A Hybrid *in Silico* Model of the Rabbit Bulbospongiosus Nerve

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OBJECTIVE

The objective of this project was to develop a method to construct a recruitment curve of a nerve in the bladder when stimulated by an electrode. The algorithm involves plotting the number of stimulated axons (y-axis) at various electrode currents (x-axis) using a 3D model of a bulbospongiosus nerve from a rabbit sample(BsN).

BACKGROUND

- Sudden Urinary Incontinence (SUI) is a medical condition characterized by the abrupt and involuntary release of urine. This can occur during physical activities such as coughing, sneezing, or exercising, or even spontaneously without warning [1].
- A variety of factors can cause SUI, including weakened pelvic muscles, hormonal changes, pregnancy, childbirth, and underlying medical conditions [1].
- Pelvic floor muscle electrical stimulation using electrical current can improve Sudden Urinary Incontinence (SUI) by causing the muscles to contract and relax through electrical impulses, imitating natural muscle activity. Over time, this strengthens the muscles and improves urinary control [2].

METHODS & MATERIALS

Step 1: Bulbospongiosus nerve (BsN) samples from rabbit models were imaged using both TEM (high resolution) and Toluidine Blue staining (lower resolution) by researchers Farial R. and Laura R. (Figure 1).

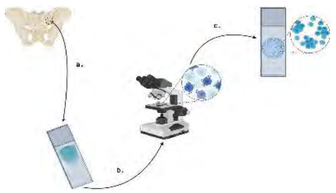

Figure 1: Imaging process of BsN New Zealand White rabbit nerve samples: (a) Histology of nerve cells, (b) TEM visualization of nerve cells, and (c) Observation of the slide at multiple levels of magnification.

Step 2: The nerve anatomy was segmented by hand using ImageJ. We utilized the multi-point tool to extract the segmentations, which were then saved in a CSV file as x and y pixel points (refer to Figure 2).

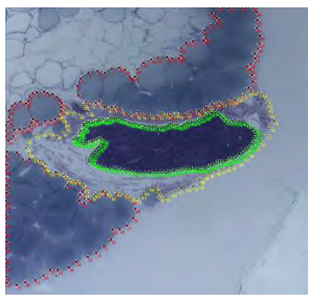

Figure 2: Image segmentation of a cross-sectional BsN stained with Toluidine Blue at 10x magnification. Color-coded boundaries indicate the fascicle containing myelinated axons (green), epineurium (yellow), and adipose/fat tissue (red).

Step 3: We created a script for random axon generation to accommodate any nerve shape, axon density, and radius range. The axons are strictly placed within the boundary of the fascicle (Figure 3).

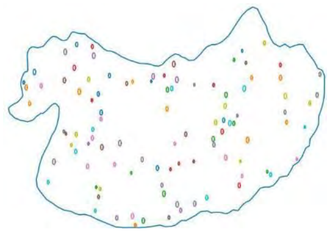

Figure 3: Random population of 100 axons within fascicle boundary. The axon diameters were automatically generated within the range of 2.796 um to 5.771 um.

Step 4: A 3D model of the nerve cross-section, comprising the fascicle, epineurium, and three sections of adipose tissue was produced using the Sim4Life software. In addition, we inserted a FEM unstructured mesh and ran the electrical stimulation on the grid, which ultimately led to the generation of an electromagnetic field that encompassed the electrode/nerve (Figure4).

a. b. c. d. e.

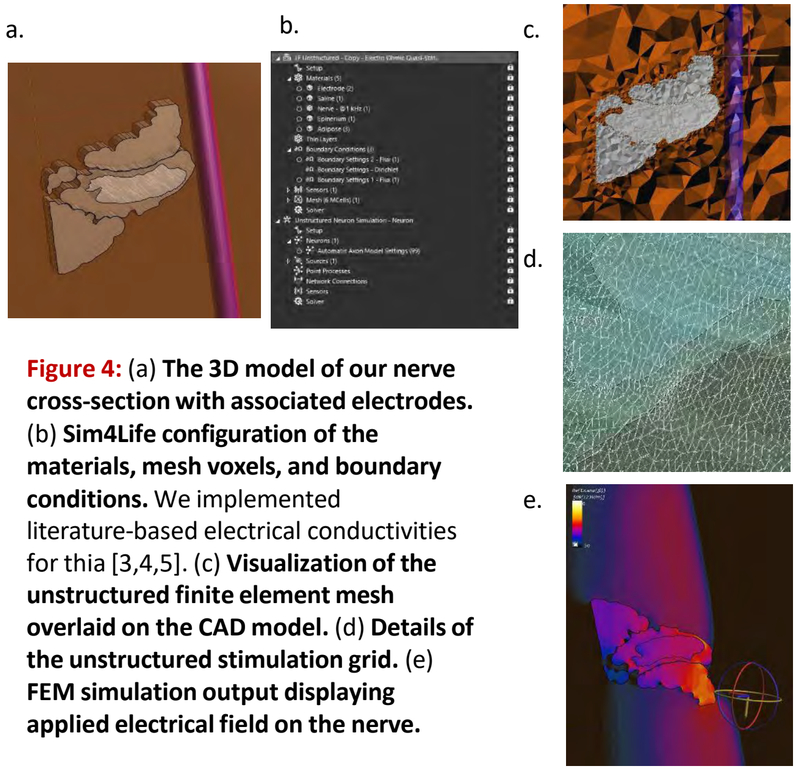

Figure 4: (a) **The 3D model of our nerve cross-section with associated electrodes.** (b) **Sim4Life configuration of the materials, mesh voxels, and boundary conditions.** We implemented literature-based electrical conductivities for thia [3,4,5]. (c) **Visualization of the unstructured finite element mesh overlaid on the CAD model.** (d) **Details of the unstructured stimulation grid.** (e) **FEM simulation output displaying applied electrical field on the nerve.**

Step 5: Compute the NEURON simulation, calculating axon conductance/action potentials via a set of mathematical equations which mimic biological nerve activity. Specifically, we used the Spatially Extended Non-Linear Node (SENN) model, and utilized a bipolar stimulation waveform of 0.1 millisecond pulse duration [7].

RESULTS

★ The recruitment curve was derived from NEURON simulation data through the generation of a titration factor graph, which was subsequently converted to a cumulative histogram.

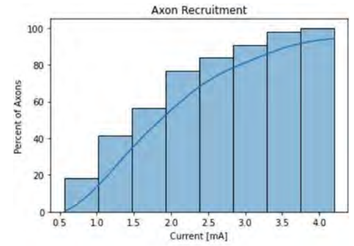

Figure 6: Calculated nerve recruitment curves for different nerve fiber diameters from 15.5 um to 9.5 um. Extracted from Koole and Holsheimer research paper [6]

★ Validation

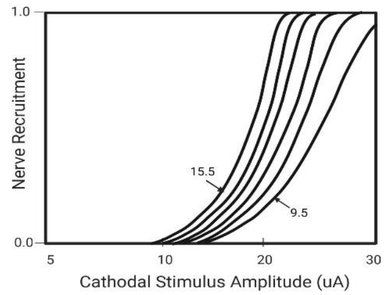

Figure 7: Recruitment curve analysis: cathodal stimulus amplitude vs. nerve recruitment [6].

CONCLUSIONS

- The project was able to demonstrate the current-based stimulation, which is the industry standard and is used in unstructured simulations.
- This result is undesirable as our project goal is to inform safe levels of electrical stimulation, indicating that further investigation should be conducted to improve our model before it is used to inform medical device/electrode specifications.
- Further analysis and validation was performed on the unstructured simulation, making this our proposed, finalized model.

AKNOWLEDGEMENTS

We would like to express our sincere gratitude to Dr. Schultz and Dr. Chen, our capstone class instructors, for their exceptional guidance, support, and valuable insights. Our heartfelt thanks also go to Dr. Romero-Ortega for his invaluable support in the development of this project, and to David Lloyd and Zuha Yousuf for their expert assistance and guidance. Additionally, we extend our appreciation to Farial Rahman and Laura Rubio for granting us permission to utilize their nerve slides.

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DISCLOSURE

MRO is a shareholder of Regenerative Bioelectronics Inc. (RBI Medical), a company that has commercial interest in neuromodulation of the PFM.