Membranes (Outline)

• Brief Review membrane structure and functions
• Physical state of membranes and its importance of fluidity
• Factors affecting fluidity; role of cholesterol in animal cells
• Functions of membrane proteins (General)
• Traffic across the membrane:
  A. Small molecules:
   – Chemical properties of substances
   – Types of transport:
     • Passive transport: diffusion & Facilitated diffusion
     • Active transport
     • Diffusion and Osmosis (lecture/lab)
   – Protein transporters
  B. Large particulate materials & Molecules
Plasma membrane

- Boundary of cell
- Selective permeability
- Composed of lipids, proteins, some carbohydrates

Phospholipids are **amphipathic molecules** with both hydrophobic and hydrophilic regions.
“The Fluid Mosaic Model” (1972)
S. J. Singer and G. Nicolson

Phospholipid bilayer

Hydrophilic region of protein

Hydrophobic region of protein

http://www.insidecancer.org/

Membrane fluidity affects activity of membrane-bound enzymes
Composition and physical properties of membranes

- **Fluid phospholipid** molecules held by 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.

![Diagram of membrane with arrows indicating lateral movement and flip-flop](a) Movement of phospholipids

Lateral movement (~10^7 times per second)  Flip-flop (~ once per month)
- Phospholipids move rapidly.

- **Proteins**
  - Some move more slowly guided/driven by the motor proteins attached to the cytoskeleton.
  - Other never move, anchored by the cytoskeleton.
Factors affecting membrane fluidity

- **Temperature**, phospholipids are more packed at low temperature (fluid to more solid)
- **Fatty acid** composition
- Presence of the steroid **cholesterol**

(b) Membrane fluidity
Cholesterol is a steroid lipid with a carbon skeleton consisting of four fused carbon rings.
• 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.

(c) Cholesterol within the animal cell membrane
Lipid Rafts
Made of special phospholipids that pack tightly with cholesterol and act as a raft for certain membrane proteins

http://www.youtube.com/watch?v=2as2bsFhoggk&feature=channel
Membranes are mosaics of structure and function

A collage of different proteins embedded in the fluid matrix of the lipid bilayer and some peripheral proteins.
Integral proteins (trans-membrane) - span the membrane.

• hydrophobic regions with non-polar amino acids, often coiled into alpha helices

• hydrophilic regions of amino acids where they contact the aqueous environment.
Functions of plasma membrane proteins

(a) Transport
(b) Enzymatic activity
(c) Signal transduction
(d) Cell-cell recognition
(e) Intercellular joining
(f) Attachment to the cytoskeleton and extracellular matrix (ECM)
Desmosomes

Intercellular joining
Traffic Across Membranes

A. Ions and monomers (small molecules)
   Move physically through the membrane

A. Macromolecules and large particles
   move across inside vacuoles & vesicles
A. Traffic of ions and monomers

Selective permeability depends on interaction of that molecule with the **hydrophobic core** and presence of specific **proteins**

- non-polar molecules can pass:

- polar and ionic molecules and inorganic ions are assisted by membrane proteins
Traffic of ions and monomers

Selective permeability depends on interaction of that molecule with the **hydrophobic core** and presence of specific **proteins**

- non-polar molecules can pass:
  - hydrocarbons, CO$_2$, and O$_2$

- polar and ionic molecules and inorganic ions are assisted by membrane proteins
  - nutrients (monomers of sugars and amino acids) and metabolic waste products
  - Na$^+$, K$^+$, Ca$^{2+}$, and Cl$^-$
Both diffusion and facilitated diffusion are forms of passive transport of molecules down their concentration gradient, while active transport requires an investment of energy to move molecules against their concentration gradient.
Movement across membranes

I. Passive transport
   From an area of high concentration to one with lower concentration, down a concentration gradient, no ATP required

II. Active transport
   From an area of low concentration to one with higher concentration, requires ATP
I. Passive Transport

1. **Simple diffusion** (gases & hydrocarbons)

2. **Osmosis** diffusion of solvent (H$_2$O)

3. **Facilitated diffusion** (via protein transporters)
   a. Translocating channels (glucose)
   b. Gated channels
I.1 Diffusion across permeable membranes

Driven by kinetic energy of individual molecules and the potential energy of the concentration gradient
Each substance diffuses down its own concentration gradient, independent of the concentration gradients of other substances.

(b) Diffusion of two solutes
1.2 Osmosis

- Passive transport of water (solvent) down its concentration gradient

http://programs.northlandcollege.edu/biology/Biology1111/animations/dissolve.html

http://physioweb.med.uvm.edu/bodyfluids/osmosis.htm
Protein channels
- water channel proteins, aquaporins
• Three types of solutions
  Isotonic- similar
  hypotonic- below
  hypertonic- above

in relation to the internal contents of the cell
(Tonicity: concentration of water soluble substances outside the cell)
Some large molecules are water-soluble

(a) Lysozyme molecule in a nonaqueous environment
(b) Lysozyme molecule (purple) in an aqueous environment such as tears or saliva
(c) Ionic and polar regions on the protein’s surface attract water molecules.

This oxygen is attracted to a slight positive charge on the lysozyme molecule.
Osmotically Active Substances (OASs)

- Water soluble substances that capture water molecules.
- Determine the direction of water movement.
- **Osmolarity**: the concentration of osmotically active particles in solution.
Effect of tonicity on eukaryotic cell shape

(a) Animal cell

- Hypotonic solution: Lysed
- Isotonic solution: Normal
- Hypertonic solution: Shriveled

(b) Plant cell

- Hypotonic solution: Turgid (normal)
- Isotonic solution: Flaccid
- Hypertonic solution: Plasmolyzed
Effect of Osmosis on Red Blood Cells

http://arbl.cvmbs.colostate.edu/hbooks/cmb/cells/pmemb/osmosis.html
Effect of salt concentration (tonicity) on plant cells

- **Turgid** cells form in hypotonic solutions and contribute to the mechanical support of the plant.

- **Flaccid** cells form in isotonic solution and the plant may wilt.

**Plasmolysis** occurs in hypertonic solution and is usually lethal.
1.3 Facilitated diffusion

The passive movement of molecules down a concentration gradient via a transport protein.

a. hydrophilic channel acts as a tunnel

b. Physically carry their molecules across the membrane

c. Specific (glucose vs. fructose)
Common features of transport proteins and enzymes

- **specific** binding sites for the solute.
- can be **saturated**
- can be **inhibited** by molecules that resemble the normal “substrate.”
- **catalyze** a *physical* process
Protein Transporters

• Interact with transported substance and other molecules

• Change conformation
  – Translocating transporter- by transported substance

  – Gated Channel (allosteric protein)- by a molecule other than the transported substance

  – Active transporter- (allosteric protein) by phosphorylation
I.3.a Translocating transporter

- Protein changes shape as solute is being transported.
- Shape changes could be triggered by the binding and release of the transported molecule.
Translocating Co-transporter
- Can bind and transport two substances together
Glucose-Na+ transport across the intestinal membrane

http://www.vivo.colostate.edu/hbooks/pathphys/digestion/smallgut/absorb_sugars.html
1.3.b. **Gated channels**

Open by a physical or chemical stimulus other than the transported molecules (Example: neurotransmitters)
II. Active transport

- Transport of solutes against their concentration gradient
- Specific transport proteins embedded in the membranes
- Requires ATP

**Phosphorylation** causes a conformational change of the transport protein translocating the solute across the membrane
The **sodium-potassium pump** actively maintains the gradient of sodium (Na+) and potassium ions (K+) across the membrane.

- Animal cell- higher concentrations of K⁺ and lower concentrations of Na⁺ inside the cell.

- The sodium-potassium pump uses the energy of one ATP to pump 3 Na⁺ ions out and 2 K⁺ ions in.

http://highered.mcgraw-hill.com/sites/0072437316/student_view0/chapter6/animations.html#

http://arbl.cvmbs.colostate.edu/hbooks/molecules/sodium_pump.html
1. Binding of cytoplasmic Na⁺ to the protein stimulates phosphorylation by ATP.

2. Phosphorylation causes the protein to change its conformation.

3. The conformational change expels Na⁺ to the outside, and extracellular K⁺ binds.

4. K⁺ binding triggers release of a phosphate group.

5. Loss of phosphate restores original conformation.

6. K⁺ is released and Na⁺ sites are receptive again; the cycle repeats.

EXTRACELLULAR FLUID

CYTOPLASM
Electrochemical gradient- a chemical concentration gradient & an electrical force

Electrogenic pumps- transport protein that generates voltage across membrane

Membrane potential- voltage generated across membrane resulting from Na+ pumps

(movement of cations into the cell and anions out of the cells)
Proton pumps

Commonly used by different organisms for multiple purposes

- **Proton gradients**: used to make ATP in mitochondria and chloroplasts.
- **Proton gradients**: used for co-transport
- **Active pumps**: generate a proton gradient using ATP
B. Transport of large macromolecules

- **Endocytosis** - Uptake of **macromolecules** and large particles

- **Exocytosis** - Secretion or excretion e.g. insulin (protein hormone) by pancreatic cells.

Endocytosis and exocytosis

Types of Endocytosis

a. Phagocytosis

b. Pinocytosis of liquid droplets, non-specific
c. Receptor-mediated endocytosis

very specific for a ligand

specific receptor on surface of cell

coat proteins line the cytoplasmic side of the pit

Once ligand is liberated inside the cell the receptors are recycled back to the membrane

e.g. Cholesterol/LDL receptor complexes

http://www.sumanasinc.com/webcontent/anisamples/molecularbiology/endocytosis.html