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CONCEPT: THE PLASMA MEMBRANE

Plasma Membrane Structure:

● The **plasma membrane** (or just "**cell membrane**") separates the cell itself from the outside extracellular fluid (ECF).

● The plasma membrane is primarily made of ___________________________.

□ Phospholipids have charged phosphate head groups on one end and two hydrocarbon chains on the other end.

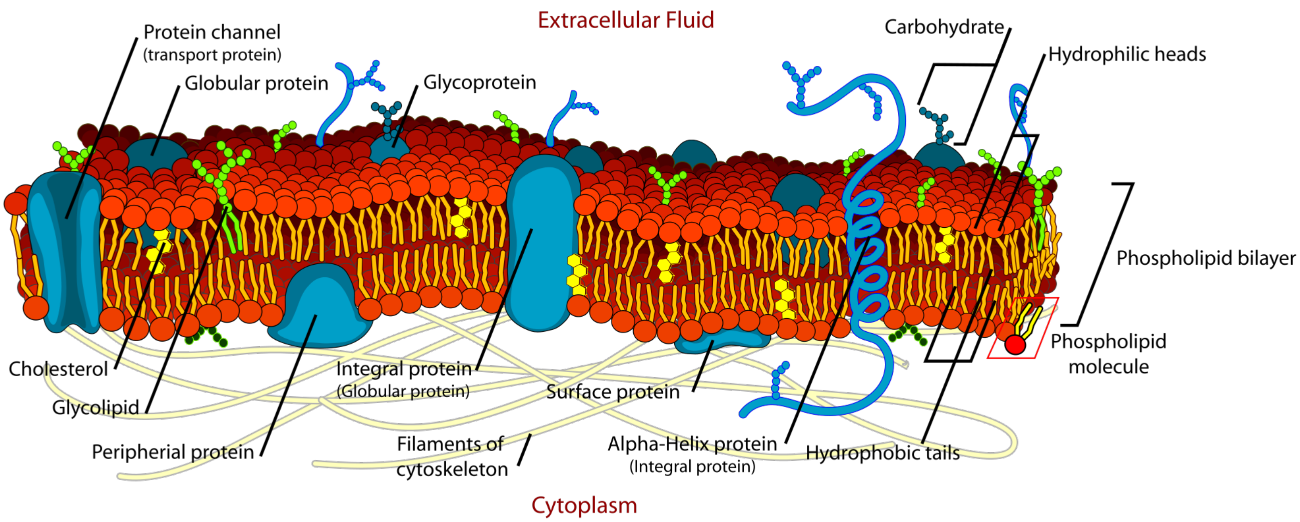
-The head groups are ___________________, so they face outward toward the aqueous cytosol or ECF.

-The hydrocarbon chains are nonpolar, so they face inward toward each other.

● The plasma membrane also has lots of proteins inserted in or on the membrane.

□ The **Fluid Mosaic Model** describes the idea that the membrane is a highly ____________________ surface with a variety of proteins and other molecules floating around.

EXAMPLE: The Fluid Mosaic Model of cell membranes.

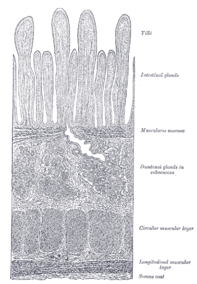


Communication at the Membrane—Membrane Surface Area

● Cell membranes are the site of ____________________________ between the cell and the outside world.

□ The surface area of the membrane is very important: ↑Surface Area→↑Contact with ECF→↑Exchange

EXAMPLE: Microvilli increase the total membrane surface area and, thus, increase exchange.



Communication at the Membrane—Membrane Proteins:

● The membrane is the key site of communication between the cell and the outside world, including other cells.

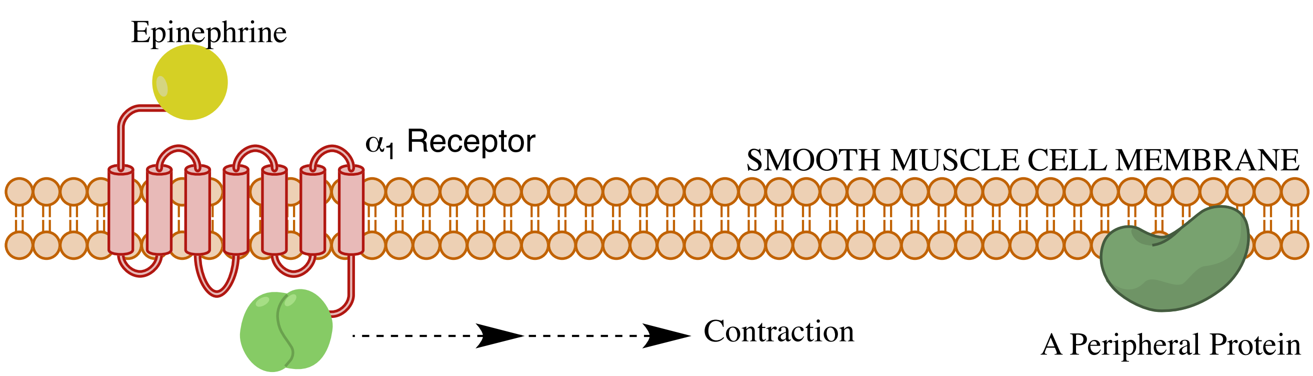
□ **Transmembrane proteins**—like receptors and ion channels—span the ____________________ membrane, allowing molecules outside of the cell to cause changes inside the cell without actually penetrating the membrane.

□ **Peripheral proteins** are anchored in the membrane and project into either the cytosol or the ECF (but not both).

□ **Junctions** are connections between the membranes of adjacent cells (more later).

-**Tight Junctions** hold adjacent cells together; **Gap Junctions** connect the cytosol of neighboring cells.

EXAMPLE: Activation of α_1 receptors—a transmembrane protein—by epinephrine causes smooth muscle contraction.



α_1 adrenergic receptors are G-protein-coupled receptors on smooth muscle. On the ECF side they bind to the hormone epinephrine. On the inside they activate a pathway that ultimately causes smooth muscle contraction. (By contrast, peripheral proteins contact only one side of the membrane.)

PRACTICE 1: The epithelial cells that line the small intestine have microvilli, which helps them to absorb macro- and micronutrients from food within the lumen of the small intestine. Microvilli accomplish this by:

a) Mixing the food.
b) Increasing the surface area of the membrane.
c) Keeping the food close to the cell surface.

PRACTICE 2: Muscarinic acetylcholine receptors (mAchRs) are proteins inserted in the membranes of various body cells. On the outside of the cell these proteins bind acetylcholine. On the inside of the cell they bind to and activate a type of protein called a GTPase. For an mAchR to bind to molecules that are both outside and inside of the cell, which of the following must it be?

a) Transmembrane protein.
b) Peripheral protein.
c) Junction.

CONCEPT: CELL-TO-CELL CONNECTIONS AND SIGNALING

Gap and Tight Junctions:

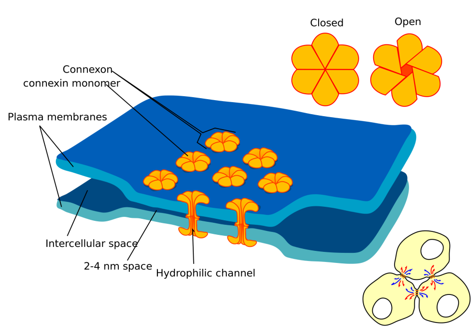
● *Adjacent* cells communicate and hold on to each other via **junctions.** Two important kinds:

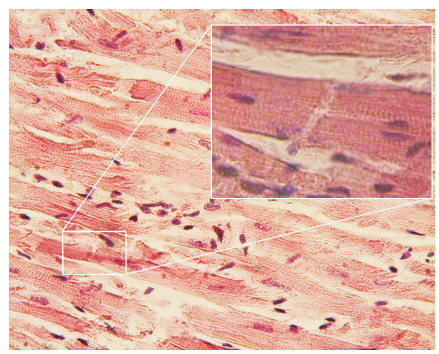
● **Gap Junctions** are small connections—like ________________—between the cytoplasm compartments of adjacent cells.

□ Allow for free exchange of small molecules and ions.

□ Made from an outgrowth of hexagonal proteins with a pore in the middle called a **connexon.**

EXAMPLE: Gap junctions in the heart allow heart muscle cells to freely exchange ions. These ions cause contraction. So, this arrangement allows heart cells to “communicate” with each other and contract in a uniform, coordinated manner.





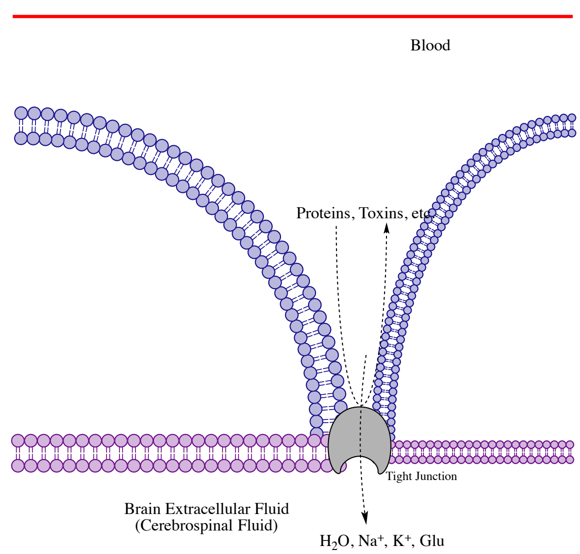
● **Tight Junctions** hold adjacent cells together, creating a layer of cells and forming a __________________________.

□ Common and important in epithelial and endothelial cell layers, like in the capillaries or gut.

□ The relative “leakiness” of tight junctions determines what can cross these cell layers.

□ *Paracellular* transport happens through/across tight junctions.

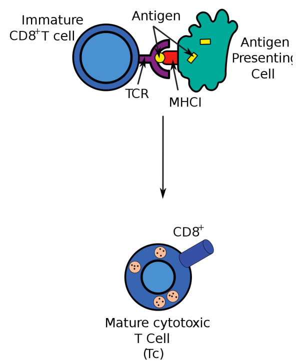
EXAMPLE: Tight junctions in the liver are very open and loose, allowing large molecules (even many proteins) to freely pass. The tight junctions in the brain are very, very tight, allowing only the smallest molecules—ions and glucose—to pass. (This is called the Blood Brain Barrier.)



Contact-Dependent Signaling:

● In **contact-dependent signaling**, one cell expresses a ligand on its membrane and the other expresses a receptor.

EXAMPLE: In the immune system, CD8+ T cells (Killer T Cells) are activated by having the T-cell receptor (TCR) on their cell membranes bind to a ligand called MHC I on antigen-presenting cells.



Secreted Signaling Molecules:

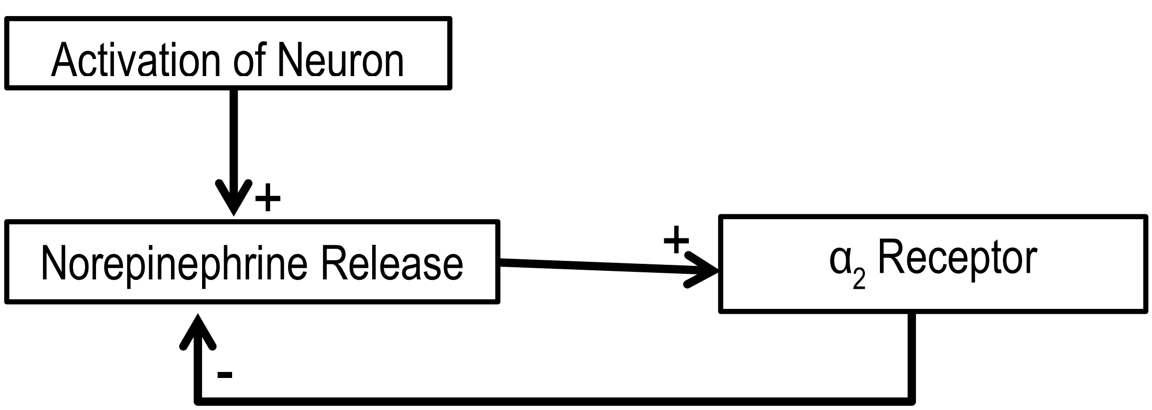
● Many cells secrete (export) proteins that act on other cells by activating __________________ on their cell membranes.

□ **Endocrine** signals are secreted into the bloodstream and travel throughout the whole body.

□ **Paracrine** signals are secreted into the ECF and affect only neighboring cells.

□ **Autocrine** signals are secreted into the ECF and bind back onto itself—receptors on the same cell's membrane.

EXAMPLE: Specific neurons in the peripheral nervous system, upon being activated, release a neurotransmitter called norepinephrine (NE). NE binds to receptors on target organs and causes various effects. NE *also* binds to α_2 receptors on the neuron itself, stopping the release of more NE. This is autocrine signaling and a small negative feedback loop.



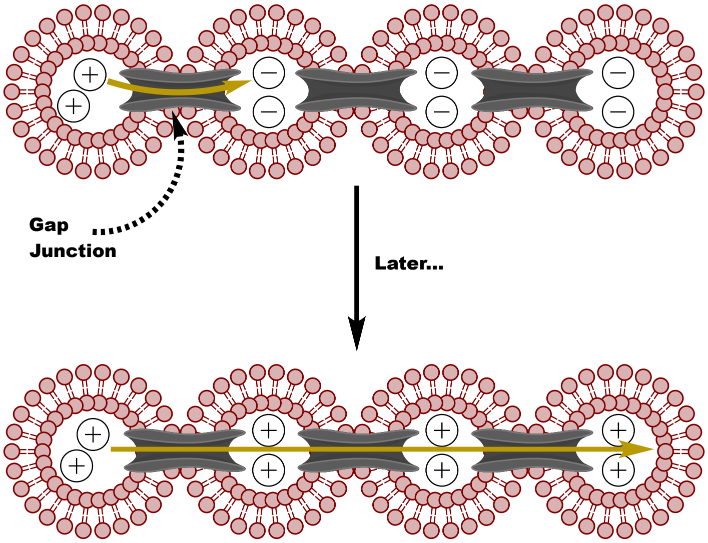
Activation of Neuron→↑NE Release→↑α_2 Receptor Activation→↓NE Release

Electrical Signaling:

● Finally, many cells communicate with one another by causing changes in their respective membrane potentials.

□ Every cell has an inside-negative V_m at rest. If they become flooded with positive charge, V_m changes.

EXAMPLE: Gap junctions between heart cells let them “share” and spread electrical messages.



As mentioned earlier, heart cells are connected by gap junctions, which allow neighboring cells to exchange ions between their respective cytoplasm. So, if one cell becomes flooded with positive charge and thus has a change in membrane potential, that will also happen to the cells with which it is in contact.

PRACTICE 1: Cells in the adrenal medulla secrete a molecule called epinephrine into the *bloodstream.* Epinephrine travels through the body to affect a variety of organs, including the heart and gut. Which of the following describes the type of signaling exhibited by epinephrine secreted from the adrenal medulla?

a) Exocrine.
b) Endocrine.
c) Paracrine.
d) Autocrine.

PRACTICE 2: ECL cells in the stomach secrete a molecule called histamine. That histamine then diffuses through the *extracellular fluid* to bind to and affect neighboring cells. Which of the following describes the type of signaling exhibited by histamine secreted secreted from ECL cells in the stomach?

a) Exocrine.
b) Endocrine.
c) Paracrine.
d) Autocrine.

CONCEPT: DIFFUSION

Diffusion, Qualitatively:

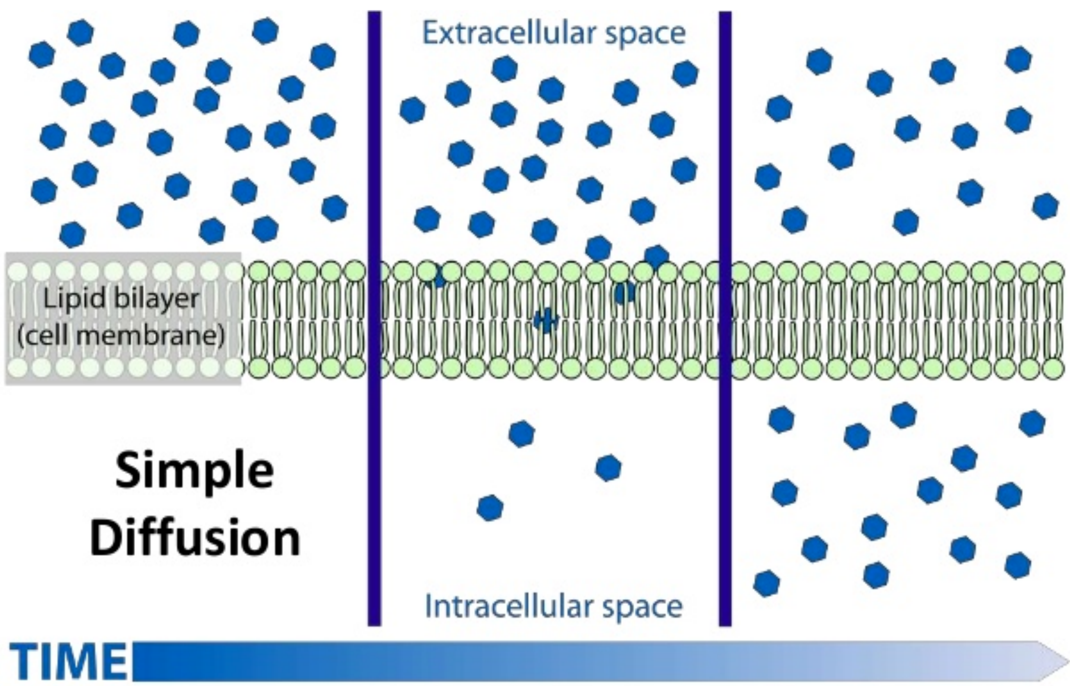
● **Diffusion** is the simple movement of solute from an area of higher concentration to an area of lower concentration.

- □ Entirely passive—no ______________________ expenditure is required.
- □ Happens from higher concentration→lower concentration.
  - - Net movement until concentrations are equal everywhere.
- □ ↑Diffusion rate for ↑Temperature and ↓Molecular Size/Weight.

● Diffusion into and out of cells must happen across cell membranes, which are __________________________.

- □ Lipophilic (i.e. nonpolar) solutes are the major solutes that enter cells via simple diffusion.
- □ Hydrophilic (i.e. polar) solutes need to be transported across the membrane (more later).

EXAMPLE: Nonpolar solutes cross the cell membrane into cells via diffusion, moving from an area of higher concentration (the extracellular space) to an area of lower concentration (the intracellular space).



Diffusion, Quantitatively—Fick's Law:

● Mathematically, the rate of diffusion through membranes can be described by **Fick's Law: J=PA(ΔC)**, where:

□ J is the **flux** (the amount of solute moving per unit time) across the membrane.

□ P is the **permeability** of the membrane to the solute; if the solute can cross more easily, it crosses more quickly.

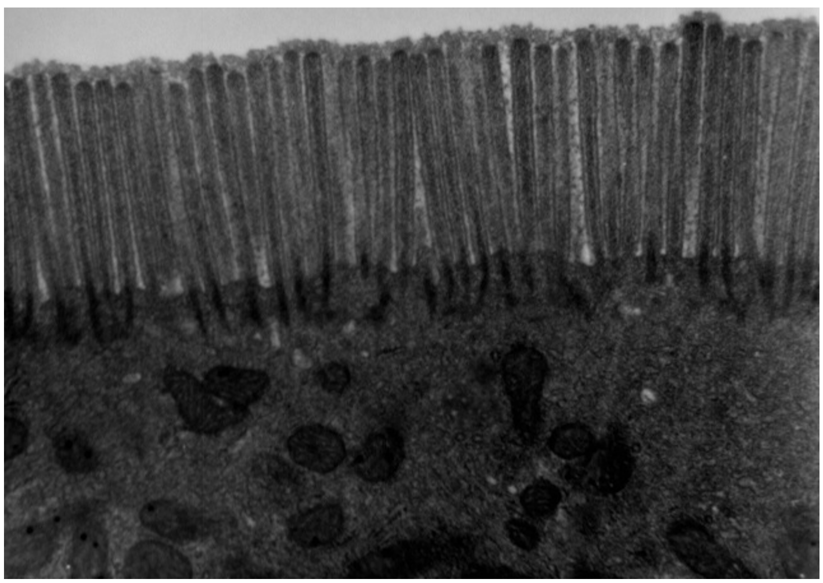
- A higher value of P means that the solute crosses more _______________________.

- Nonpolar molecules or molecules that can be transported typically have higher values of P.

□ A is the **surface area** of the membrane. More surface area means more "opportunity" for solute to cross.

□ ΔC is **concentration gradient** (the difference in solute concentration between the two side).

EXAMPLE: Microvilli that increase the available membrane surface area (↑A in Fick's Law), increasing the diffusion rate.



PRACTICE 1: The walls of capillaries—where all of the exchange between the blood and body takes place—are made of endothelial cells. Tight junctions are proteins that hold adjacent endothelial cells together and prevent too much from crossing. After injury, damaged cells release molecules that loosen tight junctions. Which variable in Fick's Law is affected by injury?

a) Permeability (P).
b) Surface Area (A).
c) Concentration Gradient (ΔC)

PRACTICE 2: The walls of capillaries—where all of the exchange between the blood and body takes place—are made of endothelial cells. Tight junctions are proteins that hold adjacent endothelial cells together and prevent too much from crossing. After injury, damaged cells release molecules that loosen tight junctions. How will this affect flux (J)?

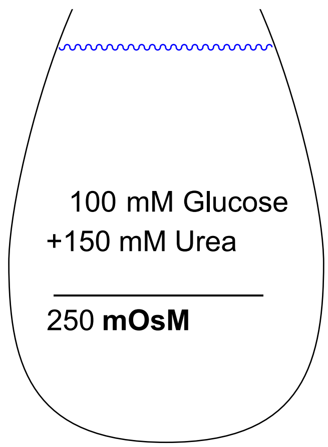
a) Increase J (more flux).
b) Decrease J (less flux).
c) No change.

CONCEPT: OSMOSIS: OSMOLARITY, OSMOTIC PRESSURE, AND TONICITY

Osmolarity:

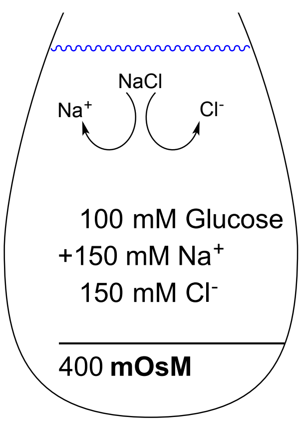
- The concentration of a *specific* solute is calculated by taking the amount of *that solute* and dividing by the volume it's in.
  - □ Concentrations are expressed in units like **molar** (M, mols/liter) or **millimolar** (mM, millimoles/liter).
- **Osmolarity** (adjective: osmolar, OsM) is the concentration of *any and every* solute in a ________________.
  - □ OsM=Total Solutes/Total Volume.

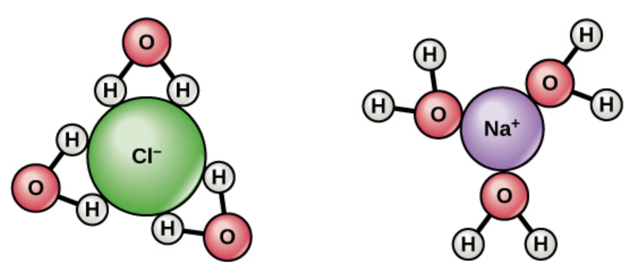
EXAMPLE: The osmolarity of a solution containing 100 mM glucose *and* 150 mM urea is 250 mOsM.



- Many ionic solutes ________________________ in water. This must be accounted for when calculating osmolarity.
  - □ For example, NaCl dissociates in water into Na^+ and Cl^-, two separate solutes that individually add to osmolarity.

EXAMPLE: OsM of a solution containing 100 mM glucose and 150 mM NaCl is 400 mOsM because NaCl dissociates.



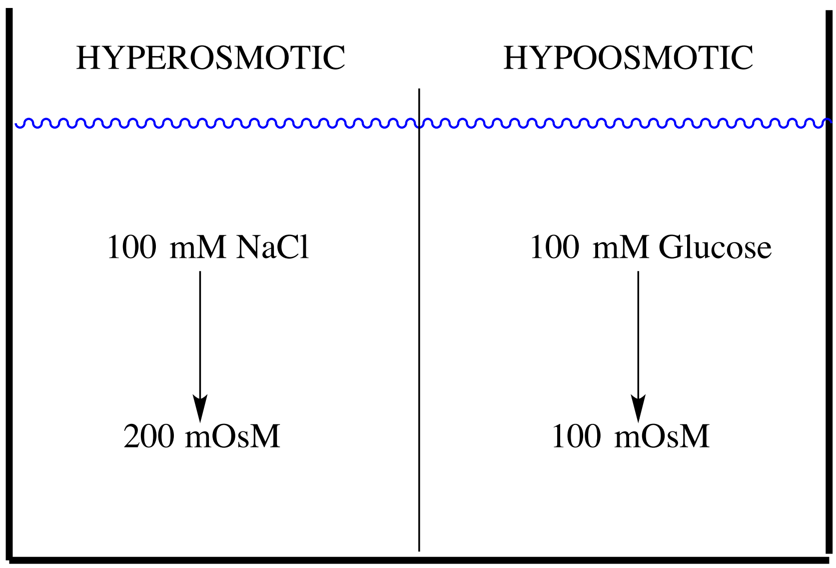


Hyper- vs. Hypo- vs. Iso*osmotic*:

● It's often useful to compare the osmolarities of 2+ solutions separated from each other by a ______________________.

- □ **Hyperosmotic** means the OsM of one solution is *greater* than the OsM of the other.
- □ **Hypoosmotic** means the OsM of one solution is *less* than the OsM of the other.
- □ **Isoosmotic** means that both solutions have the same OsM.

EXAMPLE: Two solutions—one with 100 mM NaCl, the other with 100 mM Glucose are separated by a membrane. The NaCl solution is 200 mOsM, and is therefore hyperosmotic to the 100 mOsM solution.



Osmosis:

● **Osmosis** is the process by which water moves across a _______________________ from one solution to another.

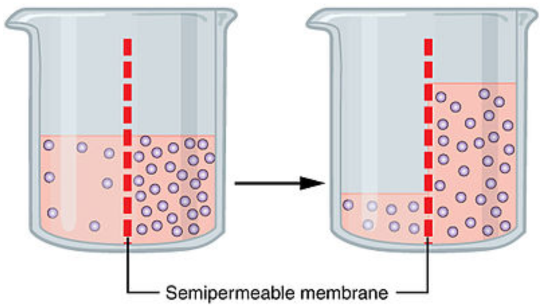
□ This depends heavily on the **permeability** of the membrane—what can cross the membrane and what can't.

● If the membrane separating two solutions is permeable to *both* the solute and water, the two solutions will equilibrate so that there are equal volumes, concentrations of individual solutes, and osmolarities on both sides.

● If the membrane is permeable to *water but impermeable to solute*, water will move to the more concentrated solution.

□ This serves to dilute the more concentrated solution with increased volume, thus equilibrating osmolarities.

EXAMPLE: Water moves into the compartment with the higher osmolarity, increasing its volume.



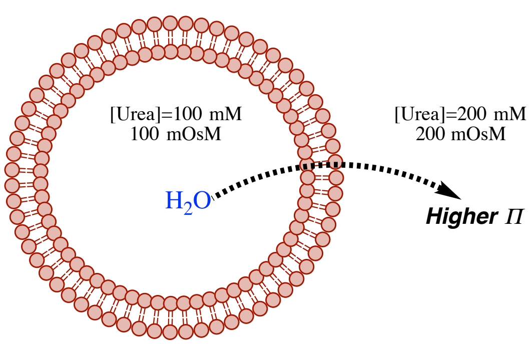
Osmotic Pressure:

● **Osmotic Pressure (Π)** is the tendency of more concentrated solutions to ________________ water toward themselves.

□ (Technically, osmotic pressure is the pressure that must be applied to *stop* that movement of water.)

□ *Hyperosmotic* solutions have higher osmotic pressures, and thus pull water toward themselves more.

EXAMPLE: The inside of a red blood cell and the extracellular fluid are separated by the cell membrane, which is permeable to water but not to urea. If $[Urea]_{inside}$=100 mM and $[Urea]_{outside}$=200 mM, then the outside of the cell has a higher osmotic pressure, and will pull water toward itself.



Tonicity:

● Osmotic pressure determines the direction that water actually travels across a membrane.

● The **tonicity** of a solution describes whether or not water actually moves into it.

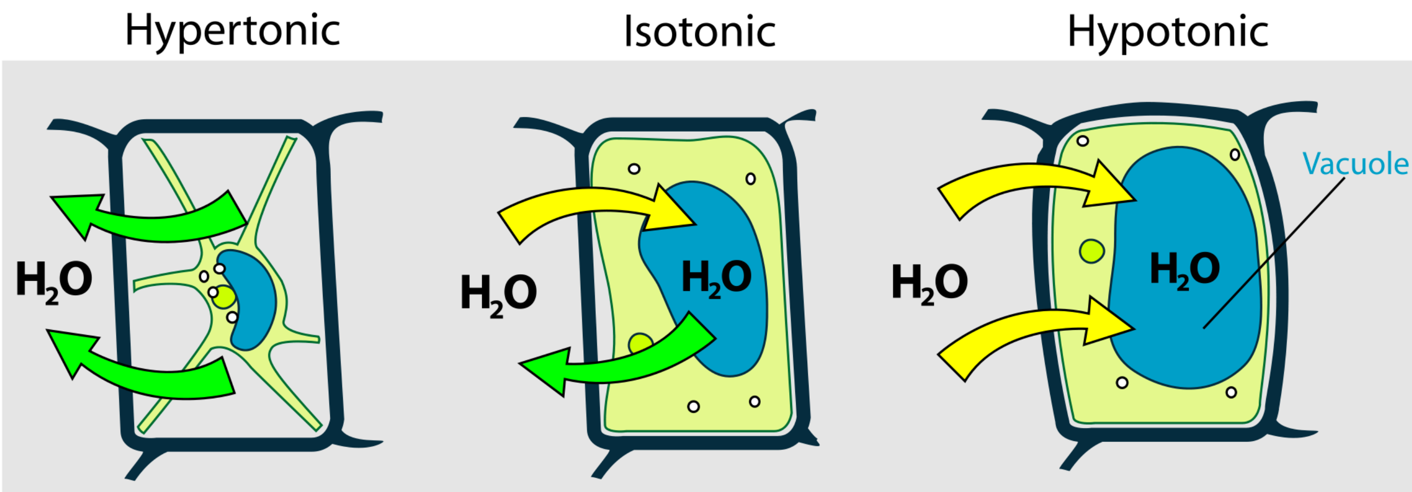
  □ The **hypertonic** side of a membrane pulls water more strongly, and thus *gains volume*.

  □ The **hypotonic** side of a membrane loses water, and thus loses volume.

  □ In an **isotonic** state, neither side's volume changes.

● *Hyperosmotic Solution→Higher Osmotic Pressure→Hypertonic Solution*.

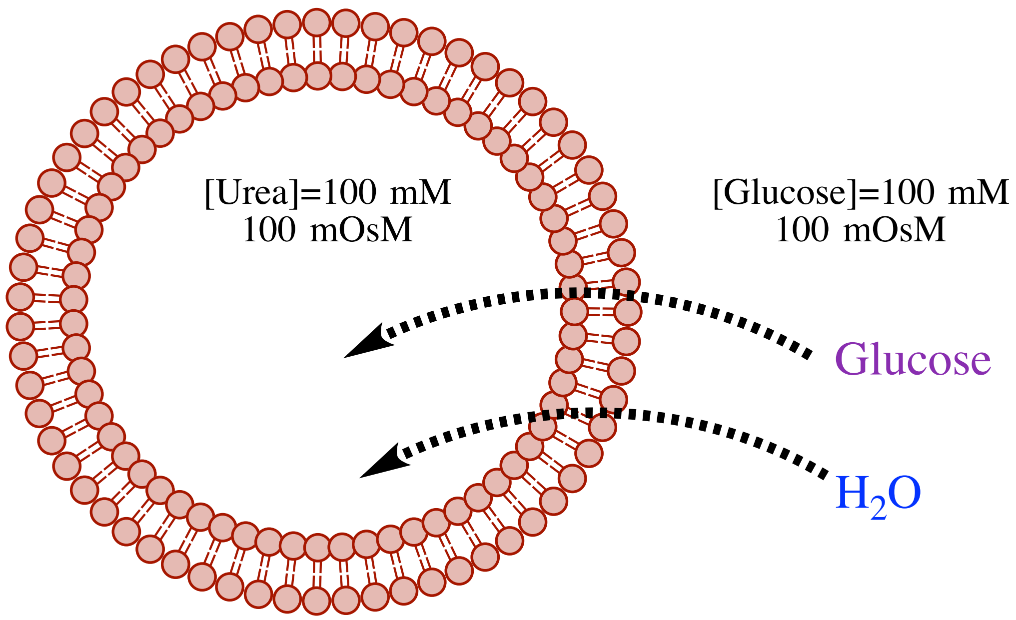
EXAMPLE: Cells suspended in hypertonic solutions shrink, while cells in hypotonic solutions swell.



Isoosmotic But Not Isotonic—A More Complicated Example:

● There are cases where each side starts out isosmotic. But, because of the permeability of the membrane, individual solutes may follow their concentration gradients and cross the membrane, bringing water with them.

EXAMPLE: This cell is in an isoosmotic solution. But, because of the permeability of the membrane, the cell is hypertonic.



A cell—filled only with 100 mM Urea—is placed in a solution of 100 mM Glucose. The membrane is permeable to glucose, but not to urea. At the beginning, the two sides are isoosmotic. However, there's a concentration gradient for glucose. Glucose will move down its concentration gradient into the cell. This will briefly increase the OsM inside the cell. So, water will follow, and the cell will swell. The sides were isoosmotic to begin with, but the cell is hypertonic.

PRACTICE 1: An undergraduate playing around in lab combines 1 L of pure water, 150 mmols of glucose, and 150 mmols of KCl. Assuming complete dissociation, which of the following is the *osmolarity* of the resulting solution?

a) 150 mOsM.
b) 300 mOsM.
c) 450 mOsM.
d) 600 mOsM.

PRACTICE 2: Filtrate inside of the nephron (part of the kidney) has an osmolarity of 500 mOsM. Fluid outside of the nephron has an osmolarity of 750 mOsM. Which of the following describes the fluid *inside of the nephron relative to the fluid outside of the nephron.*

a) Hyperosmotic.
b) Hypoosmotic.
c) Isoosmotic.

PRACTICE 3: Filtrate inside of the nephron (part of the kidney) has an osmolarity of 500 mOsM. Fluid outside of the nephron has an osmolarity of 750 mOsM. Assume that water can move between the compartments, but solute cannot. Which compartment is hypertonic, and what is going to happen to the volume of that compartment?

a) Inside the nephron; increase in volume.
b) Inside the nephron; decrease in volume.
c) Outside the nephron; increase in volume.
d) Outside the nephron; decrease in volume.

PRACTICE 4: The cytosol of red blood cells is approximately 300 mOsM, mostly from NaCl. You place the RBC in a extracellular solution of 600 mM sucrose. RBC membranes are not permeable to NaCl or sucrose. Circle the answer.

a) Which solution is hyperosmotic? (Cytosol / Extracellular Solution)

b) Which solution has a higher osmotic pressure? (Cytosol / Extracellular Solution)

c) Which direction will water move? (Toward Cytosol / Toward Extracellular Solution)

d) Which solution is hypertonic? (Cytosol / Extracellular Solution)

e) What will happen to the volume of the RBC? (Increase / Decrease)

CONCEPT: PROTEIN-MEDIATED TRANSPORT

Passive Transport:

● **Passive Transport** is the movement of molecules across cell membranes *down their concentration* ________________.

□ No energy/ATP required.

□ Accomplished by transmembrane channel proteins and carrier proteins.

● **Channel Proteins** form open passageways from the outside of the cell to the inside.

□ Passages filled with water, allowing hydrophilic molecules to cross otherwise hydrophobic cell membrane.

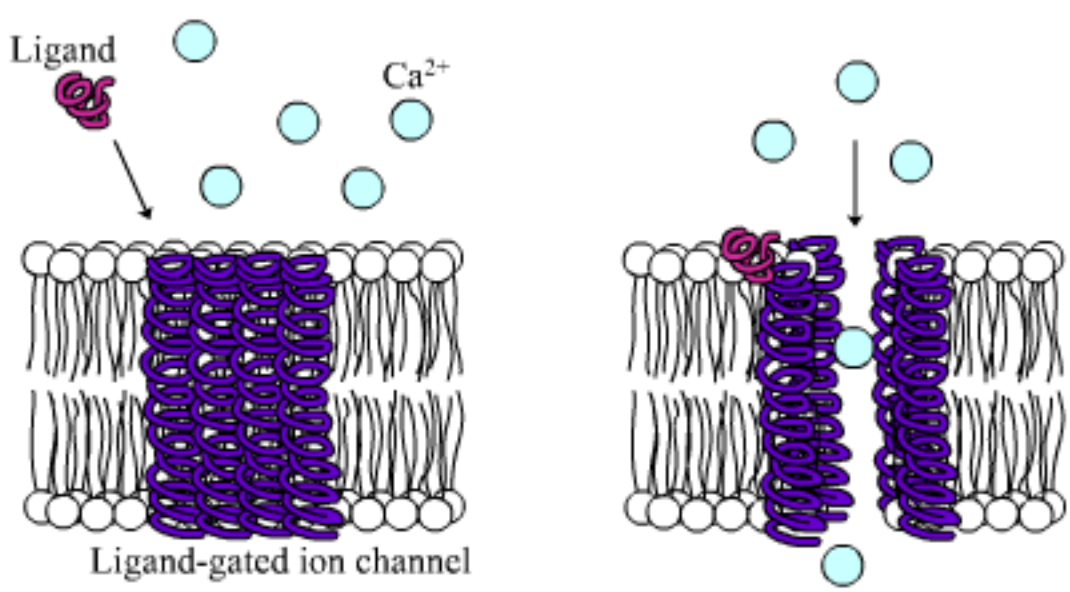
● Some channels are constantly open, while others are closed ("gated") and opened by specific _____________________.

□ **Chemically-gated channels** open when activated by an intracellular or extracellular molecular messenger.

□ **Voltage-gated channels** open when the transmembrane _____________________ changes (more later).

□ **Mechanically-gated channels** respond to outside physical forces—pressure, temperature, etc.

EXAMPLE: Ligand-gated channels are chemically-gated—a ligand binds to the channel, and it opens.



Carrier Proteins and Facilitated Diffusion:

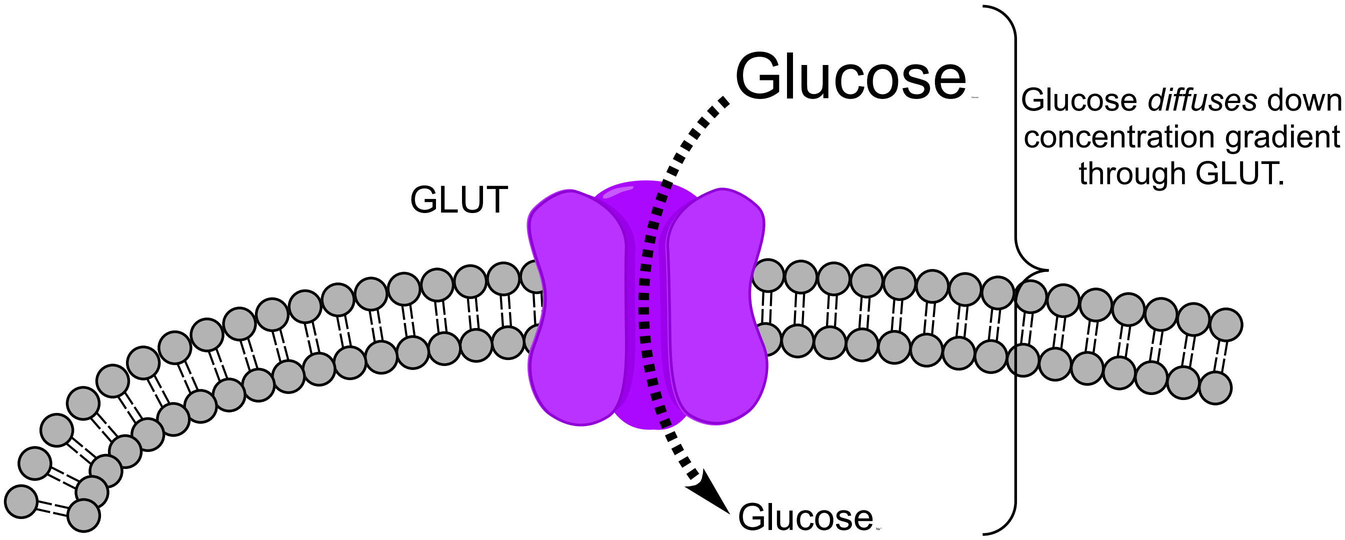
● **Carrier Proteins** bind to a molecule or molecules and change conformation, moving the molecules across the membrane as they do so. This process is also called **facilitated diffusion.**

□ **Uniporters** move just _______________ kind of molecule.

□ **Cotransporters** move more than one kind of molecule.

- **Symporters** move 2+ types of molecules in the same direction (both move into the cell or both move out).
- **Antiporters** (AKA "**Exchangers**") move 2+ types of molecules in the opposite direction.

EXAMPLE: The Glucose Transporters (GLUT) provide a way for hydrophilic glucose (which otherwise wouldn't be able to cross the membrane) to flow down its concentration gradient into cells.



Active Transport:

● **Active Transport** moves molecules across cell membranes *against their concentration gradients*.

□ This process requires some source of ____________________.

- **Primary Active Transport** uses ATP as the energy source.

- **Secondary Active Transport** uses the concentration gradients of *one* molecule to power the movement of another molecule.

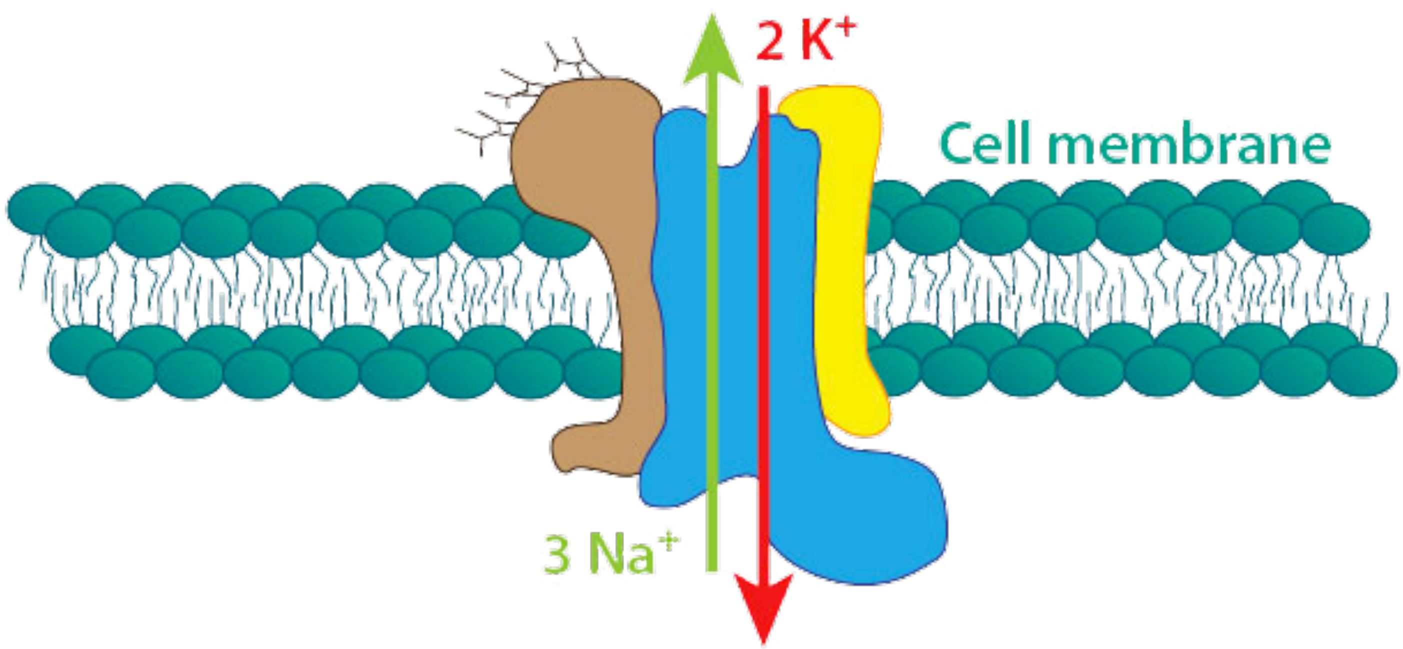
● Primary Active Transport uses ATP as the energy source, so the proteins doing this are called **ATPases**.

□ Cells can use primary active transport to establish concentration gradients across their membranes.

● Normally, the cell maintains a variety of concentration gradients across its membrane.

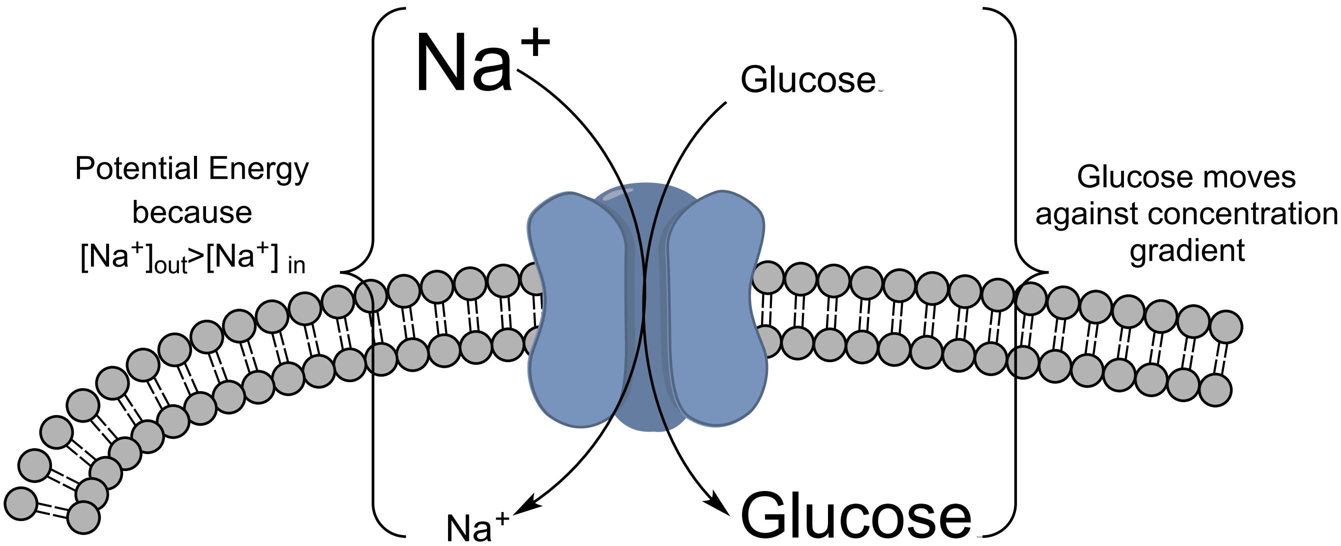
□ The most important is the Na^+/K^+ gradient—essentially every cell maintains high $[Na^+]_{out}$ and high $[K^+]_{in}$ thanks to the Na^+/K^+ ATPase.

EXAMPLE: The Na^+/K^+ ATPase uses energy from ATP to move 3 Na^+ out of the cell and bring 2 K^+ into the cell.



● **Secondary Active Transport** uses the energy in these already-existing gradients as the source of potential energy to power the movement of other molecules.

EXAMPLE: The Na^+/Glucose Cotransporter (SGLT) uses the energy in the Na^+ gradient to power the movement of Glu against its concentration gradient into a cell.



PRACTICE 1: A transporter moves Na^+, K^+, and Cl^- into the cell. What type of protein-mediated transport does this channel perform? (Hint: [Na^+] is higher outside the cell, [K^+] and [Cl^-] are higher inside the cell).

a) Passive transport through a chemically-gated channel.
b) Facilitated Diffusion.
c) Primary Active Transport.
d) Secondary Active Transport**.**

PRACTICE 2: Nicotinic acetylcholine receptors (nAchRs) are inserted in the membranes of skeletal muscle fibers. When they bind to acetylcholine, a channel within them opens and allows Na^+ and K^+ to cross the skeletal muscle cell membrane. Which of the following describes the category into which nAchRs fit?

a) Mechanically-gated ion channels.
b) Voltage-gated ion channels.
c) Ligand-gated ion channels.

PRACTICE 3: Parietal cells of the stomach express H^+/K^+ ATPase proteins. These proteins use energy from the hydrolysis of ATP to pump one H^+ out of the cell into the stomach while, at the same time, bringing one K^+ from the stomach into the cell. Which of the following accurately describes this type of transport?

a) Facilitated diffusion.
b) Primary active transport.
c) Secondary active transport.

CONCEPT: VESICLE-BASED TRANSPORT—ENDOCYTOSIS AND EXOCYTOSIS

Bulk Transport:

● **Bulk Transport** is the movement of larger solutes—carbohydrates and proteins, mostly—across cell membranes.

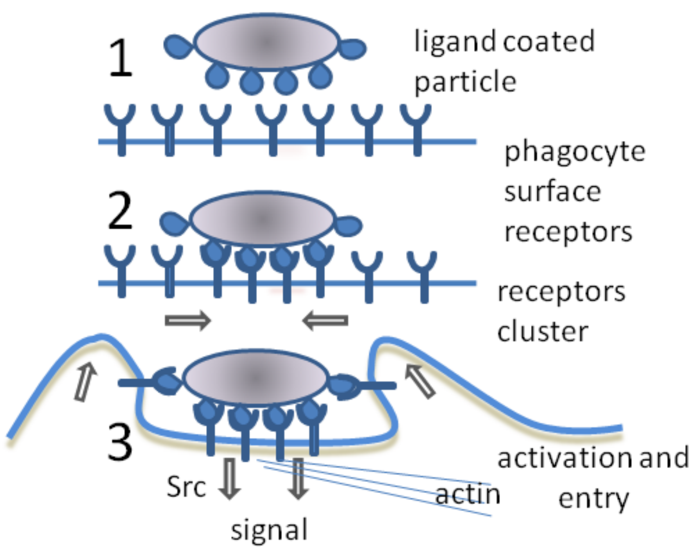
● In **Phagocytosis,** or "cell-eating," the cell wraps its membrane around a large target—like a bacterium—and brings it in.

□ Initiated when some ligand on the target's ______________________ binds to a receptor on the cell membrane.

□ The resulting membrane-bound particle—now called a **phagosome**—then fuses with the **lysosome**.

-The corrosive chemicals held in lysosomes degrade the phagosome's contents.

EXAMPLE: Macrophages—part of the immune system—engulf and kill bacteria via phagocytosis.



Endocytosis:

● **Endocytosis** is the general term for a cell taking in some substance by wrapping it in membrane.

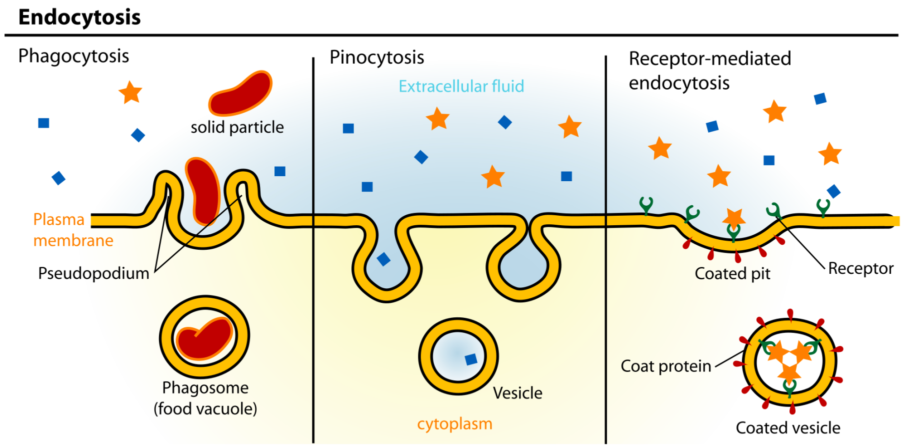
□ Like phagocytosis, but generally for smaller targets.

□ **Pinocytosis**, or "cell-drinking," is a very non-selective form. Cell just grabs some extracellular fluid.

□ In **receptor-mediated endocytosis,** the binding of a ligand to a receptor activates the engulfment.

-A cage-like protein called **clathrin** pulls the region of membrane inward the new vesicle pinches off.

EXAMPLE: A comparison of phagocytosis, pinocytosis, and receptor-mediated endocytosis (which involves clathrin).



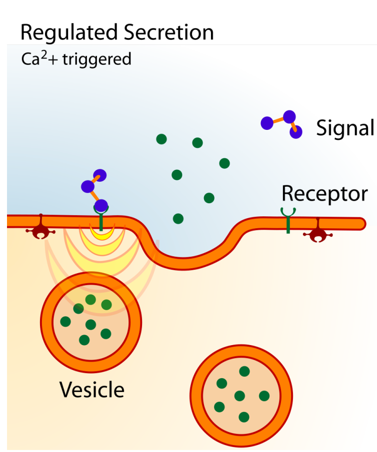
● **Exocytosis** is when an intracellular vesicle fuses with the cell membrane, releasing its contents to the ______________.

□ Opposite process from endocytosis.

□ Used to "export" large, hydrophilic molecules made in the cell, like ________________________________.

□ May be "constitutive"—happening all the time—or activated by some sort of signal.

EXAMPLE: At a synapse between neurons, exocytosis of neurotransmitter is triggered by an increase in intracellular Ca^{2+}.

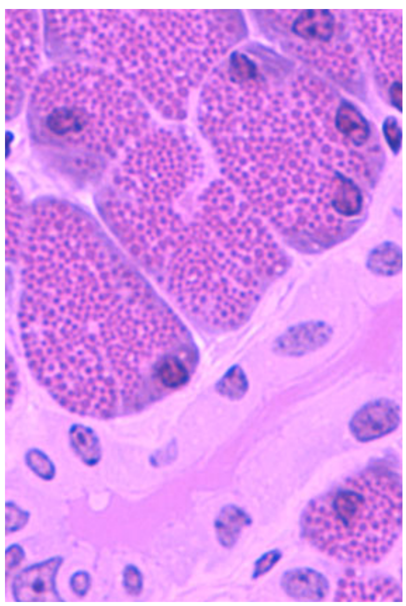


PRACTICE 1: One of the functions of antibodies—proteins that are part of the immune system—is to bind to and coat bacteria. This makes the bacteria more likely to be engulfed and destroyed by macrophages. Which of the following processes is likely facilitated by antibodies?

a) Endocytosis.
b) Exocytosis.
c) Phagocytosis.

PRACTICE 2: Below is a microscope slide of pancreatic acinar cells (the darker purple ones). All of those circles within the cell are vesicles packed with proteins to be released. The large number of granules stored by pancreatic acinar cells suggest that they do lots of which of the following processes?

a) Endocytosis.
b) Exocytosis.
c) Phagocytosis.

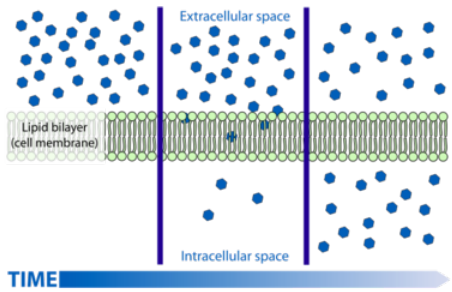


CONCEPT: THE RESTING MEMBRANE POTENTIAL I: FORCES AND OHM'S LAW

Concentration Gradients as Forces:

● Concentration gradients can be "forces"—if there is more solute on one side of a membrane than other, solute will move to eliminate that concentration gradient (assuming membrane is permeable):

EXAMPLE: If you put a cell without any glucose in it into a 100 mM glucose solution, glucose will move into the cell until the concentrations of glucose are equal inside the cell and outside.



Voltages as Forces:

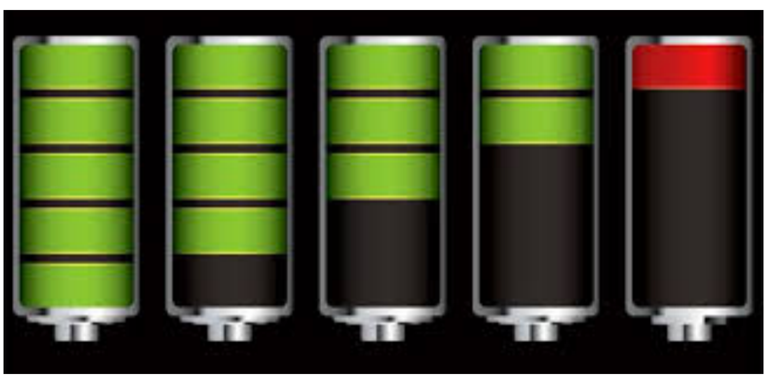
● **Voltage** is another force—it's electrical potential energy that results from ____________________ *of opposite charges*.

□ AKA a "potential difference," or "electrical potential," or "electrical potential difference," or "electrical gradient."

□ Voltages are the forces that cause charge to _____________________.

-Given voltage and a way for charge to move, the charge will move in a way that will eliminate the voltage.

EXAMPLE: Batteries have a voltage between their two ends. So, when you connect the ends using a wire, charge moves. After a while, the charge distribution has dissipated, so the voltage drops to zero and the battery dies.

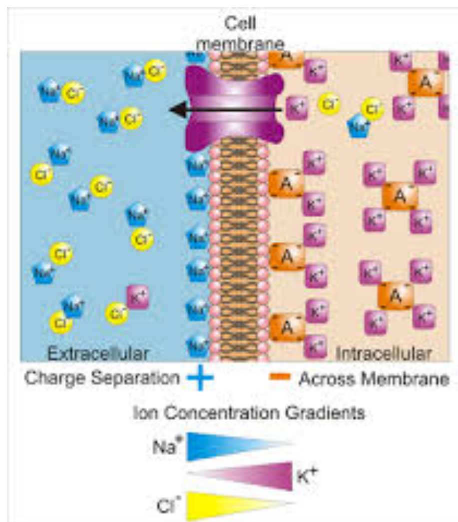


The Dual Nature of Ions:

● Ions—like Na^+ and K^+—are special because they're subject to ___________________ of these kinds of forces.

- □ They're chemicals, so they move down their concentration gradients.
- □ They're also charged, which means they're subject to electrical forces and voltages (and can generate voltages).

EXAMPLE: There is a separation of ions across cell membranes that generates a voltage.

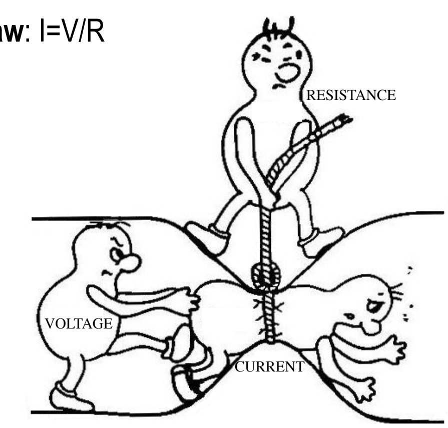


Ohm's Law:

● Ions are charged, so we can talk about their movement as a *current*, just like electricity.

● The movement of charge (a current) as the result of a voltage is described by **Ohm's Law**: I=V/R

- □ I is the **current**—how much charge is moving.
- □ V is the voltage—how hard the charges are being pulled (the driving *force*).
- □ R is the **resistance**—how hard it is for the charge to move on a pathway.
  - -There *must be* a resistance—a pathway—for charge to move.
  - -In cells, transmembrane **ion channels** are usually this pathway.



● The more common physiological form of Ohm's Law is: I=Vg.

- □ g is **conductance**—how *easy* it is for charge to move.
- □ Conductance is the *reciprocal* of resistance: g= 1/R

PRACTICE 1: Normally, Na^+ ions can't cross cell membranes very easily, because they're hydrophilic cations and the membrane is lipophilic. If a Na^+ channel in the membrane opens and increases the permeability of the membrane to Na^+, which variable in Ohm's Law (I=Vg) is directly changed by the opening of the channel?

a) Current (I).
b) Voltage (V).
c) Conductance (g).

PRACTICE 2: Normally, Na^+ ions can't cross cell membranes very easily, because they're hydrophilic cations and the membrane is lipophilic. If a Na^+ channel in the membrane opens and increases the permeability of the membrane to Na^+, how will that change affect the transmembrane current of Na^+?

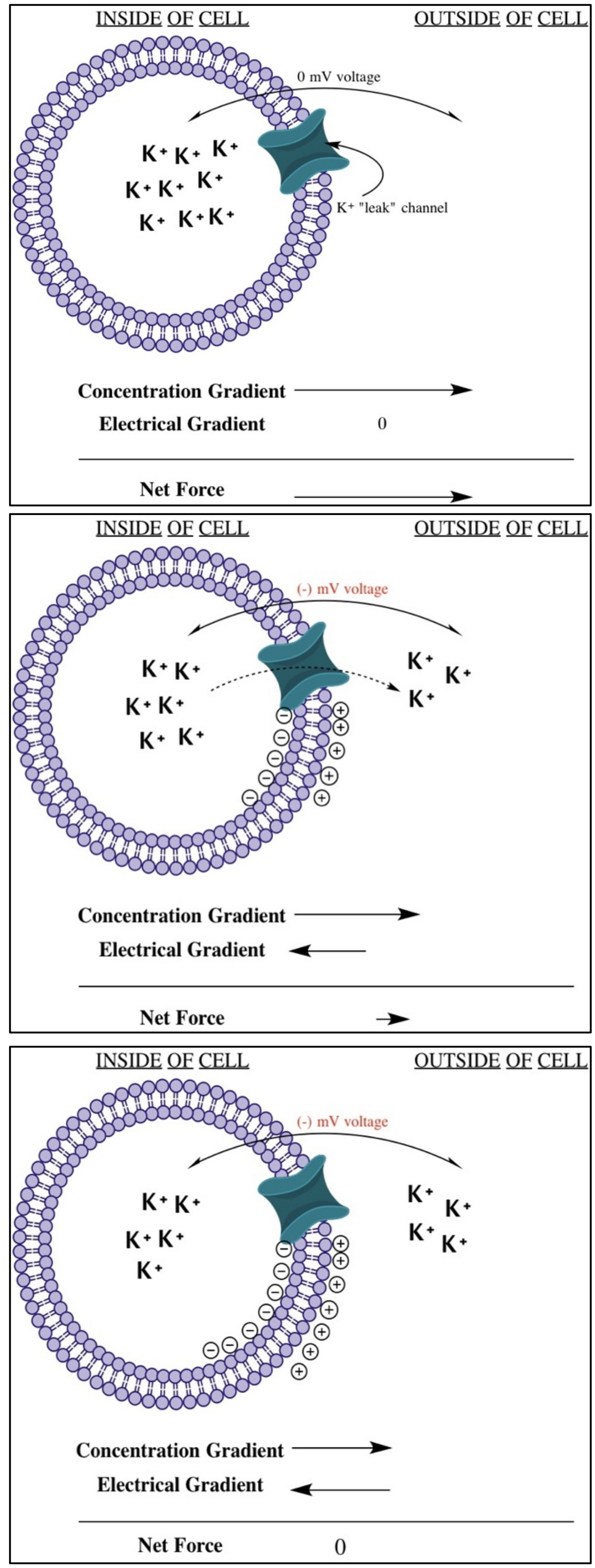
a) Increase I_{Na+}.
b) Decrease I_{Na+}.
c) No change in I_{Na+}.

PRACTICE 3: A cell is sitting in a KCl solution. Outside the cell, $[K^+]$=10 mM. Inside of the cell, $[K^+]$=100 mM. As a result of this separation of K^+, there is a transmembrane voltage V= -61 mV (i.e. the inside of the cell is more negative than the outside). Which of the following accurately describes the type(s) and direction of force(s) acting on the K^+ *inside* of the cell? (Choose all that apply.)

a) Concentration gradient; out of the cell.
b) Concentration gradient; in to the cell.
c) Electrical force; out of the cell.
d) Electrical force; in to the cell.

CONCEPT: THE RESTING MEMBRANE POTENTIAL II: DEVELOPMENT OF A MEMBRANE POTENTIAL

Development of Charge Separation Across a Membrane:



● The punchline: There's a charge separation across cell membranes, with the inside being more negative than the outside. Why?

1) Imagine a cell filled only with K^+. There is no K^+ on the outside, but there's also enough positive charge to balance the K^+.

- □ There's a *concentration gradient* pushing K^+ out of the cell, but no electrical gradient.
- □ There's a channel that will allow K^+ to cross the membrane. So, K^+ will follow the net force, moving out of the cell.

2) K^+ is positively-charged. As it leaves the cell it adds positive charge to the outside of the cell and leaves behind relative negative charge.

- □ Because K^+ is moving, the concentration gradient decreases.
- □ The resulting separation of charge creates an electrical gradient (a voltage) pushing back against the K^+. So, now two opposing forces.

3) Eventually, the system will reach a point where the concentration gradient and electrical gradient oppose each other perfectly.

- □ Neither force will actually be zero—there will still be a voltage and still be a concentration gradient.
- □ The forces resulting from each will just be equal and opposite.
- □ This is an *equilibrium*, which means there will be no more *net* movement of ion—no more current.

● In sum: If you stick an electrode across a cell membrane and compare the inside of the cell to the ECF, you'll measure a voltage—called a **membrane potential (V_m)**—between -70 and -90 mV.

- □ The **Resting Membrane Potential (V_{rest})** is the specific value of V_m when a cell is at rest.

PRACTICE 1: A neuron is sitting at rest in a dish. Its membrane potential is at V_{rest}= -70 mV; $[K^+]_{inside}$=100 mM and $[K^+]_{outside}$=10 mM. Which of the following force(s) acting on the K^+ is *equal to zero*? (Choose all that apply.)

a) Concentration gradient force.
b) Electrical gradient force.
c) Concentration Gradient Force+Electrical Gradient Force (i.e. the net force).
d) Force of sexual attraction.

CONCEPT: THE RESTING MEMBRANE POTENTIAL III: THE NERNST AND GOLDMAN-HODGKIN-KATZ EQUATIONS

The Nernst Equation and The Equilibrium Potential:

● The **Nernst Equation** lets us calculate the V_m at which the concentration gradient force and electrical gradient force are ___________________ *and opposite to each other* for a particular ion. This value is called the **Equilibrium Potential (E_{ion}).**

□ General form: $E_{ion} = \frac{RT}{z\mathcal{F}} \ln \left(\frac{[ion]_{out}}{[ion]_{in}}\right)$

-R= universal gas constant, T=temp (in Kelvin), *z*=ionic charge (z=$^+$1 for Na^+ and K^+), F=Faraday Constant.

□ Simplified: $\mathbf{E_{ion} = \frac{61}{z} \log \left(\frac{[ion]_{out}}{[ion]_{in}}\right)}$.

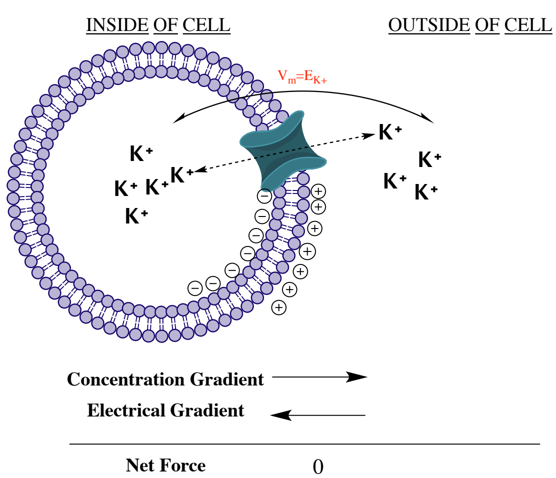
-Assumes body temperature and a base-10 logarithm.

● The Nernst Equation—the E_{ion}—tells you *the value of V_m at which there is no net* _________________ *on a particular ion*.

□ If an ion can cross the membrane, *it will move in a way that will work to bring V_m toward E_{ion}.*

● Nernst is used when you have an ionic concentration gradient and an ionic current and want to know *how that ionic current will affect V_m.*

EXAMPLE: When V_m=E_{K+}, there is no *net force* on the ions.



The Goldman-Hodgkin-Katz Equation—Estimating V_m:

● The Nernst Equation tells us the value that V_m will approach because of a particular ionic current.

□ But, it doesn't give any information about the instantaneous *value* of V_m.

● The **Goldman-Hodgkin-Katz Equation** provides an estimate of V_m for a cell by calculating a *weighted* ______________ of equilibrium potentials for all the ions capable of crossing the membrane. For Na^+, K^+, and Cl^- :

□ $V_m = 61log\frac{(P_{Na^+}[Na^+]_{out}+P_{K^+}[K^+]_{out}+P_{Cl^-}[Cl^-]_{in})}{(P_{Na^+}[Na^+]_{in}+P_{K^+}[K^+]_{in}+P_{Cl^-}[Cl^-]_{out})}$, where P_{ion} is the permeability of the membrane to that ion.

□ Ions that can cross the membrane more easily—can make a larger current—have a larger effect on V_m.

Why Does $V_{rest} \cong$ -70 mV?

● Essentially every cell in the body expresses **Na^+/K^+ ATPase pumps** in their cell membranes.

□ These pumps continuously pump *Na^+ out of the cell and K^+ into the cell*→a concentration gradient for these ions:

- Typically: $[Na^+]_{out} \cong 150$ mM and $[Na^+]_{in} \cong 15$ mM ⇒ $E_{Na+} \cong +61$ mV.

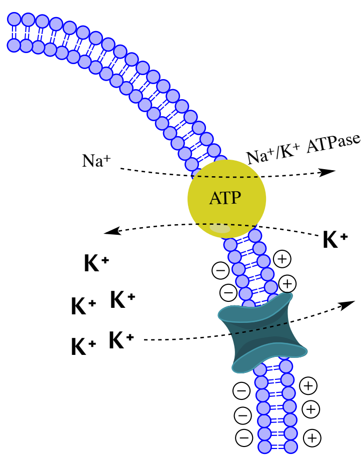
- Typically: $[K^+]_{out} \cong 5$ mM and $[K^+]_{in} \cong 150$ mM ⇒ $E_{K+} \cong -90$ mV.

● Essentially every cell in the body also expresses **K^+ leak channels** in their cell membranes.

□ These channels provide a ________________ for K^+ to cross the membrane and pull V_m toward E_{K+} *even at rest*.

□ This is why the resting membrane potential of most cells is so close to E_{K+} at about -70 to -90 mV.

EXAMPLE: The combination of the concentration gradients for Na^+ and K^+ established by the Na^+/K^+ ATPase and the presence of K^+ leak channels causes the membrane potential of resting cells to be close to E_{K+}.



PRACTICE 1: Assume that, for a given cell: $[Ca^{2+}]_{extracellular\ fluid}$=120 mM and $[Ca^{2+}]_{cytosol}$=1.2 mM. Which of the following is true for this cell?

a) E_{Ca2+}= +61 mV
b) E_{Ca2+}= -61 mV
c) E_{Ca2+}= +122 mV
d) E_{Ca2+}= -122 mV

PRACTICE 2: A typical neuron is sitting at V_{rest}=- 70 mV. Many Na^+ channels in the neuron's membrane open and stay open. $[Na^+]_{outside}$=150 mM and $[Na^+]_{inside}$=15 mM. After a new equilibrium is reached, you measure the new membrane potential. Which of the following is likely to be the value of that new membrane potential?

a) V_m= -70 mV.
b) V_m= -10 mV.
c) V_m= 0 mV.
d) V_m= +61 mV.

PRACTICE 3: You discover an alien neuron and take some measurements. At rest, the membrane is most permeable to which ion?

V_{Rest}=+40 mV	**$[Ion]_{ECF}$**	**$[Ion]_{cytosol}$**
Na^+	15 mM	150 mM
K^+	100 mM	10 mM

a) Na^+
b) K^+
c) Mo^{2+} (Molybdenum)
d) Plutonium

PRACTICE 4: A cell is initially at V_m=0 mV. The concentrations of K^+ inside and outside the cell are: $[K^+]_{out}$=5 mM, $[K^+]_{in}$=150 mM. If a channel for K^+ opens, will K^+ flow into or out of the cell?

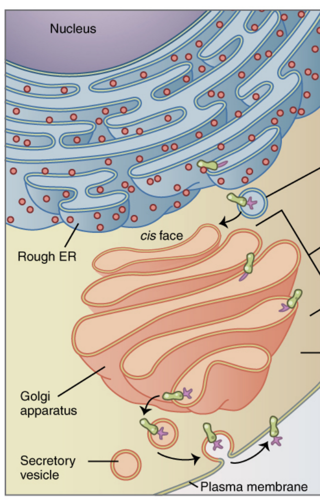
PRACTICE 5: Complete the table for a cell with $[Na^+]_{out}$=150 mM and $[Na^+]_{in}$=15 mM.

Membrane Potential (V_m):	**Direction of I_{Na+}:**
0 mV	
+30 mV	
+100 mV	
-90 mV	
+61 mV	

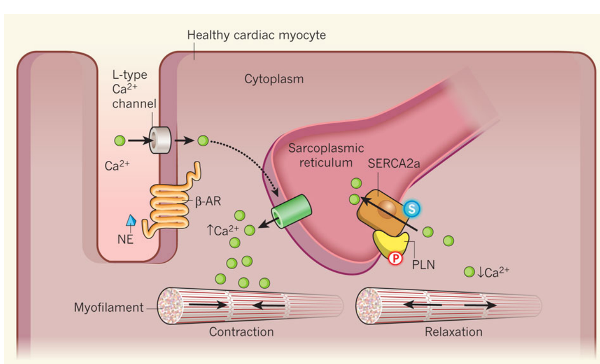
CONCEPT: REVIEW OF PHYSIOLOGICALLY-RELEVANT ORGANELLES

- Within the cell are **organelles**, which carry out specific jobs necessary for cell life and function. Some are:
  - □ The **mitochondria** perform the aerobic ("with oxygen") parts of ____________________ to make ATP.
  - □ The **Golgi complex** "packages" proteins into vesicles to be sent out of the cell.
  - □ The **smooth endoplasmic reticulum** (or **sarcoplasmic reticulum** in muscle cells) stores Ca^{2+}.
  - □ The **nucleus** holds DNA and is the site of mRNA _________________________________.
  - □ The **ribosomes** bind to mRNA and tRNA, translating the former into polypeptides.
  - □ The **lysosomes** hold corrosive chemicals used to break down intracellular toxins or pathogens.
- Some organelles also have membranes of their own—e.g. the nucleus, Golgi, Endoplasmic Reticulum, and Mitochondria.

EXAMPLE: In the pituitary (a gland in the brain), cells make signaling proteins called hormones that get released into the blood. These must be "packaged" into membrane-bound vesicles beforehand. This packaging happens at the Golgi.



EXAMPLE: Skeletal and cardiac muscle cells contract when Ca^{2+} levels increase in the cytosol. For both of these cell types, most of this Ca^{2+} is released from the sarcoplasmic reticulum, which stores the Ca^{2+}.



CONCEPT: PROTEIN SYNTHESIS AND GENE EXPRESSION

● Essentially everything a cell does is determined and carried out by ___________________________.

□ How a cell "behaves" (if it responds to a stimulus, how it responds) depends on the proteins the cell expresses.

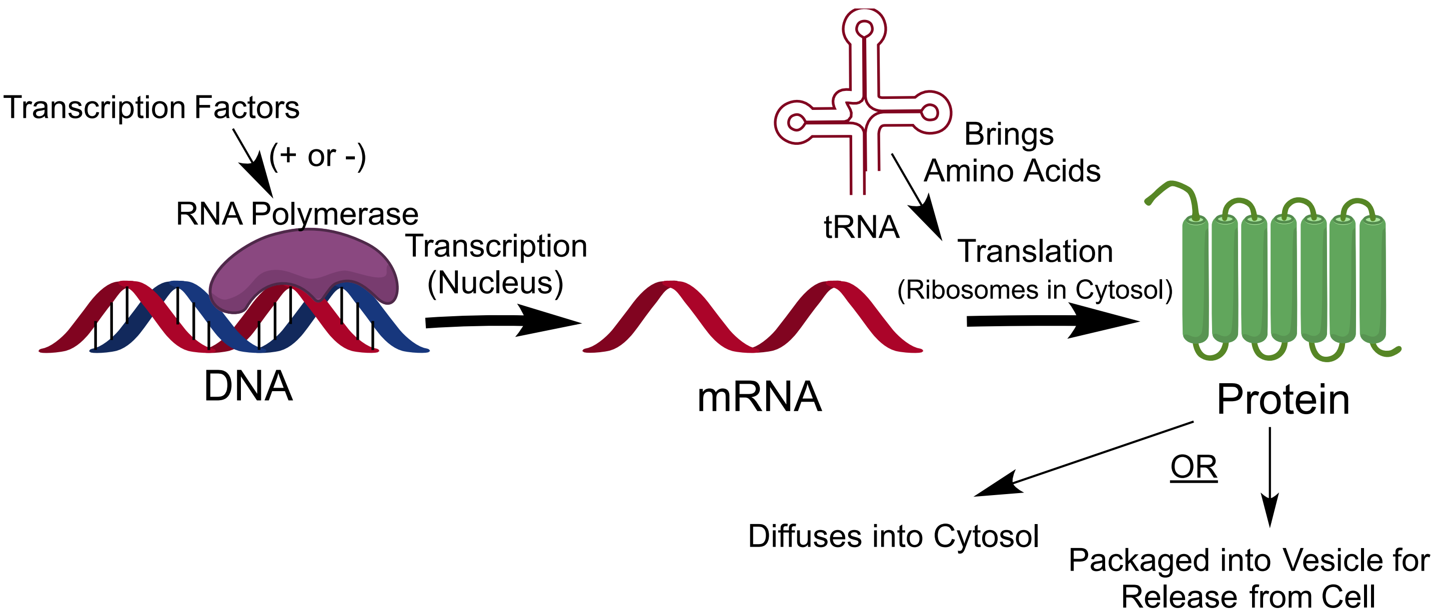
The Central Dogma of Molecular Biology:

● The **Central Dogma of Molecular Biology** describes the process a cell uses to make a protein.

□ DNA→RNA→Protein.

□ The DNA→RNA=**transcription** (in the ___________________________).

□ The RNA→Protein=**translation** (performed by **ribosomes** in the _____________________________).



Regulation of Gene Expression:

● A family of molecules called **transcription factors** determine which specific genes get ________________________.

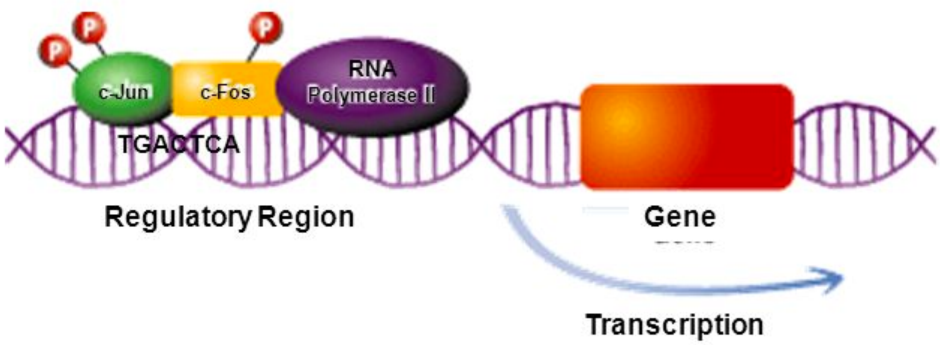
  □ In the nucleus, transcription factors bind to specific DNA sequences.

  □ A transcription factor may **activate/up-regulate/promote** transcription.

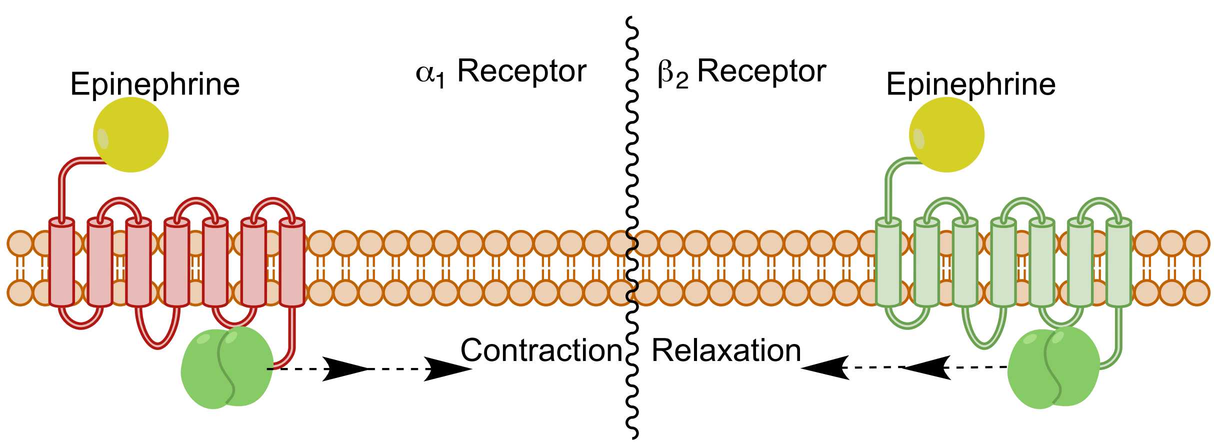
  □ Or, a transcription factor may **inhibit/down-regulate/repress** transcription.

● **Steroid hormones** activate transcription factors, and thus change which genes a cell is expressing.

EXAMPLE: Transcription factors that promote expression recruit RNA Polymerase and initiate transcription of a gene.



EXAMPLE: Why this matters—different receptors can mean a different response to the same stimulus in smooth muscle.



Smooth muscle can express two different receptors that can bind to epinephrine—α_1 receptors and β_2 receptors. Activation of α_1 receptors causes contraction, while activation of β_2 receptors causes relaxation. So, how a smooth muscle cell responds to epinephrine depends on which receptor (or the ratio) it is expressing.