

**PHYS 4xx Mem 8 - Model for signal propagation**

(Note: the equation numbers start from the previous lecture)

The propagation speed of a signal along an axon depends on both a time scale and a length scale. We examine each of these quantities within the framework of electrical circuit theory from introductory physics courses. Our first observation is that the plasma membrane may be regarded as a parallel plate capacitor with the charges  $Q$  on each side of the membrane supporting a potential difference  $V$  via

$$Q = CV, \quad (8)$$

where  $C$  is the capacitance of the membrane. Potentially, there are several contributions to the membrane capacitance; in the problem set, we examine an idealized membrane to show that the capacitance per unit area  $\mathcal{C}$  is expected to be around  $1 \times 10^{-2} \text{ F/m}^2$ , which is in the range measured experimentally. For a membrane potential of  $-70 \text{ mV}$ , the capacitance per unit area  $\mathcal{C} = 1 \times 10^{-2} \text{ F/m}^2$  corresponds to a charge density  $Q/A$  of  $0.7 \times 10^{-3} \text{ C/m}^2$ .

A single loop circuit with just a resistor and capacitor in series will discharge exponentially with time. This can be seen by substituting Ohm's Law  $V = IR$  into Eq. (8) to obtain a differential equation for  $Q(t)$ :

$$Q = -CRI = -CR(dQ/dt)$$

or

$$dQ/dt = -Q/RC, \quad (9)$$

where the current  $I$  is  $dQ/dt$  and where the signs of  $I$  and  $V$  have been taken into account. The solution to Eq. (9) is  $Q(t) = Q_0 \exp(-t/\tau)$ , where the decay time  $\tau$  is

$$\tau = RC. \quad (10)$$

Expressed in terms of conductivity and capacitance per unit area, Eq. (13.10) can be rewritten as

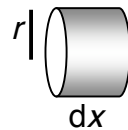
$$\tau = \mathcal{C} / \gamma. \quad (11)$$

For example, the conductivity is about  $5 \Omega^{-1}\text{m}^{-2}$  (or less) for the passage of individual ionic species across a membrane; see end-of-chapter problems. Taking this value and  $\mathcal{C} = 1 \times 10^{-2} \text{ F/m}^2$  leads to a decay time  $\tau$  of 2 ms according to Eq. (11). For future reference, we rearrange Eq. (9) in terms of the change in the membrane potential as

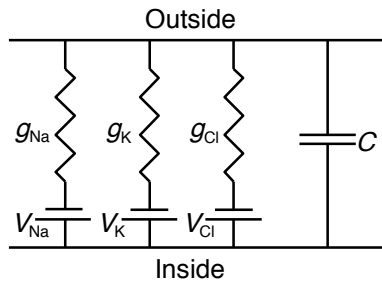
$$dV/dt = -V/RC, \quad (12)$$

where the decay time for  $V(t)$  from this expression is the same as that in Eq. (9).

Now make  $V$  a function of position as well as time, and consider the behavior of a small ring of membrane surface with area  $A = 2\pi r dx$ , where  $r$  is the radius of the axon and  $dx$  is a distance along its length, assumed to lie parallel to the  $x$ -axis.

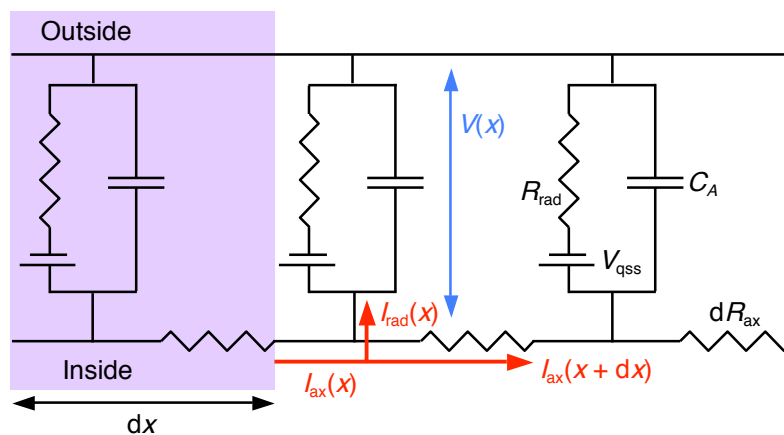


The flow of ions through this membrane patch can be viewed using the circuit diagram below for the three principal ions ( $\text{Na}^+$ ,  $\text{K}^+$  and  $\text{Cl}^-$ ). Each ionic species is shown as having its own path within the circuit, as there is a separate Nernst potential (shown by the battery symbol) and conductivity (shown by the resistor symbol) for each ionic species. The capacitance doesn't depend on the individual species, so only one capacitive element is required for this section of the axon. The horizontal wire at the top of the circuit represents the current outside of the axon while the wire at the bottom represents the current in the interior of the axon.



- The circuit element can be simplified by combining individual Nernst/resistive elements:
- the conductance for the overall current is just the sum of the individual conductances, so only one resistive element is required, with conductivity  $\gamma = \gamma_{\text{Na}} + \gamma_{\text{K}} + \gamma_{\text{Cl}}$ ,
  - the Nernst potentials for each ion can be replaced with the quasi-steady state potential  $V_{\text{qss}}$  defined in Eq. (7).

The effective circuit is the magenta box:



Now add the resistance of the axonal fluid  $dR_{ax}$ ; a similar resistance should appear in the top wire of the diagram representing current flow outside of the axon, but because the exterior fluid region is so large, this resistance can be neglected.

When the current  $I_{ax}$  flows to the right along the bottom wire and encounters the loop circuit at location  $x$  linking the interior of the axon to the exterior, it divides such that its value after the loop  $I_{ax}(x + dx)$  is less than its value before,  $I_{ax}(x)$ . The difference in these values,

$$I_{rad} = I_{ax}(x) - I_{ax}(x + dx), \quad (13)$$

is the amount of current lost to the loop.

$I_{rad}$  can either leak through the membrane via  $V_{qss}$  and  $R_{rad}$  or it can add to the charge on the membrane at the capacitive element  $C_A$ . The current that leaks out is equal to the radial current density  $\mathcal{I}_{rad}(x)$  multiplied by the area of the membrane at location  $x$ , namely  $2\pi r dx$ . The charge  $dQ$  that accumulates at the capacitor is just  $dQ = C_A dV$ , which arises from the current  $dQ/dt = d/dt(C_A V)$  in time interval  $dt$ . Thus,

$$I_{rad}(x) = \mathcal{I}_{rad}(x) \cdot 2\pi r dx + d/dt(C_A V). \quad (14)$$

Here,  $C_A$  is equal to the product of the capacitance per unit area  $\mathcal{C}$  multiplied by the area element  $2\pi r dx$ ; hence,

$$I_{rad}(x) = 2\pi r \{ \mathcal{I}_{rad}(x) + \mathcal{C} (dV/dt) \} dx. \quad (15)$$

Substituting Eq. (15) into Eq. (13) yields

$$I_{ax}(x) - I_{ax}(x + dx) = 2\pi r \{ \mathcal{I}_{rad}(x) + \mathcal{C} (dV/dt) \} dx, \quad (16)$$

or

$$dI_{ax}/dx = -2\pi r \{ \mathcal{I}_{rad}(x) + \mathcal{C} (dV/dt) \}. \quad (17)$$

The minus sign comes from the reversed order of the currents on the left-hand side of Eq. (16) compared to the conventional definition of a derivative  $df/dx$ .

The axial current can be related to the decrease in potential from  $x$  to  $x + dx$  through Ohm's law:

$$V(x + dx) - V(x) = -I_{ax}(x) dR_{ax}(x), \quad (18)$$

where  $dR_{ax}(x)$  is the resistance of the interior of the axon over a distance  $dx$ . The minus sign arises because current flows in the direction of decreasing potential; here, a positive value for  $dV/dx$  means that the potential increases with  $x$ , which drives the current toward negative  $x$ , the opposite direction than what is assumed in the circuit diagram. The resistance  $dR_{ax}$  of the axon segment is equal to the length of the segment  $dx$  divided by the product of its cross sectional area  $\pi r^2$  and the axial conductivity  $\kappa_{ax}$  (in three dimensions; units of  $\Omega^{-1}m^{-1}$ )

$$dR_{ax} = dx / \pi r^2 \kappa_{ax}. \quad (19)$$

Thus, Eq. (18) becomes

$$I_{ax}(x) = -(\pi r^2 \kappa_{ax}) \cdot (dV(x) / dx). \quad (20)$$

and

$$dI_{ax}/dx = -(\pi r^2 \kappa_{ax}) \cdot (d^2V(x) / dx^2)$$

Eqs. (17) and (20) can be combined to yield a differential equation for the voltage  $V(x, t)$ . The first step is to take the spatial derivative of Eq. (20) to obtain  $dI_{ax}/dx$ , and then substitute the result into Eq. (17). After some algebraic manipulations,

$$(r\kappa_{ax}/2) \cdot (d^2V(x) / dx^2) = I_{rad}(x) + \mathcal{C} (dV/dt). \quad (21)$$

This is one version of the cable equation. The next step is to relate the radial current density  $I_{rad}(x)$  to the potential. To obtain Eq. (7) for the quasi-steady state potential  $V_{qss}$ , we imposed the condition that there was no net current density out of the three parallel circuits for each ionic species. However, if the applied potential  $V$  varies from  $V_{qss}$ , then there will be a current density  $I$  governed by Ohm's law  $I = \gamma \Delta V$ , where the relevant  $\Delta V$  is  $V(x, t) - V_{qss}$  and the relevant (two-dimensional conductivity)  $\gamma$  is  $\gamma_{tot}$  because the current is the sum over all ionic contributions:

$$\gamma_{tot} = \sum_{\alpha} \gamma_{\alpha}. \quad (22)$$

That is, the radial current per unit area is

$$I_{rad}(x) = \gamma_{tot} (V - V_{qss}). \quad (23)$$

Placing this into Eq. (21) yields

$$(r\kappa_{ax}/2) \cdot (d^2V / dx^2) = \gamma_{tot} (V - V_{qss}) + \mathcal{C} (dV/dt). \quad (24)$$

As a last step, we shift the voltages by defining the local voltage as  $v(x, t)$  as

$$v(x, t) = V(x, t) - V_{qss}, \quad (25)$$

to extract the linear cable equation:

$$\lambda^2 (d^2v / dx^2) - \tau (dv/dt) = v. \quad \text{linear cable equation} \quad (26)$$

By comparison with Eq. (24) the length and time scales are

$$\lambda = (r\kappa_{ax} / 2\gamma_{tot})^{1/2} \quad \tau = \mathcal{C} / \gamma_{tot}. \quad (27)$$

The time scale  $\tau$  has appeared before in Eq. (11) for  $RC$  circuits.

If the initial disturbance applied to the axon is small (*i.e.*,  $V - V_{qss}$  is small) then the linear cable equation is not far from Fick's law and the disturbance should spread out with time but will not propagate intact. The predicted time scale for the disturbance to dissipate is around a millisecond.

To make the cable equation a proper description of signal propagation, the two-dimensional conductivities  $\gamma_\alpha$  in Eq. (22) must be modified to reflect the experimental observation that sodium channels open as the action potential rises at its leading edge. When channels open in the membrane, the conductivity increases in proportion to the number of open channels per unit area,  $n_{\text{open}}$ , as in

$$\gamma_\alpha(V) = n_{\text{open}} G_{\text{channel}} + \gamma_\alpha(0) \quad (28)$$

where  $G_{\text{channel}}$  is the conductance of a single channel and where  $\gamma_\alpha(V)$  is the conductivity of species  $\alpha$  at voltage  $V$ . Given that more channels open as the voltage increases, then  $\gamma_{\text{tot}}$  is voltage-dependent. Considering only the sodium and potassium conductivities, Eq. (24) can be rearranged to read

$$(r\kappa_{\text{ax}}/2\gamma_K) \cdot (d^2V/dx^2) - (\mathcal{C}/\gamma_K) \cdot (dV/dt) = (\gamma_{\text{Na}}/\gamma_K) (V - V_{\text{Na}}) + (V - V_K). \quad (29)$$

For a squid axon under resting conditions are  $\gamma_{\text{Na}} = 0.11 \Omega^{-1}\text{m}^{-2}$ ,  $\gamma_K = 3.7 \Omega^{-1}\text{m}^{-2}$ , and  $\gamma_{\text{Cl}} = 3.0 \Omega^{-1}\text{m}^{-2}$ . For the two-species (Na and K) system here,  $\gamma_{\text{tot}} \equiv \gamma_K$  and the two prefactors in Eq. (13.29) are approximately equal to  $\lambda^2$  and  $\tau$  in Eq. (26)

$$\lambda \equiv (r\kappa_{\text{ax}}/2\gamma_K)^{1/2} \quad \tau \equiv \mathcal{C}/\gamma_K, \quad (30)$$

so long as the number of open sodium channels is small. Hence, the left-hand sides of Eqs. (26) and (29) are very similar, while the right-hand side of Eq. (29) reveals the presence of the voltage-dependent sodium conductivity  $\gamma_{\text{Na}}(V)$ . Note that  $\lambda$  is proportional to the square root of the axon radius.

Taking the potassium conductivity to be constant at the leading edge of the action potential, the  $\gamma_{\text{Na}}:\gamma_K$  ratio changes from 1:25 in the resting state to 20:1 at the peak of the potential. This dramatic variation is sufficient to completely change the behavior of Eq. (29) from signal dissipation below the threshold voltage to signal propagation above it.

The speed of the propagating signal is proportional to  $\lambda/\tau$ , the length and time scales of the equation. We have already estimated  $\tau$  to be about 1 - 2 milliseconds. To estimate  $\lambda$ , we take the (three dimensional) conductivity of the axonal fluid to be  $\kappa_{\text{ax}} = 1 \Omega^{-1}\text{m}^{-1}$ ; seawater has  $\kappa = 5 \Omega^{-1}\text{m}^{-1}$ . Taking  $r = 10 \mu\text{m}$  for the axon radius and  $\gamma = 5 \Omega^{-1}\text{m}^{-2}$  yields  $\lambda = 10^{-3} \text{m}$ . Thus, the propagation speed of the action potential with these parameter values should be about 0.5 - 1 m/s within the cable equation approach.