

SPECIAL SECTION GUEST EDITORIAL

Optics in Neuroscience

In recent years there has been a strong trend to enhance traditional research techniques in neuroscience with optical-based techniques. The trend is evident on every level of neuroscience research, spatially spanning submicron to centimeters and temporally spanning submillisecond to seconds. Optical techniques are attractive because they enable researchers to study brain function from the smallest functional unit, ion channels in small patches of excitable membranes, to its largest unit, monitoring the correlates of cognitive activity in the human brain. Another major advantage of optical imaging methods is that in most cases using light as a probe enables the researcher to study the neural tissue without any direct contact; being noninvasive to the tissue is especially important in *in vivo* studies. Finally, most optical research is performed with compact, mobile, and affordable equipment that can be readily integrated in existing research facilities.

The aim of this special section is to give the readers a state-of-the-art report on the current status of optical techniques in neuroscience and their applications. For various reasons, the gamut of optical techniques could not be represented here and this section has a heavier representation of techniques for noninvasive monitoring of human brain activity. Nevertheless, we hope that the readers will find their interest covered by these papers.

The first paper is a review by Demuro and Parker on optical single channel recording. This is an exciting example for the growing superiority of optical techniques. Single channel recordings have been dominated in recent decades by the “patch-clamp” recording technique, a very successful technique that revolutionized the study of single channels and was acknowledged by a Noble prize to its inventors. However, patch-clamp recording has its limitations: it can only probe one channel at a time, and the pipette used for recording has to create a strong seal around the membrane, which can damage the probed tissue. Demuro and Parker demonstrate that one can record from a channel (albeit with weaker temporal resolution) by using optical recording techniques without damaging the tissue. Furthermore, their optical techniques enable them to record from up to hundreds of channels simultaneously, enabling the study of the spatiotemporal characteristics of many channels. In other words, optical techniques enable research to move from a single channel focus to a population focus, providing obvious advantages.

Electrodes are typically used to either record or stimulate the neuronal tissue, and the move from electrodes or pipettes to optical methods is also evident in the next paper. Kötter et al. describe how optical techniques can be successfully used for precise stimulation of cortical tissue by using light to release the caged neurotransmitter glutamate and by measuring the effects of the release within cortical networks. The authors use a combination of experimental results and modeling to highlight the advantages of this technique for elucidating functional networks in the cortex.

Guiou et al., using a combination of intrinsic signal optical imaging and field-potential measurements, report on the disruption in the process of neurovascular coupling and cerebral blood volume related to the phenomenon of cortical spreading depression—a pronounced depolarization of neurons and

glia that spreads slowly across the cortex followed by a period of depressed electrophysiological activity. The use of intrinsic signal optical imaging—an optical method that is based on measuring activity-induced reflection changes from the illuminated brain—enables the researchers not only to image patterns of cortical activity *in vivo* with high spatial and temporal resolutions, but also with the use of the right filters to extract additional results on cerebral blood volume changes and neurovascular coupling. Quantification of the blood volume and hemoglobin concentration changes requires accurate knowledge of the photon path length through the cortical tissue. Yokoyama et al. describe a novel approach for estimating the spectral dependence of this path length factor from the temporal variance of the spectral measurements. As discussed by Okui and Okada, inaccurate knowledge of these path length factors can cause cross-talk in the estimate of the hemoglobin concentrations. These works are important steps towards obtaining greater quantitative accuracy in the estimation of the physiological parameters.

The next two papers examine the use of novel technologies for diagnosing the diseased brain. Bizheva et al. utilize ultra-high-resolution optical coherence tomography to characterize the signatures of healthy and diseased brain tissue. Their initial results in *ex vivo* tissue samples demonstrates that optical coherence tomography has the ability to visualize and identify morphological features such as microcalcifications, enlarged nuclei of tumor cells, small cysts, and blood vessels. This technology could ultimately prove useful during brain surgery to identify tumor boundaries for conservative resection. Skoch et al. discuss the development of near-infrared fluorescence imaging for detecting amyloid- β peptide in the brain associated with Alzheimer's disease. The advancement of such a molecular imaging approach would serve an important role in the diagnosis of Alzheimer's disease as well as guide treatment.

The remaining seven papers address the use of near-infrared spectroscopy (NIRS) for measuring brain function and cerebral oxygenation utilizing continuous-wave, frequency-domain, and time-domain methods. Gratton et al. provide a review of their recent results in noninvasively measuring neuronal signals and the resultant hemodynamic response. They confirm the cerebral origin of the hemodynamic response with simultaneous optical and functional magnetic resonance imaging (fMRI).

An exciting application for NIRS of brain function is in the study of the developing infant brain, since this population is not easily studied with fMRI or positron emission tomography (PET). In addition, NIRS could complement electrically evoked responses measured by electroencephalography (EEG) that are currently being used to study the developing brain. NIRS could give access to the hemodynamic response to a stimulus and enable the design of behavioral experimental paradigms that do not lend themselves well to EEG. The pros and cons of NIRS for studying brain correlates of perceptual, cognitive, and language development in human infants is reviewed by Aslin and Mehler. Wilcox et al. illustrate the potential for NIRS in this field of research by measuring hemodynamic responses associated with an infant's ability to differentiate objects of different shapes and colors through the

activity in the inferior temporal cortical region associated with the behavior of object differentiation.

The hemodynamic responses to brain activation will evolve with the behavioral maturation of an infant. In addition, the hemodynamic responses will also change as the baseline blood volume, blood flow, and metabolism of the infant brain develops. These baseline parameters vary significantly over the first years of human life. Thus, accurate quantitative interpretation of the hemodynamic response to brain activation will likely depend on knowledge of these baseline parameters. Frequency-domain and time-domain NIRS can be used to assess these parameters. D'Arceuil et al. show, with a frequency-domain NIRS measurement, the significant developmental changes that occur in blood volume and hemoglobin oxygen saturation in a neonatal rabbit brain. The time scale of the volume and saturation changes were different, indicating differing developmental trajectories for capillary density, blood flow, and oxygen metabolism. This method applied on animal models and in human studies will lead to a greater understanding of the developing normal brain and potentially enable diagnosis of an abnormally developing brain.

The majority of brain activation studies with NIRS have used measures of the diffuse light intensity changes to discern the hemodynamic changes resulting from brain activation. Time-domain methods offer the potential for improved depth sensitivity to brain activation, as well as the ability to discriminate superficial scalp signals from the deeper brain signals. This depth discrimination has the potential to significantly improve the contrast-to-noise ratio in the estimate of the hemodynamic response by differentiating systemic physiological fluctuations in the scalp from the brain activation signal. This is shown theoretically and experimentally by Selb et al. who use a time-domain system to measure brain activation in a human adult and compare the contrast-to-noise ratio obtained

with the time-domain system to that of a continuous-wave measurement. They show that the time-domain system has a better contrast-to-noise ratio because of its theoretically superior depth sensitivity. Future advancement of this technology should increase the number of brain regions detectable by NIRS. One such example is provided in the paper by Quaresima et al., which illustrates the use of time-domain NIRS for measuring brain activity associated with letter-fluency.

Signal processing algorithms can be developed to discriminate systemic physiological signals from brain activation signals. One classic approach is to use a principle component analysis of an appropriate data covariance matrix to design a filter to discriminate components of the data with large variance. The paper by Zhang et al. examines the utility of such an approach and finds some promise in its use for improving the signal-to-noise ratio in the estimated hemodynamic response. This is an area of research that should provide significant improvement for NIRS measurements of brain activation in the near future.

We hope that these papers can serve as a snapshot of this field as of 2004. We expect rapid growth in the development and application of optical techniques in neuroscience; a bright future for the interactions of light and brain.

David A. Boas, Ph.D.

Massachusetts General Hospital
Harvard Medical School

Ron D. Frostig, Ph.D.

University of California, Irvine

Special Section Guest Editors