Fundamentals of Neuroengineering - 2019
NEURON exercise - Modelling Electrical Stimulation of the Nervous System

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Introduction

In this lab the purpose is to study electrical stimulation of the nervous system trough the software environment NEURON which simulate a myelinated fiber response to different stimulation protocols according to the Hodgkin-huxley model which explains the ionic mechanisms underlying the initation and propagation of action potentials. We assesse the effect of intracellular versus extracellular stimulation and the effect of cathodic versus anodic stimulation. The simulated fiber is modeled with 101 nodes and is located in the grey matter (=2 S/m). By looking at the induced electric potential V along the direction of the fiber, we were able to draw conclusions on the stimulation parameters, which are the frequency, the amplitude, the pulse width and spacial modulation.

Part 1 - External electric potential and activation function (Rattay 1986)

Question 1 and 2:

A source point electrod placed at z=100um away from the fiber generates an induced electric potential on the membrane of the fiber. On Figure 1, we can see both the electric field and the activation function relativ to the x position of the fiber for a cathodic source of -1 μm. According to the following formula:

$$Ve = \frac{amplitude}{4 * \pi * rho * distance}$$

we were able to compute and model the electic field.

The activation function is given by:

$$S = \frac{\partial^2 Ve}{\partial x^2}$$

On figure 2 we can see the same but for a positive current applied of 1 μm, which is an anodic current source. The shape we get for the electric field is like a spike which is negative for the cathodic and positive for the anodic source. The activation function looks the same but with the opposite sign and we can observe two additional small spikes pointing to the opposite direction. For the cathodic source, the fiber will clearly be recruited at point x=0 but for the anodic source it is unclear, there are two points x=-0.002m and x=0.002m where the fiber can be recruited.

Question 3:

According to the plots, we can conclude that the cathodic stimulation is more efficient. For the same magnitude of current applied, the depolarization (which corresponds to the positive spikes from the activation function) is much higher and also it is at a unique point. For the anodic source, there are two depolarization points. In other words, for cathodic stimulation, less current is needed to reach the threshold to initiate the propagation of the action potential.

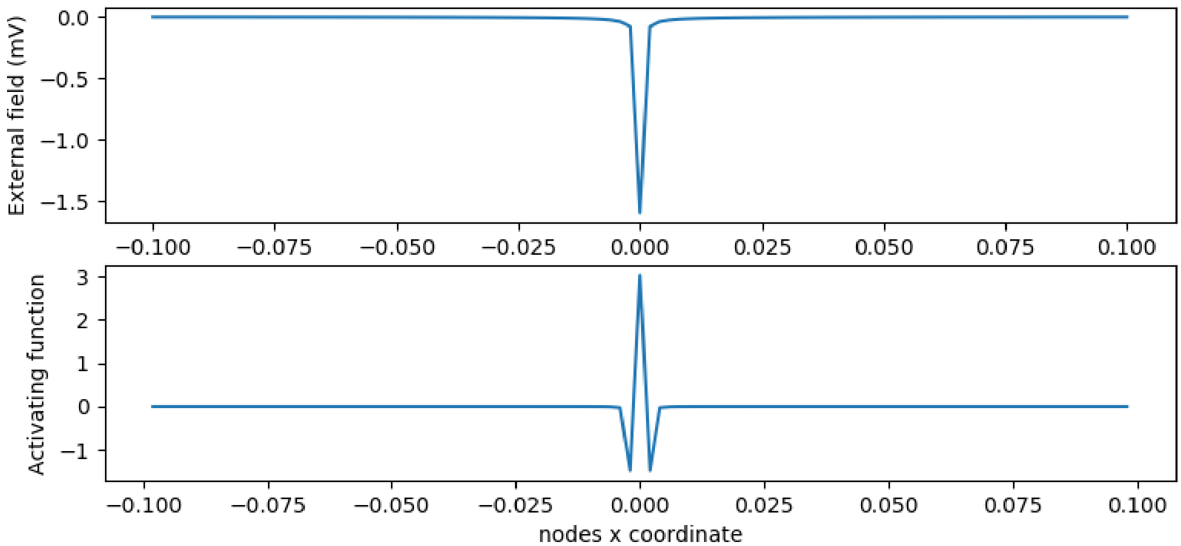


Figure 1: Electric field and action potential of the membrane along the fiber with cathodic current I = -1 uA

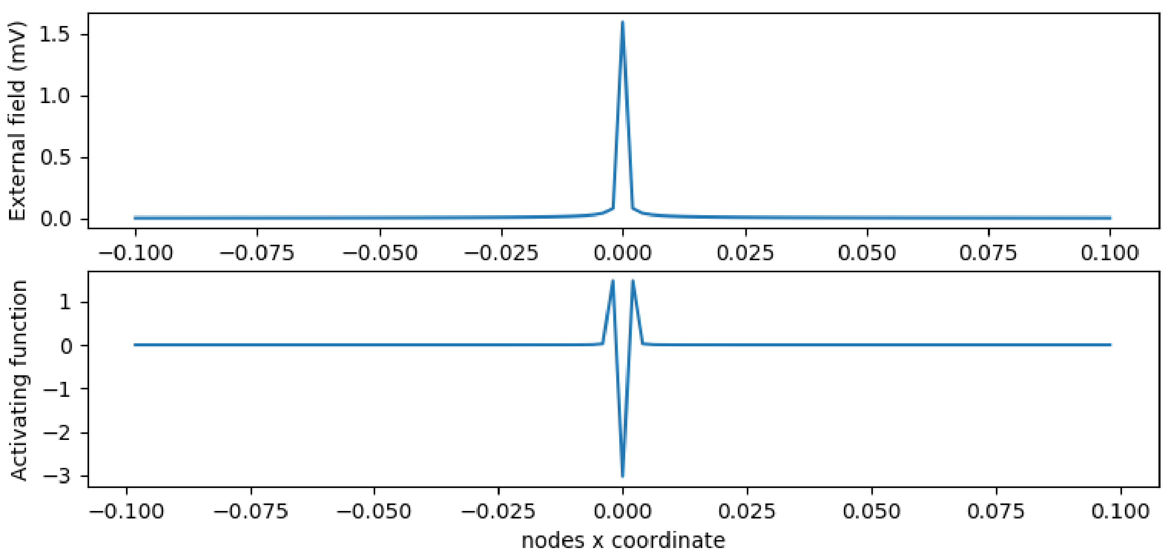
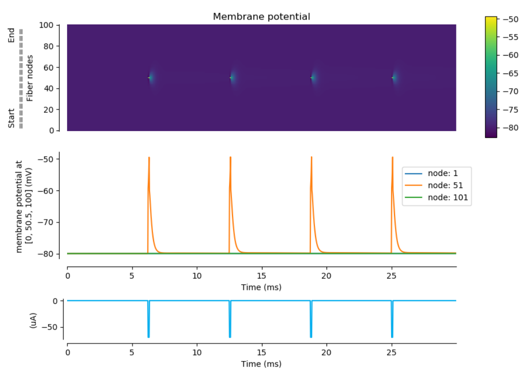


Figure 2: Electric field and action potential of the membrane along the fiber with anodic current I = 1 uA

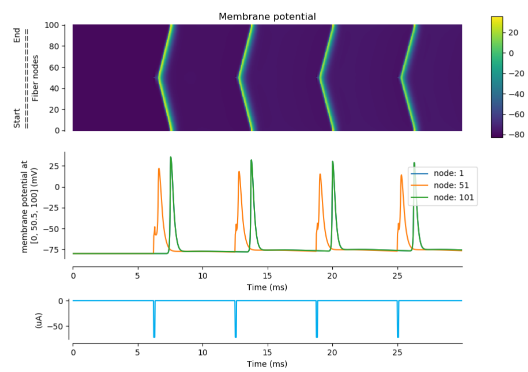
Part 2 - Modelling the membrane dynamics: extracellular stimulation

Question 4:

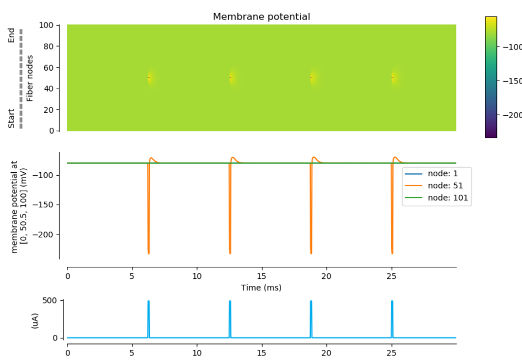
In this part, we analyze the effect of the amplitude and sign of extracellular stimulation on the myelinated fiber membrane. The current pulse width applied is again fixed at $100\mu s$. For this part, the membrane diameter is also fixed to $20\mu m$. After trying out different values, we found that the minimal current necessary is -$72\mu A$. At this point the membrane potential reaches the threshold to make the action potential propagate in the cell for a cathodic source. $500\mu A$ is needed for an anodic source. There is a factor of 7 which means that a cathodic stimulation is 7 times more efficient. On figure 3 (for both cathodic (top) and anodhic (bottom) sources), we can observe the case where the threshold is not reached and the case where the action potential is transmitted.



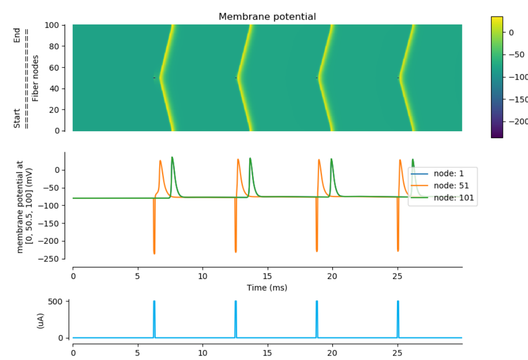
(a) -$70\mu A$ applied



(b) -$72\mu A$ - minimal current magnitude needed to observe action potential propagation



(c) $490\mu A$ applied

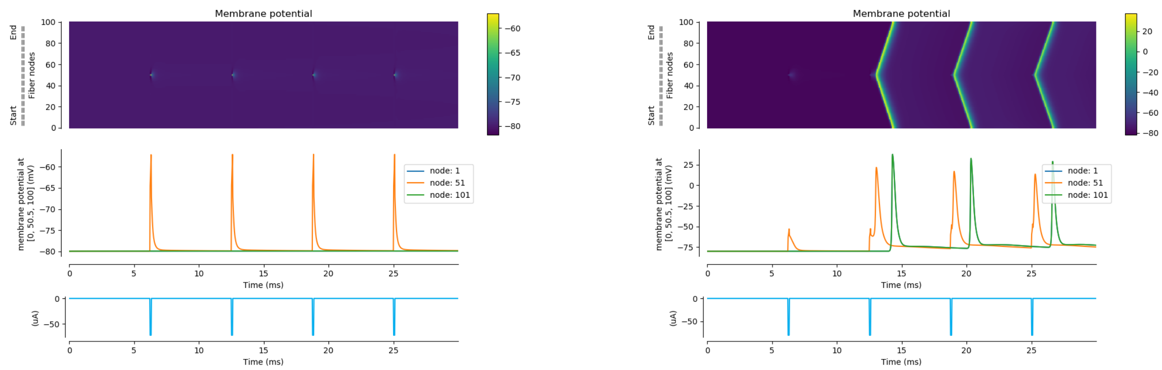


(d) $500\mu A$ - minimal current magnitude needed to observe action potential propagation

Figure 3: cathodic (top) and anodic (bottom) stimulation

Question 5:

We concluded in question 4 that the cathodic stimulation is more efficient, here we analyze the effect of the diameter of the fiber. In the previous question. The diameter was fixed to 20μm. Now we will look at what point were we reach the threshold for a diameter of 5um and 10um. On figure 4, we observe the case where the threshold is not reached and the case where the action potential is transmitted for a 5μm diameter. A magnitude current source of -72μA was able to recruit the 20μm so we can conclude that in fact, a higher diameter fiber is more easily excitable.



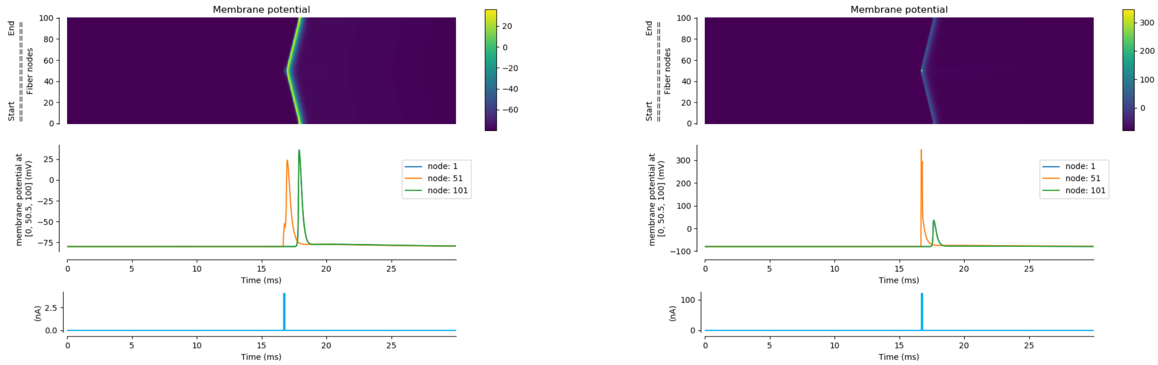
(a) -72μA applied on a 5um diameter fiber (b) -80μA applied on a 5um diameter fiber

Figure 4: extracellular cathodic stimulation

Part 3 - Modelling the membrane dynamics: intracellular stimulation

Question 6:

In this part we evaluate the case of intracellular stimulation with a current-clamp for a fixed fiber diameter of 20μm. After trying several cathodic source current values with the intracellular stimulation software model, we can say that it does not work. This is due to the fact that injecting negative current will here only hyperpolarize. But the anodic stimulation is extremely efficient. Only 4 nA are required to propate the membrane action potential. Also interestingly, when the current is too high, the signal is not as good according to the NEURON simulation (see figure 5). Comparing with the extracellular stimulation, the required current is extremely lower. So the compromise to make is between efficiency or invasivness.



(a) action potential with 4nA (b) action potential with 120nA: degradation

Figure 5: intracellular anodic stimulation: Low and high current applied

Part 4 Interactions between induced and physiological neural activity

Previously, the study of the myelinated fiber was done when it was in the resting state. Physiological activity is however present in reality and electrical stimulation can be used to modulate it. Here the natural activity is modeled with a firing at a constant rate of 55 Hz while being stimulated, with the extracellular electrode, at 100 Hz and an amplitude of -80 μA. The physiological activity is initiated at the first node of the fiber while the induced one is initiated as before at the node 55.

Question 7:

On table 1, we report the origin of the spike felt on the fiber nodes. The second spike has an interesting shape on the membrane potential 2D plot because in fact both the physiological and induced were close to simultaneously generated and the two spikes will collide at the node 40.

. Spike 1 and 3 are purely Induced. Finally, for the last spike is the purely physiological because it occurs before the induced one and when the induced stimulation occurs, the fiber is already busy propagating the physiological one so the induced do not appear.

Voltage	spike 1	spike 2	spike 3	spike 4
Node 40	induced	induced+physiological (collision)	induced	physiological
Node 0	induced	physiological	induced	physiological
Node 100	induced	induced	induced	physiological

Table 1: Type of spike observed along the fiber

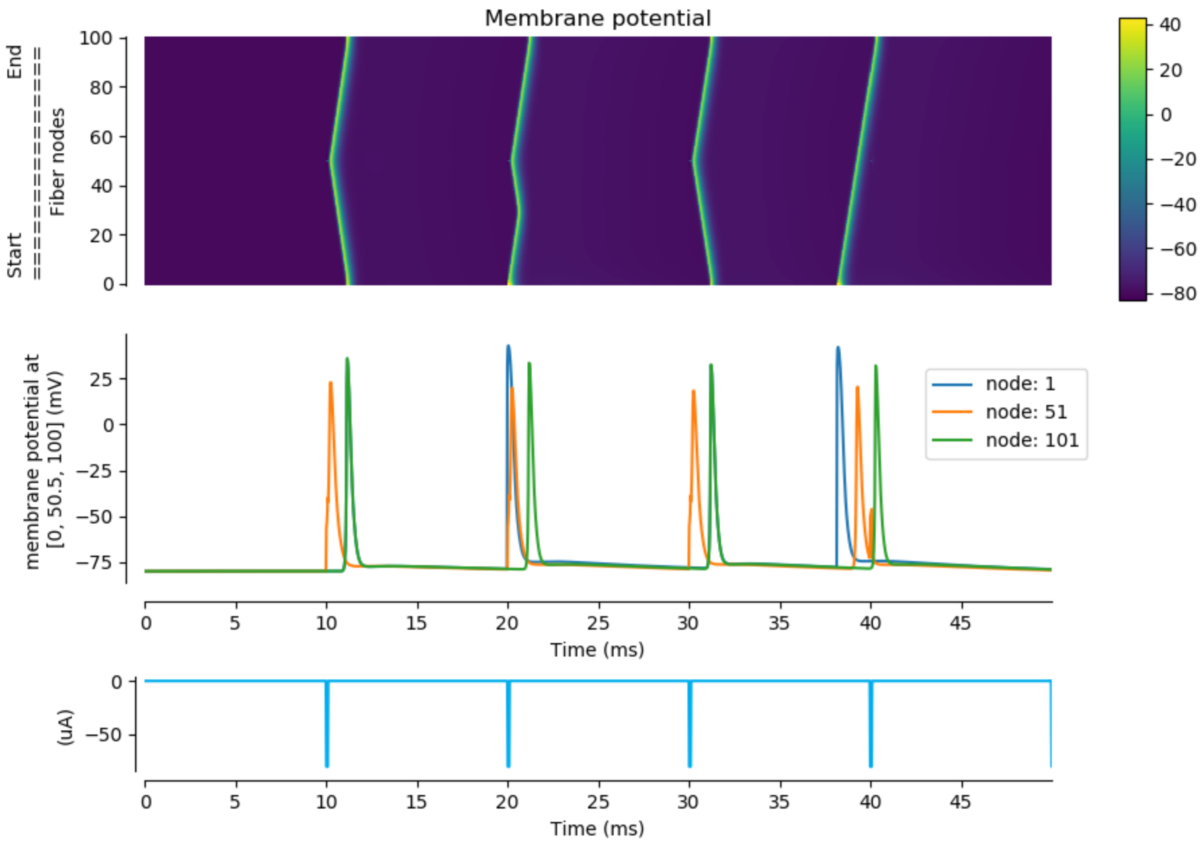


Figure 6: cathodic current = -1 uA