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6

Biology in Mathematics at the University of Richmond

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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

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- 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.