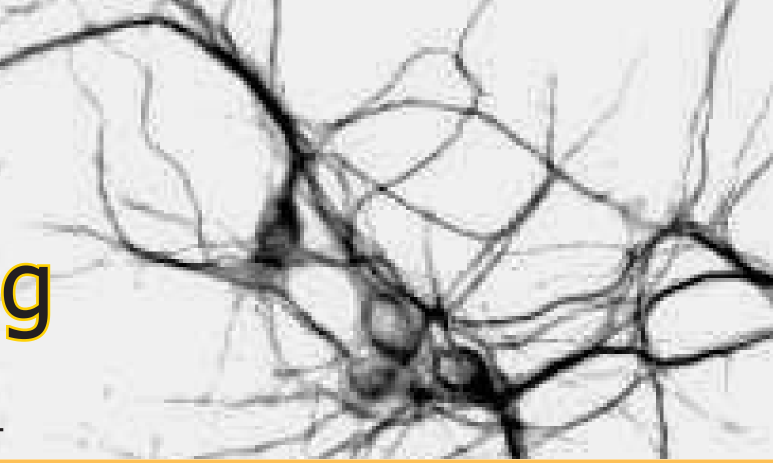


Center for Neuroengineering Newsletter

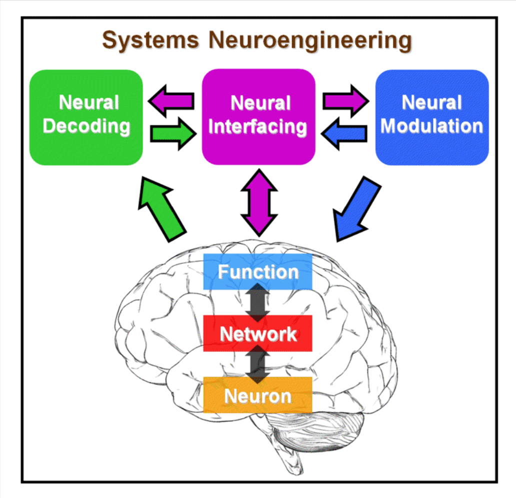
Fall 2011

University of Minnesota

University of Minnesota Awarded NSF IGERT Training Grant in Neuroengineering

The University of Minnesota has been awarded a new grant from the National Science Foundation (NSF) for a new Integrative Graduate Education and Research Traineeship (IGERT) program in Systems Neuroengineering, which is directed by Dr. Bin He with the participation of over two dozens of training faculty across engineering and brain sciences. Over the next five years the NSF grant will provide $3 million in funding, supporting six new doctoral trainees per year. The IGERT program is designed to provide interdisciplinary graduate education and research training to exceptionally qualified doctoral students who will work with Neuroengineering faculty at the university.

Bridging engineering and neuroscience, Systems Neuroengineering is an emerging field that translates research discoveries into neuro-technologies that provide new and powerful tools for basic and clinical neuroscience research, and lead to enhanced patient care. Exploration of neural systems has long focused on understanding how neural systems work at the molecular, cellular, network and system levels. Engineering methodologies have always played an important role in the study of neural systems, providing tools needed to detect, process, and model neural signals. Tremendous progress has been made in the field of neuroengineering in recent years, both in the application of engineering concepts and methodologies to the study of neural systems, and in the interfacing of neural systems with external devices for restoration of lost neural function. The rapid progress and tremendous translational potential of neuroengineering includes examples of systems that electrically pace brain activity in order to restore function, or that use brain activity for diagnosing disease or controlling external devices such as computers or robotic devices.



The Systems Neuroengineering IGERT program is motivated by the notion that future breakthroughs in this rapidly-growing area of research will be made by engineers who understand the fundamental issues and principles of neuroscience, and by neuroscientists who are truly competent in engineering concepts and tools. This IGERT program is open to doctoral students who major in biomedical engineering, electrical engineering, mechanical engineering, or neuroscience at the University of Minnesota. IGERT Trainees will participate in a newly-designed, integrated graduate curriculum that will provide them with a solid foundation in the interdisciplinary field of neuroengineering, with broad research training using a team advising model, and with practical experience for the successful application of neuroengineering concepts and methods to real-world problems.

IGERT

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Trainees will develop the interdisciplinary skills to tackle the grand challenges in systems neuroengineering, including neural decoding, neural interfacing and neuromodulation. The program will lower the barriers to interdisciplinary, collaborative education and research by training graduate students with diverse biological and quantitative backgrounds to possess expertise in multiple fields so that they can serve as catalysts for the cross-fertilization of neuroscience with engineering sciences in academia, industry and government.

The IGERT training program includes the following features: a) Choice of research advisors from over 2 dozens of participating training faculty across engineering and the brain sciences; b) Joint faculty mentoring and team advising of dissertation research; c) New neuroengineering curriculum; d) Lab rotations in engineering and basic/clinical brain sciences labs; e) Industrial internship rotations; f) Generous stipend ($30,000/year for two years on IGERT program) and tuition coverage. Trainees must be U.S. citizens or permanent residents who have been admitted to one of the four participating University of Minnesota doctoral programs: Biomedical Engineering, Electrical Engineering, Mechanical Engineering, and Neuroscience. For more information on this highly selective training program and how to apply, please visit the program website at http://www.igert-ne.umn.edu/

The IGERT training grant proposal was initiated from the CNE faculty meeting held during the Annual Symposium in February 2010. A number of center faculty participated in the IGERT program, with Dr. Bin He as the PI and Drs. Tim Ebner, Matt Johnson, Kamil Ugurbil and Jerry Vitek as the Co-PIs. Medtronic, Inc. and St. Jude Medical, Inc. are industrial partners on practical training of IGERT fellows. The IGERT program is NSF's flagship training program, which is aimed at transforming the nation's graduate education and research training. The IGERT award is timely and will provide opportunities to transform neuroengineering graduate education and research training, and further enhance the quality and visibility of neuroengineering activities at the University of Minnesota.

Message from Director

DIrector, Bin He, PhD

Faculty of the Center for Neuroengineering are continuously striving for excellence in interdisciplinary research as well as graduate training in neuroengineering. A major initiative in which many center faculty members participated was the NSF IGERT (Integrative Graduate Education and Research Traineeship) training grant. The successful application of IGERT - NSF's flagship training program - in the area of systems neuroengineering represents peer recognitions of our vision and activities of CNE, the quality of faculty and students, and the graduate programs of the University of Minnesota. The intellectual themes we have organized in the IGERT proposal strongly reflect the strengths of the CNE faculty research as well as the significance of emerging areas in neural decoding, neural interfacing and neuromodulation. We hope the IGERT award will be one step further towards our goal to establish CNE as a center for excellence in neuroengineering research and training at a national and global scale. In addition to the NSF IGERT award, you will also find the exciting news of a new NIH/NINDS Center Grant and two equipment initiative grants of UMN led by CNE faculty, as well as exciting research discoveries by CNE faculty and their groups.

Neuroengineering Annual Symposium Scheduled for February 16, 2012

The next Annual Symposium for the Center for Neuroengineering will be held in Coffman Union on February 16, 2012. The last Annual Symposium held on Feb 2011 attracted over 170 faculty, staff, students, and industrial colleagues. The Annual Symposium is a free event and will consist of CNE faculty presentations and student/postdoc poster sessions. E-mail to cne@umn.edu with your full name and institution/department if you plan to attend.

Ebner and Colleagues Receive NIH/NINDS Center Core Grant

The recently funded P30 Institutional Center Core grant is an exciting opportunity to enhance basic and translational neuroscience research at the University of Minnesota. This five-year, $3,750,000 award from the National Institute of Neurological Disease and Stroke will provide core research facilities with a focus on the use of mouse models to study neurological diseases. Drs. Tim Ebner (CNE faculty and Neuroscience Department Head) and Harry Orr (ITN Director) are the co-directors of the new Center. The cores provide a range of services and techniques to our neuroscience investigators. The overall goal is to increase productivity, promote new research directions, and foster collaborations among neuroscientists on campus. The three Cores are: 1) Genetic Manipulation (Co-Directors: Drs. Harry Orr and Lorene Lanier), 2) Behavioral Phenotyping (Director: Dr. Mark Thomas), and 3) Imaging and Tract Tracing (Co-Directors: Drs. Tim Ebner, Glenn Giesler and Paul Mermelstein). The Genetic Manipulation Core uses the newest technology to generate mouse models, which is a major tool used to study neurological diseases. This core also produces viruses that can deliver genes to the nervous system, a powerful technique that can be used to manipulate the nervous system of any species and test new therapies. The Behavioral Phenotyping Core vastly expands the capability and throughput capacity for evaluating behavior in mice, including sensory, motor and cognitive functions. The Imaging and Tract Tracing Core provides investigators with expertise in optogenetics in the central nervous system, dye tracing methods with histological preparation of mouse nervous system tissue, and modern optical imaging tools. Each core provides services and tools that few laboratories can provide individually. Neuroscientists in a variety of departments are already using the facilities. The Cores are located at various locations in the Medical School to best serve the user base, including the Wallin Medical Biosciences Building and the newly-remodeled first floor of Jackson Hall. The latter was made possible by a $3.4 million grant from NIH. The Institutional Center Core grant came at an ideal time, with major investments in advanced imaging tools. Two other recent grants, a $5.4 million Infrastructure Investment Initiative and a $1.4 million Minnesota Partnership grant will be used to provide state-of-the-art optical imaging systems for our neuroscience researchers. This includes a super resolution microscope, making the University of Minnesota one of only a handful of research institutes in the world with the technical capability to visualize individual proteins. The combined effect of the Institutional Center Core grant and the investments in imaging will make it possible for our researchers to tackle the most pressing and important problems in neuroscience.

Engel and Colleagues Receive I3 Major Equipment Grant for New 3.0 T MRI

CNE faculty member Steve Engel (Psychology) and colleagues have received an Infrastructure Investment Initiative grant of $1.5 million to acquire an additional 3.0 Tesla MRI (Magnetic Resonance Imaging) system. MRI is now a critical research tool for cutting-edge research in many disciplines at the University of Minnesota. Its use has expanded from fields that have traditionally valued neuroimaging data, such as psychology, neuroscience, psychiatry, radiology, and child development, into a host of other domains, including economics, political science, public health, and even design. The University of Minnesota has been a pioneer in MRI research with a variety of labs pursuing active research using the MRI scanner. The current 3.0 T MRI scanner has been heavily used by a number of investigators - making scheduling highly competitive. The new 3.0 T MRI scanner will greatly enhance the ability of investigators on campus to pursue basic and applied neuroscience as well as neuroimaging research. Dr. Steve Engel serves as the PI of the grant, with Drs. Kelvin Lim, Cheryl Olman, John Sullivan, Kathleen Thomas, and Bin He as the Co-PIs.

University of Minnesota

Nick and Colleagues Research Brain Connectivity

Although cellular and molecular factors have been linked to human disease, a large gap remains in understanding how genes and events at the cellular level produce complex behaviors. Specifically, how neurons work together in networks to process sensory information, store information for later use, and organize movements is not well understood. A stumbling block has been the inability to identify the same types of neurons from preparation to preparation in vertebrate recordings. To begin to address this problem and bridge a significant gap in neuroscientific knowledge, Nancy Day and colleagues in CNE faculty member Teresa Nick's (Neuroscience) lab have developed a method to record many neurons while at the same time identifying a subset based on their projection patterns. They combined two established techniques, multi-electrode (tetrode) recording, which enables the simultaneous recording of many neurons, and antidromic stimulation, which enables the identification of neurons by the location-specific stimulation of their axons. They found that corticocortical and corticostriatal principal neurons could be reliably identified in a songbird brain area, which is used for both sensory processing and motor control. As proof-of-concept, they showed that both types of principal neurons fire action potentials in population bursts that are characteristic of the neural song system, suggesting that near simultaneous signals are sent to diverse brain areas. This work was recently published in the Journal of Neurophysiology.

Parhi, Netoff and Colleagues Advance Seizure Prediction Research

CNE faculty member Keshab Parhi (Electrical and Computer Engineering) and Tay Netoff (Biomedical Engineering) started collaborating on seizure prediction about three years ago. Parhi was interested in combining machine learning with signal processing features to design classifiers for biomedical problems. Netoff, a neuroscientist, was looking for a classifier for predicting seizures. Their collaboration with Electrical Engineering Ph.D. student Yun-Sang Park and MSEE student Lan Luo led to some unexpected results in predicting seizures. A paper from the group was recently published in Epilepsia as a cover article. This paper shows that out of 80 seizures among 18 patients in the commonly used Freiburg database, 78 could be predicted using bipolar or spatial-differential processing of the EEG signals with only 1 false positive every 4 hours. This paper applied machine learning approaches in a rigorous way based on the double cross-validation approach using a support vector machine (SVM) classifier. While the SVM classifier does not make use of any temporal processing, this weakness was overcome by using a second order Kalman filter to filter the decision variable output of the SVM classifier. The post-processing filter is the key to reducing the number of false positives. This work further suggests the promise of potentially predicting seizures from electrophysiological recordings.

Redish and Colleagues Publish Paper to Nanomedicine

CNE faculty member Dr. A. David Redish (Neuroscience) and his recent PhD graduate Dr. John Ferguson (Biomedical Engineering), along with an interdisciplinary team of colleagues (Joshua Puhl, Tyler Stigen, Jadin Jackson, Kevin Crisp, Karen Mesce, and Tay Netoff), have recently published a paper in Nanomedicine entitled "Nanowires precisely grown on the ends of microwire electrodes permit the recording of intracellular action potentials within deeper neural structures". This paper describes a new method of fabricating nanoelectrodes for intracellular neural recordings. The authors also used the nanoelectrodes to record intracellular action potentials in a rat brain slice preparation and in isolated leech ganglia. These novel nanoelectrodes have the potential to revolutionize intracellular recording technology and applications.

Faculty Spotlight
Taner Akkin, PhD

Dr. Taner Akkin, a CNE faculty member and Assistant Professor in the Department of Biomedical Engineering, developed optical techniques for 3D visualization of the nerve fiber tracts in the brain, and for depth resolved detection of neural action potentials.

Dr. Akkin's group, in collaboration with Dr. Tay Netoff's group and Dr. Aviva Abosch, and with support from the Institute of Engineering in Medicine, recently published a research article in NeuroImage that showed brain anatomy and nerve fiber orientation with an unprecedented level of detail. The optical imaging technique - multi-contrast optical coherence tomography - was also developed in Dr. Akkin's Biomedical Optics Laboratory. This technique is capable of generating depth-resolved images of reflectivity, phase retardance/birefringence, optic axis orientation and, for in-vivo studies, blood flow - all simultaneously. This technique works in reflection-mode and allows serial block-face imaging for large samples. In this study, Dr. Akkin's group demonstrated that imaging with retardance and axis orientation contrasts is valuable for distinguishing between white matter and gray matter in the brain, and for visualizing nerve fiber tracts that are as small as a few tens of micrometers (Fig. 1). Derived from the polarization property of light, these contrasts provide a significant level of signal for the white matter, which consists mostly of myelinated axons that are known to be birefringent. This optical tractography technique has the potential to co-validate diffusion tensor magnetic resonance images (DTI), a study that is underway. It can also contribute to the understanding of brain disorders, such as schizophrenia and autism, in which abnormal connectivity presumably plays a major role. Moreover, development of an endoscopic device that can discern white matter, grey matter and blood vessels in the brain would be a benefit to neurosurgical interventions, which include optimal placement of deep brain stimulation (DBS) electrodes for the treatment of conditions such as Parkinson's disease and Dystonia. These tasks are certainly challenging, but at the same time within reach of Dr. Akkin's optical fiber-based imaging technology.

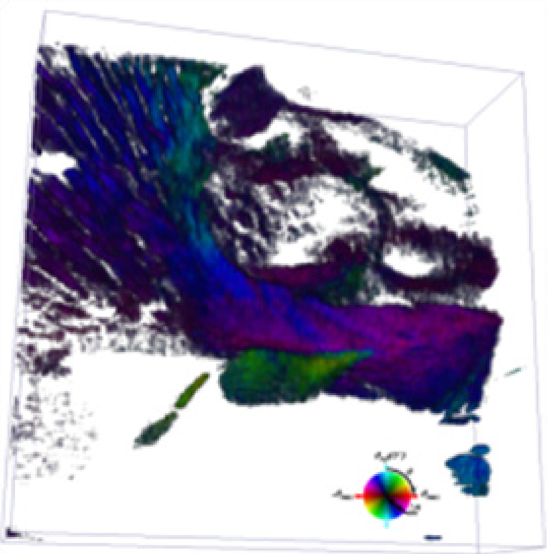

Fig. 1: The 3D optical tractography of a rat brain section (6×6×0.45 mm3). Colors indicate axis orientations, and birefringence controls the brightness of colors (from Wang et al., NeuroImage 58: 984-992, 2011).

In addition to his recent publication in Neuroimage, Dr. Akkin has recently received an R01 grant from the National Institutes of Health (NIH; EB012538) for a separate study on depth-resolved optical imaging of neural action potentials (APs). Together with co-investigator Dr. David Landowne (U. of Miami), the group is developing phase- and polarization-sensitive optical coherence tomography techniques and contrast enhancement methods for imaging neural activity in various preparations including squid giant axon, pike olfactory nerve, and salamander and mouse retinas. After Dr. Akkin's pioneering work on detecting APs with phase sensitive interferometry, the emerging technology of spectral-domain optical coherence tomography has allowed them to simultaneously detect AP related phase changes at various depths from invertebrate axons on a millisecond time scale (Akkin et al, J Membrane Biology 231: 35-46, 2009). Although these techniques do not require exogenous chemicals, the group demonstrated that axons stained with voltage-sensitive infrared dyes produce significant change in the local back-scattered light intensity around the membrane during AP propagation (Akkin et al, Frontiers in Neuroenergetics 2:22:1-10, 2010). The method will be developed for measuring and localizing APs (as a depth-resolved optical voltmeter) with high spatiotemporal resolution. Moreover, their novel polarization sensitive imaging systems present exceptional sensitivity that may allow for imaging compound APs without dyes, and the near infrared techniques are applicable for imaging layer-specific retinal activity (opto-retinogram). With further investigation, results from Dr. Akkin's group could open a new era in functional imaging technology to localize neural activity at different depths in situ. If the functional and dysfunctional neural regions are imaged selectively, the methods may lead to early detection of neural diseases.

CNE Co-Organized UMN-SJTU Bilateral Workshop

A group of CNE faculty (Wei Chen, Kelvin Lim, Geoff Ghose, Bin He, Sheng He, Matt Johnson) participated in a two-day bilateral workshop with neuroengineering faculty from Shanghai Jiaotong University (SJTU), in Shanghai, China. Six faculty from each institution gave presentations on neural decoding and imaging, neural interfacing, and neuromodulation. Intensive discussions were held between UMN and SJTU faculty on subjects of mutual interest. Topics included research collaboration and potential exchange for graduate students and visiting scholars in the field of neuroengineering. SJTU is one of China's leading universities, with the College of Engineering ranked among the top three engineering schools in China, and has about ten affiliated hospitals. SJTU has the second oldest biomedical engineering program in China, which was recently ranked second by the Chinese Government. Many SJTU BME faculty - including its Executive Dean who was a tenured faculty member in Purdue Engineering School – were trained or worked in the United States before returning to SJTU. The workshop was co-organized by CNE with partial financial support from the Institute of Engineering in Medicine and Institute of Translational Neuroscience.

Flying High With Brain Waves: SEE Innovation

The work of CNE faculty member Bin He (Biomedical Engineering) and his colleagues on BCI (brain-computer interface) was recently featured in the National Science Foundation (NSF) highlights on the Science, Engineering & Education (SEE) Innovation website. The NSF highlight describes how Dr. He's research team developed a unique BCI that allows humans to control a virtual helicopter in real time, using only their imaginations. Using electrical signals recorded from the scalp to control the flight of the helicopter, the BCI experience occurs in three dimensions. Such BCIs provide individuals with nervous system disabilities and spinal cord injuries with the opportunity to enhance their quality of life by controlling their environment and participating in society. This research was recently published in the Public Library of Science (PLoS ONE) which was featured by news medias including ABC News, Washington Post, Scientific American, and Economist . Other contributors to the PLoS ONE article include Alex Doud, JP Lucas and Marc Pisansky.

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