BME Discovery

FALL 08

The Henry Samueli School of Engineering

University of California, Irvine

Department of Biomedical Engineering

Dear Friends,

The 2008-09 academic year is upon us, and the Department of Biomedical Engineering (BME) at UC Irvine continues to develop and grow in exciting new ways. I would like to highlight just a few activities we have been involved with over the summer, as well as several new endeavors planned for the fall quarter, and encourage you to read more about our program in the following pages.

The fiscal year ended on June 30, 2008, and our extramural research expenditures were nearly $9 million over the past year. This is equivalent to $560,000 per faculty member, and is indicative of our growing and strengthening research programs amidst an ever-increasing competitive environment. Additional benchmarks for our program continue to improve as well. We currently have 85 doctoral students (5.2 doctoral students per faculty member) in the program, and conferred 16 Ph.D. degrees in the last year. Our undergraduate program has reached a steady level of approximately 500 students, and we graduated 98 bachelor's degrees this past year. Our number of undergraduate students remains strong, and we anticipate continued growth of our doctoral program commensurate with the growth of our faculty.

BME is also actively recruiting four new faculty members, which will increase the total number of faculty lines to 16.5, distributed among 20 professors. The positions include the founding director of The Edwards Lifesciences Center for Advanced Cardiovascular Technology, one associate professor, and two assistant professors. After a thorough search, we are nearing the completion of these exciting recruitment opportunities, and look forward to ultimately welcoming four faculty members to BME.

The BME Corporate Advisory Board also added four new members during the past year – Robert A. Boghosian, recently retired senior vice president of quality and regulatory affairs, Beckman Coulter, Inc., Kenneth A. Charhut, president and CEO, Orquis Medical Corporation, Palmi Einarsson, vice president, Ossur North America, and Robert E. Grant, president, Allergan Medical – who bring additional strength and insight from both large and small companies, as well regional expertise in cardiovascular, cosmetic, and analytical instrumentation industries. The advisory board now has 15 external members, and continues to play an integral role in the development of BME, particularly on the capstone design course in the undergraduate program.

Please take a few moments to learn more about BME, including our faculty profile, Assistant Professor Elliot Botvinick, additional information about our undergraduate and graduate programs, outstanding student highlights, and the upcoming seminar series schedule.

Best Regards,
Steven C. George, M.D., Ph.D.
William J. Link Professor and Chair

FACULTY PROFILE

Elliot Botvinick, Ph.D., assistant professor of biomedical engineering and surgery, is the principle investigator of the Mechanobiology Laboratory in the Beckman Laser Institute at UC Irvine, which is part of the National Institutes of Health-sponsored Laser Microbeam and Medical Program (LAMMP). The lab uses biophotonics to study mechanotransduction, biomechanics, and the role of extracellular mechanical properties in cellular physiology.

Since the lab's establishment in 2007, Botvinick's research group has grown to three Ph.D. students, two postdoctoral researchers, and several exceptional undergraduate students. Botvinick's lab has also recently been awarded additional funds to develop holographic optical tweezers for parallelization of his research methods. Most recently, Botvinick and Samueli School colleague Andrew J. Putnum, Ph.D., associate professor of biomedical engineering and chemical engineering and material science, have received funding through the National Science Foundation Biomaterials Program for their project, "Integrating Biomaterials and Biophotonics to Assess How ECM [Extracellular Matrix] Mechanics Regulate Cell Function in 3-D."

One of Botvinick's research areas is mechanotransduction by arteriolar endothelial cells. These cells measure fluid shear stress in small arteries, and signal vessel dilation in order to lower vascular resistance. There is considerable debate as to whether endothelial cells measure fluid shear stress at their apical surface via the cell membrane and the glycocalyx, or if stress is measured at the basolateral membrane via the stretching of adhesion molecules. The cells must differentiate fluid shear stress from circumferential stresses arising from pulsatile blood pressure and active dilation (or contraction) of the vessel.

Figure 1

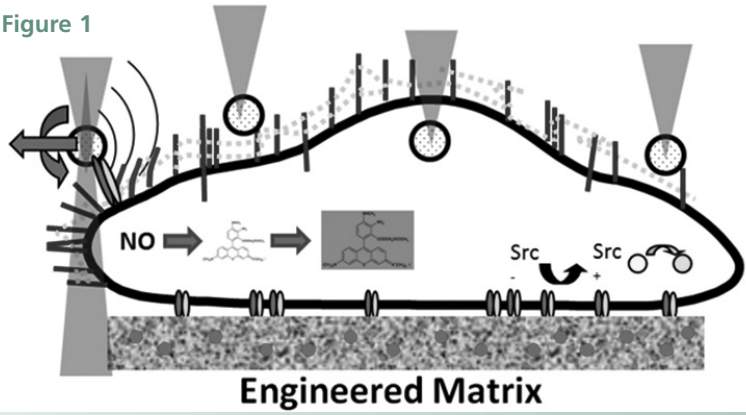


Figure 1. *Experiment Diagram. Endothelial cells are grown on protein-coated engineered polymer surfaces containing fluorescent microspheres. Cells are transfected with the Src Kinase reporter and labeled by a NO activated fluorescent indicator. Spherical crystals will be trapped and rotated by circularly polarized light, which is collected and analyzed to measure torque, particle rotation and particle fluctuation. Protein coated microspheres are attached to cells via integrin binding and pulled or twisted by laser tweezers. Confocal images of the fluorescent microspheres embedded within the engineered matrix are analyzed to measure matrix deformation and thus cell adhesion forces.*

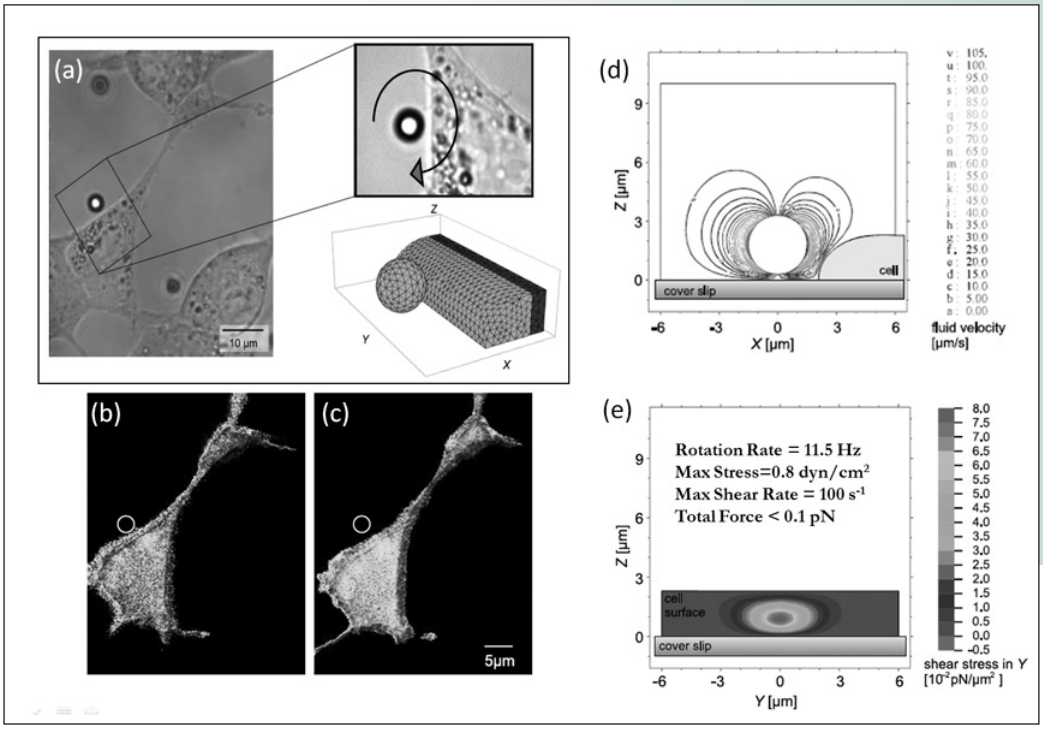
In Figure "1," vertical lines on the apical surface represent the glycocalyx, and the oval pairs at the basolateral surface represent integrin adhesion molecules. Research publications present contradictory results regarding the role of the glycocalyx in mechanotransduction, a consequence of the ubiquitous use of laminar flow chambers in studying mechanotransduction.

In a laminar flow chamber, stress at the basolateral and apical surfaces are balanced. Therefore, signaling at each surface cannot be isolated. Botvinick's research lab utilizes polarized light to apply known optical torque to home-grown, micron-sized, spherical vaterite crystals. The rotating spheres set-up laminar flow that extends a few microns from the sphere's surface. When rotating spheres are brought close to a cell, Botvinick's models predict physiological magnitude shear stress. The small area of interaction nets small forces. These forces distributed across the basolateral surface result in low- to-no detectable signaling from adhesion molecules. In this way, his lab is quantifying glycocalyx shear stress sensitivity independent of basolateral adhesion-mediated signaling.

By measuring microsphere rotation and applied torque, the lab can measure apparent viscosity, apply localized flow to a cell, and predict fluid stress at the cell surface via finite element models.

Botvinick's team is currently combining these techniques with traction force microscopy to measure the distribution of fluid stresses across the basolateral surface, and to monitor any reactionary contractility by the cell. They are also developing experimental protocols to measure the dependency of apparent viscosity on key structural components of the endothelial glycocalyx by enzymatic digestion, knock-outs, and RNAi knock down.

Figure 2. *Cell responds to localized fluid flow. (a) Brightfield image of a 3:0± 0:2 Ìm diameter vaterite sphere rotating near a cell transfected with the Src FRET biosensor. The geometrically significant region of the image is used as a template for finite element (FEM) modeling. (b) CFP/YFP Ratio image of membrane-bound Src biosensor before rotating the vaterite particle (white circle), and (c) after 16 minutes of continuous rotation. Rotation induced a slight ratio increase as well as cell migration. (d) Equi-velocity lines calculated for a sphere rotating at 11.5 Hz. Viscosity of water was assumed. (e) Front view of cell showing shear stress distribution. Stress is primarily confined to a 2 Ìm by 1 Ìm elliptical region with a total force < 0.1 pN. Crystals can rotate at rates exceeding 100 Hz yielding arterial wall-magnitude shear stress (10 dyn/cm2) on the cell. Stress also increases as the bead moves closer to the cell (not shown).*



FACULTY BRIEFLY

Michael W. Berns, Ph.D., professor of biomedical engineering, surgery and developmental and cell biology, has been elected a Fellow of the International Society of Optics and Photonics (SPIE). Berns was acknowledged for his major contributions in the field of biomedical optics, especially regarding light interactions with cells and tissues. Berns is also the co-founder of the Beckman Laser Institute and Medical Clinic at UC Irvine, which focuses on the use of light and lasers as applied to biology and disease.

Andrew J. Putnam, Ph.D., associate professor of biomedical engineering and chemical engineering and materials science, was awarded $2.1 million from the state to support a study on the effect of embryonic stem cells on heart disease. Putnam is one of 22 scientists statewide to receive a New Faculty Award from the California Institute for Regenerative Medicine (CIRM), the state agency tasked with distributing funds for stem cell research. He also received the 2008 Fariborz Maseeh Best Faculty Research Award at the Seventh Annual "California: Prosperity Through Technology" Industry Research Symposium, hosted by The Henry Samueli School of Engineering.

GRADUATE PROGRAM NEWS

The Department of Biomedical Engineering is excited to welcome the graduate student class of 2008. The graduate committee was pleased to consider a large pool of 274 applicants, with truly stellar academic records and achievements. Despite fierce competition from top biomedical engineering programs around the nation, 14 Ph.D. students and 12 M.S. degree students were accepted, all with excellent academic records.

In an effort to continuously improve our Ph.D. program, third-year students will now present results of their Ph.D. work in the course of the BME seminar series, which will not only develop their presentation skills, but also inform a broader audience about recent research conducted in BME labs.

Professor Frithjof Kruggel, M.D., now serves as the new biomedical engineering graduate advisor, following Professor Abraham Lee, Ph.D.

UNDERGRADUATE PROGRAM NEWS

On August 15, 2008, the Department learned that the undergraduate biomedical engineering program was accredited by the American Board for Engineering and Technology, Inc. (ABET), retroactive to October 1, 2006. We are one of only two accredited bioengineering or biomedical engineering degree programs in the state of California, and one of about fifty accredited programs in the United States.

ABET, founded in 1932, is a federation of professional societies that accredits university degree programs in engineering and technology. The Biomedical Engineering Society establishes program criteria for bioengineering and biomedical engineering degree programs, while ABET evaluates whether degree programs have met these standards.

Accreditation is a standard that helps to show how graduates of our biomedical engineering program are prepared to become part of the professional community of biomedical engineers. The accreditation also signals to employers that our graduates are fully prepared to begin practicing their profession. Accreditation of our degree program has been a major goal since the formation of the Department. The recognition of this milestone is a cause for celebration among faculty, staff, and students.

OUTSTANDING STUDENT HIGHLIGHTS

Aparajita Bhattarcharya, a fifth-year Ph.D. student in the Hearing and Speech Laboratory of Professor Fan-Gang Zeng, Ph.D., was recently awarded the prestigious international scholarship from the Phi Beta Kappa Alumni Association in Southern California. The Alumni Association funds and administers a scholarship program for foreign students engaged in graduate study in academic institutions in Southern California with Phi Beta Kappa chapters. The Phi Beta Kappa Alumni Association in Southern California, founded in 1918, is the largest Phi Beta Kappa alumni association in the nation.

Bhattarcharya received a B.Sc. degree in physics and a B.Tech. degree in instrumentation and electronics from Jadavpur University, Kolkata, India. She also earned a M.Tech degree in biomedical engineering from the Indian Institute of Technology, Bombay, India. Her research involves understanding and improving the speech performance of cochlear implant (CI) users in noisy conditions. Although these implants provide significant benefit in quiet listening conditions, their performance in noise is severely impeded. She is also investigating the relative importance of temporal envelope and fine structure cues to speech understanding in a noisy environment.

Justin Ducote, a fifth-year Ph.D. student in the Imaging Physics Laboratory, led by Professor Sabee Molloi, Ph.D., recently presented his research at the 50th Annual Meeting of the American Association of Physicists in Medicine July 27-31, 2008, in Houston, Texas. He is developing a method to measure the percent glandular content of a woman's breast, a quantity strongly associated with the risk of developing breast cancer. The technique makes use of dual energy X-ray imaging, where overlapping tissues can be isolated and quantified. The technique is used to separate and measure the two principle breast components, glandular and adipose tissue. His future research will focus on investigating the possibility of incorporating this method into routine screening mammography.

OUTSTANDING STUDENT HIGHLIGHTS *(continued)*

Ekaterina Kniazeva, who recently completed her second year of graduate studies working in the laboratory of Associate Professor Andrew J. Putnam, Ph.D., was recently awarded a two-year extramural fellowship from the American Heart Association to further her studies on the mechanical role of the extracellular matrix in capillary morphogenesis. She also won a best poster award at The Henry Samueli School of Engineering's Seventh Annual "California: Prosperity Through Technology" Industry Research Symposium on May 19, 2008, for her poster, "Impact of Cell-Generated Forces on 3-D Capillary Morphogenesis." Kniazeva, originally from Estonia, has a B.S. degree from Harvey Mudd College.

James "Lee" Puckett, a fifth-year M.D./Ph.D. student, was recently awarded a 2008 Brython Davis Fellowship. The fellowship is awarded to students who demonstrate outstanding past academic achievement, as well as future promise, with at least one parent who is currently, or has been, a regular member of either the United States Navy or Marine Corps. Puckett received his B.S. degree in bioengineering from the University of California, San Diego in 2002, and joined the Medical Scientist Training Program at UC Irvine in 2004. He is currently studying under the mentorship of Steven C. George M.D., Ph.D., the William J. Link chair and professor of biomedical engineering. For his doctoral thesis, Lee is investigating the relationship between exhaled nitric oxide, a non-invasive marker of pulmonary inflammation, and the clinical management of pediatric asthma. His translational clinical research is performed under the supervision of Stan P. Galant, M.D., on the Children's Hospital of Orange County's Breathmobile, a mobile asthma van that provides state-of-the-art health care to medically underserved populations in Orange County.

He has authored numerous peer reviewed publications, has presented at multiple international medical research conferences, and has received numerous awards, including the UC Irvine Basic Science Certificate of Excellence, Pathology Honor Society Award and Membership, Warren L. Bostick Award for Excellence in Clinical Pathology, and the American Society of Clinical Pathologist Award for Academic Excellence and Achievement. In 2007, he received the UCI Medal Fellowship. Following completion of his medical and doctorate education, he will pursue a medical residency position, and ultimately hopes to have a career as a professor of medicine.

Upcoming Events 2008–09

Distinguished Lecturer Series

"Biomimetic Biomaterials"
Featuring Jennifer West, Ph.D.
Rice University
Friday, November 14, 2008, 3:30 – 4:30 p.m.
Location: Natural Sciences II, Room 3201
Host: Professor Bernard Choi

"Nanotechnology Driven New Approaches for Combating Cancer"
Featuring Sadik Esener, Ph.D.
University of California, San Diego
Friday, November 21, 2008, 3:30 – 4:30 p.m.
Location: Natural Sciences II, Room 3201
Host: Professor Abraham Lee

"What are Cells "Thinking?" (And How Might We Think About This...?): A Bioengineering Approach to Understanding How Signaling Networks Govern Cell Behavior"
Featuring Doug Lauffenburger, Ph.D.
Massachusetts Institute of Technology
Friday, December 5, 2008, 3:30 – 4:30 p.m.
Location: Natural Sciences II, Room 3201
Host: Professor Andrew Putnam
Co-Sponsor: Center for Complex Biological Systems, UC Irvine

"Molecular Engineering and Regulation of Synaptic Function in Dendrites"
Featuring David Meaney, Ph.D.
University of Pennsylvania
Friday, January 23, 2009, 3:30 – 4:30 p.m.
Location: Natural Sciences II, Room 3201
Host: Professor Zoran Nenadic

"Mechanical Properties of Actin Stress Fibers in Living Cells"
Featuring Frank Yin, M.D., Ph.D.
Washington University, St. Louis
Friday, February 13, 2009, 3:30 – 4:30 p.m.
Location: Natural Sciences II, Room 3201
Host: Professor Bruce Tromberg

"The Cutting Edge of Soft Tissue Wound Healing"
Featuring David Hom, M.D., F.A.C.S.
University of Cincinnati
Friday, February 27, 2009, 3:30 – 4:30 p.m.
Location: Natural Sciences II, Room 3201
Host: Professor Brian Wong

"Science and Technology Discovery to Meet Global Health Needs"
Featuring Carol A. Dahl, Ph.D.
The Bill and Melinda Gates Foundation
Friday, March 6, 2009, 3:30 – 4:30 p.m.
Location: Natural Sciences II, Room 3201
Host: Professor Abraham Lee

"Functional and Molecular Imaging of Articular Cartilage: Toward a New Medical Paradigm for Osteoarthritis"
Featuring Martha L. Gray, Ph.D.
Harvard-MIT Health Sciences and Technology
Massachusetts Institute of Technology
Friday, April 3, 2009, 3:30 – 4:30 p.m.
Location: Natural Sciences II, Room 3201
Host: Professor Bruce Tromberg

"Functional Neuroimaging: Translating Basic Research to Clinical Application"
Featuring Kristina Ropella, Ph.D.
Marquette University
Friday, May 8, 2009, 3:30 – 4:30 p.m.
Location: Natural Sciences II, Room 3201
Host: Professor Steven George

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University of California, Irvine
The Henry Samueli School of Engineering
Department of Biomedical Engineering
3120 Natural Sciences II
Irvine, CA 92697-2715

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