BME Discovery

SPRING 09

The Henry Samueli School of Engineering

University of California, Irvine

Department of Biomedical Engineering

Dear Friends,

The 2008-09 academic year is nearly complete, and we are encouraged by the continual growth and development of our educational and training programs. I would like to describe just a few exciting examples of news in our Department, and encourage you to read more about our program in the following pages.

This past year we hired new Assistant Professor Elliot Hui. Dr. Hui completed his doctoral work in electrical engineering at the University of California, Berkeley, and then completed postdoctoral work with Dr. Sangeeta Bhatia at MIT. Dr. Hui's research program focused on the use of Micro-Electro-Mechanical Systems (MEMS) to investigate biological problems, most notably cell-cell interaction and communication to better understand liver physiology and oncogenesis. We look forward to Dr. Hui's contributions to our research and educational mission.

In January, the 4,000-square-foot Bio-Organic Nanofabrication (BiON) facility in the California Institute for Telecommunications and Information Technology building opened, providing a tremendous resource for our program emphasis in BioMEMS (biomedical MEMS). The facility is a shared resource for faculty and other researchers developing devices that focus on organic systems, in particular biological systems.

We are actively recruiting four new faculty members, which will bring our total number of faculty lines to 17.5, distributed among 21 faculty members. The positions include the founding director of The Edwards Lifesciences Center for Advanced Cardiovascular Technology, an associate professor, and two assistant professors. The searches have been very dynamic over the past year, and we are close to filling these open positions.

Our BME Corporate Advisory Board, together with our undergraduate students in the Biomedical Engineering Society, planned the second annual Biomedical Engineering Industry Night, where representatives from local biomedical device companies interacted with students seeking summer internships and full-time employment. The event featured eleven companies and nearly 100 students participated.

I invite you to learn more about these events and additional stories in this issue, including our faculty profile featuring Dr. Bernard Choi, BME Industry Night, outstanding student highlights, academic news, and information about upcoming BME events.

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

FACULTY PROFILE

Bernad Choi, Ph.D., assistant professor of biomedical engineering in the Beckman Laser Institute and Medical Clinic, primarily focuses his research efforts in the following areas: the biological response to selective microvascular injury caused by light-based protocols, and non-invasive microvascular imaging methods for clinical application.

Understanding the microvascular response to light-based therapy is in its infancy. Much of what is known about the response is derived from computational modeling of tissue optics and short-term (less than 24 hours) monitoring of the microvasculature. Recently, Choi's lab has demonstrated that the chronic microvascular response to light-based injury can differ substantially from that predicted with modeling or from short-term in vivo experiments. Specifically, they have observed a robust microvascular repair process, resulting in a stronger resiliency of the microvascular network to light-based therapy than previously predicted.

The key questions Choi is analyzing include the underlying biological processes of the microvascular remodeling process, and how can they modulate this remodeling process. To address these issues, Choi and his research colleagues are:

- Studying metabolic and biochemical dynamics associated with various regimes of selective microvascular injury achieved with phototherapies.
- Evaluating the translational potential of novel combination therapeutic protocols.

To achieve these aims, Choi's lab has developed laser speckle imaging (LSI) to characterize blood flow dynamics in a microvascular network animal model, with high spatial and temporal resolution (Figure 1). With funding from the National Institutes of Health, they are working with other researchers at the Beckman Laser Institute to develop an integrated, wide-field functional imaging (WiFI) platform to perform quantitative, depth-resolved characterization of tissue metabolism during disease progression and therapeutic intervention.

Choi also conducts research in optical clearing. Functional optical characterization of disease is well-suited for study of specific animal preparations, such as a rodent dorsal window chamber model. However, such characterization of subsurface processes suffers from loss of spatial resolution and imaging depth due to the blurring effects of optical scattering, impacting the ability of researchers to both localize and quantify molecular and cellular processes.

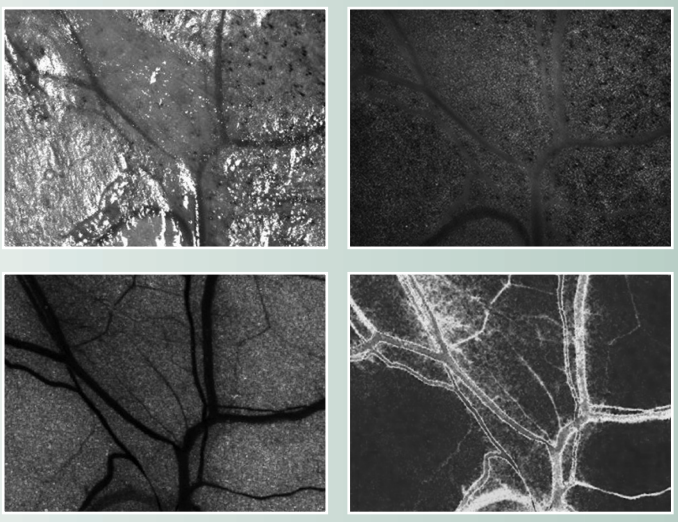


Figure 1 - Laser speckle imaging (LSI) of blood flow dynamics.

LSI permits non-invasive, wide-field imaging of blood flow dynamics, with high spatial (tens of mm) and temporal (ms scale) resolution. (Reflectance Image) With standard lamp illumination, the microvascular architecture is visible, but the degree of blood flow in each vessel is unknown. (Raw Speckle Image) With laser excitation, a grainy pattern is observed. The speckle pattern is blurred by light collected from moving red blood cells. (Speckle Contrast Image) With use of a convolution filter, we obtain a high-contrast blood flow map. The darker the pixel intensity, the higher the flow. (Speckle Flow Index Map) With assumptions made on the distribution of flow velocities, we compute a blood flow map. We use LSI as a research and clinical tool to study the microvascular response to therapy, in preclinical and clinical studies.

Choi is exploring how to improve the accuracy and precision of quantitative visualization of subsurface molecular and cellular processes, and how to improve clinical monitoring of hemodynamic parameters. To tackle these topics, Choi and his research colleagues are:

- Studying the efficacy and safety of a chemical-based method known as optical clearing (Figure 2), to improve visualization and quantitative accuracy of biomarkers related to subsurface tissue characteristics in vitro and in vivo.

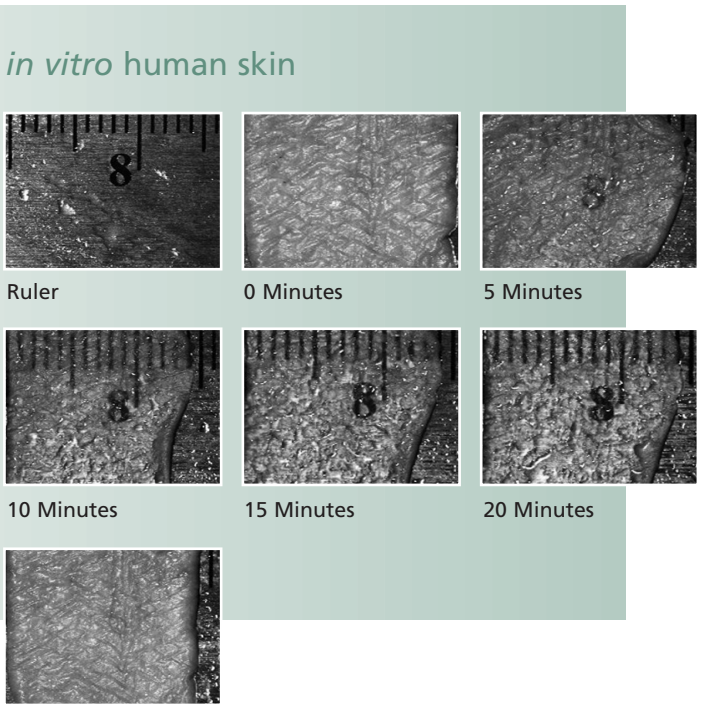
- Developing practical, user-friendly instrumentation to provide clinical personnel with real-time diagnostic information to guide ensuing decisions regarding treatment planning.

Collectively, this research is expected to contribute to the fields of biophotonics, dermatology, neurobiology, cancer therapy, ophthalmology, vascular biology, wound healing, and drug discovery.

Choi received a B.S. degree from Northwestern University, and M.S. and Ph.D. degrees in biomedical engineering from the University of Texas at Austin.

Figure 2 - Representative example of optical clearing for enhanced optical imaging.

Visualization of an opaque metal ruler that was placed underneath human skin samples immersed in glycerol for different periods of time demonstrates the dynamic and dramatic changes in skin transparency. Within 10 minutes of immersion in glycerol, scale marks on the opaque metal ruler underneath the skin were easily discernible. (Bottom Row) To demonstrate the reversible nature of optical clearing, the sample was then placed in phosphate-buffered saline for 20 minutes, after which scattering of the sample returned.



FACULTY BRIEFLY

Bernard Choi, Ph.D., assistant professor of biomedical engineering and the Beckman Laser Institute, was recently selected as the Biomedical Engineering Professor of the Year by the Engineering Student Council (ESC) at the annual National Engineers Week Awards Banquet.

Abraham Lee, Ph.D., professor of biomedical engineering and mechanical and aerospace engineering, and director of the Micro/Nano Fluidics Fundamentals Focus (MF3) Center, recently received two grants for his research in targeted drug delivery vehicles and cell-sorting technology.

The National Institutes of Health awarded Lee and co-investigator Paul Dayton, Ph.D., associate professor in the Joint Department of Biomedical Engineering at the University of North Carolina at Chapel Hill and North Carolina State University, a grant to further research the precision engineering of ultrasonically-targeted drug delivery vehicles. Lee and co-investigator Lisa Flanagan, Ph.D., a research scientist in the UC Irvine department of pathology, were also awarded a California Institute for Regenerative Medicine Technology and Tools grant to develop a device to sort stem cells by distinguishing their electrical properties.

Zoran Nenadic, D.Sc., assistant professor of biomedical engineering, in collaboration with An Do, M.D., neurology resident physician, and Luis Chui, M.D., clinical professor of neurology, received a $75,000 grant from the Roman Reed Spinal Cord Injury Research Fund of California to develop a brain-computer interface controlled walking simulator.

Announcing **New Faculty**

Elliot Hui, Ph.D., joined the Department of Biomedical Engineering as assistant professor in September 2008. His research interests primarily focus on the use of microtechnology to solve problems in biology and human health. For example, his lab is developing tools for constructing and manipulating biological tissue at a cellular level in order to study how cells communicate with each other. His group is also pursuing non-electronic control systems to drive low-cost, miniaturized devices for global health diagnostics.

BME Industry Night

Nearly 100 students attended this year's Biomedical Engineering Industry Night on March 5, 2009. BME Industry Night, a collaborative effort between the Biomedical Engineering Society (BMES) student chapter and the BME Department, provided an opportunity for leading biomedical industry representatives to meet undergraduate and graduate biomedical engineering students from a top-tier public university, and to recruit for internships and full-time employment within their company. Students had the chance to speak one-on-one with representatives from 11 leading biomedical companies, including:

Abbott Medical Optics, Inc.
Allergan, Inc.
Bausch & Lomb Inc.
Edwards Lifesciences LLC
Ignite Health
Medtronic, Inc.
Orqis Medical Corporation
RAH Consulting Group, Inc.
Scholler Scientific Corporation
Straddling, Yocca, Carlson & Rauth
Versant Ventures

The UC Irvine BMES student chapter's mission is to create awareness among the campus community and other engineering students about the biomedical engineering field. This chapter also serves to promote the biomedical engineering profession by providing their members with resources and networks for professional development. One of their most important efforts is building relationships with local biomedical engineering companies, and connecting their members with career opportunities.

BMES would like to express sincere thanks to all of the participating companies for their support of the program and BME's outstanding students.

OUTSTANDING STUDENT HIGHLIGHTS

So Hyun "Sophie" Chung is a Ph.D. candidate in biomedical engineering conducting research in the Beckman Laser Institute (BLI) under the supervision of Professor Bruce J. Tromberg, Ph.D. Chung received her M.S. degree in biomedical engineering from Seoul National University in 2004 and B.S. degree in electronics engineering from Ewha Woman's University in 2002. She served as the president (co-chair) of the engineering student council in both undergraduate and graduate schools.

Her research focuses on breast cancer detection and treatment monitoring using a non-invasive optical imaging technology, Diffuse Optical Spectroscopic Imaging. In her recently published paper, she measured tissue water state (bound/free) in breast cancer tissues non-invasively, and found that histopathological tumor grades have a high correlation with the tissue water state. Her research includes clinical breast cancer studies and validation studies by comparing optical imaging to MRI.

The originality and potential of her research was recognized with a "Susan G. Komen for the Cure – AACR Scholar-in-Training Award," and a "Newport Spectra-Physics Research Excellence Award." She was also awarded a "Chancellor's Club for Excellence Fellowship" that is intended to recognize and reward UC Irvine's most academically superior doctoral students who exhibit outstanding promise as scholars, researchers, and public leaders.

Samuel A. Danziger's primary research focuses on improving the accuracy and effectiveness of computational machine learning systems using computer models and in silico predictions applied to in vivo and in vitro experimentation for biomedical projects. Specifically, he developed novel computational active learning methods in conjunction with homology modeling and feature extraction techniques for the p53 cancer rescue mutant problem.

A prominent protein in the human cancer prevention pathway, p53 is encoded by the TP53 gene. Certain p53 cancer mutants regularly occur in human tumors and are inactive in biological assays. When some p53 cancer mutants are given additional

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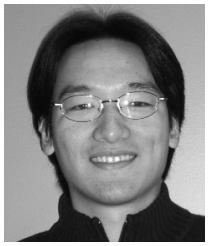
OUTSTANDING STUDENT HIGHLIGHTS *(continued)*

second site rescue mutations, the p53 is reactivated. It is theorized that understanding the p53 rescue mechanism can aid in the design of small molecule drugs that mimic the rescue effect. Danziger used his initial in silico predictions to find p53 rescue mutants that are active in vivo and in vitro, and to predict the behavior of those mutants with up to 77 percent accuracy. Danziger also expressed mutant p53 in yeast, and developed software to aid in the design of mutant oligonucleotides and primers.

Danziger's subsequent research developed novel active learning strategies for rapidly and efficiently building an accurate classifier using the fewest number of expensive data points. His most recent research developed a novel active learning strategy specialized to find positive examples quickly. The p53 prediction algorithms were extended to detect cancer rescue hot-spot domains with proficiency similar to that of an expert biologist. These algorithms found p53 cancer rescue mutants in silico 44 percent faster than regular active learning, and rescued for the first time the previously unrescuable cancer mutant P152L.



Yu-Hsiang (Shawn) Hsu, a doctoral student in the Microbiomechanics Laboratory directed by Professor William C. Tang, Ph.D., is currently working on a project in the Micro/Nano Fluidics Fundamentals Focus (MF3) Center, funded by the Defense Advanced Research Projects Agency (DARPA), industry, and university support. This project aims to demonstrate a lab-on-a-chip micro-instrument for rapid disease diagnosis, including identification of cancer cells and infection-induced cell abnormalities. This microfluidic platform offers a potentially rapid and cost-effective alternative to conventional tools in biology and clinical laboratories for studying the biomechanics of cells. By applying the concept of smart structure with thin-film piezoelectric transducers and integrating into a microfluidic bioreactor array, the mechanical characteristics and behaviors of adherent cells can be studied in a massively parallel approach. By focusing on the detection of cell-traction-modulated electro-mechanical signals, the concept of using the mechanical characteristics of cells to perform disease diagnosis can be put into practice.

Hsu presented his work during an oral session in the International Conference on Adaptive Structure and Technologies (ICAST) held in Ascona, Switzerland on Oct. 6 – 9, 2008. ICAST is an important international conference that gathers worldwide leading scientific researchers and engineers to discuss the latest progress and applications of the highly interdisciplinary field of smart materials and structures. His paper was selected for one of the five Best Student Contribution Awards to recognize the quality, importance, and originality of his research.

Hsu, originally from Taiwan, received B.S. and M.S. degrees from the National Taiwan University in Taiwan, and is currently a Ph.D. student in the Department of Biomedical Engineering. Hsu has been involved in research topics related to the design of flexible structure control, smart structures, sensors and actuators, piezoelectric transformers, the developments of MEMS-based piezoelectric transducers, bioreactors and acoustic micro-mixers, and studies of cell mechanics and bio-electro-mechanical coupled systems, etc.

ACADEMIC NEWS

In an effort to advance the curriculum of the M.S. degree program, all future students are required to conduct a focused research project leading to a thesis to emphasize a better balance between theoretical and practical education. A thesis project may be conducted via an internship in the biomedical industry, supervised by a faculty member.

The 2008-09 academic year also brought changes to the undergraduate curriculum. Students will no longer receive credit for the first physics course taken by incoming freshmen, which allowes the BME Department to expand the biomechanics sequence to encompass three quarters. The first two quarters cover statics and dynamics, providing the background for the third quarter, which covers the biomechanics of cells, blood flow and the circulatory system, interstitial flow, the eye, and muscles and the skeletal system.

Upcoming Events 2009

Biomedical Engineering Society 2009 Annual Fall Meeting
"Bridging the Three Rivers of Biology, Engineering and Medicine"
October 7-10, 2009
Hosted by the University of Pittsburgh and Carnegie Mellon University
Location: David Lawrence Convention Center, Pittsburgh, PA
http://www.bmes.org/

"Functional Neuroimaging: Translating Basic Research to Clinical Application"
BME Distinguished Lecturer Series
Featuring Kristina Ropella, Ph.D.
Marquette University
Friday, October 23, 2009, 3:30 - 4:30 p.m.
Location: Natural Sciences II, Room 3201
Host: Professor Steven George

The Fourth Laboratory for Fluorescence Dynamics Workshop in Advanced Fluorescence Imaging and Dynamics
Laboratory for Fluorescence Dynamics
UC Irvine Department of Biomedical Engineering
October 26-30, 2009
For more information, please visit
http://www.lfd.uci.edu/workshop/

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