STUDENTS

Undergraduate Program Growing

The BME undergraduate program continued its steady growth in 2005, with an incoming freshman class of 107 students. Of these students, 31 declared the Biomedical Engineering major and 76 declared the Biomedical Engineering: Premedical major. One point of significance is that the SAT scores and GPAs of these students were higher than those of the incoming Fall 2004 class. We also admitted 12 transfer students, of which 10 declared the Biomedical Engineering major, and two declared the Biomedical Engineering: Premedical major.

Graduate Students Move Ahead

In 2005 we celebrated our first graduating class with the conferral of 21 B.S. degrees. Of these students, 12 received the B.S. degree in Biomedical Engineering and nine received the Biomedical Engineering: Premedical degree. Ten of these alumni are going on to higher education in pursuit of their M.S. or Ph.D. degree, four are pursuing a medical degree, and two took jobs in industry. We are very proud of this group of students and their achievements.

In the Classroom

The Biomedical Engineering Laboratory course (BME 170) was offered for the first time in spring 2005. This lab introduced students to the measurement and analysis of biological systems through a series of laboratory rotations involving in-vitro and in-vivo experiments.

Distinguished Lecturer Series 2006

January 25, 2006
Micro-tools for Biology
Featuring Dr. George M. Whitesides
Harvard University

Location: Crystal Cove Auditorium
UC Irvine Student Center

February 2, 2006
Two-phase Flows in Microfluidic Devices
Featuring Dr. Dorian Liepmann
University of California, Berkeley

March 16, 2006
Non-invasive Assessment of Cardiovascular Control in Sleep Apnea: Basic and Translational Research Studies
Featuring Dr. Michael Khoo
University of Southern California

April 20, 2006
Control of Cell and Tissue Function via Protein Biomaterials
Featuring Dr. David Kaplan
Tufts University

May 4, 2006
Digital Humans: From Biomechanical Models to Simulated Surgery
Featuring Dr. Scott Delp
Stanford University

May 18, 2006
Structurally and Functionally Integrated Computational Biology of the Heart
Featuring Dr. Andrew McCulloch
University of California, San Diego

All lectures will take place from Noon - 1 p.m. in UC Irvine's McDonnell Douglas Engineering Auditorium
(unless otherwise noted)

BMEDiscovery

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

WINTER 06

INSIDE THIS ISSUE:

BMEDiscovery

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

Dear Friends,

The Biomedical Engineering Department is continuing its robust growth, and we are excited to introduce two new faculty members in this issue of BMEDiscovery. Dr. Zoran Nenadic joined the department as an assistant professor on April 1, 2005. His research focus is on engineering neural systems. On October 1, 2005, six months after Dr. Nenadic's arrival, Dr. Frithjof Kruggel joined us as a full professor. Dr. Kruggel's research focuses on biomedical imaging and signal analysis in neuroscience, and represents the second faculty member hired into the area of neuro-engineering.

Another exciting development includes the building of the BioNEMOS (Bio-Nano-Electro-Mechano-Optical Systems) laboratory, which is located in the state-of-the-art California Institute of Telecommunication and Information Technology (Calit2) building. This laboratory provides co-located research and teaching capabilities that combine molecular, cell, and tissue experiments on nano- and micro-scale platforms with multiple probing and imaging capabilities in electrical, mechanical, and optical domains.

The latest research activities in cancer study, as well as an event calendar, are also in this issue of BMEDiscovery. More information can be found on our website www.bme.uci.edu.

Best Regards,
William C. Tang
Professor and Interim Chair

FACULTY

UC Irvine Welcomes Professors Kruggel and Nenadic

Dr. Kruggel is Focused on Biomedical Image and Signal Analysis in Neuroscience

Professor Frithjof Kruggel, M.D., joined UC Irvine's Department of Biomedical Engineering in October. Dr. Kruggel, a German native, received his Diploma in Chemistry and his Medical License from the Ruhr-University Bochum (Germany). Doctoral work brought him to the Max-Planck-Institute of Psychiatry in Munich, where he designed a psychophysiological test for human olfaction in order to better characterize disturbances of taste and smell in patients with focal brain damage.

He received his M.D. with highest honors from the Ludwig-Maximilian-University in Munich. After finishing his training in Clinical Neurology and Neuropsychology, he moved to Leipzig and assisted in building the newly founded Max-Planck-Institute of Cognitive Neuroscience, heading the Workgroup on Signal and Image Analysis from 1995-2004. From 2002-2004, he organized the education in Signal and Image Analysis as a deputy professor in the Department of Computer Science at the University of Leipzig. In his career he has published more than 100 scientific papers.

As a member of the UC Irvine faculty, Dr. Kruggel has focused his research in two main areas: computational neuroanatomy and human brain mapping. His work in computational neuroanatomy aims at developing methods for describing individual brain structures by meaningful characteristics such as size, shape, and texture.

Once these quantitative parameters are extracted from the neuroimage data, and they can be related to physical, cognitive or clinical parameters of a patient. Similar to values in clinical chemistry (i.e., blood glucose level, liver enzymes), normal ranges and distributions were determined for structural brain parameters to better interpret individual values with respect to a normal population. This data provides a better understanding of gender-related differences and age-related changes. These parameters also help discriminate healthy and pathological aging, thus increasing the likelihood of early detection of degenerative brain diseases such as Alzheimer's disease.

His work in human brain mapping is directed on improving techniques to analyze data from functional neuroimaging experiments. Examples include (1) the detection and description of single hemodynamic responses in functional MRI, (2) techniques to combine functional MRI and EEG, functional MRI and near infrared spectroscopy, (3) the set-up of physiologically oriented finite element models of the head to localize electromagnetic sources in the brain. Emphasis is led on the study of individual subjects to better relate functional activation to neuroanatomical structures, and to have these techniques applicable for clinical patients.

Structural and functional imaging may converge, as recent developments in high resolution imaging promise. Cytoarchitectonic fields of the human neocortex are defined by characteristic variations in the composition of a general six-layered structure. It is commonly accepted that these fields correspond to functionally homogeneous entities. Diligent techniques were developed to characterize cytoarchitectonic fields by staining sections of post-mortem brains and subsequent statistical evaluation. However, recent advances from Kruggel and his co-workers in high resolution MRI techniques have demonstrated the feasibility to study the neocortical fine-structure in anatomical MRI images, thus, defining cytoarchitectonic fields by in-vivo techniques.

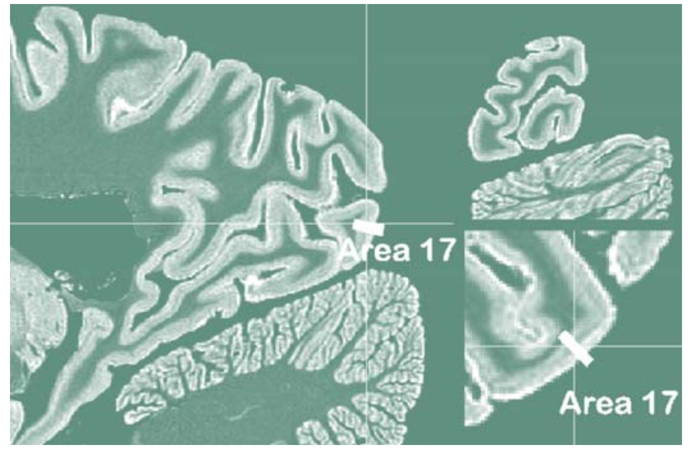


Figure 1: *The visual cortex is distinguishable from the surrounding Area 18 by the presence of Gennari's band, which corresponds to layer IVb of this cortex and consists of an intracortical horizontal fiber system. This structure is easily detected in the high-resolution MRI dataset as a darker band in the bright cortex.*

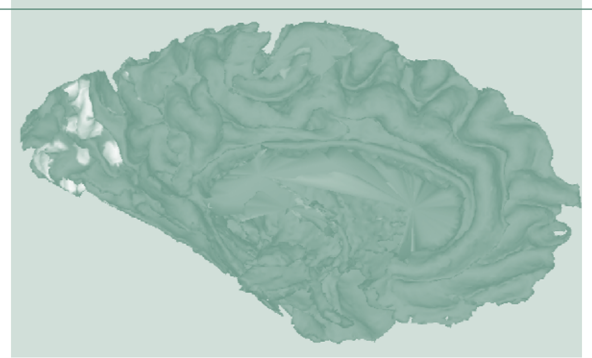


Figure 2: *Medial view of the brain hemisphere. Using statistical characteristics of a model region marked in the figure above, it is possible to detect the extent of the visual cortex (in light grey). Thus, structural properties of a cortical region were used to define a functionally uniform patch on the brain surface.*

Dr. Nenadic Designs Autonomous Biomedical Control Algorithms

Zoran Nenadic, D.Sc., joined UC Irvine's faculty as an assistant professor in the Department of Biomedical Engineering in April 2005. Nenadic received his diploma in Control Engineering from the University of Belgrade, and M.S. and D.Sc. degrees in Systems Science and Mathematics from Washington University. Prior to joining UC Irvine, he was a postdoctoral fellow with the Division of Engineering and Applied Science at the California Institute of Technology, where he is currently a visiting associate.

Nenadic's research interests fall into three major areas: the design of control algorithms for autonomous biomedical devices, unsupervised adaptive biomedical signal processing, and computational modeling of biological neural networks and development of neural decoding algorithms.

While at Caltech, Nenadic worked on the development of control algorithms for extra cellular recordings from the brain in both rats and monkeys. The goal of the algorithm is to autonomously guide the recording electrodes to an optimal recording position, and then to maintain the optimal signal quality by compensating for various disturbances inherent to the process of extracellular recordings, most notably, tissue drifts and signal nonstationarity. The major benefits of such an algorithm have implications in both acute and chronic recording experiments. Capable of operating in a fully unsupervised mode, the algorithm could free the human operator from the tediousness of acute recordings, while making fast and unbiased decisions leading to the ending and maintenance of the optimum recording position. This is especially important in experiments with a large number of electrodes, where it is impractical, if not impossible, for the operator to manually adjust and move all electrodes simultaneously. In chronic recording applications, these "smart probes" are useful because they could prolong the life of recording arrays by being able to move the electrodes once they become encapsulated by the scar tissues, or the useful neural signal is lost due to other reasons (inammatory reaction, cell expiration, cell-electrode separation due to mechanical shocks, and so forth).

To operate recording electrodes autonomously, a computer needs to be able to interpret the recorded signals based on very little, or no prior information. The detection and recognition of useful neural signals in noise become challenging when both signal and noise properties are unknown. Furthermore, to account for non-stationary phenomena and variable recording conditions, these signal processing algorithms have to be adaptive and robust. Nenadic has developed a set of robust signal processing tools, useful for blind neural data processing. In addition, he has developed an ancient stochastic optimization algorithm for regression curve maximization based on noisy samples alone. The applications of this method reach beyond the realm of neural signal processing and neural recording device control.

The future of brain-machine interface and neural prostheses, in particular, hinges upon a proper deciphering of the neural code. By analyzing the neural correlates of movement intentions in real time, the information can be decoded and used to drive external devices such as computer cursors, autonomous vehicles, or artificial limbs. Massively parallel recording devices, typically used in neuroprosthetic applications, quickly generate large sets of neural data, not all of which contain the information useful for the task at hand. Nenadic tackles this problem with the help of information theory, which is used to guide the extraction of the most informative data subset. To develop and validate these algorithms, he uses both recorded data and data generated by large networks of biologically realistic neural models. The advantage of the modeling approach is that it allows the exibility in simulating different neural configurations, and it helps identify the critical model parameters, useful for the design of future experiments. Finally, the model of an electrode-neuron interface may provide important guidelines for the design of future neural recording implants.

Nenadic has authored more than 25 scientific publications. He is a member of the IEEE, the Mathematical Association of America, and the Society for Neuroscience.

RESEARCH

Multidisciplinary Approach Enables Multi-Dimensional Study of Cancer

The study of cancer by biologists, oncologists, and other life science researchers is well renowned. However, many do not realize that this field is also the subject of intense research by physicists, mathematicians and engineers who study this disease from a physical perspective. For example, whereas molecular biologists elucidate genetic mechanisms of tumor growth, mathematicians and physicists establish basic principles that underpin this growth. The goal for these principles is to enable the study of cancer from a universal perspective that allows prediction of disease progression and treatment response for individual patients.

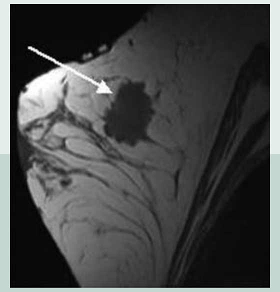
The Biomedical Engineering Department of The Henry Samueli School of Engineering is at the forefront of this activity with the work conducted in the Computational Biology Laboratory. Under the direction of Vittorio Cristini, assistant professor of biomedical engineering, some of the world's most sophisticated mathematical models of cancer are being developed at UC Irvine.

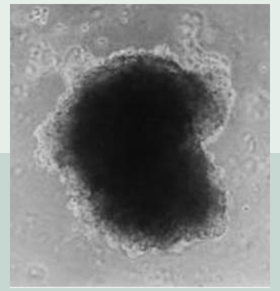
For example, Biomedical Engineering Ph.D. candidate, Hermann Frieboes, has been working on establishing two- and three-dimensional computer models of cancer that integrate biology, physics, and mathematics. Parameters for the model are based on experimental data obtained from tumors grown in the laboratory, as well as from clinical data. This approach ensures that the underlying mathematics and physics will accurately model tumor growth, invasion, and response to treatment. Frieboes' work in Cristini's computational lab is funded by the National Cancer Institute and the National Science Foundation.

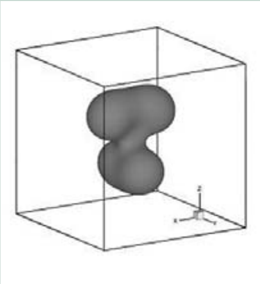
In collaboration with the Beckman Laser Institute at UC Irvine, Cristini's group has obtained data on tumor growth in the laboratory. Working at the Translational Oncology Laboratory of Dr. John Fruehauf at the UCI Medical Center, they have been studying how tumors grown in the lab respond to drug treatment. In addition, they have obtained MRI data from tumors in patients through collaboration with the UCI Center for Functional Onco-Imaging.

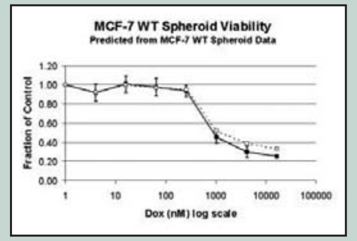
"We have the opportunity to dramatically advance our understanding of this disease through the integration of knowledge from many different fields, such as biology, mathematics, and imaging," said Frieboes. "We also hope that the ever-increasing advancement of knowledge in each of these disciplines will benefit from an integrated approach and lead to treatment optimization on an individual patient basis."

In particular, Cristini's group is studying the transport issues and biological barriers that hamper delivery of chemotherapeutics to tumors, including nanoparticle-mediated drug delivery. They are also examining how an impaired vasculature can create gradients of oxygen and cell nutrients that affect tumor morphology and response to treatment. Their work has been published in several journals, including *Cancer Research*, *Biomedical Microdevices* and *Clinical Cancer Research*, along with several other manuscripts currently under review.









Top left: MRI of a patient tumor. Top right: Microscope image of tumor grown in laboratory. Bottom left: Tumor modeled in 3-D. Bottom middle: Tumor cross-section modeled in 2-D showing development of necrosis and angiogenesis. Bottom right: Comparison of laboratory tumor drug response (solid line) and model prediction (dashed line). Note: figures are not to scale.