AP Biology

A Semicomprehensive Review
Version 3.1415–γ

Created by Charles Feng
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Contents

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It's that time of the year again! Thankfully, for many of us, this round of finals will be the last we'll have to take in high school. However, all of us are still faced with the challenge of kicking the basal bodies out of finals, and so this guide has come into existence. While not intended to be an exhaustive review of everything we learned in biology[1], it should do a pretty good job of letting you recall everything we did this past semester.

Without further ado, let us begin.

1 Introduction to Biology

Biology. What a strange word. *Biolo* and *gy* combine to form this word – nobody knows what either of them mean. Strange. Anyhow, biology supposedly means "the study of life". However, in many cases, it requires using dead organisms. Therefore to study life we must end it. How quaint.

1.1 Themes

There are several main themes that occur frequently in many areas of biology. The first of these deals with emergent properties in biological organization.

Basically, there is a hierarchy of structural levels, with each level made up of the levels below it. The lowest level is 1) atoms, and then progresses to 2) molecules, 3) organelles, 4) cells, 5) tissue, 6) organs, and 7) organisms. A group of organisms in the same species is a *population*, lots of populations of different species make up a *biological community*, and lots of these communities make up an *ecosystem*. *Emergent properties*, or new special functions and stuff, appear as you go up levels – kind of like how teams can do more complicated things than individuals.

The second theme dictates that cells are an organism's basic units of structure and function. We'll talk more about cells later, but I'll mention that there are two types of cells – prokaryotic and eukaryotic – and that one type is more complicated than the other. Do you remember which one?

The third theme is about DNA. Again, we'll talk about it later so bah. Similarly, the fourth theme tells us that structure and function are correlated in biology (form fits function) but is quite useless because of its triviality. The fifth says that organisms interact with their environments, again pretty obvious.

The next one is a little more important. It tells us that regulatory mechanisms ensure equilibrium in living systems, or more specifically that feedback processes and such regulate which reactions occur at which rates and so keeps the cell alive and healthy. *Negative feedback* is where feedback slows or stops processes. An example of negative feedback is when enzymes turn A to B to C to D, and then a high concentration of D goes back and turns off the A→B enzyme, stopping the process. *Positive feedback* is when a product of the reaction sequence (D) goes back and enhances one of the enzymes in the process, making it faster. Positive feedback is pretty rare in living systems.

The next theme is pretty useless too. It tells us that there is a lot of diversity in biology (different species of animals, plants, and such) but there is also unity in all of that. It seems to contradict until we realize that DNA determines what most of us look like, making us almost the same. But as the King Lego said to his subordinate building blocks, you can make a lot of stuff with only several varieties of pieces if you have lots and lots and lots of pieces.

Next, we learn that evolution and natural selection is core to biology. Nothing new here; let's move on. We arrive at the (I lost count)th theme, which tells us about the scientific method. Basically, you make *Observations*, which lead you to ask a *Question*, then make a *Hypothesis* and a *Prediction*, which can be tested through an *Experiment*. If the test doesn't support the hypothesis, make a new one; if it supports it, make some more predictions and test them. Scientific *Induction* means that you're going from specific to general (Rohan has no legs, Nish has no legs, our whole class has no legs, thus all humans have no legs); *Deduction* means that you're going from general to specific (Indians are melanous, Rohan is Indian, thus Rohan is melanous).

[1] That means that you should try to study the book and your class notes as well, regardless of how hugely bloated this guide is. This disclaimer is small so hopefully you do not see it. If you do in fact see it, shhh... don't tell anyone...

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1.2 Dainty Biochemistry

Atoms are dainty. — Unknown

Organisms are made of *matter*, or anything that has mass and takes up space. An element is a substance that can't be broken down further by chemical reactions. A *compound* is a substance consisting of two or more elements combined in a fixed ratio. Life needs about 25 elements, including carbon, oxygen, hydrogen, and nitrogen. *Trace elements* are only needed in small quantities, and include iron and iodine.

An atom is made up of neutrons (no charge) and protons (positive charge), which are located in a densely packed nucleus. Clouds of electrons (negative charge) orbit the nucleus. The *atomic number* is the number of protons, whereas the *mass number* is the number of protons plus the number of neutrons. Some atoms with the same atomic number have different mass numbers due to different numbers of neutrons. These are called *isotopes*.

A *fishhead* is the head of a fish, and is sometimes used in Asian soup to increase intelligence or something. There are different energy levels in the electrons surrounding the atom's nucleus; these matter in photosynthesis when light energy kicks an electron up some energy levels. Electrons are located in shells; the outermost shell is the *valence* and is the shell that matters most to reactions.

There are several kinds of bonds that can occur between atoms. The first is a *covalent bond*, in which the atoms share electrons. Atoms connected by these bonds form molecules. Polar covalent bonds occur when there is a sufficient difference in electronegativity between the two atoms and the shared electrons tend to stay closer to the more electronegative atom. This gives the two atoms slight partial charges; the more electronegative one with a negative charge (δ^-) and the other one with a positive charge (δ^+). The whole molecule becomes polar if the polar bonds don't cancel each other out. Water is an example of a polar molecule. Nonpolar covalent bonds are where the electrons are shared almost equally.

Ionic bonds occur when one atom completely yanks an electron away from another. These form actual full charges; the positively charged atom is called a *cation* and the other one is an *anion*. Compounds formed by ionic bonds are called salts.

Hydrogen bonds form between polar molecules. The δ^- portion of one molecule forms a weak bond with the δ^+ portion of another molecule. Hydrogen bonds are really really important in biology because of their significance in water. We'll talk about that later.

Van der Waals interactions occur because electrons aren't evenly distributed in nonpolar molecules – sometimes more electrons are on one side and such. These are even weaker than hydrogen bonds but help reinforce the three-dimensional shapes of large molecules.

1.3 Water – Not Just Good For Drinking

Wow, did you know that?! Life is utterly dependent on water because of several fun properties that water has.

Firstly, water is polar (see above if you don't what that is) and thus forms hydrogen bonds with other polar molecules. This causes water to exhibit *cohesion* with other water molecules and *adhesion* to non-water polar molecules. These two mean about the same thing – water likes sticking to other polar things. This enables some cool effects, such as capillary action (lets water travel up xylem of plants and thus lets plants stand tall) and surface tension (little insects and stuff can walk on water).

Water also has a high specific heat, meaning that it is resistant to change in temperature. This is caused by hydrogen bonding again. When the temperature is increased, hydrogen bonds break and the temperature decreases a bit; when the temperature is decreased, hydrogen bonds form and increase the temperature a little bit. This helps oceans and stuff not boil away under the hot hot *yellow* sun. Since we're made of water too (except Charles, who is a robot) it helps with keeping the same temperature in our body, called *homeostasis*.

Water has a high heat of vaporization, which makes it absorb a lot of energy when it evaporates. This contributes to *evaporative cooling*, which contributes to the stability of temperature in bodies of water and in us. Recall that when sweat evaporates, we feel cool; this is due to evaporative cooling.

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Water's also cool because in ice (hahaha get the pun?) the molecules are actually spaced farther apart than in liquid water due to a crystal lattice of hydrogen bonds. Therefore, *ice floats* and so ponds don't freeze due to insulation by a top ice layer, helping life thrive in them.

Finally, water is a very good solvent, meaning it can dissolve lots of things, helping us be able to transport many molecules and such easily in our body.

Water sometimes loses hydrogen atoms to other water molecules, forming two ions:

$$H_2O \rightleftharpoons H_3O^+ + OH^-$$

This *dissociation* is very important to life, as it is the basis of pH and acids and bases. An *acid* is a substance that donates hydrogen (H^+) or more accurately hydronium (H_3O^+) ions. A *base* absorbs these ions, reducing the H^+ concentration. The pH of the solution tells us how acidic or basic a solution is; lower pH means more acidic and higher means more basic. A pH of 7 is neutral.

One reason acids and bases are important is for buffers. Most of the chemical processes in our body are dependent on pH; they need a specific pH range to run or else they won't work. Buffers are substances that lessen changes in pH; when acid is added, the H^+ ions are absorbed the buffer; when base is added, H^+ ions are donated by the buffer to neutralize the base. An example of a buffer is carbonic acid:

$$H_2CO_3 \rightleftharpoons HCO_3^- + H^+$$

If the solution becomes more acidic, the equilibrium shifts to the left; when it becomes more basic, the equilibrium shifts to the right.

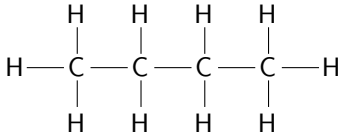
2 Organic Compounds

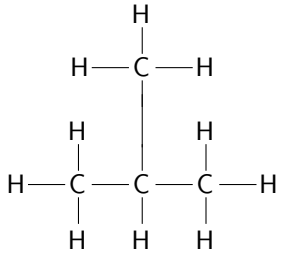
2.1 Carbon

Carbon is also really important to life because they are the basic building blocks of most molecules in organisms. Carbon has 4 valence electrons, letting it have a maximum of four covalent bonds (tetravalence) which adds to its versatility, letting it form covalent bonds with many different elements. Also, carbon is able to form chain or ring skeletons, in which the huge potential for variation bring more diversity to organic molecules. Carbon skeletons can vary in length, branching, and can have double bonds or even exist in ring shapes.

Variation in organic molecules can exist in the form of *isomers*, or compounds that have the same molecular formula (i.e. $C_6H_{12}O_6$) but have different structures (i.e. glucose, fructose). There are three types of isomers:

Structural isomers have a different arrangement of covalent partners among the carbon atoms. Below left is butane; below right is isobutane.





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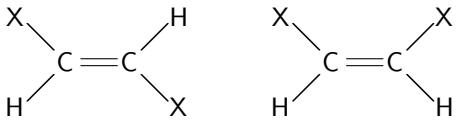
Geometric isomers differ in arrangement around a double bond. Note that in the left image, the X's are on opposite sides of the structure, while on the right image, they're on the same side.



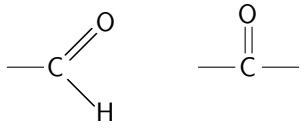
Enantiomers are basically "mirror images" of each other, like your right and left hands. Usually, one enantiomer has an effect while the other has none or even a harmful effect.

2.2 Functional Groups

Functional groups are components of organic molecules that are commonly involved in chemical reactions as groups and have special properties. These functional groups behave consistently from one molecule to another.

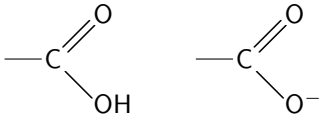
The *hydroxyl* group consists of an oxygen atom bonded to a hydrogen. Organic compounds containing a hydroxyl group are called alcohols. It looks like —OH.

The *carbonyl* group consists of a carbon atom joined to an oxygen atom by a double bond. There are two types of carbonyl groups: if it is located at the end of a carbon chain, it has a hydrogen connected to the carbon, is called a *aldehyde*, and has a formula of —COH. If it is located in the middle of a carbon chain, it's just a C double bonded to an O and is called a *ketone*.



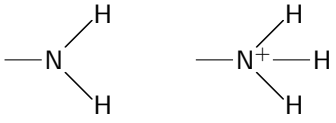
aldehyde *ketone*

The *carboxyl* group (—COOH) consists of a carbon atom doubled bonded to an oxygen and also bonded to a hydroxyl group. Compounds containing these are called carboxylic acids, and are acidic since they are a source of hydrogen ions.



non-ionized *ionized*

The *amino* group (—NH_2) consists of a nitrogen atom bonded to two hydrogen atoms. Compounds with these are called amines. This group acts as a base; it absorbs protons and gets a positive charge.



non-ionized *ionized*

The *sulfhydryl* (—SH) group is a sulfur attached to a hydrogen and the carbon skeleton. Substances containing these are called thiols. Sulfhydryl groups can interact to hold proteins together.

The *phosphate* (—OPO_3^{2-}) group consists of a phosphorus attached to four oxygens, one of which is attached to the carbon skeleton, the second doubled bonded to the phosphorus and the remaining two single bonded to the phosphorus and with negative charges. This is especially important in the body, being the primary source of energy in the form of ATP.

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3 Macromolecules – Bigger is better!

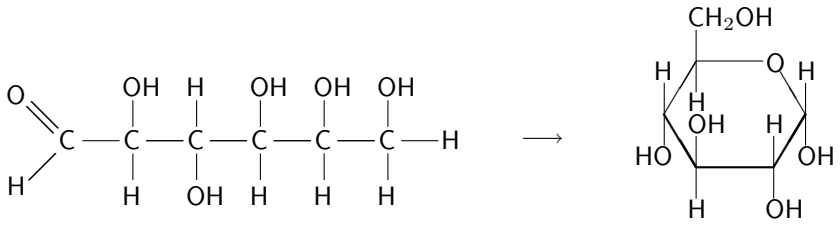
These molecules are very very very very big - some may even have more than 100000 atoms. Usually, macromolecules are polymers, or are formed from long chains of small, nearly identical subunits called monomers; however, in some cases, they are not. You haven't had any fun in a long time, have you? I'm dreadfully sorry; I agree that studying for an AP Biology final can be quite tedious sometimes. Therefore, now is the time to head to the nearest refrigerator and grab yourself a cool drink. Do it; it'll make you much happier.

Macromolecule monomers are bound together through a *dehydration reaction*, in which water is removed (H from an —OH on one molecule; the whole OH is removed from the other molecule) and the resulting molecules bound together. Polymers are disassembled into monomers by *hydrolysis*, in which water is added to break them apart. We'll look at each type of molecule one by one.

3.1 Carbohydrates

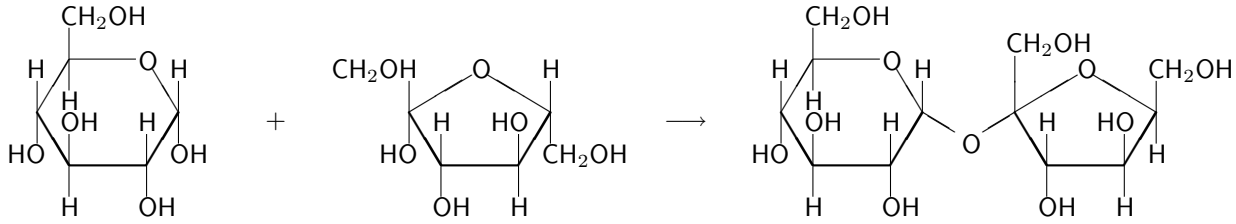
These are sugars. Their monomers are called *monosaccharides*, dimers are called *disaccharides*, and polymers are called *polysaccharides*.

Glucose ($C_6H_{12}O_6$) is the most commonly known monosaccharide. It has a carbonyl (aldehyde) group, and therefore is an *aldose*. Fructose is like glucose except its carbonyl is a ketone and therefore is a *ketose*. Although sometimes glucose is in linear form, when it is immersed in aqueous solution, it is actually a ring structure, in which the 1-carbon attaches to the oxygen on the 5-carbon. The image below shows glucose in its linear and ring forms.



Galactose is another hexose (6 carbons like glucose) and resembles glucose.

A *disaccharide* is formed by two monosaccharides joined by a *glycosidic linkage*, a covalent bond formed by a dehydration reaction. Some common disaccharides include *sucrose*, which is glucose + fructose; *maltose*, which is glucose + glucose, and *lactose*, which is glucose + galactose. The image below shows how glucose and fructose link to form starch.



A *polysaccharide* is a polymer with lots and lots of monosaccharides joined by glycosidic linkages. Some polysaccharides are used to store energy to be metabolized later. For example, *starch*, used in plants, is a chain of 1-4 linkages of α glucose[2] monomers. It exists in a helix due to hydrogen bonds. There are two types of starch: amylose (unbranched, meaning there are no side helices coming off the main helix) and amylopectin (branched). Animals use *glycogen*, which is much more branched than starch.

[2] α glucose is different from β glucose due to the placement of the hydroxyl group on the 1-carbon in the ring form. Basically, β glucose is like a mirror image of α.

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Another type of polysaccharide is the structural polysaccharide, which serves to protect the cell or the organism. One of these, *cellulose*, is formed from alternating α and β glucose, forming a straight chain that is used in bunches as a strong building material. Another is *chitin*, which resembles cellulose but also has a nitrogenous appendage on each monomer. It is used in exoskeletons of arthropods and in many fungi.

3.2 Lipids

Lipids are not polymers. They have almost no affinity for water and consist mainly of hydrocarbons.

Fats are constructed from a glycerol and three fatty acids which are connected to the glycerol through *ester linkages*. The fat consisting of a glycerol and three fatty acids is also called a *triacylglycerol* or simply *triglyceride*. The fatty acids are formed from hydrogen molecules attached to carbon chains and can be *saturated*, meaning that as many hydrogens as possible are attached, or *unsaturated*, having some double bonds. Saturated fats are solid at room temperature, whereas unsaturated fats are liquid. Fats make you fat because they're such rich sources of energy. *Muktuk* is whale fat and is often eaten by Eskimos.

Phospholipids are used in cell membranes and consist of a hydrophilic head and two hydrophobic tails. They are used in cell membranes as a bilayer, wich the tails pointing inward and the heads on the outside, kind of like O= =O.

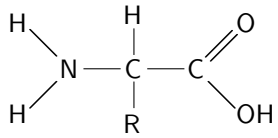
Steroids are lipids with a carbon skeleton of four fused rings. Cholesterol is a steroid.

3.3 Proteins

Drink Smarter. Live Better. Drink V8. — Advertisement.

Proteins are polymers constructed from a set of 20 different *amino acids*. Polymers of amino acids are actually called *polypeptides*; proteins can be one or more polypeptides that are coiled into special conformations.

Amino acids are cool little molecules containing carboxyl and amino groups connected to a central carbon, which is further connected to a hydrogen and a R group, which can be one of twenty different side chains. Since carboxyl can donate a hydrogen ion and the amino can accept a hydrogen ion, amino acids are both acidic and basic, making them *amphoteric*. There are twenty amino acids depending on what the side chain is, and each can be nonpolar, polar, or electrically charged. Amino acids are connected through dehydration reactions, forming *peptide bonds*. Here's an amino acid:



There are four levels of protein structure. Since proteins only work if they are in the right conformation and not *denatured*, the structure is especially important. A change in one level affects all the levels above it.

Primary structure is the sequence of amino acids. A change in a single amino acid can lead to Bad Things, as in the case of sickle-cell anemia.

Secondary structure is the way the chain of amino acids is coiled or folded. It has two possibilities: an α helix or a β pleated sheet. The former is caused by hydrogen bonds between every fourth amino acid; the latter by hydrogen bonds between strips of amino acids.

Tertiary structure is other interactions between side chains of amino acids. There can be hydrogen bonds, hydrophobic interactions (i.e. Van der Waals forces) between hydrophobic groups, strong *disulfide bridges* between sulfhydryl groups of cysteine monomers, and ionic bonds between ionic side chains.

Quaternary structure is how two or more polypeptides are arranged to form a protein.

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3.4 Nucleic Acids

Nucleic acids make up DNA which make up genes which define primary structure of proteins. Girls and maybe Nish sometimes wear makeup to look pretty.

There are two types of nucleic acids, DNA and RNA, both of which are formed by a polymer of nucleotides. Each nucleotide is formed from a *nitrogenous base*, a *pentose* (deoxyribose in DNA, ribose in RNA) and a phosphate group. *Pyrimidines* are small nitrogenous bases, containing only a single ring of carbon. C, T, and U are pyrimidines. *Purines* are double ringed bases. A and G are purines.

DNA is structured like a double helix. A only pairs with T; C only pairs with G. We'll talk more about DNA later.

4 Energy and Metabolism

4.1 Energy

An organism's chemical reactions considered as a whole is called its *metabolism*, with each related series of reactions organized into *metabolic pathways*. Processes that break down molecules are called *catabolic pathways*; processes that build complex molecules are called *anabolic pathways*[3].

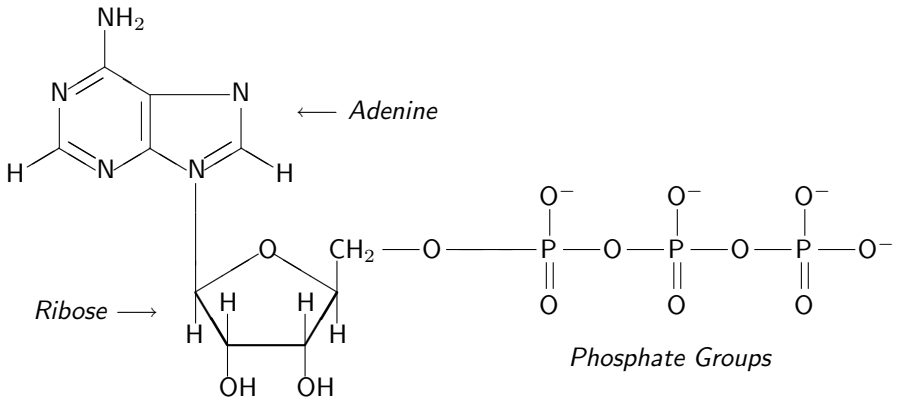
Organisms live at the expense of free energy, or the amount of energy available to do work. We have the equation $\Delta G = \Delta H - T\Delta S$, or free energy equals the difference of total energy and entropy, or the amount of disorder in a system. Note that in a *spontaneous process*, the free energy of a system always decreases.

An *exergonic reaction* is one that loses free energy to its surroundings, or ΔG decreases. Spontaneous processes are exergonic. An *endergonic reaction* absorbs free energy so ΔG increases. These are nonspontaneous reactions. *Energy coupling* is when energy from an exergonic process is used to drive an endergonic one.

If a cell is at *equilibrium*, then it cannot do any more work and therefore is dead. A cell prevents this from happening through the constant flow of materials into and out of the cell.

4.2 ATP

ATP, or *adenosine triphosphate*, is the immediate form of energy that powers most cellular work. It consists of an adenine bonded to a ribose sugar which is then bonded to three high-energy phosphate groups[4].



[3]To remember this, recall that *anabolic* steroids *build up* your muscles.

[4]Phosphate groups are considered to have *high energy* because of the repulsion between successive negatively charged oxygen atoms. The bonds *want* to break and so release a lot of energy by doing so.

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ATP performs work by *phosphorylating* (donating a phosphate group to) substances, thereby releasing energy to the substance. It is regenerated through energy from catabolism in a cycle known as the *ATP cycle*.

4.3 Enzymes

An enzyme is a biological *catalyst*, or it changes the rate of a reaction.

Every chemical reaction involves bond breaking and bond forming. Because bonds must absorb energy in order to break and reform, there needs to be a little bit of energy added to the molecule (called the *activation energy*, or E_A) for it to become unstable. Normally, if the activation energy is relatively high, the reaction would only occur very rarely. However, enzymes *lower the activation energy* by putting stress on the bonds and therefore make the reaction more likely to occur.

The reactant an enzyme catalyzes is called its *substrate*. An enzyme has a specific substrate that it catalyzes; very few other molecules will work. This is because the 3-D region of the enzyme that does the catalysis, its *active site*, is very specific as to what kinds of molecules it can accept. When a substrate goes into the active site, an *induced fit* occurs: the enzyme changes its conformation to grab the substrate tightly, enhancing the catalyzing ability of the enzyme.

The rate at which a quantity of a substrate is converted to products is dependent on several factors. Generally, the more substrate, the faster rate of catalysis; this is because there is more cf a chance that enzymes and substrates will bounce together the right way for the reaction to occur. However, when all the enzymes in the area have their active sites full of substrate, the enzyme population is said to be *saturated* and the only way to increase productivity is to add more enzymes.

A cell's physical and chemical environment has an effect on enzyme activity. There is a temperature and pH range, called the optimal temperature and pH, in which an enzyme functions best. If the environment's properties do not fall in this range, the enzyme can denature and not function as well.

Some enzymes also require nonprotein buddies for them to work (talk about insecurity! O.O). These buddies, called *cofactors*, can bind permanently or loosely to the active site to improve function. Organic cofactors are called *coenzymes*.

Other chemicals, called *inhibitors*, are mean and disrupt the action of enzymes. If an inhibitor covalently bonds with the enzyme, the enzyme is pretty much doomed and inhibition is irreversible. *Competitive inhibitors* compete for admission to the active site (reminds me of applying to colleges). These block the substrate from entering the active site. *Noncompetitive inhibitors* bind to the enzyme at a location away from the active site, but cause the active site's conformation to change and refuse to accept any more substrate.

4.4 Control of Metabolism

It is obvious that without control, a cell's metabolic processes would go insane and probably end up blowing up the cell in a small thermonuclear reaction. In this section, we'll talk about how the cell implements control by switching certain enzymes on and off at certain times.

In many cases, molecules that naturally regulate enzyme activity behave like reversible noncompetitive inhibitors. These bind to an *allosteric site* on the enzyme. Most allosterically regulated enzymes have more than one polypeptide chain, or subunit, and each of these chains can catalyze the reaction. These enzymes repeatedly alternate between an active and an inactive form. If an allosteric regulator binds to an allosteric site on an enzyme, all of the subunits on the enzyme will be activated or inhibited at the same time and the form it's in will be stabilized.

Allosteric regulation usually works with feedback inhibition. The products of a series of enzyme reactions sometimes are the allosteric regulators for an enzyme near the beginning of the series; therefore, when the product concentration gets too high, the enzyme near the beginning will be inhibited and so the reaction will slow down. When the concentration decreases, the enzyme will be activated again and the reaction will return to its original pace.

In enzymes composed of more than one subunit, if a substrate binds to one unit, all the other units usually become primed to accept substrates. This is called *cooperativity*.

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5 Cell Structure and Physiology

Some cells have arms and legs and play baseball with ribosomes. The Leaping Lymphocytes won last year by pounding the Ancient Amoebae 77-1. I hear that final game was legendary.

5.1 Cell Structures

There are two different types of cells: prokaryotic and eukaryotic. Only bacteria and archaea have prokaryotic cells; protists, plants, fungi, and animals have eukaryotic cells. Prokaryotic cells are characterized by their lack of membrane-bound organelles, lack of nuclei (chromosomes are located in a region called the *nucleoid* in the cytosol), and are much smaller than their eukaryotic counterparts. Both types of cells have a plasma membrane, cytosol, chromosomes, and ribosomes. Because prokaryotic cells are so simple, they kind of suck and thus we'll only look at eukaryotic cells.

The *nucleus* contains most of the genes in a eukaryotic cell. A *nuclear envelope* encloses the nucleus. This envelope is a double membrane that is perforated by pores, which regulate the transfer of large macromolecules in and out of the nucleus. The inside of the inner membrane is lined by the *nuclear lamina* with maintains the shape of the nucleus. Inside, the DNA is in the form of a fibrous material called *chromatin*. There also may be *nucleoli*, which synthesize ribosomal RNA. The nucleus itself synthesizes mRNA.

Ribosomes are little organelles created by the nucleoli. They aren't membrane-enclosed and are made up of a large and a small subunit. They are located in the cytoplasm or are bound to the rough endoplasmic reticulum. They facilitate the synthesis of polypeptides.

The *endomembrane system* consists of lots of membranes in the cell, including the nuclear envelope, the endoplasmic reticulum, the Golgi apparatus, lysosomes, vacuoles and the plasma membrane.

The *endoplasmic reticulum* or ER consists of a network of connected membranous sacs called cisternae. The space inside the cisternae is called the *cisternal space*. Oooh profound! There are two distinct regions of ER that differ in structure and function: smooth ER and rough ER. Smooth ER functions in the synthesis of lipids, the metabolism of carbohydrates, detoxification of drugs and poisons, and helps with the contraction of muscle cells. Rough ER is studded with ribosomes and secretes proteins for use in other membrane-bound organelles or for transport out of the cell. Most secretory proteins are *glycoproteins*, which are proteins bonded to carbohydrates, more specifically oligosaccharides[5]. The rough ER also creates membranes and sends them off in the form of transport vesicles.

The *Golgi apparatus* processes products of the ER and is involved in manufacturing, warehousing, sorting, and shipping. It's formed from unconnected cisternae and has two different faces differing in thickness and molecular composition. The *cis* face is the receiving end and the *trans* face is the sending end. The cisternae between the two faces are used to modify and/or store products before sending them off in transport vesicles. Functions of the Golgi apparatus include altering products of the ER and manufacturing some macromolecules like non-cellulose polysaccharides. I eat Golgi apparati. They taste like lemons.

Lysosomes are membrane-bound sacs of hydrolytic enzymes that are used to digest macromolecules. The interior is pretty acidic because the enzymes used work best in that environment. Most lysosomes are piecewise made in the rough ER and bud off of the Golgi apparatus. They are used in intercellular digestion, autophagy (recycling of cell's organic material) and are involved in programmed cell death, or apoptosis.

Vacuoles are big *vesicles*, both of which are membrane-bound sacs. There are three types of vacuoles: 1) food vacuoles created by phagocytosis, 2) contractile vacuoles used to pump water out of the cell in freshwater protists, and 3) central vacuoles, located in plant cells, which are enclosed by the *tonoplast*, store organic and inorganic molecules and pigments, help with cell growth by absorbing water, and can be disposal sites for metabolic byproducts.

Mitochondria are bean-shaped organelles that generate ATP through cellular respiration. A mitochondrion is enclosed by two membranes: the outer membrane is smooth while the inner membrane is convoluted with foldings called *cristae*. The membranes are made by free ribosomes in the cytosol and ribosomes in the mitochondrion itself. The *intermembrane space* is located between

[5]Small polymer of monosaccharides – recall that "oligo" means "few".

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the two membranes. The *mitochondrial matrix* is enclosed by the inner membrane.

Plastids are organelles found in plant and some protist cells. There are several types of plastids: *amyloplasts* store starch, *chromoplasts* have pigments that make plants colorful, and *chloroplasts* which convert light energy to chemical energy through photosynthesis. A chloroplast has two membranes, and the interior is made up of a fluid called the *stroma* in which lots of flattened sacs called *thylakoids* are stacked together to form *grana*.

Peroxisomes are single-membrane organelles that create and destroy hydrogen peroxide while performing functions such as breaking down fatty acids and detoxifying alcohols and other harmful compounds. A special type of peroxisome, the *glyoxysome*, is found in fat-storing tissues of plant seeds and contain enzymes that convert fatty acids into sugar to nourish the emerging seedling. Peroxisomes increase in number by splitting in two.

The *cytoskeleton* is made up of microtubules, microfilaments (actin filaments) and intermediate filaments. It provides structural support to the cell, helps anchor organelles and enzymes, is involved in cell movement and can regulate biochemical activities in the cell. *Microtubules* are hollow tubes consisting of 13 columns of tubulin molecules; they are involved in cell motility as flagella and cilia and help move around organelles and chromosomes. They also maintain the cell's shape. *Microfilaments* are made up of two intertwined strands of actin; they help with changes in cell shape, cytoplasmic streaming, help to move the cell through pseudopodia, and form the cleavage furrow during cell division[6]. They are used in muscle cells, in which they are arranged with myosin filaments to enable contraction and expansion. Finally, *intermediate filaments* are fibrous proteins supercoiled into thick cables and help anchor the nucleus and certain organelles.

Flagella and *cilia* are used in cell movement. Both of these are formed by a "$9 + 2$" arrangement of microtubules, or nine pairs arranged in a circle with two separate ones in the middle, and are moved by dynein "arms" that crawl up and down each pair on the outer ring. They are anchored in the cell by a *basal body*. Flagella beat back and forth in an *undulating motion* to propel the cell forwards; cilia are like oars and use an active stroke and a recovery stroke. Cells (notably amoebae) can also move by using actin filaments to squeeze the cytosol forwards into *pseudopodia*.

The *cell wall* is the outermost layer of plant cells and unicellular organisms. It protects the cells, maintains the cells' shapes, and prevents cells from taking in too much water. It is comprised of cellulose embedded in a matrix of other polysaccharides and proteins. Alex Inman is very white and very awesome.

The *extracellular matrix* is found in animal cells and are formed from glycoproteins such as collagen which are embedded in a network of *proteoglycans*. Cells are attached to the ECM by *fibronectins*, which bind to receptor proteins called *integrins* on the cell membranes. It is theorized that changes in the ECM of a particular tissue could help coordinate the behavior of all cells in that tissue.

Intercellular junctions help with cell-to-cell communication and interaction. In plants, the cell walls are perforated with *plasmodesmata*, which are basically small holes that actually unify most of the plant into one continuous bulk of cytosol. Small solutes and such can pass through plasmodesmata. In animal cells, *tight junctions* fuse membranes of neighboring cells, preventing leakage of extracellular fluid. *Desmosomes* or anchoring junctions fasten cells together. *Gap junctions* provide pores surrounded by special proteins that allow small molecules to pass through.

Some plants have another layer, called the secondary cell wall, underneath the primary cell walls. The primary cell walls of adjacent cells are held together by the *middle lamella* layer, which is rich in sticky polysaccharides called *pectins*.

5.2 Membrane Structure

The plasma membrane surrounding the cell controls the movement of molecules into and out of the cell. Exhibiting *selective permeability* (only some substances can pass through), it is fundamental to cell life. The membrane is formed from a *phospholipid bilayer*, or two layers of phospholipids with the hydrophobic tails pointing towards each other and the hydrophilic heads on the outside, forming a O=== ===O membrane. The *fluid mosaic model* states that the membrane is a fluid structure, with various proteins embedded in the bilayer.

The membrane is held together by weak hydrophobic interactions, making it very susceptible to movement and change (lateral

[6] This is a lonely little footnote that doesn't really have much to say. :(

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movement of phospholipids, etc). Phospholipids with unsaturated fatty acid tails make the membrane more fluid; saturated hydrocarbon tails make it viscous. Cholesterol reduces membrane fluidity at moderate temperatures by reducing phospholipid movement and hinders solidification at low temperatures by disrupting the packing of phospholipids. The membrane must be fluid to work properly.

Integral proteins penetrate the phospholipid bilayer and usually are *transmembrane proteins*, meaning that they stick out on both sides. *Peripheral proteins* aren't embedded in the bilayer.

Cell-cell recognition is a crucial function performed by carbohydrates on the plasma membrane. These carbohydrates are usually oligosaccharides, and are bonded to proteins extruding from the surface (forming glycoproteins) and some are bonded to lipids (forming glycolipids).

Other functions of the plasma membrane include transport, enzymatic activity, signal transduction, intercellular joining, and attachment to the extracellular matrix.

5.3 Diffusion and Osmosis

Diffusion describes the tendency for molecules of a substance to spread out into all the available space, causing a net movement of molecules from high concentration to low concentration, or down their *concentration gradient*. Diffusion does not require energy as it is a spontaneous process. When a substance diffuses across a cell membrane, it is called *passive transport*.

When comparing two solutions of different concentrations, the solution with higher concentration is said to be *hypertonic* and the other solution is said to be *hypotonic*. Solutions that are of same concentration are called *isotonic*. If we were to have a U-tube with a semipermeable membrane in the center and equal levels of water but unequal concentrations on the two sides, then the water will diffuse to the side with more concentration until the concentrations are equal. The diffusion of water is called *osmosis*.

Diffusion of water can be considered a flow of water down a *water potential* gradient. Water potential, designated ψ, has two components: osmotic potential caused by solutes and pressure potential due to physical pressure on the solution. Water will always move from high water potential to low water potential (kind of like you can only fall from high ground to low ground; you can't fall up). An addition of solute to the solution will decrease the water potential; the addition of pressure on the solution increases water potential. A hypertonic solution has lower ψ; a hypotonic solution has higher ψ.

If an animal cell is in hypotonic solution, water will rush in and it will burst. If it is in a hypertonic solution, water will rush out and the cell will shrivel up. Animal cells functional normally in isotonic environments.

If a plant cell is in hypotonic solution, water will rush in and create pressure inside the cell against the cell wall. This *turgid* state is normal for plant cells. If it is in an isotonic solution, it will become flaccid and wilt. If it is in a hypertonic solution, the cell will *plasmolyze*, or the plasma membrane will shrink away from the cell wall.

Therefore, cells living in non-optimal conditions must have special adaptations for *osmoregulation*. For example, *Paramecium* lives in a hypotonic environment, and therefore water will continually diffuse into the cell. *Paramecium* compensates for this by using a *contractile vacuole* to pump water out of the cell.

5.4 Traffic Across Membranes

Blingocytosis is pretty cool. I don't know if it exists though.

The plasma membrane is selectively permeable, taking up only some substances at various rates. Hydrophobic molecules can cross the membrane with ease; however, it is very difficult for polar molecules and ions to pass through. This problem is remedied through integral transport proteins that range from simple channels to complex shape-changing units that are extremely selective.

Hydrophilic molecules can only[7] diffuse through the membrane with the help of transport proteins, called *facilitated diffusion*. A

[7] Actually, we're only using "can only" in a general sense here; some molecules like hydrogen ions can sometimes randomly cross the membrane. Kinda reminds me of quantum tunneling.

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transport protein is specialized for the solute it transports and can even have a specific binding site, like the active site of an enzyme. It can also be inhibited by molecules that pretend to be its solute but actually screw it up. Some transport proteins include *aquaporins*, which allow for diffusion of water, and *gated channels*, which open and close on either sides of the membrane to transport molecules.

Active transport is the pumping of solutes against their concentration gradients. This transport requires the expenditure of energy, usually donated through phosphorylation of the transport protein by ATP. One type of active transport is the *sodium-potassium pump*, which trades sodium ions inside the cell for potassium ions outside, with a trade balance of three sodiums for two potassiums. Note that this also generates a voltage across the membrane; the inside of the cell becomes more negatively charged than the outside. This forms a *electrochemical gradient*, a combination of both a concentration gradient and a membrane potential across the membrane. Another type of active transport is the *proton pump*, used in plants, bacteria, and fungi, which pumps hydrogen ions out of the cell. This also generates an electrochemical gradient.

A pump that transports a specific solute can also indirectly drive the active transport of other solutes through *cotransport*. For example, if a hydrogen ion is pumped out of a plant cell through a proton pump, it can diffuse back into the cell *with a sucrose molecule attached* through a sucrose-H^+ transporter, supply the cell with the nutrients that it needs.

Exocytosis is used to transport large molecules out of the cell. A transport vesicle containing the molecule fuses with the plasma membrane, expelling the molecule. Similarly, *endocytosis* is used to take in macromolecules; the plasma membrane surrounds the molecule and pinches in to form a vesicle. There are three types of endocytosis: *phagocytosis*, in which a cell engulfs a particle by wrapping pseudopodia around it; *pinocytosis*, where a cell gulps water into tiny vesicles; and *receptor-mediated endocytosis*, in which specific extracellular substances or *ligands* bind to special receptors on the cell's surface (these are usually located in *coated pits* which are covered with fuzzy protein) and then are ingested.

6 Cellular Respiration

Monkeys. There's still so many chapters to go! Big bald purple monkeys. Boohoohoohoo

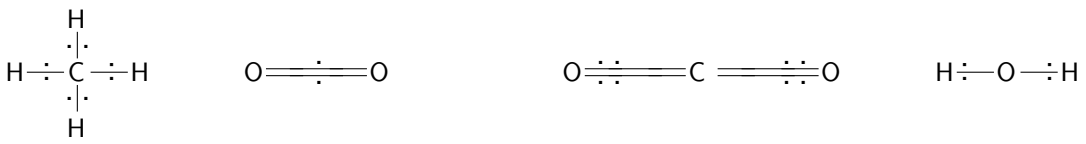
6.1 Oxidation-Reduction Reactions

Oxidation-reduction reactions, or *redox reactions* for short, there is a transfer of electrons from another substance to another. The substance that loses electrons is said to be *oxidized* and the substance that gains them is said to be *reduced*[8].

A redox reaction can be summarized like $Xe^- + Y \longrightarrow X + Ye^-$. Substance X is the electron donor and the *reducing agent*. Substance Y is the electron acceptor and is the *oxidizing agent*.

Not all redox reactions involve the complete transfer of electrons. Some only change the degree of electron sharing in bonds. Electrons in more polar bonds have less energy than electrons in nonpolar bonds. For example, we look at the combustion of methane:

$$CH_4 + 2\ O_2 \longrightarrow CO_2 + 2\ H_2O$$



During the reaction, equally shared electrons move away from carbon and hydrogen atoms and closer to oxygen, which is much more electronegative. This reaction releases energy to the surroundings because electrons lose potential energy as they move closer

[8] A helpful way to remember the order is through the acronym OIL RIG, or Oxidation Is Loss [of electrons of course] and Reduction Is Gain.

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to more electronegative reactions. Carbon is said to be *oxidized* because the distances of electrons from carbon in the product is greater than that in the reactants. Similarly, oxygen is said to be *reduced* because the distances of electrons from oxygen is less in the products than in the reactants.

During cellular respiration, electrons "fall" from organic molecules to oxygen. In the equation for cellular respiration,

$$C_6H_{12}O_6 + 6\,O_2 \longrightarrow 6\,CO_2 + 6\,H_2O$$

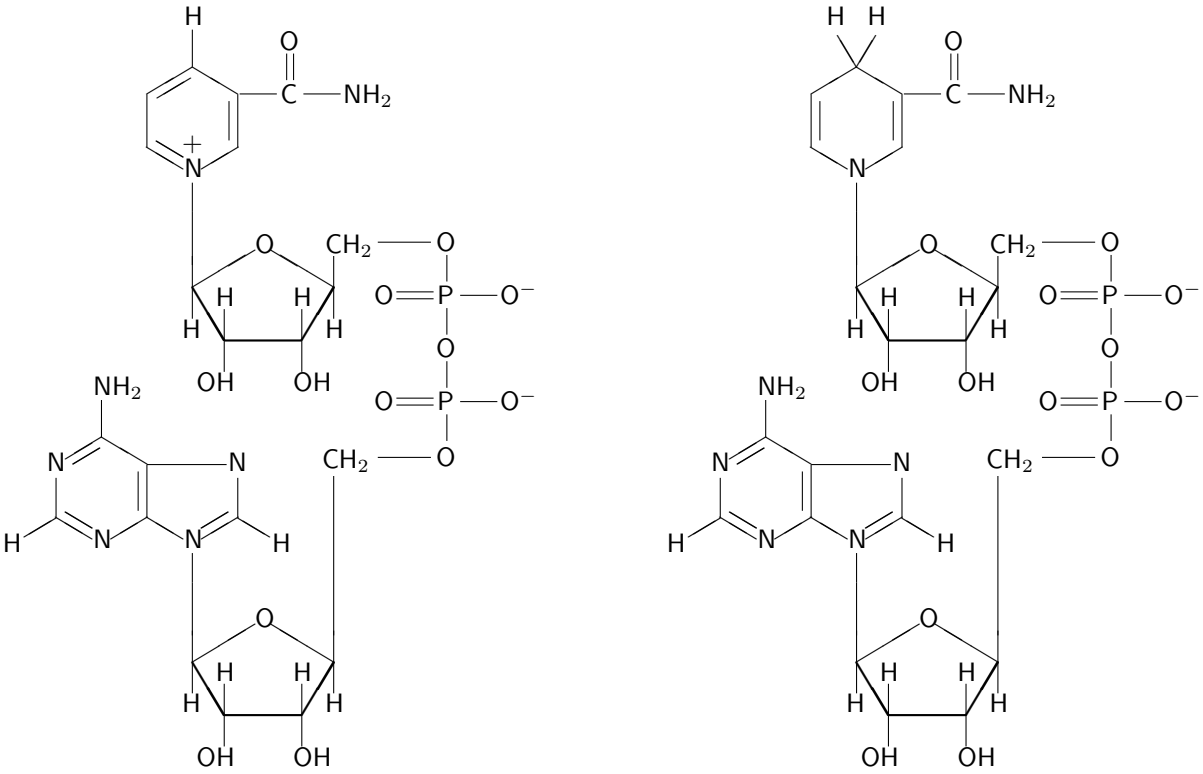
glucose, $C_6H_{12}O_6$, is oxidized to $6\,CO_2$ and $6\,O_2$ is reduced to $6\,H_2O$. Generally, in a combustion reaction (like above), the fuel is oxidized and oxygen is reduced.

6.2 NADH and the "Fall" of Electrons

If a glucose molecule were to release all its energy at once, it would be quite useless for the cell, as none of the energy would be harvested for use in cellular work. Therefore, the energy is released slowly when hydrogen atoms are stripped and passed to a coenzyme called NAD^+ or *nicotinamide adenine dinucleotide*. Therefore, the NAD^+ functions as an oxidizing agent during cellular respiration (thus it's reduced), and the reduced NADH donates its energy to cellular work via the electron transport chain and the resulting ATP synthesis.

Below left is the oxidized NAD^+. Note the lovely structure (it took over an hour to get all the \put commands right in LaTeX O.O). The double-ringed structure to the bottom left is adenine; there are also two five-carbon sugars and two phosphate groups. The ring and tail on the top is the nicotinamide group, which is the important part of the whole thing.

When $2[H]$ is added from food, it undergoes reduction and turns into the diagram to the right, NADH. Later, NADH gives the electrons to the electron transport chain and is oxidized back into NAD^+.



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6.3 Cellular Respiration I – Glycolysis

Glycolysis, which occurs in the cytosol, literally means "splitting of sugar" and does just that. Glucose, a 6-carbon sugar, is split into two 3-carbon sugars. These 3-carbon sugars are then oxidized and transformed into two molecules of pyruvate. The net yield of glycolysis is 2 ATP from substrate-level phosphorylation and 2 NADH.

Glycolysis is divided into two phases, the *energy investment phase* and the *energy payoff phase*.

In the energy investment phase, glucose enters the cell, is phosphorylated by 2 ATP (through *phosphoglucoisomerase* and *phosphofructokinase*) and then is split apart by aldolase into 2 *glyceraldehyde-3-phosphate*, or G3P.

In the energy payoff phase, 2 NAD^+ receive some electrons and H^+ from the 2 G3P and become 2 NADH. Then, in a series of steps, the resulting 2 *1,3-bisphosphoglycerate* molecules are converted to 2 pyruvate with the release of 4 ATP.

Each pyruvate then enters the mitochondrion through a transport protein. It goes through a complex series of enzymes, and after 1) releasing carbon dioxide, 2) reducing NAD^+ to form NADH, and 3) bonding to Coenzyme A (to make it more reactive), it converts to acetyl coenzyme A, or *acetyl CoA*. It is now ready to proceed to the Krebs Cycle.

6.4 Cellular Respiration II – Krebs Cycle

In the matrix of the mitochondrion, the acetyl CoA takes part in a secret ritual – the *Krebs Cycle*. No one knows what this strange name even means[9], let alone know the secret processes that occur in this terrible cycle. However, our Great Biology Book Of Doom seems to know, and it explains the Krebs Cycle thusly:

In the whole cycle, two carbons enter in the form of acetate and two carbons leave in the form of CO_2.

The acetyl CoA enters, is added to *oxaloacetate* (4 carbons) and releases CoA—SH to form *citrate*, a 6-carbon compound. This then is converted to *isocitrate* by the removal and addition of water; then α*-ketoglutarate* by the expulsion of carbon dioxide and the donation of an electrons and H^+ to NAD^+ to form NADH. The α-ketoglutarate emits another CO_2 and reduces another NAD^+ and then combines with the CoA—SH to form *succinyl CoA*. This releases CoA—SH, converts a GDP to GTP (which then powers the conversion of a ADP to ATP) and turns into *succinate*. Succinate sucks. Two hydrogens are transferred to FAD (flavin adenine dinucleotide) to form $FADH_2$ and the succinate turns into *fumarate*. Addition of water turns into into *malate*, which reduces another NAD^+ to NADH and changes to oxaloacetate, which starts the cycle all over again.

In summary, each turn of the Krebs Cycle releases 3 NADH, 1 $FADH_2$, and 1 ATP[10]. Since the beginning of celluar respiration, 8 NADH, 2 $FADH_2$, and 4 ATP have been produced from glucose. The NADH and $FADH_2$ now move to the inner mitochondrial membrane to go through the *electron transport chain*.

6.5 Cellular Respiration III – Electron Transport Chain

NADH donates electrons to the beginning of the electron transport chain, a flavoprotein containing a *flavin mononucleotide* (FMN). The flavoprotein then passes the electrons to Fe·S, an iron-sulfur protein. Then, the electrons reach a lipid called ubiquinone (Q). Meanwhile, $FADH_2$ donates electrons to the electron transport chain at Q since the electrons on $FADH_2$ have less potential energy than those on NADH.

While the electrons travel through each successive protein in the electron transport chain, their energy is slowly released to pump hydrogen ions (H^+) from the matrix to the intermembrane space in the mitochondrion.

After reaching Q, the electrons go through another multiprotein complex, containing two cytochromes and another iron-sulfur protein. They then go to *cytochrome C* and are taken to another multiprotein complex, this one containing two more cytochromes. Finally, the electrons are added to $2\ H^+ + 1/2\ O_2$ to form water.

[9] Actually, it's named after Hans Krebs who discovered it. But that's no fun.
[10] Since there are two pyruvates, the actual net output is 6 NADH, 2 $FADH_2$ and 2 ATP.

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All the energy that is released in the electron transport chain pumps a bunch of hydrogen ions across the inner mitochondrial membrane. The resulting H^+ (electrochemical) gradient then creates a *proton-motive force* across the membrane, causing H^+ to diffuse through ATP synthase and thus generate the conversion of ADP + P_1 to ATP through a process called *oxidative phosphorylation*.

In total, glycolysis generates about 2 ATP; Krebs cycle generates another 2 ATP, and the electron transport chain and oxidative phosphorylation generates about 34 ATP. Therefore, cellular respiration of one glucose molecule yields a maximum of 38 ATP. However, the actual total is rarely this high because of several reasons, including "accidental" diffusion of hydrogen ions across the inner mitochondrial membrane itself, without going through ATP synthase.

6.6 Fermentation

Food can also be oxidized without oxygen through a process called *fermentation*. In anaerobic (oxygen-less) conditions, organisms are forced to undergo fermentation to produce energy. Since only glycolysis can work in anaerobic conditions, then each molecule of glucose will only produce 2 ATP, making fermentation very inefficient.

In *alcoholic fermentation*, pyruvate is converted to ethanol by releasing carbon dioxide and being reduced by the 2 NADH produced by glycolysis. This way, the supply of NAD^+ is regenerated for use in glycolysis and 2 ATP is generated. An organism that uses alcoholic fermentation is yeast; the released carbon dioxide is why you see bubbles in baked bread.

In *lactic acid fermentation*, pyruvate is directly reduced by 2 NADH to form lactate, a mild poison. Meanwhile, the NAD^+ reserve is regenerated and 2 ATP is released. The lactate is converted back to pyruvate in the liver. Human muscles cells undergo lactic acid fermentation when oxygen is scarce.

Fermentation is used in the brewing of beer. Like writing biology guides, beer makes one insane. Bear sounds like beer, and bears are cute. Therefore, fermentation is cute.

6.7 Other Pathways and Feedback Mechanisms

Cellular respiration does not have to utilize glucose as fuel. For example, proteins can be hydrolyzed into amino acids, which can be converted to pyruvate, acetyl CoA, or can feed into the Krebs cycle. Carbohydrates can be broken down into monosaccharides and undergo glycolysis. Fats can be broken down into glycerol and fatty acids, the former converted into G3P and the latter broken apart by *beta oxydation* into 2-carbon fragments which enter the Krebs cycle as acetyl CoA. Fats are excellent fuel.

Intermediate compounds in the Krebs cycle can also be siphoned away and modified to make many other organic molecules such as amino acids in a process called *biosynthesis*. Glucose can be made from pyruvate, and fatty acids can be made from acetyl CoA.

Feedback mechanisms control cellular respiration so that the cell does not waste more of a substance than it needs. For example, in an anabolic pathway (i.e. biosynthesis), an excess of a particular product amino acid can prompt an enzyme that steals a certain compound from the Krebs cycle to stop working. Also, the cell can control its catabolism – an excess of ATP can inhibit phosphofructokinase way back in glycolysis; citrate from the Krebs cycle also inhibits the same enzyme. An excess of AMP (adenosine monophosphate) means that energy is scarce in the cell and so stimulates phosphofructokinase.

Overall, cellular respiration is cool. Yay.

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7 Photosynthesis

Si j'étais président de la République... je mangerais vos biscuits.

Autotrophic organisms, or those that acquire all the energy they need from carbon dioxide and other inorganic raw materials, are the major sources of organic compounds for all nonautotrophic organisms. For this reason, they are referred to as the *producers* of the biosphere. Many autotrophs, called *photoautotrophs*, convert light energy from sunlight into chemical energy in a process called *photosynthesis*.

7.1 Structures Involved in Photosynthesis

All green parts of a plant have chloroplasts and therefore are able to undergo photosynthesis, but leaves are the major sites in most plants. Chloroplasts are mainly found in the *mesophyll* cells, or the tissue in the interior of the leaf. Carbon dioxide enters the leave and oxygen exits it through pores on the leaf's surface called *stomata* which are flanked by *guard cells*. Water absorbed by the roots are delivered to the cells through veins.

As a review, recall that a chloroplast has two membranes and stacks of *thylakoids* called *grana* (singular: *granum*) inside, surrounded by a fluid called the *stroma*.

The general equation for photosynthesis is $6\ CO_2 + 12\ H_2O + \text{Light Energy} \longrightarrow C_6H_{12}O_6 + 6\ O_2 + 6\ H_2O$.

7.2 The Light Reactions

We will begin our investigation of the first "half" of photosynthesis, the light reactions, by looking at the nature of light. Light is a form of energy known as *electromagnetic radiation* and travels in squiggly waves. The distance between the crests of these waves is called the *wavelength*, and range from less than a nanometer (gamma rays) to over a kilometer (radio waves). The entire range of radiation is called the *electromagnetic spectrum*. Between about 380 and 750 nanometers lies visible light, which is most important in our study of photosynthesis.

Light also behaves like a stream of particles called *photons*. These small bundles of energy are what fuels the conversion from light energy to chemical energy in photosynthesis.

Plants are able to absorb light energy through photosynthetic pigments, the most notable of which is *chlorophyll*. There are two types of chlorophyll, α and β, both of which absorb best in the bluish and orange-red range of the spectrum of visible light and worst in green (that's why leaves appear green; the green light isn't absorbed). An *action spectrum* that plots the rate of photosynthesis versus the wavelength of light seems to show that this is the case. Other pigments, called *accessory pigments*, help broaden the range of light absorbed a bit; however, their most important function seems to be to absorb excess light energy that may otherwise damage chlorophyll. Examples of accessory pigment include *carotenoids*.

Chlorophyll consists of a porphyrin ring attached to a hydrocarbon tail. When a photon hits a chlorophyll molecule, an electron becomes excited for a while and then when it drops down to its *ground state*, it releases some heat and another photon, which strikes another chlorophyll molecule nearby. Chlorophyll, along with other pigment molecules, is organized into *photosystems*, which provides an array of pigment molecules for light to strike and bounce around until it reaches the *reaction center*, which is composed of a *reaction-center chlorophyll* and a *primary electron acceptor*. After the reaction-center chlorophyll is hit with a photon, it donates its excited electron to the primary electron acceptor.

There are in fact two different types of photosystems that cooperate in the light reactions. *Photosystem I* absorbs best at a wavelength of 700 nm, whereas *Photosystem II* absorbs best at a wavelength of 680 nm.

The light reaction begins when a photon of light energy strikes Photosystem II, bouncing along the numerous pigment molecules until it reaches P680, the reaction-center chlorophyll. Two electrons from P680 are excited and hop to the primary acceptor; these are replenished in P680 by the splitting of water to form hydrogen ions and oxygen gas. Meanwhile, the electrons in the primary

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acceptor go down an electron transport chain where they provide energy for the synthesis of ATP through a proton gradient (and proton-motive force) like described above in cellular respiration.

While all that is happening, a photon also strikes Photosystem I, exciting two electrons in P700 (its reaction-center chlorophyll) which hop to the primary acceptor. The electrons from Photosystem II that are "worn out" after the electron transport chain replenish the departee electrons in P700.

The electrons in the primary acceptor of Photosystem I now can go to one of two paths. In *noncyclic electron flow*, they travel down another electron transport chain, where they end up in an enzyme called $NADP^+$ reductase which adds them to $NADP^+$ to form NADPH, which temporarily stores the energy in the electrons.

In *cyclic electron flow*, the electrons go back to the first electron transport chain, which uses their energy to generate ATP, and finally arrive back at P700 to be excited again. Cyclic electron flow is used because the next step, the Calvin Cycle, needs more ATP than NADPH and noncyclic electron flow creates the same amount of each.

7.3 Calvin Cycle

The Calvin Cycle uses the ATP and NADPH produced in the light reactions to create a sugar, glyceraldehyde-3-phosphate (G3P). This sugar can be later used to form many organic compounds including glucose.

To start off the cycle, three carbons from 3 CO_2 are added to 3 *ribulose bisphosphate* (RuBP) by the enzyme *rubisco* to form 6 molecules of *3-phosphoglycerate*. Then, phosphorylation by 6 ATP converts them to 6 *1,3-bisphosphoglycerate*, which then is reduced by 6 NADPH into 6 molecules of *glyceraldehyde-3-phosphate*, or G3P. One G3P is output and used to create glucose and other organic compounds. The rest are changed back to 3 molecules of RuBP by consuming 3 ATP, and the cycle begins anew. Note that each turn of the cycle actually only fixes 1 carbon dioxide; we are looking at it three turns at a time so that we can have meaningful output after each cycle.

7.4 Alternative Carbon Fixation Mechanisms

On hot, arid days, plants are often faced with a problem: if they leave their stomata open, they will lose too much water through transpiration; if they close their stomata, they won't be able to intake enough carbon dioxide to proceed with photosynthesis. Several alternative mechanisms have been developed to fix this problem.

In C_3 plants, those that go through the cycle illustrated above, a process called *photorespiration* occurs. When oxygen concentrations overtake carbon dioxide concentrations, rubisco adds oxygen to the Calvin cycle instead of carbon dioxide. This causes a two-carbon compound to leave the chloroplast (instead of the 3-carbon G3P) which then is converted to CO_2 by mitochondria and peroxisomes. This completely wastes the organic material because it produces no ATP and no food, and so decreases photosynthetic output.

C_4 plants have evolved to overcome this difficulty in a more advanced way – they go through an alternate mode of carbon fixation that produces a 4-carbon compound as its first product. In C_4 plants, *bundle-sheath* cells are tightly packed around the veins of the leaf, and are the sites for the Calvin cycle. Between the bundle-sheath cells and the leaf surface lie the mesophyll cells. The mesophyll cells absorb carbon dioxide from the air and incorporate it into oxaloacetate (4-carbon) using the enzyme *PEP carboxylase*, which has much more of a carbon dioxide affinity than rubisco and therefore can still incorporate CO_2 when the stomata are closed. The oxaloacetate then is converted to malate, which then gives off CO_2 to be used in the Calvin Cycle. The remaining pyruvate is converted to PEP through phosphorylation and ready to accept CO_2 once again.

Another adaptation to arid conditions has evolved in succulent plants, including cacti and pineapples. This mode of carbon fixation is called *crassulacean acid metabolism*, or CAM. Stomata of CAM plants open at night, when the rate of transpiration is much less, and incorporate carbon dioxide into a variety of organic acids. Then, during the daytime, the stomata close and the organic acids supply the carbon dioxide needed for the Calvin cycle.

Woohoo, now we're done. Time to have some fun. In the sun. With the... CELLCYCLE!

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8 The Cell Cycle

I see the light at the end of the tunnel... it is very bright indeed! Huzzah!

8.1 Introduction

A cell's endowment of DNA as a whole is called its *genome*. Although each cell has so much DNA (a typical human cell has 3 m of it), replication is possible due to the packaging of DNA into *chromosomes*. Each species has a characteristic number of chromosomes in each cell nucleus. *Somatic cells* are non-reproductive cells, and in every human being, they contain 46 chromosomes. Reproductive cells, or *gametes*, contain 23 chromosomes in humans, half the number of somatic cells.

Prior to condensation into chromosomes, the DNA of a cell is in a form known as *chromatin*, which includes DNA and various proteins. When a cell prepares for division, the chromatin duplicates and condenses into a double-stranded *chromosome*, which is composed of two identical *sister chromatids* joined at a region known as the *centromere*.

8.2 Interphase

The actual division of a somatic cell, karyokinesis or mitosis, is just one small part of the cell cycle. Most of a cell's life is spent in *interphase*, which contains three different phases: G_1, S, and G_2. In the G_1 phase, the cell grows a bit; chromatin is duplicated in the S phase, and in the G_2 phase, the cell grows some more and prepares for mitosis. The cell's progress through these phases is regulated by the *cell cycle control system*, consisting of three *checkpoints* that require go-ahead signals to continue.

The first of these checkpoints and the most important one is the G_1 checkpoint, located in the G_1 phase. This checkpoint seems to dictate what the cell does – if the cell receives the go-ahead signal at this point, it is basically destined to divide; if the cell does not receive the signal; it goes into a nondividing state called the *G_0 phase*.

The events of the cell cycle are paced by fluctuations in the abundance and activity of certain cycle control proteins, which are divided into two main classes. *Protein kinases* activate or deactivate other proteins by phosphorylating them and give the go-ahead signals at the G_1 and G_2 checkpoints. These kinases, called *cyclin-dependent kinases*, or Cdks, are naturally in an inactive form and must be attached to a *cyclin* to become active. The activity of a Cdk fluctuates according to the changes in concentration of its cyclin partner.

One cyclin-Cdk complex, MPF or *maturation-promoting factor*, triggers the cell's passage past the G_2 checkpoint and into mitosis. MPF then degrades its cyclin which detaches from the Cdk, inactivating it.

8.3 Mitosis

Mitosis is usually broken down into five subphases.

In *prophase*, chromatin begins to coil into chromosomes, the nucleoli disappear, and the mitotic spindle begins to form and push the centrosomes to opposite ends of the cell.

In *prometaphase*, the nuclear envelope fragments. The spindle microtubules interact with the of the condensed chromosomes. Each sister chromatid in a chromosome has a *kinetochore* on the centromere, which connects to kinetochore microtubules. Nonkinetochore microtubules from one end of the cell interact with those at the other end.

In *metaphase*, the centrosomes are now at opposite ends of the cell. All the chromosomes are lined up at an imaginary plane on the middle of the cell, called the *metaphase plate*.

In *anaphase*, the sister chromatids separate and become known as single-stranded chromosomes. These chromosomes are pulled to opposing ends of the cell by kinetochore microtubules. Meanwhile, nonkinetochore microtubules interact with each other and make the cell longer.

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In *telophase*, the nuclear envelopes reform, the chromosomes begin condensing, and the cells prepare for cytokinesis. In animal cells, a *cleavage furrow* caused by a contractile ring of actin microfilaments forms on the metaphase plate and begins to pinch the cells apart. In plant cells, vesicles containing cell wall material form along the metaphase plate and fuse together to form a *cell plate*, which eventually separates daughter cells.

Mitosis may have evolved from a simpler type of cell division found in bacteria called *binary fission*. In binary fission, the single bacterial chromosome is replicated starting from the *origin of replication* and then move apart. Meanwhile, the plasma membrane grows inward in the middle of the cell, and finally the two daugher cells come apart.

8.4 Cell Cycle Regulation

In addition to the checkpoints mentioned earlier, the cell cycle is also regulated by internal and external signals. Internal signals include one that delays anaphase until all the kinetochores on chromosomes are connected to spindle microtubules. External signals include *growth factors*, which are proteins released by certain cells that stimulate others to divide.

Density-dependent inhibition of cell division is a phenomenon in which crowded cells stop dividing. *Anchorage dependence* means that cells must be attached to a non-cell substratum to divide. Cancerous cells do not exhibit either of these dependences, and thus they divide excessively and invade other tissues.

Transformation is the process in which a normal cell turns into a cancer cell. If the cancer cell grows unchecked, it will develop into a tumor. A *benign* tumor occurs when the abnormal cells remain at the original site; however, when the cells *metastasize* and travel throughout the body, a *malignant tumor* forms and could lead to death.

9 Meiosis and Sexual Life Cycles

Back in the day, when men were real men, women were real women and nonkinetochore microtubules were REAL nonkinetochore microtubules...

9.1 Introduction

Like begets like. The transmission of traits from one generation to another is called *inheritance* or *heredity*. The inherited traits are coded in *genes*, which are segments of DNA located at specific points on a chromosome called *loci*.

Actually, "like begets like" only applies to asexual reproduction, or mitosis, in which each daughter cell is identical to its parent. In sexual reproduction, through a process called *meiosis*, variation is introduced in offspring.

A *karyotype* is an organized display of all the chromosomes in the cell. *Homologous chromosomes*, or chromosomes that define the same traits, are grouped together. Note that *somatic cells*, or cells that aren't gametes, are *diploid* and have 46 chromosomes – 22 pairs of homologous *autosomes* and 2 *sex chromosomes*. In humans, the sex chromosomes are grouped together. Recall that females have XX and males have XY.

Gametes, or sex cells, are the product of meiosis and are *haploid* and have a single set of the 22 autosomes and one sex chromosome. The union of gametes is called *fertilization* or *syngamy*. The resulting fertilized egg, or *zygote*, is diploid.

9.2 Various Sexual Life Cycles

In animals, the multicellular individual is diploid. A male and female multicellular individual produce haploid gametes through meiosis whicih combine through fertilization to form a diploid zygote, which then undergoes mitosis to become the multicellular individual.

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In most fungi and some algae, the multicellular organism is haploid and produces gametes through mitosis. Two of these gametes combine to form a diploid zygote, which then undergoes meiosis to form haploid cells that undergo mitosis to reform the multicellular organism.

Plants and some algae go through a type of life cycle called *alternation of generations*, in which there is both a haploid multicellular organism called the *gametophyte* and a diploid multicellular organism called the *sporophyte*. The haploid gametophyte produces haploid gametes by mitosis, which combine to form a diploid zygote which matures into the sporophyte. The sporophyte then produces spores through meiosis which undergo mitosis to become the gametophyte.

9.3 Meiosis

Meiosis reduces the chromosome number from diploid to haploid. This is important because if two diploid gametes were to fertilize, the resulting organism would be *quadruploid*, and each generation would have twice the number of chromosomes as the last. This would suck to be the organism.

Meiosis has one DNA replication but two consecutive cell divisions, called *meiosis I* and *meiosis II*. This results in four haploid daughter cells.

In *interphase* that precedes meiosis, each chromosome replicates and attaches to its identical sister chromatid at its *centromere*.

In *prophase I*, the chromosomes begin to condense, and in a process called *synapsis*, homologous chromosome pairs are joined by the *synaptonemal complex* to form *tetrads* which look like XX. At places called *chiasmata*, chromatids of homologous chromosomes are crossed and trade segments. This *crossing over* is important for introducing variation to the offspring. Meanwhile, the nuclear envelope and nucleoli fragment and spindle microtubules that are forming connect to the kinetochores on the chromosomes.

In *metaphase I*, the tetrads are lined up at the *metaphase plate*. A kinetochore microtubule from one pole is connected to the kinetochore of one chromosome in the tetrad, and a microtubule from the other pole is connected to the kinetochore of the other chromosome.

In *anaphase I*, the double-stranded chromosomes forming the tetrad split apart, bringing one double-stranded chromosome to each pole for each tetrad. Note that the sister chromatids are still attached.

In *telophase I*, cytokinesis occurs – cleavage furrows and cell plates form. There is no further replication of genetic material.

Meiosis II is very similar to Mitosis.

In *prophase II*, a spindle apparatus forms and attaches to the kinetochores of each sister chromatid. In *metaphase II*, the chromosomes are aligned at the metaphase plate. In *anaphase II*, the centromeres of sister chromatids separate, bringing individual single-stranded chromosomes to each pole. In *telophase II*, nuclei reform and cytokinesis occurs. Now we have four haploid daughter cells.

9.4 Genetic Variation

Sexual life cycles introduce genetic variation among offspring. They do this by three aways:

Independent assortment of chromosomes along the metaphase plate in both meiosis I and II cause different combinations of mother and father chromosomes in the daughter cells. The number of different daughter cells that can be produced is equal to 2^n, where n is the haploid number of chromosomes.

Crossing over occurs during prophase I, which enables both mother and father genes to appear in the same gamete. Crossing over produces *recombinant chromosomes*.

Random fertilization is due to the chance that any sperm can fertilize the egg. Since each sperm and each egg can have one of over 8 million different possibilities for chromosome combinations, the number of possibilities is simply astronomical.

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10 DNA

Watson and Crick came up with a double-helical model for DNA in 1953. Griffith discovered the idea of *transformation*, or a change in genotype and phenotype due to assimilation of external DNA by a cell. Hershey and Chase discovered that genetic information was located on nucleic acids, not protein. Chargaff showed that in all species, the proportions of the four nucleotide bases are in a characteristic ratio – $\%$ A $\approx \%$ T and $\%$ G $\approx \%$ C.

10.1 Structure of DNA

DNA is double-stranded and is arranged in a *double helix*. The backbones of the DNA strands are made of alternating 5-carbon sugar (in DNA, deoxyribose; in RNA, ribose) and phosphate groups. The sugars are attached to *nitrogenous bases* which are attached to the bases on the other strand through hydrogen bonds.

The nitrogenous bases are adenine (A) and guanine (G), which are double-ringed *purines*, and thymine (T), and cytosine (C), which are single-ringed *pyrimidines*. Adenine only hooks with thymine and guanine only hooks with cytosine, therefore explaining Chargaff's rules.

The two strands in DNA are *antiparallel*, which means that they are parallel but go in different directions. Each strand as a 3' end and a 5' end; the 3' end is a hydroxyl group at the end of a ribose and the 5' end is a phosphate group. On one strand, the 3' end is on the "top", and on the other strand, the 3' end is on the "bottom" of the structure.

RNA, another nucleic acid, is like DNA, but there are several major differences. Firstly, RNA is single-stranded. Like DNA, RNA has four different nitrogenous bases; however, T is replaced by uracil in RNA. Therefore, in RNA, adenine bonds with uracil and guanine bonds with cytosine.

10.2 DNA Replication

During DNA replication, what basically happens is the two DNA strands separate, then some nucleotides come by and attach to the base pairs on both strands of DNA, and then we are left with two identical strands of DNA.

Several models have been proposed for how DNA replicates; the *conservative model* says that the parent DNA strand emerges from the replication process intact; the *semiconservative model* (which we now know is true) says that the parent strand gives one strand to each resulting replication; the *dispersive model* says that each strand strand of both daughter molecules contain a mixture of old and new parts. The Meselson-Stahl experiment proved that the semiconservative model was correct.

The replication of DNA starts at special sites called *origins of replication*. Bacteria have only one origin of replication because it has one strand of DNA; eukaryotic replication could have hundreds of thousands of origins of replication. Once an origin of replication is identified, a *replication bubble* forms which spreads in both directions until all the bubbles meet and the whole strand is replicated. At either end of a bubble is a *replication fork*, a Y-shaped region where the new strands of DNA are elongating.

Elongation of DNA is catalyzed by *DNA polymerases*. Each nucleotide before joining an existing strand is actually what is called a *nucleoside triphosphate*, which resembles ATP except the sugar is deoxyribose instead of ribose.

DNA polymerase breaks off two phosphate groups and uses the energy released to link the other phosphate group to the sugar on the 3' end of the strand. This is why DNA strands can only elongate on the 3' end. The two phosphates broken off, called *pyrophosphate*, then breaks down into two inorganic phosphate molecules.

Because DNA polymerase can only attach nucleotides to the 3' end of a DNA strand, one side of the DNA fork, called the *leading strand* will be easily written in one continuous strand. However, the other side, the *lagging strand*, runs in the opposite direction and so must be written in lots of little segments called *Okazaki fragments*[11] These fragments are usually about 100 to 200 nucleotides long and are linked together by *DNA ligase*.

[11] As the DNA unzips at the replication fork, the leading strand can just keep on adding nucleotides, but the lagging strand must start writing at the replication fork and proceed *away from it*. That's why there needs to be so many fragments.

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DNA polymerase cannot start DNA synthesis; it can only add more nucleotides on the end of an already existing strand. Starting DNA replication is done by *primase*, which first joins RNA nucleotides to the parental strand in a small fragment called the *RNA primer*. Then, DNA polymerase joins DNA nucleotides to the end of that primer. Finally, a different DNA polymerase replaces the RNA primer with a DNA segment.

Other enzymes involved in DNA replication include *helicase*, which unwinds the double helix, and *single-strand binding protein*, which holds the two strands apart during replication.

10.3 DNA Repair

During DNA replication, DNA polymerase itself checks to see if the nucleotide added was the right one; if not, it replaces it. This is a simple form of proofreading that fixes many errors that could develop.

Mismatch repair fixes problems that occur after DNA synthesis. A *nuclease* first cuts the damaged DNA strand at two points; *DNA polymerase* then fills the gap, and finally *DNA ligase* seals the newly added strand to the original strand. This type of repair is called *nucleotide excision repair*. One common type of damage is a *thymine dimer*, or a covalent bond between adjacent thymine nucleotides.

Another potential problem that arises from the DNA replication process is due to the ability of DNA polymerase to only add nucleotides to 3' ends of strands. Therefore, the RNA primer that appears on the 3' end of the lagging strand cannot be replaced by DNA. This causes the DNA strand to shorten with each replication, which is potentially dangerous. However, the cell minimizes the effects of this problem by having really long useless nucleotide sequences at the ends of DNA molecules called *telomeres*. In humans, telomeres are usually the sequence TTAGGG. When telomeres get too short, they are elongated by an enzyme called *telomerase*. Telomerase isn't found in all cells and therefore may be a limiting factor in organism life span.

11 From Gene to Protein

The relationship between genes and proteins can be easily and somewhat inaccurately described as the *one gene–one polypeptide hypothesis*. In a cell, there are two processes involved in creating a gene from a protein: *transcription* synthesizes messenger RNA from DNA in the nucleus, and *translation* synthesizes a polypeptide based on the transcribed mRNA. Translation occurs in ribosomes.

11.1 Transcription

Transcription is divided into three phases: initiation, elongation, and termination.

Specific sequences of nucleotides along the DNA strand tell *RNA polymerase* where to start and stop transcription. The DNA sequence where RNA polymerase attaches is called the *promoter*; the sequence that signals end of transcription is called the *terminator*. Eukaryotic promoters often include a nucleotide sequence called a *TATA box*. The stretch of DNA that is to be transcribed into an RNA molecule is called the *transcription unit*.

In eukaryotes, several proteins called *transcription factors* help with the binding of RNA polymerase and the initiation of transcription. These transcription factors usually attach to the promoter. The whole complex consisting of transcription factors and RNA polymerase attached to the promoter is called the *transcription initiation complex*. Transcription is now ready to commence.

During *elongation*, RNA polymerase moves down the DNA double helix, unzipping and rezipping the helix as it goes along. It continually elongates the RNA transcript which peels away from its DNA template.

Finally, when the RNA polymerase transcribes a terminator sequence, it stops transcribing soon afterwards. RNA polymerase leaves the DNA strand and the RNA strand detaches from its DNA parent strand.

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11.2 RNA Processing

Before the transcribed RNA can leave the nucleus, it must undergo special modifications through *RNA processing*.

One of the modifications is alteration of both ends of the mRNA. On the 5' end, a *5' cap*, made from a modified form of a guanine nucleotide, is added to protect the mRNA from degradation and also used as a "attach here" sign for ribosomes once the mRNA leaves the nucleus. On the 3' end, a *poly(A) tail* is added, consisting of lots and lots of adenine nucleotides. The poly(A) tail probably has the same function as the 5' cap.

A major part of RNA processing is *RNA splicing*, in which noncoding segments in the RNA strand, called *introns*, are excised and the remaining *exons* are spliced together[12]. The signals for RNA splicing are located at the ends of introns. Little thingies called *small nuclear ribonucleoproteins* or *snRNPs* (pronounced "snurps") recognize these splice sites. snRNPs contain some snRNA and some protein. Several different snRNPs join with more proteins to form a complex called a *spliceosome* which interacts with the splice sites at the ends of an intron. It then cuts at specific points to release the intron, and joins together the two exons on both sides.

In some organisms, the intron RNA catalyzes its own excision. Wow, nucleic acids can catalyze reactions too! The RNA molecules that function as enzymes are called *ribozymes*.

Why are there introns when they are thrown away anyway? Perhaps introns separate protein *domains*, which are areas of distinct structure and function in a protein. Or perhaps under different circumstances, different segments of the DNA are designated as introns and therefore one gene could be used to create more than one protein.

The processed mRNA now leaves the nucleus to fulfill its purpose in life.

11.3 Translation and Protein Synthesis

In translation the cell interprets the mRNA and builds a protein accordingly. The interpreter is *transfer RNA*, or tRNA. The function of tRNA is to transfer amino acids to a ribosome.

On the mRNA strand, each codon, or group of three nucleotides, defines an amino acid. There are about 64 different codons possible; three of them are stop codons (that stop translation) and one is a start codon.

tRNA consists of a single RNA strand that is about 80 nucleotides long. It folds to a L-shaped structure, with the amino acid attachment site on one side and the anticodon on the other. tRNA's 2-dimensional structure is cross-shaped, with loops at the ends of three points of the cross and the amino acid attachment site on the fourth point. There are about 45 varieties of tRNA; some varieties of tRNA can match with more than one codon through a relaxation of base-pairing rules called *wobble*.

tRNA and an amino acid arrive at an enzyme called *aminoacyl-tRNA synthetase* and through phosphorylation by ATP, are bonded together, forming an *aminoacyl tRNA*, which is now free to go to the ribosome. When tRNA arrives at a ribosome, the anticondon will match with its counterpart on the mRNA strand (for example: a tRNA with an anticodon of AAA will match with a codon (nucleotide triplet) on the mRNA strand of UUU.

Ribosomes are made up of proteins and *ribosomal RNA*. The subunits of ribosomes are made in the nucleoli. A ribosome has two parts, a *large subunit* and a *small subunit*. The large subunit has three sites: the P site (*peptidyl-tRNA site*) holds the tRNA carrying the growing polypeptide chain; the A site (*aminoacyl-tRNA site*) holdes the tRNA carrying the next amino acid to be added to the chain. Discharged tRNAs leave the ribosome from the E site (*exit site*).

Basically, translation is devided into three stages: initiation, elongation, and termination.

In *initiation*, a small ribosomal subunit binds to the mRNA. The initiator tRNA containing the anticodon UAC pairs with the start codon, AUG. The first amino acid in a polypeptide sequence is therefore always Met. A large ribosomal subunit then arrives and attaches to the small subunit by the expenditure of GTP, forming a *translation initiation complex*.

In *elongation*, a tRNA recognizes and attaches to the mRNA codon in the A site with the expenditure of GTP. Then, the existing

[12] Remember that EXons are the pieces that eventually EXit the nucleus. INtrons are left behind IN the nucleus.

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chain on a tRNA in the P site transfers to the tRNA in the A site. Both tRNAs shift down a site; the tRNA that was in the P site is now in the E site and detaches. The tRNA that was in the A site is now in the P site and is attached to the whole polypeptide chain. The process can now repeat.

In *termination*, a *release factor* recognizes the stop codon, and when it enters the A site, it hydrolyzes the bond between the tRNA in the P site and the attached polypeptide chain. The polypeptide chain is now free, and the whole structure disassembles.

Typically, a single strand of mRNA is used to make lots of copies of a polypeptide simultaneously through strings of ribosomes called *polyribosomes* working on it at the same time.

When a polypeptide is translated, some *posttranslational modifications* must be applied before it can be used as a protein. Sometimes, at the end of a polypeptide, there is a *signal peptide* that must be removed. It binds to a protein-RNA complex called a *signal-recognition particle* (SRP; its RNA is called SRP RNA) which then attaches to a SRP receptor protein on the endoplasmic reticulum. Then, the polypeptide goes into the ER and its signal peptide is removed. The ER can now transport it to the Golgi apparatus which then can send it where it belongs.

In prokaryotes, transcription and translation can occur at the same time since the DNA strand is located in the cytosol as well. As RNA polymerase moves down the DNA strand, a polyribosome can attach to the growing mRNA strand and begin creating many copies of the polypeptide.

11.4 The Control of Gene Expression

How are bacteria able to cope with the rapid changes in environment? For example, a *E. coli* cell living in the human colon is utterly dependent on the contents of the human's meal. If the bacterium is deprived of the amino acid tryptophan, it will activate a metabolic pathway that synthesizes the compound. However, if the human eats a tryptophan-rich meal, the bacteria does not need to waste resources to produce its own and so stops the pathway. How do bacteria do this?

The five genes coding for the polypeptide chains that catalyze the production of tryptophan are clustered together and are served by a single promoter, making all five a single transcription unit. An "on-off switch" called the *operator* is located within the promoter or between the promoter and the enzyme-coding genes helps to regulate the access of RNA polymerase to the genes and therefore the whole pathway. All together, the promoter, the operator, and the genes they control is called an *operon*. We are now looking at the *trp* operon.

The *trp* operon can be switched off by a protein called the *repressor*, which binds to the operator and blocks atachment of RNA polymerase to the promoter. The repressor is coded in an inactive state by a *regulatory gene* outside the operon. In the presence of tryptophan, the repressor is activated and binds to the operator, switching the operon off. Tryptophan functions in this sytem as a *corepressor*.

The *trp* operon is said to be a *repressible operon* because its transcription is *inhibited* when a small molecule (tryptophan) binds to a regulatory protein. An *inducible operon*, however, is *stimulated* when a specific small molecule binds to a regulatory protein.

This is the case in the *lac* operon, which creates enzymes to metabolize lactose. In the *lac* operon, the regulatory gene codes for an *active* repressor, which immediately binds to the operator in the promoter and prevents synthesis of the *lac* enzymes. However, allolactose, an isomer of lactose, allosterically inhibits the repressor, so in the presence of allolactose, the operon is activated.

Although the presence of allolactose does let the *lac* operon work, it can't really be considered an inducer because it only indirectly does its job – it deactivates a repressor. An example of positive gene regulation lies also in the *lac* operon. In the presence of the small molecule *cyclic AMP* (cAMP), a certain regulatory protein, the *cAMP receptor protein* or CRP, is activated. The CRP then binds to a site on the *lac* promoter and makes it easier for RNA polymerase to bind to the promoter and start transcription. Therefore, an increase in concentration of cAMP will directly cause an increase in production of the lactose-metabolizing enzymes.

11.5 Mutations

Mutations are changes in genetic material. We will now look at *point mutations*, or chemical changes in just one base pair.

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A *base-pair substitution* is where one base pair is replaced by another. It can be a *missense mutations*, or the codon still codes for an amino acid but not the right one; or a *nonsense mutation*, which changes an amino acid codon to a stop codon and therefore leads to a nonfunctional protein.

Insertions and *deletions* are additions or losses of nucleotide pairs in a gene. They can cause a *frameshift mutation*, or the whole pattern of codons is changed. For example, in the sentence "THE BIG RED DOG ATE THE CAT," if the G in "BIG" is removed, the sentence would become "THE BIR EDD OGA TET HEC AT," which is nonsense. Unless they are near the end of a gene, frameshift mutations almost always lead to a nonfunctional protein.

Mutations can be caused by physical and chemical agents called *mutagens*.

12 Animal Reproduction

We're getting closer to the end of this guide now!

Let's take a little break. Take a deep breath, and imagine yourself lying on a soft, warm beach, with the palm trees swaying in the wind and water lapping on the shores around you. You can hear soft sounds of a beautiful violin melody. Gently rub your shoulders against the soft sand and take a sip of deliciously fresh coconut milk. It is sweet and cool on your tongue.

Then, calmly remember that you have a biology final coming up very very soon, and watch as scorpions come out of the searing hot sand and sting you repeatedly and the sky suddenly turns black. You can now hear thunder and see lightning flashes all around you. Then a swarm of vampire bats come and attack your face, sucking out all your blood through your eyelids. You scream and scream to no avail, and finally, a bolt of lightning strikes your gonads and you die a violent, gruesome death.

Oops. I forgot that I was supposed to calm you down; I got a little carried away. Sorry about that. :(

12.1 Gametogenesis

Spermatogenesis, or the production of mature sperm cells, is a continuous process in the human male. It occurs in the seminiferous tubules of the testes. The stem cells that give rise to sperm, *spermatogonia*, divide repeatedly by mitosis and produce many replications. Then, one spermatogonium, called the *primary spermatocyte*, differentiates and goes through meiosis I to form two *secondary spermatocytes*. These then undergo meiosis II to form *spermatids* which differentiate into *spermatozoa*, or sperm cells.

Oogenesis is the development of ova – mature, unfertilized egg cells. In the developing female embryo, *oogonia* multiply and then begin meiosis but the process stops at prophase I. The cells at this stage are called *primary oocytes*. On the onset of puberty, they complete meiosis I to form *secondary oocytes*. It is the secondary oocytes that are released from the ovary. When a secondary oocyte is fertilized, meiosis completes and it finally becomes an ovum.

There are so many jokes we can make about Nish and gametogenesis, but they probably wouldn't be appropriate here and so we won't mention them. These lines are just to waste your printer ink. Wastewastewaste hehe save a tree kill a whale. The combustion of Barney yields carbon dioxide and water because Barney is a hydrocarbon.

12.2 Hormonal Patterns

In males, stimuli from other areas in the brain cause the hypothalamus to release *gonadotropin-releasing hormone* (GnRH), which prompts the release of *follicle-stimulating hormone* (FSH) and *luteinizing hormone* (LH) from the anterior pituitary gland. Both travel down to the testes; the former stimulates spermatogenesis and the latter stimulates androgen production, which gives rise to primary and secondary sex characteristics. Androgens have a negative feedback effect on the secretion of hormones by both the hypothalamus and the anterior pituitary.

In females, the process is much more complicated. There are two cycles in females: a *menstrual cycle* and a *ovarian cycle*.

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The menstrual cycle has three phases: in the *menstrual flow phase*, menstrual bleeding occurs because the endometrium disintegrates; in the *proliferative phase*, the thin remaining endometrium begins to regenerate and thicken for a week or two; in the *secretory phase*, the endometrium becomes more vascularized and develops glands that secrete a glycogen-rich fluid. The beginning of the secretory phase corresponds with ovulation.

The ovarian cycle has two phases: in the *follicular phase*, several follicles in the egg begin to grow. The maturing follicle grows big and fat and creates a bulge in the ovary. The follicular phase ends with *ovulation*, when the follicle and adjacent wall rupture, releasing the secondary oocyte. Afterwards, the remains of the follicle turn into the *corpus luteum* and in the *luteal phase* of the cycle, hormones are secreted by endocrine cells of the corpus luteum.

The female pattern begins with the release of GnRH from the hypothalamus. This stimulates the anterior pituitary gland to release a small amount of FSH and LH. FSH causes growth of follicles (follicular phase of ovarian cycle), which corresponds with the proliferative phase of the menstrual cycle. Then, the LH causes the follicle to mature and secrete estrogen. Ovulation soon follows and the pattern enters the luteal phase. The corpus luteum forms due to stimulation by LH and secretes estrogen and progesterone, which stimulate development and thickening of the endometrium in the secretory phase of the menstrual cycle. Very high levels of estrogen and progesterone then have a negative effect on the release of GnRH and therefore the release of LH. A decrease in the amount of LH causes the corpus luteum to atrophy. Finally, levels of estrogen and progesterone drop and the endometrium disintegrates in the menstrual flow phase of the menstrual cycle. So much stuff to memorize for female pattern; I could make a sexist joke here but I won't.

Females generally undergo menopause, or the cessation of ovulation and menstruation, between the ages of 46 and 54. During those years, the ovaries lose their responsiveness to FSH and LH and therefore estrogen production declines.

12.3 Fetal Development

Human gestation can be divided into three *trimesters* of three months each.

About one day after fertilization, the zygote begins dividing in a process called *cleavage*. The embryo becomes a *blastocyst*, a hollow ball of cells, after about a week and implants into the endometrium. Differentiation of body structures now begins. Meanwhile, tissues grow out of the embryo and mingle with the endometrium to form the *placenta*, which provides a medium for nutrients to diffuse from maternal blood vessels to fetal ones without mingling of blood. The first trimester is also the main period of *organogenesis*, the development of organs. By the end of the first trimester, all the major structures of the adult are present in the embryo.

Also during the first trimester, the embryo secrets hormones that signal its presence to the mother's reproductive system. One of these, *human chorionic gonadotropin*, maintains secretions of progesterone and estrogens by the corpus luteum to prevent accidental menstration of the embryo.

During the second trimester, the fetus grows rapidly and is very active. The uterus will grow enough for the pregnancy to become obvious.

During the third trimester, the fetus grows rapidly and its activity may decrease as it fills the available space within the embryonic membranes. *Oxytocin*, produced by the fetus and the mother's posterior pituitary, stimulates contractions of the uterus. Oxytocin also stimulates the placenta to secret *prostaglandins*, which enhance the contractions. The contractions then prompt the production of more oxytocin and prostaglandins, a positive feedback system.

Birth, or *parturition*, then occurs.

Why doesn't the mother reject the fetus, which has antigens from the father? It could be because of the *trophoblast*, which acts like a barrier between the embryo and maternal tissue. It contains paternal antigens as well, but perhaps it prevents an immune response by interfering with the mother's T lymphocytes, perhaps by blocking the action of *interleukin-2*, a cytokine required for an immune response. Another hypothesis is that the trophoblast secrets an enzyme that rapidly breaks down local supplies of *tryptophan*, an enzyme required for T cell survival and function.

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13 Animal Development

13.1 Fertilization

Fertilization occurs when the sperm and egg unite to form a *zygote*. The main function of fertilization is to combine haploid sets of chromosomes from two individuals into a single diploid cell.

The eggs of sea urchins are fertilized externally after the animals release gametes into the surrounding seawater. When a reaches the jelly coat that covers the egg, a vesicle at the tip of the sperm called the *acrosome* discharges its contents, including hydrolytic enzymes, onto the jelly coat in a process called the *acrosomal reaction*. The hydrolytic enzymes enable the *acrosomal process* to penetrate the jelly coat of the egg and finally reach a receptor on the *vitelline layer* right underneath the jelly coat. The fusion of the sperm and egg membranes allows sodium ions to flow into the egg cell and change the membrane potential, depolarizing the membrane and not allowing any more sperm in. This is called the *fast block to polyspermy*.

Then, the *cortical reaction* initiates, releasing a wave of calcium ions (Ca^{2+}) that sweeps across the whole egg and triggers small vesicles called *cortical granules* to discharge their contents into the layer between the egg cytoplasm and the vitelline layer, called the *perivitelline space*. This causes the vitelline layer to become the *fertilization envelope*, a hard shell that prevents entry of additional sperm. This is called the *slow block to polyspermy*. By this time, the voltage across the membrane has returned to normal and the fast block stops functioning.

In mammals, fertilization occurs *in vivo*. The sperm migrates through a layer of follicle cells until it reaches the *zona pellucida* which cloaks the egg's cytoplasm. The acrosomal vesicle ruptures and release hydrolytic enzymes that penetrate the *zona pellucida*, and then the sperm fuses with the egg. This triggers depolarization of the egg membrane, which functions as a fast block to polyspermy. A cortical reaction then occurs which modifies the *zona pellucida*, leading to the slow block to polyspermy. Note that in contrast to sea urchins, the whole mammal sperm is absorbed into the egg. The basal body of the sperm's flagellum divides and forms the two centrosomes in the zygote which will generate the mitotic spindle for cell division.

13.2 Cleavage

Cleavage, or rapid cell division, occurs after fertilization. During cleavage, the cells basically skip the G_1 and G_2 phases of mitosis, and so the embryo does not enlarge and the divided cells, called *blastomeres*, become successively smaller.

Most animals, with the exception of mammals, have eggs and zygotes with a definite polarity. The polarity is defined by the uneven distribution of substances in the cytoplasm, and in many frogs, the distribution of *yolk*, or stored nutrients, is a key factor in influencing the pattern of cleavage. Yolk is most concentrated at the *vegetal pole* and least concentrated at the *animal pole*. When an amphibian egg is fertilized, the plasma membrane rotates towards the point of sperm entry, exposing a region of cytoplasm called the *gray crescent* that will later become the dorsal side of the embryo. Because yolk tends to impede cell division, cleavage of the frog zygote occurs more rapidly in the animal hemisphere, resulting in an embryo with different-sized cells.

In zygotes with less yolk, cleavage divisions all occur at about the same rate, producing blastomeres of about equal size.

Continued cleavave produces a ball of cells called a *morula*[13]. Then, a fluid-filled cavity called the *blastocoel* forms inside, creating a hollow ball called the *blastula*. In eggs with lots of yolk, cleavage is restricted to a small disk of yolk-free cytoplasm at the animal pole. This incomplete division is called *meroblastic cleavage*. *Holoblastic cleavage* is the complete division of eggs having less yolk.

13.3 Gastrulation

In *gastrulation*, three cell layers are established to form the *gastrula*. The three layers are called the *ectoderm*, *endoderm*, and *mesoderm*. The ectoderm forms the outer layer of the gastrula and will eventually develop into the nervous system and the

[13]The textbook says that "morula" means "mulberry." That's funny, because I'd never think of a ball of cells as a berry. But maybe biologists are just weird that way.

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epidermis. The endoderm lines the embryonic digestive tract and will eventually become the digestive tract and associated organs. The mesoderm fills the space between the endoderm and mesoderm and will eventually become most other organs in our body.

In sea urchins, gastrulation begins when *mesenchyme cells* detach from the vegetal pole and enter the blastocoel. These cells will eventually become the mesoderm. The vegetal pole buckles inwards in a process called *invagination* and then develops into a deeper, narrower pouch called the *archenteron*, the primitive gut. The open end of the archenteron is called the *blastopore*. Then, another opening forms on the other side of the archenteron, forming the mouth of a primitive digestive tube or endoderm.

In frogs, invagination occurs to form the *dorsal lip* of the blastopore. Gastrulation continues with cells on the surface of the embryo rolling over the edge of the dorsal lip into the interior in a process called *involution*. The three layers develop, and as the process is completed, the blastopore encircles a *yolk plug* that decreases in size due to expansino of the ectoderm. Finally, all three layers are in place and organogenesis can begin.

13.4 Organogenesis

In frogs, the *notochord*, which will define the vertebral, is formed from mesoderm that condenses just above the archenteron, and the *neural tube*, which will become the brain and spinal cord, is formed by the folding of the neural plate inwards. Strips of mesoderm next to the notochord separate into blocks called *somites*, which will become the vertebrae and the muscles around there.

In birds, the meroblastic cleavage forms the *blastodisc*, a cap of cells that rests on the undivided yolk. The blastomeres then arrange into two layers, the *epiblast* and *hypoblast*. I know that this is pretty boring, but we're almost done so keep it up! Then, during gastrulation, the blastodisc folds inwards on the *primitive streak* to form the three gastrulation layers. Finally, in organogenesis, the neural tube, notochord, and somites develop like in frogs. The tissue layers that are outside the embryo develop into four *extraembryonic membranes*: the yolk sac, the amnion, the chorion, and the allantois. The *yolk sac* will digest the large amount of yolk to feed the growing embryo, the *amnion* encloses the embryo in a fluid-filled amniotic sac and along with the *chorion* will cushion the embryo against mechanical shocks. The *allantois* functions as a disposal sac for uric acid.

In mammals, the eggs have very little yolk and go through holoblastic cleavage that is relatively slow. The *inner cell mass* that exists in the blastocyst stage arranges into the *epiblast* and *hypoblast* and will develop into the embryo and some extraembryonic membranes. The *trophoblast* is the outer layer of the blastocyst and will later form the fetal portion of the placenta. After implantation, the four extraembryonic membranes form: the *chorion*, which develops from the trophoblast, completely surrounds the embryo and the other extraembryonic membranes; the *amnion* will eventually enclose the embryo in a fluid-filled cavity; the *yolk sac* is a site of early formation of blood cells which later migrate into the embryo; and the *allantois* forms blood vessels that transport oxygen and nutrients from the placenta to the embryo and rid the embryo of carbon dioxide and nitrogenous wastes.

13.5 Morphogenesis and Differentiation

The cytoskeleton is especially important in changing the shape, position and adhesion of the cell. Microfilaments and microtubules help to form invaginations and evaginations of tissue layers during development. The cytoskeleton also helps cells to "crawl" from one place to another. Cell crawling is important in *convergent extension*, in which cells in a tissue layer arrange themselves so that the sheet of cells becomes narrower and longer.

The extracellular matrix is also important in development. It may help with holding cells together when migrating cells reach their destinations. Also contributing to cell migration and tissue structure are glycoproteins in the ECM called *cell adhesion molecules* (CAMs) which bind to CAMs on other cells. Other important cell-adhesion molecules include *cadherins*, which have been shown to be essential to the correct formation of the frog blastula.

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13.6 Cell Determination and Differentiation

Through marking cells at different stages of development and seeing what structures they develop into, scientists have found that as development proceeds, a certain cell's *developmental potential* (the range of structures it can give rise to) becomes restricted.

The fates of embryonic cells are mostly determined by the distribution of cytoplasmic determinants but can also be affected by the zygote's pattern of cleavage. Sometimes, the cells resulting from the first division zygote are both *totipotent*, meaning that both can become a normal embryo. As development progresses, however, most cells lose their totipotency, but some keep their ability to turn into more than one kind of cell for a while – for example, if the dorsal ectoderm of a sufficiently young embryo is replaced with ectoderm from somewhere else, the ectoderm will still turn into a neural plate. However, if this is done in a late-stage gastrula, the transplanted ectoderm will not respond to its new location anymore and not form a neural plate.

Induction, or when a cell is influenced by cells around it to change in some way, is also very important to organism development. It usually plays a role in *determination*, or setting the fate of cells.

14 Cell Communication

One topic of cell conversation is sex. This is the case in mating yeast cells; the two mating types, a and α, exchange chemical signals called a *factor* and α *factor* respectively which cause the cells to grow towards each other and eventually fuse.

Communicating cells can be close together or far apart. In *paracrine signaling*, a secreting cell acts on nearby cells by secreting molecules of a *local regulator* into the extracellular fluid. Another form of local signaling is *synaptic signaling*, in which a nerve cell releases *neurotransmitter* molecules across a *synapse*, a narrow space between two nerve cells. This passes a neural signal from cell to cell. Long-distance signaling is accomplished through *hormones*, special molecules that travel through the bloodstream to their target destinations.

Cell signaling is divided into three stages: *reception*, *transduction*, and *response*.

14.1 Signal Reception

In signal reception, a signal molecule called a *ligand*[14] binds to a receptor protein on the target cell. Most signal receptors are plasma membrane proteins as most signal molecules are water-soluble and are too large to pass through the plasma membrane.

There are three types of membrane receptors: G-protein-linked receptors, tyrosine-kinase receptors, and ion-channel receptors.

A *G-protein-linked receptor* works with the help of a *G protein*. When a ligand binds with the *signal-binding site* on the receptor, the receptor changes shape and activates the G protein by replacing the GDP on it with a GTP. Then, the G protein moves to an enzyme and activates it, triggering the pathway leading to cellular response. Then G protein then catalyzes the hydrolysis of its GTP and leaves the enzyme, becoming available for use. All three proteins are attached to the plasma membrane throughout the whole cycle.

Many diseases affect the action of G-protein-linked receptors, including cholera, which chemically modifies a G protein invoved in regulating salt and water secretion.

A *tyrosine-kinase receptor* is made from two originally disjoint tyrosine-kinase receptor monomers. When signal molecules attach to the binding sites of both receptors, the receptors come together, forming a dimer. This aggregation activates the tyrosine-kinase parts of both polypeptides, which adds phosphates to each other. The phosphates then activate the relay proteins. Each tyrosine-kinase receptor dimer can activate 10 or more different intracellular proteins simultaneously.

Some membrane receptors are *ligand-gated ion channels*. When a signal molecule binds to the receptor, a channel opens and ions flow through. The change in ion concentratino triggers cellular responses. Then, the ligand dissociates and the channel closes again.

[14] The actual term *ligand* refers to a small molecule that specifically binds to a large one.

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Other signal receptors are located inside the cell. Several important signaling molecules, including steroid hormones, thyroid hormones, and nitric oxide (NO), are able to pass through the plasma membrane and bind to receptors located inside the cell. For example, testosterone passes through the plasma membrane and binds to a receptor protein in the cytosol. The complex that results enters the nucleus and binds to specific genes as a *transcription factor*, stimulating the transcription of the genes into mRNA. The mRNA is then translated into a specific protein.

14.2 Signal-Transduction Pathways

The transduction state of cell signaling is usually a multistep pathway. This usually occurs in the form of a chain of protein phosphorylation in which each protein is phosphorylated by the last and helps to phosphorylate the next, creating a *phosphorylation cascade*. An enzyme that transfers phosphate groups from ATP to a protein is a *protein kinase*. The effects of protein kinases are quickly reversed in the cell by *protein phophatases* which remove phosphate groups from proteins.

Certain small molecules or ions, called *second messengers*, also help to transfer a signal in a cell. One of these is cyclic AMP or cAMP. An enzyme in the membrane, *adenylyl cyclase*, converts ATP to cAMP in response to an extracellular signal. The cAMP then triggers the activation of another protein, usually protein kinase A.

Other second messengers include calcium ions and *inositol trisphosphate*, or IP_3. When signal molecules attach to a membrane receptor, an enzyme called *phospholipase C* converts a molecule called PIP_2 into two second messengers, DAG and IP_3. The IP_3 prompts the opening of a calcium channel on the ER membrane, which causes the release of calcium ions into the cytosol. The calcium binds to a protein called *calmodulin* which changes conformation and binds to other proteins, activating them and leading to the cellular response.

14.3 Cellular Response

Elaborate pathways amplify and specify the cell's response to signals. A cell's response to a particular signal depends on the type of receptor protein, relay molecules, and proteins needed to carry out the response. Different pathways may have the same molecules in common but occur in different cells.

The efficiency of signal transduction can be increased through the presence of *scaffolding proteins*, large relay proteins to which several other relay proteins are simultaneously attached.

And on that note, you have now reviewed all the concepts you need to know for finals. Good luck, and godspeed[15]!

15 Special Thanks

Many many people deserve special thank-yous.

Firstly, I'd like to thank Rohan Puranik for being an awesome lab partner and knowing how to cut agar cubes very well. He is also Indian, making him quite melanous in hue, in sharp contrast to my excellent yellowish complexion. Rohan is also the primary editor of this guide, and helped greatly with finding and fixing errors. The guide is much improved due to his hard work. Of course, I take full responsibility for any errors that remain.

More thanks go to the entire 5/6th period AP Biology class. Without you, I am nothing. You all make biology the most fun class in my day! I would try to name all of you, but I'm afraid I'll forget somebody, and that would suck.

Special thanks to those of you who kept me alive through the making of this guide. Lingyu Xie, Julie Bai, Lawrence Chan (Llamaru-chan!), Katrina Cruz... woohoo! You guys rock! Also great thanks to Alex Inman; without his "encouragement", this guide wouldn't have been finished in time.

[15] I'm actually not sure what this word means but it sounds cool so I'll use it.

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I'd also like to thank our great biology teacher, Mr. Smiley. His eyes are like diamonds and his breath is like fire and his voice is like thunder! His counsel is wise and his ability to instill fear in the hearts of biology students is unsurpassed. There is nobody in the world who is as awesome as he is. Hail Mr. Smiley!

Lastly, but MOST CERTAINLY not the least, I would like to thank YOU, oh patient reader, for being able to put up with my nonsensical blabbings and read through this guide. You rock!

16 References

1. Campbell, Neil A. and Reece, Jane B. *Biology.* 6th ed. San Francisco: Pearson Education Inc., 2002.

17 An Addendum

This guide was written on a Windows computer and typeset in LaTeX using the excellent TeXnicCenter program (please visit www.toolscenter.org for more information), which has simplified much of the process of compiling and reviewing. It uses the plugins *fancyhdr*, *amsmath*, *aliphat*, *hcycle*, and *hetarom*, the last three of which are from the package XyMTeX and were used to typeset the structural formulas used throughout.

Please immediately notify me at fenguin@gmail.com if you find any errors or omissions in this guide; I will be eternally grateful if you do so. This version is dated **December 26, 2005**; there may be an update available at http://www.fenguin.net.

Overall, thank-you greatly for reading, and I sincerely hope that you overcome all your AP Biology challenges!

Charles Feng

December 26, 2005

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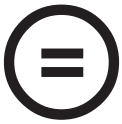

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