Dynamics of Neural Systems
Cable Theory and Multi-compartment Models

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Overview

- Cable theory
- Multi-compartment modeling

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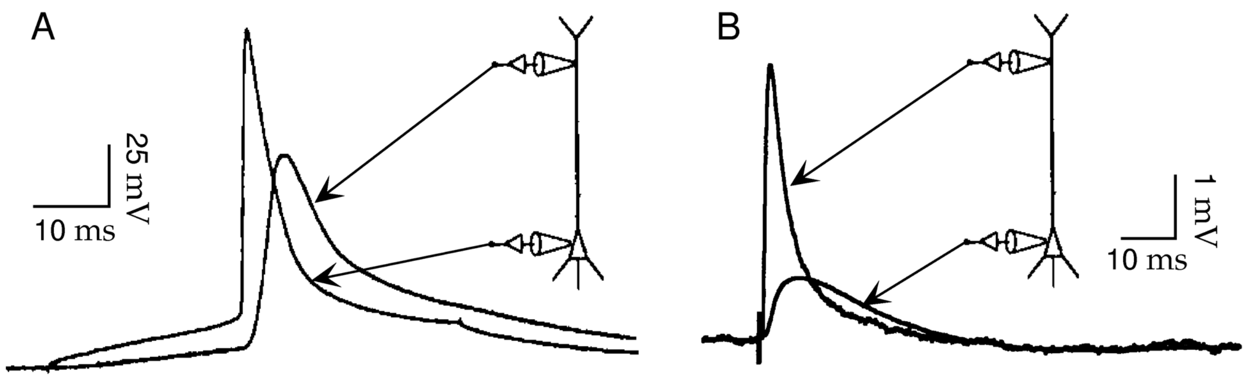
- Multi-compartment modeling

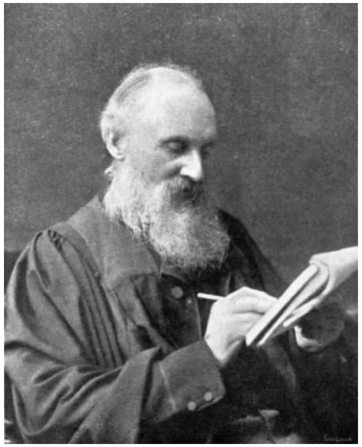
Cable theory

- Assumption for single compartment models often not justified.
- Especially for neurons with thin processes or fast changes of potential, or for cable-like long structures.
- **Continuous deformation** of signals along neuron surface (A: action potential; B: EPSP).
- Idealized model: spatially extended **neural cable**

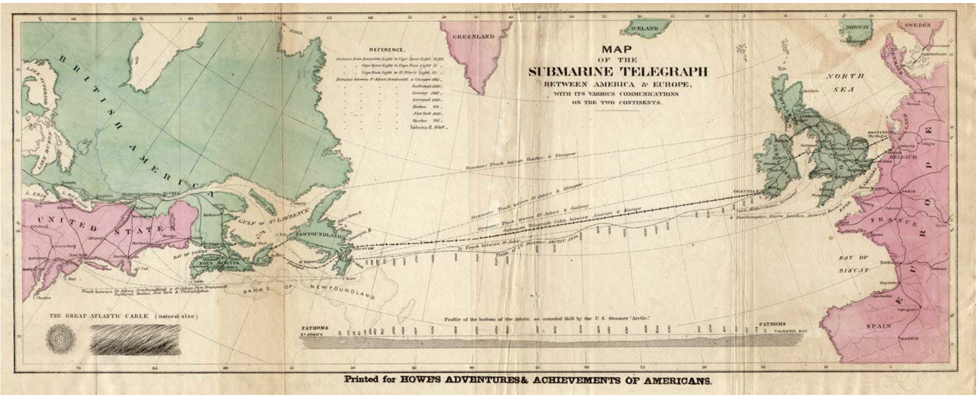


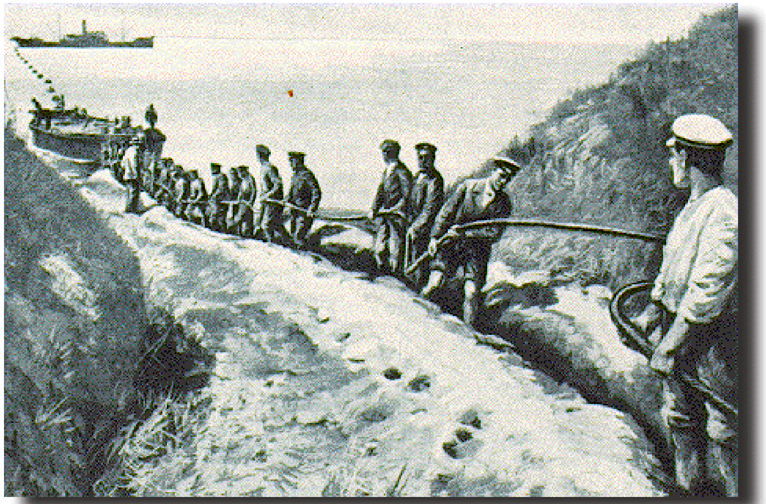
Cable theory: history

- Helmholtz (1850) measured finite speed of signal propagation along nerve fibers.
- Basic theory developed 1855 by William Thompson (Lord Kelvin) motivated by telegraphy using long underwater cables.
- Later combination with theory of excitable membranes by Hodgkin and Huxley.



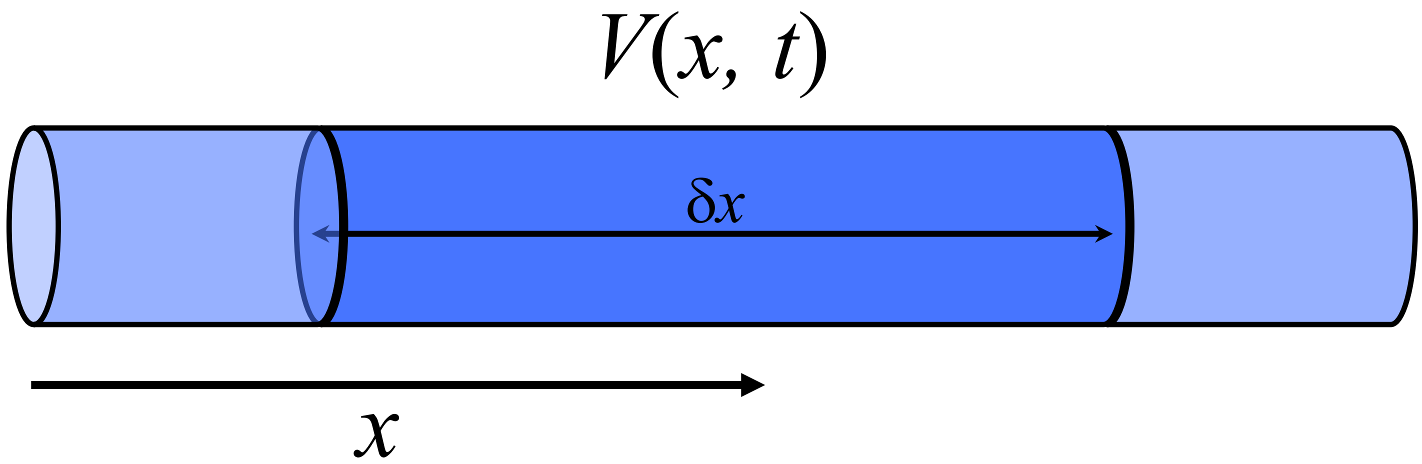
Lord Kelvin



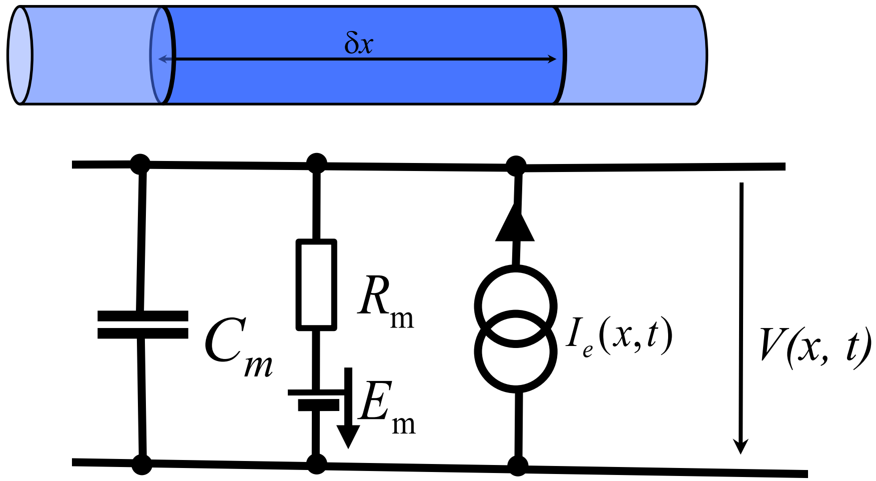


Modeling of a piece of cable I

- Short segment of neural cable; length δx.
- Membrane voltage as function of position: $V(x, t)$
- Apply Kirchhoff's laws:

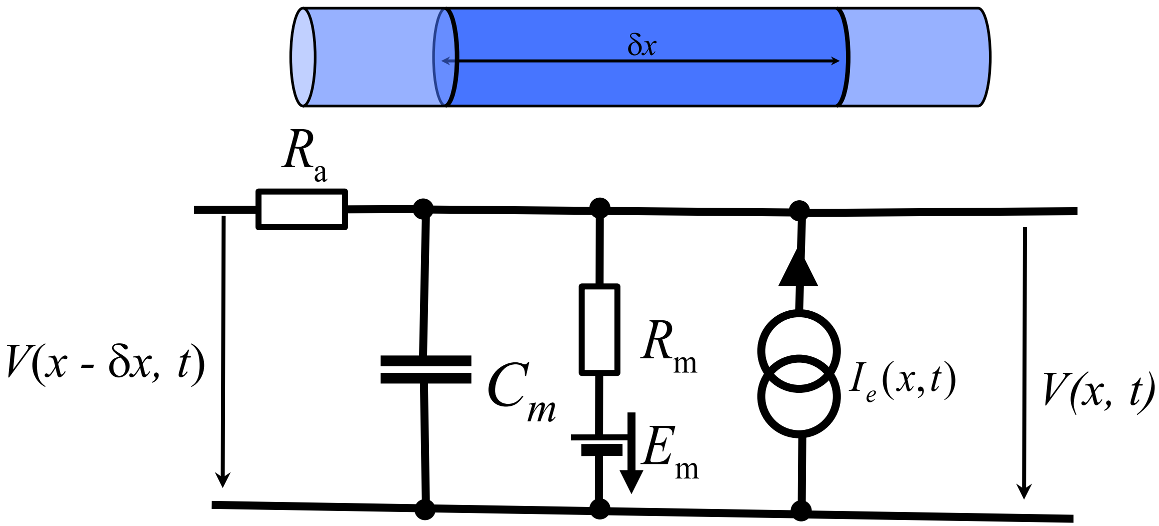


Modeling of a piece of cable II



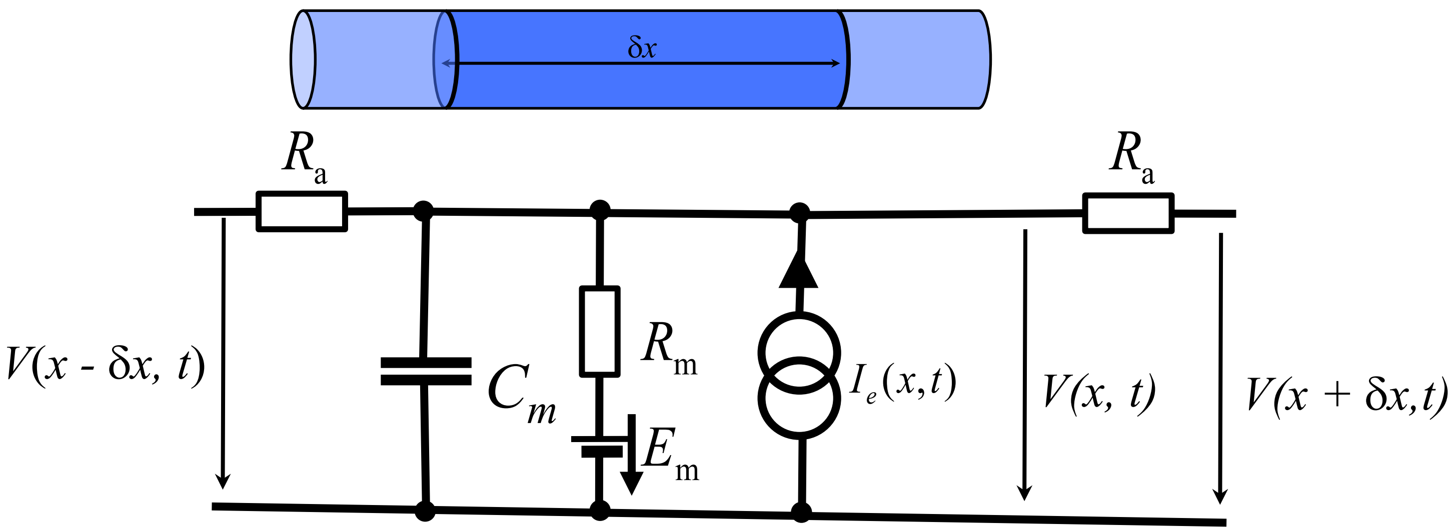
$$\underbrace{C_{\mathrm{m}} \frac{\partial V(x,t)}{\partial t}}_{\text{capacitive current}} + \frac{V(x,t) - E_{\mathrm{m}}}{R_{\mathrm{m}}} = I_{\mathrm{e}}(x,t)$$

Modeling of a piece of cable II



$$C_m \frac{\partial V(x,t)}{\partial t} + \frac{V(x,t) - E_m}{R_m} + \underbrace{\frac{V(x,t) - V(x - \delta x, t)}{R_a}}_{\text{Length current from left neighbor compartment}} = I_e(x,t)$$

Modeling of a piece of cable II



$$C_m \frac{\partial V(x,t)}{\partial t} + \frac{V(x,t) - E_m}{R_m} + \frac{V(x,t) - V(x-\delta x,t)}{R_a} + \underbrace{\frac{V(x,t) - V(x+\delta x,t)}{R_a}}_{\text{Length current from right neighbor compartment}} = I_e(x,t)$$

Modeling of a piece of cable III

- Short segment of neural cable; length δx.
- DEQ with concentrated elements:

$$C_\mathrm{m}\frac{\partial V(x,t)}{\partial t}+\frac{V(x,t)-E_\mathrm{m}}{R_\mathrm{m}}+\frac{V(x,t)-V(x-\delta x,t)}{R_\mathrm{a}}+\frac{V(x,t)-V(x+\delta x,t)}{R_\mathrm{a}}=I_\mathrm{e}(x,t)$$

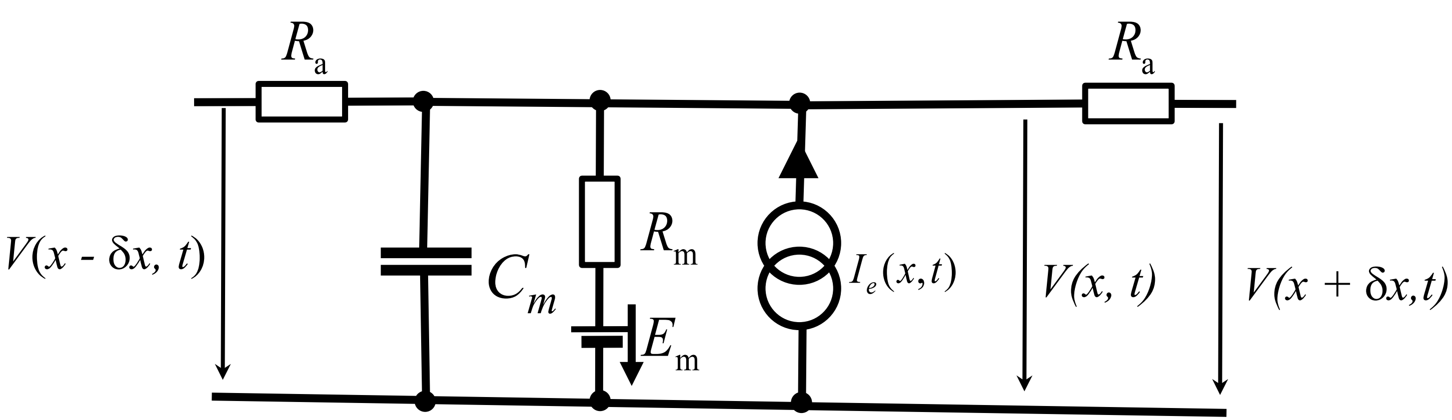
- Reformulation with **length-normalized parameters**:

$$C_\mathrm{m}=c_\mathrm{m}\delta x \quad \text{[F/m]}$$

$$R_\mathrm{m}=r_\mathrm{m}/\delta x \quad [\Omega\ \mathrm{m}]$$

$$R_\mathrm{a}=r_\mathrm{a}\delta x \quad [\Omega\ /\ \mathrm{m}]$$

$$I_\mathrm{e}(x,t)=i_\mathrm{e}(x,t)\delta x \quad [\mathrm{A}\ /\ \mathrm{m}]$$



Modeling of a piece of cable IV

- DEQ with concentrated elements:

$$C_{\mathrm{m}}\frac{\partial V(x,t)}{\partial t}+\frac{V(x,t)-E_{\mathrm{m}}}{R_{\mathrm{m}}}+\frac{V(x,t)-V(x-\delta x,t)}{R_{\mathrm{a}}}+\frac{V(x,t)-V(x+\delta x,t)}{R_{\mathrm{a}}}=I_{\mathrm{e}}(x,t)$$

- Resulting partial differential equation:

$$\cancel{\delta x}\,c_{\mathrm{m}}\frac{\partial V(x,t)}{\partial t}+\cancel{\delta x}\,\frac{V(x,t)-E_{\mathrm{m}}}{r_{\mathrm{m}}}+\cancel{\delta x}\,\frac{V(x,t)-V(x-\delta x,t)}{(\delta x)^2 r_{\mathrm{a}}}+\cancel{\delta x}\,\frac{V(x,t)-V(x+\delta x,t)}{(\delta x)^2 r_{\mathrm{a}}}=i_{\mathrm{e}}(x,t)\,\cancel{\delta x}$$

- Remark that for $\delta x \to 0$ we can write:

$$\frac{V(x,t)-V(x-\delta x,t)}{(\delta x)^2}+\frac{V(x,t)-V(x+\delta x,t)}{(\delta x)^2}\to\frac{1}{\delta x}\left[\frac{\partial V(x-\delta x/2,t)}{\partial x}-\frac{\partial V(x+\delta x/2,t)}{\partial x}\right]$$

$$\to-\frac{\partial^2 V(x,t)}{\partial x^2}$$

Cable equation

- Reordering of terms gives the **cable equation**:

$$\boxed{\underbrace{\frac{r_\mathrm{m}}{r_\mathrm{a}}}_{\lambda^2\text{: length constant } (\lambda > 0)} \frac{\partial^2 V(x,t)}{\partial x^2} = \underbrace{r_\mathrm{m} c_\mathrm{m}}_{\tau_\mathrm{m}\text{: time constant}} \frac{\partial V(x,t)}{\partial t} + \underbrace{V(x,t) - E_\mathrm{m}}_{v(x,\,t)} - r_\mathrm{m} i_\mathrm{e}(x,t)}$$

- Standardized form (with $v(x,\, t) = V(x,\, t) - E_\mathrm{m}$):

$$\boxed{\lambda^2 \frac{\partial^2 v(x,t)}{\partial x^2} = \tau_\mathrm{m} \frac{\partial v(x,t)}{\partial t} + v(x,t) - r_\mathrm{m} i_\mathrm{e}(x,t)}$$

Steady state solutions

- In general solutions depend on space and time.
- Assume a constant current $i_\mathrm{e}(x)$ is injected at end of cable (neurite) and neuron relaxes to a stable solution.
- Since $\partial / \partial t = 0$ one obtains the ordinary DEQ:

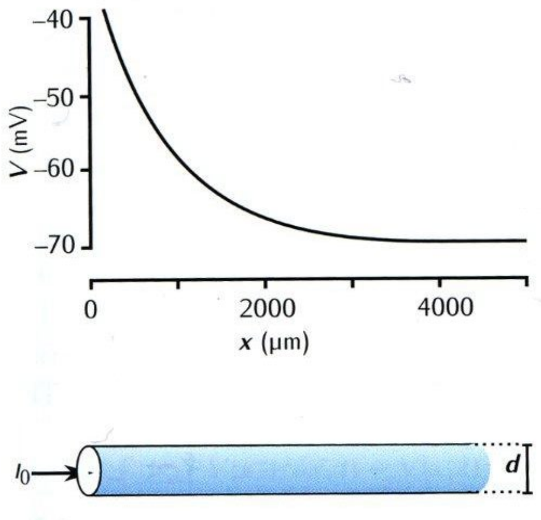
$$\boxed{\lambda^2 \frac{\mathrm{d}^2 v(x)}{\mathrm{d}x^2} = v(x) - r_\mathrm{m} i_\mathrm{e}(x)}$$

Steady state solution: semi-infinite cable

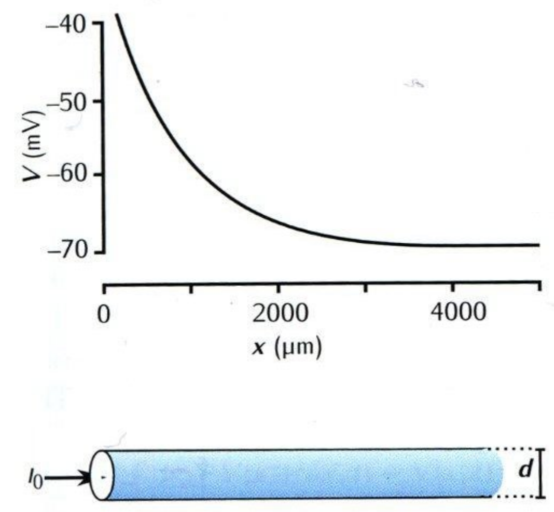
- Semi-infinite cable: extending over the interval $x \in [0, \infty)$
- Assume: current I_0 injected at at the open end $x = 0$, i.e. $i_e(x) = I_0\, \delta(x)$.
- Since $x > 0$, we find by solving the DEQ:

$$\lambda^2 \frac{d^2 v(x)}{dx^2} = v(x) \quad \Rightarrow$$

$$v(x) = K_1 e^{-x/\lambda} + K_2 e^{x/\lambda}$$
$$= K_3 \cosh(x/\lambda) + K_4 \sinh(x/\lambda)$$



Steady state solution: semi-infinite cable

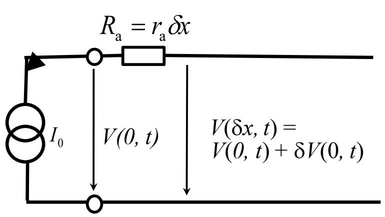


- For $x \rightarrow \infty$ follows from $v(\infty) = 0$ (i.e. $V(\infty) = E_{\mathrm{m}}$) that $K_2 = 0$ for a finite solution.
- This implies: $v(x) = K_1 e^{-\frac{x}{\lambda}}$

$$v'(x) = -\frac{K_1}{\lambda} e^{-x/\lambda}$$

- With the boundary condition $v'(0) = -r_{\mathrm{a}} I_0$ follows: $-\left.\frac{\mathrm{d}v(x)}{\mathrm{d}x}\right|_{x=0} = K_1/\lambda = I_0 r_a$

Derivation:



$$\Rightarrow \delta V(0,t) = -r_{\mathrm{a}}\delta x \cdot I_0$$

$$\Leftrightarrow \frac{\partial V(0,t)}{\partial x} = -r_{\mathrm{a}} \cdot I_0$$

- Final result:

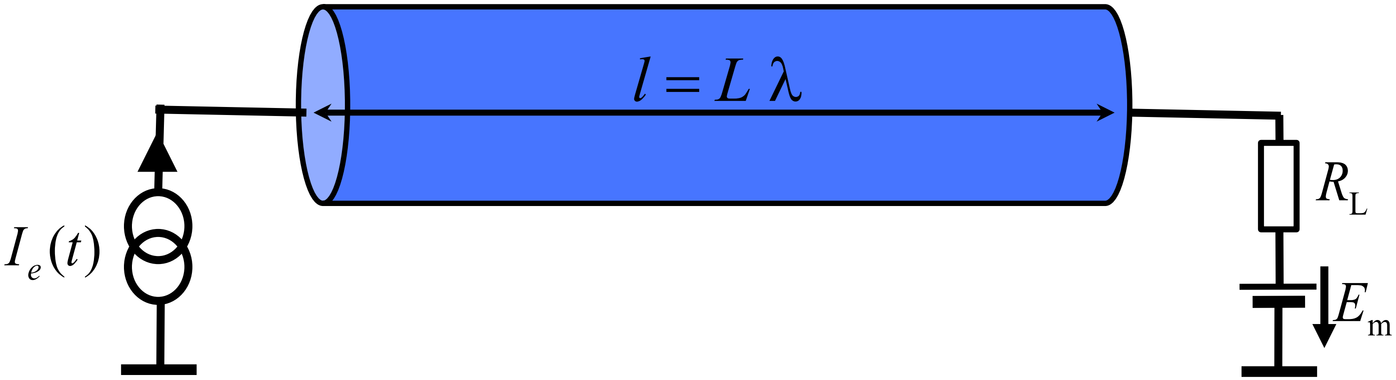
Input resistance for the semi-infinite cable

$$\boxed{V(x) = E_{\mathrm{m}} + R_\infty I_0 e^{-x/\lambda} \qquad \text{with} \qquad R_\infty = \sqrt{r_{\mathrm{m}} r_{\mathrm{a}}}}$$

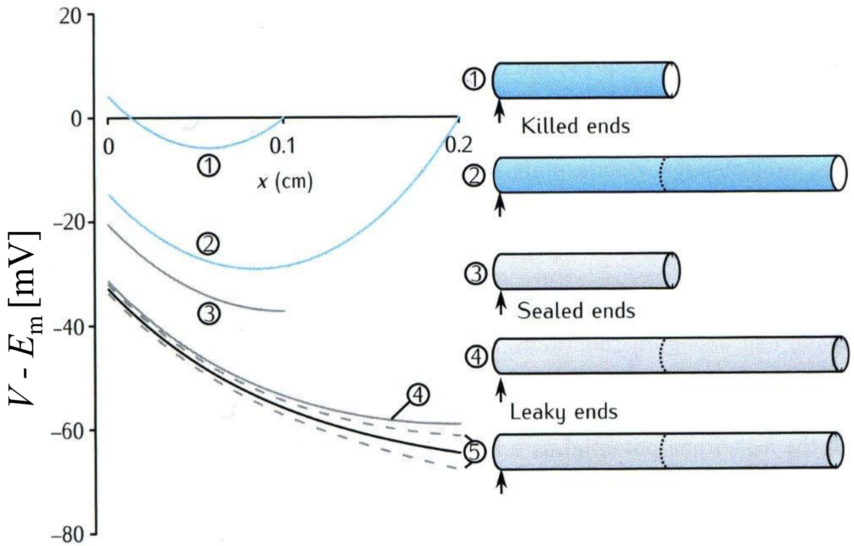
Steady state solution: finite cable

- **Finite cable** with length l and resistor R_L at the end.
- Defining $X = x/\lambda$ and $L = l/\lambda$, the general steady state solution can be computed as:

$$\boxed{V(X) = E_m + R_\infty I_0 \frac{R_L / R_\infty \cosh(L-X) + \sinh(L-X)}{R_L / R_\infty \sinh(L) + \cosh(L)} \quad \text{with } R_\infty = \sqrt{r_m r_a}}$$



Boundary conditions



- Killed end (short cut): $V(X) = E_{\mathrm{m}} + \dfrac{R_\infty I_0 \sinh(L - X) - E_{\mathrm{m}} \cosh(X)}{\cosh(L)}$
  ($R_{\mathrm{L}} = 0$, for $V(L) = 0$)
- For sealed end: $V(X) = E_{\mathrm{m}} + R_\infty I_0 \dfrac{\cosh(L - X)}{\sinh(L)}$
  ($R_{\mathrm{L}} = \infty$)

$X = 0 \Rightarrow$ **Input resistance**: $R_{\mathrm{in},L} = R_\infty \coth(L) = \dfrac{V(0) - E_m}{I_0}$

Time-dependent solution I

- Appropriate reparametrization of time axis $T = t / \tau_{\mathrm{m}}$ and spatial axis by $X = x / \lambda$ results in the simplified equation:

$$\boxed{\frac{\partial^2 v(X,T)}{\partial X^2} = \frac{\partial v(X,T)}{\partial T} + v(X,T) - r_{\mathrm{m}} i_{\mathrm{e}}(X,T)}$$

- Solution for infinite cable using **Green's function**:
  The Green's function $h(X, T)$ is the solution for a delta pulse input of the form: $r_{\mathrm{m}} i_{\mathrm{e}}(X,T) = \delta(X)\delta(T)$
- Construction of the solution for any arbitrary input $r_{\mathrm{m}} i_{\mathrm{e}}(X,T)$ by superposition, exploiting the fact that the partial differential equation defies a **linear operator**.

Time-dependent solution II

- Green's function (impulse response): simpler example: Compute the solution of the linear membrane dynamics with $E_m = 0$:

$$\underbrace{R_m C}_{\tau\text{: time constant}} \frac{\mathrm{d}V}{\mathrm{d}t} + (V(t) - E_\mathrm{m}) = R_m\, I_\mathrm{e}(t)$$

- The Green's function $h(t)$ is the solution of this equation for an input that is a delta function: $R_m\, I_\mathrm{e}(t) = \delta(t)$:

$$\tau \frac{\mathrm{d}h}{\mathrm{d}t} + h(t) = \delta(t) \;\Rightarrow\; h(t) = 1(t)\,\frac{1}{\tau}\,e^{-t/\tau}$$

Proof: Fourier transformation of the DEQ:

$$\tau\, i\omega\, \tilde{h}(\omega) + \tilde{h}(\omega) = 1 \;\Leftrightarrow\; \tilde{h}(\omega) = \frac{1}{1+\tau\, i\omega}$$

Fourier transformation pairs

Time-dependent solution III

- The DEQ can be interpreted as **linear operator** $\mathcal{D}$ that maps the input signal onto the solution, e.g:

$$\delta(t) \xrightarrow{\mathcal{D}} V(t) \equiv h(t)$$

- The differential equation as linear operator maps linear combinations of inputs onto linear combinations of the outputs with the same linear weights.
- You learned the following property of the delta function:

$$f(t) = \int_{-\infty}^{\infty} \delta(t - t')\, f(t')\; dt'$$

  This implies the function is a superposition of delta function peaks weighted by the function values at the individual times.

Time-dependent solution IV

- Obviously, because of the linearity the DEQ maps a weighted and time-shifted delta peak to the weighted and time shifted Green's function (for $a \in \mathrm{IR}$):

$$a\,\delta(t-t') \xrightarrow{D} V(t) \equiv a\,h(t-t')$$

- This implies that the solution of the DEQ is just a linear superposition if the Green's functions, weighted by the function values and time-shifted, defined by the **convolution integral**:

$$\boxed{V(t) = \int_{-\infty}^{\infty} h(t-t')\; R_m I_e(t')\; dt'}$$

Time-dependent solution V

- Example (cf. last lecture): $R_m\, I_\mathrm{e}(t) = R_m I_0\, 1(t)$ and $h(t) = 1(t)\frac{1}{\tau}e^{-t/\tau}$ implies:

$$V(t) = \int_{-\infty}^{\infty} h(t-t')\ R_m\, I_0 1(t')\, dt'$$

$$= \begin{cases} \int_0^t \frac{1}{\tau} e^{-t-t'/\tau} R_m I_0\, dt' = R_m\, I_0 \left[-e^{-t/\tau}\right]_0^t = R_m I_0 \left(1 - e^{-t/\tau}\right) & \text{for} \quad t \geq 0 \\ 0 \quad \text{for} \quad t < 0 \end{cases}$$

$$= R_m I_0 \left(1 - e^{-t/\tau}\right) 1(t)$$

- Knowing the Green's function, we can thus compute solutions for arbitrary inputs very easily.

Time-dependent solution VI

- The cable equation defines also a linear differential operator D that maps the space-time input $r_{\mathrm{m}} i_{\mathrm{e}}(X,T)$ onto the solution $v(X,T)$.
- The corresponding Green's function for this operator can be found by solving the partial differential equation for $r_{\mathrm{m}} i_{\mathrm{e}}(X,T) = \delta(X)\delta(T)$:

$$h(X,T) = \frac{1(T)}{\sqrt{4\pi T}} e^{-T - X^2/(4T)}$$

- The general solution is then given by the (space-time) convolution integral:

$$\boxed{v(X,T) = \int_{-\infty}^{\infty}\int_{-\infty}^{\infty} h(X - X', T - T')\, r_{\mathrm{m}} i_{\mathrm{e}}(X', T')\, \mathrm{d}X' \mathrm{d}T'}$$

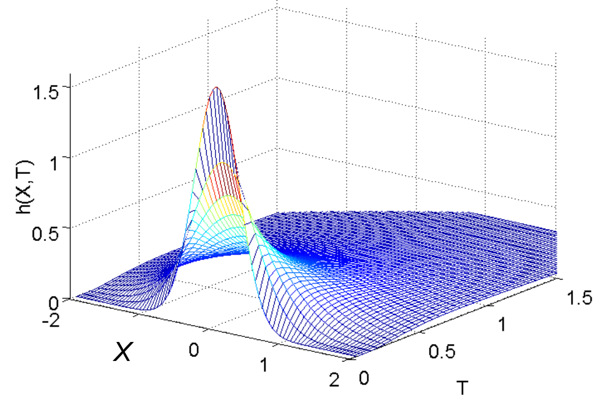
Time-dependent solution VII

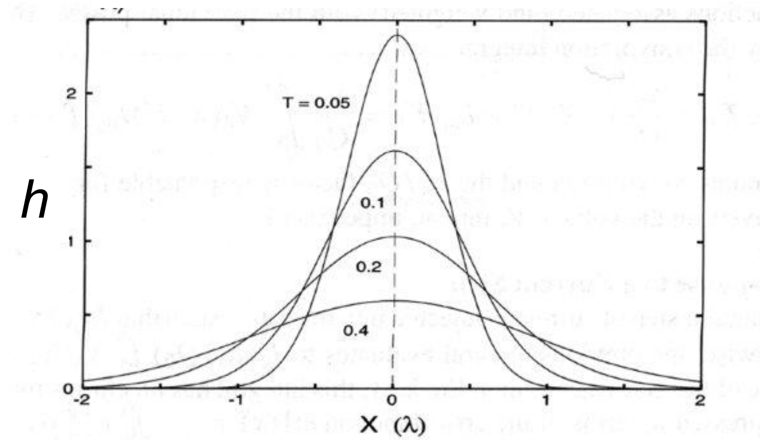
- Green's function for an infinite cable: 'dissipating Gaussian pulse'
- Time of maximum:

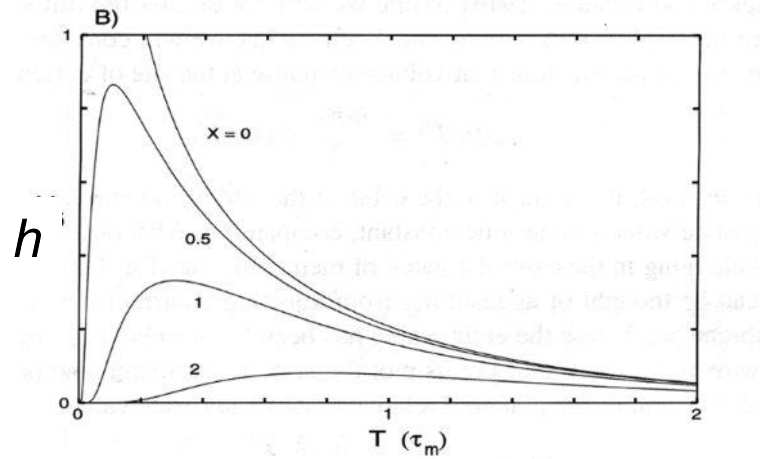
$$T_{\max} = \frac{t_{\max}}{\tau_m} = \frac{\sqrt{1+4X^2}-1}{4} \approx \frac{X}{2}$$

- Green's functions can also be constructed for cables with finite length.

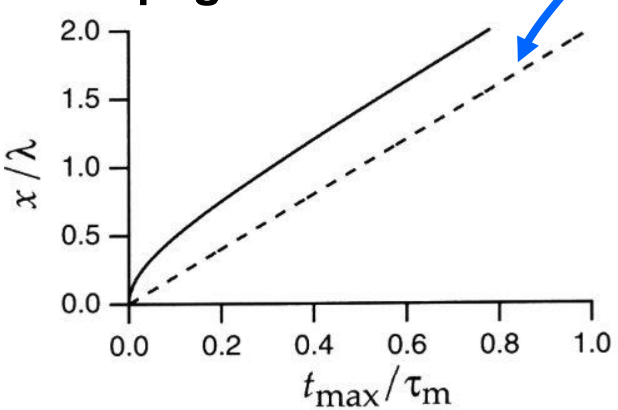
Green's function







Propagation of maximum



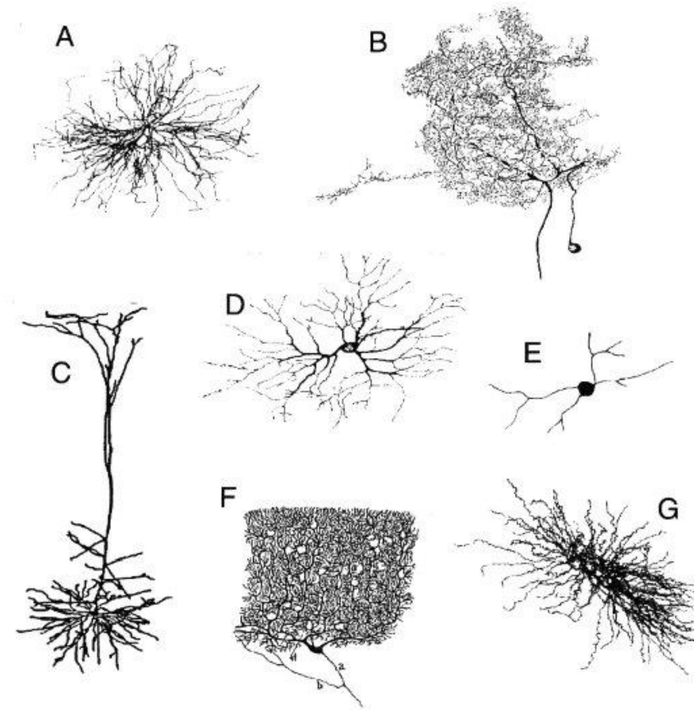
Overview

- Cable theory
- Multi-compartment modeling

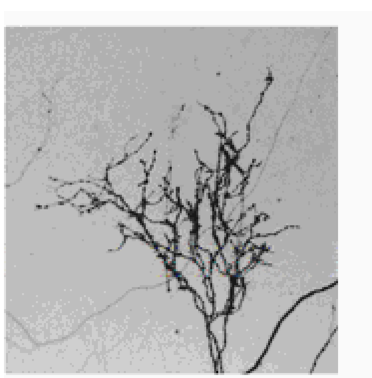
Axonal + dendritic trees

- Many different morphological shapes.
- Typically axons branch in processes with smaller diameter.
- Tight relationship between size of dendritic tree and receptive field, e.g. in the retina.

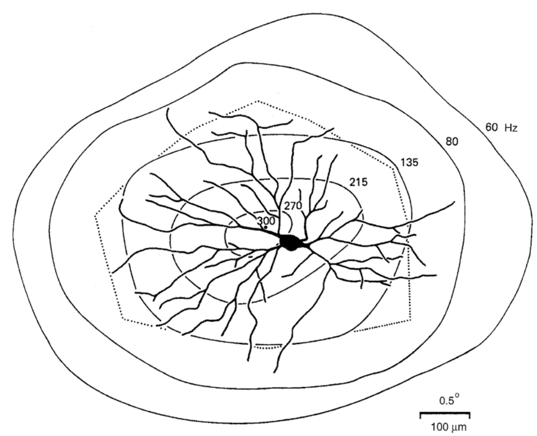
Dendritic trees



Axonal tree



Dendritic tree of retinal ganglion cell and receptive field



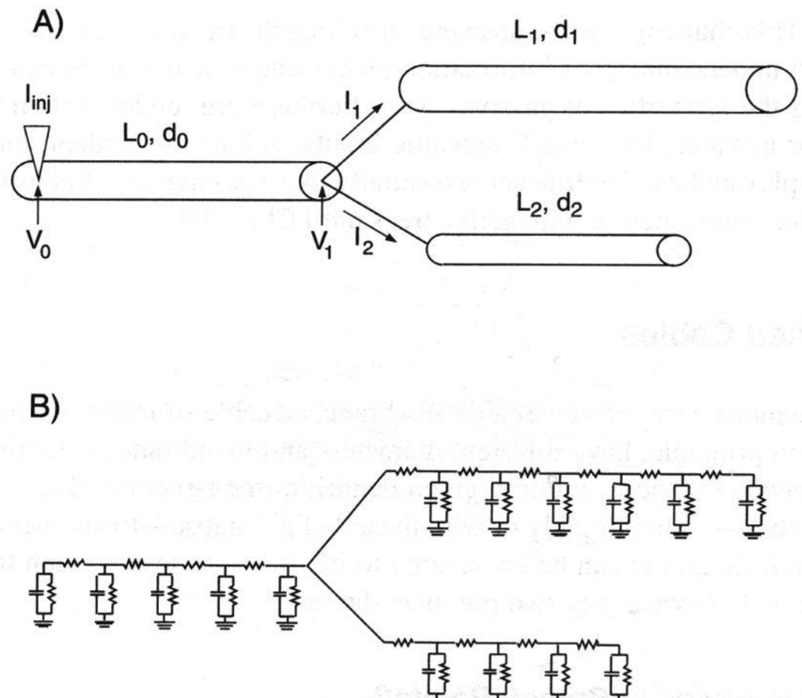
Branching I

- Typically, axons branch in processes with smaller diameter.
- Model: connected cable segments; end segments specify leak resistance for the previous ones.
- Example: steady state solution; sealed ends:

$$R_{L,i} = R_{\infty,i}\coth(L_i) \quad \text{for } i = 1,2$$

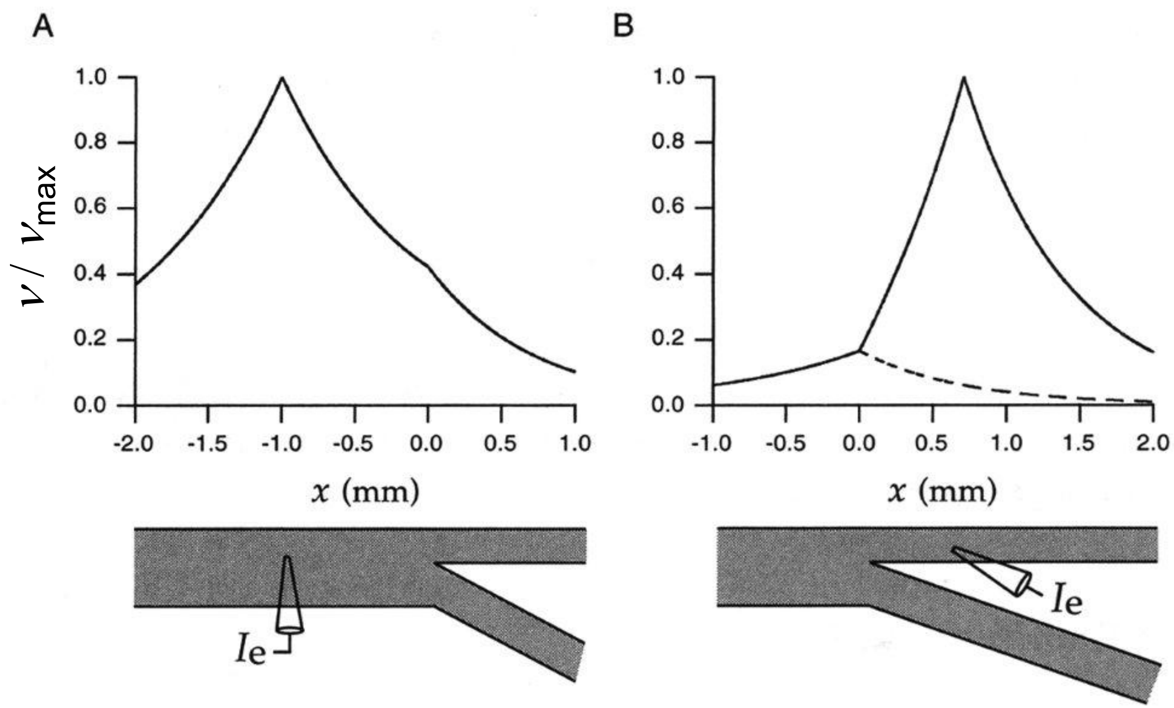
- Effective leak resistance for segment 0:

$$\left(R_{L,0}\right)^{-1} = \left(R_{L,1}\right)^{-1} + \left(R_{L,2}\right)^{-1}$$



Branching II

- Similar procedure can be applied for time dependent solutions.
- Example: three connected semi-infinite cables.



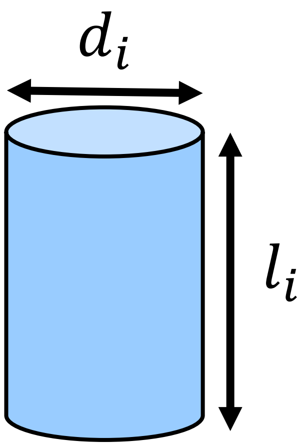
Branching III

- Necessity to compute cable properties for neurites (with same electrical properties) for different diameters d_i.
- For this purpose, electrical membrane properties are typically given in a form independent of the diameter:

$\tilde{r}_{m,i} = r_{m,i} \pi d_i$ — Area-specific membrane resistance [Ω m²] $\Rightarrow$ $R_{m,i} = \tilde{r}_{m,i} \frac{1}{\pi d_i l_i}$

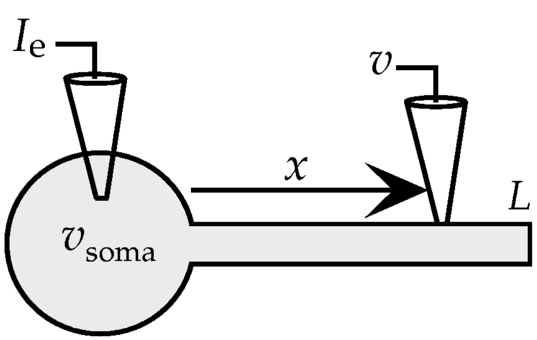
$\tilde{r}_{a,i} = r_{a,i} \pi (d_i/2)^2$ — Axial resistance per area [Ω m] $\Rightarrow$ $R_{a,i} = \tilde{r}_{a,i} \frac{l_i}{\pi (d_i/2)^2}$

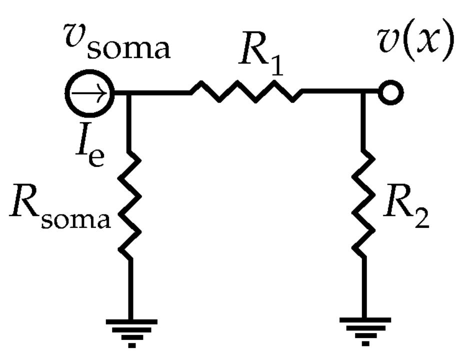
$\tilde{c}_{m,i} = \frac{c_{m,i}}{\pi d_i}$ — Area-specific membrane capacity [F/m²] $\Rightarrow$ $C_{m,i} = \tilde{c}_{m,i} \pi d_i \, l_i$



Rall model I

- Highly simplified model for a neuron.
- Consists of a single-compartment model for the soma and a single cylindrical cable that models the dendrites.
- Length and diameter of the cable adjusted to average properties of modeled dendritic system.
- Input resistance of soma: $R_e = R_{soma} \,||\, (R_1 + R_2)$
- Voltage at electrode: $v(x) = v_{soma} \cdot \underbrace{R_2 \,/\, (R_1 + R_2)}_{\text{Attenuation}}$





$$v_{soma} = \frac{I_e(R_1 + R_2)R_{soma}}{R_1 + R_2 + R_{soma}}$$

$$v(x) = \frac{I_e R_2 R_{soma}}{R_1 + R_2 + R_{soma}}$$

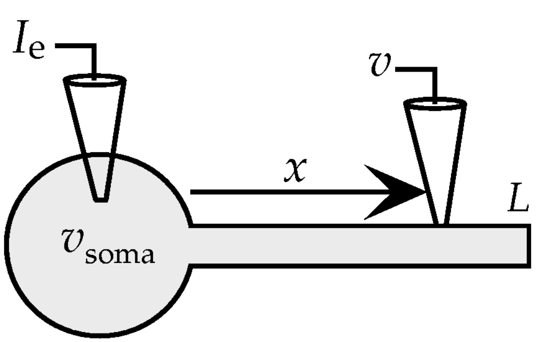
Rall model II

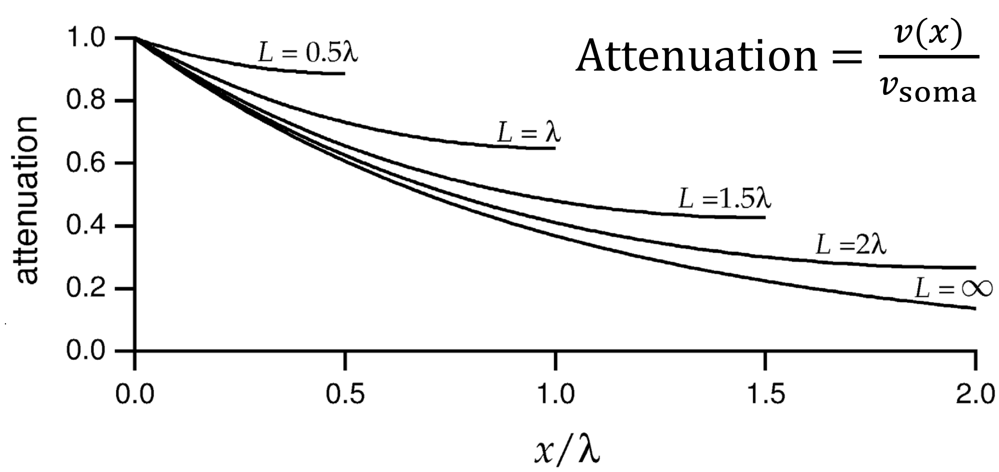
- The resistances follow from what we had before:

$$R_2 = R_\infty \frac{\cosh(L-X)}{\sinh L} \qquad \text{(sealed end)}$$

$$R_1 = R_\infty \frac{\cosh L - \cosh(L-X)}{\sinh L} \qquad \text{(input resistance of cable with length } L \text{ minus } R_2\text{)}$$

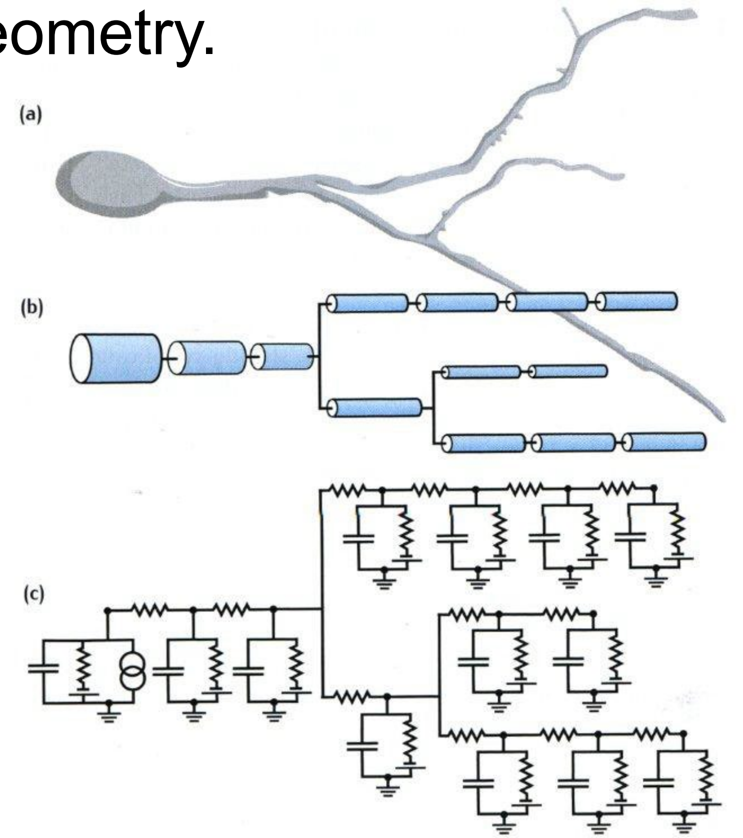
- Remark: Using a soma-only model can result in wrong time scales (see Sterratt et al. book for details).





Multi-compartment models I

- More realistic models contain membrane nonlinearities; in this case cable equation cannot be solved analytically.
- Neuron is ‘discretized’ and approximated by finite number of compartments with simple geometry.
- Each compartment has own membrane voltage and follows discussed equat-ions for membrane potential.
- In addition, currents to neighboring compartments have to be added.



Multi-compartment models II

- Typical equation for a single compartment:

Coupling conductances

$$C_{\mathrm{m}} \frac{\mathrm{d}V_n(t)}{\mathrm{d}t} + \frac{V_n(t)-E_{\mathrm{m}}}{R_{\mathrm{m}}} + \underbrace{g_{n,n-1}(V_n(t)-V_{n-1}(t)) + g_{n,n+1}(V_n(t)-V_{n+1}(t))}_{\text{coupling terms to neighbor compartments}} = I_{\mathrm{e},n}(t)$$

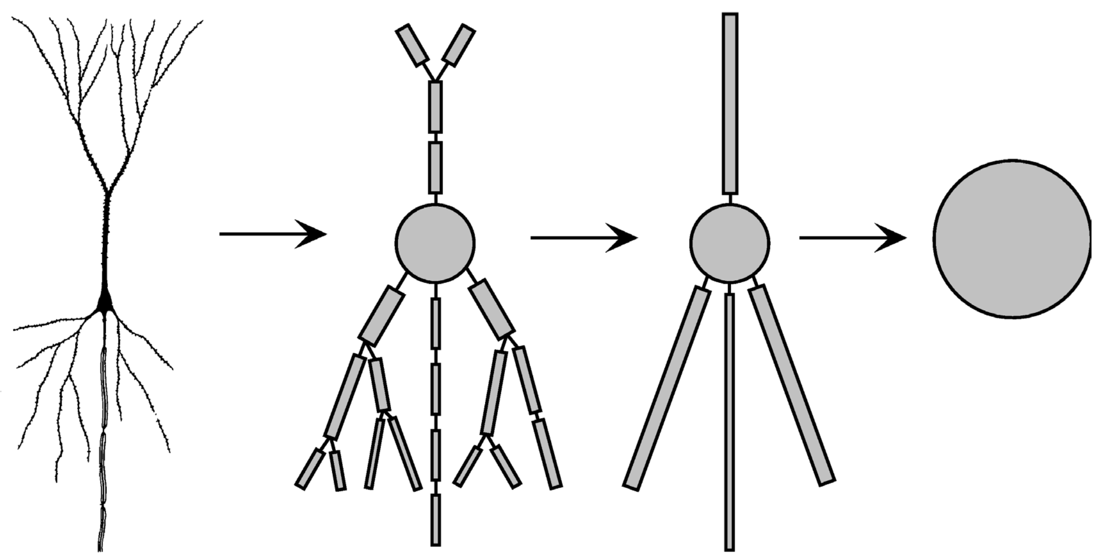
Multi-compartment models II

- Typical equation for a single compartment:

Coupling conductances

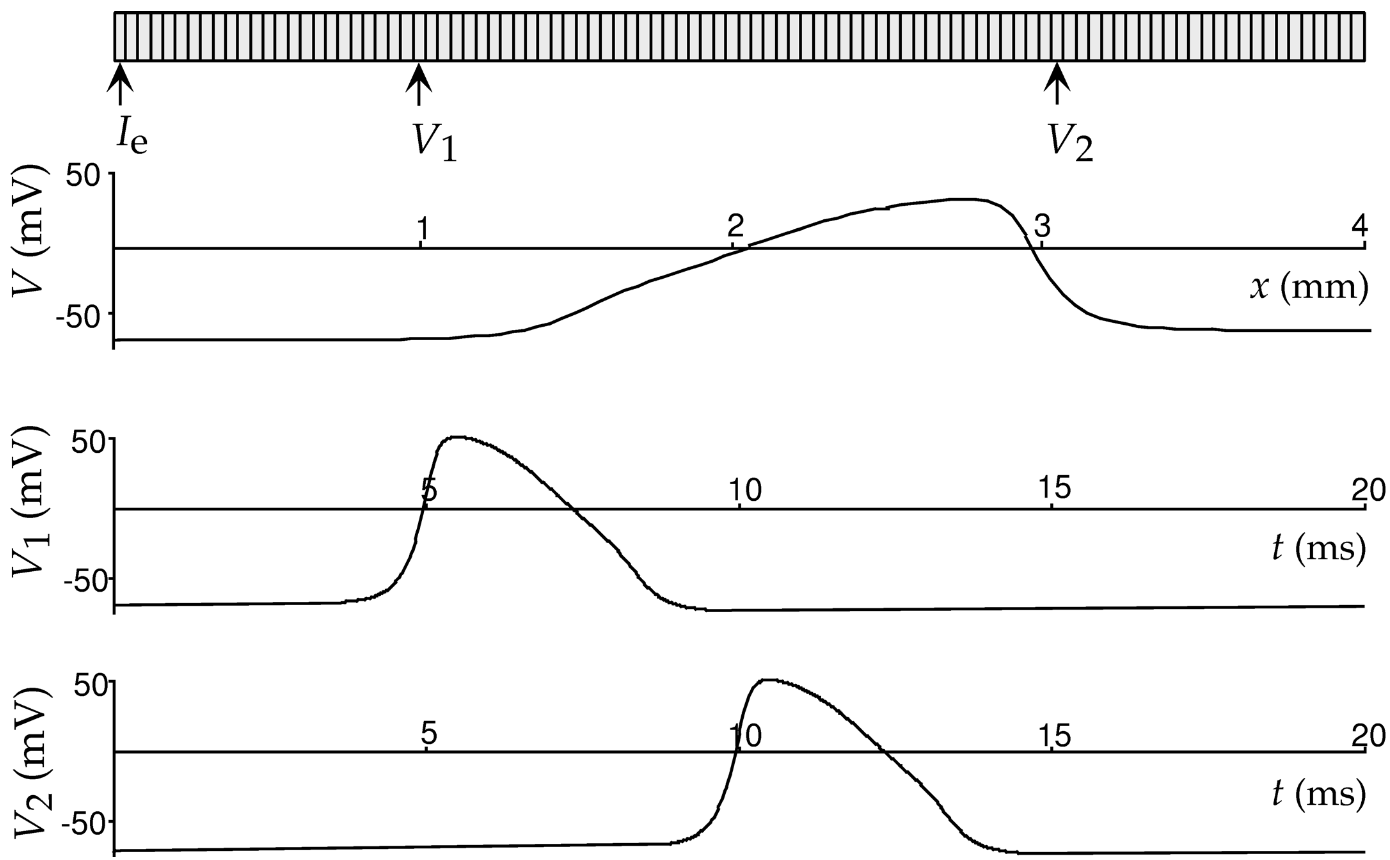
$$C_{\mathrm{m}} \frac{\mathrm{d}V_n(t)}{\mathrm{d}t} + \frac{V_n(t) - E_{\mathrm{m}}}{R_{\mathrm{m}}} + \underbrace{g_{n,n-1}(V_n(t) - V_{n-1}(t)) + g_{n,n+1}(V_n(t) - V_{n+1}(t))}_{\text{coupling terms to neighbor compartments}} = I_{\mathrm{e},n}(t)$$

- Addition of synaptically controlled currents (nonlinear).
- Accuracy and computational effort grow with number of compartments.



Example: action potential propagation along unmyelinated axon

- 100 compartments like Hodgkin-Huxley model (next lecture); non-branching cable.



Things to remember

- Cable equation $\rightarrow$ 1,2,3,4)
- Form of stationary solution $\rightarrow$ 4)
- Green's function approach $\rightarrow$ 2)
- Boundary conditions (sealed, killed, leaky) $\rightarrow$ 4)
- Modeling of branching $\rightarrow$ 1,4)
- Rall model $\rightarrow$ 1)
- Idea of multi-compartment modeling $\rightarrow$ 4)

(Numbers relate to literature on next page.)

Literature (for this lecture)

1) Dayan P. & Abbott, L.F. (2001 / 2005) *Theoretical Neuroscience: Computational and Mathematical Modeling of Neural Systems.* MIT Press, Cambridge MA, USA. Chapter 5.

2) Gerstner, W. & Kistler, W. (2002) *Spiking Neuron Models - Single Neurons, Populations, Plasticity*. Cambridge University Press, UK. Chapter 2.

3) Koch, C. (1999) *Biophysics of Computation*. Oxford University Press, UK. Chapters 2 and 3.

4) Sterratt, D., Graham, B, Gillies, A., Willshaw, D. (2011) *Principles of Computational Modelling in Neuroscience.* Cambridge University Press, UK. Chapters 2 and 4.