A Freshman Based Approach to the Integration of Mathematics, Science and Computation Within a Biological Science Department

HHMI Quantitative Biology Workshop Curriculum and Institutional Transformation at the Math/Biology Interface July 2008

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Outline

Rethinking The Presentation of Calculus

Currently we are embarking on a plan to develop an integration between biology, mathematics and computational tools for placement within a typical existing department of biological sciences. We posit a *traditional* college entity having the following structure

- 80% or more tenured faculty having little interest in the use of the triad of mathematics, computation and science in their own course development and teaching.
- Incoming majors having uneven training in mathematics and computer science and who may be biased against mathematics and computer science as part of the discipline of biology.
- An existing mathematics requirement of two semesters of engineering based calculus.

Our Basic Plan

Here is the basic plan:

- Keep the existing First Semester Calculus Course for engineers and teach it as a baseline. Call this course Math-One-Engineering , here MTHSC 106.
- Replace the existing Second Semester Calculus Course which is called Math-Two-Engineering (here MTHSC 108) with a new course specifically designed for Biology majors called Math-Two-Biology , here MTHSC 108-Biology.
- Add model based points of view to the first year fundamental biology sequence Biology-One and Biology-Two , here BIOL 110 and 111.

Rethinking The Presentation of Calculus

Since Spring 2006, MTHSC 108-B for biologists has been offered at Clemson University and taken by about 250 students. We have developed the course using the following point of view:

- Mathematics is subordinate to the biology: the course builds mathematical knowledge needed to study interesting nonlinear biological models.
- We emphasize that more interesting biology requires more difficult mathematics and concomitant intellectual resources.
- We choose a few nonlinear models and discuss them very carefully; logistics, Predator - Prey and disease models.
- Since graphical interfaces lose value with more variables, we explore how to obtain insight from a six variable linear Cancer model.
- We always stress how we must abstract out of biological complexity the variables necessary to build models and how we can be wrong.

Combining Threads from Mathematics Courses

In outline, these are the topics we have chosen to use:

- From Calculus 2: here MTHSC 108
  - Simple substitution.
  - The Fundamental Theorem of Calculus.
  - The Logarithm and Exponential Function
  - Integration by Parts and Partial Fraction Decomposition Methods.
  - Approximating functions by tangent lines and the error that is made.
- From Linear Algebra: Here MTHSC 311
  - Vectors and matrices.
  - Linear systems of equations.
  - Determinants and what they mean.
  - Eigenvalues and Eigenvectors for 2×2 matrices.

Combining Threads from Mathematics Courses Continued

Linear Ordinary Differential Equations: here MTHSC 208

- Simple Rate Equations and their applications.
- The idea of an integrating factor.
- Building a Newton's Cooling model from data.
- The logistics model.
- Complex numbers and complex functions.
- Second order linear homogeneous equations.
- Systems of two linear differential homogeneous equations.
- Graphical analysis of systems of two linear differential homogeneous equations.

Combining Threads from Mathematics Courses Continued

Nonlinear Ordinary Differential Equations: here MTHSC 208 level material but not usually covered.

- The Predator - Prey model.
  - Conservation law.
  - Restriction of positive solutions.
  - Periodicity of solutions.
  - Graphical analysis.
  - Usefulness in explaining some data.
- The Predator - Prey model with self-interaction.
  - Restriction of positive solutions.
  - periodicity of solutions.
  - Graphical analysis.
  - Failure to explain data and what that means for modeling.

Combining Threads from Mathematics Courses Continued

- A disease model.
  - Restriction of positive solutions.
  - Graphical analysis.
  - Usefulness in explaining epidemics.
- Higher Dimensional Differential Equation Systems: here MTHSC 208
  - A six variable linear cancer model.
  - Model used to find important relationships between factors that cause mutations in tumor suppressor genes.
  - Asymptotic behavior not useful. Behavior over typical human lifetime is what is important.
  - Graphical analysis not useful.
  - Numerical methods not useful.
  - Determining validity of the model is the most important thing. Errors made in approximations determine this.

Combining Threads from Mathematics Courses Continued

Numerical Methods for Differential Equations: here MTHSC 208 and MTHSC 360.

- Euler's Method and its error analysis.
- Using MatLab to solve first order differential equations with Euler's method using scripts.
- Learning how to plot results.
- Discussion of Runga-Kutte methods and their use via MatLab scripts.
- MatLab scripts for the numerical solution of systems of differential equations.
- MatLab scripts for the numerical solution of Predator - Prey models.
- MatLab scripts for the numerical solution of disease models.

How Do We Do The Implementation?

We interweave the calculus, differential equations, MatLab and numerical methods, linear algebra and modeling material carefully.

- Mathematics is introduced as needed for the modeling. The first part of the course must introduce specific mathematic material and they are not quite ready for models. So they find this more challenging.
- Daily homework with lots of algebra and manipulation is used. Doing 1 or 2 problems encourages mimicry, while doing 6 of each type builds mastery.
- Graders help with the daily busywork.
- The lectures and textbook use many examples with daily comments and anecdotes on how this stuff relates to biology.

The Working Course

- Course uses discussion boards.
  - www.ces.clemson.edu/∼petersj/discus
  - Click on the MTHSC 108 For Biologists site and navigate to the syllabus to see how it has been implemented in practice.
  - Typical Homeworks and class interaction are in the Homework and Examination sites.
- The ideas discussed above have been used to develop a textbook.
  - In Spring 2006 started as handwritten notes given to the class via handouts.
  - Now a full textbook available at www.lulu.com/GneuralGnome .

Our Four Year Quantitative Emphasis Idea

To build a more cohesive plan for the development of these points of view within Biological Sciences, we are planning to implement a new four year **Quantitative Emphasis Area** (QEA) within the biological sciences degree program.

- We think of it as a precursor to a new reasoned approach to making these ideas a *core* part of the entire biological sciences curriculum.
- In Table 1, we show a first attempt at designing a quantitative emphasis approach for biological science majors.
- We have avoided course numbers specific to Clemson University and replaced them with more generic labels.
- All of this is still in flux, of course, as the content in the Junior and Senior year depends a lot on the background the students get in the first two years.

Four Year Quantitative Emphasis Plan

Year	Semester	Course	Description
Freshman	Fall	Biology-One	Simple statistics, graphical modeling
		Math-One-Engineering	Derivatives, basic integration
	Spring	Biology-Two	Simple statistics, graphical modeling
		Math-Two-Biology	Nonlinear ODE biological models, calculus, linear algebra
Sophomore	Fall	Ex-Stat-One	First course in experimental statistics
	Spring		
Junior	Fall	Math-Three-Biology	PDE biological models, partial derivatives, integral transforms control theory
	Spring	Quant-Bio-One	modeling in biological contexts statistical and bioinformatics ideas
		BioInfo-One	Bioinformatics One
Senior	Fall	BioInfo-Two	Bioinformatics Two
		CapStone-One	Capstone research project Part I
	Spring	CapStone-Two	Capstone research project Part II

Table: The Initial Quantitative Emphasis Approach

Undergraduate Research Experience

The Capstone courses are research project courses where the students can get involved in topics closer to the frontier.

- Senior years are typically very busy and student engagement and learning would probably be higher if we could get them involved in a research venue earlier.
- At Clemson University, we call these approaches **Creative Inquiry** courses and they can be taken as early as the sophomore year.
- Our challenge is to find ways to insert such research into the busy schedules of our students!
- To prepare for such **Creative Inquiry**, more mathematical and computational training needed. Part of this is provided in the the followup course, Math-Three-Biology listed in the **QEA** plan.

The Followup Mathematics Course

Our goals are to

- Add more mathematical tools that lead the students into modeling realms involving partial differential equations.
- Discuss models which require abstraction of biological detail to gain insight.
- Continue to develop computer modeling skills via an increased use of MatLab.
- Always remember that the mathematical content is subservient to the biology.

More Calculus for Biologists Design Philosophy

Our design philosophy is as follows:

- All parts of the course must be integrated, so we don't want to do mathematics, science or computer approaches for their own intrinsic value.
- Models are carefully chosen to illustrate the basic idea that we know far too much detail about virtually any biologically based system we can think of. We must always remember that throwing away information allows for the possibility of mistakes. This is a hard lesson to learn, but important.
- Models from population biology, genetics, cognitive dysfunction, regulatory gene circuits and many others are good examples to work with. All require massive amounts of abstraction and data pruning to get anywhere, but the illumination payoffs are potentially quite large.

More Calculus For Biologists: Math-Three-Biology

We have decided to focus on these topics for the followup course.

- Analysis of predator-prey dynamics using both linear and nonlinear theory.
- General ideas from nonlinear differential equation systems.
- The cable equation (used to study transmission of depolarization in neurons).
- Laplace transforms.
- Fourier transforms.
- Solution of the cable equation and its use to model organogenesis in developmental biology.
- The Hodgkin-Huxley models of action potentials.
- A model of the brain.
- A model of schizophrenia which includes an introduction to control theory

Why These Topics?

Why these topics?

- The students have not yet seen partial derivatives as they are not taking the traditional Calculus 3 for engineers, so they need to be exposed to that right away.
- The analysis of Predator - Prey models (using graphical tools and conservation laws as done in the first course) can naturally be augmented by looking at the eigenvalues of the appropriate Jacobian matrix.
- Deriving the cable equation from Biophysical principles ties together many ideas from mathematics and science.
- Laplace and Fourier transform techniques require extending Riemann integration to improper integrals and show the students new abstract ways of looking at problems.
- The cable equation has many applications and so is a good vehicle for further modeling.

Why Neuroscience?

Why neuroscience models?

- Modeling the brain requires many trade-offs between biological detail and abstraction.
- Dopamine regulation models require many lumped sum approximations and hence allow us to discuss validity of these models in a complicated context.
- The schizophrenia model treats dopamine as a control parameter which allows us to introduce rudimentary control ideas.

Creative Inquiry Design

Our **CI** design criteria are then as follows:

- The **CI** course is designed to run from the sophomore year to the junior year. Hence, we add some credits each semester in each of these years for **CI**.
- The CI-One to CI-Four are the precursors to the CapStone courses in the senior year so careful integration required.
- These courses must choose a problem amenable to study using the triad of mathematics, computational tools and science. This endeavor must
  - start low enough to engage sophomores who are just beginning to achieve the triad training they need,
  - develop over the course of the sophomore year into a self - contained bioscience problem where triad skills are essential to the solution.
  - segue into a mini-research problem in the senior year that does not necessarily have to be publishable but contains creative sparks and insights.

Creative Inquiry?

To the outline of Table 1, we now add **Creative Inquiry** (**CI**) courses to the CapStone courses as seen in Table 2:

Year	Semester	Course	Description
Freshman	Fall	Biology-One	Simple statistics, graphical modeling
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	Spring	Biology-Two	Simple statistics, graphical modeling
		Math-Two-Biology	Nonlinear ODE biological models, calculus, linear algebra
Sophomore	Fall	Ex-Stat-One	First course in experimental statistics
		CI-One	Creative Inquiry Sophomore One
	Spring	CI-Two	Creative Inquiry Sophomore Two
Junior	Fall	Math-Three-Biology	PDE biological models, partial derivatives, integral transforms, control theory
		CI-Three	Creative Inquiry Junior One
	Spring	Quant-Bio-One	modeling in biological contexts statistical and bioinformatics ideas
		BioInfo-One	Bioinfomatics One
		CI-Four	Creative Inquiry Junior Two
Senior	Fall	BioInfo-Two	Bioinformatics Two
		CapStone-One	Capstone research based on CI-One to CI-Four, Part I
	Spring	CapStone-Two	Capstone research based on CI-One to CI-Four, Part II

Table: An Expanded Quantitative Emphasis Approach

Calculus For Biology: Spring 2006 to Spring 2008

- We serve approximately 60 students each Spring semester and $40 - 50$ students each Fall semester. This is 3 sections per year. So about 100 students per year. In Fall 2008, preregistration is at 55.
- So far about 260 students and most get at least a **C** grade.
- A textbook has been written to support these clients and has been field tested over since Spring 2006. This started as handwritten notes and progressed to typed lecture notes which were set up as a **Print On Demand** book in June 2008.
- A usable philosophy has emerged.
  - Lots of graded homework and feedback;
  - many office hours
  - lots of help for the 3 or 4 students/ year who have mathematics anxiety (they will get at least a **B** if helped).
  - Lots of biology anecdotes and hooks on a daily basis to emphasize the mathematics and computational stuff is relevant.

What Are The Teaching Problems

- It is not easy to teach this course:
  - Training in biology, mathematics and computation is needed.
  - The teacher has to really like this stuff as an enthusiastic and energetic delivery is important.
- Hard to train new people
  - learning this course while teaching at normal load is very hard.
  - funds are generally not available to give release time
- Course is very successful and more sections might be needed.
  - other departments are becoming interested. If they choose to make this course required the Fall and Spring student count could jump to 200 per year.
  - Where do we get the instructors if this happens?

What Resources Are Needed?

To make this happen

- Course Development
  - A vision for each course must be implemented and fielded.
  - A textbook must be written as our needs are quite special
- Training Resources: external funding needed
  - As the course scales up, for training for teachers from both departments.
  - To support for course development.