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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BME Discovery

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SAMUELI SCHOOL OF ENGINEERING · UNIVERSITY of CALIFORNIA · IRVINE | Department of Biomedical Engineering

Elliot Hui Receives DARPA Young Faculty Award

Assistant Professor **Elliot Hui** received a DARPA Young Faculty Award (YFA) in May 2013, worth $425,000 over two years. His proposal is titled "Directed Evolution of Phytochrome Absorption Spectra for Multichannel Optogenetic Cellular Interfaces."

"We plan to create a set of proteins that will be able to activate different cellular functions in response to specific wavelengths of light," says Hui. "Starting with the proteins that are used by plants to steer themselves toward sunlight, we want to harness evolution to create a set of modified proteins that are sensitive to different colors of light. Ultimately, we hope to use light to accomplish tasks such as steering cell migration or patterning the differentiation of stem cells."

The DARPA Young Faculty Award program aims to identify and engage rising stars in junior faculty positions in academia and equivalent positions at non-profit research institutions and expose them to Department of Defense (DoD) and National Security challenges and needs. In particular, the YFA provides high-impact funding to elite researchers early in their careers to help them develop innovative new research directions in the context of enabling transformative DoD capabilities. The program's long term goal is to develop the next generation of scientists and engineers in the research community who will focus a significant portion of their future careers on DoD and National Security issues.

Hui received a bachelor's degree in physics from MIT and a doctorate in electrical engineering from UC Berkeley. Following his doctoral work in microelectromechanical systems (MEMS) under Roger Howe, he trained as an NIH Kirschstein fellow in the laboratory of Sangeeta Bhatia at MIT, where he developed MEMS tools to probe cell-cell interactions in the liver. In 2008, he joined the UC Irvine faculty. His research group employs tools such as MEMS, microfluidics, and optogenetics to control biological systems dynamically at the microscale. His interests include tumor progression and stem cell differentiation as well as point-of-care diagnostics. He is a member of the Center for Complex Biological Systems, the Edwards Lifesciences Center for Advanced Cardiovascular Technology, and the Chao Family Comprehensive Cancer Center.

Bernard Choi Receives Grant from NIH

The National Institute of Dental and Craniofacial Research awarded Associate Professor **Bernard Choi** a three-year R01 research grant to develop a device that will enable dentists and endodontists to assess the health of the pulpal chamber within teeth. A reliable device is expected to reduce the number of unnecessary root canal procedures performed after traumatic injury. The project involves translation of the laser speckle imaging technology under development in Choi's laboratory, to evaluation in the clinics of Drs. Petra Wilder-Smith (co-PI) and Jan O'Dell. The proposed research is expected to develop a simple, low-cost, quick method that enables dentists and endodontists finally to accurately assess pulpal health status.

Choi has been named the Samueli School of Engineering Honoree for Excellence in Undergraduate Education (2013), and for the third time over the last five years, he has been selected by the Engineering Student Council as Biomedical Engineering Faculty of the Year (2012- 2013).

OUTSTANDING STUDENT HIGHLIGHTS

Tim Smith Earns NSF Graduate Research Fellowship

Tim Smith, biomedical engineering doctoral student is one of five UC Irvine engineering graduate students who won the highly competitive NSF Graduate Research Fellowship. Smith studies ways to reduce the inflammatory response to implanted materials in Assistant Professor **Wendy Liu**'s laboratory.

The highly competitive NSF Graduate Research Fellowship Program (GRFP) recognizes and supports outstanding graduate students in science, technology, engineering and mathematics who are pursuing research-based master's and doctoral degrees at accredited U.S. institutions. NSF received more than 13,000 applications for the 2013 competition and made 2,000 award offers. Fellows receive a three-year annual stipend, opportunities for international research and professional development.

Hamed Alavi Awarded Seed Grant from Edwards Lifesciences

Graduate student **Hamed Alavi** has been awarded a seed grant from Edwards Lifesciences to continue his research on development and testing of our hybrid tissue-engineered heart valve at KLAB. This project addresses the efforts to complete the proof of concept of the first patient-specific heart valve prostheses with lifelong durability, enhanced biocompatibility, and self-regenerating capacity. The patient-specific heart valve is designed to be a living implant with the capacity to self-regenerate and the potential to last a lifetime, similar to a native heart valve. Rather than being a device that palliates a disease, it promises to be curative; a living replacement for a diseased component of our physiology.

Michelle Sangalang Wins Statewide Business Plan Competition for Youth

Biomedical engineering student **Michelle Sangalang** credits her senior design classes for helping her win a statewide business plan competition. She and her partner Andrew Ekelem, a UC Berkeley bioengineer alumnus, brought home the grand prize of $5,000 in their age category (18 to 27 year olds) in the Youth Entrepreneurship Program's Boost Business Plan Competition. Sangalang and Ekelem attended high school together. Their business is called Chariot Mobility, and its focus is to make the best in-class customized manual wheelchair that uses an advanced propulsion system and materials. They are creating the first manual wheelchair to be maneuvered solely from a lever system.

"Our primary goal is to provide a chair that sustains the user's health better than the traditional wheelchairs," says Sangalang. "Our patent-pending lever system improves the stability of the wrist and shoulder, and enables the user to propel more efficiently than current push-rim wheelchairs. Ergonomic propulsion reduces the occurrence of repetitive strain injury, improving the quality of life for wheelchair users."

Ekelem, a paraplegic, came up with the idea and turned to Sangalang for help in making it happen. "My senior design classes and the entrepreneurship class led by Goran Matijasevic stimulated my interest in the business side of technology," says Sangalang. "I learned about the intricacies of bringing a product to market, and about the business plan competition."

BME Students Achieve a Strong Showing at Merage Business Plan Competition

Biomedical engineering students put their entrepreneurial skills on the line in the 2013 Business Plan Competition at UC Irvine's Paul Merage School of Business. The Merage Business Plan Competition offers UCI students, staff and researchers the opportunity to form a team, create a business plan and potentially fund their business idea, all within seven months. Nineteen teams competed in the final leg of this year's competition with four of the winning teams including one or more BME student.

SAVE THE DATE

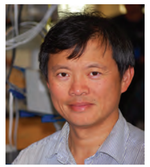
The UC Irvine Samueli School Department of Biomedical Engineering will proudly host the
15th annual UC Systemwide Bioengineering Symposium
June 18-20, 2014

The symposium provides a forum for collaboration and networking among bioengineering faculty, students and researchers at the 10 University of California campuses.

Bioengineering Institute of California, visit bic.ucop.edu

BME Discovery

"Inspiring **Engineering Minds** to Advance **Human Health**"



Dear Friends of BME,

Greetings from Irvine! As I begin my fourth year as department chair, I am reminded of the special opportunity we have as biomedical engineers for improving peoples' lives today and for generations to come. Located in the heart of Orange County (between Los Angeles and San Diego counties), UC Irvine is home to more than 300 biomedical companies and several major medical centers. The pillars are in place for UCI to become an engine of innovation for biomedical devices and biotechnology. In fact, this fall we are launching the first professional master's program under the BioENGINE acronym (ENGINE stands for Engineering, Innovation, and Entrepreneurship). This first class will be part of the Master of Science in Engineering Management program. In the next few years, we anticipate broadening BioENGINE to include two additional degree programs in engineering innovation and clinical translation. It is our mission to educate and inspire students who have the innovative engineering skills, the business and management know-how, and the strong desire to create products that transform medicine.

As a BME department, it is easy to focus on the technical aspects of new biomedical advancements and lose sight of the ultimate motivation of helping people and improving lives. The purpose of our existence is to advance human health. This all begins with a focus on people – students, staff, faculty, friends in the community, and people of all walks of life who we would like to touch. This newsletter is about the people we cherish at UCI, their stories, their aspirations, their visions, and their accomplishments.

This year, the BME team adds three new faculty members and a department manager. We welcome Cathy Ta as department manager. She hails from the UCI School of Medicine (SOM) and has been instrumental in making the Department of Otolaryngology one of the most innovative and financially healthy departments on campus. Cathy will play a key role in the BME department's increasingly critical relationship with SOM in medical education and clinical research. In January, Chang Liu joined BME as an assistant professor and the 20th core faculty member. Professor Liu's research focuses on the engineering of genetic systems and the rapidly advancing field of synthetic biology. In July and September, new assistant professors Michelle Digman and Beth Lopour joined as the 21st and 22nd core faculty members. More detailed introductions will be provided in the next newsletter (spring 2014).

I'm pleased to report that BME students are proving to be naturally gifted entrepreneurs. In the 2013 Merage Business Plan Competition, BME students were key members on the first, second, and third place teams, each which received a substantial cash prize by the corporate sponsors. Even the undergraduate division winning team had three BME students on the eight-person team. Furthermore, BME student Michelle Sangalang was on a two-person team that won a statewide Business Plan Competition for Youth. With all this buzz and excitement, we just might be witnessing the birth of a "Medical Device Coast," with UCI being the center hub of innovation.

Also this year, we partnered with UCI's Public Health Program and Angel Heart International, to provide three BME senior design teams the chance to witness firsthand the challenges of delivering healthcare in resource poor settings of developing nations. Three teams were selected for overseas expeditions (Peru, Thailand-Myanmar, China). The students came back inspired to make a difference in global health. Visit the Samueli School's YouTube channel to see a documentary (search for Thailand-Myanmar Malaria Project), that takes viewers through the touching and gut-wrenching journey of one of these teams.

On the research front, BME faculty are bucking the national trend of funding uncertainties by garnering awards and grants at a record pace. Most noteworthy, Assistant Professor Elliot Hui was awarded the DARPA Young Faculty Award to use specific frequencies of light to activate cellular functions. Professor Lisa Flanagan was awarded the prestigious NSF CAREER Award. Professor Bernard Choi received a major NIH RO1 grant to develop a device that would help endodontists reduce the number of unnecessary root canal procedures, a prevalent problem, which this proposed research could have a major impact on. And finally, a trio of BME professors was awarded over $2M to create novel diabetes treatments.

I welcome you to read about these and many more of our accomplishments in this newsletter and on our website, www.eng.uci.edu/dept/bme.

Sincerely,
Abe Lee, *William J. Link Professor and Chair, BME at UCI*

FACULTY HIGHLIGHTS

Researchers Awarded $2.27 Million to Create Novel Diabetes Treatments

Two UC Irvine research groups have received $2.27 million from the JDRF to develop innovative methods of treating and possibly curing Type 1 diabetes.

The JDRF, formerly the Juvenile Diabetes Research Foundation, awarded one grant to Jonathan Lakey, associate professor of surgery and biomedical engineering, and Elliot Botvinick, assistant professor of surgery and biomedical engineering; and another to Weian Zhao, assistant professor of pharmaceutical sciences and biomedical engineering. Lakey and Zhao are affiliated with the Sue and Bill Gross Stem Cell Research Center.

With $1.27 million in funding over three years, Lakey and Botvinick will try to find a way to successfully transplant encapsulated, stem cell-created pancreatic islets. In Type 1 diabetes, the pancreas cannot produce insulin – a hormone key to regulating carbohydrate and fat metabolism in the body – making daily insulin treatments necessary.

In a previous study, Lakey helped show that transplanted encapsulated islets can create and secrete insulin. A major hurdle, though, is overcoming immune-system rejection of these transplanted islets.

The Lakey-Botvinick team – which includes researchers and products from UCI, the University of Oxford, the Netherlands' University of Groningen, Eastern Virginia Medical School, Islet Sheet Medical in San Francisco, Islet Sciences in New York and Danish pharmaceutical company Novo Nordisk – will explore the use of isolated islets in which the cells are encased in an ultrapure algae membrane.

The encapsulation chemistry allows for selective permeability, meaning that some small molecules, such as glucose and insulin, can pass across the barrier, while large antibodies and immunological molecules are blocked from entering into the space containing the islets.

"Perhaps the greatest challenge in the field of islet transplantation is to make the metabolic benefits available to patients with Type 1 diabetes without the need for chronic immunosuppression," says Lakey, who's also director of UCI's Health's Clinical Islet Program. "I believe that this technology has great promise for realizing our goal. And this welcome support from the JDRF should speed our progress."

With the other grant, Zhao and his colleagues will try to develop an insulin sensor for the JDRF's Artificial Pancreas Project, which supports the creation of an automated system to dispense insulin based on real-time changes in blood sugar levels. Central to such a device is a mechanism that can accurately determine blood insulin amounts to provide feedback control for the artificial pancreas.

Existing systems deliver insulin via a pump under closed-loop control, using data from a continuous glucose sensor. They are, however, associated with severe risks – especially insulin overdose – when any of their components malfunction.

Zhao will receive $1 million for the two-year effort, with the potential for further funding if his team comes up with a promising model. "Integrating a real-time insulin sensor into the artificial pancreas system will allow us to precisely monitor and control the levels of both sugar and insulin, ultimately leading to safe and effective management of diabetes," he says.

New Assistant Professor Chang Liu Brings Synthetic Biology Expertise to UCI

Chang Liu was hired as an assistant professor in BME in January by the Center for Complex Biological Systems. Professor Liu received his bachelor's degree in chemistry with highest honors, summa cum laude at Harvard University, and his doctorate in chemistry at the Scripps Research Institute. He was most recently a Miller Fellow at the Miller Institute for Basic Research in Science at UC Berkeley.

Professor Liu's research focuses on the engineering of genetic systems. His doctoral work focused on expanded genetic codes and their use to evolve proteins, including anti-HIV antibodies, containing novel unnatural amino acids. In the natural genetic code, 20 amino acids are used, each assigned to a three-base sequence of DNA called a codon. Genetic engineering has allowed codons to be reassigned to specify new, unnatural amino acids and thus create completely new biological functionality. Liu was successful in the genetic encoding of sulfotyrosine in E. coli, which enabled a new avenue to study this common posttranslational modification. Furthermore, Liu leveraged his expanded genetic codes to ask the question of whether additional amino acids could provide a selective advantage in protein evolution. He found that by utilizing sulfotyrosine and other unnatural amino acids, he could generate stronger antibodies against HIV and other disease targets. This work is described in first-author papers published in leading journals such as *Nature Biotechnology, PNAS, JACS,* and *Annual Reviews of Biochemistry*. During his postdoctoral training, Liu expanded his expertise into the field of synthetic biology. Specifically, he exploited regulatory leader peptides to control gene expression in a programmable way, allowing cells to respond to environmental stimuli based on Boolean logic operations and higher-order functional relationships. This work has been published as first-author papers in *Nature Biotechnology* and *Nature Methods*, with additional papers to come.

Looking forward, Liu is aiming to improve the process of directed evolution, in which we harness the power of natural selection to create genes and proteins with characteristics that are defined by the scientist, rather than nature. Currently, this is a slow process because mutations must be introduced slowly, or else the genome of the host cell becomes compromised too quickly. Liu's vision is to create an orthogonal genetic system. That is, the host cell will still have its own natural DNA and its own genetic machinery for duplicating and reading its genome; this natural genetic machinery will function with a low error rate, keeping the host cells healthy. At the same time, Liu will introduce a separate genetic system with completely new replication machinery. The two sets of genetic machinery will be separate and will not replicate each other. Thus, the second set of genetic machinery can be engineered to replicate genes using a high error rate, allowing for very rapid evolution of desired genes while protecting the integrity of the natural host genome. This will represent a seminal advancement and transform directed evolution into a much more powerful tool than it is currently.

Liu will provide the BME department with a formidable foothold in the burgeoning field of synthetic biology. Over the past five to 10 years, a number of leading research institutions have begun investing resources into developing programs in synthetic biology. Liu's unique expertise will make him a powerful collaborator not only within the department, but also cross-departmentally through the Center for Complex Biological Systems.

Students Travel Overseas for Firsthand Experience

Twelve senior biomedical engineering students got the experience of a lifetime this past spring when they were selected for international expeditions that provided a firsthand understanding of medical care delivery in resource-poor settings of developing nations.

A six-person team traveled to Lanzhou, China, to work with the families of underprivileged pediatric patients who were in need of heart surgery. A two-person team visited HIV/STD patients at clinics serving the gay/transgender sex worker population in Lima, Peru. And a four-person team journeyed to the Thailand-Myanmar border to witness the frontline of the malaria battleground.

The overseas trips, funded by a $25,000 gift from Edwards Lifesciences, were part of a larger effort to enhance the senior capstone design course.

"Industry folks were telling us that our students were good on theory and technical expertise but needed more hands on experience and people skills," says **William Tang**, professor of biomedical engineering and associate dean for research, who led the effort to implement new ideas to the design course in response to industry representatives' comments.

The international trips were an opportunity for students to put their teamwork and leadership skills to the test, providing genuine care and help to people in disparate need. The department partnered with UC Irvine's Public Health Program for the trips to Peru and Thailand, and with Angel Heart International for the trip to China.

Reaz Rahman went on the Thailand-Myanmar trip and his senior project was a portable and low-cost malaria diagnostic platform that proposes diagnosing malaria with a saliva sample instead of blood from a finger prick.

"The experience I gained from doing field research on malaria is unlike any education I have ever received," says Rahman. "It was something I could never have learned from a book. Seeing the diagnostic process helped me understand the need for better and more advanced diagnostics to improve lives."

"I was extremely excited with the outcomes from these expeditions," says Tang, who accompanied the teams to China and Thailand. "Even though traveling to these areas was strenuous and taxing, even a hardship for some, in the end, all the students came back transformed in their ideas about biomedical engineering. They were fired up and excited about continuing on in this line of profession, almost as a life calling or mission."