

Modeling Peripheral Nerve to improve Selective Stimulation

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Abstract

We present in this paper the model of a whole nerve bundle constructed under Neuron software. This model is being used to reproduce any internal physical configuration of a nerve bundle from the peripheral system and it allows building any other type of nerves. Simulation results prove the validity of the model and allow to confirm the feasibility of performing selective activation of fibers depending on frequency variability.

1. INTRODUCTION

Functional electrical stimulation has become a prolific clinical method over years in neurophysiology. With spinal cord injuries, the neural connection between the Central Nervous System (CNS) and some peripheral organs may be damaged. FES bypasses the CNS by electrically stimulating the peripheral nerves in order to re-enable normal organ functions such as bladder and bowel management, etc. The activation of muscle by FES is quite different than natural one conducted by the CNS; one of the most important issues is the reversed recruitment order, which results on large motor units recruited first with very low stimulus threshold [1]. Another important limitation comes from the so-called selectivity; in many clinical applications, it is necessary to stimulate only specific fibers and not others to prevent dyssynergia between muscles [2]. One approach consists of accurately modeling [3] and simulating nerve conduction when various types of FES are used through a bipolar cuff electrode instead of going by trial-and-error. We propose a new modeling technique based on Neuron software [4].

2. METHODS

2.1 The axon model

A double cable model of the axon was used. We then turned one axon into a template in order to generate as many as needed. This template was later used to create one fascicle; and then, we turned it again into a template to

generate the whole nerve bundle. In order to create an accurate model, properties and parameters of mammalian nerve fibers are required. The current project makes use of an available model [5] to create fascicles of different properties and position them in 3D space.

Figure 1 shows a myelinated axon with a close up to see the different compartments within a section. Each internodal segment is subdivided into two paranodal myelin sheath attachments region (MYSA), two fluted internodal regions (FLUT) and six stereotype internodal regions (STIN) [6]. As can be seen from the electrical model, the nodal compartment comprises several membrane dynamics including fast (Naf) and persistent (Nap) sodium, slow potassium (Ks) and linear leakage conductance (Lk) in parallel with the nodal capacitance (Cn). Each non-nodal compartment was represented as a double cable structure in order to add the effect of myelin. They are basically comprised of membrane conductances and capacitances; Gm and Cm are for myelin while Gi and Ci stands for the internodal axolemma.

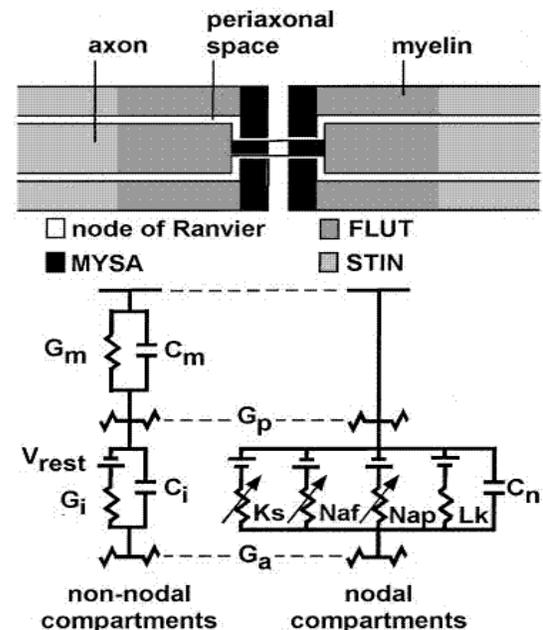


Figure 1: Axon electrical and physical model (Adapted from 5).

2.2 The axon template

What is needed then, is to be able to call an axon template, pass to it some parameters (such as diameter, position in xy-plane and nerve length), and then the 3D model will be automatically generated and will grow in the z-direction. Position in the xy-plane passed to the template is used to group a certain amount of axons together in order to reproduce the fascicles.

2.3 The fascicle template

A fascicle is a grouping of axons surrounded by a connective tissue called endoneurium and packed in yet another connective tissue, the perineurium. The whole nerve bundle is composed of several fascicles surrounded by the epineurium and of a layer of fat surrounding everything. Figure 2 shows a nerve bundle cross-section with all its tissues.

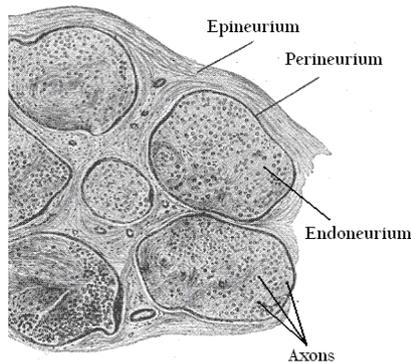


Figure 2: Nerve bundle cross-section

The “driver program” is responsible for opening the input files that Neuron will read in order to create the necessary number of fascicles and in turn, create all the different axons within each fascicle.

2.4 Finite Element Analysis

Next step is to take into account the effect of the current driven by the cuff electrodes on the individual nerve fibers. We should account for the presence and effect of various connective tissues. The method used is Finite Elements Analysis (FEA); in FEA, the volume conductor is divided into several tiny and connected volume elements in form of a mesh. FEA software (SCIRun [7]) can then analyse the passage of the current through each tiny volume elements and therefore derive values for current and potentials at any point within the volume. It is then used to extract the exact potential at the position of each and every axon in our simulated model. Those values are then input to Neuron which simulates the propagation of the action potential throughout the nerve.

3. RESULTS

By representing the fiber geometry as close as possible to reality and with accurate representation of membrane dynamics, we allowed the model to reproduce multiple sets of independent experimental data. The model results prove that it can be used to simulate the reaction of a real nerve to electrical stimulation. Furthermore, it is used to determine the best set of parameters in order to achieve consistent results.

The first validation has been made between experimental records from rat [8] and our model. When 2 subthreshold pulses were applied, the second one fired an action potential (figure 3 (A) & (B)). This supernormal activity is mainly caused by a passive phenomenon called “depolarisation after potential” but also from the slight activation of the persistent Na^+ conductance proposed by McIntyre et al. [4]. It is also shown that this phenomenon depends on fiber diameter.

The second validation has been made between experimental records from Baker et al. [9]. It consists of showing that afterhyperpolarization’s (AHP) amplitude and duration are impulse-dependent. This means that AHP’s amplitude and duration increased as we increase the number of suprathreshold applied stimuli (100 μs pulse width) at a frequency of 200 Hz (figure 3 (C) & (D)). The model matched well the experimental data. Note that amplitudes are truncated for clarity.

The last validation is about spike frequency adaptation; this is a common phenomenon in FES techniques. The model showed spike frequency accommodation after 1-5 spikes. These results matched well experimental records on rat made by Baker et al. [9] (figure 3 (E) & (F)). This phenomenon is also diameter-dependent.

Results also demonstrate certain selectivity from the frequency of the stimulus. As the frequency increases, some axons stop firing action potential (AP). At the beginning, each stimulus fired an AP, but their amplitude tends to decrease (figure 4). As we increase more and more the frequency we see that many stimuli do not fire any AP (at 960Hz figure 5).

These results demonstrate the feasibility to achieve selective stimulation with frequency.

4. DISCUSSION AND CONCLUSIONS

We used computational models of a nerve in order to have a proper tool to simulate the response of a whole nerve bundle to electrical

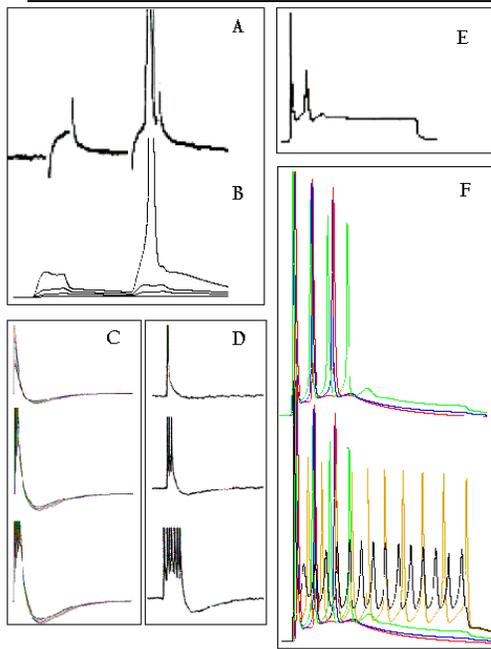


Figure 3: - Two subthreshold 3 ms stimuli separated by 10 ms (A) Experimental records [8] (B) Model data - AHP amplitude & duration increases with the number of stimuli (C) Model data (D) Experimental records [9] - Spike frequency accommodation (E) Experimental records [9] (F) Model data.

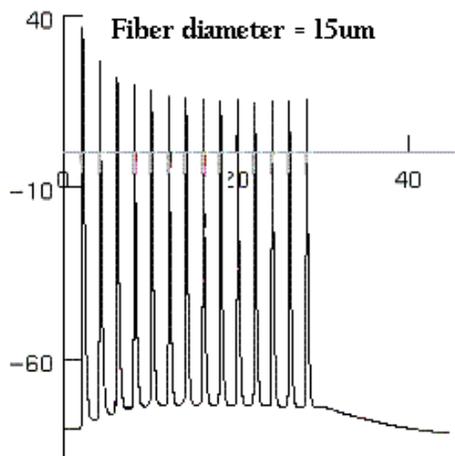


Figure 4: Firing AP with a 500Hz stimulus

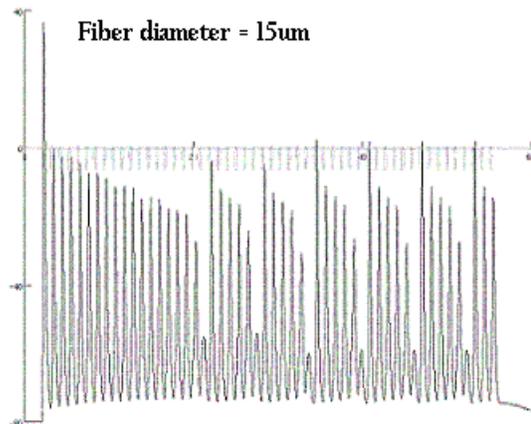


Figure 5: Firing AP with a 960Hz stimulus

stimulation. The results presented in this paper showed that the model correctly reproduced common experimental data.

Although, there are some model limitations; the first one comes from the axon models itself. There are also limitations coming from the FEA software; the extracted voltage values are not for the whole nerve length but only for a finite portion. The 3D resolution of the mesh is not infinitely small so, an approximation has to be made when the voltage to extract (at the axon position) is between two nodes.

Future work will be made in order to get rid of some of those limitations. This model will be used to determine the stimulation parameters (amplitude, frequency and pulse width) in order to get the best possible selectivity.

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Acknowledgements

The authors would like to acknowledge the financial support from the National Sciences and Engineering Research Council of Canada (NSERC) and from the Canadian Institute of Health Research (CIHR).