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ELEC436/536 SPRING 2020

Homework 4

Q1) *(20 points)* Consider an action potential with a waveform that can be approximated by a triangle, as given in the figure below. Assume that the tail of the action potential spatial waveform is at position x = 0 , 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 =1.25 MΩ/cm and r_e =12.5 kΩ/cm, respectively. If this action potential is propagating (without dissipation) along an unmyelinated axon in the +x direction with velocity 2 m/s, calculate the resulting local circuit currents, i.e., the transmembrane current per unit length i_m and the axial intra- and extra-cellular currents I_i and I_e , respectively, as a function of position x .

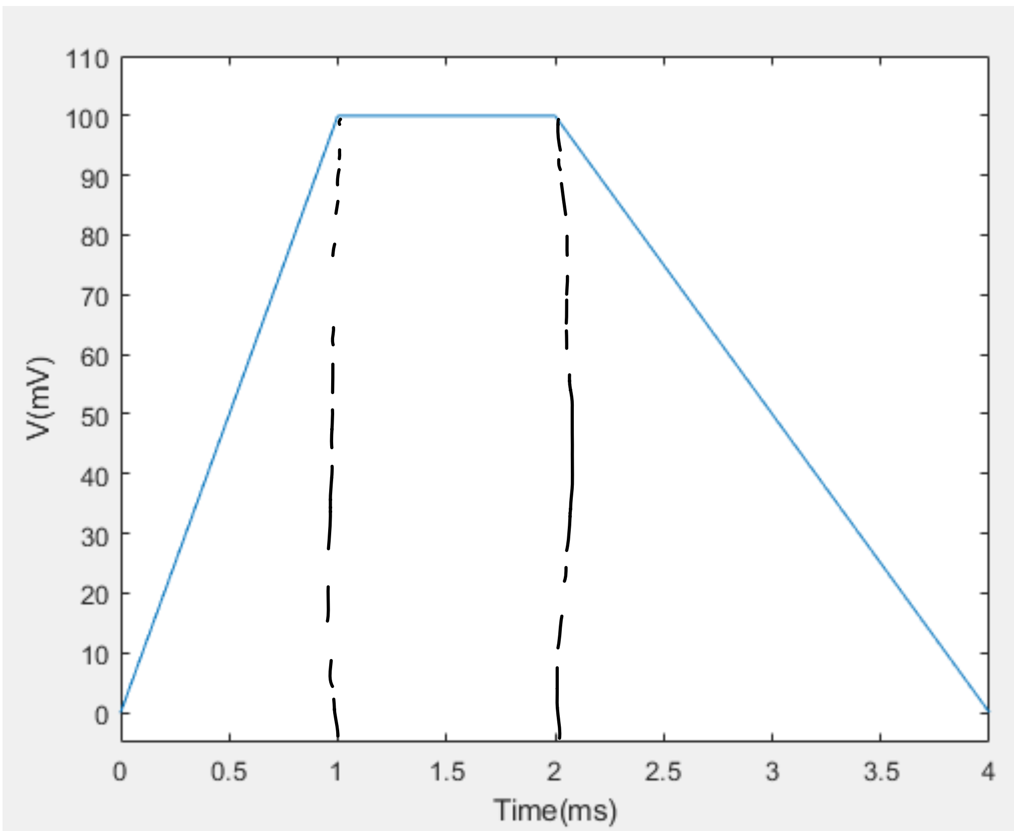


Fig. Membrane Voltage

Answer for 1 :

From the information that propagating action potential is propagating at a constant velocity 2 m/s;

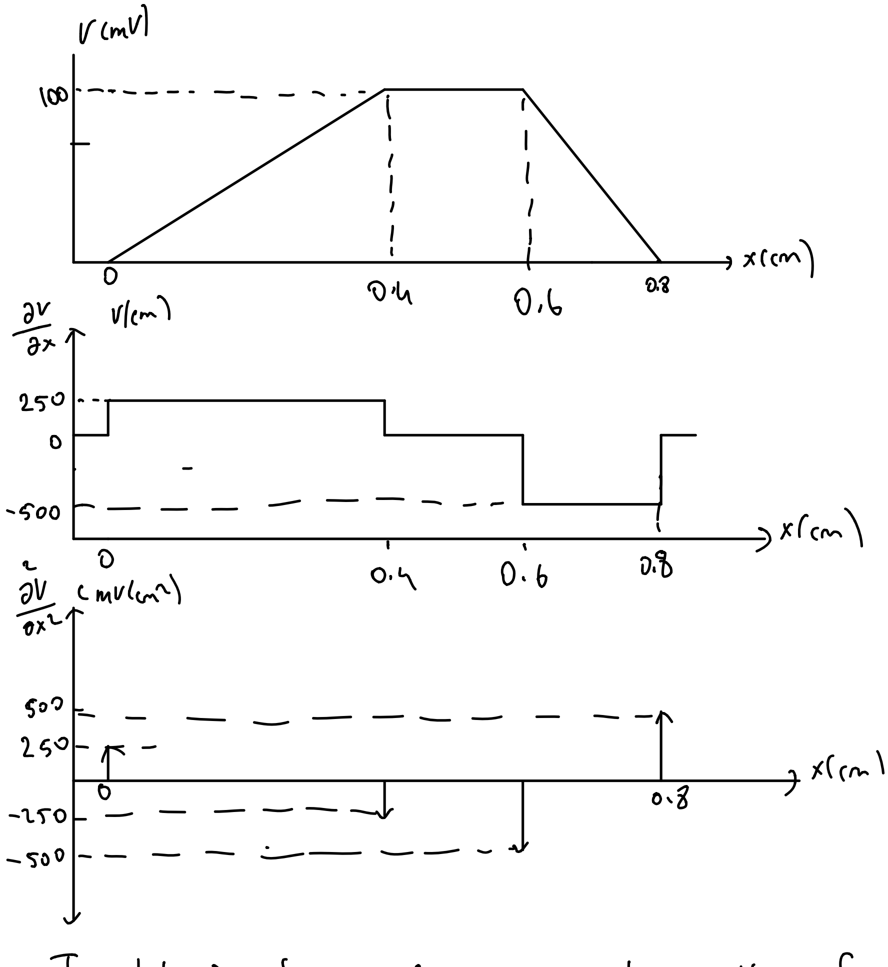
- The axon is active (nonlinear), cable equations, that apply to nonlinear membranes, can be only used.

- The spatial action potential waveform must be:

$$V(x,t) = V(x - 0.2t);$$ where x: position along axon in units cm

t: time in ms

For temporal action potential waveform shown above, spatial extent will be 0.8 cm, and for propagation in +x direction, the spatial action potential waveform will be pointing in the opposite direction.



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

$$I_m = \frac{1}{r_e + r_i} \cdot \frac{\partial^2 V}{\partial x^2}$$ valid for linear and nonlinear cables.

The first and second spatial derivatives of action potential waveform are shown in the middle and bottom panels of the figure above. The delta dirac functions at $x = 0, 0.2, 0.4, 0.8$ cm have areas

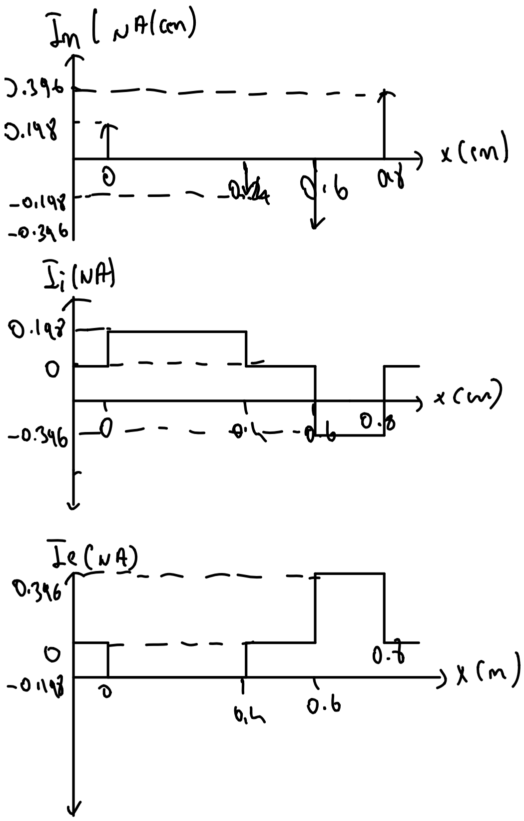
Dividing sum of extra- and intra-cellular resistances per unit length gives the transmembrane currents I_m shown in the top panel of the figure below. The delta dirac functions at $x = 0, 0.2, 0.4, 0.8$ cm have areas of

To obtain intra- and extra-cellular currents I_i and I_e respectively, use cable equations;

$$\frac{\partial I_e}{\partial x} = I_m \; ; \quad \frac{\partial I_i}{\partial x} = -I_m,$$ valid for both non-linear and linear cables.

Integrating solution for I_m, from 0 to x gives solutions for I_i and I_e; shown below.

Note that solutions for I_i, I_e, I_m satisfies Kirchoff current law



$$V_m(x,t) = V_m\left(t - \frac{x}{\theta}\right)$$

Q2) *(20 points)*

The relative transmembrane potential at time t = 0 can be described by:

$$v_m(x) = \begin{cases} 0, & \text{for } x < 0\ cm, \\ 20\sin\left(\frac{4\pi x}{d}\right)\cos\left(\frac{4\pi x}{d}\right), & \text{for } 0 \le x \le 1\ cm, \\ 0, & \text{for } x > 1\ cm, \end{cases}$$

where x is in units of cm, v_m is in units of mV, and d = 2 cm .

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 MΩ/cm and r_e = 10 kΩ/cm , respectively.

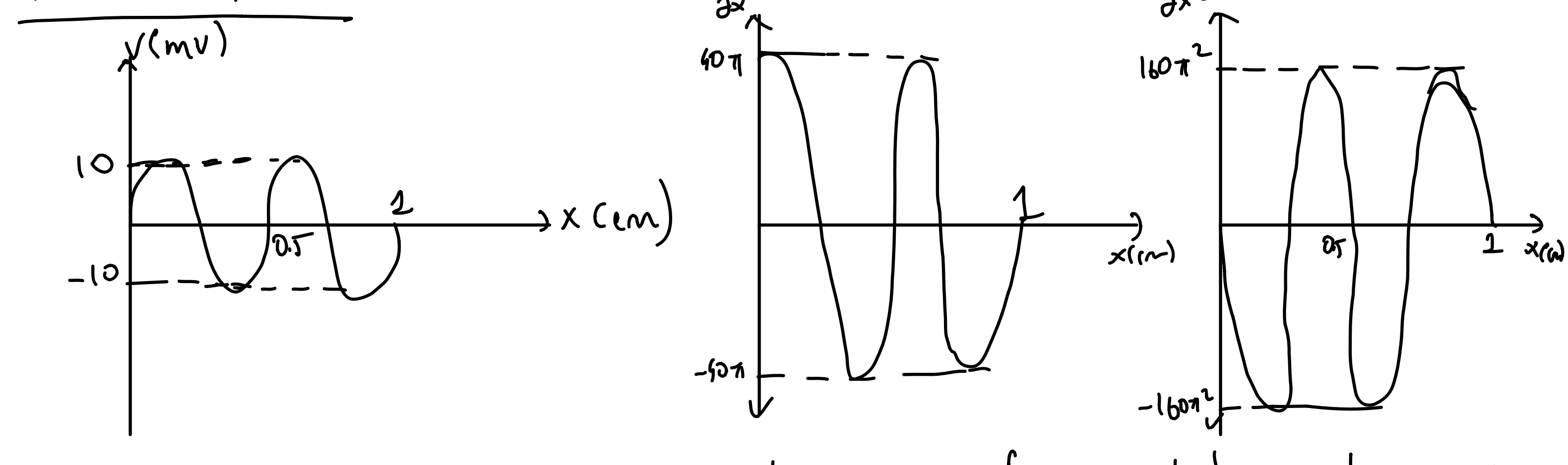
a. Calculate the local circuit currents, i.e., the transmembrane current per unit length i_m and the axial intra- and extra-cellular currents I_i and I_e, respectively, as a function of position x.

b. If the action potential is propagating stably with a velocity of - 6 m/s, find an expression for the temporal action potential waveform $v_m(t)$ at the position x = 0.2 cm, and sketch this waveform.

Q3) (20 points) The following questions from the textbook: 1-5 (pages 449-452 in 3rd Edition of the textbook.)

Q4) (40 points) The following questions from the textbook: 16-21 (pages 449-452 in 3rd Edition of the textbook.)

Answer for 2:



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

$$i_m = \frac{1}{r_i + r_e} \cdot \frac{\partial^2 V_m}{\partial x^2}$$ valid for both linear and nonlinear cables.

The first and second derivatives in the regions $x < 0$ and $x > 1$ cm are 0.

In region $0 \le x \le 1$ cm, the first and second derivatives are:

$$\frac{\partial V_m}{\partial x} = 20 \cdot \frac{4\pi}{d} \cos^2\left(\frac{4\pi x}{d}\right) - 20 \cdot \frac{4\pi}{d} \sin^2\left(\frac{4\pi x}{d}\right) = \frac{20 \cdot 4\pi}{d}\left(\cos^2\left(\frac{4\pi x}{d}\right) - \sin^2\left(\frac{4\pi x}{d}\right)\right)$$

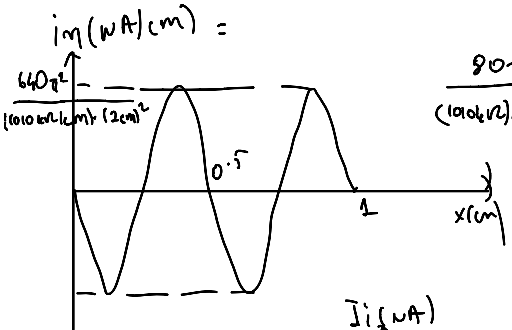
$$= \frac{20.4\pi}{d} \cos\left(\frac{8\pi x}{d}\right)$$

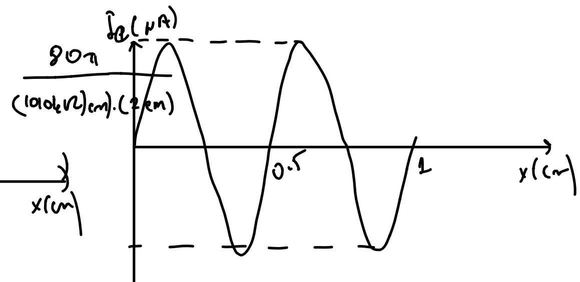
$$\frac{\partial^2 V_m}{\partial x^2} = -\frac{20.4\pi}{d} \cdot \frac{8\pi}{d} \sin\left(\frac{8\pi x}{d}\right)$$

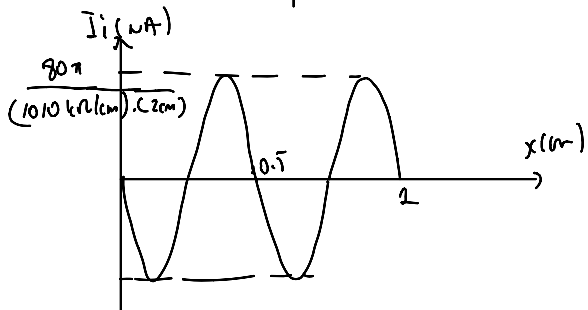
Dividing the second spatial derivate by the sum of extra- and intra-cellular resistances per unit length gives the transmembrane current per unit length i_m as use of cable eqns i

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

which are valid for both linear and nonlinear cables. These can be integrated over x to give I_i and I_e as being equal to $-\frac{1}{r_i + r_e} \cdot \frac{\partial V_m}{\partial x}$ and $\frac{1}{r_i + r_e} \cdot \frac{\partial V_m}{\partial x}$, as plotted.







2.6 $V_m(x,t) = V_m\left(t - \frac{x}{\theta}\right)$

$$V_m(x, t=0) = V_m\left(-\frac{x}{\theta}\right) = \begin{cases} 0 & x<0\,cm \\ 20 \cdot \sin\left(\frac{4\pi x}{d}\right) \cdot \cos\left(\frac{4\pi x}{d}\right) & 0<x<1cm \\ 0 & x>1\,cm \end{cases}$$

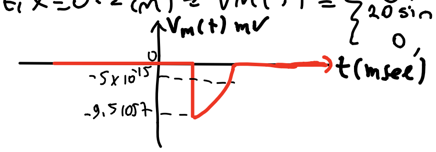
$$\boxed{d = 2cm}$$

$$= V_m\left(-\frac{(x-\theta t)}{\theta}\right) = \begin{cases} 0 & x-\theta t<0\,cm \\ 20 \sin\left(\frac{4\pi}{d}(x-\theta t)\right) \cos\left(\frac{4\pi}{d}(x-\theta t)\right) & 0 \le x-\theta t \le 1\,cm \\ 0 & x-\theta t > 1cm \end{cases}$$

$$= V_m(t,x)$$

$$\boxed{\theta = -0.6\ cm/ms\ , \ x = 0.2\ cm}$$

$$V_m(t, x=0.2\,cm) = V_m(t) = \begin{cases} 0, & 0.2+0.6t<0 \Rightarrow t<\frac{1}{3}msec \\ 20 \sin(0.4\pi + 1.2\pi t) \cdot \cos(0.4\pi + 1.2\pi t) & \frac{1}{3} \le t \le \frac{4}{3}\ msec \\ 0, & t > \frac{4}{3}\ msec \end{cases}$$



Q3

1. In the core-conductor model, what units often are used for each of the following:

a. c_m, the core-conductor's membrane capacitance.

$\mu F/cm$

b. r_m, the core-conductor's membrane resistance.

$\Omega.cm$

c. r_i, the core-conductor's intracellular resistance.

Ω/cm

d. R_i, the intracellular resistivity.

$\Omega \cdot cm$

2. Consider a cylindrical HH fiber at rest. The radius of the membrane is 30 micrometers. Extracellular currents flow to twice the membrane radius. The extracellular resistivity is 50 Ωcm. The intracellular resistivity is three times that of the extracellular. The membrane capacitance is 1 μF/cm^2. The HH resting conditions apply. The fiber is passive. Find each of the following, in suitable units, using the linear core-conductor model:

a. What is the membrane resistivity, R_m?

b. What is the membrane resistance r_m?

c. What is the intracellular resistance per unit length r_i?

d. What is the extracellular resistance per unit length r_e?

2.a) Hodgkin-Huxley model has a linear response to transmembrane voltage changes near the resting potential, so the membrane resistance can be found from the conductances in the HH model. Using table 13.5, gives resting values of HH membrane, to find conductances (g values) of HH membrane at rest.

$$Rm = \frac{1}{(g_K + g_{Na} + g_L)} = 1.475\ \Omega\text{-cm}^2$$

2.b) The resistance R in ohms of segment of membrane is

$$R = Rm/A_s = \frac{R_i}{2\pi a L} = \frac{rm}{L} \Rightarrow rm = \frac{Rm}{2\pi a}$$

Using results for Rm found in part(a) ; $rm = \frac{1.475\ \Omega\text{-cm}^2}{(2\pi \cdot 0.003)} = 78{,}248\ \Omega\text{-cm}$

2.c) The intracellular resistance per unit length characterizes the volume inside the membrane in a way that takes into account the medium resistivity and the fiber's radius. After ri has been found, one need only make a later choice of length L (distance along axis) to find resistance R of the segment - R:

$$R = riL = \frac{Ri.L}{Ai} = \frac{Ri.L}{\pi a^2} \rightarrow ri = \frac{Ri}{\pi a^2} \rightarrow ri = 5{,}305{,}169\ \Omega/cm$$

2.d) The connection of intracellular resistance per length with region inside membrane seems obvious, but "extracellular currents flow to twice of membrane radius" seems much less. In the absence of physical boundary of some kind, asserting that extracellular current flows most intensively near the membrane, and it provides a specific basis for computing re, even if it is only an estimate. Note that cross sectional area inside a is one-third the cross section btw a and 2a. 2a is limiting radius for extracellular current assumes that extracellular current flows through greater cross-section, but still within radius of fiber membrane.

$$R = \frac{ReL}{Ae} = \frac{Re.L}{(\pi(2a)^2 - \pi a^2)} = re.L$$

$$re = \frac{Re}{3\pi a^2} \Rightarrow re = 589{,}463\ \Omega/cm$$

3. A cylindrical fiber's membrane has a certain radius. The intracellular volume is within this radius. The extracellular volume is outside the membrane extending to a radius of twice this amount. (The membrane itself is considered to have negligible thickness relative to these dimensions.) The membrane resistance at rest is 2,000 Ωcm^2, and the membrane capacitance is 1.2 μF/cm^2. The intracellular resistivity is 100 Ωcm, and the extracellular resistivity is 40 Ωcm. The radius is 50 μm. Find each of the following, in suitable units. Use the linear core-conductor model.

$a = 50 \cdot 10^{-4}$ cm

a. What is the membrane resistance per unit length?

$$r_m = \frac{R_M}{2\pi a} = \frac{2{,}000\ \Omega cm^2}{2\pi(50\times10^{-4})} = 63{,}700\ \Omega cm$$

b. What is the membrane capacitance per unit length?

$$C_m = 1.2\ \mu F/cm^2 \times (2\pi(50\times10^{-4})) = 0.0377\ \mu F/cm$$

c. What is the intracellular resistance per unit length?

$$L r_i = \frac{R_i L}{A_i} \Rightarrow r_i = \frac{R_i}{\pi a^2} = 1{,}273{,}000\ \Omega/cm$$

d. What is the extracellular resistance per unit length?

$$r_e = \frac{R_e}{3\pi a^2} = 169\ \Omega/cm$$

4. A cylindrical fiber is represented by the core- conductor model. Known quantities are the following: the transmembrane potential, $V_m(x)$, the fiber's radius a, and intracellular and extracellular resistances r_i and r_e. Note that r_i and r_e are in "unit length" form. At the time of interest, there is no stimulus of any kind. Write the mathematical expression by which each of the following can be found, from the known quantities.

a. Intracellular axial current I_i. $I_i = \frac{-1}{(r_i+r_e)} \cdot \left[\frac{\partial V_m}{\partial x} - I \cdot r_e\right]$

when $I = 0$, 2nd term drops out, since there is no stimulus.

b. Extracellular axial current I_e. $I_e = \frac{1}{(r_i+r_e)} \cdot \left[\frac{\partial V_m}{\partial x} + I \cdot r_e\right]$

when $I = 0$, 2nd term drops out, since there is no stimulus.

c. Transmembrane current (per cm^2) I_m.

$$I_m = \frac{1}{(2\pi a)(r_i+r_e)} \cdot \left[\frac{\partial^2 V_m}{\partial x^2} - r_e i_p\right]$$

when $i_p = 0$, 2nd term drops out, since there is no stimulus.

question asks for I_m, i.e., current per cm^2, the I_m equation requires that dimensions are in cm.

5. A cylindrical fiber is represented by the core- conductor model. The upstroke of the transmembrane potential is given by a template function as $V_m(x) = 50\tanh(x)$ (x in mm). The fiber's radius is a, and the intracellular and extracellular resistances are r_i and r_e. (Note that r_i and r_e are in "unit length" form.) V_m is understood to be the spatial distribution of V_m at one moment during propagation of an action potential. At this time, which is after propagation began, there are no stimuli. Give the mathematical expression for the answer, and plot normalized wave shapes, (wave shapes having peaks scaled to ±1), for each part below.

a. Plot $V_m(x)$ from x of –4 to 4 mm. Which direction would this action potential be moving?

b. Find and plot $I_i(x)$. At its peak, which is the direction of the current?

c. Find and plot $I_e(x)$. At its peak, which is the direction of the current?

d. Find and plot $I_m(x)$. Interpret the sign of the peaks in relation to the direction of AP movement.

5.a) $V_m(x) = a_v \cdot \tanh(x)$ has negative potentials for $x < 0$, positive for $x > 0$. The action potential is moving left, toward the more negative region.

5.b) $I_i(x) = -a_i\, \mathrm{sech}^2(x)$. Intracellular current is flowing left.

5.c) $I_e(x) = +a_e\, \mathrm{sech}^2(x)$. Extracellular current is flowing right.

5.d) $I_m(x) = -2a_m\, \mathrm{sech}^2(x) \cdot \tanh(x)$. Membrane current is outward left, inward right.

a_v, a_i, a_e, a_m are undefined constants that are proportionality constants that include such factors as radius and axial resistance.

Q4

For Exercises 16–26, assume that the upstroke of a uniformly propagating action potential is described by the V_m template equation (13.3):

$$V_m(x,t) = 50\tanh\left[t - \frac{(x-x_0)}{\theta}\right] \tag{13.3}$$

In (13.3) V_m is in mV, t is time in msec, and x is distance along the axis in mm. Distance x_0 is a constant, in mm, and θ is the velocity of propagation, in mm/msec (i.e., in m/s). Assume the fiber radius is 50 μm, the intracellular resistivity 100 Ωcm, and the extracellular resistivity 0.

Use of mathematical functions such as hyperbolic tangent to create artificial V_m waveforms as a function of time and space is useful, in that the template function can be used to give one insight across a wide range of responses in space and time, and as calibration waveforms for equipment or display. One can regenerate them much more quickly than experimental measurements, even with HH simulations. Even so, one must keep in mind that the waveforms may be similar to real action potentials in some respects but differ markedly from real action potentials in other respects. For example, the wave shape defined in (13.3) does not show effects at fiber ends, with stimuli, or in response to changes in rate of stimulation. Also, the tanh waveform is unnaturally symmetric. Further, the tanh template function as given models only the action potential upstroke; thus it leaves out the recovery phase. Even so, in part because of the simplification that it embodies, use of the template waveform allows other fundamental relationships in time and space to stand out, and thus to be more evident to the student.

16. Using Eq. (13.3) with the assumptions of the core-conductor model. derive an equation for the longitudinal current $I_i(x,t)$.

17. Using Eq. (13.3) with the assumptions of the core-conductor model, derive an equation for the longitudinal current $I_e(x,t)$.

18. If $x_0 = 2$ mm and $\theta = 2$ m/sec, plot $V_m(t)$ as it will be seen at $x = 10$ mm.

19. If $x_0 = 2$ mm and $\theta = 2$ m/sec, plot $V_m(x)$ as it would exist at $t = 3$ msec.

20. Under the same conditions as in Ex. 19, plot $I_i(x)$.

21. Under the same conditions as in Ex. 19, plot $I_e(x)$.

$$\frac{\partial I_i}{\partial x} = -I_m$$

$$I_m = \frac{1}{r_e + r_i} \cdot \frac{\partial^2 V_m}{\partial x^2}$$

$$\frac{\partial V_m}{\partial x} = \left(-\frac{1}{\theta}\right) \cdot \frac{\partial V_m}{dt}$$

$$\frac{\partial^2 V_m}{\partial x^2} = \left(\frac{1}{\theta^2}\right) \cdot \frac{\partial^2 V_m}{dt^2}$$

$$I_m = \frac{a}{2R_i\,\theta^2}\frac{\partial^2 V_m}{\partial t^2}$$

$$\frac{\partial V_m}{\partial x} = -\frac{50}{\theta}\,\mathrm{sech}^2\left[t - \frac{(x-x_0)}{\theta}\right]$$

$$\frac{\partial V_m}{\partial t} = -\theta \cdot \frac{\partial V_m}{\partial x} = 50\,\mathrm{sech}^2\left[t - \frac{(x-x_0)}{\theta}\right]$$

$$\frac{\partial^2 V_m}{\partial x^2} = -\frac{100}{\theta^2}\cdot\tanh\left[t - \frac{(x-x_0)}{\theta}\right]\mathrm{sech}^2\left[t - \frac{(x-x_0)}{\theta}\right]$$

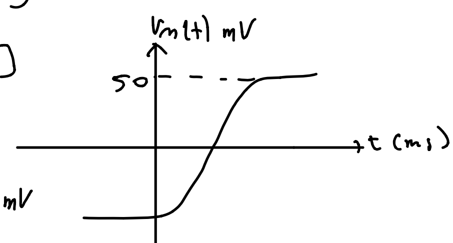
$$\frac{\partial^2 V_m}{\partial t^2} = -100\cdot\tanh\left[t - \frac{(x-x_0)}{\theta}\right]\mathrm{sech}^2\left[t - \frac{(x-x_0)}{\theta}\right]$$

16) $I_i(x,t) = \frac{-1}{(r_i + r_e)} \cdot \left[\frac{\partial V_m}{\partial x} - I r_e\right] = \frac{-1}{r_i}\frac{\partial V_m}{\partial x}$ $\dashrightarrow r_i = \frac{R_i}{\pi a^2} = \frac{100\,\Omega cm}{\pi(0.05)^2 cm^2} = 1273240\ \Omega/cm$

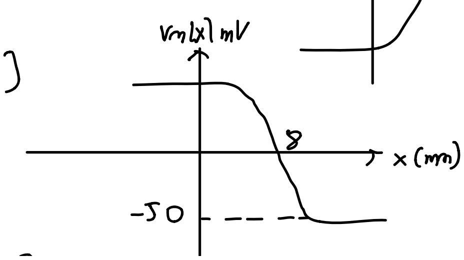
$$I_i(x,t) = \frac{-1}{127324} \cdot \frac{-50}{\theta} \cdot \mathrm{sech}^2 h\left[t - \frac{(x-x_0)}{\theta}\right]\ nA$$

17) $I_e(x,t) = -I_i(x,t) = -\frac{50}{1273240\theta} \cdot \mathrm{sech}^2\left(t - \frac{(x-x_0)}{\theta}\right)\ nA$

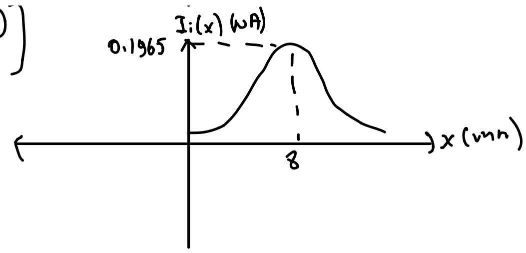
18) $V_m(x=10,t) = 50\tanh\left(t - \frac{8}{2}\right) = 50\tanh(t-4)$



19) $V_m(x, t=3) = 50\tanh\left(3 - \frac{x-2}{2}\right)$



20) $I_i(x, t=7) = \frac{0.393}{2} \operatorname{sech}^2\left[3 - \frac{(x-2)}{2}\right]$



21) $I_e(x, t=7) = -\frac{0.393}{2} \operatorname{sech}^2\left[3 - \frac{(x-2)}{2}\right]$