Passive cell models

Comp Neuroscience

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1 Ionic basis of the membrane potential

The key feature in maintaining a voltage difference between a neuron and the external world is the cell membrane which has the property of selectively allowing different ions in and out of the cell. There are many different ions in the intra- and extracellular media. For our purposes, the most important are calcium [Ca], potassium [K], sodium [Na], chloride [Cl], and magnesium [Mg]. Potassium and sodium have a single positive charge per ion, chloride has a single negative charge, and calcium and magnesium have two positive charges per ion. Positive ions are called cations and negative are called anions.

1.1 Nernst Equation

Each ion has an equilibrium potential associated with it whereby the diffusive forces and the electrical forces balance. This is given by the Nernst Equation

$$E_i \equiv V_{in} - V_{out} = \frac{RT}{zF} \ln \frac{[C]_{out}}{[C]_{in}} \tag{1}$$

where T is the absolute temperature $273.16 + {}^\circ C$, $R = 8.31451\ j/(mol - K)$ is the ideal gas constant, $F = 96485.3\ C/mol$ is Faraday's constant, and z is the valence of the ion. Generally people use the logarithm base 10 in which case the Nernst equation is multiplied by the factor 2.303. At $T = 20^\circ C$ just multiply the logarithm base 10 of the ratio of outside to inside by 58 mV to get the equilibrium potential. At $T = 37^\circ C$ the multiplication factor is just 62 mV. The table at the end of this section shows the typical equilibrium potentials for various membranes at various temperatures.

1.2 Goldman-Hodgkin-Katz

In the presence of several different ions, the equilibrium of the cell depends on the relative permeability of the ions. For this, we use the Goldman-Hodgkin-Katz equation:

$$V_{rest} = \frac{RT}{F} \ln \frac{P_K[K^+]_{out} + P_{Na}[Na^+]_{out} + P_{Cl}[Cl^-]_{in}}{P_K[K^+]_{in} + P_{Na}[Na^+]_{in} + P_{Cl}[Cl^-]_{out}} \tag{2}$$

Permeability of an ion is dependent on a number of factors such as the size of the ion, its mobility, etc. During rest in the squid giant axon, the permeabilities have the ratio $P_K : P_{Na} : P_{Cl} = 1 : 0.03 : 0.1$ so that

$$V_{rest} = 58 \log \frac{1(10) + 0.03(460) + 0.1(40)}{1(400) + 0.03(50) + 0.1(540)} = -70mV$$

Since P_K dominates, this is close to E_K. During an action potential the ratio is $P_K : P_{Na} : P_{Cl} = 1 : 15 : .1$ so that

$$V_m = 58 \log \frac{1(10) + 15(460) + 0.1(40)}{1(400) + 15(50) + 0.1(540)} = +44mV$$

Later on we will approximate the GHK equations by a linearized version:

$$V_{eq} = \frac{g_{Na}E_{Na} + g_K E_K + g_{Cl}E_{Cl}}{g_{Na} + g_K + g_{Cl}}$$

where the conductances g are proportional to the permeabilities.

HOMEWORK

1. Suppose the external potassium in a mammalian cell is increased by a factor of 10. What is the new value of E_K?
2. At $10°C$ a cell contains 80 mM sodium inside and has only 100 mM sodium outside. What is the equilibrium potential for sodium?
3. Using the same permeabilities for the mammalian cell as were used for the squid axon, compute V_{rest}, V_m using the table below.

2 Ion concentrations and equilibrium potentials

Ion	Inside (mM)	Outside (mM)	Equilibrium Potential $E_i = \frac{RT}{zF} \ln \frac{[C]_{out}}{[C]_{in}}$
Frog Muscle			$T = 20°C$
K^+	124	2.25	$58 \log \frac{2.25}{1.24} = -101mV$
Na^+	10.4	109	$58 \log \frac{109}{10.4} = +59mV$
Cl^-	1.5	77.5	$-58 \log \frac{77.5}{1.5} = -99mV$
Ca^{2+}	10^{-4}	2.1	$29 \log \frac{2.1}{10^{-4}} = +125mV$
Squid Axon			$T = 20°C$
K^+	400	20	$58 \log \frac{20}{400} = -75mV$
Na^+	50	440	$58 \log \frac{440}{50} = +55mV$
Cl^-	40-150	560	$-58 \log \frac{560}{40-150} = -66 \text{ to } -33mV$
Ca^{2+}	10^{-4}	10	$29 \log \frac{10}{10^{-4}} = +145mV$
Mammalian cell			$T = 37°C$
K^+	140	5	$62 \log \frac{5}{140} = -89.4mV$
Na^+	5-15	145	$62 \log \frac{145}{5-15} = +90 - (+61)mV$
Cl^-	4	110	$-62 \log \frac{110}{4} = -89mV$
Ca^{2+}	10^{-4}	2.5-5	$31 \log \frac{2.5-5}{10^{-4}} = +136 - (+145)mV$

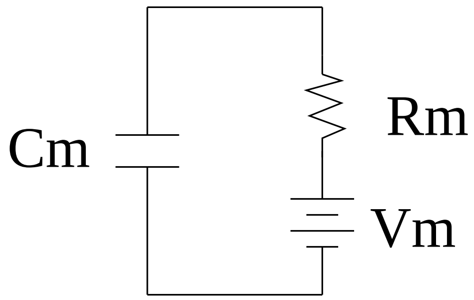

Figure 1: Passive Membrane Model

3 Electrical properties of a membrane

The simplest representation of a piece of nerve membrane is a simple $RC-$ circuit as shown in Figure 1. The capacitance of a typical membrane, C_m arises due to the fact that there are layers of conductive and nonconductive (lipids) media. The capacitance of a typical patch of membrane is $C_M = 1\mu F/cm^2$. That is the membrane capacitance is measured in terms of the area of the membrane. The larger the area, the larger the capacitance. Since we will be doing most measurements in microns but most constants are in centimeters, the conversion factor is 10^4 microns per centimeter. The actual capacitance is then $C_M A$ where A is the area of the membrane patch. Thus, a spherical cell which is 20 microns in diameter has a total capacitance of

$$C_m = C_M 4\pi r^2 = 1 \times 10^{-6} 4\pi (20 \times 10^{-4})^2 = 5 \times 10^{-11} \text{ farad} = 50pF.$$

The membrane also has an associated resistance. As you might guess, the smaller the patch of membrane, the larger is the resistance. The resistance of a typical patch of membrane, R_M is $10000\Omega cm^2$ so that for our sphere, the actual resistance is $R_m = R_M/A$ or

$$R_m = R_M/(4\pi r^2) = 1 \times 10^4/(4\pi(20 \times 10^{-4})^2) = 198M\Omega.$$

There are two main points to emphasize: (i) Associated with any membrane are certain *material* constants that are independent of the shape of the membrane, (ii) the actual electrical properties of a membrane depend on its geometry.

We can now write the equation for a patch of membrane:

$$C_m \frac{dV}{dt} = -(V - V_m)/R_m \tag{3}$$

which, if we multiply both sides by R_m obtain

$$\tau_m \frac{dV}{dt} = -(V - V_m) \tag{4}$$

where $\tau_m = R_m C_m = R_M/A \times C_M A = R_M C_M$ is called *the membrane time constant.* **It is independent of geometry.** For our present choice of parameters, $\tau_m = 10^{-6} \times 10^4 = 10msec$. The true membrane resistance is difficult to measure since electrodes will puncture the membrane and thus decrease the apparent resistivity. This simple equation is called a one-compartment model for a passive membrane. In general, as we will see, all neural models are made up of pieces just like this and ultimately so are connectionist models that can be derived from these biophysical models. This is the **EVE** of GENESIS!

The solution to (4) is easy:

$$V(t) = V_m + (V(0) - V_m)e^{-t/\tau}$$

where $V(0)$ is the initial voltage.

We could apply a steady current to this membrane as well. Typically, currents are measured in terms of the area of membrane stimulated or current density. The units are typically microamperes per centimeter.

This is convenient since one micro-farad times one milli-volt per one milli-second gives one micro-ampere. Positive currents are inward relative to the cell and are called *depolarizing* while negative currents which are outward relative to the cell are called *hyperpolarizing.* Suppose we take $V_m = -70mV$ and apply a step of current to our spherical cell. Let's apply $2\mu A/cm^2$. What is the voltage as a function of time? The equation is

$$C_m \frac{dV}{dt} = -(V - V_m)/R_m + \bar{I} \tag{5}$$

whose solution is again easy to obtain if I is constant:

$$V(t) = (V_m + R_m\bar{I})(1 - e^{-t/\tau}) + V(0)e^{-t/tau} \tag{6}$$

Thus the voltage rises or falls to a new value dependent on the current density. The current, $\bar{I} = IA$ where I is the current density. Note that the final value of the potential is dependent on the current density and not the actual geometry of the cell since the final potential is $V_m + R_m\bar{I} = V_m + (R_M/A)IA = V_m + IR_M$. For our present example, the steady state voltage is

$$V_{ss} = -70mV + 1000 \times (1 \times 10^4\Omega - cm^2)(2 \times 10^{-6}Amp/cm^2) = -50mV.$$

Note the factor of 1000 is necessary to convert to millivolts.

HOMEWORK

1. Calculate R_m and C_m for a cylindrical cell with diameter of 10 microns and length of 50 microns. Ignore the area at the ends of the cylinder.
2. How much current is needed to raise the potential to -55 mV in the spherical cell example above?
3. Suppose that R_M is $20000\Omega - cm^2$. What is the time constant of the membrane.
4. Suppose that the spherical cell above is initially at rest. Write the equation for the voltage as a function of time if the current is stepped up to 10 $\mu A/cm^2$ for 20 msec and then set to 0 again. (HINT: Use (6) twice, once for the time when the stimulus is on. Then again, using the voltage at the end of the stimulus as initial voltage.) Sketch the voltage response to this current pulse.

4 Numerical solution of passive models

Once we get beyond a single compartment model, it is much easier to simulate the behavior rather than attempting to explicitly solve the differential equations that you derive. In particular, once that are more than 2 compartments and once channels and synapses are added, simulation is just about the only generally applicable tool for studying behavior. There are many simulation programs available and we will talk about some of them later in the term; notably GENESIS and NEURON, both of which are specifically designed for neural simulations. Both of these simulators solve differential equations, but their interface essentially removes the actual equations from you. We will use a general purpose differential equation solver in which we must explicitly provide the relevant equations. The simulator is called XPPAUT and runs on any UNIX system with X windows. A version that is similar but with some interface differences is avaliable for Windows 95/NT.

The first model we will simulate is the single compartment injected by a current (3)

$$C_M A \frac{dV}{dt} = A \frac{V_m - V}{R_M} + A\bar{I}(t)$$

where A is the area of the membrane compartment. We can divide this whole thing by A to get rid of it. We are interested in a scale of millivolts, milliseconds and picoamps. Dividing by AC_M we obtain:

$$\frac{dV}{dt} = (\frac{V_m - V}{R_M} + \bar{I}(t))/C_M.$$

We use the following values for the parameters: $R_M = 10000\Omega - cm^2$, $C_M = 1\mu F/cm^2$. The with units of milliseconds and millivolts, we can set $C_M = 1$ and obtain:

$$\frac{dV}{dt} = (1000\frac{V_m - V}{R_M} + \bar{I}(t))/C_M$$

where $\bar{I}(t)$ is measured in $\mu A/cm^2$. We can view the reciprocal of the resistance as a conductance measured in $Siemens/cm^2$. The factor of 1000 comes from the conversion to millivolts and from the factor of 10^{-6} from the capacitance. We typically measure the conductance, $g_M = 1/R_M$ in $\mu S/cm^2$ so that we finally obtain:

$$\frac{dV}{dt} = (g_M(V_m - V) + \bar{I}(t))/C_M$$

where $g_M = 10^3/R_M$ is the membrane conductance in $\mu S/cm^2$. All units are now in terms of millivolts, milliseconds, and microamps, microsiemens, microfarads per square centimeter.

4.1 Writing an ODE file

To simulate this in XPPAUT we must create an ODE file which has information such as the number of equations, the parameters, initial conditions, names of variables and function definitions. The following file does the trick:

```
# passive membrane with step function current: passive.ode
dV/dt = (1000*(E-V)/R_M + I_0*f(t))/C_M
V(0)=-70
# I in microamps/cm^2 C_m in microfarads/cm^2 R_M in Ohm cm^2 E in mV
# t in msecs
parameter R_M=10000, C_m=1, I_0=2, E=-70
parameter t_on=5, t_off=10
# define a pulse function
f(t)=heav(t_off-t)*heav(t-t_on)
# track the current
aux ibar=f(t)*I_0
done
```

There is little explanation needed except for the following points:

- `heav(t)` is the Heaviside step function which is 0 for $t < 0$ and 1 for $t > 0$. Thus $f(t)$ is a pulse function which turns on at $t = t_{on}$ and turns off at $t = t_{off}$.
- `V(0)=-70` is the initial condition.
- `aux` means that what follows is something that we want to plot but does not satisfy a differential equation.
- XPPAUT is case insensitive so upper and lower cases are synonymous.
- `#` means that what follows is a comment.
- `param ...` defines parameters
- `dV/dt = ...` tells XPPAUT that this is a differential equation
- `done` tells the parser the file is done.

Notes: (1) All the declarations at the beginning of each line can be abbreviated to their first letter; all others are ignored until a space is encountered. (2) Variables, functions, and parameters can have up to 9 letters. (3) There are at most 300 differential equations allowed, 200 parameters, and 50 functions.

4.2 Running the simulation

Create this file with your editor and fire up XPPAUT with the following command:

```
xpp passive.ode
```

where `passive.ode` is the file name. If the program typed in is OK, then a series of 7 windows will be created. If you are using TWM (the manager on an xterm or the NeXT) you must click where you want the windows. The seven windows are:

1. The main window with all of the commands
2. The parameter window with the names of the parameters and their current values
3. The initial data window with the variables and their current values
4. The delay window (ignore this for now)
5. The boundary condition window (ignore this too)
6. The equation window (lists the equations)
7. The data browser. This lets you look at the numbers and manipulate them like a spreadsheet.

(**NOTE.** Some Window managers (fvwm) produce dead windows instead of iconified windows. To resurrect these windows, iconify them manually and then uniconify them and they will spring back to life!) There are two windows that accept commands and several other windows that are for input and/or inform you about parameters, boundary conditions, and initial conditions. The main window is for most of the commands and the browser window is the "spreadsheet" for viewing, saving, and manipulating the numbers. The main things one wants to do are:

1. Integrating the equations and changing initial data. All of the commands in xpp have keyboard shortcuts so that you can avoid using the mouse. To change initial conditions and parameters, click in the appropriate window and change the value. When you are happy with the values, just click the OK button to tell XPP. You can also change initial conditions from the Command Window (the top line of the main window – thers is no analogue in Win95.) Similarly, you can click on the Parameters item in the main menu and type the name of the parameter you want to change and then give it a value. Type Enter a few times to exit this mode.

To run the simulation, click on the Initial Conds menu and then on Go, or type `I G`. (In Win95 click on Run Go or Ctrl G) The trajectory is invisible since the window only goes from -1 to 1. To get a bigger window, click on the "Window" bar and then on "Window" or type `W W`. A new window will appear in which you can specify the max and min of your axes. Click on OK when you are done and the data will be redrawn in the new window. There are two quicker ways to do it. Click on "X vs T" and choose V as the variable to plot versus time. The window will automatically be redrawn and fitted. Alternatively, use the "Window" command but then click on "Fit". (In Win95 use the Graphics View or Graphics Fit or Graphics XvsT).

2. Changing parameters. The parameters can be changed like the initial conditions by changing them in the parameter window. Another way to change parameters is to click on "Parameter" in the main window or type "P" the keyboard shortcut. Hit `<Enter>` repeatedly to exit this mode. Change some of the parameters and reintegrate.

3. Changing numerical parameters. Click on "nUmerics" or type "U" to get a new menu. The main items of interest are

- "Total" Clicking on this lets you set the total amount of time for the integration. The default is 20.
- "Dt" This is the time step for integrating the equations. Smaller steps take longer but are more accurate. The default is 0.05

- "Bounds" This sets the total magnitude that any trajectory can take. The integration is stopped if the bounds are exceeded. Increase it if you want; the default is 100.
- "Ncline control" This controls the grid for nullcline computation. Increase it for finer nullclines. The default is 40.
- "Method" This is the method of integration. The only ones of interest to you are:
  - Euler
  - Modified Euler
  - Runga Kutta
  - QualRK
  - Gear
  - CVode

  The first two are fast and inaccurate. The next two are more accurate and the last two are the most accurate and require additional input.
- "Esc-exit" This takes you back to the main menu.

In Win95 click on Numerics Int Params to get a window with most of the useful numerical parameters. There are others that may be of use; read the full doc for them. At this point you may want to run the full tutorial.

TO QUIT! click on File Quit Yes in X and Ctrl Q or File Quit in Win95.

HOMEWORK

In the compartmental model above, change the current stimulus to be a sinusoid with frequency of 40 Hz and plot the solution for 200 msec. Use `Dt=.2`. To do this, you will have to modify the ODE file. Please print out the ODE file and also make a copy of your solution. (Use the postscript option under graphics.) (Instead of editing the file, you can edit the right-hand sides, replacing $f(t)$ with a sinusoid, `sin(2*pi*t/25)`.

5 The passive cable equation

Information flows in the nervous system from the soma to the axon and then to the dendrites. In most models, the dendrites are regarded as being passive electrical cables. In this section, the cable equation is derived, steady state cable properties are studied and total input resistance of a cell is defined.

We will model the cable as a continuous piece of membrane that consists of a simple RC circuit coupled with an axial resistance that is determined by the properties of the axoplasm. Figure 2 shows a piece of a cable broken into small parts. From this figure, we obtain the following equations

$$C_m \frac{dV_j}{dt} = \frac{E - V_j}{R_m} + \frac{V_{j+1} - 2V_j + V_{j+1}}{R_a} \tag{7}$$

We have introduced a new quantity, R_a which is the axial resistance. This as you would guess depends on the geometry of the cable, in this case, the diameter, d and the length, ℓ. As with the membrane resistance, there is also a material constant, R_A associated with any given cable. This is measured in $\Omega - cm$. A typical value is $100\Omega - cm$. As anyone who has ever put a stereo will attest, the resistance along a cable is proportional to its length and inversely proportional to the cross-sectional area (the fatter the cable, the less resistance) thus we have the following (using our definitions above)

$$C_m = \pi d \ell C_M \tag{8}$$

$$R_m = \frac{R_M}{\pi d \ell} \tag{9}$$

$$R_a = \frac{\ell R_A}{\pi (d/2)^2} = \frac{4 \ell R_A}{\pi d^2} \tag{10}$$

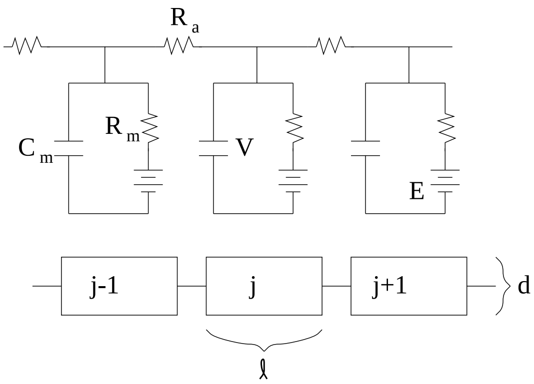

Figure 2: Cable broken up into discrete segments

We plug these into (7), let $x = j\ell$ define distance along the cable, and then take the limit as $\ell \to 0$ to obtain the continuum equation for the cable:

$$\pi d C_M \frac{\partial V(x,t)}{\partial t} = \pi d \frac{E - V(x,t)}{R_M} + \pi \frac{d^2}{4} \frac{\partial^2 V(x,t)}{\partial x^2}. \tag{11}$$

We multiply both sides by $R_M/\pi d$ and obtain the following equation:

$$\tau_m \frac{\partial V}{\partial t} = E - V + \lambda^2 \frac{\partial^2 V}{\partial x^2} \tag{12}$$

where τ_m is the time constant $R_M C_M$ and

$$\lambda = \sqrt{(d/4)R_M/R_A} \tag{13}$$

is called the space constant of the cable. The space constant depends on the diameter while the time constant depends only on the material constants. Using $R_M = 10000\Omega cm^2$ and $R_A = 100\Omega cm$ we obtain

$$\lambda = \sqrt{25d}$$

so if the dendrite has a diameter of, say, 10 microns, or 0.001 centimeters, the space constant is 0.07 centimeters or 0.7 mm. The space constant determines how quickly the potential decays down the cable.

An alternate derivation is given by Segev in the Book of GENESIS. The longitudinal current, I_i is given by the following:

$$\frac{1}{r_i} \frac{\partial V}{\partial x} = -I_i \tag{14}$$

where r_i is the *cytoplasmic resistivity* as resistance per unit length along the cable. This is just $4R_A/(\pi d^2)$.

5.1 Steady state and boundary conditions

To make life easier, we set $E = 0$. The solution to (12) depends on the initial spatial distribution of voltage and the conditions at the ends of the cable, *the boundary conditions.* We will consider either a finite cable of length l or a semi-infinite cable where one end goes to infinity. We will first look only at the steady state behavior of the cable. In this case, we drop the derivative with respect to t and obtain:

$$0 = \lambda^2 \frac{d^2 V}{dx^2} - V \tag{15}$$

whose general solution is one of the following forms:

$$\begin{aligned}
V(x) &= A_1 e^{-x/\lambda} + A_2 e^{x/\lambda} && (16)\\
V(x) &= B_1 \cosh((l-x)/\lambda) + B_2 \sinh((l-x)/\lambda) && (17)\\
V(x) &= C_1 \cosh(x/\lambda) + C_2 \sinh(x/\lambda) && (18)
\end{aligned}$$

We define the *input resistance* of a cable as the ratio of the steady state potential divided by the current injected.

5.1.1 Semi-infinite cable

In this case, we assume that at $x = 0$ the voltage is clamped to $V = V_0$. The boundedness of the voltage as $x \to \infty$ means that we must take

$$V(x) = V_0 e^{-x/\lambda} \tag{19}$$

It is now clear why λ is called a *space-constant*, it determines the voltage attenuation with distance.

Alternatively, we could demand that the current at $x = 0$ be specified as I_0. From (14) we see that

$$-I_0 = \frac{1}{r_i}\frac{dV}{dx}$$

and since $V(x) = V_0 e^{-x/\lambda}$ we get

$$V(x) = r_i I_0 \lambda e^{-x/\lambda}$$

The input resistance is the ratio of $V(0)/I_0$ is thus

$$R_\infty = r_i\lambda = (4R_A/(\pi d^2))\sqrt{(d/4)R_M/R_A} = \frac{2\sqrt{R_M R_A}}{\pi d^{3/2}} \tag{20}$$

The input conductance for the semi-infinite cable is thus

$$G_\infty = \frac{\pi d^{3/2}}{2\sqrt{R_M R_A}}$$

Note: It is often convenient to introduce the dimensionless space variable, $X = x/\lambda$ and the *electrotonic length* of the cable, $L = l/\lambda$. This gets rid of all the divisions by λ in the exponentials and hyperbolic functions.

5.1.2 Finite cable

There are a variety of possible end conditions we can apply to the cable. Among them are the (a) *sealed end* where no current can pass and so $dV/dx = 0$, (b) *short circuit* or *open end* where the voltage is clamped to 0, (c) *leaky ends* which is a mixture of the two, some current escapes but not an infinite amount. Let's revert to the dimensionless equations $X = x/\lambda$ and $L = l/\lambda$. Assume that the voltage at $X = 0$ is V_0. Then the general solution to the steady-state equation is:

$$V(X) = V_0 \frac{\cosh(L-X) + B_L \sinh(L-X)}{\cosh L + B_L \sinh L}$$

where B_L is an arbitrary constant. This general solution is equivalent to asserting that the boundary condition at $X = 0$ is V_0 and that at $X = L$

$$B_L V(L) + \frac{dV}{dX}(L) = 0$$

The free parameter, B_L is the ratio of the input conductance for the cable, G_L to that of the semi-infinite cable, G_∞. That is, $B_L = G_L/G_\infty$.

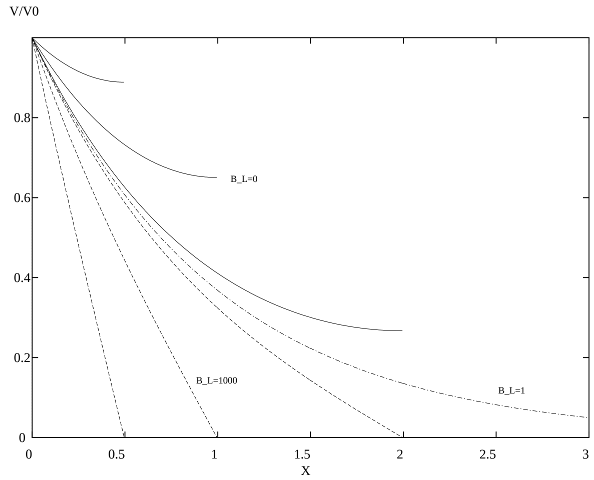

Figure 3: Steady state voltages for a variety of electrotonic lengths and for different end conditions

For example, if we want the sealed end condition at $X = L$ we take $B_L = 0$ so that

$$V(X) = V_0 \frac{\cosh(L-X)}{\cosh L}$$

If we want the open end conditions, we take $B_L = \infty$ so that

$$V(X) = V_0 \frac{\sinh(L-X)}{\sinh L}$$

If we choose $B_L = 1$ then

$$V(X) = V_0 e^{-X}$$

which is precisely the solution to the semi-infinite cable. In figure 3 we plot the steady state voltages for a variety of different cables and at different electronic lengths. These could be solved analytically, but the plots were in fact generated by using XPPAUT.

5.1.3 Solving boundary value problems with XPPAUT

We want to solve:

$$\begin{aligned} \frac{d^2V}{dX^2} - V &= 0 \\ V(0) &= V_0 \\ B_L V(L) + \frac{dV}{dX}(L) &= 0 \end{aligned}$$

Since XPPAUT can only solve systems of first order equations, we rewrite this as a system of two first order equations:

$$\begin{aligned} \frac{dV}{dX} &= V_X \\ \frac{dV_X}{dX} &= V \\ V(0) &= V_0 \\ B_L V(L) + V_X(L) &= 0 \end{aligned}$$

which translates into the following ODE file

```
# steady state cable  sscab.ode
dv/dt = vx
dvx/dt = v
# boundary condition at left end:
bndry v-1
# boundary condition at right end:
bndry bl*v'+vx'
#
parameter bl=1
done
```

Since XPPAUT use t as its independent variable, we have changed the name of "x" to "t". Boundary conditions are set by using the declaration, `bndry`. XPPAUT will try to set these to zero. Primes mean to evaluate the variable at the end of the integration while unprimed variables evaluate at the beginning. To generate these picture, I just set the total amount for the integration to either of 0.5, 1, 2, 3, corresponding to different electrotonic distances. Then I used the `Bndry (N)o show` combination to solve the equations. I used the `Graphics Freeze Freeze` combination to make a permanent copy of the given curve. I repeated this for each curve and used the `Text Text` option to draw the text on the curves and the `View 2d` combination to set the axes and labels.

HOMEWORK

1. What is the electrotonic length for a cable with $R_M = 20000\Omega cm^2, R_A = 75\Omega cm, d = 8\mu, C_M = 1\mu F/cm^2$, $\ell = 1mm$
2. Find the input resistance for the semi-infinite cable with the above parameters
3. Solve the steady state voltages for $B_L = 0, .25, 1, 10, 100$ on a cable with electrotonic length 3 using XPPAUT.

6 Equivalent Cylinders

Recall that the input conductance for the semi-infinite cable is given by:

$$G_\infty = \frac{\pi d^{3/2}}{2\sqrt{R_M R_A}}$$

Recall also that the space constant is

$$\lambda = \sqrt{(d/4)R_M/R_A}$$

The *electrotonic length* of a cable of physical length, ℓ is $L \equiv \ell/\lambda$. The input conductance at $X = 0$ for a finite cable of electrotonic length, L with a sealed end at $X = L$ is just

$$G_{in} = G_\infty \tanh(L).$$

There are many other possibilities, but the sealed end is the most common.

The idea that Rall discovered is that if the dendrites were related in a particular fashion, then the whole thing could be collapsed to a single cylindrical cable. This is called the *equivalent cylinder.* Consider the tree shown in the figure 4. Suppose that the branches, 0,1 and 2 have the same membrane resistivities, R_M and R_A. Assume that the daughter branches, 1 and 2, have the same electrotonic length, that is, their physical length divided by their space constants (which of course depend on their diameters) are all the same. (For example, if both have equal diameters and are the same physical length.) Also, assume that the two have the same end conditions, eg sealed. We want to know if it is possible to combine the branches of the dendrite into a single equivalent cylinder. The key is that we must avoid impedence mismatches. Thus, to combine the dendrites, 1 and 2 with 0, we require:

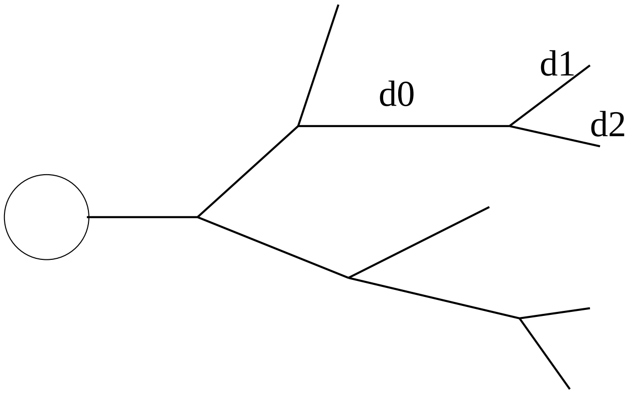

Figure 4: Dendritic tree

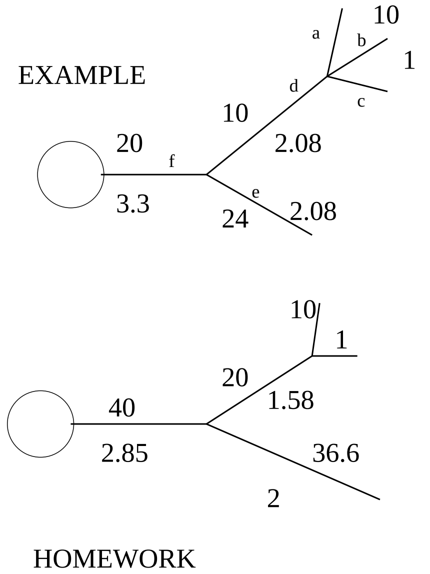

Figure 5: Example and exercise

1. All the ends are the same conditions, sealed.
2. The electrotonic lengths of 1 and 2 are the same
3. The diameters match as follows:

$$d_0^{\frac{3}{2}} = d_1^{\frac{3}{2}} + d_2^{\frac{3}{2}}$$

It is clear that this last condition is a consequence of the impedance of the parent branch equalling that of the sum of the daughters. If these conditions hold then 0,1,and 2 can be collapsed into a single cylinder with diameter equal to that of dendrite 0 and total electrotonic length as the sum of 1 and 0 (or equivalently 2 and 0.)

Example

In the above figure, we depict a dendritic tree consisting of several branches with their lengths and diameters in microns. (a) Can they be reduced to an equivalent cylinder (b) What is the electrotonic length (c) What is the input conductance. Assume sealed ends for all terminal dendrites and assume that $R_M = 2000\Omega\text{cm}^2$ and that $R_A = 60\Omega\text{cm}$.

Answer.

$$d_a^{3/2} + d_b^{3/2} + d_c^{3/2} = 1 + 1 + 1 = 3 = 2.08^{3/2} = d_d^{3/2}$$

$$d_d^{3/2} + d_e^{3/2} = 3 + 3 = 6 = 3.3^{3/2} = d_f^{3/2}$$

so the 3/2 rule is obeyed. Clearly a,b,c are all the same electrotonic length. The space constants are:

$$\lambda_a = \lambda_b = \lambda_c = \sqrt{d_a R_M / 4R_A} = 289\mu$$

$$\lambda_d = \lambda_e = \sqrt{d_e R_M / 4R_A} = 416\mu$$

$$\lambda_f = \sqrt{d_f R_M / 4R_A} = 524\mu$$

Thus, the total electrotonic length of abc with d is

$$L_{abcd} = \frac{\ell_a}{\lambda_a} + \frac{\ell_d}{\lambda_d} = \frac{10}{289} + \frac{10}{416} = .0586$$

$$L_e = \frac{\ell_e}{\lambda_e} = \frac{24}{416} = .0576$$

which are close enough to be considered equal (2% difference). Thus, we can combine the whole thing into an equivalent cylinder. The total electrotonic length is then:

$$L = L_f + L_e = L_f + L_{abcd} = \frac{\ell_f}{\lambda_f} + L_e = 0.096 \approx 0.1$$

Finally, the input conductance is

$$G_{in} = G_\infty \tanh(L) = \frac{\pi d^{3/2}}{2\sqrt{R_M R_A}} \tanh(L)$$

which is

$$G_{in} = \frac{\tanh(0.1)(3.14159)(3.3 \times 10^{-4})^{3/2}}{2\sqrt{2000 \times 60}} = 2.7 \times 10^{-9}\mathrm{S}$$

Exercise

Apply the same analysis to the bottom dendrite in the figure.

7 Exploring transients in the passive cable

Starting from the cable equation (12) we can rescale time by the membrane time constant, τ_m and space by the space constant, λ and shift the voltage so that $V = 0$ is rest. With inputs, $s(t,x)$ the full equation is:

$$\frac{\partial V}{\partial T} = -V(X,T) + \frac{\partial^2 V}{\partial T^2} + s(t,x).$$

So far, we have only considered the steady state effects of inputs and the role of the cable in decrementing the steady state inputs. However, the temporal filtering of dendrites is also very important. Dendrites can produce effective delays and thus can have far reaching consequences for synchronization and other temporal coding aspects. It is possible to mathematically address this question for a variety of cable types. Since this is beyond what we have time to do, I will instead approach the question of dendritic transients computationally. Let L be the total electrotonic length of the cable and assume sealed ends. We will break the cable into 21 compartments labeled 0 to 20. We will explore the effects of a synaptic current of the form:

$$a(t/\tau)e^{-t/\tau}$$

where τ is the time constant of the synapse. Since this is a linear problem, the actual amplitude of the input doesn't matter and what we will be concerned with is the relative amplitudes, the time to peak of the inputs relative to the stimulus site, and the rate of decay of the inputs.

The ODE file that we will use is

```
# a 20 compartment mode with a synaptic input and sealed conditions
# [x0-.5,x0+.5] is position of input
s(t,x)=heav(x+.5-x0)*heav(x0+.5-x)*amp*t*exp(-t/tau)/tau
v0'=-v0+(v1-v0)/(dx^2)+s(t,0)
v[1..19]'=-v[j]+(v[j+1]-2*v[j]+v[j-1])/(dx^2) + s(t,[j])
v20'=-v20+(v19-v20)/(dx^2) + s(t,20)
dx=L/20
par tau=1,amp=5,x0=0,L=2
@ total=20,meth=cvode,toler=1e-5,atoler=1e-4,dt=.1,yhi=.2,ylo=0
@ xhi=20,yp=v0
done
```

which is a "discretization" of the continuous model. There are several parameters that are useful. The parameter `x0` is the position of the input and corresponds to the compartment number,0-20. The parameter `L` is the electrotonic length and `tau` is the decay constant of the synaptic input. (Note that this is relative to the membrane time constant since the time scale is relative to the membrane time constant τ_m. Thus, `tau=.1` means that the time constant of the synapse is ten times faster than the membrane time constant.)

HOMEWORK

We will call compartment 0 the soma. So that `x0` is the distance of the input relative to the soma. Here are some things to look at:

1. Sketch the potential at the soma for the synaptic input at compartments 0, 5, 10, and 20. Determine the following parameters, the time to peak, the amplitude of the peak, and the time to decay to half the peak voltage. How do the peak amplitudes depend on distance? How about the time to peak? Does the peak appear to decay slower or faster for more distant inputs?

2. Set the total integration time to 50 and the length of the x-axis to be 50. Put the synapse at `x0=5` and now look at the following three sets of parameters. Set `tau=1,amp=5` and solve the equations. Repeat with `tau=.1, amp=20`. Repeat with `tau=10, amp=2`. Observe that the decay rate of the input for the two smaller values of `tau` is roughly the same. But the decay rate for the slower synapse is much greater. Explain why the two faster synapses decay at about the same rate. (Hint: For the faster synapses, what dominates the decay of the synapse or the membrane decay rate?)