentration. Students extend the derivation to more interesting biological processes and use graphical and algebraic methods to evaluate stability.

Finally, in the section on probability, students meet diffusion from the molecular perspective as a stochastic process. They see that the probabilities that describe the location of a molecule follow exactly the discrete-time dynamical system found with macroscopic reasoning about volumes. After deriving the binomial distribution, they see that the ensemble of molecules, assuming independence, obeys it, and in the limit the ensemble behaves like its expectation. They have then come full circle to see that the deterministic discrete-time dynamical systems and differential equations derived and studied in the first part of the course are the equations for the expectation of a stochastic process.

The familiarity of diffusion allows students to use their intuition to derive and understand mathematical models that can then challenge and extend that intuition. The multiplicity of modeling approaches illustrates that the tool chosen to study a problem depends on the problem and the question being asked, and shows that apparently different methods can be closely related.

4.5   Successes and Failures

Although no formal assessment has been done, students seem to enjoy the course, and some show evidence of having used the material in other courses. The University of Utah has a tradition of encouraging undergraduate research in biology (the initial Hughes grant funding the development of the course was focused on further strengthening these programs), and many students have been attracted to this course because of the benefits for research.

The course was to be taught to a single section of students in the pilot phase and then scaled up to serve all biology majors. This has not occurred, primarily because of scheduling difficulties, and the course remains at one or two sections. Strong advising from the biology department has maintained enrollment although the course is not required and is widely considered to be harder than the ordinary calculus sequence. The majority of the students have not taken calculus before, and are comparable in mathematical background to their peers who enroll in the ordinary calculus sequence.

We have found that separating biologists from physicists and engineers has promoted a positive and collaborative atmosphere, which extends to the instructors. Over the years, the course has been successfully staffed by both faculty and advanced graduate students, thanks to the large mathematical biology group at the University of Utah. The shared motivation of life science students and the choice of biologically relevant topics provides the best argument for such a course, with its implementation depending on an institution's requirements and goals.

The course has faced many problems. The pressure to develop a second edition of the book took energy away from improving the teaching of the course, leading to a period of relative stagnation. Work on the second edition coincided with a switch to semesters that broke up the elegant three part structure in an unnatural way, with differential equations being divided over two semesters.

There is little doubt that the course is more difficult than the standard calculus sequences because of the challenges of modeling, the open-ended material, and the diversity of topics. Given the wide range of mathematical backgrounds and abilities among students, the goals of the course must be adjusted along a sliding scale. The weakest students at least gain familiarity with concepts such as models, differential equations, and statistics. The strongest students can apply what they have learned to work in other courses and in research. Those with the most mathematical enthusiasm and ability can in principle move on to advanced calculus, linear algebra, or mathematical biology, but the department advisors have discouraged this, assuming that students from this course will lack the background needed for more advanced work.

In response to pressure from advisors and reviewers, and in part for completeness, I added several topics to the third edition:

- Double-log graphs and an introduction to allometry,
- Implicit differentiation and related rates,
- Infinite series, Taylor series, and improper integrals,
- Integration by partial fractions,
- Trigonometric substitutions,
- Computing volumes of solids of revolution.

Whether these additions will help integrate this course with the rest of the mathematics curriculum will depend on the idiosyncrasies of particular institutions.

Modernizing the course will probably take two directions. First, the introductory part of the course needs to be closer to real biological problems. One of the difficulties is balancing elucidation of general principles with the complexity of real biology. The themes of growth, diffusion, and selection could be better introduced with real data, ideally student-generated. A bit of preliminary statistical analysis would help motivate the models and their analysis. Second, the lack of bioinformatics is frustrating. At the University of Utah, we believe that a course for beginning undergraduates must avoid methods presented as a black box, and methods for dealing with complex genetic data cannot be developed from scratch at this level. However, carefully chosen examples should reveal the methods, challenges, and excitement of modern biology.

Even in the biology-friendly atmosphere of the University of Utah Department of Mathematics, integrating this course with the rest of the curriculum has been challenging. We have failed to integrate the material learned with the rest of the biology curriculum, due to a historical inability of the University of Utah to enforce prerequisites (currently being improved) and to the challenges of incorporating any new material in already over-stuffed biology courses.

4.6   Looking Ahead

Today's college educator must contend with two conflicting problems. Entering students generally have poor quantitative skills of all sorts, from number sense through algebra and including lack of real computer programming experience and knowledge of statistics. However, real biological problems, whether in the realm of research or in medicine, are becoming ever more complex. Those of us trained in the step-by-step logic of mathematics find it unacceptable to present students with a series of black boxes that can be used to solve problems. But the jump from solving and understanding a linear discrete-time dynamical system to appreciating the logic required to make inferences from genetic data seems too large to make in a single year. Much lip service is paid to integrating quantitative material into biology courses, but few institutions have succeeded in doing so in a serious way due to the limitations of both faculty and students.

The different sizes, emphases, and personalities of institutions make a one-size fits allmodel for integrating calculus-level mathematics with a life science curriculum inappropriate. Each institution needs to use its strengths (such as the large mathematical biology group at the University of Utah) to advance quantitative education and initiate the long-awaited generational shift in biological thinking.

References

Adler, F.R., 1998: *Modeling the Dynamics of Life: Calculus and Probability for Life Scientists*, Brooks/Cole.

Adler, F.R., 2011: *Modeling the Dynamics of Life: Calculus and Probability for Life Scientists, Third Edition*, Brooks/Cole.

5

The First Year of Calculus and Statistics at Macalester College

Dan Flath[1], Tom Halverson[2], Danny Kaplan[3], and Karen Saxe[4]
Department of Mathematics, Statistics, and Computer Science, Macalester College

Name of Institution	Macalester College
Size	about 2000 students
Institution Type	selective 4-year undergraduate liberal arts college
Student Demographic	first semester calculus students; required course sequence for all mathematics, biology, and economics students; often taken by others fulfilling distribution requirement.
Department Structure	Mathematics and statistics are housed in same department, together with computer science and applied mathematics.

Abstract

At Macalester College, we have redesigned our introductory calculus course to make a more useful mathematics sequence for life science students, a change that also works better for students from the physical sciences, economics, and other social sciences. The redesigned curriculum consists of a two semester course sequence: Applied Calculus (AC) and Introduction to Statistical Modeling (ISM).

5.1 Course Structure

- Weeks per term: 14-week semester
- Classes per week/type/length: three 1-hour lecture periods each week

---

[1] flath@macalester.edu
[2] halverson@macalester.edu
[3] kaplan@macalester.edu
[4] saxe@macalester.edu

- Labs per week/length: none required, but AC meets frequently in lab; ISM meets every day in lab
- Average class size: AC has 30–40 students in 5–6 sections per year; ISM has 30 in 3–4 sections per year
- Enrollment requirements: AC—Macalester admission; ISM—either AC, or Multivariable Calculus, or Linear Algebra
- Faculty/dept per class, TAs: One department faculty member per section, plus one undergraduate assigned to help with grading, and to help in lab, as instructor sees fit
- Next course: After AC either ISM, or second semester calculus; After ISM, Applied Multivariate Statistics

5.2   Introduction

Macalester College is a selective liberal arts college in Saint Paul, Minnesota with about 2000 students. The median SAT scores for current students are 670 in mathematics and 700 in critical reading; the ACT composite median is 31. The vast majority of the students who take our introductory courses fall into one of two categories: those who take quite a bit of mathematics, including Linear Algebra and Multivariable Calculus, or those who are interested in another discipline and are required (or limited by time) to take two mathematics courses. Our former Calculus I was designed as the first semester of a two or three course calculus sequence, and we found that it was no longer meeting the needs of the type (2) students and that very few of the type (1) students were enrolling in it (one or two per year), since they placed into Calculus II or higher. This motivated us to change the role of Calculus I and to think of it as part of a two-course sequence in Calculus and Statistics. During this same time (November 2000), our department was host to a Curriculum Foundations Workshop in Biology (Dilts and Salem, 2004) and Chemistry (Craig, 2004), where members of these disciplines gathered to discuss the ways that the mathematics curriculum supports their students. The themes that arose from these workshops—especially multivariable relationships, scale and estimation, modeling, and data analysis—were the foundation of our vision for our new courses. Applied Calculus (AC) is our entry-level mathematics course; we do not offer precalculus. Mathematics majors typically enter Macalester with calculus credit; since they all take Introduction to Statistical Modeling (ISM), which requires some multivariable background, most take ISM following their Multivariable Calculus or Linear Algebra course. Students from client departments for whom the AC/ISM sequence is required can instead take Multivariable Calculus and ISM (this is what many economics students do).

5.3   The First Semester—Applied Calculus

Applied Calculus (AC) is a one semester course on mathematics for modeling. It is distinctive for the range of topics covered, the active approach taken in the classroom, and the significant computer component using the software R[5]. This is professional-level software and is used for the entire year in AC and its follow-up course (discussed below). Algebraic techniques are present but deemphasized; there is no calculus prerequisite. Most students go from this course to the statistics class described in the next section.

   The content of the course has four broad sections. The first section (roughly nine classes) focuses on families of functions and modeling. Single and multivariable phenomena are discussed. The emphasis is on building intuition about families of functions of one variable—linear, exponential, and sinusoidal—and how they are used in modeling. Later in the course, the logistic family is added. The graphical significance of parameters is explored through curve fitting, with the aid of semi-log graphs for exponential functions. After a computer lab on defining and graphing functions with R, students model experimental data by a graphical curve fit—exponential decay is represented by automatically recorded heights of successive bounces of a ball, and a sinusoidal model is fit to a recording of a human whistle. The importance of keeping track of units of measurement is emphasized. Functions of two and more variables

---

[5] R is a language and environment designed for statistical computing and graphics. One of R's strengths is the ease with which well-designed publication-quality plots can be produced, including mathematical symbols and formulae where needed. It is a numerical computation environment, like Matlab, and is popular with biologists. R is free software, available at www.r-project.org/

are introduced with a Cobb-Douglas model and the connection between rectangular tables of values and their contour diagram representations are made with a class activity of creating a contour diagram from a large table of values by drawing the diagram right on the table.

The second section (roughly fourteen classes) is on differentiation of functions of one and several variables. The derivative is introduced as a sensitivity parameter that can be approximated by difference quotients. This is reinforced with a computer lab on numerical differentiation that features experimentation with the size of Δx. Symbolic differentiation, including the chain rule and the product rule, are treated but not dwelt on. Partial and directional derivatives are introduced as natural extensions of derivatives to functions of two or more variables and students learn how to estimate them from contour plots and tables of data. Second order derivatives are used to make local approximation of 1- and 2-variable functions with quadratic Taylor polynomials. Gradient vectors are developed in a class activity with a contour map. A lab lets students explore how to use gradients in the steepest descent method to find the minimal potential energy of a configuration of two masses and two springs. Constrained optimization including Lagrange multipliers is taught graphically and the significance of the multiplier λ is explained.

The third section (roughly eight classes) is on modeling with differential equations. The focus is on interpreting the equations, and a variety of extended examples. Differential equations are introduced as mathematical models of population and pollution that are based on rate of change assumptions. Presentation as a slope field permits graphical solution. The exact solution of the linear differential equation $y' = ky$ is taught, but solutions are produced and graphed by computer for all other differential equations. A common sense explanation of Euler's method suggests how numerical solutions may be generated. First order models include population growth, predator-prey dynamics, susceptible-infected-removed (SIR) model of the spread of disease, passage of a cold medication through the body, and a general first order constant coefficient linear system of two coupled functions of time. In a computer lab, students graphically explore the solutions of the coupled system that arise by changing the signs and magnitudes of the parameters. As a last example, the second order harmonic oscillator equation is studied, and students learn to interpret a curve in the y-y' phase plane.

The course ends with a section (roughly seven classes) on linear algebra, which is included to facilitate a geometric understanding of linear least squares curve fitting. This material is critical for, and has proven a good prelude to, the next semester on statistical modeling. Students come to the course understanding that solving two simultaneous linear equations means finding the point of intersection of two lines in the plane. They are taught the dual interpretation, that of finding a linear combination, if any, of given vectors that hits a target vector. In the computer lab, students play a video game in which they attempt to hit a target on the screen by changing the lengths of vectors that are added. Since the vectors are in 3-space, they must view the system from different angles, leading to some challenge and fun. Consideration of existence and uniqueness of solutions in examples leads naturally to the concepts of span and linear independence. In the applied setting the target vector, given by data, belongs to a high dimensional space and is not in the span of the few vectors available. What to do? The students are told to find the linear combination that gets closest to the target. Students see that finding a least squares fit can be interpreted in just this way, the parameters sought being the coefficients in a linear combination of vectors determined by the model. Using low dimensional examples, lengths, angles, dot products, and ultimately orthogonal projections are introduced that are used to solve the least squares problem.

Many locally written materials, including daily syllabi, class activities and a module on linear algebra, are available at the course website. They supplement the basic textbook (Hughes-Hallett et al., 2009).

5.4 The Second Semester—Introduction to Statistical Modeling

The development of our Introduction to Statistical Modeling course (ISM) stemmed from a rethinking of the goals of introducing college-level statistics. ISM is typically taken right after AC. To accommodate students who have taken calculus in high school, students can also enter ISM after taking Multivariable Calculus or Linear Algebra; students in ISM must have some exposure to calculus of several variables and basic vector techniques. Most of our students take Multivariable Calculus before Linear Algebra, though the former is not required for the latter. Students who have taken AP Statistics in high school do not place out of ISM, as ISM is a multivariate modeling course.

ISM students should be able to describe realistic systems in meaningful ways. Descriptive statistics in ISM emphasizes multivariate modeling: how two variables are related in the context set by other variables. The idea of a partial

derivative is important in describing relationships. To illustrate, consider the analysis of data from a trial of a cancer drug. Our previous course involved a t-test comparing patients who received the drug and those who got a placebo. In ISM, the effect of the drug can be analyzed in terms of the dose, adjusting for the sex and condition of the patients.

ISM students see the central concepts of statistical inference, and we teach inferential statistics as built on a core framework that unifies the various tests from the t-test to analysis of covariance. The central idea is that models partition variability into deterministic and random components (or explained and unexplained or modeled and unmodeled) and that inference involves comparing the sizes of the two components.

Students should be equipped to build and interpret statistical models that can be used in their work in client disciplines. Computational statistics in ISM includes organizing multivariate data, simulation and bootstrapping, and of course the interpretation of standard reports such as the regression and ANOVA reports.

ISM starts with building and interpreting linear models in a deterministic framework. The emphasis is on how to choose explanatory model terms that can capture important aspects of the variability in a response variable, and how to interpret the coefficients found by fitting. The central decision that a modeler makes is which terms (the columns of the model matrix A, in algebraic language) to include. Since the modeling is multivariate, we can introduce both main effects and interactions early.

To describe the process of fitting a model, we introduce some mathematical abstractions: data as a point in an N-dimensional space and fitting as a projection onto a subspace. We emphasize the geometry of the situation. A central concept is the model triangle, a right triangle whose hypotenuse is the response variable b and whose legs are the fitted values (Ax) and the residuals ($b - Ax$). Correlation coefficients are cosines of angles, variances are square lengths, R^2 is a ratio of square lengths.

We move out of the deterministic framework half-way through the course. Confidence intervals are introduced through resampling. The importance of $\sqrt{N}$ is highlighted and reinforced by teaching about the nature of random walks.

The central inferential paradigm of hypothesis testing is also presented geometrically. The null hypothesis is that the explanatory vectors (the columns of A) point in random directions. In this framework, the one-sample t-test can be done with a protractor. To teach ANOVA and ANCOVA, we build on the idea of a sequence of models and how adding a new model term moves the fitted values (Ax) closer to the response variable (b). The F statistic compares how far our new term took us to what would be expected for a randomly pointing term.

The result is a course that is very mathematical and perceived by the students as useful. They emerge with a set of concepts and skills in statistical reasoning that are a match for their native reasoning skills. Statistics becomes a way to describe and understand relationships of some complexity.

ISM is an ambitious course. There are rich and powerful ideas to cover and it's important not to spend time on technicalities. For example, we do not spend time on the difference between $z = 1.96$ and $t = 2.09$. We do not talk about the unequal variance t-test. Non-parametrics are covered concisely: take the rank before modeling. As mentioned above, we use professional-level software (the R package), presenting carefully selected aspects to the students. Since this is the second semester of using R, we can expect students to learn them fluently.

Students emerge from ISM with a sense of the power of statistics and why many fields rely on statistical methodology. The course is challenging, but not inaccessible; it is taken by about one-quarter of all students at Macalester. A typical course section includes a mix of students heading toward majors in biology (the biology major requires the ACM/ISM sequence), economics, and several other disciplines. It is also taken by all mathematics majors, who benefit from seeing practical applications of mathematics such as linear algebra.

The textbook (Kaplan, 2011) is available at the mosaic website given above.

5.5   Results and Challenges

We are happy with the way the AC/ISM sequence is working at Macalester. Students enjoy the courses, find them useful in further courses and in jobs, and faculty members in other departments (most notably, in biology and economics) appreciate the topics we teach. The big picture view and wide variety of topics that students are exposed to early in college serves students majoring in these client disciplines well. The biggest challenge we face is that of integrating these courses into our majors' plans, in mathematics, applied mathematics, and statistics. On the mathematics side, we need to work on the transition from AC to second semester calculus for those few students who come to us with no calculus at all, start in AC, and then want to consider a mathematics major. For them, AC lacks some of the

algebraic formulations of a more traditional first calculus course that they might need to go on in theoretical or applied mathematics. That said, they too get a very good feel for calculus and are often better prepared for Multivariable Calculus and Linear Algebra when they take them. On the statistics end, there is perhaps too much overlap between ISM and the next Applied Multivariate Statistics course, which is taken by students who decide to complete a statistics major or minor. In short, the courses work very well as terminal courses in our department, which was our intent. Our challenge is that their success has attracted more students with a greater diversity of mathematical backgrounds to want to go on in our department than we saw with a traditional calculus sequence in place. We are happy to continue dealing with this challenge.

References

Craig, N.C., 2004: Chemistry. *Curriculum Foundations Project: Voices of the Partner Disciplines*, S. Ganter and W. Barker, Eds., MAA, 27–35.

Dilts, J. and A. Salem, 2004: Biology. *Curriculum Foundations Project: Voices of the Partner Disciplines*, S. Ganter and W. Barker, Eds., MAA, 15–18.

Hughes-Hallett, D., P.F. Lock, A.M. Gleason, D.E. Flath, S.P. Gordon, D.O. Lomen, D. Lovelock, W.G. McCallum, B.G. Osgood, A. Pasquale, J. Tecosky-Feldman, J. Thrash, K.R. Rhea, Thomas W. Tucker, 2009: *Applied Calculus*. 4th ed., Wiley.

Kaplan, D.T., 2011: *Statistical Modeling: A Fresh Approach*. 2nd ed., Project MOSAIC.

6

Biology in Mathematics at the University of Richmond

Lester Caudill[1]

Department of Mathematics & Computer Science, University of Richmond

Name of Institution	University of Richmond
Size	about 3,000 students
Institution Type	small four-year private college
Student Demographic	recent high school graduates with high potential and interests in mathematics or biology
Department Structure	Mathematics and Biology are individual departments in the School of Arts and Sciences

Abstract

In an effort to meet the needs of science students for modeling skills, three new courses have been created at the University of Richmond: Scientific Calculus I and II, and Mathematical Models in Biology and Medicine. The courses are described, and lessons learned and future directions are discussed.

6.1   Course Structure (Scientific Calculus)

- Weeks per term: 15

- Classes per week/type/length: three 50-minute class meetings each week

- Average class size: 17–20 students

---

[1] lcaudill@richmond.edu

- Enrollment requirements: For freshmen with previous calculus experience.
- Faculty/dept per class, TAs: Taught by one mathematics faculty member.
- Next course: Mathematical Models in Biology and Medicine (see below)

6.2   Course Structure (Mathematical Models in Biology and Medicine)

- Weeks per term: 15
- Classes per week/type/length: three 50-minute class meetings each week
- Average class size: 8–12 students
- Enrollment requirements: Completion of Scientific Calculus sequence. Alternatively: completion of regular calculus sequence, along with linear algebra.
- Faculty/dept per class, TAs: Taught by one mathematics faculty member.
- Next course: There is currently no course specifically designed to be a follow-up to this course.

6.3   Introduction

Some of us believe in the inherent beauty and elegance of mathematics and that it is an important subject worthy of study in its own right. For others, appreciation for mathematics hinges not on its inherent goodness but on its being good *for something*. For years, I have been a proponent of applications in introductory-level mathematics (especially calculus), as long as the applications are modern and real. They are best if they are relevant to the class members, relating to something that interests them.

An opportunity to put this philosophy into practice came as part of a multi-year Science Initiative at the University of Richmond. Part of this program, funded by a grant from the Howard Hughes Medical Institute, was an effort to increase interdisciplinarity in our introductory science and mathematics courses. Within mathematics, our goals were to revise the content of our calculus sequence to emphasize the relevance of mathematics to the sciences, and to help science students understand and use the role of mathematical modeling in scientific investigation. This effort resulted in the creation of three new math courses:

- A two-semester course called Scientific Calculus I–II
- A one-semester upper-division biomedical modeling course: Mathematical Models in Biology and Medicine

Scientific Calculus is intended for students who intend to major in one of the sciences, and is open to students who have completed a good high school calculus course. The modeling course is open to students who have completed the scientific calculus sequence, and to students who took the mainstream calculus sequence and linear algebra.

The University of Richmond is a small (about 3000 students), private, primarily undergraduate liberal arts institution in Richmond, Virginia. The typical Richmond student arrives with a good background in mathematics, including success in AP (or comparable level) calculus. Thus we assume familiarity with calculus fundamentals, as is done in Scientific Calculus.

6.4   Development of Scientific Calculus

There were three steps in the design of the Scientific Calculus sequence:

1. Identify the most relevant calculus and modeling topics for the sciences.
   To identify historically absent or underrepresented topics, we consulted with faculty members from the sciences, to identify important mathematics topics and to solicit topics and examples from their science courses that could be used in Scientific Calculus. We also conducted research into the modern uses of mathematical modeling in the sciences, through a review of current literature. The result was the following list:
   - □ Early exposure to multivariate calculus.
   - □ More emphasis on worst-case error estimates, error propagation, and practical estimation.

 □ Responsible data set management, including regression techniques.
 □ Discrete probability.
 □ Linear algebra and dynamical systems.
 □ Modern and relevant illustrations, examples, and applications.

2. Make room in the mainstream two-semester calculus sequence for topics from Step 1 that are not currently included.

   We accomplished this in two ways. First, we omitted some topics that remain in calculus curricula because they have somehow earned "tenure" by enduring for so many years, in spite of being of little value to science. These topics include the endpoint convergence tests for Taylor series, as well as some of the old traditional physics/geometry applications, like computing the work done in carrying a leaky sand bag up a ladder. Next, we restricted the course to students who already have a good calculus background. This permits us to relegate some simple or review topics to outside readings and assignments, thereby opening more class time to the new topics. Some of the relegated topics include functions and other pre-calculus review, derivative shortcut formulas (except for the chain rule and implicit differentiation), vector basics, and single-variable optimization.

3. Fill the resulting room in the topics list with the topics from Step 1, and organize the topics into a logical and coherent order.

This is best illustrated by the current sequence of topics in the courses, as listed below.

6.5 Scientific Calculus Topic Sequence

The new course sequence was first offered during the 2005–6 academic year, and has been offered each year since. The sequence of topics now is

- Scientific Calculus I:
  ○ Fitting models to data (linear and nonlinear regression)
  ○ Building assumptions and hypotheses into models via rates-of-change
  ○ Average rate of change, instantaneous rate of change, and the derivative, with emphasis on linear approximations and optimization
  ○ Multivariate differential calculus, with emphasis on linear approximations and optimization
  ○ Definite integrals
- Scientific Calculus II:
  ○ Applications of definite integrals
     In pharmacokinetics
     Distribution and density functions
     Survival-renewal models
  ○ Probability and uncertainty (including both discrete and continuous random variables and distributions)
  ○ Polynomial approximation of functions; Taylor series and intervals of convergence
  ○ Dynamical systems models
     Single difference equation models
     Single differential equation models
     Discrete dynamical systems and linear algebra (culminating in the dominant eigenvalue theorem)

It is critical to motivate and introduce each major topic with science questions and applications. Without this, the relevance of the material to other fields can be lost.

   Finding a text for the course was difficult. We reviewed texts that purport to present calculus from a scientific (usually biological) perspective, but none could do all of

- present all the topics in Scientific Calculus in the sequence we cover them
- motivate and introduce the topics in a manner consistent with the theme and philosophy of the course

We elected to use the same text as we use in our mainstream calculus sequence. This gave us material for about 60% of the two semesters. The remaining 40%, as well as motivational and contextual materials for many of the text sections, is covered by homemade materials, including many handouts, computer labs, data sets, assignments, and examples. These homemade materials will be made publicly available soon.

6.6   **Biomedical Modeling Course**

As a follow-up to the Scientific Calculus sequence, we created an upper-level mathematics course, Mathematical Models in Biology and Medicine, with the goal of teaching science students to construct and analyze mathematical models of scientific processes, using difference and differential equations.

The strategy in the course is to teach some modeling principles and then use them to study differential and difference equation models in biology and medicine. The topics and their order were planned to introduce successively higher-level model-building and analysis skills. The mathematical theme is an extended notion of compartment modeling, developed specifically for the course. The course topics follow. For each, the new model-building skills introduced are noted in parentheses.

- Biological control of pest populations (modeling principles and single compartment models)
- Spotlight #1: Tumor growth dynamics (more single population models)
- Pharmacokinetics (multi-compartment systems with linear transfer rates)
- Spotlight #2: Models of chemotherapy (combines population and PK models)
- Epidemiology (multi-compartment systems with nonlinear transfer rates)
- Interacting populations (two or more multi-compartment systems that interact)
- Spotlight #3: Leukemia dynamics (an application of interacting populations models)
- Immunology of the HIV virus (a combination of several previous model types)
- Age- or Stage-structured population models (different compartment dynamics)
- Biochemical kinetics (more-complicated types of interactions)

The three spotlights reflect a recurring theme of mathematical modeling in cancer research, showing students the range of modeling problems and opportunities in a single biomedical field.

The course combines lecture, hands-on activities, and outside-of-class assignments. Each unit has the same structure, illustrated by the components of the unit on epidemiology:

1. Begin with a discussion of the biological and medical information needed to model epidemiological processes.

2. Introduce some simple modeling situations (e.g., direct person-to-person spread of a disease in a closed population), and construct difference equation and differential equation models for them. Students explore variants (e.g., other modes of transmission) in homework assignments.

3. After constructing models that are nonlinear autonomous systems, we learn how to perform local stability analysis at equilibria of a system of difference equations or differential equations. Students continue to construct and analyze variants of the models we construct in class.

4. The final class day of the unit is devoted to an in-class modeling challenge, in which students work in pairs to create (and defend!) a model for a situation that is related, but different from previous models (a disease with a different mode of transmission). They must assume:

    a. A closed population, except for disease-related deaths.
    b. No immunity conferred.
    c. The disease is spread by a vector (i.e., another creature, like mosquitos with malaria or West Nile Virus).

    This was an interesting activity because it required the students to combine epidemic models with population models, a topic from a previous unit.

The course culminates in a major modeling project, which the students work in pairs to complete. Projects from recent years include:

- *Antibiotic treatment of bacterial infections.*
  Develop models of two strains of bacteria with differing susceptibility to a particular antibiotic. (The models are more like population models than pharmacokinetic models.)

- *The spread of nosocomial (i.e. hospital-acquired) infections*.
  Develop models of an infection that is spread between hospital patients by healthcare workers.

- *Chemotherapy of cancer tumors.*
  Develop models of tumor growth, under chemotherapy treatment, that account for the fact that cells on the tumor surface are more susceptible to drug-induced death than the interior cells are. (This project was proposed by a math/pre-med major in the course.)

- *Cancer tumor growth and radiation therapy.*
  Develop more-realistic models of tumor growth, by accounting for different types of mutant cells, and incorporate the effects of radiation therapy.

- *Drug dosing regimens.*
  Develop models that aid in designing an outpatient drug administration schedule.

- *Dynamic instability of cytoskeleton components called microtubules.*
  This project was proposed by a pair of biochemistry and molecular biology majors in the course. In each project, the students constructed one or more mathematical models, analyzed them, and studied variants.

There is currently no text for this course. There are many modeling books that focus on the analysis of a model, but few that focus primarily on the *construction* of models. Model-building skills are the primary focus of this course, so the class operates from a homemade set of notes, homework assignments, and computer labs.

6.7 Discussion

After the initial offering of Scientific Calculus in 2005–6, the sequence of topics was significantly revised. We discovered that the students, because they had all taken a calculus course previously, were not seeing enough new material in the first semester. In response, we moved the unit on multivariate differential calculus into the first semester, resulting in a better balance of new and familiar material across the semesters. The course has now been offered enough years to achieve a stable topic sequence. The next improvement is likely to involve a small number of data-gathering wet labs, to provide students with their own data sets.

Mathematical Models in Biology and Medicine has been added as a regular course in our mathematics curriculum. This course has also been offered enough times to reach a stable syllabus.

7

A Terminal Post-Calculus-I Mathematics Course for Biology Students[†]

Glenn Ledder [1]

Department of Mathematics, University of Nebraska-Lincoln

Name of Institution	University of Nebraska-Lincoln
Size	about 24,000 students
Institution Type	large state university with PhD program
Student Demographic	recent high school graduates with high potential and interests in math and/or biology
Department Structure	Mathematics and Biology are individual departments in the College of Arts and Sciences

Abstract

Most innovative mathematics curricula for biology students assume the form of a two-semester calculus sequence that diverges quickly from the standard calculus sequence. However, there are important groups of students for whom this plan is not ideal. The University of Nebraska-Lincoln has developed a model in which the first course can be any introductory calculus course and the second course is a terminal calculus-based mathematics course that focuses on modeling, probability, and dynamical systems. In this paper, we consider the pedagogical issues raised by such a course and provide details on the topics taught in the course and the methods used to teach them.

7.1 Course Structure

- Weeks per term: 15

- Classes per week/type/length: five 1-hour lecture/lab/recitation periods each week

---

[1] gledder@math.unl.edu

- Labs per week/length (if any): 1-hour laboratory periods as needed
- Average class size: 5–10 students, but could accomodate 30
- Enrollment requirements: One calculus course
- Faculty/dept per class, TAs: Taught by one mathematics instructor, with a TA for grading.
- Next course: This course gives students the necessary background to take more advanced interdisciplinary courses in mathematical biology. Both the Department of Mathematics and the School of Biological Sciences have such a course.

7.2   Introduction

The need for a new mathematics curriculum for biology students has been well documented (National Research Council, 2003). Most of the response to this need has come in the form of two-semester curricula that distinguish biology students from other science students at the beginning of their academic careers. We have taken a different approach at UNL because

1. In the American educational system, many students enter college uncertain of their major and career plans. It is desirable to have a flexible curriculum that allows them to defer their choice of program until after their first semester. This suggests a two-semester curriculum that is sufficiently similar to the standard engineering calculus to allow students to transfer from one to the other after the first semester.

2. In addition to an undergraduate major in biology, UNL has a major in fisheries and wildlife biology. Students in this program are required to take any one calculus course, and most choose the 3-credit business calculus course over the 5-credit engineering calculus or biocalculus courses. After encountering quantitative problems in their major courses, some of these students are interested in developing more mathematics background, but lack the prerequisites for a biocalculus II course. This suggests a terminal course in useful mathematics for which any calculus I course can serve as a prerequisite.

3. UNL has faculty in the life sciences who are interested in mathematical biology. These faculty members have PhD students who need to learn mathematical tools for their research. Such students do not have the background for courses in differential equations, linear algebra, or mathematical biology, and they lack the time to take an entire calculus-for-biology sequence. This suggests a terminal course in useful mathematics beyond calculus—a course that allows them to succeed in spite of having no recent work in calculus.

These considerations led to the development of a course called Mathematical Methods for Biology and Medicine (MMBM), which was taught at UNL five times from 2005 through 2010. The course gradually evolved in an effort to better meet the needs of its several student populations:

- Undergraduate biochemistry majors who have recently taken a 5-credit calculus I course;
- Undergraduate biology majors who have recently taken a 5-credit calculus I course;
- Undergraduate fisheries and natural resources majors who have recently taken a 3-credit business calculus course;
- Graduate students from various life science departments, for whom calculus is but a distant memory.

The needs of these groups were determined by consultation with the undergraduate curriculum committees of the client departments and the mathematically-oriented ecology and natural resources faculty. The standard biochemistry curriculum requires two 5-credit calculus courses but lacks statistics or differential equations. The standard biology curriculum requires a 5-credit calculus I course and either the second calculus course or a 3-credit non-calculus-based statistics course; most biology students take the latter because of the smaller number of credits, and nearly all students find it to be of little value.

7.3 Course Overview

We decided to offer Mathematical Methods for Biology and Medicine as a 5-credit course to accommodate the biochemists' desire for an alternative to calculus II worth the same number of credits. This provided ample time for important topics but made the course less attractive to undergraduate biology majors. Because the course met the needs of the biochemistry students better than calculus II, our hope was that it would eventually become the default second course for biochemistry majors, assuring us of a stable enrollment. The class met for a 50-minute period five days each week in a classroom with computers. Having me in the classroom every day gave me the flexibility of being able to mix lecture and computer laboratory activities according to pedagogical needs. For continuing viability, we would have eventually needed to have a teaching assistant take the course one day each week for computer laboratory activities and review—this move is necessary for institutionalization of the course because faculty loads are never more than seven credits in a semester.

Table 1 shows the outline of topics for the course. The first four items are lecture units, which will be discussed in more detail later. The student presentations are informal, with each student giving a talk about ten minutes long using either a slide presentation or the board. The students are asked to find a journal article or book chapter in which mathematics is used for research in a life science area. I provide guidance if they need help finding a source. They are instructed to focus on the biological setting, a very general description of the mathematics used, and the biological significance of the results. The mathematics must go beyond mere statistical analysis of data, but I do not expect them to understand the details. The point of this assignment is to give the class a sample of the many uses of mathematics in biology. I allow a couple of minutes for friendly questions, and I can almost always add a little additional information to the presentations using my general knowledge of mathematical models in biology.

Mathematical Modeling	2–3 weeks
Review of Calculus	1 week
Probability	4–5 weeks
Dynamical Systems	5 weeks
Student Presentations	1 week

Table 1. General Outline of Mathematical Methods for Biology and Medicine

The lecture portion of the course used my lecture notes, as I could not find a suitable textbook.[2] The main reasons for this are that there is no published treatment of mathematical modeling as I envision it and that all the published materials on dynamical systems require more background knowledge than I can expect from my students. In the following discussion of the lecture materials, I emphasize my strategies for teaching these advanced subjects to students with minimal background.

7.4 Mathematical Modeling

Mathematical modeling involves constructing mathematical models from a conceptual model (a simplified narrative description of the biological principles believed to be at work), determining parameter values from data, characterizing and testing models, and using them to make predictions about scientific experiments. These skills are not generally taught anywhere in the mathematics curriculum. I introduce them in a precalculus setting so that I can start the course with an area that is familiar to everyone and the modeling skills can be reinforced in the calculus review portion of the course. The topics in the modeling unit are listed in Table 2; each is discussed in some detail below.

1. Functions with Parameters

Parameters are an essential feature of mathematical models, as they provide ways to incorporate numerical data that may be uncertain or may differ among cases. Previously, students have learned to interpret symbols as either

---

[2] My book *Mathematics for the Life Sciences: Calculus, Modeling, Probability, and Dynamical Systems* will be published by Springer-Verlag in 2013.

Functions with Parameters
Concepts of Modeling
Fitting Models to Data
Empirical and Statistical Modeling
Mechanistic Modeling

Table 2. Mathematical Modeling Topics

dependent or independent variables, and they find it difficult to understand parameters and to manipulate functions that contain them. Lack of experience with parameters is one reason why calculus students have trouble understanding the definition of the derivative, which is based on a family of secant slopes with the horizontal distance between the points as the parameter. Understanding parameters is useful, but not central, in calculus; most students complete calculus in spite of not understanding them. We make this possible by avoiding problems with parameters on exams. In contrast, parameters are so integral to mathematical modeling that students are unable to learn the subject at all without a minimal facility.

In my introduction to parameters, I focus on the ways they affect the graphs and analytical properties of functions. Figure 1 illustrates the function $f(x) = x^3 - 2x^2 + bx$. The parameter b changes the shape of the graph, qualitatively as well as quantitatively. When we reexamine this function in the calculus review unit, we can determine the bifurcation point; that is, the value of the parameter where the function changes from monotone to not monotone.
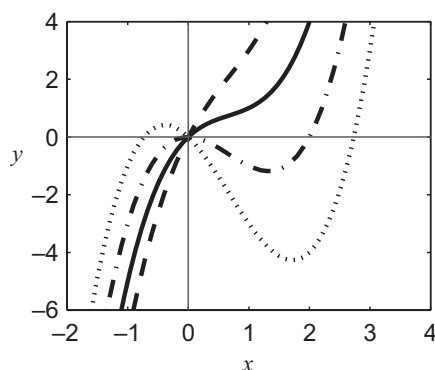
Figure 1. $f(x) = x^3 - 2x^2 + bx$ with $b = -2$ (dotted), $b = 0$ (dash-dot), $b = 2$ (solid), and $b = 4$ (dashed)

2. Concepts of Modeling

In their previous experience with applications of mathematics, students have been misled into thinking that the scientific value of a model is equivalent to its mathematical value. It is important to disabuse students of this notion. At best, we may claim that a mathematical model is *valid* or *useful*; we should not be so bold as to say that it is *correct* or *true*. Results obtained from mathematical models are often mathematically correct but counterintuitive. Such results are usually wrong. This is not a mathematical issue. Mathematics can determine the properties of models, but it cannot determine their validity. Validation of models requires comparison with data.

I want my students to understand that mathematical models can be treated in two ways. The general case of a model can be analyzed mathematically using the ideas learned in an initial study of parameters. Specific instances of a model can be worked out by numerical simulations, which is useful if a valid set of parameter values is known. It is also important for students to appreciate that the same model can take different symbolic forms by using different parameters. As an example, the mathematical formulations $f(t) = f_0 e^{-kt}$ and $f(t) = Be^{-t\ln2/T}$ represent the same model, despite the different symbols for the initial value parameter and the use of the decay constant k in one and the half-life constant T in the other. This is far from obvious to students and needs emphasis. Similarly, the relationship between these dimensional models and the corresponding dimensionless model $F(\tau) = e^{-\tau}$ is difficult for students to understand.

3. Fitting Models to Data

The parameter values used in the examples for the previous sections were chosen for mathematical convenience. In practice, students need to know how to choose parameter values to fit a set of data. I focus on three simple models,

$$Y = mX, \quad y = b + mx, \quad z = Ae^{-kt},$$

which I do using linear least squares. I've never seen the 1-parameter model $Y = mX$ treated as a separate case, but I find it useful when the graph of the function is expected on scientific grounds to pass through the origin. The mathematical benefit from treating this special case first is that we can define a one-variable function,

$$F(m) = \left(\sum X^2\right) m^2 - 2 \left(\sum XY\right) m + \left(\sum Y^2\right)$$

to represent the residual sum of squares for any slope m. Its minimum is the vertex of the parabola, which can be found algebraically if necessary (for students who have not had any calculus). Once the students have learned to fit the one-parameter straight line, the two-parameter straight line follows easily from the assumption that the best fit line must go through the mean $(\bar{x}, \bar{y})$ of the data (this can be proven using multi-variable calculus, but I ask the students to accept it on intuitive grounds). The original xy data can be converted to XY data by

$$X = x - \bar{x}, \quad Y = y - \bar{y}.$$

The slope m can then be found as before, and the intercept b follows by replacing X and Y in the model $Y = mX$ by the same formulas.

4. Empirical and Statistical Modeling

In biology, it is common to choose mathematical models by reverse engineering from data. As a simple example, we can try to choose between a power function model and an exponential function model by plotting the data as $\ln y$ vs $\ln x$ and as $\ln y$ vs x; a power function model is used if the former plot suggests a straight line, while an exponential function model is used when the latter plot is more suggestive of a straight line. In scientific practice, choosing between competing models by looking at graphs has been supplanted by the use of the Akaike Information Criterion (AIC), which assesses the relative statistical support for competing models, given a particular data set, by balancing residual error against complexity (see McQuarrie and Tsai (1998)). It is curious that this useful tool has not become part of the standard elementary statistics syllabus since its discovery in 1974. Perhaps this is because the derivation of the formula is quite difficult.[3] Nevertheless, its application is simple, and anyone doing mathematical modeling in biology should be able to use it. The simplest example of its benefit is that it shows the one-parameter model $y = mx$ to be superior to the two-parameter model $y = b + mx$ in just those cases for which scientific principles suggest the simpler model. For example, if x is the number of prey animals available to a predator and y is the number of prey animals consumed in a unit time interval, it is a logical necessity that $y(0) = 0$. A minimum error fit of real data to the model $y = b + mx$ yields nonzero b; the more complicated model has smaller error, but is qualitatively wrong. With reasonably good data, AIC is almost certain to select the simpler model.

It is particularly important for students to understand why complexity in a formula is a drawback. It is not merely because simple formulas are easier to work with. It is because complex formulas often have complicated behavior that does not match the simple behavior expected by theory. Figure 2 shows a data set generated by adding a small amount of random noise to the function $Y = 0.3X$, along with two attempts to fit the data to a model. The dashed line is the model $Y = mX$, while the curve is a quartic polynomial; both models were parameterized using the odd-numbered points, with the result shown in Figure 2a. The quartic polynomial fits the data exactly and would therefore be preferred if accuracy were the only criterion. However, the inclusion of the even-numbered points in Figure 2b shows that the quartic polynomial is oversensitive to variations in the data, which more than compensates for the advantage of perfect accuracy of fit to a small data set. Of course we could fit a quartic polynomial to the full data set, but the fit would again be problematic if we added more data points.

---

[3] While I agree that we should not teach unmotivated (black box) methods, I think most mathematicians go too far with their insistence that everything must be rigorously proved. I like to characterize mathematicians as people who believe that you shouldn't drive a car unless you have built it yourself.
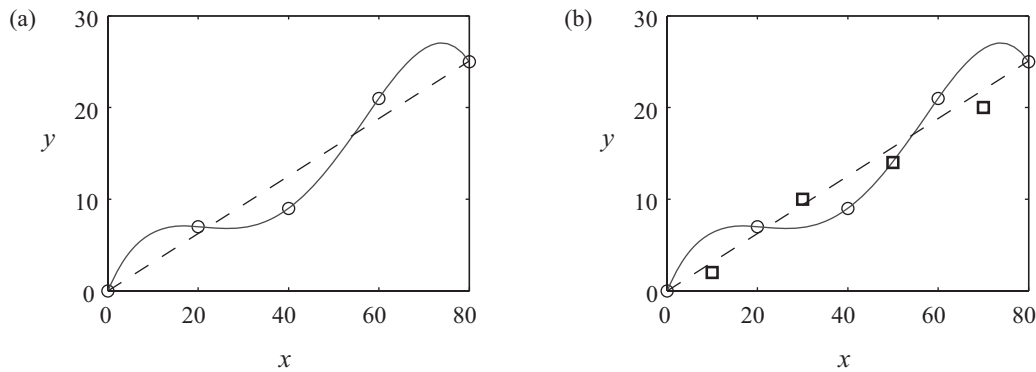
Figure 2. A dataset fitted by linear and quartic models; the parameters were determined using only the odd-numbered points, as shown in (a), while (b) shows the same parameter choices with all of the data.

5. Mechanistic Modeling

Here we discuss the derivation of models from assumptions based on biological principles, a topic that has been discussed elsewhere (Ledder, 2008). I also indicate a relatively simple method for parameterizing models of the form $y = mf(x; p)$, where m and p are parameters. The method utilizes the special structure of a model in which one parameter enters nonlinearly while the other appears only as a scaling factor:

1. Let $t_i(p) = f(x_i; p)$ for each data point (x_i, y_i) and a range of p.
2. Define a function $G(p)$ by

$$G(p) = \min_{m \in \mathbb{R}} \sum [y_i - mt_i(p)]^2.$$

3. The best fit for p is the value that minimizes the function G.
4. The best fit for m is the value that minimizes the sum when p is the best fit value.

The method works because the nonlinear model reduces to the linear model $y = mt$ for any particular p, allowing us to determine the residual sum of squares as a function of p. The function $G(p)$ can be computed numerically and plotted to obtain an estimate for the best fit value of p. Of course we could use nonlinear optimization software as a black box, but it is much more instructive to use a method that students can understand.

7.5   Calculus

The course requires one calculus course as a prerequisite, but some of the students have not seen calculus in several years. This poses a difficulty, as some of them could use a semester-long refresher course while others need at most a day or two of review. I address this problem by deemphasizing use of techniques of calculus in the subsequent units on probability and dynamical systems and using functions with parameters whenever possible. I expect my students to be able to use the basic differentiation rules for simple functions, the fundamental theorem for definite integrals that require only elementary antiderivative formulas and substitution, and Simpson's rule for definite integrals that cannot be calculated by the fundamental theorem. The primary focus of the review is on the concepts of calculus, because it is the concepts that generate the applications. Thinking of the derivative as the slope of a graph leads naturally to its use for optimization. Similarly, thinking of the definite integral as accumulation in time, space, or structure leads to more obvious applications, such as obtaining distance from velocity or total population from spatial population density, and to more subtle applications, such as obtaining the total population from an age-distribution function. From here, one can derive Euler's equation for the growth rate of an age-structured population fairly simply. If $l(x)$ and $m(x)$ are the probability of survival to age x and the rate of offspring production per parent of age x respectively, then the population of parents of age x is $B(t - x)l(x)dx$ and so the total rate of offspring production is

$$B(t) = \int_0^\infty B(t - x)l(x)m(x)\,dx.$$

However, if the population grows at rate r, then the birth rate must also grow at rate r; hence, we also have $B(t) = B(0)e^{rt}$. Substituting this formula into the integral equation yields Euler's equation

$$1 = \int_0^\infty e^{-rx} l(x) m(x) \, dx,$$

which students can explore by using specific functions for survival and fecundity, obtaining an estimate for r by trial and error (Comar, 2008).

7.6 Probability

Table 3 lists the topics in the unit on probability. The topics and their order are based on two principles:

1. Students learn best when probability is approached experimentally rather than axiomatically.

2. Biologists are most interested in having their students learn how to work with probability distributions.

Characterizing Data
Concepts of Probability
Discrete Distributions
Continuous Distributions
Distribution of Sample Means
Conditional Probability
Estimating Parameters with Likelihood

Table 3. Probability Topics

My first principle is motivated by the pedagogical work of Lock and Lock (2008). The second is the result of conversation with biologists at my institution. A consequence of these principles is that I don't spend much time on the usual introductory problems that use a uniform discrete distribution with combinatorics. I do work with probabilities of various nucleotide combinations in DNA, but I avoid problems with card games or colored marbles in an urn. Another consequence is that I do probability distributions before conditional probability. It is logical to progress from studying sample means, which are the results of multiple experiments, all similar, to studying probability in multiple experiments, each different.

I think of a probability distribution as model of an infinite population, so it is natural to begin with elementary descriptive statistics of finite samples and move directly to probability distributions. Our study of distributions emphasizes the definitions of the fundamental distributions, using the probability distribution function for discrete distributions and the cumulative distribution function for continuous distributions, and using them to calculate probabilities. I spend a lot of time on distributions of sample means because they are central to understanding what biologists actually measure. Each measurement made by a biologist corresponds to drawing a number from a probability distribution. However, the variances of distributions in biology are high. Biologists thus take multiple measurements, so measurements in biology are means of samples from a distribution. Biologists need to understand that their measurement constitutes a single number drawn from a distribution of sample means rather than a number drawn from a distribution of individual experimental values. If an experiment is conducted flawlessly, there is still a 4% chance that the true mean of the population lies more than two standard deviations (of the distribution of means, not the distribution of individuals) from the mean calculated from the experimental data. This probability of anomalous results cannot be decreased; the only way to be confident in a biological measurement is to average together so many individual measurements that an error of two standard deviations in the mean is acceptable.

My coverage of the final two topics depends on the makeup of the class. Conditional probability is particularly important in the understanding of medical test design. Rare conditions are hard to test for because a small probability of false positives can nevertheless yield more false positives than true ones. The last topic is of special value to practicing ecologists, so I present it only if there are ecology graduate students in the class.

7.7   Dynamical Systems

Discrete and continuous dynamical systems are usually treated separately. I find it beneficial to treat them together in the context of one-dimensional systems before separating them for multi-dimensional systems. The outline of topics appears in Table 4. My presentation follows several pedagogical principles:

1. Students should have experience with dynamical systems in scalar form before attempting a more mathematical treatment with vector notation.

2. The primary goal of mathematical analysis is to determine the long-term behavior of a system in different regions of the parameter space. (In particular, I have my students obtain analytical solutions only for the trivial exponential growth equations.)

Single Variable Dynamics
    Discrete Models
    Continuous Models
    Cobweb Plots
    The Phase Line
    Stability Analysis
Discrete Dynamical Systems
    Discrete Linear Models
    A Matrix Algebra Primer
    Eigenvalues and Eigenvectors
    Theoretical Results
Continuous Dynamical Systems
    Continuous Models
    The Phase Plane
    Stability for Linear Systems
    Stability for Nonlinear Systems

Table 4. Dynamical Systems Topics

Elementary genetics serves as a nice introductory example for discrete one-variable models (Comar, 2008). Suppose p is the gene pool frequency of the malaria susceptibility trait **A** and $q = 1 - p$ is the frequency of the sickle cell trait **a**. Suppose these traits are randomly distributed[4] among individuals in a population. Then the genotypes **AA**, **Aa**, and **aa** have frequencies p^2, $2pq$, and q^2, respectively. If we assign a value of 1 to the fitness of the heterozygote **Aa**, then the fitness of the homozygote **AA** is some number $m \in (0, 1]$ whose value depends on the risk of malaria. The homozygote **aa** results in sickle cell anemia, with fitness 0. Given these assumptions, the relative frequencies of parents are in the ratio $(1 - m)p^2 : 2pq$. Hence, the next generation has traits **A** and **a** with relative frequencies given by the ratio $[2(1 - m)p^2 + 2pq] : 2pq$, from which we can obtain the difference equation

$$q_{t+1} = \frac{q_t}{(1 - m)(1 - q_t) + 2q_t}$$

for the sickle cell trait. Students can experiment with this model, with questions such as

1. If the risk of malaria is extremely high ($m \to 0$), what happens to the gene pool?

2. Suppose a population with a given initial q moves to a non-malarial environment. How does the frequency of the sickle cell trait change over 100 generations?

---

[4] This discussion is facilitated by my opting to discuss probability before studying dynamical systems.

My favorite continuous model is the resource utilization model

$$\frac{dx}{dt} = f(x) - Cg(x),$$

where x is the level of some resource, f is a function representing its natural change, g is a function representing the decrease in level caused by an average consumer, and C is the fixed number of consumers. We can use the prey equation from any predator-prey model, with the level of predators taken as a parameter rather than a dynamic variable. We use Matlab's built-in numerical differential equation solver to run simulations with models of this form. Students quickly discover the concepts of stable and unstable equilibria, which are then explored mathematically in the subsequent sections on the phase line and stability computation.

I have my students develop a stage-structured population model as an example of a discrete system. Numerical experiments (see Ledder et al. (2012)) lead naturally to the discovery of the dominant eigenvalue and its eigenvector as the long-term stable growth rate and stage-distribution ratio. I present the formal theory of eigenvalues only after this initial exploration.

There are a number of good models to use as introductory examples for continuous dynamical systems. Pharmacokinetics provides a good example of a linear system, and Michaelis-Menten kinetics provides a relatively simple example of a nonlinear system. Depending on the student populations, I will also use the Perelson and Nelson (1999) HIV model or a predator-prey model with logistic growth in the prey and a Holling Type 2 functional response (Brauer and Castillo-Chavez, 2001). These examples help students to learn nullcline analysis and linearized stability analysis.

7.8   Postscript

Unfortunately, the 5-credit course described here never caught on with biochemistry freshmen, in spite of its acceptance by the biochemistry faculty. The difficulty was the tendency of students to take advice from their peers rather than their professors. Establishment of a course depends on satisfying one of two conditions: either the course must be required, or the curriculum must be such that the course is clearly the path of least resistance for a large number of students. Biochemistry students could not be persuaded to select an unfamiliar course to replace the familiar Calculus II. I am now working with the School of Biological Sciences at UNL to repackage the course material in a way that makes the course part of the path of least resistance for biology majors. This will require the course to be offered as an alternative to Calculus I, which means a 5-credit course in calculus and dynamical systems. The irony is that this change will take me back to tracking students into biomath courses in the first semester, precisely what my project was intended to avoid. The clear lesson, stated in terms of the parts of this volume, is that no *model* can survive unless it is part of a successful *process*.

7.9   Conclusions

Mathematical Modeling for Biology and Medicine never had enough students to produce formal data regarding its success. However, I collected feedback from the students each time I taught the course, and I kept track of student success with the various topics. Students have consistently given positive evaluations of the course, but my analysis of the outcomes of the course is mixed. The dynamical systems portion of the course has been most successful. While topics such as nullcline analysis and linearized stability analysis are normally taught late in a differential equations course, they do not require background other than facility with algebra and graphing, an understanding of the derivative as a rate of change, and some ability to compute derivatives. The probability portion of the course has improved in the last two runs, perhaps owing to the topic list and pedagogical methods presented here, which were somewhat different from prior implementations of the course. The mathematical modeling portion of the course is the one that seems most difficult to the students. They generally do well with fitting models to data, but they have trouble working with parameters, in spite of the attention I give to the topic. In particular, my classes have not done well in understanding dimensionless form. However, the idea presented here of beginning the course by studying functions with parameters is new and as yet untested. I am optimistic that the mathematical modeling portion of the course can be as successful as the other portions, given enough class time and a pedagogy that subdivides the topic into a hierarchy of skills.

Ultimately, the success of any new course depends on attaining two goals:

1. It must develop a steady enrollment so that it can be taught as a regular (not externally-funded) course offering.

2. It must become a department course rather than an individual instructor course; that is, the materials and pedagogy need to be sufficiently well documented that other faculty can teach it. I am hopeful that future publication of my materials in book form will make it possible for courses such as mine to be successful.

References

Brauer, F., and C. Castillo-Chavez, 2001: *Mathematical Models in Population Biology and Epidemiology*, Springer-Verlag.

Comar, T.D., 2008: The integration of biology into calculus courses. *PRIMUS* **18**, 49–70.

Ledder, G., 2008: An experimental approach to mathematical modeling in biology. *PRIMUS* **18**, 119–138.

Ledder, G., B. Tenhumberg, and G.T. Adams, 2013: An interdisciplinary research course in mathematical biology for young undergraduates. This volume, 69–82.

Lock, R.H. and P.F. Lock, 2008: Introducing statistical inference to biology students through bootstrapping and randomization. *PRIMUS* **18**, 39–48.

McQuarrie, A.D.R. and C.-L. Tsai, 1998: *Regression and Time Series Model Selection*, World Scientific.

National Research Council, 2003: *Bio 2010: Transforming Undergraduate Education for Future Research Biologists*, National Academies Press.

Perelson, A.S. and P.W. Nelson, 1999: Mathematical analysis of HIV-1 dynamics *in vivo*. *SIAM Rev.* **41**, 3–44.

8

Modeling Nature and the Nature of Modeling—an Integrative Modeling Approach

Claudia Neuhauser[1]
University of Minnesota Rochester

Name of Institution	University of Minnesota Twin Cities
Size	About 52,000 students
Institution Type	Large land grant university with graduate and professional programs
Student Demographics	Undergraduate and graduate students in biological sciences programs
Department Structure	The Department of Ecology, Evolution, and Behavior is in the College of Biological Sciences

Abstract

Modeling Nature and the Nature of Modeling is a sophomore level course that covers aspects of linear algebra, differential equations, difference equations, and stochastic processes that are relevant to biology majors. The course emphasizes active learning, in-class computer experiments, and integrates data into modeling. While the course is mathematically rigorous, it emphasizes experimental exploration of concepts before their rigorous treatment.

8.1   Course Structure

- Weeks per term: 15

- Classes per week/type/length: two 75-minute integrated lecture/computer lab each week

---

[1] neuha001@umn.edu

- Labs per week/length: integrated with lecture
- Average class size: 15–20 students in one section
- Enrollment requirements: some familiarity with calculus (one semester)
- Faculty/dept per class, TAs: Taught by one instructor
- Next course: This course gives students an introduction to modeling that can serve as the basis for graduate level research in the biological sciences or prepare students for interdisciplinary mathematics courses with a biology focus that are available in the School of Mathematics
- Website: http://bioquest.org/numberscount/courses/bshs-calculus-2/

8.2   Introduction

The course Modeling Nature and the Nature of Modeling was offered at the University of Minnesota Twin Cities through the Department of Ecology, Evolution, and Behavior between 2003 and 2007. It is now being redesigned for a degree program in the Health Sciences at the new University of Minnesota campus in Rochester, Minnesota. The University of Minnesota is a large public research university with over 65,000 students system-wide. In Fall 2012, the Twin Cities campus had about 30,400 undergraduate students, 13,100 graduate students, and 3,800 students enrolled in professional programs. The Twin Cities has a separate College of Biological Sciences (CBS). CBS's total enrollment of undergraduate students is about 1,700. Most of the undergraduate students choose biology as their major. Other majors are biochemistry; ecology, evolution & behavior; genetics, cell biology & development; microbiology; neuroscience; and plant biology. The campus in Rochester was established December 2006 to provide graduate and undergraduate education in health sciences and biotechnology. It started to admit undergraduate students into a Bachelor of Science in the Health Sciences in Fall 2009.

The course Modeling Nature and the Nature of Modeling was offered for the first time in Fall 2003 and subsequently every fall semester to undergraduate and graduate students on the Twin Cities campus until Fall 2007. A version of the course was offered on the Rochester campus starting Fall 2010. Originally, the course was designed to meet the need for further mathematical training after biology students completed a year of calculus to better prepare them for the increasingly quantitative nature of biology. The course is currently being redesigned to serve as the second semester of calculus for students in the new degree program in the Health Sciences on the Rochester campus.

Undergraduate students can take the course after completing a semester of calculus. There is no requirement for an upper division biology course. Graduate students who enrolled in the course on the Twin Cities campus came from various graduate programs in the life sciences and often took their last mathematics course years prior to enrolling in the course. While their understanding of biology and their exposure to primary literature is greater than that of the undergraduate students in the course, they remember little of the calculus they learned as undergraduate students.

When the course was originally designed, all the CBS biology majors were required to take a full year of calculus. Biology majors at the University of Minnesota, Twin Cities, have a choice between regular Calculus or Calculus with Biological Emphasis. The regular calculus course is based on Stewart (2007). Calculus with Biological Emphasis is based on Neuhauser (2004). While the regular calculus course does not cover linear algebra, multivariable calculus, and differential equations in the first year, Calculus with Biological Emphasis introduces students to these topics in the second semester. Since these two first-year calculus courses are taught in large lectures with weekly recitations and no computer labs, the experience of biology majors was limited to what could be done using paper and pencil and graphing calculators. This traditional approach, even in the calculus course for biology majors, makes it difficult for students to experience the rich behavior of these models. The course described here can replace a standard or biology-emphasis second semester of calculus. Materials for the course are available for download at http://bioquest.org/numberscount/courses/bshs-calculus-2/. In addition, I used my Calculus for Biology and Medicine books as supporting material.

The design for the Modeling of Nature and Nature of Modeling course was based on the need for students to learn some of the theory behind the major modeling approaches in biology and to be able to experiment with models, much as biologists explore the natural world, and to be able to interpret in biological terms the equations that describe the models. Connecting mathematical concepts to examples from the natural world is a powerful way to

enhance students' conceptual understanding and their ability to read the equations that describe models. Specifically, connecting mathematical symbols with concrete examples helps students to make sense out of the often overwhelming mathematical expressions in journal articles. With funding from the Howard Hughes Medical Institute, the course is being redesigned to provide a deeper link to data and to integrate it with biology courses, including physiology and biochemistry.

8.3 Course Description

The course covers major modeling approaches in biology: difference equations, differential equations, partial differential equations, and stochastic processes. Obviously, it is impossible to provide a thorough coverage of all these topics in one semester; instead, the focus is on introducing students to them using biological examples for motivation. The goal is to make students comfortable with the mathematical description, providing them with tools for analysis, and experimental ways to explore the models. Theory is introduced when needed and primary literature is provided as background reading.

The course starts with a data set of exponential growth of monk parakeets in the U.S. (Van Bael and Pruett-Jones 1996) and asks students to build a model to describe it. Students are given the data in a spreadsheet and asked to plot it and transform axes to determine the kind of growth. The data has a stochastic component, which students learn to separate from the general trend. The data set introduces students to the simplest growth model, motivates the study of deterministic, discrete-time models and the need to understand how to model stochasticity. These concepts are explored subsequently, using spreadsheet exercises and introducing the students to a more powerful and sophisticated modeling software (Matlab). Students learn to simulate stochastic processes in both a spreadsheet and Matlab. They also learn how to mathematically describe and analyze deterministic growth and growth in a random environment, including how pseudo-random numbers are generated and the importance of the geometric mean of the growth parameter.

The first two-thirds of the course moves quickly through difference and differential equations, emphasizing in-class exploration of the models on the computer, and in-class short group projects where students can practice the more theoretical aspects of the analysis. Difference and differential equations are introduced using population models, and students learn about equilibria and stability. After covering some of the concepts of linear algebra that are needed to analyze systems of difference or differential equations (primarily eigenvectors and eigenvalues), students learn how to solve systems of linear difference and differential equations and to analyze the long-term behavior of systems of non-linear difference and differential equations by linearizing about the equilibrium. The biology behind population models is easy to understand and allows students with different levels of biological understanding to become familiar with modeling biological phenomena without being overwhelmed by both the mathematics and the biology.

A brief introduction to reaction-diffusion and advection-dispersion equations gives students a taste of more complex models. Because of their mathematical complexity, the focus is on understanding the physical meaning of the terms that appear in the equations and to show some of the complex behavior they may exhibit, including pattern formation.

For most students, this is the first time that they experience complex behavior exhibited by mathematical models, and they are surprised by the rich behavior. Whether in a single discrete time equation or in systems of partial differential equations, they begin to appreciate the value of mathematical modeling in aiding our understanding of complex behavior. Students are also introduced to bifurcation analysis. This is rarely taught to biologists but is a very powerful way to analyze the behavior of a mathematical model.

Once students feel comfortable with the various modeling approaches, more complex applications are studied. Examples include biochemical networks, genetic switches, and models of the cell cycle. The purpose of studying these examples is to give students the opportunity to read and understand theoretical papers, using the knowledge they gained in the first two-thirds of the course.

Because of the diverse backgrounds of the students and their different levels of mathematical preparedness, exams in the course are take-home exams where students are allowed to consult books, course notes, and the web. They can seek help from the instructor, and depending on the amount of help they receive, they might have to sacrifice some points. Students are encouraged to view exams as small research projects and are expected to explain their answers as if they were writing a technical report. For instance, one exam question gave students a Leslie matrix for a population of ruffed grouse and asked them to examine the viability of the population (the growth parameter was below the critical value for survival) and to justify management strategies that would rescue the population. Students were told that the

information was limited and that they should view the data as a first step in initiating further study to develop a more comprehensive management plan. Their answer was to be given to a manager at a Department of Natural Resources and so had to include explanations that went beyond just listing the largest eigenvalue of the Leslie matrix for different scenarios.

The course also includes short writing assignments that ask students to reflect on the material or on aspects of learning mathematics.

8.4   Discussion

I have taught the course five times and continue to revise it to incorporate what I learn from teaching the materials. In its first year, the course was split into a weekly lecture followed by a computer lab. The seventy-five minute lecture proved to be too much theory at once. Students could not absorb all the theory and then apply it in the following computer lab. The course felt disconnected.

Starting in the second year, I increasingly combined lecture and lab. Lecture and lab are now completely integrated, seamlessly moving between in-class model explorations and short segments of theory as needed. The course was taught in a computer lab to groups of 10–15 students. The next iteration of this course will integrate data sets into the modules to allow students to explore model behavior using real data with the goal of providing better motivation for the various models.

A major change in the mathematics requirements in CBS on the Twin Cities campus required a redesign of the course to accommodate those who had less exposure to calculus. Most undergraduate majors in the College of Biological Sciences are now required to take only one semester of calculus. The requirement for the second semester of calculus was replaced by either a non-calculus-based statistics course or a computer science course. Fortunately, a second semester of traditional calculus with its focus on integration techniques is not needed to learn modeling based on difference and differential equations. In fact, the course will serve as the second semester of calculus in the new degree program at the University of Minnesota Rochester and will be offered again starting Fall 2010.

One semester is short for a course that covers the major modeling approaches, and we cannot expect students to be proficient modelers after one semester. The course, however, removes some of the barriers biology students with just one semester or one year of calculus face when reading scientific papers that include modeling.

Since students typically do quite well in the course (being able to use books, notes, and the internet during exams contributes to their success), the course also serves as a confidence builder. After it, students can read equations that describe mathematical models more effectively and are less likely to skip over equations in papers. They are also more willing to experiment with models and explore their behavior.

References

Neuhauser, C., 2004: *Calculus for Biology and Medicine*. 2nd edition. Prentice Hall.

Stewart, J., 2007: *Calculus: Early Transcendentals*. 6th edition. Cengage Learning.

Van Bael, S., and S. Pruett-Jones, 1996: Exponential population growth on Monk Parakeets in the United States. *Wilson Bulletin*, **108**, 584–588.

9

Mathematical Biology and Computational Algebra at the Sophomore Level

Rohan Attele* and Dan Hrozencik†
Department of Mathematics, Chicago State University

Name of the Institution	Chicago State University
Size	about 7500 students.
Institution Type	Chicago State University is a public, comprehensive university that provides access to higher education for students of diverse backgrounds and educational needs.
Student Demographic	Mathematics majors with prerequisites of linear algebra, probability and statistics, and two specific freshman biology courses. Biology majors with prerequisites of a sophomore botany course and a sophomore zoology course.
Department Structure	Mathematics and Biology are two MS degree granting departments in the College of Arts and Sciences.

Abstract

Biology provides a rich source of problems that can be solved by non-infinitesimal algebraic techniques. This article discusses the content of an interdisciplinary research-oriented sophomore course in computational algebra and biology created at Chicago State University. The course is part of an attempt to teach abstract algebra on a foundation of computational algebra done at the sophomore level.

9.1 Course Structure

Weeks per term: 16 weeks.

Classes per week: Two 100 minutes sessions.

---

* kattele@csu.edu
† dhrozenc@csu.edu

Labs per week: No specific time set aside for labs; computer or experiment assignments done as needed.

Average class size: Three in the pilot; 15–20 can be accommodated.

Faculty/dept per class, TAs: Team-taught by one mathematics instructor and one biology instructor. No TAs.

Next course: Not yet approved. It will be a course in computational algebra.

9.2   Chicago State University, CSU

Chicago State University has consistently led Illinois public universities in the conferring of baccalaureate and master's degrees to African American students. CSU graduates more African Americans with a master's degree in mathematics than all other Illinois private and public colleges and universities combined, and is a national leader in graduating African Americans with a masters' degree in mathematics.

9.2.1   Department of Mathematics and Computer Science

The department has nineteen faculty members whose active research areas include mathematical biology, geometric algebras, logic, network security, software engineering, programming languages, and analysis (real, complex, and numerical, ODE, PDE). It has shifted focus from being service oriented to offering a research oriented curriculum that prepares students to work in academic and industrial settings.

The following table summarizes the distribution of students in the undergraduate majors and graduate programs.

MAJOR	02–03	03–04	04–05	05–06	06–07	07–08	08–09
Math UG	73	79	76	70	53	35	46
Math GR	27	30	21	25	22	22	19
Computer science UG	204	184	134	119	94	87	82
Computer science GR	4	9	15	14	12	13	8

9.3   Background and Motivation

This paper describes a part of an on-going attempt to develop a computational algebra curriculum at the sophomore level that will lay a foundation for abstract algebra done at the junior/senior level. Genetics provides a source of real-world problems for computational algebra. The authors made a presentation on the project at the MAA MathFest 07.

In private industry, mathematicians are most often part of interdisciplinary teams working closely with biologists, physicists, economists, etc., to solve complex problems (U.S. Department of Labor, 2010). Where in the undergraduate curriculum do students get an experience that will help them to see how mathematicians work, and to decide if that is right for them? Can we get it to them early enough so that it can be useful to their career planning?

In particular, mathematics curricula should prepare majors to have the skills needed to work in teams and bring their mathematics expertise to bear upon interdisciplinary problems. Thus mathematics majors should gain experience in solving a significant real-world problem and in working with individuals having other majors.

We designed *Introduction to Research in Mathematical Biology I*, Math 2180, to provide such an experience. In particular, it provides:

- An early opportunity for students to work in interdisciplinary teams on a real-world research problem.
- An opportunity for students to be the experts in their content areas.
- An opportunity to use relatively elementary mathematics to work on research problems.
- An opportunity to work on a research problem that could continue throughout their undergraduate careers.

9.4   Description of the Course

The course was open to both mathematics and biology majors as an elective. It was team-taught by a mathematics and biology professor, and was offered concurrently by both departments to ensure a mix of both majors.

A key idea was to build teams of students with differing abilities. Biology and mathematics majors brought different experience and expertise to the class, and then worked together to develop and analyze mathematical models. Both mathematics and biology majors needed to know enough about the other area so that they could combine their ideas. For that reason, the prerequisites for biology majors and mathematics majors were different. A mathematics major needed to have a first course in linear algebra, a probability and statistics course, and two freshman biology courses: A Survey of the Plant Kingdom, and A Survey of the Animal Kingdom. A biology major needed to have College Algebra, a sophomore botany course (Biology of Algae, Plants and Fungi), and a sophomore zoology course (Biology of Animals).

The initial class (Spring 2007) had only four students (one biology major and three mathematics majors, one of whom also was a biology minor). One of the mathematics students attended the summer 2007 mathematical biology workshop at the Mathematical Biology Institute of The Ohio State University. The low enrollment had two causes: the advisors were not well aware of the course and the course was an elective. The department has asked that the course satisfy the college interdisciplinary requirement beginning with Fall 11.

The course met twice a week in a computer lab or a biology lab. The beginning of the course had a heavier emphasis on mathematics instruction. Students used Excel spreadsheets to study difference equations, Excel add-ins (PopTools) for analyzing population demography data, and MATLAB[1] in matrix modeling of population dynamics. Students learned structured population models, transition matrices, methods for finding eigenvalues and eigenvectors and their interpretations in terms of stability. We covered most of Chapter 4 of Caswell's *Matrix Population Models* (2006) with introductory material from Allman and Rhodes' *Mathematical Models in Biology* (2004). Students learned to compute powers of matrices using eigenvalues and to approximate eigenvalues using the power method.

Once the students have enough mathematics background, they move on to the more biological aspects of the course. They study models of molecular evolution and phylogenetics, using Excel to explore the evolution of an invasive plant over time and space. This is Chapters 4 and 5 of the Allman and Roads text, omitting the mathematical background material. Also discussed were the Jukes-Cantor and Kimura models, corresponding phylogenetic distances, and log-det distance. The students constructed phylogenetic trees and learned neighbor joining and maximum parsimony methods.

We wanted to have mathematics majors and biology majors work in pairs (or small groups) on a research project, but the small initial class size did not permit the full realization of this goal. Students collected population demography data using plants in the university's Research and Teaching Prairie Garden and used long-term population demography data of endangered plants collected by the biology professor. The students then used matrix population models learned in the course to project population persistence.

The course was offered at the sophomore level in order for students to do a subsequent long-term research project. One of the mathematics undergraduate students ultimately joined the graduate program in mathematics and took two classes in genetics. As an extension of her work in population models, she is now finishing her masters' research project to model endangered plant populations incorporating inbreeding, with data gathered from Illinois and Indiana state parks.

The course was again offered in Fall 10 but only for two senior graduating mathematics majors needing an elective. One of them became interested in mathematical biology and is now in the process of applying for a NSF Graduate Fellowship Program (GRFP). The student's research plan for the GRFP is based on Chicago State's aquaponics program, and is a theoretical extension of her research done for the course. She is gathering data on the length, relative positions, and velocities of fish, the concentration of nitrites in fish effluent before and after being absorbed by the plants, and the total weight of supported plants. The data will be used for computations on the angle between velocities of different fish, minimal distance between fish, plant absorption rates of nitrites, and estimating the total weight of the fish. This research will span at least two semesters.

9.5 Conclusion

Promoting the use of relatively elementary non-infinitesimal modeling techniques and reliance on technology is a hallmark of this project. It demonstrates that even at the sophomore level, mathematics and biology students can

---

[1] MATLAB was acquired with an internal grant from the Research Development Office of the College of Arts and Sciences.

interact significantly. Students inclined toward applied mathematics can meaningfully experience mathematics in a biological setting.

References

Allman, E.S. and J.A. Rhodes, 2004: *Mathematical Models in Biology*. Cambridge University Press, 370 pp.

Caswell, H., 2006: *Matrix Population Models*. Updated 2nd ed. Sinauer Associates, Inc., 722 pp.

U.S. Department of Labor, Bureau of Labor Statistics, 2010–2011 ed: Occupational Outlook Handbook: Mathematicians. [Available online at http://stats.bls.gov/oco/ocos043.htm.]

10

An Interdisciplinary Research Course in Theoretical Ecology for Young Undergraduates[†]

Glenn Ledder[1]
Department of Mathematics, University of Nebraska-Lincoln

Brigitte Tenhumberg
School of Biological Sciences and Department of Mathematics, University of Nebraska-Lincoln

G. Travis Adams[2]
Department of English, University of Nebraska-Lincoln

Name of Institution	University of Nebraska-Lincoln
Size	about 24,000 students
Institution Type	large state university with PhD program
Student Demographic	recent high school graduates with high potential and interests in mathematics and biology
Department Structure	Mathematics and Biology are individual departments in the College of Arts and Sciences

Abstract

As part of an interdepartmental effort to attract promising students to research at the interface between mathematics and biology, we created a course in which groups of recent high school graduates and first-year college students conducted a research project in insect population dynamics. The students set up experiments, collected data, used the

---

data to develop mathematical models, tested their models against further experiments, and prepared their results for dissemination. The course was self-contained in that the lecture portion developed the mathematical, statistical, and biological background needed for the research. A special writing component helped students learn the principles of scientific writing and presentation. The success of the course was indicated by the high quality of student work and positive feedback from the students.

10.1   Course Structure

- Weeks per term: 5-week summer session
- Classes per week/type/length: five 1-hour lecture periods each week
- Labs per week/length: five 1-hour laboratory periods each week
- Average class size: 8–14 students in one section
- Enrollment requirements: For high school students and university freshmen. Students had to apply for the program and get a recommendation from a teacher.
- Faculty/dept per class, TAs: Team-taught by one mathematics instructor and one biology instructor, with the mathematics instructor doing the quantitative portion of the lecture.
- Next course: The purpose of this course was to teach research skills. There were no related courses, but many of the students did research projects later in their program. Some students chose to take additional courses in mathematics and/or biology, including interdisciplinary courses offered by either department.
- Website: http://www.math.unl.edu/programs/rute/

10.2   Introduction

Research Skills for Theoretical Ecology (RSTE) was an interdisciplinary research-based course for beginning undergraduates that was taught at the University of Nebraska-Lincoln in a five-week summer session from 2006 through 2010. The genesis of this course is described elsewhere in this volume (Ledder and Tenhumberg, 2013). The course was intended as a recruitment and preparation tool for a subsequent extended research program; hence, we expected applicants for it to have completed one year of college, including two courses in calculus and at least one in biology.

Our initial offering of RSTE was in the summer of 2006. This first attempt at an entry-level undergraduate research program highlighted both the promise and the challenge of our course design. We found it difficult to fill the program with fully-qualified students. Financial constraints cause most of our undergraduates to plan their summer around a full-time job, while our program could pay them for only five weeks; this kept some of the most qualified students from applying. We were unable to enforce our intended prerequisites, as few biology students had taken mathematics beyond Calculus I and few mathematics students had taken even one biology course. We recruited three new high school graduates to augment the five post-freshmen. Several of the students were unable to do the mathematical work, and none had adequate scientific writing skills. Nevertheless, the research work yielded excellent experimental data that was used to estimate parameters for a mathematical model and to validate it. The students indicated that the course was well worth taking. Two of the biology students continued to do interdisciplinary research after the course, one in microbiology and one in natural resources. One student is doing PhD work in epidemiology and another in statistical modeling. Two other students are doing PhD work in other areas of mathematics.

The difficulties exposed by our pilot offering were addressed in our subsequent course planning. For recruiting, we eliminated all prerequisites and targeted talented college-bound high school graduates as our primary clientele. Our purpose changed from training students already planning a research career to offering a potential career-altering experience to students at the beginning of their college experience. Reaching students at this early stage of an academic career allowed us to influence undergraduate course selection and career plans. We changed our strategy for teaching the mathematics without lowering our expectations. We hired a teaching assistant (Mr. Adams) to teach scientific writing for 2007.

In this paper, we describe the Research Skills for Theoretical Ecology course that grew out of our initial effort and was taught in the summers of 2007 through 2010. We discuss the research plan; the assignments, activities, and

teaching methods; and the outcomes and student feedback. We conclude with recommendations for similar courses at other institutions.

10.3 Student Profile

Some recruiting was done in our own freshman-level mathematics and biology courses, but most of it was done through our extensive contact list of high school mathematics teachers and through announcements sent to prospective biology majors by the Admissions Office. College-bound students in Nebraska take four years of mathematics, so it is easier for mathematics teachers than biology teachers to identify strong seniors; we also felt that ability and interest in mathematics was more critical than ability and interest in biology. Our experience showed the focus on high school mathematics to be a good decision, as nearly all of the applicants had their principal interest in biology but proved capable of doing the mathematics.

Our applicant pool remained small, but of high quality. In 2007, for example, we received eighteen applications and offered positions to sixteen students, yielding a class of fourteen. All fourteen had outstanding academic records and strong letters of support from a teacher. Our group included ten new high school graduates, all planning to major in life science areas including biology, biochemistry, pre-medicine, and pre-veterinary medicine. Six were from Nebraska's urban centers (Omaha and Lincoln), one from a small city, and three from rural high schools. Four were from Catholic high schools and six from public schools. Four were enrolled at the University of Nebraska-Lincoln (UNL) for the coming year and six were going elsewhere. We also had three current UNL students, all in mathematics, and one student about to be a (high school) senior at a highly-regarded mathematics and science academy in Illinois. There were six males and eight females. Six of the fourteen students identified scientific research as a possible career choice. The student profiles in subsequent years were similar.

10.4 Objectives and Design Principles

The goal for the course was to engage students in interdisciplinary research. By "interdisciplinary," we meant a unified whole, with experimental biology and mathematical modeling as critical and interrelated components, not biology augmented by statistical analysis, mathematics problems motivated by biology, or a loose confederation of the two. We interpreted "research" as a verb that refers to the process of generating new knowledge, not a noun that refers to work suitable for publication. We wanted our students' work to be a serious investigation of an extended open-ended problem, with conclusions supported by experimental data and mathematical models. The objectives and design principles are discussed elsewhere in this volume (Ledder and Tenhumberg, 2013); here we simply state them to provide context.

Objectives for a Research-Based Course in Theoretical Ecology:

1. Learn knowledge and skills for theoretical ecology research.
2. Conduct theoretical ecology research.
   a. Collect laboratory data on ecological problems.
   b. Use laboratory data to construct mathematical models.
   c. Use mathematical models to make predictions.
   d. Use additional laboratory experiments to test the predictions.
   e. Draw appropriate conclusions.
3. Learn scientific communication skills.
   a. Read primary literature in ecology.
   b. Write scientific research papers/posters.

Design Principles for a Research-Based Course in Theoretical Ecology:

1. The course should be about skills rather than content. Everything in it should be based on a coherent research plan.
2. The research program should be both experimental and theoretical, with a clear focus.

3. The research program needs to be devised primarily by the biologist with the mathematician's approval because the biologist needs to have the laboratory expertise for the project and the mathematician needs to be able to devise a mathematics component to complement the given biology component.

4. The course should be fully integrated: biology and mathematics, theory and experiment, laboratory and lecture.

5. An authentic research experience must lead to a research paper, although the research need not be publishable.

6. The course must be self-contained: it must provide the necessary biology background, teach the laboratory methods, build the mathematics up from a pre-calculus background, and teach scientific writing.

10.5   The Research Program

The general theme of our research program was biological pest control. Within this broad theme, the research focused on insect herbivore population dynamics, with and without predation. Our system consisted of the pea aphid *Acyrthosiphon pisum* (a widely-distributed North American insect pest), the broad bean plant *Vicia faba*, and the coccinellid (ladybird beetle) *Hippodamia convergens* (adults and larvae eat aphids).

Pea aphids are small insects that feed on the phloem of a several plant species, including the broad bean. They pass through four nymphal (immature) stages before molting to the adult stage. In the laboratory and during the summer in the field, pea aphids reproduce asexually, with offspring born live. They mature in about ten days and seldom live for more than four weeks. Their rapid life cycle makes them an excellent study species for a five-week course. Furthermore, their relatively large size and general immobility when undisturbed makes aphid handling and counting straightforward; even newborns are visible by eye. Adult coccinellids can be purchased from commercial suppliers (Carolina Biological Supply Co.) and maintained on a pea aphid diet in large chiffon-netted aluminum cages. Adult coccinellids start mating right after arrival and oviposit eggs one week later. In the lab the larvae hatch after about three days and start consuming aphids right away. The larvae go through four instars (immature stages) before pupation.

The research project combined an aphid population dynamics component with a predator-prey dynamics component, each of which required two experiments and one mathematical model. The mathematical modeling was challenging, but feasible, for good students at the high school level. Because the course lasted only five weeks, the experiments were conducted simultaneously and the models were introduced sequentially during lecture. Figure 1 indicates the logical connections among the components. Those components that appear to the left of the vertical dotted lines represent simulated experiments done with the BUGBOX models, while everything to the right represents empirical experiments on the real biological system or mathematical modeling of the biological data.

10.5.1   Aphid Population Dynamics

In the *vital rates experiment*, the students first transferred individual adult aphids in numbered 4 cm diameter clip cages fastened to bean leaves on a living plant. After 24 hours, the students removed all aphids from each cage except for one newborn. The fate of the newborn aphid could then be followed from birth to death. Each day thereafter, each clip cage was examined to record all life history events, including the days when the aphid molted to the next developmental stage (determined by observing the cast-off exoskeletons), the day of the aphid's death, and the daily number of offspring produced after the aphid becomes an adult. These data were used to determine average developmental time, fecundity, and survival rates for each stage. Because of the large variation in aphid demographic rates, we used 40–60 clip cages with one aphid each.

In conjunction with their experimental work, the students studied the density-independent population dynamics model

$$x_{t+1} = \mathbf{M}x_t, \tag{1}$$

where x_t is the population vector consisting of the six (four nymph, two adult) stages on day t. We split the adult stage into two stages because pea aphids do not reproduce in the first 1–2 days after becoming adults. $\mathbf{M}$ is a 6×6 matrix comprised of the survival, development, and fecundity rates obtained from the *vital rates experiment* data. The students used the R software package (R Development Core Team 2012)) to calculate the asymptotic population growth rate (the dominant eigenvalue of the matrix) and to simulate how the average aphid abundance changes over

Aphid Population Dynamics
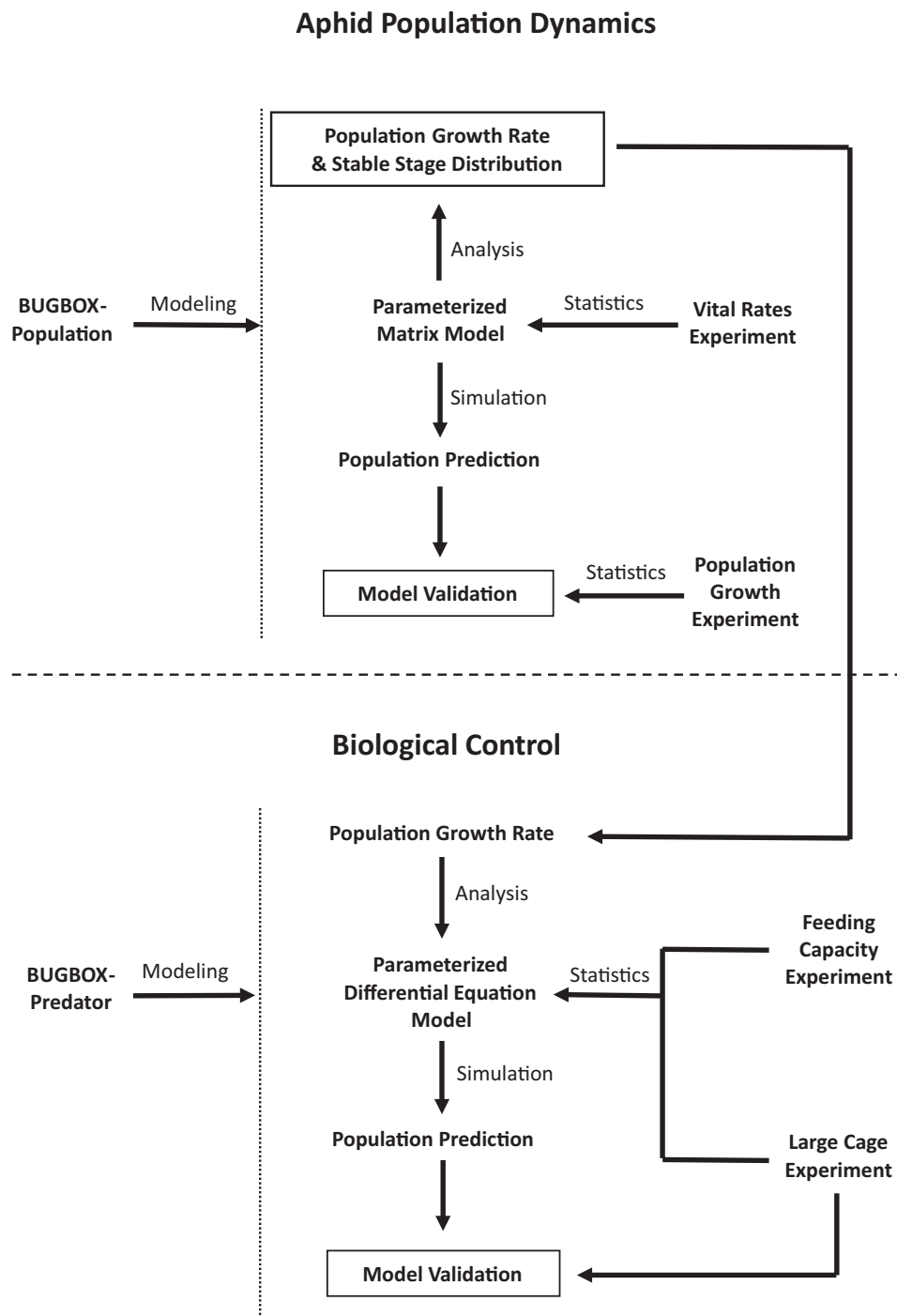
Figure 1. Schematic Representation of the Aphid Population Dynamics and Biological Control Research Plans

time. Of particular interest is the quantity N_t/N_{t-1}, the ratio of the total number of aphids on day t to the total number on day $t-1$. This ratio is sensitive to changes in the population age structure. Given enough time, it should approach a constant value, which represents the asymptotic population growth rate under ideal conditions.

The *population growth experiment* began with one adult aphid on a healthy bean plant in each of several large chiffon-netted aluminum cages ($44 \times 51 \times 61$ cm); a minimum of three cages was required. The aphid populations were counted each day for twenty days, with additional plants added as needed to prevent density-dependent mechanisms, such as reduced survival and reproduction, from influencing the population dynamics. The ratios N_t/N_{t-1} were computed from

the data and compared with the ratios predicted by the model. This experiment tested the validity of the stage-structured linear model predictions.

10.5.2   Predator-Prey Dynamics

In the *feeding capacity experiment*, the students placed individual first-instar coccinellid larvae in plastic containers with an excess number of aphids. They estimated the maximum consumption in a 24-hour period by comparing the numbers of aphids at the beginning and end of the period. Each day, all remaining aphids were replaced with fresh ones. Students continued feeding the coccinellids until they either died or pupated. A similar experiment was used to determine the maximum consumption rate for adults.

The simplest feasible model for aphid population dynamics in the presence of coccinellids is

$$\frac{dx}{dt} = rx - qy, \tag{2}$$

where x is the total aphid population size, t is the time in days, y is the fixed number of coccinellids, q is the maximum predation per coccinellid per day as determined from the *feeding capacity experiment*, and the relative growth parameter r is given by

$$r = \ln \lambda, \tag{3}$$

where λ is the value at which the N_t/N_{t-1} ratio stabilizes. We tested the model (2) by adding 7–9 adult coccinellids (an average of one predator for each 60–70 aphids) to each cage at day 20 of the *population growth experiment*. The students kept counting daily for an additional 3–4 days. The daily population totals showed that the model (2) significantly overestimated the impact of the coccinellids because it does not incorporate the effect of depletion on the searching efficiency (longer search times are needed to find prey when prey density is low). A better model, using the Holling type II functional response (Holling, 1959), is

$$\frac{dx}{dt} = rx - \frac{qyx}{a + x}. \tag{4}$$

The extra parameter a, called the *semi-saturation parameter*, represents the population size at which the capture rate per predator is one half of its asymptotic maximum. In principle, we could fit a from the additional *population growth experiment* data by using nonlinear regression analysis. In practice, this was difficult to accomplish because x represents the population density rather than the actual population size. The population density is the population size divided by an appropriate measure of the habitat size. If habitat size were the volume of the cage, it would be possible to convert population counts into population densities; however, habitat size should be based on the plant surface area, which cannot easily be estimated.

10.5.3   Research Results

Each time we taught the course, we had excellent results for the aphid population dynamics component. With an initial population of one adult and no nymphs, the N_t/N_{t-1} ratio starts high. It decreases for about eight days while the population of nymphs continues to increase. Once the first nymphs mature, the proportion of reproducing adults increases, leading to an increase in the N_t/N_{t-1} ratio. It takes about two weeks of diminishing oscillations for the N_t/N_{t-1} ratio to stabilize, with the stable value very close to that predicted by the model.

Results for the *feeding capacity experiment* were mixed. Our first supply of coccinellids was infested with a parasitoid, so we got no results at all. Generally, the feeding rate increases with larval age, but with a high degree of variability. The adult feeding rate experiment showed an even larger variation among individuals. The addition of adult coccinellids to the *large cage experiment* never yielded results that agreed with either model (2) or model (4), indicating that neither is adequate.

10.6   Student Work in and Out of Class

Because we wanted to provide a research experience for students, we would have liked to have them spend all their work time on laboratory work, statistical analysis, mathematical modeling, computer simulation, and documentation.

Our course focused on these activities, but it also included activities needed to teach students the scientific background, statistical methods, mathematical models and techniques, computer programming, and scientific writing. Our class met formally for two hours on each of twenty week days (ten hours in the laboratory, four hours in biology class, eighteen hours in mathematics class, seven hours in writing class, and one hour for assessment). Outside of class, the students read biology literature; did homework, data analysis, and writing; and took turns collecting data on weekends. The class met informally in the final week, with the students working on their papers. Altogether, we expected the students to work approximately thirty hours per week for each of the five weeks, which is roughly equivalent to the workload of a 3-credit course.

10.6.1   Laboratory Class

The instructor provided the experimental design and taught the laboratory skills; the students set up the experiments and collected the data. Each student took a turn at each of the experiments, with half of the students doing laboratory work in any given day. The laboratory class became routine after the first few days of intensive instruction.

10.6.2   Biology Class

The first hour of the course consisted of a PowerPoint lecture by the biology instructor on the biology of aphids and coccinellids. The remaining three hours were used for discussion of six research and survey papers on biological pest control (Messing and Wright, 2006), aphid ecology (Hutchinson and Hogg, 1984; Sandstrom, 1996), coccinellid ecology (Obrycki et al., 2001; Wyss et al., 1999), and aphid behavior in the presence of predators (Nelson and Rosenheim, 2006). The students read these outside of class and prepared written summaries prior to a 30-minute classroom discussion with the biology instructor.

10.6.3   Mathematics Class

The students met with the mathematics instructor for one hour on each day of the first four weeks to learn the quantitative material of the course. There were three largely independent topics:

1. Mathematical models of predation, including the simple linear functional response and the Holling type II saturation response (Holling, 1959).

2. The mathematical concepts, analytical techniques, statistical analysis of laboratory data, and computer simulation for stage-structured discrete linear models (1).

3. Derivation and phase line analysis (Brauer and Castillo-Chavez, 2001) of the differential equation models (2) and (3).

10.6.4   Writing Class

Rather than giving the students a style guide for their research paper, we expected them to develop their own. This was done in the writing class with genre analysis. We began by asking the students to look for common features in the assigned articles from the course reading packet. Then we discussed scientific writing conventions and how the students were to use these in their writing. In this way, the students discovered the correct style for scientific writing rather than having it imposed as a set of rules. By the time the genre analysis was finished, the students were already beginning to write their papers. Remaining writing class sessions were used for peer responses. We asked the students to bring a portion of their writing along with author's notes (brief reflective statements about their writing that places the piece in the writing process and guides peer or instructor responses). Pairs of students then exchanged papers and responded to each other's writing as guided by the author's notes. In this way, the students were able to focus their feedback on those aspects of writing that their partners wanted to improve.

10.6.5   Mathematics Paper

The mathematics paper was on the derivation of the Holling type II functional response from data the students collected from a virtual laboratory experiment (see below). It consisted of an introduction, experimental methods and

results sections, a mathematical modeling section that presented the derivation of the model in their own words, and a discussion section that described the success of the model in fitting the data and identified model assumptions that are not satisfied in the real biological system. We collected these short papers at the end of the second week, responded to them quickly, and had the students revise them.

10.6.6   Research Paper

The research paper was the culmination of the course, but writing began at the end of the second week. All the writing was done outside of class, with concentrated editing in the writing class. The students wrote the paper section by section, beginning with the experimental methods section. Each section had due dates for a first draft and a revised draft, and the final paper was due on the last day of class. The format for the paper was not specified by the instructors, but developed by the students in their writing class. The instructor helped the students discover appropriate scientific conventions for ecology papers with mixed experimental and mathematics content.

10.6.7   Homework

Most of the work the students did outside of class was directly related to their research project. The data analysis started in the mathematics class and was completed outside of class. Both the research paper and the mathematics paper were written entirely outside of class. The biological readings were done outside of class, and there was a small amount of mathematics homework necessary for understanding the mathematical methods used in the research.

10.7   Pedagogical Challenges

10.7.1   Teaching Biology

The biggest challenge in designing the biology component of the course was to find a meaningful interdisciplinary research project that could be completed within five weeks. First, we needed to find a topic students would recognize as important after only a single introductory lecture because the experiments had to start on the first day of the course. Second, we wanted an empirical model that would allow students to collect all necessary data within four weeks, allowing the final week for data analysis and presentation of the results. Third, the experimental procedures had to be sufficiently simple for students to carry out after a minimal training period, with additional instruction as needed. Fourth, the experiments had to provide data that could be incorporated into mathematical models (providing all required parameter estimates). Fifth, we wanted to find an ecological topic where we knew predictions were likely to match observations. These requirements prohibited us from creating a novel research project that could be published; rather we used aspects of Dr. Tenhumberg's published research (Tenhumberg, 1995; Tenhumberg, 2004; Tenhumberg et al., 2009; Tenhumberg, 2010).

We framed our research project in the general theme of biological pest control, a topic that our mostly rural students could immediately appreciate as important. We specifically wanted to do demographic research that would predict pest population dynamics. We chose aphids as a model species because of their short generation time (approximately 2–3 aphid generations coexist on a single plant in the field); this makes them a perfect study system for the laboratory. Aphids have distinct life history stages that make them ideally suited for a stage-structured modeling approach. Furthermore, aphids are sufficiently large that no extra equipment is required for population counts. Lastly, based on Dr. Tenhumberg's research (Tenhumberg, et al., 2009; Tenhumberg, 2010), we knew that the asymptotic population growth rate of *A. pisum* predicted from a matrix model would match the observed population growth rate in the laboratory. We did not have similar assurances for the predator-prey model, and the match of prediction to observation was not very good. It was instructive for the students to see that the success of mathematical modeling depends heavily on how adequately the model assumptions describe the biological system. Predator behavior is more complicated than what we could incorporate into our model.

To understand the challenges of biological control fully, students need an understanding of the natural history of pest and biological control organisms, the large spatial and temporal variation of life history traits between populations, and population dynamics. Delivering this much material was challenging. First, teaching the quantitative course material was time consuming, leaving little time for presenting the ecological background knowledge. Second, we had to use

primary literature since there was no textbook available. Reading and digesting primary literature is hard for lower-division students; in particular, most of the papers include specialized vocabulary and statistical methods that are inaccessible to students with no prior statistics course. Older papers are generally easier to understand, but they tend to use outdated experimental methods, such as extremely small sample sizes. We selected recent papers and encouraged the students to focus on the main results and general conclusions, skipping over any complicated details. With the help of the biology instructor, the students acquired the most important content of the papers but were generally dissatisfied with only partially understanding the papers.

10.7.2 Teaching Mathematics and Mathematical Modeling

Our philosophical principle that theoretical work should be motivated by an ecological question has the benefit of showing the value of mathematics, but it poses a pedagogical problem. Theory begins with observation, but full observation of the aphid life cycle requires most of four weeks and we needed to start the theoretical work much earlier. We solved this problem by providing means for collecting simulated experimental data to motivate the theory when needed. The BUGBOX-predator computer applet (Ledder, 2007b) simulates interaction between a moving predator and stationary prey. Experiments performed with this applet yield a data set with which to examine the influence of handling time on predation rates and derive the Holling type II functional response model (Ledder, 2008). The BUGBOX-population computer applet (Ledder, 2007a) simulates stage-structured population growth for a virtual insect species with a simplified life history. The students derived a stage-structured model and obtained numerical values for the parameters by collecting data corresponding to the real aphid data from the *vital rates experiment*. We investigated the model with a simple simulation that the students wrote in R (R Development Core Team 2012). This was the first computer programming experience for nearly all of the students and nearly all found it difficult. We wrote the program together in class, line by line with each line explained, over the course of an hour. The crucial feature of our simulation is the chosen output format: a graph of N_t/N_{t-1}, where N is the total population. This graph led the students to discover that the growth rate converges to a fixed value independent of initial conditions, which in turn leads to the eigenvalue problem of matrix algebra (Ledder, 2008).

Thus far, all mathematical work was done from first principles, rather than using out of the box methods. For the statistical work and mathematical analysis of the real data, we used a combination of basic statistics instruction and instructor-supplied R scripts. We used R rather than Excel because of the easy portability of computer program statements from one program to the next.

Our final three days of work in mathematics class consisted of a very fast introduction to first-order differential equation models. Since we did not require any calculus background for the course, we restricted ourselves to graphical and numerical methods for autonomous scalar differential equations. We constructed the models (2) and (4) in stages:

1. We introduced the derivative as the slope of a tangent line and as the value approached by the secant slope $\Delta x/\Delta t$ as Δt becomes arbitrarily small.

2. We examined the linear model for unrestricted population growth without predators, asserting the exponential solution formula without proof. We used this solution to calculate the rate constant r from the dominant eigenvalue λ_1.

3. We obtained the models (2) and (4) by adding a predation model to the linear growth model.

We then studied the models (2) and (4) using phase line arguments and computer simulations written by Dr. Ledder.

10.7.3 Teaching Scientific Writing

The two major challenges in teaching scientific writing in a mathematics or science course are limits of time and instructor expertise. Students entered the course with widely disparate writing ability; even the best had little, if any, prior experience in scientific writing. Lab reports written in high school are more often a source of misconceptions than a valuable writing experience. Time for writing had to come at the expense of time that could instead be spent on mathematics or science content and is likely to be undervalued by instructors who are content experts but who are not trained teachers of writing (teaching of writing being a distinct skill from writing itself). We approached this problem

in 2007 by hiring Mr. Adams as a writing specialist; after observing the 2007 writing classes, Dr. Ledder taught the writing classes in 2008 and 2009. The graduate students who taught the biology and mathematics components in 2010 also taught the writing.

Because most of our students were generally good writers already, we did not need to spend time on remedial or basic writing instruction, but we did need to teach students the expectations for scientific writing. Once the students had learned the appropriate stylistic conventions of scientific writing, the quality of their scientific writing improved considerably. We have learned that lecturing about writing styles does not improve student writing; it is much better to have students read well-written scientific papers and identify the conventions themselves. After a classroom discussion, most of the students were able to articulate the elements of scientific writing style.

Improvement in writing comes largely from directed revision, which means that someone has to read and comment on drafts of student work. The use of author's notes to direct review saves time by focusing the reviewer's attention on the points the writer has targeted for improvement. Peer review significantly lessens the time commitment for each instructor and can be done during writing class. In our experience, the willingness of students to accept suggestions from peers makes up for their decreased editing ability compared to instructors. The instructors were available for review of any work voluntarily submitted by email. The combination of peer response, optional submission to an instructor, and author's notes stresses student ownership of their writing, which we believe leads to better results.

Many of the students were surprised that they were not given class time for their writing, a concern we attributed to their being used to the high school setting and which helps explain the limited effort many freshmen put into their writing for mathematics and science courses.

10.8   Assessment

10.8.1   Outcomes

The principal outcomes of the course were the scholarly products, which originally consisted of a group poster and a group research paper, but became an individual research paper. A typical student paper was written in a style approximating professional academic style. The introduction indicated a good understanding of the purpose and context of the research. The experimental methods descriptions were good, although not as careful as in a professional paper. The results section included good descriptions and graphical displays of data and also indicated some understanding of the statistical work, the mathematical models, and the interplay between the models and the experimental data. The short conclusion section (rather than the complete discussion section of a professional paper) stated appropriate conclusions restricted to what could justifiably be claimed from the experimental work. We judged this typical paper worthy of an A- grade; there were always weaker papers, as well as A+ papers from students who we judged to be potential PhD students. Several such students are in PhD programs now or have already finished. Several research posters, all of which we evaluated as A work or better, can be found on the RUTE web page (University of Nebraska-Lincoln, 2012); we welcome feedback on the quality of the student work in the posters. One of the posters was presented at a conference at the National Academy of Sciences in 2010, alongside posters of research projects done by advanced undergraduates.

Our one traditional assessment was a quiz on stage-structured models, including modeling, simulation, and eigen-value analysis. The median quiz score in 2007 was 76%, which we judged to be a B given the difficulty of the questions. Those students who did poorly were given a second chance with a make-up quiz, which was substantially different from the first quiz but comparable in difficulty. All the students who took the second quiz showed significant improvement, increasing the median to 90%. With improvements in teaching, we achieved a median of 88% on the quiz in subsequent years without a make-up.

10.8.2   Feedback

Student feedback was illicited by two questionnaires, one for attitudes and beliefs and the other for content. We used categorical responses (Strongly Disagree, Disagree, Neutral, Agree, Strongly Agree) for all items, supplemented by written responses on questions about the value of the writing class. We computed a numerical score in the usual way, with scores of -2, -1, 0, 1, and 2 for the responses from Strongly Disagree to Strongly Agree. The key results appear in Table 1.

Statement	Score
1. Math is a worthwhile and necessary subject for biologists.	1.57
2. I don't need to know the math when I can do a problem using a computer.	0.86
3. Mathematical models help me to think about biology.	0.43
4. I learned a lot of mathematical modeling from the course.	1.29
5. I learned a lot from writing the research paper.	1.29
6. I learned a lot from writing the mathematics paper.	1.29
7. Before this program, I was considering a research career.	0.07
8. I am now considering a research career.	0.57

Table 1. Average student agreement on some subjective statements, on a scale from -2 for complete disagreement to 2 for complete agreement.

The first item indicates our success in helping the students experience the synergy between biology and mathematics. An anecdote shows the extent to which this lesson took hold. Towards the end of our 2007 class, two of the students went through advising and registration procedures at the small college they were enrolled in for Fall 2007. Their academic advisor told them that biology students should take only the minimum number of mathematics courses. We asked them what they did with that information; they replied that "of course we went to talk to a different advisor!" Both students marveled at how they could get such ignorant advice from someone who should know better.

The broad agreement that getting an answer by computer means not having to understand the mathematics seems inconsistent with the recognition of the importance of mathematics in biology, but the weak response to item 3 suggests that many of the students saw mathematics as a tool rather than a way of thinking. The agreement is less than what we would have liked, but more than it would have been without our course.

Item 4 was one of a number of similar items; responses for learning of biology, mathematics, statistics, and computing obtained average scores of 0.86 to 1.14.

Based on items 5 and 6 and the written comments, our students judged the writing assignments to have significant value beyond the value of the work on which they were reporting. That is, having to write about their work contributed to improving their writing and also to their learning of science and mathematics.

10.9 Recommendations

We believe that courses such as ours can be successful at other institutions. Some features of the course are universal and some are local. Our design principles are essential, with the possible exception of item 6. Any course intended to introduce research skills must be based on a coherent experiment plan, must integrate the components of that plan with the course material and structure, and must require serious scientific writing. The mathematics part of an interdisciplinary course should be taught from a modeling perspective (Ledder, 2008), and scientific writing should be taught explicitly.

Some aspects of our program are not easily duplicated because of the level of resources that was available. During the period of NSF funding, *RUTE* students received a $1500 stipend for the five-week program. We also paid for room and board in a university dorm and some travel expenses for students coming from more than 100 miles away, so we could create a summer program for students from a variety of institutions. With the funding gone, we considered running the course as a Freshman Honors course during the academic year. Because data needs to be collected every day, it would have been tricky to manage the laboratory work with an academic year schedule, but we do not believe this difficulty to be insurmountable. Every student does not need to work in the laboratory every day. The most serious resource problems are the need for a dedicated laboratory space and the necessity for having two instructors, each of whom needs to have the course count as part of their teaching load. Teaching as one half of an interdisciplinary team requires more time and energy than teaching one half of a standard course. We did not give serious consideration to solving the staffing problem because of the impossibility of finding laboratory space.

The choice of research topic for a freshman-level research course needs to be based on local facilities and expertise. There are many topics that could be used for laboratory research conducted by beginning undergraduates, given sufficient instruction in biological principles and laboratory methods. Other population dynamics projects would have

similar mathematical requirements, and other areas of biology may have mathematical models that could be presented at the introductory level.

We hope that other institutions will try interdisciplinary research courses, and we are interested to hear about faculty experiences with them.

One other issue merits mention, although it is beyond the scope of what the creators of a single college course can do. We believe that students who are interested in mathematics primarily because of its value in theoretical science learn more mathematics when it is presented in a modeling context than when it is presented as mathematical theory. Many topics, such as the matrix eigenvalue problem, can be taught in a scientific context rather than from a strictly mathematical point of view (Ledder, 2008). It remains difficult to teach mathematics in a modeling context to students who have not done any modeling before; this problem could be addressed in part by incorporating parameters into mathematics problems beginning with secondary school mathematics. Early experience with parameters would also help prepare mathematics majors for the mathematical abstraction they need in advanced mathematics courses.

References

Brauer, F. and C. Castillo-Chavez 2001: *Mathematical Models in Population Biology and Epidemiology*, Springer-Verlag.

Holling, C. S., 1959: Some characteristics of simple types of predation and parasitism. *Canadian Entomologist*, **91**, 293–320.

Hutchinson, W. D. and D. B. Hogg, 1984: Demographic statistics for the pea aphid (*Homoptera: Aphididae*) in Wisconsin and a comparison with other populations. *Environmental Entomology*, **13**, 1173–1181.

Ledder, G., 2007a, cited in 2012: BUGBOX-population. [Available online at http://www.math.unl.edu/∼ gledder1/ BUGBOX/.]

Ledder, G., 2007b, cited in 2012: BUGBOX-predator. [Available online at http://www.math.unl.edu/∼ gledder1/ BUGBOX/.]

Ledder, G., 2008: An experimental approach to mathematical modeling in biology. *PRIMUS*, **18**, 119–138.

Ledder, G. and B. Tenhumberg, 2013: Creating an interdisciplinary research course in mathematical biology. This volume, 133–138.

Messing, R. H. and M. G. Wright, 2006: Biological control of invasive species: solution or pollution? *Frontiers in Ecology and the Environment*, **4**, 132–140.

Nelson, E. H. and J. A. Rosenheim, 2006: Encounters between aphids and their predators: the relative frequencies of disturbance and consumption. *Entomologia Experimentalis et Applicata*, **118**, 211–219.

Obrycki, J. J., E. S. Krafsur, C. E. Bogran, L. E. Gomez, and R. E. Cave, 2001: Comparative studies of three populations of the lady beetle predator *Hippodamia convergens* (Coleoptera: Coccinellidae). *Florida Entomologist*, **84**, 55–62.

R Development Core Team (2012). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. ISBN 3-900051-07-0, URL http://www.R-project.org/.

Sandstrom, J., 1996: Temporal changes in host adaptation in the pea aphid, *Acyrthosiphon pisum*. *Ecological Entomology*, **21**, 56–62.

Tenhumberg, B., 1995: Estimating the predatory efficiency of *Episyrphus balteatus* in cereal fields. *Environmental Entomology*, **24**, 687–691.

Tenhumberg, B., 2004: Predicting predation efficiency of biocontrol agents: linking behavior of individuals and population dynamic. *Complexity and Integrated Resources Management, Transactions of the 2nd Biennial Meeting of the International Environmental Modelling and Software Society*, C. Pahl-Wostl, S. Schmidt, A. E. Rizzoli, and A. J. Jakeman, A.J., Ed. (eds), Vol. 2, iEMSs, 2004. 864–869. [Available online at http://www.iemss.org/iemss2004/proceedings/iEMSs2004_vol2.pdf.]

Tenhumberg, B., A. J. Tyre, and R. Rebarber, 2009: Model complexity affects predicted transient population dynamics following a dispersal event: A case study with *Acyrthosiphon pisum*. *Ecology* **90**, 1878–1890.

Tenhumberg, B., 2010: Ignoring population structure can lead to erroneous predictions of population size. *Nature Education Knowledge* **1**, 2. [Available online at http://www.nature.com/scitable/knowledge/library/ignoring-population-structure-can-lead-to-erroneous-15128671.]

University of Nebraska-Lincoln, cited 2012b: Research for Undergraduates in Theoretical Ecology. [Available online at http://www.math.unl.edu/programs/rute/.]

Wyss, E., M. Villiger, J. L. Hemptinne, and H. Muller-Scharer, 1999: Effects of augmentative releases of eggs and larvae of the ladybird beetle, *Adalia bipunctata*, on the abundance of the rosy apple aphid, *Dysaphis plantaginea*, in organic apple orchards. *Entomologia Experimentalis et Applicata*, **90**, 167–173.

11

An Interdisciplinary Course, Textbook, and Laboratory Manual in Biomathematics with Emphasis on Current Biomedical Research[†]

Raina Robeva[1]
Department of Mathematical, Sciences, Sweet Briar College

Robin Davies
Department of Biology, Sweet Briar College

Michael L. Johnson
Departments of Pharmacology and Medicine, University of Virginia Health System

Name of Institution	Sweet Briar College
Size	about 750 students
Institution Type	liberal arts college
Student Demographic	mathematics and biology majors and minors with interests in biomathematics
Department Structure	Mathematical Sciences and Biology are separate departments at Sweet Briar College

Abstract

We describe an interdisciplinary course and a textbook in mathematical biology developed by faculty from Sweet Briar College (SBC) and the University of Virginia (UVA) School of Medicine with support from the National Science Foundation (NSF) and the National Institutes of Health (NIH). The course and textbook were designed to supply a

bridge between the mathematical and biological sciences at the lower undergraduate level. The topics, except for the introductory material, are based on current research at the UVA School of Medicine and are attractive to mathematics majors who wish to learn how their skills can be applied to problems in the life sciences and biology majors who intend to pursue medical or health-related careers. Their modular structure makes the material adaptable to audiences with different backgrounds, needs, and levels of expertise. The course was developed for and is being taught at SBC, but some of the advanced modules are used in a course at UVA for advanced undergraduate and beginning graduate students. Individual modules can be used as stand-alone projects in conventional mathematics and biology courses.

11.1 Course Structure

- Weeks per term: 14-week semester
- Classes per week/type/length: three 1-hour lecture periods each week
- Labs per week/length: one 3-hour laboratory periods each week
- Average class size: 7–10 students
- Enrollment requirements: One semester of calculus, one semester of biology, and one semester of statistics.
- Faculty/dept per class, TAs: Team-taught by one mathematics professor and one biology professor, with both doing portions of the lectures and supervising the laboratory periods.
- Next course: The purpose of this course is to introduce students to the field of biomathematics. There are no specific follow-up courses, but some students will choose biomathematics related projects to satisfy the research requirements of their majors.
- Website: http://www.biomath.sbc.edu

11.2 Introduction

Sweet Briar College (SBC), located in central Virginia, is a selective four-year liberal arts and sciences college for women that awards Bachelor of Arts and Bachelor of Science degrees. SBC has approximately 650 students in residence. The average class size is 12 and the student-faculty ratio is 8:1. SBC is consistently cited by the *Princeton Review Guide to the Best 373 Colleges* and *U.S. News & World Report* as one of the nation's leading liberal arts institutions.

Over the past ten years, SBC has implemented extensive science curricular revisions with strong emphasis on faculty-student research that culminates in a Senior Research experience. As required by the general education requirements of the college, emphasis is placed on developing oral and writing skills. The importance of independent research has been recognized by the administration of the college and is a key element of SBC's strategic plan. In the last decade, over three million dollars has been awarded to SBC by the NSF in support of these initiatives, in addition to grants from the NIH and private foundations. Since 2000, an average of 4% of the degrees at SBC has been awarded to mathematics majors, substantially higher than the national average of less than 1% (National Center for Education Statistics, 2010). Biology at SBC has also seen an increase in majors, in line with trends reported by the Department of Education for biological sciences (NCES, 2010) and an increased number of graduates who go on to graduate and professional school.

Yet, when we began this project in 2000,[2] almost nothing in our science curriculum targeted the need for integration of mathematics with biology, a need that all of us doing biomedical research identify as pressing. Because the characterization of biological systems was reaching an unparalleled level of detail, there was clear need to apply tools from mathematics to solve the frontier problems in biology. Modeling of biological systems had also become an important component of experimental work and there was a growing demand for graduates with interdisciplinary training.

---

[2] This was prior to the release of the report Bio2010 (National Research Council, 2003) that drew national attention to the lack of interdisciplinary interaction between mathematics and biology.

Unfortunately, a program to provide such training for our undergraduate students did not exist and, even worse, there was no place in the curriculum where students could see the exciting role of mathematics in biomedical research. The causes of this were easily identifiable.

Too often in traditional math courses, simplistic material is used for applications to the life sciences. These brief examples, often out of context, have little appeal to the students and are often restricted to a few class sessions on word problems having little modeling content. Most mathematics majors complete their degrees with a rich repertoire of mathematical skills but almost no experience in applying them to problems that arise in science. In spite of the need for integrating mathematics with the life sciences, the emphasis in the mathematics courses is still on techniques rather than on applications.

Meanwhile, many of the courses in the biology curriculum make no significant use of mathematical models and theory, regardless of their increasing importance. The students who take these courses have normally completed their major's mathematical requirements (one or two semesters of calculus and a semester of statistics), have memorized a list of algorithms, and have mastered the technical use of some software packages, but have not gained enough conceptual understanding to be able to apply the algorithms in novel situations or to adequately interpret the computer output.[3] As a result, few mathematics majors and biology majors are equipped to use biomathematics techniques required by modern biological research.

In this paper, we describe in detail the undergraduate course Topics in Biomathematics that we have created and now teach at SBC. This course is a first step in integrating mathematics and biology in the undergraduate curriculum.

11.3 Course Description

The course is designed for sophomores through seniors and requires prerequisites of one semester of calculus, one semester of statistics, and a one-semester general biology or cell biology course. Our pedagogy focuses on the fundamental concepts, ideas, and biological applications of mathematical tools, and not on rigorous mathematical analysis. We do not attempt systematic presentation of mathematical material, although there are important threads that run through several of the course topics. Instead, by using specialized software (e.g., Berkeley-Madonna, MATLAB, MINITAB, and PULSE_XP) and avoiding most of the mathematical details, our goal is to enable students to experience the usefulness of mathematical techniques applied to biological problems.

11.4 Innovative Features of the Course

Our course differs from other mathematics and biology courses at SBC because

1) It is taught by a biologist and a mathematician to students who have different mathematics and biology backgrounds. Usually, about 50% of the students are biology majors and about 50% are mathematics majors. Each group brings its own expertise into the discussions of solution strategies.

2) It targets mathematics students wishing to learn applications of mathematics in the life sciences and life sciences students wanting to improve their quantitative skill, which we define as the ability to look at an unfamiliar problem, analyze it to determine the necessary data, select appropriate mathematical tools, and draw conclusions on the adequacy of the results. As mentioned above, many significant research projects now require cross-disciplinary collaboration and our attempt is to replicate this experience in the classroom.

3) It reinforces students' mathematical background by exposing them to current ideas and presenting familiar mathematical topics from a novel point of view. Often after taking a course in mathematics, students never have to use the material again except in subsequent mathematics courses. This can convey the false impression that mathematics is present in the undergraduate curriculum and requirements solely as an abstract logical and algebraic exercise. We counter this with a focus on creative applications.

---

[3] It might be worth mentioning that faculty who teach these courses may also, at times, feel unprepared to engage in a substantive debate on the relevant mathematical content.

4) It enables students to think in terms of mathematical models and motivates them to develop and apply modeling skills. We hope that this course will be just the first step—an introduction—to an exploration of applied mathematics that our students will undertake. We anticipate that some of the students who take the course will choose to work on more complex projects as part of SBC's summer research program or apply their expertise in different fields of the life sciences and in other courses.

11.5   Course Structure

The course has three fifty-minute lectures and one three-hour lab period per week. It is divided into five relatively independent biology and physiology topics: population studies, genetics, epidemiology, endocrinology, and biological clocks. Each topic consists of smaller projects and takes from two to four weeks of class time to complete. For each topic, students are divided into research teams of (ideally) two biology and two mathematics students. Group work is required to develop collaborative analytical and evaluative skills. No solution strategies are provided for the projects and students are asked to discuss possible approaches and find appropriate mathematical techniques.

During lectures, in addition to introducing or reviewing information in biology and mathematics, we emphasize development of quantitative skills: how to ask the right questions, how to answer them, and how to use the conclusions to reevaluate the situation. During the laboratory sessions, through collaborative efforts and group discussions, students propose solution strategies, identify solutions coming from them, and compare outcomes, if more than one solution strategy appears appropriate.

As our students gain proficiency, the course projects become more detailed, more realistic, and closer to actual research projects. The mathematics describing the models does not become more difficult by design, but becomes more diverse as the students discover what is needed to describe the biological process. Student grades are based on homework, laboratory assignments, and two midterm and one final course projects.

11.6   Course Topics

The content of the five biological topics listed above is

- *Population Studies*: Continuous and discrete single population growth models; unlimited growth; doubling times; Verhulst's logistic growth model; chaos; continuous models governing the sizes of interacting populations; predator-prey, competition, and symbiotic models.
- *Genetics*: Dynamics of gene frequencies in a closed population; Hardy-Weinberg equilibrium; disappearance of recessive genes; analysis of continuous traits and polygenic inheritance; Gaussian distribution of polygenic traits.
- *Epidemiology*: Epidemic models in a closed system: the SIS model; the SIR model and SIR with intermediate groups; threshold of an epidemic; epidemic models with delay.
- *Endocrinology*: Pulsatile nature of hormone release, peaks in hormone time series; applications to treatment of infertility; modeling of hormone feedback networks; endocrine oscillators and the effect on growth patterns in rats; assessing the risk of severe hypoglycemia in diabetes from self monitoring blood glucose data.
- *Biological Rhythms*: Assessing the risk of neonatal sepsis from EKG data; circadian rhythms; rhythm analyses of confounded time series; microarrays and biological clocks.

11.7   Course Materials

More detailed descriptions of these topics appear in our textbook *An Invitation to Biomathematics* and the accompanying *Laboratory Manual of Biomathematics* (Robeva et al, 2008a, 2008b). The textbook provides in-depth coverage and we do not cover all of its sections in our course. More details about the course, textbook, and our entire initiative are available on our website www.biomath.sbc.edu.

11.8 Discussion

Our biggest challenge was to create an interdisciplinary curriculum that was not limited to a collection of mathematical topics with biological applications or biology topics that use mathematical methods. Biomathematics is a discipline whose methods are not a mere mix of mathematics and biology. Our course and textbook provide an interdisciplinary approach to those methods.

We considered the first offering of the course in 2002 experimental and offered it as an honors course in an attempt to attract only strong students. The results were encouraging and, since then, we have offered the course three times as a cross-listed course that students can take for mathematics or biology credit.

Although the course is accessible to sophomores, the presence of juniors and seniors enhances the learning process. We found that a form of student mentoring emerges with juniors and seniors acting as liaisons between the sophomores and the teaching faculty. This was an unexpected benefit that we have come to rely upon. It is like the peer-mentoring practices common in actual interdisciplinary research.

We found that sophomores are able to absorb ideas and information from high-level biomathematics research and, by the end of the course, provide solutions to open-ended biomathematical problems. We also found that interdisciplinary team-teaching is different from teaching traditional courses and that teamwork created synergy between students with different backgrounds. The course structure, topic selection, and pedagogy were praised in the student evaluations. All students stressed their increased understanding of the importance of interdisciplinary collaboration. One student described the course as "the learning environment of the future" and another one said the course was "the most intellectual class offered at SBC." We attribute our success to the small class size, the informality of the seminar-like format, and the use of software that allows us to keep focused on the big picture while leaving technical details aside.

As part of our broader initiative to integrate the mathematics and biology curricula, we have used some of the course topics as stand-alone modules in conventional mathematics and biology courses including Calculus II, Statistics, Ordinary Differential Equations, Mathematical Modeling, Genetics, and Microbiology. This may be an alternative way to use our approach and materials at institutions where an integrated course in biomathematics may not be feasible.

Acknowledgements

References

National Center for Education Statistics, Institute of Education Science, cited 2012: Digest of Education Statistics 2010. [Available online at http://nces.ed.gov/programs/digest/d10/tables/dt10_282.asp?referrer=list.]

National Research Council, 2003: *BIO2010: Transforming Undergraduate Education for Future Research Biologists*. The National Academies Press, 208 pp.

Robeva, R., J. Kirkwood, R. Davies, M. Johnson, L. Farhy, B. Kovatchev, and M. Straume, 2008a: *An Invitation to Biomathematics*. Elsevier/Academic Press, 480 pp.

Robeva, R., J. Kirkwood, R. Davies, M. Johnson, L. Farhy, B. Kovatchev, and M. Straume, 2008b: *Laboratory Manual of Biomathematics*. Elsevier/Academic Press, 192 pp.

12

Teaching Bioinformatics in a Mathematics Department

Steven Deckelman[1]
University of Wisconsin-Stout

Name of Institution	University of Wisconsin-Stout
Size	about 9,000 students
Institution Type	Primarily undergraduate institution
Student Demographic	Majors in the Applied Mathematics and Computer Science Program with a Bioinformatics Concentration
Department Structure	Mathematics, Statistics, and Computer Science are in the same department.

Abstract

Undergraduate programs in bioinformatics are usually in a life science department, a computer science department, or both. A bioinformatics program in a mathematics department can include much more mathematics. We describe the discipline of bioinformatics, connections between bioinformatics and the mathematical sciences, undergraduate research possibilities, and resources for mathematicians who want to learn more about bioinformatics or develop a bioinformatics curriculum. Our concentration in bioinformatics in the Department of Mathematics, Statistics and Computer Science at the University of Wisconsin-Stout, and part of a BS degree in Applied Mathematics and Computer Science, will be described as an example.

12.1   Course Structure

- Weeks per term:16 week semester

- Classes per week/type/length: Three fifty-five minutes classes each week.

---

[1] deckelmans@uwstout.edu

- Labs per week/length: One fifty-five minute lab per week in bioinformatics capstone. Required science courses will have science labs.

- Average class size: 20 Students; 10 or fewer students the bioinformatics capstone.

- Enrollment requirements: Students should be in the bioinformatics concentration within the Applied Mathematics and Computer Science major.

- Faculty/dept per class, TAs: Taught by a single faculty member.

- Next course: Students in bioinformatics may want to take related courses in biology.

- Web pages: UW Stout, 2012a; UW Stout, 2012b.

12.2   What is Bioinformatics?

The term *informatics* has sometimes been used to describe fields in which massive amounts of data are generated and need analysis, interpretation, and application. For example, medical informatics refers to ways of organizing, using, and making sense out of the massive amount of medical research and patient record data that are being generated. Bioinformatics may be described as informatics that arise from the huge amounts of data generated by technologies for genomic sequencing. It is an area that draws on biology, chemistry, and physics, as well as mathematics, computer science, and statistics. There is no universally accepted definition of bioinformatics, and practitioners of different fields emphasize different aspects of it. Biologists may view bioinformatics as a collection of software to be used as tools in life science research, while computer scientists may regard it as a subspecialty of computer science. A mathematician exploring the subject will find it to be rich in mathematical structure. Bioinformatics is all of these things. Different conceptions of the field are emphasized to different degrees depending on the department in which the undergraduate bioinformatics curriculum resides. Bioinformatics is interdisciplinary, which makes its definition hard to nail down. It is sometimes likened to discrete computational biology, as in matching DNA sequences, as contrasted with the partial differential equations, energy equations, and approximate algorithms used to analyze protein folding. In this article, we use a broad definition that includes health informatics, computational biology, and algebraic statistics.

Much of the mathematical content of bioinformatics falls within the realm of traditional discrete mathematics. Indeed, bioinformatics could be thought of as applications of discrete mathematics in a particular biological context. Graph theory provides a natural framework for formulating fundamental problems such as biological sequence alignment. The problem of globally aligning two DNA sequences can be viewed as finding a longest path in a weighted directed graph (Jones, 2004). Tools such as generating functions arise naturally in the biological problem of restriction mapping, where the objective is to reconstruct a genomic sequence from a sequence of fragments cleaved by restriction enzymes. The notion of permutation is fundamental in the study of genome rearrangements in which organismal genomes are shuffled by evolutionary processes. Bioinformatics also uses statistics. Cluster analysis is a statistical technique that is useful in analysis of gene expression data from DNA arrays and in molecular phylogenetics—the reconstruction of evolutionary family trees. Probability (Waterman, 1995) arises in connection with hidden Markov models, a machine learning tool used in gene hunting (Durbin, 1998). Other ideas such as NP-completeness and complexity analysis are useful in understanding the nature and limitations of computational approaches to solve the problems of bioinformatics. The field has been developing rapidly and extending far beyond what mathematicians would recognize as traditional discrete mathematics. Algebraic statistics is a new subdiscipline that uses ideas of computational algebra and algebraic geometry to the study of statistical problems (Pachter, 2005). The statistical models of bioinformatics are viewed as algebraic varieties (zero sets of polynomial equations in several variables. This leads to applications such as Gröbner bases to bioinformatics. The related field of biomedical informatics has seen application of mathematical ideas from number theory and quantum mechanics (Robson, 2007). Systems biology is a field which straddles bioinformatics (as in functional genomics) and mathematical biology. It is concerned with the study of biological information networks (metabolic pathways, biochemical networks, gene regulatory networks) and uses mathematical modeling techniques involving calculus, discrete dynamical systems, and differential equations (Alon, 2007). Additional resources on these ideas and their possible inclusion in the undergraduate curriculum will be given below.

12.3   Institutional Profile

The University of Wisconsin-Stout is a four-year comprehensive institution in the University of Wisconsin system located about an hour from Minneapolis-St. Paul. There are about 9000 students, mostly undergraduates. The Department of Mathematics, Statistics, and Computer Science has about twenty-five staff members, representing the three discipline areas. There are approximately 130 applied mathematics and computer science majors with about twenty graduates per year. There is also infrastructure to support bioinformatics. The university has recently been designated as a Polytechnic Institution, defined as one having a mission that focuses on STEM disciplines and emphasizes the use of scientific theory and research to solve real-world problems and contribute to the economy and society. There is interest in and support for biotechnology research and curriculum development. We have a biology faculty active in research who use bioinformatics tools. Indeed, the proposal to create an undergraduate program in bioinformatics came from our biology faculty. The Minneapolis-St. Paul area has a growing biomedical technology industry, and the campus is about two hours away from the Mayo Clinic in Rochester, Minnesota, and one hour away from the Marshfield Clinic in Marshfield, Wisconsin, both of which have active biomedical research divisions that make use of bioinformatics. The Marshfield Clinic has close research and exchange ties with the University of Wisconsin.

12.4   Our Program at the University of Wisconsin-Stout

Our program offers a BS degree in Applied Mathematics and Computer Science with a concentration in bioinformatics. The concentration combines mathematics, computer science, statistics, biology, and chemistry. In many respects the program is like a double Math-CS major. In mathematics, students take course work up to and including the traditional junior-senior level curriculum of modern algebra and real analysis, including a year of calculus-based statistics. In computer science, students take courses in computer organization, data structures and database systems, and upper division electives. The courses are described on our websites (UW Stout, 2012c; UW Stout, 2012d).

12.5   Mathematics Courses in the Bioinformatics Curriculum

Bioinformatics students take the same mathematics core courses as all majors, including three semesters of calculus, one semester of linear algebra, and a foundations course in mathematical language and proofs. Graph theory and numerical analysis are recommended electives. Although they are not required, our bioinformatics students typically take courses in real analysis and modern algebra to fill out their programs. These courses reflect our view that our bioinformatics students are still mathematics majors, albeit with a bioinformatics emphasis. There are additional required courses in computer science, statistics, biology, and chemistry. A two-semester senior capstone course in bioinformatics (see below) rounds out the curriculum.

12.6   Bioinformatics Content in the Curriculum

Because our degree program is in the mathematical sciences, albeit with an applied slant, part of the philosophy of the program has been to teach bioinformatics as a subject at the intersection of mathematics, statistics, and computer science. But since bioinformatics is a fundamental tool in the life sciences, we also teach students how these tools are used by scientists. We want our graduates to understand how to use bioinformatics tools as biologists do and to understand the mathematical ideas on which these tools are based. Resource constraints prevent us from developing very many new courses. Instead, our approach has been to develop a small number of bioinformatics courses, while putting additional bioinformatics content in existing courses in biology and chemistry as well as in computer science and mathematics.

In our computer science Data Structures class, Dr. Terry Mason (Mason, 2010) includes a module that shows students how to build a map data structure that translates a gene sequence into a protein sequence. Projects such as this expose students to the nucleotide representation of DNA and how it maps to RNA and eventually to protein. In our Database System course, Dr. Mason has students work on design and implementation of a biological database to collect information for various agents such as chemicals and nucleotide sequences. This work is part of a project in

collaboration with the biology department to build web tools to run computations and data mining on their collected data. In our Advanced Biochemistry course, Dr. Marcia Miller-Rodeberg (Miller-Rodeberg, 2010) introduces students to the use of bioinformatics through examination of protein structures and the effects of mutations on protein function, specifically focusing on metabolic diseases. Protein sequencing and homology are discussed in relation to evolutionary trees, the evolution of new enzymes, etc. Students are also required to do a research paper and talk on a disease caused by mutations in an enzyme, with bioinformatics used to analyze structure and genetic relations. Biologist Steve Nold (Nold, 2010) integrates research questions into the laboratory and has his students create clone libraries and sequence DNA for bacteria in the Red Cedar watershed, sinkhole microbes, and grasshoppers. They take those sequences to GenBank, the National Center for Biotechnology Information Sequence Database, (NCBI, 2012a) for identifications using utilities such as Blast (Basic Local Alignment Search Tool, NCBI, 2012b).

12.7   The Bioinformatics Capstone

Our capstone course is a two-semester sequence. The first course (MSCS 492), which is taught by a mathematician or computer scientist, focuses on mathematical and computational aspects of bioinformatics, while the second (MSCS 493), taught by a life scientist, focuses on application in the life sciences. The prerequisite for MCSC 492 is senior standing in the bioinformatics major. This usually means that students have taken the full slate of courses mathematics majors typically take, from calculus to real analysis and modern algebra.

Topics in MSCS 492 include bioinformatics algorithms and programming in PERL, complexity and analysis of algorithms, proofs of correctness, software tools, and languages (Perl, Matlab etc.). It also provides an introduction to the classical problems of bioinformatics (motif finding, genome rearrangements, sequence alignments, gene prediction, phylogenetics), and some of the classical approaches to these problems (dynamic programming, combinatorial and statistical methods, hidden Markov models, graph theoretic formulations). We use the text by Jones and Pevzner, *An Introduction to Bioinformatics Algorithms*, MIT Press, 2004. Students also have a senior project on which they have to give a talk. Some of the projects have dealt with computational methods for protein structural analysis (software tools for obtaining, visualizing, and performing *in silico* analysis on protein models). Other projects have dealt with experimental methods for obtaining biological data such as gel electrophoresis, DNA probing and sequencing. Other possibilities for a project include reading a research paper in the field such as "Bounds For Sorting by Prefix Reversal," an undergraduate researcher paper by Bill Gates from his Harvard days under Christos Papadimitriou.

The second course, MSCS 493, is called Bioinformatics Practicum. In it, biologist Michael Pickart has students work on projects with bioinformatics content. For example, one student focused on improving access to multiple-species sequence data for comparative genomics. The student examined existing genomics data portals at resource sites such as the National Human Genome Research Institute (NHGRI), National Center for Biotechnology Information, National Institutes of Health Intramural Sequencing Center, and UC Santa Cruz Genome Browser to determine the existing methods for mapping of human genes to ENCODE (The Encyclopedia of DNA Elements) regions. The ENCODE consortium was launched by NHGRI. Its goal is to produce a comprehensive catalog of about 1% of the structural and functional components encoded in the genomes of humans and other species. As the number of fully sequenced genomes grows, it becomes easier for researchers to use comparative genomic data; however, our student found that current access to this data was not straightforward, limiting our students' ability utilize this resource. To assist student genomic research of ENCODE data, a student project explored ways of restricting the data for human and zebrafish genes to facilitate mapping to ENCODE regions. Students mapped protein sequences of genes involved in pigment development from the zebrafish genome to the human genome. Zebrafish are a model organism, a non-human species whose genomic structure gives insight into the human genome due to the common evolutionary descent of all species.

12.8   Special Curriculum Challenges (Theory vs. Real World)

Teaching bioinformatics at the undergraduate level involves curriculum challenges. Depending on the clientele, we may have to look for simple ways to teach mathematical ideas to biology students with minimal mathematics background. Likewise, when teaching mathematics students, there is the challenge of making the material biologically meaningful by connecting the theory to real world applications. An advantage to housing a bioinformatics program in a mathematics department is that the curriculum can be developed for students with a solid grounding in mathematics. One way

of bridging the gap between theory and practice is to use real world biological sequence data. The National Center for Biotechnology Information website (NCBI, 2012c) contains links to large public databases of DNA and protein data. The European Bioinformatics Institute (EBI, 2012a) is another good resource. A student can gain a sense of the applicability of bioinformatics by downloading a genome and analyzing it. The curriculum experience for students can be enhanced through either team teaching with biologists or developing paired biology courses that complement the mathematical bioinformatics. In a mathematics class, for example, students can be taught the mathematical basis of cluster analysis, and to understand the nature of the data furnished by DNA microarrays and how to analyze these data. In a paired biology or biotechnology class, students can gain valuable wet lab experience using DNA arrays. Likewise, students can learn the ideas of hidden Markov models in a mathematics class while applying the technique to gene finding in a biology laboratory. This approach is currently under development at the University of Wisconsin-Stout.

12.9   Undergraduate Research Possibilities in Bioinformatics

Bioinformatics is rife with opportunities for interdisciplinary undergraduate research. Because bioinformatics is a relatively new field, there is a wealth of open problems (Pevzner, 2000), many of which are understandable by undergraduates. At the same time, the life sciences are generating large data sets in need of analysis. Student projects can involve studies of mathematical and algorithmic ideas for solving problems or software development for the analysis of available biological sequence data. Partnering with biologists who make use of genomics in their research creates an opportunity for interdisciplinary student projects with interdisciplinary mentoring. Finally, there are a growing number of REU and similar opportunities for students in various biomedical, industrial, educational, and research settings. The Rochester Institute of Technology maintains a list of these (RIT, 2012a).

12.10   Some Process Issues

Originally the suggestion for a bioinformatics concentration at UW-Stout came from the biology faculty. With an undergraduate major of applied mathematics and computer science, the Department of Mathematics, Statistics, and Computer Science already had the necessary infrastructure for a bioinformatics program with a strong mathematics component. With the exception of the capstone course and a lower level introduction to bioinformatics course still under development, the program was put together with minimal additional resource requirements by using existing courses. Thus the administrative hurdles that can arise with new programs were never an issue. Once the program was up and running, advising of majors has been done jointly by mathematics and biology faculty who meet with students together.

12.11   Resources for Retooling in Bioinformatics and Bioinformatics Curriculum Development

How much biology does a mathematician need to know to get involved with bioinformatics? While it helps to have some exposure to biology, it's not necessary to be a credentialed biologist or to have wet lab skills to get involved in bioinformatics. Indeed, most mathematicians have minimal or no real training in biology and most biologists lack advanced mathematics or computational training; this makes interdisciplinary collaboration especially fruitful. It is helpful to know enough about molecular biology to be able to understand, at least conceptually, the nature of data produced by biological experiments and the questions biologists are interested in. At the undergraduate level, much of the biology needed for bioinformatics can be distilled down into what is often referred to as the central dogma of molecular biology: "DNA makes RNA makes proteins." The molecular biology text by Alberts, Bray, et. al. (Alberts, et al 1994) gives a readable introduction to the subject. The MAA publication *Math & Bio 2010* (Steen, 2005) includes a list of bioinformatics resources, as does Claudia Neuhauser and Kristine Fowlers' *Recommended Resources in Mathematical Biology* (Fowler, 2004). Bioinformatics may also be regarded as a subspecialty of mathematical biology. The Mathematical Biosciences Institute at the Ohio State University offers visiting and sabbatical opportunities for mathematics faculty. The institute also has a wealth of curriculum-relevant resources on its website (MBI, 2012a), and offers regular tutorial and workshops in all areas of mathematical biology including bioinformatics. The BioQUEST

Curriculum Consortium is specifically aimed at integrating undergraduate mathematics and biology curriculum (Bio-quest, 2012a). It offers workshops and a series of publications and maintains the BEDROCK (Bioinformatics Education Dissemination: Reaching Out, Connecting, and Knitting-together) project, a repository of curriculum resources that support "an inquiry-based approach in which students explore and analyze actual data in a way that recreates the experience of conducting research." Both the Mathematical Association of America and the Society for Industrial and Applied Mathematics have interest groups in mathematical biology that include bioinformatics, and there is also a Society for Mathematical Biology. Curriculum development resources are now available online at such sites as Pavel Pevzner's page, (Bioalgorithms, 2012a), and Lior Pachter's homepage, (Pachter, 2012a).

Summary

Bioinformatics employs computational methods and technologies to analyze biological sequence data. Its methods have origins in computational biology, a field at the junction of mathematics and computer science in which the underlying problems are mathematical in nature. To acquire an understanding of the field and its tools, students need to understand the underlying mathematical problems, which draw on discrete mathematics, theoretical computer science, probability and statistics, algebra, and algebraic geometry. Mathematicians are ideally suited to contribute to bioinformatics curriculum development and the education of the next generation of life scientists.

References

Alberts, Bray, et al. (1994). *Molecular Biology of the Cell.* New York: Taylor and Francis.

Alon, U. (2007). *An Introduction to Systems Biology: Design Principles of Biological Circuits*. Boca Raton: Chapman Hall/CRC.

Bioalgorithms, 2012a, http://www.bioalgorithms.info

Bioquest, 2012a, http://www.bioquest.org

Durbin, et al. (1998). *Biological Sequence Analysis: Probabilistic Models of Proteins and Nucleic Acids*. Cambridge: Cambridge University Press.

EBI, 2012a, http://www.ebi.ac.uk/2can/genomes/genomes.html

Fowler, K. (2004). *Using the Mathematics Literature.* New York: Marcel Dekker.

Gates, W. and Papadimitriou, C. (1978). Bounds For Sorting By Prefix Reversal, *Discrete Mathematics* (27).

Mason, T. (2010). Private Communication.

MBI, 2012a, http://www.mbi.osu.edu

Miller-Rodeberg, M. (2010). Private Communication.

NCBI, 2012a, http://www.ncbi.nlm.nih.gov/genbank

NCBI, 2012b, http://blast.ncbi.nlm.nih.gov/Blast.cgi

NCBI, 2012c, http://www.ncbi.nlm.nih.gov

Nold, S. (2010) Private Communication.

Pacheter, 2012a, http://mathematics.berkeley.edu/~lpachter

Pachter, Sturmfels. (2005). *Algebraic Statistics for Computational Biology.* New York: Cambridge University Press.

Pevzner, P. (2000). *Computational Molecular Biology: An Algorithmic Approach*. Cambridge Massachusetts: MIT Press.

Pevzner and Jones. (2004). *An Introduction to Bioinformatics Algorithms.* Cambridge Massachusetts: MIT Press.

RIT, 2012a, http://www.rit.edu/∼gtfsbi/Symp/bioinformatics.htm

Robson, B. (2007). The New Physician as Unwitting Quantum Mechanic: Is Adapting Dirac's Inference System Best Practice for Personalized Medicine, Genomics, and Proteomics? *Journal of Proteome Research* , 3114–3126.

Pickart, Michael. (2010) Personal Communication.

Steen, L. (2005). *Mathematics & Bio 2010: Linking Undergraduate Disciplines.* Washington D.C.: The Mathematical Association of America.

Tymann, P. E. (2005). Computer Science and Bioinformatics. In L. Steen, *Mathematics & Bio 2010, Linking Undergraduate Disciplines* (pp. 75–82). Washington D.C.: The Mathematical Association of America.

UW Stout, 2012a, http://www3.uwstout.edu/programs/bsamcs/index.cfm

UW Stout, 2012b, http://www3.uwstout.edu/programs/bsamcs/upload/c_bsamcs_bio.pdf

UW Stout, 2012c, http://www3.uwstout.edu/programs/bsamcs/index.

UW Stout, 2012d, http://www3.uwstout.edu/programs/bsamcs/upload/c_bsamcs_bio.pdf

Waterman, M. (1995). *Introduction to Computational Biology: Maps, Sequences, and Genomes*. Boca Raton: Chapman & Hall/CRC.

13

SYMBIOSIS: An Integration of Biology, Math and Statistics at the Freshman Level: Walking Together Instead of on Opposite Sides of the Street[†]

Karl H. Joplin[*], Istvan Karsai, and Darrell Moore, Hugh A. Miller III
Dept. of Biological Sciences

Edith Seier, Anant Godbole, and Michel Helfgott
Dept. of Mathematics & Statistics
all of East Tennessee State University

Name of Institution	East Tennessee State University
Size	about 15,000 students
Institution Type	regional state institution with graduate programs
Student Demographic	freshman curriculum for all biology majors
Department Structure	Mathematics and Statistics, and Biological Sciences are individual departments in College of Arts and Sciences

Abstract

SYMBIOSIS is a novel three-semester curriculum that teaches biology, statistics and mathematics in an integrated curriculum at the introductory level for freshmen. It was developed by faculty in the Departments of Biological Sciences and Mathematics and Statistics. We describe the goals, organization, and aims of this project and processes used to establish it and we discuss the pedagogical and cultural barriers between these disciplines that needed to be addressed.

---

[*] joplin@etsu.edu

13.1   Course Structure

- Weeks per term: 15 weeks
- Classes per week/type/length: M (Lec-2 hrs), T (Lab-2 hrs), W (Lec-2 hrs), Th (Lec-2 hrs), F (Lec-2 hrs)
- Labs per week/length: one 2-hr lab/wk
- Average class size: 16 students in one section
- Enrollment requirements: Students supported by our NSF STEP grant
- Faculty/dept per class, TAs: One biology and one mathematics instructor, two TAs
- Next course: IBMS 1200, Integrated Biology and Calculus
- Website: http://www.etsu.edu/cas/symbiosis/default.aspx

13.2   Introduction

Picture a busy thoroughfare through a city with cars speeding by and people standing on the sidewalk. Viewpoints of the people on the sidewalk depend on which side of the street they are on. This is the state of affairs in biology and mathematics education, with biologists standing on one side, mathematicians and statisticians standing on the other side, and little connection between them. This situation was addressed in 2003 by the National Academies in the publication *BIO 2010* (National Resource Council, 2003), an analysis and set of recommendations calling for the integration of biology and mathematics for academic development and pre-professional training. *BIO 2010* has been followed by *Math & BIO 2010: Linking Undergraduate Disciplines* (Steen, 2005) and by federally and privately funded initiatives. Some programs have been started in response to these reports, but most of them have focused on introducing mathematical topics into biology classes, usually at the upper undergraduate and graduate levels.

East Tennessee State University (ETSU) is a regional university of approximately 15,000 students and 700 faculty. It is primarily an undergraduate teaching institution with masters programs in biology and mathematics (http://www.etsu.edu). Faculty of the departments of Biological Sciences and Mathematics at ETSU have a history of interdepartmental cooperation in biological research. This led to the creation of the Institute of Quantitative Biology (IQB) in 2003 to enhance interdepartmental integration. Two groups of faculty drawn from both departments applied for and received an NSF-UBM grant, an NSF-funded STEP grant in 2005, and a curriculum grant funded by the Howard Hughes Medical Institute (HHMI) in 2006. These programs are connected but represent different aspects of our approach to undergraduate biology and mathematics education. The STEP program is meant to recruit students and introduce them to research and the goal of the HHMI grant is to design and implement an integrated curriculum of mathematics and biology.

The design and implementation of the HHMI-supported curriculum change has been and continues to be a major undertaking requiring rethinking of the pedagogy of both disciplines. This paper describes the process used for this project and the resulting curriculum model. Other aspects of SYMBIOSIS are described in an accompanying paper (Moore, et al., 2012).

13.3   Description

Our HHMI-funded curriculum grant is titled SYMBIOSIS: An Introductory Integrated Mathematics and Biology Curriculum. The award was to create an integrated curriculum that would count as three semesters of introductory biology for majors, one semester of statistics, and one semester of calculus. The four-year grant was funded in the fall of 2006 and SYMBIOSIS I was taught for the first time in Fall 2007.

SYMBIOSIS is our response to the *BIO 2010* report, which calls for creation of integrated courses. Most responses to this call have taken the form of mathematical modules added to existing biology courses, biological applications added to existing mathematics courses, or integrated research projects for upper division students and mainly directed at mathematics content.

We have taken a different approach with SYMBIOSIS by integrating statistics, calculus, and biology in a three-semester course at the introductory level. We describe the material used to teach SYMBIOSIS I, which combines the

topics in General Biology I for majors and the introductory probability and statistics course. During the development of the course, we realized that this approach of teaching biology with statistics has added to the conceptual richness of biology instruction while providing a biological context for statistics instruction.

The purposes of the SYMBIOSIS curriculum are to introduce a quantitative viewpoint into the introductory biology curriculum, develop mathematical concepts using biological applications, and investigate biological phenomena using analytical tools. The use of an integrative method rather than a juxtaposition method pedagogy (Jean and Iglesias, 1990) means that students see the relevance of a quantitative approach to biology. The problem with the traditional juxtaposition method is that it treats mathematics and biology as separate subjects, with students in one major viewing the other course as nothing more than a general education requirement.

The integrative method is based on the observation "Biology students are prepared to receive the mathematical concepts once they see their applications" (Riego, 1983). The same can be said of mathematics students, in that they are not taught the applicability of mathematics to biology. By presenting biology and mathematics as an integrated subject, we hope to overcome the reluctance of biology students to consider mathematical methods as essential to full understanding of biological processes.

The material for SYMBIOSIS I was developed by a year-long collaborative effort between mathematics, statistics, and biology faculty. The process required that each group develop an understanding for the approach that they use to develop their material. As one faculty member said, "You biologists don't use mathematics like a physicist does." Much of the work in integrating the material revolved around this realization. Some of the biology faculty were envious of the mathematicians' ability to develop a full lecture showing relationships and applications on the board. Math faculty were surprised that biologists needed so much illustration to show the three-dimensional structure of biology components or the effects of change over time. However, we found that each group could adjust its approach and that the disciplines could be presented in an integrated manner.

The course was first taught to a cohort of students from the NSF-funded STEP program. The students had a summer bridge program before their freshman year in which they were exposed to biological research activity and mathematical concepts. In future years, the course will be open to biology and mathematics majors who have been previously advised about its nature, and no additional prerequisites will be required. The lectures are team-taught by biology and mathematics faculty. Biology is used to introduce each module and to define the topic; this is followed by the statistics or mathematics concepts and tools that address the biological issues. Although the organization of the course is based on biological considerations, we still wanted the mathematical and statistical topics to be presented completely and in a logical order. These goals required us to decide what biological and mathematical components can be covered (see discussion below). Lectures are taught using Powerpoint and class notes are also available to the students through the university's D2L platform. The labs are taught by graduate teaching assistants with participation and overview by faculty. Typically there are two labs for each module, and experimental lab and a lab for data analysis and preparation of presentations or lab reports. Minitab and R are used in lectures and in labs to analyze data. Students complete two projects involving analysis of datasets and prepare posters of the results. The initial projects were on bird allometry and analysis of DNA sequence patterns.

We have found that statistics and biology are easy to pair, both conceptually and operationally. They have a long history together, since many statistical methods that appeared at the end of the nineteenth century and beginning of the twentieth century were developed by statisticians, such as R.A. Fisher, working in genetics and agricultural research and motivated by the need of tools to analyze the data they produced. Recent advances in genetics and bioinformatics and the acquisition of large data sets and high speed computers are again challenging the discipline of statistics with the need of tools for analysis.

The development of the material for the first semester depends on the contextual needs of biology and the developmental needs of statistics. Statistics, as with much of mathematics, depends on a logical development of concepts. Thus, both the statistics development and the biology content were considered in developing the framework for the modules. We believe that modern biology pedagogy is based too much on a pseudo-logical framework of going from small-to-big and is based on what biology has done historically and not why or how it is done. An examination of modern biology textbooks supports this contention, because they are encyclopedic in content and there is little carryover of material from chapter to chapter (Moore, et al., 2012). There is little quantitative methodology, with at most two or three equations presented in an entire book. Graphs commonly lack statistical information such as error bars, which are important because they demonstrate the variation in a population that is the basis of evolutionary change, which is

basic to biology. Thus, students are presented with a collection of facts that have no logical connection to the whole. Instructors observe that this approach produces students who do not know the introductory material needed for upper level courses.

We are attempting to address this concern by presenting students with "5 Themes of Biology" in the introductory modules, and to address each theme explicitly in each of the subsequent modules. The themes that we focus on in SYMBIOSIS are energy utilization, homeostasis, growth and reproduction, adaptation, and evolution. So when we present material on cells, we also examine how physical properties, such as surface-to-volume ratio, affect cell size and transport of material in and out of the cell. Mathematical functions can be used to show how these properties affect the energy, homeostasis, and growth and reproduction themes. In the same module, the number of erythrocytes of humans living at different altitudes (Spector, 1956) permits us to talk about the adaptation and evolution themes.

We use "module" to denote a unit of class content or chapter. Our modules define the biology and mathematics or statistical components of the semester. Each module consists of ten hours of lectures, a two-hour "wet" experimental lab, and a two-hour "dry" analytical lab.

The modules developed for SYMBIOSIS I include:

Introduction and the scientific method. A biologist's viewpoint of the scientific method and the role that statistics and mathematics plays in developing models and testing hypotheses. The binomial distribution is introduced to test hypotheses about population proportions and the randomization test is introduced to test hypotheses about the equality of means.

The cell. Cellular functions are a logical topic for the introduction of biological concepts. When we study a certain type of cell, such as an erythrocyte, its form can be classified as normal or abnormal. Counting the number of red blood cells in a sample and measuring cell dimensions provides student-generated data we can use to introduce descriptive statistics, correlation, and statistical graphs. Students are shown how to go beyond descriptive statistics and take the step toward inference. Estimation (by bootstrapping) and tests of hypotheses (randomization test) are used to arrive at conclusions based on experimental data. The biological implications of the surface to volume ratio of a cell are discussed as well as the strategies of cells to increase their surface area.

Size and scale. The concepts of scaling and allometry are used to study relationships among variables. Differences between isometric and allometric scaling are introduced, as are fractal branching for surface area and volume problems. Slope as a rate of change of scaling and log-log plots and the power law are also discussed. Exponential functions, the normal distribution, linear regression, and transformations are used to describe biological processes.

Mendelian genetics. Genetics provides an ideal motivation for the study of probability, including conditional probability, independence, and tests of independence. Mendel's original data are used to draw conclusions based on probability and to discuss the basics of Mendelian genetics. Meiosis is discussed as the biological basis of genetic probability and the rationale of why Punnett's square and probability trees demonstrate how the probability of allelic combination represents the meiosis process. Mendel's actual experimental data are used to perform goodness of fit tests for a coin-based model of genotype and phenotype. Conditional probability, Bayes rule, Poisson and normal approximation to the binomial distribution and an introduction to sampling methods are statistical topics of this module. In the Mendelian genetics module, biology and statistics integrate very well; biology provides a motivation for statistics and probability helps to understand the random nature of inheritance. The binomial distribution has always been useful in discussing the probability of each phenotype. The situation in which the sample size is large and the probability of success is small serves as a motivation for introducing the Poisson distribution as an approximation to the binomial.

DNA genetics and the genome is the natural topic to follow Mendelian genetics. DNA replication and sequence analysis are discussed and provide the opportunity to apply probability and hypothesis testing to new problems such as calculating the probability of palindromes, specific sequences of nucleotides, and specific palindromes related to enzyme restriction sites, the probability of matches, and so on. DNA databases from the internet allow us to use real data to discuss nucleotide frequency, GC content, non-independence in the two letters of a di-nucleotide, presence of palindromes, and distances between palindromes. Terms and tools that can be useful later in the understanding of

topics in bioinformatics are introduced in this module, including random walks, transition probabilities, matrices, and transition probability graphs. Classic topics of statistical inference (confidence interval estimation, test of hypotheses for proportions using large samples, the t-tests) that are part of our introductory statistics course are also included in this module. Examination of genomes and genome sequences for defined elements are used to statistically describe mitochondrial DNA sequences of insect species. Students compare the analysis of their sequence with another insect mitochondrial sequence analyzed by another pair of students, and both groups compare their sequence with the *Drosophila* mitochondria as a reference. They become aware of the differences between species at the DNA level and how to use statistical tools for this analysis. Data bases and free software available in the internet such as NCBI, Genomatrix (Genomatrix Software Suite, 2012), and ClustalW (European Molecular Biology Laboratory/European Bioinformatics Institute, 2012) are used.

Evolution is taught using probability functions to demonstrate changes in gene frequency over generational times. The Hardy-Weinberg equation is derived from allelic frequency data and the underlying assumptions are discussed. Its application as a standard against situations in which the assumptions are violated allows us to use the chi-square test.

In SYMBIOSIS II, the mathematical topics belong mainly to calculus, but with a statistical component that includes nonlinear estimation and the use of the periodogram. The biological topics of the models are populations, ecology, behavioral ecology, structured populations, chronobiology, energy, and enzymes.

In SYMBIOSIS III, the emphasis of the quantitative component is on additional topics of calculus, matrices, graph theory, some multivariate statistical methods, and an introduction to bio-informatics. The biological topics are neurons, membranes, photosynthesis, development, bioinformatics and evolution. For a further description of these modules see our Symbiosis website (East Tennessee State University, 2012).

13.4   Discussion

The reason for developing this course is simple and straightforward: to present the statistical concepts that biology and mathematical students need to do modern biology. The development and implementation have not been as simple as the goal. Each module was developed by a team consisting of at least one biologist and at least one mathematician or statistician. Members of the team need to be comfortable working together for the development process to succeed, and this is easiest for teams that have a prior working relationship, as did many of ours. The process benefited from the unqualified support of our respective chairs and college and university administration. The process is ongoing, but the results to date are encouraging. We have taken SYMBIOSIS I as the basis of a successful Governor's School program (a summer enrichment program for gifted high school students).

There are still problems at various levels of the university system, such as policies for transferring SYMBIOSIS credits to other institutions, accepting credit from transfer students, and obtaining acceptance from committees that determine appropriate credentials for admission to professional schools.

An important course design issue was to look for the best matching of biology topics and statistics topics to form the modules, but this posed some pedagogical difficulties. It is natural to start a course for future scientists with the scientific method, which implies that we need an early introduction to statistical hypotheses testing. How could we do that in the first week of the course when sampling distributions had not yet been covered? Fortunately, randomization methods (permutations test) can be included at this time to test hypotheses about the means of two populations. To test hypotheses about a population proportion, the exact test can be used; basics of probability and the binomial distribution are introduced and the exact test appears as a simple application of the binomial distribution.

The criteria that have guided the development of the statistical component of the first semester of SYMBIOSIS are as follows: do an early introduction of inference in order to be able to answer research questions from the beginning, give examples of the sequence rationale-algorithm-computer program, use a problem oriented approach presenting statistical methods when they are needed, give importance to the study of variability, take a multivariate view whenever possible, and include topics at the elementary level that can serve as a preparation for understanding the language and methods of biostatistics/bioinformatics, including exposure to R (The R Project for Statistical Computing, 2012)[1]

---

[1] R is free software, similar to Matlab, that is used extensively in bioinformatics and biostatistics; we use it to perform simple calculations and plots.

Active learning and critical thinking are promoted through class discussion and activities, homework, and poster assignments. The statistical analysis of real biological data drives the students into discovering facts instead of listening to facts in a passive way. We have created a textbook that we are using in our statistics sections (Seier and Joplin, 2011).

13.5   Suggestions

The development of this course has led us to examine many of the assumptions that traditional pedagogy makes for the biology and mathematics curricula. This is not easy and requires good communication between the mathematics and biology developmental teams. All faculty have to be willing to eliminate or restructure material. For example, our biologists agreed to move much of the biochemistry from the first to the third semester, at which point the mathematics is advanced enough to begin modeling chemical kinetics, and to eliminate time spent on biological groups (phyla and class descriptions), while the mathematicians agreed to reduce the number of Calculus II topics that lack important biological applications.

What is required is a rethinking of undergraduate education in this day of advancing biology and increasing computational power. Students must be taught to think conceptually from a critical viewpoint and this is not served by the traditional approaches.

13.6   Conclusion

SYMBIOSIS I covers somewhat more than the traditional introductory statistics course since it introduces classical parametric methods and randomization methods for inference. The biology component focus on topics that can be used to illustrate the statistics topics but nevertheless covers much of the standard first-semester biology curriculum, with the exception of atomic and molecular biochemical structure and metabolism, which are covered in SYMBIOSIS III after the mathematics has been developed in SYMBIOSIS II.

In SYMBIOSIS II, the mathematics portion is primarily concerned with the introduction and development of calculus. Thus, we are creating an introductory mathematics curriculum that emphasizes a biological, instead of the traditional physics-engineering, approach to calculus. In our collaboration, we are beginning to realize how different this approach really is.

Although the integrated approach works for small classes, implementation for large (300+) lecture sections introduces additional obstacles, since mathematics courses are typically limited to sections of 50–75. We are in the process of adapting the material for our introductory biology curriculum to address this difference. One approach is to create a co-requisite requirement so that students who enroll in Biology I must also enroll in one of the sections of the probability and statistics course that use biology for material development. Interestingly the statisticians feel that these sections would be considered more rigorous than their standard statistics course. Thus, this is not a 'baby biology' mathematics approach, but is a vigorous approach to an integrated curriculum.

In summary, because the material has been team-taught, we have noticed that both the students and the faculty have become more comfortable with the two subjects, creating a *symbiotic* approach to both biology and statistics that is developing as we walk together on the same side of the street.

Acknowledgements

References

East Tennessee State University, cited 2012: Symbiosis, the Whole is Greater than its Parts. [Available online at http://www.etsu.edu/cas/symbiosis/default.aspx].

European Molecular Biology Laboratory/European Bioinformatics Institute, cited 2012: ClustalW [Available online at http://www.ebi.ac.uk/Tools/clustalw/index.html].

Genomatrix Software Suite, cited 2012. [Available online at http://www.genomatix.de/cgi-bin/tools/tools.pl].

Jean, R.V., and A. Iglesias, 1990: The juxtaposition vs. the integration approach to mathematics in biology. *Zentralblatt fur Didaktik der Mathematik*, **22**, 147–153.

Moore, D., M. Helfgott, A. Godbole, K.H. Joplin, I. Karsai, H.A. Miller, III, E. Seier, 2013: Creating Quantitative Biologists: The immediate future of SYMBIOSIS. This volume, 201–205.

National Research Council, 2003: *Bio 2010*: *Transforming Undergraduate Education for Future Research Biologists*. National Academies Press, Washington, D.C.

National Center for Biotechnology Information, cited 2012 [Available online at http://www.ncbi.nlm.nih.gov/].

Riego L., 1983: Mathematics and the Biological Sciences—Implications for teaching. *Proceedings of the Fourth International Congress on Mathematical Education*. Zweng, M., T. Green, J. Kilpatrick, H. Pollak, M. Suydam. Birkhauser Boston, 207.

Seier E. and K.H. Joplin, 2012: *Introduction to STATISTICS in a biological context*. Createspace.

Spector, W., 1956: *Handbook of Biological Data*. National Academy of Science., Philadelphia and London: W.B. Saunders Company.

Steen L., Ed., 2005: *Math & Bio 2010: Linking Undergraduate Disciplines*. The Mathematical Association of America, Washington, D.C.

The R Project for Statistical Computing, cited 2012 [Available online at http://www.r-project.org/.]

II

Processes
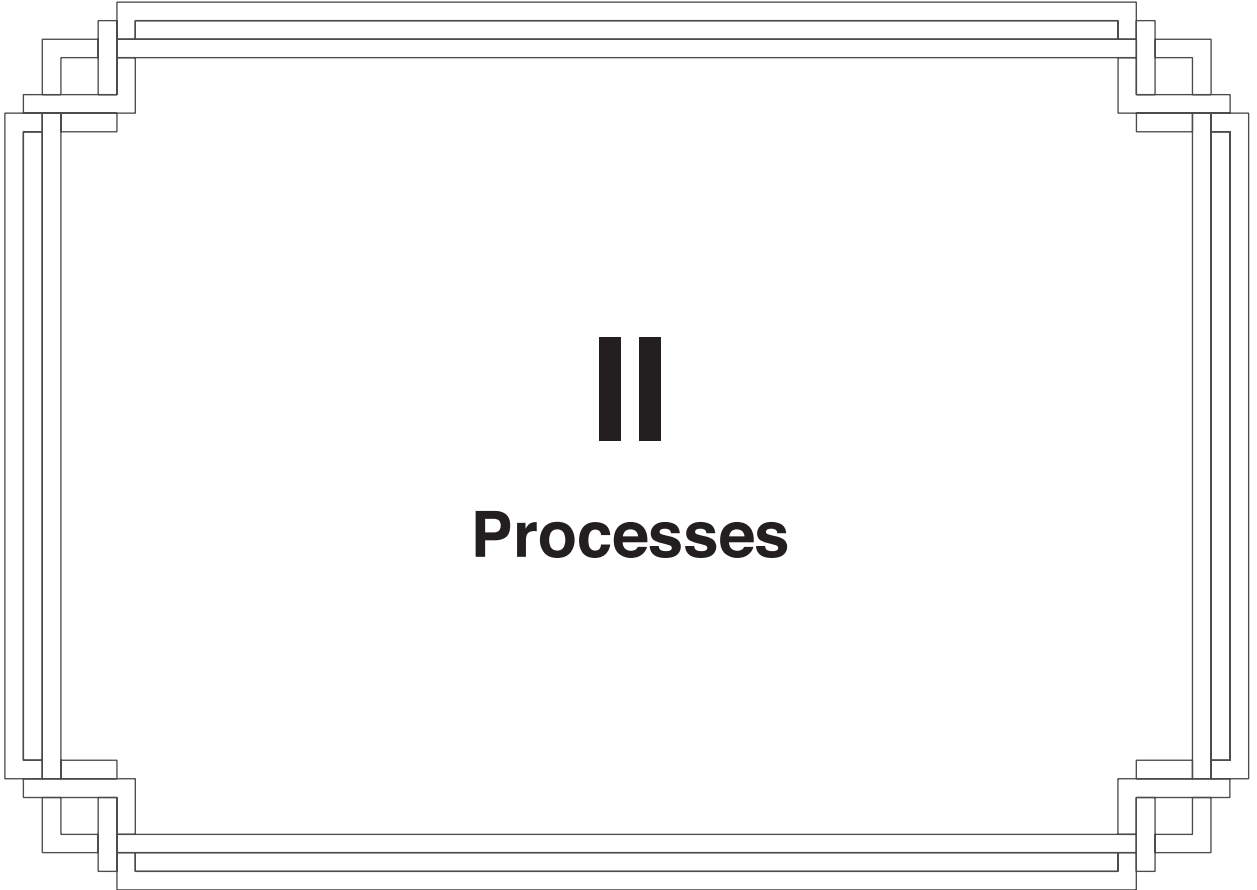
Introduction

There is a wide variety of wonderful projects described in the Models section of this book. However, as the authors of those projects will tell you, successful curriculum development in mathematics for biology requires more than an exciting course built on sound pedagogical ideas. An academic system based on standard courses distributed among standard departments is resistant to innovation and interdisciplinary teaching. The enthusiasm that accompanies new pedagogical ideas are often dampened by difficulties encountered in the implementation. In the hope of encouraging readers who are interested in emulating the projects in this volume or developing different ones, our goal in this section is to focus on the processes of creating, implementing, and institutionalizing undergraduate mathematics curricula for life science students. The authors have described the strategies and approaches they have used in pursuit of the goals of serving students and institutionalizing courses, highlighting unique features of their particular situation, constraints that affected their project, special support or collaboration they enjoyed, and their suggestions for others interested in pursuing similar projects and recommendations for the future. Not all of the authors are able to report successes, but all of them have thought carefully about why their projects did or did not work. The papers represent a broad spectrum in almost every category—type and size of institution; background and level of student population; curricular level; and size, scope and age of project.

The first four papers in this section represent long-term projects, some of which have remained successful over time and others that have not. *Science One: Integrating Mathematical Biology into a First-Year Program* by Mark Mac Lean from the University of British Columbia (UBC) details the year-long interdisciplinary math/science course at that institution. UBC is a large institution that attracts strong students. The project has been well supported by the university and has remained very successful. It stands as a testament to the possibility of long-term curricular reform. *Planning for the Long Term* by Meredith Greer from Bates College discusses a long-term project that met with initial success, but has declined over time and is now being revised by utilizing faculty and resources at other nearby small institutions. Drawing on her experience, Greer has some good suggestions for those starting out in pedagogical development. Lou Gross from the University of Tennessee reflects on a well-established two-course entry-level mathematics sequence for bioscience majors in *Some Lessons from Fifteen Years of Educational Initiatives at the Interface between Mathematics and Biology: the Entry-Level Course*. This sequence has been taught by over eighty different faculty, an unusually high degree of institutionalization for an innovative course. Gross recommends the inclusion of a sound assessment plan from the outset. The last long-term project in this section, *A "Wet-Lab" Calculus for the Life Sciences: Processes*, is by Jim Cornette and colleagues, an interdisciplinary team of faculty from Iowa State and Michigan State. The authors share some valuable lessons about course development from their experience with a project that has declined over time and not been maintained.

The remaining projects represent a wide variety of mostly newer projects that span the spectrum of institutions and student populations.

In *Creating an Interdisciplinary Research Course in Mathematical Biology*, Glenn Ledder and Brigitte Tenhumberg from the University of Nebraska-Lincoln discuss the creation of their summer course for early undergraduates (described in a companion paper in the Models section). This paper focuses on overall design principles for an interdisciplinary research-based course and offers suggestions for creating interdisciplinary partnerships in teaching. For another perspective on creating an interdisciplinary mathematical biology course, this time with a computer science twist and at a smaller master's-granting institution, see *Bioinformatics: An Example of a Cooperative Learning Course* by Namyong Lee and Ernest Boyd of Minnesota State University, Mankato.

A particularly innovative project at the community-college level, where a large number of students start their higher education career, is described in *Integrating Statistics and General Biology I in a Learning Community* by Bill Ardis and

Sukanya Subramanian at Collin County Community College in Texas. They discuss the use of learning communities and strategies for working with limitations caused by the need for community college courses to match up with courses at institutions to which their students will transfer. Readers interested in precalculus courses should also see the paper by Gordon and Gordon in the Directions section.

The final two papers describe projects at large public universities, which have their own set of challenges and opportunities. In *Constructing an Undergraduate BioMath Curriculum at a Large University: Developing First Year Biomath Courses at The Ohio State University,* Tony Nance and Laura Kubato discuss the genesis of their three course calculus and statistics sequence for life science majors, which is described in a companion piece in the Models section of this volume. In *Initial Steps Toward an Integration of Quantitative Thinking into the Teaching of Biology at a Large Public University*, Carole Hom, Eric Leaver, and Martin Wilson of the University of California, Davis, discuss a program of one-credit mathematics courses that students may choose to add as a quantitative accompaniment to an associated biology course. These innovative courses offer a possible solution to the problem of how to add mathematical content to biology courses, but with difficulties in timing the mathematics to fit the biology course. This paper presents some useful assessment data in addition to the discussion of processes.

These authors have done their part. They have worked to make changes at their institution and shared their wisdom, which is every good researcher's obligation. Your job is to find among these projects intriguing ideas, engaging approaches, an institution and student body similar to yours in some way, and some practical advice on how to successfully navigate the process of creating and implementing innovative undergraduate mathematics curricula for your own life sciences majors. We will look forward to reading about the success of your projects next time.

14

Science One: Integrating Mathematical Biology into a First-Year Program

Mark Mac Lean[1]

Department of Mathematics, The University of British Columbia, Vancouver, BC, Canada

Name of Institution	University of British Columbia, Vancouver
Size	about 45,000 students on the Vancouver campus
Institution Type	large public medical-doctoral university
Student Demographic	recent high school graduates with interests across the scientific disciplines
Department Structure	Faculty of Science has separate departments for each discipline sending instructors to Science One

Abstract

Since 1993, the Science One Program at The University of British Columbia (UBC) has been integrating mathematical biology into a team-taught, first-year interdisciplinary science program. The mathematical biology component of this program introduces students to aspects of mathematical modeling and ensures that they have a solid foundation in calculus and elementary differential equations. About 70% of the students subsequently pursue life sciences majors. Science One has shown itself to be an enriching experience for both students and faculty. Strong support from UBC administrators was essential to its early success, and has enabled many lessons learned from Science One to be applied broadly at UBC.

14.1 Course Structure

- Weeks per term: 26 weeks over two terms plus two exam periods in December and April

- Classes per week/type/length: 12 1-hour lecture periods each week; 4 1-hour tutorials each week

---
[1] maclean@math.ubc.ca

- Labs per week/length: 3 3-hour laboratory periods each week
- Average class size: 75 students in one section broken down into three tutorial/lab groups of 25 students each
- Enrollment requirements: For students entering first-year sciences; students must apply for the program; admission based on an essay, list of science-related activities, and high school grades
- Faculty/dept per class, TAs: Team-taught by eight instructors, two for each discipline
- Next course: Prepares students for entry to any major program in the Faculty of Science.
- Website: http://www.scienceone.ubc.ca

14.2   Introduction

There has been much interest in improving the mathematical education of future research biologists (Bialek and Botstein 2004; National Research Council 2003). Something as basic, and essential, to 21st Century biology as improving our understanding of the structure of the information contained in a genome will require deep training in both the biological sciences and the mathematical sciences. Moreover, mathematical biology continues to make contributions to such diverse areas as ecology, evolution, the study of diseases (both at the cellular and population levels), and to neurobiology, for example. Because most life sciences majors are required to take at least some quantitative courses, it makes sense to use them as opportunities to show students the important roles mathematics can play in the biological sciences.

In 1991, the Faculty of Science at The University of British Columbia (UBC) began to develop an interdisciplinary first-year program in science. The goal was to provide an educational experience to train new scientists who will be able to tackle problems that require tools from outside their specialized disciplines (Dryden et al. 2011). First implemented in 1993, the Science One Program is a learning community of students and faculty members that emphasizes scientific process and the interrelationships between disciplines (biology, chemistry, mathematics, and physics are the core disciplines in the program) while giving students essential technical skills for their majors or honors degrees. About 70% of the Science One students choose life sciences majors.

In the past twenty years, Science One has proven to be a crucible for new teaching ideas and has been an inspiration for new programs throughout UBC (Benbasat and Gass 2002; Dryden et al. 2011). Moreover, there is evidence that Science One students outperform other B. Sc. students at UBC in upper-year courses, including students with similar grades who have participated in highly selective majors programs (Dryden et al. 2011; Dryden and Mac Lean 2004; Dryden and Mac Lean 2008). We hypothesize that the advantage Science One students have over their peers is some combination of self-selection, our admissions process, and taking the program (Dryden et al. 2011).

From the beginning, mathematical biology played a central role in the Science One curriculum. While mathematics is obvious in many parts of first-year chemistry and physics, it traditionally has remained hidden in biology. Our goal is to help students find opportunities to see mathematics in the biological world around them. This goal matches with the goal of the UBC first-year biology courses to have students see biology as more than a collection of fact. Furthermore, the richness of the biological sciences leads to excellent examples that provide contexts in which to learn both specific mathematical concepts and mathematical modeling. Mathematical modeling is an important contributor to the growth of students' critical thinking and analytical skills.

In this note, we will focus on key aspects of Science One related to teaching mathematical biology to first-year students, and on ideas we have found to be important to building institutional support.

14.3   Program Description

UBC is a large, public, research-intensive university offering a full range of PhD programs. Our 45,000 member student body (37,000 undergraduates, 8,000 graduate students) has strong international representation. The Faculty of Science attracts top students (Wieman and Sudmant 2008), and the Science One Program attracts first-year students who seek a challenging program of studies. More than half of Science One students go on to graduate and professional schools.

Science One is a learning community of 75 first-year students, eight instructors, and a program director who also contributes to the teaching. It is structured as a single 27-credit course (of a 36-credit typical load), taught over two semesters, that integrates biology, chemistry, mathematics, and physics. The students are selected competitively on the basis of their grades and their interest in science, as judged on the basis of an essay and a list of their science-related extra-curricular activities.

Each week, students attend twelve hours of lectures, which are led by one or more faculty members. In addition, there are two tutorial hours per week during which 24 students meet with one or two instructors for a structured activity, two hours of small groups in which nine students work with one instructor, and nine hours of labs. Each component represents a different kind of opportunity for integrating disciplines.

To give the course a clear interdisciplinary feel, at least two faculty members share the classroom at one time. Even during classes in which one faculty member is the primary instructor, the presence of a peer, usually from a different discipline, helps create vibrant dynamics, especially where there are exchanges of differing viewpoints. The students see how mathematicians and scientists talk to each other, and because of the comfortable environment in the classroom, they quickly become engaged in classroom discussions.

Students also do two independent research projects, one each term. Many of these projects incorporate mathematical models in one way or another. Students present the results of one project at a spring research conference. Samples of projects can be found online in the UBC Information Repository (https://circle.ubc.ca/handle/2429/6927).

A more detailed description of the Science One Program and its operation is found in Dryden et al. (2011).

14.4 Discussion

14.4.1 Integrating Mathematical Biology through Mathematical Modeling

The mathematical content of Science One is based on the UBC standard curriculum in differential and integral calculus. Additional topics include some elementary differential equations, basic ideas from probability, difference equations, and dimensional analysis. For each topic, we have a collection of examples that use those particular concepts in a biological context. This curriculum is consistent with our goal that students who complete Science One should be able to do well in higher-level mainstream mathematics courses. The data show this to be the case (Dryden et al. 2011; Dryden and Mac Lean 2004; Dryden and Mac Lean 2008).

We break from traditional first-year pedagogy by teaching mathematical modeling in Science One. Our goal is to help students develop mathematical modeling skills, including learning to see mathematical concepts in nature, learning to work with ready-made models, learning to modify a given model to better capture actual features of a real-world system, and learning to create and analyze their own models.

Our experience is that, over the course of a year, first-year students are capable of incredible growth as modelers. There are some key factors that contribute to their growth.

1. The best examples connect to real problems in biology. Students know when they are presented with a contrived example designed to teach them a bit of mathematics, and often this approach will cause them to disengage. One of our most successful units is on modeling aspects of HIV/AIDS. Students engage enthusiastically and deeply in this unit because HIV/AIDS is a serious issue that they wish to understand. Many of the models they construct are at the edge of current understanding (e.g., modeling HIV transmission dynamics on social networks represented by graphs). It is a powerful experience for them to learn that, even as first-year students, they are close to much of the mathematics they would need to work on such problems at a research level.

2. Embrace your own ignorance. Students learn a lot by seeing how mathematicians use their mathematical viewpoints to build understanding of biological systems, or by seeing biologists use their biological intuition to work through analyzing a mathematical model. Students fear their own ignorance, and work to hide it: In their past experiences, they have been penalized for being wrong. They need to learn that it is ignorance that drives curiosity and leads to discovery. Do not underestimate the value of the instructor as a role model in this. (I frequently declare my incompetence in biology to the class.)

3. Recognize that learning to become a mathematical modeler takes time. Deliberately design a progression of experiences that help students build skills over time, and be explicit in showing them how to use prior experiences to learn new tools or to build new models.

4. Be in control. Understand your expected learning outcomes for each modeling exercise and have a clear plan in mind as to how the students will achieve them. This does not mean that you should not try new teaching ideas, nor does it mean that you will avoid disasters (even the best teachers can get caught by a pedagogic problem they did not anticipate—this is part of what makes teaching exciting!). It is easy to be enamored by a bit of mathematical biology and to forget that it must be made approachable by novices.

5. Believe in your students. Even if students do not become mathematicians, they gain a lot from learning how to communicate using mathematics. Many biology professors at UBC talk about former Science One students in their upper-year courses who would spontaneously present mathematical models on examinations, even though no real mathematics had been taught in the course. Many Science One students, including those who had been judged as weak in mathematics, have gone on to do significant mathematical modeling in their life sciences graduate degrees, thus demonstrating that we are accomplishing our goal of having students reach beyond their own specializations when they solve real problems.

   These factors have been identified through the experiences of the team teaching Science One. In some cases, they arose out of challenges faced by instructors in the face of their preconceived notions of the students and of teaching and learning. For example, the process of learning to understand the nature of even the simplest differential equation takes students much longer than most faculty members anticipated when they started teaching. The logistic equation, which seems easy to us, takes even the top students a long time to appreciate to the point where they can use it to tell scientific stories. At the outset, most of the faculty members believed the main barrier to understanding differential equations was student effort. Once instructors had seen the learning cycle in detail, they understood that there are cognitive processes that dominate what happens when students struggle to learn new ideas. The intensity (depth and frequency) of faculty-student interactions that happens in Science One gives the faculty opportunities to gain insight into student learning as it is happening. This does not happen in most standard courses. These interactions allow more insight into learning and reshape our understanding of the interplay between the roles of instructor and student.

14.4.2   Building Institutional Support

One of the questions we are often asked by people is, "How do you convince your administrators to support you?" Usually, what they mean is, "How do you pay for this?"

   At UBC, the cost-per-student of the Science One Program is between 1.5 and 2 times the average cost-per-student for a first-year student taking mainstream courses. The main component of this cost difference is faculty time. We have a small student-to-instructor ratio, and the interactions between faculty members necessary to prepare interdisciplinary classes are time-intensive, meaning that Science One has been the full teaching load for each instructor. (Starting in 2008, we implemented a model of shared teaching between two instructors per discipline that improved the cost ratio and also makes it more attractive for early-career faculty to participate.) The "on stage" time is roughly equivalent to one course per semester, and a typical teaching load is 1.5 courses per semester. The additional time is spent preparing classes and materials, and attending classes taught by others. There is a large gain to be made from the spontaneous interactions that happen because of this high level of faculty participation. Space commitments, support staff salaries, and a small operational budget add to the cost. It is important to be able to justify the higher cost of such a program to the university community, not just to the administration, since the view will be that these resources could be used to support and improve existing programs.

   It is critical to develop sustainable courses and programs. I am encouraged by the large number of initiatives to develop courses that integrate mathematics and biology at a wide range of colleges and universities. Often, the development of these courses and programs is funded by the National Science Foundation or private foundations. While much of the focus is naturally on curriculum development and its implementation, it is equally important to engage administrators in substantial ways from the beginning; ultimately they will be the ones who will decide on the future institutional funding for any project once the initial grant runs out.

14.5 Suggestions

A complete discussion of the implementation of Science One, including the many early administrative and pedagogic challenges, can be found in (Benbasat and Gass 2002). Some of the key ideas that contributed to our success are as follows:

1. We treated Science One as an educational experiment and received a five-year funding commitment from the Dean of Science, the final two years of funding contingent on a favorable interim review at the end of the first three years. Our Dean was willing to make this commitment because he was interested in interdisciplinary education, he felt in control of the expectations for our project, and he trusted that we were open to a serious evaluation of our efforts.

2. We engaged our colleagues one-on-one in our departments to keep them up to date on our work. The initial responses to Science One ranged from supportive, to skeptical, to hostile, and we knew that ultimately we would have to convince the participating departments to support the program in the long term. We hid from no one, taking any opportunity to talk about our work, even if the result was an agreement to disagree.

3. Our success is judged on how our students perform as they progress through their degrees. Some departments looked at the marks of Science One students in later courses for several years and were pleased with the results. We do detailed analyses of some key courses for our regularly scheduled program reviews. Ultimately, mathematicians and scientists like numbers, as do administrators, so it is helpful to spend some time considering what data would be useful in assessing whether or not the program is accomplishing its goals.

4. We recognize, and defend, the idea that some important data that can be used to analyze our successes and failures is not quantitative. Perhaps the most influential data that marked us as successful were the behavioral changes in our students that showed up in later courses: They spoke up more in class discussions than their peers, life sciences majors among them took more quantitative courses than usual, and a large number of our colleagues started recruiting them to work in their labs and on other research. These recruits included many students who had average looking transcripts.

5. Our views on teaching are challenged continually. All of the team members who teach in Science One are well-respected teachers. Because we interact with students so directly and so regularly, we quickly see when we succeed and when we fail, and all of us have been surprised and had some of our beliefs challenged. This happens also when we interact with our teaching teammates through our teaching.

6. Team meetings are important. We meet weekly as a team. Each week we set a schedule, which varies to accommodate our goals for that week. We discuss at a deep level what we hope to accomplish the next week, and how we might do it. We also discuss our students. These meetings are fun and often described as important to faculty development.

7. We export what we learn. Faculty members return to their departments after teaching Science One and bring a renewed sense of commitment to teaching. Standard courses in all participating departments have changed over the years in response to the lessons learned in Science One. As well, UBC has seen the growth of many exciting courses and programs inspired by the Science One model. This demonstrates how committed our university community is to creating new learning opportunities, and that our administration views such activities as valuable, and hence worth funding. Fortunately, this commitment goes beyond high-profile projects to the heart of our teaching mission.

14.6 Conclusion

Perhaps the main lesson we have learned over the past seventeen years is that it is possible to harness the energy and enthusiasm of faculty, students, and administrators to implement new teaching ideas. Given how much interest there is in increasing the mathematical expertise of future biologists, it is an exciting time to be building new courses and programs that integrate mathematical biology into the early undergraduate experience for life sciences majors. Perhaps Science One is simply an example to say that it can be done.

References

Benbasat, J. A. and C. L. Gass, 2002: Reflections on Integration, Interaction, and Community: the Science One Program and Beyond. *Conservation Ecology* 5(2), 26.

Bialek, William and David Botstein, 2004: Introductory Science and Mathematics Education for 21st-Century Biologists. *Science*, 303 (5659), 788–790.

Dryden, Neil and Mark Mac Lean, 2004: Academic Performance of Former Science One students. [Available online at http://www.scienceone.ubc.ca/grad_performance.pdf.]

Dryden, Neil, Celeste Leander, Domingo Louis-Martinez, Hiroko Nakahara, Mark Mac Lean, and Chris Waltham, 2012: Are We Doing Any Good? A Value-added Analysis of the UBC's Science One Program. *Canadian Journal for the Scholarship of Teaching and Learning,* 3(2).

Dryden, Neil and Mark Mac Lean, 2008: *Quantitative Assessment of Student Performance without Control Groups: A Case Study*. UBCV Internal Report.

National Research Council (NRC) of the National Academies, Committee on Undergraduate Biology Education to Prepare Research Scientists for the 21st Century, 2003: *BIO 2010: Transforming Undergraduate Education for Future Research Biologists.* National Academies Press.

Wieman, Carl and Walter Sudmant, 2008: Quality of UBC students relative to other BC and major US Universities. [Available online at http://www.cwsei.ubc.ca/resources/files/selectivity_report.pdf.]

15

Planning for the Long Term

Meredith Greer[1]
Department of Mathematics, Bates College

Name of Institution	Bates College
Size	about 1750 students
Institution Type	small 4-year private college
Student Demographic	students elect this course for their math major or minor, biology major, or Gen Ed quantitative requirement
Department Structure	Mathematics and Biology are individual departments in the College

Abstract

Bates College offered its first mathematical biology course in 1995. Over time, the student population and involvement of faculty have changed. Our recent redesign process yields suggestions for any mathematical biology course in its early years. We share those suggestions with you in this essay.

15.1   Course Structure

- Weeks per term: 12-week semester
- Classes per week/type/length: Three 55-minute or two 80-minute lecture periods each week
- Average class size: 25–30 students in one section
- Enrollment requirements: There is a Calculus 1 prerequisite
- Faculty/dept per class, TAs: One mathematics instructor
- Next course: None !!

---

[1] mgreer@bates.edu

15.2   Introduction

Many mathematics faculty members are extremely enthusiastic these days. We are working together with our colleagues in biology, and perhaps other sciences, to create and teach new mathematical biology courses. What will result from our efforts after five years go by? Ten? More? Will our mathematical biology courses remain vital, current, cross-disciplinary, engaging? Many aspects of these courses, given careful attention from the start, can help us attain long-lived, healthy mathematical biology courses that are still going strong many years from now.

Bates College offered its first Mathematical Models in Biology (MMB) course in early 1995. It changed significantly over the years, and our most recent process for updating it sheds light on long-term issues facing mathematical biology courses.

Bates is a liberal arts college in Maine with an enrollment of about 1750 students. General education requirements in 1995 included a quantitative course and three courses in the natural sciences. MMB satisfied both these requirements, along with serving as an elective for the biology major and for the mathematics minor. Many students at Bates aim to graduate with as many credentials as possible, whether multiple majors, several minors, or unusual student research experiences with Bates faculty. To best achieve their many goals, students seek the most efficient way to satisfy their general education requirements. When they can complete several requirements with a single course, they sometimes jump in, regardless of their interest in the course and their own background. MMB was offered as an introductory-level course, with no prerequisite, only a suggestion that students take some other biology course first. Therefore a single class could mix students having an astounding, and daunting, mix of backgrounds.

MMB began as a cross-disciplinary project, engaging both the Mathematics and Biology Departments, equally and actively. Over the years, mathematics faculty became the exclusive teachers of the course, and the Biology Department's connection lessened correspondingly. The biology topics in the course were not updated as often or as thoroughly as they might have been. Biology students, deciding which courses to take, received less and less advice regarding MMB.

As a result, Bates decided to restructure, even recreate, MMB. We know what pitfalls came about last time, and we have plans in mind to keep them from recurring. By sharing our past and present experiences with our readers, we hope to share ideas for keeping mathematical biology courses robust for a very long time.

15.3   Description

The story began in 1993. A biology professor and two mathematics professors began to talk about incorporating more mathematics into an introductory biology course. They wrote, and were awarded, an NSF grant to do that. Students in the biology class were eager, embracing mathematics in the context of their biology labs. As a result, the three professors wrote a proposal to develop a biomathematics course.

The proposal went to the Howard Hughes Medical Institute grant at Bates, an ideal source for funding this sort of curriculum development project. During the review process, the group of professors associated with the project changed. The new group had four professors, with only one from the original group. The biologist was replaced with two different biologists; one mathematician remained, and a statistician joined. This group met regularly during Winter 1994. They continued through the summer, joined by two students they had hired. Those students stayed on as teaching assistants the first time the new course was taught, Winter 1995. (Bates, located in Maine, has a winter semester rather than a spring semester.)

During the planning process, the group discussed and debated the central focus of the course. It would have been easy to view mathematics as a toolbox for biology. Instead, the group opted to give center stage to both mathematics and biology. To that end, they created a course on mathematical models of biological processes. Creating, analyzing, and visualizing models, along with data collection, gave many opportunities for studying mathematics and statistics. Mathematical topics included linear and nonlinear population modeling, Markov and Leslie models, matrices, eigenvalues, and eigenvectors, among others. At the same time, a variety of biological concepts played a part. These included predator-prey systems, models for immune systems, molecular evolution, and phylogenetic trees.

Besides specific topics, computer use, typically Minitab and MATLAB, was a focus. Furthermore, the earliest iterations of the course emphasized service learning. Students went into nearby hospitals in small groups. They worked with administrators and analyzed data using techniques they had learned in the class. They experienced firsthand the connections between classroom learning and its applicability in the community.

Since 1995, MMB has undergone several changes. Originally there was a heavy emphasis on statistics, but this was reduced to allow time for extended service learning projects, or for other topics. The course began with professor-created modules in Minitab and MATLAB; over time, new software updates mandated module updates, and students were hired to create new modules during the summer.

The bigger issue was student change. In its first few offerings, the course drew eight to twelve students. In later offerings, class sizes ranged from twenty-four to thirty. It is hard enough to arrange service learning opportunities for eight to twelve students, and more so for much larger class sizes. As a result, service learning has not been part of the course in recent years.

The student profile for the course has also changed. Originally, students were biology majors with an interest in mathematics, or vice versa. MMB is cross-listed, counting for both mathematics and biology credit. Since each department had several faculty members very involved with the course, each department regularly advised students to take it, and faculty members in each department knew a lot about the course and could answer questions about it. As time went by, biology faculty members had less connection to the course and less ability to advise their students to take it. In recent years, biology students have rarely been advised to take the course, and the biology faculty members have known very little about how the course is run. In fact, all three biology faculty members who were once involved have now retired or moved on to other jobs. No one remains in biology who was directly connected with the original MMB.

This course was designated from the start to fulfill multiple general education requirements. At the time, this made sense because mathematical biology was largely unheard of, and students were more likely to take the course having the extra encouragement of satisfying some of their requirements. Over the years, however, students with no interest in the subject began taking the course merely to satisfy multiple requirements. Some of them had such minimal mathematical background that they could not keep up with the most basic algebra steps; they did not mesh well with senior mathematics and physics majors. Other students proudly stated that they neither knew nor cared about mathematical biology, and were taking this course only because it satisfied multiple general education requirements. For these reasons and more, it became difficult to lead classes that were appropriate for all, or even most, of the students.

15.4 Discussion

One goal of the original MMB was accessibility to all. For that reason, the course had no prerequisites. Since then, increased pre-college access to calculus courses has meant that the vast majority of Bates students arrive with some prior exposure to calculus. We thus felt confident requiring a Calculus 1 prerequisite for MMB. We also gave MMB a 200-level course number instead of a 100-level number. The changes allow us to include a wider range of mathematics in the course while suggesting to registering students that they will need to remember their earlier mathematics classes in order to succeed in this course.

We also knew to think carefully about general education requirements. As it happens, Bates changed them starting with students entering the college in 2007. That made this an ideal time to change the set of requirements satisfied by MMB. Our new system prescribes different rules for "double-dipping" (or "triple-dipping")—satisfying two (or three) requirements with a single course. In the new system, we can still designate MMB as counting toward multiple requirements. However, students can no longer use it to fulfill all the requirements it theoretically can satisfy. So, for example, students must decide whether this will count as their scientific reasoning credit or their quantitative literacy credit. Our vision was that this would keep the course appeal broad without drawing undue numbers of students who claim to have no interest in either mathematics or biology. The course is currently being offered for the second time in its new incarnation, and both times, there has been a pleasant mix of students with majors across the sciences. Almost all appear very interested in mathematical biology.

Meanwhile, we have re-devoted ourselves to making sure that MMB deserves its cross-listing in the mathematics and biology departments. We have had several discussions with biology faculty members on this. Our goal was to tie the newly-designed MMB to examples from the introductory biology course offered each year at Bates and to examples from upper-level biology courses. The connections serve many purposes: we can use MMB to advertise subsequent biology and mathematics courses, advising students that the topics are covered in greater depth in later courses. Team-teaching is not a possibility right away, with MMB continuing to be taught mainly by the mathematics department,

but the new structure makes it easier for biology faculty to speak in MMB as guests. Some of our examples tie in to the expertise of Bates biologists, students benefit from the expertise of many faculty members, and our department connections continue to grow. Furthermore, both departments will feel secure in counting MMB toward their major.

We have retained many of the central mathematical and biological topics from earlier incarnations of MMB, yet left room for individual instructor preferences and unique opportunities to invite guest speakers. Our course now centers mathematically on population models using difference equations, differential equations, matrices, eigenvalues and eigenvectors, and Markov approaches. Biologically, we focus on single-species population growth, multiple-species interactions, and epidemiological models. Optional topics include phylogenetic trees, vaccination theory, game theory, spatially distributed phenomena, and cellular automata. Additional topics may be generated by student projects that help us to address specific student interests that may have been the main reason a student registered for this class. Regardless of their origin, the class examines all topics from the viewpoints of biological reasoning, mathematical theory, and computer simulation of model outcomes.

In the long term, we will maintain our mathematics-biology connections and nurture new connections over time. We need ways of staying in contact, staying current with each other's research, and meeting new and visiting faculty members as they arrive. This is not always easy, we admit, but we have already implemented several strategies:

- I began auditing biology courses, and faculty from other Natural Sciences departments have audited all or part of the new MMB. Besides gaining a glimpse into each others' courses by doing this, we discover opportunities for working together in the future.

- We held several joint meetings of a mathematics course (Differential Equations) and a biology course (Epidemiology) after the outbreak of H1N1 at Bates in Fall 2009. The students and faculty members involved had to explain their approaches to each other and combine areas of expertise to better track the timing and reasons for the outbreak. The project strengthened faculty collaboration and introduced a wider range of students to the possibilities of mathematical biology, which helped us to advertise future offerings of MMB. We plan more collaborations of this type for future semesters.

- The departments in the Natural Sciences and Mathematics Division at Bates have held several joint meetings to discuss curricular issues affecting students at all levels. These meetings initially felt like introductions of each department to the others. Now, however, they function as an ongoing conversation among the departments as entities, and among the faculty members making up the departments. We all know much more about what is happening in each others' courses, and we continually seek to further connect our courses. We plan to continue these meetings.

Despite the increase in cross-departmental collaborations, we have only a small number of faculty members even potentially involved in mathematical biology. With so few people, it has been hard to create consistent mathematical biology programming. To address this, Bates teamed up with two nearby small colleges, Bowdoin and Colby, for a series of mathematical biology events in the 2007–2008 academic year. We held a mathematical biology seminar series, funded by a grant from the Mellon Collaborative. Faculty from each of the colleges spoke, typically at a college other than their home institution, about their research in mathematics or biology. Talks did not need to be cross-disciplinary: the goal was to share our research with a general faculty audience. Seminars were preceded by refreshments and followed by a social hour or dinner, giving us all a chance to talk about our work. The overwhelming response to this was that we finally had a critical mass: many faculty members at each of the colleges, and in several departments at each college, had interests in mathematical biology, and the seminar series provided a way and a reason to communicate regularly.

In the few years since, the speaker series coordinators from each of Bates, Bowdoin, and Colby have maintained contact, letting each other know about mathematical biology events at their own colleges and discussing future collaborations on research or grant proposals. We all work, as always, to further the mathematical biology connections within our own colleges, yet having this larger pool of people to work with adds even more opportunity.

15.5   Suggestions

All in all, we now have the benefit of experience on our side. We have concrete approaches regarding prerequisites, satisfying requirements, and long-term viability of a course requiring input from many faculty with many areas of expertise.

To summarize some specific plans:

1. Use prerequisites, or other institutional structures, to allow an appropriate class mix (years, abilities, etc.) while keeping the course available to the students you hope will take it.

2. Think from the start about building, and maintaining, connections with faculty and courses across disciplines. Team-teaching and guest lectures are ideal if you can arrange them. Overlapping topics between biology and mathematics courses are additional ways to promote the interrelatedness of these fields.

3. Seek out ways to enlarge, engage, and sustain your bio/math community. This may mean connecting with nearby colleges, arranging interdisciplinary seminars within your own institution, seeking partnerships with nearby industries, or any other activities that work best at your own institution.

We wish much luck—and creativity!—for those involved with mathematical biology courses.

References

Bates College, cited 2010: about Bates. [Available online at http://www.bates.edu/about/.]

Bates College, cited 2010: general education requirements at Bates. [Available online at http://www.bates.edu/dof/general-education/the-requirements/.]

Harder, M. H., 1996: Mathematical Models and Statistics in Biology, a Noncalculus Based Course. *Proceedings of the Section on Statistical Education*, Alexandria, VA, American Statistical Association.

16

Some Lessons form Fifteen Years of Educational Initiatives at the Interface between Mathematics and Biology: The Entry-Level Course

Louis J. Gross[1]

Departments of Ecology and Evolutionary Biology and Mathematics,
University of Tennessee-Knoxville

Name of Institution	University of Tennessee, Knoxville
Size	About 28,000 students
Institution Type	Large comprehensive state university
Student Demographic	One of two possible mathematics sequences for biology majors, and required for some agriculture majors
Department Structure	Sequence is based in the Mathematics Department but is sometimes taught by faculty and students based in the Division of Biology

Abstract

In 1992, I led a workshop devoted to undergraduate quantitative education for life science students. One outcome was a suggested set of topics for the entry-level mathematics course for life science undergraduates. With NSF support, I developed a two-semester course that followed this recommended topic coverage and represented a considerable departure from the emphasis on calculus that was (and is) prevalent for undergraduates in the sciences. This two-semester course sequence involves an hypothesis testing and data-rich view of mathematics, includes computer-based projects, and has been taught by instructors with widely varying backgrounds and levels of biological expertise over

---
[1] gross@NIMBioS.org

the past eighteen years. It is the main mathematics sequence for biological science undergraduates at UTK, with approximately 300 students enrolled each semester, and was included as one of the case studies in the National Research Council's Bio2010 report. I discuss the goals of the course (a focus on conceptual development rather than on skills), provide details on the topic coverage and student assessment methods, note how the course sequence has changed since it was initiated, and discuss the challenges arising from the diversity of backgrounds of instructors.

16.1   Course Structure

- Weeks per term: 15-week semester
- Classes per week/type/length: two 50-minute periods and one 75-minute lab
- Labs per week/length: one 75-minute lab/recitation
- Average class size: 150 students with 35–40 students per section
- Enrollment requirements: Placement exam evaluation based upon high school algebra and trigonometry.
- Faculty/dept per class, TAs: One math/biology faculty member with several TAs teaching the labs/recitations.
- Next course: Calculus-based statistics or Models in Biology.
- Website: http://www.tiem.utk.edu/~gross/math151.html

16.2   Background

The history of courses in mathematics in the U.S. designed specifically for undergraduate students with interests in the biological sciences dates back at least to the early 1970s with the text by Batschelet (1971). A number of texts and courses appeared in this period, with the majority emphasizing elementary calculus and its prerequisites (Arya and Lardner 1979, Cullen 1983, DeSapio 1977, Gentry 1978, Levin 1975). Many courses had disappeared by the early 1990s, with those remaining mainly at institutions with research emphases in mathematical biology. In 1991, I began a project funded by the National Science Foundation, with a goal of developing a quantitative curriculum for life science students. The initial focus was on entry-level mathematics courses and started with a survey of quantitative course requirements for life science students at U.S. universities. The results indicated that about 80% of institutions had some calculus requirements, while the others required only pre-calculus or had no explicit requirement.

In 1992, I convened a workshop, attended by many leading mathematical and quantitative biologists with interests in undergraduate education, to discuss all aspects of undergraduate mathematics preparation for life science students. Among the recommendations from the workshop was a strong suggestion that students are not well served by being exposed only to a calculus course, because a broader array of quantitative concepts were necessary for students to be successful in careers in modern biology. At UTK we had been teaching an elementary calculus for life sciences course since the late 1970s. As an outcome of this workshop, I revised the course to incorporate a more diverse set of topics and moved the focus towards conceptual understanding and away from hand calculations based upon standard calculus rules.

16.3   Structure of the Entry-Level Course

The 1992 workshop provided specific suggestions on topic coverage for an entry-level course, including the addition of descriptive statistics, matrix algebra, discrete probability, and difference equations. Additional suggestions included ensuring that the calculus portion included an introduction to differential equations and incorporated the notions of equilibria and stability. Many additional suggestions were provided to incorporate specific biological concepts as part of this course, with the objective being to encourage problem-based learning. The full workshop report (Gross 1992) also provided suggestions for upper division courses and methods to link the mathematical and biological portions of the curriculum.

Based on the recommendations of the workshop, I implemented a pilot version of the course in place of the two-semester, 3-credit hour course we had been teaching at UTK. There had been concern expressed at the workshop that it would be extremely difficult to squeeze in all the suggested material into two 4-credit courses, let alone 3-credit

ones. Our experiences over the fifteen years that this course sequence has been offered it that is possible. The pilot course followed closely the suggestions of the workshop, which had focused mostly on specific mathematical topics. Over the next several years, I developed a set of concepts, rather than explicit mathematical methods, that served as a focus for much of the material included in the course sequence. These have been expanded upon elsewhere (NRC 2003), so I will simply list them here:

- Rate of Change
- Scale
- Equilibria
- Stability
- Structure
- Interactions
- Stochasticity
- Visualization

The mathematics needed to formalize these concepts provided the motivation for the revisions to the entry-level course that have occurred since the pilot version was offered. The first semester of the course covers discrete mathematics topics through limits of sequences, and the second semester covers the calculus up to first order linear and simple non-linear differential equations.

The goals of the current course are to

1. Develop the ability to analyze problems quantitatively that arise in the biological areas of interest to the students.
2. Illustrate the utility of mathematical models to provide answers to biological problems.
3. Develop appreciation of the diversity of mathematical approaches useful in the life sciences.
4. Provide experience using computer software to analyze data, investigate mathematical models, and provide some exposure to programming.

The course methods to meet these goals include

1. Encouraging hypothesis formulation and testing for both the biological and mathematical topics covered.
2. Encouraging investigation of real-world biological problems through the use of data in class, for homework, and in examinations.
3. Reducing rote memorization of mathematical formulas and rules through the use of software such as MATLAB and Maple.
4. Providing biological motivation for each main mathematical component of the course through a central example that is returned to regularly.

I will here give a brief example of each of these methods. For hypothesis formulation, the first course begins with each class section going to the field in groups of three students to measure leaf lengths and widths (we do not provide details as to how to do this, but leave it up to each group) and to make a hypothesis concerning the relationships between the variables they are measuring. The class then goes to a computer lab, where we provide an introduction to basic MATLAB commands, have the groups enter data, and produce histograms and scatter plots to evaluate their hypotheses. This requires a complete lab session (1 1/4 hours) but serves an essential purpose by pointing out that mathematics connects to data, that hypothesis evaluation is part of science, and that mathematics can assist in the scientific process.

For real-world biology, the class is presented with a recently published paper (typically from *Science*, *Nature*, or *Proceedings of the National Academy of Sciences*) that includes mathematics related to the topic of the day. Although few of the students are capable of reading the paper in detail, they point out the importance of mathematical ideas in biological research, and some of the data are used directly to motivate the mathematics as well as appearing on tests and quizzes in the course. The course web page includes links to the papers and a brief summary I compose that discusses the results and how they relate to the course topics.

On the use of software, there are several objectives beyond reducing the need for hand calculation. One is the ability to include much larger data sets or deal with much more complex (and realistic) projects than could be included otherwise. For example, one project asks students to make a hypothesis about whether their height changes overnight, which the class evaluates by collecting data on themselves for several nights. The data are then combined and analyzed using MATLAB to illustrate histograms and regressions, point out the importance of looking carefully at data for bad values (e.g., data which imply a student gained 10 cm in height overnight!), and to discuss the obligation to deal carefully with human data (through discussion of the Institutional Review Boards that oversee human data collection at every institution). We have chosen to use MATLAB as the software for the initial portion of the course (we move to Maple for much of the calculus portion) because it introduces students to basic coding and logic and the idea of an algorithm.

For the matrix algebra section students are shown images of landscapes, asked how to characterize them, and asked to develop hypotheses about how they might change as the images are retaken over several decades. This leads naturally to the use of vectors to characterize the distribution of states across the landscape and provides an introduction to ecological succession, which is typically familiar to students. It serves to motivate students to develop the notion of a Markov chain, which they can readily do themselves, though not with any detail on how the mathematics might work. The concept of an eigenvector as the long-term fraction of the landscape in each state (such as urban, forest, or agricultural) then arises naturally and the notion of stability is readily motivated through consideration of different initial landscape state distributions.

16.4   Student Assessment

Over time we have developed three major and one minor assessment method to evaluate student performance in the course sequence. There is a formal set of written exams covering the basic concepts and a comprehensive final exam that account for 60% of the course grade. The exams often include examples taken from data or research papers discussed in class. Students are encouraged to use standard calculators as they wish in the exams, though we do not emphasize their use in the course assignments. The exams are structured and evaluated, however, so that the use of a calculator is not necessary–the focus is on basic concepts and calculations or graphs that can be done readily by hand. Students find calculators helpful if their arithmetic skills are weak (and our focus in the sequence is not at all on arithmetic skills).

The course includes a set of weekly quizzes that cover the material assigned for homework (which we do not collect or grade). The quizzes are supplemented currently by a required solution at the board of a homework problem that counts as an additional quiz. These count for 20% of the course grade. Finally, we have a set of computer-based projects. Some require students to collect their own data, but most involve writing a formal laboratory report on a set of simulation experiments carried out using MATLAB or Maple. Sometimes we supply the code and the students modify it in a few places, and sometimes the students must develop their own code. The more complex of the projects are essentially research-level (such as the impact of random environmental variation on the dynamics and long-term structure of matrix population models), the motivation for which is readily understood by the students, although carrying out a full analysis would require extensive graduate-level mathematics. A collection of material, including syllabi, exams, basic lecture notes, and descriptions of the scientific journal publications used as examples, is available at the project website.

16.5   Challenges

Since its development in 1993, the sequence has been taught by approximately eighty different people. Most teachers have been from the Mathematics Department, faculty as well as part-time instructors and graduate students, while some have been from the Biology Department. The majority have had some exposure to mathematical biology (through our long-standing graduate education programs in this field) but quite a few have not. This has created challenges because there is less emphasis on the biological aspects of the course when taught by someone with little biological background. To deal with this we have developed a course supplement and instructors guide to provide motivating examples for the course. Additional lecture notes that develop the biological connections for the course and provide the various links to and explanations of research papers used to motivate sections of the course are provided on the

course web site. To assist biologically naïve instructors, modules were developed to motivate many of the concepts in a general biology course through a connection with mathematics (Harrell et al. 2002).

The first course in the sequence is the most difficult to teach for those with little biological background (the second course focuses on calculus). It has been taught recently to about 200 students in a lecture that meets twice weekly and breaks into smaller sections for a once-a-week lab. Instructors have included other faculty members and graduate students with an extensive mathematical biology background. The large-lecture, small-lab section format has allowed only limited small-group discussion except in the weekly lab sessions. With only two meetings a week in lecture, topic coverage proceeds at a much more rapid pace than might be preferable.

An additional challenge has been the lack of an appropriate text for the sequence. Until recently we used one of the older texts (Cullen 1983) supplemented by notes and on-line materials. Although several new texts have appeared, they have a different topic coverage (often too extensive for this course) and have little emphasis on data and its relation to course topics. Thus we have developed a new text, used it for two years, and expect publication in 2014 (Bodine et al., submitted).

16.6   Lessons and Suggestions

In many ways the course is substantially more challenging, both for the students and the instructors, than the standard science and engineering calculus sequence or the standard two-semester calculus for business and social science students. It covers a vast array of topics very quickly, and students who are not well-prepared find it quite difficult. However, they represent a majority of the students majoring in pre-health sciences and are extremely motivated, realize the importance of working hard in order to be accepted by various professional schools, and often appreciate the connection between this course and their other biology courses. The class typically includes students with varying levels of biological experience (some of them delay taking the course until much later in the undergraduate program than we prefer). I view this as beneficial because they can point out to their peers how the topics relate to those covered in more advanced biology courses. An example is the Hardy-Weinberg equilibrium that students see in their general genetics course, but which we derive mathematically.

Despite the fact that students taking this course have had a pre-calculus background (mostly in high school) and have taken a mathematical skills placement exam to be recommended for the course, their comprehension of some pre-calculus concepts is weak. So, we start with descriptive statistics, including semi-log and log-log graphs, with application to biological growth and decay processes and allometry. This refreshes students understanding of exponentials and logarithms, motivated through biological observations, and introduces new scaling concepts. Providing a new perspective, based upon observations, of a topic that many students did not grasp completely may let students develop an understanding of non-linear scaling and why logarithms appear so often in biology.

Few students enter the course with any understanding of programming or the logic that underlies computer coding. It requires considerable effort on their part to follow basic MATLAB codes given them, and they have great difficulty developing their own programs. Initially, we gave students much of the MATLAB codes required for the course, but we have since reassessed the situation and now require the students to develop their own codes for at least the simpler computer projects. Otherwise we found that students had little understanding of the steps in the code. We include basic guides to MATLAB commands associated with each project.

16.7   Conclusion

We have had no way to assess the course's impact. Well over two thousand students have taken the courses over the past fifteen years, but we have not tracked students to compare them with those who take the standard science and engineering calculus sequence. Students complete evaluations but none have been compiled to allow for comparisons either across time or between students in different courses. Those beginning to teach such a course should design assessments, find funding to implement it over a number of years, and track student success and behavior. Student information systems are now commonly available that would allow a comparison of subsequent undergraduate success between students following a different mathematics course sequence and those in a sequence such as the one described here. At this point, all I can point to is anecdotal information, including one student who told me that he was instructed

by his doctor to take the course, as it had been beneficial in their own medical career. As gratifying as this is, we need to do better in assessing the impact of courses that fall at the interface between mathematics and biology.

References

Arya, J. C., and R. W. Lardner, 1979: *Mathematics for the Biological Sciences.* Prentice-Hall, 712 pp.

Batschelet, E., 1971: *Introduction to Mathematics for Life Sciences.* Springer-Verlag, 643 pp.

Bodine, E., S. Lenhart, and L. Gross, (submitted): *Mathematics for the Life Sciences*. Princeton University Press.

Cullen, M. R., 1983: *Mathematics for the Biosciences*. PWS, 751 pp.

DeSapio, R., 1977: *Calculus for the Life Sciences.* Freeman, 739 pp.

Gentry, R. D., 1978: *Introduction to Calculus for the Biological and Health Sciences.* Addison-Wesley, 686 pp.

Gross, L. J., cited 2010: Summary Report 1992: Workshop on a Quantitative Sciences Curriculum for Life Science Students. [Available online at http://www.tiem.utk.edu/~gross/WorkshopReport92.txt.]

Harrell, S., M. Beals, and L. J. Gross, cited 2010: General Biology Modules (2002). [Available online at http://www.tiem.utk.edu/~gross/bioed/modulelist.html.]

Levin, S. A., 1975: *Mathematics for the Biological Sciences.* Cornell University, 654 pp.

National Research Council, 2003: *BIO2010: Transforming Undergraduate Education for Future Research Biologists*. National Academies Press, 192 pp.

17

A "Wet-Lab" Calculus for the Life Sciences†

James L. Cornette[1], Gail B. Johnston
Department of Mathematics, Iowa State University

Ralph A. Ackerman
Department of Ecology, Evolution and Organismal Biology, Iowa State University

Brin A. Keller
Department of Mathematics, Michigan State University

Name of Institution	Iowa State University
Size	31,000 students (25,500 undergraduate and 5500 graduate)
Institution Type	Land grant university, comprehensive undergraduate and graduate programs
Student Demographic	Freshman and sophomore life sciences majors take this course or the engineering calculus course
Department Structure	Mathematics and several life sciences departments are in the College of Liberal Arts and Sciences

Abstract

In 1994, faculty at Iowa State University introduced a calculus and differential equations course for life sciences students, the unique characteristic of which was an associated wet-lab laboratory. The students gathered data from living systems and simulations of living systems, which they analyzed using difference equations, differential equations, derivatives, or integrals. Here we describe steps that we took to introduce and develop a two-semester calculus and difference and differential equations course for biology students, and we discuss the value of biological data in such courses. We also discuss the change in course format to large lecture and no laboratory as faculty who introduced the course left the university and extreme financial restrictions were placed on universities during the first decade of the 21st century.

---

[1] cornette@iastate.edu

17.1   Course Structure

- Weeks per term: Two 15-week semesters
- Classes per week/type/length: Four 50-minute lectures per week
- Labs per week/length: Seven 2-hour laboratories per semester
- Average class size: 34 students
- Enrollment requirements: Competence in high school algebra, geometry and trigonometry
- Faculty/dept per class, TA's: Mathematics faculty teach the lectures; Biology teaching assistants teach the laboratory with biology faculty supervision
- Next Course: This course and possibly a semester of statistics constitute the mathematics taken by these students
- Website: The textbook for the course is posted on http://cornette.public.iastate.edu/CLS.html
- A black and white print version of the text is now available from CreateSpace, a subsidiary of Amazon

17.2   Introduction

In 1994 conditions were good for introducing a calculus for the life sciences course at Iowa State University, a university of 28,000 students that is very strong in science and technology. Interdisciplinary studies were encouraged, the life sciences faculty were becoming aware of the need for more mathematics, statistics and computer science in their own work and for their students, weekly seminars in computational and mathematical biology had been held for six years, and there were mathematicians who had published in biological journals and a biologist who used mathematics in his research and was auditing mathematics courses. There was strong administrative support and support from the National Science Foundation.

Our job was to develop the content of the course. We began with the (correct) premise that life sciences students would respond well to mathematics that grew out of life science laboratories and data from their literature. There was no lab manual or a text coordinated with laboratories, but we said we would write them. That turned out to be a large task, however, and only in May of 2005 was a text based on the course delivered to a publisher. The text is now posted on the web at http://cornette.public.iastate.edu/CLS.html, and a hard copy is available in two volumes (Cornette and Ackerman, 2011, 2012).

17.3   Discussion

In the first years, the main task was to plan and write material; classes and laboratories were often preceded by a quick trip to the university printing office. Cornette (a mathematician) wrote the text and Ackerman (a biologist) organized the laboratories and wrote lab material. After most of the text had been developed and there were some 150 students, a major impediment was copyright permission to use some of the data from the literature. The most extreme was the cost of $2 per student copy for two figures from *Scientific American*. They are excellent figures but we excluded them.

We began with four one-hour class meetings per week and seven or eight three-hour laboratories per semester. It is difficult to add a laboratory to the schedules of life sciences students, and after two years we moved to a two-hour laboratory, one hour of which replaced one of the four one-hour class meetings. In this arrangement, some bacterial growth laboratories were run in relay. One group of students inoculated a bacterial culture and monitored the first hour of growth and later growth was monitored by other students.

The laboratories illustrated

- exponential and logistic growth of bacteria,
- quadratic growth of mold,
- exponential decay of light intensity with depth in a lake,
- reciprocal of distance squared and reciprocal of distance decrease of light intensity in air,
- one- and two-compartment models of pharmacokinetics,

- Torricelli's quadratic decrease with time of water flow from the bottom of a reservoir,
- speed of falling objects and harmonic oscillations,
- Fick's law used to measure cardiac output
- The approximately cubic decrease in the weight of a melting ice ball,
- Newton's law of cooling,[2]
- solar radiation,
- cooling and dehydration of an egg,
- simulated breaking of whelk by crows,
- cricket chirp rate dependence on temperature,
- air compression in a syringe,
- areas of leaves, and
- butyl chloride decomposition rate.

Light depletion with increasing water depth and simulated breaking of whelk by crows have been described in (Keller 1998) and (Keller and Thompson 1999). These and simulation of cardiac output, are included in the National Council of Teachers of Mathematics website, Illuminations (Keller and Thompson 2012a,b,c).

An enzyme kinetics lab led towards the important Henri-Michaelis-Menton equation, but was sufficiently difficult that we used it only twice. We were not successful in developing a laboratory on diffusion in a medium (diffusion across a membrane is easy) and would welcome suggestions for one.

The students also were assigned six-week projects in which they could either find a data set from their respective majors or select a project from a list that we provided. Many of the students did find data from their own major, and it is not a surprise that their projects were outstanding. Students submitted written reports and presented verbal reports to the class. The final examination included questions related to the projects. As with the lab reports, the projects were done by groups of three students. We had 34–38 students per lecture section and 16 (better) and sometimes 18 students in the laboratory.

The students appreciated and enjoyed the laboratories and ownership of the data. Statistical analysis of messy real life data and the discussion of residuals were important experiences for the students. We tried to find appropriate biological models to use for homework assignments, classroom examples, and exams, but finding them was not easy.

Laboratory reports descriptive of the data and the students' proposed mathematical models of the underlying process served to solidify the students' understanding of the connection between the biology and the mathematics. Students were motivated by the laboratories, and the mathematics was perhaps more easily understood, but the algebraic operations were not easier for them. Group laboratory reports were assigned to keep the evaluation manageable. Many of the reports were well written and reports that were poorly written were returned for improvement.

It is our hypothesis that the goal of calculus in the life sciences is primarily modeling living systems with difference equations and differential equations. Understanding the concepts of derivative and integral is crucial, but the ability to compute many specific derivatives and integrals is not important. The derivative and integral were carefully defined, however, and distinguished from the discrete data of the laboratories. The analysis of calculus thus extends the discrete laboratory observations. The Fundamental Theorem of Calculus was clearly explained analytically, as it did not seem suited for a laboratory exercise.

We also included some not necessarily biological applications of the derivative and integral (max-min, related rates, area, volume, surface area problems). For example,

1. A 2-meter tall vertical fence stands 1 meter away from a 5-meter vertical wall. What is the shortest ladder that will reach across the fence from the ground to the wall and just touch the top of the fence? Assume the ground to be horizontal.
2. Find the centroid of the right circular cone with base radius r and height h.

---

[2] We did not use Torricelli, Fick, and Newton in discussion with the students.

It was correctly argued (Mathematical Biosciences Institute Curriculum Workshop 2007) that Problem 1 is not of much interest to the life sciences students. Few students in any calculus class find the problem entertaining. An alternate, 'What length ladder can be carried horizontally around a 90° turn from a 2 meter wide hallway into a 1 meter wide hallway?' usually is met with slightly greater interest. But both are clearly defined exercises where students identify relevant variables, find relations between them, and obtain a function of a single variable whose extrema give a solution. Until the life sciences provide a rich supply of such problems, we should continue to use the geometry problems that have proved over many years to be useful to students in gaining an understanding of calculus.

After three years, the course had grown to four sections in the fall and two or three in the spring. It was beyond our ability to teach all of the sections, and some faculty and graduate students who were sympathetic, but without biology experience, filled in quite well. We were fortunate to have several laboratory assistants from biology who had taken or were taking serious mathematics. Most of the mathematics faculty and teaching assistants, however, found it very time consuming to grade lab reports and semester projects and to make good use of the laboratory data. It is easier to teach engineering calculus.

Laboratories are an expensive add-on to a mathematics course. The chair of zoology initially arranged with the college dean for funding of laboratory assistants and made available a 16-student laboratory space, and continued support after our NSF grant expired. Some equipment had to be scrounged, but generally the laboratories were well equipped. The students responded well, wrote substantial laboratory reports and grasped the mathematics emerging from the laboratories. The biggest laboratory difficulty was that bacteria do not always grow, even when properly stimulated, so the resulting growth curve may be a horizontal line. Furthermore, the butyl chloride decomposition curve was not the simple exponential decay that is illustrated in the students' chemistry text. The real world does not always conform to our expectations.

The laboratory is not now being offered and the class is taught as lectures to groups of 100 to 120 students. The reasons for discontinuing the laboratories were budget reductions that began in 2001 and the retirement or departure from ISU of mathematics faculty wishing to use them.

It was a useful statement to students that the laboratories were held in the building of a biology department. We have found, however, that the laboratory concept can be used even in mathematics lectures to 100 to 120 students. Some of the laboratories can be performed as demonstrations by the lecturer or a group of two or three students in a mathematics classroom. For example, we measure the temperature of an egg (or a pint of water) as 37° C initially and perhaps 34° C ten minutes later. We ask the students to estimate what the egg temperature will be thirty minutes later. There can be a discussion about how long an egg can safely remain uncovered in a nest during which we hope that a student inquires what the ambient temperature is. Other experiments suitable for large lectures include light decay with depth of water, simulated cardiac output, one- and two-compartment models of pharmacokinetics, water draining from a reservoir, and work done in compressing air.

The project and the participants greatly benefitted from the National Science Foundation Grant number DUE 9354437, for the financial support and especially for the recognition from our university community that it was a worthwhile project.

17.4   Suggestions

A calculus for life sciences course requires life science curricula to expand mathematics requirements from none or only three or four semester credits to eight semester credits, which will displace something else from that curriculum. It also requires an expansion of freshman-level mathematics teaching, not highly valued in faculty evaluations. Nevertheless, an outstanding course can change the way students think about the life sciences. Mathematics departments have an inglorious practice of teaching a one-semester three-credit course about calculus for social sciences and business. We will be failures if that becomes the norm for life science calculus courses.

17.5   Conclusion

The role of data in life science calculus courses is still under debate. At the Mathematical Biosciences Institute Curriculum Workshop (Mathematical Biosciences Institute 2007), one speaker looked for the first occurrence of a data set in most of the current texts. All of them had at least one data set, with the first occurrence ranging from about page

10 to about page 800. Calculus has been taught for many years without reference to data, so why bother? Our answer (though, without hard data) is that students are more apt to be accepting of a course that includes real data and are more apt to use calculus and to incorporate modeling in their subsequent biological studies.

References

Cornette, J. L., and R. A. Ackerman, 2011, *Calculus for the Life Sciences: A Modeling Approach, Volume I, The First Year Course.* Self Published, Available from CreateSpace, http://www.createspace.com/3686251, 592 pp.

Cornette, J. L., and R. A. Ackerman, 2012, *Calculus for the Life Sciences: A Modeling Approach, Volume II, Difference and Differential Equations.* Self Published, Available from CreateSpace, http://www.createspace.com/3680768, 480 pp.

Keller, B. A., 1998: Shedding light on the subject. *Mathematics Teacher* **91**, 756–771.

Keller, B. A., and H. A. Thompson, 1999: Whelk-come to mathematics, *Mathematics Teacher*, **9**, 475–489.

Keller, B. A., and H. A. Thompson, cited in 2012a: *Whelk-Come to Mathematics,* in National Council of Teachers of Mathematics: Illuminations [Available online at http://illuminations.nctm.org//LessonDetail.aspx?id=U143]

Keller, B. A., and H. A. Thompson, cited in 2012b: *Shedding Light on the Subject*, in National Council of Teachers of Mathematics: Illuminations [Available online at http://illuminations.nctm.org//LessonDetail.aspx?id=U137

Keller, B. A., and H. A. Thompson, cited in 2012c: *Cardiac Output, Rates of Change, and Accumulation*, in National Council of Teachers of Mathematics: Illuminations [Available online at http://illuminations.nctm.org/LessonDetail.aspx?ID=U136

Mathematical Biosciences Institute, 2007: Over the Fence—Mathematicians and Biologists Talk About Bridging the Curricular Divide Curriculum Workshop at The Ohio State University.

18

Creating an Interdisciplinary Research Course in Mathematical Biology[†]

Glenn Ledder[1] and Brigitte Tenhumberg
University of Nebraska-Lincoln

Name of Institution	University of Nebraska-Lincoln
Size	about 24,000 students
Institution Type	large state university with PhD program
Student Demographic	recent high school graduates with high potential and interests in mathematics and biology
Department Structure	Mathematics and Biology are individual departments in the College of Arts and Sciences

Abstract

An integrated interdisciplinary research course in biology and mathematics is useful for recruiting students to interdisciplinary research careers, but there are difficulties involved in creating and implementing it. We describe the genesis, objectives, design policies, and structure of the Research Skills in Theoretical Ecology course at the University of Nebraska-Lincoln and discuss the difficulties that can arise in designing and implementing interdisciplinary courses.

18.1   Course Structure

- Weeks per term: 5-week summer session
- Classes per week/type/length: five 1-hour lecture periods each week

---

[1] gledder@math.unl.edu

- Labs per week/length: five 1-hour laboratory periods each week
- Average class size: 8–14 students in one section
- Enrollment requirements: For high school students and university freshmen. Students must apply for the program and get a recommendation from a teacher.
- Faculty/dept per class, TAs: Team-taught by one mathematics instructor and one biology instructor, with the mathematics instructor doing the quantitative portion of the lectures.
- Next course: The purpose of the course is to teach research skills. There are no related courses, but many of the students will do research projects later in their programs. Some students may choose to take additional courses in mathematics and/or biology, including interdisciplinary courses.
- Website: http://www.math.unl.edu/programs/rute/

18.2   Introduction

In 2005, I (Dr. Ledder) led an effort at the University of Nebraska-Lincoln to obtain a UBM (Interdisciplinary Training for Undergraduates in Biological and Mathematical Sciences) grant from the National Science Foundation. The principal purpose of the UBM program is to develop a cadre of undergraduate students who have developed the skills and interests needed to become productive interdisciplinary researchers in mathematical biology; accordingly, the chief component of our Research for Undergraduates in Theoretical Ecology (*RUTE*) program is the *RUTE Scholars Program*, in which teams of students and faculty mentors from both mathematics and life sciences work together on a research project. Because obtaining large competitive grants is a priority at our institution, we had the services of a team of consultants to help us polish the proposal. The consultants said that we needed a transition program for the period between when the students arrive on campus and when they are ready for the research program. With just two weeks before the proposal was due, I created a 5-week summer session course called Research Skills in Theoretical Ecology, whose purpose was to teach interdisciplinary research skills to lower division students. The word "created" is an overstatement because at that time the course was only a title and a rough idea. I had no idea what we would teach in it or even how to design it. That was a problem to face later. It was like jumping out of an airplane with a bag of material and expecting to build a parachute on the way down.

Our proposal was funded in October 2005. Research Skills in Theoretical Ecology was to be offered in early June 2006. All I had at the outset was a goal:

- Introduce *interdisciplinary research* in mathematics and biology to talented students *at an early stage* in their careers.

18.3   Assembling the Team

The crucial step was the first one: finding the right biologist to work with. The University of Nebraska-Lincoln had just hired Dr. Tenhumberg (for a joint appointment to the School of Biological Sciences and the Department of Mathematics, with tenure home in Biological Sciences), a theoretical ecologist who was interested in the project. There was a significant problem to face at the outset. As a new hire, with her tenure track appointment to begin in Fall 2006, she had to concentrate her energy on tasks that would strengthen her tenure file. Time spent during the summer teaching a course, rather than working on research, was not something that she could afford. This situation tested the commitment of our administration, which rose to the occasion. The School of Biological Sciences' department chair offered to count the course toward her teaching load for the following academic year, thus freeing time for research in the fall that would be equivalent to what she lost in the summer.

Interdisciplinary courses pose a significant staffing problem at most institutions. They can be taught by a single faculty member, but are then unlikely to be interdisciplinary in viewpoint. If taught by faculty from two departments, then each faculty member is likely to do as much work as for a full course, while each department is likely to count the work as only half a course. This problem was solved for the first year by the School of Biological Sciences' policy of counting a team course as a full course for each faculty member in the first run of the course and Dr. Ledder's willingness to teach his part for summer pay equivalent to that for half a course. Subsequent years proved more difficult

because we could not fully fund two faculty members to teach the course. After the initial offering, we saved some of Dr. Tenhumberg's time by hiring a teaching assistant to help with the laboratory instruction. More of the workload shifted to teaching assistants: in 2009 and 2010, the biology component was taught by biology graduate students from Dr. Tenhumberg's lab; in 2010, we turned the mathematics component over to a mathematics graduate student who had taken a modeling course from Dr. Ledder and had begun a research program in mathematical biology with Dr. Tenhumberg as co-advisor. These staffing arrangements worked because our graduate student teachers combined high levels of knowledge of the laboratory procedures needed for the experiments, the relevant biological literature, and the principles of mathematical modeling.

18.4 Objectives and Constraints

Most courses begin with a minimalist design process. We choose a body of material, then a text, then a syllabus, and then decide on the assignments. The course goal is generally implicit in our choices rather than a guiding principle for them. This is a blessing in that it makes the design quick and easy, but it is also a curse because courses so defined can be unfocused.

Since Research Skills in Theoretical Ecology was unlike any other course in our experience, we used an intentional design process, beginning with the course goal, progressing to a list of objectives, a list of outcomes, and finally a set of in-class activities and outside assignments. We started by deciding on our interpretation of key words and phrases in the course goal. By "interdisciplinary" we meant a unified whole with experimental biology and mathematical modeling as critical components, rather than biology augmented by statistical analysis, mathematics motivated by biology, or a loose confederation of the two. We intended the students' work to be a serious attempt to investigate aspects of a single open-ended problem and reach conclusions supported by experimental data and mathematical modeling. Originally, we intended the course to be for students who had taken freshmen courses in biology and mathematics. Recruiting difficulties led us to pitch the course instead to talented students in the summer between high school and college, so we had to interpret "at an early stage" as meaning that we should not expect our students to have any laboratory experience or any useful knowledge of calculus or statistics.

We established three objectives for the course.

1. Learn knowledge and skills for theoretical ecology research.
2. Conduct theoretical ecology research.
   a. Collect laboratory data on ecological problems.
   b. Use laboratory data to estimate the parameters of mathematical models.
   c. Use mathematical models to make predictions.
   d. Use additional laboratory experiments to test the model predictions.
   e. Draw appropriate conclusions.
3. Learn scientific communication skills.
   a. Read and discuss primary literature in ecology.
   b. Write scientific research papers/posters.

The structure of the course was dictated by these objectives. The course would have a lecture and a laboratory component, like most science courses, but the relationship between them was to be the reverse from what is usually done. Introductory science courses start with a body of material to be taught. This determines the lecture topics, and then the laboratory topics are chosen to supplement the lecture. Instead, the design of Research Skills in Theoretical Ecology would begin with a research agenda. This would determine the laboratory experiments, and then the lecture topics would be chosen to supplement the laboratory.

The chief constraint for the course had to do with the students. Straight-A students from a variety of high schools, with little or no college experience, have vastly different backgrounds. While we could expect that some of our students had studied calculus and some had studied ecology, we could not assume any specific background in biology, statistics, or mathematics beyond precalculus, nor could we assume any laboratory experience.

18.5   Design Principles

Our objectives and constraints resulted in a coherent set of design principles. We believe that the first five of our six principles could serve as design principles for any interdisciplinary research-based course in mathematics and biology, regardless of its level or content. We offer them as a general set of principles for research courses in mathematics and biology.

1. *The course should be about skills rather than content. Everything in it should be based on a coherent research plan.*

This principle reflects a paradigm shift that is occurring throughout education. General education in the 20th Century was almost universally thought of in terms of content. Distribution requirements are based on the principle that students need to know something about many different areas. In contrast, some new general education programs, such as the Achievement Centered Education (ACE) program (University of Nebraska-Lincoln, 2012a) that was implemented at the University of Nebraska-Lincoln in Fall 2009, are based on the principle that students need to develop important skills. Similarly, many institutions acclimate freshmen to academics with a freshman seminar course; such courses differ by institution, with many choosing interdisciplinary or nonstandard content, but they share the purpose of teaching freshmen the academic skills of careful reading, critical thinking, and writing.

2. *The research program should be both experimental and theoretical, with a clear focus.*

Science is a combination of theory and experiment, although individual scientists commonly focus on one or the other. Theoretical work needs to be firmly grounded in observation or else it is mere speculation. Experimental work needs to be informed by theory or else it is merely a collection of disjointed facts. The best way to teach science is to give students a course that integrates experiment and theory.

3. *The research program needs to be devised primarily by the biologist with the mathematician's approval.*

The biologist needs to have the laboratory expertise for the project, and the mathematician has to have to flexibility to devise a mathematics component to match the given biology component. This was an easy principle for us to follow, because Dr. Ledder's training is in mathematical modeling (see Ledder (2008)) rather than mathematics *per se*. Any mathematician working with a biologist on a research course needs to make the same concession. Mathematicians do not need specialized mathematical knowledge to write down population dynamics models for many different experiments, but biologists need in depth knowledge about the organisms being studied to be able to design quantitative experiments. It can be challenging to design research projects in which experiment and mathematical modeling go hand in hand. Dr. Tenhumberg's experience in constructing and using mathematical models facilitated our accomplishment of this goal.

4. *The course should be fully integrated: biology and mathematics, theory and experiment, laboratory and lecture.*

This is a crucial distinction between a research-based course and a knowledge-based course. In knowledge-based courses, it is not possible to support every theoretical statement with an experimental investigation, nor is it possible to plan a laboratory to match every lecture topic. In a research-based course, all the experiments have to be supported by theoretical work. Our motivation for integrating the biology and mathematics was to impress on students that there is a connection between these fields that they have probably always seen as unrelated.

5. *An authentic research experience must lead to a research paper, although the research need not be publishable.*

We have found that having to explain work in writing contributes to the student's understanding of the work (Ledder et al., 2013). Instead of a final exam, our students write a paper (in groups the first two years, individually thereafter) that looks as much like a professional research paper as they can manage. We get best results by having students write one section at a time, with feedback and rewrites of one section concurrent with the first draft of the next. We also devote time to examining professional research papers to discover scientific writing style and conventions.

6. *The course must be self-contained; it must provide the necessary biology background, teach the laboratory methods, build the mathematics up from a pre-calculus background, and teach scientific writing.*

This principle was required because of the uncertain background of our students. It might not be necessary for a course that is a capstone rather than an introduction. Even so, it is probably best to include too much background rather than too little. We found that talented students with a precalculus background could learn some matrix algebra and differential equations in population dynamics, provided that it was introduced appropriately (Ledder et al., 2013).

18.6 Discussion

The details of our research program, mathematics content, and pedagogy appear elsewhere. (Ledder et al., 2013; University of Nebraska-Lincoln, 2012b) Here we discuss the challenges one encounters when intimately-connected course components are designed and taught by people from different academic cultures.

- Notation and vocabulary

The first time we taught the course, Dr. Tenhumberg attended all of the mathematics lectures and Dr. Ledder attended all of the laboratory instruction sessions and some of the data collection sessions. This was helpful in standardizing the notation and vocabulary for the course. The next time we taught the course, we suffered from a bit of notation drift. Dr. Ledder used the symbol r for the *dominant* eigenvalue of a matrix so as to avoid using a Greek letter. Some of the mathematics literature uses r in this manner. He also used r for the relative growth rate in a differential equation model, which is standard in both mathematics and biology. For a mathematician, using r to mean one thing in the discrete context and something different in the continuous context causes no problem. Although the demographic literature is not fully consistent in notation, λ is typically used for discrete time models and r for continuous time models, so using r for both types of model is potentially confusing for students using textbooks written for biologists or primary literature. In retrospect, it is clear that notation should conform to biological standards as much as possible. Similarly, it is important to append biological names ("asymptotic growth rate") to mathematical names ("dominant eigenvalue").

- Software

For our first class, we used Excel for the statistical analysis because it is available on most student computers and all university computers. We used Matlab for programming simulations because it was already installed on the computers in the mathematics computer classroom. Most of our students did not want to purchase a Matlab license just for this course, which meant that they had to do all their programming in department facilities. In the second year, we instead tried Octave, which is free and similar to Matlab, but it did not work well in Windows and we went back to Matlab. In the third and subsequent years, we used R (R Development Core Team (2012)) for statistics and programming, and this turned out to be an excellent choice. R is popular among biologists, has similar functionality to Matlab, can be downloaded from the internet for free, and installs seamlessly in either a Linux or Windows environment.

- Data analysis and presentation

In the first year, we completed data collection before starting data analysis. We underestimated how long the data analysis would take because students were ignorant of the most basic statistics, like the normal distribution. Thus we resorted to using the built-in routines provided by Excel without a detailed explanation of the statistical methods. In the following years, we restricted the statistical analysis to a minimum, with instruction in statistical data analysis beginning in the second week of the course using simulated data (see Ledder (2013)). The students were happier with their understanding of statistics, but our requirement that they write their own statistics routines made them more intimidated by computer programming. We eventually lowered our expectations for the data analysis part of the computer programming while still requiring the students to write their own programs for simulations.

The style and conventions of research papers in mathematics and biology differ, which meant that we had to negotiate stylistic elements for student papers. Biology journals usually use author's name and year for citations, whereas many mathematics journals use a number corresponding to the reference list. We used the name and year method. Biology papers usually have an Experimental Methods section, which contains the mathematical models as well as the laboratory procedure. Mathematics papers usually have a separate Modeling section that does not easily fit into the structure of biology papers. We settled on following the biology structure because our research emphasized

experimental work and the students were reading primary literature in biology. We extended the Experimental Methods section to include more mathematical content than is typical for biologists.

18.7   Conclusions

Differences in academic culture between mathematics and biology provide challenges to creating an integrated interdisciplinary course to teach research skills. Several design principles provide a basis for a research-based course designed and taught by a biologist and a mathematician: the course should focus on skills rather than content, be driven by a research agenda created largely by the biologist; integrate all components; and culminate in a written paper. Cultural differences need to be appreciated, but can be bridged through planning and communication. The resulting course can provide students with an authentic scientific research experience delivered as an academic course.

References

Ledder, G., 2008: An experimental approach to mathematical modeling in biology. *PRIMUS*, **18**, 119–138.

Ledder, G., cited 2012: BUGBOX Mathematical Modeling Simulations. [Available online at http://www.math.unl.edu/~gledder1/BUGBOX/.]

Ledder, G., B. Tenhumberg, and G. T. Adams, 2013: An interdisciplinary research course in mathematical biology for young undergraduates. This volume, 69–82.

R Development Core Team (2012). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. ISBN 3-900051-07-0, URL http://www.R-project.org/.

University of Nebraska-Lincoln, cited 2012a: Achievement Centered Education. [Available online at http://ace.unl.edu/.]

University of Nebraska-Lincoln, cited 2012b: Research for Undergraduates in Theoretical Ecology. [Available online at http://www.math.unl.edu/programs/rute/.]

19

Bioinformatics: An Example of a Cooperative Learning Course*

Namyong Lee[1] and Ernest Boyd

Dept. of Mathematics & Statistics, Minnesota State University, Mankato

Institution	Minnesota State University, Mankato
Size	about 15,000 students
Institution Type	medium size state university with Master of Science
Student Demographic	recent high school graduates with high potential and interests in math, biology or computer science
Department Structure	Mathematics, Biology, and Computer Science are separate departments in the College of Science, Engineering Technology

Abstract

In this paper, we describe how our bioinformatics course was born as an interdisciplinary and cooperative learning course. Three departments—Mathematics and Statistics, Biology, and Computer and Information Science—participated in this project. We describe how our team designed the course, prepared group projects, and secured funds for it.

19.1 Course Structure

- Weeks per term: 15-week regular semester course
- Classes per week/type/length: Two 75 minute lecture/computer lab (hybrid) per week
- Labs per week/length: Two 75 minute lecture/computer lab (hybrid) per week

---

- Average class size: 12–20 students
- Enrollment requirements: Each student must interview one of the three instructors to enroll in the course
- Faculty/dept per class, TAs: Team-taught by three instructors, one from each of the mathematics, biology, and computer science departments
- Next course: Students are encouraged to take Mathematical Models in Biology (Math 490/ Biol 490). Both Bioinformatics and Math Models in Biology courses focus on interdisciplinary undergraduate research
- Website: https://d2l.mnsu.edu/ (need class account)

19.2   Introduction

Colleges and universities face significant challenges when they plan to offer bioinformatics courses to undergraduate students. The literature strongly suggests the necessity of truly interdisciplinary courses where students from different majors work closely in small teams on bioinformatics research problems (National Research Council 2003; Bialek and Botstein 2004; Steen 2005; Fetrow and John 2006). Moreover, the courses ought to be taught by a team of instructors from different disciplines, an unusual situation for most traditional institutions of higher education.

The departments of Mathematics and Statistics, Biology, and Computer and Information Science at Minnesota State University, Mankato, have created an interdisciplinary and cooperative learning bioinformatics course. It is taught by three faculty members (one from each department) and draws advanced undergraduate and graduate students from other departments as well as those three. The course is taught as a problem-solving seminar focused around group projects. Students and instructors are expected and encouraged to learn from each other. We do not expect each student to have a complete background in all three disciplines. Students work in interdisciplinary teams so that each student can contribute prior expertise in one of the fields.

The course is listed for three credits in each department so that students can register within their own disciplines. The dean of the College of Science, Engineering, and Technology agreed to pay a one-credit overload to each faculty member. This kind of course credit split is one of the constraints that make a team teaching project more difficult to administer. Fortunately, our university provides some financial support from small internal grants as an incentive to faculty members to create interdisciplinary courses.

19.3   Designing a Course

The course is still evolving. Here we describe the current design.

Faculty. Our design team consisted of six faculty members, two each from Mathematics and Statistics, Computer and Information Science, and Biology. In a given year, primary responsibility for the course is given to a team of one faculty member from each department. Having more people on the design team than are needed to teach the course allows us to deal with retirements and sabbatical leaves, and initially helped build the knowledge base necessary to prepare the course materials and group projects.

Students and Prerequisites. Initially we wanted to require introductory courses in statistics, discrete mathematics, data mining, programming, molecular biology, and physiology. We realized, however, that we might not have enough students who could satisfy all the prerequisites. Thus, we posted our course announcement without any prerequisites, but required students to obtain an instructor's permission before registration. In this manner we could make sure that each student would bring enough advanced knowledge to be a productive member of a team. Unexpectedly, students came from more than the three departments. The enrollment ranged from 12 to 20 each semester.

Scheduling Logistics. The next challenge was developing a course listing that would be relevant to students from each department. Fortunately, we have a generic seminar course in each department and could use those course names. Students can register for their own department's seminar course with the course title Bioinformatics Seminar on their transcripts without a lengthy procedure to create a new course. Scheduling a classroom is another challenge in multi-disciplinary courses, because many departments do not communicate with each other when they schedule their

courses and classrooms. We have been lucky to have a classroom at the Academic Computer Center, which solves the space problem and also makes it easier to do computer labs.

Lectures and Projects. The course has two major parts. The first half is an introduction to standard bioinformatics topics, such as molecular biology, sequence alignment, phylogenetic trees, microarrays, statistical analysis for biological data, and data mining. Students have reading assignments to broaden their knowledge and to discuss as a group. Each student is also asked to build a bioinformatics glossary journal to learn the terminology to communicate with a multi-disciplinary team.

Before the second half of the course, we introduce several research problems and divide the class into groups, each with at least one biology student, one mathematics student, and one student familiar with computer programming. In the second half, we focus on group projects, covering material necessary for the projects. In the last week of the course, each group presents the results of their research project orally and submits a written report for a course grade.

Class meets twice a week, with each 75-minute class period typically consisting of 40–45 minutes of lecture and discussion and 30–35 minutes of computer lab. Thanks to our grant, we also have had outside speakers who have given inspiring overviews of topics in bioinformatics and ideas for new projects.

Computer Lab. An essential component of the course is the computer lab. Each instructor demonstrates software with tutorials. We have used R and Bioconductor for statistical analysis and visualization of microarray data, Orange and Weka for data mining, CLC Free Workbench, BioEdit, ClustalX, TreeV32, and Cn3D for sequence alignment and phylogenetic trees. Most of these programs are in the public domain. We make a course resource CD-Rom and distribute it so that students can get familiar with the tools on their own computers. We have also used web databases and their tools, such as NCBI, BioCyc, and ExPASy.

19.4 Suggestions

Through years of experience with the course, we have seen many encouraging possibilities as well as obstacles to interdisciplinary courses. One great discovery has been the joy of working together with faculty in other disciplines. Unlike experimental sciences, such as biology, or team-project-oriented computer science, mathematicians do not frequently work in teams of people with complementary expertise. Faculty members can demonstrate to students how to collaborate with each other and contribute to a team project.

It is important to present the three disciplines as interconnected and interwoven. It would be a mistake to divide such a course into three separate presentations. When the members of the team present mathematical concepts, we often ask the group "Is this mathematical assumption reasonable for biology?" When they present a computer algorithm, we ask, "Is this method robust and efficient for large data sets? How sensitive are the results to parameter values?" It is easier to understand how to use a BLAST search at NCBI if it is preceded by a discussion of the mathematical concepts behind the Smith-Waterman algorithm and the Needleman-Wunsch algorithm. To appreciate how to use ClustalX and TreeV32 for phylogenetic trees, students need a discussion of neighborhood joining trees, UPGMA, and maximum likelihood algorithms. Clustering algorithms to analyze microarrays need to be accompanied by mathematical foundations for distance measures.

Support is needed from the departments and the college, including compensation for extra or reassigned teaching, flexibility to adjust departmental schedules, and even moral support from colleagues. It works better to confer with our Dean as a team rather than as individuals. Many institutions now realize the need for such interdisciplinary work, so we have a better chance to gain support.

Computer lab and hands-on experiments are essential. Selection of software is also important. For instance, there are many different software packages for sequence alignments and phylogenetic trees, each with its own pros and cons. To conserve time, only one should be presented.

Collective efforts to apply and receive funding are important to building the faculty team and to giving life to the course. We started with a small grant from our university system for new course design and then applied for larger funds such as an NSF CCLI grant. The process of applying for an outside grant is worthwhile, as it provides an opportunity to discuss what we can do and what we wish to do with the teaching and learning project.

Building a quality term project is another time and energy consuming task. Experts in the field should be consulted. Good ideas are available and do not need to be reinvented. We invited a number of external speakers that range from mathematicians to ecologists. They delivered insightful lectures and suggested team projects.

Short courses or workshops are useful to extend knowledge and to exchange ideas. MAA's PREP workshop (http://www.maa.org/prep), MBI (http://mbi.osu.edu), NIMBioS (http://www.nimbios.org), or DIMACS (http://dimacs.rutgers.edu) all have excellent programs. Joining a national society such as SMB (http://www.smb.org) and MAA's BioSIGMAA (http://sigmaa.maa.org/bio) is another way to extend knowledge and network.

19.5　Conclusion

Creating an interdisciplinary seminar using cooperative learning strategies is rewarding but difficult. The team of faculty members must have the support of the administration. They must be able to interact and complement each other's work. Students need to be self-motivated. The curriculum must be planned so that the component disciplines are not separate strands, but interwoven. Bioinformatics is a rich and challenging field of study, and we need to bring those characteristics to the course.

References

Bialek, W. and D. Botstein, 2004: Introductory Science and Mathematics Education for 21st-Centry Biologists. *Science*, **303**, 788–790.

Campbell, A. M., and L. J. Heyer, 2007: *Discovering Genomics, Proteomics and Bioinformatics*. 2nd ed. Benjamin Cummings, 352 pp.

Fetrow, J. and D. John, 2006: Bioinformatics and Computing Curriculum: A New Model for Interdisciplinary Courses. *SIGCSE'06*, Houston, TX, Association for Computing Machinery, 185–189.

Isaev, A., 2004: *Introduction to Mathematical Methods in Bioinformatics*. Springer-Verlag, 312 pp.

National Research Council, 2003: *Bio 2010: Transforming Undergraduate Education for Future Research Biologists*. National Academy Press, 208 pp.

Steen, L. A. Ed., 2005: *Math & BIO2010, Linking Undergraduate Disciplines*. Mathematical Association of America, 150 pp.

20

Integrating Statistics and General Biology I in a Learning Community

William Ardis
Mathematics, Collin College[1]

Sukanya Subramanian
Biology, Collin College[2]

Name of Institution	Collin College
Size	27,000 with three campuses in Collin County, Texas
Institution Type	Two-year college with core offerings for students transferring to a university, associates degrees, and certificates
Student Demographic	Core courses, required courses for students seeking associates degree in Nursing or in Physical Therapy
Department Structure	Separate Mathematics and Biology departments in the same division

Abstract

Community colleges can play an important role in integrating biology and mathematics at the freshman and sophomore level. Collin College uses a combination of introductory freshman and sophomore level courses and learning communities to show students the cross-disciplinary role of mathematics in biology.

20.1 Course Structure

- Weeks per term: 16-week semester

- Classes per week/type/length: two 2-hour, 30-minute lecture class meetings per week

---

[1] bardis@collin.edu
[1] ssubramanian@collin.edu

- Labs per week/length: one three-hour lab each week

- Average class size: 24 students

- Enrollment requirements: students must assess into a college level mathematics course, or pass MATH 0310—Intermediate Algebra for the statistics class, no requirement for the biology class

- Faculty/dept per class, TA's: Lecture section team taught by one math professor and one biology professor, lab section taught by one of the lab instructors or an associate faculty member in the biology department

- Next Course: after completing this biology course, students are eligible to take BIOL 1407—General Biology II

- Website: Only available during the semester the learning community is offered

20.2   Introduction

Science teachers have emphasized statistics in various natural science disciplines. In biology, there is a need to effectively prepare the next generation of biological researchers for the tremendous opportunities ahead. Undergraduate biology students who use statistics from the start of their education will be better positioned to contribute to future discoveries in biomedical research. Unfortunately, for most biology students, statistics has been isolated from biology. One of the recommendations from *BIO2010: Transforming Undergraduate Education for Future Research Biologists* (2003) is "Connections between biology and other scientific disciplines need to be developed and reinforced so the interdisciplinary thinking and work become second nature." One way to facilitate interdisciplinary connections is with a learning community. At Collin College we created an interdisciplinary connection by combining two core courses in the learning community, *Chances in Life: A Quantitative Approach to Biology*.

20.3   Background

The Collin County Community College District was founded in 1986, and today Collin College has three campuses. The population of Collin County has increased by 42% since 2000, making it one of the fastest growing counties in Texas. The college's enrollment is also increasing, from 11,572 in Fall 1998 to 27,593 in Fall 2011.

Of Collin College students, 52% are between the ages of 18 and 22 and 80% plan on transferring to a university. Collin College offers associate of arts, science, and applied sciences degrees, and certificates and marketable skills achievement awards. Associate degrees are offered in traditional academic disciplines such as biology and mathematics, and in specialized health science areas, such as nursing and respiratory care. Collin College has dual enrollment agreements with nine universities and colleges in the state, including Texas A&M, Texas Tech, Southern Methodist University, the University of Texas at Dallas, and the University of North Texas.

Collin College began offering learning communities in the fall of 1994, and now provides learning community courses at all three of the campuses. In the fall of 2007, the district offered eighteen learning communities, including *Chances in Life: A Quantitative Approach to Biology*. A learning community consists of two or more classes that enroll a common group of students and are linked. At Collin College, we use an integrated model. Students are required to register for the statistics and biology classes, as well as a section of the biology lab. The lecture classes are scheduled consecutively, so students are in class for three hours, twice a week, with both instructors present and active. Longer class periods build a sense of community among the students and between the students and the faculty. The model allows the faculty and students time to explore the connections between the disciplines.

20.4   Process

The options for new or different courses that a community college in Texas can offer are limited. A community college can offer any course listed in the Academic Course Guide Manual (ACGM) (Texas Higher Education Coordinating Board, 2012). The best option for us was to create a learning community combining two courses, a statistics course and a biology course.

We wanted the learning community to reinforce interdisciplinary thinking in the uses of statistics in biological research, to help students learn how statistics plays an important part in biology and show topics in biology that are integrated with the principles of statistics. Students might not see these connections in separate biology and statistics courses. We concentrated on

- Experimental design
- Evolutionary principles
- Data collection and interpretation
- Genetic principles
- Bioinformatics: relationship among gene, and protein sequences

The laboratory for biology was not initially included with the lecture; students had to sign up for a separate lab section. To give *Chances in Life* the best chance of running the first time it was offered, no particular lab section was specified. It is department policy that the biology lab must count for 25% of the students' final course grade. We had to have the combined tests account for 75% of the grade for both statistics and biology. The other 25% of the biology grade was determined by the biology lab grade, while the other 25% of the statistics grade was determined by a statistics lab component, which has varied over the three years *Chances in Life* has been offered. In the first year, it consisted of eight quiz grades and a five to seven page critique that examined a medical study (Greco et al. 1996). In the second year, it consisted of several labs using either the graphing calculator or EXCEL, and the critique. For the third year, it consisted of designing a statistical study, which students would write up as an eight to eleven page paper and present as a five minute PowerPoint presentation.

20.5 Discussion

We faced challenges in integrating the two courses, and the development of this learning community has been ongoing. It is difficult to find good examples that integrate the two subjects for use in class. We are continually looking for biological and medical studies that are accessible to our students. We have used several of the studies mentioned in the biology text. In our discussion of statistical studies and the scientific method, we examined two research articles (Bromhall et al. 2000; Davidson et al 2001) that were discussed in the biology textbook (Purves et al. 2004). Another good source has been the sessions on biomathematics at the Joint Mathematics Meetings and MathFest. Professor Ardis attended the short course *Implementing Biology across the Mathematics Curriculum*, which was held prior to MathFest in 2007, and he came away with the idea to use the paper (Luria and Delbruck 1943) to introduce the chapter on probability distributions. We have used one or two of the experiments from the biology lab. Early in the semester, students performed a hypothesis test in the lab before that topic is covered in the statistics class. In the biology lab, the lab instructors assume students have not had statistics, so the hypothesis test was little more than a black box procedure. We have the students use the data from the experiment in class when we cover hypothesis testing. This gives us an opportunity to discuss experimental design, formulation of the hypothesis, and hypothesis testing.

Because *Chances in Life* consists of two courses, its content is no different from the content of the individual courses. Consistency is important, since many of our students plan on transferring to a four-year institution. For both courses, it is difficult to change the order in which material is presented. In some cases, topics match, enabling discussion by both professors, as when we discuss the scientific method and statistical studies using the two studies noted above. In other instances, one of the professors might have to return to a topic covered earlier. For instance, while evolution is covered early on in the biology course, we returned to it when discussing the Luria and Delbruck (1943) paper as part of the introduction to probability distributions. So, while the schedule in which material was presented did not change, we worked together to determine topics that would tie the biology into the statistics lecture, or statistics into the biology lecture.

Not all of the cross-disciplinary examples are planned. One of the advantages of having both professors in the class at the same time is the opportunity for spontaneous input during the lecture. Several of the statistics examples come from the health field, and the biology professor was able to provide more background information than in the problem. Often this was the result of a student's inquiry.

Chances in Life was offered again in Fall 2008 and Fall 2009. In both instances, we required that students sign up for a particular section of the biology lab. We had hoped this would allow us to integrate statistics into the lab, and thus allow us to integrate the course grade completely. Unfortunately, the learning community was cancelled both times due to low enrollment.

Over the five years that *Chances in Life* has been offered, the largest group of students taking the course has been pre-nursing majors. To obtain an associates degree in nursing at Collin College, students must take MATH 1342–Statistics. BIOL 1406–General Biology I, is not specifically required for nursing majors, but it is a prerequisite for BIOL 2401–Anatomy and Physiology I, which is required. Since many of the pre-nursing students needed BIOL 1406 in order to take BIOL 2401, *Chances in Life* provided an opportunity for students to satisfy both requirements with the same course. We have also attracted the occasional respiratory care student; both courses are required for an Associates degree in this area. Unfortunately, we have not been able to attract many biology majors; only one or two over the past three years have enrolled in the class. In the future we will have to be more aggressive in recruiting students for the learning community. The biggest obstacle is students' lack of awareness of the program. The most effective approach is to heavily recruit students for the course. The learning community faculty need to visit other classes (and not just prerequisite mathematics classes) to explain the learning community concept and promote their biology and statistics learning community.

20.6   Suggestions

We recommend that schools without a learning community program investigate the possibility of starting one. It is important to gain the support of the administration and involve as many disciplines as possible. Because of the time and work involved in developing a learning community, we recommend that the administration consider extra compensation for teaching in one. Since Collin College uses the integrated model for learning communities, both faculty members are compensated for teaching both courses, and this encourages their development. Of course this requires an additional financial commitment from the administration. Learning communities are a form of professional development, so the information gained by faculty participants can also be used in stand alone courses. For schools that have a learning community program, we recommend that the institution encourage mathematics and science faculty to develop courses like *Chances in Life*. At Collin College, the learning community faculty members provide a professional development workshop each semester for other faculty members who might consider creating a learning community.

If a learning community program is not possible, there is an alternative. Some schools use a linked-course model, in which students co-enroll in two courses that meet separately. While the instructors might not participate in the teaching of the other class, they could work together to integrate the material into both courses. This model can be used as a starting point to encourage your college or university to consider a learning community program. It requires the initiative of the administration to encourage faculty to develop pairs of linked courses.

In any case, we recommend that faculty members attend at least one conference for the other discipline. This provides the faculty member with a view into the other discipline's world. Dr. Subramanian attended the Joint Mathematics Meeting in January 2007 because it included several sessions on biomathematics. This helped her get more examples and resources for integrating the two subjects and she felt it was enlightening to get a mathematical perspective on biological phenomena.

Another recommendation is to make sure students are aware of what a learning community is when they enroll, and make them aware of what is expected in class. One point of confusion we try to correct with students is that while this is one learning community, it consists of two classes. Students sometimes think that they will have less work to do in a learning community. It is important to stress that the learning community consists of two classes, with corresponding work loads.

20.7   Conclusion

The college has been supportive of the learning community program. Dr. Tracey McKenzie, Director of Learning Communities at Collin College, commented about *Chances in Life*:

The integration of mathematics and biology was an important expansion of our Learning Communities program that had been dominated by social sciences and humanities. This course was the first Learning Community taught that included biology, and it has been an especially attractive course option for our nursing students.

The Dean of Mathematics and Natural Sciences, was happy to approve our Learning Community when it was proposed. He has also been supportive of the learning community program, encouraging his faculty to develop learning communities that include a mathematics or science course.

The Learning Communities program at Collin College operates on the principle that learning in context provides a deeper, more durable type of learning. Courses like *Chances in Life* provide students an opportunity to place both biological and mathematical information into context. Since both courses are in the field of study curriculum for nursing, students can see that the curriculum elements have a purpose, and that purpose can be exemplified through practical examples.

The logistical problems in setting up a learning community deal not only with space and time, but also with assuring that the instructors are compatible and willing to be participants in learning about the other discipline. Certainly, with these two faculty there were no issues about that cooperation. There is also the practical consideration that the course needs to make in order to justify the time spent in preparing for it. Faculty have to be encouraged to recruit students, but a significant part of that recruiting hinges on them showing to their students that they are still active learners who will work hard to create a well-integrated course. Again, for this course that was not an issue.

Learning communities such as *Chances in Life* are ideally suited for two-year institutions where there is little ability to create new courses. We strongly feel that this type of approach to interdisciplinary thinking is beneficial to both faculty and students. Learning communities certainly give an edge to students in achieving excellences in their pursuit of knowledge.

References

Bromhall, S. D., W. S. Osborne, and R. B. Cunningham, 2000: Comparative Effects of Ambient Ultraviolet-B Radiation on Two Sympatric Species of Australian Frogs. *Conservation Biology*, **14**, 420–427.

Davidson, C., H. B. Shaffer, and M. R. Jennings, 2001: Declines of the California Red-Legged Frog: Climate, UV-B, Habitat, and Pesticides Hypothesis. *Ecological Applications*, **11**, 464–479.

Greco, D., et al., 1996: A Controlled Trial of Two Acellular Vaccines and One Whole-Cell Vaccine Against Pertussis. *The New England Journal of Medicine*, **334**, 341–348.

Luria, S. E. and M. Delbruck, 1943: Mutations of Bacteria from Virus Sensitivity to Virus Resistance. *Genetics*, **28**, 491–511.

National Research Council, 2003: *BIO 2010: Transforming Undergraduate Education for Future Research Biologists*. National Academies Press, 208 pp.

Purves, W. K., D. Sadava, G. H. Orions, and H. C. Heller, 2004: *Life: The Science of Biology*. 7th ed. W. H. Freeman and Company, 1121 pp.

Samuels, M. L., and J. A. Witmer, 2003: *Statistics for the Life Sciences*. 3rd ed. Prentice Hall, 724 pp.

Texas Higher Education Coordinating Board, cited 2012: Lower-Division Academic Course Guide. [Available online at www.thecb.state.tx.us/AAR/UndergraduateEd/WorkforceEd/acgm.htm.]

21

Constructing an Undergraduate Biomath Curriculum at a Large University: Developing First Year Biomath Courses at The Ohio State University

Tony Nance[1]
Associate Director, Mathematical Biosciences Institute, and Assistant Professor, Department of Mathematics, The Ohio State University

Laura Kubatko[2]
Associate Professor, Departments of Statistics and of Evolution, Ecology, and Organismal Biology, The Ohio State University

Name of Institution	The Ohio State University
Size	about 38,000 undergraduate students
Institution Type	large state university with graduate program
Student Demographic	recent high school graduate with interests in mathematics, statistics or biology
Department and Program Structures	six departments (Mathematics, Statistics, and four Biology), plus the biology major, administered by the Center for Life Sciences Education, all in the College of Arts and Sciences

Abstract

All curriculum development shares standard decisions and processes, and all curriculum development also has wrinkles particular to the courses and institution. In this article, we describe both as they pertain to developing first-year courses in calculus and statistics in the Mathematics and Statistics Departments that are aimed at biology students.

---

[1] nance.1@osu.edu
[2] kubatko. 2@osu.edu

21.1   Course Structure

- Weeks per term: 10 weeks (will convert to semesters in 2012)
- Classes per week/type/length: three 48-minute lectures, two 48-minute recitations
- Average class size: Calculus I = up to 120; Calculus II = up to 60; Statistics = up to 40
- Enrollment requirements: standard for 1st-year Calculus; Statistics = Integral Calculus prerequisite
- Faculty per class, TAs: 1 faculty; 2 TAs for Calculus I; 1 TA for Calculus II; 1 TA for Statistics

21.2   Introduction

Development and revision of a curriculum to meet the educational needs of students is one of the most important and most difficult jobs of faculty and administrators at the nation's colleges and universities. This especially applies when the topics of interest overlap distinct disciplines, which is becoming increasingly common. When we set out to develop a curriculum in BioMathematics at The Ohio State University (OSU), we were faced with the considerable challenge of navigating these difficulties at one of the nation's largest universities; OSU hosts more than 50,000 students on the main campus in Columbus, Ohio, approximately 38,000 of whom are undergraduates. Development of the curriculum we envisioned involved the participation of several departments belonging to two of OSU's eighteen Colleges. The curriculum developed thus far has resulted from a collaboration of faculty within the College of Mathematical and Physical Sciences (MAPS), including faculty from the Departments of Mathematics and of Statistics, and within the College of Biological Sciences (CBS).

   While our task seemed daunting, several factors were working in our favor. Motivation for the course development came from the growing interaction between MAPS and CBS (after the development of the first year courses mentioned here, the two colleges merged), and was boosted by efforts within CBS to make their curriculum more quantitative and by the NSF's establishment of the Mathematical Biosciences Institute (MBI) at OSU. While the two colleges have historically worked well with each other, interactions between them tended to be driven by specific projects. However, the establishment of the MBI required two levels of interaction, one administrative, largely at the level of the Deans, and one oriented toward specific research, largely at the level of the faculty. The result has been a strengthened partnership and frequent conversation between the colleges, and has also created a group of people who are experienced and at ease with working in the middle.

   The relevance here is that we took advantage of this network when investigating what to do and whom to talk to. We have now developed a sequence of four first-year courses in BioMathematics, three of which have been taught regularly since the 2006–07 academic year. (The fourth will be piloted in Spring 2013, its delay caused by OSU's switch to semesters in Summer 2012.) In this article, we describe the process of developing these courses, focusing specifically on the challenges we faced due to the size of our university. We discuss what aspects of the process worked well, what we could have done better, and we make suggestions for others who may be considering development of such courses in a similar setting.

21.3   Description

The three courses that have run regularly include a two-quarter sequence in Calculus for the Life Sciences and a one-quarter course in Statistics for the Life Sciences (see Kubatko et al. 2013). Other courses were later created or modified to complete an undergraduate major in mathematical biology, as well as a Masters program, in the Mathematics Department. Following the semester conversion, we will resume work on cross-departmental minor and major programs, and on a PhD program.

   The four courses were designed to serve freshmen who place into differential calculus and express an interest in the life sciences (including pre-medicine). We have learned, however, that the third-quarter courses will also enroll sophomore biology majors, as many freshman biology majors are unable to fit these courses into their schedule.

The courses were first offered during the 2006–2007 academic year, but planning began much earlier. A first step, facilitated by the MBI, was to verify the desire, demand, and audience for them. After receiving some informal positive feedback from faculty and administrators in CBS, conversations began within the Departments of Mathematics and Statistics concerning the viability of such courses. One issue within Mathematics was that biology-themed math courses had been attempted in the past, with less than stellar success; in particular, a less rigorous Calculus for Life Sciences sequence had been abandoned only recently. Thus, initial conversations for the new courses had to consider how the newly proposed courses would differ from the prior ones, in rigor and scope.

Within the Department of Statistics, there was enthusiasm for developing a course for students majoring in biology. An existing (and popular) 200-level statistics course served several populations of students, ranging from students getting degrees in computer science to those in the life sciences. There was agreement that dividing the group into life science and non-life science students would be useful, provided that the audience from life sciences was large enough.

With the support of our departments, we worked with the Deans of both MAPS and CBS to develop the courses. We were happy to receive enthusiastic support from both colleges. The problem of scheduling the courses at a large institution is non-trivial. We talked with the set of academic advisors for students majoring in the eight majors offered by CBS to obtain an idea of what courses freshmen majoring in the biological sciences would be taking; then we scheduled our courses at times that didn't conflict with required courses.

Of course, content is important and we took several approaches to selecting material to include. We looked to learn from other people's experiences. The BIO 2010 report (NRC 2003) and subsequent Math & Bio 2010 (MAA 2005) gave us a picture of efforts around the country and starting points to access the existing community. We also talked with several of the MBI's long term visitors. While the vast majority of them are in residence for research, nearly all of them are involved with interdisciplinary curricular efforts at their home institutions. From them we received valuable advice and learned from their experiences. We talked with the people who run the introductory biology program within CBS, looking for places we could reinforce each other in the classroom, referring to specific labs or tailoring specific problems for example. The instructors for the calculus sequence (T.N. and others) met throughout the academic year with the instructor (L.K.) for the statistics course, both to ensure that the students would be prepared for the statistics course (which assumes calculus) and so that the Statistics course could build on the material covered in calculus (thereby increasing the students' opinion of their "relevance").

The next step was to recruit students. To make sure the target audience was aware of the courses, we worked with student counselors from both colleges. The summer freshmen orientation advisors were extremely helpful in recruiting students into the first-quarter calculus sequence. However, recruiting students into the third quarter statistics course was much more difficult. We attempted to recruit by making the academic advisors aware of the course and by distributing information in the calculus courses. However, the response was much lower than we had hoped during the first offering of the Statistics course in Spring 2007 (of 160 students enrolled in two sections of calculus II, only a handful continued in the statistics course; however, the course enrolled 38 students total, and thus there was significant interest from other life science students). The subsequent offerings have been similarly populated. In the Discussion, we describe how have worked to improve recruitment into the third quarter courses.

Both the calculus and statistics courses were taught in a lecture-recitation format, in which students met with a faculty member for three hours of lecture per week and with a graduate teaching assistant (GTA) for two recitation session per week (see Kubatko et al 2012)). Considerable thought was given to the use of GTAs, because the courses had not been offered before and were interdisciplinary, thus we asking a bit more of a GTA than the usual assignment. It proved beneficial to have early conversations with the GTA Coordinators in the Department of Mathematics and of Statistics. Pilot courses often succeed because the designers have a passion for the course and the GTAs are hand-chosen for their experience and high teaching ability. While that can be important, we felt it imperative to have GTAs who were at ease with the biology. If they happened to be excellent teachers, that would be a bonus. Our GTAs were good, but it was their knowledge of biology that secured their selection for this position and helped make them effective with the students.

We received important feedback from teaching the pilot versions of the calculus and statistics courses during the 2006–2007 academic year, and we used it to improve the courses in their second offering during the 2007–2008 academic year. With the support of our departments and administration, we have made the courses permanent offerings, with their own distinct courses numbers.

A next step is the development of a third quarter course in mathematics, to provide an option for students wishing to continue their quantitative training following the calculus sequence. This course has been developed by one of us (T.N.) and is designed to complete a (second) semester course in the upcoming conversion. The first offering of this course is in Spring Semester 2013.

21.4   Discussion

While it took a great deal of time and effort, the process of developing these courses went very smoothly. We feel that this was largely due to how much communication there was throughout the process. Initial conversations were critical due to their content and they firmly established relationships and lines of communication that we used to foster a sense of active participation and teamwork. We were conscious of the need to keep all parties informed of progress on the development of the courses, even while keeping a core group of faculty involved in the day-to-day efforts of course development.

Also crucial has been our willingness to keep an open mind about how these courses should be set up and to solicit and consider the suggestions of students and faculty. We feel that maintaining openness will be vital as the courses continue to develop, so that we can meet the needs of students.

Our primary difficulty was recruiting students for the third quarter statistics course. The course size has been large (approximately 40 students), but only a small percentage were students who continued on from the calculus courses. We have worked to improve our recruiting, including visiting the calculus II courses and meeting with the bioscience academic advisors closer to the start of the course, so that students will be aware of the optional third quarter courses. We are also talking with the undergraduate committees for majors within CBS that require a statistics course in the hope that this will be considered a desirable option to satisfy this requirement. The course requires two quarters of calculus, so that it will likely be listed as a choice of several courses for B.A. degrees; most B.S. degrees require calculus, and so it may be the favored course for B.S. degrees.

21.5   Suggestions

Our experience suggests that keeping all groups informed at all stages in the development is crucial. It is equally important to listen carefully to the advice of colleagues and students. Ask faculty in the biological sciences what topics from mathematics and statistics they feel are valuable for their students. Ask for specific examples of where mathematics and statistics are used in the laboratory experiments the students perform. Ask about what students would be expected to know for graduate work in the biological sciences.

Communication will lead to the development of a community of faculty, staff, and administrators who care about the success of this curricular venture. While we were fortunate to have the MBI to help us build this initial community at OSU, we feel that a few networked and enthusiastic professionals who can draw others in can be enormously successful in creating such a community.

The process requires work: selecting the textbook, deciding on topics to cover, and figuring out what approach will work best are difficult and time-consuming tasks. It is important to be flexible and willing to learn by trial and error. We also recommend taking advantage of the ever-growing set of resources available in this area (this volume being one example!).

Finally, we suggest advertising courses extensively and enthusiastically. This is particularly important at a large institution like OSU, where students have many options in course scheduling. Advertising should be aimed at students and the faculty and staff who advise them.

We have learned a great deal from developing and teaching the courses. While difficult at times, we have enjoyed our work in developing courses to meet the needs of students in the biological sciences, and hope to continue to adapt our courses to provide the best experience possible for them.

Acknowledgments

References

Kubatko, L., J. Best, T. Nance, and Y. Lou, 2013: Constructing an Undergraduate BioMath Curriculum at a Large University: Implementation of First-Year BioMath Courses at The Ohio State University. This volume, 25–31.

Lynn Arthur Steen, ed., 2005: Math & Bio 2010: Linking Undergraduate Disciplines. MAA, 161pp. NRC, 2003: BIO2010: Transforming Undergraduate Education for Future Research Biologists. National Academies Press, 191 pp.

22

Initial Steps Towards an Integration of Quantitative Thinking into the Teaching of Biology at a Large Public University

Carole L. Hom[1]

Department of Evolution and Ecology, University of California, Davis

Eric V. Leaver, Martin Wilson

Department of Neurobiology, Physiology, and Behavior, University of California, Davis

Name of Institution	University of California, Davis
Size	32,000
Institution Type	Large comprehensive land grant university, offering bachelors through doctoral degrees, with four professional schools
Student Demographic	Students majoring in the life sciences
Department Structure	Life sciences courses are taught in sixteen departments in two undergraduate colleges, with mathematics, statistics, and computer science in separate departments in two other undergraduate colleges

Abstract

Faculty at the University of California, Davis, have addressed the need for integrating quantitative approaches in the biology curriculum by implementing new courses: an introductory two-hour per week modeling course and several one-hour per week quantitative "Q courses" associated with required upper division courses. The new courses are aimed at the general student population, are designed to be taught by biological faculty with minimal input of additional resources, and complement existing specialized modeling courses.

---

[1] clhom@ucdavis.edu

22.1   Course Structure

- Weeks per term: ten-week quarter
- Classes per week/type/length: one lecture per week in lower division course, with computer-based tutorial in all courses
- Labs: one hour computer lab per week, optional
- Average class size: up to 50 per section
- Enrollment requirements: lower division course: integral calculus (may be taken concurrently); upper division courses: any prerequisites that correspond to the accompanying lecture course
- Faculty/dept per class, TA's: coordinating faculty member plus one TA
- Next Courses: students who satisfy appropriate prerequisites may elect upper division courses on modeling in biology taught in life sciences, mathematics, or engineering departments
- Website: http://biosci3.ucdavis.edu/qcourses/

22.2   Introduction

All aspects of biology–the central ideas, the intellectual tools available, the practical methods used in the laboratory, the organization of research effort—have changed dramatically in the last two decades. This has great significance, because biology promises to shape human affairs in the 21st century as much or more than physics did in the 20th century. The changes have occurred so quickly that the way biologists are trained is ill-suited to the emerging reality of biological research, as virtually everyone in the business of biology, whether as a practicing scientist or as a teacher, agrees. Moreover, there is agreement about how undergraduate education must be transformed to prepare biology students for future research and discovery (e.g., see Association of American Medical Colleges and the Howard Hughes Medical Institute 2009; and National Research Council 2003).

Virtually every major problem in biology now requires the use of quantitative models, and the time is fast approaching when quantitative thinking will be as much a part of a biology degree as it is of a physics degree (Hastings and Palmer 2003; Levin *et al*. 1997, Marsteller 2010; Steen 2005). But there is a gap between the current reality and the inevitable future. At present, most biology students lack the familiarity and skills needed to apply or even to acquire the quantitative tools necessary for modern biological research. Many still regard calculus as a filter, rather than a pump that impels them toward success (Steen 1987). Because of this attitude and inertia, faculty members have generally been reluctant to introduce more quantitative material into biology curricula.

How do we get from here to there? This is the question we have tried to answer at the University of California, Davis. We believe it must be tackled at the undergraduate level. While it is admirable to have specialized classes in quantitative biology for graduate students and to cultivate a small cadre of gifted undergraduates acquainted with mathematics and biology, we need changes that affect the average student. Mathematical and physical principles must be seamlessly integrated with biology from the earliest stages of an undergraduate career (Bialek and Botstein 2004). Here we describe our first steps along that path.

At the University of California, Davis, we have introduced two types of new courses: an introductory two-hour (per week) modeling course for freshmen and sophomores and one-hour (per week) quantitative courses ("Q courses" in local parlance) associated with core upper division courses that build on the skills established in the two-hour introductory course. Both types of courses are aimed at the general student population, complement existing upper division modeling courses, and are designed to be taught by biology faculty with minimal input of additional resources. We developed the Q courses to accompany specific biology lecture courses by partnering with faculty who use models but do not regard themselves as quantitative biologists. In this paper, we explain the institutional context for our curricular renovations, describe the courses we have developed, and discuss the successes we have enjoyed and the challenges we continue to face.

22.3   The Institutional Setting

The University of California, Davis (UC Davis), is a large public research university that graduates over 2000 life science students every year. Curriculum changes at our institution and institutions like ours have a major impact on the future of national research (Hastings et al. 2002). Although research universities make up only 3% of the 3,600 colleges and universities in the United States, over 47% of the nation's college graduates receive their undergraduate degrees from a research university (Carnegie Foundation 2001).

   The nature of our institution makes curricular change difficult. First, the size of research universities makes curricular change logistically complex (see also Nance and Kubatko 2013). UC Davis biologists are housed within five autonomous departments within the College of Biological Sciences, with nine undergraduate majors within that college. In addition, fifteen other majors in the College of Agricultural and Environmental Sciences can be considered as "life sciences." Second, governance at our institution imposes a further constraint: power is decentralized and faculty and administrators share governance. Changes cannot be made by administrative fiat, no matter how visionary the administrators. Instead, large numbers of faculty must reach consensus. Third, like many institutions, we have limited amounts of time and money. New courses that require a large amount of faculty or teaching assistant time are not feasible.

   In other ways UC Davis is well positioned for implementing a more quantitative curriculum. First, a substantial number of faculty within the life sciences are trained in both modeling and bench or field biology. Second, all life science majors at UC Davis must take a year of calculus, with biological calculus as an option. Most life science majors also take statistics, which can include a statistics course aimed at a biological audience. Third, we planned the quantitative courses as part of a larger revision of the biology curriculum. The revision entailed discussion and study that led to a document approved by the faculty of the College of Biological Sciences. Both faculty and administrators strongly supported developing an introductory modeling course for lower division biology undergraduates and augmenting upper division options that integrate biology with mathematics or computation.

22.4   Modeling in Biology: the Introductory Course

In Modeling in Biology, a two-hour per week introductory course, we show freshmen and sophomores how quantitative approaches can yield insight into biological problems. We seek to increase students' comfort with quantitative ideas, rather than mastery of a set of skills. We use a practical and intuitive perspective rather than the abstract and rigorous approach taken in mathematics courses. We present mathematics and computation–specifically simulation, algorithms,

Module	Topic	Quantitative Skills and Ideas	Biological Examples and Ideas
1	Introduction to Mathcad	functions, sequences, graphing, scaling	population growth, biomechanics, caffeine metabolism
2	Manipulating data	arrays, Boolean operations, fitting a line to data, correlation vs. causation	beetles and tree ecology
3	Probability and stochastic behavior	probability, stochastic behavior, manipulating arrays	ion channels
4	Rates of change	differential equations	population growth, HIV, ion channels
5	Scaling	data plots (arithmetic, semi-log, and double-log)	scaling, brain size, allometry
6	Sex lives of primates	integrating skills previously introduced	mating systems
7	Protein sequences	matrices, bioinformatics, public database access	amino acid sequences, homology, phylogenetic trees

Table 1. Content of modules used in the course Modeling in Biology

elementary programming, and symbolic computations–to answer a specific biological question. Making a model to address the question may simultaneously answer it while raising others. The cycle of exploration and discovery helps students to think of science as a process and way of knowing (Moore, 1984) rather than as a collection of facts.

Offering the course to freshmen and sophomores has several advantages. We equip students with intellectual and practical tools to use throughout their undergraduate education. The course can also serve as a feeder for other academic programs, e.g., the NSF-funded Undergraduate Biology and Mathematics research program at UC Davis, or the minor in Quantitative Biology and Bioinformatics. Last but not least, this introductory course may broaden students' research opportunities with faculty.

Our course is based around a software package called Mathcad (http://www.ptc.com/products/mathcad/). Mathcad can be readily mastered, uses notation similar to mathematical notation, and can integrate text, images, and computations in a single document. Mathcad is installed in computer labs on our campus and student versions are available under our license agreement for under $20. Students who purchase a license can complete coursework on their own computers. The licenses are valid indefinitely, giving students a powerful quantitative tool to use in future classes or in research.

The Modeling in Biology course implements many of the recommendations of the National Research Council (2003) for mathematics and computer science in biology curricula. Students gain skills in manipulating, processing, and graphically displaying data. They examine data for correlation and suggest experiments to test causation. Students

Now that you've worked with the **if** function a bit, let's use it to create a new **state** vector that tracks the open/closed state of our single channel.

Enter the formula below, then go through it to make sure you understand how it corresponds to the statement described above:

$$\text{state}_t := \text{if}\left(\text{state}_{t-1} = 1, \text{rnd}(1) \geq 0.01, \text{rnd}(1) \geq 0.99\right)$$

4.04

$$\text{state}_t := \text{if}\left(\text{state}_{t-1} = 1, \text{rnd}(1) \geq 0.01, \text{rnd}(1) \geq 0.99\right)$$

Remember how we broke the transitions down into a list of events (1a, 1b, etc.) for the barking dog example above? In the space below, do the same thing for the expression you just typed, including the probability of each event. It's kind of tricky to understand, so take your time. Start by considering what can happen if the channel was open at time t-1, and then consider what can happen if the channel was closed at time t-1.

4.05

Plot your **state** vector, and see if it looks reasonable. Click on the blank region below and create a new x-y plot of **state**$_{\text{time}}$ against **time**. Adjust the y-axis to range from **-1** to **2** instead of the default.
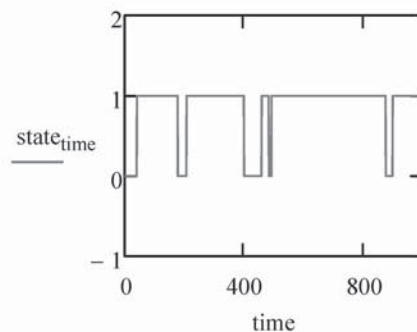
4.06

Figure 1. Excerpt from a module used in Modeling in Biology

carry out computer experiments to test biological hypotheses, and examine the relationships between theoretical constructs and experimental data.

The course consists of weekly lectures and six modules. Each module is based on a Mathcad file, similar in appearance to a word processor document. Each module (see Table 1) includes goals, background about the biological question, instructions, prompts for student work that completes the Mathcad document, and solutions so students can check their work. Modules are independent so instructors can vary their order or add new modules. Module assignments vary from one to two weeks in duration, with about three hours of student effort per week. A weekly lecture by the instructor sets the context for the module and student discussions (for a discussion of this approach, see Boyer Commission (1998)).

Each problem is presented step-by-step, with regions of text and instruction interspersed with regions where students generate computations and document their interpretations. Figure 1 shows excerpts from a module on membrane ion channels. Because we assume no prior knowledge of either ion channels or the mathematics used to model channel opening and closing, the module includes information about both, and instruction in modeling. As the student works through the module, instructions become less specific. Each module culminates with a problem in which the student is given only a general description of how to solve it.

In all modules, we present information and instructions for an action that the student is to perform; in the modules, these appear as unnumbered and numbered regions, respectively. Students type their responses into white regions of the Mathcad file where calculations are immediately computed by Mathcad. In the example of a completed module, students use random events and Boolean logic to model ion channel opening and closing. After an introduction to Boolean logic, students create a number sequence (a vector, in Mathcad's terminology) that describes whether a membrane channel is open or closed. They graph the values versus time and compare the graph to experimental recordings of a single ion channel. For the complete module, see the Ion Channels module at http://biosci3.ucdavis.edu/qcourses/.

22.5 Student Support and Assessment

Students who have difficulty with parts of a module have several options for assistance. Students can work on the module during a designated laboratory period in a computer lab with the instructor and teaching assistant (TA). Students can also email the faculty member and TA with questions. In several offerings of the class we have arranged for virtual office hours in which the TA is available at designated times to interact online with students who have difficulties with the material.

Students upload completed modules to a secure server for grading. The TA grades a subset of pages within each module. Corrections and grades are noted directly in the Mathcad file, and the modules are returned to students electronically. A key is later posted in pdf format. We feel that posting a key is important, but we take two steps to minimize cheating by subsequent students. First, the key shows all the correct mathematics, but omits answers to essay-style exercises. Second, math regions in the key do not produce functional math regions if copied directly into Mathcad. Grades in Modeling in Biology are based on work on the modules, results of an in-class midterm, and a final examination. We cannot administer a computer-based examination to large classes, so exams are on paper, instead of in a Mathcad document.

22.6 Subsequent Revisions: Modeling in Biology

The initial implementation of Modeling in Biology consisted only of lab sessions. After the first offering, we modified the curriculum and course structure. Students acknowledged that the modules familiarized them with the tools of modeling, but they requested more direction about which tools to choose for a new problem. As a response to this, we added a weekly one-hour lecture in which the instructor presented examples of different approaches to modeling and their advantages and drawbacks.

We found that the style of the modules evolved through revisions of the course material. Initially, we included instructions that mostly consisted of keystrokes and verbal descriptions of results. We subsequently included screen-capture images that depict the formula or graph that results from the appropriate keystrokes. They provide students with a less mechanical and more integrative view of the modeling process.

We discovered that many students needed reminders of how to perform Mathcad tasks they had learned several weeks earlier. Rather than including details of these procedures each time they arose in a module, we created short tutorials. We refer to these mini-modules as needed.

Finally, we found that students' mastery of computational skills improved when we included a short midterm exam. To reduce the demands on instructors, we created a bank of test questions from which faculty can draw.

On the whole, Modeling in Biology has gone well. Students seem to like the course and say that they intend to use their new quantitative skills in upper division courses. Two faculty members have requested to teach the course, and we offer it in winter and spring quarters. Three students from Modeling in Biology have gone on to take additional modeling courses, with one participating in a collaborative mathematics and biology training grant.

22.7   Upper Division Courses

In addition to the introductory course, aimed at lower division students, we sought to integrate similar content in large-enrollment upper division courses. A difficulty is that each course is taught by many instructors, with varying degrees of quantitative backgrounds and little incentive to come together to coordinate the effort required for course redevelopment. We avoided it by developing one-hour per week adjunct courses–Q courses–to run concurrently with upper division courses (referred to as parent courses). The Q courses complement the parent course with quantitative treatments of topics covered in it. We have completed modules to accompany parent courses in animal behavior, biochemistry, biomechanics, and neurobiology. They are large-enrollment courses (from 120 to over 400 students per lecture section) offered every quarter.

Like the Modeling in Biology course, the Q courses exist as a series of Mathcad modules in which students complete a series of exercises. The background biology and context for the Q course is covered in the parent course's lecture. There is no separate Q course lecture. Completed modules are submitted to a teaching assistant, who grades a subset of exercises and posts a key as in the Modeling in Biology course. Participation in the Q course by the parent course instructors is at their discretion.

Our goal in developing Q courses was to provide a quantitative supplement to upper division courses. However, we soon found that the details of the goal were subject to interpretations by students and faculty that ran counter to our own vision.

The first myth we sought to dispel was that the Q courses were targeted at high-achievers who wanted to hone their already substantial quantitative skills. On the contrary, we see Q courses as being for all biology undergraduates. Unfortunately, our attempts to dispel the myth generated another misinterpretation–that Q courses are designed to help students with the quantitative aspects of the parent course. Q courses probably do help students but they were not designed for that and may be an inefficient method.

Q courses have some goals independent of the parent course and others that depend on it. Regardless of the parent course, students gain experience using computer software, in particular Mathcad, to solve quantitative problems and visualize solutions. If a student is given a model (e.g., a set of equations), he or she should be able to use a computer to implement it and generate simulations. These are skills that continue naturally from the Modeling in Biology course.

In developing Q courses, we found that the parent course plays a large role in determining the other goals we can set. For example, our neurobiology Q course takes advantage of Mathcad's ability to solve ordinary differential equations, so students are able to construct the Hodgkin-Huxley model of the action potential and see the effects of changing model parameters (see http://biosci3.ucdavis.edu/qcourses). Prior to the Q course, the topic was treated only qualitatively or by demonstrating the model in class. In this case, the Q course has the purpose of putting the student in the driver's seat, getting them to construct the model, seeing the components involved, and understanding the quantitative role of the input parameters.

The qualitative nature of the neurobiology parent course contrasts with a more quantitative biochemistry parent course for which we developed a Q course. Many of the biochemistry models are of acid-base reactions that can be solved without a computer, given a single set of input parameters. However, the equations are non-linear. Students can calculate single points, but understanding how the equations behave is difficult. In the biochemistry Q course, students work with the models graphically, gaining an understanding in their mind's eye. Rather than calculating a solution

at one pH value, they calculate the solutions at 100 pH values and use Mathcad's 3-D graphing abilities to calculate solutions over a 100×100 surface.

In the biochemistry parent course, models are already used and solved, so our goal is an understanding of the equations. In neurobiology, the equations are so daunting to begin with that simply playing with them provides major insight.

22.8 Subsequent Revisions: Upper Division

In planning the upper division Q courses, we consulted with faculty members teaching the parent courses and obtained their input. When possible, we made each module independent of others to accommodate individual instructors' scheduling preferences while allowing lectures to motivate and provide background information. Initially, we envisioned a close association between lecture and quantitative material so that students would enhance their understanding of lecture material by completing exercises in the Q course. This was not always possible in practice.

For example, notation varies between instructors. Students became confused when Q course notation differed from that used in the parent course. Further, when students from three different parent sections of biochemistry simultaneously enrolled in a single biochemistry Q course, we learned that we could not assume a tight connection between lecture and Q course modules. Faculty in the lecture sections covered material in different orders. As a result, some students were able to use modeling exercises to reinforce biological concepts that appeared on the midterm examination in their parent course, but other students saw this material in the Q course after their midterm examination.

This led us to decouple the Q course from the parent course. We gave students in the Q course notice that they might see modeling exercises on a particular topic in conjunction with, well before, or after their lecture course midterm examination. This means that modules, on average, are longer because of the need to introduce biological background information that would otherwise be provided by the parent course. We also encouraged students who had completed the parent course to take the Q course to enrich their knowledge of the parent course topics.

In general, faculty who have taught with Q courses have been pleased with the way the quantitative material complements the parent lecture course. Because of this, faculty members encourage students to take the Q course. To date, we have offered Q courses in biochemistry and animal behavior twice each and in neurobiology four times. The difference in frequency stems from the ability of the home department of the parent course to provide a TA to support the Q course. Until instructional resources become more available, it is unlikely that we will be able to offer Q courses regularly.

22.9 Assessment: Upper Division Courses

The structure of upper division Q courses provides a straightforward means of assessing one measure of their efficacy: the grade in the parent lecture course. We compared the lecture course grades of students who simultaneously enrolled in a Q course for a letter grade (neurobiology—two offerings with combined enrollment of sixteen; biochemistry—one offering with twenty-eight students) with lecture course grades of students who took the lecture course only in the same quarter (neurobiology, combined enrollment of 235; biochemistry, 674). Grades used in the analyses were converted to a 4-point scale: A $= 4.0$, A$- = 3.7$, B $+ = 3.3$, etc.

There appear to be no differences between Q course students and lecture-only students with regard to cumulative grade point average (GPA) at the start of the term. Q course students generally earned higher grades in the lecture course than students enrolled in the lecture course only; they averaged about 0.2 grade points higher (2.7 vs. 2.5). This result is similar for separate students in biochemistry and in neurobiology (Table 2). Further, the impact is greater for women than for men (Table 2) and for weaker students than stronger ones, based on aggregating students by cumulative GPA prior to the term. For example, students with cumulative GPA < 2.75 earned a course grade of 2.0 if enrolled in the Q course versus 1.7 if enrolled in the lecture course only.

Students enrolled in the Q course may outperform lecture-only students because they spend additional time each week on concepts associated with lecture material. Given student schedules with a full load of coursework and, in

	Men Only		Women Only		Biochemistry		Neurobiology	
	Lecture only (n = 402)	Lecture & Q (n = 20)	Lecture only (n = 507)	Lecture & Q (n = 24)	Lecture only (n = 674)	Lecture & Q (n = 28)	Lecture only (n = 235)	Lecture & Q (n = 16)
D or F	10.1%	12.5%	12.4%	0%	11%	3.6%	11.5%	12.5%
C	37.1%	12.5%	30.1%	25%	32.8%	17.9%	37.4%	18.8%
B	38.1%	58.3%	39.1%	55%	40.8%	64.3%	31.9%	43.8%
A	14.8%	16.7%	18.4%	20%	15.5%	14.3%	19.1%	25.0%
GPA	2.5	2.6	2.5	2.9	2.5	2.8	2.5	2.7

Table 2. Percentages of students with a particular lecture course grade, based on enrollment in the lecture only vs. the lecture plus Q course, by gender (with courses pooled) and by course (with gender pooled). Sample sizes shown parenthetically.

many cases, part-time employment and internships, it may be difficult for students to increase study time for a subject without the additional incentive provided by a course.

22.10   General Challenges

The biggest challenge to our curriculum revision has been the conflict between the desire of faculty to include quantitative instruction and the uncomfortable consequences of realizing that vision. For example, biology faculty members were initially enthusiastic about incorporating a lower division modeling course into the curriculum. However, when faced with the question of requiring the course for majors, departments were slow to make this curriculum change (see also Adler 2013). Possible reasons include reluctance to add requirements to an already difficult major or modify existing major requirements to make room for a quantitative requirement; a perception that the course is not germane to a particular major; concern that incorporating what students may perceive as a math course will drive math-phobic students into a similar major in another college within our university.

Similarly, our faculty members were initially eager to augment our upper division offerings with the Q courses but departments lack the funds to assign teaching assistants to the Q course.

Our choice of software, Mathcad, has presented us with successes and challenges. The look of Mathcad documents is reassuring to students. Equations written in Mathcad look more or less like equations on paper. Even complex operations like solving ordinary differential equations can be accomplished visually, without anything that looks like a program. Problems often can be framed in ways that make the most intuitive sense, rather than in the way that is most efficiently processed. A generous student discount establishes Mathcad as an affordable tool for students to use beyond our courses.

However, Mathcad has its drawbacks. We intended to use a worksheet protection feature to prevent students from editing or copying anything more than their own answers in the modules but it was so bug-ridden that we had to abandon our plan. Other Mathcad bugs forced us to include workarounds and other inefficiencies in the modules that distract from the teaching.

Alternatives to Mathcad include Matlab, Excel, R, XPP, Mathematica, and Maple, and there are many criteria on which we could base our software choice, such as ability to do mathematics beyond arithmetic computations (e.g., solve differential equations), ease of use, quality control (i.e., lack of bugs), availability on multiple platforms, cost to students, and popularity (i.e., likelihood it will be used in post-graduate employment). With so many factors potentially affecting our choice of software, it is easy to lose sight of the primary goal of the courses: *to develop quantitative thinking in biology*. The most important consideration is how well a software package can facilitate that goal. We are not training students to use a particular software platform to enhance their marketability. We are teaching them to think quantitatively. In the 21st century, that involves computer software training; but this is a means to our end, not an end in itself.

We have exerted considerable effort to convince others (and ourselves) that Mathcad is the right platform to use for our courses. Faculty agree that students would be well-served by proficiency in one platform used across many classes.

However, confidence that Mathcad is the best platform to choose is so far lacking, and the issue of which to use is often revisited. The unfortunate truth is that we have to choose, and there will always be those who disagree with our choice.

22.11   Conclusions

On the whole, we are pleased with our curricular revision. The lower division modeling course and upper division Q courses provide the general undergraduate population with a biological introduction to quantitative thinking. Because the Q courses are separate, we were able to develop a more quantitative curriculum without having to revise existing lecture courses. However, our efforts to integrate these courses into the biology curriculum have been thwarted by the zero-sum nature of unit requirements, as well as the hyper-democratic and resource-limited environment of our university. While faculty widely agree that quantitative treatments should be added to the biology curriculum, they widely disagree on what should be removed to make room for these.

Acknowledgments

References

Adler, F.R., 2013: Teaching calculus, probability, and statistics to undergraduate life science majors: A unified approach. This volume, 33–38.

Association of American Medical Colleges and the Howard Hughes Medical Institute, 2009: *Scientific Foundations for Future Physicians.* [Available online at http://www.hhmi.org/grants/pdf/08-209_AAMC-HHMI_report.pdf]

Bialek, W., and D. Botstein, 2004: Introductory mathematics and science education for 21st century biologists. *Science,* **303**, 788–790.

Boyer Commission on Educating Undergraduates in the Research University, 1998: *Reinventing Undergraduate Education: A Blueprint for America's Research Universities*. [Available online at http://naples.cc.sunysb.edu/pres/boyer.nsf/]

Carnegie Foundation for the Advancement of Teaching, 2001: *The Carnegie Classification of Institutions of Higher Education: 2000 Edition,* 197 pp.

Hastings, A., P. Arzberger, B. Bolker, A. Ives, N. Johnson, and M. Palmer, 2002: *Quantitative Biology for the* 21 st *Century*. Report from an NSF-funded workshop on Quantitative Environmental and Integrative Biology held at the University of California, San Diego. [Available online at http://www.sdsc.edu/QEIB/QEIB_final.html]

Hastings, A., and M.A. Palmer, 2003: A bright future for biologists and mathematicians? *Science,* **299**, 2003–2004.

Levin, S.A., B. Grenfell, A. Hastings, and A.S. Perelson, 1997: Mathematical and computational challenges in population biology and ecosystems science. *Science,* **275**, 334–343.

Marsteller, P., 2010: Beyond *BIO2010*: Integrating Biology and Mathematics: Collaborations, Challenges, and Opportunities. *CBE—Life Sciences Education,* **9**, 41–42.

Moore, J.A., 1999: *Science as a Way of Knowing: The Foundations of Modern Biology*. Harvard University Press, 544 pp.

Nance, T., and L. Kubatko, 2013: Constructing an Undergraduate BioMath Curriculum at a Large University: Developing First Year BioMath Courses at The Ohio State University. This volume, 149–154.

National Research Council, 2003: *Bio 2010: Transforming Undergraduate Education for Future Research Biologists.* The National Academies Press, 192 pp.

Steen, L.A., 1987: *Calculus for a New Century: A Pump, Not a Filter*. MAA Notes No. 8, 258 pp.

Steen, L.A., 2005: The gift of mathematics in the era of biology. *Math & Bio 2010: Linking undergraduate disciplines*. L.A. Steen, Ed., Mathematical Association of America, 13–26.

III
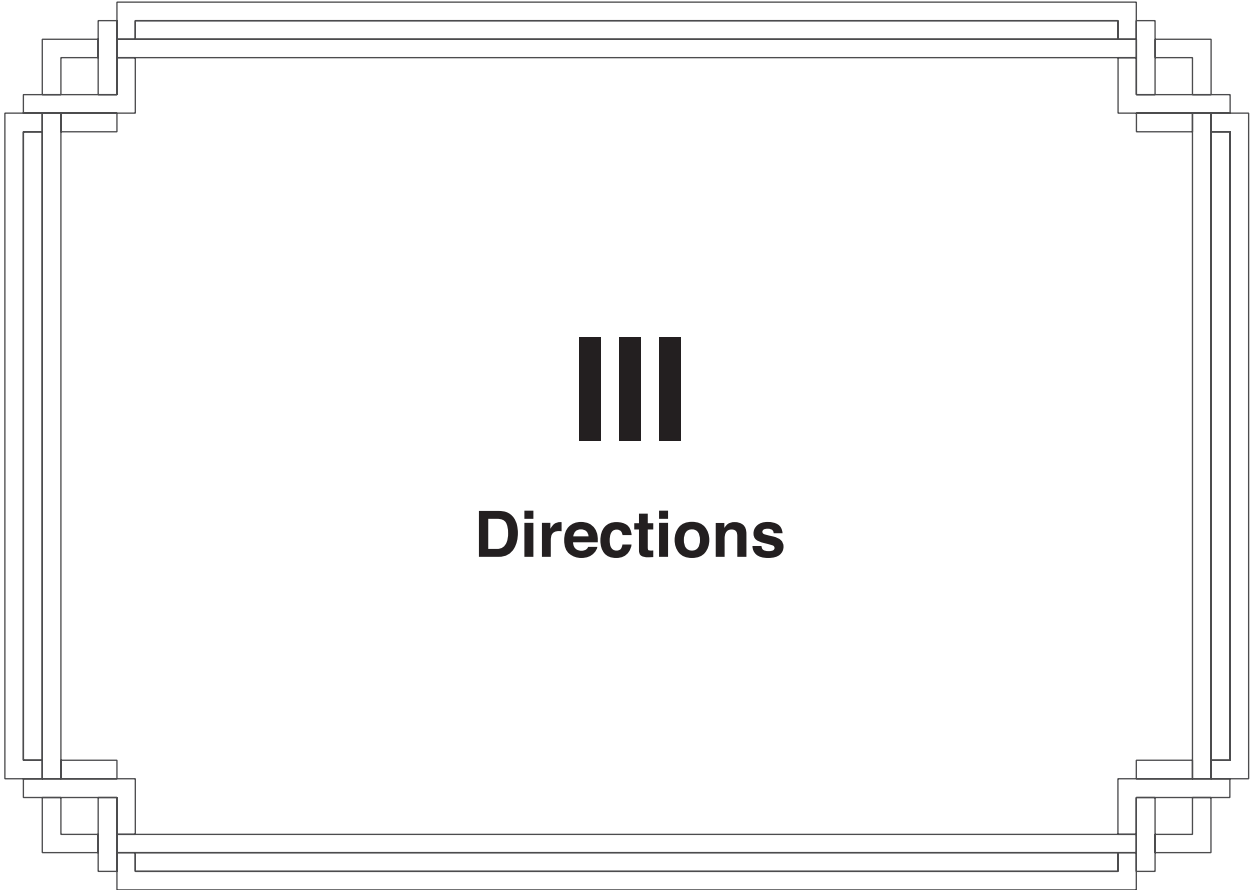
Directions

Introduction

Each of the papers in the Directions section addresses some perceived, but largely unmet, need in curricular development for undergraduate mathematical biology. Of course the question of what developments ought to occur is a matter of opinion. Each of these papers lays out a strong case and offers insights on how to introduce and develop the topics. As editors, we endorse these calls for a change in emphasis.

The section begins with the paper *Integrating Statistics into College Algebra to Meet the Needs of Biology Students*, by Sheldon Gordon of Farmingdale State University and Florence Gordon of the New York Institute of Technology. These authors are well known for their efforts to revitalize college algebra and precalculus courses. They argue for an algebra course designed to prepare students for statistics rather than calculus. The course would be more relevant to the life science students who constitute a large portion of the enrollment. The authors offer many suggestions for ways to bring statistical ideas and methods into the college algebra course while recommending a greater focus on concepts rather than techniques. Readers interested in precalculus courses should also see the paper by Ardis and Subramanian in the Processes section.

In *Motivating Calculus with Biology*, Sebastian Schreiber of the University of California at Davis argues that mathematics for biology should emphasize mathematical modeling. While all mathematics books contain word problems, some with biological themes, the typical word problem falls short of providing students with experience in mathematical modeling. A word problem provides just enough data to uniquely determine parameter values, while a modeling problem provides an excess of stochastic data that requires statistical methods to match to model parameters. Where a word problem ends with a quantitative answer, a modeling investigation continues with a comparison of the mathematical answer with biological data. Other issues important in mathematical modeling are similarly missing from the typical word problem. Schreiber offers examples with two common themes: scaling laws and population growth.

In *Computational Systems Biology: Discrete Models of Gene Regulation Networks*, Ana Martins, Paulo Vera-Licona, and Reinhard Laubenbacher of the Virginia Biomathematics Institute present a primer on molecular biology and Boolean network analysis, focusing on the *lac* operon found in *Escherichia coli.* This operon consists of a collection of genes that allow the cell to adjust to changes in the environment. While the biological system can be modeled using a variety of tools, Boolean network analysis has the advantage of being accessible to students who do not have any calculus background—the material presented in this paper forms a portion of a workshop the authors have conducted for high school teachers. Boolean network analysis could therefore be used to introduce mathematical modeling ideas much earlier in the curriculum than is currently the case. The reader interested in computational biology should also look at the papers by Attele and Hrozencik and by Robeva, Davies, and Johnson in the Models section and the paper by Lee and Boyd in the Processes section.

The Directions section concludes with the paper *Creating Quantitative Biologists: The Immediate Future of SYMBIOSIS* by Darrell Moore and colleagues at East Tennessee State University. SYMBIOSIS is an interdisciplinary curriculum project that focuses on linked mathematics and biology courses at the freshman level. The authors offer a critique of standard biology textbooks and discuss how to make biology courses more quantitative and more conceptual. While the focus of the paper is more on biology education than mathematics education, the issues are also relevant to mathematicians. Students who take mathematics courses with applications in physics take concurrent or subsequent physics courses that make use of the mathematics. In contrast, students whose mathematics courses have applications in biology are generally unable to take a concurrent or subsequent course in biology that uses the mathematics. No amount of success in mathematics curriculum development will matter unless the shoots propagated

in a mathematics course ultimately flower in a biology course. The reader interested in interdisciplinary freshman courses will also want to read the article by Mark MacLean in the Processes section.

We hope that the four papers in this section will stimulate further discussion of these topics and other broader issues of curriculum reform. Biology is a diverse area, as are the mathematical needs of biologists. The last word on what mathematical topics should be offered to biologists and when they should be offered will not be spoken for a long time. It is best to emphasize these discussions now, before a consensus on curriculum needs has formed. As is obvious in other areas of curriculum development, it is harder to renovate a curriculum area that has crystallized into a rigid form than it is to innovate in an area that is still being shaped.

23

Integrating Statistics into College Algebra to Meet the Needs of Biology Students[†]

Sheldon P. Gordon[1]

Department of Mathematics, Farmingdale State College

Florence S. Gordon

Department of Mathematics, New York Institute of Technology

Size	6500
Institution Type	Medium-sized state college with focus on technology
Student Demographic	Diverse student body with many first-generation and minority students
Department Structure	Mathematics and Biology are individual departments in the College of Arts and Sciences

Abstract

Most of the mathematics used by students in introductory biology and other laboratory science courses arises in the laboratory when students are faced with experimental data to analyze and to use as the basis for answering predictive questions. In this article, we build a case for integrating, in natural ways, significant amounts of statistical ideas and methods into courses in college algebra and precalculus to provide students with the mathematical skills they use in biology and other science courses. We provide examples to illustrate how statistics can be incorporated in ways that are natural extensions and applications of mathematical topics that are usually included in mathematics courses.

23.1 Course Structure

- Weeks per term: 15

- Classes per week/type/length: two 75-minute and one 50-minute class each week

---

[1] gordonsp@farmingdale.edu

- Labs per week/length: none
- Average class size: 30 students per section
- Enrollment requirements: For high school students and freshmen, though many postpone taking the mathematics course as long as possible.
- Faculty/dept per class, TAs: Taught by one mathematics instructor (usually a full-time instructor).
- Next course: The purpose of the course is to teach the mathematical ideas and methods needed by students who plan to major in biology or who want a mathematical approach that reflects the needs of biology and other laboratory sciences. It is also taken by some business majors. The biology majors will subsequently take at least one semester of calculus and one semester of statistics.
- Website: http://www.farmingdale.edu/faculty/sheldon-gordon/

23.2   Introduction

Each year, some one million students (Lutzer et al. 2007) take college algebra and related courses. Most of the courses were designed to prepare students for the mainstream calculus sequence by focusing almost entirely on developing the algebraic skills needed for calculus.

However, only about 10% of those who complete college algebra successfully ever go on to take Calculus I and virtually none have gone on to take Calculus III (Dunbar 2006). This suggests that offering college algebra courses to prepare students for calculus is doing a disservice to the vast majority of the students.

The challenge we face is to change the focus in these courses to make them meaningful to the departments, especially the biology department, that require them, so as to better meet the needs of the students and the disciplines that are our clients and partners.

23.3   Why do so Many Students Take the Courses?

The overwhelming majority of students take college algebra and related courses to fulfill general education requirements (particularly at large state universities and state colleges) or to fulfill the mathematics requirements of other departments. One of the partner disciplines that sends us a large proportion of our students at this level is biology. But, according to leading educators from biology and from other partner disciplines (Ganter and Barker 2004), their students do not need or ever use the algebraic manipulation that is a hallmark of most of these courses. Corporate and government leaders say we need a quantitatively literate workforce and public to compete in today's technological world and function effectively as citizens (Steen and Madison 2003). The primary mathematics needed – by the other disciplines, for today's workplace, and for effective citizenship – is more knowledge of statistics, not computational skill in algebra.

In many states, a course in college algebra is the primary mathematics requirement for students planning to become elementary and middle school teachers. The traditional college algebra course with its predominant focus on algebraic skills is not particularly appropriate for these students, especially if they will be teaching in schools that use NCTM Standards-based curricula.

Across the country, traditional college algebra courses have been identified as the primary barrier preventing students from gaining access to careers in quantitative fields. For instance, the Economic Development Council of San Antonio has identified the college algebra courses offered in the city's colleges as an impediment to the city not having the quantitatively-trained workforce needed for the high-tech economy that they envision as the future of San Antonio. In response, the mayor has appointed a taskforce, including representatives of all eleven public and private colleges in San Antonio and representatives of business, industry, and government to consider the problem and change the nature of the college algebra experience.

Most students who take college algebra are poorly served by the traditional courses. There is a need to change the focus to better serve the students who take them, to meet the increasingly quantitative needs of most other disciplines, and to meet the needs for a well-educated workforce and citizenry that can function effectively in a quantitative environment. In all of these instances, college algebra has little to do with moving on to calculus.

These issues are discussed in considerably greater detail in (Gordon 2009) and in the articles in the volume edited by Hastings (Hastings 2006).

23.4 What do the Students Need from these Courses?

What do other disciplines, particularly the biological sciences, want their students to bring to their courses from the mathematics courses they require? The MAA's committee on Curriculum Renewal Across the First Two Years (CRAFTY) recently brought together leading educators from seventeen quantitative disciplines in workshops to discuss the current mathematical needs of their disciplines and to make recommendations about what should be in the mathematics offerings to satisfy their needs. The seventeen discipline reports and a summary of all Curriculum Foundations project recommendations appear in (Ganter and Barker 2004); a discussion of their implications for courses at the college algebra and precalculus level appears in (Gordon 2009). The reports provided background for the recommendations on the undergraduate mathematics curriculum in the MAA's *Curriculum Guidelines 2004* (Lutzer et al. 2004) developed by CUPM (the Committee on the Undergraduate Program in Mathematics).

For almost all of the disciplines involved in the project, the focus was on courses below calculus, particularly college algebra. As mentioned, virtually all the disciplines see a need for a different focus in the mathematical training of their students, one that stresses conceptual understanding, mathematical modeling and problem solving, and a heavy emphasis on statistical reasoning and interpretation of real-world data. Among the points that the biologists made were

1. The collection and analysis of data that is central to biological investigations inevitably leads to the use of mathematics.

2. Mathematics provides a language for the development and expression of biological concepts and theories. It allows biologists to summarize data, to describe it in logical terms, to draw inferences, and to make predictions.

3. Statistics, modeling, and graphical representation should take priority over calculus.

The biologists said:

> Biology students need to understand the meaning and use of variables, parameters, functions, and relations. They need to know how to formulate linear, exponential, and logarithmic functions from data or from general principles. They must also understand the basic periodic nature of the sine and cosine functions. It is fundamentally important that students are familiar with the graphical representation of data in a variety of formats (histograms, scatterplots, pie charts, log-log and semi-log graphs).

Perhaps most telling is the biologists' comment that "The current mathematics curriculum for biology majors does not provide biology students with appropriate quantitative skills."

One of the themes in virtually every discipline report in the Curriculum Foundations document is the need for more statistical training. In discussions with faculty in biology and the other laboratory sciences (such as chemistry and earth and space science), it has become clear that the mathematical limitations of their students appear most dramatically in the laboratory when they are asked to analyze and interpret experimental data. In most of the courses in these fields, little if any mathematics arises in the classroom; it is in the labs that students need to apply mathematics and that mathematics is almost always statistical. Typically, they need to find trends (usually linear) in a data set and to answer predictive questions (that is, solve the resulting equation). These are the primary connections to topics in college algebra courses. Many of the social sciences, especially business, focus on using data to produce models that can be used to answer predictive questions. Their students also need more exposure to statistics.

At many schools, college algebra is the mathematical prerequisite for the first course in statistics. The introductory statistics course is already crammed with too many topics, and it is usually not possible to cover everything that students should know. One solution is to require a second statistics course, but crowded curricula make that an unrealistic option. A better solution is to provide an introduction to standard statistical topics in the prerequisite course, so that the full treatment in statistics courses can go more quickly and smoothly.

Repeating the statistics topics may seem to be a waste of time. However, it is not. Our students see the equation of a line in pre-algebra classes, again in elementary algebra, in intermediate algebra, in college algebra, and in precalculus.

Yet, sadly, many students still seem not to have fully mastered the concepts or the ability to find the equation of a line in Calculus I, despite the repetition. And this is one of the simplest things that they see in their mathematical training. The concepts and methods of an introductory statistics course are less intuitive and are much broader in variety. Despite this, we expect the students who take a one semester introductory statistics course to understand and be able to apply them based on a single exposure in one semester. Also the students are mathematically weaker than the ones who go through the traditional mathematics curriculum toward calculus. So, it is unrealistic to assume that one exposure to the ideas and methods of statistics is sufficient. Students need to see statistical ideas repeatedly, just as calculus-bound students need to see many techniques and ideas repeatedly.

Accordingly, we feel that there are compelling reasons to try to integrate a substantial amount of statistical reasoning and methods into college algebra and related courses.

23.5   Statistical Analysis and Reasoning

The challenge we face is finding ways in which statistical ideas and data analysis can be integrated into a college algebra course so as to support and reinforce the concepts and methods of college algebra. Data analysis, in the sense of fitting functions to data, has become a common topic in most textbooks as a way in which interesting and realistic applications of families of functions (linear, exponential, power, logarithmic, polynomial, and even sinusoidal) covered in the course can be applied. The extent to which this material is actually used by instructors is, unfortunately, uncertain.

Several reform college algebra texts include a chapter that looks at some simple statistical ideas such as finding the center and spread in a data set and displaying data graphically. However, the texts have been written so that the course will satisfy quantitative literacy requirements for students who will take no more mathematics. They do not meet the needs of students in biology and the other laboratory sciences, nor do they provide a broad introduction to statistical ideas. Also, the statistical ideas arise only in the free-standing chapter, so they are neither extensive nor integrated into the entire course.

How then could we incorporate statistical ideas and methods in a natural way throughout an entire college algebra course? The question is complicated by the wide variety of audiences for the course, including those who have not seen statistics previously, and who would be best served by a good introduction, and those who have previously taken a statistics course, and who would be best served by seeing many of the same ideas in a new and more mathematical context.

Many students in college algebra courses lack a sense of what mathematical notation is all about–the symbols that stand for variables, the types of variables that arise in connecting mathematics to the real world where everything is not mindlessly x and y, and the notion of the scales in reading and interpreting (let alone creating) graphs and charts. All the concepts can be reinforced by looking at real-world data and creating tables and graphs. This gives a wonderful opportunity to stress the difference between the dependent and the independent variables and the practical meaning of the domain and range of functions. These are some of the key notions that biologists called for in their report in the Curriculum Foundations project (Ganter and Barker 2004).

In introducing different types of behavior for functions (increasing versus decreasing, concave up versus concave down, turning points, and inflection points), we can look at a normal distribution as an example. It provides an effective way of reinforcing the notion of the mean (the center of a data set) and the standard deviation (the spread in a data set). Subsequently, the idea of the z-value associated with a measurement x can be introduced as nothing more than a linear function relating the variables.

In discussing the regression line to fit a data set, particularly if it is laboratory data, it is natural to point out that there could be many different sets of data for the same experiment, each leading to a different regression line. A computer graphics simulation provides visual support to make the different lines come to life and to investigate the effects of different sample sizes. We have developed an effective version of such a simulation in Excel that is available to any interested reader (Gordon cited 2012). We illustrate the possible results in Figures 1 and 2, which show, respectively, the outcomes associated with samples of size $n = 4$ and $n = 20$. In the first case, we see that many of the sample regression lines have slopes that vary dramatically from that of the population's regression line (the heavy line in the figure); in the second case, almost all of the sample regression lines have slopes that are close to that of the population regression line.
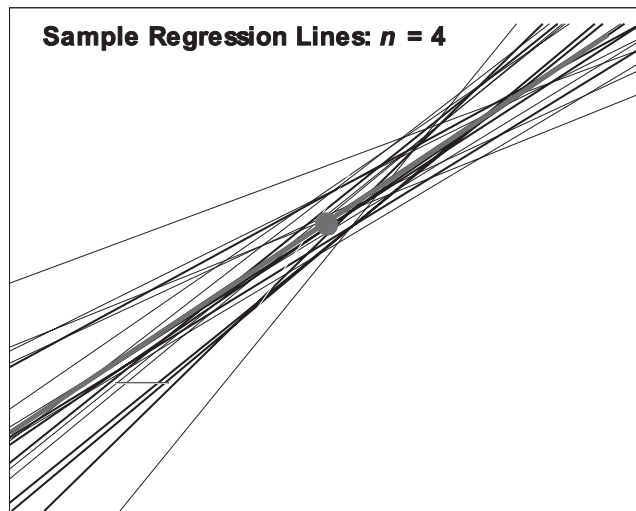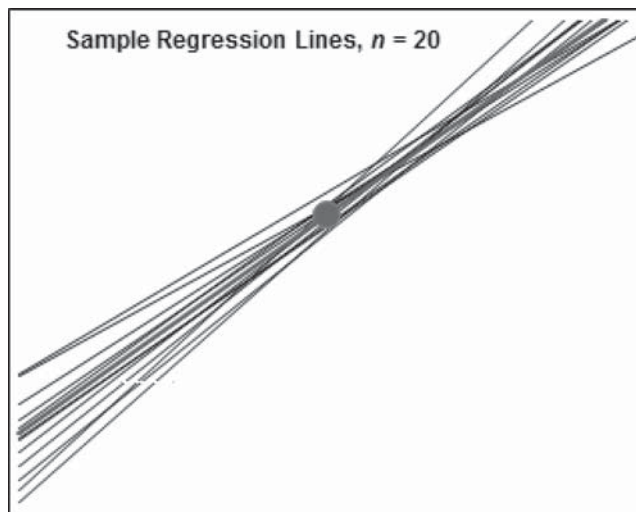
Figure 1. Sample size $n = 4$

Figure 2. Sample size $n = 20$

Such an investigation provides a wonderful opportunity to stress two of the key themes in statistics—the effect of sample size on the outcome and the variation that occurs within a sample and between different samples. These notions are critical for anyone who will be working with laboratory data.

At a later stage in the course, in discussing shifting and stretching of functions, we can return to the normal distribution function

$$N(x) = \frac{1}{\sigma\sqrt{2\pi}}e^{-(x-\mu)^2/2\sigma^2}$$

that is centered at the mean μ and has standard deviation σ. We can emphasize the fact that the standard normal distribution curve has been shifted horizontally by an amount equal to μ because of the presence of the $(x - \mu)$ term, stretched or squeezed horizontally by the effect of σ^2 as a divisor in the exponent, and stretched or squeezed vertically by the effect of σ as a factor in the denominator of the coefficient.

We can also look at the normal distribution function as an example of a composite function. Unlike the artificial functions we typically use to illustrate the idea of a function of a function, the normal distribution provides a meaningful example that the students will see again. This makes the concepts more meaningful to the students and provides motivation that is often not present in the standard treatment of composite functions.

Subsequently, we can introduce the notion of the distribution of sample means. It consists of the means of all possible samples of a given size n drawn from an underlying population having mean μ and standard deviation σ. The Central Limit Theorem, which is probably the single most important result in inferential statistics, provides information on the characteristics of the population of sample means. It tell us

1. The mean of the distribution is $\mu_{\bar{x}} = \mu$.
2. The standard deviation of the distribution is

$$\sigma_{\bar{x}} = \frac{\sigma}{\sqrt{n}}.$$

3. If the underlying population is roughly normally distributed, then the sample means are also normally distributed.
4. If the sample size n is sufficiently large, then the distribution of sample means is roughly normally distributed whatever the underlying population is. Typically, samples of size $n > 30$ are sufficiently large to assure approximate normality.

The distribution of sample means provides a wonderful opportunity to reinforce the notions of shifting and stretching functions. A computer graphics simulation that draws repeated random samples and displays their means in a histogram can provide visual and numerical support. We would start with the case of large samples means, so that the distribution of sample means will be roughly normal. The distribution of sample means is centered at the mean of the underlying population, μ, so the center of the histogram representing the sample means is typically very close to the center of the underlying population, and the numerical value for the mean of all the sample means typically comes out close to the population mean μ. Therefore, we have the same horizontal shift in the distribution of sample means as in the underlying population.

The spread in the distribution of sample means clearly depends on the sample size n. Using the simulation with large numbers of samples of size $n = 4, 9, 16$, and 25, it quickly becomes clear to the students, both visually from the graphs and numerically from the calculated values of the mean of the standard deviations of the samples, that the spread is, respectively, about $1/2$, $1/3$, $1/4$, and $1/5$ of σ. Since we are dealing with fractional multiples of σ, the distribution of sample means is clearly equivalent to a horizontal squeeze of a normally distributed population and the formula that quickly materializes is

$$\sigma_{\bar{x}} = \frac{\sigma}{\sqrt{n}}.$$

Once the Central Limit Theorem has been introduced, it is a simple matter to develop the idea of a confidence interval for the mean of an unknown population and tie it to the standard problem that arises in many laboratory experiments where the student is expected to estimate the mean of a population based on a single experimental sample.

In discussions with some biology faculty, it has become clear that there is also a need to introduce hypothesis testing. It is a fundamental statistical tool, particularly in an introductory biology course that addresses genetics. We have not been able to devise a natural way to integrate that into the flow of topics that would normally be considered part of a course at the college algebra level. The alternatives appear to be either to incorporate hypothesis testing as part of an additional unit on probability (and there simply does not appear to be adequate time in a four-hour course to do that) or to introduce it on its own without it being a natural application of a mathematical topic being addressed.

23.6   Classroom Experiences

To implement the ideas outlined above, we have developed a full set of classroom materials, including text materials and accompanying Excel spreadsheets. Much of it has been tried in a new four-credit, four-hour per week semester-long precalculus/college algebra course designed for bioscience and business students. Not all of the statistical ideas and methods have been tried yet; in particular, the ideas relating to the Central Limit Theorem and confidence intervals have not been covered, but most of the others have been implemented.

The fact that the course is intended for both the bioscience students and business students make for some interesting compromises, but also provide the opportunity to see how different kinds of students reacted to the materials. For the bioscience students, the course serves as a precalculus experience. For most of the business students, the course is a

terminal one, although some of the specific majors within our business school require a subsequent business calculus course. While we view the course as something that the students in both programs should take early in their academic careers, both groups tended to put it off as long as possible. So, most of the business students previously had taken a required introductory statistics course offered through the business school, while virtually none of the bioscience students had had any formal experience with statistics, other than what they may have done in lab reports in some of their biology courses.

With both groups, the reaction to including the statistical ideas was positive. Rather than being bored by the repetition, the business students seemed happy with the reminders about what they had seen in their first statistics course and it seemed to help them make new connections between the mathematical concepts and the statistical ones. The bioscience students seemed to find that the statistical ideas made the course more valuable because they saw direct connection to what they had been doing in their lab courses. This was facilitated by the gentle introduction of statistical ideas with little formal emphasis on the computations; that was left for a subsequent statistics course, which we hope the students might consider taking.

Although the statistical ideas were not tested on exams, the students generally did better on test problems on topics that were enhanced by some of the statistical ideas than students in comparable courses have done in recent years. For instance, the students had no trouble with problems on shifting and stretching functions, which was reflected in the examples on the normal distribution curve; in previous years, this kind of problem invariably elicited numerous "solutions" that displayed absolutely no idea of what was going on, while this year, virtually every student solved them easily.

23.7   Some Concluding Thoughts

At most schools, college algebra is the prerequisite for introductory statistics, though virtually none of the ideas and algebraic techniques in traditional college algebra courses are relevant to introductory statistics. Introductory statistics courses are typically much too crowded and rushed and many students are poorly served by them. If a significant amount of statistical thinking can appear in the prerequisite college algebra course, as we have done, we believe that it can make the subsequent statistics course more reasonable and more successful for many of the students.

Integrating statistics into college algebra and other math offerings will become increasingly imperative as the Common Core in Mathematics program begins to be implemented. Already approved by at least 45 states, this curriculum calls for introducing statistical ideas starting in sixth grade and anticipates that *every* high school graduate will have the equivalent of a solid introductory statistics course. Statistics will be a thread throughout the curriculum, but will not be integrated into the other mathematics topics. Students coming out of the Common Core will need reminders about statistical ideas, as discussed here. Eventually, the introductory statistics course as we know it today will become a new developmental offering, while those students who really need statistics in college will start with what we currently consider a second course.

References

Dunbar, S., 2006: Enrollment Flow to and from Courses below Calculus, in *A Fresh Start for Collegiate Mathematics: Rethinking the Courses below Calculus*, N. B. Hastings, Ed., MAA Notes, Mathematical Association of America.

Ganter, S. and W. Barker, editors, 2004: *The Curriculum Foundations Project: Voices of the Partner Disciplines*, Mathematical Association of America.

Gordon, S.P., 2009: What's Wrong with College Algebra?, *PRIMUS*, **18**, 516–541.

Gordon, S.P., cited in 2012: DIGMath Software Packages [Available online at http://www.farmingdale.edu/faculty/sheldon-gordon/].

Hastings, N.B. Ed., 2006: *A Fresh Start for Collegiate Mathematics: Rethinking the Courses below Calculus*, MAA Notes #69, Mathematical Association of America.

Lutzer, D.J., S.B. Rodi, E.E. Kirkman, and J.W. Maxwell, 2007: *CBMS 2005*: *Statistical Abstract of Undergraduate Programs in the Mathematical Sciences in the United States*, American Mathematical Society.

Pollatsek, H., W. Barker, D. Bressoud, S. Epp, S. Ganter, and B. Haver, 2004: *Undergraduate Programs and Courses in the Mathematical Sciences: CUPM Curriculum Guide 2004*, Mathematical Association of America.

Steen, L. and B. Madison, 2003: *Quantitative Literacy: Why Numeracy Matters for Schools and Colleges*, Woodrow Wilson National Foundation Press, Princeton, NJ.

24

Motivating Calculus with Biology

Sebastian J. Schreiber[1]

Department of Evolution and Ecology, University of California, Davis

Name of Institute	University of California, Davis
Size	32,000
Institution Type	Large comprehensive land grant university, offering bachelors through doctoral degrees, with four professional schools
Student Demography	Students majoring in the life sciences
Departmental Structure	Life sciences courses are taught in sixteen departments in two undergraduate colleges, with mathematics, statistics, and computer science in separate departments in two undergraduate colleges

Abstract

Applications of calculus concepts to real, data-driven biology problems provide students with a glimpse of the "unreasonable effectiveness" of mathematics in providing fundamental insights into biological processes. These applications can motivate key calculus concepts when chosen appropriately, provide a vehicle that links concepts throughout a calculus course. To illustrate this thematic development, I show how biological scaling laws and models of population growth link topics in precalculus fundamentals, derivatives, optimization, integration, probability, and differential equations.

24.1   Course Structure

- Weeks per term: 10-week quarter
- Classes per week/type/length: three 50-minute lecture class meetings per week
- Labs per week/length (if any): one 50-minute lab each week
- Average class size: 250 students

---

[1] sschreiber@ucdavis.edu

- Enrollment requirements: Entering students
- Faculty/dept per class, TAs: One mathematics faculty and 4 TAs.
- Next Course: N/A

24.2   Introduction

As Leo Breiman said, calculus has a right hand and a left hand.[2] On the right hand is the rigorous foundation of limits and infinitesimals. The left hand thinks physically in terms of rates of change and accumulated change. In the historical development of calculus, the left hand came first, driven by applications to planetary motions, classical mechanics, and optics. Only hundreds of year later did the rigor of the right hand enter and put calculus on a firm mathematical foundation. Given that calculus is the entry level mathematics course for most undergraduate programs, we as instructors are faced with the challenge of balancing the amount of time students spend with each hand. The right hand involves precise definitions and the derivation of properties of and relations between them. It exposes students to the elegance, power, and subtlety of mathematical rigor. The left hand involves developing and analyzing models to answer real world questions. It exposes students to the effectiveness of mathematics in describing the natural world. The right balance depends on the goals of the program. Hence, rather than presenting my personal view of the right balance of rigor and applications, I will illustrate how arming the left hand with biological applications can motivate and link a diversity of calculus concepts.

Why use biological applications? My answer comes in three parts. First, from a scientific perspective it is quite likely, in the words of Joel Cohen, that "Mathematics is biology's next microscope, only better; biology is mathematics' next physics, only better" (Cohen 2004). Mathematics can help extract patterns from large biological data sets and provide a theoretical framework for developing hypotheses for mechanisms underlying biological processes. Alternatively, the complexity of living things and how they interact is motivating the development of new mathematics. Calculus can provide students with their first exposure to the developing synergy between the two disciplines. Second, there are more students majoring in biology than physics (e.g., 64,611 biology bachelor's degrees conferred in 2004–05 versus 18,905 in physics). Thus, including some biological examples into calculus is likely to interest (and hopefully excite!) a larger number of students. Finally, there exists a rich collection of biological applications of calculus. Many of them require a minimal biological background, are supported by data sets, and can create biological themes that can be sustained throughout the calculus curriculum.

To illustrate how biological applications can motivate and connect calculus concepts, I present two classes of applications, scaling laws and population growth. My discussion of them is far from exhaustive and should be viewed as presenting the tip of the iceberg. Pedagogical suggestions are kept at a minimum. When discussing the topics in my classes, I have students (through an instructor-student dialog) identify the main questions, determine an appropriate set of assumptions, develop and analyze a model, and evaluate the model (e.g., comparing to a data set, interpreting the results from a biological perspective, etc.). After presenting the two applications, I provide a description of a topic from evolutionary biology—the growth-reproduction tradeoff—that could serve as a group project. The project combines ideas from scaling laws and population growth and can provide an opportunity for students to learn about collaboration, to delve deeper into an application, and to synthesize a diversity of calculus topics.

24.3   Scaling Laws

Scaling laws are a fundamental modeling concept in all the sciences. They describe how one quantity y (e.g,. respiration rate, strength, etc.) scales with respect to another quantity x (e.g,. body size). Scaling laws typically involve power functions $y \propto x^b$, a class of elementary functions that appear in most calculus courses. Although calculus students have seen them in pre-calculus, it is unlikely that they were exposed to modeling with them. Hence, revisiting these functions and their properties in modeling keeps students slightly off balance (i.e., they don't assume right away that this stuff is easy) and maintains their interest. I will illustrate how to motivate scaling laws in biology and how they can make repeated appearances throughout a calculus course.

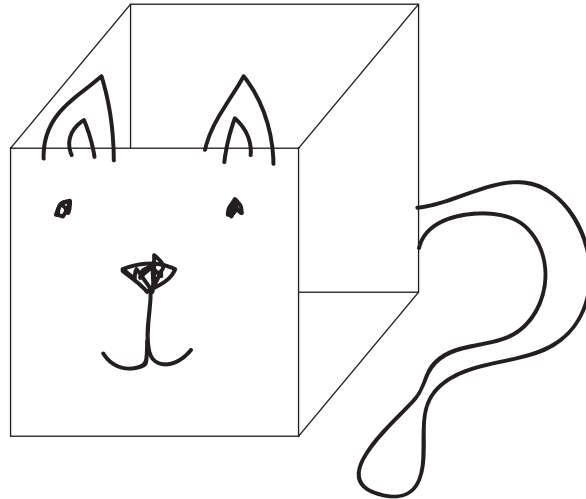
[2] With apologies to Leo Breiman.

Figure 1. A Cubical Critter

J. B. S. Haldane's 1926 article, *On being the right size* (Haldane 1926), provides many wonderful examples of scaling laws in biology. For example, when discussing the challenges faced by large and small organisms, Haldane writes

> To the mouse and any smaller animal it [gravity] presents practically no dangers. You can drop a mouse down a thousand-yard mine shaft; and, on arriving at the bottom, it gets a slight shock and walks away, provided that the ground is fairly soft. A rat is killed, a man is broken, a horse splashes. For the resistance presented to movement by the air is proportional to the surface of the moving object. Divide an animal's length, breadth, and height each by ten; its weight is reduced to a thousandth, but its surface only to a hundredth. So the resistance to falling in the case of the small animal is relatively ten times greater than the driving force.

> An insect, therefore, is not afraid of gravity; it can fall without danger, and can cling to the ceiling with remarkably little trouble. It can go in for elegant and fantastic forms of support like that of the daddy-longlegs. But there is a force which is as formidable to an insect as gravitation to a mammal. This is surface tension. A man coming out of a bath carries with him a film of water of about one-fiftieth of an inch in thickness. This weighs roughly a pound. A wet mouse has to carry about its own weight of water. A wet fly has to lift many times its own weight and, as everyone knows, a fly once wetted by water or any other liquid is in a very serious position indeed. An insect going for a drink is in as great danger as a man leaning out over a precipice in search of food. If it once falls into the grip of the surface tension of the water—that is to say, gets wet—it is likely to remain so until it drowns. A few insects, such as water-beetles, contrive to be unwettable; the majority keep well away from their drink by means of a long proboscis.

To interpret these comments mathematically, we can begin by viewing all organisms as cubical critters characterized solely be their size differences (Figure 1). If L is the length of one side of the cubical critter, then it has a surface area of $6L^2$ cm^2, and a volume of L^3 m^3. If we assume that the cubical critters are "ugly bags of mostly water,"[3] then a critter of length L weighs $m = L^3$ grams. Hence, surface area is proportional to $m^{2/3}$ and the ratio of mass to surface area is proportional to $m^{1/3}$. Hence, the larger you are, the harder you fall. Conversely, the ratio of surface area to mass is $m^{-1/3}$. Therefore, the smaller you are, the more water weight you carry per unit biomass when you get wet.

There are many data sets that can be modeled by scaling laws. One of my favorites is the mass lifted by an Olympic weightlifter versus his body mass (Figure 2). Assuming that Olympic weightlifters are geometrically similar and that

---

[3] Star Trek fans may remember this line as an alien's description of humans as mostly water encased in a bag of skin. The "ugly" part is a matter of extraterrestrial taste.
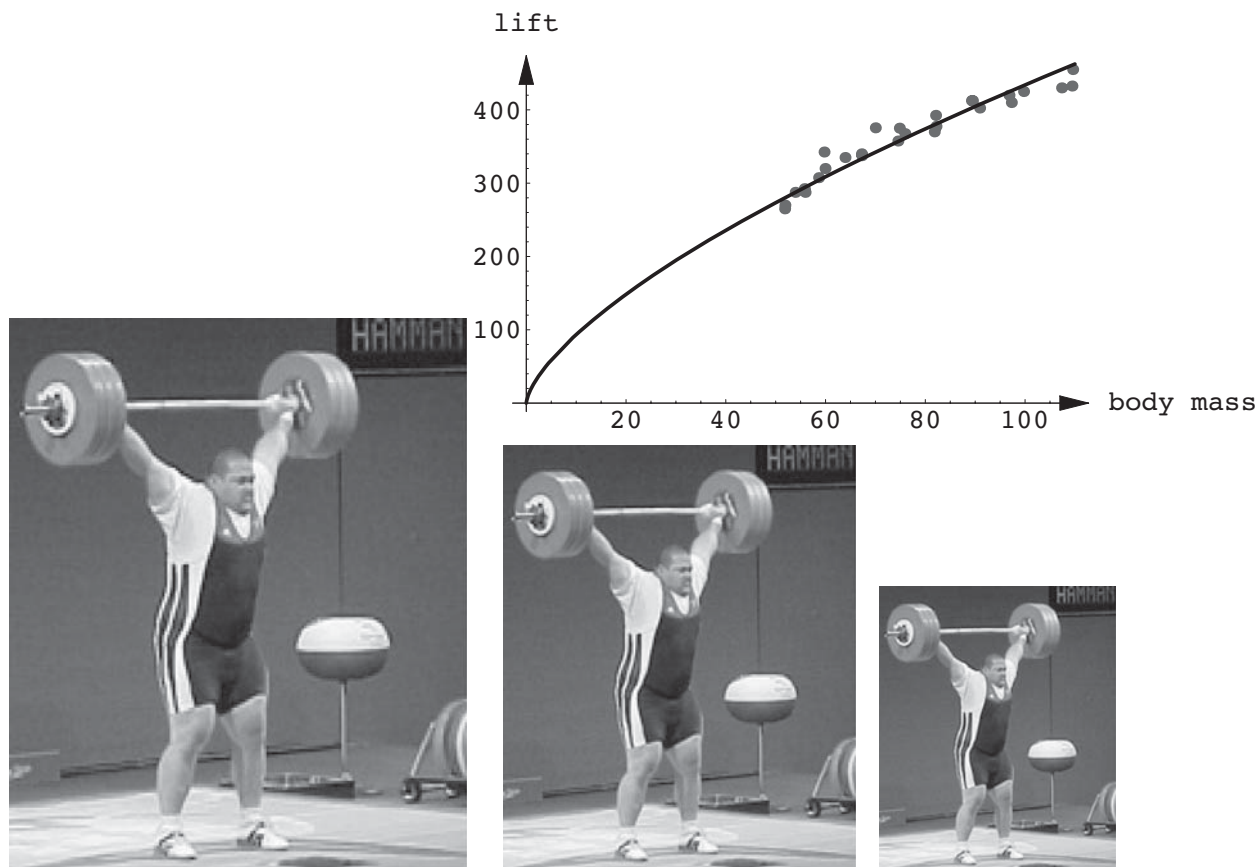
Figure 2. Geometrically similar weight lifters. The inset is a graph showing lifts of Olympic gold medalists as a function of their body mass. The fitted curve is $y = 20.15x^{2/3}$

strength is proportional to cross sectional area of the arm muscles,[4] we predicts that the mass lifted, call it y, should be proportional to $x^{2/3}$, where x is the body mass. To test the prediction, we can use linear regression on the log transformed data ($\ln y = \ln a + b \ln x$) to find the best proportionality constant a and exponent b. Linear regression yields an exponent close to 2/3 and generates a reasonable fit to the data. Using this relationship, one can also try to choose the best weightlifter by giving each weightlifter a weight-adjusted score of lift divided by $x^{2/3}$. The one with the highest score should be the gold winner. Interestingly, for two of the Olympics represented in the data set, Naim Suleymanoglu was the gold winner. Suleymanoglu was the first Olympic weightlifter to win three gold medals. The World Sports Writers' Union has identified him as one of the Top 25 Athletes of the 20th Century; we can add mathematical support to their opinion with our use of scaling laws to compare weightlifters of different sizes.

We can revisit scaling laws when computing derivatives. For instance, what is $\frac{d}{dx}\big|_{x=100} 20.15x^{2/3}$ and what does it mean? A calculation for Olympic weight lifters reveals that this derivative is approximately 2.9 kg per kg. Hence, a 1 kilogram increase in the mass of a 100 kg Olympic weight lifter results in an approximately 2.9kg increase in the mass he can lift. Even better, we can introduce the notion of elasticity: the relative change in y due to a relative change in x. More precisely, the *elasticity* of $y = f(x)$ at $x = a$ is $f'(a)\frac{a}{f(a)}$. For scaling laws, $f(x) = ax^b$, the elasticity is simply b. Hence, for the Olympic weightlifters, a 10% increase in weight results in approximately a 6.7% increase in the mass lifted.

---

[4] The assumption of geometric similarity is obviously violated for the heaviest weight class as they have no weight restriction and therefore have no reason to keep their body tight. For this reason, the fit to the 2/3rd law only seems to hold when you exclude this weight class from the data.
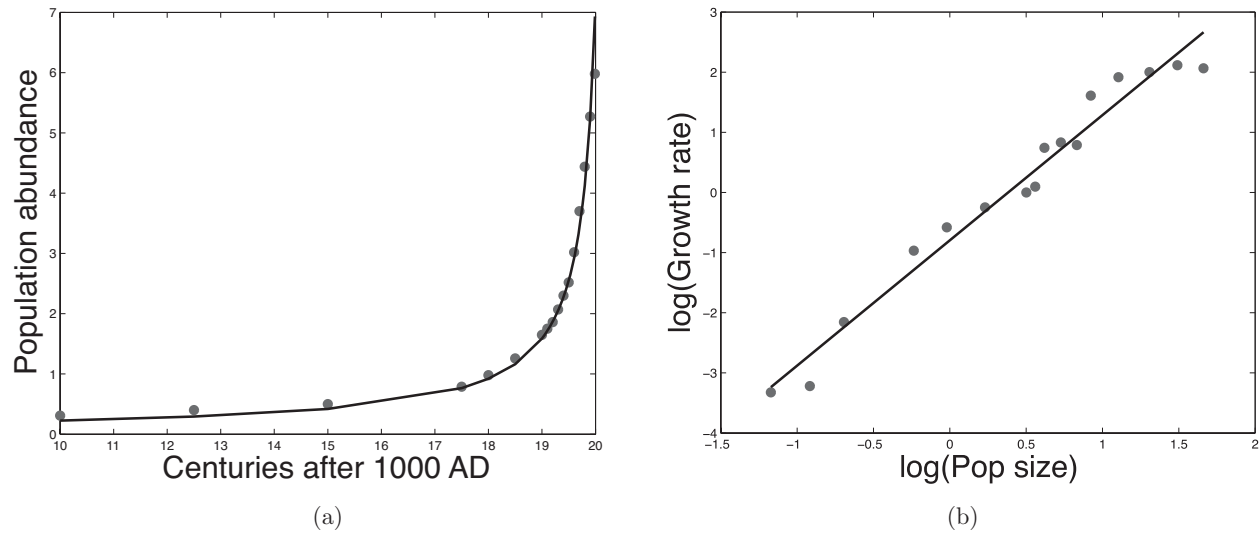
(a)   (b)

Figure 3. World population growth from 1000 A.D. to 1999 A.D. Data are plotted in small circles and the solid curve is the model fit is the solid curve. In (b), growth rates are estimated by difference quotients and the best fitting line of a log-log scale is plotted

We can also introduce optimization problems involving scaling laws, but before doing that, lets consider two examples of scaling laws in differential equations. The first example involves the *Science* paper, "Doomsday: Friday, 13 November A.D. 2026," published in 1960 by three electrical engineers at the University of Illinois (Foerster et al. 1960). World population growth data from 1000 A.D. to 1960 A.D. suggests that if N is the population size, then the population growth rate $\frac{dN}{dt}$ is proportional to N^{1+b} for some positive constant $b > 0$ and some proportionality constant $a > 0$. Letting t denote centuries after 0 A.D., plotting the log of the growth rate of world population (estimated by difference quotients) yields a roughly linear plot (Figure 3b). Using linear regression, we estimate $a \approx 0.4507$ and $b \approx 1.0827$. Solving the differential equation $\frac{dN}{dt} = a\,N^b$ yields a solution of the form $N(t) = (a\,b(T-t))^{-1/b}$ where T is the time at which, in the words of a Pogo cartoon, "everyone gets squeezed to death". Since we have estimates of a and b, we can use nonlinear least squares regression (a nice calculus exercise in of itself!) to find the value of T that gives the best fit to the data set (Figure 3a). The value turns out to be $T \approx 20.24$ for the U.N. estimates of world population growth. Hence, one gets the updated Doomsday prediction of 2024. The reliability of the prediction and the limitations of the model makes for a good classroom discussion.

The von Bertalanffy equation, which describes the growth of an organism, is another example of a differential equation that uses scaling laws. To derive it, consider a cubical critter with length L. If we assume length is measured in centimeters and the critter is mostly made of water, then its mass M is L^3 grams. If it ingests food at a rate proportional to its surface area and respires at a rate proportional to its mass, then

$$\frac{dM}{dt} = aL^2 - bL^3$$

where a and b are positive proportionality constants. Since $M = L^3$, we obtain

$$\frac{dM}{dt} = 3L^2 \frac{dL}{dt}.$$

Combing the equations yields

$$\frac{dL}{dt} = k\,(L_\infty - L)$$

where $k = b/3$ and $L_\infty = a/b$. Thus, somewhat magically, the growth of an organism can be described by a linear differential equation. With it, the student can be given many fun examples and questions. For instance, the von
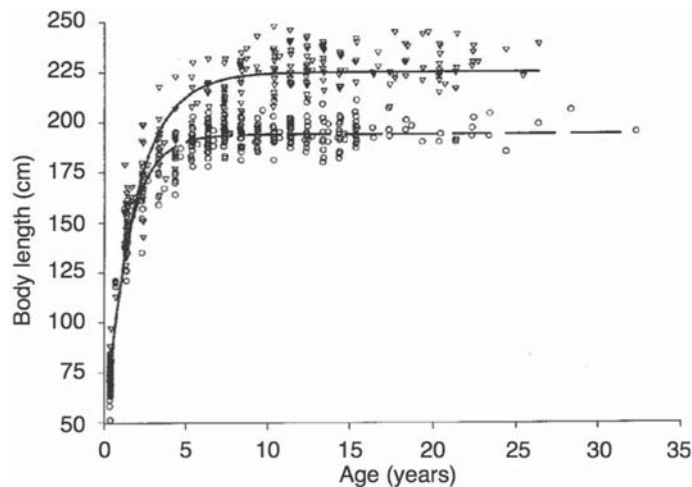
Figure 4. The von Bertalanffy curve fitted to age and body length. Data for female ($\circ$, dashed line) and male ($\triangledown$, solid line) polar bears *Ursus maritimus* captured in the Svalbard area. (Derocher and Wiig 2002)

Bertalanffy curve was used to examine growth patterns in body length and mass of female and male polar bears (*Ursus maritimus*) live-captured near Svalbard, Norway (Derocher and Wiig 2002). With information about the parameters and body sizes at different ages, we can discover various properties about the pronounced sexual dimorphism of body size. We can ask questions such as "At what length is the body mass increasing most rapidly?" (The answer is 2/3 of L_∞.) An extension of this problem is discussed in Section 24.5.

24.4   Population Growth

Modeling the growth of populations has a long rich history in mathematical biology. The richness occurs because the populations may consist of drug particles, viral particles, cells, or multicellular organisms. Hence, models of population growth have applications to genetics, ecology, evolution, immunology, physiology, and epidemiology. The models can connect calculus topics (e.g., elementary functions, optimization, differential equations, and probability density functions) and can be tested using widely available data. To illustrate their utility, I will focus on tumor growth and the spread of diseases and rumors.

A tumor is an abnormal population of cells (i.e., tissue) created when the natural balance of cell division and death is disturbed. Slow growing harmless tumors are called benign, while harmful faster growing tumors are called malignant. The simplest model of tumor growth is one of exponential growth and decay: $V(t) = V(0)e^{at}$ where $V(t)$ is the volume of the tumor at time t and a is its per-capita growth rate. Although exponential growth can not continue unabated, there are many data sets supporting this simple model during the initial phase of tumor growth. For instance, Looney and colleagues (Looney et al. 1975) used exponential growth and decay to model untreated rat tumors and strongly radiated rat tumors. Using linear regression,[5] the per-capita growth rates for non-radiated and strongly radiated tumors can be estimated as illustrated in Figure 5a. With them, we can compute the doubling time for the untreated tumors (a little over a week) and the half-life for the strongly radiated tumors (approximately 12.5 days).

Malignant tumors can be treated with radiation therapy and chemotherapy. For both, rarely is a single treatment is sufficient. Typically, the first treatment reduces the tumor, but eventually it begins to regrow, as not all cancerous cells have been killed. Since chemotherapy and radioactive therapy have many harmful side effects, determining the timing between treatments and their intensity is important. Treatments have to be sufficiently intense to cause a reduction in the tumor size, but not so intense as to place the patient at great risk from side effects. After a treatment, ideally the next treatment should occur just before the tumor starts to regrow. Estimating the time until tumor regrowth is a

---

[5] Even if one does not have immediate access to the data, it is easy to digitize the image from the paper and extract the data using a variety of utilities that are available as free ware.

great optimization problem. Consider, for example, an experimental study (Demidenko 2004) in which two groups of mice with tumors were treated with the chemotherapeutic drug cisplatin. Prior to the therapy, the tumor consisted of proliferating cells (also known as clonogenic cells) that grew exponentially with a doubling time of approximately 2.9 days. Each mouse was given a dosage of 10mg/kg of cisplatin. At the time of the therapy, the average tumor size was approximately 0.5 cm^3. After treatment, 99% of the proliferating cells became quiescent cells. Quiescent cells do not divide, and decay with a half life of approximately 5.7 days. With these assumptions, the tumor volume t days after therapy is given by

$$V(t) = 0.005e^{0.24t} + 0.495e^{-0.12t}.$$

Taking derivatives reveals that V decreases until $t \approx 10.84$ days and then begins to grow again. This prediction is close to what the data reveals (Figure 5b).

While exponential growth can provide a reasonable description of population growth when the population is not too large, it clearly can not be sustained indefinitely (e.g., a quick internet search and computation with the exponential model of the untreated mouse tumor shows that the tumor will be the size of the earth in approximately 670 days!). This can be illustrated in a classroom by simulating the spread of a rumor or disease amongst the students. Randomly choose a person in the classroom to infect with the rumor or disease. To see how the disease or rumor spreads, invoke an iterative procedure. At every iteration, ask everyone that is infected to randomly choose another individual in the classroom (e.g., by using a random number generator). If the person chosen is not infected, the person becomes infected. Everyone that is infected remains infected. Record the fraction of infected. Iterate until everyone is infected. Doing this in a class of 29 gave the data shown in Figure 6a. While an exponential growth model does a reasonable job of describing the first four iterations, it grossly overestimates the number of infected in the long term (the dashed curve in Figure 6a). If $y(t)$ denotes the fraction of infected individuals by time t, then the exponential growth model $y(t) = y(0)e^{at}$ satisfies the differential equation

$$\frac{dy}{dt} = a\,y,$$

which explains why a is called the per-capita growth rate of the population; i.e., $a = \frac{dy}{dt}\frac{1}{y}$ whenever $y \neq 0$. The problem with this model is that as the infection spreads, the fraction of those uninfected decreases and, consequently,
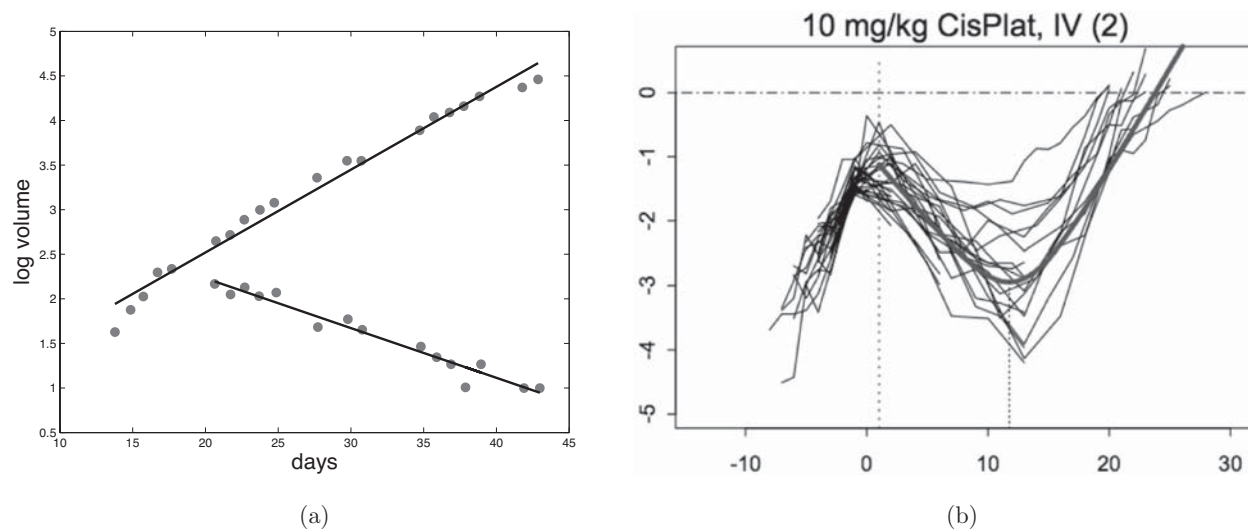

(a)   (b)

Figure 5. Tumor growth in rats: (a) growth of untreated tumors and the decay of tumors treated with 3750R of radiation data (Looney et al. 1975) (Linear regression yields per-capita growth rate estimates of $a = 0.0929$ for a non-radiated tumor and $a = -0.0558$ for a tumor with a strong radiation treatment of 3750R); (b) tumor size for mice treated with cisplatin (Demidenko 2004)
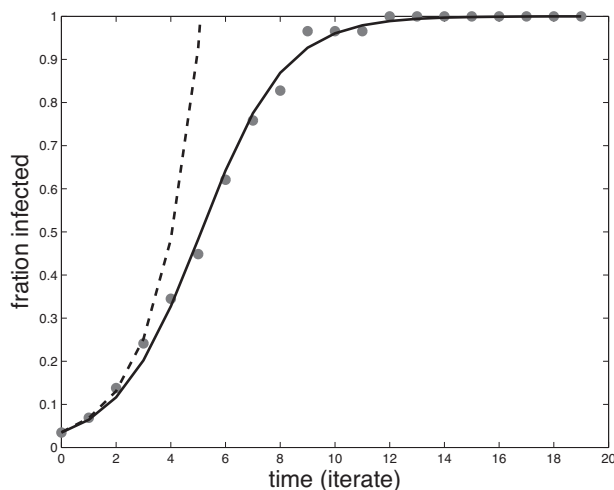
Figure 6. The spread of a rumor in a classroom of 29 individuals: actual data (circles), exponential growth model (dashed curve), and logistic growth model (solid curve)

the per-capita growth rate of y must decrease as y increases. The simplest assumption is to assume that the per-capita growth rate is proportional to the fraction of uninfected individuals. If r denotes the proportionality constant, then we set at the logistic equation

$$\frac{dy}{dt} = r\,y(1 - y) \qquad y(0) = 1/29.$$

For the classroom data, we can estimate r from the exponential growth phase of the data. Solving the differential equation using separation of variables and partial fractions yields

$$y(t) = \frac{e^{rt}}{28 + e^{rt}}$$

(see the solid curve in Figure 6a). Using this function, we can estimate when two-thirds of the population was infected. How accurate is the prediction? How does the answer depend on r?

Population growth curves can provide a nice introduction to cumulative distribution functions (CDFs), probability density functions (PDFs), and other statistical concepts. For instance, consider the exponential decay of a strongly radiated tumor. If $V(t) = V(0)e^{-at}$ is the volume of the tumor at day t, then the fraction of cells lost by day t is given by

$$F(t) = \begin{cases} 0 & \text{if } t \leq 0 \\ 1 - e^{-at} & \text{if } t > 0. \end{cases}$$

Differentiating yields the associated PDF

$$f(t) = \begin{cases} 0 & \text{if } t \leq 0 \\ a\,e^{-at} & \text{if } t > 0. \end{cases}$$

If $y(t)$ is the fraction of individuals infected with our classroom rumor by time t, then it is easy to verify that $y(t)$ is a CDF of the logistic distribution with PDF

$$y'(t) = ry(t)(1 - y(t)) = \frac{28\,r\,e^{rt}}{(28 + e^{r\,t})^2}.$$

Using the CDFs, we can answer a variety of questions. At what time is half of the classroom infected? What fraction of tumor is lost by the third day? Using PDFs and improper integrals, we can find the expected time for the loss of a particular tumor cell (i.e., $\frac{1}{a}$ days, which provides another interpretation for the parameter a) or the expected time for an individual in the classroom to become infected using the symmetry of the logistic distribution. Working with CDFs

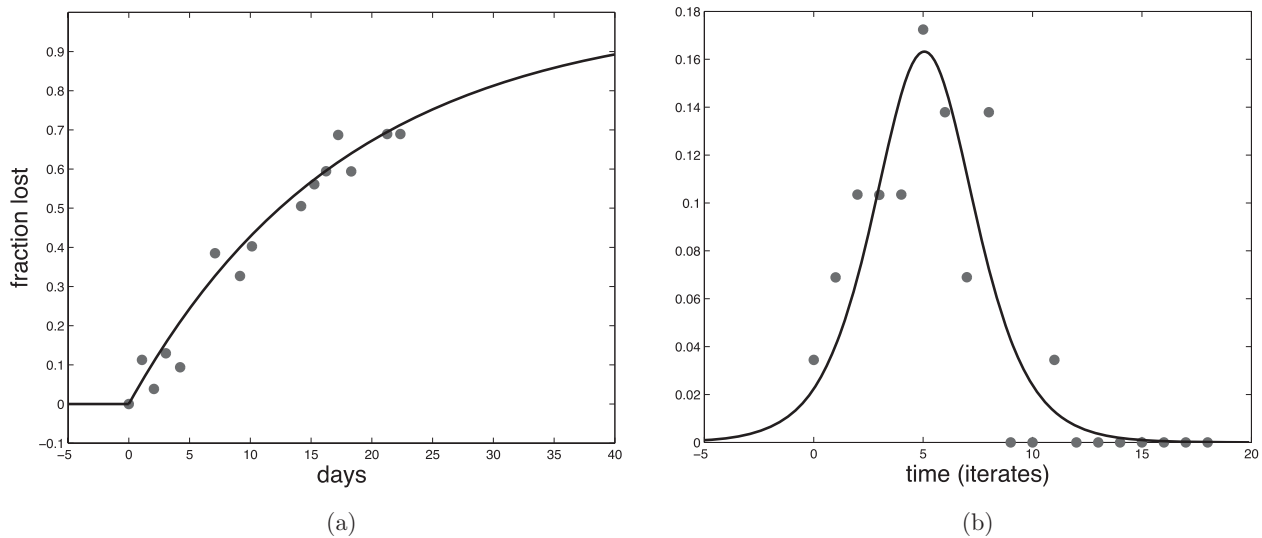(a)   (b)

Figure 7. CDFs and PDFs for decay of tumors and spread of rumors: (a) the empirical CDF (circles) and the model (solid curve); (b) the empirical PDF (circles) and the model (solid curve). Source of data as in Figures 5 and 6, respectively

and PDFs provides an opportunity to review both parts of the fundamental theorem of calculus, as getting a CDF from a PDF involves integration and getting a PDF from a CDF involves differentiation.

24.5   Projects: Putting it all Together!

Projects provide students with an opportunity to pull together and apply the calculus concepts they have learned and an opportunity to collaborate. Here I will illustrate one project, optimal investment into reproduction and growth, that pulls together several of the applications from this article.

   All organisms have a finite amount of energy at their disposal and must divide it into three fundamental biological processes: growth, maintenance, and reproduction. Since natural selection tends to weed out organisms with lower fitness (e.g., total number of offspring produced per individual), we would expect natural selection to favor organisms that divide their energies to optimize the number of offspring produced. According to Gadgil and Bossert (1970)

> If fitness is being measured entirely in the currency of offspring, the advantage of devoting resources to maintenance and growth is only insofar as this enhances the reproduction at further stages in the life history. Maintenance is essential to enable an organism to survive to these stages. Growth may enhance both survival and reproductive ability. A continuous increase in fecundity with size is well known in fishes, where gonads comprise a fairly constant proportion of the body weight. A basic challenge confronting all organisms is at what point in their life should they invest into reproduction rather than growth. On the one hand, by growing to a larger size an individual may be able to collect more resources and, thereby, produce more progeny than if it remained smaller. On the other hand, by waiting too long to start producing young, an individual may die before producing any young. Using models, one can investigate how various factors such as per-capita mortality rates, size-specific respiration rates, and size-specific consumption rates influence the optimal time to start investing energy into reproduction.

   To explore optimal reproductive schedules, consider an individual that experiences a constant risk of dying. In other words, the probability of an individual surviving to age t, call it $l(t)$, is exponentially distributed with a hazard rate of

a, i.e., a mean life expectancy of $1/a$. Assume that during its growth phase (i.e., before the switch to its reproductive phase), the individual's growth is determined by the von Bertalanffy growth equation

$$\frac{dL}{dt} = k(L_\infty - L) \qquad L(0) = 0,$$

where $L(t)$ is the length of the organism at time t, L_∞ is its asymptotic size, and $k > 0$ is a proportionality constant determining the rate of growth. As discussed earlier, this equation accounts for maintenance costs with the $-k\,L$ term. Its solution is

$$L(t) = L_\infty \left(1 - e^{-k\,t}\right).$$

Suppose at age T, the organism invests of all its growth in reproduction. The rate of growth of mass at this age is

$$\frac{d}{dt}\Big|_{t=T} L(t)^3 = 3L(T)^2 L'(T)$$
$$= 3\left(L_\infty \left(1 - e^{-kT}\right)\right)^2 k L_\infty e^{-kT}.$$

Hence, if we assume that its rate of production of progeny is proportional to its growth rate at age T, then its birth rate for $t \geq T$ is

$$b(T) = \alpha \left(1 - e^{-kT}\right)^2 e^{-kT},$$

where α is a proportionality constant. The total number of progeny expected to be produced by the individual is

$$R_0 = \int_T^\infty (t - T)b(T)e^{-at} a \, dt$$
$$= \beta e^{-(k+a)T} \left(1 - e^{-kT}\right)^2$$

for an appropriately defined constant $\beta > 0$. Solving for the time T that maximizes R_0 yields

$$T = \frac{1}{k} \ln\left(1 + \frac{2k}{k + a}\right).$$

This shows that higher hazard rates (i.e., larger values of a) lead to smaller optimal T values. Hence, organisms with shorter life expectancies should reproduce sooner rather than later. Taking the limit as $a \to 0$ results in $T = \frac{1}{k} \ln 3$. This corresponds to the time at which the organism reaches two-thirds of its limiting length and, consequently, corresponds to the time at which its mass grows most rapidly. Hence, according to this model, organisms should begin to invest in reproduction when they reach two-thirds of their limiting size. We can verify that T is decreasing with the growth rate parameter k. Thus, organisms that grow faster should reproduce sooner. To see that this simple model is just the tip of the iceberg, students should be encouraged to conduct a literature search to see what else has been done.

24.6   Discussion

Many of the perspectives and ideas in this article stem from almost two decades of teaching calculus and a decade-long collaboration with Wayne Getz and Karl Smith on writing a calculus text (Schreiber et al. 2012). This upcoming text, *Calculus for the Life Sciences* with John Wiley and Sons, is based on and elaborates on many of the ideas presented here. It highlights how biological phenomena naturally motivate and pull together all the key ingredients of differential and integral calculus. Texts like this and the diversity of pedagogical approaches described in this MAA volume can result in the next generation of biology students seeking out further connections between mathematics and the life sciences and will help the next generation of faculty to facilitate this process.

References

Demidenko, E., 2004: *Mixed Models: Theory and Applications*, Wiley.

Derocher, A.E. and Ø. Wiig, 2002: Postnatal growth in body length and mass of polar bears (*Ursus maritimus*) at Svalbard, *Journal of Zoology*, **256**, 343–349.

Foerster, H., P.M. Mora, and L.W. Amiot, 1960: Doomsday: Friday, 13 November, AD 2026, *Science* **132**, 1291–1295.

Gadgil, M. and W.H. Bossert, 1970: Life historical consequences of natural selection, *American Naturalist*, **104**, 1–24.

Haldane, J.B.S., 1926: On being the right size, *Harpers*.

Looney, W.B., J.S. Trefil, J.C. Schaffner, C.J. Kovacs, and H.A. Hopkins, 1975: Solid tumor models for the assessment of different treatment modalities: I: Radiation-induced changes in growth rate characteristics of a solid tumor model, *Proc. Natl. Acad. Sci.*, **72**, 2662–2666.

Schreiber, S.J., W. Getz, and K. Smith, 2012: *Calculus for the Life Sciences*, Wiley.

25

Computational Systems Biology: Discrete Models of Gene Regulation Networks

Ana Martins*, Paola Vera-Licona*, and Reinhard Laubenbacher[1]
Virginia Bioinformatics Institute, Virginia Polytechnic Institute and State University

Name of Institution	Virginia Tech
Size	About 28,000
Institution Type	Large research-intensive state university
Student Demographic	Regional, national and international students
Department Structure	Interdisciplinary research institute (Virginia Bioinformatics Institute) without a formal teaching mission

Abstract

This article describes a 2–3 day workshop offered at regional undergraduate teaching institutions and high schools. Its goal is to use discrete dynamic models, in particular Boolean networks, to illustrate mathematical modeling of biological networks, such as gene regulatory networks, to a broad audience that can include undergraduate faculty, undergraduate students, high school teachers, and even high school students. The workshop covers the basics of biology, mathematical modeling, and model analysis, using the well-known *lac* operon network in *E coli* as a model system. The workshop materials can be used independently or as one or several modules in a college or high school class. Supplementary materials are available at admg.vbi.vt.edu/home/Outreach/Workshops/2.

25.1 Course Structure

- 2–3 days

- Average audience size: 5–15 participants

---

* these authors contributed equally to this work
[1] reinhard@vbi.vt.edu

- Enrollment requirements: High school algebra and biology.
- Team-taught by one mathematics instructor and one biology instructor
- Web site: http://admg.vbi.vt.edu/home/Outreach/Workshops/2

25.2   Introduction

Mathematical biology uses theoretical and computational tools from mathematics to describe or analyze biological systems (Murray 1993). Biological problems are considered mathematically (such as effective drug targeting (Caplan and Rosca 2005) or inferring cancer-inducing genes (Ribba et al. 2006)). Mathematical models provide a language in which to encode the key features of a biological system, which can then be analyzed with mathematical tools to obtain insight into its structure and properties. Mathematical models can be designed for regulatory networks of genes and proteins, in which the expression of key units regulates the expression of other components in the network (deJong 2002). The modeling tools come from a broad range of mathematical fields. Most models of biological systems have been formulated as systems of differential equations, but other areas of mathematics have been used successfully to model and analyze biological systems, including algebra (Jarrah et al. 2007), control and optimization theory (Laubenbacher and Stigler 2004), graph theory (Barabasi and Oltvai 2004), logic (Albert and Othmer 2003), and statistics (Friedman et al. 2000).

The material presented in this paper is based on a workshop that was designed by us, researchers at that time at the Virginia Bioinformatics Institute (VBI) at Virginia Tech, and conducted in collaboration with the Institute for Advanced Learning and Research (IALR) in Danville, Virginia, for high school teachers from the area. The aim was to provide background and materials for the teachers to introduce into their mathematics classes, in accordance with the Standards of Learning (SOL) curriculum (Virginia Department of Education 2012), and the NCTM standards (National Council of Teachers of Mathematics 2012). We introduced key concepts in biochemistry, biology, and discrete mathematics, which were applied using graphical modeling software to explore the regulation of the lactose (*lac*) operon, an example of gene transcription in prokaryotes (Jacob and Monod 1961). The participants completed the project and developed activities to show students the value of mathematical modeling in understanding biochemical network mechanisms and dynamics.

The bar to understanding and appreciating mathematical models of biological systems is high since students need to understand the mathematics and biology used. If differential equations models are used, then students need to be familiar with some of the subtleties of the subject to appreciate topics like steady state analysis and bifurcation behavior. Therefore, we decided to use the simpler modeling tool of Boolean networks, which can be appreciated without sophisticated mathematical training. Boolean network models have been used in molecular biology since the 1960s (see Kauffman 1969) and have provided insights into the qualitative dynamical behavior of some important molecular networks, such as the cell cycle and the gene regulation mechanisms during embryonic development of organisms (Albert and Othmer 2003). The discrete analog of a continuous state space analysis is a graph-theoretic analysis of the state space graph (defined below). The material in this chapter can be used as examples in a variety of discrete mathematics courses.

We provide a basic introduction to genomics and a description of a much-studied model system, the *lac* operon in prokaryotic organisms, which regulates lactose metabolism. We also introduce Boolean networks and the tools for their analysis. We describe an example of a multi-component research project on Boolean network models of the *lac* operon and the biological insights that come from it. The project might be viewed as a case study of the utility of mathematical models in the discovery of new biology. While current molecular networks under study are substantially bigger and more complex than the *lac* operon, this simple example provides a template and interested readers can explore the recent literature.

There are, of course, other modeling frameworks that are being used successfully in systems biology, including ordinary differential equation models (see Veliz-Cuba et al. 2009), a classroom module that includes a guide to model analysis using the open source software package Copasi (Hoops et al. 2006), agent-based models, Petri net models, and Bayesian network models.

25.3   Gene Regulation and the Lac Operon

The *Escherichia coli lac* operon is one of the earliest and best understood examples of regulation of gene expression (Jacob and Monod 1961; Koolman and Röhm 1996; Lodish et al. 2000). Gene regulation in bacteria allows the cell to adjust to changes in the nutritional environment so that growth and division can be optimized. *E. coli* can use glucose or lactose as energy and carbon sources, and when cells grow in a glucose-based medium, the activity of the enzymes involved in the metabolism of lactose is very low, even if lactose is available. When glucose is exhausted from the medium and lactose is present, there is an increase in the activity of enzymes involved in lactose metabolism (Lodish et al. 2000). Before describing in detail the molecular mechanisms, we need to introduce some of the fundamental concepts of gene regulation.

25.4   Fundamentals of Gene Regulation

The modern era of molecular biology began with the great discovery, by James Watson and Francis Crick, of the DNA structure (Watson and Crick 1953). Later, the central dogma of molecular biology revolutionized science. This was first enunciated by Francis Crick (1958):

> The central dogma of molecular biology deals with the detailed residue-by-residue transfer of sequential information. It states that such information cannot be transferred from protein to either protein or nucleic acid.
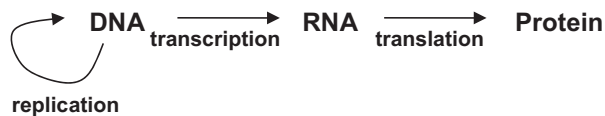

Figure 1. The central dogma of molecular biology

The representation of the central dogma in Figure 1 shows the routes in the processing and transfer of information. DNA replication allows information to be passed from a cell to daughter cells, while transcription and translation pass the information through RNA to proteins, which serve to enact instructions coded in the DNA. The concept has been extended by the discovery of several additional processes, such as reverse transcription. A description of these processes can be found in any molecular cell biology textbook (see for example Lodish et al. 2000; Watson 2003) and will not be explained here. For our purpose, it suffices to provide an overview of the transcription process, by which information is transferred from DNA to RNA.

25.4.1   Nucleic Acids: DNA and RNA

Nucleic acids are macromolecules–polymers of small subunits called nucleotides. All nucleotides have a common structure: a *phosphate* group linked to a *pentose* (a five-carbon sugar molecule) that is linked to an organic *nitrogen base* (Figure 2). The pentose in RNA is ribose (hence the name ribonucleic acid) while the one in DNA is deoxyribose (hence the name deoxyribonucleic acid). There are two types of nitrogen bases: the one-ring pyrimidines, and the two-ring purines. Both DNA and RNA contain the bases adenine (A), guanine (G) and cytosine (C). Thymine (T) exists only in DNA, while uracil (U) is only present in RNA.

The primary structures of RNA and DNA are similar, but the way polynucleotides twist and fold into stable three-dimensional conformations are different. DNA exists mainly as a single three-dimensional structure, the famous DNA double helix, while RNA can exist in several conformations. There are three main types of RNA: messenger RNA (mRNA), transfer RNA (tRNA), and ribosomal RNA (rRNA). Messenger RNA (mRNA) is involved in the transcription process, in which it serves as an information carrier from DNA to proteins. Transfer RNA (tRNA) is involved in translation, the building of proteins from its amino acid constituents. Ribosomal RNA (rRNA) is also
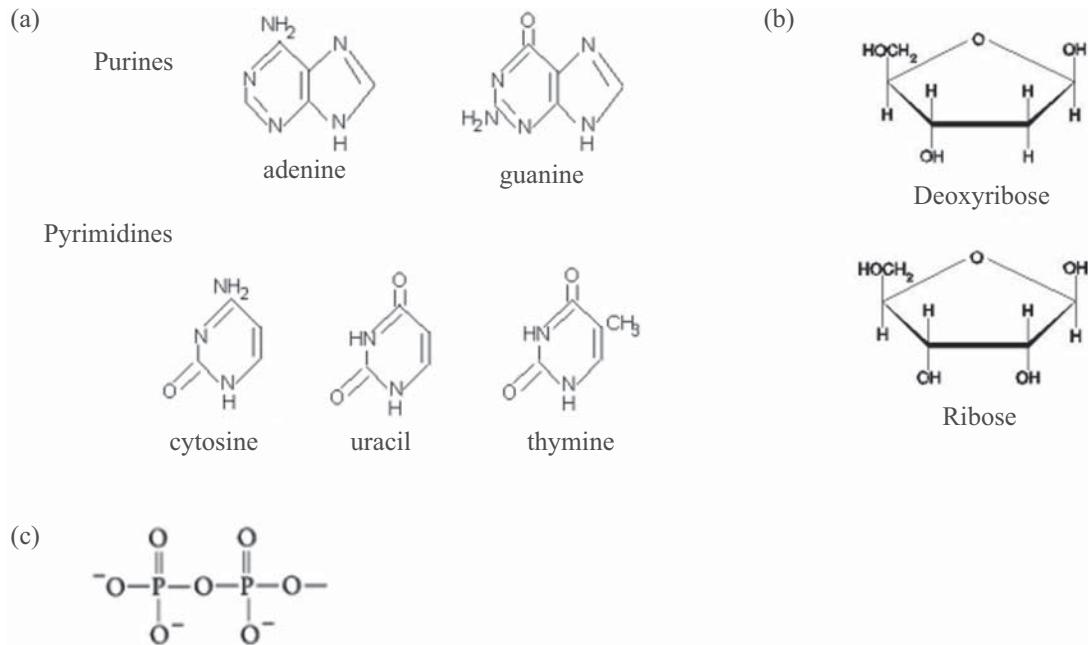
Figure 2. The constituents of nucleotides. (a) the nitrogen bases (purines and pyrimidines). Adenine, guanine and cytosine are common to RNA and DNA. Only DNA contains thymine, while only RNA contains uracil; (b) the sugars, ribose (constituent of RNA) and 2-deoxyribose (constituent of DNA); (c) a phosphate group

involved in translation, being a constituent of the ribosomes, large ribonucleoprotein complexes where proteins are synthesized.

25.4.2   The Genetic Code

The DNA molecule contains four building blocks based on four nucleobases: adenine, cytosine, guanine, and thymine. Similarly, the RNA language is written in a four-letter alphabet, with uracil taking the place of thymine. Proteins may contain twenty different amino acids that are obtained from a genetic code in which three consecutive nucleobases function as a triplet called a *codon*. Of the sixty-four possible codons in the genetic code, sixty-one encode amino acids and three are called stop codons, which indicate that it is time to stop adding amino acids when building a protein. Most of the amino acids can be encoded by more than one codon (Table 1). This is why the genetic code is said to be degenerate; that is, there are synonyms.

25.4.3   Transcription

The word "double" in the description of DNA as a double helix refers to the structure of DNA as two complementary strands that have bases that alternate according to the base-pair rule: G in one strand corresponds to C in the other, and vice versa, and A is similarly linked with T. One strand serves as the functional strand, which encodes an amino acid sequence, while the other is the template strand used to synthesize an RNA molecule in the transcription process through the action of enzymes called RNA *polymerases*. Each T, C, A, and G in the template strand results in a corresponding A, G, U, and C in the RNA molecule; hence, the resultant RNA molecule is complementary to the template strand of DNA and identical to the functional strand except that uracil replaces thymine (Figure 3). RNA polymerases find an initiation site on the DNA duplex, bind it, temporarily separate the two strands, and begin generating a new RNA strand. Transcription is controlled by regulatory proteins called *transcription factors* (TF) that bind to specific sequences in DNA and activate or inhibit the transcription of genes. A TF that inhibits the transcription is called a *repressor*, while those that stimulate transcription are called *inducers*. The sequences of DNA to which the TF binds are called *control elements*; they are *promoters* when they are involved in induction of transcription (binding of RNA polymerase) and

First Position	Second Position				Third Position
	U	**C**	**A**	**G**	
U	Phe	Ser	Tyr	Cys	**U**
	Phe	Ser	Tyr	Cys	**C**
	Leu	Ser	STOP	STOP	**A**
	Leu	Ser	STOP	Trp	**G**
C	Leu	Pro	His	Arg	**U**
	Leu	Pro	His	Arg	**C**
	Leu	Pro	Gln	Arg	**A**
	Leu	Pro	Gln	Arg	**G**
A	Ile	Thr	Asn	Ser	**U**
	Ile	Thr	Asn	Ser	**C**
	Ile	Thr	Lys	Arg	**A**
	Met (Start)	Thr	Lys	Arg	**G**
G	Val	Ala	Asp	Gly	**U**
	Val	Ala	Asp	Gly	**C**
	Val	Ala	Glu	Gly	**A**
	Val	Ala	Glu	Gly	**G**

The nucleotides are A = adenine, C = cytosine, G = guanine, and U = uracil. The amino acids are Phe = phenylalanine, Leu = leucine, Ser = serine, Tyr = tyrosine, Cys = cysteine, Trp = tryptophan, Pro = proline, His = histidine, Gln = glutamine, Arg = arginine, Ile = isoleucine, Met = methionine, Thr = threonine, Asn = asparagine, Lys = lysine, Val = valine, Ala = alanine, Asp = aspartic acid, Glu = glutamic acid, and Gly = glycine. The proteins always begin with a methionine, encoded by AUG (start codon), and the codons UAA, UAG, and UGA do not encode any amino acid, indicating the termination of translation.

Table 1. The genetic code. Each codon (triplet of three nucleotides) encodes an amino acid (except for the three stop codons). Most amino acids can be encoded by more than one codon. The DNA code is equivalent, with T in place of U.

operators when they are involved in repression of gene expression. These concepts will be important when we discuss the *lac* operon.

Operons

Prokaryotes are single-cell organisms, like bacteria, that consist of a single closed compartment of cytoplasm surrounded by a plasma membrane. In contrast with *eukaryotes,* such as yeast and all multi-celled organisms, prokaryotes do not possess internal organelles surrounded by membranes. Prokaryotic DNA exists as large circular chromosomes, associated with polyamines and small proteins and folded into a compact structure. The most common arrangement of protein-coding genes in prokaryotes has a powerful and appealing logic: genes devoted to a single metabolic goal are most often found in a continuous array in DNA. The arrangement of genes in a functional group is called an *operon*. The full set of genes is transcribed into a single mRNA molecule. Ribosomes initiate translation at the beginning of each the genes in the mRNA produced from an operon and produce the polypeptides encoded in it.
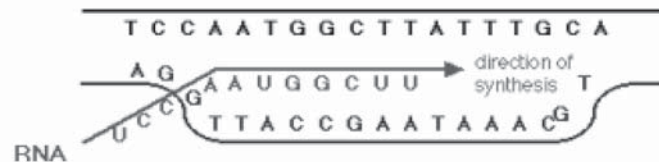
25.5   The *lac* Operon

Much of the pioneer work on the *lac* operon in *Escherichia coli* was done by François Jacob and Jacques Monod (1961). *E. coli* can regulate its gene expression depending on the carbon source used in the culture medium: when

The top strand of the DNA double helix is the temple for RNA synthesis.

DNA

T C C A A T G G C T T A T T T G C A
A G G T T A C C G A A T A A A C G T

3'   5'

The enzyme RNA polymerase pairs bases with the bottom DNA strand, to build the new RNA strand Notice the use of U instead of T in the RNA strand.

T C C A A T G G C T T A T T T G C A

A G
  C G A A U G G C U U   direction of   T
 C C G   T T A C C G A A T A A A C G   synthesis
U   G

RNA

The new RNA molecule is complementary to the bottom DNA strand, hence it is the same as the top DNA strand, except that U replaces T.

RNA 5'   3'
      U C C A A U G G C U U A U U U G C A

Figure 3. A simplified schematic view of the transcription process

cells grow in glucose-based medium, the activity of the enzymes needed to metabolize lactose is very low, but in a lactose-containing medium there is an increase in the activity of the enzymes involved in lactose metabolism.

In *E. coli,* the enzymes induced in the presence of lactose are encoded by the *lac* operon, which contains structural genes for three enzymes involved in the metabolism of lactose (*LacZ, LacY, LacA*), one structural gene encoding a repressor protein (*LacR*), and three control elements involved in the regulation of transcription, P_R, P, and O (Figure 4). The *LacZ* gene encodes β-galactosidase, an enzyme that converts lactose into glucose and galactose, and the *LacY* gene encodes lactose permease, which is involved in the transport of lactose into the cell. The *LacR* gene encodes a control element called *lac*-repressor, involved in the regulation of the three structural genes in response to nutrient changes in the culture medium.

The structural genes *LacZ, LacY* and *LacA* are expressed only when lactose is present in the cell. In its absence, the *lac*-repressor (R) binds to the operator region O, and RNA polymerase, bound to the promoter P, is unable to move past this region. Hence, no transcription of *LacZ, LacY* and *LacA* occurs (Figure 5A). When lactose enters the cell, it is converted by β-galactosidase into a similar molecule (isomer) called allolactose, which binds to the *lac*-repressor and induces a conformational change that prevents it from fitting into and binding to the operator region in the DNA. Without the *lac*-repressor blocking the DNA, the RNA polymerase is able to move along the DNA, transcription of the three genes occurs, and lactose is metabolized (Figure 5B).

| Lac | P_R | | P | O | LacZ | LacY | LacA |

Figure 4. Schematic structure of the lac operon and the regions it contains. The operon contains regulatory regions and regions coding for proteins. The regulatory regions include P_R, a promoter for *lacR*; the operator O, binding site for the repressor R; and the promoter P, a binding site for RNA polymerase. The coding regions include the genes *LacR,* encoding the regulatory protein (repressor), and *LacZ, LacY*, and *LacA*, encoding proteins involved in the utilization of lactose by *E. coli* cells
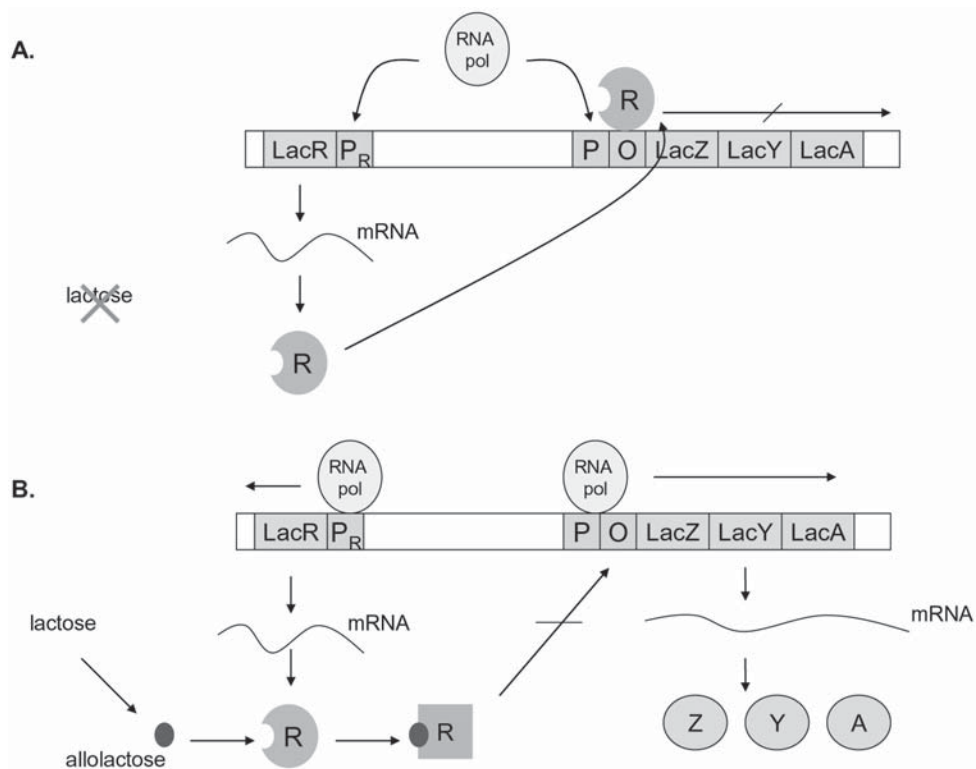
Figure 5. Regulation of gene expression in response to nutrients in *E. coli*: the *lac* operon (Koolman and Röhm 1996; Lodish et al. 2000). Details are in the text

25.6   Boolean Networks

A *Boolean function* in n variables is a function that takes an n-bit string of 0s and 1s as input and produces a one bit output, using Boolean operators such as *and* ($\wedge$), *or* ($\vee$), and *not* ($\sim$). We call an n-bit string of 0s and 1s a binary *n-string*.

Example 1. A Boolean function in three variables is $f(x, y, z) = (x \wedge y) \vee (\sim z)$.
We observe:

$$f(0, 1, 0) = (0 \wedge 1) \vee (\sim 0) = 0 \vee 1 = 1$$
$$f(1, 0, 1) = (1 \wedge 0) \vee (\sim 1) = 0 \vee 0 = 0$$
$$f(1, 1, 1) = (1 \wedge 1) \vee (\sim 1) = 1 \vee 0 = 1$$

If $k = F_2$ denotes the binary system $\{0,1\}$, then a Boolean function in n variables is a function $f : k^n \to k$. Here, k^n denotes the space of binary n-tuples. (It can be shown that any function $f : k^n \to k$ can be represented by a Boolean function).

Definition 1. A *Boolean network* F on n variables is a function $F = (f_1, \ldots, f_n) : k^n \to k^n$, where the f_i are Boolean functions. That is, F is a function that transforms binary n-strings into other binary n-strings, with the rule for transforming the i-th coordinate given by f_i.

Mathematically, we may view Boolean networks as time-discrete dynamical systems on a finite state space, where a state of the system is a binary n-tuple.

Example 2. Consider the Boolean network in 3 variables described by $F = (f_1, f_2, f_3)$, where

$$f_1 = \sim (x_1 \vee x_2) = \sim \{(x_1 \vee x_2) \wedge [\sim (x_1 \wedge x_2)]\},$$
$$f_2 = (x_1 \wedge x_2) \wedge x_3,$$
$$f_3 = x_1.$$

Note that since f_1 is the negative of the *exclusive or*, $f_1 = 1$ if $x_1 = x_2$ and $f_1 = 0$ otherwise.

　　There are two interesting directed graphs associated to a Boolean network: the dependency graph, or wiring diagram, and the state space graph. The *dependency graph* encodes the dependencies of a variable on the other variables. The nodes of the dependency graph correspond to the variables of the Boolean network. A directed edge from variable x to variable y indicates that x appears in the Boolean function of variable y. For the Boolean network in Example 2, the dependency graph is given in Figure 6.
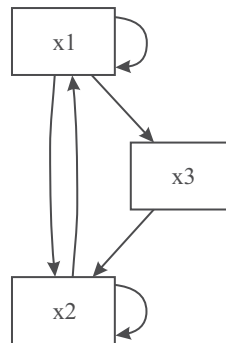

Figure 6. Boolean network of Example 2

The dynamics of the network is given by the iterations of F:

$$F(1, 0, 1) = (0, 0, 1), \ F(0, 0, 1) = (1, 0, 0), \ F(1, 0, 0) = (0, 0, 1), \text{ etc.}$$

The dynamics of a Boolean network F on n variables can also be represented by a directed graph, the *state space* of F. It has 2^n vertices consisting of all binary n-strings, representing all possible states of the network. There is an edge from vertex a to vertex b if and only if $F(a) = b$.

　　The state space of the Boolean network in Example 2 is given in Figure 7.

Definition 2. A node a in the phase space is called a *fixed point* if $F(a) = a$. A *limit cycle* in the phase space is a set of points $c_1, \ldots, c_t$ such that $F(c_i) = c_{i+1}$ and $F(c_t) = c_1$.
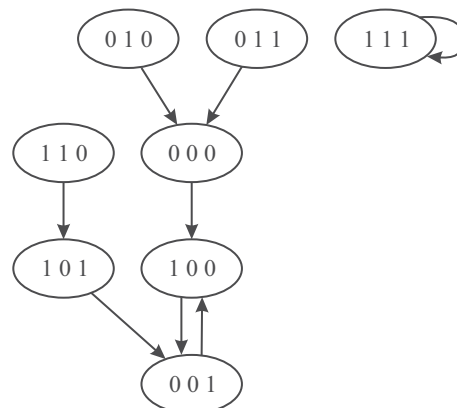

Figure 7. Dynamics of the network of Example 2

The state space of the Boolean network of Example 2 contains one fixed point $c = (1, 1, 1)$ and a limit cycle of length 2, consisting of the states $(1, 0, 0)$ and $(0, 0, 1)$.

25.7 Student Projects

The goal of the projects we designed is to let students experience modeling a molecular network with a minimum amount of preparation and prior knowledge. As mentioned earlier, this motivated our choice of Boolean networks as models. Molecular data describing the components of the *lac* operon are complicated to explain and to use, so we chose a modeling activity consisting of partial model validation based on the faithfulness of the model to basic biological features of the system.

25.7.1 Project 1

Based on the *lac* operon system described on the previous section, construct a Boolean network model F that contains the following as variables:

M = mRNA for *lac* genes, Z = beta − galactosidase, S = Allolactose (inducer), L = Lactose (intracellular), Y = Lactose permease

The dynamical system will be described as $F = (f_M, f_Z, f_S, f_L, f_Y)$, where each function indicates the presence or absence of the corresponding entity in terms of the state at the previous time step. For the model, we assume that each of transcription, translation, mRNA degradation, and protein degradation require one time unit and that extracellular lactose is always available.

One possible outcome of this activity is the Boolean model:

$$
\begin{aligned}
f_M &= S \\
f_Z &= M \\
f_S &= S \vee (L \wedge Z) \\
f_L &= Y \vee (L \wedge \sim Z) \\
f_Y &= M
\end{aligned}
$$

Each of the functions encodes a mechanism in the system that affects the corresponding molecular species. The first function, for instance, encodes the fact that the *lac* genes are expressed at time $t + 1$ if and only if the inducer allolactose (S) is present at time t. The function f_S indicates that allolactose is present at time $t + 1$ if it was present at time t or if lactose was present at time t together with β-galactosidase, which converts lactose into allolactose in one time step. We can assemble the functions into a Boolean network

$$F \colon \{0, 1\}^5 \rightarrow \{0, 1\}^5$$

that transforms a 5-tuple representing a system state into another 5-tuple representing another system state. Long-term dynamics are obtained by iteration of F.

Using the software package DVD (Jarrah et al. 2004), the participants can construct and visualize the topological and dynamical properties of the model. The model dynamics are depicted in Figure 8. Each node of the directed graph represents one model state, including all $2^5 = 32$ states. A directed arrow from one state to another indicates a state transition. That is, if the functions in the model F are evaluated at the state at the origin of the arrow, then the resulting value is the node at the tip of the arrow.

25.7.2 Project 2

Based on the biological properties of the *lac* operon, analyze the model constructed in Project 1 and decide whether it is biologically realistic.

This project can be used to demonstrate how a mathematical model can be used to test and further understanding of the underlying biology. Assuming the Boolean model above as the outcome of Project 1, it has three possible long-term dynamic outcomes corresponding to the three fixed points of the state space graph. Since the *lac* operon is basically a bi-stable system which is either ON or OFF, only $(0, 0, 0, 0, 0)$ and $(1, 1, 1, 1, 1)$ should be fixed points;
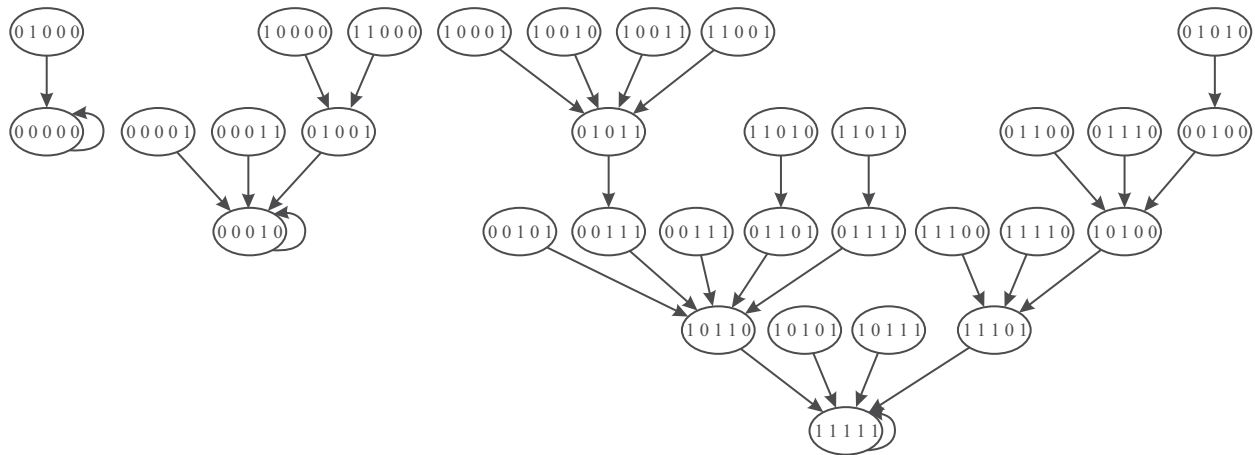
Figure 8. The topology and dynamics of the *lac* operon model. The figure was obtained using the software package DVD (Jarrah et al. 2004). The interpretation is described in the text

hence, the dynamics show that the model is not quite correct. Specifically, the additional steady state of the model represents a situation in which lactose is present in the cell, but the machinery to metabolize it is turned off. Thus, the mathematical analysis points to a flaw in understanding the underlying biological mechanisms used to formulate the individual logical rules used in the model.

25.7.3   Project 3

Using additional biological insight and analysis of the model constructed in Project 1, modify it to better conform with biological knowledge.

In search of a way to modify the functions in the model so that the state $(0, 0, 0, 1, 0)$ transitions to the steady state $(0, 0, 0, 0, 0)$ participants need to understand more of the biology and reexamine the Boolean functions. One place to make a modification is the function for S. Its first term assures that S will be present at time $t + 1$ if it was present at time t. Several modifications are possible, for instance deleting the first term or expanding it to include the presence of other variables. The process of model improvement leads to fruitful discussions that provide further insight into the biology, the modeling process, and the utility of models. The DVD software is a helpful tool that allows an easy visualization of the basic model properties (Jarrah et al. 2004). It also allows the participants to discuss whether the model constructed exhibits the expected properties of the biological system, how to test it, and how to improve the results obtained. This discussion is most useful if it is conducted in a team that contains different areas of expertise, e.g., math majors and biology or biochemistry majors.

25.8   Discussion

Mathematical modeling is becoming an essential tool in the life sciences and in biomedicine, and several fields of expertise contribute to increasingly larger projects to understand the variety of biological networks that make organisms function. We believe that students should be exposed to this area at the interface of biology and mathematics as early as possible. We have designed a collection of projects that try to capture the essence of mathematical modeling in biology, with a minimum of mathematical and biological background requirements. The projects are structured as open-ended hands-on team science activities that engage the students and encourage interaction.

While the *lac* operon has been studied for a long time, it continues to be an interesting and fruitful topic for ongoing research, as demonstrated by the recent literature on the subject. The projects thus bring students directly to a basic understanding of a topic at the forefront of current research. Depending on the setting, the projects can be expanded and extended in several directions, leading students to the intricacies of molecular data and mathematical models.

The projects are a case study for introducing real mathematical biology projects into the undergraduate and even high school curriculum. There are other biological topics that lend themselves to a similar approach, for example,

the workshop introduced by Rivera-Marrero and Stigler (2004) applied to an epidemiology problem of viral epidemic prediction and prevention.

Acknowledgements

References

Albert, R., and H.G. Othmer, 2003: The topology of the regulatory interactions predicts the expression pattern of the segment polarity genes in *Drosophila melanogaster*, *J. Theor. Biol.* **223**, 1–18.

Barabasi, A.L., and Z.N. Oltvai, 2004: Network biology: understanding the cell's functional organization, *Nat. Rev. Genet.* **5**, 101–113.

Caplan, M.R. and E.V. Rosca, 2005: Targeting drugs to combinations of receptors: a modeling analysis of potential specificity, *Ann. Biomed. Eng.* **33**, 1113–1124.

Crick, F.H., 1958: On protein synthesis, *Symp. Soc. Exp. Biol*. **XII**, 138–163.

de Jong, H., 2002: Modeling and simulation of genetic regulatory systems: a literature review, *J. Comput. Biol.* **9**, 67–103.

Friedman, N., M. Linial, I. Nachman and D. Pe'er, 2000: Using Bayesian networks to analyze expression data*, J. Comput. Biol.* **7**, 601–620.

Hoops, S., S. Sahle, R. Gauges, C. Lee, J. Pahle, N. Simus, M. Singhal, L. Xu, P. Mendes and U. Kummer, 2006: COPASI–a COmplex PAthway SImulator, *Bioinformatics* **22**, 3067–74.

Jacob, F., and J. Monod, 1961: Genetic regulatory mechanisms in the synthesis of proteins, *J. Mol. Biol.* **3**, 318–356.

Jarrah, A., R. Laubenbacher and H. Vastani, 2004, cited in 2012: DVD: Discrete Visual Dynamics [Available online at http://dvd.vbi.vt.edu].

Jarrah, A., R. Laubenbacher, B. Stigler, and M. Stillman, 2007: Reverse-engineering of polynomial dynamical systems, *Adv. Appl. Math.* **39**, 477–489.

Kauffman, S.A., 1969: Metabolic stability and epigenesis in randomly constructed genetic nets, *J. Theor. Biol.* **22**, 437–467.

Koolman, J., and K.-H. Röhm, 1996: *Color Atlas of Biochemistry*, Thieme.

Laubenbacher, R., and B. Stigler, 2004: A computational algebra approach to the reverse engineering of gene regulatory networks, *J. Theor. Biol.* **229**, 523–537.

Lodish, H., L. Berk, L. Zipursky, P. Matsudaira, D. Baltimore, and J. Darnell, 2000: *Molecular Cell Biology*, W.H. Freeman.

Murray, J.D., 1993: *Mathematical Biology*, Springer-Verlag.

National Council of Teachers of Mathematics: Principles and Standards for School Mathematics, cited 2012: [Available online at http://standards.nctm.org/].

Ribba, B., T. Colin and S. Schnell, 2006: A multiscale mathematical model of cancer, and its use in analyzing irradiation therapies, *Theor. Biol. Med. Model.* **3**, 7–25.

Rivera-Marrero, O., and B. Stigler, 2004, cited 2012: Model Your Genes the Mathematical Way I [Available online at http://admg.vbi.vt.edu/home/Outreach/Workshops/1].

Veliz-Cuba, A., R. Laubenbacher, and M. Beeken, 2009, cited 2012: A Mathematics Classroom Module [Available online at http://admg.vbi.vt.edu/home/Outreach/OR/MathModule].

Virginia Department of Education, Standards of Learning Currently in Effect for Virginia Public Schools [http://www.pen.k12.va.us/VDOE/Superintendent/Sols/home.shtml].

Watson, J.D., 2003: *DNA–The Secret of Life*, Alfred A. Knopf.

Watson, J.D., and F.H. Crick, 1953: Molecular structure of nucleic acids; a structure for deoxyribose nucleic acid, *Nature* **171**, 737–738.

26

Creating Quantitative Biologists:
The Immediate Future of SYMBIOSIS[†]

Darrell Moore[1], Karl H. Joplin, Istvan Karsai, and Hugh A. Miller III
Dept. of Biological Sciences, East Tennessee State University

Michel Helfgott, Anant Godbole, and Edith Seier
Dept. of Mathematics & Statistics, East Tennessee State University

Name of Institution	East Tennessee State University
Size	about 15,000 students
Institution Type	regional state institution with graduate programs
Student Demographic	freshman curriculum for all biology majors
Department Structure	Mathematics and Biology are individual departments in College of Arts and Sciences

Abstract

The SYMBIOSIS project is an innovative sequence of three courses designed for the first three semesters of the undergraduate curriculum. They involve a thorough integration of biology, mathematics, and statistics. In order to maintain our interdisciplinary approach beyond the SYMBIOSIS courses, a number of pedagogical and cultural barriers must be bridged.

26.1   Course Structure

- Weeks per term: 15 weeks

- Classes per week/type/length: M (Lec-2 hrs), T (Lab-2 hrs), W (Lec-2 hrs), Th (Lec-2 hrs), F (Lec-2 hrs)

- Labs per week/length: one 2-hr lab/wk

- Average class size: 16 students in one section

- Enrollment requirements: Students supported by our NSF STEP grant

---

[1] moored@etsu.edu

- Faculty/dept per class, TAs: One biology and one math instructor, two TAs
- Next course: IBMS 1200, Integrated Biology and Calculus
- Website: http://www.etsu.edu/cas/symbiosis/default.aspx

26.2   Introduction

Biological research is undergoing a major transformation, but biological education is not keeping up. Biology is becoming much more quantitative and computational, incorporating concepts and methods that integrate the biological sciences with mathematics, the physical sciences, and computer science. Because most undergraduate biology programs are not designed to prepare students for the changes, the National Research Council issued a call, published in their *Bio2010* report (National Research Council 2003) to incorporate more mathematics and physical sciences into the undergraduate biology curriculum, suggesting that it be done early in the student's academic career. We at East Tennessee State University have created the SYMBIOSIS project (Joplin et al. 2012), funded by the Howard Hughes Medical Institute, as an answer to the *Bio2010* call.

Our approach is atypical, even among those programs that integrate mathematics and biology. We present the biology and the mathematics in a mutually reinforcing, storytelling methodology, starting in the first semester of college. There is no separation between the disciplines, in contrast to more traditional curricula.

The SYMBIOSIS program comprises the first stage of an effort to incorporate more mathematics into the biology major. By introducing students to an interdisciplinary program from the start of their academic careers, we hope to make lasting connections between the two disciplines. However, to make an enduring impression on the students, the program must be expanded so that the lessons learned early are reinforced in upper division courses. A way to plan the future direction of the SYMBIOSIS program is to ask what we expect of graduating students who have successfully navigated our quantitative biology curriculum. Of course, we expect them to think like practicing scientists! But what will it take, beyond the three semesters of integrated SYMBIOSIS courses, to get them there?

26.3   Overcoming Textbook Inadequacies

A reading of introductory biology textbooks provides insight into the state of pedagogy in the biological sciences. All the popular introductory texts contain over 1200 densely packed pages and are authoritatively written, up-to-date, and profusely illustrated. There is little difference among them in subject matter. Each has a glossary defining nearly 2000 terms. Although the authors make an effort to reinforce major concepts in each chapter, they are difficult to discern (especially for the novice student) through the dense jungle of facts and new terms. Most of the material is presented as factual, and therefore students cannot get a sense of the thought processes behind the discoveries. Some introductory textbooks include shaded boxes separate from the text proper that show examples of important experiments and the testing of hypotheses. Rather than being treated as side issues, they should be developed in more detail and form the core of the textbook. None of the introductory biology textbooks includes references: if students want to pursue the subject in greater detail, they must go elsewhere to find the original literature. In many ways, the introductory texts resemble encyclopedias. The compendium approach to biology, evident in the introductory textbooks, serves to reinforce rote memorization rather than problem-solving.

Introductory biology textbooks de-emphasize quantitative thinking. For example, numerical results are reported as means, but without error bars. Graphs may show the results of treatments relative to each other and to controls, but without mention of statistical significance. Perhaps the authors of introductory biology textbooks assume that beginning students do not have the background to understand the importance of probability and statistics or that they are not necessary. We believe that to comprehend how biology is done, students must come to grips with the issues of variability, sample size, and significance. The earlier in the student's education this is accomplished, the better the student will be prepared to go beyond a superficial level of understanding. The non-statistical trend is not confined to the introductory texts: it is present in upper level textbooks as well. Such simplification of the data may, at first glance, appear to allow the student to focus on larger issues. However, by omitting statistical details, the authors are asking students to accept conclusions on faith, without essential supporting evidence. We don't operate this way within the scientific community. As role models for our students, we should deliver and accept nothing less in the classroom.

Convincing authors and editors to make extensive changes to their textbooks is not realistic. However, we can begin the process in the direction of textbook reform by adhering to a new set of standards in the classroom. We need to jettison the encyclopedic approach to biology (as exemplified by biology textbooks) and infuse our classes with the process and excitement of biological discovery (National Research Council 2005). We need to incorporate discussions of how biological concepts were discovered, including the quantitative methods used to analyze data, so that we give students a more accurate picture of how science is conducted. Students should see principles that can be applied to new situations. If the goal is for our students to think like practicing scientists, then the process of doing science is much more important than a description of the end results of that process.

A more quantitative, process-driven approach takes time. Therefore, rather than trying to cover every subject in the textbook, we need to cover fewer items but do them well. But what subjects do we sacrifice? These are tough decisions, but we should not lose sight of our ultimate goal–we are training our students to become problem-solvers, not fact-recalling automatons.

Standard first-year biology textbooks (and texts for more advanced courses) could be enhanced by using some basic mathematical techniques, drawn mainly from high school algebra and geometry. For instance, when discussing the phenomenon of diffusion across cell membranes, we can take advantage of Fick's law to make a quantitative analysis of the surface to volume ratio for cells of fixed volume but different shapes (spheres, cylinders, etc.). When discussing enzymes, the opportunity should not be lost to analyze the Michaelis-Menten equation qualitatively and quantitatively. This leads to important conclusions through the use of transformations of variables and linear and nonlinear regression (Ledder 2013).

Biology textbooks are full of opportunities to use mathematics to help illuminate the biological processes. Although mathematical formulae are few and far between in introductory biology textbooks, several texts present the Nernst equation used to calculate the equilibrium potential for a single ion species in terms of the ion's concentrations outside and inside of the cell. Typically, the equilibrium potential is given for potassium ions (E_K) and the point is made that potassium is at equilibrium when the inside of a cell membrane is more negative than the outside ($E_K \simeq -75$ millivolts for squid giant axon at $20°$ Celsius). Since the resting membrane potential (V_m) is somewhat more positive than E_K($V_m \simeq -70$ millivolts), other ions besides potassium must contribute to V_m. Rather than stopping here, why not employ the Goldman-Hodgkin-Katz equation (Nicholls et al. 2012), which incorporates the concentration gradients from several permeant ions simultaneously and the membrane's relative permeabilities to them? The GHK equation can be shortened to include just sodium and potassium ions:

$$V_m = 58 \ \log \ \frac{p_K[K]_{out} + p_{Na}[Na]_{out}}{p_K[K]_{in} + p_{Na}[Na]_{in}}.$$

We can make the analogy between permeability and membrane conductance to different ion species (the more open ion channels there are in the membrane, the higher will be the conductance). Also, by increasing the permeability (and, by analogy, conductance) of the membrane to sodium, V_m moves toward the equilibrium potential for sodium, which is exactly what happens during the initial phase of the action potential or during excitatory postsynaptic potentials. Thus, mathematical manipulation of the relative permeabilities sets the stage for understanding the biological changes in membrane conductances that underlie action, synaptic, and receptor potentials.

Many standard first-year textbooks of mathematics used by biology majors present few if any examples related to the biological sciences. And when an example is presented, say the flow of blood across an artery, no explanation is provided for the startling fact that the volume of blood that flows through a cross section of an artery in unit time is proportional to the fourth power of the radius. An application of Poiseuille's law, in the developing the main ideas of integration, could shed light on the problem of blood flow.

26.4 Changing Teaching Strategies

We need to incorporate more of the learning approaches that have been shown to promote transfer learning – the ability to use information in a new situation. Currently at our institution, we are dismayed by our students' lack of retention from the introductory to the upper division classes. Our students perform much like novices (Larkin et al. 1980) when confronted with problems and intellectual challenges: they do not seem to be able to form connections. We are continually doing remedial teaching of basic concepts in our upper division courses. Instead of a coherent set

of unifying principles, biology (for many students) is an amorphous collection of facts. So, it should not be surprising that retention is low. The literature provides some suggestions for improving transfer learning.

- Insightful problem solving can be trained by showing students how to improve their metacognitive ("thinking about thinking") skills (Davidson and Sternberg 1998)

- The application of hypothetico-deductive reasoning is like the way that people naturally process thoughts and, therefore, instruction should provide students with increasingly complex opportunities to propose and test hypotheses (Lawson 2005).

- Rather than continually boosting students' self-confidence, a better approach may be to give them a challenging task early in the semester, thus giving them a healthy "shock" to stimulate their effort and reasoning skills (Lawson et al. 2007).

Our SYMBIOSIS curriculum encompasses only the first three semesters of college. To reinforce the integrative approach to biology, upper division biology courses must include more quantitative examples and incorporate more quantitative approaches to solving problems. It is imperative that the interdisciplinary approach not disappear in the remaining two and a half years in their course of study. How can this be accomplished? The following suggestions certainly are not novel, but we consider them to be vital to the continuation of our SYMBIOSIS initiatives.

- Make modifications to current biology courses, such as including quantitative modules – if a few modules are added, the entire course does not need to be overhauled. One or two new modules can be added each time the course is taught.

- Make modifications to current mathematics courses, using biological examples rather than the more traditional engineering problems.

- Have a greater emphasis on handling and analyzing data sets in biology courses, in the lecture and the laboratory. Incorporate statistical tests of hypotheses as often as possible.

- Create new interdisciplinary courses, with biologists and mathematicians as co-instructors. This takes a great deal of effort and cooperation between departments and perhaps a reorganization of teaching responsibilities.

26.5 Culture Shock

"It is not the strongest of the species that survives, nor the most intelligent that survives. It is the one that is the most adaptable to change."

–Charles Darwin

Change is difficult. Sweeping changes, such as those envisioned by *Bio2010,* require a concerted effort by entire departments and institutions. What are some of the barriers to implementing the *Bio2010* suggestions? First, while most biology professors recognize the need for a more quantitative pedagogy, inertia must be overcome before there can be any progress. For many, the quantitative approach evokes an almost reflexive defensiveness. Others may be willing to change, but feel that they are already overburdened or unprepared. Still others may believe that they already are doing enough in their own classes and see no need to participate in any large-scale initiatives. A second set of barriers comes from the students. Many choose to major in biology because they see it as less mathematical than physics and chemistry, the age-old math phobia problem. We hope that an integrated curriculum (such as SYMBIOSIS), where students are shown from the beginning that mathematics and biology are complementary to each other, may help treat this malady. How can we minimize the loss of biology majors (many of whom will be pre-medicine) and encourage more faculty members to make modifications to our undergraduate curriculum? We think it will require nothing less than a change in the culture of biology instruction.

How can a tradition of teaching, firmly entrenched over many decades, be transformed? How can we convince students that a more quantitative biology will better prepare them? Somehow, the subject matter has to be relevant and accessible to the students and the professors. The old perception that mathematics and biology are in different domains must be dispelled. We must establish a community of scholarship in which interdisciplinary interactions are recognized, encouraged, and rewarded. Here are some recommendations:

- Encourage research publications in which both mathematicians and biologists are co-authors. Publications are rewards that can benefit all participants. With some success, others may see benefits. At our institution, we have established several collaborative research groups that are beginning to yield publications.

- Encourage publishing articles in education journals describing ways of incorporating quantitative approaches to traditionally qualitative lectures and laboratories. The publications should be rewarded in the tenure and promotion process.

- Have courses taught by colleagues from both departments.

- Design interdisciplinary graduate and undergraduate student projects with quantitative and biological components. Assign at least one committee member from each of the mathematics and biology departments.

- Teaching assistants in the biology department must be trained and prepared to help the permanent faculty in making the transition.

- Invite seminar speakers with quantitative biological research and who have the ability to make the mathematics accessible to a general biological audience.

- We desperately need a program for faculty development. Many biologists would like to have more quantification, but don't have the mathematical skills. Such development typically requires time, motivation, and funding. We need to identify some mechanisms by which the biology faculty can improve their competence in mathematics.

- Hire new faculty members who have quantitative skills and who can establish both research and teaching interdisciplinary collaborations.

- A cultural change within the Mathematics Department is needed as well; more mathematicians need to appreciate that linking mathematics to biological applications enriches learning mathematics as well as biology.

References

Davidson, J.E., and R.J. Sternberg, 1998: Smart problem solving: how metacognition helps. *Metacognition in Educational Theory and Practice*, D.J. Hacker, J. Dunlosky, and A.C. Graesser, Eds., Lawrence Erlbaum Associates, 47–68.

Joplin, K.H., E. Seier, A. Godbole, M. Helfgott, I. Karsai, J. Knisley, D. Moore, and H.A. Miller III, 2012: SYMBIOSIS: An integration of biology, math and statistics at the freshman level: walking together instead of on opposite sides of the street. This volume, xx–yy.

Larkin, J., J. McDermott, D.P. Simon, and H.A. Simon, 1980: Expert and novice performance in solving physics problems. *Science*, **208**, 1335–1342.

Lawson, A.E., 2005: What is the role of induction and deduction in reasoning and scientific inquiry? *J. Res. Sci. Teach.*, **42,** 716–740.

Lawson, A.E., D.L. Banks, and M. Logvin, 2007: Self-efficacy, reasoning ability, and achievement in college biology. *J. Res. Sci. Teach.*, **44**: 706–724.

Ledder, G., 2013: A terminal post-calculus-I mathematics course for biology students, this volume, 51–60.

National Research Council, 2003: *Bio2010: Transforming Undergraduate Education for Future Research Biologists*, National Academies Press.

National Research Council, 2005: *How Students Learn: Science in the Classroom*, M. S. Donovan and J.D. Bransford, Eds., National Academies Press.

Nicholls, J.G., A.R. Martin, P.A. Fuchs, D.A. Brown, M.E. Diamond, and D.A. Weisblat, 2012: *From Neuron to Brain*, 5th ed., Sinauer.

About the Editors

Glenn Ledder was born in Aurora, CO and currently resides in Lincoln, Nebraska. He received his B.S. in ceramic engineering from Iowa State University and his M.S. in mathematics and Ph.D. in applied mathematics from Rensselaer Polytechnic Institute. He is currently an Associate Professor of Mathematics at the University of Nebraska-Lincoln (UNL). He is the author of *Differential Equations: A Modeling Approach* (2005) and *Mathematics for the Life Sciences: Calculus, Modeling, Probability, and Dynamical Systems* (2013). Ledder has served as Program Chair for the Special Interest Group for Mathematical and Computational Biology of the MAA (BIO SIGMAA). He was co-director of the NSF-funded Research for Undergraduates in Theoretical Ecology (RUTE) program at UNL. He has mentored 40 undergraduate research students, including four groups of students in the Nebraska Research Experience for Undergraduates (REU) site. His students have won awards at the Undergraduate Poster Session at the Joint Mathematics Meetings and regional meetings of the MAA. He was an invited speaker at the Beyond BIO2010 symposium at the National Academy of Sciences in 2010 and had a student present an undergraduate research poster at that conference. Ledder has been a member of the organizing committee for the Nebraska Conference for Undergraduate Women in Mathematics (NCUWM) for a number of years and is currently co-chair of that committee.

Jenna P. Carpenter was born in Corsicana, Texas, grew up in Hope, Arkansas, and currently resides in Ruston, Louisiana. She received her B.S. in Mathematics from Louisiana Tech University and her M.S. and Ph.D. in Mathematics from Louisiana State University where she was an LSU Alumni Federation Fellow. She has spent fourteen years as a university administrator and is currently Associate Dean for Administration and Strategic Initiatives, Wayne and Juanita Professor of Mathematics in the College of Engineering and Science at Louisiana Tech University. Carpenter has been active for the last two decades in innovative STEM curricula and initiatives to encourage the success of women in STEM fields, with approximately $3 million in federal funding. She is currently on the Steering Committee for the MAA Committee on the Undergraduate Program in Mathematics (CUPM) Curriculum Guide, serves on the MAA Professional Enhancement Program (PREP) Leadership Team, is chair of the MAA Professional Development Committee, and is the MAA Louisiana-Mississippi Section Governor. She chairs the Steering Committee for the National Academy of Engineering Grand Challenge Scholars Program. She served two terms on the MAA Committee on Curriculum Renewal Across the First Two Years (CRAFTY), is a past Vice President of the American Society for Engineering Education, and served three terms on the Board of Directors for the Women in Engineering ProActive Network. She is also on several other state and national-level boards. Carpenter actively mentors faculty, undergraduate students, graduate students, and women in STEM, both at her own institution and through professional organizations and her state and national-level activities.

Timothy D. Comar was born in Chicago, IL and currently resides in the northern suburbs of Chicago. He received his Sc.B. in mathematics from Brown University and his Ph.D. in mathematics from the University of Michigan. Comar is currently an Associate Professor of Mathematics at Benedictine University. He is a member of the MAA, AMS, SIAM, and the Society for Mathematical Biology and has served as the chair of the Special Interest Group for Mathematical and Computational Biology of the MAA (BIO SIGMAA). He also serves on the Mathematics Across the Disciplines Subcommittee of the CUPM of the MAA, the Education Committee of the Society for Mathematical Biology, and the Board of Directors of the Illinois Section of the MAA (ISMAA). Comar is a Project NExT Fellow. He has been teaching courses in mathematical biology since 2003 and has mentored many undergraduate research students in mathematical biology, some of whom have won MAA Outstanding Speaker Awards at Mathfest.

UNDERGRADUATE
MATHEMATICS FOR

THE
LIFE
SCIENCES

MODELS
PROCESSES
AND
DIRECTIONS

THIS VOLUME contains 26 articles for mathematics and biology faculty who want to develop courses and programs in mathematics for life science students. The authors represent a wide variety of academic institutions, from universities to community colleges, and all of the articles begin with information about the institutional context. Many of the articles also include links to resources that can be found on the internet, and some have associated books in print as well. All emphasize features that could be applied to similar projects at other institutions and offer useful advice for the newcomer to mathematics curriculum development for life science students.

Glenn Ledder, Jenna P. Carpenter, Timothy D. Comar

EDITORS