York University BPHS 4080 (Winter 2020) - HW 5 SOLUTIONS

Questions

1. Assume that an action potential is traveling at constant velocity, v, in the positive z-direction along an axon. Assume that the core conductor model is valid so that

$$\frac{\partial^2 V_m(z,t)}{\partial z^2} = (r_i + r_0)\, K_m(z,t)$$

The waveshape of the action potential at one point in space, $z = z_0$ is shown in the figure below

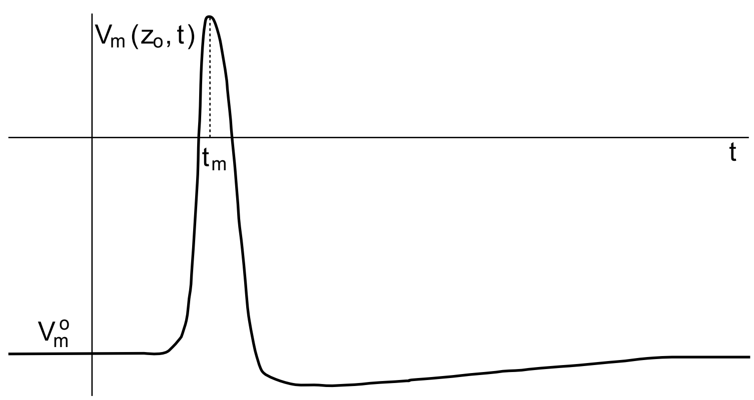

Figure 1: Waveforem of a propagated action potential

a) Sketch $K_m(z,t)$ on the same time scale as $V_m(z_0,t)$.

⇒ **Solution (5 pts):**

From the core conductor model (with no externally applied currents)

$$\frac{\partial^2 V_m(z,t)}{\partial z^2} = (r_i + r_o)\, K_m(z,t)$$

For an action potential propagating in the $\pm z$ **direction,** $V_m(z,t) = f(t \pm z/\nu)$ **so that the membrane potential must satisfy the wave equation.**

$$\frac{\partial^2 V_m(z,t)}{\partial z^2} = \frac{1}{\nu^2}\frac{\partial^2 V_m(z,t)}{\partial t^2}$$

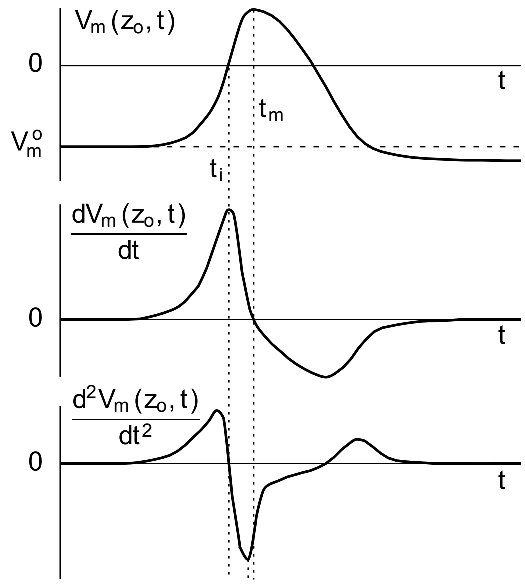

Figure 2: Membrane potential and its first two time derivatives plotted versus time. The time of occurence of the maximum value of the action potential is t_m, and the point of inflection at the onset of the action potential is t_i.

Therefore,

$$K_m(z,t) = \frac{1}{(r_i + r_o)\,\nu^2} \frac{\partial^2 V_m(z,t)}{\partial t^2}$$

The membrane potential and its first and second partial derivatives are shown in figure 3.

b) Prove that one cannot account for $K_m(z,t)$ by assuming that the membrane can be represented by the equivalent circuit for an incremental element of length δz shown in the figure below. g_m and c_m are constant conductances and capacitances per unit length. [HINT: Consider the polarity of the current through the parallel combination of g_m and c_m prior to the time of occurence of the peak of the action potential, t_m.]

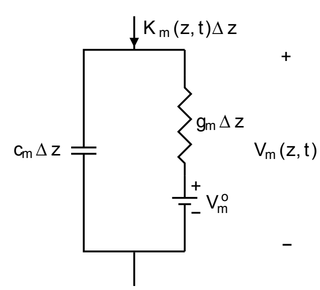

Figure 3: Equivalent network for the membrane of an axon.

⇒ **Solution (5 pts):**

For the linear model of the membrane, the membrane current per unit length is

$$K_m = c_m \frac{\partial V_m(z,t)}{\partial t} + g_m \left(V_m(z_0,t) - V_m^o \right)$$

For the time interval $0 < t < t_m$ both $\partial V_m(z_0,t)/\partial t$ and $V_m(z_0,t) - V_m^o$ are positive quantities. Therefore, the linear cable model predicts that $K_m > 0$ in this interval. However, the core conductor model for a propagated action potential shows that K_m is positive in the interval $0 < t < t_i$ but is negative in the interval $t_i < t < t_m$. Therefore, the linear resistance/capacitance model of a membrane is not consistent with the membrane current during a propagated action potential.

2. A cylindrical fibre's membrane has a certain radius r. The extracellular volume is outside the membrane extending to a radius of twice this amount. It can be noted that the membrane itself is considered to have negligible thickness relative to r. The membrane resistance at rest is 2 $k\Omega/\text{cm}^2$, the membrane capacitance is 1.2 μF / cm^2, the intracellular resistivity is 100 $\Omega\cdot$cm, the extracellular resistivity is 40 $\Omega\cdot$cm and the radius is 50 μm. Find each of the following values listed below along with their corresponding units, and ensure to use the linear core-conductor model.

a) What is the membrane resistance per unit length?

⇒ **Solution (5 pts):**

Since it is assumed that the thickness of the cylindrical fibre is uniform, then the resistance of a unit area (which is given) can be defined as:

$$R = \mathcal{R} \cdot A = \rho \cdot l$$

Therefore, to obtain the resistance of the sheet made of material whose specific resistance is R, the specific resistance can be divided by the area of the sheet such that:

$$\mathcal{R}_m = \frac{R}{2\pi r} = \frac{2k\Omega \cdot \text{cm}^2}{2\pi(0.005\text{cm})} = 63,661.98\ \Omega\text{cm} \approx 63.7\ \text{k}\Omega\text{cm}$$

b) What is the membrane capacitance per unit length?

⇒ **Solution (5 pts):**

Since a similar idea as the one stated above can be applied to calculating the membrane capacitance, the following holds true:

$$\mathcal{C}_m = C \cdot 2\pi r = 1.2\ \frac{\mu\text{F}}{\text{cm}^2} \cdot 2\pi(0.005\text{cm}) = 0.0377\ \frac{\mu\text{F}}{\text{cm}} \approx 3.77 \cdot 10^{-6}\frac{\text{F}}{\text{m}}$$

c) What is the intracellular resistance per unit length?

⇒ **Solution (5 pts):**

For the linear core-conductor model, the voltage difference across the volume element is equal to the product of the current through the element and the resistance of the element (ΔR_i) such that:

$$V_i(z,t) - V_i(z+\Delta z,t) = \Delta R_i I_i(z+\Delta z,t)$$

Therefore, by claiming ρ_i to be the resistivity of the inner conductor (cytoplasm), the resistance of the element ΔR_i can be expressed as:

$$\Delta R_i = \frac{\rho_i \Delta z}{\pi r^2}$$

Thus, for the resistance per unit length, the following expression is obtained:

$$r_i = \frac{\Delta R_i}{\Delta z} = \frac{\rho_i}{\pi r^2} = \frac{100\Omega\ \text{cm}}{\pi(0.005\ \text{cm})^2} = 1,273,239.5\ \frac{\Omega}{\text{cm}} \approx 127,324\ \frac{k\Omega}{\text{m}}$$

d) What is the extracellular resistance per unit length?

⇒ **Solution (5 pts):**

The same principles for solving for the extracellular resistance per unit length can be used as stated above; however, it must be noted that the difference in radii must be used in the calculations such that:

$$r_o = \frac{\Delta R_i}{\Delta z} = \frac{\rho_o}{\pi \Delta r^2} = \frac{40\Omega\ \text{cm}}{\pi(2r)^2 - \pi(r)^2} = \frac{40\Omega\ \text{cm}}{4\pi(0.005\text{cm})^2 - (0.005\text{cm})^2} = 169,765.3\ \frac{\Omega}{\text{cm}} \approx 16,976.5\ \frac{k\Omega}{\text{m}}$$

3. The following two experiments are performed on a squid giant axon:

- *Experiment #1:* The axon is placed in a large volume of sea water, and the size of the *transmembrane* action potential is measured by means of an intracellular micropipette and is found to have a peak-to-peak value of 100 mV. The conduction velocity is 36 m/s.
- *Experiment #2:* The axon is placed in oil and the transmembrane potential is still found to 100 mV peak-to-peak. The peak-to-peak size of the *extracellular* action potential is 75 mV.

Estimate the expected conduction velocity in Experiment # 2. State your assumptions.

⇒ **Solution (5 pts):**

The magnitudes of the extracellular and transmembrane potentials and the conduction velocity depend upon the intracellular and extracellular resistance per unit length. Designate the extracellular resistance per unit length as r_{o1} and r_{o2}, for Experiments 1 and 2, respectively. Assume that the intracellular resistance per unit length is the same for both experiments. The core conductor model implies that

$$2\pi a\,(r_o + r_i)\,\nu^2 = \mathcal{K}_m$$

where $\mathcal{K}_m$ is a property of the membrane and not of the dimesions of the cell. In Experiment 1 the axon is in a large volume of sea water so that $r_{o1} << r_i$. Therefore, the conduction velocity for Experiment 1 implies that

$$2\pi a\left(r_i\right)(36)^2 = \mathcal{K}_m$$

From Experiment 2, the ratio of the external to the transmembrane potential is 75/100=3/4. Since

$$\Delta V_o = -\frac{r_o}{r_i + r_o}\Delta V_m$$

it follows that

$$\frac{r_{o2}}{r_{o2} + r_i} = \frac{3}{4}$$

Which can be solved to give $r_{o2} = 3r_i$. The conduction velocity of the axon in Experiment 2 can be found from the relation

$$2\pi a\left(r_{o2} + r_i\right)\nu_2^2 = \mathcal{K}_m$$

which can be written as

$$2\pi a(4r_i)\nu_2^2 = \mathcal{K}_m$$

Therefore, a combination of expressions for the conduction velocity in the two experiments yields $4\nu_2^2 = 36^2$ or $\nu_2 = 18$ m/s.

4. A cylindrical cell has a diameter of 500 μm and a length equal to $L = 4\ cm$. After brief experimentation, it is discovered that the cell has the following cable parameters: A membrane conductance $g_m = 100\ \frac{\mu S}{cm}$, a membrane capacitance $c_m = 150\ \frac{nF}{cm}$, and an internal resistance $r_i = 10\ \frac{k\Omega}{cm}$ such that $r_0 \ll r_i$. Two experiments are later conducted:

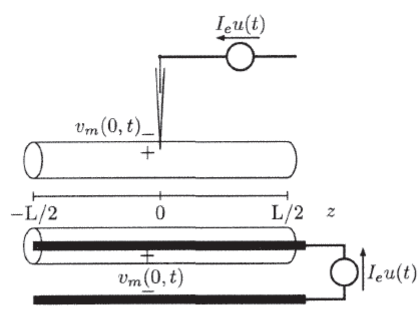

Figure 4: Image denoting the two conducted experiments with the given cylindrical cell with (top) a micropipette and with (bottom) an axial electrode

- *Experiment #1:* The cell is impaled, as seen in the top image in the following figure, with a micropipette at its center so that the membrane potential could be measured
- *Experiment #2:* Axial electrodes are impaled, as seen in the bottom image in the following figure, along the length of the cell to record the potential across the membrane - these electrodes have a resistance per unit length $r = 5\ \frac{\Omega}{cm}$.

a) Determine the cell space constant and the membrane time constant

⇒ **Solution (5 pts):**

Given the definition of the cell space constant, the following can be shown:

$$\lambda_C \approx \frac{1}{\sqrt{g_m \cdot r_i}} = \frac{1}{\sqrt{10^{-4} \cdot 10^4}} = 1 \text{ cm}$$

Therefore, given the cell space constant, the time constant of the cell can be calculated as:

$$\tau_M = \frac{c_m}{g_m} = \frac{150 \cdot 10^{-9}}{10^{-4}} = 1.5 \text{ ms}$$

b) Given the set-up of the experiment 1 explained above, determine the measured potential across the membrane at $z = 0$ (i.e determine $\nu_m(0, t)$)

⇒ **Solution (5 pts):**

The cell is 4 space space constants long. Hence, it is an electrically large cell. The step response of an electrically large cell of infinite length is given in Equation 3.55 (Weiss, 1996b). This relation gives an approximation to the step response of this cell. A more involved treatment is required to get a more accurate answer for a cell that is 4 space constants long. The approximate solution is as follows (where the t below is expressed in ms):

$$\nu_m(0, t) \approx \frac{\lambda_C r_i}{2} \cdot I_e \cdot \mathrm{erf}\Big(\frac{\mathrm{t}}{\tau_\mathrm{M}} \cdot \mathrm{u(t)}\Big) = 5 \cdot 10^3 \cdot \mathrm{I_e} \cdot \mathrm{erf}\Big(\frac{\mathrm{t}}{1.5} \cdot \mathrm{u(t)}\Big)$$

c) Given the set-up of the experiment 2 explained above, determine the measured potential across the membrane at $z = 0$ (i.e determine $\nu_m(0, t)$)

⇒ **Solution (5 pts):**

It must be noted that the axial electrode has a resistance per unit length that is 2000 times smaller than that of cytoplasm. Therefore, the space constant has increased by a factor of $\sqrt{2000} \approx$ 45, to about 45 cm. Therefore, the use of the axial electrodes has made this cell an electrically small cell whose step response is given in Equation 3.54 (Weiss, 1996b) shown below:

$$\nu_m(0, t) = \mathcal{R} \cdot I_e(1 - \exp\Big[\frac{-\mathrm{t}}{\tau_\mathrm{M}}\Big] \cdot \mathrm{u(t)}$$

Therefore, given this result, the total resistance of the membrane of the cell, ignoring the resistance of the two ends of the cylindrical cell, can be expressed as follows:

$$\mathcal{R} = \frac{1}{g_m \cdot L} = \frac{1}{10^{-4} \cdot 4} = 2.5 \cdot 10^3 \ \Omega$$

Plugging this result into the first given equation for $\nu_m(0, t)$, the following is received (where the t below is again expressed in ms):

$$\nu_m(0, t) = (2.5 \cdot 10^3) \cdot I_e(1 - \exp\Big[\frac{-\mathrm{t}}{1.5}\Big] \cdot \mathrm{u(t)}$$

Finally, the two results can be compared to one another in the figure below, where the unclamped cable response is a plot of $\nu_m(0,t)/(5 \cdot 10^3 \cdot I_e = \mathrm{erf(t/1.5)} \cdot \mathrm{u(t)}$**; for the clamped cable response, the plot below is expressed mathematically as** $\nu_m(0,t)/(5 \cdot 10^3 \cdot I_e = (1 - \exp[-\mathrm{t}/1.5]) \cdot \mathrm{u(t)}$**.**

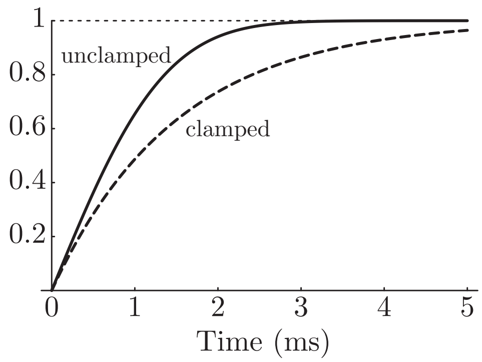

Figure 5: Image denoting the results of the unclamped/clamped experiments with the given cylindrical cell

5. In fresh man physics, one learns that electrical circuits always form closed loops. Put another way, the current has a return path such that the charge can 'flow'. Examine this figure from Weiss' book. Does this represent a 'circuit'? If so, sketch what the circuit looks like. If not, explain why.

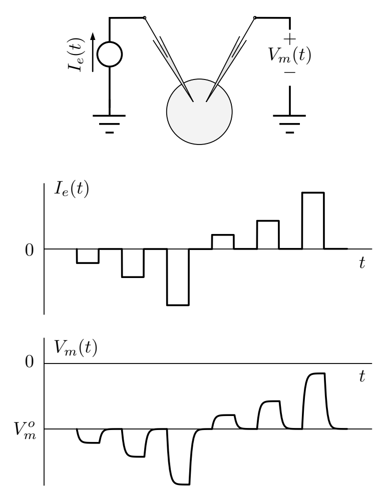

Figure 1.1

⇒ **Solution (5 pts):**

The diagram does indeed, represent a closed circuit, shown equivalently in the diagram below. In the diagram, both the voltage source and the current source are grounded to the extracellular matrix. Ground is merely a reference point to measure potential differences and is conveniently defined to be zero. It is also a matter of convenience as to where one might label ground, as voltage measurements are only concerned about differences, not absolute values. As such, the intracellular space could be defined as ground, however due to convention, electrical measurements of cells are taken with respect to extracellular bath.

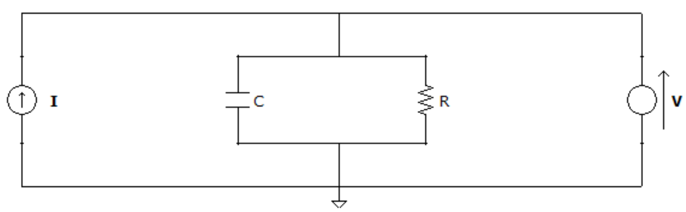

Figure 6: An equivalent circuit for problem 5. C is the membrane capacitance and R its resistance.