

# The Cell and Its Chemistry

January-13-11  
1:09 AM

**Cell:** smallest unit with the capacity to live and reproduce

## Cell Theory

1. All organisms are composed of one or more cells
  - unicellular vs. multicellular organisms
2. The cell is the smallest unit that has the properties of life
3. Cells arise only from the growth and division of pre-existing cells

## Eukaryotes vs Prokaryotes

### **Eukaryotes**

- have a nucleus/nuclear envelope
- presence of membrane-bound organelles
- motor proteins that move cells and internal cell parts

**Endomembrane System:** collection of interrelated internal membranous sacs that divide into functional & instructional compartments called organelles. Ex. Nuclear envelope, ER, and Golgi complex

### **Nucleus:**

- nuclear envelope
- nuclear pores
- nucleolus
- DNA and protein organized into chromosomes

### **Endoplasmic Reticulum:**

- tubular network of membranous channels and vesicles
- smooth ER and rough ER
- rough ER: studded with ribosomes; synthesizes proteins
- smooth ER: synthesizes lipids and steroids; detoxification

### **Golgi Complex:**

- stack of flattened membranous sacs
- located between rough ER and plasma membrane
- receives proteins of ER, sorts and modifies them, and transports them elsewhere

### Vesicles

- transport among organelles and/or to plasma membrane

### Lysosomes, Peroxisomes

- contain hydrolases, catalases

### Vacuole

- temporary storage
- turgor pressure in plant cells

### Mitochondrion

- ~2micrometers
- double membrane, cristae
- powerhouse of the cell
- turn chemicals into ATP
- uses oxygen to yield ATP
- circular mDNA

- reproduce by fission
- possess ribosomes (bacterial type)

### Chloroplast

- ~5 micrometers
- double membrane and thylakoids
- converts light to chemical energy
- circular cpDNA
- reproduce by fission
- possess ribosomes (bacterial type)

### Endosymbiont Theory

- theory that mitochondria and chloroplast are descendants of prokaryotes
- states that the prokaryotic ancestors( aerobic bacteria, photosynthetic bacteria) of modern mitochondria and chloroplast were engulfed by larger prokaryotic cells forming a mutually advantageous relationship called a symbiosis
- seemed to occur as a result of an increase in oxygen
- mitochondria are from the incorporation of aerobic prokaryote
- chloroplast from incorporation of cyanobacteria
- eukaryotic cells with chloroplasts found in plants and some protists
- eukaryotic cells lacking chloroplasts found in animals, fungi and some protists
- evidence: size, circular DNA, ribosomes, fission
  - ex. -Symbiont animals containing green photobionts
  - kleptoplasty (solar-powered sea slugs)
    - when they feed, the chloroplasts they ingest are not later excreted but rather stay in the body, allowing the slugs to produce their own food through photosynthesis

### Proof of the Endosymbiont Theory

1. Morphology/shape
  - similar shape as prokaryotic
2. Reproduction
  - derived from pre-existing mitochondria and chloroplasts
  - divide by binary fission (just like prokaryotic cells)
3. Genetic Information
  - contain their own DNA
4. Transcription and translation
  - mitochondria and chloroplast contain complete transcription and translational machinery
5. Electron transport
  - mitochondria and chloroplast generate energy (ATP) through their own electron transport chains

### Non-membrane Bound Organelles (Eukaryotes)

1. Cytoskeleton
  - support, shape, internal organization, cell movement, and movement within cell
  - ex. Microfilaments, microtubules, intermediate filaments
2. Ribosomes
  - protein synthesis

### Prokaryotes

- simplest organisms known; example are stromatolites
- single cell/unicellular
- found in 2 domains: the bacteria and Archaea (extremophiles)
- lack a nucleus
- DNA is localized in a central region of the cell-the nucleoid
- 10x smaller than eukaryotes
- less internal membrane organization compared to eukaryotes
- synthesize almost all their needed organic molecules from simple inorganic raw materials
- the prokaryotes, cyanobacteria, were first found to use oxygenic photosynthesis- which uses water to produce O<sub>2</sub>

# Cell Chemistry

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## The Chemistry of Life

- Cell chemistry= Carbon chemistry
- Carbon is essential in all important molecules of the cell
- Valence=4
- forms stable bonds
- bond energy= 70-100 kcal/mol (single covalent bond)
- visible light (400-700nm) = 40-70 kcal/mol photons
- the danger of UV light- has energy strong enough to break carbon bonds
- molecules can be linear, branched or cyclic C chains

## Common Functional Groups

- common presence of O,N,P, and S
- def. the reactive groups in atoms that occur in positions in which their covalent bonds are more readily broken or rearranged

Chemical formula	Name	Properties
-OH	Hydroxyl group	Neutral, polar
-C=O	Carbonyl group	Neutral, polar
-SH	Sulphydryl group	Neutral, polar
-COOH	Carboxyl group	-ve charge at cellular pH
-PO <sub>3</sub> <sup>2-</sup>	Phosphate group	-ve charge at cellular pH
-NH <sub>2</sub>	Amino group	+ve charge at cellular pH

## Cell chemistry

- is water based
- 75-85% H<sub>2</sub>O by weight
- polar and formation of H bonds
- properties as solvent
  - hydrophilic
    - polar molecules
    - ions
  - hydrophobic interactions
    - non polar molecules
    - molecules are excluded from hydrogen bonding

Inorganic precursors-> Small organic molecule->Macromolecule->Supramolecular structures-> Organelles/structures-> Cell

Ex. Co<sub>2</sub> and H<sub>2</sub>O (photosynthesis)-> glucose-> cellulose-> Cellulose microfibrils-> cell wall -> cell

Dehydration reaction: components of water are removed as subunits join to form a larger molecule

Hydrolysis: the components of water are added as molecules split into smaller subunits

## Intro to Macromolecules

### Major Classes of Organic Molecules

- 1.carbohydrates
- 2.Lipids
- 3.Proteins

## 4. Nucleic Acids

### Carbohydrates

- polymers of monosaccharides/simple sugars (polysaccharides) linked by glycosidic bonds between C1 and C4
- most abundant biological molecules
- form cellulose (of plant cell wall)
  - Function:
    - energy storage
    - structural molecules
    - ex. Starch, glycogen, cellulose, chitin
- Monosaccharides/ Simple sugars
  - $C_nH_{2n}O_n$ 
    - $n=3$  to  $7$
    - Trioses, pentoses and hexoses most common
  - linear vs. ring (5 or more C)
    - ring structure tends to be more stable
  - isomers
    - enantiomers (or optical isomers)- isomers that are mirror images of each other
    - structural isomers- molecules with the same chemical formula but with atoms arranged differently
    - D-glucose most commonly used by the cell
      - alpha D glucose(-OH below the ring) and beta D glucose(-OH above the ring)
      - starches of a-glucose are digestible while cellulose (of b-glucose) is not digestible
      - ex. Glyceraldehyde (D- and L- form)
  - soluble in water and have a sweet taste
- Polysaccharides
  - glycosidic bond
  - C1 to C4
  - as a result of dehydration synthesis reactions that join monomers (monosaccharides) together to form a polymer (polysaccharides)
  - cellulose: beta glucose linked together
  - alpha vs. beta
  - may be linear-branched or unbranched
  - ex. Starches, glycogen and cellulose

Polymer: string of units

Polysaccharide: string of sugar units; example of a polymer

Glycogen and starch

Hexose

Double bond in the linear structure; In the ring structure, there are different structures possible

Cellulose; No we cannot digest it

### Nucleic Acids

- Polymers of nucleotides
  - informational- the order of the proteins matter
  - DNA vs. RNA (has several different functions)
- Nucleotides
  - 5 C sugar

- ribose (RNA) or deoxyribose (DNA)
- nitrogenous base
  - purine: adenine, guanine - double C rings
  - pyrimidine: cytosine, thymine (only DNA), uracil (only RNA) - single C ring
- up to 3 phosphate groups
- sugar + base = nucleoside (if it is missing the phosphate group)
- functions: transfer of energy from one process to another; building blocks of nucleic acid
- Adenosine triphosphate (ATP)- provide energy
- the arrangement of alternating sugar and phosphate groups form the backbone of a nucleic acid
- Phosphodiester bond: the linkage of a single bridging phosphate group between the 5' carbons of one sugar to the 3' carbon of the next sugar in line
- RNA-> single stranded
  - RNA nucleotide= ribose, phosphate and one of the four bases A,U,G or C
  - involved in turning DNA material into proteins
- DNA-> double stranded
  - genetic material
  - nucleic acid sequence is listed from the 5' end to the 3' end
  - DNA nucleotide= deoxyribose, phosphate group, and one of the four bases A,T, G, or C
  - double helix molecule or double stranded molecule
    - as proposed by James Watson and Francis Crick
  - A-T form two stable hydrogen bonds
  - G-C form three stable hydrogen bonds
  
- dGTP- deoxyguanosine triphosphate
  - deoxyribose (sugar)
  - guanine (base)
  - three phosphate groups
- GTP
  - ribose
  - guanine
  - three phosphate groups

## **Proteins**

- Polymers of amino acids
- Informational (the types of amino acids present and the sequences in which they exist matter and changes will result in a different protein molecule)
- Proteins are constructed from the L glucose
- Functions:
  - Enzymes: accelerate the rate of cellular reactions (carbonic anhydrase)
  - Structural: supporting framework of cells (keratin, collagen)
  - Motility: impart movement to cells and cellular structure (actin)
  - Transport: transport substances across biological membranes (Na-K ATPase)
  - Regulatory: regulate the activity of other proteins and DNA (transcription factors, hormones)
  - Receptors: serve as recognition and receptor molecules at cell surfaces (beta adrenoreceptors)
  - Defensive (antibodies)
- Amino Acids
  - About 20 used to build proteins

- Structure;
  - Central carbon attached to:
    - Carboxyl group\amino group
    - H atom
    - Side chain/group (R group- determine the chemical characteristic of the amino acid- 1to 19 different types)
- R group
  - Hydrocarbon groups or rings are hydrophobic, non polar
  - Properties of amino acid determined by R group
    - Non polar
    - Polar, uncharged
    - Polar, acidic (-ve charge)
    - Polar, basic (+ve charge)
    - Reactive functional groups
      - ◆ Be able to tell which of the above a protein is by looking at its R group
    - Cystine- has a reactive sulhydryl group-> forms a disulphide bridges-> strong proteins that resist denaturing

### Peptide

### Polypeptide

- Peptide: Chain or polymer of amino acids
  - Polypeptide: greater than 50 amino acids in length
  - form a peptide (covalent) bond between adjacent amino acids (carboxyl group of one amino acid and the amino group of another)
    - Bond is formed by a dehydration synthesis reaction between the N and C terminus
  - N terminus (has a complete amino group- NH<sub>2</sub>) vs. C terminus (complete carboxyl group-COOH)
    - By convention, list amino residues from the N to the C terminus
  - In cells, amino acids are added only to the -COOH end
  - avg 200-500 amino acid residues (amino acids are called residues when linked in a peptide chain)
  - From polypeptide to protein
- Proteins
- One or more polypeptides folded into native conformation
  - Monomeric-Single polypeptide chain
  - Multimeric- Many polypeptide chain (ex. Hemoglobin)
    - Heteromeric- different polypeptide chains , ex. Hb- beta chains & alpha chains
    - Homomeric- all the same polypeptide chains)
- Conformation
    - Three dimensional structure determined by its amino acid sequence
    - Must occur in order for a polypeptide chain to become a protein and functional
    - Conformation is dependent on covalent and non-covalent interactions in backbone and/or R groups
  - Polypeptide and Protein
  - Have the same chemical composition
    - String of amino acids
    - Only a protein when it has folded into its conformation

Motif- area of secondary structure

Domain- area of tertiary structure

Usually associated with conserved function; can predict what it is doing in the structure

- Monomeric proteins do not exhibit quaternary structure

### **Protein structure**

-Proteins potentially have four levels of structure, each imparting different characteristics and degrees of complexity to the molecule

#### **Primary structure**

- Is the linear sequence of amino acid
- $20^n$  possibilities, where  $n = \#$  amino acids
- Changing a single aa in the primary structure alters the following types of structures and can alter or even destroy the biological function of that protein

#### **Secondary structure**

- Repeatedly coil or fold into patterns that contribute to the overall shape of a protein
- Due to Hydrogen bonding in backbone
- Alpha helix (cylinder) vs. beta pleated sheet (arrows)
  - Beta pleated sheet- Same hydrogen bonds form but they form across two backbones, giving the maximum amount of hydrogen bonding; stable
  - Alpha helix- Maximum amount of hydrogen bonds along the backbone; stable
- Motifs
  - Conserved function
  - Recognizable secondary structures
  - ex. Hairpin loop, helix-turn-helix

#### **Tertiary Structure**

- Results in the overall shape or conformation of the protein as a whole
- Due to Interactions between R groups
  - disulphide
  - These bonding interactions may be Hydrogen bonds, ionic bonds, hydrophobic interactions, disulphide bridges, & van der Waals interactions (electrons always in motion)
- The specific bonding arrangements between the R groups give rise to the protein's distinctive final 3D shape or conformation, which displays limited shape changes
- Extreme conditions can unfold a protein from its conformation, causing denaturation (loss of structure and function of the protein)
- Relative contributions of 2° and 3°
  - Fibrous vs. globular (tertiary structures most important) proteins
- Domains (contain motifs)
  - Regions of a single polypeptide chain that fold independently of each other
  - Ex. Domain containing zinc-finger motifs
- A denatured protein loses its tertiary (3°) structure and hence its function but may retain its primary (1°) structure

#### **Quaternary Structure**

- Comprises of 4 individual folded polypeptides
  - Bonds involved in holding multiple polypeptide chain together include

hydrogen bonds, polar and unpolar attractions, disulphide linkages and the others mentioned for the tertiary structure

- Describes how multiple polypeptide chains interact or link together to form a functional protein
  - Ex. Hemoglobin exhibits this structure
  - Interactions of subunits to form multimeric protein
  - Multi-protein complexes
- Prosthetic Groups
- Many proteins require a non-protein components, prosthetic groups, in order to function (and not just properly folded peptides)
  - Ex. Chlorophyll is a prosthetic group of many proteins of the photosynthetic apparatus

### **Lipids**

- Water insoluble, primarily nonpolar biological molecules composed mostly of hydrogen and carbon (hydrocarbons)
- Are not considered polymers of defined monomeric subunits
- Due to their nonpolar character, lipids dissolve much more readily in nonpolar solvents, such as acetone and chloroform rather than in water (polar)
- Due to insolubility in water they are able to form cell membranes
- Are stored and used in cells as an energy source
- 6 main classes
  - Considering only fatty acids, phospholipids, steroids, triglycerides
- Functions: energy storage, membrane structure, signalling
- Serve as hormones that regulate cellular activities
- Can be grouped as either- fats, phospholipids, or steroids

### **Isoprenes and Fatty Acids**

- Structural backbone of all lipids is derived from one of two hydrocarbon molecules: isoprene or fatty acids
- Isoprenes
  - Five-carbon molecules that when linked together can form long hydrocarbon chains
  - Structural unit in steroids and a number of phospholipids
- Fatty Acids
  - Consists of single hydrocarbon chain with a carboxyl group (-COOH) linked at one end
    - The carboxyl group gives the fatty acid its acidic properties
    - As chain length increases, fatty acids become less soluble and more solid
    - If hydrocarbon chain of a FA has the maximum number of hydrogen atoms= FA is saturated with hydrogen atoms (linear)
    - If one or more double bonds exist, FA is unsaturated (has a kink)
      - 1 double bond= monounsaturated (MUFAs)
      - More than one double bond= polyunsaturated (PUFAs)
    - 14-22 carbon fatty acids are very common

### **Fats/ Triglycerides**

- Consist of three fatty acid chains linked to a single molecule of glycerol by a ester bonds
- Fats are also referred to as triacylglycerols or triglycerides
- Triglycerides become less fluid as the length of their fatty acid chains increases

- Used widely as stored energy/ energy storage (adipocytes)
- Yield more than twice as much energy as carbohydrates; excellent source of energy
- Insulating
- In birds, can serve as a water repellent for their feathers
- Fat vs. Oil
  - o Fat- Are saturated (do not have double bonds) and linear= more viscous
  - o Oil- Are unsaturated (have double bonds)= kink in the molecule= less viscous/ oil like consistency

### Phospholipids

- Phosphate-containing lipids
- Primary lipid of cell membranes/ structural component of membranes
- Glycerol forms the backbone
  - o Only two of its binding sites are linked to fatty acids
  - o Other site is linked to a polar phosphate group, which binds to another polar unit
- Structure: 2 hydrophobic fatty acids at one end attached to hydrophilic polar group called the head group
- Molecules containing both hydrophobic and hydrophilic regions are called **amphipathic**
- Phosphoglycerides
  - o Glycerol
  - o 2 fatty acids (16-18C)
    - Most phospholipids have one saturated and one unsaturated fatty acid (involved with achieving the right degree of fluidity)
  - o Phosphate
  - o Hydrophilic R group= serine, ethanolamine, choline, inositol

### Steroids

- Structure: 4 ringed hydrocarbon skeleton/ 4 carbon rings
- Only in eukaryotic cells
- Are still amphipathic (hydroxyl group is hydrophilic, other parts of structure are hydrophobic) but on a lesser degree
- Group of lipids with structures based on a framework of four carbon rings that are derived from isoprene units
- Sterols, the most abundant steroids- have a hydrocarbon chain and a hydroxyl group attached to the 4 ring carbon structure
  - o Ex. Cholesterol (plasma membrane of animal cells) and phytosterols (plant cell membranes)
  - o Ergosterols (bacteria)
  - o You wouldn't expect to find sterols in the inner membrane of a mitochondria or chloroplast- they arise from prokaryotes which lack sterols
- Steroids Aldosterone, cortisol
- Steroids play a structural and signalling role

Be able to draw macromolecule structures

phosphatidyl- choline

Phosphatidylethanolamine

# Cell Plasma Membrane and Transport

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## Plasma Membrane

- Selectively permeable barrier
- Allows the uptake of key nutrients
- Elimination of waste products while maintaining a protected environment where metabolic processes can occur

## Fluid Mosaic Model

- Proposed by Singer and Nicholson (1972)
- Proposes that membranes are not rigid with molecules locked into place but rather consist of fluid lipid molecules in which proteins are embedded and float freely
- Lipid molecules exist in a double layer, called a bilayer, that is less than 10nm thick
- Lipid-protein assembly in which components are held together in a thin sheet by non-covalent bonds
  - o Two fluid lipid layers- structural backbone., permeability barrier
  - o Mosaic of proteins- unique complement responsible for specific functions (ex. Transport)
- The membrane is highly dynamic (lipids exchange places within one layer constantly)
- Contains a wide assortment of different types of proteins, each with a specific function
- Proteins are larger than lipids, and thus move slower in the membrane
- Proteins and other membrane components in one layer/half of the lipid bilayer, differ from those that make up the other half
  - o Referred to as **membrane asymmetry** and it reflects the differences in the functions performed by each side of the membrane
  - o Established during membrane biogenesis
  - o Flipflops vs. rotation and lateral diffusion
    - Hydrophilic head of phospholipid
- Functions:
  - o Define boundaries; selectively permeable barrier
    - Allow lipid-soluble molecules to pass easily; water soluble molecules do not pass through easily
  - o Localisation and organization
    - Scaffold for biochemical activities (enzymes)
    - Ex. mitochondria
  - o Regulation of solute transport
    - Across the cell membrane and/or organelles
    - Uphill or downhill
    - Ex. Na-K ATPase
  - o Responses to external signals
    - Receptors and signal transduction
    - Ex. B adrenoreceptor
  - o Cell to cell communication
    - Recognition, adhesion, exchange of materials through gap junctions (animal cells) or plasmodesmata (plant cells)
- Experiments to prove membrane fluidity
  - o FRAP- Fluorescence Recovery After Photobleaching
    - Cell membrane proteins labelled with fluorescent dye
    - Part of membrane is bleached using a laser
    - Recovery of the bleached spot occurs by the movement of other fluorescent labelled proteins
    - Protein's diffusion rate can be calculated
- Typical cell membrane
  - o 50/50% protein and lipids
- Inner mitochondrial membrane
  - o 76% protein
  - o 24% lipid
- Plasma membrane of Schwann Cells (Myelin sheath)
  - o 18% proteins
  - o 82% lipids

## Phospholipids

- Dominant lipids found in membranes
- Consists of two fatty acids 'tails' linked to one of several types of alcohols or amino acids by a phosphate group
- Are amphiphatic- contain a region that is hydrophobic, nonpolar (fatty acids chains) and a region that is hydrophilic, polar (charged phosphate-containing head group)
  - o Hydrophobic interactions (non covalent interaction) is critically important in determining the membrane structure
- When added to an aqueous solution, phospholipids aggregate with each other and assemble into a bilayer
  - o As a result of the tendency of hydrophobic fatty acids to aggregate together while the polar head groups associate with water

## Membrane Fluidity

- Fluid nature of membrane essential for function
- Dependent on how densely the individual lipid molecules are pack together
- Two factors: composition of lipids that make up the membrane and temperature
  - o Saturated hydrocarbons=straight=more tightly pack=less fluidity; opposite is true for unsaturated hydrocarbons
  - o Low temperature=more tightly packed=more viscous membrane; opposite is true for high temperatures
    - C chain length (shorter=more fluid) and saturation (unsaturated=more fluid)
    - Head group polarity (more polar=more fluid)
    - Buffering effect of sterols
- Mixture of saturated and unsaturated hydrocarbons is ideal to achieve normal fluidity
- Sterols, beside lipids, also increase membrane fluidity
- Homeoviscous adaptation: alterations in lipid composition to maintain membrane fluidity at different environmental temperatures

## Unit membrane

- Gorter and Grendel, 1925
- Lipid bilayer
  - o Key component of permeability barrier
- Composition
  - o Phosphoglycerides (main component)
    - Serine, choline, ethanolamine, inositol
    - 16-18 C
    - Saturated and unsaturated
  - o Glycolipids
    - Single sugars or oliogosachhatides
    - Marker (e.g. ABO blood groups)
  - o Sterols
    - Cholesterol, phytosterols
    - Cholesterol: increases fluidity at low temperatures, but lower fluidity at higher temperature
    - Absent from prokaryotes
    - Hydrophilic hydroxyl group end located at the surface of the membrane
    - Hydrophobic tail and end located within the membrane
  - o Variable
    - C:P ratio cholesterol: phophglyceride ratios
    - This ratio is high in Sharks
    - As a method of retaining urea
      - They have a high content of urea; live in an area where there is relatively no urea

## Desaturases

- a group of enzymes, that produce unsaturated fatty acids during fatty acids synthesis.
- This increases fluidity in the organism that has this enzyme
- All fatty acids are initially saturated (straight).
- Desaturases creates a double bond, to form an unsaturated hydrocarbon (kink)
- Changes in the desaturase gene, increases its production, when temperatures lowered (occurring in organisms with the desaturase gene)

## Semi-palmated Sandpiper

- Have a 2 week stopover at the Bay of Fundy to feed on mudshrimp (enough to double their weight)

- PUFA-rich diet (mudshrimp) results in increased PUFA in membranes
  - o Which in turn increases fluidity
- They use fatty acids to facilitate endurance flight exercises

### **Lipid Raft**

- Areas of low fluidity floating in areas of higher fluidity
- Have saturated fatty acid chains, long chains
- Allow proteins to be clustered together to allow for cell signalling mechanisms

A protist moves from warm to cold water. What can be done to maintain its membrane fluidity?

- Shorter chains
- Decrease ratio of p-choline to p-amine

### **Membrane Proteins**

- Mosaic component of the fluid mosaic model
- Functions: transport, enzymes, signal transduction, attachment/recognition
- 3 types: integral, peripheral, lipid-anchored

### **Integral Membrane Proteins**

- Amphiphatic with one or more hydrophobic regions
- Usually transmembrane (single or multipass)
- Transmembrane regions typically  $\alpha$ -helix of 20-30 hydrophobic aa residues
- Have to break open the membrane in order to fully study this protein

### **Peripheral Membrane Proteins**

- Membrane associated through non-covalent interactions
- Dynamic relationship with membrane
- Can attach and detach from the membrane
- Makes links with plasma membrane and the cytoskeleton (ex. Adherin)

### **Lipid-anchored Membrane Proteins**

- Membrane associated through covalent linkages to phospholipids
  - o Fatty acid anchored
    - Intracellular orientation
  - o GPI anchor
    - Extracellular orientation
    - Can be cleaved (detached from anchor) with phospholipase C
    - Ex. Type IV carbonic anhydrase

### **Cell Transport**

- Hydrophobic Membranes- can pass through
- Small, uncharged polar molecules - can pass through
- Large, uncharged polar molecules
- Ions
- Charged ions are unable to pass freely through the membrane (attract water molecules around them)

### **Passive Transport**

#### **Diffusion**

- Spontaneous; based on random movement
- Driven by diffusion gradient (downhill)
  - o For solutes without a charge-> concentration gradient
  - o For gases-> partial pressure gradient
  - o For ions-> electrochemical gradient
  - o For water-> osmotic gradient-> from low solute concentration to high solute concentration

Hypotonic (low solute concentration) solution-> cell expand solution is hypotonic; cell is hypertonic

Hypertonic (solution-> cells shrink solution is hypertonic; cell is hypotonic)

Isotonic solution-> cell remains the same

## Membrane Permeability

- Lipophilic molecules
  - o Partition coefficient-> ratio of solubility in organic solvent to that in water

## Facilitated Diffusion

### Channel Proteins

- o Ions, water (aquaporins)
- o Hydrophilic channel that allow ions and water to transfer along their gradients
- Highly selective
- Leak vs. Gated (ex. Voltage-gated: membrane potential (neuron), ligand-gated : have a binding site that opens and closes the channel (muscles))

### Carrier Proteins

- Change conformation when bonded by a solute and in so doing moves the solute across the membrane according to its gradient
- Ions, larger and/or polar molecules
- Can be inhibited by some drugs (that block channels; inhibit conformational changes)
- Rate of transport depends not only on concentration gradient but also the amount of proteins present to allow the transfer; saturation kinetics
  - o Transferring will continue till all the carrier proteins are used
- Highly selective
- Types
  - o Uniporter (urea transporter) - move one solute in one direction
  - o Symporter (Co-transporter)- move two solutes in the same direction
  - o Antiporter (exchanger)- move two solutes in opposite direction
- Urea movement in the Gulf toadfish
  - o Saturated kinetics involved
  - o Active is unidirectional; urea blood level decreases when excreted
  - o Facilitated- bidirectional; urea blood level increases during excretion when urea is present in the water of the fish

## Active Transport

- Carrier-mediated movement against gradient (uphill) via coupled input of energy ("pumps")
- Highly selective
- Unidirectional

### A. Primary Active Transport

- ATP hydrolysis directly coupled to transport of solute
- Several types
  - o P type
    - Move cations (Na, K, Ca, H)
    - Reversibly phosphorylated
    - Ex. Na, K-ATPase
  - o V-type
    - Move H<sup>+</sup> into organelles
    - Vacuole pumps

### B. Secondary Active Transport

- Use carriers
  - Variation of the primary active transport
  - Uses ATP
  - Simultaneous transport of two solutes
  - Downhill transport along gradient established by primary active transport allows uphill transport of second solute
    - Na<sub>+</sub> gradient in animal cells
    - H<sup>+</sup> gradient in plant cells
  - Transport in the mammalian kidney
    - Filtration maximum for glucose and diabetes mellitus

- Structural specialization- mitochondria & microvilli
- Symporter system/Co-transporter: Na is moved into the cell with its gradient established by the Na/K pump; at the same time, glucose is carried into the cell against its gradient
- Saturation kinetics is important

An experiment to distinguish between facilitated diffusion and secondary active transport

1. Deprive the cell of ATP (inhibit mitochondria with drugs)-> primary and secondary active transport will stop working. Facilitated diffusion would continue because it doesn't rely on ATP
2. Check direction of movement of solutes. F. driven by gradients. Reverse the gradient, it stops working. S.A.T. reverse the gradient, transport still happens

***MIDTERM STARTS AT 11:15AM - (2nd midterm= feb 16)***

POP QUIZ

Peripheral membrane protein-held to the membrane by non covalent interactions- easy to knock off  
 GPI-anchored- covalent linkage- need an enzyme to knock it off

Integral membrane protein- buried in the membrane;  
 Channel protein-type of integral membrane; has a hydrophilic core

Non charge particle- moves according to its concentration gradient  
 Water- moves according to its osmotic gradient

Hypertonic solution- shrink  
 Hypotonic- expand

# The Cytoskeleton

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## **Cytoskeleton**

- extremely dynamic; changes in accordance with what the cell needs
- Functions include:
  - The provision of structure and support
  - Intracellular transport - molecules can move within the cell
  - The positioning of organelles within the cell
  - The generation of force for cell movement (ex. movement of microfilaments in the case of muscle cells)
  - Contributing to cell division
- Prokaryotes do not have a cytoskeleton as we know it

## **Intermediate Filaments**

### *Structure:*

- Strong, rope-like fibres of 10-12nm in diameter
- Family of fibrous proteins
  - Ex. Keratin, neurofilament proteins, nuclear lamins
  - Tissue specific
  - $\alpha$ -helix (strong secondary structures) domain flanked by variable globular domains
- Coiled-coil dimer: building block of an intermediate filament
- Protofilament- tetramer: formed by dimers
- Filament: formed by 8 protofilaments; when twisted form the intermediate filaments

### *Dynamic Character*

- Relatively stable, but do turn over
  - Ex. Nuclear lamins

### *Functions:*

- Mechanical strength in animal cells
- Ex. Keratin Ifs
  - Link to desmosomes and hemidesmosomes
  - Epidermolysis bullosa simplex: as a result of defective IFs
- Only nuclear lamins in other eukaryotes

## **Microfilaments**

### *Structure:*

- Flexible, helical fibres of ~7nm diameter
- G-actin
  - Central cavity binds ATP or ADP
- F-actin
  - Polymer of G-actin monomers
  - Helix
  - Filament has polarity
- Non-covalent interactions hold the monomers together
- Grow at the + end (G-actins added at this end) and shrink at the - end (ATP is hydrolyzed into ADP causing the G-actin to break off)
  - Can rapidly grow or rapidly disappear
- Dynamic character
- ATP-G-actin polymerizes more readily than ADP-G-actin

Hydrolysis follows polymerization

- ADP-G-actin dissociates more readily than
- ATP-G-actin
- Actin-binding proteins regulate the rate and form of polymerization and network formation
  - o Cell signalling mechanisms regulate actin-binding proteins

### Functions:

- Shape/support and motility (of cell and within cell)
  - o All eukaryotic cells
- Shape/support
- Cell cortex
  - o networks
- Micro-villi
  - o bundles
- Adherens junctions

### Motility

- Motor proteins = ATP-dependent “motors”
- Myosins
  - o Heavy chain = globular head + tail
  - o Move towards + end
- Motility based on muscle contraction
  - o Thin filaments - microfilaments
  - o Thick filaments - myosin II
  - o Sarcomere
- Motility based on muscle contraction cont'd
  - o Sliding filament model
  - o Cross-bridge cycle
  - o Regulated by Ca<sup>2+</sup>
- Contractile assemblies also occur in non-muscle cells
  - o Sliding filaments
  - o myosin II
  - o e.g. cytokinesis
- Cell crawling – motility by polymerization
  - o Amoeboid motion (pseudopodia)
  - o Cell migration and invasion (lamellipodia, filapodia)
  - o phagocytosis
- Motility within the cell
  - o “unconventional” myosin, e.g. myosin I

Motif- an area of secondary structure within a domain (cafeteria in the university)

Domain- an area that fold independently of each other (university)

### Pop Quiz

Cross bridge cycle

Allows muscles to contract

Needs calcium

## Types of Actin Binding proteins

### Capping proteins

Microtubules- straw like, hollow

Microfilaments-Two strands of actin forming a helix

- Both have polarity- Building blocks formed in the same direction

### Pop Quiz

#### Axonemal dynein

- Used within a cilium or flagellum
- Moves microtubules across each other
- Significant? Causes the flagellum or cilium to move

#### Plant Cell Primary Wall

- For protection & rigidity, regulates permeability, involved in linking cells together, support
- Made of cellulose embedded in the hydrated matrix ( made of hemi cellulose and pectin-hold together cell walls)
- Cellulose fibres are loose which allows the cell to continue to grow

Test that cellulose microfibril orientation relies on movement of enzyme rosettes along microtubules

- Destroy the microtubules
  - o Observe whether the enzymes move or not
  - o Calchocine (drug): Prevents tubulin from adding to microtubulins (depolymerization)

#### Plasmodesmata

- Lined with plasma membrane
- Desmotubules (smooth ER)
- Route for ions, small molecules; growth factors, hormones, rNa may pass too
- Created at the time the cell wall is formed
- Adjacent cells are in communication due to the plasmodesmata (cytoplasmic connection)

### **Animal Cells: Cell-Cell Connections**

A variety of types

- Adhesive (anchoring) junctions: adherens junction, desmosome
- Tight junctions (hold cells together; sealing junction)
- Gap junctions (cytoplasmic connection between the cells)

Adhesive (anchoring) junctions

#### **Adherens junctions**

- Connect to MFs
- Small areas or continuous zones of attachment in epithelia
- Tie cadherins to MF

#### **Desmosomes**

- Connect to Intermediate filaments
- Protein plaque for strong adhesion (skin, cardiac muscle, cervix of uterus)
- Plaque holds cadherins to Ifs

## Cadherins

- Transmembrane glycoprotein
- Repeats in extracellular domain "zip" together
- Cell-cell separation

## Intracellular linking proteins

### **Tight Junctions**

- Seals cell together
- Permeability barrier in epithelia
  - o Ex. Intestine, bladder, skin, gill
- Barrier to lateral diffusion in plasma membrane
  - o Polarized cell; polarizes the cell- keeping one side different and separate the other side
- Structure
  - o Ridges formed of junctional proteins-> claudins, occludin
    - The more ridges, the more tighter the junction
    - Ridges of proteins on one membrane connect with the protein ridges of an adjacent cells

### **Gap Junctions**

- Cytoplasmic contact - cytoplasmic pool extending between two cells
  - o Electrical and chemical communication
- Muscle and nerve tissue
  - o Ex. Coordination of heart beat (cells of the heart are connected by gap junctions to allow them to contract as a unit)
- Structure
  - o Cell-cell separation 3nm
  - o Connexin- integral membrane protein
  - o 6 form linking structure

### **Extracellular Matrix (ECM) of Animal Cells**

- Organized network of ..

### **Structure Involves 3 Classes of Molecules**

- Structural proteins- collagens (provide strength- are crosslinked), elastins (provide elasticity, resiliency- held together by covalent bonds)
- Matrix- proteoglycans- they carry a negative charge (proteins-polysaccharide complexes)
- Adhesive glycoproteins - ex. Fibronectin (dimers made of several fibrin binding domains; links the ECF together)

## Integrins

- Heterodimer (alpha and beta chains)
- Integrate ECM with cytoskeleton
  - Extracellular binding site for adhesive glycoproteins
  - Intracellular binding sites for linking proteins
- Focal adhesions and hemidesmosomes

### **Recall**

#### *Extracellular structure*

- ECM- animal

- Cell wall- plant

*Structural fibre*

- Collagen and elastin- animal
- Cellulose- plant

*Matrix*

- Proteoglycans- animals
- Hemicellulose and pectin - plants

*Adhesive molecules*

- Pectins- plants
- Fibronectins- animals

# Cell-to-Cell Signalling

February-09-11

2:11 PM

## Types of Cell Communication

- Gap junctions and plasmodesmata
- Contact
- Chemical messengers

## The Elements of A Signalling System

- Signalling molecule (first/primary messenger)
- Reception
  - o Receptor- membrane, cytosolic or nuclear
- Transduction
  - o Signalling cascades and second messengers
- Response
  - o Changes in gene expression
  - o Changes in activities of enzymes, transcription factors or other regulatory proteins, transporters, cytoskeleton, et
- Termination

## Membrane Receptor Signalling Systems

- Signals are water-soluble chemicals
  - o Signalling molecule does not enter cell
  - o Signal removal
  - o e.g. environmental chemicals, neurotransmitters, hormones
- Membrane receptors are integral membrane glycoproteins
  - o Ligand-gated channels
  - o Receptor tyrosine kinases
  - o G protein-coupled receptors

### Ligand-gated channels

- e.g. Skeletal muscle activation by acetylcholine

### Signalling cascades

- Role of phosphorylation: kinases vs phosphatases
- Amplification
- Termination
  - o Removal of ligand-receptor complex
  - o Inactivation of receptor
  - o Inactivation of signalling cascade

### Receptor tyrosine kinases

- Dimer formation
- Activation of cytoplasmic protein kinase domain
- Autophosphorylation (tyrosine residues)
- Phosphorylation of target proteins
- Typically regulate cell growth and proliferation

### G protein-coupled receptors

- Activate guanine nucleotide-binding proteins (G protein)
- G protein activates enzyme to produce 2nd messenger
- 2nd messenger activates protein kinases

G proteins are molecular switches

- GTP bound = on
- GDP bound = off

G proteins are heterotrimers

- G $\alpha$  binds GTP or GDP
- G $\beta$  and G $\gamma$  form a unit

G proteins are diverse

- Adenylyl cyclase activation (Fig. 8.10)
- Phospholipase C activation (Fig. 8.12)
- Adenylyl cyclase inhibition

Example – control of pigment dispersion in chromatophores

### **Lipid-soluble signals & intracellular receptors**

Signals enter cells by diffusion

- e.g. steroid hormones

Receptors are ligand-activated transcription factors

- Ligand-binding domain
- DNA-binding domain

Regulate gene expression

- Response elements

Example

- Testosterone and muscle