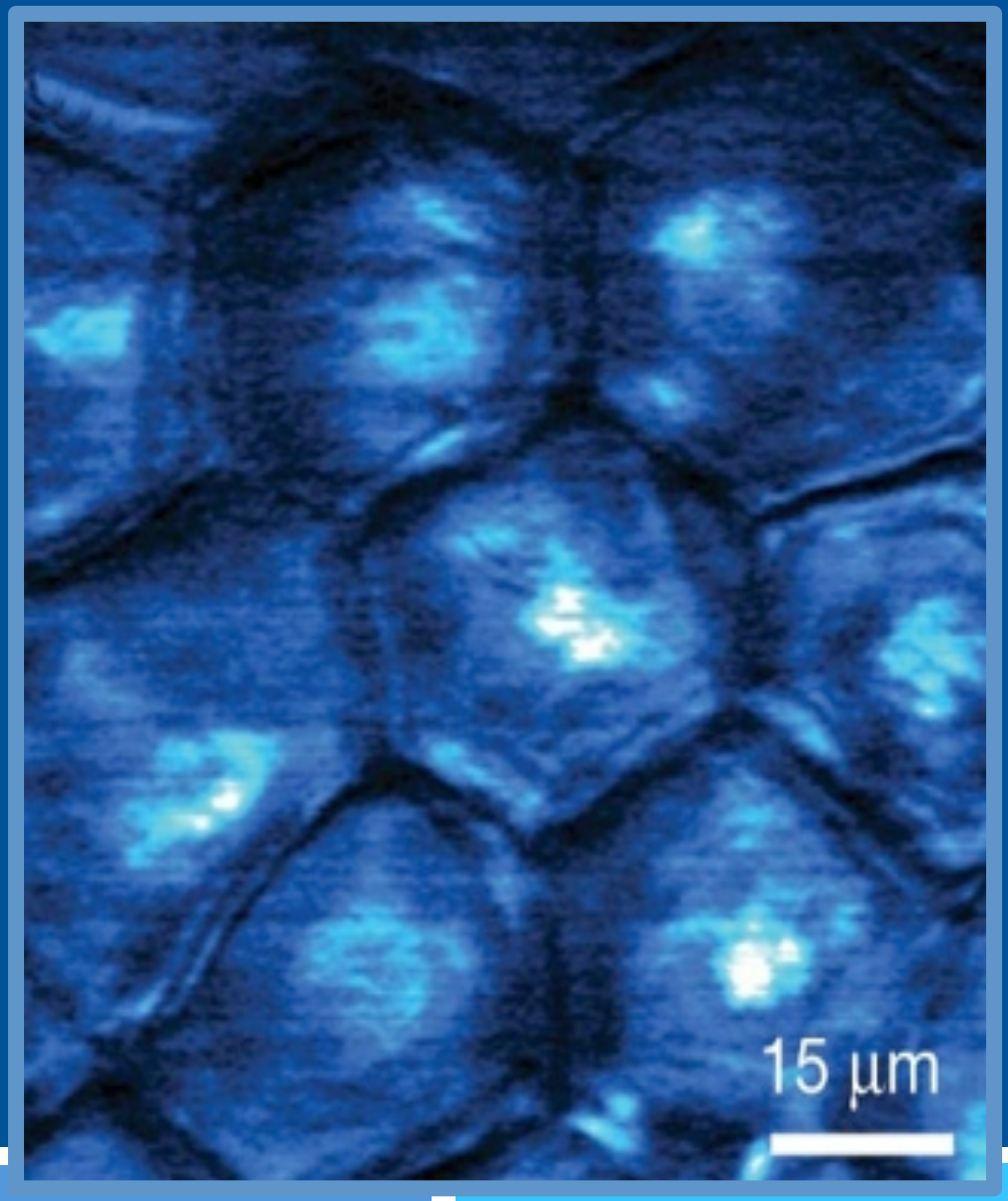


# MEMBRANE STRUCTURE

## Lecture 9

BIOL 266/4

2014-15

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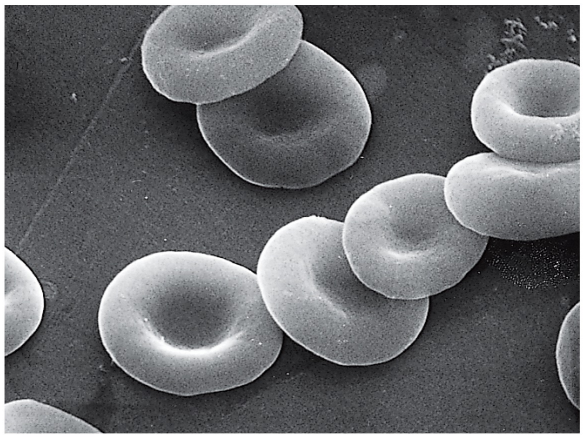
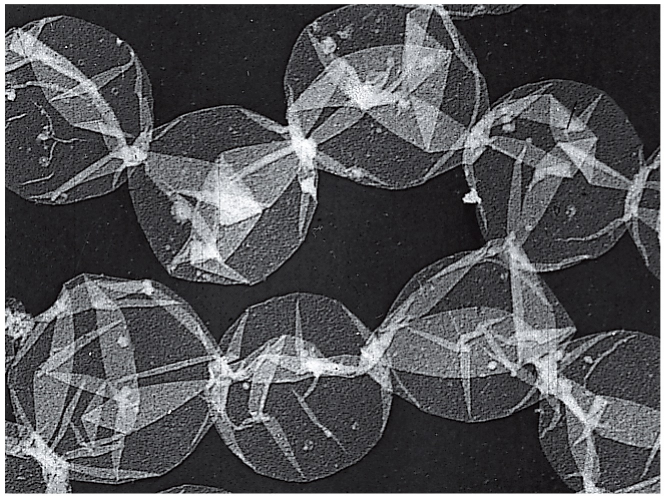
# RED BLOOD CELL MEMBRANE PROTEINS

# The Dynamic Nature of the Plasma Membrane




Courtesy François M.M. Morel, Richard F. Baker and Harold Wayland.

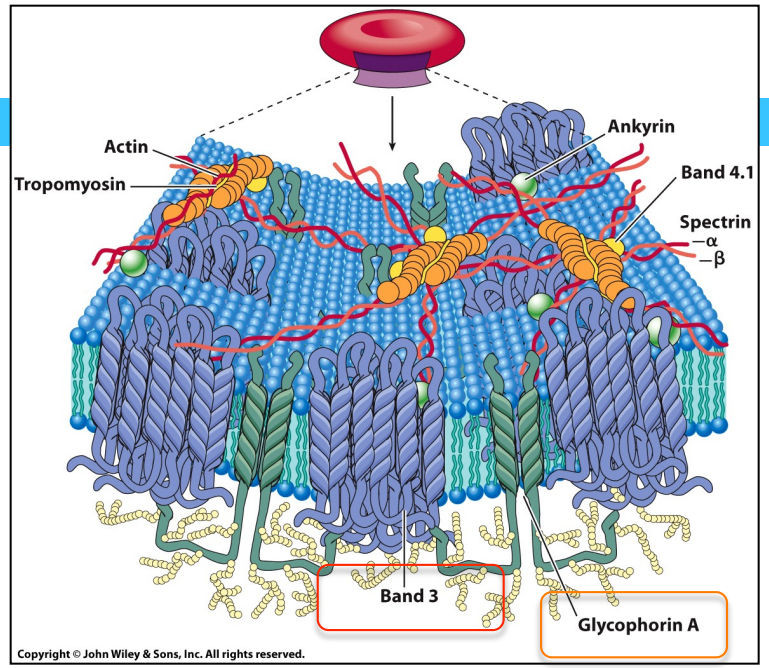
SEM of human erythrocytes and membrane ghosts



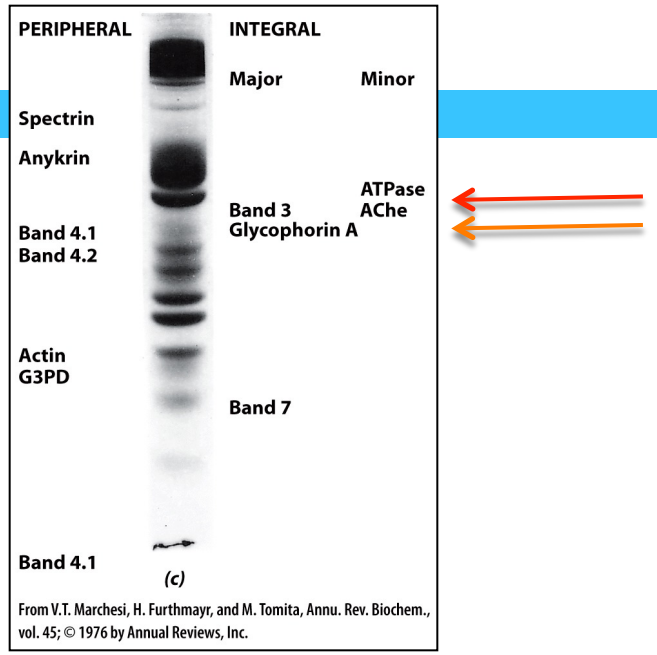
Courtesy Joseph Hoffmann, Yale University

- The Red Blood Cell: An Example of Plasma Membrane Structure
  - Homogeneous preparation of membrane "ghosts" can be prepared by *hemolysis*.
  - Membrane proteins can be purified and characterized by fractionation using SDS-PAGE electrophoresis.

# The Dynamic Nature of the Plasma Membrane




Erythrocyte plasma membrane model viewed from the internal surface

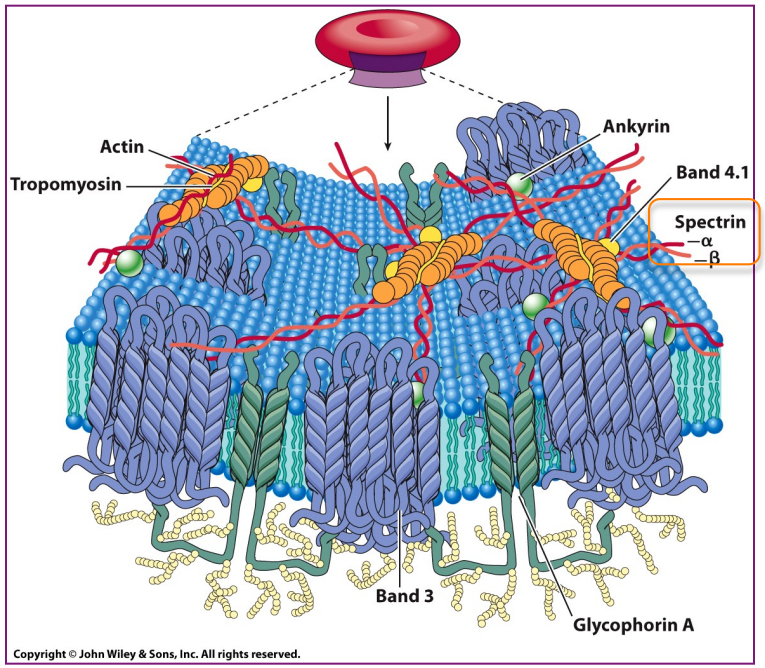


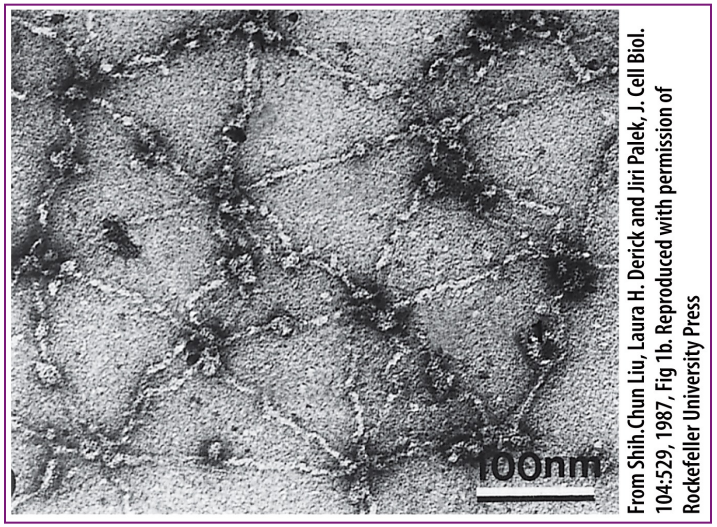

SDS–PAGE of membrane proteins

## Integral Proteins of the Erythrocyte Membrane

- Band 3 is composed of two *homodimers* of a glycoprotein that exchanges $Cl^-$ and $HCO_3^-$ across the red cell membrane.
- Glycophorin A is a dimer with negative charges that may prevent red cells from clumping.

# The Dynamic Nature of the Plasma Membrane




EM: inner membrane skeleton proteins

## The Erythrocyte Membrane Skeleton

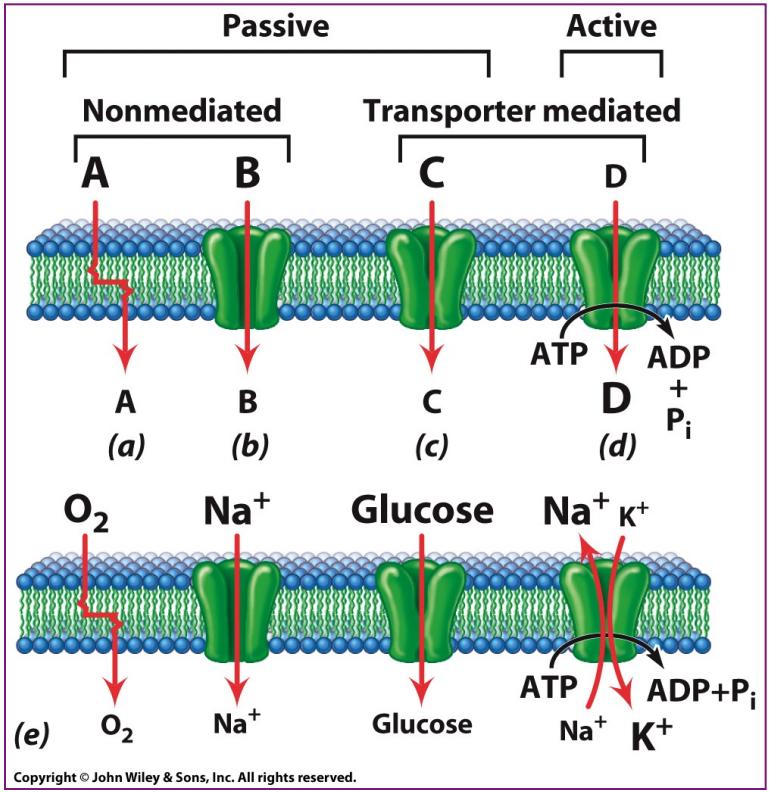
- The major component of the internal membrane skeleton is *spectrin*.
- Spectrin molecules are attached to the membrane surface by noncovalent bonds to *ankyrin*, a peripheral membrane protein which is noncovalently bonded to band 3.
- Spectrin is linked to other cytoplasmic proteins, such as *actin* and *tropomyosin*, which maintains the integrity of the membrane.

# MEMBRANE TRANSPORTATION

# Movement of Substances Across Cell Membranes

Selective permeability allows for separation and exchange of materials across the plasma membrane

- *Net flux* is the difference between *influx* and *efflux* of materials.
- Flux can occur by passive and/or active transport.

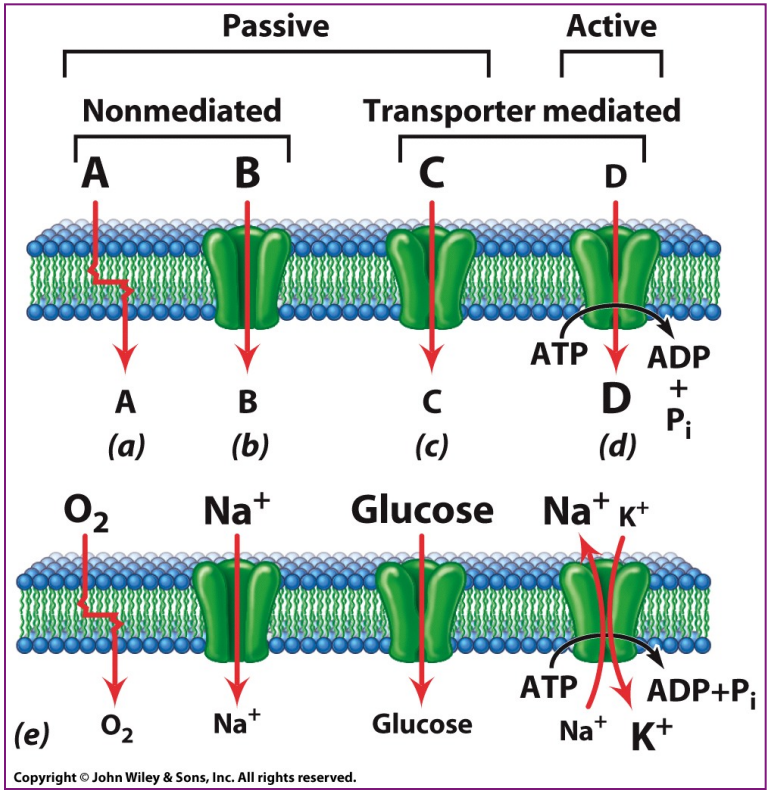



Four basic mechanisms by which solute molecules move across membranes

# Movement of Substances Across Cell Membranes

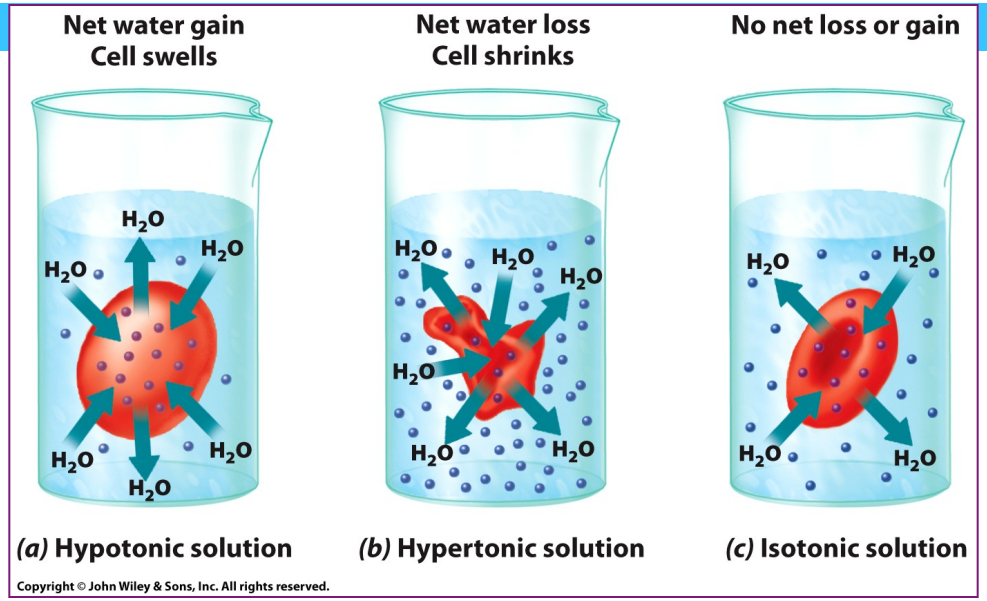
## The Energetics of Solute Movement

- **Diffusion** is the spontaneous movement of material from a region of high concentration to a region of low concentration.
- Movement during diffusion of nonelectrolytes depends on the concentration gradient.
- Movement during diffusion of electrolytes depends on the electrochemical gradient.




Four basic mechanisms by which solute molecules move across membranes

# Movement of Substances Across Cell Membranes




The effects of differences in the concentration of solutes on opposite sides of the plasma membrane

## The Diffusion of Water through Membrane

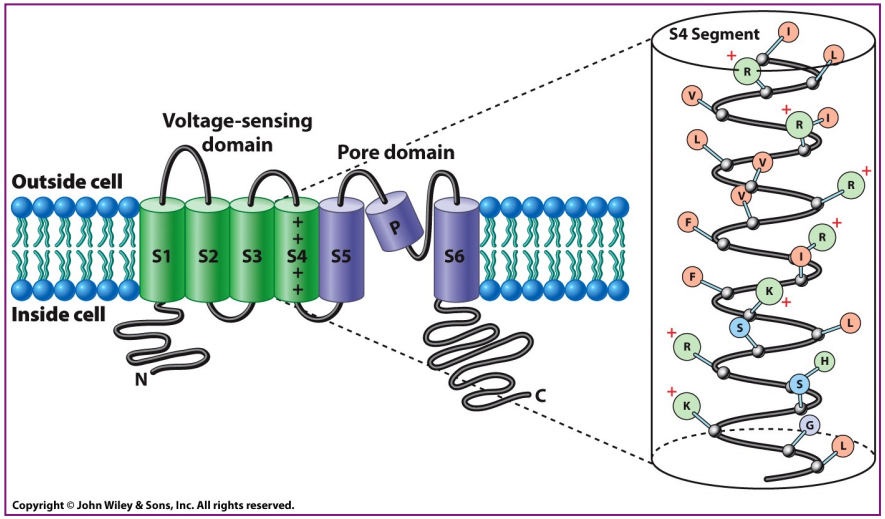
- Diffusion of water through a semipermeable membrane is called **osmosis.**
- Water diffuses from areas of lower solute concentration to areas of higher solute concentration.
- Cells swell in **hypotonic** solution, shrink in **hypertonic** solutions, and remain unchanged in **isotonic** solutions.

# Movement of Substances Across Cell Membranes

## Voltage-gated Potassium ($K_v$) channel

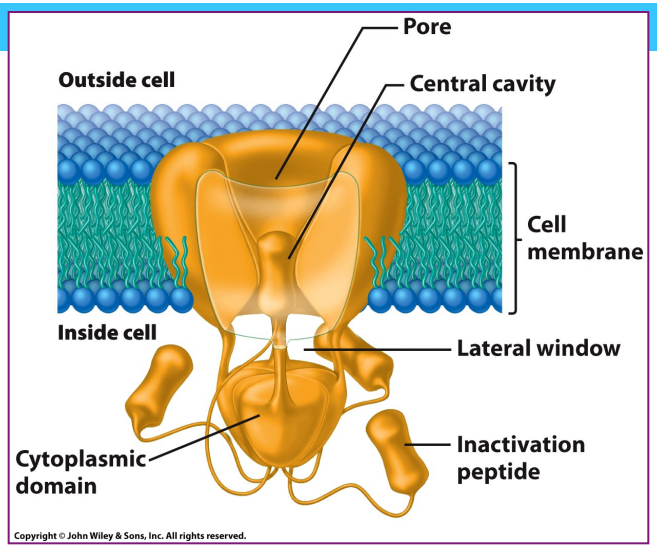
- both N and C termini are cytoplasmic
- contains six membrane-spanning helices. (S1-S6)
- Six helices can be grouped into two domains:
  - **Pore domain** – permits the selective passage of $K^+$ ions.
  - **Voltage-sensing domain** – consists of helices S1-S4 that senses the voltage across the plasma membrane.

The structure of a eukaryotic, voltage-gated $K^+$ channel

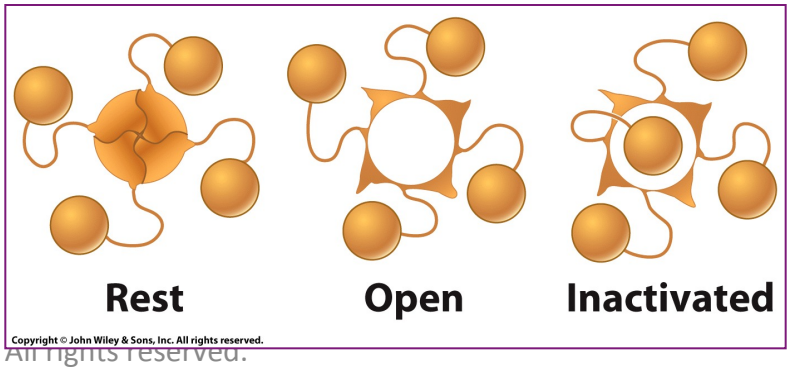


# Movement of Substances Across Cell Membranes

- K Channel can be opened, closed, or inactivated.
- Once opened, more than 10 million $K^+$ ions can pass through per second.
- After the channel is open for a few milliseconds, the movement of $K^+$ ions is "automatically" stopped by a process known as inactivation.




Conformational states of a voltage-gated $K^+$ ion channel



# Active Transport

# Movement of Substances Across Cell Membranes

## Active Transport

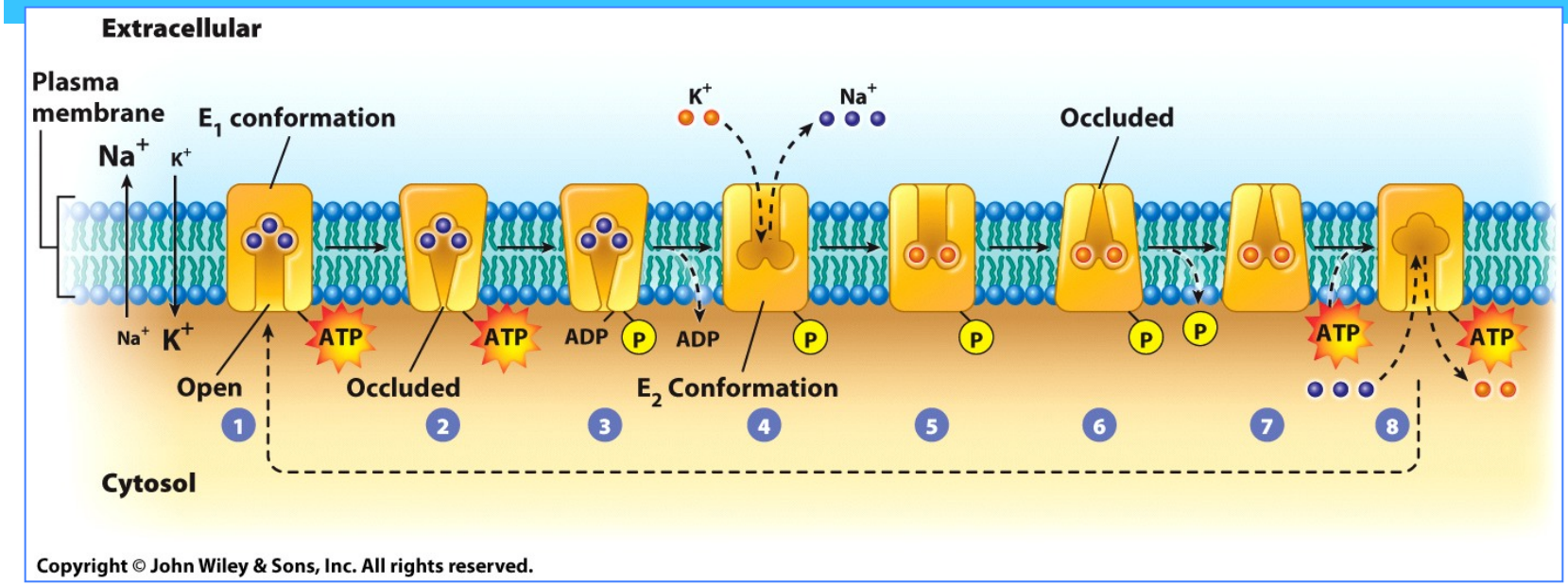
- Maintains the gradients for potassium, sodium, calcium, and other ions across the cell membrane.
- Couples the movement of substances against gradients to ATP hydrolysis.

**Table 4.3 Ion Concentrations Inside and Outside of a Typical Mammalian Cell**

| | Extracellular concentration | Intracellular concentration | Ionic gradient |
|---|---|---|---|
| $Na^+$ | 150 mM | 10 mM | 15× |
| $K^+$ | 5 mM | 140 mM | 28× |
| $Cl^-$ | 120 mM | 10 mM | 12× |
| $Ca^{2+}$ | $10^{-3}$ M | $10^{-7}$ M | 10,000× |
| $H^+$ | $10^{-7.4}$ M (pH of 7.4) | $10^{-7.2}$ M (pH of 7.2) | Nearly 2× |

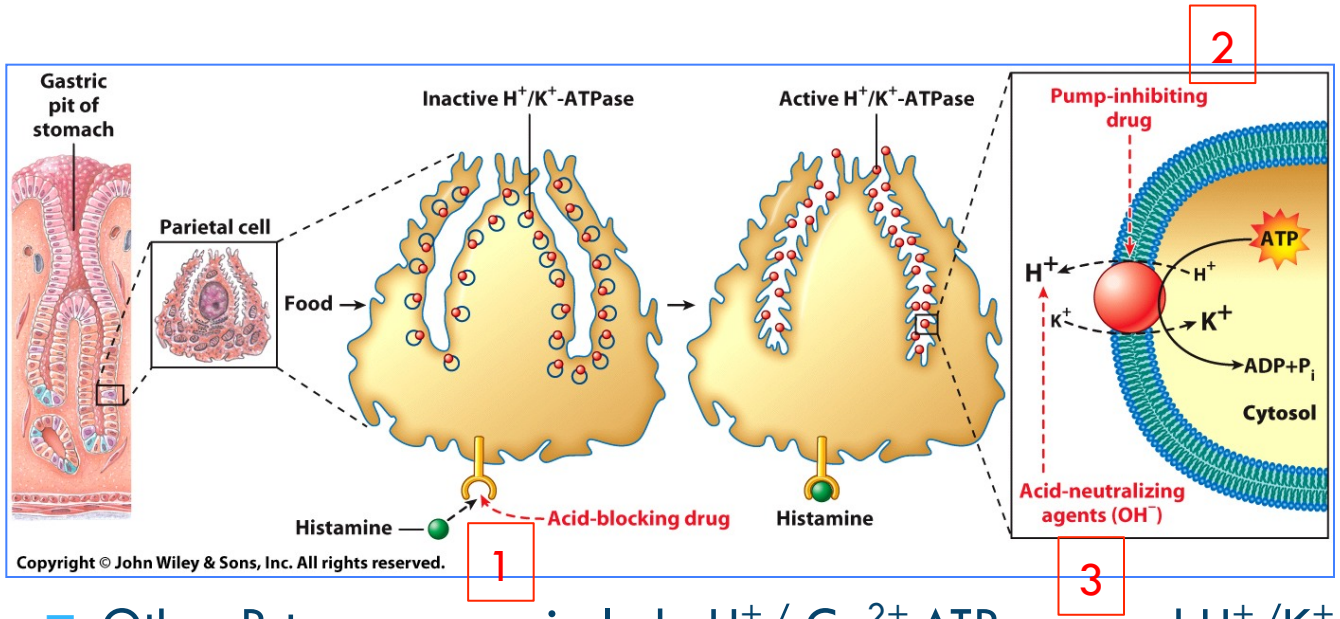
The ion concentrations for the squid axon are given on page 177.

# Movement of Substances Across Cell Membranes




- Coupling Active Transport to ATP Hydrolysis
  - The $Na^+/K^+$ ATPase (*sodium-potassium pump*) moves $K^+$ inside/$Na^+$ outside, and is inhibited by ***ouabain.***
  - The ratio of $Na^+$: $K^+$ pumped is 3:2.
  - The ATPase is a P-type pump, in which phosphorylation causes changes in conformation and ion affinity that allow transport against gradients.

# Movement of Substances Across Cell Membranes



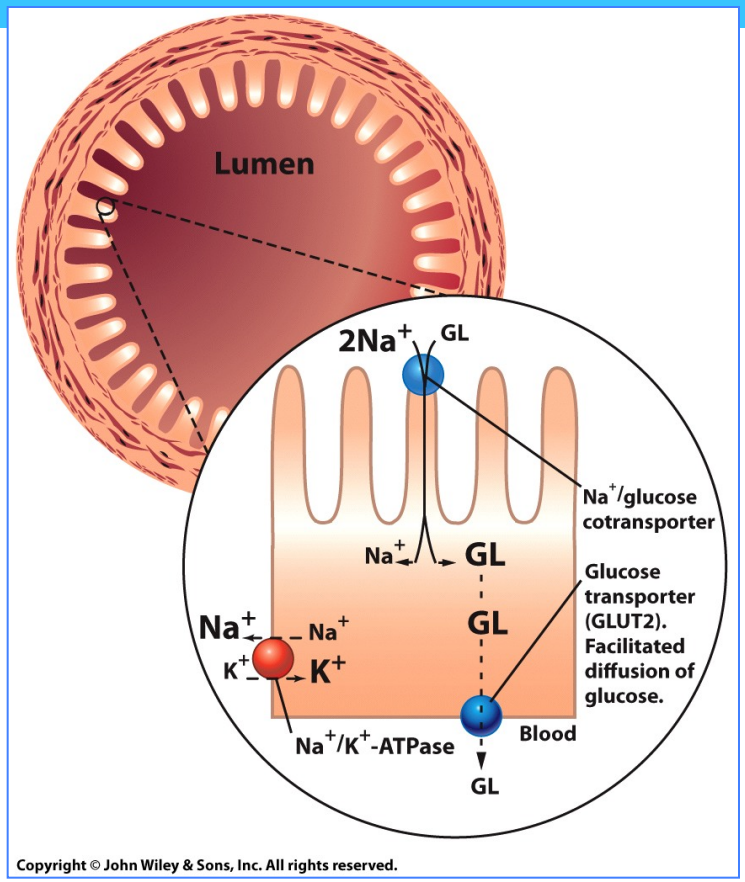

Control of acid secretion in the stomach

- Other P-type pumps include $H^+$/ $Ca^{2+}$ ATPases and $H^+/K^+$ ATPases.
- Vacuolar (V-type) pumps use ATP, but are not phosphorylated during pumping.
- Histamine activates the $H^+/K^+$ ATPase and thus transport of $H^+$ in the stomach lumen
- Acid formation in the stomach can be blocked by several mechanisms

# Movement of Substances Across Cell Membranes

**Secondary transport:**

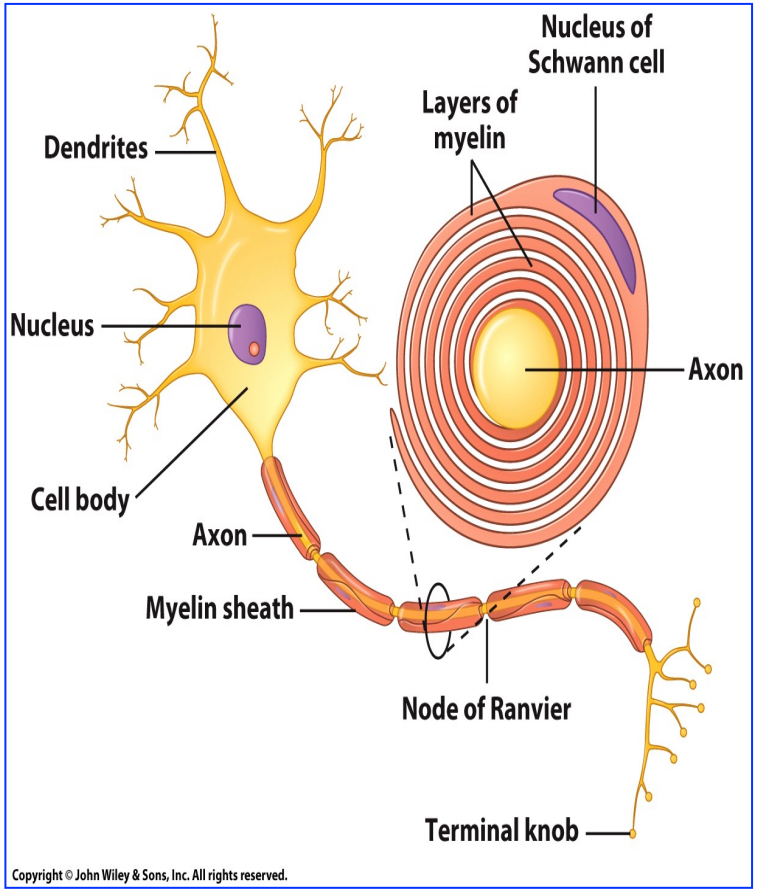
- Use of energy stored in an ionic gradient
- Coupling Active Transport to Existing Ion Gradients
  - Gradients created by active ion pumping store energy that can be coupled to other transport processes.




**Secondary transporter**: the Na+ gradient helps to transport glucose by a Na+/glucose co-transporter

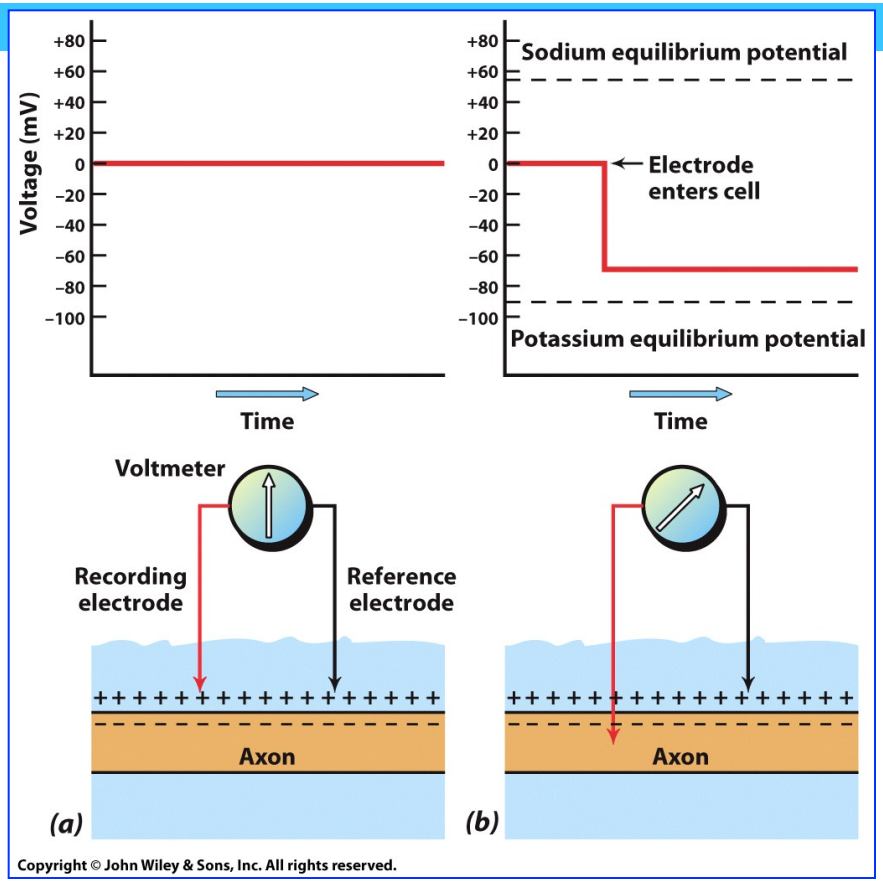
# Membrane Potentials and Nerve Impulses

- Potential differences exist when charges are separated.
- *Neurons* are specialized cells for information transmission using changes in membrane potentials.
  - **Dendrites** receive incoming information.
  - **Cell body** contains the nucleus and metabolic center of the cell.
  - The **axon** is a long extension for conducting outgoing impulses.
  - Most neurons are wrapped by **myelin-sheath.**



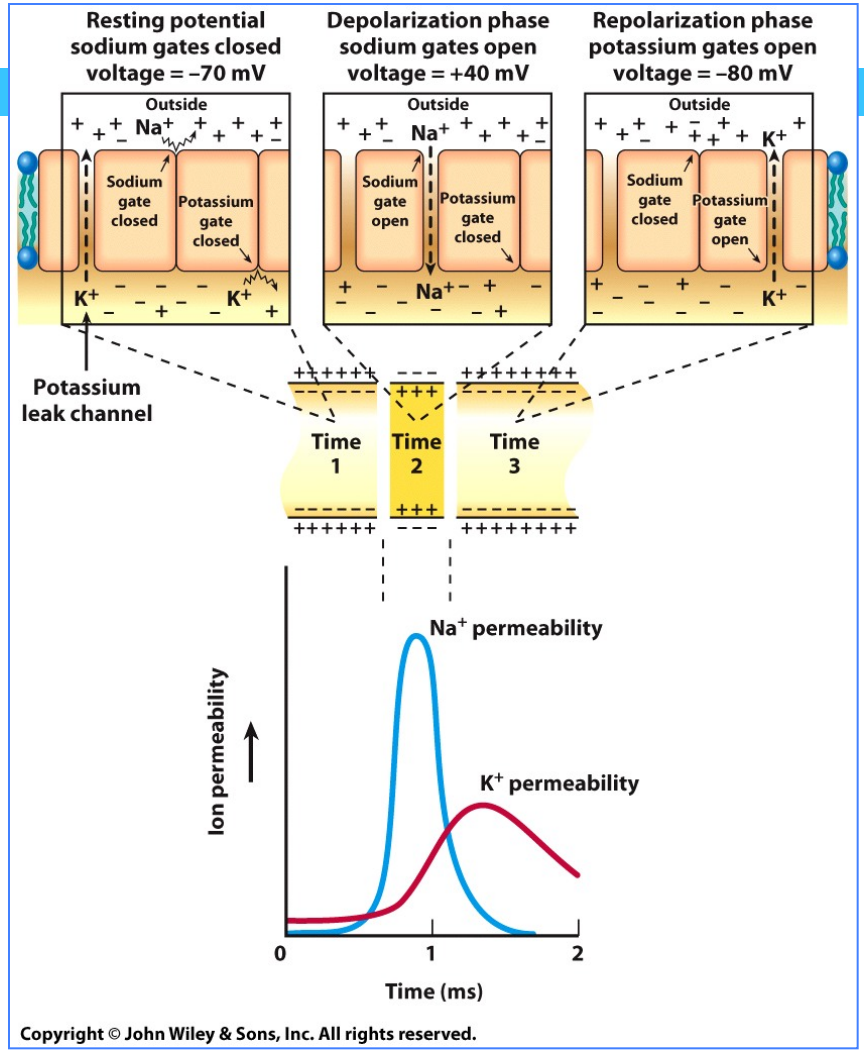
# Membrane Potentials and Nerve Impulses

- The **Resting Potential**
  - It is the membrane potential of a nerve or muscle cell, subject to changes when activated.
  - $K^+$ gradients maintained by the $Na^+/K^+$-ATPase are responsible for resting potential.



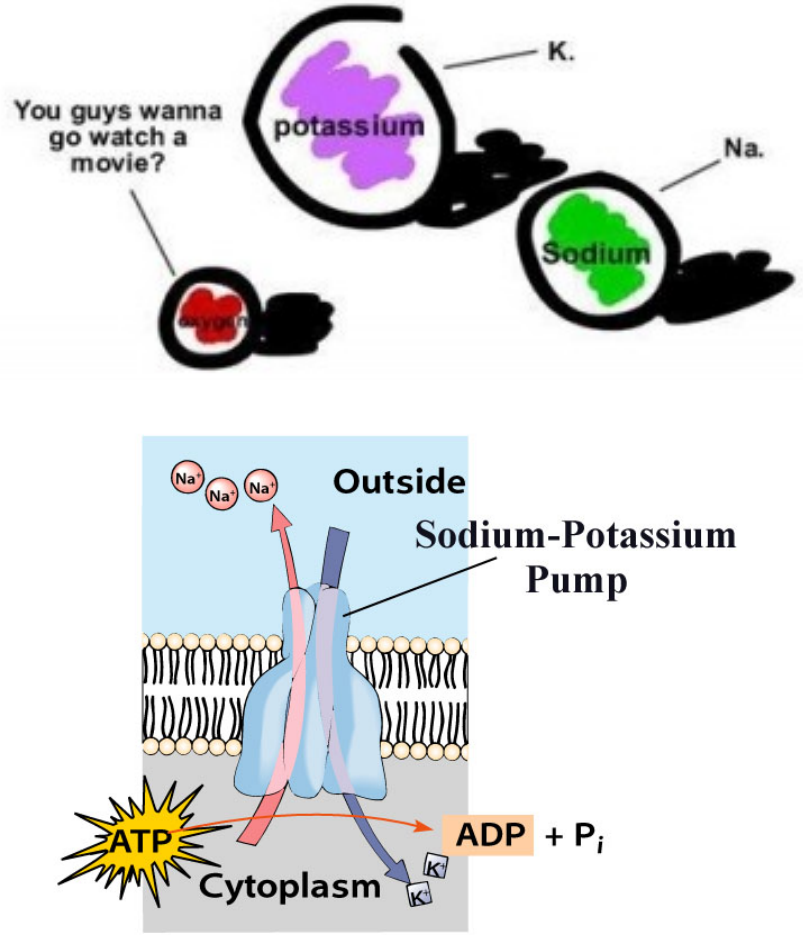
# Membrane Potentials and Nerve Impulses

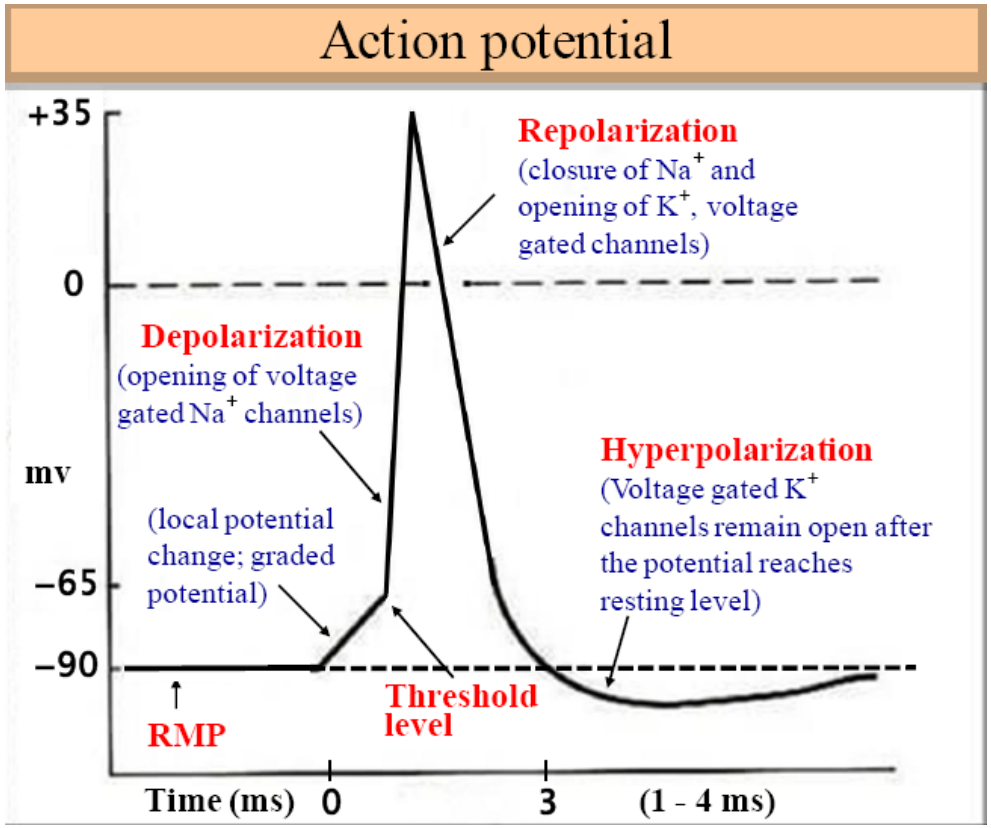
- The Action Potential (AP)
  - When cells are stimulated, voltage-gated $Na^+$ channels open, triggering the AP.
  - Opening of $Na^+$ channels, causes membrane **depolarization**.
  - $Na^+$ channels are inactivated immediately following an AP, producing a short *refractory period* when the membrane cannot be stimulated.




Formation of an action potential

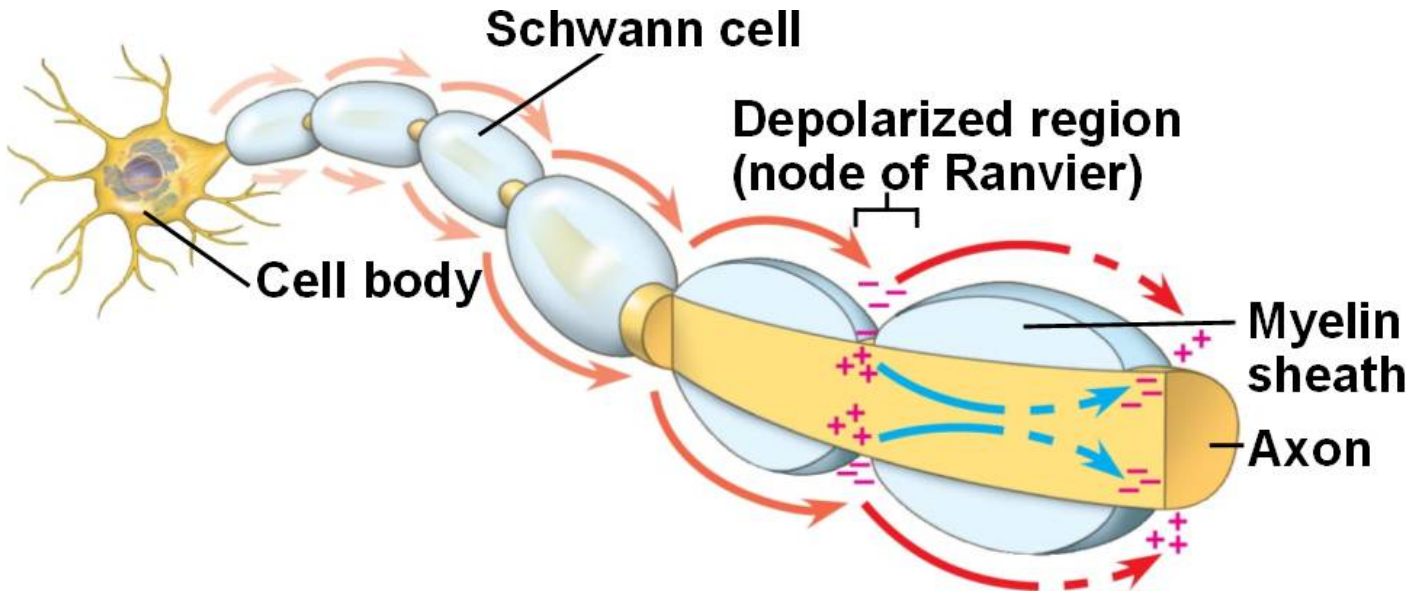
# Membrane Potentials and Nerve Impulses




Formation of an action potential

# Membrane Potentials and Nerve Impulses

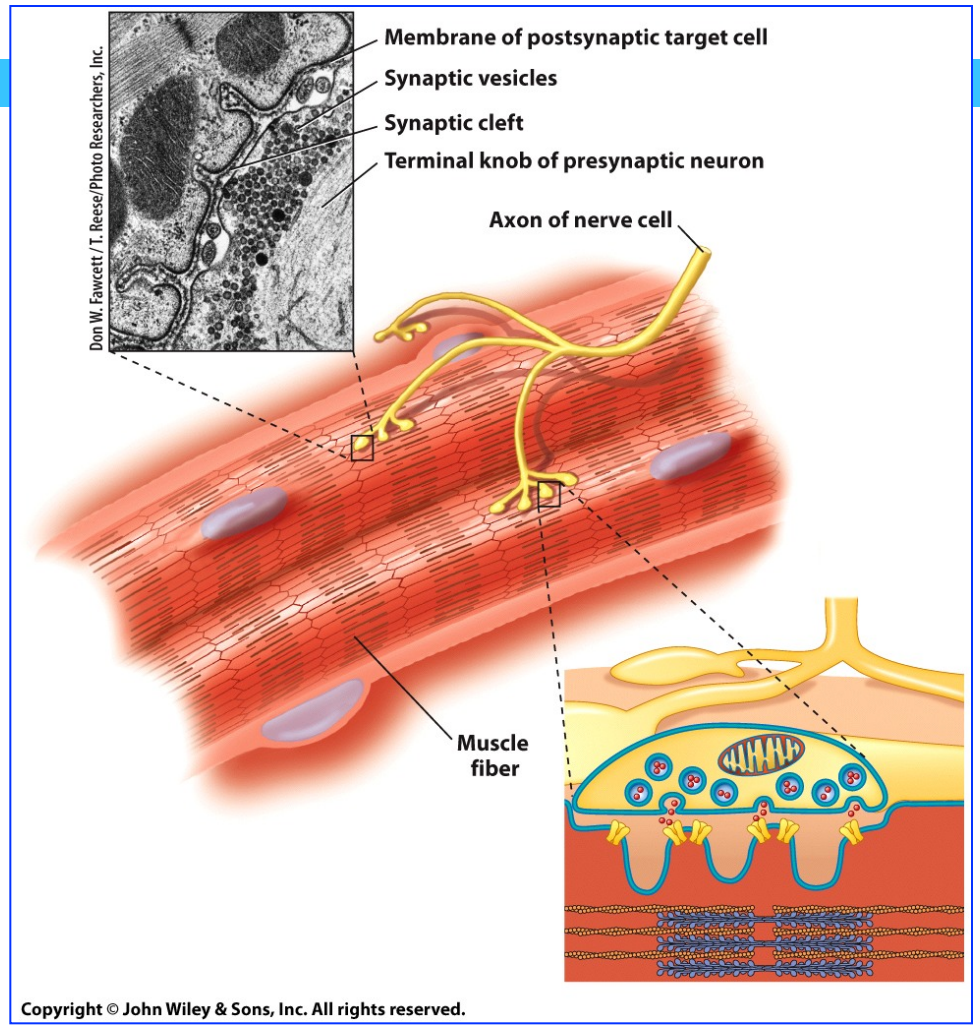



Saltatory Conduction is the propagation of action potentials along myelinated axons from one node of Ranvier to the next

# Membrane Potentials and Nerve Impulses

## Neurotransmission: Jumping the Synaptic Cleft

- **Presynaptic neurons** communicate with **postsynaptic neurons** at a specialized junction, called the **synapse,** across a gap (**synaptic cleft**).
- Chemicals (**neurotransmitters**) released from the presynaptic cleft diffuse to receptors on the postsynaptic cell.
- Bound transmitter can depolarize (excite) or hyperpolarize (inhibit) the postsynaptic cell.
- Transmitter action is terminated by reuptake or enzymatic breakdown.

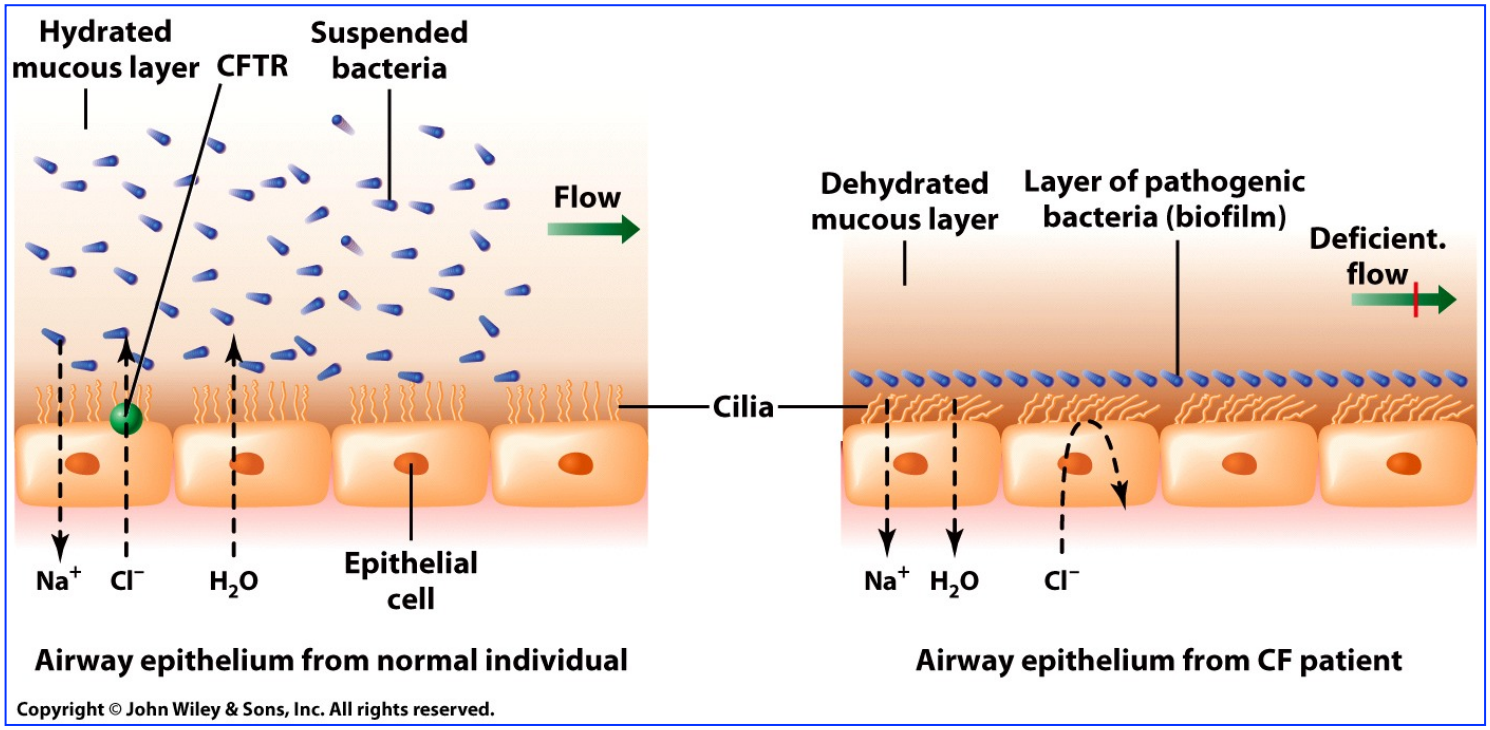



The neuromuscular junction

# The Human Perspective:
## Defects in Ion Channels as a Cause of Inherited Disease

- Several inherited disorders have been linked to mutations in genes encoding ion proteins channels.
- ***Cystic fibrosis (CF)*** is a genetic disease characterized by abnormal fluid secretions from tissues and caused by a defective chloride channel.
- A defect prevents normal insertion of the Cystic fibrosis transmembrane conductance regulator (CFTR) polypeptide into the membrane.
- Abnormal CFTR leads to a blockage of the movement of salt and water into and out of cells.
- Thick mucous traps bacteria that give rises to chronic infections

# The Human Perspective:
## Defects in Ion Channels as a Cause of Inherited Disease



# Some interesting links

https://www.youtube.com/watch?v=P-imDC1txWw
https://www.youtube.com/watch?v=yQ-wQsEK21E
https://www.youtube.com/watch?v=_slUL3kMZlU

# Put your thinking cap on….


1. Explain the correlation between Na/K pump and action potential.
2. What are the respective functions of phospholipids, proteins and carbohydrates of the cell membrane?