Branching Dendritic Trees and Motoneuron Membrane Resistivity

Wilfrid Rall

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The View of Dendrites at the Time

- The working hypothesis during the 1950s was that synapses on the dendrites, in particular on distal branches, are essentially ineffective, and that only the synapses at the soma and the proximal dendrites contribute to a neuron's output.
- Partially due to the need for simplifying assumptions in facing the complexity of the nervous system.
- "Standard Motoneuron" model of Eccles and collaborators consisted of a 70 μm diameter soma with six 5 μm diameter dendrites of infinite length.

Goals of the Paper

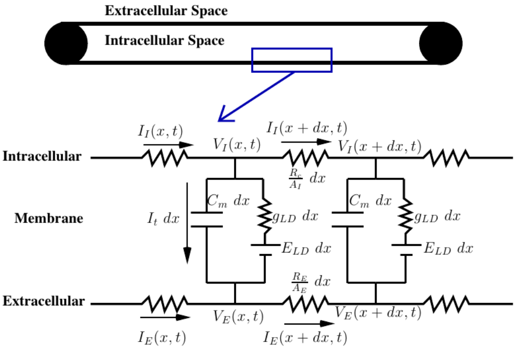
- Address the how the geometry of the dendritic tree relates to estimates of the specific membrane resistivity.
- Provide a method for reducing the geometrical complexity of a branching dendritic tree, while preserving its electrical properties.
- Take away message, Rall's meticulous calculations show that Eccles severely underestimated the size of the dendritic tree which lead to an underestimation of the dendritic membrane resistivity and dendritic-to-soma conductance value.

Goals of the Paper

Cable Theory: Assumptions

- Each section of the dendritic tree is a cylindrical piece of a phospholipid bilayer membrane surrounding an interior of cytoplasm.
- The electric properties of the membrane are assumed to be uniform over the entire soma-dendritic surface.
- The electric current inside any cylindrical component is assumed to flow axially through an ohmic resistance which is inversely proportional to the area of cross section.
- The electric current across the membrane is assumed to be normal to the membrane surface.
- A membrane electromotive force, E_{LD}, is assumed to be in series with the membrane resistance, and is assumedto be constant for all of the membrane.

Cable Equation



Membrane Current — Change in Axial Current

$$\pi d\left(C_m\frac{\partial v}{\partial t}+\frac{1}{R_m}(v-E_{LD})\right)=\frac{\partial}{\partial x}\left(\frac{1}{\frac{R_c}{A_I}+\frac{R_E}{A_E}}\frac{\partial v}{\partial x}\right)$$

$$v=v_I-v_E,\ \ A_I=\pi d^2$$

Assumptions Specific to the Current Paper

- Resistance of the external medium is zero ($R_E = 0$).
- Isopotential soma.
- The internal potential and current are assumed to be continuous at all dendritic branch points and at the soma-dendritic junction.

$$\tau \frac{\partial v}{\partial t} = \lambda^2 \frac{\partial^2 v}{\partial x^2} - (v - E_{LD})$$

$$\lambda = \sqrt{\frac{dR_m}{4R_c}}$$

$$\tau = R_m C_m$$

Assumptions Specific to the Current Paper

- Resistance of the external medium is zero ($R_E = 0$).
- Isopotential soma.
- The internal potential and current are assumed to be continuous at all dendritic branch points and at the soma-dendritic junction.

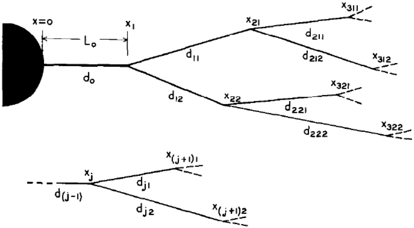
$$\tau \frac{\partial V}{\partial t} = \lambda^2 \frac{\partial^2 V}{\partial x^2} - V$$

$$V = v - E_{LD}$$

$$\lambda = \sqrt{\frac{dR_m}{4R_c}}$$

$$\tau = R_m C_m$$

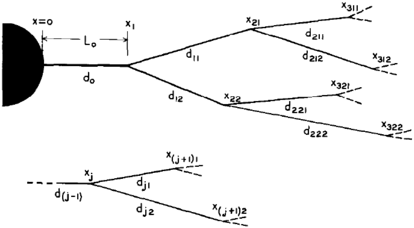
Steady-State Solutions of the Cable Equation



$$\frac{d^2V}{dx^2} = \frac{V}{\lambda_0^2},\ 0 < x < x_1$$
$$V(x_1) = V_1$$

$$V(x) = A\cosh[(x_1 - x)/\lambda_0] + B\sinh[(x_1 - x)/\lambda_0]$$

Steady-State Solutions of the Cable Equation



$$\frac{V}{V_1}(x) = \cosh[(x_1 - x)/\lambda_0] + B_1 \sinh[(x_1 - x)/\lambda_0],\ 0 \leq x \leq x_1$$

$$\frac{V}{V_1}(0) = \frac{V_0}{V_1} = \cosh[L_0/\lambda_0] + B_1 \sinh[L_0/\lambda_0]$$

- B_1 is related to the amount of axial current flowing at $x = x_1$.

$$I = -\frac{\pi d_0^2}{R_c} \frac{dV}{dx}\bigg|_{x=x_1} = \frac{\pi d_0^2}{R_c \lambda_0} V_1 B_1$$

Dependence of B_1 on Boundary Conditions

- Semi-Infinite Cylinder: $B_1 = 1$

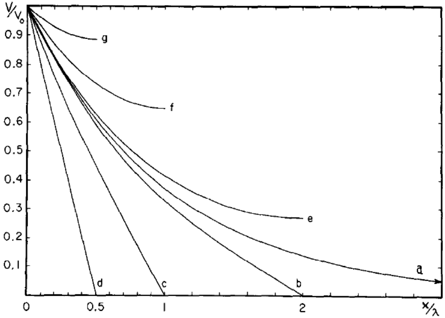
$$V/V_0 = e^{(x_1 - x)/\lambda_0}$$

- Sealed End (No Flux): $B_1 = 0$

$$V/V_0 = \frac{\cosh[(x_1 - x)/\lambda_0]}{\cosh[(L_0)/\lambda_0]}$$

- Killed End: $B_1 = \infty$ ($V(x_1) = 0$)

$$V/V_0 = \frac{\sinh[(x_1 - x)/\lambda_0]}{\sinh[(L_0)/\lambda_0]}$$



Why Is B_1 Important?

- B_1 (along with the length of the dendritic trunk L_0/λ_0) determines the input conductance of a dendritic tree.

$$I = -\frac{\pi d^2}{R_c}\frac{dV}{dx}$$

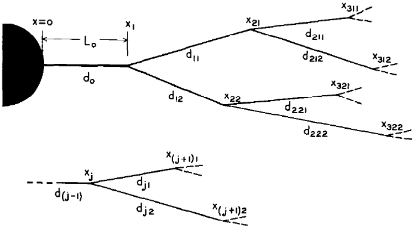
$$I/V_1 = G_\infty(\sinh[(x_1 - x)/\lambda_0] + B_1 \cosh[(x_1 - x)/\lambda_0]),\ 0 \le x \le x_1$$

$G_\infty = \frac{\pi d_0^2}{R_c \lambda_0} = \frac{\pi d_0^{3/2}}{\sqrt{R_m R_c}}$ is the input conductance of the semi-infinite dendritic trunk.

$$G_D = I_0/V_0 = B_0 G_\infty$$

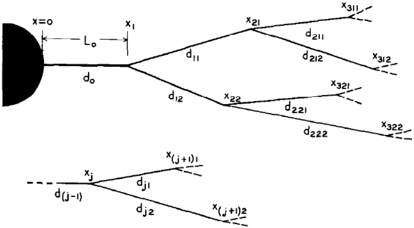
$$B_0 = \frac{B_1 + \tanh(L_0/\lambda_0)}{1 + B_1 \tanh(L_0/\lambda_0)}$$

Dependence of B_1 on Branching



$$\frac{I_1}{V_1} = B_1 G_\infty$$

Dependence of B_1 on Branching

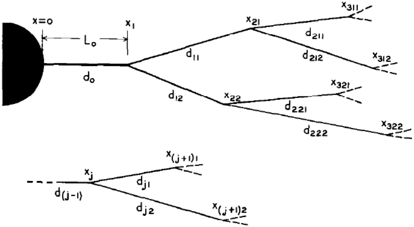


$$\frac{d^2V}{dx^2} = \frac{V}{\lambda_{1k}^2},\; x < x < x_{2k}$$

$$V(x_{2k}) = V_{2k}$$

$$V(x) = A\cosh[(x_{2k}-x)/\lambda_{1k}] + B\sinh[(x_{2k}-x)/\lambda_{1k}]$$

Dependence of B_1 on Branching

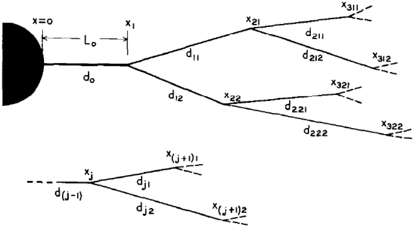


$$\frac{d^2V}{dx^2} = \frac{V}{\lambda_{1k}^2},\ x_1 < x < x_{2k}$$

$$V(x_{2k}) = V_{2k}$$

$$\frac{V}{V_{1k}}(x) = \cosh[(x_{2k}-x)/\lambda_{1k}] + B_{2k}\sinh[(x_{2k}-x)/\lambda_{1k}],\ x_1 \le x \le x_{2k}$$

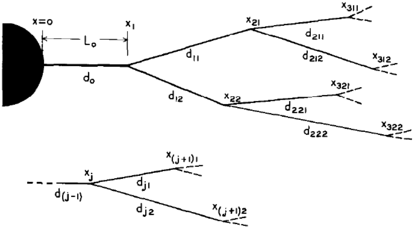
Dependence of B_1 on Branching



$$\frac{V}{V_{1k}}(x) = \cosh[(x_{2k} - x)/\lambda_{1k}] + B_{2k}\sinh[(x_{2k} - x)/\lambda_{1k}],\ x_1 \le x \le x_{2k}$$

$$\frac{I}{V_{1k}}(x) = \frac{\pi d_{1k}^2}{\lambda_{1k} R_c}\left\{\sinh[(x_{2k} - x)/\lambda_{1k}] + B_{2k}\cosh[(x_{2k} - x)/\lambda_{1k}]\right\},\ x_1 \le x \le x_{2k}$$

Dependence of B_1 on Branching

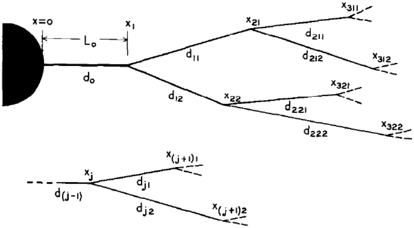


$$\frac{\frac{I}{V_{1k}}(x_1)}{\frac{V}{V_{1k}}(x_1)} = \frac{I_{1k}}{V_1} = \frac{\pi d_{1k}^{3/2}}{\sqrt{R_m R_c}} \frac{\sinh[(x_{2k}-x_1)/\lambda_{1k}] + B_{2k}\cosh[(x_{2k}-x_1)/\lambda_{1k}]}{\cosh[(x_{2k}-x_1)/\lambda_{1k}] + B_{2k}\sinh[(x_{2k}-x_1)/\lambda_{1k})}$$

$$= \frac{\pi d_{1k}^{3/2}}{\sqrt{R_m R_c}} \frac{\sinh[L_{1k}/\lambda_{1k}] + B_{2k}\cosh[L_{1k}/\lambda_{1k}]}{\cosh[L_{1k}/\lambda_{1k}] + B_{2k}\sinh[L_{1k}/\lambda_{1k}]}$$

$$= \frac{\pi d_{1k}^{3/2}}{\sqrt{R_m R_c}} \frac{B_{2k} + \tanh(L_{1k}/\lambda_{1k})}{1 + B_{2k}\tanh(L_{1k}/\lambda_{1k})}$$

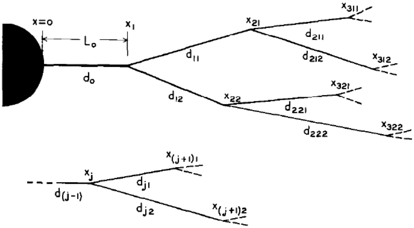
Dependence of B_1 on Branching



$$\frac{I_{1k}}{V_1} = B_{1k} G_\infty (d_{1k}/d_0)^{3/2}$$

$$B_{1k} = \frac{B_{2k} + \tanh(L_{1k}/\lambda_{1k})}{1 + B_{2k}\tanh(L_{1k}/\lambda_{1k})}$$

Dependence of B_1 on Branching



$$\frac{I_1}{V_1} = \sum_k \frac{I_{1k}}{V_1}$$

$$B_1 G_\infty = \sum_k B_{1k} G_\infty (d_{1k}/d_0)^{3/2}$$

$$B_1 = \sum_k B_{1k} (d_{1k}/d_0)^{3/2}$$

Example Calculation

$$B_j = \sum_k B_{jk}[d_{jk}/d_{(j-1)}]^{3/2}$$

$$B_{jk} = \frac{B_{(j+1)k} + \tanh(L_{jk}/\lambda_{jk})}{1 + B_{(j+1)k}\tanh(L_{jk}/\lambda_{jk})}$$

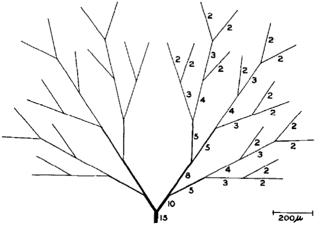


TABLE 1
BRANCHING TREE CALCULATION

		$R_m = 3600\ \Omega cm^2$				$R_m = 900\ \Omega cm^2$			
d_{j-1} to d_{jk}	$(d_{jk}/d_{j-1})^{3/2}$	tanh (L_{jk}/λ_{jk})	$B_{(j+1)k}$	B_{jk}	B_j	tanh (L_{jk}/λ_{jk})	$B_{(j+1)k}$	B_{jk}	B_j
3 μ to 2 μ	0.54	0.32	0	0.32	0.34	0.58	0	0.58	0.62
3 μ to 2 μ	0.54	0.32	0	0.32		0.58	0	0.58	
4 μ to 2 μ	0.35	0.32	0	0.32	0.47	0.58	0	0.58	0.75
4 μ to 3 μ	0.65	0.26	0.34	0.55		0.50	0.62	0.85	
5 μ to 3 μ	0.46	0.26	0.34	0.55	0.70	0.50	0.62	0.85	1.02
5 μ to 4 μ	0.71	0.24	0.47	0.64		0.44	0.75	0.89	
8 μ to 5 μ	0.49	0.21	0.70	0.80	0.78	0.40	1.02	1.01	0.98
8 μ to 5 μ	0.49	0.21	0.70	0.80		0.40	1.02	1.01	
10 μ to 5 μ	0.35	0.21	0.70	0.80	0.88	0.40	1.02	1.01	1.05
10 μ to 8 μ	0.71	0.17	0.78	0.84		0.32	0.98	0.99	
15 μ to 10 μ	0.54	0.08	0.88	0.90	0.98	0.15	1.05	1.03	1.12
15 μ to 10 μ	0.54	0.08	0.88	0.90		0.15	1.05	1.03	
15 μ (at $x = o$)		0.03	0.98	$B_0 =$	0.98	0.06	1.12	$B_o =$	1.11

RALL

Relating Input Resistance to Membrane Resistance

- Goal is to estimate R_m.
- The whole neuron conductance G_N (or resistance $R_N = \frac{1}{G_N}$) can be measured experimentally.
- How does G_N relate to R_m?

Relating Input Resistance to Membrane Resistance

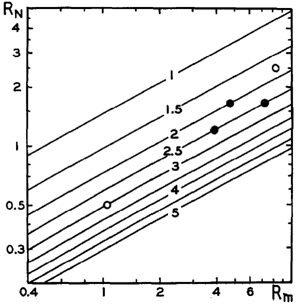
$$
\begin{aligned}
G_N &= \sum_j G_{Dj} + G_S \\
&= \frac{\pi}{2\sqrt{R_c}} \frac{1}{\sqrt{R_m}} \sum_j B_{0j} d_{0j}^{3/2} + \frac{S}{R_m} \\
&= \frac{C D^{3/2}}{\sqrt{R_m}} + \frac{S}{R_m}
\end{aligned}
$$

- $D^{3/2} = \sum_j B_{0j} d_{0j}^{3/2}$ is the combined dendritic tree parameter.
- $\sum_j d_{0j}^{3/2}$ is the combined dendritic trunk parameter.

Relating Input Resistance to Membrane Resistance

$$R_m = (1+\varepsilon)C^2D^3R_N^2$$

$$1+\varepsilon = \frac{1}{4}\left[1+\sqrt{1+\frac{4S}{CD^3R_N}}\right]^2$$



- Since $D^{3/2}$ depends on R_m through B_{0j}, Rall assumes each $B_{0j} = 1$ and uses $D^{3/2} \approx \sum_j d_{0j}^{3/2}$ in his subsequent calculations.

Dendritic to Somatic Conductance Ratio

$$\rho = \frac{\sum_j G_{Dj}}{G_S}$$
$$= C[D^{3/2}/S]\sqrt{R_m}$$

Anatomical Results

TABLE 2
MAMMALIAN MOTONEURONS

Mammal	Geometric quantities: Dendrites $\Sigma d^{3/2}$ [a] (10^{-6} cm$^{3/2}$)	Soma S [b] (10^{-6} cm^2)	Ratio $\Sigma d^{3/2}/S$ (cm$^{-1/2}$)	Hypothetical estimates[h] (for $R_m = 4000\ \Omega$cm^2): ρ	R_N (megohms)	(for $R_m = 600\ \Omega$cm^2): ρ	R_N (megohms)
Human, adult							
(Chu)[c]							
Fig. 2	249	149	1.67	21	1.21	8.2	0.44
Fig. 3	205	129	1.59	20	1.47	7.8	0.53
Fig. 12	281	103	2.73	34	1.09	13.4	0.40
Fig. 13	226	109	2.07	26	1.35	10.1	0.50
Fig. 18	217	87	2.49	32	1.41	12.2	0.52
Fig. 21	244	98	2.49	32	1.26	12.2	0.46
Mean	237	112	2.17	27	1.30	10.6	0.48
Standard Deviation	27.1	22.7	0.47	5.9	0.14	0.23	0.05
Cat, adult							
(Haggar and Barr)[d]	204	94	2.17	28	1.49	11	0.55
(corrected for shrinkage)	261	130	2.01	25	1.17	10	0.43
(Fatt)[e]	226	107	2.11	27	1.35	10	0.50
Cat, "Standard Motoneurone"							
(Eccles, 1957)[f]	67	150	0.45	5.7	4.0	2.2	1.25
(Coombs, *et al.*, 1959)[f]	78	150	0.52	6.6	3.5	2.6	1.13
Human, adult, chromatolytic							
(Chu)[c]							
Fig. 14	80	73	1.1	14	3.7	5.4	1.28
Fig. 15	104	126	0.83	10	2.8	4.1	0.93
Mean	92	100	0.92	12	3.2	4.5	1.09

TABLE 2 (*Continued*)

Mammal	Geometric quantities: Dendrites $\Sigma d^{3/2}$ [a] (10^{-6} cm$^{3/2}$)	Soma S [b] (10^{-6} cm^2)	Ratio $\Sigma d^{3/2}/S$ (cm$^{-1/2}$)	Hypothetical estimates[h] (for $R_m = 4000\ \Omega$cm^2): ρ	R_N (megohms)	(for $R_m = 600\ \Omega$cm^2): ρ	R_N (megohms)
Human, infant							
(Chu)[c]							
Fig. 1	100	63	1.59	20	3.0	7.8	1.08
Fig. 5	113	49	2.31	29	2.7	11.3	1.0
Fig. 6	135	76	1.78	22	2.2	8.7	0.81
Fig. 7	132	75	1.76	22	2.3	8.6	0.83
Fig. 20[g]	83	29	2.87	36	3.7	14.1	1.37
	(139)	(58)	(2.40)	(30)	(2.2)	(11.8)	(0.81)
Mean[g]	113	58	2.06	26	2.7	10.1	0.93
	(124)	(64)	(1.97)	(25)	(2.4)	(9.7)	(0.88)
Standard Deviation[g]	21.9	19.8	0.53				
	(16.6)	(11.3)	(0.36)				

Anatomical Results

- The values of the standard motoneuron model are ignificantly different from the adult and infant data presented.
- Comparison of the $\sum_j d_0 j^{3/2}$ values with the group of eight adult neurons using the t-test gives a $p < 0.001$ for chance occurrence of such a deviation.
- The standard motoneurone value for the ratio, $\sum_j d_0 j^{3/2}/S$, is about one-fourth the mean value found for both adult and infant neurons; the t statistic gives a $p < 0.01$ for chance occurrence of such a deviation.

Estimates

- Using a range of physiologically estimated R_N values, Rall estimates R_m to be within 1000 to 8000 Ωcm^2 as opposed to between 500 to 600 Ωcm^2 proposed by Eccles and colleagues.
- Rall also estimates the ratio of the dendritic to somatic conductance to be between 10 and 47, as opposed to the value of 2.3 put forth by Eccles and colleagues.

Legacy of Rall

- Demonstrated that dendrites could be analyzed by a rigorous mathematical and biophysical approach.
- Showed that the interrelations between the unique morphology and the specific electrical properties of neurons can be critical for their input-output functions.
- Challenged the dominant hypothesis of contemporary neurobiologists and modelers that neurons are essentially isopotential units.