MASSACHUSETTS INSTITUTE OF TECHNOLOGY

May 2010

The BioTECH

Volume 7, Issue 1

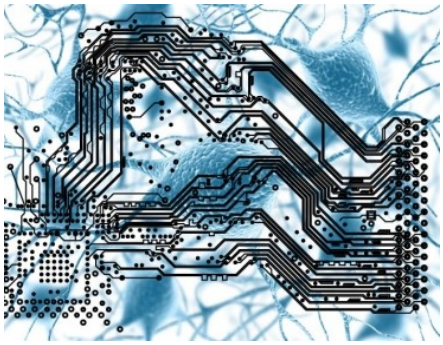
BIOLOGICAL ENGINEERING-BIOMEDICAL ENGINEERING SOCIETY

$25 million NSF Grant Awarded

By *SABINA SOOD, '13*
BIOTECH EDITOR

Source: from MIT News, published February 23, 2010, "With $25 million grant, NSF funds center to investigate the creation of biological machines"

The National Science Foundation (NSF) has given MIT, along with the University of Illinois at Urbana-Champaign and the Georgia Institute of Technology, a $25 million grant to launch the Emergent Behaviors of Integrated Cellular Systems Center (EBICS). The center is being funded by NSF's Science and Technology Centers Integrative Partnerships program and will have its headquarters at MIT.



Graphic from MIT News

"Ultimately, we envision being able to create biological modules — sensors, processors, actuators"

The purpose of the center is to "dramatically advance research in complex biological systems, create new educational programs based on this research and demonstrate leadership in its involvement of groups traditionally underrepresented in science and engineering." The center's founding director and Course 2 /20 Professor Roger Kamm states, "Ultimately, we envision being able to create biological modules — sensors, processors, actuators — that can be assembled in various ways to produce different capabilities. If successful, this will open up an entirely new field ofresearch with wide-ranging implications, ranging from regenerative medicine to developmental biology."

In order to accomplish the goal of the center, scientists are working to uncover the properties and mechanisms of cells and generate basic cellular machines that can carry out specific functions. The educational aspect of EBICS consists of "an integrated graduate program for engineers to learn biological science, and for biologists to learn engineering methods."

BE Faculty Awards, 2009-10

- Profs. Roger Kamm and Bruce Tidor named AAAS Fellows
- Prof. Angie Belcher wins ENI Prize for Renewable & Non-Convential Energy
- Prof. Leona Samson selected for NIH Pioneer Award
- Professor Linda Griffith receives NIH Transformative Research Grant
- Prof Doug Lauffenburger receives inaugural Systems Biology Foundation Award
- Prof Linda Griffith receives Society for Biomaterials Clemson Award for Basic Research
- Prof. Jay Han wins Analytical Chemistry Young Innovator Award

Inside this Issue

Meet the 2009 – 2010 BE-BMES Exec!

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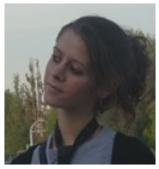

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The BioTECH

MIT Bioengineering-Biomedical Engineering Publication

web.mit.edu/bmes/www

Interested in writing for the BioTECH?
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Professor of BE, ChemE, Biology

New BE Faculty

Professors Ron Weiss and **Katharina Ribbeck** joined the BE faculty in the past year.

Ron Weiss joined the BE faculty in September 2009 from Princeton University's Electrical Engineering Department. At MIT, he is jointly appointed in the Department of Electrical Engineering and Computer Science and Biological Engineering. Professor Weiss completed his PhD in the area of programming biological cells from MIT EECS/CSAIL.

A pioneer in synthetic biology, his group works on the construction and analysis of synthetic gene networks, as well as using computer engineering principles of abstraction to program cells with sensors and actuators precisely controlled by analog and digital logic circuitry.

Picture from MIT BE Website

Professor Weiss was also heavily involved in the new $25million grant from NSF for the creation of biological machines (*see front page*).

Interview with Prof Katharina Ribbeck

By ***Jessica Perez '11***
Assistant Editor

Katharine Ribbeck joined the BE faculty this March after finishing a Bauer fellowship at Harvard University Center for Systems Biology. Ribbeck earned a Biology degree from the University of Heidelberg in 1998 with highest honors, and her PhD at the same institution in 2001. Her current research is on biological transport barriers focusing on the physical properties of mucus barriers and its invasion by pathogens. Ribbeck answered a few questions on her new position.

BE-BMES: How was your group's transition from Harvard to MIT?
Ribbeck: It was a very smooth transition. I already had an excited group of postdocs set up at Harvard [who joined me at MIT]. The department was also very supportive by allowing me to access my lab space and office before my official start date.

BE-BMES : What challenges have you faced with your new position?:
Ribbeck: There are challenges at many levels. One challenge is to set up a group of people that interact well with each other. It is also challenging to come up with balanced projects. You want low hanging fruit, but yet bold aims, high merit, but not too risky. Then each person has a very different style in doing science, so I have to take that into account. But I have great, independent, excited students. We are a good team. Although stress is apart of it, I look forward to every day. It is a luxury to be able to follow your curiosity. I can't imagine a more wonderful situation.

BE-BMES: Why did you choose to go the academic route?
Ribbeck: In academia you design and communicate your research in different ways than in industry. Also important for me is the exposure to students, and the opportunity to teach. I enjoy this.

Picture from MIT BE Website

BE-BMES: Why do you think there are so few women professors at MIT?
Ribbeck: I personally have not experienced a gender-based difference in treatment at MIT. I am treated well and have fantastic support. However, having a family is very demanding. Here I think having the right family model is important. A partner who supports you in pursuing your career, and splits responsibilities at home, is crucial.

BE-BMES: Can you describe your current research?:
Ribbeck: (eyes light up) We study the physical properties of mucus, a biological gel that serves as the body's first line of defense against foreign invaders in the stomach, lungs, nose, urogenital tract. It has fantastic properties: it blocks bacteria, viruses, and toxins, but at the same time passes nutrients, scents, or sperm. The techniques we use in my lab range from single particle tracking to live imaging of macrophage migration through the mucus. One new project is to look at live mucus (and the cells therein) in the digestive tract of zebrafish. This project is in collaboration with Nancy Hopkins.

Ribbeck will be teaching 20.450 (Molecular & Cellular Pathophysiology) next semester. The Ribbeck lab is currently seeking UROPs. Most important criteria is excitement and enthusiasm.

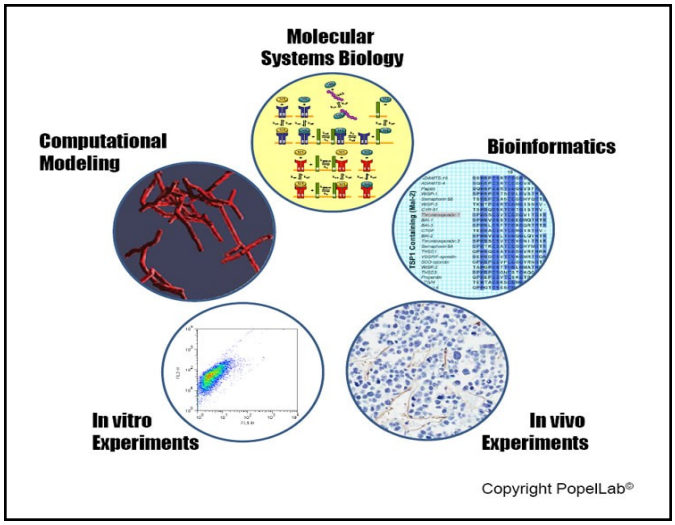
Biological Engineering: the

By *MASHAAL SOHAIL, '11*
BIOTECH EDITOR

Nature does not tend to be organized into neatly bounded compartments representing different disciplines; particularly in biological systems, we usually see a mixture of many fields all at once. Thus, in order to completely understand these living systems, to develop better therapeutic solutions and to manipulate these systems for various applications, it is important to understand not only the biology but also the physics and chemistry involved. Moreover, it is also essential to have a grasp of various different engineering principles. These include, for example,

- **Computational Modeling** which can be used to predict protein folding and determine drug targets for various diseases
- **Fluid and Field Dynamics** to help understand various transport phenomenon in living systems and to develop new tools to separate, sense and analyze biomolecules
- **Thermodyamics and Mechanics** to understand the energetics of biological events such as folding, binding, signaling and tissue contraction and to develop better therapeutics and clinical practices

The evolution of the field of biological engineering is, therefore, an inevitable consequence of this growing need for a synthesis of these various disciplines and skills in the context of biological problems. One way to visualize MIT's department is to imagine a multidimensional landscape with axes of biology, chemistry, physics, mechanical engineering, chemical engineering and computer science and to orient a sphere somewhere on the landscape so that it encompasses varying amounts of each discipline. Biological engineering, however, is not standardized across schools in the U.S., let alone across countries. Continuing the sphere analogy— each school's take on biological engineering may be oriented differently in our multidimensional scientific coordinate system, encompassing more of one field and less of another. In fact, the snapshot of each program may be better described as an ellipse rather than as a sphere.



Graphic from www.jhu.edu/apopel/images/research2.jpg

Biological engineers from all over can still communicate effectively though. This is because they have all studied the same problems and approaches even though they may have studied them in varying depths. Just looking at the portfolio of the faculty, one realizes the uniqueness of the department, with backgrounds ranging from Electrical Engineering to Biochemistry, all brought together by their shared interest in similar problems.

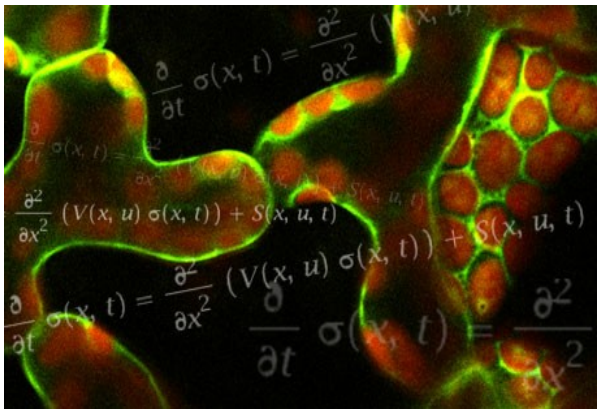
According to Professor Manalis, since its inception, the major has seen some evolution in the student body itself. The first class was predominantly concentrated with students who, if the BE major had not existed, would probably have majored in Biology. Over the years, as awareness of what the field is has increased, the major is attracting more students that are also inclined towards Mech E or Comp Sci for example. The newer BE

field and MIT's take on it

classes see a higher number of students who are pursuing minors or taking classes in other engineering fields to achieve more depth where the BE major might provide just a sampling.

In BE, probably more so than in other departments at MIT, the classes significantly map to the research that is being done by the faculty. As a direct consequence, the classes constantly draw on current real world problems. Since BE provides a new lens for looking at many of these problems, the classes present very realistic depictions of the problems as well as of the current approaches to solve them, their limitations and the practical hurdles involved. For example, in the fourth unit of 20.330 (Fields, Forces and Flows in Biological Systems), Professor Han prefaces teaching about electroosmotic flow by presenting the actual dilemma he faced in his own research as a graduate student developing a DNA separation device in which he observed DNA moving from the cathode to the anode instead of vice versa. On teaching new concepts, he would then constantly refer back to this problem and how the concepts from the class helped to explain and correct it.

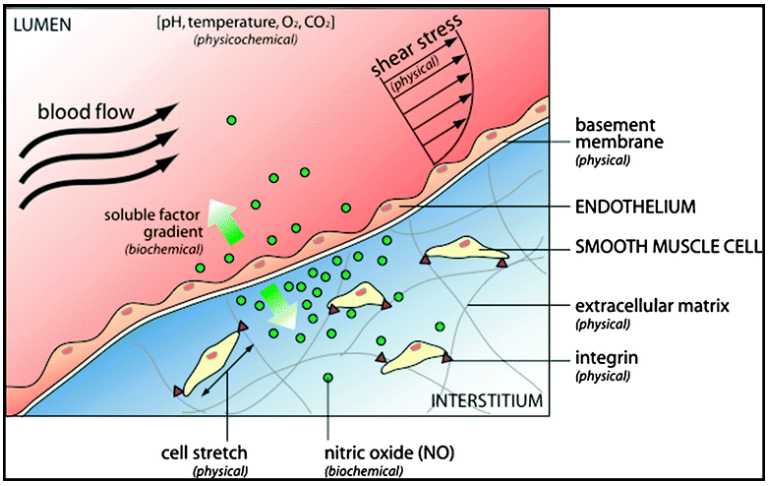
The real world applications of BE can be seen clearly in health-related aspects such as the development of novel therapeutics and diagnostics for disease. MIT's Department, however, provides avenues for students across other aspects of BE as well. For those interested in Synthetic Biology for example, Natalie Kuldell and Ron Weiss' 20.020 (Introduction to Biological Engineering Design) serves as a freshman class which sets the framework for Synthetic Biology and lets students try their hand at it.



Graphic from University of Exeter

This year's class has student groups developing projects which include using microorganisms to harvest Lithium from seawater, building an enclosed sustainable ecosystem comprising of Algae and Bacteria for biofuel production and using gut-residing bacteria for treatment of lactose-intolerance. The scope of BE, therefore, goes much beyond just health and medicine and the field has applications in areas ranging from more efficient energy generation and promotion of environmental health to the design of new biomaterials and synthetic biological systems.

A sincere thanks to Professor Manalis and Natalie Kuldell for sharing their perspectives.



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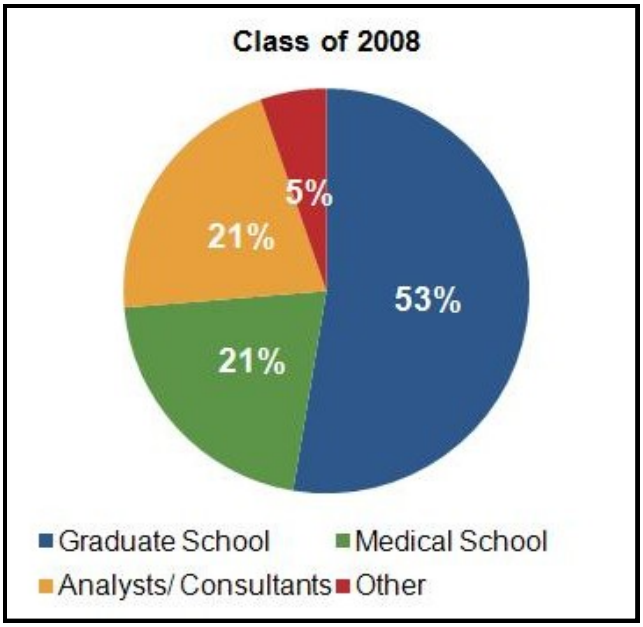
MIT Biological Engi



Amanda Morris, Class of 2008

After graduating from MIT's Biological Engineering major, I am attending Johns Hopkins School of Medicine. A frequently asked question during medical school interviews and medical school training has been - how is a Biological Engineering degree going to help in medical school? My experience has been that a BE background has helped me to better understand how the human body works. For instance, during summer research in cardiothoracic surgery, I have seen how pressure and volume principles guide the development of new heart valves. In addition, understanding the anatomy of muscle movement requires a firm grasp of force-balance principles. Coordinating both heart and muscle is the central nervous system, which we can better understand through mathematical and computational modeling. In sum, engineering is applied in vivo. Medicine is hard yet rewarding work, and BE is my foundation.

Justin Lo, Class of 2008

I'm a second-year MD/PhD student at Harvard Medical School and will be in the HST MEMP program for my PhD. I see myself on a track towards academic medicine, with both research and clinical practice as part of my future career. I'm particularly interested in gastroenterology and medical oncology. The whole idea behind BE (engineering and design based on biological principles and foundations) is quite applicable to the HST MD track at HMS. Particularly, the lab courses were useful for helping me understand research frontiers and the concepts behind medical devices for diagnosis and treatment. As for advise, I would just say it's best to follow your heart, really. No mentor, parent, or large sum of $$$ should ever take the place of your gut instinct.

Consulting Firms
DRW Trading
Allston Trading
Fletcher Spaght Inc.
Applied Predictive Technologies
Decision Resources
Rosetta

Medial Schools
Harvard
Mt. Sinai
Washington Univ
Case Western
Univ. of Pittsburgh

Sasha Brophy, Class of 2008

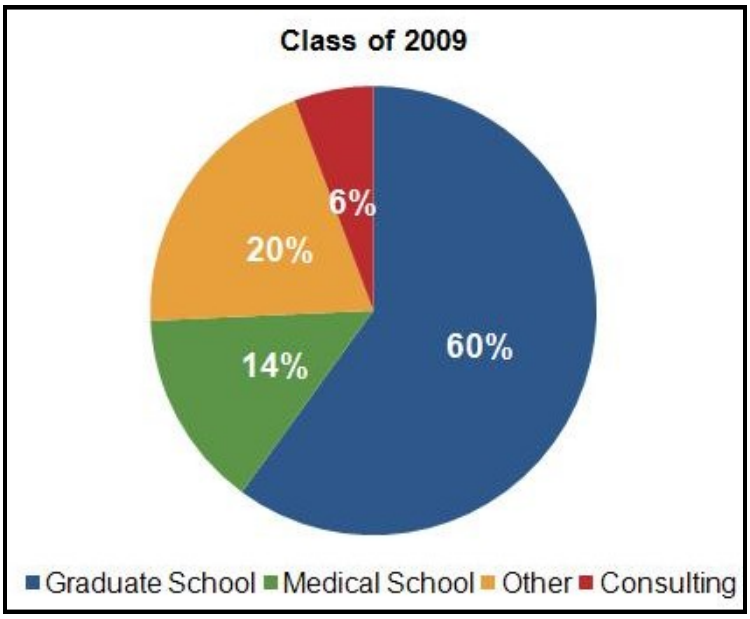
Since graduation with the first MIT BE class in 2008, I have been working at Fletcher Spaght, a healthcare consulting and venture capital company here in Boston. While I've moved over to the company strategy aspect, my biotech background has been instrumental in my valuations of these medical devices and life science tools. To understand where the latest research is moving and what tools are needed, I read up on Pubmed articles as I learned to do in Essigmann's thesis class. When we were looking at some flow cytometer companies, I was able to draw on my lab experience from Natalie Kuldell's 20.109. And the business valuation software skills I needed to pick up were a breeze after 20.180 and 20.181 DNA database programming.

Other
World Traveling
Teach for American
Lab Technician
Taking a year off
US Navy (Naval Nuclear Propulsion Program)
Start-up Company

neers in the World

Programs
Bioengineering
HIV Immunology
Systems Biology
MD/PhD
Plant and Microbial biology

Graduate Schools
MIT
UPenn
Harvard
Duke
Caltech
University of Wisconsin
University of Washington
Oxford University
NIH Academy
University of Florida
Boston University
UT Southwestern
UC Berkeley
UCSF
Ecole de Neurosciences de Paris
UCSD
Stanford
Johns Hopkins
University of Michigan



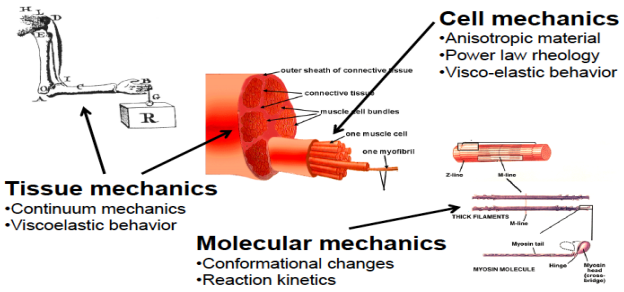
Iny Jhun, Class of 2009

Since graduating, I've been doing research at the Samson Lab / Center for Environmental Health Sciences for a clinical study on inflammatory bowel disease. Meanwhile, I also applied to several Environmental Health graduate programs, and will be attending Harvard School of Public Health this coming Fall of 2010 for a doctoral program in Environmental Epidemiology. My undergraduate training in both biological sciences and quantitative methods will certainly be relevant and useful in my graduate studies, as epidemiological methods are rooted in statistics, and understanding the effect of environmental factors on health outcomes will require a solid background on biology. I think biological engineering at MIT is one of the most relevant majors for those interested the field of epidemiology.

Bryan H, Class of 2009

In the time since I've left MIT I have traveled. After graduation I took on a research project in bioenergy at the Ben Gurion University of the Negev in Be'er-Sheva, Israel. My BE degree got me the job, and I got the chance to see the Middle East and learn about the bioenergy sector. When I wasn't working, I traveled through Jordan and Egypt meeting people, visiting friends, and experiencing a completely different world. By fall I was back at MIT figuring out my next project, hopefully one that would export me to somewhere new again. Inside of a month I was in Barcelona, Spain, where I currently reside, working on an Atherosclerosis project at the Institut Químic de Sarrià. Again, it was my connection to the MIT community that afforded me this opportunity. I will be here until the end of the summer when I'll join a bioinformatics company based out of Bangalore, India for a brief 3-month internship.

I have a BS in Biological Engineering, but upon graduating from the Institute, I wanted to see the world, not just more lab benches. I think I'm doing that, and although I still find myself in lab from time to time, at least it's not Eastern Standard Time. As for my future, I'm still uncertain. World traveling has pulled me into the nearly orthogonal fields of international relations and development, journalism, and even entrepreneurship. My advice to the younger classes is to study what you like, not what you think you need to know. And see the world, it's very different from MIT.



20.310: Molecular, Cellular and Tissue Biomechanics — Mashaal Sohail '11

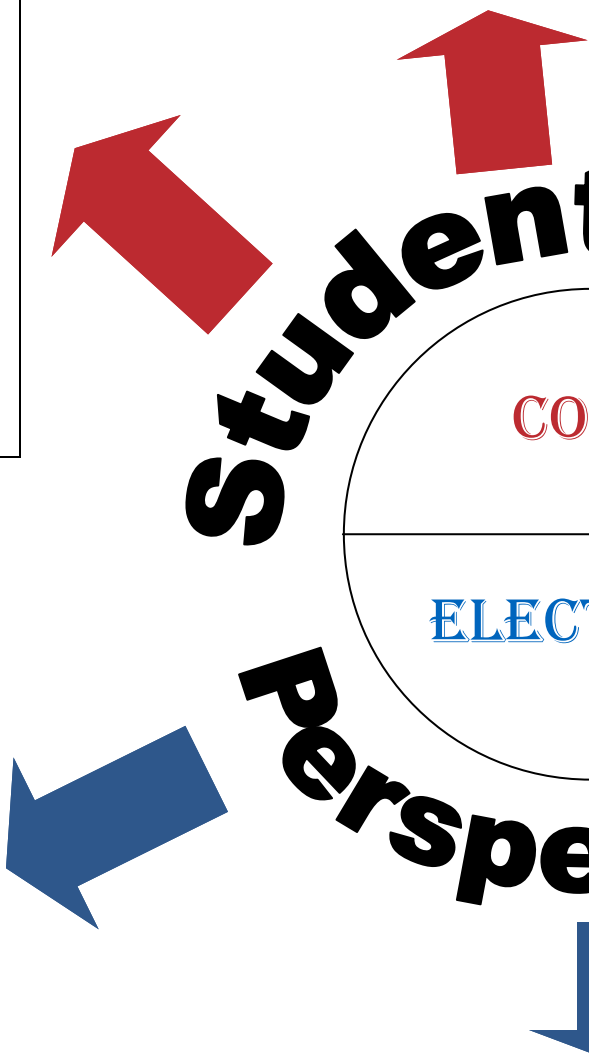
This class studies biomechanics on many scales ranging from protein-ligand binding, DNA packaging, protein folding, cell adhesion/migration to mechanotransduction pathways and tissue mechanics. The relevance of these events is emphasized in the context of examples such as wound healing, muscle contraction, hearing and the propagation of bacterial infections. Since defects in mechanotransduction can lead to many diseases such as cancer, hearing and development disorders, understanding the relevant biomechanics can lead to improvements in tissue engineering, medical procedures and current therapeutics. The class is divided into 3 units (molecular, tissue and cellular) and covers a range of concepts both qualitatively and quantitatively including single molecule models, reaction kinetics, force balances, continuum mechanics, visco and poroelastic behaviors, cell membrane mechanics and mechanics of the cytoskeleton and the nucleus. Evaluation is based on 3 exams (one for each unit), weekly problem sets and a final group research paper + short presentation.

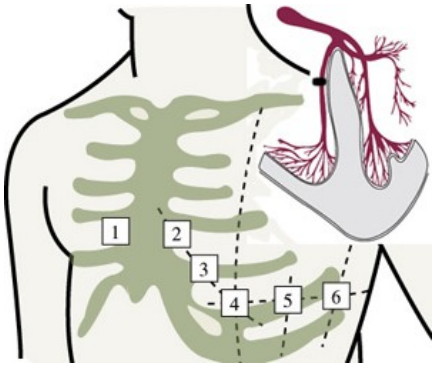
6.047: Computational Biology — Layla Barkal '11

This is a wonderful, intense, class. It's listed as undergrad but undergrads are the slight minority – there are course 6 grads, Harvard MPH students, BU grads and undergrads, and HST grads. The diversity is great in terms of class discussions and perspectives. Content wise, the course is divided into two halves: foundations and frontiers. The foundations portion has psets to teach you the tools of computational biology. The frontiers part is a series of guest lectures in which researchers from the Boston area come in to tell you about their awesome projects while you are simultaneously working on your own final project. And because you're given half the semester to work on the final project, it's possible to actually delve into it and accomplish something. As for pre-reqs, 6.041 is useful; it's a generally useful course that you should take anyways. My formal coding experience prior to 6.047 consisted only of 6.00, not 6.006 as recommended, and though the psets took quite a while, I don't think I was missing much background. Overall, the class is a lot of work, very rewarding, and I would absolutely recommend it.

20.380: Biological Engineering Design (Sen

The class puts a lot of emphasis on designing
is done closely within large groups of 7-8, and
experience to me in that way. The general aim
those who seek to work in larger companies ra
Each group of students chooses a disease, an
different parts in the final report: background, c
testing, modeling, clinical testing and business
properties. Personally, I do not find diseases o
interesting, but I must admit that the class has
'reading of medically oriented papers' dimensio





6.022: Quantitative Physiolo

This class is an engineer's int
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respiratory system, and the re
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***Perspectives compiled from various students.**

ior Capstone) — Anonymous

a therapeutic. Work
it has been quite a 'real world'
of this class is more directed to
ather those interested in research.
d each individual is responsible for
design, in vivo and in vitro
aspects or intellectual
r business start-ups very
been the only one to add this
on to my education .

20.330: Fields, Forces & Flows in Biological Systems — Mashaal Sohail '11

As the need for new sophisticated tools to study biological systems grows, it is becoming increasingly important to understand the dynamics that govern interactions between biomolecules. Examples include microfluidic systems, biosensors, mass spectrometers, sequencing tools, cell counters, single cell traps, electrophoresis devices and diagnostic tools for viral diseases. This class teaches an understanding of the relevant governing dynamics and kinetics in the context of events like binding/separation of biomolecules, cell movement in response to other cells/factors, cell differentiation, and transport within living systems. It manages to establish both an intuitive higher level understanding of these concepts and develop more quantitative mathematical applications (you will see a lot of differential equations!). The class is logically divided into 4 units (Transport, Fields, Fluids, Electrokinetics and Forces), each of which ends with a non cumulative exam. Part of the final evaluation is also based on the weekly problem sets. The class is very well organized and leaves one with a comprehensive sense of the various interactions that exist in a biological system.

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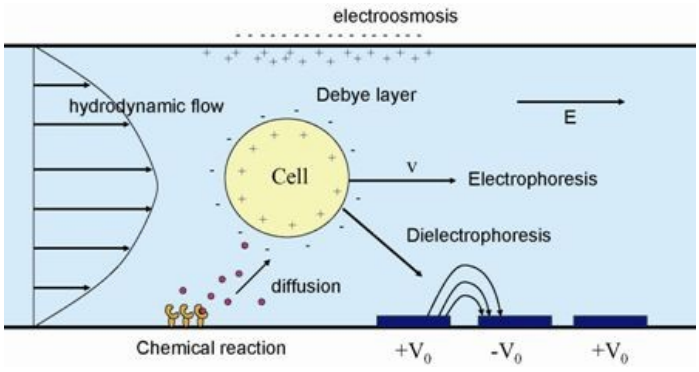


20.441: Biomaterials-Tissue Interactions — Eric Gomez '11

This class is an introduction to applications of material science and biology in medical implants, artificial organs, and scaffolds in tissue engineering. Professors Spector and Yannas do a great job of covering a wide spectrum of topics involving biomaterials in a non-convoluted or certain course-heavy manner, so that this class can be handled by students of most any major with applications to biology. I took the class fall of 2009, and it was filled with students from course 2, 3, 5, 7, 10, and 20. The course work consists of psets due weekly or every other week, and three tests that are open book, notes, and internet. There is no final! In their tests and psets, the professors like to put you in the positions of a surgeon or CEO of a biomaterials company, giving you a cool way of applying what you've learned in class. The class also focuses on the most up to date biomaterial technology, emphasizing tissue regeneration. I recommend this class to anybody who is interested in the field of tissue engineering and regeneration.

gy — Matthew Luchette '11

troduction to medical school. The class
ms (the cardiovascular system, the
nal system) and applies principles of
ineering to understand how the sys-
. What really makes the class a blast,
s has three labs throughout the year,
e semester goes on. The class culmi-
t lab" at the end of the semester,
terventions on a live, anesthetized rab-
ts.

Briefings: Semester in Review

Career Panel, How to Choose a Major, Student Research Prizes, and more!

Every semester, our exec works diligently to share exciting events and opportunities with our community. Here is a brief overview of highlights from the past semester!

Launch of the MIT Center for Gynepathology Research

December 4, 2009

Padma Lakshmi, model, celebrity host of Top Chef and co-founder of the Endometriosis Foundation of America, spoke at the launch of the MIT Center for Gynepathology Research. Ms. Lakshmi visited to raise awareness of the toll endometriosis takes on society and shared her personal experience with endometriosis. During her speech Lakshmi announced her pregnancy. This is a great triumph over endometriosis because many patients suffer from infertility. After her MIT address, a private reception was held for selected patients and family members of patients suffering with endometriosis.

Panel Discussion: Career paths in Biomedical and Biological Engineering

February 24, 2010

The speakers present on the panel were able to discuss their experiences from different stages of their careers, share ideas regarding career paths, and answer questions from the audience. The panel consisted of the following speakers:
Mike Benedetto - Project Executive at Skanska (Science and technology business development)
Geoffrey von Maltzahn - New Ventures Principal at Flagship Ventures (venture capital firm), HST PhD - Feb. '10. Winner of 2009 Lemelson-MIT $30,000 Student Prize
Nicholas Marcantonio - Consultant at ClearView Healthcare Partners (life sciences consulting firm), MIT BE Ph.D.- June '08
Matthias Reumann – Postdoctoral fellow at IBM Research and EMBS Administrative Committee member, Universitat Karlsruhe Ph.D – Feb '07
Kelly Sullivan – Clinical Development and Regulatory Affairs (pharmaceutical industry), Harvard PhD '01.

CPW Festival
April 8, 2010

Photo by Jessica Perez

How to Choose a Major Panel

March 9, 2010

Professor and student representatives from Course 2, 3, 6, 7, 8, 10, 20 shared their take and perspective on how their major is relevant to bioengineering research. They also highlighted special tracks in certain majors that accommodates the more bio-focused student.
Course 2: Prof Peter So; Shanette Go
Course 3: Prof Michael Cima; Hannah Rice, Elizabeth Tsai, Cameron Brow, Justin Breucop
Course 6: Profs Eric Grimson and Jay Han; Daniel Kim
Course 7: Prof Hazel Sive; Lauren Shields
Course 8: Prof Jeff Gore; Stephen Serene, Helen Hou
Course 10: Prof Paula Hammond; Diana Wu, Hilda Buss, Alan Leung
Course 20: Prof Ernest Fraenkel; Kevin Hu, Roli Mandhana

Photo by Andrea Fabre

Students Showcase Their Research at Merck/BE-BMES Undergraduate Research Poster Session

November 16, 2009

The 5th annual Merck/BE-BMES Undergraduate Research Poster Session gave students the opportunity to present their research at a poster session to judges from academia and industry. Merck generously funds $500, $300, and $100 cash prizes to the top 3 winners. Omar Abudayyeh received first place, Anne Ye received second place and Yadir Guerrero received third place. The 2010 Merck/BE-BMES Research Poster Competition submission deadline is early October 2010.

STUDENT RESEARCH HIGHLIGHTS

EMILY HOUSTON

Design of a Lens Cleaning Device for Laparoscopy Use

Advisor: Prof Alex Slocum

Laparoscopic surgical procedures have revolutionized many gynecological and abdominal procedures, leading to dramatic reductions in recovery time and scarring for the patient. However, the surgeon's vision through the endoscopic lens is frequently obscured by fog, liquid, and solid debris. I worked in a team to design a mechanical solution to this problem, providing a clean image through the scope with the click of a button, without requiring external hookups to power or fluids. Multiple prototypes and tests show that the device can successfully restore vision up to 90 times in one surgery and the device recently received promising feedback at the Design of Medical Devices Conference. Working on this project is extremely fulfilling. It allows me to apply engineering fundamentals to design a biomedical device that could have a huge impact on the quality of current laparoscopic procedures.

Student Research Spotlight

Why? Research is an ongoing dialogue — share your work with peers from different backgrounds but similar interests!

How? Submit a concise and informative description of research in a BE-related field.

Interested? Contact be-bmes-exec@mit.edu!

DANIEL KIM

A Remote Control for Gene Expression

Advisor: Prof Sangeeta Bhatia

Modifying genetic networks from the outside of the cell can be made simpler with the use of nanotechnology. In my current research, I use gold nanoparticles to change laser energy into heat energy. This heat energy is then used to toggle a "genetic switch" in bacteria, turning on a gene that was previously off. Thus, we can remotely control gene expression using light as our input; this allows fast modifications to gene expression without having to use chemicals. As the main investigator in this project, I work on all aspects of implementation. Currently, I am working on attaching gold nanorods to the surface of the bacterium to create a biological "module." Being an electrical engineer with a minor in biomedical engineering has helped me understand the key limitations and constraints in the system, as well as the best methods to actually implement this idea.

BE in the World: News, Business, Policy Perspectives

Cancer Fight: Unclear Tests for New Drug

Taken from The NYTimes, Published April 19, 2010 by Gina Kolata

The news was not good: she had cancer. Then the complications began. Dr. Griffith, director of the Center for Gynepathology Research at M.I.T., had a test to see whether her tumor had extra copies of a protein, HER2. If it did, it would respond to a drug, Herceptin, which blocks the protein and stymies the tumor's growth. Drugs aimed at disabling proteins that spur cancer are, many oncologists say, the future of cancer therapies. Only a few are available now but almost every new drug under study is designed to disable cancer-fueling proteins. But these so-called targeted therapies are only as good as tests to find their protein targets. And while most patients do not yet know it, those tests can be surprisingly unreliable. Acknowledging the problem, cancer specialists on Monday announced new testing guidelines for one protein target, but as new targets are identified, the problem continues to grow.

Article continued on NYTimes.

***Professor Griffith, a faculty advisor for BE-BMES, founded the MIT Center for Gynepathology Research in** the fall of 2009. The center's aim is to bring new frontiers of engineering to understand the basic biology, physiology, and pathophysiology of the female reproductive tract, in collaboration with biologists and clinicians. It also includes research efforts focused on developing new technologies for diagnosis and treatment of these diseases, and fosters liaisons with industry. A particular emphasis of the center is "biological engineering' -- fusing approaches from tissue engineering and systems biology to understand disease etiology and progression.*

Judge Invalidates Human Gene Patent

Taken from The New York Times, Published March 29, 2010 by John Schwartz and Andrew Pollack

A federal judge struck down patents on two genes linked to breast and ovarian cancer. The decision, if upheld, could throw into doubt the patents covering thousands of human genes and reshape the law of intellectual property. United States District Court Judge Robert W. Sweet invalidated seven patents related to the genes BRCA1 and BRCA2, whose mutations have been associated with cancer. The American Civil Liberties Union and the Public Patent Foundation argued that genes, products of nature, fall outside of the realm of things that can be patented, stifle research and innovation, and limit testing options.

Article continued on NYTimes.

The Next Human Genome Project: Our Microbes

Taken from Technology Review, Published May 2, 2010 by Emily Singer

Much as we might like to ignore them, microbes have colonized almost every inch of our bodies, living in our mouths, skin, lungs, and gut. Indeed, the human body has 10 times as many microbial cells as human cells. They're a vital part of our health, breaking down otherwise indigestible foods, making essential vitamins, and even shaping our immune system. Recent research suggests that microbes play a role in diseases, such as ulcers, heart disease, and obesity. While microbes make up such an intimate part of us, most of our microbial inhabitants remain a mystery. The bacteria in the human body are very difficult to study, since only about 1 percent of them can be grown in the lab. Now a proposed new project to sequence all our microbial residents could change that.

Article continued on Technology Review.

U.S. Congress Moves On Open Public Access Bill

Taken from Publishers Weekly, Published April 19, 2010 by Andrew Albanese

The U.S. Congress last week formally re-introduced the Federal Research Public Access Act of 2010 (FRPAA) in the U.S. House of Representatives, a bill that would mandate public access to publicly-funded research in the U.S. The bill would require federal agencies with annual extramural research budgets of $100 million or more to provide the public with online access to research manuscripts within six months after publication in a peer-reviewed journal.

Article continued on Publishers Weekly.

Amyris Files to go Public—Biofuels from Microbes

Taken from GreentechMedia, Published April 16, 2010 by Eric Wesoff

This synthetic biology firm, which has raised more than $244 million in private funding from notable VC firms, including Kleiner Perkins Caufield & Byers and Khosla Ventures, is looking to raise $100 million. The company, which was spun out of research conducted at UC Berkeley, feeds sugars to custom microbes which exude hydrocarbons to order which are then converted to fuels or industrial chemicals. Amyris is focusing on Brazilian sugarcane as its primary feedstock. They plan to commence commercialization starting in 2011 using contract manufacturers.

Article continued on Greentech-Media.

BE-BMES
Excellence in Biomedical Engineering Research Awards 2010

Below are abstracts from the winning reports for the 2010 Research Prize Competition! Each winner will receive $500 in cash, graciously supported by the BE Department.

Liver Tissue Engineering for the Assessment of Drug Metabolism and Toxicity — Nayoon Kim (Course 7)

The liver is responsible for metabolizing nutrients and detoxifying drugs introduced into the body, making it vulnerable to drug-induced liver injury. Hence liver cells are routinely used to study hepatotoxicity in-vitro, as part of the drug safety evaluation process. However, liver cells that are plated as 2-D monolayers on various substrates lose their specialized function rapidly in culture and sometimes may not accurately predict toxicological outcome. A possible reason could be due to the absence of the complex 3-D structure and blood flow effects and the resultant environmental cues seen in-vivo. We studied a 3-D flow-based in-vitro liver system development by the Griffith laboratory for cell survival and functionality and compared it to 2-D monolayer controls. The system consists of multiple reactor units that house scaffolds containing capillary sized channels in which cells are continuously perfused by medium. We discovered that cells seeded into the system reorganized into 3-D tissue aggregates with high survival rates and minimal variability between individual reactor wells as well as biological replicates. Cell survival and function (determined by albumin and bile acid production rates per cell) were enhanced in our 3-D system compared to 2-D monolayer controls. Because functional attributes like albumin and bile acid were much closer to the physiological levels than those in the 2-D system, we concluded that our 3-D flow-based system can

serve as an effective alternative that retains liver like properties to study drug metabolism and hepaotoxicity in humans.

Multifunctional virus-single-walled carbon nanotube complex as a platform for simultaneous targeted second window near infrared fluorescence imaging and efficient chemotherapy — Aditya Kohli (Course 20)

We report a virus-based platform for manipulating single-walled carbon nanotubes (SWNTs) in biological solutions for multimodal near-infrared (NIR) fluorescent cell-specific imaging and therapy. SWNTs are stably dispersed by major coat proteins of the M13 bacteriophage through molecular recognition and retain band-gap fluorescence in the 900 – 1350 nm wavelength range, which may allow for deep tissue imaging. Minor coat protein p3, located at the proximal tip of M13, was genetically engineered to specifically target SPARC matricellular protein, a marker overexpressed on metastatic breast and prostate tumors. The targeted virus-SWNT complex serves as a NIR imaging agent and allowed for sensitive and selective NIR imaging of cells with varying expression levels of SPARC. Controlling M13-SWNT stoichiometry allowed further functionalization of the viral major coat with a chemotherapeutic agent for targeted drug delivery in vitro. Doxorubicin (DOX) delivered by the M13-SWNT complex inhibited cell growth 400x more

efficiently than free DOX, and was restricted to SPARC expressing cells. This approach provides an 'all-in-one' platform for targeted NIR fluorescence imaging and efficient drug delivery.

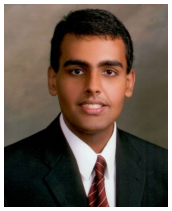
Engineering PEG hydrogel scaffolds for the development of a 3-D Hepatitis C model
Luvena Ong (Course 10)

Hepatitis C (HCV) afflicts millions of people world-wide. Unfortunately, no vaccine currently exists for HCV, and treatments are effective in less than 50% of patients. Furthermore, no small animal is natively susceptible to HCV infection. As a result, we are interested in developing an efficient in vivo model using polyethylene glycol hydrogels that encapsulate Huh 7.5 hepatoma cells. These constructs would be implanted in mice to serve as chimeric hu-

manized liver animal models. To aid in developing a stable model, we have been optimizing the infectivity and viability of the constructs in vivo and in vitro via Lenti-Fluc-Alb and Jc1-Fluc or Jc1-RFP viruses and by studying how J2-3T3 fibroblasts and RGD peptide ligands serve to stabilize Huh 7.5 cells and HCV infection over time. We found that a co-culture of Huh 7.5 and J2-3T3s with RGD stabilized the Huh 7.5 cells in vitro and in vivo; furthermore, we found increased infection with addition of the supportive factors. As a result of this work, we are continuing optimization of the constructs and probing the molecular mechanisms by which infection persists through the model in vitro and in vivo.

Effect of histone H1 on PBAE-mediated gene delivery in HepG2 cells
Jay Rajan (Course 7)

The nonviral delivery of genes to human cells is vital in developing treatments for many genetic diseases that involve the loss of gene function. One such method of nonviral gene delivery is the use of positively charged polymers called poly(ß-amino-esters), or PBAEs. PBAEs are able to penetrate the cell membrane with DNA, deliver DNA safely to the nucleus, and be degraded by the cell after the DNA is delivered. Because they are positive, PBAEs are able to combine well with negatively charged DNA to form particle complexes that can be packaged and delivered, or "transfected", into cells. Histone proteins, which naturally bind to DNA in units called nucleosomes, help keep DNA in a compact form while it remains in the cell nucleus. With respect to improving nuclear delivery of DNA, the combination of DNA with histone proteins prior to transfection has previously had success in improving the expression of luciferase. Hence, it is hypothesized that the use of histones in cell transfection by PBAE-DNA complexes can improve DNA delivery. The optimization of PBAE-mediated DNA delivery can hopefully lead to insights on developing gene therapies for many diseases, namely hemophilia. Many hemophiliacs are not able to stop bleeding when their blood vessels are ruptured by cuts or bruises, because they lack expression of a protein called Factor IX that aids in blood clot formation to stop blood flow. Through delivery of Factor IX DNA to liver cells, where the Factor IX protein is normally produced, hemophiliacs can obtain the necessary genetic material to produce functional protein and clot blood normally. Thus, extensive studies are currently being performed to find methods to model PBAEs into effective and therapeutic gene delivery vehicles.

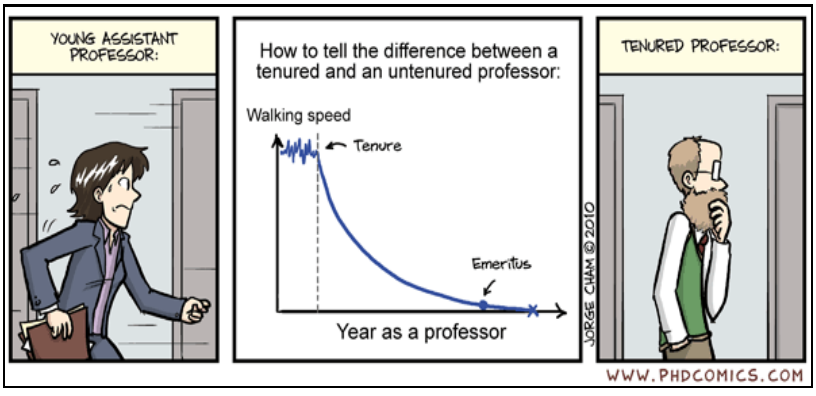


Optimizing Cell-free Expression of Bioengineered G-Protein Coupled Receptors
Deepali Ravel (Course 7)

G-protein coupled receptors (GPCRs) are involved in cell-signaling and are an integral part of many human systems. Olfactory receptors (ORs) make up the largest family of GPCRS and are crucial to behavior. Yet, much is unknown about the molecular basis of olfactory receptor-odorant binding, and, to date, no crystal structure has been obtained for these GPCRs. This lack of structural knowledge is due to the fact that olfactory receptors and other GPCRs are notoriously difficult to produce and crystallize, the first steps to obtaining a crystal structure of a protein. Using recently developed detergent-based methods, we sought to optimize production of thirteen wild-type ORs and one bioengineered OR, designated hOR17-4 T4L, in quantities and levels of stability suitable for crystallization. An Escherichia coli-based cell-free expression system was used to produce human, mouse, and rat olfactory receptor proteins. Eight non-ionic and zwitter-ionic detergents were evaluated for their ability to promote expression and maintenance of soluble protein product, which was quantified by western blotting. Circular dichroism was used for secondary structure analysis. Detergent screens showed that addition of 0.2% Brij 35 to the cell-free synthesis reaction caused a several-fold increase in soluble hOR17-4 T4L yield (amount of soluble hOR17-4 T4L produced) as well as yield of other ORs. hOR17-4 T4L monomer and dimer produced by this method migrated in SDS gel similarly to hOR17-4 T4L produced in human embryonic kidney cells. Several ORs produced in this cell-free system were shown to have correct secondary structure. We have shown that this E.coli-based cell-free expression system can be used to produce many correctly folded olfactory receptors. Our preliminary data suggest a direct relationship between olfactory receptor yield and likelihood of proper folding. Improvements to OR production methods will enable further inquiry into the structure and function of ORs, leading to a more informed development of GPCR-targeting drugs.

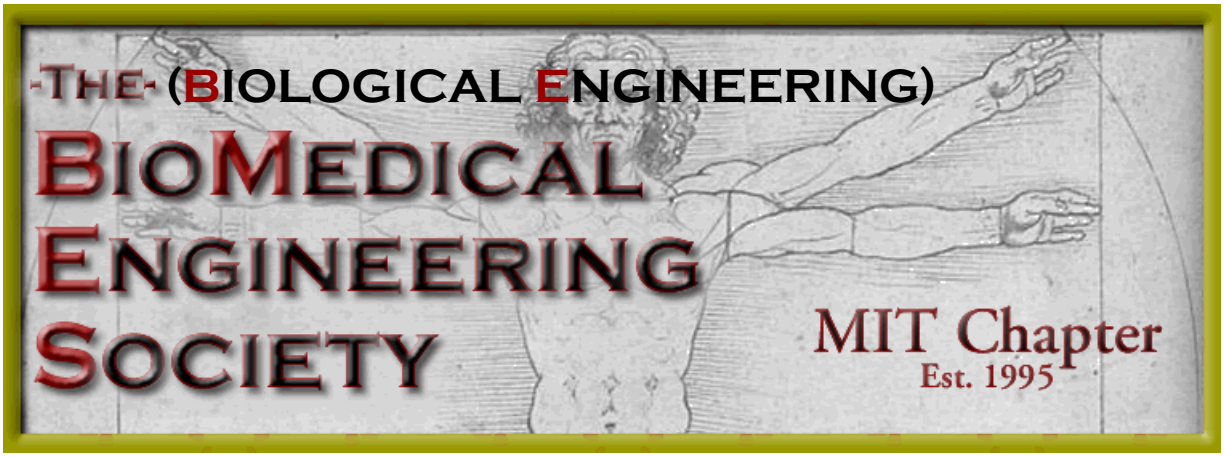
Graphic from http://www.cs.duke.edu/brd/NIH/tips/comic.jpg

Bench Humor



Graphic from PhD Comics

Graphic from offthemark.com



BE-BMES is aimed at the professional development of students pursuing the BE Major, the BME Minor, and/or similar educational interests, and serves as the nexus of communication between faculty and students regarding courses and educational programs in BE and BME. The Society welcomes students from any major with interests at the Biology/Engineering interface.

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