Establishing the Bio-interface for Neural Electrophysiology with a Diamond Voltage Imaging Microscope

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Solution voltage imaging enables the measurement of localized electric potentials, such as those occurring at solid-liquid interfaces, across membranes, and within electrogenic biological systems. However, standard techniques such as micro-electrode arrays, scanning probes, and all-optical fluorescence methods are limited in resolution, restricted to serial imaging, and require the use of short-lived dyes respectively [1-2]. An electro-optic approach wherein optical signals are produced directly by a voltage-sensitive substrate material would overcome these limitations by providing massively parallel readout without the need for dyes or resolution-limiting electronics. We have recently reported the successful execution of such an approach by embedding fluorescent lattice defects near the surface of a transparent semiconducting diamond substrate, the surface of which is electrochemically tuned to enable quantitative, non-invasive, and photostable optical voltage imaging [3]. The practical use of this technology, which we call a diamond voltage imaging microscope (DVIM), in neural electrophysiology research now requires the realization of a robust, stable, and low-impedance interface between the diamond chip and the neural cell membrane.

Here, I will introduce DVIM technology and present some of our recent results [3] before discussing the applicability of the technology in three different regimes of electrophysiological recording: intracellular, quasi-intracellular, and extracellular. I will then focus on our progress to date in achieving stable intracellular recordings of neuronal action potentials using ordered arrays of fluorescent diamond 'nanoneedles'. With tip diameters and surface functionalities/coatings which may enable spontaneous yet non-toxic penetration of the cell membrane, these structures offer a rapid pathway toward enabling network-scale electrical recordings *in vitro* with micron resolution.

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