OUTSTANDING STUDENT HIGHLIGHTS

Luis Alonzo, a second-year Ph.D. student from Venezuela, was awarded a Miguel Velez Fellowship worth $10,000 from the UC Irvine Graduate Division. Alonzo is working in the Cardiopulmonary Transport and Tissue Remodeling laboratory under Professor **Steven C. George**, M.D., Ph.D., where he is working on creating a 3-D dynamic model of the tumor microenvironment to characterize the role of macrophages on tumor progression and metastasis.

Phillip Duncan, a third-year Ph.D. student studying under Assistant Professor **Elliot Hui**, Ph.D., received an honorable mention Public Impact Fellowship from the UC Irvine Graduate Division. Duncan's research centers on the development of a microfluidic oscillator. In the future, he hopes to develop a new manufacturing process utilizing micromachining instead of lithography to create more complicated microfluidic circuits. The platform he is developing would allow for point-of-care diagnostic devices that are low-cost, portable and simple to use.

Inas Morsy, a fourth-year undergraduate student, was named Engineering Student Council's BME Student of the Year. Morsy has balanced her course workload while being involved in Tau Beta Pi, Engineering Student Council, and the Society of Women Engineers, and has been on the Dean's List every quarter since coming to UC Irvine. Her final project involves designing a device to measure the degree of cataract formation in the lens of the eye with LenSx Lasers.

Claire Robertson, a third-year biomedical engineering graduate student in the laboratory of Professor **Steven C. George**, M.D., Ph.D., has been selected as one of 591 young researchers from around the globe to attend the 61st Lindau Nobel Laureate Meetings in Germany this summer. Robertson's research looks at how the airways of the lung change with diseases like asthma or smoke inhalation, and whether the fibrosis seen in these diseases causes changes in their mechanical behavior.

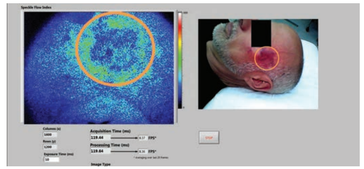
DEPARTMENT NEWS

Fan-Gang Zeng Elected IEEE Fellow

The Institute of Electrical and Electronics Engineers (IEEE) recently named BME Professor **Fan-Gang Zeng**, Ph.D., as a Fellow. Zeng was honored for his contributions to auditory prostheses.

Zeng's laboratory uses a systems and modeling approach to understand how the ear and brain work together to process sounds, including human speech and music. Working with faculty and students in engineering, neurobiology and cognitive sciences, he also develops and designs innovative prosthetic devices and training procedures for people who have lost hearing and balance functions.

Biomedical Engineering Paper Featured in Journal of Biomedical Optics



Bernard Choi, Ph.D., BME assistant professor, and **Owen Yang**, a third-year graduate student in the Samueli School, teamed with **David Cuccia**, CEO of Modulated Imaging, Inc., on a project in the Microvascular Therapeutics and Imaging Laboratory at the Beckman Laser Institute at UC Irvine to improve the removal of port wine stain birthmarks. The findings of the group have led to a paper published in the *Journal of Biomedical Optics*.

Two BME Professors Earn $3.8 million grant from NIH Heart Lung & Blood Institute

A four-year R01 grant from the National Heart, Lung, and Blood Institute of the National Institutes of Health (NIH) has been awarded to **Brian J. Wong**, M.D., Ph.D., BME professor and director of the Division of Facial Plastic Surgery in the Department of Otolaryngology–Head and Neck Surgery, **Zhongping Chen**, Ph.D., BME professor, and **Said E. Elghobashi**, Ph.D., professor of mechanical and aerospace engineering, for their proposal, "Modeling the pediatric upper airway using anatomic optical coherence tomography and computational fluid dynamics." The three professors will be researching ways to improve airway flow in children and individualize surgery procedures for pediatric patients.

BME Discovery

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

INSIDE THIS ISSUE:

SPRING 11

BME Discovery

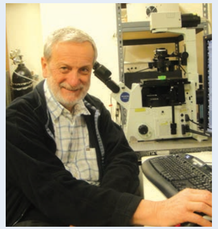
SPRING 11

THE HENRY SAMUELI SCHOOL OF ENGINEERING
UNIVERSITY OF CALIFORNIA, IRVINE
DEPARTMENT OF BIOMEDICAL ENGINEERING

RESEARCH HIGHLIGHTS

Biomedical Researchers Awarded $1 Million Keck Foundation Grant

Three UCI researchers receive funds to develop a nanoscale imaging microscope



Biomedical Engineering Professor **Enrico Gratton**, Ph.D., Research Associate **Michelle Digman**, Ph.D., and Developmental and Cell Biology Professor **J. Lawrence Marsh**, Ph.D., have been awarded a $1 million grant from the W. M. Keck Foundation to engineer a nanoscale imaging microscope capable of observing single-cell migration in vivo. Matching funds were also awarded by the UC Irvine Office of Research to support the establishment of the "W. M. Keck Nanoimaging Laboratory," whose mission is to develop state-of-the art technologies that will revolutionize how protein dynamics are measured.

The nanoimaging microscope is specifically designed to probe fluctuations of protein numbers and their interactions in real space and time at the nanoscale inside live tissues. The instrument will provide researchers with a detailed description of the dynamics of molecular associations at the nanoscale by viewing them directly in the cells of living organisms, which is important for understanding how protein complexes, that are responsible for cell migration in tissues, assemble and disassemble.

This technology will help gain insight into protein signaling mechanisms in the native intra- and extracellular environment. According to Digman, "The main advantage of this technology is that the laser beam can be positioned at any point in the cell. We can detect single molecular events while the cells are migrating and, with our fast feedback algorithm, we can maintain the focal position while at the same time 'tracking' the cell movement."

Probing the molecular interactions at the nanoscale inside native tissue and capturing the exact point as tumor cells invade is considered the next frontier in fluorescence imaging and cancer research. Developing this enabling technology will allow investigators studying many aspects of developmental processes to measure the dynamics of protein interactions that drive cellular behavior in living tissues during actions such as wound repair, neuronal targeting, angiogenesis and metastasis.

The researchers have developed the enabling technologies for imaging deep into tissues with the sensitivity necessary to detect single molecules in their own research activities. However, these technologies have not yet been combined into a single integrated platform and applied to cancer research.

Gratton said, "We are appreciative and enthusiastic that the W. M. Keck Foundation is willing to support our research, and are certain that many researchers will benefit from this development."

Based in Los Angeles, the W. M. Keck Foundation was established in 1954 by the late W. M. Keck, founder of the Superior Oil Company. The Foundation's grant making is focused primarily on pioneering efforts in the areas of medical research, science and engineering, and undergraduate education. The Foundation also maintains a Southern California Grant Program that provides support for the Los Angeles community, with a special emphasis on children and youth.

BME: Bridging the Disciplines - Mobilizing the Students - Empowering the Faculty

Dear Friends of BME:

The last nine months have been a whirlwind experience for me as I learned the ropes of being a department chair while getting to know more about the people in the Department of Biomedical Engineering (BME). Even though I have been at UC Irvine for more than nine years, I can honestly say that I am now prouder than ever to be part of BME. I am impressed by what we have collectively accomplished in our short history, and am even more excited about what the future holds. Some of my "discoveries" include:

Did you know?

■ BME faculty lead four highly visible and well-funded research centers that bridge fundamental discoveries to applied clinical studies, and arguably are the best in their respective fields: Beckman Laser Institute and Medical Clinic (BLI); Laboratory for Fluorescence Dynamics (LFD); The Edwards Lifesciences Center for Advanced Cardiovascular Technology; and the Micro/Nano Fluidics Focus Center (MF3). The annual budget for each of these centers exceeds $1 million per year.

■ BME faculty are integral members of key UC Irvine schools across campus: the School of Biological Sciences (e.g the Center for Complex Biological Systems); School of Medicine (e.g. the Chao Family Comprehensive Cancer Center, Sue and Bill Gross Stem Cell Research Center, Gavin Herbert Eye Institute, Institute for Clinical and Translational Science); and The Paul Merage School of Business (e.g. the annual Stradling Yocca Carlson & Rauth Business Plan Competition). BME has 55 affiliated faculty from other schools on campus, encouraging and participating in cooperative research across fields of discipline.

■ BME faculty are competitive in garnering extramural grants, with research expenditures exceeding $10 million in 2010 ($588,235 per core faculty member). Recent highlights include our junior faculty receiving the prestigious National Institutes of Health (NIH) Innovator's Award (Assistant Professor Michelle Khine) and National Science Foundation Faculty Early Career Development (CAREER) Award (Assistant Professor Zoran Nenadic), and the LFD receiving a grant from NIH for more than $7 million over the next five years (Professor Enrico Gratton).

■ BME faculty are respected and renowned leaders in their fields, as evidenced by their positions as chief editors and editorial board members in the top journals of their fields *(e.g. Journal of Biomedical Optics, Lasers in Surgery and Medicine, Lab on a Chip)*

■ BME has established strong ties to local biomedical device industry, with a Corporate Advisory Board whose members include the most reputable biomedical industry leaders in Orange County. Many of these board members have supported our program since its inception in 1998. Our undergraduate Senior Design Class relies heavily on local companies to mentor student projects and lecture on industry-relevant topics. Each year, BME students are hired into these local companies, completing the cycle from education to research to economic growth.

■ BME is one of only three programs in the state of California accredited by the Accreditation Board for Engineering and Technology (ABET), ensuring a quality UC Irvine education that takes into account design content, mathematic rigor and solid measures of outcome.

■ BME students are active entrepreneurs, placing in the top three of The Paul Merage School of Business's Stradling Yocca Carlson & Rauth Business Plan Competition on a yearly basis. At least 10 BME graduates, alumni and/or faculty are in the process of starting companies in California.

Going forward, with the foundation of a high quality and large student population, supportive network of companies, and highly reputable research operation, I am convinced that BME is poised to be the innovation and economic engine of Orange County and beyond through biomedical technologies.

I invite you to take a moment and read through the rest of the newsletter, including the "Research Highlights," "Faculty Profile," "Department News," and "Outstanding Student Highlights" sections.

Best Regards,

Abraham P. Lee, Ph.D.
William J. Link Professor and Chair, BME
Director, Micro/Nano Fluidics Fundamentals Focus Center

RESEARCH HIGHLIGHTS

BME Assistant Professor Receives CAREER Award for Neuron Research

Zoran Nenadic, D.Sc., assistant professor of biomedical engineering and electrical engineering and computer science, has received a Faculty Early Career Development (CAREER) Award from the National Science Foundation for his proposal, "CAREER: Estimation of Neuron's Position, Size and Dendritic Tree Morphology via Multi-sensor Extracellular Recording Technology."

Extracellular recording of the electrical activity of neurons in the brain has become the method of choice in experimental neuroscience. These types of recordings, performed with an electrode positioned near an individual neuron, have characterized much of what is known about brain function.

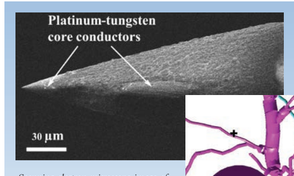
In recent decades, this technology has progressed to the point where multiple electrodes, each equipped with multiple sensors and integrated within a single microdrive device, can be lowered independently into an area of interest within the brain. Despite these advances, the process of extracellular recording remains tedious and time consuming, which limits the full potential of multi-electrode and multi-sensor technology.

Constant human supervision is required in studies of this nature due to the lack of information about the relative position and migration trends of neurons with respect to the recording electrodes. Very little is also known about the properties of neurons whose activities are being recorded, which can lead to interpretative errors in research data.

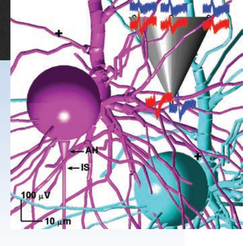
Nenadic's proposal seeks to use advanced mathematical and engineering techniques to develop a statistical framework to estimate a neuron's position, size and dendritic tree morphology (or shape), based on multi-sensor measurements of the neuron's extracellular electric field. Once Nenadic has developed this framework, it will then be tested, first computationally, using detailed computational neuron models, and then experimentally, using animal brain slices, and then compared for accuracy.

The proposed framework will enable more efficient positioning and guidance of electrodes, estimation of neuron's migration trends, and experimental separation of neurons according to their size and shape. The study will also lead to the development of optimal design criteria for multi-sensor recording electrodes. By bringing together ideas from engineering, mathematics, and neuroscience, this interdisciplinary research plan will fundamentally transform the way extracellular recording experiments are conducted, while addressing important problems arising at the neuron-electrode interface. These advances will allow scientists to tackle many open questions in neuroscience, and fundamentally advance scientific understanding of the animal brain.

As part of the proposal's educational component, Nenadic will devise, implement and test educational tools and measures designed to address the concerns U.S. engineering education faces today, and will face in the future. Specifically, he plans to enhance the educational experience of biomedical engineering students to help them better prepare for the challenges imposed by the changing global context of engineering. He will also promote engineering education and the pursuit of engineering careers in underrepresented students from kindergarten through high school, and contribute to the professional development and retention of math and science teachers.



Scanning electron microscope image of a 4-sensor electrode—tetrode (Thomas Recording GmbH, Giessen, Germany). Two sensors are visible from this perspective.



Simulated action potentials (duration 2 ms) of two model neurons sensed by a tetrode tip (gray cone) with sensors marked by . Red traces are from the left cell and blue traces are from the cell on the bottom right. Estimated source locations are marked by +.

New BME Professor Develops Innovative Cardiovascular Technology

Arash Kheradvar, M.D., Ph.D., is the newest assistant professor of BME and medicine in The Henry Samueli School of Engineering. Kheradvar conducts research in The Edwards Lifesciences Center for Advanced Cardiovascular Technology, and mainly focuses on cardiovascular engineering, particularly in the areas of cardiac mechanics, cardiovascular devices and cardiac imaging.

Kheradvar is a known scientist in the field of cardiovascular engineering whose contributions to cardiovascular vortex formation and heart valve engineering are internationally recognized by the cardiovascular communities. He is the inventor of 15 issued and pending patents, mostly in cardiovascular devices. He was also selected as a Vivien Thomas Young Investigator finalist by the council of Cardiovascular Surgery and Anesthesia at the American Heart Association Scientific Sessions in 2009.

Kheradvar is working to develop a patient-specific, predictive model for congenital heart defects, one of the most common heart problems that affect approximately nine out of 1,000 newborns. Among the different types of the defects, Kheradvar and his research group are interested in Tetralogy of Fallot, which classically involves four anatomical abnormalities, and is the most common cyanotic heart defect. In this project, they study the disease at multiple stages of embryonic, postnatal and early childhood to define a multiscale, predictive model for determining the fluid-structure interaction in these patients. This model will eventually provide valuable insights into the effect of flow-field on phenotypical variations of the disease. This information also improves the understanding of the remodeling process after the initial repair, and will contribute to decision-making concerning patient follow-up.

Kheradvar received his medical degree from Tehran University of Medical Sciences in 2000. He joined the California Institute of Technology in 2002, and completed his Ph.D. in bioengineering in 2007. He is a member of multiple national and international study sections, including the National Institutes of Health, National Science Foundation, American Heart Association, Natural Sciences and Engineering Research Council of Canada, Canadian Institutes of Health Research and National Medical Research Council of the Singapore Ministry of Health. He is also an editorial board member of the *American Society of Artificial Internal Organs Journal, International Journal of Medical Engineering and Informatics, and International Journal of Biomedical Engineering and Consumer Health Informatics*.

A recent achievement by Kheradvar and his group is the development of an advanced technology for percutaneous heart valves (PHVs) that uses a fundamentally different concept for packaging and deployment than current technologies, resulting in a much smaller pre-valve delivery profile (12 French Catheter vs. 18-45 French Catheter for other technologies). This new PHV can perform as well as any surgically-implanted valve due to its standard tri-leaflet shape, and is deliverable into the body through multiple routes, including trans-femoral, trans-apical, and Subclavian routes. This technology has been licensed by FOLDA, LLC, an Orange County start-up company that Kheradvar co-founded. More information about Kheradvar's research can be found at his group website: http://klab.eng.uci.edu.

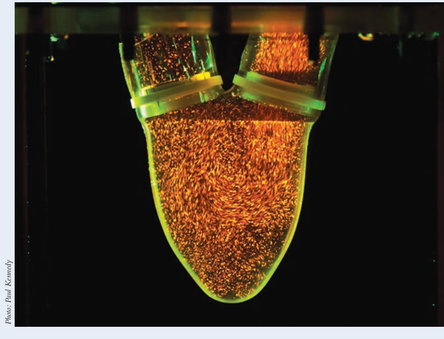


Photo: Paul Kennedy

Photo Caption: A vortex formation phenomenon in an in-vitro transparent model of the left ventricle. The flow seeded by the fluorescent particles is illuminated by a laser sheet passing through the ventricle model. The ventricular sac is a part of the advanced cardiac flow simulator at Kheradvar's laboratory.