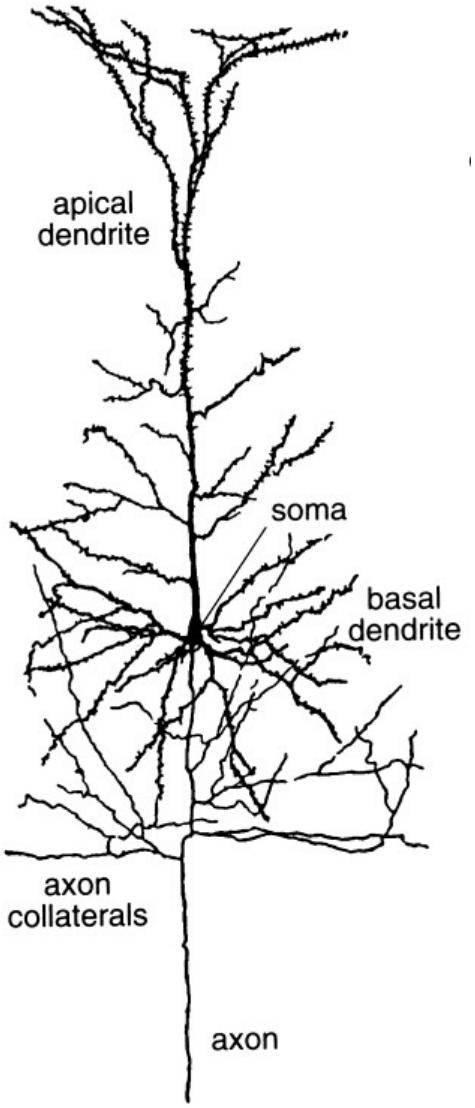
Single Neuron Biophysics & Models

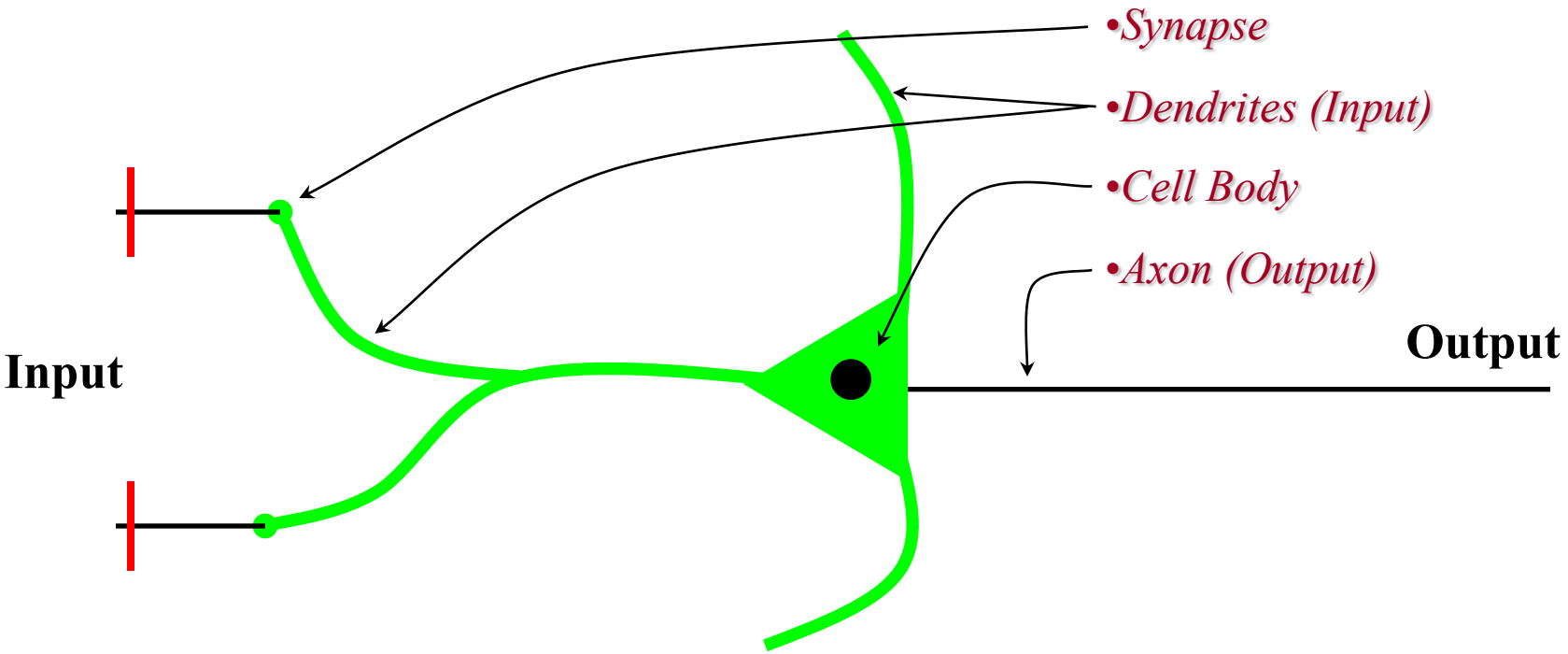
Basics of proteins

- https://youtu.be/78QUeXVKiJ4

The Neuron


apical
dendrite
soma
basal
dendrite
axon
collaterals
axon

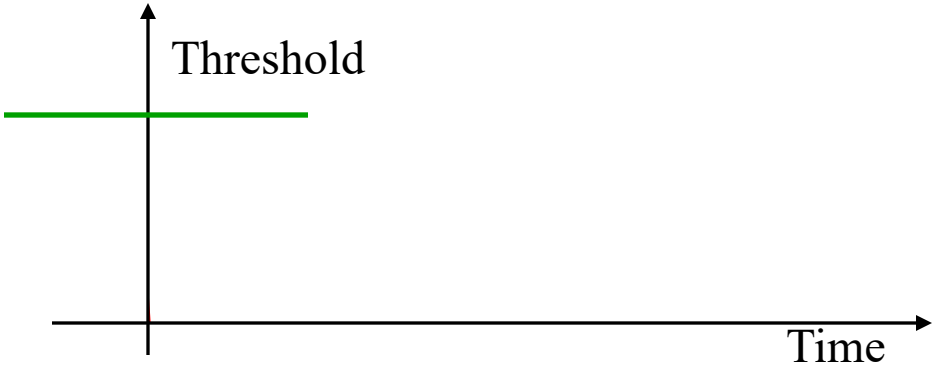
Neuron: The Device

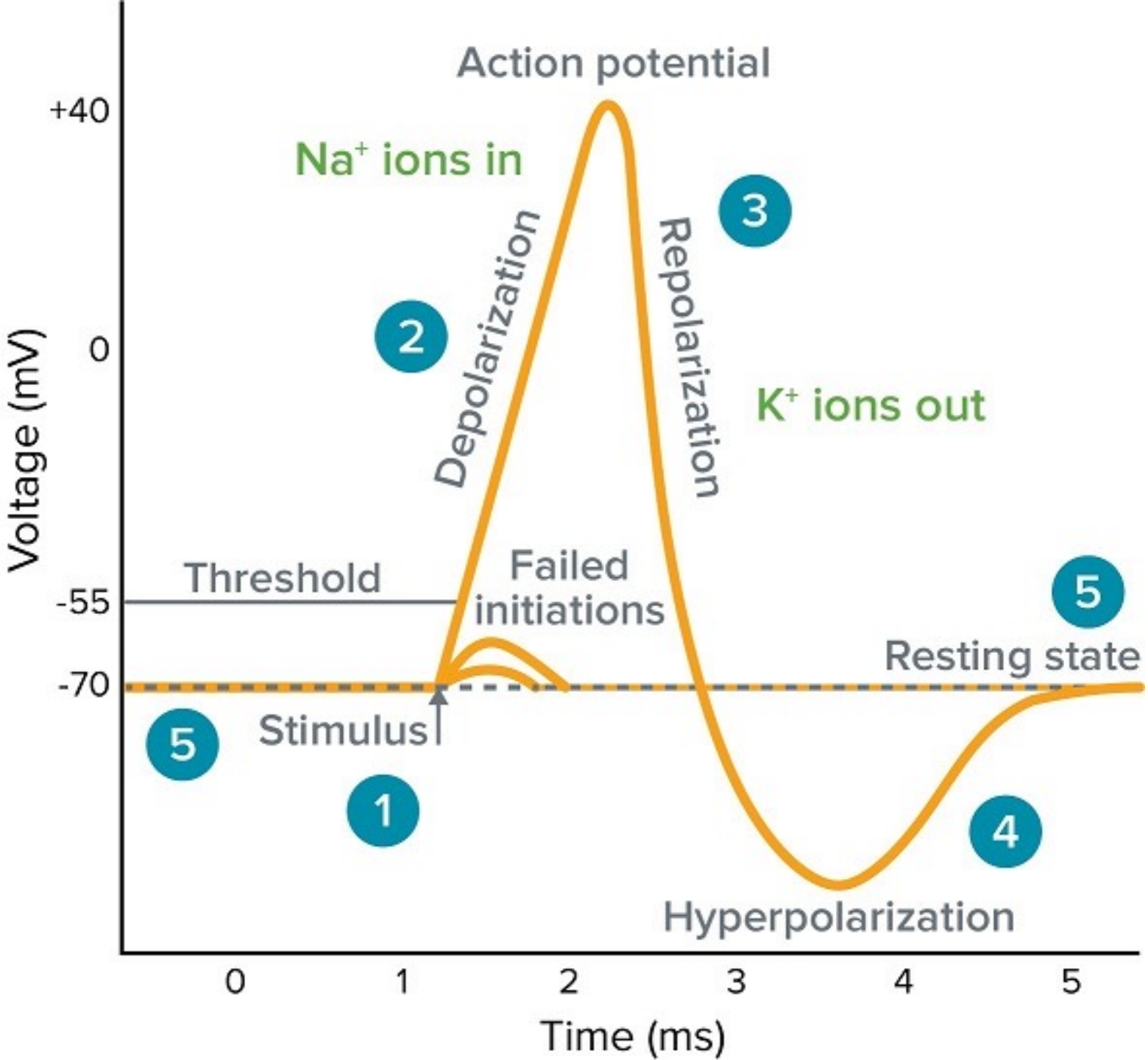


Equilibrium: Membrane Potential

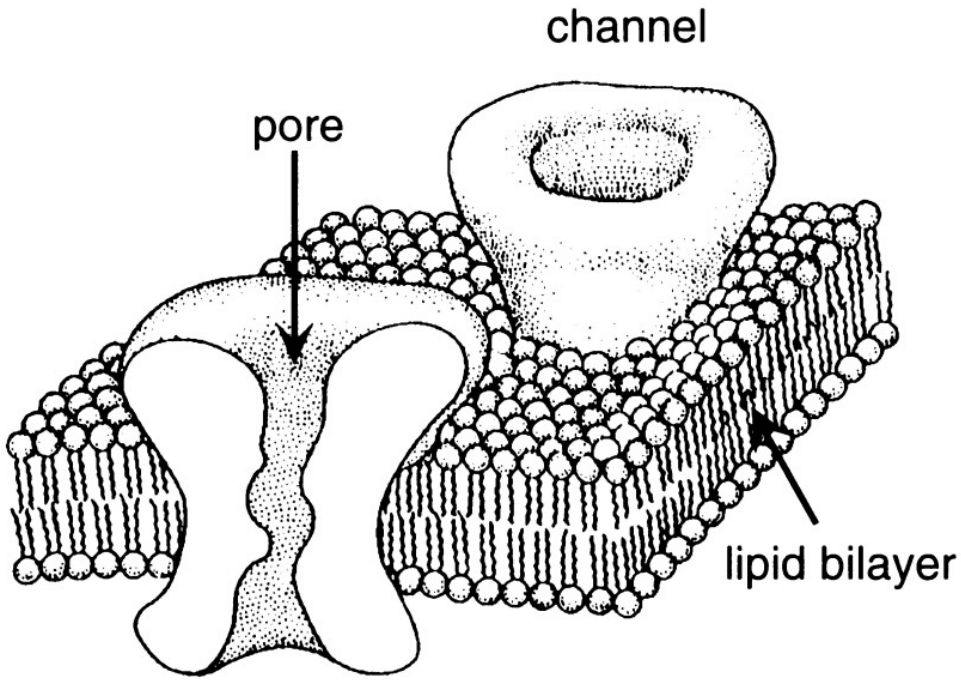
Dendrites: Passive Conductance

Axon: Spikes (Hodgkin Huxley Eqns)




Action potential
+40
Na+ ions in
3
Depolarization
Repolarization
2
0
K+ ions out
Voltage (mV)
Threshold
Failed
initiations
5
-55
Resting state
-70
5
Stimulus
1
4
Hyperpolarization
0
1
2
3
4
5
Time (ms)

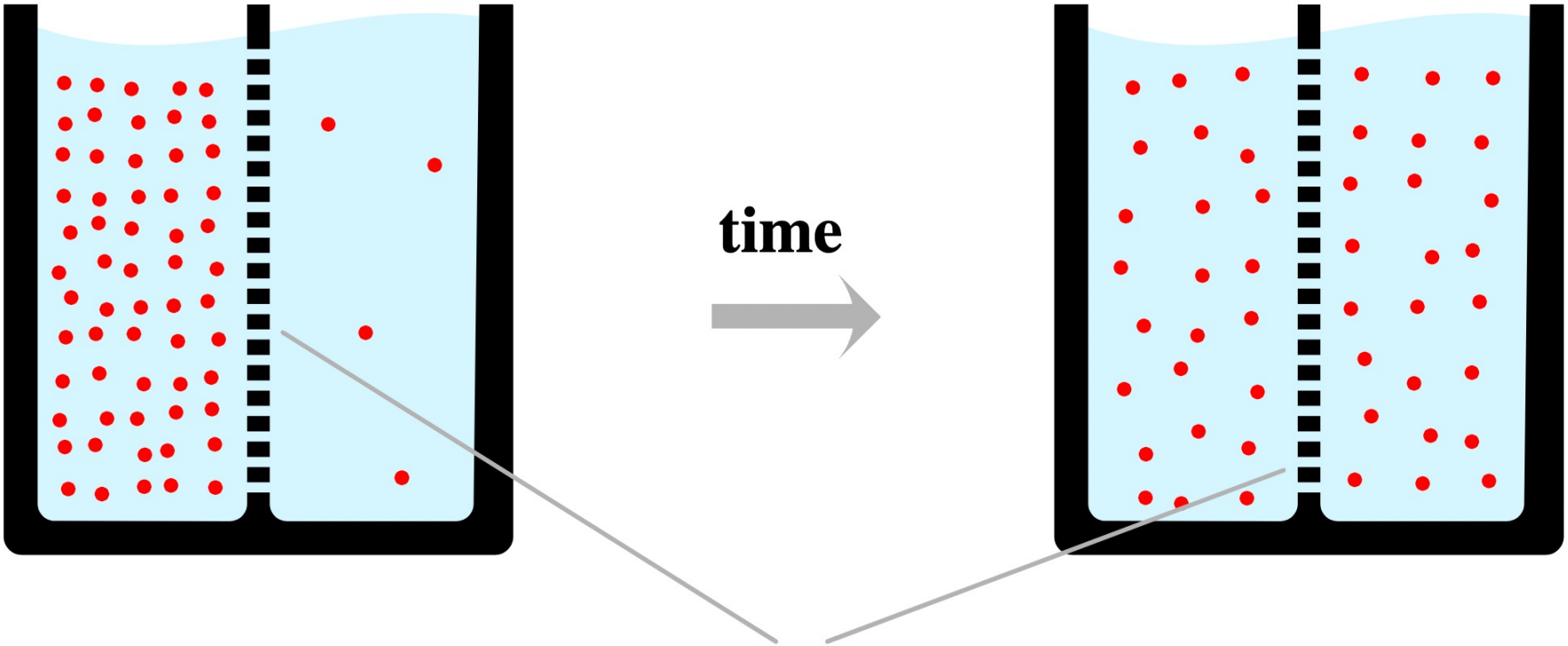
The Membrane



Membrane: 3 to 4 nm thick, essentially impermeable

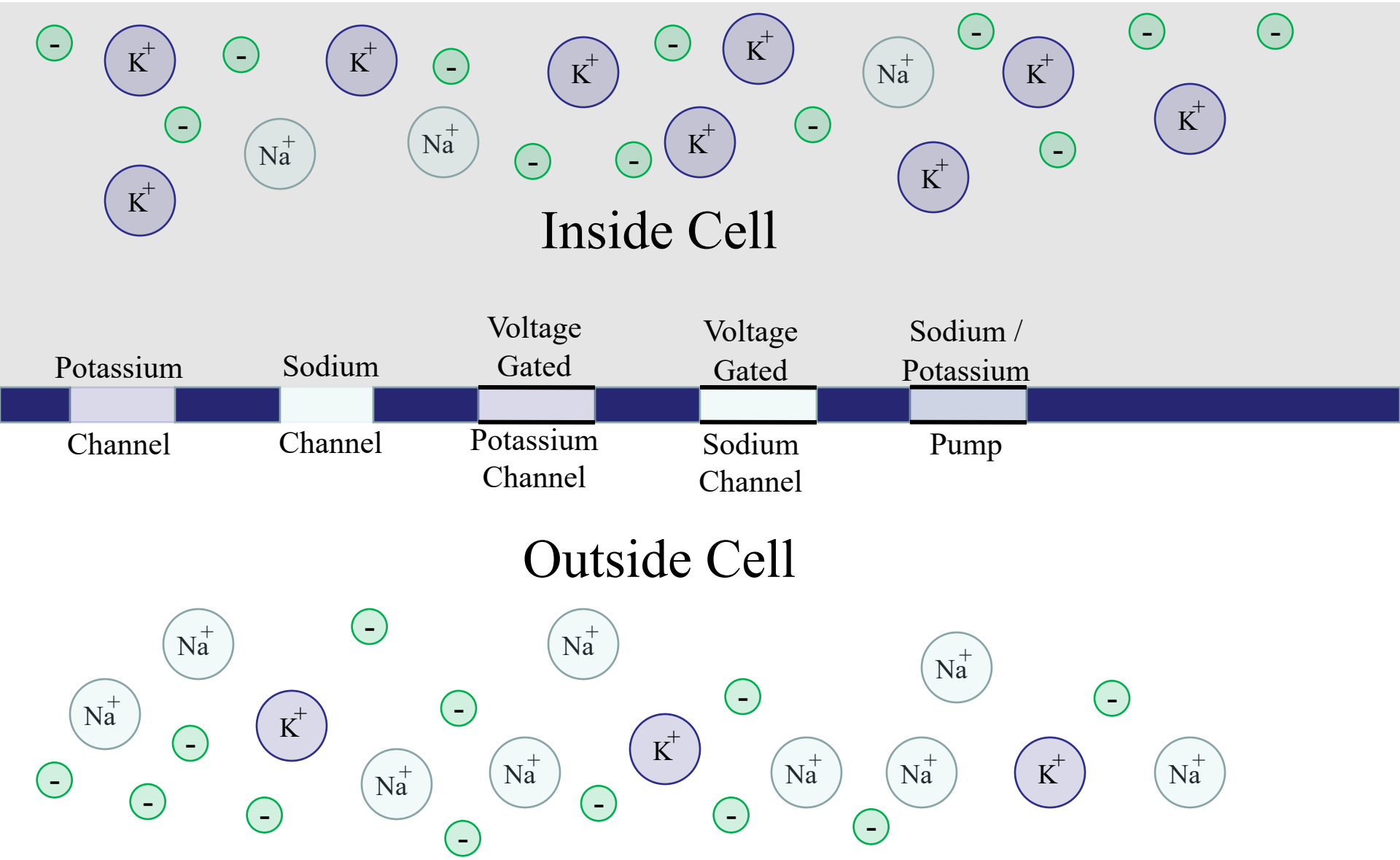
Ionic Channels: Selectively permeable (10,000 times smaller resistance)

Diffusion

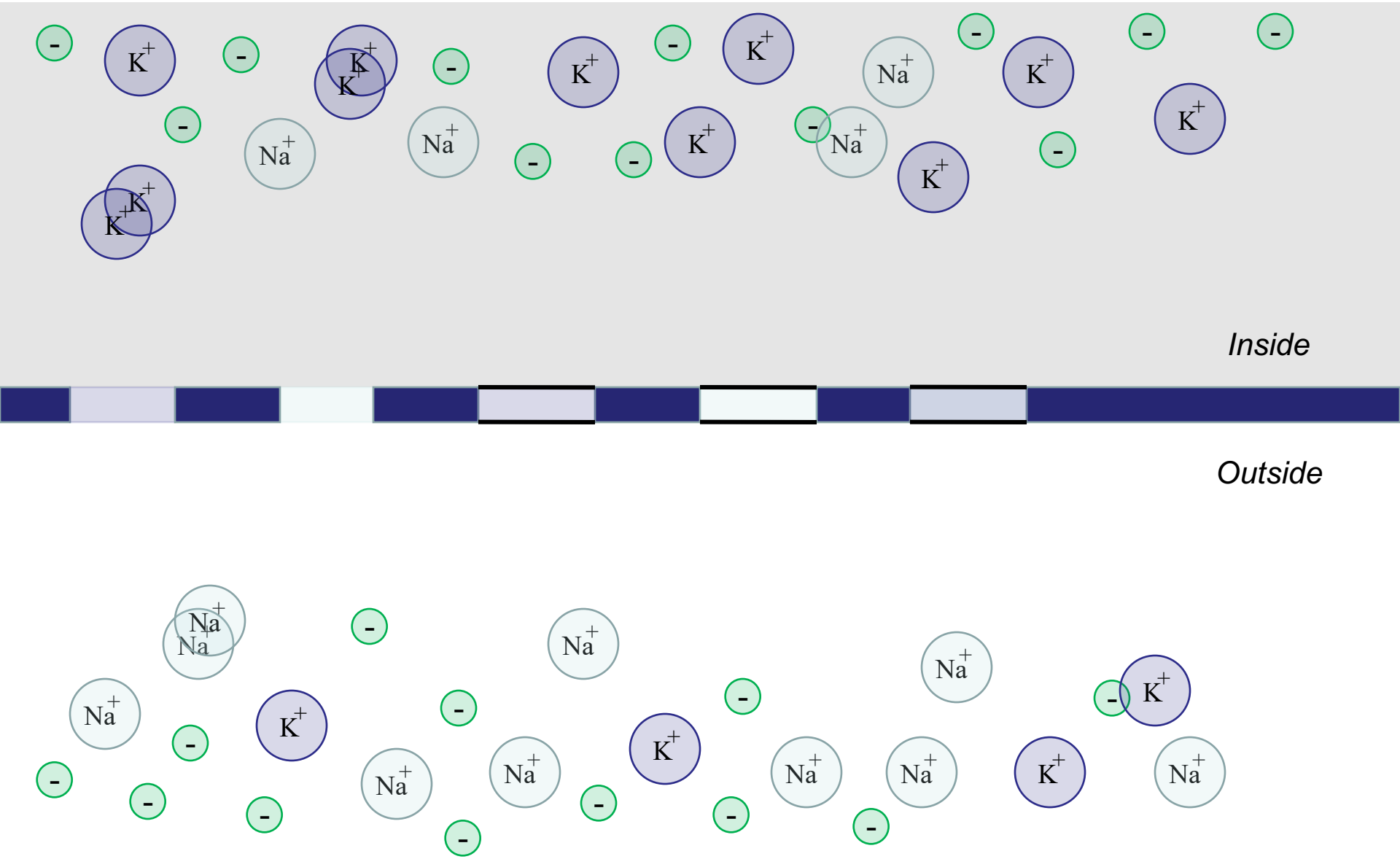


Electric field

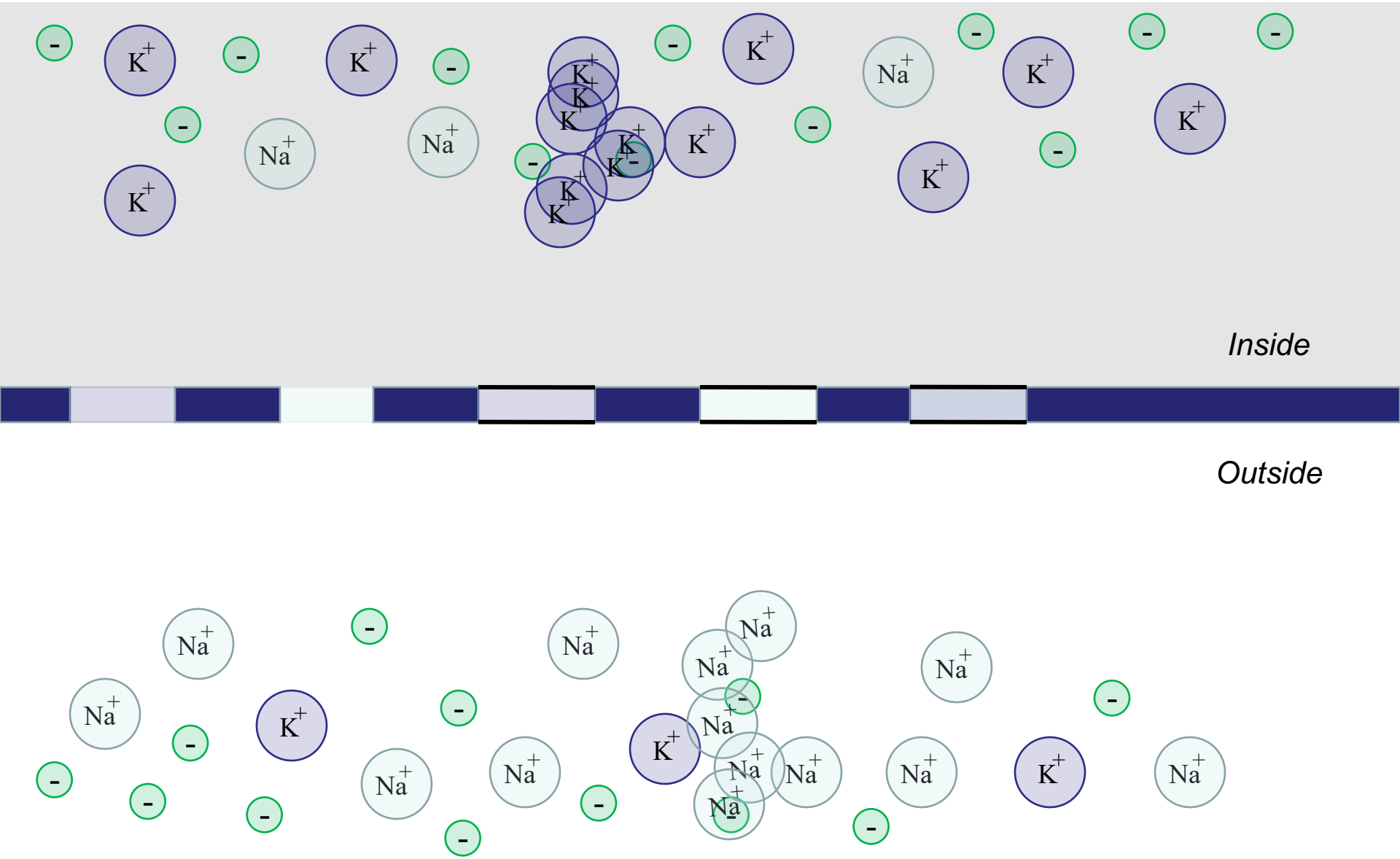
Basic Biophysics of the neuron



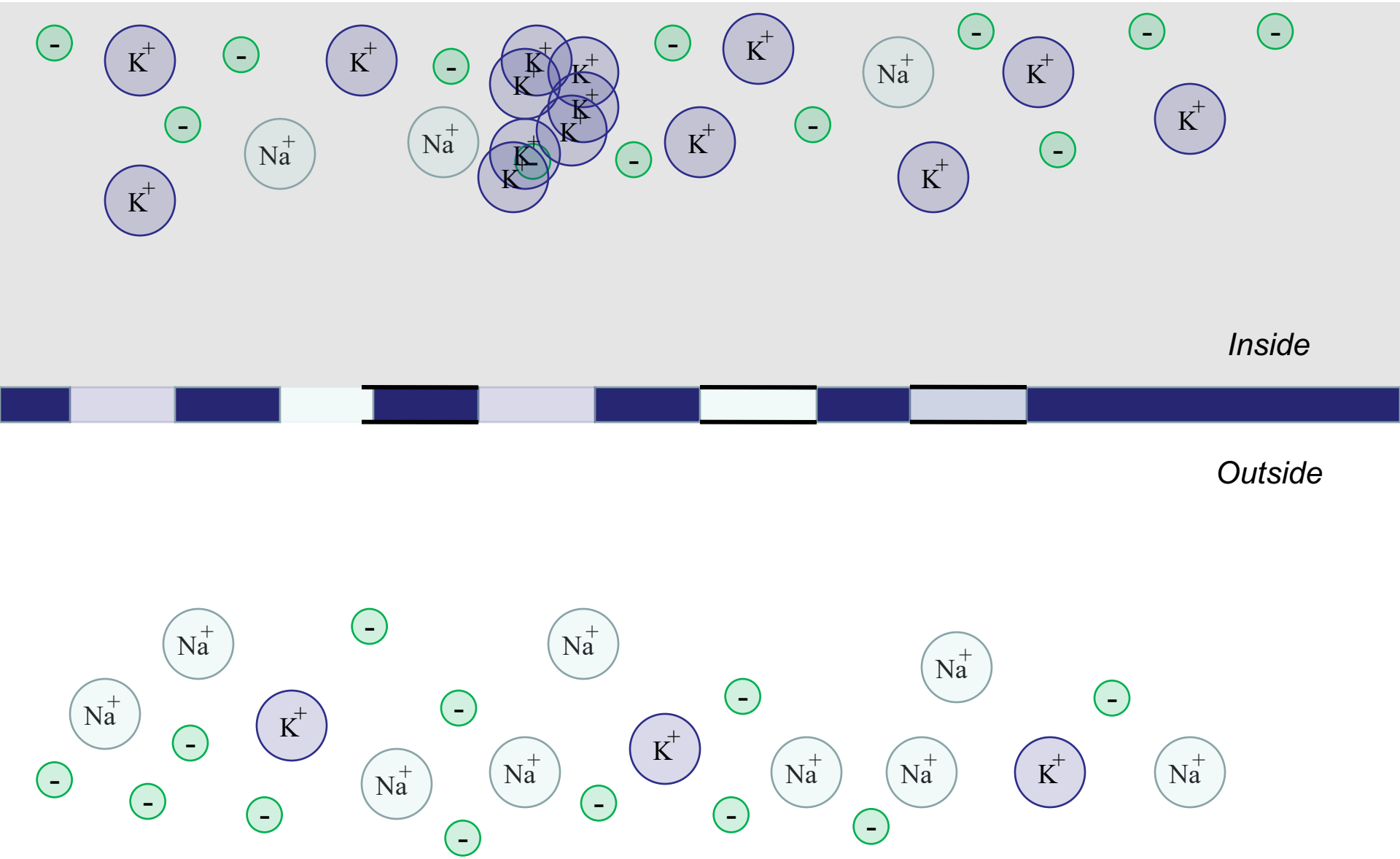
Basic Biophysics of the neuron - equilibrium



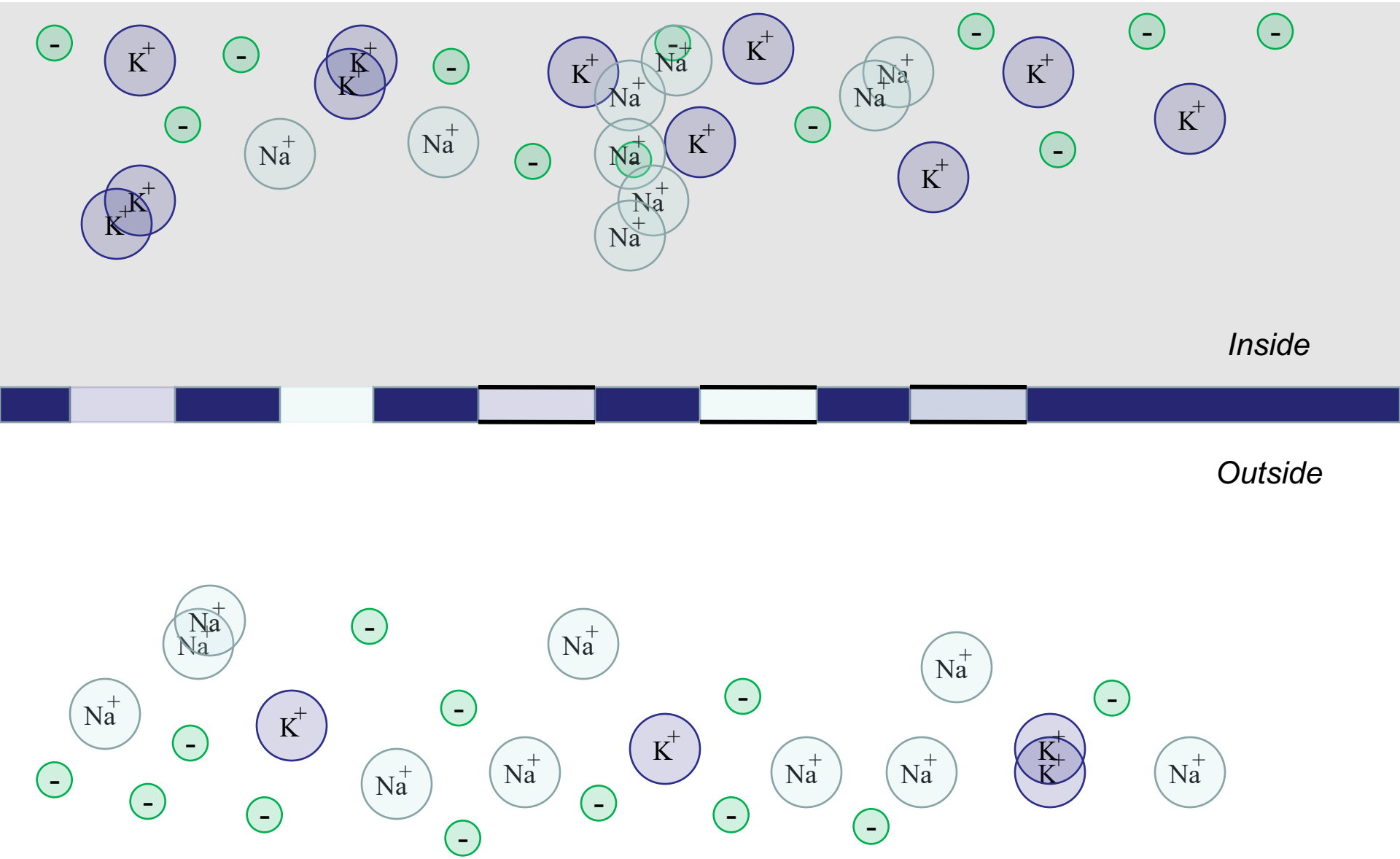
Basic Biophysics of the neuron – Action Potential



Basic Biophysics of the neuron – Action Potential



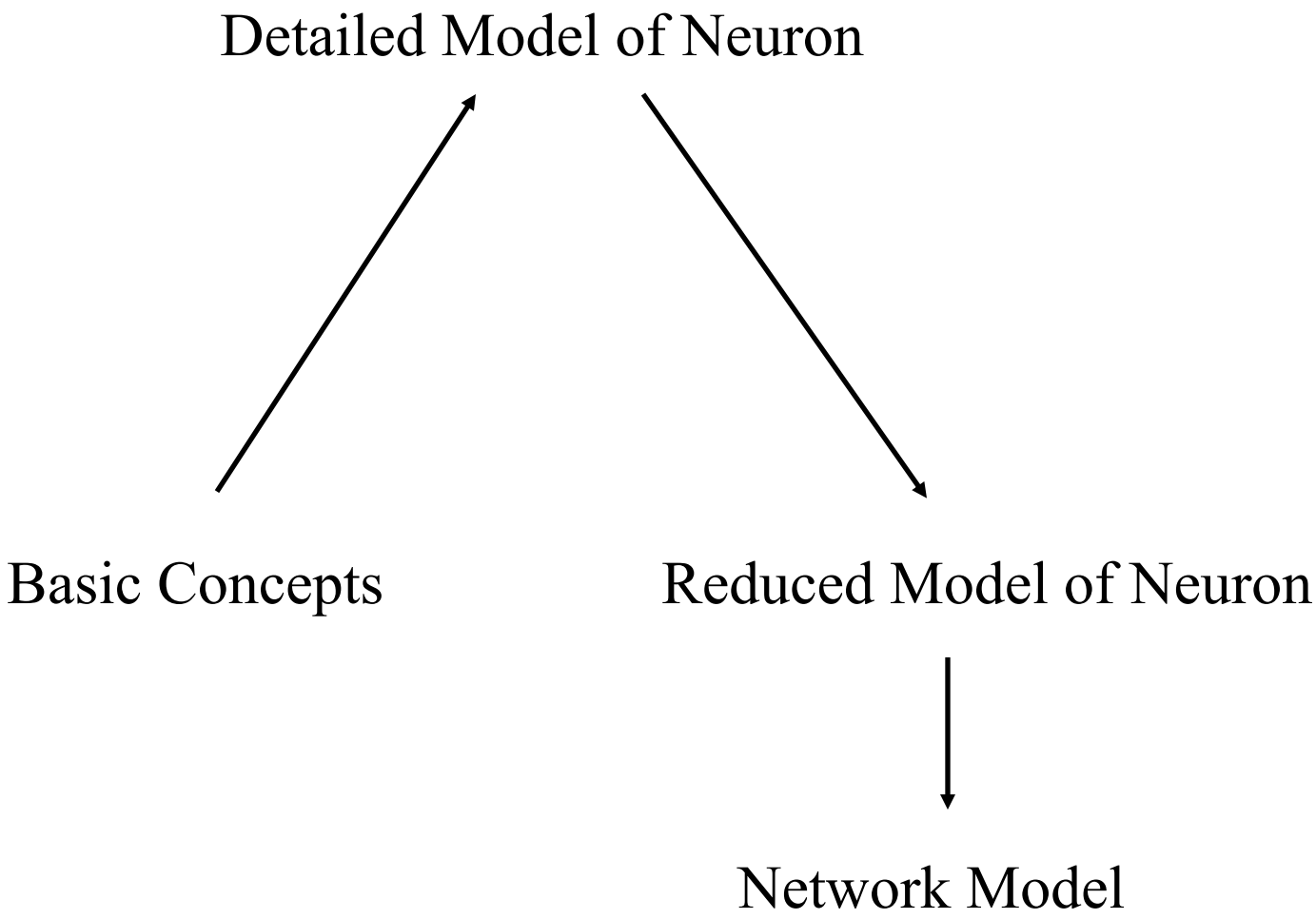
Basic Biophysics of the neuron – Action Potential



Some more intricacies

- More types of ions
- A zoo of ion channels, receptors
- Varied anatomical features

Approach


Detailed Model of Neuron
Basic Concepts
Reduced Model of Neuron
Network Model

- René Magritte, 1929

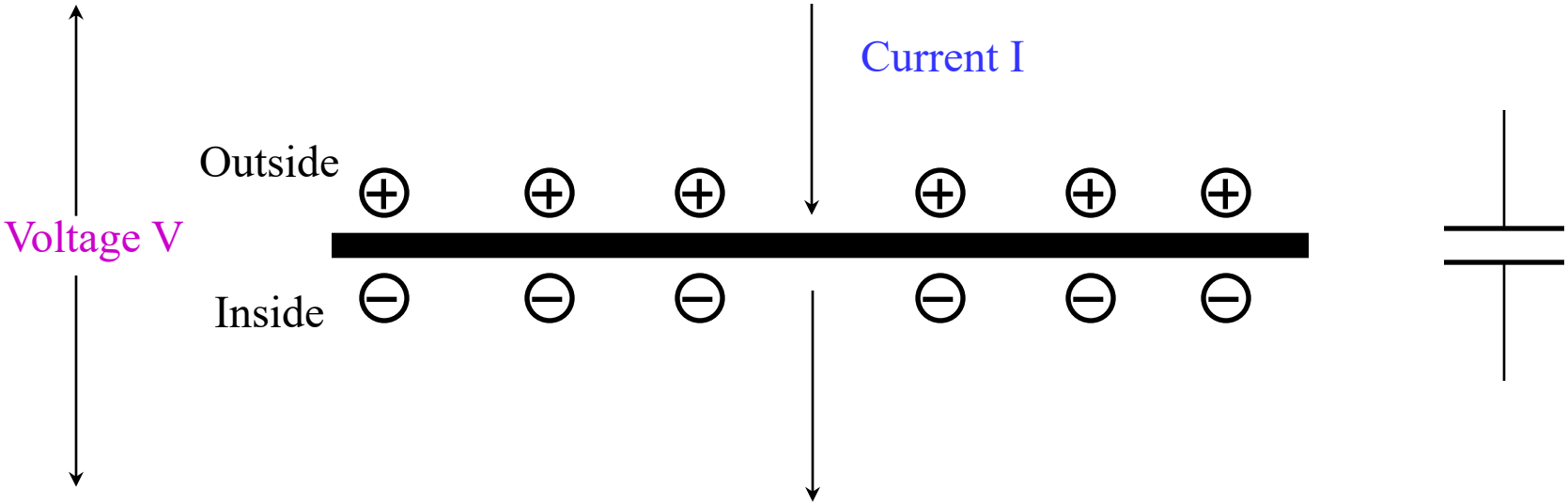
On Exactitude in Science
Jorge Luis Borges, *Collected Fictions*, translated by Andrew Hurley.

…In that Empire, the Art of Cartography attained such Perfection that the map of a single Province occupied the entirety of a City, and the map of the Empire, the entirety of a Province. In time, those Unconscionable Maps no longer satisfied, and the Cartographers Guilds struck a Map of the Empire whose size was that of the Empire, and which coincided point for point with it. The following Generations, who were not so fond of the Study of Cartography as their Forebears had been, saw that that vast Map was Useless, and not without some Pitilessness was it, that they delivered it up to the Inclemencies of Sun and Winters. In the Deserts of the West, still today, there are Tattered Ruins of that Map, inhabited by Animals and Beggars; in all the Land there is no other Relic of the Disciplines of Geography.

—Suarez Miranda, *Viajes de varones prudentes*, Libro IV, Cap. XLV, Lerida, 1658

Rodin vs. Brancusi

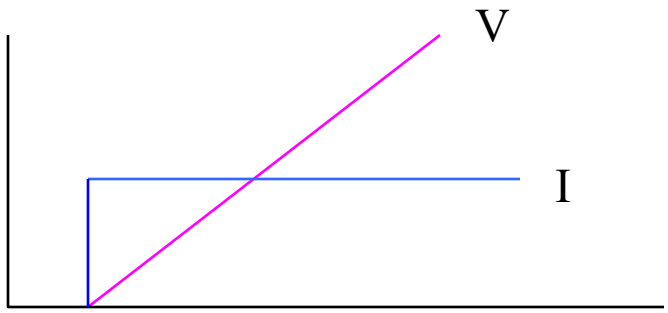
The Membrane: Capacitance



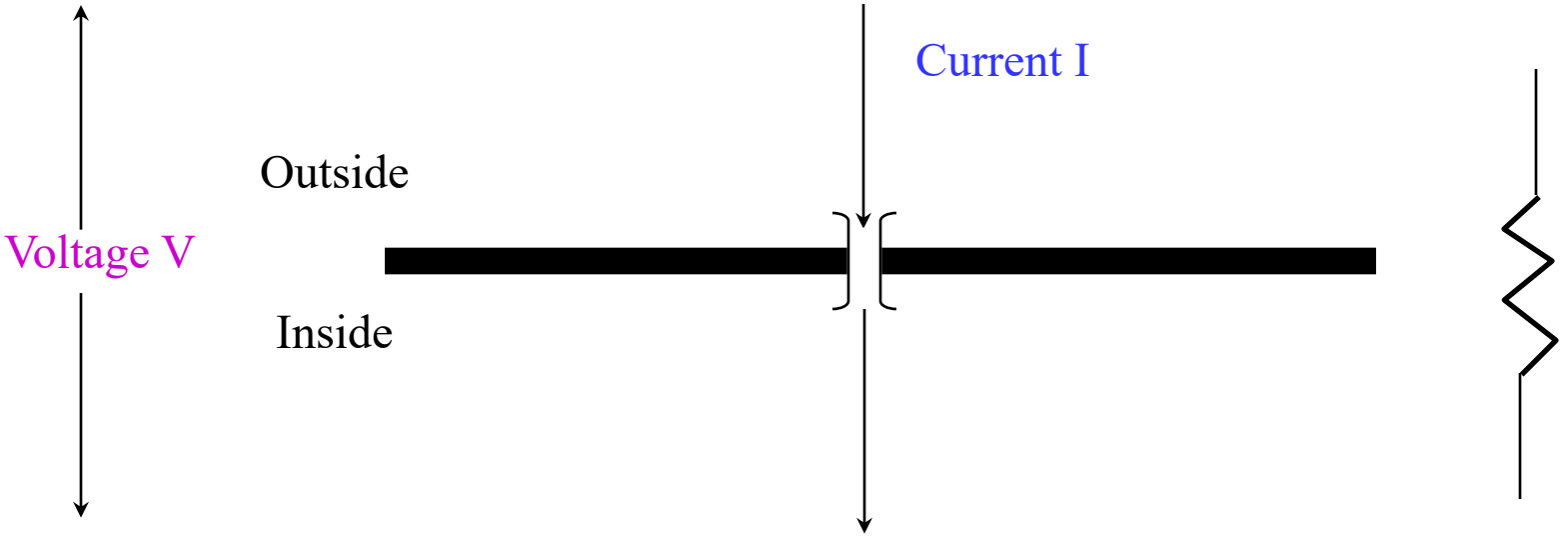
$C = Q/V$ 1 Farad = 1 Coulomb/ 1 Volt
$(Q = CV)$;

$dQ/dt = I$

$I = C\ dV/dt$

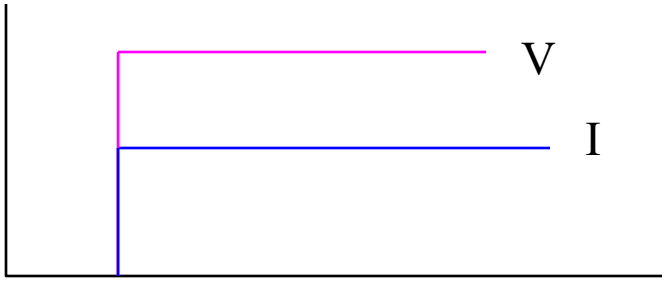


The Membrane: Resistance

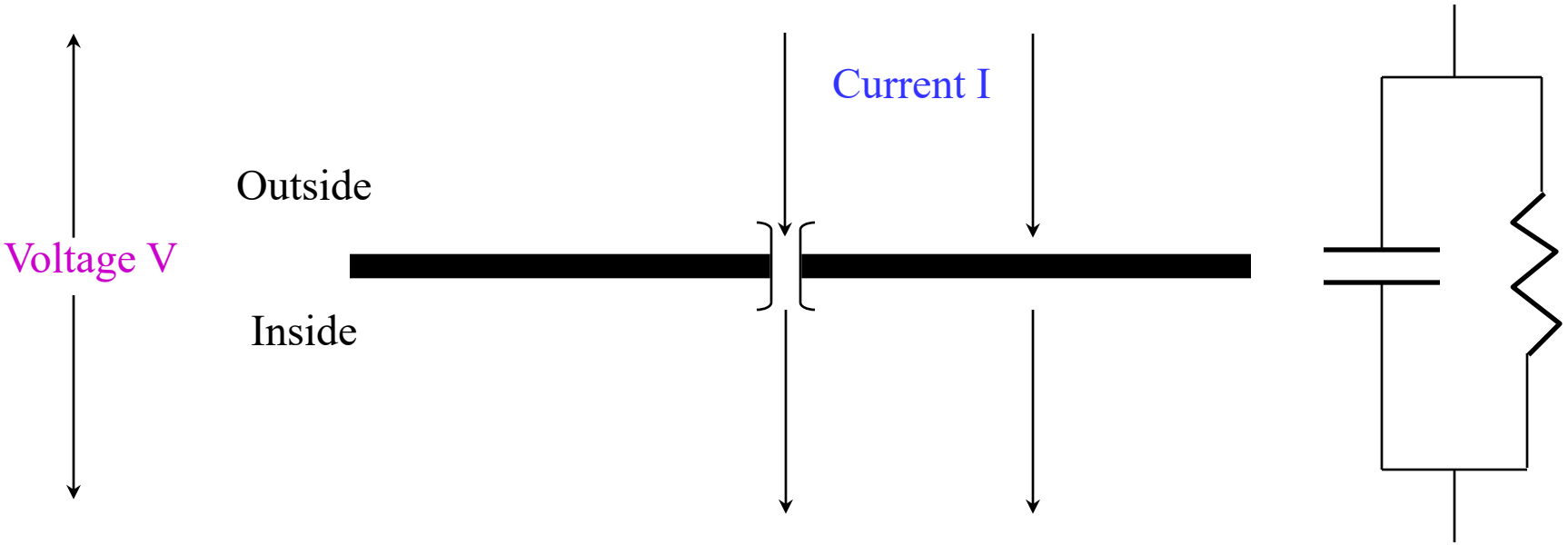


R = V/I 1 Ohm = 1 Volt/ 1 Ampere

I = V/R

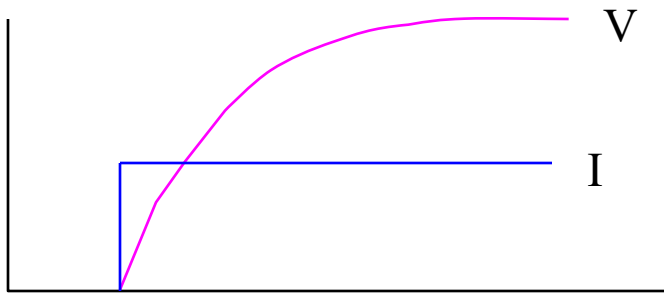


The Membrane: Capacitance and Resistance



$$I = C\,dV/dt + V/R$$

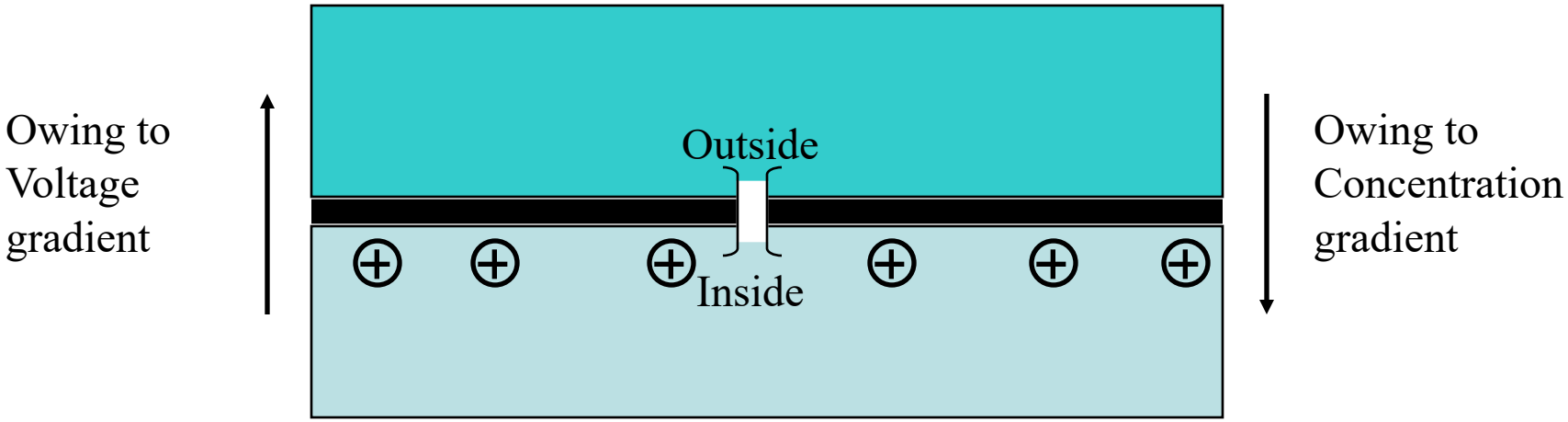
$$(C*R)\,dV/dt = -V + IR$$



The Membrane: Membrane Potential

Case 1: Single type of Ion (Na^+)

Charge Balanced out by impermeable ion



Reversal Potential : When opposing currents balance each other out.

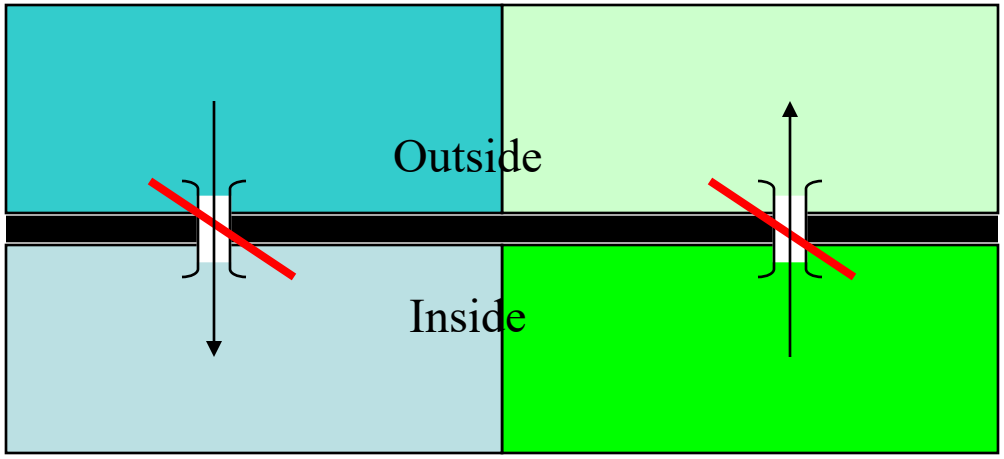
Nernst Equation: $E = (RT/z) \ln([outside]/[inside])$

Reversal Potential for Na^+ is around *+50 mV* (based on typical concentration gradients)

Note: Reversal potential **does not** depend upon *resistance.*

The Membrane: Membrane Potential

Case 1: Two types of Ions (Na^+ and K^+)



Equilibrium Potential : When opposing currents balance each other out (*-70 mV)*.

Goldman-Hodgkin-Katz Equation:

$$V_m = \frac{RT}{F} \ln \frac{P_K[K^+]_o + P_{Na}[Na^+]_o + P_{Cl}[Cl^-]_i}{P_K[K^+]_i + P_{Na}[Na^+]_i + P_{Cl}[Cl^-]_o} \qquad (2\text{–}1)$$

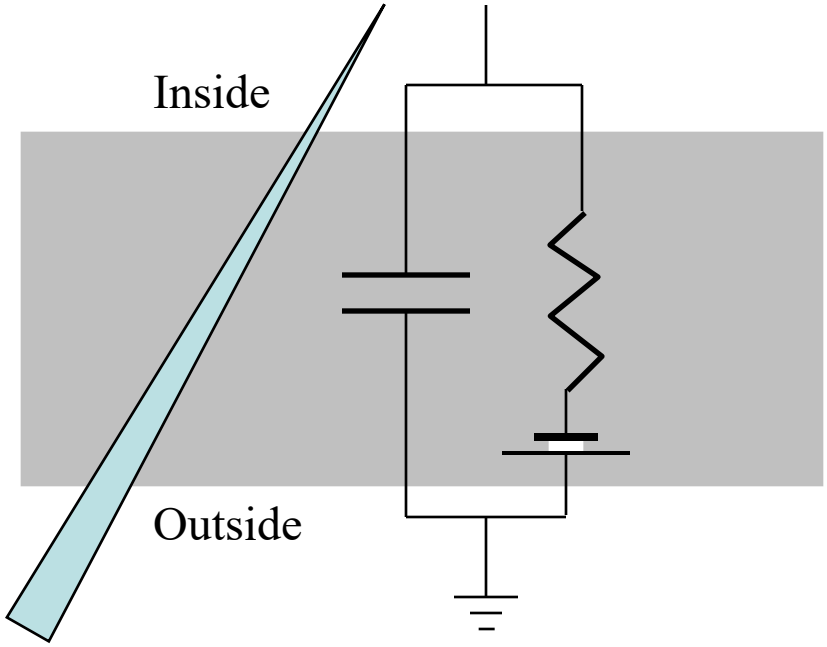
where R is the gas constant, T the absolute temperature, F Faraday's constant, $[\cdot]_i$s

Why ingesting Pottasium Cloride is deadly; ingesting Sodium Cloride is not.

Note: Equilibrium potential **does** depend upon relative *resistances.*

Reversal potentials ---- Na^+ *: +50 mV* K^+ *: -80 mV*

Passive membrane: Equivalent Circuit



Voltage independent channels

Single Compartment

Electrotonically compact neuron.

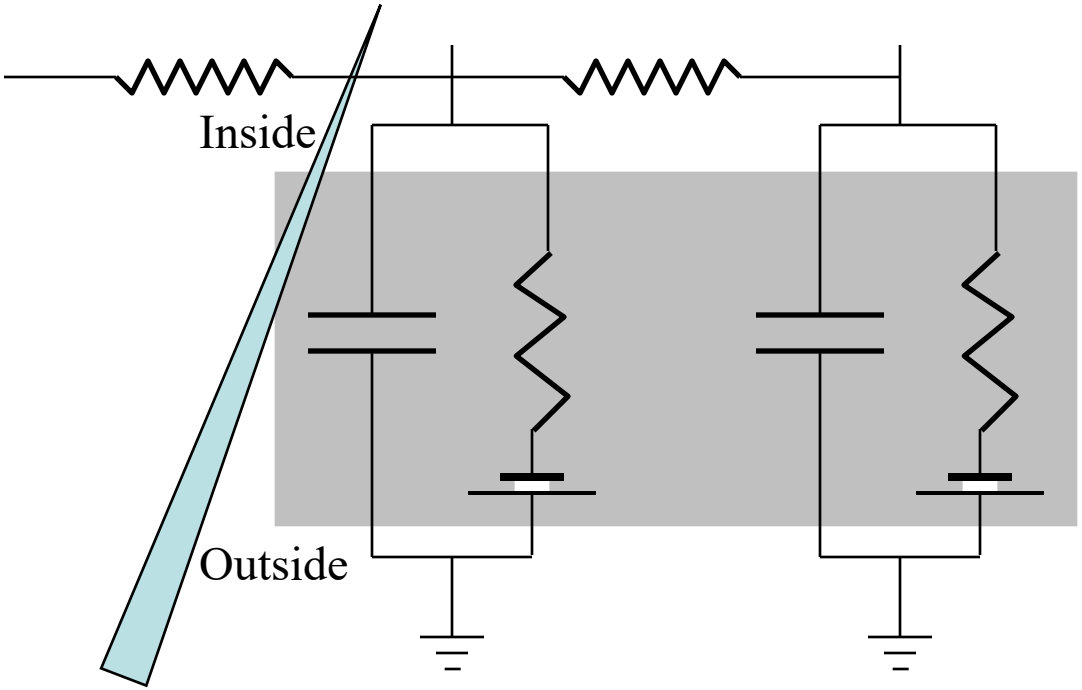
$\mathbf{I_{INJ} = I}$

$\mathbf{I = C\ dV/dt + (V\text{-}E_L)/R}$

Use new variable: $V = V - E_L$

$\mathbf{(C*R)\ dV/dt = -V + IR}$

Passive membrane: Cable Equation



Voltage independent channels

Multiple Compartments

Electrotonically non-compact neuron.

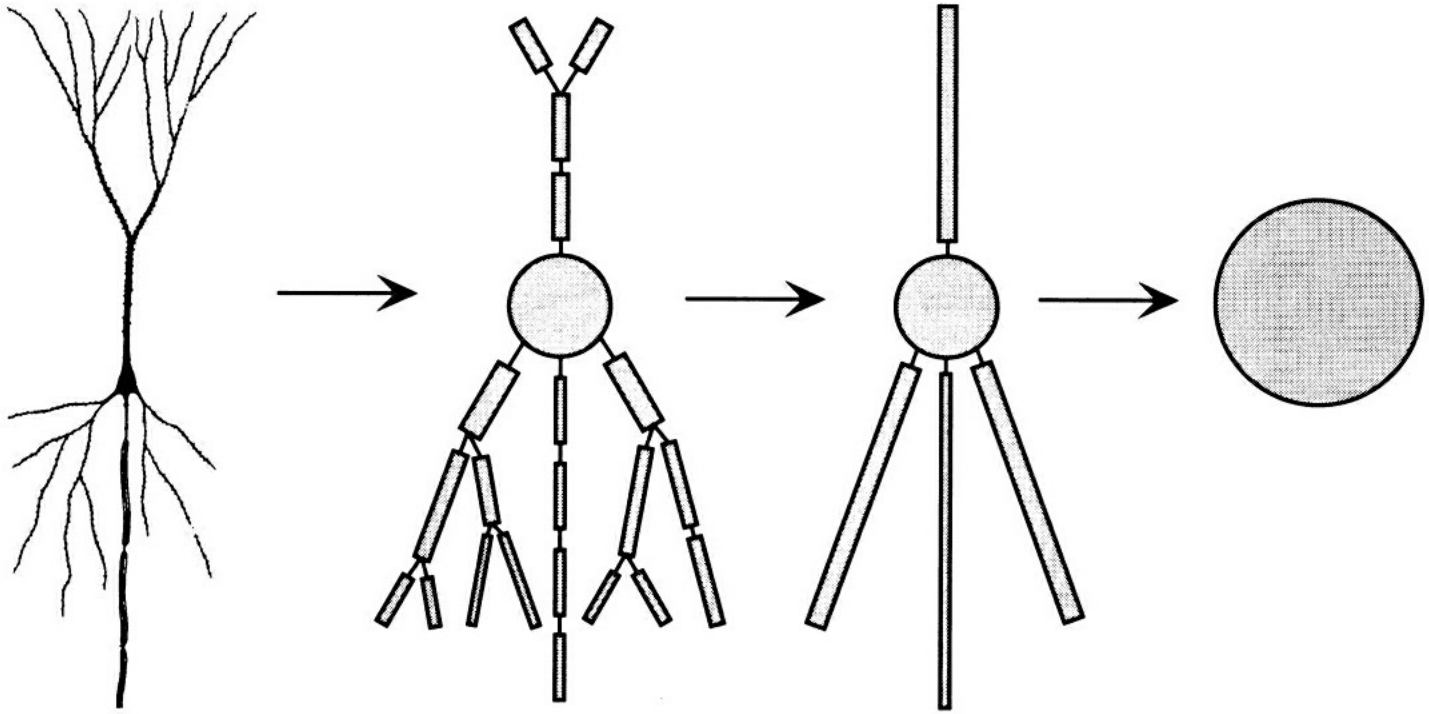
$$C\,\partial V/\partial t = -V/R + I$$

$$\partial V/\partial x = ir \qquad \text{hence } \partial^2 V/\partial x^2 = r\partial i/\partial x$$

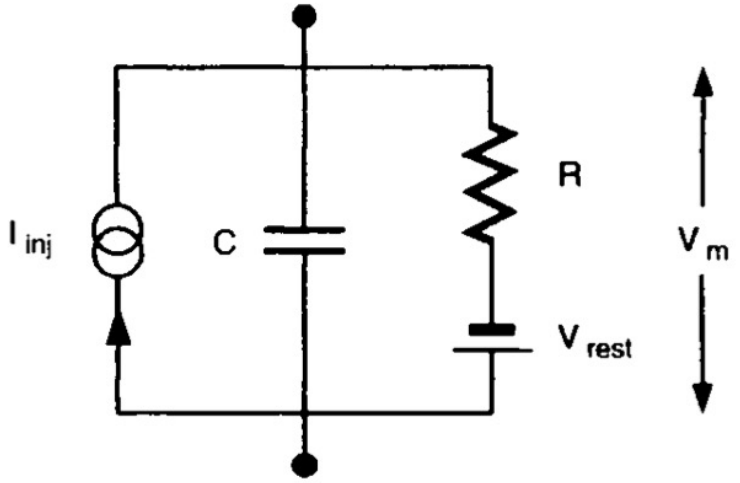
$$I_{INJ} = I - \partial i/\partial x \quad \text{hence } I = I_{INJ} + \partial i/\partial x$$

$$C\partial V/\partial t = (1/r)\,\partial^2 V/\partial x^2 - (1/R)V + I_{INJ}$$

Passive membrane: Compartmental Model



Solving the membrane equation



$$C\frac{dV_m(t)}{dt} + \frac{V_m(t) - V_{\text{rest}}}{R} = I_{\text{inj}}(t)\,.$$

With $\tau = RC$, with units of $\Omega \cdot \text{F} = \text{sec}$, we can rewrite this as

$$\tau\frac{dV_m(t)}{dt} = -V_m(t) + V_{\text{rest}} + RI_{\text{inj}}(t)\,.$$

Let us assume that the membrane potential starts off at $V_m(t = 0) = V_{\text{rest}}$.

If I_inj=0, this means V_m(t) = V_rest

Suppose we switch on a constant current of amplitude I_0 at t=0.

The general form of the solution of the differential equation is:

$$V_m(t) = v_0 e^{-t/\tau} + v_1 \tag{1.7}$$

where v_0 and v_1 depend on the initial conditions. Replacing this into Eq. 1.6 and canceling identical variables on both sides leaves us with

$$v_1 = V_{\text{rest}} + R I_0 . \tag{1.8}$$

We obtain the value of v_0 by imposing the initial condition $V_m(t = 0) = v_0 + v_1 = V_{\text{rest}}$. Defining the steady-state potential in response to the current as $V_\infty = R I_0$, we have solved for the dynamics of V_m for this cell,

$$V_m(t) = V_\infty(1 - e^{-t/\tau}) + V_{\text{rest}} . \tag{1.9}$$

This equation tells us that the time course of the deviation of the membrane potential from its resting state, that is, $V_m(t) - V_{\text{rest}}$, is an exponential function in time, with a time constant equal to τ. Even though the current changed instantaneously from zero to I_0, the membrane potential cannot follow but plays catch up. This is demonstrated graphically in Fig. 1.3. How slowly V_m changes is determined by the product of the membrane resistance and the capacitance; the larger the capacitance, the larger the current that goes toward charging up C. Note that τ is independent of the size of the cell,

$$\tau = RC = R_m C_m . \tag{1.10}$$

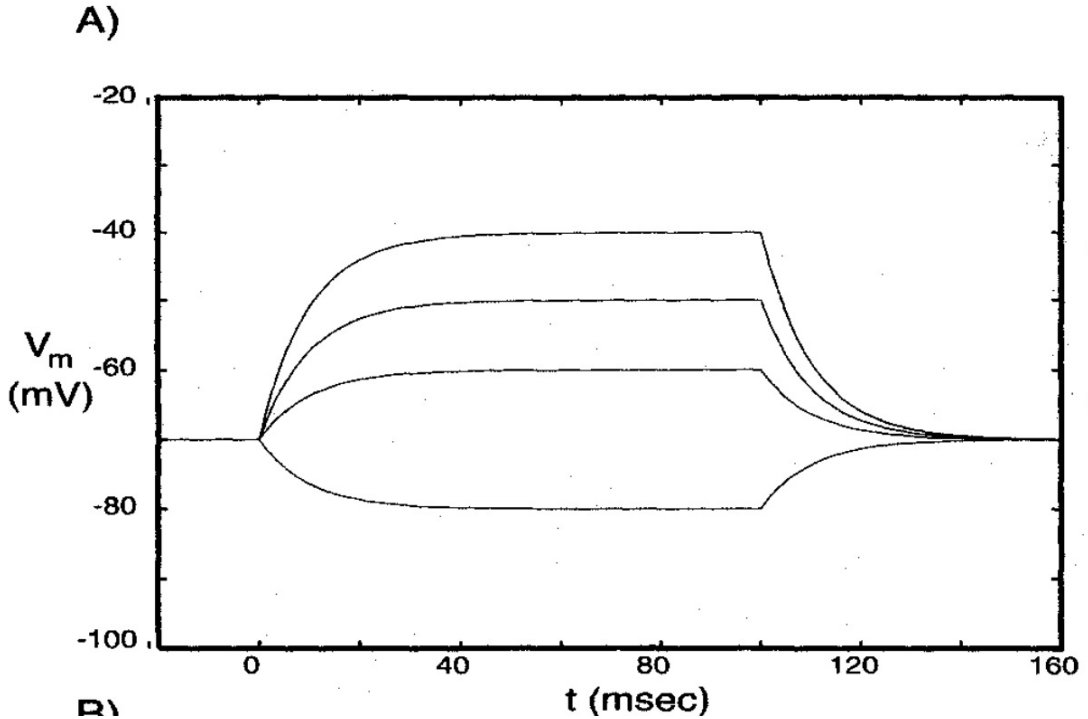
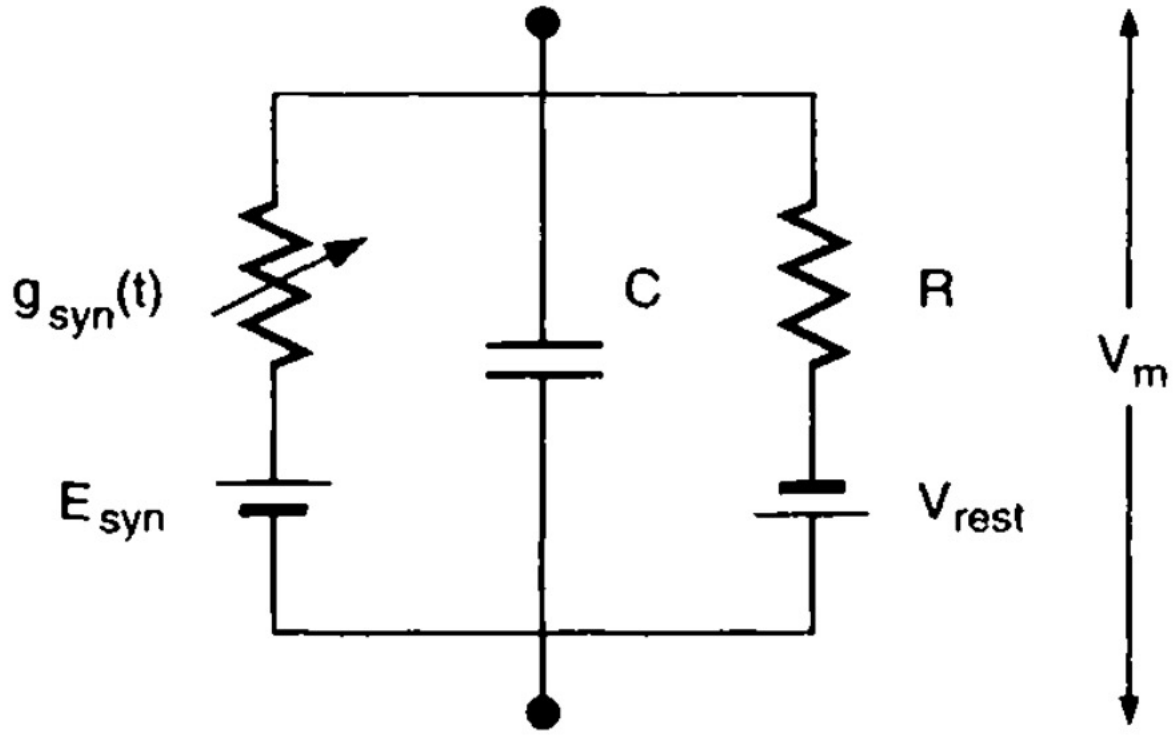


Fig. 1.3 BEHAVIOR OF AN *RC* CIRCUIT **(A)** Evolution of the membrane potential $V_m(t)$ in the single *RC* compartment of Fig. 1.2B when a current step of different amplitudes I_0 (see Eq. 1.9) is switched on at $t = 0$ and turned off at 100 msec. Initially, the membrane potential is at $V_{\text{rest}} = -70$ mV. We here assume $R = 100$ MΩ, $C = 100$ pF, $\tau = 10$ msec, and four different current amplitudes, $I_0 = -0.1, 0.1, 0.2$, and 0.3 nA. **(B)** Normalized *impulse response*

Synaptic input

- https://www.youtube.com/watch?v=8-m_J2CnYho

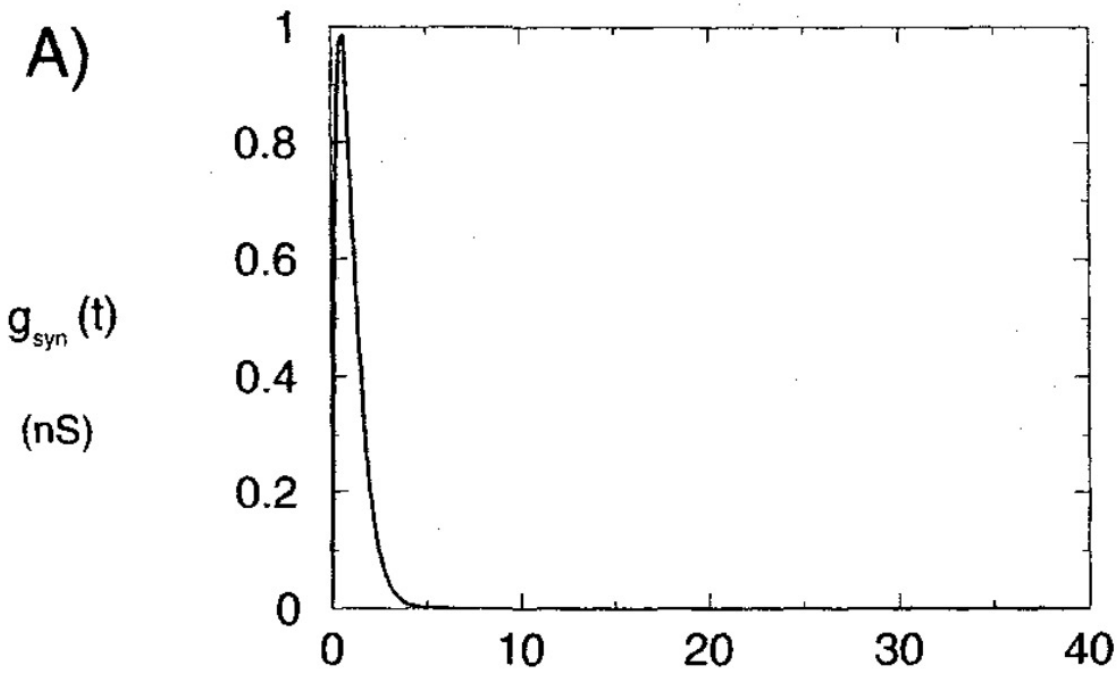
- https://www.youtube.com/watch?v=bQIU2KDtHTI



$$C\frac{dV_m}{dt} + g_{syn}(t)(V_m - E_{syn}) + \frac{V_m - V_{rest}}{R} = 0$$

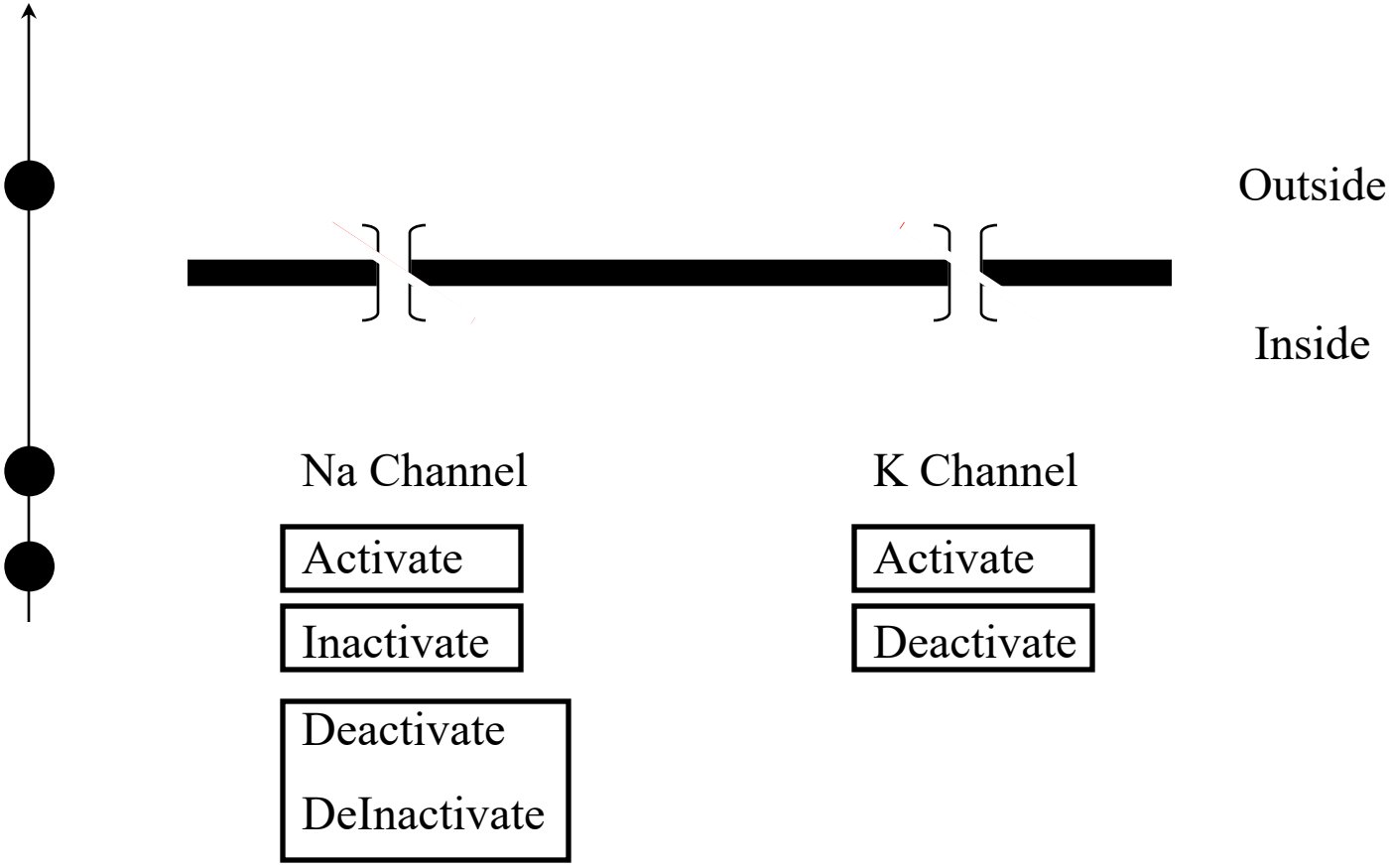
Frequently the time course of synaptic input is approximated by a so-called α function.

$$g_{\mathrm{syn}}(t) = \mathrm{const} \cdot t e^{-t/t_{\mathrm{peak}}} .$$

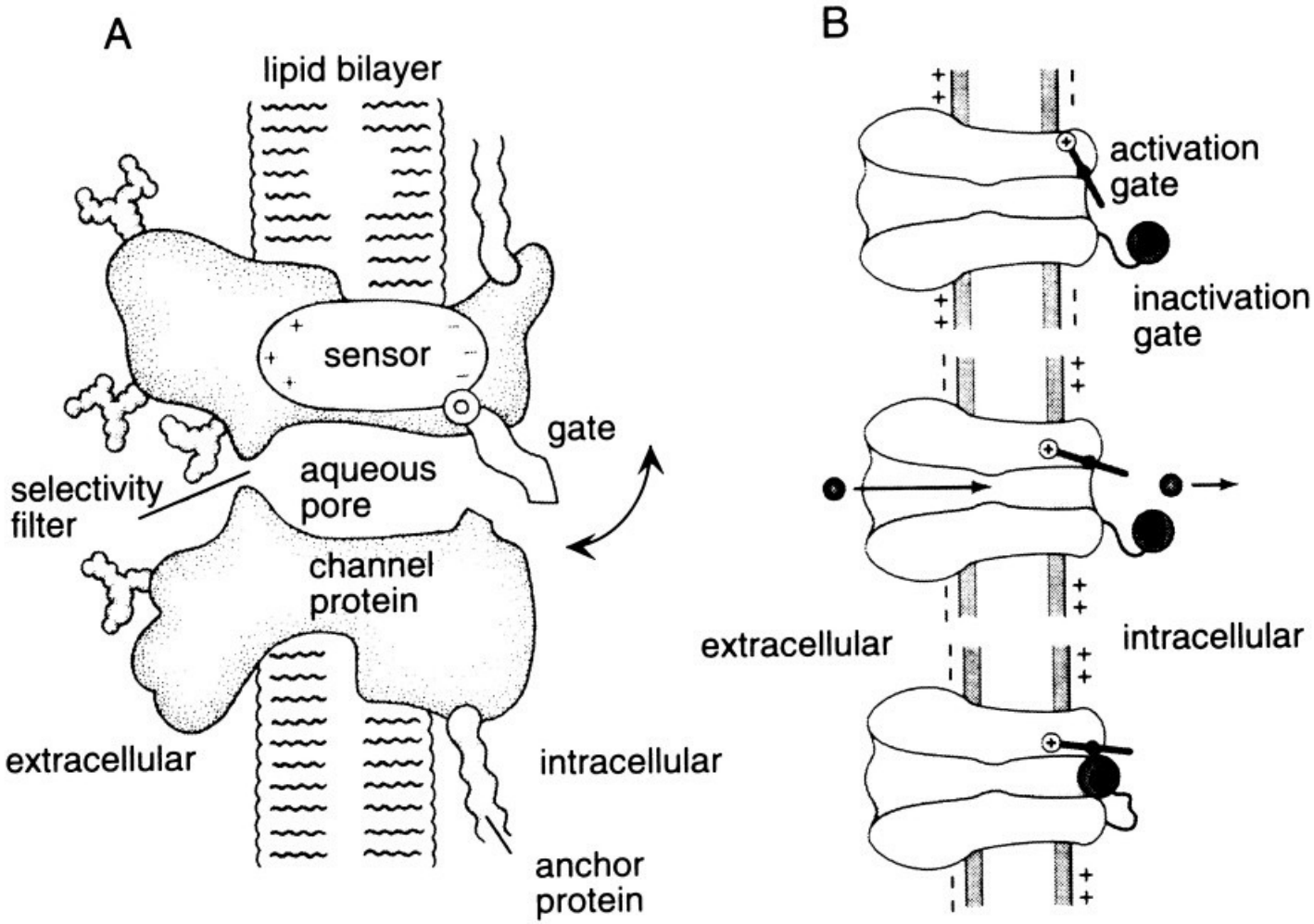


Hodgkin Huxley Experiments

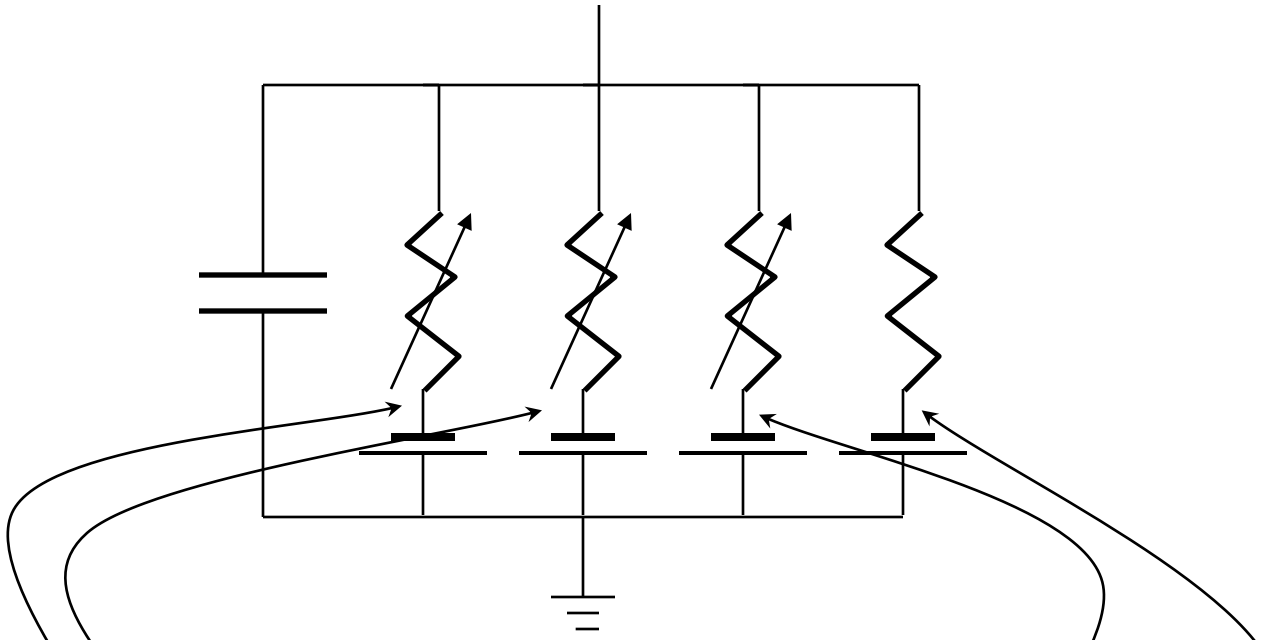
Active membrane: Voltage Dependent Conductance



Active membrane: Sodium Channel



Active membrane: Voltage Dependent Conductance



Na^+ Channels: $G_{Na} = (1/R_{Na})$ and E_{Na}

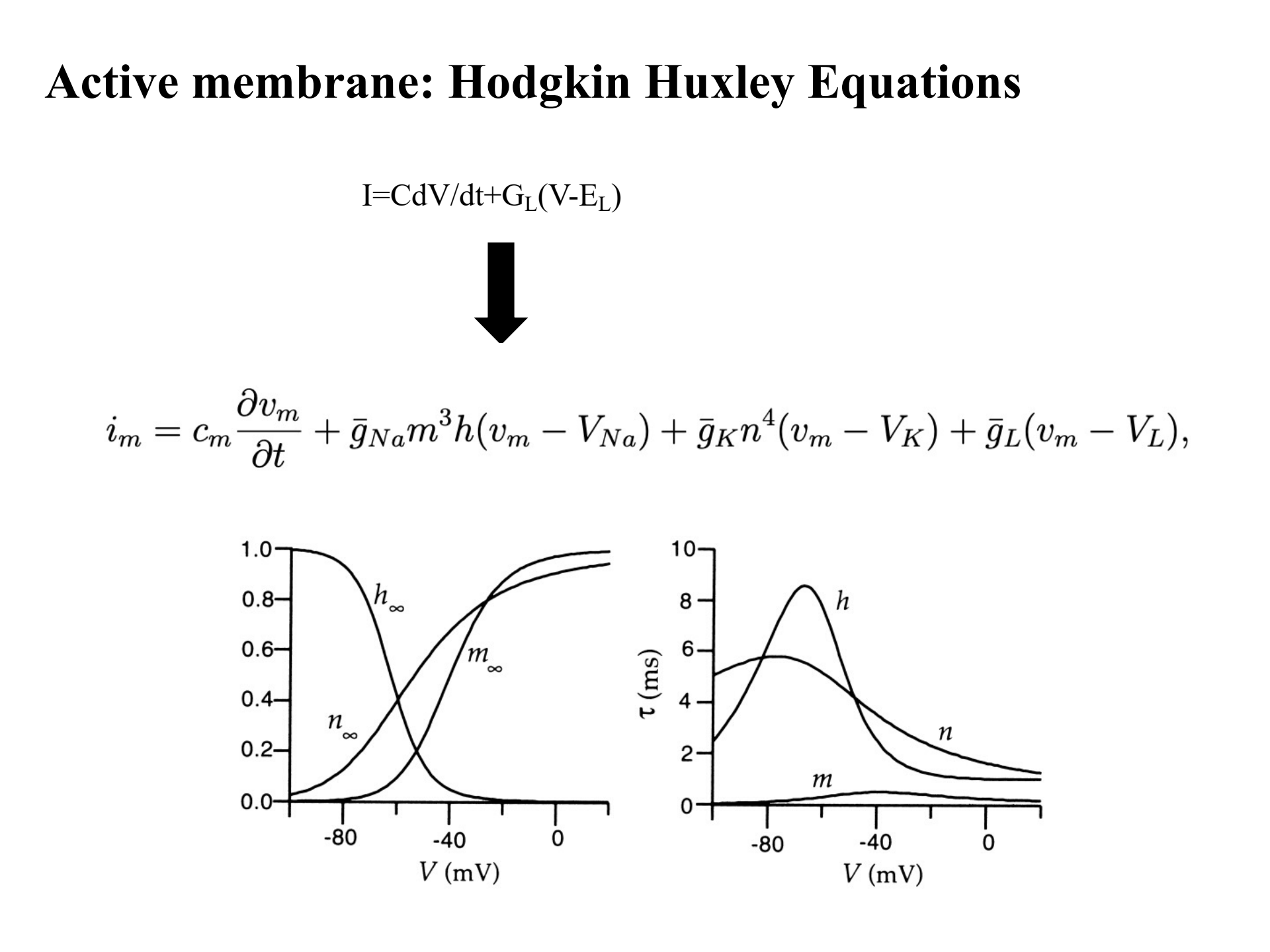
K^+ Channels: $G_K = (1/R_K)$ and E_K

Ca^{2+} Channels: $G_{Ca} = (1/R_{Ca})$ and E_{Ca}

Leak Channels: $G_L = (1/R_L)$ and E_L

Active membrane: Hodgkin Huxley Equations

$I=CdV/dt+G_L(V-E_L)$



$$i_m = c_m \frac{\partial v_m}{\partial t} + \bar{g}_{Na} m^3 h (v_m - V_{Na}) + \bar{g}_K n^4 (v_m - V_K) + \bar{g}_L (v_m - V_L),$$

$$i_m = c_m \frac{\partial v_m}{\partial t} + \bar{g}_{Na} m^3 h (v_m - V_{Na}) + \bar{g}_K n^4 (v_m - V_K) + \bar{g}_L (v_m - V_L), \tag{2–10}$$

$$\frac{dm}{dt} = \alpha_m (1 - m) - \beta_m m, \tag{2–11}$$

$$\frac{dh}{dt} = \alpha_h (1 - h) - \beta_h h, \tag{2–12}$$

$$\frac{dn}{dt} = \alpha_n (1 - n) - \beta_n n, \tag{2–13}$$

These are called the Hodgkin-Huxley Equations. α_m, β_m, α_h, β_h, α_n and β_n are functions of v_m as below:

$$\alpha_m = \frac{0.1(v_m + 25)}{e^{\frac{v_m + 25}{10}} - 1}, \qquad \beta_m = 4e^{\frac{v_m}{18}}, \tag{2–14}$$

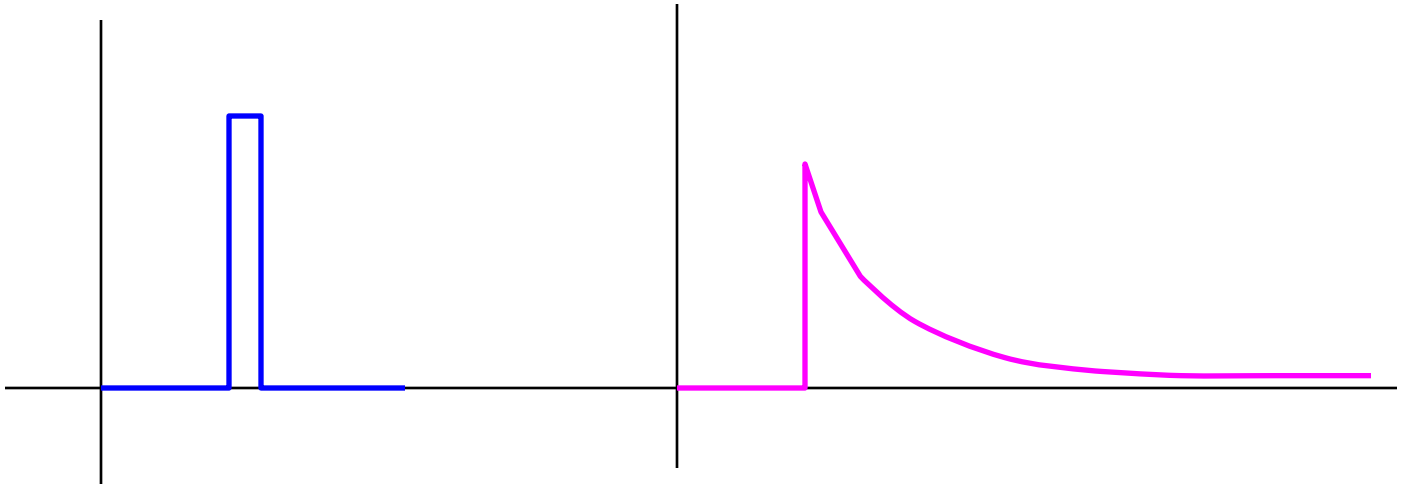
$$\alpha_h = 0.07e^{\frac{v_m}{20}}, \qquad \beta_h = \frac{1}{e^{\frac{v_m + 30}{10}} + 1}, \tag{2–15}$$

$$\alpha_n = \frac{0.01(v_m + 10)}{e^{\frac{v_m + 10}{10}} - 1}, \qquad \beta_n = 0.125e^{\frac{v_m}{80}}. \tag{2–16}$$

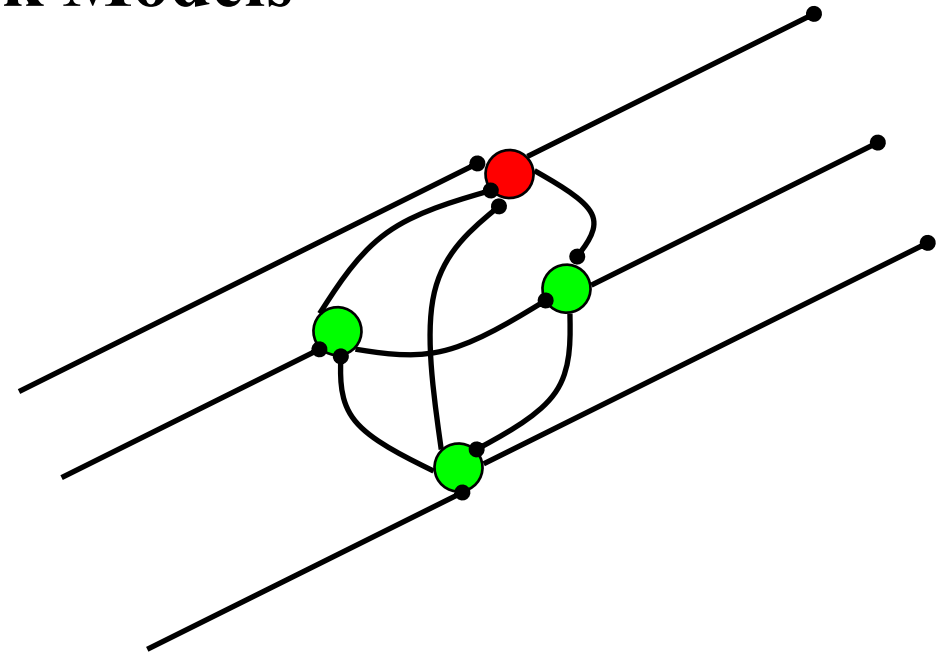
Reduced Model: Leaky Integrate and Fire [Lapicque, 1907]

$CdV/dt = -G_L(V-E_L) + I$

- Assume that synaptic response is an injected current rather than a change in conductance.
- Assume injected current is a δ function; Results in PSP
- Linear System: Total effect at soma = sum of individual PSP's
- Neuron Spikes when total potential at soma crosses a threshold.
- Reset membrane potential to a reset potential (can be resting potential)



Network Models



Biggest Difficulty:

Spikes ⟶ Membrane Potential ⟶ Spikes

Firing Rate Model

Exact spike sequence converted into instantaneous rate r(t)

Justification: Each neuron has large number of inputs which are generally not very correlated.

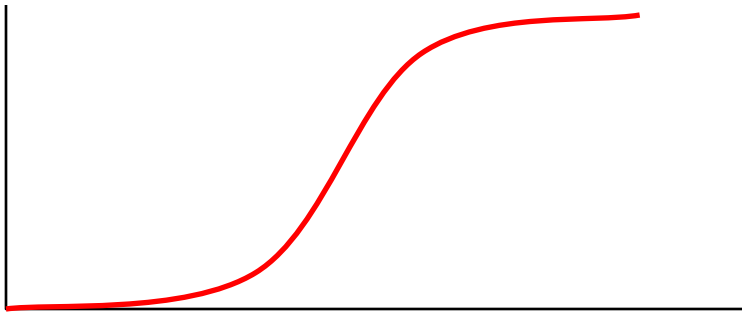
2 Steps:

Firing Rate of Presynaptic Neuron → Synaptic Input to Postsynaptic Neurons

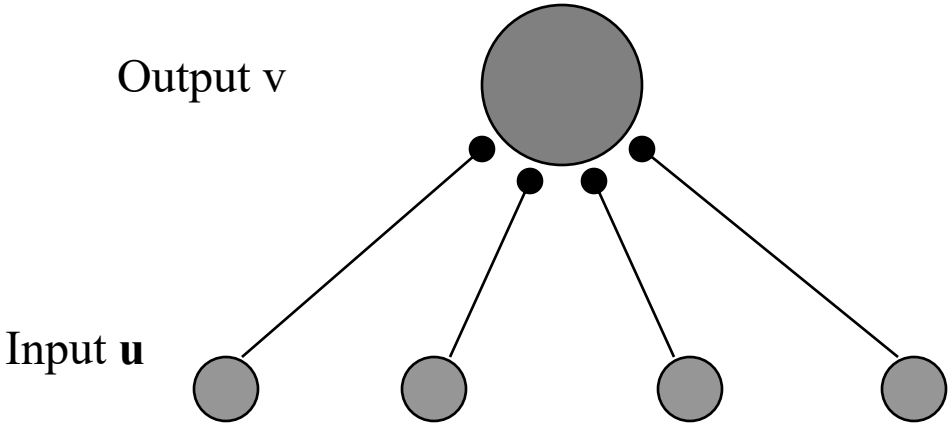
Total Input to Postsynaptic Neuron → Firing rate of Postsynaptic Neuron

Total Synaptic Input modeled as total current injected into the soma

f-I curve: Output Spike Frequency vs. Injected Current curve



Firing Rate Model

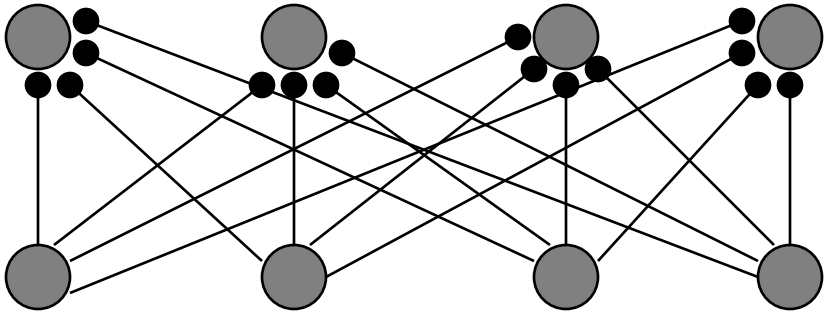


Firing rate does not follow changes in total synaptic current instantaneously, hence

$\tau \, dv/dt = -v + F(I(t))$

$I(t) = \mathbf{w}.\mathbf{u}(t)$

Firing Rate Network Model



$\mathbf{v}(t)$

$\mathbf{u}(t)$

$$\tau \, d\mathbf{v}/dt = -\mathbf{v} + F(\mathbf{w}.\mathbf{u}(t))$$

BULLETIN OF
MATHEMATICAL BIOPHYSICS
VOLUME 5, 1943

A LOGICAL CALCULUS OF THE IDEAS IMMANENT IN NERVOUS ACTIVITY

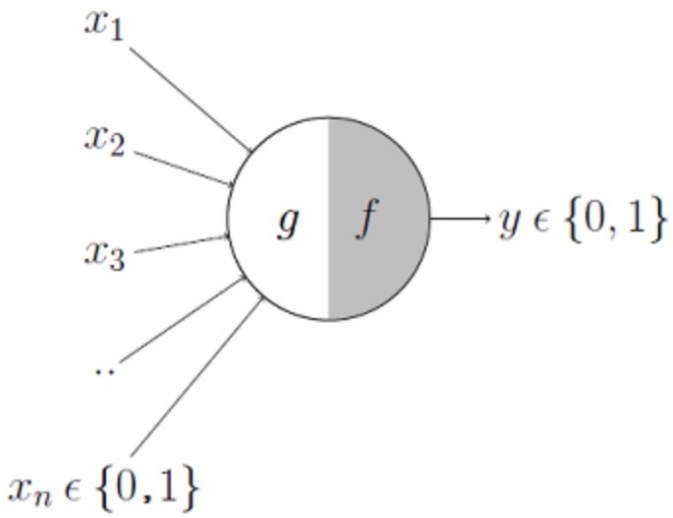
WARREN S. MCCULLOCH AND WALTER PITTS

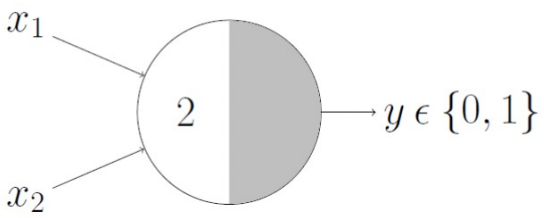
FROM THE UNIVERSITY OF ILLINOIS, COLLEGE OF MEDICINE,
DEPARTMENT OF PSYCHIATRY AT THE ILLINOIS NEUROPSYCHIATRIC INSTITUTE,
AND THE UNIVERSITY OF CHICAGO

Because of the "all-or-none" character of nervous activity, neural events and the relations among them can be treated by means of propositional logic. It is found that the behavior of every net can be described in these terms, with the addition of more complicated logical means for nets containing circles; and that for any logical expression satisfying certain conditions, one can find a net behaving in the fashion it describes. It is shown that many particular choices among possible neurophysiological assumptions are equivalent, in the sense that for every net behaving under one assumption, there exists another net which behaves under the other and gives the same results, although perhaps not in the same time. Various applications of the calculus are discussed.

$$g(x_1, x_2, x_3, ..., x_n) = g(\mathbf{x}) = \sum_{i=1}^{n} x_i$$

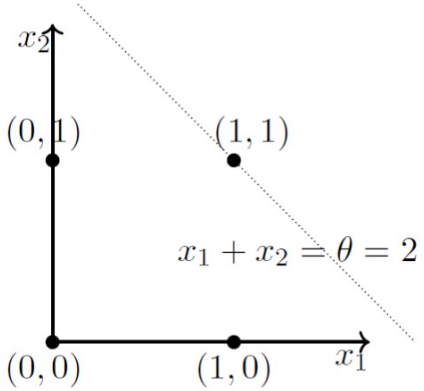
$$\begin{aligned} y = f(g(\mathbf{x})) &= 1 \quad if \quad g(\mathbf{x}) \geq \theta \\ &= 0 \quad if \quad g(\mathbf{x}) < \theta \end{aligned}$$





AND function

$$x_1 + x_2 = \sum_{i=1}^{2} x_i \geq 2$$



Donald O Hebb

- Wrote The Organization of Behavior in 1949
- “When an axon of cell A is near enough to excite cell B and repeatedly or persistently takes part in firing it, some growth process or metabolic change takes place in one or both cells such that A's efficiency, as one of the cells firing B, is increased” (Hebb 1949)