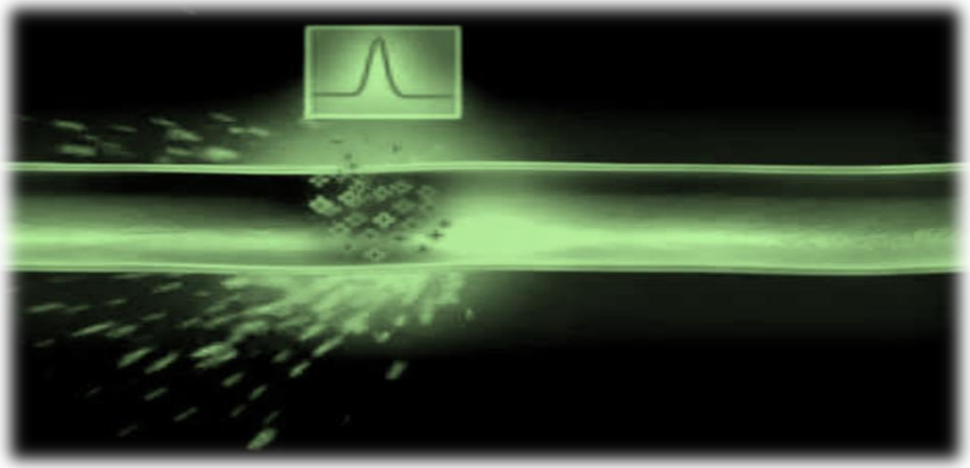

Membrane Potentials

Faculty of Dentistry
Nervous System

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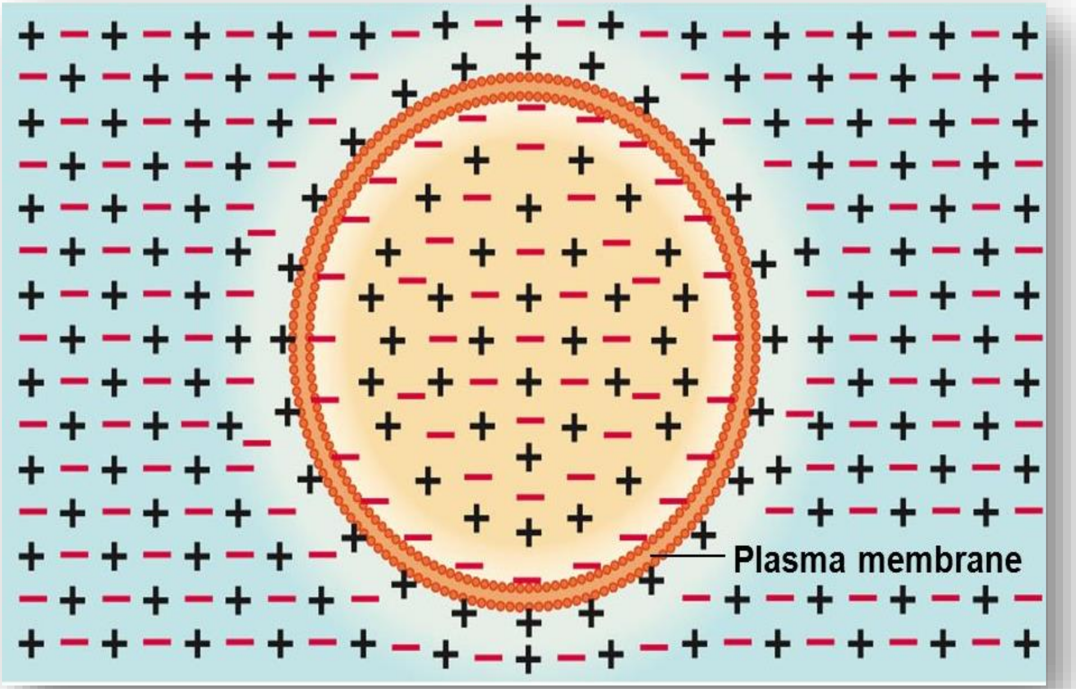
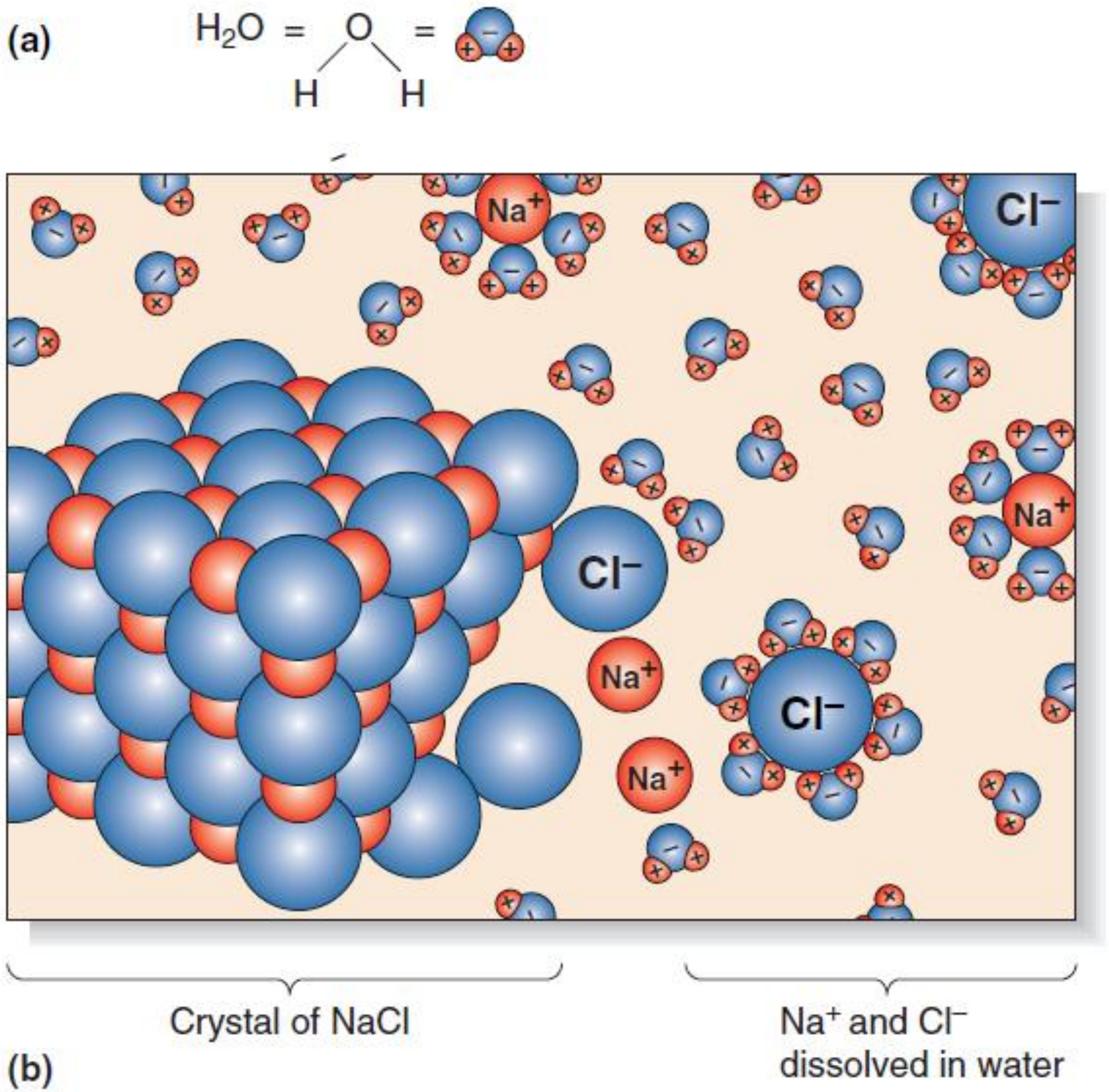
Lecture outline

- Resting membrane potential
  - Ionic basis of resting membrane potential
  - Equilibrium potentials
  - Nernst equation
  - Goldman-Hodgkin-Katz equation
- Graded potentials
- Action potentials



- There is an electrical potential difference between the two sides of the membrane in all body cells: Membrane Potential
- Some cells (excitable cells) such as nerve and muscle cells can rapidly and transiently change their membrane potential and generate electrochemical impulses.



(a)
H2O =
O
H H
=
Na+
Cl−
Cl−
Na+
Na+
Cl−
Na+
Crystal of NaCl
Na+ and Cl−
dissolved in water
(b)

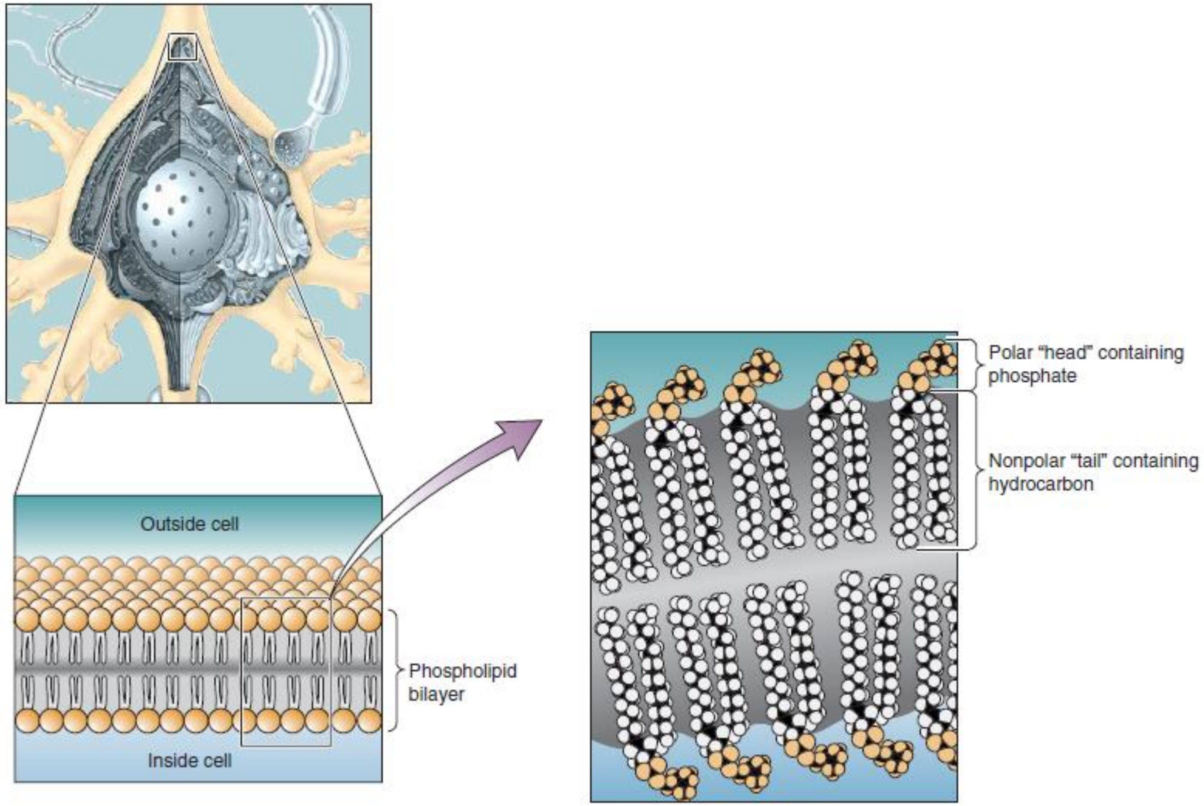
Intracellular and extracellular ion concentrations in a typical mammalian cell

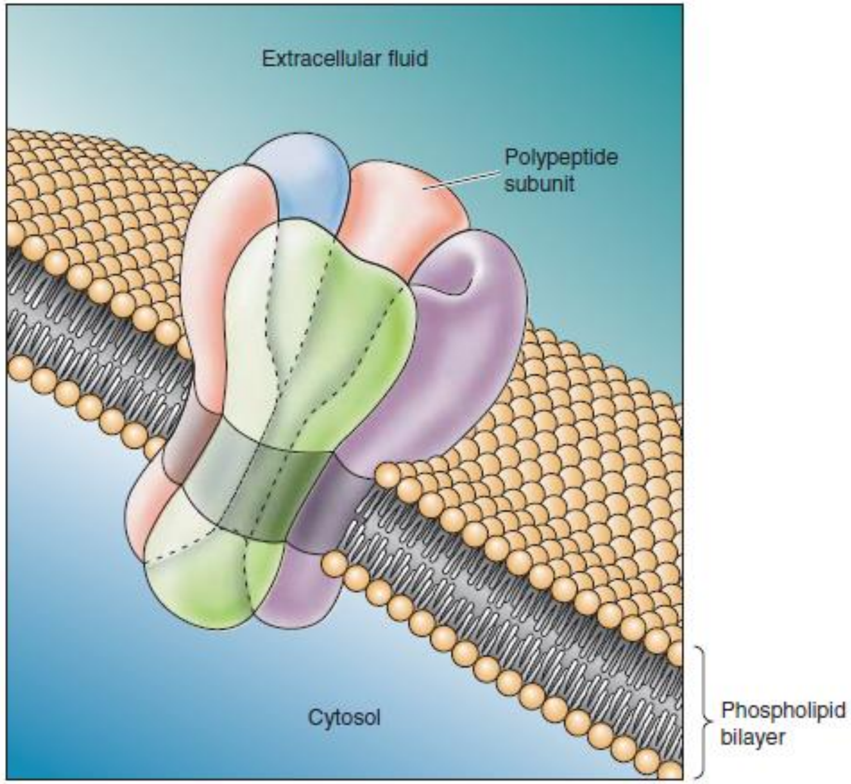
Component	Cytoplasmic concentration (mM)	Extracellular concentration (mM)
Cations		
Na^+	5–15	145
K^+	140	5
Mg^{2+}	0.5	1–2
Ca^{2+}	10^{-4}	1–2
H^+	7×10^{-5} ($10^{-7.2}$ M or pH 7.2)	4×10^{-5} ($10^{-7.4}$ M or pH 7.4)
Anions		
Cl^-	5–15	110

	EXTRACELLULAR FLUID	INTRACELLULAR FLUID
Na^+	142 mEq/L	10 mEq/L
K^+	4 mEq/L	140 mEq/L
Ca^{++}	2.4 mEq/L	0.0001 mEq/L
Mg^{++}	1.2 mEq/L	58 mEq/L
Cl^-	103 mEq/L	4 mEq/L
HCO_3^-	28 mEq/L	10 mEq/L
Phosphates	4 mEq/L	75 mEq/L
$SO_4^=$	1 mEq/L	2 mEq/L
Glucose	90 mg/dl	0 to 20 mg/dl
Amino acids	30 mg/dl	200 mg/dl ?
Cholesterol Phospholipids Neutral fat	0.5 g/dl	2 to 95 g/dl
PO_2	35 mm Hg	20 mm Hg ?
PCO_2	46 mm Hg	50 mm Hg ?
pH	7.4	7.0
Proteins	2 g/dl (5 mEq/L)	16 g/dl (40 mEq/L)

Resting Membrane Potentials

The phospholipid membrane and membrane proteins

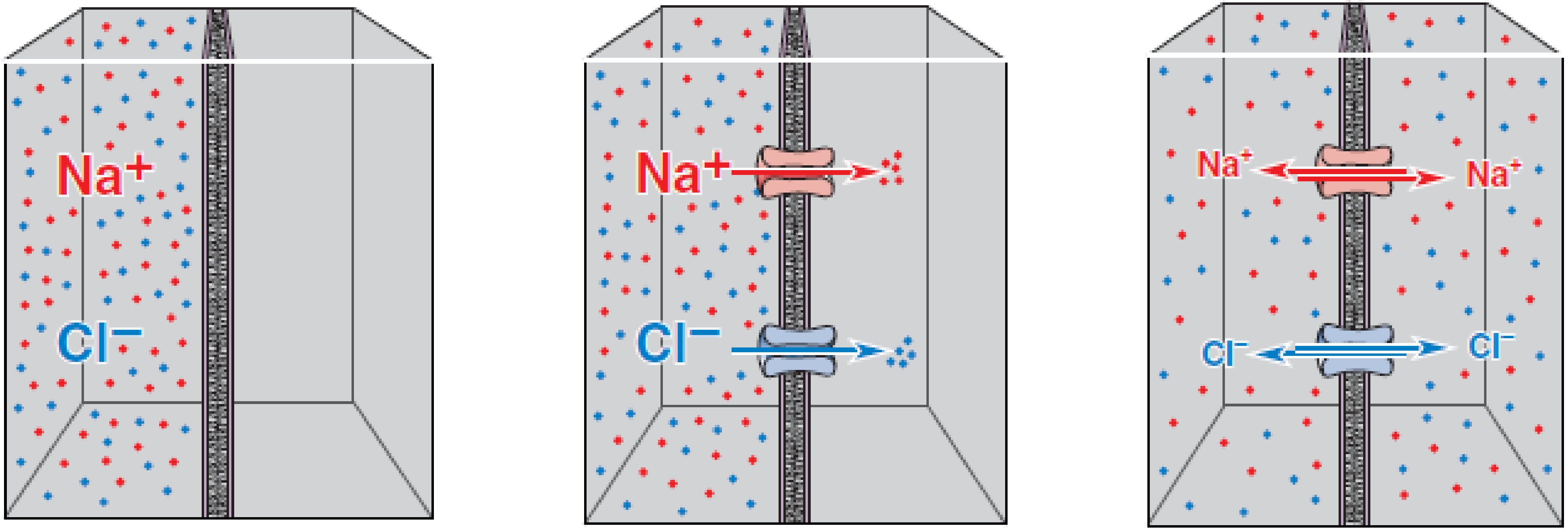




The Movement of Ions

Ionic movements through channels are influenced by two factors: **Diffusion and Electricity.**

Diffusion



The movement of ions across the membrane by diffusion, therefore, happens when

- ✓ The membrane has channels permeable to the ions
- ✓ There is a concentration gradient across the membrane.

Electricity

- The movement of electrical charge is called **electrical current (I)**
- Two important factors determine how much current will flow:
  - **Electrical potential (voltage, V)**
  - ✓ is the force exerted on a charged particle
  - ✓ reflects the difference in charge between the anode and the cathode.
  - **Electrical conductance (g, Siemens)**
  - ✓ is the relative ability of an electrical charge to migrate from one point to another
  - ✓ depends on the number of ions or electrons available to carry electrical charge, and the ease with which these charged particles can travel through space

- **Electrical resistance** is simply the inverse of conductance
- The relative inability of an electrical charge to migrate.
- It is represented by the symbol **R** and measured in units called ohms (Ω).

Ohm’s law

$$\mathbf{I = g \cdot V}$$

$$\mathbf{I = V / R}$$

Driving an ion across the membrane electrically requires:

Channel proteins permeable to that ion (to provide conductance)

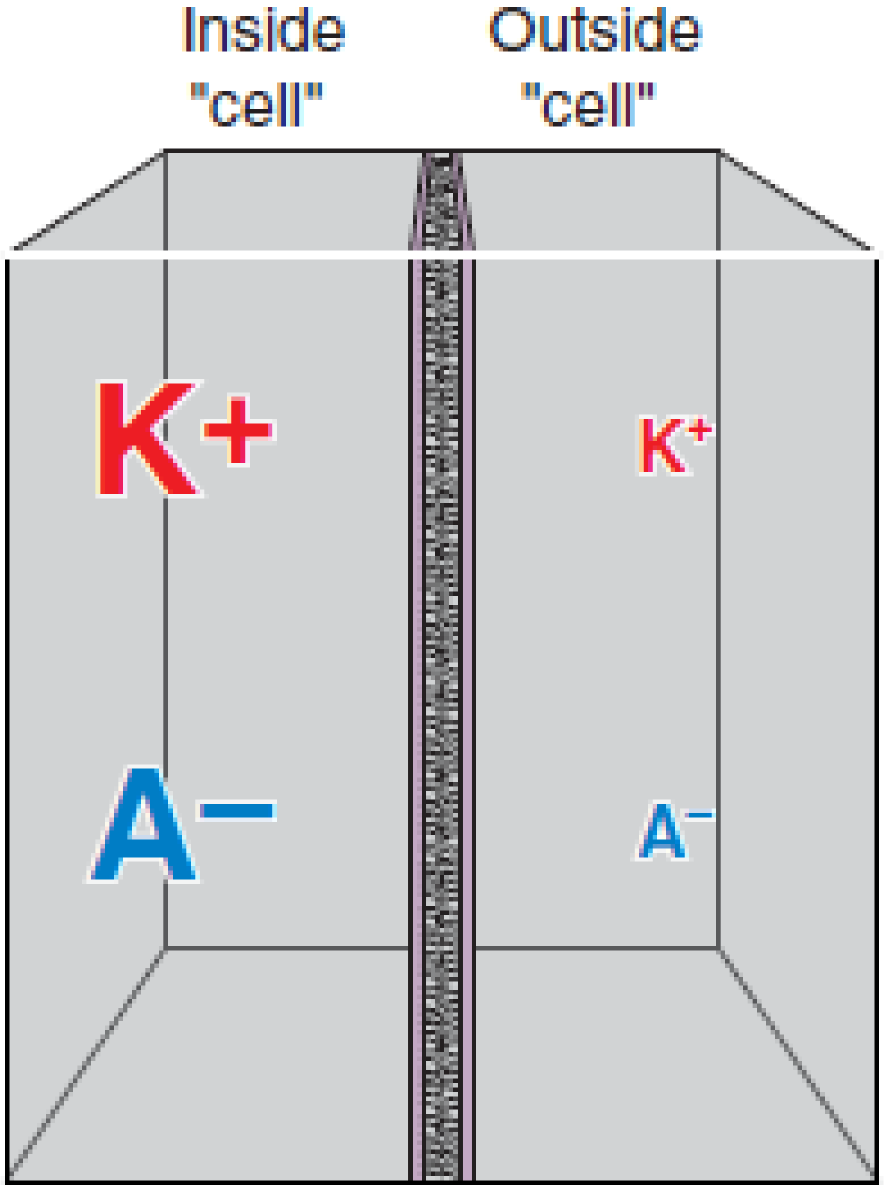
Electrical potential difference across the membrane

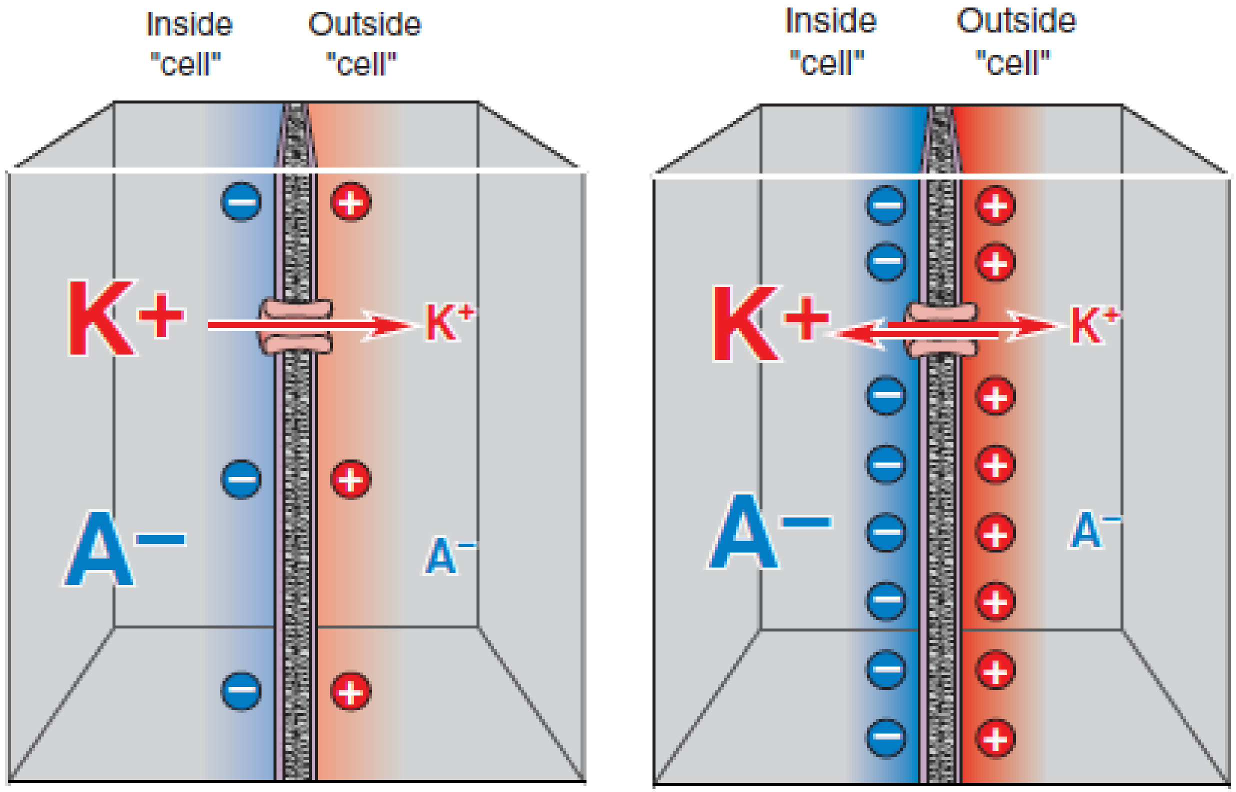
The Ionic Basis of The Resting Membrane Potential

- Membrane potential (V_m): the voltage (i.e. electrical charge difference) across the cell membrane at any moment.
  - Sometimes V_m is «at rest»: **Resting membrane potential**
  - At other times it is not (e.g. during graded and action potential)
- Vm = - 65 mV

Equilibrium Potentials

20X





Ionic equilibrium potential , or simply **equilibrium potential** is the electrical potential difference that exactly balances an ionic concentration gradient

E ion.

E_K = - 80 mV.

If the concentration difference across the membrane is known for an ion, the equilibrium potential can be calculated for that ion: ***NERNST EQUATION***

$$E_{ion} = 2.303\,\frac{RT}{zF}\,\log\frac{[ion]_o}{[ion]_i}$$

where

E_{ion} = ionic equilibrium potential
R = gas constant
T = absolute temperature
z = charge of the ion
F = Faraday's constant
log = base 10 logarithm
$[ion]_o$ = ionic concentration outside the cell
$[ion]_i$ = ionic concentration inside the cell

At body temperature (37°C), the Nernst equation for the important ions—K^+, Na^+, Cl^-, and Ca^{2+} — simplifies to:

$$E_K = 61.54\text{ mV}\log\frac{[K^+]_o}{[K^+]_i}$$

$$E_{Na} = 61.54\text{ mV}\log\frac{[Na^+]_o}{[Na^+]_i}$$

$$E_{Cl} = 61.54\text{ mV}\log\frac{[Cl^-]_i}{[Cl^-]_o}$$

$$E_{Ca} = 30.77\text{ mV}\log\frac{[Ca^{2+}]_o}{[Ca^{2+}]_i}$$

If $\dfrac{[K^+]_o}{[K^+]} = \dfrac{1}{20}$

and $\log\dfrac{1}{20} = -1.3$

then $E_K = 61.54\text{ mV} \times -1.3$
$= -80\text{ mV}.$

Ions are driven across the membrane at a rate proportional to the difference between the membrane potential and the equilibrium potential

Ionic driving force = $V_m - E_{ion}$

Relative ion permeabilities of the membrane at rest

The resting membrane potential can be calculated using the **Goldman-Hodgkin-Katz equation,** that takes into consideration the relative permeability of the membrane to different ions.

$$V_m = 61 \log \frac{P_K [K_{out}] + P_{Na} [Na_{out}] + P_{Cl} [Cl_{in}]}{P_K [K_{in}] + P_{Na} [Na_{in}] + P_{Cl} [Cl_{out}]}$$

where V_m is the membrane potential, P_K and P_{Na} are the relative permeabilities to K^+ and Na^+, respectively, and the other terms are the same as for the Nernst equation.

If the resting permeability to K^+ is 40 times greater than its to Na^+, then solving the Goldman equation yields:

$$\begin{aligned} V_m &= 61.54 \text{ mV} \log \frac{40\,(5) + 1\,(150)}{40\,(100) + 1\,(15)} \\ &= 61.54 \text{ mV} \log \frac{350}{4015} \\ &= -65 \text{ mV} \end{aligned}$$

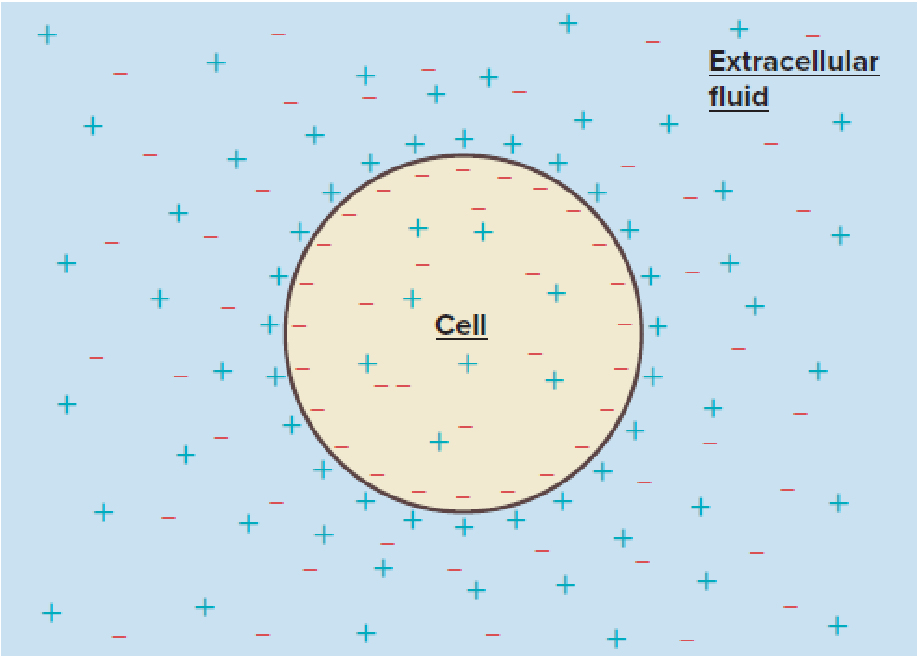
- *Membrane potential depends on the ionic concentrations on both sides of the membrane.*
- **How do these concentration gradients arise?**

Ionic concentration gradients are established by the **actions of ion pumps** in the cell membrane

Resting membrane potential

- RMP is generated largely because of the movement of K^+ out of the cell down its concentration gradient through **K^+ leak channels**.
  - The plasma membrane is more permeable to K^+ in resting state than Na^+ because the membrane has more leak channels for K than for Na^+
  - Hydrated form of K^+ is smaller than hydrated form of Na^+

Inside of the cell becomes negative with respect to the outside.

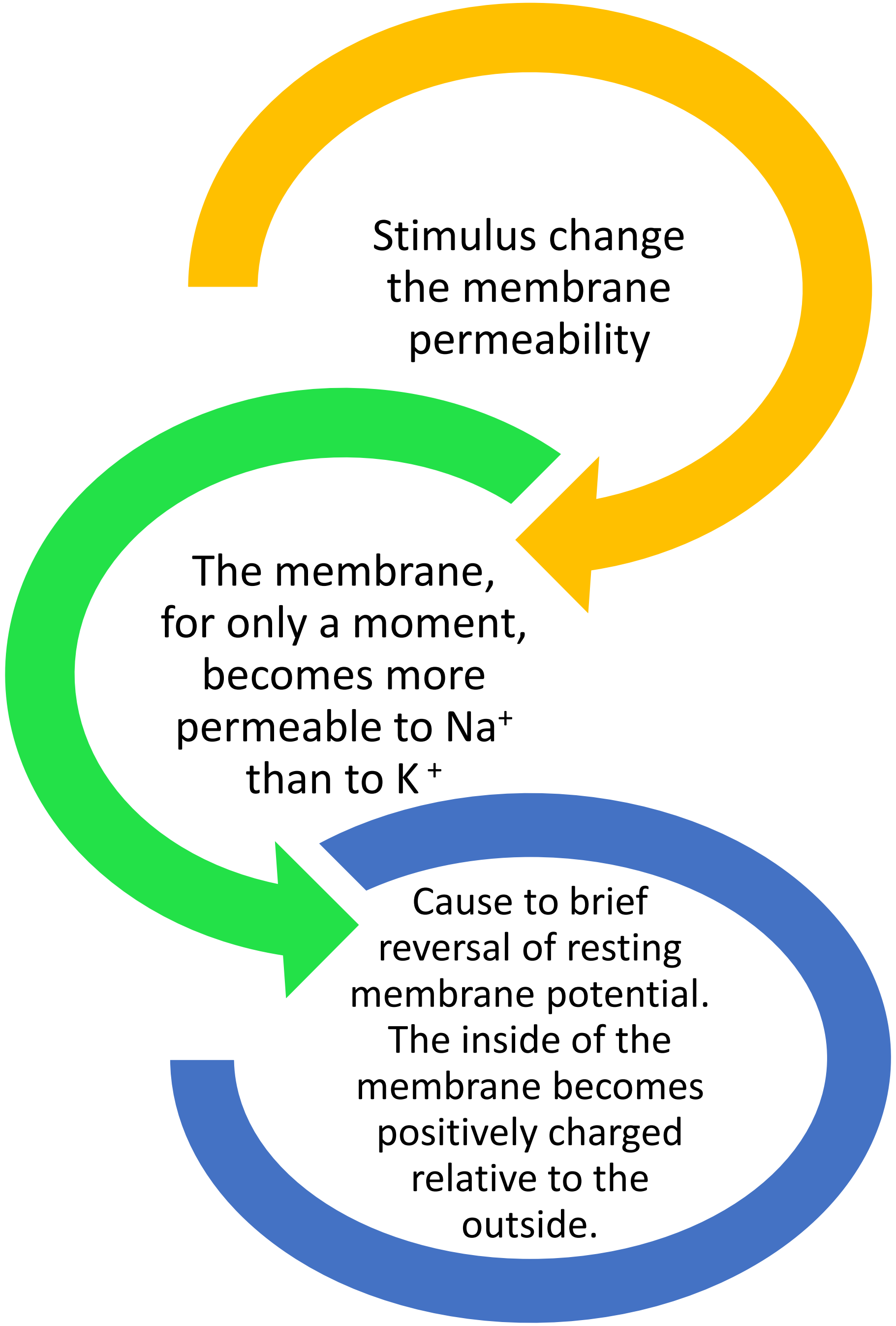


Resting membrane potential

- **The Na^+–K^+ pump contributes only indirectly** to the resting membrane potential by maintaining, across the cell membrane, the Na^+ and K^+ concentration gradients that then produce diffusion potentials.
  - The direct **electrogenic** contribution of the pump (3 Na^+ pumped out of the cell for every 2 K^+ pumped into the cell) is small (~20%).
- Since the plasma membrane is imperable to proteins so A- are inside the membrane

Inside of the cell becomes negative with respect to the outside.

Graded Potentials and Action Potentials



Two types of signals are produced by a change in membrane potential

- ✓**Graded potentials** (short-distance signals)
- ✓**Action potentials** (long-distance signals)

Basic terminology for membrane potential changes

Term	Meaning
Polarization	Outside and inside of a cell have a different net charge
Depolarization	A decrease in the potential difference between the inside and outside of the cell Less negative potential
Hyperpolarization	An increase in the potential difference between the inside and outside of the cell More negative membrane potential
Repolarization	Returning of membrane potential to the resting value
Overshoot	When the inside of the cell becomes positive due to the reversal of the membrane potential polarity

What makes a cell excitable?

- **Gated ion channels**

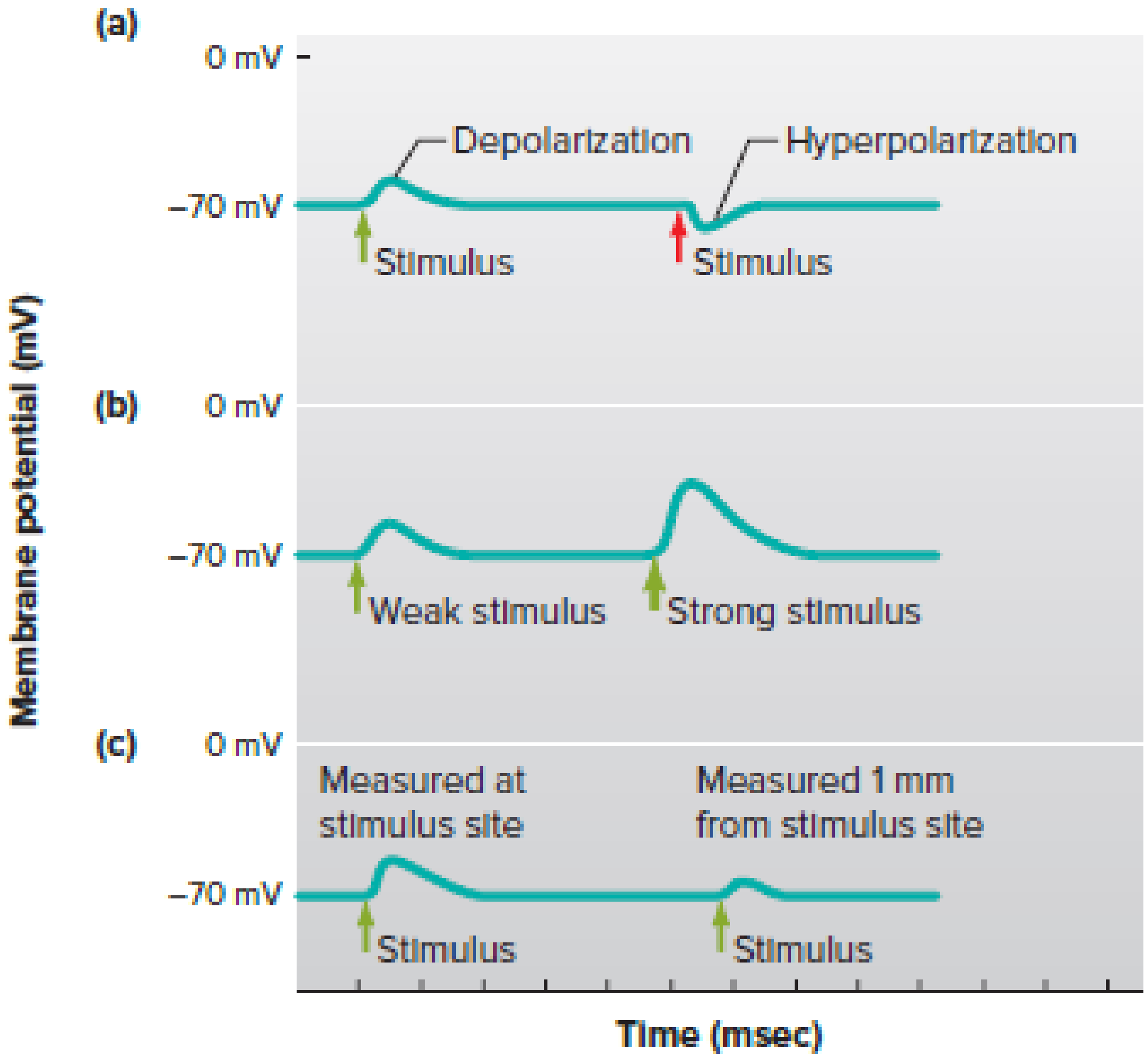
- Gated channels give a cell the ability to produce electrical signals (*excitability*) that can transmit information between different regions of the membrane(*excitable membranes*-neuronsandmusclecells)

Voltage-gated channels

- Have sequences of charged amino acids that make the channels reversibly change their conformation in response to changes in membrane potential
- At negative potential (during resting) they stay closed
- Membrane depolarization tends to them open
- Voltage-gated Na^+ channels respond faster and have *inactivation gates* which blocks channel shortly after depolarization and opens at repolarization

Graded potentials

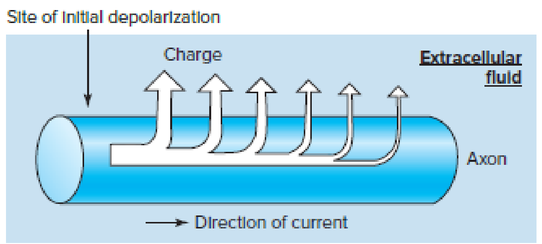
- Changes in membrane potential that are confined to a relatively small region of the plasma membrane.
- Usually produced when some specific change in the cell's environment acts on a specialized region of the membrane.
- Magnitude of potential varies directly with the magnitude of the triggering event
- Are given various names related to the location of the potential or the function they perform
  - Receptor potential
  - Synaptic potential
  - Pacemaker potential



Can be either depolarizing or hyperpolarizing

Magnitude is related to the magnitude of the initiating event (graded)

Charge is lost with the distance because of the leak channels (predominantly K^+)

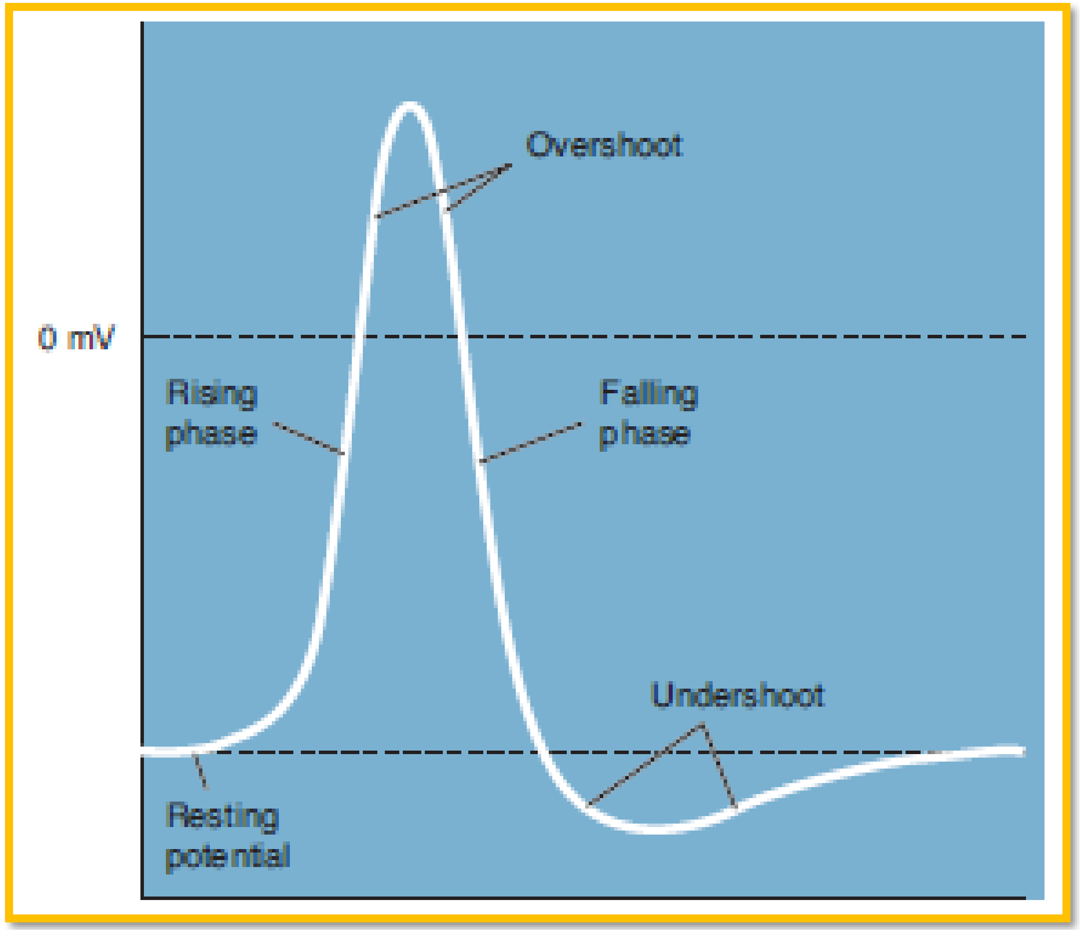


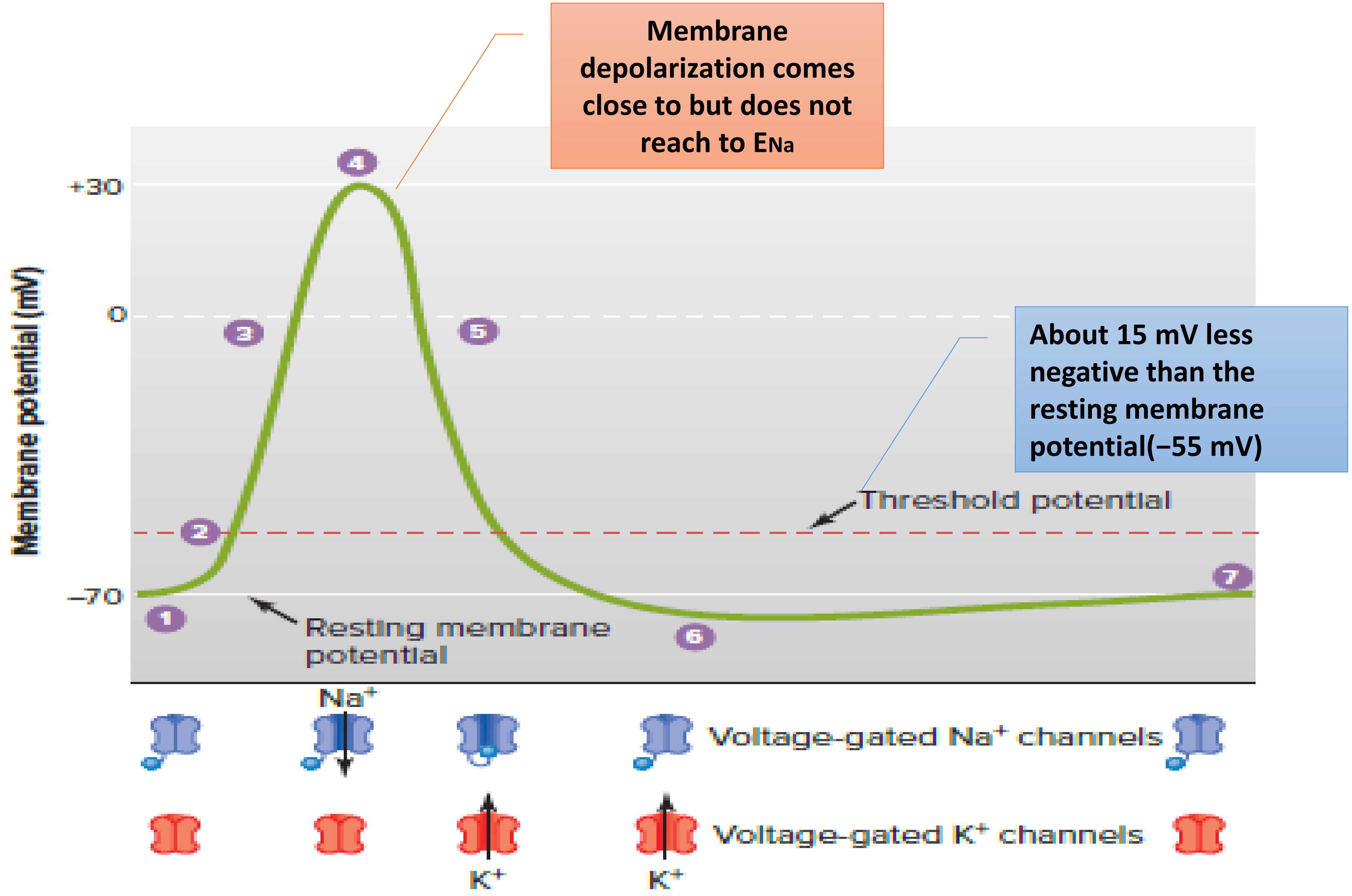
Action Potentials

Large alterations in the membrane potential (upto100 mV)

Very rapid (1-4 msec)

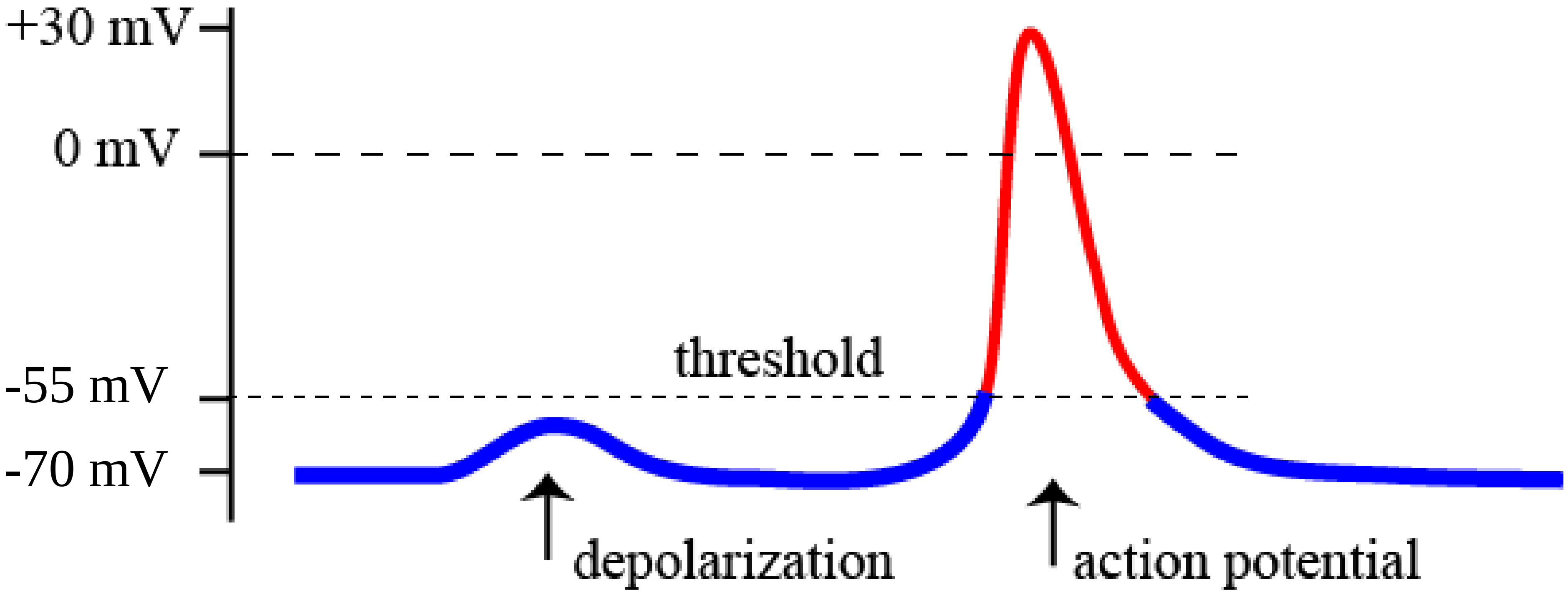
Voltage-gated Na^+ and voltage-gated K^+ channels are resposible for most neuronal action potential





Membrane depolarization comes close to but does not reach to ENa
About 15 mV less negative than the resting membrane potential(−55 mV)
Membrane potential (mV)
+30
0
−70
1
2
3
4
5
6
7
Threshold potential
Resting membrane potential
Na+
K+
K+
Voltage-gated Na+ channels
Voltage-gated K+ channels

Action Potential



Action potentials are all-or-none

Action potentials either occur maximally or they do not occur at all.

After passing the threshold, all the stimuli triggers same action potentials at the same amplitude

Difference between «weak» and «strong» stimuli

- Number and patterns of action potentials transmitted per unit of time (frequency) differs

- The frequency of action potentials (**firing rate**) depends on the magnitude of depolarizing current

Refractory Periods

Absolute refractory period

- During the action potential a second stimulus can not produce another action potential
- Voltage-gated Na+ channels are already open or in inactive state

Relative refractory period

- Coincides with the after hyperpolarization
- A stimulus stronger than normal can produce action potential
- Fewer Na+ channels available and some of the K+ channels are still open

Refractory Periods

✓Limits the number of action potentials

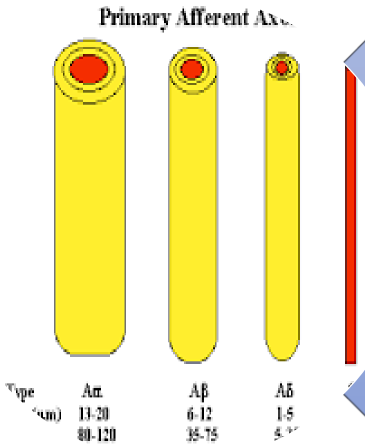
✓Helps separation of action potentials from each other

✓Determines direction of action potential propogation

Propagation of Action Potential

- Sequential opening and closing of voltage-gated Na^+ and K^+ channels along the membrane
- An action potential initiated at one end of an axon propagates only in one direction; it does not turn back on itself.
- This is because the membrane just behind it is refractory, due to inactivation of the sodium channels.

Velocity of Action Potential



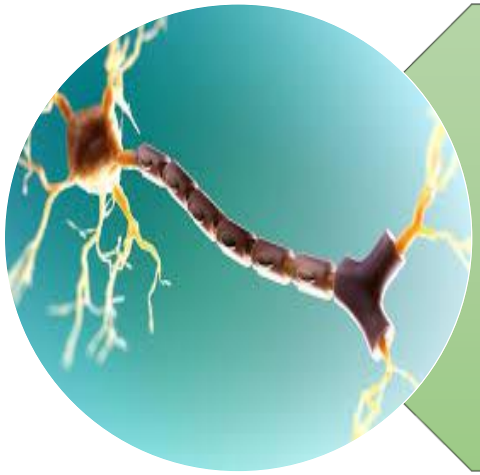
Fiber diameter

Velocity

Less internal resistance to local current

0.5 m/sec → 100 m/sec

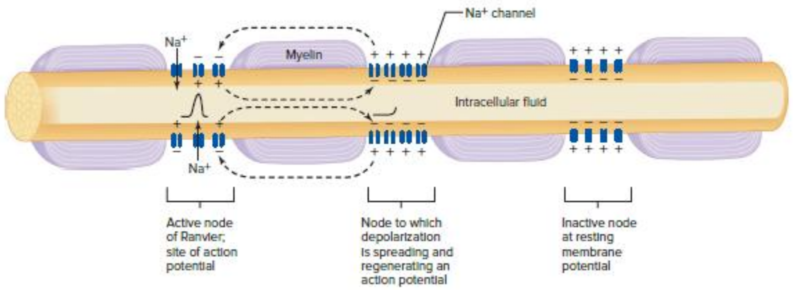
small diameter, unmiyelinated fiber = 0.5 m/sec
•4 sec from toe to brain
large diameter, myelinated fiber = 100 m/sec
•0.02 sec from toe to brain



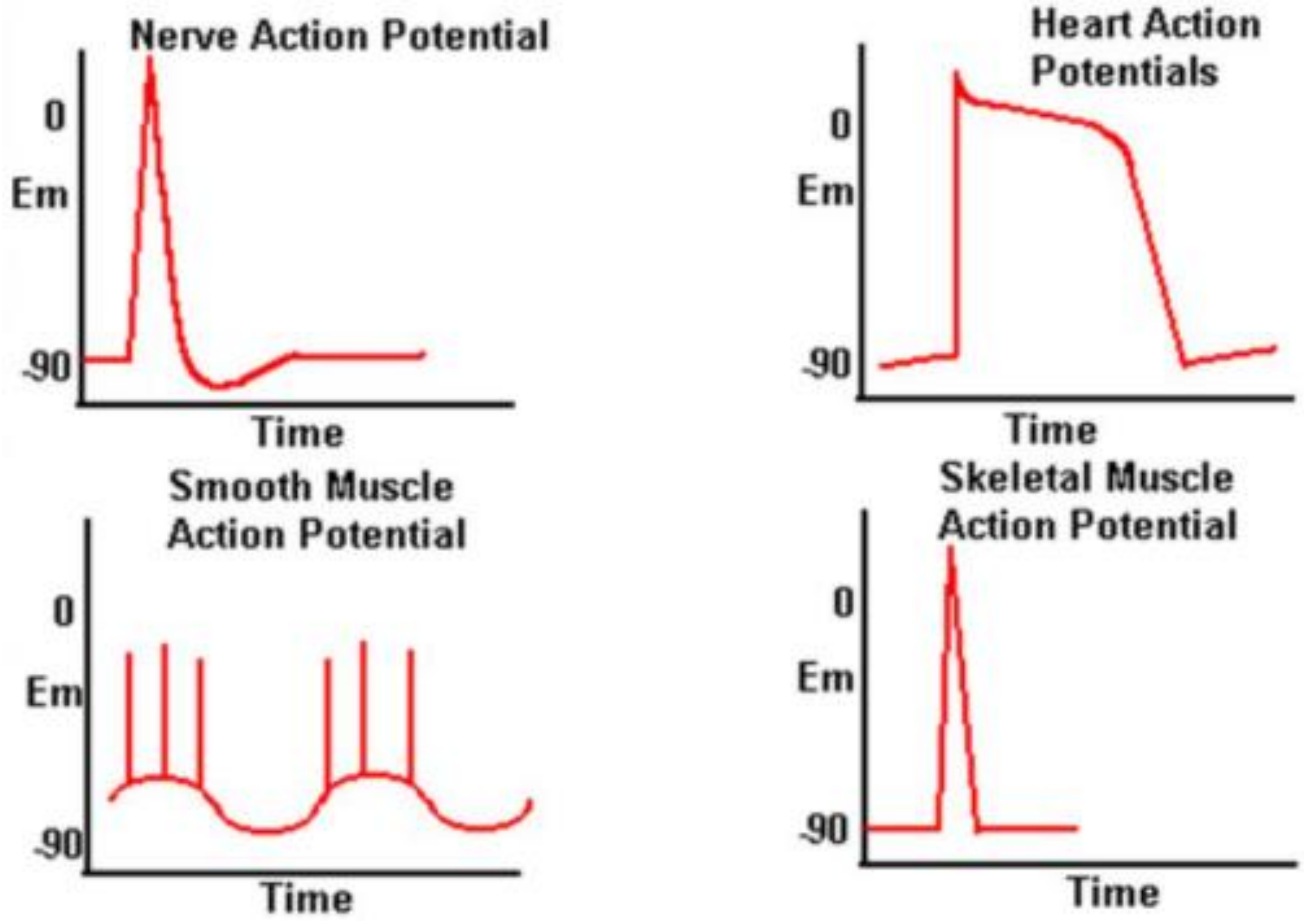
Myelination

Velocity

Less charge flow between intracellular and extracellular fluid



Different types of action potentials



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