Objectives:
The student should be able to:
1. List the major fluid compartments and their relative size.
2. List the major chemical components of cell membranes.
3. State the major functions of a cell membrane.
4. List the types of membrane junctions that can be formed by cells.
5. Indicate the direction of passive net flux of a substance of known concentration.
6. Explain the dependence of flux magnitude on concentration difference, temperature, molecule mass, and surface area.
7. Identify the factors in Fick’s law.
8. Define diffusion coefficient.

Outline:
I. Fluid compartments
   A. Total body water (TBW). Approximately 60% of the total body weight is water.
   B. Intracellular fluid (ICF). Approximately two-thirds of the TBW.
   C. Extracellular fluid (ECF). Approximately one-third of the TBW.
   D. The ionic composition of ICF and ECF are different.
E. The ECF is compartmentalized.
1. Plasma. Approximately 20% of the ECF circulates as the plasma component of blood.
2. Interstitial. Approximately 80% of ECF surrounds the cells that are not in the vascular system.
3. Protein concentration is higher in plasma than in the interstitial fluid.

F. The ICF is compartmentalized within the cell:
1. cytosolic fluid, the fluid within the cells that surrounds the organelles (e.g., nuclei, mitochondria);
2. organellar fluid, the fluid within the organelles.

G. Movement of substances and water between compartments is an important process.

II. Cell membranes
A. A cell’s plasma membrane is a selective barrier to water and ion movement.
1. It separates the cytoplasm (cytosolic and organellar fluid) from the extracellular fluid.
2. It allows tightly coupled cells to act as a barrier between fluid compartments (e.g., the cells that separate the plasma from the interstitial fluid).

B. Composition
1. Lipid bilayer (plasmalemma)
   a. consists of amphipathic phospholipids molecules
   b. arranged in a bilayer with hydrophilic head groups pointed toward the aqueous phase
   c. hydrophobic fatty acid side-chains are in the interior of the bilayer
   d. the membrane is fluid
   e. cholesterol and unsaturated fatty acid side-chains help maintain fluidity of the bilayer
2. Proteins
   a. integral
      i. transmembrane
      ii. single-sided
   b. peripheral
   c. glycoproteins – extracellular carbohydrate attached to membrane proteins

3. Other substances
   a. cholesterol
   b. hydrophobic substances
      i. hormones
      ii. fatty acids
      iii. drugs

C. The fluid mosaic model of membrane structure
D. Membrane junctions
   1. Junctional proteins (e.g., integrins) are transmembrane proteins that link cells to one another and to the extracellular matrix.
   2. Desmosomes provide a mechanical linkage between cells.
   3. Tight junctions and their proteins provide an impermeant barrier by closely linking adjacent cells. This produces a “sidedness” to the cells so that substances moving from one side to the other must cross through the cells.
   4. Gap junction proteins allow cell-to-cell communication.
III. Diffusion in free solution

A. Diffusion direction and magnitude
   1. Diffusion is a random process
      a. random thermal motion
      b. probability of directional movement depends upon concentration
   2. If fluid compartments are separated by a permeable membrane, the difference in probability of movement from one compartment to another is the net flux.
   3. In the absence of transport mechanisms (discussed later), net flux is always from high concentration to low concentration (passive net flux).
   4. The magnitude of flux of a molecule across a permeable membrane depends upon:
      a. concentration difference of the molecule on both sides of the membrane;
      b. temperature of the solutions;
      c. size of the molecule;
      d. area of the membrane.

B. Diffusion as a function of time and distance (Fick’s equation)
   1. Net flux from diffusion in free solution depends upon the concentration gradient of the substance: $\frac{\Delta c}{\Delta x}$.
   2. The larger the concentration gradient, the larger the net flux.
   3. The constant of proportionality that relates flux ($J$) to the concentration gradient is the Diffusion coefficient ($D$). Fick’s equation is:
      $$J = -D \cdot \left( \frac{\Delta c}{\Delta x} \right)$$
   4. The units of $D$ are cm$^2$/sec.
   5. Diffusion over short distances is fast, but over long distances diffusion is very slow.

IV. Diffusion across cell membranes

A. Adaptation of Fick’s equation
   1. Net flux across a cell membrane depends upon the concentration difference of the substance: $(C_o - C_i)$, where $C_o$ is the concentration outside the cell, and $C_i$ is the concentration inside the cell.
   2. The net flux depends on the surface area of the cell membrane, $A$.
   3. The constant of proportionality that relates flux ($J$) to the concentration difference and the membrane area is the permeability coefficient ($k_p$). Flux from outside to inside is:
      $$J = k_p \cdot A \cdot (C_o - C_i)$$

B. The diffusion of a hydrophilic substance (e.g., an ion) across a hydrophobic membrane is very slow because the permeability coefficient is usually very small.

C. Hydrophobic substances and gases have a much higher permeability coefficient.
D. Integral membrane proteins can selectively increase the permeability coefficient for particular substances, such as ions.

1. These “channels” (pores) and transporters (carriers) recognize specific substances, and thus are selective.
2. Channels provide a semi-aqueous path for free diffusion.
3. Transporters provide a protein-mediated transport mechanism that may couple the transport of one substance against its gradient to the flux of another substance “down” its flux gradient (discussed later).
4. They can be regulated to increase or decrease permeability
   a. transporters may be modified to change the rate of transport
   b. channels can be “gated” on and off by:
      i. electrical activity
      ii. ligand binding
      iii. modification by enzymes
      iv. mechanical deformation.

E. Separation of charge across a membrane will also affect diffusion of ions across the membrane.

1. A net charge will attract or repel an opposite or like charged ion, respectively. This will affect the flux of the ion.
2. The electrical force acting on an ion may be opposite in direction from the chemical force driving diffusion (chemical gradient). Thus, an ion experiences an “electrochemical gradient” that influences flux.