**Topic 4: THE CELL MEMBRANE**

I Membrane Structure and Composition
- A Lipid Bilayer
  - 1 Phospholipids are primary component
    - a fatty acid chains (hydrophobic) point into the membrane
    - b glycerol, phosphoric acid (hydrophilic) point outside the membrane (= cell interior or cell exterior)
  - 2 Cholesterol is embedded
    - a more cholesterol = more fluid membrane, but better barrier to $H_2O$
  - 3 Physical barrier, also hydrophobic interior is difficult to pass through
  - 4 Fluidity – a medium (solvent) for other substances to function in
- B Proteins
  - 1 span membrane: hydrophilic regions at ends, hydrophobic central region.
  - 2 stud outside or inside – may interact with other membrane components by ionic interactions or hydrogen bonds
  - 3 Channels for small water soluble molecules, e.g., ions
  - 4 Receptor sites for hormones, neurotransmitters, etc. (ligands = molecules that bind receptors)
  - 5 Membrane bound enzymes
  - 6 Link membrane to cytoskeleton
  - 7 Cell adhesion molecules
  - 8 Recognition markers
- C Carbohydrates
  - 1 only on outer surface
  - 2 glycoproteins
  - 3 glycolipids
  - 4 modify/change function of proteins they are linked to
  - 5 recognition markers
  - 6 cell adhesion
- D Fluid Mosaic Model

II Cell to Cell Adhesions
- A Extracellular matrix
  - 1 meshwork of fibery proteins

2 acts as glue, and to maintain proper spacing between cells

B Cell junctions
1 desmosomes
a place where filaments tie cells together
b can form continuous protein network of intracellular proteins with extracellular proteins
2 tight junctions = adherens junction
a impermeable junctions that join lateral edges of epithelial cells
b allows epithelial cells to have "sides", and to themselves act as specialized selectively permeable barriers
3 gap junctions
a gaps between cells joined by tunnel composed of protein

C Other cell adhesion molecules (CAMs)
1 cell-matrix adhesion
2 cell-cell adhesion (e.g. N-CAM)
3 some are loose: allow rapid binding/unbinding for movement
4 some are tight and permanent

III Membrane Transport
A Overview
1 Plasma membrane is selectively permeable
2 Factors that affect **permeability** of a molecule across LIPID BILAYER
a solubility in lipid
i gases ($O_2$, $CO_2$), fatty acids cross
ii ions (Na+) and hydrophilic molecules don't
iii $H_2O$?
b size: smaller easier to cross
3 Presence of membrane proteins allows additional (selective) permeability because of
a channels
b carriers

B Passive Diffusion

1 Requires <u>no energy</u>
2 Substances move down/with concentration gradient

3 Factors that affect **rate of diffusion**

  a magnitude of **concentration gradient** – greater the difference in concentration, the greater the rate of diffusion
  b permeability of membrane to substance
  c surface area of membrane – greater surface area = greater rate of diffusion
  d molecular weight of substance – small particles have a higher rate of diffusion
  e distance over which it occurs

4 By diffusion across bilayer (gases, lipids)

5 By diffusion through channels (ions)

6 By osmosis

  a "Special case" of diffusion
  b Net diffusion of water down its concentration gradient
  c Or "up" the concentration gradient of all other solutes combined = up the osmolarity gradient
  d Water moves across lipid bilayer OR through channels

3 By carrier Mediated Transport = "facilitated diffusion"

  a Carrier proteins span membrane
  b No energy required
  c Assists movement of substance down concentration gradient

C Active Transport

  1 Requires energy (ATP)
  2 Can move molecules against/up concentration gradient
  3 By "primary active transport"
    a called pumps (also called ATPases)
    b Example: Na+/K+ ATPase pump: pumps Na+ out; K+ in

  4 By secondary active transport

a An energy-requiring process is linked to one that does not require energy
b frequently coupled to the Na+K+ ATPase
c Na+K+ ATPase makes K+ high inside, Na+ high outside
d additional carrier molecules couple transport with the re-intake of Na+

5 Special case of secondary active transport: transport across epithelia

- a epithelia with adherens junctions have ‘sides’ with different distributions of carrier proteins, pumps, and channels
- b allows selective transport of materials
- c example: glucose from intestinal lumen to blood

Vesicular transport

1 Transport in or out of cell in membrane bound vesicle

2 Endocytosis: surrounding & engulfing of substance

- a two fates of endocytosed material:
  - i endosome fuses with lysosome and material is digested/released within the cell
  - ii endosome travels across the cell to be released on the other side, can be used to transport material across a cell layer

3 Exocytosis: fusion of vesicle with membrane & release

- a mechanism of secretion
- b mechanism of maintaining the plasma membrane

**Topic 5: MEMBRANE POTENTIAL; REGULATION/COORDINATION OF CELLULAR ACTIVITIES**

I Membrane Potential

A Overview

1 Definition: a separation of charges across a membrane (unequal distribution)

2 Energy is required to separate charges that want to be together (opposites attract)

3 This means that separated charges have potential to do work

4 Unit of measure is mV (1/1000 of a volt)

B All living cells have membrane potential

1 Slight excess of positive outside

2 Slight excess of negative inside

3 Ions responsible: Na+, K+, A- (A- is large intracellular particles = anions)

C Causes of Membrane Potential in Living Cells

1 Effect of K+ alone (hypothetical situation: cell filled with only K+ and A-, in a bath of Na+ and Cl-, membrane permeable to only K+)

a Concentration gradient stronger than Electrical gradient

b So K+ diffuses out of cell

c A- stays in cell

d Results in increase of electrical gradient

e Continues until electrical gradient balances concentration gradient:

f balance is called equilibrium potential = -90mV

g this is a negative potential because of the net negative charge inside the cell

2 Effect of Na+ alone (hypothetical situation; same cell as above, but membrane is permeable to only Na+)

a concentration gradient stronger than electrical gradient

b Na diffuses into cell

c Cl- stays outside

d diffusion of Na+ continues till a balance is achieved

e equilibrium potential = +60 mV

f this is a positive potential because of the net positive charge inside the cell

3 All together now; “real cell”
  a Membrane is more permeable to K+ than Na+
  b K+ wants to move out of cell with its own concentration grad but against electrical gradient.
  c Na+ wants to move in with its own concentration gradient and its own electrical gradient
  d membrane is more permeable to K+ so more K+ moves out relative to Na+
  e but enough Na moves in to reduce membrane potential from -90 to -70mV
  f this is still hypothetical – something needs to keep Na+ high outside and K+ high inside
  g Na+K+ ATPase pump counterbalances diffusion of K+ and Na+ to maintain the -70 potential
  h ALL PASSIVE FORCES BALANCE BY ACTIVE FORCES; NO NET DIFFUSION

5 Cl-
  a Does not influence membrane potential
  b Is influenced by membrane potential
  c Cl- diffuses passively across membrane until its concentration gradient is balanced by overall electrical gradient established by membrane potential

II Cell-Cell Communication

A Types of communication
  1 direct communication
    a gap junctions:  small molecules pass through “tunnel” between cells
    b cell-surface communication, direct contact of cell-surface proteins

  2 diffusible signaling molecules
    a paracrine
      i short-range diffusion
      ii neurotransmitters = specialized type of paracrine signaling
    b endocrine
      iv long-range diffusion via blood

v hormones and neurohormones are examples

B Action of chemical messengers (ligands) on cell-surface receptors

1 initial effect on receptor is a conformational change
2 direct effect on receptor
  a receptor is a channel (e.g. Ach receptor = Na+ channel)
  b receptor is an enzyme (e.g. phosphatase, receptor then adds phosphates to other proteins to change their activity)
3 second messenger systems
  a activates a cascade of chemical reactions
  b cyclic AMP and Ca++ are common second messengers

III Regulation of cellular activites. Consider an example of a secretory cell regulating production of a hormone.

A Homeostatic maintenance of a desired level of hormone
1 End-product inhibition: end product of metabolism (hormone) is an inhibitor of an enzyme in the metabolic pathway
  a metabolic pathway: series of enzyme-catalyzed steps that result in a final product
2 Autocrine signaling: end product of metabolism (hormone) acts on a cellular receptor – binding leads to inhibition of an enzyme in the pathway
3 Both are examples of negative feedback at the cellular level

B Regulated change of hormone levels
1 Activity of enzyme is changed (inhibited/stimulated)
2 Amount of enzyme is changed
  a change in rate of protein synthesis (RNA ➔ protein is inhibited)
  b change in rate of gene transcription (change in gene expression; DNA➔RNA is inhibited)
3 Other processes can be regulated
4. How is the change accomplished?
  a. An additional signal from outside the cell binds to a receptor, initiates change
  b. A number of mechanisms within the cell can also result in change