Optimizing the Manufacturing of Porous Poly ε-caprolactone Scaffold Conduits for Nerve Repair

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Introduction

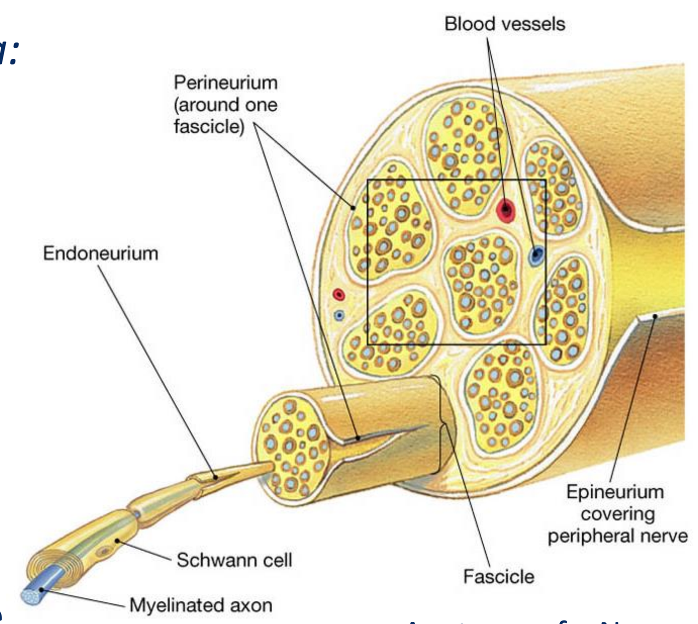
Millions suffer from nerve injury, which can have a devastating effect on a person's quality of life due to limited sensory and motor functions. Porous poly ε-caprolactone (PCL) multi-channeled scaffolds, developed in the Sakamoto lab, have recently been demonstrated to improve nerve regeneration following traumatic nerve injury, due to a 60% open volume and cellular guidance, characterized by micro-computed tomography (micro-CT). However, the micro-channels within PCL scaffolds are difficult to manufacture, because of their small dimensions and high aspect ratio (200 µm inner diameter, 60 µm wall thickness, 10 mm length). **We aim to improve the quality control of scaffold manufacturing by ensuring consistent reproducibility and we also aim to decrease the scaffold manufacturing time.**

Optimum PNS Scaffold Criteria:

1. Biocompatible
2. Stiffness and surface roughness
3. Month-long degradation rate

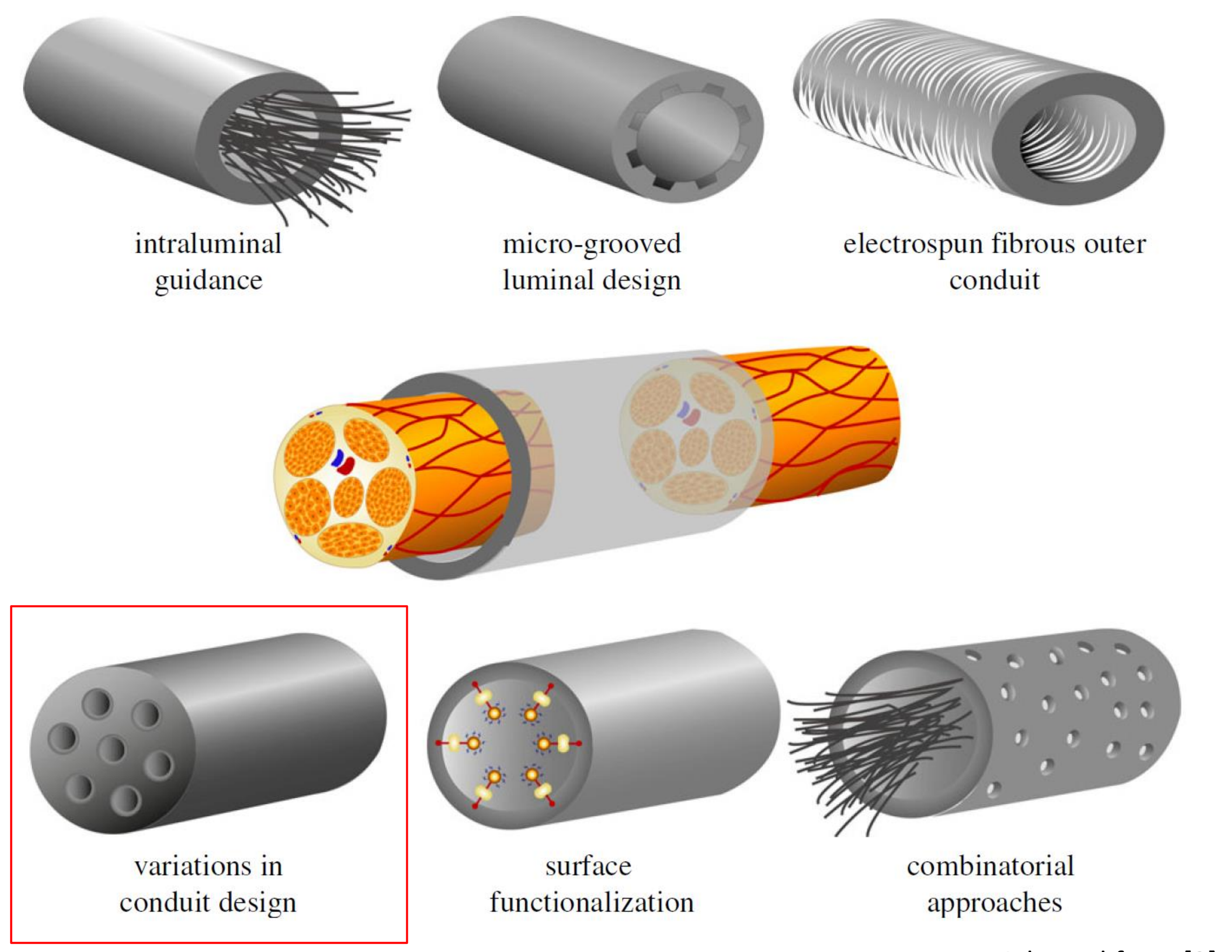
Structural Design Criteria:

1. Micro-channel diameter (20 µm to 200 µm)
2. Maximum lumen volume
3. 1 cm length

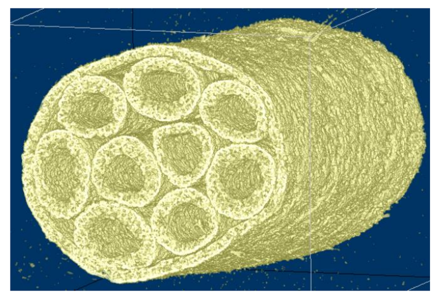


Anatomy of a Nerve
Adapted from droualb.faculty.mjc.edu

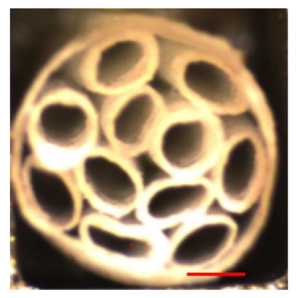
Possible Conduit Designs for Nerve Repair



Adapted from [3].

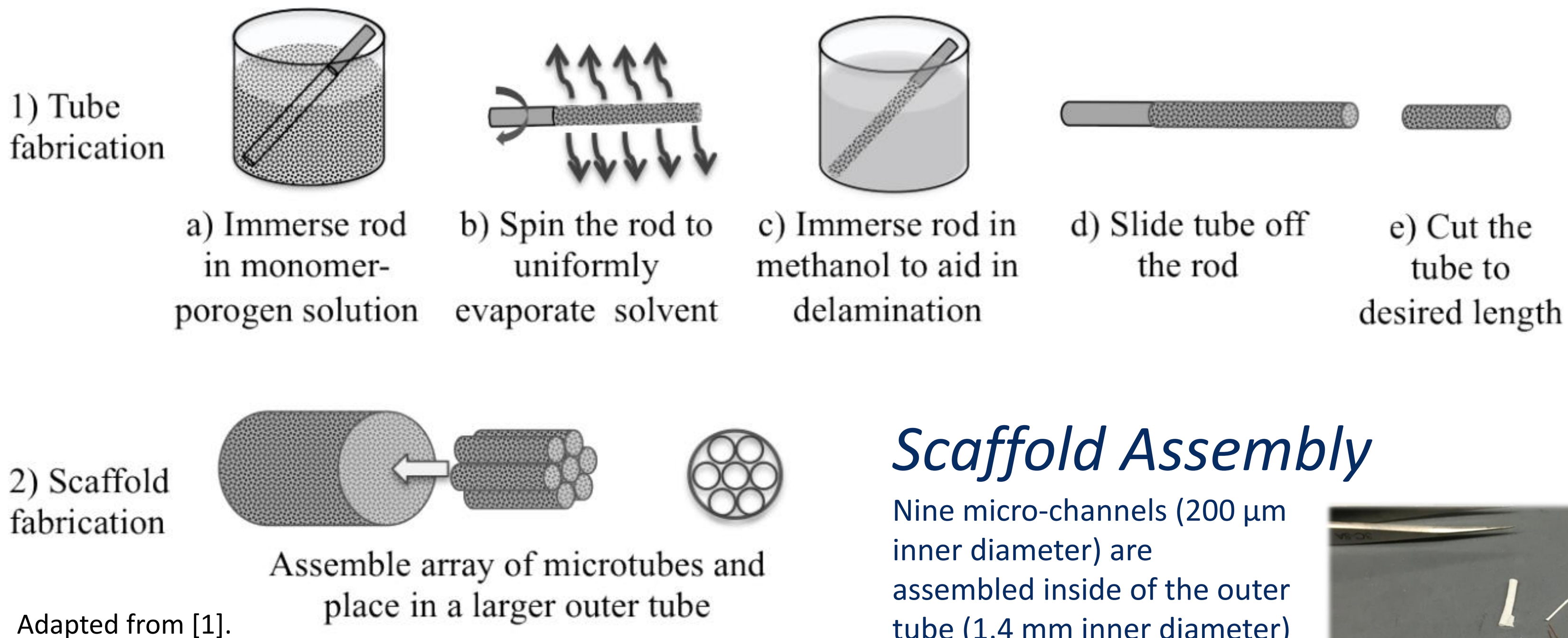


Micro-CT Image of Assembled PCL Conduit



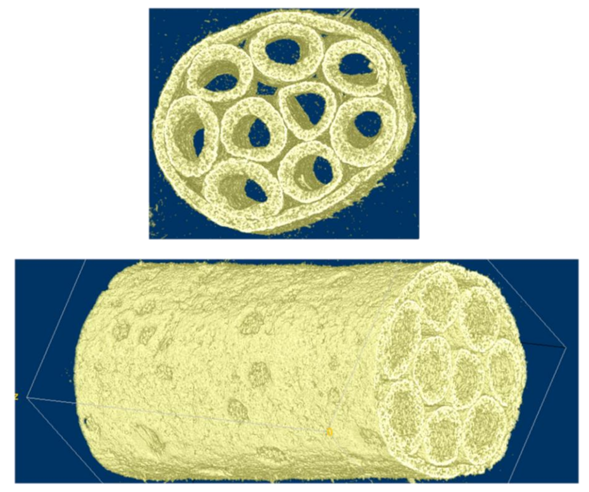
Optical image of an assembled PCL scaffold. 0.260 mm micro-channel diameter. 0.060 mm wall thickness. 70 vol% porosity. Scale bar is 0.2 mm. Adapted from [1].

Current Scaffold Manufacturing Process



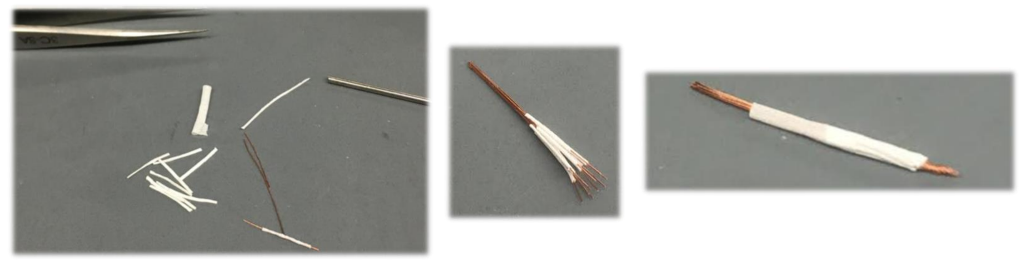
Adapted from [1].

Micro-CT Scaffold Images



Scaffold Assembly

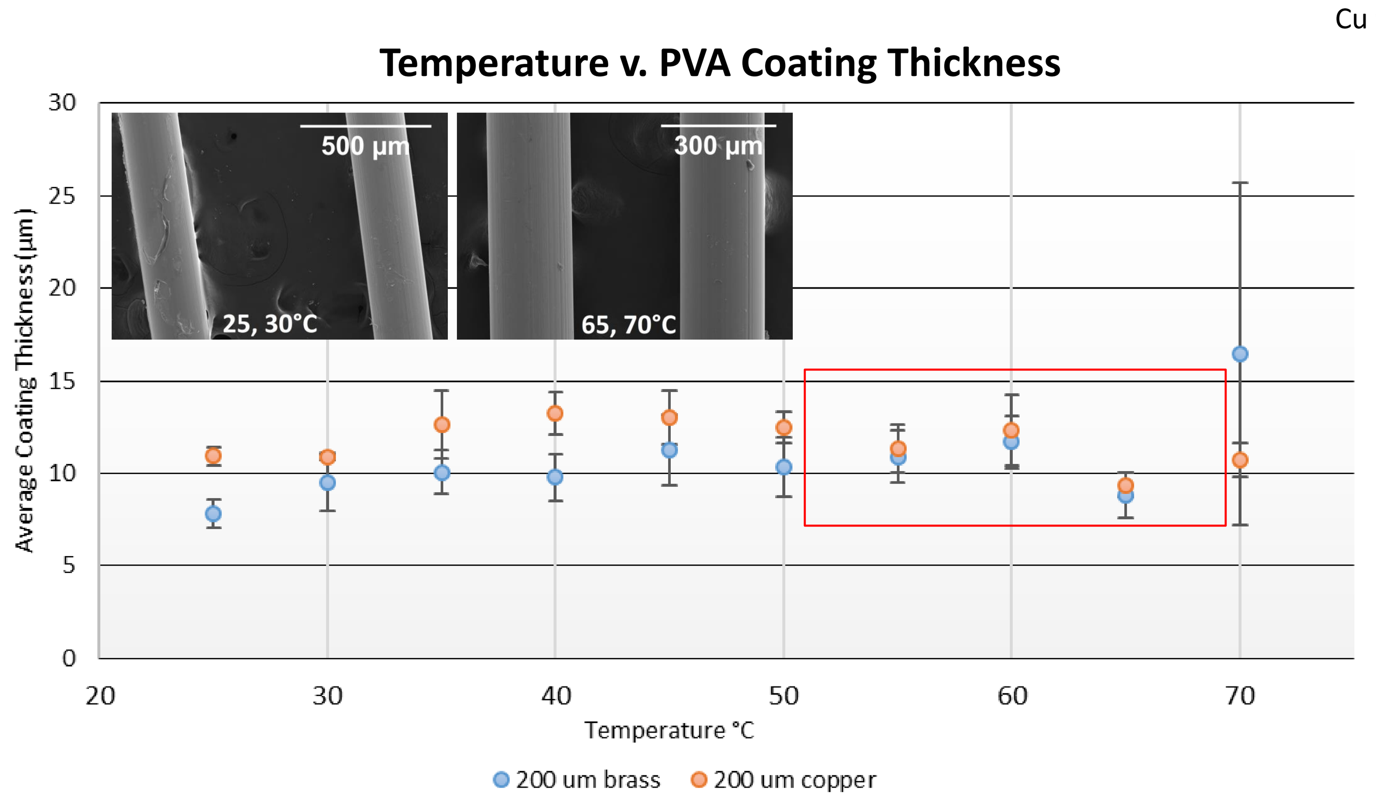
Nine micro-channels (200 µm inner diameter) are assembled inside of the outer tube (1.4 mm inner diameter)

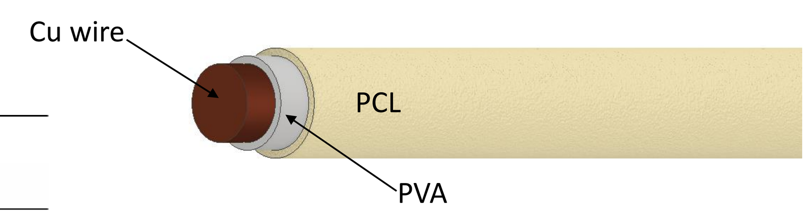


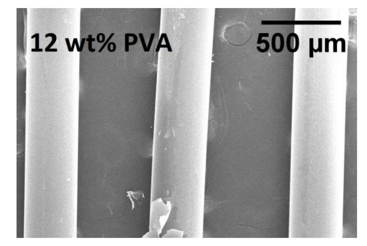
New Assembly Methods:

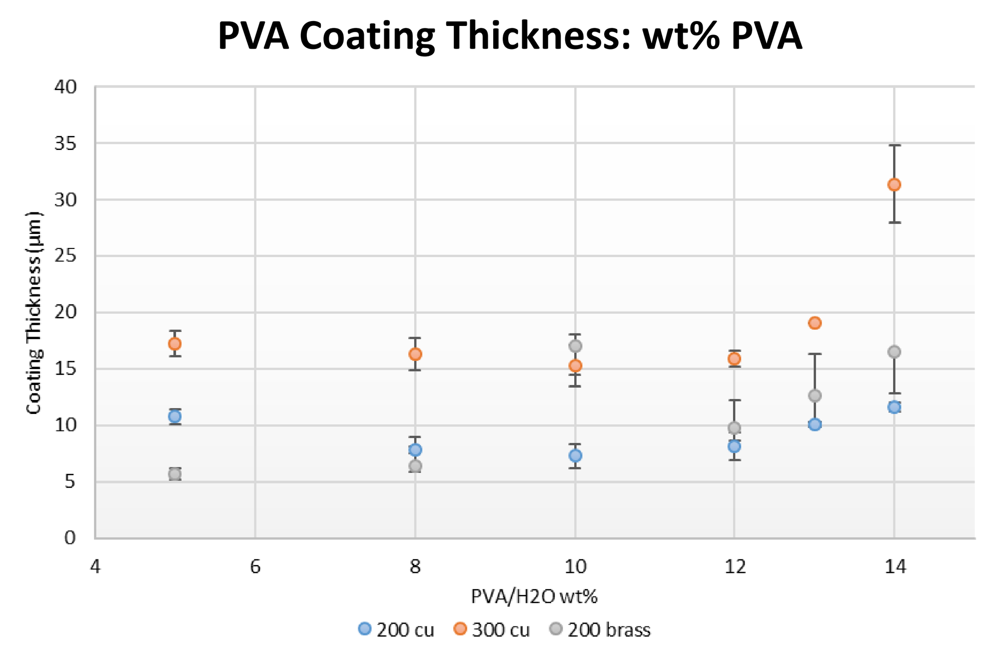
1. *Poly(vinyl alcohol) (PVA) Release Layer*

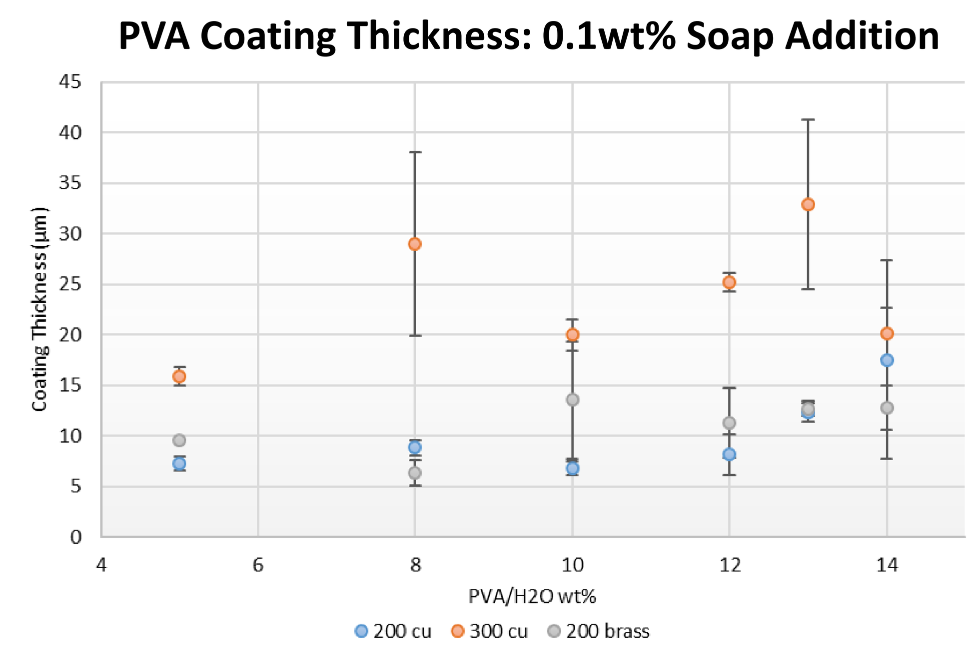
To improve micro-channel manufacturing, a release layer of poly(vinyl alcohol) (PVA) was incorporated to help remove the channels from the wire. PVA was chosen for its chemical compatibility with the PCL solvent. In order to coat the wires with a thick homogeneous layer to facilitate micro-channel removal, 200 µm copper, 200 µm brass and 300 µm copper wires were dip coated with different PVA solutions (from 5 to 14 wt%). Soap (0.1%) was added to the PVA solutions and the dipping temperature was varied (from 25 to 70°C), to reduce surface tension.





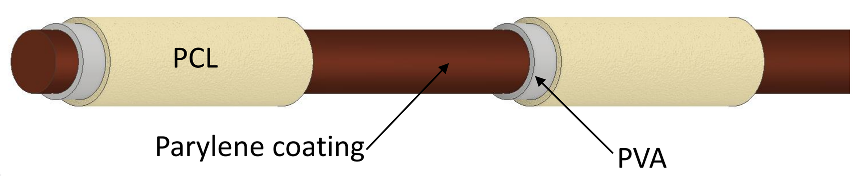


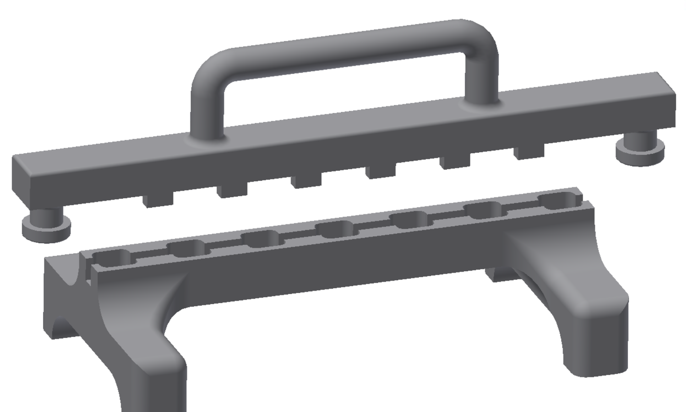




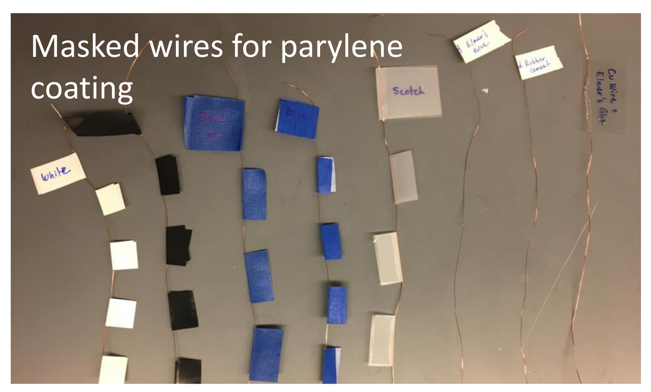
2. *Masking Materials*

To ease scaffold reproducibility, the PVA coating was used in masking and casting methods. Sections were masked with tape or glue, then coated with parylene, prior to PVA coating, to help create the scaffold micro-channels in sections.





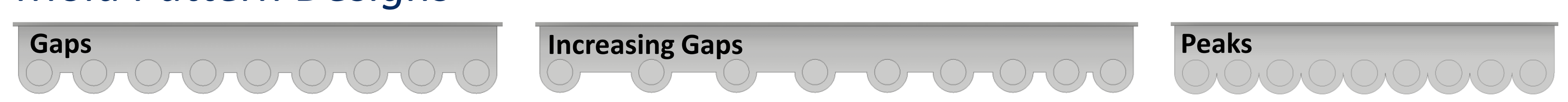
3D printed apparatus for masking wire with glue.



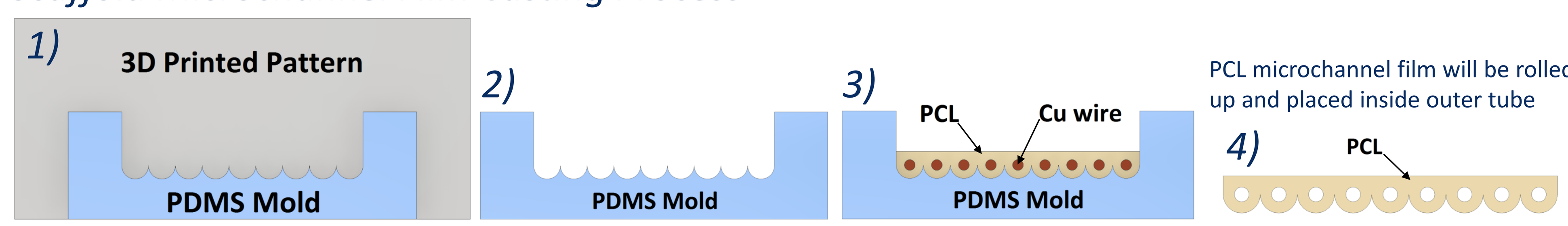
3. *Roll-able Casted Films*

A casting method was used to create a contiguous sheet of micro-channels around PVA coated wires, which can be rolled up into larger tubes. Several mold pattern designs were computer modeled and 3D printed, before casting in polydimethylsiloxane (PDMS), used because of its resistance to chloroform and its flexibility.

Mold Pattern Designs



Scaffold Microchannel Film Casting Process



Conclusion

PVA Release Layer

- Wire size – thicker wire creates a thicker PVA coating
- Wire material – does not affect coating thickness
- PVA solution wt% - coating thickness increases as you increase the PVA wt% from 12 wt%
- Homogeneity decreases as you increase PVA wt%
- Optimum coating temperature is between 50°C and 70°C

Masking Materials

- Tapes are not effective at masking parylene on Cu wires
- Elmer's glue and rubber cement are effective masks, but do not come off the wire easily

Roll-able Casted Films

- Patterns will be 3D printed and used to make molds

Future Directions

- New masking materials for PVA coating
- 3D printing - Design scaffold templates and test for printability
- Experiment 3D printing with photocrosslinkable PCL or PVA
- Investigate different microchannel scaffold designs to optimize cell adhesion
- Characterize the effect of micro-channel design on nerve growth
- Identify scaffold design features and materials which are optimal for nerve regeneration

References

1. Shahriari, D. (2016). Degradable Microchannel Nerve Guidance Scaffolds for Central and Peripheral Nerve Repair (Doctoral dissertation, University of Michigan, 2016). 1-174.
2. Spinal Cord and Autonomic NS. (n.d.). Retrieved March 28, 2017, from http://droualb.faculty.mjc.edu/Lecture%20Notes/Unit%205/chapters_14_and_17%20spinal%20cord%20with%20figures.htm
3. Daly, W., Yao, L., Zeugolis, D., Windebank, A., & Pandit, A. (2011). A biomaterials approach to peripheral nerve regeneration: bridging the peripheral nerve gap and enhancing functional recovery. *Journal of The Royal Society Interface,9*(67), 202-221. doi:10.1098/rsif.2011.0438

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