A Model of Nerve-Bundle Fibre-Stimulation using Implantable Cuff Electrodes - Summary of Research Articles

Joseph Radford
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1 Principles of Physiology

This comprehensive textbook[1] covers the fundamentals of nerve fibres and nerve bundles: their structure, how they are activated under normal circumstances and their relationship with muscle functions.

A motor neuron (nerve fibre) from the spinal cord innervates multiple muscle fibres, and each fibre is innervated by only one motor neuron. As the bundle leaves the spinal cord, it furcates into individual motor neurons. These neurons are approximately cylindrical and have membranes consisting of a lipid bilayer which allows some ions through but not others. The aim of the model to be implemented in this assignment is to interface with the bundles.

This gives some basic ideas about the geometry of the model. The model will likely be cylindrical, consisting of the fibres within a bundle. The materials it contains have properties of conductivity to ions that are most definitely relevant. The dominant effects will be seen in the relationship:

\[ i_{Na} = g_{Na}(V_m - E_{Na}) \]  \hspace{1cm} (1)  

\[ i_K = g_K(V_m - E_K) \]  \hspace{1cm} (2)

Where \( V_m \) is the membrane potential, which can be calculated using the Goldman, Hodgkin, Katz equation; \( g \) is the conductance of that ion and \( E \) is the equilibrium potential of that ion.

The expressions for ionic currents in equations (1) and (2) may seem to be useful information for the model, but what we are most interested in is the propagation of a voltage along the membrane, that is, an action potential, caused by some current we have successfully steered to the fibre. This is achieved by pushing the membrane potential, \( V_m \), above a certain threshold voltage.

It follows that one way to model this system is by attempting to map the voltage field for any given input from the electrodes to produce a voltage above the action potential threshold.

Another point to consider is that the action potential itself is a process of ionic currents coming in and out of the membrane. This is important to note as the current that stimulates the action potential must not interfere with this process.
This provides details of the desired characteristics of the current waveform - that it should be a short enough pulse to stimulate the action potential, but then stop so that it does not interfere with the propagation. Other characteristics of the waveform such as amplitude and frequency are determined by what the human body can handle without being damaged.

2 Simulation of Intrafascicular and Extraneural Nerve Stimulation

This article[2] uses a volume conduction model for a simulated nerve, implementing two concentric cylinders. This models a fascicle inside a connective tissue, together forming a nerve. The inner cylinder has medium $i$ and radius $r_i$ and between the two cylinders is medium $o$, and outer cylinder has radius $r_0$.

$$V(z,r) = \frac{1}{2\pi} \int_{-\infty}^{\infty} \left[ g_0(k) \cdot I_0(|k| \cdot r) + h_0(k) \cdot K_0(|k| \cdot r) \right] e^{jkz}dk$$

Equation (3) shows electric potential solved from fulfilling the Laplace equation. The article goes on to define $I_0$ and $K_0$ as modified Bessel functions with order zero, and determines $g_0(k)$ and $h_0(k)$ from boundary conditions, continuity in potential and normal current density at the cylinder surfaces. The model also accounts for anisotropy.

Two different conditions are then considered, an extraneural ring electrode (electrode at $r = r_0$) and an intrafascicular point electrode (electrode at $r = 0$), providing different boundary conditions.

The article obtains constants for the materials and the geometry from the literature.

Should the voltages appear above the threshold (taken here to be 50mV above resting potential) (at a node of Ranvier) then an action potential will propagate.

3 A toolchain to simulate and investigate selective stimulation strategies for FES

This article[3] looks at the processes involved in Neural Functional Electrical Stimulation (NFES). This nonphysiological recruitment activates axons with the biggest diameter first then activates ones with smaller diameters as the amplitude of the stimulus current increases. This causes fatigue as it activates type II fast twitch muscles first, then activates the type I slow twitch fatigue resistant fibres. Physiological recruitment in an able bodied individual activates type I first, then type II if needed. Reversing the recruitment order is something this article and the model being researched for would like to achieve.

The strategies used here include multipolar electrodes and advanced stimulators trying geometrically or diameter selective methods. Multipolar cuff electrodes have limited selectivity, although the article proposes using a non-cylindrical flat cuff to reshape the nerve and improve selectivity. A diameter
selective method uses an anodal block, which employs hyperpolarisation to stop the first action potentials passing a certain point - these will most likely be those associated with larger diameters as they have a lower threshold. Also, a high frequency component in the stimulation is considered, as this will inhibit some action potentials.

In this article, the potential generated by a cylindrical cuff is given by:

\[ V(p) = \frac{1}{4\pi} \sum_j \left( \sum_{i,j \in T_i} \int_{T_i} \frac{\Phi_j(p')(p - p') \cdot n}{||p - p'||^3} ds(p') \right) v_j + \frac{1}{4\pi} \sum_i \int_{T_i} \left( \frac{ds(p')}{||p - p'||} \right) (\delta_n v)_i \]

where \(j\) is the index of the vertices of the triangular mesh, \(T_i\) are triangles, \(p'\) are points of \(T_i\), \(n\) is the normal to \(T_i\) and \(\Phi_j\) is the piecewise linear finite element of node \(j\) on triangle \(T_i\).

It claims that this method, the Symmetric BEM, has a higher accuracy and convergence rate than the classical finite element methods.

The Hodgkin-Huxley method is used to simulate the excitation of the nerves. The article goes on to adjust the parameters and observe the effects and outcomes of the different strategies on the voltage fields and excitation. The work has been validated with animal tests.

4 Evaluation of the Cable Model for Electrical Stimulation of Unmyelinated Nerve Fibres

This model\cite{4} uses a similar three dimensional cylinder volume conductor model as in \cite{2} and compares it to the cable model. However, it considers the case for a domain with and without a current source (equations (5) and (6)) for the primary potential (infinite medium model):

\[ \Phi_p^{(i)}(\rho, \theta, z) = 0 \quad (5) \]

\[ \Phi_p^{(i+)}(\rho, \theta, z) = \frac{I_s}{4\pi \sigma R} \quad (6) \]

and a secondary potential (due to inhomogeneities) using a finite element method. Thus it obtains:

\[ \Phi = \Phi_p^{(i)} + \Phi_s^{(i)} \quad (7) \]

Equation (8) shows how the all important membrane voltage can be calculated.

\[ \Phi_m(\theta, z) = \Phi^{(i)}(\rho_1, \theta, z) - \Phi^{(2)}(\rho_2, \theta, z) \quad (8) \]
The article compares this with the membrane voltage derived from the passive steady state cable model and modifies it to obtain:

\[ V_m - \lambda^2 \frac{\partial^2 V_m}{\partial z^2} = \lambda^2 \frac{\partial^2 V_e}{\partial z^2} + 2aE_{\text{trans}} \cos(\theta - \theta_{E_{\text{trans}}}) \]  (9)

where \( \lambda = \sqrt{\frac{\rho_m}{\sigma_m}} \), \( a = \rho_2 \) and \( E_{\text{trans}} \) is the electric field transverse to the fibre with an azimuthal orientation of \( \theta_{E_{\text{trans}}} \).

It is determined that equation (9) is a good approximation of the 3D conduction model.

5 Point source nerve bundle stimulation: effects of fibre diameter and depth on simulated excitation

This model[5] also selects a cylinder to represent the nerve structure, similar to that outlined in [2] and [4]. However, it only has one cylinder that represents the entire nerve bundle, and a point source of \( I_s \) outside the cylinder in the extracellular medium.

The potential fields outside and inside the bundles are modelled as:

\[ \Phi_e(\rho, \theta, z) = \sum_{n=-\infty}^{\infty} \int_{-\infty}^{\infty} D_n(k)K_n(|k|\rho) \cdot \cos n\theta e^{-jkz} dk + \frac{I_s}{4\pi\sigma_e R} \]  (10)

\[ \Phi_o(\rho, \theta, z) = \sum_{n=-\infty}^{\infty} \int_{-\infty}^{\infty} C_n(k)I_n\left(\frac{|k|\eta(k)}{\sqrt{\sigma_o \sigma_p}}\rho\right) \cdot \cos n\theta e^{-jkz} dk \]  (11)

After defining this, the article investigates fibre diameter and radial depth on the excitation threshold. This is a relevant relationship as when selectively activating nerves in a bundle, each nerve may have a different threshold to be considered.

The effects are quantified with the space constant:

\[ \lambda = \sqrt{\frac{r_m}{r_{il} + r_{ol}}} \]  (12)

where \( r_{il} \) is intracellular resistance per unit length, \( r_{ol} \) is the interstitial resistance per unit length and \( r_m \) is the lumped membrane resistance times unit length.

However, if the fibres are in a tightly packed bundle:

\[ r_{ol} = \frac{(\rho_o/f_o)}{\left(\pi a_{fib}^2/(f_i + f_m)\right)} \]  (13)
where \( f_o, f_i, f_m \) are interstitial, intracellular and membrane spaces and \( a_{f_{sb}}^2 \) is the outer radius of the fibre.

Finally, an intracellular potential distribution function is determined from the space constant and the interstitial potential:

\[
\Phi_i^F = \frac{1}{\lambda^2 k^2 \delta + 1} \Phi_o^F
\]

(14)

where \( \delta \) is a function of (anisotropic) conductivity and \( k \) is the \( z \) direction spatial frequency.

Equation (14) gives an evaluated model of the potential within a nerve bundle when fibre diameter and radial depth are included. This function needs to be considered carefully when determining voltage thresholds and how they may change within a modelled bundle domain.

References


