Quantitative Initiatives in College Biology

Profiles of Projects at Undergraduate Institutions

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The following profiles of campus initiatives in quantitative aspects of undergraduate biology is the result of a targeted study of interdisciplinary efforts at two-year and four-year colleges and comprehensive universities undertaken by Project Kaleidoscope (PKAL) at the Independent Colleges Office (ICO) in Washington, DC. The goal of this effort is to inform those involved with undergraduate education in both the biological and mathematical sciences of the current state of integration between the two fields. The PKAL effort was lead by a project team of faculty who are part of PKAL's Faculty of the 21st Century (F21) initiative: Debra Hydorn, Chair of Mathematics at the University of Mary Washington; Stokes Baker, Associate Professor of Biology at the University of Detroit Mercy; and Jeffe Boats, Assistant Professor of Mathematics, also at the University of Detroit Mercy. After surveying the community to identify exemplary programs that translate collaborations into the undergraduate curriculum, they interviewed faculty leaders to profile how students at different campuses are being prepared for the "New Biology."

Capital University
College of Wooster
Davidson College
Duquesne University
Harvey Mudd College
Hope College
James Madison University
Macalester College
Montana State University
Pomona College
Seattle Central Comm. College
University of Detroit Mercy
University of Mary Washington
University of Redlands
University of Richmond
Univ. of Wisconsin-La Crosse
Wheaton College

Computational Sciences Across the Curriculum

Capital University

Located in a suburb of Columbus, Ohio, Capital University is one of the largest Lutheran-affiliated universities in the country. Half of its 4000 students are undergraduates pursuing one of six different bachelor's degrees awarded by the university. Capital offers one of the nation's few undergraduate programs in Computational Science Across the Curriculum (CSAC).

Computational science is an emerging and rapidly growing interdisciplinary field at the intersection of mathematics, computing, and science that investigates ways of using mathematics, computing and visualization to solve complex scientific problems. Capital University mathematician Ignatios Vakalis notes that many consider computational science to be a "third methodology in the development of scientific knowledge, alongside theory and experimentation."

Funded by grants from the National Science Foundation[1] and Battelle, Capital's undergraduate program in computational science is designed primarily for mathematics, science, and pre-engineering majors. The two chief goals of CSAC are to present mathematics within the context of science problems and to demonstrate how computing technology (symbolic, numeric, parallel, graphical/visualization) is used to solve problems from different scientific disciplines. Since modeling is an integral part of any computational experiment, all courses have a mathematical component.

Currently the CSAC program is offered as a minor that complements any mathematics or science major. For example biology or mathematics majors can supplement their major with the formal minor in computational science. All computational science courses make use of inquiry-based pedagogy, and all homework and projects are team based, pairing a science major with a mathematics or computer science major to work together on a single project. All projects require full written reports and oral presentations.

A number of computational science courses have been modified to include biology applications, and some have been developed specifically for computational biology. For example, one of the modules in Computational Science I[2] is the investigation, creation, and solution of mathematical models for the spread of infectious diseases. Students are guided to develop an SIR (Susceptible, Infected, Recovered) model[3], generate the appropriate non-linear coupled system of differential equations, use Maple[4] to solve the system numerically, use graphing tools to visualize the solution, and assess the results. Multiple homework projects are assigned for investigating extensions of the SIR model. In addition, case studies for modeling the spread of Malaria and SARS are presented using the STELLA[5] modeling package.

[1] NSF CLLI-EMD grant (DUE: 9952806)

[2] www.capital.edu/acad/as/csac/Comp_Sci1/compsci1.htm

[3] mathworld.wolfram.com/Kermack-McKendrickModel.html
www.math.duke.edu/education/ccp/materials/diffcalc/sir/sir2.html

[4] www.maplesoft.com/products/maple/

[5] www.iseesystems.com

The CSAC curriculum[6] consists of two courses in Computational Science, one (Computational and Applied Mathematics) in differential equations and dynamical systems and a capstone team-based undergraduate research experience. Elective courses include two in parallel and high performance computing; one in scientific visualization; and an array of courses on computational methods in biology,[7] chemistry, environmental science, finance, psychology, neuroscience, and physics.

The impact of biology on CSAC is already broad, and still expanding. In addition to Computational Science I, the courses in parallel computing and computational mathematics have been enriched with modules that address the integration of biology concepts with mathematical modeling and computer implementation. In addition, the mainstream calculus courses include more applications to biology, and a new calculus course geared specifically to the life sciences is in development.

Modules and other educational materials that are generated for those courses address real-world issues through the following paradigm:

Problem → Model → Method
→ Implementation → Assessment

All are taught using inquiry-based methods and involve students in interdisciplinary teams. Many students conduct research in bioinformatics with companies at the Columbus Business and Technology Center, the Ohio Supercomputer Center, and the Medical Informatics Division at Ohio State University.

In addition, with funding from the W.M. Keck Foundation, Capital University leads the twelve-member Keck Undergraduate Consortium for Computational Science Education (KUCSEC).[8] The goal of the KUCSE project, and its 26 faculty co-PIs, is the creation of online educational materials for teaching a variety of undergraduate computational science courses.[9] All materials demonstrate the connection of mathematics with a variety of disciplines. Examples from biology include modeling tumor-immune interactions,[10] modeling malaria,[11] and gene identification.[12] Capital plans to develop an additional course in bioinformatics and will soon offer a

[6] www.capital.edu/acad/as/csac

[7] www.capital.edu/acad/as/csac/Comp_Bio/compbio.htm

[8] www.capital.edu/acad/as/csac/Keck

[9] www.capital.edu/acad/as/csac/Keck/modules.html

[10] www.capital.edu/acad/as/csac/Keck/modules/Depillis/depillis.html

[11] www.capital.edu/acad/as/csac/Keck/modules.html#malaria

[12] www.capital.edu/acad/as/csac/Keck/modules.html#gene

certificate program in Computational Biology/ Bioinformatics via its Summer Science Institute.

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Developing Computer Information Skills

College of Wooster

The College of Wooster is a small liberal arts college located in the rural community of Wooster, Ohio with an enrollment of 1700. The institution is strong in the humanities, and has approximately 20% of its students majoring in science and math. Biology is the largest science major, with approximately 80 students.

The availability of web-based resources makes genomic information and analysis tools readily available to undergraduates. Thus, institutions of all sizes and resources can train their students in the use of bioinformatics tools and in connecting these skills to the primary scientific literature. Faculty at the College of Wooster have taken advantage of these resources to reform their Biochemistry and Molecular Biology program. One of the driving forces behind their reform efforts is the National Research Council's Bio2010 report. Although Wooster faculty would like to add a course in bioinformatics, with only seven faculty teaching in the life sciences there is no room to add such a course. Adding bioinformatics-based assignments to existing courses represents a pragmatic solution to this problem. Additionally, faculty and students at Wooster have only limited access to information technology personnel, so they cannot create database-mining software on their own. Biologist Dean Fraga states, "the fact these resources are available free is a great way for smaller institutions to provide students with a taste of this type of research and to access the same data that university researchers have access to."

Using a number of on-line bioinformatics tools, Fraga has created an assignment that is an integral part of his Cell Biology course and provides an opportunity for Biochemistry and Molecular Biology majors to gain the computer expertise that will be needed by future scientists. In this assignment, Fraga has students write a mock grant proposal[13] for a series of experiments to elucidate the function of a gene in Paramecium based solely on a DNA sequence. In describing the learning outcomes of the assignment, Fraga tells his students, "You will need to develop skill in two areas: searching the scientific literature and bioinformatics. We have constructed this course so that you will develop skills in both."

To accomplish their assignment, students are lead through a series of tasks in which they learn about resources and tools needed to access and analyze sequence data. The students gain an overview of bioinformatics, the concept of genomic database mining, and the development of testable hypotheses on the structure and function of genetic sequences from information gained in other organisms. To accomplish this assignment, students: Download sequence data from Genbank, the DNA sequence database of the National Center for Biotechnology Information (NCBI); Download and use free software that identifies putative open reading frames, the DNA sequences that encode proteins; Use NCBI[14] tools to analyze the predicted open reading frame and discover information known about related genetic sequences.

Fraga's students use these database mining results to "construct a plausible hypothesis as to the role of the identified Paramecium PP1 genes." To do this, students need to use additional web-based NCBI resources. The first is BLAST, a web-based software that uses algorithms that identify Genbank sequences with significant sequence homology. A text-base search and retrieval system, Entrez, is then used to identify other database information (protein sequence, taxonomy, etc.). Another computer-based algorithm, ClustalW, is then used to develop phylogenetic trees based on sequence data. To aid in the analysis of their data, the students are introduced to the mathematical tools of cladistics such as matrix analysis and bootstrapping.

Before writing their mock research proposal, Fraga's students must read the primary research literature related to their sequence. This literature is accessed through Entrez. The students then use computer-generated algorithms to make predictions on the protein folding from their sequence data. Once these assignments are completed, the information is used by the students in the development of their hypothesis concerning the role of the identified Paramecium PP1 genes.

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[13] www.wooster.edu/biology/dfraga/BIO_305/305_grant_exercise.html
[14] www.ncbi.nlm.nih.gov

The College of Wooster plans to build on their success in bioinformatics undergraduate instruction. "Our philosophy is to embed bioinformatics in four required courses in our biochemistry & molecular biology curriculum rather than develop a new bioinformatics course" reports Fraga. "Our vision is that each course will embed a different aspect of bioinformatics." In the future, Fraga plans to have his students in Cell Physiology actually advance science, by having them study unanalyzed data from the Paramecium genome project.[15] "If I am successful in adding this to my course," observes Fraga, "students will use software for stitching together sequences and identifying coding regions." By addressing the question, "How many genes code for gene X?" undergraduates at the College of Wooster will be helping annotate the Paramecium genome project.

Faculty who are not widely versed in database mining can learn how to use NCBI resources. They provide online instruction manuals and tutorials relating to their resources. Additionally, NCBI will present free workshops on their database tools anywhere in the country, as long as the institution provides 50 attendees.

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Genomics and Computational Biology

Davidson College

Davidson College is a highly selective residential liberal arts college of 1700 students in central North Carolina. Its largest majors are biology, English, and history with about 25% of a graduating class majoring in science or mathematics.

In a two-semester sequence, the Biology and Mathematics Departments at Davidson College provide students with a course on genomics followed by a course on the mathematics needed to understand genomics research. The first course in the sequence is Genomics, Proteomics and Bioinformatics, taught by biologist Malcolm Campbell. The text used for this course is *Discovering Genomics, Proteomics, and Bioinformatics*, coauthored by Campbell and mathematician Laurie Heyer, who teaches the second course in the series, Computational Biology. According to the course description, students in Campbell's course "will utilize print and online resources to understand how biological information (e.g., DNA sequences, microarrays, proteomics, and clinical studies) is obtained at the genomic level. This information will be integrated into a 'cell web' of molecular interactions."

This first course makes extensive use of a series of "Math Minutes" written by Heyer that are a part of the course textbook. According to Campbell, the Math Minutes are integrated into the textbook "so students can see how the math illuminates the biology. Bioinformatics contains a lot of math and students need to understand the importance of mathematical interpretation of biological data." Campbell also reports that students in this course are required to use their knowledge to answer real-world problems in genomics, proteomics and systems biology (which is a lot of modeling). Through a series of web page assignments, students explore genes and their expressions, along with gene-encoded proteins. Examples of student pages can be viewed on the web.[16]

Computational Biology, which is cross-listed with the mathematics department, is a "survey of bioinformatics techniques used to extract meaning from complex biological data." Heyer has two goals for her students in this course: First, "to understand and apply various algorithms and statistical tests for analyzing DNA, RNA and protein sequences, microarray data, and gene circuits." Second, to "gain practical experience with Perl, a programming language widely used in molecular biology." As part of interdisciplinary teams, students complete two projects that involve building interactive web sites using Perl. The first time the course was offered, students' first project was to describe and demonstrate web sites with Kyte-Doolittle hydropathy plots. Users of these web sites input an amino acid sequence; information on the web page that is produced helps in interpreting the resulting plot. The purpose of the second web project was to introduce hierarchical clustering of gene expression data. For this web site, users input a subset of genes and specify a subset of experimental conditions. Example student projects are on the course web site.[17]

Campbell and Heyer's success is due to several factors. First, both are members of supportive departments. According to Campbell, "neither the College nor our departments had requested that we develop the courses.

15 www.genoscope.cns.fr/externe/English/Projets/Projet_FN/FN.html

16 www.bio.davidson.edu/courses/genomics/studentpages.html

17 www.bio.davidson.edu/courses/compbio/webpage/home.htm

However both departments were keen to support our initiatives." This support came in the form of moral support as well as money to purchase computers and research equipment. In addition, Heyer's department made a commitment to support changes in the curriculum to include more applied mathematics and computational science.

Second, both Campbell and Heyer created their courses using well-developed pedagogical principles. For example, Campbell used his sabbatical to read papers and meet with research-active faculty to enrich the case-based, real-data approach of his course. Heyer created her course around the goals of preparing students to "build new bioinformatics tools" and "develop new approaches to bioinformatics problems." She meets these goals through the use of Perl and a sequence of fundamental bioinformatics algorithms.

Third, their collaborations are an integral part of both courses. "The potential to collaborate with Heyer opened up a new venue for the course," reports Campbell. "Often cell and molecular biology students are told they should study more math, but they are never shown examples of why this is good advice. Heyer was able to identify some interesting biological statements that were founded upon mathematical principles."

Currently, Campbell and Heyer have plans to develop a laboratory genomics course and a genomics concentration that will attract all science majors. "We want to be a funnel rather than a sieve when it comes to attracting students to the intersection of math and biology."

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Applying Mathematics in the Sciences

Duquesne University

Located in Pittsburgh, Duquesne is a Catholic university with 5,500 undergraduates and nearly 3,000 graduate students. Business and marketing are the most common major areas but health sciences are second at 17%. The middle 50% of students have SAT scores between 1000 and 1200.

In an attempt to answer the age-old question "why do we have to study all this math?" the mathematics department at Duquesne designed a new course for science majors under the broad title Topics in Math. Taught every semester in the mathematics department, it is required of students majoring in biology, chemistry, physics, and physical therapy. Topics in Math is intended to be a capstone mathematics course for science majors that shows them real science applications of mathematics.

The course is taught as a series of three modules, typically four-and-a-half weeks each, covering various topics in mathematics. Each module is geared toward a specific scientific application of mathematics, although the mathematics itself remains the primary emphasis. In the short history of the course, modules have been offered covering such diverse topics as image processing, mathematical modeling, statistical modeling, and knot theory. The topics vary from semester to semester, as do the instructors.

Each of the three modules is designed by a team consisting of one mathematics and one science faculty member. Together, they decide on what to cover, but the mathematician does the instruction. The collaboration goes farther than just course design: typically the science faculty member who has collaborated on design of the module gives one lecture to explain the scientific view on why this mathematical topic is important for science.

Mathematician Eric Rawdon tells of the final assignment where students work in groups of two or three on a project they select from a short list of topics. Each group is assigned a faculty member to work with, and often volunteers from the science departments take part.

"They complete the project and do a short write-up. In their final presentation, they are supposed to apply ideas and techniques from the module to something they have done in a science class. When this isn't possible, the students are allowed to do further research on the subject, the idea being to get them to think beyond the module."

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Mathematical Biology

Harvey Mudd College

Harvey Mudd College (HMC) is a small, highly selective, private undergraduate college in southern California with major programs in physics, chemistry, engineering, mathematics, biology, and computer science. The curriculum emphasizes breadth in science and engineering. All HMC students complete a rigorous technical core curriculum that includes courses in all of the above subjects. Students then devote about one-third of their additional course-work efforts to completing major requirements, and another one-third of their course units are focused in the humanities and social sciences. HMC is one of the five colleges in the Claremont Colleges consortium.

HMC offers a new major in mathematical biology that is anchored in two newly designed courses, Mathematical Biology I and II (Math 118 and Math 119),[18] that study mathematical models of biological processes (e.g., population genetics, epidemiology, matrix population models, physiology, and neurobiology). Students in these courses interact with experts in different areas of mathematical biology. Actual topics are determined based on papers written by expert guest lecturers for each semester.

Mathematician Lisette de Pillis and biologist Steve Adolph created these two eight-week courses in 2002 when the new mathematical biology major was established.[19] According to de Pillis, "the main goal of these courses is to expose students to a wide variety of areas in which mathematics and biology are inextricably linked. In order to best do this, we felt students should become acquainted with current research and literature in mathematical biology. This led to the course structure being much like a seminar, in which students read research papers, and experts came to speak on various topics."

In describing the process of developing these courses, de Pillis notes that "Math 118 focuses on continuous dynamic models (PDE and ODE models), while Math 119 focuses on discrete models (including evolutionarily stable systems and discrete dynamic models). With support from a grant that supports the Keck Quantitative Life Sciences Center[20] at Harvey Mudd, several top researchers in mathematical biology were invited to visit HMC and lecture to the class. In addition to arranging for invited guest speakers, we assembled a comprehensive research literature and textbook readings package, and created new sets of lectures."

The prerequisites for the two courses are one semester of Differential Equations and one semester of Linear Algebra along with a course in Introductory Biology. Additional requirements for the mathematical biology major include courses in mathematics, biology and computation. To prepare students for the guest lecturers, both mathematical and biological topics are reviewed or introduced at the beginning of the course. For example, in a recent offering of the first course, students first participated in a workshop on two-species competition models and then learned about partial differential equations. The first guest lecturer, an expert in tumor modeling, then followed. Visits by modeling experts are supplemented in each course with assigned readings, mathematical exercises, and a final project that requires students to review and summarize a pair of articles from research journals in biology or medicine that each present a model of some biological process.

The mathematical biology courses and mathematical biology major are products of the Center for Quantitative Life Sciences at Harvey Mudd. The idea for this Center emerged from discussions among HMC mathematics and biology faculty. In 2000, mathematics department chair Michael Moody wrote a proposal to the Keck Foundation seeking funding to establish a Center. The proposal was funded a year later, and de Pillis and Adolph were named co-directors. The aim of the Center is to introduce students and faculty of HMC and the Claremont Colleges to a "rapidly moving scientific field" through new educational experiences and opportunities for research. In addition to supporting visiting researchers and on-campus research, the Center also promotes course development and provides summer undergraduate research opportunities.

De Pillis and Adolph worked through a number of challenges in implementing their courses, including getting "up to speed in areas outside of our specialties… to help students become ready for the visitors" and not finding a suitable textbook. However, de Pillis reports that, "The most challenging hurdle we have to face … will come in the future: we will have to transition from giving a course which is dominated by outside visitors, to a course which will be taught fully by the two of us."

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[18] www.math.hmc.edu/~depillis/MATHBIO/index.html
[19] www2.hmc.edu/www_common/biology/academics/biomath.html
[20] www.math.hmc.edu/~depillis/KECK_QLS/index1.html

Mathematical Biology

Hope College

Hope College is a selective residential liberal arts college of 3000 students located in western Michigan. The largest majors are management and psychology, with approximately 50% of graduates having at least one major in the social sciences. The third and fourth largest majors are biology and chemistry, with approximately 20% of graduates having at least one major in the natural science division.

Mathematician Janet Andersen[21] and biologist Leah Chase team-teach Mathematical Biology, a sophomore-level course that is cross-listed in biology and mathematics. The course is based on biology research papers and, according to Andersen, it "fosters interactions between mathematics majors and biology majors that mimic those that occur in interdisciplinary research groups." Objectives outlined in the course description include "communicating across disciplinary boundaries; critically reading research papers; giving oral presentations on technical material to a general audience; learning about areas of research that combine the study of mathematics and biology."

Throughout the course students work in teams to complete both computer labs and wet labs on topics that include population studies, infection dynamics, neuroscience, and animal behavior. Teams have both biology and mathematics student members. "The students work together," says Anderson, "so that the math students help the biology students understand the math and the biology students help the math students understand the biology." The mathematical content covered in the course includes applications in linear algebra and differential equations. Students who elect this course for mathematics credit need to have completed both Linear Algebra and Differential Equations, while the mathematics prerequisite for students seeking biology credit is Calculus I. The prerequisite for biology students is Ecology & Evolution; the mathematics students have no biology prerequisite.

The biology research papers used in the course incorporate both experimental data and mathematical models. Andersen describes a recent unit of the course: "We are currently doing a unit on Hogkin & Huxley's papers based on their research with the squid axon. Students read the Hogkin & Huxley paper, "A quantitative description of membrane current and its application to conduction and excitation in nerve." We present background lectures on cell signaling and analyzing differential equations. We incorporate a wet lab on the isolation and stimulation of the frog sciatic nerve. The students do an oral presentation on the Hodgkin & Huxley paper."

Andersen indicates that the course was developed following a revision of the general education requirements at Hope. "The science requirement for non-majors became a choice of interdisciplinary courses. This began a tradition of faculty in the science division collaborating on course development." Andersen received an NSF grant[22] to support the development of the course which "provided summer stipends for myself, a biologist, and students. It also provided money to hire a part-time instructor, freeing up one of the instructors so that the course could be co-taught."

Commenting on the process of course development, she says, "Two hardest things… have been (1) finding appropriate biology research papers that incorporate mathematical models, and (2) developing the wet labs to accompany the research papers. Most of the faculty summer work was devoted to finding research papers and developing materials to go with them, while most of the student summer work was developing the labs."

"Interdisciplinary conversation is harder and more rewarding than most people think" continued Anderson. "You must learn the vocabulary of the other discipline and develop an understanding of what you don't know in order to effectively communicate."

Mathematical Biology was first offered as a cross-listed course in 2002. It is an elective for both mathematics and biology majors and is offered yearly; typical enrollment is 8 students. In addition to the computer labs and wet labs, students complete a number of oral presentations on their labs and also complete quizzes, homework assignments and discussion questions. All students enrolled in the course must also attend two mathematics and two biology colloquium during the semester, for which they are required to write a brief summary.

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[21] math.hope.edu/andersen/

[22] Course, Curriculum and Lab. Improv. (CCLI) award DUE-0089021.

A New General Education Science Sequence

James Madison University

James Madison University is a largely undergraduate public university in the Shenandoah Valley of Virginia. JMU was founded as a teacher preparation institution but now serves 15,000 students in five colleges.

Faculty at JMU have created a new three-semester package of science courses for students in their Interdisciplinary Liberal Studies (IDLS) program. The courses were created to provide students with a learning experience that models the kind of learning environment that these future teachers will use in their own teaching. The sequence, Understanding our World,[23] consists of six one- or two-credit block courses that provide one option for students in the IDLS program to meet JMU's natural science general education requirements. The last two courses in the sequence, How Life Works—A Human Focus[24] and The Environment in Context, integrate both quantitative and technology applications within the science content.

How Life Works deals with the patterns, energy, information, life's machinery, feedback, community and evolution. Environment in Context uses environmental issues as a unifying concept to introduce ecology, environmental chemistry, and evolution. Topics such as resource utilization and conservation, air and water quality issues, ecological succession, community processes, biological diversity and evolution are used to illustrate concepts and demonstrate the relationship between science and public policy.

According to Cindy Klevickis of JMU's Integrated Science and Technology Department and a member of the development team, "the initiative for this course sequence came from the School of Education as we were developing the IDLS major for future Elementary and Middle School teachers. We wanted students to come away from the class not just knowing science. We wanted them to be able to see science as a possible center for interdisciplinary theme-based learning and ideally we wanted our students to love and appreciate science."

To accomplish this, these IDLS courses are limited to an average class size of 30 so they can provide hands-on, inquiry-based investigations that are tied to the standards of learning. For example, How Life Works is divided into a series of biology topics, each one of which involves a quantitative or technology component. The topics are:

- Pedigree Workshop
- Ethics and Human Genetic Testing
- Bacteria, Viruses and Infectious Diseases
- Neuromuscular Connections
- Cancer

Technology is a significant component of many of the activities and assignments in Klevickis' courses. "We use Rasmol[25] molecular modeling software to teach the students how to create their own animated computer models of biomolecules."[26] Klevickis adds, "I want my students to be able to use computer applications as a tool to help understand the science content."

Although intended for students in the pre-professional education program, the IDLS program can be selected as a second major for students not in the education program. The Understanding Our World sequence is also taken by some students in the secondary education program and by students who have had negative experiences in the traditional general education science courses.

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Calculus and Statistics with Biology Applications

Macalester College

Macalester College is a highly selective liberal arts college located in St. Paul, Minnesota. The college is well known for its large international student population and attracts domestic students from every state in the US. Three of the most popular departments, economics, biology, and psychology, all require introductory statistics as part of their majors. The mathematics and computer science department accounts for about 8% of all declared majors.

In a new two-semester sequence of courses, calculus and statistics are taught at Macalester College using sim-

[23] www.isat.jmu.edu/users/klevicca/idls/scicore.htm

[24] www.isat.jmu.edu/users/klevicca/idls/GSCI_165.htm

[25] www.umass.edu/microbio/rasmol/

[26] www.isat.jmu.edu/users/klevicca/vism/vism.htm

ple biological examples. The two courses provide an alternative to the more traditional presentation of these topics, and are the work of mathematicians Daniel Kaplan, Karen Saxe and Tom Halverson. According to Kaplan, "the point of our work has not been to airlift biology examples into a standard curriculum, but to redo the curriculum so that the methods and concepts taught are directly applicable to biology." Biology topics used in these courses range from ecological modeling of single species and of competing/predating species to the action potential of nerve cells.

Beginning with an introduction to the human wake cycle to motivate the need for mathematical models, Calculus with Biology Applications progresses through linear, exponential and logarithmic functions, recursion, and functions of two variables on to derivatives, differential equations, and optimization. To complete a series of computer labs, students make use of the software package "R"[27] made available to them free through the course web site. "The calculus course has been completely redone," reports Kaplan, "de-emphasizing symbolic content and replacing it with geometrical approaches that can be used to analyze the biology applications."

Students also use "R" in Statistics with Biology Applications, which follows the traditional curriculum of introductory statistics courses. Beginning with basic descriptive statistics and graphs, the course continues with probability and probability distributions, regression analysis, statistical inference, analysis of variance, and multiple regression. According to Kaplan, "the most important thing is to emphasize concepts and methods that are directly applicable to the biology as taught by biologists. This means that we don't indulge ourselves in thinking, 'if we teach them how to reason rigorously, the students will somehow figure out how to carry this over to their work in biology.'"

To create these new courses, several steps were taken. First, Kaplan wrote a portion of the biology department's renewal of a grant from the Howard Hughes Medical Institute to provide more advanced mathematics and computer skills for biology majors. In this renewal request, Macalester mathematicians proposed to "revamp the entire introductory mathematics sequence taken by biology majors." Second, the biology department agreed to increase from one to two the number of mathematics department courses required of its majors. To make this change worthwhile to biologists, Kaplan promised that the new required courses would "double the amount of statistics covered, in addition to giving other mathematical skills that would be useful in studying biology."

Third, Kaplan evaluated the topics in calculus and statistics with an eye towards including only those topics that are important to biology. For more advanced topics, particularly in statistics, he "worked backwards from these to figure out what mathematics the students would need to know." Fourth, with support from the Hughes Institute, Kaplan organized a seminar for biology, mathematics and statistics faculty to go over the topics to be included in the new courses. "The seminar helped to guarantee that the topics would be of interest to the biologists, and created some excitement in the biology department that they would be getting something worthwhile." "At the same time," continued Kaplan, "the seminar helped us justify some seemingly radical steps, such as omitting the topic of symbolic integration almost entirely. The statisticians, I think, were surprised at the sophistication of the statistical techniques that the biologists are interested in."

Originally taught as Special Topics courses, the calculus course will be taught as Math 135 Applied Calculus in the fall of 2004 followed by Math 155 Introduction to Statistical Modeling, pending approval by the College's Educational Policy and Governance Committee.

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Introductory Biology from a Quantitative Approach

Montana State University

Montana State University, a land-grant institution located in Bozeman, offers baccalaureate degrees in 51 fields and doctoral degrees in 17 fields. Enrollment at MSU is over 12,000 students, including undergraduate and graduate students.

Introductory Biology: Cells to Organisms[28] is the first course in a new three-course sequence being offered at Montana State University. The course was developed

[27] www.r-project.org

[28] www.neuron.montana.edu/academics/index.php?fileName=BIOL213/index.html

under the Hughes Undergraduate Biology (HUB) program[29] at MSU, which was funded by a Howard Hughes Medical Institute grant. According to HUB Program Coordinator Martha Peters, "quantitative approaches are infused in the laboratory exercises, which are original, open-ended labs asking students to explore the experimental process including making hypotheses, designing experiments and analyzing data." Further, the labs are "less content-based and more process-based with a progression of computational approaches used starting from descriptions of measurement and precision to more complex statistical analysis of data."

In the first lab of the course, students study locomotion by measuring the hips and hind limb bones of five cats. Peters says, "In this activity students learn some anatomy and have a discussion of biomechanics, but there is heavy emphasis on measurement and data collection." Summarizing the lab activities she says, "Students are given little direction in how to gather, organize and present their data, but are guided to develop graphs and brainstorm about precision and accuracy of measurement." To complete the lab, students are asked to describe any patterns seen in their data and to verify their results and compare methodologies with other groups in the class.

Offered for the first time in the spring of 2004, Cells to Organisms was taught by Gwen Jacobs from the Cell Biology and Neuroscience Department and Cathy Cripps from Plant Sciences and Plant Pathology. Throughout the course, biology lectures by Jacobs and Cripps are intermixed with lectures on quantitative topics by Neuroscientist Alexander Dimitrov, also from the Cell Biology and Neuroscience Department. For example, following lectures on "Water balance in animals" and "Gas exchange and circulation," Dimitrov lectures on "Uncertainty, measurement and probability" and "Models, relations and graphs."

Materials for Cells to Organisms identify a series of themes that are repeated throughout this first course and its labs and that will be a part of the other two courses in the sequence:

- Scientific processes
- Discovering patterns
- Biological causation
- Balance in dynamic systems
- Levels & scale

[29] hughes.montana.edu/curriculum_dev/index.php?fileName=syllabi.html

The other two courses in the sequence, Molecules to Cells and Organisms to Populations, will be taught in the fall of 2004 and the spring of 2005, respectively. The prerequisites for all three courses are the first semester of General Chemistry and either a course in Elementary Statistics or the Survey of Calculus.

According to the HUB web site "the thematic focus of the program is the quantitative analysis of complex biological systems." Course development within HUB is an interdisciplinary endeavor. "No single discipline commands the perspective and depth to surmount the intrinsic challenges in elucidating the structural, organizational, and mechanistic principles of complex biological systems." Faculty from Cell Biology and Neuroscience, Veterinary Molecular Biology, Ecology, Plant Sciences and Plant Pathology and Mathematical Sciences are currently developing new courses under the HUB program.

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The Many Phases of Mathematical Modeling

Pomona College

One of seven institutions with contiguous campuses in Claremont, California, that comprise The Claremont Colleges, Pomona College is a highly selective institution of about 1,500 students whose median SAT scores are 1450. Biology is one of the top five majors for Pomona students. In addition, 4% major in neuroscience and 4% in mathematics.

Pomona mathematician Ami Radunskaya is always eager to talk about her applied mathematics students' forays into mathematical modeling. "We have developed a six-week module centered around a two-dimensional ODE model of tumor growth with immune competition. Students explore a detailed analysis of this model and show how it can explain some phenomena observed—but not understood—by clinicians, such as tumor regrowth after a long period of remission and asynchronous response to chemotherapy."

This module is part of Mathematical Modeling, a course that guides students as they explore the process of developing, analyzing, simulating, and interpreting scientific data. Although this course is not part of the biology program but rather a requirement of mathematics majors in the "applied math" track, and eighty percent of student projects deal with topics in biology or the life sciences.

Pomona students' work in this course gives evidence that mathematics is present everywhere you find life. Past student projects have included different models of tumor growth (with or without chemotherapy), urban sprawl and the preservation of green space, the behavior of bats in a cave, the synchronization of women's menstrual cycles, the perception of rhythm, and the organization of memory.

But how does a teacher get students to recognize patterns and think about them methodically in a scientific framework? To do so effectively, the instructors concluded that students need a yardstick by which to measure their progress. They have since adopted a detailed approach with a rubric for evaluation provided at each of the following stages: telegraphic reports, project outline, oral presentation, and written presentation.

First, students are asked to search scientific literature for papers on prescribed mathematical models, and to report back to the class in pairs using the "telegraphic report" format. This means they give both a written report and an oral report before the class. Homework assignments are also given, designed to give practice in the analysis of mathematical models.

Second, students present preliminary write-ups for their modeling projects, each of which includes elements such as a project proposal, bibliography, project outline, and poster. Timely feedback is the key at this stage offering possible avenues of improvement early enough for it to be of real help.

Later, students give both an oral and written presentation of their completed project in as professional a manner as possible. "Making the final project presentations a more formal affair encourages the students to take these presentations seriously," Rudanskaya says. "I have seen a distinct improvement in overall output since I started inviting other faculty and students to attend the final presentations."

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Six Billion People and Counting

Seattle Central Community College

Seattle Central Community College, located in downtown Seattle, serves about 10,000 students per quarter, divided equally into college transfer and professional-technical programs. SCCC was named "College of the Year" in 2001 by Time magazine.

"The main focus of this dual course is to apply mathematics to science, to put mathematics and science together the way they are supposed to be. In this course, mathematics is one of the languages of science, expressing the amount of lead in drinking water in quantitative terms. In this course, mathematics is the tool of science, forecasting how often giant oil spills take place. In this course, mathematics is used to understand environmental issues and problems, and help devise solutions that are based in reality, not appearance."

This is how geologist Joseph Hull and mathematician Greg Langkamp describe the course Six Billion People and Counting[30] they have designed as part of the Coordinated Studies Program (CSP) at Seattle Central Community College. Their course combines introductory environmental science and introductory college-level mathematics in a concentrated learning experience that involves weekly, multi-day projects that are based on real ecological and environmental data and problems. Students receive instruction in the use of Excel for graphing and modeling data, and also take field trips to rivers and forests to gather real data for their examination. At 13 credits, this combined-course experience satisfies both the mathematics/quantitative reasoning and integrated studies requirements of the college's associate of arts degree.

Six Billion People and Counting fits nicely into the philosophy of CSP courses at Seattle Central, which is to give students the opportunity to satisfy several college requirements through the focused integration of topics from different disciplines. According to Hull, the college currently offers both intra- and inter-divisional coordinated studies courses each quarter. Intra-divisional coordinated studies courses within the Science and Mathematics Division are organized under guidelines developed by the Programs Integrating Science and Mathematics (PRISM) committee.

[30] seattlecentral.org/faculty/jhull/6bill.html

Hull and Langkamp first started teaching their course as two "linked" but separately taught courses. Starting with lists of 11 mathematics topics and 11 environmental topics, they paired and reorganized the topics to allow a smooth development for both environmental science and mathematics. Multi-day environmentally-based projects are a focus of the course. "We had some project ideas already in mind (e.g., water pollution in a series of lakes modeled with systems of difference equations) that dictated which math and science topics would go together," Hull reports. "Other projects were invented to correspond to the remaining pairs of topics. That was challenging!"

For example, to introduce students early in the semester to studying the relationship between two quantitative variables (as well as to demonstrate the linkages between mathematics and science) 80 shells of the butter clam Saxidomus giganteus were collected for students to measure their lengths and widths. After graphing these data on their TI-83+ calculators, students fit a line first through two selected points and then, using the regression routine, the entire data set. "The purpose of this exercise," says Hull, "is to learn about the real-world application of linear functions, to learn that characteristics of the linear function such as the slope and y-intercept have real physical meaning when applied to real data, and to develop skills in graphically and mathematically representing quantitative information." Students also learn about the random variability of data, outliers, extrapolation, and growth sequences.

Other projects used in this course were generated from classroom materials that are a part of Hull and Langkamp's NSF-funded grant that supported the Quantitative Environmental Learning Project (*QELP*).[31] Hull and Langkamp are currently preparing a liberal arts mathematics textbook with an environmental theme based on their course.[32]

Even though no quantitative assessment of the impact of this interdisciplinary course on student learning has been made, Hull indicates that the course attracts 40–50 students each time it is offered, and that anecdotal evidence and end-of-class surveys reveal an extremely high satisfaction level. Although the target group for this course is students who are not planning to major in science or mathematics, Hull reports also that they are enrolling an increasing number of science students who are eager to see real applications of mathematics. "With few exceptions, all students felt they learned more mathematics when the mathematics was in a socially relevant context and when the mathematics utilized real data and information. A number of liberal arts students from this course have actually gone on to major in science."

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Overcoming Pre-Med Barriers

University of Detroit Mercy

The University of Detroit Mercy is a private, religious, moderately selective master's degree university offering student-centered undergraduate and graduate education in an urban context. The university was established in 1990 by the merger of the Jesuit University of Detroit and Mercy College of Detroit. Today it enrolls about 6000 students in over 100 different academic degrees and programs.

One of the barriers to curriculum reform identified by the *Bio2010* report is the content of high-stakes exams such as the Medical College Admissions Test (MCAT) and the Dental Admissions Test (DAT). Both faculty and students feel that biology courses must teach to these pivotal exams. Time pressure excludes content not directly related to these important evaluations. This creates a dilemma: how to address the curriculum goals of *Bio2010* in a department for which preparation of pre-health professionals is the main educational mission.

The Biology Department of the University of Detroit Mercy (UDM) is just such a department, eager to meet the challenges of *Bio2010* yet constrained by admission tests. The Biology Department offers a broad program to prepare students for graduate or professional school. Approximately 80% of the entering science students are pre-med, pre-dental or pre-physician assistant. The College of Engineering and Science has formal undergraduate programs in each of these health professions.[33]

As a result of the institution's urban location, the Biology Department has diverse demographics. Of the 110 declared biology majors, 75% are female, 17% are African American, 10% are of Middle Eastern descent,

31 seattlecentral.edu/qelp

32 seattlecentral.edu/qelp/NewBook.html

33 eng-sci.udmercy.edu/bio/premed.html

5% are Asian, and 4% are Hispanic. The acceptance rate to medical school and dental school is "appreciably above the national average." However, not all students who enter the pre-health profession program enter professional school. Addressing students on its web site, the Biology Department promises that if students decide not to go to medical school after all, faculty will "assist you in revising your plans and getting started in a new direction." As a result of faculty advising, UDM students enter a variety of life sciences related careers, such as biomedical research.

Increasingly, the Biology Department addresses the concerns of *Bio 2010* by introducing quantitative skills into pre-existing courses. "Our students see the value of taking Physiology Laboratory," reports Biology Department chair Greg Grabowski, "but they enter our program with abysmal math skills. To effectively analyze their data, students need to have a firm grasp of statistics, especially parametric tests and standardization of data." To help train students as scientists, the biology department now introduces statistical concepts during the freshmen laboratory experience.

The department introduced statistical thinking in the General Biology Laboratory course as a way to replace cookbook laboratory exercises with inquiry-based instruction. Students learn how to use confidence intervals by measuring the size of brachiopods in fossil casts coming from different rock strata. "Once my students learn how to use this statistical tool [confidence intervals]," reports course instructor Stokes Baker, "they use it in inquiry laboratory exercises." In one exercise, students study the phenomenon of plant cold acclimation, the gaining of freezing resistance once a plant has been exposed to low nonfreezing temperature. To observe this process without specialized equipment, students must compare the growth of acclimated and non-acclimated plant populations. After completing this directed-inquiry laboratory, the students are then challenged to use their newly-acquired statistical skills in an open-ended laboratory investigation. Reporter genes in transgenic plants are used to show that other abiotic stresses, such as drought, induce some of the same genes as cold-stress. The students are assigned an abiotic stress and asked to design and execute an experiment that determines if their assigned stress induced resistance to freezing. "The only way students can answer this question with the resources available to them," observes Baker, "is through the use of statistics."

A formal assessment study of the General Biology Laboratory students showed that incorporating statistics into an inquiry setting had an impact on learning outcomes. Chi-squared analysis showed that those students given a statistics-based inquiry curriculum, as compared to a course section that used traditional laboratory experiences, were more likely to analyze data involving repeated measurements by calculating a mean ($p = 0.0119$), were more likely to try some method to quantify variability ($p = 9.4 \times 10^{-6}$) and were more likely to correctly deduce that data with excessive overlap cannot be used to make a reasonable conclusion ($p = 0.0122$).

Statistical training is reinforced in a course in Biometrics, which is designed for second year biology and biochemistry students. The rationale in requiring this course for biology majors was that health practitioners are consumers of statistical analysis when they read the scientific literature. Thus UDM's biology graduates should be fluent in these tools even though they are not emphasized on medical entrance exams. Statistical analysis involving standardization of data, parametric analysis, and linear regression are then incorporated into upper level laboratory courses, such as Ecology, Physiology and Animal Behavior.

Modeling using Excel is introduced in upper-level courses. Interactive spreadsheet models are first introduced in the Biometrics course as part of a just-in-time teaching strategy. As Baker observes, "Excel has the advantages of being interactive, readily available and flexible. For example, really complex concepts, like the central limit theorem, can be presented with interactive spreadsheets." Students find modeling an effective tool in their learning. For example, in an anonymous survey with 20 respondents, 80% percent indicated that they agreed or strongly agreed with the statement, "Overall, this demonstration helped me see the concepts in the central limit theorem." 20% were neutral and 0% disagreed.

Students learn how to do modeling by comparing theoretical probability distributions. Baker reports that the skills students learn are "directly transferred to my Ecology course, where students create computer models that simulate predator-prey relationships and logistic growth. With the power and availability of commercial spreadsheets, there is no reason why ecology should be taught purely as a descriptive science."

Students have reported that the addition of mathematics content to biology course has had an impact on their professional lives. One example is Lisa Dosmann, a senior who works part time at Tank Automotive and Armament Command (TACOM), a product development arm of the US Department of Defense. According to Dosmann, she was hired by TACOM, because they were looking for someone with a background other than engineering who also had good research skills. TACOM has asked her to help evaluate the robustness of water quality tests used by soldiers in the field to determine the safety of potential potable water supplies. These tests are being evaluated by receiver operator characteristic (ROC) curves. Referring to her course work in Biometrics, Dosmann said "it was very exiting that we covered what I had to do at work, because ROC curves and regression are integral components of the research at TACOM." "This class [Biometrics] has made me a more valuable employee," she continued. Ms. Dosmann feels that a research-oriented course has been a liberating experience for her. "This is the first class I felt was not pre-med oriented at UDM." Her future plan is to pursue graduate work in biology.

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Introduction to Mathematical Modeling

University of Mary Washington

The University of Mary Washington is a highly selective residential public liberal arts college of 4000 students in central Virginia. Its largest majors are Business Administration, English, Biology and Psychology; approximately 20% of its graduates major in the natural sciences, mathematics and computer science.

In Introduction to Mathematical Modeling, Mary Washington students learn the process of mathematical modeling by exploring a variety of environmental issues. Recognizing that student interest in the environment was significantly greater than student interest in mathematics, two mathematics faculty—Suzanne Sumner and Debra Hydorn—designed a course that introduces students to the use of mathematical models in understanding environmental issues.

Students first learn to model data with biological and life sciences implications using functions. Sample data sets include mercury concentration in the livers of female dolphins, the number of species of the Galapagos Islands, the number of breeding pairs of Sandwich Terns, and sulphur dioxide pollution potential. Scatter plots of these and other data sets reveal the need for both linear and non-linear models such as exponential, power, and logarithmic models. The method of least square regression is then presented as a tool for fitting lines to data, along with the log transformation as a means for fitting curves. At each step in the modeling process, students are asked to consider what information a potential model provides about the environment as well as the appropriateness and goodness-of-fit of each model. After finding a "best fit" model for a data set, students are asked to combine what they learned through their model with library and on-line research on the underlying environmental issue to draw conclusions and make recommendations.

Next, students explore the use of difference equations to understand the balance between "restocking" and "harvesting" that is required, for example, in monitoring the population size of species such as Canada Geese, black bears, or zebra mussels in the Great Lakes. Students compare models with different restocking and harvesting requirements and select a best model based on the implications of the environmental situation. The logistic model is then introduced as a modification of the exponential growth model to include an inhibiting factor more appropriate for modeling population growth. The modified logistic model is then explored along with an introduction to chaotic sequences. The final topic typically covered is probability models. Students explore the use of some discrete and continuous probability models, including the exponential and normal distributions, to understand the natural variability within populations.

Course material is supplemented with one or two guest lecturers each semester who provide insights into the usefulness of modeling in understanding environmental problems. Past lecturers include scientist and author John Harte who discussed population models, wildlife photographer and Mary Washington graduate Lynda Richardson who shared her experiences, and geneticist Wyatt Mangum who discussed modeling the impact of habitat fragmentation on a population's gene pool.

In addition to quizzes and exams, students write several papers and complete two group projects. For the papers students examine current research as presented in articles published by NASA's Earth Observatory[34] and then summarize the environmental issues and modeling methods described in the article. Many of the articles presented at this site concern biological or life science research, including "Watching Plants Dance to the

[34] earthobservatory.nasa.gov

Rhythms of the Oceans"[35] and "A Delicate Balance: Signs of Change in the Tropics."[36] For the group projects, students complete one data analysis using functions and regression as a modeling tool and one using difference equations. Students use SPSS for the regression project and Excel for the difference equations project.

Sumner and Hydorn have studied the impact of course participation on students' perceptions of their mathematical and analytical abilities. Results thus far suggest an improvement in students' assessment of their abilities and an improved attitude concerning the usefulness of mathematics. Although designed for students who are not planning to major in mathematics or science, the course is enjoying an increased enrollment of mathematics, computer science and science majors, along with students from all disciplines across campus. The course satisfies the general education mathematics requirement at Mary Washington, along with two or more of the college's "across-the-curriculum" requirements (environmental awareness, writing intensive, speaking intensive).

Originally offered as just one section in the Spring of 1998, the mathematics department now offers four sections each semester. Introduction to Mathematical Modeling was developed as part of the Virginia Collaborative for Excellence in the Preparation of Teachers (VCEPT)[37], an NSF-funded program, using interdisciplinary course materials created by Sumner at the 1995 Project Kaleidoscope National Assembly.

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Mathematical Consulting

University of Redlands

The University of Redlands is a selective liberal arts university located in southern California. With 2200 students in the residential undergraduate program, and another 2000 enrolled in evening programs in education and business, the University blends a traditional liberal arts college with offerings in several pre-professional and master's degree programs.

One course at Redlands, Mathematical Consulting,[38] offers students the opportunity to work as part of a team on interdisciplinary projects that link mathematics to problems in environmental and life sciences, economics, and other areas. "On campus, faculty, staff, and administration are able to present problems of academic interest or operational need to the consulting lab; off campus, non-commercial interests and agencies such as schools, social and environmental groups and the police are sources of interesting projects."

The prerequisites for the course are one semester of statistics (selected from courses offered in mathematics, psychology, economics, or business) and permission of the instructor. Additional mathematics and statistics training is provided at the beginning of the course based on the projects for that semester. Much of the first part of the course is also devoted to filling in gaps in the technological preparation of students coming from statistics courses in different disciplines.

Mathematical Consulting was created under Project Intermath[39], an NSF-funded consortium of institutions with the goal of more fully integrating mathematics into the undergraduate curriculum. The course was created by Steve Morics, Rick Cornez and Mike Bloxham, and is currently being taught by Jim Bentley. According to Morics, the course "was created with an eye toward incorporating problems supplied by the life sciences, and several of our students have pursued projects related to life and environmental sciences." Two projects described by Morics include an analysis of bird count data supplied by the local Audubon Society and research with a member of the faculty concerning fish populations in the local mountains. Other projects described on the course web site include "bringing modeling expertise to an EPA-funded effort partly centered on this campus and aimed at saving the Salton Sea" and "assisting in faculty research, such as drawing inferences from aerial imaging in studies of vegetation."

In describing the development of this course, Morics states, "There were two guiding principles. We took as a model a course offered in our environmental sciences program. That course, the Environmental Design Studio, uses teams of students with different strengths to work on actual problems of environmental design. We took

[35] earthobservatory.nasa.gov/Study/SSTNDVI

[36] earthobservatory.nasa.gov/Study/DelicateBalance

[37] vcept.longwood.edu/vcept_course_materials.htm

[38] newton.uor.edu/Departments%26Programs/MathematicsDept/comap/ broch1.html

[39] www.projectintermath.org/

that concept and conceived it as an opportunity to bring students from different majors together working on projects under the guidance of a mathematics professor and an instructor from a project's 'home discipline.' Secondly, we used this as an opportunity to identify what other departments are doing with quantitative information and to try to engage them in the discussion of it. We thought that by inviting them to share their projects with us, they would be more willing to use our expertise in future quantitative endeavors."

The course may be taken for two to four credits; however, according to Steve Morics, "practically every student takes it for four credits, and with a couple of weeks at the front end covering software and other details, research time, and preparing the presentation of the results, most projects take the full 13 weeks of our semester." The course is conducted much like the consulting labs typical of programs in statistics. Although some faculty bringing projects to the course may also recruit students from their disciplines to work on the projects, students who sign up for the course are assigned to a project and will conduct research on the topic of the project and on the methods of analysis needed to complete it. Both students and clients sign a non-disclosure statement and students only report on the result of their analysis without making recommendations to the client.

To prepare for the course, mathematics faculty line up projects from individuals and groups, both on and off campus. "I worked a semester ahead," said Morics. "Our class was new and the campus was full of projects, so it wasn't very hard to drum up business. Indeed, that turned out to be the easiest part of the preparation. The current instructor has far more contacts off-campus than I did, so more projects come in that way, but I don't think he's had to look very far to find them. We offer free consulting to our clients, and they seem fairly eager to take advantage of it." The course is offered on a yearly basis with a typical class size of 10 students.

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Making the Microscope a Quantitative Instrument

University of Richmond

The University of Richmond is a comprehensive university in Richmond, Virginia, with about 2800 undergraduates. The Biology Department has 14 full time faculty and graduates 50 majors per year.

The microscope is the symbol of biology because to many people it represents the descriptive nature of this science. Most adults recall that much of their biology education consisted of looking at and drawing objects on microscope slides. However, "anatomy and microscopy can be more than pretty pictures," notes University of Richmond biologist Gary Radice. "Quantitative differences in tissue structure are important and not that difficult to measure."

Thanks to the availability of computer technology, Radice has transformed a traditionally descriptive course, Microanatomy (Bio311), into a highly quantitative course. "My main motivation was that I wanted students to learn to examine images in the microscope critically, and to gather as much information from images as possible," says Radice. "One of the problems novices face is not appreciating the scale of objects they see in the microscope."

In the laboratory component of Microanatomy, students are now asked to compare tissues quantitatively, for example, to compare the capacity and air-exchange areas of frog and mice lungs based on histological sections (microscope slides). One challenge is that images observed from microscope slides are of two-dimensional slices going through complicated three-dimensional tissues; another is that they have no absolute scale. However, it is possible to produce accurate estimates of the volumes of microscopic objects by clever use of statistics and solid geometry. Radice leads his students through a series of activities that teach them how to apply mathematics to histology and then his students use these skill in further inquiry-based investigations.

Stereology is the determination of three-dimensional quantitative attributes of a microscopic specimen by sampling two-dimensional features. Parameters such as size, surface area, volume or volume fraction are estimated using systematic uniform random sampling, a technique where a grid overlay is randomly placed on a microscopic image. Size attributes are then estimated by counting the number of grid points that land within the structure of interest. Once the size of the grid has been calibrated against a standard, equations based on solid geometry are then used to estimate the parameter in question.

The key to stereology is a principle first articulated by the 17th century Jesuit theologian and mathematician Bonaventura Cavalieri: if the equidistant cross sections of two solids with the same altitude are always equal, then the volumes of the two solids are the same. Students gain knowledge about and faith in the accuracy of Cavalieri's principle by determining the volume of yolk and white of a hard boiled egg. Students first determine the volume of their egg by water displacement in a graduated cylinder. Serial sections meeting the requirements of the Cavalieri method are created by using a common kitchen egg-slicer. The egg disks are arranged on a piece of plastic wrap along with a 15 cm length standard. The serial section is then digitized using a common computer scanner.

To measure tissue areas and volumes, grids of regularly spaced crosses are photocopied onto transparent plastic sheets which are then "thrown" onto the images so the grid points fall in a random position. It is then a simple matter to count the number of points that land on white and the number that land on yolk. The area of each square is determined using the scale, and the area of white and yolk on each section is then estimated by multiplying the number of points by the area per square. The volume of the egg is then the sum of the volume of each slice (area times thickness). The calculated volume is then compared to the volume measured by displacement. The method is surprisingly accurate as long as the point grid is placed randomly and the slices are made starting from a random position relative to the end of the egg.

Once students gain skill and confidence in this technique, they then repeat the exercise with commercially available histology serial sections (chicken embryos or frog embryos) or with serial sections the students have prepared as lab projects. The analysis of these microscopic images is accomplished by capturing the slide images with a digital camera attached to a compound microscope. After capturing their images, students transfer them either to CD or over a wireless network to laptop computers. Image analysis is then done using off-the-shelf computer software, either Adobe Photoshop[40] or ImageJ. ImageJ can be downloaded free from the National Institutes of Health (NIH) web site.[41]

[40] www.reindeergraphics.com/iptk/

[41] rsb.info.nih.gov/ij/

Stereology grids can be photocopied onto plastic sheets and applied onto computer monitors or applied onto printed images. Alternately, stereology plug-ins for Photoshop and ImageJ[42] are also available that will scale and draw a randomly-positioned grid of lines, crosses or points directly onto the images. The software method is no more accurate or faster that plastic overlays, but does keep material costs down because large numbers of images do not need to be printed but instead can be analyzed as they are opened on screen. Spreadsheet software is then used to record and statistically analyze the data.

Radice added the quantitative analysis of histological sections as part of his efforts to reform biology education at the University of Richmond. "The general approach I have used in the microanatomy course is to limit the "survey and memorize" aspects of learning tissue structure and focus more on tools and principles. If undergraduates can learn to examine a few organs in depth (e.g., kidney, small intestines, lung) with a variety of tools, they can use those skills later to learn on their own the structure of a liver or some other organ.

As a result of his curriculum reform, Radice has been able to secure National Science Foundation funding to improve his course. The Course Curriculum and Laboratory Improvement (CCLI) program has supported the purchase of imaging equipment and laptop computers for the course. Several web sites[43] and at least one textbook[44] offer good introductions to stereology.

Radice urges others to consider incorporating stereology into their teaching labs. The procedures are simple and easy to learn, the costs of digital microscope cameras have fallen dramatically in recent years, and the necessary computer hardware and software is widely available. "It is a great way to generate data quickly for lessons in basic statistical analysis and experimental design."

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[42] The most-used plug-ins are "Draw line" and "Point grids."

[43] www.liv.ac.uk/fetoxpath/quantoxpath/stereol.htm
www.stereologysociety.org/
www.reindeergraphics.com/tutorial/index.shtml

[44] Howard, C. V. and M. G. Reed, Unbiased Stereology: Three-Dimensional Measurement in Microscopy, Springer-Verlag, New York, 1998.

Bioinformatics Across the Curriculum

University of Wisconsin—La Crosse

The University of Wisconsin—La Crosse is one of 13 comprehensive universities in the University of Wisconsin System. The University offers associate, bachelor's and master's degree programs, enrolling 8700 undergraduates and 650 master's-level students. The school's most popular majors are business/marketing and social sciences/history; roughly 22% of their students earn a degree in STEM (science, technology, engineering, mathematics) fields.

By creating a series of exercises to be incorporated into existing courses, nine faculty from three different departments established a "Bioinformatics Across the Curriculum" program at the University of Wisconsin-La Crosse. According to Biologist David R. Howard, "the project started with a retreat [whose goal was] to rationally design a program that would introduce students to bioinformatics in a step-wise process throughout their careers." In addition to five biologists, two chemists and two microbiologists are also involved. Howard reports that the faculty involved in the planning phase decided which bioinformatics concepts should be taught in the various courses. A workshop was then given to teach other faculty how to design and incorporate bioinformatics exercises into their courses.

During the summer of 2002, the group created exercises for a total of twelve different courses that span required and elective courses in four disciplines (Biology, Cell and Molecular Biology, Microbiology and Biochemistry). Howard reports that there are numerous activities depending on the level. "In General Biology, students are shown in lecture how sequence alignments are done and used to develop phylogenetic trees. In upper level courses, computational activities include BLAST searches, sequence alignments, protein modeling from x-ray crystal structures, genomics, determining phylogenetic relationships, etc." Of the University's sole Bioinformatics course (Microbiology 440), Howard observes that students "have the opportunity to use virtually every in-silico technique available."

Each bioinformatics exercise created by the group went through a rigorous review process, starting with a presentation to the entire group of participating faculty and an in-depth evaluation by two other faculty. The exercises were then modified based on peer-review and incorporated throughout the academic year. Information about the exercises for five of the courses is available on the Bioinformatics Across the Curriculum project web page[45], which can be accessed through BioWeb[46], a collaborative project among the fourteen different University of Wisconsin System universities and centers to improve undergraduate biology education. The Bioinformatics Across the Curriculum web page is a part of the Molecular genetics resources available under the GenWeb section of BioWeb.[47]

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Algorithms and DNA

Wheaton College

Wheaton College is a selective residential liberal arts college of 1600 students in eastern Massachusetts. Its most popular majors are from the social sciences; typically 10% of graduates major in a natural science or mathematics.

Students at Wheaton College have the opportunity to explore genomic research in two separate courses. Algorithms and DNA[48], a required course for computer science majors offered by the Department of Mathematics and Computer Science, is "linked" to a major course in biology. The other, DNA,[49] is a general education, non-science-majors course that is team-taught by faculty in biology and computer science.

Mark LeBlanc, the computer scientist who teaches Algorithms and DNA, says to prospective students: "The sequencing of genomes (e.g., files filled with megabytes of A, C, G, T's) provides a new and rich source of data that is screaming for programmers to help make sense of it all. Said differently, the biologists know that they cannot do the work alone: they need you!"

The value of computer scientists and biologists working together to conduct DNA research is strengthened by

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45 bioweb.uwlax.edu/GenWeb/Molecular/ bioinfo%20curric.htm

46 bioweb.uwlax.edu/

47 bioweb.uwlax.edu/GenWeb/Molecular/molecular.htm

48 cs.wheatonma.edu/mleblanc/215/

49 cs.wheatoncollege.edu/mleblanc/dna

linking Algorithms and DNA to one of two courses in the biology department— Genetics or Cell Evolution—that are offered independently but taught at the same time. This "linking" happens as students in the Algorithms and DNA course are paired with a student in one of the biology courses to collaborate in several lab projects throughout the semester and to conduct a final joint research project. This arrangement models a work environment that computer science students will likely encounter in their careers where research and software development is built upon the work of expert scientists.

Toward this end, LeBlanc works closely with biologist Betsey Dexter Dyer who is the instructor of the biology courses to which his course is linked to help define the projects his students will conduct. LeBlanc says this partnership has been invaluable at a small liberal arts college without a formal bioinformatics program. About her collaborations with LeBlanc, Dyer says, "In general we have quite a bit of freedom with constructing our syllabi and we were able to make this connection between our courses without much difficulty." "It helped enormously to be at a small college with one Science Center housing all of the sciences including computer science and mathematics. We (in the Science Center) get to know each other well and share many of the same students. This seems to lead to collaborations."

Algorithms and DNA offers computer science majors an introduction to the mathematical foundations, design, implementation and computational analysis of fundamental algorithms. LeBlanc says, "Algorithms are full of quantitative approaches; it is the essence of the entire course." The emphasis on DNA provides real problems through which students implement procedures such as "heuristic searching, sorting, several graph theory problems, string matching, and the theoretical expression of their orders of growth." This question is most relevant for the biology students as they work with their computer science partner in designing and running a quantitative experiment that searches DNA. One such project required students to design an "Olfactory Gene Finder," i.e., an experiment to search for hydrophobic regions of DNA.

DNA, team-taught by Dyer and LeBlanc, is the second course at Wheaton that gives students opportunity to study the genome. First taught in the fall of 2003 with an enrollment of 18 students, DNA is a general-education elective intended for non-science majors that also satisfies Wheaton's quantitative analysis requirement. The course is designed to show the "amazing blend of biology, chemistry, computing, and mathematics that emerges when considering DNA." The course description states: "This course explores DNA from four points of view: molecular biology, applied mathematics, organismal and evolutionary biology, and computer science." To conduct DNA analysis, students learn to program in Perl, a string-matching language. Dyer reports that students "design and build (in Perl) 'finders' for genes that possibly code for seven transmembrane proteins." According to Dyer and LeBlanc, student reactions to the course have been "very encouraging." "Anecdotal evidence suggests that many of the non-majors began with misgivings about their ability to program. However, by the end of the semester, many of these same students reported the experience to be 'rewarding' and 'enjoyable.'" Pre- and post-course student evaluations conducted by Dyer and LeBlanc indicate that, "almost the entire class had gained a much greater sophistication in describing topics relevant to DNA."

Student understanding and appreciation for DNA research is further enriched by Wheaton College's curriculum that is centered around the notion of "connections." Wheaton students are required to take at least two connected courses[50] that bridge the traditional divisions. Under the title Genes in Context, Algorithms and DNA and DNA are both connected with the course Ethics, offered by the Philosophy Department. The goal of this connection is "increasing students' awareness and understanding of the ethical issues stemming from the use of our growing knowledge of DNA and the genome."

Dyer and LeBlanc are also the faculty leaders of Wheaton College's Genomics Research project,[51] which provides opportunities for students to contribute to ongoing genomics research. Starting with two student researchers in 1999, this research group now has five student researchers and has produced papers published in *The Journal of Computing Sciences in Colleges and Genome Research*. Dyer and LeBlanc have received grants from NSF for setting up their research lab and for hosting two workshops to help faculty incorporate genomics into the undergraduate curriculum. Recently they received a new NSF award to help disseminate their course and lab materials.

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50 www.wheatoncollege.edu/catalog/conx/

51 genomics.wheatoncollege.edu