

CABLE EQUATION DERIVATION

Last time we briefly reviewed the range of morphology types in the nervous system, discussed the basic means by which neurons communicate with each other, talked a bit about the usefulness of modeling and described different levels of modeling from the molecular to synapse to neuron to network to system to behavior.

We discussed how, if you are going to do models of neurons, that the first thing you need to decide is what morphology to use for your model neuron, whether you want to include all of the detail from an anatomical reconstruction or whether you want to use a simplified morphology that contains the essential features of the cell under study.

Whether you use a detailed morphology or a reduced morphology you need to divide the model's morphology into segments or compartments to model appropriately the spatial extent of the dendrites, but when you do this, how should you model these individual segments?

Because the voltage inside a neuron is negative relative to the outside, and because the membrane has the ability to store and separate charge, and because the membrane is studded with proteins, some of which are ion channels that allow current to pass, it is natural to develop a conceptual model of a patch of neuron membrane as an electric circuit, with a capacitor in parallel with a resistor representing the membrane current. Patches of membrane are connected together with another resistance representing the intracellular media.

We can represent the segment of dendrite as a cylinder with current flowing across the membrane and also down the cylinder. Technically current should have a 3-dimensional representation, but as we discussed, we can neglect the angular and radial current flows and reduce our consideration to 1-dimensional longitudinal current flow. This keeps our conceptual model electric circuit simple as shown on the top of this overhead

2-1. Today we will show how we can get from this conceptual model of a dendritic segment to the basic equation of neuron modeling, the CABLE EQUATION. The hardest thing about understanding how we get the cable equation is keeping the definitions of the various terms and their units straight.

The first set of terms all have something to do with voltage.

V_i is the potential inside the cell

V_{i1} is the potential inside at location x_1

V_{i2} is the potential inside at location x_2

V_e is the potential outside the cell

V_{e1} is the potential outside at location x_1

V_{e2} is the potential outside at location x_2

E_r is the resting membrane battery or the difference in voltage inside vs outside. This is the voltage where no net current flows, or where $V_i - V_e = E_r$. It represents the resting membrane potential

V_m is the membrane potential or $V_i - V_e$

Finally, for simplicity, we define $V = V_i - V_e - E_r$ so that V is 0 at rest

2-2. Next we define terms that have something to do with properties of the intracellular fluid and the membrane.

r_i is axial resistance per unit length with units of ohms/cm. In recent years, this term has been called r_a and I will use the terms interchangeably. The intracellular cytoplasm provides a resistance to current flow and r_i expressed this in terms of a unit length of dendrite. Note that the actual resistance will depend on the diameter of dendrite, so dendrites with different diameters will have different r_i values even though it is for the same length of dendrite.

$r_i\Delta x$ is the axial resistance of a length Δx of dendrite in cm. It has units of ohms, purely ohms

r_e is the extracellular resistance per unit length of dendrite with units of ohms/cm. The extracellular fluid also provides a resistance to current flow, just as the intracellular fluid does.

$r_e\Delta x$ is the extracellular resistance of a length Δx of dendrite in cm. It has units of ohms.

c_m is capacitance per unit length of membrane with units of F/cm

$c_m\Delta x$ is capacitance of a patch of dendrite Δx long. Units are Farads (F).

g_m is the conductance per unit length of membrane with units S/cm

$g_m\Delta x$ is the conductance of a membrane patch Δx long. Units are Siemens or S. We present definitions in terms of conductance first rather than the more familiar resistance because to make the non-intuitive definitions of resistance that follow more palatable. You might think of current being conducted across the membrane rather than the membrane providing a resistance, although these are the same thing

$r_m/\Delta x$ is the resistance of a patch of dendrite Δx long. Units are ohms. Since conductance is the inverse of resistance and ohms are the inverse of Siemens (also called mhos), this definition follows from $\text{resistance} = 1/(g_m\Delta x) = r_m/\Delta x$.

r_m is the resistance of a unit length patch of membrane in units of ohms-cm. Again this is the inverse of g_m .

So in the membrane circuit at the top of the page, we have labeled the resistances and capacitances in terms that represent resistance and capacitance in ohms and Farads.

Given these definitions, we are in position to derive the cable equation.

2-3. First of all we use Ohm's law. Which is what? $V=iR$. Before doing so, let's add two more definitions. If we consider two locations in a cylinder x_1 and x_2 where $x_2 > x_1$ (for convenience) then

$$\Delta x = x_2 - x_1 \text{ and } \Delta V = V_2 - V_1$$

also we assume that current i is positive with positive x (or in our illustrated cylinder, current flows to the right)

Then consider the portion of the circuit represented by current flowing through the resistance $r_i \Delta x$. By Ohm's law

$$V_{i1} - V_{i2} = i_i r_i \Delta x \text{ or } -\Delta V_i = i_i r_i \Delta x \text{ using our definition of } \Delta V$$

Then divide by Δx to get $\Delta V / \Delta x = i_i r_i$ and take the limit as Δx goes to 0. This is the definition of a derivative. We end up with (partial derivative)

$$\frac{\partial V_i}{\partial x} = -i_i r_i \text{ Similarly, if we consider the extracellular circuit we get } \frac{\partial V_e}{\partial x} = i_e r_e$$

2-4. Secondly we use Kirchoff's current law. Which says what? In any circuit representation the sum of currents coming into a node equals the sum of currents exiting the node. Before applying this equation, let's add some more definitions.

First, with current being positive with positive x we define

$$\Delta i = i_2 - i_1 \text{ We will use this for the intracellular and extracellular currents}$$

Second, let

i_m be the membrane current per unit length with units of A/cm and

$i_m \Delta x$ be the membrane current across a section of dendrite Δx long. Units are A (amps)

Also, using a convention mentioned last quarter, outward current is positive, inward current is negative.

Now, let's consider the currents meeting at the intracellular node at x_1 . The current coming into the node i_1 must equal the currents leaving this node $i_2 + i_m \Delta x$ or $i_1 = i_2 + i_m \Delta x$

Using our definition of Δi we get $-\Delta i = i_m \Delta x$

Dividing by Δx gives $\Delta i / \Delta x = -i_m$ and then taking the limit as Δx goes to zero gives

$$\frac{\partial i_i}{\partial x} = -i_m \text{ Similarly, considering the extracellular current we get } \frac{\partial i_e}{\partial x} = +i_m$$

2-5. Thirdly, we use Ohm's law and $Q=CV$

From $Q=CV$, we take the derivative with respect to time of both sides and get $dq/dt = C dV/dt$ (Note, C is not dependent on time)

But then what is dq/dt , the change of charge with time? This is the definition of current. We get

$i_m \Delta x|_{cap} = c_m \Delta x \frac{dV_m}{dt}$ where $V_m = V_i - V_e$ and the current is through the capacitance arm of the circuit. Dividing by Δx and we have simply

$$i_{m(cap)} = c_m \frac{dV_m}{dt}$$

From Ohm's law $V=iR$, we analyze the resistive arm of the membrane circuit. For V we consider the difference from V_i through the battery E_r to V_e and for i and R we take the terms from the illustrated circuit to get

$V_i - (V_e + E_r) = i_m \Delta x|_{res} r_m / \Delta x$ If we replace $V_i - V_e$ with V_m and cancel the Δx terms and divide by r_m we have

$$i_{m(res)} = V_m/r_m - E_r/r_m = (V_m - E_r)/r_m$$

Putting the capacitive and resistive currents together we get

$$i_m = c_m \frac{dV_m}{dt} + \frac{V_m - E_r}{r_m}$$

2-6. Now we gather our various equations together

Our equations for intracellular and extracellular current flow $\frac{\partial V_i}{\partial x} = -i_i r_i$ and $\frac{\partial V_e}{\partial x} = i_e r_e$ imply

that $\frac{\partial V}{\partial x} = -i_i r_i + i_e r_e$ and if we take another derivative with respect to x we get

$\frac{\partial^2 V_m}{\partial x^2} = -r_i \frac{\partial i_i}{\partial x} + r_e \frac{\partial i_e}{\partial x}$. Now if we substitute $\frac{\partial i_i}{\partial x} = -i_m$ and $\frac{\partial i_e}{\partial x} = +i_m$ into this equation we get

$\frac{\partial^2 V_m}{\partial x^2} = +r_i i_m + r_e i_m = i_m (r_i + r_e)$. Finally we substitute $i_m = c_m \frac{dV_m}{dt} + \frac{V_m - E_r}{r_m}$ in for i_m and get

$\frac{\partial^2 V_m}{\partial x^2} = (r_i + r_e) \left(c_m \frac{dV_m}{dt} + \frac{V_m - E_r}{r_m} \right)$. Now rearrange terms to get

$$\frac{r_m}{r_i + r_e} \frac{\partial^2 V_m}{\partial x^2} = r_m c_m \frac{\partial V_m}{\partial t} + (V_m - E_r).$$

2-7. Now if we consider voltage in terms of displacement from a resting potential and substitute $V = V_m - E_r$, then we get

$$\lambda^2 \frac{\partial^2 V}{\partial x^2} = \tau \frac{\partial V}{\partial t} + V \text{ which is the CABLE EQUATION, where } \lambda = \sqrt{\frac{r_m}{r_i + r_e}} \text{ and } \tau = r_m c_m \text{ and}$$

λ is the space constant and τ is the time constant

Note that r_m and c_m and r_i (r_a) are in terms of a length of dendrite and have units of ohm-cm, F/cm and ohm/cm. These values will vary with diameter. It is much more convenient to consider terms that take diameter into account and which are themselves independent of diameter. Consequently we define

R_m as the resistance of a unit area of membrane. Units are ohm-cm²

$$R_m = r_m \pi d \text{ or } r_m / \Delta x (\pi d \Delta x) = R_m \text{ Note } \pi d \Delta x \text{ is the membrane area of a cylinder}$$

C_m as the capacitance per unit area. Units are F/cm².

$$C_m = c_m / \pi d$$

R_i (or R_a) as the axial resistance through a cross-sectional area per unit length. Units are ohm-cm

$$R_a = r_a \pi a^2 \text{ (a = radius)}$$

With these definitions we get $\lambda = \sqrt{\frac{R_m d}{4 R_a}}$ and $\tau = R_m C_m$

2-8. Most of the time you will see the space constant λ defined without the r_e term. We typically neglect the extracellular resistance. We know that r_e is not zero, right? Why? If r_e were zero then we would not be able to make extracellular recordings. Furthermore ephaptic coupling has been observed among tightly coupled neurons. However we generally neglect r_e and in models of single neurons, this is a reasonable assumption because r_e is generally very small compared to the resistance of the membrane. The voltage difference outside the cell differs far less than the voltage across the membrane.

Rall did some calculations in 1959 to justify the neglect of r_e assuming that the neuron was either a sphere or a cylinder. If we consider a neuron as a sphere and calculate the voltage change from the cell to a distant point (infinity) using Ohm's law, we get

$$V_e = i \int_b^\infty \frac{R_e}{4\pi r^2} dr = \frac{i R_e}{4\pi} \int_b^\infty \frac{1}{r^2} dr = \frac{i R_e}{4\pi} \left(\frac{-1}{r} \right) \Big|_b^\infty = \frac{i R_e}{4\pi b}.$$

Now the voltage drop across the membrane (using Ohm's law is

$V = i R_m / 4\pi b^2$ so if the radius of the cell is 30 μm , R_e is 222 Ωcm and R_m is 4000 Ωcm^2 then $V_e/V = b R_e/R_m = 1.5 \text{ e-4}$.

Similarly for a cylinder we can calculate the voltage change from the cell with radius a to a distant point ($1000a$) using Ohm's law to get

$$V_e = i \int_a^{1000a} \frac{R_e}{2\pi r \ell} dr = \frac{iR_e}{2\pi \ell} \int_a^{1000a} \frac{1}{r} dr = \frac{iR_e}{2\pi \ell} \ln(r) \Big|_a^{1000a} = \frac{iR_e}{2\pi \ell} [\ln(1000a) - \ln(a)]$$

$$= \frac{iR_e}{2\pi \ell} \ln\left(\frac{1000a}{a}\right) = \frac{iR_e}{2\pi \ell} 6.9$$

Now across the membrane $V = iR_m/2\pi a \ell$ so $V_e/V = R_e/R_m \cdot 6.9a = 1.9e-4$ (assuming $a=5\mu\text{m}$)

So whether the cell is considered as a sphere or a cylinder, the voltage change extracellularly is very small compared to the change across the membrane and so we neglect it.

2-9. Often the mathematicians get rid of pesky constants with a change of variables, and this is often done with the cable equation. If we let $X = x/\lambda$ and $T = t/\tau$ then

$$\frac{\partial V}{\partial x} = \frac{\partial V}{\partial X} \frac{\partial X}{\partial x} = \frac{\partial V}{\partial X} \frac{1}{\lambda} \quad \text{and} \quad \frac{\partial^2 V}{\partial x^2} = \frac{\partial^2 V}{\partial X^2} \frac{1}{\lambda^2}$$

Similarly

$$\frac{\partial V}{\partial t} = \frac{\partial V}{\partial T} \frac{\partial T}{\partial t} = \frac{\partial V}{\partial T} \frac{1}{\tau}$$

so the cable equation $\lambda^2 \frac{\partial^2 V}{\partial x^2} = \tau \frac{\partial V}{\partial t} + V$ becomes $\frac{\partial^2 V}{\partial X^2} = \frac{\partial V}{\partial T} + V$ in non-dimensional form

2-10. This page summarizes the definitions of the various terms used in the derivation.

Next time we will look at some solutions to the cable equation.