

Passive Conduction - Cable Theory

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Biological Structure

Theoretical models describing propagation of synaptic potentials have evolved significantly over the past century. Synaptic potentials are the root of neural activity, electrical potential differences caused by fluxes of biological ions across the neural membrane. The first important breakthrough came through affirmation of the “leaky cable” theory proposed by Hermann. His theory described the way synaptic potentials propagate in lieu of excitatory membrane facilitation, i.e., passively. Passive conduction is an important behavior associated with the dendritic and terminal branches of the neuron. In the passive regime, the synaptic potential propagates with attenuation which prompted Hermann to ascribe a correlation with theory which describes “lossy” transmission lines [1].

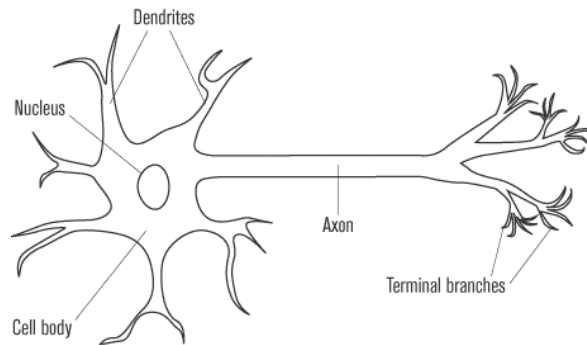


Figure 1: A neuron with basic components labeled. The dendrites are the region most often associated with Cable Theory, though the terminal branches are often proponents of passive conduction as well.

Cable Theory

Cable Theory is based on a small number of principles. The first principle is that local circuit currents, which are depicted below, are a medium for diffusive propagation of synaptic potentials along the axon membrane. The ion

fluxes, i.e., local currents, change local potentials which induce local currents in neighboring locales with diminishing amplitudes.

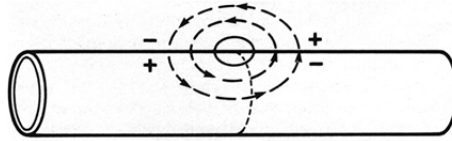


Figure 2: An example of local ion channel currents flowing across the membrane of a cylindrical section of neuron. Local denotes that the current loops exist on a small scale compared to the radius of the cylindrical membrane.

The second tenet of Cable Theory models the cell membrane as discrete, compartmentalized electrical circuits. The cellular membrane necessarily exhibits a capacitance due to the imbalance of ion concentrations in the extracellular and intracellular fluids. The cell membrane also exhibits an intrinsic conductivity depending on characteristics of embedded ion channels. The cytoplasm also displays an axial conductance which depends primarily on the ion concentration throughout the fluid. A sample scheme for modeling passive conduction membrane as a set of circuits is shown in *figure 3* below.

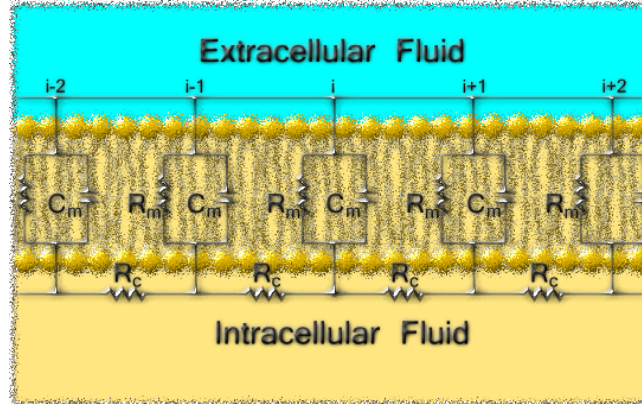


Figure 3: A diagram of the electrical components which approximate the cellular membrane and cytoplasm in Cable Theory. Using information in the diagram, one can employ basic circuit physics and differential equations to derive the Cable Equation which describes the electrical potential across the membrane.

Now, we venture into the mathematical derivation. Recall Kirchhoff's Current Law, $\sum_{j=1}^{j=n} I_k = 0$, as well as Ohm's Law, $V = IR$ and an equation for capacitive current, $I = \frac{dQ}{dt} = C \frac{dV}{dt}$. Using the marked node in the diagram above, the following equations fall out.

$$I_1 - I_2 - I_3 = 0 \quad (1)$$

$$I_1 = (V_i - V_{i-1})/R_c \quad (2)$$

$$I_2 = (V_{i+1} - V_i)/R_c \quad (3)$$

$$I_3 = -C_m \frac{\Delta V}{\Delta t} + (V_{rest} - V_i)/R_m \quad (4)$$

The resting potential outside the cell is relative, so it can be defined as zero and removed from the equations. Substitute the subsequent equations back into (1) and rearrange slightly to get

$$\frac{\Delta V}{\Delta t} = \frac{1}{R_c C_m} [V_{i-1} - 2V_i + V_{i+1}] - \frac{V_i}{R_m C_m} \quad (5)$$

The electrical constants appearing in the equations above are described in non-standard units to neutralize their length dependence. For example, the membrane capacitance is measured experimentally in *Farads/cm²* because $C_m \propto A_{membrane}$. It is best to redefine measurements per unit length as per the model. The following table depicts the relevant unit conversions as well as approximate values of the constants relative to the model [3] [1]. The radius of the axon ($\approx 0.5 \text{ mm}$ for giant squid) is denoted by a , and tildes denote the experimentally measured value.

convenient constant	units	substitution	experimental value	conversion
r_c	$k\Omega/cm$	$r_c \cdot \Delta x = R_c$	12.5	$r_c = \tilde{r}_c / (\pi a^2)$
r_m	$k\Omega \cdot cm$	$r_m / \Delta x = R_m$	15.0	$r_m = \tilde{r}_m (2a\pi)$
c_m	$\mu F/cm$	$c_m \cdot \Delta x = C_m$	0.30	$c_m = \tilde{c}_m / (2a\pi)$

When substitution are made for R_c , R_m , and C_m , the equation begins to look like familiar differential equations.

$$\frac{\Delta V}{\Delta t} = \frac{1}{r_c c_m} \left[\frac{V_{i-1} - 2V_i + V_{i+1}}{\Delta x^2} \right] - \frac{V_i}{r_m c_m} \quad (6)$$

The differential form of the Cable Equation arrives in the limit that Δx and Δt are taken to zero.

$$\frac{\partial V(x, t)}{\partial t} = \frac{1}{r_c c_m} \frac{\partial^2 V(x, t)}{\partial x^2} - \frac{V(x, t)}{r_m c_m} \quad (7)$$

Substituting $D = \frac{1}{r_c c_m}$ and $\tau = r_m c_m$ to get the Cable Equation an elegant form.

$$\dot{V} = D \frac{\partial^2 V}{\partial x^2} - \frac{1}{\tau} V \quad (8)$$

Unlike many partial differential equations, fortunately, the Cable Equation can be solved explicitly with a bit of work. The first order of business is simplifying the system through some initial guesswork. The last term looks very much like the time derivative of an exponential, so let's see what happens if we substitute $V(x, t) = e^{-t/\tau}W(x, t)$. Equation (8) simplifies to

$$\frac{\partial W}{\partial t} = D \frac{\partial^2 W}{\partial x^2}. \quad (9)$$

After this useful transformation, the partial differential equation appears much more tractable. A variable substitution will reduce the equation to an ordinary differential equation; let $\phi = x^2/t$. The resulting ordinary differential equation

$$-\frac{dW}{d\phi} = 4D \frac{d^2W}{d\phi^2}. \quad (10)$$

With minimal effort $W(x, t)$ can be solved explicitly then normalized over all spatial coordinates. Reverse the variable substitution to attain the solution in terms of x and t .

$$W(x, t) = \frac{1}{\sqrt{4\pi D(t-t_0)}} \exp \left[\frac{-(x-x_0)^2}{4D(t-t_0)} \right] \quad (11)$$

Combine (11) with the term which was exponential in time to arrive at $V(x, t)$, the solution to the Cable Equation.

$$V(x, t) = \frac{1}{\sqrt{4\pi D(t-t_0)}} \exp \left[\frac{-(x-x_0)^2}{4D(t-t_0)} - \frac{t-t_0}{\tau} \right] \quad (12)$$

Applications of the Cable Equations

Example 1

Suppose we have two dendritic branches coming to a union as a model system. We want to investigate the outcome of two different synaptic pulses coming together. The pulse on the top branch initiates at a point which is an arc length of a from the union while the bottom branch's pulse begins at an arc length of b from the union. Let's use the union to define the origin of both of our coordinate systems, so that the stimulus point of each pulse is $x_a = -a$ and $x_b = -b$. The stimulus voltages are defined as:

$$V_a(t=0) = \alpha \delta(x_a + a)$$

$$V_b(t=0) = -\beta \delta(x_b + b).$$

The diffusion constant, D , and the time constant, τ , can be assumed to be constant in all regions of the system although this is not necessarily true in a realistic case.

The first step in solving the problem is simply realizing that the differential form of the Cable Equation is linear. Solutions to linear differential equations can be

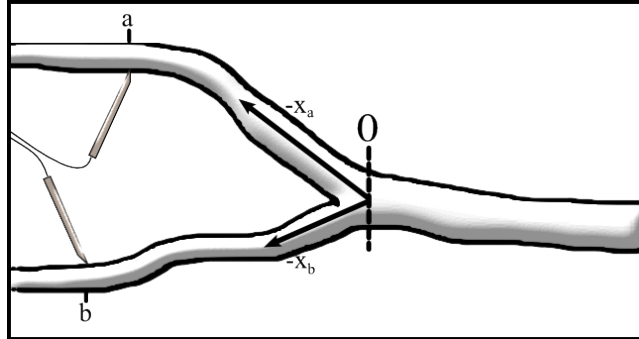


Figure 4: The setup for the problem below: two synaptic pulses initialized on different dendritic branches which come to a union.

superimposed solutions for each of the stimuli can be solved separately. Each solution evolves from a delta-function stimulus, so the solution derived earlier, equation 12, is applicable. The solutions for the two branches are then:

$$V_a(x_a, t) = \frac{\alpha}{\sqrt{4\pi D(t-t_0)}} \exp \left[\frac{-(x_a + a)^2}{4D(t-t_0)} - \frac{t-t_0}{\tau} \right]$$

$$V_b(x_b, t) = \frac{-\beta}{\sqrt{4\pi D(t-t_0)}} \exp \left[\frac{-(x_b + b)^2}{4D(t-t_0)} - \frac{t-t_0}{\tau} \right].$$

The combined solutions at the union of the two branches is then simply

$$V(x, t) = V_a(x_a, t) + V_b(x_b, t) \quad (13)$$

Now, the behavior of interest in this problem is the time evolution of the voltage at $x_a = x_b = 0$. For instance, what type of initial parameters allow the pulses to exactly cancel one another at any point in time. Using equation 13 solve for the time at which the synaptic pulses exactly cancel each other. Set $V(0, t) = 0$, $x = 0$ and $t_0 = 0$, and one arrives at

$$\frac{\alpha}{\sqrt{4\pi Dt}} \exp \left[\frac{-a^2}{4Dt} - \frac{t}{\tau} \right] = \frac{\beta}{\sqrt{4\pi Dt}} \exp \left[\frac{-b^2}{4Dt} - \frac{t}{\tau} \right].$$

Simplify.

$$\alpha \exp [-a^2/4Dt] = \beta \exp [-b^2/4Dt]$$

Take the natural logarithm of both sides.

$$\ln \alpha - a^2/4Dt = \ln \beta - b^2/4Dt$$

Now we can solve for values of t which yield zero voltage at the point of union.

$$t = \left(\frac{a^2 - b^2}{4D} \right) \ln \alpha/\beta \quad (14)$$

Seeing as $t > 0$ is a necessary condition, total interference can occur only if $(a > b)$ and $(\beta > \alpha)$, $(b > a)$ and $(\alpha > \beta)$ or $(a = b)$ and $(\alpha = \beta)$. This makes sense intuitively and affirms that we have arrived at a reasonable solution.

Example 2

Now for an example modeled to be more relevant to physical systems, take a system which includes a dendrite and connecting soma at the far end of the cable. The other end of the dendrite can only be excited by a -70 mV pulse once every 5 ms . To make the example even a little more concrete, employ the measured experimental values of squid axons given in the table previously for electrical constants and let the model dendrite have a length $L = 2 \text{ cm}$. The connecting soma needs to reach a voltage of -5 mV to exceed its threshold and fire. Will the train of synaptic pulses in system described above excite the connecting soma? If so, how many excitations must occur before the soma fires?

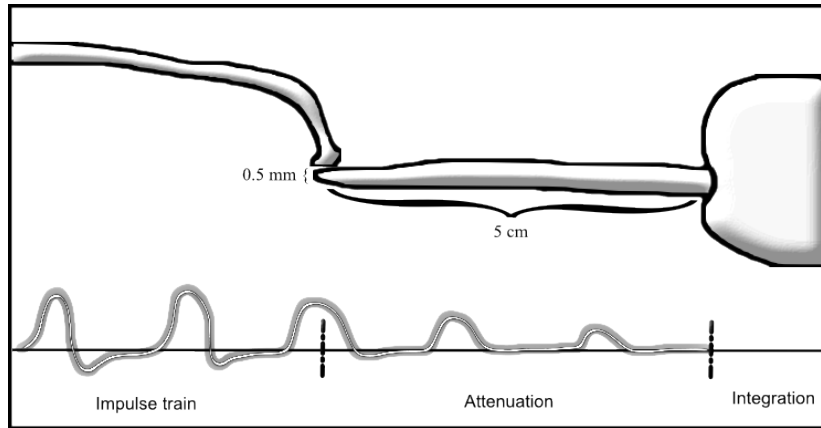


Figure 5: The setup for the problem above: a train of synaptic impulses is incident on a single, 5 cm dendritic branch. The diagram is very roughly consistent with giant squid neurons.

The solution for a single excitation has been well established. This solution suits the purpose of this example as well. Therefore, for a single excitation one attains

$$V(x, t) = \frac{-70mV}{\sqrt{4\pi Dt}} \exp \left[\frac{-(x)^2}{4Dt} - \frac{t}{\tau} \right]. \quad (15)$$

First order of business, plug the experimental values back into the equation.

$$V(5, t) = -38.24t^{-1/2} \exp \left[\frac{-0.9375}{t} - \frac{t}{4.5} \right] mV \quad (16)$$

Now, find the time at which the voltage on the soma is highest from a single excitation. The task is best accomplished using a mathematical modeling program such as Mathematica or Matlab as the differential solution cannot be solved explicitly. One finds that the voltage on the soma peaks at about -3.253 mV after around 3.12 ms ; the solution then decays exponentially. Therefore, the soma does not fire from the first pulse at any rate.

To resolve whether the incoming excitations can excite the soma, the fact that solutions are additive needs to be employed once again; this instance in the time domain. The solution with two pulses at 5 ms offsets is now considered for $t > 5 \text{ ms}$.

$$\begin{aligned}
 V(5, t) = & -38.24t^{-1/2} \exp \left[\frac{-0.9375}{t} - \frac{t}{4.5} \right] \\
 & -38.24(t-5)^{-1/2} \exp \left[\frac{-0.9375}{(t-5)} - \frac{t-5}{4.5} \right] \quad (17)
 \end{aligned}$$

The peak voltage at the soma is assumed to be very near 8.12 ms , so the system can simply be evaluated at this point. The soma voltage still falls short of the firing threshold, so proceeding in a similar manner, three pulses are now included at 5 ms spacing.

$$\begin{aligned}
 V(5, t) = & -38.24t^{-1/2} \exp \left[\frac{-0.9375}{t} - \frac{t}{4.5} \right] \\
 & -38.24(t-5)^{-1/2} \exp \left[\frac{-0.9375}{(t-5)} - \frac{t-5}{4.5} \right] \\
 & -38.24(t-10)^{-1/2} \exp \left[\frac{-0.9375}{(t-10)} - \frac{t-10}{4.5} \right] \quad (18)
 \end{aligned}$$

This time the solution yields -5.07 mV at $t = 8.12 \text{ ms}$, therefore the soma is indeed excited two subsequent excitatory pulses after the first.

Further Experimental Development

The majority of experiments involving Cable Theory center around measuring the electrical constants of the dendrites. The first measurements were made some time after equivalent experiments were carried out on squid axons. The dendrites are much smaller in stature; therefore, more refined measurement techniques were necessary. Eventually measurements of r_c , r_m , and c_m were performed using simple, fine electrodes. Years later, patch-clamp methods were developed to make the same measurements [3]. The patch-clamp measurements results assert that the previous measure were underestimates by a factor of 2-4 for different values. Though the constants differ, the experiments do observe attenuation of the synaptic signal in very good agreement with expectations from Cable Theory.

Another more recent method of observing synaptic potentials involves the application of voltage sensitive dyes [4] [2]. A fluorescent dye which binds to the

cellular membrane is injected into the axon and allowed to diffuse throughout the neuron. The neuron is then electrically excited and the observed changes in light intensity are proportional to voltage changes. The method shows great promise, as it allows observation of the entire neuron at once rather than a relatively small number of separate points. However, it is not without flaw. Calibration between voltage and fluorescence intensity has proven difficult, because of a number of factors involving nonlinearity as well as fluorescent dye placement and numbers.

References

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