# Chapter 5 – Cell Membrane Transport and Membrane Transporters

## *Objectives*

Given the synopsis in this chapter, competence in each objective will be demonstrated by responding to multiple choice, matching, put-in-order, or fill-in questions, at the level of 85% or greater proficiency for each student.

A. To explain how the phospholipid bilayer is organized to prevent the unrestricted passage of water-soluble ions and molecules, such as sodium and glucose, from one side to the other.
B. To explain the composition and organization of transmembrane proteins, including channels, facilitative transporters, co-transporters and counter-transporters, and pumps.
C. To explain the process of passive transport across cell membranes.
D. To explain the process of active transport across cell membranes.
E. To explain the role of pumps and channels in determining the electrical potential across the cell membranes.
F. To explain the process of epithelial transport across the apical and basolateral membranes.

# Phosphopid bilayer

To review basic cellular anatomy, please go to Appendix D. There you will find summaries of the structure of membranes, membranous organelles, and non-membranous organelles. As shown in Figure D.2, the plasma membrane is composed of a phospholipid bilayer. Make a special note that the membranous organelles are also composed of one or more phospholipid bilayers.

As shown in Figure 5.1, the phospholipid bilayer provides the framework to tightly regulate the transport of various molecules and ions into and out of the cell.

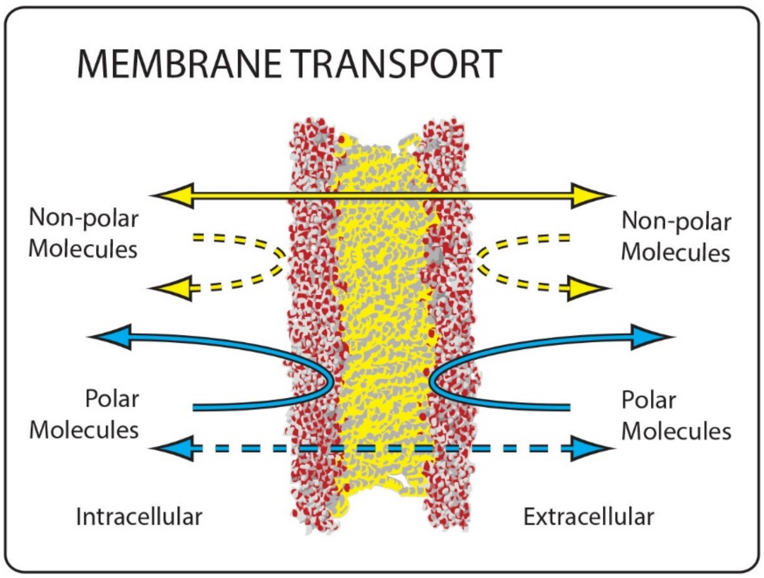


**Figure 5.1 © 2019 David G. Ward, PhD**

- The surfaces of the plasma membrane facing the intracellular fluid and facing the extracellular fluid are phosphate based and generally hydrophilic (polar).
- The interior of the plasma membrane is lipid and cholesterol based and generally hydrophobic (non-polar).
    - The phospholipid bilayer allows many non-polar molecules (such as $O_2$, $CO_2$, and small lipid soluble molecules), but not others, to *penetrate* the cell membranes.
    - The phospholipid bilayer p*revents* the unrestricted passage of polar molecules (such as ions and water-soluble molecules), through the cell membranes. However, slow, limited passage of water can occur.

### Transport of Lipid Soluble Molecules across Cell Membranes:

Because of the organization of the phospholipid bilayer, many non-polar molecules (such as cortisol, and small fatty acids) can pass through cell membranes without the use of specialized transporters, as shown in Figure 5.2.

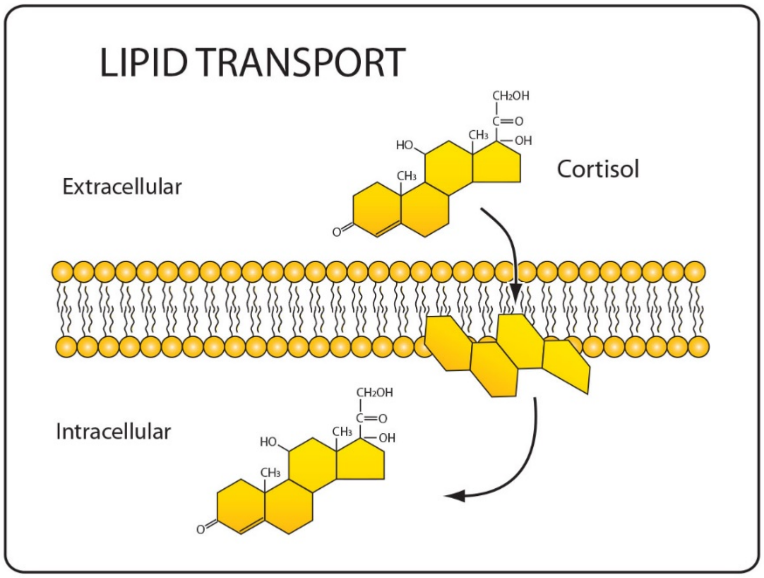


**Figure 5.2 © 2014 David G. Ward, PhD**

- The movement of non-polar molecules through cell membranes is often a **passive** process that depends predominantly on the process of diffusion; the movement of molecules from an area of high concentration to an area of low concentration.
- However, recent findings suggest that the movement of specific lipids through cell membranes involves novel transport proteins

## Transport of Ions, Water, and Water-Soluble Molecules across Cell Membranes:

Because of the composition of the phospholipid bilayer, most polar molecules (such as ions, water, and water-soluble molecules) require the use of specialized transporters to pass through cell membranes.

- Water molecules, although polar, are small enough to pass slowly in small volumes through cell membranes by diffusion.

  - *However, most cells require much larger volumes of water to pass through their membranes and thus also require the use of specialized transporters*.

- Accordingly, transport of ions, water, and water-soluble molecules through the cell membranes depend critically on transmembrane transport proteins, that include:

  - Channels
  - Facilitative transporters
  - Co- and counter-transporters
  - Pumps

# Transmembrane Transport Proteins

Because the phospholipid bilayer is relatively impermeable to water and water-soluble molecules, transmembrane proteins play a central role in transport across the cell membranes. Some transmembrane proteins function in membrane transport and are the subject of this chapter. Other transmembrane protein functions in cellular communication and are the subject of chapter 6. Transmembrane proteins with dual functions are discussed where appropriate. The classification of the various transmembrane proteins involved in membrane transport is summarized in a schematic (cartoon) form in Figure 5.3

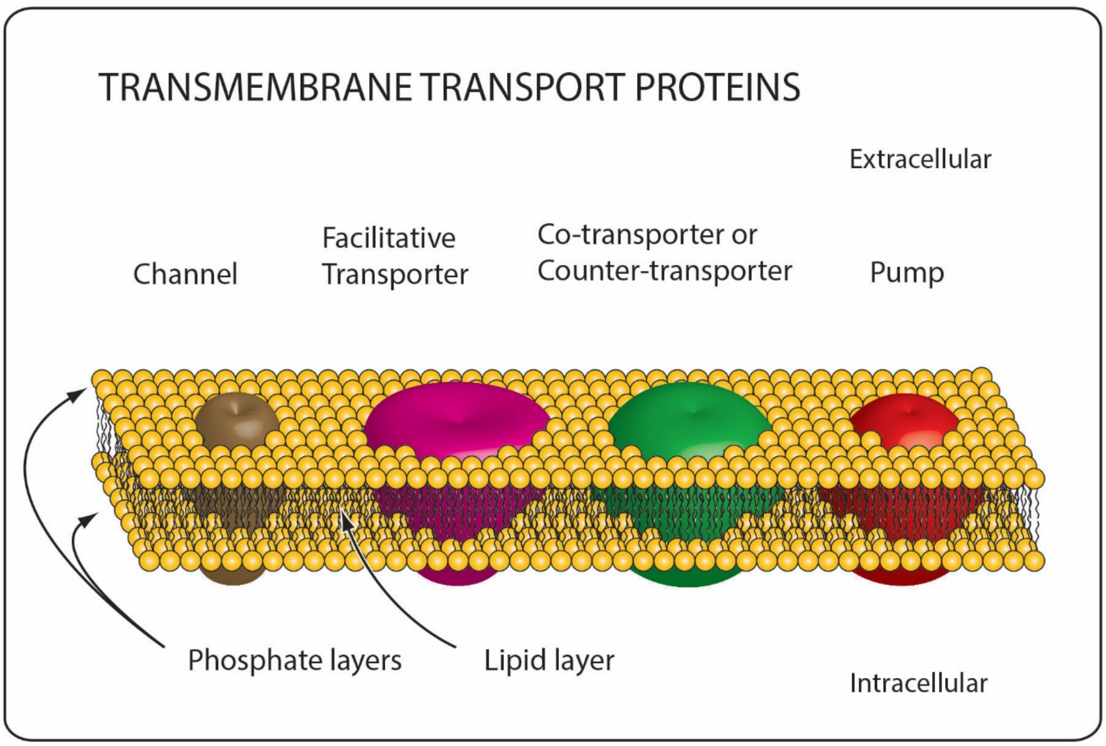


**Figure 5.3 © 2018 David G. Ward, PhD**

## Channels: Diffusion of Ions and Water

Movement of ions (such as $Na^+$, $K^+$, $Ca^+$, and $Cl^-$) through cell membranes depends, in part, on the use of **channels** and the **passive** process of **diffusion**, the movement of ions or molecules from an area of higher concentration to an area of lower concentration. These will be considered in subsequent chapters, especially 7, 8, 9, 11, 12, 16, 17, 20-22.

- Ions pass through channels selectively
  - For example, $Cl^-$ passes through $Cl^-$ channels
  - $Cl^-$ moves from the area of higher $Cl^-$ concentration to the area of lower $Cl^-$ concentration

- Water passes through channels selectively
  - For example, $H_2O$ passes through $H_2O$ channels
  - $H_2O$ moves from the area of higher $H_2O$ concentration to the area of lower $H_2O$ concentration

Transport of $Cl^-$ and $H_2O$ through their respective channels is shown in Figure 5.4.

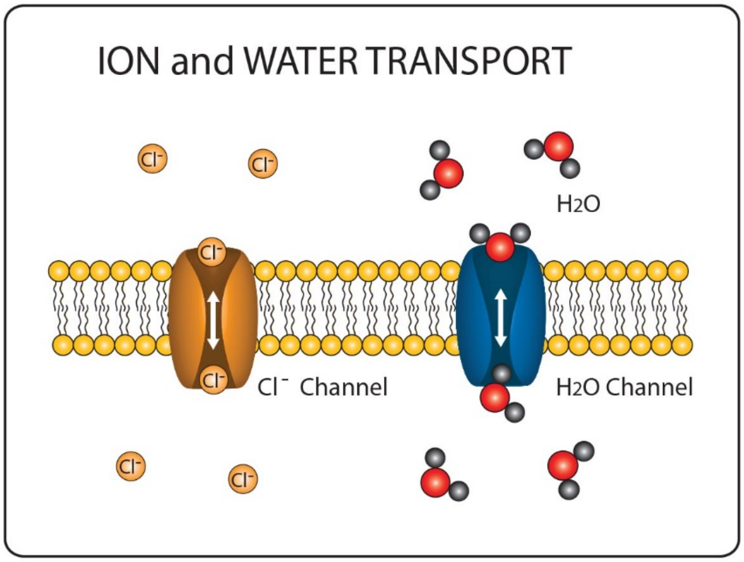


**Figure 5.4 © 2019 David G. Ward, PhD**

### Osmolarity and Movement of Water and Ions

Osmolarity is a measure of the concentration of dissolved ions in water. A high osmolarity (hypertonic) is associated with a lower water concentration; A low osmolarity (hypotonic) is associated with a higher water concentration, as shown in Figure 5.5.

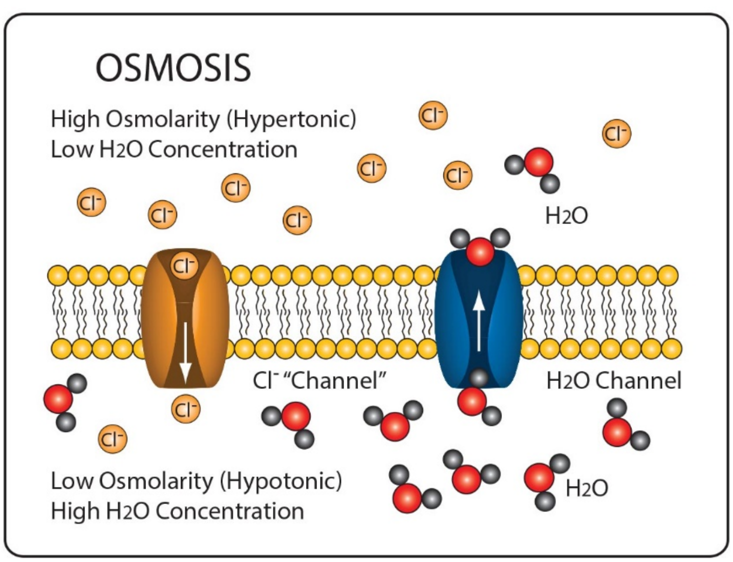


**Figure 5.5 © 2019 David G. Ward, PhD**

Water will move from an area of higher water concentration to an area of lower water concentration, especially when water channels (aquaporins) are present. A solute ($Cl^-$, for example) will move from an area of higher $Cl^-$ concentration to an area of lower $Cl^-$ concentration, when $Cl^-$ "channels" are present.

- Osmosis is the movement of water through a membrane due to a water concentration gradient. That is, from a higher water concentration to a lower water concentration. Osmosis is often described as water movement from a **hypotonic** solution to a **hypertonic** solution
  - When the extracellular fluid and the intracellular fluid have the same osmolarity, they are said to be isotonic.
- Osmolarity is the concentration of solute (ions or molecules) per L of solution
  - The concentration is expressed as Osm /L or as mOsm/L
- Osmolality is the concentration of solute (ions or molecules) per kg of solvent
  - The concentration is expressed as Osm/kg or as mOsm/kg

## Facilitative Transporters: Diffusion of Glucose and Other Small Molecules

Movement of some molecules (such as glucose) that are too large to pass through the membrane channels depend on the use of **facilitative transporters** (carrier proteins) and the **passive** process of facilitated **diffusion**, as shown in Figure 5.6. These will be considered more in chapters 14, 20-23.

- For example, glucose binds to a facilitative transporter (such as GLUT2 or GLUT4), that in turn changes the conformation of the protein.
  - **GLUT2** is not insulin-regulated; found in liver, pancreas, intestine, and kidney.
  - **GLUT4** is insulin-regulated; is found primarily in adipose tissues and muscle.
- Glucose moves from the area of higher to lower glucose concentration

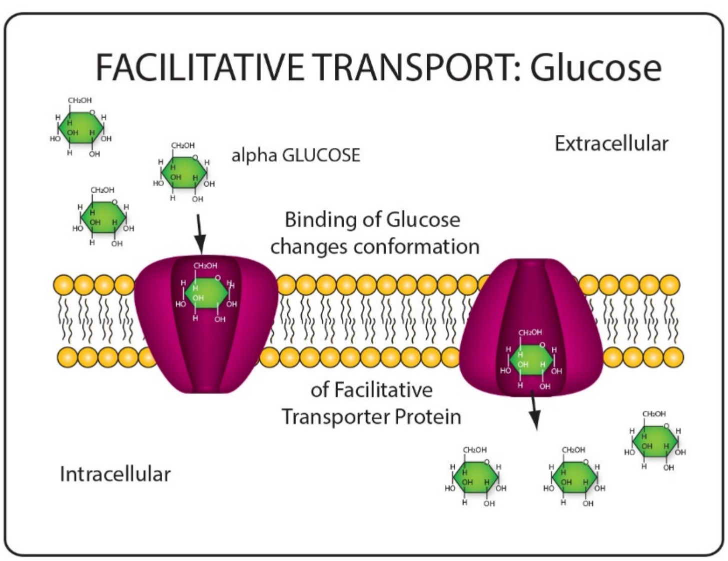


**Figure 5.6 © 2019 David G. Ward, PhD**

## Co- and Counter-Transporters: Ion Coupled Movement of Small Molecules or Other Ions

Movement of small molecules or ions through cell membranes often depends on the use of **cotransporters** or **counter-transporters** and a process often called **secondary active transport**. This process uses the concentration gradient of an ion (a driving ion, commonly $Na^+$) to provide the energy to move other solutes (the driven molecule or ion). Examples of a sodium coupled glucose cotransporter (SGLT1) and a sodium coupled hydrogen counter-transporter (NHE1), are shown in Figure 5.7. These will be considered more in chapters 20-22.

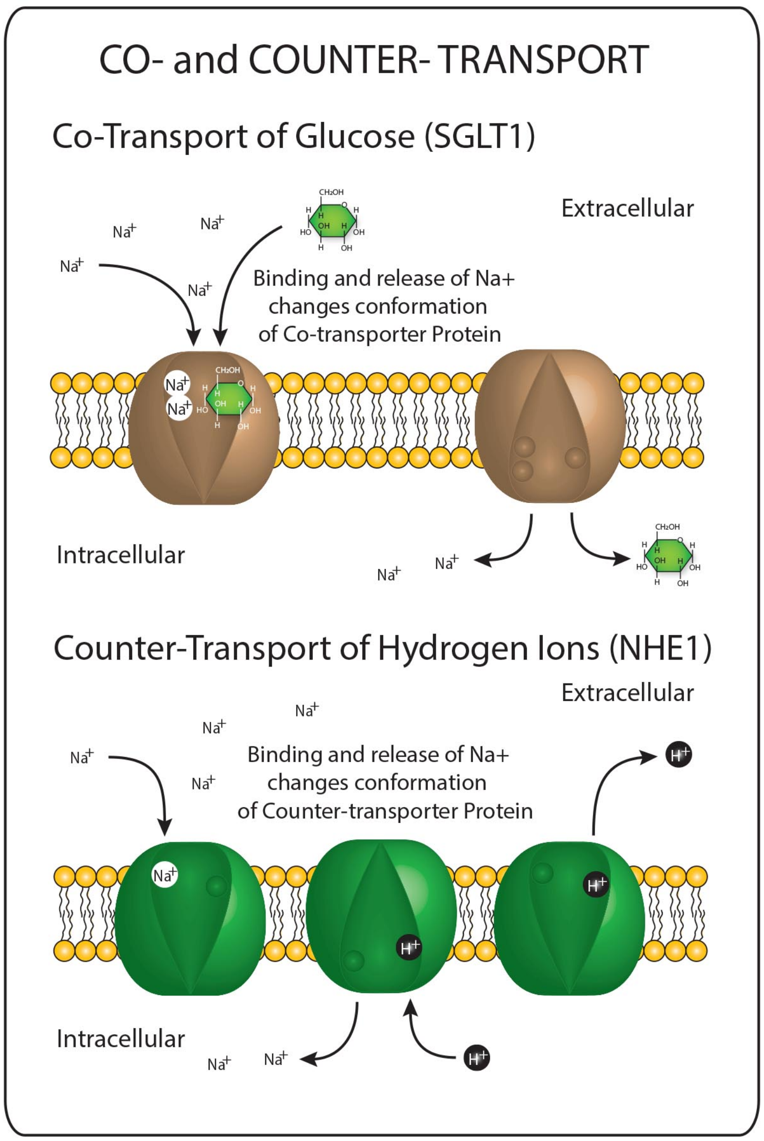


**Figure 5.7 © 2019 David G. Ward, PhD**

- **Cotransporters** (Symporter); for example, $Na^+$/Glucose cotransporter (**SGLTs**).
  - $Na^+$ and Glucose bind to the transporter protein, that in turn changes the conformation of the protein.
    - **SGLT1** transporters are found predominantly in the small intestine and require the binding of two sodium ions in order to transport glucose.
    - **SGLT2** transporters are found predominantly in the kidney, and require the binding of only one sodium ion to transport glucose.
  - Glucose moves through the cell membrane in the same direction as the $Na^+$, from the area of higher $Na^+$ concentration to the area of lower $Na^+$ concentration.
- **Counter-transporters** (Antiporter, Exchanger); an example is a $Na^+$ coupled $H^+$ counter-transporter (**NHEs**).
  - $Na^+$ and $H^+$ bind to the counter-transporter, that in turn changes the conformation of the protein.
  - $H^+$ moves through the cell membrane in the opposite direction to the $Na^+$, from the area of lower $Na^+$ concentration to the area of higher $Na^+$ concentration.

In addition to $Na^+$/Glucose cotransporter (**SGLTs**) and $Na^+/H^+$ counter-transporter (**NHEs**), there are several other co- and counter-transporters. These will be considered more in chapters 7, 9, 20, 21.

- $K^+/Cl^-$ cotransporter (**KCC**) is found in neurons and kidney.
- $Na^+/K^+/2Cl^-$ cotransporter (**NKCC**);
  - **NKCC1** is found in developing brain, cochlea, and exocrine glands;
  - **NKCC2** is found in kidney and is Furosemide sensitive.
- $Na^+/Cl^-$ cotransporter (**NCC**) is found in kidney and is Thiazide sensitive.

## Pumps: ATP dependent Movement of Ions

Movement of ions through cell membranes often depends on **pumps**, which use ATP to provide the energy to move ions from an area of low concentration to an area of high concentration. Examples of pumps are calcium pumps and sodium-potassium pumps. These will be considered more in subsequent chapters, especially 7, 8, 9, 11, 12, 20, 21.

- $Ca^{2+}$ pumps move $Ca^{2+}$ out of cells (or into sarcoplasmic reticulum)
- $Na^+/K^+$ pumps, during each cycle, move 3 $Na^+$ out of cells and 2 $K^+$ into cells

The operation of the sodium-potassium exchange pump is shown in Figure 5.8. Three $Na^+$ ions bind to the transporter proteins. The transporter protein is phosphorylated by the hydrolysis of ATP which changes the conformation of the protein. Two $K^+$ ions bind to the transporter protein and the three $Na^+$ ions move into the extracellular fluid. The removal of the $Na^+$ ions allows the transporter protein to return to its original conformation. The two $K^+$ ions move into the intracellular fluid.

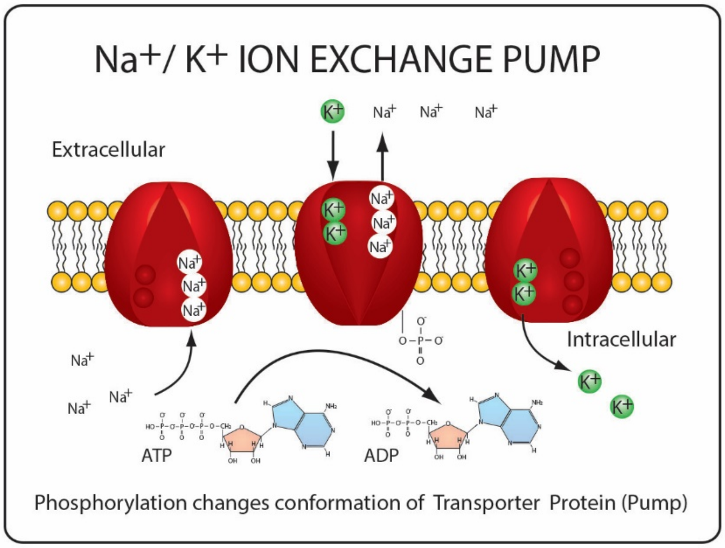


**Figure 5.8 © 2018 David G. Ward, PhD**

## Transmembrane Ion Concentrations and Membrane Potentials

Due to the $Na^+/K^+$ pumps and Cl- transporters the concentrations of ions vary considerably between the extracellular and intracellular fluid. Please refer to chapter 1b, Table 1.2.

- Extracellular fluid contains large numbers of sodium and chloride ions.
- Intracellular fluid contains large numbers of potassium ions.

A membrane potential of about - 70 mV is generated due to:

- The uneven distribution of charges
- The $Na^+/K^+$ pumps moves 3 $Na^+$ for every 2 $K^+$
- $K^+$ ions diffuse out of the cell through leak(y) potassium channels faster than $Na^+$ ions diffuse into the cells.

We will explore this process further in chapter 7.

# Epithelial Transport

Epithelial tissue forms a barrier between the external and internal environments, and between fluid compartments of the body.

- **Absorption** is transport from outside to inside. For example, from the luminal fluid of the intestines or renal tubules, into the interstitial fluid.
- **Secretion** is transport from inside to outside. For example, from the interstitial fluid, into the luminal fluid of the intestines or renal tubules.

Typical transport mechanisms are illustrated in Figure 5.9

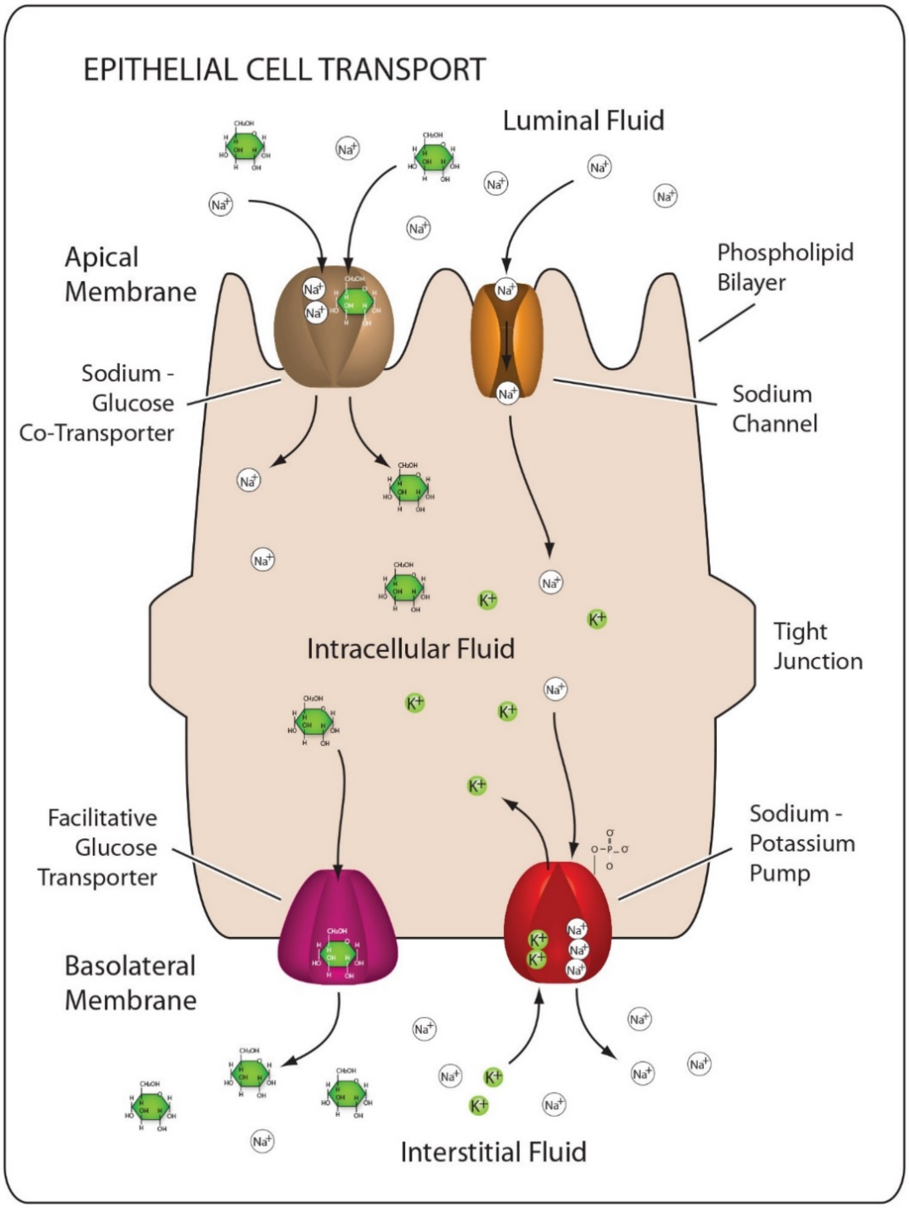


**Figure 5.9 © 2014 David G. Ward, PhD**

## Membrane Structure

The composition and function of the plasma membrane of the epithelial cells varies depending on whether the membranes face the lumen or faces the interstitial fluid.

- The membrane that faces the luminal fluid is called the **apical** membrane.
- The membrane that faces the interstitial fluid is called the **basolateral** membrane.

## Solute Transport

Much of the energy that drives the transport of solutes through epithelial cells is derived from the $Na^+/K^+$ pumps in the basolateral membrane. As described above, extracellular fluid contains a high concentration of sodium and chloride ions and a low concentration of potassium ions, and intracellular fluid contains a high concentration of potassium ions and a low concentration of sodium and chloride ions. Therefore, concentration gradients exist for sodium ions, potassium ions, and chloride ions.

## Water Transport

Secondary to solute transport, water follows changes in the osmotic gradient and moves from areas of higher water concentration to lower water concentration.

- The apical membrane of epithelial cells contains $Na^+$ channels, and sodium ions can diffuse into the **intracellular fluid**.
- Epithelial cells can absorb glucose across the apical membrane by means of a $Na^+$/glucose co-transporter.
- Epithelial cells can secrete glucose across the basolateral membrane into the **interstitial fluid** by means of a facilitative glucose transporter (glucose carrier).
- Epithelial cells transport potassium ions ($K^+$) and sodium ions ($Na^+$) across the basolateral membrane by means of $Na^+/K^+$ pumps. Potassium in pumped into the intracellular fluid and sodium is pumped into the interstitial fluid.

# Quiz Yourself

1-5. Matching

A) Surface of membrane facing extracellular fluid
B) Surface of membrane facing intracellular fluid
C) Interior core of membrane
D) None of the above
E) A and B

hydrophilic 1) _____
hydrophobic 2) _____
phosphate based 3) _____
lipid and cholesterol based 4) _____
water soluble ions and molecules cannot enter this region 5) _____

6-10. Matching (general membrane transport)

A) Can move through membrane rapidly without transporter
B) Cannot move through membrane without transporter

Ions 6) _____
$O_2$, $CO_2$ 7) _____
Small lipids 8) _____
Small sugars 9) _____
Small amino acids 10) _____

11-15. Matching

A) Pumps
B) Channels
C) Co-Transporters
D) Facilitative Transporters
E) all of the above

Transport depends on concentration gradient of a driving ion 11) _____
Allow facilitated diffusion of small molecules (e.g. glucose) 12) _____
Transport of ions depends on energy from ATP 13) _____
Are transmembrane proteins 14) _____
Allow diffusion of ions 15) _____

16-20. Matching (epithelial transport)

A) Basolateral membrane
B) Apical membrane

Often has $Na^+$ channels 16) _____
Faces the interstitial fluid 17) _____
Commonly has $Na^{+}/K^+$ pumps 18) _____
Often has $Na^+$/Glucose Co-transporters 19) _____
Often has facilitative glucose transporters 20) _____

Fill in

21. In a membrane, the _______________ of the phospholipids in one monolayer face the _______________ of the phospholipids in the other monolayer.

22. It is difficult for polar molecules to pass through the phospholipid bilayer because _______________ _______________ attract one another.

23. The passage of solutes through channels is an example of _______________ transport.

24. The passage of solutes using co-transporters is an example of_________________ _______________ transport.

25. In diffusion water or solutes pass from an area of high to _______ concentration.

Study Questions

1. Explain the process of diffusion and its role in the movement of molecules and ions across the plasma membrane.
2. Explain the role of channels and pumps in the movement of water or electrolytes across the plasma membrane.
3. Compare and contrast the roles of channels, facilitative transporters, co- and counter-transporters, and pumps.