199b Hydrogel-Electrode Interfaces for Directed Tissue Remodeling in the Retinal Implant

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It has been suggested that a retinal implant, consisting of electrodes in contact with remaining neural structures, may be able to replace lost visual function. However, the high current and charge densities required to elicit visual perceptions limit clinical applications. These electrical requirements result in part from resistive native and scar tissues that obstruct the device from its target cells. We are examining the potential use of one type of tissue-engineered interface, composed of hydrogels, as a mechanism for improving tissue-electrode interactions in the retinal implant. Hydrogels are particularly promising in this application, as they offer several modes to reduce tissue obstruction, and thereby electrical resistance.

The hydrogel that we are investigating consists of poly (ethylene glycol) – poly (lactic acid) (PEG-PLA) copolymers and is designed to elute neurotrophins. PEG subunits were selected because they are biocompatible with retinal tissue and are non-adhesive potentially reducing glial cell attachment and scar tissue formation, both of which increase electrical resistance. PLA subunits allow for gel degradation through the slow hydrolysis of their ester linkages, providing a means of encapsulated drug release. Gel degradation also limits the possibility of electrical interference between the gel and the electrode surface. Gels are designed to release neurotrophins (e.g., brain-derived neurotrophic factor (BDNF), ciliary neurotrophic factor (CNTF)) that may attract neurites to the electrode surface, thereby reducing the electrical pathway between the electrode and its target. Our initial investigations are focused primarily on the short-term interactions (i.e., < 8 weeks) of neurites with electrode structures. Additional modifications, such as adhesive coatings, may be required to promote long-term neurite adhesion/attraction to the electrode following hydrogel dissolution.

The selected PEG-PLA hydrogels were synthesized using standard protocols and deposited on electrode surfaces using micropipettes. The hydrogels were applied as liquid precursors over the active sites of multi-electrode arrays (MEAs) and were polymerized *in situ* by UV radiation. The MEAs are comprised of 15 individually addressable, 400 mm diameter (1.3×10^{-3} cm^2) gold electrode sites coated with either activated iridium oxide (AIROF) or sputtered iridium oxide (SIROF) to increase charge injection capacity. Gels demonstrated adhesion to AIROF activated IrO_2 electrode surfaces and some surrounding polyimide insulating structures. These studies suggest that the relative degree of hydrogel precursor spreading over the iridium oxide and polyimide surfaces is controlled by altering the hydophobicity of the precursor. To examine the impact of the gel on electrode performance, gel electrical properties were characterized using cyclic voltammetry, electrochemical impedance spectroscopy (EIS), and potential transient measurements during current pulsing in buffered physiological saline at 37^oC. Gel degradation and drug release were evaluated using bovine serum albumin (BSA) as a model protein in microplate total protein assays. The final film could be designed to release a number of neurotrophins that enhance retinal survival or neurite extension. Currently, the effects of one possible neurotrophin, brain derived neurotrophic factor (BDNF), are being evaluated *in vitro* using retinal slice cultures. Ultimately, hydrogel films will be evaluated *in vivo* using histology and electrophysiology to confirm improved tissue contact and a reduction in electrical charge and current requirements.

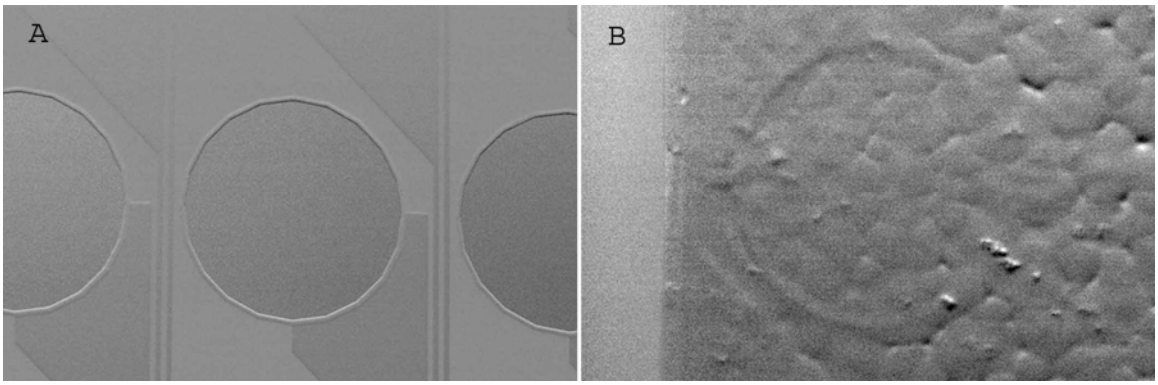

Figure 1: SEM Micrographs of 400 Micron Diameter Microelectrodes (A) Before and (B) After Hydrogel Addition.

These hydrogel films may reduce scar tissue and the distance from target neurons, thereby decreasing the electrical requirements of the retinal implant. However, this application is just one example of a broader class of tissue-engineered electrical devices capable of manipulating their environment. These devices present a method to overcome present limitations in biocompatibility and tissue interactions, expanding the reach of present prosthetic devices, implants, and biosensors.