A New Curriculum in Neural Engineering with Emphasis on Design of Neural Systems

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Introduction. Academic and commercial research teams are currently developing a new generation of devices that will interact with, incorporate, and/or emulate living nervous systems. Neural prostheses to restore hearing, mobility or sight will offer a wider range of function; robotic devices will become more effective with "neuromorphic" control systems; fundamentally new methods for processing information will be motivated by biological systems. Neural Engineering is the intellectual force behind these developments, supported by recent advances in cellular neurobiology, microfabrication and neural modeling. Based on decades of quantitative approaches to increase our *understanding* of neural systems, bioengineers are now beginning to *design* neural systems and neural interfaces. Neural engineers have new tools to control aspects of these systems such as guided axon growth and multielectrode arrays for stimulation and recording. In addition to potential applications attracting the attention of biotech and defense industries, these efforts in turn increase our understanding of natural neural systems.

One of the most intriguing aspects of contemporary Neural Engineering is the increasing degree to which scientists can repair and exploit the properties of neural systems, including applications such as neural prostheses, biosensors, or hybrid neural computing devices. The former application currently supports significant industrial involvement; for example, Clarion and Medtronic have commercially available cochlear implants, and Optobionics Inc. (IL) and Second Sight (CA) are companies developing prostheses for vision (in existence for approximately 14 and 4 years, respectively). The latter applications are being funded strongly by federal agencies (e.g. DARPA, NSF), with anticipation of future commercial opportunities. New interface technologies suggest potential new applications in information processing, wherein neurons inspire novel silicon structures for computing, or where neurons themselves perform signal processing operations as part of a hybrid device. A funding mechanism was recently developed between the National Science Foundation and the Department of Energy specifically to fund basic research in these areas [Biological Information Technology and Systems, BITS, (***1***)].

In light of such advances and demonstrated commitment by industry and federal funding sources, it is both appropriate and advantageous to now train students as Neural Engineers. Student training in this evolving area should emphasize the cellular and molecular interfaces between biological and artificial systems. However, training in *Neural Engineering* at the undergraduate level has been slow to develop, impeded by the compartmentalization of the requisite skills in traditionally separate curricula (Neuroscience and Engineering). The UIC Departments of

Bioengineering and Biological Sciences have addressed this problem in a three-year cross-college effort to establish both undergraduate and graduate course tracks in *Neural Engineering*.

The objective of this paper is to describe the Neural Engineering curriculum and its core courses at the University of Illinois at Chicago. Largely defined during the last four years, an important aspect of the curriculum is the adaptation of research-level approaches to cutting edge, interdisciplinary problems in bioengineering to the undergraduate teaching environment. Key features of the curriculum are pointed out, and course evaluations from pilot offerings are described. One particular course, *Bioengineering / Biological Sciences 474* (*BioE/BioS 474*), *Neural Engineering I*, which serves as the capstone for the undergraduate track and the starting point for the graduate track, is described in detail. Development of *BioE/BioS 474* is currently supported by an NSF-CCLI grant, and a preliminary description of this course was presented at the Whitaker Foundation Summit on Education in Biomedical Engineering (2001).

Need for integrated undergraduate training in neuroscience and engineering. It is well-recognized that major improvements in the education of scientists and engineers will require more active learning experiences that address real-world problems, and that effective curricula should expose students to interdisciplinary connections (***2***). In fact, explicit recommendations for the improvement of courses and curricula in the first decade of the 21st century stress that practical training extending beyond traditional fields of inquiry is essential for moving undergraduates quickly into graduate and professional schools and into the technology workforce (***3***).

One field which spans traditional science and engineering boundaries, and which seems poised for major advances, is Neural Engineering. This relatively new field combines cellular and molecular neurobiology with the analytic and modeling tools of engineering, and with electronics, materials science, and fabrication technologies (Figure 1). It is the intellectual foundation supporting such practical developments as prosthetic devices to repair defective sensory organs, electrode implants to restore movement to those paralyzed, neuromorphic chips that mimic the information processing capacities of animal and human brains, and biologically inspired robots. In anticipation of increased clinical applications and growing industry arising from neural engineering research, this focus is experiencing an increased presence at universities, with new research centers (e.g. University of Southern California, Case Western Reserve) and emerging graduate programs (e.g. Arizona State University, University of Pennsylvania).

As a result, one model for educating neural engineers would be to expect those completing a Bachelor's degree in engineering to then train in neuroscience at the graduate level (or vice-versa). However, most engineering graduates enter the work force with their engineering bachelor's degree and no other degrees (***4***). Thus drawing engineering students into a new field that goes beyond traditional boundaries, such as Neural Engineering, is probably best accomplished by creating tracks within undergraduate programs that combine traditional curricula. We have identified a set of quantitative skills, a minimum level of knowledge in neurobiology, and a core of engineering paradigms which, when combined in an efficient curriculum, will train students who will be highly competitive in the commercial and academic job markets as well for admission to graduate and professional schools.

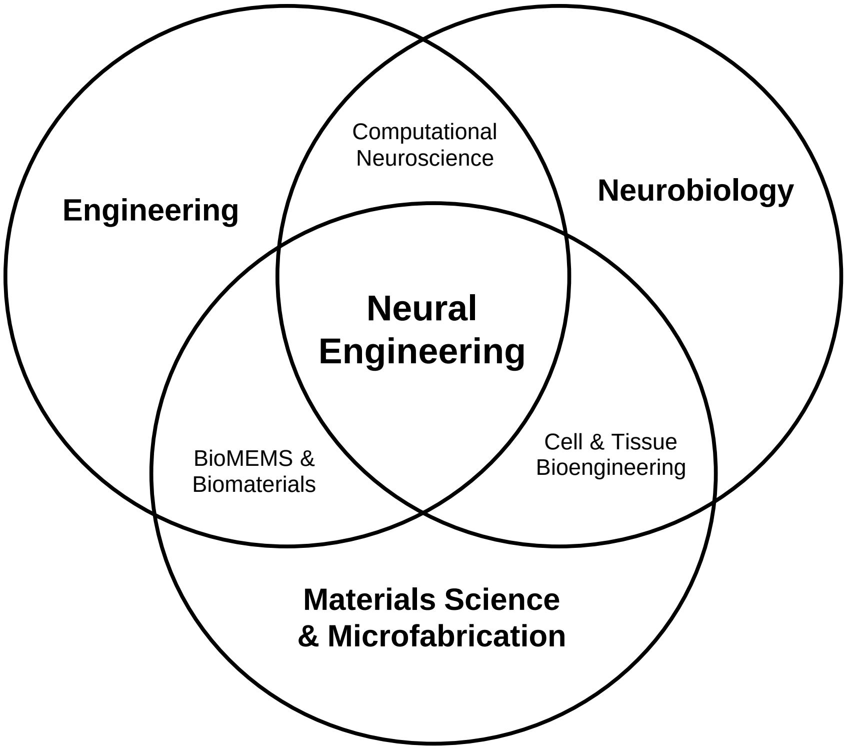

Figure 1. Component areas of the field of Neural Engineering, as emphasized in the UIC curriculum, and in the capstone undergraduate course, *Neural Engineering I*. The interdisciplinary nature of the field, spanning several traditional curricula, is apparent. A primary objective of the curriculum is to present contemporary Neural Engineering topics as design problems. This approach, which utilizes engineering paradigms within the context of neurobiology, is most efficiently taught in a highly integrative setting emulating the research environment. BioMEMS: Bio-Micro-Electromechanical Systems.

***Neural Engineering* curriculum.** As stated above, it is now appropriate and advantageous to provide undergraduates with training in neural engineering. Building an undergraduate Neural Engineering curriculum was challenging for three reasons:

1. The intellectual domain of neural engineering spans several traditional curricula,
2. The methods of the neural engineer are often technically complex and founded in advanced principles of the supporting fields (neurobiology, electronics, signal processing, etc.), and
3. The instrumentation needed for technical training is not generally available in an undergraduate learning environment.

Based on institutional strengths in research and teaching, UIC Bioengineering and Biological Sciences faculty have met these challenges by:

1. Organizing an undergraduate course track in neural engineering that spans three departments and two colleges.
2. Developing a capstone course for this track, in which prerequisite knowledge is synthesized and applied in a model approach to problems in neural engineering.

3. Leveraging and expanding upon existing laboratory resources to provide hands-on technical training.

The Neural Engineering curriculum at UIC has both undergraduate and graduate course tracks. While Biological Sciences undergraduate students may elect to take a concentration of courses in Neural Engineering, and several Biological Sciences students currently enroll in Neural Engineering courses, there is no recognized Neural Engineering minor for those students at this time (the process has begun to establish this cross-college minor as part of a larger initiative to develop an Interdisciplinary Training Program in Neuroscience). Therefore, this paper is focused on the Neural Engineering course track as taken by Bioengineering students, as outlined in Figure 2 below.

In first year undergraduate courses, both Bioengineering and Biology students are introduced to Neural Engineering in course segments providing a survey of applications and a hands-on experience (e.g. building a robot guided by a sensorimotor reflex strategy). Should a student elect to follow the Neural Engineering course track, elective courses are chosen to address requisite areas of knowledge not provided in the student's traditional major. In the fourth year, the undergraduate track culminates with *BioE/BioS 474*, *Neural Engineering I*, a capstone course which synthesizes electives and core knowledge into a coherent picture of Neural Engineering through a series of lectures and experimental activities (this course is described in detail below).

The defining activities of an engineer are to design and build. In order to design with living components (neurons), they must be described quantitatively. A second course, *BioE 472*, *Models of the Nervous System*, serves as a prerequisite for *Neural Engineering I* (however the material in both courses is organized such that they may be taken concurrently). The primary objective of *Models of the Nervous System* is to describe neural systems quantitatively, and can be thought of as a course in computational neuroscience for engineers. This course builds upon the students' background in neurobiology and mathematics (through differential equations). System levels covered include single channels (described by stochastic models), patches of membrane (described with Hodgkin-Huxley biophysics), single neurons (described by compartmental models with simplified or accurate morphology), and small groupings of neurons (integrate-and-fire models). Material related to information processing in neural systems is introduced, including spike train analysis and information theory. Analysis tools for multi-unit recording are also presented, such as spike detection, spike sorting, and rate and coincidence detection. All of these topics directly support material and activities in *Neural Engineering I*.

The current text for *Models of the Nervous System* is Foundations of Cellular Neurophysiology, by Johnston and Wu (The MIT Press). This is an excellent treatment of computational neuroscience which we have found to be approachable by upper-division engineers and biologists alike.

The preparatory coursework in neurobiology includes at least one year of courses taught by the biological sciences department, and must include the *BioS 442* course, a rigorous treatment of *Nerve and Muscle Physiology*. The remaining one-semester course is chosen in coordination with the student's advisor to reflect the student's interests, and generally consists of a course in neuroscience methods or cellular neurobiology. The entire curriculum, with course titles and descriptions, can be viewed at www.uic.edu/depts./bioe.

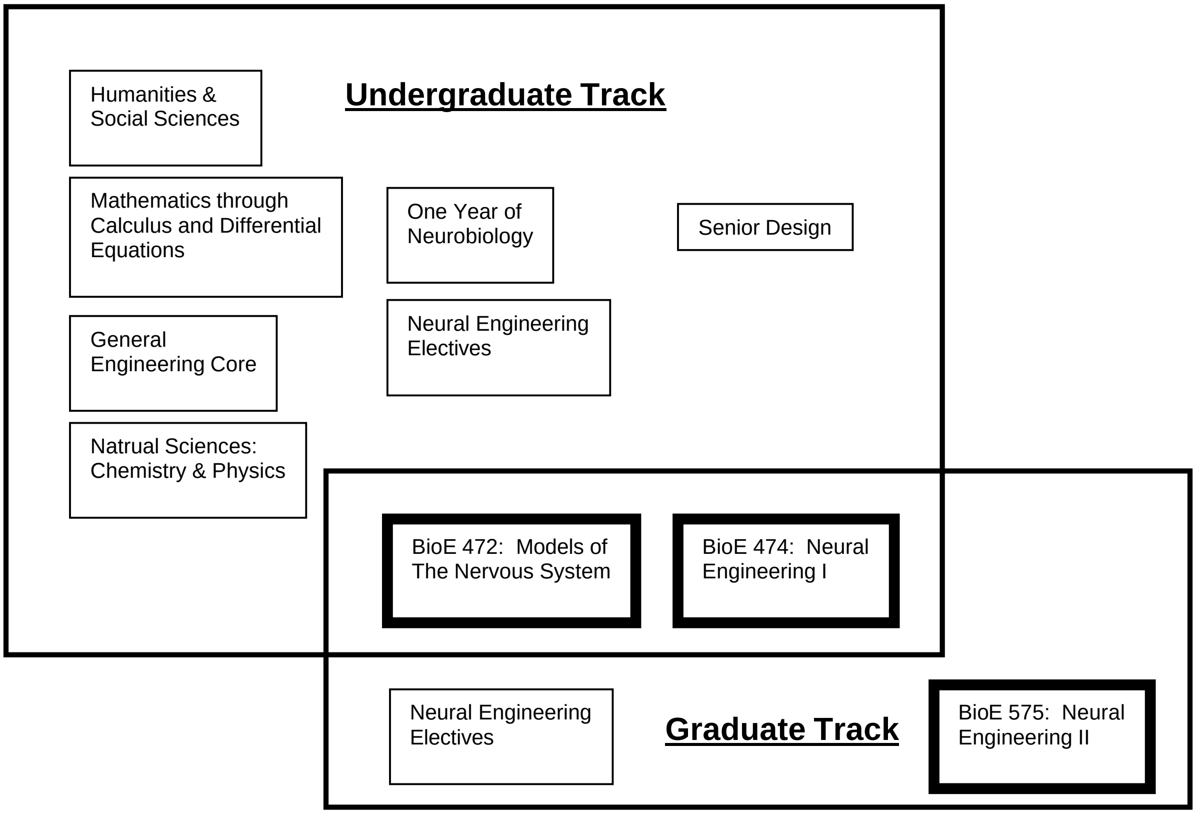

Figure 2. Undergraduate and graduate *Neural Engineering* course tracks, as approached by students majoring in Bioengineering. Courses are depicted in approximate chronological order from left to right. Core Neural Engineering courses, highlighted with bold boxes, are taken by all students following this track within Bioengineering or Biological Sciences.

The graduate course track in Neural Engineering includes the two courses noted above, and adds an additional required core course, *BioE 575, Neural Engineering II*. (The Ph.D. in Bioengineering currently requires a total of 64 hours of coursework, 32 hours of which are at the 500 level.) This course focuses on more complex neural systems, including the brain. *Models of the Nervous System* is a prerequisite for *Neural Engineering II*, but *Neural Engineering I* is not. While *Neural Engineering* graduate students generally take both, this allows for more flexibility in course timing.

In *Neural Engineering II*, a quantitative treatment of electromagnetism is stressed, from the perspective of treating neurons as sources of electric fields contained in volume conductors. Highly developed mathematics is used to solve inverse electromagnetic problems, where areas of neural activity in the brain interior are mapped from measurements of potentials on the scalp, and serve as a basis for understanding clinically relevant functional brain imaging. Key topics are given below:

- Brain and Activation
  - Anatomical and Physiological Basics of Brain
  - Brain as a Bioelectric Generator
  - Brain as a Biomagnetic Generator
  - Brain as a Volume Conductor
  - Bidomain Model of Brain Tissue
  - Brain Activity
- Measurement of Neural Signals
  - Bioelectrical Measurement
  - Biomagnetic Measurement
- Stimulation of Neural Tissue
  - Functional Electrical Stimulation
  - Functional Magnetic Stimulation
- Eelctromagnetic Imaging and Localization of Neural Sources
  - Isopotential/Isofunction Mapping
  - Laplacian Mapping
  - Noninvasive Cortical Imaging
  - Dipole Source Localization

Detailed Course description: ***Neural Engineering I.*** A key course in the neural engineering curriculum at both the graduate and undergraduate levels is *BioE/BioS 474*, *Neural Engineering I*. The course objective is to emphasize application-driven design of neural systems. This is done in a highly integrative format strongly reminiscent of the Neural Engineering research environment, involving critical examination of current literature, computer simulations and modeling, and experimental measurements from living systems. This integration dictates the course content and the student activities in each class, as described below.

The reading for *Neural Engineering I* consists primarily of a set of recent papers from the literature which illustrate the methods and approaches of *Neural Engineering*. A mix of review, methods, and research papers are included. The course packet is photocopied and bound by an on-campus service which also pays the copyright fees and distributes the packets to the students for a modest fee. The list of papers changes from year to year; the current list being used during the Spring 2002 semester is given below [full references available in the bibliography (***5-18***)]. Students are encouraged to refer to the text from *Models of the Nervous System* as a reference when needed.

Reading List for *Neural Engineering I*, Spring 2002 semester:

Plonsey & Barr (1998)	Electrical field stimulation of excitable tissue.
Rattay (1998)	Analysis of the electrical excitation of CNS neurons.
Greenberg *et al.* (1999)	A computational model of electrical stimulation of the retinal ganglion cell.
Stett *et al.* (2000)	Electrical multisite stimulation of the isolated chicken retina.
Grumet *et al.* (2000)	Mulit-electrode stimulation and recording in the isolated retina.
Nadig (1999)	Development of a silicon retinal implant: cortical evoked potentials following focal stimulation of the rabbit retina with light and electricity.
Norman *et al.* (1999)	A neural interface for a cortical vision prosthesis.
Rousche *et al.* (2001)	Flexible polyimide-based intracortical electrode arrays with bioactive capability.
Peyman *et al.* (1998)	Subretinal semiconductor microphotodiode array.

Zrenner *et al.* (1999)	Can subretinal microphotodiodes successfully replace degenerated photoreceptors?
Humayun *et al.* (1999)	Pattern electrical stimulation of the human retina.
Liang *et al.* (1999)	The nerve-electrode interface of the cochlear implant: current spread.
Tykocinski *et al.* (2001)	Chronic electrical stimulation of the auditory nerve using high surface area (HiQ) platinum electrodes.
Marzella & Clark (1999)	Growth factors, auditory neurons and cochlear implants: a review.

One of the most important features of the *Neural Engineering I* course is the student-student teaching that takes place during each problem-based team activity. With only modest recruitment effort, the two offerings of *BioE/BioS 474* have had almost equal enrollment from the two departments (Biological Sciences and Bioengineering; class size has ranged from 16-20 students). When working with computer simulations or with living systems in the wet lab, students are divided into small teams of 2-3, with at least one representative from each department. Each student feels most comfortable in one environment or the other, and the nearly constant transfer of information between students results in almost full-time one-on-one instruction. This serves to increase the speed of learning (students are quicker to ask another student a “dumb” question as opposed to asking the instructor), and effectively emphasizes the importance of interdisciplinary collaboration in a problem-solving environment.

The integration of course content was chosen carefully to demonstrate the importance of breadth of knowledge, and the interdependence between various fields in practical applications. Material spans a wide range of topics, and is generally reinforced by repeated exposure in different contexts. For example, students hear a lecture on single-cell modeling, then work with a computational model of a single cell, and finally record from a single neuron in the lab, comparing experimental results with model predictions. For each neural engineering application, the following aspects of the problem are covered (examples of specific topics given to illustrate a course segment on neural prostheses):

- current research activities (from the current literature),
- key aspects of neurobiology relevant to a *Neural Engineering* application (e.g. retinal circuitry),
- methods and techniques used in research (e.g. multi-unit recording from isolated retina on a microelectrode array),
- modeling of neurons and stimuli (e.g. fields generated by microelectrodes, and cellular responses to these fields),
- available technology for interfacing artificial systems with neurons (e.g. implantable microelectrode arrays),
- current methods in *Neural Engineering* (e.g. experimental protocols for evaluating retinal prostheses), and
- the design, performance and limitations of commercially available devices (e.g. cochlear implants).

Student activities from day to day are varied, with time divided roughly equally between traditional lecture, computer simulations and models, and hands-on experience with engineered living systems. The lecture material is a way to supplement reading and to emphasize or clarify key concepts. Reading is carefully chosen to directly support an interactive experience such as a problem-guided computer simulation. A lecture format which has worked very well is to randomly choose students to present key figures from the reading, with the instructor making necessary clarifications, relating the figure to the objectives of the paper or Neural Engineering in general, and encouraging / facilitating any resulting discussion. Guiding the class to critical conclusions about the reading through Socratic questioning has resulted in lasting and insightful impressions of key concepts in each student, as reflected in answers to exam questions.

For computer simulations, students are quickly trained by walking them through key menus and demonstrating relevant syntax for a given software environment (e.g. NEURON or MatLab) using a computer and video projector. Small teams of students (2-3) are then given a problem to solve using the simulation tools at their disposal.

A notable feature of the course is the laboratory component, in which students gain hands-on experience with research techniques rarely encountered in a teaching environment, especially at the undergraduate level. While rigorous training in any single method is not possible in the available time, we believe that exposure to the techniques provides some practical technical training, as well as providing a critical view of the research problems discussed. Namely, where the data come from, and the associated challenges of working with living systems. Two key learning modules will be described below; the themes for each module are adapted from faculty research involving:

- Neurons patterned on a microelectrode array, demonstrating fabrication and principles of biosensors and implantable neuroprosthetics, and illustrating progress toward hybrid devices for biocomputation and complex hybrid prostheses.
- Integration of a robot with a living neuromuscular system, illustrating neuromorphic control of artificial devices, as well as spike train analysis and practical interface technologies for advanced neuromuscular prostheses.

A significant challenge to the development of this course was adapting research activities to an undergraduate teaching environment. Advanced, graduate-level materials are often distinguished from undergraduate materials by complexity of theory, and/or by degree of integration of previous course-work. During the pilot offerings of the *Neural Engineering I* course, we found that adaptation of advanced material was facilitated by the following circumstances:

- The interdisciplinary nature of the prerequisite coursework prepared students well for the wide range of material covered in the course.
- Pairing of students of dissimilar backgrounds during the guided-learning portions of the course allows each student to interact constantly with a relative “expert” in the unfamiliar material (engineering or biology-based).
- By the time students reach the laboratory, the experimental objective has been covered in lecture, and the relevant system has been modeled in the computer lab. The students are therefore aware of the theory and purpose of the experimental techniques, and usually only a demonstration of the specifics of using particular pieces of instrumentation was required.

Learning module: Neurons patterned on a microelectrode array. An issue central to many Neural Engineering applications is the interface between neurons and microelectrodes used for stimulating (e.g. a retinal prosthetic implant, ***19-22***) or recording (e.g. an olfactory biosensor, ***23-24***). In addition, controlling synapse formation is key to patterning neurons into functional circuits and networks; applications range from biocomputers to hybrid, implantable neuroprosthetics (***25-28***). This course segment includes the following, over approximately eight weeks:

- Lecture material covering clinical and industrial applications of neuron/microelectrode systems (prostheses, neuromorphic chips, biosensors), mechanisms of electrical coupling, electrochemistry of electrode materials, and design and fabrication of microelectrodes.
- Computer models to predict the response of analytical neurons to idealized and realistic electrical stimuli.
- The physiology of B104 neuroblastoma cells is described, and culture procedures are demonstrated. This cell line is reasonably well characterized, easy to maintain, and has been used as an assay for neural patterning (***29***).
- Students use microcontact printing to alter the surface chemistry of the floor of a culture dish [via soft lithography (***30,31***)]). Localization of cells over micropatterned areas of fluorescently labeled collagen is quantified. This requires each student team to count cells every 6 hours.
- In a separate class, collagen micropatterning is used to position cells over planar microelectrodes in the floor of the culture well.
- Whole-cell patch clamp techniques are used to measure responses of cells to electrical stimulation from the planar microelectrodes. Data are analyzed to reveal the mechanisms of electrical coupling, and compared to computer model predictions.
- Cell responses (i.e. impedance changes between the microelectrode beneath the cell and the bath reference electrode) to superfused toxins are measured as a demonstration of biosensor design. Sensor specificiations (sensitivity, linearity, dynamic range) are determined.

The following describes an extension of this module still under development (with support from an NSF CCLI grant), and will be ready for the Fall 2003 semester.

- Lecture material covering clinical and industrial applications of patterned neurons, substrate materials, techniques for micropatterning substrates, and signal processing strategies in single- or multi-synaptic systems.
- Computer models of simple neural circuits will be built using NEURON software.
- Students will use microcontact printing to alter the surface chemistry of a cell culture substrate in a grid pattern (***30***). Localization of neurons (most likely rat hippocampal cells) over micropatterned areas of fluorescently labeled collagen will be quantified.
- Intracellular and/or extracellular planar microelectrodes will be used to measure synaptic efficacy between pairs of cells with apparent physical contact; information transfer across the synapse will be quantified, and compared to model predictions.

Learning module: Neuromorphic control of robot locomotion. There is an established history of neuroscience and robotics influencing each other for basic research or specific applications. This learning module explores our understanding of a sensorimotor pathway in the cockroach by trying to emulate it with an analog circuit. The stereotypical avoidance behavior of the cockroach is to turn away from the stimulus when an antenna is touched. The challenge posed to the students in this module is to have a robot demonstrate the appropriate avoidance behavior when the input signals to the robot originate in the sensory neurons of a living cockroach. This engaging activity serves to establish a model of biopotential control of an electric device, and illustrates a number of concepts central to advanced neuromuscular prostheses and biopotential-controlled aids for persons with chronic paralysis (e.g. internet navigation or control of a motorized wheelchair).

The students first hear lecture material describing what is known about the biological system that controls escape behavior in response to antennal stimulation. This material includes basic neurobiology, as well as quantitative models describing the input-output relationship of the system. Based upon this information, and with guidance from the instructor, an analog circuit is built (using basic op-amp-based filters, integrators, summers and amplifiers) with the goal of performing the signal processing accomplished by the natural system (including integration and contralateral inhibition). The conditioned electronic signal is then converted to a variable voltage via a push-pull amplifier. In the lab, sensory neuron activity from the right and left antennae of a living cockroach is recorded using hook electrodes and standard electrophysiology amplifiers. These signals are then fed into the student teams' circuits. The output of each circuit then becomes input to the actuators of a robot built with the Leggo Mindstorms Robotics Invention System^{TM}. If the robot exhibits the stereotypical escape response when the living cockroach antenna is touched, then the students have implemented neuromorphic control, and constructed a model of a neuromuscular prosthesis. The material for this module is presented in the same structure as the one described above, including lecture, computer modeling, and hands-on experience with the living system. A simpler version of this module has also been used, where the biopotentials originate in the students' biceps muscles and are recorded using a differential amplifier and disposable ECG electrodes.

Outcomes of first two pilot offerings. Initial evaluation consisted of examination of student work and a written course evaluation administered by the University of Illinois Survey Research Laboratory (SRL). This survey asked 16 questions about instructor effectiveness and course quality. Overall score for instructor effectiveness was 4.2/5.0, and overall score for course quality was 3.8/5.0. Course features rated highest were appropriateness of exam questions (3.9), usefulness of homework assignments (3.9), and the text (3.8). The weakest feature was course organization (3.2), which is understandable during a pilot offering. Instructor qualities rated highest were ability to answer questions thoroughly (4.6) and clarity of communication (4.6).

Student work showed an assimilation of material learned in biology and engineering courses that became more seamless as the semester progressed. For example, first attempts to use current-loop laws learned in a circuits course to analyze the passive response of a cell to membrane channel opening were awkward. However, later in the semester, students took the initiative in explaining cockroach behavior with relatively complex electrical analogs to cross-inhibitory sensorimotor pathways. We found that two strong features of the course were **1)** pairing biology and bioengineering students during problem-solving activities, and **2)** the interdisciplinary experiences it afforded.

By pairing students with complimentary backgrounds, each student was constantly interacting with a relative "expert" in the unfamiliar field. We feel that this enhanced learning significantly, and hope to measure this outcome in future course assessment.

As emphasized in the student evaluation comments, exposure to computational tools (e.g. MATLAB) or wet-lab techniques (e.g. intracellular recording) represented experiences outside the traditional curriculum for one or the other group, and were very well received.

Summary. By developing three new courses to serve as the backbone of the *Neural Engineering* curriculum (*Models of the Nervous System*, *Neural Engineering I*, *Neural Engineering II*), we have coalesced a large amount of material from traditionally separate curricula. We believe that the undergraduate courses, when combined with appropriately chosen electives, provide both a broad bioengineering skill set, as well as a useful concentration in *Neural Engineering*. The two laboratory modules described above successfully adapt cutting-edge research material to an undergraduate teaching environment.

The key feature of our results is the recreation of the collaborative, integrative atmosphere of a successful research environment in the classroom. This was accomplished through the integration of course material from traditionally disparate curricula, a multi-modal approach to problem solving, where students are presented with the same issues from a number of directions, and the pairing of students with dissimilar backgrounds for team activities. While the specific laboratory activities described here would be difficult to simulate at other institutions which do not already perform similar research activities, we believe that our efforts can serve as an example for the adaptation of any appropriate research activity to the teaching arena. We feel strongly that this type of approach will become increasingly critical as technologies and applications in bioengineering become more interdisciplinary and technically complex, and it is being adopted by other focus areas in our department (Cell & Tissue Engineering; Bioinformatics & Genomics).

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