Electrophysiology of Neurons

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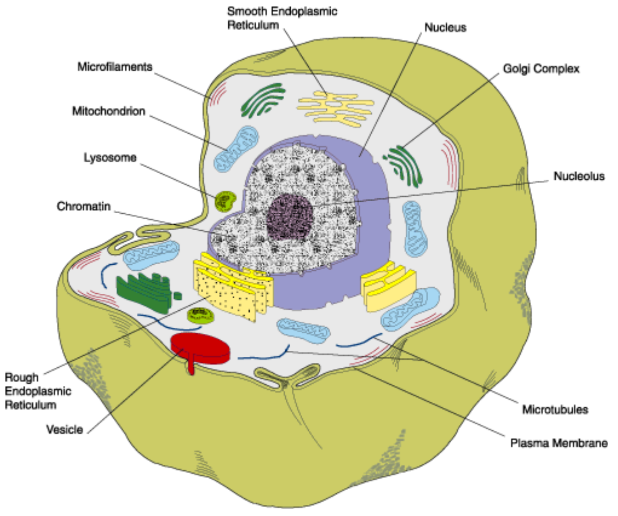
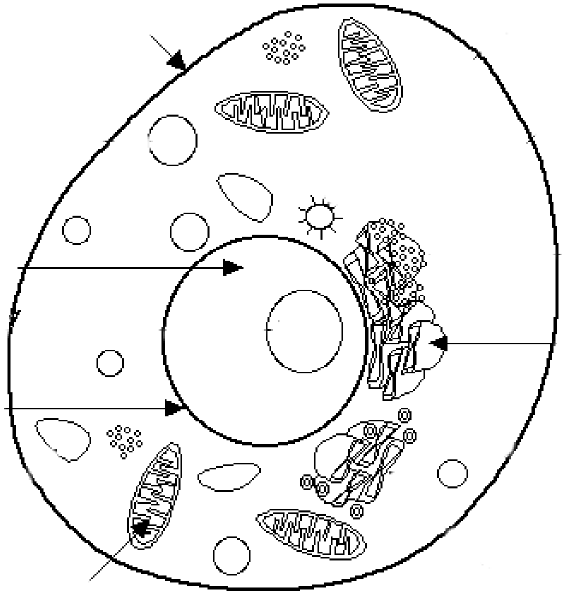
Autumn 2018

Outline

- Cell Membrane & Ions
- Electrochemical gradients
- Equivalent circuit
- Hodgkin-Huxley gate model
- Hodgkin-Huxley Model

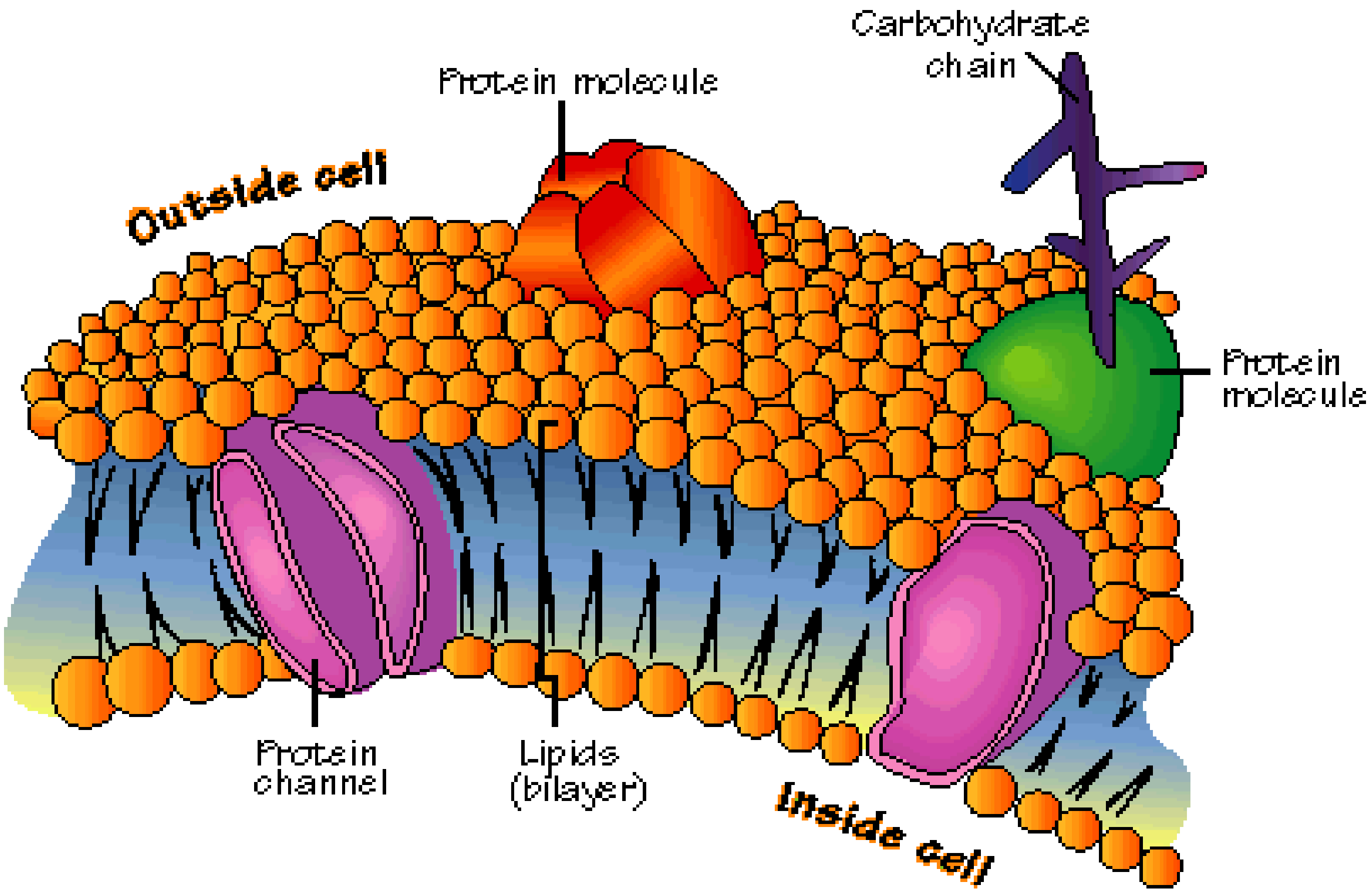
Cell Membrane & Ions



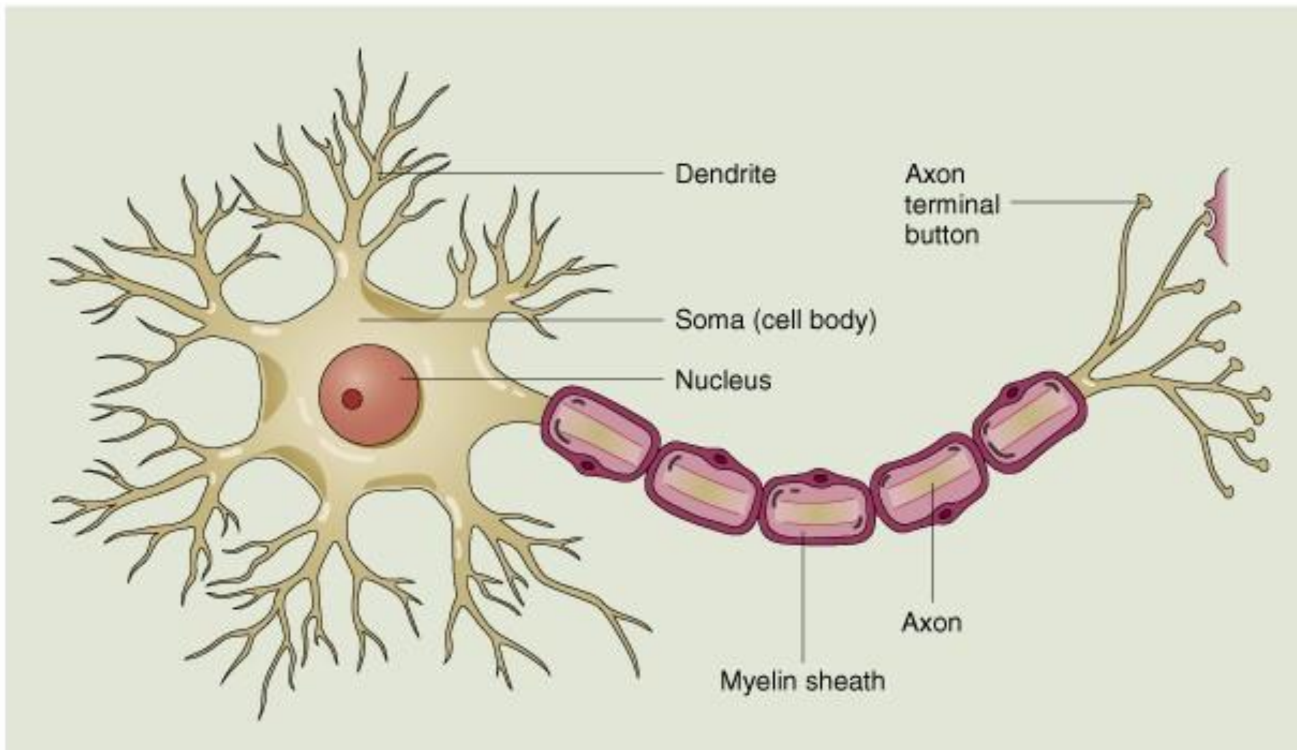


Cell Membrane
Cell Body
Nuclear Membrane
Nucleus
Endoplasmic Reticulum
Mitochondria

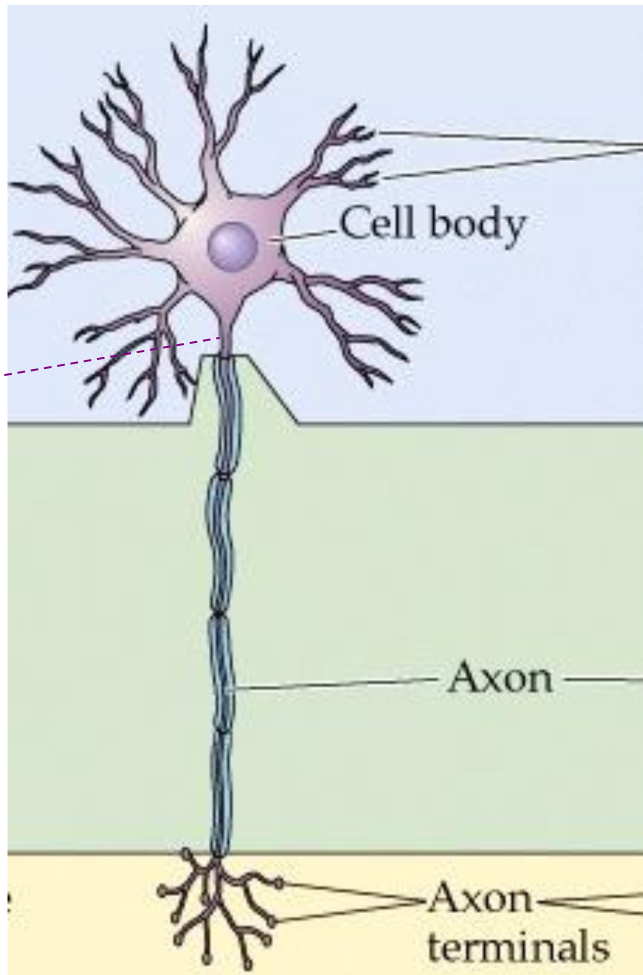
Cell Membrane & Ions

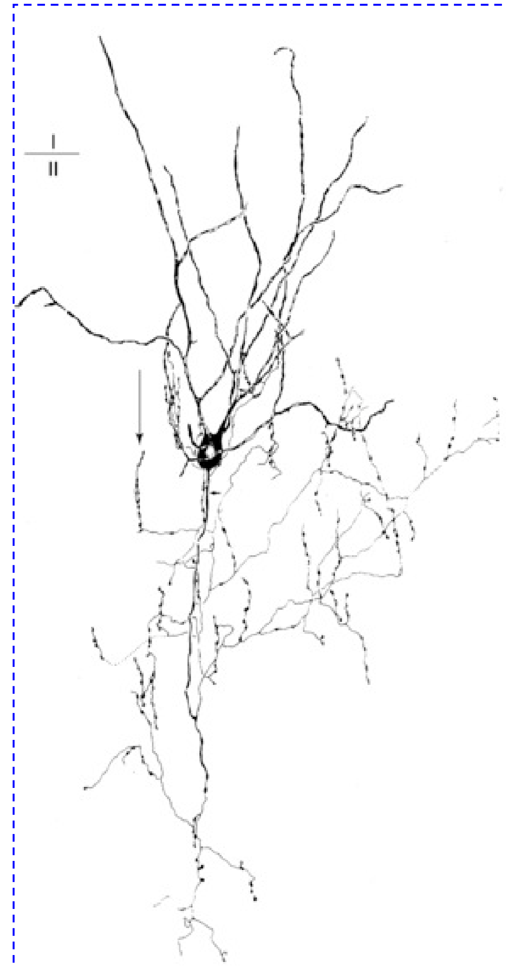


Neuron

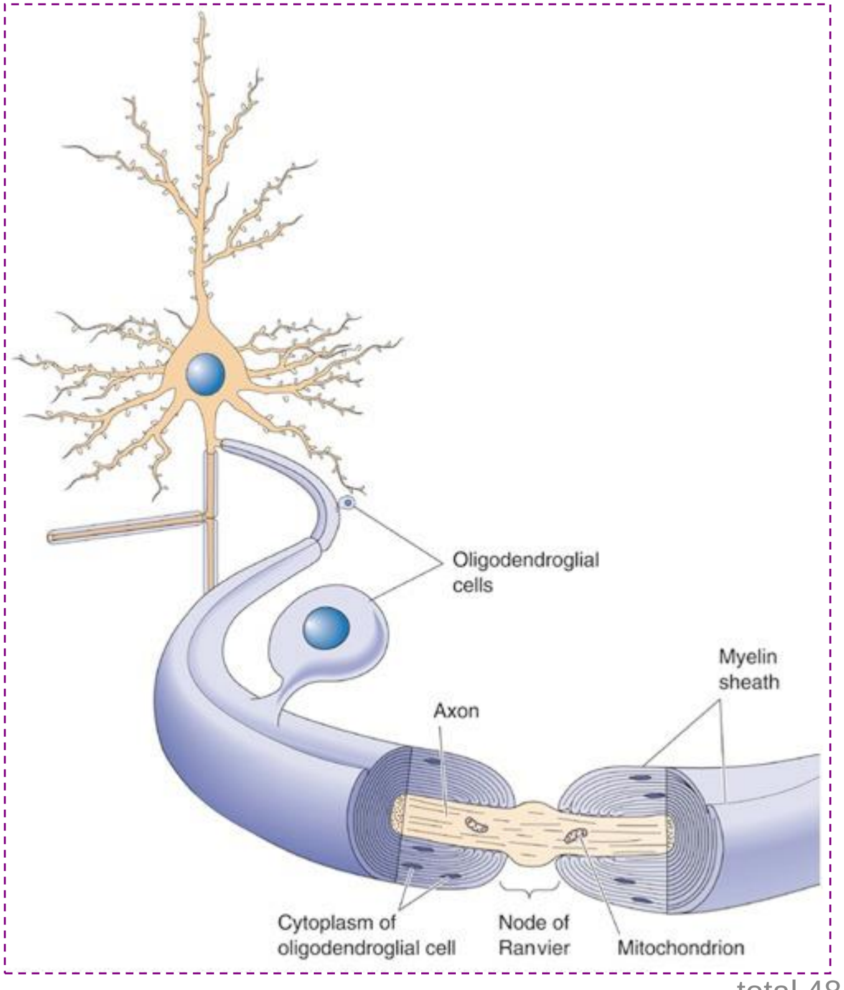

Dendrite
Axon
terminal
button
Soma (cell body)
Nucleus
Axon
Myelin sheath

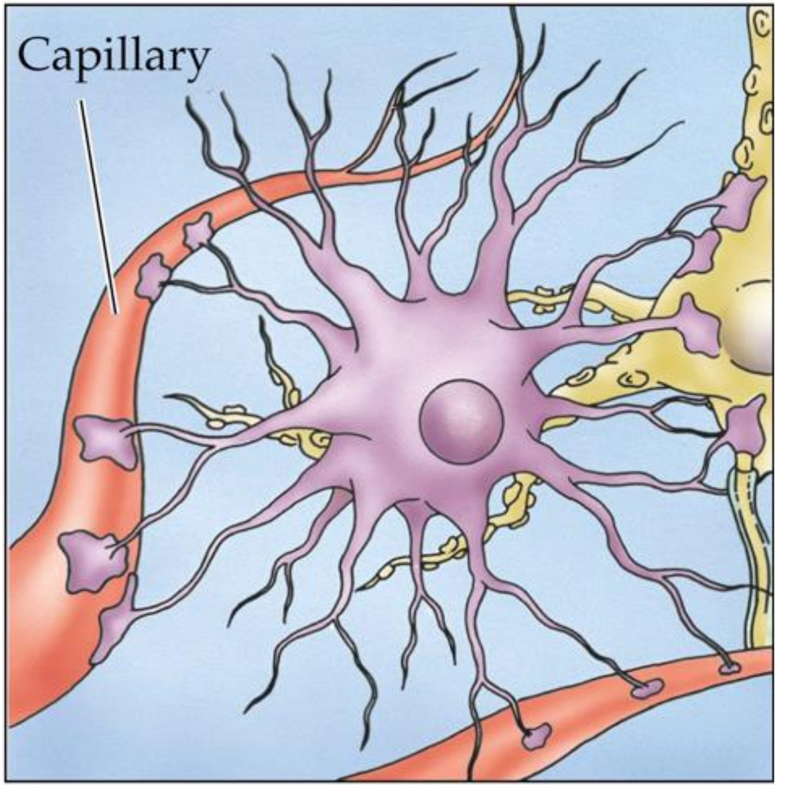
Neuron



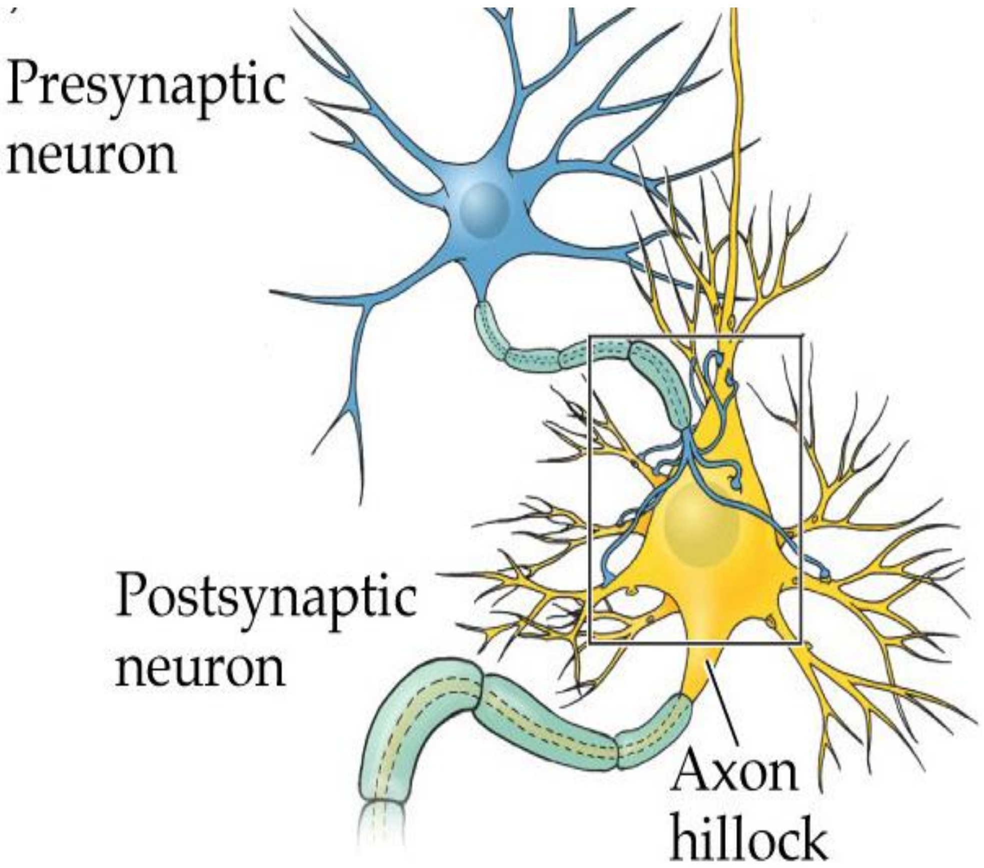


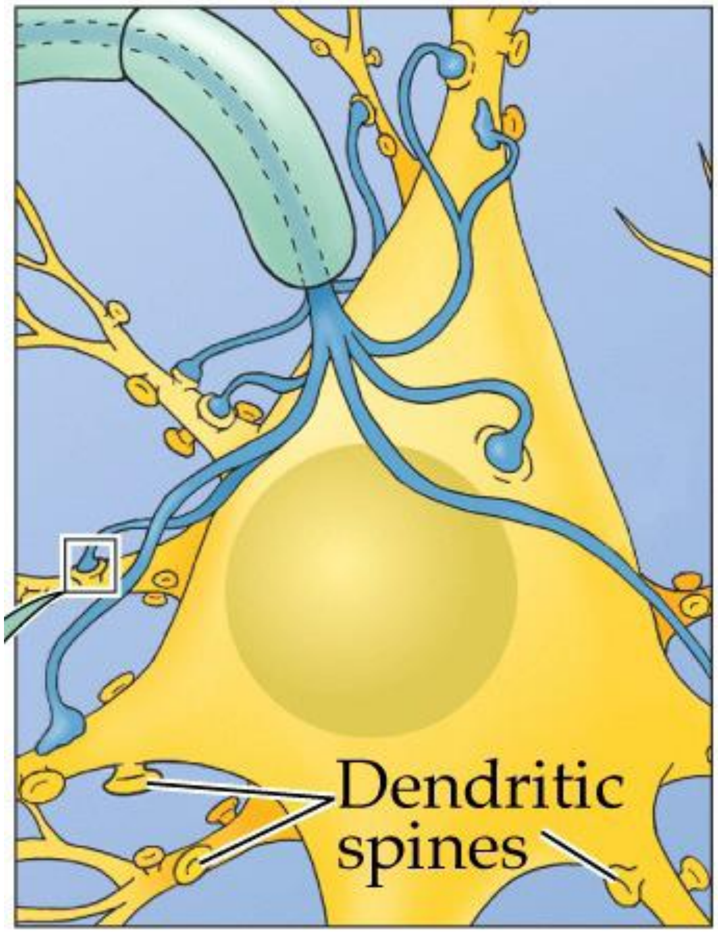
Neuron


Oligodendroglial cells
Myelin sheath
Axon
Cytoplasm of oligodendroglial cell
Node of Ranvier
Mitochondrion

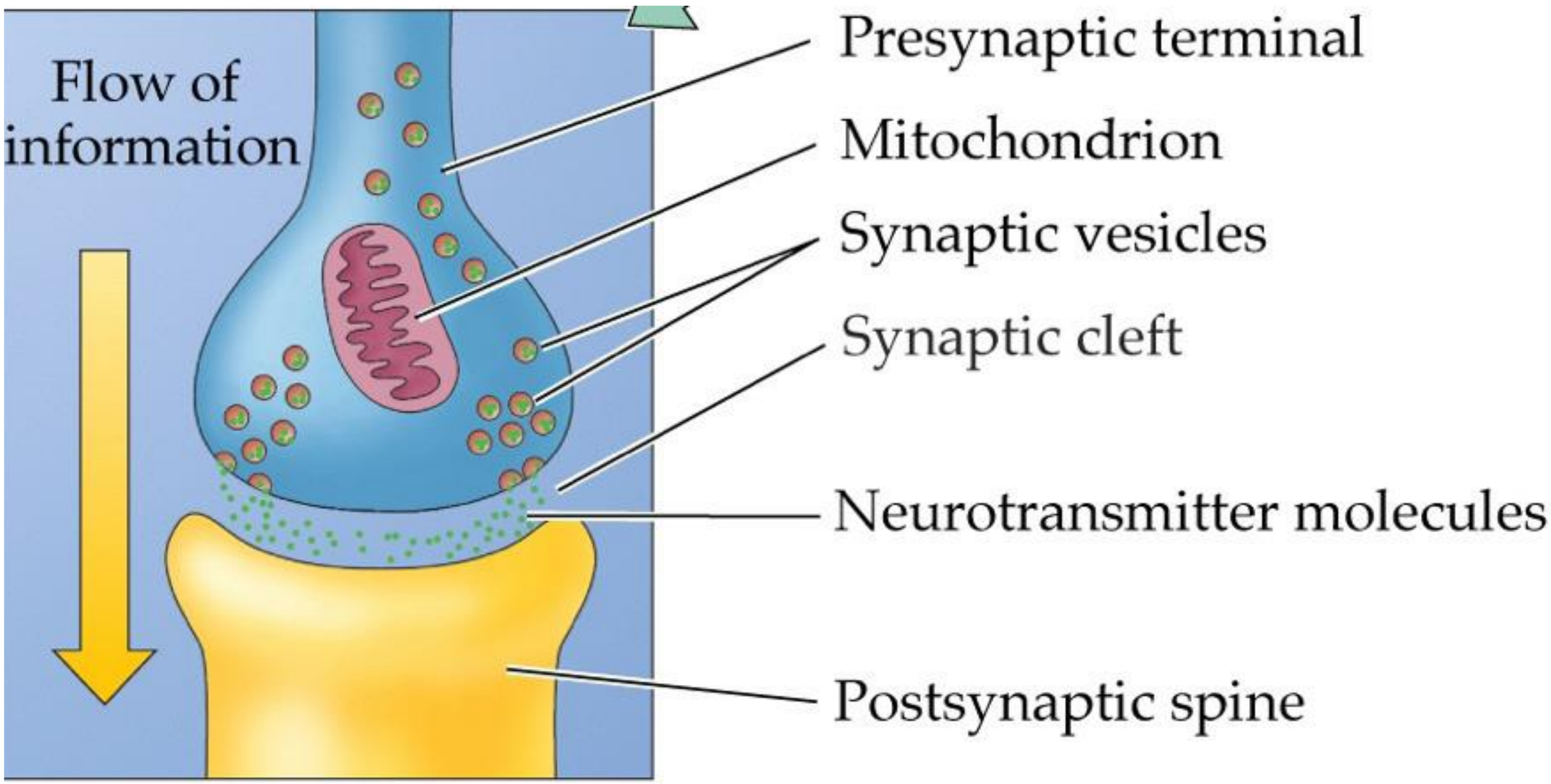

Capillary

Connection of Neurons

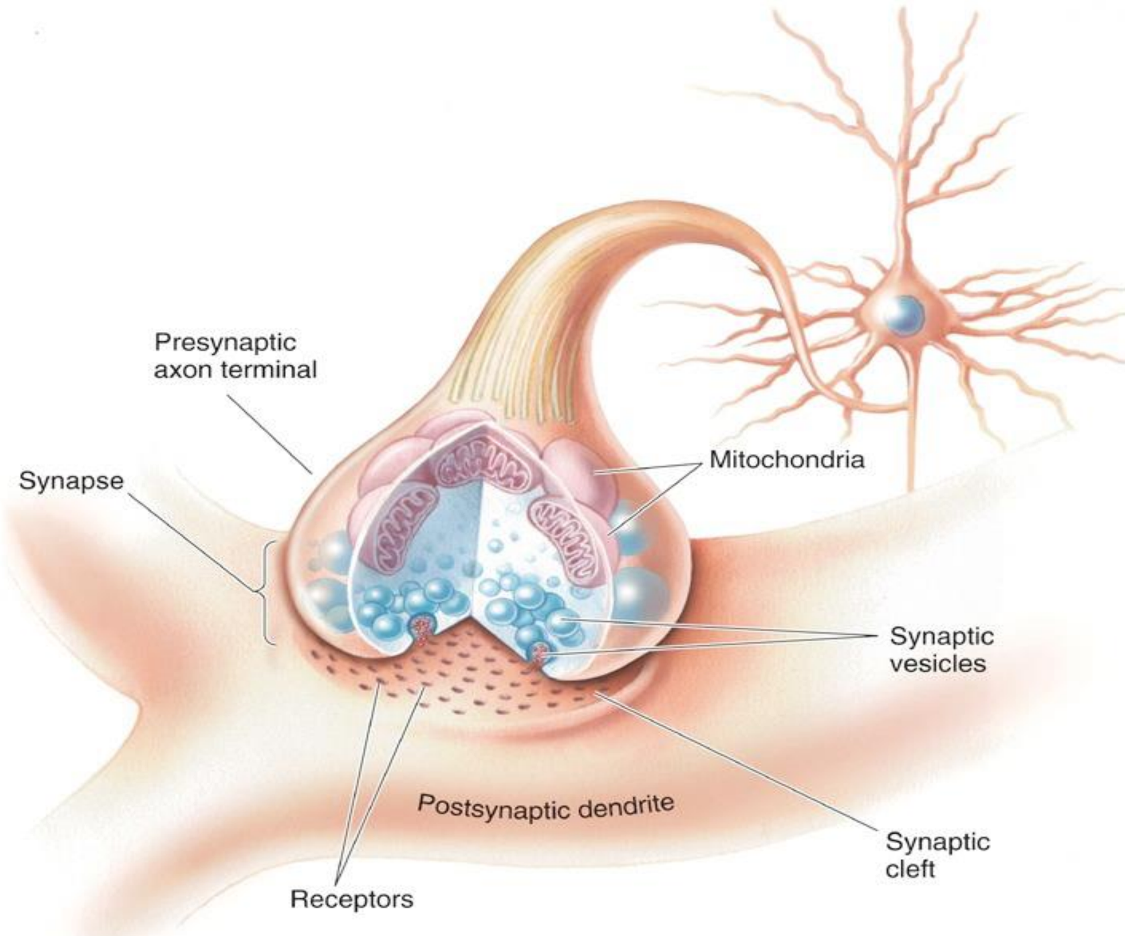




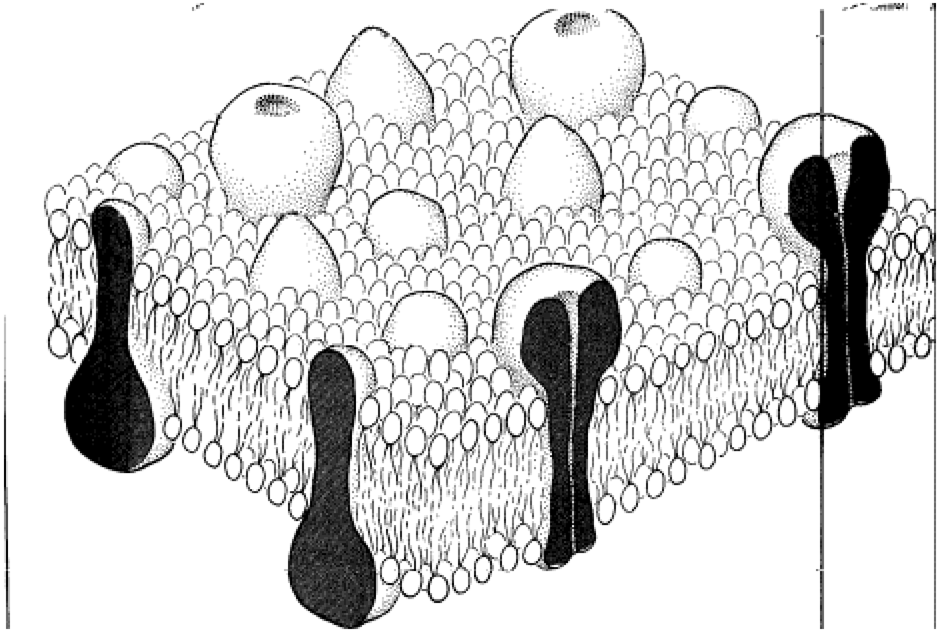
An Individual Synapse



An Individual Synapse

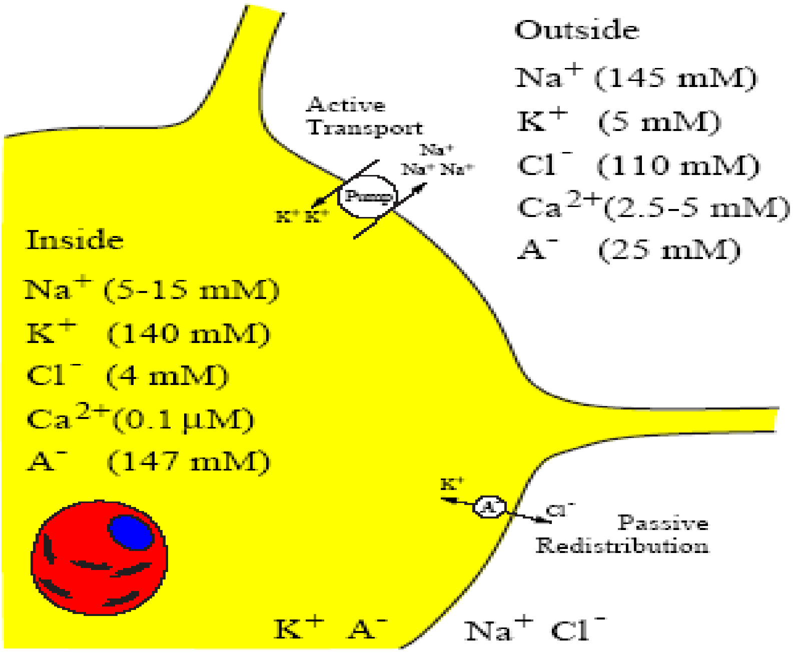


Neuron membrane



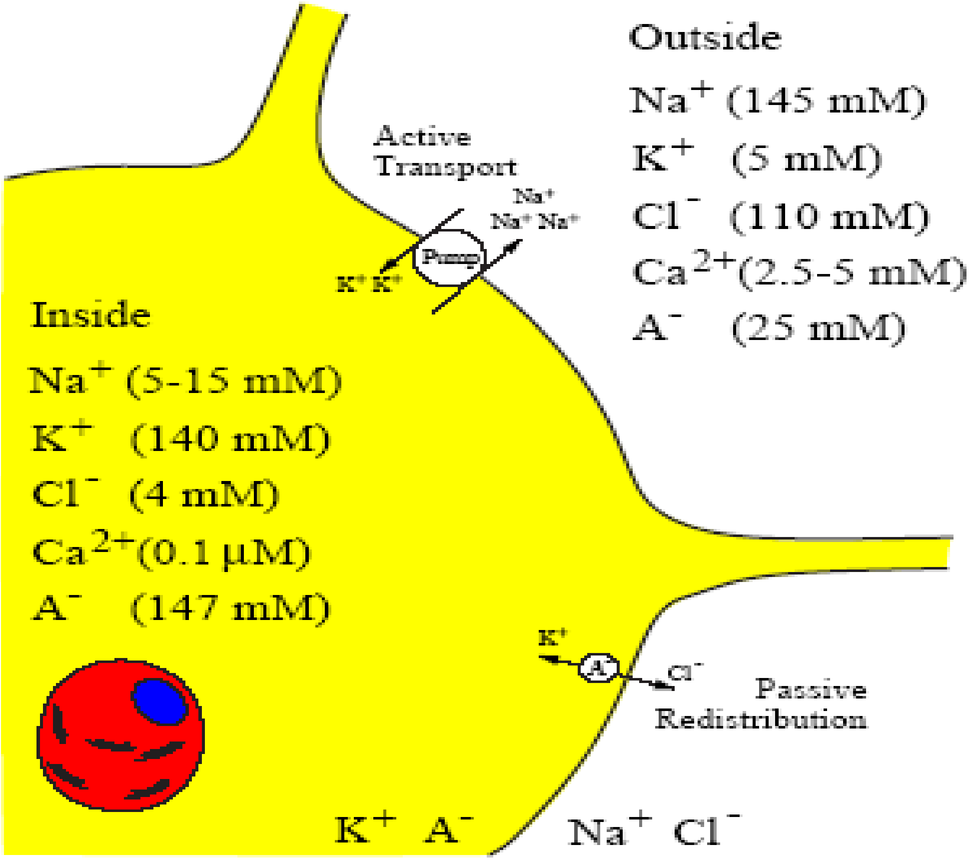
Neurons & Ions

Electrical activity in neurons is sustained and propagated via ionic currents through neuron membranes. Most of these transmembrane currents involve four ionic species: sodium (Na^+), potassium (K^+), calcium (Ca^{2+}), and chloride (Cl^-).

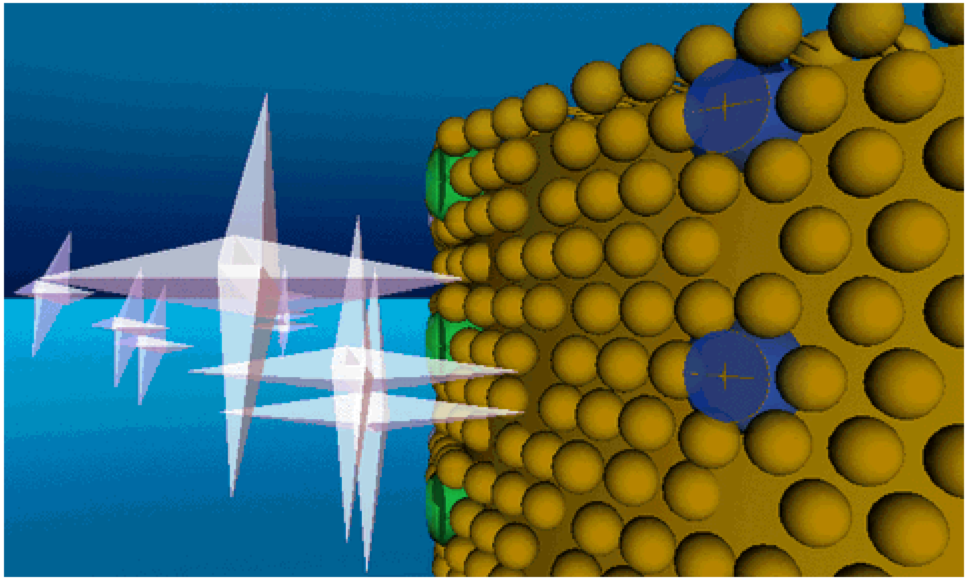


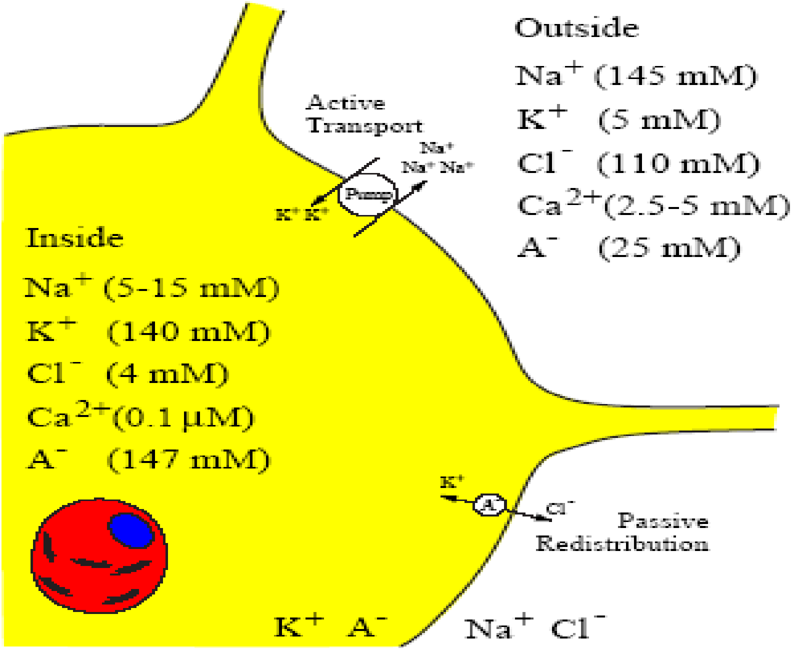
Electrochemical gradients

Different concentrations on the two sides --- major driving forces of neural activity.

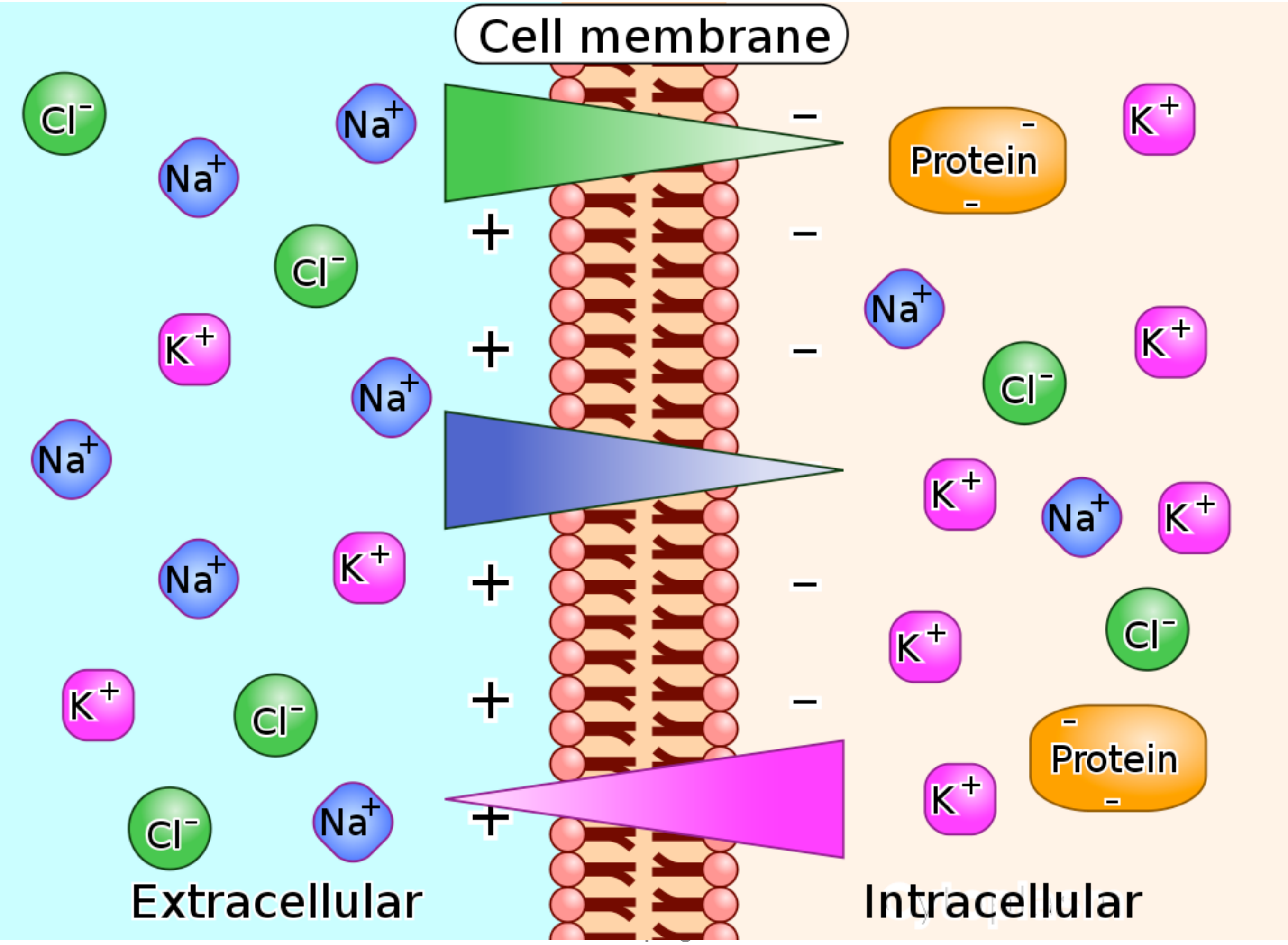


Ions

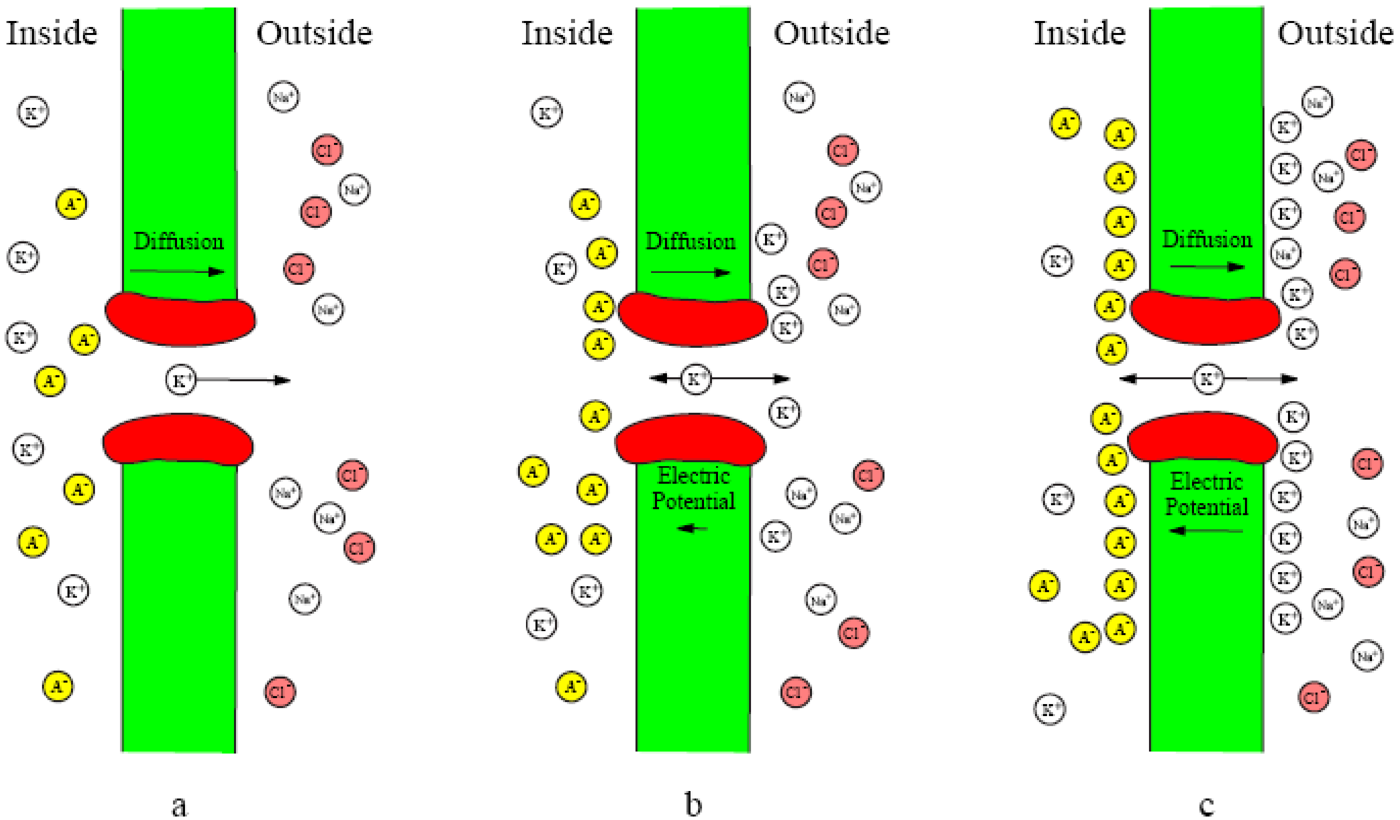



Outside
Na+ (145 mM)
K+ (5 mM)
Cl- (110 mM)
Ca2+(2.5-5 mM)
A- (25 mM)
Active
Transport
Pump
Inside
Na+ (5-15 mM)
K+ (140 mM)
Cl- (4 mM)
Ca2+(0.1 µM)
A- (147 mM)
Passive
Redistribution
K+ A-
Na+ Cl-

Ionic diffusion



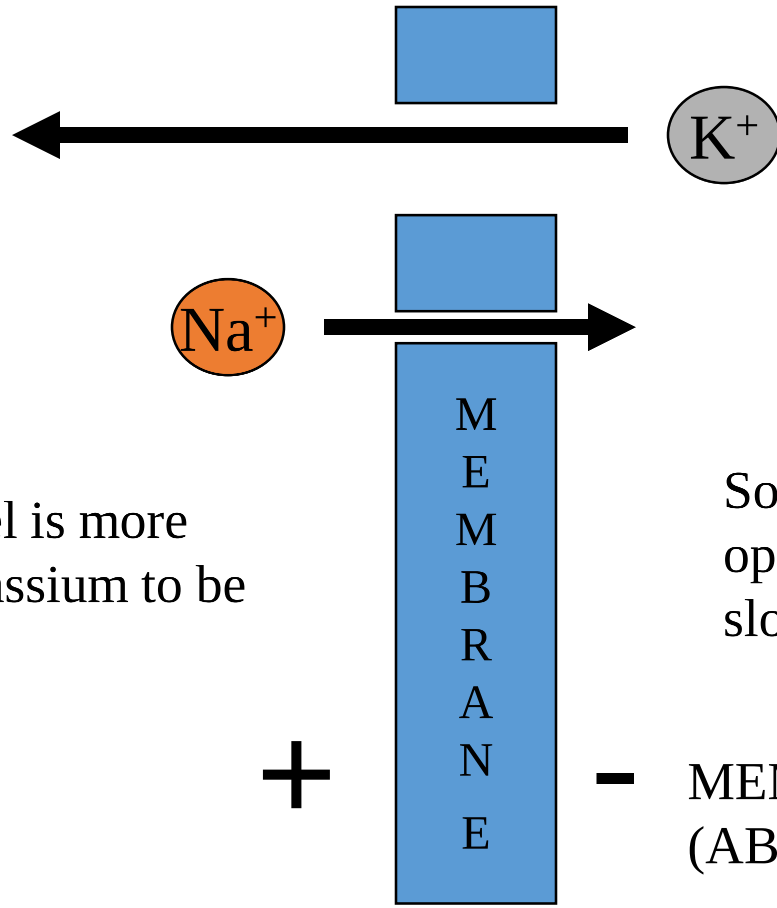
Ionic diffusion



The Membrane Potential

Extracellular Fluid

Intracellular Fluid

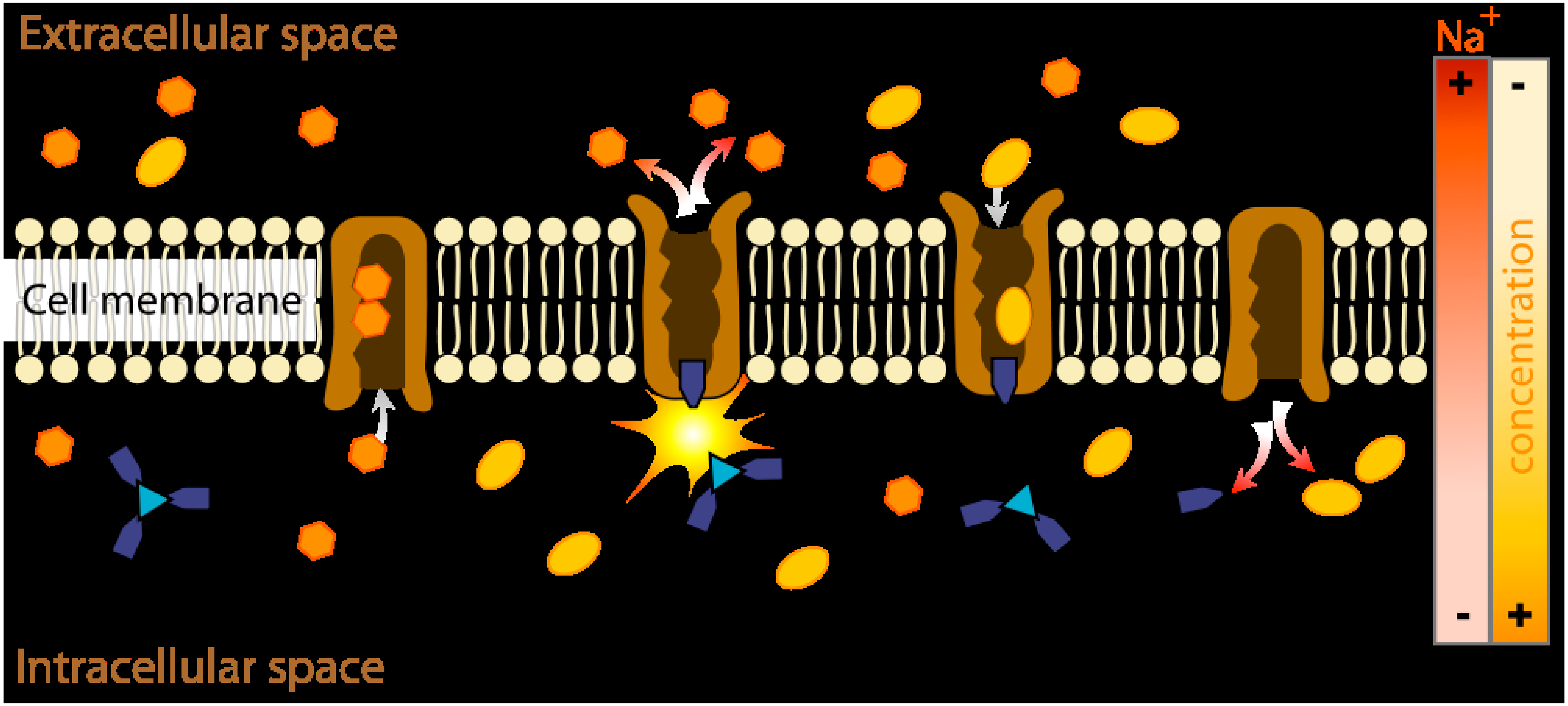


Potassium channel is more open causing potassium to be faster

Sodium channel is less open causing sodium to be slower

MEMRANE POTENTIAL (ABOUT 90 -120 mv)

The Membrane Potential



Nernst potential

Nernst equilibrium potential:

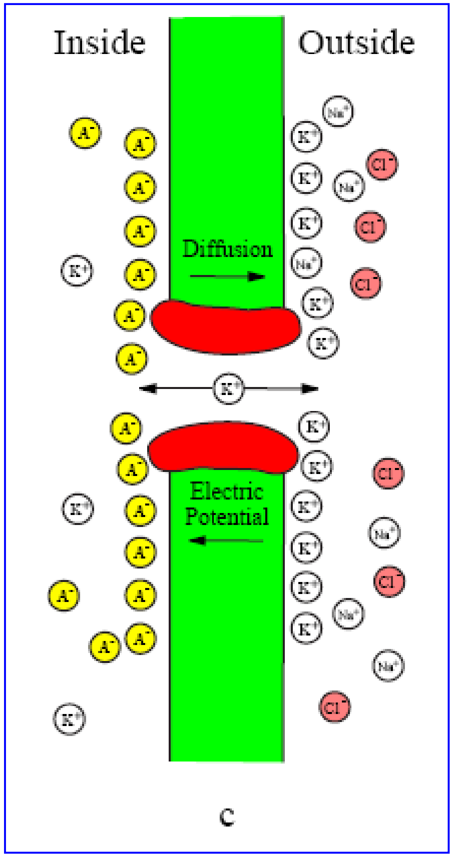
$$E_{ion} = \frac{RT}{zF} \ln \frac{[\text{Ion}]_{\text{out}}}{[\text{Ion}]_{\text{in}}}$$

R - *the universal gas constant*

T - *temperature*

F - *Faraday constant*

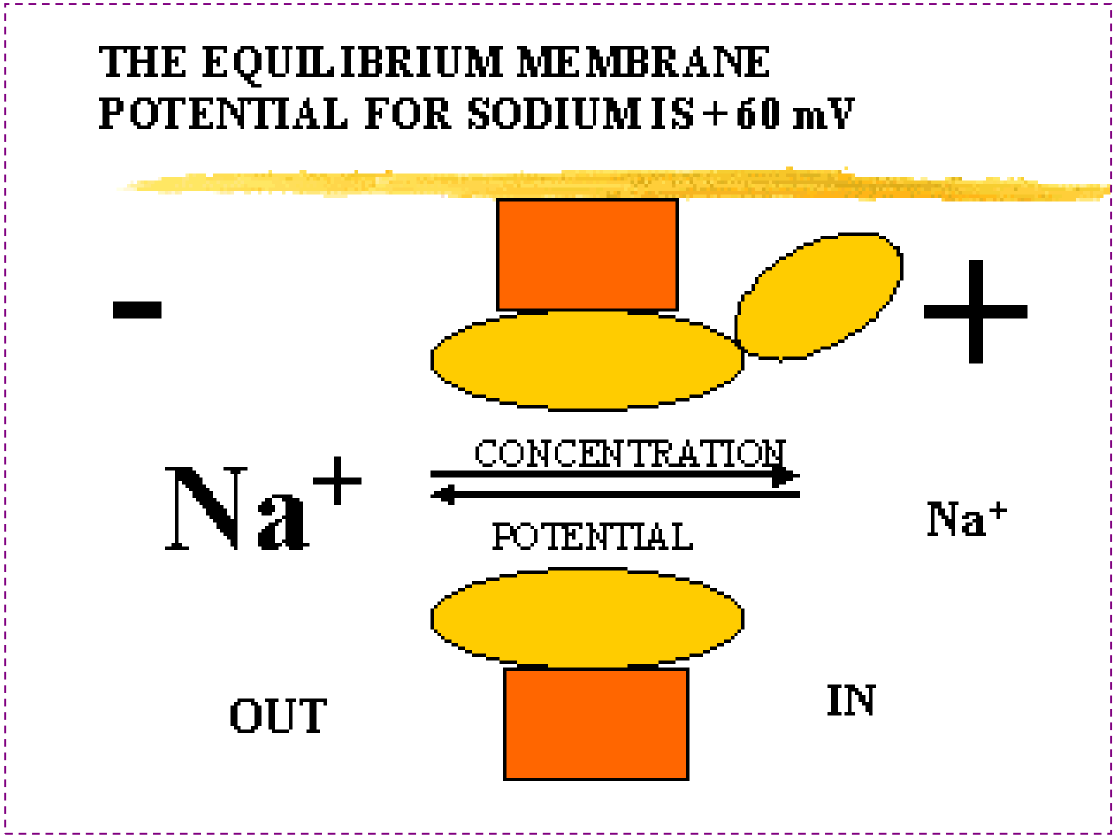
z - *the valence of the ion*



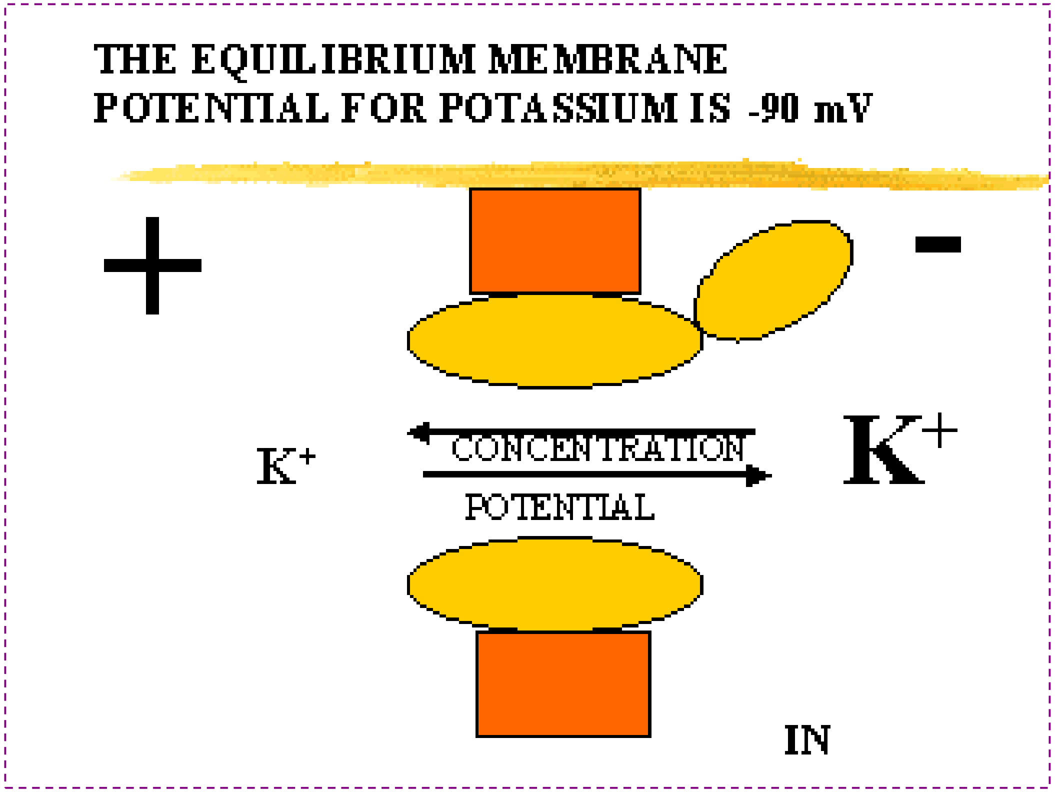
Sodium equilibrium potential

Outside 145mM

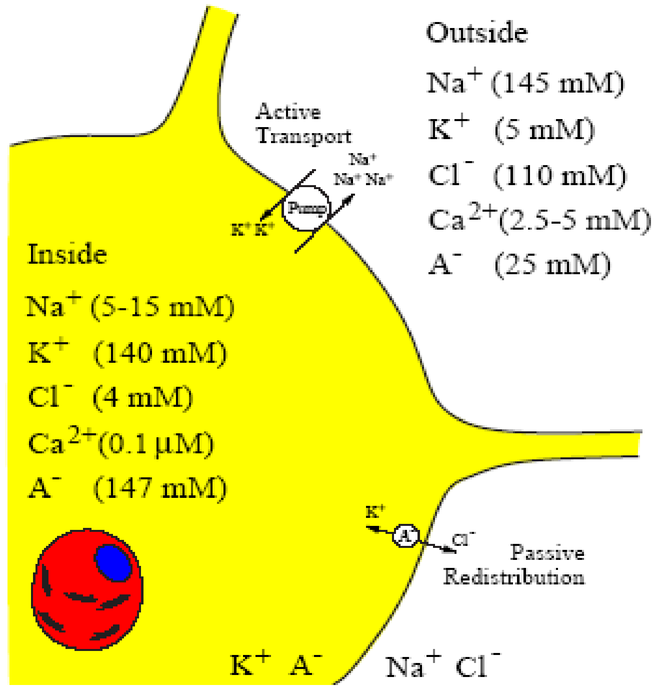
Inside 5-15mM



Equilibrium potential



Equilibrium potentials

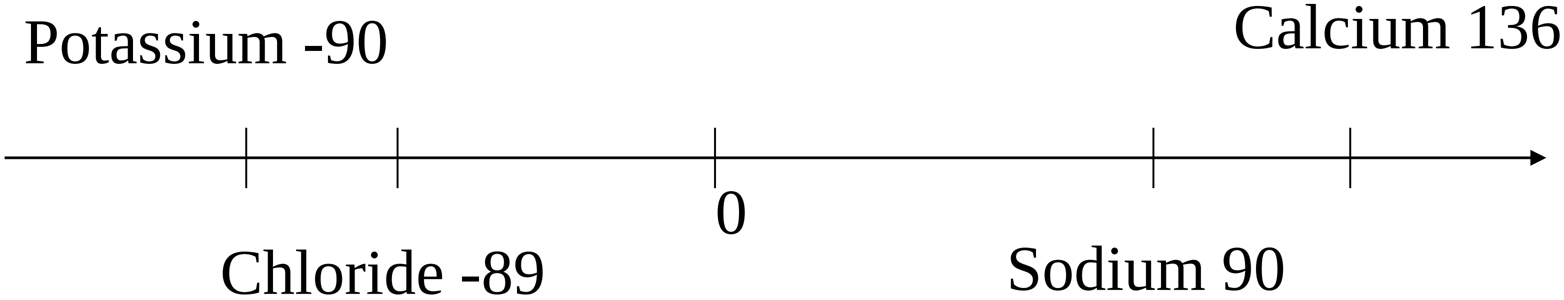


Equilibrium Potentials

$$
\begin{array}{llcl}
Na^+ & 62\log\frac{145}{5} & = & 90\ \mathrm{mV} \\
 & 62\log\frac{145}{15} & = & 61\ \mathrm{mV} \\
K^+ & 62\log\frac{5}{140} & = & -90\ \mathrm{mV} \\
Cl^- & -62\log\frac{110}{4} & = & -89\ \mathrm{mV} \\
Ca^{2+} & 31\log\frac{2.5}{10^{-4}} & = & 136\ \mathrm{mV} \\
 & 31\log\frac{5}{10^{-4}} & = & 146\ \mathrm{mV}
\end{array}
$$

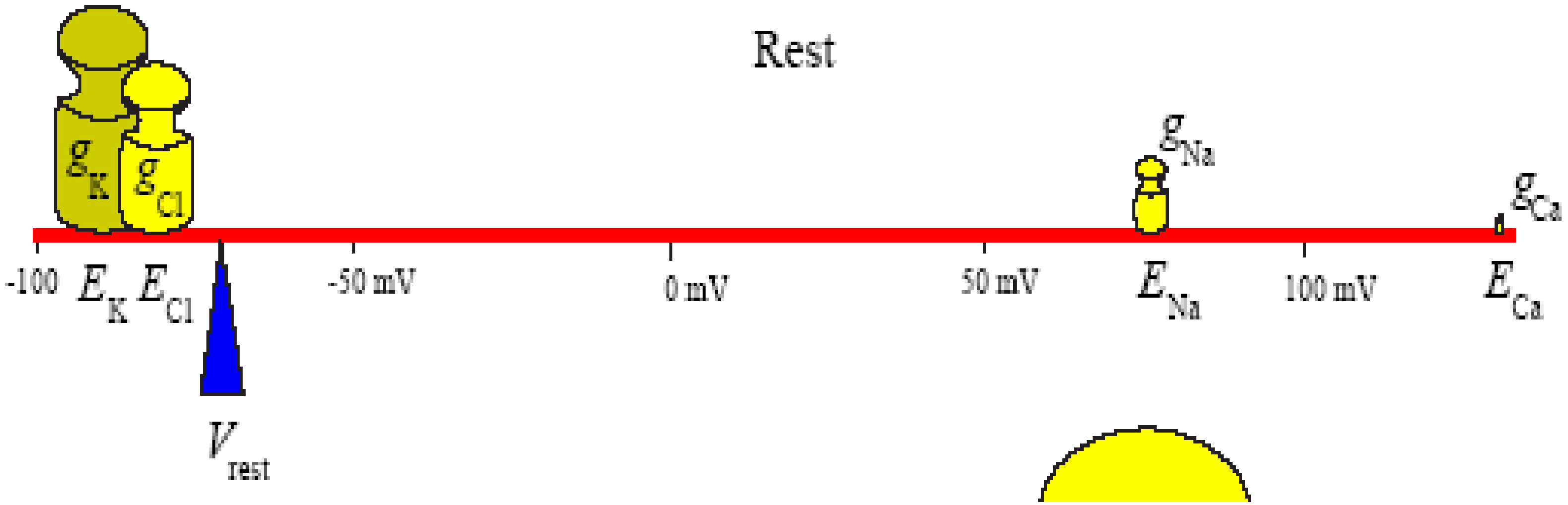
$$T = 37^o C$$

Equilibrium potentials



Resting Potential

I=0, dV/dt=0



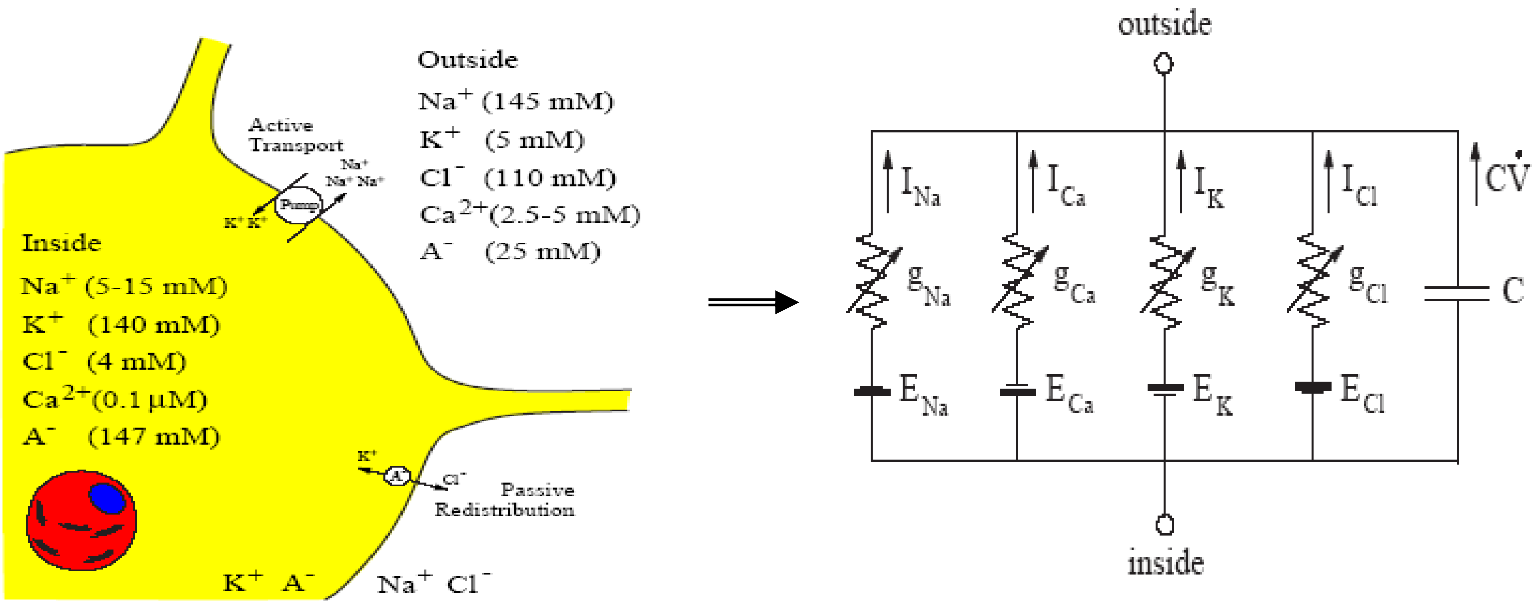
Inward on outward currents

$$E_K < E_{Cl} < V_{(at\ rest)} < E_{Na} < E_{Ca}$$

$$I_{Na},\ I_{Ca} < 0 \text{ (inward currents)}$$

$$I_K,\ \ I_{Cl} > 0 \ \text{ (outward currents)}$$

Mapping neural activity to circuits



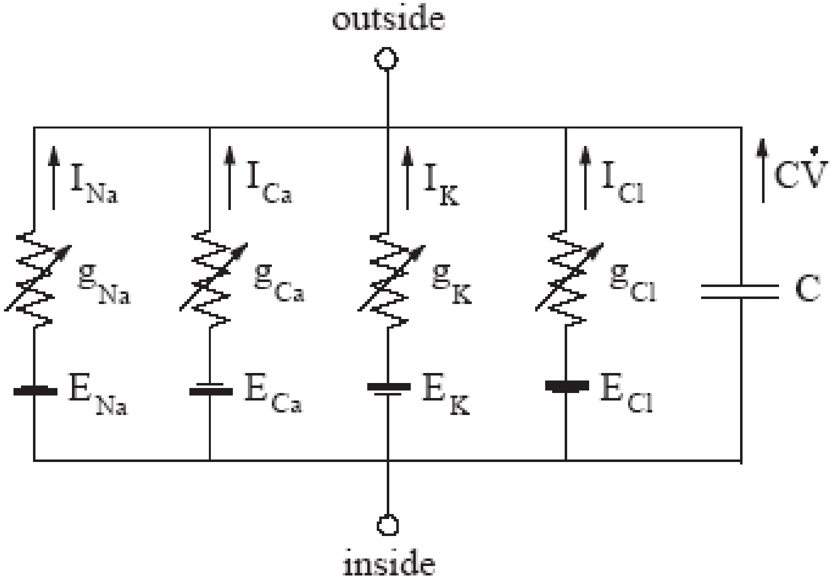
Equivalent circuit

$$I_K = g_K\left(V - E_K\right)$$

$$I_{Na} = g_{Na}\left(V - E_{Na}\right)$$

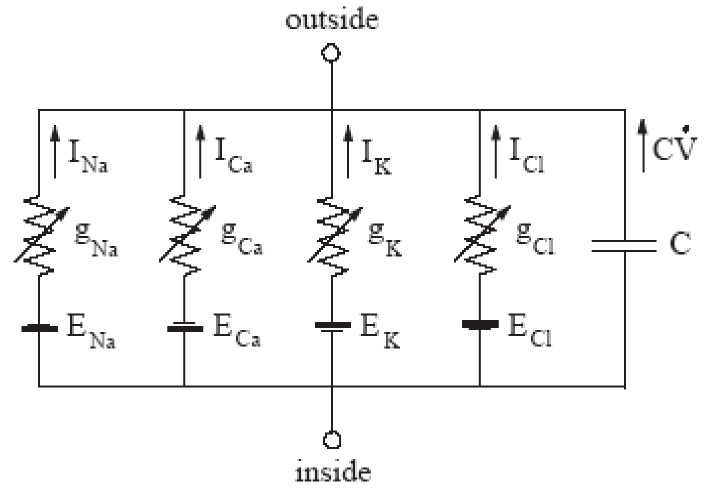
$$I_{Ca} = g_{Ca}\left(V - E_{Ca}\right)$$

$$I_{Cl} = g_{Cl}\left(V - E_{Cl}\right)$$



Equivalent circuit

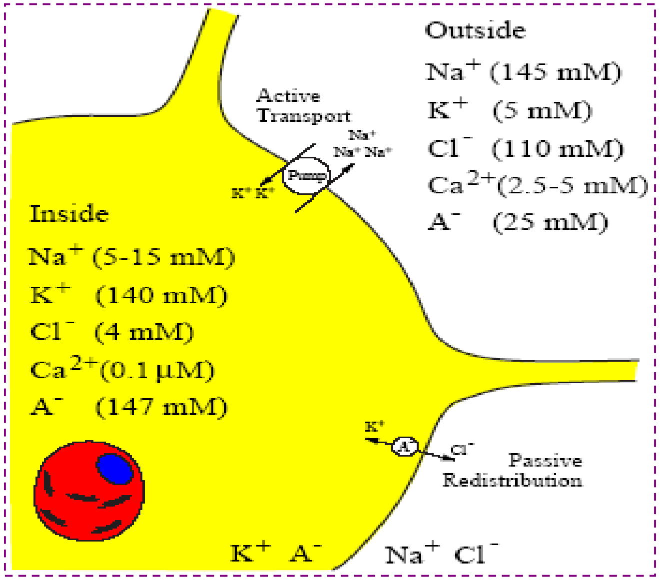
$$I_K = g_K\left(V - E_K\right)$$
$$I_{Na} = g_{Na}\left(V - E_{Na}\right)$$
$$I_{Ca} = g_{Ca}\left(V - E_{Ca}\right)$$
$$I_{Cl} = g_{Cl}\left(V - E_{Cl}\right)$$

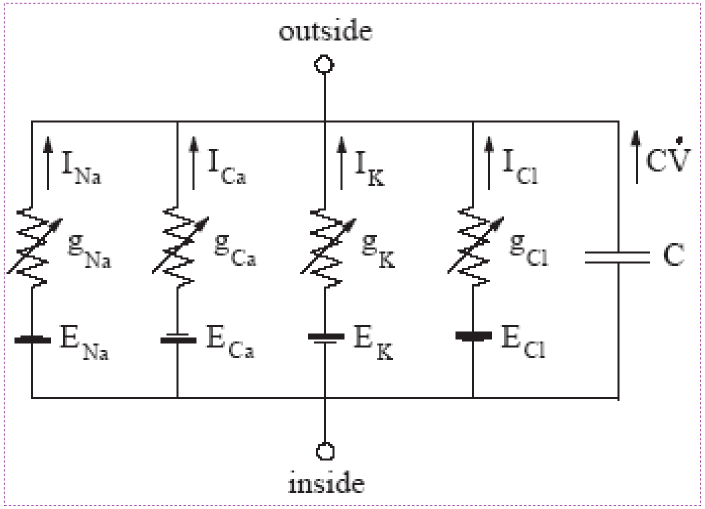


$$I = C\dot{V} + I_{Na} + I_{Ca} + I_K + I_{Cl}$$
$$C\dot{V} = I - I_{Na} - I_{Ca} - I_K - I_{Cl}$$

$$\boxed{C\dot{V} = I - g_{Na}\left(V - E_{Na}\right) - g_{Ca}\left(V - E_{Ca}\right) - g_K\left(V - E_K\right) - g_{Cl}\left(V - E_{Cl}\right)}$$

Equivalent circuit





$$C\dot{V} = I - g_{Na}\left(V - E_{Na}\right) - g_{Ca}\left(V - E_{Ca}\right) - g_K\left(V - E_K\right) - g_{Cl}\left(V - E_{Cl}\right)$$

Equivalent circuit

$$C\dot{V} = I - g_{Na}\left(V - E_{Na}\right) - g_{Ca}\left(V - E_{Ca}\right) - g_K\left(V - E_K\right) - g_{Cl}\left(V - E_{Cl}\right)$$

by setting $\dot{V} = 0$ and $I = 0$

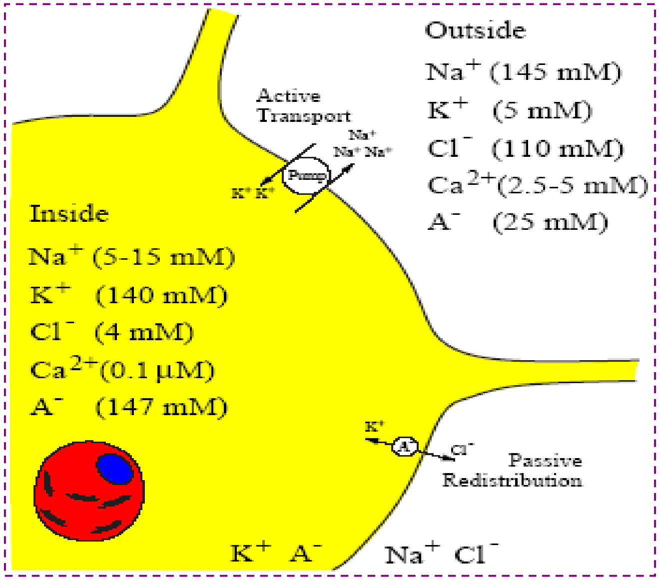
$$V_{rest} = \frac{g_{Na}E_{Na} + g_{Ca}E_{Ca} + g_K E_K + g_{Cl}E_{Cl}}{g_{Na} + g_{Ca} + g_K + g_{Cl}}$$

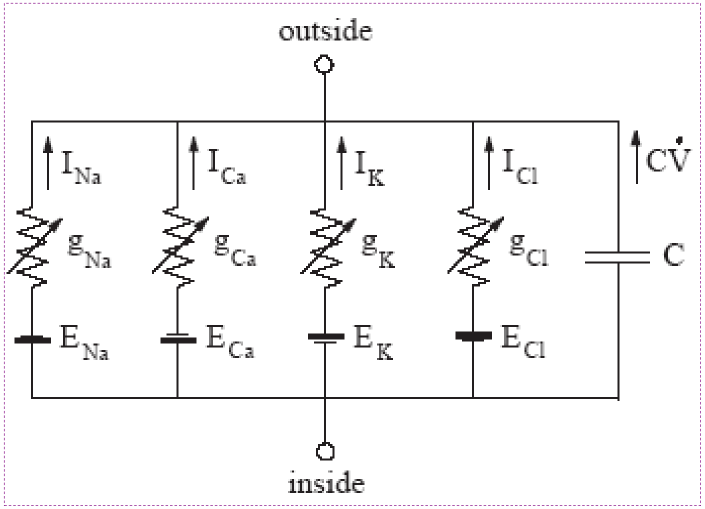
$$C\dot{V} = I - g_{inp}\left(V - V_{rest}\right)$$

where

$g_{inp} = g_{Na} + g_{Ca} + g_K + g_{Cl}$ --- input conductance.

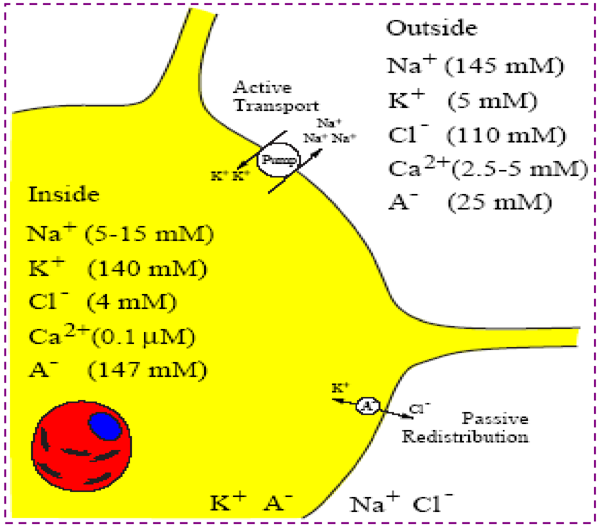
Equivalent circuit

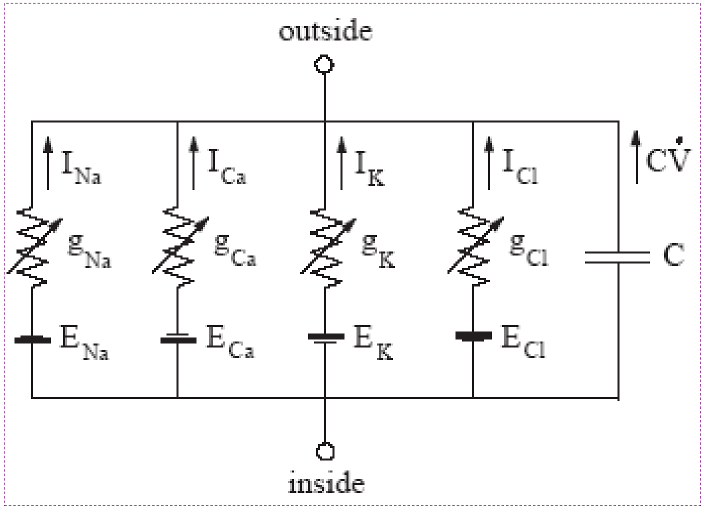




$$C\dot{V} = I - g_{inp}\left(V - V_{rest}\right)$$

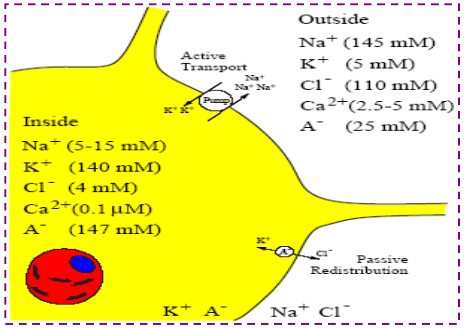
Equivalent circuit

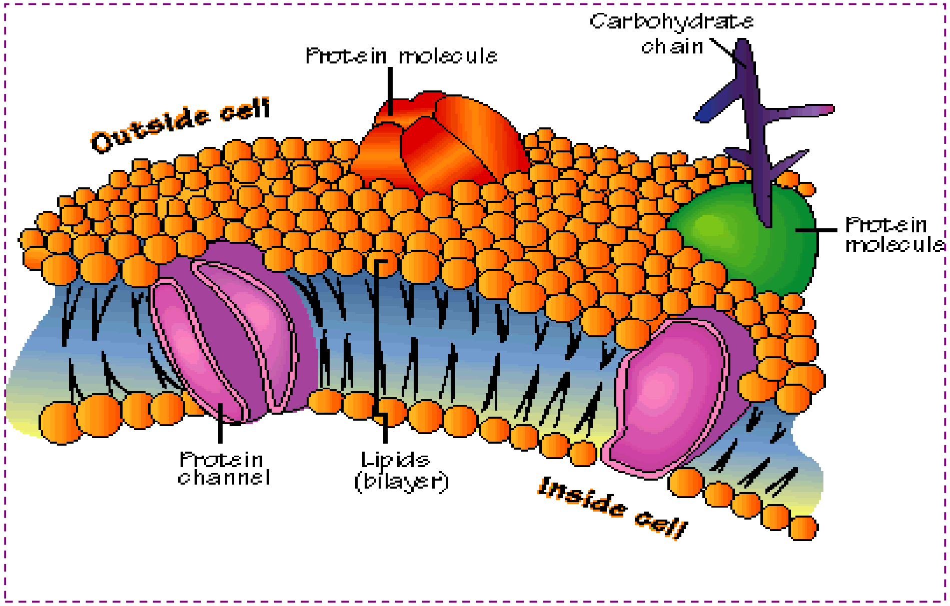




$$C\dot{V} = I - g_{inp}\left(V - V_{rest}\right)$$

Ionic channels

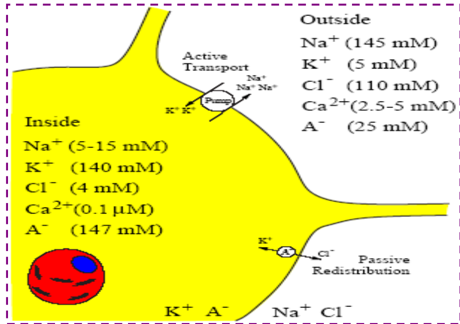


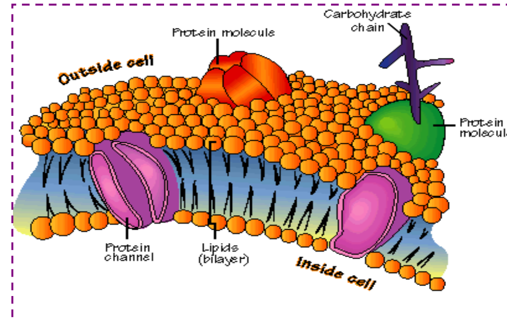


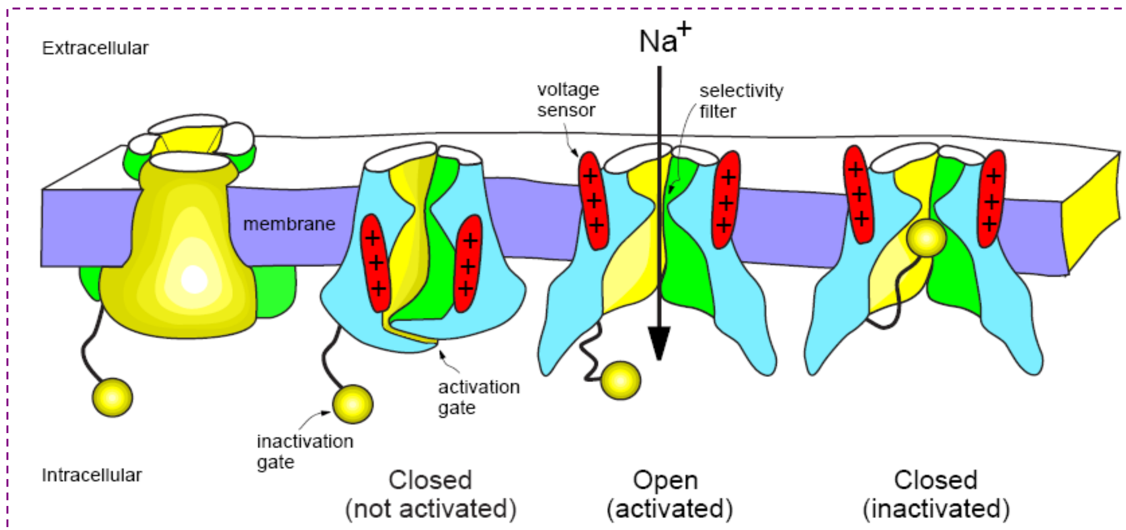
Electrical conductance of individual channels can be controlled by gating particles.

Ionic channels are large transmembrane proteins having aqueous pores through which ions can flow down their electrochemical gradients.

Ionic channels

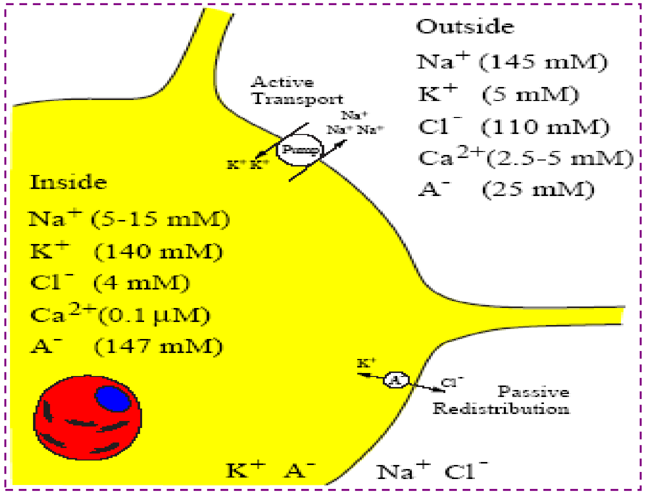


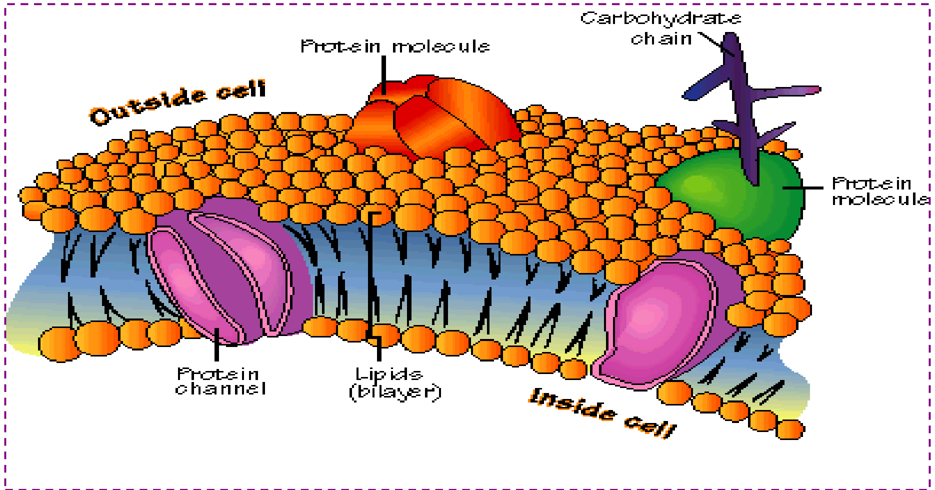




Electrical conductance of individual channels can be controlled by gating particles.

Hodgkin-Huxley gate model





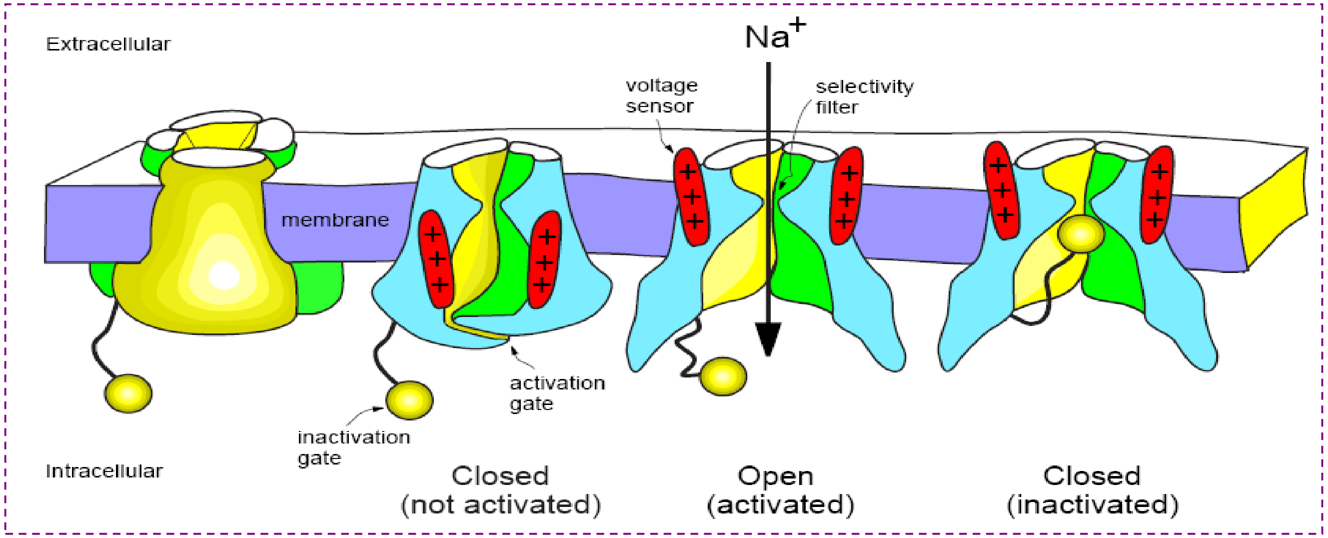
Electrical conductance of individual channels can be controlled by gating particles.

$$g_{inp} = \bar{g}\, p$$

p - average proportion of channels in the open state

$\bar{g}$ - maximal conductance of the population

Hodgkin-Huxley gate model



$$g_{inp} = \bar{g}\, p \Rightarrow p = m^a h^b \Rightarrow g_{inp} = \bar{g}\, m^a h^b$$

m - probability of the activation gate to be in open state

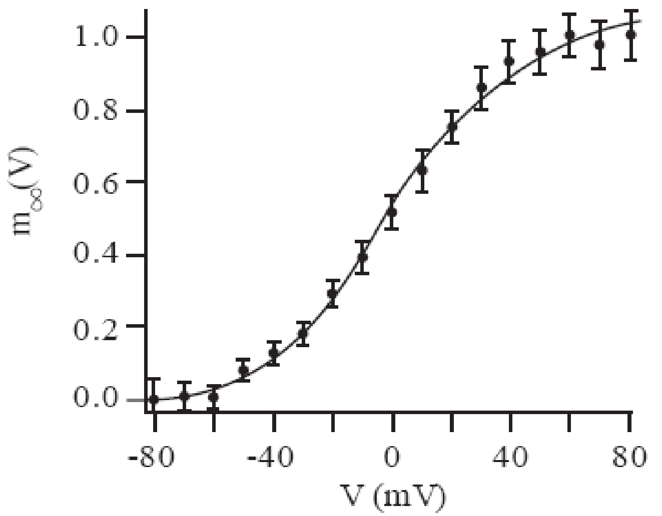
h - probability of the inactivation gate to be in open state

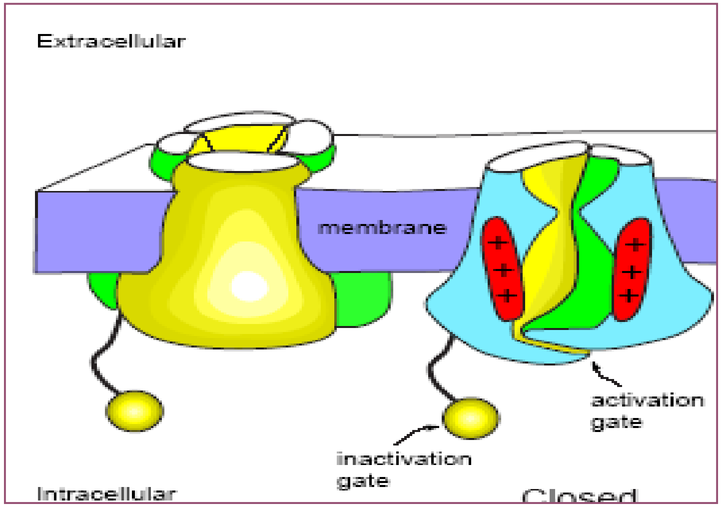
a - number of activation gates

b - number of inactivation gates

Activation gate

$$\tau(V)\dot{m} = \left(m_\infty(V) - m\right)$$



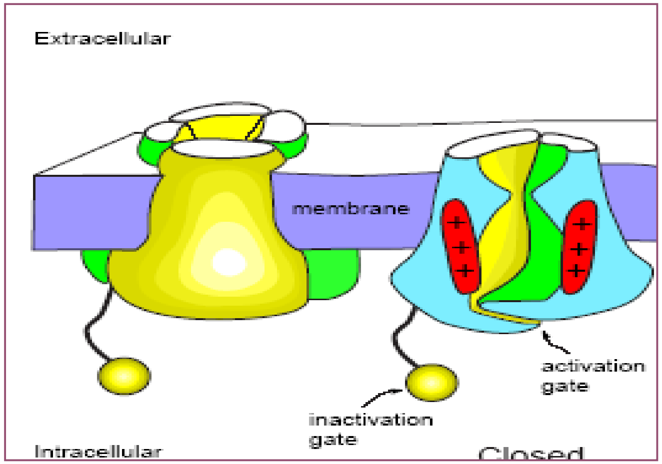


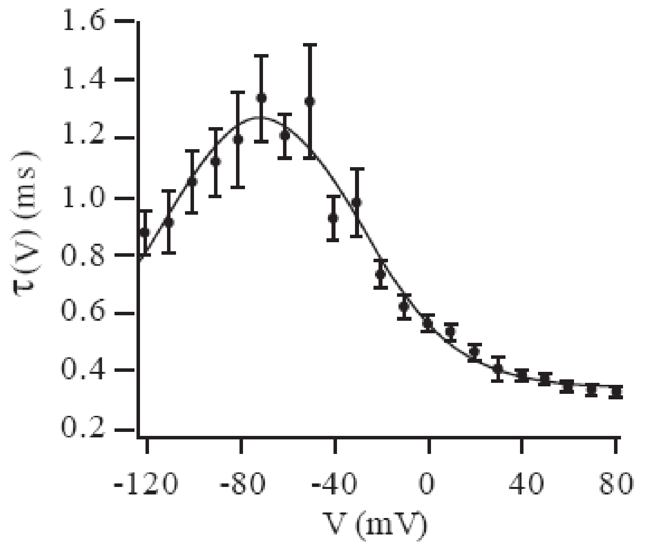
Activation fuction:

$$m_\infty(V) = \frac{1}{1 + \exp\left\{\left(V_{1/2} - V\right)/k\right\}}$$

Time constant

$$\tau(V)\dot{m} = \left(m_\infty(V) - m\right)$$

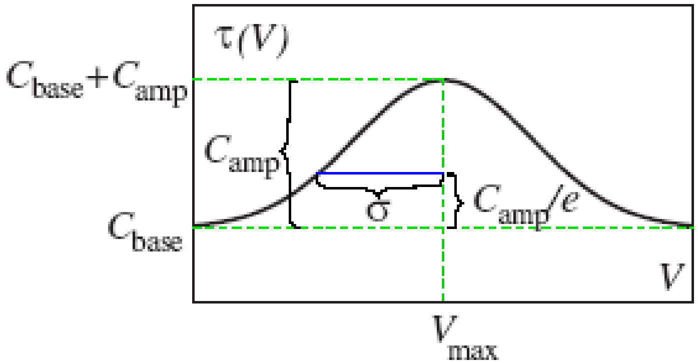




Time constant:

$$\tau(V) = C_{base} + C_{amp}\exp\frac{-\left(V_{\max} - V\right)^2}{\sigma^2}$$

Time constant

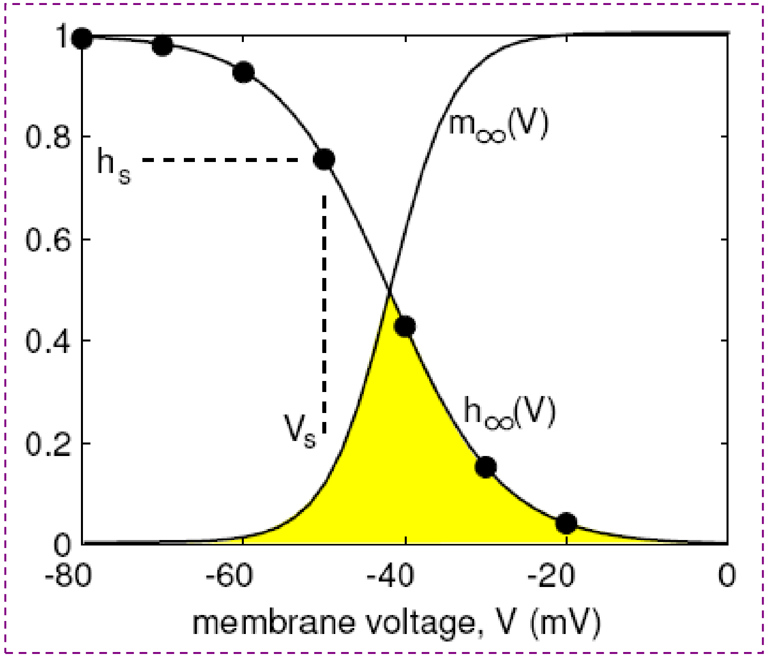


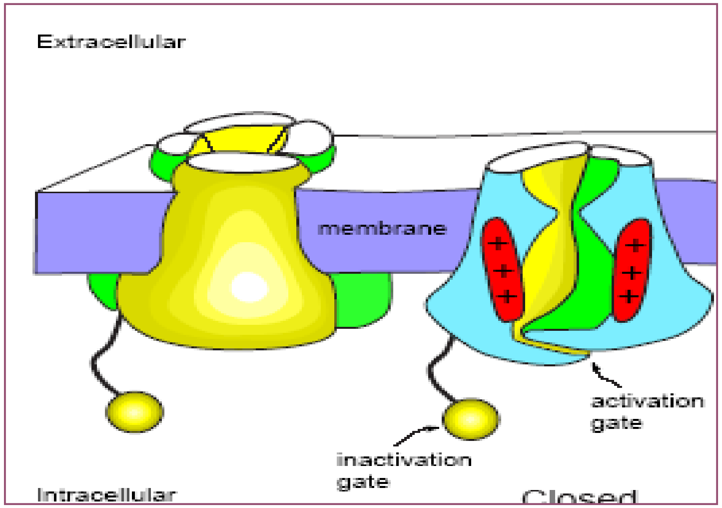
Time constant:

$$\tau\left(V\right)=C_{base}+C_{amp}\exp\frac{-\left(V_{\max}-V\right)^{2}}{\sigma^{2}}$$

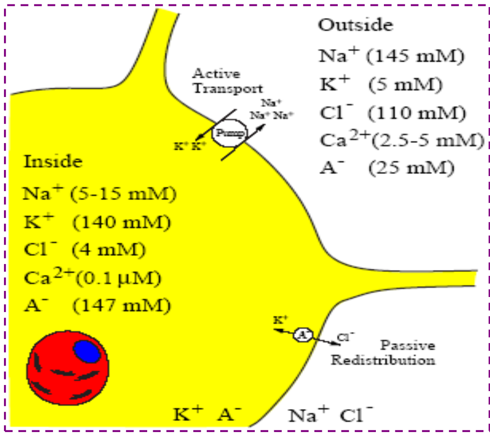
Inactivation gate

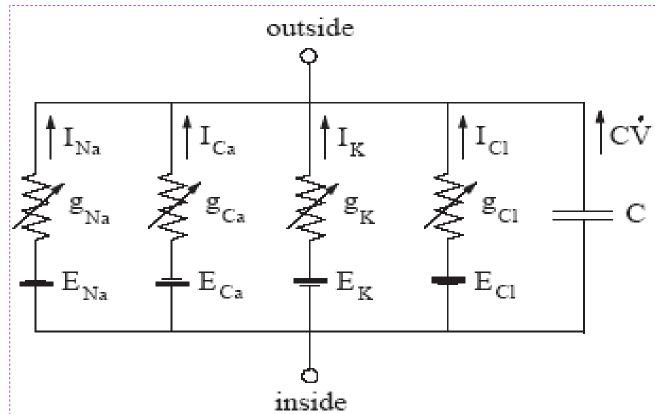
$$\boxed{\tau(V)\dot{h} = \left(h_\infty(V) - h\right)}$$





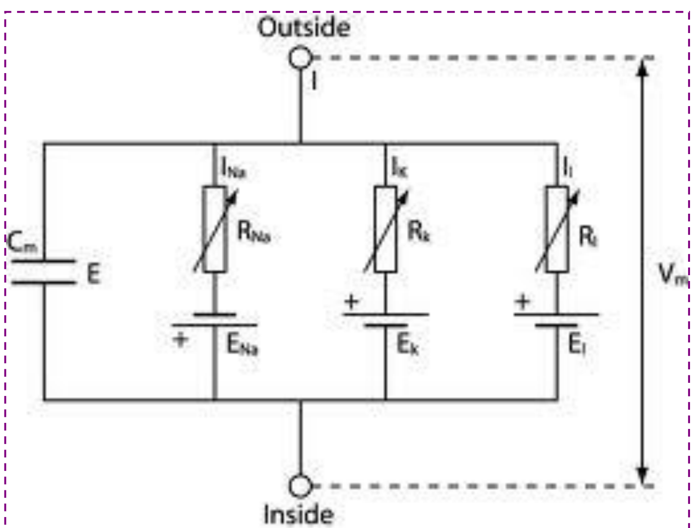
Hodgkin-Huxley Model

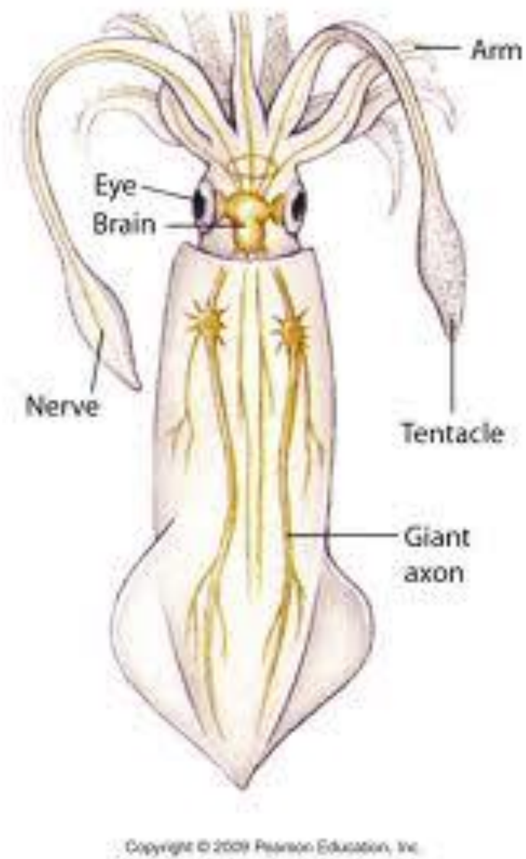




$$
\begin{cases}
C\dot{V} = I - \bar{g}\, m^a p^b \left(V - V_{rest}\right) \\
\tau(V)\dot{m} = \left(m_\infty(V) - m\right) \\
\tau(V)\dot{h} = \left(h_\infty(V) - h\right)
\end{cases}
$$

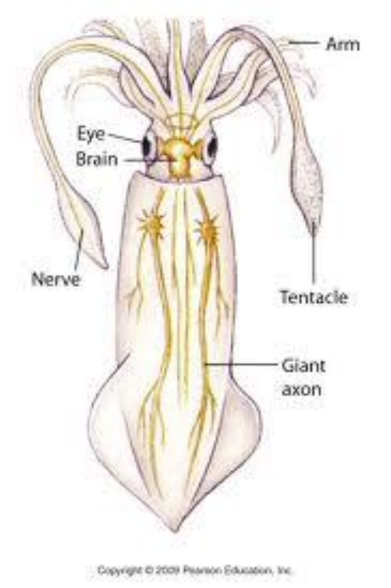
Hodgkin-Huxley model of the squid giant axon





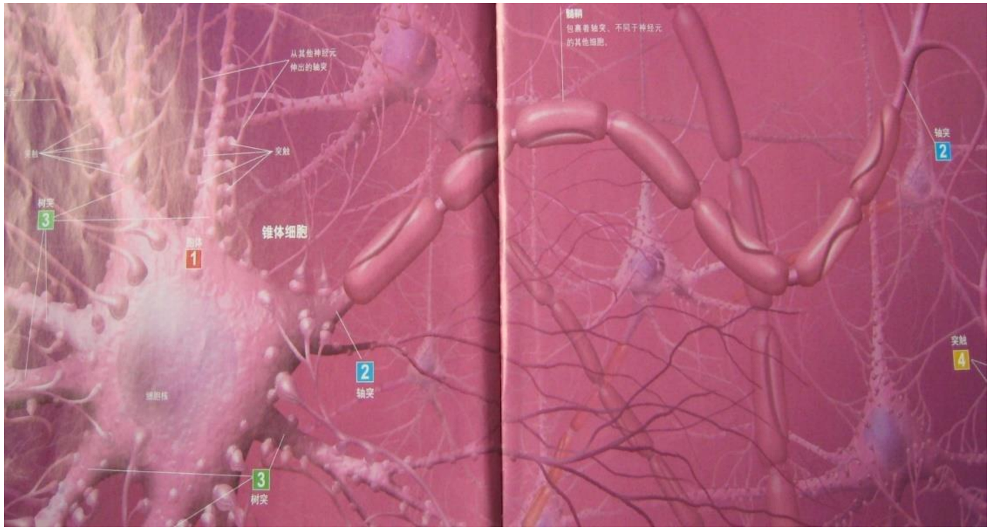
Hodgkin-Huxley model of the squid giant axon

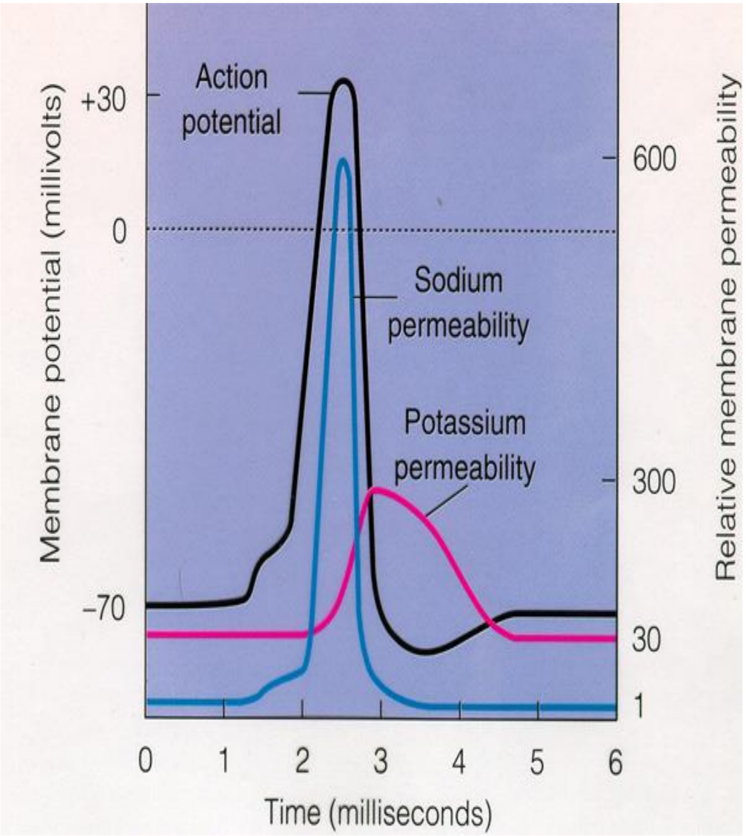
$$
\begin{cases}
C\dot{V} = I - \underbrace{\bar{g}_K n^4 (V - E_K)}_{I_K} - \underbrace{\bar{g}_{Na} m^3 h (V - E_{Na})}_{I_{Na}} - \underbrace{\bar{g}_L (V - E_L)}_{I_L} \\
\dot{n} = \alpha_n(V)(1-n) - \beta_n(V)n \\
\dot{m} = \alpha_m(V)(1-m) - \beta_m(V)m \\
\dot{h} = \alpha_h(V)(1-h) - \beta_h(V)h
\end{cases}
$$



1963 Nobel prize in physiology or medicine

Action potential





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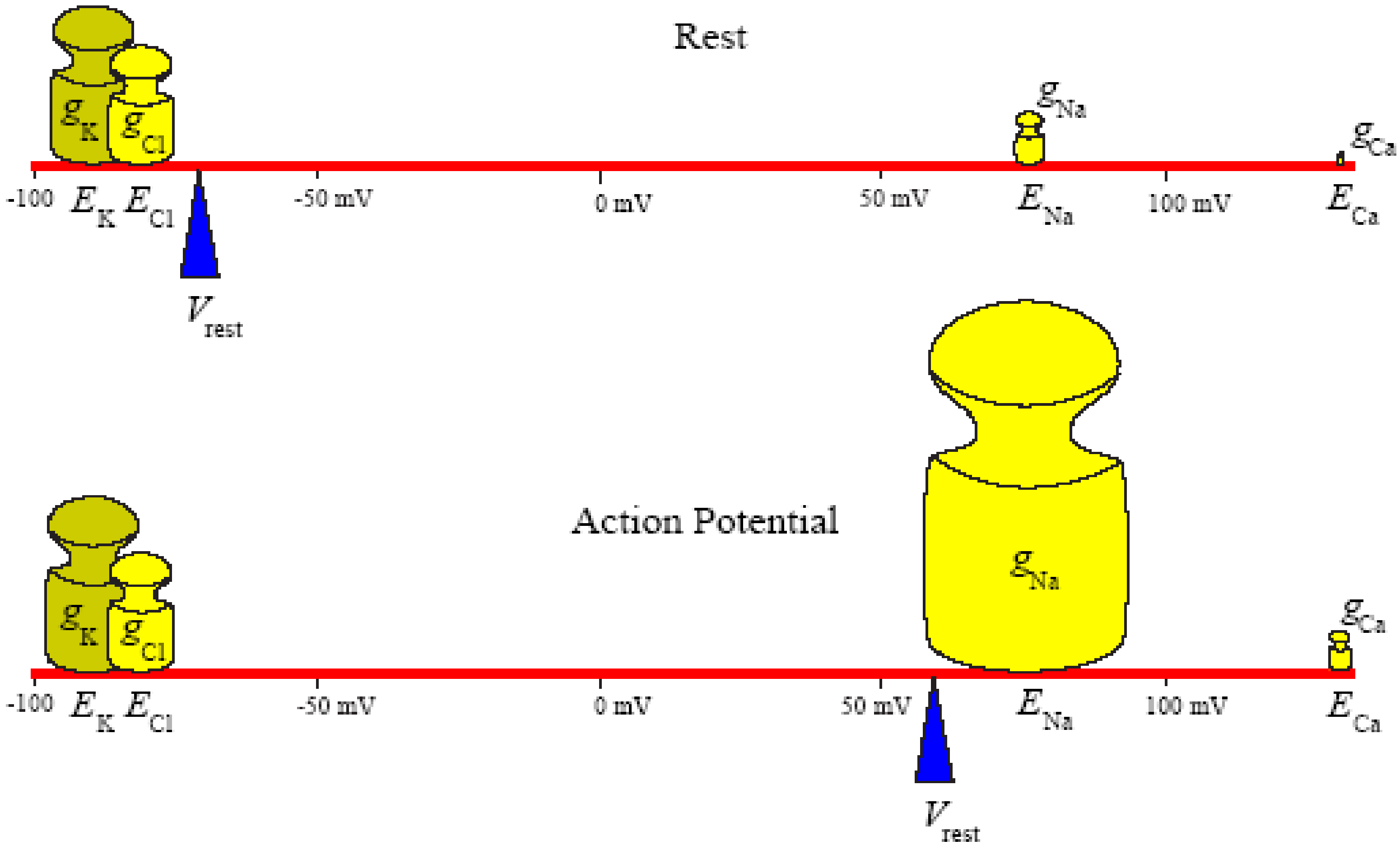

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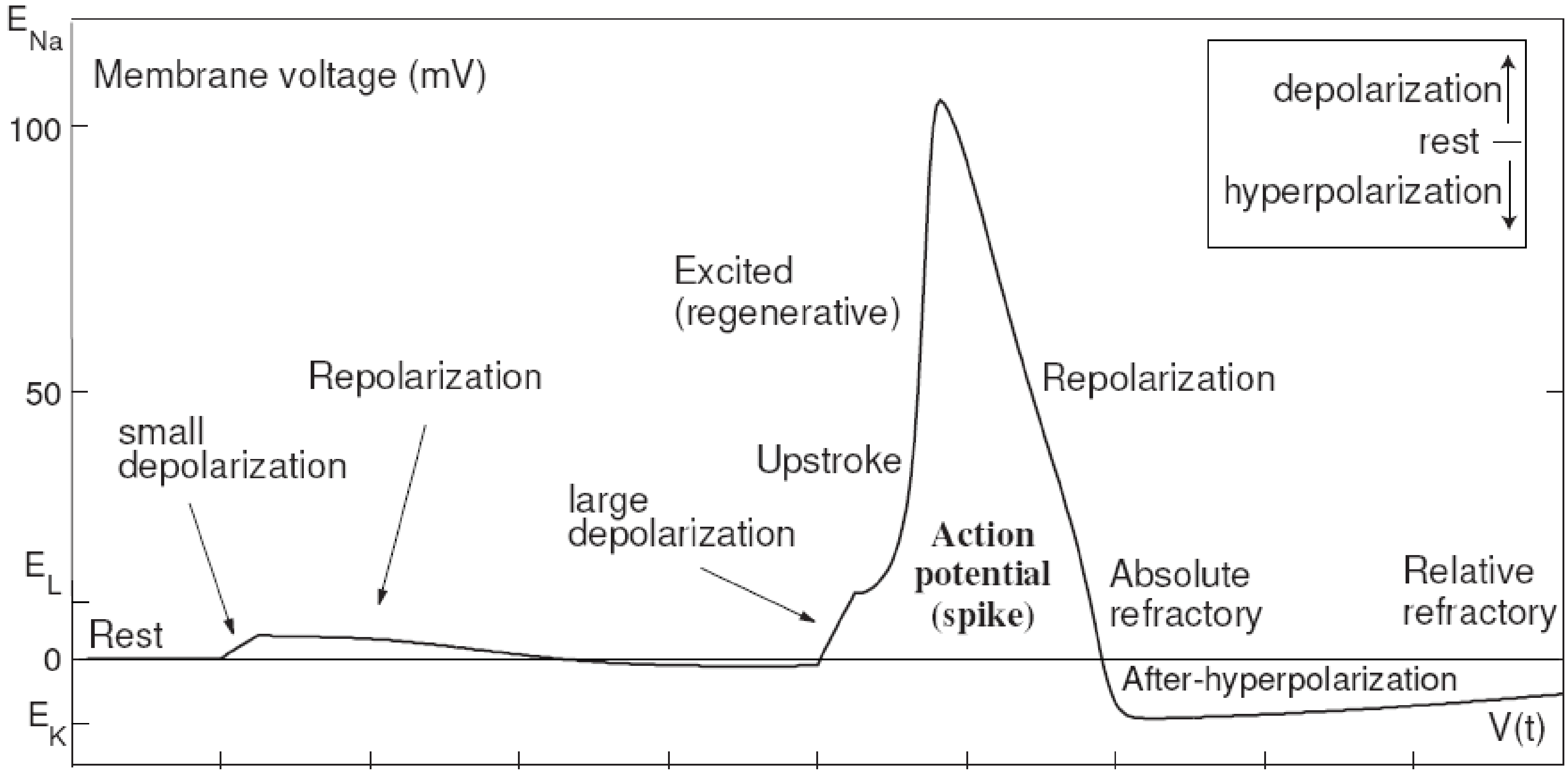

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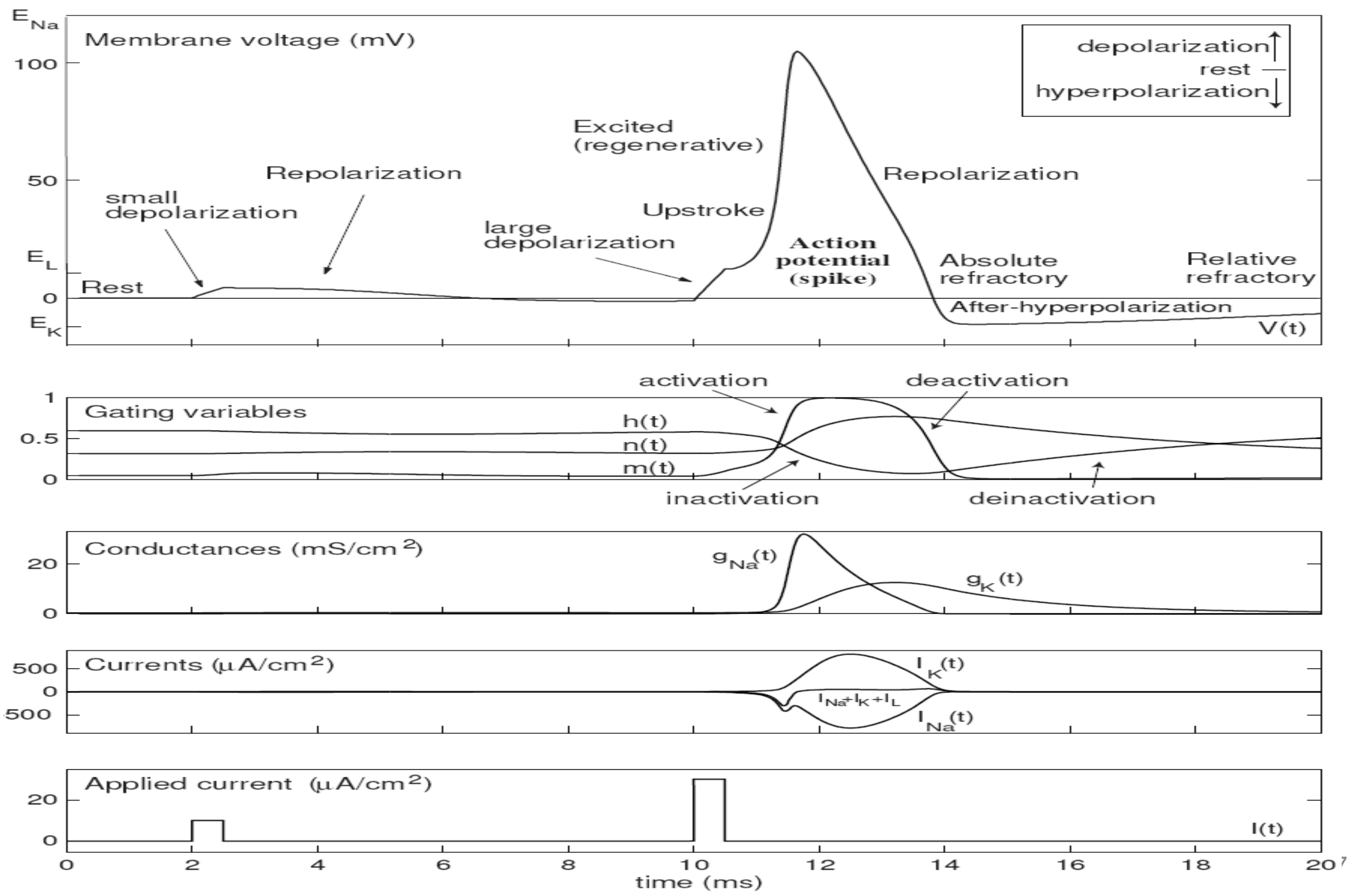

The End