CLUTCH

www.clutchprep.com

CONCEPT: BIOLOGICAL MEMBRANE TRANSPORT

●Recall: Molecules have natural tendency to diffuse _____ *their* concentration gradients (from _____ to _____).

□ Biological membranes are _____ *permeable* & can act as _____ to prevent diffusion.

□ *Selectively Permeable* (or *semi-permeable*): "_____" about what crosses *in/out* of the cell membrane.

EXAMPLE: Diffusion & Selectively Permeable Membranes.

Which Molecules Freely Cross Membranes?

Freely Diffuse *without facilitation:*	____	**Uncharged**	**Nonpolar/Hydro_____**
Cannot* Freely Diffuse *without facilitation:	**Large**	_____ (+/-)	**Polar/Hydrophilic**

EXAMPLE: Diffusion Across a Membrane.

PRACTICE: Which molecule most easily diffuses across a biological membrane's lipid bilayer, without facilitation?

a) H_2O. b) O_2. c) $H_2PO_4^-$. d) Glucose. e) Na^+.

CONCEPT: BIOLOGICAL MEMBRANE TRANSPORT

PRACTICE: Rank the unfacilitated transmembrane diffusion of the following molecules from least → most permeable.

a) Acetamide → Urea → Butyramide.
b) Urea → Acetamide → Butyramide.
c) Butyramide → Acetamide → Urea.
d) Acetamide → Butyramide → Urea.
e) Urea → Butyramide → Acetamide

Map of Biological Membrane Transport

●Molecular transport across biological membranes can occur in a _____ of ways.

EXAMPLE: Membrane Transport Map.

CONCEPT: PASSIVE VS. ACTIVE TRANSPORT

- _____ general types of processes transport molecules across biological membranes: 1) *Passive* & 2) *Active*.

EXAMPLE: Passive vs. Active Membrane Transport.

	_____ Transport	_____ Transport
Energy Input?	_____	_____ ATP
Movement Relative to Gradient?	_____/With	Up/Against
Thermodynamically favorable?	Yes	_____
Spontaneous?	Yes (*Exergonic*, _____)	No (*Endergonic*, _____)
Protein Facilitation?	Sometimes	Always

PRACTICE: Passive membrane transport processes include_____.

a) Consumption of ATP for energy.
b) The use of transport proteins to move a substance from low to high concentration.
c) Movement of a substance down its concentration gradient.
d) Movement of a substance up its concentration gradient.

PRACTICE: What is the difference between active and passive transport across a plasma membrane?

a) Active transport is used to move substances down their concentration gradient, where passive transport is used to move substances against their concentration gradient.
b) Active transport is ATP dependent, whereas passive transport does not require energy for movement across the plasma membrane.
c) Active transport implies that the cell is working with other cells, whereas passive transport implies that the cell does not cooperate with other cells.
d) Active transport means that the cell is aggressively going after substances that it wants to bring into the cell, whereas passive transport means that the cell just waits for the substance to cross the membrane.

CONCEPT: PASSIVE VS. ACTIVE TRANSPORT

Classes of Passive/Active Membrane Proteins

- _____ types of *passive/active* membrane proteins are classified according to how they operate:
  - **1)** _____porters: transport _____ molecule at a time in just _____ direction.
  - **2)** _____porters: cotransport ≥ 2 molecules at a time in the _____ direction.
  - **3)** _____porters: cotransport ≥ 2 molecules at a time in _____ directions.

PRACTICE: A transport protein that simultaneously transports two different molecules in different directions is called:

a) A uniporter.
b) A symporter.
c) An equilibrium protein.
d) An antiporter.
e) A simple diffuser.

PRACTICE: Which option below best describes a transporter that requires ATP to move molecules A and B out of the cell?

a) An active antiporter.
b) A passive antiporter.
c) A passive symporter.
d) An active uniporter.
e) An active symporter.

CONCEPT: PASSIVE MEMBRANE TRANSPORT

Simple & Facilitated Passive Transport

- _____ types of *passive transport*:
  1) _____ *Diffusion*: simple & direct diffusion through the membrane (squeezing between phospholipids).
  2) *Facilitated Diffusion*: non-energetic diffusion that is _____ by a membrane-*protein*.

EXAMPLE: Passive Transport: Simple vs. Facilitated Diffusion.

PRACTICE: The difference between simple and facilitated diffusion is that facilitated diffusion:

a) Requires a protein transporter.
b) Moves molecules against their concentration gradient.
c) Requires energy.
d) Freely diffuses molecules against their concentration gradient.

PRACTICE: Simple diffusion and facilitated diffusion across a membrane both _____:

a) Move molecules against their concentration gradient.
b) Move molecules with their concentration gradient.
c) Require ATP.
d) Use a protein transporter.
e) Transport charged molecules from low to high concentration.
f) Transport large, charged molecules from high to low concentration.
g) Both b and f are true.

CONCEPT: PASSIVE MEMBRANE TRANSPORT

Kinetics of Passive Transport

- *Rate/velocity* of passive transport: driven by the extent of the *concentration gradient* across the membrane.
  - □ The *greater* the concentration, the *faster* the *rate* of _____ *diffusion* (forms _____ data).
- Rate of _____ diffusion is even *faster*; HOWEVER, its *limited* by the amount of transport protein.
  - □ Therefore, passive *facilitated* diffusion rates form a _____, *Michaelis-Menten* curve.
  - □ **K_{tr}**: "substrate" concentration at which the **tr**ansport-protein is _____-saturated (analogous to the K_m).

$$V_0 = \frac{V_{max}[S]}{K_{tr} + [S]}$$

$$y = mx + b$$

PRACTICE: The rate of movement (flux) of a substance X into cells was measured at different concentrations of X to construct the following graph. Does the graph's data suggest diffusion of X into cells is mediated by a protein transporter?

a) Yes, diffusion of X is mediated by a protein transporter (facilitated diffusion).
b) No, diffusion of X is not mediated by a protein transporter (simple diffusion).

PRACTICE: The rate of transfer across a membrane is measured for a given molecule. The diffusion rate is seen to be hyperbolic with respect to the concentration of the diffusing molecule. The method of transport is which of the following?

a) Facilitated diffusion.
b) Active transport.
c) Simple Diffusion.
d) Symporter diffusion.

CONCEPT: FACILITATED DIFFUSION

●Recall: *Facilitated Diffusion*: passive, non-energetic diffusion that is *facilitated* by a membrane-_____.

□ This integral membrane-protein can either be:

1) a *Carrier/Transporter*: undergoes _____changes to move a solute across a membrane.

2) a *Porin/Channel*: form an obvious *membrane-spanning*-_____.

EXAMPLE: Carrier/Transporters & Porins/Aquaporins/Ion-Channels.

PRACTICE: What type of transport does not require the assistance of a membrane protein?

a) Simple diffusion.
b) Facilitated diffusion.
c) Passive transport.
d) Symport of more than one molecule.
e) All of the above require a protein.

PRACTICE: Movement of water across a membrane is facilitated by proteins called _____:

a) Annexins.
b) Aquaporins.
c) Pores.
d) Hydroporins.
e) Selectins.
f) Symporters.

CONCEPT: ERYTHROCYTE FACILITATED TRANSPORTER MODELS

Erythrocyte Glucose Uniporter (GLUT1)

●Classic example of *facilitated passive transport* are erythrocyte (red blood cell) *Glucose Transporters* (_____).

□ GLUT1 *conformationally changes* as it transports glucose *down* its concentration gradient as a _____.

□ Due to glucose metabolism, [Glucose] inside cells is generally kept _____ with respect to blood [glucose].

□ _____ glucose transporters exist in *different* tissues with *varied* functional roles.

Transporter	Tissue Expression	Biological Role
_____	Ubiquitous	Basal Glucose Uptake
GLUT2	Intestine, Liver, Pancreas	*Intestine*: Pump digested glucose into blood. *Liver*: replenishes blood glucose. *Pancreas*: Regulation of insulin release
GLUT4	Muscle, Fat, Heart	Glucose import, increased by insulin

PRACTICE: Glucose transport into erythrocytes (not into intestinal epithelial cells) is an example of:

a) Primary active transport.
b) Secondary active transport.
c) Facilitated symport.
d) Facilitated Uniport.
e) Simple Diffusion.
f) None of the above.

CONCEPT: ERYTHROCYTE FACILITATED TRANSPORTER MODELS

PRACTICE: Which of the following correctly ranks the steps of erythrocyte glucose transport by GLUT1?

a) II, I, III, IV. b) II, I, IV, III. c) IV, III, II, I d) I, II, IV, III. e) IV, II, III, I

I. A conformational change exposes glucose to the opposite site of the membrane.

II. Glucose binds to the transporter on one side of the membrane.

III. The GLUT1 transporter reverts back to its initial conformation.

IV. The glucose molecule has a weakened affinity to GLUT1 and dissociates from the transporter.

Erythrocyte Cl^-/HCO_3^- Antiporter

- Recall: CO_2 produced by respiring tissues *diffuses* into erythrocytes, where _____ *anhydrase* converts it to HCO_3^-.
  - □ *Cl^-/HCO_3^- Antiporters:* passively transport Cl^- & HCO_3^- in _____ directions (called *Chloride-*_____).
- *Chloride-Shift*: phenomenon of Cl^-/HCO_3^- _____ near the *tissues* & near the *lungs*.
  - □ Cl^- acts as *counterion* to _____ charge across membrane.
  - □ HCO_3^- buffer *maintains* blood pH & _____ *blood's capacity to transport CO_2* from tissues to lungs.

How Does the Chloride-Shift Work?

1. Near *tissues*, ↑ $[HCO_3^-]$ *inside* cell diffuses *down* its gradient to the _____ (via Cl^-/HCO_3^- antiporters).
2. Near *lungs*, the _____ events occur.

CONCEPT: ERYTHROCYTE FACILITATED TRANSPORTER MODELS

PRACTICE: What is the chloride shift?

a) The excretion of Cl^- by the kidney, preventing bicarbonate ions from causing an increase in plasma pH.
b) The production of carbaminohemoglobin by chloride infusion from the plasma.
c) The exchange of Cl^- for bicarbonate ions in erythrocytes, causing HCO_3^- to leave the cell.
d) The production of bicarbonate by enzymatic degradation of chloride.

PRACTICE: The Chloride-Shift occurs when:

a) Carbon dioxide moves into the RBCs.
b) Hemoglobin binds carbon dioxide.
c) Oxygen moves into the red blood cells.
d) Bicarbonate moves out of the red blood cells.
e) Chloride shifts across the nuclear membrane.

PRACTICE: Which of the following statements is FALSE concerning the chloride-bicarbonate exchanger?

a) The exchanger increases the rate of bicarbonate transport across the membrane.
b) The exchanger uses ATP as an energy source to drive bicarbonate transport.
c) The exchanger transports chloride ions across the membrane.
d) The exchanger is classified as an antiporter.

PRACTICE: In the "chloride shift" diagrams below, label each scenario (**A** & **B**) as occurring in either the tissues or lungs:

A) a) Tissues. b) Lungs.

B) a) Tissues. b) Lungs.

CONCEPT: MEMBRANE TRANSPORT OF IONS

Charged Ions Flow Down Electrochemical Gradients

- Direction that charged ions diffuse across membranes depends on its _____ & *electrochemical* gradient.
- *Electro-chemical Gradient*: a *combination* & *balance* of the following _____ gradients:
  - **1)** _____ *gradient*: a difference in *chemical concentration* between two regions.
    - □ Recall: Chemicals flow *down* their concentration gradients, (from ↑ to ↓) to reach *chemical* ⇌
  - **2)** _____ *gradient*: a difference in the sum of *electrical charges* between two regions.
    - □ Charged ions flow toward _____ charged regions to reach *electrical* ⇌ (net charge = 0).

Transmembrane Potential

- *Transmembrane Potential/Voltage* ($\Delta\Psi$ or V_m): difference in electrical charge between inside & outside of a membrane.
  - □ *Usually* presented from relative position of inside a membrane & expressed in units of volts or millivolts (V or mV).
- Generally, *inside* of cells are more _____ with respect to the outside ($\Delta\Psi$ is *usually* negative).
  - □ When $\Delta\Psi \neq 0$, it establishes *opposite* _____ gradients for *anions* & *cations*.

$\Delta\Psi = \Psi__ - \Psi__ = \ominus$

OR

$\Delta\Psi = \Psi__ - \Psi__ = \oplus$

CONCEPT: MEMBRANE TRANSPORT OF IONS

Types of Ion Channels

- Ion channels selectively & passively transport *specific* _____ (such as Na^+, K^+, and Cl^-) across a membrane.
- _____ types of *ion-channels*:
  1) _____ Ion Channel: remain open, *always* allowing *leakage* of ions down their electrochemical gradients.
  2) _____-*gated* Ion Channel: opens/closes due to regulation by _____cellular *ligand* molecules.
  3) _____-*gated* Ion Channel: opens/closes due to regulation by _____cellular *signaling* molecules.
  4) _____-*gated* Ion Channel: opens/closes due to changes in *transmembrane potential/voltage* ($\Delta\Psi$).
  5) _____-*gated* Ion Channel: opens/closes due to *mechanical* stimulation (ex. touch, sound, pressure).

PRACTICE: Which of the following describes ion channels that are coupled to membrane receptors, such that their gating (opening or closing) is altered by messenger binding?

a) Ligand-gated channels.
b) Mechanical-gated channels.
c) Leakage channels.
d) Voltage-gated channels.

CONCEPT: MEMBRANE TRANSPORT OF IONS

PRACTICE: Facilitated diffusion of charged ions across a biological membrane is _____:

a) Generally irreversible.
b) Endergonic.
c) Driven directly by ATP.
d) Not specific with respect to the type of ion.
e) Driven by a difference in the electrochemical gradient.

PRACTICE: Which of the following statements is false about a signal-gated ion channel receptor?

a) They are present in the cell membrane.
b) They respond to the presence of intracellular signaling molecules.
c) Differences in membrane potential can affect whether the channel receptors are open or close.
d) They are a type of gated-ion-channel that can open and close under different conditions.

PRACTICE: The voltage-gated potassium channels associated with an action potential provide an example of what type of membrane transport?

a) Simple diffusion.
b) Facilitated diffusion.
c) Coupled transport.
d) Primary active transport.
e) Secondary active transport.

CONCEPT: PRIMARY ACTIVE MEMBRANE TRANSPORT

●*Recall*: *Active transport*: an active, _____-driven process transporting molecules *against* their concentration gradient.

2 Types of Active Membrane Transport

1. _____ *Active Transport*: directly driven by energy source (such as ATP hydrolysis).
2. _____ *Active Transport*: directly driven by an *electrochemical ion gradient*.

EXAMPLE: Primary vs. Secondary Active Transport.

Types of Primary Active Transport ATPases

●*Primary Active Transport ATPase*: transporters that *hydrolyze* _____ to pump molecules *against* their gradients.

- □ _____ types of *Primary Active Transport* ATPases:

ATPase Type	Function
1) ____-type ATPase	Transports cations (ex. Na^+ & K^+) & are reversibly **P**hosphorylated by ATP.
2) ____-type ATPase	Transports H^+ to *acidify* intracellular regions of **V**esicles. Lysosome
3) ____-type ATPase	Transports **F**ree H^+ across mitochondrial membranes producing ATP (ATP synthase). You're Free!
4) ____-type ATPase	Transports **A**nions across **A**rchaeal cell membranes.
5) _____ Transporters	Transports many types of solutes (ex. drugs) utilizing an **A**TP-**B**inding **C**assette. ATP Mixtape

CONCEPT: PRIMARY ACTIVE MEMBRANE TRANSPORT

PRACTICE: What initial effect would the loss of ATP production have on a cell's ability to transport substances?

a) The cell would only be able to transport substances using active transport.
b) The cell would be able to transport substances using active and passive transport.
c) The cell would only be able to transport substances using passive diffusion.
d) The transport of all substances across the membrane would stop.

PRACTICE: What is the main difference between active transport and facilitated transport?

a) Facilitated transport uses proteins, but active transport does not.
b) Active transport uses ATP to power transport, but facilitated transport does not.
c) Active transport occurs across the plasma membrane, but facilitated transport does not.
d) Active transport moves a substance from higher concentration low concentration, while facilitated transport moves a substance from low concentration to high concentration.
e) All of the above are differences between active and facilitated transport.

PRACTICE: P-type ATPases _____.

a) Transport phosphate against its concentration gradient.
b) Undergo reversible phosphorylation by ATP hydrolysis.
c) Transport anions only.
d) Transports phosphate with its concentration gradient.
e) Phosphorylates cations so they can be transported into the cell.

CONCEPT: SODIUM-POTASSIUM ION PUMP

●Recall: *inside* of cells are more _____ with respect to the outside, which dictates the *electrical* gradient.

●Most cells maintain an *opposite chemical* gradient of sodium (_____) & potassium (_____) ions:

□ Inside cell: ↓ [Na^+] & ↑ [K^+].

Sodium-Potassium Ion Pump: a P-Type ATPase

●*Na^+/K^+ Pump*: a _____*-type ATPase* that transports Na^+ & K^+ cations in *opposite* directions (antiport).

□ ____ _____ ions are _____; while ____ _____ ions are _____ (pump-K^+-in).

□ *ATP-dependent process*: ATP-hydrolysis *phosphorylates* _____ residue on pump, causing a *conformational* shift.

EXAMPLE: Sodium-Potassium Ion Pump.

CONCEPT: SODIUM-POTASSIUM ION PUMP

PRACTICE: The critical function of the sodium-potassium pump is to move:

a) Na^+ and K^+ into the cell.
b) Na^+ and K^+ out of the cell.
c) Na^+ out of the cell and K^+ into the cell.
d) Na^+ into the cell and K^+ out of the cell.
e) Na^+ and K^+ into the cell and H^+ out of the cell via antiport.

PRACTICE: Which of the following defines the type of transport by the sodium-potassium ATPase?

a) Active transport through a symporter.
b) Passive transport through a symporter.
c) Active transport through an antiporter.
d) Passive transport through a symporter.
e) Facilitated diffusion through a symporter.

PRACTICE: Which of the following statements about the mechanism of the sodium-potassium ATPase is FALSE?

a) It helps to create a transmembrane potential that is more negative on the inside and more positive on the outside.
b) It pumps 3 Na^+ ions out of the cell.
c) It pumps 2 K^+ ions into the cell.
d) The ATPase is phosphorylated by ATP to transport of Na^+ into the cell.
e) All of the statements above are correct.

PRACTICE: Which of the following shows the correct order of steps for the mechanism of the sodium-potassium ATPase?

a) II, I, V, III, IV, VI.
b) IV, II, III, I, V, VI.
c) I, II, III, IV, V, VI.
d) IV, II, I, III, V, VI.
e) IV, III, I, II, VI, V.

I. 2 K^+ Ions bind.
II. Phosphorylation of an Asp residue.
III. Conformational change releasing 3 Na^+ ions outside the cell.
IV. 3 Na^+ ions bind.
V. Release of the phosphate group.
VI. Conformational change releasing 2 K^+ ions inside the cell.

CONCEPT: SERCA: CALCIUM ION PUMP

●Another example of a P-type ATPase is the **S**arcoplasmic/**E**ndoplasmic **R**eticulum **C**a^{2+} **A**TPase (_____) Pump.

□ SERCA functions as a _____ to pump Ca^{2+} into the SR or ER (keeping *cytoplasmic* [Ca^{2+}] _____).

SERCA Pump

●When released into the cytoplasm, _____ acts as an *intracellular signal* in virtually all cells.

□ *Muscle Contraction*: occurs when nerve impulse induces *release* of Ca^{2+}, _____ cytoplasmic [Ca^{2+}].

□ *Muscle Relaxation*: occurs when SERCA pumps Ca^{2+} into SR, _____ cytoplasmic [Ca^{2+}].

PRACTICE: The calcium ATPase is an example of what type of transport model?

a) Facilitated diffusion via antiport.
b) Secondary active transport via symport.
c) Primary active uniport.
d) Simple diffusion.
e) Primary active symport.

PRACTICE: The calcium ATPase (SERCA) _____:

a) Is a V-type ATPase that transports calcium inside vesicles.
b) Is a P-type ATPase that maintains cytosolic [Ca^{2+}] around 0.1 μM & sarcoplasmic reticulum [Ca^{2+}] at 1.5 mM.
c) Is a P-type ATPase and an example of passive facilitated diffusion.
d) Is a P-type ATPase that transports calcium from the ER to the cytoplasm.
e) None of the above are true.

CONCEPT: ABC TRANSPORTERS

ABC Transporters Provide Multidrug Resistance

●***A**TP-**B**inding-**C**assette* (_____) *Transporters*: integral membrane proteins with > 1 ABC structural motif.

□ Pump substances across a membrane, _____ their concentration gradient.

●All ABC Transporters share _____ common *structural* elements:

1) _____ **T**rans-**M**embrane **D**omains (_____) which make the pore through the membrane.

2) _____ *cytosolic* **N**ucleotide-**B**inding **D**omains (_____) that bind & hydrolyze ATP (**A**TP **b**inding **c**assette).

●Some called **m**ulti**d**rug **r**esistance (_____) *transporters*, since they're responsible for *resistance* to multiple _____.

□ In humans, ***P**-**g**lyco**p**rotein* (___-_____) is an MDR transporter that removes *anti-cancer* drugs from tumor cells.

EXAMPLE: ABC Transporter.

PRACTICE: ABC transporters are a part of a superfamily of transporters that have two nucleotide binding domains that bind _____, which is necessary for primary active transport.

a) ADP. b) Phosphate. c) ATP. d) GTP. e) AMP.

PRACTICE: What side of a membrane has a higher concentration of the toxin Limbricide after ABC transporter activity?

a) Inside the cell. b) outside the cell.

PRACTICE: Which of the following statements is TRUE for BOTH P-type ATPases and ABC transporters?

a) They each have two ATP-binding protein domains.

b) They both contain a phosphorylated Asp residue.

c) They both are examples of multi-drug resistant proteins that pump toxins out of the cell.

d) They are both dependent on the presence of ATP.

e) They both require ATP binding before substrate binding and transport.

CONCEPT: SECONDARY ACTIVE MEMBRANE TRANSPORT

●Recall: _____ *Active Transport*: directly driven by an *electrochemical ion gradient*.

□ HOWEVER, its *indirectly* driven by **p**rimary **a**ctive **t**ransport (since electrochemical gradients are built by PAT).

□ Co-transports ions _____ their electrochemical gradient & other molecules _____ their gradient.

EXAMPLE: Secondary Active Transport.

EXAMPLE: The sodium–potassium pump is an example of a system that uses primary active transport to set up conditions that can ultimately allow for secondary active transport. All of the following are true except:

a) The Na^+–K^+ pump is an antiporter fueled by the hydrolysis of ATP.
b) Secondary active transport of glucose into cells moves glucose against its concentration gradient.
c) The Na^+–K^+ pump exports Na^+ ions to the outside of the cell, establishing a concentration gradient for Na^+.
d) K^+ and Na^+ both diffuse into the cell along their concentration gradients to drive the transport of glucose.
e) Secondary active transport of glucose into cells is indirectly driven by ATP hydrolysis.

PRACTICE: Which of the following is a way in which primary and secondary active transport may work together?

a) Primary active transport can be used to create a concentration gradient of sodium such that sodium and glucose can move into the cell together via antiport mechanism.
b) Primary active transport is used to create ATP necessary to drive secondary active transport.
c) Primary active transport can be used to create a concentration gradient of sodium such that sodium and glucose can move into the cell together via secondary active symport.
d) Primary and secondary active transport always oppose each other so they never work together.

CONCEPT: GLUCOSE ACTIVE SYMPORTER MODEL

- Classic & relevant example of *secondary active transport* are *intestinal epithelial Na^+-Glucose* _____.
  - **A** *Primary Active Transport*: _____/_____ *pump* maintains transmembrane Na^+ gradient.
  - **B** *Secondary Active Transport*: *Na^+-Glucose symporters* _____ *Na^+* & glucose in *same* direction.
    - □ ____ Na^+ imported _____ their gradient *powers* ____ glucose imported _____ its gradient.
  - **C** As glucose is pumped into epithelial cell, it is simultaneously moved into the blood via a *GLUT2* _____.
    - □ *Na^+-Glucose symporter* & *GLUT2 uniporter* operate on _____ sides of epithelial cells.

EXAMPLE: Intestinal Epithelial Glucose Active Symporter.

PRACTICE: Which of the following is TRUE about the Na^+-glucose symporter?

a) The transporter moves glucose down its concentration gradient.

b) The transporter is directly powered by ATP hydrolysis.

c) The energy stored in the Na^+ gradient is harvested for the movement of glucose.

d) The energy stored in the glucose gradient is harvested for the movement of K^+.

e) The protein is an ABC transporter.

CONCEPT: GLUCOSE ACTIVE SYMPORTER MODEL

PRACTICE: The Na^+-Glucose symporter effectively transports glucose inside of cells against its concentration gradient using energy stored in the Na^+ concentration gradient. This energy for glucose transport is derived from the _____.

a) Glucose-Na^+ antiporter.
b) Na^+-K^+-ATPase.
c) Chloride-bicarbonate antiporter.
d) Glucose erythrocyte uniporter (GLUT1).
e) Epithelial glucose uniporter (GLUT2).
f) SERCA pump.

PRACTICE: The Na^+-Glucose symporter transports the two molecules into the cell, while the Na^+-K^+ ATPase uses ATP to transport Na^+ ions out of the cell. What would be the result of a mutation leading to a nonfunctional Na^+-Glucose symporter?

a) Increased levels of intracellular K^+.
b) Increased levels of intracellular glucose.
c) Decreased activity of the Na^+-K^+ ATPase.
d) Overactivation of the Na^+-K^+ ATPase.
e) Increased levels of ATP.

PRACTICE: Imagine that you perform a series of experiments to test the rate of glucose transport (V_0) into epithelial cells using the Na^+-Glucose symporters. These experimental epithelial cells contain no intracellular Na^+ but have the same glucose concentration as their surroundings. In experiment #1, you transfer your cells to test tubes that contain different extracellular [Na^+] & then measure the rate of glucose transport (V_0). In experiment #2, you introduce leakage Na^+ channels into the cell membranes & then repeat the same experiment. Label the data on the plot below as showing results to either Experiment #1 or Experiment #2.

CONCEPT: ENDOCYTOSIS & EXOCYTOSIS

- *Macro*molecules (ex. proteins, polysaccharides, DNA) are too _____ to diffuse through membranes or channels.
  - □ Instead, macromolecules are transported across cell membranes via *endocytosis* &/or *exocytosis*.
  - □ _____ *Proteins*: integral membrane proteins that help *fuse* membranes in both endocytosis & exocytosis.

Endocytosis Allows Entry to the Cell

- _____*docytosis*: macromolecule **en**gulfment by the cell-membrane, allowing _____ to the cell inside a lipid vesicle.
  - □ _____ main types of *endocytosis*:
  - 1 _____: *large*, *solid* material is taken in by endocytosis (cell "_____").
  - 2 _____: *small*, *liquid* material taken in by endocytosis (cell "_____").
  - 3 *Receptor-Mediated-Endocytosis*: specific form of *pinocytosis* using _____ proteins.

EXAMPLE: Endocytosis.

PRACTICE: Which of the following is FALSE about endocytotic movements?

a) Phagocytosis could be used against invading microorganisms.

b) Ingestion of plasma membrane along with extracellular fluid is a kind of pinocytosis.

c) Phagocytosis is a means of feeding in some eukaryotes and is important in animal nutrition.

d) The materials engulfed will be enclosed by a small portion of the ER membrane.

CONCEPT: ENDOCYTOSIS & EXOCYTOSIS

Exocytosis Allows Exiting from the Cell

- _____*ocytosis*: vesicle fusion with cell membrane, allowing vesicle contents to _____ cell into the **ex**tracellular space.
  - □ Neurotransmitters & zymogens of digestive enzymes are released by exocytosis.

PRACTICE: Which of the following is NOT a true statement regarding exocytosis?

a) It forms intracellular vesicles from inward folding of the plasma membrane.
b) It requires fusion of vesicles with the plasma membrane.
c) It secretes large molecules out of the cell.
d) It is responsible for neurotransmitter release of acetylcholine to stimulate muscle contractions.

PRACTICE: Label the following phrases based on if they apply to A) Only Endocytosis, B) Only Exocytosis, or C) Both:

a) Decreases the surface area of the plasma membrane: _____.
b) Increases the surface area of the plasma membrane: _____.
c) Secretes large molecules out of the cell: _____.
d) Brings molecules into the cell: _____.
e) Requires cellular energy: _____.

PRACTICE: Which means of particle transport is shown in the figure below?

a) Exocytosis.
b) Endocytosis.
c) Facilitated diffusion.
d) Simple diffusion.

CONCEPT: NEUROTRANSMITTER RELEASE

Neurotransmitters

●A well-studied example of exocytosis is *release* of _____ in the final step of a neuron's signal.

□ *Neurotransmitter*: chemical released by end of *neuron* to _____ a signal (ex. _____).

□ *Acetylcholine* is stored in *vesicles* & released by *neurons* (via *exocytosis*) to trigger *muscle* _____.

SNARE Fusion Proteins

●Vesicles & plasma membranes naturally _____ each other.

●Neurotransmitter exocytosis involves many proteins, including integral-membrane *fusion proteins* called _____.

1) ____-SNAREs: on an intracellular **V**esicle's *cytoplasmic* surface (outside of **V**esicle); also called ____-SNARE.

2) ____-SNAREs: on the **T**arget membrane's *cytoplasmic* surface; also called ____-SNARE.

EXAMPLE: V/R-SNARE vs. T/Q-SNARE.

CONCEPT: NEUROTRANSMITTER RELEASE

PRACTICE: V-SNARE proteins deliver _____ to T-SNARE receptor sites.

a) Ribosomes. b) mRNA. c) Transport vesicles. d) Lysozymes.

PRACTICE: True or False: All transport vesicles in the cell have T-SNARE proteins in their membrane.

a) True. b) False.

Neurotransmitter Exocytosis

●Neurotransmitter release via exocytosis occurs in a _____-step process:

1) *SNARE Binding*: V & T SNARE _____, inducing _____ *changes*, drawing membranes together.

2) *Hemifusion*: changes in *curvature* & *lateral tension* induce _____ *sheets* of membranes to *fuse*.

3) *Fusion Pore*: *continued* changes in curvature & lateral tension *fuse* both membrane sheets, creating a _____.

4) *Release*: Fusion pore *expands* to _____ neurotransmitter & fused membrane relaxes.

EXAMPLE: Neurotransmitter Release via Exocytosis.

EXAMPLE: The toxin produced by *Clostridium tetani* (which causes tetanus) is a protease that cleaves/destroys SNAREs. Explain why this would lead to muscle paralysis.

PRACTICE: The R-SNARE and Q-SNARE proteins are involved in what process?

a) Formation of vesicles.

b) Fusion of transport vesicles with the target membrane.

c) Targeting of transport vesicle to intracellular destinations.

d) Packaging of neurotransmitters into transport vesicles.

e) Ligand-gated channel opening.

CONCEPT: SUMMARY OF MEMBRANE TRANSPORT

CONCEPT: SUMMARY OF MEMBRANE TRANSPORT

CONCEPT: SUMMARY OF MEMBRANE TRANSPORT

EXAMPLE: Match each term with the correct description:

a) Integral membrane protein _____.
b) Peripheral membrane protein _____.
c) Channel _____.
d) Passive Transport _____.
e) Active transport _____.
f) Na^+-K^+ ATPase _____.
g) Secondary transporter _____.
h) Antiporter _____.
i) Symporter _____.
j) Ion channel _____.

1. Facilitated diffusion.
2. Use the energy of one gradient to create another.
3. Interacts tightly with membrane interior.
4. Molecules moving in opposite directions.
5. Interacts with the border of a membrane.
6. Allows rapid movement of molecules down a gradient.
7. Movement against a concentration gradient.
8. Molecules moving in the same direction.
9. Can be voltage-gated or ligand-gated.
10. Creates an electrical gradient across the membrane.

PRACTICE: Classify each of the following transport systems according to the terms in the list on the right by putting the appropriate letter or letters in the blank next to each transport system. More than one term may apply to each transporter.

_____ GLUT1 transporter of erythrocytes.

_____ Cl^-/HCO_3^- transporter of erythrocytes.

_____ Na^+/K^+ ATPase.

_____ Ca^{2+} ATPase of sarcoplasmic reticulum.

_____ Glucose uptake driven by a Na+ gradient.

a) Primary active transport.
b) Secondary active transport.
c) Symport.
d) Antiport.
e) Uniport.
f) Facilitated diffusion.

CONCEPT: THERMODYNAMICS OF MEMBRANE DIFFUSION: UNCHARGED MOLECULE

●Recall: the *change* in Gibbs Free Energy Equation: Gibbs Free Energy Under Any Conditions $\Delta G = \Delta G^{\circ} + RT \ln(Q)$ $Q = \frac{[\text{Products}]}{[\text{Reactants}]}$

□ Describes ΔG due to _____ *gradients/concentrations*.

●$\Delta G_{transport}$: the Gibbs Free Energy change associated with *membrane* _____.

□ When the "reaction" is simply *membrane transport*, ΔG˚ = _____, (since no bonds are created/formed).

EXAMPLE: $\Delta G_{transport}$ for Membrane Diffusion of Uncharged Solutes.

$$\Delta G_{transport} = \underbrace{RT \ln\left(\frac{[C_{____\ side}]}{[C_{____\ side}]}\right)}_{\text{Chemical Gradient}}$$

R = 8.315 J/mol*K
T = Degrees Kelvin (K)

EXAMPLE: Calculate $\Delta G_{transport}$ for glucose diffusion across a cell membrane to the inside if [Glucose] outside cell = 10 mM, [Glucose] in cytosol = 0.1 mM, & the temperature = 20˚C.

STEP 1: Determine *net charge* of diffusing molecule: Uncharged. Charged (+/–).

STEP 2: Determine *direction* of diffusion (establish *initial* & *final* sides). Drawing a sketch may be helpful.

STEP 3: Check *units* on all numbers & if necessary, *convert* units to ensure *compatibility*. (Ex. Temp. = *Kelvin* ; [X] = $M_{olarity}$).

STEP 4: *Plug in* all given values (with *appropriate units*) into the *correct equation* & *algebraically solve* for missing variable.

CONCEPT: THERMODYNAMICS OF MEMBRANE DIFFUSION: UNCHARGED MOLECULE

PRACTICE: Calculate $\Delta G_{transport}$ for the diffusion of glucose from *outside to inside* a cell if extracellular [Glucose] = 5 mM, intacellular [Glucose] = 0.5 mM, & the temperature = 20˚C. Would this be an exergonic or endergonic process?

a) –5.61 KJ/mol.
b) 5.61 KJ/mol.
c) –0.383 KJ/mol.
d) 0.383 KJ/mol.

PRACTICE: Calculate $\Delta G_{transport}$ for the diffusion of glucose from *inside to outside* a cell if extracellular [Glucose] = 1 M, intacellular [Glucose] = 2.0 mM, & the temperature = 20˚C. Would this be a spontaneous or nonspontaneous process?

a) –15.15 KJ/mol.
b) 15.15 KJ/mol.
c) –1.03 KJ/mol.
d) 1.03 KJ/mol.

PRACTICE: Calculate the energy cost ($\Delta G_{transport}$) of pumping an uncharged solute across a cell's plasma membrane, against a 1.0×10^4-fold concentration gradient at 25˚C. Would this be an exergonic or endergonic process?

a) –95 KJ/mol.
b) 2 KJ/mol.
c) 23 KJ/mol.
d) –10 KJ/mol.

CONCEPT: THERMODYNAMICS OF MEMBRANE DIFFUSION: CHARGED ION

- When _____ diffuse across a membrane, the *transmembrane potential/voltage* (_____) must be considered.
  - □ Recall: *Transmembrane Potential/Voltage* ($\Delta\Psi$): the difference in *electrical* _____ across the membrane.
- $\Delta G_{transport}$ of ions due to *only* the transmembrane potential (_____ *gradient*) *alone* is given as: $\Delta G_{transport} = zF\Delta\Psi$.
  - □ _____: net charge of the diffusing ion.
  - □ _____ (*Faraday constant*): charge of 1 mole of electrons = 96,485 JV^{-1}/mole (Coulombs/mole).
- HOWEVER, recall: *ion* diffusion depends on _____ gradient (combination of *chemical* & *electrical* gradients).

EXAMPLE: $\Delta G_{transport}$ for Membrane Diffusion of Charged Ions.

R = 8.315 J/mol˚K
T = Degrees Kelvin (K)

$$\Delta G_{transport} = \underbrace{RT \ln\left(\frac{[C_{final\ side}]}{[C_{initial\ side}]}\right)}_{\text{Chemical Gradient}} + \underbrace{___\ \mathscr{F}\ \Delta___}_{\text{Gradient}}$$

EXAMPLE: Calculate the energy cost ($\Delta G_{transport}$) of pumping Ca^{2+} from the cytosol to the extracellular space if the temperature is 37˚C, $\Delta\Psi$ = 0.05 V (inside negative), cytosolic $[Ca^{2+}] = 1.0 \times 10^{-7}$ M, & extracellular $[Ca^{2+}] = 1.0 \times 10^{-3}$ M.

STEP 1: Determine *net charge* of diffusing molecule: Uncharged. Charged (+/–): _____.

STEP 2: Determine *direction* of diffusion (establish *initial* & *final* sides). Determine *sign* of $\Delta\Psi$ (+ or –). Draw a sketch.

STEP 3: Check *units* on all numbers & if necessary, *convert* units to ensure *compatibility*. (Ex. Temp. = *Kelvin* ; $\Delta\Psi$ = Volts).

STEP 4: *Plug in* all given values (with *appropriate units*) into the *correct equation* & *algebraically solve* for missing variable.

CONCEPT: THERMODYNAMICS OF MEMBRANE DIFFUSION: CHARGED ION

PRACTICE: Calculate the free energy change ($\Delta G_{transport}$) for the movement of Na^+ into a cell when its concentration outside is 150 mM and its cytosolic concentration is 10 mM. Assume that T = 20°C and $\Delta\Psi$ = –50 mV (inside negative).

a) –1.7 KJ/mol.
b) –11.4 KJ/mol.
c) –11,600 KJ/mol.
d) 11.4 KJ/mol.
e) 14.3 KJ/mol.

PRACTICE: Calculate the $\Delta G_{transport}$ required to move 1 mole of Na^+ ions from inside the cell ([Na^+] inside = 5 mM) to the outside of the cell ([Na^+] outside = 150 mM) when $\Delta\Psi$ = –70 mV (inside negative) & the temperature is 37°C.

a) –15.5 KJ/mol.
b) 2.0 KJ/mol
c) 15.5 KJ/mol.
d) –2.0 KJ/mol.

PRACTICE: Calculate the $\Delta G_{transport}$ when Ca^{2+} ions move from the endoplasmic reticulum ([Ca^{2+}] = 1 mM) to the cytoplasm ([Ca^{2+}] = 0.1 μM). Assume that $\Delta\Psi$ = 0 and T = 25°C.

a) 23 KJ/mol.
b) –23 KJ/mol.
c) –17 KJ/mol.
d) 17 KJ/mol.