SBI OA0

CORE UNIT 2: ENERGY AND THE LIVING CELL

Chapters 3, 4, & 5

Chapter 4: Cell Membranes: A Study of Structure and Function

- some of the diverse functions of membranes are...

  1. transport – a message sent along nerve pulse travels because Na and K ions are rapidly moving across the plasma membrane of the nerve cell

  2. reaction sites – a sequence of chemical reactions occurring between proteins in the blood and proteins embedded in the membranes of blood platelets - blood cells with no nuclei

  3. recognition sites – proteins in the membranes of white blood cells that recognize foreign substances and bind to them

  4. communication surfaces - the binding of one white blood cell's membrane proteins to invaders triggers messages to other neighbouring white blood cells that a foreign substance is around, via their membranes

- the cell membrane is simple in structure, yet complex in its function (see figure 4.1, p. 78)

4.1 *Membrane Constituents*

- made of **lipids** (neutral or other) and **proteins** (see p. 78, figure 4.2)

- attached to the lipids or to the proteins could be carbohydrates – these are called **glycolipids**, and **glycoproteins** respectively

  1. **Lipids**

     (i) ***Neutral Lipids*** (sterols) – soluble in hydrocarbon solvents (eg. Cholesterol)

     - the most important neutral lipid is cholesterol (p. 41, figure 2.23) – especially in mammalian membranes

     - the ring system is rigid, the tail branch is flexible

     - cholesterol usually "sits" just inside the membrane (p. 85, figure 4.11, and fig. 8.3 of handout), but closer to its surface – resulting in the membrane being more rigid at its surface and more fluid at its center

     - the fluidity and rigidity character of a membrane, at various locations throughout it, play a major role in the proper functions of the membrane

     (ii) ***Other Lipids*** – not soluble in hydrocarbon solvents (eg. Phospholipids and glycolipids)

a. *Phospholipids*

- 2 long fatty acids attached to a triglycerol by an ester linkage make a lipid molecule
- when the glycerol attaches to a phosphate group, this creates a “phosphotidyl” molecule
- when the phosphate group attaches to a final **head group** (p. 79, figure 4.1), the molecule is called a phospholipid
- the specific class a phospholipid molecule is dictated by the kind of head group it possesses (p. 79, fig. 4.2)
- the length and physical properties of a phospholipid molecule is dictated by the kind of fatty acid chain it possesses (p. 79, figure 4.3)
- three kinds of head groups are **choline**, **ethanolamine**, and **serine** produce three classes of phospholipids – phosphotidyl*choline* (a zwitter ion), phosphotidyl*ethanolamine* (a zwitter ion), and phosphotidyl*serine* (a negatively charged ion) respectively
- saturated fatty acids in phospholipids produce less fluid structures
- unsaturated fatty acids in phospholipids produce more fluid structures – due to the more flexible double bonds within the chain

b. *Glycolipids*

- contain a pair of hydrocarbon tails and a polar head group consisting of one or more carbohydrate groups
- found in the membranes of neurons – abundant in brain cells

2. **<u>Membrane Proteins</u>** (p. 80, figure 4.4)

- the functions of membrane proteins can vary (fig. 8.6 of handout)

(i) ***Peripheral Proteins*** – soluble in water, can easily be moved, and bound to other proteins that are in the membrane

(ii) ***Integral Proteins*** – insoluble in water and can only be removed when the membrane is broken apart

4.2 Spontaneous Assembly of Membranes

- all natural components of membranes are amphophilic (both water fearing and water liking)

1. **<u>Monolayers and Soap Bubble Bilayers</u>**

    - a monolayer is seen on p. 81, figure 4.6
    - a soap bubble bilayer is seen on p. 82, figure 4.7

2. **<u>Micelles and Bilayer Membranes</u>**

    - placed in water, amphophilic molecules tend to form micelles or clusters (p. 82, figure 4.8) since the cross-sectional area of the head group tends to be larger than that of the fatty acid hydrophobic tails
    - phospholipids don't form stable micelles because the hydrophobic tails have a larger cross-sectional area than the hydrophilic heads do
    - instead of micelles, phospholipids in water result in the basic structure of a membrane (p. 83, figure 4.9) – where the only way to avoid exposure to water is to have the hydrophobic tails together in a bilayer
    - basically, the bilayer separates two regions of water into the "out-side" region and the "inside" region (figure 8.1, of handout)

Homework: define from "lipid" to "bilayer hypothesis" in vocabulary, p. 98 , and do ques. 1-8, pp. 98-99

Reminder: UNIT 2, QUIZ #1 – next class!!

4.3 <u>Development of Models of Membrane Structure</u>

- once the structure of the lipid bilayer was established, other questions arose....where do the proteins occur?.....Do hydrophobic molecules pass more readily through the membrane?....What determines permeability?....etc.
- one model - the Danielli-Davson model - proposed that proteins formed **transmembrane pores** (p. 84, figure 4.10 and figure 8.2 of handout)
- this model is not entirely incorrect since proteins actually do span the entire membrane structure
- as the 3-D nature of proteins became understood, the details of the membrane models improved
- it became evident that the interior of membranes are fluid, since molecules within them could move around and mix – rather than being static in a matrix (evidence of this - fig. 8.4 of handout)
- the fluid mosaic model is the most current accepted to date – OVERHEAD (p. 85, figure 4.11 and fig. 8.2 of handout) – notice glucose chains attached to proteins and lipids creating glycoproteins and glycolipids, respectively
- the fluidity of the membrane is a very important feature that it possesses (figure 8.3 of handout)

4.4 Special Properties of Membranes

- any given membrane possesses a large variety of lipids, differing in the nature of the head group, and in the make-up of the fatty acid chains
- of the three classes of phospholipids, it is believed that the outer, extracellular half of the membrane has a larger proportion of phosphotidylcholine and is the only site of the glycolipids
- the cytoplasmic (inner) half contains a larger fraction of phosphotidylserine and phosphotidylethanolamine
- this results in an asymmetric distribution of lipids such that the more negative class exist on the inner half, next to the cytoplasm
- integral proteins are always oriented in one specific direction – glycoproteins have their carbohydrates attached on the extracellular side (figure 4.12, p. 86, and fig. 8.5 of handout)
- the portion of the protein that lies in the interior of the membrane has a large number of hydrophobic amino acid residues
- the portion of the protein that lies beside the hydrophilic heads of the membrane, possess charges as well as hydrophilic amino acid residues – this causes strong physical interactions with the polar surfaces and provides extremely strong binding of the integral proteins to the membrane
- proteins on the periphery of membranes are asymmetrically associated with it – they could also be associated with, or bound to, other proteins in the cytoplasm of a cell (figure 4.13, p. 86)
- sometimes a phospholipid on one side of a bilayer actually moves laterally or translocates to the opposite side (p. 86, figure 4.14, and fig. 8.3 of handout)

Homework: define from "transmembrane pore" to "fluid mosaic model" in vocabulary, p.98 , and do ques.9, p. 99.

4.5 Transport Across Membranes

- the first essential function of the membrane is the containment of cellular constituents -- to keep all biological components that interact with one another for life functions, together in one fixed area
- all membranes allow for the movement of non polar molecules and small polar molecules, like water, across it
- the spontaneous movement of solute molecules across a membrane in response to a electrochemical gradient is called **passive transport**
- large polar molecules, and charged molecules pass through the membrane by **facilitated diffusion**
- this take place through protein pores, so long as a concentration gradient across the membrane exists
- when necessary ions needed to be transported against a concentration gradient, energy is required to do so – this is called **active transport**

- the different classes of transport in a cell are seen on p. 87, figure 4.15
- the type of molecule that is transported is regulated by the cell in response to changes in the environment
- to respond to the environment means that the membrane is able to transport information
- three kinds of potential that result in the movement of matter...(p. 88, figure 4.16)
    - *gravitational potential* (due to gravity)
    - *magnetic potential* (due to magnetic fields)
    - *electric potential* (due to charges on species)
- in all three cases, matter moves from a region of higher potential to a region of lower potential
- molecules that are in a region of high concentration are at a higher *chemical potential* than those in a region of low concentration
- when the potential gradient is zero, then there is no net transport of molecules or ions – equilibrium is established (fig. 8.8 of handout)
- for ions, sometimes high chemical potential may favor one direction of movement, while high electric potential may favor another, at the same time (figure 4.17, p. 88)
- when the effect of the difference in chemical potential is equal, but opposite, to the effect of the difference in electric potential, the net transport is zero
- the result of the two added together is called electrochemical potential
- the natural spreading of molecules from regions of high chemical potential to regions of low chemical potential is called **diffusion** (figure 4.18, p. 89)
- the larger the gradient in chemical potential, the faster the movement of molecules
- even when a substances spreads across (and through) another it eventually reaches equilibrium, however, the individual molecules will continue to move throughout the entire solution – giving this system a dynamic characteristic
- the degree of chemical potential difference across a membrane, as well as the permeability of the membrane itself, both affect the rate of movement of molecules
- the permeability of a molecule through pure lipid membranes is related to how soluble it is in the interior of the membrane relative to its solubility in water – since hydrophobic molecules are more soluble in the membrane, they have higher permeabilities
- diffusion of a solvent through a selectively permeable membrane is called **osmosis** (fig. 8.9 of handout)
- in living systems, the solvent is usually water
- the reason why water has a high permeability through cell membranes, even though it's not soluble in hydrocarbons, is because it is very small
- water potential is measured as a result of how many solute molecules it solvates

- low solute concentrations in water means high water potential (or osmotic potential)
- the osmotic potential across a cell membrane is zero when the amount of water on both sides of the membrane is equal – the two solutions on both sides of the membrane are called **isotonic**
- solutions with more solute are **hypertonic** solutions
- solutions with low solute concentrations, therefore high water potential, are **hypotonic**
- the affects of each type of solution can be extremely important to the health of a cell (figure 4.20, p. 90, and figure 8.11 of handout)
- when the cytoplasmic osmotic potential increases, as a result of water entering a cell, the **osmotic pressure** inside the cell increases (a pushing from the cytoplasmic side toward the outside of the cell)
- in very dilute solutions (with high osmotic potential) a cell can burst – called **lysis** (figure 4.21, p. 90, and fig. 8.10 of handout)
- the cell walls of plant cells are able to withstand the large amounts of osmotic pressure from the cytoplasm...why? -- ans. The slight modification in the orientation of the alcohol group of carbon 1, causing the characteristic alternating, diagonal, 1-4 linkage of glucose, making cellulose instead of starch, results in a tough-to-break polymer – the polymers bunch up in strands to make extremely resistant fibres
- solute molecules must cross both the polar regions and the non-polar regions of the membrane before they can move into the cell's interior
- the relative permeabilities of various substances across a pure lipid bilayer are seen in figure 4.22, p. 91
- ***Passive Transport*** (figure 4.23, p. 91 and fig. 8.14 of handout)
  - small uncharged molecules may occur through the lipid bilayer by simple diffusion
  - the passive transport of larger polar molecules and ions require special channels or permanent pores in the membrane – these are usually created by transmembrane proteins called *transport proteins* -- they contain a narrow channel filled with water – helps to bring in hydrophylic molecules
  - the passive transport of large molecules takes place through channels that are only created by special transport proteins when the right type of molecule binds to the surface of the transport protein itself (figure 4.24, p. 92 and fig. 8.12 of handout)
  - the rate of passive transport of substances across a membrane via facilitated diffusion is affected by two factors:
    1. the concentration gradient (electrochemical gradient) difference across the membrane
    2. how fast a protein can change its structure to allow the substance to cross the lipid bilayer
  - the rate of passive transport of a substance across a membrane via simple diffusion is affected solely by the electrochemical gradient
  - therefore, facilitated diffusion is slower than simple diffusion
- ***Active Transport*** (figure 4.23, p. 91 and fig. 8.14 of handout)

- this kind of transport moves substances across a membrane to oppose an electrochemical gradient – i.e. like rolling a ball up hill
- this is done using proteins that are called *pumps*
- these proteins are highly selective in what they will pump into and out of cells (figure 4.25, p. 93) – this way, only the right molecules are transported, wasting no energy
- one very common kind of active transport is the **sodium-potassium pump**
- not just in plasma membranes of cells, but in many other types of membranes
- it functions to move Na^+ out of the cell or organelle (where the $[Na^+]$) is normally 10X higher), and K^+ into the cell or organelle (where the $[K^+]$ is 10X lower)
- the energy to function comes from individual ATP (adenosine triphosphate) molecules
- every one ATP is hydrolyzed to produce ADP and phosphate, which releases a certain amount of energy such that three Na^+ ions are pumped out, and two K^+ ions are pumped in (figure4.26, p. 93 and fig. 8.13 of handout)

- ***Two Important Features of the Na^+-K^+ Pump***
    - <u>Efficient energy use in the transport of ions</u>
        - part of the energy from the ATP is used to change the shape of the protein to allow transport of the Na^+ ion and part of it is saved as a protein-phosphate chemical bond
        - the part saved as a protein-phosphate chemical bond is used to change the protein back into its original shape while it transports K^+ ions in through the membrane
    - <u>Effective reverse-use property</u>
        - the pump can run backward – the cell uses the energy released in the transport of the ions down their chemical potential gradients to make ATP
- since this effective reverse use of the pump is linked with its transport property, the entire system is referred to as the **sodium-potassium ATPase**
- since the pump moves two different ions across it in opposite directions, it is called **antiport**
- when the transport of one molecule toward lower chemical potential causes the transport of another molecule against its chemical potential gradient, it is called **symport**
    - an example of this is when Na^+ ions come back into the cell, after they have been pumped out, they bring back with them, a glucose molecule (figure 4.27, 4.28, p. 94
- the sodium-potassium pump is an example of an electrogenic pump (or proton pump) that stores energy by generating a charge separation (voltage) across a membrane
- first it establishes a more "positiveness" in the cytoplasm and "negativeness" in the ECF, from the use of ATP energy as a power source, by pumping positive ions (Na^+ or H^+) into the ECF

- then it uses this electric gradient across the membrane to drive other processes – one of them is to take in sugar and other nutrients that are higher in concentration in the cytoplasm (fig. 8.15 and 8.16 of handout)

- ***Regulated Transport***
  - the transport of materials into and out of cells is regulated

    1. Voltage-gated Channels: some cell membranes (like those of nerve cells) have channels in them that open and close based on the electric potential gradient across them – when the potential is great, the membrane is said to be polarized and the channels are closed -- when the potential difference decreases to a certain point the membrane is depolarized and the channels open (figure 4.29, p. 95)
    2. Ligand-gated Channels: cell membrane channels respond to the binding of other protein molecules – they and open when the concentration of this protein is high, and close when this compound is absent (figure 4.29, p. 95)

  - regulated channels are used in facilitated diffusion
  - active transport channels are regulated, but by the availability of ATP, not by the availability of transport protein molecules

- ***Macromolecule Transport***
  - very large molecules don't penetrate the membranes of cells
  - they are taken in by a process called **endocytosis** (phagocytosis/pinocytosis) and released by the cell by a process called **exocytosis** (figure 4.30, p. 95 and fig. 8.17 of handout)
  - both processes involve the reorganization of the membrane into small *membrane vessicles*
  - hormones, insulin, lipoproteins, neurotransmitters, histamines are all released and taken in by cells through endo- and exocytosis

- Membrane Potential
  - the relative concentrations of sodium and potassium in the cytoplasm and in the ECF establishes an electric potential gradient across a membrane – this is called the **membrane potential**
  - most animal cells have a potential of -40 mV to -60 mV
  - this is maintained by the Na^+-K^+ pump at the expense of ATP (approx. 1/3 of all ATP made)
  - the role of membrane potential in nerve cells is crucial
  - neurotransmitters bind to receptors in the membrane causing a rapid change in the permeability of the sodium ion – this results in the membrane potential increasing above the normal value of -60 mV
  - if the change is large enough to reach a threshold potential, the Na^+ ion channels open fully to produce a rapid change in membrane potential toward +100 mV

- reaching this value causes the Na^+ ion channels to close, and the K^+ ion channels to fully open
- this efflux of K^+ ions causes the membrane potential to restore to -60 mV
- this very large positive potential, which occurred for a brief moment, is conducted along the cell membrane, which in turn, causes other Na^+ ion channels to open and depolarize the membrane
- the cycle is repeated as the nerve impulse travels along the membrane
- 2/3 of the ATP made by nerve cells is used for the Na^+-K^+ pump

Hmwrk: define from "passive transport" to "membrane potential" in vocab, p.98 , and ques.10-18, p. 98

Reminder: UNIT 2, QUIZ #2 – next class!!

4.6 Special Membranes

- of all the membranes, the plasma membrane has the greatest variety of functions...
  1. encloses cell and keeps the cell content concentrated
  2. using its specialized protein receptors, it serves as the communication link between the inside of the cell and the outside
  3. together with the cytoskeleton and the exoskeleton of the cell, it is responsible for maintaining and changing the shape of cells
- the mitochondria and the chloroplasts of each cell contain their own double membranes
- the ER membrane system runs throughout the cell and constitutes between 1/3 and ½ of the membrane mass of a cell – the rough ER (with ribosomes) membrane system is responsible for the synthesis of many proteins, while the smooth ER (without ribosomes) membrane system is responsible for the production of small membrane vessicles for the transport of glycoproteins during their synthesis
- the Golgi apparatus is a large network of membranes which is involved in the control and production of transport vessicles
- membrane vessicles are highly specialized and throughout entire cell's cytoplasm – they function as small "shuttles" which transport material from one region of the cell to another, and to keep toxic chemicals from the rest of the cell (i.e. lysosome contents of low pH)

4.7 The Effect of Drugs on Membranes

- polyene antibiotics
  - these drugs are used to fight fungal infections (i.e. yeast)

- they kill cells since they bind to sterols in the membranes of cells and form large pores
- the pores allow ions to freely pass through the membrane, down their concentration gradients -- Na^+ ions to enter, and K^+ ions exit the cell
- this causes a loss of control of osmotic balance – water enters the cell and the cell lyses and dies
- they bind much more strongly to ergosterol, the major sterol in yeast cells, than to cholesterol, the major sterol in human cells – however, if taken in large amounts, they could kill human cells as well
- these drugs have no effect on bacteria, since bacteria have no sterols in their membranes at all

- <u>anesthetics</u>
    - it is believed that lidocaine (local) or general (non-local) anesthetics act by physically disrupting the membrane structure to the point where the proteins in the plasma membranes of nerve cells do not function properly
    - nitrous oxide (laughing gas) induces laughter which causes special neurotransmitters to be released that bind to nerve receptors to reduce pain sensation

4.8 Variations on a Basic Theme

- all membranes are basically structurally similar, however, each has its own specialized function
- differences may be within the same cell (i.e. plasma membrane vs. mitochondrial membrane), or from cell to cell within the same organism (i.e. liver cell membrane vs. brain cell membrane)
- ***Review: answer objectives 1-9, pp. 98.***