Electrical Engineering 3BB3: Cellular Bioelectricity (2014)

Solutions to Midterm 2

1. **In the cable equations for a uniform cylindrical fiber, if the extracellular space between a fiber and its surrounding fibers or cells is very extensive, then a reasonable approximation is:**
   - **a.** $r_m \approx 0$**,**
   - **b.** $r_i \approx 0$**,**
   - **c.** $r_e \to \infty$**, or**
   - **d.** $r_e \approx 0$**.** **(5 pts)**

   The answer is **d.** $r_e \approx .0$

2. **The minimum stimulus amplitude required to just reach threshold as the duration of a stimulating pulse tends towards infinity is referred to as the:**
   - **a. robitussin,**
   - **b. rheobase,**
   - **c. chronaxie, or**
   - **d. cronkite.** **(5 pts)**

   The answer is **b. rheobase**.

3. **For a cylindrical fiber with space constant** λ**, the temporal response of the membrane potential to a current step at the spatial origin is exponential with time constant** τ **at:**
   - **a.** $x = 0$**,**
   - **b.** $x = \lambda$**,**
   - **c. all values of** x**, or**
   - **d. no values of** x**.** **(5 pts)**

   The answer is **b.** $x = \lambda$.

4. **The larger the diameter of a *spherical excitable cell*, then:**
   - **a. the smaller the membrane time constant,**
   - **b. the smaller the membrane capacitance,**
   - **c. the smaller the membrane potential, or**
   - **d. the smaller the membrane resistance.** **(5 pts)**

   The answer is **d. the smaller the membrane resistance**.

5. **The larger the diameter of a *cylindrical axon*, then:**
   a. **the larger the space constant,**
   b. **the smaller the space constant,**
   c. **the larger the axoplasmic longitudinal resistance, or**
   d. **the smaller the membrane capacitance.** **(5 pts)**

   The answer is **a. the larger the space constant**.

6. **Consider the extracellular potential produced by a short action potential (AP) propagating along a long axon. If the AP waveform has no hyperpolarizing or depolarizing afterpotentials, then the normal lumped-source model for this AP would be:**
   a. **a single monopole source,**
   b. **a single dipole source,**
   c. **a pair of equal and opposite dipole sources, or**
   d. **a pair of equal and opposite monopole sources.** **(5 pts)**

   The answer is **c. a pair of equal and opposite dipole sources**.

7. **In cardiac tissue, action potentials spread from cell to cell via:**
   a. **tropomyosin and troponin,**
   b. **ACh receptors,**
   c. **gap junctions, or**
   d. **the neurotransmitter GABA.** **(5 pts)**

   The answer is **c. gap junctions**.

8. **Atrial repolarization can be observed in the component of an ECG lead voltage waveform known as the:**
   a. **P wave,**
   b. **T wave,**
   c. **ST segment, or**
   d. **none of the above.** **(5 pts)**

   The answer is **d. none of the above**. Atrial repolarization is obscured by the larger QRS complex produced by ventricular activation.

9. Briefly explain:

a. what are *miniature* endplate potentials (MEPPs), and

b. how do they indicate that neurotransmitter release is quantal at the neuromuscular junction?

(15 pts)

a. MEPPs are the postsynaptic potentials that are generated at the neuromuscular junction in response to the spontaneous exocytosis of a single presynaptic neurotransmitter vesicle and the subsequent binding of the ACh to some number of post-synaptic receptor channels and the opening of these channels. MEPP amplitudes are typically on the order of around 0.5 mV. (See p. 9 of Lecture #22.)

b. All EPPs in a neuromuscular junction elicited by a motor axon action potential tend to have an amplitude that is an integer multiple of the MEPP amplitude, suggesting that neurotransmitter can only be released in discrete packets or *quanta*. Experimental modification of the calcium signalling for neurotransmitter release appears to change the release probability but not size of the neurotransmitter quanta. (See pp. 9–12 of Lecture #22.)

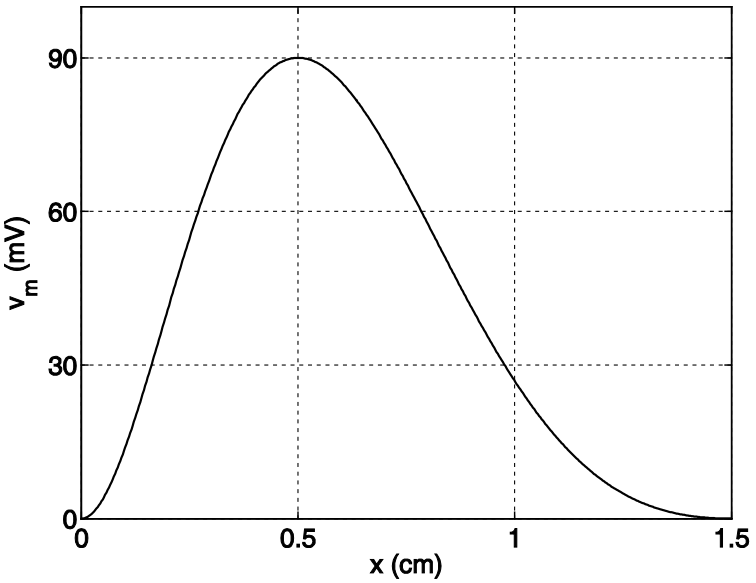
10. Compare and contrast how the propagation velocity for action potentials depends on the axonal diameter in *unmyelinated* vs. *myelinated* axons. (15 pts)

From Hodgkin & Huxley's equation for a stably propagating action potential in an unmyelinated axon (Eq. 6.68), the propagation velocity is constrained to be proportional to the square-root of the fiber diameter (Eq. 6.70). This arises because of the relative contributions of the membrane resistance and the axoplasmic longitudinal resistance to the length of the local circuit currents, such that the space constant for an unmyelinated uniform fiber is proportional to the square-root of the fiber diameter.

For a myelinated axon, the local circuit currents are elongated due to the myelination of the internodes increasing the membrane's leakage resistance. The Schwann cells in the PNS and the oligodendrocytes in the CNS regulate the length of the internodes such that they are proportional to the fiber diameter. Consequently, the propagation velocity in myelinated axons is directly proportional to the fiber diameter.

Thus, the propagation velocity increases with increasing diameter for both types of axons, but the increase in velocity is more pronounced for myelinated axons.

11. Consider an action potential (AP) with the *spatial* waveform illustrated in the figure below.



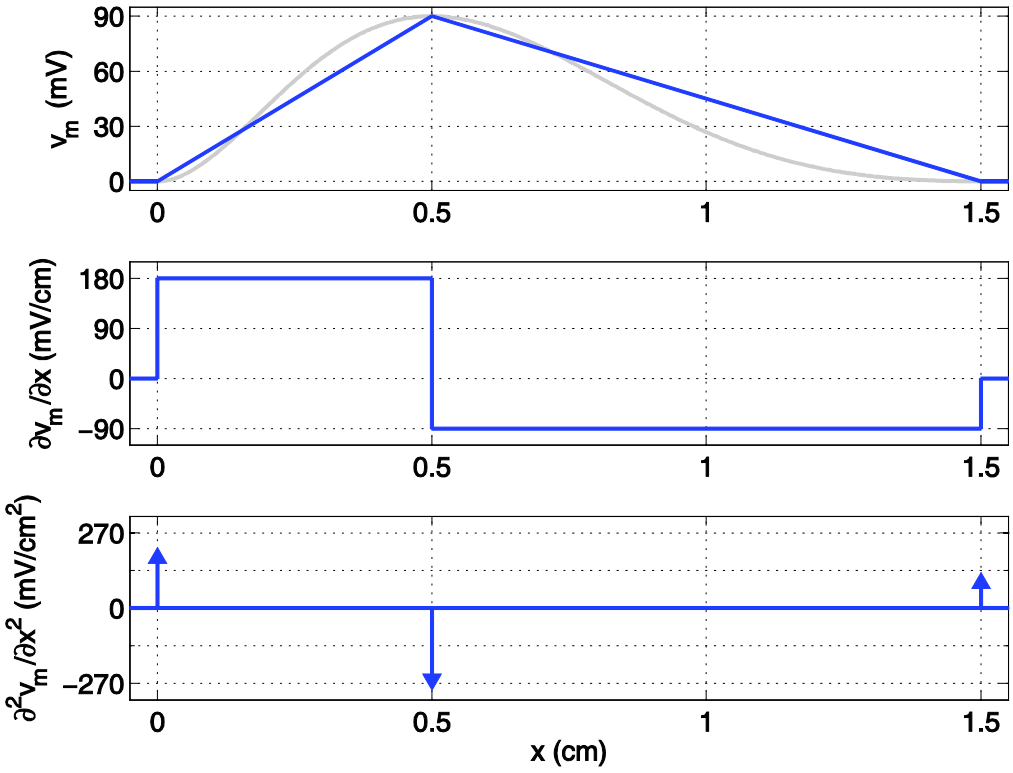
Assume that no currents are being injected into the intra- or extra-cellular space from external sources and the intra- and extra-cellular resistances per unit length are $r_i = 1\ \text{M}\Omega/\text{cm}$ and $r_e = 20\ \text{k}\Omega/\text{cm}$, respectively.

a. Calculate the local circuit currents, i.e., the transmembrane currents and the axial intra- and extra-cellular currents as a function of position x, *in the case where this waveform is approximated by a triangle*.

b. If the spatial waveform shown above occurs at time $t = 0$ and the AP is propagating at a constant velocity $\theta = -5\ \text{m/s}$ (i.e., to the left), sketch the *temporal* AP waveform that would be observed at position $x = 0.5\ \text{cm}$ (for times $t < 0$ as well as for $t > 0$). Make sure to include in your sketch the times at which the foot, peak and tail of the AP are each at position $x = 0.5\ \text{cm}$. (15 pts)

a. The simplest triangular approximation of the given waveform has the foot of the AP starting at $x = 0$, the peak at $x = 0.5\ \text{cm}$, and the end of the tail at $x = 1.5\ \text{cm}$, as shown in the top panel of the figure below.

The first spatial derivate is zero in the regions $x < 0$ and $x > 1.5\,\text{cm}$, a constant value of 180 mV/cm in the region from 0 to 0.5 cm, and a constant value of $-90\ \text{mV/cm}$ in the region 0.5 to 1.5cm, as shown in the middle panel of the figure below. The second spatial derivative is a Dirac delta function of area 180 mV/cm at position $x = 0$, a Dirac delta function of area $-270\ \text{mV/cm}$ at position $x = 0.5\,\text{cm}$, a Dirac delta function of area 90 mV/cm at position $x = 1.5\ \text{cm}$, and zero elsewhere, as shown in the bottom panel of the figure below.



To determine the transmembrane currents resulting from the spatial waveform, we make use of the cable equation for the transmembrane currents:

$$i_m = \frac{1}{r_i + r_e} \cdot \frac{\partial^2 v_m}{\partial x^2},$$

which is valid for both linear and nonlinear cables.

Dividing the second spatial derivate by the sum of the intra- and extra-cellular resistances per unit length gives i_m consisting of Dirac delta function of areas:

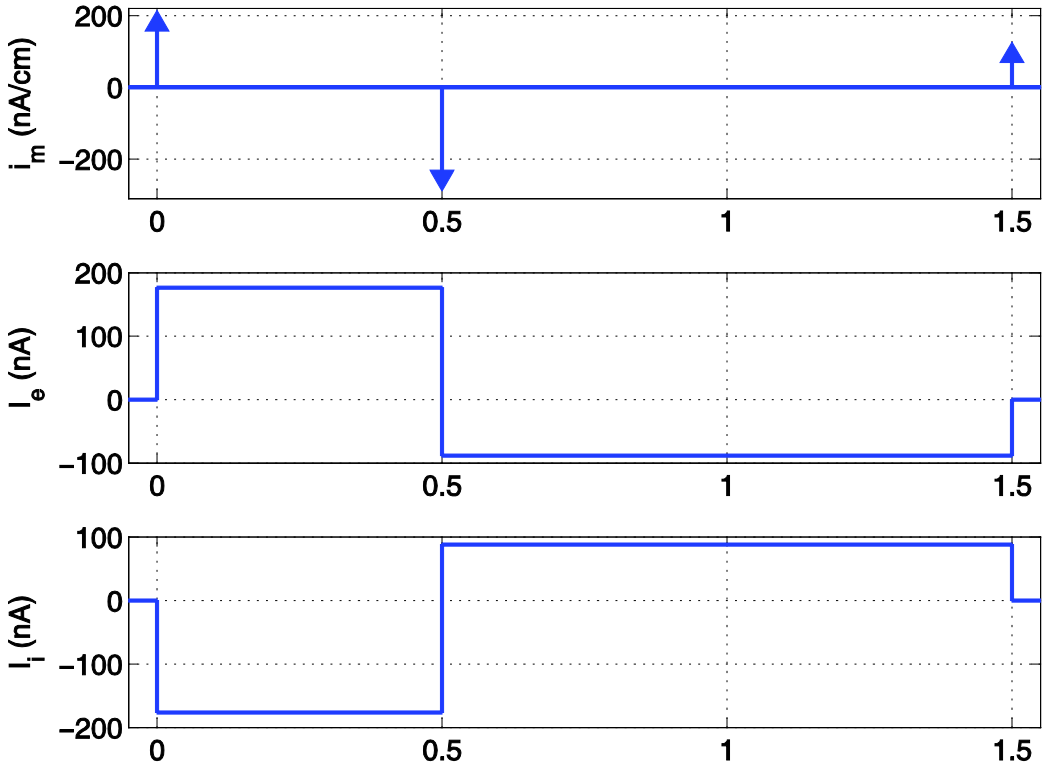
- $\frac{(180\ \text{mV/cm})}{(1020\ \text{k}\Omega/\text{cm})} = 176.5\ \text{nA}$ at position $x = 0$,
- $\frac{(-270\ \text{mV/cm})}{(1020\ \text{k}\Omega/\text{cm})} = -264.7\ \text{nA}$ at position $x = 0.5\ \text{cm}$,
- $\frac{(90\ \text{mV/cm})}{(1020\ \text{k}\Omega/\text{cm})} = 88.2\ \text{nA}$ at position $x = 1.5\ \text{cm}$,

and zero elsewhere,, as shown in the top panel of the figure below.

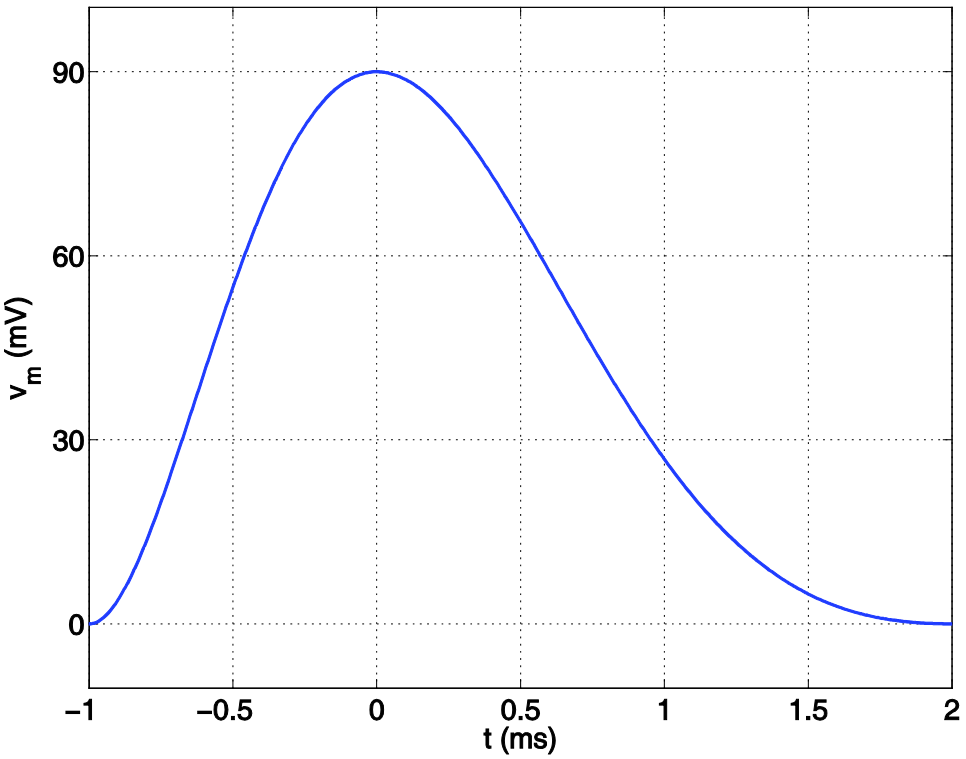
To obtain the extra- and intra-cellular axial currents I_e and I_i, respectively, we make use of the cable equations:

$$\frac{\partial I_e}{\partial x} = i_m; \quad \frac{\partial I_i}{\partial x} = -i_m,$$

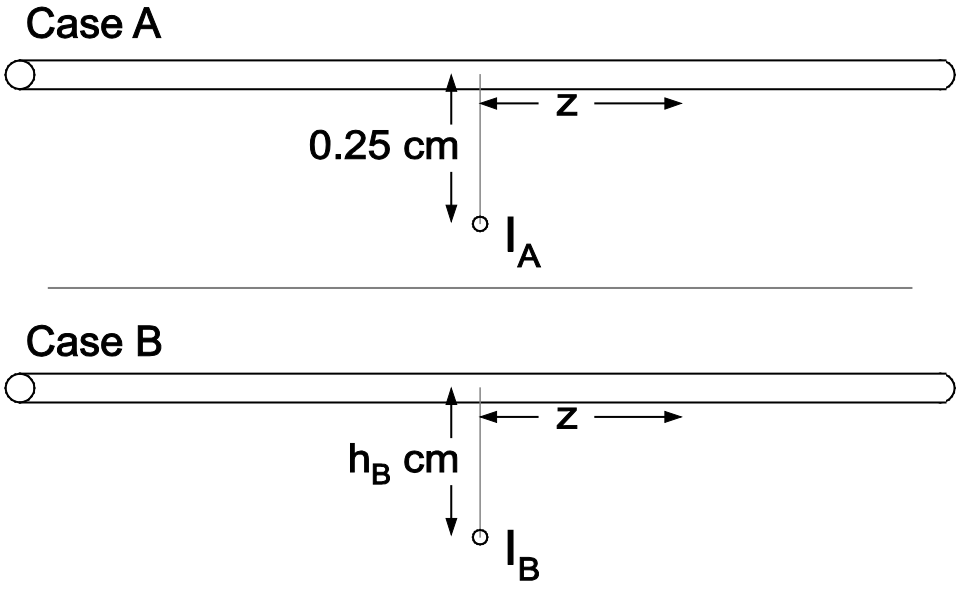
which are valid for both linear and nonlinear cables. These can be integrated over x to give $I_e = \frac{1}{r_i + r_e}\frac{\partial v_m}{\partial x}$ and $I_i = -\frac{1}{r_i + r_e}\frac{\partial v_m}{\partial x}$, such that I_e and I_i are zero in the regions $x < 0$ and $x > 1.5\,\text{cm}$, have constant values of $\pm 176.5\,\text{nA}$ (respectively) in the region from 0 to 0.5 cm, and constant values of $\mp 88.2\,\text{nA}$ (respectively) in the region 0.5 to 1.5cm, as plotted in the middle and bottom panels, respectively, of the figure below.



b. From the information given, the peak of the AP is at position $x = 0.5$ cm at time $t = 0$ ms. Since the foot of the AP is 0.5 cm to the left of the peak and the propagation velocity is $\theta = -5\,\text{m/s} = -0.5\,\text{cm/ms}$, the foot of the AP must have been at position $x = 0.5$ cm at time $t = -1$ ms. The tail end of the AP waveform is 1 cm behind the peak, so it will arrive at position $x = 0.5$ cm at time $t = 2$ ms. The corresponding temporal waveform is plotted in the figure below.


90
60
30
0
v_m (mV)
−1
−0.5
0
0.5
1
1.5
2
t (ms)

12. Consider two cases (A & B) of extracellular stimulating electrodes well approximated by idealized monopole sources with the geometry relative to an unmyelinated axon as shown below.



In both cases the extracellular medium has a conductivity of $\sigma_e = 20\ \mathrm{mS/cm}$ and the axon is identical. The two stimulating electrodes have step currents of $I_A = -1\ \mathrm{mA}$ and $I_B = +1\ \mathrm{mA}$, respectively. Electrode A is known to be 0.25 cm from the axon, while electrode B is an arbitrary distance h_B.

a. Find the extracellular potential *in units of mV* as a function of z (in units of cm), i.e., $\phi_e(z)$, for both case A and case B.

b. Find the activating function $\frac{\partial^2 \phi_e}{\partial z^2}$ *in units of mV/cm²* for both case A and case B.

c. At what distance h_B is the *maxim (i.e., peak) positive value* of the activating function for case B equal to the *maximum (i.e., peak) positive value* of the activating function for case A? (15 pts)

a. The two cases have the same basic geometry and stimulation characteristics, just with different current amplitudes and electrode-fiber distances. Therefore, it is possible to solve for the general case and then substitute in the appropriate values for the specific cases. For a monopole source at a perpendicular distance of h from the fiber, the distance r from the electrode to the position z on the fiber is:

$$r = \sqrt{h^2 + z^2}\,.$$

Therefore the extracellular potential at position z on the fiber is:

$$\phi_e(z) = \frac{I_0}{4\pi\sigma_e}\frac{1}{\sqrt{h^2 + z^2}}\,.$$

For Case A this corresponds to:

$$\phi_{e,\mathrm{A}}(z) = \frac{-1}{4\pi \cdot 20}\frac{1}{\sqrt{0.25^2 + z^2}}\ \mathrm{V} = \frac{-3.9789}{\sqrt{0.25^2 + z^2}}\ \mathrm{mV},$$

and for Case B:

$$\phi_{e,\mathrm{B}}(z) = \frac{+1}{4\pi \cdot 20}\frac{1}{\sqrt{h_\mathrm{B}^{\,2} + z^2}}\ \mathrm{V} = \frac{3.9789}{\sqrt{h_\mathrm{B}^{\,2} + z^2}}\ \mathrm{mV}.$$

Note that for I_A & I_B in units of mA being divided by σ_e in units of mS/cm, the resulting units of $\phi_e(z)$ will be V, not mV, so we need to multiple by 1×10^3 to get the result in units of mV.

b. The activating function $\frac{\partial^2 \phi_e}{\partial z^2}$ is then:

$$\frac{\partial \phi_e}{\partial z} = -\frac{I_0}{4\pi\sigma_e}\frac{z}{\left(h^2 + z^2\right)^{3/2}} \quad \Rightarrow$$

$$\frac{\partial^2 \phi_e}{\partial z^2} = \frac{I_0}{4\pi\sigma_e}\frac{3z^2 - \left(h^2 + z^2\right)}{\left(h^2 + z^2\right)^{5/2}}$$

$$= \frac{I_0}{4\pi\sigma_e}\frac{2z^2 - h^2}{\left(h^2 + z^2\right)^{5/2}}.$$

For Case A this corresponds to:

$$\frac{\partial^2 \phi_{e,\mathrm{A}}}{\partial z^2} = \frac{-3.9789\left(2z^2 - 0.25^2\right)}{\left(0.25^2 + z^2\right)^{5/2}}\ \mathrm{mV/cm^2},$$

and for Case B:

$$\frac{\partial^2 \phi_{e,\mathrm{B}}}{\partial z^2} = \frac{3.9789\left(2z^2 - {h_\mathrm{B}}^2\right)}{\left({h_\mathrm{B}}^2 + z^2\right)^{5/2}}\ \mathrm{mV/cm^2}.$$

c. The peaks of the activating function $\frac{\partial^2 \phi_e}{\partial z^2}$ are located where its derivate equals zero:

$$\frac{\partial^3 \phi_e}{\partial z^3} = \frac{I_0}{4\pi\sigma_e}\frac{9zh^2 - 6z^3}{\left(h^2 + z^2\right)^{7/2}} = 0$$

$$\Rightarrow \frac{9zh^2 - 6z^3}{\left(h^2 + z^2\right)^{7/2}} = 0$$

$$\Rightarrow 9zh^2 - 6z^3 = 0$$

$$\Rightarrow z^3 = \tfrac{3}{2} zh^2$$

$$\Rightarrow z = 0, \pm\sqrt{\tfrac{3}{2}}h.$$

Evaluating $\partial^2 \phi_e / \partial z^2$ at these three locations reveals that there is a single positive peak at $z = 0$ for Case A, with a magnitude of:

$$\left.\frac{\partial^2 \phi_{e,\mathrm{A}}}{\partial z^2}\right|_{z=0} = \frac{-3.9789\left(0 - 0.25^2\right)}{\left(0.25^2 + 0\right)^{5/2}}\ \mathrm{mV/cm^2} = 254.65\ \mathrm{mV/cm^2},$$

while the positive peaks for Case B are found at $z = \pm\sqrt{\tfrac{3}{2}}h_\mathrm{B}$. Solving for the value of h_B that produces $\partial^2 \phi_{e,\mathrm{B}} / \partial z^2 = 254.65\ \mathrm{mV/cm^2}$ at $z = \sqrt{\tfrac{3}{2}}h_\mathrm{B}$ gives:

$$\left.\frac{\partial^2 \phi_{e,\mathrm{B}}}{\partial z^2}\right|_{z=\sqrt{\frac{3}{2}}h_\mathrm{B}} = \frac{3.9789\left(2\left(\sqrt{\tfrac{3}{2}}h_\mathrm{B}\right)^2 - {h_\mathrm{B}}^2\right)}{\left({h_\mathrm{B}}^2 + \left(\sqrt{\tfrac{3}{2}}h_\mathrm{B}\right)^2\right)^{5/2}}\ \mathrm{mV/cm^2} = 254.65\ \mathrm{mV/cm^2}$$

$$\Rightarrow \frac{3.9789\left(2 \cdot \tfrac{3}{2}{h_\mathrm{B}}^2 - {h_\mathrm{B}}^2\right)}{\left({h_\mathrm{B}}^2 + \tfrac{3}{2}{h_\mathrm{B}}^2\right)^{5/2}} = 254.65 \qquad \Rightarrow \frac{3.9789\left(2{h_\mathrm{B}}^2\right)}{\left(\tfrac{5}{2}{h_\mathrm{B}}^2\right)^{5/2}} = 254.65$$

$$\Rightarrow \frac{3.9789 \cdot 2 \cdot {h_\mathrm{B}}^2}{\left(\tfrac{5}{2}\right)^{5/2} \cdot {h_\mathrm{B}}^5} = 254.65 \qquad \Rightarrow {h_\mathrm{B}}^3 = \frac{3.9789 \cdot 2}{\left(\tfrac{5}{2}\right)^{5/2} \cdot 254.65}$$

$$\Rightarrow h_\mathrm{B} = \sqrt[3]{\frac{3.9789 \cdot 2}{\left(\tfrac{5}{2}\right)^{5/2} \cdot 254.65}} = 0.1468\ \mathrm{cm}.$$

The activating functions for these two cases are shown in the figure below. It can be seen that the positive peak value for case A is equal to the positive peak value for case B with electrode B at a distance of 0.1468 cm from the fiber.