UNIVERSITY of HOUSTON
CULLEN COLLEGE of ENGINEERING
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PhD Dissertation Announcement

DEVELOPMENT OF FLEXIBLE NEURAL PROBES FOR STIMULATION AND RECORDING IN THE CENTRAL NERVOUS SYSTEM

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The functionality of cortical neurons depends on the strength of its local and long-range synapses and the interpretation of the anatomy – physical and functional depends on the understanding of these circuits.[1] Optogenetics[2,3] uses genetic manipulations to insert opsin containing ion channels into neurons in highly localized regions of the brain. Then light can be used to optically gate ion-transport across the plasma membrane to stimulate or silence spiking activity with millisecond precision. This enables the neuroscientist to 1) determine of the frequency and strength of synaptic connections and 2) differentiate between the influences of multiple pathways between two regions (e.g. between the pulvinar and the primary visual cortex). This capability enables the mapping of neural circuits with greater cellular specificity and spatio-temporal resolution than previously possible.

While great progress has been made in the genetic methods used in optogenetics, little progress has been made in improving the devices (optrodes) used to simultaneously photostimulate and record neural activity. Currently, these devices are made by gluing microwires or electrodes to thick optical fibers[4,5]. To realize the full potential of optogenetic methods, a new type of optrode is required.

In this thesis we describe the development of a new probe concept based on the integration of micrometer-scale thin film electrodes and associated interconnect wiring on the

cylindrical surface of fine optical fibers with tight manufacturing tolerances. The use of optical fibers as probe substrates provides high intensity, multi-spectral light delivery with essentially no coupling loss, as well as the strength and stiffness required for deep-brain applications. The use of *thin film conductors* contributes negligibly to the probe diameter, *high resolution* permits a very high electrode count on thin fibers, and *high dimensional precision* enables accurate 3-D localization of neuronal sources.[6] Moreover, the technology is compatible with high throughput manufacturing at very low cost, an important consideration for wide dissemination of the technology, particularly for linear and 2D-array applications. A second crucial development is the design and implementation of a multi-electrode interface between thin-film wiring on the (cylindrical) probe and state-of-the-art common neuro-amplifier and signal processing systems.

2-channel prototypes have been fabricated and used in preliminary experiments to 1) record photostimulated neural activity in a group of genetically identified neurons in the primate primary visual cortex at the Vanderbilt University School of Medicine (VUSM) and 2) demonstrate source localization in the rat hippocampus at the Baylor College of Medicine (BCM). The prototypes had 15x15 μm^2 gold electrodes on 60 μm optical fibers with lengths up to 3 cm. Owing to a smaller diameter, they displaced about 90% less tissue than competing optrodes. In future work, we propose to further reduce probe diameter to the ~30 μm range, corresponding to an additional 75% reduction in probe volume, development of probes with advanced functionality, extend the technology to 1- and 2-D arrays.

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