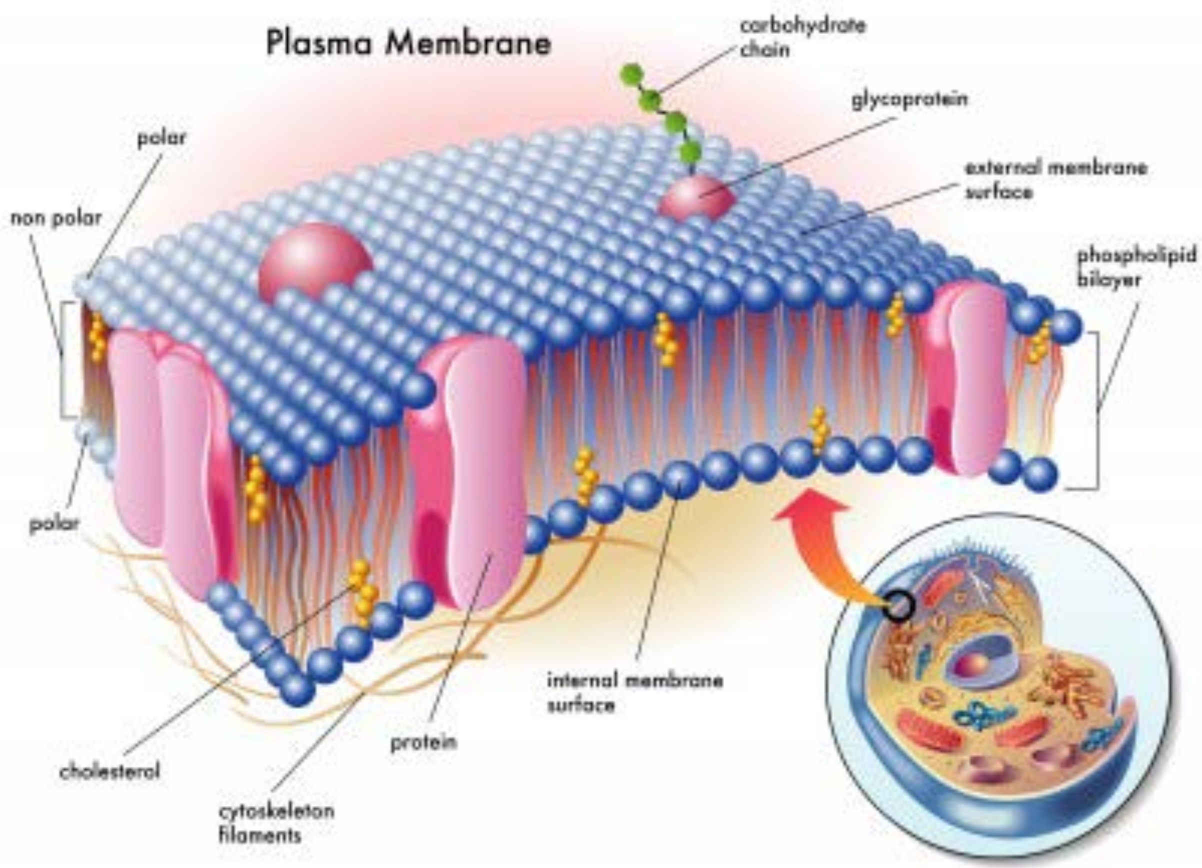
Physiology



Cell Membrane & Membrane Potential

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Outline

① Properties of Cell Membrane

② Membrane Potential

Reading Assignment

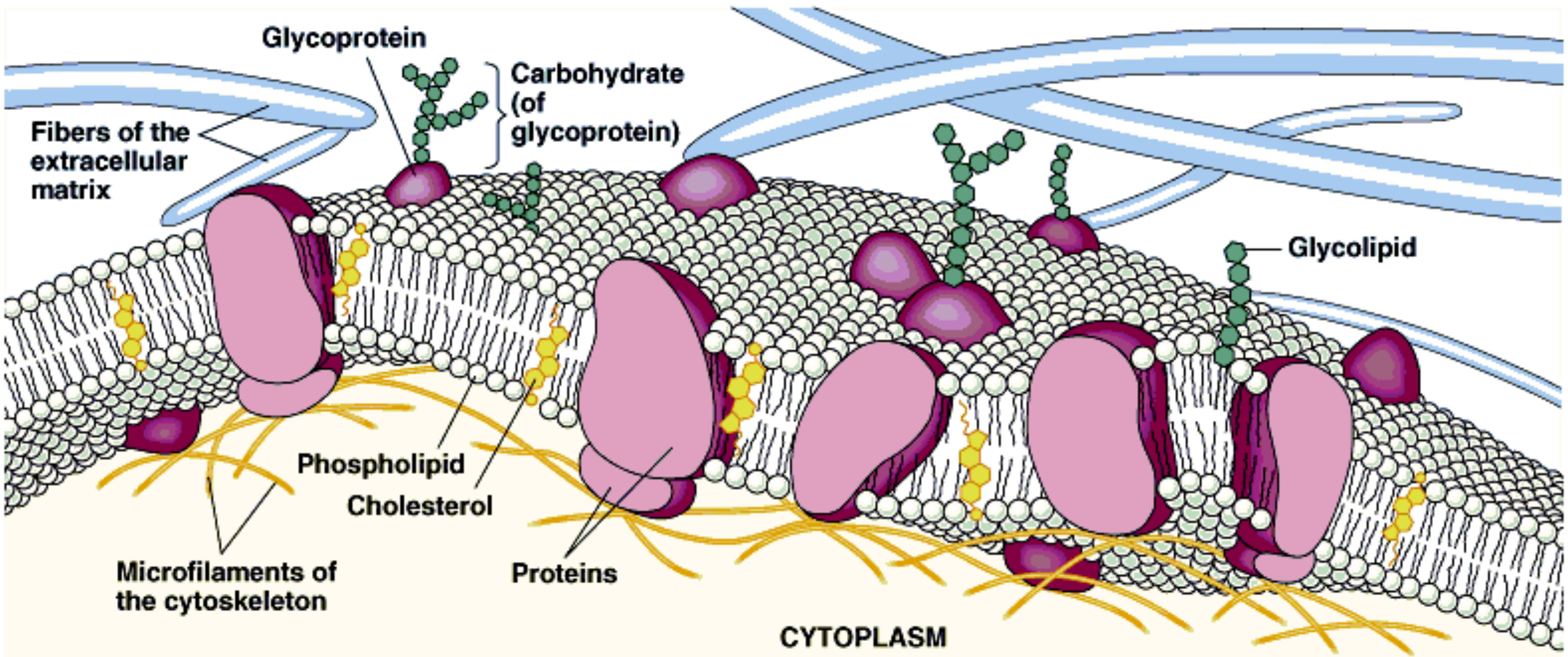
Guyton And Hall Textbook Of Medical Physiology, 13 Edition, Chapter 2, pg; 12-14, Chapter 5 pg; 61

Cell membranes protect and organize cells

- ✓ Gatekeeping

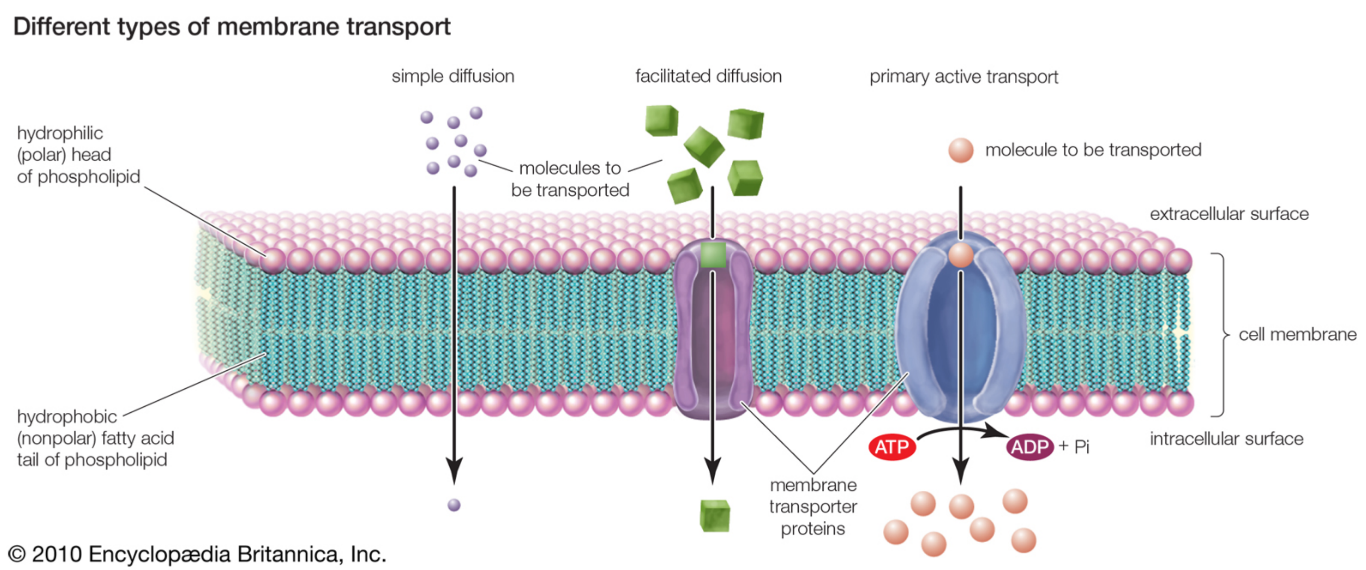
What Do Membranes Do?

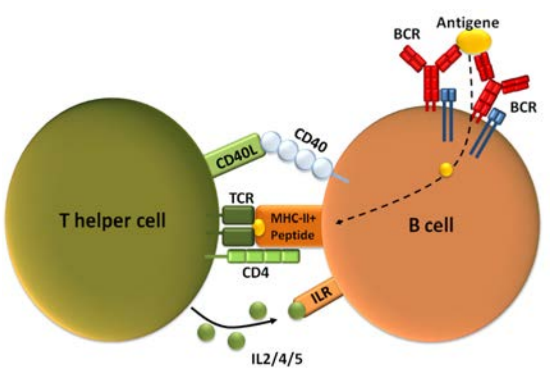
- Cell membrane surrounds the cell
- Protects the cell
- Semi-permeable barrier- channel&transporter



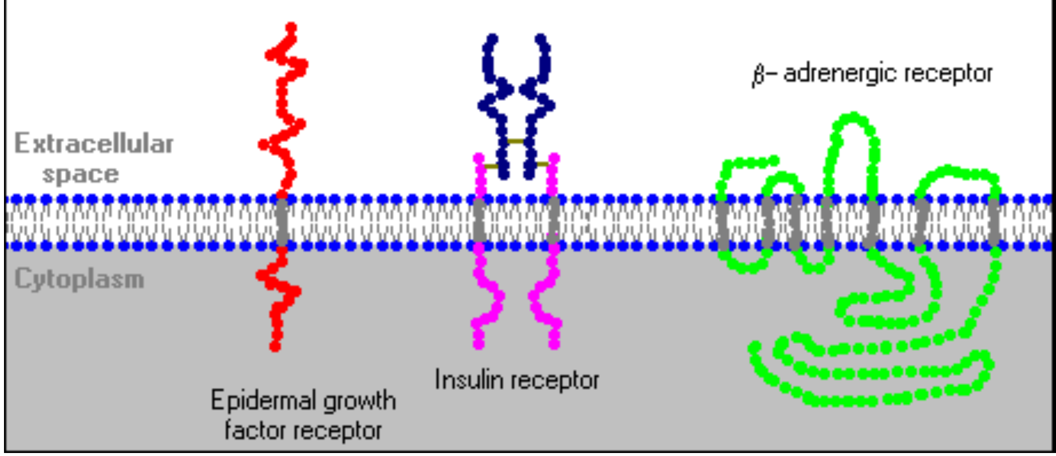
What Do Membranes Do?

- Maintain concentration of various substances
  - Homeostasis
- Allows cell recognition/communication
  - Proteins and carbohydrates

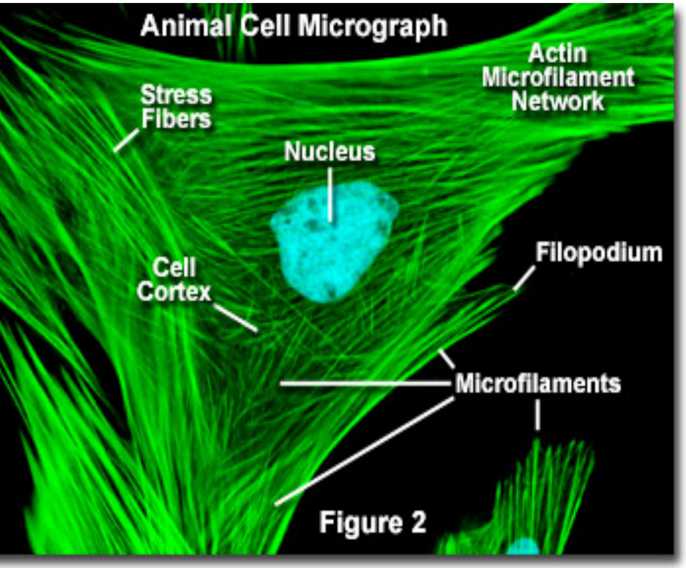


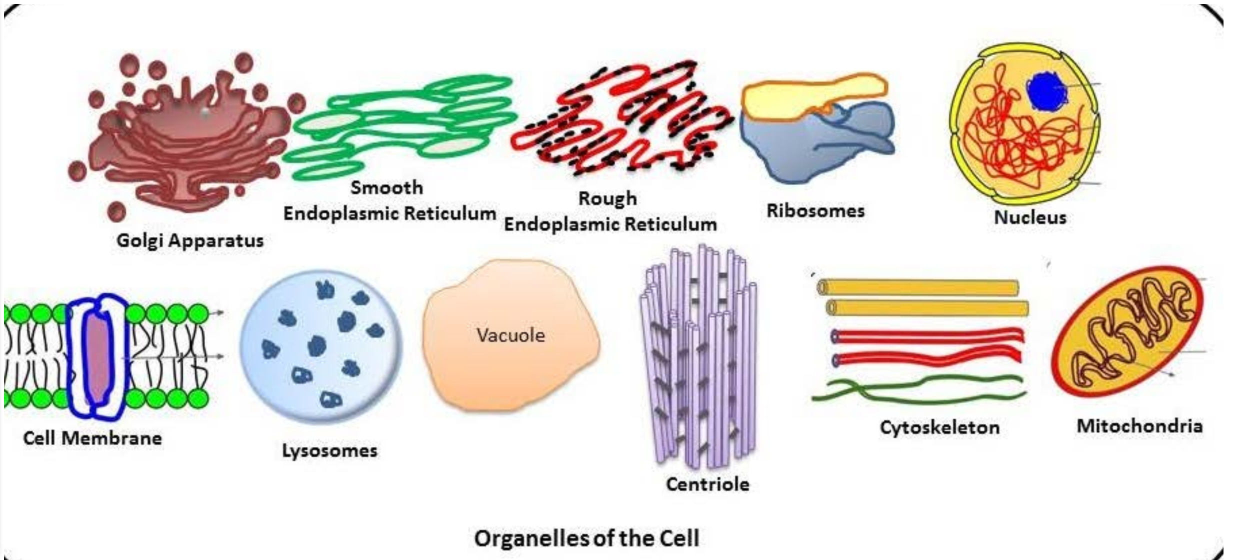


What Do Membranes Do?



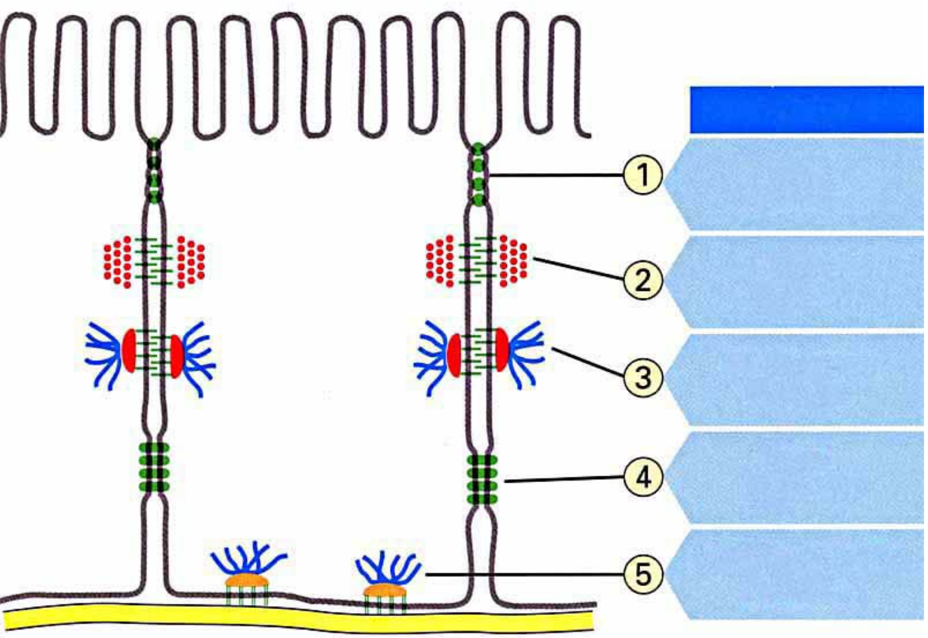
- Allows receptivity
- Allows to maintain cell shape
- Helps to compartmentalize subcellular domains

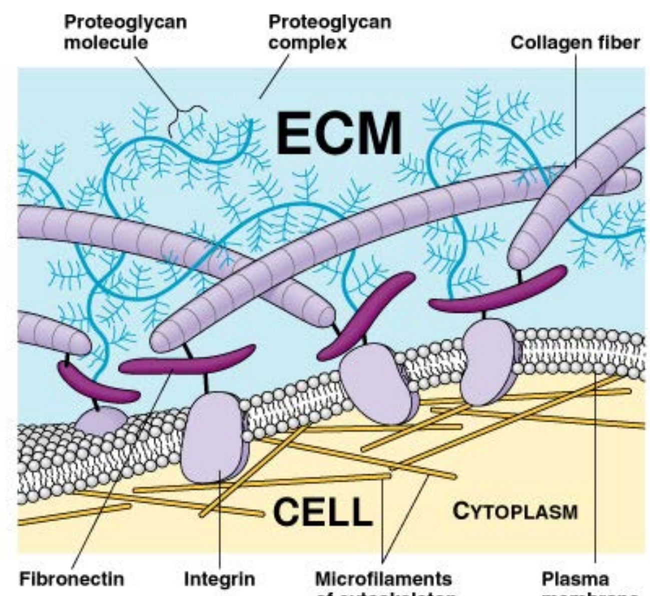




What Do Membranes Do?

- Links adjacent cells together by membrane junctions. Desmosome (selectin)
- Anchors cells to the extracellular matrix. hemidesmosome (integrin)





What Are Cellular Membranes Made Of?

- Lipids 42%
  - Phospholipids … 25%
  - Cholesterol ……. 13%
  - Other lipids …….. 4%

Lipids

- Proteins 55%
- Carbohydrates 3%

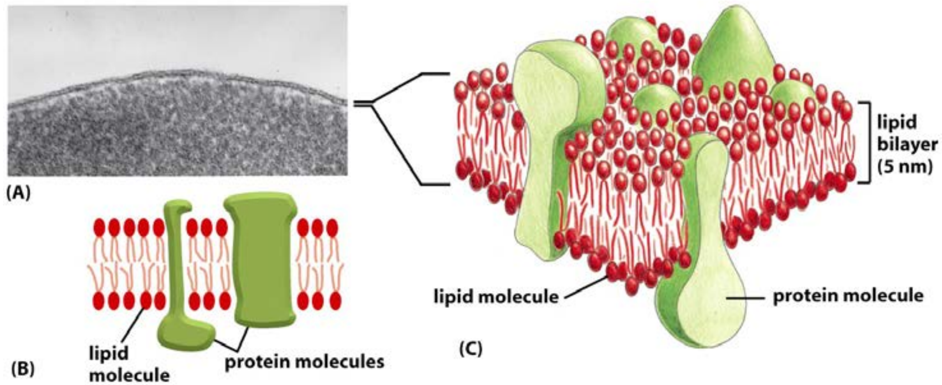
Core of membrane-barrier

high permeability to lipid-soluble substances CO_2, steroid

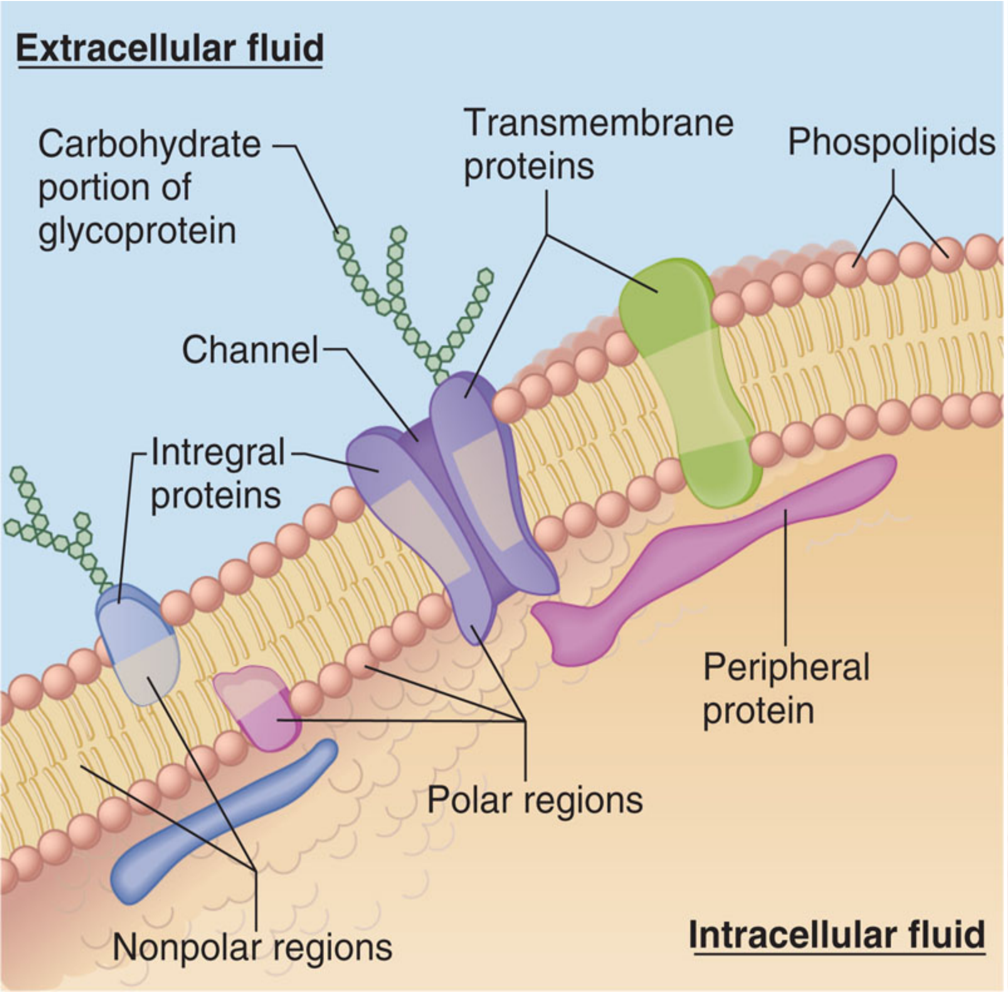
low permeability to water-soluble substances ions, glucose

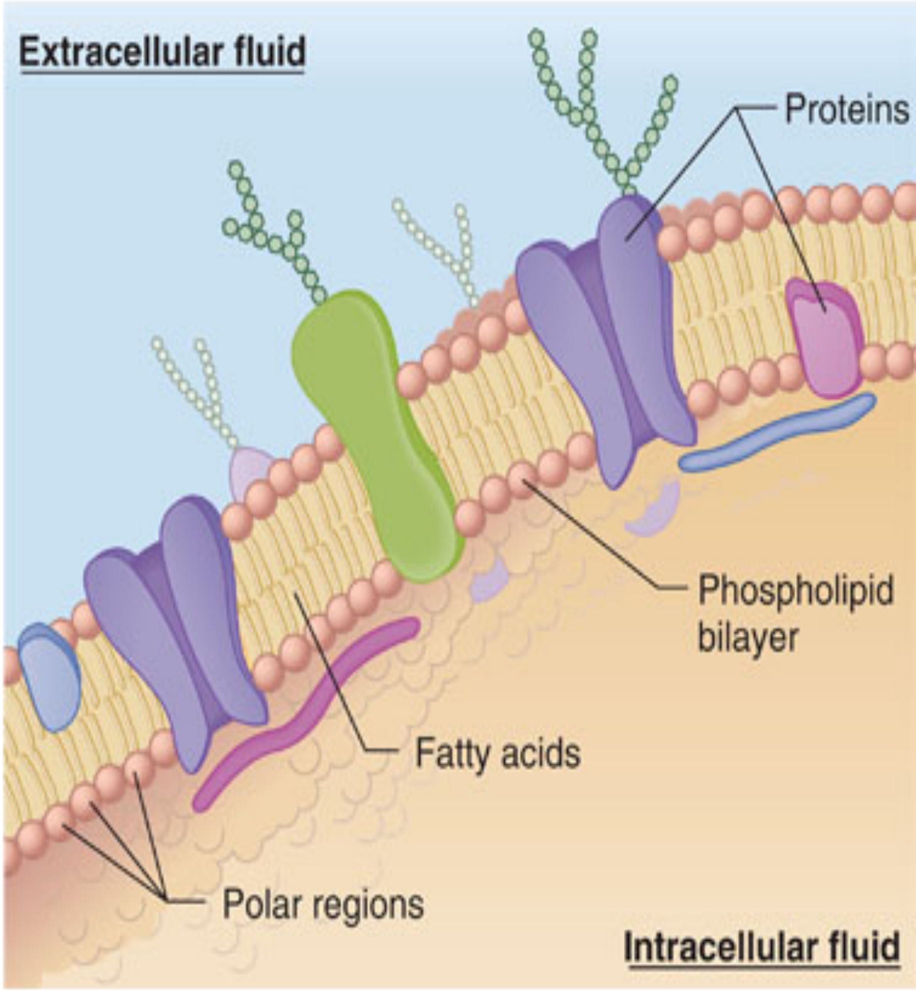
transporters, enzymes, hormone receptors, cell-surface antigens

Cell coat- cell-cell int. antigenicity

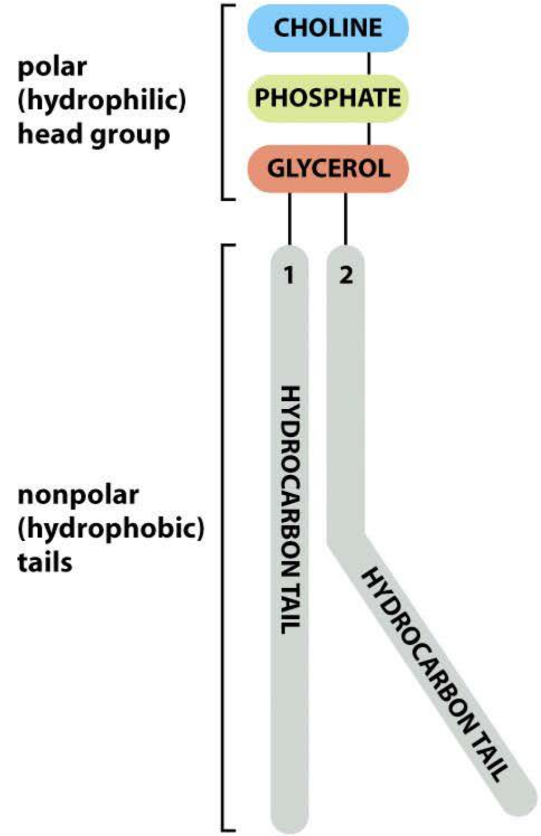


Cell Membrane Structure and Function





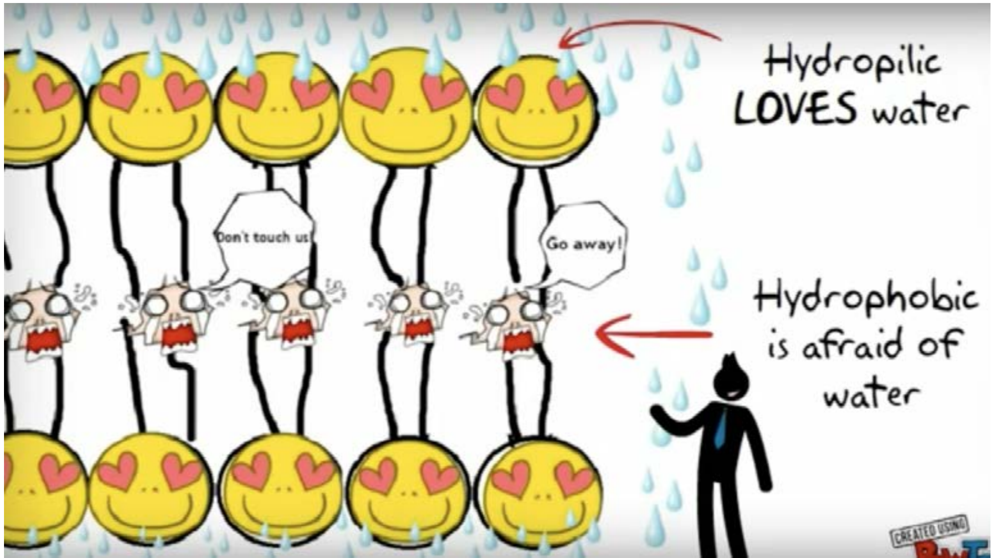
Phospholipid Component of Cell Membranes



✓ **Phosphorylated Glycerol Head** (polar & hydrophilic).

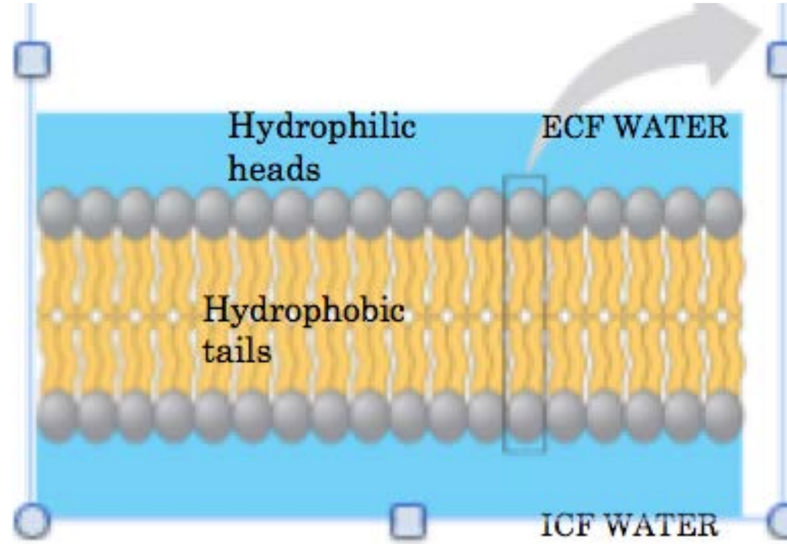
✓ Hydrocarbon chains of **2 fatty acid tails** (nonpolar & hydrophobic)

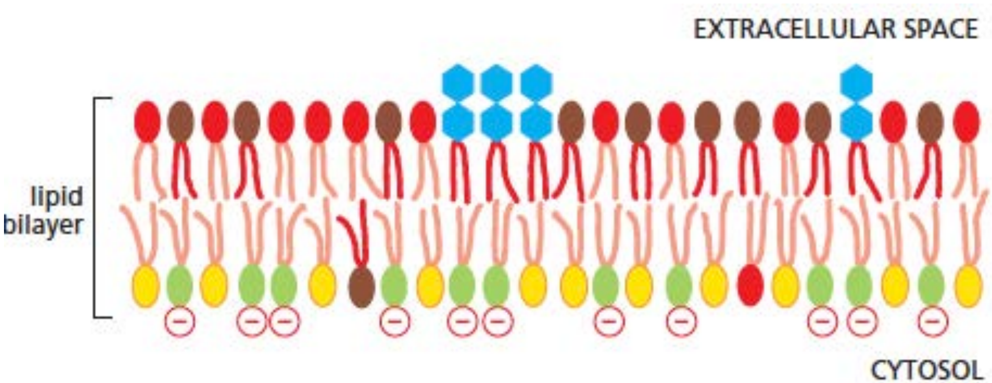
Hydrophilic (water-loving)
Hydrophobic (water-fearing)
Amphipathic (both)- phospholipid molecules



Lipid Bilayer

In cell membranes, phospholipids orient so the lipid-soluble fatty acid tails face each other and the water soluble glycerol heads point away from each other





Dominant phospholipids

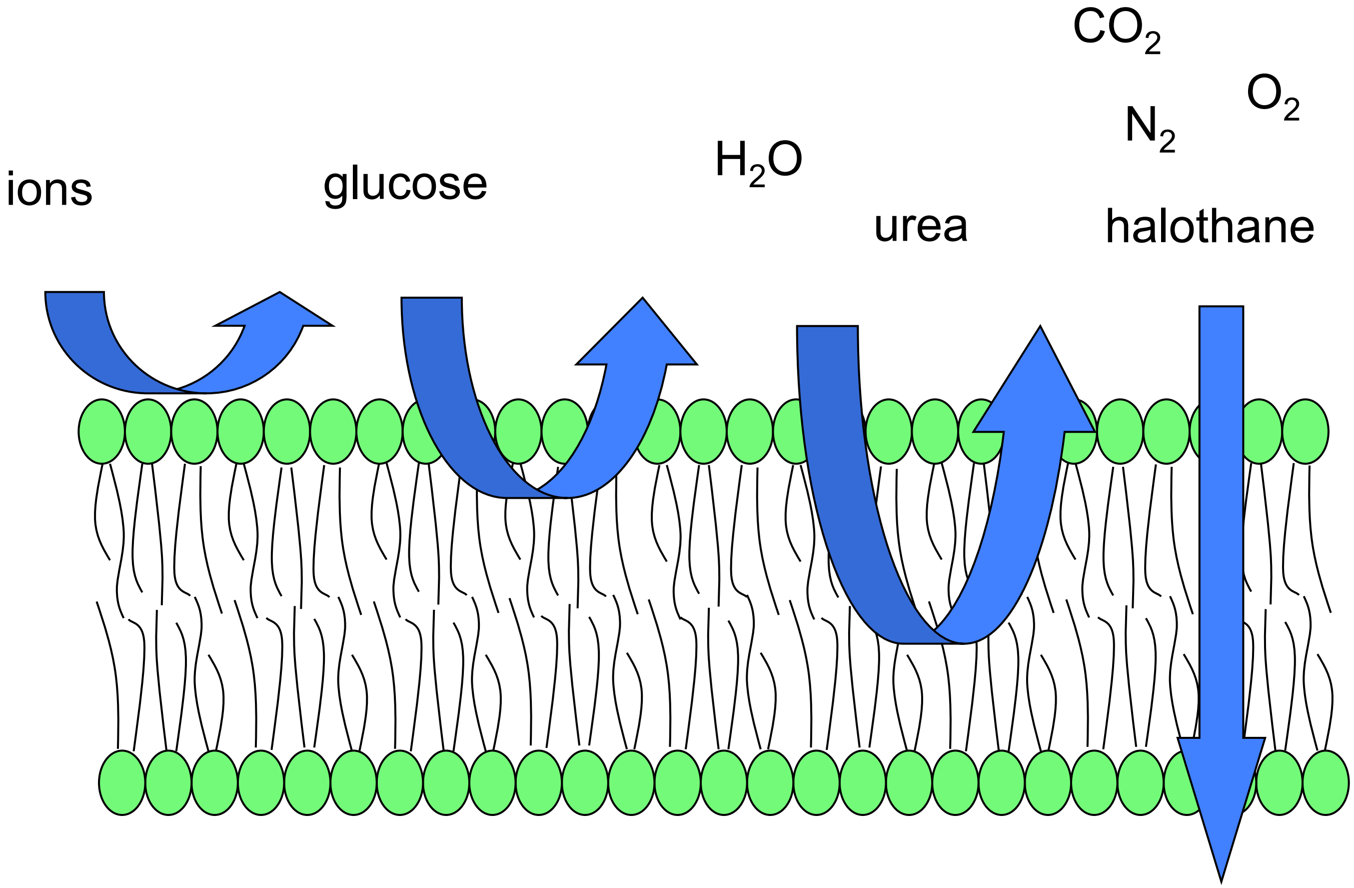
1. **Phosphoglycerides**
   - Phosphatidylethanolamine
   - **Phosphatidylserine**
   - Phosphatidylcholine

2. Sphingomyelin

- Phosphatidylinositol

Cell Membrane
Lipid Bilayer

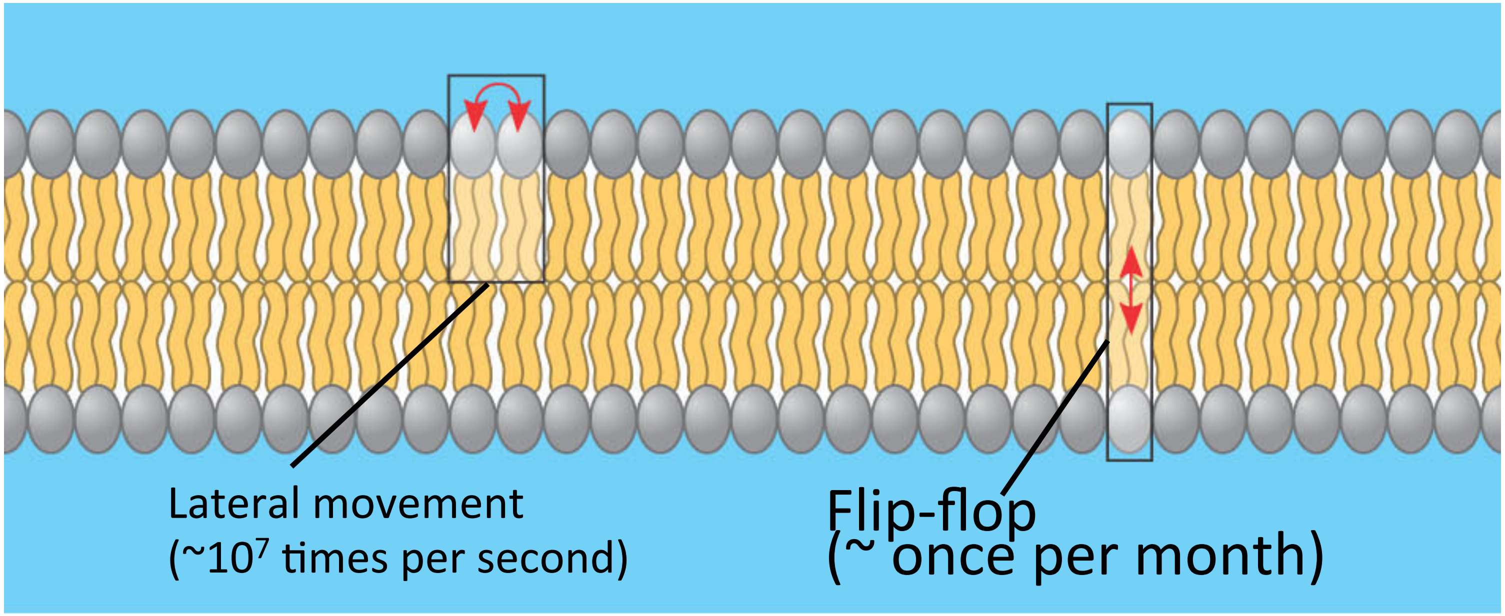
- *barrier to water and water-soluble substances*



The Fluidity of Membranes

- Membrane molecules have weak hydrophobic interactions.

- Components drift laterally, but rarely flip-flop.

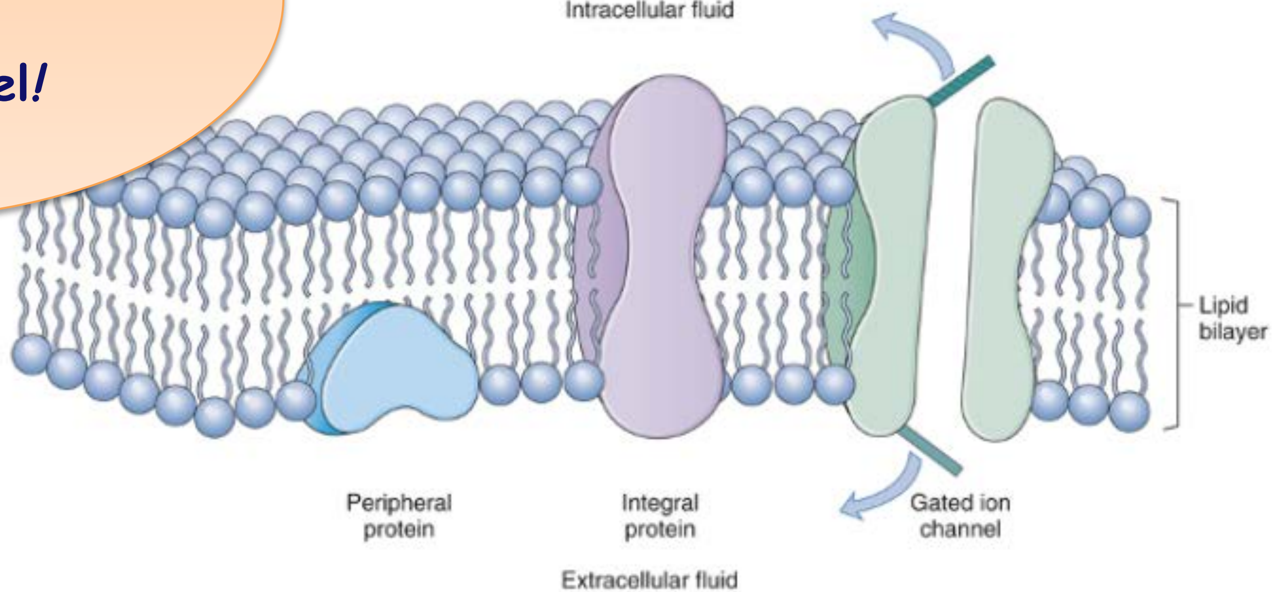


Cell membrane must be more than lipids…

- In 1972, S.J. Singer & G. Nicolson proposed that membrane proteins are inserted into the phospholipid bilayer

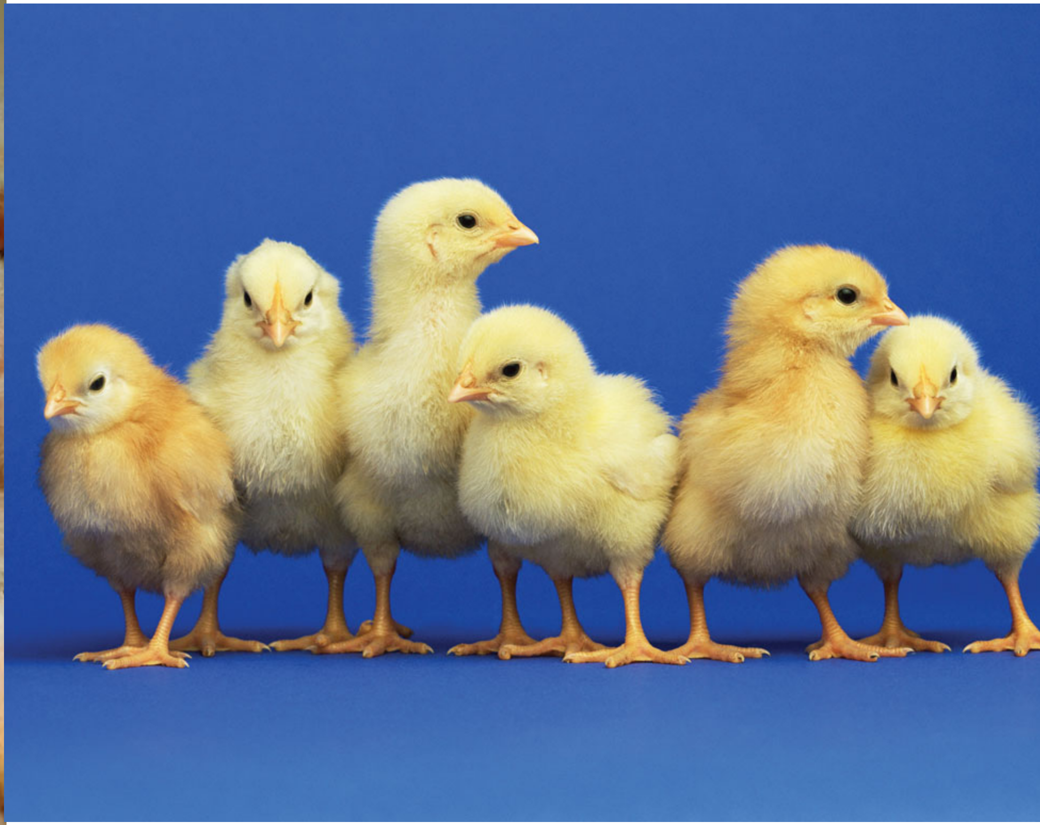
It's like a fluid…
It's like a mosaic…
It's the
Fluid Mosaic Model!

Membrane is a collage of proteins & other molecules embedded in the fluid matrix of the lipid bilayer



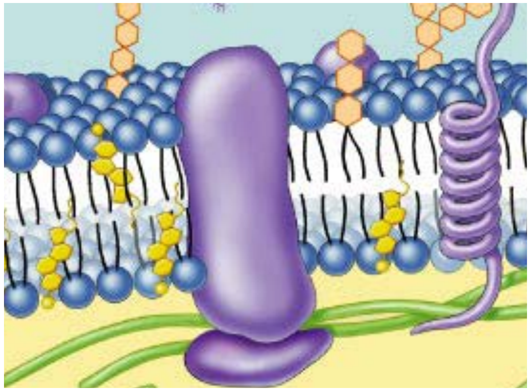
The Fluidity of Membranes

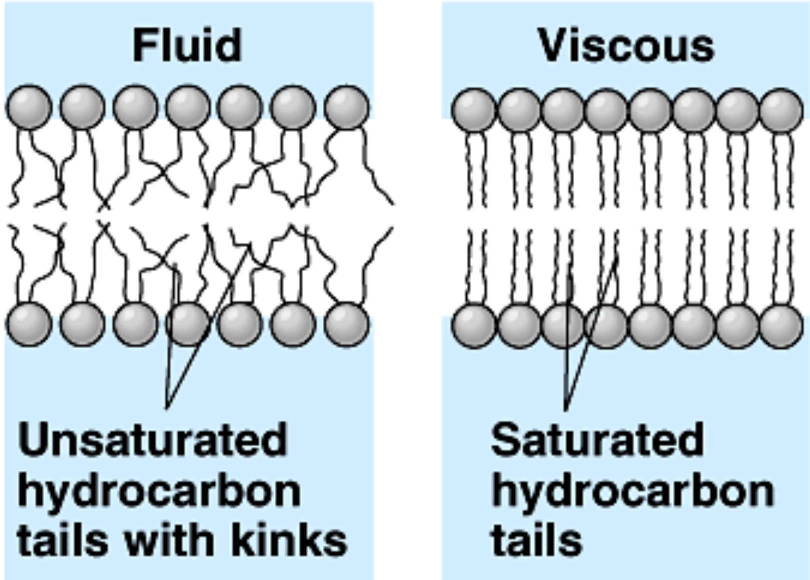
- ➢ The fluidity of a lipid bilayer depends on both its **composition and its temperature**
- ***Temperature***



Membrane Lipid Composition Varies

- ➢ **Lipid composition affects flexibility**
- o membrane must be fluid & flexible
- o about as fluid as thick salad oil
- • **% unsaturated fatty acids in phospholipids**
- o keep membrane less viscous
- o cold-adapted organisms, like winter wheat
- o increase % in autumn
- • **cholesterol** in membrane

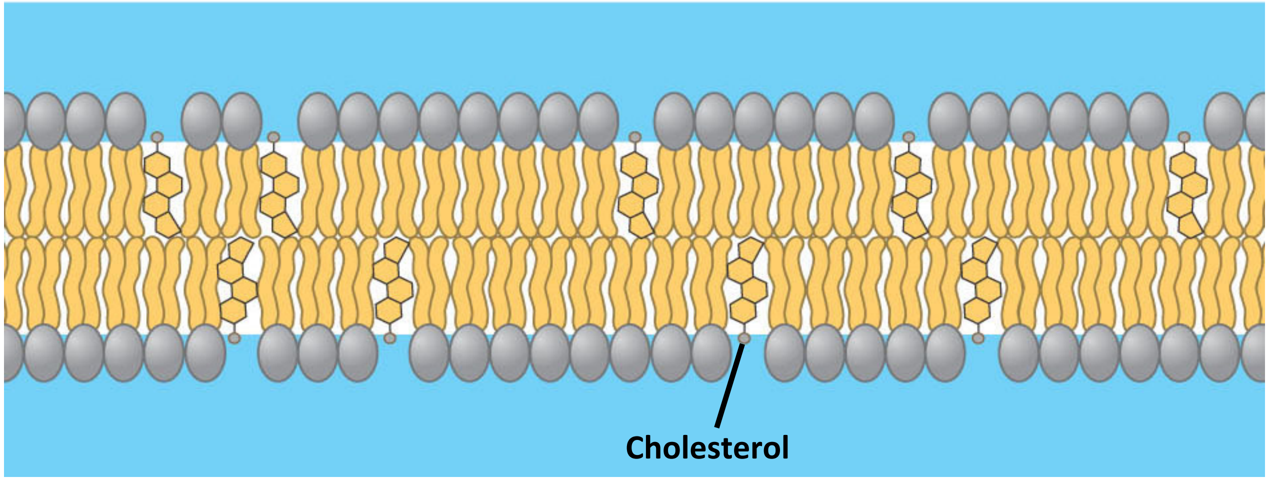




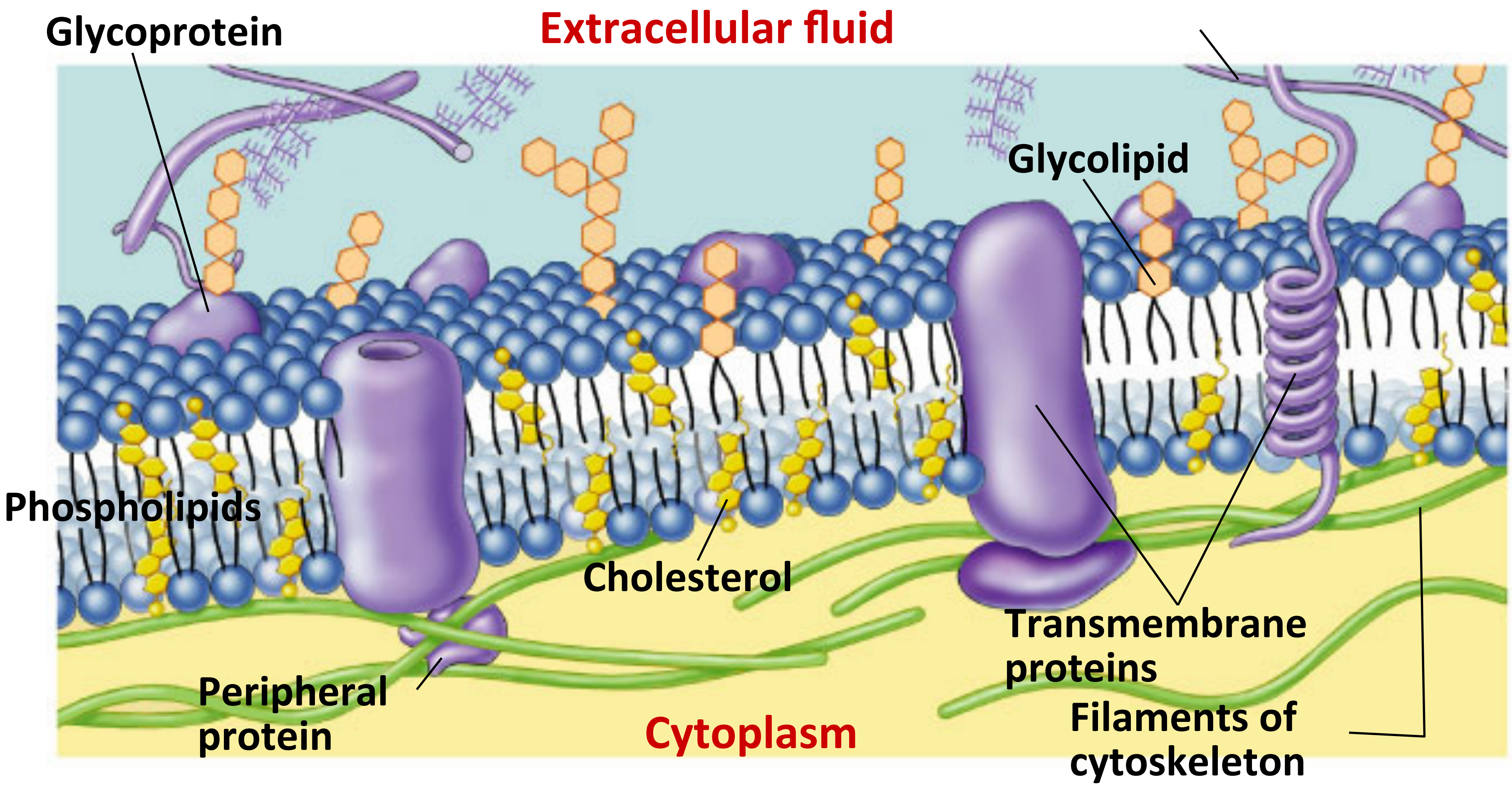
Cholesterol Component of Cell Membranes

- Cholesterol modulates the properties of lipid bilayers.
- Between phospholipid molecules
- At warm temperatures (such as 37°C), ↓ fluidity.
- At cool temperatures, it maintains fluidity by preventing tight packing.

"temperature buffer"

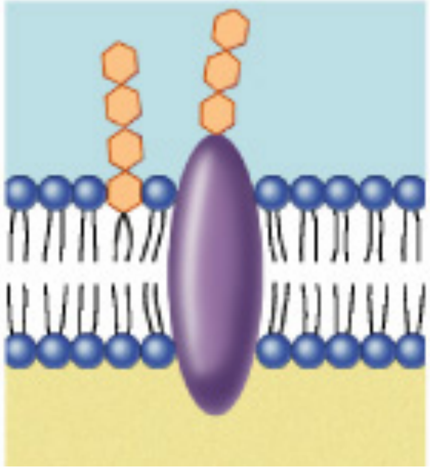


The carbohydrates are not inserted into the membrane, they are too hydrophilic for that.

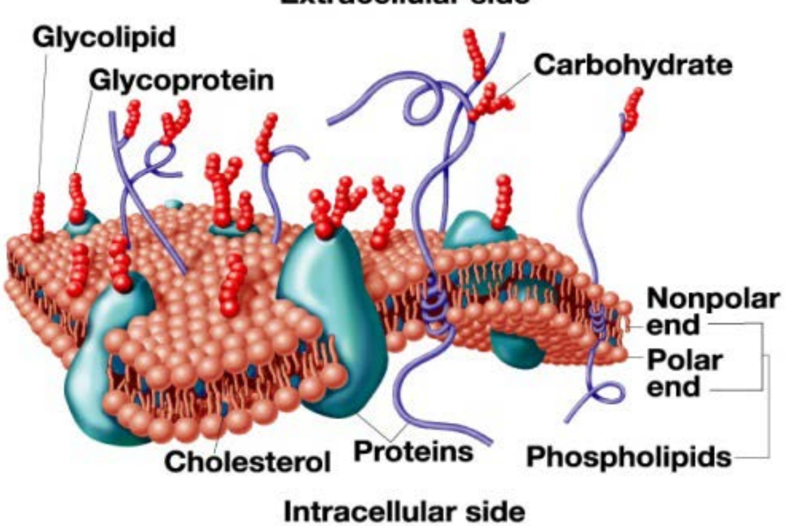


They are attached to proteins- glycoproteins, Lipids- glycolipids

General Functions of Cell Membrane Carbohydrates

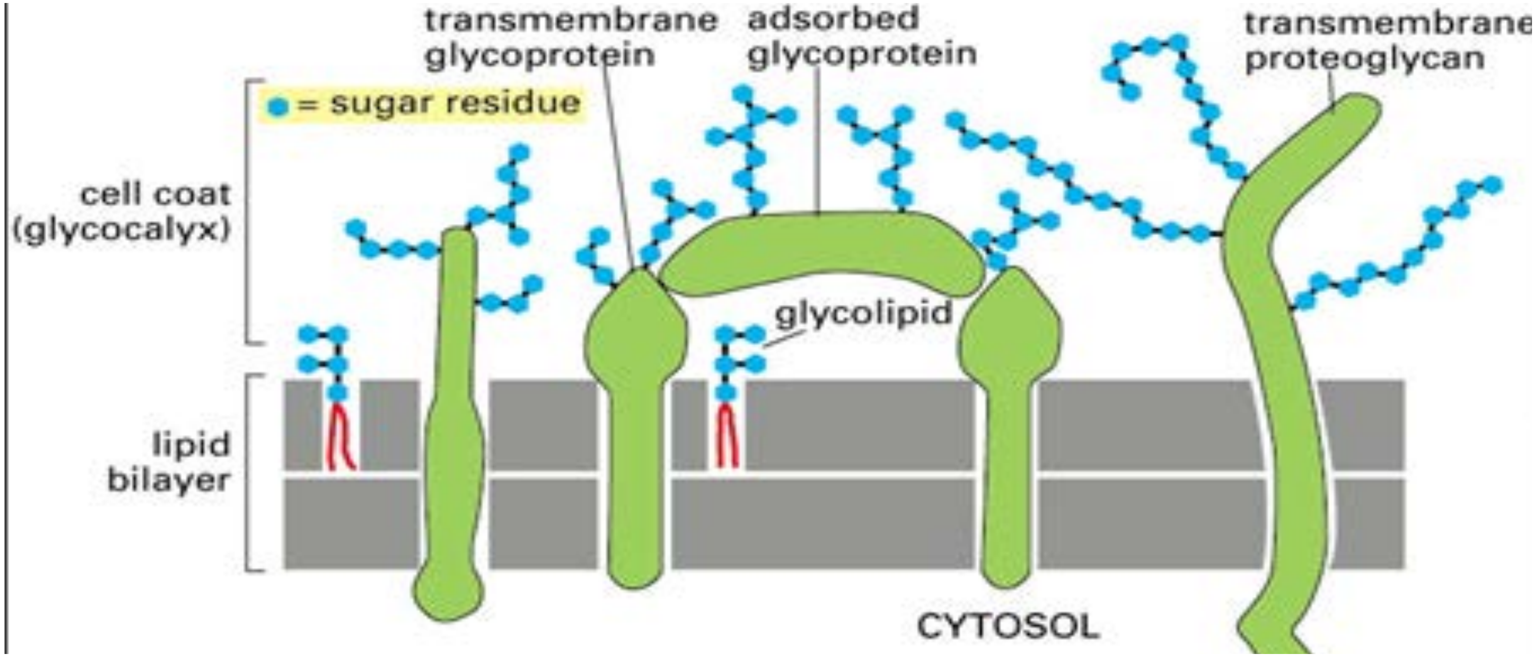


- Play a key role in cell-cell recognition
  - ability of a cell to distinguish one cell from another (antigens)
- Attach cells to each other.
- Act as receptor sides. Some involved in immune reactions.
- important in organ & tissue development
- Give most of cells overall negative surface charge.



✓ **Primarily attached to the outer surface of the membrane as:**

- Glycoproteins … (most of it).
- Glycolipids …… (1/10).



Surface molecules constitute a layer at the surface of the cell called **«cell coat or glycocalyx»**. **Made inside the cell and secreted**

Other Functions

- protect the membrane against the harsh conditions
- preventing unwanted cell–cell interactions

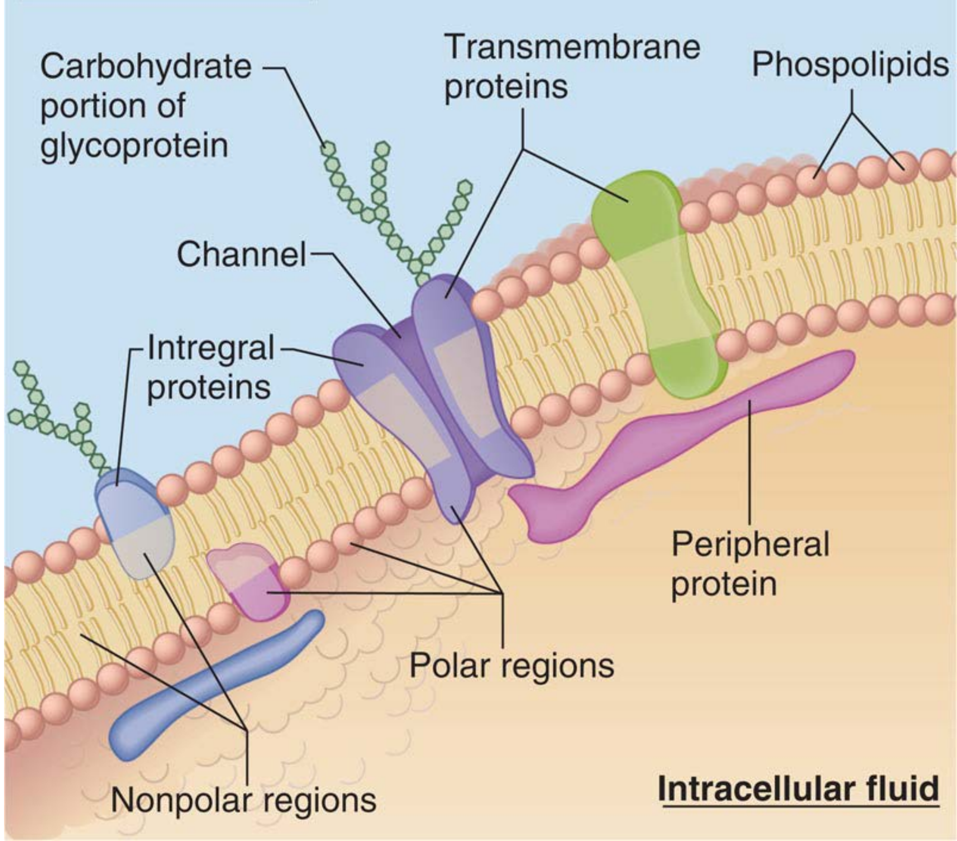
Protein Component Of Cell Membranes

- Proteins determine membrane's specific functions

– cell membrane & organelle membranes each have unique collections of proteins

- Membrane proteins:

1. Integral proteins
2. Peripheral proteins



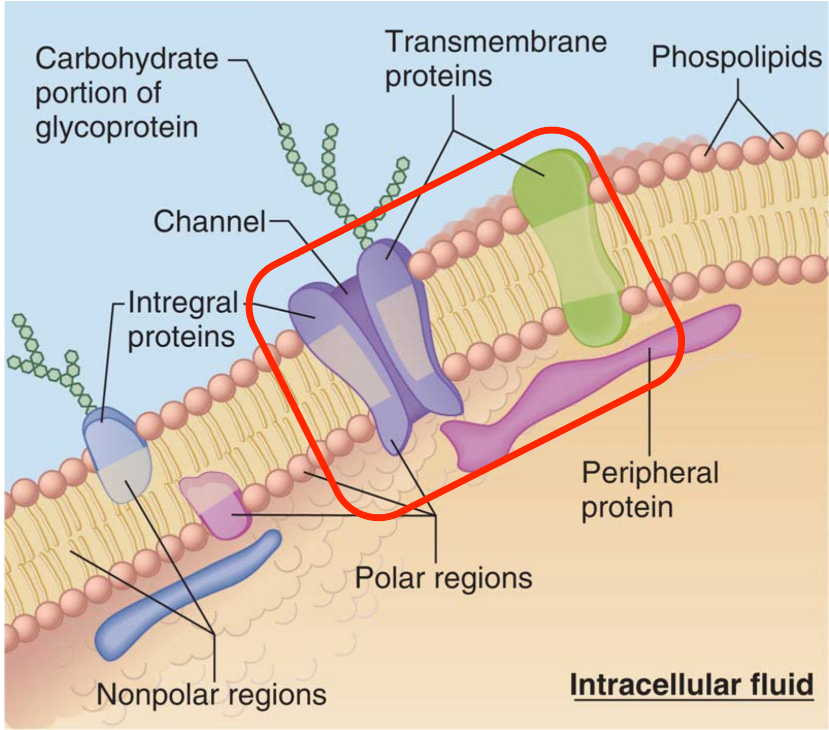
Cell Membrane Proteins

1. Integral proteins: / Internal or intrinsic

- Permanently embedded in, and anchored to the cell membrane by hydrophobic interactions
- They can be defined as those proteins which require a detergent (such as SDS or Triton X-100) or some other a polar solvent to be displaced.

E.G

- Ligand-binding receptors (hormones)
- Transporter proteins (Na+-K+)
- Cell adhesion molecules
- GTP-binding proteins
- Ion channels

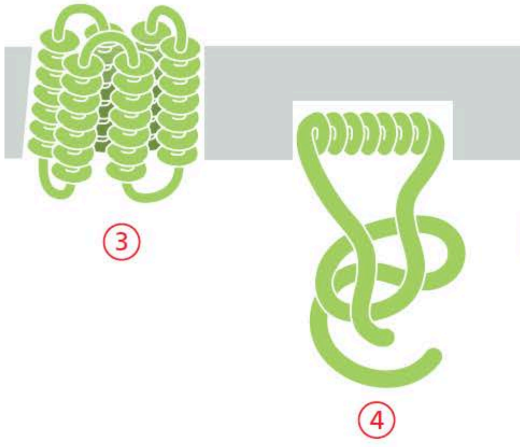


Integral Proteins

- **Integral polytopic proteins (transmembrane)** are permanently attached to the lipid membrane and span across the membrane
- **provide structural channels or pores,** Cell-surface receptors**.**
- **Only transmembrane proteins** can function on both sides of the bilayer or transport molecules across it.

- **Integral monotopic proteins** are permanently attached to the lipid membrane from only one side

  and do not span across the membrane.



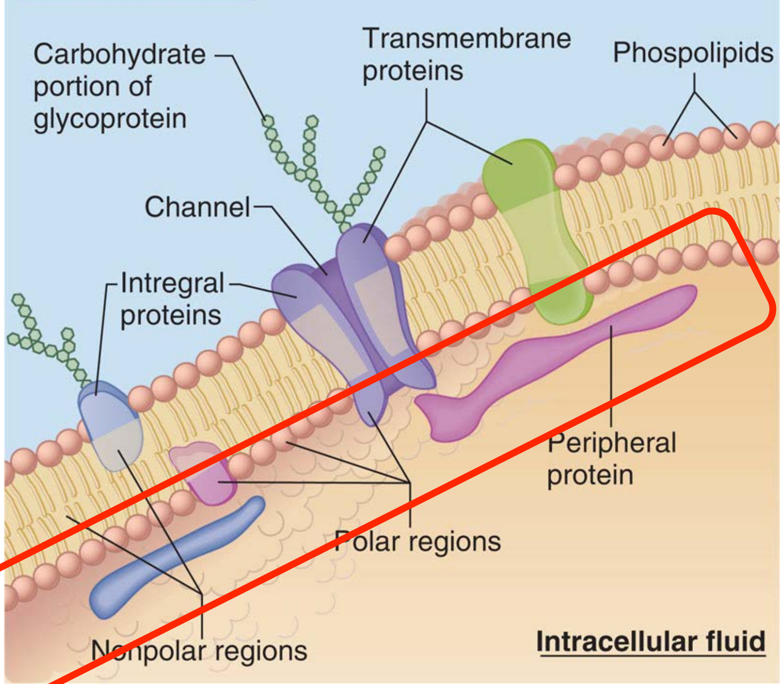
Cell Membrane Proteins

2. Peripheral proteins: / external or extrinsic proteins

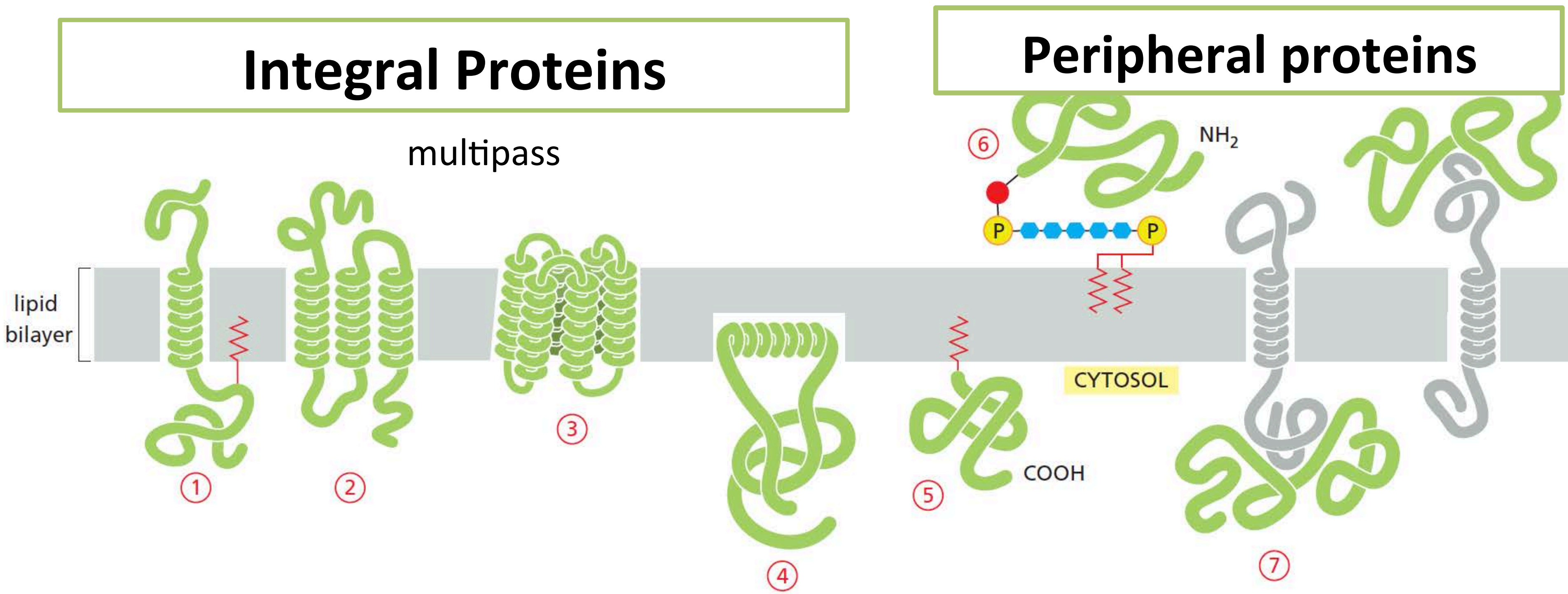
- Found on one side (face) of the membrane. (not covalently bound) loosely bound to surface of membrane
- temporarily associated with lipid bilayer or with integral membrane proteins
- Easily removed by high salt solutions or elevated pH

Intracellular; enzymes, regulatory side of ion channels, carrier, vesicle trafficking

Extracellular; Receptors, enzymes, Antigens, adhesion molecules.



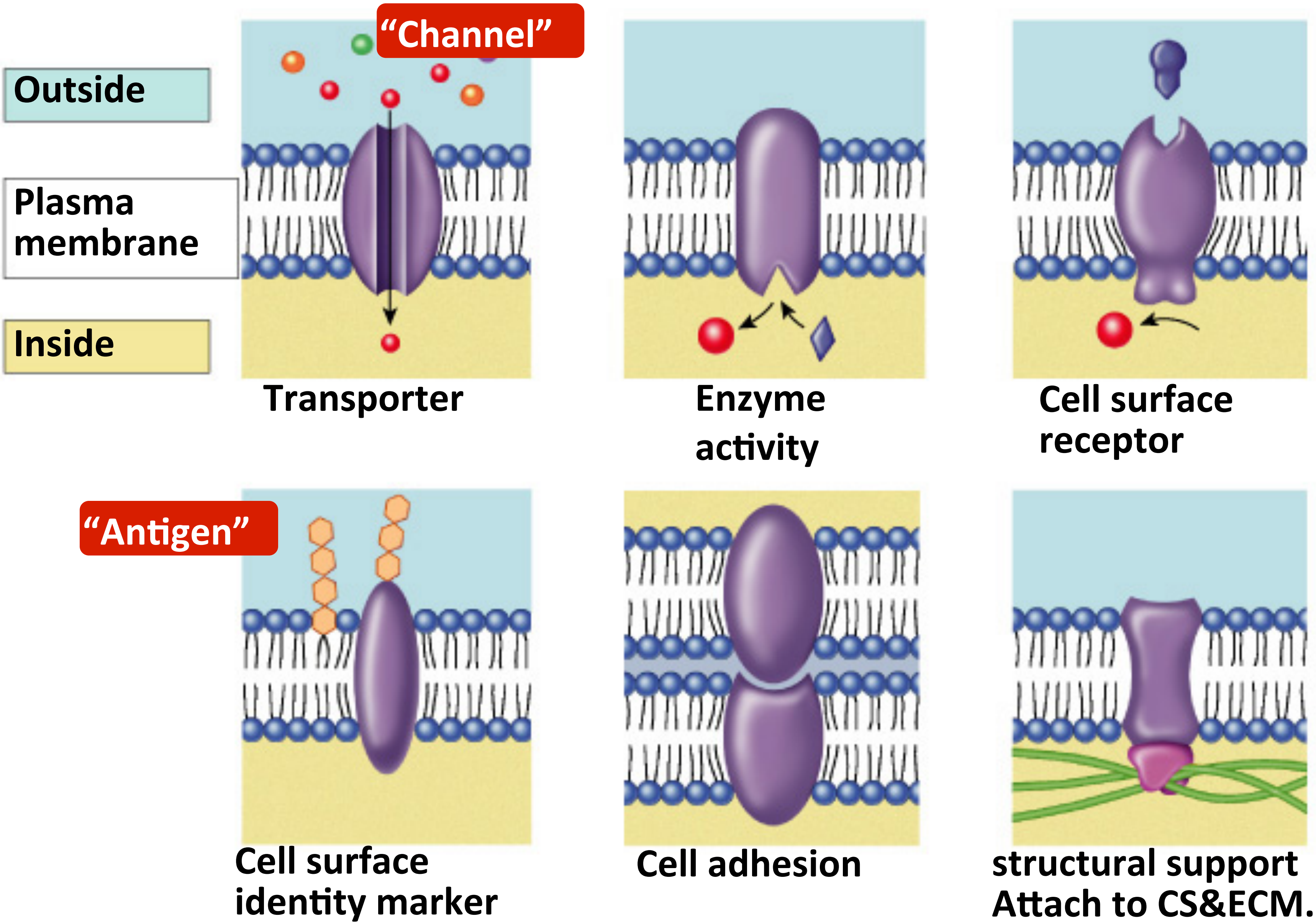
- membrane proteins are **amphiphilic** having hydrophobic and hydrophilic regions.



Many Membrane Proteins Are Glycosylated

- Most **transmembrane proteins** in animal cells
- sugar residues are added in the lumen of the **ER and the Golgi apparatus**
- oligosaccharide chains are always present **on the noncytosolic side** of the membrane
- polysaccharide chains of integral membrane **proteoglycan** molecules as part of the extracellular matrix
- carbohydrate-binding proteins called lectins

Many Functions of Membrane Proteins



Membrane Potentials

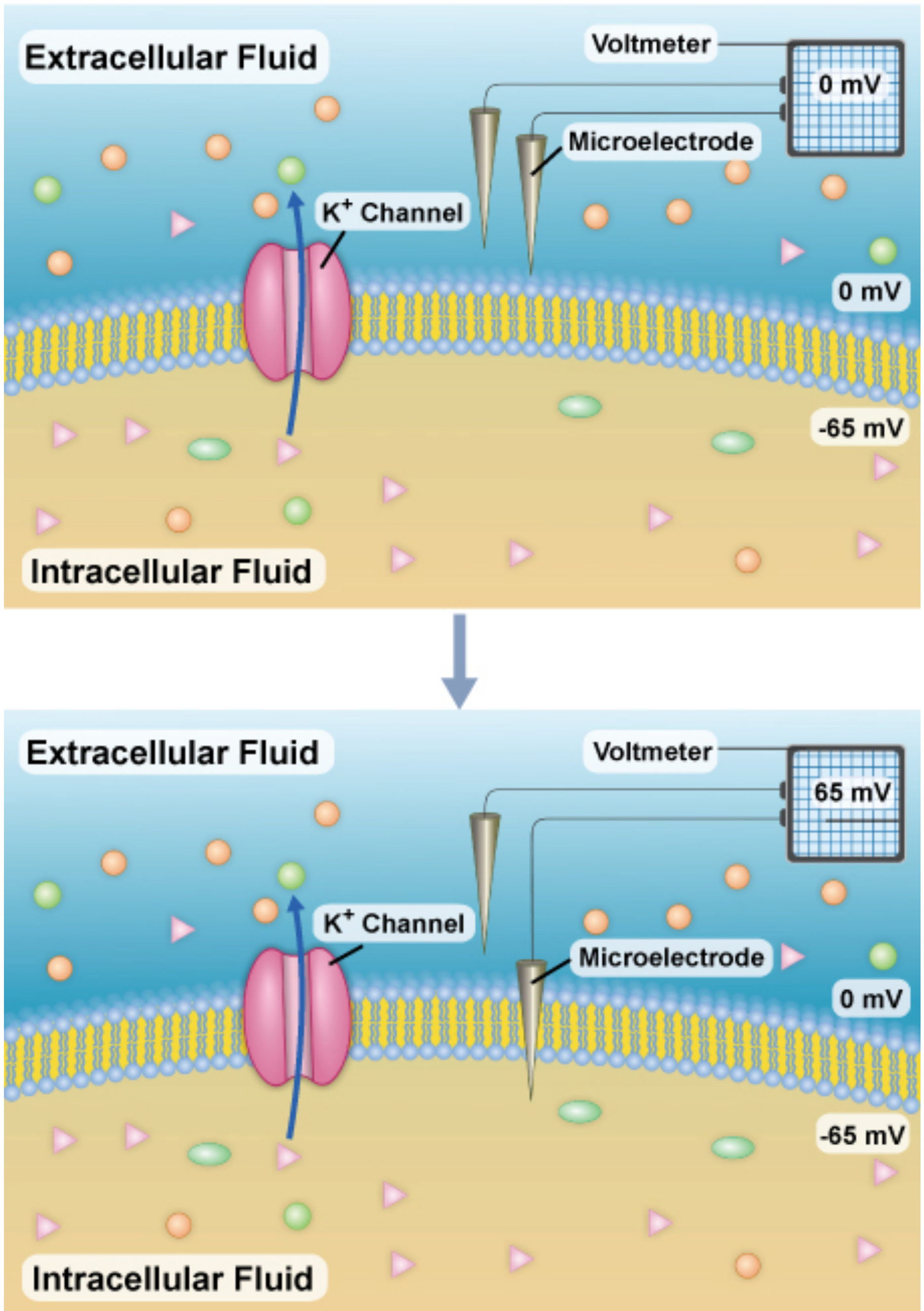
Outline

① Membrane Potentials
② Membrane Excitations

Membrane Potential

✧Electrical potential difference across the cell membrane

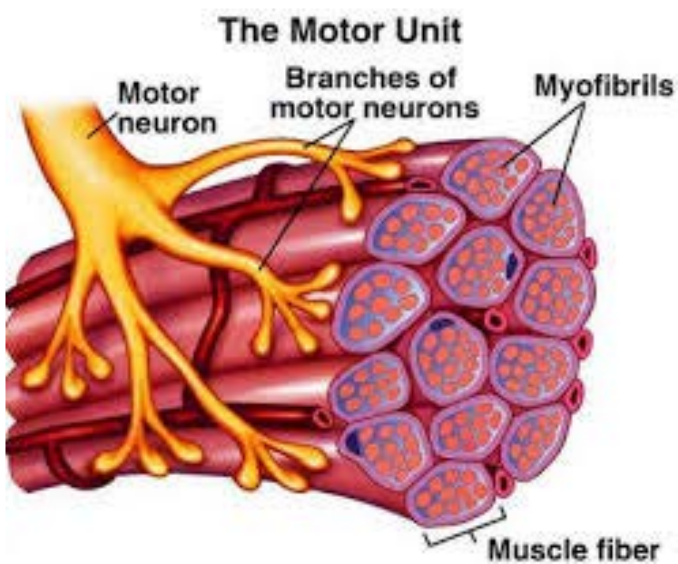
✧caused by different concentrations of **K⁺**, Na⁺, and Cl⁻ ions on each side of the membrane.



Functions of The Membrane Potential

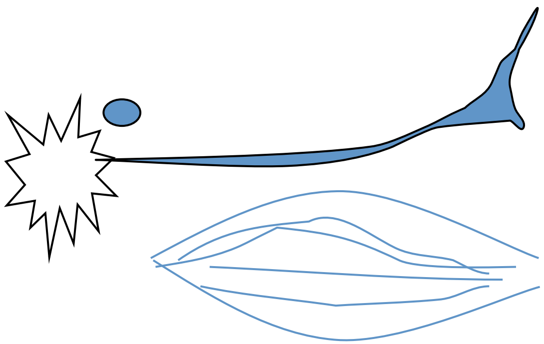
*It allows a cell to function as a **battery**

*In electrically excitable cells such as **neurons** and mu**scle cells**, it is used for transmitting signals between different parts of a cell.



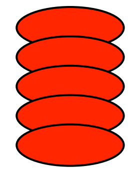
Excitable Tissues

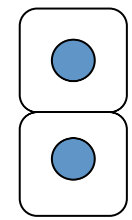
Excitable



- **Neuron**
- **Muscle**
  - Skeletal
  - Cardiac
  - Smooth

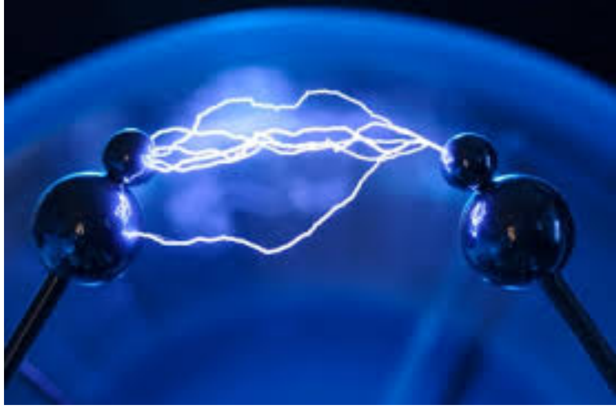
Non-excitable



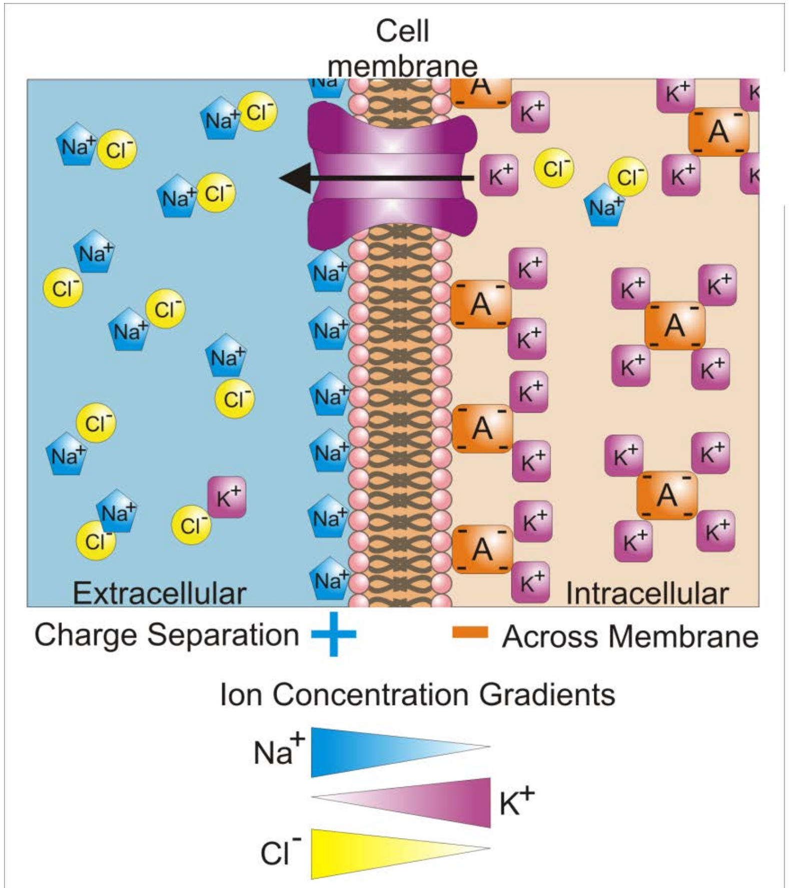


- RBC
- Intestinal cells
- Fibroblasts
- Adipocytes

Electrical Properties of Membranes

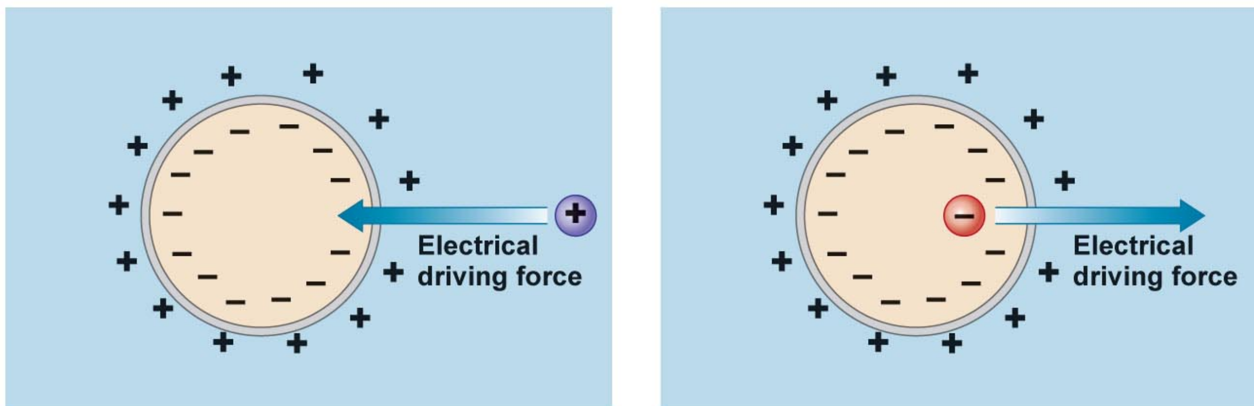


- All cells have *electrical properties*.
- Cell interior is **negative** with respect to the exterior
- *voltage difference (Vm)* that exists across the plasma membrane
  - Moving ions into or out of a cell **Charge imbalance** between the ICF and the ECF



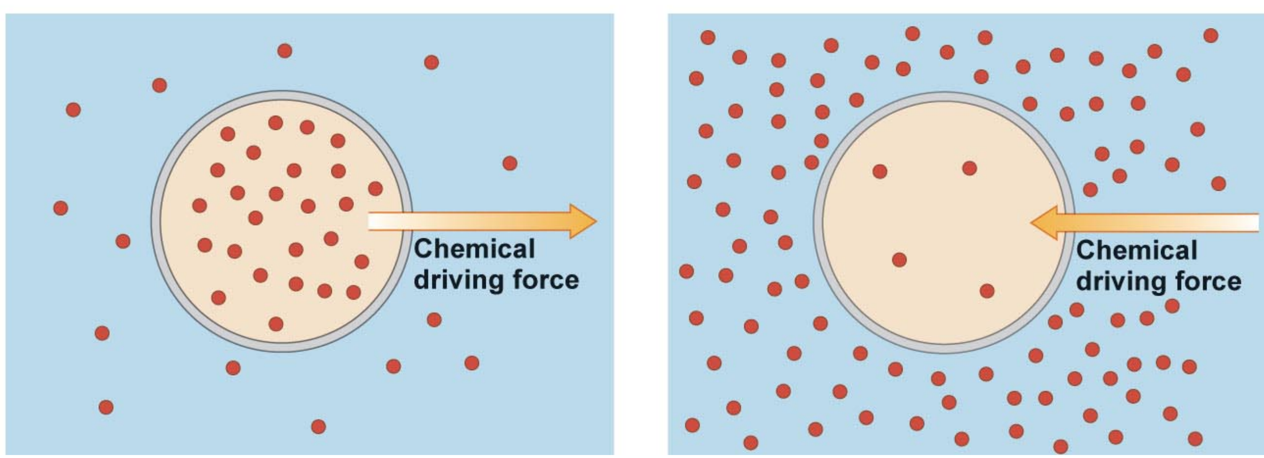
Formation of Membrane Potentials

"**Electro**" due to the charges of the ions



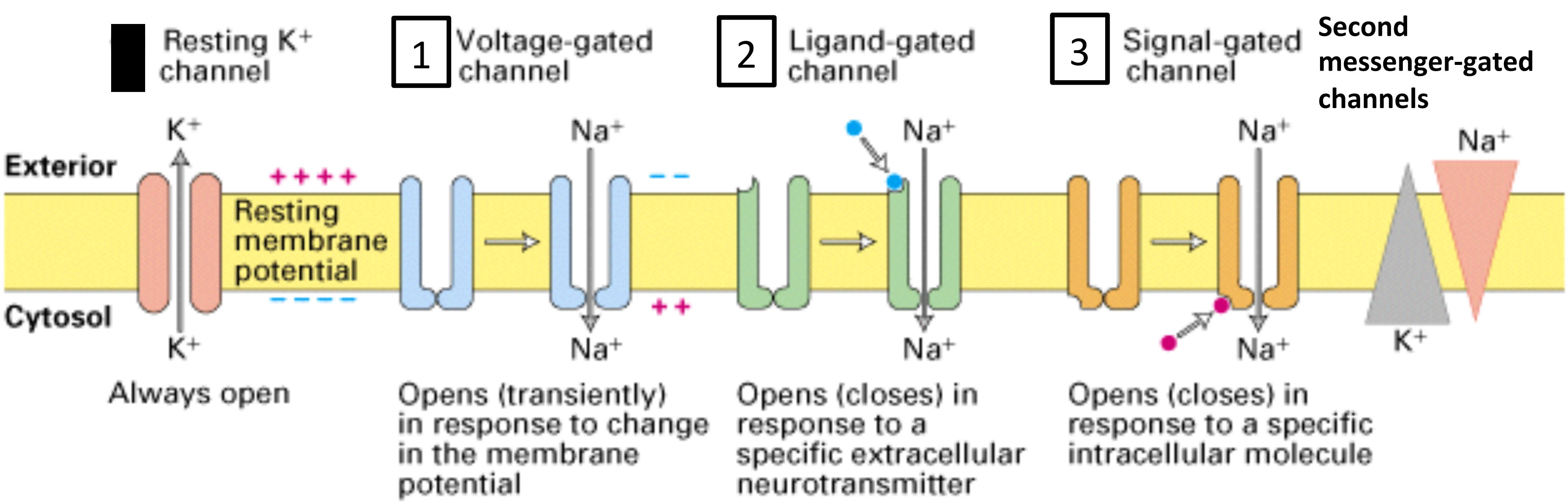
(a) (b)

"**Chemical**" due to the number and types of ions



ION CHANNELS

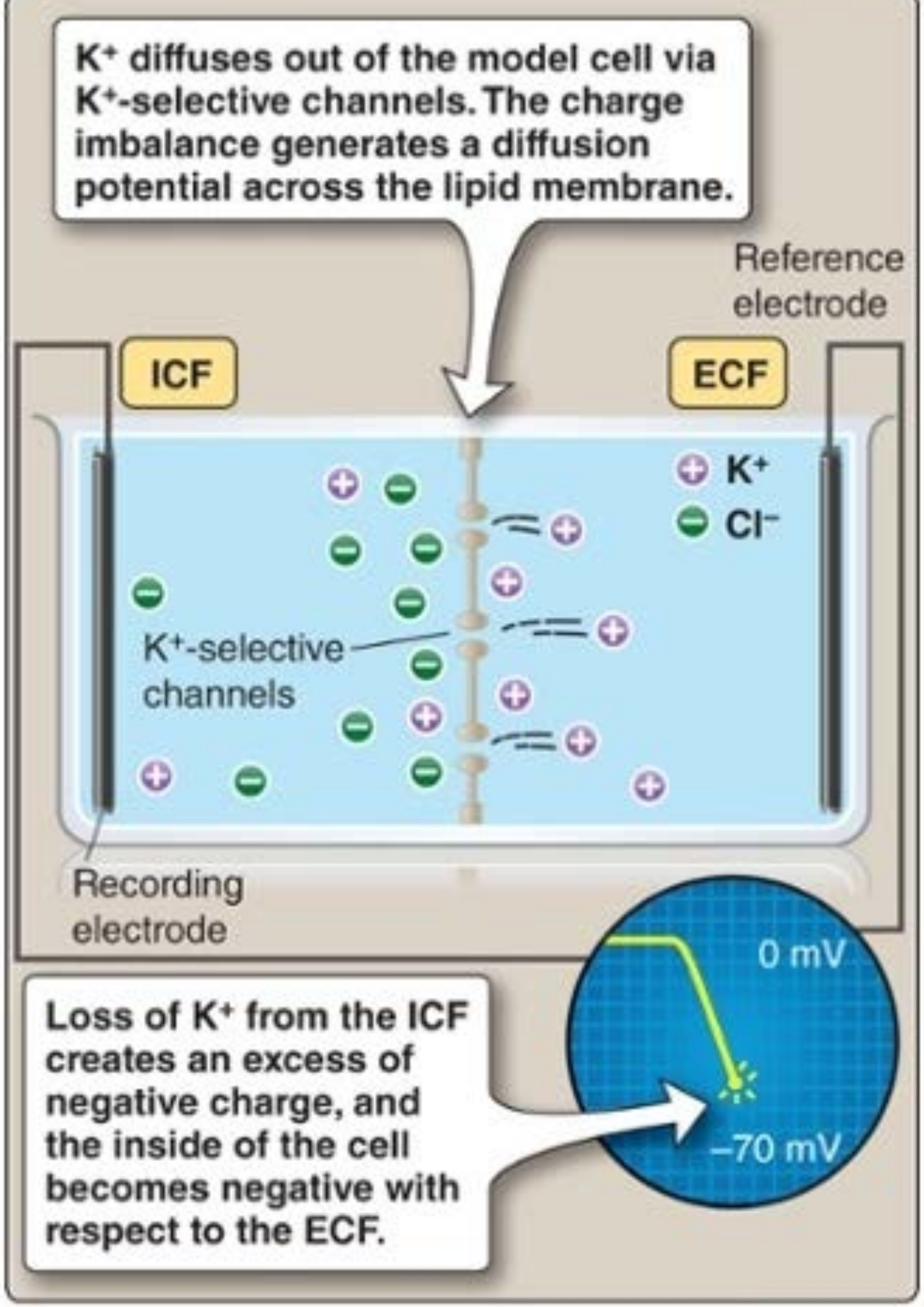
- **Integral** membrane spanning proteins
- when open, permit the passage of certain ions
- **Selective;** size, charges
- controlled by **gates**
- The gates on ion channels are controlled by three types of **sensors.**



Na, Ca, Cl, K Nerve-Hormones, NT cardiac sinoatrial node- cAMP

Types of Membrane Potentials

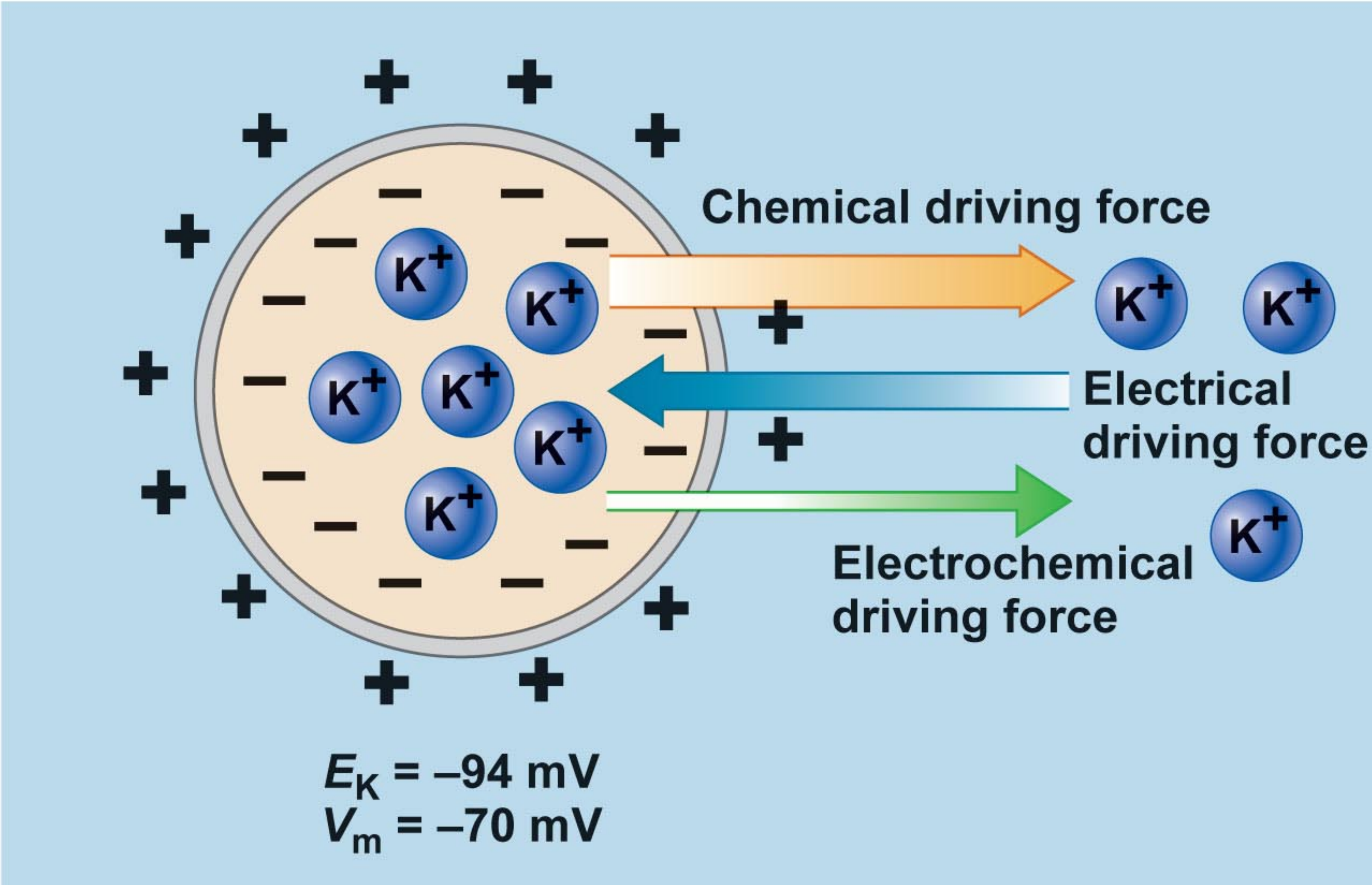
- Diffusion potentials
- Equilibrium potentials
- Resting potentials
- Threshold membrane potential
- Action potentials



Diffusion Potentials

potential difference generated across a membrane when a charged solute diffuses **down its concentration gradient**.

potassium ions have charge, so their movement causes a **diffusion potential** to form across the membrane.

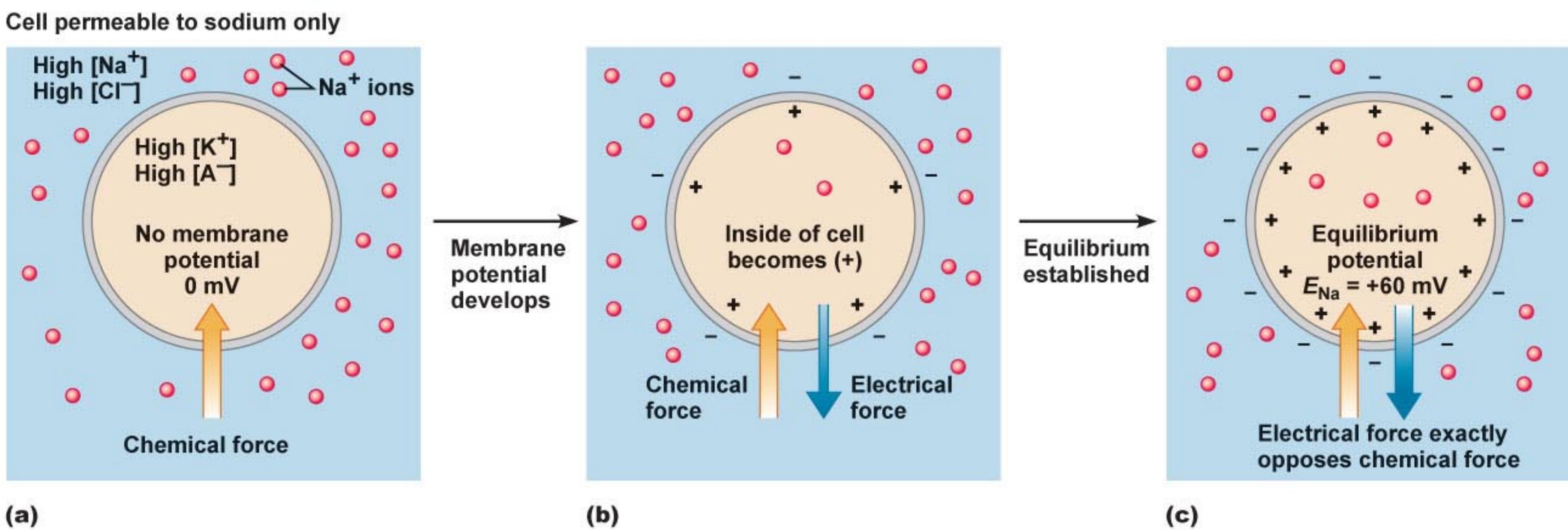


Cl-

Opposite charges attract to each other,
potassium movement slow down and eventually it stops.

Equilibrium Potentials (E)

At **electrochemical equilibrium,** the chemical and electrical driving forces acting on an ion are equal and opposite, and no further net diffusion occurs



in other words, if a cation diffuses down its concentration gradient, it carries a positive charge across the membrane, which will retard and eventually stop further diffusion of the cation.

Resting Membrane Potential (V_R) RMP

Constant membrane potential present in cells of non excitable tissues and those of excitable tissues when they are at rest

- Some ion channels are open at rest.
- Resting V_m (**resting potential=** sum of the diffusion) potentials generated by each of these ions flowing through open channels.
- The equilibrium condition, in which there is **no net flow of ions** across the plasma membrane, defines the resting membrane potential for this idealized cell.

The Membrane potential: Balance of Two Forces

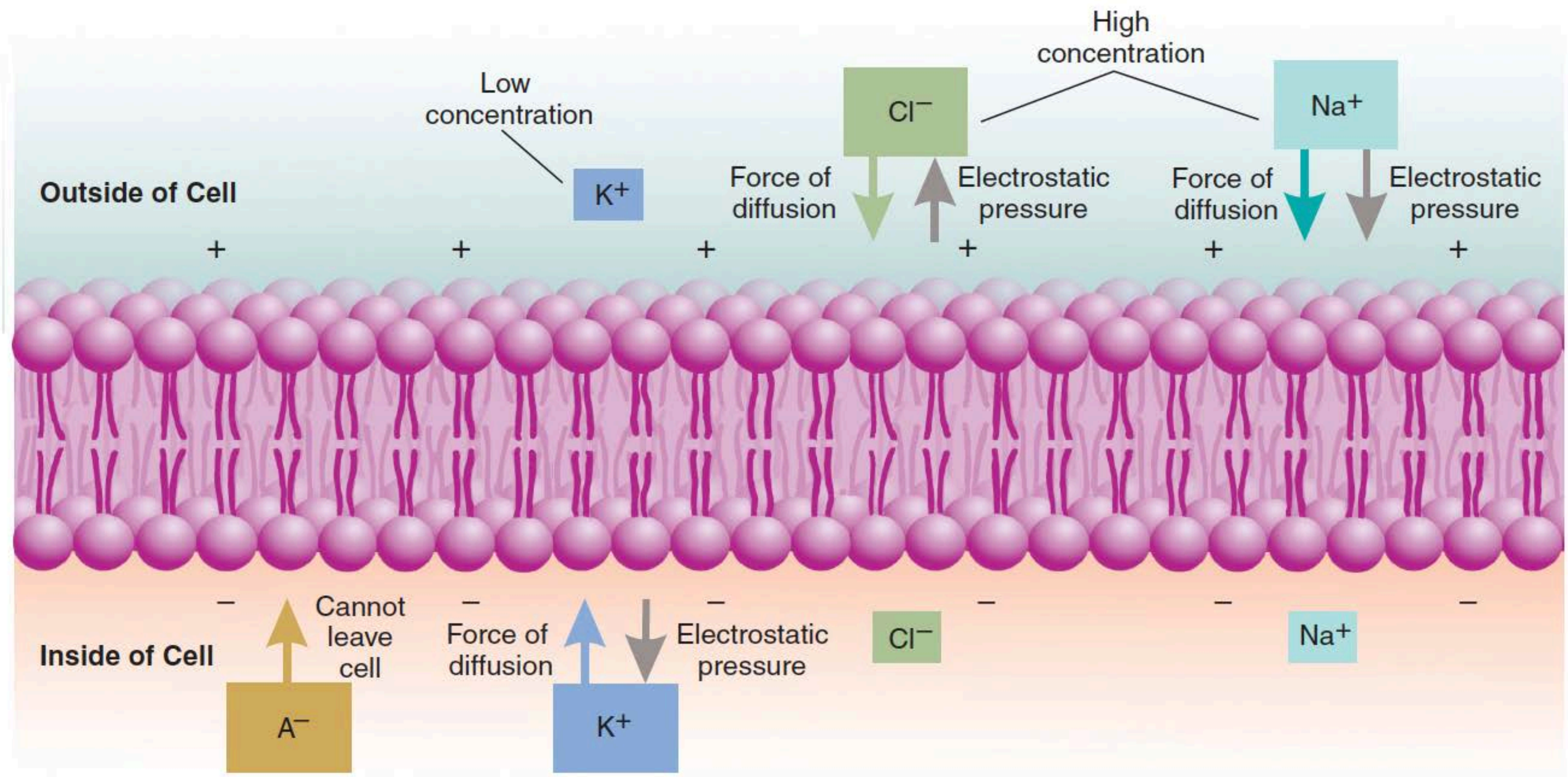


FIGURE 2.15 Control of the Membrane Potential. The figure shows the relative concentration of some important ions inside and outside the neuron and the forces acting on them.

Membrane Potential

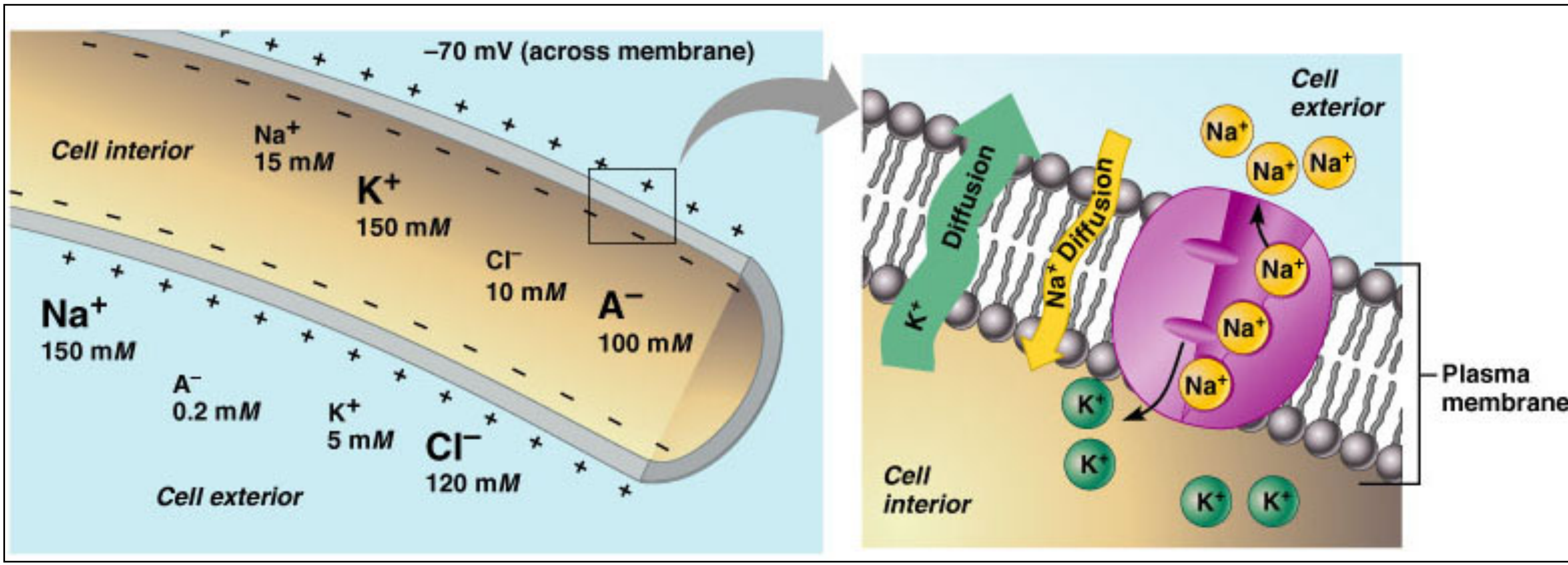
- Proteins and phosphates are negatively charged at normal cellular pH.
- These anions attract positively charged cations that can diffuse through the membrane pores.
- Membrane more permeable to K^+ than Na^+.
  - Concentration gradients for Na^+ and K^+.
- Na^+/ K^+ATP pump 3 Na^+ out for 2 K^+ in.

➢ All contribute to unequal charge across the membrane.

Resting Membrane Potential (V_R)

*Different membrane permeabilities due to passive ion channels for Na+, K+, and Cl-

*The **K+ permeability is higher than Na+**
***more of the K$^+$ leakage channels** than Na$^+$



Ions in the Extracellular and Intracellular Fluid

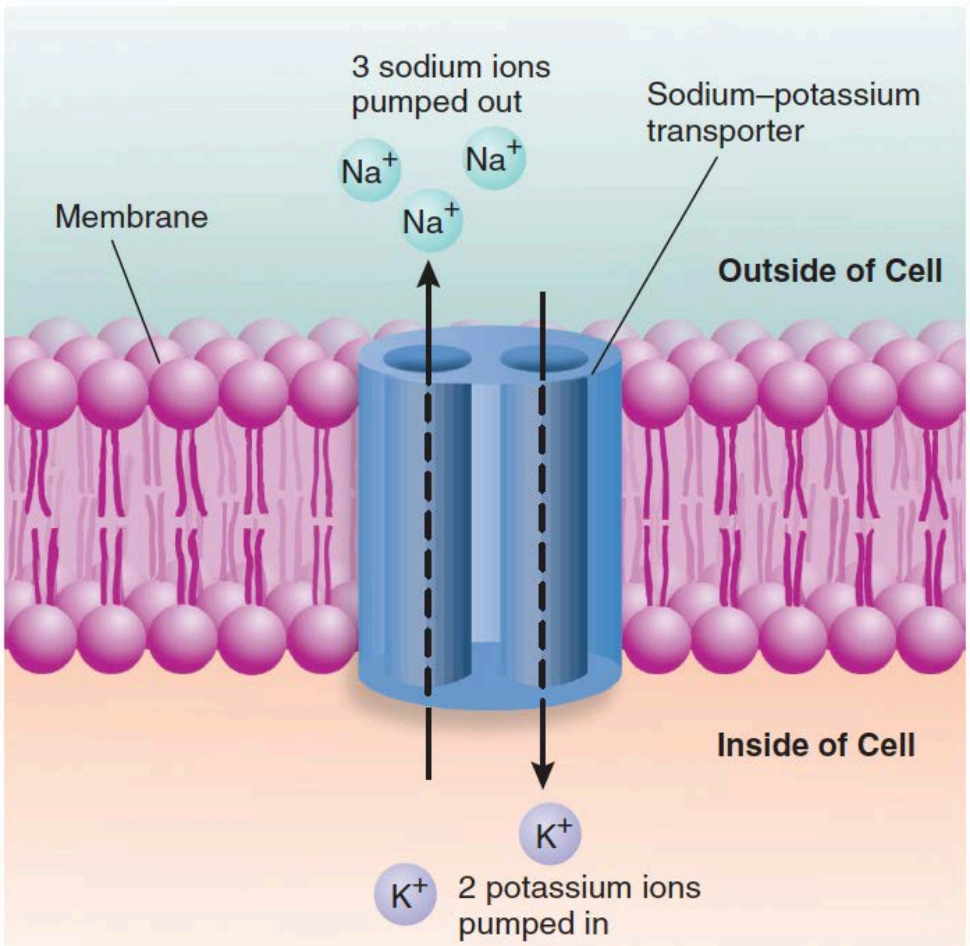


FIGURE 2.16 A Sodium–Potassium Transporter. These transporters are found in the cell membrane.

*Na^+ ions are **actively transported** to maintain the resting potential.

*The **sodium-potassium pump** exchanges three Na^+ ions for two K^+ ions.

*Na^+ K^+ pump is an active, it needs energy taken from ATP

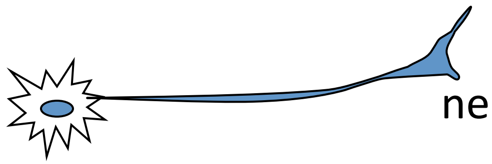
*Very important to **maintain the concentration gradient across the cell membrane**

Maintenance of Membrane Potential- Transporter Contribution

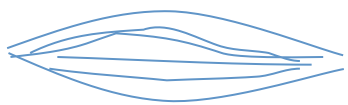
- Without energy, the membrane potential would eventually be destroyed as
  - ***K^+ leaks* out** the cell due to membrane leakage channels
  - ***Na^+ leaks* in** due to membrane leakage channels
- **Na^+/K^+ ATPase (Sodium-Potassium Pump)** restores the balance pumping Na^+ out and K^+ back in.

Excitable Tissues

excitable

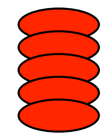


neuron

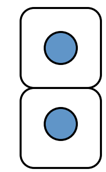


muscle

Non-excitable



Red cell



GIT

- Excitable tissues have more negative RMP

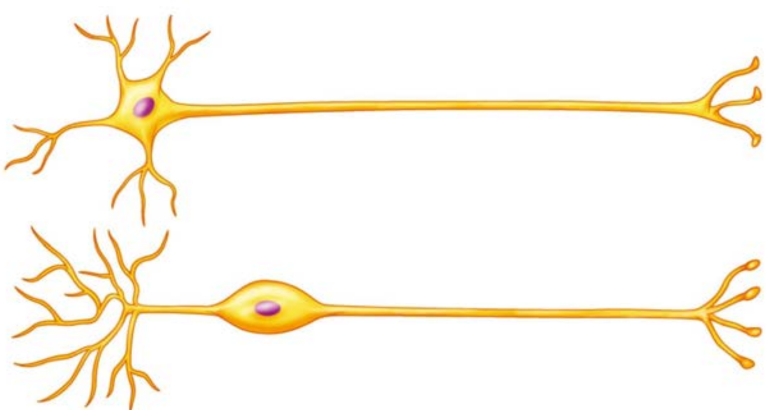
- ○ -70 mV Neurons
- ○ -90 mV Skeletal Muscle

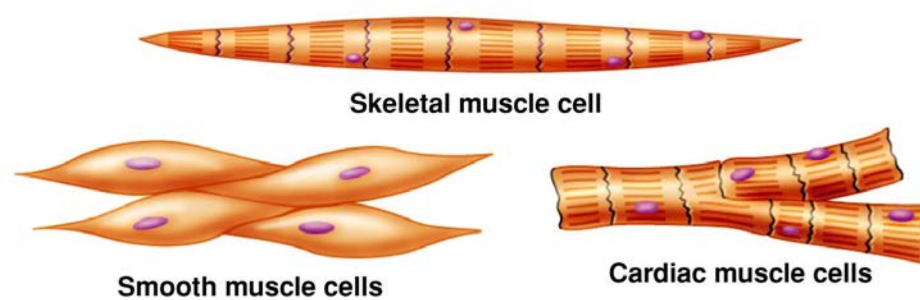
- Non-excitable tissues have less negative RMP
- ○ -53 mV epithelial cells
- ○ -8.4 mV RBC
- ○ -20 to -30 mV fibroblasts
- ○ -58 mV adipocytes

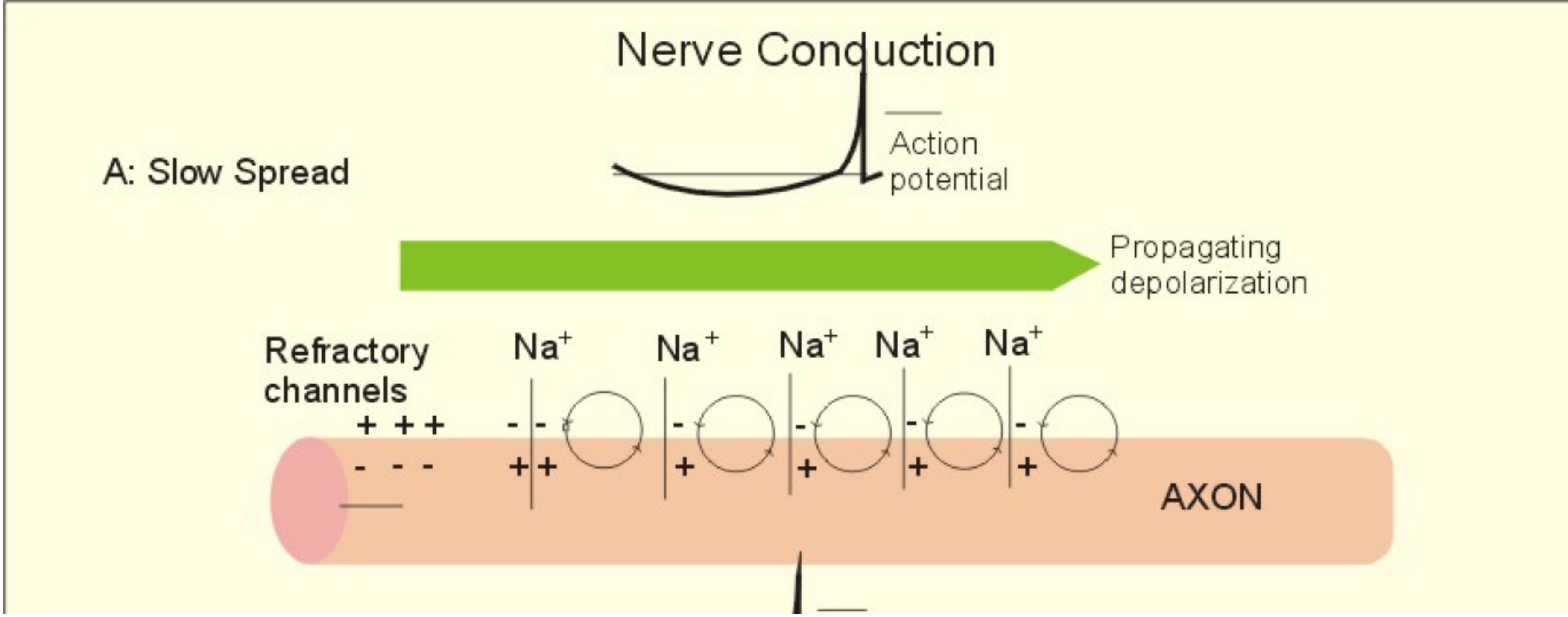
Excitable Membranes

- **Excitable Tissues** – electrically active tissues

- Tissues which are capable of generation and transmission of electrochemical impulses
  - nervous tissue
  - muscle tissue







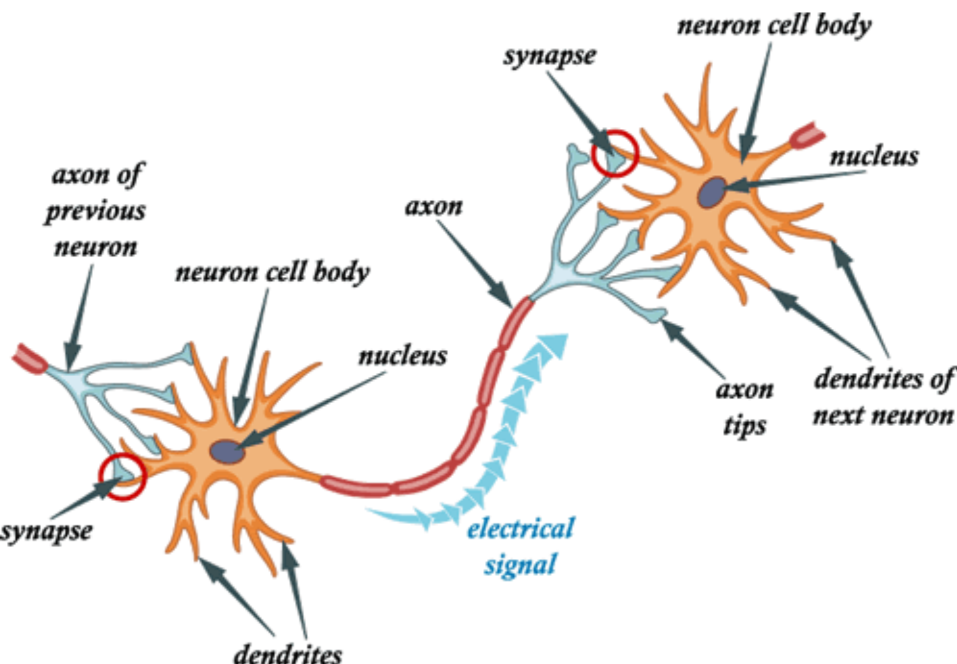
ExCitation

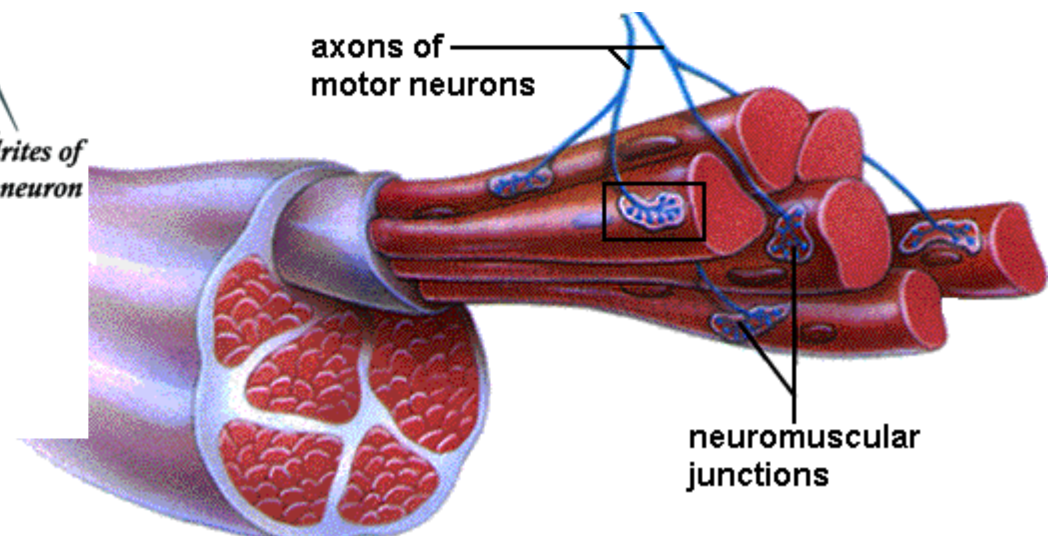
The electrical changes caused by increased membrane permeability to ions

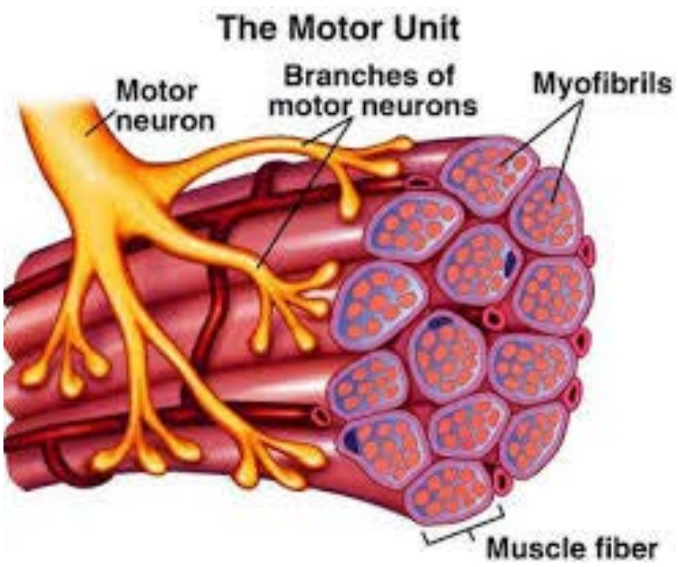
(e.g., Na^+ *versus* K^+ or Cl^-)

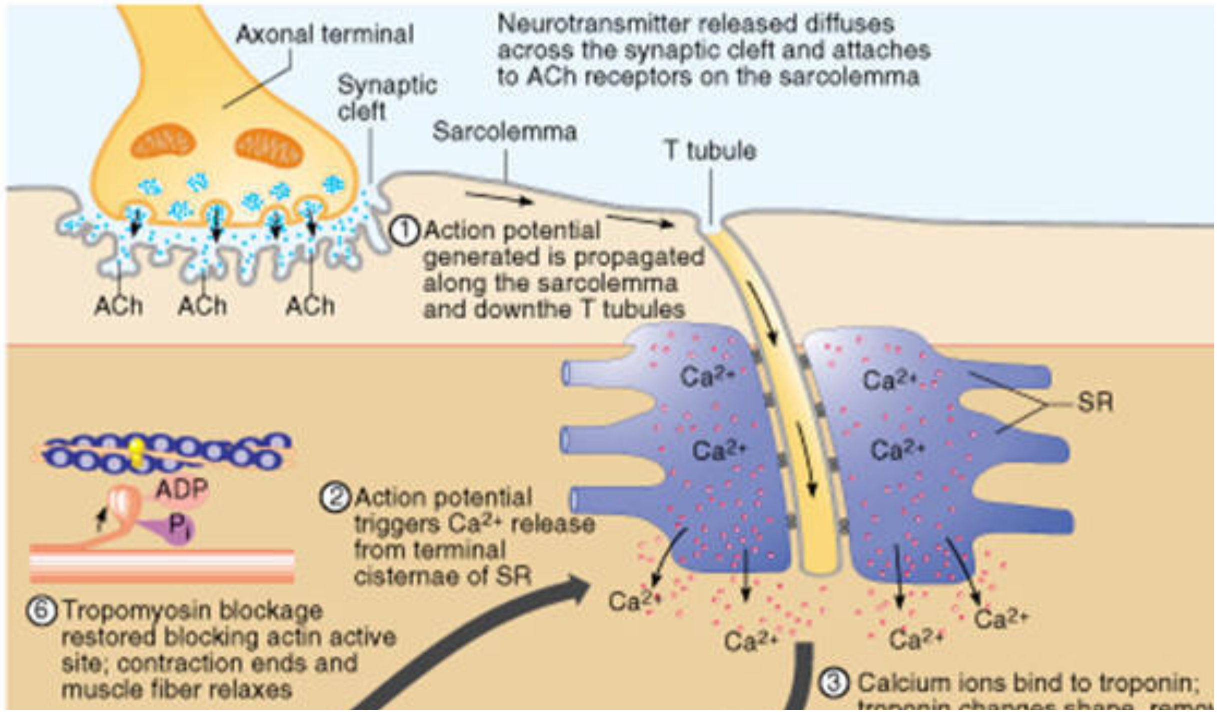
How These Cells Use This Exitaiton???

- Nerve cells use **this exitation for signaling**
  nerve to muscle or nerve to nerve





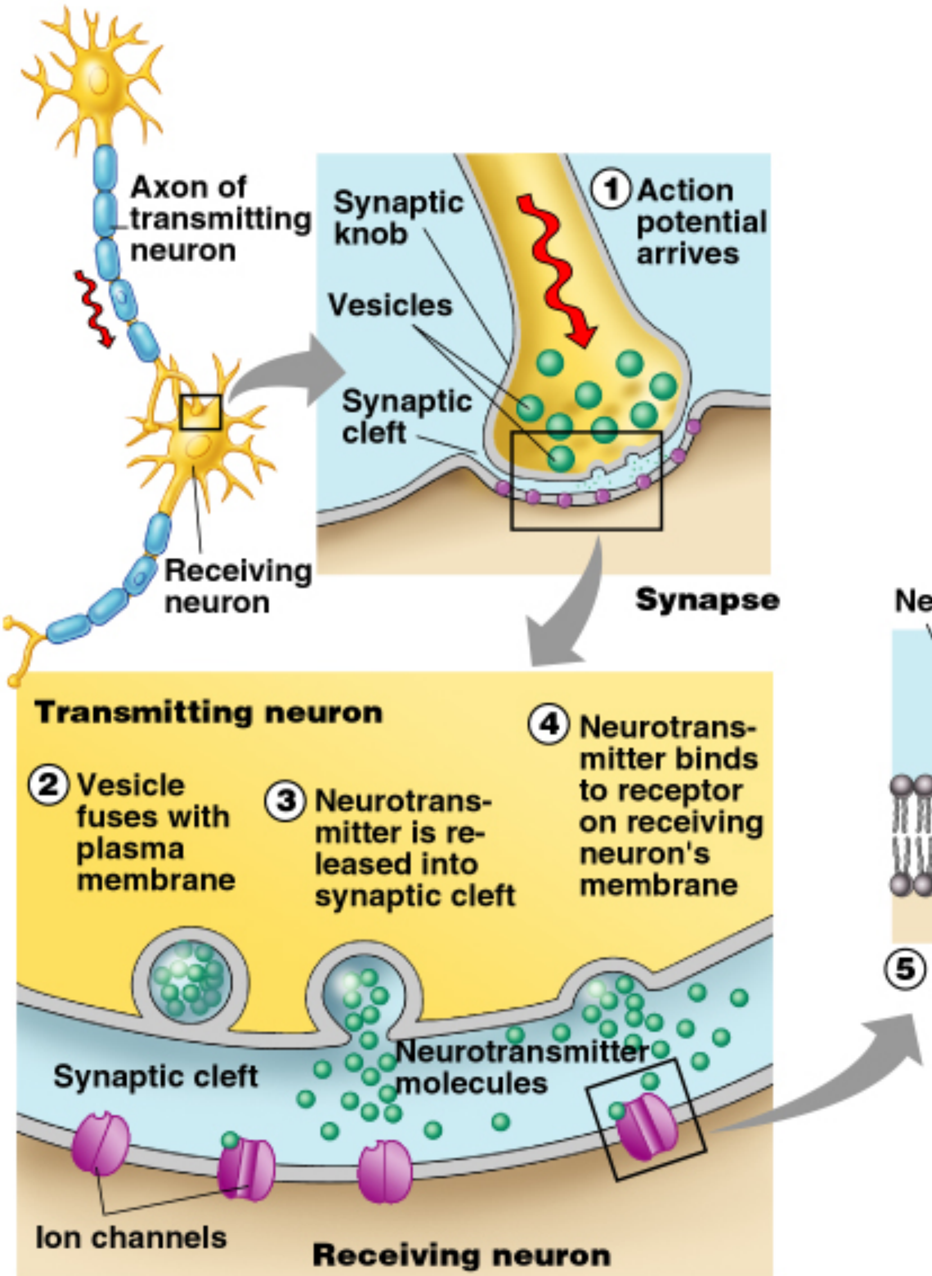




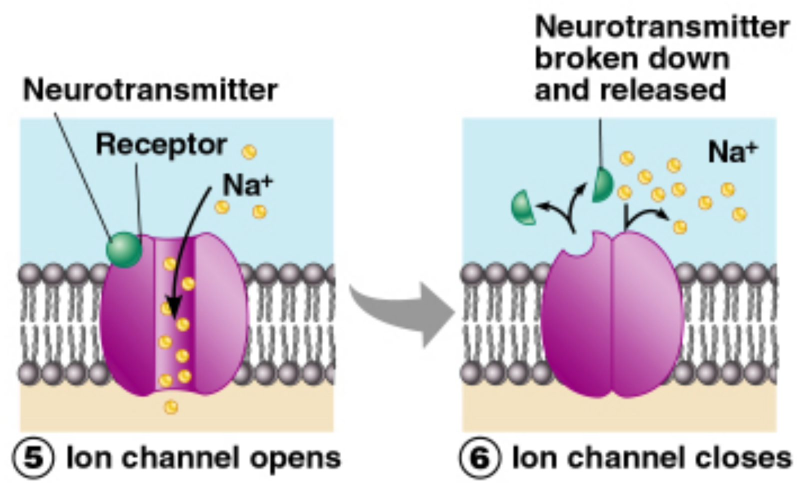
- The muscle cell, in turn, uses a change **exitation** to initiates muscle **contraction.**

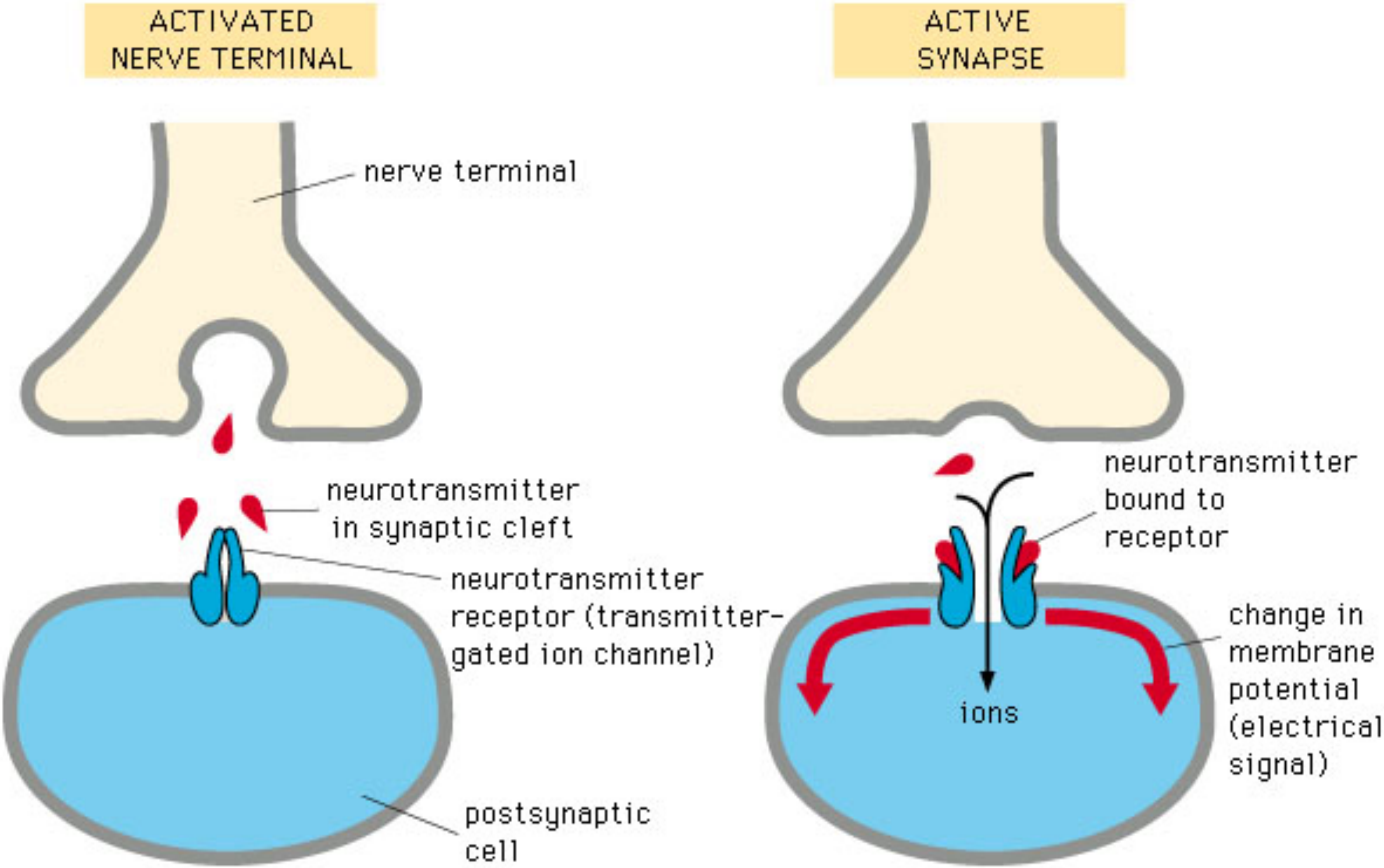
- Neuronal and muscle action potentials coordinated selective passage of ions (Na^+, Ca^{2+}, and K^+) between ICF and ECF.

How Neurons Communicate at Synapses



"information" must not only be conducted along nerve cells information" BUT ALSO, be transferred from one nerve cell to another across the *synapse*



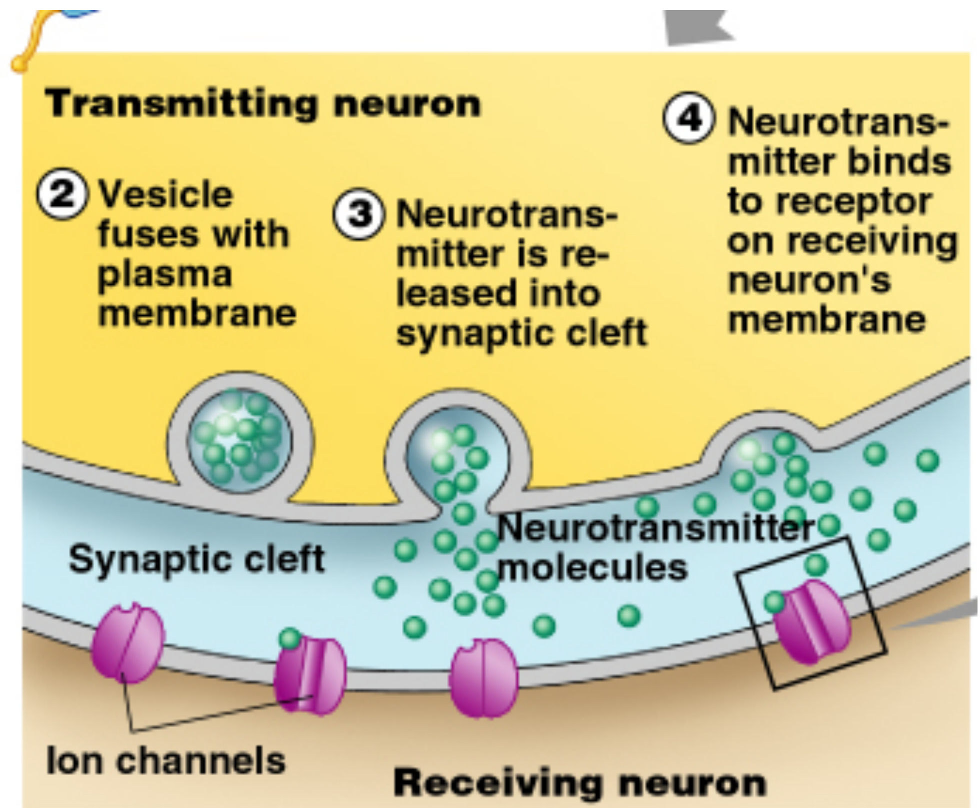


ACTIVATED NERVE TERMINAL
ACTIVE SYNAPSE
nerve terminal
neurotransmitter in synaptic cleft
neurotransmitter receptor (transmitter-gated ion channel)
postsynaptic cell
neurotransmitter bound to receptor
ions
change in membrane potential (electrical signal)

Continuation of the Nerve Impulse between Neurons

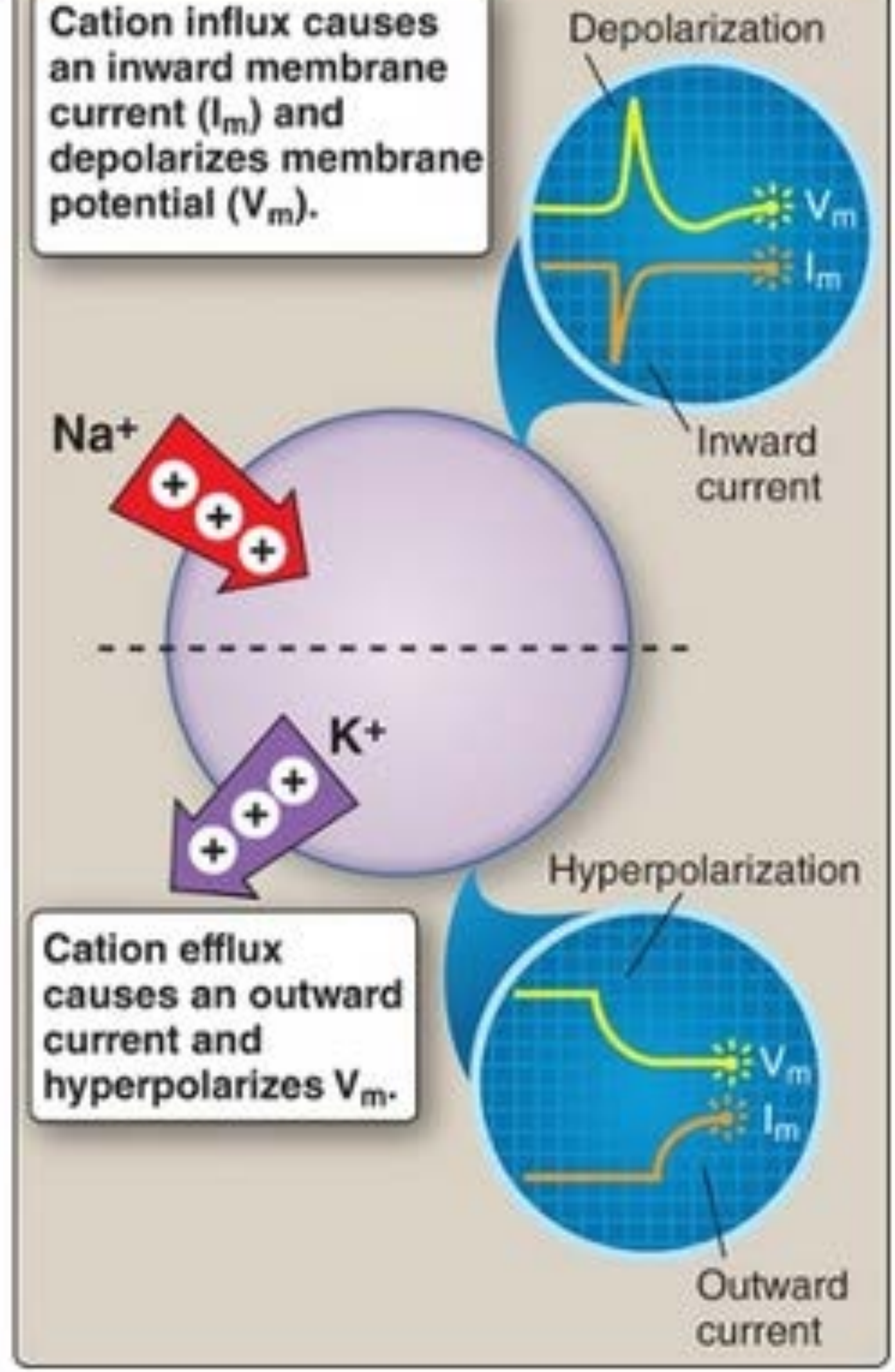
- Impulses are able to cross the synapse to another nerve

1. **Neurotransmitter is released** from a nerve's axon terminal
2. The dendrite of the next neuron has receptors **(Ach gated Na channel)** that are stimulated by the neurotransmitter
3. An action potential is started in the dendrite



Membrane Potential Changes

- **The inside of a cell negative than ECF**.
- Na+ in: Membrane loses polarization called **membrane depolarization**.
- K+ out: Caused **membrane hyperpolarization**.

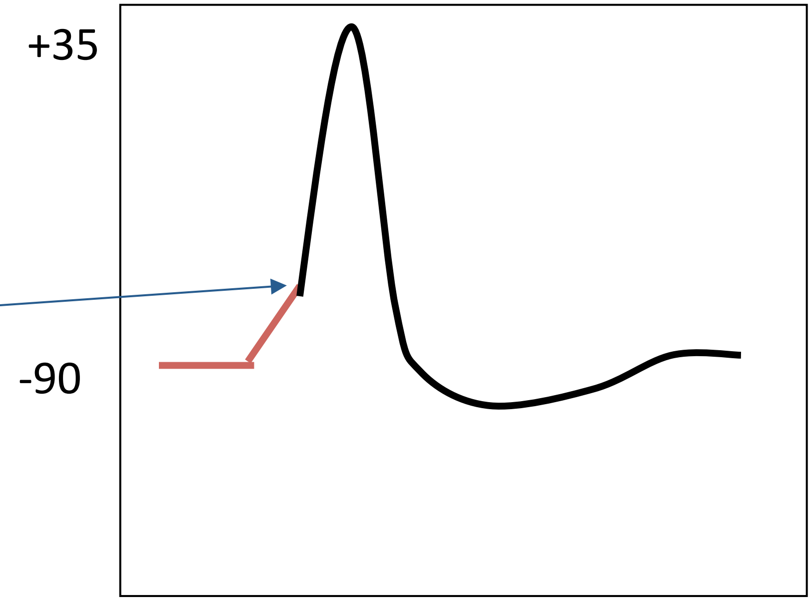


Action Potential

3. Initially membrane is **slowly depolarised** (Na influx)

- Until the **threshold level** is reached
  - (This may be caused by the stimulus)

Threshold level

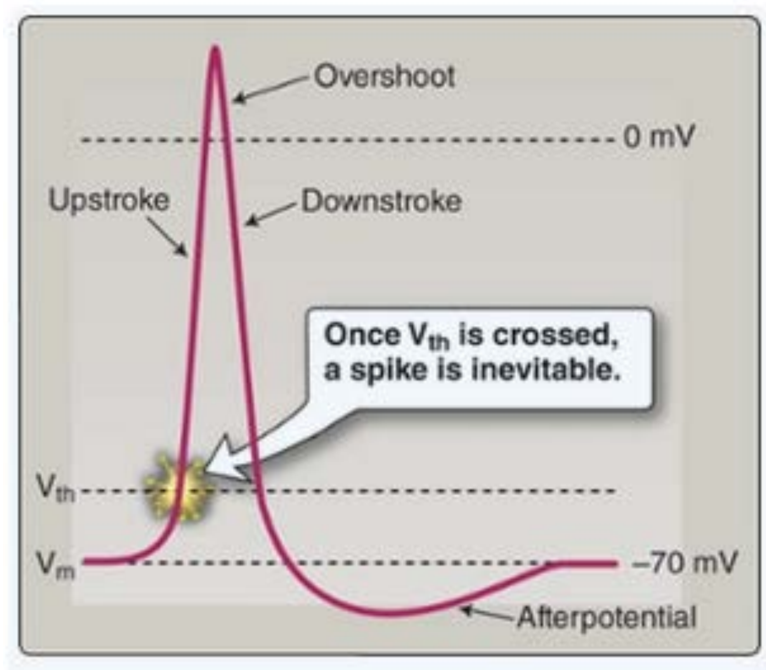


Action Potentials-Threshold potential

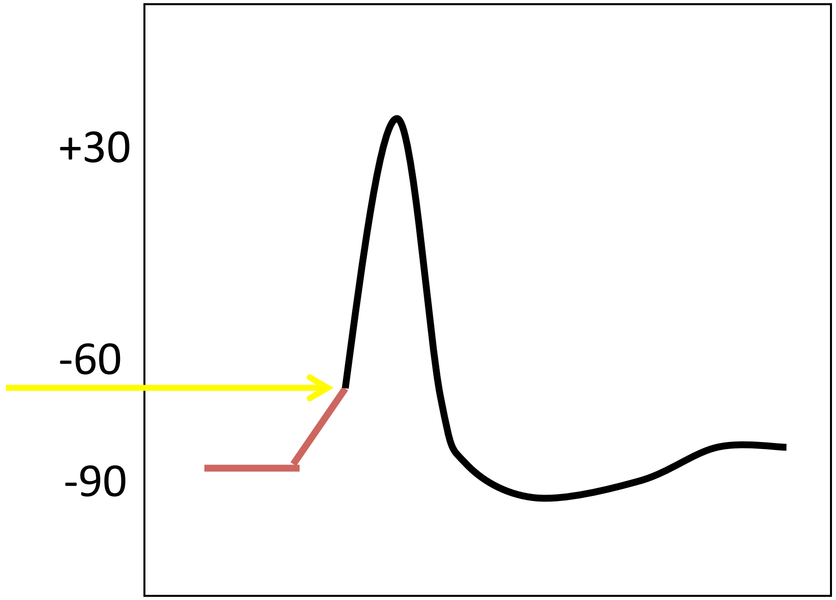
4. The electrical voltage needed to open the **voltage dependent Na^+ channels** required to trigger an action potential.

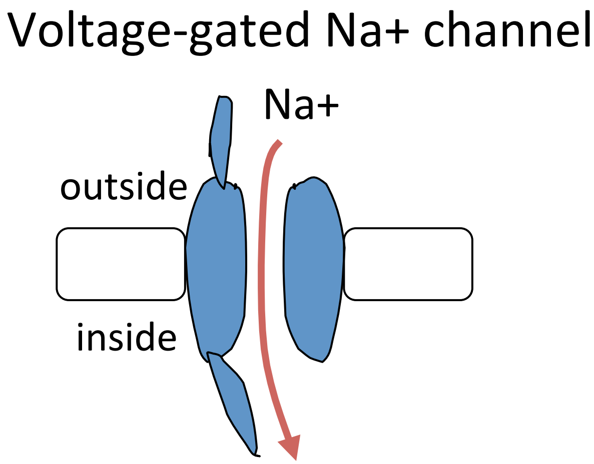
- This occurs in most excitable tissues at **-60mV**

- Once the threshold level is reached
  - AP is set off and *no one can stop it ! Like a gun*



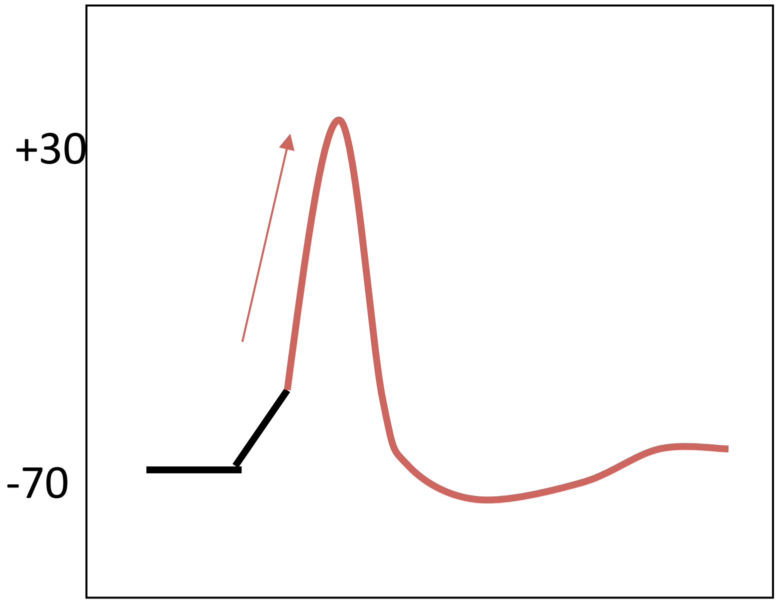
Physiological Basis of Depolarisation

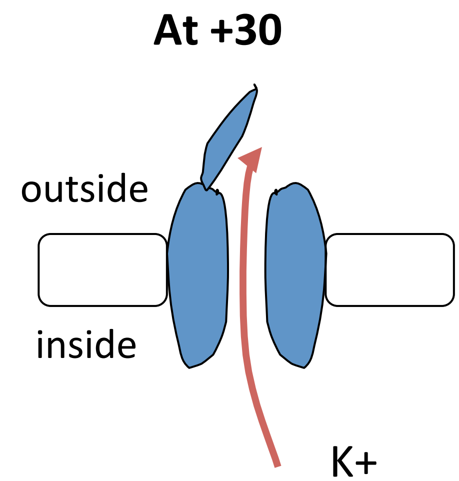




4. When the threshold level is reached
   - **Voltage-gated Na+** channels open up
     - (Na+ conc. outside is higher than the inside)
   - More Na^+ goes inside the cell
   - The positivity of the membrane potential increases and causes **depolarisation**

Physiological basis of Repolarisation



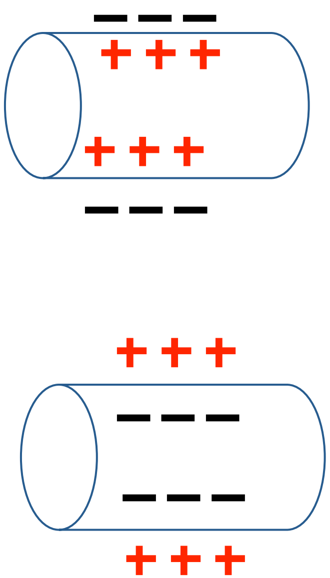


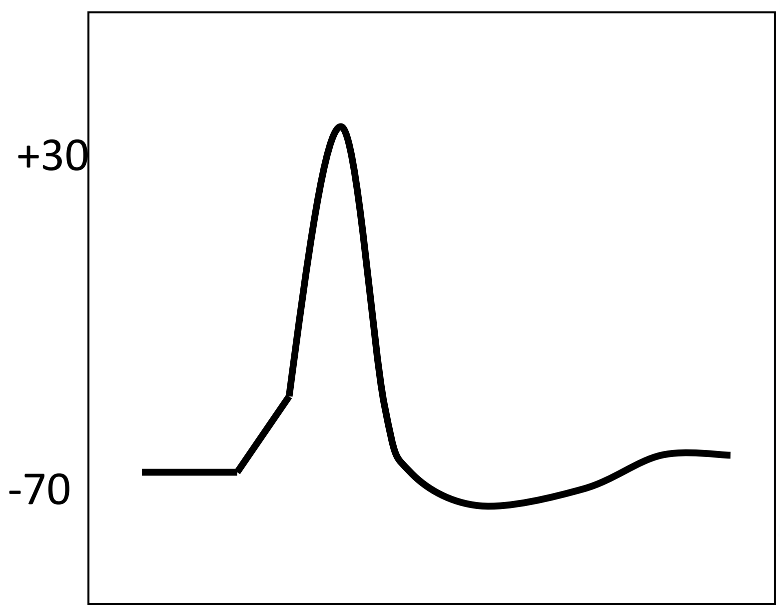
5. When membrane potential reaches **+30 mV**, **Na+ channels are inactivated**

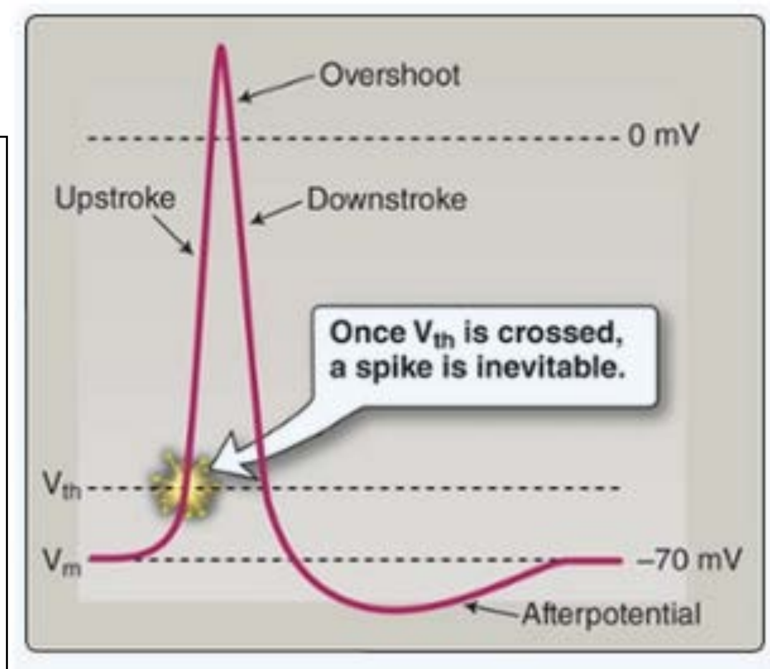
- Then K+ channels open, K+ goes outside
- Positive ion leaving the inside causes negativity at ICF
- **Repolarisation** occurs

Action Potentials-Overshoot

- The action-potential peak often “overshoots” the zero-potential line, and the inside of the cell becomes positively charged with respect to the ECF.







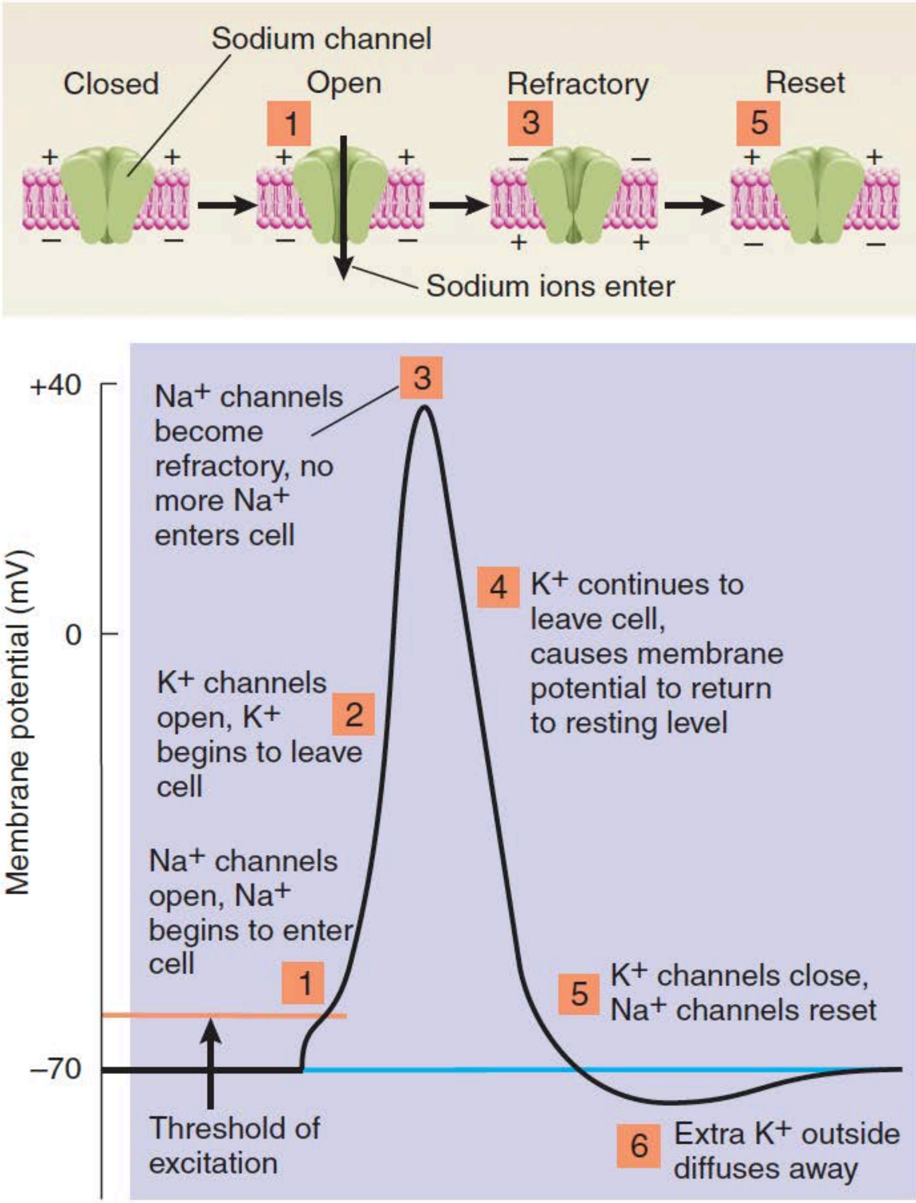
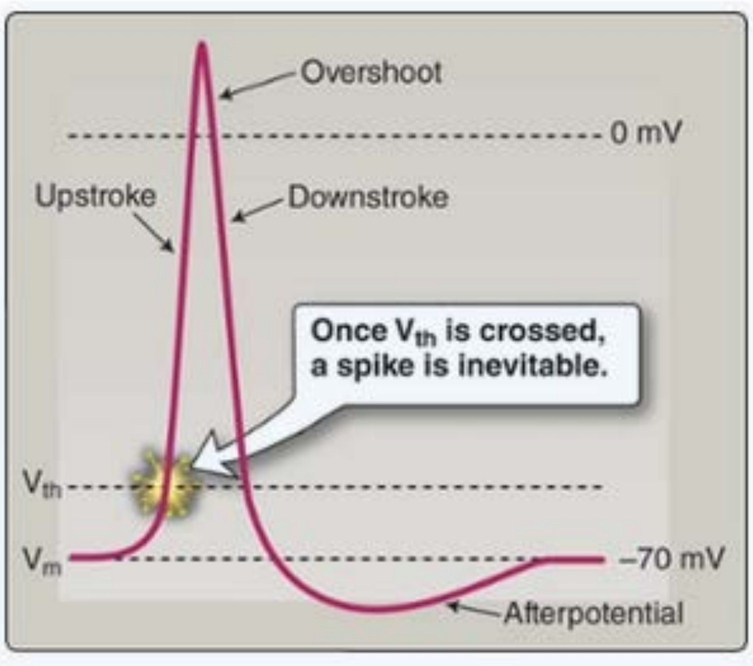


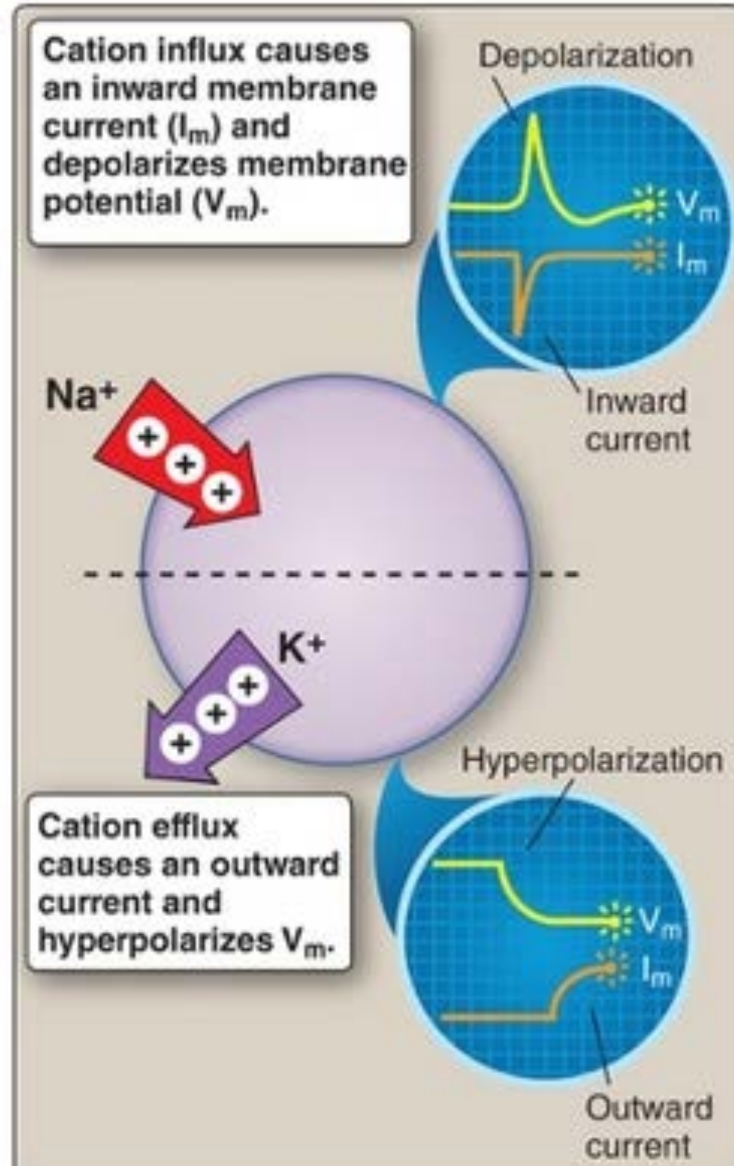
FIGURE 2.18 Ion Movements During the Action Potential. The shaded box at the top shows the opening of sodium channels at the threshold of excitation, their refractory condition at the peak of the action potential, and their resetting when the membrane potential returns to normal.

- **Refractory period** is a period during which another normal action potential cannot be elicited in an excitable cell.

Action potentials-After Potentials

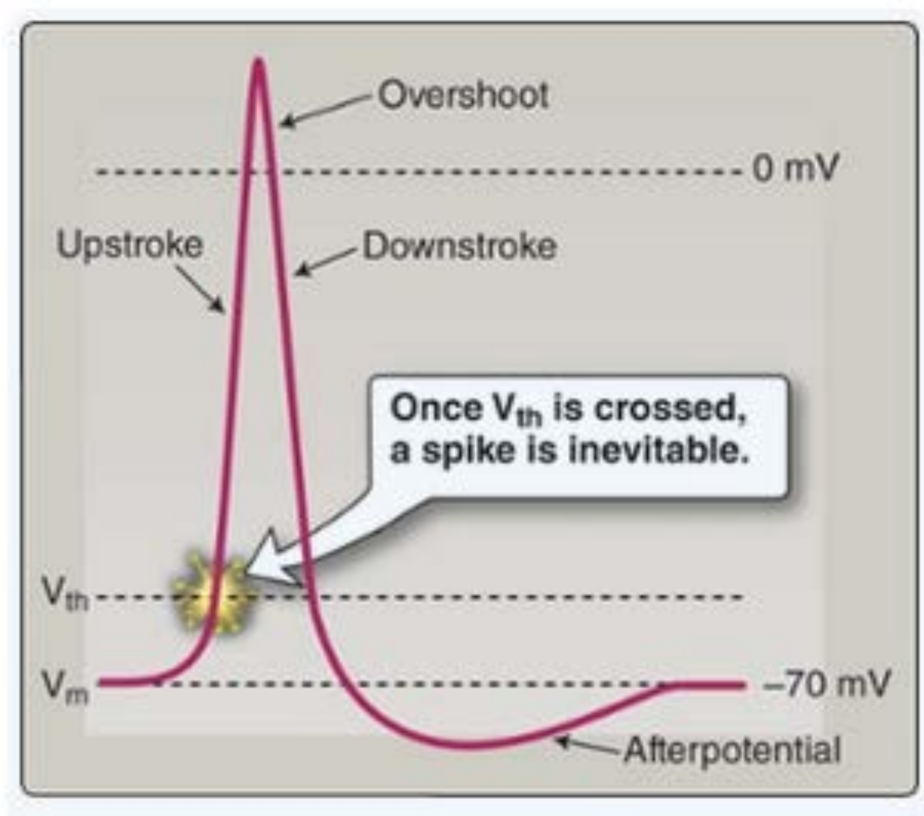
5. The **downstroke** is caused in part by voltage-dependent K^+ channels that open to allow K^+ efflux, causing V_m to **repolarize**.





Action potentials-After Potentials

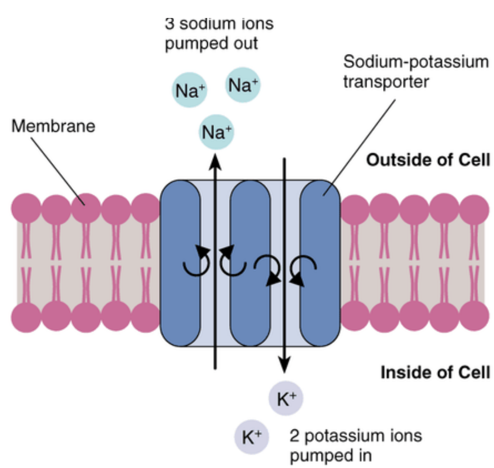
6. A hyperpolarizing afterpotential (hyperpotential) takes the membrane negative to V_m for a period before eventually settling at the normal resting potential.

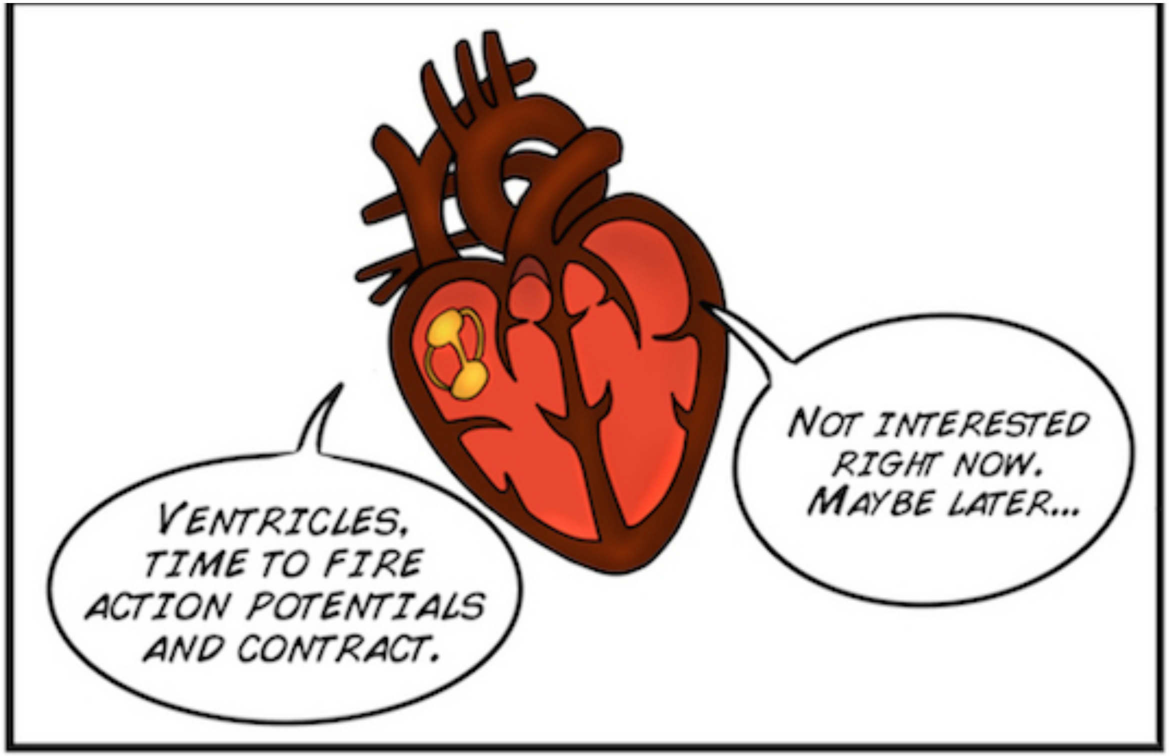


Role of Na+/K+ pump

- Since Na+ has come in and K+ has gone out
- Membrane has become **negative**
- But ionic distribution has become **unequal**

- **Na+/K+ pump restores Na+ and K+ conc. slowly.**
  – By pumping 3 Na+ ions outward and 2+ K ions inward




VENTRICLES, TIME TO FIRE ACTION POTENTIALS AND CONTRACT.
NOT INTERESTED RIGHT NOW. MAYBE LATER...