Neurophotonics

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Brain Mapping and Therapeutics

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This special section of *Neurophotonics* evolved from a shared interest between SPIE and the Society for Brain Mapping and Therapeutics (SBMT)[1] in advancing the ways in which photonics can be applied to the understanding of the physiological structure and function of the brain and improving the diagnosis and treatment of brain disorders. The collection of papers presented here captures some of the multidisciplinary work in these areas that is typical of what is presented at SBMT annual meetings.

We are pleased to present an excellent collection of papers including overviews of the field and original research with cutting edge data and technological innovations. The common

[1]The Society for Brain Mapping and Therapeutics (SBMT) is a non-profit society organized for the purpose of encouraging basic and clinical scientists who are interested in areas of brain mapping, engineering, stem cell, nanotechnology, imaging and medical device to improve the diagnosis, treatment and rehabilitation of patients afflicted with neurological disorders. The society promotes the public welfare and improves patient care through the translation of new technologies/therapies into lifesaving diagnostic and therapeutic procedures. The society is committed to excellence in education and scientific discovery and achieves its mission through multidisciplinary collaborations with government agencies, patient advocacy groups, educational institutes, and industry as well as philanthropic organizations.

theme in this collection is the interaction of technology, engineering, and science to further our understanding of the brain as a fundamental science and to work together toward treating, curing, and perhaps preventing neurological disease and disorders.

The number of neural connections in a cubic millimeter of the human brain has been compared to the number of stars in the Milky Way. What we know about the universe changes every day as astronomers use more and more powerful telescopes and sensors, but the idea is intriguing. The human brain with its hundred billion neurons and hundred trillion connections rivals the cosmos in sheer complexity, and the future of neuroscience will certainly depend on multidisciplinary approaches and advances in technology.

The paper by Segev et al. takes the complexity head on. Optogenetics has enabled optical activation and suppression of specific neuronal activities, but the field has been hampered by fundamental limitations posed by light scattering in neural tissue which prevent deep brain stimulation. Segev et al.'s innovative approach seeks to overcome this significant limitation by developing neurophotonic probes that take advantage of integrated nanophotonics and microelectromechanical systems (MEMS). The paper demonstrates the delivery of complex illumination patterns deep within brain tissue using these mass-producible ultranarrow silicon-based probes. Inspired by the revolution in silicon microelectronics, the authors argue that large-scale integration of such neurophotonic probes is necessary to understand the complexity of the human brain.

Visualization of neuronal activity *in vivo* is of great importance for understanding brain functions. Localizing neural activities is a critical step in understanding the functional characteristics of neuronal interactions in the brain. Light scattering as a challenge and opportunity for this visualization has been discussed in the paper by Tang et al. as a review of laminar optical tomography (LOT) which is based on light transport in tissue. While scattering, absorption, and fluorescence are the primary processes of light transport in tissue, scattering is the prevalent phenomenon for this *in vivo* imaging. By detecting the emerging light for a range of positions with different source–detector separations, it is possible to perform depth-resolved imaging of subsurface tissue structures through a proportional relationship between the source–detector separations and the average investigation depths. The detection geometry used in LOT allows collection of information from a relatively shallow depth (millimeter or mesoscopic scale), enabling higher resolution tomographic imaging.

Neurofeedback-based learning studies have been performed using real-time analysis of brain signals with various neuroimaging techniques to enable self-regulation of brain function. Electroencephalography (EEG) has been used since the 1960s as a way of providing feedback to allow control of brain activity. Neurofeedback has since been extended to other neuroimaging techniques, such as functional near-infrared spectroscopy (fNIRS) to take advantage of better spatial resolution source location accuracy, smaller instrumentation footprint, and ease of use of optical-based neuroimaging techniques when compared with functional magnetic resonance imaging (fMRI). Liu et al. have used fNIRS in a proof of concept human subject study. Impaired facial processing may contribute to social dysfunction in certain individuals with autism spectrum disorder (ASD). Prior studies show that EEG-based and fMRI-based neurofeedback might help some individuals with ASD learn to modulate regional brain activity and thus reduce symptoms. This paper reports on the feasibility of employing fNIRS-based neurofeedback training in children with ASD. In another paper, Kashou et al. use fNIRS in a study to elucidate functional developmental processes in the newborn brain with reference to the effects of somatic stimulation and to assess the feasibility of NIRS in the clinical intensive care unit setting.

Three papers in this special section relate the use of the eye-brain connection for neurofeedback, for understanding the disease and abnormality, and ultimately for understanding the brain, and for therapeutic purposes: Hu et al. study age-related macular degeneration through special analysis of retina in three-dimensional spectral-domain optical coherence tomography (OCT) images, while Makarov et al. offer a fundamental and quantum-mechanics basis of understanding the transparency of certain cells by studying the retinal cell transparency through their quantum mechanics (QM)-based model. Zelinsky and Feinberg used EEG to investigate cortical effects from wearing therapeutic eyeglasses, hypothesizing that they can create measureable changes in EEG. Their hypothesis is based on the idea that the brain is equipped with a complex system for processing sensory information, including retinal circuitry comprising part of the central nervous system. Retinal stimulation can influence brain function via customized eyeglasses at both subcortical and cortical levels.

Gottschalk et al. discuss the importance of visualization of whole brain activity during epileptic seizures as fundamental for both understanding of the underlying disease mechanism, as well as the development of treatment strategies. They further present the challenge of studying deep brain neural activity with the existing functional neuroimaging methods due to lack of adequate resolution and low penetration into subcortical areas. The authors use temporal correlation between the real-time volumetric optoacoustics imaging and electrophysiological recordings of the whole-brain responses as functional neuroimaging. The authors use this technique's ability to noninvasively visualize real-time thalamo-cortical activity inducing epileptic seizures in mice.

Precise delineation of normal tissue from tumor tissue for a complete resection of brain tumor mass is a significant challenge in neurosurgery. In a review paper, Vasefi et al. discuss various optical and thermal imaging as potential techniques for cancer diagnosis in neurosurgery. They discuss OCT, thermal infrared imaging, and various fluorescence-based imaging while correlating the advancement of the brain mapping field with the advances in optical technologies. C. J. Liu et al. use a serial optical coherence scanner, which integrates a vibratome slicer and polarization-sensitive OCT for *ex vivo* imaging for visualization of the mouse cerebellum and adjacent brainstem. The scanner provides intrinsic optical contrasts to distinguish the cerebellar cortical layers and white matter. Images from serial scans reveal the large-scale anatomy in detail and map the nerve fiber pathways in the cerebellum and brainstem. They show high-resolution tiled images for delineation of fine structures in the cerebellum and brainstem by incorporating a water-immersion microscope objective. Huang et al. present a review of use of a specific fluorescence technique for tumor surgery. In their paper, they discuss aminolevulinic acid (ALA)-mediated exogenous fluorescence of protoporphyrin IX (PpIX) as a sensitive approach for tumor imaging. This review paper highlights the challenges and progress in PpIX-mediated fluorescence-guided resection.

The last two papers in the collection show the power of imaging as an intraoperative guide during neurosurgery. In the first paper, a review of long-wavelength infrared imaging with quantum well infrared photodetector or QWIP arrays—originally developed for space-based observation—Khoshakhlagh and Gunapala describe how their uniform and high-resolution images can provide an additional tool for neurosurgeons in delineating tumor cells. Bae et al. describe the innovation of 4-mm diameter stereoscopic imaging endoscope with tilt control that is based on a single CMOS camera for minimally invasive brain tumor surgery. In addition to use of photonic imaging as intraoperative tools, these two papers are examples of space technology for neurophotonics and intraoperative neurosurgery.

In accepting the 2015 SBMT Beacon Award, Stephen Hawking, the preeminent cosmologist and amyotrophic lateral sclerosis (ALS) patient, stated, “I have spent my life thinking about the universe, its inception, its destiny, its seeming anomalies and how it can all be explained. Understanding one’s own brain is ... a different type of challenge... and it is hard to emphasize enough how important technology can be in diagnosing and treating neurological diseases.” We agree. We hope that you enjoy this special section.

Shouleh Nikzad, **PhD**, is a senior research scientist, principal engineer, co-lead, and technical director for JPL’s Medical Engineering Forum, and lead for Advanced Detectors, Systems, and Nanoscience at NASA’s Jet Propulsion Laboratory, California Institute of Technology. She holds visiting faculty and lecturer appointments including at Caltech’s Medical Engineering Department as well as the Division of Physics, Math, and Astronomy. She has held visiting scientist positions at USC Keck School of Medicine and Cedars-Sinai Medical Center Neurosurgery Department. She is a Fellow of the American Physical Society, a Fellow of SPIE, president of SBMT (2014-2015), and recipient of the 2013 Pioneer in Medicine award of SBMT. Her research focus is on developing novel UV/visible/NIR photonics technologies, imagers, and instruments for astronomy, planetary and Earth observation space applications, and their spinoffs into medical applications. Dr. Nikzad received her PhD from Caltech in applied physics, MSEE from Caltech, and BSEE from USC.

Yu Chen, **PhD**, is an associate professor at the University of Maryland in College Park, Maryland. He received his bachelor’s degree in physics from Peking University, China, in 1997 and his Ph.D. in bioengineering from the University of Pennsylvania in 2003. His research interests include optical coherence tomography (OCT), laminar optical tomography (LOT), multiphoton microscopy (MPM), development of novel quantitative optical sensing and imaging devices for clinical translation, and preclinical and clinical applications of optical technologies in imaging brain function, renal physiology, cancer therapy, and tissue engineering. He received the NSF CAREER Award in 2012. Dr. Chen has been an associate editor of *Medical Physics* and a guest editor of *IEEE Journal of Selected Topics on Quantum Electronics* and the SPIE journal *Neurophotonics*. He is a member of IEEE, SPIE, and the Optical Society of America (OSA) and has served as conference program chair and general chair for the OSA Conference on Lasers and Electro-Optics (CLEO): Applications and Technologies. He is member of the board of SBMT and co-editor of the textbook *Neurophotonics and Brain Mapping*.

Vassiliy Tsytsarev, **PhD**, obtained his Ph.D. in neuroscience from Saint-Petersburg State University in Russia. Soon after graduating he moved to Japan and started work in the Brain Science Institute of RIKEN, and the Human Brain Research Center, Kyoto. After seven years in Japan he moved to the United States and is now working in the University of Maryland. Functional brain mapping, neural circuits, and different types of brain optical imaging are his main scientific interests. In Japan, he worked in the field of auditory neuroscience using intrinsic optical imaging and voltage-sensitive dye imaging of the brain activity, at the same time being included into the fMRI team. After moving to the U.S., he switched to the somatosensory cortex, while maintaining interest in new methods of brain imaging. He is currently focusing on functional brain mapping, epileptic studies, and neural network functioning of the rodent somatosensory system, a perfect object for many types of neuroscience research, including models of neural diseases. He is member of the board of SBMT and member of the science committee of SBMT.

Babak Kateb, **MD**, is a neuroscientist whose research focuses on introducing advanced diagnostics and therapeutics into clinical neuroscience to rapidly identify and treat neurological disorders such as brain cancer, Alzheimer’s disease, Parkinson’s disease, and brain and spinal disorders. He did his clinical research fellowship at the USC Keck School of Medicine and studied neuroengineering at USC Ming Hsieh Institute. Dr. Kateb is founding chairman and CEO of the Society for Brain Mapping & Therapeutics (SBMT), president and scientific director of the Brain Mapping Foundation, director of the National Center for Nano-Bio-Electronics. He collaborates with Los Alamos National Lab and had an appointment with NASA/JPL as a visiting scientist. Previously Dr. Kateb was director of R&D at the Department of Neurosurgery at City of Hope Cancer Center and a research scientist at Cedars-Sinai Medical Center, where he developed a partnership between Cedars-Sinai and NASA. He received a NASA Tech Brief Award for his pioneering work on sniffing cancer cells using NASA’s electronic nose and the 2015 SBMT Pioneer in Medicine award. He is editor of *The Textbook of Nanoneuroscience and Nanoneurosurgery*, and editor of *Neurophotonics and Brain Mapping*. Currently, he is the Scientific Director and Director of Strategic Alliance at the California Neurosurgical Institute.

Warren Grundfest, **MD**, is the past president of SBMT (2006–2007) and the recipient of the 2007 Pioneer in Medicine award of SBMT. Dr. Grundfest received his M.D. from Columbia University in 1980. He trained in General Surgery at UCLA Medical Center and Cedars-Sinai Medical Center, and joined the Cedars-Sinai Staff in 1985. In 1987 he was appointed Director of Surgical Research. In 1991 he received the Dorothy and E. Philip Lyon Endowed Chair in Laser Research and became Director of the interdisciplinary program collaborating with all branches of the institution entitled “The Laser Research and Technology Development Department.” Between 1995 and 1998 he was a Visiting Associate in Mechanical Engineering at the California Institute of Technology working on surgical robotics. Between 1994 and 1999 he was also a Research Professor of Bioengineering at the University of Southern California. In 1999 Dr. Grundfest became the Founding Chair of the Bioengineering Program at UCLA, which he helped build into a Department. He currently serves as a Professor of Bioengineering, Electrical Engineering, and Surgery at UCLA.