

# Conduction in excitable cells - the cable equation

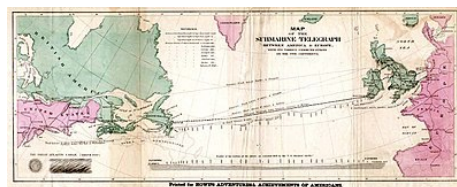
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## Outline

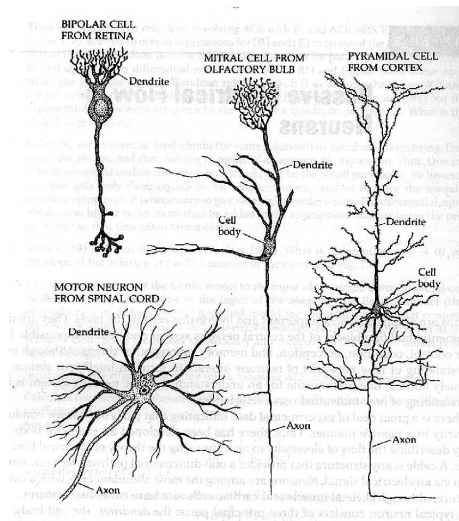
- Introduction
  - History
  - Brief overview of neurons
- Derivation of the cable equation
- Scaling/dimensionless form
- Example models

## History lesson





## Neurons (1)



## Neurons (2)

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. We will first look at conduction in the dendrites, passive conduction.

## Why is the cable equation important?

- Fundamental for modeling neurons
- Signal propagation in Purkinje network
- Extends to cardiac conduction in 3D (bidomain, monodomain)

## Fundamental quantities and assumptions

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

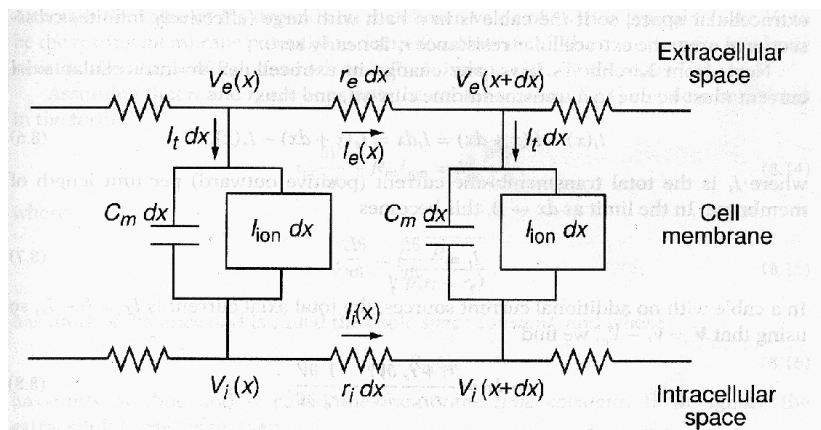
- $V_i$  and  $V_e$  are intra- and extracellular potentials
- $I_i$  and  $I_e$  are intra- and extracellular (axial) current
- $r_i$  and  $r_e$ ; intra- and extracellular resistance per unit length

We have

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

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

## Sketch of a discrete cable



## Currents are assumed to be Ohmic

We assume Ohmic resistance:

$$\begin{aligned} V_i(x + \Delta x) - V_i(x) &= -I_i(x)r_i\Delta x \\ V_e(x + \Delta x) - V_e(x) &= -I_e(x)r_e\Delta x \end{aligned}$$

In the limit:

$$\begin{aligned} I_i &= -\frac{1}{r_i} \frac{\partial V_i}{\partial x} \\ I_e &= -\frac{1}{r_e} \frac{\partial V_e}{\partial x} \end{aligned}$$

## Conservation of current (1)

Any current leaving the intracellular domain has to enter the extracellular domain, and vice-versa. Total current is conserved between  $x$  and  $x + \Delta x$ :

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

where  $I_t$  is transmembrane current, per unit length.

Taking the limit  $\Delta x \rightarrow 0$  yields

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

## Conservation of current (2)

We now have the membrane current  $I_t$  expressed in terms of  $I_i, I_e$ . We want a relation between the  $I_t$  and the membrane potential  $V$ .

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

## Conservation of current (3)

cont.

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

so

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

## Incorporating cell membrane physiology

From the membrane model previously derived we have

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

where  $p$  is the circumference of the cable. The total 1D cable model is then:

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

## Physical units

So far we have not considered the physical units of the terms. Typical units are

Quantity	Dimension	Typical unit
$p$	length	$cm$
$C_m$	capac./area	$\mu F/cm^2$
$V$	voltage	$mV$
$I_{ion}$	current/area	$\mu A/cm^2$
$r_i, r_e$	res./length	$10^3 \Omega/cm$
$x$	length	$cm$
$t$	time	$ms$

## Exercise

Verify that all the terms in the cable equation have the same physical units:

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

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$t$	time	$ms$

What is the unit of the terms in the equation?

## Scaling the cable equation (1)

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

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

where  $V_0$  is the resting potential. Multiply with  $R_m$  to get

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

Here we have assumed  $r_i$  and  $r_e$  constant.

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

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

## Scaling the cable equation (2)

We introduce the dimensionless variables:

$$T = t / \tau_m, X = x / \lambda_m$$

We can then write:

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

A solution  $\hat{V}(T, X)$  of (??) implies that  $V(t, x) = \hat{V}(t / \tau_m, x / \lambda_m)$  will satisfy the unscaled equation.

The scaled equation has units of voltage, but can easily be non-dimensionalized by introducing  $V = V_0 + \tilde{V} \bar{V}$ , where  $\bar{V}$  is a characteristic voltage and  $\tilde{V}$  is a dimensionless variable.

## The reaction term

The form of  $f$  depends on the cell type we want to study. For the axon  $I_{ion}(m, n, h, V)$  of the HH-model is a good candidate.

For the dendrite, which is non-excitable, a linear resistance model is good:

$$I_{ion} = \frac{1}{R_m} (V - V_{eq})$$

or in dimensionless form  $f = -V$ :

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

## Boundary- and initial conditions

Need boundary and initial values. Initially at rest:

Initially at rest:

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

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:

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

## Passive conduction

The linear cable in dimensionless form

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

We consider a semi-infinite (i.e. long) cable with voltage clamped to a constant  $V_c$  at  $X = 0$ . At steady state, we have

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

with solution

$$V = V_c e^{-X} = V_c e^{-x/\lambda_m}$$

What does this tell you about how a signal decays along the cable? How strong is the signal one space constant from the source? How about ten space constants?

## Exercise

Remember the expression for the space constant:

$$\lambda_m = \sqrt{R_m/(p(r_i + r_e))} \approx \sqrt{R_m/(pr_i)} = \sqrt{R_m/(pR_c/A)},$$

Assume a circular cross section with diameter  $d$ . Typical values for a mammalian neuron are  $R_m = 7000\Omega\text{cm}^2$ ,  $R_c = 150\Omega\text{cm}$ ,  $d = 10.0\mu\text{m}$

Calculate the space constant  $\lambda_m$ . How does it compare to the length of a human axon?

## The bistable equation (1)

The simplest model of active conduction in neuron is obtained by choosing the reaction term

$$f(V) = AV(1 - V)(V - \alpha),$$

where  $\alpha$  is a parameter between 0 and 1, and  $A$  is a scaling parameter for the reaction term.

## The bistable equation (2)

We have

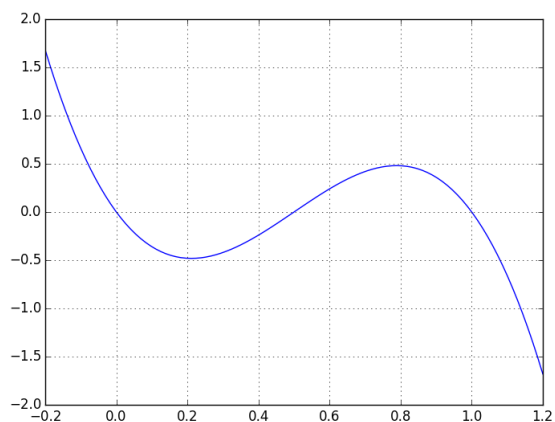
$$\frac{\partial V}{\partial t} = \frac{\partial^2 V}{\partial x^2} + AV(1 - V)(V - \alpha),$$

and if we neglect the diffusion term we get

$$\frac{\partial V}{\partial t} = AV(1 - V)(V - \alpha),$$

The right hand side has three zero's;  $V = 0$ ,  $V = 1$ ,  $V = \alpha$ . These are equilibrium points for the equation ( $\partial V/\partial t = 0$ ).

### The bistable equation (3)



Here  $\alpha = 0.5$ . What happens if the solution is perturbed away from the three equilibrium points  $V = 0, V = 1, V = \alpha$ ? (Recall that  $\partial V / \partial t = f(V)$ )

### The bistable equation (4)

- The equation has one unstable and two stable equilibrium points
- Any initial condition  $V < \alpha$  will approach  $V = 0$
- Any initial condition  $V > \alpha$  will approach  $V = 1$

In 1D (with diffusion), the solution is a traveling front.

### The FitzHugh-Nagumo model (1)

- The bistable equation describes a traveling front, but never returns to the resting potential
- To describe a propagating action potential we need to add a *recovery variable*
- The result is the FitzHugh-Nagumo (FHN) model, the simplest model for qualitatively realistic propagation in excitable cells



$$\begin{aligned}\frac{\partial V}{\partial t} &= \frac{\partial^2 V}{\partial x^2} + AV(1-V)(V-\alpha) - w, \\ \frac{\partial w}{\partial t} &= \epsilon(V - \gamma w),\end{aligned}$$

with  $\epsilon, \gamma > 0$  and  $w(0, x) = 0$ .

## The FitzHugh-Nagumo model (2)

Again, we can examine the behavior of the model by neglecting diffusion:

$$\begin{aligned}\frac{\partial V}{\partial t} &= AV(1-V)(V-\alpha) - w, \\ \frac{\partial w}{\partial t} &= \epsilon(V - \gamma w),\end{aligned}$$

- Initially, the model behaves as the bistable equation
- As  $V$  increases,  $\frac{\partial w}{\partial t} > 0$
- $w > 0$  will "pull"  $V$  back towards  $V = 0$
- In 1D, the solution is a traveling wave resembling an action
- potential

## Summary

- The cable equation describes signal propagation in *leaky* cables
- 1D reaction-diffusion equation, the form of the reaction term depends on the application (properties of the membrane):
  - Linear; passive membrane
  - Cubic; bistable equation (propagating front)
  - FHN; coupled to ODE (propagating AP)
  - Hodgkin-Huxley, cardiac cell models, etc...