The Effect of Myelination on Action Potential Conduction Velocity in the Hodgkin & Huxley Axon Model

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1 Introduction

A mathematical model describing the propagation of action potentials through nerve axons was first developed by Hodgkin and Huxley, after they recorded a large amount of quantitative data from giant squid axons using the voltage-clamp method[1]. Their model, largely known as the Hodgkin & Huxley model or HH for short, consisted of four nonlinear ordinary differential equations (ODEs), which can be easily solved numerically. The classically used HH model considers three ion channel gates each with a probability of being open: n for K^+ channels; m and h for Na^+[1]. In order to numerically solve the four ODEs describing the HH model, we have to treat the axon as made of spatially discrete "sections". Thus, a discrete HH model can be built by solving these 4 ODEs to give the states (V, n, m, and h) of each discrete section of the axon. Using MatLab, a simulation of the discrete HH model was built and a propagating action potential is shown in Figure 1.

However, unlike the giant squid axons that Hodgkin & Huxley developed their model for, most neuron axons are wrapped with insulating myelin sheaths, which significantly increase the amount of myelin around an axon. This myelin serves to decrease the membrane capacitance and conductance of an axon, effectively increasing the conduction velocity of the propagating action potential. In order to better model myelinated axons, we extended the HH model to incorporate myelin and ran a simulation in MatLab to validate it.

2 Methods

In our extended HH model, the myelinated sections (internodes) of the axon are modeled as passive cables without ion channels, while the unmyelinated sections (nodes of Ranvier) are modeled using the classical HH model with ion channels. The first step is to find the appropriate myelin thickness to use for the myelinated sections. Myelin thickness varies depending on the dimensions and type of axons, so a valid assumption to make, according to *Sanders et. al*[2], is to use myelin thickness equal to the axon radius. As the simulation runs for each discrete section, it checks the myelin thickness value. If it is zero, the standard HH model (with ion channels) is used for that section. Otherwise, if the myelin thickness is non-zero, that section is considered a passive cable with membrane capacitance per area $c_{\text{myelin}} = 5 \cdot 10^{-9}\text{F/cm}^2$ and membrane resistivity $\rho_m = 4 \cdot 10^5 \Omega \cdot \text{cm}^2$, with values similar to *Waxman et. al*[3].

Four different myelination patterns were used, and the amount of myelin is shown as a normalized value for the number of sections that have myelin. The first pattern used was an axon that had no myelin at all. The second had 63.3% myelin with one unmyelinated section every two myelinated sections. The third pattern had 86.6% myelin with one unmyelinated section every nine myelinated sections. The last pattern (voltage response shown in Figure 2) had 90% myelin with an unmyelinated section at the first, middle, and last sections.

3 Results

The simulation was run in MatLab for each myelination pattern, and both the average conduction velocity and firing frequency were calculated: the first by dividing the length of the axon by the time it took the action potential to travel from the beginning to the end of the axon. The latter was calculated by counting the number of full spikes minus one and dividing that by the time between the first and last spikes. Thus, both the conduction velocity and firing frequency, shown in table below, are average values and not instantaneous.

normalized amount of myelin (%)	average conduction velocity (cm/s)	firing frequency (Hz)
0.00	245.1015	59.46
63.3	431.116	75.97
86.6	670.63	96.67
90.0	778.7903	104.59

4 Discussion

The results described above suggest that the addition of myelin increases conduction velocity, with the highest myelination pattern (90%) having a three-fold increase in conduction velocity when compared to the unmyelinated pattern. The results also suggest that a longer internode (myelinated) length further increases conduction velocity, which can be seen with the doubled conduction velocity of the 900 μm internode pattern (90%) when compared to the 630 μm internode pattern (63.3%). The results are in agreement with the already established notion[4, 5] that myelination results in higher conduction velocity, and this validates the use of the HH axon model for myelinated axons.

The classic HH model was the first conductance-based model of the neuron, and it is based on representing the cell membrane with an equivalent circuit. According to this model, current flow across the cell membrane is due to charging by the membrane capacitance and movement of ions across ion channels having variable conductances. When Hodgkin and Huxley first worked on the giant squid axon, they used devices such as the voltage-clamp to gather experimental data on the electrical activity of unmyelinated neurons. They used the experimental data to fit their conductance-based model, but their model did not include myelinated axons. As previously mentioned[5], most neurons are myelinated, rendering the HH model inapplicable for these neurons. In order to include myelin in the HH model, we simply add internodes between the usual HH-modeled sections, and these myelinated internodes have no ion channels and act as passive cables with a certain membrane capacitance and resistance. This allows us to adapt the HH model to a broader range of neurons, simply by incorporating myelin into the model. As the results of the simulation have demonstrated, the addition of myelin produces the expected effects and validates the extended HH model that was developed.

5 Figures

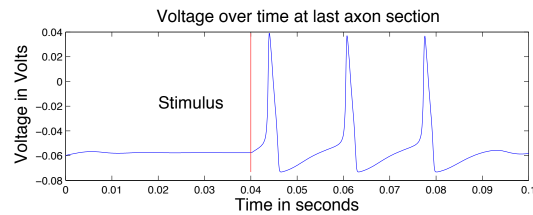

Figure 1: Voltage response of an unmyelinated axon after an input stimulus using the standard HH model.

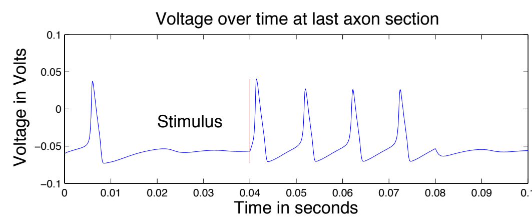

Figure 2: Voltage response of a 90% myelinated axon after an input stimulus using the described extended HH model. Note the much faster conduction velocity shown by short time between stimulus and response spike.

References

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The source code for the MatLab simulation can be found at:
`https://bitbucket.org/basheersubei/hh-model-with-myelin`