Methods of Applied Mathematics II (Math451H): Neuronal Dynamics

Bibliography:

MIT Open Courseware – Physics II: Electricity & Magnetism
http://ocw.mit.edu/OcwWeb/Physics/8-02Spring-2007/CourseHome/index.htm

Membrane Potential. Elmslie, K. S. (2001) Encyclopedia of Life Sciences. John Wiley & Sons, Elmslie, K. S. (2001) Encyclopedia of Life Sciences. John Wiley & Sons, http://www.mrw.interscience.wiley.com/emrw/9780470015902/els/article/a0000182

Figures were taken from some of these books

Passive membrane

Passive membrane properties

- Review of electric circuits
- Membrane potential
- Equilibrium potentials (Nernst-Planck & Nernst equations)
- Passive membrane potential
- Passive membrane potential: Electric circuit model
- Passive membrane potential: Mathematical model

Electric circuits - quick review

Q: electric charge

- positive and negative
- unit of charge: Coulomb (C)

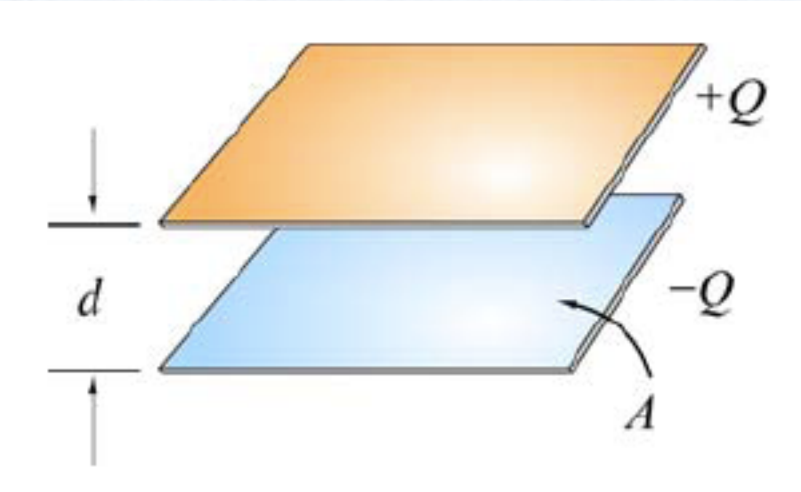
ΔV: potential difference

- It represents the amount of work done per unit charge to move a test charge q0 from point A to point B, without changing its kinetic energy
- unit of electric potential: volt (V)
- 1 volt = 1 joule/coulomb (1 V = 1 J/C)

Electric circuits - quick review

Capacitor:

- Device that stores electric charge
- Basic configuration: two conductors carrying equal but opposite charges
- Simplest example: two conducting plates of area A, which are parallel to each other, and separated by a distance d



- The amount of charge Q stored in a capacitor is proportional to ΔV (the electric potential difference between the plates)

Electric circuits - quick review

Capacitor:

- The amount of charge Q stored in a capacitor is proportional to ΔV (the electric potential difference between the plates)

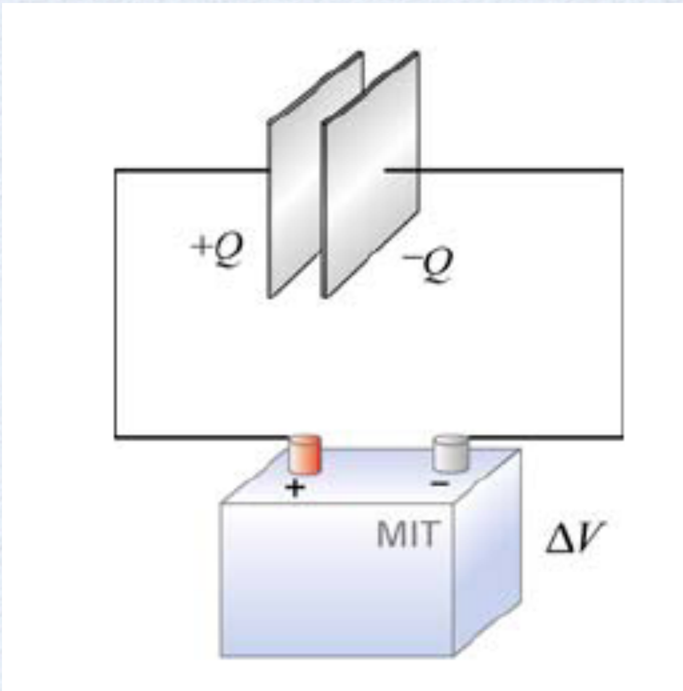
$$Q = C\,|\Delta V|$$

C: Capacitance

- It is a measure of the capacity of storing electric charge for a given ΔV
- Unit of capacitance: farad (F)
- 1 F = 1 C / V   (Coulomb / volt)

Electric circuits - quick review

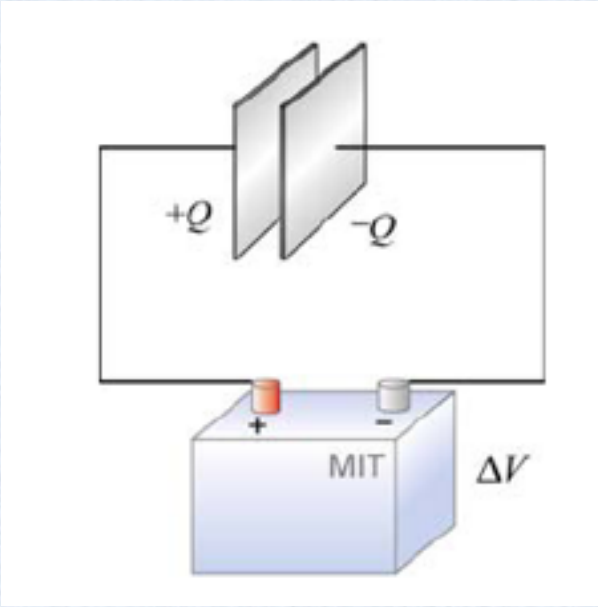
A capacitor can be charged by connecting the plates to the terminal of a battery, which are maintained at a potential difference ΔV called the terminal voltage



The connection results in sharing the charges between the terminals and the plates

Electric circuits - quick review

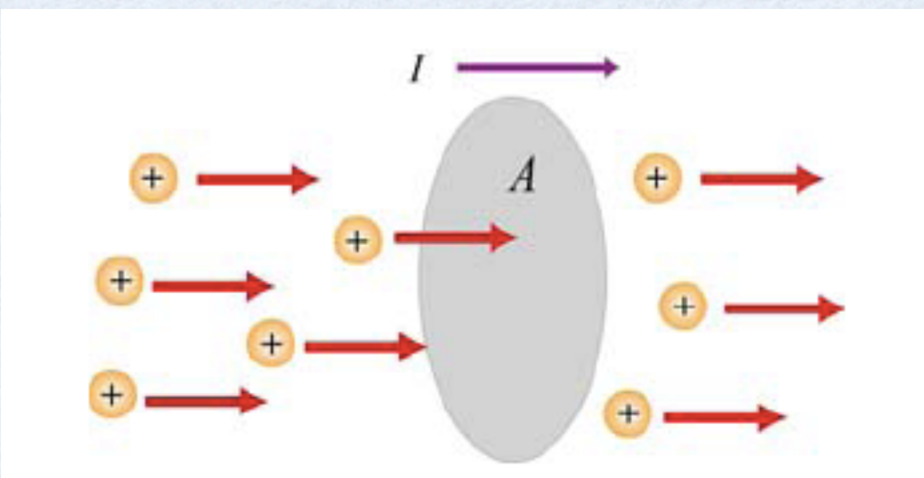
- The plate that is connected to the + terminal will acquire some + charge
- The plate that is connected to the - terminal will acquire some – charge
- The sharing causes a momentary reduction of charges on the terminals, and a decrease in the terminal voltage
- Chemical reactions are then triggered to transfer more charge from one terminal to the other to compensate for the loss of charge to the capacitor plates, and maintain the terminal voltage at its initial level
- The battery could be thought of as a charge pump that brings a charge Q from one plate to the other

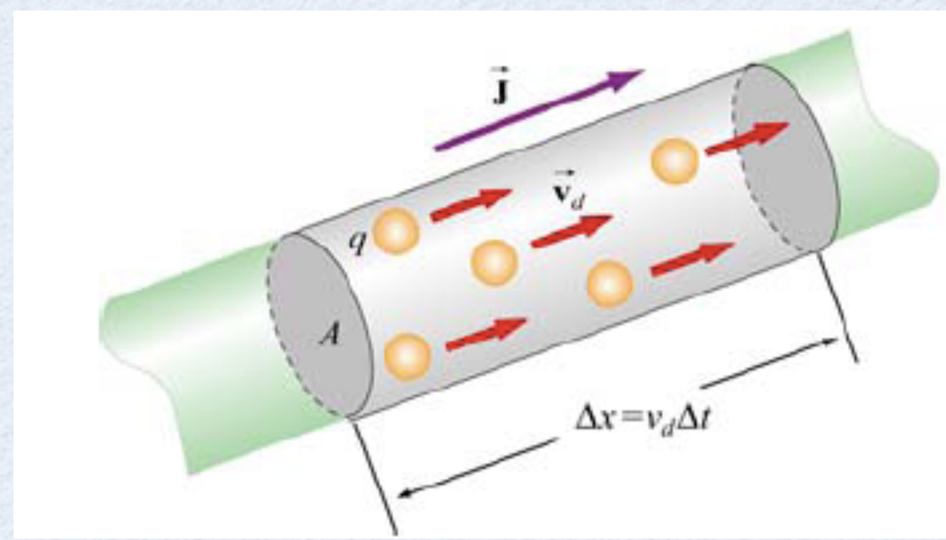


Electric circuits - quick review

I: Electric current

- Flows of electric charge
- Defined as the rate at which charges flow across any cross-sectional area

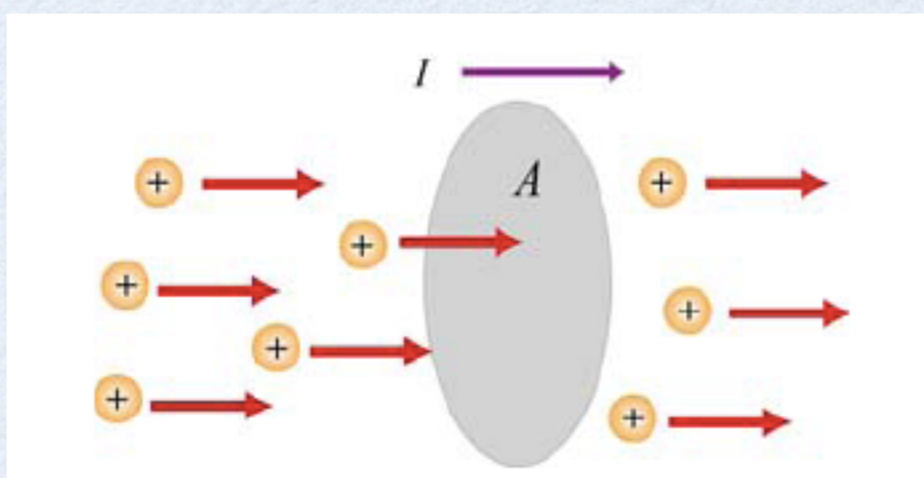




Electric circuits - quick review

I: Electric current

- Unit of current: Ampere (A)
- 1 A = 1 C / sec (Coulomb / second)
- $I_{avg} = \Delta Q / \Delta t$
- In the limit $\Delta t \rightarrow 0$, $I = dQ / dt$
- Convention: The direction of current corresponds to the direction in which positive charge is flowing



Electric circuits - quick review

R: Resistance

- Unit of resistance: Ohm (Ω)
- 1 Ω = 1 V / A   (Volt / Ampere)

G: Conductance

- Unit of resistance: Siemens (S)
- 1 S = 1 Ω^{-1} = 1 A / V   (Ampere / Volt)

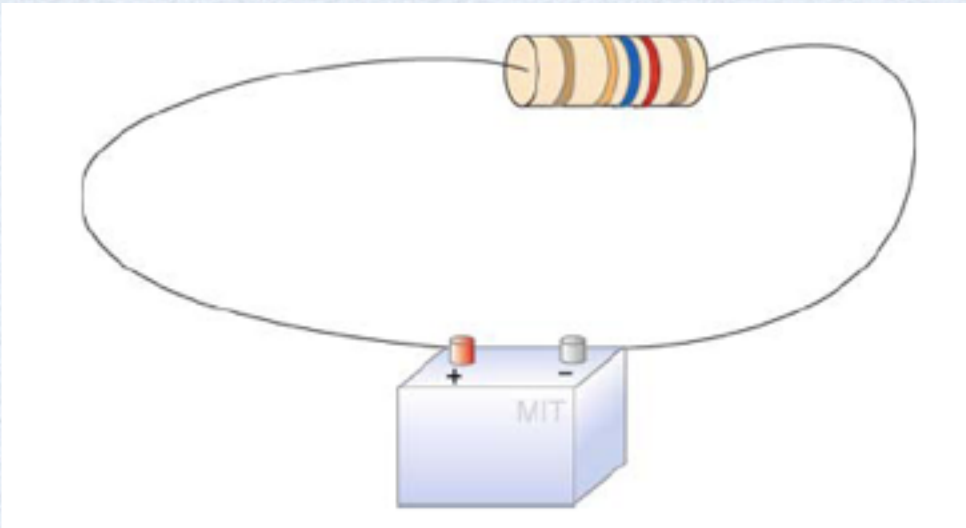
Electric currents flow in conductors, but it is impeded in insulators
Ohm's law:

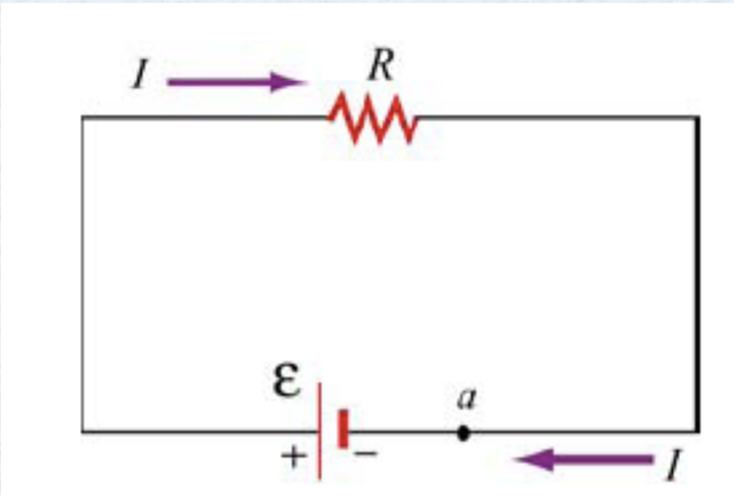
$$\Delta V = I\,R$$

Electric circuits - quick review

Electromotive force (emf or ε): Electrical energy that must be supplied to maintain a constant current in a closed circuit

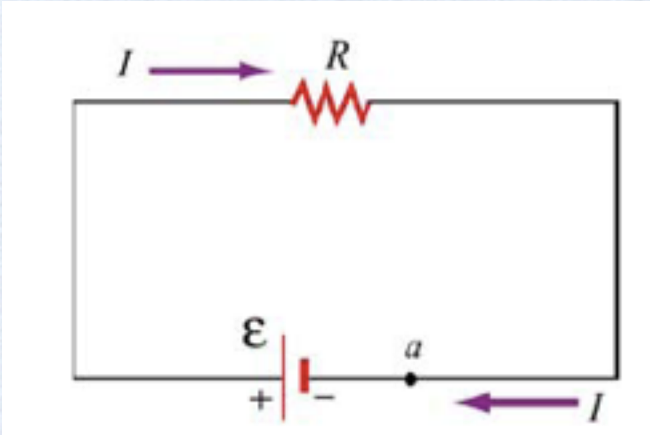
Simple circuit: battery + resistor





Electric circuits - quick review

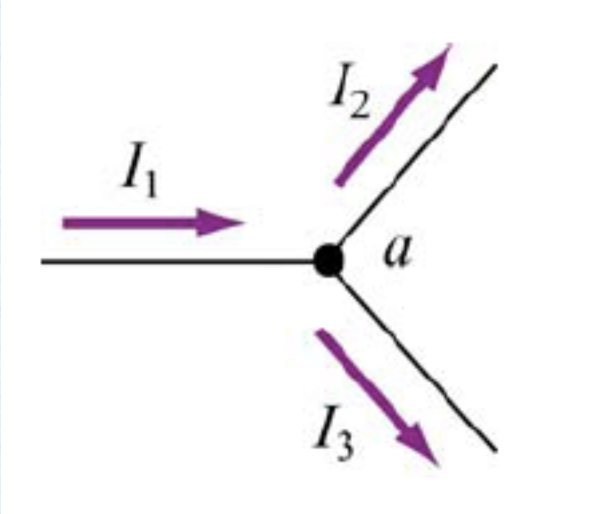
Simple circuit: battery + resistor



- $\Delta V = V_b - V_a > 0$
- If a charge Δq is moved from a through the battery, its potential energy is increased by $\Delta q\, \Delta V$
- As the charge Δq moves across the resistor, the potential energy is decreased (due to collisions with atoms in the resistor).
- If we neglect the internal resistance of the battery and the connecting wires, upon returning to a the potential energy of Δq remains unchanged
- The battery compensates the energy loss through the resistor.
- it converts chemical energy into emf to drive the current around the circuit

Electric circuits - quick review

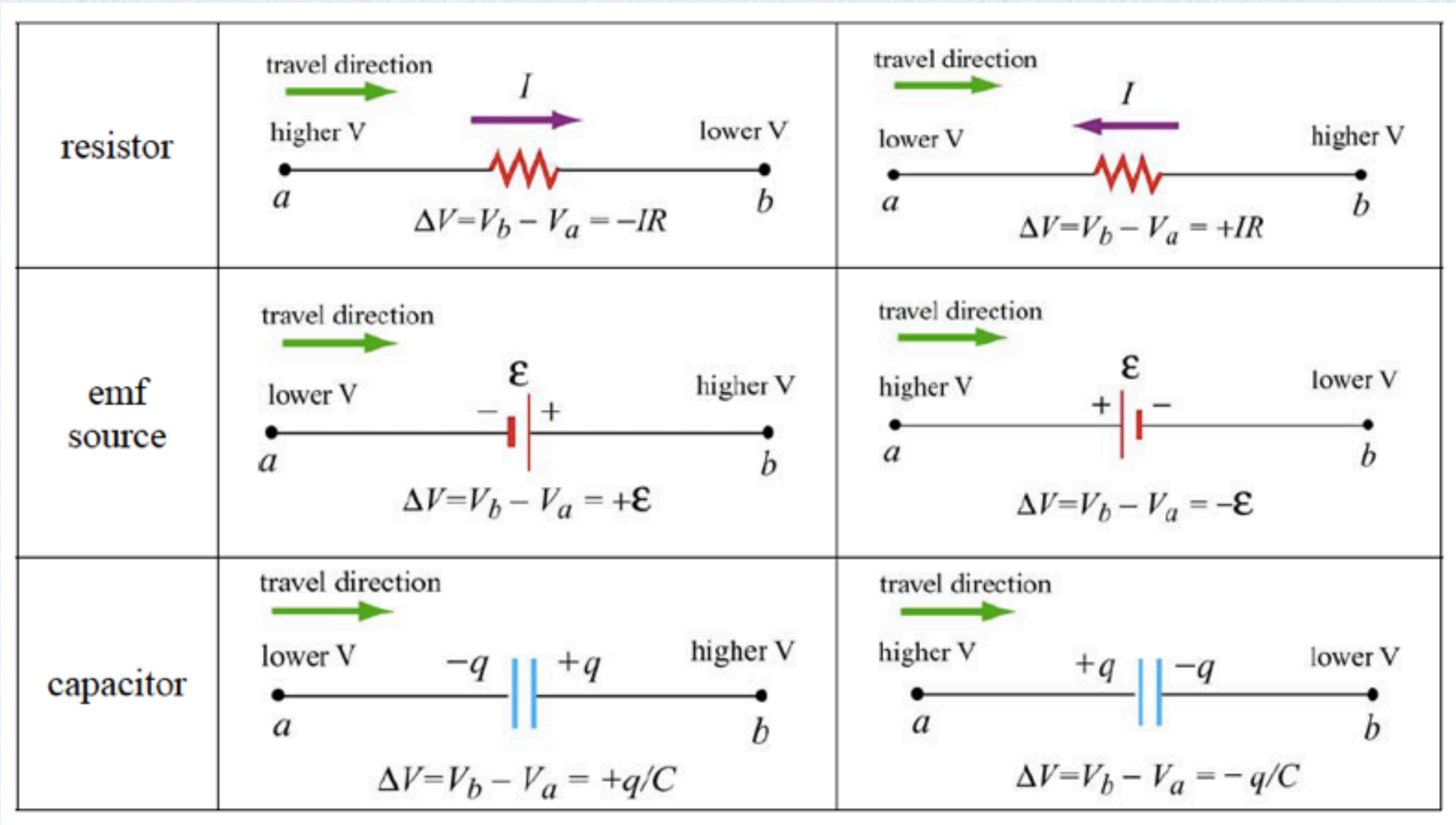
Kirchhoff's current law: The sum of the currents into the node must equal the sum of currents out of the node (current conservation)



Kirchhoff's voltage law: The sum of the voltage drops ΔV across any circuit elements that form a closed circuit is zero

Electric circuits - quick review

Convention



Cellular neurophysiology

Membrane potential

- Potential difference between the inside and the outside of the cell
- $V_M = V_{in} - V_{out}$

Resting potential

- Membrane potential when the cell is at rest
- Typical neuron: $V_M = -70$ mV

Cellular neurophysiology

Membrane potential

- The potential difference arises from differences in the concentrations of various ions within and outside the cell
- Na^+, K^+, Cl^-, Ca^{2+}
- $[K^+]_i$ is much higher than $[K^+]_o$ (~ 10 times)
- $[Na^+]_o$ is much higher than $[Na^+]_i$
- $[Cl^-]_o$ is much higher than $[Cl^-]_i$
- Transport of ions across the cell membrane
- Selective permeability of the membrane to these ions.

$[X^+]_o$: Concentration of ions X in the outside of the cell
$[X^+]_i$: Concentration of ions X in the inside of the cell

Cellular neurophysiology

Inward current

- Positively charged ion entering the cell
- Depolarization
- Negatively charged ion leaving the cell

Outward current

- Positively charged ion leaving the cell
- Hyperpolarization
- Negatively charged ion entering the cell

Cellular neurophysiology

Cell membrane:

- Lipid bilayer (not permeable to ions, poor conductor)
- Ion channels (proteins)

Ion channels:

- Non-gated: always open
- Gated: open and close

Cellular neurophysiology

Non-gated ion channels:

- Primarily responsible for establishing the resting potential

Gated ion channels:

- Probability of opening often depends on the membrane potential (voltage-gated ion channels)
- Typically selective for a single ion
- Permeability of the membrane to a particular ion depends on the number of open channels for the ion

- Action potentials are generated when gated channels open allowing for the flux of ions across the membrane

Cellular neurophysiology

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Cellular neurophysiology

Electric signals

- Action potentials are generated when gated channels open allowing for the flux of ions across the membrane

Influenced by electrochemical potentials:

- Concentration gradients or chemical potentials (Non-uniform distribution of ionic concentrations).

- Electric fields (separation of charge across the membrane, nonzero electric field, etc). of opening often depends on the membrane potential (voltage-gated ion channels)

Cellular neurophysiology

Concentration differences (and appropriate channels open):

- Na^+ and Cl^- tend to diffuse inward
- K^+ tends to diffuse outward

Cell permeable only to K^+

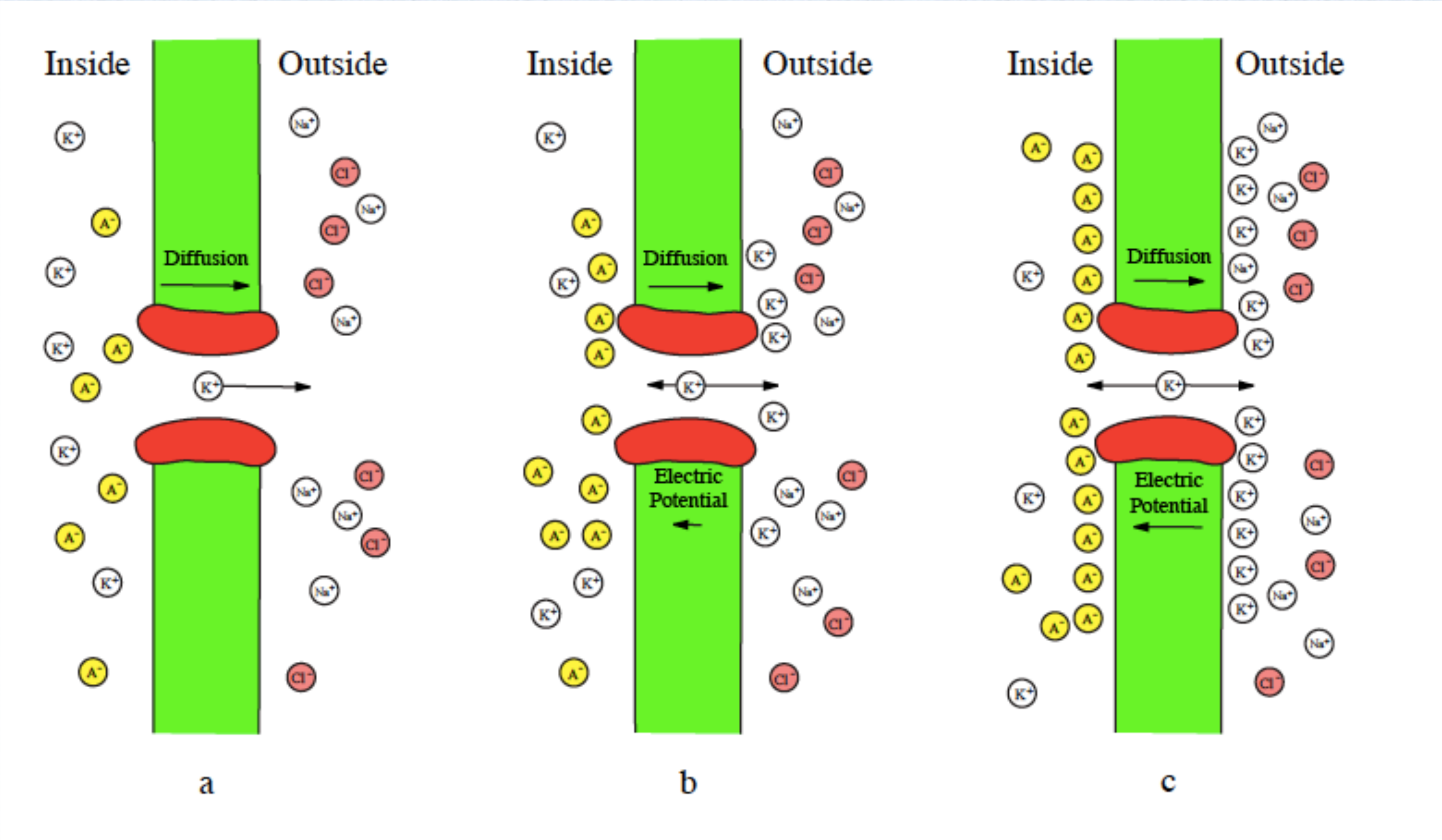
- Concentration gradient of K^+ moves K^+ ions out of the cell
- Excess of positive charge builds up outside the cell
- Excess of negative charge builds up inside the cell (A^-, i impermeable organic anions)
- Buildup of charge acts to impede the further efflux of K^+

- Equilibrium: electrical and chemical forces are equal and opposite

Cellular neurophysiology

Cell permeable only to K^+

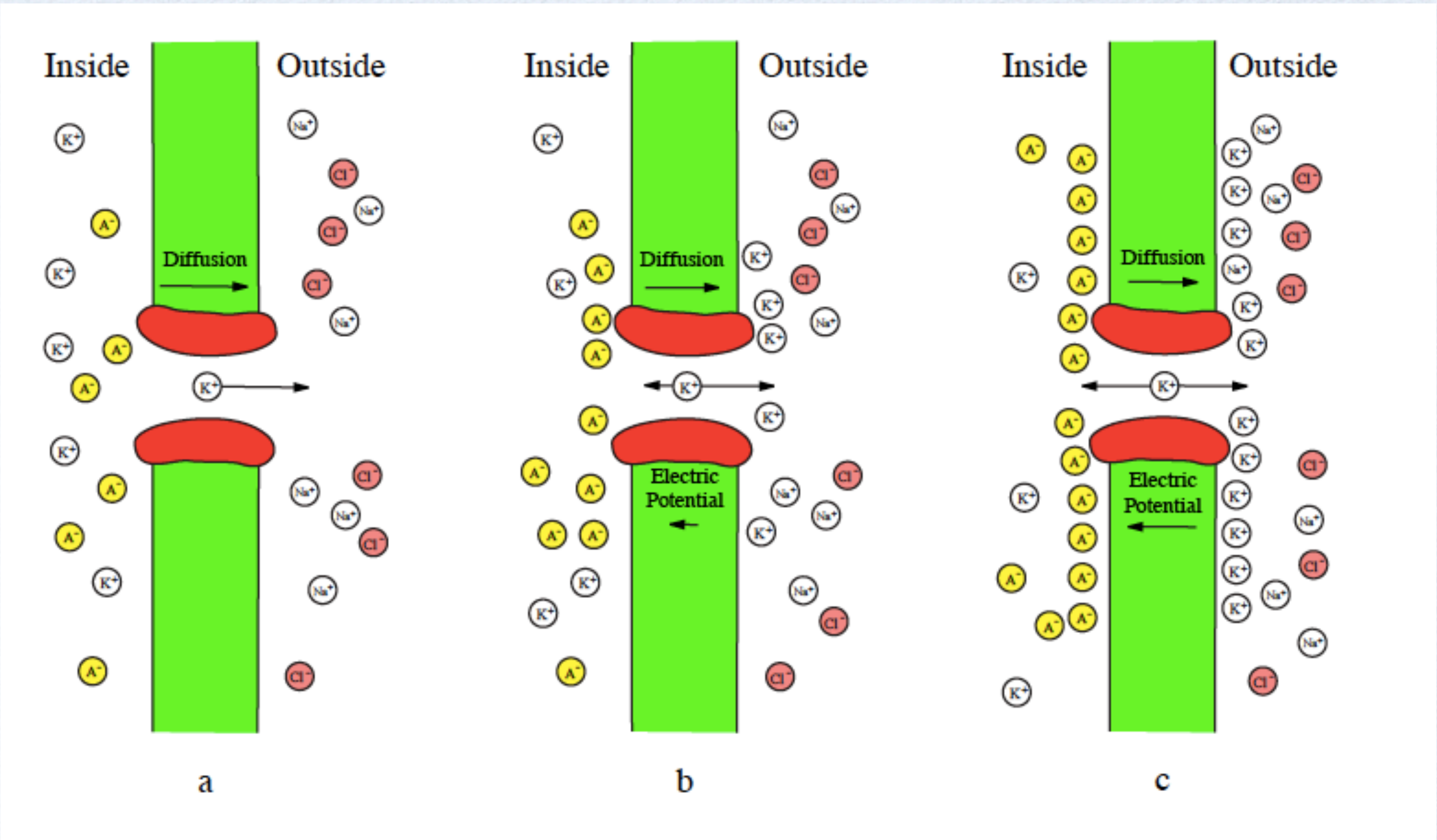
- Concentration gradient of K^+ moves K^+ ions out of the cell



Cellular neurophysiology

Cell permeable only to K^+

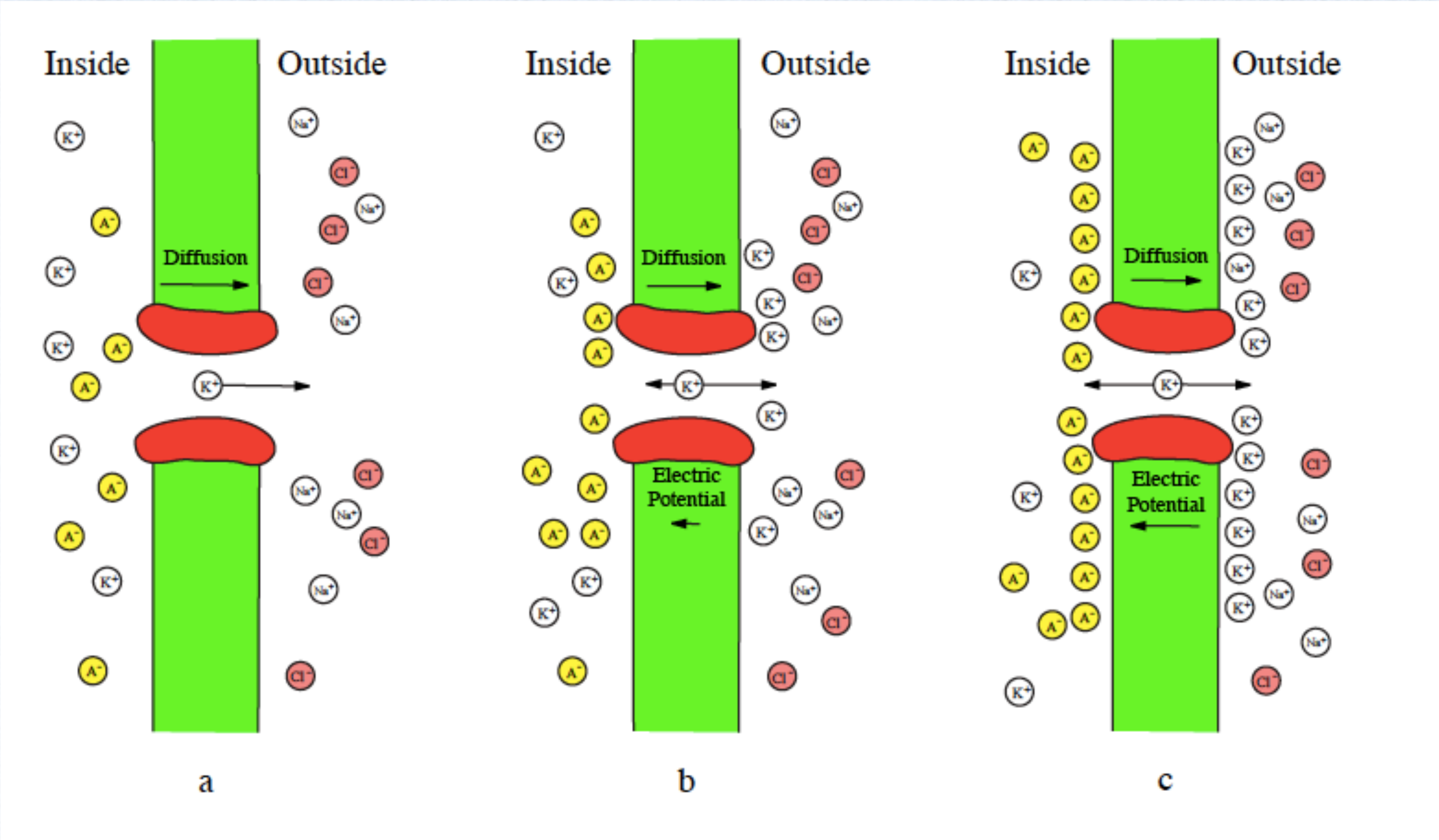
- Electric potential pointing in the opposite direction is created



Cellular neurophysiology

Cell permeable only to K^+

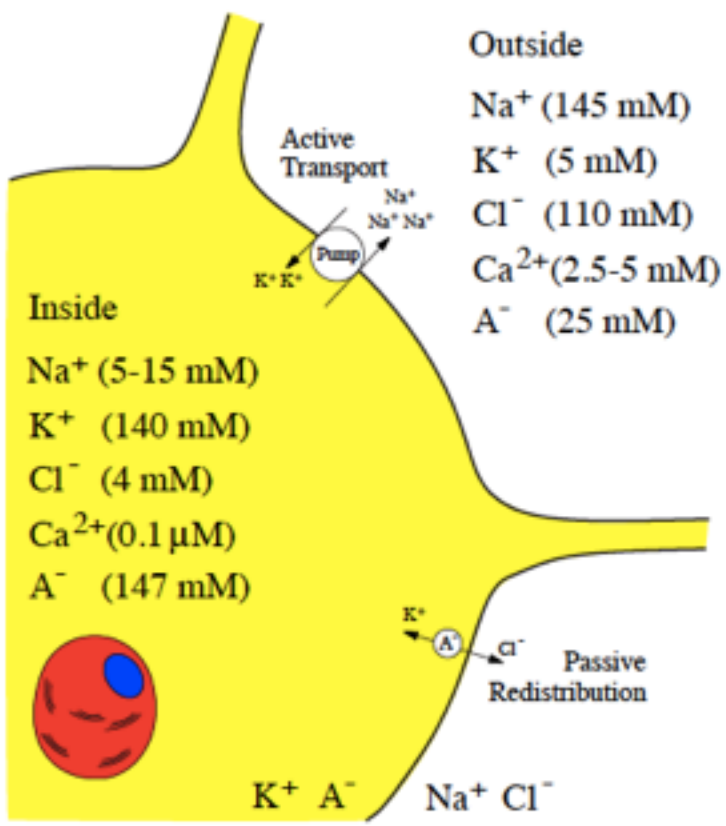
- Equilibrium is reached



Cellular neurophysiology

Reversal potential or Nernst equilibrium

- Membrane potential at which a specific ion concentration is in equilibrium across the membrane



Equilibrium Potentials

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

Figure 2.1: Ion concentrations and Nernst equilibrium potentials (2.1) in a typical mammalian neuron (modified from Johnston and Wu 1995). A^- are membrane-impermeant anions. Temperature $T = 37°\text{C}$ (310°K).

Cellular neurophysiology

Resting membrane potential

- All living cells maintain differential ion concentrations across the cell membrane
- At equilibrium molecules still cross the membrane, but the movement into the cell equals the movement out of the cell; that is, the net movement of molecules is zero
- The concentration force is generated by a class of proteins called ion pumps that use cellular energy (ATP)
- The cell must expend energy in the form of ATP to pump the ions against their concentration gradient

Cellular neurophysiology

Resting membrane potential

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Two factors generate the resting membrane potential

- Differential ion concentrations
- Selective permeability of the membrane

Cellular neurophysiology

Fick's law for diffusion

$$J_{\text{diff}} = -D\frac{\partial C}{\partial x}$$

J: diffusion flux (molecules/sec-cm2)
D: diffusion coefficient (cm2/sec)
C: concentration of ions (molecules/cm3)

✓Diffusion takes place down the concentration gradient

Cellular neurophysiology

Fick's law for diffusion

$$J_{\mathrm{diff}} = -D\frac{\partial C}{\partial \mathrm{x}}$$

J: diffusion flux (molecules/sec-cm^2)
D: diffusion coefficient (cm^2/sec)
C: concentration of ions (molecules/cm^3)

✓ Diffusion takes place down the concentration gradient

- D depends on the size of the molecule and the medium in which it is diffusing
- Typical value (K^+, Na^+, Cl^-) = 2.5 x 10^{-6} cm^2/sec

Cellular neurophysiology

Ohm's law for drift

$$J_{\text{drift}} = -\mu \; z \, C \; \frac{\partial V}{\partial x}$$

J: drift flux (molecules/sec-cm^2)
μ: mobility (cm^2/ V-sec)
V: electric potential (V)
C: concentration of ions (molecules/cm^3)
z: valence of the ion (dimensionless)

✓ The drift of positively charged particles takes place down th
electric potential gradient

Cellular neurophysiology

Total flux across the membrane

$$J = J_{diff} + J_{drift} = -D \frac{\partial C}{\partial x} - \mu \, z \, C \frac{\partial V}{\partial x}$$

Cellular neurophysiology

Total flux across the membrane

$$J = J_{\mathrm{diff}} + J_{\mathrm{drift}} = -D\,\frac{\partial C}{\partial x} - \mu\, z\, C\,\frac{\partial V}{\partial x}$$

Diffusion and drift processes in the same medium are additive because the resistance presented by the medium to the two processes are the same

Cellular neurophysiology

Total flux across the membrane

$$J = J_{\text{diff}} + J_{\text{drift}} = -D\,\frac{\partial C}{\partial x} - \mu\, z\, C\,\frac{\partial V}{\partial x}$$

Einstein relation

$$D = \frac{k\,T}{q}\mu$$

k: Boltzmann's constant (1.38 x 1023 joule/°K)
T: absolute temperature (°K)
q: charge of the molecule (molecules/sec-cm^2)

Cellular neurophysiology

Total flux across the membrane

$$J = J_{diff} + J_{drift} = -D\ \frac{\partial C}{\partial x} - \mu\ z\ C\ \frac{\partial V}{\partial x}$$

Using Einstein relation

$$J = -\left(\frac{\mu\ k\ T}{q}\ \frac{\partial C}{\partial x} + \mu\ z\ C\ \frac{\partial V}{\partial x} \right)$$

Cellular neurophysiology

- ✓ Nernst-Planck Equation (NPE)

$$I = -\left(u\,z\,R\,T\,\frac{\partial C}{\partial x} + u\,z^2\,F\,C\,\frac{\partial V}{\partial x} \right)$$

R: gas constant (1.98 cal/ºK-mol)
F: Faraday's constant (96,480 C/mol))
$u = \mu / N_A$: molar mobility (cm^2/V-sec-mol)
I: $J \cdot z F$ (A/cm^2)
N_A: Avogadro's number

Cellular neurophysiology

The membrane potential is at rest when the net cross-membrane current is equal to zero; i.e., $I = 0$

✓ Nernst Equation:

$$E_X = \frac{R\,T}{z\,F} \ln \frac{C_{X,out}}{C_{X,in}}$$

E_X: Equilibrium potential of ion X

Cellular neurophysiology

- ✓ Reversal potentials:

Table 1.1 Typical ion concentrations in cells (from Johnston and Wu [139])

Ion	Inside (mM)	Outside (mM)	Equilibrium potential (mV), $E_i = \frac{RT}{zF} \ln \frac{[C]_{out}}{[C]_{in}}$
Frog muscle			$T = 20°C$
K^+	124	2.25	$58 \log \frac{2.25}{124} = -101$
Na^+	10.4	109	$58 \log \frac{109}{10.4} = +59$
Cl^-	1.5	77.5	$-58 \log \frac{77.5}{1.5} = -99$
Ca^{2+}	10^{-4}	2.1	$29 \log \frac{2.1}{10^{-4}} = +125$
Squid axon			$T = 20°C$
K^+	400	20	$58 \log \frac{20}{400} = -75$
Na^+	50	440	$58 \log \frac{440}{50} = +55$
Cl^-	40–150	560	$-58 \log \frac{560}{40-150} = -66$ to -33
Ca^{2+}	10^{-4}	10	$29 \log \frac{10}{10^{-4}} = +145$
Mammalian cell			$T = 37°C$
K^+	140	5	$62 \log \frac{5}{140} = -89.7$
Na^+	5–15	145	$62 \log \frac{145}{5-15} = +90 - (+61)$
Cl^-	4	110	$-62 \log \frac{110}{4} = -89$
Ca^{2+}	10^{-4}	2.5–5	$31 \log \frac{2.5-5}{10^{-4}} = +136 - (+145)$

Simple neuron models

Simple Neuron models

- Single compartment: The spatial dependency of the neuron is reduced to a single point
- Passive neuronal membrane model: It does not include ionic currents; i.e., it does not describe the generation of action potential
- Integrate-and-fire neuron: Spikes can be added artificially to the passive neuronal membrane model

Equivalent circuit model

Components

- Capacitors: representing the ability of the membrane to store charge
- batteries: representing the concentration gradients of the ions
- conductors or resistors: representing the ion channels

Equivalent circuit model

Components

- Capacitors: representing the ability of the membrane to store charge
- batteries: representing the concentration gradients of the ions
- conductors or resistors: representing the ion channels

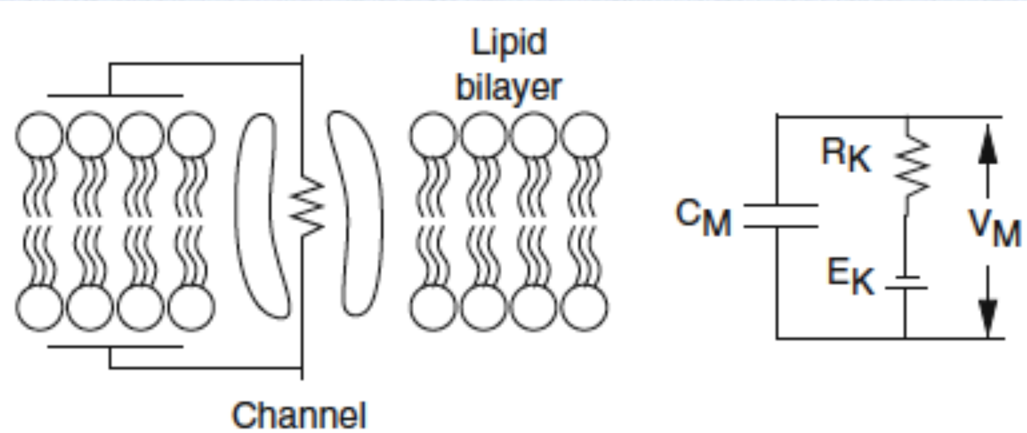


Fig. 1.2 The cell membrane showing the insulating lipid bilayer and a K^+ channel, which allows current to flow. The equivalent electrical circuit is shown on the *right*

membrane only permeable to K^+

Equivalent circuit model

Capacitors:

- The lipid bilayer (cell membrane) has dielectric properties (it behaves like a capacitor)

- Store charge that builds up on both sides of the lipid bilayer due to the membrane potential

$$Q = C\,V$$

Q: charge
C: membrane capacitance (also C_M)
V: membrane potential (also V_M)

C is a measure of how much charge Q needs to be distributed across the membrane in order for a certain potential V to build up

Equivalent circuit model

- Capacitors release this charge in the form of current

$$I_C = C\frac{dV}{dt}$$

- Capacitive current (due to changes of voltage across the capacitance

- There is never an actual movement of charge across the membrane. There is only a redistribution of charge across the two sides.

- The membrane has a very high resistivity.

- The thinner the membrane the stronger the mutual interaction of the charges across it.

Equivalent circuit model

Capacitance:

$$C = C_m A$$

C: membrane capacitance (μF)

C_m: specific membrane capacitance (μF/cm^2)

A: area (cm^2)

Typical values: C_m = 0.7 to 1.0 μF/cm^2

Equivalent circuit model

Resistance:

- Proteins imbedded within the membrane allow ions to pass from one side to the other (ion channels).

- Ionic currents flow through these channels

$$R = \frac{R_m}{A}$$

R: membrane resistance (Ω)
R_m: specific membrane resistance ($\Omega\ cm^2$)
A: area (cm^2)

Equivalent circuit model

Conductance:

- Inverse of the resistance

$$G = R^{-1}$$

$$G_m = R_m^{-1}$$

G: membrane Conductance (S)
G_m: specific membrane conductance (S / cm^2)
A: area (cm^2)

Equivalent circuit model

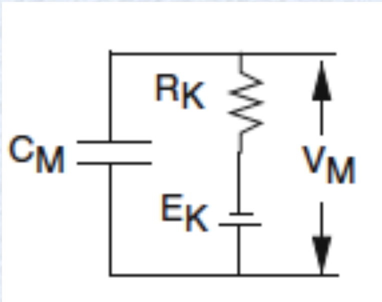
Ohm's law:

- Inverse of the resistance

$$I_K = G_K\,(V - E_K)$$

or

$$I_L = G_L\,(V - E_L)$$



I_L: leak current

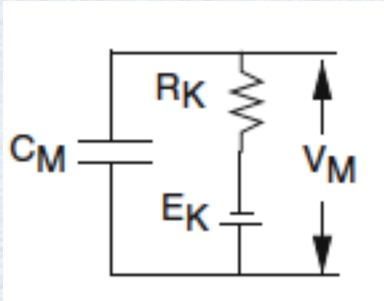
$G_L\,(V - E_L)$: driving force

Passive membrane equation

Kirchhoff's current law:

The total current into the cell must add up to zero

$$C\frac{dV}{dt} = -G_L(V - E_L)$$

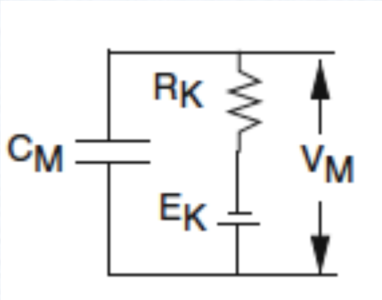


Passive membrane equation

Injected current I_{inj} or applied current I_{app}

Kirchhoff's current law:

The total current into the cell must add up to zero



$$C\frac{dV}{dt} = -G_L(V-E_L) + I_{inj}(t)$$

$$C\frac{dV}{dt} = -G_L(V-E_L) + I_{app}(t)$$

Passive membrane equation

time constant:

$$\tau = R\,C$$

$$C\frac{dV}{dt} = -G_L(V-E_L)+I_{inj}(t)$$

$$\tau\frac{dV}{dt} = -V+E_L+I_{inj}(t)R$$