Chapter 1: Themes in the Study of Life

- **Biology**: The scientific study of life.
- **Systems Biology**: Construct models for the dynamic behavior of who biological systems.
- **Reductionism**: the reduction of complex systems to simpler components that are more manageable to study.
- **Eukaryotic cell** is subdivided by internal membranes.
- **Prokaryotic cell:** DNA is not separated from the rest of the cell in a nucleus.
- **Inquiry**: a search for information and explanation
- **Data**: Recorded observations
- **Hypothesis**: a tentative answer to a well-framed question.
- **Theory**: Much broader in scope than a hypothesis, is general enough to spin off many new, specific hypotheses, generally supported by a much greater body of evidence.
- **Technology**:applied scientific knowledge for some specific purpose

- **Evolution**: the process of change that has transformed life on Earth from its earliest beginnings to the diversity of organisms living today.
- **Properties of life**: Order, Evolutionary Adaption, Response to the Environment, Regulation, Energy processing, Growth and Development, Reproduction.

1. <u>Themes connect the concepts of Biology</u>

1. New properties emerge at each level in the biological hierarchy (emergent properties). Thus, the study of life can be divided into different levels of biological organisation.
2. Organisms interact with their environments, exchanging matter and energy: cycling of nutrients, flow of energy. Work requires a source of energy
3. Structure and function are correlated at all levels of biological organization.
4. Cells are an organism's basic units of structure and function.
5. The continuity of life is based on heritable information in the form of DNA
    1. **Genes:** the units of inheritance that transmit information from parents to offspring.
    2. **DNA:** the substance genes are made of.
    3. **Genome**: The entire "library" of genetic instructions that an organism inherits.
6. Feedback mechanism regulate biological systems.
    1. **Negative feedback**: Accumulation of an end product of a process slows that process.
    2. **Positive feedback**: Accumulation of an end product of a process speeds up that process.

2. ***<u>The Core Theme:</u>* <u>Evolution accounts for the unity and diversity of life</u>**

1. Organizing the diversity of life

1. *The Three Domains of Life:* Domain **Bacteria** and domain **Archaea** are prokaryotic. Domain **Eukarya** is eukaryotic.

2. Domain **Eukarya** is further divided into the kingdoms *Protista, Plantea, Fungi,* and *Animalia.*

2. Charles Darwin and the Theory of Natural Selection.

1. Nov. 1859: Charles Robert Darwin publishes *On the Origin of Species by Means of Natural Selection.*
2. "Decent with modification" and "natural selection"

3. The Tree of Life

1. Biologists' diagrams of evolutionary relationships generally take treelike forms.

3. <u>Scientists use two main forms of inquiry in their study of nature</u>

1. **Discovery science** (descriptive science): Describing natural structures and processes as accurately as possible through careful observation and analysis of data.
    1. **Inductive reasoning**: Deriving generations from a large number of specific examples.
2. **Hypothesis-based science**: Explaining nature.
    1. **Deductive reasoning**: From general premises, we extrapolate to the specific results we should expect if the premises are true.
    2. Hypotheses must be testable and falsifiable.
    3. Scientific method: The way scientists conduct experiments.
        1. **Controlled experiment**: Compares an experimental group with an control group.
4. **Scientific Models**: A tool used to help explain a scientific concept.

Chapter II: The Chemical Context of Life

Living organisms are subject to basic laws of physics and chemistry.

- **atom**: the smallest unit of matter that still retains the properties of an element.
- **Dalton**: a unit of measurement the same as the amu.
- **Energy:** the capacity to cause change.
- **Potential energy**: the energy that matter possesses because of its location or structure.
- **Chemical bonds**: Interactions that hold atoms together.
- **Valence**: the number of unpaired electrons required to complete an atom's outermost shell.
- **Electronegativity**: The attraction of a particular kind of atom for the electrons of a covalent bond.

1. Matter consists of chemical elements in pure form and in combinations called compounds

1. **Matter**: anything that takes up space and has mass.
2. **Element**: a substance that cannot be broken down to other substances by chemical reactions.
3. **Compound**: a substance consisting of two or more different elements combined in a fixed ratio.
4. About 25% of the 92 elements are essential to life.
5. Carbon, Hydrogen, Oxygen and Nitrogen make up 96% of living matter.
6. Most of the remaining 4% is made up of phosphorous, potassium, and sulfer.
7. **Trace elements:** elements required by an organism in only minute quantities.

2. An element's properties depend on the structure of its atoms

1. **Subatomic particles:** neutrons (N), protons (+), electrons (-). Protons and neutrons are tightly packed together in the **atomic nucleus**.
2. **Atomic number**: the number of protons in the nuclei of an atom.
3. **Mass number**: the sum of the protons plus neutrons in the nucleus of an atom.
4. **Atomic mass**: the mass of an atom (in daltons)
5. **Isotope**: the different atomic forms of an element. A **radioactive isotope** is one in which the nucleus decays spontaneously.
6. **Electron shells**: where electrons are found.
    1. **Valence electrons** are the outermost electrons and they are found in the **valence shell**.
    2. **Orbital:** the three-dimensional space where an electron is found 90% of the time. The first shell only has 1 *s* orbital. The second shell has 1 *s* orbital and 3 *p* orbitals. The third shell has more complex orbitals.

3. The formation and function of molecules depend on chemical bonding between atoms

1. **Covalent bond**: the sharing of a pair of valence electrons by two atoms.
    1. **Molecule**: two or more atoms held together by covalent bonds.

- **Ion**: a charged atom or molecule
- **Cation**: Positively charged ion
- **Anion**: Negatively charged ion

2. **Single bond**: only one pair of electrons shared.
3. **Structural Formula**: A way of representing molecular structure. Ex... H—H
4. **Molecular Formula**: Indicates what atoms are in a molecule. Ex.... H_2
5. **Double bond**: two pairs of electrons shared.
6. **Nonpolar covalent bond**: Electrons are shared equally
7. **Polar covalent bond**: Electrons are shared equally.

2. **Ionic Bonds**: In some cases, two atoms are so unequal in their attraction for valence electrons that the more electronegative atom strips an electron completely away from its partner. An **ionic bond** is formed when cations and anions attract each other.
   1. Compounds formed by ionic bonds are called **ionic compounds** or **salts**.
   2. The formula for an ionic compound indications only the ratio of elements in a crystal of the salt.

3. Weak Chemical Bonds

1. **Hydrogen Bond**: Formed when a hydrogen atom covalently bonded to one electronegative atom is also attracted to another electronegative atom. In living cells, the electronegtaive atom is usually nitrogen or oxygen.
2. **van der Waals interactions**: When atoms, by chance, become slightly polarized and molecules stick together slightly. Very weak force, but allows geckos to walk up a wall.

4. Molecular Shape and Function

1. A molecule has a characteristic size and shape, determined by the positions of the atoms' orbitals. The shape of the molecule is very important to its function. Molecules with similar shapes have similar biological effects.
2. For water (H_20), the molecule is shaped like a V with its two covalent bonds spread apart at an angle of 104.5º
3. The methane molecule (CH_4) has the shape of a completed tetrahedron because all four hybrid orbitals of carbon are shared with hydrogen atoms.
4. Only molecules with complementary shapes can form weak bonds with each other.

- **Chemical reactions**: the making and breaking of chemical bonds.
- **Reactants**: starting materials
- **Products**: ending materials.
- **Chemical equilibrium**: the point at which the reactions offset one another equally

4. Chemical Reactions Make and Break Chemical Bonds

1. All atoms of the reactants must be accounted for in the products: Reactions cannot create or destroy matter but can only rearrange it.
2. All chemical reactions are reversible, with the products of the forward reaction becoming the reactants for the reverse reaction.

Chapter 3: Water and the Fitness of the Environment

- Cells are about 70-95% water
- **Polar Molecule**: A molecule in which the two ends of the molecule have opposite charges.
- **Adhesion**: The clinging of one substance to another
- **Surface tension**: a measure of how difficult it is to stretch or break the surface of a liquid.
- **Kinetic energy**: the energy of motion.
- **Heat**: a measure of the matter's total kinetic energy due to motion of its molecules. Depends on the volume.
- **Temperature**: a measure of heat intensity that represents the average kinetic energy of the molecules, regardless of volume.
- **Heat of vaporization**: the quantity of heat a liquid must absorb for 1 g of it to be converted from the liquid to the gaseous state.

2. The Polarity of Water Molecules Results in Hydrogen Bonding

1. Water is a polar molecule. The slightly positive hydrogen of one molecule is attracted to the slightly negative oxygen of a nearby molecule.

3. Four emergent properties of water contribute to Earth's fitness for life

1. *Cohesion:* a phenomenon that appears because hydrogen bonds hold water together.
1. Cohesion due to hydrogen bonding contributes to the transport of water and dissolved nutrients against gravity in plants.
2. Water also has a greater surface tension than most other liquids.

2. *Moderation of Temperature:* Water moderates air temperature by absorbing heat from air that is warming and releasing the stored heat to air that is cooler. Water is good for heat storage because it has a high specific heat.
1. **Calorie**: the amount of heat it takes to raise the temperature of 1 g of water by 1ºC.
2. **Joule:** The work exerted when one applies a force of one newton to move an object 1m. 1 calorie equals 4.184 joules.
3. **Specific Heat**: the amount of heat that must be absorbed or lost for 1g of a substance to change its temperature by 1ºC.
1. Water's high specific heat is due to the hydrogen bonding that requires a lot more energy to break. This can moderate temperature near and in large bodies of water.

4. **Evaporative Cooling:** as a liquid evaporates, the surface of the liquid that remains behind cools down.
1. Water's high heat of vaporization is another emergent property caused by hydrogen bonds, which must be broken before the molecules can make their exodus from the liquid.
2. Evaporative cooling of water contributes to the stability of temperature in lakes and ponds and also provides a mechanism that prevents terrestrial organisms from overheating.

3. *Insulation of Bodies of Water by Floating Ice*
1. Water is one of the few substances that are less dense as a solid than as a liquid. This is because hydrogen bonding locks solid water into a crystalline lattice and holds the molecules slightly apart. Water actually reaches its greatest density at 4ºC. Ice at 0ºC is actually 10% less dense than liquid water at 4ºC.
2. Because ice floats on top of water, it insulates the water below it and prevents deep bodies of water from freezing completely, allowing life to survive under the frozen surface.

4. *The Solvent of Life.*
1. Water is the best solvent out there, but it is not a universal solvent.
2. **Hydration shell**: the sphere of water molecules around each dissolved ion.
3. **Hydrophilic**: Any substance that has an affinity for water. Substances can be hydrophilic without actually dissolving if the molecules are large enough.
4. **Colloid**: a stable suspension of fine particles in a liquid.
5. **Hydrophobic**: Substances that seem to repel water.
6. **Molecular Mass**: the sum of the masses of all the atoms in a molecule.
7. **Mole (mol)**: represents an exact number of objects—6.022×10^{23}.
8. **Molarity**: the number of moles of solute per liter of solution.

- **Solution**: a liquid that is a completely homogeneous mixture of two ore more substances.
- **Aqueous solution**: one in which water is the solvent.
- **Solvent**: the dissolving agent.
- **Solute**: the substance that is dissolved.

4. Acidic and basic conditions affect living organisms

1. Occasionally, a hydrogen atom participating in a hydrogen bond between two water molecules shifts from one molecule to the other. The hydrogen leaves its electron behind.
1. Hydroxide ion: OH^- ; Hydronium ion:H_3O^+. By convention, it's represented by H^+, even though H^+ does not exist on its own in an aqueous solution. OH^- and H^+ are very reactive.
2. This is a reversible reaction. In pure water, only one water molecule in every 554 million is dissociated.
3. Biologists use the pH scale to describe how acidic or basic a solution is.
2. Strong acids and bases completely dissociate in water. Ex. HCl and NaOH. Weak acids and bases reversibly release and accept back hydrogen ions. Ex. NH_4 and H_2CO_3.
3. In any aqueous solution at 25ºC, the *product* of the H^+ and OH^- concentrations is constant at 10^{-14}.
4. The internal pH of most living cells is close to 7. The pH of human blood is very close to 7.4. A person cannot survive for more than a few minutes if the blood pH drops to 7 or rises to 7.8. **Buffers** are substances that minimize changes in the concentrations of H^+ and OH^- in a solution.
5. Considering the dependence of all life on water, contamination of rivers, lakes, seas and rain is a dire environmental problem.
6. Carbon dioxide, the main product of fossil fuel combustion, also causes other problems. It is one of the chemicals implicated in global warming.
7. When CO_2 dissolves in seawater, it reacts with water (H_2O) to form carbonic acid (H_2CO_3). Almost all of the carbonic acid in turn dissociates, producing protons and a balance between two ions, bicarbonate (HCO_3^-) and carbonate (CO_3^{2-}). As seawater acidifies due to the extra protons, the balance shifts towards HCO_3^-, lowering the concentration of CO_3^{2-}. Because calcification is directly affected by the concentration of CO_3^{2-}, any decrease in CO_3^{2-} is therefore of great concern because calcification accounts for the formation of coral reefs in our tropical seas. The expected doubling of CO_2 emissions by the year 2065 could lead to a 40% decrease in coral reef calcification, according to a study by Chris Langdon and colleagues.

- Acid: a substance that increases the hydrogen ion concentration of a solution.
- Base: a substance that reduces the hydrogen ion concentration of a solution.
- **pH**: the negative common logarithm of the hydrogen ion concentration: pH=-log[H^+]. The lower the number, the more acid the solution. Most biological fluids are within the range pH 6-8.
- **Acid precipitation** refers to rain, snow or fog with a pH lower than pH 5.2. It affects lakes, streams and soil adversely.

- **Organic chemistry**: the study of compounds containing carbon. Of all chemical elements, carbon is unparalleled in its ability to form molecules that are large, complex, and diverse.
- **Vitalism**: the belief in a life force outside the jurisdiction of physical and chemical laws
- **Mechanism**: the view that physical and chemical laws govern all natural phenomena.

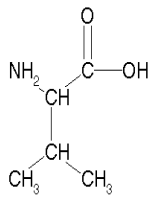
- **Hydrocarbons**: organic molecules consisting of only carbon and hydrogen. They can release a relatively large amount of energy.

1. Organic chemistry is the study of carbon compounds

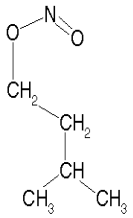
1. The science of organic chemistry originated in attempts to purify and improve the yield of other organisms.
2. Early 1800s: chemists could make many simple compounds but could not synthesize the complex molecules extracted from living matter.
3. 1828: Friedrich Wöhler attempted to make ammonium cyanate by mixing solutions of ammonium ions (NH_4^+) and cyanate ions (CNO^-). However, he managed to make urea instead.
4. Hermann Kolbe, a student of Wöhler's made the organic compound acetic acid from inorganic substances that could be prepared directly from pure elements.
5. 1953: Stanley Miller helped bring this abiotic synthesis of organic compounds into the context of evolution by simulating the early earth.
6. All this discredited vitalism and supported mechanism.

2. Carbon atoms can form diverse molecules by bonding to four other atoms

1. The key to an atom's chemical characteristics is its electron configuration. This configuration determines the kinds and number of bonds an atom will form with other atoms.
2. Carbon usually completes its valence shell by sharing its 4 valence electrons. When a carbon atom forms four single covalent bonds, the bonds angle towards the corners of an imaginary tetrahedron. When two carbon atoms are joined by a double bound, however, all bonds around those carbons are in the same plane.
3. Carbon chains form the skeletons of most organic molecules. The skeletons vary in length and may be straight, branched or arranged in closed rings.
4. **Isomers**: compounds that have the same numbers of atoms of the same elements but different structures and hence different properties.
    1. **Structural isomers** differ in the covalent arrangements of their atoms.

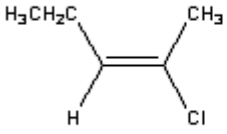


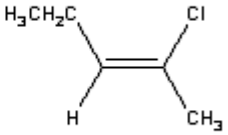
$C_5H_{11}NO_2$
valine
white solid
essential amino acid



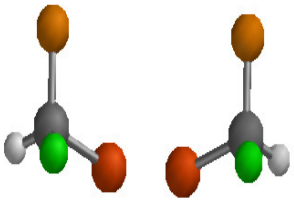
$C_5H_{11}NO_2$
amyl nitrate
volatile liquid
drug (poppers)

    2. **Geometric isomers** have the same covalent partnerships, but they differ in their spatial arrangements.





    3. **Enantiomers** are isomers that are mirror images or each other.



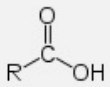
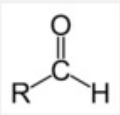
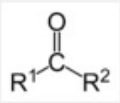
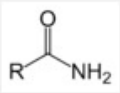
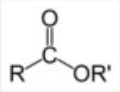
3. A small number of chemical groups are key to the functioning of biological molecules

1. The distinctive properties of an organic molecule molecule also depend on the molecular components attached to the carbon skeleton.
2. **Functional Group**: the chemical groups affect molecular function by being directly involved in chemicals reactions.

Table of Functional groups

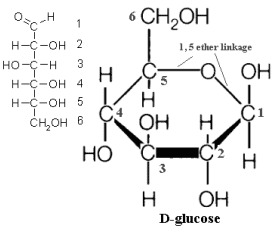
[edi

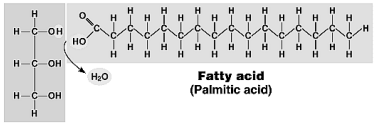
Alk is the prefix of the group (Meth, Eth, Prop, etc.)

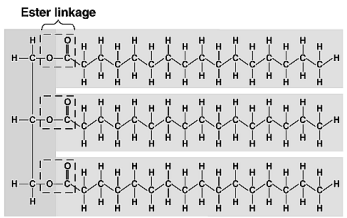
Family	Structure	IUPAC nomenclature	IUPAC nomenclature for cyclic parent chains (if different from straight chains)	Common nomenclature
Alkyl groups	R—	***Alk*yl**	-	***Alk*yl**
Halogens	R—halogen	***Halo'alk*ane**	-	***Alk*yl *hal*ide**
Alcohols	R—OH	***Alk*anol**	-	***Alk*yl alcohol**
Amines	$R—NH_2$	***Alk*anamine**	-	***Alk*yl amine**
Carboxylic acids		***(Alk + 1)*anoic acid**	**Cyclo*alk*anecarboxylic acid**	-
Aldehydes		***Alk*anal**	**Cyclo*alk*anecarboxaldehyde**	-
Ketones		***Alk*anone**	-	$Alk_{(1)}$yl $Alk_{(2)}$yl ketone
Thiols	R—SH	***Alk*anethiol**	-	-
Amides		***(Alk + 1)*anamide**	**Cyclo*alk*anecarboxamide**	-
Ethers	$R_1—O—R_2$	***alk*oxy*alk*ane**	-	$Alk_{(1)}$yl $Alk_{(2)}$yl ether
Esters		$Alk_{(1)}$yl ***Alk*** $_{(2)}$ aneoate	$Alk_{(1)}$yl Cyclo$alk_{(2)}$anecarboxylate	$Alk_{(1)}$yl ***(Alk + 1)*** $_{(2)}$ anoate

Chapter 5: The Structure and Function of Large Biological Molecules.

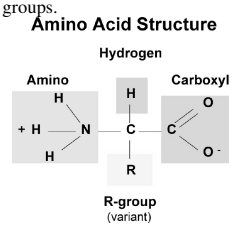
- **Macromolecules**: enormous molecules that can have a mass well over 100,000 amu.





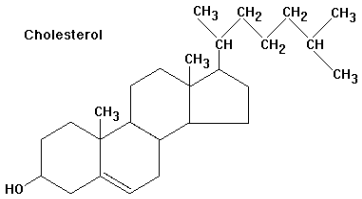


- **Enzymes**: biological **catalysts**. Most are proteins.
- **Amino acids**: organic molecules possessing both carboxyl and amino groups.



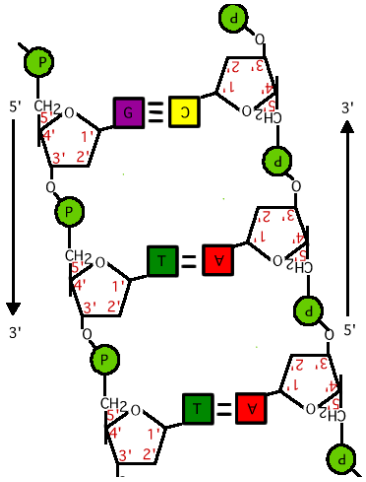
- **X-ray crystallography**: A method used to figure out the structure of molecules.
- **Nuclear Magnetic Resonance spectroscopy**: A method used to figure out the structure of molecules which does not require crystallization.
- **Bioinformatics**: Predicting the 3D structure of proteins from their amino acid sequences.

1. **Macromolecules are polymers, built from monomers**:
   1. **Polymer**: long molecule consisting of many similar or identical building blocks (**monomers**) linked by covalent bonds. Monomers are joined by **dehydration reactions**, which are facilitated by **enzymes**. The reverse reaction of dehydration synthesis is **hydrolysis**.
2. **Carbohydrates serve as fuel and building material**
   1. **Carbohydrates** include both sugars and polymers of sugars.
   2. The simplest carbohydrates are monosaccharides, which usually have empirical formulas of CH_2O. Glucose is the most common monosaccharide. It has a carbonyl group and multiple hydroxyl groups. Monosaccharides are classified by the number of carbon atoms and the location of the carbonyl groups.
      1. In aqueous solutions, most sugar molecules will form rings.
      2. Monosaccharides are major nutrients. Not only are they a major fuel for cellular work, they also serve as the raw material for the synthesis of other organic molecules.
   3. A **disaccharide** consists of two monosaccharides joined by a **glycosidic linkage**.
   4. **Polysaccharides** are macromolecules formed monosaccharides. They are generally used as energy storage and as structural materials.
      1. Plants tend to store **starch**, a polymer of glucose monomers. **Starch** is made of alpha-glucose and is helical. Generally, starch has few to no branching. The unbranched version is amylose; the branched version is amylopectin.
      2. Animals store **glycogen**, a more highly branched glucose polymer, instead.
      3. **Cellulose** is a major component of the tough walls that enclose plant cells. Because it is made of beta-glucose, the molecule is straight, and hydrogen-bonding between parallel cellulose molecules hold them together. About 80 cellulose molecules associate to form a microfibril, which weaves itself into the cell wall. Very few things can digest cellulose.
      4. **Chitin**: the carbohydrate used by arthropods to build their exoskeletons and fungi to build their cell ways.
3. **Lipids are a diverse group of hydrophobic molecules**
   1. **Fats** are constructed from glycerol, an alcohol with three carbons, each bearing a hydroxyl group; and **fatty acids**, long chains of carbon with a carboxyl group at one end. Fats separate water because the water molecules hydrogen-bond to each other and exclude the fats. Three fatty acids each join to a glycerol with ester linkages, forming a **triacylglycerol**.
      1. **Saturated fatty acid-**contains only single bonds between the carbon molecules. Usually solid at room temperature.
      2. **Unsaturated fatty acid**-contains one or more double bonds. A *cis* double bond creates a kink in the molecule, preventing the molecules from packing too tightly together so they are liquid at room temperature.
      3. Major function of fats is energy energy storage, insulation, and cushioning.
   2. **Phospholipids** make up the cell membranes. They have two fatty acids joined to a glycerol; the third hydroxyl group of glycerol is joined to a phosphate group. The fatty acids are hydrophobic, the phosphate group is hydrophilic. In water, phospholipids form a lipid bilayer to keep the fatty acid tails away from water.
   3. **Steroids**: lipds characterized by a carbon skeleton consisting of four fused rings.
      1. **Cholesterol** is a common component of animal cell membranes and is also the precursor from which other steroids are synthesized.



4. **Proteins have many structures, resulting in a wide range of functions**
   1. Proteins account for more than 50% of the dry mass of most cells. Some proteins speed up chemical reactions, while others play a role in structural support, storage, transport, cellular communication, movement, and defense against foreign substances.
   2. All proteins are polymers constructed from the same set of 20 amino acids. A protein consists of one or polypeptides. A functional protein is not just a polypeptide chain, but one or more polypeptides precisely twisted, folded, and coiled into a molecule of unique shape. There are four levels of protein structure:
      1. Primary structure: the unique sequence of amino acids.
      2. Secondary Structure: either a coil (alpha-helix) or folds (beta-pleated sheet) that result from the hydrogen bonds between the repeating constituents of the polypeptide backbone.
      3. Tertiary structure: the overal shape of a poly peptide resulting from interactions between the side chains (R groups).
         1. **Hydrophobic interaction:** water molecules exclude non-polar substances as they form hydrogen bonds with each other and the hydrophilic parts of the protein. Non-polar amino acids then attract each other with van der Waals intercations.
         2. **Polar side chains and ionic bonds:** form between positively and negatively charged side chains to help stabilize tertiary structure.
         3. **Disulfide bridges:** the sulfur of cysteine bonds to the sulfur of another cysteine.
      4. Quaternary structure: the overall protein strcture that results from the aggregation of several polypeptide subunits.
   3. Proteins are joined by dehydration synthesis, which forms **peptide bonds.**
   4. **Denaturation:** the processes that causes a protein to lose its structure and function.
   5. **Chaperonins:** proteins molecules that assist in the proper folding of other proteins.

- **Gene**: a unit of inheritance. Codes for the amino acid sequence of a polypeptide.

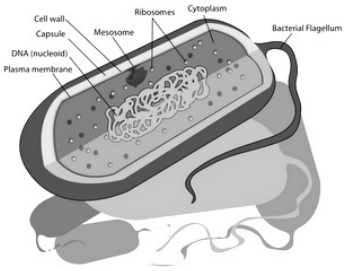


5. Nucleic acids store and transmit hereditary information

1. **Nucleic acids**: enable living organisms to reproduce their complex components from one generation to the next. There are two types:
   1. **Deoxyribonucleic acid**
   2. **Ribonucleic acid**
2. Sites of protein synthesis are tiny structures called ribosomes.
3. Nucleic acids are macromolecules that exist as polymers called **polynucleotides,** which consist of monomers called **nucleotides**.
   1. There are two types of nucleotides:
      1. **pyrimidines**, which have a six-membered ring of carbon and nitrogen atoms. They include cytosine, thymine, and uracil.
      2. **Purines**: which have a six-membered ring fused to a five-membered ring. They include adenine and guanine.
   2. The sugars connected to the nitrogenous base are **ribose** and **deoxyribose;** the later lacks an oxygen atom on the second carbon of its ring. Because the atoms in both the nitrogenous base and the sugar are numbered, the sugar atoms have a prime (') after the number to distinguish them.
   3. Adjacent nucleotides are joined by a phosphodiester linkage. The two free ends of the polymer are distinctly different from each other. One end has a phosphate attached to a 5' carbon, and the other end has a hydroxyl group on the 3' carbon.
4. DNA molecules have two polynucleotides that spiral around an imaginary axis, forming a double helix.
   1. The two sugar-phosphate backbones run in opposite 5'→3' directions from each other, an arrangement referred to as **antiparallel.**
   2. One long DNA double helix includes many genes.
   3. Adenine always pairs with thymine, and guanine always pairs with cytosine (in DNA).
5. The linear sequences of nucleotides in DNA molecules are passed from parents to offspring. Siblings have greater similarity in their DNA and proteins than do unrelated individuals of the same species.
6. Molecular biology has added a new tape measure to the toolkit biologists use to assess evolutionary kinships.

Chapter 6: A Tour of the Cell

- **Light microscope**: visible light is passed through the specimen and then through glass lenses. Cannot resolve detail finer than about 200 nanometers.
- **Electron Microscope**: Focuses a beam of electrons through the specimen or onto its surface. For practical purposes they usually cannot resolve biological structure smaller than about 2 nm. Invented in the 1950s. Disadvantage: the processes to prepare the slides kills them.
- **Cell fractionation**: takes cells apart and separates the major organelles and other subcellular structures from one another.
- **cytosol**: the aqueous part of the cytoplasm within which various particles and organelles are suspended



- **Nucleus**: contains most of the genes in the eukaryotic cell.
- **Nuclear lamina**: a netlike array of protein filaments that maintains the same of the nucleus by mechanically supporting the nuclear envelope.
- **Nuclear matrix**: a framework of fibers extending throughout the nuclear interior.

- **Endomembrane system:** synthesizes proteins, transports proteins into membranes and organelles or out of the cell, metabolism and movement of lipids, and detoxification of poisons.

- **Transport vesicles**: vesicles in transit from one part of the cell to another.

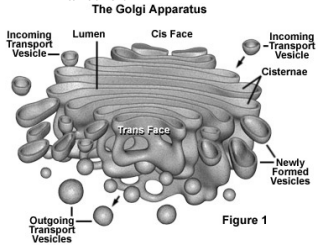


Figure 1

1. To study cells, biologist use microscopes and the tools of biochemistry

1. **1665:** Robert Hooke sees cell walls from the bark of an oak tree.
2. **1674**: Antoni van Leeuwenkoek sees living cells.
3. **Organelles**: Membrane-enclosed compartments within cells.
4. **Scanning electron microscope**: The electron beam scans the surface of the sample, which is usually coated with gold. The beam excites electrons on the surface, and these secondary electrons are detected by a device that translates the pattern of electrons into an electronic signal to a video screen.
5. **Transmission electron microscope**: aims an electron beam through a very thin section of the specimen, similar to the way a light microscope transmits light through a slide. The specimen has been stained with atoms of heavy metals, which attach to certain cellular structures, thus enhancing the electron density of some parts of the cell more than others. The electrons passing through the specimen are scattered more in the denser regions, so fewer are transmitted.
6. Microscopy techniques can introduce **artifacts**, structural features seen in micrographs that do not exist in the living cells.

2. Eukaryotic cells have internal membranes that compartmentalize their functions

1. All cells have several basic features in common:
    1. They are all bounded by selective membrane called the *plasma membrane.*
    2. They contain **chromosomes**, which carry genes in the form of DNA.
    3. They have **ribosomes**, which make proteins according to instructions from the genes.
2. In **eukaryotic cells**:
    1. Most of the DNA is in an organelle called the nucleus, which is bounded by a double, porous membrane.
    2. Have membrane-bound organelles. These provide different local environments that facilitate specific metabolic functions.
3. In **prokaryotic cells**:
    1. the DNA is concentrated in a region that is not membrane-enclosed, called the **nucleoid**.
    2. Lack membrane-bound organelles.
4. The **plasma membrane** functions as a selective barrier that allows sufficient passage of oxygen, nutrients and wastes to service the entire cell. Like most biological membranes, plasma membranes consist of a double layer of phospholipids and other lipids.

3. The eukaryotic cell's genetic instructions are housed in the nucleus and carried out by the ribosomes

1. The **nuclear envelope**, which encloses the **nucleus**, is a double membrane. Each membrane is a lipid bilayer and the two are separated by a space of about 20-40 nm. The envelope has many pores. At the lip of each pore, the inner and outer membranes are continuous. A *pore complex,* made out of proteins, lines each pore and regulates the entry and exist of proteins, RNAs, and macromolecules.
2. **Chromosomes**: structures that carry genetic information. Each chromosome is made of **chromatin**.
3. **Nucleous**: a mass of densely stained granules fibers in the nucleus that synthesizes rRNA.
4. The nucleus directs protein synthesis by synthesizing mRNA according to instructions provided by the DNA. The mRNA is then transported to the cytoplasm via the nuclear pores. Once an mRNA molecule reaches the cytoplasm, ribosomes translate the mRNA's genetic message into the primary structure of a specific polypeptide.
5. *Free ribsomes* are suspended in the cytosol while *bound ribosomes* are attached to the outside of the endoplasmic reticulum or nuclear envelope. Most of the proteins made by free ribosomes function within the cytosol. Bound ribosomes generally make proteins that are destined for insertion into membranes, for packaging within certain organelles such as lysosomes, or for export from the cell.

4. **The endomembrane system regulates protein traffic and performs metabolic functions in the cell**.

1. The membranes of the endomembrane system are related either through direct physical continuity or by the transfer of membrane segments as tiny *vesicles.*
2. The endomembrane system includes the nuclear envelope, the endoplasmic reticulum, the Golgi apparatus, lysosomes, various kinds of vacuoles, and the plasma membrane.
3. **Endoplasmic reticulum**: accounts for more than half the total membrane in many eukaryotic cells. The ER consists of a network of membranous tubules and sacs called cisternae. The ER membrane separates the internal compartment of the ER, called the ER lumen or cisternal space, from the cytosol. The ER membrane is continuous with the nuclear envelope. The space between the two membranes of the nuclear envelope is continuous with the lumen of the ER.
4. The **smooth ER** synthesizes lipids, including oils, phospholipids, and steroids. Other enzymes of the smooth ER help detoxify drugs and poisons, especially in liver cells. The smooth ER also stores calcium ions.
5. Many types of cells secrete proteins produced by ribosomes attached to **rough ER**. As a polypeptide chain grows from a bound ribosomes, it is threaded into the ER lumen through a pore formed by a protein complex in the ER membrane. Most secretory proteins are **glycoproteins**. Secretory proteins depart from the ER wrapped in the membranes of vesicles that bud like bubbles from a specialized region called the *transitional ER.*
6. Rough ER is also a membrane factory for the cell; it grows in place by adding membrane proteins and phospholipids to its own membrane.
7. After leaving the ER, many transport vesicles travel to the **Golgi apparatus**, where products of the ER are modified, stored, and sent to other destinations. The Golgi apparatus consists of flattened membranous sacs—cisternae--looking like a stack of pita bread. Vesicles concentrated in the vicinity of the of the Golgi apparatus are engaged in the transfer of material between parts of the Golgi and other structures. The two poles of a Golgi stack are referred to as the *cis* face, which receives material, and the *trans* face, which ships material. The *cis* face is usually located near the ER. The *trans* face gives rise to vesicles, which pinch off and travel to other sites. Products of the ER are usually modified during their transit from the *cis* region to the *trans* region of the Golgi. The Golgi apparatus also manufactures certain macromolecules by itself, such as pectins and other noncellulose polysaccharides. The Golgi manufactures and refines its products in stages, with different cisternae containing unique teams of enzymes. Before a Golgi stack dispatches its products by budding vesicles from the *trans* face, it sorts these products and targets them for various parts of the cell.
8. **Lysosomes**: a membranous sac of hydrolytic enzymes that an animal cell uses to digest macromolecules. Hydrolytic enzymes and lysosomal membrane are made by rough ER and then transferred to the Golgi apparatus for further processing.
    1. Amoebas and many other protists eat by engulfing smaller organisms or other food particles, a process called **phagocytosis**. The *food vacuole* formed in this way then fuses with a lysosome, whose enzymes digest the food.

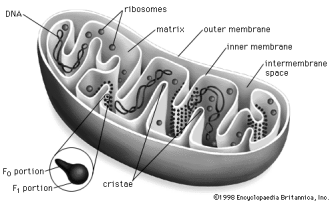
2. *Autophagy:* the process in which lysosomes use their hydrolytic enzymes to recycle the cell's own organic material.
3. In plants and fungi, which lack lysosomes, vacuoles carry out hydrolysis.
4. In Tay-Sachs disease, a lipid-digesting enzyme is missing or inactive, the lysosomes become engorged with lipids and begin to interfere with other cellular activities. This causes the brain to become impaired by an accumulation of lipids in the cells.

9. **Vacuoles**: Diverse Maintenance Compartments.
   1. Mature plant cells generally contain a large **central vacuole**. The solution inside, called cell sap, differs in composition from the cytosol. The central vacuole can hold reserves of important organic compounds, inorganic ions, and can also contain metabolic by-products, pigments, or poisons to prevent predators. Vacuoles also help plants grow faster by absorbing water.

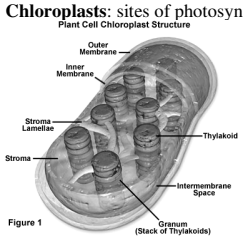
- **Food vacuoles**: store food
- **Contractile vacuoles**: pump water out of cell.

5. **Mitochondria and chloroplasts change energy from one form to another**
   1. Mitochondria have two membranes separating their innermost space from the cytosol, and chloroplasts typically have tree. (Chloroplasts and related organelles in some algae have *four* membranes.) The membrane proteins of mitochondria and chloroplasts are made not by ribosomes bound to the ER, but by free ribosomes in the cytosol and by ribosomes contained within these organelles themselves. Mitochondria and chloroplasts also contain a small amount of DNA. They are semi-autonomous organelles that grow and reproduce within the cell.
   2. Mitochondria are found in nearly all eukaryotic cells. They are about 1-10 μm long. Time-lapse films of living cells reveal mitochondria moving around, changing their shapes, and fusing or diving into two. The mitochondrion is enclosed by two membranes, each phospholipid bilayer with a unique collection of embedded proteins. The outer membrane is smooth, but the inner membrane is convoluted, with infoldings called **cristae**.
      1. **Intermembrane space**: the narrow region between the inner and outer membranes.
      2. **Mitochondrial matrix**: is enclosed by the inner membrane and contains mitochondrial DNA and ribosomes, in addition to many different enzymes.
   3. The chloroplast is a specialized member of a family of closely related plant organelles called **plastids**. Chloroplasts contain the green pigment chlorophyll, along with enzymes and other molecules that function in the photosynthetic production of sugar. Their shapes are changeable, and they grow and occasionally pinch in two, reproducing themselves.
      1. **Thylakoids**: flattened, interconnected sacs inside chloroplasts. They are sometimes arranged into stacks called **grana.** The fluid outside the thylakoids is the **stroma**, which contains the chloroplast DNA and ribsomes as well as many enzymes. The membranes of the chloroplast divide the chloroplast space into three compartments: the intermembrane space, the stroma, and the thylakoid space.
   4. The peroxisome is a specialized metabolic compartment that is bounded by a single membrane. They contain enzymes that transfer hydrogen from various substrates to oxygen, producing hydrogen peroxide as a by-product, from which the organelle derives its name. Some peroxisomes use oxygen to break fatty acids down. Peroxisomes in the liver detoxify alcohol and other harmful compounds. H_2O_2 itself is toxic, but peroxisomes also contains an enzyme that converts it to water.
      1. Specialized peroxisomes called *glyoxysomes* are found in the fat-storing tissues of plant seeds. They convert fatty acids to sugar.
      2. Peroxisomes do not bud from the endomembrane system. They grow larger by incorporating proteins made primarily in the cytosol, lipids made in the ER, and lipids synthesized within the peroxisome itself. They may increase in number by splitting in two when they reach a certain size.

- **Mitochondria**: sites of cellular respiration.



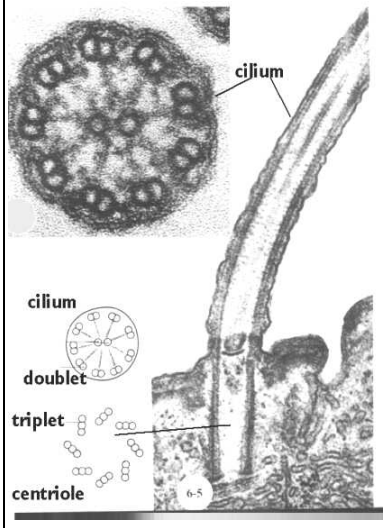
- **Chloroplasts**: sites of photosynthesis



- **Peroxisome**: oxidative organelle that is not part of the endomembrane system. Imports its proteins primarily from the cytosol.

- **Cytoskeleton**: a network of fibers extending throughout the cytoplasm.

6. **The cytoskeleton is a network of fibers that organizes structures and activities in the cell**
   1. The cytoskeleton plays a major role in organizing the structures and activities of the cell, is composed of three types of molecular structures: microtubules, microfilaments, and intermediate filaments.
      1. *Microtubules* are the thickest of the three types. They are hollow rods measuring about 25 nm in diameter and from 200 nm to 25 μm in length. They are constructed of tubulin proteins. Each tubulin protein is a *dimer*, a molecule made up of two subunits. One end of the microtubule can accumulate or release tubulin dimers at a much higher rate than the other, thus growing and shrinking significantly during cellular activities. This is called the "plus end". Microtubules shape and support the cell and also serve as tracks along which organelles equipped with motor proteins can move. They resist compression forces.
         1. In animal cells, microtubules grow out from a **centrosome**, a region that is often located near the nucleus and is considered a "microtubule-organizing center." Within the centrosome are a pair of **centrioles**, each composed of nine sets of triplet microtubules arranged in a ring. Although centrosomes with centrioles may help organize microtubule assembly in animal cells, they are not essential for this function in all eukaryotes.
         2. A specialized arrangement of microtubules is responsible for the beating of **flagella** and **cilia**. **Flagella** and **cilia** can act as locomotor appendages or they can move fluid over the surface of a tissue. Motile cilia usually occur in large numbers of the cell surface. They are about 0.25 μm in diameter and about 2-20 μm long. Flagella are the same diameter but longer, 10-200 μm and are typically limited to just one or a few per cell. A flagellum has an undulating motion while cilia work more like oars.
            1. A cilium may also act as a signal-receiving "antenna" for the cell. Cilia that have this function are generally nonmotile, and there is only one per cell. (In vertebrate animals, almost all cells seem to have such a cilium, which is called a *primary cilium.).*
            2. Motile cilia and flagella share a common ultrastructure. Both have a core of microtubules sheathed in an extension of the plasma membrane. Nine doublets of microtubules, the members of each pair sharing part of their walls, are arranged in a ring. In the center of the ring are two single microtubules. Nonmotile primary cilia lack the central pair of microtubules. The microtubule assembly of a cilium or a flagellum is anchored in the cell by a **basal body**, which is structurally very similar to a centriole.
            3. In flagella and motile cilia, flexible cross-linking proteins, even spaced along the length of the cilium or flagellum, connect the outer doublets to each other and to the two central microtubules. Each outer doublet also has pairs of protruding proteins, called **dyneins,** spaced along its length and reaching toward the neighboring doublet. The mechanics of dynein-based bending involve a process that resembles walking. A typical dynein protein has two "feet" that "walk" along the microtubule of the adjacent doublet, one foot maintaining contact while the other releases and reattaches one step further along the microtubule. Microtubule doublets seem to be to be held in place by cross-linking proteins just inside the outer doublets and by the radial spokes and other structural elements, so the forces exerted by dynein "walking" cause the doublets to curve.

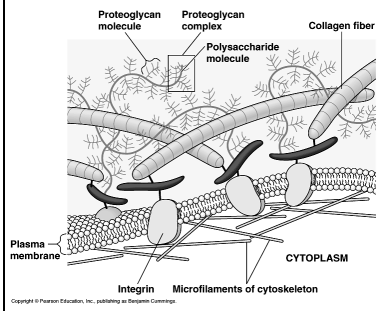


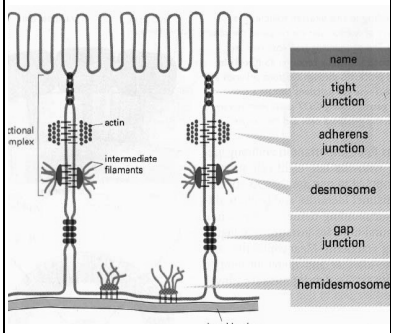
2. *Microfilaments* (also known as actin filaments) are the thinnest. They are solid rods about 7 nm in diameter and are made out of molecules of **actin**. A microfilament is a twisted double chain of actin subunits. Beside occurring as linear filaments, microfilaments can form structural networks. They seem to be present in all eukaryotic cells. They bear tension. A three-dimensional network formed by microfilaments (*cortical microfilaments)* just inside the plasma membrane helps support the cell's shape. This network gives the out cytoplasmic layer of a cell (the **cortex**) the semisolid consistency of a gel. In animal cells specialized for transporting materials across the plasma membrane, bundles of microfilaments make up the core of microvilli.
    1. Microfilaments are well known for their role in cell motility, particularly as part of the contractile apparatus of muscle cells. Contraction of the muscle cell results from the actin and myosin filaments sliding past one another. In other kinds of cells, actin filaments are associated with myosin in miniature and less elaborate versions of the arrangement in muscle cells. These actin-myosin aggregates are responsible for localized contraction of cell. A contracting belt of microfilaments forms a cleavage furrow that pinches a dividing animal cell into two daughter cells. Localized contraction also plays a role in amoeboid movement. In plant cells, both actin-myosin interactions and sol-gel transformations brought about by actin may be involved in **cytoplasmic streaming**.
3. *Intermediate filaments* have diameters in a middle range, 8 nm-12 nm. They are specialized for bearing tension. Each type is constructed from a different molecular subunit belonging to a family of proteins whose members include keratins. Intermediate filaments are more permanent fixtures of cells than are microfilaments and microtubules. Even after cells die, the intermediate filament networks often persist. Intermediate filaments are especially important in reinforcing the shape of a cell and fixing the position of certain organelles. The nucleus commonly sits within a cage of made of intermediate filaments. Other intermediate filaments make up the nuclear lamina. In cases where the shape of the entire cell correlated with function, intermediate filaments support that shape.

2. The most obvious function of the cytoskeleton is to give mechanical support to the cell and maintain its shape. The cytoskeleton provides anchorage for many organelles and even cytosolic enzyme molecules. It can be quickly dismantled in one part of the cell and reassembled in a new location, changing the shape of the cell.
3. Cell motility generally requires the interaction of the cytoskeleton with **motor proteins.** Vesicles and other organelles often travel to their destinations along "monorails" provided by the cytoskeleton.
4. The cytoskeleton is also involved in regulating biochemical activities in the cell in response to mechanical simulation. Cytoskeleton transmission of naturally occurring mechanical signals may help regulate and coordinate the cell's response.

7. **Extracellular components and connections between cells help coordinate cellular activities**.
    1. The plasma membrane is usually regarded as the boundary of the living cell, but most cells synthesize and secrete materials that are external to the plasma membrane.
    2. Plant cell walls are much ticker than the plasma membrane, ranging from 0.1 μm to several micrometers. The exact chemical composition of the wall varies from species to species and cell type to cell type. Microfibrils made of the polysaccharide cellulose are secreted to the extra cellular space, where they become embedded in a matrix of other polysaccharides and proteins.
        1. A young plant cell first secretes a relatively thin and flexible wall called the **primary cell wall**. In actively growing cell, the cellulose fibrils are oriented at right angles to the direction of cell expansion. Microtubules in the cell cortex guide cellulose synthase as it synthesized and deposits the fibrils.
        2. Between the primary walls of adjacent cells is the **middle lamella**, a thin layer rich in sticky polysaccharides called pectin. It glues adjacent cells together.
        3. When a plant cell matures and stops growing, it strengthens its wall. Some just secrete hardening substances into the primary cell wall. Others add a **secondary cell wall** between the plasma membrane and the primary wall.
    3. Although animal cells lack walls akin to those of plant cells, they do have an elaborate **extracellular matrix**. The main ingredients of the ECM are glycoproteins secreted by the cells. The most abundant glycoprotein in the ECM of most animal cells is **collagen**, which forms strong fibers outside the cells. The collagen fibers are embedded in a network woven from **proteoglycans**. Some cells are attached to the ECM by still other ECM glycoproteins, such as **fibronectin**. Fibronectin and other ECM proteins bind to cell surface receptor proteins called **integrins** that are built into the plasm membrane. Integrins span the membrane and bind on their cytoplasmic side to associated proteins attached to microfilaments of the cytoskeleton. By communicating with a cell through integrins, the ECM can regulate a cell's behavior.
    4. **Intercellular junctions**
        1. **Plasmodesmata**: The channels that perforate cell walls in plants. Cytosol passes through the plasmodesmata and connects the chemical environments of adjacent cells. The plasma membranes of adjacent cells line the channel of each plasmodesmata and thus are continuous.
        2. In animals, there are three main types of intercellular junctions: *tight junctions, desmosomes,* and *gap junctions.* All three types of intercellular junctions are especially common in epithelial tissue.
            1. **Tight junctions**: the plasma membranes of neighboring cells are very tightly pressed against each other, bound together by specific proteins. Tight junctions prevent leakage of extracellular fluid across a layer of epithelial cells.
            2. **Desmosomes** function like rivets, fastening cells together into strong sheets. Intermediate filaments made of sturdy keratin proteins anchor desmosomes in the cytoplasm. Desmosomes attach muscle cells to each other.
            3. **Gap junctions** provide cytoplasmic channels from one cell to an adjacent cell are are similar to plasmodesmata in plant cells. They consist of membrane proteins that surround a pore through which ions, sugars, amino acids, and other small molecules may pass.

- ***Cell Wall****:* an extracellular structure of plant cells that protects the cell, maintains its shape, and prevents excessive uptake of water.





Chapter 7: Membrane Structure and Function.

- **Selective permeability**: Some substances can cross easier than others.

1. **Cellular membranes are fluid mosaics of lipids and proteins**
    1. The plasma membrane is the edge of life, the boundary that separates the living cell from its surroundings.
    2. The most abundant lipids in most membranes are phospholipids, which are **amphipathic** molecules.
    3. In the **fluid mosaic model**, the membrane is a fluid structure with a "mosaic" of various proteins embedded in or attached to a double layer (bilayer) of phospholipids.
    4. **1915**: membranes isolated from red blood cells were chemically analyzed and found to be composed of lipids and proteins.
    5. **1925:** Two Dutch scientists, E. Gorter and F. Grendel, reasoned that cell membranes must be phospholipid bilayers.
    6. **1935**: Hugh Davson and James Danielli suggested the cellular membrane was a sandwich of phospholipids between two layers of hydrophilic proteins. Although the heads of phospholipids are hydrophilic, the surface of a membrane consisting of a pure phospholipid bilayer adheres less strongly to water that does the surface of a biological membrane. By the 1960s, the Davson-Danielli sandwich had become widely accepted as the structure of all of a cells membranes. However, not all cellular membranes are identical and membrane proteins are actually amphipathic.
    7. **1972**: S. J. Singer and G. Nicolson proposed that membrane proteins are dispersed, individually inserted into the phospholipid bilayer with their hydrophilic regions protruding.
    8. A method of preparing cells from electron microscopy called freeze-fracture has demonstrated visually that proteins are indeed embedded in the phospholipid bilayer of the membrane. Freeze-fracture splits a membrane along the middle of the phospholipid bilayer, somewhat like pulling apart a chunky peanut butter sandwich.
    9. Most of the lipids and some of the proteins can shift about laterally, but it is quite rare for a molecule to flip-flop transversely across the membrane, switching from one phospholipid layer to the other.
    10. A membrane remains fluid as temperature decreases until finally the phospholipids settle into a closely packed arrangement and the membrane solidifies. The temperature at which a membrane solidifies depends on the types of lipids it is made of. The membrane remains fluid to a lower temperature it is rich in phospholipids with unsaturated hydrocarbon tails.
        1. The steroid cholesterol, which is wedged between phospholipid molecules in the plasma membranes of animal cells, has different effects on membrane fluidity at different temperatures. At relatively high temperatures (like 37 ºC, the body temperature of humans), cholesterol makes the membrane less fluid by restraining phospholipid movement. However, because cholesterol also hinders the close packing of phospholipids, it lowers the temperature required for the membrane to solidify.
        2. Membranes must be fluid to work properly.
    11. A membrane is a collage of different proteins embedded in the fluid matrix of the lipid bilayer. Proteins determin most of the membrane's function.
        1. **Integral proteins** penetrate the hydrophobic core of the lipid bilayer. Many are *transmembrane proteins* which span the membrane. Other integral proteins extend only partway into the hydrophobic core. The hydrophobic regions of an integral protein consist of one or more stretches of nonpolar amino acids, usually coiled into α helices.
        2. **Peripheral proteins** are not embedded in the lipid bilayer at all; they are appendages loosely bound to the surface of the membrane, often to exposed parts of integral proteins.
        3. There are six major functions performed by proteins of the plasma membrane.
            1. **Transport**: A protein that spans the membrane my provide a hydrophilic channel across the membrane that selected for a particular solute. Other transport proteins shuttle a substance from one side to the other by changing shape.
            2. **Enzymatic activity**: a protein built into the membrane may be an enzyme with its active site exposed to substances in the adjacent solution. In some cases, several enzymes in a membrane are organized as a team that carries out sequential steps of a metabolic pathway.
            3. **Signal transduction**: A membrane protein (receptor) may have a binding site with a specific shape that fits the shape of a chemical messenger, such as a hormone. The external messenger may cause a shape in the protein the relays the message to the inside of the cell.
            4. **Cell-cell recognition**: Some glycoproteins serve as identification tags that specifically recognized by membrane proteins of other cells. Cells recognize other cells by binding to surface molecules, often carbohydrates, on the plasma surface. Some membrane carbohydrates are covalently bonded to lipids (**glycolipids**). Most are covalently bonded to proteins (**glycoproteins**).
            5. **Intercellular joining**: Membrane proteins of adjacent cells may hook together in various kinds of junctions, such as gap junctions or tight junctions.
            6. **Attachment to the cytoskeleton and extracellular matrix**: Microfilaments or other elements of the cytoskeleton may be non-covalently bound to membrane proteins, a function that helps maintain cell shape stabilizes the location of certain membrane proteins. Proteins that can bind to ECM molecules can coordinate extracellular and intracellular changes.
    12. Membranes have distinct inside and outside faces. The asymmetrical arrangement of proteins, lipids, and their associated carbohydrates in the plasma membrane is determined as the membrane is built by the ER and Golgi apparatus.
2. **Membrane structure results in selective permeability**
    1. The biological membrane has the ability to regulate transport across cellular boundaries, a function essential to the cell's existence.
    2. Cell membranes are selectively permeable, and substances do not cross the barrier indiscriminately.
    3. Nonpolar molecules, such as hydrocarbons, carbon dioxide, and oxygen, are hydrophobic and can therefore dissolve in the lipid bilayer of the membrane and cross it easily, without the aid of membrane proteins.
    4. Polar molecules such as glucose and other sugars pass only slowly through a lipid bilayer, and even water, an extremely small polar molecule, does not cross very rapidly. These hydrophilic substances can avoid contact with the lipid bilayer by passing through **transport proteins** that span the membrane.
        1. Some transport proteins, called *channel proteins,* function by having a hydrophilic channel that certain molecules or atomic ions use as a tunnel through the membrane. (Water passes through channels called *aquaporins).*
        2. Other transport proteins, called *carrier proteins,* hold onto their passengers and change shape in a way that shuttles them across the membrane.
        3. A transport protein is specific for the substance it translocates, allowing only a certain substance to cross the membrane.

- **Diffusion:** the movement of molecules of any substance so that they spread out evenly into the available space
- **Concentration gradient:** The region along which the density of a chemical substance decreases. No work must be done in order to make this happen. Each substance diffuses down its *own* concentration gradient, unaffected by the concentration differences of other substances.
- **Osmoregulation**: the control of water balance.

- **Membrane potential**: the voltage across a membrane (ranges between -50 to -200 mV).

- **Ligand**: any molecule that binds specifically to a receptor site of another molecule.

3. **Passive transport is diffusion of a substance across a membrane with no energy investment**
    1. The diffusion of a substance across a biological membrane is called **passive transport** because the cell does not have to expend energy to make it happen.
    2. **Osmosis:** The diffusion of water across a selectively permeable membrane.
    3. **Tonicity:** The ability of a solution to cause a cell to gain to lose water.
        1. If a cell without a wall is immersed in an environment that is **isotonic** to the cell, there will be no *net* movement of water across the plasma membrane.
        2. If it is immersed in a solution that is **hypertonic** to the cell, the cell will lose water to its environment, shrivel, and probably die.
        3. If it is immersed in a solution that is **hypotonic** to the cell, water will enter the cell faster than it leaves, and the cell will swell and lyse like an overfilled water balloon.
        4. A cell without rigid walls can tolerate neither excessive uptake nor excessive lose of water.
        5. However, the relatively inelastic cell wall will expand only so much before it exerts a back pressure on the cell that opposes further water uptake. At this point, the cell is **turgid**, which is the healthy state for most plant cells. If a plant's cells and their surroundings are isotonic, there is no net tendency for water to enter, and the cells become **flaccid** (limp).
        6. In a hypertonic environment, a plant cell will lose water to its surroundings and shrink. Its plasma membrane will pull away from the cell wall (**plasmolysis**), and the plant will wilt.
    4. Many polar molecules and ions impeded by the lipid bilayer of the membrane diffuse passively with the help of transport proteins that span the membrane. This phenomenon is called **facilitated diffusion.**
        1. Channel proteins simply provide corridors that allow a specific molecule or ion to cross the membrane.
        2. A group of channel proteins are **ion proteins,** many of which function as **gated channels**, which open or close in response to a stimulus.
        3. Carrier proteins seem to undergo a subtle change in shape that somehow translocates the solute-binding site across the membrane.
        4. In certain inherited diseases, specific transport systems are either defective or missing altogether.
    5. Despite the help of transport proteins, facilitated diffusion is considered passive transport because the solute is moving down its concentration gradient.
4. **Active transport uses energy to move solutes against their gradients.**
    1. Some transport proteins can move solutes against their concentration gradients., across the plasma membrane from the side where they are less concentrated to the side where they are more concentrated.
    2. To pump a molecule across a membrane against its gradient requires work; the cell must expend energy. Therefore, this type of membrane traffic is called **active transport.** As in other types of cellular work, ATP supplies the energy for most active transport.
    3. Active transport enables a cell to maintain internal concentrations of small molecules that differ from concentrations in its environment.
        1. One transport system that works this way is the **sodium-potassium pump,** which exchanges sodium for potassium across the plasma membrane of animal cells.
    4. The cytoplasm is negative in charge relative to the extracellular fluid because of an unequal distribution of anions and cations on opposite sides of the membrane. Thus, *two* forces drive the diffusion of ions across a membrane: a chemical force (the ion's concentration gradient) and a electrical force (the effect of the membrane potential on the ion's movement.) This combination of forces action on an ion is called **electrochemical gradient.**
        1. A transport protein that generates voltage across a membrane is called an **electrogenic pump**. The sodium-potassium pump seems to be the major electrogenic pump of animal cells. The name electrogenic pump of plants, fungi, and bacteria is a **proton pump,** which actively transports hydrogen ions (protons) out of the cell.
    5. A single ATP-powered pump that transports a specific solute can indirectly drive the active transport of several other solutes in a mechanism called **cotransport.** A plant cell uses the gradient of hydrogen ions generated by its proton pumps to drive the active transport of amino acids, sugars, and several other nutrients into the cell.
5. **Bulk transport across the plasma membrane occurs by exocytosis and endocytosis.**
    1. Large molecules, such as proteins and polysaccharides, as well as larger particles, generally cross the membrane in bulk be mechanism that involve packaging vesicles. Like active transport, these processes require energy.
    2. The cell secretes certain biological molecules by the fusion of vesicles with the plasma membrane (**exocytosis**).
        1. Many secretory cells use exocytosis to export products.
    3. In **endocytosis**, the cell takes in biological molecules and particulate matter by forming new vesicles from the plasma membrane. Although the proteins involved in the processes are different, the events of endocytosis looks like the reverse of exocytosis. There are three types of endocytosis:
        1. **Phagocytosis:** Cellular eating.
        2. **Pinocytosis:** Cellular drinking.
        3. **Receptor-mediated endocytosis:** Human cells use receptor-mediated endocytosis to take cholesterol for use in the synthesis of membranes and other steroids. Cholesterol travels in the blood in particles called low-density lipoproteins (LDLs), complexes of lipids and proteins. LDLs act as *ligands* by binding to LDL receptors on plasma membranes and then entering the cells by endocytosis.

Chapter 8: An Introduction to Metabolism

- **Metabolism**: the totality of an organism's chemical reactions.
- **Bioenergetics**: The study of how energy flows through living organisms.
- **Energy**: the capacity to cause to change.
- **Thermodynamics**: The study of the energy transformations that occur in a collection of matter.

1. An organism's metabolism transforms matter and energy, subject to the laws of thermodynamics.

1. A **metabolic pathway** begins with a specific molecule, which is then altered in a series of defined steps, result in a certain product. Each step of the pathway is catalyzed by a specific enzyme.
    1. **Catabolic pathways** release energy by breaking down complex molecules into simpler compounds.
    2. **Anabolic pathways** consume energy to build complicated molecules from simpler ones.
2. Energy exists in various forms, and the work of life depends on the ability of cells to transform energy from one type into another.
    1. **Kinetic energy:** Energy associated with the relative motion of objects. **Heat**, or **thermal energy**, is kinetic energy associated with the random movement of atoms or molecules.
    2. **Potential energy:** The energy that matter possesses because of its location or structure. **Chemical energy** is a term used by biologist to refer to the potential energy available for release in a chemical reaction.
3. An *isolated system*, such as that approximated by liquid in a thermos bottle, is unable to exchange either energy or matter with its surroundings. In an *open system*, energy and matter can be transferred between the system and its surroundings.
4. **First law of thermodynamics:** Energy can be transferred and transformed, but it cannot be created or destroyed. (Principle of conservation of energy).
5. **Second law of thermodynamics:** Every energy transfer or transformation increases the entropy of the universe. For a process to occur spontaneously, it must increase the entropy of the universe.
    1. It is true that cells create ordered structures from less organized starting materials. However, an organism also takes in organized forms of energy from the surroundings and replaces them with less ordered forms.
    2. On a larger scale, energy flows into an ecosystem in the form of light and exists in the form of heat.
    3. The entropy of a particular system, such as an organism, may actually decrease as long as the total entropy of the *universe*—the system plus its surroundings—increases.

- **Entrophy:** a measure of disorder or randomness.
- **Spontaneous process**: a process that can occur without an input of energy. Does not imply that such a process would occur quickly.

2. The free-energy change of a reaction tells us whether or not the reaction occurs spontaneously.

1. The change in free energy, ΔG, can be calculated for a chemical reaction with the following formula: $\Delta G = \Delta H - T\Delta S$ when ΔH is the change in the system's *enthalpy,* ΔS is the change in the system's entropy, and T is the absolute temperature in Kelvin units. Only experiments with a negative ΔG are spontaneous.
2. We can think of free energy as a measure of a system's instability—its tendency to change to a more stable state. Unless something prevents it, systems will move towards greater stability.
3. As a reaction proceeds towards equilibrium, the free energy of the mixture of reactants and products decreases. Free energy increases when a reaction is somehow pushed away from equilibrium. Because a system at equilibrium cannot spontaneously change, it can do no work. A process is spontaneous and can perform work only when it is moving towards equilibrium.
4. An **exergonic reaction** proceeds with a net release of free energy. Because the chemical mixture loses free energy, ΔG is negative for an exergonic reaction.
5. An **endergonic reaction** is one that absorbs free energy from its surroundings. Because this kind of reactions essentially *stores* free energy in molecules, ΔG is positive. Such reactions are nonspontaneous.
6. Reactions in an isolated system eventually reach equilibrium and can then do no work. Because systems at equilibrium are at a minimum of *G* and can do no work, a cell that has reached metabolic equilibrium is dead. The fact that metabolism as a whole is never at equilibrium is one of the defining features of life.
7. A living cell is not in equilibrium. The constant flow of materials in and out of the cell keeps the metabolic pathways from ever reaching equilibrium.

- **Free energy** is the portion of a system's energy that can perform work when temperature and pressure are uniform throughout the system.

3. ATP powers cellular work by coupling exergonic reactions to endergonic reactions.

1. A cell does three main kinds of work:
    1. *Chemical work*: the pushing of endergonic reactions, which would not occur spontaneously.
    2. *Transport work:* the pumping of substances across membranes against the direction of spontaneous movement.
    3. *Mechanical work:* such as the beating of cilia, the contraction of muscle cells, and the movement of chromosomes during cellular reproduction.
2. **Adenosine triphosphate** contains the sugar ribose, with the nitrogenous base adenine and a chain of three phosphate groups bounded to it. The bonds between the phosphate groups of ATP can be broken by hydrolysis. When the terminal phosphate bond is broken, 7.3 kcal of energy per mole is released. All three phosphate groups are negatively charged. These like charges are crowded together, and their mutual repulsion contributes to the instability of this region of the ATP molecule. The triphosphate tail of ATP is the chemical equivalent of a compressed spring.
3. The cell's proteins harness the energy released during ATP hydrolysis in several ways to perform the three types of cellular work—chemical, transport, and mechanical. Thus, the cell is able to use the energy released by ATP hydrolysis directly to drive chemical reactions that, by themselves, are endergonic. This usually involves the transfer of a phosphate group from ATP to some other molecule, such as the reactant. The recipient of the phosphate group is then said to be **phosphorylated.**
4. ATP is a renewable resource that can be regenerated by the addition of phosphate to ADP. The free energy required to phosphorylate ADP comes from exergonic breakdown reactions in the cell. The chemical potential energy temporarily stored in ATP drives most cellular work.

- **Energy coupling**: the use of an exergonic press to drive an endergonic one.

4. Enzymes speed up metabolic reactions by lowering energy barriers

1. The laws of thermodynamics tell us what will and will not happen under give conditions but say nothing about the rate of these processes.
2. Every chemical reaction between molecules involves both bond breaking and bond forming.
3. The initial investment of energy for starting a reaction is known as the *free energy of activation,* or activation **energy,** abbreviated E_A. We can think of activation energy as the amount of energy needed to push the reactants over an energy barrier, or hill, so that the "downhill" part of the reaction can begin. At the summit, the reactants are in an unstable condition know as the *transition state.* Activation energy is often supplied in the form of heat that the reactant molecules absorb from the surroundings.
4. An enzyme catalyzes a reaction by lowering the E_A barrier. An enzyme cannot change the ΔG for a reaction; it cannot make an endergonic reaction exergonic.
5. The reaction catalyzed by each enzyme is very specific; an enzyme can recognize its specific substrate even among closely related compounds, such as isomers.
6. Only a restricted region of the enzyme molecule actually binds to the substrate. This region is called the **active site**. As the substrate enters the active site, interactions between its chemical groups and those on the R groups of the amino acids that form the active site of the protein cause the enzyme to change its shape slightly so that the active site fits even more snugly around the substrate. This **induced fit** brings chemical groups of the active site into positions that enhance

- **Enzyme**: a macromolecule that acts as a catalyst.
- **Substrate**: the reactant an enzyme acts on. The enzyme binds to its substrate, forming an **enzyme-substrate complex**.

their ability to catalyze the chemical reaction.

7. In most enzymatic reactions, the substrate is held in the active site by so-called weak interactions, such as hydrogen bonds and ionic bonds.
8. Enzymes use a variety of mechanism that lower activation energy and speed up a reaction.
    1. The active site provides a template on which the substrates can come together in the proper orientation for a reaction to occur between them.
    2. As the active site of an enzyme clutches the bound substrates, the enzyme may stretch the substrate molecules towards their transition-state form, stressing and bending critical chemical bonds that must be broken during the reactions.
    3. The active site may also provide a microenvironment that is more conductive to a particular type of reaction than the solution itself would be without the enzyme.
    4. Sometimes the active site directly participates in the reaction. The process sometimes even involves brief covalent bonding between the substrate and an R group of an amino acid of the enzymes. Subsequent steps of the reaction restore the R groups.
9. The rate at which a particular amount of enzyme converts substrate to products is partly a function of the initial concentration of the substrate: The more substrate molecules that are available, the more frequently they access the active sites of the enzyme molecules.
10. The activity of an enzyme—how efficiently the enzyme functions—is affected by general environmental factors, such as temperature and pH. It can also be affected by chemicals that specifically influence that enzyme.
11. Each enzyme works better under some conditions than under others, because these *optimal conditions* favor the most active shape for the enzyme molecule.
    1. Up to a point, the rate of an enzymatic reaction increases with increasing temperature, partly because substrates collide with active sites more frequently when the molecules move rapidly.
    2. Above that temperature, however, the speed of the enzymatic reaction drops sharply.
    3. Most human enzymes have optimal temperatures of about 35-40°C (close to human body temperature.)
    4. Just as each enzyme has an optimal temperature, it also has a pH at which it is most active. The optimal pH values for most enzymes fall in the range of pH 6-8, but there are exceptions.
12. Many enzymes require nonprotein helpers (**cofactors**) for catalytic activity. Cofactors may be found tightly to the enzyme as permanent residents, or they may bind loosely and reversibly along with the substrate.
    1. The cofactors of some enzymes are inorganic. Ex: Zn, Fe, or Cu ions.
    2. **Coenzyme**: a cofactor that is an organic molecule.
13. Certain chemicals selectively inhibit the action of specific enzymes.
    1. Toxins and poisons are often irreversible enzyme inhibitors.
    2. Many antibiotics are inhibitors of specific enzymes in bacteria.

- **Competitive inhibitors**: reduce the productivity of enzymes by blocking substrates from entering active sites.
- **Noncompetitive inhibitors**: bind to another part of the enzyme in a way that changes the shape of the active site and make it less effect.

5. Regulation of enzyme activity helps control metabolism

1. Chemical chaos would result if all of a cell's metabolic pathways were operating simultaneously.
2. A cell controls its metabolic pathways either by switching on and off the genes that encode specific enzymes or by regulating the activity of enzymes
3. **Allosteric regulation** is the term used to describe any case in which a protein's function at one site is affected by the binding of a regulatory molecule to a separate site.
    1. Most enzymes know to be allosterically regulated are constructed from two or more subunits, each composed of a polypeptide chain and having its own active site. The entire complex oscillates between two different shapes, one active and the other nonactive. The binding of an *activator* to a regulator site stabilized the shape that has the functional active sites, whereas the binding of an *inhibitor* stabilizes the inactive for of the enzyme.
    2. If an enzyme has two or more subunits, a substrate molecule causing induced fit in one subunit can trigger the same favorable shape change in all the other subunits of the enzyme (**cooperativity**).
    3. Allosteric regulators are attractive drug candidates for enzyme regulation because they exhibit higher specificity for particular enzymes than do inhibitors that bind to the active site.
4. Cellular structures help bring order to metabolic pathways. In some cases, a team of enzymes for several steps of a metabolic pathway are assembled into a multienzyme complex.
    1. Some enzymes and enzyme complexes have fixed locations within the cell and act as structural components of particular membranes.
    2. Others are in solution within specific membrane-enclosed eukaryotic organelles, each with its own internal chemical environment.

- **Feedback inhibition**: a metabolic pathway is switched off by the inhibitory binding of its end product to an enzyme that acts early in the pathway.

Chapter 9: Cellular Respiration: Harvesting Chemical Energy.

- **Fermentation**: the partial degradation of sugars that occurs without the use of oxygen.
- **Aerobic respiration**: Oxygen is consumed as a reactant along with the organic fuel.
- **Anaerobic respiration**: Used by some prokaryotes; uses substances other than oxygen as the final oxidizing substance.
- **Cellular respiration**: includes both aerobic and anaerobic respiration but is usually used to refer to only aerobic respiration.

- **Oxidation**: loss of electrons.
- **Reduction**: gain of electrons.
- **Reducing agent**: donates electrons
- **Oxidizing agent**: accepts electrons.

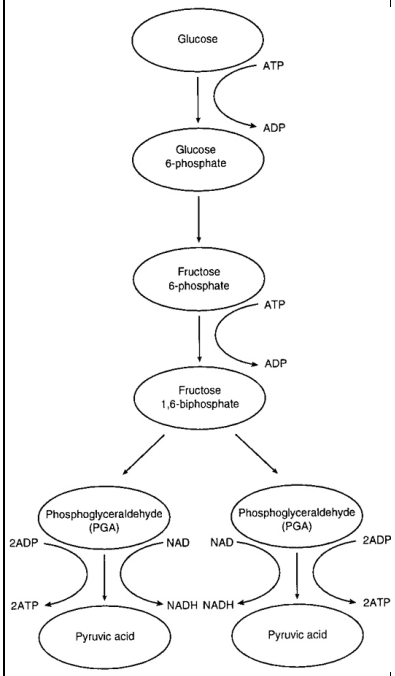
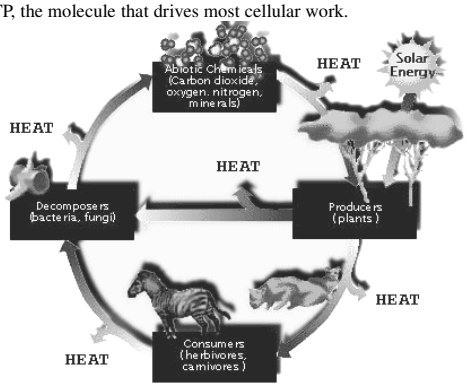


Illustration 1: Glycolysis

0. Overview: Life is Work

1. Living cells require transfusions of energy from outside sources. Energy flows into an ecosystem as sunlight and leaves as heat. Photosynthesis generates oxygen and organic molecules used by the mitochondria of eukaryotes as fuel for cellular respiration. In this chapter, we consider how cells harvest the chemical energy stored in organic molecules and use it to generate ATP, the molecule that drives most cellular work.

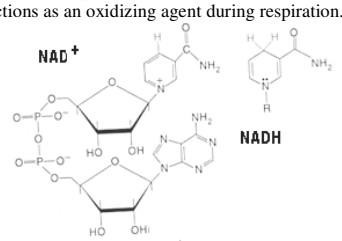


1. Catabolic pathways yield energy by oxidizing organic fuels

1. Organic compounds possess potential energy as a result of their arrangement of atoms. Compounds that can participate in exergonic reactions can act as fuels.
2. Although carbohydrates, fats, and proteins can all be processed and consumed as fuel, it is helpful to learn the steps of cellular respiration by tracking the degradation of the sugar glucose ($C_6H_{12}O_6$):

$$C_6H_{12}O_6 + 6\ O_2 \rightarrow 6\ CO_2 + H_2O + \text{Energy (ATP+heat)}$$

3. This breakdown of glucose is exergonic, having a free energy change of $\Delta G = -686$ kcal/mol.
4. The relocation of electrons releases energy stored in organic molecules, and this energy ultimately is used to synthesize ATP.
    1. In many chemical reactions, there is a transfer of one or more electrons from one reactant to another (redox reactions)
    2. Not all redox reactions involve the complete transfer of electrons from one substance to another; some change the degree of electron sharing in covalent bonds.
    3. During cellular respiration, the glucose is oxidized and oxygen is reduced. Cellular respiration does not oxidise glucose in a single explosive step, however. Rather, the cell breaks down glucose and other organic fuels in a series of steps, each one catalyzed by an enzyme. At key stops, electrons are stripped from the glucose. Each electron travels with a proton, forming a hydrogen atom. The hydrogen atoms are not transferred directly to oxygen, but instead are usually passed first to an electron carrier, a coenzyme called **NAD^+**. As an electron acceptor, NAD^+ functions as an oxidizing agent during respiration.



    4. Respiration uses an **electron transport chain** to break the fall of electrons to oxygen into several energy-releasing steps.
    5. In summary, during cellular respiration, most electrons travel the following "downhill" route: glucose → NADH → electron transport chain → oxygen.
    6. Respiration is a cumulative function of three metabolic stages:
        1. Glycolysis—Occurs in the cytosol; breaks glucose into two molecules of a compound called pyruvate.
        2. The citric acid cycle—Takes place within the mitochondrial matrix;
        3. Oxidation phosphorylation: electron transport and chemiosmosis.
    7. The energy released at each step of the chain is stored in a form the mitochondrion can use to make ATP. This mode of ATP synthesis is called **oxidative phosphorylation** because it is powered by the redox reactions of the electron transport chain.
    8. Oxidative phosphorylation accounts for almost 90% of the ATP generated by respiration. A smaller amount of AT is formed directly in a few reactions of glycolysis and the citric acid cycle by a mechanism called **substrate-level phosphorylation.**

2. Glycolysis harvests chemical energy by oxidizing glucose to pyruvate

1. The world *glycolysis* means "sugar splitting" and in glycolysis, glucose is split into two three-carbon sugars, which are then oxidized and their remaining atoms rearranged to form two molecules of pyruvate.
2. Glycolysis can be divided into two phases: energy investment and energy payoff. The net energy yield from glycolysis is 2 ATP and 2 NADH per glucose molecule. The net energy yield from glycolysis, per glucose molecule, is 2 ATP plus 2 NADH.

3. The citric acid cycle completes the energy-yielding oxidation of organic molecules

1. If molecular oxygen is present, the pyruvate enters a mitochondrion.
2. Pyruvate is first converted to a compound called acetyl coenzyme A, or **acetyl CoA,** the steps of which are as follows:
    1. Pyruvate's carboxyl group is removed and given off as a molecule of CO_2.
    2. The remaining two-carbon fragment is oxidized, forming a compound named acetate. An enzyme transfers the extracted electrons to NAD^+.
    3. Coenzyme A, a sulfur-containing compound derived from a B vitamin, is attached to the acetate by an unstable

- **ATP synthase**: the enzyme that actually makes ATP from ADP and inorganic phosphate. It works like an ion pump in reverse.
- A H^+ gradient across a membrane is called a **proton-motive force** because it can perform work.

bound that makes the acetyl group very reactive.

3. The citric acid cycle is also called the tricarboxylic acid or the Kerbs cycle. The cycle has eight steps, each catalyzed by a specific enzyme.
    1. The acetyl group of acetyl CoA joins the cycle by combining with the compound oxaloacetate, forming citrate. The next seven steps decompose the citrate back to oxaloacetate, making this process a cycle.
4. In total, 6 NADH, 2 $FADH_2$ and 2 GTP (or ATP) are formed per glucose molecule.
5. Most of the ATP produced by respiration results from oxidative phosphorylation, when the NADH and $FADH_2$ produced by the citric acid cycle relay the electrons extracted from food to the electron transport chain.

4. During oxidative phosphorylation, chemiosmosis couples electron transport to ATP synthesis

1. At this point, molecules of NADH and $FADH_2$ account for most of the energy extracted from the glucose.
2. The electron transport chain is a collection of molecules embedded in the inner membrane of the mitochondrion in eukaryotic cells. Most components of the chain are proteins, which exist in multiprotein complexes numbered I through IV. Tightly bound to these proteins are *prosthetic groups,* nonprotein components essential for the catalytic functions of certain enzymes.
3. During electron transport along the chain, electron carriers alternate between reduced and oxidized states as they accept and donate electrons.
4. NADH transfers its electrons to the first molecule of the electron transport chain in complex I, a **flavoprotein (FMN).** FMN then passes the electrons to an iron-sulfur protein (Fe·S in complex I), which then passes the electrons to **ubiquinone,** a small hydrophobic molecule and the only member of the electron transport chain that is not a protein. Most of the remaining electron carriers between ubiquinone and oxygen are proteins called **cytochromes.**
5. $FADH_2$ adds its electrons to the electron transport chain at complex II, so its electrons provides about one-third less energy than do the electrons of NADH.
6. The electron transport chain makes no ATP directly. Its function is to ease the fall of electrons from food to oxygen, breaking a large free-energy drop into a series of smaller steps that release energy manageable amounts. It also establishes the H^+ gradient used to power ATP synthase.
7. **Chemiosmosis**: the process in which energy stored in the form of a hydrogen ion gradient across a membrane is used to drive cellular work such as the synthesis of ATP.
8. ATP synthase is a multisubunit polypeptide with four main parts, each made of multiple polypeptides. It is the smallest molecular rotary motor known in nature. Protons move one by one into binding sites on one of the parts (the rotor), causing it to spin in a way that catalyzes ATP production from ADP and inorganic phosphate.
9. During respiration, most energy flows in this sequence: glucose → NADH → electron transport chain → proton-motive force→ATP.
10. Oxidative phosphorylation produces about 32 or 34 ATP per glucose. This is an approximate because phosphorylation and the redox reactions are not directly doubled to each other.
    1. Although 1 $NADH^+$ results in 10 H^+ being transported out across the inner mitochondrial membrane, it takes somewhere between 3 and 4 H^+ to make a molecule of ATP. A molecule of $FADH_2$ can only provide enough energy to make 1.5 to 2 ATP. It also takes energy to move ATP to the cytosol.
    2. It also takes a shuttle to move the electrons into the mitochondrial matrix. The electrons are either passed to FAD or NAD^+.
    3. The proton-motive force is also used by the mitochondrion to do other work, such as transporting pyruvate.
11. At full efficiency (38 ATP produced per glucose molecule; 2 from glycolysis, 2 from the citric acid cycle, and 34 from oxidation phosphorylation), about 40% of the potential chemical energy in glucose has been transferred to ATP.

5. Fermentation and anaerobic respiration enable cells to produce ATP without the use of oxygen

1. Because most of the ATP generated by cellular respiration is due to the work of oxidative phosphorylation, our estimate of ATP yield from aerobic respiration is contingent on an adequate supply of oxygen to the cell.
2. Fermentation is a way of harvesting chemical energy without using either oxygen or any electron transport chain.
3. The oxidizing agent of glycolysis is NAD^+, and neither oxygen nor any electron transfer chain is involved. Fermentation is an expansion of glycolysis that allows continuous generation of ATP by the substrate-level phosphorylation of glycolysis. It recycles NADH by transferring the electrons to pyrvuate.
4. There are two types of fermentation:
    1. **Alcohol fermentation**: pyruvate is converted to ethanol in two steps.
    2. **Lactic acid fermentation**: pyruvate is reduced directly by NADH to form lactate as an end product, with no release of CO_2.
5. Both fermentation and aerobic cellular respiration use glycolysis to oxidize glucose and other organic fuels to pyruvate, with a net production of 2 ATP by substrate-level phosphorylation.
6. In fermentation, the final electron acceptor is an organic molecule such as pyruvate or acetaldehyde. In aerobic respiration, the final electron acceptor is oxygen.
7. Respiration yields as much as 19 times more ATP per glucose molecule that does fermentation. (38 vs 2).
8. **Obligate anaerobes:** carry out only fermentation or anaerobic respiration and in fact cannot survive in the presence of oxygen.
9. **Facultative anaerobes**: can make enough ATP to survive using either fermentation or respiration.
10. Ancient prokaryotes probably used glycolysis to make ATP long before oxygen was present in Earth's atmosphere.

6. Glycolysis and the citric acid cycle connect to many other metabolic pathways

1. Glycolysis can accept a wide range of carbohydrates for catabolism
2. Proteins can also be used for fuel, but first the must be digest to their constituent amino acids. Before amino acids can feed into glycolysis or the citric acid cycle, their amino groups must be removed, a process called deamination.
3. After fats are digested to glycerol and fatty acids, the glycerol is converted to glyceraldehyde-3-phosphate, an intermediate of glycolysis. **Beta oxidation** breaks down fatty acids into two-carbon fragments, which enter the citric acid cycle as acetyl CoA. A gram of fat oxidized by respiration prodcues more than twice as much AT as a gram of carbohydrate.

7. Regulation of cellular respiration via feedback mechanisms

1. The most common mechanism for regulation is feedback inhibition: the end product of the anabolic pathway inhibits the enzyme that catalyzes an early step of the path way.
2. If the cell is working hard and its ATP concentration begins to drop, respiration speeds up. When there is plenty of ATP to meet demand, respiration slows down. Control is based mainly on regulating the activity of enzymes at strategic points in the catabolic pathway.

Chapter 10: Photosynthesis

- **Photosynthesis**: the conversion of light energy to chemical energy by plants.
- **Autotrophs**: "self-feeders" who sustain themselves without eating anything derived from other living beings.
- **Heterotrophs**: obtain their organic material by consuming other organisms.

1. Photosynthesis converts light energy to the chemical energy of food

1. The original chloroplast is believed to have been a photosynthetic prokaryote that lived inside a eukaryotic cell.
2. Leaves are the major sites of photosynthesis in most plants. The color of the leaf is from **chlorophyll**, the green pigment located within chloroplasts. It is the light energy absorbed by chlorophyll that drives the synthesis of organic molecules in the chloroplast. Chloroplasts are found mainly in the cells of the **mesophyll**, the tissue in the interior of the leaf.
3. Carbon dioxide enters the leaf, and oxygen exits, by way of microscopic pores called **stomata**. A typical mesophyll cell has about 30-40 chloroplasts.
4. An envelope of two membranes encloses the **stroma**, the dense fluid within a chloroplast. An elaborate system of interconnected membranous sacks called **thylakoids** segregates the stroma from the *thylakoid space.* In some cells, thylakoid sacs are stacked in columns called *grana*. Chlorophyll resides in the thylakoid membranes.
5. We can summarize the complex series of chemical reactions in photosynthesis with this chemical equation:

$$6\ CO_2 + 12\ H_2O + \text{Light energy} \rightarrow C_6H_{12}O_2 + O_2 + 6\ H_2O$$

6. O_2 give off by plants is derived from H_2O. The chloroplast splits water into hydrogen and oxygen. Because the electrons increase in potential energy as they move from water to sugar, this process require energy (from light).
7. The two stages of photosynthesis are known as the **light reactions**, and the **Calvin cycle**.
    1. The **light reactions** are the steps of photosynthesis that convert solar energy to chemical energy. Water is split, providing a source of electrons and protons and giving off O2 as a by-product. Light absorbed by chlorophyll drives a transfer of the electrons and hydrogen ions from water to an acceptor called $NADP^+$, a molecule similar to NAD^+. The light reactions also generate ATP, using chemiosmosis to power **photophosphorylation**.
    2. The **Calvin cycle** begins by incorporating CO2 from the air into organic molecules already present in the chloroplast (**carbon fixation**). The Calvin cycle then reduces the fixed carbon to carbohydrate by the addition of electrons from NADPH. The cycle requires energy in the form of ATP. Thus, it is the Calvin cycle that makes sugar, but it can do so only with the help of the NADPH and ATP produced by the light reactions.
    3. The thylakoids of the chloroplast are the sites of the light reactions, while the Calvin cycle occurs in the stroma.

- **Wavelength**: the distance between crests of electromagnetic waves.
- **Visible light** can be detected as various colors by the human eye (380 nm-750 nm in wavelength)
- The ability of a pigment to absorb various wavelengths of light can be measured with **spectrophotometer**.
- **Absorption spectrum:** A graph plotting a pigment's light absorption verses wavelength.
- **Chlorophyll *a*** participates directly in the light reactions.
- **Active spectrum**: plots the relative effectiveness of different wavelengths for photosynthesis.

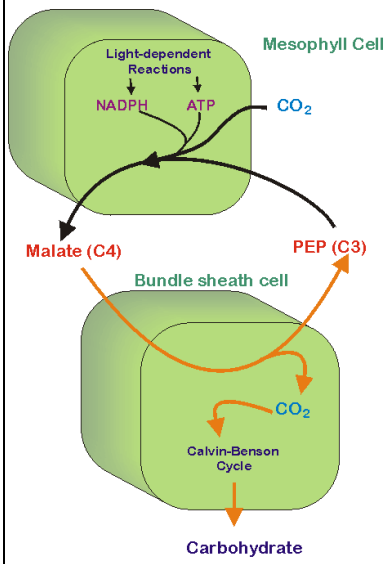
2. The light reactions convert solar energy to the chemical energy of ATP and NADPH

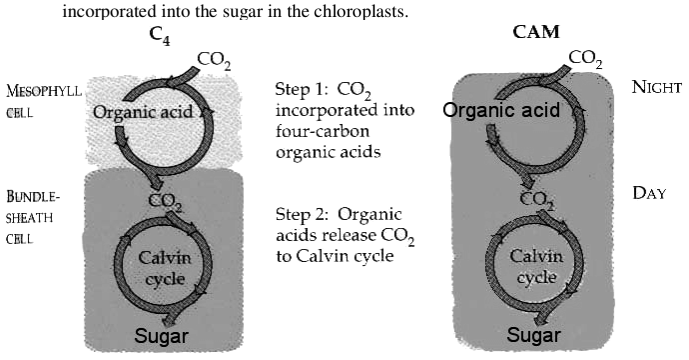
1. Chloroplasts are chemical factories powered by the sun.
2. Light is a form of energy known as electromagnetic energy, which exists as both a particle (photons) and a wave.
3. The amount of energy a photon carries is inversely related to the wavelength of the light: the shorter the wavelength, the greater the energy of each photon of that light.
4. Substances that absorb visible light are known as *pigments*. Different pigments absorb light of different wavelengths. The color we see is the color most reflected or transmitted by the pigment. We see green when we look at a leaf because chlorophyll absorbs violet-blue and red light while transmitting and reflecting green light.
5. The active spectrum for photosynthesis does not exactly match the absorption spectrum of chlorophyll *a,* because accessory pigments with different absorption spectra are also photosynthetically important in chloroplasts and broaden the spectrum of colors that can be used for photosynthesis. The accessory pigments include **chlorophyll *b*** and **carotenoids**.
6. When a molecule absorbs a photon of light, one of the molecule's electrons is elevated to an orbital where it has more potential energy. When the electron is in its normal orbital, the pigment molecule is said to be in its ground state. Absorption of a photon boosts an electron to an orbital of higher energy, and the pigment molecule is then said to be in an excited state. The excited state, like all high-energy states, is unstable. As excited electrons fall back to the ground state, photons are given off. This afterglow is called fluorescence. If a solution of chlorophyll isolated from chloroplasts is illuminated, it will fluoresce in the red-orange part of the spectrum and also give off heat.
7. A **photosystem** is composed of a protein complex called a **reaction-center complex** surrounded by several light harvesting complexes. Each **light-harvesting complex** consists of various pigment molecules bound to proteins. The reaction-center complex contains a molecule capable of accepting electrons (**primary electron acceptor**) and a very special pair of chlorophyll *a* molecules.
8. The solar-powered transfer of an electron from the reaction-center chlorophyll *a* pair to the primary electron acceptor is the first step of the light reactions.
9. The thylakoid membrane is populated by two types of photosystems that cooperate in the light reactions of photosynthesis. They are called **photosystem II (PS II)** and **photosystem I (PS I).** They were named in order of their discovery, but photosystem II functions first in the light reactions. The reaction-center chlorophyll *a* of photosystem II is know as P680 because this pigment is best at absorbing light having a wavelength of 680 nm. The chlorophyll *a* at the reaction-center complex of photosystem I is called P700 because it most effectively absorbs light of wavelength 700 nm.
10. **Linear electron flow**: a flow of electrons through the photosystems and other molecular components built into the thylakoid membrane.
    1. A photon of light strikes a pigment molecule in a light-harvesting complex, boosting one of its electrons to a higher energy level. As this electron falls back to its ground state, an electron in a nearby pigment molecule is simultaneously raised to an exited state. This process continues, with the energy being relayed to other pigment molecules until it reaches the P680 pair of chlorophyll *a* molecules in the PS II reaction-center complex. It excites an electron in this pair of chlorophylls to a higher energy state.
    2. This electron is transferred from the excited P680 to the primary electron acceptor. We can refer to the resulting form of P680, missing an electron, as $P680^+$.
    3. An enzyme catalyzes the splitting of a water molecule into two electrons, two hydrogen ions, and an oxygen atom. The electrons as supplied one by one two the $P680^+$ pair, each electron replacing one transferred to the primary electron acceptor. ($P680^+$ is the strongest biological oxidizing agent known.) The oxygen atom immediately combines with an oxygen atom generated by the splitting of another water molecule, forming O_2.
    4. Each photoexcited electron passes from the primary electron acceptor of PS II to PS I via an electron transport chian, the components of which are similar to those of the electron transport chain that functions in cellular respiration. The electron transport chain between PS II and PS I is made of the electron carrier plastoquinone (Pq), a cytochrome complex, and a protein called plastocyanin (Pc).
    5. The exergonic "fall" of electrons to a lower energy level provides energy for the synthesis of ATP. As electrons pass through the cytochrome complex, the pumping of protons builds a proton gradient that is subsequently used in chemiosmosis.
    6. Meanwhile, light energy was transferred via light-harvesting complex pigments to the PS I reaction-center complex, exciting an electron of the P700 pair of chlorophyll *a* molecules located there. The photoexcited electron was then transferred to PS I's primary electron acceptor, and the $P700^+$ can now accept the electron that reaches the bottom of the electron transport chain from PS II.

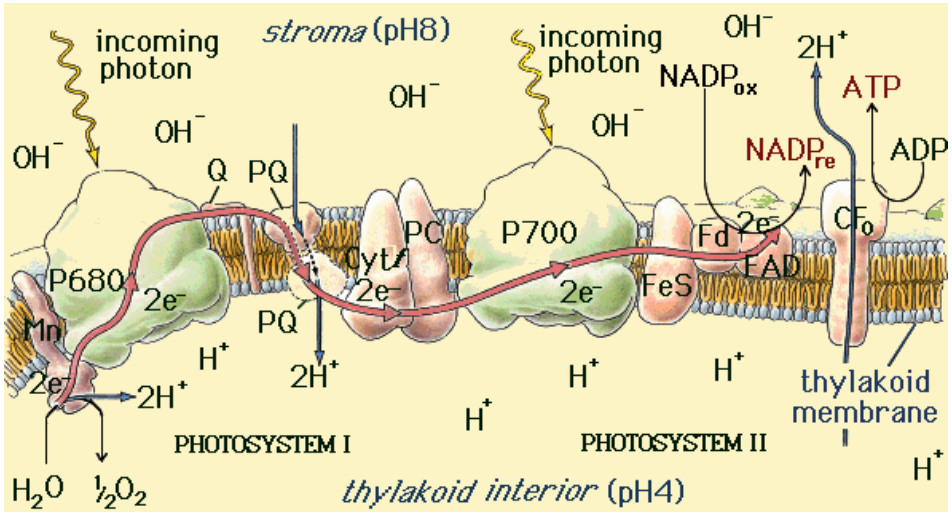
7. Photoexcited electrons are passed in a series of redox reactions from the primary electron acceptor of PS I down a second electron transport chain through the protein ferredoxin (Fd). This chain does not create a proton gradient and thus does not produce ATP.
8. The enzyme $NADP^+$ reductase catalyzes the transfer of electrons from Fd to $NADP^+$. Two electrons are required for its reduction to NADPH. This molecule is at a higher energy level than water, and its electrons are more readily available for the reactions of the Calvin cycle than were those of water.

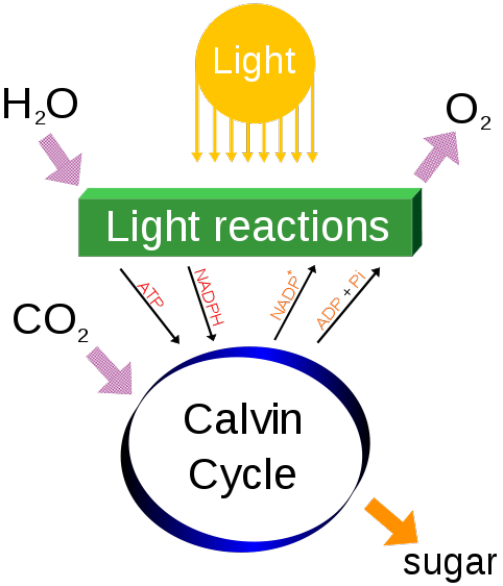
11. **Cyclic electron flow**: which uses photosystem I but not photosystem II. There is no production of NADPH and no release of oxygen. Cyclic flow does, however, generate ATP. Several of the currently existing groups of photosynthetic bacteria are known to have photosystem I but not photosystem II. Evolutionary biologists believe that these bacterial groups are in which photosynthesis first evolved, in a form similar to cyclic electron flow. Cyclic electron flow may be photoprotective, protecting cells from light-induced damage.
12. Chloroplasts and mitochondria generate ATP by the same basic mechanism: chemiosmosis. Although the spatial organization of chemiosmosis differs slightly between chloroplasts and mitochondria, it is easy to see similarities in the two.
13. Notice that NADPH, like ATP, is produced on the side of the membrane facing the stroma, where the Calvin cycle reactions take place.

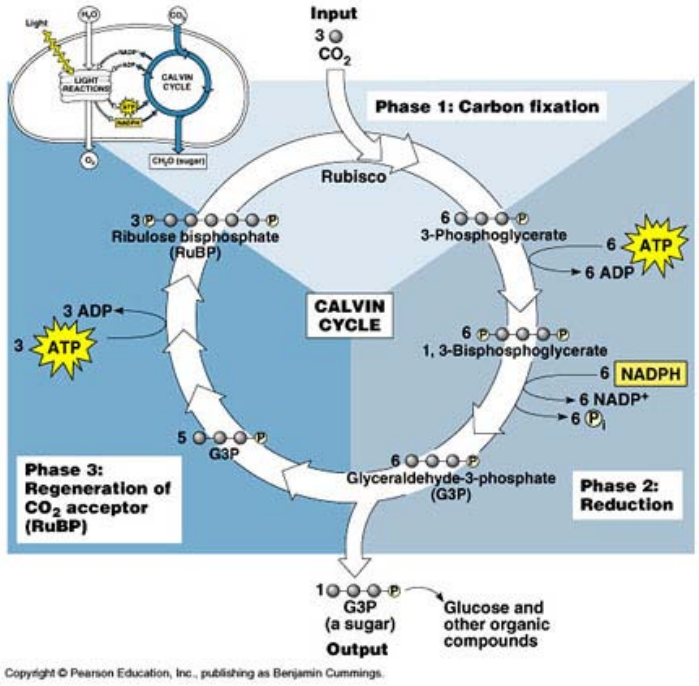
3. **The Calvin cycle uses ATP and NADPH to convert CO_2 to sugar.**
   1. The Calvin cycle is similar to the citric acid cycle in that a starting material is regenerated after molecules enter and leave the cycle. The cycle spends ATP as an energy source and consumes NADPH as a reducing power for adding high-energy electrons to make the sugar.
   2. The carbohydrate produced directly from the Calvin cycle is actually not glucose, but a three carbon sugar (glyceraldehyde-3-phosphate). For the net synthesis of one molecule of G3P, the cycle must take place three times, fixing three molecules of CO2. The Calvin cycle can be divided into three phases.
      1. Carbon fixation: The Calvin cycle incorporates each CO_2 molecule, one at a time, by attaching it to a five-carbon sugar named ribulose bisphosphate. The enzyme that catalyzes this first step is RuBP carboxylase, or **rubisco.** The product of the reaction then splits into two molecules of 3-phosphorglycerate (for each CO_2 fixed).
      2. Reduction: Each molecule of 3-phosphorglycerate receives an additional phosphate group from ATP, forming 1,3-biphosphorglycerate, which is reduced by NADPH and also loses phosphate group, becoming glyceraldehyde-3-phosphate. One molecule exits the cycle; the other five must be recycled to regenerate the three molecules of RuBP.
      3. Regeneration of CO_2 acceptor RuBP. In a complex seiries of reactions, the carbon skeletons of five molecules of G3P are rearranged by the last steps of the Calvin cycle into three molecules of RuBP.
   3. **Alternative mechanisms of carbon fixation have evolved in hot, arid climates**
      1. The problem of dehydration is important to plants. Solutions often involve trade-offs. An important example is the compromise between photosynthesis and the prevention of excessive water lost from the plast.
      2. On a hot, dry day, most plants close their stomata, a response that conserves water. This response also reduces photosynthetic yield by limiting access to CO_2, which favors an apparently wasteful process called photorespiration.
      3. In most plants, initial fixation of carbon occurs via rubisco. Such plants are called C_3 plants because the first organic product of carbon fixation is a three-carbon compound. However, when CO_2 becomes scarce, rubisco adds O_2 to the Calvin cycle instead. The product splits, and a two carbon-compound leaves the chloroplast, where it is further degraded into CO_2 by peroxisomes and mitochondria. The process is called photorespiration because it occurs in the light and consumes O_2 while producing CO_2.
      4. Photorespiration is evolutionary baggage—a metabolic relic from a much earlier time when the atmosphere had less O_2 and more CO_2.
      5. In some cases, photorespiration plays a protective role in plants, neutralizing the otherwise damaging products of the light reactions, which build up when a low CO_2 concentration limits the progress of the Calvin cycle.
      6. C_4 plants are so named because they preface the Calvin cycle with an alternative mode of carbon fixation that forms a four-carbon compound as its first product.. In C_4 plants, there are two distinct types of photosynthetic cells: bundle-sheath cells and mesophyll cells.
         1. Bundle-sheath cells are arranged into tightly packed sheaths around the veins of the leaf.
         2. Between the bundle sheath and the leaf surface are the more loosely arranged mesophyll cells.
         3. The Calvin cycle is confined to the chloroplasts of the bundle-sheath cells. However, the cycle is preceded by incorporation of CO_2 into organic compounds in the mesophyll cells.
            1. The first step is carried out by an enzyme present only in mesophyll cells called PEP carboxylase, which adds CO2 to phosphoenolpyruvate (PEP), forming oxaloacetate. PEP carboxylase has a much higher affinity to CO_2 than rubisco and no affinity for O_2.
      7. **Crassulacean acid metabolism (CAM):**
         1. The mesophyll cells of CAM plants store the organic acids they make during the night in their vacuoles until morning, when the stomata close. During the day, when the light reactions can supply ATP and NADPH for the Calvin cycle, CO2 is released from the organic acids made the night before to become incorporated into the sugar in the chloroplasts.






incoming photon
stroma (pH8)
incoming photon
OH⁻
NADP$_{ox}$
2H⁺
ATP
ADP
NADP$_{re}$
Q
PQ
PC
P700
Fd
2e⁻
CF$_o$
Cyt
FAD
P680
2e⁻
FeS
Mn
H⁺
2H⁺
thylakoid membrane
PHOTOSYSTEM I
PHOTOSYSTEM II
H$_2$O
½O$_2$
thylakoid interior (pH4)


Light
H$_2$O
O$_2$
Light reactions
ATP
NADPH
NADP⁺
ADP + Pi
CO$_2$
Calvin Cycle
sugar


Input
3 CO$_2$
Phase 1: Carbon fixation
Rubisco
3 Ribulose bisphosphate (RuBP)
6 3-Phosphoglycerate
6 ATP
6 ADP
CALVIN CYCLE
3 ADP
3 ATP
6 1, 3-Bisphosphoglycerate
6 NADPH
6 NADP⁺
6 P$_i$
5 G3P
6 Glyceraldehyde-3-phosphate (G3P)
Phase 3: Regeneration of CO$_2$ acceptor (RuBP)
Phase 2: Reduction
1 G3P (a sugar)
Output
Glucose and other organic compounds
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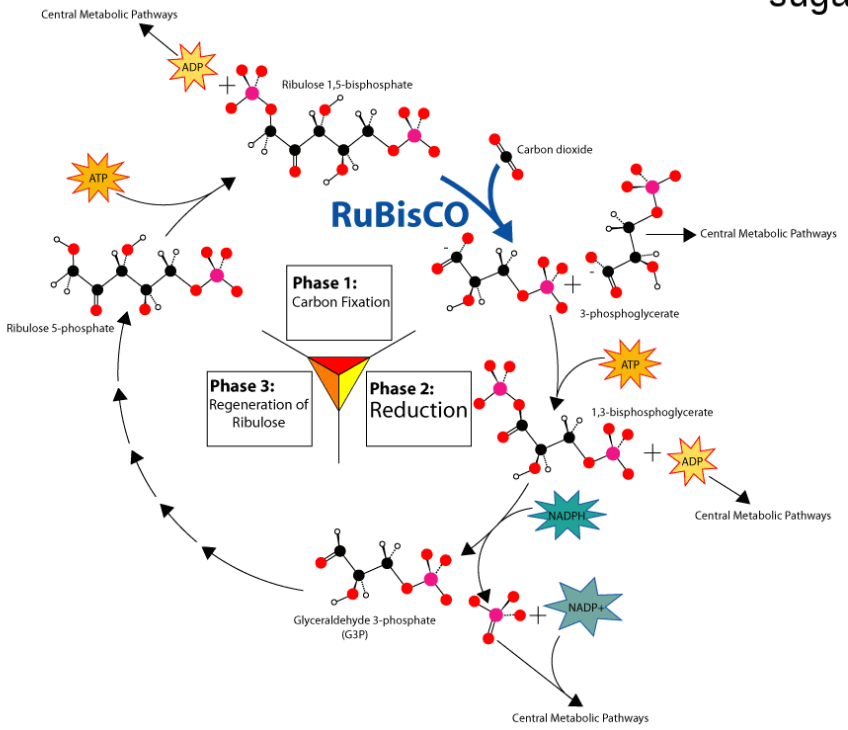
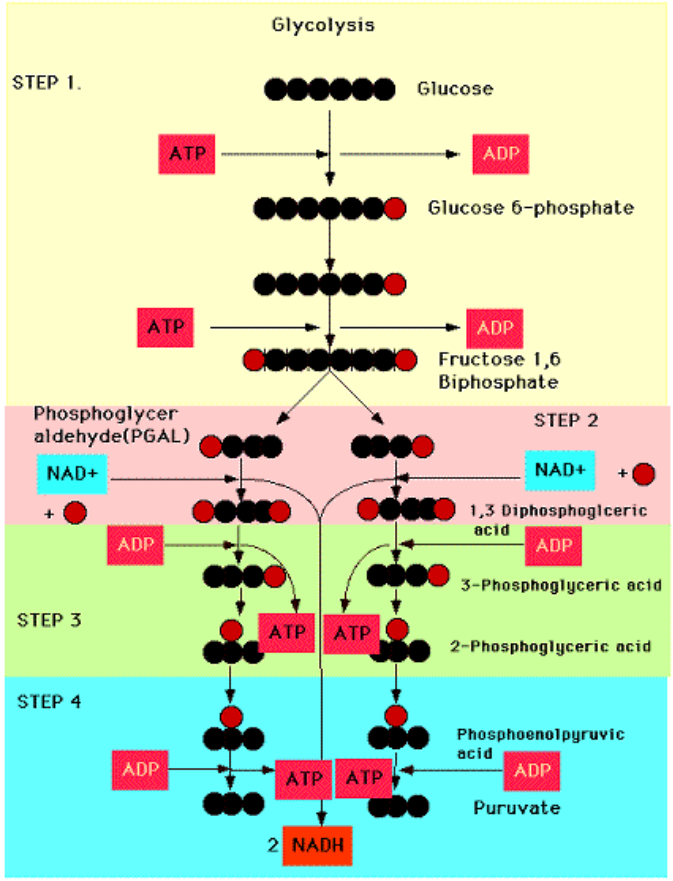
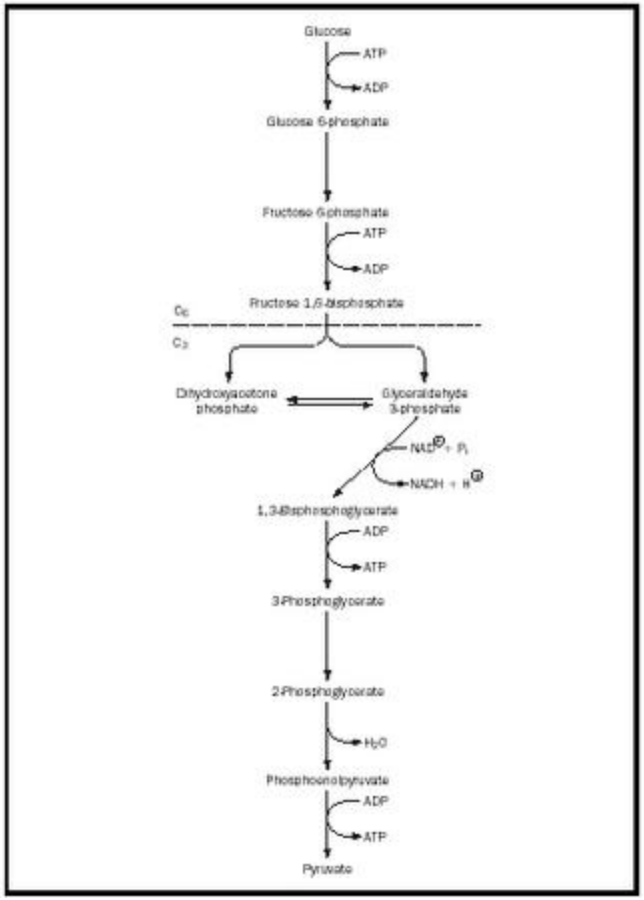
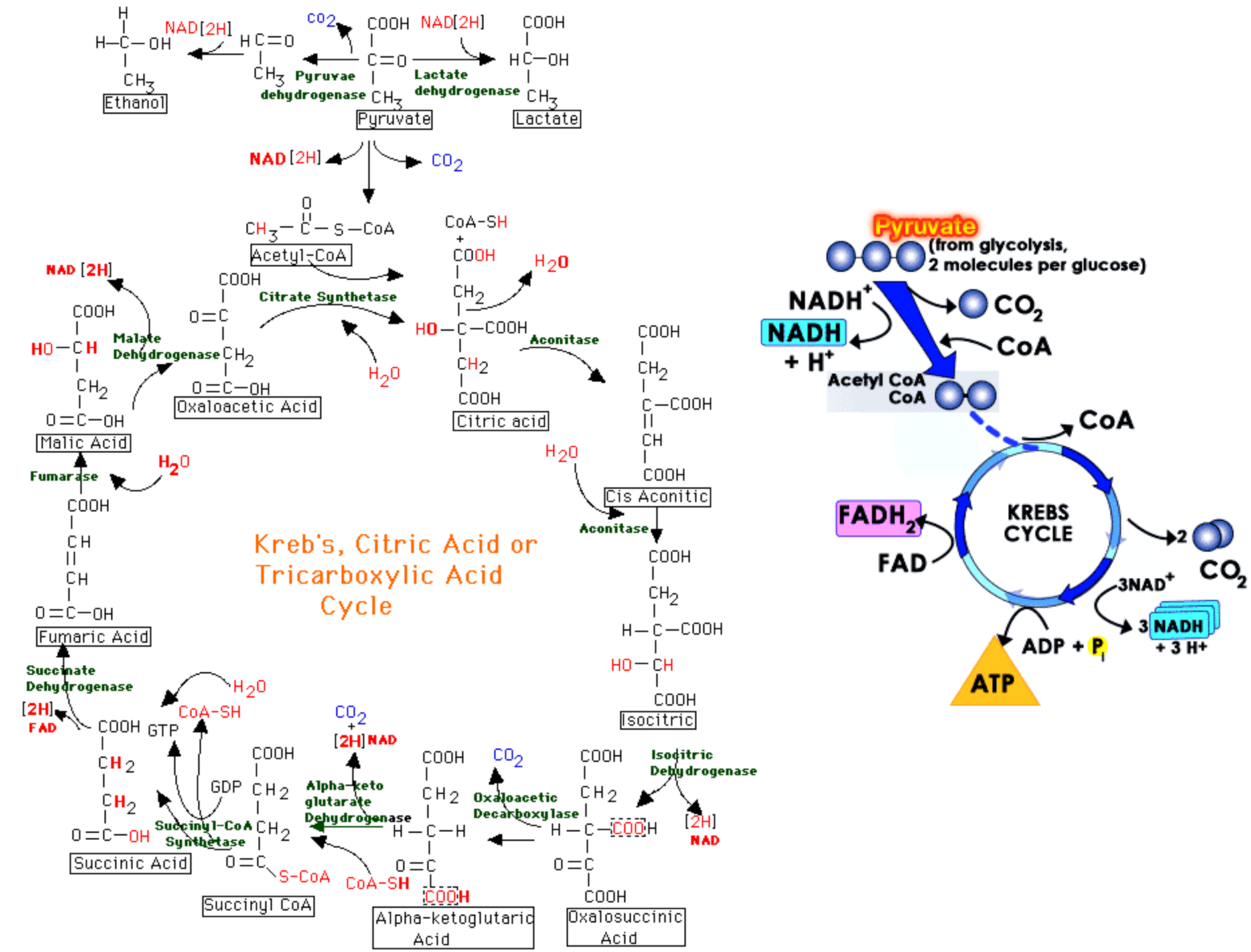
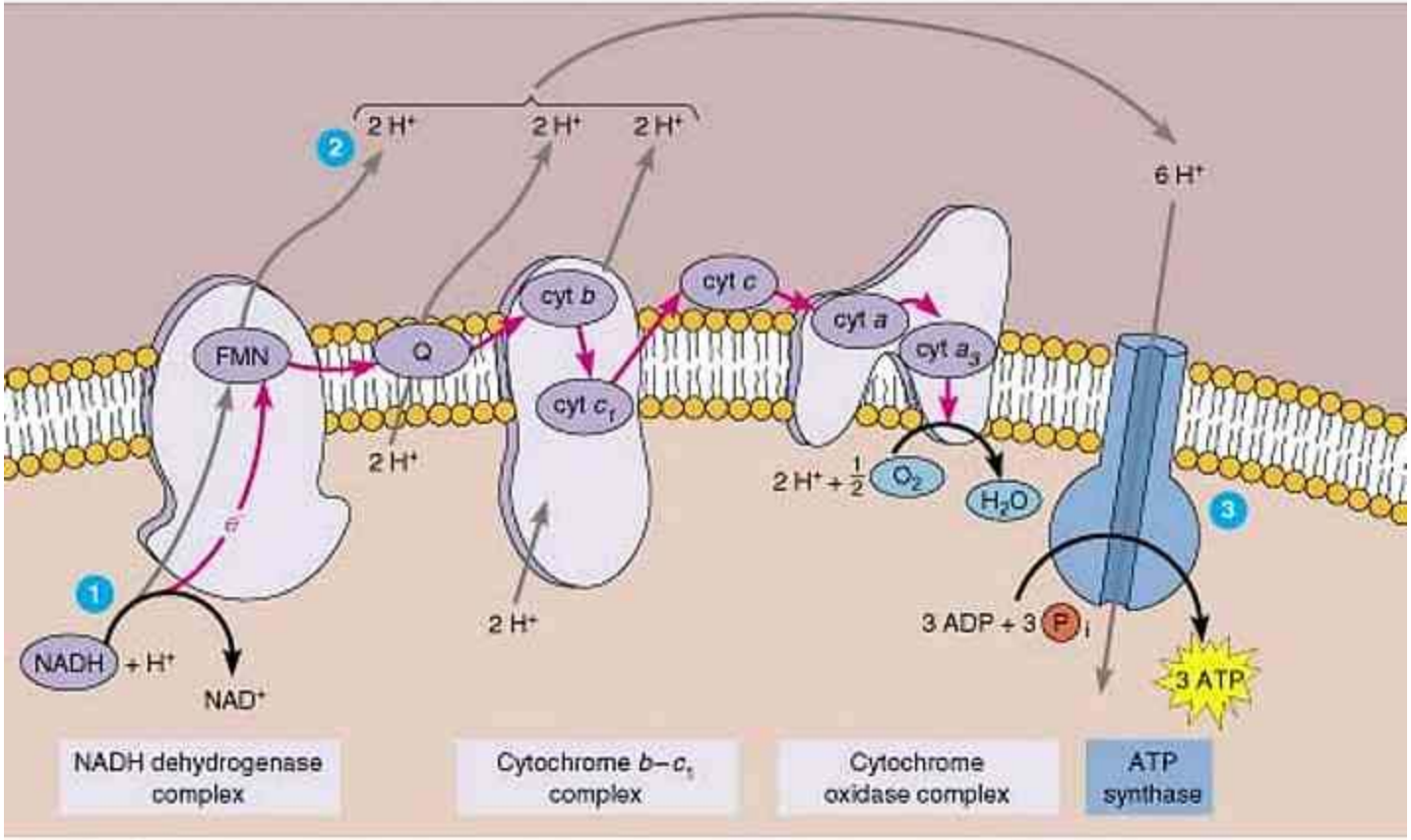

Central Metabolic Pathways
ADP
Ribulose 1,5-bisphosphate
ATP
Carbon dioxide
RuBisCO
Central Metabolic Pathways
Ribulose 5-phosphate
Phase 1: Carbon Fixation
3-phosphoglycerate
Phase 3: Regeneration of Ribulose
Phase 2: Reduction
ATP
1,3-bisphosphoglycerate
ADP
Central Metabolic Pathways
NADPH
NADP+
Glyceraldehyde 3-phosphate (G3P)
Central Metabolic Pathways


Glycolysis
STEP 1.
Glucose
ATP
ADP
Glucose 6-phosphate
ATP
ADP
Fructose 1,6
Biphosphate
Phosphoglycer
aldehyde(PGAL)
STEP 2
NAD+
NAD+
+
+
1,3 Diphosphoglceric
acid
ADP
ADP
3-Phosphoglyceric acid
STEP 3
ATP
ATP
2-Phosphoglyceric acid
STEP 4
Phosphoenolpyruvic
acid
ADP
ATP
ATP
ADP
Puruvate
2 NADH

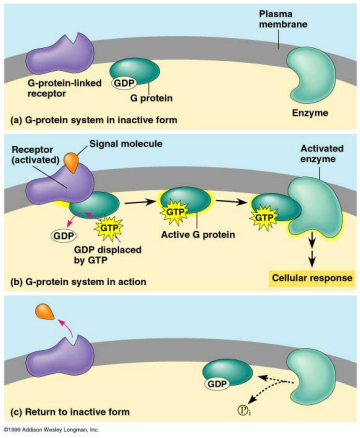

Glucose
ATP
ADP
Glucose 6-phosphate
Fructose 6-phosphate
ATP
ADP
Fructose 1,6-bisphosphate
Dihydroxyacetone
phosphate
Glyceraldehyde
3-phosphate
1,3-Bisphosphoglycerate
ADP
ATP
3-Phosphoglycerate
2-Phosphoglycerate
Phosphoenolpyruvate
ADP
ATP
Pyruvate


Ethanol
NAD[2H]
CO2
Pyruvae dehydrogenase
Pyruvate
Lactate dehydrogenase
Lactate
NAD [2H]
CO2
Acetyl-CoA
CoA-SH
Citrate Synthetase
H2O
Oxaloacetic Acid
Citric acid
Aconitase
Cis Aconitic
Isocitric
Isocitric Dehydrogenase
Oxalosuccinic Acid
Oxaloacetic Decarboxylase
Alpha-ketoglutaric Acid
Alpha-keto glutarate Dehydrogenase
Succinyl CoA
Succinyl-CoA Synthetase
GTP
GDP
Succinic Acid
Succinate Dehydrogenase
FAD
Fumaric Acid
Fumarase
Malic Acid
Malate Dehydrogenase
Kreb's, Citric Acid or Tricarboxylic Acid Cycle
Pyruvate
(from glycolysis, 2 molecules per glucose)
NADH+
NADH + H+
CO2
CoA
Acetyl CoA
KREBS CYCLE
FADH2
FAD
2 CO2
3NAD+
3 NADH + 3 H+
ADP + Pi
ATP

ELECTRON TRANSPORT CHAIN



- **Ligand**: a molecule that specifically binds to another, usually larger, molecule.
- **G-protein:** a protein that binds the energy-rich molecule GTP.



- **Kinase:** an enzyme that catalyzes the transfer of phosphate groups.

- **Protein kinase**: the general name for an enzyme that transfers phosphate groups from ATP to a protein.
- **Protein phosphatases**: enzymes that can rapidly remove phosphate groups from proteins, a process called dephosphorylation.

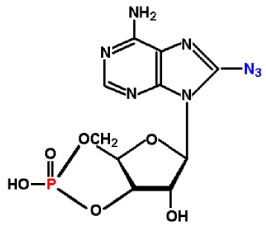


Illustration 1: cAMP

1. External signals are converted to responses within the cell.

1. **Signal transduction pathway**: the process by which a signal on a cell's surface is converted to a specific cellular response. The molecular details of signal transduction between yeast and mammals are similar, suggesting that early versions of the cell-signaling mechanisms used today evolved well before the first multicellular creatures appeared on Earth.
2. Cells in a multicellular organism usually communicate via chemical messengers targeted for cells that may or may not be immediately adjacent.
    1. Both animals and plants have cell junctions that directly connect the cytoplasms of adjacent cells.
    2. Animal cells may communicate via direct contact between membrane-bound cell-surface molecules (cell-cell recognition).
    3. Messenger molecules are also used. **Local regulators** only travel short distances. **Hormones** are used for long-distance signaling.
3. Earl W. Sutherland (who won the Nobel prize in 1971) investigated how the animal hormone epinephrine stimulates the breakdown of glycogen. His work suggested that the signal transduction pathway can be broken into three stages:
    1. **Reception:** A signaling molecule binds to a receptor protein located at the cell's surface or inside the cell.
    2. **Transduction:** The binding of the signaling molecule changes the receptor protein. The transduction stage converts the signal to a form that can bring about a specific cellular response. Transduction sometimes occurs in a single step but more often requires a sequence of changes in a series of different molecules (relay molecules.)
    3. **Response**: The transduced signal finally triggers a specific cellular response.

2. Reception: A signaling molecule binds to a receptor protein, causing it to change shape.

1. A signaling molecule behaves as a **ligand.**
2. Most signal receptors are plasm membrane proteins. For many receptors, their shape change directly activates the receptor, enabling it to interact with other cellular molecules.
3. Most water-soluble signaling molecules bind to specific sites on receptor proteins embedded in the cell's plasma membrane. There are three major types of membrane receptors:
    1. **G protein-coupled receptors:** A plasm membrane receptor that works with the help of a **G-protein.** Many different signaling molecules use G protein-coupled receptors. G protein-coupled receptor proteins are remarkably similar in structure; they all have seven α helices spanning the membrane.
        1. Loosely attached to the cytoplasmic side of the membrane, the G protein functions as a molecular switch that is either on or off. When GDP is bound to the G protein, the G protein is inactive.
        2. When the appropriate signaling molecule binds to the extracellular side of the receptor, the receptor is activated and changes shape. Its cytoplasmic side then binds an inactive G protein, causing a GTP to displace the GDP. This activates the G protein.
        3. The activated G protein dissociates from the receptor, diffuses along the membrane, and then binds to an enzyme, altering the enzyme's shape and activity. When the enzyme is activated, it can trigger the next step in a pathway leading to a cellular response.
        4. The G-protein then hydrolyses the GTP to GDP and a phosphate ion, causing the G-protein to become inactive and detach from the enzyme, which returns to its original shape.
    2. **Receptor tyrosine kinases** belong to a major class of plasm membrane receptors characterized by having enzymatic activity. Receptor tyrosine kinases are membrane receptors that attach phosphates to tyrosines.
        1. Many receptor tyrosine kinases have an extracellular, an α helix spanning the membrane, and an intracellular tail containing multiple tyrosines. Before the signal molecule binds, the receptors exist as individual polypeptides.
        2. The binding of a signaling molecule causes two receptor polypeptides to associate closely with each other, forming a dimer.
        3. Dimerization activates the tyrosine kinase region of each polypeptide.
    3. **Ion channel receptors:** a ligand-gated ion channel is a type of membrane receptor containing a region that can act as a "gate" when the receptor changes shape. When a signaling molecule binds as a ligand to the receptor protein, the gate opens or closes, allowing or blocking the flow of specific ions through a channel in the receptor.
        1. When the ligand binds to the receptor and the gate opens, specific ions can flow through the channel and rapidly change the concentration of that particular ion inside the cell. This change may directly affect the activity of the cell in some way. When the ligand dissociates from this receptor, the gate closes and ions no longer enter the cell.
        2. Some gated ion channels are controlled by electrical signals instead of ligands.
4. **Intracellular receptor proteins** are found either in the cytoplasm or nucleus of target cells. A chemical messenger must pass through the target cell's plasma membrane to reach these receptors. Thus, they must be hydrophobic. Examples include steroids and the thyroid hormones. The hormone binds to the receptor protein, activating it.
5. Specific proteins called *transcription factors* control which genes are turned on in particular cell at particular time.

3. Tranduction: Cascades of molecular interactions relay signals from receptors to target molecules in the cell.

1. The transduction stage of cell signaling is usually a multistep pathway, which can greatly amplify a signal and provide more opportunities for coordination and regulation than simpler systems do.
2. Like falling dominoes, the signal-activated receptor activates another molecule, which activates yet another molecule, and so on, until the protein that produces the final cellular response is activated. The relay molecules are often proteins. At each step, the signal is transduced into a different form, commonly a shape change in a protein.
3. The phosphorylation/dephosphorylation system acts a molecular switch in the cell, turning activities on or off as required.
4. Many signaling pathways also involve small, nonprotein, water-soluble molecules or ions called **second messengers**. These readily spread throughout the cell by diffusion. Second messengers participate in pathways initiated by both G protein-coupled receptors and receptor tyrosine kinases.
5. The two most widely used second messengers are cyclic AMP and calcium ions.
    1. The binding of epinephrine to the plasma membrane of a liver cell elevates the cytosolic concentration of **cyclic AMP (cAMP).** An enzyme embedded in the plasma membrane, **adenylyl cyclase,** converts ATP to cAMP in response to an extracellular signal.
    2. Another enzyme, phosphodiesterase, converts cAMP to AMP.
    3. The immediate affect of cAMP is usually the activation of a serine/threonine kinase called *protein kinase A.*
    4. Further regulation of cell metabolism is provided by other G-protein systems that *inhibit* adenylyl cyclase.
    5. Many signaling molecules in animals induce responses in their target cells via signal transduction pathways that increase the cytosolic concentration of calcium ions. Calcium is even more widely used that cAMP as a second

messenger. The pathways leading to calcium release involve still other second messengers, **inositol trisphosphate (IP_3)** and **diacylglycerol (DAG).** These two messengers are produced by cleavage of a certain kind of phospholipid in the plasma membrane.

4. Response: Cell signaling leads to the regulation of transcription or cytoplasmic activities.

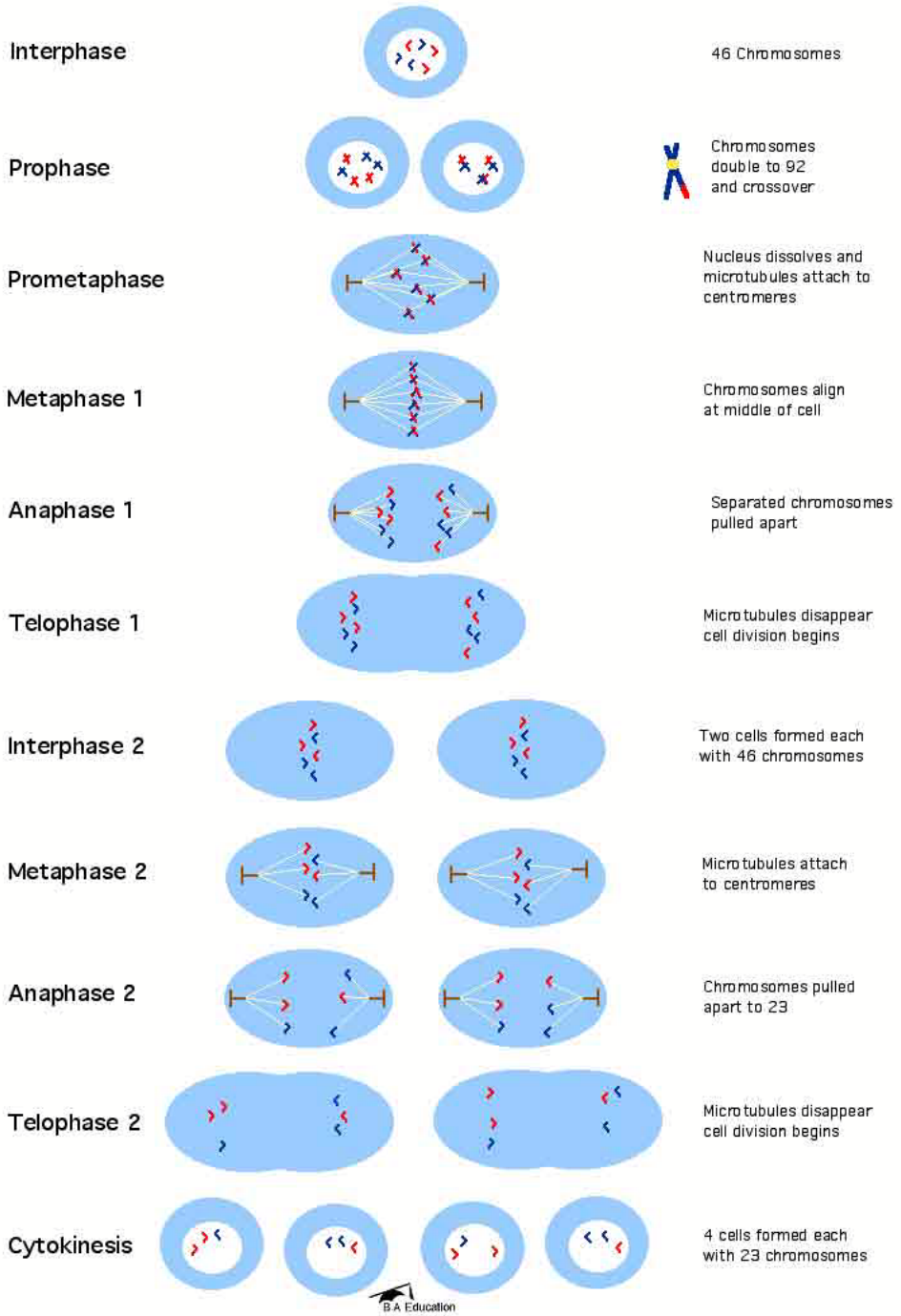
1. Ultimately, a signal transduction pathway leads to the regulation of one or more cellular activities. The response at the end of the pathway may occur in the nucleus of the cell or in the cytoplasm.
2. Many signaling pathways ultimately regulate protein synthesis, usually by turning specific genes on or off in the nucleus. The final activated molecule in a signaling pathway may function as a transcription factor.
3. Sometimes a signaling pathway may regulate the *activity* of proteins rather than their *synthesis,* directly affecting proteins that function outside the nucleus.
4. In addition to the regulation of enzymes, signaling events may also affect other cellular attributes, such as overall cell shape.
5. Signaling pathways with numerous steps between a signaling event at the cell surface and the cell's response have two important benefits: They amplify the signal and they provide different points at which a cell's response can be regulated.
    1. Elaborate enzyme cascades amplify the cell's response to a signal. At each catalytic step in the cascade, the number of activated products is much greater than the preceding step.
    2. *Different kinds of cells have different collections of proteins:* The response of a particular cell to a signal depends on its particular collectrion of signal receptor proteins, relay proteins, and proteins needed to carry out the response.
6. Recent research suggests the efficiency of signal transduction may in many cases be increased by the presence of **scaffolding proteins,** large relay proteins to which several other relay proteins are simultaneously attached.
7. Some proteins may participate in more than one pathway, either in different cell types or in the same cell at different times or under different conditions.
8. A key to a cell's continuing receptiveness to regulation by signaling is the reversibility of the changes that signals produce.

5. Apoptosis (programmed cell death) integrates multiple cell-signaling pathways.

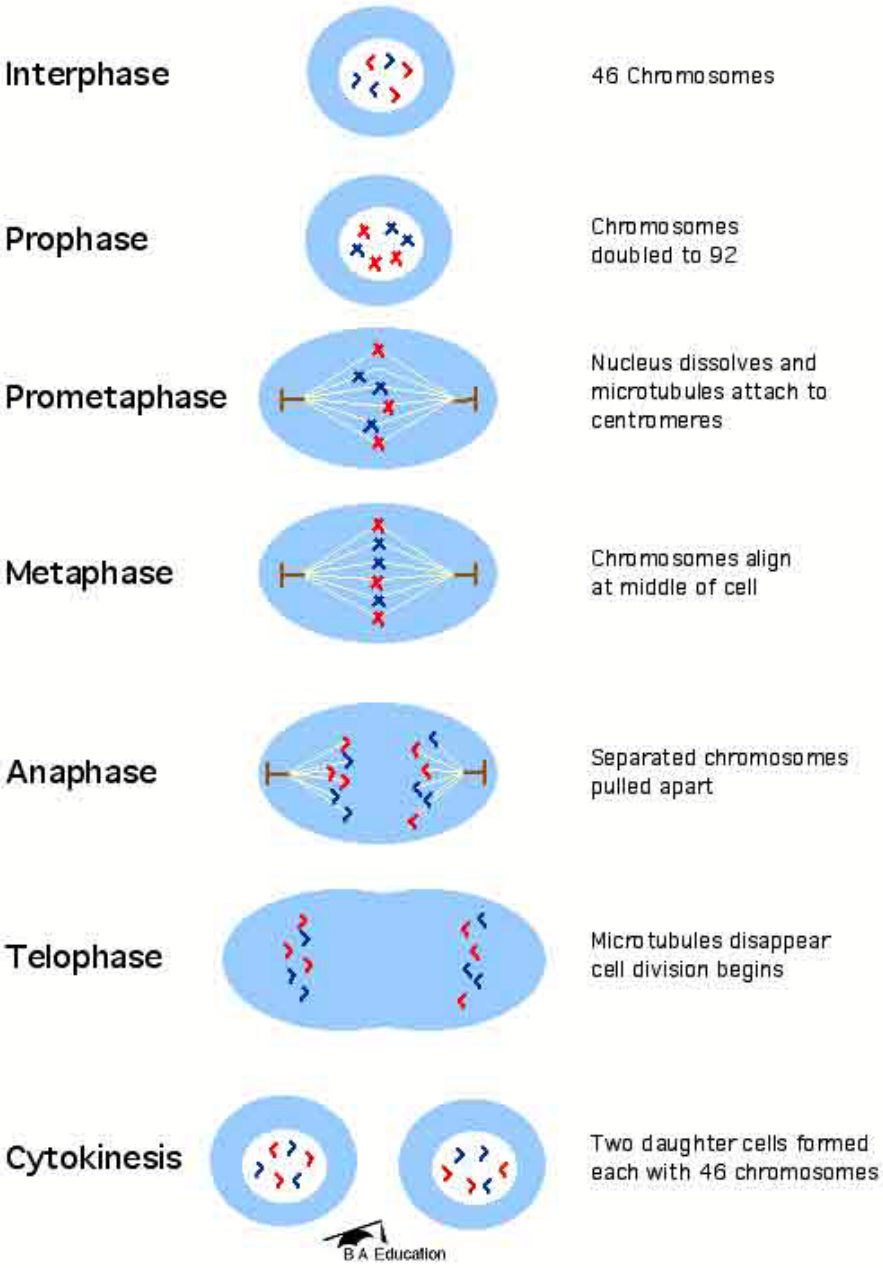
- **Proteases**: enzymes that cut up proteins. The main proteases of apoptosis are called *caspases.*
- **Nucleases**: enzymes that cut up DNA.

1. Cells that are infected or damaged or that have simply reached the end of their functional life span often enter a program of controlled cell suicide called **apoptosis.**
2. During this process, cellular agents chop up the DNA and fragment the organelles and other cytoplasmic components. The cell shrinks and becomes lobed, and the cell's parts are packaged up in vesicles that are engulfed and digested by specialized scavenger cells, leaving no trace.
3. Most proteins involved in apoptosis are continually present in cells, but in inactive form; thus, protein activity is regulated rather than protein synthesis.
4. In humans and other mammals, several different pathways, involving about 15 different caspases, can carry out apoptosis.
    1. One major pathway involves mitochondrial proteins. Apoptotic proteins can form molecular pores in the mitochondrial outer membrane, causing it to leak and release proteins that promote apoptosis.
    2. At key points in the apoptotic program, proteins integrate signals from several different sources and can send a cell down an apoptotic pathway.
    3. When a death-signaling ligand occupies a cell-surface receptor, this binding leads to activation of caspases are other enzymes that carry out apoptosis, without involving the mitochondrial pathway.
    4. Two other types of alarm signals originate from *inside* the cell. One comes from the nucleus, generated when the DNA has suffered irreparable damage, and a second comes from the endoplasmic reticulum when excessive protein misfolding occurs.
    5. A built-in cell suicide mechanism is essential to development and maintenance in all animals.

Meiosis


Interphase
46 Chromosomes
Prophase
Chromosomes double to 92 and crossover
Prometaphase
Nucleus dissolves and microtubules attach to centromeres
Metaphase 1
Chromosomes align at middle of cell
Anaphase 1
Separated chromosomes pulled apart
Telophase 1
Microtubules disappear cell division begins
Interphase 2
Two cells formed each with 46 chromosomes
Metaphase 2
Microtubules attach to centromeres
Anaphase 2
Chromosomes pulled apart to 23
Telophase 2
Microtubules disappear cell division begins
Cytokinesis
4 cells formed each with 23 chromosomes
B.A Education

Mitosis


Interphase
46 Chromosomes
Prophase
Chromosomes doubled to 92
Prometaphase
Nucleus dissolves and microtubules attach to centromeres
Metaphase
Chromosomes align at middle of cell
Anaphase
Separated chromosomes pulled apart
Telophase
Microtubules disappear cell division begins
Cytokinesis
Two daughter cells formed each with 46 chromosomes
BA Education

Chapter 12: The Cell Cycle

- **Cell division**: reproduction of cells.
- **Cell cycle**: the life of a cell from the time it is first formed from a dividing parent cell until its own division into two cells.
- **Genome**: A cell's endowment of DNA.

0. OVERVIEW: THE KEY ROLES OF CELL DIVISION

1. When a unicellular organism, such as an amoeba, divides and forms duplicate offspring, the division of one cell reproduces an entire organism.
2. Cell division also enables sexually reproducing organisms to develop from a single cell—the fertilized egg, or zygote.

1. CELL DIVISION RESULTS IN GENETICALLY IDENTICAL DAUGHTER CELLS

1. A typical human cell has about 2 m of DNA. The replication and distribution of so much DNA is manageable because DNA molecules are packaged into **chromosomes.**
2. Every eukaryotic species has a characteristic number of chromosomes in each cell nucleus. The nuclei of human **somatic cells** each contain 46 chromosomes. Human **gametes** have half as many chromosomes as somatic cells.
3. Eukaryotic chromosomes are made of **chromatin,** a complex of DNA and associated protein molecules.
4. Each duplicated chromosome has two **sister chromatids,** which are initially attached all along their lengths by adhesive protein complexes called *cohesions;* this attachment is called *sister chromatid cohesion.* The duplicated chromosome has a narrow "waist" at the **centromere**, a specialized region where the two chromatids are most closely attached.
5. **Mitosis**, the division of the nucleus, is usually followed immediately by **cytokinesis,** the division of the cytoplasm. Gametes are produced by **meiosis**.

2. THE MITOTIC PHASE ALTERNATES WITH INTERPHASE IN THE CELL CYCLE

1. In 1882, a German anatomist named Walther Flemming developed dyes that allowed him observe, for the first time, the behavior of chromosomes during mitosis and cytokinesis.

2. Phases of the Cell Cycle:

1. The **mitotic (M) phase,** which includes both mitosis and cytokinesis, is usually the shortest part of the cell cycle.
2. **Interphase** often accounts for about 90% of the cycle. Interphase can be divided into subphases: the **G_1 phase,** the **S phase,** and the **G_2 phase.** A cell grows (G_1), continues to grow as it copies its chromosomes (S), grows more as it completes preparations from cell division (G_2), and divides (M).
3. Mitosis is conventionally broken down into five stages: **prophase, prometaphase, metaphase, anaphase,** and **telophase.**
4. Many of the events of mitosis depend on the **mitotic spindle,** which consists of fibers made of microtubules and associated proteins.
    1. In animals, the assembly of spindle microtubules starts at the **centrosome,** a subcellular region containing material that functions throughout the cell cycle to organize the cell's microtubules.
    2. During interphase in animal cells, the single centrosome replicates, forming two centrosomes, which remain together near the nucleus.
    3. By the end of prometaphase, the two centrosomes, one at each pole of the spindle, are at opposite ends of the cell. An **aster,** a radial array of short microtubules, extends from each centrosome.
    4. Each of the two sister chromatids of a replicated chromosome has a **kinetochore,** a structure of proteins associated with specific sections of chromosomal DNA at the centromere. During prometaphase, some of the spindle microtubules attached to the kinetochores. When one of a chromosome's kinetochores is "captured" by microtubules, the chromosome begins to move toward the pole from which those microtubules extend. However, this movement is checked as soon as microtubules from the opposite pole attach to the other kinetochore. The chromosome finally settles midway between the two ends of the cell, on an imaginary plane called the **metaphase plate.**
    5. By metaphase, the microtubules of the asters have also grown are in contact with the plasma membrane.
    6. Anaphase commences suddenly when the cohesins holding together the sister chromatids of each chromosome are cleaved by enzymes. A clever experiment carried out in Gary Borisy's lab at the University of Wisconsin in 1987 suggested that motor proteins on the kinetochores "walk" chromosomes along the microtubules, which depolymerize at their kinetochore ends after the motor proteins have passed. However, other researchers, working with different cell types or cells from other species, have shown that chromosomes are "reeled in" by motor proteins at the spindle poles and that the microtubules depolymerize after they pass by these motor proteins.
    7. The nonkinetochore microtubules are responsible for elongating the whole cell during anaphase.
    8. At the end of anaphase, duplicate groups of chromosomes have arrived at opposite ends of the elongated parent cell. Nuclei re-form during telophase. Cytokinesis generally begins during anaphase or telophase, and the spindle eventually disassembles.
5. In animal cells, cytokinesis occurs by a process known as **cleavage.** The first sign of cleavage is the appearance of a **cleavage furrow,** a shallow groove in the cell surface near the old metaphase plate. On the cytoplasmic side of the furrow is a contractile ring of actin microfilaments associated with molecules of the protein myosin.
6. Cytokinesis in plant cells, which have cell walls, is markedly different. During telophase, vesicles derived from the Golgi apparatus move along microtubules to the middle of the cell, where they coalesce, producing a **cell plate.**
7. The asexual reproduction of single-celled eukaryotes includes mitosis and occurs by a type of cell division called **binary fission,** meaning "division by half." In *E. coli,* the process of cell division is initiated when the DNA of bacterial chromosome begins to replicate at a specific place on the chromosome called the **origin of replication,** producing two origins, which move to opposite sides of the cell.

3. The Evolution of Mitosis

1. In *dinoflagellates*, the chromosomes attach to the nuclear envelope, which remains intact during cell division. Microtubules pass through the nucleus inside cytoplasmic tunnels, reinforcing the spatial orientation of the nucleus, which then divides in a process reminiscent of bacterial binary fission.
2. In *diatoms* and *yeasts,* the nuclear envelope remains intact during cell division, and microtubules form a spindle within the nucleus.

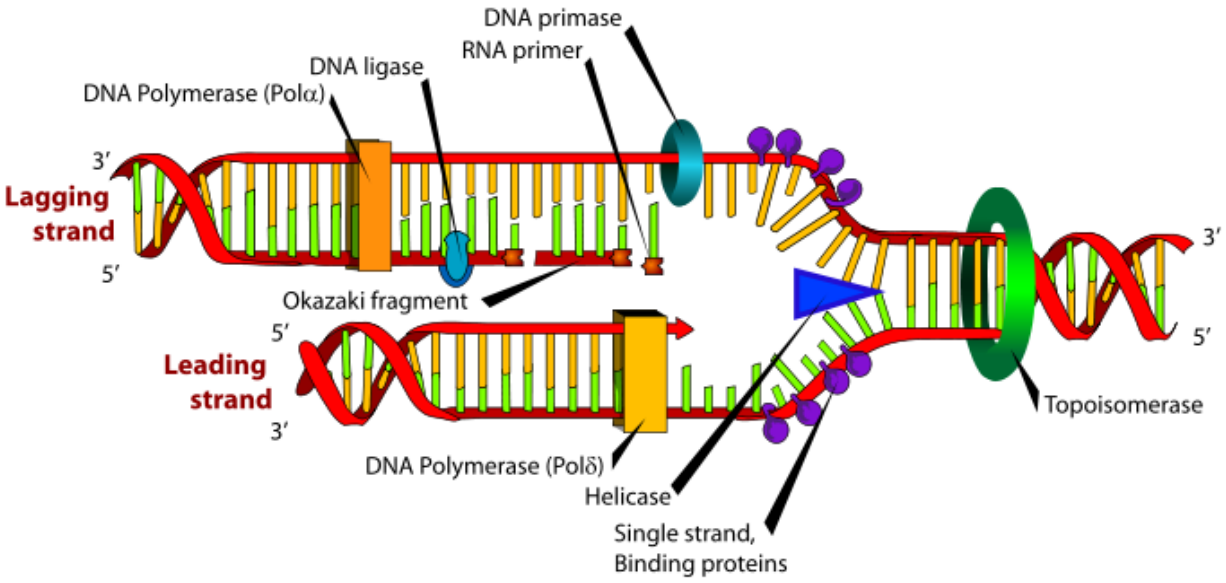
3. THE EUKARYOTIC CELL CYCLE IS REGULATED BY A MOLECULAR CONTROL SYSTEM.

1. The timing and rate of cell division in different parts of a plant or animal are crucial to normal growth, development, and maintenance.
2. In the early 1970s, a variety of experiments suggests that the cell cycle is driven by specific signaling molecules present in the cytoplasm.
3. The sequential events of the cell cycle are directed by a distinct **cell cycle control system.**
4. A **checkpoint** in the cell cycle is a control point where stop and go-ahead signals can regulate the cycle. Animal cells generally have built-in stop signals that halt the cell cycle at checkpoints until overridden by go-ahead signals. Three

- **Growth factor**: a protein released by certain cells that simulates other cells to divide.
- **Density-dependent inhibition**: a phenomenon in which crowded cells stop dividing.

major checkpoints are found in the G_1, G_2, and M phases. If a cell receives a go-ahead signal at the G_1 checkpoint, it will usually complete the G_1, S, G_2, and M phases and divide. If it does not receive a go-ahead signal at the point, it will exit the cycle, switching into a nondividing state called the **G_0 phase.**

5. Proteins kinases are enzymes that activate or inactivate other proteins by phosphorylating them. Particular protein kinases give the go-ahead signals at the G_1 and G_2 checkpoints. Many of the kinases that drive the cell cycle are actually present at a constant concentration in the growing cell, but much of the time they are in an inactive form. To be active, such a kinase must be attached to a **cyclin.** Because of this requirement, these kinases are called **cyclin-dependent kinases,** or **Cdks.**
    1. **MPF** (maturation-promoting factor) was the cyclin-Cdk complex that was discovered first. MPF causes phosphorylation of various proteins of the nuclear lamina, promoting fragmentation of the nuclear envelope.
    2. Animal cells appeared to have at least three Cdk proteins and several different cyclins that operate at the G_1 checkpoint.
    3. For the M checkpoint, the appropriate regulatory protein becomes activated only when all the kinetochores of all the chromosomes are attached to the spindle.
    4. Cells fail to divide if an essential nutrient is lacking in the culture medium. Most types of mammalian cells divide in culture only if the growth medium includes specific growth factors.
    5. Recent studies have revealed that the binding of a cell-surface protein to its counterpart on an adjoining cell sends a growth-inhibiting signal to both cells.
    6. Most animal cells also exhibit **anchorage dependence.** To divide, they must be attached to a substratum.
6. **Loss of Cell Cycle Controls in Cancer Cells**
    1. Cancer cells do not heed the normal signals that regulate the cell cycle. They divide excessively and invade other tissues. In addition to their lack of density-dependent inhibition and anchorage dependence, cancer cells do not stop dividing when growth factors are depleted. They may make a required growth factor themselves, or they may have an abnormality in the signaling pathway that conveys the growth factor's signal to the cell cycle control system even in the absence of that factor. Another possibility is an abnormal cell cycle control system.
    2. If and when they stop dividing, cancer cells do so at random points in the cycle. Cancer cells can go on dividing indefinitely in culture if they are given a continual supply of nutrients; in essence, they are "immortal". Nearly all normal mammalian cells growing in culture divide only about 20-50 times before they stop dividing, age, and die.
    3. The abnormal behavior of cancer cells can be catastrophic when it occurs in the body. The problem begins when a single cell in a tissue undergoes **transformation,** the process that converts a normal cell to a cancer cell.
    4. If the abnormal cells remain at the original site, the lump is called a **benign tumor.** In contrast, a **malignant tumor** becomes invasive enough to impair the functions of one or more organs.
    5. The cells of malignant tumors are abnormal in many ways besides their excessive proliferation. They may have unusual numbers of chromosomes. Their metabolism may be disabled, and they may cease to function in any constructive way. Abnormal changes on the cell surface cause cancer cells to lose attachments to neighboring cells and the extracellular matrix, which allows them to spread into nearby tissues. The spread of cancer cells to locations distant from their original site is called **metastasis.**
    6. To treat known or suspected metastatic tumors, chemotherapy is used, in which drugs that are toxic to actively dividing cells are administered through the circulatory system.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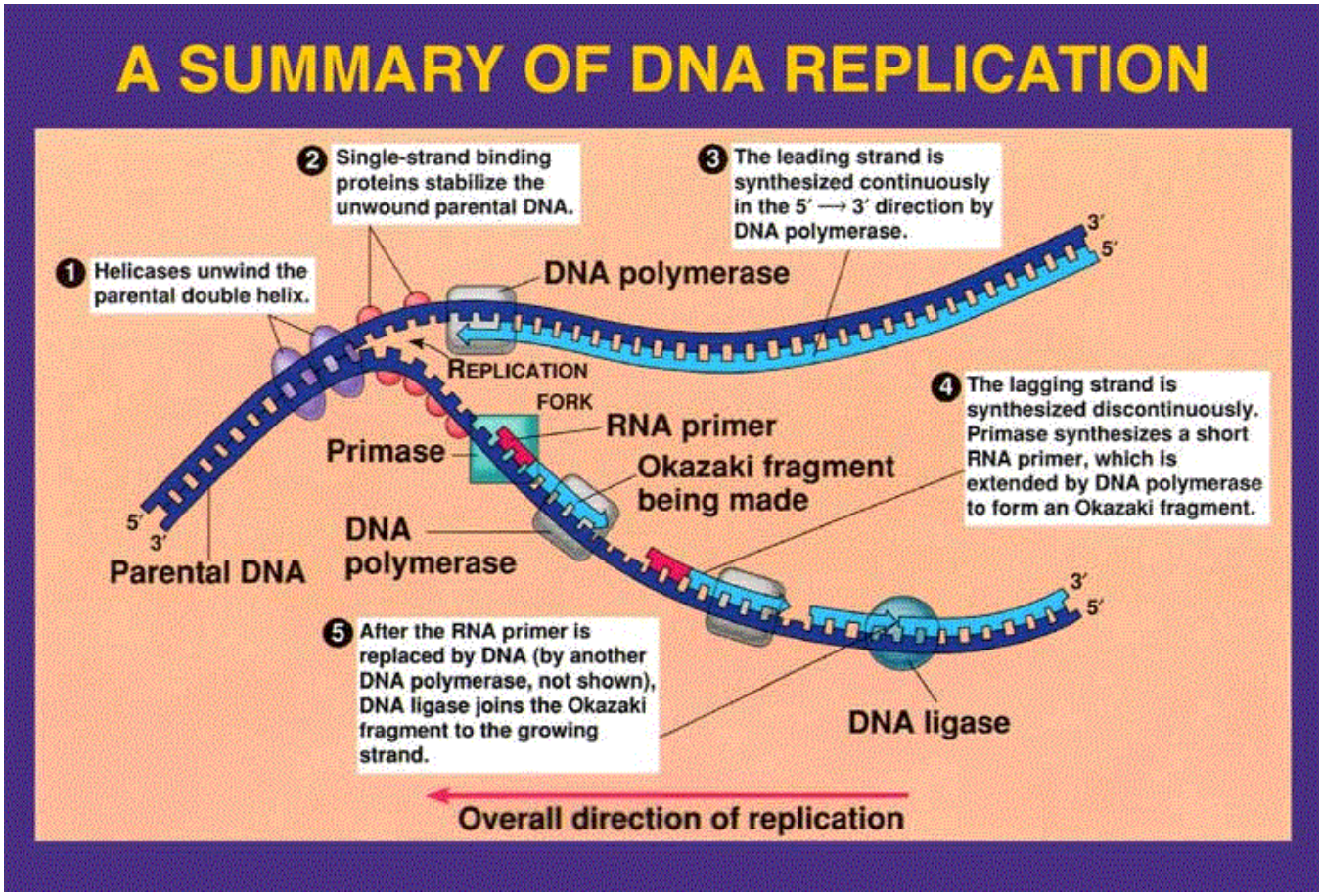

A SUMMARY OF DNA REPLICATION
1 Helicases unwind the parental double helix.
2 Single-strand binding proteins stabilize the unwound parental DNA.
3 The leading strand is synthesized continuously in the 5′ ⟶ 3′ direction by DNA polymerase.
4 The lagging strand is synthesized discontinuously. Primase synthesizes a short RNA primer, which is extended by DNA polymerase to form an Okazaki fragment.
5 After the RNA primer is replaced by DNA (by another DNA polymerase, not shown), DNA ligase joins the Okazaki fragment to the growing strand.
DNA polymerase
REPLICATION FORK
RNA primer
Primase
Okazaki fragment being made
DNA polymerase
Parental DNA
DNA ligase
Overall direction of replication
3′
5′

- **Heredity**: The transmission of traits from one generation to the next.
- Along with inherited similarity, there is also **variation**.
- **Genetics**: the scientific study of heredity and hereditary variation.
- **Locus**: A gene's specific location along the length of a chromosome.

- **Life Cycle**: the generation-to-generation sequence of stages in the reproductive history of an organism.

- **Fertilization**: The union of gametes, culminating in fusion of their nuclei.
- **Zygote**: the resulting fertilized egg. It is diploid.
- **Meiosis**: a type of cell division that produces haploid cells.

- **Chiasma**: the physical manifestation of crossing over due to the fact that sister chromatid cohesion still holds the two original sister chromatid together.
- *Independent assortment*: Because each homologous pair of chromosomes is positioned independently of the other pairs at metaphase I, the first meiotic division results in each pair sorting its maternal and paternal homologs into daughter cells independently of every other pair.

- **Character**: a heritable feature that varies among individuals, such as flower color.
- **Trait**: Each variant for a character.

1. Offspring acquire genes from parents by inheriting chromosomes.

1. Parents endow their offspring with coded information in the form of hereditary units called **genes**.
2. In animals and plants, reproductive cells called **gametes** are the vehicles that transmit genes from one generation to the next.
3. Except for small amounts of DNA in mitochondria and chloroplast, the DNA of a eukaryotic cell is packaged into chromosomes within the nucleus.
4. In **asexual reproduction**, a single individual is the sole parent and passes copies of all its genes to its offspring. An individual that reproduces asexually gives rise to a **clone**.
5. In **sexual reproduction**, two parents give rise to offspring that have unique combinations of genes inherited from the two parents.

2. Fertilization and meiosis alternate in sexual life cycles.

1. In humans, each **somatic cell—**any cell other than those involved in gamete formation—has 46 chromosomes.
2. **Karyotype**: images of the chromosomes are in arranged in pairs, starting with the longest chromosomes. The two chromosomes composing a pair have the same length, centromere position, and staining pattern: These are called **homologous chromosomes.**
3. The two distinct chromosomes referred to as X and Y are an important exception to the general pattern of homologous chromosomes in human somatic cells. Because they determine an individual's sex, the X and Y chromosomes are called **sex chromosomes.** The other chromosomes are called **autosomes.**
4. Any cell with two chromosome sets is called a **diploid cell** and has a diploid number of chromosomes, abbreviated 2*n*.
5. Gametes (sperm and eggs) contain a single chromosome set. Such cells are called **haploid cells,** and each has a haploid number of chromosomes (*n*).
6. Although the alteration of meiosis and fertilization is common to all organisms that reproduce sexually, the timing of these two events in the life cycle varies, depending on the species.
    1. In humans and most other animals, gametes are the only haploid cells.
    2. Plants and some species of algae exhibit a second type of life cycle called **alteration of generations.** Both diploid and haploid stages are multicellular. The multicellular diploid stage is called the **sporophyte.** Meiosis in the sporophyte produces haploid cells called **spores**, which divide, forming a multicellular haploid stage called the **gametophyte.**
    3. A third type of life cycle occurs in most fungi and some protists, including some algae. After gametes fuse and form a diploid zygote, meiosis occurs without a multicellular diploid offspring developing.

3. Meiosis reduces the number of chromosome sets from diploid to haploid.

1. Meiosis, like mitosis, is preceded by the replication of chromosomes. However, this single replication is followed by not one but two consecutive cell divisions, called **meiosis I** and **meiosis II.**
2. Three events unique to meiosis occur during meiosis I.
    1. **Synapsis and crossing over:** During prophase I, replicated homologs pair up and become physically connected along their lengths by a zipper-like protein structure, the *synaptonemal complex* (**synapsis**). Genetic rearrangement between nonsister chromatids (**crossing over**) occurs. Following diassembly of the synaptonemal complex in late prophase, the two homologs pull apart slightly but remain connected by at least chiasma.
    2. **Homologs on the metaphase plate**: At metaphase I of meiosis, chromosomes are positioned on the metaphase plate as pairs of homologs.
    3. **Separation of homologs**: At anaphase I of meiosis, the replicated chromosomes of each homologous pair move toward opposite poles, but the sister chromatids of each replicated chromosome remain attached. At anaphase I, cohesions are cleaved along the arms, allowing homologs to separate. At anaphase II, cohesions are cleaved at the centromeres, allowing chromatids to separate. A protein named shugoshin protects cohesins from cleavage at the centromere during meiosis I.
    4. Meiosis I is called the *reductional division* because it halves the number of chromosomes sets per cell. During meiosis II (*equational division*) the sister chromatids separate, producing haploid daughter cells.

4. Genetic variation produced in sexual life cycles contributes to evolution.

1. One aspect of sexual reproduction that generates genetic variation is the random orientation of homologous pairs of chromosomes at metaphase of meiosis I. The number of possible combinations when chromosomes sort independently during meiosis is 2^n.
2. Crossing over produces **recombinant chromosomes**, individual chromosomes that carry genes derived from two different parents. Crossing over begins very early in prophase I, as homologous chromosomes pair loosely along their lenghts. A chiasma forms as the result of a crossover occurring while sister chromatid cohesion is present along the arms. Chiasmata hold homologs together as the spindle forms for the first meiotic division.
3. At metaphase II, chromosomes that contain one or more recombinant chromatids can be oriented in two alternative, nonequivalent ways with respect to the other chromosomes.

Chapter 14: Mendle and the Gene Idea

0. Overview: Drawing from the Deck of Genes
    1. The explanation of heredity most widely in favor during the 1800s was the "blending" hypothesis, the idea that genetic material contributed by the two parents mixes in a manner analogous to the way blue and yellow paints blend to make green.
    2. An alternative to the blending model is a "particulate" hypothesis of inheritance: the gene idea.
1. Mendel Used the Scientific Approach to Identify Two Laws of Inheritance.
    1. Mendel grew up on his parents' small farm, received agricultural training in school along with his basic education, and overcame financial hardship and illness to excel in high school and, later, at the Olmutz Philosophical Institute.
    2. In 1843, the then 21-year-old Mendel entered a monastery.
    3. After failing the exam necessary to become a teacher, Mendel left the monastery and studied physics and chemistry at the University of Vienna for two years. Two professors affected him greatly:
        1. Christian Doppler encouraged his students to learn science through experimentation and trained Mendel to use mathematics to help explain natural phenomena.
        2. Franz Unger aroused Mendel's interest in the causes of variation in plants.
    4. Afterwards, Mendel returned to the monastery and was assigned to teach at a local school. Around 1857, Mendel began breeding garden peas in the abbey garden to study inheritance.

- **Punnett square**: a handy diagrammatic device for predicting the allele composition of offspring from a cross between individuals of known genetic makeup.
- **Homozygous**: identical alleles
- **Heterozygous**: two different alleles.
- **Phenotype**: observable traits. Can refer to a specific character or the organism in its entirety.
- **Genotype**: genetic makeup. Can refer to a specific gene or the organism's entire genome.
- **Monohybrids**: heterozygous for one character.
- **Dihybrids**: individuals heterozygous for two characters.

5. Mendel made sure that he started his experiments with varieties that, over many generations of self-pollination, hard produced on the same variety as the parent plant. Such plants are said to be **true-breeding.**
6. **Hybridization**: The mating, or *crossing*, of two true-breeding barieties.
    1. **P generation:** the true-breeding parents.
    2. **F_1 generation:** The first generation of hybrid offspring.
    3. Allowing the F_1 generation to self-pollinate produces an **F_2 generation**.
7. **Mendel's Model**
    1. Alternative versions of genes account for variations in inherited characters. These alternative versions of a gene are called **alleles.**
    2. For each character, an organism inherits two alleles, one from each parent.
    3. If the two alleles at a locus differ, then one, the **dominant allele,** determines the organism's appearance; the other, the **recessive allele**, has no noticeable effect on the organism's appearance.
    4. **Law of Segregation:** The two alleles for a heritable character segregate (separate) during gamete formation and end up in different gametes.
8. Breeding an organism of unknown genotype with a recessive homozygote is called a **testcross** because it can reveal the genotype of that organism.
9. The results of Mendel's dihybrid experiments are the basis for the **law of independent assortment:** each pair of alleles segregates independently of each other pair of alleles during gamete formation. Strictly speaking, this law applies only to genes located on different chromosomes.

2. THE LAWS OF PROBABILITY GOVERN MENDELIAN INHERITANCE.
    1. Mendel's laws of segregation and independent assortment reflect the same rules of probability that apply to tossing coins, rolling dice, and drawing cards from a deck.
    2. The *multiplication rule* states that to determine the probability of two events *both* happening, we multiply the probability of one event by the probability of the other event.
    3. *Addition rule*: the probability that any one of two or more mutually exclusive events will occur is calculated by adding their individual probabilities.
3. INHERITANCE PATTERNS ARE OFTEN MORE COMPLEX THAN PREDICTED BY SIMPLE MENDELIAN GENETICS.
    1. **Complete dominance:** the phenotypes of the heterozygote and the dominant homozygote are indistinguishable.
    2. **Incomplete dominance**: Neither allele is completely dominant, and the F_1 hybrids have a phenotype somewhere between those of the two parental varieties.
    3. **Codominance**: the two alleles both affect the phenotype in separate, distinguishable ways.
    4. For any character, the observed dominate/recessive relationship of alleles depends on the level at which we examine phenotype. Ex: **Tay-Sachs disease**, an inherited lack of a certain enzyme that metabolizes certain lipids. As these lipids accumulate in brain cells, the victim begins to suffer seizures, blindness, and degeneration of motor and mental performance and dies within a few years.
        1. Only children who are homozygous recessive have the disease. Thus, at the *organismal* level, the Tay-Sachs allele qualifies as recessive.
        2. The activity level of the lipid-metabolizing enzyme in heterozygotes is intermediate between that in individuals homozygous for the normal allele and that in individuals with Tay-Sachs disease. At the *biochemical level*, Tay-Sachs allele displays incomplete dominance.
        3. Heterozygous individuals produce equal numbers of normal and dysfunctional enzyme molecules. At the *molecular* level, the moral allele and the Tay-Sachs allele are codominant.
    5. The dominant allele for a particular character may be less common in a population that the recessive allele.
    6. Most genes exist in more than two allelic forms.
    7. **Pleiotropy**: When genes have multiple phenotypic effects. Most genes display pleiotropy.
    8. For many characters, an either-or classification is impossible because the characters vary in population along a continuum. (**Quantitative characters**). This usually indicates **polygenic inheritance**, where two or more genes affect a single phenotypic character.
    9. Environment contributes to the quantitative nature of some characters. These characters are **multifactorial**.

- **Epistasis**: a gene at one locus alters the phenotypic expression of a gene at a second locus.
- **Norm of reaction**: the phenotypic range for a genotype.

4. MANY HUMAN TRAITS FOLLOW MENDELIAN PATTERNS OF INHERITANCE
    1. **Pedigree:** contains information describing the traits of parents and children across the generations arranged into a family tree.
    2. Although phenotypically normal with regard to the disorder, heterozygous may transmit the recessive allele to their offspring and thus are called **carriers.**
    3. In general, genetic disorders are not evenly distributed among all groups of people. This uneven distribution results from the different genetic histories of the world's peoples during less technological times, when populations were more geographically (and hence genetically) isolated. When a disease-causing recessive allele is rare, it is relatively unlikely that two carriers of the same harmful allele will meet and mate. However, if the man and woman are close relatives, the probability of passing on recessive traits increases greatly.
    4. The most common lethal genetic disease in the United States is **cystic fibrosis**, which strikes one out of every 2,500 people of European descent, though it is much rarer in other groups. The disorder is caused by a defect or absence of a chloride ion channel.
    5. The most common inherited disorder of among people of African descent is **sickle-cell disease**, which affects one out of 400 African-Americans. Heterozygotes, said to have *sickle-cell trait*, are usually healthy, but they may suffer some sickle-cell symptoms during prolonged periods of reduced blood oxygen content.
    6. Although many harmful alleles are recessive, a number of human discovers are due to dominate alleles. One example is *achondroplasia*, a form of dwarfism that occurs in one of every 25,000 people.
    7. A lethal dominate allele can escape elimination if it causes death only after an individual who carries the allele has reached a relatively advanced age. For example, **Huntington's disease**, a degenerative disease of the nervous system, is caused by a lethal dominate allele that has no obvious phenotypic effect until the individual is about 35-45 years old.
    8. The hereditary diseases we have discussed so far are sometimes described as simple Mendelian disorders because they result from abnormality of one or both alleles at a single genetic locus. Many more people are susceptible to diseases that have a multifactorial basis—a genetic component plus a significant environmental influence. In many cases, the hereditary component is polygenic.
    9. A preventive approach to simple Mendelian disorders is possible when the risk of a particular genetic disorder can be assessed before a child is conceived or during the early stages of the pregnancy.
    10. For an increasing number of heritable disorders, tests are available that can distinguish individuals of the normal phenotype who are dominate homozygotes from those who are heterozygotes.
    11. Some genetic disorders can be detected at birth by simple tests that are now routinely performed in most hospitals in the United States.

- **Amniocentesis**: a physician inserts a needle into the uterus and extracts about 10 mL of amniotic fluid.
- **Chorionic villus sampling**: a physician inserts a narrow tube through the cervix into the uterus and suctions out a time sample of tissue from the placenta.
- **Ultrasound**: sound waves are used to produce an image of the fetus.
- **Fetoscopy**: a needle-thin tube containing a viewing scope and fiber optics is inserted into the uterus.

Chapter 15: The Chromosomal Basis of Inheritance.

0. *Overview: Locating Genes Along Chromosomes.*
    1. Gregor Mendel's "hereditary factors" were purely an abstract concept when he proposed their existence in 1860. At that time, no cellular structures were know that could house these imaginary units.
    2. Today, we can show that genes—Mendel's "factors"--are located along chromosomes.
1. *Mendelian inheritance has its physical basis in the behavior of chromosomes.*
    1. Using improved techniques of microscopy, cytologists worked out the process of mitosis in 1875 and meiosis in the 1890s.
    2. Around 1902, Walter S. Sutton, Theodor Boveri, and others independently noted the parallels between the behavior of chromosomes and the behavior of Mendel's proposed hereditary factors. The **chromosome theory of inheritance** began to take form. According to this theory Mendelian genes have specific loci (positions) along chromosomes, and it is the chromosomes that undergo segregation and independent assortment.

- **Wild type:** the phenotype for a character most commonly observed in natural populations.
- *Mutant phenotype*: Traits that are alternatives to the wild type.

    3. **Thomas Hunt Morgan**:
        1. He first mated fruit flies until he got a single male fruit fly with white eyes instead of the normal red eyes.
        2. He then mated the white-eyed fly with a normal red-eyed fly. All the offspring had red eyes.
        3. When these offspring mated, the new offspring had the ratio of 3-red-eyed: 1-white-eyed, Morgan noticed that all the white-eyed flies produced were male.
        4. He concluded that a fly's eye color was linked to its sex.
2. *Sex-linked genes exhibit unique patterns of inheritance.*
    1. In humans and other mammals, there are two varieties of sex chromosomes, designated X and Y. A person who inherits two X chromosomes usually develops as a female. An XY person develops into a male.
    2. Researchers have sequenced the human Y chromosome and have identified 78 genes, which code for about 25 proteins. About half of these genes are expressed only in the testis, and some are required for normal testicular function.

- **Sex-linked gene**: a gene located on either sex chromosome.

    3. If a sex-linked trait is due to a recessive allele, a female will express the phenotype only if she is a homozygote. Because males have only one locus, the terms *homozygous* and *heterozygous* lack meaning for describing their sex-linked genes; the term *hemizygous* is used in such cases.
    4. A number of of human sex-linked disorders are much more serious that color blindness. An example is **Duchenne muscular dystrophy**. The disease is characterized by a progressive weakening of the muscles and loss of coordination. Researchers have traced the disorder to the absence of a key muscle protein called dystrophin and have mapped the gene for this protein to specific locus on the X chromosome.
    5. **Hemophilia**: a sex-linked recessive disorder defined by the absence of one or more of the proteins required for blood clotting.
    6. **X-inactivation in Female Mammals**
        1. One X chromosome in each cell in females becomes almost completely inactivated during embryonic development. The inactive X in each cell of a female condenses into a compact object called a **Barr body**, which lies along the inside of the nuclear envelope.
        2. British geneticist Mary Lyon demonstrated that the selection of which X chromosome will form the Barr body occurs randomly and independently in each embryonic cell present at the time of X inactivation. As a consequence, females consist of a *mosaic* of two types of cells: those with the active X derived from the father and those with the active X derived from the mother.
        3. Inactivation of an X chromosome involves modification to the DNA, including attachment of methyl groups to one of the nitrogenous bases of DAN nucleotides. Researchers also have discovered an X chromosome gene called XIST that is active *only* on the Barr-body chromosome. Multiple copies of the RNA product of this gene apparently attach to the X chromosome on which they are made, eventually almost covering it.
3. *Linked genes tend to be inherited together because they are located near each other on the same chromosome.*
    1. When 50% of all offspring are recombinants, genetics say that there is a 50% frequency of recombination. A 50% frequency of recombination is observed for any two genes that are located on different chromosomes and are thus unlinked.
    2. **Crossing over** accounts for the recombination of linked genes. In crossing over, which occurs while the replicated homologous chromosomes are paired during prophase of meiosis I, a set of proteins orchestrates an exchange of corresponding segments of one maternal and one paternal chromatid.
    3. **Genetic map**: an ordered list of the genetic loci along a particular chromosome.
    4. Alfred H. Sturtevant predicted that *the farther apart two genes are, the higher the probability that a crossover will occur between them and therefore the higher the recombination frequency.*
    5. **Linkage map:** A genetic map based on recombination frequencies. Sturtevant expressed the distances between genes in **map units** (centimorgans), defining one map unit as equivalent to a 1% recombination frequency.
    6. Other methods enable geneticists to construct **cytogenetic maps** of chromosomes, which locate genes with respect to chromosomal features.

- **Linked genes**: Genes located on the same chromosome that tend to be inherited together in genetic crosses.
- **Genetic recombination**: the production of offspring with combinations of traits that differ from those found in either parent.
- **Parental types**: have phenotypes that matches one of the parental phenotypes.
- **Recombinant types (recombinants)**: have phenotypes that differ from the parental phenotypes.

4. *Alterations of chromosome number or structure cause some genetic disorders*
    1. The phenotype of an organism can be affected by small-scale changes involving individual genes. Random mutations are the source of all new alleles, which can lead to new phenotypic traits.
    2. Large-scale chromosomal changes can also affect an organism's phenotype. They often lead to spontaneous abortion (miscarriage) of a fetus.
    3. **Aneuploidy**: a condition in which a zygote has an abnormal number of chromosomes. **Monosomic**: the zygote only has one copy of a chromosome. **Trisomic**: the zygote has three copies of a chromosome.
    4. **Polyploidy**: More than two complete chromosome sets in all somatic cells. It is fairly common in the plant kingdom. Many of the plant species we eat are polyploid. In the animal kingdom, polyploid species are much less common, although they are known to occur among fishes and amphibians. In general, polyploids are more nearly normal in appearance than aneuploids.
    5. Errors in meiosis or damaging agents such as radiation can cause breakage of a chromosome, which can lead to four types of of changes in chromosome structure.
        1. **Deletion**: a chromosomal fragment is lost.
        2. **Duplication**: a "deleted" fragment becomes attached as an extra segment to a sister chromatid.
        3. **Inversion**: the fragment reattaches to the original chromosome but in reverse orientation.

- **Nondisjunction**: the members of a pair of homologous chromosomes do not move apart properly during meiosis I or sister chromatids fail to separate during meiosis II.

4. **Translocation**: the fragment joins a non-homologous chromosome.

6. **Down syndrome**: an aneuploid condition that affects one about of every 700 children born in the United States. Down syndrome is usually the result of an extra chromosome 21. Down syndrome includes characteristic facial features, short stature, heart defects, susceptibility to respiratory infection, and mental retardation. The frequency of Down syndrome increases with the age of the mother. While the disorder occurs in just 0.04% of children born to women under age 30, the risk climbs to 0.92% for mothers at age 40 and is even higher for older mothers
7. *Klinefelter syndrome*: A condition in which a male has an extra X chromosome (XXY). People with this disorder have male sex organs, but the testes are abnormally small and the man is sterile. Some breast enlargement and other female body characteristics are common. Affected individuals may have subnormal intelligence.
8. Males with an extra Y chromosome (XYY) do not exhibit any well-defined syndrome, but they tend to be taller than average.
9. Females with trisomy X (XXX), which occurs once in approximately 1,000 live births, are healthy and cannot be distinguished from XX females except by karyotype.
10. *Turner syndrome (monosomy X):* The only viable monosomy in humans. It occurs about once in every 5,000 births. Although these X0 individuals are phenotypically female, they are sterile because their sex organs do not mature.
11. Many deletions in human chromosomes, even in a heterozygous state, cause severe problems. *Cri du chat* ("cry of the cat"), results from a specific deletion in chromosome 5. A child born with this deletion is mentally retarded, has a small head with unusual facial features, and has a cry that sounds like the mewing of a distressed cat.
12. Chromosomal translocations have been implicated in certain cancers, including *chronic myelogenous leukemia (CML).* In these cells, the exchange of a large portion of chromosome 22 with a small fragment from a top of chromosome 9.

5. Some inheritance patterns are exceptions to the standard chromosome theory.

1. Geneticists have identified two or three dozen traits in mammals that depend on which parent passed along the alleles for those traits. This is called **genomic imprinting**.
    1. Genomic imprinting occurs during the formation of gametes and results in the silencing of one allele of certain genes. This imprints are transmitted to all the body cells during development, so either the maternal or paternal allele of a give imprinted gene is expressed in every cell of that organism. In each generation, the old imprints are "erased" in gamete-producing cells, and the chromosomes of the developing gametes are newly imprinted according to the sex of the individuals forming the gametes.
    2. Consider, for example, the mouse gene for insulin-like growth factor 2 (*Igf2*), one of the first imprinted genes to be identified. Although this growth factor is required for normal prenatal growth, only the parental allele is expressed. Although heavily methylated genes are usually inactive, methylation of certain cytosines on the paternal chromosome leads to expression of the parental *Igf2* allele. In experiments with mice, embryos engineered to inherit both copies of certain chromosomes from the same parent usually die before birth, whether that parent is male or female. Apparently, normal development requires that embryonic cells have exactly one active copy—not zero, not two—of certain genes.
2. Some genes are located in organelles in the cytoplasm; because they are outside the nucleus, these genes are sometimes called *extracellular genes* or *cytoplasmic genes*.
    1. In 1909, German scientist Karl Correns observed that the coloration of offspring was determined only by the maternal parent and not by the paternal parent when it came to yellow or white patches of the leaves of otherwise green plants. In most plants, a zygote receives all its plastids from the cytoplasm of the egg and none from the pollen.
    2. Similar maternal inheritance is also the rule for mitochondrial genes in most animals and plants, because almost al the mitochondria passed on to the a zygote come from the cytoplasm of the egg.

Chapter 15: The Chromosomal Basis of Inheritance.

- **Transformation**: a change in genotype and phenotype due to the assimilation of external DNA by a cell.
- **Bacteriophages** (**phages**): viruses that infect bacteria.

0. OVERVIEW: LIFE'S OPERATING INSTRUCTIONS
    1. In April 1953, James Watson and Francis Crick shook the scientific world with an elegant double-helical model for the structure of deoxyribonucleic acid, or DNA.
    2. Of all of nature's molecules, nucleic acids are unique in their ability to direct their own replication from monomers.
1. DNA IS THE GENETIC MATERIAL.
    1. Once T. H. Morgan's group showed that genes are located along chromosomes, the two chemical components of chromosomes—DNA and proteins—became the candidates for the genetic material.
    2. Until the 1940s, the case for proteins seemed stronger, especially since biochemists had identified them as a class of macromolecules with great heterogeneity of specificity of function, essential requirements for the hereditary material. In addition, little was known about nucleic acids.
    3. We can trace the discovery of the genetic role of DNA back to 1928. While attempting to develop a vaccine against pneumonia, a British medical officer named Frederick Griffith studied *Streptococcus pneumoniae*, a bacterium that causes pneumonia in mammals. He was surprised to find that when he killed the pathogenic bacteria with heat and then mixed the cell remains with living bacteria of the nonpathogenic strain, some of the living cells become pathogenic.
    4. Griffith's work set the stage for a 14-year search by American bacteriologist Oswald Avery for the identity of the transforming substance. Avery focused on the three main candidates: DNA, RNA, and protein. Avery broke open the heat-killed pathogenic bacteria and extracted the cellular contents. In separate samples, he used specific treatments that inactivated each of the three types of molecules. He then tested each treated ample for its ability to transform live nonpathogenic bacteria. Only when DNA was allowed to remain active did transformation occur. However, his results were met with skepticism.
    5. In 1952, Alfred Hershey and Martha Chase performed experiments showing that DNA in the genetic material of a phage known as T2. They devised an experiment showing that only one of the two components of T2 actually enters *E. coli* cell during infection by using radioactive isotopes to tag proteins and DNA. They found that the phage DNA entered the host cells but the phage protein did not.
    6. Further evidence that DNA is the genetic material came from the laboratory of biochemist Erwin Chargaff. He noticed a peculiar regularity in the ratios of nucleotide bases within a single species.
    7. Once most biologists were convinced that DNA was the genetic material, the challenge was to determine how the structure of DNA could account for its role in inheritance. By the early 1950s, the arrangement of covalent bonds in a nucleic acid polymer was well established. While visiting the laboratory of Maurice Wilkins, Watson saw an X-ray diffraction image of DNA produced by Wilkins's accomplished colleague Rosalind Franklin. Watson was familiar with the types of patterns that helical molecules produce. A careful study of Franklin's X-ray diffraction photo of DNA not only told him that DNA was helical in shape, but also enabled him to approximate the width of the helix and the spacing of the nitrogenous bases along it. The presence of two strands accounts for the now-familiar term **double helix**.
    8. Franklin had concluded that the sugar-phosphate backbones were on the outside of the double helix. This arrangement was appealing because it put the relatively hydrophobic nitrogenous bases in the molecule's interior and thus away from the surrounding aqueous solution. Franklin's X-ray data indicated that the helix makes one full turn every 3.4 nm along its length. With the bases stacked just 0.34 nm apart, there are ten layers of base pairs, or rungs of the ladder, in each full turn of the helix.
    9. Because the helix has the same diameter for its entire length, Watson and Crick reasoned that pyrimidines were paired with purines and vis-versa.
2. MANY PROTEINS WORK TOGETHER IN DNA REPLICATION AND REPAIR
    1. Watson and Crick: "Now, our model for deoxyribonucleic acid is, in effect, a pair of templates, each of which is complementary to the other. We imagine that prior duplication the hydrogen bonds are broken, and the two chains unwind and separate. Each chain then acts as a template for the formation onto itself of a new companion chain, so that eventually we shall have two pairs of chains, where we only had one before. Moreover, the sequence of the pairs of bases will have been duplicated exactly.
    2. **Semiconservative model**: Each of the two daughter molecules will have one old strand, derived from the parent molecule, and one newly made strand.
    3. The bacterium *E. coli* has a single chromosome about 4.6 million nucleotide pairs. In a favorable environment, an *E. coli* cell can copy all this DNA and divide to form two genetically identical daughter cells in less than an hour.
    4. More than a dozen enzymes and other proteins participate in DNA replication. Much more is known about how this "replication machine" works in bacteria than in eukaryotes.
    5. The replication of a DNA molecule begins at special sites called **origins of replication**, short stretches of DNA having a specific sequence of nucleotides. At each end of a replication bubble a **replication fork**, a Y-shaped region where the parental strands of DNA are being unwound. Several kinds of proteins participate in the unwinding.
        1. **Helicases**: enzymes that untwist the double helix at the replication forks, separating the two parental strands and making them available as template strands.
        2. After parental strand separation, **single-strand binding proteins** bind to the unpaired DNA strands, stabilizing them.
        3. The untwisting of the double helix causes tighter twisting and strain ahead of the replication fork. **Topoisomerase** helps relieve this strain by breaking, swiveling, and rejoining DNA strands.
    6. The initial nucleotide chain that is produced during DNA synthesis is actually a short stretch of RNA, not DNA. This RNA is called a **primer** and is synthesized by the enzyme **primase.**
    7. Enzyme called **DNA polymerase** catalyze the synthesis of new DNA by adding nucleotides to a pre-existing chain. Most DNA polymerase require a primer and a DNA template strand, along which complementary DNA nucleotides line up. Each nucleotide added to a growing DNA strand comes from a nucleotide triphosphate, which is a nucleoside with three phosphate groups. As each monomer joins the growing end of a DNA strand, two phosphate groups are lost as a molecular of pyrophosphate. Subsequent hydrolysis of the pyrophosphate to two molecules of inorganic phosphate is a coupled exergonic reaction that helps drive the polymerization reaction.
    8. Because of their structure, DNA polymerases can add nucleotides only to the free 3´ end of a primer or growing DNA strand, never to the 5´ end. Along one template strand, DNA polymerase III can synthesize a complementary strand continuously by elongating the new DNA in the mandatory 5´→3´ direction.
    9. The DNA strand made by this mechanism is called the **leading strand.**
    10. To elongate the other new strand of DNA in the mandatory 5´→3´ direction, DNA pol III must work along the other template strand in the direction away from the replication fork. The DNA strand elongating in this direction is called the **lagging strand.** The lagging strand is elongated in segments called **Okazaki fragments.** Whereas only one primer is required on the leading strand, each Okazaki fragment on the ladding strand must be primed separately. Another DNA

polymerase I, replaces the RNA nucleotides of the primers with DNA versions, adding them one by one onto the 3´ end of the adjacent Okazaki fragment. Another enzyme, **DNA ligase**, accomplishes this task, joining the sugar-phosphate backbones of all the Okazaki fragments into a continuous DNA strand.

11. It is traditional—and convenient—to represent DNA polymerase molecules as locomotives moving along a DNA "railroad track," but such a model is inaccurate in two important ways. First, the various proteins that participate in DNA replication actually form a single large complex, a "DNA replication machine."
12. Second, the DNA replication complex does not move along the DNA; rather, the DNA moves through the complex during the replication process. In eukaryotic cells, multiple copies of the complex, perhaps grouped into "factories," may be anchored to the nuclear matrix.
13. Although errors in the completed DNA molecule amount to only one in 10 billion nucleotides, initial pairing errors between incoming nucleotides and those in the template strand are 100,000 times more common—an error rate of one in 100,000 nucleotides. During DNA replication, DNA polymerases proofread each nucleotide against its template as soon as it is added to the growing strand.
14. In **mismatch repair**, enzymes remove and replace incorrectly paired nucleotides that have resulted from replication errors.
15. Incorrectly paired or altered nucleotides can also arise after replication. DNA molecules are constantly subjected to potentially harmful chemical and physical agents. In addition, DNA bases undergo spontaneous chemical changes under normal cellular conditions. However, these changes in DNA are usually corrected before they become mutations perpetuated through successive replications. Many different DNA repair enzymes have evolved. Often, a segment of the strand containing the damage is cut out (excised) by a DNA-cutting enzyme—a **nuclease—**and the resulting gap is then filled in with nucleotides. One such DNA repair system is called **nucleotide excision repair.**
16. In spite of the impressive capabilities of DNA polymerases, there is a small portion of the cell's DNA that DNA polymerases can neither replicate nor repair. For linear DNA, such as the DNA of eukaryotic chromosomes, the fact that a DNA polymerase can add nucleotides only to the 3´ end of a pre-existing poly-nucleotide leads to an apparent problem. Repeated rounds of replication produce shorter and shorter DNA molecules with uneven ends. However, eukaryotic chromosomal DNA molecules have special nucleotide sequences called **telomeres** at their ends. In addition, specific proteins associated with telomeric can prevent the staggered ends of the daughter molecule from activating the cell's systems for monitoring DNA damage. Telomeres do not prevent the shortening of DNA molecules due to successive rounds of replication; they just postpone the erosion of genes near the ends of DNA molecules.

3. A Chromosome Consists of a DNA Molecule Packed Together with Proteins
   1. Stretched out, the DNA of an *E. coli* cell would measure about a millimeter in length, 500 times longer than the cell. Within a bacterium, however, certain proteins cause the chromosome to coil and "supercoil," densely packing it so that it fills only part of the cell.
   2. Together, a complex of DNA and protein, called **chromatin**, fits into the nucleus through an elaborate, multilevel system of DNA packing.
      1. DNA, the double helix, is about 2 nm apart.
      2. Histones are responsible for the first level of DNA packing in chromatin. They consist of about 100 amino acids each, and have a many positively charged amino acids that bind tightly to the negatively charged DNA. H2A, H2B, H3, and H4 are the four most common types of histones.
      3. Nucleosomes, or "beads on a string" (10nm fiber): In electron micrographs, unfolded chromatin is 10 nm in diameter. Such chromatin resembles beads on a string. Each "bed" is a nucleosome, the basic unit of DNA packaging; the "string" between beads is called linker DNA. A nucleosome consists of DNA wound twice around a protein core composed of two molecules each of the four main histone types. The N-terminus of each histone (the histone tail) extends outward from the nucleosome. In the cell cycle, histones leave the DNA only briefly during replication and gene expression.
      4. 30-nm fiber: Interactions between the histone tails of one nucleosome and the linker DNA and nucleosomes on either side cause the 10-nm fiber to coil into a 30-nm fiber. A fifth histone, H1, is involved.
      5. Looped domains (300-nm fiber). The 30-nm fiber, in turn, forms loops called *looped domains* attached to a chromosome scaffold made of proteins, thus making up a *300-nm fiber.* The scaffold is rich in one type of topoisomerase, and H1 molecules also appear to be present.
      6. Metaphase chromosome: In the mitotic chromosome, the looped domains themselves coil and fold in a manner not yet fully understood, further compacting all the chromatin to produce the characteristic metaphase chromosome. The width of one chromatid is 700 nm. Particular genes always end up located at the same places in metaphase chromosomes, indicating that the packing steps are highly specific and precise.
   3. Even during interphase, the centromeres and telomeres of chromosomes, as well as other chromosomal regions in some cells, exist in a highly condensed state similar to that seen in a metaphase chromosome. This type of interphase chromatin, visible as irregular clumped with a light microscope, visible as irregular clumps with a light microscrope, is called **heterochromatin**, to distinguish it from the less compacted, more dispersed **euchromatin**.

0. Overview: The Flow of Genetic Information.

1. **Gene expression**: the process by which DNA directs the synthesis of proteins (or, in some cases, just RNAs).

1. Genes Specify Proteins Via Transcription and Translation.

1. In 1909, British physician Archibald Garrod was the first to suggest that genes dictate phenotypes through enzymes that catalyze specific chemical reactions in the cell. Garrod may have been the first person to recognize that Mendel's principles of heredity apply to humans as well as peas.
2. Using a treatment shown in the 1920s to cause genetic changing, George Beadle and Edward Tatum bombarded *Neurospora crassa*, a bread mold, with X-rays and then looked among the survivors for mutants that differed in their nutritional needs from the wild-type mold. Wild-type *Neurospora* can survive in the laboratory on a moist support medium called agar, mixed only with inorganic salts, glucose and the vitamin biotin. Beadle and Tatum identified mutants that could not survive on minimal medium, apparently because they were unable to synthesize certain essential molecules from the minimal ingredients. To ensure survival of these nutritional mutants, Beadle and Tatum allowed them to grow on a *complete growth medium*. They then took samples from each mutant and distributed them to a number of different vials, each containing minimal medium plus a single additional nutrient. Afterwards, they pinned down each mutant's defect more specifically. Their results provided strong support for the *one-gene—one enzyme hypothesis:* the function of a gene is to dictate the production of a specific enzyme.

- **Transcription**: the synthesis of RNA under the direction of DNA.
- **Messenger RNA** carries a genetic message from the DNA to the ribosomes.
- **Translation**: the synthesis of a polypeptide under the direction of RNA. Occurs at the **ribosomes**.

3. However, many eukaryotic genes can code for a set of closely related polypeptides in a process called alternative splicing. Also, quite a few genes code for RNA molecules that have important function sin cells even though they are never translated into protein.
4. In prokaryotes, the lack of segregation between DNA and ribosomes means that translation of mRNA begins while transcription is still in progress.
5. In eukaryotes, the initial RNA transcript from any gene, including those coding for RNA that is not translated into protein, is more generally called a **primary transcript.**
6. Triplets of nucleotide bases are the smallest units of uniform length that can code for all the amino acids. The flow of information from gene to protein is based on a **triplet code**: The genetic instructions for a polypeptide chain are written in the DNA as a series of nonoverlapping, three-nucleotide words. For each gene, only one of the two DNA strands is transcribed. This strand is called the **template strand.** The mRNA base triplets are called **codons**, and they are customarily written in the 5´→3´ direction. The three codons that do not designate amino acids are "stop" signals, or termination codons, marking the end of translation. The codon AUG has a dual function: It codes for the amino acid methionine (Met) and also functions as a "start" signal, or initiation codon. There is *redundancy* in the genetic code, but no ambiguity.
7. Our ability to extract the intended message from a written language depends on reading the symbols in the correct groupings—that is, in the correct **reading frame**.
8. The genetic code is nearly universal, shared by organism from the simplest bacteria to the most complex plants and animals. Exceptions to the universality of the genetic code include translation systems in which a few codons differ from the standard ones. There are also exceptions in which stop codons can be translated into one of two amino acids not found in most organism. One of them, pyrrolysine, has only been detected so far in archaea; the other, selenocysteine is a component of some bacterial proteins and even some human enzymes.

2. Transcription is the DNA-Directed Synthesis of RNA: *a closer look.*

1. An enzyme called an **RNA polymerase** pries the two strands of DNA apart and joins the RNA nucleotides as they base-pair along the DNA template.
2. The DNA sequence where RNA polymerase attaches and initiates transcription is known as the **promoter**; in bacteria, the sequence that signals the end of transcription is called the **terminator**. The stretch of DNA that is transcribed into an RNA molecule is called a **transcription unit.**
3. Bacteria only have a single type of RNA polymerase. Eukaryotes have at least three types of RNA polymerase. The one used for mRNA synthesis is called RNA polymerase II.

- **TATA box**: a crucial promoter DNA sequence.

4. Certain sections of a promoter are especially important for binding RNA polymerase. A collection of proteins called **transcription factors** mediate the binding of RNA polymerase and the initiation of transcription, and they are required for RNA polymerase II to bind to the promoter. The whole complex of transcription factors and RNA polymerase II bound to the promoter is called a **transcription initiation complex.**
5. As RNA polymerase moves along the DNA, it continues to untwist the double helix, exposing about 10 to 20 DNA bases at a time. The enzyme add nucleotides to the 3´ end of the growing RNA molecule, and the new RNA molecule peels away from its DNA template and the DNA double helix re-forms. A single gene can be transcribed simultaneously by several molecules of RNA polymerase following each other like trucks in a convoy.
6. The mechanism of termination differs between bacteria and eukaryotes. In bacteria, a terminator sequence causes the the polymerase to detach from the DNA and release the transcript, which available for immediate use as mRNA. In eukaryotes, RNA polymerase II transcribes a sequence on the DNA called the polyadenylation signal sequence, which does for a polyadenylation signal (AAUAAA) in the pre-mRNA. Then, at a point about 10 to 35 nucleotides downstream from the AAUAAA signal, proteins associated with the growing RNA cut it free from the polymerase. However, the polymerase continues transcribing DNA for hundreds of nucleotides. The RNA produced by this continued transcription is digested by an enzyme that moves along the RNA. When the enzyme reaches the polymerase, transcription is terminated and the polymerase falls off the DNA.

3. Eukaryotic cells modify RNA after transcription.

1. **RNA processing**: The 5′ end receives a **5′ cap,** a modified form of a guanine nucleotide with three phosphate groups. The 3′ end, an enzyme adds 50 to 250 more adenine (A) nucleotides, forming a **poly-A tail**. These two modifications facilitate the export of the mature mRNA from the nucleus, protect the mRNA from hydrolytic enzymes, and help ribosomes attach to the 5′ end of the mRNA.
2. **RNA splicing:** the removal of large portions of the RNA molecule. The average length of a transcription unit along a human DNA molecule is about 27,000 base pairs; however, it takes only 1,200 nucleotides in RNA to doe for the average-sized protein of 400 amino acids. Most eukaryotic genes and their RNA transcripts have long noncoding stretches of nucleotides. Most of these noncoding sequences are interspersed between coding segments of the gene. The noncoding segments of nucleic acid that lie between coding regions are called intervening sequences, or **introns**. The other regions are called **exons**. The introns are cut out from the molecules and the exons joined together, forming an mRNA molecule with a continuous coding sequence. The signal for RNA splicing is a short nucleotide sequence at each end of an intro. Particles called *small nuclear ribonucleoproteins,* abbreviated *snRNPs,* recognize these splice sites. Several different snRNPs join with additional proteins to form an even lager assembly called a **spliceosome**, which is almost as big as a ribosome. The spliceosome interacts with certain sites along an intron, releasing the iron and joining together the two exons.
3. The idea of a catalytic role for snRNA arose from the discovery of **riboenzymes,** RNA molecules molecules that function as enzymes. In some organisms, RNA splicing can occur without proteins or even additional RNA molecules:

The intron RNA functions as a riboenzyme and catalyzes its own excision.

4. Three properties of RNA enable some RNA molecules to function as enzymes:
    1. A region of a RNA molecule may base-pair with a complementary region elsewhere in the same molecule, which gives the molecule a particular three-dimensional structure.
    2. Some of the bases in RNA contain functional groups that may participate in catalysis.
    3. The ability of RNA to hydrogen-bond with other nucleic acid molecules adds specificity to its catalytic activity.
5. **Alternative RNA splicing**: when a gene can give rise to two or more different polypeptides, based on which segments are treated as introns during RNA processing.
6. Proteins often have a modular architecture consisting of discrete structural and functional regions called **domains**.
7. The presence of introns in a gene my facilitate the evolution of new potentially useful proteins as a result a process known as *exon shuffling.*

4. **Translation is the RNA-directed synthesis of a polypeptide: *a closer look.***
    1. ***Transfer RNA*** interprets mRNA. Molecules of tRNA are not all identical. As a tRNA molecule arrives at a ribosome, it bears a specific amino acid at one end. At the other end of the tRNA is a nucleotide triplet called an **anticodon.** Translation is simple in principle by complex in its biochemistry and mechanics, especially in the eukaryotic cell.
    2. Like mRNA and other types of cellular RNA, transfer RNA molecules are transcribed from DNA templates. In a eukaryotic cell, tRNA, like mRNA, is made in the nucleus and must travel from the nucleus to the cytoplasm, where translation occurs.
    3. A tRNA molecule consist of a single RNA strand that is only about 80 nucleotide long. This single strand can fold back upon itself and form a molecule with a three-dimensional structure that is roughly L-shaped. The loop extending from one end of the L includes the anticodon. From the other end of the L-shaped tRNA molecule protrudes its 3´ end, which is the attachment site for an amino acid.
    4. A tRNA that binds to an mRNA codon specifying a particular amino acid must carry that amino acid, and no other, to the ribosome. The correct matching up of tRNA and amino acid is carried out by a family of related enzymes called **aminoacyl-tRNA synthetases.**
    5. There are 20 different synthetases, one for each amino acid; each synthetase is able to bind all the different tRNAs that code for its particular amino acids.
    6. Some tRNAs are able to bind to more than one codon. Such versatility is possible because the rules for base pairing between the third base of a codon and the corresponding base of a tRNA anticodon are relaxed compared to those at other codon positions. The flexible base pairing at this codon position is called **wobble**.
    7. Ribosomes facilitate the specific coupling of tRNA anticodons with mRNA codons during protein synthesis. A ribosome is made up of two subunits, called the large and small subunits. The ribosomal subunits are constructed of proteins and RNA molecules named **ribosomal RNAs**, or **rRNAs**. In eukaryotes, the subunits are made in the nucleolus.
    8. In both bacteria and eukaryotes, large and small subunits join to form a functional ribosome only when they attach to an mRNA molecule. About two-third of the mass of a ribosome consists of rRNAs, either three molecules (in bacteria) or four (in eukaryotes).
    9. Although the ribosomes of bacteria and eukaryotes are very similar in structure and function, those of eukaryotes are slightly larger and differ somewhat from bacterial ribosomes in their molecular composition.
    10. In addition to a binding site for mRNA, each ribosome has three binding sites for tRNA. The **P site** holds the tRNA carrying the growing polypeptide, while the **A site** holds the tRNA carrying the next amino acid to be added to the chain. Discharged tRNAs leave the ribosome from the **E site**.
    11. As the polypeptide becomes longer, it passes through an *exit tunnel* in the ribosome's large subunit.
    12. Recent research strongly supports the hypothesis that rRNA, not protein, is primarily responsible for both the structure and function of the ribosome.
    13. We can divide translation, the synthesis of a polypeptide chain, into three stages: initiation, elongation, and termination.
        1. Initiation: The initiation stage of translation brings together mRNA, a tRNA bearing the first amino acid of the polypeptide, and the two subunits of a ribosome.
            1. First, a small ribosomal unit binds to both mRNA and a specific initiator tRNA, which carries the amino acid methionine.
                1. In bacteria, the small subunit can bind these two in either order.
                2. In eukaryotes, the small subunit, with the initiator tRNA already bound, binds to the 5´ cap of the mRNA and then *scans* downstream along the mRNA until it reaches the start codon.
            2. The attachment of a large ribosomal subunit completes the *translation initiation complex.*
            3. Proteins called i*nitiation factors* are required to bring all these components together. A GTP molecule is also required. A polypeptide is always synthesized from the N-terminus to the C-terminus.
        2. Elongation: Amino acids are added one by one to the preceding amino acid. Each addition involves the participation of several proteins called *elongation factors.*
            1. **Codon recognization:** The anticodon of an incoming aminoacyl tRNA base-pairs with the complementary mRNA codon in the A site. Hydrolysis of GTP increases the accuracy and efficiency of this step.
            2. **Peptide bond formation**: An rRNA molecule of the large ribosomal subunit catalysed the formation of a peptide bond between the new amino acid in the A site and the carboxyl end of the growing polypeptide in the P site. This step removes the polypeptide from the tRNA in the P site and attaches it to the amino acid on the tRNA in the A site.
            3. **Translocation**: The ribosome translocates the tRNA in the A site to the P site. The empty tRNA in the P site is moved to the E site, where it is released. The mRNA moves along with its bond tRNAs, bringing the next codon to be translated into the A site. A GTP molecule is required.
        3. Termination: A stop codon in the mRNA reaches the A site of the ribosome. A protein called a *release factor* binds directly to the stop codon in the A site. The release factor causes the addition of a water molecule instead of an amino acid to the polypeptide chain. The translation assembly breaks apart, a process that requires 2 GTP.
        4. Multiple ribosomes translate an mRNA at the same time. Such strings of ribosomes are called **polyribosomes** or **polysomes.**
    14. **Post-translational modifications** may be required before the protein can begin doing its particular job. Certain amino acids may be chemically modified by the attachment of sugars, lipids, phosphate groups, or other additions. Enzymes may remove one or more amino acids from the leading (amino) end of the polypeptide chian. A polypeptide chian may be enzymatically cleaved into two or more pieces. Two or more polypeptides may come together, becoming the subunits of a protein that has quaternary structure.
    15. Polypeptide synthesis always begins in the cytosol, when a free ribosome starts to translate an mRNA molecule. The growing polypeptide itself may cue the ribosome to attach to the ER. A segment of the polypeptide, called the **signal polypeptide**, is recognized as it emerges from the ribosome by a protein-RNA complex called a **signal-recognization particle (SRP).**

5. Point mutations can affect protein structure and function.

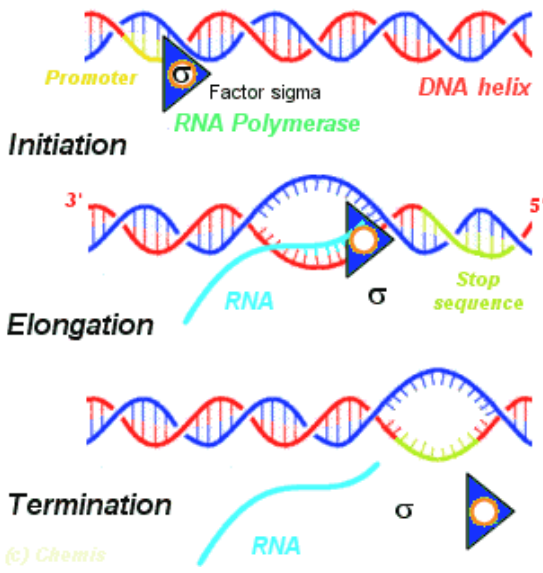
1. **Mutations** are responsible for the huge diversity of genes found among organisms because mutations are the ultimate source of new genes.
2. **Point mutation**: chemical changes in a single base pair of a gene.
    1. **Base-pair substitution**: the replacement of one nucleotide and its partner with another pair of nucleotides.
        1. *Silent mutations* have no effect on the encoded protein.
        2. *Missense mutations* exchange one amino acid to another one.
        3. *Nonsense mutation* change a codon for an amino acid to a stop codon.
    2. **Insertions and deletions** are additions or losses of nucleotide pairs in a gene.
        1. *Frameshift mutation*: Insertion or deletion of nucleotides may alter the reading frame of the genetic message.
3. Errors during DNA replication or recombination can lead to base-pair substitutions, insertions, or deletions, as well as to mutation affecting longer stretches of DNA. A number of physical and chemical agents, called **mutagens,** interact with DNA in ways that cause mutations.
    1. Chemical mutagens:
        1. Base analogs: chemicals that are similar to normal DNA bases but pair incorrectly during DNA replication.
        2. Some other chemical mutagens interfere with correct DNA replication by inserting themselves into the DNA and istorting the double helix.
        3. Other mutagens cause chemical changes in bases that change their pairing properties.

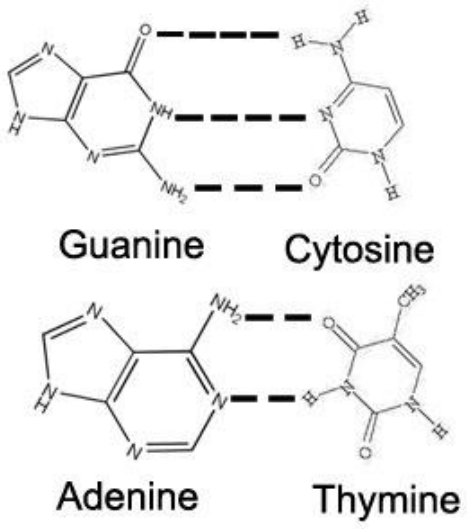
6. While gene expression differs among the domains of life, the concept of a gene is universal.

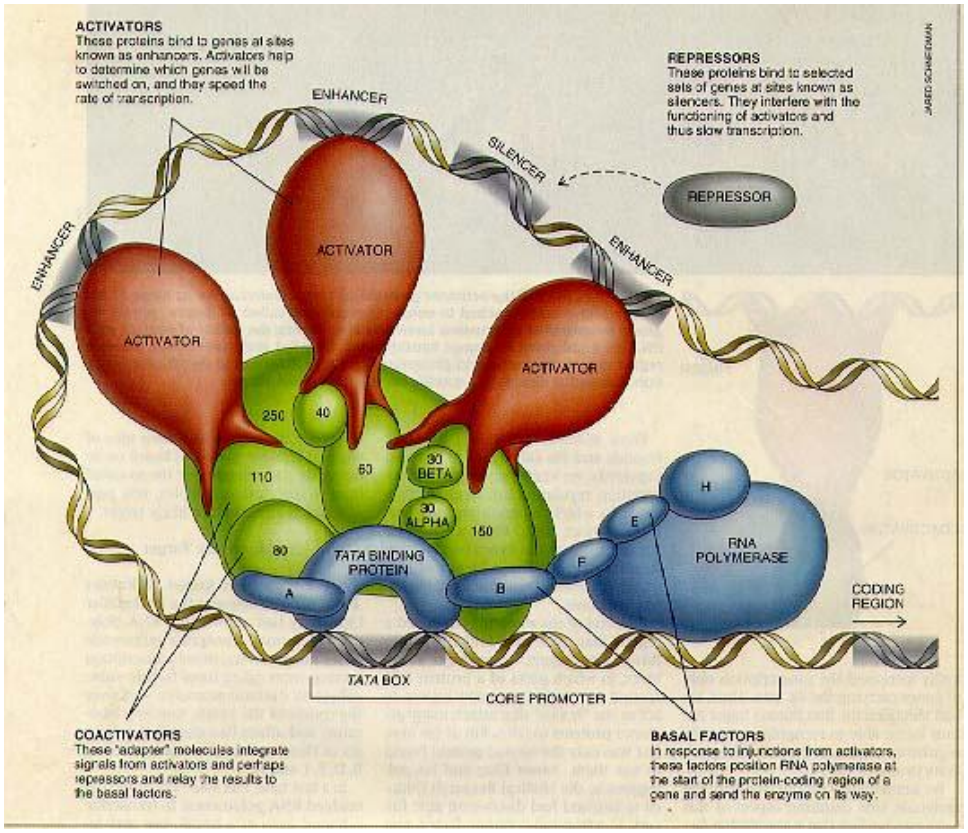
- *Gene: a region of DNA that can be expressed to produce a final functional product that is either a polypeptide or an RNA molecule.*

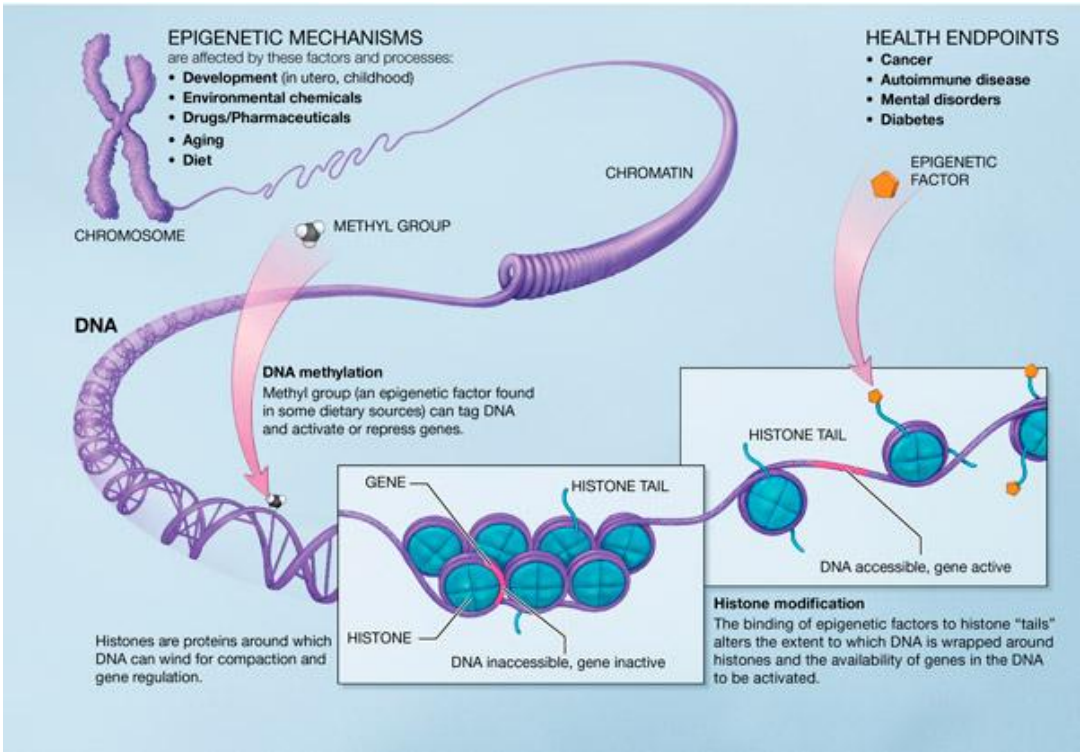
1. Bacterial and eukaryotic RNA polymerases differ significantly from each other. The single RNA polymerase of archaea resembles the three eukaryotic RNA polymerases, and archaea and eukaryotes use a complex set of transcription factors, unlike bacteria.
2. Archaeal ribosomes are the same size as bacterial ribosomes, but their sensitivity to chemical inhibitors most closely matches that of eukaryotic ribosomes. The archaeal process of initiation of translation is more like that of bacteria.
3. The most important differences between bacteria and eukaryotes with regard to gene expression arise from the bacterial cell's relative absence of compartmental organization. In the absence of a nucleus, a bacterial cell can simultaneously transcribe and translate the same gene. In contrast, the eukaryotic cell's nuclear envelope segregates transcription from translation and provided a compartment for extensive RNA processing.
4. A given type of cell expresses only a subset of its genes. Gene expression is precisely regulated.

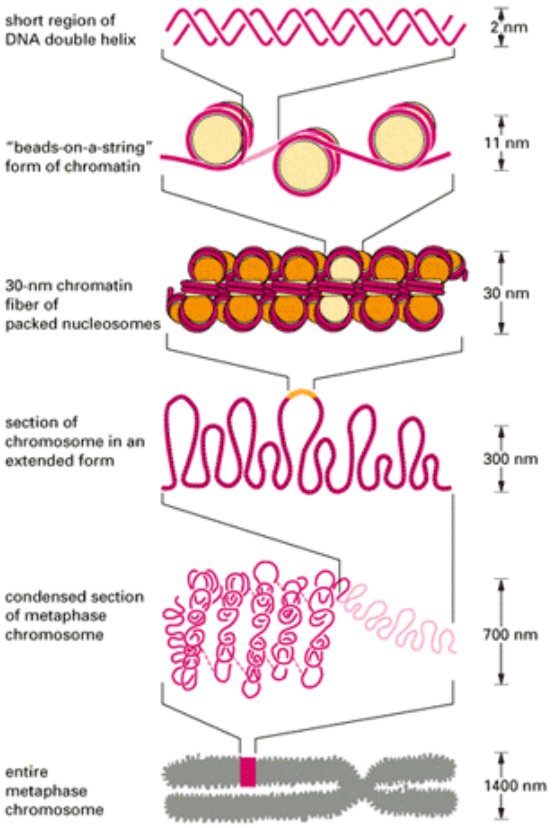
mRNA transcription for bacteria








EPIGENETIC MECHANISMS
are affected by these factors and processes:
• Development (in utero, childhood)
• Environmental chemicals
• Drugs/Pharmaceuticals
• Aging
• Diet
HEALTH ENDPOINTS
• Cancer
• Autoimmune disease
• Mental disorders
• Diabetes
CHROMOSOME
CHROMATIN
METHYL GROUP
EPIGENETIC FACTOR
DNA
DNA methylation
Methyl group (an epigenetic factor found in some dietary sources) can tag DNA and activate or repress genes.
GENE
HISTONE TAIL
HISTONE TAIL
DNA accessible, gene active
HISTONE
DNA inaccessible, gene inactive
Histones are proteins around which DNA can wind for compaction and gene regulation.
Histone modification
The binding of epigenetic factors to histone "tails" alters the extent to which DNA is wrapped around histones and the availability of genes in the DNA to be activated.


short region of DNA double helix
2 nm
"beads-on-a-string" form of chromatin
11 nm
30-nm chromatin fiber of packed nucleosomes
30 nm
section of chromosome in an extended form
300 nm
condensed section of metaphase chromosome
700 nm
entire metaphase chromosome
1400 nm

whiteboard

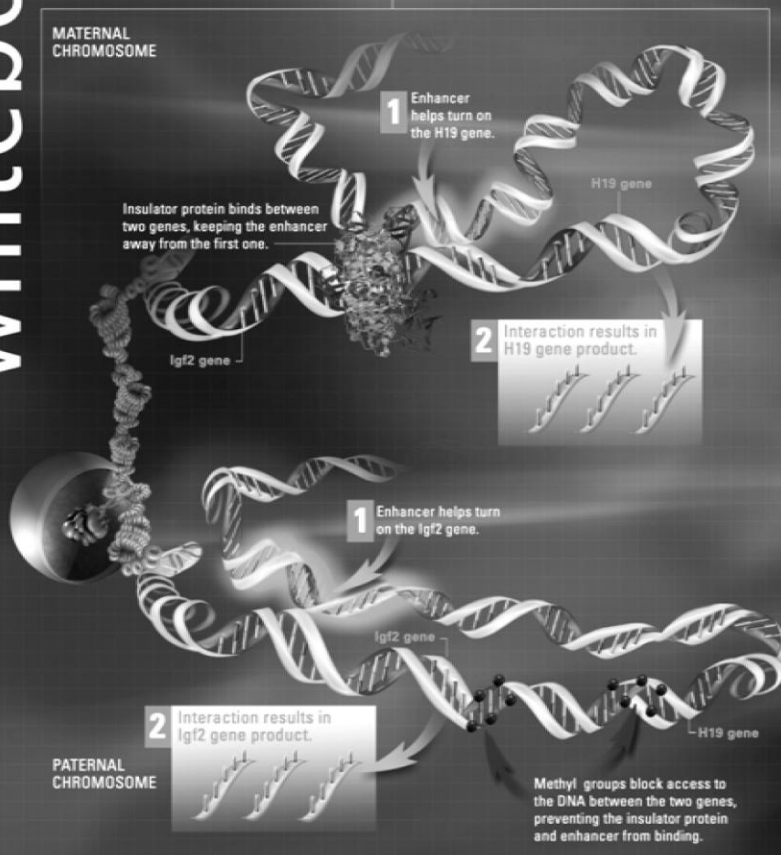
> THE LINK BETWEEN EPIGENETICS AND CANCER

GRAPHIC BY: CHRISTINA ULLMAN SCIENTIFIC ADVISOR: HEINZ LINHART

There are two known types of epigenetic marks—methyl groups and DNA packaging proteins—which help cells turn on specific genes at the right time and place. Strategically placed methyl groups (shown here in red) can block access to key regions of DNA. Each methyl group consists of a carbon atom surrounded by hydrogen. In the example on the right, misplaced methyl groups on one copy of a single chromosome contribute to cancer by disrupting the balance between two gene products. Ordinarily, only one copy of the chromosome pair is methylated at the location illustrated.

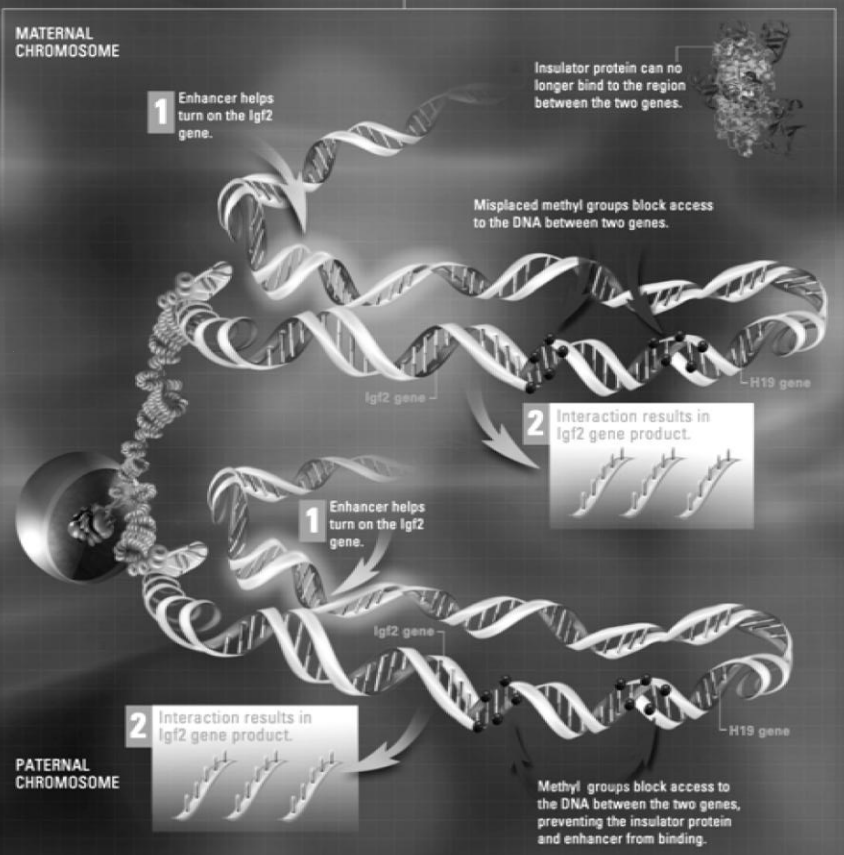
A. NON-CANCEROUS CELL

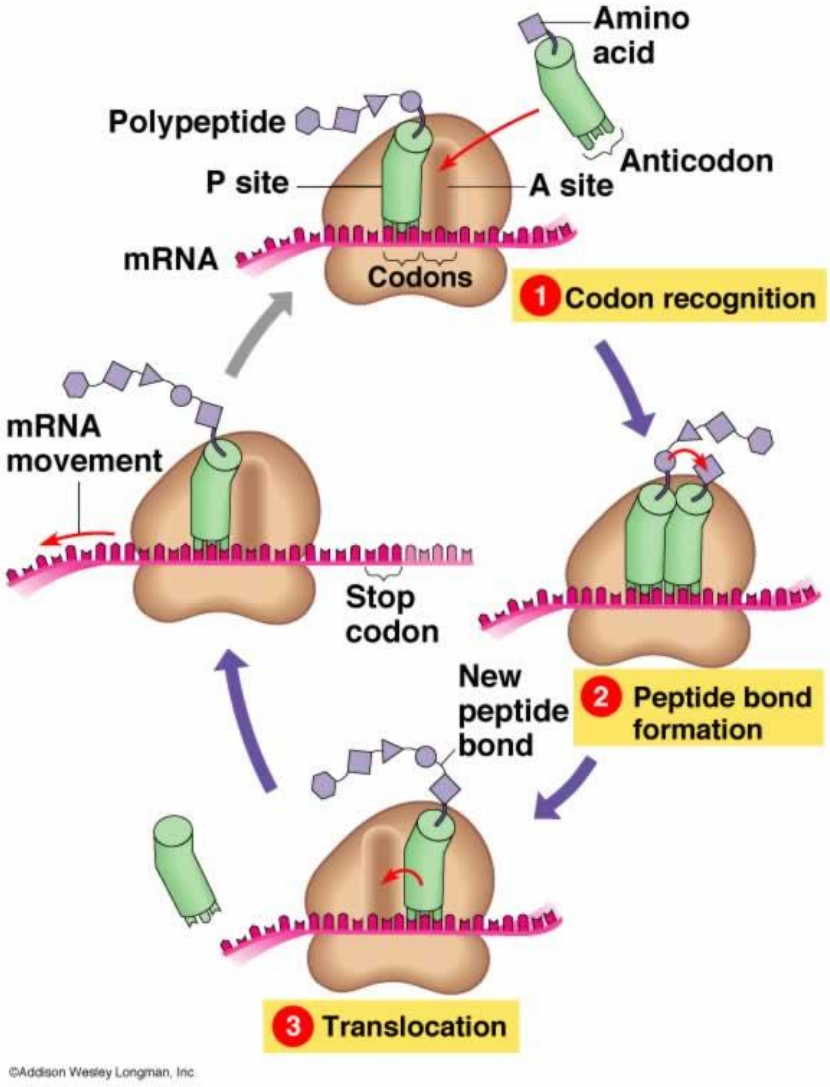
One copy of a single chromosome pair is methylated.



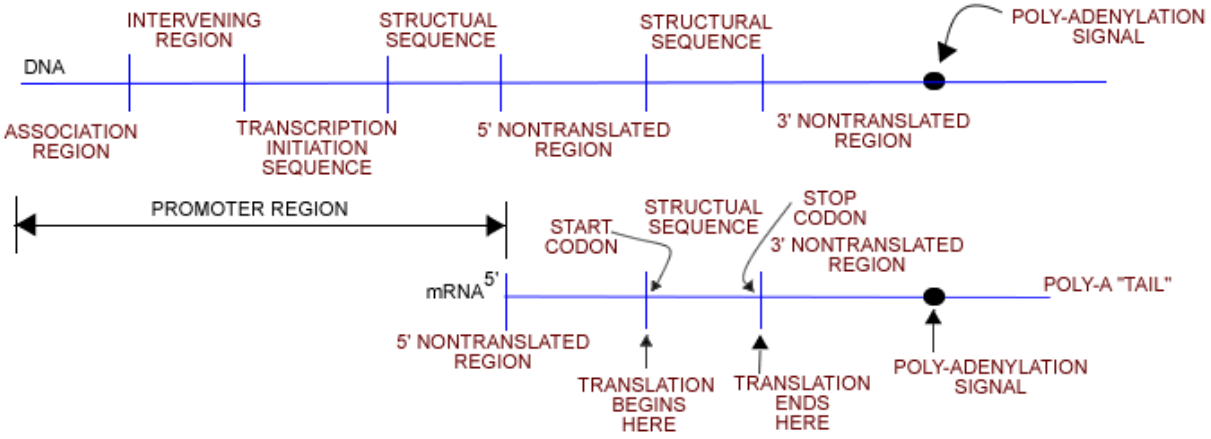
B. CANCEROUS CELL

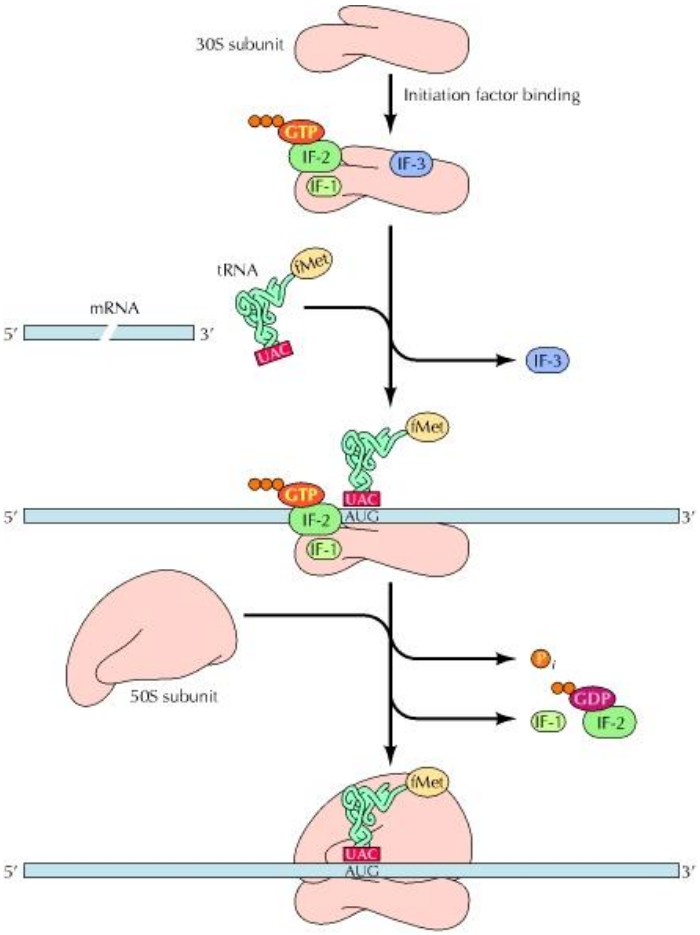
Two copies of a single chromosome pair are methylated.





Structure of a typical eukaryotic gene

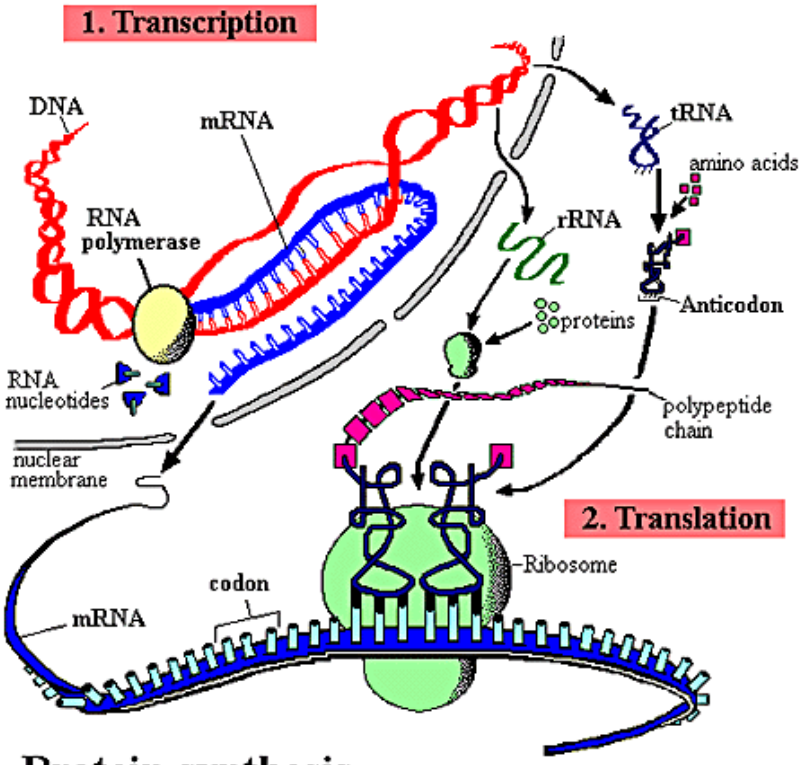




SECOND POSITION

FIRST POSITION	U	C	A	G	THIRD POSITION
U	phenyl-alanine	serine	tyrosine	cysteine	U
					C
	leucine		stop	stop	A
			stop	tryptophan	G
C	leucine	proline	histidine	arginine	U
					C
			glutamine		A
					G
A	isoleucine	threonine	asparagine	serine	U
					C
			lysine	arginine	A
	* methionine				G
G	valine	alanine	aspartic acid	glycine	U
					C
			glutamic acid		A
					G

* and start



Protein synthesis

Chapter 18: Regulation of Gene Expression

- **Differential gene expression**: the expression of different by cells with the same genome.

0. *Overview: Conducting the Genetic Orchestra*
   1. Cells intricately and precisely regulated their gene expression. Gene expression in eukaryotes, as in bacteria, is often regulated at the stage of transcription, but control at other levels of gene expression is also important.
1. *Bacteria often respond to environmental change by regulating transcription.*
   1. Metabolic control occurs on two levels. First, cells can adjust the activity of enzymes already present. Second, cells can adjust the production level of certain enzymes.
   2. A key advantage of grouping genes of related function into one transcription unit is that a single on-off "switch" can control the who cluster of functionally related genes; in other words, these genes are under *coordinate control*. The switch is a segment of DNA called an **operator.** All together, the operator, the promoter, and the genes they control constitute and **operon**.
   3. Regulation of both the *trp* and *lac* operons involves the *negative* control of genes, because the operons are switched off by the active form of the repressor protein.
      1. For the *trp* operon, the entire operon can be switched off by a protein called the *trp* **repressor**. The *trp* repressor is the product of a **regulatory gene** called *trpR*, which is located some distance from the operon it controls and has its own promoter. Regulatory genes are expressed continuously, although at a low rate.
         1. Trytophan functions in this system as a **corepressor,** a small molecule that cooperates with a repressor protein to switch an operon off.
         2. The *trp* operon is said to be a *repressible operon* because its transcription is usually on but can be inhibited (repressed) when a specific small molecule binds allosterically to a regulatory protein.
         3. *Repressible enzymes* generally function in anabolic pathways, which synthesize essential end products from raw materials.
      2. An *inducible operon* is usually off but can be stimulated (induced) when a specific small molecule interacts with a regulatory protein. The specific small molecule, called an **inducer,** *inactivates* the repressor. For the *lac* operon, the inducer is is allolactose.
         1. The enzymes of the lactose pathway are referred to as *inducible enzymes* because their synthesis is induced by a chemical signal.
   4. **Positive gene regulation:** When glucose and lactose are both present in its environment, *E. coli* preferentially uses glucose. Only when lactose is present and glucose is in short supply does *E. coli* use lactose as an energy source. The mechanism depends on the interaction of an allosteric regulatory protein with a small organic molecule, in this cAMP, which accumulates when glucose is scarce. The regulatory protein, called *catabolite activator protein (CAP),* is an **activator**, a protein that binds to DNA and stimulates transcription of a gene. By facilitating the binding of RNA polymerase to the promoter and thereby increasing the rate of transcription, the attachment of CAP to the promoter directly stimulates gene expression. Therefore, this mechanism qualifies as positive regulation.
2. *Eukaryotic gene expression can be regulated at any stage.*
   1. A typical human cell probably expresses about 20% of its genes at any given time. Highly differentiated cells, such as muscle or nerve cells, express an even smaller fraction of their genes.
   2. Only a small amount of the DNA—about 1.5% in humans—codes for protein. The rest of the DNA either codes for RNA products, such as tRNAs, or isn't transcribed at all.
   3. The structural organization of chromatin not only packs a cell's DNA into a compact form that fits inside the nucleus but also helps regulate gene expression in several ways. Genes within heterochromatin, which is highly condensed, are usually not expressed.
   4. In **histone acetylation,** acetyl groups ($-COCH_3$) are attached to lysine in histone tails; deacetylation is the removal of acetyl groups. When lysines are acetylated, their positive charges are neutralized and the histone tails no longer bind to neighboring nucleosomes. The addition of methyl groups ($-CH_3$) to histone tails (methylation) can promote condensation of the chromatin. The addition of a phosphate group to an amino acid (phosphorylation) next to a methylated amino acid can have the opposite effect.
      1. Some activators recruit proteins that acetylate histones near the promoters of specific genes, thus promoting transcription.
   5. Inactive DNA, such as that of inactivated mammalian X chromosomes, is generally more methylated than DNA that is actively transcribed, although there are exceptions.
      1. At least in some species, DNA methylation seems to be essential for the long-term inactivation of genes that occurs during normal cell differentiation in the embryo.
      2. Once methylated, genes usually stay that way through successive cell divisions in a given individual. At DNA sites where one stand is already methylated, methylation enzymes correctly methylate the daughter strand after each round of DNA replication.
      3. A methylation pattern maintained in this way also accounts for **genomic imprinting** in mammals.
      4. Alterations in normal patterns of DNA methylation are seen in some cancers, where they are associated with inappropriate gene expression.
   6. **Epigenetic inheritance**: inheritance of traits transmitted by mechanisms not directly involving the nucleotide sequence.
   7. The REGULATION OF TRANSCRIPTION INITIATION in eukaryotes involves proteins that bind to DNA and either facilitate or inhibit binding of RNA polymerase.
      1. A cluster of proteins called a *transcription initiation complex* assembles on the promoter sequence at the "upstream" end of the gene.
      2. Associated with most eukaryotic genes are multiple **control elements**, segments of noncoding DNA that help regulate transcription by binding certain proteins.
      3. To initiate transcription, eukaryotic RNA polymerase requires the assistance of proteins called transcription factors. Only a few general transcription factors independently bind a DNA sequence, such as the TATA box within the promoter; the others primarily bind proteins, including each other and RNA polymerase II.
      4. *Proximal control elements* are located close to the promoter. *Distal control elements*, groupings of which are called **enhancers**, may be thousands of nucleotides upstream or downstream of a gene or even within an intron.
      5. Protein-mediated bending of the DNA is thought to bring the bond activators in contact with a group of so-called *mediator proteins,* which in turn interact with proteins at the promoter. These multiple protein-protein interactions help assemble and position the initiation complex on the promoter.
   8. In eukaryotes, the precise control of transcription depends largely on the binding of activators to DNA control elements. The particular *combinations* of control elements in an enhancer associated with a gene turns out to be more important than the presence of a single unique control element in regulating transcription of the gene.
   9. Analysis of the genomes of several eukaryotic species has revealed some co-expressed genes that are clustered near one another on the same chromosome. However, each gene in such a cluster usually has its own promoter and is individually transcribed. Sometimes, however, several related genes do share a promoter and are transcribed into a single pre-mRNA, which is then processed into separate mRNAs. More commonly, co-expressed eukaryotic genes, such as genes

- **Alternative RNA splicing**: different mRNA molecules are produced from the same primary transcript, depending on which RNA segments are treated as exons and which as introns.

coding for the enzymes of a metabolic pathway, are found scattered over different chromosomes. Coordinate control of dispersed genes in a eukaryotic cell often occurs in response to chemical signals from outside the cell.

10. The life span of mRNA molecules in the cytoplasm is important in determining the pattern of protein synthesis in a cell. mRNA breakdown begins with the enzymatic shortening of the poly-A tail. Enzymes later remove the 5` cap. Once the cap is removed, nuclease enzymes rapidly chew up the RNA.
11. Translation presents another opportunity for regulating gene expression; such regulation occurs most commonly at the initiation stage.
    1. Some mRNAs can be blocked by regulatory proteins that bind to specific sequences or structures within the 5' UTR of the mRNA.
    2. Some stored mRNAs initially lack poly-A tails of sufficient length to allow translation initiation. A cytoplasmic protein adds adenine nucleotides to prompt translation.
12. Translation of *all* the mRNAs in a cell may be regulated simultaneously. In an eukaryotic cell, such "global" control usually involves the activation or inactivation of one more of the protein factors required to initiate translation.
13. The final opportunities for controlling gene expression occur after translation. Often, eukaryotic polypeptides must be processed to yield functional protein molecules. Many proteins undergo chemical modifications that make them functional.
14. Finally, the length of time each protein functions in the cell is strictly regulated by means of selective degradation. To mark a particular protein for destruction, the cell commonly attaches molecules of a small protein called ubiquitin to the protein. Giant protein complexes called **proteasomes** then recognize the ubiquitin-tagged proteins and degrade them

3. Noncoding RNAs play multiple roles in controlling gene expression.

1. Only 1.5% of the human genome codes for proteins. A significant amount of the genome may be transcribed into non-protein-coding RNAs, including a variety of small RNAs.
2. Regulation by noncoding RNAs is known to occur at two points in the pathway of gene expression: mRNA translation and chromatin configuration.
3. Since 1993, a number of research studies have uncovered small single-stranded RNA molecules, called **microRNAs (miRNAs),** that are capable of binding to complementary sequences in mRNA molecules. The miRNAs are formed from longer RNA precursors that fold back on themselves, forming one or more short double-stranded hairpins structures, each held together by hydrogen bonds. After each hairpin is cut away from the precursor, it is trimmed by an enzyme (Dicer) into a short double-stranded fragment of about 20 nucleotide pairs. One of the two strands is degraded, while the other strand, the miRNA, forms a complex with one or more proteins; the miRNA allows the complex to bind to any mRNA molecule with the complementary sequence. The miRNA-protein complex then either degrades the target mRNA or blocks its translation.
4. Researchers had found that that injecting double-stranded RNA molecules into a cell somehow turned off expression of a gene with the same sequence as the RNA (**RNA interference, RNAi**), which was later shown to be due to **small interfering RNAs (siRNAs),** which are similar in size and functions to miRNAs.
5. The distinction between miRNAs and siRNAs is based on the nature of the precursor molecule for each. While an miRNA is usually formed from a single hairpin in a precursor RNA, siRNAs are formed from much longer double-stranded RNA molecules, each of which gives rise to many siRNAs.
6. In addition to affect mRNAs, small RNAs can cause remodelling of chromatin structure. siRNAs produced by yeast cells appear to be crucial for the formation of heterochromatin at the centromeres of chromosomes.

4. A program of differential gene expression leads to the different cell types in a multicellular organism.

- **Cell differentiation**: the process by which cells become specialized in structure and function.
- **Morphogenesis**: the physical processes that give an organism its shape.
- **Cytoplasmic determinates**: maternal substances in the egg that influence the course of early development.
- **Induction**: the process in which signals cause changes in target cells.
- **Determination**: the events that lead to the observable differentiation of a cell.
- **Pattern formation**: The development of a spatial organization in which the tissues and organs of an organism are all in their characteristic places.
- **Homeotic genes**: control pattern formation in the late embryo, larva, and adult.
- **Embryonic lethals**: mutations with phenotypes causing death at the embryonic or larval stage.
- **Maternal effect gene**: a gene that, when mutant in the mother, results in a mutant phenotype in the offspring, regardless of the offspring's own genotype. Because they control the orientation (polarity) of the egg and consequently of the fly, maternal effect genes are also called **egg-polarity genes**.

1. In the embryonic development of multicellular organisms, a fertilized egg (a zygote) gives rise to cells of many different types, each with a different structure and corresponding function.
2. The specific genes expressed in any particular cell of a developing organism determine its path.
3. It turns out that materials placed into the egg by the mother set up a sequential program of gene regulation that is carried out as cells divide. One important source of information early in development is the egg's cytoplasm. The cytoplasm of an unfertilized egg is not homogeneous. Proteins, mRNA, other substances, and organelles, are distributed unevenly in the unfertilized egg, and this unevenness has a profound impact on the development of the future embryo in many species.
4. The other major source of developmental information, which becomes increasingly important as the number of embryonic cells increases, is the environment around a particular cell. Most influential are the signals impinging on an embryonic cell from other embryonic cells in the vicinity, including contact with cell-surface molecules on neighboring cells and the binding of growth factors secreted by neighboring cells.
5. Once it has undergone determination, an embryonic cell is irreversibly committed to its final fate. Differentiated cells are specialists at making tissue-specific proteins.
6. *MyoD* is the protein that transforms an embryonic precursor cell to a myoblast, a cell that is committed to becoming a muscle cell. *MyoD* stimulates the production of certain proteins, as well as itself.
7. **Positional information:** the molecular cues that control pattern formation.
8. In the 1940s, scientists began using the genetic approach—the study of mutants—to investigate *Drosophila* development. In *Drosophila*, cytoplasmic determinates that are localized in the unfertilized egg provide positional information for the placement of anterior-posterior and dorsal-ventral axes even before fertilization.
9. In the 1940s, Edward B. Lewis first showed the value of the genetic approach to studying embryonic development in *Drosophila.* Lewis studied bizarre mutant flies with developmental defects that led to extra wings or legs in the wrong places.
10. In the 1970s, two researchers in Germany, Christiane Nüsslein-Volhard and Eric Wieschaus, set out to identify *all* the genes that affect segment formation in *Drosophila*. There were three major difficulties:
    1. *Drosophila* has about 13,700 genes. The genes affecting segmentation might be just a few needles in a haystack or might be so numerous and varied that scientists would be unable to make sense of them.
    2. Mutations affecting a process as fundamental as segmentation would be embryonic lethals.
    3. Cytoplasmic determinates in the egg were known to play a role in axis formation, and therefore the researchers knew they would have to study the mother's genes as well as those of the embryo.
11. Nüsslein-Volhard and Wieschaus began their search for segmentation genes by exposing flies to a mutagenic chemical that affected the flies' gametes. They mated the mutagenized flies and then scanned their descendants for dead embryos or larvae with abnormal segmentation or other defects. Using this approach, they eventually identified about 1,200 genes essential for pattern formation during embryonic development.
12. An embryo whose mother has a mutant *bicoid* gene lacks the front half of its body and has posterior structures at both ends.
13. *Morphogen gradient hypothesis*: Gradients of substances called **morphogens** establish an embryo's axes and other features of its form.
14. *Bicoid* mRNA is highly concentrated at the extreme anterior end of the mature egg. The mRNA is produced in nurse

cells, transferred to the egg via cytoplasmic bridges, and anchored to the cytoskeleton at the anterior end of the egg.

15. Scientists injected pure *bicoid* mRNA into various regions of early embryos. The protein that resulted from its translation caused anterior structures to form at the injection sites.

5. Cancer results from genetic changes that affect cell cycle control.

1. The genes that normally regulate cell growth and division during the cell cycle include genes for growth factors, their receptors, and the intracellular molecules of signaling pathways.
2. An early breakthrough in understanding cancer came in 1911, when Peyton Rous, an American pathologist, discovered a virus that causes cancer in chickens.
3. *Tumor viruses* cause cancer in various animals. The Epstein-Barr virus, which causes infections mononucleosis, has been linked to several types of cancer, notably Burkitt's lymphoma. Papillomaviruses are associated with cancer of the cervix, and a virus called HTLV-1 causes a type of adult leukemia.
4. Research on tumor viruses led to the discovery of cancer-causing genes called **oncogenes** in certain retroviruses. The normal versions of the cellular genes, called **proto-oncogenes**, code for proteins that stimulate normal cell growth and division.
5. The genetic changes that convert proto-oncogenes to oncogenes fall into three main categories: movement of DNA within the genome, amplification of a proto-oncogene, and point mutations in a control element or in the proto-oncogene itself.
    1. Cancer cells frequently contain chromosomes that have broken and rejoined incorrectly, translocating fragments from one chromosome to another. If a translocated proto-oncogene ends up near an especially active promoter (or other control element), its transcription may increase, making it an oncogene.
    2. Amplification increases the number of copies of the proto-oncogene in the cell.
    3. A point mutation either (1) in the promoter or an enhancer that controls a proto-oncogene, causing an increase in its expression, or (2) in the coding sequence, changing the gene's product to a protein that is more active or more resistant to degradation than the normal protein.
6. **Tumor-suppressor genes** code for proteins that help prevent uncontrolled cell growth. They have various functions:
    1. Repair damaged DNA, a function that prevents the cell from accumulating cancer-causing mutations.
    2. Control the adhesion of cells to each other or to the extracellular matrix; proper cell anchorage is crucial in normal tissues—and often absent in cancers.
    3. Components of cell-signaling pathways that inhibit the cell cycle.
7. The Ras protein, encoded by the ***ras* gene,** is a G protein that relays a signal from a growth factor receptor on the plasma membrane to cascade of protein kinases. The cellular response at the end of the pathway is the synthesis of a protein that stimulates the cell cycle.
8. The ***p53* gene,** named for the 53,000-dalton molecular weight of its protein product, is a tumor-suppressor gene. The protein it encodes is a specific transcription factor that promotes the synthesis of cell-cycle inhibiting proteins. The *p53* gene has been called the "guardian angel of the genome." Once activated, for example by DNA damage, the p53 protein functions as an activator for several genes. Often, it activates a gene called *p21*, whose product halts the cell cycle by binding to cyclin-dependent kinases, allowing time for the cell to repair the DNA; the p53 protein can also turn on genes directly involved in DNA repair. When DNA damage is irreparable, p53 activates "suicide" genes.
9. More than one somatic mutation is generally needed to produce all the changes characteristic of a full-fledged cancer cell. The model of a multistep path to cancer is well supported by studies of one of the best-understood types of human cancer, colorectal cancer.
10. About a half dozen changes must occur at the DNA level for a cell to become fully cancerous. These usually include the appearance of at least one active oncogene and the mutation or loss of several tumor-suppressor genes. Mutations must knock out *both* alleles in a cell's genome to block tumor suppression. Most oncogenes behave as dominate alleles. The gene for telomerase is usually activated, allowing the cancer cells to be "immortal."
11. About 15% of colorectal cancers involve inherited mutations. Many of these affect the tumor-suppressor gene called *adenomatous polyposis coli,* or *APC*. This gene has multiple functions in the cell, including regulation of cell migration and adhesion. There is evidence of a strong inherited predisposition in 5-10% of patients with breast cancer. Mutations in the *BRCA1* or *BRCA2* gene are found in at least half of inherited breast cancers. Both genes are considered tumor-suppressor genes because their wild-type alleles protect against breast cancer and their mutant alleles are recessive. Both function in the cell's DNA damage repair pathway.

0. *Overview: A Borrowed Life*

1. Lacking the structures and metabolic machinery found in cells, most viruses are little more than genes packaged in protein coats. Viruses cannot reproduce or carry out metabolic activities outside of a host cell. Most biologists studying viruses today would probably agree that they are not alive but exist in a shady area between life-forms and chemicals.

1. *A Virus Consists of a Nucleic Acid Surrounded by a Protein Coat.*

1. In 1883, Adolf Mayer, a German scientist, discovered that he could transmit mosaic disease from plant to plant by rubbing sap extracted from diseased leaves onto healthy plants. Mayer suggested that the disease was caused by unusually small bacteria that were invisible under a microscope.
2. Dimitri Ivanowsky, a Russian biologist, passed same from infected tobacco leaves through a filter designed to remove bacteria. After filtration, the sap still produced mosaic disease.
3. Dutch botanist Martinus Beijerinck carried out a classic series of experiments that showed that the infectious agent in the filtered sap could reproduce. He showed that the mysterious agent of mosaic disease could not be cultivated on nutrient media in test tubes or petri dishes.
4. In 1935, American scientist Wendell Stanley crystallized the infectious particle.
5. The tiniest viruses are only 20 nm in diameter—smaller than a ribosome.
6. Their genomes may consist of a double-stranded DNA, single-stranded DNA, double-stranded RNA, or single-stranded RNA, depending on the kind of virus. The smallest viruses known have only four genes in their genome, while the largest have several hundred to a thousand.
7. Rod-shaped viruses are commonly called *helical viruses*.
8. Some viruses have accessory structures that help them infect their hosts.
9. **Viral envelopes** are derived from the membranes of the host cell and contain phospholipids and membrane proteins of both host and viral origin.
10. Many of the most complex capsids are found among the viruses that infect bacteria, called **bacteriophages**, or simply **phages**.

- **Capsid**: the protein shell enclosing the viral genome. The capsid may be rod-shaped, polyhedral, or more complex in shame. Capsids are built from a large number of protein subunits called *capsomeres*, but the number of different *kinds* of proteins in a capsid is usually small.

2. *Viruses Reproduce Only in Host Cells*

1. Each type of virus can infect cells of only a limited variety of hosts, called the **host range** of the virus. Viruses identify host cells by a "lock-and-key" fit between viral surface proteins and specific receptor molecules on the outside of cells.
2. A viral infection begins when a virus binds to a host cell and the viral genome makes its way inside. The mechanism of genome entry depends on the type of virus and the type of host cell. Most DNA viruses use the DNA polymerases of the host cell to synthesis new genomes along the templates provided by viral DNA. In contrast, to replicate their genomes, RNA viruses use virally encoded polymerases that can use RNA as a template. After the viral nucleic acid molecules and capsomeres are produced, they spontaneously self-assemble into new viruses.
3. Bacteria are not defenseless. Natural selection favors bacterial mutants with receptors that are no longer recognized by a particular type of phage. When phage DNA successfully enters a bacterium, the DNA is often identified as foreign and cut up by cellular enzymes called **restriction enzymes**.
4. Natural selection also favors phage mutants that can bind the altered receptors ore are resistant to particular restriction enzymes.
5. Infection of an *E. coli* cell by phage λ begins when the phage binds to the surface of the cell and injects its linear DNA genome. Within the host, the λ DNA molecule forms a circle
    1. During a lytic cycle, the viral genes immediately turn the host cell into a λ-producing factory.
    2. During a lysogenic cycle, however, the λ DNA molecule is incorporated into a specific site on the *E. coli* chromosome. When integrated into the bacterial chromosome in this way, the viral DNA is known as a **prophage.** One prophage gene codes for a protein that prevents transcription of most of the other prophage genes.
    3. The term *lysogenic* implies that prophages are capable of generating active phages that lyse their cells. An environmental signal, such as a certain chemical or high-energy radiation, usually triggers the switchover from the lysogenic to the lytic mode.
    4. A few other prophage genes may be expressed during lysogeny. Expression of these genes may alter the host's phenotype. For example, the three species of bacteria that cause the human diseases diphtheria, botulism, and scarlet fever would not be harmful to humans without certain prophase genes that cause the host bacteria to make toxins.
6. One key variable is the nature of the viral genome: Is it composed of DNA or RNA? Is it double-stranded or single-stranded? Single-stranded RNA viruses are further classified into three classes (IV-VI) according to how the RNA genome functions in a host cell.
7. An animal virus equipped with an envelope—that is, an outer membrane—uses it to enter the host cell. The viral envelope is derived from the host cell's plasma membrane, although some of the molecules of this membrane are specified by viral genes. Some viruses have envelopes that are not derived from the plasma membrane.
8. In the cause of herpesviruses, copies of the viral DNA can remain behind as mini-chromosomes in the nuclei of certain nerve cells.
9. The RNA animal viruses with the most complicated reproductive cycles are the **retroviruses** (class VI). These viruses are equipped with an enzyme called **reverse transcriptase,** which transcribes an RNA template into DNA.
    1. Of particular medical importance is **HIV (human immunodeficiency virus),** the retrovirus that causes **AIDS (acquired immunodeficiency syndrome**). HIV and other retroviruses are enveloped viruses that contain two identical molecules of single-stranded RNA and two molecules of reverse transcriptase.
10. The integrated viral DNA, called a **provirus**, never leaves the host's genome, remaining a permanent resident of the cell.
11. How did viruses originate? Viruses have been found that infect every form of life—not just bacteria, animals, and plants, but also archaea, fungi, algae, and other protists.
    1. Viruses are not the descendants of precellular forms of life but evolved *after* the first cells appeared, possibly multiple times.
    2. Viruses originated from naked bits of cellular nucleic acids that moved from one cell to another, perhaps via injured cell surfaces.
    3. Candidates for the original sources of viral genomes include plasmids and transposons. Both are mobile genetic elements.
        1. Plasmids: small, circular DNA molecules found in bacteria and in the unicellular eukaryotes called yeasts.
        2. Transposons: DNA segments that can move from one location to another within a cell's genome.
12. The debate about the origin of viruses has been reinvigorated recently by reports of mimivirus, the largest virus yet

- **Lytic cycle**: A phage reproductive cycle that culminates in the death of the host cell.
- **Virulent phage**: a phage that reproduces only by a lytic cycle.
- **Lysogenic cycle**: allows replication of the plage genome without destroying the host.
- **Temperate phages**: phages capable of using both models of reproducing within a bacterium.

discovered. Mimivirus is a double-stranded DNA virus with an icosahedral capsid that is 400 nm in diameter. Its genome contains 1.2 million bases and an estimated 1,000 genes. Some of the genes appear to code for products previously thought to be hallmarks of cellular genomes: proteins involved in translation, DNA repair, protein folding, and polysaccharide synthesis. The researchers who described mimivirus propose that it most likely evolved *before* the first cells and then developed an exploitative relationship with them. Other scientists disagree, maintaining that the virus evolved more recently than cells and has simply been efficient at scavenging genes from its hosts

- **Vaccine**: a harmless variant or derivative of a pathogen that stimulates the immune system to mount defenses against the harmful pathogen.

3. *Viruses, Viroids, and Prions are Formidable Pathogens in Animals and Plants*

1. Other smaller, less complex entities known as viroids and prions also cause disease in plants and animals, respectively.
2. A viral infection can produce symptoms by a number of different routes: causing the release of hydrolytic enzymes from lysosomes, or causing infected cells to produce toxins; some viruses have molecular components that are toxic.
3. How much damage a virus causes depends partly on the ability of the infected tissue to regenerate by cell division. Many of the temporary symptoms associated with viral infections, such as fever and aches, actually result from the body's own efforts at defending itself against infection rather than from cell death caused by the virus.
4. Although vaccines can prevent certain viral illnesses, medical technology can do little, at present, to cure most viral infections once they occur. However, the few enzymes that are encoded by viruses have provided targets for other drugs.
5. *Emerging viruses*: Viruses that appear suddenly or are new medical scientists.
    1. *Hemorrhagic fever:* an often fatal syndrome characterized by fever, vomiting, massive bleeding, and circulatory system collapse.
    2. *Encephalitis*: inflammation of the brain.
6. *Severe acute respiratory syndrome (SARS)* first appeared in southern China in November 2002, infecting 8,000 people and killing more than 700 people over the next eight months. The infectious agent, a *coronavirus*, had a single stranded RNA genome (class IV) and had not previously been known to cause disease in humans.
7. Three processes contribute to the emergence of viral diseases:
    1. RNA viruses tend to have an unusually high rate of mutation because errors in replicating their RNA genomes are not corrected by proofreading.
    2. Dissemination of a viral disease from a small, isolated human population.
    3. The spread of existing viruses from other animals.
        1. Flu epidemics provide an instructive example of the effects of viruses moving between species. There are three types of influenza virus: types B and C, which infect only humans and have never caused an epidemic, and type A, which infects a wide range of animals, including birds, pigs, horses, and humans. Influenza A strains have caused three major flue epidemics among humans in the last 100 years.
8. A likely scenario for a pandemic and others is that it begins when a virus mutates as it passed from one host species to another.
    1. When an animal is infected with more than one strain of flu virus, the different strains can undergo genetic recombination if the RNA molecules making up their genomes mix and match during viral assembly, leading to a new strain of that virus. Because humans have never been exposed to that strain before, they have no immunity. If the virus can spread easily, it may become a major human outbreak
9. Different strains of influenza A are given standardized names. The name identifies which forms of two viral surface proteins are present: hemagglutinin (H) and neuraminidase (N). There are 16 different types of hemagglutinin, a protein that helps the flu virus attach to host cells, and 9 types of neuraminidase, an enzyme that helps release new virus particles.
10. Avian flu:
    1. 1997: at least 18 people in Hong Kong were infected with the H5N1 virus, which had previously killed several thousand chickens earlier that year. All of Hong Kong's domestic birds were culled.
    2. 2002: New cases of H5N1 in humans appeared in southeast Asia.
    3. 2007: The disease, now called "avian flu," had killed about 160, and had a morality rate over 50%.
11. **Viral Diseases in Plants:**
    1. More than 2,000 types of viral diseases of plants are known, and together they account for an estimated annual loss of $15 billion worldwide.
    2. Common signs of viral infection include bleached or brown spots on leaves and fruits, stunted growth, and damaged flowers or roots.
    3. Plant viruses have the same basic structure and mode of reproduction as animal viruses. Most have an RNA genome and a helical capsid; some have an icosahedral capsid.
    4. Viral diseases of plants spread by two major routes:
        1. *Horizontal transmission:* a plant is infected from an external source of the viurs.
        2. *Vertical transmission*: a plant inherits a viral infection from a parent.
    5. Once a virus enters a plant cell and begins reproducing, viral genomes and associated proteins can spread throughout the plant by means of plasmodesmata. The passage of viral macromolecules from cell to cell is facilitated by virally encoded proteins that cause enlargement of plasmodesmata.
    6. **Viroids:** circular RNA molecules, only a few hundred nucleotides long, that infect plants. Viroids do not encode proteins but can replicate in host plant cells. They tend to cause errors in the regulatory systems that control plant growth.
    7. **Prions:** infectious *proteins* which appear to cause a number of degenerative brain diseases in various animal species, including scrapie in sheep, mad cow disease, and Creutzfeldt-Jakob disease in humans.
        1. Prions act very slowly, with an incubation period of at least ten years before symptoms develop. Also, they are virtually indestructible.
        2. According to the leading model, a prion is a misfolded form of a protein normally present in brain cells. When the prion gets into a cell containing the normal form of the protein, the prion somehow converts normal protein molecules into the misfolded prion versions.

Chapter 20: Biotechnology

- **Recombinant DNA**: DNA molecules formed when segments of DNA from two different sources—often different species—are combined *in vitro*.
- **Biotechnology**: the manipulation of organisms or their components to make useful products.
- **Genetic engineering**: the direct manipulation of genes for practical purposes.
- **DNA cloning**: Methods for preparing well-defined segment of DNA in multiple identical copies.
- **Gene cloning**: The production of multiple copies of a single gene.
- **Cloning vector**: a DNA molecule that can carry foreign DNA into a host cell and replicate there.
- **Genomic library**: the complete set of plasmid-containing cell clones, each carrying copies of a particular segment from the initial genome.
- **Bacterial artificial chromosome**: large plasmids, trimmed down so they contain just the genes necessary to ensure replication.
- **Expression vector**: a cloning vector that contains a highly active bacterial promoter just upstream of a restriction site where the eukaryotic gene can be inserted in the correct reading frame.

0. OVERVIEW: THE DNA TOOLBOX
   1. 1995: Researchers sequenced the entire genome of a free-living organism, the bacterium *Haemophilus influenzae*.
   2. By 2007: Researchers had completely sequenced hundreds of prokaryotic genomes and dozens of eukaryotic ones, including all 3 billion base pairs of the human genome.
   3. Using DNA microarray analysis, researchers can quickly compare gene expression in different samples, such as those obtained from normal and cancerous tissues.

1. DNA CLONING YIELDS MULTIPLE COPIES OF A GENE OR OTHER DNA SEGMENT
   1. Naturally occurring DNA molecules are very long, and a single molecule usually carries many genes. A single human gene might constitute only .001% of a chromosomal DNA molecule. The distinctions between a gene and the surrounding DNA are subtle.
   2. *E. coli* and many other bacteria have **plasmids,** small circular DNA molecules that replicate separately from the bacterial chromosome. A plasmid only has a small number of genes; these genes may be useful when the bacterium is in a particular environment but may not be required for survival or reproduction under most conditions.
   3. To clone pieces of DNA in the laboratory, researchers isolate a plasmid from a bacterial cell and insert DNA from another source. The plasmid is then return to bacterial cell, producing a *recombinant bacterium***,** which then divides, reproducing the plasmid and the inserted DNA.
   4. Researchers can isolate copies of a cloned genes from bacteria for use in basic research or to endow an organism with a new metabolic capability. A protein with medical uses can be harvested in large quantities from cultures of bacteria carrying the cloned gene for the protein.
   5. Gene cloning and genetic engineering rely on **restriction enzymes,** which cut DNA molecules at a limited number of specific locations, called **restriction sites, yielding** a set of **restriction fragments.** The restriction fragments have at least one single-stranded end, called a **sticky end**. Sticky ends can base-pair together and be sealed together by **DNA ligase**.
   6. **Complementary DNA (cDNA)**: researchers isolate the mRNA from a cell and use reverse transcriptase to create DNA from it. The DNA is then inserted into plasmids, forming a **cDNA library**.
   7. **Nucleic acid hybridization:** Using a short, singled-stranded nucleic acid, the **nucleic acid probe**, that can be either RNA or DNA and is labelled with a radioactive isotope or a florescent tag. The probe will hydrogen-bond to a specific sequence and can be used to search for certain genes in a genomic or cDNA library.
   8. Because bacterial cells do not have RNA-splicing machinery, cDNA genes are more useful when one is attempting to actually produce a protein product.
   9. Molecular biologists can avoid eukaryotic-bacterial incompatibility by using yeasts as hosts for cloning and/or expressing eukaryotic genes. Yeasts have plasmids, a rarity among eukaryotes. Also, scientists can make **yeast artificial chromosomes (YACs),** which combine the essentials of a eukaryotic chromosome—an origin of replication, a centromere, and two telomeres—with foreign DNA. YACs are much longer than plasmid vectors.
      1. Another reason to use eukaryotic host cells for expressing a cloned eukaryotic gene is that many eukaryotic proteins will not function unless they are modified after translation. Bacterial cells cannot carry out these modification.
   10. Ways of introducing recombinant DNA into eukaryotic cells:
      1. **Electroporation**: a brief electrical pulse applied to a solution containing cells creates temporary holes in their plasma membranes.
      2. Direct injection, using microscopically thin needles.
      3. Bacteria or viruses.
   11. **Polymerase chain reaction (PCR)**: a process that amplifies a specific target segment of DNA in a test tube. A three-step cycle produces an exponentially growing population of identical DNA molecules. First, heating separates the DNA strands, then cooling allows short, single-stranded DNA primers complementary to sequences on opposite strands at each end of the target sequence to bind to the DNA. The primers are then extended by a heat-stable DNA polymerase in the 5`→3` direction. PCR is faster and more specific than replication via organisms, but PCR has a higher rate of mutation.
      1. Despite that, PCR has been used to amplify DNA from: a 40,000-year-old frozen woolly mammoth, crime scenes, single embryonic cells, viral genes.

2. DNA TECHNOLOGY ALLOWS US TO STUDY THE SEQUENCE, EXPRESSION, AND FUNCTION OF A GENE.
   1. **Gel electrophoresis**:
      1. Uses a gel made of a polymer, such as a polysaccharide, as a molecular sieve to separate nucleic acids or proteins on the basis of size, electrical charge, and other physical properties.
      2. An electrical current pulls molecules one way or another.
      3. Smaller molecules can travel faster than larger ones.
   2. *Restriction fragment analysis*: DNA fragments produced by restriction enzyme digestion of a DNA molecule are sorted by gel electrophoresis, producing a characteristic band pattern. This provides a way to identify DNA molecules. Also, because DNA can be recovered undamaged from gels, the procedure also provides a way to prepare pure samples of individual fragments.
   3. **Southern blotting**: a method that combines gel electrophoresis and nucleic acid hybridization allows us to detect certain alleles by using a radioactive probe to seek out certain sequences of base pairs.
   4. *Dideoxyribonucleotide* (or *dideoxy*, for short) *chain termination method*: A method to sequence the order of certain genes.
      1. The DNA fragment is denatured into single strands and incubated in a test tube with the necessary ingredients for DNA synthesis.
      2. Synthesis of each new strand starts at the 3` end of the primer and continues until a dideoxyribonucleotide is inserted, at random, instead of the normal equivalent deoxyribonucleotide. This prevents further elongation of the strand. Eventually, a set of labeled strands of various lenghts is generated, with the color of the tag representing the last nucleotide in the sequence.
      3. The labeled strands in the mixture are separated by passage through a polyacrylamide gel. For DNA sequencing, the gel is formed in a capillary tube rather than a slab. The small size of the tube allows a fluorescence detector to sense the color of each fluorescent tag as the strands come through. Strands differing in length by as little as one nucleotide can be distinguished from each other.
   5. **Northern blotting:** Gel electrophoresis separates samples of mRNA from different sources. The samples are then transferred to a nitrocellulose membrane and then the important parts are labeled with radiative probes.
   6. **Reverse transcriptase-polymerase chain reaction (RT-PCR):** Reverse transcriptase makes cDNA from mRNA isolated from different sources. The cDNA serves as the source for PCR amplification using primers from the gene of interest. When the products are run on a gel, copies of the amplified region will be observed as bands only in the

samples that originally contained the gene of interest.

7. ***In situ* hybridization:** Labeled probes track down the location of specific mRNAs in the intact organism.
8. **DNA microarray assays**: A DNA microarray consists of tiny amounts of a large number of single-stranded DNA fragments representing different genes fixed to a glass slide in a tightly spaced array, or grid. mRNA is isolated from a cell and transcribed into cDNA, which is labeled with a fluorescent dye. The cDNA mixture is then applied to the array, where it binds to complementary sequences. Excess cDNA is rinsed off, and the microarray is canned for fluorescence, showing which genes are expressed.
9. ***In vitro* mutagenesis**: specific mutations are introduced into a cloned gene, and then the mutated gene is returned to a cell in such a way that it disables the normal cellular copies of the same gene. If the introduced mutations alter or destroy the function of the gene product, the phenotype of the mutant cell may help reveal the function of the missing normal protein.
10. A newer method for silencing expression of selected genes exploits the phenomenon of **RNA interference (RNAi).** This uses synthetic double-stranded RNA molecules matching the sequence of a particular gene to trigger breakdown of the gene's messenger RNA or to block its translation.

3. CLONING ORGANISMS MAY LEAD TO PRODUCTION OF STEM CELLS FOR RESEARCH AND OTHER APPLICATIONS

- **Stem cell**: a relatively unspecialized cell that can both reproduce itself indefinitely and differentiate into specialized cells of one or more types.
- **Embryonic stem cells** are isolated from the blastula stage. Can reproduce indefinitely and can differentiate into all types of cells.
- **Adult stem cells**: Are not able to give rise to all cell types in the organism, although they can generate multiple types.
- **Pluripotent**: the ability of a cell to differentiate into many different kinds of cells.

1. (Organismal) cloning produces one or more organisms genetically identical to the "parent" that donated the single cell.
2. In the 1950s, F. C. Steward and his students at Cornell University found that differentiated cells taken from the root of a carrot could grow into normal adult plants.
    1. Plant cloning is new used extensively in agriculture.
    2. **Totipotent**: the ability of a mature cell to dedifferentiate and then give rise to al the specialized cell types of an organism.
3. Differentiated cells from animals generally do not divide in culture, so early researchers had to use different methods.
    1. *Nuclear transplantation*: the removal of the nucleus from an egg cell and the replacement of that nucleus with a nucleus taken from a differentiated cell.
4. Such experiments were conducted on frogs by Robert Briggs and Thomas King in the 1950s and by John Gurdon in the 1970s. They found that the older the donor nucleus, the lower the percentage of normally developing tadpoles. They concluded that something in the nucleus *does* change as animal cells differentiate.
5. In 1997, Scottish researchers cloned a sheep (Dolly) by nuclear transplantation from a differentiated cell. They achieved the necessary dedifferentiation of donor nuclei by culturing mammary cells in nutrient-poor medium. Dolly's cells were not quite as healthy as those of a normal sheep, possibly reflecting incomplete reprogramming of the original transplanted nucleus.
6. Since 1997, researchers have cloned mice, cats, cows, horses, mules, pigs, and dogs.
    1. *Reproductive cloning*: cloning with the goal of producing new individuals.
7. Cloned animals do not always look or behave identically. For example, in a herd of cows cloned from the same line of cultured cells, certain cows are dominate in behavior and others are more submissive.
8. In the early 21st century, South Korean researchers reported cloning human embryos to the blastocyte stage, although they later retracted those statements.
9. Only a small percentage of cloned embryos develop normally to birth. Many cloned animals exhibit defects. Researchers have found that the DNA in embryonic cells from cloned embryos often as more methyl groups than does the DNA in equivalent cells from uncloned embryos of the same species. Because DNA methylation helps regulate gene expression, misplaced methyl groups in the DNA of donor nuclei may interfere with the pattern of gene expression necessary for normal embryonic development.
10. The major goal of cloning human embryos is not reproduction, but the production of stem cells for treating human diseases. The ultimate aim of stem cell research is to supply cells for the repair of damaged or diseased organs.
    1. In 2007, three research groups reported transforming mouse skin cells into ES cells, simply by causing the skin cells to express four "stem cell" master regulatory genes.

4. THE PRACTICAL APPLICATIONS OF DNA TECHNOLOGY AFFECT OUR LIVES IN MANY WAYS.

- *Genetic marker*: a DNA sequence that various in a population.
- *Polymorphisms*: Variations in DNA sequence.

1. Medical Applications:
    1. Diagnosis of Diseases:
        1. Because the sequence of the RNA genome of HIV is known, RT-PCR can be used to amplify and detect HIV RNA in blood or tissue samples.
        2. Medical scientists can now diagnose hundreds of human genetic disorders by using PCR with primers that target the genes associated with these disorders. These disorders include sickle-cell disease, hemophilia, cystic fibrosis, Huntington's disease, and Duchenne muscular dystrophy.
        3. For some genetic disorders, medical scientists can detect an abnormal disease-causing allele by testing for *genetic markers* that are known to be very close (linked) to the allele.
        4. The most useful genetic marker are single base-pair variations in the genomes of the human population. A **single nucleotide polymorphism** is a single base-pair site where variation is found in at least 1% of the population. SNPs occur on average about once in 100 to 300 base pairs in the human genome and are found in both coding and noncoding DNA sequences.
        5. A **restriction fragment length polymorphism** is a SNP that alters the sequence recognized by a restriction enzyme.
    2. **Gene Therapy**: introducing genes into an afflicted individual for therapeutic purposes. Several questions still remain:
        1. How can the activity of the gene be controlled so that cells make appropriate amounts of the gene product at the right time and in the right place?
        2. How can we be sure that the insertion of the therapeutic gene does not harm some other necessary cell function?
        3. The elimination of unwanted alleles from the gene pool could backfire.
        4. In France in 2000, ten young children with severe combined immunodeficiency (SCID) were treated with gene therapy. Nine of these patients showed significant, definitive improvement after two years. However, tree of these patients subsequently developed leukemia, and one of them died.
    3. **Pharmaceutical Products**:
        1. **Synthesis of Small Molecules for Use as Drugs**: An exciting recent development has been the synthesis of small molecules that are tailored to combat certain cancers by blocking the function of a protein crucial for the tumor cell's survival.
        2. **Protein Production in Cell Cultures**: Certain human genes are vectored into host cells and the products are used to treat some diseases. Sometimes, pathogen surface protein genes are vectored into harmless bacteria to make vaccines.
        3. Protein Production by "Pharm" Animals and Plants: Sometimes, instead of using cells in cultures, scientists use whole animals to create certain proteins. These proteins, however, may be modified differently after

- **Genetic profile**: a person's unique set of genetic markers.
- **Short tandem repeats (STRs)**: tandemly repeated units of 2- to 5-base sequences in specific regions of the genome.

translation, and thus must be screened carefully for allergic reactions. Scientists are also beginning to create "pharm" plants.

1. **Transgenic**: an animal that has genes from another animal, usually an animal of a different species.

2. Forensic Evidence and Genetic Profiles:
   1. In violent crimes, small amounts of DNA may be found in body fluids or small pieces of tissue left at the scene or on the clothes or other possessions of the victim or assailant.
      1. Tests that use antibodies require fairly fresh samples in relatively large amounts and cannot prove guilt, only innocence.
      2. DNA testing can identify the guilty individual with a high degree of certainty,
   2. Using STR analysis with 13 markers, the probability of two people having identical DNA profiles is somewhere between one chance in 10 billion and one in several trillion.
3. Environmental Cleanup
   1. Scientists have created bacteria that can extract heavy metals from their environments and incorporate the metals into compounds that are readily recoverable.
   2. Genetically engineered microbes may become important in both mining minerals and cleaning up highly toxic mining wastes.
   3. *Biofuels* from crops such as corn, soybeans, and cassava have been proposed as a supplement or even replacement for fossil fuels.
4. Agricultural Applications:
   1. Animal Husbandry: Scientists can transfer genes that will cause animals to develop larger muscles. However, problems such as low fertility or increased susceptibility to disease are not uncommon among transgenic animals.
   2. Genetic Engineering in Plants: Agricultural scientists have already endowed a number of crop plants with genes for desirable traits, including delayed ripening and resistance to spoilage and disease.
      1. The **Ti plasmid** transfers new genes (known as T DNA) into plants
      2. Genetic engineering is rapidly replacing traditional plant-breeding programs, especially for useful traits, such as herbicide or pest resistance, determined by one or a few genes.
      3. Genetic engineering also has great potential for improving the nutritional value of crop plants.
5. Safety and Ethical Questions Raised by DNA Technology:
   1. Early concerns about potential dangers associated with recombinant DNA technology focused on the possibility that hazardous new pathogens might be created.
   2. Today, the most public concern about possible hazards centers not on recombinant microbes but on **genetically modified (GM) organisms.**
   3. GM crops are widespread in the United States, Argentina, and Brazil.
   4. Some people fear that transgenic plants might pass their new genes to close relatives in nearby wild areas.

Chapter 21: Genomes and their Evolution

- **Genomics**: the study of whole sets of genes and their interactions
- **Bioinformatics**: the application of computational methods to the storage and analysis of biological data.
- **Linkage map**: A genetic map based on the frequencies of recombination between markers during crossing over of homologous chromosomes.
- **Physical map:** A genetic map based on the number of nucleotides between markers.
- **Proteomics**: Systematic study of the full protein sets (proteomes) encoded by genomes.

1. NEW APPROACHES HAVE ACCELERATED THE PACE OF GENOME SEQUENCING

1. **Human Genome Project**: In 1990, an international, publicly funded consortium of scientists at universities and research institutes organized 20 large sequencing centers in six countries plus a host of other labs working on small projects, all to sequence the human genome.
2. Even before the Human Genome Project, however, earlier researchers had sketched a rough picture of the organization of the genomes of many organisms:
    1. Karyotyping of many species revealed their chromosome numbers and banding patterns.
    2. Fluorescence *in situ* hybridization (FISH): fluorescently labeled probes are allowed to hybridize to an immobilized array of whole chromosomes.
3. From the above, they first constructed a **linkage map** and then a **physical map**.
4. Whereas a productive lab could typically sequence 1,000 base pairs a day in the 1980s, by the year 2000 each research center working on the Human Genome Project was sequencing 1,000 base pairs *per second*, 24 hours a day, seven days a week.
5. In 1992, emboldened by advances in sequencing and computer technology, molecular biologist J. Craig Venter devised an alternative approach to the sequencing of whole genomes: the *whole-genome shotgun approach*. It begins with the sequencing of random DNA fragments that are pieced together with powerful computer programs.
    1. In 1995, Venter reported the first complete genome sequence of an organism, the bacterium *Haemophilus influenzae*.
    2. In 1998, he set up a company, Celera Genomics, to sequence the human genome. Five years later, Celera Genomics and the public consortium jointly announced that sequencing of the human genome was largely complete, two years ahead of schedule.

2. SCIENTISTS USE BIOINFORMATICS TO ANALYZE GENOMES AND THEIR FUNCTIONS.

1. Government-funded agencies established databases and provided software with which scientists could analyse the sequence data.
2. These large, comprehensive websites are complemented by others maintained by individual or small groups of laboratories, which are often designed for a narrower purpose.
3. The National Center for Biotechnology Information (NCBI) database of sequences is called Genbank. As of August 2007, it included the sequences of 76 million fragments of genomic DNA, totalling 80 billion base pairs. The amount of data Genbank contains is estimated to double approximately every 18 months.
4. NCBI has many programs available to help scientists. One compares a DNA sequence with every sequence in Genbank to look for similar regions. Another compares predicted protein sequences. A third can search any protein sequence for common stretches of amino acids (domains) for which a function is known or suspected, and it can show a 3D model of the domain alongside other relevant information. There is even a software program that can compare a collection of sequences and diagram in the form of an evolutionary tree by on the sequence relationships.
5. Using available DNA sequences, geneticists can study genes directly, without having to infer genotype from phenotype. However, they must find a way to recognize as-yet unknown protein-coding genes and determine their function.
    1. Software is used to scan for start and stop signals, RNA-splicing sites, and other telltale signs of protein-coding genes. The software also looks for certain short sequences that correspond to sequences present in known mRNAs. Thousands of such sequences, called *expressed sequence tags*, or *ESTs*, have been collected from cDNA sequences.
6. The identities of about half the human genes were known before the Human Genome Project began.
7. Sometimes a newly identified sequence will match, at least partially, the sequence of a gene or protein whose function is well known.
8. One basic application of the systems biology approach is to define gene circuits and protein interaction networks.
    1. The Cancer Genome Atlas is an example of systems biology in which a large group of interacting genes and gene products are analyzed together. In a three-year pilot project running from 2007 to 2010, tree types of cancer—lung cancer, ovarian cancer, and glioblastoma of the brain—are being analyzed by comparing gene sequences and patterns of gene expression in cancer cells with those of normal cells.
9. Silicon and glass "chips" have already been developed that hold a microarray of most of the known human genes. Such chips are being used to analyze gene expression patterns in patients suffering from various cancers and other diseases.
10. Ultimately, every person may carry with their medical records a catalog of their DNA sequence, with regions highlighted that predispose them to specific diseases.

3. GENOMES VARY IN SIZE, NUMBER OF GENES, AND GENE DENSITY.

1. Genome size:

1. Comparing the three domains, we find a general difference in genome size between prokaryotes and eukaryotes. While there are some exceptions, most bacterial genomes have between 1 and 6 million base pairs (Mb). Eukaryotic genomes tend to be larger: most animals and plants have genomes of at least 100 Mb.
2. A comparison of genome sizes among eukaryotes fails to reveal any systematic relationship between genome size and the organism's phenotype.

2. Number of genes:

1. Bacteria and archaea, in general, have fewer genes that eukaryotes. Free-living bacteria and archaea have from 1,500 to 7,500 genes, while the number genes in eukaryotes ranges from about 5,000 for unicellular fungi to at least 40,000 for some multicellular eukaryotes.
2. At the outset of the Human Genome Prject, biologists expected somewhere between 50,000 to 100,000 genes to be identified in the completed sequence, based on the number of known human proteins. As the project progressed, the estimate was revised downward several times, and, as of 2007, the most reliable count places the number at 20,488.
3. Nearly all human genes contain multiple exons, and an estimated 75% of these multi-exon genes are spliced in at least two different ways.
4. Additional polypeptide diversity could result from post-translational modifications such as cleavage or addition of carbohydrate groups in different cell types or at different developmental stages.

3. Gene Density and Noncoding DNA:

1. Eukaryotes tend to have a lower gene density than prokaryotes. Among the genomes that have been sequenced completely thus far, humans and other mammals have the lowest gene density.
2. In all bacterial genomes studied so fair, most of the DNA consists of genes for protein, tRNA, or rRNA; the small amount of other DNA consists mainly of transcribed regulatory sequences, such as promoters.
3. Humans have 10,000 times as much noncoding DNA as bacteria.

4. MULTICELLULAR EUKARYOTES HAVE MUCH NONCODING DNA AND MULTIGENE FAMILIES

1. The bulk of most eukaryotic genomes consists of DNA sequences that neither code for proteins nor are transcribed to produce known RNAs (junk DNA). This DNA plays important roles in the cell.

2. 24% of the human genome is gene-related regulatory sequences and introns. 15% is unique noncoding DNA (gene fragments and pseudogenes).
3. 59% of DNA is made up of repetitive DNA, sequences that are present in multiple copies in the genome. This includes:
    1. Transposable elements and related sequences (44%)
        1. L1 sequences: 17%
        2. Alu elements: 10%
    2. Repetitive DNA unrelated to transposable elements (15%)
        1. Simple sequence DNA (3%)
        2. Large-segment duplications (5-6%)
4. **Transposable elements**: stretches of DNA that can move from one location to another within the genome. Both prokaryotes and eukaryotes have them.
    1. *Transposition*: the process in which a transposable element moves from one site in a cell's DNA to a different target site by a type of recombination process.
    2. The first evidence for wandering DNA segments came from American geneticist Barbara McClintock's breeding experiments with maize in the 1940s and 1950s.
5. There are two types of eukaryotic transposable elements:
    1. **Transposons**: move within the genome by means of a DNA intermediate. They can move by a "cut-and-paste" mechanism or by a "copy-and-paste" mechanism
    2. **Retrotransposons**: move by means of an RNA intermediate that is a transcript of the retrotransposon DNA. The RNA intermediate is converted back to DNA by reverse transcriptase. They always leave a copy at the original site. Most transposable elements in eukaryotic genomes are retrotransposons.
6. Multiple copies of transposable elements and sequences related to them are scattered throughout eukaryotic genomes. A single unit is usually hundreds to thousands of base pairs long, and the dispersed "copies" are similar but usually not identical to each other.
7. In humans and other primates, a large portion of transposable element-related DNA consists of a family of similar sequences called *Alu elements*, consisting of 10% of the human genome. *Alu* elements are about 300 nucleotides long, much shorter than most functional transposable elements, and they do not code for any protein; however, they are still transcribed into RNA.
8. An even larger percentage (17%) of the human genome is made up of a type of retrotransposon called *LINE-1,* or *L1*. These sequences are much longer than *Alu* elements—about 6,500 base pairs. L1 may help regulate gene expression and may have differential effects on gene expression in developing neurons, contributing to the great diversity of neuronal cell types.
9. Repetitive DNA that is not related to transposable elements probably arises due to mistakes during DNA replication or recombination. Such DNA accounts for about 15% of the human genome. About a third of this (5% of the human genome) consists of duplications of long stretches of DNA, with each unit ranging from 10,000 to 300,000 base pairs.
    1. **Simple sequence DNA** contains many copies of tandemly repeated short sequences. Repeated units may contain as many as 500 nucleotides, but often contains fewer than 15 nucleotides. When the unit contains 2 to 5 nucleotides, the series of repeats is called a **short tandem repeat**. Although, simple sequence DNA makes up 3% of the human genome.
    2. The nucleotide composition of simple sequence DNA is often different enough from the rest of the cell's DNA to have an intrinsically different density.
    3. Much of a genome's simple sequence DNA is located at chromosomal telomeres and centromeres, suggesting that this DNA plays a structural role for chromosomes.
    4. Centromeric DNA, along with simple sequence DNA located elsewhere, may also help organize the chromatin within the interphase nucleus.
10. **Genes and Multigene Families:**
    1. In the human genome and the genome of many other animals and plants, solitary genes make up less than half of the total transcribed DNA. The rest occurs in **multigene families**, collections of two or more identical or very similar genes.
    2. In multigene families that consist of *identical* DNA sequences, those sequences are usually clustered tandemly and, with the notable exception of the genes for histone proteins, have RNAs as their final products.
    3. The classic examples of multigene families of *nonidentical* genes are two related families of genes that encode globins, a group of proteins that include the α and β polypeptide subunits of hemoglobin.
    4. One copy of a duplicated gene can undergo alterations that lead to a completely new function for the protein product. The genes for lysozyme and α-lactalbumin are good examples.

5. DUPLICATION, REARRANGEMENT, AND MUTATION OF DNA CONTRIBUTE TO GENOME EVOLUTION

1. One aspect of evolution must have been an increase in the size of the genome, with the extra genetic material providing the raw material for gene diversification.
    1. An accident in meiosis can result in one or more sets of chromosomes, which could facilitate the evolution of genes in rare cases. One set of genes can provide essential functions for the organism. The genes in the one or more extra sets can diverge by accumulating mutations.
    2. Unequal crossing over during prophase I of meiosis can result in one chromosome with a deletion and another with a duplication of a particular gene.
    3. Slippage can occur during DNA replication, such that the template shifts with respect to the new complementary strand, and a part of the template strand is either skipped by the replication machinery or used twice as a template.
2. Sometime in the last 6 million years, the fusion of two ancestral chromosomes in the human line led to different haploid numbers for humans (n=23) and chimpanzees (n=24).
3. Large blocks of genes on the human chromosome 16 are found on four mouse chromosomes, indicating that the genes in each block stayed together during the evolution of the mouse and human linages.
4. Analysis of chromosomal breakage points associated with rearrangements showed that they were not randomly distributed, but that specific sites were used over and over again.
5. *Rearrangements of Parts of Genes: Exon Duplication and Exon Shuffling:*
    1. The presence of introns in most genes of multicellular eukaryotes may have promoted the evolution of new and potentially useful proteins by facilitating the duplication or repositioning of exons in the genome.
    2. A particular exon within a gene could be duplicated on one chromosome and deleted from the other.
    3. *Exon shuffling:* The occasional mixing and matching of different exons either within a gene or between two nonallelic genes owing to errors in meiotic recombination.
6. The persistence of transposable elements as a large fraction of some eukaryotic genomes is consistent with the idea that they play an important role in shaping a genome over evolutionary time. They can promote recombination, disrupt cellular genes or control elements, and carry entire genes or individual exons to new locations.
    1. Transposable elements of similar sequence facilitate recombination by providing homologous regions for crossing

over.

2. An *Alu* element may hop into an intron in a way that creates a weak alternative splice site in the RNA transcript.

6. COMPARING GENOME SEQUENCES PROVIDES CLUES TO EVOLUTION AND DEVELOPMENT.

1. The more similar in sequence the genes and genomes of two species are, the more closely related those species are in their evolutionary history.
    1. Particular genetic differences between two recently diverged species are usually responsible for the phenotypic differences between the species.
2. Analysing highly conserved genes in distantly related species can help clarify evolutionary relationships among species that diverged from each other long ago.
3. A third of human duplications are not present in the chimpanzee genome, and some of these duplications contain region associated with human diseases. There are more *Alu* elements in the human genome that in that of the chimpanzee, and the latter contains many copies of a retroviral provirus not present in humans.
4. To discover the basis for the phenotypic differences between the two species, biologists are studying specific genes and types of genes that differ between humans and chimpanzees and comparing them with their counterparts in other mammals, revealing a number of genes that are apparently evolving faster in the human than in either the chimpanzee or the mouse. Among them are genes involved in defence against malaria and tuberculosis and at least one gene that regulates brain size.
    1. One transcription factor whose gene shows evidence of rapid change in the human lineage is called FOXP2, which functions in vocalization in vertebrates.
5. Another exciting prospect that stems for our ability to analyse genomes is increasing our understanding of the spectrum of genetic variation in humans. Because the history of the human species is so short—about 200,000 years—the amount of DNA variation among humans is small compared to that of many other species.
6. Molecular analysis of the homeotic genes in *Drosophila* has show that they all include a 180-nucleotide sequence called a **homeobox,** which specifies a 60-amino-acid *homeodomain* in the encoded proteins. An identical or very similar nucleotide sequence has been discovered in the homeotic genes of many invertebrates and vertebrates. Researchers have discovered that the homeobox-encoded homeodomain is the part of a protein that binds to DNA when the protein functions as a transcriptional regulator. However, the shape of the homeodomain allows it to bind to any DNA segment; but itself it cannot select a specific sequence. Rather, other domains in a homeodomain-containing protein, ones that are more variable, determine which genes the protein regulates.
7. Developmental biologists have found that in addition to homeotic genes, many other genes involved in development are highly conserved from species to species.
8. Homeotic genes in animals were named *Hox* genes. Differing patterns of expression of the *Hox* genes along the body axis in insects and crustaceans can explain the variation in number of leg-bearing segments among segmented animals. Recent research suggests that the same *Hox* gene product may have subtly dissimilar effects in different species.
9. In both animals and plants, development relies on a cascade of transcriptional regulators turning on or turning off genes in a finely tuned series.
10. While quite a few of the master regulatory switches in *Drosophila* are homeobox-containing *Hox* genes, those in *Arabidopsis* belong to a completely different family of genes, called the *Mads-box* gene.

- Biologists in the field of evolutionary developmental biology (**evo-devo**) compare developmental processes of different multicellular organisms.

Chapter 22: Descent with Modification: A Darwinian View of Life

- **Evolution:**
  1. Descent with modification
  2. A change in the genetic composition of a population from generation to generation.
- **Strata**: superimposed layers of rock.

1. The Darwinian Revolution Challenged Traditional Views of a Young Earth Inhabited by Unchanging Species

1. Long before Darwin was born, several Greek philosophers suggested that life might have changed gradually over time.
   1. Aristotle (384-322 B.C.), however, viewed species as fixed. He thought that life-forms could be arranged on a ladder, or scale, of increasing complexity (*scala naturae*).
   2. These ideas coincided with the Old Testament account of creation, which holds that species were individually designed by God and therefore perfect.
   3. Carolus Linnaeus (1707-1778), a Swedish physician and botanist, sought to classify life's diversity "for the greater glory of God." Linnaeus adopted a nested classification system, grouping similar species into increasingly general categories.
   4. Darwin drew many of his ideas from the work of scientists studying **fossils**, the remains or traces or organisms from the past.
   5. **Paleontology**, the study of fossils, was largely developed by French scientist Georges Cuvier (1769-1832), who noted older fossils were less similar to current lifeforms than later fossils.
      1. Cuvier opposed evolution and instead advocated **catastrophism,** the principle that events in the past occurred suddenly and were caused by mechanisms different from those operating the present
   6. 1795: Scottish geologist James Hutton (1726-1797) proposed that Earth's geologic features could be explained by gradual mechanisms still operating. Charles Lyell (1797-1875) incorporated Hutton's thinking into his principle of **uniformitarianism,** which stated that mechanisms of change are constant over time.
   7. 18th century: Several naturalists suggested that live evolves as environments change.
      1. Lamarck published his hypothesis in 1809, the year Darwin was born. His theory had two principles: *use and disuse*, the idea that parts of the body that are used extensively become larger and stronger, while those that are not used deteriorate; *inheritance of acquired characteristics*, the idea that an organism could pass these modification s to its offspring. Lamarck also thought that evolution happens because organisms have an innate drive to become more complex.

- **Adaptations**: characteristics of organisms that enhance their survival and reproduction in specific environments.
- **Natural selection**: a process in which individuals with certain inheritance traits leave more offspring than individuals with other traits.
- **Artificial Selection**: the process of modifying other species of many generations by selecting and breeding individuals that possess desired traits.

2. Descent with Modification by Natural Selection Explains the Adaptations of Organisms and the Unity and Diversity of Life.

1. As the 19th century dawned, it was generally believed that species had remained unchanged since their creation.
2. Charles Darwin (1809-1882) was born in Shrewsbury in western England. Even as a boy, he had a consuming interest in nature; however, his father set him to medical school in Edinburgh. But Charles found medicine boring and surgery before the days of anaesthesia horrifying. He quit medical school and enrolled at Cambridge University, intending to become a clergyman.
3. At Cambridge, Darwin became the protégé of the Reverend John Henslow, a botany professor. Soon after Darwin graduated, Henslow recommended him to Captain Robert FitzRoy, who was preparing the survey ship HMS *Beagle* for a long voyage around the world.
4. Darwin embarked from England on the *Beagle* in December 1831. The primary mission of the voyage was to chart poorly known stretches of the South American coastline.
5. Darwin observed that the plants and animals in temperate regions of South America more closely resembled species living in the South American tropics than species living him temperate regions of Europe.
6. Darwin hypothesized that the Galápagos had been colonized by organisms that had strayed from South America and the diversified, giving rise to new species on the various islands.
7. In 1844, Darwin wrote a long essay on descent with modification and its underlying mechanism, natural selection. Yet he was still reluctant to publish his ideas, apparently because he anticipated the uproar they would cause.
8. In June 1858, Darwin received a manuscript from Alfred Russel Wallace (1823-1913), a British naturalist working in the East Indies who had developed a hypothesis of natural selection similar to Darwin's.
9. Lyell and a colleague presented Wallace's paper, along with extracts from Darwin's unpublished 1844 essay, to the Linnean Society of London on July 1, 1858. Darwin quickly finished his book, titled *On the Origin of Species by Means of Natural Selection* and published it next year.
10. Darwin perceived unity in life, which he attributed to the descent of all organisms from an ancestor that lived in the remote past.
11. Darwin described four observations of nature from which he drew two inferences:
    1. *Observation 1:* Members of a population often vary greatly in their traits
    2. *Observation 2:* Traits are inherited from parents to offspring.
    3. *Observation 3:* All species are capable of producing more offspring than their environment can support.
    4. *Observation 4:* Owing to lack of food or other resources, many of these offspring do not survive.
    5. *Inference 1:* Individuals whose inherited traits give them a higher probability of surviving and reproducing in a given environment tend to leave more offspring than other individuals.
    6. *Inference* 2: This unequal ability of individuals to survive and reproduce will lead to the accumulation of favorable traits in the population over generations.
12. Natural selection: A summary:
    1. Natural selection is a process in which individuals that have certain heritable characteristics survive and reproduce at a higher rate than other individuals.
    2. Over time, natural selection and increase the match between organisms and their environment.
    3. If an environment changes, or if individuals move to a new environment, natural selection may result in adaptation to these new conditions, sometimes giving rise to new species in the process.
    4. Individuals do not evolve; populations do.
    5. Natural selection can amplify or diminish only *heritable traits*.
    6. Environmental factors vary from place to place and over time. A trait that is favorable in one place or time may be useless—or even detrimental—in other places or times.

- **Homology**: Similarity in characteristics resulting from a shared ancestry.
- **Evolutionary tree**: diagram that reflects the evolutionary relationships among groups of organisms.

3. Evolution is Supported by an Overwhelming Amount of Scientific Evidence.

1. For many years, John Endler, of the University of California, Santa Barbara, has studied the impact of predators in guppies (*Poecilia reticulata*). He observed that among wild guppy populations in Trinidad, the male guppies' color patterns are so variable that no two males look alike. Female guppies are attracted to males with bright colors, but the bright colors that attract females also make the males more conspicuous to predators. When guppies are placed in an environment with predators, they tend to be more drab; when the guppies are relocated to an environment without predators, they are more colorful.
2. Natural selection is a process of editing rather than a creative mechanism. A drug does not *create* resistant pathogens; it *selects for* resistant individuals that were already present in the population.
3. The fossil record shows that past organisms differed from present-day organism and that many organisms have become extinct. It also documents the origins of major new groups of organisms. The fossil record can also be used to test evolutionary hypotheses arising from other kinds of evidence.
4. **Homologous structures**: Variations on a structural theme that was present in a common ancestor.
   1. **Vestigial structures**: remnants of features tat served important functions in the organism's ancestors.

5. **Convergent evolution**: the independent evolution of similar features in different lineages.
6. **Biogeography**: the geographic distribution of species
    1. **Continental drift**: the slow movement of Earth's continents over time. About 250 mya, all of Earth's landmasses were united in a single continent called **Pangaea**.
    2. Islands generally have many species of plants and animals that are **endemic—**not found anywhere else in the world.

Chapter 23: The Evolution of Populations

- **Microevolution**: change in allele frequencies in a population over generations.
- *Discrete characters*: characters that can be classified on an either-or basis.
- *Quantitative characters* vary along a continuum within a population.

- **Population**: a group of individuals of the same species that live in the same area and interbreed, producing fertile offspring.
- **Gene pool**: all the alleles for all the loci in all individuals in a population.
-

1. Mutation and sexual reproduction produce the genetic variation that makes evolution possible

1. Darwin had abundant evidence that life on Earth had evolved over time and he proposed that natural selection was the primary mechanism for evolution. He also emphasized the importance of heritable differences among individuals, but he could not explain precisely how organisms pass heritable traits to their offspring.
2. A few years after Darwin published *The Origin of Species*, Gregor Mendel wrote a groundbreaking paper, proposing his gene model of inheritance.
3. **Genetic Variation**:
   1. **Average heterozygosity*:*** the average percent of loci that are heterozygous.
   2. **Geographic variation**: Differences in the genetic composition of separate populations.
   3. **Cline**: a graded change in a character along a geographic axis
4. **Mutation**: a change in the nucleotide sequence of an organism's DNA.
   1. Point mutations can have a significant impact on genotype, but they generally are only slightly harmful or have no effect at all. A rare mutation may be beneficial.
   2. Chromosomal changes that delete, disrupt, or rearrange many loci at once are almost certain to be harmful.
   3. Duplications of large chromosome segments are often harmful, but the duplication of smaller pieces of DNA may not be.
   4. Mutation rates tend to be low in plants and animals, averaging about one mutation in every 100,000 genes per generation, and even lower in prokaryotes.
5. In organisms that reproduce sexually, most of the genetic variation in a population results from the unique combination of alleles that each individual receives. This is due to crossing over, independent assortment of chromosomes, and fertilization.

2. The Hardy-Weinberg equation can be used to test whether a population is evolving.

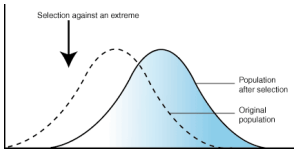
1. The **Hardy-Weinberg principle** states that the frequencies of alleles and genotypes in a population will remain constant from generation to generation, provided that only Mendelian segregation and recombination of alleles are at work. Such a gene pool is said to be in **Hardy-Weinberg equilibrium**.
2. **Conditions for Hardy-Weinberg equilibrium:**
   1. No mutations
   2. Random mating
   3. No natural selection
   4. Extremely large population size
   5. No gene flow
3. The Hardy-Weinberg equation: $p^2 + 2pq + q^2 = 1$ where p is the frequency of the dominate allele and q is the frequency of the recessive allele.

3. Natural selection, genetic drift, and gene flow can alter allele frequencies in a population.

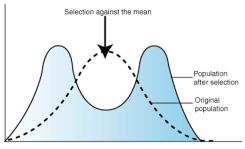
1. **Natural selection** results in alleles being passed to the next generation in proportions different from their proportions in the present generation. By consistently favoring some alleles over others, natural selection can cause *adaptive evolution*.
2. Genetic drift: Chance events can also cause allele frequencies to fluctuate unpredictably from one generation to the next, especially in small populations.
   1. **Founder effect**: When a few individuals become isolated from a larger population, this smaller group may establish a new population whose gene pool differs from the source population.
   2. **Bottleneck effect**: A sudden change in the environment may drastically reduce the size of a population. The survivors may have a different allele frequency than the original population due to chance.
3. **Effects of Genetic Drift: A Summary**
   1. Genetic drift is significant in small populations.
   2. Genetic drift can cause allele frequencies to change at random
   3. Genetic drift can lead to a loss of genetic variation within populations.
   4. Genetic drift can cause harmful alleles to become fixed.
4. **Gene flow**: the transfer of alleles into or out of a population due to the movement of fertile individuals or their gametes.

4. Natural selection is the only mechanism that consistently causes adaptive evolution.

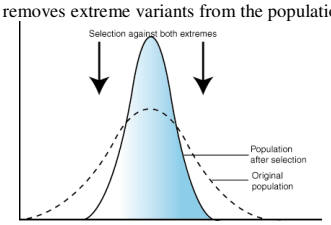
1. **Relative fitness:** the contribution an individual makes to the gene pool of the next generation, *relative to* the contributions of other individuals.
2. Natural selection can alter the frequency distribution of heritable traits in three ways, depending on which phenotypes in a population are favored.
   1. **Directional selection** shifts the overall makeup of the population by favoring variants that are at one extreme of the distribution.



   2. **Disruptive selection** favors variants at both ends of the distribution.



3. **Stabilizing selection** removes extreme variants from the population and preserves intermediate types.



3. **Sexual selection**: individuals with certain inherited characteristics are more likely than other individuals to obtain mates.

1. **Sexual dimorphism**: marked differences between the two sexes in secondary sexual characteristics.

2. **Intrasexual selection**: Selection within the same sex—individuals of one sex compete directly for makes of the opposite sex.

3. **Intersexual selection** (*mate choice*): individuals of one sex (usually the females) are choosy in selecting their mates from the other sex.

4. **The Preservation of Genetic Variation**

1. **Balancing selection**: natural selection maintains two or more forms in a population.

2. **Heterozygote advantage**: heterozygotes are more fit than the homozygotes.

3. **Frequency-dependent selection**: the fitness of a phenotype declines if it becomes too common in the population.

4. **Neutral variation**: Many of the nucleotide differences in noncoding sequences appear to confer no selection advantage or disadvantage.

5. **Why natural selection cannot fashion perfect organisms**:

1. Selection can act only on existing phenotypes.
2. Evolution is limited by historical constraints.
3. Adaptations are often compromises
4. Chance, natural selection, and the environment interact.

- **Speciation**: the process by which one species splits into two or more species.
- **Microevolution**: changes over time in allele frequencies in a population.
- **Macroevolution**: the broad pattern of evolution over long time spans.

1. The biological species concept emphasizes reproductive isolation

1. The word *species* is Latin for "kind" or "appearance". But are organisms truly divided into the discrete units we call species, or is this classification an arbitrary attempt to impose order on the natural world?
2. The primary definition of species used in this textbook is referred to as the **biological species concept**. According to this concept, a **species** is a group of populations whose members have the potential to interbreed in nature and produce viable, fertile offspring—but do not produce viable, fertile offspring with members of other such groups.
3. Gene flow has the potential to hold the gene pool of a species together, so long as it is not outweighed by effects of selection or drift.
4. The biological species concept does not apply to organisms that reproduce asexually all or most of the time, such as prokaryotes.
5. The formation of new species hinges on **reproductive isolation—**the existence of biological factors (barriers) that impede members of two species from producing viable, fertile offspring. Such barriers block gene flow between the species and limit the formation of **hybrids**, offspring that result from an interspecific mating.
    1. **Prezygotic barriers** block fertilization from occurring by impeding members of different species from attempting to mate by separating them spatially, temporally, or via behavior quirks; by preventing an attempted mating from being completed successfully; or by hindering fertilization if mating is completed successfully.
    2. **Postzygotic barriers** contribute to reproductive isolation after the hybrid zygote is formed. Hybrids may fail to complete development, be frail or sterile, or fail to produce viable and fertile offspring after mating with either of the parent species.
6. Other definitions of species:
    1. The **morphological species concept** characterizes a species by body shape and other structural features.
    2. The **ecological species concept** views a species in terms of its ecological niche, the sum of how members of the species interact with the nonliving and living parts of their environment.
    3. The **phylogenetic species concept** defines a species as the smallest group of individuals that share a common ancestor, forming one branch on the tree of life.

2. Speciation can take place with or without geographic isolation.

1. In **allopatric speciation**, gene flow is interrupted when a population is divided into geographically isolated subpopulations. Different mutations arise, natural selection acts on the separated organisms, and genetic drifts alters allele frequencies. Reproductive isolation may the arise as a by-product of selection or drift having caused the populations to diverge genetically.
    1. The importance of allopatric speciation is suggested by the fact that regions that are highly subdivided by geographic barriers typically have more species than do regions with fewer barriers.
2. In **sympatric speciation**, speciation occurs in populations that live in the same geographic area. Although such contact makes sympatric speciation less common than allopatric speciation, sympatric speciation can occur if gene flow is reduced by such factors as polyploidy, habitat differentiation, and sexual selection.
    1. A species may originate from an accident during cell division that results in extra sets of chromosomes, a condition called **polyploidy**. There are two distinct forms of polyploidy. An **autopolyploid** is an individual that has more than two chromosome sets that are all derived from a single species. A second form of polyploidy can occur when two different species interbreed and produce hybrid offspring. Various mechanisms can change a sterile hybrid into a fertile polyploid called an **allopolyploid**.
    2. Sympatric speciation can also occur when genetic factors enable a subpopulation to exploit a habitat or resource not used by the parent population.
    3. There is evidence that sympatric speciation can also be driven by sexual selection. Breeding *Pundamilia pundamilia* males have a blue-tinged back, whereas breeding *Pundamilia nyererei* males have a red-tinged back. Mate choice based on male breeding coloration is the main reproductive barrier that normally keeps the gene pools of these two species separate.

3. Hybrid zones provide opportunities to study factors that cause reproductive isolation.

1. What happens if allopatric populations come back into contact with one another? One possible outcome is the formation of a **hybrid zone**. Some hybrid zones form as narrow bands. Other hybrid zones have more complicated spatial patterns.
2. There are three possible outcomes for the hybrid zone over time. Reproductive barriers between species may be strengthened over time (limiting the formation of hybrids) or weakened over time (causing the two species to fuse into a single species). Or hybrid may continue to be produced, creating a long-term, stable hybrid zone.
    1. When hybrids are less fit than members of their parent species, we might expect natural selection to strengthen prezygotic barriers to reproduction, thus reducing the formation of unfit hybrids. Because this process involves *reinforcing* reproductive barriers, it is called **reinforcement**.
    2. Next, let's consider the case in which two species contact one another in a hybrid zone, but the barriers to reproduction are not strong. So much gene glow may occur that reproductive barriers weaken further and the gene pools of the two species become increasingly alike. In effect, the speciation process reverses, eventually causing the two hybridizing species to fuse into a single species.
    3. Many hybrid zones are stable in the sense that hybrids continue to be produced—a result you might no expect.

4. Speciation can occur rapidly or slowly and can result from changes in few or many genes.

1. The fossil record includes many episodes in which new species appear suddenly in a geologic stratum, persist essentially unchanged through several strata, and then disappear. Paleontologists Niles Eldredge, of the American Museum of Natural History, and Stephen Jay Gould (1941-2002), of Harvard University, coined the term **punctuated equilibria** to describe these periods of apparent stasis punctuated by sudden change.
2. The punctuated pattern suggests that once the process begins, speciation can be completed relatively rapidly—a suggestion confirmed by a growing number of studies. The interval between speciation events ranged from 4,000 years (in cichlids of Lake Nabugabo, Uganda) to 40 million years (in some beetles).
3. Studies of ongoing speciation (as in hybrid zones) can reveal traits that cause reproductive isolation.
4.

- **Protobionts:** collections of abiotically produced molecules surrounded by a membrane-like structure.

I. CONDITIONS ON EARLY EARTH MADE THE ORIGIN OF LIFE POSSIBLE.

1. Chemical and physical processes on early Earth, aided by the emerging force of natural selection, could have produced very simple cells through a sequence of four main stages:
    1. The abiotic synthesis of small organic molecules, such as amino acids and nucleotides.
    2. The joining of these small molecules into macromolecules, including proteins and nucleic acids.
    3. The packaging of these molecules into "protobionts."
    4. The origin of self-replicating molecules eventually made inheritance possible.
2. Earth and the other planets of the solar system formed about 4.6 billion years ago, condensing from a vast cloud of dust and rocks that surrounded the young sun. For the first few hundred million years, life probably could not have originated or survived on Earth because the planet was still being bombarded by huge chunks of rock and ice left over from the formation of the solar system. The collisions generated enough heat to vaporize the available water and prevent seas from forming. This phase likely ended about 3.9 billion years ago.
3. As the bombardment of early Earth slowed, conditions on the planet were extremely different from those of today. The first atmosphere was probably thick with water vapor, along with various compounds released by volcanic eruptions, including nitrogen and its oxides, carbon dioxide, methane, ammonia, hydrogen, and hydrogen sulfide. As Earth cooled, the water vapor condensed into oceans, and much of the hydrogen quickly escaped into space.
4. Early 1920s: Russian chemist A. I. Oparin and British scientist J. B. S. Haldane independently hypothesized that Earth's early atmosphere was probably a reducing environment, in which organic compounds could have formed from simple molecules. The energy for this organic synthesis could have come from lightning and intense UV radiation. Haldane suggested that the early oceans were a solution of organic molecules, a "primitive soup" from which life arose.
5. 1953: Stanley Miller and Harold Urey, of the University of Chicago, tested the Oparin-Haldane hypothesis by creating laboratory conditions comparable to those that scientists at the time through existed on early Earth. Their apparatus yielded a variety of amino acids found in organisms, today, along with other organic compounds. However, the early atmosphere was made up of mostly nitrogen and carbon dioxide and thus was neither reducing nor oxidizing. Small pockets of air near volcanoes are reducing, however. Perhaps instead of forming in the atmosphere, the firs organic compounds formed near submerged volcanoes, where hot water and minerals gush into the ocean from Earth's interior.
6. Miller-Urey-type experiments demonstrate that the abiotic synthesis of organic molecules is possible. Fragments of a 4.5 bya carbonaceous chondrite (a type of meteorite) found in Australia in 1969 contain more than 80 amino acids, some in large amounts.
7. By dripping solutions of amino acids onto hot sand, clay, or rock, researchers have been able to produce amino acid polymers. The polymers formed spontaneously, without the help of enzymes or ribsomes. But unlike proteins, these polymers are a complex mix of linked and cross-linked amino acids.
8. Two key properties of life are accurate replication and metabolism. While Miller-Urey-type experiments have yielded some of the nitrogenous bases of DNA and RNA, they have not produced anything like nucleotides. The necessary conditions to produce nucleotides may have been met by **protobionts**. Laboratory experiments demonstrate that protobionts could have formed spontaneously. For example, certain small membrane-bounded droplets called liposomes can form when lipids or other organic molecules are added to water. Liposomes can "reproduce," and because their bilayer is selectively permeable, liposomes undergo osmotic swelling or shrinking when placed in solutions of different solute concentrations.
9. The first genetic material was most likely RNA, not DNA. Thomas Cech, of the University of Colorado, and Sidney Altman, of Yale University, found that RNA can carry out a number of enzyme-like catalytic functions. Cech called these RNA catalysts **ribozymes**. Natural selection on the molecular level has produced ribozymes capable of self-replication in the laboratory, because single-stranded RNA molecules assume a variety of specific 3D shapes mandated by their nucleotide sequences.
10. A protobiont with self-replicating, catalytic RNA would differ from its many neighbors that did not carry RNA or that carried RNA without such capabilities. If that protobiont could grow, split, and pass its RNA molecules to its daughters, the daughters would have some of the properties of their parent.
11. Once RNA sequences that carried genetic information appears in protobionts, many further changes would have been possible. For example, RNA could have provided the template on which DNA nucleotides were assembled. Double-stranded DNA is a much more stable repository for genetic information than the more fragile single-stranded RNA.

II. THE FOSSIL RECORD DOCUMENTS THE HISTORY OF LIFE.

- **Stromatolites**: layered rocks that form when certain prokaryotes bind thin films of sediment together.

1. **The Fossil Record** shows that there have been great changes in the kinds of organisms that dominated life on Earth at different points in time. As substantial and significant as the fossil record is, it is an incomplete chronicle of evolutionary change. Many of Earth's organisms did not die in the right place at the right time to be preserved as fossils, and geologic processes destroyed many of the fossils that were formed.

2. **How Rocks and Fossils Are Dated**:
1. The order the fossils in rock strata tells us the relative ages of the fossils.
2. **Radiometric dating** is based on the decay of radioactive isotopes.

3. **The Origin of New Groups of Organisms**:
1. Tetrapods have four limbs
    1. Mammals have a lower jaw that is composed of only one bone, three bones in the middle ear to transmit sound, and differentiated teeth.

III. KEY EVENTS IN LIFE'S HISTORY INCLUDE THE ORIGINS OF SINGLED-CELLED AND MULTICELLED ORGANISMS AND THE COLONIZATION OF LAND.

1. The study of fossils has helped geologists establish a **geologic record**.
2. The first two eons—the Archaean and the Proterozoic—together lasted approximately 4 billion years. The Phanerozoic eon, roughly the last half billion years, encompasses most of the time that multicellular eukaryotic life has existed on Earth. It is divided into three eras: the Paleozoic, Mesozoic, and Cenozoic. The boundaries between the eras correspond to major extinction events seen in the fossil record.

3. **The First Single-Celled Organisms**:
1. Earliest single-celled prokaryotes appeared about 3.5-3.9 bya.
2. The amount of atmospheric O_2 increased gradually from about 2.7 to 2.2 bya, but then shot up relatively rapidly to more than 10% of its present level, causing the first mass extinction.
3. The oldest widely accepted fossils of eukaryotic organisms are about 2.1 bya. **Endosymbiosis** posits that mitochondria and plastids were formerly small prokaryotes that began living within larger cells. The model of **serial endosymbiosis** supposes that mitochondria evolved before plastids through a sequence of endosymbiotic events.

4. **The Origin of Multicellularity**:
1. The common ancestor of multicellular eukaryotes lived 1.5 bya.
2. Geological evidence indicates that a series of severe ice ages occurred from 750 -580 mya, confining life to areas near deep-sea vents, hot springs, or equatorial regions.

- **Continental drift**: the movement of earth's continental plates.
- **Pangaea**: a supercontinent that existed 250 mya.
- **Adaptive radiations**: periods of evolutionary change in which groups of organisms form many new species whose adaptations allow them to fill different niches.

3. Larger and more diverse multicellular eukaryotes do not appear in the fossil record until about 565 mya.
4. Many phyla of living animals appear suddenly in fossils formed early in the Cambrian period (535-525 mya), a phenomenon referred to as the **Cambrian explosion**.
5. Fungi, plants and animals did not begin to colonize land until about 500 mya.

4. The Rise and Fall of Dominate Groups Reflect Continental Drift, Mass Extinctions, and Adaptive Radiations.
   1. The Permian mass extinction, which defines the boundary between the Paleozoic and Mesozoic eras (251 may), claimed about 96% of marine animal species and drastically altered life in the ocean. Enormous volcanic eruptions in what is now Siberia covered an area of 1.6 million km^2 with a layer of lava hundreds to thousands of meters thick. The eruptions may have produced enough carbon dioxide to warm the global climate by an estimated 6°C.
   2. The Cretaceous mass extinction occurred about 65.5 mya and marks the boundary between the Mesozoic and Cenozoic eras. Walter Alvarez and the late Luis Alvarez, of the University of California, Berkley, and their colleagues proposed that the extinction happened because an asteroid or large comet collided with Earth, causing a huge cloud of debris to billow into the atmosphere. Research has foxed on the Chicxulub crater, a 65 mya scar beneath sediments off the Yucatán coast of Mexico. About 180 km in diameter, the crater is the right size to have been caused by an object with a diameter of 10 km.
   3. The fossil record shoes that it typically takes 5-10 million years for the diversity of life to recover to previous levels after a mass extinction.
5. Major Changes in Body form Can Result from Changes in the Sequences and Regulation of Developmental Genes.
   1. Many striking evolutionary transformations are the result of **heterochrony**, an evolutionary change in the rate or timing of developmental events. If reproductive-organ development accelerates compared to other organs, the sexually mature stage of a species may retain body features that were juvenile structures in an ancestral species—a condition called **paedomorphosis**.
   2. Substantial evolutionary changes can also result from alterations in genes that control the placement and spatial organization of body parts.
   3. Changes in *Hox* genes or in how they are expressed can have a profound impact on morphology. Two duplications of *Hox* genes have occurred in the vertebrate lineage, and all vertebrate genomes tested to date have both of these duplications.
   4. New developmental genes arising after gene duplication events very likely facilitated the origin of new morphological forms.
   5. Changes in the form of organisms often may be caused by mutations that affect the regulation of developmental genes—not their sequence.
6. Evolution is Not Goal Oriented.
   1. Evolution is like tinkering—a process in which new forms arise by the the slight modification of existing forms.
   2. Complex structures have evolved in increments from simpler versions that performed the same basic function.
   3. Evolutionary novelties can also arise when structures that originally played one role gradually acquire a different one.
   4.

- **Phylogeny**: the evolutionary history of a species or group of species.
- **Systematics**: a discipline focused on classifying organisms and determining their evolutionary relationships.
- **Taxonomy**: A scientific discipline concerned with naming and classifying the diverse forms of life.
-

1. Phylogenies show evolutionary relationships
    1. To avoid ambiguity when communicating about their research, biologists refer to organisms by Latin scientific names. The two-part format of the scientific name, commonly called a **binomial**, was instituted in the 18th century by Carolus Linnaeus. The first part is the genus name, the second part is the species name.
    2. The taxonomic system named after Linnaeus, the Linnaean system, places related genera in the same **family**, families into **orders**, orders into **classes**, classes into **phyla**, phyla into **kingdoms**, and kingdoms into **domains**. The placement of species may not reflect their evolutionary history.
    3. The evolutionary history of a group of organisms can be represented in a branching diagram called a **phylogenetic tree**.
        1. **PhyloCode** only names groups that include a common ancestor and all of its descendants (clades).
        2. A phylogenetic tree represents a hypothesis about evolutionary relationships. These relationships often are depicted as a series of dichotomies ,or two-way **branch points**.
        3. **Sister taxa** share an immediate common ancestor and are each other's closest relatives. A **polytomy** is a branch point from which more than two descendant groups emerge.
2. Shared characters are used to constructed phylogenetic trees.
    1. A potential red herring in constructing a phylogeny is similarity due to convergent evolution—called **analogy—**rather than to shared ancestry (homology). Distinguishing between homology and analogy is critical in reconstructing phylogenies. Analogous structures that arose independently are also called **homoplasies**.
    2. **Molecular systematics** is the use of DNA and other molecular data to study evolutionary relationships.
3. Phylogenies are inferred from morphological and molecular data.
    1. **Cladistics**: common ancestry is the primary criterion used to classify organisms into **clades**, a group of species that includes an ancestral species and all of its descendants. Clades are **monophyletic**. **Paraphyletic** groups consists of an ancestral species and some, but not all, of its descendants. **Polyphyletic** groups consists of taxa with different ancestors.
    2. A **shared ancestral character** is a character that originated in an ancestor of the taxon. A **shared derived character** is an evolutionary novelty unique to a particular clade.
    3. An **outgroup** is a species or group of species from an evolutionary linage that is known to have diverged before the lineage that includes the species we are studying (the **ingroup**).
    4. In some phylogenetic tree diagrams, branch lenghts are proportional to the amount of evolutionary change or to the times at which particular events occurred.
    5. According to the principle of **maximum parsimony**, we should first investigate the simplest explanation that is consistent with the facts.
    6. The principle of **maximum likelihood** states that give certain rules about how DNA changes over time, a tree can be found that reflects the most likely sequence of evolutionary events.
    7. In an approach known as **phylogenetic bracketing**, we can predict (by parsimony) that features shared two groups of closely related organisms are present in their common ancestor and all of its descendants, unless independent data indicate otherwise.
4. An organism's evolutionary history is documented in its genome.
    1. Molecular techniques allow us to trace the phylogenies of gene duplications and the influence of these duplications on genome evolution. **Orthologous genes** are homologous genes that are found in different species because of speciation. **Paralogous genes** result from gene duplication, so they are found in more than one copy in the same genome.
    2. Ninety-nine percent of the genes of humans and mice are detectably orthologous, and 50% of our genes are orthologous with those of yeast.
5. Molecular clocks help tract evolutionary time.
    1. A **molecular clock** assumes that the number of nucleotide substitutions in orthologous genes is proportional to the time that has elapsed since the species branched from their common ancestor.
    2. In the 1960s, Jack King and Thomas Jukes, at the University of California, Berkley, and Motoo Kimura, at the Japanese National Institute of Genetics, published papers supporting **neutral theory—**that much evolutionary change in genes and proteins has no effect on fitness and therefore is not influenced by Darwinian selection.
    3. However, molecular clocks do not run as smoothly as neutral theory predicts. Many irregularities are likely to be the result of natural selection in which certain DNA changes are favored over others.
6. New information continues to revise our understanding of the tree of life.
    1. Early taxonomists classified all known species into two kingdoms: plants and animals. They placed bacteria in with plants because both had a cell wall. Eukaryotic unicellular organisms with chloroplasts and fungi were also considered plants. Unicellular organisms that move and ingest food—protozoans--were classified as animals.
    2. Taxonomic schemes with more than two kingdoms did not gain broad acceptance until the late 1960s, when many biologists recognized five kingdoms: Monera (prokaryotes), Protista, Plantae, Fungi, and Animalia.
    3. Biologists later developed a three-domain structure: Bacteria, Archaea, and Eukarya.
        1. Bacteria contains most of the currently known prokaryotes.
        2. Archaea consists of a diverse group of prokaryotic organisms that inhabit a wide variety of environments.
        3. Eukarya consists of all the organisms that have cells containing true nuclei.
    4. The three-domain structure highlights the fact that much of the history of life has been about single-celled organisms.
    5. **Horizontal gene transfer** is a process in which genes are transferred from one genome to another through mechanisms such as exchange of transposable elements and plasmids, viral infection, and perhaps fusions of organisms. Because phylogenetic trees are based on the assumption that genes are passed vertically from one generation to the next, the occurrence of such horizontal transfer events helps to explain why universal trees built using different genes can give inconsistent results.
    6. Some scientists have argued that horizontal gene transfers were so common that the early history of life should be represented as a tangled network of connected branches. Others have suggested that relationships among early organisms are best represented by a ring.

1. STRUCTURAL AND FUNCTIONAL ADAPTATIONS CONTRIBUTE TO PROKARYOTIC SUCCESS.
    1. The first organisms to inhabit Earth are thought to have been prokaryotes.
    2. Prokaryotic cells typically have diameters in the range of 0.5-5 µm, much smaller than the 10-100 µm diameter of many eukaryotic cells.
    3. Most bacterial cell walls contain **peptidoglycan**, a network of modified-sugar polymers crosslinked by short polypeptides.
    4. The **Gram stain**, developed by 19th century Danish physician Hans Christian Gram, separates bacteria into two categories: **Gram positive,** which have simpler walls with a relatively large amount of peptidoglycan and **Gram-negative**, which have a more complex wall containing a smaller amount of peptidoglycan covered by an outer membrane that contains lipopolysaccharides. The lipid portions of the lipopolysaccharides in the walls of many gram-negative bacteria are toxic, causing fever or shock.
    5. The cell wall of many prokaryotes is covered by a **capsule**, a sticky layer of polysaccharide or protein. Some prokaryotes stick to their substrate or to one another by means of hair-like protein appendages called **fimbriae**.
    6. **Sex pili**: appendages that pull two cells together prior to DNA transfer from one cell to the other.
    7. Some prokaryotes call move at velocities exceeding 50 µm/sec—up to 50 times their body length per second.
    8. Flagella may be scattered over the entire surface of the cell or concentrated at one or both ends. Prokaryotic flagella are one-tenth the width of eukaryotic flagella and are not covered by an extension of the plasma membrane.
    9. Many prokaryotes exhibit **taxis**, movement toward or away from a stimulus.
    10. The cells of prokaryotes are simpler than those of eukaryotes, in both their internal structure and their genomic organization. Some prokaryotic cells do have specialized membranes that perform metabolic functions. These membranes are usually infoldings of the plasma membrane. The chromosome is located in a **nucleoid region**. A typical prokaryotic cell may also have much smaller rings of separately replicating DNA called **plasmids**, most carrying only a few genes.
    11. Certain bacteria form resistant cells called **endospores** when an essential nutrient is lacking.
2. RAPID REPRODUCTION, MUTATION, AND GENETIC RECOMBINATION PROMOTE GENETIC DIVERSITY IN PROKAYROTES.
    1. Three factors give rise to high levels of genetic diversity in prokayrotes: rapid reproduction, mutation, and genetic variation.
    2. Prokaryotic populations have large amounts of genetic variation as a result of rapid reproduction and mutation.
    3. New mutations, although individually rare, can greatly increase genetic diversity in species like *E. coli* that have short generation times and large population size. This diversity, in turn, can lead to rapid evolution.
    4. Additional diversity arises from genetic recombination. Three processes—transformation, transduction, and conjugation—can bring together prokaryotic DNA from different individuals.
        1. In **transformation**, the genotype and possibly phenotype of a prokaryotic cell are altered by the uptake of foreign DNA from its surroundings.
        2. In **transduction**, phages carry bacterial genes from one host cell to another; transduction is a type of horizontal gene transfer.
        3. In **conjugation**, genetic material transferred from one bacterial cell to another when they are temporarily joined. The donor uses sex pili to attach to the recipient. The ability to form sex pili and donate DNA during conjugation results from the presence of a particular piece of DNA called the **F factor**. The F factor can exist either as a plasmid or as a segment of DNA within the bacterial chromosome.
            1. The F factor in its plasmid form is called the **F plasmid**.
            2. A cell with the F factor built into its chromosome is called an *Hfr* cell.
3. DIVERSE NUTRITIONAL AND METABOLIC ADAPTATIONS HAVE EVOLVED IN PROKARYOTES.
    1. Organisms that obtain energy from light are called *phorotrophs*, and those that obtain energy from chemical source called *chemotrophs*. Organisms that need only an inorganic compound such as CO_2 as a carbon source are called *autotrophs. Heterotrophs* require at least one organic nutrient to make other organic compounds.
    2. Four major modes of nutrition:
        1. **Photoautotrophs:** photosynthetic organisms that capture light energy and us it to drive the synthesis of organic compounds from inorganic carbon compounds. Cyanobacteria and many other groups of prokaryotes are photoautotrophs, as are plants and algae.
        2. **Chemoautotrophs** also need only an inorganic compound as a carbon source. However, instead of using light as an energy source, they oxidize inorganic substances. Unique to certain prokaryotes.
        3. **Photoheterotrophs** harness energy from light but must obtain carbon in organic form. Unique to certain marine and halophilic prokaryotes.
        4. **Chemoheterotrophs** must consume organic molecules to obtain both energy and carbon. Widespread among prokaryotes. Fungi, animals, most protists, and even some parasitic plants are also chemoheterotrophs.
    3. **Obligate aerobes** use O_2 for cellular respiration and cannot grow without it. **Obligate anaerobes** are poisoned by O_2. Some obligate anaerobes live exclusively by fermentation; others extract chemical energy by **anaerobic respiration. Facultative anaerobes** use O_2 if it is present by can also carry out anaerobic respiration or fermentation in an anaerobic environment.
    4. Prokaryotes can metabolize nitrogen in a wide variety of forms. Some cyanobacteria and some methanogens convert atmospheric nitrogen to ammonia, a process called **nitrogen fixation**.
    5. Cooperation between prokaryotes allows them to use environmental resources they could not use as individual cells. For instance, the cyanobacterium *Anabaena* has genes that encode proteins for photosynthesis and for nitrogen fixation, but a single cell cannot carry out both processes at the same time. *Anaerobe* forms filamentous colonies. Most cells in a filament carry out only photosynthesis, while a few specialized cells called **heterocytes** carry out only nitrogen fixation.
    6. Metabolic cooperation between different prokaryotic species often occurs in surface-coating colonies known as **biofilms**.
4. MOLECULAR SYSTEMATICS IS ILLUMINATING PROKARYOTIC PHYLOGENY.
    1. Until the late 20th century, systematics based prokaryotic taxonomy on phenotypic criteria. Apply molecular systematics to the investigation of prokaryotic phylogeny has led to some dramatic conclusions.
    2. A single handful of soil could contain 10,000 prokaryotic species.
    3. Horizontal gene transfer obscures the location of the root of the tree of life.
    4. **Archaea** share certain traits with bacteria and others with eukaryotes. The first prokaryotes assigned to domain Archaea live in environments so extreme that few other organisms can survive there. Such organisms are called **extremophiles. Extreme halophiles** live in highly saline environments. **Extreme thermophiles** thrive in very hot environments.
        1. **Methanogens:** a group of archaea named for the unique way they obtain energy: They use CO_2 to oxidize H_2, releasing methane as a waste product. Methanogens are poisoned by O2. Although some methanogens live in extreme environments, others live in swamps and marshes where other microorganisms have consumed all the O_2.
        2. Many extreme halophiles and all known methanogens are archaea in the clade Euryarchaeota. The euryarchaeotes

- **Anaerobic respiration**: The use of inorganic molecules other than oxygen to accept elections at the "downhill" end of election transport chains.

also include some extreme thermophiles, though most thermophilic species belong to a second clade, Crenarchaeota. Recently, genetic prospecting has revealed many species of euryarchaeotes and crenarchaeotes that are not extremophiles. These archaea exist in habitats ranging from farm soils to lake sediments to the surface waters of the open ocean.

3. 1966: researchers discovered a new clade, Korarchaeota. 2002: researchers found extremely tiny archaeal cells (0.4 µm in diameter) attached to much larger crenarchaeote. They placed this archaea into a new clade, Nanoarchaeota.

5. **Bacteria** include the vast majority of prokaryotes that most people are aware of. Every major mode of nutrition and metabolism is represented among bacteria.

1. **Proteobacteria**: a large and diverse clade of gram-negative bacteria that includes photoautotrophs, chemoautotrophs, and heterotrophs.

1. **Alpha proteobacteria**: Many species are closely associated with eukaryotic hosts.

2. **Beta proteobacteria**: This nutritional diverse subgroup contains *Nitrosomonas*, a genus of soil bacteria that play an important role in nitrogen recycling by oxidizing ammonium (NH_4^+), producing nitrate (NO_2^-) as a waste product.

3. **Gamma proteobacteria**: This subgroup's photosynthetic members include sulfur bacteria such as *Thiomargarita namibiensis*. Some heterotrophic gamma proteobacteria are pathogens.

4. **Delta proteobacteria**: Includes the slime-secreting myxobacteria. When the soil dries out or food is scarce, the cells congregate into a fruiting body that releases resistant "myxospores". These cells found new colonies in favorable environments. Bdellovibrios are delta proteobacteria that attack other bacteria, charging at up to 100 µm/sec and boring into their prey by spinning at 100 revs/sec.

5. **Epsilon proteobacteria**: Most species in this subgroup are pathogenic to humans or other animals. Epsilon proteobacteria include *Campylobacter*, which causes blood poisoning and intestinal inflammation, and *Helicobacter pylori*, which causes stomach ulcers.

2. **Chlamydias**: These parasites can survive only within animal cells, depending on their hosts for resources as basic as ATP. The gram-negative walls of chlamydias are unusual in that they lack peptidoglycan.

3. **Spirochetes**: These helical heterotrophs spiral through their environment by means of rotating, internal, flagellum-like filaments. Many spirochetes are free-living, but others are notorious pathogenic parasites.

4. **Cyanobacteria**: These photoautotrophs are the only prokaryotes with plantlike, oxygen-generating photosynthesis. Both solitary and colonial cyanobacteria are abundant where ever there is water, providing an enormous amount of food for freshwater and marine ecosystems. Some filamentous colonies have cells specialized for nitrogen fixation.

5. **Gram-positive bacteria**: Gram-positive bacteria rival the proteobacteria in diversity. Species in one subgroup, the actinomycetes, form colonies containing branched chains of cells. Two species of actinomycetes cause tuberculosis and leprosy. However, most actinomycetes are free-living species that help decompose the organic matter in soil.

1. Gram-positive bacteria include many solitary species.
2. Mycoplasmas are the only bacteria known to lack cell walls. They are also the tiniest of all known cells, with diameters as small as 0.1 µm. They also have remarkably small genomes.

5. PROKARYOTES PLAY CRUCIAL ROLES IN THE BIOSPHERE.

1. Prokaryotes are so important to the biosphere that if they were to disappear, the prospects of survival for many other species would be dim.
2. Chemoheterotrophic prokaryotes function as **decomposers**.
3. **Symbiosis**: an ecological relationship in which two species live in close contact with one another. In general, the larger organism in a symbiotic relationship is known as the **host**, and the smaller is known as the **symbiont**.

1. **Mutualism**: an ecological interaction between two species in which both benefits.

2. **Commensalism**: an ecological interaction in which one species benefits while the other is not affected significantly.

3. **Parasitism**: an ecological relationship in which a **parasite** eats the cell contents, tissues, or body fluids of is host.

6. PROKARYOTES HAVE BOTH HARMFUL AND BENEFICIAL IMPACTS ON HUMANS.

1. **Pathogenic bacteria**: All the pathogenic prokaryotes known to date are bacteria.

1. Pathogenic prokaryotes usually cause illness by producing poisons, which are classified as exotoxins or endotoxins.

1. **Exotoxins** are proteins secreted by certain bacteria and other organisms.

2. **Endotoxins** are lipopolysaccharides components of the outer membrane of gram-negative bacteria.

2. **Prokaryotes in Research and Technology**:

1. Humans have long used bacteria to convert milk into cheese and yogurt.
2. Prokaryotes are the principle agents in **bioremediation,** the use of organisms to remove pollutants from soil, air, or water.
3. Bacteria can now be used to make natural plastics.

- **Protist**: An informal term applied to any eukaryote that is not a plant, animal, or fungus. Most protists are unicellular, though some are colonial or multicellular.
- **Mixotrophs** combine photosynthesis *and* heterotrophic nutrition.

I. MOST EUKARYOTES ARE SINGLE-CELLED ORGANISMS

1. Protists exhibit more structural and functional diversity than any other group of eukaryotes. Photoautotrophy, heterotrophy, and mixotrophy have all arise independently in many protists lineages. Some protists are exclusively asexual; others can reproduce sexually or at least employ the sexual processes of meiosis and fertilization. All three basic types of sexual life cycles are represented among protists, along with some variations that do not quite fit any of these types.
2. There is abundant evidence that much of protist diversity has its origins in endosymbiosis. The first eukaryotes acquired mitochondria by engulfing an aerobic prokaryote. Later in eukaryotic history, one lineage of heterotrophic eukaryotes acquired an additional endosymbiont—a photosynthetic cyanobacterium—that then evolved into plastids. On several occasions during eukaryotic evolution, red algae and green algae underwent **secondary endosymbiosis**: They were ingested in the food vacuole of heterotrophic eukaryotes and become endosymbionts themselves.

2. EXCAVATES INCLUDE PROTISTS WITH MODIFIED MITOCHONDRIA AND PROTISTS WITH UNIQUE FLAGELLA.

1. The excavates include the diplomonads, the parabasalids, and the euglenozoans.
   1. **Diplomonads** have modified mitochondria called *mitosomes,* which lack functional electron transport chains. Diplomonads have two equal-sized nuclei and multiple flagella. Many diplomonads are parasites.
   2. **Parabasalids** also have reduced mitochondria (*hydrogenosomes);* they generate some energy anaerobically, releasing hydrogen gas as a by-product.
   3. **Euglenozoans** belong to a diverse clade that includes predatory heterotrophs, photosynthetic, and parasites. The main morphological feature that distinguishes protists in this clade is the presence of a spiral or crystalline rod of unknown function inside their flagella. The two best-studied groups of euglenozoans are the kinetoplastids and the euglenids.
      1. **Kinetoplastids** have a single, large mitochondrion that contains an organized mass of DNA called a *kinetoplast*. Kinetoplastids in the genus *Trypanosoma* cause sleeping sickness; they evade immune responses with an effective bait-and-switch defense.
      2. A **euglenid** has a pocket at one end of the cell from which one or two flagella emerge. Many species are mixotrophs.

3. CHROMALVEOLATES MAY HAVE ORIGINATED BY SECONDARY ENDOSYMBIOSIS

1. The supergroup **Chromalveolata** (the chromalveolates) is a large, extremely diverse clade of protists.
   1. The **alveolates** are a group of protists whose monophyly is well supported by molecular systematics. They have membrane-bounded sacs (alveoli) just under the plasma membrane.
      1. The **dinoflagellates** are characterized by cells that are reinforced by cellulose plates. Two flagella located in perpendicular grooves in this "armor" make dinoflagellates spin as they move through water.
      2. Nearly all **apicomplexans** are parasites of animals, and some cause serious human diseases.
      3. **Ciliates** are a large, varied group of protists named for their use of cilia to move and feed. A distinctive feature of ciliates is the presence of two types of nuclei: tiny micronuclei and large marconuclei. Each marconucleus typically contains multiple copies of the ciliate's genome.
   2. The **stramenophiles** are a group of marine algae that include some of the most important photosynthetic organisms on the planet, as well as several clades of heterotrophs. They have a longer, hairy flagellum paired with a shorter, smooth one.
      1. **Diatoms** are unicellular algae that have a unique glass-like wall made of hydrated silica embedded in an organic matrix. Live diatoms can withstand pressures as great as 1.4 million kg/m^2. Much of the diatom's strength comes from the delicate lacework of holes and grooves in their walls; if the walls were smooth, it would take 60% less force to crush them.
      2. The characteristic color of **golden algae** results from their yellow and brown carotenoids.
      3. The largest and most complex algae are **brown algae**.
      4. **Oomycetes** include the water molds, the white rusts, and the downy mildews. They typically have cell walls made of *cellulose*. Although oomycetes descended from plastid-bearing ancestors, they no longer have plastids and do not perform photosynthesis.
2. A variety of life cycles have evolved among the multicellular algae. The most complex life cycles include an **alternation of generations**, the alternation of multicellular haploid and diploid forms.

- The term **thallus** refers to an algal body that is plantlike. A typical thallus consists of a rootlike **holdfast**, a stemlike **stipe**, and leaflike **blades.**
- **Heteromorphic**: The sporophytes and gametophytes are structurally different.
- **Isomorphic**: Sporophytes and gametophytes look similar to each other.

4. RED ALGAE AND GREEN ALGAE ARE THE CLOSEST RELATIVES OF LAND PLANTS

1. The clade **Rhizaria** has recently been proposed based on results from molecular systematics. Many species in Rhizaria are among the organisms referred to as amoebas. **Amoebas** were formerly defined as protists that move and feed by means of **pseudopodia**.
   1. The protists called **foraminiferans**, or **forams**, are named for their porous shells, called **tests**. Foram tests consist of a single piece of organic material hardened with calcium carbonate. The pseudopodia that extend through the pores function in swimming, test formation, and feeding.
   2. The protists called **radiolarians** have delicate, intricately symmetrical internal skeletons that are generally made of silica.

5. UNIKONTS INCLUDE PROTISTS THAT ARE CLOSELY RELATED TO FUNGI AND ANIMALS.

1. Red algae, green algae, and land plants make up the fourth eukaryotic supergroup, which is called **Archaeplastida**.
   1. Many of the 6,000 known species of **red algae** are reddish, owing to a photosynthetic accessory pigment called phycoerythrin. Red algal species may be greenish red in very shallow water, bright red at moderate depths, and almost black in deep water. Most red algae are multicellular. Red algae have especially diverse life cycles, and alternation of generations is common. But unlike other algae, they have no flagellated stages in their life cycle and depend on water currents to bring gametes together for fertilization.
   2. The grass-green chloroplasts of **green algae** have an ultrastructure and pigment composition much like the chloroplasts of land plants. Green algae are divided into two main groups, chlorophytes and charophyceans.
      1. More than 7,000 species of chlorophytes have been identified. Most live in fresh water, but there are also many marine and some terrestrial species. The simplest chlorophytes are unicellular organisms. Larger size and greater complexity evolved in chlorophytes by three different mechanisms.
         1. The formation of colonies of individual cells, as seen in *Volvox* and in filamentous forms that contribute to the stringy masses known as pond scum.
         2. The formation of true multicellular bodies by cell division and differentiation, as seen in the seaweed *Ulva*.
         3. The repeated division of nuclei with no cytoplasmic division, as seen in the multinucleate filaments of *Caulerpa*.
      2. The charophyceans are the algae most closely related to land plants.

6. UNIKONTS INCLUDE PROTISTS THAT ARE CLOSELY RELATED TO FUNGI AND ANIMALS

1. **Unikonta** is a recently proposed, extremely diverse supergroup of eukaryotes that includes animals, fungi, and some

protists.

2. There are two major clades of unikonts, the amoebozoans and the opisthokonts (animals, fungi, and closely related protist groups).
    1. **Amoebozoans** form a clade that is well supported by molecular data. This clade includes many species of ameobas that have lobe- or tube-shaped, rather than threadlike, pseudopodia. Amoebozoans include slime molds, gymnamoebas, and entamoebas.
        1. Slime molds produce fruiting bodies that aid in spore dispersal. They have diverged into two main branches, plasmodial slime molds and cellular slime molds, distinguished in part by their unique life cycles.
            1. Many **plasmodial slime molds** are brightly colored, often yellow or orange. At one stage in their life cycle, they form a mass called a **plasmodium**, which may grow to a diameter of many centimeters. Despite its size, the plasmodium is not multicellular; it is a single mass of cytoplasm that is undivided by plasma membranes and that contains many diploid nuclei.
            2. The life cycle of the protists called **cellular slime molds** can prompt us to question what it means to be an individual organism. The feeding stage of these organisms consists of solitary cells that function individually, but when food is depleted, the cells form an aggregate that functions as a unit. The cells remain separated by their individual plasma membranes. Cellular slime molds are haploid organisms (only the zygote is diploid) and in having fruiting bodies that function in asexual rather than sexual reproduction.
        2. Gymnamoebas constitute a large and varied group of amoebozoans.
        3. Entamoebas are parasites.
    2. **Opisthokonts** are an extremely diverse group of eukaryotes that includes animals, fungi, and several groups of protists.

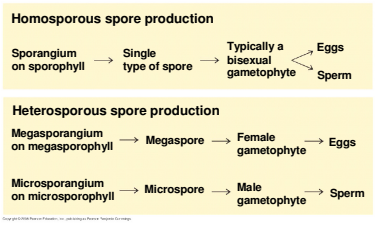
7. Protists Play Key Roles in Ecological Relationships
    1. **Symbiotic protists**: Many protists form symbiotic associations with other species. For example, photosynthetic dinoflagellates provide nourishment to their symbiotic partners, the coral polyps that build coral reefs. Other protists are parasites.
    2. Many protists are important **producers**, organisms that use energy from light (or inorganic chemicals) to convert carbon dioxide to organic compounds. Scientists estimate that up to one-quarter of the world's photosynthesis is performed by diatoms, dinoflagellates, multicellular algae, and other protists.

Chapter 29: Plant Diversity 1: How Plants Colonized Land

- **Phragmoplast**: An alignment of cytoskeletal elements and Golgi-derived vesicles that forms across the midline of a dividing plant cell.

- A **seed** is an embryo packaged with a supply of nutrients inside a protective coat.

Fig. 29-UN8



I. Land Plants Evolved from Green Algae.

1. **Morphological and Molecular Evidence:** The charophytes share the four following distinctive traits with land plants: rosette-shaped cellulose-synthesizing complexes, peroxisome enzymes, structure of flagellated sperm, and formation of a phragmoplast.

2. **Adaptations Enabling the Move to Land**: In charophytes and plants, a layer of a durable polymer called **sporopollenin** prevents exposed zygotes from drying out.

3. **Derived Traits of Plants**:

1. *Alternation of Generations*: the haploid **gametophyte**→gametes→diploid zygote→**sporophyte**→haploid **spores**.

1. Multicellular plant embryos develop from zygotes that are retained within tissues of the female parent. The embryo has specialised **placental transfer cells**.

2. *Walled Spores Produced in Sporangia*: The sporophyte has multicellular organs called **sporangia**. Diploid cells called **sporocytes** undergo meiosis and generate the haploid cells.

3. *Multicellular Gametangia*: Produce gametes. The female gametangia are called **archegonia**. Male gametangia are called **antheridia**. (A few species have bisexual gametangia).

4. *Apical Meristems*: localized regions of cell division at the tip of shoots and roots.

5. The epidermis in many species has a covering, the **cuticle**, which consists of polyester and wax polymers.

4. **The Origin and Diversification of Plants**: In the 1970s, researchers found fossil spores dating to the Ordovician period, up to 475 mya. Spores of present-day plants are typically dispersed as single grains, but the fossil spores are fused together in groups of two or four.

1. **Vascular plants** have a complex vascular tissue system. Nonvascular plants are informally called **bryophytes**.

2. **Seedless vascular plants** include **lycophytes** (club mosses and their relatives) and **pterophytes** (ferns and their relatives.)

3. **Gymnosperms** are grouped together as "naked seed" plants because their seeds are not enclosed in chambers. **Angiosperms** are a huge clade consisting of all flowering plants.

2. Mosses and Other Nonvascular Plants Have Life Cycles Dominated By Gametophytes

1. The nonvascular plants are represented today by three phyla of small herbaceous plants: **liverworts** (phylum Hepatophyta), **hornworts** (phylum Anthocerophyta), and **mosses** (phylum Bryophyta).

2. **Bryophyte Gametophytes**: Unlike vascular plants, in all three bryophyte phyla the gametophytes are the dominate stage of the life cycle: they are larger and longer-living than the sporophytes. When bryophyte spores are dispersed to a favorable habitat, such as moist soil or tree bark, they germinate and grow into gametophytes, producing **protonema**, which produces buds in favorable conditions. These buds produce **gametophores**. The gametophytes are anchored by delicate **rhizoids**, which are not composed of true tissues.

3. **Bryophyte Sporophytes**: Cannot live independently; remain attached to parental gametophytes. A typical bryophyte sporophyte consists of a **foot** (absorbs nutrients from the gametophyte), a **seta** (conducts material to sporangium), and a **sporangium** (**capsule**). Upper part of capsule features a ring of interlocking, tooth-like structures (**peristome**), which releases the spores.

4. **Stomata** allow the exchange of CO_2 and O_2 between the outside air and the sporophyte interior. Liverworts do not have stomata.

5. **The Ecological and Economic Importance of Mosses**: Mosses help retain nitrogen in the soil. One wetland moss genus, *Sphagnum*, forms **peat**.

3. Ferns and Other Seedless Vascular Plants Were the First Plants to Grow Tall.

1. **Origin and Traits of Vascular Plants**: Branched sporophytes not dependent on gametophytes for nutrition. Multiple sporangia.

1. **Life Cycles with Dominant Sporophytes**:

2. **Transport in Xylem and Phloem**: *Xylem* conducts most of the water and minerals; xylem is made of tube-shaped cells (*tracheids*) strengthened with the polymer *lignin*. Cells of *phloem* distribute sugars, amino acids, and other organic products. Advantage: being able to grow tall. Treelike plants arrived about 370 mya.

3. **Evolution of Roots**: *Roots* are organs that absorb water and nutrients from the soil and anchor the plant. Probably arose multiple times by convergent evolution.

4. **Evolution of Leaves**: *Leaves* increase the surface area of the plant body and serve as the primary photosynthetic organ of vascular plants. Lycophytes have **microphylls**, small, spine-shaped leaves supported by a single strand of vascular tissue (appeared 410 mya). Other plants have **megaphylls**, leaves with a highly branched vascular system (appeared 370 mya).

5. **Sporophylls and Spore Variations**: *Sporophylls*-modified leaves that bear sporangia. Fern sporophylls produce clusters of sporangia (**sori**). In many lycophytes and in most gymnosperms, groups of sporophylls form cone-like structures called **strobili**.

1. **Homosporous** plants: one type of sporangium produces pone type of spore, which typically develops into a bisexual gametophyte. (generally also seedless vascular plants)

2. **Heterosporous** plants have two types of sporangia and produces two kinds of spores, **megaspores** and **microspores**.

2. **Classification of Seedless Vascular Plants**: Two clades of living seedless vascular plants: the lycophytes (phylum Lycophyta: club mosses, spike mosses, quillworts) and the pterophytes (phylum Pterophyta: ferns, horsetails, whisk ferns and relatives).

1. **Phylum Lycophyta: Club Mosses, Spike Mosses, and Quillworts**: By the Carboniferous period (359 to 299 mya), there were two evolutionary lineages of lycophytes: small herbaceous plants and giant woody treelike plants. Only the small herbaceous plants have survived.

2. **Phylum Pterophyta: Ferns, Horsetails, and Whisk Ferns and Relatives**: Radiated extensively from their Devonian origins. Currently number more than 12,000 species. Currently only 15 species of horsetails in genus *Equisetum*. Whisk ferns (*Psilotum*) and the closely related genus, *Tmesipteris*, lack true roots.

3. **The Significance of Seedless Vascular Plants**:

1. Seedless vascular plants in the late Devonian and early Carboniferous grew to great heights, drawing CO_2 out from the atmosphere and triggering an ice age.

CHAPTER 30: PLANT DIVERSITY II: THE EVOLUTION OF SEED PLANTS

- **Seed**: consists of an embryo and its food supply, surrounded by a protective coat.

I. SEEDS AND POLLEN GRAINS ARE KEY ADAPTATION FOR LIFE ON LAND.

1. Traits common to seed plants: reduced gametophytes, heterospory, ovules, and pollen.
2. **Advantages of Reduced Gametophytes**: Gametophytes can develop from spores retained within the sporangia of the parental sporophyte, protecting the gametophyte from environmental stress.
3. **Heterospory: The Rule Among Seed Plants**: Megasporangia produce megaspores that give rise to female gametophytes; microsporangia produce microspores that give rise to male gametophytes.
4. **Ovules and Production of Eggs**: A layer of sporophyte tissue (**integument**) envelops and protects the megasporangium. The whole structure — megasporangium, megaspore, and their integument(s) — is called an **ovule**.
5. **Pollen and Production of Sperm**: Microspore→ **pollen grain** (consists of a male gametophyte enclosed within the pollen wall made of sporopollenin). **Pollination**: the transfer of pollen to the part of a seed plant that contains the ovules. The sperm of gymnosperms and angiosperms generally lack flagella and are nonmotile.
6. **The Evolutionary Advantage of Seeds**: The seed coat provides extra protection to the embryo.

II. GYMNOSPERMS BEAR "NAKED" SEEDS, TYPICALLY ON CONES.

1. **Gymnosperm Evolution**: First seed-bearing plants appeared in the fossil record 360 mya. Earliest fossils of gymnosperms are about 305 million years old. Drier climate conditions favored the spread of gymnosperms. **Conifers**: cone-bearing gymnosperms.
   1. *Cycadophyta:* Large cones and palmlike leaves.
   2. *Ginkgophyta: Ginkgo biloba* is the surviving species of this phylum. Tolerates air pollution well.
   3. *Gnetophyta:* Three genera: Welwitschia (one species only, *Welwitschia mirabilis*; lives in deserts of southwestern Africa), Gnetum (35 species of tropical trees, shrubs, and vines, native to Africa and Asia; seeds resemble fruits), Ephedra (40 species in arid regions.)
   4. *Coniferophyta:* Largest of the gymnosperm phyla (600 species). Mostly large trees (cypresses, redwoods). Mostly evergreens.
2. **The Life Cycle of a Pine**: In conifers, the two types of spores are produced by spearate cones: small pollen cones and large ovulate cones. Most species have both types of cones. Yellow pollen is released in large amounts and carried by wind to the ovulate cones.

III. THE REPRODUCTIVE ADAPTATION OF ANGIOSPERMS INCLUDE FLOWERS AND FRUITS.

1. **Characteristics of Angiosperms:**
   1. **Flowers**: angiosperm structure specialized for sexual reproduction. **Sepals**: green and enclose the flower before it opens. **Petals**: brightly colored in most flowers and aid in attracting pollinators. **Stamens** produce pollen and are made up of a **filament** and an **anther**. **Carpels** make megaspores and consist of a **stigma**, a **style**, and an **ovary**.
   2. **Fruits**: typically consists of a mature ovary. Protect dormant seeds and aid in their dispersal. Mature fruits can be either fleshy or dry. Some fruits have parachutes or propellers. Some fruits can float, others rely on animals for dispersal.
   3. **The Angiosperm Life Cycle**: Each male gametophyte has two haploid cells: a *generative cell* that divides into two sperm, and a *tube cell* that produces a pollen tube. Female gametophyte=**embryo sac**. Most flowers have mechanisms that ensure **cross-pollination**. Pollen reaches ovary→pollen tube penetrates through the **micropyle**, a pore in the integuments of the ovule→two sperm cells are discharged into the embryo sac→**double fertilization**: one sperm fuses with the egg, the other fuses with the two nuclei in the large central cell, producing a triploid cell→Zygote develops into a sporophyte embryo with a rudimentary root and one or two **cotyledons**; triploid cell develops into **endosperm**.
2. **Angiosperm Evolution**: Originated at least 140 mya, began to dominate by 100 mya.
   1. **Fossil Angiosperms**: late 1990s: scientists in China discover fossils of angiosperms from 125 mya.
   2. **Angiosperm Phylogeny**: Living gymnosperms are a monophyletic group who diverged from the ancestors of angiosperms 305 mya. Angiosperms may be most closely related to extinct seed plants like Bennettitales. *Amborella* and water lilies are living representatives of two of the most ancient angiosperm lineages.
   3. **Developmental Patterns in Angiosperms**: in *Amborella*, eggs form from precursor cells that differ from from the egg precursor cells of most other living angiosperms. In a variety of early angiosperms, the outer of the two protective integuments appears to be a modified leaf.
   4. **Angiosperm Diversity**: Species with one cotyledon were called **monocots**, and those with two were called **dicots**. Monocots typically have parallel leaf veins, while the veins of most dicots have a netlike pattern. Current research supports the hypothesis that monocots form a clade by dicots are paraphyletic. The vast majority of species once categorized as dicots form a large clade known as **eudicots**. The rest are group into the **basal angiosperms** and the **magnoliids**.
   5. **Evolutionary Links Between Angiosperms and Animals**: Herbivores and angiosperms are in an evolutionary arms race; plant-pollinator and other mutually beneficial interactions have also arose.

IV. HUMAN WELFARE DEPENDS GREATLY ON SEED PLANTS.

1. In forests and on farms, seed plants are key sources of food, fuel, wood products, and medicine.
2. **Products from Seed Plants**: Four thousands of years, farmers have selected the seeds of plants with desirable traits to plant for the next year's crops. Spices are derived from various plant parts, such as flowers(cloves, saffron), fruits and seeds (vanilla, black pepper, mustard, cumin), leaves (basil, mint, sage), and even bark (cinnamon).
3. **Threats to Plant Diversity:** Thirty-five million acres of tropical rain forest are cleared each year. As forests disappear, so do thousands of plant species. If current rates of loss in the tropics and elsewhere continue, scientists estimate that within the next 100 to 200 years, 50% or more of Earth's species will become extinct.

Chapter 31: Fungi

1. Fungi are Heterotrophs that Feed by Absorption.

1. **Nutrition and Ecology**: Fungi are heterotrophs that absorbs nutrients from the environment outside of its body by secreting powerful hydrolytic enzymes into their surroundings. Fungi take on many roles in ecological communities, with different species living as decomposers, parasites, or mutalists.
2. **Body Structure**: the most common fungal body structures are multicellular filaments and single cells (**yeasts**).
    1. **Fungal Morphology**: The bodies of fungi form a network of tiny filaments (**hyphae**) that consist of tubular cell walls surrounding the plasma membrane and cytoplasm of the cells. Fungal cell walls are strengthened by **chitin**. Fungal hyphae form an interwoven mass called a **mycelium**. The fungus concentrates its energy and resources on adding hyphal length. In most fungi, the hyphae are divided into cells by **septa**, which generally have pores large enough to allow ribosomes, mitochondria, and even nuclei to flow from cell to cell. **Coenocytic fungi** lack septa and consist of a continuous cytoplasmic mass having hundreds or thousands of nuclei.
    2. **Specialized Hyphae in Mycorrhizal Fungi:** Some fungi have specialized hyphae that allow them to feed on living animals. Other fungal species have **haustoria**, specialized hyphae used to extract nutrients from — or exchange nutrients with — their hosts. **Mycorrhizae**: mutually beneficial relationships between fungi and plant roots. **Ectomycorrhizal fungi** form sheaths of hyphae over the surface of a root and also grow into the extracellular spaces of the root cortex. **Arbuscular mycorrhizal fungi** extend their branching hyphae through the root cell wall and into tubes formed by invagination of the root cell membrane.

2. Fungi Produce Spores Through Sexual or Asexual Life Cycles

1. Most fungi propagate themselves by producing vast numbers of spores, either sexually or asexually.
2. **Sexual reproduction**: Hyphae from two mycelia release **pheromones**→Hyphae grow towards each other and fuse (**plasmogamy**), forming a **heterokaryon**, a mycelium that contains coexisting, genetically different nuclei→In some species, the different nuclei exchange chromosomes and genes in a process similar to crossing over. In other species, the haploid nuclei pair off two to a cell, one form each parent, forming a **dikaryotic** mycelium→**karyogamy**: fusion of the nuclei→Haploid spores form from meiosis.
3. **Sexual reproduction**: **Molds** form visible mycelia and can produce haploid spores by mitosis. **Deuteromycetes**, which include yeasts, have no known sexual stage.

3. The Ancestor of Fungi was an Aquatic, Single-Celled, Flagellated Protists.

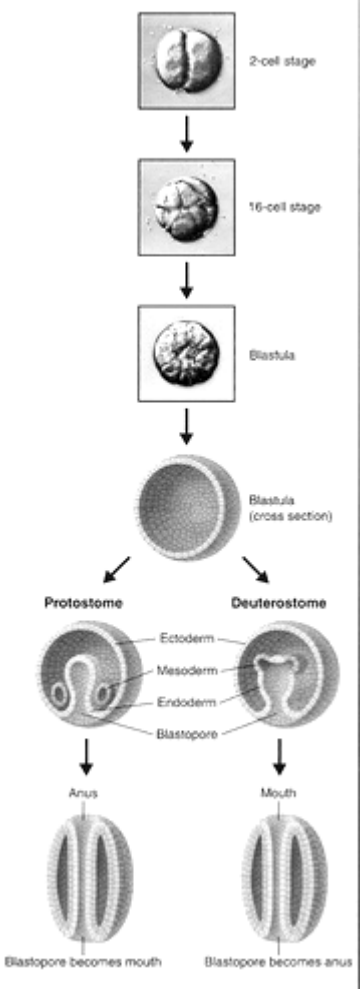
1. **The Origin of Fungi**: *Opisthokonts* are a clade made up of animals, fungi, and their protistan relatives. **Nucleariids** are protists that are mostly closely related to fungi.
2. **Are Microsporidia Closely Related to Fungi?** Microsporidia are unicellular parasites of animals and protists. They lack functional mitochondria.
3. **The Move to Land**: Fossils of the earliest known vascular plants from the late Silurian period (420 mya) contain evidence of mycorrhizal relationships between plants and fungi.

4. Fungi have Radiated into a Diverse Set of Lineages.

1. **Chytrids**: Fungi classified in the phylum Chytrdiomycota are ubiquitous in lakes and soil. They are unique among fungi in having flagellated spores (**zoospores**). Some **chytrids** form colonies with hyphae, while others exist as single spherical cells. Thought to be one of the earliest fungal groups to diverge form other fungi.
2. **Zygomycetes**: (~1,000 known species) Includes fast-growing molds responsible for causing foods to rot during storage. Other zygomycetes live as parasites or as commensal symbionts of animals.
    1. *Life Cycle of Rhizopus stolonifer*: Coenocytic hyphae spread out over the food surface, penetrate it, and absorb nutrients. In the asexual phase, bulbous black sporangia develop at the tips of upright hyphae. In sexual reproduction, plasmogamy produces a sturdy structure called a **zygosporangium**, a multinucleate structure in which karyogamy and then meiosis occur.
3. **Glomeromycetes**: (~160 species) Form arbuscular mycorrhizae
4. **Ascomycetes**: (~65,000 species) The defining feature of ascomycetes is the production of sexual spores in saclike **asci**; thus, they are commonly called **sac fungi**. Fruiting bodies are called **ascocarps**. More than 40% of all ascomycete species live with green algae or cyanobacteria in beneficial symbiotic associations called lichens. Ascomycetes reproduce asexually by producing enormous numbers of asexual spores called **conidia**. Conidia also can fuse with the hyphae from a mycelium of a different mating type. Karyogamy is followed by meiosis, then by a mitotic division to form eight ascospores.
5. **Basidiomycetes**: (~30,000 species, including mushrooms, puffballs, and shelf fungi; mutualists that form mycorrhizae, plant parasites rusts and smuts, **club fungus**) Long-lived dikaryotic mycelium. Reproduces sexually by producing elaborate fruiting bodies (**basidiocarps**). After a mushroom forms, its cap supports and protects a large surface area of dikaryotic basidia on gills. Karyogamy occurs, followed by meiosis and basidiospore formation.

5. Fungi Play Key Roles in Nutrient Cycling, Ecological Interactions, and Human Welfare.

1. **Fungi as Decomposers**: Almost any carbon-containing substrate — even jet fuel and house paint — can be consumed by at least some fungi.
2. **Fungi as Mutualists**:
    1. All plant species studied to date appear to harbor symbiotic **endophytes**, fungi that live inside leaves or other plant parts without causing harm.
    2. Leaf-cutter ants "farm" fungi by feeding the fungi leaves and eating from specialized swollen hyphae tips that contain protein and carbohydrates.
    3. A **lichen** is a symbiotic association between a photosynthetic microorganism and a fungus in which millions of photosynthetic cells are held in a mass of fungal hyphae.
3. **Fungi as Pathogens**: about 30% of the 100,000 known species of fungi make a living as parasites or pathogens, mostly of plants. The general term for a fungal infection of an animal is **mycosis**.
4. **Practical Uses of Fungi**: Fungi help produce cheese, yogurt, the citric acid in soft drinks, bread, alcoholic beverages, and medicines.



I. Animals are multicellular, heterotrophic eukaryotes with tissues that develop from embryonic layers
   1. Animals are multicellular and eukaryotic. Unlike plants, animals cannot construct all of their own organic molecules and so, in most cases, they ingest them—either by eating other living organisms or by eating nonliving organic material. They also lack the structural support of cell walls and instead use structural proteins like collagen (only found in animals) to hold them together. Many animals have two types of specialized cells not seen in other multicellular organisms: muscle cells and nerve cells.
   2. Most animals reproduce sexually, with the diploid stage usually dominating the life cycle. Sperm fertilizes a larger, nonmotile egg, forming a diploid zygote, which undergoes **cleavage**, dividing without cell growth, and forms a **blastula**. **Gastrulation** develops the layers of embryonic tissue, and the blastula develops into a **gastrula**.
   3. The life cycles of many animals also include at least one larval stage. A **larva** is a sexually immature form of an animal that is morphologically distinct from the adult. Larvae eventually undergo **metamorphosis**, a developmental transformation that turns the animal into a juvenile, which resembles an adult but is not sexually mature.
   4. Animals share a unique homeobox-containing family of genes, known as *Hox* genes. *Hox* genes play important roles in the development of animal embryos, controlling the expression of dozens or even hundreds of other genes that influence animal morphology. *Hox* genes regulate patterning of the anterior-posterior axis, as well as other aspects of development.

II. The History of Animals Spans More Than Half a Billion Years
   1. The animal kingdom includes not only the great diversity of living species, but also the even greater diversity of extinct ones. (Some palaeontologists have estimated that 99% of all animal species are extinct). Studies suggest that the common ancestor of living animals may have lived sometime between 675 to 875 mya. Morphological and molecular evidence indicates that choanoflagellates are among the closest living relatives of animals.
   2. **Neoproterozoic Era (1,000-542 mya):** The first generally accepted macroscopic fossils or animals range in age from 565-550 mya. These fossils are members of an early group of multicellular eukaryotes known as the **Ediacaran biota**, which were soft-bodied organisms similar to sponges and cnidarians. The fossil record strongly suggests that the end of the Neoproterozoic era was a time of increasing animal diversity.
   3. **Paleozoic Era (542-251 mya):** Animal diversification appears to have accelerated dramatically from 535-525 mya, during the Cambrian period of the Paleozoic era—a phenomenon often referred to as the **Cambrian explosion**. New predator-prey relationships, a rise in atmospheric oxygen, and the evolution of the *Hox* gene complex all contributed to the Cambrian explosion. The Cambrian period was followed by the Ordovician, Silurian, and Devonian periods, when animal diversity continued to increase, although punctuated by episodes of mass extinctions. By 460 mya, groups that diversified during the Cambrian period were making an impact on land. Insects and plants began influencing each other's evolution. Vertebrates made the transition to land around 360 mya and diversified into numerous terrestrial groups.
   4. **Mesozoic Era (251-65.5 mya):** The animal phyla that had evolved during the Paleozoic now began to spread into new ecological habitats. The first coral reefs formed. Large and small dinosaurs emerged, both as predators and herbivores. Flowering plants (angiosperms) and insects both underwent dramatic diversifications during the late Mesozoic.
   5. **Cenozoic Era (65.5 mya to present):** Mass extinctions of both terrestrial and marine animals ushered in the Cenozoic era. The global climate gradually cooled throughout the Cenozoic, triggering significant shifts in many animal lineages.

III. Animals Can Be Characterized by "Body Plans"
   1. A **body plan** is a set of morphological and developmental traits, integrated into a functional whole—the living animal.
   2. Some animals exhibit **radial symmetry**, others exhibit **bilateral symmetry**. Most animals with bilateral symmetry show **cephalization**, with their brain and sensory equipment concentrated at their anterior end.
   3. Sponges and a few other groups lack true tissues. In all other animals, the embryo becomes layered through the process of gastrulation, forming *germ layers*. The outermost germ layer, the **ectoderm**, gives rise to the outer covering of the animal and, in some phyla, to the central nervous system. **Endotherm**, the innermost germ layer, lines the developing digestive tube, or **archenteron**, and gives rise to the lining of the digestive tract (or cavity) and organs such as the liver and lungs of vertebrates. Animals that have only these two germ layers are said to be **diploblastic**. **Triploblastic** animals have a third germ layer as well, called the **mesoderm,** which develops into the muscles and most other organs. All bilaterally symmetrical animals are **triploblastic**.
   4. Most **triploblastic** animals possess a **body-cavity**, a fluid- or air- filled space separating the digestive tract from the outer body wall. This body cavity is also known as a **coelom**. A true coelom forms from tissue derived from the mesoderm. The inner and outer layers of tissue that surround the cavity connect dorsally and ventrally and form structures that suspend the internal organs. Animals that possess a true coelom are known as **coelomates**. A pseudocoelom is derived from the mesoderm and endoderm, and animals that have one are **pseudocoelomates**. Some triploblastic animals lack a body cavity altogether and are called **acoelomates**. The terms *coelomates* and *pseudocoelomates* refer to grades, not clades.
   5. Based on certain aspects of early development, many animals can be categorized as having one or two developmental nodes: **protostome development** or **deuterostome development**.
   6. Protostomes tend to have spiral, determinate cleavage, while deuterostomes tend to have radial, indeterminate cleavage.
   7. During gastrulation, an embryo's developing digestive tube initially forms as a blind pouch, the archenteron, which becomes the gut. As the archenteron forms in protostomes, initially solid masses of mesoderm split and form the coelom. In contrast, in deuterostomes, the mesoderm buds from the wall of the archenteron and its cavity becomes the coelom.
   8. Generally, the **blastopore** develops into the mouth in protostomes and the anus in deuterostomes.

IV. New Views of Animal Phylogeny Are Emerging from Molecular Data
   1. Researchers have long based their hypotheses about animal phylogeny on morphological data. In the late 1980s, biologists also began to study the molecular systematics of animals.
   2. **All animals share a common ancestor. Sponges are basal animals. Eumetazoa is a clade of animals with true tissues. Most animal phyla belong to the clade Bilateria. Chordates and some other phyla belong to the clade Deuterostomia**.
   3. The morphology-based tree divides the bilaterians into two clades: deuterostomes and protostomes. However, molecular phylogenies indicate that there are tree major clades of bilaterally symmetric animals: Deuterostomia, Lophotrochozoa, and Ecdysozoa. Members of Ecdysozoa shed their exoskeletons on occasion (*ecdysis*); members of Lophotrochozoa either develop a **lophophore**, a crown of ciliated tentacles that function in feeding or go through a distinctive developmental stage called the **trochophore larva**.

Chapter 33: Invertebrates

- **Invertebrates**: animals that lack a backbone.

1. Sponges are basal animals that lack true tissues.

1. Animals in the phyla Calcarea and Silicea are known informally as "sponges." Sponges are sedentary **suspension feeders**: they capture food particles suspended in the water that passes through their body, which in some species resembles a sac perforated with pores. Water is drawn through the pores into a central cavity, the **spongocoel**, and then flows out of the sponge through a larger opening called the **osculum**. Lining the interior of the spongocoel are flagellated **choanocytes**, or collar cells. The body of a sponge consists of two layers of cells separated by a gelatinous region called the **mesohyl**. Wandering through the mesohyl are cells called **amoebocytes**, named for their use of pseudopodia. Most sponges are **hermaphrodites**. Sponges produce a variety of antibiotics and other defensive compounds.

2. Cnidarians are an ancient phylum of eumetazoans

1. All animals except sponges and a few other groups belong to the clade Eumetazoa, animals with true tissues. The basic body plan of a cnidarian is a sac with a central digestive compartment, the **gastrovascular cavity**. A single opening to this cavity functions as both mouth and anus. There are two variations on this body plan: the sessile polyp and the motile medusa. **Polyps** are cylindrical forms that adhere to the substrate by the aboral end of their body and extend their tentacles, waiting for prey. The tentacles are armed with batteries of **cnidocytes**, cells unique to cnidarians that function in defense and prey capture. Specialized cnidae called **nematocysts** contain a stinging thread that can penetrate the body wall of the cnidarian's prey. A **medusa** is a flattened, mouth-down version of the polyp. Some cnidarians exist only as polyps or only as medusae; others have both a polyp stage and a medusa stage in their life cycle. Cnidaria is divided into four major classes: Hydrozoa, Scyphozoa, Cubozoa, and Anthozoa.
    1. Most hydrozoans alternate between polyp and medusa forms, as in the life cycle of *Obelia*.
    2. The medusa generally is the predominant stage in the life cycle of the class Scyphozoa.
    3. Cubozoans have a box-shaped medusa stage.
    4. Sea anemones and corals belong to the class Anthozoa.

3. Lophotrochozoans, a clade identified by molecular data, have the widest range of animal body forms.

1. Molecular evidence suggests that there are three major clades of bilaterally symmetrical animals: Lophotrochozoa, Ecdysozoa, and Deuterostomia. Lophotrochozoa was identified by molecular data.
2. There are six lophotrochozoan phyla: the flatworms, rotifers, ectoprocts, brachiopods, molluscs, and annelids.
3. **Phylum Platyhelminthes:** Flatworms are so named because they have thin bodies that are flattened dorsoventrally. They are acoelomates and their flat shape places all their cells close to water in the surrounding environment or in their gut. Their relatively simple excretory apparatus functions mainly to maintain osmotic balance with their surroundings. This apparatus consists of **protonephridia**, networks of tubules with ciliated cells known as *flame bulbs* that pull fluids through branched ducts opening to the outside. Flatworms are divided into four classes: Turbellaria (mostly free-living flatworms), Monogenea (monogeneans), Trematoda (trematodes, or flukes), and Cestoda (tapeworms).
    1. **Turbellarians** are nearly all free-living and mostly marine. The best-known freshwater tubellarians are members of the genus *Dugesia*, commonly called **planarians**.
    2. **Monogeneans** and **trematodes** live as parasites in or on other animals. Most trematodes have complex life cycles with alternating sexual and asexual stages. Many trematodes require an intermediate host in which larvae develop before infecting the final host where the adult worms live. Most monogeneans are external parasites of fish. The monogenean life cycle is relatively simple.
    3. **Class Cestoda**: Tapeworms are also parasitic. They lack a mouth and gastrovascular cavity; they absorb nutrients released by digestion in the host's intestine. The anterior end (scolex) is armed with suckers and often hooks that the worm uses to attach itself to the intestinal lining of its host. Posterior to the scolex is a long ribbon of units called proglottids, which are little more than sacs of sex organs. After sexual reproduction, proglottids loaded with thousands of fertilized eggs are released from the posterior end of a tapeworm and leave the host's body in feces.
4. **Phylum Rotifera**: Rotifers have an **alimentary canal**, a digestive tube with a separate mouth and anus. They are pseudocoelomates, and fluid in the pseudocoelom serves as a hydrostatic skeleton. Some rotifer species consists only of females that produce more females from unfertilized eggs, a type of reproduction called **parthenogenesis**. Other species produce two types of eggs that developed by parthenogenesis. One type forms females while the other type (produced when conditions deteriorate) develops into simplified males that cannot even feed themselves. The males survive only long enough to fertilize eggs, which form resistant zygotes that can survive when a pound dries up. It is puzzling that so many rotifer species survive without males.
5. **Lophophorates: Ectoprocts and Brachipods**: Bilaterians in the phyla Ectoprocta and Brachiopoda are among those known as lophophorates. These animals have a *lophophore*, a crown of ciliated tentacles that surround the mouth. Other similarities, such as a U-shaped alimentary canal and the absence of a distinct head, reflect these organisms' sessile existence. Lophophorates have a true coelom that is completely lined by mesoderm.
    1. **Ectoprocts** are colonial animals that superficially resemble clumps of moss. In most species, the colony is encased in a hard **exoskeleton** studded with pores through which the lophophores extend.
    2. **Brachiopods**, or lamp shells, superficially resemble clams and other hinge-shelled molluscs, but the two halves of brachiopod shell are dorsal and ventral rather than lateral, as in clams. All brachiopods are marine.
6. **Phylum Mollusca**: Snails and slugs, oysters and clams, and octopuses and squids are all molluscs. Most molluscs are marine, though some inhabit fresh water, and some snails and slugs live on land. Molluscs are coelomates, and their bodies have three main parts: a muscular **foot**, usually used for movement; a **visceral mass** containing most of the internal organs; and a **mantle**, a fold of tissue that drapes over the visceral mass and secretes a shell (if one is present). In many molluscs, the mantel extends beyond the visceral mass, producing a water-filled chamber, the **mantle cavity**, which houses the gills, anus, and excretory pores. Many molluscs feed by using a straplike rasping organ called a **radula** to scrape up food. Most molluscs have separate sexes, and their gonads are located in the visceral mass. Many snails, however, are hermaphrodites. There are eight classes of molluscs, we will look at four: Polyplacophora (chitons), Gastropoda (snails and slugs), Bivalvia (clams, oysters, and other bivalves), and Cephalopoda (squids, octopuses, cuttlefishes, and chambered nautiluses).
    1. **Chitons** have an oval-shaped, unsegmented body and a shell divided into eight dorsal plates.
    2. About three-quarters of all living species of molluscs are **gastropods**. A distinctive characteristic of class Gastropoda is a developmental process known as **torsion**. As a gastropod embryo develops, its visceral mass rotates up to 180°, causing the animal's anus and mantle cavity to wind up above its head.
    3. **Bivalves**: The molluscs of class Bivalvia include many species of clams, oysters, mussels and scallops. Bivalves have a shell divided into two halves. They have no distinct head. Most bivalves are suspension feeders.
    4. **Cephalopods** are active predators. Most have only a vestigial shell if they have a shell at all. Their foot has been modified into a muscular excurrent siphon and part of the tentacles. They have a closed circulatory system, well-developed sense organs, and a complex brain.

7. **Phylum Annelida:** An **annelid's** body resembles a series of fused rings. They are divided into three classes:
    1. **Oligochaeta**: Reduced head, no parapodia, but chaetae present. Includes earthworms and a variety of aquatic species.
    2. **Polychaeta**: Many have a well-developed head; each segment usually has parapodia with many chaetae; free living. Most members are marine; in many marine species, the parapodia function as gills.
    3. **Hirudina**: Body usually flattened, with reduced coelom and segmentation; chaetae usually absent, suckers at anterior and posterior ends, parasites, predators, and scavengers. Majority inhabit fresh water.

4. Ecdysozoans are the most species-rich animal group.

1. Ecdysozoa includes animals that shed a tough external coat (**cuticle**) as they grow; in fact, the group derives its name from this process, which is called **molting**, or ecdysis.
2. **Nematodes**: Roundworms are found in most aquatic habitats, in the soil, in the moist tissues of plants, and in the body fluids and tissues of animals. They have unsegmented bodies covered by a tough cuticle; as the worm grows, it periodically sheds its old cuticle and secretes a new, larger one. In most species, the sexes are separate and females are larger than the males. 25,000 species are known; perhaps 20 times that number actually exist.
    - Phylum Nematoda includes many significant agricultural pests that attack the roots of plants. Other species of nematodes parasitize animals. Parasitic nematodes have an extraordinary molecular toolkit that enables them to redirect some of the cellular functions of their hosts and evade their immune systems.
3. **Arthropods**: Two out of every three known species are arthropods, and members of the phylum Arthropoda can be found in nearly all habitats of the biosphere. Arthropods have segmented bodies, hard exoskeletons, and jointed appendages. The earliest fossils with this body plan are from the Cambrian explosion.
    - Early arthropods showed little variation from segment to segment. As arthropods evolved, the segments tended to fuse and become fewer in number, and the appendages became specialized for a variety of functions, including walking, feeding, sensory reception, reproduction, and defense.
    - The body of an arthropod is completely covered by the cuticle, and exoskeleton constructed from layers of protein and the polysaccharide chitin.
    - Arthropods have an **open circulatory system**. A variety of specialized gas-exchange organs have evolved in arthropods.
    - Morphological and molecular evidence suggests that living arthropods consist of four major lineages that diverged early in the evolution of the phylum: **cheliceriforms** (sea spiders, horseshoe crabs, scorpions, ticks, mites, and spiders); **myriapods** (centipedes and millipedes); **hexapods** (insects and their wingless, six-legged relatives); and **crustaceans** (crabs, lobsters, shrimps, barnacles, and many others).
    1. **Cheliceriforms** are named for clawlike feeding appendages called *chelicerae*, which serve as pincers or fangs. The earliest cheliceriforms were **eurypterids**, or water scorpions. Most of the marine cheliceriforms, including all of the eurypterids, are extinct. Among the marine cheliceriforms that survive today are the sea spiders (pycnogonids) and horseshoe crabs. The bulk of modern cheliceriforms are **arachnids**, a group that includes scorpions, spiders, ticks, and mites. Arachnids have a cephalothorax that has six pairs of appendages: the chelicerae; a pair of appendages called *pedipalps* that function in sensing, feeding, or reproduction; and four pairs of walking legs. In most spiders, gas exchange is carried out by **book lungs**, stacked platelike structures contained in an internal chamber. A unique adaptation of many spiders is the ability to catch insects by constructing webs of silk, a liquid protein produced by specialized abdominal glands.
    2. Millipedes and centipedes belong to the subphylum **Myriapoda**, the myriapods. The myriapod head has a pair of antennae and three pairs of appendages modified as mouthparts, including the jaw-like **mandibles**.
        1. Millipedes (class **Diplopoda**) have a large number of legs. Each truck segment is formed from two fused segments and bears two pairs of legs. They eat plant matter.
        2. Centipedes (class **Chilopoda**) are carnivores. Each segment of a centipede's trunk region has one pair of legs.
    3. Insects and their relatives (subphylum **Hexapoda**) are more species-rich than all other forms of life combined. They live in almost every terrestrial habitat and in fresh water. The internal anatomy of an insect includes several complex organ systems. A fossil record of diverse insect mouthparts indicates that specialized feeding on gymnosperms and other Carboniferous plants also contributed to early adaptive radiations of insects. Later, the evolutionary expansion of flowering plants stimulated another major increase in insect diversity.
        1. Flight is one key to the great success of insects because an animal that can fly can escape many predators, find food and mates, and disperse to new habitats much faster than an animal that must craw about on the ground.
        2. Many insects undergo metamorphosis during their development. In **incomplete metamorphosis**, the young (called nymphs) resemble adults but are smaller, have different body proportions, and lack wings. The nymph undergoes a series of molts, each time looking more like an adult. In **complete metamorphosis**, the larval stages are specialized for eating and growing and are known as caterpillar, maggot, or grub. The larval stage looks entirely different from the adult stage.
        3. Reproduction in insects is usually sexual, with separate male and female individuals. Adults come together and recognize each other as members of the same species by advertising with bright colors, sound, or odors.
        4. Insects are classified in more than 30 orders.
        5. We depend on bees, flies, and many other insects to pollinate our crops and orchards. On the other hand, insects are carriers for many diseases, including Africa sleeping sickness.
    4. Crustaceans (subphylum **Crustacea**) typically have highly specialized appendages. Most crustaceans have remained in marine environments. Sexes are separate in most crustaceans
        1. One of the largest groups of crustaceans is the **isopods**, which include terrestrial, freshwater, and marine species. Among the terrestrial isopods are the pill bugs.
        2. Lobsters, crayfishes, crabs, and shrimps are all relatively large crustaceans called **decapods**.
        3. Planktonic crustaceans include many species of **copepods**, which are among the most numerous of all animals, as well as the shrimplike krill, which grow to about 5 cm long.
        4. Barnacles are a group of mostly sessile crustaceans whose cuticle is hardened into a shell containing calcium carbonate.

5. Echinoderms and chordates are deuterostomes.

1. Sea stars, sea urchins, and other echinoderms (phylum **Echinodermata**) may seem to have little in common with phylum Chordata, which includes the vertebrates—animals that have a backbone. In fact, however, echinoderms and chordates share features characteristic of a deuterostome mode of development, such as radial cleavage and formation of the mouth at the end of the embryo opposite the blastopore.
2. Sea stars and most other **echinoderms** are slow-moving or sessile marine animals. A thin epidermis covers an

endoskeleton of hard calcareous plates. Unique to echinoderms is the **water vascular system**, a network of hydraulic canals branching into extensions called **tube feet** that function in locomotion, feeding, and gas exchange. Sexual reproduction of echinoderms usually involves separate male and female individuals that release their gametes into the water. Living echinoderms are divided into six classes:

1. **Asteroidea (sea stars)**: Sea stars have multiple arms radiating from a central disk, the undersurfaces of which bear tube feet. By combination of muscular and chemical actions, the tube feet can attach to or detach from a substrate. Sea stars can regrow lost arms, and members of one genus can even regrow an entire body from a single arm if part of the central disk remains attached.
2. **Ophiuroidea (brittle stars)**: Brittle stars have a distinct central disk and long, flexible arms. They move primarily by lashing their arms in serpentine movements.
3. **Echinoidea (sea urchins and sand dollars)**: Sea urchins and sand dollars have no arms, but they do have five roes of tube feet that function in slow movement.
4. **Crinoidea (sea lilies and feather stars)**: Sea lilies live attached to the substrate by a stalk; feathers stars crawl about by using their long, flexible arms.
5. **Holothuroidea (sea cucumbers)**: Sea cucumbers do not look much like other echinoderms. They lack spines, and their endoskeleton is much reduced. Sea cucumbers have five rows of tube feet. Some of the tube feet around the mouth are developed as feeding tentacles.
6. **Concentricycloidea (sea daisies)**: Sea daisies were discovered in 1986, and only three species are known.

3. **Phylum Chordata** consists of two subphyla of invertebrates as well as the hagfishes and the vertebrates. The close relationship between echinoderms and chordates does not mean that one phylum evolved from the other. Echinoderms and chordates have evolved independently of one another for at least 500 million years.

- **Morphology**: external form.
- **Tissue**: group cells with a common function, structure, or both.
- **Organ**: consists of several types of tissues that together carry out particular functions.

I. The Plant Body has a Hierarchy of Organs, Tissues, and Cells.

1. **The Three Basic Plant Organs: Roots, Stems, and Leaves:** The ability to acquire resources arose from the evolution of three basic organs—roots, stems, and leaves. These organs form a **root system** and a **shoot system**, the latter consisting of stems and leaves.
    1. **Roots**: a multicellular organ that anchors a vascular plant in the soil, absorbs minerals and water, and often stores carbohydrates. Tiny **root hairs** increase the surface area of the root. In gymnosperms and eudicots: **taproot**: the one main vertical root. **Lateral roots** extend from the taproot. In seedless vascular plants and most monocots: many small (*adventitious*) roots grow from the stem (*fibrous root system*).
    2. **Stems**: an organ consisting of an alternating system of **nodes**, the points at which leaves are attached, and **internodes**, the stem segments between nodes. In the upper angle (axil) formed by each leaf and the stem is an **axillary bud**, which can form a lateral shoot (branch). The **apical bud** is at the shoot tip. **Apical dominance**: the inhibition of axillary buds by an apical bud.
    3. **Leaves**: In most vascular plants, the **leaf** is the main photosynthetic organ. They generally consist of a flattened **blade** and a stalk, the **petiole**. Grasses lack petioles. Monocots have parallel major veins. Eudicots have a branched network of major veins. There are three major types of leaf shape: simple, compound, and double-compound.
2. **Dermal, Vascular, and Ground Tissues**:
    1. **Tissue system**: a functional unit connecting all of the plant's organs.
    2. **Dermal tissue system**: the plant's outer protective covering. In nonwoody plants, it is usually a single tissue (**epidermis**). The **cuticle** helps prevent water loss. In woody plants, **periderm** replaces the **epidermis** in older regions of stems roots.
    3. The **vascular tissue system** carries out long-distance transport of materials between the root and shoot systems. **Xylem** transports water and minerals; **phloem** transports sugars. The vascular tissue of a root or stem is collectively called the **stele**.
    4. Tissues that are neither dermal nor vascular are part of the **ground tissue system**. Ground tissue that is internal to the vascular tissue is known as **pith**, and ground tissue that is external to the vascular tissue is called **cortex**.
3. **Common Types of Plant Cells**:
    1. **Parenchyma cells** have primary walls that are relatively thin and flexible, and most lack secondary walls. Perform most of the metabolic function so the plant. Retain the ability to divide and differentiate into other types of plant cells.
    2. **Collenchyma cells** help support young parts of the plant shoot. Lack secondary walls and lignin; provide flexible support without restraining growth.
    3. **Schlerenchyma cells**: have thick secondary walls supported by lignin. Mostly dead at functional maturity. Two types of schlerenchyma cells (**sclereids** and **fibers**) are specialized entirely support and strengthening. Sclereids, which are shorter than fibers and irregular in shape, have very thick, lignified secondary walls. Fibers are long, slender, and tapered.
    4. **Water-Conducting Cells of the Xylem** (**tracheids** and **vessel elements**): tubular, elongated cells that are dead at functional maturity. Nearly all plants have tracheids; only angiosperms, a few gymnosperms and a few seedless vascular plants have vessel elements. Tracheids are long and thin, with tapered ends. Vessel elements are wider, shorter, thinner-walled, and less tapered.
    5. **Sugar-Conducting Cells of the Phloem**: Alive at functional maturity. Sugars are transported through cells called **sieve-tube elements**, which lack a nucleus, ribosomes, a distinct vacuole, and cytoskeletal elements and depend entirely on nonconducting **companion cells**.

II. Meristems Generate Cells for New Organs.

1. Growth occurs throughout a plant's life (**indeterminate growth**). In contrast, most animals and some plant organs — such as most leaves, thorns, and flowers — undergo **determinate growth**; that is, they stop growing after reaching a certain size.
2. **Annuals** complete their life cycle in a single year or less. **Biennials** generally require two growing seasons to complete their life cycle, flowering and fruiting only in their second year. **Perennials** live many years and include trees, shrubs, and some grasses.
3. Plants are capable of indeterminate growth because they have perpetually embryonic tissues (**meristems**). **Apical meristems,** located at the tips of roots and shoots and in the axillary buds of shoots, provide additional cells that enable the plant to grow in length (**primary growth**). Growth in thickness (**secondary growth**) is caused by the activity of **lateral meristems** called the vascular cambium and cork cambium. The **vascular cambium** adds layers of vascular tissue called secondary xylem (wood) and secondary phloem. The **cork cambium** replaces the epidermis with the thicker, tougher periderm.
4. Cells that remain as sources of new cells are called *initials*. The new cells displaced from the meristems are called *derivatives*.

III. Primary Growth Lengthens Roots and Shoots

1. The results of primary growth are the **primary plant body**.
2. **Primary Growth of Roots**: The tip of a root is covered by a thimble-like **root cap**, which secretes a polysaccharide slime that lubricates the soil around the tip of the root.
    1. The *zone of cell division* includes the root apical meristem and its derivatives. New root cells are produced in this region, including the root cap.
    2. In the *zone of elongation*, root cells elongate and push the root tip farther into the soil.
    3. In the *zone of differentiation*, or zone of maturation, cells complete their differentiation and become distinct cell types.
    4. The innermost layer of the cortex is called the **endodermis**, a cylinder one cell thick that forms the boundary within the vascular cylinder. Lateral roots arise from the **pericycle**, the outermost cell layer in the vascular cylinder. A lateral root pushes through the cortex and epidermis until it emerges form the established root.
3. **Primary Growth of Shoots**: A shoot apical meristem is a dome-shaped mass of dividing cells at the shoot tip. Leaves develop from **leaf primordia**, finger-like projections along the sides of the apical meristem.
    1. **Tissue Organization of Stems**: The epidermis covers stems as part of the continuous dermal tissue system. Lateral shoots develop from axillary bud meristems on the stem's surface and disrupt no other tissues. In most eudicot species, the vascular tissue consists of vascular bundles arranged in a ring. In most monocot stems, the vascular bundles are scattered throughout the ground tissue.

2. **Tissue Organization of Leaves**: The epidermal barrier is interrupted by **stomata**, which allow gas exchange between the surrounding air and the photosynthetic cells inside the leaf. Two **guard cells** regulate the opening and closing of the stomata.
    1. The ground tissue of a leaf (**mesophyll**) is sandwiched between the upper and lower epidermal layers. The *palisade mesophyll* consists of one or more layers of elongated parenchyma cells on the upper part of the leaf. The *spongy mesophyll* is below the palisade mesophyll.
    2. The vascular system of each leaf is continuous with the vascular tissue of the stem. Each vein is enclosed by a protective *bundle sheath*.

4. **SECONDARY GROWTH ADDS GIRTH TO STEMS AND ROOTS IN WOODY PLANTS.**

1. The **secondary plant body** consists of the tissues produced by the vascular cambium and cork cambium. All gymnosperm species and many eudicot species have secondary growth, but its rare in monocots.

- *Dendrochronology*: the science of analyzing tree ring growth patterns.

2. **The Vascular Cambium and Secondary Vascular Tissue**: The vascular cambium is a cylinder of meristematic cells, often only one cell thick. In a typical woody stem, the vascular cambium consists of a continuous cylinder of undifferentiated parenchyma cells, located outside the pith and primary xylem and to the inside of the cortex and primary phloem. In a typical woody root, the vascular cambium forms to the exterior of the primary xylem and interior to the primary phloem and pericycle. *Heartwood*: old xylem that no longer transports water. *Sapwood*: xylem that still transports water.
3. **The Cork Cambium and the Production of Periderm**: Periderm consists of two tissues: *phelloderm,* a thin layer of parenchyma cells that forms to the interior of the cork cambrium; and cork, a layer of dead cells with waxy *suberin*. Dotting the periderm are small, raised areas (**lenticles**), in which there is more space between cork cells, enabling living cells within a woody stem or root to exchange gases with the outside air. **Bark** includes all tissues external to the vascular cambium.

5. **GROWTH, MORPHOGENESIS, AND DIFFERENTIATION PRODUCE THE PLANT BODY**

- **Morphogenesis**: the development of body form and organization.

1. **Molecular Biology: Revolutionizing the Study of Plants**: Researchers are attempting to create mutants for every gene in the genome of *Arabidopsis thaliana*.
2. **Growth: Cell Division and Cell Expansion:**
    1. **The Plane and Symmetry of Cell Division:** Microtubules in the cytoplasm become concentrated into a ring (**preprophase band**) that predicts the future plane of cell division.
    2. **Orientation of Cell Expansion**: In a growing cell, enzymes weaken the cross-links in the cell wall, allowing it to expand as water diffuses into the vacuole by osmosis. Plant cells rarely expand equally in all directions. Their greatest expansion is usually oriented along the plant's main axis. The orientation of microtubules in the cell's outermost cytoplasm that determines the orientation of cellulose microfibrils. Cells expand perpendicular to the grain of the microfibrils.
    3. **Microtubules and Plant Growth**: *fass* mutants lack organized microtubules, so they have unusually squat cells with random planes of cell division.
3. **Morphogenesis and Pattern Formation**:
    1. **Pattern formation**: the development of specific tissues in specific locations. **Positional information** tells each cell where it is. Positional information includes **polarity**, the condition of having structural or chemical differences at opposite ends of an organism.
4. **Gene Expression and Control of Cellular Differentiation:** Cellular differentiation depends on the control of gene expression. The activation or inactivation of specific genes depends on positional information. Differential expression of a homeotic gene called *GLABRA-2* is required for appropriate root hair distribution.
5. **Location and a Cell's Developmental Fate**:
    1. *Clonal analysis*: the cell lineages derived from each cell in an apical meristem are mapped during organ development.
    2. The cell's *final* position in a emerging organ determines what kind of cell it will become.
6. **Shifts in Development: Phase Changes**
    1. **Phase change:** morphological changes that arise when the apical meristem matures. Juvenile nodes and internodes retain their juvenile status even after the shoot continues to elongate and the shoot apical meristem has changed to the adult phase.
7. **Genetic Control of Flowering**: Floral growth is determinate: the production of a flower by a shoot apical meristem stops the primary growth of that shoot. The transition from vegetative growth to flowering is associated with the switching on of floral **meristem identity genes**. Plant biologists have identified several **organ identity genes** that regulate the development of the characteristic floral patterns. According to the **ABC model**, each class of organ identity genes is switched on in two specific whorls of the floral meristem.

0. Overview: Underground Plants:

1. A peculiar genus of perennial plants called stone plants (*Lithops*) live a subterranean lifestyle. Except for the tips of two succulent leaves that are exposed to the surface, a stone plant lives entirely below ground. Each leaf tip has a region of clear, lens-like cells that allow light to penetrate to the photosynthetic issues underground.

1. Land Plants Acquire Resources Both Above and Below Ground.

1. Above ground: Sunlight and CO_2. Below ground: Water and minerals.
2. Algal ancestors obtained everything absorbed water, minerals and CO_2 directly from the water in which they lived.
3. Early land plants had cuticles and few stomata to avoid excessive water loss and rhizoids. ↑surface area→↑evaporation. ↑Height→↑anchorage→multicellular, branching roots. ↑Height also → ↑ efficiency of transport→Evolution of xylem and phloem.
4. **Shoot Architecture and Light Capture**: stems serve as supporting structures for leaves and as conduits for the transport of water and nutrients. Variations in shoot systems arise largely from the form and arrangement of leaves, the outgrowth of axillary buds, and the relative growth in stem length and thickness.
    1. **Phyllotaxy**: the arrangement of leaves on a stem. Alternate/spiral=one leaf per node. Opposite=two leaves per node. Whorled= 3 or more leaves per node. Most angiosperms have alternate phyllotaxy, each successive leaf emerging about 137.5° from the site of the previous ones.
        I. *Leaf area index*: the total upper leaf surface of a single plant or an entire crop divided by the surface area of the land on which the plant or crop grows. *Self-pruning*: non-productive leaves or branches undergo programmed cell death.
        2. Some plants have horizontally orientated leaves; others have vertically orientated leaves.
        3. Plants must choose between branching or growing tall.
5. **Root Architecture and Acquisition of Water and Minerals**: Tall plants typically have strong taproot systems. Most monocots have a fibrous root system that does not anchor as well as the taproot system does. Physiological mechanisms reduce competition within the root system of a plant. **Mycorrhizae**: mutalistic associations between roots and fungi.

2. Transport Occurs by Short-Distance Diffusion or Active Transport and by Long-Distance Bulk Flow.

1. **Diffusion and Active Transport of Solutes:** Diffusion is considered passive transport because it does not require energy. Most solutes must pass through **transport proteins** embedded in the membrane. **Proton pumps** use energy from ATP to pump protons out of the cell, resulting in a H^+ gradient, creating a **membrane potential**. In **cotransport**, a transport protein couples the diffusion of one solute with active transport of another.
2. **Diffusion of Water (Osmosis)**: The combined effects of solute concentration and physical pressure are incorporated into a quantity called the **water potential** (measured in **megapascals**)**.** Free water moves from regions of higher water potential to regions of lower water potential.
    1. **How Solutes and Pressure Affect Water Potential**: The **solute potential** (Ψ_S) of a solution is proportional to the molarity. Solute potential is also called **osmotic potential** because solutes affect the direction of osmosis. **Pressure potential** (Ψ_P) is the physical pressure on a solution.
    2. **Measuring Water Potential**: $\Psi = \Psi_S + \Psi_P$.
    3. **Aquaporins Facilitate Diffusion of Water.**
3. **Three Major Pathways of Transport**: **apoplastic**: through extracellular spaces. **Symplastic**: through intracellular spaces. **Transmembrane**: goes through both extracellular and intracellular spaces.
4. **Bulk Flow in Long-Distance Transport**: *Bulk Flow*: the movement of a fluid driven by pressure.

3. Water and Minerals are Transported from Roots to Shoots.

- **Xylem sap**: the water and dissolved minerals in the xylem.
- **Transpiration**: the loss of water vapor from leaves and other aerial parts of the plant.
- **Guttation**: the exudation of water droplets that can be seen in the morning on the tips or edges of some plant leaves.

1. **Absorption of Water and Minerals by Root Cells**. Root cells have root hairs to increase surface area. Some minerals are transported actively inside.
2. **Transport of Water and Minerals into the Xylem**: The **endodermis**, the innermost layer of cells in the root cortex, surrounds the stele and functions as a last checkpoint for the selective passage of minerals from the cortex into the vascular tissue. Minerals and water taking the *apoplastic route* are blocked by the **Casparian strip** and must enter a cell to pass into the stele.
3. **Bulk Flow Driven by Negative Pressure in the Xylem**:
    1. **Pushing Xylem Sap: Root Pressure**: Endodermis pumps ions into the stele, and water follows. If root pressure > transpiration, then **guttation** occurs.
    2. **Pulling Xylem Sap: The Transpiration-Cohesion-Tension Mechanism**: Water evaporates from leaves, and cohesion and tension pull water up from the roots. *Cavitation* is the formation of a water vapor pocket.

4. Stomata Help Regulate the Rate of Transpiration.

- **Xerophytes**: plants adapted to deserts.

1. **Stomata: Major Pathways for Water Loss**: About 95% of the water a plant loses escapes through stomata.
2. **Mechanisms of Stomatal Opening and Closing**: ↑$[K^+]$ in guard cell→water follows→guard cell becomes turgid→ stomata opens.
3. **Stimuli for Stomatal Opening and Closing**: At least three cues contribute to stomatal opening at dawn: light, CO_2 depletion, and an internal "clock" in guard cells (**circadian rhythms**). Abscisic acid signals guard cell closing.
4. **Effects of Transpiration on Wilting and Leaf Temperature**: If transpiration is too high, the plant wilts. Transpiration also results in evaporative cooling.
5. **Adaptations That Reduce Evaporative Water Loss**: Some plants complete their short life cycles during the brief rainy seasons. Many have reduced leaves and carry out photosynthesis with their stems. Some have CAM photosynthesis.

5. Sugars are Transported From Leaves and Other Sources to Sites of Use or Storage.

- **Phloem sap**: the aqueous solution that flows through sieve tubes.
- **Sugar source**: plant organ that is a net producer of sugar.
- **Sugar sink**: plant organ that is a net consumer or depository of sugar.

1. **Translocation**: transportation of the products of photosynthesis via the phloem.
2. Sinks usually receive sugar from the nearest sugar sources. Neighboring sieve tubes may carry sap in opposite directions if they originate and end in different locations. Sugars are actively transported into the sieve tube elements, and water follows. In some plants, the walls of the companion cells feature many ingrowths, enhancing solute transfer between apoplast and symplast (**transfer cell**). Sugars are actively transported into sugar sinks.
3. The phloem transports sugars by positive pressure.
4. If there are more sinks that can be supported by sources, a plant might abort some flowers, seeds or fruits (*self-thinning*).

6. The Symplast is Highly Dynamic.

1. Plant transport is a dynamic process: the transport needs of a plant cell typically change during its development.
2. Plasmodesmata are highly dynamic structures that can change in permeability and number. They can open or close rapidly in response to changes in turgor pressure, cytoplasmic calcium levels, or cytoplasmic pH.
3. **Electrical Signaling in the Phloem**: The phloem serves a nerve-like function in the Venus flytrap.
4. **Phloem**: **An Information Superhighway**: Hormones and RNA can travel via the phloem, influencing cell growth in many areas of a plant.

- **Anatomy**: the biological form
- **Physiology**: biological function

1. Animal form and function are correlated at all levels of organization
    1. An animal's size and share are fundamental aspects of form that significantly affect the way an animal interacts with its environment.
    2. Animals need to exchange materials with their environment, and this need imposes limitations on their body plans. Exchange occurs as substances dissolved in an aqueous medium move across the plasma membrane of each cell. The rates of exchange for nutrients, waste products, and gases are proportional to membrane surface area.
    3. The opportunity for exchange is strongly influenced by cell number. Many animals will a simple internal organization have body plans that enable direct exchange between the external environment and nearly all cells. In whales and most other animals, extensively branched or folded surfaces are the evolutionary adaptation that enables sufficient exchange with the environment.
    4. In all animals, the spaces between cells are filled with fluid, often called **interstitial fluid**. Complex body plans also include a circulatory fluid, such as blood.
    5. With a complex body plan, an animal can maintain a relatively stable internal environment while living in a variable external environment. A complex body plan is especially advantageous for animals living on land, where the external environment may be highly variable.
    6. Cells are organized into **tissues**, groups of cells of similar appearance and a common function. Different tissues are further organized into function units called **organs**. Groups of **organs** that work together provide and additional level of organization and coordination and make up an **organ system**.
    7. Animal tissues fall into four main categories: epithelial tissue, connective tissue, muscle tissue, and nervous tissue.
        1. **Epithelial tissue** covers the outside the body and lines organs and cavities within the body. They are often closely packed and contain many tight junctions to create a watertight seal. Epithelial cell shape may be *cuboidal*, *columnar*, or *squamous*. Cells may be arranged in a *simple epithelium*, a *stratified epithelium*, or a *pseudostratified epithelium*.
        2. The most common functions of **connective tissues** are to bind and support other tissues in the body. Connective tissue consists of a sparse population of cells scattered through an extracellular matrix. The matrix generally consists of a web of fibers embedded in a uniform foundation that may be liquid, jellylike, or solid. There are six major types of connective tissue in vertebrates: loose connective tissue, cartilage, fibrous (dense) connective tissue, adipose tissue, blood, and bone.
            1. Connective tissue fibers, which are made of protein, are of three kinds: *Collagenous fibers* to provide strength combined with flexibility; *elastic fibers* that are easily stretched but snap back to their original length when tension is released, and *reticular fibers*.
            2. Two cell types dominate in connective tissue: **fibroblasts** to secrete the protein ingredients of the extracellular fibers, and **macrophages** to engulf foreign particles and dead cells.
        3. The tissue responsible for nearly all types of body movement is **muscle tissues**. There are three types of muscle tissue in the vertebrate body: skeletal, cardiac, and smooth muscle
        4. The function of **nervous tissue** is to sense stimuli and transmit signals in the form of nerve impulses from one part of the animal to another. Nervous tissue contains **neurons**, which have extensions called axons that are unique specialized to transmit nerve impulses. It also includes different forms of **glial cells**, or **glia**, which help nourish, insulate, and replenish neurons.
    8. There are two different control loops in the body: the endocrine system and the nervous system.
        1. The signaling molecules broadcast throughout the body by the endocrine system are called **hormones**. Depending on which cells have receptors for that hormone, the hormone may have an effect in just a single location or in sites throughout the body. Hormones are relatively slow acting but often long-lasting because they remain in the bloodstream and target tissues for seconds, minutes, or even hours.
        2. In the nervous system, a single is not broadcast throughout the entire body. Instead, each single, called a nervous impulse, travels a target cell along a dedicated communication line, consisting mainly of the neuron extensions called axons. Four types of cells receive nerve impulses: other neurones, muscle cells, endocrine cells, and exocrine cells. Unlike the endocrine system, the nervous system conveys information by the *pathway* the signal takes. Overall, transmission is extremely fast.

- **Homeostasis** means "steady state," or internal balance.
- **Negative feedback**: the response reduces the stimulus.
- **Positive feedback**: triggers mechanisms that amplify rather than diminish the stimulus.

2. Feedback control loops maintain the internal environment in many animals
    1. Faced with environmental fluctuations, animals manage their internal environment by either regulating or conforming.
        1. An animal is said to be a **regulator** for a particular environmental variable if it uses internal control mechanisms to regulate internal change in the face of external fluctuation.
        2. An animal is said to be a **conformer** for a particular environmental variable it it allows its internal condition to conform to external changes in the variable.
    2. Like a home heating system, an animal achieves **homeostasis** by maintaining a variable, such as body temperature or solute concentration, at or near a particular value, or **set point** or **normal range**. Fluctuations in the variable above or below the set point serve as the **stimulus**. A receptor, or **sensor**, detects the stimulus and triggers a **response**, a physiological activity that helps return the variable to the set point.
    3. The set points and normal ranges for homeostasis can change under various circumstances. One way in which the normal range of homeostasis may change is through **acclimatization**, he process by which an animal adjusts to changes in its external environment.
3. Homeostatic processes for thermoregulation involve form, function, and behavior
    1. **Thermoregulation** is the process by which animals maintain an internal temperature within a tolerable range.
    2. Birds and mammals are mainly **endothermic**, meaning that they are warmed mostly by heat generated by metabolism
    3. In contrast, amphibians, lizards, snakes, turtles, many fishes, and most invertebrates are mainly **ectothermic**, meaning that they gain most of their heat from external sources.
    4. Because their heat source is largely environmental, ectotherms generally need to consume much less food than endotherms of equivalent size—an advantage if food supplies are limited. Ectotherms also usually tolerate larger fluctuations in their internal temperatures. Many adjust body temperature by behavioral means, such as seeking out shade or basking in the sun.
    5. An animal whose body temperature varies with its environment is called a **poikilotherm**. In contrast, a **homeotherm** has a relatively constant body temperature.
    6. Any organism, like any object, exchanges heat by four physical processes: conduction, convection, radiation, and evaporation. In mammals, several of these mechanisms involve the **integumentary system**, the outer covering of the body, consisting of the skin, hair, and nails.

7. A major thermoregulatory adaptation in mammals and birds is insulation, which reduces the flow of heat between an animal and its environment. Sources of insulation include hair, feathers, and layers of fat formed by adipose tissue.
8. Adaptations that regulate the extent of flood flow near the body surface or that trap heat within the body core play a significant role in thermoregulation. In response to changes in the temperature of their surroundings, many animals alter the amount of blood flowing between their body core and their skin. Nerve signals that relax the muscles of the vessel walls result in *vasodilation*, an increase in the diameter of superficial blood vessels. Blood flow in the skin is elevated. The reverse process, *vasoconstriction*, reduces blood flow and heat transfer by decreasing the diameter of superficial vessels.
9. In many birds and mammals, reduction of heat loss relies on **countercurrent exchange**, the flow of adjacent fluids in opposing directions that maximizes transfer rates of heat or solutes. Heat transfer involves an antiparallel arrangement of blood vessels called a *countercurrent heat exchanger.* Certain sharks, bony fishes, and insects also use countercurrent heat exchange. Many endothermic insects have a countercurrent exchanger that helps maintain a high temperature in the thorax, where their flight muscles are located.
10. Water absorbs considerable heat when it evaporates; this heat is carried away from the body surface with the water vapor. Adaptations can greatly augment this cooling effect. Panting is important in birds and many mammals. Sweating or bathing moistens the skin and enhances evaporative cooling.
11. Both endotherms and ectotherms control body temperature through behavioral responses. Some terrestrial invertebrates have certain postures than enable them to maximize or minimize their absorption of heat from the sun.
12. Endotherms can vary heat production to match changing rates of heat loss. Heat production—thermogenesis—is increased by muscle activity like moving and shivering. Through shivering and nonshivering thermogenesis, mammals and birds in cold environments can increase their metabolic heat production by as much as five to ten times the levels that occur in warm conditions.
13. In bird and mammals, acclimatization to seasonal temperature changes often includes adjusting the amount of insulation —by growing a thicker coat of fur in the winter and shedding it in the summer, for example.
14. Some ectotherms that experience subzero body temperature protect themselves by producing “antifreeze” compounds that prevent ice formation in the cells.
15. The sensors that control thermoregulation are concentrated in the **hypothalamus**, a region of the brain near the ears. The hypothalamus contains a group of nerve cells that functions as a thermostat. A variety of experiments have shown that fever reflects an increase in the set point for the biological thermostat.

4. Energy requirements are related to animal size, activity, and environment.
   1. The overall flow and transformation of energy in an animal—its **bioenergetics—**determines nutritional needs and is related to an animal’s size, activity, and environment.
   2. Heterotrophs, such as animals, must obtain their chemical energy from food, which contains organic molecules synthesized by other organisms. They use this energy to fuel metabolism and activity.
   3. Most energy-containing molecules are used to generate ATP. ATP produced by cellular respiration and fermentation powers cellular work, enabling cells, organs, and organ systems to perform the functions that keep an animal alive. Energy in the form of AT is also used in biosynthesis, which is needed for body growth and repair, synthesis of storage material such as fat, and production of gametes.
   4. The amount of energy an animal uses in a unit of time is called its **metabolic rate—**the sum of all the energy-requiring biochemical reactions over a give time interval. Metabolic rate can be measure by monitoring an animal’s rate of heat loss. Metabolic rate can also be determined from the amount of oxygen consumed or carbon dioxide produced by an animal’s cellular respiration.
   5. The minimum metabolic rate of a nongrowing endotherm that is at rest, has an empty stomach, and is not experiencing stress is called the **basal metabolic rate (BMR)**. The metabolic rate of a fasting, nonstressed ectotherm at rest at a particular temperature is called its **standard metabolic rate (SMR)**.
   6. Metabolic rate is affected by size activity, and whether or not the animal is an endotherm or an ectotherm.
   7. Remarkably, the relationship between overall metabolic rate and body mass is constant across a wide range of sizes and forms. The reason for the inverse relationship of metabolic rate per unit of body mass to body size is still a subject of debate. Correlated with its higher metabolic rate per gram, the smaller animal has a higher breathing rate, blood volume (relative to its size) and heart rate. Also it must eat much more food per unit of body mass.
   8. For both ectotherms and endotherms, activity greatly affects metabolic rate. In general, the maximum metabolic rate an animal can sustain is inversely related to the duration of activity.
   9. **Torpor**: a physiological state in which activity is low and metabolism decreases, is an adaptation that enables animals to save energy while avoiding difficult and dangerous conditions. **Hiberation** is long-term torpor that is an adaptation to winter cold and food scarcity. Similarly, the slow metabolism and inactivity of *estivation*, or summer torpor, enables animals to survive long periods of high temperatures and scarce water supplies. Many small mammals and birds exhibit a daily torpor that seems to be adapted to feeding patterns.

- **Nutrition**: food being taken in, taken apart, and taken up.
- **Herbivores**: dine mainly on plants or algae.
- **Carnivores** mostly eat other animals.
- **Omnivores** regularly consume animals as well as plants or algea.

1. AN ANIMAL'S DIET MUST SUPPLY CHEMICAL ENERGY, ORGANIC MOLECULES, AND ESSENTIAL NUTRIENTS.
    1. The activities of cells, tissues, organs, and who animals depend on sources of chemical energy in the diet. This energy, after being converted to ATP, powers processes ranging from DNA replication and cell division to vision and flight.
    2. Animals need a source of organic carbon and a source of organic nitrogen. Starting with these materials, animals can construct a great variety of organic molecules.
    3. The materials that an animal's cells require but cannot synthesize are called **essential nutrients**. Obtained from dietary sources, these nutrients include both minerals and preassembled organic molecules.
    4. There are four classes of essential nutrients: essential amino acids, essential fatty acids, vitamins, and minerals.
        1. **Essential amino acids**: any amino acid that must be obtained in prefabricated form. A diet that provides insufficient amounts of one or more essential amino acids causes protein deficiency, the most common type of malnutrition among humans. The proteins in animal products such as meat, eggs, and cheese are "complete," which means they provide all the essential amino acids in their proper proportions. In contrast, most plant proteins are "incomplete," being deficient in one or more essential amino acids.
            1. Some animals have adaptations that help them through periods when their bodies demand extraordinary amounts of protein.
        2. Animals can synthesize most, but not all, of the fatty acids they need. The **essential fatty acids**, the ones they cannot make, are certain fatty acids that are unsaturated. Deficiencies in this class of nutrients are rare.
        3. **Vitamins** are organic molecules with diverse functions that are required in the diet in very small amounts. For humans, 13 essential vitamins have been identified. Vitamins are classified as water-soluble or fat-soluble.
        4. Dietary **minerals** are inorganic nutrients, such as zinc and potassium, that are usually required in small amounts —from less than 1 mg to about 2,500 mg per day.
    5. **Undernourishment** is the result of a diet that consistently supplies less chemical energy than the body requires. When an animal is undernourished, a series of events unfold: the body uses up stored fat and carbohydrates and begins breaking down its own proteins for fuel; muscles begin to decrease in size, and the brain may become protein-deficient. Some of the damage by be irreversible. The animal will eventually die.
    6. **Malnourishment** is the long-term absence from the diet of one or more essential nutrients. The potential effects of malnourishment include deformities, disease, and even death.
    7. Many insights into human nutrition have come from *epidemiology*, the study of human health and disease at the population level.
2. THE MAIN STAGES OF FOOD PROCESSING ARE INGESTION, DIGESTION, ABSORPTION, AND ELIMINATION.
    1. **Ingestion** is the act of eating.
        1. There are four major feeding mechanisms for animals. **Suspension feeders** sift small food particles from the water. **Substrate feeders** are animals that live in or on their food source. **Fluid feeders** suck nutrient-rich fluid from a living host. Most animals, including humans, are **bulk feeders**, which eat relatively large pieces of food.
    2. In **digestion**, food is broken down into molecules small enough for the body to absorb. The hydrolysis of food inside vacuoles, called **intracellular digestion**, begins after a cell engulfs solid food by phagocytosis or liquid food by pinocytosis. In **extracellular digestion**, the breakdown of food happens in compartments that are continuous with the outside of the animal's body.
        1. Many animals with relatively simple body plans have a digestive compartment with a single opening. This pouch, called a **gastrovascular cavity**, functions in digestion as well as in the distribution of nutrients throughout the body.
        2. More complex animals have a digestive tube extending between two openings, a mouth and an anus. Such a tube is called a **complete digestive tract** or, more commonly, an **alimentary canal**. The tube can be organized into specialized compartments that carry out digestion and nutrient absorption in a stepwise fashion.
    3. In the third stage, **absorption**, the animal's cells take up (absorb) small molecules such as amino acids and simple sugars.
    4. **Elimination** completes the process as undigested material passes out of the digestive system
3. ORGANS SPECIALIZED FOR SEQUENTIAL STAGES OF FOOD PROCESSING FORM THE MAMMALIAN DIGESTIVE SYSTEM
    1. In mammals, the digestive system consists of the alimentary canal and various accessory glands that secrete digestive juices through ducts into the canal. The accessory glands of the mammalian digestive system are three pairs of salivary glands, the pancreas, the liver, and the gallbladder.
    2. Food is pushed along the alimentary canal by **peristalsis**, alternating waves of contraction and relaxation in the smooth muscles lining the canal. At some of the junctions between specialized compartments, the muscular layer forms ringlike valves called **sphincters**.
    3. Ingestion and the initial steps of digestion occur in the mouth, or **oral cavity**. Mechanical digestion begins as teeth of various shapes cut, smash, and grind food, making the food easier to swallow and increasing its surface area. Meanwhile, the presence of food stimulates a nervous reflex that causes the **salivary glands** to deliver saliva through ducts to the oral cavity. **Amylase**, an enzyme in saliva, hydrolyzes starch and glycogen into smaller polysaccharides and the disaccharide maltose. After food is deemed acceptable and chewing commences, tongue movements manipulate the food, helping shape it into a ball called a **bolus**.
    4. The **pharynx**, or throat region, opens to two passage-ways: the esophagus, which connects to the stomach, and the trachea, which connects to the lungs. When you swallow, a flap of cartilage called the *epiglottis* prevents food from entering the trachea by covering the *glottis*—the vocal cords and the opening between them. Guided by the movements of the *larynx*, the upper part of the respiratory tract, this swallowing mechanism directs each bolus into the entrance of the esophagus. If the swallowing reflex fails, food or liquids can reach the windpipe and cause choking.
    5. The **stomach** is located just below the diaphragm in the upper abdominal cavity. It secretes a digestive fluid called **gastric juice** and mixes this secretion with the food through a churning action. This mixture of ingested food and digestive juice is called **chyme**. Two components of gastric juice carry out chemical digestion. One is hydrochloric acid (HCl), which disrupts the extracellular matrix that binds cells together in meat and plant material. Protein bonds are attacked by the second component of gastric juice—a **protease**, or protein-digesting enzyme enzyme, called **pepsin**. *Parietal cells* secrete hydrogen and chloride ions, which form hydrochloric acid (HCl). Meanwhile, *chief cells* release pepsin into the lumen in an inactive form called **pepsinogen**. HCl converts pepsinogen to active pepsin by clipping off a small portion of the molecule and exposing its active site. The stomach lining protects against self-digestion by secreting **mucus**, a viscous and slippery mixture of glycoproteins, cells, salts, and water. However, damaged areas of the stomach lining called gastric ulcers may appear. Infection by the acid-tolerant bacterium *Helicobacter pylori* causes ulcers. Chemical digestion by gastric juice is accompanied by the churning action of the stomach. This coordinated

series of muscle contractions and relaxations mixes the stomach contents about every 20 seconds. The sphincter between the esophagus and the stomach normally opens only when a bolus arrives. The sphincter located where the stomach opens to the small intestine helps regulate the passage of chyme into the small intestine, allowing only one squirt at a time.

6. Most enzymatic hydrolysis of macromolecules from food occurs in the **small intestine**. The small intestine is the alimentary canal's longest compartment. The first 25 cm or so of the small intestine forms the **duodenum**, a major crossroad in digestion. It is here that chyme from the stomach mixes with digestive juices from the pancreas, liver, and gallbladder, as well as from gland cells of the intestinal wall itself.
    1. The **pancreas** aids chemical digestion by producing an alkaline solution rich in bicarbonate as well as several enzymes. The bicarbonate neutralizes the acidity of chyme and acts as a buffer. Among the pancreatic enzymes are trypsin and chymotrypsin, proteases secreted into the duodenum in inactive forms.
    2. Digestion of fats and other lipids begins in the small intestines and relies on the production of **bile**, a mixture of substances that is made in the **liver**. Bile is stored and concentrated in the **gallbladder**.
    3. The epithelial lining of the duodenum is the source of several digestive enzyme.

    While enzymatic hydrolysis proceeds, peristalsis moves mixture of chyme and digestive juices along the small intestine. Most digestion is completed in the duodenum. The remaining regions of the small intestine, called the *jejunum* and the *ileum,* function mainly in the absorption of nutrients and water. The small intestine has a huge surface area. Large folds in the lining have finger-like projections called **villi**. In turn, each epithelial cell of a villus has on its apical surface many microscopic appendages, or **microvilli**, that are exposed to the intestinal lumen. The enormous surface area presented by microvilli is an adaptation that greatly increases the total capacity for nutrient absorption.
    4. The sugar fructose moves by facilitated diffusing down its concentration gradient from the lumen of the small intestine into the epithelial cells. From there, fructose exists the basal surface and is absorbed into microscopic blood vessels, or capillaries, at the core of each villus.
    5. Other nutrients, including amino acids, small peptides, vitamins, and most glucose molecules, are pumped against concentration gradients by the epithelial cells of the villus.
    6. After being absorbed by epithelial cells, fatty acids and monoglycerides are recombined into triglycerides. These fats are then coasted with phsopholipids, cholesterol, and proteins, forming water-soluble globules called **chylomicrons**. These are then transported into a **lacteal**, a vessel at the core of each villus. Lacteals are part of the vertebrate lymphatic system.
    7. In contrast with the lacteals, the capillaries and veins that carry nutrient-rich blood away from the villi all converge into the **hepatic portal vein**, a blood vessel that leads directly to the liver. This allows the liver to regulate distribution of nutrients to the rest of the body and remove toxic substances before the blood circulates broadly.
7. The alimentary canal ends with the **large intestine**, which includes the colon, cecum, and rectum. The small intestine connects to the large intestine at a T-shaped junction. One arm of the T is the 1.5-m-long **colon**, which leads to the rectum and the anus. The other arm forms a pouch called the **cecum**. The cecum is important for fermenting ingested material, especially in animals that eat large amounts of plant material. The **appendix**, a finger-like extension of the human cecum, has a minor and dispensable role in immunity. A major function of the **colon** is recover water that has entered the alimentary canal as the solvent of digestive juices. The **feces**, the wastes of the digestive system, become increasingly solid as they are moved along the colon by peristalsis.
    1. A rich flora of mostly harmless bacteria resides in the human colon, contributing approximately one-third of the dry weight of feces. As by-products of their metabolism, many colon bacteria generate gases, including methane and hydrogen sulfide, which has an offensive odor. These gases and ingested air are expelled through the anus. Some of the bacteria produce vitamins, such as biotin, vitamin K, and several B vitamins, including folic acid.

    The terminal portion of the large intestine is the **rectum**, where feces are stored until they can be eliminated. Between the rectum and the anus are two sphincters, the inner one being involuntary and the outer one being voluntary. Periodically, strong contractions of the colon create an urge to defecate.

4. EVOLUTIONARY ADAPTATIONS OF VERTEBRATE DIGESTIVE SYSTEMS CORRELATE WITH DIET.
    1. The digestive systems of mammals and other vertebrates are variations on a common plan, by there are many intriguing adaptations, often associated with the animal's diet.
    2. Dentition, an animal's assortment of teeth, is one example of structural variation reflecting diet. Poisonous snakes have fangs, modified teeth that inject venom into prey, and an elastic ligament that permits the mouth to open very wide, allowing snakes to swallow prey whole.
    3. In general, herbivores and omnivores have longer alimentary canals relative to their body size than do carnivores.
    4. Many herbivores house large populations of mutalistic bacteria and protists in fermentation chambers in their alimentary canals. These microorganisms have enzymes that can digest cellulose. The location of mutalistic microbes in alimentary canals varies, depending on the type of herbivore. For example:
        1. The hoatzin has a large, muscular crop that houses mutalistic microorganisms.
        2. Horses and many other herbivorous mammals house mutalistic microorganisms in a large cecum.
        3. In rabbits and some rodents, mutalistic bacteria living in the large intestine as well as in the cecum. Nourishing by-products of fermentation by bacteria in the large intestine are initially lost with the feces and recovered by *coprophagy*, feeding on some of the feces.
        4. The koala, and Australian marsupial, also has an enlarged cecum.
        5. The most elaborate adaptations for an herbivorous diet have evolved in the animals called **ruminants**, which include deer, sheep, and cattle.
    5. Giant tubeworms that live at deep-sea hydrothermal vents have no mouth or digestive system. Instead, they rely entirely on mutalistic bacteria to generate energy and nutrients from the carbon dioxide, oxygen, hydrogen sulfide, and nitrate available at the vents.

5. HOMEOSTATIC MECHANISMS CONTRIBUTE TO AN ANIMAL'S ENERGY BALANCE.
    1. Food balances the expenditure of energy for metabolism and activity, and storage. Nearly all of an animal's AT generation is based on the oxidation of energy-rich organic molecules—carbohydrates, proteins, and fats—in cellular respiration. In humans, the primary sites of storage are liver and muscle cells. Excess energy from the diet is stored there in the form of glycogen. Adipose (fat) cells represent a secondary site of energy storage. When more energy is required than is generated from the diet, the human body generally expends liver glycogen first and then draws on muscle glycogen and fat.
    2. **Overnourishment**, the consumption of more calories than the body needs for normal metabolism, causes obesity, the excessive accumulation of fat. Obesity, in turn, contributes to a number of health problems, including the most common type of diabetes (type 2), cancer of the colon and breast, and cardiovascular disease that can lead to heart attacks and strokes.
    3. Researchers have discovered several homeostatic mechanisms that help regulate body weight. Operating as feedback

circuits, these mechanisms control the storage and metabolism of fat. Several hormones regulate long-term and short-term appetite by affecting a "satiety center" in the brain. Leptin is a product of adipose cells, so levels rise when body fat increases, cuing the brain to suppress appetite.

4. Though fat hoarding can be a health liability, it may have been an advantage in our evolutionary past.
5. The relationship between fat storage and evolutionary adaptation in animals is sometimes complex. Consider the plump offspring of the seabirds called petrels. Their parents must fly long distances to find food. Most of the food that they bring to their chicks is very rich in lipids. To get all the protein they need, young petrels have to consume many more calories than they burn in metabolism and consequently become obese. The youngsters must then fast for several days to lose enough weight to be capable of flight.

3. CIRCULATORY SYSTEMS LINK EXCHANGE SURFACES WITH CELLS THROUGHOUT THE BODY.
   1. In simple animals, every body cell is in direct contact with the environment. Each cell can thus exchange materials directly with the surrounding medium.
      1. In cnidarians, a central gastrovascular cavity functions both in digestion and in the distribution of substances throughout the body. Since the body wall is a mere two cells thick, the nutrients must diffuse only a short distance to reach the cells of the outer layer. Some cnidarians, such as jellies, have gastrovascular cavities with a much more elaborate branching pattern.
      2. A flat body, such of flatworms and planarians, optimizes diffusional exchange by increasing surface area and minimizing diffuse distances.
   2. In more complex animals, a circulatory system moves fluid between each cell's immediate surroundings and the tissues where exchange with the environment occurs. A circulatory system has three basic components: a circulatory fluid, a set of interconnecting tubes, and a muscular pump, the **heart**.
      1. Arthropods and most mollusks have an **open circulatory system**, in which the circulatory fluids bathes the organs directly. In these animals, the circulatory fluid, called **hemolymph**, is also the interstitial fluid.
      2. In a **closed circulatory system**, blood is confined to vessels and is distinct from the interstitial fluid. The benefits of close circulatory systems include relatively high blood pressures, which enable the effective delivery of O_2 and nutrients to the cells of larger and more active animals. Closed systems are also particularly well suited to regulating the distribution of blood to different organs.
   3. The closed circulatory system of humans and other vertebrates is often called the **cardiovascular system**.
      1. Arteries, veins, and capillaries are the tree main types of blood vessels. Arteries and veins are distinguished by the *direction* in which they carry blood. Arteries carry blood from the heart *towards* capillaries, and veins return blood to the heart *from* capillaries. There is one exception: the portal veins, which carry blood between pairs of capillary beds.
      2. The hearts of all vertebrates contain two or more muscular chambers. The chambers that receive blood entering the heart are called **atria**. The chambers responsible for pumping blood out of the heart are called **ventricles**.
   4. In bony fishes, rays, and sharks, the heart consists of two chambers: an atrium and a ventricle. The blood passes through the heart once in each complete circuit, an arrangement called **single circulation**. In single circulation, blood that leaves the heart passes through two capillary beds before returning to the heart.
   5. The circulatory system of amphibians, reptiles, and mammals have two distinct circuits, an arrangement called **double circulation**. The right side of the heart delivers oxygen-poor blood to the capillary beds of the gas exchange tissues. This part of the circulation is called a **pulmonary circuit** if the capillary beds involved are all in the lungs, as in reptiles and mammals. It is called a **pulmocutaneous circuit** if it includes capillaries in both the lungs and the skin, as in many amphibians. The left side of the heart pumps oxygen-rich blood to the rest of the body in the **systemic circuit**. Double circulation provides a vigorous flow of blood to the brain, muscles, and other organs because the heart re-pressurizes the blood destined for these tissues after it passes through the capillary beds of the lungs or skin. Indeed, blood pressure is often much higher in the systemic circuit than in the gas exchange circuit.
      1. Frogs and other amphibians have a heart with three chambers: two atria and one ventricle. A ridge within the ventricle diverts most of the oxygen-poor blood from the right atrium into the pulmocutaneous circuit and most of the oxygen-rich blood from the left atrium into the systemic circuit. When underwater, a frog adjusts its circulation, for the most part shutting off blood flow to its temporarily ineffective lungs.
      2. Turtles, snakes, and lizards have a three-chambered heart, with a septum partially dividing the ventricle into separate right and left chambers. In alligators, caimans, and other crocodilians, the septum is complete, but the pulmonary and systemic circuits are connected where the arteries exit the heart.
      3. In all mammals and birds, the ventricle is completely divided, such that there are two atria and two ventricles. The left side of the heart receives and pumps only oxygen-rich blood, while the right side receives and pumps only oxygen-poor blood.

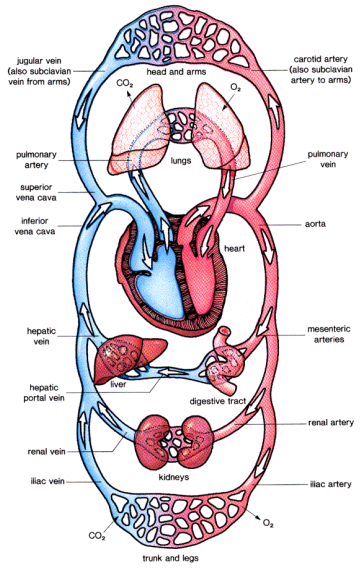


Illustration 1: Human circulatory system

4. COORDINATED CYCLES OF HEART CONTRACTION DRIVE DOUBLE CIRCULATION IN MAMMALS.
   1. The timely delivery of O_2 to the body's organs is critical: Brain cells, for example, die within just a few minutes if their O_2 supply is interrupted.
   2. Contraction of the right ventricle pumps blood to the lungs where it loads O_2 and unloads CO_2. Oxygen-rich blood returns from the lungs via the pulmonary veins to the left atrium of the heart. Next, the oxygen-rich blood flows into the left ventricle, which pumps the oxygen-rich blood out to the body tissues. Blood leaves the left ventricle via the aorta, which branches into the arteries and then the capillary beds. In the capillary beds, the blood unloads O_2 and loads CO_2. Oxygen-poor blood from the head, neck and forelimbs is channeled into a large vein, the superior vena cava. Another large vein, the inferior vena cava, drains blood from the trunk and hid limbs.
   3. The heart contracts and relaxes in a rhythmic cycle. When it contracts, it pumps blood; when it relaxes, its chambers fill with blood. One complete sequence of pumping and filling is referred to as the **cardiac cycle**. The contraction phase of the cycle is called **systole**, and the relaxation phase is called **diastole**. **Heart rate** multiplied by **stroke volume** determines the cardiac output. Four valves in the heart prevent backflow and keep blood moving in the correct direction. An **atrioventricular (AV) valve** lies between each atrium and ventricle. **Semilunar valves** are located at the two exists of the heart: where the aorta leaves the left ventricle and where the pulmonary artery leaves the right ventricle. The first heart sound ("lub") is created by the recoil of blood against the closed AV valves. The second sound ("dup") is produced by the recoil of blood against the closed semilunar valves. If blood squirts backwards through a defective valve, it may produce an abnormal sound called a **heart murmur**.
   4. **Maintaining the Heart's Rhythmic Beat**: Some cardiac muscle cells are autorhythmic, meaning they contract and relax repeatedly without any signal from the nervous system. The **sinoatrial (SA) node**, or *pacemaker*, sets the rate and timing in which all cardiac muscle cells contract by generating electrical impulses much like the ones in nerve cells. The impulses originating at the SA node reach other autorhythmic cells that are located in the wall between the left and right atria. These cells form a relay point called the **atrioventricular (AV) node**. The signals from the AV node are conducted throughout the ventricular walls by specialized muscle fibers called bundle branches and Purkinje fibers. The medical test called an **electrocardiogram** (**ECG** or, sometimes, **EKG**) uses electrodes placed on the skin to detect and record these currents. Two sets of nerves, the sympathetic and parasympathetic nerves regulate the pace of the heart. Hormones secreted into the blood also influence the pacemaker, as does body temperature.

5. PATTERNS OF BLOOD PRESSURE AND FLOW REFLECT THE STRUCTURE AND ARRANGEMENT OF BLOOD VESSELS.
   1. The same physical principles that govern the operation of plumbing systems apply to the functioning of blood vessels.
   2. Blood vessels contain a central lumen (cavity) lined with an **endothelium**, a single layer of flattened epithelial cells.

- **Pulse:** the rhythmic bulging of the artery walls with each heartbeat.

Capillaries have very thin walls, which consist of just the endothelium and its basal lamina. Both arteries and veins have two layers of tissue surrounding the endothelium: an outer layer of connective tissue containing elastic fibers and a middle layer containing smooth muscle and more elastic fibers. An artery has a wall about three times as thick as that of a vein to accommodate blood pumped at high pressure by the heart. The thinner-walled veins convey blood back to the heart at a lower velocity and pressure and have valves to prevent backflow.

3. **Blood Flow Velocity**: Each artery conveys blood to so many capillaries that the *total* cross-section area is much greater in capillary beds than in arteries or any other part of the circulatory system. The result is a dramatic decrease in velocity from the arteries to the capillaries. The slower flow through capillaries allows time for exchange to occur.
4. **Blood Pressure**: Arterial blood pressure is highest when the heart contracts during ventricular systole. The pressure at this time is called **systolic pressure**. There is a lower but still substantial blood pressure when the ventricles are relaxed (**diastolic pressure**). **Vasoconstriction** raises blood pressure and **vasodilation** decreases blood pressure. **Endothelin** is a potent inducer of vasoconstriction.
    1. Blood pressure is generally measured for an artery in the arms at the same height as the heart. For a healthy 20-year-old human at rest, arterial blood pressure in the systemic circuit is typically about 120 mm Hg at systole and 70 mm Hg at diastole, a combination designated 120/70.
    2. If the blood pressure in your brain is too low to provide adequate blood flow, you will likely faint. The challenge of pumping blood against gravity is particularly great for animals with very long necks. A giraffe, for example, requires a systolic pressure of more than 250 mm Hg near the heart.
5. Rhythmic contractions of smooth muscles in the walls of venules and veins aid in the movement of blood. The contraction of skeletal muscles during exercise squeezes blood through the veins toward the heart. The change in pressure within the thoracic cavity during inhalation causes the venae cavae and other large veins near the heart to expand and fill with blood.
6. Capillaries in the brain, heart, kidneys, and liver are usually filled to capacity, but at man other site the blood supply varies over time as blood is diverted from one destination to another. There are two mechanisms that regulate flow into capillaries. One mechanism involves contraction of the smooth muscle in the wall of an arteriole, which reduces the vessel's diameter and decreases blood flow to the adjoining capillary beds. The other mechanism involves the action of *precapillary sphincters*, rings of smooth muscle located at the entrance to capillary beds.
7. In places where the blood pressure is greater than the osmotic pressure difference, there is a net loss of fluid from the capillaries. In contrast, where the osmotic pressure difference exceeds the blood pressure, there is a net movement of fluid from the tissues into the capillaries.
8. Only about 85% of the fluid that leaves the capillaries reenters them. The lost fluid returns to the blood via the **lymphatic system**. After entering the lymphatic system by diffusion, the fluid is called **lymph**; its composition is about the same as that of interstitial fluid. Along a lymph vessel are organs called **lymph nodes**, which filter the lymph and house cells that attack viruses and bacteria.

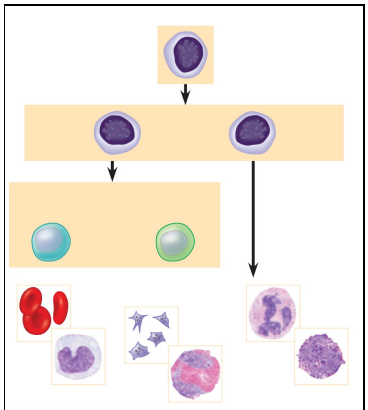


Illustration 2: Figure 42.19: Differentiation of blood cells

4. Blood components function in exchange, transport, and defense.
    1. Vertebrate blood is a connective tissue consisting of cells suspended in a liquid matrix called **plasma**. Dissolved in the plasma are ions and proteins that, together with the blood cells, function in osmotic regulation, transport, and defense. Some of these ions buffer the blood. Salts are also important in maintaining the osmotic balance of the blood. To serve all of these functions, plasma electrolytes must be kept within narrow concentration ranges. Plasma proteins act as buffers against pH changes, help maintain the osmotic balance between blood and interstitial fluid, and contribute to the blood's viscosity. The immunoglobulins, or antibodies, help combat viruses and other foreign agents that invade the body. Some proteins are escorts for lipids. A third group of plasma proteins are clotting factors that help plug leaks when blood vessels are injured. Plasma also contains a wide variety of other substances in transit from one part of the body to another, including nutrients, metabolic wastes, respiratory gases, and hormones.
    2. Suspended in blood plasma are two classes of cells: red blood cells, which transport O_2, and white blood cells, which function in defense. Blood also contains **platelets**, fragments of cells that are involved in the clotting process. All blood cells develop from multipotent **stem cells** that are dedicated to replenishing the body's blood cell populations.
        1. Red blood cells (**erythrocytes**) transport O_2. Mature mammalian erythrocytes lack nuclei, leaving more space for **hemoglobin**. Human erythrocytes are small disks that are biconcave. Erythrocytes also lack mitochondria and generate their ATP exclusively by anaerobic metabolism. A negative-feedback mechanism, sensitive to the amount of O2 reaching the body's tissues via the blood, controls erythrocyte production via a hormone called **erythropoietin** (**EPO**) that stimulates erythrocyte production.
        2. The blood contains five major types of white blood cells (**leukocytes**): monocytes, neutrophils, basophils, eosinophils, and lymphocytes
        3. . Their function is to fight infections.
        4. **Platelets** are pinched-off cytoplasmic fragments of specialized bone marrow cells. They have no nuclei and serve both structural and molecular functions in blood clotting.
    3. Clotting involves the conversion of fibrinogen to its active form, **fibrin**, which aggregates into threads that form the framework of a clot.
        1. Sometimes clots form within a blood vessel, blocking the flow of blood. Such a clot is called a **thrombus**.
    4. **Cardiovascular disease**:
        1. **Atherosclerosis**: the hardening of the arteries by accumulation of fatty deposits.
        2. A **heart attack**, also called a *myocardial infarction*, is the damage or death of cardiac muscle tissue resulting from blockage of one or more coronary arteries.
        3. A **stroke** is the death of nervous tissue in the brain due to a lack of O_2.
        4. **Low-density lipoprotein (LDL)** is associated with the deposition of cholesterol in arterial plaques. **High-density lipoprotein (HDL)** appears to reduce the deposition of cholesterol.
        5. **Hypertension** (high blood pressure) is yet another contributor to heart attack and stroke as well as other health problems.

- **Gas exchange**: the uptake of molecular O_2 from the environment and the discharge of CO_2 to the environment.
- **Partial pressure**: the pressure exerted by a particular gas in a mixture of gases.

5. Gas exchange occurs across specialized respiratory surfaces.
    1. The conditions for gas exchange vary considerably, depending on whether the respiratory medium—the source of O_2—is air or water. Air is less dense and less vicious than water, so breathing air is relatively easy and need not be particularly efficient. The warmer and saltier the water is, the less dissolved O_2 it can hold. Aquatic animals must expend considerable energy to carry out gas exchange.
    2. The movement of O_2 and CO_2 across moist respiratory surfaces takes place entirely by diffusion. The rate of diffusion is proportional to the surface area across which it occurs and inversely proportional to the square of the distance through which molecules must move.
    3. The structure of a respiratory surface depends mainly on the size of the animal and whether it lives in water or on land, but it is also influenced by metabolic demands for gas exchange.
    4. In some relatively simple animals, such as sponges, cnidarians, and flatworms, every cell in the body is close enough to the external environment that gases can diffuse quickly between all cells in the environment.

5. The skin serves as a respiratory organ in some animals, including earthworms and some amphibians, but the general body surface of most animals lack sufficient area to exchange gases for the whole organism.
6. **Gills** are outfoldings of the body surface that are suspended in the water. Movement of the respiratory medium over the respiratory surface, a process called **ventilation**, maintains the partial pressure gradients of O_2 and CO_2 across the gill that are necessary for gas exchange. The arrangement of capillaries in a fish gill allows for **countercurrent exchange**, the exchange of a substance or heat between two fluids flowing in opposite directions.
7. Although the most familiar respiratory structure among terrestrial animals is the lung, the most common is actually the **tracheal system** of insects. Made up of air tubes that branch throughout the body, this system is one variation on the theme of an internal respiratory surface.
8. **Lungs** are localized respiratory organs. In mammals, a system of branching ducts conveys air to the lungs, which are located in the thoracic cavity. Air enters through the **nostrils** and is then filtered by hairs, warmed, humidified, and sampled for odors as it flows through a maze of spaces in the **nasal cavity**. The nasal cavity leads to the **pharynx**, which leads to the **larynx** (voicebox). From there, air travels to the **trachea**, which forks into two **bronchi** and later **bronchioles**. Gas exchange occurs in the **alveoli**. Alveoli are so small that specialized secretions are required to relieve the surface tension in the fluid that coats their surface. These secretions, called **surfactants**, contain a mixture of phsopholipids and proteins. Lacking cilia or significant air currents to remove particles from their surface, alveoli are highly susceptible to contamination.

G. Breathing ventilates the lungs.

1. The process that ventilates lungs is **breathing**, the alternating inhalation and exhalation of air.
2. An amphibian such as a frog ventilates its lungs by **positive pressure breathing**, inflating the lungs with forced airflow.
3. Unlike amphibians, mammals employ **negative pressure breathing**, pulling, rather than pushing, air into their lungs. Expanding the thoracic cavity during inhalation involves the animal's rib muscles and the **diaphragm**, a sheet of skeletal muscle that forms the bottom wall of the cavity. Depending on activity level, additional muscles may be recruited to aid breathing. During exercise, other muscles of the neck, back, and chest increase the volume of the thoracic cavity by raising the rib cage.
4. The volume of air inhaled and exhaled with each breath is called **tidal volume**. The tidal volume during maximal inhalation and exhalation is the **vital capacity**. The air that remains after a forced exhalation is called the **residual volume**.
5. **How a Bird Breathes**: Ventilation is both more efficient and more complex in birds than in mammals. When bird breathe, they pass air over the gas exchange surface in only one direction, and incoming, fresh air does not mix with air that has already carried out gas exchange. Bird use eight or nine air sacs situated on either side of the lungs as bellows to keep air flowing through the lungs. Instead of alveoli, which are dead ends, the sites of gas exchange in bird lungs are tiny channels called *parabronchi*.
6. **Control of breathing in humans**: Although you can voluntarily hold your breath or breathe faster and deeper, most of the time your breathing is regulated by involuntary mechanisms. Networks of neurons that regulate breathing, called **breathing control centers**, are located in two brain regions, the medulla oblongata and the pons. Control circuits in the medulla establish the breathing rhythm, while neurons in the pons regulate its tempo. In regulating breathing, the medulla uses the pH of the surrounding tissue fluid as an indicator of blood CO_2 concentration. The O_2 concentration in the blood usually has little effect on the breathing control centers. However, when the O_2 level drops very low, O_2 sensors in the aorta and the carotid arteries send signals to the breathing control centers. When you breathe deeply, a negative-feedback mechanism prevents the lungs from overexpanding. Breathing control is only effective if it is coordinated with control of the cardiovascular system so that ventilation is matched to blood flow through alveolar capillaries.

H. Adaptations for gas exchange include pigments that bind and transport gases.

1. Animals transport most of their O_2 bound to certain proteins called **respiratory pigments**. These pigments greatly increase the amount of O_2 that can be carried in the circulatory fluid. With a few exceptions, these molecules have a distinctive color and consist of a protein bound to a metal.
2. Vertebrate hemoglobin consists of four subunits, each with a cofactor called a heme group that has an iron atom at its center. Like all respiratory pigments, hemoglobin binds O_2 reversibly. This process depends on cooperativity between the hemoglobin subunits.
3. Low pH decreases the affinity of hemoglobin for O_2, an effected called the **Bohr shift**.
4. In addition to its role in O_2 transport, hemoglobin helps transport CO_2 and assists in buffering the blood.
5. Animals vary greatly in their ability to temporarily inhabit environments in which there is no access to their normal respiratory medium. One adaptation of diving mammals to prolonged stays underwater is an ability to store large amounts of O_2, both in hemoglobin and **myoglobin**, a protein similar to hemoglobin in the the muscles.

CHAPTER 43: THE IMMUNE SYSTEM

*Animals are constantly under attack by **pathogens**, infectious agents that cause disease. The **immune system** enables an animal to avoid or limit many infections. An animal's most basic defense against pathogens is a barrier. **Innate immune** responses are active immediately upon infection and are the same whether or not the pathogen has been encountered previously. Innate immunity includes the barrier defenses as well as defenses that combat pathogens after they enter the body. A second defense system, found only in vertebrates, is **acquired immunity,** also known as adaptive immunity.*

I. IN INNATE IMMUNITY, RECOGNITION AND RESPONSE RELY ON SHARED TRAITS OF PATHOGENS.

1. **Innate Immunity of Invertebrates**:

1. **Lysozyme**, an enzyme that digests microbial cell walls, and a low pH protect the insect digestive system.

2. Some hemocytes carry out a cellular defense called **phagocytosis**: the ingestion and digestion of bacteria and other foreign substances. Others produce chemicals that kill microbes and help entrap multicellular parasites. They also secrete *antimicrobial peptides*.

3. Fungal cell walls contain certain unique polysaccharides, while bacterial cell walls have polymers containing combinations of sugars and amino acids not found in animal cells.

2. **Innate Immunity of Vertebrates:**

1. **Barrier Defenses**: In mammals, epithelial tissues block the entry of many pathogens. Saliva, tears, and mucous secretions that bathe various exposed epithelia provide a washing action that inhibits colonization by microbes and contain lysozyme.

2. **Cellular Innate Defenses**: Phagocytic white blood cells (leukocytes) recognize pathogens via the **Toll-like receptors (TLR)**. TLR4 detects lipopolysaccharides and TLR3 detects double-stranded RNA.

1. The most abundant phagocytic cells in the mammalian body are **neutrophils.**

2. **Macrophages** provide an even more effective phagocytic defense.

3. **Eosinophiles** defend against multicellular invaders.

4. **Dendritic cells** populate tissues that are in contact with the environment and stimulate development of acquired immunity.

3. **Antimicrobial Peptides and Proteins**:

1. **Interferons** are proteins that provide innate defense against viral infections.

2. The **complement system** consists of roughly 30 proteins in blood plasma that function together to fight infections.

4. **Inflammatory Responses**: changes brought about by chemical signals released upon injury or infection

- **Pus**: a fluid rich in white blood cells, dead microbes, and cell debris.

1. **Mast cells** produce **histamine**, an important inflammatory signal. Triggers: dilation of nearby blood vessels,

2. A minor injury causes local inflammation, but severe tissue damage or infection may cause a systemic response.

3. Some toxins released by pathogens, as well as *pyrogens* released by activated macrophages, can rest the body's thermostat to a higher temperature.

4. *Septic shock* is an overwhelming systemic inflammatory response characterized by very high fever, low blood flow, and low blood pressure.

5. **Natural Killer Cells**: help recognize and eliminate certain diseased cells in vertebrates. With the exception of RBCs, all cells in the body normally have on their surface a protein called a class I MHC molecule. NK cells attack any cell without a class I MHC molecule (that is not a RBC).

3. **Innate Immune System Evasion by Pathogens**

1. The outer capsule that surrounds certain bacteria hides the polysaccharides of their cell walls.

II. IN ACQUIRED IMMUNITY, LYMPHOCYTE RECEPTORS PROVIDE PATHOGEN-SPECIFIC RECOGNITION.

- **Cytokines**: proteins that help recruit and activate lymphocytes.

1. **Lymphocytes** are critical for acquired immune defense.

1. **T cells** mature in the **thymus**.

2. **B cells** mature in the bone marrow.

2. Both T cells and B cells contribute to *immunological memory*: an enhanced response to a foreign molecule encountered previously.

- **Antigen**: Any foreign molecule that is specifically recognized by lymphocytes and elicits a response from them.

3. **Acquired Immunity: An Overview:** Each B or T cell has on its surface many receptor proteins that can each bind to particular foreign molecule. If a receptor protein binds to a foreign molecule, it activates the B or T cell, which undergoes mitosis. Activated T cells activate other cells and detect and kill infected host cells. Activated B cells secrete antibodies.

4. **Antigen Recognition by Lymphocytes**:

1. **The Antigen Receptors of B cells and T cells**: A single B or T lymphocyte has about 100,000 **antigen receptors** on its surface. B cells can give rise to *plasma cells*, which produce **antibodies** (**immunoglobulins**).

1. Each **B cell receptor** for an antigen is a Y-shaped molecule consisting of four polypeptide chains: two identical **heavy chains** and two identical **light chains**. Each chain consists of a variable region and a constant region.

2. Each **T cell receptor** for an antigen consists of two different polypeptide chinas, an *α chain* and a *β chain.* Each chain consists of a variable region and a constant region.

3. Each of the genes in a group called the **major histocompatibility complex (MHC)** produces a host cell protein that can present an antigen fragment to a T cell receptor.

2. **The Role of the MHC**: Once a pathogen is in a host cell, enzymes in the cell cleave he pathogen proteins into small pieces. These pieces are bound to MHC molecules inside the cell. Movement of the MUC molecule and bound peptide to the cell surface results in **antigen presentation**. T cells can bind to the presented antigen.

1. **Class I MHC molecules**: Found on all nucleated cells. Displays peptides to **cytotoxic T cells**.

2. **Class II MHC molecules**: Found only on dendritic cells, macrophages, and B cells (**antigen-presenting cells**). Displays peptides to **helper T cells**.

5. **Lymphocyte Development**:

1. **Generation of Lymphocyte Diversity by Gene Rearrangement**: Differences in the amino acid sequence of the variable region account for the specificity of antigen receptors on lymphocytes. A receptor light chain is assembled from three pieces: a variable (*V*) segment, a joining (*J*) segment, and a constant (*C*) segment. The light-chain gene contains a single C segment, 40 different V segments, and 5 different J segments. Early in B cell development, a set of enzymes collectively called recombinase randomly links one V gene segment to one J gene segment. Heavy-chain genes undergo a similar rearrangement.

2. **Origin of Self-Tolerance**: As lymphocytes mature in the bone marrow or thymus, their antigen receptors are tested for self-reactivity. The ones that react to the body's own molecules are destroyed or disabled.

3. **Amplifying Lymphocytes by Clonal Selection**: The binding of an antigen receptor to its specific antigen

activates the lymphocyte. Activated lymphocytes divide rapidly, producing effector cells and memory cells (**clonal selection**)

1. **Effector cells**: attack the antigen, are short-lived.
2. **Memory cells**: long-lived, remember the antigen.

The production of effector cells from a clone of lymphocytes during the first exposure to an antigen represented the **primary immune response**. B cells produce *plasma cells*, and T cells become helper T cells and cytotoxic T cells. If an individual is exposed again to the same antigen, the response is faster, or greater magnitude, and more prolonged (**secondary immune response**).

- **Humoral immune response**: Activated B cells produce antibodies.
- **Cell-mediated immune response**: activates cytotoxic T cells.

3. ACQUIRED IMMUNITY DEFENDS AGAINST INFECTION OF BODY CELLS AND FLUIDS

1. **Helper T Cells: A Response to Nearly All Antigens**: Helper T cells uses **CD4** to bind to the class II MHC molecule. Both the antigen-presenting cell and the helper T cell produce cytokines, which activate the helper T cell. The three principle types of antigen-presenting cells interact with helper T cells in different contexts. Dendritic cells trigger the primary immune response. Macrophages help initiate the secondary immune response, while B cells activate the humoral response.
2. **Cytotoxic T Cells: A Response to Infected Cells**: Cytotoxic T cells are the effector cells in a cell-mediated immune response. They are activated by helper T cells and antigen-presenting cells. Class I MHC molecules display non-self proteins to the protein **CD8** on the surface of cytotoxic T cells. Cytotoxic T cells release proteins that cause cell rupture and cell death.
3. **B Cells: A Response to Extracellular Pathogens**: The humoral response consists of clonally selected B cells secreting antibodies. B cells and helper T cells activate this pathway, as well as proteins or polysaccharides on the surface of bacteria.
4. **Antibody Classes**: The five major types of heavy-chain C regions determine five major classes of antibodies.
5. **The Role of Antibodies in Immunity**:
   1. *Neutralization*: antibodies bind to surface proteins of a virus or bacterium, thereby blocking the pathogen's ability to infect a host cells.
   2. *Opsonization*: antibodies bound to antigens present a readily recognized structure for macrophages and therefore increase phagocytosis.
   3. *Activation of the complement system and pore formation*.
6. **Active and Passive Immunization**
   1. **Active immunity**: memory B cells.
   2. **Passive immunity**: transfer of antibodies from one organisms to another, temporarily protecting the second organism.
   3. Active immunity can develop from the introduction of antigens into the body through **immunization** (**vaccination**).
   4. In artificial passive immunization, antibodies from an immune animal are injected into a nonimmune animal.
7. **Immune Rejection**: the body can reject non-self cells that were transplanted in.
   1. **Blood Groups**: To avoid harmful immune reactions in human blood transfusions, ABO blood groups must be taken into account.
   2. **Tissue and Organ Transplants**: In the case of tissue and organ transplants, or grafts, it is MHC molecules that stimulate the immune response that leads to rejection. The wide diversity of MHC molecules almost guarantees that no two people, except identical twins, will have exactly the same set.

4. DISRUPTIONS IN IMMUNE SYSTEM FUNCTION AND ELICIT OR EXACERBATE DISEASE

1. **Allergies**: Allergies are exaggerated (hypersensitive) responses to certain antigens called **allergens**. An acute allergic response sometimes leads to *anaphylatic shock*, a whole-body, life-threatening reaction that can occur within seconds of exposure to an allergen. Abrupt dilation of peripheral blood vessels, causing a precipitous drop in blood pressure.
2. **Autoimmune Diseases**: The immune system turns against particular molecules of the body.
   1. *Systemic lupus erythematosus* (*lupus*): The immune system generates antibodies against histones and DNA released by the normal breakdown of body cells.
   2. *Rheumatoid arthritis*: damage and painful inflammation of the cartilage and bone of joints.
   3. *Type 1 diabetes mellitus*: Cytotoxic T cells destroy beta cells in the pancreas.
   4. *Multiple sclerosis*: T cells destroy the myelin sheath of neurons in the CNS.
3. **Exertion, Stress, and the Immune System:** Moderate exercise improves immune system function, but exercise to the point of exhaustion suppresses the immune system. Psychological stress also disrupts the immune system.
4. **Immunodeficiency Diseases**: a disorder in which the ability of an immune system to protect against pathogens is defective or absent.
   1. *SCID*: functional lymphocytes are rare or absent.
   2. **Acquired immunodeficiency syndrome (AIDS)**: caused by HIV.
5. **Acquired Immune System Evasion by Pathogens**
   1. **Antigenic Variation**: changes in epitope expression by pathogens.
   2. **Latency**: Viruses remain in a host without activating immune defenses, ceasing production of viral products targeted by lymphocytes.
   3. **Attack on the Immune System: HIV**: HIV infects helper T cells with high efficiency, binding to the CD4 molecule. HIV also infects macrophages and brain cells. The virus mutates at a very high rate during replication. The virus also spends about a decade dormancy.
6. **Cancer and Immunity**: The frequency of certain cancers increases when the immune response is impaired.

- *Inborn immunodeficiency*: genetic or developmental defect in the immune system.
- *Acquired immunodeficiency* develops later in life following exposure to chemical or biological agents.

- **Osmoregulation**: the general process by which animals control solute concentrations and balance water gain and loss.
- **Excretion**: the process that rids the body of nitrogenous metabolites and other water products.
- **Osmolarity**: osmotic pressure.

I. Osmoregulation balances the uptake and loss of water and solutes.

1. Regulating the chemical composition of body fluids depends on balancing the uptake and loss of water and solutes.
2. An animal can maintain water balance in two ways. One is to be an **osmoconformer**, which is isoosmotic with its surroundings. All osmoconformer are marine animals. The second is to be an **osmoregulator**, which controls its internal osmolarity independent of that of its environment. Osmoregulators must expend energy to maintain the osmotic gradients that cause water to move in or out.
3. Most animals, whether osmoconformers or osmoregulators, cannot tolerate substantial changes in external osmolarity and are said to be **stenohaline**. In contrast, **euryhaline** animals, which include certain osmoconformers and osmoregulators, can survive large fluctuations in external osmolarity.
4. Most marine invertebrates are osmoconformers. Their total osmolarity is the same as that of seawater. However, they must actively transport some solutes to maintain homeostasis
5. Many marine vertebrates and some marine invertebrates are osmoregulators. For most of these animals, the ocean is a strongly dehydrating environment. Such fishes balance the water loss by drinking large amounts of seawater. They then make use of both their gills and kidney to rid themselves of salts.
6. A distinct osmoregulatory strategy evolved in marine sharks and most other chondrichthyans. Their tissues contain high concentrations of urea and trimethylamine oxide (TMAO), a compound that protects proteins from damage by urea.
7. The osmoregulatory problems of freshwater animals are the opposite of those of marine animals. The body fluids of freshwater animal must be hyperosmotic because animals cells cannot tolerate salt concentrations as low as those of lake or river water. Many freshwater animals, including fishes, solve the problem of water balance by drinking almost no water and excreting large amounts of very dilute urine.
8. Extreme dehydration, or *desiccation*, is fatal for most animals. Some animals enter a dormant state when their habitats dry up, an adaptation called **anhydrobiosis**. Andrydrobiosis requires adaptations that keep cell membranes intact. In particular, a disaccharide called trehalose seems to protect the cells by replacing the water that is normally associated with proteins and membrane lipids.
9. The threat of dehydration is a major regulatory problem for terrestrial plants and animals. The body coverings of most terrestrial animals help prevent dehydration. Despite this, most terrestrial animals lose water through many routes: in urine and feces, across their skin, and from moist surfaces in gas exchange organs. Land animals maintain water balance by drinking and eating most foods and by producing water metabolically through cellular respiration.
10. In most animals, osmotic regulation and metabolic waste disposal rely on one or more kinds of **transport epithelium**.
11. A specialized nasal gland enables the albatross and other marine birds to maintain internal salt balance.

II. An animal's nitrogenous wastes reflect its phylogeny and habitat.

1. Because most metabolic wastes must be dissolved in water to excreted from the body, the type and quantity of waste products may have a large impact on an animal's water balance.
2. When proteins and nucleic acids are broken apart for energy or converted to carbohydrates or fats, enzymes remove nitrogen in the form of **ammonia**.
3. Because ammonia can be tolerated only at very low concentrations, animals that excrete nitrogenous wastes as ammonia need access to lots of water. Therefore, ammonia excretion is most common in aquatic species.
4. Mammals, most adult amphibians, sharks, and some marine bony fishes and turtles mainly excrete **urea**. Urea is much less toxic, but animals must expend energy to produce urea from ammonia.
5. Insects, land snails, and many reptiles, including birds, excrete **uric acid** as their primary nitrogenous wastes. Many animals, including humans, produce a small amount of uric acid as a product of purine breakdown.
6. In general, the kind of nitrogenous wastes excreted depend on an animal's evolutionary history and habitat, especially the availability of water. In addition, reproductive mode seems to have been an important factor in determining which type of nitrogenous waste has become the major form during the evolution of a particular group of animals.

III. Diverse excretory systems are variations on a tubular theme

1. In most causes, hydrostatic pressure drives a process of **filtration.** Water and small solutes, such as salts, sugars, amino acids, and nitrogenous wastes, cross the membrane, forming a solution called the **filtrate**. **Reabsorption** recovers useful molecules and water from the filtrate and returns them to the body fluids. Nonessential solutes and wastes are left in the filtrate or are added to it by selective **secretion**, which also occurs by active transport.
2. Flatworms, which lack a coelom or body cavity, have excretory systems called protonephridia. The **protonephridia** from a network of dead-end tubules connected to external openings. Cellular units called flame bulbs cap the branches of each protonephridium. The urine excreted by freshwater flatworms has a low solute concentration, helping to balance the osmotic uptake of water from the environment. Protonephridia are also found in rotifers, some annelids, mollusc larvae, and lancelets.
3. Most annelids, such as earthworms, have **metanephridia**, excretory organs that open internally to the coelom. Each segment of a worm has a pair of metanephridia, which are immersed in coelomic fluid and enveloped by a capillary network. The metanephridia of an earthworm have both excretory and osmoregulatory functions.
4. Insects and other terrestrial arthropods have organs called **Malpighian tubules** that remove nitrogenous wastes and also function in osmoregulation. The nitrogenous wastes—mainly insoluble uric acid—are eliminated as nearly dry matter along with the feces.
5. In vertebrates and some other chordates, a specialized organ called the **kidney** functions in both osmoregulation and excretion. In humans, each kidney is about 10 cm long and is supplied with blood by a **renal artery** and drained by a **renal vein**. Urine exits each kidney through a duct called the **ureter**, and both ureters drain into a common **urinary bladder**. During urination, urine is expelled from the bladder through a tube called the **urethra**, which empties to the to the outside.
6. The mammalian kidney has an outer **renal cortex** and an inner **renal medulla**. Microscopic excretory tubules and their associated blood vessels pack both regions. Weaving back and forth across the cortex and medulla is the **nephron**, the functional unit of the vertebrate kidney. A nephron consists of a single long tubule as well as a ball of capillaries called the **glomerulus**. The blind end of the tubule forms a cup-shaped swelling, called **Bowman's capsule**, which surrounds the glomerulus.
7. From the **Bowman's capsule**, the filtrate passes into the **proximal tubule**, then the **loop of Henle**, and then the **distal tubule**, which empties into a **collecting duct**. All the collecting ducts lead into the **renal pelvis**.
8. Among the vertebrates, only mammals and some birds have loops of Henle. In the human kidney, 85% of the nephrons are **cortical nephrons**, which have short loops of Henle and are almost entirely confined to the renal cortex. The other 15%, the **juxtamedullary nephrons**, have loops that extend deeply into the renal medulla and thus allow hyperosmotic urine.
9. Each nephrons is supplied with blood by an **afferent arteriole**, an offshoot of the renal artery that branches to form the capillaries of the glomerulus. The capillaries converge as they leave the glomerulus, forming an **efferent arteriole**. Branches of this vessel form the **peritubular capillaries**, which surround the proximal and distal tubules. A third set of

10. capillaries extend downward and form the **vasa recta**, hairpin-shaped capillaries that serve the long loop of Henle of juxtamedullary nephrons.

c. The nephron is organized for stepwise processing of blood filtrate.

1. **Proximal tubule**: reabsorption in the proximal tubule is critical for the recapture of ions, water, and valuable nutrients from the huge initial filtrate volume. Processing of filtrate in the proximal tubule helps maintain a relatively constant pH in body fluids.

2. **Descending limb of the loop of Henle**: Reabsorption of water continues. Here numerous water channels formed by **aquaporin** proteins make the transport epithelium freely permeable to water.

3. **Ascending limb of the loop of Henle**: Contains ion channels but no aquaporins; is impermeable to water. NaCl diffuses out of the filtrate.

4. **Distal tubule**: the distal tubule plays a key role in regulating the K^+ and NaCl concentration of body fluids.

5. **Collecting duct**: The collecting duct carries the filtrate through the medulla to the renal pelvis.

6. The mammalian kidney's ability to conserve water is a key terrestrial adaptation. In a mammalian kidney, the production of hyperosmotic urine is possible only because considerable energy is explended for the active transport of solutes against concentration gradients.

7. *The Two-Solute Model*:

3. Hormonal circuits link kidney function, water balance, and blood pressure.

- **Hormone** is a molecule that is secreted into the extracellular fluid, circulates in the blood or hemolymph, and communicates regulatory messages throughout. Only the target cells that have the receptors that enable a response.
- **Pheromones**: chemicals that are released into the external environment.

1. Hormones and other signaling molecules bind to target receptors, triggering specific response pathways
    1. Hormones and other signaling molecules trigger responses by binding to specific receptor proteins in or on target cells; other cells are unresponsive to that molecule.
    2. Hormones secreted into extracellular fluids by endocrine cells reach target cells via the bloodstream. Some endocrine cells are grouped in ductless organs called **endocrine glands**. Endocrine glands thus contrast with *exocrine glands*, such as salivary glands, which have ducts that carry secreted substances onto body surfaces or into body cavities.
    3. Hormones serve a range of functions in the body. They maintain homeostasis; mediate responses to environmental stimuli; and regulate growth, development, and reproduction. They also control the appearance of characteristics that distinguish a juvenile animal from an adult.
    4. Many types of cells produce **local regulators**, secreted molecules that act over short distances and reach their target cells solely by diffusion. Local regulators function in many other processes, including blood pressure regulation, nervous system function, and reproduction. In **paracrine** signaling, target cells lie near the secreting cell. In **autocrine** signaling, the secreted molecules act on the secreting cell itself. Some secreted molecules have both paracrine and autocrine activity. One secreted, local regulators act on their target cells within seconds or even milliseconds, eliciting responses more quickly than do hormones.
        1. Polypeptide local regulators include **cytokines**, which play a role in immune responses and **growth factors**, which stimulate cell proliferation and differentiation.
        2. The gas **nitric oxide (NO)**, which consists of nitrogen double-bonded to oxygen, serves in the body as both a neurotransmitter and a local regulator. Highly reactive and potentially toxic, NO usually triggers changes in a target cell within a few seconds of contact and then breaks down.
        3. A group of local regulators called **prostaglandins** are modified fatty acids. In semen that reaches the reproductive tract of a female, prostaglandins stimulate the smooth muscles of the female's uterine wall to contract, helping sperm reach an egg. At the onset of childbirth, prostaglandin-secreting cells of the placenta cause the nearby muscles of the uterus to become more excitable, helping to induce labor. In the immune system, prostaglandins promote fever and inflammation and also intensify the sensation of pain. Prostaglandins also help regulate the aggregation of platelets. Prostaglandins also help maintain a protective lining in the stomach.
    5. At many synapses, neurons secrete molecules called **neurotransmitters** that diffuse at very short distance to bind receptors on the target cells. In neuroendocrine signaling, *neurosecretory cells*, specialized neurons typically found in the brain, secrete molecules (neurohormones) that diffuse from nerve cell endings into the bloodstream.
    6. Hormones are often divided into three groups: polypeptides, amines, and steroid hormones.
        1. Polypeptides are usually formed by cleavage of a longer protein chain. Polypeptides and many amine hormones are water-soluble. Water-soluble hormones are secreted by exocytosis, travel freely in the bloodstream, and bind to cell-surface receptors.
        2. Steroid hormones are lipids that contain four fused carbon rings. Steroid hormones, as well as other largely nonpolar hormones, such as thyroxine, are lipid-soluble and can pass through cell membranes readily. Lipid-soluble hormones diffuse out across the membranes of endocrine cells and travel in the bloodstream bound to transport proteins. They bind to intracellular receptors.
    7. The binding of a water-soluble hormone to a receptor protein triggers events at the plasma membrane that result in a cellular response. The series of changes in cellular proteins that converts the extracellular chemical signal to a specific intracellular response is called **signal transduction**. When you find yourself in a stressful situation, your adrenal gland secretes **epinephrine**.
    8. When a steroid hormone binds to its cytosolic receptor, a hormone-receptor complex forms, which moves into the nucleus. The receptor portion of the complex interacts with DNA or with a DNA-binding protein, stimulating transcription of specific genes. Thyroxine, vitamin D, and other lipid-soluble hormones have receptor that are typically located in the nucleus. Recent experiments indicate that lipid-soluble hormones can sometimes trigger responses at the cell surface without first entering the nucleus.
    9. Many hormones elicit more than one type of response in the body. The effects brought about by a particular hormone can vary if target cells differ in the molecules that receive, transduce, or respond to that hormone.
2. Negative feedback and antagonistic hormone pairs are common features of the endocrine system.
    1. Low pH in the small intestine stimulates certain endocrine cells of the duodenum, called S cells, to secrete the hormone *secretin*. Secretin enters the bloodstream and reaches target cells in the **pancreas**, which releases bicarbonate, which raises the pH in the duodenum. This pathway is self-limiting because the response to secretin reduces the stimulus.
    2. For secretin and many other hormones, the response pathway involves **negative feedback**, a loop in which the response reduces the initial stimulus.
    3. Simple hormone pathways are widespread among animals.
    4. Maintaining blood glucose concentrations near 90 mg/ 100 mL is a critical bioenergetic and homeostatic function. Two antagonistic hormones, insulin and glucagon, regulate the concentrating of glucose in the blood. When blood glucose rises above the set point, release of **insulin** triggers uptake of glucose from the blood, decreasing the blood glucose concentration. When blood glucose drops below the set point, the release of **glucagon** promotes the release of glucose into the blood, increasing the blood glucose concentration. Scattered throughout the pancreas are clusters of endocrine cells known as the **islets of Langerhans**. Each islet has *alpha cells*, which make glucagon, and *beta cells*, which make insulin. Thus, the pancreas is both an endocrine gland and an exocrine gland with functions in the endocrine and digestive systems.
    5. Insulin lowers blood glucose levels by stimulating nearly all body cells outside the brain to take up glucose from the blood, by slowing glycogen breakdown in the liver and inhibiting the conversion of amino acids and glycerol to glucose. Glucagon only affects cells of the liver by signalling them to increase glycogen hydrolysis, convert amino acids and glycerol to glucose, and release glucose into the bloodstream.
    6. The antagonistic effects of glucagon and insulin are vital to managing fuel storage and consumption by body cells. Glucose homeostasis also relies on responses to glucagon and insulin elsewhere in the body as well as responses to other hormones.
    7. A disruption in glucose homeostasis can be quite serious. **Diabetes mellitus** is caused by a deficiency of insulin or a decreases response to insulin in target tissues. In people with diabetes mellitus, the high level of glucose in blood exceeds the capacity of the kidneys to reabsorb this nutrient. As glucose is concentrated in the urine, more water is excreted along with it, resulting in excessive volumes of urine.
        1. *Type 1 diabetes*: or insulin-dependent diabetes, is an autoimmune disorder in which the immune system destroys the beta cells of the pancreas. Stem cell research may someday provide a cure for type 1 diabetes by generating replacement beta cells that restore insulin production by the pancreas.

2. *Type 2 diabetes* (non-insulin-dependent diabetes): is characterised by a failure of target cells to respond normally to insulin. Excess body weight and lack of exercise significantly increase the risk. Nevertheless, type 2 diabetes is the seventh more common cause of death in the United States and a growing public healthy problems worldwide.

3. The endocrine and nervous systems act individually and together in regulating animal physiology

1. In all animals but the simplest invertebrates, the endocrine and nervous systems are integrated in the control of reproduction and development.
2. Before hormones stimulate the metamorphosis of the caterpillar, a larva, into the adult butterfly, they regulate development of a newly hatched egg into the fully grown larva. The signals that direct molting and metamorphosis in insects originate in the brain. There, neurosecretory cells produce *prothoracicotropic hormone* (PTTH), a peptide neurohormone that prompts the prothoracic glands, a pair of endocrine glands just behind the brain, release **ecdysone**.
3. The corpora allata secrete a third signaling molecule, **juvenile hormone**, which maintains juvenile characteristics, as well as other things. In the presence of high levels of juvenile hormone, ecdysone stimulates molting that results in a larger larva. When the juvenile hormone level is low, ecdysone-induced molting produces the cocoon, or pupal form, within which metamorphosis occurs.
4. Synthetic versions of juvenile hormone are used as a biological pest control method to prevent insects from maturing into reproducing adults.
5. In vertebrates, the **hypothalamus** plays a central role in integrating the endocrine and nervous systems. The hypothalamus receives information from nerves throughout the body and from other parts of the brain. In response, it initiates endocrine signaling appropriate to environmental conditions. Signals from the hypothalamus travel to the **pituitary gland**, a gland located at its base. The **posterior pituitary**, or *neurohypophysis*, stores and secretes two hormones made by the hypothalamus. The **anterior pituitary**, or *adenohypophysis*, is regulated by hormones secreted by the hypothalamus.
6. **Posterior Pituitary Hormones**: The posterior pituitary releases two neurohormones, oxytocin and antidiuretic hormone (ADH).
    1. One function of **oxytocin** in in mammals is to regulate milk release during nursing; this function is mediated by a simple neurohormone pathway. The initial stimulus is the infant's suckling. Stimulation of sensory nerve cells in the nipples generates signals in the nervous system that reach the hypothalamus. In response to circulating oxytocin, the mammary glands secrete milk. The oxytocin pathway regulating the mammary gland provides an example of a positive-feedback mechanism. Activation of the pathway is sustained until the baby stops suckling. When mammals give birth, oxytocin induces target cells in the uterine muscles to contract. It drives the birth process to completion. Oxytocin also functions in regulating mood and sexual arousal in both males and female.
    2. **Antidiuretic hormone (ADH)**, or *vasopressin*, helps regulate blood osmolarity. ADH increases water retention the kidneys, thus decreasing urine volume.
7. **Anterior Pituitary Hormones**: *Thyrotropin-releasing hormone (TRH)* is a product of the hypothalamus that stimulates the anterior pituitary to secrete thyrotropin, also know as *thyroid-stimulating hormone (TSH)*. Signals to the brain stimulate the hypothalamus to produce hormones. Each hypothalamic hormone is either a *releasing hormone* or an *inhibiting hormone*, reflecting its role in promoting or inhibiting release of one or more specific hormones by the anterior pituitary.
    1. They hypothalamic releasing and inhibiting hormones are secreted nearly capillaries at the base of the hypothalamus. The capillaries drain into short blood vessels, called portal vessels, which subdivide into a second capillary bed within the anterior pituitary.
    2. The hypothalamus secretes TRH, which prompts the anterior pituitary to secrete TSH, which prompts the thyroid to release thyroid hormone, which increases metabolic rate. Like simple hormone pathways, hormone cascade pathways typically involve negative feedback.
    3. Four anterior pituitary hormones act primarily or exclusively as tropic hormones: **follicle-stimulating hormone (FSH), luteinizing hormone (LH), adrenocorticotropic hormone (ACTH),** and **TSH**.
        1. FSH and LH (the *gonadotropins*) stimulate the activities of the male and female gonads, the testes and ovaries, respectively.
        2. ACTH stimulates the production and secretion of steroid hormones by the adrenal cortex.
    4. Two anterior pituitary hormones are nontropic: prolactin (PRL) and melanocyte-stimulating hormone (MSH). Prolactin stimulates mammary gland growth and milk synthesis in mammals, regulates fat metabolism and reproduction in birds, delays metamorphosis in amphibians, and regulates salt and water balance in freshwater fishes. Melanocyte-stimulating hormone regulates the activity of pigment-containing cells in the skin of some amphibians (as well as fishes and reptiles). In mammals, MSH inhibits hunger.
    5. **Growth hormone (GH)** stimulates growth through tropic and nontropic effects. The liver responds to GH by releasing *insulin-like growth factors (IGFs),* which circulate in the blood and directly stimulate bone and cartilage growth. Hypersecretion of GH during childhood can lead to gigantism, in which the person grows unusually tall —as tall as 8 feet—though body proportions remain relatively normal. Excessive GH production in adulthood results in an overgrowth of the extremities called acromegaly. Hyposecretion of GH in childhood retards long-bone growth and can lead to pituitary dwarfism If diagnosed before puberty, pituitary dwarfism can be treated successfully with human GH.

- **Tropic hormone**: a hormone that regulates the function of endocrine cells or glands.

4. Endocrine glands respond to diverse stimuli in regulating metabolism, homeostasis, development, and behavior.

1. **Thyroid Hormone: Control of Metabolism and Development**.
    1. Thyroid hormone regulates bioenergetics; helps maintain normal blood pressure, heart rate, and muscle tone; and regulates digestive and reproductive functions. In vertebrates, the **thyroid gland** consists of two lobs on the ventral surface as the trachea.
    2. The term *thyroid hormone* actually refers to a pair of very similar hormones derived from the amino acid tyrosine: **triiodothyronine (T_3)** contains three iodine atom, whereas tetraiodothyronine, or **thyroxine (T_4)** contains four iodine atoms.
    3. Hyperthyroidism can lead to high body temperature, profuse sweating, weight loss, irritability, and high blood pressure. In Graves' disease, the immune system produces antibodies that bind to the receptor for TSH and activate sustained thyroid hormone production. Protruding eyes are a typical symptom.
    4. Hypothyroidism produces weight gain, lethargy, and intolerance to cold. Proper thyroid function requires dietary iodine.
    5. The thyroid controls the metamorphosis of a tadpole into a frog.
    6. All vertebrates require thyroid hormones for the normal functioning of bone-forming cells and the branching of nerve cells during embryonic development of the brain. Congenital hypothyroidism results in markedly retarded

skeletal growth and poor mental development.

2. **Adrenal Hormones: Response to Stress**:
    1. The **adrenal glands** of vertebrates are in each case associated with the kidneys. The *adrenal cortex* is the outer portion, and the *adrenal medulla* is the central system. The adrenal cortex consists of true endocrine cells, whereas the secretory cells of the adrenal medulla derive from neural tissue during embryonic development.
    2. Fight-or-flight responses is triggered by two hormones of the adrenal medulla, epinephrine (adrenaline) and norepinephrine (noradrenaline). Both are **catecholamines**, a class of amine hormones synthesized from the amino acid tyrosine. The adrenal medulla secretes epinephrine and norepinephrine in response to stress—whether extreme pleasure or life-threatening danger. Both increase the rate of glycogen breakdown in the liver and skeletal muscles, promote glucose release by liver cells, and stimulate the release of fatty acids from fat cells. They increase both the rate of stroke volume of the heartbeat and dilate the bronchioles in the lungs, actions that raise the rate of oxygen delivery to body cells. They also alter blood flow, causing constriction of some blood vessel and dilation of others. The overall effect is to shunt blood away from the skin, digestive organs, and kidneys, while increasing the blood supply to the heart, brain, and skeletal muscles. Epinephrine generally has a stronger effect on heart and metabolic rates, while the primary role of norepinephrine is in modulating blood pressure. The adrenal medulla is controlled by involuntary nerve signals
    3. The adrenal cortex responds to endocrine signals. Stressful stimuli cause the hypothalamus to secrete a releasing hormone that stimulates the anterior pituitary to release the tropic hormone ACTH. When ACTH reaches the adrenal cortex via the bloodstream, it stimulates the endocrine cells to synthesize and secrete a family of steroids called **corticosteroids**: glucocorticoids and mineralocorticoids.
        1. Glucocorticoids effect glucose metabolism. They promote glucose synthesis from noncarbohydrate sources, such as proteins. They also suppress certain components of the body's immune system.
        2. **Mineralocorticoids** act principally in maintaining salt and water balance.
    4. The corticosteroid products of the adrenal cortex include small amounts of steroid hormones that function as sex hormones. The sex hormones produced by the adrenal cortex are mainly "male" hormones (androgens), with small amounts of "female" hormones (estrogens and progestions).
3. Sex hormones affect growth, development, reproductive cycles, and sexual behavior. The gonads produce and secrete three major categories of steroid hormones: androgens, estrogens, and progestins. The testes primarily synthesize **androgens**, the main one being **testosterone**. Androgens are responsible for the development of human male secondary sex characteristics. Use of anabolic steroids while effective in increasing muscle mass, can cause severe acne outbreaks and liver damage. In addition, anabolic steroids have a negative-feedback effect on testosterone production, causing significant decreasing in sperm count and testicular size.
4. **Extrogens**, of which the most important is **estradiol**, are responsible for maintenance of the female reproductive system and the development of female secondary sex characteristics. **Progestins**, which include **progesterone**, are primarily involved in preparing and maintaining tissues of the uterus required to support the growth and development of an embryo.
5. The **pineal gland**, a small mass of tissue near the central of the mammalian gland, synthesizes and secretes the hormone **melatonin**, a modified amino acid. Melatonin regulates functions related to light and to seasons marked by changes in day length. Its primary functions relate to biological rhythms associated with reproduction.

1. Both asexual and sexual reproduction occur in the animal kingdom

- *Fragmentation*: the breaking of the body into several pieces.
- *Regeneration*: The regrowth of lost body parts.
- **Ovulation**: the release of mature eggs.

1. In **sexual reproduction**, the fusion of haploid gametes forms a diploid cell, the **zygote**. The female gamete, the **egg**, is a large, nonmotile cell. The male gamete, the **sperm**, is generally a much smaller, motile cell. The vast majority of eukaryotic species reproduce sexually. The unique combinations of parental genes formed during meiotic recombination may help survival if the environment changes, concentrates good genes and allows a population to rid itself of sets of harmful genes more easily.
2. **Asexual reproduction** is the generation of new individuals without the fusion of egg and sperm. Many invertebrates can reproduce asexually by **fission**, the separation of a parent organism into two individuals of approximately equal size. Also common among invertebrates is **budding**, in which new individuals arise from outgrowths of existing ones. In another form of asexual reproduction, some invertebrates, including certain sponges, release specialized groups of cells that can grow into new individuals. **Parthenogenesis** is a form of asexual reproduction in which an egg develops without being fertilized. Asexual reproduction is expected to be most advantageous in stable, favorable environments because it perpetuates successful genotypes faithfully and precisely.
3. Most animals exhibit cycles in reproductive activity, often related to changing seasons. Reproductive cycles are controlled by hormones, which in turn are regulated by environment cues. Common environmental cues are changes in day length, seasonal temperature, rainfall, and lunar cycles. Animals may reproduce exclusively asexually or sexually, or they may alternate between the two modes. Asexual reproduction occurs when conditions are favorable, whereas sexual reproduction occurs during times of environmental stress.

- *Hermaphroditism*: each individual has both male and female reproductive systems.
- *Sex reversal*: The process in which an individual changes its sex during its lifetime.

4. Several genera of fish, amphibians, and reptiles reproduce exclusively by a complex form of parthenogenesis that involves the doubling of chromosomes after meiosis, producing diploid offspring. An individual adopts female behavior prior to ovulation, when the level of the female sex hormone estradiol is high, then switches to male-like behaviour after ovulation, when the level of progesterone is highest. Isolated lizards lay fewer eggs than those that go through the motions of sex.
5. Sexual reproduction that involves encounters between members of the opposite sex presents a problem for sessile animals, burrowing animals, and some parasites.

2. Fertilization depends on mechanisms that bring together sperm and egg of the same species.

- *Spawning*: Individuals in the same area release their gametes into the water at the same time.

1. **Fertilization—**the union of sperm and egg—can be either external or internal. A moist habitat is almost always required for external fertilization, both to prevent the gametes from drying out and two allow the sperm to swim to the eggs.

2. When external fertilization is not synchronous across a population, individuals may exhibit specific mating behaviors leading to the fertilization of the eggs of one female by one male, which allows for mate selection and increases the probability of successful fertilization.

3. Internal fertilization is an adaptation that enables sperm to reach an egg efficiently, even when the environment is dry. The mating animals may make use of *pheromones*, chemicals released by one organism that can influence the physiology and behavior of other individuals of the same species.

4. All species generally produce more offspring than can survive to reproduce. Species with external fertilization tend to produce very large numbers of gametes, but the fraction that zygotes that survive is often quite small. Internal fertilization usually produces fewer zygotes, and is often associated with a variety of mechanisms that provided greater protection of the embryos and parental care of the young.

5. Rather than secreting a protective eggshell, some animals retain the embryo for some portion of its development within the female's reproductive tract. Embryos of marsupial mammals spend only a short period in the uterus; the embryos then craw out and complete fetal development attached to a mammary gland in the mother's pouch. The embryos of eutherian mammals remain in the uterus throughout fetal development.

- **Gonads**: the organs that produce gametes in most animals.

6. Sexual reproduction in animals relies on sets of cells that serve as precursors for ova and sperm.

7. Annelids have separate sexes but do not have distinct gonads; rather, the eggs and sperm develop from undifferentiated cells lining the coelom. As the gametes mature, they are released from the body wall and fill the coelom.

8. More elaborate reproductive systems include sets of accessory tubes and glands that carry, nourish, and protect the gametes and sometimes the developing embryos. In many insect species, the female reproductive system includes a **spermatheca**, a sac in which sperm may be stored for extended periods, a year or more in some species. Because the female releases male gametes from the spermatheca only in response to the appropriate stimuli, fertilization occurs under conditions likely to be well suited to embryonic development.

9. In many non-mammalian vertebrates, the digestive, excretory, and reproductive systems have a common opening to the outside, the **cloaca**. Many non-mammalian vertebrates lack a well-developed penis and instead ejaculate sperm by turning the cloaca inside out.

10. Although fertilization involves the union of a single egg and sperm, animals often mate with more than one member of the other sex. Mechanisms have evolved, however, that enhance the reproductive success of a male with a particular female and diminish the change of that female mating successfully with another partner.

3. Reproductive organs produce and transport gametes

1. **Female Reproductive Anatomy**:
    1. The clitoris and two sets of labia make up a female's external reproductive anatomy. The internal organs are the gonads and a system of ducts and chambers which receive and carry gametes and house the embryo and fetus.
    2. The female gonads are a pair of ovaries that flank the uterus and are held in place in the abdominal cavity by ligaments. The outer layer of each ovary is packed with **follicles**, each consisting of an **oocyte**, a partially developed egg, surrounded by a group of support cells. The surrounding cells nourish and protect the oocyte during much of **oogenesis**, the formation and development of an ovum. During a typical 4-week menstrual cycle, one follicle matures and expels its egg, a process called ovulation. After ovulation, the residual follicular tissue grows within the ovary, forming a mass called the **corpus luteum**. If the egg cell is not fertilized, the corpus luteum degenerates, and a new follicle matures during the next cycle.
    3. An **oviduct**, or fallopian tube, extends from the uterus toward each ovary. Wavelike contractions and cilia covey an egg down the oviduct to the **uterus**. The inner lining of the uterus, the **endometrium**, is richly supplied with blood vessels. The neck of the uterus is the **cervix**, which opens into the vagina.
    4. The **vagina** is a muscular but elastic chamber that is the site for insertion of the penis and deposition of sperm during copulation. Outside of it is the **vulva**, the collective term for the external female genitals, which consists of the **labia majora**, the **labia minora**, the **hymen**, and the **clitoris.** The clitoris conists of a short shaft supproting a rounded **glans**, or head, covered by a small hood of skin, the **prepuce**.
    5. **Mammary glands** are preset in both sexes but normally produce milk only in females.

2. **Male Reproductive Anatomy**:
    1. The male gonads, or **testes**, consist of many highly coiled tubes surrounded by several layers of connective tissue. These tubes are the **seminiferous tubules**, where sperm form. The **Leydig cells**, scattered between the seminiferous tubules, produce testosterone and other androgens. The **scrotum**, a fold of the body wall, maintains testis temperature about 2°C below that in the abdominal cavity.
    2. From the seminiferous tubules of a testis, the sperm pass into the coiled tubules of the **epididymis**. During **ejaculation**, the sperm are propelled from each epididymis through a muscular duct, the **vas deferens**. Each vas deferens extends around and behind the urinary bladder, where it joins a duct from the seminal vesicles, fomring a short **ejaculatory duct**, which open into the **urethra**, the outlet tube for both the excretory system and the reproductive system.
    3. Three sets of accessory glands—the seminal vesicles, the prostate gland, and the bulbourethral glands—produce secretions that combine with sperm to form **semen**, the fluid that is ejaculated. Two **seminal vesicles** contribute about 60% of the volume of semen. The **prostate gland** secretes its products directly into the urethra through several small ducts. The **bulbourethral glands** are a pair of small glands along the urethra below the prostate and they secrete pre-cum.
    4. The human **penis** contains the urethra, as well as three cylinders of spongy erectile tissue. For individuals with long-term erectile dysfunction, drugs such as Viagra promote the vasodilating action of the local regulatory nitric oxide. The penis of rodents, raccoons, walruses, whales, and several other mammals also contains a bone, the baculum, which probably further stiffens the penis for mating. The human glans is covered by a fold of skin called the prepuce, or foreskin, which may be removed by circumcision.
3. **Human Sexual Response**: The same embryonic tissues five rise to the glans of the penis and the clitoris, the scrotum and the labia majora, and the skin on the penis and the labia minora.
    1. The sexual response cycle can be divided into four parts: excitement, plateau, orgasm, and resolution.
        1. The excitement phase prepares the vagina and penis for coitus. Myotonia may occur, resulting in nipple erection or tension of the arms and legs.
        2. In the plateau phase in females, the outer third of the vagina becomes vasocongested, while the inner two-thirds slightly expands.
        3. **Orgasm** is characterised by rhythmic, involuntary contractions of the reproductive structures in both sexes. In males, orgasms are two-fold: emission occurs when the glands and ducts of the reproductive tract contract, forcing semen into the urethra; expulsion, or ejaculation, occurs when the urethra contracts and the semen is expelled.
        4. The resolution phase completes the cycle and reverses the responses of the earlier stages.

- **Vasocongestion**: the filling of a tissue with blood.
- **Myotonia**: increased muscle tension.
- **Coitus**: sexual intercourse.

4. The timing and pattern of meiosis in mammals differ from males and females

1. Sperm are small and motile. In contrast, eggs, which provide the initial food stores for the embryo, are typically much larger.
2. Spermatogenesis and oogenesis in three significant ways
    1. Only in spermatogenesis do all four products of meiosis develop into mature gametes.
    2. Spermatogenesis occurs throughout adolescence and adulthood. During oogenesis in human females, mitotic divisions are thought to be complete before birth, and the production of mature gametes cease at about age 50.
    3. Spermatogenesis produces mature sperm from precursor cells in a continuous sequence, whereas oogenesis has long interruptions.

- **Gametogenesis**: the production of gametes.
- **Spermatogenesis**: the formation and development of sperm cells.
- **Oogenesis**: the development of mature oocytes.

5. The interplay of tropic and sex hormones regulates mammalian reproduction

1. In both males and females, the coordinated actions of hormones from the hypothalamus, anterior pituitary, and gonads govern human reproduction. The principle sex hormones are steroid hormones: in males, androgens, especially testosterone; in females, estrogens, especially estradiol, and progesterone. Like the gonadotropins, the sex hormones regulate gametogenesis directly and indirectly.
2. Androgens are responsible for male vocalizations. During human embryogenesis, androgens promote the development of the primary sex characteristics of males.
3. At puberty, sex hormones in both males and females induce formation of secondary sex characteristics. Androgens cause the voice to deepen, facial and pubic hair to develop, and muscles to grow. Androgens also promote specific sexual behaviors and sex drive, as well as an increase in general aggressiveness. Estradiol stimulates breast and public hair development, induces fat deposition in the breasts and hips, increases water retention, and alters calcium metabolism.
4. In males, the FSH and LH secreted in response to GnRH are both required for normal spermatogenesis. FSH promotes the activity of Sertoli cells. Within the seminiferous tubules, these cells nourish the developing sperm. LH regulates Leydig cells, cells located in the interstitial space between the seminiferous tubules., causing them to secrete androgens. Testosterone regulates blood levels of GnRH, FSH, and LH through inhibitory effects on the hypothalamus and anterior pituitary, as does **inhibin**, a hormone that is produced by the Sertoli cells.
5. Ovulation occurs only after the endometrium has started to thicken and develop a rich blood supply, preparing the uterus for the possible implantation of an embryo. If pregnancy does not occur, the uterine lining is sloughed off, and another cycle begins. The cyclic shedding of the endometrium from the uterus, which occurs in a flow through the cervix and vagina, is called **menstruation**. The changes in the uterus define the **menstrual cycle**, also called the **uterine cycle**. The cyclic events that occur in the ovaries define the **ovarian cycle**.
6. **The Ovarian Cycle:** During the **follicular phase**, the follicles grow and the oocytes mature. The low levels of estradiol inhibit secretion of the pituitary hormones, keeping the levels of FSH and LH relatively low. When the estradiol secretion by the growing follicle beings to rise steeply, the FSH and LH levels rise as well, causing the follicle to rupture and release the secondary oocyte. There is sometimes a distinctive pain in the lower abdomen at or near the time of ovulation; this pain localizes to the left or right side, corresponding to whichever ovary has matured a follicle during that cycle. The **luteal phase** of the ovarian cycle follows ovulation. The corpus luteum secretes progesterone and estradiol, reducing LH and FSH secretion. Low gonadotrophin levels near the end of the luteal phase cause the corpus luteum to disintegrate, causing the pituitary gland to begin secreting more FSH.
7. **The Uterine Cycle**: Prior to ovulation, ovarian steroid hormones stimulate the uterus to prepare for support of an embryo. Increased estradiol levels cause the endometrium to thicken (**proliferative phase**). The luteal phase of the ovarian cycle is coordinated with the **secretory phase** of the uterine cycle. Menstruation is the **menstrual flow phase** of the uterine cycle. The first day of menstruation is designated day 1 of the new uterine (and ovarian) cycle.
8. About 7% of women of reproductive age suffer from **endometriosis**, a disorder in which some cells of the uterine lining migrate to an abdominal location that is abnormal, or **ectopic**.

9. After about 500 cycles, a woman undergoes **menopause**, the cessation of ovulation and menstruation. The ovaries lose their responsiveness to FSH and LH, resulting in a decline in estradiol production by the ovary. One intriguing hypothesis proposes that during early human evolution, undergoing menopause after bearing several children allowed a mother to provide better car for her children and grandchildren.
10. Non-primate mammals have **estrous cycles**, in which in the absence of a pregnancy, the uterus reabsorbs the endometrium and no extensive fluid flow occurs. Mammals with estrous cycles typically copulate only during the period surrounding ovulation. Extrus is sometimes called heat, and indeed, the female's body temperature increases slightly.

6. In placental mammals, an embryo develops fully within the mother's uterus.

1. The alkalinity of the semen helps neutralize the acidic environment of the vagina, protecting the sperm and increasing the motility. When first ejaculated, the semen coagulates, but soon after anticoagulants liquefy the semen.
2. Fertilization (**conception**) occurs when a sperm fuses with an egg in the oviduct. About 24 hours later, the resulting zygote begins dividing, a process called **cleavage**. By about 1 week after fertilization, the **blastocyte**, a sphere of cells surrounding a central cavity, forms. Several days after that, the embryo implants into the endometrium. One embryonic hormone, **human chorionic gonadotropin (hCG)**, acts like pituitary LH in maintaining secretion of progesterone and estrogens by the corpus luteum through the first few months of pregnancy. Levels of hCG in the maternal blood are so high that some is excreted in the urine, where its presence is the basis of a common early pregnancy test.
3. Many pregnancies terminate spontaneously as a result of chromosomal or developmental abnormalities. Much less often, a fertilized egg lodges in the oviduct, resulting in a tubal, or ectopic, pregnancy.
4. Human gestation can be divided for convenience into three **trimesters** of about three months each.

- **Pregnancy (gestation):** the condition of carrying one or more embryos in the uterus.

5. **First Trimester**: the endometrium responds to implantation by growing over the blastocyst. The embryo's body structures now begin to differentiate. During its first 2-4 weeks of development, the embryo obtains nutrients directly from the endometrium. The outer layer of the blastocyte (**trophoblast**) grows outward and mingles with the endometrium, forming the **placenta**. Material diffusing between the maternal and embryonic circulatory systems supplies nutrients, provides immune protection, exchanges respiratory gases, and disposes of metabolic wastes for the embryo. Blood from the embryo travels to the placental through the arteries of the umbilical cord and returns via the umbilical vein.
6. Splitting of the embryo during the first month of development can result in identical, or *monozygotic*, twins. Fraternal (*dizygotic*) twins arise when two follicles mature in a single cycle.
7. The first trimester is the main period of **organogenesis**, the development of the body organs. At 8 weeks, all the major structures of the adult are present in rudimentary form, and the embryo is called a **fetus**. It is about 5 cm long.
8. High levels of progesterone initiates changes in the mother: increased mucus in the cervix forms a plug to protect against infection, the maternal part of the placenta stop, the uterus gets larger, and ovulation and menstrual cycling stop. The breasts enlarge rapidly and are often quite tender, and three-fourths of all pregnant women experience nausea.
9. **Second trimester**: The uterus grows enough for the pregnancy to become obvious. The fetus grows to about 30 cm in length and is very active. hCG declines, the corpus luteum deteriorates, and the placenta completely takes over the production of progesterone.
10. **Third trimester**: the fetus grows to about 3-4 kg in weight and 50 cm in length. Fetal activity decreases as the fetus fills the available space. The mother's abdominal organs become compressed and displaced, leading to frequent urination, digestive blockages, and strain in the back mucles.

- **Labor**: the process by which childbirth occurs.

11. **Labor**: Local regulators (prostaglandins) and hormones (estradiol and oxytocin) induces and regulates **labor**. A series of strong, rhythmic uterine contractions during the three stages of labor bring about birth, or *parturition*. The first stage is the opening up and thinning of the cervix, ending with complete dilation. The second stage is expulsion, or delivery, of the baby. The final stage is delivery of the placenta.
12. **Lactation** is unique to mammals. The hypothalamus signals the anterior pituitary to secrete prolactin, which stimulates the mammary glands to produce milk. The secretion of oxytocin triggers release of milk from the mammary glands.
13. **Maternal Immune Tolerance of the Embryo and Fetus**: the overall regulation of the immune system appears to be altered by the reproductive process.

- **Contraception:** the deliberate prevention of pregnancy.
- **Abortion**: the termination of a pregnancy in progress.

14. **Contraception and Abortion**:
    - Fertilization can be prevented by abstinence. Temporary abstinence, often called the **rhythm method** of birth control or **natural family planning**, depends on refraining from intercourse when conception is most likely. A pregnancy rate of 10-20% is typically reported fro couples practising natural family planning
    - As a method of preventing fertilization, *coitus interruptus*, or withdrawal, is unreliable.
    - The several **barrier methods** of contraception that block the sperm from meeting the egg have pregnancy rates of less than 10%. Examples include the condom, the diaphragm, the cervical cap, and the vaginal pouch (aka female condom).
    - Except for complete abstinence from sexual intercourse, the most effective means of birth control are sterilization, intrauterine devices, and hormonal contraceptives (typically **birth control pills**).
    - The most commonly prescribed birth control pills are a combination of a synthetic estrogen and a synthetic progestin. Combination birth control pills can also be used in high doses as "morning-after" pills. For women taking a combination pill, cardiovascular problems are the most serious concern. Among nonsmokers, birth control pills slightly raise a women's risk of abnormal blood clotting, high blood pressure, heart attach, and stroke. However, the pill decreases the risk of ovarian and endometrial cancers.
    - Hormonal male contraceptives are still in the testing stage.
    - Sterilization is the permanent prevention of gamete release. **Tubal ligation** in women usually involves cauterizing or tying off a section of each oviduct to prevent eggs from traveling into the uterus. **Vasectomy** in men is the tying off or excision of a small section of each vas deferens to prevent sperm from entering the urethra. Both procedures are difficult to reverse.
    - A drug called mifepristone, or RU486, enables a woman to terminate pregnancy non-surgically within the first 7 weeks.
15. **Modern Reproductive Technologies**:
    1. Ultrasound imaging is commonly used to analyze the fetus's size and condition. Amniocentesis and chorionic villus sampling are techniques in which a needle is used to obtain fetal cells from fluid or tissue surrounding the embryo. A blood sample from the mother can also yield fetal cells.
    2. To date, almost all detectable disorders remain untreatable in the uterus, and many cannot be corrected even after birth.

3. For women, the risk of reproductive difficulties, as well as genetic abnormalities of the fetus, increases steadily past age 35; evidence suggests that the prolonged period of time oocytes spend in meiosis is largely responsible.
4. Hormone therapy can sometimes increase sperm or egg production, and surgery can often correct ducts that have failed to form properly or have become blocked.
5. **Assisted reproductive technologies** generally involve surgically removing eggs from an woman's ovaries after hormonal stimulation, fertilizing the eggs, and returning them to the woman's body. For ***in vitro*** **fertilization (IVF)**, oocytes are mixed with sperm in culture dishes. **Intracytoplasmic sperm injection (ICSI)** involves directly injecting the head of a sperm into an egg.
6. Evidence indicates that abnormalities arising as a consequence of IVF procedures are rare.

CHAPTER 47: ANIMAL DEVELOPMENT

- **Cell differentiation**: process of cell specialization.
- **Morphogenesis**: the process by which an organism takes shape.
- **Model organism**: a species that lends itself to the stud of a particular question, is representative of a larger group, and is easy to grow in the lab.

*The question of how a zygote becomes an animal has intrigued scientists for centuries. In the 1700s, the prevailing notion was **preformation**: the idea that the egg or sperm contains an embryo—a preformed, miniature infant, or "homunculus"—that simply became larger during the development. The competing explanation of embryonic development was **epigenesis**: the idea that the form of an animal emerges gradually from a relatively formless egg.*

I. After fertilization, embryonic development proceeds through cleavage, gastrulation, and organogenesis.

1. During the first stage (*cleavage*), cell division creates a hollow ball of cells, the blastula, from the zygote. *Gastrulation* rearranges the blastula into a three-layered embryo, the gastrula. During *organogenesis*, the three layers become rudimentary organs.

2. Fertilization: Combines the haploid gametes into a diploid zygote. Fertilization has been studied extensively in sea urchins.

1. The Acrosomal Reaction: When the head of a sea urchin sperm contacts the jelly coat of a sea urchin egg, molecules in the egg's coat trigger the **acrosomal reaction** in the sperm. A specialized vesicle (**acrosome**) at the tip of the sperm discharges hydrolytic enzymes, which digest the jelly coat of an egg. The acrosomal process elongates, and certain proteins on its tip adhere to sperm receptor proteins extending from the egg. The sperm and egg plasma membranes then fuse, causing sodium ion channels to open and the cell to depolarize, preventing additional sperm from fusing with the egg's plasma membrane (**fast block to polyspermy**).

2. The Cortical Reaction: Within seconds after a sperm binds to the egg, a calcium ion surge causes vesicles called **cortical granules** fuse with the egg plasma membrane, secreting enzymes and other macromolecules into the *perivitelline space* between the plasma membrane and the vitelline layer. These molecules push the vitelline layer away from the egg and harden the larger, forming a protective **fertilization envelope**. An enzyme clips off and releases the external portions of the sperm receptor proteins and any sperm attached to them.

3. Activation of the Egg: The calcium ion spike also triggers an increase in the rates of cellular respiration and protein synthesis by the egg.

3. Fertilization in Mammals: The mammalian egg is clocked by follicle cells released along with the egg during ovulation. The extracellular matrix of the egg is called the **zona pellucida**. Mammals do not have a fast block to polyspermy. The entire sperm is taken into the egg.

- **Holoblastic cleavage**: Egg contains relatively little yolk. The blastocoel is centrally located, and the cleavage furrow passes all the way through cells.
- **Meroblastic cleavage**: the incomplete division of a yolk-rich egg.

4. Cleavage: The cells carry out the S and M phases of the cell cycle; however, they often virtually skip over the G_1 and G_2 phases. Cleavage simply partitions the cytoplasm of one large cell, the zygote, into many smaller cells called **blastomeres**, each with its own nucleus. The **blastocoel**, a fluid-filled cavity in the middle of the embryo, begins to form, and the embryo becomes a **blastula.**

1. Eggs often have a definite polarity defined by the uneven distribution of substances in the cytoplasm. Yolk is often concentrated toward one pole of the egg, called the **vegetal pole**; the other end is called the **animal pole**.

2. In the frog, a movement called *cortical rotation* establishes the dorsal-ventral axis. The animal hemisphere cortex moves toward the vegetal inner cytoplasm on the side where the sperm nucleus entered, which is always in the animal hemisphere. The vegetal hemisphere cortex across from the side of sperm nucleus entry moves toward the inner cytoplasm of the animal hemisphere. Proteins in the vegetal cortex interact with molecules of the animal medulla and initiate the development of dorsal structures. This rotation exposes a light gray region of cytoplasm, the **gray crescent.** Unequal division of the cytoplasm cause the blastocoel to be located in the animal hemisphere.

5. Gastrulation: The cells of an embryo rearrange itself to become a three-layered **gastrula**. Gastrulation is driven by changes in cell motility, changes in cell shape, and changes in cellular adhesion to other cells and to molecules of the extracellular matrix. The three layers produced are called the **germ layers**: the **endoderm**, the **mesoderm**, and the **ectoderm**.

1. In an sea urchin embryo, gastrulation begins at the vegetal pole, where individual cells detach from the blastocoel wall and become *mesenchyme cells* that migrate in the blastocoel. The remaining cells near the vegetal pole become a *vegetal plate*, which buckles inwards (**invagination**), forming a blind-ended tube called the **archenteron**. The open end of the **archenteron** is called the **blastopore**. The blind end of the archenteron fuses with the ectoderm to produce a rudimentary digestive tube.

2. Gastrulation is more complicated in frog embryos because of the yolk and because the wall of the blastula is more than one cell thick. Gastrulation begins when a group of cells on the dorsal side begin to invaginate, forming a **dorsal lip**. The future endoderm and mesoderm cell layers on the surface of the embryo roll over the edge of the lip into the interior of the embryo (**involution**). The blastocoel collapses. As gastrulation is completed, the circular lip of the blastopore encircles a **yolk plug**.

3. In birds, the inward movement of cells during gastrulation is affected by the large mass of yolk pressing against the bottom of the embryo. Instead of becoming a blastula, bird embryos become a **blastoderm** consisting of upper and lower layers—the *epiblast* and *hypoblast*—lying atop the yolk mass. During gastrulation, some epiblast cells move toward the midline of the blastoderm, forming a primitive **streak**. Then they detach and move inward toward the yolk, forming the endoderm and the mesoderm. The hypoblast cells do not contribute to the embryo.

6. Organogenesis: The three germ layers develop into rudimentary organs.

1. In chordates, the neural tube and the **notocord** develop first. The notochord forms from dorsal mesoderm that condenses when cells associate tightly as a group just above the archenteron. The ectoderm above the notochord becomes the *neural plate*, which rolls itself into a **neural tube**. **Neural crest cells** develop along the boarders where the neural tube pinches off and migrate to various parts of the embryo, forming peripheral nerves, parts of teeth, skull bones, and many other different cell types. Strips of cells lateral to the notochord separate into blocks called **somites**. Parts of the somites dissociate into mesenchyme cells, which migrate individually to new locations. Some mesenchyme cells gather around the notochord and form the vertebrae. Others form the muscles associated with the vertebral column and the ribs. Lateral to the somites, the mesoderm splits into two layers that form the lining of the coelom.

2. In chickens, the borders of the blastoderm fold downward and come together, pinching the embryo into a three-layered tube joined under the middle of the body to the yolk. Neural-tube formation, development of the notochord and somites, and other events in organogenesis occur much as in the frog embryo.

3. In flies and other insects, tissues of the nervous system form when ectoderm along the anterior-posterior axis rolls into a tube inside the embryo. The tube is on the ventral side of the fly embryo rather than the dorsal side.

7. Developmental Adaptations of Amniotes:

1. All vertebrate embryos require an aqueous environment for development. The shelled egg of birds and other reptiles, as well as a few mammals (monotremes), and the uterus of marsupial and eutherian mammals provide an aqueous environment. Reptiles (including birds) and mammals are called **amniotes**.

2. In aminote embryos, four **extraembryonic membranes** also form: the **chorion** functions in gas exchange; the **amnion** encloses the embryo in a protective, fluid-filled amniotic cavity; the **yolk sac** encloses the yolk; and the

allantois disposes of waste.

8. **Mammalian Development**: Fertilization takes place in the oviduct, and the earliest stages of development occur while the embryo completes its journey down the oviduct to the uterus. Mammalian gastrulation and early organogenesis follow pattern similar to that of birds and other reptiles.
    1. At the completion of cleavage, the embryo has more than 100 cells arranged around a central cavity (**blastocyst**). Clustered at one end of the blastocyte cavity is a group of cells called the **inner cell mass**, which forms the embryo and most of the extraembryonic membranes.
    2. The **trophoblast**, the outer epithelium of the blastocyst, does not contribute to the embryo itself but instead provides support services. It secretes enzymes that break down molecules of the endometrium and extends fingerlike projections into the surrounding maternal tissue. Around the time of implantation, the inner cell mass of the blastocyst forms a flat disk with an upper layer of cells, the *epiblast*, and a lower layer, the *hypoblast.*
    3. As implantation is completed, gastrulation begins. Extraembryonic membranes begin to form. The trophoblast, mesodermal cells derived from the epiblast, and adjacent endometrial tissue all contribute to the placenta.
    4. The fluid from the amniotic cavity is the "water" expelled from the mother's vagina when the amnion breaks just prior to childbirth. The yolk sac in mammals actually contains no yolk; it bears the name because it is homologous with the yolk sac in birds. The yolk sac membrane in mammals is a site of early formation of blood cells, which later migrate into the embryo proper. The allantois in mammals is incorporated into the umbilical cord.
    5. Identical twins can arise when embryonic cells become separated. If the separation occurs quite early, before the trophoblast and inner cell mass become differentiated, then two embryos will grow, each with its own chorion and amnion. If the separation occurs a little later, after the chorion forms but before the amnion forms, the two embryos will share a chorion but have separate amnions. If the separation occurs even later, the two embryos will share a chorion and an amnion.

2. Morphogenesis in animals involves specific changes in cell shape, position, and adhesion.
    1. Morphogenesis is a major aspect of development in both animals and plants, but only in animals does it involve the *movement* of cells.
    2. Changes in the shape of a cell usually involve reorganization of the cytoskeleton. Microtubules oriented parallel to the dorsal-ventral axis of the mbryo apparently help lenghten the cells in that direction. Actin microfilaments at the dorsal end of each cell contract to give the cells a wedge shape that forces the ectoderm layer to bend inwards.
    3. The cytoskeleton also drives cell migration. The cellular protrusions of migrating embryonic cells are usually flat sheets (lamellipoda) or spikes (filopodia).
    4. During gastrulation in some organisms, invagination begins when cuboidal cells on the surface of the blastula become wedge-shaped. Movement of cells deeper into the embryo involves the extension of filopodia. The cells that first move through the blastopore and up along the inside of the blastocoel wall drag others behind them.
    5. There are also many situations in which cells migrate individually.
    6. Cell crawling is also involved in **convergent extension**, a type of morphogenetic movement in which the cells of a tissue layer rearrange themselves so that the sheet becomes narrower while it becomes longer. It occurs, for example, as the archenteron elongates in the sea urchin embryo and during involution in the frog gastrula.
    7. **Cell adhesion molecules (CAMs)** contribute to cell migration and stable tissue structure. One important class of CAMs is the **cadherins**, which require calcium ions outside the cell for proper function. Janet Heasman, Chris Wylie, and colleagues demonstrated the importance of one particular cadherin in the formation of the frog blastula. Cadherins are also involved in the tight adhesion of cells in the mammalian embryo.
    8. Cell migration and tissue organization also involve the extracellular matrix. Membrane proteins may act as receptors that bind specific ECM molecules. An organized array of ECM fibers may function as tracts; some have substances that inhibit migration off that path. Nonmigratory cells can affect cell migration by secreting things into the ECM.
    9. Some extracellular glycoproteins (ex. fibronectin) provide specific molecular anchorage for moving cells. Fibronectin fibers line the roof of the blastocoel; cells at the free edge of the involuting mesoderm migrate along the fibers.
    10. Moving cells engage in an ongoing dialogue with the ECM and other cells in the vicinity. As migrating cells move along specific paths, a variety of receptor proteins on their surfaces pick up directional cues from the immediate environment. Cell-ECM and cell-cell binding systems affect each other during convergent extension: fibronectin binding to its receptor provides a molecular signal to the cell that ultimately affects the function of cadherins.

3. The developmental fate of cells depends on their history and on inductive signals.
    1. Virtually every cell in an organism has the same genome: different cells make different proteins by expressing different genes.
    2. Two general principles integrate our current knowledge of the genetic and cellular mechanisms that underlie differentiation during embryonic development.
        1. *During early cleavage divisions, embryonic cells must somehow become different from one another.* In many animal species, initial differences between cells result from the uneven distribution of cytoplasmic determinants in the unfertilized egg.
        2. *Once initial cell asymmetries are set up, subsequent interactions among the embryonic cells influence their fate, usually by causing changes in gene expression*. This mechanism is called **induction;** it may be mediated by diffusible signaling molecules or cell-surface interactions.
    3. The lineages of cells making up the three germ layers created by gastrulation are traceable to cells in the blastula, before gastrulation has begun. Later researchers developed techniques that allowed them to mark an individual blastomere during cleavage and then follow the maker as it was distributed to all the mitotic descendants of that cell.
    4. In nonamniote vertebrates, basic instructions for forming the body axes are established early, during oogenesis or fertilization.
    5. In chicks, gravity is involved in establishing the anterior-posterior axis as the egg travels down the hen's oviduct before being laid. Later, pH differences between the two sides of the blastoderm cells establish the dorsal-ventral surface.
    6. In many species that have cytoplasmic determinants, only the zygote is **totipotent—**that is, capable of developing into all the different cell types of that species.
    7. The fates of embryonic cells can be affected not only by the distribution of cytoplasmic determinants but also by how this distribution relates to the zygote's characteristic pattern of cleavage.
    8. Once embryonic cell division creates cells that differ from each other, the cells begin to influence each other's fates by induction. In frogs, the dorsal lip of the blastopore in the early gastrula functions as an "organizer" of the embryo's body plan by initiating a chain of inductions that results in the formation of the notochord, the neural tube, and other organs.
    9. Inductive signals play a major role in **pattern formation—**the development of an animal's spatial organization, the arrangement of organs and tissues in their characteristic places in three-dimensional space. The molecular cues that control pattern formation, called **positional information**, tell a cell where it is with respect to the animal's body axes

- **Fate maps**: territorial diagrams of embryonic development.
- *Developmental potential*: the range of structures a cell can give rise to.

and help to determine how the cell and its descendants will respond to molecular signaling.

10. The wings and legs of chicks, like all vertebrate limbs, begin as limb buds, bumps of mesodermal tissue covered by a layer of ectoderm. Each component of a chick limb, such as a specific bone or muscle, develops with a precise location and orientation relative to three axes: the proximal-distal axis, the anterior-posterior axis, and the dorsal-ventral axis. One limb-bud organizer region is the **apical ectodermal ridge (AER)**, a thickened area of ectoderm a the tip of the bud. The second major limb-bud organizer region is the **zone of polarizing activity (ZPA)**, a block of mesodermal tissue located underneath the ectoderm where the posterior side of the bud is attached to the body.

11. *Hox* genes play various roles at several distinct points during limb pattern formation.

CHAPTER 48: NEURONS, SYNAPSES, AND SIGNALING

- Neurons: the nerve cells that transfer information within the body.
- In more complex animals, higher-order processing is carried out largely in groups of neurons organized into a **brain** or into simpler clusters called **ganglia**.

1. NEURON ORGANIZATION AND STRUCTURE AFFECT FUNCTION IN INFORMATION TRANSFER

1. The squid has some extraordinarily large nerve cells that are well suited for physiological studies.
2. Three stages in information processing: sensory input, integration, and motor output:
   1. **Sensory neurons** transmit information from eyes and other sensors that detect external stimuli or internal conditions.
   2. Neurons in the brain or ganglia integrate the sensory input. The vast majority of neurons in the brain are **interneurons**, which make only local connects.
   3. **Motor neurons** transmit signals to muscle cells, triggering muscle activity.
3. The **central nervous system** (CNS) consists of the brain and a longitudinal nerve cord. The neurons that carry information into and out of the CNS consitute the **peripheral nervous system (PNS)**.
4. Most of a neuron's organelles, including its nucleus, are located in the **cell body**. A typical neuron has numerous **dendrites**, highly branched extensions that *receive* signals from other neurons. A neuron also has a single **axon**, an extension that *transmits* signals to other cells. The cone-shaped region of an axon where it joins the cell body is called the **axon hillock**.
5. Each branched end of an axon transmits information to another cell at a junction called a **synapse**. The part of each axon branch that forms this specialization junction is a **synaptic terminal**. At most synapses, chemical messengers called **neurotransmitters** pass information from the transmitting neuron to the receiving cell. In describing a synapse, we refer to the transmitting neuron as the **presynaptic cell** and the neuron, muscle, or gland cell that receives the signal as the **postsynaptic cell**.
6. To function normally, the neurons of vertebrates and most invertebrates require supporting cells called glial cells, or **glia**.

2. ION PUMPS AND ION CHANNELS MAINTAIN THE RESTING POTENTIAL OF A NEURON.

1. All cells have a **membrane potential**: a voltage across their plasma membrane. In neurons, inputs from other neurons or specific stimuli cause changes in this membrane potential that act as signals, transmitting and processing information. The membrane potential of a rest neuron—one that is not sending signals—is its **resting potential** and is typically between -60 and -80 mV.
2. The concentration of K^+ is 140 m*M* inside the cell, but only 5 m*M* outside. The Na^+ concentration gradient is nearly the opposite: 150 m*M* outside and only 15 m*M* inside. These Na^+ and K^+ gradients are maintained by *sodium-potassium pumps* in the plasma membrane.
3. The ion channels that establish the membrane potential have *selective permeability*; they allow only certain ions to pass. Outflow of K^+ leads to an excess of negative charge inside the cell. This buildup of negative charge within the neuron is the source of the membrane potential.
4. The magnitude of the membrane voltage at equilibrium for a particular ion is called that ion's **equilibrium potential (E_{ion}):** $E_{ion} = 62mV\,(\log \frac{[ion]_{outside}}{[ion]_{inside}})$, at 37°C and for an ion with a net charge of 1+.

3. ACTION POTENTIALS ARE THE SIGNALS CONDUCTED BY AXONS

1. Neurons contain **gated ion channels**, ion channels that open or close in response to stimuli. The opening or closing of ion channels alters the membrane's permeability to particular ions, which in turn alters the membrane potential. Opening more potassium channels increases the membrane's permeability to K^+, increasing the net diffusion of K^+ out of the neuron. The inside of the membrane becomes more negative. The increase in the magnitude of the membrane potential is called a **hyperpolarization**. A reduction in the magnitude of the membrane potential is called a **depolarization**. If the gated sodium channels open, the membrane's permeability to Na^+ increases, causing a depolarization as the membrane potential shifts toward E_{Na} (+62 mV at 37°C). The types of hyperpolarization and depolarization we have considered so far are called *graded potentials* because the magnitude of the change in membrane potential varies with the strength of the stimulus.
2. Many of the gated ion channels in neurons are **voltage-gated ion channels**. If a depolarization opens voltage-gated sodium channels, the resulting flow of Na^+ into the neuron results in further depolarization.
3. Action potentials occur whenever a depolarization increases the membrane voltage to a particular value, called the **threshold**. Because action potentials occur fully or not at all, they represent an *all-or-none* response to stimuli. Because action potentials are so brief, a neuron can produce hundred of them per second. Differences in action potential frequency convey information about signal strength. There are four stages to action potentials:
   1. At the resting potential, most voltage-gated sodium channels are closed. Some potassium channels are open, but most voltage-gated potassium channels are closed.
   2. A stimulus depolarizes the membrane. Gated sodium channels open, allowing more Na^+ to diffuse into the cell.
   3. Once the threshold is crossed, the membrane potential quickly rises close to E_{Na}. (*Rising phase).*
   4. Voltage-gated sodium channels inactivate soon after opening, halting Na^+ inflow; and most voltage-gated potassium channels open, causing a rapid outflow of K^+.
   5. *Undershoot*: The membrane's permeability to K^+ is higher than at rest, so the membrane potential is closer to E_K than it is at the resting potential. The gated potassium channels eventually close, and the membrane potential returns to the resting potential.
4. An action potential functions as a long-distance signal by regenerating itself as it travels from the cell body to the synaptic terminals. At the site where an action potential is initiated (usually the axon hillock), Na^+ inflow during the rising phase creates an electrical current that depolarizes the neighboring region of the axon membrane. In the repolarized zone, the sodium channels remain inactivated. Consequently, the inward current that depolarizes the axon membrane *ahead* of the action potential cannot produce another action potential *behind* it. An action potential that starts at the axon hillock moves in only one direction—toward the synaptic terminals.
5. Wider axons conduct action potentials more rapidly than narrow ones. In **saltatory conduction**, the **myelin sheath** insulates a neuron and helps it conduct signals faster. Myelin sheaths are produced by **oligodendrocytes** in the CNS and **Schwann cells** in the PNS. Voltage-gated sodium channels are restricted to gaps in the myelin sheath called **nodes of Ranvier**.

- **Action potential**: a massive change in membrane voltage.
- **Refractory period**: The "downtime" following an action potential when a second action potential cannot be initiated. It is due to the inactivation of sodium channels.

4. NEURONS COMMUNICATE WITH OTHER CELLS AT SYNAPSES.

1. Electrical synapses contain gap junctions, which allow electrical current to flow directly from one neuron to another.
2. *Chemical synapses* involve the release of a chemical neurotransmitter. A synaptic cleft separates the two neurons. The arrival of an action potential at a synaptic terminal opens calcium ion channels. The influx of calcium ions cause **synaptic vesicles** to bind with the plasma membrane and release neurotransmitters.
3. Binding of a neurotransmitter to a particular part of an ion channel opens the channel and allows specific ions to diffuse across the postsynaptic membrane. **Excitatory postsynaptic potentials (EPSPs)** bring the membrane potential of the

postsynaptic cell closer to the threshold; **inhibitory postsynaptic potentials (IPSPs)** bring the membrane potential further away.

4. A single EPSP is usually too small to trigger an action potential. **Temporal summation**: two EPSPs occur at a single synapse in such rapid succession that the postsynaptic neuron's membrane potential has not returned to the resting potential. **Spatial summation**: two EPSPs produced nearly simultaneously by *different* synapses.
5. Various mechanisms rapidly clear neurotransmitters from the synaptic cleft.
6. **Modulated Synaptic Transmission**: The neurotransmitter binds to a receptor that activates a signal transduction pathway involving a second messenger, which may alter the postsynaptic cell in many diverse ways. The effects of these second-messenger systems have a slower onset but last longer.
7. **Neurotransmitters**: There are more than 100 known neurotransmitters. Nearly all fall into one of a few groups based on chemical structure. The major classes of neurotransmitters are acetylcholine, biogenic amines, amino acids, neuropeptides, and gases.
    1. **Acetylcholine**: Excites noncardiac muscles. Acetylcholine activity is terminated by *acetylcholinesterase*. Inhibits cardiac muscle.
    2. **Biogenic amines** are neurotransmitters derived from amino acids. **Serotonin** is synthesized from tryptophan. The catecholamines are derived from tyrosine. One catecholamine, **dopamine**, acts only as a neurotransmitter. Two others—**epinephrine** and **norepinephrine—**act both as neurotransmitters and as hormones.
    3. **Amino acids**: Two amino acids serve as the major neurotransmitters in the vertebrate CNS: **gamma-aminobutyric acid (GABA)** and **glutamate**.
    4. **Neuropeptides**: relatively short chains of amino acids. **Substance P** is a key excitatory neurotransmitter that mediates our perception of pain. **Endorphins** decrease pain perception.
    5. **Gases**: Some neurons in vertebrates release dissolved gases that act as local regulators. Nitric oxide (NO) is a gast that is synthesized on demand. Carbon monoxide also acts as a neurotransmitter.

CHAPTER 49: NERVOUS SYSTEMS

- **Reflexes**: the body's automatic responses to ceratin stimuli.

1. *Nervous systems consist of circuits of neurons and supporting cells.*

1. In most cnidarians, a series of interconnected nerve cells a diffuse **nerve net**.
2. In more complex animals, the axons of multiple nerve cells are often bundled together, forming **nerves**.
3. Animals with elongated, bilaterally symmetrical bodies have even more specialized nervous systems. Such animals exhibit cephalization. One or more nerve cords connect the anterior "brain" with other nerves. The brain and nerve cords make up the *central nervous system* (CNS); nerves and ganglia comprise the *peripheral nervous system* (PNS).
4. The brain takes care of complex integrations; the spinal cord relays instructions and **reflexes**.
5. Invertebrates have a ventral nerve cord, vertebrates a dorsal one. Ganglia are found just outside the spinal cord in vertebrates.
6. The brain and spinal cord of vertebrates are derived from the dorsal embryonic nerve cord, which is hollow. The hollow cavity of the embryonic nerve cord becomes the **central canal** of the spinal cord and the **ventricles** of the brain. Both the central canal and the four ventricles are filled with **cerebrospinal fluid(CSF)**.
7. The brain is composed of gray matter and white matter. **Gray matter** consists mainly of neuron cell bodies, dendrites, and unmyelinated axons. **White matter** consists of bundled axons that have myelin sheaths.
8. **Glia in the CNS**: *Ependymal cells* line the ventricles and have cilia that circulate the CSF. *Microglia* protect against invading microorganisms. *Oligodendrocytes* myelinate axons in the CNS. **Astrocytes** provide structural support for neurons and regulate the extracellular concentrations of ions and neurotransmitters. They may facilitate information transfer at synapses or even release neurotransmitters. They regulate blood supply to the neurons as well. During development, they induce the cells that line the capillaries in the CNS to form tight junctions, forming the **blood-brain barrier**. In an embryo, **radial glia** form tracks along which newly formed neurons migrate from the neural tube. Astrocytes and radial glia can also generate new neurons and glia.
9. **The Peripheral Nervous System**:
    1. *Afferent* neurons bring in information; *efferent* neurons send out commands.
    2. The **cranial nerves** connects the brain with locations mostly in organs of the head and upper body. The **spinal nerves** run between the spinal cord and parts of the body below the head.
    3. The **motor system** consists of neurons that carry signals to skeletal muscles. The **autonomic nervous system** regulates the *internal* environment by controlling smooth and cardiac muscles and the organs of the digestive, cardiovascular, excretory, and endocrine systems. Three divisions—sympathetic, parasympathetic, and enteric—together make up the autonomic nervous system.
        1. Activation of the **sympathetic division** corresponds to arousal and energy generation.
        2. Activation of the **parasympathetic division** generally causes the opposite responses that promote calming and a return to self-maintenance function.
        3. The **enteric division** regulates secretion and peristalsis.

2. *The vertebrate brain is regionally specialized.*

1. In vertebrates, three anterior bulges of the neural tube—the **forebrain**, **midbrain**, and **hindbrain—**become evident as the embryo develops. By the 5th week of embryonic development, there are five brain regions. The three derived from the midbrain and hindbrain become the brain stem. The *telencephalon* becomes the adult **cerebrum**. Rapid, expansive growth of the telencephalon during the 2nd and 3rd months causes the outer portion of the cerebrum (**cerebal cortex**) to extend over and around much of the rest of the brain. The *diencephalon* becomes the thalamus, hypothalamus, and epithalamus.
2. The **brainstem** ("lower brain") functions in homeostasis, coordination of movement, and conduction of information to and from higher brain centers. The adult brainstem consists of the midbrain, the **pons**, and the **medulla oblongata**. All axons carrying sensory information to and motor instructions from higher brain regions pass through the brainstem. The medulla and pons also help coordinate large-scale body movements. Signals from the brainstem affect attention, alertness, appetite, and motivation. The medulla contains centers that control several automatic, homeostatic functions, including breathing, heart and blood vessel activity, swallowing, vomiting, and digestion. The pons also participates in some of these activities.
    1. The **reticular formation determines** which incoming information reaches the cerebral cortex.
    2. All birds and mammals show characteristic sleep/wake cycles controlled by levels of melatonin, which is synthesized from serotonin and reaches peak levels during the night.
    3. Sleep and dreams are involved in consolidating learning and memory. Some animals display evolutionary adaptations that allow for substantial activity during sleep.
3. The **cerebellum**, which develops from part of the hindbrain, coordinates movements and balance.
4. The **diencephalon** develops into three adult brain regions: the thalamus, hypothalamus, and epithalamus. The thalamus and hypothalamus are major integrating centers that act as relay stations for information flow in the body. The epithalamus also contains the pineal gland, which secretes melatonin. The **thalamus** is the main input center for sensory information going to the cerebrum. The **hypothalamus** is one of the most important brain regions for the control of homeostasis.
    1. **Biological Clock Regulation by the Hypothalamus**: In mammals, circadian (daily) rhythms are coordinated by a group of neurons in the hypothalamus called the **suprachiasmatic nucleus**.

- **Biological clock**: a molecular mechanism that directs periodic gene expression and cellular activity.

5. The **cerebrum** handles most of the information processing in mammals. It is divided into right and left **cerebral hemispheres**. Each hemisphere consists of an outer covering of gray matter, the cerebral cortex, internal white matter; and groups of neurons collectively called *basal nuclei* that are located deep within the white matter. In humans, the cerebral cortex accounts for 80% of total brain mass. A thick band of axons known as the **corpus callosum** connects the two hemispheres. If damage occurs to the cerebrum early in development, the normal functions of the damaged area are frequently redirected elsewhere.
6. In humans, the outermost part of the cerebral cortex forms the *neocortex*, six parallel layers of neurons arranged tangential to the brain surface. Birds lack a neocortex but they are also capable of *cognition*.

3. *The cerebral cortex controls voluntary movement and cognitive functions*

- *Primary sensory areas* receive and process a specific type of sensory information.
- *Association areas* integrate the information from various parts of the brain.
- *Somatosensory* receptors provide information about touch, pain, pressure, temperature, and the position of muscles and limbs.

1. Each side of the cerebral cortex has four lobes: frontal, temporal, occipital, and parietal. The thalamus directs different types of input to distinct locations: visual information to the occipital lob, auditory input to the temporal lobe, and somatosensory and taste information to the parietal lobe. Olfactory information is sent first to regions of the cortex that are similar in mammals and reptiles and then via the thalamus to an interior part of the frontal lobe.
2. Actions and movement result from the motor cortex, which lies near the rear of the frontal lobe. Generally, neurons that control inferior areas of the body are located superior to neurons that control superior areas of the body.
3. The mapping of high cognitive functions to specific brain areas began in the 1800s. *Broca's area* produces speech and is located in front of the part of the primary motor cortex that controls muscles in the face.
4. *Wernicke's area* in the left temporal lobe helps comprehend speech.

5. **Lateralization:** the establishment of differences between the two hemispheres of the cerebrum. The left hemisphere is more adept at math and logical operations. The right hemisphere appears to be dominate in the recognition of faces and patterns, spatial relations, and nonverbal thinking.
6. Individuals with a severed corpus callosum exhibit a "split-brain" effect.
7. **Emotions** require many parts of the brain, including the *limbic system*. The limbic system consists of the amygdala, the hippopotamus, and parts of the thalamus. Structures within the limbic system have diverse functions, including emotion, motivation, olfaction, behavior, and memory. Emotions that manifest themselves in behaviors such as laughing and crying involve an interaction of parts of limbic system with sensory areas of the cerebrum. Structures in the forebrain also attach emotional "feelings" to basic, survival-related functions controlled by the brainstem, including aggression, feeding, and sexuality. The focus of emotional memory is the **amygdala** in the temporal lobe. The prefrontal cortex is also important in temperament and decision making.
8. **Consciousness** is an emergent property of the brain, and it recruits activities in many areas of the cerebra cortex.

4. *Changes in synaptic connections underlie memory and learning.*
   1. Developing neurons must compete for growth-supporting factors. Half of the neurons formed in the embryo are eliminated.
   2. Synapse elimination is the second major process that shapes nervous system development in the embryo.
   3. **Neural plasticity**: The capacity of the nervous system to be remodeled. Synapses can be created or removed, and signaling at a synapse could be increased or weakened.
   4. **Memory and Learning**: Both short and long-term memories are stored in the cerebral cortex. The hippocampus is essential for acquiring long-term memories, but not for maintaining them. The delay in forming long-term memories allows them to be integrated gradually into the existing store of knowledge and experience, providing a basis for more meaningful associations. Motor skills are usually learned by repetition.
   5. **Long-term potentiation (LTP):** a lasting increase in the strength of synaptic transmission.
5. *Nervous system disorders can be explained in molecular terms.*
   1. Disorders of the nervous system include schizophernia, depression, drug addiction, Alzheimer's disease, and Parkinson's disease.
   2. About 1% of the world's population suffer from **schizophernia**, a severe mental disturbance characterized by psychotic episodes in which patients have a distorted perception of reality.
   3. Individuals affected by **major depressive disorder** undergo periods—often lasting many months—during which once enjoyable activities provide no pleasure and provoke no interest.
   4. **Bipolar disorder**, or manic-depressive disorder, involves swings of mood from high to low and affects about 1% of the world's population.
   5. **Drug Addiction and the Brain Reward System**: Drugs increase the activity of the brain's reward system. The key neurotransmitter of the reward system is dopamine. Inputs to the reward system are received by neurons in a region near the base of the brain called the *ventral tagmental area (VTA).*
   6. **Alzheimer's disease** is a dementia characterized by confusion, memory loss, and a variety of other symptoms. Its incidence is age-related. The disease is progressive, and leads to the death of neurons in many areas of the brain. There is often massive shrinkage of brain tissue. Amyloid plaques and neurofibrillary tangles are characteristic of Alzheimer's.
   7. A motor disorder, **Parkison's disease,** is characterized by difficulty in initiating movements, slowness of movement, and rigidity. It is a progressive brain illness that is more common with advancing age. Generally results from the death of neurons in the midbrain that release dopamine in the basal nuclei.
   8. The mammalian CNS cannot fully repair itself when damaged or diseased, although surviving neurons can compensate. However, the hippocampus has dividing cells, which means the brain has stem cells that can become neurons.

- **Sensory reception**: The detection of a stimulus by sensory cells.
- **Sensory transduction:** the conversion of a physical or chemical stimulus to a change in the membrane potential or a sensory receptor.
- **Receptor potential**: the change in membrane potential caused by a stimulus.

1. Sensory Receptors Transduce Stimulus Energy and Transmit Signals to the Central Nervous System

1. Most sensory cells are specialized neurons or epithelial cells. Sensory cells and organs, as well as the structures within sensory cells that respond to specific stimuli, are called **sensory receptors**.
2. For many sensory receptors, transducing the energy in a stimulus into a receptor potential initiates **transmission** of action potentials to the CNS.
3. When action potentials reach the brain via sensory neurons, circuits of neurons process this input, generating the **perception** of the stimuli.
4. **Amplification** refers to the strengthening of stimulus energy during transduction. Upon continued stimulation, many receptors undergo a decrease in responsiveness termed **sensory adaptation**.
5. **Types of Sensory Receptors:**
    1. **Mechanoreceptors** sense physical deformation caused by forms of mechanical energy such as pressure, touch, stretch, motion, and sound.
    2. **Chemoreceptors** include general receptors for total solute concentration and specific receptors that respond to individual kinds of molecules.
    3. **Electromagnetic Receptors** detect various forms of electromagnetic energy, such as visible light, electricity, and magnetism.
    4. **Thermoreceptors** detect heat and cold.
    5. **Nociceptors (Pain receptors)** detect stimuli that reflect noxious (or harmful) conditions.

2. The Mechanoreceptors Responsible for Hear and Equilibrium Detect Moving Fluid or Settling Particles

1. Hear and the perception of body equilibrium, or balance, are related in most animals.
2. To sense gravity and maintain equilibrium, most invertebrates rely on sensory organs called **statocytes.** A common type of statocyst contains a layer of ciliated receptor cells surrounding a chamber that contains one or more **statoliths**, which are grains of stand or other dense granules.
3. Many (perhaps most) insects have body hairs that vibrate in response to sound waves. Many insects also detect sound by means of "ears" consisting of a tympanic membrane (eardrum) stretched over an internal air chamber.
4. **Hearing and Equilibrium in Mammals**:
    1. **Hearing**: Moving air→tympanic membrane→Three bones of middle ear→Oval window (membrane of cochlea's surface)→fluid inside the cochlea→Cochlear duct and basilar membrane (and attached hair cells)→Receptor potential. One pressure waves travel through the vestibular canal, they pass around the apex of the cochlea and then continue through the tympanic canal, dissipating as the strike the **round window**.
        1. Louder sounds cause more action potentials. Each region of the basilar membrane is tuned to a particular vibration frequency.
    2. **Equilibrium**:
        1. Situated in a vestibule behind the oval window, the **utricle** and **saccule** allow us to perceive position with respect to gravity or linear movement. Small calcium carbonate particles (otoliths) press on hair cells, causing the hair cells to send action potentials. The utricle is oriented horizontally and the saccule is positioned vertically.
        2. Three **semicircular canals** detect turning of the head and other forms of angular acceleration.
5. **Hearing and Equilibrium in Other Vertebrates**: Most fishes and aquatic amphibians also have a **lateral line system**.

3. The Senses of Taste and Smell Rely on Similar Sets of Sensory Receptors.

- The perceptions of **gustation** (taste) and **olfaction** (smell) both depend on chemoreceptors that detect specific chemicals in their environment.

1. Many animals use their chemical senses to find mates, to recognize territory that has been marked by some chemical substance, and to help navigate during migration. Animals such as ants and bees that live in large social groups rely extensively on chemical "conversation".
2. The taste receptors of insects are located within sensory hairs (sensilla) on the feet and mouthparts.
3. The receptor cells for taste in mammals are modified epithelial cells organized into **taste buds**. There are five types of tastes: sweet, sour, salty, bitter, and umami. The sensation of sweet, umami, and bitter requires a G protein-coupled receptor. In humans, there are more than 30 different receptors for bitter taste, each able to recognize multiple bitter tastants. In contrast, humans have one type of sweet receptor and one type of umami receptor. The receptor for sour tastants belongs to the TRP (transient receptor potential) family. The salty receptor(s) have yet to be identified.
4. **Smell in Humans**: In olfaction, the sensory cells are neurons. The receptive ends of the cells contain cilia that extend into the layer of mucus coating the nasal cavity. When an odorant diffuses into this region, it binds to a specific GPCR protein called an odorant receptor (OR) on the plasma membrane of the olfactory cilia→production of cAMP→Opens Na^+ and Ca^{2+} channels in the plasma membrane. Humans can distinguish thousands of different odors, each caused by a structurally distinct odorant. There are more than 1,000 OR genes—each olfactory receptor cell appears to express one OR gene.

4. Similar Mechanisms Underlie Vision Throughout the Animal Kingdom.

1. **Vision in Invertebrates**: Most invertebrates have some kind of light-detecting organ.
    1. One of the simplest is the ocellus of planarians. The ocelli are surrounded on three sides by a layer of darkly pigmented cells that block light. Light shining on the planarian stimulates light-sensitive cells called **photoreceptors** in each ocellus only through the opening where there are no pigmented cells.
    2. **Compound eyes** are found in insects and crustaceans and in some polychaete worms. A compound eye consists of up to several thousand light detectors called **ommatidia**.
    3. **Single-lense eyes** are found in some jellies and polychaetes, as well as spiders and many molluscs. Light enters through the **pupil**. The **iris** changes the diameter of the pupil.
2. **Vertebrate Visual System**:
    1. **Structure of the Eye**: The globe of the eyeball consists of the **sclera**, a tough white outer layer of connective tissue, and the **choroid**, a thin, pigmented layer. At the front of the eye, the sclera is transparent and called the **cornea**. The **retina** forms the innermost layer of the eyeball and contains layers of neurons and photoreceptors. The **lens** and **ciliary body** divide the eye into two cavities. The ciliary body produces **aqueous humor** to fill the anterior cavity. Blockage of the ducts that drain the aqueous humor can produce glaucoma. The posterior cavity, filled with the jellylike **vitreous humor**, constitutes most of the volume of the eye. The lens is a transparent disk of protein: fishes, squids and octopi focus by moving the lens forward or backward. Humans and other mammals focus by changing the shape of the lens.
    2. The human retina contains **rods** and **cones**. Rods are more sensitive to light but do not distinguish color; cones

distinguish color but are less sensitive to light. There are three types of cones. The **fovea** has no rods, only cones. The peripheral regions only have rods, no cones.

3. **Sensory Transduction in the Eye**: Each rod or cone in the vertebrate retina contains visual pigments (**rhodopsin**) that consist of a light-absorbing molecule (**retinal**) bound to a membrane protein (**opsin**). Rhodopsin absorbs light→a bond in retinal shifts from a *cis* to a *trans* arrangement→activating ("bleaching") rhodopsin→activating transducin (a G-protein)→activating phosphodiesterase→hydrolyzes cGMP attached to Na^+ channels→Na^+ channels close→Cell hyperpolarizes→Cell stops releasing glutamate→**bipolar cells** either depolarize or hyperpolarizes. **Ganglion cells** synapse with bipolar cells and transmit action potentials to the brain via axons in the optic nerve. **Horizontal cells** and **amacrine cells** function in neural pathways that integrate visual information before it is sent to the brain.
    1. Within the brain: Ganglion cell axons→**lateral geniculate nuclei→primary visual cortex**.
3. **Evolution of Visual Preception**: Melanopsin helps animals regulate circadian rhythms by syncing the rhythm with the day.

- **Lateral inhibition**: sharpens edges and enhances contrast in the image. Occurs at all levels of visual processing in the brain.
- *Receptive field:* the part of the visual field to which a ganglion can respond.
- The two optic nerves meet at the **optic chiasm** near the center of the base of the cerebral cortex.

5. The Physical Interaction of Protein Filaments is Required for Muscle Function.

1. Vertebrate **skeletal muscle** is characterized by a hierarchy of smaller and smaller units: multi-nucleated muscle fibers→**myofibrils**→Thin filaments (**actin**) and thick filaments (**myosin**). Skeletal muscle is **striated** because the regular arrangement of the filaments creates a pattern of light and dark bands. Each repeating unit is a **sarcomere**. Thin filaments are attached at the Z-lines and project toward the center of the sacromere; thick filaments are attached at the M lines centered in the sacromere.
2. **Sliding-Filament Model**: The thick and thin filaments slide past each other longitudinally, increasing the overlap of the thick and thin filaments. Each myosin molecule consists of a long "tail" region and a globular "head" region extending to the side. The myosin head begins in a low-energy configuration and bound to ATP→myosin head hydrolyzes ATP and moves to high-energy configuration→Myosin head binds to actin→Myosin head releases the ADP and phosphate group and returns to low-energy configuration, sliding the thin filament→Myosin binds to a new molecule of ATP and releases actin.
3. Creatin phosphate and glycogen store energy for muscles.
4. **The Role of Calcium and Regulatory Proteins**: **Tropomyosin**, a regulatory protein, and the **troponin complex**, a set of additional regulatory proteins, are found to the actin strands of thin filaments. When Ca^{2+} binds to the troponin complex, the tropomyosin shifts in a way to expose myosin-binding sites on the actin.
5. Arrival of action potential at the synaptic terminal of a motor neuron→release of acetylcholine→depolarization of muscle→Action potential spreads to the interior of the muscle fiber via **transverse (T) tubules**→Action potential reaches the **sarcoplasmic reticulum (SR)**→Ca^{2+} channels in the SR open, allowing Ca^{2+} to diffuse into the cytosol→ Ca^{2+} binds to troponin complex. When motor neuron input stops, the Ca^{2+} is pumped back into the SR and the tropomyosin returns to its original position.
6. In amyotrophic lateral sclerosis (ALS), aka Lou Gehrig's disease, motor neurons in the spinal cord and brainstem degenerate. Myasthenia gravis is an autoimmune disease in which a person produces antibodies to the acetylcholine receptors on skeletal muscle fibers.
7. There are two basic mechanisms by which the nervous system produces graded contractions of whole muscles: (1) by varying the number of muscle fibers that contract and (2) by varying the rate at which muscle fibers are stimulated.
8. In most muscles, the number of muscle fibers in different motor units ranges from a few to hundreds. The force (tension) developed by a muscle progressively increases as more and more of the motor neurons controlling the muscle are activated (**recuitment**). When the rate of action potentials is high enough that the muscle fiber cannot relax at all between stimuli, the twitches fuse into one smooth, sustained contraction called **tetanus**.
9. **Types of Skeletal Muscle Fibers:**
    1. **Oxidative and Glycolytic Fibers:** Oxidative fibers rely mostly on aerobic respiration and contain many mitochondria and **myoglobin**. Glycolytic fibers use glycolysis as their primary source of ATP and have a larger diameter and less myoglobin than oxidative fibers.
    2. **Fast-Twitch and Slow-Twitch Fibers:** Fast-twitch fibers develop tension two to three times fast than slow-twitch fibers. A slow-twitch fiber has less SR than a fast-twitch fiber. Whereas all slow-twitch fibers are oxidative, fast-twitch fibers can be either glycolytic or oxidative.
10. **Other types of Muscle**:
    1. Vertebrate **cardiac muscle** is found in only one place—the heart. Cardiac muscle has **intercalated disks**, where gap junctions provide direct electrical coupling between cells.
    2. **Smooth muscle** in vertebrates is found mainly in the walls of hollow organs. The thick filaments are scattered throughout the cytoplasm, and the thin filaments are attached to structures called dense bodies. They have no troponin complex or T-tubules, and the SR isn't as well developed. Calcium ion cause contraction by binding to the protein calmodulin, which activates an enzyme that phosphorylates the myosin head.

- **Motor unit**: consists of a single motor neuron and all the muscle fibers it controls.

6. Skeletal Systems Transform Muscle Contraction Into Locomotion.

1. The skeleton provides a rigid structure to which the muscles can attach. Generally, muscles work in antagonistic pairs.
2. **Types of Skeletal Systems:**
    1. **Hydrostatic Skeletons**: consists of fluid held under pressure in a closed body compartment.
    2. **Exoskeletons**: a hard encasement deposited on an animal's surface. About 30-50% of the arthoropod cuticles consists of **chitin**.
    3. **Endoskeleton**: hard supporting elements, such as bones, buried within the soft tissues of a animal.
3. **Size and Scale of Skeletons**: The strength of a building support depends on its cross-sectional area, which increases with the square of its diameter. The strain on that support depends on the building's weight, which increases with the cube of its height or other linear dimension.
4. **Types of Locomotion:**
    1. **Swimming:** Gravity is generally not a problem, but friction is a big problem. Thus, most fast organisms are fusiform.
    2. **Locomotion on Land**: Friction is usually not a problem, but gravity is. Maintaining balance is another problem. For crawlers, friction is a problem.
    3. **Flying**: Gravity is the major problem for fliers. All types of wings are airfoils.
5. **Energy Costs of Locomotion:**
    1. The energy cost of locomotion depends on the mode of locomotion and the environment.

- **Locomotion**: Active travel form place to place. Must overcome friction and gravity.

Chapter 51: Animal Behavior

- **Behavior**: an action carried out by muscles or glands under control of the nervous system in response to a stimulus.
- **Ethology**: the scientific study of how animals behave.

- **Signal**: a stimulus transmitted from one animal to another.
- **Communication:** the transmission and reception of signals

- **Innate behavior**: Behavior that is developmentally fixed.
- **Learning**: the modification of behavior based on specific experiences.

I. Discrete sensory inputs can stimulate both simple and complex behaviors.

1. Collectively, an animal's behavior is the sum of its responses to external and internal stimuli.
2. **Proximate causation**: "how" a behavior occurs or is modified. **Ultimate causation**: "why" a behavior occurs in the context of natural selection.
3. **Behavioral ecology**: the study of the ecological and evolutionary basis for animal behavior.
4. **Fixed Action Patterns**: a sequenced of unlearned acts that is essentially unchangeable and, once initiated, usually carried to completion. Triggered by a **sign stimulus**.
5. **Oriented Movement:**
    1. **Kinesis**: a change in activity or turning rate in response to a stimulus.
    2. **Taxis**: an oriented movement toward or away from some stimulus.
    3. **Migration**: a regular, long-distance change in location.
6. **Behavioral Rhythms**: The circadian clock has a major role in the daily activity of all animals. Behavior rhythms linked to the yearly cycle of seasons are called *circannual rhythms*. Other behavior patterns are linked to the lunar cycle.
7. **Animal Signals and Communications.**
    1. *Visual Communication:* the flow of information to the visual system
    2. *Chemical Communication:* the transmission and reception of signals in the form of specific molecules.
    3. *Tactile Communication:* Communication via touch.
    4. *Auditory Communication:*
    5. ***Pheromones**:* chemical substances used for communication between members of the same species.

II. Learning establishes specific links between experience and behavior.

1. **Habituation**: a loss of responsiveness to stimuli that convey little or no new information.
2. **Imprinting**: The formation at a specific stage in life (**sensitive period**) of a long-lasting behavioral response to a particular individual or object.
3. **Spatial learning**: the establishment of a memory that reflects the environment's spatial structure.
    1. **Landmarks**: location indicators.
    2. **Cognitive Map**: A representation in the nervous system of the spatial relationships between objects in an animal's surroundings.
4. **Associative Learning**: the ability to associate one environmental feature with another
    1. **Classical conditioning**: an arbitrary stimulus becomes associated with a particular outcome.
    2. **Operant conditioning**: an animal learns to associate one of its own behaviors with a reward or punishment and then tends to repeat or avoid that behavior.
5. **Cognition and Problem Solving**:
    1. **Cognition**: the process of knowing represented by awareness, reasoning, recollection, and judgement.
    2. **Problem-solving**: the cognitive activity of devising a method to proceed from one state to another in the face of real or apparent obstacles.
6. **Development of Learned Behaviors**:
    1. Most acquired behaviors involve learning that takes place over a relatively short time. Development of some other behaviors, such as singing in some bird species, occurs in distinct stages.

III. Both genetic makeup and environment contribute to the development of behaviors.

1. Although the DNA sequence of the genome provides instructions for the development of behavior, many factors—including the environment of the fertilized egg and the animal's diet, social interactions, and surroundings—modify how these instructions are carried out.
2. **Cross-fostering study:** the young of one species are placed in the care of adults from another species. The extent to which the offspring's behavior changes in such a situation is one measure of how the social and physical environment influences behavior.
3. **Twin study**: researchers compare the behavior of identical twins raised apart with those raised in the same household.
4. **Regulatory Genes and Behavior**: *Fru* programs fruit flies for male courtship behavior by overseeing a male-specific wiring of the central nervous system.
5. **Genetically Based Behavioral Variation in Natural Populations**:
    1. **Case Study:** *Variation in Migratory Patterns*: The wintering area of the blackcap (*Sylvia atricapilla*), a small migratory warbler, is genetically determined.
    2. **Case Study**: *Variation in Prey Selection*: Banana slugs appear to be a genetically acquired taste for the western garter snake (*Thamnophis elegans*).
6. **Influence of Single-Locus Variation**: Male meadow voles (*Microtus pennsylvanicus*) are solitary and do not form lasting relationships with mates. Male prairie voles (*Microtus ochrogaster*) *pair-bond* with a single female after they mate. This is influenced solely by the levels of the neurotransmitter vasopressin (ADH).

IV. Selection for individual survival and reproductive success can explain most behaviors

1. **Foraging Behavior**: *Foraging* (food-obtaining behavior) includes not only eating but also any activities an animal uses to search for, recognize, and capture food items.
    1. **Evolution of Foraging Behavior**: Variation in a gene called *forager* (*for*) dictates the food search behavior of *Drosophila melanogaster (*fruit fly) larvae. On average, larvae carrying the for^R ("rover") allele travel nearly twice as far while feeding as larvae with the for^S ("sitter") allele. The for^R allele is more advantageous for highly dense populations, while the for^S allele is more advantageous for more sparse populations.
    2. **Optimal foraging model**: natural selection should favor a foraging behavior that minimizes the costs of foraging and maximizes the benefits.
    3. **Balancing Risk and Reward**: Maximizing energy gain and minimizing energy costs are of little benefit if the behavior makes the forager a likely meal for a predator. Predation risk influences foraging behavior.
2. **Mating Behavior and Mate Choice:**
    1. **Mating Systems and Parental Care:**
        1. **Promiscuous**: no strong pair-bonds or lasting relationships.
        2. **Monogamous**: one male pair-bonds with one female. Generally, males and females are similar morphologically.
        3. **Polygamous**: A single male mates with many females (**polygyny**), or a single female mates with many

males (**polyandry**). Polygamous species are generally dimorphic, with the single male or the single female larger and showier.

4. *Certainty of paternity*: Young born to or eggs laid by a female definitely contain that female's genes. In internal fertilization, the certainty of paternity is rather low→exclusively male parental care is very rare in birds and mammals, and males birds or mammals tend to engage in behaviors that increase their certainty of paternity. In external fertilization, certainty of paternity is much higher and both males and females care for offspring exclusively.

2. **Sexual Selection and Mate Choice:**
   1. **Mate Choice by Females**: Mate preferences by females by play a central role in the evolution of male behavior and anatomy through *intersexual selection*.
   2. **Male Competition for Mates**: a source of sexual (*intrasexual*) selection that can reduce variation among males.
      1. **Agonistic behavior**: an often ritualized contest that determines which competitor gains access to a resource.
   3. **Applying Game Theory**:
      1. **Game Theory** evaluates alternative strategies in situations where the outcome depends on the strategies of all the individuals involved.

5. Inclusive fitness can account for the evolution of altruistic social behavior.
   1. Many social behaviors are selfish; that is, they benefit the individual at the expense of others, especially competitors.
   2. **Altruism**: a behavior that reduces an individual's fitness but increases the fitness of other individuals in the population.
   3. **Inclusive fitness**: the total effect an individual has on proliferating its genes by producing its own offspring *and* by providing aid that enables other close relatives, who share many of those genes, to produce offspring.
      1. **Hamilton's rule**: $rB>C$
         1. r: **coefficient of relatedness**: the fraction of genes that, on average, are shared.
         2. B: average number of *extra* offspring that the beneficiary of an altruistic act produces.
         3. C: how many *fewer* offspring the altruist produces.
      4. **Kin selection**: the natural selection that favors altruistic behavior by enhancing reproductive success of relatives.
      5. **Reciprocal altruism**: An altruistic behavior performed with an expectation of similar altruism returned at a later time.
         1. *Tit-for-tat*: an individual treats another in the same way it was treated the last time they met.
      6. **Social Learning**: Modification of behavior through the observation of other individuals.
         1. **Culture**: a system of information transfer through social learning or teaching that influences the behavior of individuals in a population.
         2. **Case study**: *Mate choice copying*: a behavior in which individuals in a population copy the mate choice of others.
         3. **Case study**: *Social Learning of Alarm Calls*: Infant velvet monkeys learn when to give alarm calls from the adults in the population.
         4. **Sociobiology**: the study of human culture in relation to evolutionary theory.