

Lester Wolfe Workshop in Laser Biomedicine

Neural Imaging with Optics

Tuesday, April 13, 2004 4:00-6:00 PM
Massachusetts General Hospital
Wellman 1 Conference Room
50 Blossom Street, Boston

Dynamic neural imaging is a growing field that is improving our understanding of neural structure and function from the level of single neurons to whole brain systems. This workshop will provide an introduction to this field and explore new optical methods for imaging changes in the brain.

Using Optical Microscopy to Study Synaptic Structure and Function

Venkatesh Murthy, PhD, Morris Kahn Associate Professor of Molecular and Cellular Biology, Harvard University

Low Coherence Interferometry for Noninvasive Monitoring of Nerve Signals

Christopher Fang-Yen, PhD, Massachusetts Institute of Technology

Two-Photon Imaging of Synaptic Morphology in the Visual Cortex in vivo

Ania Majewska, PhD, Massachusetts Institute of Technology

SUMMARY 4/13/2004

The meeting was devoted to a single topic, “Neural Imaging with Optics”, and was jointly sponsored by the MIT Spectroscopy Laboratory, the Wellman Center and CIMIT. The emphasis was on using dynamic neural imaging to understand neural structure and function. Venkatesh Murthy, PhD, Harvard, described “Using Optical Microscopy to Study Synaptic Structure and Function”. The mouse brain is being studied, using various

staining techniques to show synapses. The brain properties of interest include morphology, protein distribution, electrical activity, synaptic activity and the transport of calcium ions or intracellular messengers. Proteins are now relatively easy to study using transgenic mice which express green or yellow fluorescent proteins (GFP/YFP). Staining can also be achieved using genetically-encoded fluorophores. Measurements of synaptic function are now possible using pH-sensitive GFPs (synaptopHfluorins) together with confocal microscopy; fusion of vesicles can be detected via changes in pH. Two-photon fluorescence microscopy, which allows deeper optical imaging, is being used to study the mouse brain via a window model.

Christopher Fang-Yen, PhD, MIT, described the use of “Low Coherence Interferometry for Noninvasive Monitoring of Nerve Signals”. The goal is to develop an optical electrode for noninvasive long-term recording of such signals. There are a number of possible intrinsic changes in the optical properties of tissue during neural activity. These include changes in scattering, hemodynamic changes such as the changes in blood oxygen which have been detected by diffuse optical tomography and electro-optical modulation of membrane refractive index by nerve potential changes. Mechanical motion in nerves during neural activity has already been measured by atomic force microscopy; the displacements are small, 0.1-1.0 nm, but should be measurable by interferometry. A system based on a Michelson interferometer and a low coherence source has been built and is being evaluated; a number of techniques to eliminate noise due to specimen and instrument motions have been developed. Initial experiments on a lobster nerve used external electrodes to apply a stimulating voltage and measure its transmission. The optical beam from the interferometer probed the region between the electrodes and was able to detect 5 nm of displacement. Currently, the system cannot distinguish between nerve swelling and nerve bundle motion. A newer version of the system using a fiber optic probe is being developed and will be the basis of a scanning probe microscope.

Ania Majewska, PhD, MIT, described “Two-Photon Imaging of Synaptic Morphology in the Visual Cortex in vivo”. Two-photon microscopy of dendritic spines reveals Ca compartmentalization as well as transport in and out of cells. The spine structure has been shown to be very dynamic, although the function of the observed structural changes is not understood. Use of a mouse window model allows imaging over time periods as long as a week and showed that most spines were stable over that period. Initial work in a ferret model appears to show changes in spine structure in response to exposure to specific visual patterns.

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