Cells and Transport Processes

• Cells and cellular compartments are able to accumulate a variety of substances in concentrations that are very different from those of the surroundings.

• Most of the substances that move across membranes are dissolved gases, ions, and small organic molecules; solutes.
The Movement of a Solute Across a Membrane Is Determined by Its Concentration Gradient or Its Electrochemical Potential

- The movement of a molecule that has no net charge is determined by its concentration gradient.
- Simple or facilitated diffusion involve exergonic movement “down” the concentration gradient (negative $\Delta G$).
- Active transport involves endergonic movement “up” the concentration gradient (positive $\Delta G$).
The electrochemical potential

- The movement of an ion is determined by its *electrochemical potential*, the combined effect of its concentration gradient and the charge gradient across the membrane.

- The active transport of ions across a membrane creates a charge gradient or *membrane potential* \( (V_m) \) across the membrane.
Active transport of ions

- Most cells have an excess of negatively charged solutes inside the cell.

- This charge difference favors the inward movement of cations such as Na$^+$ and outward movement of anions such as Cl$^-$.

- In all organisms, active transport of ions across the plasma membrane results in asymmetric distribution of ions inside and outside the cell.
Figure 8-2

(a) Simple diffusion. Oxygen, carbon dioxide, and water diffuse directly across the plasma membrane in response to their relative concentrations inside and outside the cell.

(b) Facilitated diffusion mediated by carrier proteins. The movement of glucose across the plasma membrane is facilitated by a specific glucose transporter called GLUT1. An anion exchange protein facilitates the reciprocal transport of chloride ($Cl^-$) and bicarbonate ($HCO_3^-$).

(c) Facilitated diffusion mediated by channel proteins. Aquaporin channel proteins can facilitate the rapid inward or outward movement of water molecules.

(d) Active transport. Driven by the hydrolysis of ATP, the Na$^+$/K$^+$ pump moves three sodium ions outward for every two potassium ions moved inward, establishing an electrochemical potential across the plasma membrane for both ions.
Simple Diffusion: Unassisted Movement Down the Gradient

• The most straightforward way for a solute to cross a membrane is through **simple diffusion**, the unassisted net movement of a solute from high to lower concentration

• Typically this is only possible for gases, nonpolar molecules, or small polar molecules such as water, glycerol, or ethanol
Diffusion Always Moves Solutes Toward Equilibrium

• Diffusion always tends to create a random solution in which the concentration is the same everywhere

• Solutes will move toward regions of lower concentration until the concentrations are equal
  – Diffusion always proceeds from regions of higher to lower free energy

• Thus diffusion is always movement toward equilibrium
Osmosis Is the Movement of Water Across a Selectively Permeable Membrane

• The properties of water cause it to behave in a special way

• Water molecules are uncharged and so are not affected by the membrane potential

• Water concentration is not appreciably different on opposite sides of a membrane
Osmosis

- If two solutions are separated by a \textit{selectively permeable membrane}, permeable to the water but not the solutes, the water will move toward the region of higher solute concentration

- This movement is called \textbf{osmosis}

- For most cells, water tends to move inward
Figure 8-8A-1

HYPERTONIC SOLUTION

ANIMAL CELL

(a) Shriveled

ISOTONIC SOLUTION

Normal

H2O

H2O

(b) Lysed

HYPOTONIC SOLUTION

PLANT CELL

(c) Plasmolyzed

H2O

(d) Flaccid

Turgid
The use of liposomes to study diffusion

- Bangham trapped solutes inside liposomes, and measured the rate at which they diffused out

- Ions were trapped inside the liposomes for days, and small uncharged molecules such as oxygen diffused too rapidly to measure

- Factors affecting diffusion: size, polarity, and charge
Solute Size

• In general, lipid bilayers are more permeable to small molecules—water, oxygen, carbon dioxide—than larger ones.

• But without a transporter even these small molecules move more slowly than in the absence of a membrane.

• Still, water diffuses more rapidly than would be expected for a polar molecule.
Diffusion of water

- It is thought that membranes contain tiny pores that allow water to diffuse more rapidly than predicted based on its polarity.

- Alternatively, perhaps membrane lipid movement creates temporary “holes” through which the water can move.

- There is little evidence for these hypotheses.
Solute Polarity

• Lipid bilayers are more permeable to nonpolar substances than to polar ones

• Nonpolar substances dissolve readily into the hydrophobic region of the bilayer

• Large nonpolar molecules such as estrogen and testosterone cross membranes easily, despite their large size
A measure of solute polarity

- Polarity of a solute can be measured by the ratio of its solubility in an organic solvent to its solubility in water

- This is called the *partition coefficient*

- In general, the more nonpolar (hydrophobic) a substance is, the higher the partition coefficient
Solute Charge

• The relative impermeability of polar substances, especially ions, is due to their association with water molecules

• The molecules of water form a *shell of hydration* around polar substances

• In order for these substances to move into a membrane, the water molecules must be removed, which requires energy
The Rate of Simple Diffusion Is Directly Proportional to the Concentration Gradient

• Thermodynamically, simple diffusion is always an exergonic process, requiring no input of energy

• Kinetically, the net rate of transport for a substance is proportional to its concentration difference across the membrane
\( V_{\text{inward}} \)

- \( \nu_{\text{inward}} = P \Delta [S] \)
  - \( V_{\text{inward}} = \) rate of diffusion in moles/sec*cm\(^2\)
  - \( \Delta [S] = [S]_{\text{outside}} - [S]_{\text{inside}} \)
  - \( P = \) permeability coefficient, which depends on thickness and viscosity of the membrane

- Simple diffusion has a linear relationship between inward flux of solute and the concentration gradient of the solute
Figure 8-5

\[ V = \text{rate of diffusion} \]

\[ \Delta [S] = \text{solute concentration gradient} \]

- Facilitated diffusion (hyperbolic)
- Simple diffusion (linear)
Facilitated Diffusion: Protein-Mediated Movement Down the Gradient

- Most substances in the cell are too large or too polar to cross membranes by simple diffusion.
- These can only move in and out of cells with the assistance of transport proteins.
- If the process is exergonic, it is called facilitated diffusion; the solute diffuses as dictated by its concentration gradient.
Transport proteins in facilitated diffusion

- No input of energy is needed in facilitated diffusion
- The role of the transport proteins is just to provide a path through the lipid bilayer, allowing the “downhill” movement of a polar or charged solute
Carrier Proteins and Channel Proteins Facilitate Diffusion by Different Mechanisms

- Transport proteins are large, integral membrane proteins with multiple transmembrane segments.

- **Carrier proteins** (*transporters* or *permeases*) bind solute molecules on one side of a membrane, undergo a conformation change, and release the solute on the other side of the membrane.

- **Channel proteins** form hydrophilic *channels* through the membrane to provide a passage route for solutes.
Carrier Proteins Alternate Between Two Conformational States

- The alternating conformation model states that a carrier protein is allosteric protein and alternates between two conformational states.

- In one state the solute binding site of the protein is accessible on one side of the membrane.

- The protein shifts to the alternate conformation, with the solute binding site on the other side of the membrane, triggering solute release.
Carrier Proteins Are Analogous to Enzymes in Their Specificity and Kinetics

• Carrier proteins are analogous to enzymes
  
  - Facilitated diffusion involves binding a substrate, on a specific solute binding site
  - The carrier protein and solute form an intermediate
  - After conformational change, the “product” is released (the transported solute)
  - Carrier proteins are regulated by external factors
Specificity of Carrier Proteins

• Carrier proteins share the property of high specificity with enzymes, too

• Transport proteins are often highly specific for a single compound or a small group of closely related compounds

• The carrier protein for glucose in erythrocytes is specific to a few monosaccharides, and is stereospecific for only their $D$-isomers
Kinetics of Carrier Protein Function

• Carrier proteins can become saturated as the concentration of the solute rises

• This is because the number of carrier proteins is limited and each functions at a finite maximum velocity

• So, carrier-facilitated transport (like enzyme catalysis) exhibits *saturation kinetics*
Saturation kinetics of carrier proteins

- Carrier facilitated transport has an upper limiting velocity, $V_{\text{max}}$, and a constant $K_m$ corresponding to the concentration of solute needed to achieve $\frac{1}{2}(V_{\text{max}})$

- Initial rate of solute transport can be described:
  
  \[ \nu = \frac{V_{\text{max}}[S]}{K_m + [S]} \]
Competitive inhibition of carrier proteins

- *Competitive inhibition* of carrier proteins can occur in the presence of molecules or ions that are structurally related to the correct substrate.

- For example, the transport of glucose by glucose carrier proteins can be inhibited by the other monosaccharides that the carrier accepts (such as mannose and galactose).
Carrier Proteins Transport Either One or Two Solutes

• When a carrier protein transports a single solute across the membrane, the process is called uniport

• A carrier protein that transports a single solute is called a uniporter

• When two solutes are transported simultaneously, and their transport is coupled, the process is called coupled transport
Coupled transport

- If the two solutes are moved across a membrane in the same direction, it is referred to as **symport** (or **cotransport**)

- If the solutes are moved in opposite directions, it is called **antiport** (or **countertransport**)

- Transporters that mediate these processes are **symporters** and **antiporters**
Figure 8-6B

OUTER SURFACE

INNER SURFACE

Sympport

Antiport

(b) Coupled transport
The Erythrocyte Glucose Transporter and Anion Exchange Protein Are Examples of Carrier Proteins

- The glucose transporter is a uniport carrier for glucose
- The anion exchange protein is an antiport anion carrier for $\text{Cl}^-$ and $\text{HCO}_3^-$
- Both are found in the plasma membrane of erythrocytes
The Glucose Transporter: A Uniport Carrier

• The erythrocyte is capable of glucose uptake by facilitated diffusion because the level of blood glucose is much higher than that inside the cell

• Glucose is transported inward by a glucose transporter (GLUT; GLUT1 in erythrocytes)

• GLUT1 is an integral membrane protein with 12 transmembrane segments, which form a cavity with hydrophilic side chains
1. Glucose binds to a GLUT1 transporter protein that has its binding site open to the outside of the cell ($T_1 \text{ conformation}$).

2. Glucose binding causes the GLUT1 transporter to shift to its $T_2$ conformation with the binding site open to the inside of the cell.

3. Glucose is released to the interior of the cell, initiating a second conformational change in GLUT1.

4. Loss of bound glucose causes GLUT1 to return to its original ($T_1$) conformation, ready for a further transport cycle.
Transport by GLUT1 is reversible

- A carrier protein can facilitate transport in either direction
- The direction of transport is dictated by the relative solute concentrations outside and inside the cell
- Glucose concentration is kept low inside most animal cells
The Erythrocyte Anion Exchange Protein: An Antiport Carrier

• The anion exchange protein (also called the chloride-bicarbonate exchanger) facilitates reciprocal exchange of Cl\(^{-}\) and HCO\(_3\)^{−} ions only

• Exchange will stop if either anion is absent

• The ions are exchanged in a strict 1:1 ratio
The “ping-pong” mechanism

• The anion exchange protein is thought to alternate between two conformational states

• In the first, it binds a chloride ion on one side of the membrane, which causes a change to the second state

• In the second state, the chloride is moved across the membrane and released
The “ping-pong” mechanism (continued)

- The release of chloride causes the protein to bind bicarbonate

- The binding of bicarbonate causes a shift back to the first conformation

- In this conformation, bicarbonate is moved out of the cell, allowing the carrier to bind chloride again
Biological relevance of anion exchange

- In tissues, waste CO$_2$ diffuses into the erythrocytes where it is converted to HCO$_3^-$ by the enzyme *carbonic anhydrase*.

- As the concentration of bicarbonate rises it moves out of the cell, coupled with uptake of Cl$^-$ to prevent a net charge imbalance.

- In the lungs, the entire process is reversed.
Channel Proteins Facilitate Diffusion by Forming Hydrophilic Transmembrane Channels

- Channel proteins form hydrophilic transmembrane channels that allow specific solutes to cross the membrane directly.

- There are three types of channels: ion channels, porins, and aquaporins.
Ion Channels: Transmembrane Proteins That Allow Rapid Passage of Specific Ions

- **Ion channels**, tiny pores lined with hydrophilic atoms, are remarkably selective.

- Because most allow passage of just one ion, there are separate proteins needed to transport \( \text{Na}^+ \), \( \text{K}^+ \), \( \text{Ca}^{2+} \), and \( \text{Cl}^- \), etc.

- Selectivity is based on both binding sites involving amino acid side chains, and a size filter.
Gated channels

• Most ion channels are *gated*, meaning that they open and close in response to some stimulus

  - *Voltage-gated channels* open and close in response to changes in membrane potential

  - *Ligand-gated channels* are triggered by the binding of certain substances to the channel protein

  - *Mechanosensitive channels* respond to mechanical forces acting on the membrane
Functions of ion channels

- Ion channels play roles in many types of cellular communication, such as muscle contraction and electrical signaling of nerve cells.

- Ion channels are also needed for maintaining salt balance in cells and airways linking the lungs.

  - A chloride ion channel, the *cystic fibrosis transmembrane conductance regulator (CFTR)*, helps maintain the proper $\text{Cl}^-$ concentration in lungs; defects in the protein cause cystic fibrosis.
Porins: Transmembrane Proteins That Allow Rapid Passage of Various Solutes

• Pores on outer membranes of bacteria, mitochondria and chloroplasts are larger and less specific than ion channels.

• The pores are formed by multipass transmembrane proteins called **porins**.

• The transmembrane segments of porins cross the membrane as $\beta$ barrels.
Structure of porins

- The $\beta$ barrel has a water-filled pore at its center

- Polar side chains line the inside of the pore, allowing passage of many hydrophilic solutes

- The outside of the barrel contains many nonpolar side chains that interact with the hydrophobic interior of the membrane
Figure 8-8A,B

(a) Porin side view

(b) Porin end view
Aquaporins: Transmembrane Channels That Allow Rapid Passage of Water

- Movement of water across cell membranes in some tissues is faster than expected given the polarity of the water molecule

- **Aquaporin (AQP)** was discovered only in 1992

- Aquaporins allow rapid passage of water through membranes of erythrocytes and kidney cells in animals, and root cells and vacuolar membranes in plants
Aquaporin structure

• All aquaporins are tetrameric integral membrane proteins

• The identical monomers associate with their 24 transmembrane segments oriented to form four central channels

• The channels, lined with hydrophilic side chains, are just large enough for water molecules to pass through one at a time
Active Transport: Protein-Mediated Movement Up the Gradient

- Facilitated diffusion is important, but only accounts for movement of molecules down a concentration gradient, toward equilibrium.

- Sometimes a substance must be transported against a concentration gradient.

- In this case active transport is used to move solutes up a concentration gradient, away from equilibrium.
Functions of active transport

• Active transport couples endergonic transport to an exergonic process, usually ATP hydrolysis

• Active transport performs three important cellular functions
  - Uptake of essential nutrients
  - Removal of wastes
  - Maintenance of nonequilibrium concentrations of certain ions
Nonequilibrium conditions

- Active transport allows the creation and maintenance of an internal cellular environment that differs greatly from the surrounding environment.

- Many membrane proteins involved in active transport are called pumps, because energy is required to move substances against their concentration gradients.
Active transport is *unidirectional*

- Active transport differs from diffusion (both simple and facilitated) in the direction of transport.

- Diffusion is *nondirectional* with respect to the membrane and proceeds as directed by the concentrations of the transported substances.

- Active transport has an intrinsic *directionality*.
The Coupling of Active Transport to an Energy Source May Be Direct or Indirect

- Active transport mechanisms can be divided based on the sources of energy and whether or not two solutes are transported at the same time

- Active transport is categorized as *direct* or *indirect*
(a) Direct active transport involves a transport system coupled to an exergonic chemical reaction, most commonly the hydrolysis of ATP. As shown here, ATP hydrolysis drives the outward transport of protons, thereby establishing an electro-chemical potential for protons across the membrane.
Indirect active transport

- Indirect active transport depends on the simultaneous transport of two solutes

- Favorable movement of one solute *down* its gradient drives the unfavorable movement of the other *up* its gradient

- This can be a symport or an antiport, depending on whether the two molecules are transported in the same or different directions
(b) Indirect active transport involves the coupled transport of a solute $S$ and ions—protons, in this case. The exergonic inward movement of protons provides the energy to move the transported solute, $S$, against its concentration gradient or electrochemical potential.
Direct Active Transport Depends on Four Types of Transport ATPases

• Four types of transport ATPases have been identified
  - $P$-type
  - $V$-type
  - $F$-type
  - $ABC$-type

• They differ in structure, mechanism, location, and roles
P-type ATPases

- **P-type ATPases** are members of a large family, and are reversibly phosphorylated by ATP on a specific aspartic acid residue.

- They have 8-10 transmembrane segments in a single polypeptide, which crosses the membrane multiple times.

- They are sensitive to inhibition by vanadate, $\text{VO}_4^{3-}$, which resembles phosphate, $\text{PO}_4^{3-}$. 
V-type ATPases

- **V-type ATPases** pump protons into organelles such as vacuoles, vesicles, lysosomes, endosomes, and the Golgi complex.

- They have two multisubunit components: an integral component embedded in the membrane and a peripheral component that juts out from the membrane surface.
F-type ATPases

- **F-type ATPases** are found in bacteria, mitochondria and chloroplasts
- They transport protons and have two components: a transmembrane pore \((F_0)\) and a peripheral membrane component \((F_1)\) that contains the ATP binding site
- Both are multisubunit components
F-type ATPases also function in reverse

• The F-type ATPases can facilitate the reverse process

• In this case, ATP is synthesized, driven by the exergonic flow of protons down their gradients

• In the reverse direction, the ATPases are more accurately called **ATP synthases**
ABC-type ATPases

• The **ABC-type ATPases** are also called **ABC (ATP binding cassette) transporters**

• The term *cassette* describes the catalytic domain that binds ATP as part of the transport process

• ABC-type ATPases comprise a very large family of transport proteins found in all organisms
Importers and exporters

- Most of the ABC transporters initially discovered from bacteria were *importers*, involved in uptake of nutrients

- But many are now known to be *exporters*, some of which are medically important
Medical significance of ABC-type ATPases

- ABC transporters are medically important because some of them pump antibiotics or drugs out of cells, rendering the cell resistant to the drug.

- Some human tumors are resistant to drugs that normally inhibit growth of tumors; the resistant cells have high concentrations of an ABC transporter called MDR (multidrug resistance) transport protein.
The cystic fibrosis transporter

- *CFTR*, the transporter responsible for cystic fibrosis (when defective), is similar in sequence and structure to the core domains of ABC transporters

- However, CFTR is an ion channel and does not use ATP to drive transport
Indirect Active Transport Is Driven by Ion Gradients

- Indirect active transport (or secondary active transport) is not powered by ATP hydrolysis.

- The inward transport of molecules up their electrochemical gradients is often coupled to and driven by simultaneous inward movement of Na+ (animals) or protons (plant, fungi, bacteria) down their gradients.
Symport mechanisms of indirect active transport

- Most cells continuously pump either sodium ions or protons out of the cell (e.g., the Na\(^+\)/K\(^+\) pump in animals)

- The resulting high extracellular concentration of Na\(^+\) is a driving force for the uptake of sugars and amino acids

- This is indirectly related to ATP because the pump that maintains the sodium ion gradient is driven by ATP
Proton gradients drive indirect active transport in many organisms

- Most organisms rely on proton gradients rather than the Na\(^+\) gradients used by animals.

- For example, fungi and plants use proton symport for the uptake of organic solutes, with ATP driving the proton pump that creates and maintains the proton electrochemical potential.

- Proton or ion gradients can be used for export as well as import.
Examples of Active Transport

- The Na+/K+ ATPase (or pump) in all animal cells is a well-understood example of direct active transport by a P-type ATPase.

- The Na+/glucose symporter is an example of indirect active transport.

- Light-driven proton transport in some bacteria is an example of an unusual type of transport.
Direct Active Transport: The Na+/K+ Pump Maintains Electrochemical Ion Gradients

- In a typical animal cell, $[\text{K}^+]_{\text{inside}}/[\text{K}^+]_{\text{outside}}$ is about 35:1 and $[\text{Na}^+]_{\text{inside}}/[\text{Na}^+]_{\text{outside}}$ is around 0.08:1

- The electrochemical potentials for sodium and potassium are essential as a driving force for coupled transport and for transmission of nerve impulses
Requirement for energy

- The pumping of both Na\(^+\) and K\(^+\) ions against their gradients requires energy.

- The pump that is responsible, the Na\(^+\)/K\(^+\) ATPase (or pump), uses the exergonic hydrolysis of ATP to drive the transport of both ions.

- It is responsible for the asymmetric distribution of ions across the plasma membrane of animal cells.
Figure 8-11

OUTSIDE OF CELL

K⁺ K⁺

Oligosaccharides

INSIDE OF CELL

β α α β

Na⁺ Na⁺ Na⁺

Binding site for ATP
The Na\(^+\)/K\(^+\) pump is an allosteric protein

- The Na\(^+\)/K\(^+\) pump has two alternative conformational states, E\(_1\) and E\(_2\)

- The E\(_1\) conformation is open to the inside of the cell and has high affinity for Na\(^+\) ions

- The E\(_2\) conformation is open to the outside of the cell and has high affinity for K\(^+\) ions
Figure 8-12

1. Three Na⁺ from inside the cell bind to E₁.
2. Na⁺ binding triggers phosphorylation of α subunits by ATP.
3. A conformational change to E₂ following phosphorylation expels three Na⁺ to the outside of the cell.
4. Two K⁺ from outside the cell bind to E₂.
5. K⁺ binding triggers dephosphorylation, causing a conformational change back to E₁.
6. Two K⁺ expelled to the inside as the pump returns to initial state.

Initial state: pump open to inside (E₁ conformation)

OUTSIDE OF CELL

INSIDE OF CELL

Pump open to outside, ready to start second half of cycle (E₂ conformation)
Indirect Active Transport: Sodium Symport Drives the Uptake of Glucose

• Although most glucose into and out of our cells occurs by facilitated diffusion, some cells use a Na⁺/glucose symporter.

• For example, the cells lining the intestine take up glucose and some amino acids even when their concentrations are much lower outside than inside the cells.
Uptake of glucose via sodium symport requires energy

- A steep Na+ gradient that is maintained across the plasma membrane (via the Na+/K+ pump) is used to provide the energy needed

- The proteins responsible for sodium symport are called sodium-dependent glucose transporters, or SGLT proteins
Figure 8-13

1. Two sodium ions from outside the cell are bound.

2. Binding of sodium ions allows glucose binding and a subsequent conformational change.

3. Symporter opens to inside.

4. Sodium ions are released inside, but are continually extruded to outside by a separate sodium-potassium pump (dashed line).

5. Loss of sodium ions is followed by glucose release to inside.

6. Release of glucose allows the empty symporter to return to initial state.
The Energetics of Transport

• Every transport event in the cell is an energy transaction

• For uncharged solutes, the only variable is the concentration gradient across the membrane

• For charged solutes, both concentration and electrical potential are relevant
For Uncharged Solutes, the $\Delta G$ of Transport Depends Only on the Concentration Gradient

- For solutes with no net charge, we are concerned only with their concentration gradient across the membrane

- Because of this, the $\Delta G$ for transport of uncharged solutes is relatively easy to calculate
Calculating $\Delta G$ for the Transport of Molecules

- The general reaction for solute transportation

$$- [S]_{\text{outside}} \rightarrow [S]_{\text{inside}}$$

- And $\Delta G$ can be calculated as

$$- \Delta G = \Delta G^\circ + RT \ln \frac{[S]_{\text{inside}}}{[S]_{\text{outside}}}$$
$K_{eq}$ for transport of uncharged solutes

- The $K_{eq}$ for uncharged solutes will always be 1

\[
K_{eq} = \frac{[S]_{\text{inside}}}{[S]_{\text{outside}}} = 1.0
\]

- And $\Delta G^\circ$ is always 0

\[
\Delta G^\circ = -RT \ln K_{eq} = -RT \ln 1 = 0
\]
ΔG of inward transport

- The ΔG of inward transport simplifies to

\[ ΔG_{\text{inward}} = +RT \ln \frac{[S]_{\text{inside}}}{[S]_{\text{outside}}} \]

- If \([S]_{\text{inside}} < [S]_{\text{outside}}\), ΔG is negative and the transport is exergonic

- But, if \([S]_{\text{inside}} > [S]_{\text{outside}}\), ΔG is positive and transport is against the concentration gradient
An Example: The Uptake of Lactose

- Suppose the [lactose] inside a bacterium must be kept at 10mM, and the external [lactose] is 0.20 mM

- We can determine the energy requirement for inward transport of lactose
An Example: The Uptake of Lactose

\[ \Delta G_{\text{inward}} = + RT \ln \frac{[\text{lactose}]_{\text{inside}}}{[\text{lactose}]_{\text{outside}}} \]

\[ = + (1.987)(273 + 25) \ln \frac{0.010}{0.0002} \]

\[ = +592 \ln 50 \]

\[ = +2316 \text{ cal/mol} \]

\[ = +2.32 \text{ kcal/mol} \]

- For outward transport of lactose \([S]_{\text{inside}}\) and \([S]_{\text{outside}}\) must be interchanged
## Table 8-3

### Calculation of $\Delta G$ for the Transport of Charged and Uncharged Solutes

<table>
<thead>
<tr>
<th>Transport Process</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image" alt="Diagram showing inward and outward transport" /></td>
</tr>
</tbody>
</table>

### $\Delta G$ for Transport of Uncharged Solutes:

\[
\Delta G_{\text{inward}} = +RT \ln \frac{[S]_{\text{inside}}}{[S]_{\text{outside}}} \quad R = 1.987 \text{ cal/mol} \cdot \text{K} \\
\Delta G_{\text{outward}} = -\Delta G_{\text{inward}} \quad T = K = ^\circ C + 273
\]

### $\Delta G$ for Transport of Charged Solutes:

\[
\Delta G_{\text{inward}} = +RT \ln \frac{[S]_{\text{inside}}}{[S]_{\text{outside}}} + zFV_m \quad z = \text{charge on ion} \\
F = 23,062 \text{ cal/mol} \cdot \text{V} \\
V_m = \text{membrane potential (in volts)} \\
\Delta G_{\text{outward}} = -\Delta G_{\text{inward}}
\]
For Charged Solutes, the $\Delta G$ of Transport Depends on the Electrochemical Potential

- For charged solutes we must consider both concentration gradient and the membrane potential, $V_m$

- Because $V_m$ is nearly always negative, it usually favors the inward movement of cations and opposes their outward movement
Calculating $\Delta G$ for the Transport of Ions

If $S^z$ is a solute with charge $z$, then

$$\Delta G_{\text{inward}} = +RT \ln \frac{[S]_{\text{inside}}}{[S]_{\text{outside}}} + zFV_m$$

For a typical cell $V_m$ is negative, so a positive ion will give a negative $\Delta G$ for inward transport, and a negative ion gives a positive $\Delta G$.
Outward transport

- For outward transport, $\Delta G$ has the same value as inward, but with the sign changed

\[ \Delta G_{\text{outward}} = - \Delta G_{\text{inward}} \]
An Example: The Uptake of Chloride Ions

- Consider a nerve cell with $[\text{Cl}^-]_{\text{inside}} = 50\text{mM}$, in a solution with $[\text{Cl}^-] = 100\text{mM}$ and membrane potential of $-60\text{mV}$

- The inward movement of Cl$^-$ ions is *down* the concentration gradient but *up* the charge gradient

- To determine the direction of transfer, we need to take both into account
Calculate $\Delta G$ for $\text{Cl}^-$ intake

- $\Delta G_{\text{inward}} = +RT \ln \frac{[S]_{\text{inside}}}{[S]_{\text{outside}}} + zFV_m$

  
  
  $= +(1.987)(273 + 25) \ln \left( \frac{0.05}{0.10} \right)$
  
  $= +(-1)(23,062)(-0.06)$

  $= +592 \ln (0.5) + (23,062)(0.06)$

  $= -410 + 1384$

  $= 974 \text{ cal/mol}$

  $= +0.97 \text{ kcal/mol}$

- So, though $[\text{Cl}^-]$ is higher outside the cell, energy is still required for import