AC 2007-2611: A REAL INTRODUCTION TO ENGINEERING AND BIOTECHNOLOGY

Rachael Schmedlen, University of Michigan

Mimi Adam, University of Michigan

Robert Sulewski, University of Michigan

Matthew O'Donnell, University of Washington

A Real Introduction to Engineering and Biotechnology

Abstract

We have developed a unique section of the required Freshman Introduction to Engineering course for the College of Engineering, University of Michigan, Ann Arbor: *Biotechnology and Human Values.* Our course is predicated on the assumptions that a meaningful introduction to Biomedical Engineering and biotechnology includes 1. solving problems for a real client, 2. exploring the leading edges of the field, and 3. learning strategies to solve novel problems. Our challenge has been to turn teenagers straight out of high school into individuals with a real appreciation, based on experience, of what it takes to be an engineer. To this end, the course is organized as a company, Blue Genes Research and Development, and our students are formed into project teams, each assigned to a client, a specialist physician at the University of Michigan Hospitals. Each team must work with the physician to develop a diagnostic test to detect a disease before the onset of symptoms. Course material emphasizes the fundamental doctrines of systems biology, the central role of quantification in design and validation, and the economic, legal, social and ethical implications of our technology. In class, students explore basic sciences and emerging diagnostic technologies for genetic disease, including lab-on-a-chip, gene chip, and MRI imaging. Students receive hands on experience through lab modules dealing with genetic sequencing and molecular imaging of proteins. In addition, students receive formal instruction in technical communications, and problem solving strategies, including brain-storming and research organization. Performance on an individual and team basis is evaluated through a series of homework sets, exams, lab reports, journals, team minutes, and oral project reports, in addition to a final formal report prepared for the client. As students attest, this course stretches them, but the experience with their clients encourages them to perform beyond their own expectations and also provides them with invaluable confidence in their ability to tackle new challenges.

Introduction

Biotechnology and Human Values, one section of the Introduction to Engineering course required of all incoming College of Engineering freshmen at the University of Michigan, Ann Arbor, was originally designed and developed by Matthew O'Donnell, former chair of the Biomedical Engineering Department, under a Life Sciences Grant. The pilot for this course was initially taught by two instructors - lead engineer, Prof. O'Donnell, and a co-lead in technical communications, Mimi Adam. Over time, the course expanded to include two wet labs under the lead of Dr. Robert Sulewski, a technical communication instructor with background in pharmacology and public health. At the conclusion of the 3 year grant, Dr. Rachael Schmedlen was recruited to assume the position of lead engineering instructor and has continued to develop and refine the course together with the instructional team. Although the Introduction to Engineering course has undergone a number of evolutionary cycles, in its present form it is a project based, experiential course, with each section representing a different engineering discipline. The stated objectives of the Freshman course, in accordance with ABET guidelines, include the introduction of basic engineering concepts, including design concept, basic statistics, ethics, environmental and societal impact of technology, technical communications and team management. Although the college provides specific guidelines regarding both general and specific objectives of the freshman introductory course, how these objectives are met is left fairly open to interpretation, as is the engineering content. From the outset, the vision for Biotechnology and Human Values was ambitious and challenging. We wanted this course to provide our students with a realistic experience in biotechnology and engineering. The question then was how could an introductory course, in 14 short weeks, give students the first taste of the expectations awaiting them as professionals? How would we drive home an appreciation for the realities of our profession without sacrificing basic sciences and technical content, communication and problem solving skills, team interactions, and ethical, societal and legal issues? How would we impress on students that these are not isolated topics and skills, but rather integral facets of good design and engineering? How would we give students an appreciation for the scope of biotechnology and multi-disciplinary nature of this field.

We decided from the outset that we wanted to introduce students to real life learning – that non-linear, complex process that underpins experience and expertise. We wanted students to undergo a shift from the prepackaged linear approach of secondary education to a more integrated approach to learning that would emphasize the multifaceted nature of the problems we solve in science and engineering. In short, we wanted students to make the shift from linear to systems thinking. The concept of systems is not foreign to most students. Most students have already encountered systems thinking in team sports such as football, baseball and soccer. Students are 'taught' the basic skills and rules of the game, but the real learning occurs on the field where constantly changing dynamics and situations challenge student skills and strategies. Perhaps the most important lesson one learns in this context is that there is more than one strategy to obtaining the goal – more than one way to skin the proverbial cat. Furthermore, nothing fuels passion and commitment as does the rich sense of achievement that accompanies good teamwork and success on the playing field. We wanted our students to experience this type of learning, but how to achieve it?

We decided that the most effective way to integrate content, skills, and experience into a single semester was complete immersion. To that end, we created our company, Blue Genes R & D – our playing field. Blue Genes R & D specializes in genotypic and/or phenotypic diagnostic tests to detect the presence of disease before the onset of symptoms. Our real life clients are specialist physicians from the University of Michigan Hospitals, Ann Arbor. Project teams consist of 5 to 6 students. To better simulate interdisciplinary teams in the workplace, the course is cross-listed under Liberal Sciences and Arts (LS&A) so that a given number of life science students can enroll each semester. Each project team is assigned to a physician client and is responsible for initiating contact, interviewing the client and determining with the client, which disease to target for pre-symptomatic diagnosis. Instructors form a management team. Although management oversees the progress of the project, they are not directly involved in the project team – client interaction. Instructors recruited for this course have industry and/or research experience in biomedical engineering, health care, or related fields. Lecture material and lab modules present fundamental concepts, issues, and techniques needed to develop a solution for the client.

Although the course was originally designed to handle 100 engineering students and approximately 20 science majors, the College of Engineering has recently reduced the enrollment to 80 engineering students and we continue to accept up to 20 LS&A students. Although AP biology is a requirement for science majors, it is not required for incoming engineering students. We have taught this course once per year since 2000, with a current average enrollment of 80 students.

Course Objectives

In addition to the guidelines outlined by ABET for the Introduction to Engineering Course, we had a number of specific objectives for *Biotechnology and Human Values.* To provide students with an appreciation for the scope of biotechnology and biomedical engineering, we wanted to introduce them to some of the leading edges of biomedical engineering and technology – what we affectionately refer to as "taking them where no Freshman has gone before". Hence, in addition to exploring new developments in basic sciences, we also introduce emerging and/or evolving diagnostic technologies for genetic disease, including lab-on-a-chip, gene chips, and MRI imaging.

We also wanted students to appreciate the central role of quantification and metrics in systems biology, design and validation. The objective of the core content was to introduce key concepts in systems biology, with special emphasis on metrics and quantification. The control feedback loop is an example of a key concept underlying systems biology that we tackle at a very early stage in the curriculum. Moreover, we wanted students to become sensitive to the role of stakeholders, identifying stakeholders as well as prioritizing their needs and demands in the design process. Finally, we wanted students to learn to exploit resources, including their own and those of their team mates, through effective research, brainstorming, and problem solving strategies.

Business Organization

In order to provide the students with a strong sense of what it means to be an engineer, we have organized the course as a company, Blue Genes Research and Development. The technical lead for the course is considered the CEO, the lab director is the CTO and the co-lead in communications, is the marketing director and team project manager. The students are placed in teams of 5-6 and assigned to solve a problem facing a real client. Expectations and responsibilities are communicated through memos and meetings between the teams and the instructor (manager). We have a web site on the college network, c-tools, where assignments and deliverables are posted, as well as lectures, library resources and web resources.

Project Teams

After students are welcomed to the company on the first day of class, they fill out forms regarding their interests, background and skills, and are assigned to six person teams by the end of the first week. Although teams are primarily assigned by residence hall locale, each team is made as diverse as possible in terms of academic background and skill. Every attempt is made to include at least one Life Science major in each team. Teams are encouraged to sit together in lecture and discussion sections so that they can engage in activities as a unit. To encourage team identity and bonding, each team has to create a team name, logo and e-mail as well as a team letterhead. All assignments are turned in on team letterhead.

Trial and error soon made it clear that 6 member teams were best able to handle the workload and least likely to breakdown into 2 opposing cliques as often happened with 4 person teams. In addition, when a member or two fails to perform to group expectations, the remainder of the team tends to form a more cohesive unit that can exert positive peer pressure and fend off a major team conflict. Oddly enough, 5 person teams seem to be the most susceptible to serious divisions and are often run by a dominant leader who unites with another member to take over all the work and exclude other members from the decision making process.

In addition to lectures, labs and discussion sections, students are expected to schedule meetings with management to review their projects and to attend office hours to discuss questions, problems or concerns. Furthermore, they are required to turn in individual journals and team minutes weekly. The team minutes allow instructors to keep their pulse on the team and the individual journals provide insight into the state of mind and concerns of the individuals on each team.

Course Content

Before the students can solve their client's problem, they must be able to understand the basic concepts of molecular biology, fundamental doctrines of systems biology, quantification in design and validation, and the economic, legal, social, and ethical implications of cutting edge biotechnology techniques. These topics are presented in a collection of lectures, discussion sections, and lab modules. Table 1 presents the topics covered in lecture throughout the semester. Lectures focus on biology and engineering principles while discussion sections emphasize technical communication topics. Student comprehension of the lecture material is assessed through two exams, a midterm and final, and homework sets on sequencing, statistics, and imaging.

Table 1: Biology and engineering topics covered in lecture

Cellular and Molecular Biology	Nucleotides, DNA, RNA (1 lecture) Transcription (1 lecture) Translation (1 lecture) Mutations (1 lecture)
Systems Biology	Feedback model (2 lectures) Disease as errors in feedback model (1 lecture) Quantification of disease (1 lecture)
Sequencing Technology	PCR (1 lecture) Electrophoresis (1 lecture) Low, medium, high resolution (1 lecture) Sanger method (1/2 lecture) Lab-on-a-chip (1 lecture)
Statistics	Probability (1 lecture) Mean, standard deviation (1/2 lecture) Confidence intervals, hypothesis testing (1/2 lecture) Receiver operating characteristic curves (1 lecture)
Expression Technology	Gene chip technology (1 lecture) Serial analysis of gene expression (1 lecture)

Molecular Imaging	Immunostaining for protein expression (1 lecture) Quantification of protein expression (1 lecture) Nanosystems (2 lectures)
Imaging Technology	MRI (3 lectures) Precession, Lamor frequency Longitudinal recovery and transverse relaxation Spin echo, gradient echo sequences

In this course, we focus on understanding the current scientific concepts and leading edge technologies utilized in the diagnosis of disease. Thus, the course begins by introducing students to the fundamental dogma of molecular biology. We briefly review nucleotides, DNA, and RNA characteristics before describing the process of replication, transcription, and translation. The majority of our students are already familiar with these concepts, but a significant fraction of our students were not exposed to these concepts in high school. For these students, and anyone that wants to sharpen their skills, we post links to animation modules on the web, such as the Dolan Learning Center (www.dnalc.org).

Once the students understand the biology concepts, the lectures shift focus to understanding systems biology. We present how transcription and translation can be represented as a feedback model and that disease results from errors in the model. To diagnose a disease, students learn that they must identify what component of the feedback model is broken and how to quantify that component to detect it. An example of the upregulation of integrin receptors in response to injury is presented to illustrate the principle.

Quantification and certainty of measurement for accurate diagnosis is reinforced through the presentation of statistics. Mean, standard deviation, confidence intervals, and hypothesis testing are all presented to the students as tools employed in the laboratory for assessing the reliability of biological measurements. From the lecture, students also learn how to generate receiver operating characteristic (ROC) curves for ascertaining the quality of diagnostic tests.

Once students recognize the importance of quantification in the diagnosis of disease, we discuss examples of different cutting edge diagnosis techniques. Students learn the principles behind PCR and electrophoresis, which they receive hands-on experience with in one of the lab modules. They learn the differences between low, medium, and high resolution and the appropriate applications for each. Emerging sequencing technologies, such as lab-on-a-chip are presented as well.

In addition to genotypic diagnostic tests, the students are exposed to expression technologies. Principles of gene chip techniques and serial analysis of gene expression are presented to the students and contrasted with sequencing technologies. Students learn that they can obtain spatial information about protein expression with molecular imaging techniques, which they witness first hand in a second lab module.

Finally, the reminder of the course covers in depth the principles behind MRI as a future expression diagnostic test. Students learn the fundamental concepts of MRI including precession, Lamor frequency, longitudinal recovery, transverse relaxation, spin echo sequence, gradient echo sequence, and image processing. These concepts are used to demonstrate applications of MRI technology, like fMRI. MRI applications of the future, such as molecular imaging, tie together the ideas of molecular biology, feedback models, and expression technologies covered over the duration of the course.

In this course, the lectures move at a swift pace to cover all of the material mentioned; therefore, we have developed some methods to assist the students in grasping the concepts quickly. As already mentioned, we include links to websites for the students to reference, some of which include animation modules, such as the Dolan Learning Center site, MRI Tutor (www.mritutor.org/mritutor/index), and Simplyphysics.com. We also include several in-class exercises to demonstrate the concepts and give the students opportunities to tackle problems. Using paper coated with PTC to detect mutations on a taste receptor, students receive a physical demonstration of how mutations affect cellular function[1,2]. We reinforce the principles of transcription, translation, and sequencing by having the students work out scenarios using pop beads as nucleotides. Other activities involve the students creating a human DNA strand, representing different types of bonds with different connections (hand on shoulder = covalent, hand in hand = hydrogen bond), for example. To better understand the MRI concepts, students act out the precession of protons gradient fields and relaxation and recovery.

Lab Modules

The two lab modules used in this course reinforce lecture material, provide students with hands-on experience in sequencing and expression technologies, and present real-life problems to the students. In the first module, the students collect a sample of cheek cells, isolate DNA, amplify it with PCR, and separate it using electrophoresis. The instructions for this module are presented in a memo from their company, Blue Genes Research and Development. In the memo, the students' manager requests that the students evaluate the feasibility of developing this technology in a fictitious developing country, Bangi-Bangi. After performing the lab, the students must evaluate and write a report on the reliability of the technique from their own results and the feasibility of recreating a lab in the developing country.

The second lab exposes the students to a different kind of diagnostic technology covered in lecture, molecular imaging. Students monitor the expression of heat shock protein to mammalian cells incubated at different temperatures. From the images collected, students must assess the fluorescence intensity to quantitatively measure the expression of the protein. In both this lab and the PCR lab, the students analyze their results and results from the rest of the class.

Term Project

To demonstrate what engineers face everyday, we developed a term project in which student teams must solve a problem from a real client, a physician from the University of Michigan Hospitals. Each team is assigned a different physician and they must interview him/her and identify a disease which could benefit from a novel, pre-symptomatic diagnostic test. Using the information learned from the interviews, lectures, lab modules, and literature searches, the students design a pre-symptomatic sequencing or expression test to diagnose the target disease.

Students report their progress and results over the course of the semester through two oral presentations and a formal report.

Assignments

Each assignment, including technical homework is designed to give students the opportunity to apply core concepts and principles to a variety of problems, all of which represent different aspects of the central project. The first assignment is a Lab Prospectus which requires students to evaluate the feasibility and suitability of a common DNA sequencing technique that they will perform in lab for a potential client, UNICEF, who hopes to use the information to budget for possible future outbreaks of disease in outreach areas. The students have to conduct a qualitative analysis of the protocol and also determine the economic, practical, legal, ethical, and environmental feasibility of conducting the test in outreach areas and consider the limitations of the tests for predicting disease outbreaks. In the second assignment, the Lab Report, focuses on the results of the lab test, individual team results as well as overall results for all teams. Students are asked to re-examine their initial assessment of the test in light of the test results. In this assignment, the concept of quantification is introduced with a required statistical analysis of the performance and reliability of the test. Now the same issues of feasibility and suitability have to be redefined in terms of actual results. In the second lab, the molecular imaging lab, the students are introduced to different ways of quantifying a result. In the first lab the result is determined by the length of a sequence and whether or not a sequence band appears. In the second lab, concentration of gene expression is being measured in terms of light intensity. However, students still have to evaluate this test in the same qualitative terms they evaluated the first test. Hence, the concepts of societal and environmental impact are revisited in the second lab report as well.

Although the workload is demanding, the organization of assignments, one building on the other, helps students to constantly re-examine and re-apply core concepts and issues critical to the success of their design. By midterm, students become aware of how the labs, homework and assignments all fit together to provide the basis for their project. This is the time teams have dubbed the "aha" moment in the course. Despite various attempts to make students aware of this process from the beginning, it seems to require time and experience to finally be recognized.

In short, the business model is extremely useful in removing the instructor as the sole source of knowledge. Instructors do not intrude in the team – physician dialogue. Students are empowered to become proactive in their learning and to learn to listen to their client's needs and wants. Placing students between management and client allows them to experience the role of stakeholders in the decision-making process. With the help of management and client, students are then introduced to the potential secondary stakeholders in their project.

Assessment

Looking at the student evaluations from the last semester this course was offered, our key objectives all received scores of 4.00/5.00 or better: I have a sense of pride and accomplishment as a result of completing my projects; I have became more aware of the responsibilities engineers have as professionals; this course helped me understand the range of skills/discipline needed in engineering; I enhanced my technical knowledge in at least one field of engineering in this class; this course helped me understand the social and economic considerations in engineering.

Particularly gratifying has been the physician response to our program. Many physicians have been with our course since its inception. One physician, a senior attending in pathology, was so impressed with the performance of his project team that he sent an e-mail to the head of the department after receiving a copy of the final report from his project team stating that the team's work had exceeded his expectations and frankly, amazed him. A second physician was so delighted by the performance of his team that he hired the entire team for a paid internship in his hospital lab.

Generally, students enjoy the lab modules and are enthusiastic about the opportunity to perform genetic testing techniques they learned about in lecture and see on TV. Because they analyze a sample of their own DNA, the lab becomes more real to them. We frequently encounter comments from students' journals that support these observations, like this one: "The most exciting thing for me this week was getting into the lab to perform the macro procedure. It was really cool to actually get to do a procedure that you hear so much about for yourself. All throughout high school, we did plenty of labs for biology and chemistry, but the labs were all kind of boring and never really involved any processes that I really cared about that much. But because I really understand the concept of PCR and electrophoresis, and I have heard and read so much about the procedure, I was actually interested in what I was doing, which made it very exhilarating to be working in the lab. I cannot wait to finish the procedure and look forward to analyzing the results. I think that as a result of this lab, I appreciate the lab and genetics more because it makes me feel as though I have a personal connection to the procedure (since my DNA was used for one of the samples). It grounds the test in reality in my mind instead of having it feel as though such genetic tests were something that happened only in movies and sophisticated labs."

As the years have passed, former freshman from our introductory courses are starting to populate our capstone senior design course. The senior design course is set up much as the introductory course and it is interesting to observe that the more pro-active and confident students in the course are generally our former freshman. One such student recently made an unsolicited comment during a conference that confirmed this impression: " Whenever my team-mates freak out at the workload or the project, I tell them not to worry – they can do it. Just keep your eyes on the mark. I told them you don't make them do more than they can do and they can do more than they think. All of us who took the freshman class tell them the same thing. That's probably the most important thing I learned from that course."

Conclusion

We have developed an introductory engineering course that immerses freshmen into a real-life engineering setting by organizing the course like a company and assigning students to real physician clients. The course integrates biotechnology concepts, technical communication skills, laboratory techniques, and design skills. As students attest, this course stretches them, but the experience with their clients encourages them to perform beyond their own expectations and also provides them with invaluable confidence in their ability to tackle new challenges. Physician response to the students' solutions has been very positive. From this class, students take the lessons learned and apply them to other courses later on in their undergraduate careers. In the future, we would like to incorporate more active learning exercises in class to improve understanding of concepts and assess student understanding of lecture material in real time. Additionally, we plan to develop methods to more quantitatively assess student learning from the physician client design project, the level of student interest generated, and the impact of the course on the students' academic careers.

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