Microchannel Scaffolds as Regenerative Peripheral Nerve Interfaces

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Statement of Purpose:

There is a great need to design neurally controlled prosthetics that cosmetically and functionally mimic amputated limbs. This remains a largely unmet clinical need because state of the art neural prosthetics provide a small fraction of the functionality of a natural limb. While the robotics side of neural prosthetics has seen many advances recently, it is the ability to read the body's neural signals and send them to the robotics that lags behind.

The *objective* of this project is to engineer a thin-film polydimethylsiloxane (PDMS) based regenerative microchannel scaffold with microelectrodes incorporated in the microchannels for the purpose of reliable, high-throughput peripheral nerve interfacing. Our *central hypothesis* is that forcing axons from an amputated nerve to regenerate through microchannels (Figure 1A) will provide intimate and isolated contact with integrated microelectrodes and facilitate more selective recording and stimulation. This abstract describes our first-stage development and characterization of implanted PDMS-based microchannel scaffolds. The goal was to assess the capability of the scaffolds to sequester regenerated axons in the microchannels and determine the filling density of each microchannel so future maturation of axons can be accommodated. In the second stage of the project, microelectrodes will be incorporated into the base PDMS layer and evaluated for the ability to record action potentials from regenerated yet compartmentalized small nerve bundles.

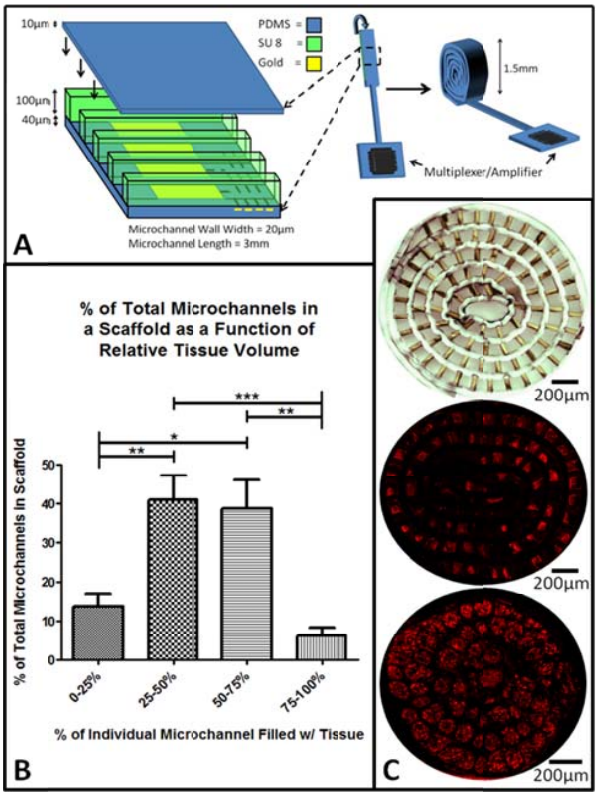
Methods:

In order to fabricate the microchannel scaffolds, a base PDMS layer was created that would house electrodes and a multiplexer/amplifier for interfacing in the second stage of the project (Figure A). Secondly, SU-8 microchannel walls (with a 100µm separation) were patterned on top using standard photolithography. A PDMS cover layer was bonded to the top of the SU-8 microchannel walls creating closed microchannels. Finally, the sheet of microchannels was rolled to form a tubular structure.

Six scaffolds were implanted in the rat sciatic nerve amputee animal model for 8 weeks, explanted, cryosectioned, and stained for axons. The scaffolds were analyzed for axon regeneration into and through the scaffold as well as the degree to which microchannels containing axons were filled with tissue.

Results:

An entrance view of a fabricated and rolled microchannel scaffold is shown in Figure C (top). A representative cross-section through the middle of an explanted scaffold stained for axons (red) is shown in Figure C (middle). Figure C (bottom) shows a representative tissue section distal to the scaffold, also stained for axons (red). Figure B depicts the average distribution of microchannels containing axons in a



scaffold as a function of the relative area of tissue in the individual microchannel. For example, approximately 5% of the total microchannels containing axons in a scaffold were more than 75% filled with regenerated tissue (right most column).

Conclusions:

In conclusion, we have developed a PDMS-based regenerative microchannel scaffold. We have verified the ability for transected axons to regenerate into and through the microchannels. Furthermore, we observed that the macroscopic microchannel morphology was retained by the regenerating nerve up to 1mm distal of the scaffold. Finally, we have demonstrated that approximately 95% of all microchannels containing tissue have at least 25% free area for future axon and tissue maturation. We believe this microchannel scaffold will be a robust, biologically stable platform through which high-throughput peripheral nerve interfacing can occur in future generations of the device.

References:

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