1 Cell Membrane Structure and Function

Chapter 8

2 Introduction

- The plasma membrane separates the living cell from its nonliving surroundings.
- This thin barrier, 8 nm thick, controls traffic into and out of the cell.
- Like other membranes, the plasma membrane is **selectively permeable**, allowing some substances to cross more easily than others.

3 Membrane Molecules

- The main macromolecules in membranes are lipids and proteins, but include some carbohydrates.
- The most abundant lipids are phospholipids.
- Phospholipids and most other membrane constituents are amphipathic molecules.
  - Amphipathic molecules have both hydrophobic regions and hydrophilic regions.

4 Phospholipids constitute a fluid membranes

- The phospholipids and proteins in membranes create a unique physical environment, described by the **fluid mosaic model**.
  - A membrane is a fluid structure with proteins embedded or attached to a double layer of phospholipids.

5 Membrane models have evolved to fit new data

- Models of membranes were developed long before membranes were first seen with electron microscopes in the 1950s.
  - In 1895, Charles Overton hypothesized that membranes are made of lipids because substances that dissolve in lipid enter cells faster than those that are insoluble.
  - Twenty years later, chemical analysis confirmed that membranes isolated from red blood cells are composed of lipids and proteins.

6 Discovering Structure of Membrane through experimentation

- Attempts to build artificial membranes provided insight into the structure of real membranes.
  - In 1917, Irving Langmuir discovered that phosphilipids dissolved in benzene would form a film on water when the benzene evaporated.
    - The hydrophilic heads were immersed in water.

7 Phospholipids form a film on water

8 Bilayer

- In 1925, E. Gorter and F. Grendel reasoned that cell membranes must be a phospholipid bilayer, two molecules thick.
- The molecules in the bilayer are arranged such that the hydrophobic fatty acid tails are sheltered from water while the hydrophilic phosphate groups interact

with water.

9 Bilayer: hydrophobic interior

10 Davson & Danielli Model

- Actual membranes adhere more strongly to water than do artificial membranes composed only of phospholipids.
- One suggestion was that proteins on the surface increased adhesion.
- In 1935, H. Davson and J. Danielli proposed a sandwich model in which the phospholipid bilayer lies between two layers of globular proteins.

11 Davson-Danielli Model

- Early images from electron microscopes seemed to support the Davson-Danielli model and until the 1960s, it was considered the dominant model.

12 Membranes are not identical

- Further investigation revealed two problems.
  - First, not all membranes were alike, but differed in thickness, appearance when stained, and percentage of proteins to lipids.
  - Second, measurements showed that membrane proteins are actually not very soluble in water.
    - Membrane proteins are amphipathic, with hydrophobic and hydrophilic regions.
    - If at the surface, the hydrophobic regions would be in contact with water.

13 Singer - Nicholson Model

- In 1972, S.J. Singer and G. Nicolson presented a revised model that proposed that the membrane proteins are dispersed and individually inserted into the phospholipid bilayer.
  - In this fluid mosaicmodel, the hydrophilic regions of proteins and phospholipids arein maximum contact with water and the hydrophobic regions are in a nonaqueous environment.

14 Singer - Nicholson Model

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- A specialized preparation technique, freeze-fracture, splits a membrane along the middle of the phospholid bilayer prior to electron microscopy.
- This shows protein particles interspersed with a smooth matrix, supporting the fluid mosaic model.

16 **Membranes are fluid**

- Membrane molecules are held in place by relatively weak hydrophobic interactions.
- Most of the lipids and some proteins can drift laterally in the plane of the membrane, but rarely flip-flop from one layer to the other.

17 Fluid membrane allows drift

18 Movements of phopholipids

- The lateral movements of phospholipids are rapid, about 2 microns per second.
- Many larger membrane proteins move more slowly but do drift.
  - Some proteins move in very directed manner, perhaps guided/driven by the motor proteins attached to the cytoskeleton.
  - Other proteins never move, anchored by the cytoskeleton.

19 Lateral movements

20 Factors affecting fluidity

- Membrane fluidity is influenced by temperature and by its constituents.
- As temperatures cool, membranes switch from a fluid state to a solid state as the phospholipids are more closely packed.

21 Structure contributes to fluid quality

- Membranes rich in unsaturated fatty acids are more fluid that those dominated by saturated fatty acids because the kinks in the unsaturated fatty acid tails prevent tight packing.

22 Role of cholesterol

- The steroid cholesterol is wedged between phospholipid molecules in the plasma membrane of animals cells.
- At warm temperatures, it restrains the movement of phospholipids and reduces fluidity.
- At cool temperatures, it
- maintains fluidity by
- preventing tight packing.

23 Significance of fluidity

- To work properly with active enzymes and appropriate permeability, membrane must be fluid, about as fluid as salad oil.
- Cells can alter the lipid composition of membranes to compensate for changes in fluidity caused by changing temperatures.
  - For example, cold-adapted organisms, such as winter wheat, increase the percentage of unsaturated phospholipids in the autumn.
  - This allows these organisms to prevent their membranes from solidifying during winter.

24 **Membranes are mosaics of structure and function**

- A membrane is a collage of different proteins embedded in the fluid matrix of the lipid bilayer.

25 Proteins determine membrane function

- There are two populations of membrane proteins.
  - Peripheral proteins are not embedded in the lipid bilayer at all.
  - Instead, they are loosely bounded to the surface of the protein, often connected to the other population of membrane proteins.

26 Integral proteins

  - Integral proteins penetrate the hydrophobic core of the lipid bilayer, often completely spanning the membrane (a transmembrane protein).
    - Where they contact the core, they have hydrophobic regions with nonpolar amino acids, often coiled into alpha helices.
    - Where they are in contact with the aqueous environment, they have hydrophilic regions of amino acids.

27 Membrane proteins reinforce structure

- One role of membrane proteins is to reinforce the shape of a cell and provide a strong framework.
  - On the cytoplasmic side, some membrane proteins connect to the cytoskeleton.
  - On the exterior side, some membrane proteins attach to the fibers of the extracellular matrix.

28 Membranes have distinctive inside and outside faces

The two layers may differ in lipid composition, and proteins in the membrane have a clear direction.

  - The outer surface also has carbohydrates.
  - This asymmetrical orientation begins during synthesis of new membrane in the endoplasmic reticulum.

29 Inside and OUTside

30 The proteins in the plasma membrane may provide a variety of major cell functions.

31 **Membrane carbohydrates are important for cell-cell recognition**

- The membrane plays the key role in cell-cell recognition.
  - Cell-cell recognition is the ability of a cell to distinguish one type of neighboring cell from another.

    - This attribute is important in cell sorting and organization as tissues and organs in development.
    - It is also the basis for rejection of foreign cells by the immune system.
    - Cells recognize other cells by keying on surface molecules, often carbohydrates, on the plasma membrane.

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- Membrane carbohydrates are usually branched oligosaccharides with fewer than 15 sugar units.
- They may be covalently bonded either to lipids, forming glycolipids, or, more commonly, to proteins, forming glycoproteins.
- The oligosaccharides on the external side of the plasma membrane vary from species to species, individual to individual, and even from cell type to cell type within the same individual.
    - This variation marks each cell type as distinct.
    - The four human blood groups (A, B, AB, and O) differ in the external carbohydrates on red blood cells.

33 A membrane's molecular organization results in selective permeability

- A steady traffic of small molecules and ions moves across the plasma membrane in both directions.
    - For example, sugars, amino acids, and other nutrients enter a muscle cell and metabolic waste products leave.
    - The cell absorbs oxygen and expels carbon dioxide.
    - It also regulates concentrations of inorganic ions, like Na$^+$, K$^+$, Ca^{2+}, and Cl$^-$, by shuttling them across the membrane.
- However, substances do not move across the barrier indiscriminately; membranes are selectively permeable.

34 Permeability of a molecule

- depends on the interaction of that molecule with the hydrophobic core of the membrane.
    - Hydrophobic molecules, like hydrocarbons, CO2, and O2, can dissolve in the lipid bilayer and cross easily.
    - Ions and polar molecules pass through with difficulty.
        - This includes small molecules, like water, and larger critical molecules, like glucose and other sugars.
        - Ions, whether atoms or molecules, and their surrounding shell of water also have difficulties penetrating the hydrophobic core.

35 Polar molecules can pass through transport proteins

- Some transport proteins have a hydrophilic channel that certain molecules or ions can use as a tunnel through the membrane.
    - Others bind to these molecules and carry their passengers across the membrane physically.
- Each transport protein is specific as to the substances that it will translocate (move).
    - For example, the glucose transport protein in the liver will carry glucose from the blood to the cytoplasm, but not fructose, its structural isomer.

36 Passive transport is diffusion across a membrane

- **Diffusion** is the tendency of molecules of any substance to spread out in the available space
    - Diffusion is driven by the intrinsic kinetic energy (thermal motion or heat) of molecules.

- Movements of individual molecules are random.
- However, movement of a population of molecules may be directional.

37 Dynamic equilibrium

- At this dynamic equilibrium as many molecules pass one way as cross the other direction.

38 **concentration gradient**

  - This spontaneous process decreases free energy and increases entropy by creating a randomized mixture.
- Each substance diffuses down its own concentration gradient, independent of the concentration gradients of other substances.

39 Passive transport

- The diffusion of a substance across a biological membrane is passive transport because it requires no energy from the cell to make it happen.
  - The concentration gradient represents potential energy and drives diffusion.

40 Passive transport has different rates for different molecules

- However, because membranes are selectively permeable, the interactions of the molecules with the membrane play a role in the diffusion rate.
- Diffusion of molecules with limited permeability through the lipid bilayer may be assisted by transport proteins.

41 **Osmosis is the passive transport of water**

- Differences in the relative concentration of dissolved materials in two solutions can lead to the movement of ions from one to the other.
  - The solution with the higher concentration of solutes is **hypertonic**.
  - The solution with the lower concentration of solutes is **hypotonic**.
  - Solutions with equal solute concentrations are **isotonic**.

42 Osmosis movement of water

- Imagine that two sugar solutions differing in concentration are separated by a membrane that will allow water through, but not sugar.
- The hypertonic solution has a lower water concentration than the hypotonic solution.
  - More of the water molecules in the hypertonic solution are bound up in hydration shells around the sugar molecules, leaving fewer unbound water molecules.

43 osmosis

- Unbound water molecules will move from the hypotonic solution where they are abundant to the hypertonic solution where they are rarer.

44 Direction of osmosis

- The direction of osmosis is determined only by a difference in total solute concentration.
  - The kinds of solutes in the solutions do not matter.
  - This makes sense because the total solute concentration is an indicator of the abundance of bound water molecules (and therefore of free water molecules).

- When two solutions are isotonic, water molecules move at equal rates from one to the other, with no net osmosis.

45 **Cell survival depends on balancing water uptake and loss**

- An animal cell immersed in an isotonic environment experiences no net movement of water across its plasma membrane.
  - Water flows across the membrane, but at the same rate in both directions.
  - The volume of the cell is stable.

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- The same cell is a hypertonic environment will loose water, shrivel, and probably die.
- A cell in a hypotonic solution will gain water, swell, and burst.

47 Maintaining osmotic pressure

- For a cell living in an isotonic environment (for example, many marine invertebrates) osmosis is not a problem.
  - Similarly, the cells of most land animals are bathed in an extracellular fluid that is isotonic to the cells.
- Organisms without rigid walls have osmotic problems in either a hypertonic or hypotonic environment and must have adaptations for osmoregulation to maintain their internal environment (contractile vacuole, cell wall.)

48 Mechanical Support of the plantt

- The cells of plants, prokaryotes, fungi, and some protists have walls that contribute to the cell's water balance.
- An animal cell in a hypotonic solution will swell until the elastic wall opposes further uptake.
  - At this point the cell is turgid, a healthy state for most plant cells. Turgid cells contribute to the mechanical support of the plant.
- If a cell and its surroundings are isotonic, there is no movement of water into the cell and the cell is **flaccid** and the plant may wilt.

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- In a hypertonic solution, a cell wall has no advantages.
- As the plant cell looses water, its volume shrinks.
- Eventually, the plasma membrane pulls away from the wall.
- This **plasmolysis** is usually lethal.

50 **Specific proteins facilitate passive transport of water and selected solutes**

- Many polar molecules and ions that are normally impeded by the lipid bilayer of the membrane diffuse passively with the help of transport proteins that span the membrane.
- The passive movement of molecules down its concentration gradient via a transport protein is called **facilitated diffusion**.

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Transport proteins are similar to enzymes

- They may have specific binding sites for the solute.
- Transport proteins can become saturated when they are translocating passengers as fast as they can.
- Transport proteins can be inhibited by molecules that resemble the normal “substrate.”
  - When these bind to the transport proteins, they outcompete the normal substrate for transport.
- While transport proteins do not usually catalyze chemical reactions, they do catalyze a physical process, transporting a molecule across a membrane that would otherwise be relatively impermeable to the substrate.

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Channel proteins

- Many transport proteins simply provide corridors allowing a specific molecule or ion to cross the membrane.
  - These channel proteins allow fast transport.
  - For example, water channel proteins, aquaprorins, facilitate massive amounts of diffusion.

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Gated channel proteins

- open or close depending on the presence or absence of a physical or chemical stimulus.
  - The chemical stimulus is usually different from the transported molecule.
  - For example, when neurotransmitters bind to specific gated channels on the receiving neuron, these channels open.
    - This allows sodium ions into a nerve cell.
    - When the neurotransmitters are not present, the channels are closed.

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Transport proteins

- Some transport proteins do not provide channels but appear to actually translocate the solute-binding site and solute across the membrane as the protein changes shape.

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Transport protein

- These shape changes could be triggered by the binding and release of the transported molecule.

56

Active transport is the pumping of solutes against their gradients

- Some facilitated transport proteins can move solutes against their concentration gradient, from the side where they are less concentrated to the side where they are more concentrated.
- This **active transport** requires the cell to expend its own metabolic energy.
- Active transport is critical for a cell to maintain its internal concentrations of small molecules that would otherwise diffuse across the membrane.

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Role of ATP in active transport

- Active transport is performed by specific proteins embedded in the membranes.
- ATP supplies the energy for most active transport.
  - Often, ATP powers active transport by shifting a phosphate group from ATP (forming ADP) to the transport protein.

    - This may induce a conformational change in the transport protein that translocates the solute across the membrane.

58 Na-K Pump

- The sodium-potassium pump actively maintains the gradient of sodium (Na+) and potassium ions (K+) across the membrane.
    - Typically, an animal cell has higher concentrations of K+ and lower concentrations of Na+ inside the cell.
    - The sodium-potassium pump uses the energy of one ATP to pump three Na+ ions out and two K+ ions in.

59 Sodium-potassium pump

60 **diffusion and facilitated diffusion are forms of passive transport of molecules-no ATP**

61 **Some ion pumps generate voltage across membranes**

- All cells maintain a voltage across their plasma membranes.
    - The cytoplasm of a cell is negative in charge compared to the extracellular fluid because of an unequal distribution of cations and anions on opposite sides of the membrane.
    - This voltage, the **membrane potential**, ranges from -50 to -200 millivolts.

62 Electrochemical gradient

- The membrane potential acts like a battery.
- The membrane potential favors the passive transport of cations into the cell and anions out of the cell.
- Two combined forces, collectively called the electrochemical gradient, drive the diffusion of ions across a membrane:
    - a chemical force based in an ion’s concentration gradient
    - an electrical force based on the effect of the membrane potential on the ion’s movement.

63 Obey electrochemical gradient over concentration gradient

- Ions diffuse not simply down its concentration gradient, but diffuses down its electrochemical gradient.
    - For example, before stimulation there is a higher concentration of Na+ outside a resting nerve cell.
    - When stimulated, a gated channel opens and Na+ diffuse into the cell down the electrochemical gradient.

64 Electrogenic pumps

- Special transport proteins, **electrogenic pumps**, generate the voltage gradients across a membrane
    - The sodium-potassium pump in animals restores the electrochemical gradient not only by the active transport of Na^+ and K^+, but because it pumps two K^+ ions inside for every three Na^+ ions that it moves out.
    - In plants, bacteria, and fungi, a **proton pump** is the major electrogenic pump, actively transporting H^+ out of the cell.

65 Proton pumps

- Protons pumps in the cristae of mitochondria and the thylaloids of chloroplasts, concentrate H+ behind membranes.
- These electrogenic pumps store energy that can be accessed for cellular work.

66 In cotransport, a membrane protein couples the transport of two solutes

- A single ATP-powered pump that transports one solute can indirectly drive the active transport of several other solutes through **cotransport** via a different protein.
- As the solute that has been actively transported diffuses back passively through a transport protein, its movement can be coupled with the active transport of another substance against its concentration gradient.

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- Plants commonly use the gradient of hydrogen ions that is generated by proton pumps to drive the active transport of amino acids, sugars, and other nutrients into the cell.
  - The high concentration of H^+ on one side of the membrane, created by the proton pump, leads to the facilitated diffusion of protons back, but only if another molecule, like sucrose, travels with the hydrogen ion.

68 Exocytosis and endocytosis

- Small molecules and water enter or leave the cell through the lipid bilayer or by transport proteins.
- Large molecules, such as polysaccharides and proteins, cross the membrane via vesicles.
- During **exocytosis**, a transport vesicle budded from the Golgi apparatus is moved by the cytoskeleton to the plasma membrane.
- When the two membranes come in contact, the bilayers fuse and spill the contents to the outside.

69 Endocytosis and exocytosis

- During endocytosis, a cell brings in macromolecules and particulate matter by forming new vesicles from the plasma membrane.
- Endocytosis is a reversal of exocytosis.
  - A small area of the plasma membrane sinks inward to form a pocket
  - As the pocket into the plasma membrane deepens, it pinches in, forming a vesicle containing the material that had been outside the cell

70 phagocytosis is a form of endocytosis

- In phagocytosis, the cell engulfs a particle by extending pseudopodia around it and packaging it in a large vacuole.
- The contents of the vacuole are digested when the vacuole fuses with a lysosome.

71 **pinocytosis**, “cellular drinking”

- a cell creates a vesicle around a droplet of extracellular fluid.
  - This is a non-specific process.

72 Receptor-mediated endocytosis

- Receptor-mediated endocytosis is very specific in what substances are being transported.
- This process is triggered when extracellular substances bind to special receptors, ligands, on the membrane surface, especially near coated pits.
- This triggers the formation of a vesicle

73 Receptor Mediated Endocytosis

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- Receptor-mediated endocytosis enables a cell to acquire bulk quantities of specific materials that may be in low concentrations in the environment.
  - Human cells use this process to absorb cholesterol.
  - Cholesterol travels in the blood in low-density lipoproteins (LDL), complexes of protein and lipid.
  - These lipoproteins bind to LDL receptors and enter the cell by endocytosis.
  - In familial hypercholesterolemia, an inherited disease, the LDL receptors are defective, leading to an accumulation of LDL and cholesterol in the blood.
  - This contributes to early atherosclerosis.