

Transient Solutions, Equivalent cylinder, Insights from Passive Models

5-1. Up to this point we have considered solutions to the steady-state cable equation. Now we move on to the transient case. We will consider the non-dimensional form of the cable equation

in this discussion or $\frac{\partial^2 V}{\partial X^2} = V + \frac{\partial V}{\partial T}$ where $X=x/\lambda$ and $T=t/\tau$. The classic means to solve this

equation is the method of separation of variables. The assumption is that the solution is of the form $V(x,t) = X(x) T(t)$ or the product of a function only of x with a separate function only of t .

If we substitute this into the cable equation we get $X''T = XT + XT'$ since the second derivative of V with respect to x equals the second derivative of X with respect to x times T , etc. We

divide this by XT and get $\frac{X''}{X} = 1 + \frac{T'}{T} = -\alpha^2$. You might wonder where the $-\alpha^2$ came from.

This term is called a separation constant. The first expression on the left is only a function of X and the second expression is only a function of T . The only way a function of X can equal a function of T is if the functions are equal to a constant. We choose the separation constant to be $-\alpha^2$ because we have some idea of where this solution will end up. α^2 is positive and $-\alpha^2$ will guarantee a negative constant. We want a negative constant because the solution as a function of time will blow up if the solution is positive. We don't want that. Also α^2 means we will not have a square root sign in our solution.

Since the function of X and the function of T are both equal to this separation constant we have

two equations: $X'' = -\alpha^2 X$. The first requires a function whose second derivative is the
 $T' = -(1 + \alpha^2)T$

negative of itself (multiplied by a constant) and the second requires a function whose first derivative returns the function, again multiplied by a constant. The second case we have seen before. This is just the exponential function. The first case is new. Previously, when we looked at the steady-state solutions, we wanted a function whose second derivative returned the function, but without the minus sign. We used cosh and sinh. However, here we have a minus sign. Functions that work here are cos and sin, the standard trig functions. Our solution

becomes $V(X, T) = (A \sin(\alpha X) + B \cos(\alpha X)) \exp\left[-(1 + \alpha^2)T\right]$.

As with the steady-state equation, we use boundary conditions to evaluate the arbitrary constants, only here we must also use the initial condition. We have 3 arbitrary constants. We have 2 boundaries and 1 initial condition.

5-2. For the boundary conditions, let's use sealed end conditions at both ends. What are these

boundary conditions? They are: $-\frac{1}{\lambda r_i} \frac{\partial V}{\partial X} \Big|_{X=0} = 0$. Note that there is an extra λ on the left side
 $-\frac{1}{\lambda r_i} \frac{\partial V}{\partial X} \Big|_{X=L} = 0$

of these conditions because we are using the non-dimensional form of the equation with X and T instead of x and t .

What is the derivative with respect to X here? The derivative of $\sin(x)$ is $\cos(x) dx$ and the derivative of $\cos(x)$ is $-\sin(x) dx$. We get:

$$\frac{\partial V(X,T)}{\partial X} = (\alpha A \cos(\alpha X) - \alpha B \sin(\alpha X)) \exp\left[-(1 + \alpha^2)T\right]$$

For this derivative to equal 0 at $X=0$ implies that $A=0$ since $\sin(0)=0$

With $A=0$, this derivative will equal 0 at $X=L$ only if $\sin(\alpha L) = 0$.

We know that \sin is a periodic function whose value is 0 at $0, \pi, 2\pi, 3\pi$, etc.

So $\alpha L = n\pi$ where $n=0, 1, 2$, etc. Or $\alpha = n\pi/L$

So we have

$$V(X,T) = \sum_{n=0}^{\infty} B_n \cos\left(\frac{n\pi X}{L}\right) \exp\left[-\left(1 + (n\pi/L)^2\right)T\right]$$

Now the B_n will still have to be determined from the initial conditions $V(X,0)$

The importance of this solution is that the voltage decay has an infinite number of time constants. The solution for an isopotential cell or sphere had only one time constant, the membrane time constant. Here there are an infinite number. Now the coefficients of most of these time constants are small and the fastest time constants won't contribute much to the signal. However these time constants exist and are the reason why charging and decay are both faster in a cylinder than in an isopotential cell.

Recall that τ_m is the time voltage decays to $1/e$ of its initial value in an isopotential sphere. The decay is faster in a cylinder because of these extra "equalizing" time constants.

When $n=0$ the exponential part of the solution is just $\exp(-t/\tau_0)$. $\tau_0 = \tau_m = R_m C_m$, the membrane time constant. For $n>0$ the coefficient of t in the exponential term is $\left[1 + (n\pi/L)^2\right]/\tau_0$ where again we have $\tau_0 = \tau_m$. We can define the "equalizing" time constants as

$$1/\tau_n = \left[1 + (n\pi/L)^2\right]/\tau_0 \text{ or } \tau_n = \tau_0 / \left[1 + (n\pi/L)^2\right]. \text{ Then the solution is } V(x,t) = \sum_{n=0}^{\infty} C_n e^{-t/\tau_n}$$

This solution, given by Rall in 1969, replaces the $B_n \cos$ term in the previous solution with C_n . Also we have reverted back to the solution with real x and t . The C_n will depend on the initial conditions.

The importance of this solution is easily demonstrated. If one applies a brief or sustained current and then records the voltage decay once this current is turned off, then this voltage decay is described by $C_0 \exp(-t/\tau_0) + C_1 \exp(-t/\tau_1) + \dots$. The coefficients and time constants can be estimated from the experimental voltage trace by standard curve fitting procedures. We are particularly interested in the time constants, because, we can rearrange the expression above to

$$\text{get } L = \frac{\pi}{\sqrt{\tau_0/\tau_1 - 1}}. \text{ Thus if we have } \tau_0 \text{ and } \tau_1 \text{ we can get an estimate of the cell's electrotonic}$$

length $L = \ell/\lambda$.

Estimating electrotonic length in this way was very important before morphological reconstructions started to be done, because it gave us an estimate of the electrotonic structure of a cell.

5-3. The procedure outlined above could theoretically be used to compute the voltage transient in a cell, but already we see that the mathematical solution will be messy and will involve infinite sums.

Another approach for obtaining the transient solution is with Laplace Transform techniques. The advantage of Laplace Transform techniques is that the PDE is transformed into an ODE in the

Laplace domain. That is $\frac{\partial^2 V}{\partial X^2} = V + \frac{\partial V}{\partial T}$ becomes $\frac{\partial^2 W}{\partial X^2} = W(1+s) - V(x,0)$

where W is the Laplace transform of V. In the dimensional form this becomes

$\lambda^2 \frac{\partial^2 W}{\partial x^2} = W(1+\tau s) - V(x,0)$. If we assume $V(x,0)=0$ or the cell is at rest everywhere, then a solution to this equation is

$W(x,s) = A(s)\cosh(\gamma(\ell-x)) + B(s)\sinh(\gamma(\ell-x))$ where $\gamma = \frac{\sqrt{1+\tau s}}{\lambda}$. If we express A(s) and B(s) in terms of the voltage in the Laplace domain at $x=0$ and $x=\ell$, $W(0,s)$ and $W(\ell,s)$ then we have

$$W(x,s) = W(\ell,s)\cosh(\gamma(\ell-x)) + \frac{W(0,s) - W(\ell,s)\cosh(\gamma\ell)}{\sinh(\gamma\ell)}\sinh(\gamma(\ell-x))$$

5-4. To determine $W(0,s)$ and $W(\ell,s)$ we apply boundary conditions of sealed end at $x=\ell$ and current input at $x=0$. The sealed end condition at $x=\ell$ gives

$$-\frac{1}{r_i} \frac{\partial W}{\partial x} \Big|_{x=\ell} = 0 \Rightarrow \frac{\gamma}{r_i} \frac{W(0,s) - W(\ell,s)\cosh(\gamma\ell)}{\sinh(\gamma\ell)} = 0 \quad \text{and the current condition at } x=0 \text{ gives}$$

$$-\frac{1}{r_i} \frac{\partial W}{\partial x} \Big|_{x=0} = I(t) \Rightarrow \frac{W(0,s)}{\tanh(\gamma\ell)} - \frac{W(\ell,s)}{\sinh(\gamma\ell)} = \frac{r_i}{\gamma} \hat{I}(s) \quad \text{where } \hat{I}(s) \text{ is the Laplace transform of } I(t)$$

This is a system of 2 equations in 2 unknowns $W(0,s)$ and $W(\ell,s)$ which is easily solved. However the hard part then is inverting back from the Laplace domain to the time domain and this is usually done numerically.

The branched case can be solved in the Laplace transform domain in a manner similar to how the steady-state system was solved back in OH 4-6. This gets exceptionally messy. For more details see Butz and Cowan Biophys J. 1974; Horwitz Biophys. J. 1981, 1983 or Holmes Biol. Cybern. 1986.

5-5. Clearly these solutions are complicated. Is there a way to simplify the mathematics? In particular is there a way to simplify a branched structure to a cable? Well, it turns out that this is possible. The procedure for this leads to Rall's EQUIVALENT CYLINDER MODEL.

We will motivate how this works. Consider a cable that branches into two cables. The boundary condition of the original cable is a leaky end with a leak conductance G_L which is equal to the sum of the input conductances of the two daughter cables $G_1 + G_2$ as we saw before. Can we construct a cable having input conductance of $G_1 + G_2$ but also having the same diameter as the parent cable?

Recall the input conductance for a finite cylinder

$$G_N = G_\infty \tanh(\ell / \lambda) = \frac{\tanh(\ell / \lambda) d^{3/2}}{(2/\pi) \sqrt{R_m R_a}} \quad (\text{Note before we saw } R_N. \quad G_N = 1/R_N)$$

Then the sum of the input conductances of the two daughter cables is

$$G_{N1} + G_{N2} = \frac{\pi}{2\sqrt{R_m R_a}} \left\{ \tanh\left(\frac{\ell_1}{\lambda_1}\right) d_1^{3/2} + \tanh\left(\frac{\ell_2}{\lambda_2}\right) d_2^{3/2} \right\}.$$

The input conductance of a single cable G_3 would be

$$G_{N3} = \frac{\pi}{2\sqrt{R_m R_a}} \left\{ \tanh\left(\frac{\ell_3}{\lambda_3}\right) d_3^{3/2} \right\}$$

If the two cables have the same input conductance as a single cable, then $G_{N1} + G_{N2} = G_{N3}$. When does this happen?

Let's suppose that R_m and R_a are the same in all cylinders, and also suppose that the electrotonic lengths of the cylinders is also the same, that is, $\ell_1/\lambda_1 = \ell_2/\lambda_2 = \ell_3/\lambda_3$. Then $G_{N1} + G_{N2} = G_{N3}$ when $d_1^{3/2} + d_2^{3/2} = d_3^{3/2}$. This is called the "3/2 rule".

So we can construct a single cable equivalent to two cables in input conductance that also has the same diameter as the parent cable if the above assumptions are satisfied, the "3/2 rule" is satisfied and d_3 equals the parent cable diameter. So we can replace the two cables with one cable.

5-6. This discussion was designed to motivate what Rall proved, which is that a branched dendritic tree is equivalent mathematically to a cylinder if the following conditions are satisfied:

- 1) R_m and R_a are the same in all branches
- 2) All terminal branches end with the same boundary condition (sealed end)
- 3) All terminal branches end at the same electrotonic distance, L from $x=0$ ($L = \sum \ell_i / \lambda_i$ is the same for all paths from $x=0$ to all tips)
- 4) At every branch point $d_{\text{parent}}^{3/2} = \sum d_{\text{children}}^{3/2}$
- 5) Any dendritic input must be delivered proportionally to all branches at a given electrotonic distance.

Do dendritic trees satisfy these constraints? Which do you think are most likely to be violated? Clearly 5) is problematic for inputs. Inputs can occur at a variety of locations. It might be surprising to learn that 4) is satisfied in many trees, but also not in others. 3) is rarely satisfied. Clearly this assumption is violated in pyramidal cells with long apical dendrites and short basilar dendrites. Even in motoneurons that might appear at first glance to be equivalent cylinders, branches drop out distally, making a cable with constant diameter early followed by tapering the more appropriate representation.

Is there any reason why the $3/2$ rule should be satisfied? If it is there is impedance matching at branch points and no possible “reflections”. Voltage attenuation in the soma to distal direction proceeds smoothly. If the $3/2$ rule is not satisfied, then there are abrupt changes in attenuation at the branch point in the soma to distal direction. If daughter diameters are thinner than the $3/2$ rule then voltage attenuation will be less steep before the branch point and more steep after the branch point than would be the case if the $3/2$ rule were satisfied. If daughter diameters are thicker than the $3/2$ rule, the opposite occurs. Voltage attenuation will be steeper before the branch point and less steep after the branch point than when the $3/2$ rule is satisfied. This might have important implications for the relative effectiveness of inhibition delivered at the soma for changing the voltage at distances away from the soma.

5-7. Here we illustrate collapsing a tree into a cylinder for analysis. Clearly the collapsing is not exact in this case, but it is a useful approximation.

5-8. So what are some insights from passive models?

1) Steady-state attenuation is given by the space constant only for infinite cylinders. The boundary conditions matter for finite length cables. (OH 3-5)

2) Voltage attenuation into a sub-tree depends on how much the sub-tree resembles a “sealed end” or a “short circuit” condition (OH 4-7)

3) Voltage attenuation is asymmetric. Attenuation is steep in the dendrite to soma direction and shallow in the soma to dendrite direction. This is a consequence of the relative input resistances at proximal and distal locations and differences in the perceived boundary conditions by currents flowing in the two directions.

3a) There is reciprocity in the voltage response. The term reciprocity comes from engineering. Here we mean that the response at location 1 due to input at location 2 is the same as the response at location 2 due to input at location 1. To be clear, the voltage responses at the two input sites are very different. However the paths between the sites face the same conditions.

3b) Voltage attenuation for transient inputs is much greater than the steady-state attenuation. However, the attenuation of the integral of the transient response equals the steady-state attenuation. So despite the steep attenuation in transient inputs, much of the current still makes its way to the soma to make a contribution there.

4) To a first approximation, dendrites can be modeled as an equivalent cylinder

5) Electrotonic length, L of a cylinder can be obtained from experimental estimates of the first two time constants in a voltage transient, τ_0 and τ_1 .

Regarding this latter point we have not discussed what the time constants mean in a branched structure that does not follow equivalent cylinder constraints. It turns out that the time constants have a different interpretation (but still are “equalizing” time constants in that charge is equalized according to these time constants). It turns out that τ_1 represents charge equalization between the longest tip to tip path in the cell instead of along the path from the soma to the tips when the cell is not an equivalent cylinder. This can cause errors in the estimates of L with the formula based on the equivalent cylinder.