AC 2007-1803: INTEGRATIVE DESIGN AND EXPERIMENTAL ANALYSIS: A YEARLONG LABORATORY COURSE IN BIOMEDICAL ENGINEERING

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Integrative Design and Experimental Analysis: A Yearlong Laboratory Course in Biomedical Engineering

Abstract

Undergraduate degree programs in biomedical engineering and bioengineering require a very broad array of topics in engineering and biology if they are to adequately prepare graduates for the fast-growing biotech industry, as well as for graduate and professional school. To provide this breadth of expertise, BME programs typically include coursework in cell and molecular biology, physiology, biomaterials, bioinstrumentation (including signals and systems, circuits, and biomedical imaging analysis), biomechanics, transport phenomena, and mathematical modeling of BME systems in their core curricula. Given this breadth, however, there is a pressing need for not only providing sufficient practical depth in these topics through hands-on laboratory components, but also for allowing the students to integrate the concepts learned in these diverse courses towards solving real-world BME problems. Towards meeting these needs, we have developed a yearlong laboratory course that is required of all BME majors at the University of Virginia. This course is divided into 12 separate lab modules taught by eight different faculty members throughout the year, in accordance with their respective areas of expertise. BME-relevant applications and methods covered in this lab span the topics listed above, including cell culture, microscopy, RNA and protein extraction, western blotting, RT-PCR, biomaterials and tissue engineering, ultrasound, EKG, biomechanics, microfluidics, biofluid dynamics, and quantitative clinical measurement methodologies. The end of this course consists of a four-week project which empowers the students to integrate the skills and knowledge accumulated throughout the year towards independently addressing a relevant hypothesis or question in BME. Student lab proficiency and analytical ability were assessed via detailed group lab reports on each module, weekly quizzes, in-lab observation by the instructors and TAs, and a final written practicum exam. Additionally, feedback on the course was gathered from: 1) student evaluations, surveys, and individual interviews; 2) input from industry and professional school representatives; and 3) internal input from a majority of the faculty in our department. Over the first three years this course has been offered, assessment of student learning as well as feedback from all sources (which has been used to enhance and revise the lab modules as needed in successive years) have both been very positive. The laboratory course described in this paper thus represents a viable curricular means by which to provide students with not only the topical breadth but also the practical depth and integrative analysis necessary to prepare the next generation of biomedical engineers.

Introduction

The field of biomedical engineering (BME) is widely regarded as the fastest growing engineering discipline at most universities.[1] Undergraduate curricula in BME must include a very broad array of topics in engineering and biology in order to adequately prepare graduates for the fast-growing biotech industry and for graduate and professional school. To provide this breadth of expertise, BME programs typically include coursework in cell and molecular biology, physiology, biomaterials, bioinstrumentation (including signals and systems, circuits, and biomedical imaging analysis), biomechanics, transport phenomena, and mathematical modeling of BME systems in their core curricula.[2] This extremely wide breadth of core coursework and concepts poses a significant educational challenge in providing the students with sufficient depth of experience in experimental design and hands-on laboratory skills spanning all facets of BME.[3] Many core curricula in undergraduate BME programs offer a semester- or quarter-long lab course which is split into roughly 5-6 modules, each of which covers a different subject area within BME.[4] Additionally, some core courses may include a lab component that focuses specifically on the material in that course.

A large body of educational research indicates that hands-on, active participation by students is significantly more conducive to learning than traditional lectures and rote memorization of material, thus prompting the National Academy of Science to issue a call for improved methods in teaching science, technology, engineering, and mathematics (STEM).[5] The evidence strongly suggests that inquiry- and problem-based learning is more valuable to students in laboratory courses than merely following a "cookbook"-style set of instructions.[6] Undergraduate laboratories in BME face the additional challenge of integrating concepts across the wide breadth of the field while still effectively teaching students a critical set of core competencies (not just skills and concepts in specific subject areas).[7] In the experience of the authors, achieving this combination of goals (breadth and depth, taught in an inquiry-based fashion emphasizing development of core competencies) is challenging within a single semester or quarter course.

Towards meeting these curricular needs in the biomedical engineering undergraduate program at the University of Virginia, we have developed a yearlong laboratory course sequence called Integrative Design and Experimental Analysis (IDEAS). This two-semester course sequence is required of all majors in our program. Below we describe the overall organization of the IDEAS course, the aspects of the course that promote active inquiry-based learning, the specific course content, and the course objectives and assessment to date.

Course Objectives

The stated course objectives for the IDEAS lab sequence are as follows:

1. To develop basic understanding of underlying principles in biological, molecular, chemical, mechanical, and electrical techniques and systems as it applies to biomedical engineering practices;
2. To promote integration of knowledge from biomedical engineering courses in a practical, hands-on laboratory experience. This is done by exposing students to traditional and state-of-the-art equipment and techniques, and by relating concepts in individual and multiple lab modules to those encountered in medical, biomedical science, and engineering disciplines;
3. To introduce students to the process of scientific writing, including reporting of data, data analysis, and relevant discussion based on relevance to the biomedical field. This is conducted through group laboratory reports; and
4. To promote group teamwork and ethics in scientific experiments and experimental design.

Overall Course Organization

The IDEAS lab is a two-semester course sequence which is taken by BME majors in their third year of study in our program. The lab is divided into topical modules which introduce the students to fundamental and cutting-edge skills in the broader field of biomedical engineering. Each module (described in a later section) provides students with experience using laboratory techniques and quantitative analysis of data. Modules vary in duration from one to two weeks, with the exception of the final "IDEAS Module," discussed below. Each week of the lab includes a 50-minute lecture (attended by all students in the class) and a four-hour lab session (held three times a week to reduce the number of students in lab at any one time).

<u>Lab lecture</u>: At the beginning of each week throughout both semesters of the IDEAS course sequence, students attend a 50-minute lecture in which the following three pieces of information are presented: 1) The motivation and BME context for the particular lab technique(s) and/or analysis method(s) the students will experience later in the week; 2) A detailed review of the core concepts relating to the week's lab; and 3) A brief preview of what is expected in the lab that week. These lectures are critically important not only for providing students with the knowledge base necessary to understand the importance and purpose of the labs, but also for conceptually linking each lab with those performed in previous weeks. These lectures also continually refer back to core courses in the BME major that the students have already taken (see Prerequisites section below), thereby reminding them of factual details they may have since forgotten and reinforcing concepts they have learned.

<u>Lab session</u>: Students divide into teams of three or four for the lab sessions, and they perform the labs and write the reports as a group. Each lab lasts four hours and includes the following four components: 1) A pre-lab quiz designed to ensure that the students have read the current lab module handout and have adequately understood the concepts covered in the weekly lecture; 2) A 20-30 minute orientation by the instructors, summarizing the steps to be taken during the lab, the equipment and/or supplies needed, any safety warnings or reminders, and any additional information or concepts that were not covered in the lecture, often including a demonstration of particular techniques or lab equipment; 3) The actual lab, in which the instructors and TAs are constantly present and offering hands-on instruction and advice to the students; and 4) Final approval of each team's lab notebook by an instructor or TA (to ensure that the notebook is not filled in after the fact).

After each module is completed, each team of students must turn in a rigorously-graded lab report that describes and discusses the lab, the results, the data analysis, and the team's conclusions. To better assess whether individual students have learned the core concepts from the lab modules, at the end of each semester the students must take a final written exam. Additionally, the weekly pre-lab quizzes are individual assignments that are intended to assess student understanding throughout the semester.

Prerequisites

Given the breadth of topics covered in the IDEAS lab sequence, there are several prerequisites and co-requisites for this course that necessitate limiting it to students with junior standing. Prior to taking IDEAS, students have taken all of their foundational engineering courses (chemistry, physics, calculus, ordinary differential equations, and statistics). Within the BME department, enrolled students must also have taken one semester of cell and molecular biology, two semesters of human physiology, and one semester of biomechanics. These BME prerequisites do not include a lab component, and in the IDEAS lab itself we teach the introductory techniques necessary to complete later modules.

As described below, the first semester of IDEAS is largely focused on molecular and cell biology, biomaterials, and tissue engineering, and the second semester is geared more towards instrumentation and systems design. During the fall semester of their junior year (when they are also taking the first half of IDEAS), students in our program take a BME Systems and Analysis class, providing them with the background needed to complete the instrumentation-oriented modules in the following spring semester of IDEAS. As a co-requisite during that spring semester, students take a Computational Biomedical Engineering class, which covers numerical methods and fundamental BME modeling techniques. This course is synchronized with IDEAS so that methods (e.g. numerical integration) are learned prior to using them in data analysis in the IDEAS lab. Students usually have not taken an introductory circuits class prior to IDEAS, but have covered some of the theory the prior fall in the BME Systems and Analysis course. We thus include basics of operational amplifiers and active filters in the first week of the spring semester in IDEAS.

Enhancing Inquiry-based Active Learning in Undergraduate BME Labs

Inductive learning is widely seen as the most effective mechanism by which students retain core concepts and critical skills.[8-9] A laboratory teaching environment is especially well-suited to engaging BME students in inductive, inquiry-based learning.[7] Accordingly, we have incorporated several active learning methods into the IDEAS lab course:

Lab module handouts: The students are given detailed module handouts corresponding to each week's labs. However, a danger inherent in any lab manual or handout is that it merely gives the class a "cookbook"-like list of steps to accomplish, while requiring only minimal independent inquiry or analysis on the part of the students.[6] To avoid this potential pitfall commonly found in instructional lab handouts, we often leave some aspects of the lab (especially the data analysis) deliberately vague. On the other hand, descriptions of fundamental skills and techniques (e.g. operating a pipette or extracting RNA from cells) have remained very detailed, since there is little to be gained conceptually from students having to "discover" the intricacies of established procedures such as Western blotting and PCR.

Lab reports: Most of the lab modules require a significant amount of quantitative data analysis and critical evaluation of the results, but the students are not usually given a list of steps needed to complete the data analysis. In fact, they are not told specifically what figures or data need to be included in the report in the first place. It is left completely up to the students to decide what data are important, and how best to present these data within a strict page limit. This autonomy in performing data analysis and synthesizing a lab write-up empowers students to think critically about experimental design in "real-world" BME research and is far more valuable than giving them what amounts to a lab report "template" that they simply fill in with their data. Students also learn how to engage in clear scientific written communication, and a strong grading emphasis is placed on precision in writing. Since undergraduates typically do not have extensive background knowledge of the literature in the field (and thus may not be able to write a truly deep and thoughtful discussion section), the instructor responsible for a given module furnishes a list of inquiry-based questions (IBQs), which take the place of a traditional discussion section. These IBQs force the students to think very deeply about the implications of their experiments and about potential pitfalls and sources of error.

Written practicum exams: Each semester concludes with a final "written practicum" exam administered to each student individually. This exam tests the major concepts and lab procedures covered in the semester's modules. Exam questions frequently have required students to think through the design of experiments that build on what those they have already studied and performed in lab. Some questions also provide data and then probe the students' understanding of important lab procedures (e.g. showing a Western blot and then asking, "What step was left out in the protein extraction and purification?"). As a result, the written practicum does not merely test the students' memorization of facts, but rather their critical understanding of core competencies and their ability to synthesize new information and design experiments.

Final IDEAS project: The final IDEAS project at the end of the second semester of the course sequence will be described in greater detail in a separate section below, after the description of the topical modules. In brief, the entire premise behind the final four-week project is to empower the students to integrate all the myriad concepts, skills, analysis methods, and techniques that they have learned throughout the year towards solving a problem relevant to biomedical engineering. With respect to enhancing inquiry-based learning, the students are not given detailed steps or protocols for their projects, but rather the underlying motivation for the project and a short list of key specific questions that must be addressed. They can choose to answer those questions any way they see fit (within reason, provided the cost is not excessive, and pending approval of the faculty or TA "consultant" on each project) using the skills learned in previous modules. The autonomy that the students experience in executing this four-week "mini-Capstone" project provides invaluable experience in experimental design and critical thinking and analysis. We feel that this final project is really the most important module in the entire course sequence because it exemplifies the active learning methodology recognized to be optimal for best teaching students BME content and competencies within a laboratory setting.[7]

Description of Specific Lab Modules

The IDEAS lab consists of 13 modules which span two semesters. Most modules are one or two weeks in duration and culminate in a written module report by the student teams. The modules that we have developed for the IDEAS course sequence are described below. It should be noted that these module topics are in constant flux and have evolved (and will continue to evolve) in response to regular assessment (both of the core competencies and skills in BME that are most important for undergraduate majors to attain, and of the effectiveness of the lab modules at imparting these competencies to the students). The various modules are taught by a total of eight faculty members, according to expertise in particular areas of BME. All of the students experience the same labs for each module, with the exception of the final IDEAS Module. Since this final "capstone" module integrates skills and concepts from throughout the yearlong course, it will be discussed in the next section, rather than in this list of module descriptions.

<u>Fall Semester modules</u>:

<u>Introductory Module – Fundamental Skills in BME Laboratories:</u> The purpose of the very first week of the IDEAS lab is for the students to become familiar with 1) basic laboratory equipment (e.g. pipettes, digital microscopy) and basic lab math (i.e. dilutions) that will be used throughout the semester. The skills taught in this module are essential for laboratory research and generating repeatable, high quality results. Lab groups are expected to become familiar with using pipettes, operating the inverted microscope and acquiring digital microscopy images, and performing dilutions.

While the use of pipettes to transfer prescribed amounts of volume is certainly not difficult, it does require an appropriate level of instruction and orientation for undergraduates who might not have encountered a pipette before. The proper use of this instrument is especially critical for performing most of the modules the first semester of IDEAS and is a valuable skill in many undergraduate research endeavors. The instructors and TAs provide students with hands-on instruction on the proper use of pipettes, requiring approximately 30-60 minutes for all members of each group to become comfortable using the pipettes. The students first measure the weight of specified amounts of water, and then they conduct a simple standard curve for protein analysis and calibrate the protein intensity of the colorimetric assay to known protein concentration standards. Thus, both of these activities provide a measure of pipette volume accuracy for each individual in the class. We have found that this somewhat remedial introduction is necessary to ensure that all students (not just students who have already been working in faculty research labs) gain confidence in this fundamental skill, thus empowering them to participate more fully in the remaining labs during the semester.

Another critical skill that students often lack (or seem to forget when they enter a "wet" lab) is how to perform basic lab math – e.g. calculating dilutions and concentrations when assembling solutions and reaction mixtures. This material is generally covered in introductory chemistry, but a few pre-lab homework problems ensure that each student is competent making these calculations quickly and accurately in a lab setting. The final activity in this short introductory module is calibrating the area of the inverted microscope field of view using a scale slide. The students learn to collect digital images using a CCD camera, and they gain a basic understanding of the components of the microscope and ImageJ analysis software. (Fluorescent microscopy is covered in detail in Modules 4 and 5, discussed below.)

<u>Module 1 – Techniques in Cell Culture</u>: In the first actual module in the IDEAS lab, students learn the cell culture techniques used to expand and grow adherent cell monolayers in culture. The skills taught in this module are essential in working with, handling, and sustaining the viability of mammalian cells (and those of other organisms) outside of their natural environment. The first week of the module involves measuring growth kinetics over a span of seven consecutive days (a group member has to volunteer to come in each day to image the team's cells). Each team is given three cultures of freshly-plate bovine aortic endothelial cells (BAECs) with media at three different serum concentrations. On each day, the three plates are imaged,

and analysis is performed to quantify the number and density of cells present on each plate. The IDEAS Lab Staff maintains the cells throughout the week by feeding them, thus minimizing the risk of infection by students. These results are then used to derive an equation for growth from first principles (not based on curve-fitting). In the second week of Module 1, the students extract protein and mRNA from BAECs that have been stimulated with a high concentration of serum relative to a control population. For the mRNA extraction, students learn to properly use sterile RNAse-free technique. The collected protein and mRNA samples are then frozen at the end of the lab session for use in subsequent modules.

Module 2 – Quantification and Manipulation of Proteins: During the first week of Module 2, lab groups are expected to successfully: 1) Prepare their stimulated and control protein lysates collected from the second week of Module 1 for SDS-PAGE electrophoresis; 2) Run specific stages of a Western blot to detect proteins and determine their molecular weights; and 3) Analyze the resulting blot to quantify the relative activation (i.e. phosphorylation) of a mitogen activated protein kinase (MAPK) called ERK1/2 (Extracellular Regulated Kinase) in the stimulated and control samples. In this way, the students will be able to see the tangible evidence of their serum stimulation in Module 1, while learning critical skills of protein measurement on a gel and quantification using image analysis software. In the second week of this module, intracellular protein concentrations are not quantified from a lysate as in the first week, but, instead, cytoskeletal proteins are stained within fixed cells using immunofluorescence techniques. (Since the staining techniques are fairly time-consuming, the actual fluorescent microscopy will occur in Module 4.)

Module 3 – Molecular Evaluation of the Genome: While Module 2 focused on the detection of proteins within the cell, Module 3 involves the detection of specific mRNA levels to quantify gene expression. The isolated RNA from Module 1 is used in a reverse transcriptase reaction to generate cDNA for a specific gene (whose expression is sensitive to serum stimulation, as was performed in Module 1). Students also receive a grade based on the quality of their mRNA yields as measured in a UV spectrophotometer. Then in the second week of Module 3, this cDNA is run on a real-time PCR machine, and the students analyze the results to determine the quantitative impact of serum stimulation on the gene of interest. In order to complete this lab within a manageable length of time, the lab primarily involves preparation of the treatment and control samples to be run in the PCR, in addition to setting up the machine and thermocycler software. The PCR runs overnight, and the TAs collect the data the following day and e-mail it to all student teams from that section. Students then compute the fold changes in expression of the target genes.

Module 4 – Fundamentals in Digital Microscopy and Fluorescence Imaging: The objective of Module 4 is to learn the basics of fluorescence microscopy, learn how to spatially calibrate a microscope, and improve image quality using deconvolution. The skills taught in this module are essential for measuring quantitatively the spatial distribution of subcellular components. Lab groups: 1) Measure the resolution and point-spread function of the microscope using sub-wavelength fluorescent microspheres; 2) Acquire images of fluorescence-labeled cytoskeleton from the immunofluorescence samples prepared in the second week of Module 2; and 3) Improve the quality and resolution of those images using deconvolution. In Module 2, some cell cultures were treated with toxins that affected assembly of specific proteins in the cytoskeleton.

The students thus have to conceptually link the immunofluorescence, microscopy, and image analysis with the cell biology they have covered in a previous course.

Module 5 – Nano-Systems for Cellular and Molecular Evaluation: Module 5 builds on the principles of fluorescence microscopy and image analysis covered in Module 4 by having the students investigate how systems of molecular motors may be reconstituted *in vitro* to give motility, and how fluorescence microscopy can be extended to view single molecules. The students set up an actin-myosin motility assay, and the velocity of actin filaments is imaged and analyzed for different ATP concentrations. They also review Michaelis-Menten kinetics and analyze the kinetics of the actin-myosin cycling as a function of ATP concentration, computing the V_{max} and K_m constants of the reaction. In this module, three completely different concepts relevant to BME are thus taught and/or reinforced: 1) High-resolution microscopy of single molecules; 2) Molecular motor function; and 3) Enzyme kinetics. This is a cutting-edge assay that, to our knowledge, has not been implemented in any undergraduate lab elsewhere.

Module 6 – Principles in Tissue Engineering, Biomaterials, and Drug Delivery: In the final module of the fall semester of the IDEAS course sequence, the students examine the surface properties of polymers that have applications in tissue engineering and drug delivery. Using a goniometer, surface contact angles are measured for several combinations of polymers and liquids, and various PLAGA polymers having different degradation rates are prepared by the students. In the second week of Module 6, an *in vitro* wound healing experiment is performed using an electric cell-substrate impedance sensing (ECIS) system. After applying a wounding electric pulse, this cutting-edge technology can measure cell proliferation onto the wounded site at the resolution of a single cell. The students are expected to: 1) Use the inverted microscope and software to take images of confluent ECIS chambers of BAECs and estimate the percent confluence in the field of view surrounding the electrode; 2) Apply media conditions containing different levels of lysophosphatidic acid (LPA) or control media using sterile technique in a laminar flood hood; 3) "Wound" the cell chambers using the ECIS control software; and 4) Quantify wound closure rate and cumulative wound closure over an 18-24 hour period. The set of skills taught in this module is one among several standard *in vitro* modeling methods to study the wound healing behavior of cultured cells in response to selected chemical and mechanical cues. Students also calculate the diffusivity of different polymers from raw data of cumulative release of a model small molecule from different polymer substrates.

Spring Semester modules:

Module 7 – BME Signals and Systems: Biopotentials, EKG Measurements, and Vectorcardiography: The first module of the spring semester shifts in focus from techniques in cell and molecular biology to those more traditionally associated with BME. Students review basic operational amplifiers and active filter circuits (both in lecture and in lab), and then they build a 4-stage EKG amplifier. Using this circuit, they measure the frontal and horizontal plane EKGs on one or more of the team members. Using these results, the 3-D instantaneous cardiac vector is then computed. The results are then compared to blood pressure and heart sound data measured using the Biopac Student Lab kit. Thus, the students integrate concepts relating to electronics, signals and systems, and physiology.

Module 8 – Biomedical Imaging: Principles of Ultrasound and Image Processing: To gain an introduction into BME imaging, the students perform B-mode ultrasound imaging with a single transducer. The transducer moves along a motorized stage over a phantom, and the motor and the transducer data (collected via an oscilloscope) are coordinated using LabVIEW. Additionally, transducers having different focal depths are used to collect data so that the students can learn the effect of focal depth on the final reconstructed image. This lab not only teaches the principles of ultrasound imaging, but also a simple control system in LabVIEW. The students are given a non-functioning version of a LabVIEW interface, and they must add the components necessary for the system to operate correctly. The data are then reconstructed into a 2-D image in Matlab using image processing techniques (filtering, Hilbert transform, etc.). The student-generated ultrasound image must then be compared with known phantom configuration.

Module 9 – Bio-fluid Dynamics: Principles of Blood Flow, Transport, and Clinical Measurement Techniques: One of the critical concepts in biotransport and fluid dynamics is the distinction between low- and high-Reynolds flow. The first week of Module 9 involves setting up a very low-Reynolds number flow system using a microfluidics “T-sensor” chamber. The students inject fluids containing fluorescently-tagged molecules of two widely varying molecular weights, each with a different fluorophore attached. Both of these fluids are injected into the two T-sensor inputs using syringe pumps, and the microfluidics chamber is viewed under the fluorescence microscope. The diffusivities of both molecules can be computed from images taken at varying distances along the channel (downstream of the T-inputs). The key assumption is that no convective mixing will occur at the low volumes and flow rates being tested, and any dissipation of fluorescent material perpendicular to the direction of flow will be due to diffusion, not convection.

The second portion of the bio-fluid dynamics module involves macro-flow setups meant to mimic the flow of blood in large arteries. Using a flow loop with gravity-induced constant water flow (adjustable by varying the height of a reservoir), two clinically relevant measurements are made by the students. The first is the measurement of flow using the method of thermodilution. In the flow-loop version of this common clinical procedure, a Swan-Ganz catheter is inserted into the flow loop, and ice water is injected into the proximal injection port. Downstream, a thermistor measures the temperature of the water via a Wheatstone bridge circuit that has been calibrated. From the transient change in temperature after the small volume of cold water is injected, the flow rate can be computed. This experiment requires students to integrate three key concepts: 1) Thermistor measurement device with a balanced Wheatstone bridge circuit and oscilloscope; 2) The basic principle of thermodilution itself, and why it is useful in a clinical setting; and 3) The indirect calculation of fluid flow using the measured temperature change, based on the Stewart-Hamilton relationship. As is the case in many of the IDEAS modules, the importance of accurate calibration and quantitative analysis of data are heavily emphasized.

The final portion of Module 9 involves the use of clinical pressure transducers to measure the pressure drop across a “stenosis” in the flow loop setup described above. As the flow rate is altered, the Reynolds number at which turbulent flow begins can be estimated. Additionally, as part of the continued emphasis on calibration when making clinical measurements, the frequency response of the transducers is measured. The students use a balloon “pop test” to generate a step reduction in pressure at the transducer, and the underdamped nature of the transducer/flow-loop system can be observed on the oscilloscope. The frequency characteristics of this system are then computed assuming a second-order linear system, thus integrating concepts learned in physiology with those in the controls portion of the signals and systems class.

Module 10 – Biomechanics of Soft Tissues: Tensile Strength and Viscoelasticity: The tensile strength of chicken skin is measured using an Instron materials testing device. Tissue samples are treated with collagenase and elastase in order to alter the mechanical properties of the skin, and these samples are tested and compared with the control skin. Additionally, the effects of strain rate and cyclical testing are analyzed and fit within a viscoelastic model, and a constitutive equation is derived. This module thus integrates concepts of strength of materials and biomechanics with the extracellular matrix structural molecules and resulting properties learned in cell and molecular biology.

Module 11 – Fundamental Tools in Bioinformatics: Perhaps the fastest growing fields within BME are computational systems biology and bioinformatics. However, very few BME curricula currently include exercises in sequence analysis and network modeling within their core courses, despite the significant utility of these tools in many avenues of BME-relevant research. In Module 11, students learn the basic tools of gene sequence analysis (BLAST and FASTA), and they apply these to the reconstruction of a simple metabolic pathway that is related to the signaling network probed in Modules 2 and 3 in the prior semester. One of the enzymes in this pathway will be missing, and students will have to run a BLAST against other sequenced organisms in order to identify this gap in the network. This module thus not only teaches concepts of the most prevalent bioinformatics algorithms, but also integrates these concepts with those of understanding biomedical systems at the integrated, network level. Such holistic thinking in BME will be critical going forward as new mechanisms of diseases (e.g. atherosclerosis) are uncovered.

Final Project – The IDEAS Approach to BME: Integrating knowledge to find a solution

As mentioned above in the section on inquiry-based learning, the final "module" of the IDEAS lab course sequence is a four-week project that integrates material from other modules covered throughout the year in this course sequence. These projects, which take place at the end of the spring semester, are solicited each year from numerous faculty members within the department and are often in a cutting-edge area of research. The IDEAS instructors and TAs act as "consultants" to the student teams for these projects, providing guidance and advice as the project proceeds. This guidance is especially important given that four weeks is a relatively short amount of time in which to complete a sophisticated project, and one of the key goals of the instructors and TAs is to make sure that none of the teams proceeds down a "dead-end" path in addressing their research questions.

During the lecture period at the outset of the four-week module, each student team receives a randomly assigned project description (approximately half a page), which includes a bulleted list of questions they need to address by the time their project is completed. (There is no lecture corresponding to the final project, given the diversity of topics covered.) The teams then meet with an instructor or TA to discuss the details of the problem statement and the questions on the assigned project handout, and the instructor gives guidance to point the students in a viable direction. Within the first week, the students must develop a detailed experimental design project plan (with team member responsibilities throughout the remaining three weeks), which they discuss again with the instructor or TA (or both). After that point, the students are free to work on their projects when they choose and are not required to show up in lab for their regularly-assigned four-hour sessions. Each week the students must submit a brief progress report and discuss any data with their "consultant," and at the end of the semester the students turn in a final report.

The specific projects assigned vary depending on the faculty feedback received in a given year. Past projects have included measurement and quantification of focal adhesions in mammalian endothelial cells, determination of fluid velocity through a flow loop setup using ultrasound, characterization of the mechanical properties of porcine spinal ligaments subjected to cyclical tensile testing, and the design of a real-time EKG peak detection algorithm implemented in LabVIEW and its application to EKG data from patients with heart disease. Each of these projects required students to either delve much more deeply into the subject matter covered in one of the modules, and/or they necessitated the integration of material from two or more modules. Students were given a significant degree of flexibility in the execution of their projects, subject to instructor approval. Students thus have an opportunity to engage in experimental design at a level that prepares them for the upcoming Capstone projects the following year.

Course Assessment

Assessment of the course after each module was conducted using oral and written communication from the students. Course evaluations were collated at the end of each semester, and individual exit interviews and anonymous surveys were conducted for two graduating classes. Students complete peer evaluations each semester regarding the performance of their fellow group members in the lab and in writing the reports. Summative assessment of student learning consisted of pre-lab quizzes each week, laboratory reports for each module, one final written report at the end of the second semester, and two final written practicum exams (one after each semester). Thus far, the IDEAS lab course sequence has been taught 3.5 times to a total of 226 students (59 of whom have so far completed just the first semester, Modules 1-6).

Most students (typically >75-85%) have met all four course objectives thus far. To determine Objective 1, a cutoff of 70% was selected on the pre-lab quizzes, the final exam each semester, and the results section of the written lab reports (which have counted 40-60% of each report). Approximately 70-85% of students (depending on the semester and the particular group of students) have met this objective. Course Objectives 2 and 3 were evaluated from the lab reports and in-class interactions with the students. In-class interaction was subjective, but critical in evaluating the depth course content and the amount the students were able to absorb. Objective 4 was determined not only from personal interactions with students and the quality of their group lab reports, but also from their performance in the final IDEAS project and from peer evaluations that they submit each semester. Greater than 95% have met Objectives 2-3, and approximately 94% have met Objective 4. The 6% who have not met Objective 4 (regarding teamwork) have been rated poorly by their peers on their contribution to the in-lab activities, the data analysis, and the lab reports.

Student exit interviews from the first two classes who took the IDEAS lab indicated that student opinion of the course sequence has been very positive. In a rating of most "helpful or inspirational" classes in the program, both semesters of the IDEAS lab rated in the top 4 out of 19 courses in our program. Some representative positive comments were: "These labs were amazing – my favorite thing about BME"; "helpful for learning about different types of research"; "very helpful and interesting experience, especially because I didn't do research"; and "I thought the IDEAS labs were an excellent/unique way to introduce a variety of important biomedical engineering concepts and lab techniques and fostered critical thinking & technical writing skills that were extremely beneficial for my senior design/thesis projects." In end-of-course evaluations, students have also commented very favorably on the useful skills learned, the hands-on instruction by multiple faculty, the breadth of topics covered, and that they "learned a lot." While most of the comments have been positive, some constructive negative feedback has been gathered in the exit interviews and evaluations, as well. Generally, the negative comments have either stemmed from organizational issues (especially the first couple of times the lab was taught, since this is still a relatively new course) or from the steep expectations, strict grading of lab reports, and the length of time required to complete the data analysis and lab reports.

As time has elapsed from the actual lab and the students have had an opportunity to put what they have learned into practice and perspective, the student opinion of the course has grown even more positive. Our institution participated in the EBI Engineering Assessment Survey[10] last year, and out of 26 comparable institutions with BME majors, our institution ranked 1st in the following two categories relating to instructional laboratory facilities: "Established an atmosphere conducive to learning" and "Allowed use of modern engineering tools," and ranked 3rd in "Fostered student/faculty interaction." Additionally, in the ABET skill development category in the EBI survey, our institution ranked 2nd in "Design experiments" and 4th in "Conduct experiments."

Conclusions and Future Directions

Overall, we feel that the IDEAS laboratory course sequence developed and implemented at the University of Virginia has been successful in providing students with both breadth and depth in biomedical engineering techniques and experimental design and analysis. Student performance in the course has been good, and student feedback via evaluations, exit interviews, and surveys has been very positive for the most part. The negative feedback thus far has generally been constructive, leading us to make improvements in some aspects of the course. Some changes have been practical as well as principled (e.g. switching from individual to group lab reports, thereby encouraging teamwork while simultaneously reducing the grading load).

We also regularly solicit feedback from a majority of faculty in the department regarding the specific lab content in the modules and final IDEAS project topics. When initially selecting the modules to include in the course, we obtained input from medical and graduate school administrators and industry representatives in BME. As a result, most medical schools have readily granted credit for this lab in lieu of traditional biology labs required of applicants, and many of our student industrial interns have been praised for their proficiency in the lab following their experience in the IDEAS course.

In future years, we plan to revise IDEAS in the following key ways: 1) The module content and experiments will be revised every year, both to improve the quality and efficiency of the lab sessions and to include new skills and techniques to keep the lab up-to-date as the field of BME progresses. One such example is the addition of Module 11 (on bioinformatics tools and network analysis), which is new this semester. This module was added because several members of the faculty felt that students from a BME program should not graduate without first gaining an understanding of basic sequence analysis and an appreciation for high-throughput biology. 2) One negative aspect of the lab that the instructors and TAs have noticed is a tendency in some groups for one or two students to dominate the activities in the lab. To alleviate this issue, we will plan more individual activities within the modules (i.e. provide more in-lab activities that can be performed in parallel to reduce "down time" when only one or two students can make meaningful contributions). 3) Students sometimes struggle with writing high-quality lab reports since IDEAS is usually the first time they have written a rigorous report in the style of a scientific journal publication. Thus, enhanced instruction in report-writing would be beneficial to most of the students.

In conclusion, the assessment of student learning and the feedback gathered from multiple sources (which has been used to enhance and revise the lab modules as needed each year) have both been very positive over the first three and a half years this course has been offered in our program. The laboratory course described in this paper thus represents a viable curricular means by which to provide students with not only the topical breadth but also the practical depth and integrative analysis necessary to prepare the next generation of biomedical engineers.

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