Biomedical Instrumentation I

Lecture-5: The Origin of Biopotentials

Dr Muhammad Arif, PhD

m.arif@faculty.muet.edu.pk

https://sites.google.com/site/mdotarif/teaching/bmi

Source of Bioelectric Potentials

- Bioelectric potentials are produced as a result of electrochemical activity of a certain class of cells, known as *excitable cells*.

- The excitation cells are the main components of nervous tissue, muscular tissue, & glandular tissue.

Electrical States of Excitable Cells

There are two main states of the excitation cells;

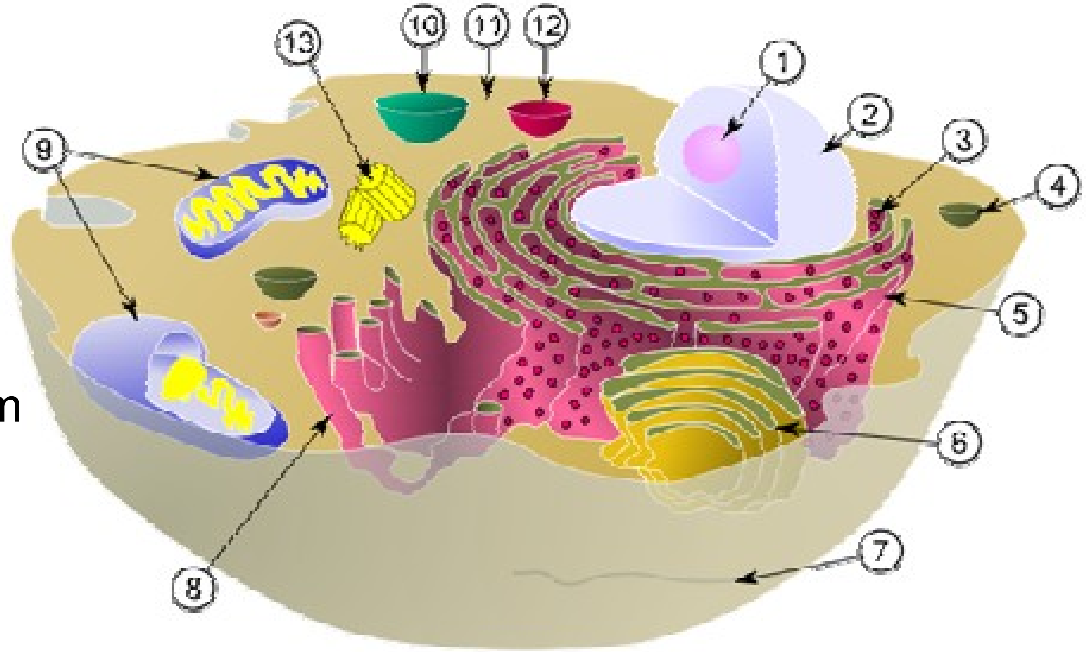
1. Resting State
2. Action State

Recordings of Bioelectric Phenomena

- Electrocardiogram (ECG or EKG)
- Electroencephalogram (EEG)
- Electroneurogram (ENG)
- Electromyogram (EMG)
- Electroretinogram (ERG)
- Electroretinography (ERG)
- Electrooculography (EOG)

Human Cell Structure

(1) Nucleolus
(2) Cell Nucleus
(3) Ribosome
(4) Vesicles
(5) Rough Endoplasmic Reticulum
(6) Golgi
(7) Cytoskeleton
(8) Smooth Endoplasmic Reticulum
(9) Mitochondria
(10) Vacuole
(11) Cytoplasm
(12) Lizosom
(13) Centrioles

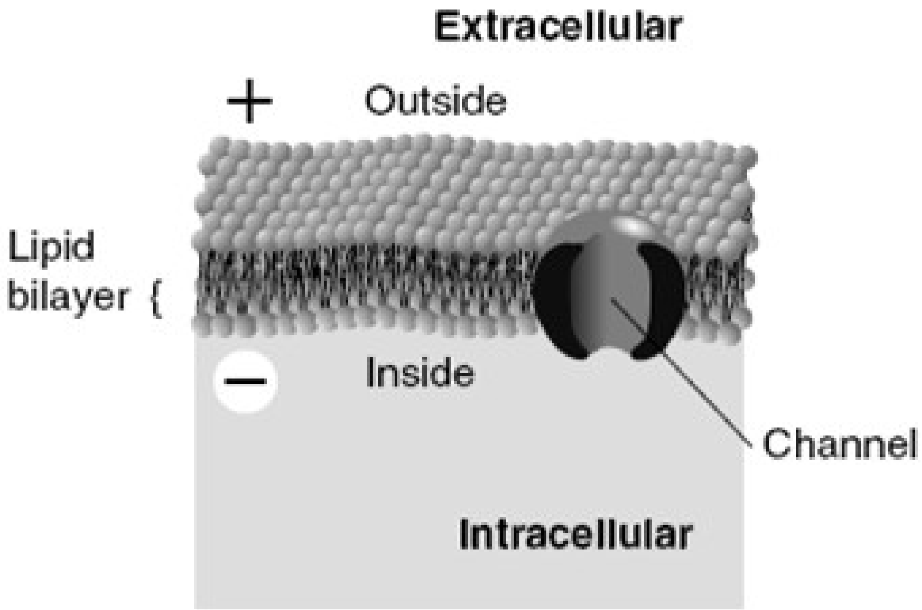


Cell Membrane

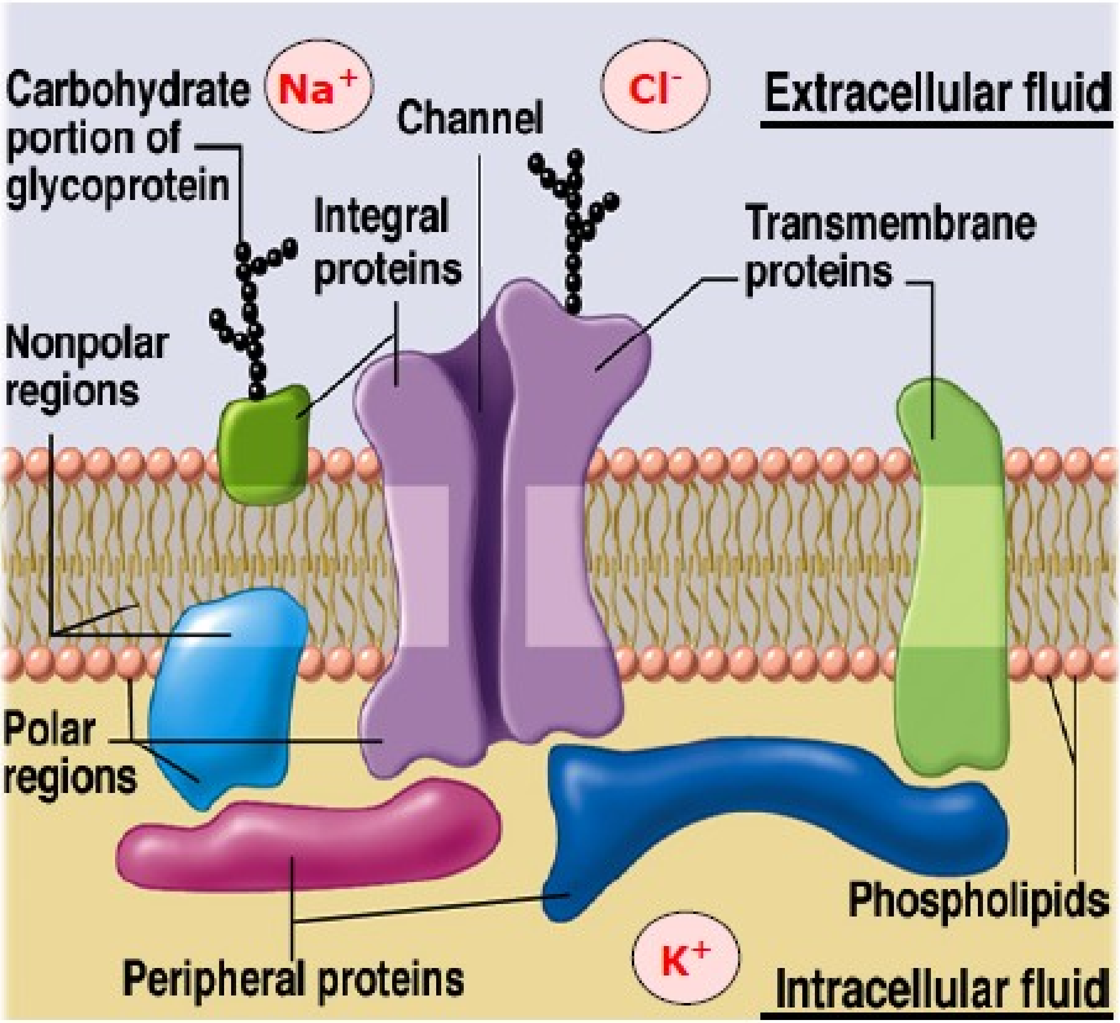
- Cell membrane is semipermeable lipid bilayer made of lipids and proteins that separates the intracellular part from the extracellular environment.

- The cell membrane is very thin with the thickness of 7-15 nm.

- Transmembrane ion channels (pores having the width of 8 nm) allow flow of ions across the membrane.



Cell Membrane



Cell Membrane

- The cell membrene is a thin dielectric material acts as a charge separator (like a leaky capacitor) with a dielectric constant of $\varepsilon = 5$, and spec. capacity of $C = 0.5$ to $1\ \mu F/cm^2$

- The cell membrane is impermeable to intracellular protein and other organic anions.

- The cell membrane is semipermeable to sodium (Na^+), potassium (K^+) and chlorine (Cl^-) ions.

- Separation of charge due to selective permeability of the membrane to ions is responsible for the membrane potential.

Cell Membrane

Transit of substances in and out of cells is regulated by:

1. **Diffusion** is the passive process of transfer of ions or substance from regions of higher concentration to regions of lower concentration.

2. **Osmosis** is the process diffusion of water through a semipermeable membrane.

3. **Active transmission** is the process of transfer of ions or substance from region of lower concentration to regions of higher concentration, and it requires energy.

Cell Membrane

- Ion concentration difference across membrane creates a diffusion gradient.
- Movement of ions across the membrane causes an electrical current to travel along the membrane.
- The ions flow by diffusion create a potential difference which inhibits further flow of charged ions similar to P-N junction.
- The current in electric circuits is the flow of free electrons. Similarly, the current in biological tissue is the flow of free ions.

Cell Membrane

The rules governing the ionic current are:

- Fick's law diffusion
- Drift equation
- Einstein relation

Cell Membrane

1. Fick's Law

Diffusion through semipermeable membrane that is if there is a high concentration [C] of particles in one region that are free to move, they will flow in a direction to equalize the concentration [C] throughout the region.

$$J_{diff} = -D \frac{d[C]}{dx} \text{ for positive ions.}$$

J_{diff} is the current density in (A/m^2).

C is the concentration of ions as a function of distance (C/m^3)

D is the diffusion constant (m^2/s)

K^+ ions can easily leave the cell, creating an excess positive charge and the potential difference occurs - diffusion takes place until the electric field is established and it stops the process of diffusion.

Cell Membrane

2. Particle Drift

Charged particles such as ions in an electric field will move under the forces of electrical attraction and repulsion. The resulting ionic flow is called the drift current.

$$J_{drift} = -\mu Z \frac{d[V]}{dx}[C] \text{ for positive ions.}$$

J_{drift} is the current density in (A/m^2).

C is the concentration of ions as a function of distance (C/m^3)

Z is the number of charges on the ion.

μ is the proportionality constant, mobility $(m^2/V.s)$

V is the voltage drop, (V)

Cell Membrane

3. Einstein Relationship

Two physical constants, mobility **μ** and diffusion coefficient ***D*** are related to each other:

$$\frac{D}{\mu} = \frac{kT}{q}$$

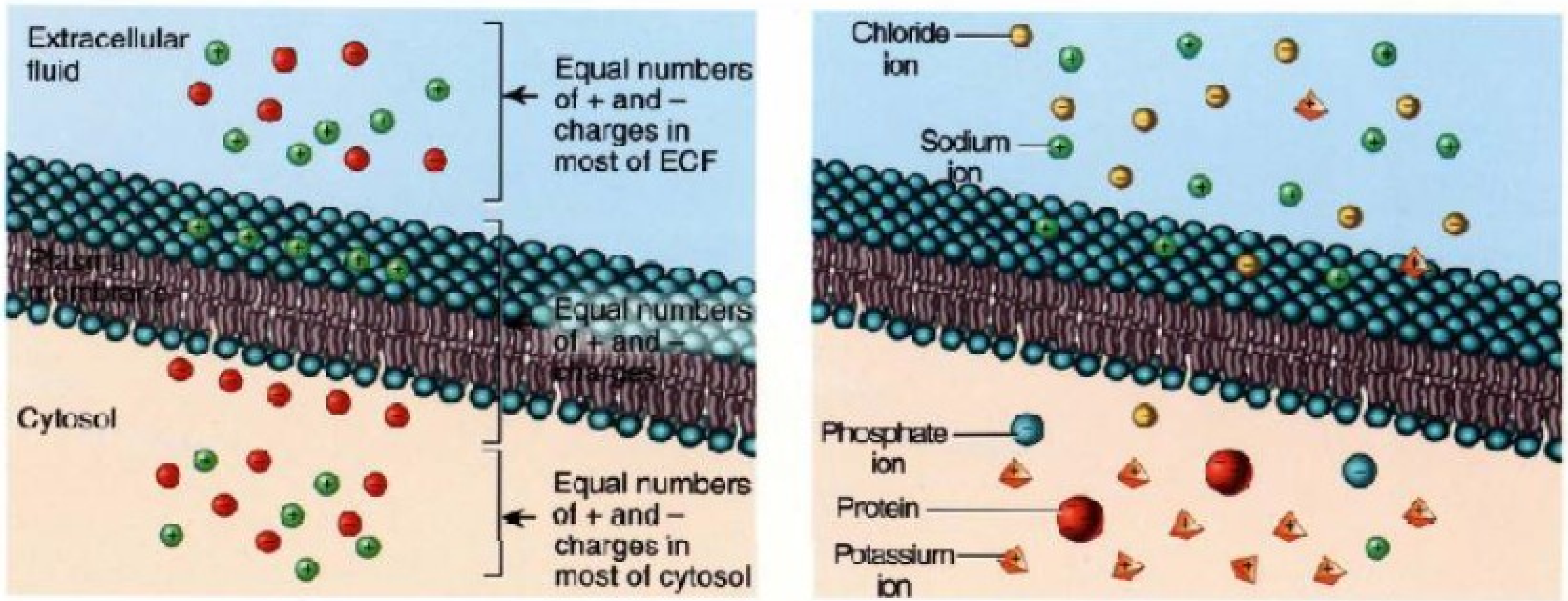
k is the Boltzmann's constant

q is the charge (C)

T is the absolute temperature (K)

Equilibrium Potential

- At equilibrium transmembrane (resting) potential, the net current through the cell membrane is zero.



(a) Distribution of charges (b) Distribution of ions

Equilibrium Potential

Nernst Equation

- The Nernst equation is used for single ionic species.
- Assumes K^+ to be the main ionic species involved in the resting state that is, $P_k >> P_{na}$.

$$E_K = \frac{RT}{nF} \ln \frac{[K]_o}{[K]_i}$$

$$E_K = 0.0615 \log_{10} \frac{[K]_o}{[K]_i}$$

n is the valence of the K^+

$[K]_i$ and $[K]_o$ are the intracellular and extracellular concentrations of K^+ in moles per liter

R is the universal gas constant

T is absolute temperature in K

F is the Faraday constant

Equilibrium Potential

Example: The intracellular K+ concentration of a group of cells averages I50 x 10^{-6} moles/cm^3. The extracellular concentration of K^+ averages 6 x 10^{-6} moles/cm^3.

a)Calculate the concentration ration.

b)Calculate the diffusion potential for K^+.

Solution

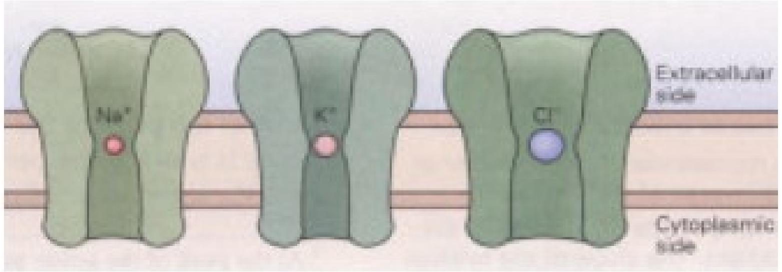
a) $$\frac{C_o}{C_i} = \frac{6 \times 10^{-6}\ \text{moles/cm}^3}{150 \times 10^{-6}\ \text{moles/cm}^3} = \frac{5}{20} = \mathbf{1/4}$$

b) $$E^{K+} = 61\ \text{Log}\ C_o/C_i = 61\ \text{Log}\ 1/25 = \mathbf{-85.3\ mV}$$

Equilibrium Potential

Goldman–Hodgkin–Katz (GHK) Equation

The Goldman equation accounts for influence of other ionic species in internal and external fluid media.



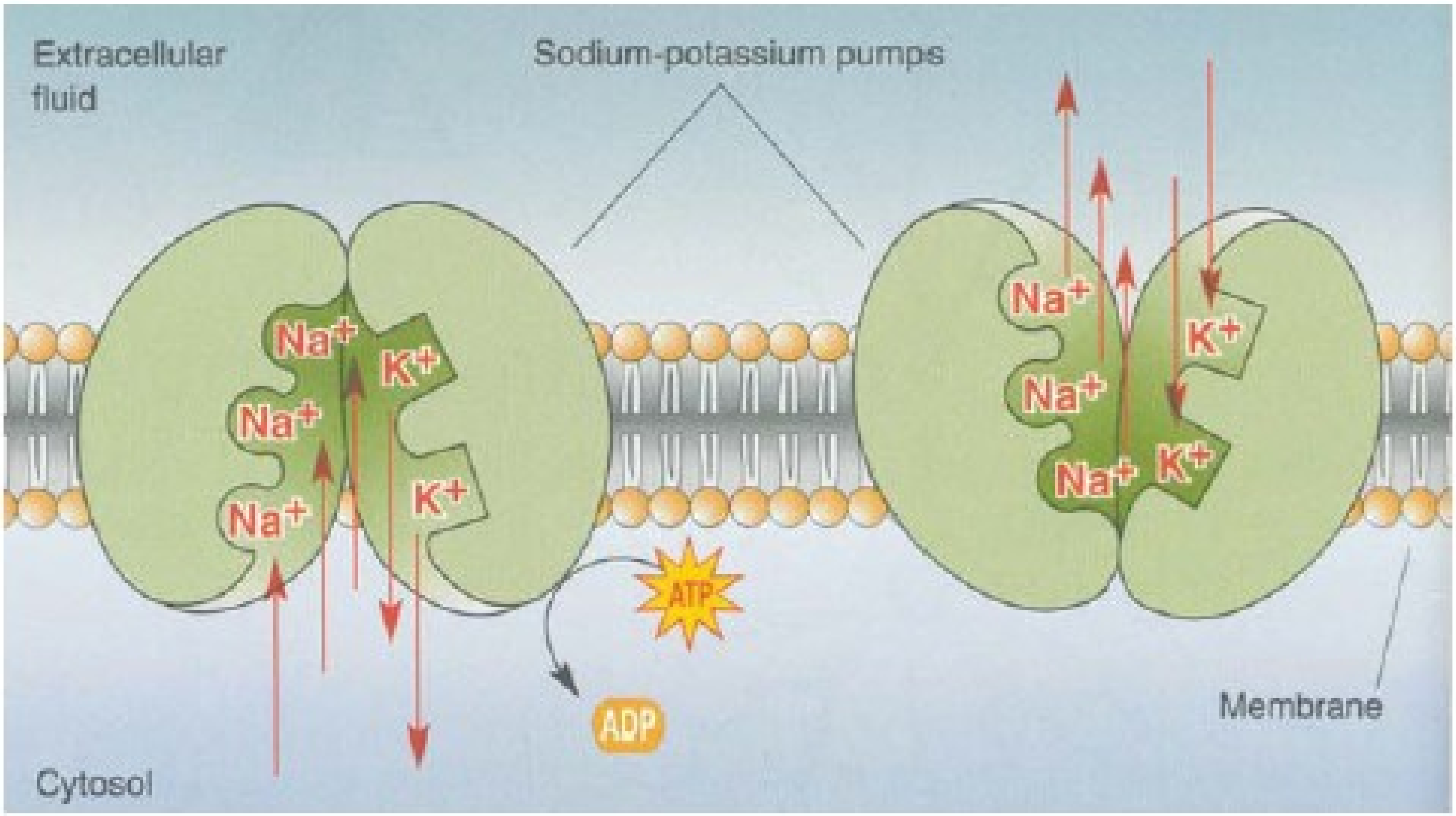
$$E = \frac{RT}{F} \ln\left\{ \frac{P_K[K]_o + P_{Na}[Na]_o + P_{Cl}[Cl]_i}{P_K[K]_i + P_{Na}[Na]_i + P_{Cl}[Cl]_o} \right\}$$

- **R** is the universal gas constant
- **T** is absolute temperature in K
- **F** is the Faraday constant
- P_M is the permeability coefficient of the membrane for a particular ionic species M (K, Na, Cl)

Active Channel: Sodium-Potassium Pump

- Maintaining steady state ionic imbalance requires continuous transport of ions against electrochemical gradients.
- Active transport mechanism located in the membrane, and is known as the ***sodium–potassium pump***.
- The sodium–potassium pump actively transports Na^+ out of cell and K^+ into cell in the ratio $3Na^+ : 2K^+$.
- Associated pump current i_{NaK} is a net outward current that tends to increase the negativity of the intracellular potential.
- The energy for the pump is provided by a common source of cellular energy, adenosine triphosphate (ATP) produced by mitochondria in the cell.

Active Channel: Sodium-Potassium Pump



Factors Influencing the Flow of Ions Across the Cell Membrane

- Diffusion gradients
- Inwardly directed electric field
- Membrane structure (availability of pores)
- Active transport of ions against an established electrochemical gradient

The Active State

Polarization: the cell membrane is at a steady resting potential (more negative inside the cell).

Depolarization: lessening the magnitude of cell polarization by making inside the cell less negative.

Hyperpolarization: increasing the magnitude of cell polarization by making inside the cell more negative.

Action Potential: brief transient disturbance of membrane potential.

- change in membrane potential due to a stimulus adequate to bring about depolarization sufficient to exceed its threshold potential and thereby elicit an all-or-none action potential.
- change in potential from resting level.
- further increases in intensity or duration of stimulus beyond that required for exceeding the threshold level produce only the same result.

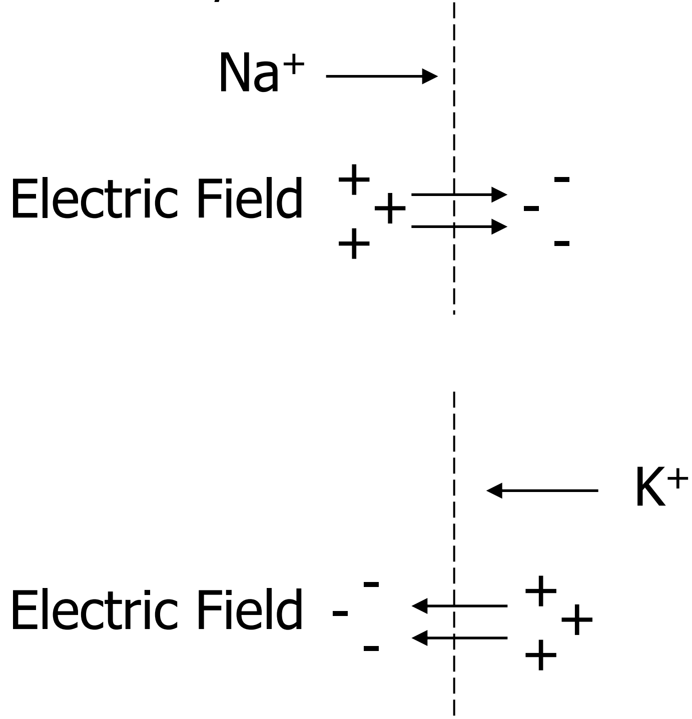
Repolarization: return to membrane equilibrium after action potential.

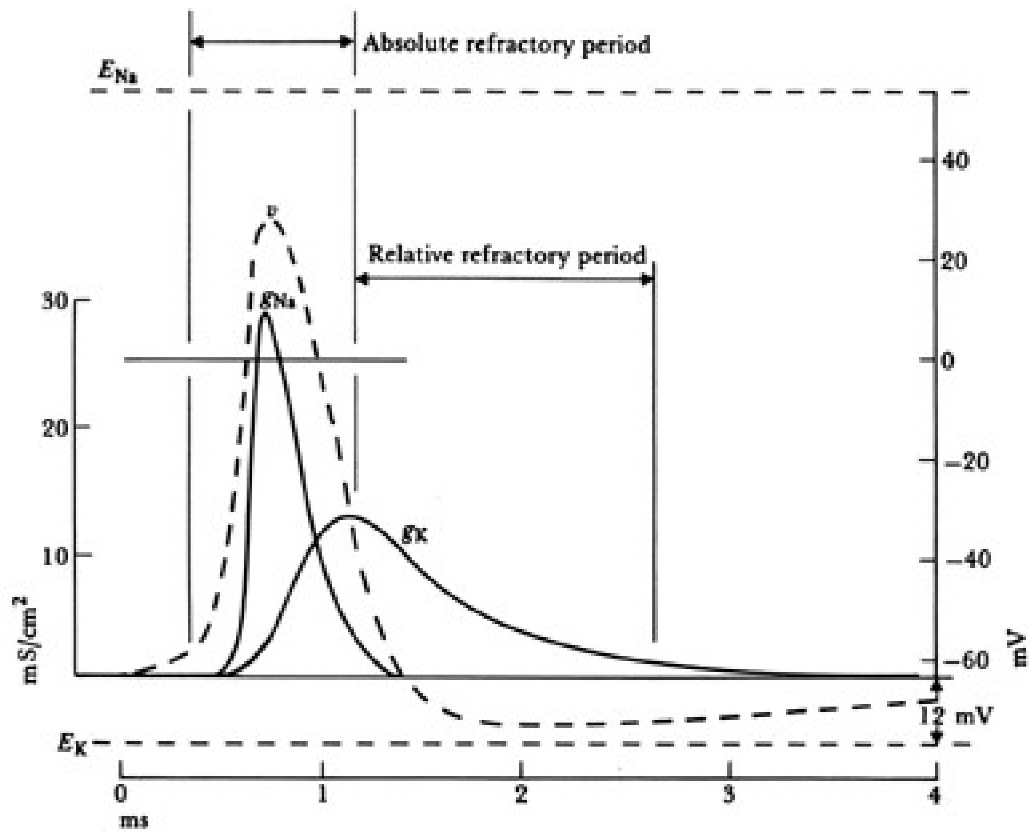
Action Potential

If a stimulus depolarizes the cell such that $V_{cell} > V_{threshold}$, an *action potential* is generated.

Exteracellular | Interacellular

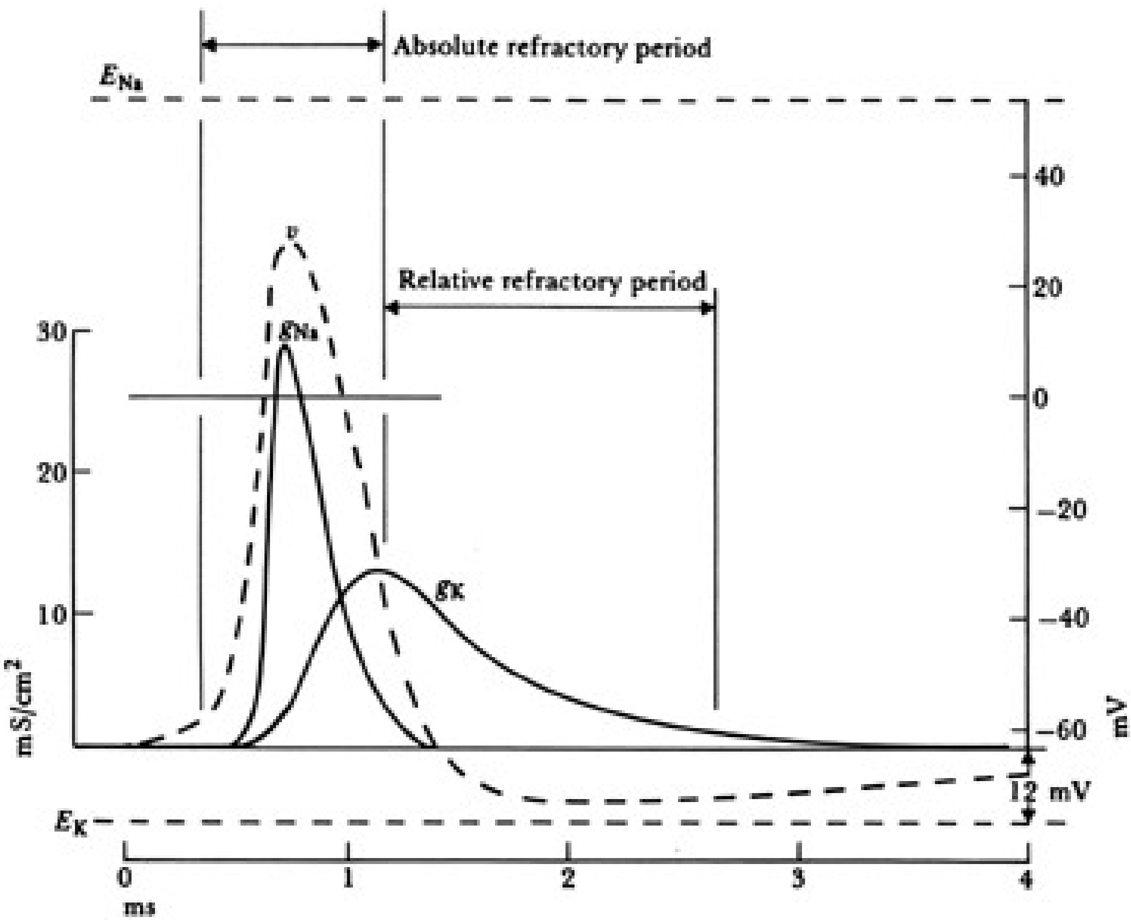
2.5 mmol/liter of K^+ | 140 mmol/liter of K^+





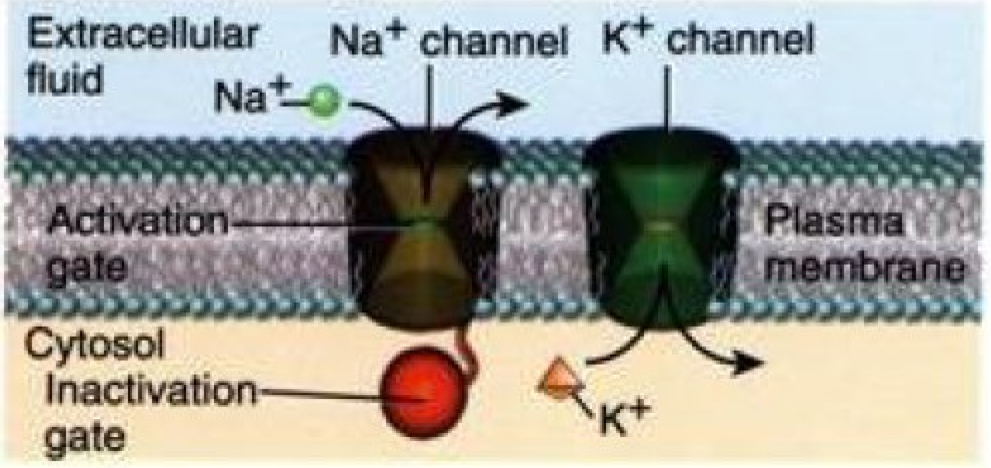
Action Potential

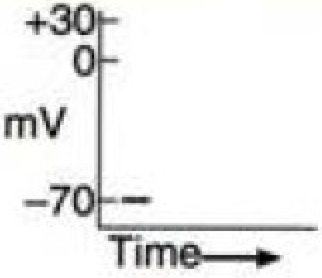
Absolute refractory period: membrane can not respond to any stimulus.
Relative refractory period: membrane can respond to an intense stimulus.



Resting Membrane Potential

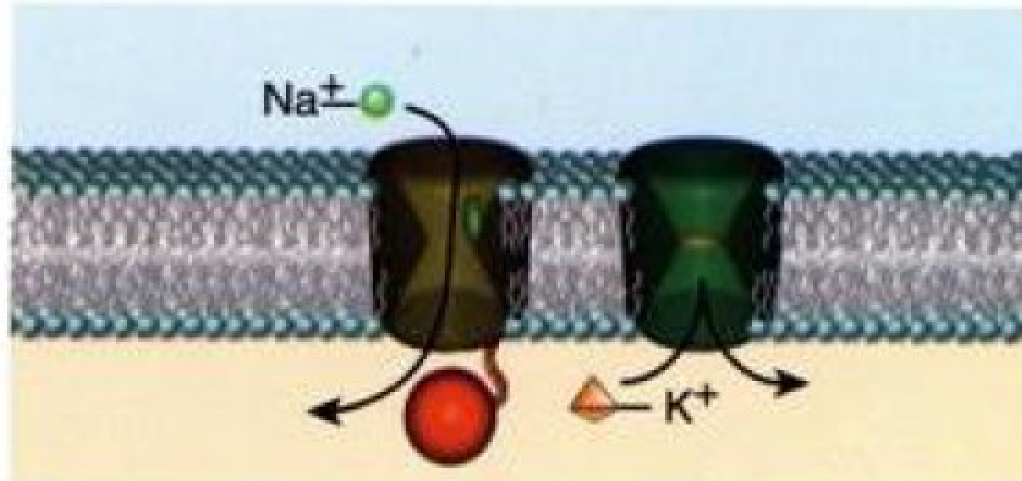
1. **Resting state:** Voltage-gated Na^+ channels are in resting state and voltage-gated K^+ channels are closed.

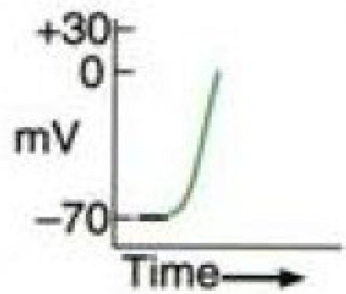




Action Potential

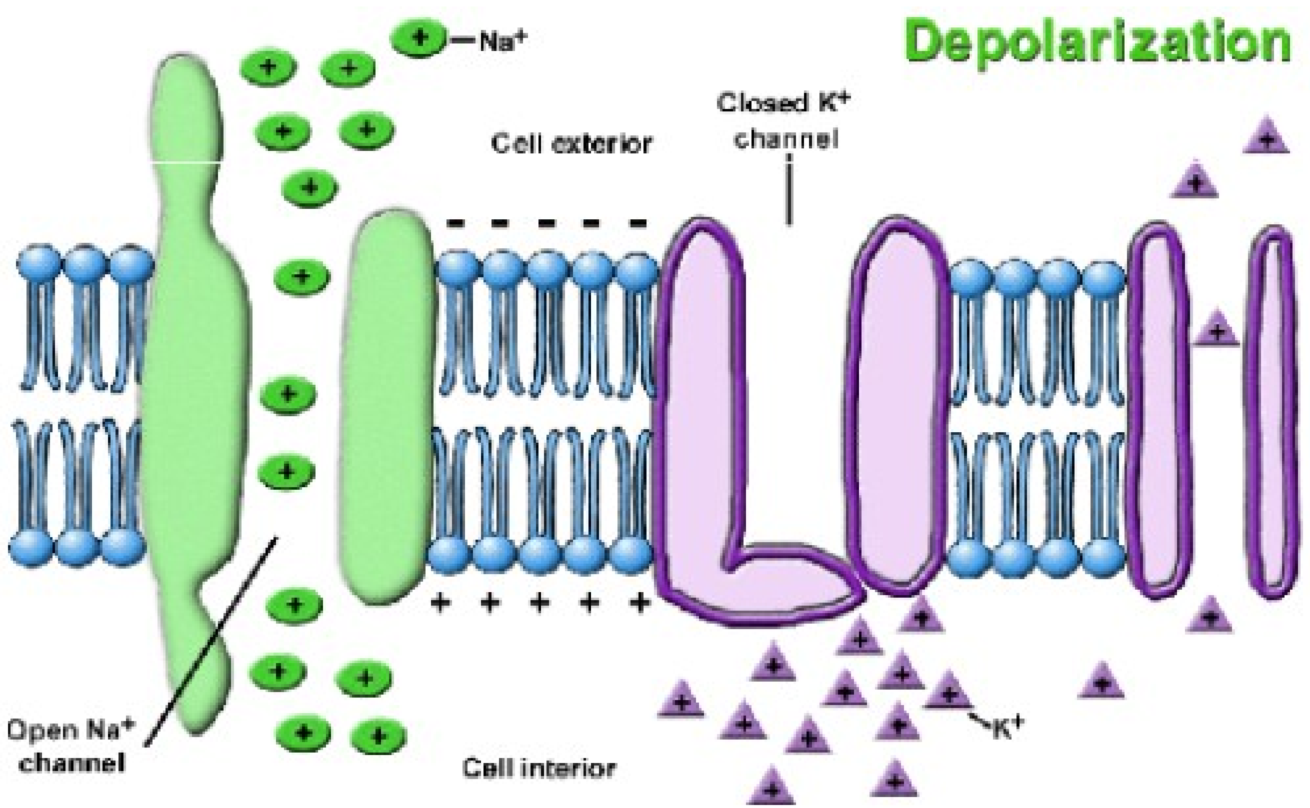
2. Depolarizing phase: Depolarization to threshold (about –55 mV) opens Na^+ channel activation gates. The inflow of Na^+ further depolarizes the membrane until its polarity is reversed.





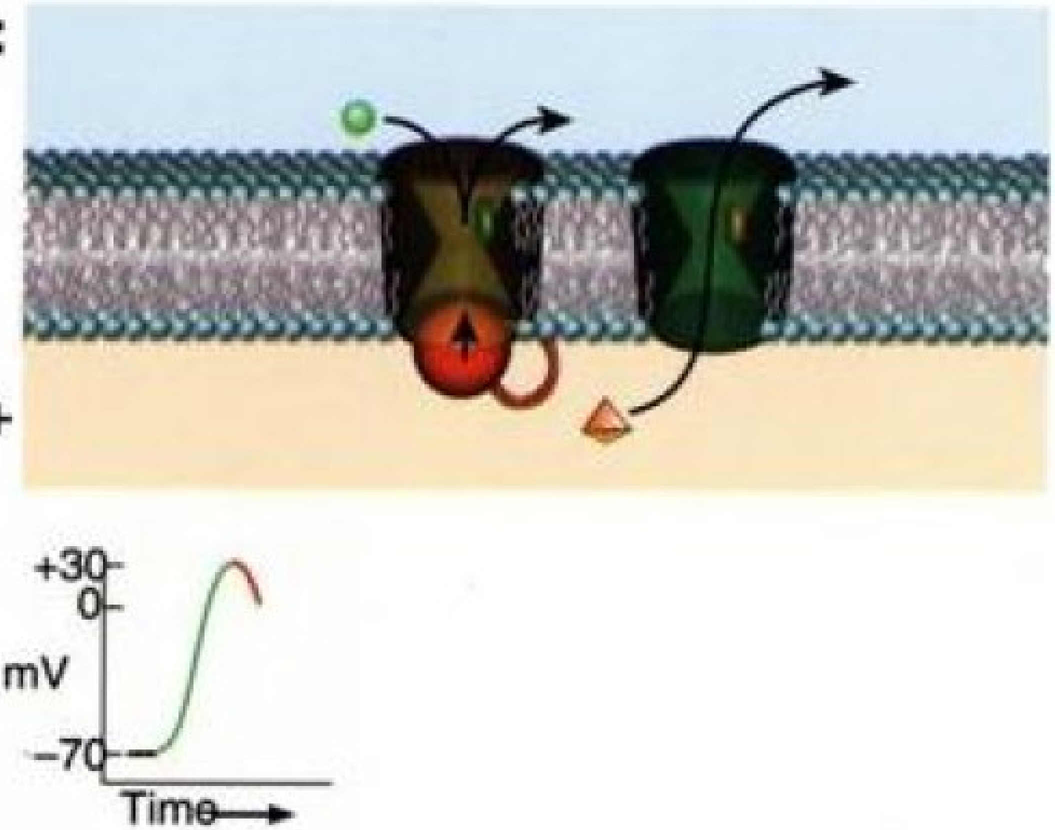
Action Potential

As a result of stimulus, the permeability of membrane to Na+ increases up to 1000 times folds. Therefore, the Na+ rush into the cell carrying enough positive charges to change the membrane potential. This is called “Depolarization”.



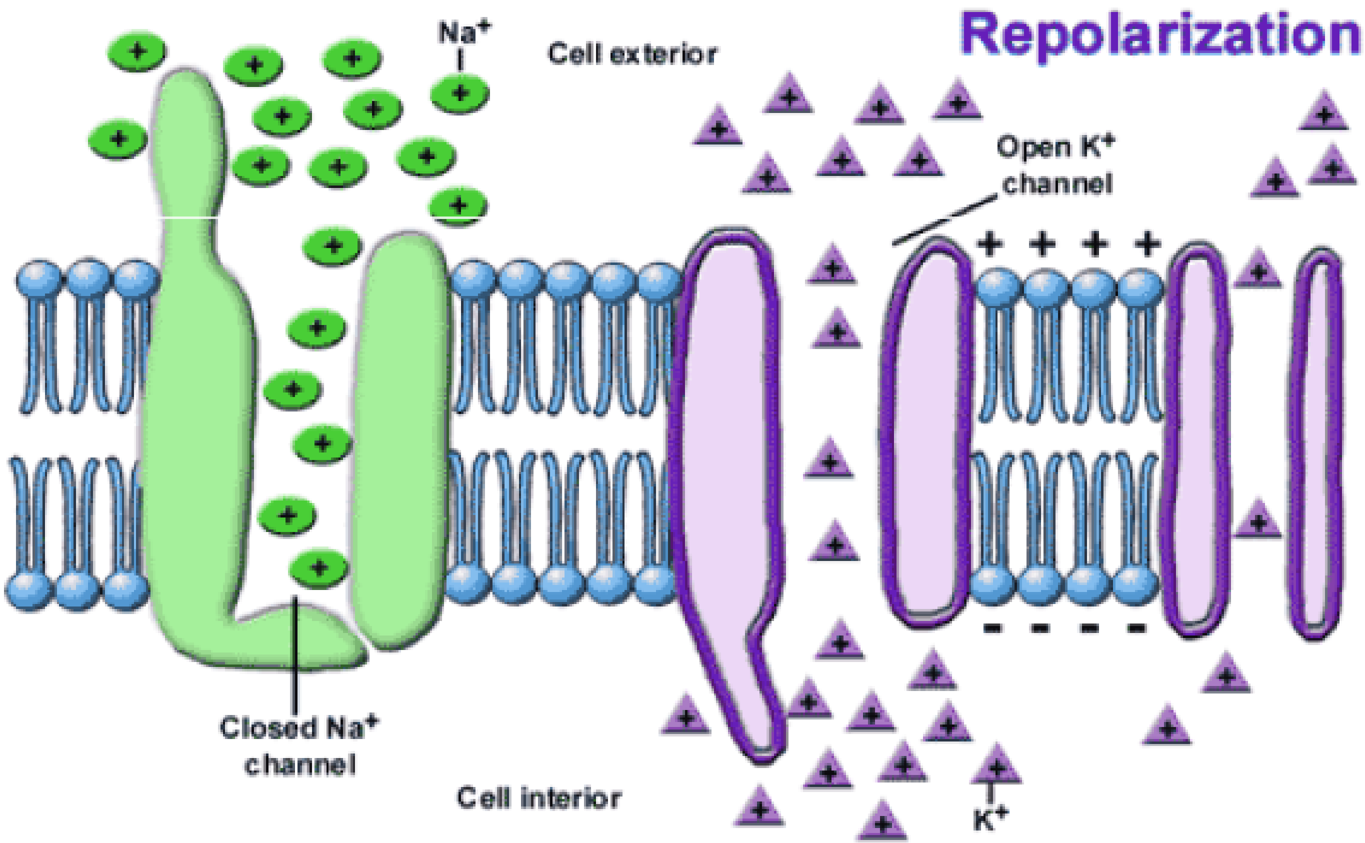
Action Potential

3. Repolarizing phase: More slowly, depolarization also opens voltage-gated K^+ channels, which permit outflow of K^+. At the same time Na^+ channel inactivation gates are closing.



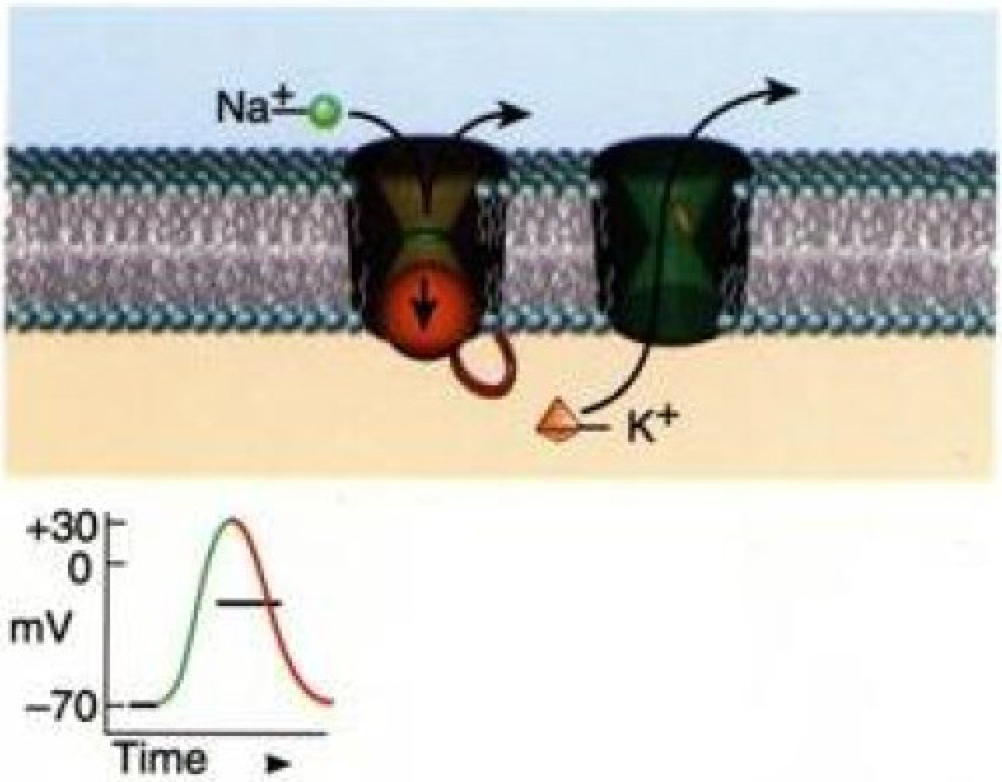
Action Potential

Almost immediately after depolarization, the pores of membrane again become almost impermeable to Na+ and the membrane potential goes back to its resting state. This is called “Repolarization”.

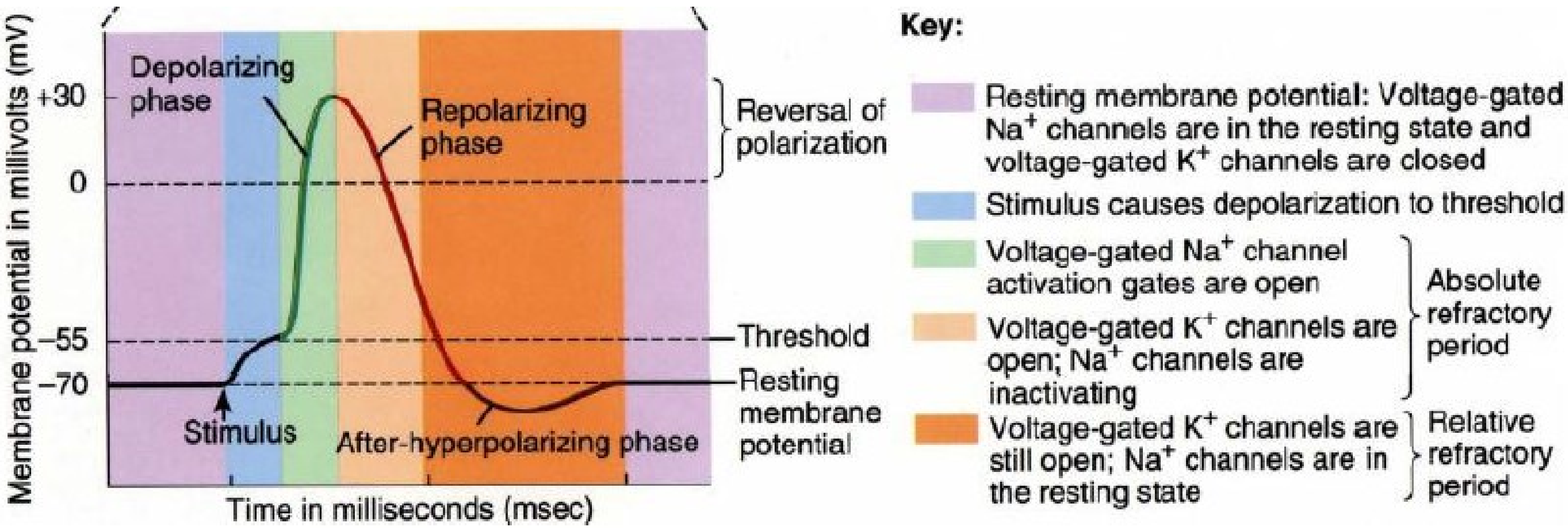


Action Potential

4. Repolarization continues:
Outflow of K^+ restores the resting membrane potential, Na^+ channel inactivation gates are opening and K^+ channels are closing.



Action Potential



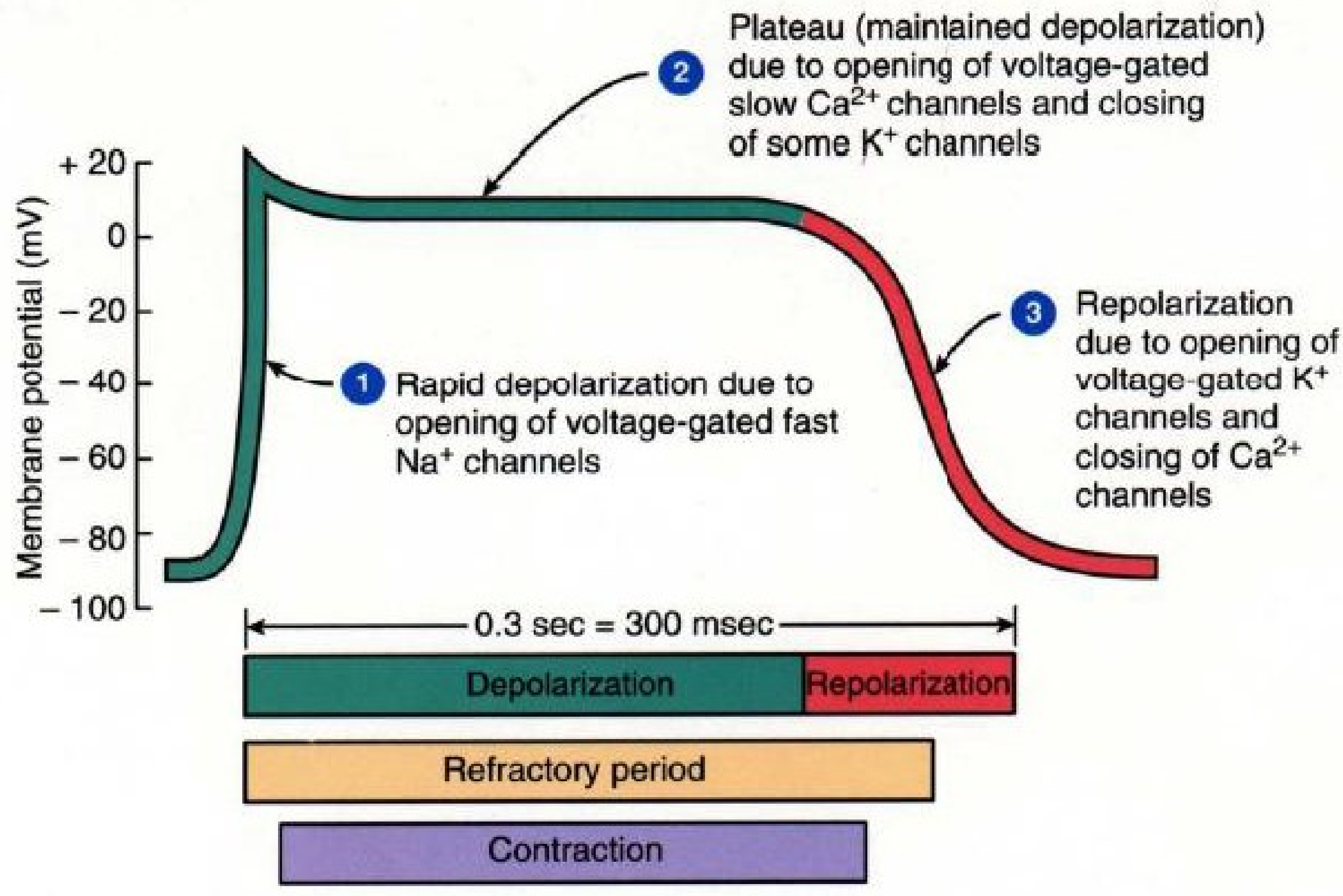
Action Potential

- An action potential elicited at any point on a membrane, usually excites adjacent portions of the membrane, resulting propagation of the action potential in any direction.

- The action potential moves and depolarizes through the entire membrane or it fails to travel at all.

- This is called “all-or-none law”.

The ECG: Cardiac Action Potential



(a) Action potential, refractory period, and contraction

Questions?