Neuroprothetics Exercise 6
Electric Stimulation

Dominik Scherer

21. January 2024

1 Multicompartment model with electric stimulation

In this exercise, we replace the stimulating current I_{stim} that was directly fed to the model by an external current stimulation, as it would be possible with an electrode. For that, we will simulate how the potential due to the external current is distributed over a linear axon and how the axon reacts to different external stimuli.

1.1 External Potential

How a potential will build up along a linear axon, depending on the external current and its distance to the axon, can be calculated with the equation

$$\Phi(I, r) = \frac{\rho}{4\pi} \frac{I}{r} , \tag{1}$$

which gives the potential at a given distance r from the source. For a linear axon, that means we need to replace r with $\sqrt{{r_0}^2 + x^2}$ to get to an equation that gives the potential at a given point along the axon (x). The equation for the potential along the axon is now given by:

$$\Phi(I, x) = \frac{\rho}{4\pi} \frac{I}{\sqrt{{r_0}^2 + x^2}} . \tag{2}$$

In Figure 1, the potential distribution is depicted for a source that is placed in the middle of an $l_{axon} = 300\,\mu$m long axon at a minimal distance of $r_0 = 10\,\mu$m. The graph is plotted once for $I_1 = 1\,$mA and for $I_2 = -1\,$mA.

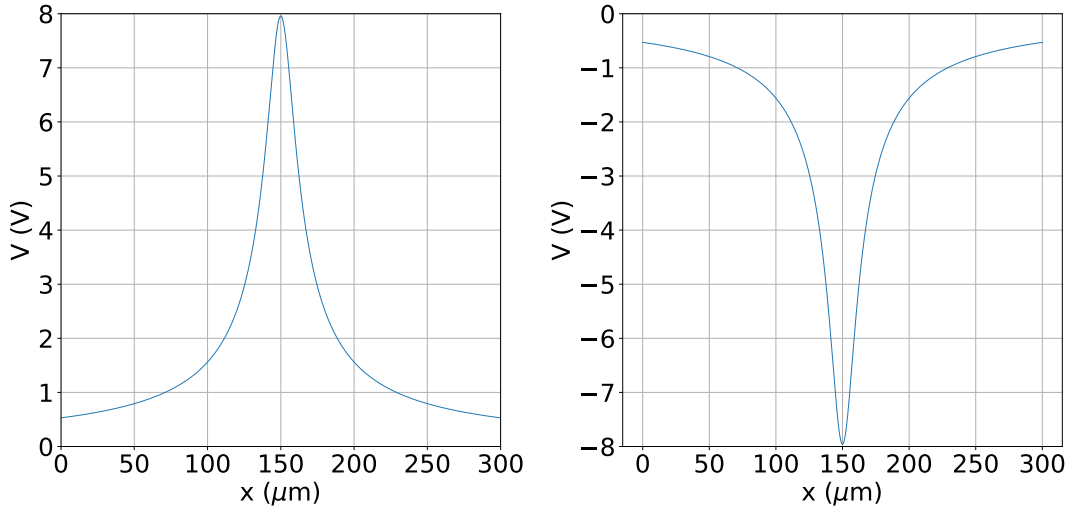

Figure 1: Potential distribution along a linear axon due to a point-like current source spaced 10 μm away from the middle of the axon.

Similarly, the electric field along the axon can be calculated as the negative first derivative of the potential ($E = -\frac{d\Phi(x)}{dx}$) and is shown in Figure 2.

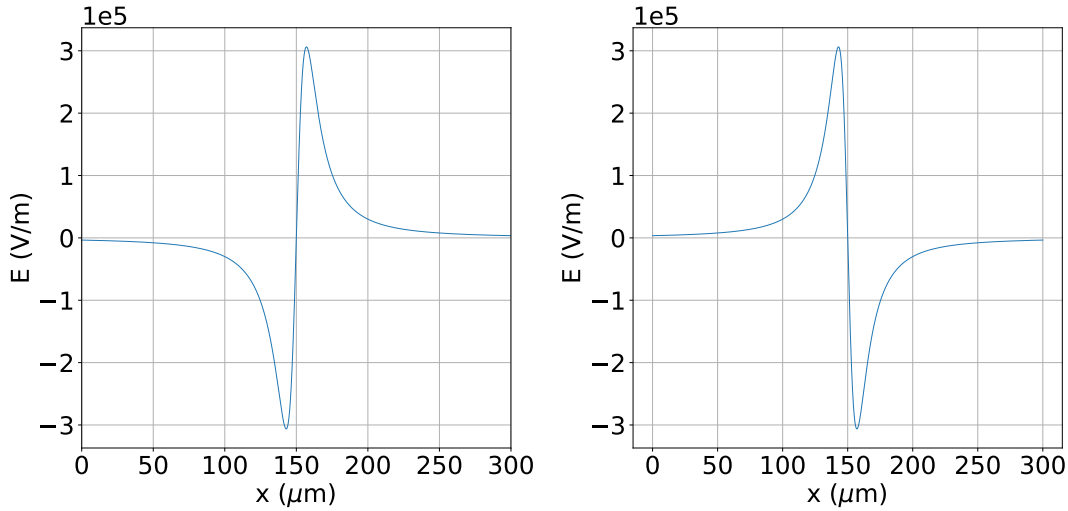

Figure 2: Distribution of an electric field along a linear axon due to a point-like current source spaced 10 μm away from the middle of the axon.

The activation function, which is given by the second derivative of the external potential (at least for compartment lengths converging to zero), describes the activation of a neuron due to an external potential. This might seem counterintuitive, but it makes

sense when considering that due to the membrane capacity, the internal potential will directly compensate for an applied positive external potential by being decreased. Thus, no action potential will form. Even a linearly changing external potential won't have such an effect since the compartments are interconnected, and the (spacially) constantly changing intercellular potential would lead to opposing currents of the same magnitude going in and out of every compartment. Thus, the net current in each department is zero, which leads to an unchanged membrane potential. Therefore, what is needed to achieve an action potential is an external potential whose second derivative is non-zero to obtain a net positive membrane potential.

With the external potential given by the equation 2, the activation function

$$A(x) = \frac{d^2\Phi(x)}{dx^2} \tag{3}$$

for the given currents is shown in Figure 3.

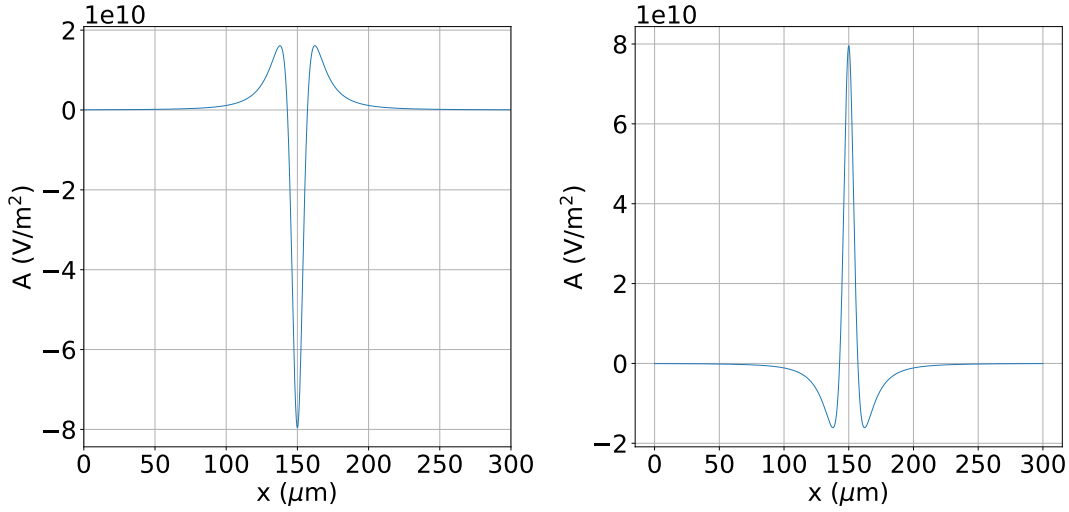

Figure 3: Activation function along a linear axon due to a point-like current source spaced 10 μm away from the middle of the axon.

1.2 External potential applied on HH model

To see how the multicompartment HH model will actually respond to an external potential, its function to calculate the potential was modified. The old model considered a current stimulus I_{stim} but no external potential:

$$\frac{d}{dt}V_m = \frac{1}{C_m}(-I_{HH} + I_{stim}) + \frac{1}{C_M R_a}\mathbf{C}V_m \,. \tag{4}$$

The adapted model now takes the external potential (V_e) into account:

$$\frac{d}{dt}\vec{V}_m = \frac{-\vec{I}_{HH}}{C_m} + \frac{1}{C_M R_a}\mathbf{C}V_m + \frac{1}{C_M R_a}\mathbf{C}\vec{V}_e \,. \tag{5}$$

In both equations, $\mathbf{C}$ is the connection matrix (not a capacitance), as already explained in the last task. The internal stimulus current used to trigger an action potential in the exercises before is now zero.

Equation 5 then is again solved with the implicit Euler ODE solver. Thanks to the matrix form, the implementation of the implicit Euler solver can be expressed as a set of linear equations of the form

$$\mathbf{A}\vec{x} = \vec{b}\,, \tag{6}$$

where

$$\mathbf{A} = \mathbf{I} - \frac{\Delta t}{C_m R_a}\mathbf{C} \tag{7}$$

and

$$\vec{b} = \vec{V}_m(t) + \frac{\Delta t}{C}(-\vec{I}_{HH}(t+\Delta t)) + \frac{\Delta t}{C_m R_a}\mathbf{C}\vec{V}_e(t+\Delta t)\,. \tag{8}$$

In equation 7, $\mathbf{I}$ is the identity matrix of the dimensions $\mathbf{n} \times \mathbf{n}$, where $\mathbf{n}$ is the number of compartments.

The different potentials resulting from external current stimuli at $x = 150\,\mu$m and $r_0 = 10\,\mu$m were fed to the model which was run for 30 ms with a step size of $\Delta t = 25\,\mu$s. The current stimuli had a mono-phasic or a bi-phasic shape, as shown in Figure 4.

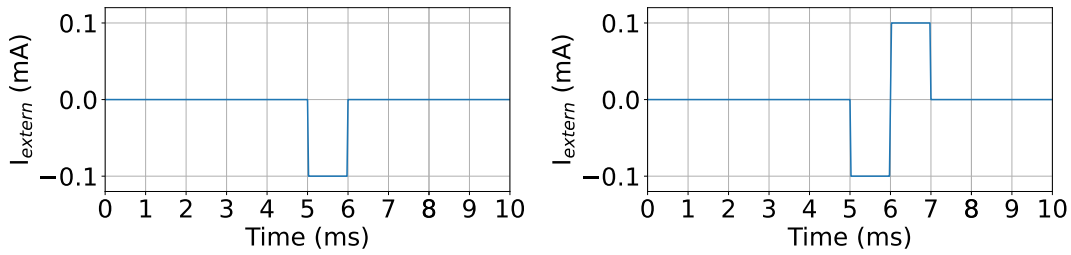

Figure 4: Examples of a mono-phasic (left) and a bi-phasic (right) external current.

The following external current pulses were applied to the model from $t_0 = 5\,\mathrm{ms}$ on for $1\,\mathrm{ms}$ each phase:

- Mono-phasic, $I = -0.05\,\mathrm{mA}$
- Mono-phasic, $I = -0.1\,\mathrm{mA}$
- Bi-phasic, $I = \mp 0.1\,\mathrm{mA}$
- Bi-phasic, $I = \mp 0.15\,\mathrm{mA}$
- Mono-phasic, $I = 0.2\,\mathrm{mA}$
- Mono-phasic, $I = 0.4\,\mathrm{mA}$

Note: a sign of "$\mp$" for the bi-phasic currents means that the first pulse is the negative one, as in the right plot in Figure 4.

2 Results

The model's responses to the different external stimuli are shown in Figures 5 and 6.

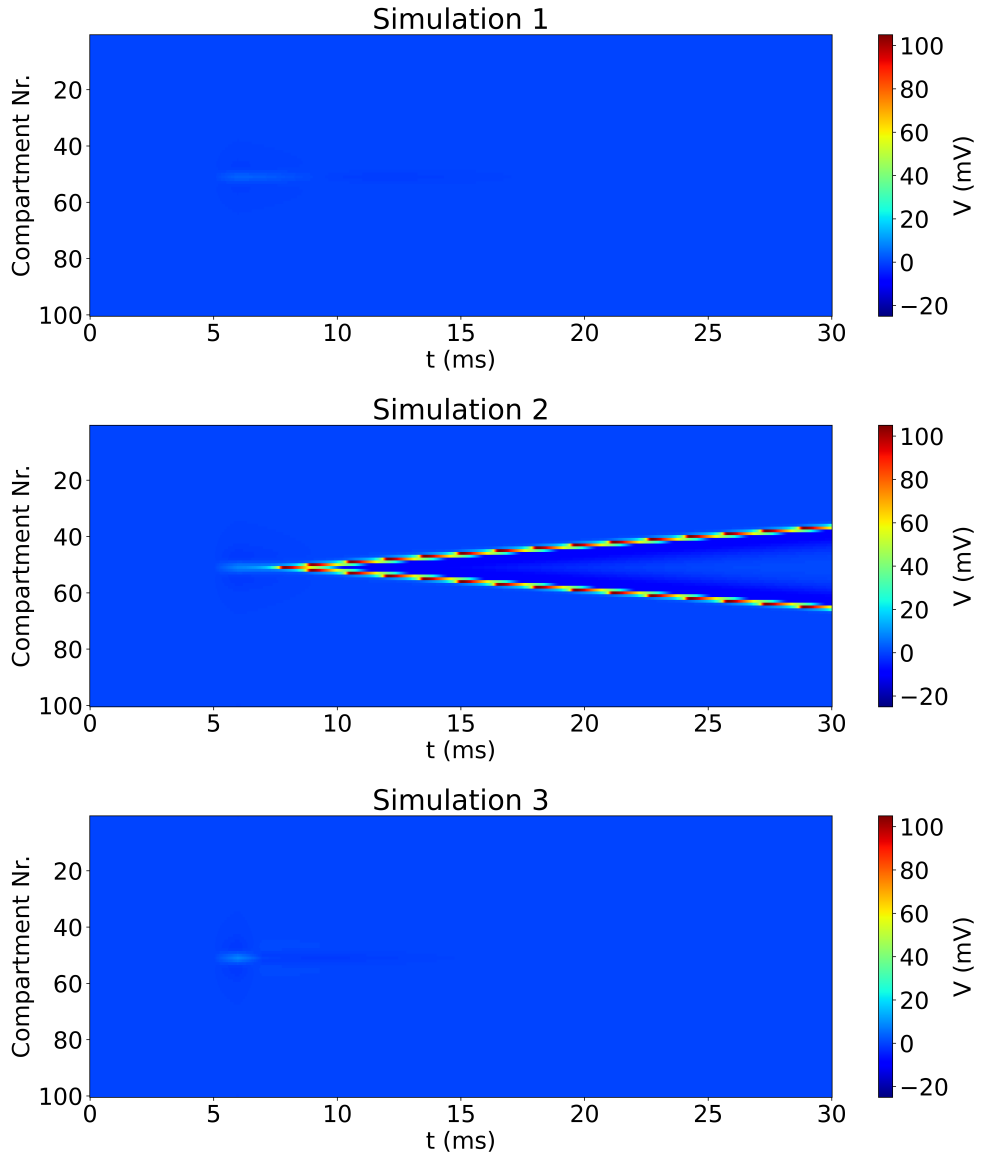

Figure 5: Membrane potential when stimulated as described in section 1.2. Simulation 1: Mono-phasic, $I = -0.05\,\mathrm{mA}$. Simulation 2: Mono-phasic, $I = -0.1\,\mathrm{mA}$. Simulation 3: Bi-phasic, $I = \mp 0.1\,\mathrm{mA}$.

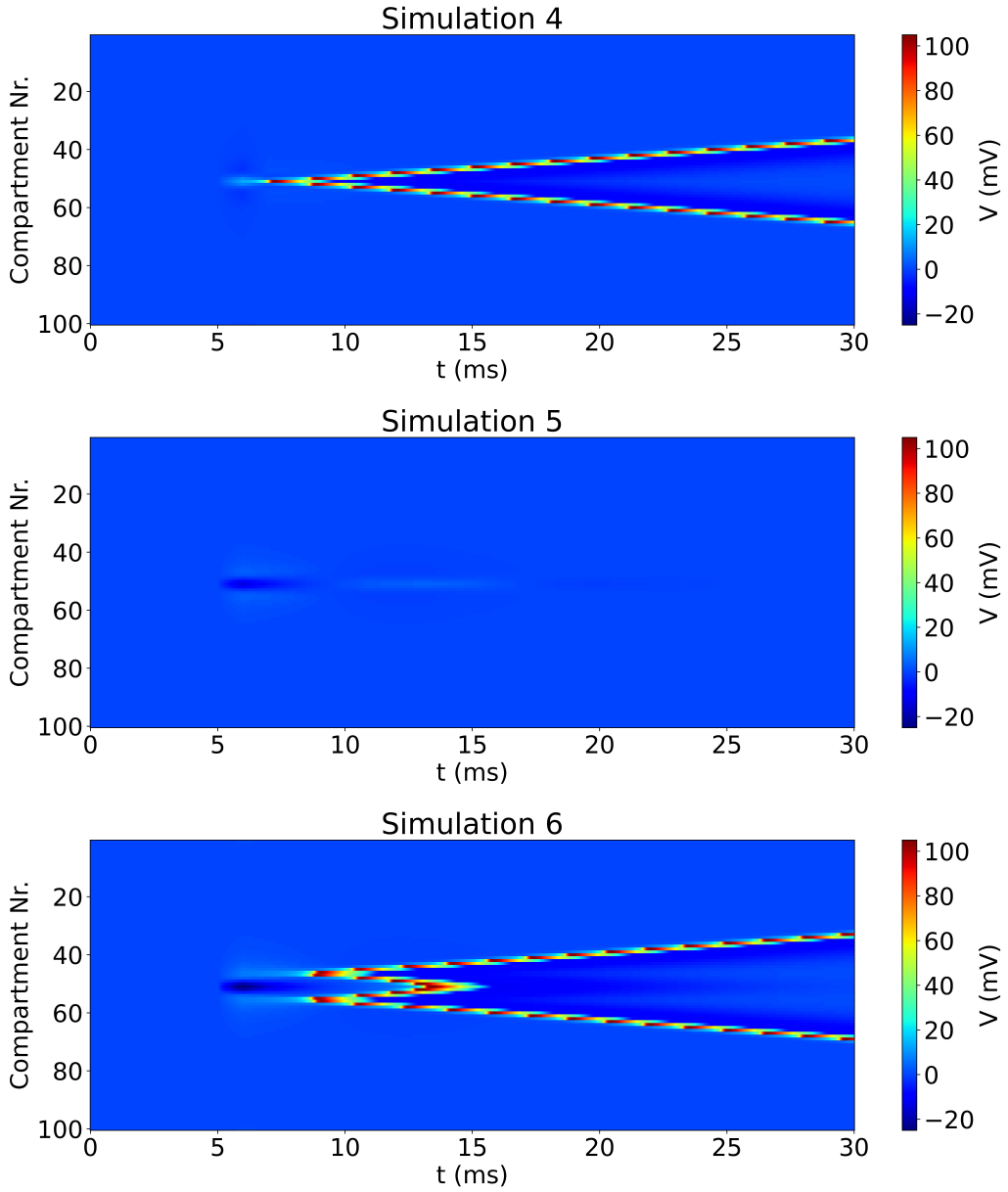

Figure 6: Membrane potential when stimulated as described in section 1.2. Simulation 4: Bi-phasic, $I = \mp 0.15\,\mathrm{mA}$. Simulation 5: Mono-phasic, $I = 0.2\,\mathrm{mA}$. Simulation 6: Mono-phasic, $I = 0.4\,\mathrm{mA}$.

3 Discussion

3.1 Relationship between stimulus shape and amplitude necessary for AP generation

Simulations 1 and 2 show that for a mono-phasic negative current pulse, $I = -0.1\,\mathrm{mA}$ is sufficient to deploy an AP, but $I = -0.05\,\mathrm{mA}$ is not. For bi-phasic pulses, Simulation 3 and 4 show that $I = \mp 0.15\,\mathrm{mA}$ is required while $I = \mp 0.1\,\mathrm{mA}$ is not enough. Simulations 5 and 6 show that a positive mono-phasic current, not even $I = 0.2\,\mathrm{mA}$, suffices, but with $I = 0.4\,\mathrm{mA}$, actually two AP will develop in compartments right and left of the center one.

The observations suggest that an AP induced by a negative mono-phasic shape requires the lowest current, a bi-phasic shape (negative phase first), a higher one, and a positive mono-phasic stimulus has to be applied with the highest current to obtain an AP. Also, it is clearly visible that the APs don't occur at $t = 5\,\mathrm{ms}$ where the stimulus happens but is delayed. This can be explained by the fact that the external potential doesn't directly induce the AP but leads to a current flow across the membrane, which itself leads to the membrane potential crossing the firing threshold. Therefore, the delay is dependent on the membrane resistance and membrane capacitance.

3.2 Relationship between activating function and excitation profile

The excitation profile relates strongly to the activation function. From section 1.2, we know that a positive activation function is needed to induce an AP. From Figure 3, we can derive that for negative currents, the activation function gets much more positive in comparison to a positive current stimulus since the activation function is flipped with the sign of the input current. This explains why the excitation profile in the model will result in an AP at much lower currents when the current is negative. However, Figure 3 also shows that when a positive current is large enough to induce an AP, two AP will be triggered since the activation function has two maxima. In the excitation profile, this will result in an action potential propagating in both directions from each of the two compartments where the activation function reaches its maximum. Due to the refractory period of the compartments, however, the signals propagating to the middle of the axon will result in a depletion of the signal at the compartment where they meet since none of them can trigger an AP in a compartment which was recently triggered by the other. This is nicely visible in Figure 6, Simulation 6.

The reason why a bi-phasic pulse starting with a negative current has to be larger to trigger an action potential than a negative mono-phasic stimulus is due to the aforementioned delay between stimulus and AP. Because in the given examples, the delay was longer than one phase of the bi-phasic current, the positive phase of the stimulus will lead to an activation function that directly counters the activation function of the first phase before it could raise the membrane potential above the firing threshold. This leads to a forced decrease in membrane potential at the midpoint, where you would expect

an AP from the first phase. The second phase is also too weak to induce an action potential itself since we already discussed that for positive currents, the magnitude of the current has to be much larger to induce an AP than for a negative one. When, however, the current of the first phase of the bi-phasic pulse is large enough, the time until the second phase comes into action is long enough to raise the membrane potential above the threshold, from where on even the counteracting activation function can't stop the formation of an action potential as shown in Figure 6, Simulation 4.