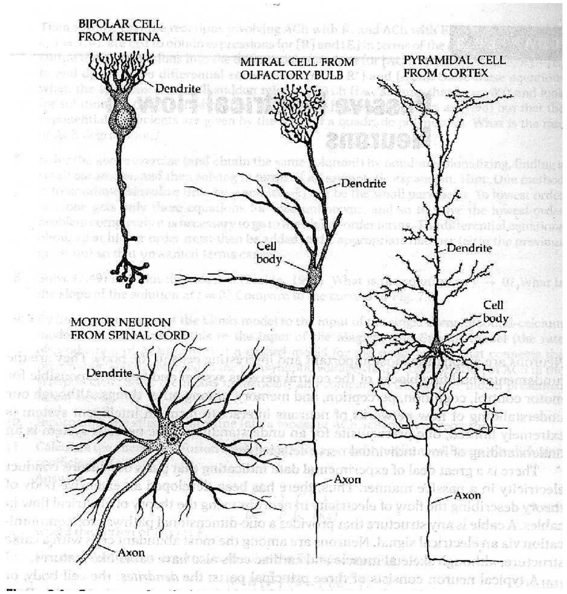
The cable equation A.K.A. the monodomain model

Neurons



Electric flow in neurons

The neuron consists of three parts:

- Dendrite-tree, the “input stage” of the neuron, converges on the soma.
- Soma, the cell body, contain the “normal” cellular functions
- Axon, the output of the neuron, may be branched. Synapses at the ends are connected to neighboring dendrites.

The axon has an excitable membrane, gives rise to active conduction. Will first look at conduction in the dentrites, passive conduction.

The cable equation, 4.1

The cell typically has a potential gradient along its length. Radial components will be ignored.

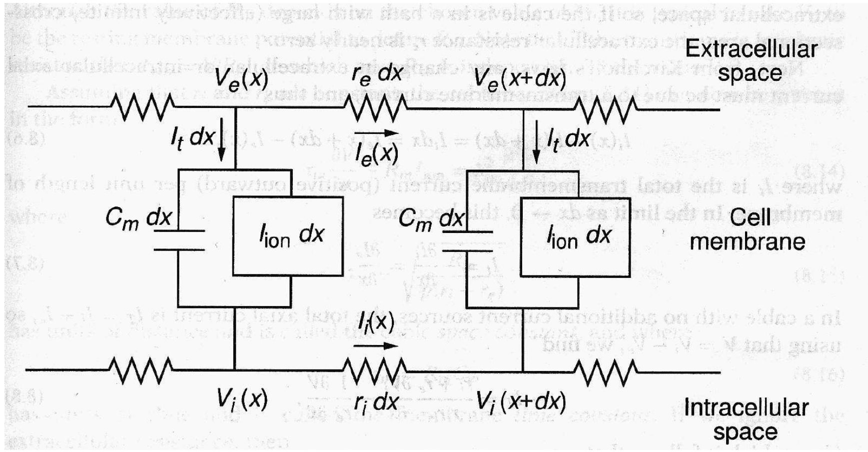
Notation:

V_i and V_e are intra- and extra cellular potential
I_i and I_e are intra- and extra cellular (axial) current
r_i and r_e are intra- and extra cellular resistance per unit length

$$r_i = \frac{R_c}{A_i}$$

where R_c is the cytoplasmic resistivity and A_i is the cross sectional area of the cable.

Discrete cable



Ohmic resistance assumed:

$$V_i(x+\Delta x) - V_i(x) = -I_i(x) r_i \Delta x$$

$$V_e(x+\Delta x) - V_e(x) = -I_e(x) r_e \Delta x$$

In the limit:

$$I_i = -\frac{1}{r_i}\frac{\partial V_i}{\partial x} \quad \text{and} \quad I_e = -\frac{1}{r_e}\frac{\partial V_e}{\partial x}$$

Conservation of current yields:

$$I_i(x) - I_i(x+\Delta x) = -(I_e(x) - I_e(x+\Delta x)) = I_t \Delta x \qquad (1)$$

where I_t is transmembrane current, per unit length. In the limit (1) yields:

$$I_t = -\frac{\partial I_i}{\partial x} = \frac{\partial I_e}{\partial x}$$

We would like to express I_t in terms of V.

$$\frac{1}{r_e}\frac{\partial^2 V_e}{\partial x^2} = -\frac{1}{r_i}\frac{\partial^2 V_i}{\partial x^2} = -\frac{1}{r_i}\left(\frac{\partial^2 V}{\partial x^2} + \frac{\partial^2 V_e}{\partial x^2}\right)$$

$$\left(\frac{1}{r_e} + \frac{1}{r_i}\right)\frac{\partial^2 V_e}{\partial x^2} = -\frac{1}{r_i}\frac{\partial^2 V}{\partial x^2}$$

cont.

$$\left(\frac{1}{r_e} + \frac{1}{r_i}\right)\frac{\partial^2 V_e}{\partial x^2} = -\frac{1}{r_i}\frac{\partial^2 V}{\partial x^2}$$

$$\frac{\partial^2 V_e}{\partial x^2} = -\frac{\frac{1}{r_i}}{\frac{1}{r_e} + \frac{1}{r_i}}\frac{\partial^2 V}{\partial x^2} = -\frac{r_e}{r_e + r_i}\frac{\partial^2 V}{\partial x^2}$$

so

$$I_t = \frac{\partial I_e}{\partial x} = -\frac{1}{r_e}\frac{\partial^2 V_e}{\partial x^2} = \frac{1}{r_e + r_i}\frac{\partial^2 V}{\partial x^2}$$

From the membrane model previously derived we have

$$I_t = p(C_m \frac{\partial V}{\partial t} + I_{\text{ion}})$$

where p is the circumference of the cable. The total expression will be in Ampere/meter.

The total 1D cable model is then:

$$p(C_m \frac{\partial V}{\partial t} + I_{\text{ion}}(V)) = (\frac{1}{r_e + r_i} \frac{\partial^2 V}{\partial x^2})$$

Dimensionless form

We can scale the variables to reduce the number of parameters. Defines a membrane resistance:

$$\frac{1}{R_m} = \frac{\Delta I_{\text{ion}}}{\Delta V}(V_0)$$

where V_0 is the resting potential. Multiplication with R_m

$$C_m R_m \frac{\partial V}{\partial t} + R_m I_{\text{ion}} = \frac{R_m}{p(r_i + r_e)} \frac{\partial^2 V}{\partial x^2}$$

Here we have assumed r_i and r_e constant.

Defining $f = -R_m I_{\text{ion}}$, $\tau_m = C_m R_m$ (time constant) and $\lambda_m^2 = R_m/(p(r_i + r_e))$ (space constant squared) we can write

$$\tau_m \frac{\partial V}{\partial t} - f = \lambda_m^2 \frac{\partial^2 V}{\partial x^2} \qquad (2)$$

Introduces the dimensionless variables:

$$T = t/\tau_m \quad \text{and} \quad X = x/\lambda_m$$

We can then write:

$$\frac{\partial V}{\partial T} = f + \frac{\partial^2 V}{\partial X^2} \qquad (3)$$

A solution $\hat{V}(T, X)$ of (3) will imply that $V(t, x) = \hat{V}(t/\tau_m, x/\lambda_m)$ will satisfy (2).

The reaction term, 4.2

The form of f depends on the cell type we want to study.

For the axon $I_{\text{ion}}(m, n, h, V)$ of the HH-model is a good candidate.

For the dendrite, which is non-excitable, a linear resistance model is good. Shift V so $V = 0$ is the resting potential:

$$\frac{\partial V}{\partial T} = \frac{\partial^2 V}{\partial X^2} - V$$

Need boundary and initial values. Initially at rest:

$$V(X, 0) = 0$$

Boundary conditions

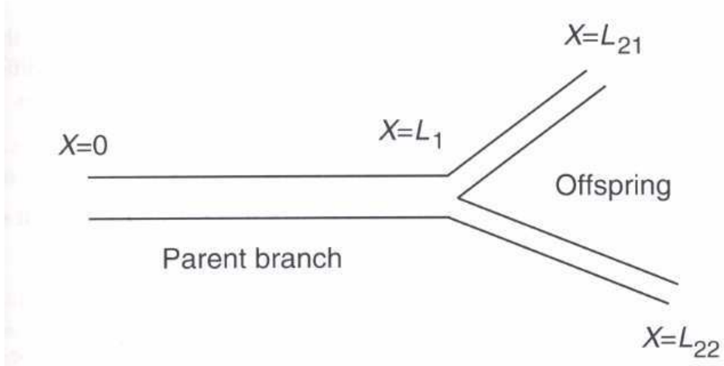
Types of boundary conditions:

- Dirichlet: $V(x_b, T) = V_b$, voltage clamp.
- Neumann: $\frac{\partial V}{\partial X} = -r_i \lambda_m I$, current injection.

Justification:

$$\frac{\partial V_i}{\partial x} = -r_i I_i \Rightarrow \frac{\partial V}{\partial x} - \frac{\partial V_e}{\partial x} = -r_i I_i \overset{r_e=0}{\Longrightarrow} \frac{\partial V}{\partial x} = -r_i I_i$$

Branching structures, 4.2.3



Linear cable equation used in each branch:

$$\frac{\partial V}{\partial T} = \frac{\partial^2 V}{\partial X^2} - V$$

General solution in the steady state:

$$V = Ae^{-X} + Be^{X}$$

Two parameters per branch, six in total to determine.
Three taken from boundary conditions: current injection in X=0 and voltage clamp at $X = L_{21}$ and $X = L_{22}$.
Two more from continuity of voltage:

$$V_1(L_1) = V_{21}(L_1) = V_{22}(L_1)$$

The sixth condition is obtained from continuity of current:

$$\frac{1}{R_{1,in}} \frac{dV_1}{dX} = \frac{1}{R_{21,in}} \frac{dV_{21}}{dX} + \frac{1}{R_{22,in}} \frac{dV_{22}}{dX}$$

where the input resistance is

$$R_{in} = \lambda_m r_i = \sqrt{\frac{R_m}{pr_i} \frac{R_c}{A_i}}$$

Assuming a circular crossection:

$$R_{in} = \frac{2}{\pi} \sqrt{R_m R_c} d^{-3/2}$$

If R_m and R_c is not changing the condition becomes:

$$d_1^{3/2} \frac{dV_1}{dX} = d_{21}^{3/2} \frac{dV_{21}}{dX} + d_{22}^{3/2} \frac{dV_{22}}{dX}$$

Equivalent cylinders

With certain assumptions the dendrite tree can be modelled with a single cable equation. $L_{21} = L_{22}$, and they have the same boundary conditions:
This gives $V_{21} = V_{22}$ and thus:

$$d_1^{3/2}\frac{dV_1}{dX} = (d_{21}^{3/2} + d_{22}^{3/2})\frac{dV_{21}}{dX}$$

The critcal assumption is then:

$$d_1^{3/2} = d_{21}^{3/2} + d_{22}^{3/2}$$

If so, then we can use a single equation for the whole system.
Similar arguments can be made for more complex branching.

Wave propagtion in Excitable Systems, 6

The bistable equation

$$\frac{\partial V}{\partial t} = \frac{\partial^2 V}{\partial x^2} + f(V) \qquad (4)$$

Where $f(V)$ has three zeros, say at $V = 0, \alpha, 1$. For example:

$$f(V) = aV(V-1)(\alpha - V)$$

The solution will be a travelling wave.

Traveling wave

Assume a solution on the form:

$$V(x,t) = U(x+ct) = U(\xi)$$

Inserting this into the bistable equation yields a 2. order ODE:

$$U_{\xi\xi} - cU_\xi + f(U) = 0$$

Or equivalently a system of two 1. order ODEs:

$$U_\xi = W$$
$$W_\xi = cW - f(U)$$

We seek solutions where

$$(U, U_\xi) \overset{\xi\to-\infty}{\longrightarrow} (0,0), \quad \text{and} \quad (U, U_\xi) \overset{\xi\to\infty}{\longrightarrow} (1,0).$$

Traveling wave

In general not possible to solve the system analytically.
We can say something about the sign of c, e.g. the direction of propagation. Multiplying the scalar ODE with U_ξ and integrating from $-\infty$ to ∞ yields:

$$c\int_{-\infty}^{\infty} W^2 d\xi = \int_0^1 f(u)du$$

So c has the same sign as $\int_0^1 f(u)du$.

Used these two facts:

$$(V_x^2)_x = 2V_xV_{xx} \Rightarrow \int V_xV_{xx} = \frac{1}{2}V_x^2$$

$$\int_{x_0}^{x_1} f(V(x))V_x dx = \int_{V(x_0)}^{V(x_1)} f(V)dV$$

Analytical solution in the cubic case

With

$$f(V) = A^2V(V-1)(\alpha - V)$$

the solution is given as

$$U(\xi) = \frac{1}{2}\left[1 + \tanh\left(\frac{A}{2\sqrt{2}}\xi\right)\right]$$

with

$$c = \frac{A}{\sqrt{2}}(1-2\alpha)$$

Propagation failure, 12.3.2

- Signal propegates from the pacemaker through the AV-node and into the bundle of HIS
- This bundle divides in several branches
- Bundle branch block occurs when the action potential fails to propgate through the enitre branch.
- We will derive conditions for block using the cable equation

Modeling branching

If we assume negligbile resitance $r_e = 0$, the cable equation reads:

$$C_mR_m\frac{\partial V}{\partial t} = \frac{R_m}{p}\frac{\partial}{\partial x}\left(\frac{A}{R_c}\frac{\partial V}{\partial x}\right) + f(V)$$

As usual p is the circumferance, and A is the cross sectional area of the cell. R_m is the membrane resistance and R_c the intracellular resistance.
$f(V) = 0$ at three points: $V = 0 < \alpha < 1$
We define $x = 0$ as the brancing point and use subscript 1 and 2 for the geomtritcal properities to left and right side of the branch, respectively.

Comparison property of the bistable equation

If we have two initial conditions where:

$$V_A(0,x) \leq V_B(0,x)$$

Then for all $t \geq 0$:

$$V_A(t,x) \leq V_B(t,x)$$

If we can find a *stationary* solution of the cable equation, then, due to the property above this represent an upper bound, e.g. a block.

We look for a solution where
$V(-\infty) = 0$, $V(+\infty) = 1$
and
$V_x(-\infty) = V_x(+\infty) = 0$.

Equation for stationary wave

$$x < 0: \frac{R_m}{p_1}\frac{\partial}{\partial x}\left(\frac{A_1}{R_c}\frac{\partial V}{\partial x}\right) + f(V) = 0$$

$$x > 0: \frac{R_m}{p_2}\frac{\partial}{\partial x}\left(\frac{A_2}{R_c}\frac{\partial V}{\partial x}\right) + f(V) = 0$$

Multiply by V_x and integrate:

$$x < 0: c_1 \int_{-\infty}^{0} V_{xx} \cdot V_x + \int_{-\infty}^{0} f(V) \cdot V_x = 0$$

$$x > 0: c_2 \int_{0}^{\infty} V_{xx} \cdot V_x + \int_{0}^{\infty} f(V) \cdot V_x = 0$$

where $c_i = (A_i R_m)/(p_i R_c), \quad i = 1,2$

Integrate

Note that

$$(V_x^2)_x = 2V_x V_{xx} \Rightarrow \int V_x V_{xx} = \frac{1}{2}V_x^2$$

and from the chain rule of derivation:

$$\int_{x_0}^{x_1} f(V(x))V_x dx = \int_{V(x_0)}^{V(x_1)} f(V)dV = F(V_1) - F(V_0)$$

where $F(V) = \int_0^V f(u)du$
So:

$$x < 0: c_1\frac{1}{2}[V_x^2]_{-\infty}^{0} + F(V(0)) - F(V(-\infty)) = 0 \Rightarrow c_1 V_x^2 + F(V) = 0$$

$$x > 0: c_2\frac{1}{2}[V_x^2]_{0}^{\infty} + F(V(\infty)) - F(V(0)) = 0 \Rightarrow -c_2 V_x^2 + F(1) - F(V) = 0$$

cont.

$$\frac{1}{2}\frac{R_m A_i}{R_c p_i}V_x^2 + F(V) = \begin{cases} 0, & i = 1 \\ F(1), & i = 2 \end{cases}$$

Formulated in terms of current: $I = -(A/R_C)V_x$.

$$\frac{1}{2}\frac{R_m R_c}{A_i p_i}I^2 + F(V) = \begin{cases} 0, & i = 1 \\ F(1), & i = 2 \end{cases}$$

Continuity of current yields:

$$F(V)\left(\frac{A_1 p_1}{A_2 p_2} - 1\right) = -F(1)$$

Possible to find such a V?

If $A_1p_1 = A_2p_2$, then obviously not.
Must have:

$$\frac{A_1p_1}{A_2p_2} = 1 - \frac{F(1)}{F(V)} = \gamma$$

We assume $F(1) > 0$, e.g. left going wave.
Note that $F(1) > F(V)$
If $F(V) > 0$, then no solution is possible because $\gamma < 0$.
Thus $F(V) < 0$ and $\gamma > 1$.
Therefore block is only possible when $A_1p_1 > A_2p_2$.
The smallest value of $\gamma^* = 1 - F(1)/F(\alpha)$.
Thus block is not possible if $\frac{A_1p_1}{A_2p_2} < \gamma^*$
Conclusion: there exists a standing wave solution if:

$$\frac{A_1p_1}{A_2p_2} > 1 - \frac{F(1)}{F(\alpha)}$$

For the cubic case:

$$\frac{A_1p_1}{A_2p_2} > 1 + \frac{1-2\alpha}{\alpha^3(2-\alpha)}$$