Neuroprothetics Exercise 6
Electric Stimulation

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1 Potential Field

This exercise continues to explore the responses of the multi-compartment axon model under electrical stimulation. However, unlike in exercise 5, this time the stimulus current will not be injected into the axon, but is applied via an extracellular electric field.
Given a homogeneous extracellular medium characterized by a resistivity of ρ, the potential Φ at any given point located a distance r from a point-source of current I can be determined using the formula presented in equation 1.

$$\Phi = \frac{\rho}{4\pi} \cdot \frac{I}{r} \tag{1}$$

1.1 Activating Function

The extracellular potential can be calculated according to equation 1. The electric field is obtained as the negative first derivative of the potential, while the activating function, which is a critical parameter indicating how changes in the extracellular potential can lead to neuron activation, is derived as the second derivative of the potential.
When ρ_{medium} is set to $1\Omega m$, and currents of $I = 1mA$ and $I = -1mA$ are applied separately, the values of the extracellular potential, the electric field, and the activating function can be calculated along a 300μm straight segment of an axon positioned 10μm from a point source of current. These values are respectively presented in Figure 1, Figure 2, and Figure 3.

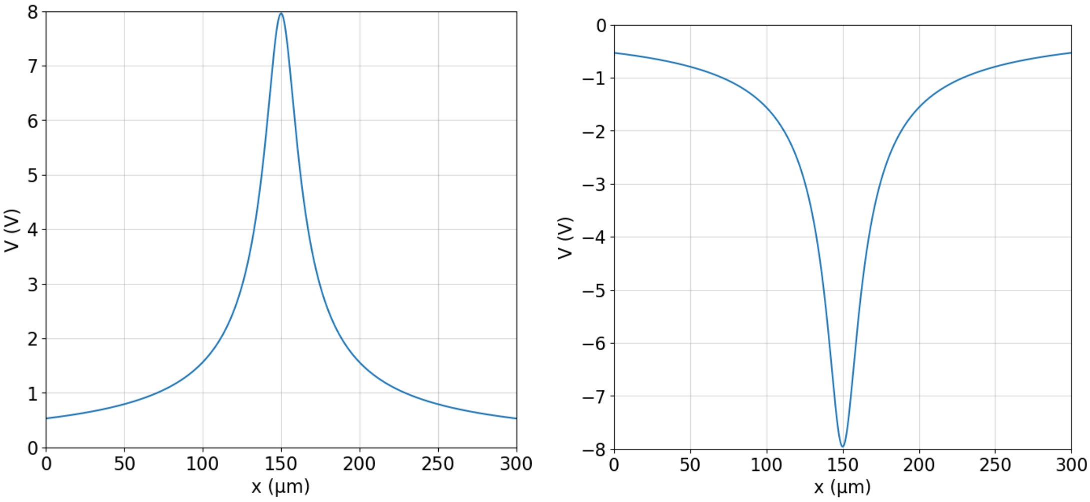

Figure 1: Extracellular potential for $d = 10\,\mu m$ for I = 1 mA (left) and $I = -1\,mA$ (right)

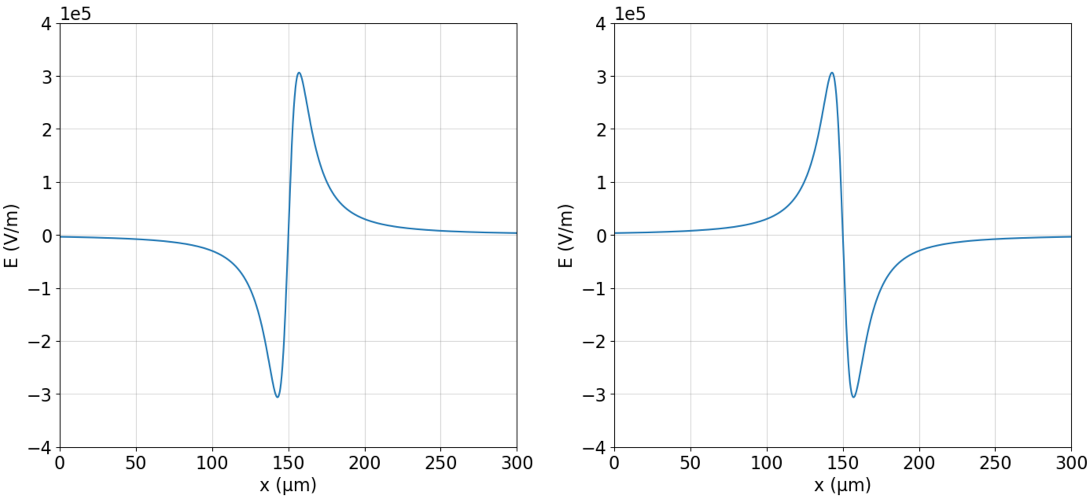

Figure 2: Electric field for $d = 10\,\mu m$ for I = 1 mA (left) and $I = -1\,mA$ (right)

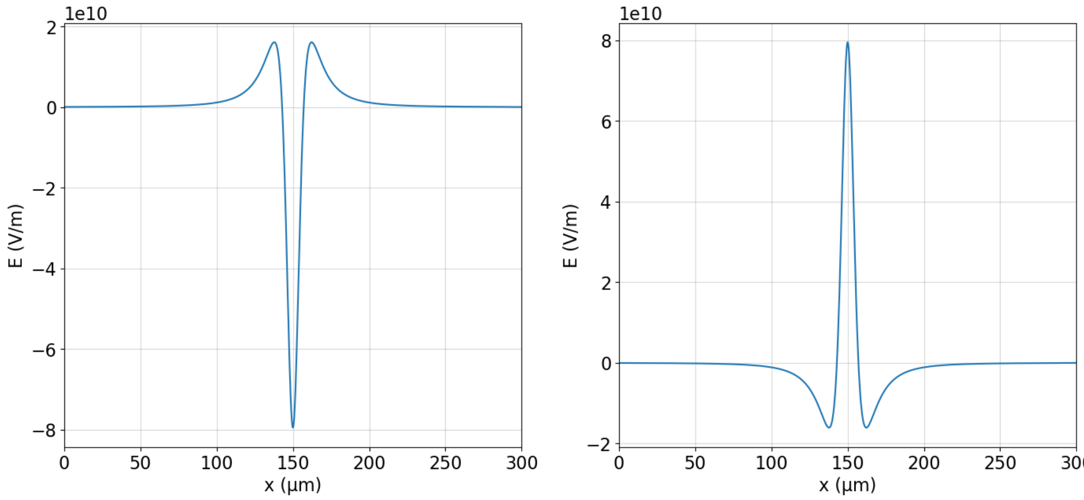

Figure 3: Activating function for $d = 10\,\mu m$ for I = 1 mA (left) and $I = -1\,mA$ (right)

2 Neuron Model

In this exercise, the axon will be stimulated only by the extracellular potential, which means I_{stim} will be zero, so the re-derived Implicit Euler equation will be like:

$$(I - \frac{\Delta t}{C_m R_a} C) \cdot \vec{V}_m(t + \Delta t) = \vec{V}_m(t) + \frac{\Delta t}{C_m}(-\vec{I}_{HH}(t + \Delta t) + \frac{1}{R_a} C \cdot \vec{V}_e(t + \Delta t)) \quad (2)$$

2.1 Stimulate the Axon

We construct the six stimulation sequences I_1 to I_6 as presented in Table 1 and depicted in Figure 4. Simulations are run with the following parameters: axoplasmatic resistivity $\rho_{\text{axon}} = 7 \times 10^{-3} \Omega \cdot m$, axonal radius $r_{\text{axon}} = 1 \mu m$, and compartment length $l_{\text{comp}} = 3 \mu m$. The simulation duration is set to 30 ms with a time step $\Delta t = 25 \mu s$, and the pulse initiation is positioned at $t = 5 ms$.

Polarity / Current pulse type	Negative	Positive
Mono-phasic	$I_1 = -0.05$ mA, $I_2 = -0.1$ mA	$I_5 = 0.2$ mA, $I_6 = 0.4$ mA
Bi-phasic	$I_3 = \mp 0.1$ mA, $I_4 = \mp 0.15$ mA	

Table 1: The six stimulation sequences

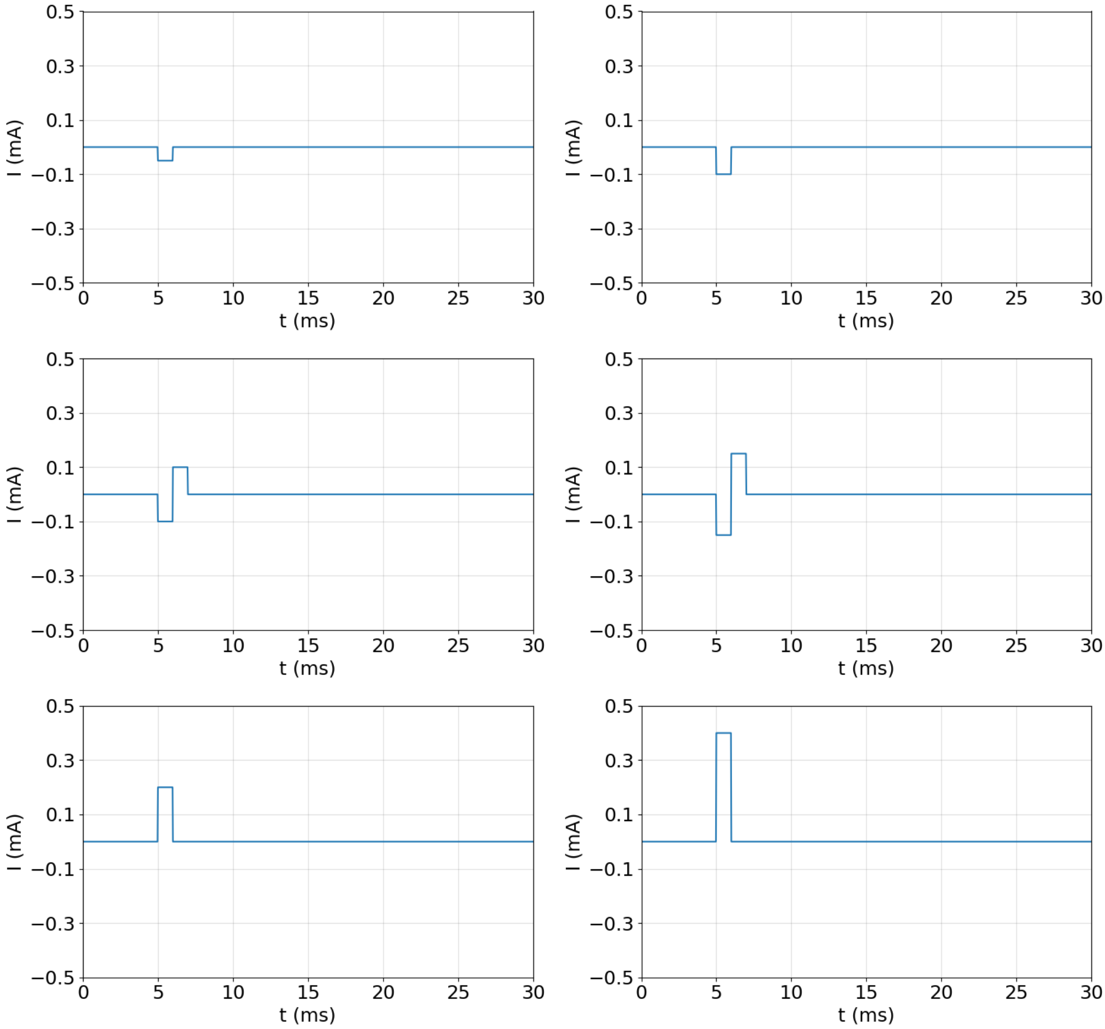

Figure 4: Current waveform patterns for the stimulation sequences

The propagation of the action potential in these six simulation sequences is depicted in Figures 5 and 6. The results can be interpreted as follows:

- how different stimulus shapes relate to necessary stimulus amplitudes for generation of APs.
  (1) the effect of mono-phasic pulse on stimulation:
  For the monophasic pulses I_1, I_2, I_5 and I_6, we observe that negative currents are more likely to elicit neuronal stimulation compared to positive currents. For instance, a current of $I_2 = -0.1$ mA is sufficient to generate stimulation, whereas a positive current requires an increase to $I_6 = 0.4$ mA to achieve the same effect.
  (2) the effect of bi-phasic pulse on stimulation:
  The efficacy of bi-phasic pulses I_3 and I_4 is related to the timing of the electrical stimulus. In the case of I_3, the negative current pulse occurring around 5ms to 6ms is on the verge of forming a stimulus while the subsequent positive pulse interrupts this process. Since the reverse direction positive current does not reach the necessary threshold, no stimulation occurs (as shown at the bottom of Figure 5). When the stimulus current of I_4 is increased, the time required to reach the stimulation threshold decreases, allowing the formation of a stimulus before the arrival of the reverse current, hence a stimulation is observed (as shown at the top of Figure 6).

- how the activating function relates to the observed excitation profiles.
  Based on the activation function graph at the bottom of Figure 3, we can observe the following characteristics:
  (1) The activation function for positive current displays two positive peaks, whereas the activation function for negative current has only one positive peak. Typically, a positive peak in the activation function corresponds to the generation of a stimulus, thus positive current may induce two stimuli, while negative current would result in one stimulus. This is corroborated by Figure 5 Middle for I_2, where only one AP is observed, and Figure 6 Bottom for I_6, where two APs are observed which appear upon collision.
  (2) The activation function for negative current shows a very high peak, indicating that negative current more easily generates a stimulus. In contrast, the activation function for positive current has gentle peaks, indicating that a sufficiently large positive current is needed to produce a stimulus. As shown in Figure 5 Middle and Figure 6 Bottom, a current of -0.1 mA I_2 is sufficient to trigger a stimulus, while a positive current of 0.4 mA I_6 is required to produce a stimulus.

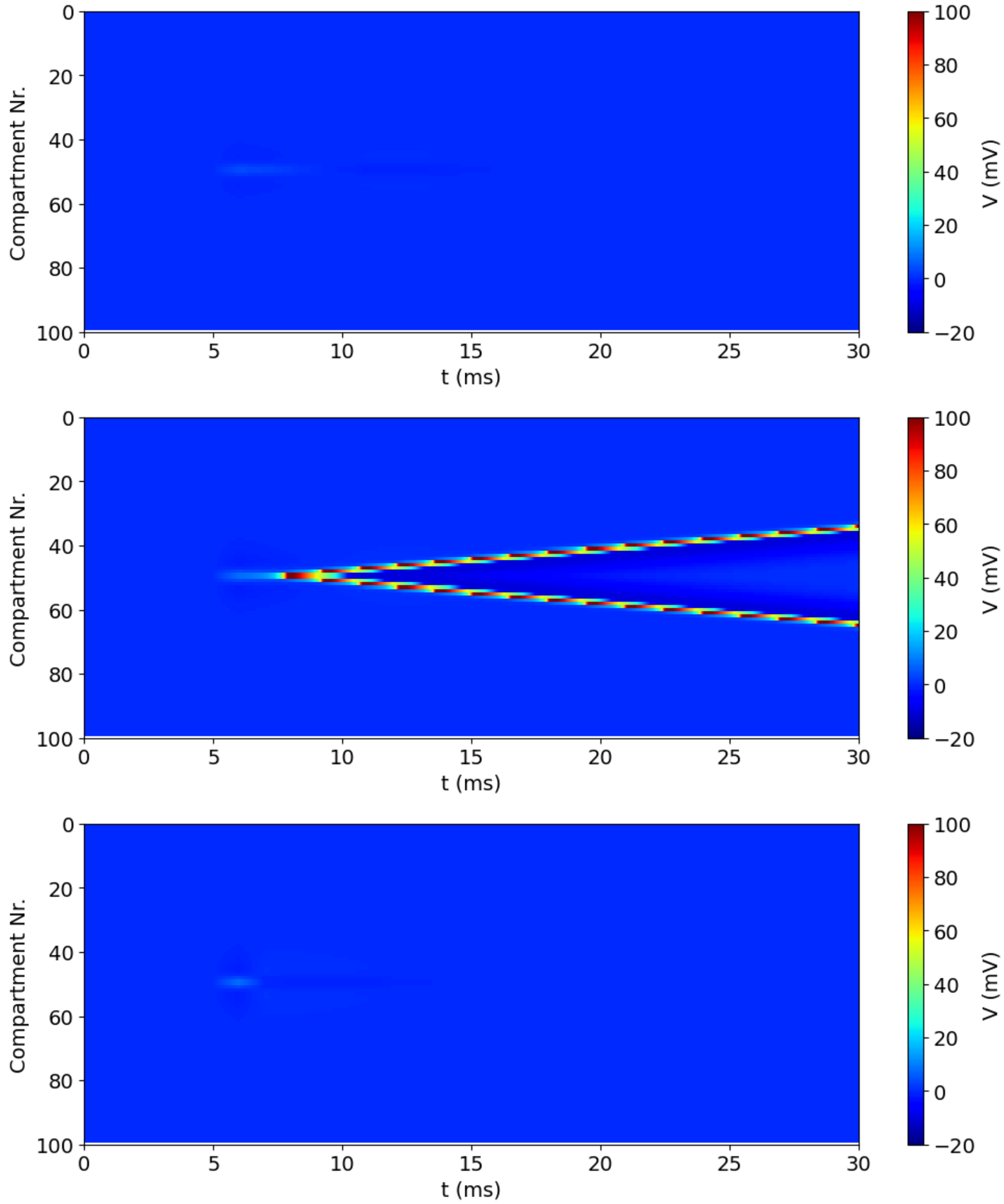

Figure 5: Propagation of the action potential when stimulated at $t = 5\,\mathrm{ms}$ with a phase duration of $1\,\mathrm{ms}$. Top: mono-phasic pulse with $-0.05\,\mathrm{mA}$. Middle: mono-phasic pulse with $-0.1\,\mathrm{mA}$. Bottom: bi-phasic pulse with $\mp 0.1\,\mathrm{mA}$

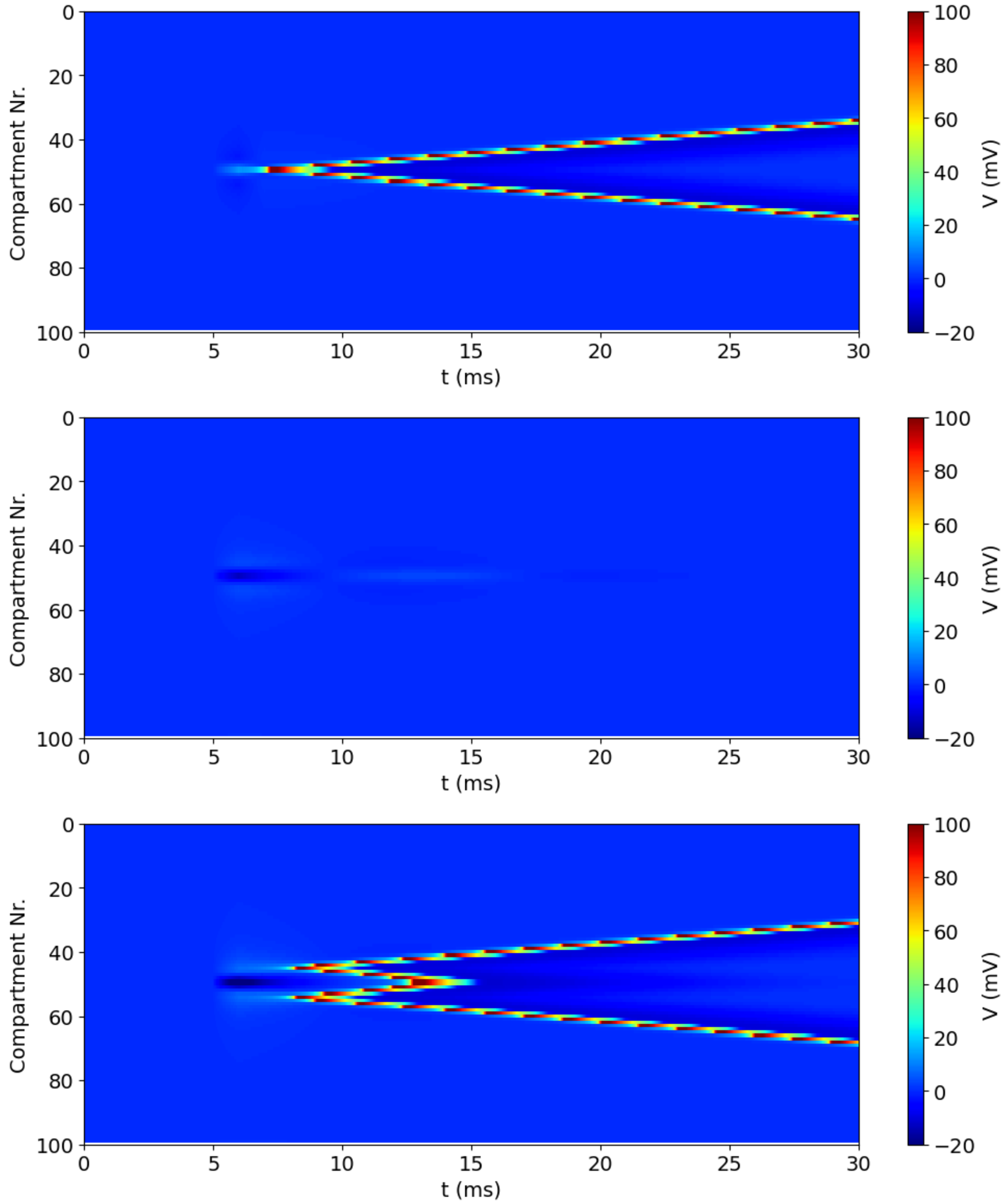

Figure 6: Propagation of the action potential when stimulated at $t = 5\,\mathrm{ms}$ with a phase duration of $1\,\mathrm{ms}$. Top: bi-phasic pulse with $\mp 0.15\,\mathrm{mA}$. Middle: mono-phasic pulse with $0.2\,\mathrm{mA}$. Bottom: mono-phasic pulse with $0.4\,\mathrm{mA}$