UC Irvine Establishes Center to Study Small-Scale Fluidic Behavior

With the support of $7.2 million over three years, UC Irvine has created a center for the study of micro- and nano-fluidics – the science and technology of preparing and handling small amounts of fluids on microchips.

The Micro/Nano Fluidics Fundamentals Focus Center (MF3) brings together 17 leading micro- and nano-fluidics professors from 10 universities nationwide to advance the basic science and applications of a field seen as key to creating a vast array of new technologies. With scientists representing the disciplines of biomedical, mechanical and electrical engineering, as well as chemistry, research is expected to apply to areas such as health care, electronics, and environmental and food monitoring.

"The promise of fluidics technology is broad and exciting," said Abraham Lee, principal investigator of MF3 and professor of biomedical engineering and mechanical and aerospace engineering at UCI. "In the health sciences, it can allow for the automated collection of fluid samples, such as water or blood; or the separation and detection of biological components such as cells, proteins or DNA; and chemicals such as toxins or pollutants. In a field like heat management, fluidics can facilitate the more efficient transport of fluids."

Additionally, MF3 will provide graduate students the opportunity to interact with researchers and professors from multiple fields to learn the skills necessary to design modular micro- and nano-fluidic components and handheld, portable devices, as well as build the technology cost-effectively.

The center is a spin-off of activities completed at the Integrated Nanosystems Research Facility, an interdisciplinary research laboratory in The Henry Samueli School of Engineering that focuses on work with a broad range of nanoscale systems.

MF3 is being funded by the Defense Advanced Research Projects Agency in the amount of $4.3 million, and more than a dozen company sponsors will contribute $2.9 million to the center over three years. For more information, visit the MF3 center Web site at www.inrf.uci.edu/mf3/.

Upcoming Events 2007

California: Prosperity Through Technology
6th Annual Industry Research Symposium
May 15-16, 2007
Hosted by The Henry Samueli School of Engineering, UC Irvine
Location: Arnold and Mabel Beckman Center of the National Academies of Sciences and Engineering and UC Irvine
http://www.eng.uci.edu/cptt

Biomedical Engineering Society 2007 Annual Fall Meeting
"Engineering the Future of Biology and Medicine"
September 26-27, 2007
Hosted by UC Irvine, UCLA and USC
Location: Renaissance Hollywood Hotel, Los Angeles, CA
http://bme.usc.edu/bmes2007/

Frontiers in Biomedical Devices 2007 Conference
June 7-8, 2007
Sponsored by the ASME Nanotechnology Institute
Co-chaired by Professor Abe Lee, UC Irvine, and Dr. Walt Baxter, Medtronic Cardiac Rhythm Management
Location: Hyatt Regency Irvine, Irvine, CA
http://www.asmeconferences.org/BioMed07/

2nd LFD Workshop in Advanced Fluorescence Imaging and Dynamics
October 22–26, 2007
Sponsored by Carl Zeiss Inc., UC Irvine, and Globals Software
Location: Laboratory for Fluorescence Dynamics, UC Irvine
http://www.lfd.uci.edu/workshop/

For more information please visit www.bme.uci.edu or call 949.824.6284

BME Discovery

SPRING 07

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INSIDE THIS ISSUE:

The Henry Samueli School of Engineering
University of California, Irvine
Department of Biomedical Engineering

Dear Friends,

The 2006-07 academic year has moved swiftly with many exciting developments in the Biomedical Engineering Department. Our research and training programs continue to expand with tremendous energy, and I would like to highlight just a few recent and future activities.

The Department hired two new junior faculty this past year – Dr. Elliot Botvinick and Dr. Bernard Choi. Dr. Botvinick obtained his formal training in bioengineering from the University of California, San Diego, and has proven to be an exceptional experimentalist in the pursuit of biomedical imaging and investigation at the biomolecular level. Dr. Choi obtained his bachelor's degree in biomedical engineering from Northwestern University, and master's and doctoral degrees, also in biomedical engineering, from the University of Texas at Austin. His postdoctoral training was completed at the Beckman Laser Institute here at UC Irvine. He has a well-focused research program in the field of biophotonics for cutaneous and subcutaneous investigations.

This coming fall, the Department is co-hosting the Annual Fall Meeting of the Biomedical Engineering Society with the University of Southern California and the University of California, Los Angeles. This is a wonderful opportunity to showcase our talented faculty and students on a national stage, which will include more than 2,000 presentations over a broad array of biomedical topics. The meeting will be held at the Renaissance Hollywood Hotel, Los Angeles, Calif., from September 26–29, 2007.

The Frontiers in Biomedical Devices Conference is another meeting opportunity, which will take place June 7–8, 2007 at the Hyatt Regency Irvine, Irvine, Calif., and is sponsored by the American Society of Mechanical Engineers Nanotechnology Institute. The conference is co-chaired by Professor Abe Lee, and Dr. Walt Baxter of Medtronic Cardiac Rhythm Management. Dr. Baxter is also a member of the Department's Corporate Advisory Board.

Finally, it is with great pride, I announce the recent DARPA-supported center led by Professor Lee named the Micro/Nano Fluidics Fundamentals Focus Center (MF3). This Center involves 17 faculty members (seven from UC Irvine) from 10 universities across the country, and is one of only 10 nationally established by DARPA. MF3 will study micro- and nano-fluidics – the science and technology of preparing and handling small amounts of fluids on microchips. With scientists representing the disciplines of biomedical, mechanical and electrical engineering, as well as chemistry, research is expected to apply to areas such as health care, electronics, and environmental and food monitoring.

Please take a few minutes to learn more about the Department and additional stories highlighted in this issue, including a faculty profile on Professor Enrico Gratton, graduate student profiles, and additional information regarding biomedical engineering undergraduate and graduate programs.

Best Regards,

Steven George
William J. Link Professor and Chair

FACULTY

Professor Enrico Gratton Shares Information about Fluorescence Across the Globe

Enrico Gratton, Ph.D., professor of biomedical engineering, joined UC Irvine in 2006 after 30 years at the University of Illinois at Urbana-Champaign. Gratton is the principal investigator of the Laboratory for Fluorescence Dynamics (LFD), a national research resource center for biomedical fluorescence spectroscopy supported by the University and by a grant from the National Institutes of Health.

The LFD, founded in 1986, re-located from Illinois to Irvine, and is now housed in the Natural Sciences II building, employing about two dozen people. Scientists from all over the world visit the LFD to learn about the latest techniques in fluorescence research – including Fluctuation Correlation Spectroscopy (FCS), Raster Image Correlation Spectroscopy (RICS), Fluorescence Lifetime Imaging (FLIM), 3-D Particle Tracking, and Frequency-Domain Fluorescence Lifetime Spectroscopy – and to take advantage of the LFD resources for spectroscopy, microscopy, biochemistry, cell culture and data analysis.

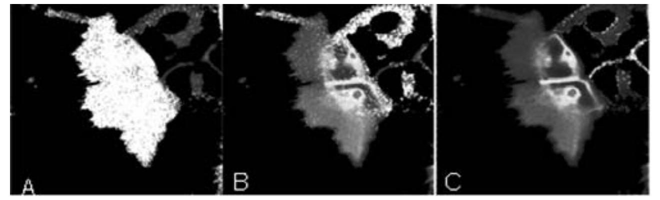
As principal investigator of the LFD, Gratton is firmly committed to spreading information about fluorescence spectroscopic principles, instrumentation and applications to the scientific community. He travels to workshops, conferences and society meetings, spanning the globe, to train and advise other researchers and students.

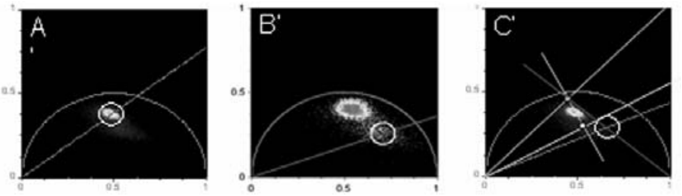
"Enrico's greatest contribution to the fluorescence research field is the dissemination of his knowledge, which keeps us in contact with other researchers and brings in new students because of his enthusiasm about the science," said Susana Sanchez, Ph.D., LFD user coordinator. "He can talk to young people anywhere—in the United States, Europe, South America. Students like him and are not afraid to talk to him."

Gratton was born in Italy and received his doctorate in physics from the University of Rome. He authored Globals software for multiple-file spectroscopy analysis and image analysis, holds nine issued patents, and has more than 400 publications. His research interests include designs of new fluorescence instruments, protein dynamics, hydration of proteins and I.R. spectroscopy of biological substances.

He has served on the editorial board of *Biophysical Journal* and other peer-reviewed publications, and is an organizer of the International Weber Symposium on Innovative Fluorescence Methodologies in Biochemistry and Medicine.

Lifetime Phasors is a new method designed at the Laboratory of Fluorescence Dynamics for the analysis of lifetime images. This method allows non-expert users to easily analyze lifetime data from cells. The method has been used for fluorescence resonance energy transfer (FRET) and ion concentration analysis in cells. For FRET analysis, the operator can move the cursor along the quenching line and calculate the FRET image. Either visual inspection or computer recognition methods can tell us if pixels along the FRET line form clusters in specific portions of the cell.





Selecting the region in A' (donor + acceptor) the part in white lights up (A). Selecting the region in B' (autofluorescence) the part in white lights up (B). Selecting the region in C' (along the donor quenching line as shown, HEK293 transfected with a donor labeled EGFPuPAR chimera, an acceptor mRFP1-uPAR in the presence of ligand to induce FRET.

For more about Gratton's research and the Laboratory for Fluorescence Dynamics, please visit http://www.lfd.uci.edu.

GRADUATE PROGRAM

The 2007 fall quarter looks to be the start of another promising academic year with a strong applicant pool. The Department of Biomedical Engineering has admitted 32 Ph.D. students, and 20 master's degree students - all of whom excel in academics, research, and preparedness. The department hosted a recruitment visitation day on Friday, March 2, welcoming 19 of the admitted students. The day's activities introduced the students to the graduate program, and included tours of the Beckman Laser Institute and the Integrated Nanosystems Research Facility, an informal poster presentation series, one-on-one interactions with various faculty members, and an "open lab session" for students to tour the many faculty laboratories. After the Department hosted an outdoor barbeque lunch, the Biomedical Engineering Society (BMES) graduate student chapter gave the prospective students a tour of graduate student housing and also brought them to view the famous "O.C." Pacific sunset at Newport Beach.

The day concluded with dinner at a local restaurant, where prospective students were able to socialize with current biomedical engineering students in a relaxed atmosphere, and the Department looks forward to welcoming many of these talented students in the fall.

UNDERGRADUATE PROGRAM

A Cost-Effective Upper Extremity Prosthesis Design

Upper extremity prostheses are a scarce necessity in less developed countries due to lack of medical facilities, economic resources and prevalent warfare. The demand for prostheses has continued to grow as 50,000 amputations occur annually. The current market focuses primarily on lower extremities because prosthetic legs cost less and provide full functionality when compared to upper extremity prostheses. Prosthetic legs only need to fulfill basic motions such as walking and running, while upper extremity prostheses include complicated hands that encompass 22 degrees of motion.

The design of a cost-effective upper extremity prothesis began as a class project in the senior biomedical engineering design course sequence during the 2006 fall quarter. Fourth-year students Steven Chen, Vanessa Pau, Theresa Shar, Stephanie Tiaden and Anthony Wong set out to design an affordable and easily assembled upper limb prosthetic device that would provide basic arm function and could be widely distributed. Cost, availability, functionality and simplicity were the project's primary considerations.

With the help of their instructors, Professors Abraham Lee and William Tang, the team found a mentor, David Coe, a certified orthotist, from Hanger Prosthetics and Orthotics. Consulting Coe and conducting a cost-benefit analysis of material and manufacturing processes yielded a project budget of less than $400. The design team worked to select the least costly materials that still fulfilled primary functions, including Dacron straps and harnesses instead of costly leather or neoprene materials. Aluminum was selected for the friction wrist unit and terminal device because it was both lightweight and affordable, unlike pricey titanium and heavier stainless steel units.

The final design constitutes an aluminum terminal device and wrist unit attached to a vacuum-molded polypropylene forearm, with movement controlled by an adjustable harness and cable system. Three standardized adult forearm sizes (small, medium and large), with prototypes designed with CAD, will be manufactured for universal fitting. Additional socks for fitting between a patient and the device may be included to enhance user comfort.

The prosthesis design is unique, providing a solution to a problem that is many times overlooked because of the financial aspects of product marketing. By creating a low-cost prosthetic, and minimizing production and training costs, the design team hopes to help improve the lives of patients in developing countries at an affordable price.

In the current market, prosthetic arms can cost up to $40,000. The team's model prosthetic produced a below-the-elbow, upper limb prosthesis for under $400, bringing their prosthesis one step closer to mass production and availability. The final product consists of an easily assembled mobile kit that contains one prosthetic arm. The arm can easily be re-fitted and adjusted to the patient, either on-site or at a medical facility.

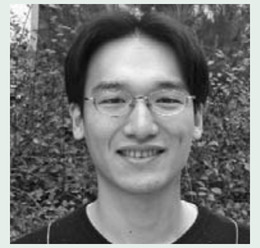
Currently, the team has finished building a working model of the prosthetic arm. In coming weeks, they plan to build more prostheses to conduct trial tests, and intend to make an instructional video or pamphlet on how to wear and assemble the prosthesis. They hope to gain FDA approval, and ultimately aim to collaborate with charitable organizations for widespread distribution of the prosthesis design to economically disadvantaged amputees worldwide in three years.

The team said that they valued the opportunity to work under the guidance of Lee, Tang, and Coe. Building the prosthesis with a certified orthotist allowed the team to work in a rapidly-growing industry, and they said learning more about limb loss and landmine victims also proved to be a humbling experience. As aspiring biomedical engineers, team members hope their design and cooperative efforts can have a positive impact on the less fortunate. The design team members expressed gratitude for the experience to gain expertise in the area of prosthetics, build valuable mentor relationships, and, most importantly, provide a small helping hand (pun intended) to the community along the way.

OUTSTANDING GRADUATE STUDENT PROFILES

Kanaka Hettiarachchi, a Ph.D. student in Professor Abraham Lee's BioMiNT lab, is developing new microfluidic systems for creating microbubbles for ultrasound imaging and therapeutics. Ultrasound is the most widely used imaging technique in the world, but unlike X-ray and magnetic resonance imaging, the technology has until recently been limited by the lack of effective contrast agents. In echocardiography procedures, only a small portion of a microbubble contrast agent population is optimally sized for imaging systems.

Using microfluidic devices, Hettiarachchi is able to produce a stable and monodispersed contrast agent population so that similar microbubble radial oscillations from pulses of ultrasound lead to a smaller variation in the received echoes. The work has been presented at two international conferences, and published in the journal *Lab on a Chip*. Through collaboration with UC Davis, a NIH grant has been awarded to fund Hettiarachchi's continued development efforts. His future research focuses on microbubble-based biosensors and generating functionalized drug carriers for delivering bioactive substances to desired sites of the vascular endothelium for the treatment of disease. Hettiarachchi also designed the logo and application wall slide for the recently established Micro/Nano Fluidics Fundamentals Focus Center (MF3).



Yu-Hsiang (Shawn) Hsu, a Ph.D. student in Professor William Tang's lab, is one of 16 UC Irvine graduate students named a 2006-07 Calit2 Emulex Fellow, a one-year award funded by Calit2 corporate partner Emulex Corp. Currently, he is working on a project in Tang's lab that aims to establish the critical engineering feasibility that will lead to a micro-platform with massive arrays of micro chambers, each instrumented with a resonant transducer capable of interrogating the mechanical properties of a cell.

In every major cellular event, including cell division and cell migration, the cytoskeleton changes dynamically in a highly complex and coordinated manner to help complete the cellular activities. Since many of the mechanical properties of a cell are defined by cytoskeleton morphology, including viscosity and stiffness, it is hypothesized that viscosity and stiffness measurements can be used to infer the different morphological behaviors of a cytoskeleton, which in turn are directly driven by cellular activities. Conventional molecular probes will be used to simultaneously visualize cytoskeleton changes while resonance is measured. Such correlation does not yet exist, but holds tremendous promise in enabling massively parallel drug screening, cancerous cell identification and quantification, and other rapid turn-around studies of single-cell physiologies.

FACULTY BRIEFLY

Elliot Botvinick, Assistant Professor

Botvinick's research focuses on the relationship between mechanical stresses on cells and molecular signaling, i.e. cellular mechanotransduction. Currently, emphasis is placed on the transduction of fluid shear stresses by endothelial cells and the transduction of mechanical stress during cell migration. Cell signaling is measured on a cell-by-cell basis using fluorescent techniques, including FRAP, FRET and TIRF. Microscopes are customized to combine imaging with functional microbeams for laser ablation and laser tweezers. Spatially modulated microbeams can constitute an array of laser tweezers that can apply known mechanical or fluid stresses and measure elastic and viscous properties within sub regions on or within a single cell.

Botvinick is currently involved in research projects on the role of the glycocalix in the transduction fluid shear stress on vessel walls, and cell signaling in laminar flow chambers in which only a few cells experience unsteady or reverse flow as introduced by laser tweezers. He received his B.Sc., M.S. and Ph.D. in bioengineering from the University of California, San Diego.

Zhongping Chen, Professor

Chen, professor of biomedical engineering and electrical engineering and computer science, has recently been selected as a Fellow of the Optical Society of America. This honor is only given to ten percent of the OSA membership and is dedicated for members who have served with distinction in the advancement of optics.

Chen was honored specifically for his pioneering contributions to the development of functional optical coherence tomography (F-OCT), including Doppler, polarization-sensitive, phase-resolved and second-harmonic OCT. F-OCT allows for cross-sectional imaging of tissue structure, blood flow and birefringence simultaneously with high spatial resolution. Many of his active research projects are interdisciplinary, involving research areas in fiber optics, lasers and optoelectronics, MEMS, signal processing and biomedical instrumentation.

Bernard Choi, Assistant Professor

Choi's research interests include the development and application of in vivo optical imaging methods for novel therapy discovery, with current collaborations in dermatology and neurobiology. He also leads research efforts on the use of chemical agents to reduce the optical scattering of biological tissue. Choi received his B.Sc. degree from Northwestern University, and his M.S.E. and Ph.D. degrees in biomedical engineering from the University of Texas at Austin. After completing an Arnold and Mabel Beckman Fellowship at UC Irvine, he was appointed as an assistant professor in the Biomedical Engineering Department and the Department of Surgery, Beckman Laser Institute.