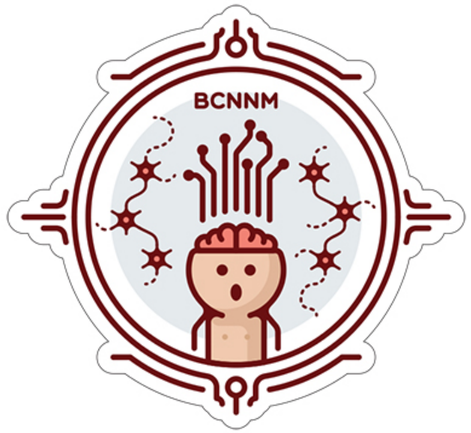


Computational Neuroscience

Lecture 3. Neuron physiology and biophysics

| Dmitry Bozhko | Georgy Galumov | Sofia Kolchanova | Vladislav Myrov |

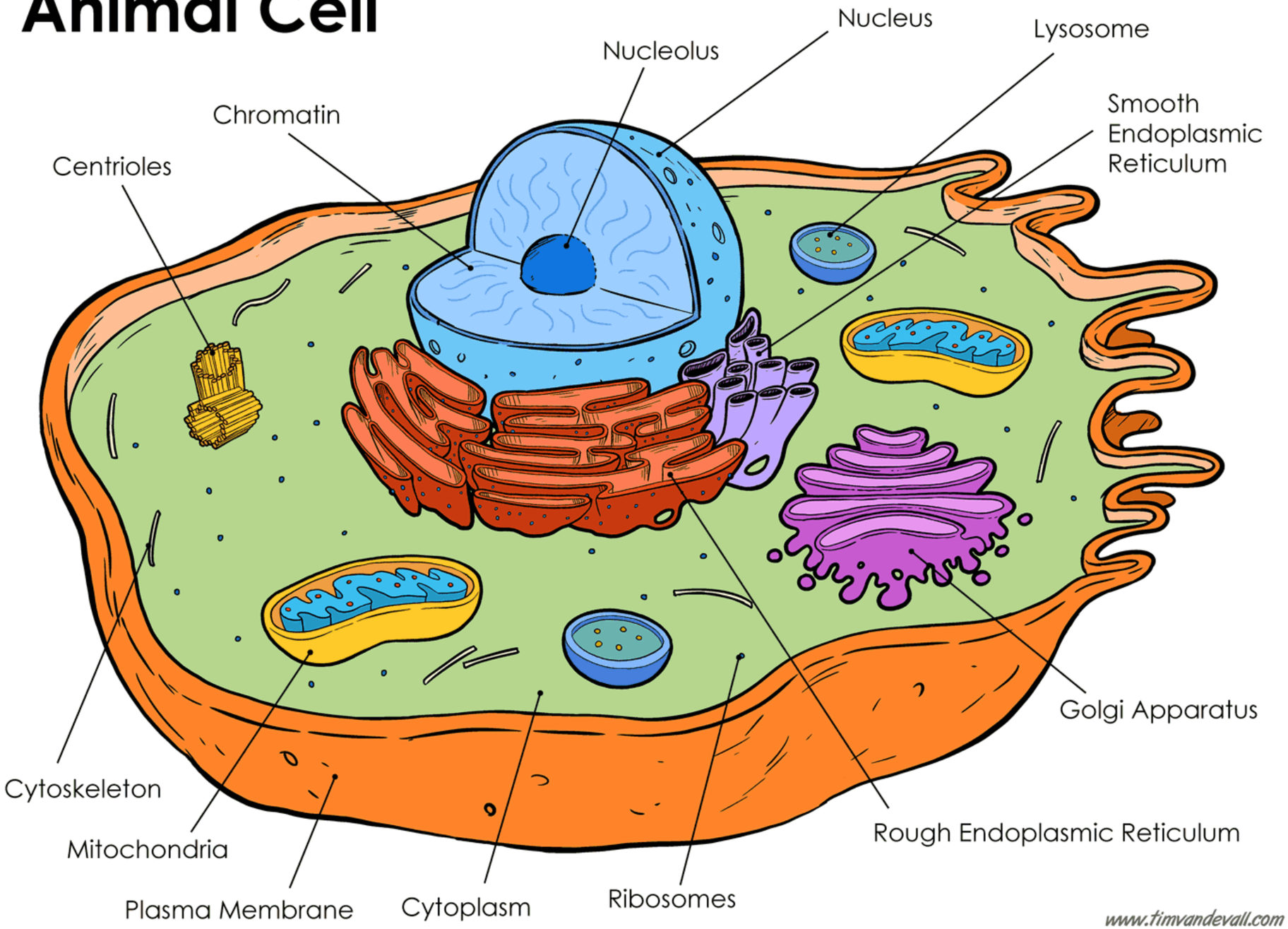
Agenda

- Neuron morphological and functional structure
- How does neuron transmit signals
- Biophysics of neuron
- Electrochemical properties

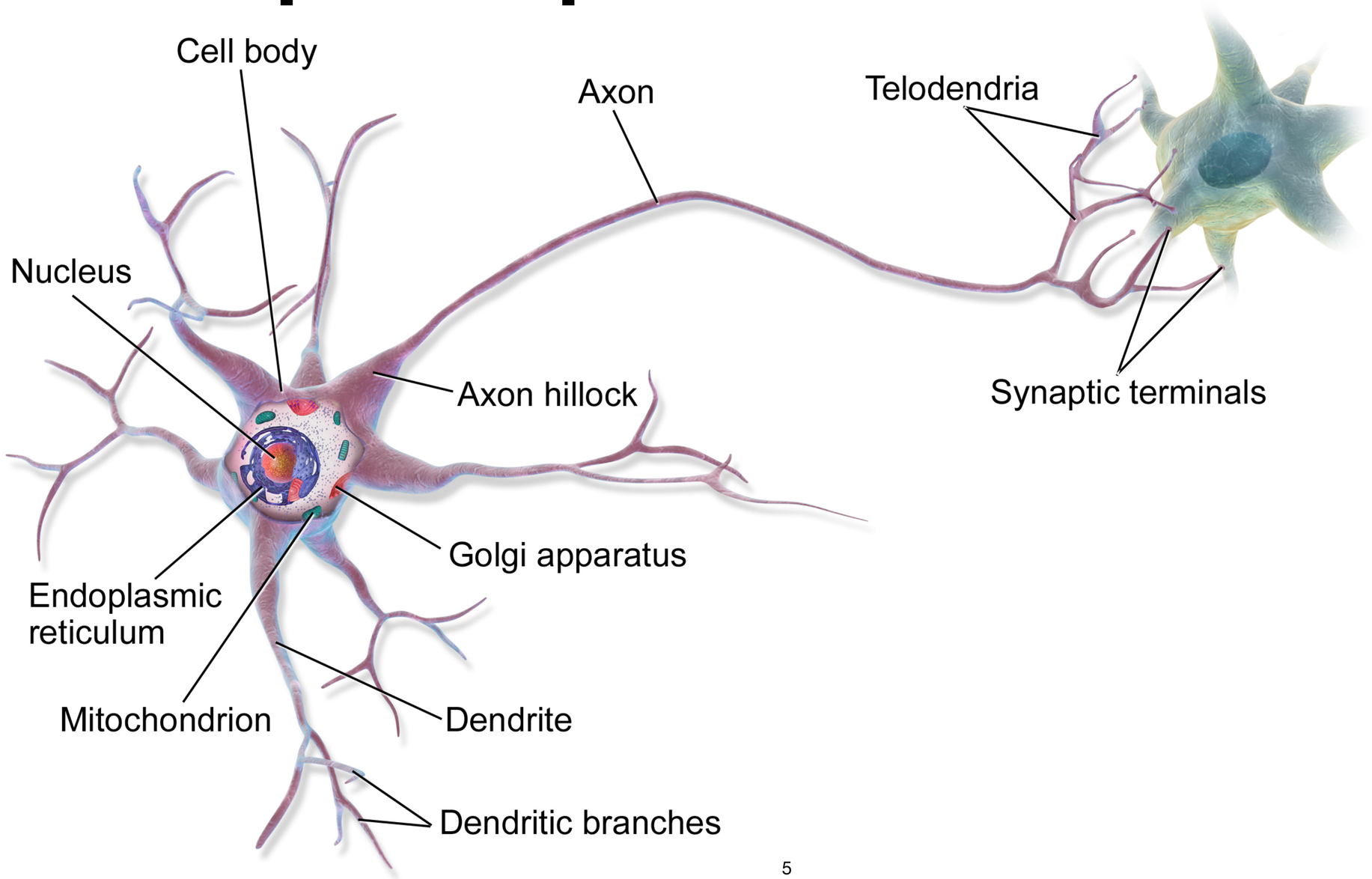
Neuron morphological and functional structure

- Neuron as a cell
- Neuron specific parts
- Morphology
- Functions
- Glial cells

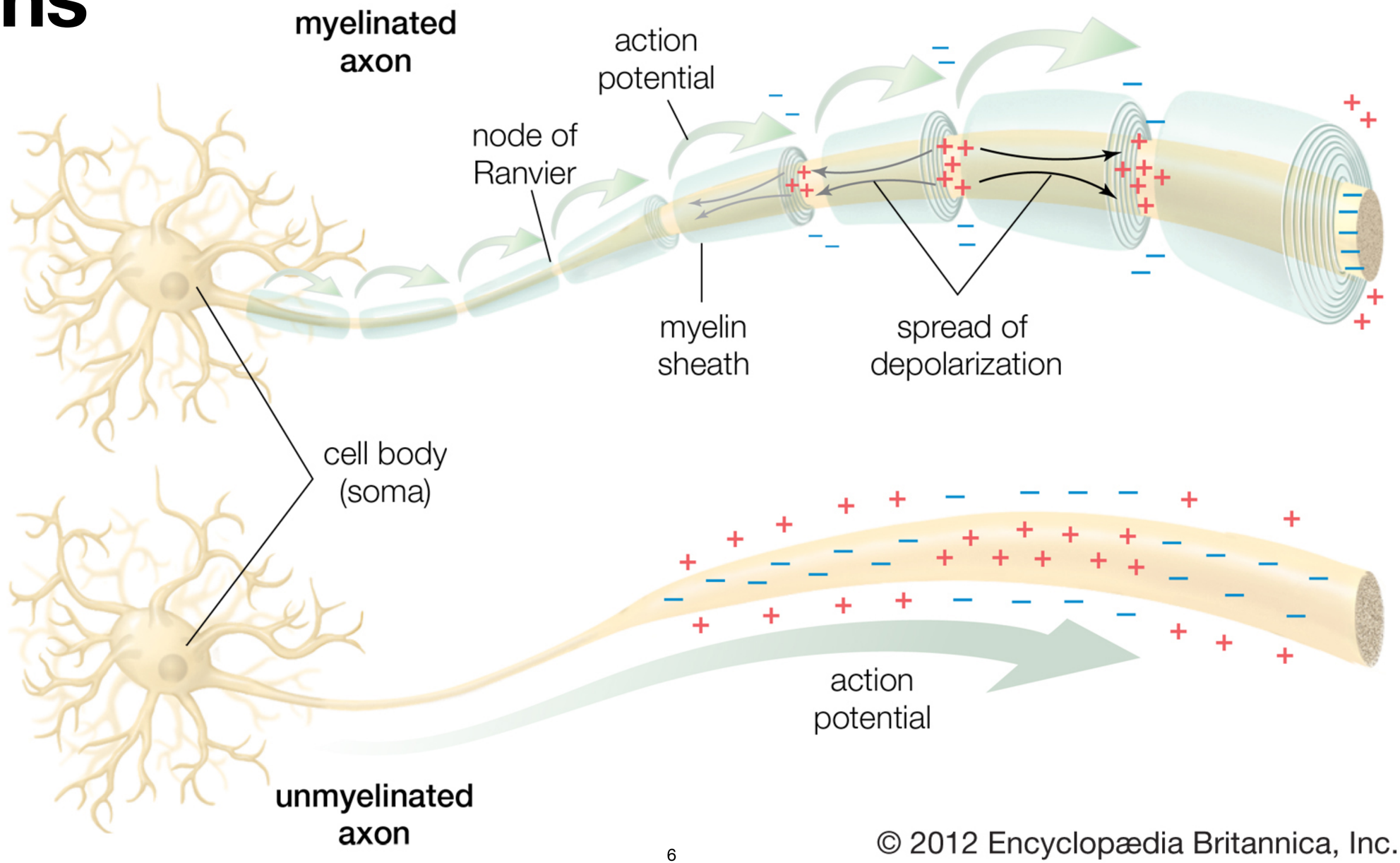
Animal Cell



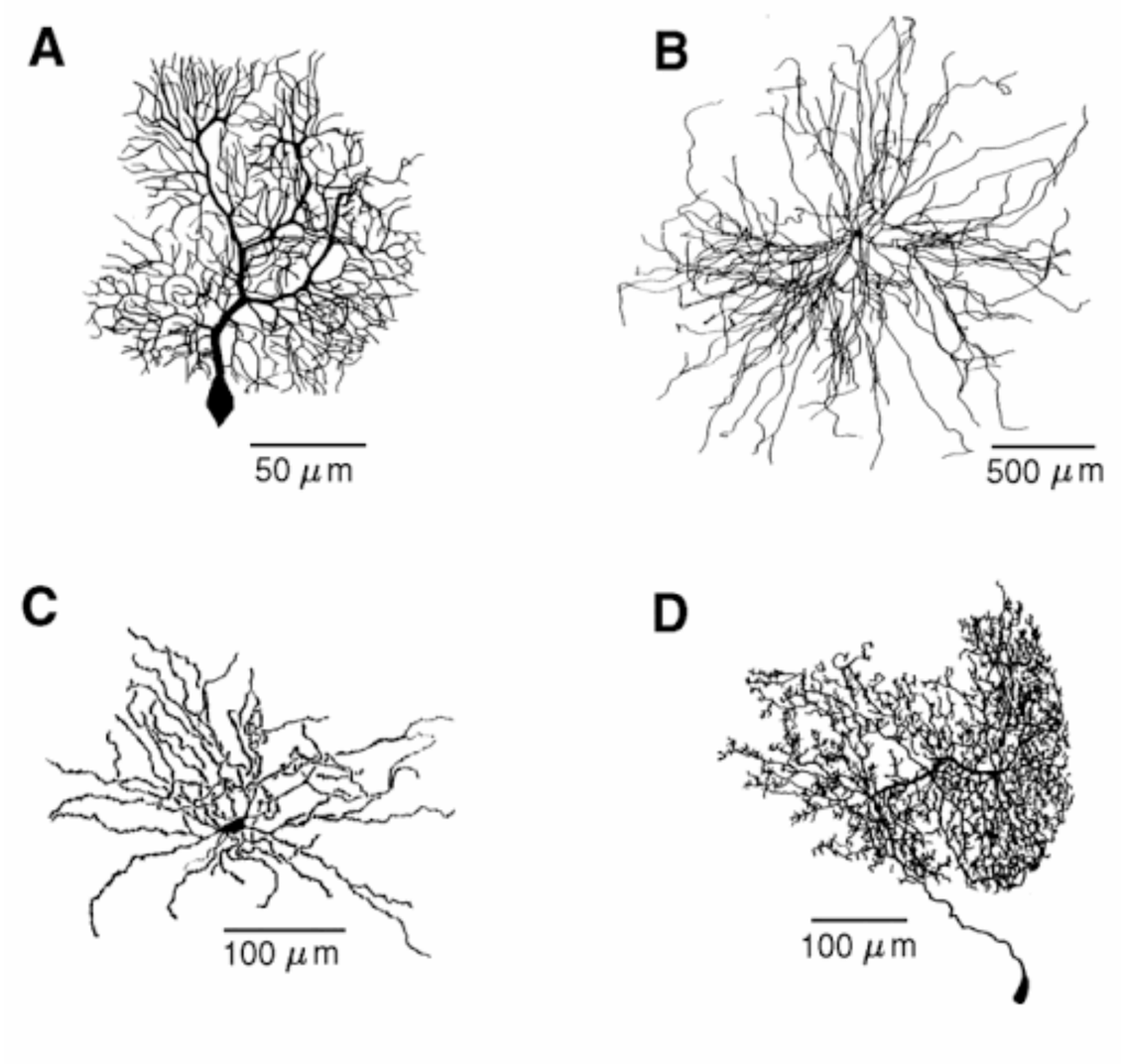
Neuron specific parts

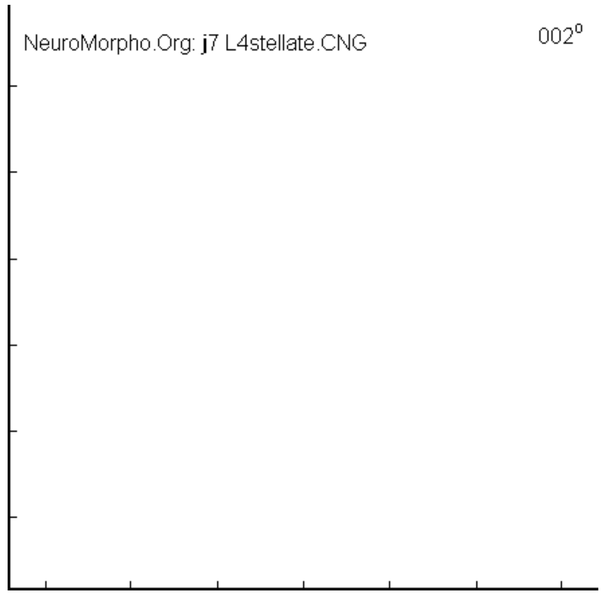


Axons

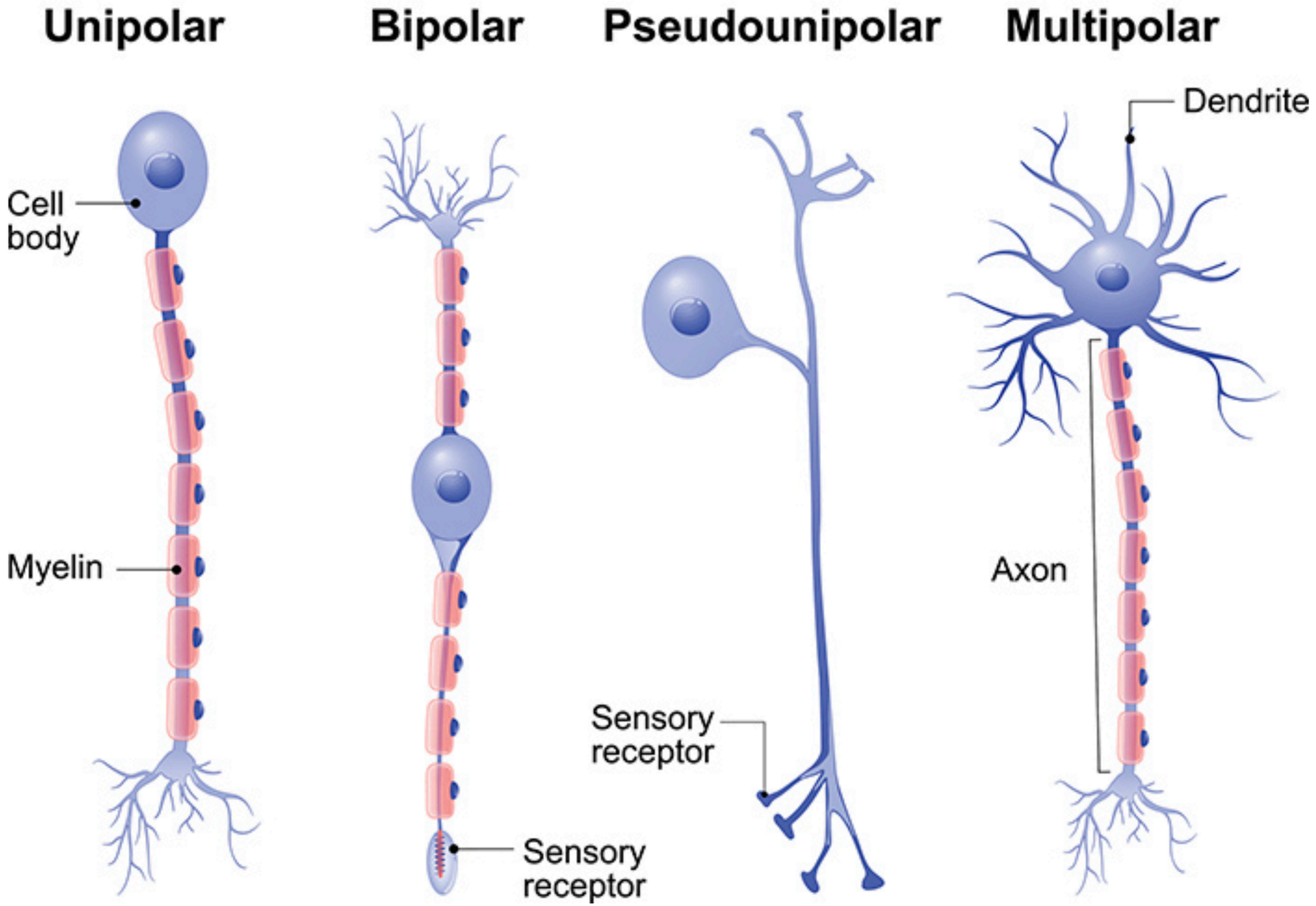


Dendrites

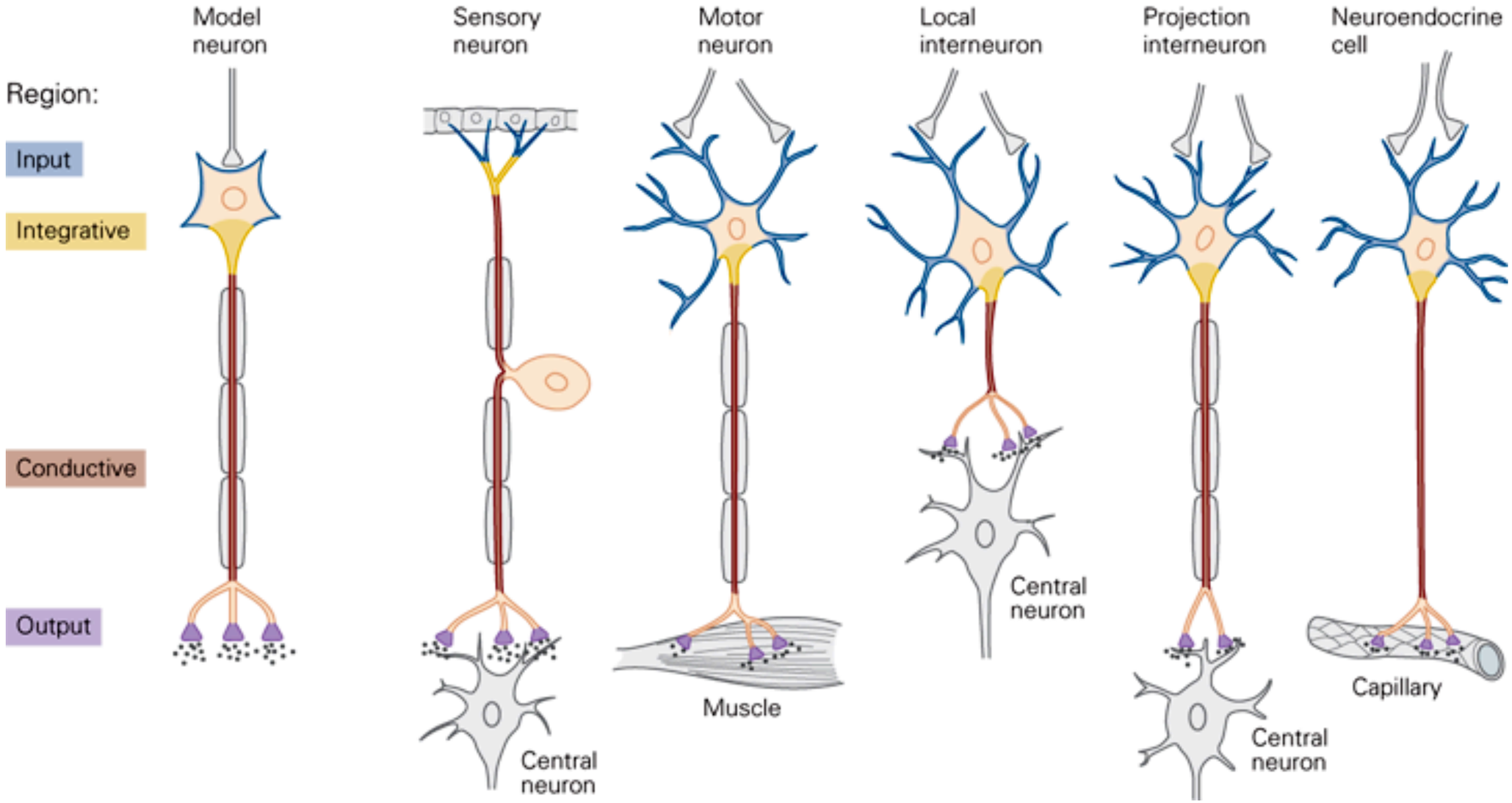

A
50 μm
B
500 μm
C
100 μm
D
100 μm


NeuroMorpho.Org: j7 L4stellate.CNG
002°

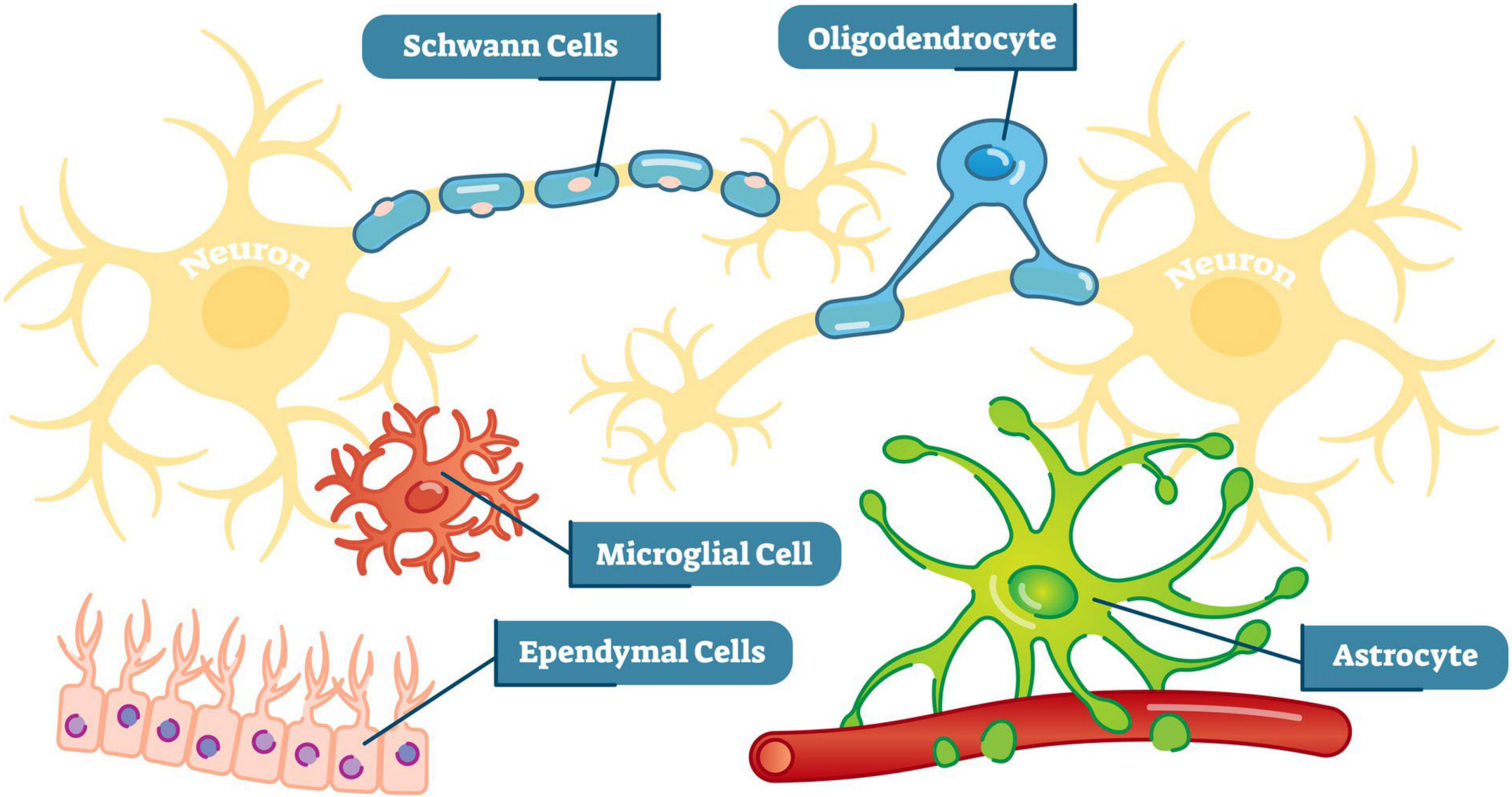
Morphology


Unipolar
Bipolar
Pseudounipolar
Multipolar
Cell body
Myelin
Sensory receptor
Sensory receptor
Dendrite
Axon

Functions


Model neuron
Sensory neuron
Motor neuron
Local interneuron
Projection interneuron
Neuroendocrine cell
Region:
Input
Integrative
Conductive
Output
Central neuron
Muscle
Central neuron
Central neuron
Capillary

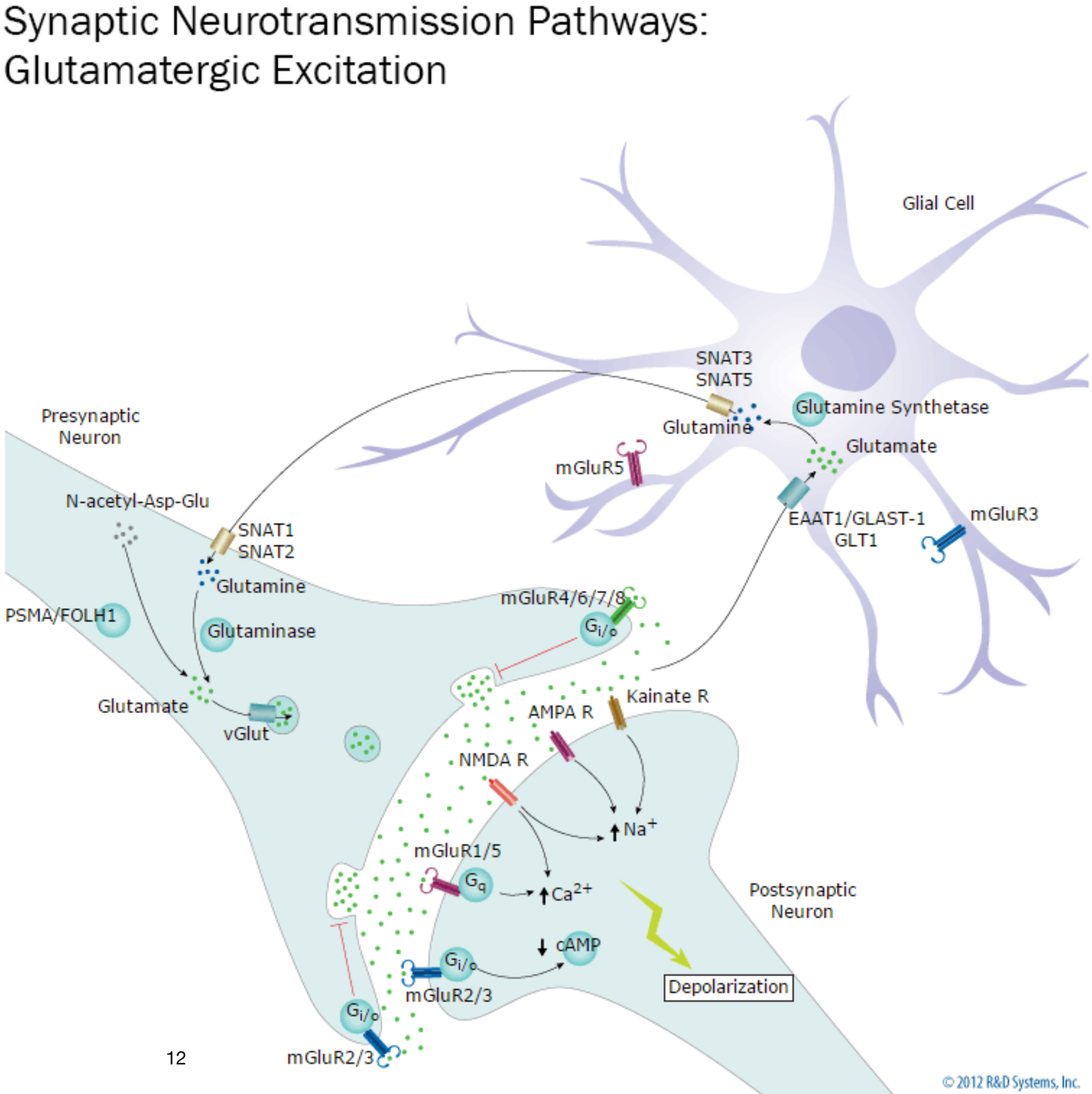
Glial cells

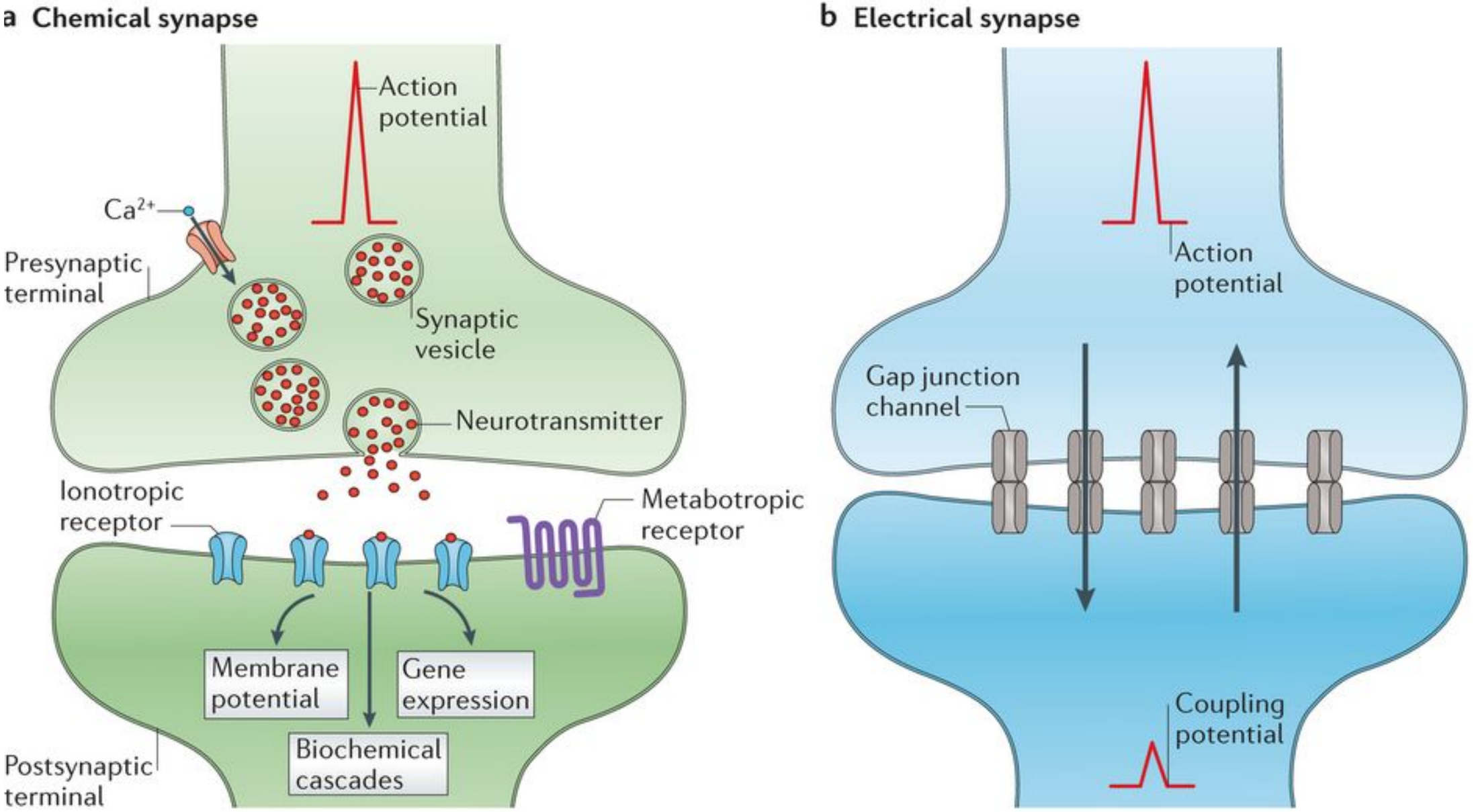

Schwann Cells
Oligodendrocyte
Neuron
Neuron
Microglial Cell
Ependymal Cells
Astrocyte

How does neuron transmit signals

- Connections (synapses, gap junctions)
- Excitation/Inhibition

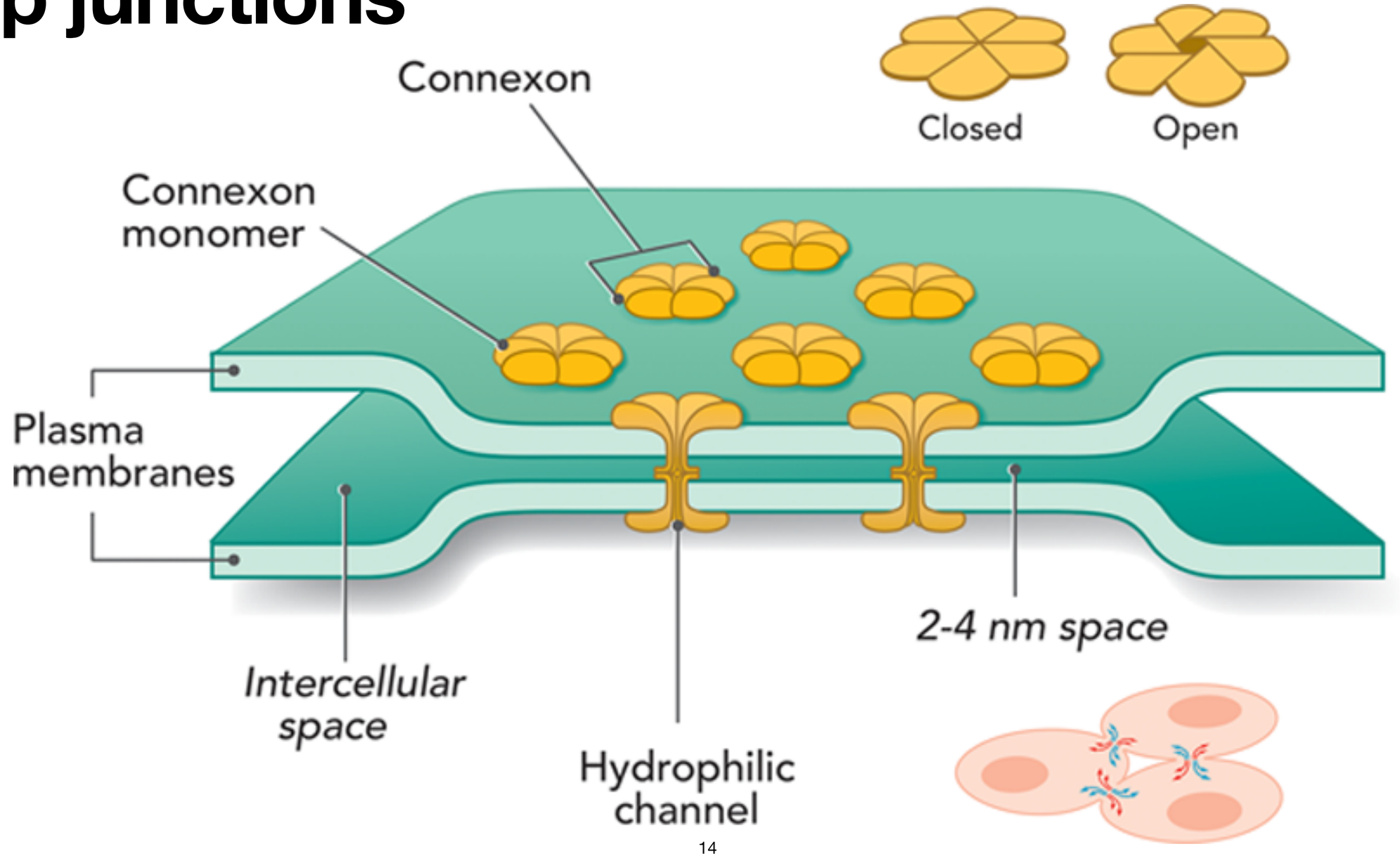
Synapses

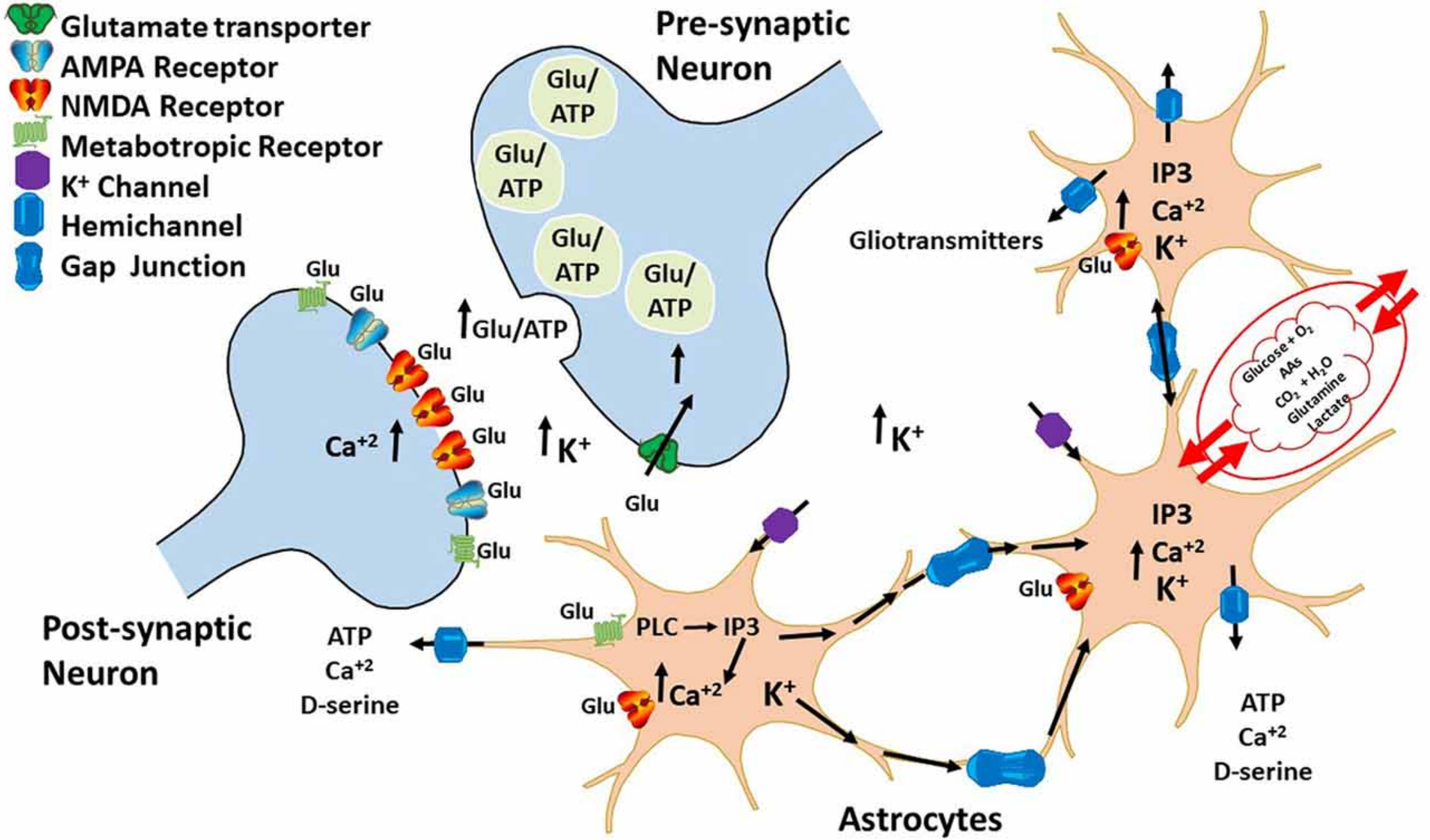

Synaptic Neurotransmission Pathways:
Glutamatergic Excitation
Glial Cell
SNAT3
SNAT5
Glutamine Synthetase
Glutamine
Glutamate
mGluR5
EAAT1/GLAST-1
GLT1
mGluR3
Presynaptic
Neuron
N-acetyl-Asp-Glu
SNAT1
SNAT2
Glutamine
PSMA/FOLH1
Glutaminase
mGluR4/6/7/8
$G_{i/o}$
Glutamate
vGlut
Kainate R
AMPA R
NMDA R
Na^+
mGluR1/5
G_q
Ca^{2+}
Postsynaptic
Neuron
cAMP
$G_{i/o}$
mGluR2/3
Depolarization
$G_{i/o}$
mGluR2/3
© 2012 R&D Systems, Inc.



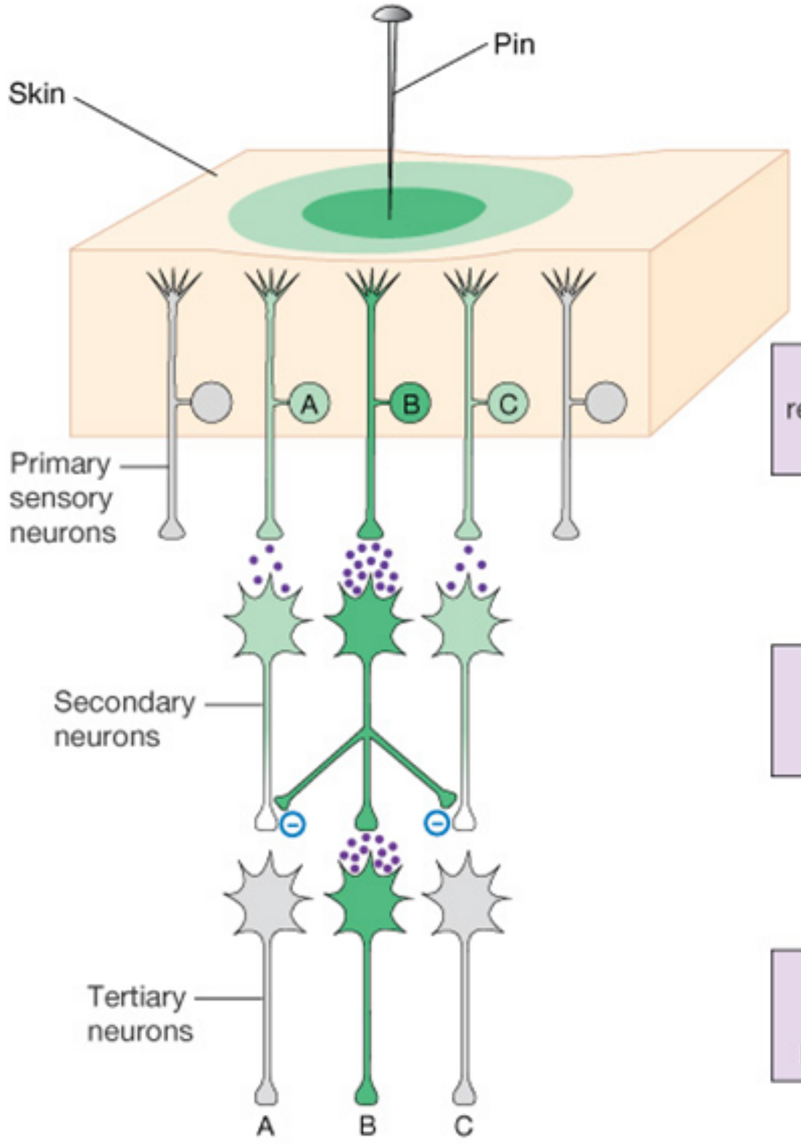
Nature Reviews | Neuroscience

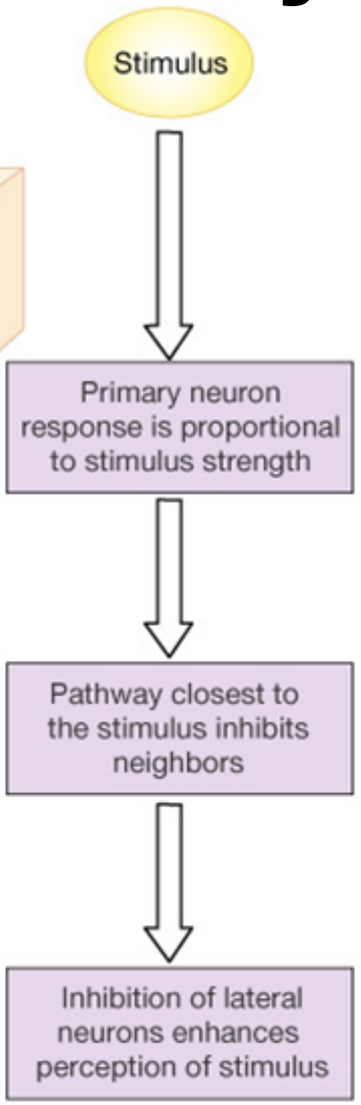
Gap junctions

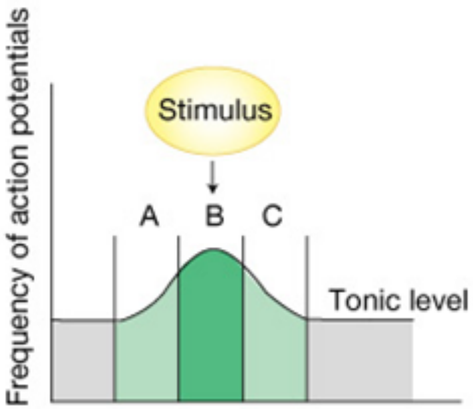


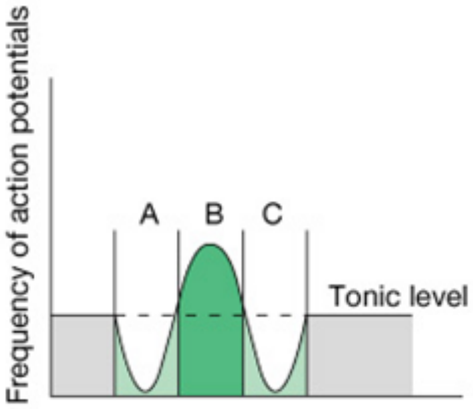

Glutamate transporter
AMPA Receptor
NMDA Receptor
Metabotropic Receptor
K+ Channel
Hemichannel
Gap Junction
Pre-synaptic Neuron
Glu/ ATP
Glu/ ATP
Glu/ ATP
Glu/ ATP
Glu/ ATP
Glu
Glu
Glu
Glu
Glu
Glu
Glu
Glu/ATP
Ca+2
K+
K+
Glu
Post-synaptic Neuron
ATP
Ca+2
D-serine
Glu
PLC → IP3
Glu
Ca+2
K+
Astrocytes
Gliotransmitters
IP3
Ca+2
K+
Glu
IP3
Ca+2
K+
Glu
Glucose + O2
AAs
CO2 + H2O
Glutamine
Lactate
ATP
Ca+2
D-serine

Lateral inhibition in sensory processing









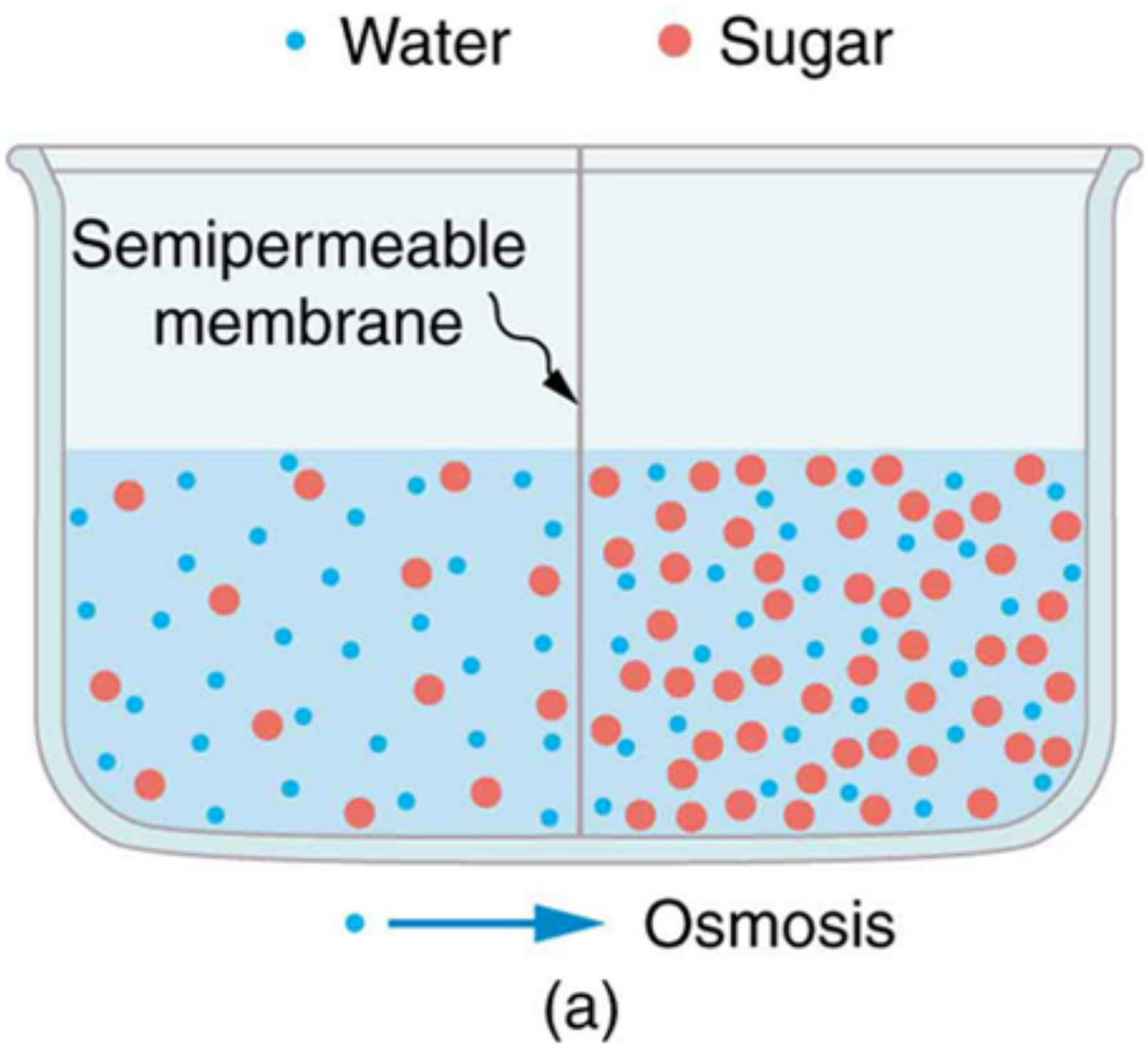
Biophysics of neuron

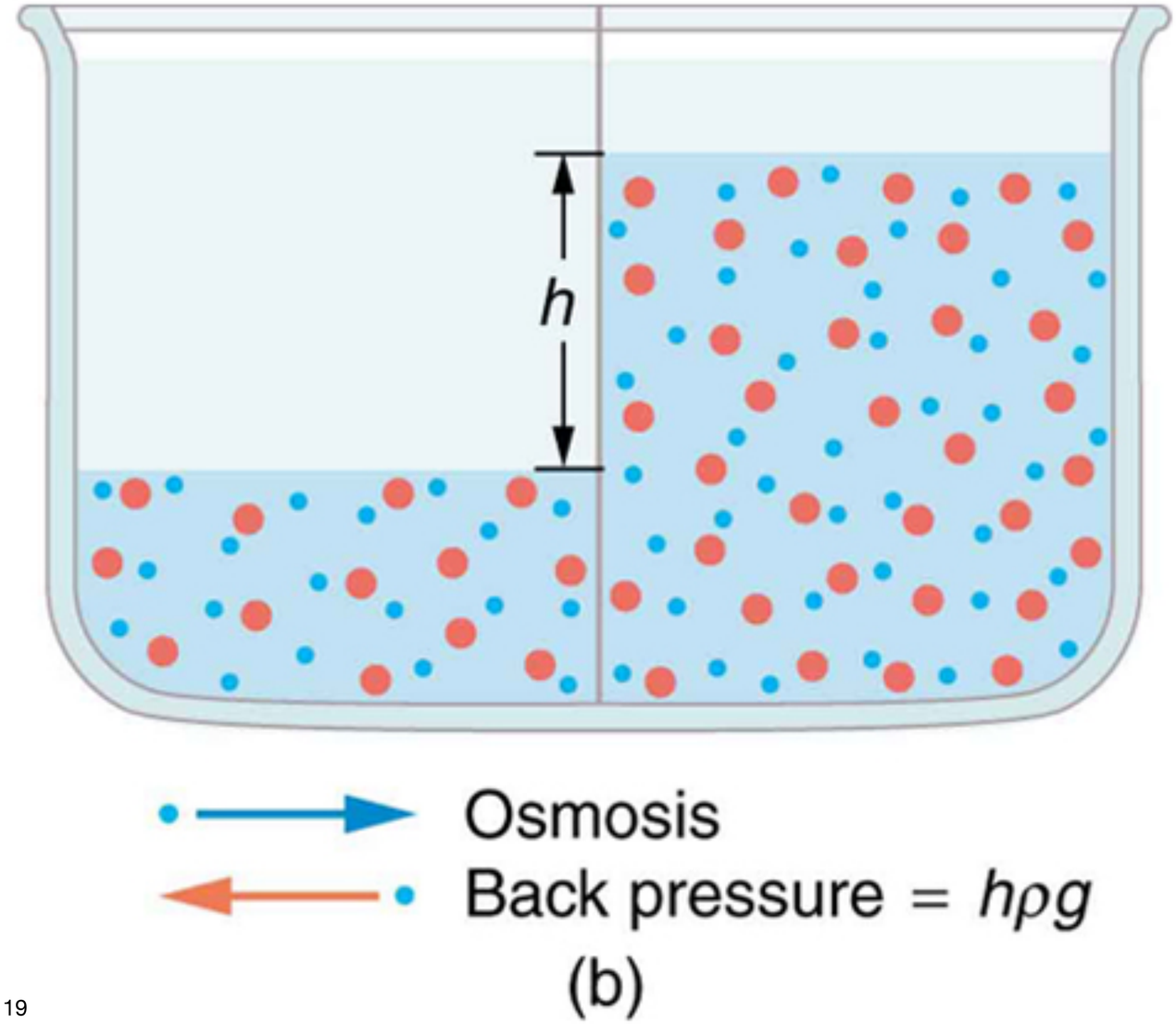
- Membrane and potential
- Osmotic effect
- Ion gradient (electrochemical gradient)
- Ion pumps (active transport)
- Ion channels (passive transport)
- Leakage

Membrane and potential

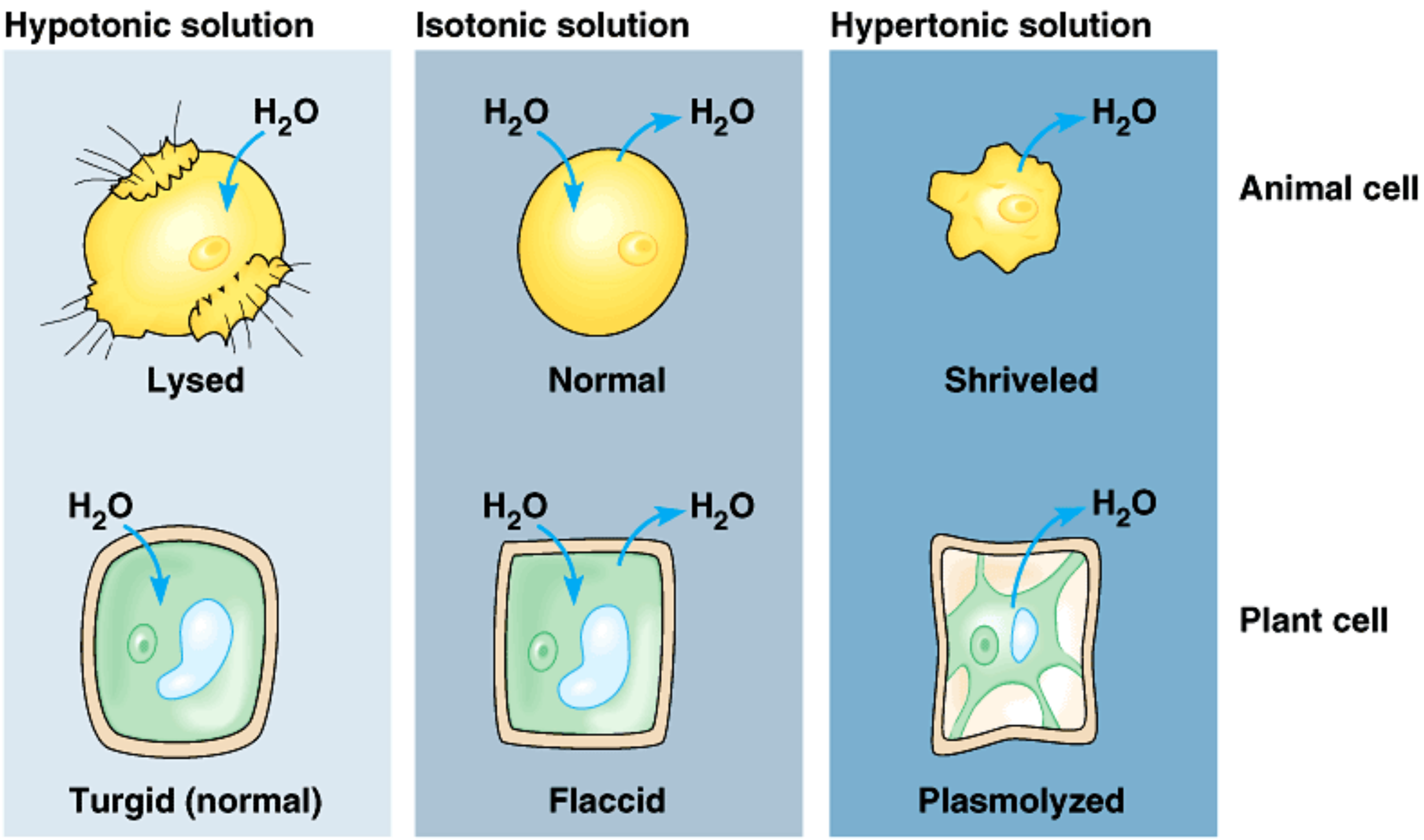
- A cubic micron of cytoplasm might contain, for example, 10^{10} water molecules, 10^8 ions, 10^8 small molecules such as amino acids and nucleotides, and 10^5 proteins
- Cell membrane acts as a capacitor by separating the charges lying along its interior and exterior surfaces
- Almost all plasma membranes have an electrical potential across them, with the inside usually negative with respect to the outside
- In electrically excitable cells such as neurons and muscle cells, it is used for transmitting signals between different parts of a cell
- The membrane potential in a cell derives ultimately from two factors: electrical force! and diffusion!

Diffusion and osmosis





Osmosis in biological cells



Ion gradient (electrochemical gradient)

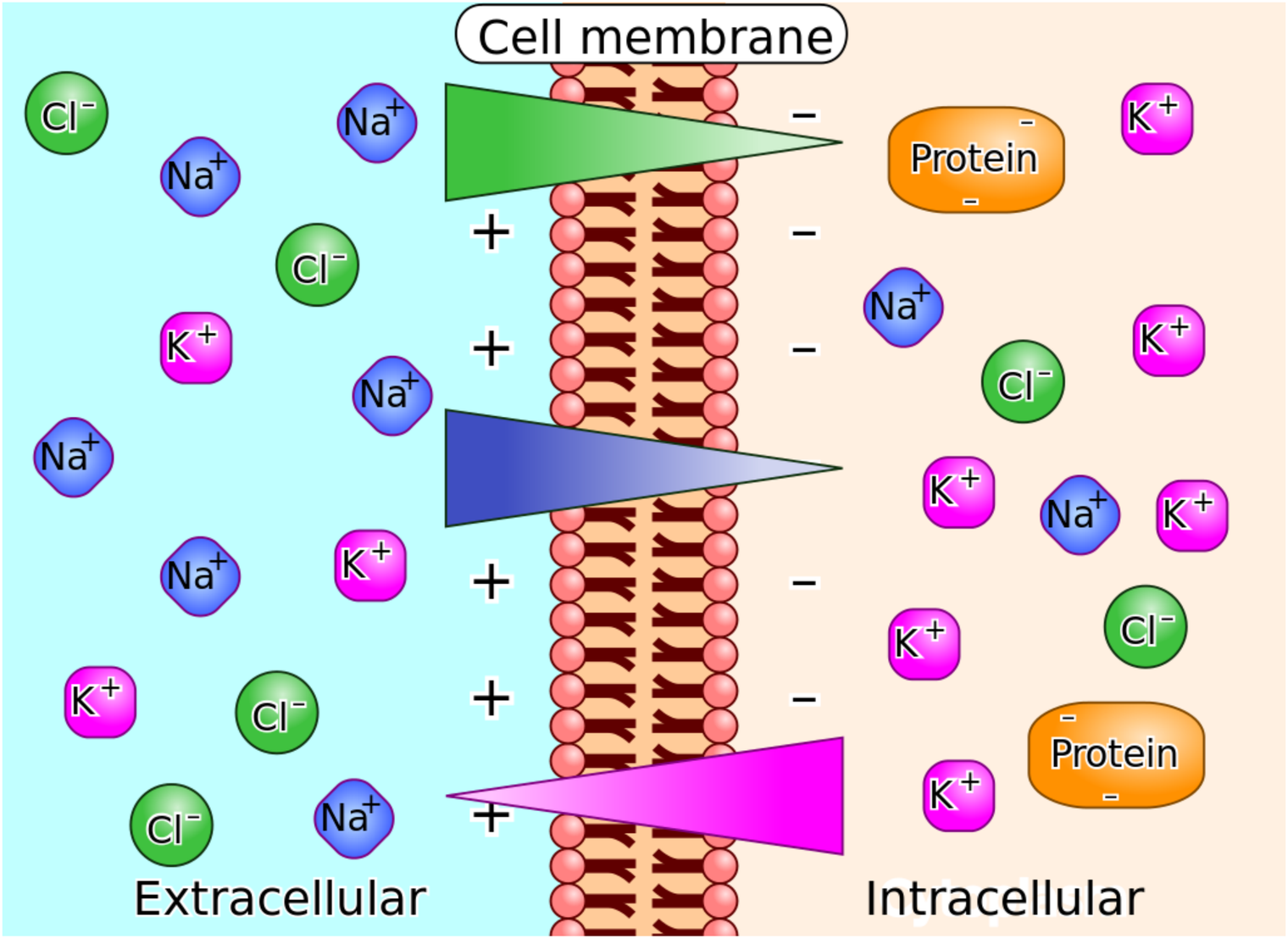
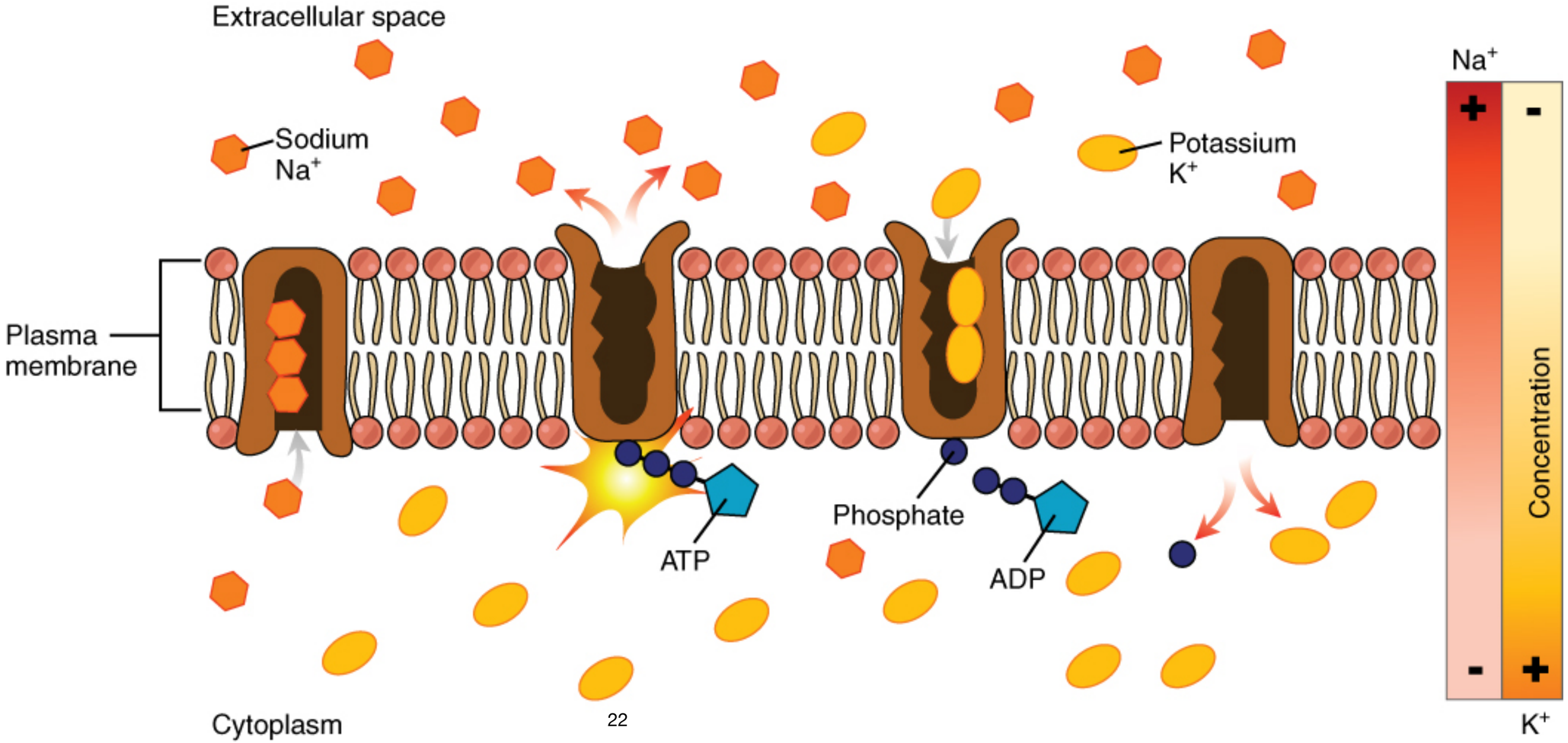


Diagram of ion concentrations and charge across a semi-permeable cellular membrane

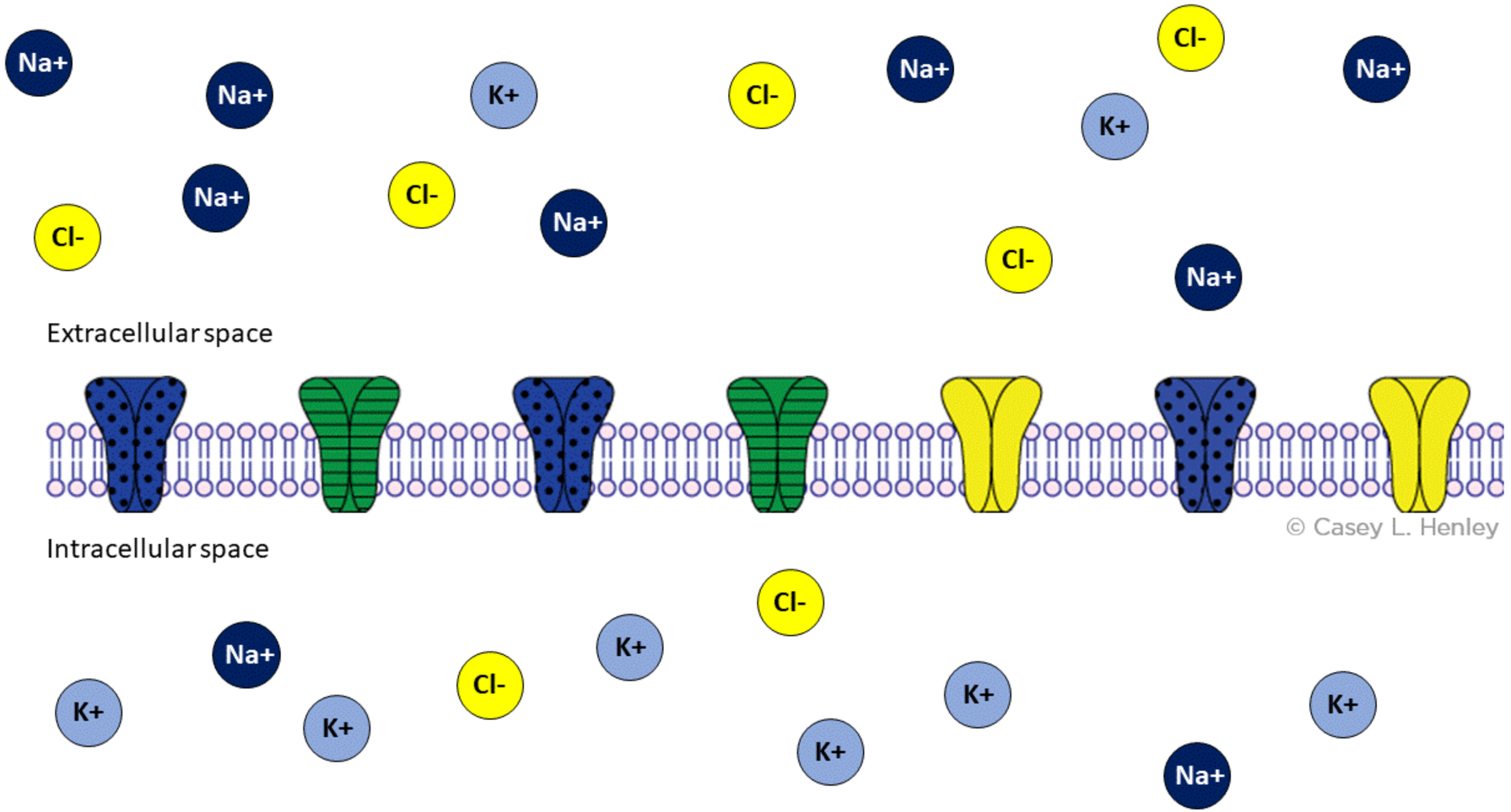
Ion pumps (active transport)

Na^+/K^+-ATPase (Na^+/K^+ adenosine triphosphatase) found in the plasma membrane of all animal cells.

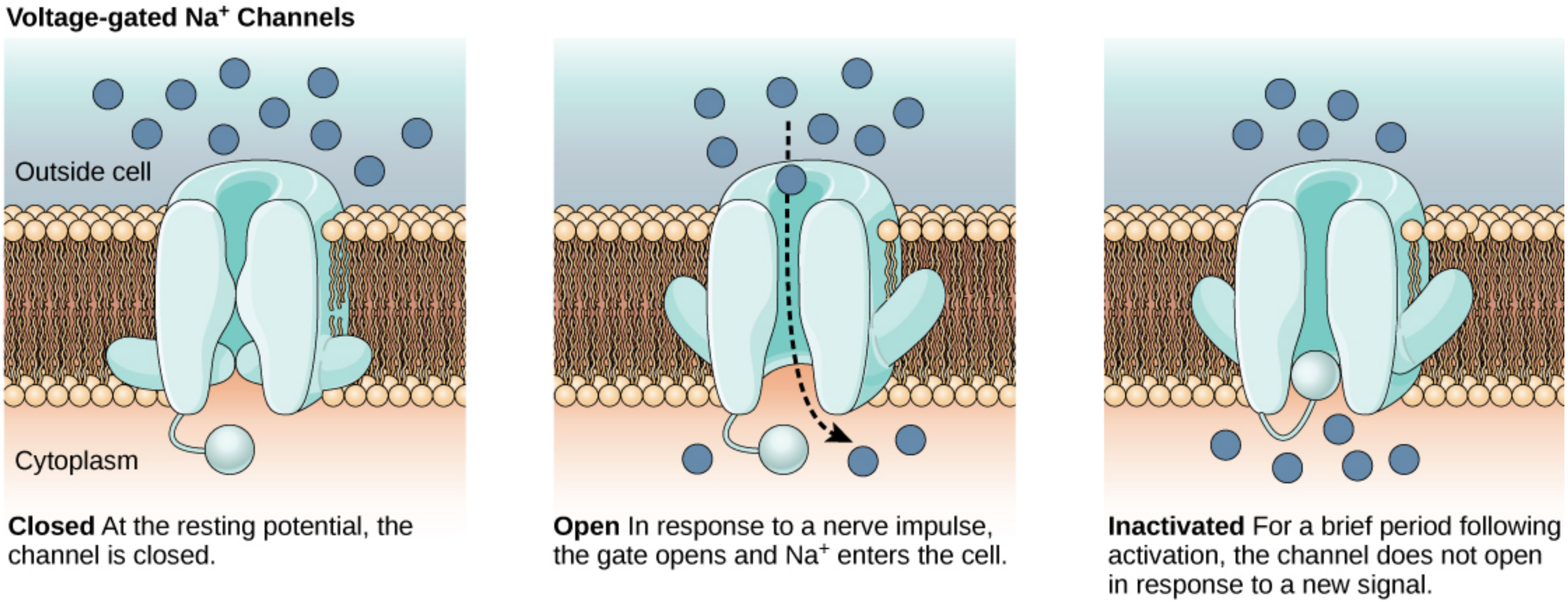
3 sodium ions ↑ of the cell and two potassium ions ↓



Ion channels (passive transport)

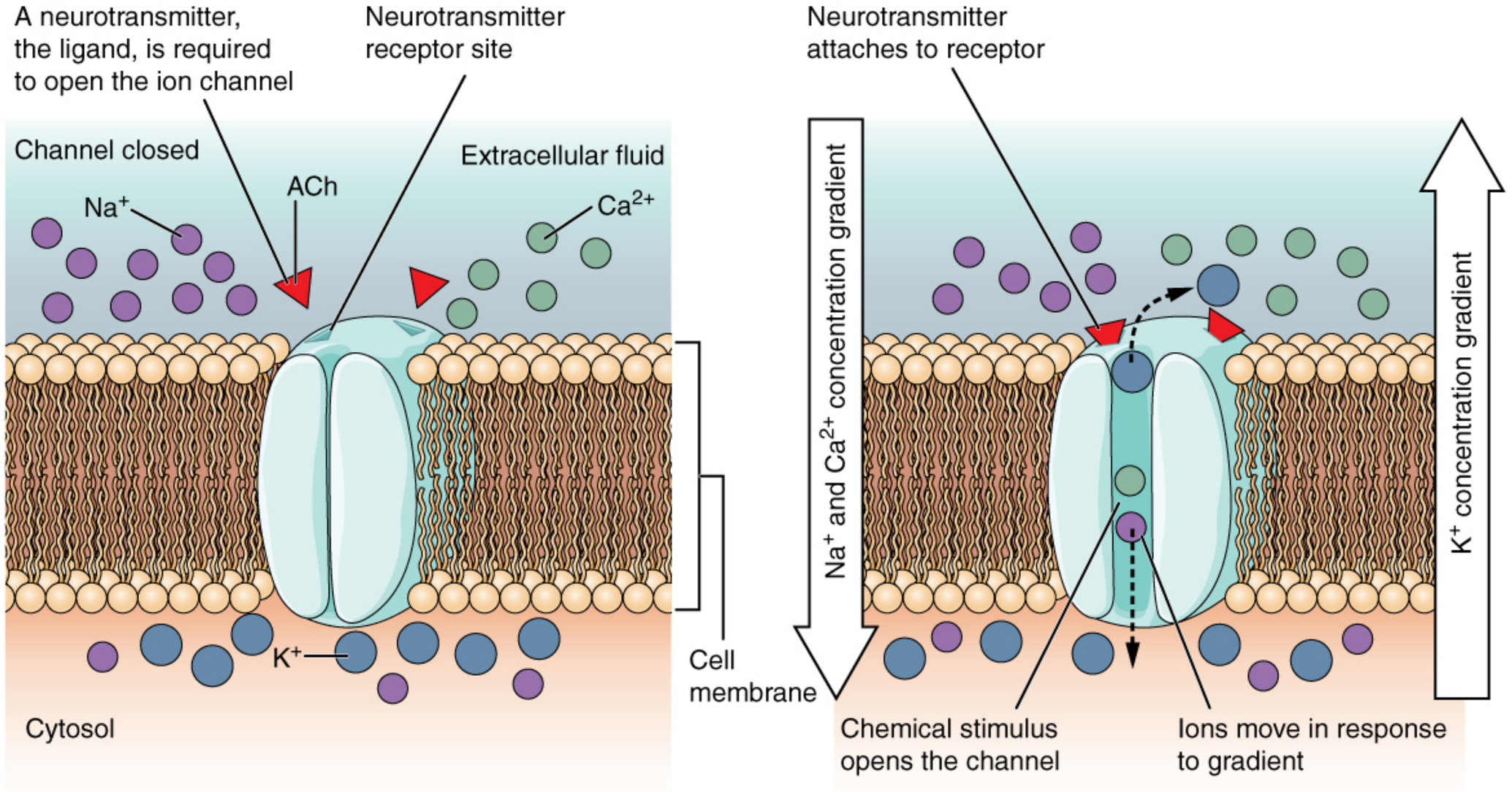


Voltage-gated



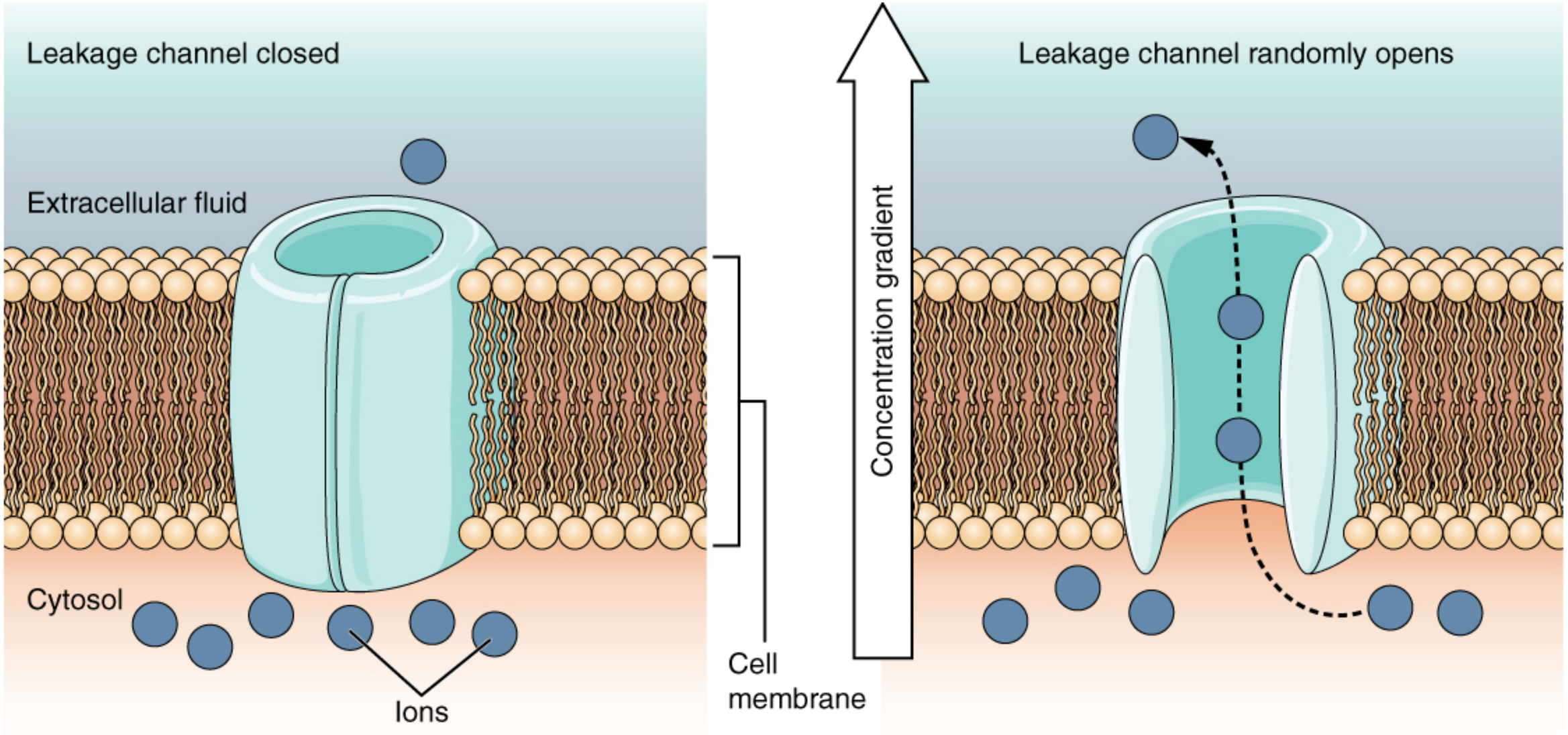
Voltage-gated Na^+channel example

Ligand-gated



Ligand-gated ACh channel example

Leakage


Leakage channel closed
Extracellular fluid
Cytosol
Ions
Cell membrane
Concentration gradient
Leakage channel randomly opens

Electrochemical properties

- Nernst equation
- Reversal potential (equilibrium)
- Resting potential
- Action potential
- Detection methods

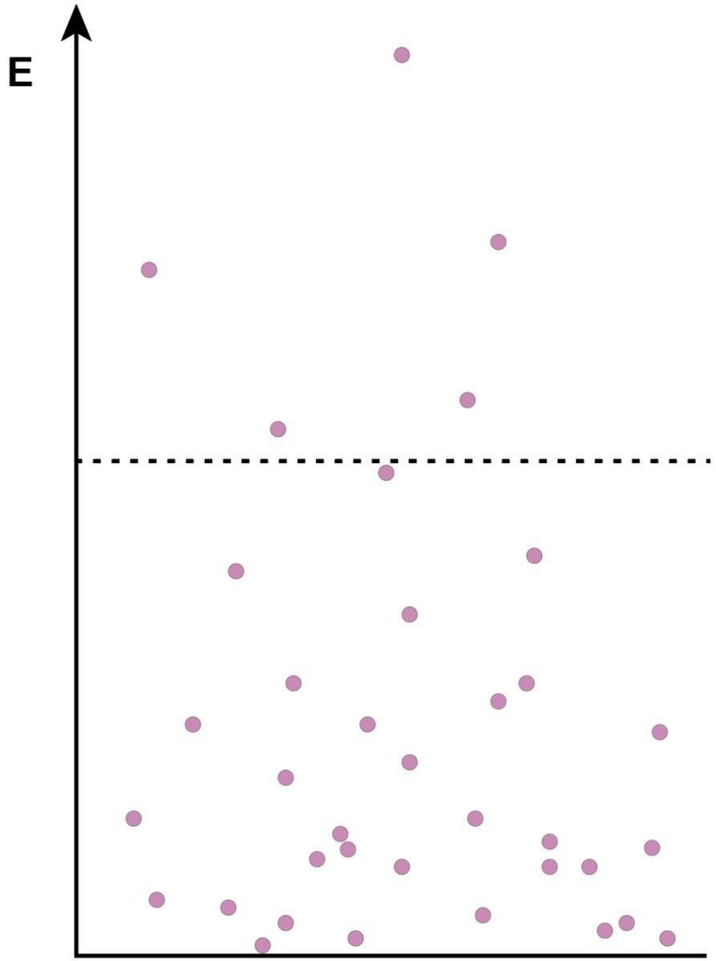
Boltzmann distribution

Boltzmann distribution: $n \propto e^{-\frac{E}{kT}}$, n - density, E - energy, k - Boltzmann's constant, T - temperature

$E = qu$, E - energy, q - charge, u - potential

$$\frac{n_2}{n_1} = e^{\frac{1}{kT}(E_1 - E_2)} = e^{\frac{q}{kT}(u_1 - u_2)}$$

$$\ln \frac{n_2}{n_1} = \frac{q}{kT}\Delta u \implies \Delta u = \frac{kT}{q} \ln \frac{n_2}{n_1}$$, where $\Delta u = u_1 - u_2$ and



u_1 - potential inside, u_2 - potential outside, n_1 - concentration inside, n_2 - concentration outside

Nernst equation

$$E_m = \frac{kT}{q} \ln \frac{[outside]}{[inside]} = \frac{RT}{F} \ln \frac{[outside]}{[inside]}$$, where

T - the absolute temperature, measured in kelvins

R - the universal gas constant, equal to 8.314 joules $\cdot K^{-1} \cdot \text{mol}^{-1}$

F - the Faraday constant, equal to 96,485 C $\cdot \text{mol}^{-1}$

Reversal potential (equilibrium)

The reversal potential (or equilibrium potential) of an ion is the value of transmembrane voltage at which diffusive and electrical forces counterbalance, so that there is no net ion flow across the membrane.

E_K in $[-90; -70]$ mV for K^+

$E_{Na} > 50$ mV for Na^+

$E_{Ca} \approx 150$ mV for Ca^{2+}

E_{Cl} in $[-65; -60]$ mV for Cl^-

Goldman–Hodgkin–Katz Equation

$$E_m = \frac{RT}{F} \ln\left(\frac{P_K[K^+]_{out} + P_{Na}[Na^+]_{out} + P_{Cl}[Cl^-]_{in}}{P_K[K^+]_{in} + P_{Na}[Na^+]_{in} + P_{Cl}[Cl^-]_{out}} \right)$$, where

P_{ion} - the permeability or selectivity for that ion type

$[\text{ion}]_{out}$ - the extracellular concentration of that ion (in moles per cubic meter)

$[\text{ion}]_{in}$ - the extracellular concentration of that ion (in moles per cubic meter)

Cl^- conductances, with reversal potentials near the resting potential, may pass little net current. Instead, their primary impact is to change the membrane resistance of the cell.

Resting potential

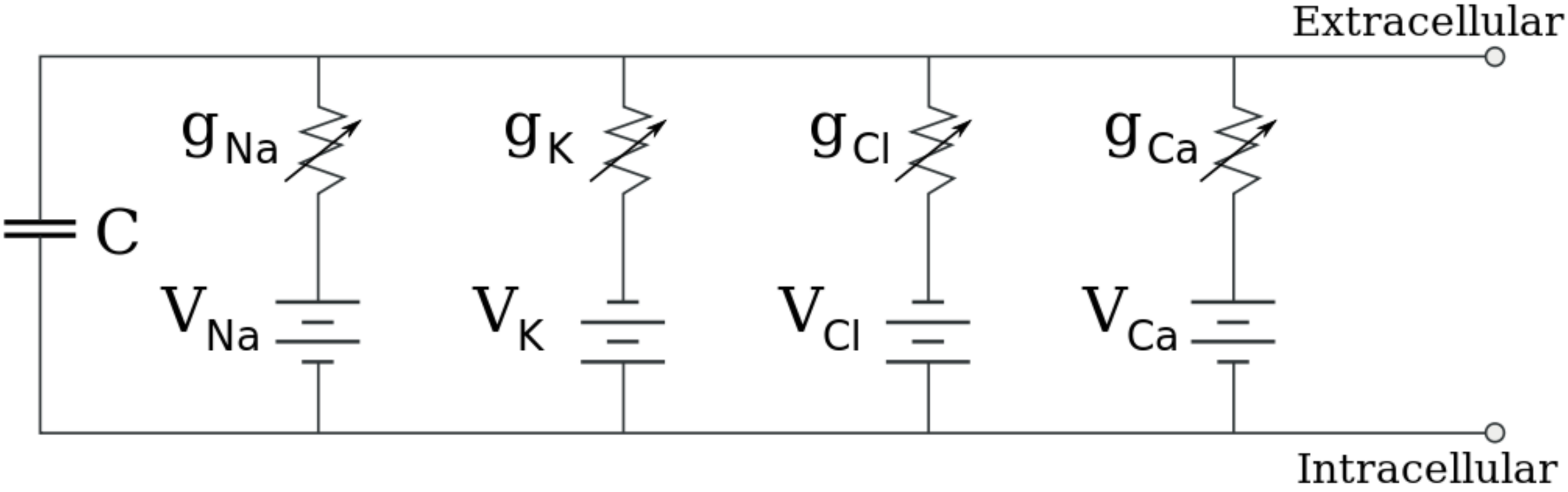
When the membrane potential of a cell goes for a long period of time without changing significantly, it is referred to as a resting potential or resting voltage. This term is used for the membrane potential of non-excitable cells, but also for the membrane potential of excitable cells in the absence of excitation.

- The Nernst equation applies for one type of ion to pass through membrane
- Some ion channels are not so selective
- Membrane potential as a weighted average of the reversal potentials for the individual ion types, weighted by permeability

Summary of resting potential values in different types of cells

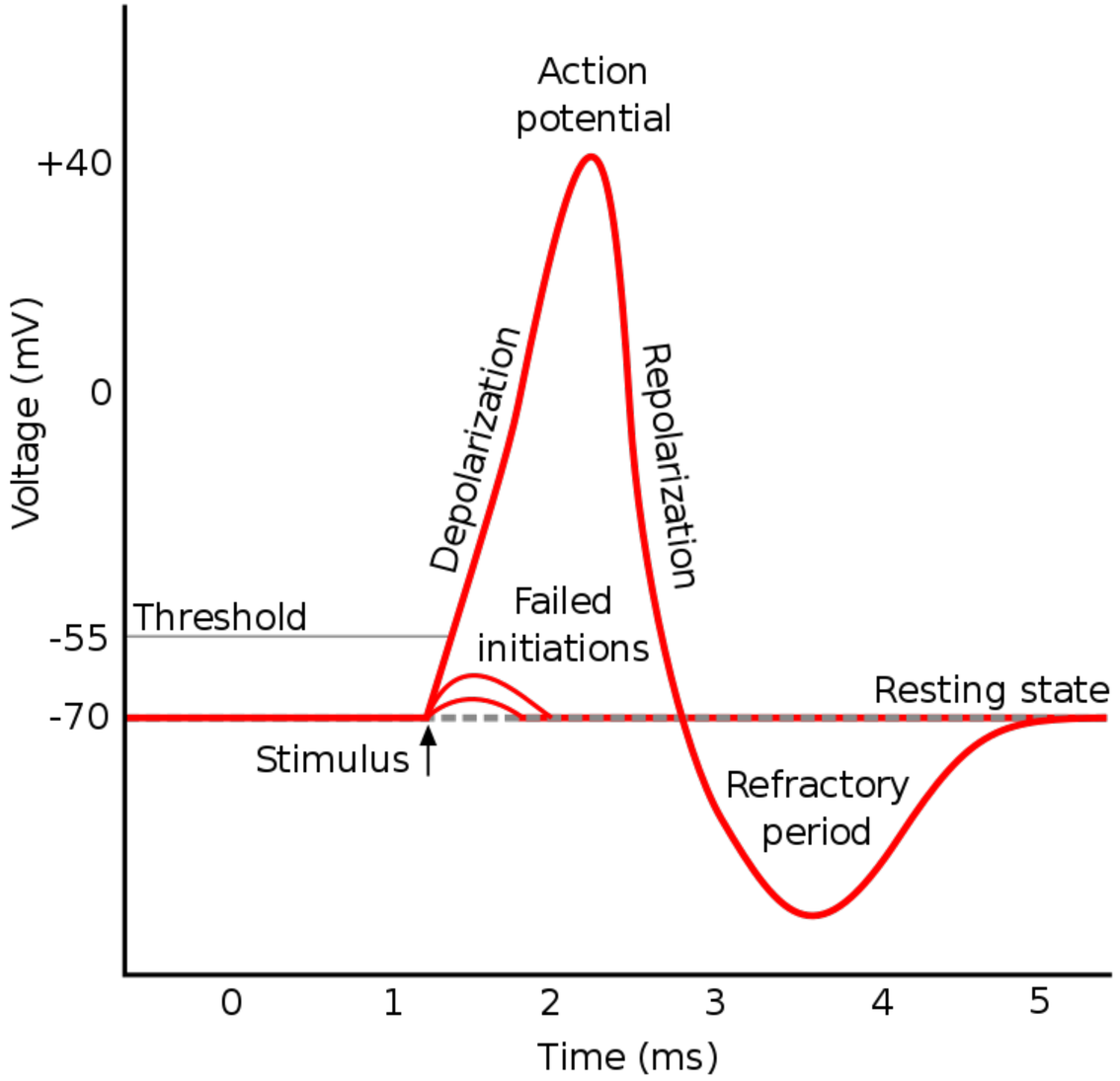
Cell types	Resting potential
Skeletal muscle cells	-95 mV
Astroglia	-80 to -90 mV
Neurons	-60 to -70 mV
Smooth muscle cells	-60 mV
Aorta Smooth muscle tissue	-45 mV
Photoreceptor cells	-40 mV
Hair cell (Cochlea)	-15 to -40mV
Erythrocytes	-8.4 mV
Chondrocytes	-8 mV

Equivalent circuit

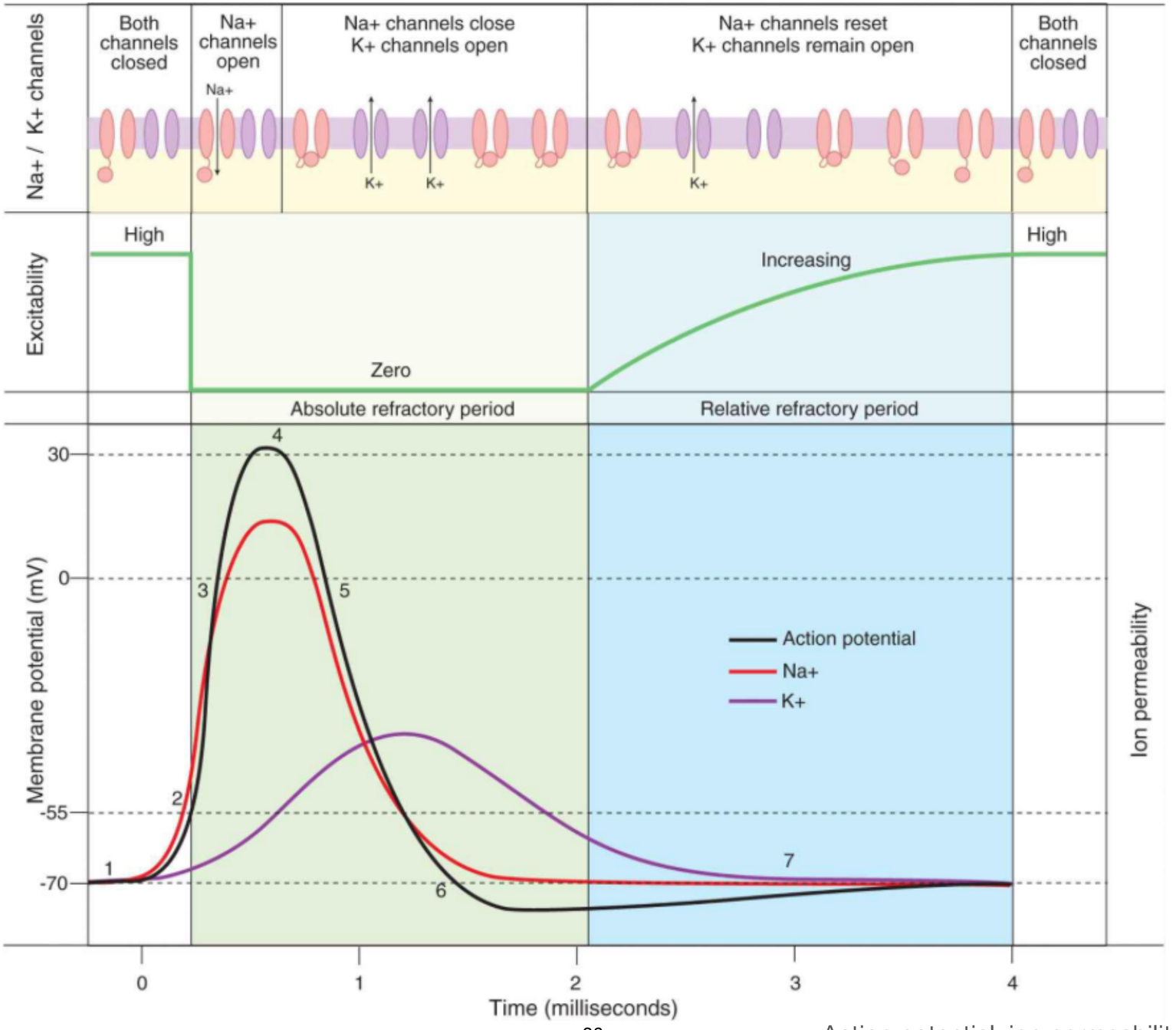


Resistance-capacitance or RC circuit in electrical terms

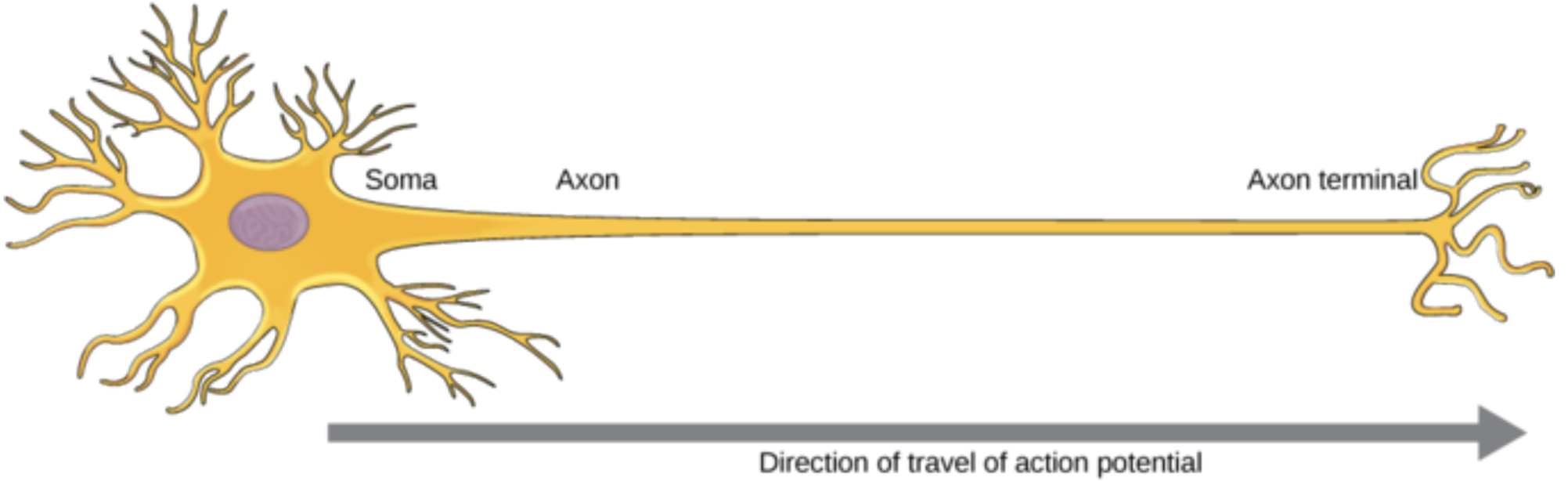
Action potential



Approximate plot of a typical action potential



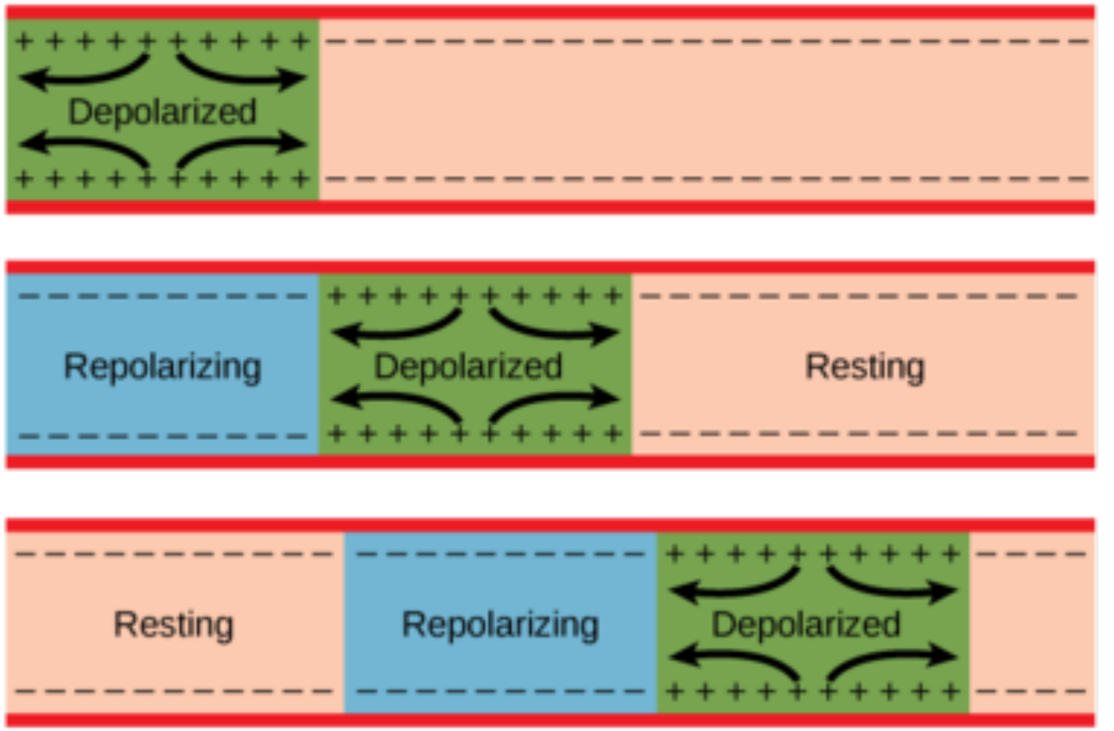
Action potential, ion permeability dynamics, excitability dynamics



a. In response to a signal, the soma end of the axon becomes depolarized.

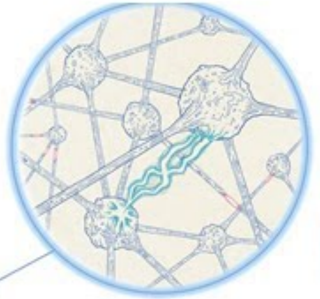
b. The depolarization spreads down the axon. Meanwhile, the first part of the membrane repolarizes. Because Na^+ channels are inactivated and additional K^+ channels have opened, the membrane cannot depolarize again.

c. The action potential continues to travel down the axon.



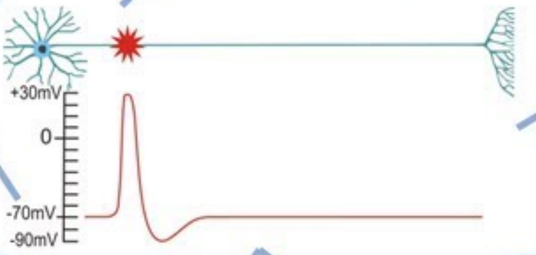
Action potential propagation along an axon

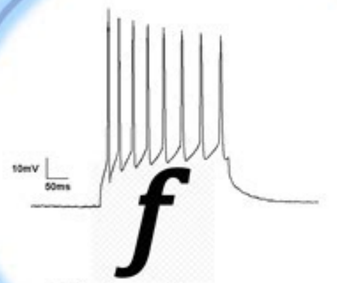
Patch clamp technique



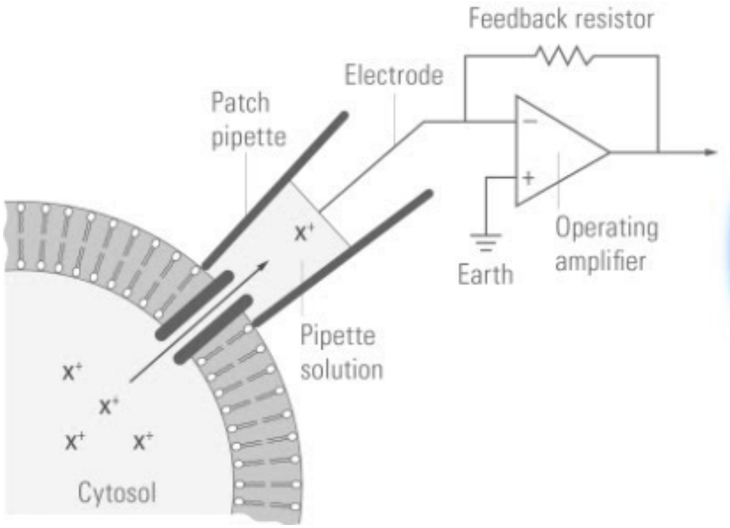
capacitance

conductance

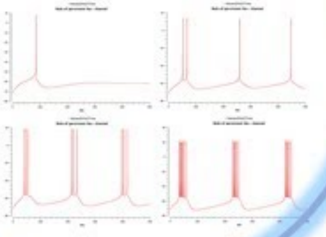




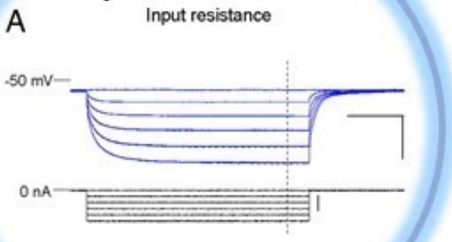
Firing frequency



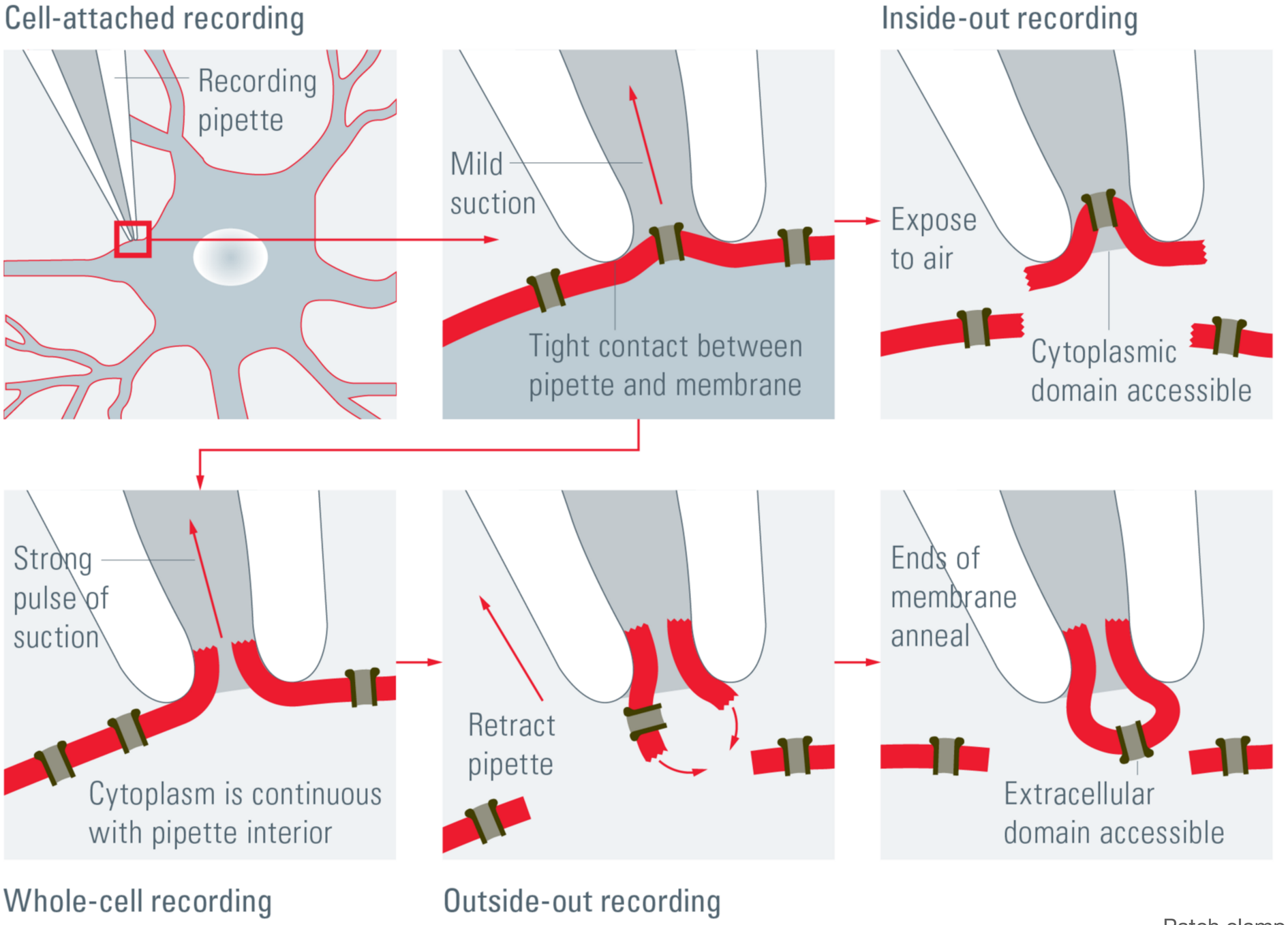
Firing pattern



Input resistance



What we can see with patch clamp



Patch clamp configurations