

Which of the following would most readily cross a lipid bilayer by simple diffusion?

- A. Oxygen**
- B. Glucose
- C. Chloride ions
- D. Proteins

4. 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. Active transport.

5. You are studying the entry of a small molecule into red blood cells. You determine the rate of movement across the membrane under a variety of conditions and make the following observations:

- i. The molecules can move across the membrane in either direction.
- ii. The molecules always move down their concentration gradient.
- iii. No energy source is required for the molecules to move across the membrane.
- iv. As the difference in concentration across the membrane increases, the rate of transport reaches a maximum.

The mechanism used to get this molecule across the membrane is most likely:

- A. simple diffusion.
- B. facilitated diffusion.**
- C. active transport.
- D. There is not enough information to determine a mechanism.

6. A particular cell has an internal chloride ion concentration of 50 mM, while outside the cell the chloride ion concentration is 100 mM. The free energy change associated with chloride transport into the cell ( $\Delta G$ ) is +970 cal/mol. Which choice below is the best explanation for this data?

- A.  $\text{Cl}^-$  ion movement into the cell is energetically favorable.
- B. Both the concentration gradient and electrical gradient favor movement of  $\text{Cl}^-$  ions into the cell.
- C. The concentration gradient for  $\text{Cl}^-$  ions favors movement into the cell, but the electrical gradient opposes inward movement of  $\text{Cl}^-$ .**
- D. Both the electrical and chemical gradients for  $\text{Cl}^-$  ions favor outward movement of  $\text{Cl}^-$  ions.

7. Place the following steps in an action potential in the correct order.

- 1. Sodium channels become inactivated and potassium channels are opened.
- 2. Sodium and potassium channel gates are closed; membrane potential is  $-60\text{mV}$ .
- 3. Sodium channel gates open in response to change in membrane potential.

4. Potassium rapidly leaves the cell; membrane potential drops to  $-75\text{mV}$ .  
5. Sodium rushes into the cell; membrane potential reaches  $+40\text{mV}$ .

A. 2, 1, 4, 3, 5, 2.  
B. 2, 1, 3, 4, 5, 2.  
C. 2, 3, 4, 1, 5, 2.  
**D. 2, 3, 5, 1, 4, 2.**

8. How are neurotransmitters released into a synapse in response to an action potential?

A. They pass through voltage-gated neurotransmitter channels.  
B. They diffuse through the cell when the action potential reverses membrane potential.  
C. They pass through gap junctions into the post-synaptic cell.  
**D. They are released by membrane fusion of vesicles in response to increased calcium concentration.**

10. Which of the following is the most likely immediate affect of G-protein activation?

A. Receptors are stimulated to bind to their ligands.  
**B. Enzymes are activated that catalyze second messenger formation.**  
C. GTP is depleted from the cell.  
D. G-proteins bind to DNA and activate gene expression.

1. (10 points) List and describe three types of membrane transport proteins. EXTRA CREDIT: Provide a specific example of each type (1 point each).

Carrier proteins - exist in two conformations, altered by high affinity binding of the transported molecule. Moves material in either direction, down concentration gradient (facilitated diffusion). EXAMPLE: GluT1 erythrocyte glucose transporter.

Channel proteins - primarily for ion transport. Form an aqueous pore through the lipid bilayer. May be gated. Moves material in either direction, down concentration gradient (facilitated diffusion). EXAMPLES: Voltage-gated sodium channel, erythrocyte bicarbonate exchange protein.

Active transporters - use energy (direct, ATPase; or indirect, ion gradient) to drive molecules across the membrane against a concentration gradient. EXAMPLES: Na<sup>+</sup>/K<sup>+</sup> ATPase, Na<sup>+</sup>/glucose transporter.

2. (10 points) Describe how a resting membrane potential is established and maintained.

The Na<sup>+</sup>/K<sup>+</sup> ATPase pump moves K<sup>+</sup> ions into the cell and Na<sup>+</sup> ions out of the cell to establish strong chemical gradients for each. The cell still maintains near electrical neutrality (K<sup>+</sup> balanced inside by large anions, Na<sup>+</sup> balanced outside by Cl<sup>-</sup>). Leaky K<sup>+</sup> channels allow some K<sup>+</sup> ions to flow out of cell, down chemical concentration gradient. This creates an electrical potential, as positive charges are leaving the cell. This electrical gradient favors movement of K<sup>+</sup> back into the cell, setting up an electrochemical equilibrium for K<sup>+</sup>, typically at about -60 mV.

3. (10 points) Describe the difference between “open”, “closed” and “inactivated” voltage-gated sodium channels. Include in your answer the role of each state in generating an action potential.

Closed channels have an internal, voltage sensitive gate that is closed. Na<sup>+</sup> ions are prevented from entering the cell by the closed gate. This state exists during the resting membrane potential. The channel is poised to respond to a signal.

Open channels have responded to a change in membrane potential by opening the internal gate. This is a protein conformational change in response to electrical changes. Na<sup>+</sup> ions rapidly enter the cell, leading to depolarization and potentially to an action potential.

Channels are inactivated in response to an action potential. A protein domain blocks the exit to the channel, preventing the flow of Na<sup>+</sup> ions. This allows the cell to restore the resting potential, and allows directional travel of the action potential by preventing another signal from occurring too soon.

4. (15 points) List and describe five different types of molecules that participate in signal transduction pathways.

Primary messengers/signal - bind receptors to initiate a cellular response pathway.

Tyrosine kinase receptors - plasma membrane receptors that transmit an external signal to the cell interior by autophosphorylation.

G-protein coupled receptors - ligand binding activates intracellular G proteins to trigger a pathway.

G proteins - activated by ligand-bound receptors. Trimeric, inactive receptors are induced to uncouple into alpha and beta-gamma subunits, as a result of the alpha subunit exchanging GDP for GTP.

SH domain proteins - bind to activated tyrosine kinase receptors to continue a pathway.

adenylyl cyclase/phospholipase C - examples of G protein targets that synthesize second messengers.

Second messengers - small molecules synthesized in response to a signal. Rapidly spread throughout a cell. Includes cAMP,  $\text{Ca}^{2+}$ , IP<sub>3</sub>, DAG, NO, etc.

Ser/Thr kinases (MAP kinases) - a cascade of protein activation that amplifies signals and leads to cellular changes.

Transcription factors - activated by upstream events to alter cellular gene expression.

$$\begin{aligned}
 F &= PA(\text{Co}-\text{Ci}) \\
 &= (.00005)(4/3)(\pi)(145-15) \\
 &= .0204
 \end{aligned}$$

With reference to the fluid mosaic model of the cell membrane, which of the following statements is

Homeostasis: maintenance of an internal environment in equilibrium through dynamic balance.

The GHK equation expresses that the membrane potential is a weighted average of the individual equilibrium potentials and the magnitude of the conductance for all ions contributing the membrane potential.

Attachment to actin depends on phosphorylation of the cross-bridge by a  $\text{Ca}^{++}$ -calmodulin-dependent myosin light-chain kinase (MLCK). Phosphorylated cross-bridges cycle until they are dephosphorylated by myosin phosphatase. Regulation of smooth muscle myosin interactions with actin by  $\text{Ca}^{++}$ -stimulated phosphorylation.

Same, but reg dep on light chain phosph by MLCK rather than  $\text{Ca}^{2+}$  and troponin C.

1. Myosin crossbridge attaches to actin filament, pulling thin fil to ctr of thick and gen force
2. ADP and  $\text{P}_i$  are rel from myosin head; ATP binds.
3. ATP dec affinity of myosin for actin, allowing rel of myosin from actin.
4. ATP energy prod conf chg in the myosin head (i.e., recocking).
5. Cross-bridge = ready for another contraction cycle. Cycle continues as long as cross-bridge = phosph (same basic steps, slower for SMCs).
6. Cross-bridge cycling = hydrolysis of 1 ATP/cyc, until myoplasmic  $\text{Ca}^{2+}$  falls.
7. MLCK becomes inactive w/ dec in  $\text{Ca}^{2+}$ , and the cross-bridges are dephosph by MP

SMC contraction initiated by increase of intracellular  $\text{Ca}^{2+}$  via

1. pacemaker cells
2. neurotransmitters (ACh, NE)
3. hormones (ATII, vasopressin, endothelin), signaling molecules (IP3)

In a living cell, the concentration gradient of  $\text{Na}^+$  tends to drive it into the cell, and the electrical gradient of  $\text{Na}^+$  (a positive ion) also tends to drive it inward to the negatively-charged interior. The situation is more complex, however, for other elements such as potassium. The electrical gradient of  $\text{K}^+$ , a positive ion, also tends to drive it into the cell, but the concentration gradient of  $\text{K}^+$  tends to drive  $\text{K}^+$  out of the cell. The combined gradient of concentration and electrical charge that affects an ion is called its electrochemical gradient.

The equilibrium potential of an ion is the potential which just balances the concentration difference of the ion across the membrane.

The calculation of the "net" potential of an ion (the difference between the resting membrane potential and the equilibrium potential) tells you how much "force" (in electrical terms), and its direction, is acting on an ion in a resting neuron.

When voltage-gated ion channels open, ions move through these channels under the influence of the combined influence of the electrical field of the membrane potential and the concentration gradients of the ions.

A neuron is said to be polarized because there is a difference of electrical potential across its membrane.

Axons generally have which of the following concentrations of ions INTERNALLY (relative to extra-cellular space)?  
High  $K^+$ , low  $Na^+$ , low  $Cl^-$ .

The extracellular space around axons generally has which of the following concentrations of ions (relative to intracellular concentrations)?  
Low  $K^+$ , high  $Na^+$ , high  $Cl^-$ .