1 Passive and Active Electrical Propagation

We consider the behavior of the transmembrane potential across a long process, first in terms of passive propagation and then in terms of active (regenerative) propagation. This is a first step toward considering spatial aspects of the electrical dynamics of neurons.

1.1 Basic Scales

The cytoplasm acts as one conductor and the extracellular space acts as the second. Let's assume, as is often but not always the case, that the conductance of the extracellular space may be taken as infinite. Then a signal that flows down the center will be attenuated over a length of axon such that the cytoplasmic and membrane impedances (don't forget the capacitance of the membranr) are about equal, i.e., over the length required to form a voltage divider. For an axon of radius a with membrane thickness L, we can estimate this length by equating the cytoplasmic and membrane resistances, i.e.,

$$\rho_c \frac{\lambda}{\pi a^2} \approx \rho_m \frac{L}{2\pi a \lambda} \tag{1.1}$$

or

$$\lambda = \sqrt{\frac{\rho_m}{\rho_c}\frac{aL}{2}} \tag{1.2}$$

Usually the product

$$r_m = \rho_m L \tag{1.3}$$

is denoted as the specific membrane resistance It has typical values of r_m =1 to 100 kΩcm^2, while the cytoplasm has resistances of order ρ_c = 30 to 300 Ωcm. The spatial attenuation length λ is seen to vary as $\lambda \propto a^{1/2}$.

The signals in neurons are confined to a small frequency band, about 10 kHz. Further, the relevant cables are lossy and have a only thin dielectric. Thus it pays to evaluate all of the physical parameters of the system to see which dominate and which may be neglected. Let's consider general expressions for the membrane (transverse) conductance, the membrane capacitance and the axial (what else!) inductance. We consider a model with a membrane, or dielectric layer, that has conductivity g, permittivity ϵ, and permeability μ. This arbitrariness of this cable will emphasize that all the bumps in real axons and dendrites can safely be ignored.

1.2 Cable Equation

We can now just consider a model with resistances and capacitances and write down a lumped parameter model for a lossy cable. The exact equation for a cable can be considered by writing the circuit equations for a segment of length Δx and letting $\Delta x \to 0$. We get

$$\tau \frac{\partial V(x,t)}{\partial t} + V(x,t) - \lambda^2 \frac{\partial^2 V(x,t)}{\partial x^2} = \frac{r_m}{2\pi a} I_m(x,t) \tag{1.4}$$

where the time-constant τ depends only on membrane constants. We have included the possibility of additional membrane currents, denoted I_m in units of Amperes per unit length; these will become evident when we study action potential propagation.

1.2.1 Steady State Response

A particularly simple case to consider is the steady state response to the continuous injection of current at a point. The cable equation turns into Helmholtz's equation (λ plays the role of 'k'), i.e.,

$$V(x) - \lambda^2 \frac{\partial^2 V(x)}{\partial x^2} = \frac{r_m}{2\pi a} I_m(x) \tag{1.5}$$

and we know that the solutions are of the form

$$V(x) = Ae^{\frac{x}{\lambda}} + Be^{-\frac{x}{\lambda}} + C \tag{1.6}$$

where here the A, B, Cs are constants. For the case of current injected at a spot into an infinitely long uniform cable, , i.e, $I_m(x) = I_o\delta(x)$, the change in voltage is

$$V(x) = \frac{I_o}{2\lambda} \frac{r_m}{2\pi a} e^{-\frac{|x|}{\lambda}} + V(\infty) \tag{1.7}$$

Thus, as we claimed above, we see directly that λ scales the length of the electrical disturbance. We also see that the input resistance scales as

$$R = \frac{V(0)}{I_o} = \frac{\sqrt{2}}{4\pi} \sqrt{\rho_c r_m}\, a^{-3/2} \tag{1.8}$$

Thus the resistance goes up faster than linear as the radius of the process decreases. To the extent that large resistances are a good thing, as least as far as not loading down the soma, one cannot be too thin ... .

We can push this result into the frequency domain to see what the low pass filtering characteristics of the cable look like. The simplest way to do this is to take the Fourier transform, with respect to time, of the original cable equation. We get

$$i\tau\omega\tilde{V}(x,\omega) + \tilde{V}(x,\omega) - \lambda^2 \frac{\partial^2 \tilde{V}(x,\omega)}{\partial x^2} = \frac{r_m}{2\pi a} \tilde{I}_m(x,\omega) \tag{1.9}$$

or

$$(1+i\omega\tau)\tilde{V}(x,\omega)-\lambda^2\frac{\partial^2\tilde{V}(x,\omega)}{\partial x^2}=\frac{r_m}{2\pi a}\tilde{I}_m(x,\omega) \tag{1.10}$$

This looks exactly like the Helmholtz equation if we make the substitutions

$$r_m \leftarrow \frac{r_m}{1+i\omega\tau} \tag{1.11}$$

$$\lambda \leftarrow \frac{\lambda}{\sqrt{1+i\omega\tau}} \tag{1.12}$$

The resistance is generalized to a steady-state impedance with

$$Z(\omega)=R\frac{1}{\sqrt{1+i\omega\tau}}=R\frac{e^{-\frac{i}{2}tan^{-1}(\omega\tau)}}{(1+(\omega\tau)^2)^{\frac{1}{4}}} \tag{1.13}$$

It is interesting that the impedance varies as $Z \sim R/\sqrt{\omega\tau}$, in contrast to the $Z \sim R/(\omega\tau)$ dependence for a lumped RC circuit. This was recently seen in motoneurons. Thus long cables provide a very soft filtering effect.

1.2.2 General Response

The full cable equation is simple to evaluate once you realize that this is really the diffusion equation in terms of the function $U(x,t)$, with

$$V(x,t)=e^{-\frac{t}{\tau}}U(x,t) \tag{1.14}$$

where $\frac{\lambda^2}{\tau}=\frac{a}{\rho_c c_m}$ plays the role of the diffusion constant. The homogeneous part of the cable equation becomes

$$\lambda^2\frac{\partial^2 U(x,t)}{\partial x^2}-\tau\frac{\partial U(x,t)}{\partial t}=0 \tag{1.15}$$

We can write down the delta function response directly. That is, for an impulse of charge so that $I_m(x,t)=Q_o\delta(x)\delta(t)$, the voltage evolves as

$$V(x,t)=\frac{Q_o}{\tau}\frac{r_m}{2\pi a}\sqrt{\frac{\tau}{4\pi\lambda^2 t}}\;e^{-\frac{t}{\tau}-\frac{x^2\tau}{4\lambda^2 t}} \tag{1.16}$$

There are two essential aspects of the response to consider. The first is that the voltage at the injection site initially decay faster than τ_m as current flows into the cable and and charge it. At later times all locations of the cable essentially discharge together and the decay is exponential. This behavior can be seen from plots of the calculated response at various distances from the origin, and in the data of Rall, who spent much effort on the issue of cables.

The second point is that the pulse is decaying as it spreads, and thus has the appearance of a front. We can ask where the front of the pulse is by calculating $\frac{\partial V(x,t)}{\partial t}=0$. We rewrite our solution of the cable equation with all of the time and space dependent terms in the exponent, so that

$$V(x,t) = V(0) e^{-\frac{1}{2} ln \frac{t}{\tau} - \frac{t}{\tau} - \frac{x^2 \tau}{4\lambda^2 t}} \tag{1.17}$$

Thus $\frac{\partial V(x,t)}{\partial t} = \frac{\partial V(0) e^{f(x,t)}}{\partial t} = V(0) e^{f(x,t)} \frac{\partial f(x,t)}{\partial t} = 0$ implies

$$\begin{aligned} \frac{d\left(\frac{1}{2} ln \frac{t}{\tau} + \frac{t}{\tau} + \frac{x^2\tau}{4\lambda^2 t}\right)}{dt} &= 0 & (1.18) \\ t\frac{\tau}{2} + t^2 - \frac{x^2\tau^2}{4\lambda^2} &= 0 & (1.19) \end{aligned}$$

which gives

$$t_{max} = \frac{\tau}{2}\left(\sqrt{\frac{1}{4} + \frac{x^2}{\lambda^2}} - \frac{1}{2}\right) \approx \frac{\tau}{2}\frac{|x|}{\lambda} \tag{1.20}$$

The ratio $\frac{|x|}{t_{max}} = \frac{2\lambda}{\tau}$ is the speed of the (exponentially decaying) peak of the voltage pulse. Note that the width of the peak increases with time as $\lambda\sqrt{\frac{2t}{\tau}}$, consistent with dispersion during passive decay.

1.3 Speed of the Action Potential

We now turn to active propagation, for which we expect the speed to be faster than that for passive propagation and, further, for which we expect the width of the action potential to be constant with time. A naive approach is to take the speed to be that from the cable equation with parameters for the cell during an action potential, i.e.,

$$u \approx \frac{\lambda(AP)}{2\tau(AP)} = \frac{\sqrt{\frac{r_m}{2\rho_c} a}}{2 r_m c_m} \tag{1.21}$$

with r_m dominated by $\overline{G}_{Na^+}$, so that

$$u \approx \frac{1}{2c_m}\sqrt{\frac{\overline{G}_{Na^+}}{2\rho_c} a} = \frac{\lambda}{2\tau}\sqrt{r_m \overline{G}_{Na^+}} \tag{1.22}$$

which is faster than passive propagation by a factor of $\frac{\sqrt{r_m \overline{G}_{Na^+}}}{4}$. To get a better approximation, we first recall that the Hodgkin-Huxley neuron in the absence of external input is given by

$$\begin{aligned} \tau\frac{\partial V(x,t)}{\partial t} &= \lambda^2 \frac{\partial^2 V(x,t)}{\partial x^2} - r_m \overline{G}_{Na^+} m^3(V,t) h(V,t)\left(V - V_{Na^+}\right) & (1.23) \\ &- r_m \overline{G}_{Ka^+} n^4(V,t)\left(V - V_{K^+}\right) - r_m \overline{G}_{leak}\left(V - V_{leak}\right) \end{aligned}$$

along with equations (three of them) for the activation parameters $n(V,t)$, $m(V,t)$, and $h(V,t)$, where the conductances have units of $(\Omega cm^2)^{-1}$, i.e., conductance per unit area, so we don't have to chase factors of $2\pi a$, where

- $V(x, t) \leftarrow$ transmembrane potential
- $m(V, t) \leftarrow$ activation parameter for Na^+ current
- $h(V, t) \leftarrow$ inactivation parameter for Na^+ current
- $n(V, t) \leftarrow$ activation parameter for K^+ current

We need consider only the leading edge or front of the action potential so that we can ignore the potassium currents.

The equation for Na^+ current will contain an essential nonlinearity to allow regenerative behavior. This is found by looking at the I-V relation for the squid axon at short times, when the Na^+ current is fully activated. It follows a cubic dependence, as discussed for our analysis of the Fitzhugh-Nagumo equation.

We take

$$f(V) = -V\left(1 - \frac{V}{V_{rest}}\right)\left(1 - \frac{V}{V_{peak}}\right) \tag{1.24}$$

with $V_{threshold} = 0$ and $V_{rest} < 0 < V_{peak}$. Thus all potentials are with respect to the threshold level. We then have an equation that is roughly valid on the time-scale of the leading edge of the spike - or the first 0.1 ms of the action potential, i.e.,

$$\tau\frac{\partial V}{\partial t} = \lambda^2\frac{\partial^2 V}{\partial x^2} + r_m\overline{G}_{Na^+}V\left(1 - \frac{V}{V_{rest}}\right)\left(1 - \frac{V}{V_{peak}}\right) \tag{1.25}$$

This equation ignores the recovery term and provides an interesting lesson about a hypothetical neuron with only noninactivating Na^+ currents (perhaps this can be built with the right molecular tools someday).

We now solve this equation for a propagating front with constant speed and width:

- Let $V(x, t) = V(x - ut) \equiv V(z)$, so that

$$-\tau u\frac{dV}{dz} = \lambda^2\frac{d^2V}{dz^2} + r_m\overline{G}_{Na^+}V\left(1 - \frac{V}{V_{rest}}\right)\left(1 - \frac{V}{V_{peak}}\right) \tag{1.26}$$

- Assume that V propagates as a front when V is not near $V = 0$ or $V = V_{peak}$, where $\frac{dV}{dz} = 0$. We define the width of the front as Λ, which has to be found self consistently, and take

$$\dot{V} \equiv \frac{dV}{dz} = -\frac{V}{\Lambda}\left(1 - \frac{V}{V_{peak}}\right) \tag{1.27}$$

- Take $V(z \rightarrow \pm\infty) = 0$

- A trick is to rewrite the equation with

$$\frac{d^2V}{dz^2} = \dot{V}\frac{d\dot{V}}{dV} \tag{1.28}$$

so that

$$\frac{d\dot{V}}{dV} = -\frac{1}{\Lambda}\left(1 - 2\frac{V}{V_{peak}}\right) \tag{1.29}$$

- Then

$$-\tau u\dot{V} = \lambda^2\dot{V}\frac{d\dot{V}}{dV} - r_m\overline{G}_{Na^+}\Lambda\left(1 - \frac{V}{V_{rest}}\right)\dot{V} \tag{1.30}$$

or after substitution, and arrnanging constants to make all terms dimensionless,

$$-u\frac{\tau}{\Lambda} + \frac{\lambda^2}{\Lambda^2} - r_m\overline{G}_{Na^+} = \left(\frac{2\lambda^2}{\Lambda^2 V_{peak}} + \frac{r_m\overline{G}_{Na^+}}{V_{rest}}\right)V \tag{1.31}$$

The terms proportional to V and those independent of V must independently sum to zero. Thus

$$\Lambda = \frac{\lambda}{\sqrt{r_m\overline{G}_{Na^+}}}\sqrt{2\left(\frac{-V_{rest}}{V_{peak}}\right)} \tag{1.32}$$

and we see that the space constant is shortened during an action potential. Further,

$$u = \frac{\lambda}{\tau}\sqrt{r_m\overline{G}_{Na^+}}\,\frac{1 + 2\left(\frac{-V_{rest}}{V_{peak}}\right)}{\sqrt{2\left(\frac{-V_{rest}}{V_{peak}}\right)}} \tag{1.33}$$

where we used $\sqrt{x} + \sqrt{\frac{1}{x}} = \frac{1+x}{\sqrt{x}}$and we see that the speed depends on the amplitude of the action potential.

The temporal width of the front is just $T \equiv \frac{\Lambda}{u}$, or

$$T = \frac{\tau}{r_m\overline{G}_{Na^+}}\,\frac{2\left(\frac{-V_{rest}}{V_{peak}}\right)}{1 + 2\left(\frac{-V_{rest}}{V_{peak}}\right)} \tag{1.34}$$

Finally, recalling that all voltages are relative to threshold, the fraction of voltages is typically $\left(\frac{-V_{rest}}{V_{peak}}\right) \approx \frac{1}{2}$. Further, the factor $r_m\overline{G}_{Na^+}$ that sets the difference between passive and active scales is 20 or more. So an action potential is a rather narrow front. Remember too that all of the above was derived just with a phenomenological model of the nonlinear fast, Na^+ current. This appears legitimate since this current is an order of magnitude faster than the slow recovery dynamics.