BIOL 130 Course Notes
Unit 1 – Introduction to the Cell

History

Robert Hooke
- First microscope, viewed slices of cork "cellula"

Antoni Van Leeuwenhoek
- 300x magnification
- Single-celled organisms "animalscules"

Theodor Schwann
- Cell Theory

Cell Theory
- All organisms consist of one or more cells
- The cell is the basic unit of structure for all organisms
- All cells arise only from pre-existing cells

Basic Properties of Cells
- Use the same genetic program - **Central Dogma** (DNA → RNA → protein)
- Engage in many mechanical activities (transport, assembly, motility)
- Respond to environmental signals (stimuli, hormones)
- Are capable of self-regulation – **Homeostasis**

Prokaryotes
- No real nucleus
- Eubacteria → all have cell wall except mycoplasma
- Archaebacteria → all have cell wall; best known are extremophiles
- Three shapes → spherical, rod-shaped, spiral

Eukaryote
- Protists → mostly single cells (algae, mold, protozoa)
- Fungi → single cell & multicellular; cells walls, heterotrophs (yeast, mushrooms)
- Plants → multicellular, cell walls
- Animals → multicellular, no cell walls, heterotrophs

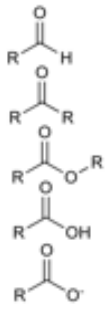
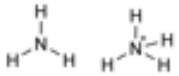
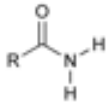
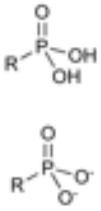
Endosymbiont Theory
- Certain organelles (mitochondria, chloroplasts) evolved from smaller prokaryotes engulfed by larger cell

Model Organisms
- Ea coli → DNA replication, gene transcription, translation
- Saccharomyces cerevisiae (yeast) → cell cycle; minimal model eukaryote
- Arabidopsis thaliana → all flowering plants are closely related
- Drosophila melanogaster → genetics, development
- Ca elegans (the worm) → first animal genome to be sequenced; location, lineage, and fate of every cell in embryo, larva and adult is known
- Mouse → model mammal; genetics well understood

Unit 2 – Cellular Chemistry & Macromolecules

Functional Groups

- Components of organic molecules typically involved in chemical reactions

Hydroxyl	OH		Alcohols
Carbonyl	C=O		Aldehyde
Amino	NH_3		Amine
			Amide
Sulfhydryl	SH		Thiol
Phosphates	PO_4		Organophosphates

Macromolecules

- Condensation Reaction → making the chain - **Anabolism**
- Hydrolysis → breaking the chain – **Catabolism**

Proteins

- Polymers made up of amino acids
- Used as enzymes, for transport, support, signalling/regulating, movement, and defense
- Amino acids are joined by an amide linkage, known as a peptide bond, making polypeptide chain
- Side chain extends from peptide-bonded backbone in polypeptide chain
- Backbone is directional – convention is to number amino acid residues starting as N terminus **(Primary Sequence)**

Structure

- Primary → Linear amino acid sequence
- Secondary → Folding into elements of structure

- Tertiary → Interaction of elements of secondary structure forming a global structure
- Quaternary → When two or more polypeptides join to form the final functional protein
- Protein Domain → Segment of polypeptide that forms a compact, stable, independently folding structure

Secondary Structure

- Made up of repeating alpha-helices and beta-pleated sheets (parallel & anti-parallel)

Tertiary Structure

- Polypeptides precisely twisted, folded, and coiled into a unique shape
- Primary sequence of amino acids determines the final shape
- Forces that determine protein shape include **ionic bonds** (electrostatic), **H-bonding**, **hydrophobic interactions**, and **disulfide bridges**

Hydrophobic Forces

- Hydrophobic core region in folded protein
- Polar side chains participate in hydrogen bonds on outside of protein

Disulfide Bonding

- Covalent stabilization of protein structure found in secreted proteins (destined from more hostile extracellular environment)
- Formed in the endoplasmic reticulum (oxidizing environment)

Denaturation

- Change in physical or chemical conditions (pH, salt concentration, temperature)
- Disruption of bonds maintaining protein's shape

Improper Protein Folding

- Any mutation that leads to a missing or incorrect amino acid can lead to incorrect folding
- Protein never functions properly/loss of function
- Protein folds properly at first but unfolds under certain conditions (eventually loss of function)
- Protein misfolds and is deposited in insoluble aggregates within cell (loss of function and disruption of other aspects of cell activity)
- Diseases related to misfolded proteins include cystic fibrosis, type II diabetes, Creutzfeldt-Jakob, Alzheimer's & Parkinson's
    - Protein misfolds, forms aggregates and is deposited in cells as **plaques** → leads to cell death and subsequent neurological dysfunction

Quaternary Structure

- Two or more polypeptide chains linked together
- All subunits are required for biological activity

Amino Acid Side Chains (R Groups)

- Nonpolar → hydrophobic R groups (inside of peptide chain as to avoid water)
- Polar → soluble in water; uncharged (partial charges can form H-bonds) or charged (containing acids or bases)

Nucleic Acids

- Deoxyribonucleic acid (DNA) → sequence of subunits in DNA polymer directs RNA synthesis
- Ribonucleic acid (RNA) → RNA directs ordering of amino acids in a peptide chain
- Information stored as DNA sequences enables living organism to pass on hereditary information, as well as cells themselves
- Linear (unbranched) polymers of nucleotides (containing nitrogenous base, pentose sugar, phosphate group)
- Backbone is composed of sugar and phosphate
- 5' end is beginning of nucleic acid, and is the start site for transcription/translation

Monomer Units

- DNA nucleotides → Phosphate + deoxyribose + base (A, G, C, or T)
- RNA nucleotides → Phosphate + ribose + base (A, G, C, or U)
- Bases are either **purines** (guanine, adenine) or **pyrimidines** (uracil, cytosine, thymine)
- Nucleotides act as **coenzymes** (organic non-protein required for enzyme function), as signal molecules within cells, and are important agents in energy transfer reactions (ATP → ADP + P_i + energy)
- Hydroxyl groups on ribose in DNA makes it much less stable than DNA (which is deoxyribose)

Polymerization Reactions

- Endergonic reaction as it requires energy
- Creation of new phosphodiester bonds from two nucleotides
- Polymerization of bases occurs because energy level of free nucleotides is first raised by addition of two phosphate groups
- Creation of **nucleoside triphosphates** (activated nucleotides)

Secondary Structure of DNA

- Antiparallel alignment of two DNA strands, with H-bonds between complimentary bases
- Entire molecule is water-soluble due to charged phosphate backbone facing outward
- Major & minor grooves are significant in regulation of gene transcription

Secondary Structure of RNA

- H-bonds form between complementary base pairs
- Pairing is usually done between bases on the same strand
- Leads to formation of **stem and loop** structures with single-stranded regions and double-stranded antiparallel regions
- H-bonding is spontaneous, which stabilizes the molecule
- Final molecule is single-stranded
- Complex fold can result in RNA have catalytic activity

Higher Order DNA Structure

- DNA molecules can adopt higher order structure
- Allows for compact packaging and strict regulation of gene expression

Types of RNA

- mRNA → code for protein

- rRNA → form core of the ribosome and catalyze protein synthesis
- miRNA → regulates gene expression
- tRNA → serve as adaptors between mRNA and amino acids during protein synthesis

Carbohydrates

- Monosaccharides → simple sugars
- Oligosaccharides → small chains; attached to proteins → **glycoproteins**; attached to lipids → **glycolipids**
- Polysaccharides → very long sugar chains
- Monosaccharides link together with C1 of one and C4 (occasionally C6) of the other
- Alpha-1,4 linkages → starch & glucose – readily **hydrolyzed**
- Beta-1,4 linkages → structural polysaccharides – very resistant to **enzymatic degradation**

Monosaccharides

- Carbonyl groups (either ketone or aldehyde) and lots of OH groups
- Often form rings in solution
- Hydroxyl group in ring form can be below (alpha glucose) or above (beta glucose) the plane of the molecule

Polysaccharides

- Starch → mixture of unbranched amylose (alpha-1,4) and branched amylopectin (alpha-1,4 and a-1,6)
- Glycogen → highly unbranched (alpha-1,4 and alpha-1,6)
- Cellulose → polymer of beta-glucose, joined by beta-1,4 linkages (each glucose is flipped)
- Chitin → joined by beta-1,4 linkages of N-acetylglucosamine; exoskeleton of anthropods
- Peptidoglycan → two different alternating monomers linked by beta-1,4 bonds; chain of amino acids attached to one of the sugars (structural polysaccharide in bacteria)

Function of Carbohydrates

- Structural → cellulose, chitin, peptidoglycan; part of nucleic acid monomer
- Cell-cell Recognition → all animal cells covered with **glycocalyx** consisting of membrane proteins covalently bonded to oligosaccharides
- Energy storage → alpha-1,4 linkages of starch and glycogen are readily hydrolyzed to release stored energy

Lipids

- Largely non-polar/hydrophobic
- Significant proportion of lipid is hydrocarbon
- Only macromolecule that is not a polymer
- Energy storage → fats/oils (contains 6x more Calories than other macromolecules)
- Signalling/membranes → sterols - cholesterol (membrane component), steroids (hormones)
- Membranes → phospholipids – major component of biological membranes

Fats (Triacylglycerols, Triglycerides)

- Glycerol backbone & three fatty acids (carboxylic acid with long hydrocarbon tail)
- **Unsaturated fatty acid (oleic acid)** → double-bonded carbon causes it to bend (plant)
    - Cis (oleic) or trans (elaidic)

- **Saturated fatty acid (stearic acid)** → no double bond causes it to be straight (animal)

Phospholipids

- Polar head group with hydrophobic fatty acid tails
- Phosphatidyl choline is model phospholipid

Lipid Bilayer

- Two closely apposed sheets of lipids (permeability), studded with proteins (functions)
- Carbohydrates attached to protein and lipids in a non-random manner
- All membrane lipids are amphipatic
- Form spontaneously and are self-sealing
- Phospholipids within membrane are constantly moving; spinning in place/travelling laterally within **leaflet**
- Occasionally flipped to the opposite leaflet during membrane synthesis but rarely flop back
- Cholesterol makes membrane less fluid

Unit 3 – Thermodynamics and Catalysis

First Law of Thermodynamics

- Energy can be transferred and transformed, it cannot be created or destroyed

Second Law of Thermodynamics

- Energy tends to spontaneously disperse, from being localized, ordered to becoming spread out, disordered; entropy → disorder

Chemical Reactions

- Exergonic → less ordered, products have lower E_p than reactants
- Endergonic → more ordered, products have higher E_p than reactants
- Gibb's Free Energy (G) → below 0 for exergonic, above 0 for endergonic

Coenzymes

- Chemically changed during the reaction; must be regenerated to complete catalytic cycle
- Organic molecules typically involved in shuttling of electrons and protons (many are vitamins)

Regulation of Enzyme Activity (Regulatory Molecules)

- Regulatory molecule has ability to bind to an enzyme and increases (activator) or decreases (inhibitor) enzyme reactivity
- **Allosteric** or **competitive** regulation

Covalent Modification

- Covalent modification of the enzyme by functional groups, rather than binding of molecules to the enzyme
- Most often phosphorylation at –OH containing side chains

Enzyme Inhibitors

- Competitive inhibition → competes with substrate to bind to active site; can be overcome by increasing substrate concentration
- Non-competitive → binds to allosteric site, changing the enzyme's conformation

Unit 4 – Energy

Substrate Level Phosphorylation

- Generates few ATP during glycolysis (initial breakdown/rearrangement of glucose)

Oxidative Phosphorylation (Aerobic Respiration)

- Electrons harvested from organic fuel molecules in redox reactions used to pump H^+ across membrane (proton pump)
- Protons are then allowed to cross back over (diffusing down their gradient) and run ATP synthase

Photophosphorylation

- Cyclic and non-cyclic phosphorylation

Electron Carriers

- Modified nucleotides
- Coenzymes that carry electrons from one reaction to another; readily accept a hydride atom and donate it
- NAD^+ → nicotinamide adenine dinucleotide (vitamin B3)
- FAD → flavin adenine dinucleotide (vitamin B2)
- $NADP^+$ → nicotinamide adenine dinucleotide phosphate

Cellular Respiration

Glycolysis

- Converts each molecule of glucose into 2 pyruvate molecules
- Results in the formation of activated carrier molecules **(ATP** & **NADH)**
- Pyruvate is transported from cytosol into mitochondrial matrix
    - Transformed into Acetyl-CoA and CO_2
    - Acetyl CoA can also be produced directly from the oxidation of fatty acids
- Two ATPs spent to make glucose more reactive
- Doubly phosphorylated sugar is split
- Each 3C sugar joins with a free phosphate, making sugar even more reactive
- In final steps, 2 phosphate groups on each sugar are transferred to ATP

Regulation of Glycolysis

- High levels of ATP inhibit the enzyme **phosphofructokinase**
    - Catalyzes fructose-6-PO_4 → fructose-1,6-bisPO_4
- Two binding sites → active site and regulatory (allosteric) site

Pyruvate Oxidation

- Decarboxylation Reaction → taking off a carbon
- Reducing (loading) NAD^+
- Activating 2-carbon acyl groups
    - Pyruvate + NAD^+ + CoA → Acetyl-CoA + NADH + CO_2
- Catalyzed by pyruvate dehydrogenase enzyme complex

Coenzyme A

- A nucleotide derivative, an organophosphate, a thiol, and coenzyme
- Thiol group reacts with carboxylic acids (carries acyl groups)

TCA (Krebs/Citric Acid) Cycle

- 2 Carbon acyl unit is fully oxidized
- Yields 2 molecules of CO_2, 1 GTP (ATP), and activated electron carriers 3 NADH, 1 $FADH_2$
- Molecule required to restart the cycle is regenerated
- Each molecule of glucose does two complete rounds

Other Fuel Molecules

- Proteins → digested to amino acids → deaminated → fed into TCA cycle
- Fats → fatty acids broken down into 2C units → acetyl-CoA (Beta-oxidation)

Regulation of Metabolic Pathways

- Feedback inhibition → when an enzyme in a pathway is inhibited by a product of that pathway

Energy Generation in Mitochondria

- Unleashing electrons in NADH and FADH (carrier molecules) allows mitochondria to generate most of the ATP for cellular function

Reduced Energy Carriers

- Loaded energy carriers (NADH, $FADH_2$) carry their electrons to the matrix side of the inner mitochondrial membrane
- They transfer electrons to a series of membrane-associated proteins that shuttle electrons in redox reactions (ETC)

Electron Transport Chain

- Series of molecules embedded in inner mitochondrial membrane
- NADH delivers electrons to top of chain, oxygen catches them at the bottom
- Oxygen is reduced with hydrogens to form water
- One O_2 is reduced to two molecules of water for every two electron carriers (4 electrons)

Chemiosmotic Theory

- Most ATP synthesis is due to electrochemical gradient across inner mitochondrial membranes, generated using energy from NADH, $FADH_2$, derived from breakdown of fuel molecule

Chemiosmosis

- Harnessing the electrochemical gradient of H^+ ions across a membrane to make ATP

Yield from Aerobic Respiration

- 30 ATP/glucose; 1a5 ATP/$FADH_2$; 2a5 ATP/NADH

Anaerobic Respiration

- No oxygen to accept final electron transfer in ETC
- Oxidative phosphorylation backs up, buildup of loaded energy carriers, TCA cycle shuts down
- Generates only 2 ATP/glucose

- Fermentation → pyruvate accepts electrons from NADH, converts NADH back to NAD^+, allowing glycolysis to continue
- Lactic acid or alcoholic fermentation

Unit 5 – Gene Expression

Transcription from a DNA Template

- Only one strand of DNA is transcribed (template strand); other strand (non-template/coding) matched RNA sequence but with U in place of T
- DNA is transcribed by RNA polymerase (**holeoenzyme** made up of a core enzyme with the ability to synthesize RNA and has a regulatory subunit – **sigma factor**)
- Sigma factor recognizes a **promoter** sequence
- Eukaryotes have three distinct types of RNApol (I, II, III)

Coding & Non-Coding Regions

- Entire gene (introns & exons) transcribed (primary transcript)
- After capping, while still being transcribed, RNA splicing (removal of introns) begins
- Spliceosomes → carry out splicing, consist of 5 small nucleau ribonucleoproteins (snRNPs)

Translation

- A site → the acceptor site for aminoacyl tRNA
- P site → where peptide bond forms
- E site → where tRNAs exit the ribosome
- Start codon (Met/AUG) is found by tRNA, large ribosomal subunit binds
- Aminoacyl-tRNA binds to A site, first peptide bond forms
- Presence of STOP codon in mRNA terminates translation
- Folding begins during translation, and it often helped with Molecular Chaperones

Post-Translational Modifications

- Glycosylation → addition of carbohydrate
- Lipoylation → addition of lipid groups
- Phosphorylation → addition of phosphate group
- Ubiquitination → addition of ubiquitin
- Methylation → addition of methyl group
- Acetylation → addition of acetyl group
- Proteolysis → cleavage of peptide bonds

Unit 6 – Biological Membranes

Regulation of Membrane Fluidity

- Fluid state must be maintained for normal cell function
- Maintaining fluidity can be done by changing composition of membranes – alter phospholipids, desaturate fatty acids, change length of fatty acid chains, adjust amounts of cholesterol
- Human red blood cells are model organisms for plasma membrane

Protein Interaction with Membranes

- Polypeptide chains usually cross as alpha-helices
- Hydrophilic channels can be formed from several alpha-helices
- Proteins folded into pleated sheets can form pores
- Membrane proteins move in the lipid bilayer
- Cells can restrict the movement of membrane proteins

Membrane Transport

- Lipid bilayers tend to block passage of polar molecules
- Substances can enter by passing through lipid bilayer, being transported across bilayer by membrane proteins acting as **carriers** or **channels**, or being engulfed by the cell
- Molecules diffuse across concentration gradient (osmosis in the case of water)

Osmotic Effects on Cells

- Animal Cell:
    - Hypotonic (excessive water) → Lysed
    - Isotonic (balanced water) → Normal
    - Hypertonic (lacking water) → Shriveled
- Plant Cell:
    - Hypotonic (excessive water) → Turgid (normal for plants)
    - Isotonic (balanced water) → Flaccid (not enough water)
    - Hypertonic (lacking water) → Plasmolyzed (really not enough water)

Maintaining Osmotic Balance

- Osmoconformers → marine organisms adjust their internal salt concentrations to math seawater
- Osmoregulators → pumping water out of cells (vacuoles)
- Turgor → most plants are hyper-osmotic, and pull water into the cell

Unit 7 – Intracellular Compartments and Protein Sorting

Importing Proteins into Organelles

- Transport through nuclear pore
- Transport across membrane
- Transport by vesicles
- Proteins to be imported have **nuclear localization sequence**
- Made on ribosomes in the cytosol, displays an addressing tag, which is then recognized and brought to next step by nuclear transport receptor (escort)
- Escort would then go look for more proteins

Nuclear Pores – Gateways of the Nucleus

- Allows small molecules to freely pass through
- Larger proteins requires energy (active)
- Proteins pass through nuclear pores **without unfolding**
- **Nuclear Localization Signal** → amino acid sequence that tags a protein for import into the nucleus by nuclear transport
- **Nuclear Export Signal** → tags a protein for export

Import of Protein into Mitochondria

- Proteins destined for mitochondria/chloroplasts made by free ribosomes in cytosol
- Has to move around until it matches up with other half
- Protein is partially folded when signal sequence on N terminus binds with receptor protein
- To fit into it, must partially unfold, then once in the mitochondrial matrix, it refolds, forming **mature protein**
- Cells used for secreting protein have ridiculous amounts of ER

Endoplasmic Reticulum

- Serves as entry point for not only proteins for itself, but rest of endomembrane system (Golgi, lysosomes, endosomes), cell surface, secretory proteins
- Once in ER (membrane or lumen), proteins will never re-enter cytosol
- Two types of proteins transferred to ER→ water soluble proteins translocated crompletely across ER (secretion), and prospective transmembrane proteins translocated partially across (membrane)
- Multi-pass proteins have multiple stop and start sequences while crossing the ER membrane

Signal Recognition Protein

- Riboprotein recognizes signal sequence (section of protein which directs protein to proper organelle) and escorts it accordingly

Vesicular Transport

- Transport vesicles carry soluble proteins (lumens) and membrane proteins (membranes) between comparments
- Outward from ER → Golgi → other organelles; Inward from plasma membrane → lysosomes
- **Clathrin-coated vesicles** → form basket that gives vesicle shape
- **Adaptin** → recognize and capture specific cargo for transport
- Clathrins recognize adaptins, adaptins recognize protein

Glycosylation in the ER

- Every time a protein comes through this channel, **Prefab** system attaches an identical sugar group
- Prefab → oligosaccharide, phosphate, and fatty acid

Unfolded Protein Response (UPR)

- If cell requires increase protein production, molecular chaperones can't always meet demand
- Buildup of misfolded protein accumalte until activated receptors pick it up, which activated transcription regulator, and more chaperones are transcribed
- These are then carried back to ER by ribosomes and are translated into the ER and more chaperones can fold protein
- If cell still can't keep up, apoptosis happens

Functions of Golgi Apparatus

- Modification of new proteins arriving from ER
- Most complex polysaccharides synthesized in the Golgi
- Glycos Amino Glycans (GAGs)

Constitutive VS. Regulated Secretion

- Constitutive → all cells, any time
    - When vesicle fuses, it becomes part of the plasma membrane
    - Leads to new membrane, and new membrane protein
    - Important mechanism in cell growth
- Regulated → only when signal comes, only in specialized cells
    - Protein are selected to be at very high concentrations in vesicles

Vesicular Transport & Endocytic (Inward) Pathways

- Pinocytosis (cell drinking) → tiny vesicles formed – **endosomes** (done by all eukaryotic cells)
- Phagocytosis (cell eating) → much larger vesicles – **phagosomes** (done by specialized cells)
- Receptor-mediated endocytosis (animal) → particular molecules (**ligands**) for which membrane has receptors, which are grouped in patched of membrane called **coated pits**
    - Gets fused with lysosome (meaning it can attack low density lipoprotein) which then spits out cholesterol

Unit 8 – Cell Communication

Long & Short Range Communication

- Endocrine → public
- Paracrine → less public
- Neuronal → long range but private (telephone)
- Contact-dependent → extremely private (whispering in ear)

Signalling Pathways

- Signalling molecule synthesized and released by signalling cell
- Signal molecule travels to target cell
- Signal binds to receptor protein on/in target cell – **signal transduction**
- Change in protein activity (activation/inactivation); changes in gene expression
- Changes in cell shape, movement, metabolism, secretion

Cell Response

- Fast → already have enzymes in cell, crank up activity (can be as fast as seconds)
- Slow → set up a cascade that will send for gene transcription, ect (can be as long as hours) – but very effective

Receptor Location

- Chemical signal suggests where receptor will be
- Receptor start in cytosol and ends up in nucleus (Steroid) → **intracellular**
    - small hydrophobic signal molecules can typically enter the cell and regulate gene transcription
- Integral transmembrane protein → signal must be transduced or transferred across the membrane → **cell-surface receptor**

Steroid Hormone

- Can cross the lipid bilayer
- Finds receptor protein, completes and activated it (transcription factor) and gets royal escort through nuclear pore
- Genomic effects → driving effects of the gene

Intracellular Signalling Cascade

- First messenger → signal molecule that couldn't enter the cell
- Intracellular messenger molecules → small, non-protein, high mobile molecules, for every one of these, you get a second messenger
- Second messenger → small (non-protein) molecules that relay signals from cell surface receptors to target molecules within cell
- Intracellular signal molecules often act as molecular switches

Signalling By Protein Phosphorylation

- When you put a phosphate on protein, you increase its activity
- Transfer phosphate from ATP onto protein
- Kinase → enzyme that transfers phosphate
- Phosphatase → takes phosphate off

- Many proteins controlled by phosphorylation are themselves kinases

Signalling By GTP-Binding Protein

- Binds to diphosphate (depends on GDP or GTP)
- If GTP is abundant in the cell, it drops the GDP and GTP takes its spot
- The protein has built in GTPase activity, meaning it has the enzymatic activity to pluck third phosphate off and revert to starting position

Regulation of Proteins by Phosphorylation

- Kinases push activating
- Phosphates push deactivating
- Two major classes: serine/theorine & tyrosine

GTP-Binding Protein

- Active → cleaves off phosphate
- Inactive → default, waiting for something to happen
- Changes signal of protein so it drops phosphate – GTP leaks in and takes that spot – active

Cell-Surface Receptors

- Ion channel-coupled receptors → binding of ligand opens/closes channel
- G-Protein Coupled Receptors (GPCRs) → binding of ligand activated G protein, which activates an enzyme or ion channel in membrane – highly conserved
    - Always 7 transmembrane alpha-helices (passes)
- Enzyme-coupled Receptors → Signal molecule in form of a dimer binds to two enzymes which activates signal **or** signal molecule binds to enzyme which activates associated enzyme

Activation of G-Protein Coupled Receptor

- Alpha subunit determines whether its active
- Drop GDP and grab GTP, now we have an active alpha subunit
- Dissociated alpha and beta
- Turns itself off by hydrolyzing GTP
- Phosphate comes off, back to default
- Only lasts for a few seconds; as long as alpha and beta are separate, hanging on to tri phosphate

Downstream Targets of G-Proteins

- Ion channels → clear, simple, straight-forward method
- Membrane bound-enzymes that catalyze synthesis of 2nd messengers

Cyclic AMP

- Many GPCRs (epinephrine) activate adenylyl cyclase, which creates cyclic AMP with cleaved off phosphates
- Cyclic AMP activates protein kinase, and signals the activation of gene transcription

Phospholipase C

- Activated by many GPCRs, which sends inositol 1,4,5-triphosphate to open Ca^{2+} channel
- Once channel is open, calcium comes blasting out into the cell and kicks PKC which has already been kicked by diacylglycerol (inositol phospholipid head)

Activation of Calmodulin (CaM) by Ca^{2+}

- Ca acts via transducer protein
- Cell is stimulated, increasing the concentration of Ca
- Ca binds to calmodulin, changing its shape, and wraps around downstream molecules

Receptor Tyrosine Kinase (RTK)

- Activate by enzyme-coupled receptors – since they are single pass membrane proteins, they are not suited to transmit a signal across membrane, so they dimerize
- Activate monomeric GTP-binding protein Ras (mitogen growth factors)
- This sets off a relay system of kinase activations

Unit 9 – Cellular Cycle, Mitosis, Meiosis

Phases of the Cell Cycle

- G_1 phase → most of cell's growth (G_0 subsection for really slow dividing cells)
- G_1/S checkpoint → commitment to mitosis, without signal, cell stays in G_0 phase
- S phase → DNA replication
- G_2 phase → Prep for mitosis (double checking synthesis)
- G_2/M checkpoint → checking for internal issues (double checking all signals)
- M phase → Mitosis

Control of the Cell Cycle

- Mitosis-promoting factor (MPF) → heter dimeric protein
    - Cycling-dependent kinase (Cdk) → catalytic subunit, transfers phosphate from ATP to certain amino acids on target protein – not active unless bound to cyclin partner – constant levels
    - Cyclin → regulatory subunit; levels oscillate throughout the cell cycle
- When cyclin is low, kinase it low, ect.
- Mitogens push cells past G_1/S restriction point

Mitosis

- Involves diploid cells only
- Prophase → chromosomes start appearing and condensing
- Prometaphase → nuclear envelope disappears
- Metaphase → chromosomes line up on metaphase plate ready to be split
- Spindle Checkpoint (Metaphase → Anaphase) → metaphase arrest if something is wrong, or apoptosis
- Anaphase → sister chromatids separate
- Telophase → nuclear envelope re-forms and spindle apparatus disintegrates
- Cytokinesis → actin filament creates cleavage furrow which separates cells (animals)
    - In plant, golgi helps to build new wall by congregating budding vesicles

Cancer → Failure to Respect Checkpoints

- Inappropriate start signals → RTKpathway → Ras

Brakes in Cell Cycle

- Tumor suppressors → transcription factors that drive expression of genes that code for protein that inhibits Cdks
- p53 → detects DNA damage at G_1/S checkpoint; loss of both copies associated with cancer – **guardian of the genome**
- p21 → in response to DNA damage, puts arm lock on cyclin cdks as part of tumor suppressor

Cell Cycle Accelerators

- Oncogene (oncoprotein) → mutated version of normal genes/proteins involves in driving cell division/proliferation
    - Non-mutated version → proto-oncogene (normal behaviour)

Apoptosis

- Involves protein-protein interaction and enzymes (caspases)
- Regulated by Bcl-2 (anti-apoptotic) Bax, Bak, Bad (pro-apoptotic)
- Can be triggered by release of cytochrome C
- Was studied using c. elegans (worms)
- Pruning done by releasing enough survival factors for some cells to survive but not all

Meiosis

- Involves both haploid and diploid cells
- Meiosis I → homologs line up in pairs and separate
    - Prophase I → both non-sister chromatids cross over and synapse
    - Metaphase I → tetrads migrate to metaphase plate
    - Anaphase I → homologs begin to separate
    - Telophase I & cytokinesis → chromosomes move to opposite sides of cell, cell divides
- Meiosis II → separating chromatids
    - Prophase II → spindle apparatus forms
    - Metaphase II → chromosomes line up
    - Anaphase II → sister chromatids begin to separate
    - Telophase II & Cytokinesis → chromosomes separate; cell divides

Mitosis VS. Meiosis I

- Mitosis → homologs line up independently; each cell with same gene
- Meiosis → homologs line up in pairs; positioning and allocation is random

Mistakes in Meiosis

- Improper distribution of chromosomes to each daughter cell → **non-disjunction**
- Results in gametes with abnormal number of chromosomes → **aneuploidy**
    - Extra (third) copy → trisomy
    - One copy → monosomy
    - No copy → nullisomy
- Non-disjunction of chromosome 21 in meiosis I → trisomic (downs syndrome)

Asexual Reproduction

- Organisms well adapted to its environment → bacteria, protists, plants, fungi, some insects, fish, reptiles
- Creates clones; no genetic variability

Unit 10/11 – Cells in Their Social Context

Cytoskeleton

- Microtubules → stiff, hallow tube made of tubulin
    - Alpha or Beta subunit sticking out at ends determine polarity
    - Grow fastest at plus end
    - Determine cell shape; form tracks for movement of vesicles/organelles (motor protein), mitotic spindle
    - Kinesins (toward plus end) and dyeneins (toward minus end) along rails
- Intermediate filaments → ropes
    - Cytoplasmic → ropes or nuclear → mesh
    - Keratins → epithelium
- Microfilaments → threads made of actin
    - Actin filaments contract and allow cell movement

Cancer & Tissue Renewal

- Benign → noninvasive
- Malignant → invasive – detach from original tumor and invade other tissues → **metastasis**
    - Spreads throughout body via blood or lymph (initiates secondary tumors)