Chapter 2 – Cellular Anatomy and Membrane Transport

Objectives

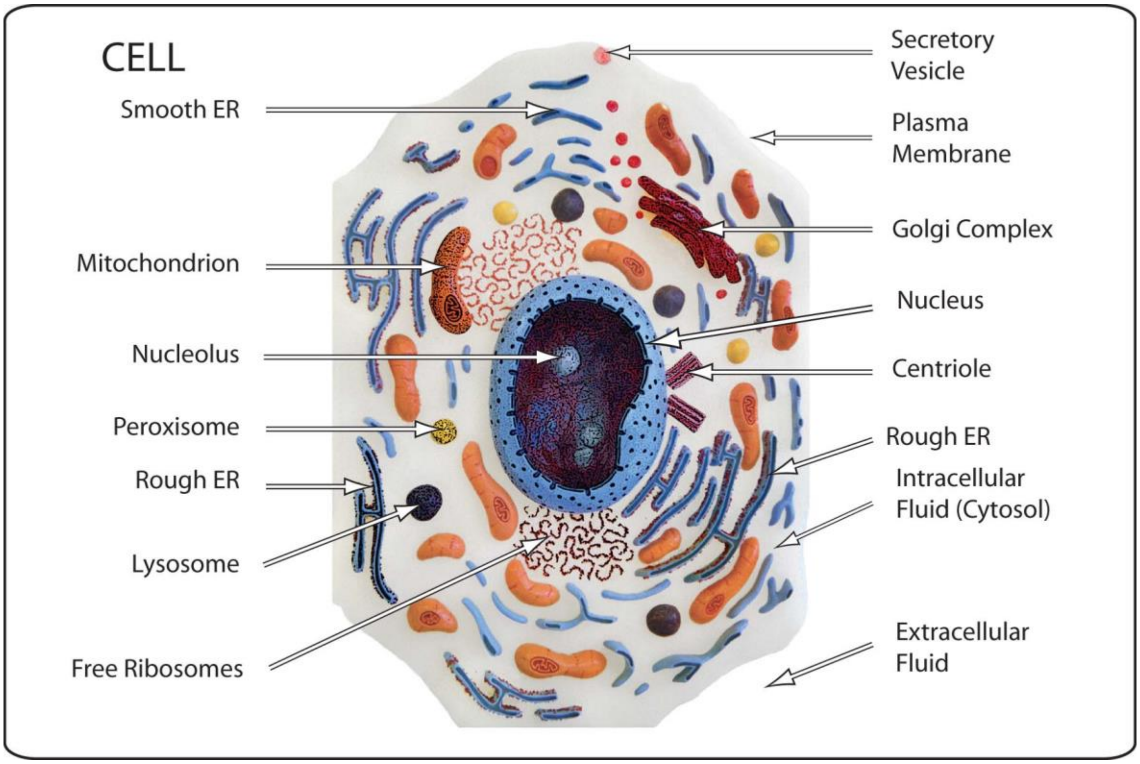
Given the synopsis in this chapter, competence in each objective will be demonstrated by responding to multiple choices or matching questions, completing fill-in questions, or writing short answers, at the level of 75% or greater proficiency for each student.

A. To identify the major features and organelles of a human cell.
B. To explain how the plasma membrane is organized anatomically and how the phospholipid bilayer limits transport through membranes.
C. To explain how chemical substances are transported across cell membranes.
D. To explain the role of transmembrane proteins in transport.
E. To explain the structure and function of the membranous organelles, including the nucleus, endoplasmic reticulum, Golgi complex, vesicles, and mitochondria.
F. To explain how the nucleus, endoplasmic reticulum, Golgi complex, vesicles, and plasma membrane are anatomically and functionally interrelated.
G. To explain the structure and function of the non-membranous organelles, including the ribosomes and cytoskeleton.

Cells are the basic organizational unit of life; all organisms are composed of cells. The functioning of cells is dictated by common physiological characteristics.

- Cells reproduce by cell duplication / division
- The information to build a cell and to permit cellular function is encoded in its genes (DNA/RNA)
- Cells respond to stimuli and produce responses.
- Cells engage in various mechanical activities and enzymatically controlled chemical reactions
- Cellular activity is fueled by chemical energy
- Cells undergo a remarkable amount of self-regulation

Cells are typically 10 to 30 microns in length (except for muscle cells and neurons). This small size is dictated by the short distance that substances can diffuse and the finite number of copies of genes. The basic organization of a mammalian cell is shown in Figure 2.1. Please use this illustration as a reference as we go through the chapter.



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Plasma Membrane

Cells are surrounded by **extracellular fluid** and contain **intracellular fluid**. Both the extracellular fluid and the intracellular fluid are composed mainly of water and various solutes. Some critical solutes are sodium, potassium, calcium and chloride ions. The plasma membrane separates the extracellular fluid from the intracellular fluid.

Phospholipid Bilayer

The plasma membrane is composed of a **phospholipid bilayer** and various proteins, either embedded in the bilayer (**transmembrane proteins**) or on the surfaces of the bilayer (peripheral proteins). The basic organization of the phospholipid bilayer is shown in Figure 2.2.

The **phospholipid bilayer** is composed predominantly of phospholipids and cholesterol. Together, these molecules:

- Enclose the contents of the cell so that cellular activity can proceed without outside interference
- Prevent the unrestricted passage of water and water soluble molecules, such as nutrients and electrolytes from one side of the membrane to the other

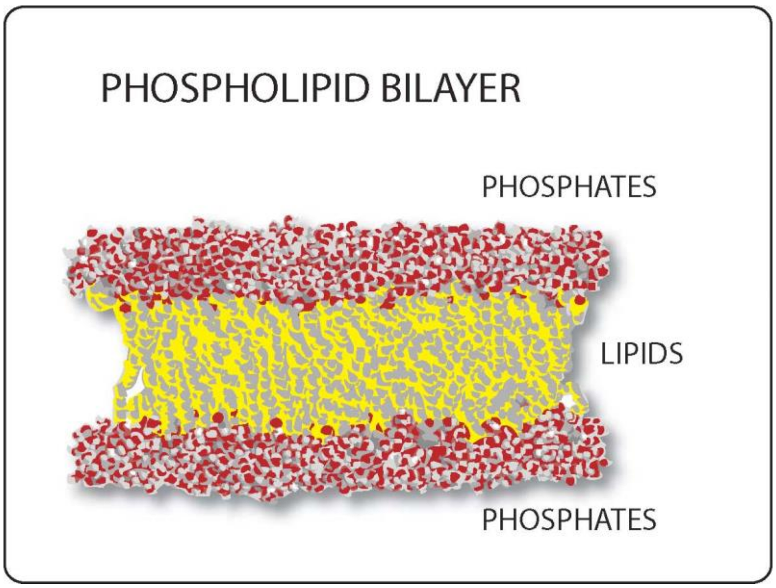


Figure 2.2 © 2007 David G. Ward, PhD

Transmembrane proteins are embedded in and pass through the phospholipid bilayer. Peripheral proteins of the plasma membrane attach to the surfaces of the phospholipid bilayer, either on the intracellular side or on the extracellular side. Together, these membrane molecules:

- Transport specific water soluble chemicals, such as nutrients and electrolytes from one side of the membrane to the other.
- Allow cells to respond to external stimuli: Membrane receptors combine with certain molecules (Ligands).
- Allow cells to interact with each other: Membrane molecules allow cells to recognize and signal one another, to adhere to each other when appropriate, and to exchange materials and information.

Membrane Transport

Membrane transport is dictated by the structure of the phospholipid bilayers.

- The surfaces of the phospholipid bilayer facing the intracellular fluid and facing the extracellular fluid are phosphate based and **hydrophilic**.
- The interior of the phospholipid bilayer is lipid and cholesterol based and **hydrophobic**.

As shown in Figure 2.3, the phospholipid bilayer allows **lipid soluble** molecules (such as steroids), to *penetrate* the cell membranes. At the same time the phospholipid bilayer p*revent* the unrestricted passage of water, ions, and water soluble molecules, through the cell membranes. The phospholipid bilayer provides the framework to tightly regulate the transport of various molecules and ions into and out of the cell.

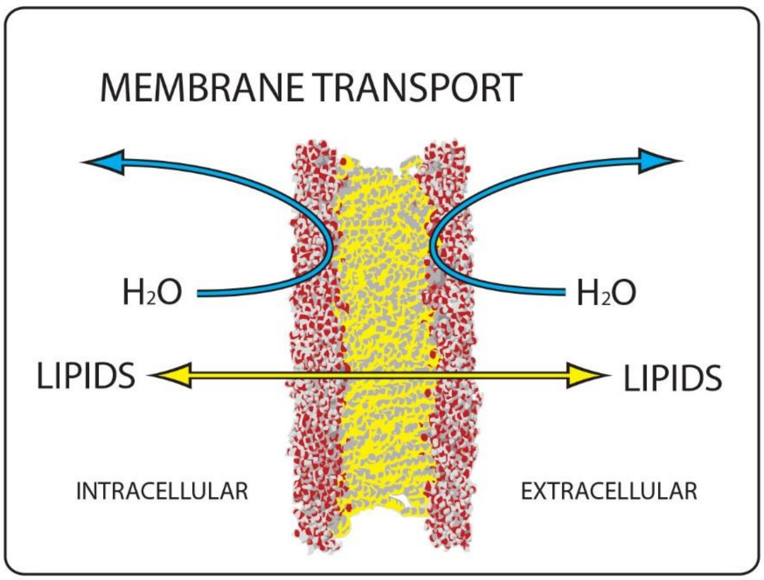


Figure 2.3 © 2014 David G. Ward, PhD

Transport of Lipid Soluble Molecules across Cell Membranes:

Because of the organization of the phospholipid bilayer, **lipid soluble** molecules (such as steroid and thyroid hormones) <u>*can*</u> readily pass through cell membranes <u>without the use of specialized transporters</u>, as shown in Figure 2.4.

- Cell membranes, by their nature, are permeable to lipid soluble molecules.

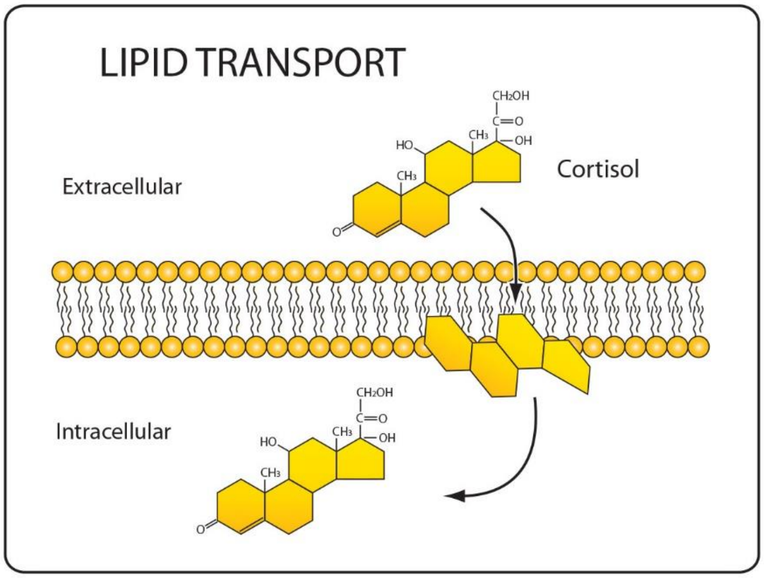


Figure 2.4 © 2014 David G. Ward, PhD

The movement of lipid molecules through cell membranes is a passive process that depends predominantly on diffusion. **Diffusion** is the movement of molecules from an area of high concentration to an area of low concentration. The process of diffusion is driven by the random activity of molecules.

- The difference in concentration between the area of high concentration and the area of low concentration is referred to as the **concentration gradient**.
- Concentration gradients provide the driving force for passive transport and secondary active transport.

Transport of Water and Water Soluble Molecules across Cell Membranes:

Because of the composition of the phospholipid bilayer water, ions, and **water soluble** molecules <u>require the use of specialized transporters</u> to pass through cell membranes.

- Cell membranes, by their nature, are impermeable to water soluble molecules.

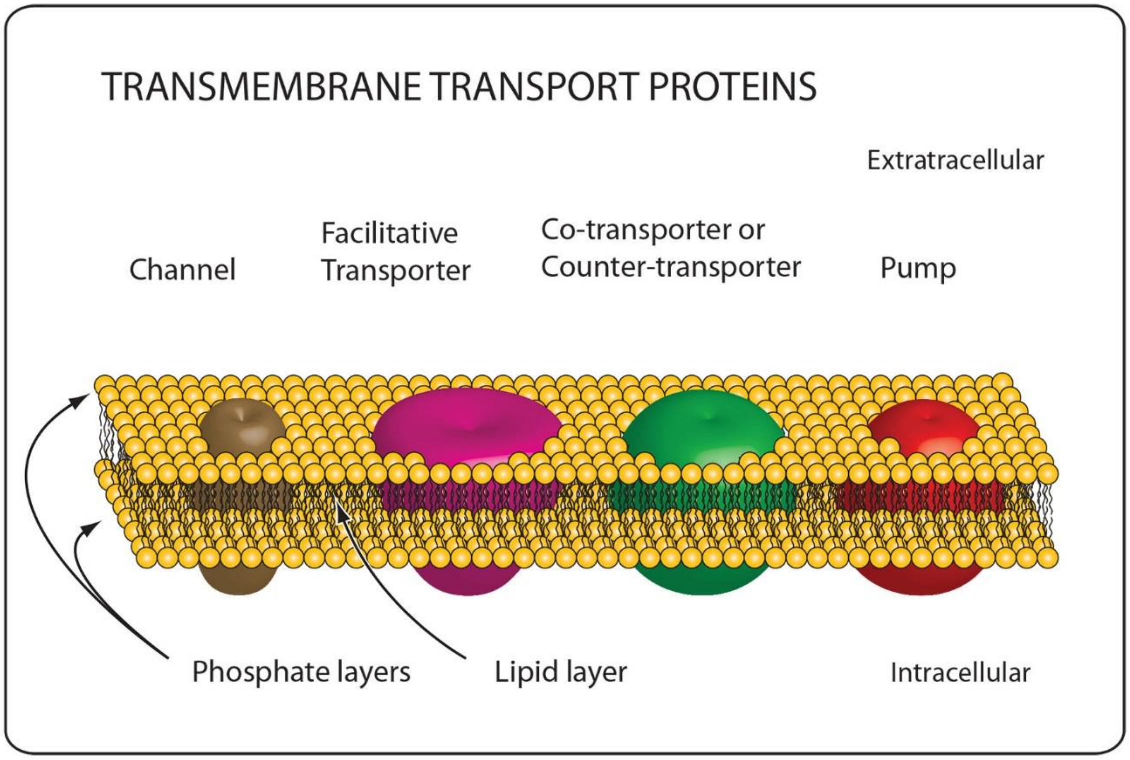
Accordingly, additional mechanisms are required to transport water, ions, and other water soluble molecules through the cell membranes.

These mechanisms involve four major classes of transmembrane transport proteins:
- Channel proteins
- Facilitative transporter proteins
- Co-and counter-transporter proteins
- Pump proteins

In addition the mechanisms involve two major classes of transport processes
- Passive transport processes
- Active transport processes

Over view of 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 current subject. Other transmembrane protein functions in cellular communication and will be considered at a later time. The organization of the various transmembrane proteins involved in membrane transport is summarized in Figure 2.5



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Channels

Channels are transmembrane proteins that form passageways in the cell membrane. Channels allow for the diffusion of water and ions through the cell membrane. Molecules and ions move from a region of high concentration to a region of lower concentration. Diffusion through channels is classified as a **passive transport** process.

- **Leak(y) Channels** are passageways in the cell membrane that are always open. (These types of channels are sometimes called passive channels.)

- **Gated Channels** are passageways in the cell membrane that can open or close in response to chemical, electrical, or other types of signals. Accordingly, gated channels also function as receptors.

Facilitative Transporters

Facilitative transporters are transmembrane proteins that are often called **carrier proteins**. These proteins allow for the movement of larger water soluble molecules (such as glucose) through the cell membrane. Molecules move from a region of high concentration to a region of lower concentration. The carrier proteins are not enzymatically active and move molecules by spontaneous conformational changes. Movement by facilitative transporters is classified as a **passive transport** process.

Co-Transporters and Counter-Transporters

Co-transporters and counter-transporters are transmembrane proteins. These proteins can move molecules or ions from a region of high concentration to a region of low concentration, or from a region of low concentration to a region of high concentration. Although, these transporter proteins are not enzymatically active, they depend on energy derived from the concentration gradient of ions, most commonly sodium ions, to cause conformational changes and transport. Movement by co-transporters and counter-transporters is classified as a **secondary active transport** process.

- **Co-Transporters** - As one group of ions (such as sodium ions) move through the cell membrane according to their concentration gradient, another group of molecules (such as glucose) move through the cell membrane in the <u>same</u> direction.
- **Counter-Transporters** - As one group of ions (such as sodium ions) move through the cell membrane according to their concentration gradient, another group of ions (such as hydrogen ions) move through the cell membrane in the <u>opposite</u> direction.

Pumps

Active transport pumps are transmembrane proteins. These proteins can move ions from a region of high concentration to a region of low concentration, or from a region of low concentration to a region of high concentration. Pumps are enzymatically active and obtain the energy for transport from the breakdown of ATP, to cause conformational changes and transport. Movement by pumps is classified as an **active transport** process.

Passive Transport Processes

Passive transport processes process depend predominantly on diffusion. Diffusion is the movement of molecules from an area of high concentration to an area of low concentration. The process of diffusion is driven by the random activity of molecules.

- The difference in concentration between the area of high concentration and the area of low concentration is referred to as the **concentration gradient**.
- Concentration gradients provide the driving force for passive transport and secondary active transport.

Only passive transport involving channels will be considered in this section. Passive transport involving facilitative transporters will be considered at a later time.

Diffusion across cell membranes: Water and Ions

Movement of water and ions (such as Na^+, K^+, Ca^+, and Cl^-) through cell membranes depend on the use of **channels** and the process of diffusion, as shown in Figure 2.6.

- Specific **channels** allow for the diffusion of water or ions through cell membranes.

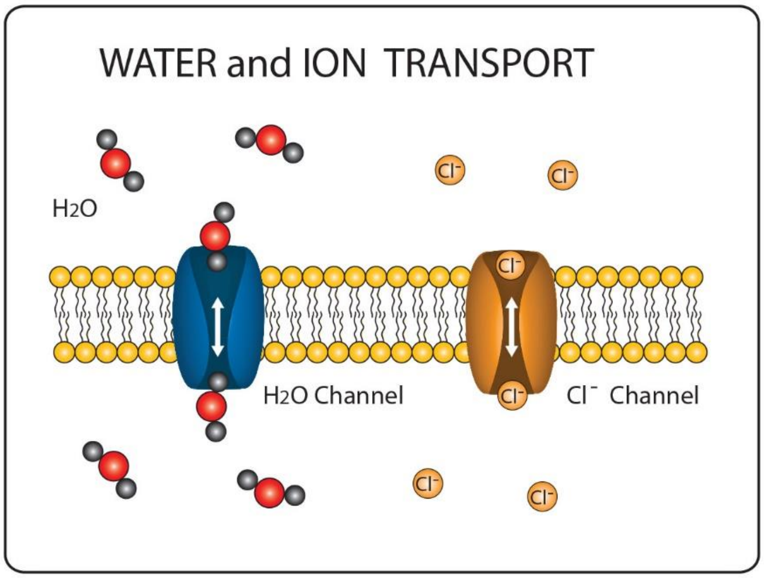


Figure 2.6 © 2014 David G. Ward, PhD

Water and ions can pass through channels only if:

- There is a concentration gradient for the ion.
- The charge of the channel permits passage of the ion.
- The channel is specifically constructed to allow passage of the ion.

For example, water passes through water channels. Na^+ ions pass through sodium channels. K^+ ions pass through potassium channels. Ca^+ ions pass through calcium channels. Cl^- ions pass through chloride channels.

Osmosis and Dialysis

Osmosis is the diffusion of water across a cell membrane. Dialysis is the diffusion of solutes across a cell membrane. However, water and ions diffuse independently, as shown in Figure 2.7. Water moves from the region of high water concentration to the region of low water concentration through water channels. Solute (such as Na^+, K^+, Ca^+, and Cl^-) moves from the region of high solute concentration to the region of low solute concentration through specific ion channels.

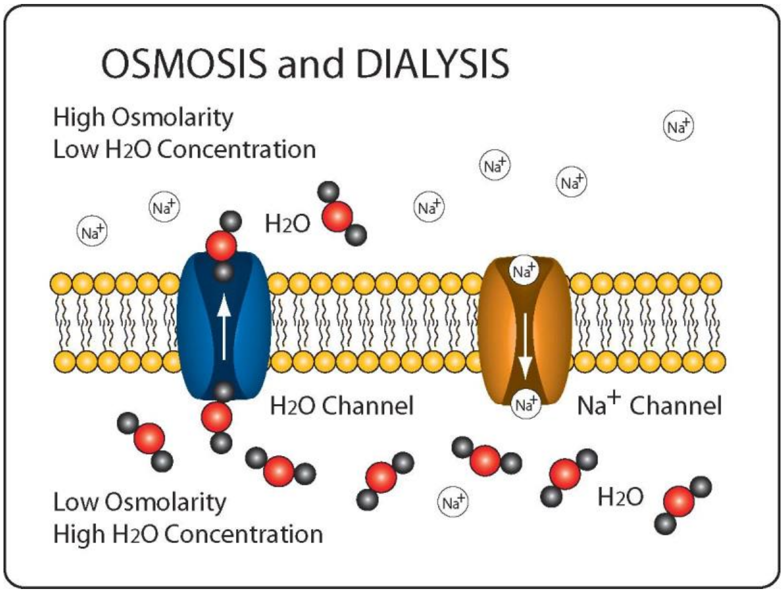


Figure 2.7 © 2007 David G. Ward, PhD

- The concentration of water and solute are inversely related. As solute concentration increases, water concentration decreases, and vice versa.

- **Osmolarity** is a measure of the concentration of dissolved solutes. As the osmolarity increases, water concentration decreases, and vice versa.

A solution that is **isosmotic** (isotonic) has the same solute and water concentration as normal blood, a solution that is **hyperosmotic** (hypertonic) has higher solute concentration, and a solution that is **hypo-osmotic** (hypotonic) has a lower solute concentration.

Active Transport Processes

Active transport involves the movement of ions across a cell membrane using an Active Transport Protein (pump) and energy from the breakdown of ATP (refer to pumps earlier in the chapter).

- Active transport allows for the movement of ions from a region of low concentration to a region of high concentration.

Only active transport involving pumps will be considered in this section. Secondary active transport involving co- and counter-transporters will be considered at a later time.

The most common active transport pumps are ion pumps and ion exchange pumps.

- **Ion pumps** actively transport a single ion, such as calcium ions.
- **Exchange pumps** actively transport a particular ion in one direction and another ion in the opposite direction. The sodium-potassium exchange pump is an example; three sodium ions are moved out of the cell and two potassium ions are moved into the cell.

The operation of the sodium-potassium exchange pump is shown in Figure 2.8. Three sodium ions bind to binding sites in the transporter proteins. The transporter protein is phosphorylated by the hydrolysis of ATP which changes the conformation of the protein. The binding sites are now exposed in the extracellular side of the membrane. Two potassium ions bind to binding sites on the transporter protein and the three sodium ions diffuse into the extracellular fluid. The removal of the sodium ions allows the transporter protein to return to its original conformation. The binding sites are now exposed on the intracellular side of the membrane and the two potassium ions diffuse into the intracellular fluid.

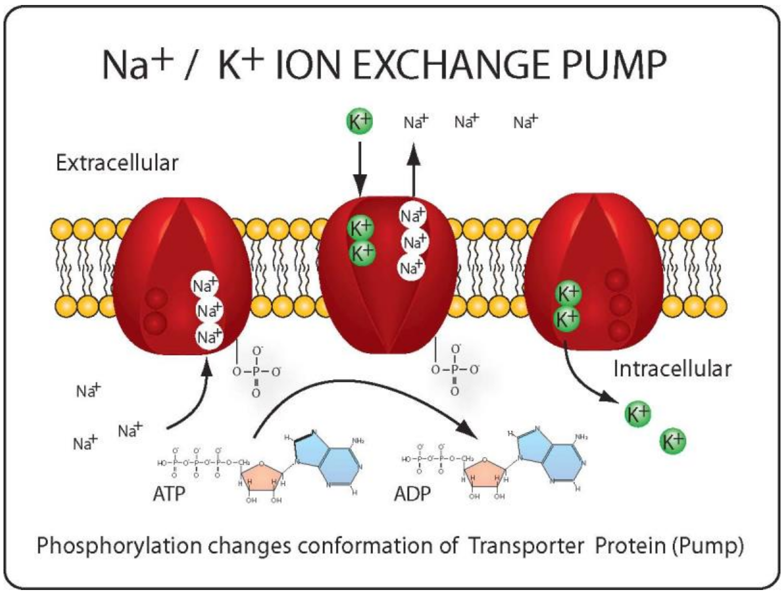


Figure 2.8 © 2007 David G. Ward, PhD

Membranous Organelles

All of the material inside of the cell except for the **nucleus** is called the **cytoplasm**. The membranous organelles include the nucleus, mitochondria, endoplasmic reticulum, Golgi complex, and various vesicles (including lysosomes, and peroxisomes). The **membranous organelles** are composed of double or single phospholipid bilayers.

Nucleus

The **nuclear envelope** is composed of double phospholipid bilayers forming a double walled membrane with pores. The membranes of the nuclear envelope serve as a barrier to keep ions, and proteins from passing between the nucleus and the cytoplasm. The basic organization of the nucleus is shown in Figure 2.9.

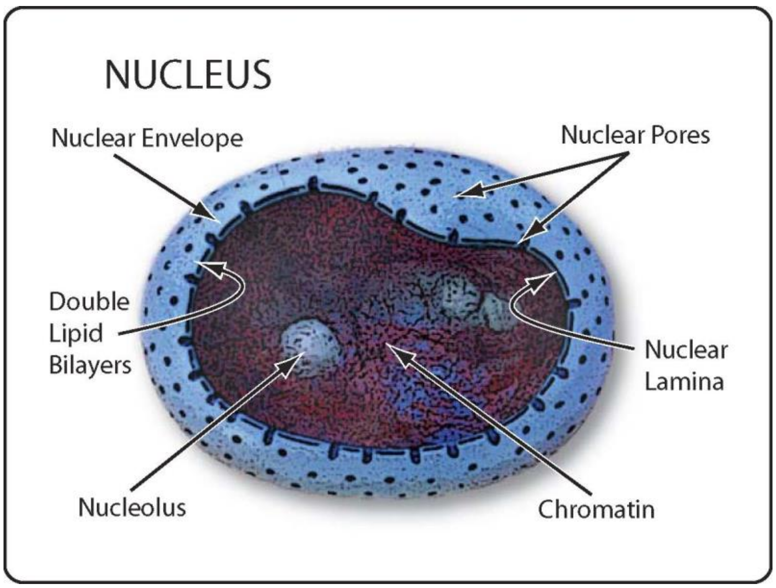


Figure 2.9 © 2007 David G. Ward, PhD

- The two membranes are fused frequently forming **nuclear pores** that contain complex assemblies of proteins.
- The inner membrane is bound to a dense filamentous meshwork called the **nuclear lamina**, inner most dark layer. The nuclear lamina provides support for the nuclear envelope and attachment sites for chromatin fibers.
- Nuclear pores allow for the movement of proteins and ribonucleic acids (RNAs) in both directions between the nucleus and cytoplasm.
- In the non-dividing cell, the portions of the DNA that encode ribosomal RNA (rRNA) are clustered in one or more irregularly shaped structures called **nucleoli**.

The nucleus contains **chromatin** which is composed of deoxyribonucleic acid (DNA) and associated histone and non-histone proteins. DNA wraps around disks of histone proteins forming **nucleosomes**. The nucleosome coils up to form the loop domains. The loop domains come together to form the chromosomes prior to mitosis. The loop domains uncoil after mitosis is complete. The organization of the chromosomes and DNA is shown in Figure 2.10.

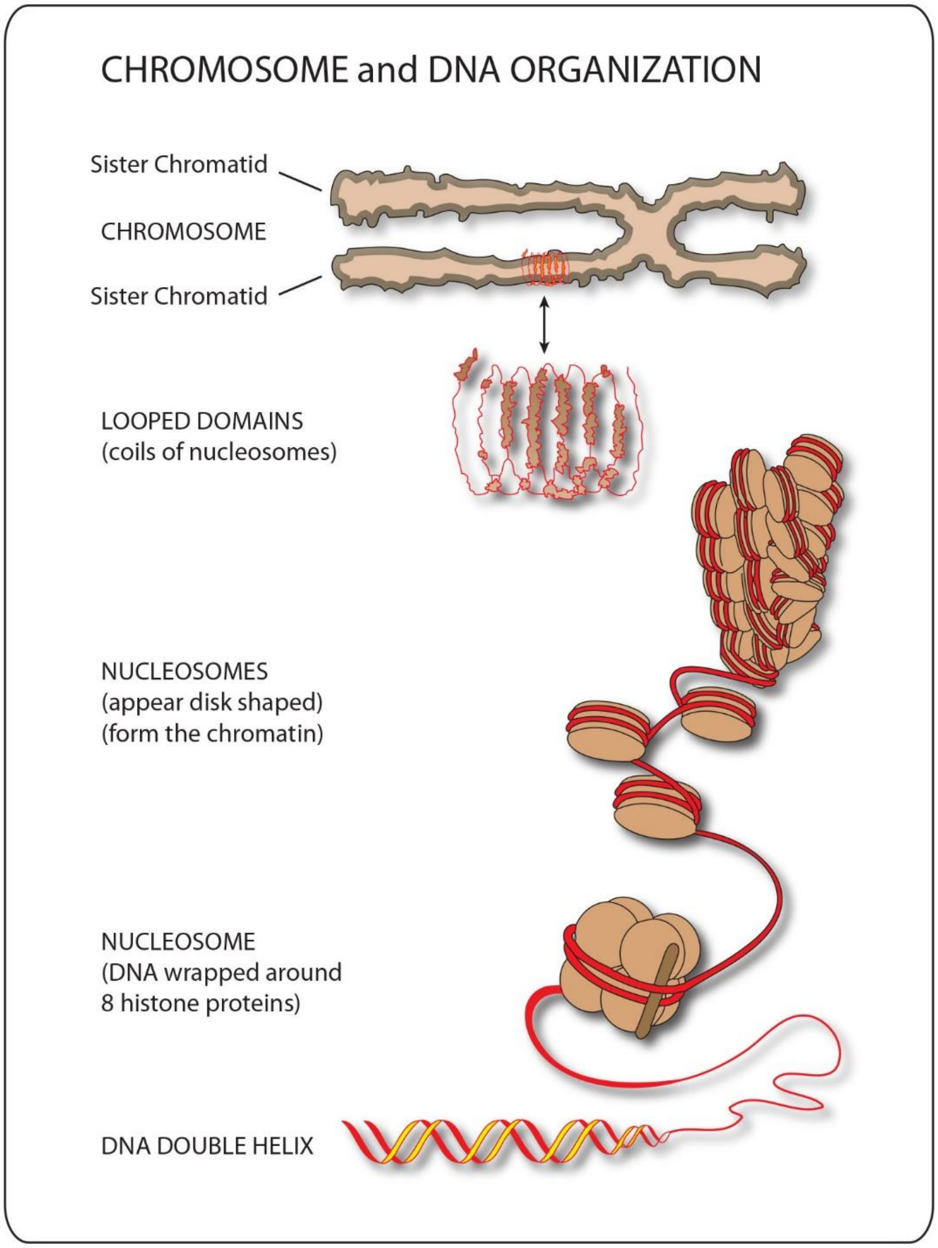


Figure 2.10 © 2014 David G. Ward, PhD

Endoplasmic reticulum (ER)

The endoplasmic reticulum consists of interconnected membranes that are composed of a single phospholipid bilayer. These membranes form tubing that act as transportation pathways and storage sites. The basic organization of rough endoplasmic reticulum is shown in Figure 2.11.

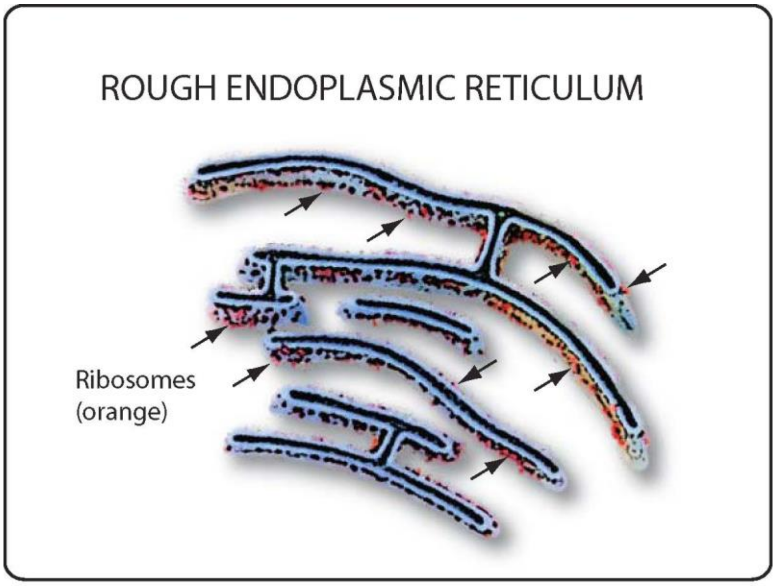


Figure 2.11 © 2007 David G. Ward, PhD

- The **Rough Endoplasmic Reticulum (RER)** consists of flattened sacs that typically are an extension of the outer membrane of the nuclear envelope. Both the nuclear envelope and the RER are covered with **ribosomes** on the surface of the membranes facing the cytosol. The RER is the site for synthesizing secretory proteins. Non-secretory proteins are synthesized on free ribosomes.
    - Proteins in the ER typically leave in transport vesicles produced by budding of the ER membrane. Budding is the pinching off of pieces of the tubular membrane.
- The **Smooth Endoplasmic Reticulum (SER)** consists of tubular structures that form an interconnecting system of pipelines curving through the cytoplasm. There are few if any ribosomes on the membranes. The functions of the SER vary with the type of cell. In endocrine cells the SER is involved in synthesizing steroid hormones. In liver cells, the SER is involved in detoxification of organic compounds and in the conversion of stored glycogen to glucose. In muscle and some other cells, calcium is stored in the SER. Regulated release of calcium from the SER triggers contraction of skeletal muscle cells and fusion of secretory vesicles with the plasma membrane. We will be considering these functions in more detail in subsequent chapters.

Golgi complex

The Golgi complex consists of flattened, disk-like membranous sacs, call **cisterna**, which are each composed of a single phospholipid bilayer. The basic organization of the Golgi complex is shown in Figure 2.12.

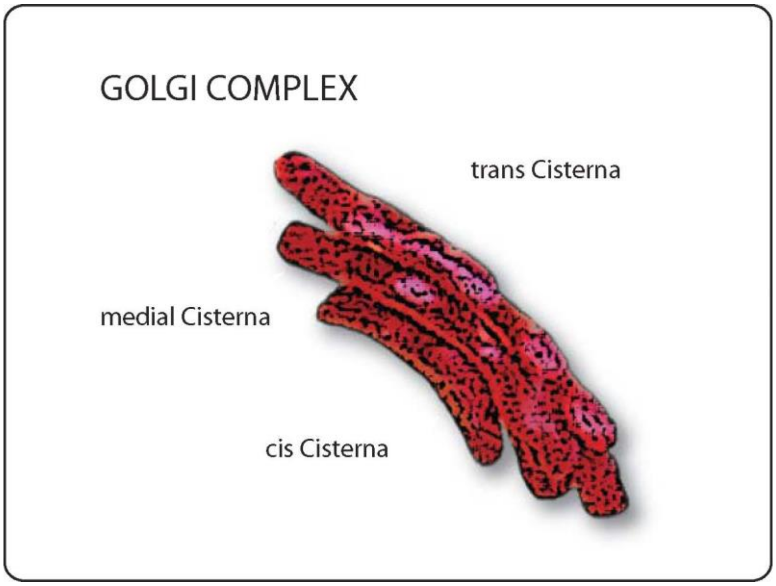


Figure 2.12 © 2007 David G. Ward, PhD

- The Golgi complex acts as a processing plant. The Golgi complex is involved in modifying proteins from the endoplasmic reticulum and in synthesizing complex polysaccharides.
- Proteins in the Golgi complex typically leave in vesicles produced by budding of the Golgi membrane.

Vesicles

There are many types of vesicles, including transport vesicles, secretory vesicles, and lysosomes and peroxisomes. Vesicles are composed of a single phospholipid bilayer.

- **Secretory Vesicles** are vesicles that have budded from the Golgi complex and contain proteins or other substances intended for secretion out of a cell.
- **Lysosomes** are vesicles that have budded from the Golgi complex and contain many digestive enzymes. Lysosomes are common in phagocytic cells and digest cellular debris and pathogens.
- **Peroxisomes** are vesicles that are derived in part from the ER, and contain many metabolic enzymes that generate hydrogen peroxide as a by-product. Peroxisomes are involved in various aspects of lipid metabolism, especially oxidation of long chain fatty acids, and synthesizing phospholipids.

Summary of Membranous organelles

Figure 2.13 summarizes the relationship among the nucleus, endoplasmic reticulum, ER buds, Golgi complex, vesicles and plasma membrane. These membranous organelles together with the ribosomes play a critical role in the synthesis and transport of proteins, lipids and carbohydrates. Details of how the nucleus, ribosomes, endoplasmic reticulum and Golgi complex work together in protein synthesis are considered further in a subsequent chapter.

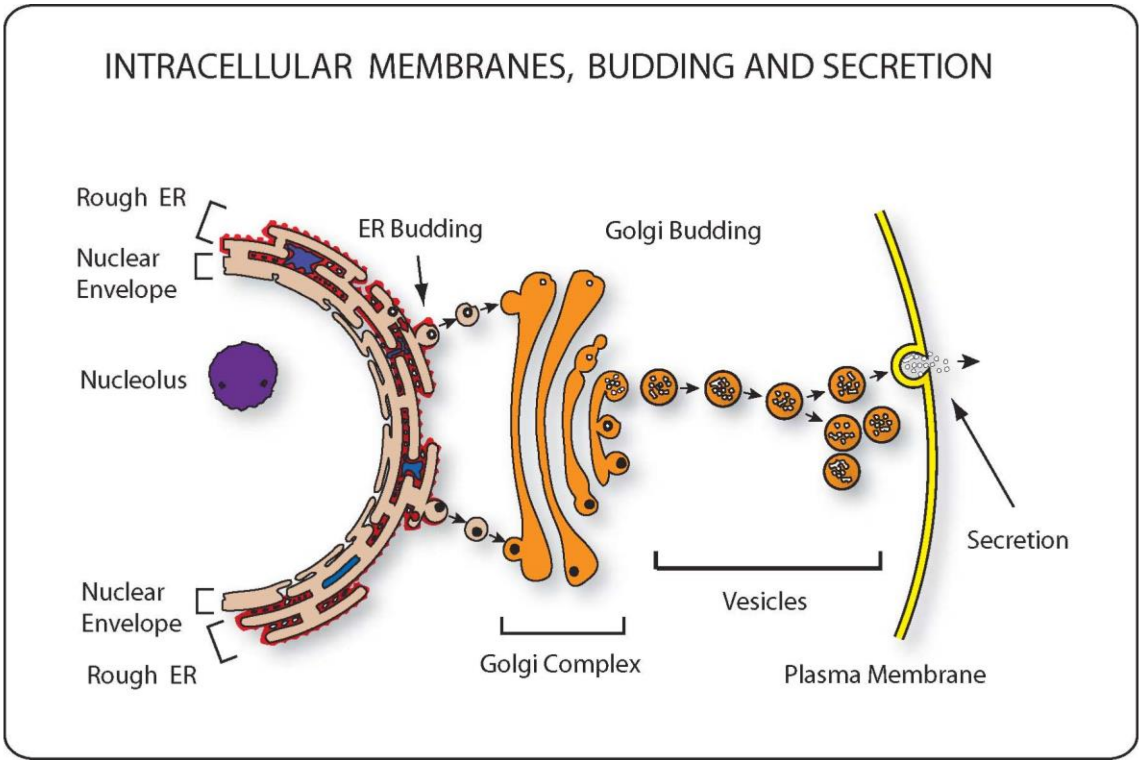
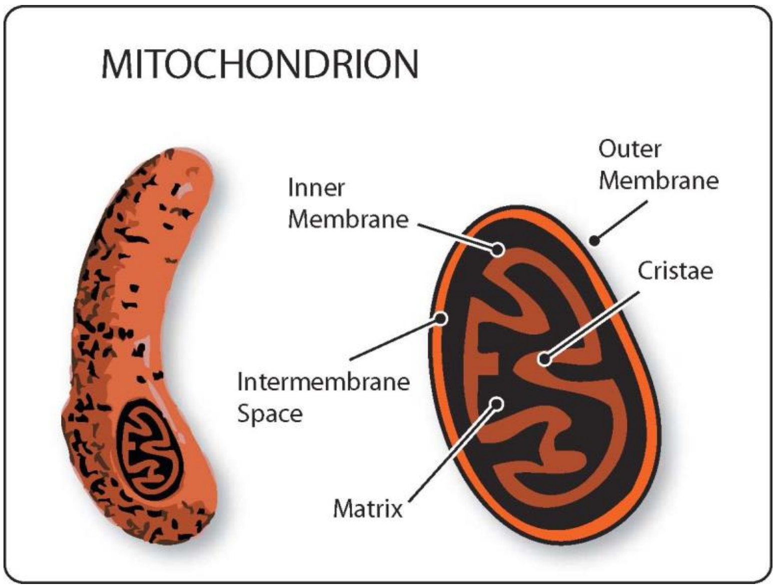


Figure 2.13 © 2007 David G. Ward, PhD

Mitochondria

Mitochondria are composed of double phospholipid bilayers forming an outer membrane and an inner membrane. Much of the inner membrane forms deep folds called **cristae**. The inner membrane surrounds an aqueous compartment called the **matrix**. The matrix contains a high concentration of water soluble proteins, especially enzymes. In addition, mitochondria contain their own genome (mitochondrial DNA). The basic organization of the mitochondrion is shown in Figure 2.14.



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- The matrix is the site for the first steps of conversion of glucose into ATP – decarboxylation of pyruvate and the tricarboxylic acid cycle (Krebs cycle).
- The inner membrane contains a large number of polypeptides and is the location of most of the machinery required for the remaining synthesis of ATP – oxidative phosphorylation (AKA electron transport chain).

Non-Membranous Organelles

The non-membranous organelles are of course the molecular clusters in the cell that are not bounded by phospholipid bilayers. These include the ribosomes, the cytoskeleton, and other structures such as the centrioles.

Ribosomes

Ribosomes are composed of subunits of ribosomal RNA and protein and may be free of or attached to ER. The basic organization of free ribosomes is shown in Figure 2.15.

- Ribosomes function to build proteins using messenger and transfer RNA. Ribosomes are made from a small ribosomal subunit (40S**)**, and a large ribosomal subunit (60S). The role of ribosomes in the construction of proteins will be considered further in later chapter.

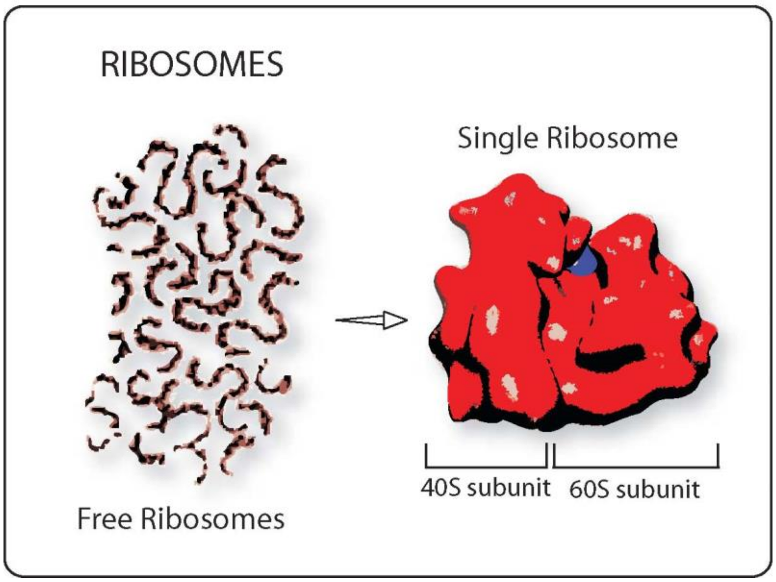

Figure 2.15 © 2007 David G. Ward, PhD

Cytoskeleton and Centrioles

The cytoskeleton is composed of microtubules, microfilaments (**actin**), and other protein filaments. They function as a cytoskeleton, in intracellular transport, and in mobility.

- **Microtubules** are hollow, cylindrical protein structures that form part of the cytoskeleton, mitotic spindles, centrioles, cilia and flagella. Microtubules move substances and organelles within cells, and anchor organelles and mRNA.
- **Microfilaments** are actin proteins involved in movement. **Myosin** proteins are motor proteins that move along **actin** proteins
- **Centrioles** are composed of 9 evenly spaced bundles of 3 microtubules per bundle and play a critical role in separation of chromatids during cell division.