Mathematics in the Life Sciences Curriculum

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"Mathematics is biology's next microscope—only better."

—Rita Colwell, director of the NSF 1998–2004

The text of this talk is available at:

www.math.tamu.edu/~phoward/talks.html

Selected References

- 2003 National Academies report: BIO2010: Transforming Undergraduate Education for Future Research Biologists
  - www.nap.edu/catalog/10497.html
- Material for M151B/M152B (Version A calculus), M147/M148 (Version B calculus), and M442 (Math Modeling)
  - www.math.tamu.edu/~phoward/M151.html etc.
- C. Neuhauser, *Calculus for Biology and Medicine*, 2nd Edition, Pearson 2004
- J. D. Murray, *Mathematical Biology*, 2nd Edition, Springer 1993
- C. L. Taubes, *Modeling Differential Equations in Biology*, Prentice Hall 2001.

Overview of the Talk

- Introduction and Background
- Curriculum Change in the Life Sciences
- Mathematics in the Life Sciences Curriculum
- Calculus for Life Science Majors
- The Role of a Modeling Course

2003 National Academies Report

The importance of quantitative biology was summarized in a recommendation from the National Academies in their 2003 report, BIO2010: Transforming Undergraduate Education for Future Research Biologists (see p. 8 of the report, the first recommendation listed):

"Given the profound changes in the nature of biology and how biological research is performed and communicated, each institution of higher education should reexamine its current courses and teaching approaches to see if they meet the needs of today's undergraduate biology students. Those selecting the new approaches should consider the importance of building a strong foundation in mathematics and the physical and information sciences to prepare students for research that is increasingly interdisciplinary in character."

The UBM Program at Texas A&M

In 2004 Texas A&M received funding from the NSF for a UBM program (Undergraduate Biological and Mathematical Sciences). The PI was Vincent Cassone, and the Co-PI in mathematics was Jay Walton (now the PI). (The other Co-PI's are Deborah Bell-Pedersen in Biology, Rodney Honeycutt in Biology and Wildlife and Fisheries Sciences, and Thomas Wehrly in Statistics.)

As part of this program, Jay Walton introduced a weekly seminar on mathematical biology and he also developed a semester-long senior level course on mathematical biology focused primarily on applications of dynamical systems, though also with a component on stochastic processes.

Since 2002 I have taught a course in mathematical modeling in which I spend roughly a quarter of the time on mathematical biology.

Life Sciences Calculus at Texas A&M

In 2006-2007 I developed a two-semester quantitative calculus sequence for students in the life sciences (fast-paced, and with a MATLAB component) (Version A). There were 22 students in this first course. In 2009-2010 I developed a second two-semester calculus sequence, this one at a slower pace, and without a MATLAB component (Version B).

Current enrollment for Version B is 250, taught in three lectures (and nine sections). (Version A is on hiatus due to ecomonic pressure.)

The second semester of Version A has been taught by a post-doc, Yuliya Gorb. The first semester of Version B has been taught by a lecturer, Heather Ramsey, who is currently teaching the second semester.

Autobiographical Notes

- Undergraduate degree in physics from Tennessee Technological University (1991)
- Master's Degree in management science from the University of Tennesee (1993)
- Ph. D. in mathematics from Indiana University (1998)
- Research interests
  - existence and stability of nonlinear waves
  - conservation laws
  - phase separation and coarsening dynamics
- Last biology course was from Coach Kamikawa at Rockwood High School

U.S. Bachelor's Degrees in the Life Sciences

Year	"Biological and biomedical sciences"	All majors	Percent
1980	46,109	929,417	5.0
1990	37,204	1,051,344	3.5
2000	63,005	1,237,875	5.1
2005	64,611	1,439,264	4.5
2006	69,178	1,485,242	4.7
2007	75,151	1,524,092	4.9

Source: 2010 Statistical Abstract of the United States

Comparison U.S. Bachelor's degrees by percent

Year	Math/Stat	Engineering	Business
1980	1.2	7.5	20.0
1990	1.4	7.8	23.6
2000	.9	5.9	20.7
2005	1.0	5.5	21.6
2006	1.0	5.5	21.4
2007	1.0	5.4	21.5

Source: 2010 Statistical Abstract of the United States

Goals for the New Life Sciences Curriculum I

- The amount of core biology that a life sciences student should master as an undergraduate increases each year with advancing research. It's unreasonable to assume students will generally take less biology in the new curriculum.

- Many advances in life sciences research will occur where biology overlaps with chemistry, physics, mathematics, engineering, and computer science. Students in the life sciences should become more familiar with these subjects.

- Faculty in these departments should incorporate relevant examples from the life sciences into their lectures.

Goals for the New Life Sciences Curriculum II

- Life science faculty should make use of material students have learned in courses from these departments.

- Laboratory work in the life sciences should emphasize the interdisciplinary nature of laboratory research.

- Interdisciplinary undergraduate research should play a critical role in the new curriculum. Projects involving co-mentors from different departments can be especially productive.

The “Special Case” of Mathematics

In the BIO2010 report the committee writes (p. 5):

“Mathematics teaching presents a special case. Most biology majors take no more than one year of calculus, although some also take an additional semester of statistics. Very few are exposed to discrete mathematics, linear algebra, probability, and modeling topics.”

In the following four slides I'll discuss mathematics topics that strike me as relevant to research in the life sciences. Aside from my inclusion of partial differential equations, this list is quite similar to the one beginning on page 42 of the BIO2010 report.

Mathematics in the Life Sciences I

- Pre-calculus and calculus
  - real and complex numbers, functions, limits, continuity, differentiability, integrability
  - multidimensional differentiation and integration

- Matrix and linear algebra
  - scalars, vectors, matrices, linear transformations, eigenvalues and eigenvectors, invariant subspaces

- Standard ODE techniques
  - separable equations, linear first and second order equations, first order linear systems

Mathematics in the Life Sciences II

- Dynamical Systems
  - nonlinear systems of difference equations
  - nonlinear systems of differential equations
  - phase plane analysis
  - equilibrium points and stability
  - limit cycles

- Modeling techniques
  - arguments based on scale
  - dimensional analysis and nondimensionalization
  - regression and parameter estimation
  - modeling with difference and differential equations
  - modeling with partial differential equations
  - modeling stochastic processes

Mathematics in the Life Sciences III

- Mathematical computation
  - rudimentary programming in a high programming language
  - familiarity with (one of) MATLAB, Maple, Mathematica etc.

- Partial differential equations
  - linear diffusion equations
  - Fourier techniques
  - reaction-diffusion equations

- Probability theory and statistics
  - combinatorics, discrete and continuous random variables, simulation, stochastic processes
  - sampling, maximum likelihood estimators, hypothesis testing

Mathematics in the Life Sciences IV

While the preceding list is overly ambitious, it certainly is not exhaustive.

- Topology and knot theory
  - strands of DNA can be regarded mathematically as topological *knots* that must be unknotted by enzymes in order for replication or transcription to occur
  - www.tiem.utk.edu/~harrell/webmodules/DNAknot.html
- Transform methods
  - the Radon transform is an important tool, for example, in imaging by tomography
  - P. Kuchment and L. Kunyansky, *Mathematics of thermoacoustic tomography*, European J. Appl. Math. 19 (2008), no. 2, 191–224.

“Traditional” Math Requirements (from Texas A&M)

- Finite math
  - logic, probability, systems of linear equations
  - the textbook is *Applied Finite Mathematics*, by E. C. Tomastik and J. Epstein
- Single variable calculus
  - fairly standard first semester in calculus
  - the textbook is *Single Variable Calculus: Concepts & Contexts*, 4th Ed., J. Stewart 2010
- Introductory Statistics
  - sampling and statistical inference; estimation and hypothesis testing
  - textbook is *The Practice of Statistics in the Life Sciences*, B. Baldi and D. Moore

A New Mathematics Sequence

Our two main questions are:

1. How much mathematics should be incorporated into the life sciences curriculum?

2. In what way should it be incorporated?

In BIO2010, the Committee proposes the introduction of:

“A new mathematics sequence that exposes students to statistics, probability, discrete math, linear algebra, calculus, and modeling without requiring that a full semester be spent on each topic. A brief overview of these topics could be presented in two semesters, but a full introduction and the inclusion of more computer science would more likely take four semesters.”

The Case Against a New Sequence

- The broad consistency of undergraduate courses such as those in the standard calculus sequence is quite useful in that we all know what a student who has taken calculus has seen.
- Students can change majors without re-taking their core mathematics classes.
- Students can easily transfer credits from junior colleges etc. for standard courses. For many programs, including those in the life sciences, student diversity is enhanced by students transferring from junior colleges.
- Developing a new sequence requires significant work, and a sequence such as this is difficult to staff. (More on this later.)

The Case For a New Sequence I

- A new sequence can be designed so that students will learn a good deal of the mathematics they need to know without taking additional classes.

- The new sequence will emphasize life science applications, so life science majors should recognize the relevance of the techniques.

- Likewise, developing a new sequence allows us to use fewer biological examples in traditional calculus courses, where students may not find them relevant.

- Introducing a new sequence allows more flexibility in setting the level of presentation. For example, do students in the life sciences need to know epsilonics?

The Case For a New Sequence II

- A mathematics course for students in the life sciences can serve as a gathering ground for students with different majors but similar interests.

- The course helps to connect faculty in mathematics with faculty in the life sciences.

Multiple Tracks

Clearly, different programs will set different mathematical requirements for the students. Also, a program might allow students to make a (limited) choice regarding how much math to take. To be specific, we will think in terms of four tracks:

- **Qualitative track**: minimal mathematics
- **Quantitative track**: a significant amount of mathematics, developed at a slow pace with little theory
- **Fast quantitative track**: a significant amount of mathematics, developed at a rapid pace with more theory
- **Math minor track:** mathematics up through partial differential equations and modeling at a level comparable with the math major curriculum

Recruitment Into Quantitative Tracks

- Goals
  - **high school to undergraduate:** recruit more students who are strong in mathematics into undergraduate life science majors
  - **undergraduate:** recruit students who would traditionally take minimal mathematics into tracks with an emphasis on mathematics
  - **undergraduate to graduate:** recruit more students who are strong in mathematics into graduate programs in the life sciences

- Selling points
  - in many life science fields mathematics is now playing as important a role as it has traditionally played in engineering and physics
  - there are better employment and graduate school prospects for students with a more quantitative degree

Broad Goals for the Quantitative Tracks

- Familiarize students with mathematics that appears in current life science publications
- Provide students in the life sciences with a vocabulary that will help them communicate with researchers in mathematics
- Prepare students for upper division undergraduate work and for graduate work in the life sciences
- Prepare students for quantitative research projects to be carried out in their departments or in an interdisciplinary environment with co-mentors

Challenges for Faculty I

From the BIO2010 Report:

"Successful redesign of courses and curricula requires a much larger investment of faculty time, departmental encouragement, and significant support from the college or university administration. Faculty must master material, delete material from preexisting courses to accomodate new material, and adapt their teaching style to the new approach. In almost all institutions, systematic change in the curriculum lies beyond the reach of individual faculty members."

Challenges for Faculty II

- Courses on mathematics in the life sciences are difficult to staff.
  - Many faculty members in math departments do not feel suitably prepared to lecture on life science topics.
  - Courses that are genuinely focused on mathematics in the life sciences differ significantly from standard courses, and this means prep work is considerable.
  - While good textbooks have appeared for a two-semester calculus sequence, few textbooks are available for upper division classes.
  - As far as I know there are no good manuals for technology (MATLAB, Maple, Mathematica) in the life sciences.
  - At many, if not most, research institutions effort toward teaching is not encouraged.

Challenges for Faculty III

- Some faculty members in life science departments do not agree that their majors need a quantitative track.
  - If quantitative applications are not covered in life science classes, students will not think their math courses are relevant.
- It's difficult to find qualified graduate students or upper division undergraduate students to staff recitation sections.
- It can be difficult to arrange help for students outside of class.
  - It's difficult to find qualified undergraduates to staff help sessions.
  - Individual student-tutors and off-campus tutoring services don't know what to do with the courses.

Challenges for Students I

- Many students in the life sciences do not have the necessary background from high school for a college-level calculus sequence, and this means they must either take an additional pre-calculus course or struggle considerably with the quantitative track.

- Many students in the life sciences still think they won't use much mathematics in their future work, and so these courses do not interest them.

- As with most introductory courses at public research universities, class sizes will generally be quite large, and while this is difficult on all students, it is particuarly difficult on (1) students with insufficient preparation, and (2) students who need to be convinced the material is relevant.

Challenges for Students II

- Many students in the life sciences are preparing for medical school, and they are competing (in GPA, for example) with students who are not taking challenging mathematics.

- These students are often specifically preparing for the Medical College Admissions Test (MCAT), and to some extent this preparation constrains what courses they should reasonably take. (The BIO2010 report suggests a reexamination of medical school admissions requirements in general and the MCAT specifically.)

The Math Minor Option

Six semester-length courses, 21 hours total (18 math, 3 statistics).

- Calculus I-III
- Ordinary and partial differential equations
- Mathematical modeling in the life sciences
- Statistics

The Calculus Sequence

- Calculus I
  - pre-calculus; standard introduction to differential and integral calculus; application to single difference equations
- Calculus II
  - linear algebra; multivariate differential calculus; application to discrete and continuous dynamical systems
- Calculus III
  - multivariate integral calculus; introduction to partial differential equations

Upper Division Courses

- Ordinary and partial differential equations
  - solution techniques; qualitative considerations; MATLAB
- Mathematical modeling in the life sciences
  - dimensional analysis; regression techniques and parameter estimation; modeling with difference equations; modeling with ODE; probability; projects
- Statistics
  - sampling and inference; hypothesis testing; estimators

Emphasis on the First-Year Sequence

Many students in the life sciences will not reasonably be able to take more than two semesters of mathematics (and one semester of statistics), so one pragmatic approach is to develop a one-year sequence that covers the most important topics in life science mathematics. Such a sequence seems to be in place or under development now at many universities and colleges.

One early quantitative first-year sequence for students in the life sciences was developed by Louis Gross at the University of Tennessee in Knoxville, starting in 1991. I'll briefly review the topics in Dr. Gross's course on the next two slides. For details, see

www.tiem.utk.edu/~gross/quant.lifesci.html

The Sequence at UTK, Fall Semester

- Descriptive statistics
  - analysis of tabular data, means, variances, histograms, linear regression
- Exponentials and logarithms, non-linear scalings, allometry
- Matrix algebra
  - addition, subtraction, multiplication, inverses, matrix models in population biology, eigenvalues and eigenvectors, Markov chains, ecological succession
- Discrete probability
  - population genetics, behavior sequence analysis

The Sequence at UTK, Spring Semester

- Difference equations
  - linear and nonlinear examples, equilibrium, stability and homeostasis, logistic models, limits

- Calculus
  - limits of functions and continuity
  - derivatives and curve sketching
  - antiderivatives and integrals
  - trigonometric functions

- Differential equations and modeling

Remarks Specific to Calculus I-II at Texas A&M

- Participating life science programs
- Two different Versions
- Broad goals for the course
- Gauges of success
- List of topics
- Topics omitted from a standard sequence
- General observations about the course

Life Sciences Programs at Texas A&M

The math department at Texas A&M has been coordinating with the following departments and undergraduate majors:

- Department of Biomedical Engineering
- Department of Biochemistry/Biophysics
  - biochemistry, genetics
- Department of Biology
  - biology (B.A. or B.S.), molecular and cell biology, microbiology, zoology
- Department of Wildlife and Fisheries Sciences

Two Different Versions

Version A. In the academic years 2006-2007, 2007-2008, and 2008-2009, I taught a version of this course primarily directed at students majoring in biochemistry and genetics. This course was fast-paced, selectively rigorous (in the spirit of most engineering calculus sequences), and employed MATLAB in a computational component.

Version B. In the current academic year we are offering a version of this course primarily directed at students in biology, molecular and cell biology, microbiology, and zoology. This course proceeds at a slower pace, is less rigorous, and has no computational component.

Both versions use the textbook by Neuhauser (see references).

Broad Goals for Calculus I-II

- Cover the mathematics most important to students in the life sciences, and illustrate the practical importance of these techniques.
- Create a cohort of students in the life sciences, including students from many different majors.
- Serve as a chance to recruit students into a math minor track in the life sciences and prepare students for further coursework on this track.

Has the Calculus Sequence Been a Success?

The first group of 22 students to take the course became seniors this year, so we haven't had much chance to evaluate the course's impact in any reasonable way. In fact, we're still trying to understand what a success would look like. Here are some anecdotal observations:

- Students seem genuinely to appreciate the relevance of this course. Student evaluations have been enormously positive, and several students have stopped by my office since taking the course to tell me how well it's served them in their upper division courses and research projects.

- It has certainly facilitated the creation of student cohort groups that extend across different majors in the life sciences. The course doesn't feel generic, and one consequence of this is that students become more vested in it. They stay in contact longer than usual both with their fellow students and with me.

What About Recruitment?

- We're not at all sure what a successful level of recruitment would be. Students in majors such as biochemistry and genetics are required to take additional math anyway. Most of the students in biology, even the very good ones, are glad to have their math requirement fulfilled.

- I'm only aware of 5 students of the 130 who have taken the course who have gone on to take more math classes than they were required to take.

Course Topics

Roughly 80% of the material covered is taken from Neuhauser's text, with some rearrangement. For example, only one section from Chapter 1 is used, and the entirety of Chapter 2 (on difference equations) is covered as an application of differentiation in Chapter 5.

First Semester Topics I

- Graphing, semilog and doublelog plots
- Limits of functions and continuity
- Theory of differentiation
  - limit definition
  - derivatives of standard functions
  - rules of differentiation
- Standard applications of differentiation
  - linear approximation
  - related rates
  - graphing
  - optimization
  - L'Hospital's rule

First Semester Topics II

- Difference equations
  - calculation of exact solutions
  - recursive solutions
  - cobwebbing
  - fixed points and stability
- Theory of integration
  - Riemann sums
  - the Fundamental Theorem of Calculus
  - standard methods of integration
- Applications of integration
  - calculations of area and volume
  - average value of a function; arclength of a function

Second Semester Topics I

- Taylor polynomials and approximation
- First order differential equations
  - modeling
  - solving separable and first order linear equations
  - equilibrium points and stability
- Linear algebra
  - matrix algebra, eigenvalues and eigenvectors
- Multivariate differential calculus
  - graphing functions of two variables, limits and continuity
  - partial derivatives and multidimensional differentiation
  - optimization

Second Semester Topics II

- Regression and parameter estimation
- Systems of difference equations
  - modeling
  - exact solutions of linear equations (2×2 and 3×3)
  - fixed points and stability
- Systems of differential equations
  - modeling
  - solving linear systems (2×2 and 3×3)
  - equilibrium points and stability

Omitted Topics

- Less emphasis on computing volumes; calculation of work is omitted
- Few trigonometric integrals and no trigonometric substitution
- Surface area of revolution is omitted
- Infinite series are omitted (!)
- The cross product is omitted

General Observations about the Students

- Many students, especially those working toward med school, are highly motivated.
- Even with a diagnostic test that places roughly half the first-year biology students in pre-calculus, we've found that the preparation gap among students in this course is enormous. Some students have had a year of calculus in high school and others have only had a weak course in pre-calculus.
- The students with weak preparation often do well at the beginning, but there is a cumulative effect with all the new material, and they are stuggling by the end of first semester.
- Much of the material covered, especially second semester, does not correspond with what students understand calculus to be, and this is confusing.

Teaching Assistants

- In Version A we had graduate students preside over a standard recitation once each week and a technology lab once each week. In Version B we had a mix of undergraduates and graduates preside over standard recitations twice each week. (There was group work during one and questions followed by a quiz in the other.)

- In most cases the teaching assistants had no special preparation in either biology or MATLAB. (We've never had a single one with preparation in both.)

- The technology lab was especially problematic because some lecture was required. In spring 2007 I ended up teaching the technology lab myself.

Use of Applications I

It's natural in a sequence like this to place considerable emphasis on applications. This can be problematic and, in cases, counterproductive.

- Setting up interesting applications takes quite a bit of time.
- While students do seem to get genuinely caught up in extended applications, they lose sight of the mathematics. It's often difficult for them to recognize the difference between calculations specific to the application and general methods that will be widely applicable.
- Setting up uninteresting textbook applications is counterproductive.

Use of Applications II

I've proceeded as follows:

- Generally, I do few applications, but I spend a considerable amount of time on the applications I cover.
- Most of the mathematics is developed without significant use of applications.
- The mathematics required for an application is completely developed before the application is considered.
- I'm cautious about using an application to motivate the development of a mathematical method, because students tend to associate the method too strongly with that particular application.

Applications Used, Fall Semester

- World population growth by regression
  - semilog plots
  - curve fitting

- U.S. population growth with difference equations
  - derivation of the discrete logistic model
  - equilibrium points and stability
  - parameter estimation from U.S. population data
  - numerical solutions with MATLAB
  - predictions and discussion

Applications Used, Spring Semester

- Modeling an African wild dog population
  - linear difference equations
  - evolution by decomposing data onto eigenspaces
- SIR model
  - derivation
  - phase plane analysis approach to stability
  - parameter estimation and numerical evolution
- HIV infection model
  - derivation
  - eigenvalue approach to stability
  - parameter estimation and numerical evolution

Future Plans

Here, I'll mention a few things that I would like to incorporate into the sequence, but haven't yet tried.

- Undergraduate research projects
  - The steady increase of class size is making this unreasonable.
- Reading projects
  - By the end of this sequence, students should be able to read some papers from the life sciences literature in which mathematics plays an important role. Several good examples are given in the book by Taubes (see references).

Mathematical Modeling in General

A course in mathematical modeling can fit naturally into the life sciences curriculum.

In staffing such a course we run into a similar problem as with courses in mathematics for the life sciences: they require a phenomenal amount of work. In particular, mathematical modeling is almost certainly the most difficult undergraduate course to teach well.

Three Varieties of Modeling

- **Lecture format.** Students are taught modeling techniques in a standard lecture format. The advantage of this approach is that quite a bit of new, useful mathematics can be introduced
- **Applications format.** Students use class time, as well as time outside of class, to work on extended projects that make use of mathematics students already know. The advantage of this approach is that it allows students to spend a considerable amount of time doing what applied mathematicians do: scratching their heads in utter bafflement at problems they're not at all sure how to start.
- **Brutal format.** Material is taught in standard lecture format, but students are also assigned extended projects that use both mathematics the students already know and mathematics that's being covered in class.

Modeling Topics and Schedule I

- MATLAB (2 weeks)
- Regression and parameter estimation (2 weeks)
- Modeling with ODE (2 weeks)
  - compartment analysis
  - chemical reactions
  - population dynamics
  - Newtonian mechanics
  - Lagrangian and Hamiltonian mechanics
- Analysis of ODE models (2 weeks)
  - mostly stability
  - maximum sustainable growth (from Murray)

Modeling Topics and Schedule II

- Modeling with Probability (5 weeks)
  - axioms of probability, definitions
  - permutations and combinations
  - conditional probability and independence
  - discrete random variables, expected value
  - game theory
  - continuous random variables
  - cumulative distribution functions
  - probability density functions
  - simulations
- Statistics (1 week)
  - maximum likelihood estimators
  - hypothesis testing

Modeling Projects I

- Dimensional analysis and parameter estimation
  - marble descending through a viscous fluid
- Ordinary differential equations
  - the world's longest parachute jump
  - the flight of a foam dart
  - HIV infection in vivo
  - the MERS landers Spirit and Opportunity
- Partial differential equations
  - sustained biodiversity among three competing species

Modeling Projects II

- Discrete probability
  - blackjack
  - Texas Hold'em
- Continuous probability
  - queueing theory
  - the stock market