Douglas College Human Anatomy & Physiology I (2nd ed.)

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DOUGLAS COLLEGE BIOLOGY DEPARTMENT

DOUGLAS COLLEGE
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Contents

Preface

Welcome to the Douglas College Anatomy & Physiology open textbook!

This textbook is a project under development by our Biology faculty to ultimately provide students with all the factual information they need to succeed in the BIOL 1103 and BIOL 1109 courses at Douglas College in BC, Canada. Readers should be aware that the information herein is subject to change at any time as corrections, additions, or other important modifications are made. Current students at Douglas College should be aware that only the most recent version of this textbook will be considered by their instructors to be complete and correct. The most recent version of this second edition will remain accessible online at https://pressbooks.bccampus.ca/dcbiol110311092nded/, and the most recent version of the second edition of the companion textbook (developed for Douglas College's BIOL 1203 and BIOL 1209 courses) will also remain accessible online at https://pressbooks.bccampus.ca/dcbiol120312092nded/.

This textbook was developed initially as an adaptation of the OpenStax Anatomy & Physiology textbook, freely and perpetually available online at http://cnx.org/content/col11496/latest/. The original adaptations of that OpenStax textbook for Douglas College are accessible online at https://pressbooks.bccampus.ca/dcbiol111031109/ and https://pressbooks.bccampus.ca/dcbiol12031209/ In the first edition of the Douglas College adaptations the chapter and section numbers were left as they were in the version of the OpenStax A&P textbook, from which they were largely drawn. However, this second edition has been more extensively edited and rearranged to correspond with the curriculum used at Douglas College, so chapter and section numbers are no longer aligned specifically with the OpenStax A&P textbook.

About this Resource

Customization

Errata

Since this textbook is primarily web based, updates can be made 'live' when deemed pedagogically necessary. If you have a correction to suggest, please submit it by email for review to Dr. Jennifer Barker, whose current contact information can be obtained from the Biology faculty page of the Douglas College website: https://www.douglascollege.ca/programs-courses/faculties/science-technology/biology/faculty

About Anatomy and Physiology

Section 1: Levels of Organization

Units 1–8 provide students with a basic understanding of human anatomy and physiology, including its language, the levels of organization, and the basics of chemistry and cell biology. These units provide a foundation for the further study of the body. They also focus particularly on how the body's regions, important chemicals, and cells maintain homeostasis.

Unit 1 Atoms & Molecules
Unit 2 The Chemistry of Water
Unit 3 Biochemistry
Unit 4 Cell Structure and Function
Unit 5 Cell Biology: Membrane Transport
Unit 6 Tissue: Structure and Function
Unit 7 Body Structure
Unit 8 Homeostasis

Section 2: Nervous Regulation and Integration

In Units 9-10, students explore the structure of the nervous system and how it functions, to prepare them to understand how it is used to regulate other body systems that are discussed in subsequent units. This section is the first to walk students through a specific system of the body.

Unit 9 The Nervous System
Unit 10 Sensory Systems

Section 3: Support and Movement

Units 11-16 introduce students to the integumentary, skeletal, and muscular systems that provide support and protection to the human body, as well as allow movement.

Unit 11 The Integumentary System
Unit 12 The Skeletal System
Unit 13 Joints
Unit 14 Biomechanics
Unit 15 Muscle Anatomy
Unit 16 Muscle Physiology

Additional sections

The remaining systems of the human body are covered in the companion textbook to this one, designed for Douglas College's BIOL 1203 and BIOL 1209 courses.

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Finally, we wish to thank the remaining faculty members of the Biology Department for their valuable input into the content and organization of this textbook, Sara McKinnon for creating the section on lever systems and its associated diagrams, and Zoir Amirdad for creating many of the scalable vector-based versions of the images found in this textbook and also available as separate auxiliary resources.

LEVELS OF ORGANIZATION

Unit 1: Atoms and Molecules

Unit outline

Part 1. Elements and compounds

- Elements and compounds
- Atoms and subatomic particles
    - Atomic structure
    - Atomic number and mass number
    - Electrons

Part 2. Chemical bonds

- Ionic bonds
- Covalent bonds
    - Non-polar
    - Polar
- Hydrogen bonds
- Water

Learning Objectives

At the end of this unit, you should be able to:

I. Define the term “chemical element”, specify the name and symbol for the four most common chemical elements in the body, and describe the importance of each.

II. Define the term “atom” and describe the structure of an atom.

III. Define the terms “molecule” and “compound”.

IV. Describe the formation of an ion and of an ionic bond.

V. Describe the formation of a covalent bond.

VI. Distinguish between organic and inorganic molecules.

VII. Describe the composition of organic molecules, specify two characteristics of organic molecules that make them useful to living organisms, and give examples of organic molecules.

VIII. Specify the chemical properties of water.

Learning Objectives and Guiding Questions

At the end of this unit, you should be able to complete all the following tasks, including answering the guiding questions associated with each task.

I. Define the term "chemical element", specify the name and symbol for the four most common chemical elements in the body, and describe the importance of each.

1. Define the term "chemical element".
2. For each of the four most common chemical elements in the human body:
    - Specify its name
    - Specify its chemical symbol
    - Name at least one molecule or type of molecule in which it is found, and briefly describe that molecule's function in the human body

II. Define the term "atom" and describe the structure of an atom.

1. Define the term "atom".
2. Draw an annotated diagram (*a diagram that includes descriptive labels, with verbs*) of the "planetary" (or "Bohr") model describing the general structure of an atom.
3. Be able to identify the number of electrons, protons and neutrons for common elements if given the atomic number and mass number.

III. Define the terms "molecule" and "compound".

1. Define the terms "molecule" and "compound".
2. Write 1-2 sentences to clearly distinguish between the terms "molecule" and "compound". *(If a question ever asks you to 'clearly distinguish between', 'compare', 'contrast', or similar terms: make sure the direct comparison is very obvious in your answer!)*

IV. Describe the formation of an ion and of an ionic bond.

1. Use an annotated diagram to describe the process by which ions are formed from neutral atoms.
2. Write one sentence that states what is meant by the term "ionic bond".

V. Describe the formation of a covalent bond.

1. Describe the process by which a covalent bond is formed between two atoms.
2. Compare and contrast *(list similarities **and** differences between)* ionic compounds and covalent molecules.

VI. Distinguish between organic and inorganic molecules.

1. Compare and contrast *(list similarities **and** difference between)* organic molecules and inorganic molecules.
2. Name at least two *specific and clear* examples of each type of molecule (i.e. name *two* organic

molecules, and *two* inorganic molecules, that could not be mistaken for anything else).

VII. Describe the composition of organic molecules, specify two characteristics of organic molecules that make them useful to living organisms, and give examples of organic molecules.

1. Describe the chemical composition of organic molecules.
2. Name the four main types of organic molecules discussed further in this course. *(Hint: you may need to look at the "Biochemistry" topic to answer this question!)*
3. Specify at least two characteristics of organic molecules that make them particularly useful to living organisms.

VIII. Specify the chemical properties of water.

1. Draw a diagram of a single water molecule. Clearly label any:
    - Oxygen atoms
    - Hydrogen atoms
    - Covalent bonds
2. Draw an annotated diagram showing two, and only two, water molecules. In your diagram you should include all the labels shown above, then add explanatory labels identifying and fully describing the following important chemical properties:
    - The molecule's polarity
    - Its molecular shape
    - The important interaction ('bond') that exists *between* two water molecules
3. Describe how the chemical properties of water affects the physical properties of water.

The smallest, most fundamental material components of the human body are chemical elements. All of the elements found in the human body — elements that include phosphorus, carbon, sodium, and calcium, to name a few — originated in stars. These elements, in turn, form both the inorganic and organic chemical compounds important to life, including, for example, water, glucose, and proteins. This chapter begins by examining elements and how the structures of atoms, the basic units of matter, determine the characteristics of elements by the number of protons, neutrons, and electrons in the atoms. The chapter then builds the framework of life from there.

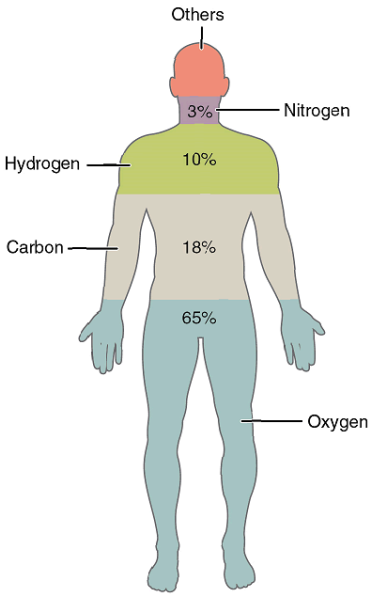
Part 1: Elements and Atoms: the Building Blocks of Matter

The substance of the universe—from a grain of sand to a star—is called **matter**. Scientists define matter as anything that occupies space and has mass.

Elements and Compounds: All matter in the natural world is composed of one or more of fundamental substances called **elements**. An element is a pure substance that is distinguished from all other matter by the fact that it cannot be created or broken down by ordinary chemical means. While your body can assemble many of the chemical compounds needed for life from their constituent elements, it cannot make elements. They must come from the environment.

The elements in the human body are shown in Figure 1, beginning with the four most abundant: oxygen (O), carbon (C), hydrogen (H), and nitrogen (N). Each element's name can be replaced by a one- or two-letter symbol;

you will become familiar with some of these during this course. All the elements in your body are derived from the foods you eat and the air you breathe.



Element	Symbol	Percentage in Body
Oxygen	O	65.0
Carbon	C	18.5
Hydrogen	H	9.5
Nitrogen	N	3.2
Calcium	Ca	1.5
Phosphorus	P	1.0
Potassium	K	0.4
Sulfur	S	0.3
Sodium	Na	0.2
Chlorine	Cl	0.2
Magnesium	Mg	0.1
Trace elements include boron (B), chromium (Cr), cobalt (Co), copper (Cu), fluorine (F), iodine (I), iron (Fe), manganese (Mn), molybdenum (Mo), selenium (Se), silicon (Si), tin (Sn), vanadium (V), and zinc (Zn).		less than 1.0

Figure 1. Elements of the Human Body. *The main elements that compose the human body are shown from most abundant to least abundant.*

In nature, elements rarely occur alone. The combination of two or more atoms joined by chemical bonds can form a molecule. A **compound** is a substance containing at least two different elements joined by chemical bonds.

All compounds can be categorized based off of the nature of its constituent elements. An **inorganic compound** is a substance that does not contain both carbon and hydrogen. A great many inorganic compounds do contain hydrogen atoms, such as water (H_2O) and the hydrochloric acid (HCl) produced by your stomach. In contrast, only a handful of inorganic compounds contain carbon atoms. Carbon dioxide (CO_2) is one of the few examples.

An **organic compound**, then, is a substance that contains carbon-hydrogen bonds. Many organic compounds can be synthesized via covalent bonds within living organisms, including the human body. Recall that carbon and hydrogen are the second and third most abundant elements in your body. You will soon discover how these two elements combine in the foods you eat, in the compounds that make up your body structure, and in the chemicals that fuel your functioning.

Carbon atoms can bind to other carbon atoms as well as atoms of other elements in multiple ways, so organic molecules come in many different shapes with different properties depending on their exact chemical composition. The fact that organic molecules can be assembled into very large molecules with complex structures makes them useful to living cells in several ways. Examples can include structural components of cells or functional components that allow chemical reactions to proceed.

Finally, the chemical energy present in the covalent bonds in many organic molecules can be transferred to other molecules, in the form of new bonds. For example, some of the energy contained in the bonds of a glucose molecule can be harvested and used by living cells to attach a phosphate group to a molecule of adenosine diphosphate, making the molecule adenosine triphosphate (ATP). The vital importance of ATP to the functioning of human cells is discussed in more detail elsewhere in this textbook.

For example, the compound glucose is an important body fuel. It is always composed of the same three elements: carbon, hydrogen, and oxygen. Since it is a carbon-based molecule that contains hydrogen, it is an organic compound. The elements that make up any given compound always occur in the same relative

amounts. In glucose, there are always six carbon units and six oxygen units for every twelve hydrogen units. But what, exactly, are these "units" of elements?

Atoms and Subatomic Particles: An **atom** is the smallest quantity of an element that retains the unique properties of that element. In other words, an atom of hydrogen is a unit of hydrogen—the smallest amount of hydrogen that can possibly exist. As you might guess, atoms are almost unfathomably small. The period at the end of this sentence is millions of atoms wide.

1. Atomic Structure and Energy: Atoms are made up of even smaller subatomic particles, three types of which are important: the **proton**, **neutron**, and **electron**. The number of positively-charged protons and non-charged ("neutral") neutrons, gives mass to the atom, and the number of protons in the nucleus of the atom determine the element. The number of negatively-charged electrons equals the number of protons.

There are different ways to illustrate the structure of an atom (Figure 2). Consider a typical atom of helium (He), that is composed of two protons, two neutrons, and two electrons. In the planetary model (or Bohr model), helium's two electrons are shown circling the nucleus in a fixed orbit depicted as a ring (Figure 2a). Although this model is helpful in visualizing atomic structure, in reality, electrons do not travel in fixed orbits, but whiz around the nucleus erratically in a so-called electron cloud (Figure 2b).

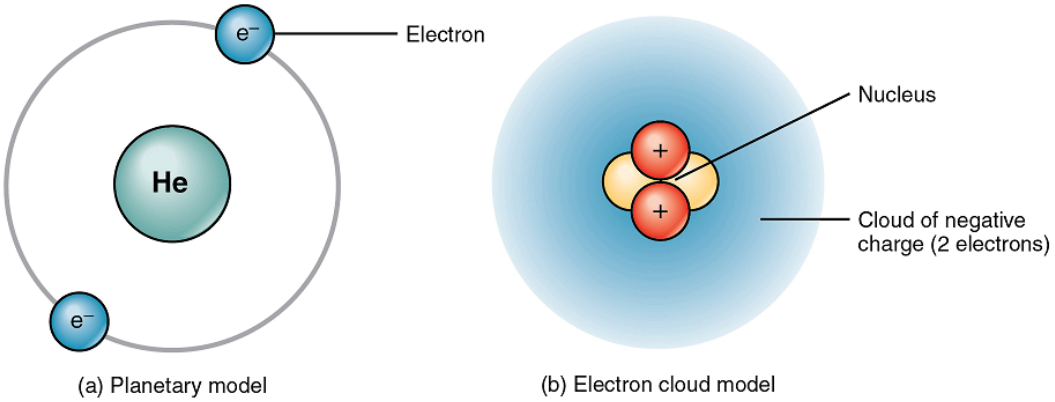


Figure 2. Two Models of Atomic Structure. *(a) In the planetary model, the electrons of helium are shown in fixed orbits, depicted as rings, at a precise distance from the nucleus, somewhat like planets orbiting the sun. (b) In the electron cloud model, the electrons of helium are shown in the variety of locations they would have at different distances from the nucleus over time.*

An atom's protons and electrons carry electrical charges. An atom's neutrons have no charge: they are electrically neutral. Just as a magnet sticks to a steel refrigerator because their opposite charges attract, the positively charged protons attract the negatively charged electrons. This mutual attraction gives the atom some structural stability. The attraction by the positively charged nucleus helps keep electrons from straying far. The number of protons and electrons within a neutral atom are equal, thus, the atom's overall charge is balanced.

2. Atomic Number and Mass Number: An atom of carbon is unique to carbon, but a proton of carbon is not. One proton is the same as another, whether it is found in an atom of carbon, sodium (Na), or iron (Fe). The same is true for neutrons and electrons. So, what gives an element its distinctive properties—what makes carbon so different from sodium or iron? The answer is the unique quantity of protons each contains. Carbon by definition is an element whose atoms contain six protons. No other element has exactly six protons in its atoms. Moreover, all atoms of carbon, whether found in your liver or in a lump of coal, contain six protons. Thus, the **atomic number**, which is the number of protons in the nucleus of the atom, identifies the element. Because an atom usually has the same number of electrons as protons, the atomic number identifies the usual number of electrons as well.

In their most common form, many elements also contain the same number of neutrons as protons. The most common form of carbon, for example, has six neutrons as well as six protons, for a total of 12 subatomic

particles in its nucleus. An element's **mass number** is the sum of the number of protons and neutrons in its nucleus. So the most common form of carbon's mass number is 12. (Electrons have so little mass that they do not appreciably contribute to the mass of an atom.) Carbon is a relatively light element. Uranium (U), in contrast, has a mass number of 238 and is referred to as a heavy metal. Its atomic number is 92 (it has 92 protons) but it contains 146 neutrons; it has the most mass of all the naturally occurring elements.

The **periodic table of the elements**, is a chart identifying the 92 elements found in nature, as well as several larger, unstable elements discovered experimentally. The elements are arranged in order of their atomic number, with hydrogen and helium at the top of the table, and the more massive elements below. The periodic table is a useful device because for each element, it identifies the chemical symbol, the atomic number, and the mass number, while organizing elements according to their propensity to react with other elements. The number of protons and electrons in an element are equal. The number of protons and neutrons may be equal for some elements, but are not equal for all.

3. The Behavior of Electrons: In the human body, atoms do not exist as independent entities. Rather, they are constantly reacting with other atoms to form and to break down more complex substances. To fully understand anatomy and physiology you must grasp how atoms participate in such reactions. The key is understanding the behavior of electrons.

Although electrons do not follow rigid orbits a set distance away from the atom's nucleus, they do tend to stay within certain regions of space called electron shells. An **electron shell** is a layer of electrons that encircle the nucleus at a distinct energy level (Figure 3).

The atoms of the elements found in the human body have from one to five electron shells; the first holds up to two, the second holds up to eight, the third holds up to 18. However, all electron shells apart from the first shell may also be considered "complete" with eight electrons, thus making the atom non-reactive. This configuration of electron shells is the same for all atoms. The precise number of shells depends on the number of electrons in the atom. Hydrogen and helium have just one and two electrons, respectively. If you take a look at the periodic table of the elements, you will notice that hydrogen and helium are placed alone on either sides of the top row; they are the only elements that have just one electron shell. A second shell is necessary to hold the electrons in all elements larger than hydrogen and helium.

Lithium (Li), whose atomic number is 3, has three electrons. Two of these fill the first electron shell, and the third spills over into a second shell. The second electron shell can accommodate as many as eight electrons. Carbon, with its six electrons, entirely fills its first shell, and half-fills its second. With ten electrons, neon (Ne) entirely fills its two electron shells. Again, a look at the periodic table reveals that all of the elements in the second row, from lithium to neon, have just two electron shells. Atoms with more than ten electrons require more than two shells. These elements occupy the third and subsequent rows of the periodic table.

The factor that most strongly governs the tendency of an atom to participate in chemical reactions is the number of electrons in its **valence shell**. A valence shell is an atom's outermost electron shell. If the valence shell is full, the atom is stable; meaning its electrons are unlikely to be pulled away from the nucleus by the electrical charge of other atoms. If the valence shell is not full, the atom is reactive; meaning it will tend to react with other atoms in ways that make the valence shell full. Consider hydrogen, with its one electron only half-filling its valence shell. This single electron is likely to be drawn into relationships with the atoms of other elements, so that hydrogen's single valence shell can be stabilized.

All atoms (except hydrogen and helium with their single electron shells) are most stable when there are exactly eight electrons in their valence shell. This principle is referred to as the octet rule, and it states that an atom will give up, gain, or share electrons with another atom so that it ends up with eight electrons in its own valence shell. For example, oxygen, with six electrons in its valence shell, is likely to react with other atoms in a way that results in the addition of two electrons to oxygen's valence shell, bringing the number to eight. When two hydrogen atoms each share their single electron with oxygen, covalent bonds are formed, resulting in a molecule of water, H_2O.

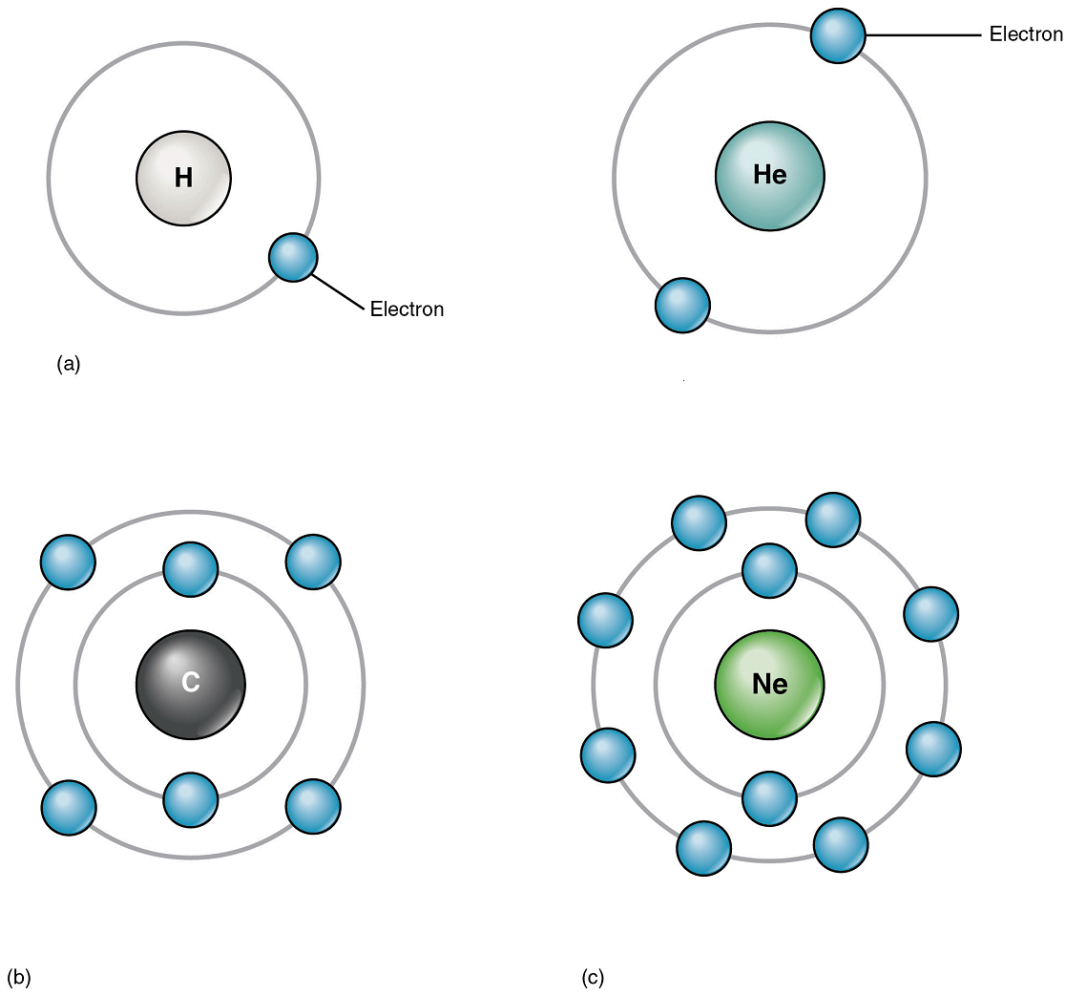


Figure 3. Electron Shells. *Electrons orbit the atomic nucleus at distinct levels of energy called electron shells. (a) With one electron, hydrogen only half-fills its electron shell. Helium also has a single shell, but its two electrons completely fill it. (b) The electrons of carbon completely fill its first electron shell, but only half-fills its second. (c) Neon, an element that does not occur in the body, has 10 electrons, filling both of its electron shells.*

Part 2: Chemical Bonds

Ions and Ionic Bonds: Recall that an atom typically has the same number of positively charged protons and negatively charged electrons. As long as this situation remains, the atom is electrically neutral. But when an atom participates in a chemical reaction that results in the donation or acceptance of one or more electrons, the atom will then become positively or negatively charged. This happens frequently for most atoms in order to have a full valence shell, as described previously. This can happen either by gaining electrons to fill a shell that is more than half-full, or by giving away electrons to empty a shell than is less than half-full, thereby leaving the next smaller electron shell as the new, full, valence shell. An atom that has an electrical charge—whether positive or negative—is an **ion**.

Potassium (K), for instance, is an important element in all body cells. Its atomic number is 19. It has just one electron in its valence shell. This characteristic makes potassium highly likely to participate in chemical reactions in which it donates one electron. (It is easier for potassium to donate one electron than to gain seven electrons.) The loss will cause the positive charge of potassium's protons to be more influential than the negative charge of potassium's electrons. In other words, the resulting potassium ion will be slightly positive. A potassium ion is written K^+, indicating that it has lost a single electron. A positively charged ion is known as a **cation**.

Now consider fluorine (F), a component of bones and teeth. Its atomic number is nine, and it has seven electrons in its valence shell. Thus, it is highly likely to bond with other atoms in such a way that fluorine accepts one electron (it is easier for fluorine to gain one electron than to donate seven electrons). When it does, its

electrons will outnumber its protons by one, and it will have an overall negative charge. The ionized form of fluorine is called fluoride, and is written as F^-. A negatively charged ion is known as an **anion**.

Atoms that have more than one electron to donate or accept will end up with stronger positive or negative charges. A cation that has donated two electrons has a net charge of +2. Using magnesium (Mg) as an example, this can be written Mg^{++} or Mg^{2+}. An anion that has accepted two electrons has a net charge of –2. The ionic form of selenium (Se), for example, is typically written Se^{2-}.

The opposite charges of cations and anions exert a moderately strong mutual attraction that keeps the atoms in close proximity forming an **ionic bond**. An ionic bond is an ongoing, close association between ions of opposite charge. The table salt you sprinkle on your food owes its existence to ionic bonding (Figure 4). Sodium commonly donates an electron to chlorine, becoming the cation Na+. When chlorine accepts the electron, it becomes the chloride anion, Cl–. With their opposing charges, these two ions strongly attract each other. Incidentally, the substances formed through ionic bonding are always referred to as compounds.

Water is an essential component of life because it is able to break the ionic bonds in salts to free the ions. In fact, in biological fluids, most individual atoms exist as ions. These dissolved ions produce electrical charges within the body. The behavior of these ions produces the tracings of heart and brain function observed as waves on an electrocardiogram (EKG or ECG) or an electroencephalogram (EEG). The electrical activity that derives from the interactions of the charged ions is why they are also called electrolytes.

Covalent Bonds: Unlike ionic bonds formed by the attraction between a cation's positive charge and an anion's negative charge, molecules formed by a **covalent bond** share electrons in a mutually stabilizing relationship. Like next-door neighbors whose kids hang out first at one home and then at the other, the atoms do not lose or gain electrons permanently. Instead, the electrons move back and forth between the elements. Because of the close sharing of pairs of electrons (one electron from each of two atoms), most covalent bonds are not broken apart in water.

1. Nonpolar Covalent Bonds: Figure 5 shows several common types of covalent bonds. Notice that the two covalently bonded atoms typically share just one or two electron pairs, though larger sharings are possible. The important concept to take from this is that in covalent bonds, electrons in the outermost valence shell are shared to fill the valence shells of both atoms, ultimately stabilizing both of the atoms involved.

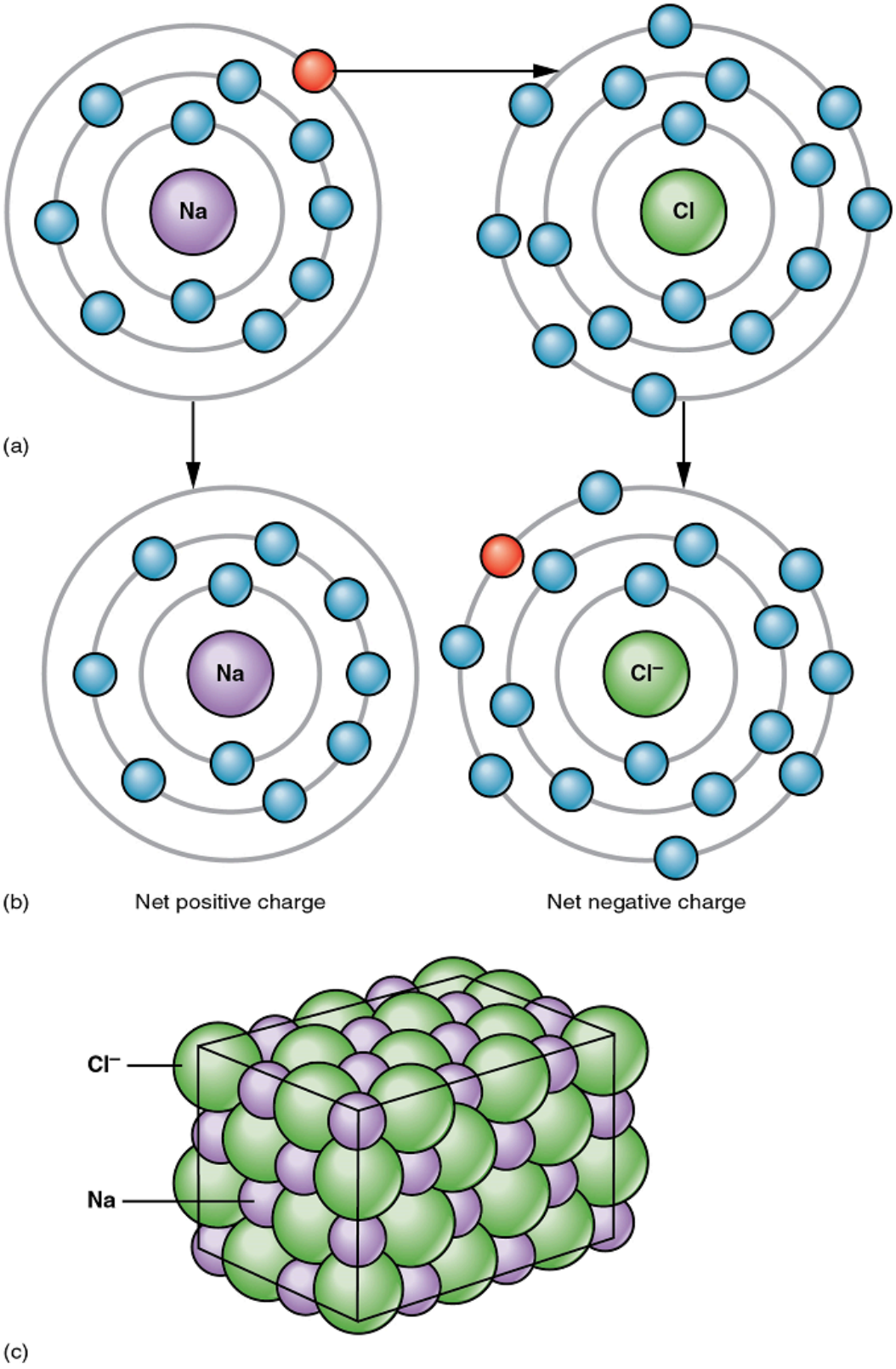


Figure 4. Ionic Bonding. *(a) Sodium readily donates the solitary electron in its valence shell to chlorine, which needs only one electron to have a full valence shell. (b) The opposite electrical charges of the resulting sodium cation and chloride anion result in the formation of a bond of attraction called an ionic bond. (c) The attraction of many sodium and chloride ions results in the formation of large groupings called crystals.*

In a single covalent bond, a single electron pair is shared between two atoms, while in a double covalent bond,

two pairs of electrons are shared between two atoms. There even are triple covalent bonds, where three atoms are shared.

You can see that the covalent bonds shown in Figure 5 are balanced. The sharing of the negative electrons is relatively equal, as is the electrical pull of the positive protons in the nucleus of the atoms involved. This is why covalently bonded molecules that are electrically balanced in this way are described as nonpolar; that is, no region of the molecule is either more positive or more negative than any other.

2. Polar Covalent Bonds: Groups of legislators with completely opposite views on a particular issue are often described as "polarized" by news writers. In chemistry, a **polar molecule** is a molecule that contains regions that have opposite electrical charges. Polar molecules occur when atoms share electrons unequally, in polar covalent bonds.

The most familiar example of a polar molecule is **water** (Figure 6). The molecule has three parts: one atom of oxygen, the nucleus of which contains eight protons, and two hydrogen atoms, whose nuclei each contain only one proton. Because every proton exerts an identical positive charge, a nucleus that contains eight protons exerts a charge eight times greater than a nucleus that contains one proton. This means that the negatively charged electrons present in the water molecule are more strongly attracted to the oxygen nucleus than to the hydrogen nuclei. Each hydrogen atom's single negative electron therefore migrates toward the oxygen atom, making the oxygen end of their bond slightly more negative than the hydrogen end of their bond.

What is true for the bonds is true for the water molecule as a whole; that is, the oxygen region has a slightly negative charge and the regions of the hydrogen atoms have a slightly positive charge. These slight charges are also referred to as "partial charges" because the strength of the charge is less than one full electron, as would occur in an ionic bond. Regions of weak polarity are indicated in diagrams with the Greek letter delta (∂) and a plus (+) or minus (–) sign (Figure 6).

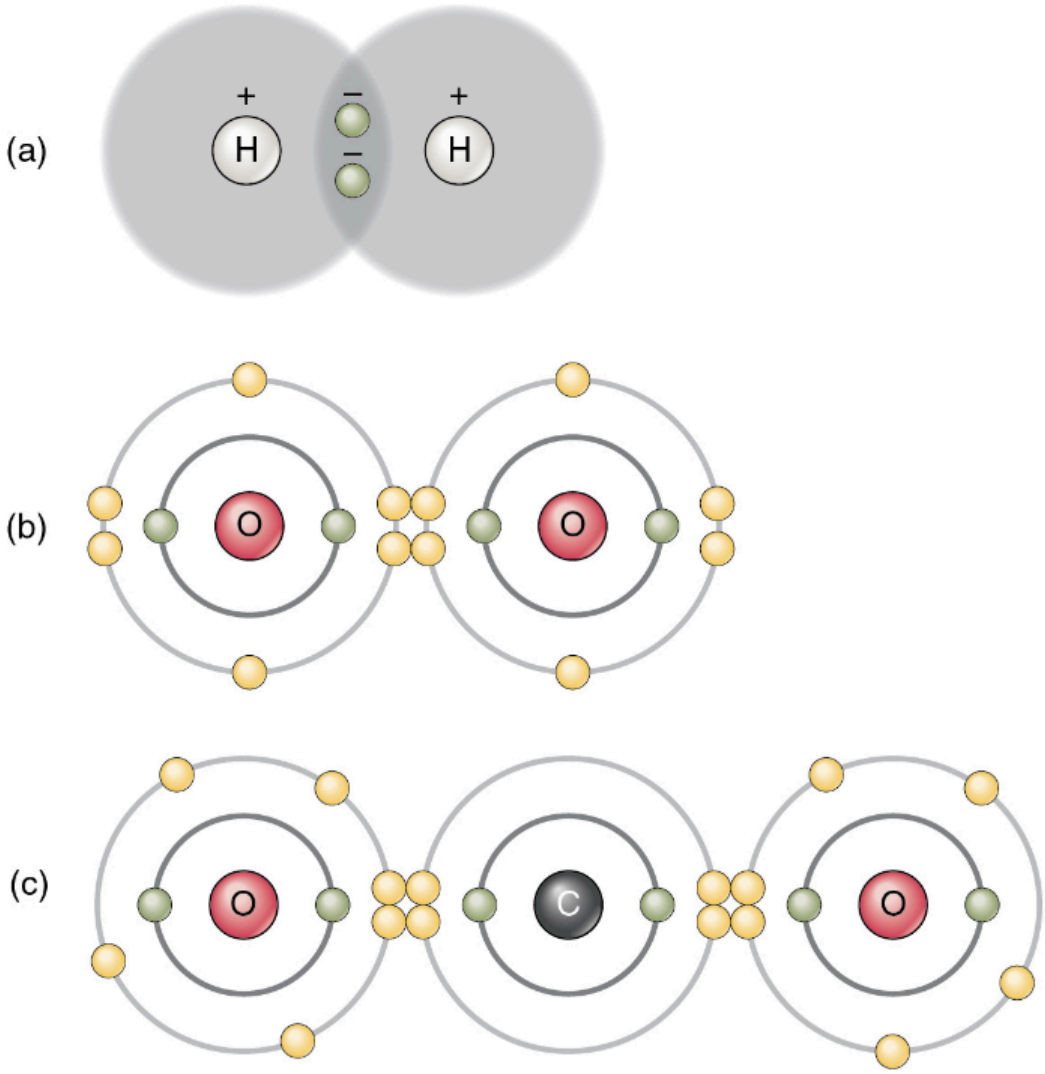


Figure 5. Covalent bonding. *a) A single covalent bond: hydrogen gas (H-H). Two atoms of hydrogen each share their solitary election in a single covalent bond. b) A double covalent bond: oxygen gas (O=O). An atom of oxygen has its electrons in its valence shell: thus, two more would make it stable. Two atoms of oxygen achieve stability by sharing two pairs of electrons in a double covalent bond. c) Two double covalent bonds: carbon dioxide (O=C=O). An atom of carbon has four electrons in its valence shell; thus, four more would make it stable. An atom of carbon and two atoms of oxygen achieve stability by sharing two electron pairs each, in two double covalent bonds.*

Even though a single water molecule is unimaginably tiny, it has mass, and the opposing electrical charges on the molecule pull that mass in such a way that it creates a shape somewhat like a triangular tent (Figure 6). The resulting dipole, with the positive charges at one end formed by the hydrogen atoms at the "bottom" of the tent and the negative charge at the opposite end (the oxygen atom at the "top" of the tent).

Hydrogen Bonds: A hydrogen bond is formed when a slightly (or weakly) positive hydrogen atom already bonded to one electronegative atom (for example, the oxygen in the water molecule) is attracted to another electronegative atom from another molecule. In other words, hydrogen bonds always include a hydrogen atom that is already part of a polar molecule.

The most common example of hydrogen bonding in the natural world occurs between molecules of water. It happens before your eyes whenever two raindrops merge into a larger bead, or a creek spills into a river. Hydrogen bonding occurs because the slightly negative oxygen atom in one water molecule is attracted to the slightly positive hydrogen atoms of two other water molecules (Figure 7).

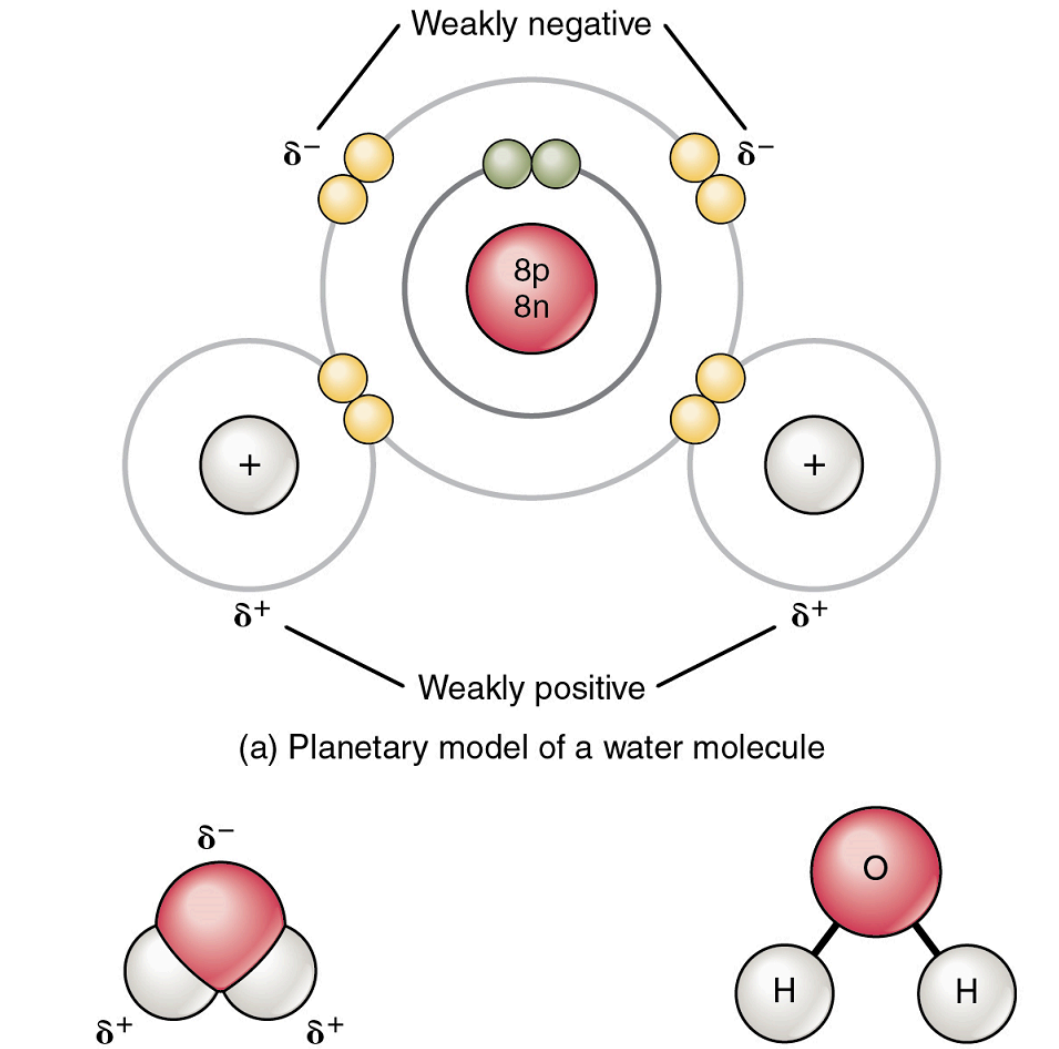


Figure 6. Polar Covalent Bonds in a Water Molecule.

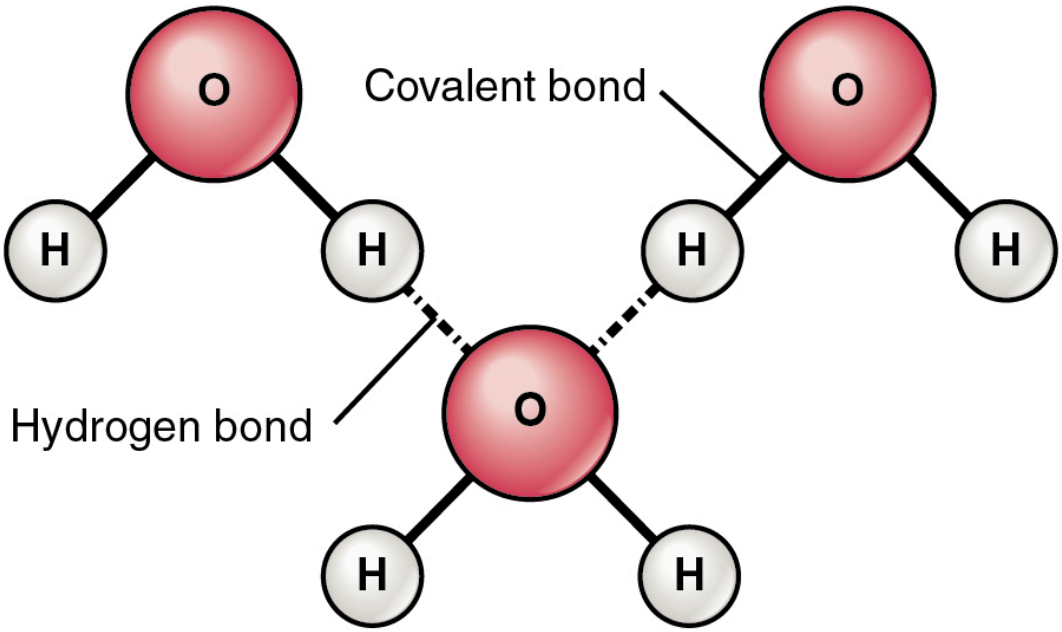


Figure 7. Hydrogen Bonds between Water Molecules. *Notice that the bonds occur between the slightly (or weakly) positive charge on the hydrogen atoms and the slightly (or weakly) negative charge on the oxygen atoms. Hydrogen bonds are relatively weak, and therefore are indicated with a dotted (rather than a solid) line.*

Water molecules also strongly attract other types of charged molecules as well as ions. This explains why sodium chloride or "table salt," for example, which consists of equal numbers of positively-charged sodium (Na^+) and negatively-charged chloride (Cl^-), dissolves so readily in water. In this case dipole-ion bonds form between the water and the electrically-charged ions (electrolytes), allowing moving water molecules to pull the Na^+ and Cl^- away from each other. Water molecules also repel molecules with nonpolar covalent bonds, like fats, lipids, and oils. You can demonstrate this with a simple kitchen experiment: pour a teaspoon of vegetable oil, a compound formed by nonpolar covalent bonds, into a glass of water. Instead of instantly dissolving in the water, the oil forms a distinct bead because the polar water molecules repel the nonpolar oil.

Physical properties of water: The formation of hydrogen bonds in water allows water to have different physical properties than other liquids. One is density; for a typical substance, the solid state is denser than the liquid state. However, this is not the case for water, as ice (solid state) is actually less dense than water (liquid state). The formation of hydrogen bonds in water also affects its boiling point. Scientific predictions based on chemical trends indicate that water should have a boiling point of 90°C. However, the actual boiling point of water is 100°C. In a similar manner, hydrogen bonding also affects the specific heat capacity of water, so that water requires an unusually high amount of energy be added to increase its temperature (and releases an unusually high amount of energy when cooled).

Watch this SciShow video to learn more about electrostatic forces! Direct link: https://youtu.be/GMnsZuEE_m8

Watch this CrashCourse video to learn more about bonding! Direct link: https://youtu.be/QXT4OVM4vXI

Unit 2: The Chemistry of Water

Unit outline

Part 1. Biological importance of water

- Water as a Lubricant and Cushion
- Water as a Heat Sink
- Water as a Component of Liquid Mixtures
- The Role of Water in Chemical Reactions

Part 2. Fluid compartments in the human body

- Body Water Content
- Fluid Compartments
    - Intracellular Fluid
    - Extracellular Fluid

Learning Objectives

At the end of this unit, you should be able to:

I. Explain the biological importance of water.

II. Specify the percentage of body weight that is composed of water and estimate the amount of body water you contain in liters.

III. Describe the distribution of body water.

Learning Objectives and Guiding Questions

At the end of this unit, you should be able to complete all the following tasks, including answering the guiding questions associated with each task.

I. Explain the biological importance of water.

1. For each of the four biologically important properties of water:
    - Identify the property.
    - Describe its importance in the human body.

II. Specify the percentage of body weight that is composed of water and estimate the amount of body water you contain in liters.

1. Given your (approximate) body weight, calculate the amount of water you contain, in liters. *You may use a calculator if necessary, but must clearly show all your work!*

III. Describe the distribution of body water.

1. For each of the major fluid compartments of the human body:
    - Name the compartment.
    - Define the compartment by specifying its location in the human body.
    - Specify the percentage of body fluid volume made up by that compartment.

As much as 70 percent of a human's body weight is water. This water is contained both within the cells and between the cells that make up tissues and organs. Its several roles make water indispensable to human functioning.

Water as a Lubricant and Cushion: Water is a major component of many of the body's lubricating fluids. Just as oil lubricates the hinge on a door, water in synovial fluid lubricates the actions of body joints, and water in pleural fluid helps the lungs expand and recoil with breathing. Watery fluids help keep food flowing through the digestive tract, and ensure that the movement of adjacent abdominal organs is friction free.

Water also protects cells and organs from physical trauma, cushioning the brain within the skull, for example, and protecting the delicate nerve tissue of the eyes. Water cushions a developing fetus in the mother's womb as well.

Water as a Heat Sink: A heat sink is a substance or object that absorbs and dissipates heat but does not experience a corresponding increase in temperature. In the body, water absorbs the heat generated by chemical reactions without greatly increasing in temperature. Moreover, when environmental temperature soars, the water stored in the body helps keep the body cool. This cooling effect happens as warm blood from the body's core flows to the blood vessels just under the skin and is transferred out to the environment as radiant heat. At the same time, sweat glands release warm water in sweat. For evaporation of this water to occur, the hydrogen bonds between the water molecules must be broken, requiring a relatively high amount of energy that in part includes heat. This removal of heat by evaporation results in a cooling of the blood in the body's periphery, near the surface of the skin, which then circulates back to the body core and cools the body.

Water as a Component of Liquid Mixtures: A mixture is a combination of two or more substances, each of which maintains its own chemical identity. In other words, the constituent substances are not chemically bonded into a new, larger chemical compound. The concept is easy to imagine if you think of powdery substances such as flour and sugar; when you stir them together in a bowl, they obviously do not bond to form a new compound. The room air you breathe is a gaseous mixture, containing three discrete elements—nitrogen, oxygen, and argon—and one compound, carbon dioxide.

For cells in the body to survive, they must be kept moist in a water-based liquid called a **solution**. In chemistry, a liquid solution consists of a solvent that dissolves a substance called a solute. An important characteristic

of solutions is that they are homogeneous; that is, the solute molecules are distributed evenly throughout the solution. If you were to stir a teaspoon of sugar into a glass of water, the sugar would dissolve into sugar molecules separated by water molecules. The ratio of sugar to water in the left side of the glass would be the same as the ratio of sugar to water in the right side of the glass. If you were to add more sugar, the ratio of sugar to water would change, but the distribution—provided you had stirred well—would still be even.

The Role of Water in Chemical Reactions: Two types of chemical reactions involve the creation or the consumption of water: dehydration synthesis and hydrolysis.

- In dehydration synthesis, one reactant gives up an atom of hydrogen and another reactant gives up a hydroxyl group (OH) in the synthesis of a new product. In the formation of their covalent bond, a molecule of water is released as a byproduct (Figure 1). This is also sometimes referred to as a condensation reaction.
- In hydrolysis, a molecule of water disrupts a compound, breaking its bonds. The water is itself split into H and OH. One portion of the severed compound then bonds with the hydrogen atom, and the other portion bonds with the hydroxyl group.

These reactions are reversible, and play an important role in the chemistry of organic compounds (which will be discussed shortly).

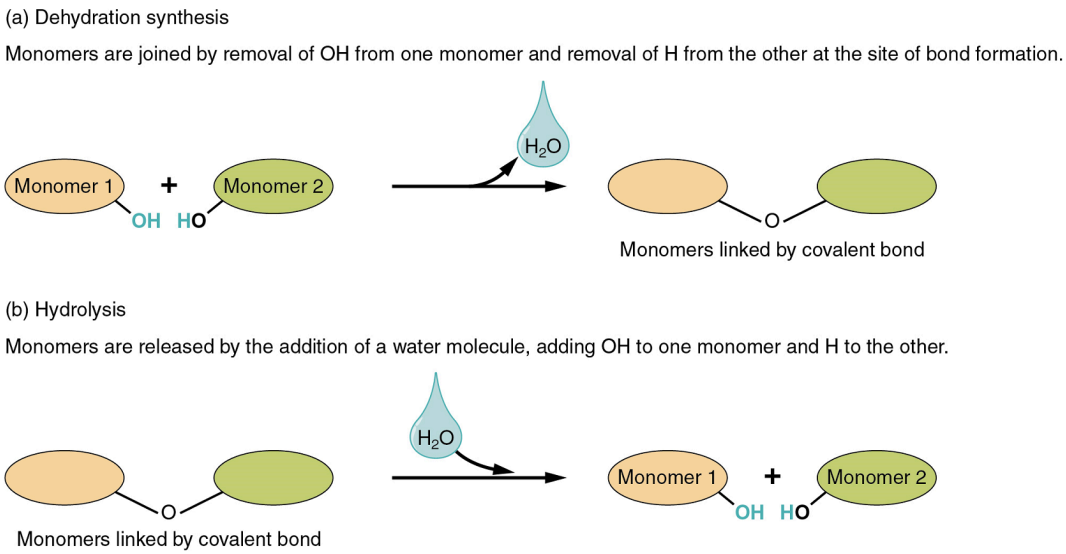


Figure 1. Dehydration Synthesis and Hydrolysis. *Monomers, the basic units for building larger molecules, form polymers (two or more chemically-bonded monomers). (a) In dehydration synthesis, two monomers are covalently bonded in a reaction in which one gives up a hydroxyl group and the other a hydrogen atom. A molecule of water is released as a byproduct during dehydration reactions. (b) In hydrolysis, the covalent bond between two monomers is split by the addition of a hydrogen atom to one and a hydroxyl group to the other, which requires the contribution of one molecule of water.*

Body Water Content: Human beings are mostly water, ranging from about 75 percent of body mass in infants to as low as 45 percent in old age. In adults, the average percent of body mass in women is 50 percent, whereas in men the average is 60 percent. The percent of body water changes with development, because the proportions of the body given over to each organ and to muscles, fat, bone, and other tissues change from infancy to adulthood (Figure 2).

Fluid Compartments: Body fluids can be discussed in terms of their specific fluid compartment, a location

that is largely separate from another compartment by some form of a physical barrier. The intracellular fluid (ICF) compartment is the system that includes all fluid enclosed in cells by their plasma membranes. Extracellular fluid (ECF) surrounds all cells in the body. Extracellular fluid has two primary constituents: the fluid component of the blood (called plasma) and the interstitial fluid (IF) that surrounds all cells not in the blood (Figure 3).

1. Intracellular Fluid: The intracellular fluid lies within cells and is the principal component of the cytosol/ cytoplasm. The intracellular fluid makes up approximately two thirds (about 60 percent) of the total water in the human body, and in an average-size adult male, the intracellular fluid accounts for about 25 liters (seven gallons) of fluid (Figure 4). This fluid volume tends to be very stable, because the amount of water in living cells is closely regulated. If the amount of water inside a cell falls to a value that is too low, the cytosol becomes too concentrated with solutes to carry on normal cellular activities; if too much water enters a cell, the cell may burst and be destroyed.

2. Extracellular Fluid: The extracellular fluid accounts for the other one-third of the body's water content. Approximately 20 percent of the extracellular fluid is found in plasma. Plasma travels through the body in blood vessels and transports a range of materials, including blood cells, proteins (including clotting factors and antibodies), electrolytes, nutrients, gases, and wastes. Gases, nutrients, and waste materials travel between capillaries and cells through the interstitial fluid. Cells are separated from the interstitial fluid by a selectively permeable cell membrane that helps regulate the passage of materials between the interstitial fluid and the interior of the cell.

The body has other water-based extracellular fluid. These include the cerebrospinal fluid that bathes the brain and spinal cord, lymph, the synovial fluid in joints, the pleural fluid in the pleural cavities, the pericardial fluid in the cardiac sac, the peritoneal fluid in the peritoneal cavity, and the aqueous humor of the eye. Because these fluids are outside cells, these fluids are also considered components of the extracellular fluid compartment.

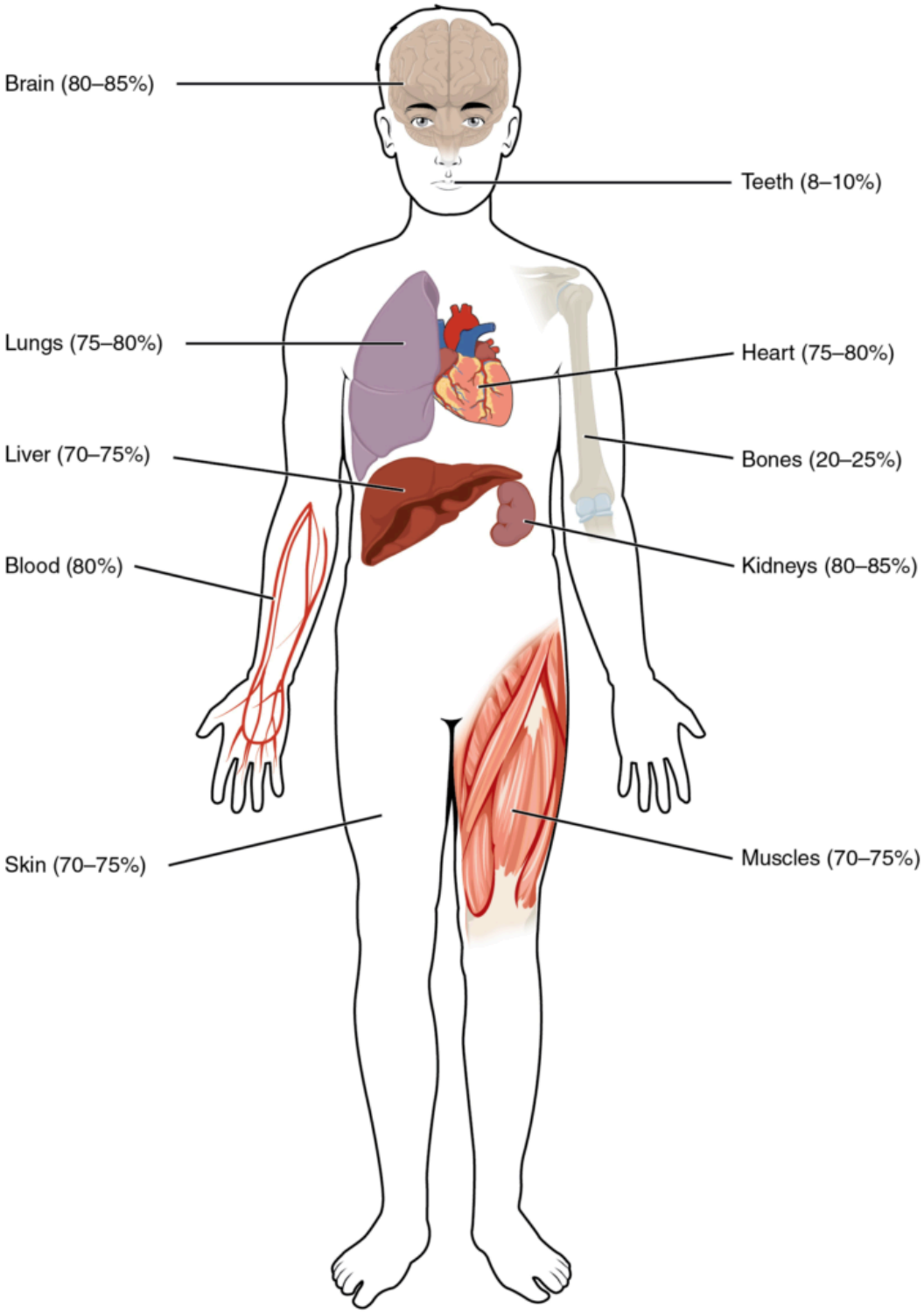


Figure 2. Water Content of the Body's Organs and Tissues. *Water content varies in different body organs and tissues, from as little as 8 percent in the teeth to as much as 85 percent in the brain.*

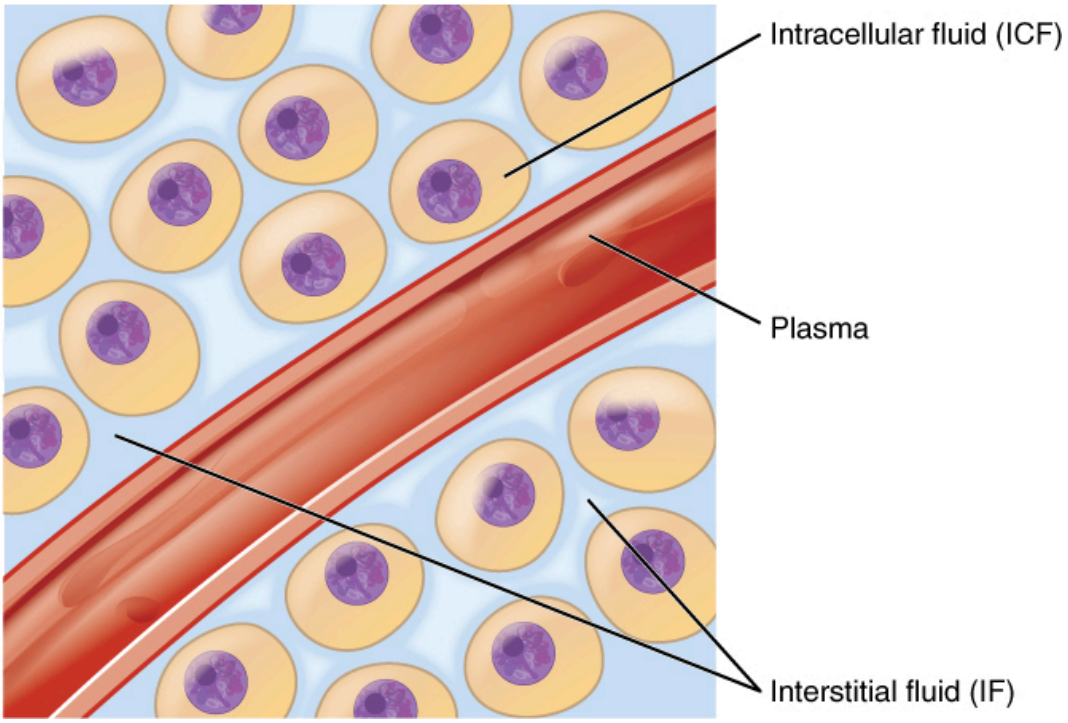


Figure 3. Fluid Compartments in the Human Body. *The intracellular fluid (ICF) is the fluid within cells. The interstitial fluid (IF) is part of the extracellular fluid (ECF) between the cells. Blood plasma is the second part of the extracellular fluid. Materials travel between cells and the plasma in capillaries through the interstitial fluid.*

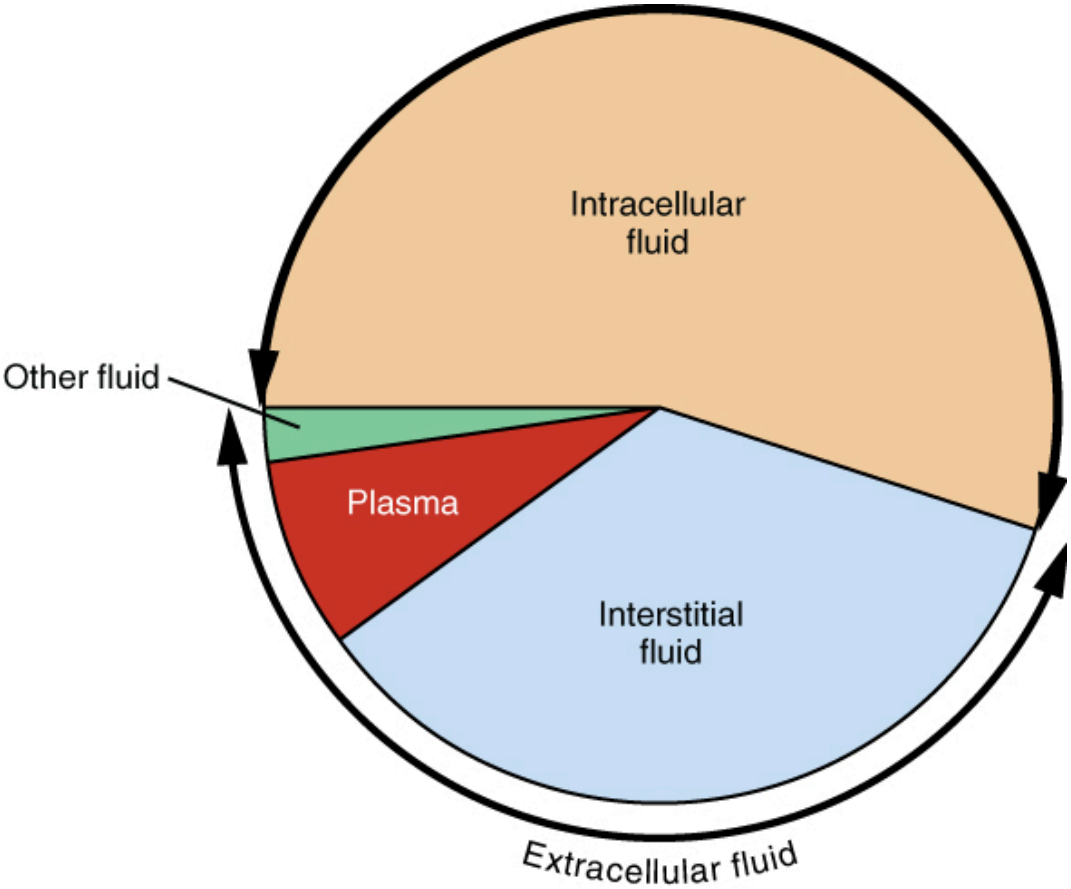


Figure 4. Proportions of Total Body Fluid in Each of the Body's Fluid Compartments. *Most of the water in the body is intracellular fluid. The second largest volume is the interstitial fluid, which surrounds cells that are not blood cells.*

Watch this Amoeba Sisters' video to learn more about the properties of water! Direct link: https://youtu.be/3jwAGWky98c

Watch this CrashCourse video to learn more about the importance of water and its chemical properties. Direct link: https://youtu.be/HVT3Y3_gHGg

Unit 3: Biochemistry

Unit outline

Part 1. Chemistry of carbon

Part 2. Carbohydrates

- Monosaccharides
- Disaccharides
- Polysaccharides
- Functions of carbohydrates

Part 3. Lipids

- Triglycerides
- Phospholipids
- Steroids

Part 4. Proteins

- Amino acids
- Shape of proteins
- Protein function

Part 5. Nucleotides and nucleic acids

- Structure
- ATP
- Nucleic acids
    - DNA
    - RNA

Learning Objectives

At the end of this unit, you should be able to:

I. Describe the chemistry of carbon.

II. Describe the structure and function of carbohydrates.

III. Describe the structure and function of lipids.

IV. Describe the structure and function of proteins.

V. Describe the structure and function of nucleic acids.

Learning Objectives and Guiding Questions

At the end of this unit, you should be able to complete all the following tasks, including answering the guiding questions associated with each task.

I. Describe the chemistry of carbon.

1. Identify the number of covalent bonds carbon can form.
2. Define the term “hydrocarbon chain”.
3. Define the term “functional group”, and identify five examples that are important in human physiology.

II. Describe the structure and function of carbohydrates.

1. Specify the three chemical elements of which carbohydrate molecules consist, and their relative (approximate) proportions in a typical carbohydrate molecule.
2. Refer to the chemical structure of carbohydrates and the chemical properties of water to explain why carbohydrates are generally hydrophilic (soluble in water).
3. Carbohydrate molecules can be grouped based on how many monomers they contain. For each of the three main size groups of carbohydrate:
    - Name and define the group (based on the number of monomers it contains)
    - Name at least three specific examples of each group
    - Briefly describe at least one major function in the human body of each group

III. Describe the structure and function of lipids.

1. Specify the major elements of lipid molecules.
2. Specify the chemical elements of which lipid molecules typically consist, and their relative (approximate) proportions in a typical lipid molecule.
3. Describe the following for triglycerides.
    - Using an annotated diagram, describe the main structural components
    - Describe their primary function in the human body
4. Describe the following for phospholipids.
    - Using an annotated diagram, describe the main structural components and distinguish between the polar head and non-polar tail ends
    - Describe their primary function in the human body
5. Describe the following for steroids.

- Describe the main structural components
- Describe their primary function in the human body

6. Refer to the chemical structure of lipids and the chemical properties of water to explain why lipids are generally insoluble in water.
7. Describe and clearly distinguish between the physical and chemical characteristics of:

- Saturated fats and unsaturated fats
- Monounsaturated fats and polyunsaturated fats

IV. Describe the structure and function of proteins.

1. Specify the chemical elements that make up protein molecules.
2. Use an annotated diagram to show the structure of a generic amino acid.
3. For each of the four levels of structure of a protein molecule:

- Name the structural level.
- Define the structural level.

4. Describe, using examples, eight major functional groups of proteins.
5. For each major functional group of proteins:

- Briefly describe the major function in the human body.
- Name one protein that is representative of each group.

V. Describe the structure and function of nucleic acids.

1. Specify the chemical elements that make up nucleotides.
2. Draw an annotated diagram to show the general structure of a generic nucleoside and a generic nucleotide.
3. For adenosine triphosphate (ATP), describe its:

- Chemical structure.
- Function in cells.
- Important chemical characteristics that allow it to perform its function.

4. Draw two annotated diagrams to compare and contrast the overall structure of the two major nucleic acids found in human cells. In your diagrams, be sure to include the three main structural components of individual nucleotides.
5. Compare and contrast the structure of RNA and DNA. For both molecules, identify:

- The name and general structure of the monomers they consist of.
- The specific nitrogenous bases present in each.
- The one major structural difference between a molecule of RNA and a molecule of DNA.
- The type of bond holding the dual strands of DNA together.
- The main function in human cells.

Organic compounds typically consist of groups of carbon atoms covalently bonded to hydrogen, usually oxygen, and often other elements as well. Created by living things, they are found throughout the world, in soils and seas, commercial products, and every cell of the human body. The four types most important to human

structure and function are carbohydrates, lipids, proteins, and nucleotides. Before exploring these compounds, you need to first understand the chemistry of carbon.

The Chemistry of Carbon: What makes organic compounds ubiquitous is the chemistry of their carbon core. Recall that carbon atoms have four electrons in their valence shell, and that the octet rule dictates that atoms tend to react in such a way as to complete their valence shell with eight electrons. Carbon atoms do not complete their valence shells by donating or accepting four electrons. Instead, they readily share electrons via covalent bonds.

Commonly, carbon atoms share with other carbon atoms, often forming a long carbon chain referred to as a carbon skeleton. It is also possible for carbon atoms to form more than one covalent bond with one another, and can form double bonds and triple bonds.

In organic compounds, carbon atoms can be found to share electrons with hydrogen. Carbon and hydrogen groupings are called hydrocarbons. If you study the figures of organic compounds in the remainder of this chapter, you will see several with chains of hydrocarbons in one region of the compound.

Carbon may share electrons with oxygen or nitrogen or other atoms in a particular region of an organic compound. Moreover, the atoms to which carbon atoms bond may also be part of a functional group. A **functional group** is a group of atoms linked by strong covalent bonds and tending to function in chemical reactions as a single unit. You can think of functional groups as tightly knit "cliques" whose members are unlikely to be parted. Five functional groups are important in human physiology; these are the hydroxyl, carboxyl, amino, methyl and phosphate groups (Table 1).

Table 1: Functional Groups Important in Human Physiology

Functional Group	Chemical formula	Importance
Hydroxyl	-OH	Polar group. Components of all four major classes of organic compounds discussed in this chapter. Involved in dehydration synthesis and hydrolysis reactions, and hydrogen bonding.
Carboxyl	-COOH	A component of the organic acids discussed in this chapter.
Amino	$-NH_2$	A component of all amino acids.
Methyl	$-CH_3$	A component of all fatty acids.
Phosphate	$-PO_4^{2-}$	A component of all phospholipids and nucleotides.

Carbon's affinity for covalent bonding means that many distinct and relatively stable organic molecules nevertheless readily form larger, more complex molecules. Any large molecule is referred to as **macromolecule** (macro- = "large"), and the organic compounds in this section all fit this description. However, some macromolecules are made up of several "copies" of single units called monomer (mono- = "one"; -mer = "part"). Like beads in a long necklace, these monomers link by covalent bonds to form long polymers (poly- = "many"). There are many examples of monomers and polymers among the organic compounds.

Monomers form polymers by engaging in dehydration synthesis (Figure 1). As was noted earlier, this reaction results in the release of a molecule of water. Each monomer contributes: One gives up a hydrogen atom (H) and the other gives up a hydroxyl group (OH). Polymers are split into monomers by hydrolysis (-lysis = "rupture"). The bonds between their monomers are broken, via the donation of a molecule of water, which contributes a hydrogen atom to one monomer and a hydroxyl group to the other.

Carbohydrates: A carbohydrate is a molecule composed of carbon, hydrogen, and oxygen; in most carbohydrates, hydrogen and oxygen are found in the same two-to-one relative proportions they have in water. In fact, the chemical formula for a "generic" molecule of carbohydrate is $(CH_2O)_n$. The structure also contains several hydroxyl groups, which makes carbohydrates polar in terms of chemical nature.

Carbohydrates are also referred to as saccharides, a word meaning "sugars.". Three forms are important in the body. Monosaccharides are the monomers of carbohydrates. Disaccharides (di- = "two") are made up of two monomers. Polysaccharides are the polymers, and can consist of hundreds to thousands of monomers.

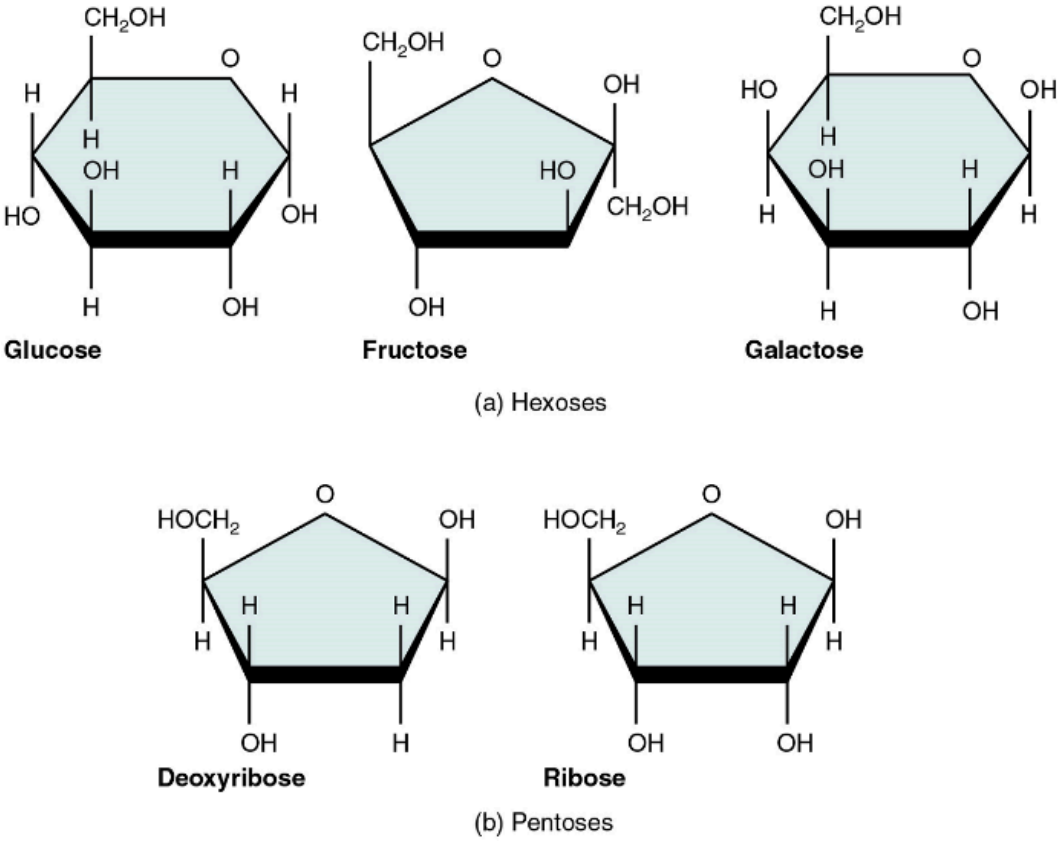
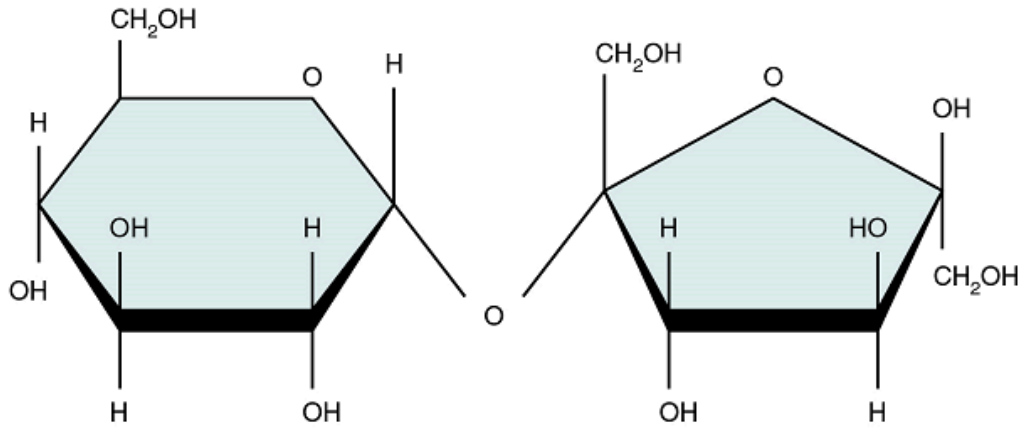


Figure 1. Five Important Monosaccharides. *Different groups of monosaccharides are defined by the number of carbon atoms in their molecular structure. In the examples shown, the hexoses each contain six carbon atoms in their molecular structure, whereas the pentoses each contain five carbon atoms.*

1. Monosaccharides: A monosaccharide is a monomer of carbohydrates. Five monosaccharides are important in the body. Three of these are the hexose sugars, so called because they each contain six atoms of carbon. These are glucose, fructose, and galactose (Figure 1a). The remaining monosaccharides are the two pentose sugars, each of which contains five atoms of carbon: ribose and deoxyribose (Figure 1b).

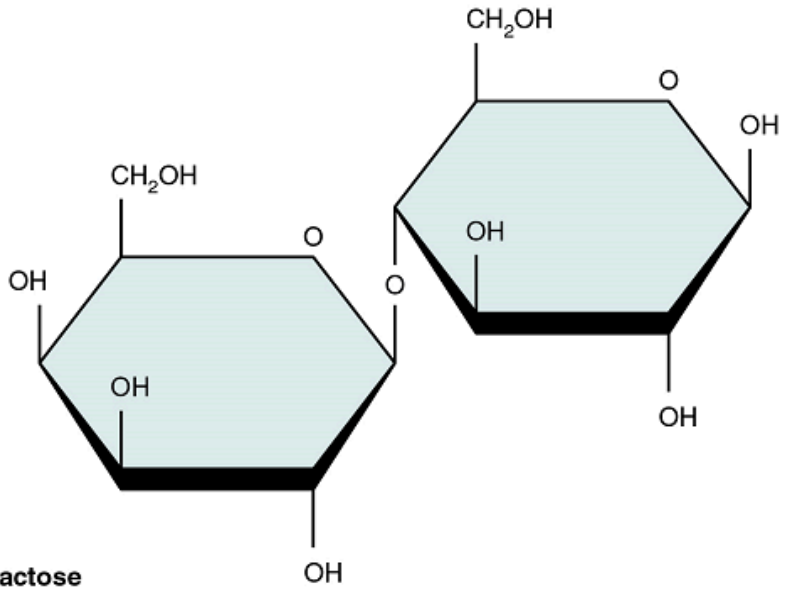
2. Disaccharides: A disaccharide is a pair of monosaccharides. Disaccharides are formed via dehydration synthesis, and the bond linking them is referred to as a glycosidic bond (glyco- = "sugar"). Three disaccharides are important to humans. These are sucrose, commonly referred to as table sugar; lactose, or milk sugar; and maltose, or malt sugar (Figure 2). As you can tell from their common names, you consume these in your diet; however, your body cannot use them directly. Instead, in the digestive tract, they are split into their component monosaccharides via hydrolysis.

(a) The monosaccharides glucose and fructose bond to form sucrose



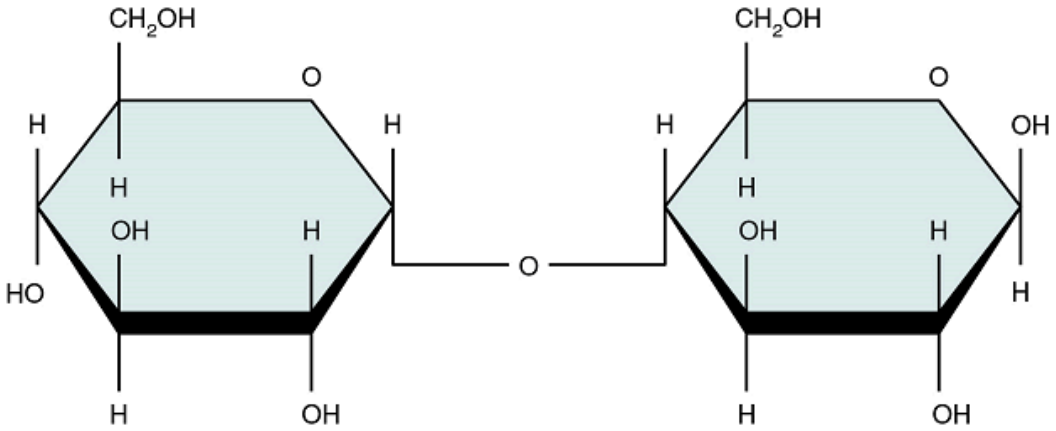
Sucrose

(b) The monosaccharides galactose and glucose bond to form lactose.



Lactose

(c) Two glucose monosaccharides bond to form maltose.



Maltose

Figure 2. Three Important Disaccharides. *All three important disaccharides are formed by dehydration synthesis.*

3. Polysaccharides: Polysaccharides can contain a few to a thousand or more monosaccharides. Three are important to the body (Figure 3):

- Starches are polymers of glucose. They occur in long chains called amylose or branched chains called amylopectin, both of which are stored in plant-based foods and are relatively easy to digest.
- Glycogen is also a polymer of glucose, but it is stored in the tissues of animals, especially in the muscles and liver. It is not considered a dietary carbohydrate because very little glycogen remains in animal tissues after slaughter; however, the human body stores excess glucose as glycogen, again, in the muscles and liver.
- Cellulose, a polysaccharide made of glucose that is the primary component of the cell wall of green plants, is the component of plant food referred to as "fiber". In humans, cellulose/fiber is not digestible; however, dietary fiber has many health benefits. It helps you feel full so you eat less, it promotes a healthy digestive tract, and a diet high in fiber is thought to reduce the risk of heart disease and possibly some forms of cancer.

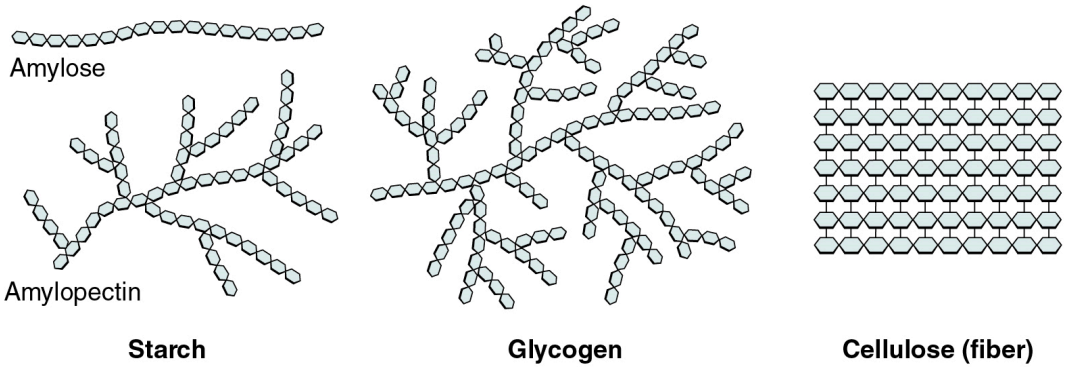


Figure 3. Three Important Polysaccharides. *Three important polysaccharides are starches, glycogen, and fiber.*

4. Functions of Carbohydrates: The body obtains carbohydrates from plant-based foods. Grains, fruits, and legumes and other vegetables provide most of the carbohydrate in the human diet, although lactose is found in dairy products. Polysaccharides such as starch, and various monosaccharides and disaccharides play a role as a primary energy source, especially glucose which is the main monosaccharide used in the body. Short chains of saccharides can also be used to form the glycocalyx (described in a later unit). The body is also capable of storing glucose in the body in the form of glycogen (a polysaccharide).

Finally, pentose sugars are critical structural components of ATP and the nucleotides that make up RNA and DNA.

Lipids: A **lipid** is one of a highly diverse group of compounds made up mostly of hydrocarbons. The few oxygen atoms they contain are often at the periphery of the molecule. Their nonpolar hydrocarbons make all lipids hydrophobic. In water, lipids do not form a true solution, but they may form an emulsion, which is the term for a mixture of solutions that do not mix well.

1. Triglycerides: A triglyceride is one of the most common dietary lipid groups, and the type found most abundantly in body tissues. This compound, which is commonly referred to as a fat, is formed by covalent bonding between two types of molecules (Figure 4):

- A glycerol backbone consists of three carbon atoms, each bonded to a hydroxyl group.
- Three fatty acids, long chains of hydrocarbons with a carboxyl group and a methyl group at opposite ends, extend from each of the carbons of the glycerol. These hydrocarbon chains are formed with nonpolar bonds, making them hydrophobic in terms of chemical nature.

Triglycerides form via dehydration synthesis. Glycerol gives up hydrogen atoms from its hydroxyl groups at

each bond, and the carboxyl group on each fatty acid chain gives up a hydroxyl group. A total of three water molecules are thereby released.

Fatty acid chains that have no double carbon bonds anywhere along their length and therefore contain the maximum number of hydrogen atoms are called saturated fatty acids. These straight, rigid chains pack tightly together and are solid or semi-solid at room temperature (Figure 5a). Butter and lard are examples, as is the fat found on a steak or in your own body. In contrast, fatty acids with one double carbon bond are kinked at that bond (Figure 5b). These monounsaturated fatty acids are therefore unable to pack together tightly, and are liquid at room temperature. Polyunsaturated fatty acids contain two or more double carbon bonds, and are also liquid at room temperature. Plant oils such as olive oil typically contain both mono- and polyunsaturated fatty acids.

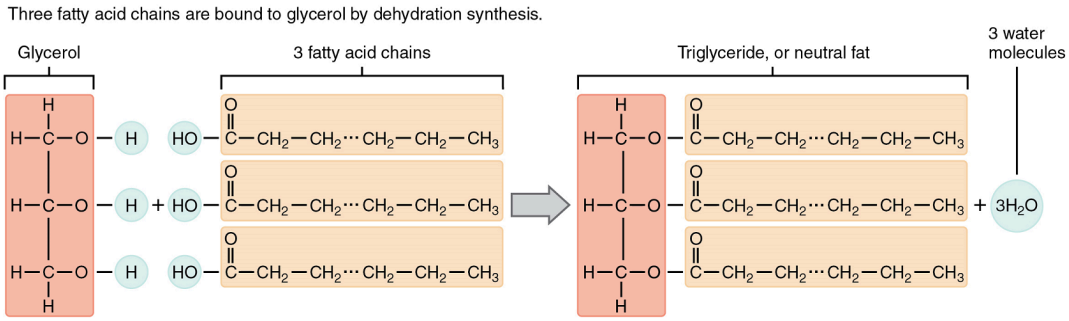


Figure 4. Triglycerides. *Triglycerides are composed of three fatty acids attached to glycerol via dehydration synthesis. Notice that glycerol gives up individual hydrogen atoms, and the carboxyl groups on each fatty acid give up a hydroxyl group.*

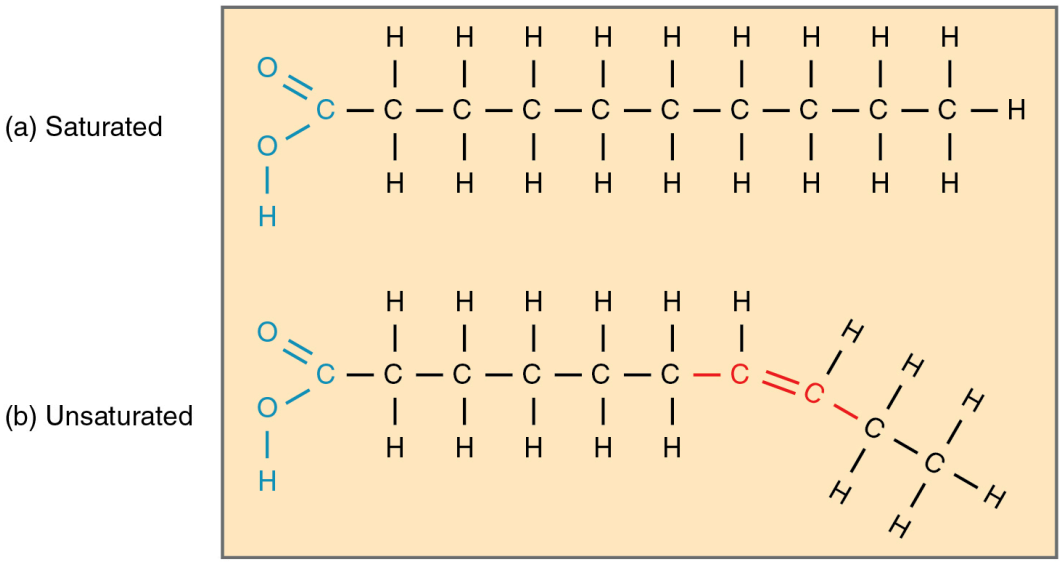


Figure 5. Fatty Acid Shapes. *The level of saturation of a fatty acid affects its shape. (a) Saturated fatty acid chains are straight. (b) Unsaturated fatty acid chains are kinked.*

As a group, triglycerides are a major fuel source for the body and are used when glucose storages are low or during extended fasting conditions. Triglycerides also fuel long, slow physical activity such as gardening or hiking, and contribute a modest percentage of energy for vigorous physical activity. Dietary fat also assists the absorption and transport of the nonpolar fat-soluble vitamins A, D, E, and K. Additionally, stored body fat protects and cushions the body's bones and internal organs, and acts as insulation to retain body heat.

Fatty acids are also components of glycolipids, which are sugar-fat compounds found in the cell membrane.

Lipoproteins are compounds in which the hydrophobic triglycerides are packaged in protein envelopes for transport in body fluids.

2. Phospholipids: As its name suggests, a **phospholipid** is a bond between the glycerol component of a lipid and a phosphorous molecule. In fact, phospholipids are similar in structure to triglycerides. However, instead of having three fatty acids, a phospholipid is generated from a diglyceride, a glycerol with just two fatty acid chains (Figure 6). The third binding site on the glycerol is taken up by the phosphate group, which in turn is attached to a polar "head" region of the molecule. Recall that triglycerides are nonpolar and hydrophobic. This still holds for the fatty acid portion of a phospholipid compound. However, the head of a phospholipid contains charges on the phosphate groups, as well as on the nitrogen atom. These charges make the phospholipid head hydrophilic. Therefore, phospholipids are said to have hydrophobic tails, containing the neutral fatty acids, and hydrophilic heads, containing the charged phosphate groups and nitrogen atom. Phospholipids for the phospholipid bilayer, which is the basis of the structure of cell membranes.

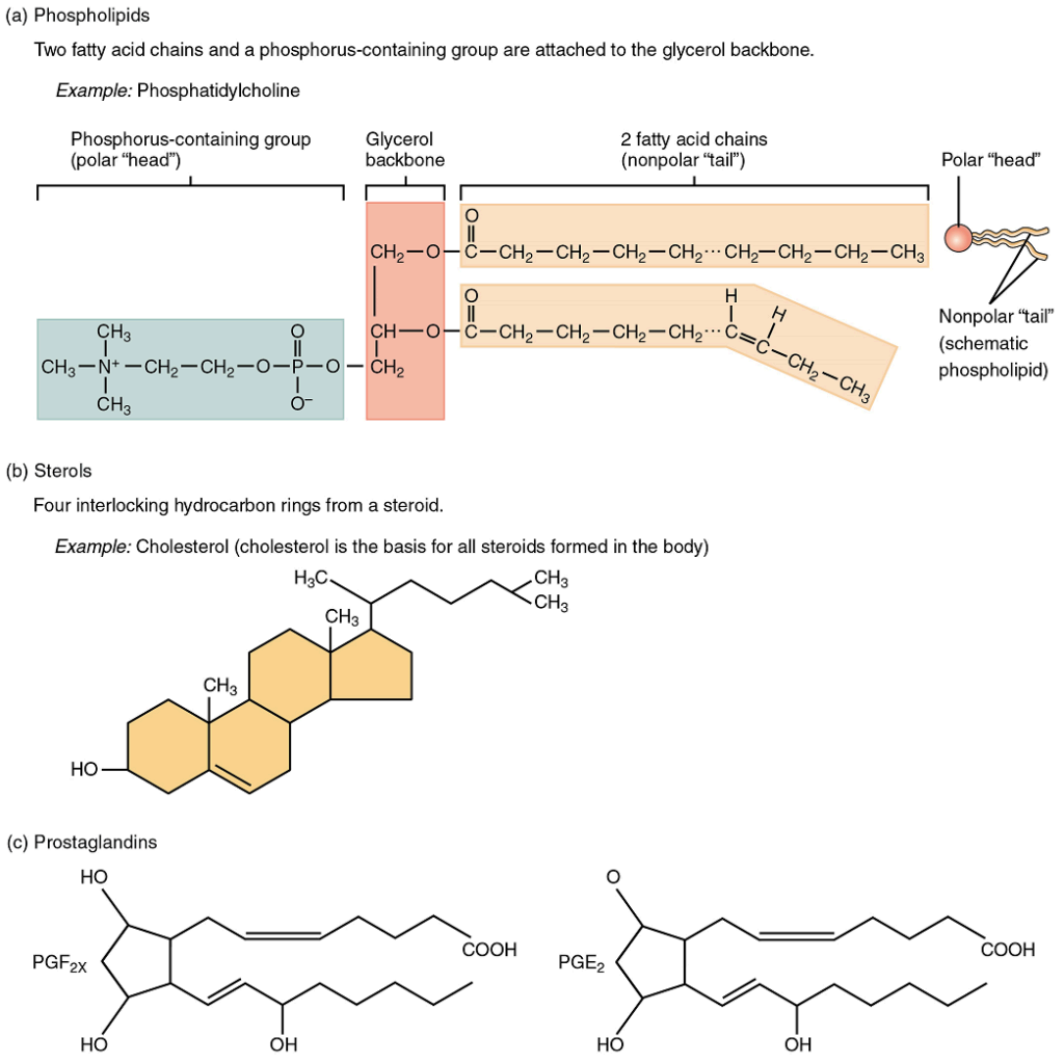


Figure 6. Other Important Lipids. *(a) Phospholipids are composed of two fatty acids, glycerol, and a phosphate group. (b) Sterols are ring-shaped lipids. Shown here is cholesterol.*

3. Steroids: A steroid compound (referred to as a sterol) has as its foundation a set of four hydrocarbon rings bonded to a variety of other atoms and molecules (see Figure 6b). Although both plants and animals synthesize sterols, the type that makes the most important contribution to human structure and function is cholesterol, which is synthesized by the liver in humans and animals and is also present in most animal-based foods.

Like other lipids, cholesterol's hydrocarbons make it hydrophobic; however, it has a polar hydroxyl head that is hydrophilic. Cholesterol is an important component of bile acids, compounds that help emulsify dietary fats. Cholesterol is also a building block of many hormones, signaling molecules that the body releases to regulate processes at distant sites.

Proteins: You might associate proteins with muscle tissue, but in fact, proteins are critical components of all tissues and organs. A **protein** is an organic molecule composed of amino acids linked by peptide bonds. Proteins include the keratin in the epidermis of skin that protects underlying tissues, the collagen found in the dermis of skin, in bones, and in the meninges that cover the brain and spinal cord. Proteins are also components of many of the body's functional chemicals, including digestive enzymes in the digestive tract, antibodies, the neurotransmitters that neurons use to communicate with other cells, and the peptide-based hormones that regulate certain body functions (for instance, growth hormone). While carbohydrates and lipids are composed of hydrocarbons and oxygen, all proteins also contain nitrogen (N), and many contain sulfur (S), in addition to carbon, hydrogen, and oxygen, in varying ratios depending on the structure.

1. Microstructure of Proteins: Proteins are polymers made up of nitrogen-containing monomers called amino acids. An amino acid is a molecule composed of an amino group and a carboxyl group, together with a variable side chain. Just 20 different amino acids contribute to nearly all of the thousands of different proteins important in human structure and function. Body proteins contain a unique combination of a few dozen to a few hundred of these 20 amino acid monomers. All 20 of these amino acids share a similar structure (Figure 7). All consist of a central carbon atom to which the following are bonded:

- a hydrogen atom
- an alkaline (basic) amino group NH_2 (see Table 1)
- an acidic carboxyl group COOH (see Table 1)
- a variable group

Notice that all amino acids contain both an acid (the carboxyl group) and a base (the amino group) (amine = "nitrogen-containing"). What distinguishes the 20 amino acids from one another is their variable group, which is referred to one another is their variable group, which is referred to as a side chain or an R-group. This group can vary in size and can be polar or nonpolar, giving each amino acid its unique characteristics.

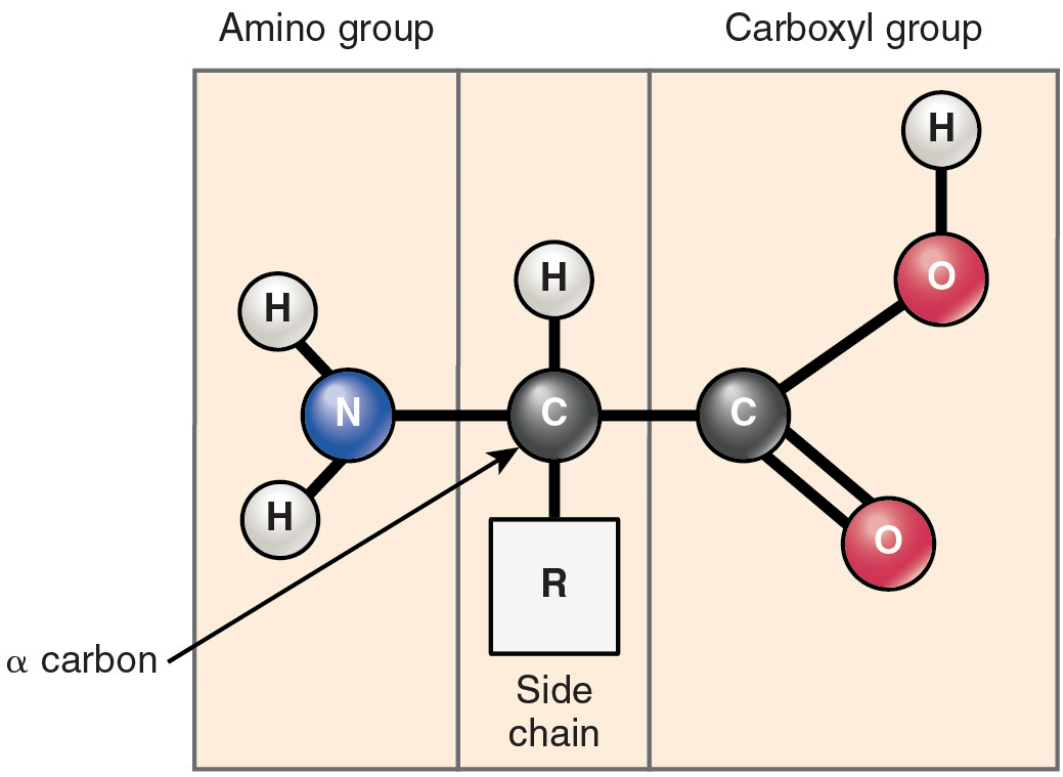


Figure 7. Structure of an Amino Acid. *The side chain, designated "R", differs between specific amino acids and is composed of one or more hydrogen, carbon, oxygen, nitrogen, and/or sulfur atoms.*

Amino acids join via dehydration synthesis to form protein polymers (Figure 8). The unique bond holding amino acids together is called a **peptide bond**. A peptide bond is a covalent bond between two amino acids that forms by dehydration synthesis. A peptide, in fact, is a very short chain of amino acids. Strands containing fewer than about 100 amino acids are generally referred to as polypeptides rather than proteins.

The body is able to synthesize most of the amino acids from components of other molecules; however, some cannot be synthesized and have to be consumed in the diet. These are known as the essential amino acids.

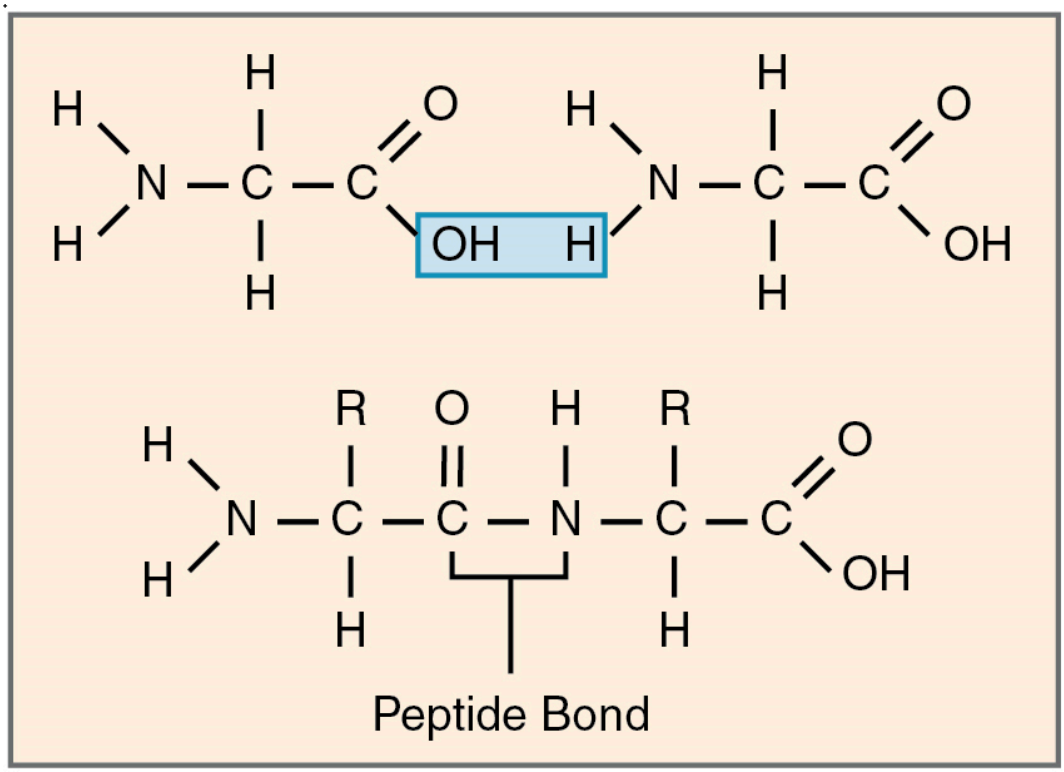


Figure 8. Peptide Bond. *Different amino acids join together to form peptides, polypeptides, or proteins via dehydration synthesis. The bonds between the amino acids are peptide bonds.*

2. Shape of Proteins: A protein's shape is essential to its function, which is fundamentally determined by the sequence of amino acids of which it is made (Figure 9a). The sequence is called the primary structure of the protein.

Although some polypeptides exist as linear chains, most are twisted or folded into more complex secondary structures that form when bonding occurs between amino acids with different properties at different regions of the polypeptide.

The secondary structure of proteins further folds into a compact three-dimensional shape, referred to as the protein's tertiary structure (Figure 9c). Often, two or more separate polypeptides bond to form an even larger protein with a quaternary structure (Figure 9d). The polypeptide subunits forming a quaternary structure can be identical or different. For instance, hemoglobin, the protein found in red blood cells is composed of four tertiary polypeptides, two of which are called alpha chains and two of which are called beta chains.

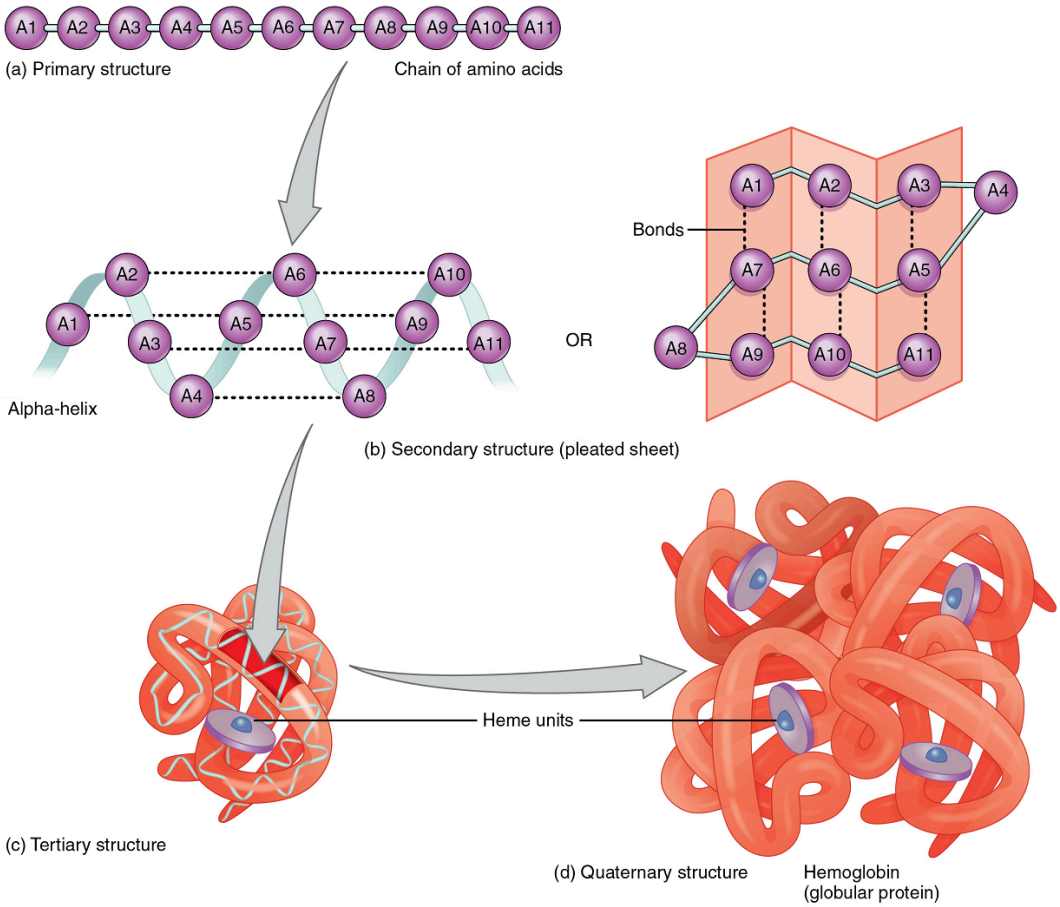


Figure 9. The Shape of Proteins. *(a) The primary structure is the sequence of amino acids that make up the polypeptide chain. (b) The secondary structure, which can take the form of an alpha-helix or a beta-pleated sheet, is maintained by hydrogen bonds between amino acids in different regions of the original polypeptide strand. (c) The tertiary structure occurs as a result of further folding and bonding of the secondary structure. (d) The quaternary structure occurs as a result of interactions between two or more tertiary subunits. The example shown here is hemoglobin, a protein in red blood cells which transports oxygen to body tissues.*

3. Functions of Proteins:

Proteins in the body have a variety of functions. Some proteins are used for **movement**, from muscle cell contraction (actin and myosin) down to intracellular transport (e.g. actin). Some proteins are also used to provide a structural framework or **mechanical support** of connective tissues (e.g. collagen, keratin, elastin), individual cells (e.g. titin), and plasma membranes (e.g. spectrin, dystrophin). Some proteins called enzymes, introduced earlier as protein catalysts, play a role in **catalytic action** (e.g., ATP synthase, etc.) to speed up chemical reactions in the body.

Some proteins are used to **transport** specific molecules (e.g. hormones or gases) or ions (e.g. iron or calcium) in blood. The hemoglobin proteins packed into red blood cells for example (Figure 9d) are used to transport the oxygen gas molecules from the lungs to other body cells. Others (e.g. albumin, hemoglobin) can help **regulate body fluid pH** by reversibly functioning as acids or bases, thus acting as buffers. Some proteins act as hormones to **regulate metabolism**, and are referred to as peptide hormones or protein hormones (e.g. insulin, growth hormone, oxytocin). Others are used to **defend the body** against foreign substances including invading pathogens and toxins (e.g. antibodies, complement proteins). Finally, some proteins known as **molecular chaperones** (e.g., heat-shock proteins, etc.) are essential to the production of other proteins and the appropriate breakdown of damaged proteins.

As was noted earlier, the basic and acidic components enable proteins to function as buffers in maintaining acid–base balance, but they also help regulate fluid–electrolyte balance. Proteins attract fluid, and a healthy concentration of proteins in the blood, the cells, and the spaces between cells helps ensure a balance of fluids in these various “compartments.” Moreover, proteins in the cell membrane help to transport electrolytes in and

out of the cell, keeping these ions in a healthy balance. Like lipids, proteins can bind with carbohydrates. They can thereby produce glycoproteins or proteoglycans, both of which have many functions in the body.

The body can use proteins for energy when carbohydrate and fat intake is inadequate, and stores of glycogen and adipose tissue become depleted. However, since there is no storage site for protein except functional tissues, using protein for energy causes tissue breakdown, and results in body wasting.

Nucleotides and Nucleic Acids: The fourth type of organic compound important to human structure and function are the nucleotides (Figure 12). A nucleotide is one of a class of organic compounds composed of three subunits:

- one or more phosphate groups
- a pentose sugar: either deoxyribose or ribose
- a nitrogen-containing base: adenine, cytosine, guanine, thymine, or uracil

Nucleotides can be assembled into nucleic acids (DNA or RNA) or the energy compound adenosine triphosphate.

1. Adenosine triphosphate: The nucleotide adenosine triphosphate (ATP), is composed of a ribose sugar, an adenine base, and three phosphate groups (Figure 10). ATP is classified as a high energy compound because the two covalent bonds linking its three phosphates store a significant amount of potential energy. In the body, the energy released from these high energy bonds helps fuel the body's activities, from muscle contraction to the transport of substances in and out of cells to anabolic chemical reactions.

When a phosphate group is cleaved from ATP, the products are adenosine diphosphate (ADP) and inorganic phosphate (Pi). This hydrolysis reaction can be written:

$$ATP + H_2O \rightarrow ADP + Pi + energy$$

Removal of a second phosphate leaves adenosine monophosphate (AMP) and two phosphate groups. Again, these reactions also liberate the energy that had been stored in the phosphate-phosphate bonds. They are reversible, too, as when ADP undergoes phosphorylation. **Phosphorylation** is the addition of a phosphate group to an organic compound, in this case, resulting in ATP. In such cases, the same level of energy that had been released during hydrolysis must be reinvested to power dehydration synthesis.

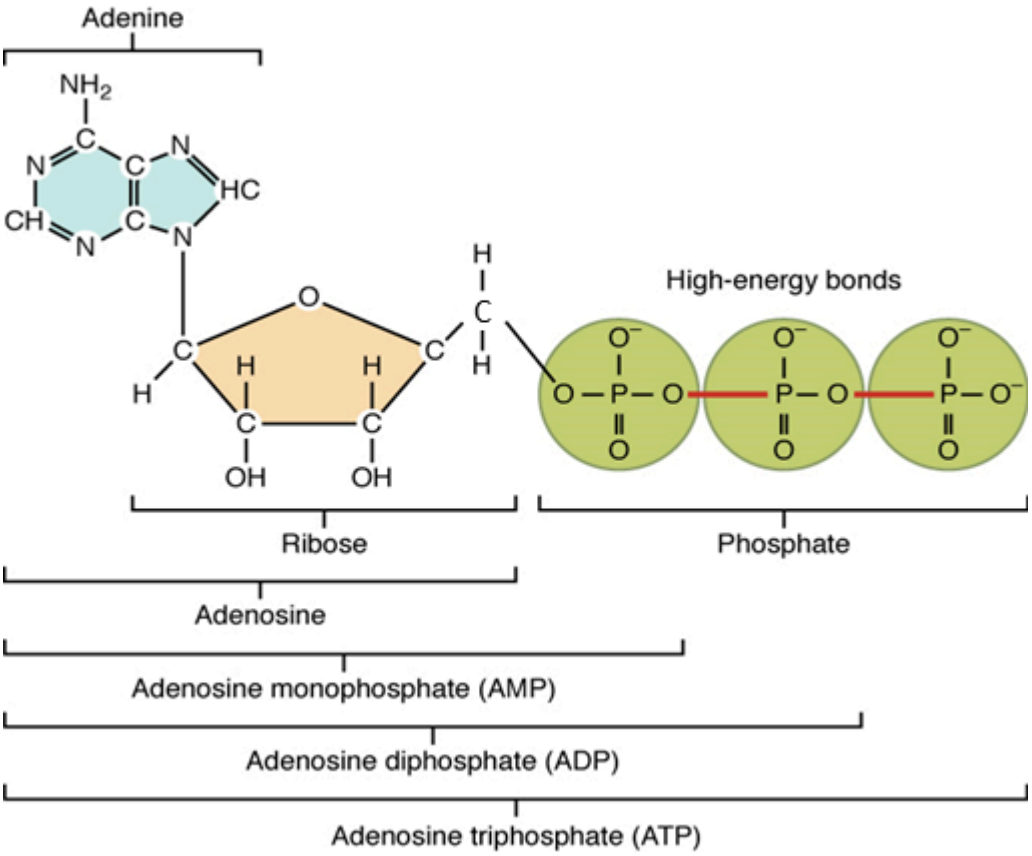


Figure 10. Structure of Adenosine Triphosphate (ATP). *Adenosine is a nucleoside to which can be attached one (mono-), two (di-), or three (tri-) phosphate groups.*

Cells can also transfer a phosphate group from ATP to another organic compound. For example, when glucose first enters a cell, a phosphate group is transferred from ATP, forming glucose phosphate ($C_6H_{12}O_6$—P) and ADP. Once glucose is phosphorylated in this way, it can be stored as glycogen or metabolized for immediate energy.

2. Nucleic Acids: The nucleic acids differ in their type of pentose sugar. **Deoxyribonucleic acid (DNA)** is nucleotide that stores genetic information. DNA contains deoxyribose plus one phosphate group and one nitrogen-containing base. The bases for DNA can be adenine, cytosine, guanine, and thymine. **Ribonucleic acid (RNA)** is a ribose-containing nucleotide that helps manifest the genetic code as protein. RNA contains ribose, one phosphate group, and one nitrogen-containing base, but the bases for RNA are one of adenine, cytosine, guanine, and uracil. (Figure 11)

Bonds formed by dehydration synthesis between the pentose sugar of one nucleic acid monomer and the phosphate group of another form a "backbone," from which the components' nitrogen-containing bases protrude. In DNA, two such backbones attach at their protruding bases via hydrogen bonds. These twist to form a shape known as a double helix (Figure 12). The sequence of nitrogen-containing bases within a strand of DNA form the genes that act as a molecular code instructing cells in the assembly of amino acids into proteins. Humans have almost 22,000 genes in their DNA, locked up in the 46 chromosomes inside the nucleus of each cell (except red blood cells which lose their nuclei during development). These genes carry the genetic code to build one's body, and are unique for each individual except identical twins.

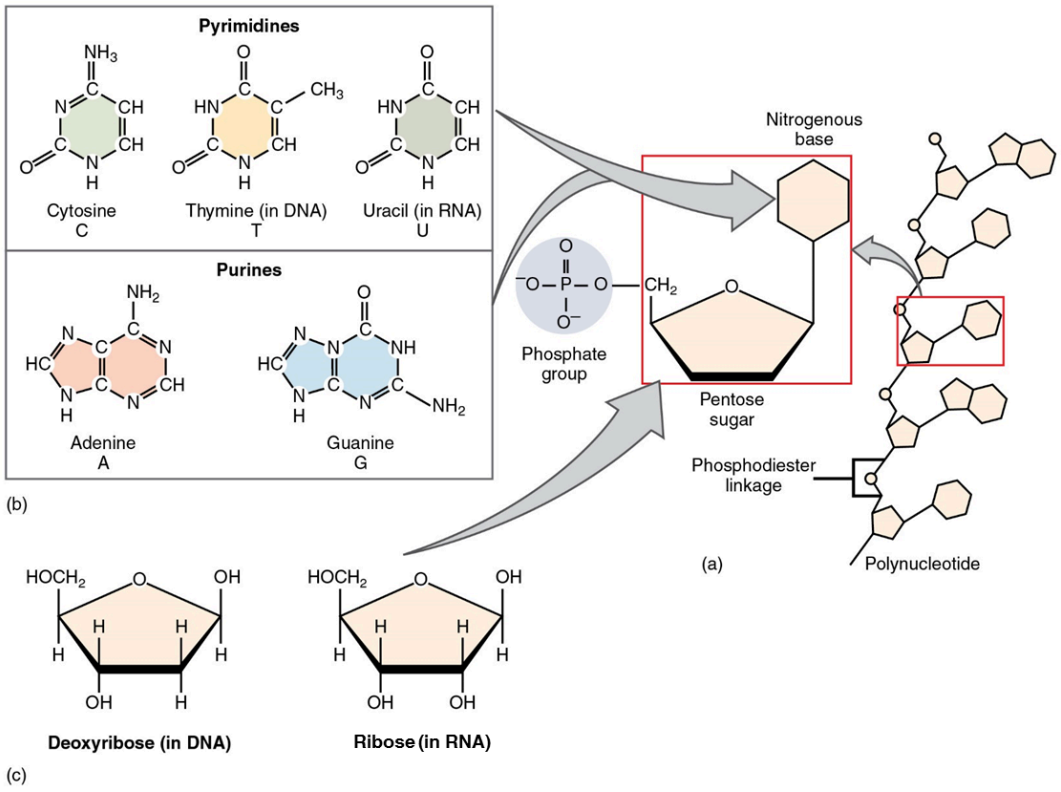


Figure 11. Nucleotides. *(a) The building blocks of all nucleotides are one or more phosphate groups, a pentose sugar, and a nitrogen-containing base. (b) The nitrogen-containing bases of nucleotides. (c) The two pentose sugars of DNA and RNA.*

In contrast, RNA consists of a single strand of sugar-phosphate backbone studded with bases. Messenger RNA (mRNA) is created during protein synthesis to carry the genetic instructions from the DNA to the cell's protein manufacturing plants in the cytoplasm, the ribosomes.

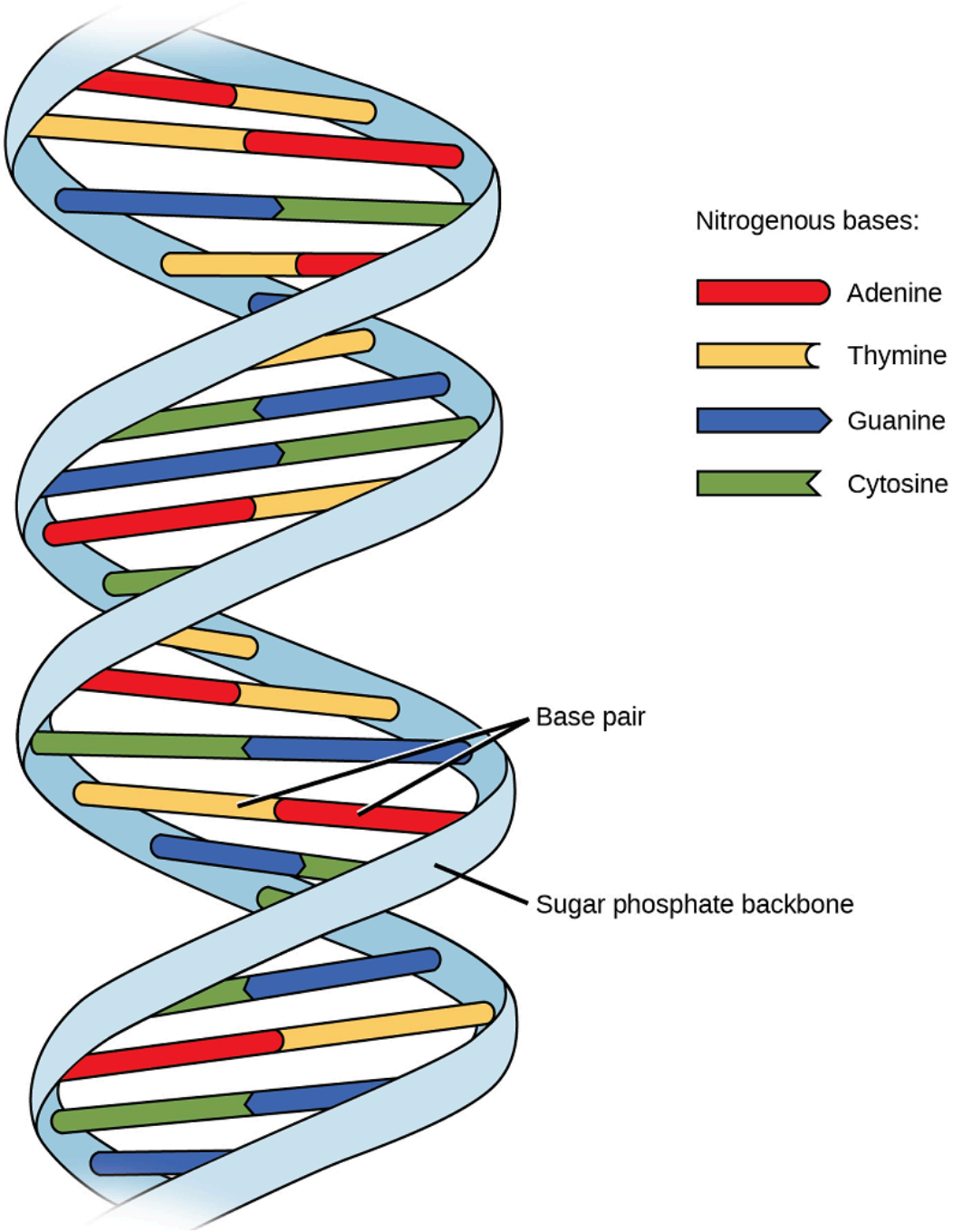


Figure 12. DNA. *In the DNA double helix, two strands attach via hydrogen bonds between the bases of the component nucleotides.*

Watch this Amoeba Sisters video to learn more about biomolecules! Direct link: https://youtu.be/YO244P1e9QM

Unit 4: Cell Structure and Function

Unit Outline

Part 1. Characteristics of life

Part 2. Structural organization of the body

Part 3. Cell structure, cellular organelles and functions

Part 4. Cellular processes involved in growth

Learning Objectives

At the end of this unit, you should be able to:

I. Specify the characteristics associated with life and explain why the cell is the basic unit of life.

II. Describe the levels of structural organization in the body.

III. Describe the structure and the functions of major components of a cell.

IV. Define metabolism, and distinguish between anabolism and catabolism.

V. Describe the cellular processes involved in the growth of the human body from a fertilized egg to an adult.

VI. Describe the importance of cell differentiation to an organism.

VII. Describe the general characteristics of each of the following cell types and relate their characteristics to their functions: nerve cell, muscle cell, red blood cell (erythrocyte), white blood cell (leukocyte).

Learning Objectives and Guiding Questions

At the end of this unit, you should be able to complete all the following tasks, including answering the guiding questions associated with each task.

I. Specify the characteristics associated with life and explain why the cell is the basic unit of life.

1. List, explain and provide examples of each of the characteristics of life.
2. In reference to your answer to question #1, above, explain in one sentence why the cell is considered to be the basic unit of life.

II. Describe the levels of structural organization in the body.

1. Define each of the following levels of organization in the body:

    - Chemical level
    - Cellular level
    - Tissue level
    - Organ level
    - Organ system level
    - Organismal level

2. Write a clear description of the relationships between the chemical, cellular, tissue, organ, organ system, and organismal levels of organization in the body.

III. Describe the structure and the functions of major components of a cell.

1. Describe the structure (be able to identify them in a diagram) and describe the functions of the following cytoplasmic components:

    - Cell membrane (plasma membrane)
    - Endoplasmic reticulum
    - Ribosomes
    - Golgi apparatus (Golgi complex)
    - Lysosomes
    - Mitochondria
    - Vesicle

2. Describe the structure (be able to identify them in a diagram) and describe the functions of the following nuclear components:

    - Nuclear envelope
    - Chromosomes
    - Nucleolus

3. Use a full page to draw (by hand, and neatly!) an annotated diagram of a cell showing all of the following structures and briefly describing the function of each (a simple, flattened diagram is fine, no need to show 3D structures, but the defining characteristics of each named structure should be clear):

    - Plasma membrane
    - Nuclear envelope
    - Nucleus
    - Nucleolus
    - Smooth endoplasmic reticulum
    - Rough endoplasmic reticulum

- Bound ribosomes
- Free ribosomes
- Golgi apparatus (or Golgi complex)
- Lysosomes
- Mitochondria
- Vesicles

4. Describe the structure (name all the components and describe their relationships to each other) and list the general functions of the "endomembrane system".

IV. Define metabolism, and distinguish between anabolism and catabolism.

1. Define the term "metabolism".
2. Write a single sentence that clearly differentiates between "anabolism" and "catabolism".

V. Describe the cellular processes involved in the growth of the human body from a fertilized egg to an adult.

1. Distinguish between cell division, cell growth and cell differentiation.
2. Provide two examples of cell types in the human body that do not undergo cell division.
3. Define the term "stem cell".

VI. Describe the importance of cell differentiation to an organism.

1. Describe how cell differentiation allows cells to serve specialized functions.
2. Explain why it is important in the human body to have cells specialized in performing particular functions, rather than having all cells be identical to each other.

VII. Describe the general characteristics of each of the following cell types and relate their characteristics to their functions: nerve cell, muscle cell, red blood cell (erythrocyte), white blood cell (leukocyte).

1. Describe the general structural characteristics (morphology) and function of each of the following cell types:
   - Neuron
   - Muscle fiber
   - Erythrocyte
   - Leukocyte

Part 1: Characteristics of Life: The different organ systems each have different functions and therefore unique roles to perform in the body. These many functions can be summarized in terms of a few that we might consider definitive of human life: organization, metabolism, exchange of materials, responsiveness, movement, development, growth and reproduction.

Organization: A human body consists of trillions of cells organized in a way that maintains distinct internal compartments. These compartments keep body cells separated from external environmental threats and keep the cells moist and nourished. They also separate internal body fluids from the countless microorganisms that grow on body surfaces, including the lining of certain tracts, or passageways. The intestinal tract, for example,

is home to even more bacteria cells than the total of all human cells in the body, yet these bacteria are outside the body and cannot circulate freely inside the body.

Cells, for example, have a membrane (also referred to as the plasma membrane) that keeps the intracellular environment—the fluids and organelles—separate from the environment outside the cell (the extracellular environment). Blood vessels keep blood inside a closed system, and nerves and muscles are wrapped in tissue sheaths that separate them from surrounding structures. In the chest and abdomen, a variety of internal membranes keep major organs such as the lungs, heart, and kidneys separate from others.

The body's largest organ system is the integumentary system, which includes the skin and its associated structures, such as hair and nails. The surface tissue of skin is a barrier that protects internal structures and fluids from potentially harmful microorganisms, toxins and the external environment.

Metabolism: The first law of thermodynamics holds that energy can neither be created nor destroyed—it can only change form. Your basic function as an organism is to consume (ingest) energy and molecules in the foods you eat, convert some of it into fuel for movement, sustain your body functions, and build and maintain your body structures. There are two types of reactions that accomplish this: **anabolism** and **catabolism**.

- Anabolism is the process whereby smaller, simpler molecules are combined into larger, more complex substances. For example, amino acids can be combined together to make proteins. Your body can assemble, by utilizing energy, the complex chemicals it needs by combining small molecules derived from the foods you eat.
- Catabolism is the process by which larger more complex substances are broken down into smaller simpler molecules. For example, sugars are broken down to carbon dioxide and water. Catabolism releases energy. The complex molecules found in foods are broken down so the body can use their parts to assemble the structures and substances needed for life.

Taken together, these two processes are called metabolism. **Metabolism** is the sum of all anabolic and catabolic reactions that take place in the body. Both anabolism and catabolism occur simultaneously and continuously to keep you alive.

Every cell in your body makes use of a chemical compound, **adenosine triphosphate (ATP)**, to store and release energy. The cell stores energy in the molecule of ATP, then moves the ATP molecules to the location where energy is needed to fuel cellular activities. Then the ATP is broken down and a controlled amount of energy is released, which is used by the cell to perform a particular job.

Watch this Crash Course video to learn more about metabolism! Direct link: https://youtu.be/00jbG_cfGuQ

Exchange of Material: Organisms do not exist solely within their own boundaries, but interact with the external environment that surrounds them. One of the ways in which they do this is by exchanging materials with their external environment: taking in materials from their external environment and by expelling waste products out into their external environment. These materials and waste products may be anything from very small, relatively simple molecules (e.g. glucose, carbon dioxide) that must cross an individual cell's plasma membrane to whole cells or foods that were ingested but not fully digested and/or absorbed and so must be excreted from the organism.

Responsiveness: Responsiveness is the ability of an organism to adjust to changes in its internal and external environments. An example of responsiveness to external stimuli could include moving toward sources of food and water and away from perceived dangers. Changes in an organism's internal environment, such as increased body temperature, can cause the responses of sweating and the dilation of blood vessels in the skin in order to decrease body temperature.

Movement: Human movement includes not only actions at the joints of the body, but also the motion of individual organs and even individual cells. As you read these words, red and white blood cells are moving throughout your body, muscle cells are contracting and relaxing to maintain your posture and to focus your vision, and glands are secreting chemicals to regulate body functions. Your body is coordinating the action of entire muscle groups to enable you to move air into and out of your lungs, to push blood throughout your body, and to propel the food you have eaten through your digestive tract. Consciously, of course, you contract your skeletal muscles to move the bones of your skeleton to get from one place to another, and to carry out all of the activities of your daily life.

Development, growth and reproduction:

- Development is all of the changes the body goes through in life. Development includes the process of cell differentiation, in which unspecialized cells become specialized in structure and function to perform certain tasks in the body. Development also includes the processes of growth and repair, both of which involve cell differentiation.
- Growth is the increase in body size. Humans, like all multicellular organisms, grow by increasing the number of existing cells, increasing the amount of non-cellular material around cells (such as mineral deposits in bone), and, within very narrow limits, increasing the size of existing cells.
- Reproduction is the formation of a new organism from parent organisms. In humans, reproduction is carried out by the male and female reproductive systems. Because death will come to all complex organisms, without reproduction, the line of organisms would end.

Part 2: Structural Organization of the Human Body: Before you begin to study the different structures and functions of the human body, it is helpful to consider its basic architecture; that is, how its smallest parts are assembled into larger structures. It is convenient to consider the structures of the body in terms of fundamental levels of organization that increase in complexity: subatomic particles, atoms, molecules, organelles, cells, tissues, organs, organ systems and organisms (Figure 1).

The Levels of Organization: To study the chemical level of organization, scientists consider the simplest building blocks of matter: subatomic particles, atoms and molecules. All matter in the universe is composed of one or more unique pure substances called elements, familiar examples of which are hydrogen, oxygen, carbon, nitrogen, calcium, and iron. The smallest unit of any of these pure substances (elements) is an atom. Atoms are made up of subatomic particles such as the proton, electron and neutron. Two or more atoms combine to form a molecule, such as the water molecules, proteins, and sugars found in living things. Molecules are the chemical building blocks of all body structures.

A **cell** is the smallest independently functioning unit of a living organism. All living structures of human anatomy contain cells, and almost all functions of human physiology are performed in cells or are initiated by

cells. Even bacteria, which are extremely small single celled, independently-living organisms, have a cellular structure.

A human cell typically consists of flexible membranes that enclose cytoplasm, a water-based fluid together with a variety of tiny functioning units called **organelles**. In humans, as in all organisms, cells perform all functions of life. A **tissue** is a group of many similar cells (though sometimes composed of a few related types) that work together to perform a specific function. An **organ** is an anatomically distinct structure of the body composed of two or more tissue types. Each organ performs one or more specific physiological functions. An **organ system** is a group of organs that work together to perform major functions or meet physiological needs of the body. Assigning organs to organ systems can be imprecise since organs that "belong" to one system can also have functions integral to another system. In fact, most organs contribute to more than one system.

The organism level is the highest level of organization. An organism is a living being that has a cellular structure and that can independently perform all physiologic functions necessary for life. In multicellular organisms, including humans, all cells, tissues, organs, and organ systems of the body work together to maintain the life and health of the organism.

The Cellular Level of Organization: You developed from a single fertilized egg cell into the complex organism containing trillions of cells that you see when you look in a mirror. Early during this developmental process, cells differentiate and become specialized in their structure and function. These different cell types form specialized tissues that work in concert to perform all of the functions necessary for the living organism. Cellular and developmental biologists study how the continued division of a single cell leads to such complexity.

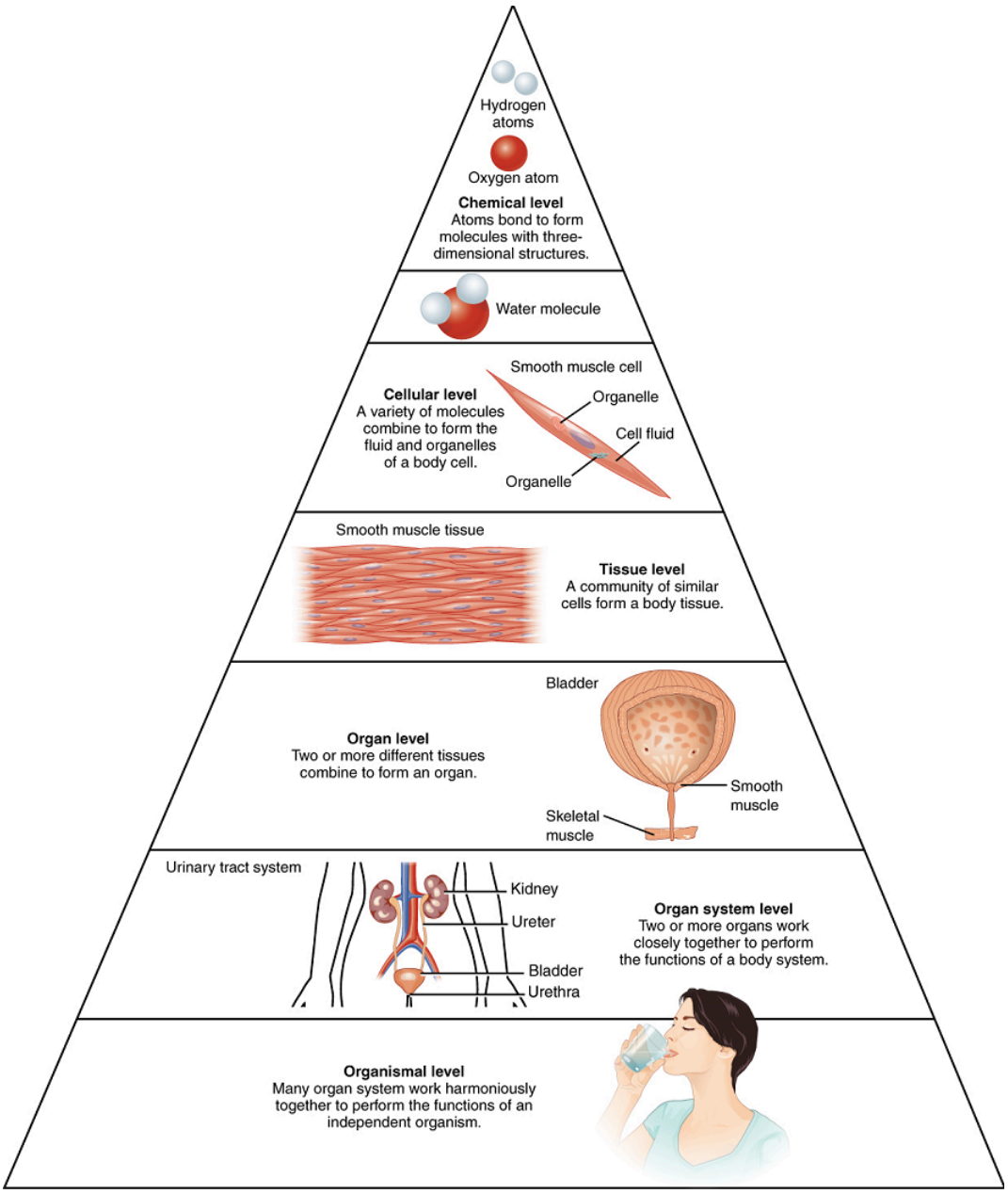


Figure 1. Levels of Structural Organization of the Human Body. *The organization of the body often is discussed in terms of six distinct levels of increasing complexity, from the smallest chemical building blocks to a unique human organism.*

Consider the difference between a cell in the skin and a nerve cell. A skin cell may be shaped like a flat plate (squamous) and live only for a short time before it is shed and replaced. Packed tightly into rows and sheets, the squamous skin cells provide a protective barrier for the cells and tissues that lie beneath. A nerve cell, on the other hand, may be shaped something like a star, sending out long processes up to a meter in length and may live for the entire lifetime of the organism. With their long winding processes, nerve cells can communicate with one another and with other types of body cells and send rapid signals that inform the organism about its environment and allow it to interact with that environment. These differences illustrate one very important theme that is consistent at all organizational levels of biology: the form of a structure is optimally suited to perform particular functions assigned to that structure. Keep this theme in mind as you tour the inside of a cell and are introduced to the various types of cells in the body.

The concept of a cell started with microscopic observations of dead cork tissue by scientist Robert Hooke in

1665. Without realizing their function or importance, Hook coined the term “cell” based on the resemblance of the small subdivisions in the cork to the rooms that monks inhabited, called cells. About ten years later, Antonie van Leeuwenhoek became the first person to observe living and moving cells under a microscope. In the century that followed, the theory that cells represented the basic unit of life would develop. These tiny fluid-filled sacs house components responsible for the thousands of biochemical reactions necessary for an organism to grow and survive. In this chapter, you will learn about the major components and functions of a generalized cell and discover some of the different types of cells in the human body.

Watch this Amoeba Sisters video for an introduction to the cell! Direct link: https://youtu.be/8IlzKri08kk

Part 3: Cell structure, cellular organelles and functions

General cell structure: Plasma Membrane, Cytoplasm and Nucleus:

The cell membrane (also known as the plasma membrane) separates the inner contents of a cell from its external environment. This membrane provides a protective barrier around the cell and regulates which materials can pass in or out. It is primarily composed of phospholipids arranged in a two layers but also contains cholesterol and a mosaic of different proteins. You will learn more about the structure and function of the plasma membrane in Unit 5. All living cells in multicellular organisms contain an internal cytoplasmic compartment, composed of cytosol and organelles. **Cytosol**, the jelly-like substance within the cell, provides the fluid medium necessary for biochemical reactions and is mostly composted of water. Eukaryotic cells, including all animal cells, also contain various cellular organelles. An **organelle** (“little organ”) is one of several different types of membrane-enclosed bodies in the cell, each performing a unique function.

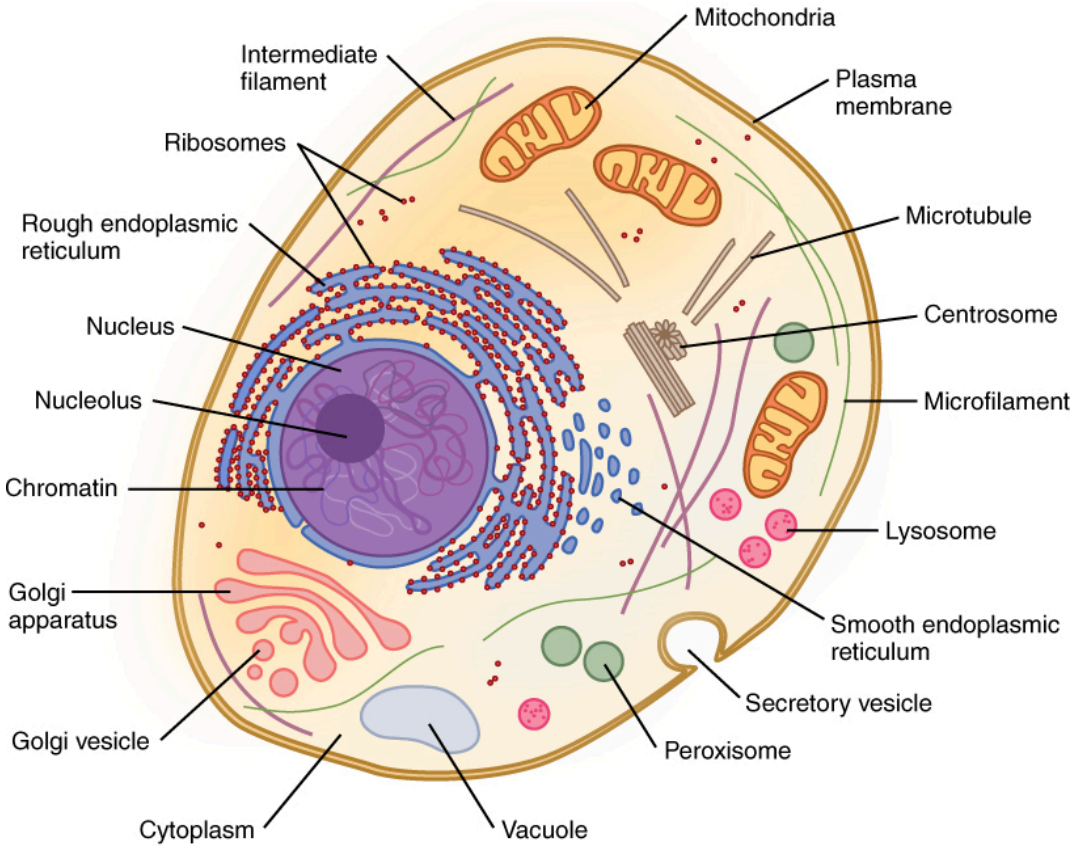


Figure 2. Typical Human Cell. *While this image is not indicative of any one particular human cell, it is a typical example of a cell containing the primary organelles and internal structures.*

Just as the various bodily organs work together in harmony to perform all of a human's functions, the many different cellular organelles work together to keep the cell healthy and performing all of its important functions. The organelles and cytosol, taken together, compose the cell's **cytoplasm**. The **nucleus** is a cell's central organelle, which contains the cell's DNA (Figure 2).

Organelles of the Endomembrane System: A set of three major organelles together form a system within the cell called the endomembrane system. These organelles work together to perform various cellular jobs, including the task of producing, packaging, and exporting certain cellular products. The organelles of the endomembrane system include the endoplasmic reticulum, Golgi apparatus, and vesicles.

Endoplasmic Reticulum: The **endoplasmic reticulum (ER)** is a system of channels that is continuous with the nuclear membrane (or "envelope") covering the nucleus (see Part 7) and composed of the same lipid bilayer material. The ER can be thought of as a series of winding thoroughfares similar to the waterway canals in Venice. The ER provides passages throughout much of the cell that function in transporting, synthesizing, and storing materials. The winding structure of the ER results in a large membranous surface area that supports its many functions (Figure 3).

Endoplasmic reticulum can exist in two forms: rough ER and smooth ER. These two types of ER perform some very different functions and can be found in different amounts depending on the type of cell. Rough ER (RER) is so-called because its membrane is dotted with embedded granules—organelles called ribosomes, giving the RER a bumpy appearance. A **ribosome** is an organelle that serves as the site of protein synthesis and it is composed of two subunits. Ribosomes can either be bound (attached to ER) or free (floating in the cytosol). Smooth ER (SER) lacks ribosomes.

One of the main functions of the smooth ER is in the synthesis of lipids. The smooth ER synthesizes phospholipids, the main component of biological membranes, as well as steroid hormones.

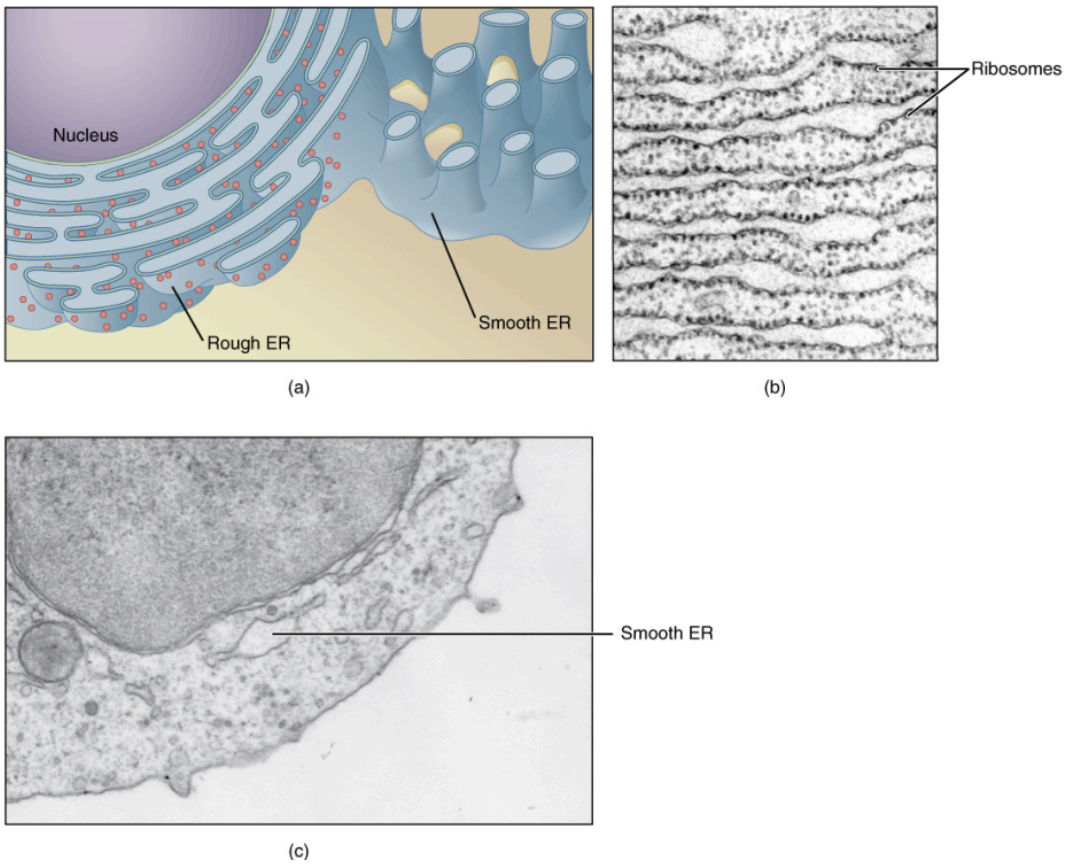


Figure 3. Endoplasmic Reticulum (ER). *(a) The endoplasmic reticulum is a winding network of thin membranous sacs found in close association with the cell nucleus. The smooth and rough endoplasmic reticula are very different in appearance and function. (b) Rough endoplasmic reticulum is studded with numerous ribosomes, which are sites of protein synthesis (source: mouse tissue). EM × 110,000. (c) Smooth endoplasmic reticulum synthesizes phospholipids, steroid hormones, regulates the concentration of cellular Ca^{2+}, and breaks down certain toxins (source: mouse tissue). EM × 110,510. (Micrographs provided by the Regents of University of Michigan Medical School © 2012)*

For this reason, cells that produce large quantities of such hormones, such as those of the female ovaries and male testes, contain large amounts of smooth ER. In addition to lipid synthesis, the smooth ER also sequesters (i.e., stores) and regulates the concentration of cellular calcium (Ca^{2+}) which is extremely important in cells of the nervous system where Ca^{2+} is the trigger for neurotransmitter release. Additionally, the smooth ER, especially in the liver, performs a detoxification role, breaking down certain toxins.

In contrast with the smooth ER, the primary job of the rough ER is the synthesis and modification of proteins destined for the cell membrane or for export from the cell. For this protein synthesis, many ribosomes attach to the ER (giving it the studded appearance of rough ER). Typically, a protein is synthesized within the ribosome and released inside the channel of the rough ER, where sugars can be added to it (by a process called glycosylation) before it is transported within a vesicle (a small fluid filled sac) to the next stage in the packaging and shipping process: the Golgi apparatus.

The Golgi Apparatus: The **Golgi apparatus** is responsible for sorting, modifying, and shipping off the products that come from the rough ER, much like a post-office. The Golgi apparatus looks like stacked flattened discs, almost like stacks of oddly shaped pancakes. Like the ER, these discs are membranous. The Golgi apparatus has two distinct sides, each with a different role. One side (the *cis* face) of the apparatus receives products in vesicles. These products are sorted through the apparatus, and then they are released from the opposite side (the *trans* face) after being repackaged into new vesicles. If the product is to be exported from the cell, the vesicle migrates to the cell surface and fuses to the cell membrane, and the cargo is secreted (Figure 4).

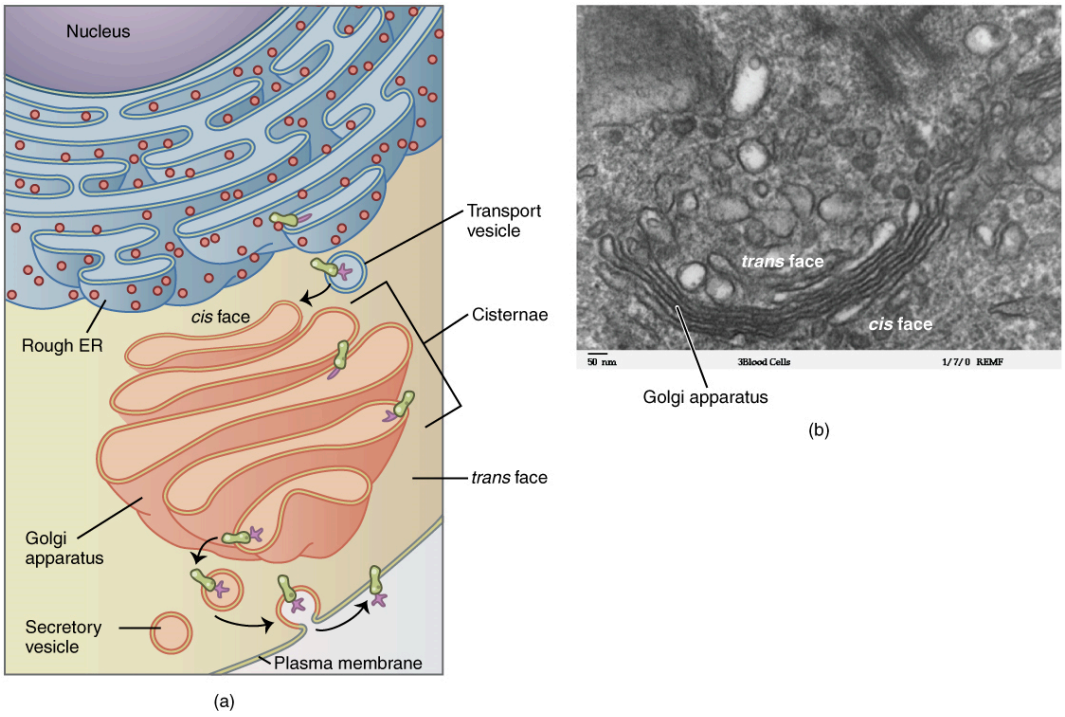


Figure 4. Golgi Apparatus. *(a) The Golgi apparatus manipulates products from the rough ER. Proteins and other products of the ER are sent to the Golgi apparatus, which organizes, modifies, packages, and tags them. Some of these products are transported to other areas of the cell and some are exported from the cell through exocytosis. Enzymatic proteins are packaged as new vesicles called lysosomes. (b) An electron micrograph of the Golgi apparatus.*

Lysosomes: Some of the protein products from the Golgi include digestive enzymes that are meant to remain inside the cell for use in breaking down certain materials. These enzymes are packaged into to vesicles called **lysosomes**. A lysosome is an organelle that contains enzymes that break down and digest unneeded cellular components, such as a damaged organelle in a process called autophagy ("self-eating").

Lysosomes are also important for breaking down foreign material. For example, when certain immune defense cells, like white blood cells, phagocytize (engulf) bacteria, the bacterial cell is transported to a lysosome and digested by the enzymes inside. Under certain circumstances, lysosomes perform a more grand and dire function. In the case of damaged or unhealthy cells, lysosomes can be triggered to open up and release their digestive enzymes into the cytoplasm of the cell, killing the cell. This "self-destruct" mechanism is called **autolysis**, and makes the process of cell death controlled (a mechanism called "apoptosis").

Organelles for Energy Processing: In addition to the jobs performed by the endomembrane system, the cell has many other important functions. Just as you must consume nutrients to provide yourself with energy, so must each of your cells take in nutrients, some of which convert to chemical energy that can be used to power biochemical reactions.

Mitochondrion: A **mitochondrion** (plural = mitochondria) is a membranous, bean-shaped organelle that is the "energy transformer" of the cell. Mitochondria consist of an outer lipid bilayer membrane as well as an additional inner lipid bilayer membrane (Figure 5). The inner membrane is highly folded into winding structures with a great deal of surface area, called cristae. It is along this inner membrane that a series of proteins, enzymes, and other molecules perform the biochemical reactions of cellular respiration.

These reactions harvest the energy stored in nutrient molecules (such as glucose) to power the synthesis of ATP, which provides usable energy to the cell. Cells use ATP constantly, and so the mitochondria are constantly at work. Oxygen molecules are required during cellular respiration, which is why you must constantly breathe it in. One of the organ systems in the body that uses huge amounts of ATP is the muscular system because ATP is required to sustain muscle contraction. As a result, muscle cells are packed full of mitochondria.

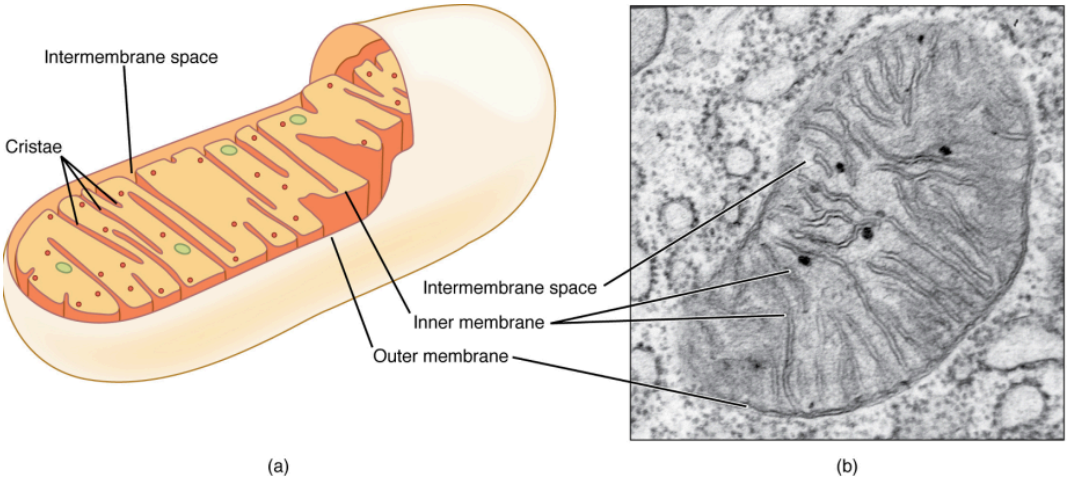


Figure 5. Mitochondrion. *The mitochondria are the energy-conversion factories of the cell. (a) A mitochondrion is composed of two separate lipid bilayer membranes. Along the inner membrane are various molecules that work together to produce ATP, the cell's major energy currency. (b) An electron micrograph of mitochondria. EM × 236,000. (Micrograph provided by the Regents of University of Michigan Medical School © 2012)*

Nerve cells also need large quantities of ATP to run their sodium-potassium pumps which are used to generate an action potential. Therefore, an individual neuron will be loaded with over a thousand mitochondria. On the other hand, a bone cell, which is not nearly as metabolically-active, might only have a couple hundred mitochondria.

The Nucleus: The nucleus is the largest and most prominent of a cell's organelles (Figure 6). The nucleus is generally considered the control center of the cell because it stores all of the genetic instructions for manufacturing proteins. Interestingly, some cells in the body, such as muscle cells, contain more than one nucleus (Figure 7), which is known as multinucleated. Other cells, such as mammalian red blood cells (RBCs), do not contain nuclei at all. RBCs eject their nuclei as they mature, making space for the large numbers of hemoglobin molecules that carry oxygen throughout the body.

Inside the nucleus lies the blueprint that dictates everything a cell will do and all of the products it will make. This information is stored within DNA. The nucleus sends "commands" to the cell via molecular messengers that translate the information from DNA. Each cell in your body (with the exception of the cells that produce eggs and sperm) contains the complete set of your DNA. When a cell divides, the DNA must be duplicated so that the each new cell receives a full complement of DNA.

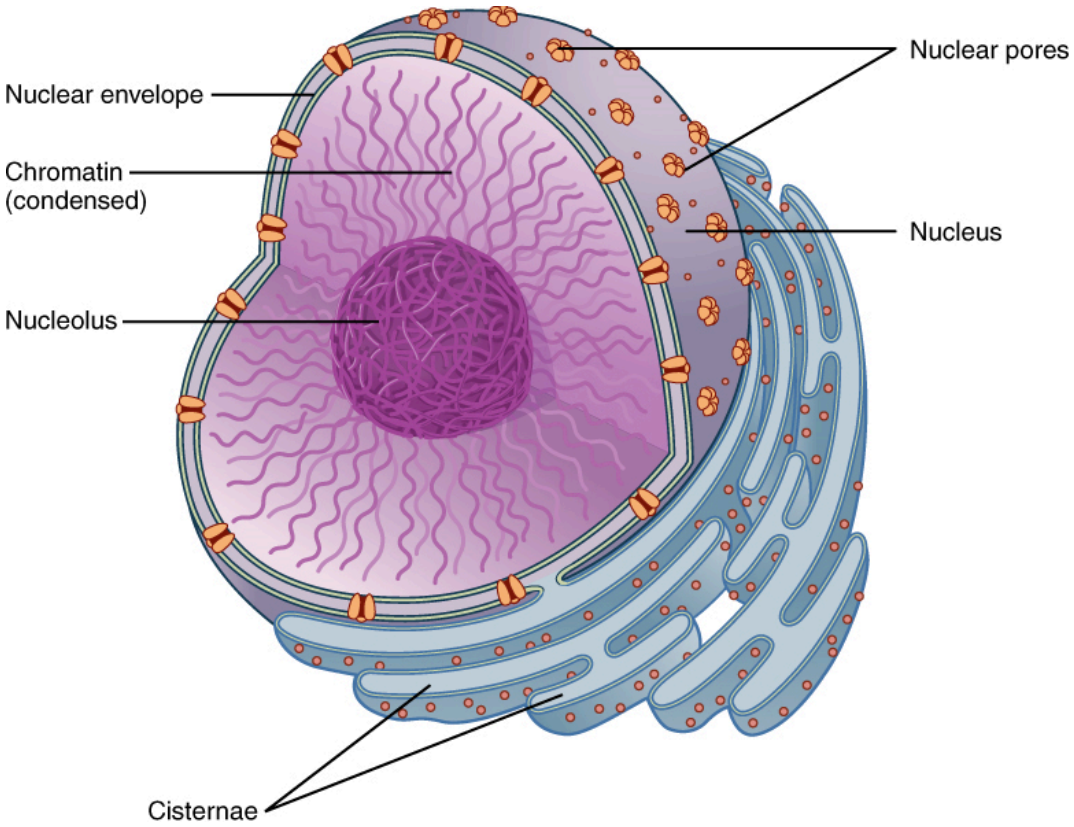


Figure 6. The Nucleus. *The nucleus is the control center of the cell. The nucleus of living cells contains the genetic material that determines the entire structure and function of that cell.*

Organization of the Nucleus and Its DNA: Like most other cellular organelles, the nucleus is surrounded by a membrane called the **nuclear envelope**. This membranous covering consists of two adjacent lipid bilayers with a thin fluid space in between them. Spanning these two bilayers are nuclear pores. A **nuclear pore** is a tiny passageway for the passage of proteins, RNA, and solutes between the nucleus and the cytoplasm..

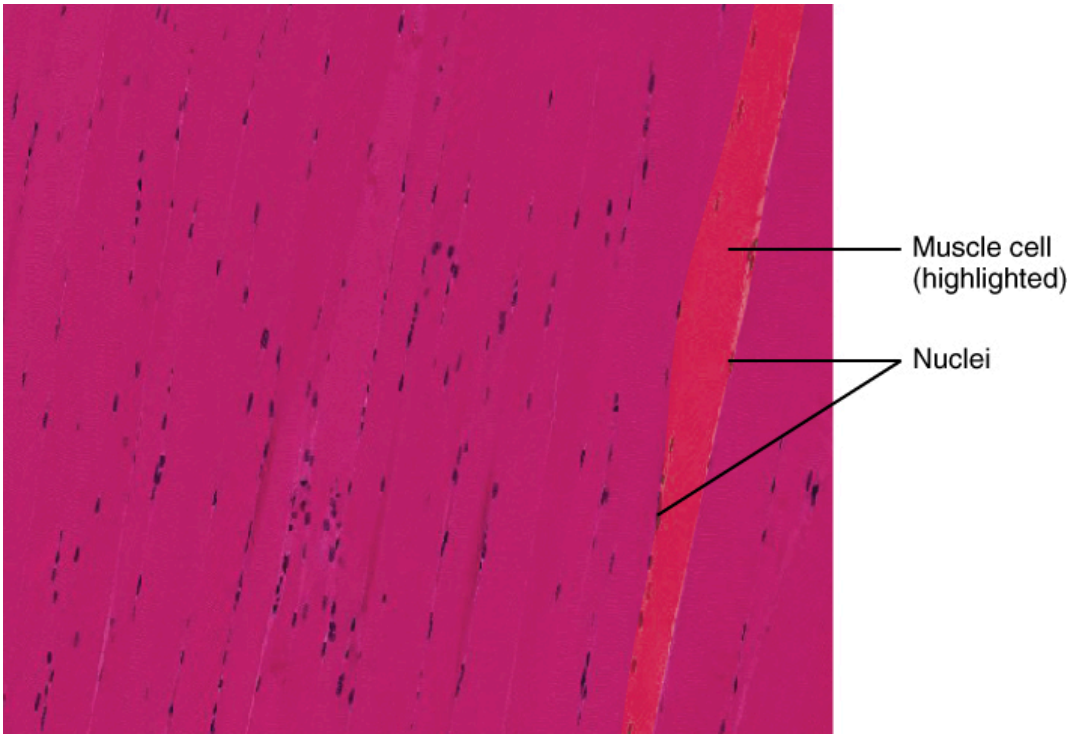


Figure 7. Multinucleate Muscle Cell. *Unlike cardiac muscle cells and smooth muscle cells, which have a single nucleus, a skeletal muscle cell contains many nuclei, and is referred to as "multinucleated." (Micrograph provided by the Regents of University of Michigan Medical School © 2012)*

Inside the nuclear envelope is a gel-like nucleoplasm with solutes that include the building blocks of nucleic acids. There also can be a dark-staining mass often visible under a simple light microscope, called a **nucleolus** (plural = nucleoli). The nucleolus is a region of the nucleus that is responsible for manufacturing the RNAs necessary for construction of ribosomes. Once synthesized, newly made ribosomal subunits exit the cell's nucleus through the nuclear pores.

The genetic instructions that are used to build and maintain an organism are arranged in an orderly manner in strands of DNA. Within the nucleus are threads of **chromatin** composed of DNA and associated proteins (Figure 8). Along the chromatin threads, the DNA is wrapped around a set of histone proteins. When a cell is in the process of division, the chromatin condenses into chromosomes, so that the DNA can be safely transported to the "daughter cells." The **chromosome** is composed of DNA and proteins; it is the condensed form of chromatin. It is estimated that humans have almost 22,000 genes distributed on 46 chromosomes.

Part 4: Cellular processes involved in growth

Cell Division, Growth, and Differentiation:

Cell Division: cells in the body must replace themselves over the lifetime of a person. For example, the cells lining the gastrointestinal tract must be frequently replaced when constantly "worn off" by the movement of food through the gut. But what triggers a cell to divide, and how does it prepare for and complete cell division? The **cell cycle** is the sequence of events in the life of the cell from the moment it is created at the end of a previous cycle of cell division until it then divides itself, generating two new cells.

While there are a few cells in the body that do not undergo cell division (such as gametes, red blood cells, most neurons, and some muscle cells), most somatic cells divide regularly. A **somatic cell** is a general term for a body cell, and all human cells, except for the cells that produce eggs and sperm (which are referred to as **germ** cells), are somatic cells.

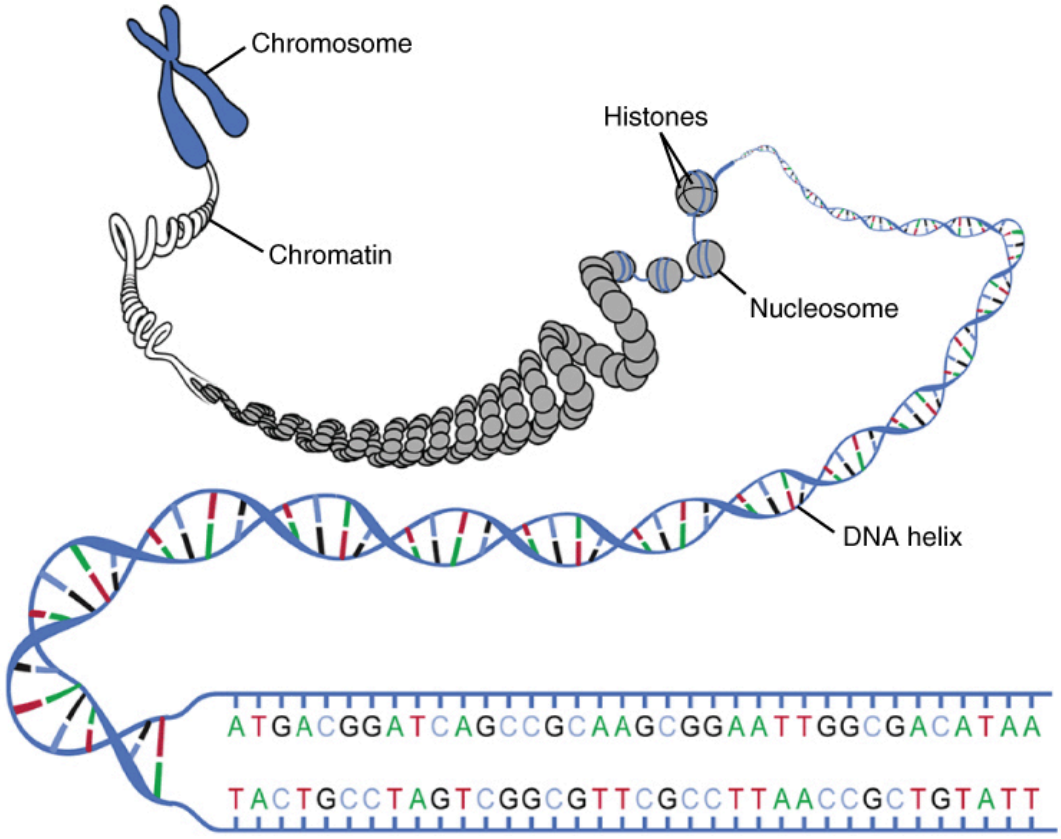


Figure 8. DNA Macrostructure. *Strands of DNA are wrapped around supporting histones. These proteins are increasingly bundled and condensed into chromatin, which is packed tightly into chromosomes when the cell is ready to divide.*

Cell Growth: Once cells divide, they grow and increase in size. For example, nerve cells first appear as relatively small cells but then they elongate to become extremely long cells. Similarly, muscle cells grow to become extremely long cells as muscles are formed.

Cell Differentiation: How does a complex organism such as a human develop from a single cell—a fertilized egg—into the vast array of cell types such as nerve cells, muscle cells, and epithelial cells that characterize the adult? Throughout development and adulthood, the process of cellular differentiation leads cells to assume their final morphology and physiology. Differentiation is the process by which unspecialized cells become specialized to carry out distinct functions.

A **stem cell** is an unspecialized cell that can divide without limit as needed and can, under specific conditions, differentiate into specialized cells. Stem cells are unique in that they can also continually divide and regenerate new stem cells instead of further specializing. There are different stem cells present at different stages of a human's life. They include the embryonic stem cells of the embryo, fetal stem cells of the fetus, and adult stem cells in the adult. One type of adult stem cell is the epithelial stem cell, which gives rise to the keratinocytes in the multiple layers of epithelial cells in the epidermis of skin.

When a cell differentiates they becomes specialized; yet all cells in the body, beginning with the fertilized egg, contain the same DNA, how do the different cell types come to be so different? The answer is analogous to a movie script. The different actors in a movie all read from the same script, however, they are each only reading their own part of the script. Similarly, all cells contain the same full complement of DNA, but each type of cell only "reads" the portions of DNA that are relevant to its own function. In biology, this is referred to as the unique genetic expression of each cell.

Cell specialization:

As cells specialize they may undertake major changes in its size, shape, metabolic activity, and overall function. The morphology (structure) of a mature cell is closely related to the function it is specialized to

serve (Figure 9). **Muscle fibers** for example are far removed in structure and function from the zygote that they ultimately arose from: they are long, slender structures that are well-suited to contracting to produce macroscopic movements over relatively long distances. Some **neurons** (nerve cells) are exceptionally long and slender in shape, again to act over relatively long distances, although in this case their function is to transmit information rather than move body structures directly. **Erythrocytes** (red blood cells) are used to transport oxygen in the blood; their tiny size and lack of a nucleus make them well-suited to squeezing through the smallest of capillaries, and their lack of mitochondria mean they do not themselves use up the oxygen they are supposed to be delivering to other cells. **Leukocytes** (white blood cells) on the other hand are noticeably larger than erythrocytes, and do have mitochondria. The large size of macrophages, for example, means they are capable of physically engulfing relatively large particles or whole cells such as bacteria by phagocytosis, and their mitochondria allow them access to the chemical energy required to move themselves through body tissues towards invading pathogens.

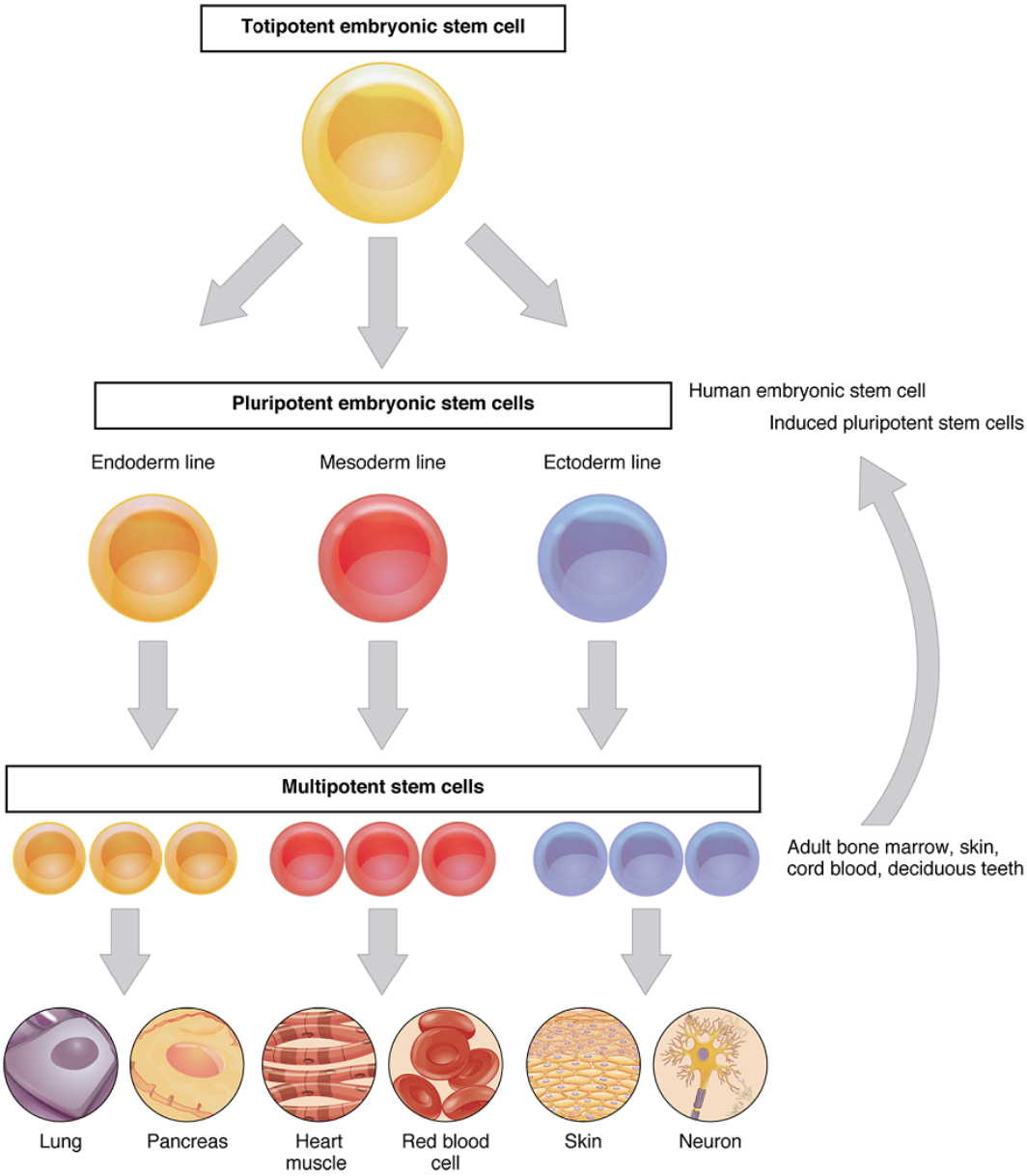


Figure 9. Stem Cells. *The capacity of stem cells to differentiate into specialized cells make them potentially valuable in therapeutic applications designed to replace damaged cells of different body tissues.*

Watch this Amoeba Sisters video to learn more about how cells become specialized! Direct link: https://youtu.be/t3g26p9Mh_k

Watch this Amoeba Sisters video for some examples of specialized cells! Direct link: https://youtu.be/wNe6RuK0FfA

Unit 5: Cell Biology: Membrane Transport

Unit Outline

Part 1. The cell membrane

- Membrane structure

Part 2. Transport across the cell membrane

- Diffusion
- Facilitated diffusion
- Osmosis
- Active transport mechanisms

Learning Objectives

At the end of this unit, you should be able to:

I. Describe the "fluid mosaic" model of membrane structure including the membrane components.

II. Describe how the structure of the cell membrane affects membrane permeability.

III. Describe the following passive processes: diffusion, facilitated diffusion and osmosis. Explain the function of each in a cell.

IV. Describe and explain the effects of placing red blood cells in hypertonic, hypotonic and isotonic solutions, respectively.

V. Describe the following active processes: primary and secondary active transport, endocytosis (phagocytosis, pinocytosis), and exocytosis. Explain the function of each in a cell.

Learning Objectives and Guiding Questions

At the end of this unit, you should be able to complete all the following tasks, including answering the guiding questions associated with each task.

I. Describe the "fluid mosaic" model of membrane structure including the membrane components.

1. Describe the characteristics of the plasma membrane that are captured by describing its structure as a 'fluid mosaic'. (i.e.: explain why it is appropriate to refer to the membrane as 'fluid' AND why it is appropriate to refer to the membrane as a 'mosaic'.)

II. Describe how the structure of the cell membrane affects membrane permeability.

1. Describe how the structural components of the plasma membrane make it "selectively permeable", rather than permeable or impermeable. In your description be sure to refer to the types of molecules that may pass easily (or not) through the membrane, and what chemical characteristics they share that makes them capable (or incapable) of doing so.

III. Describe the following passive processes: diffusion, facilitated diffusion and osmosis. Explain the function of each in a cell.

IV. Describe and explain the effects of placing red blood cells in hypertonic, hypotonic and isotonic solutions, respectively.

1. Describe and explain the effects (i.e.: on cell size, cell shape, and cytosol solute concentrations) of placing red blood cells in a solution that is:
    - Hypertonic relative to the cytosol
    - Hypotonic relative to the cytosol
    - Isotonic relative to the cytosol

V. Describe the following active processes: primary and secondary active transport, endocytosis (phagocytosis, pinocytosis), and exocytosis. Explain the function of each in a cell.

1. Compare and contrast (with the use of annotated diagrams) the characteristics of the following in terms of (a) ATP requirements, (b) molecules moved, (c) size of material moved, and (d) the direction of movement (i.e.: relative to its own concentration gradient, relative to another molecule or molecule type's concentration gradient, and/or relative to the cell's internal vs. external environment):
    - Active and passive transport mechanisms
    - Simple and facilitated diffusion
    - Facilitated diffusion and osmosis
    - Primary and secondary active transport
    - Facilitated diffusion and secondary active transport
    - Exocytosis and endocytosis
    - Pinocytosis and phagocytosis
    - Phagocytosis and receptor-mediated endocytosis

Part 1: The Cell Membrane:

Despite differences in structure and function, all living cells in multicellular organisms have a surrounding cell membrane. As the outer layer of your skin separates your body from its environment, the cell membrane (also known as the plasma membrane) separates the inner contents of a cell from its exterior environment. This cell membrane provides a protective barrier around the cell and regulates which materials can pass in or out.

Structure and Composition of the Cell Membrane: The cell (plasma) membrane is described by the fluid

mosaic model, it is an extremely pliable structure composed primarily of stacked **phospholipids** (a "bilayer"). **Cholesterol** is also present, which contributes to the fluidity of the membrane, and there are various **proteins** embedded within the membrane that have a variety of functions.

A single phospholipid molecule has a phosphate group on one end, called the "head," and two side-by-side chains of fatty acids that make up the lipid tails (Figure 1). The phosphate group is negatively charged, making the head polar and hydrophilic—or "water loving." A **hydrophilic** molecule (or region of a molecule) is one that is attracted to water. The phosphate heads are thus attracted to the water molecules of both the extracellular and intracellular environments. The lipid tails, on the other hand, are uncharged, or nonpolar, and are hydrophobic—or "water fearing." A **hydrophobic** molecule (or region of a molecule) repels and is repelled by water. An **amphipathic** molecule is one that contains both a hydrophilic and a hydrophobic region. In fact, soap works to remove oil and grease stains because it has amphipathic properties. The hydrophilic portion can dissolve in water while the hydrophobic portion can trap grease in micelles that then can be washed away.

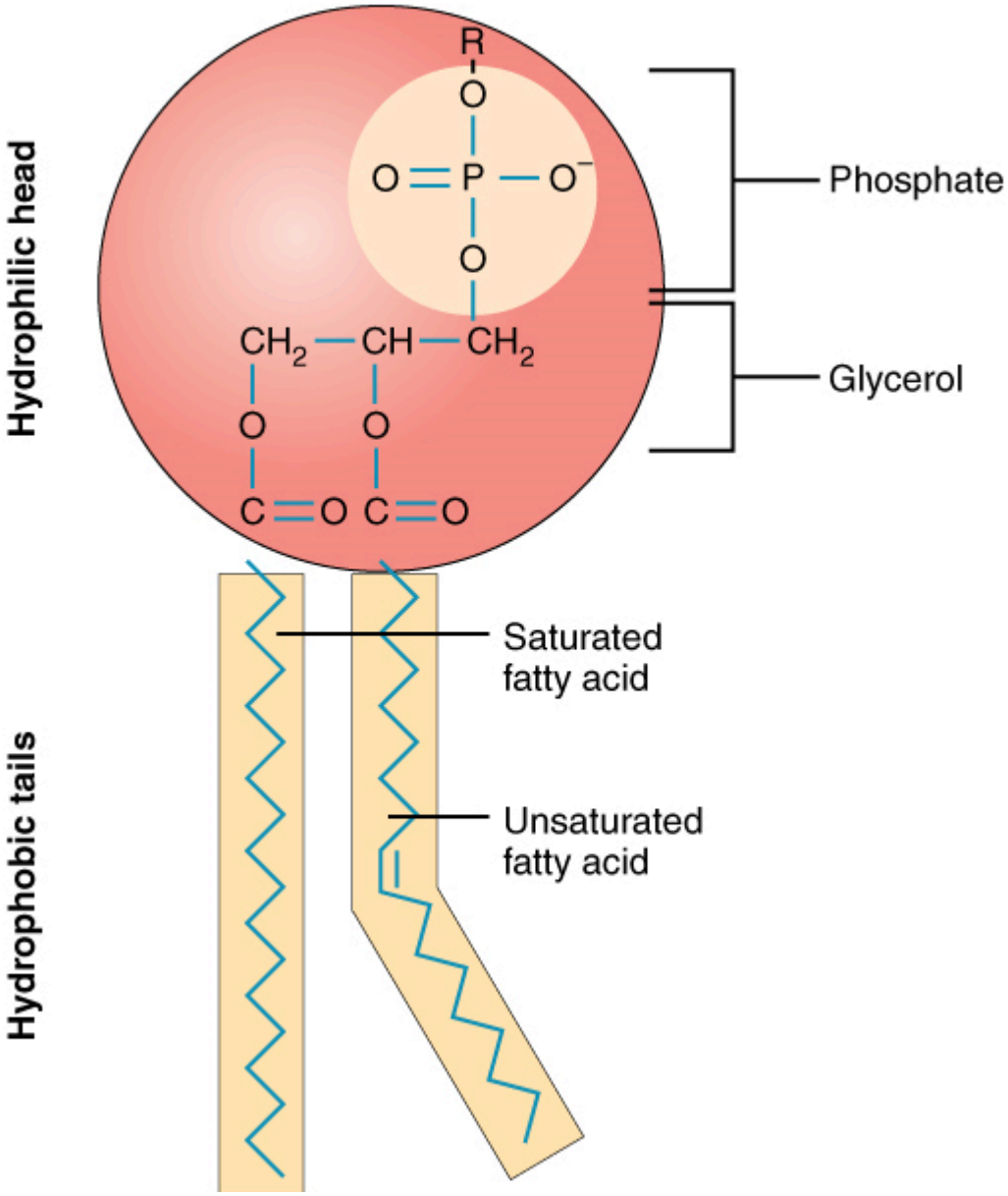


Figure 1. Phospholipid Structure. *A phospholipid molecule consists of a polar phosphate "head," which is hydrophilic and a non-polar lipid "tail," which is hydrophobic. Unsaturated fatty acids result in kinks in the hydrophobic tails.*

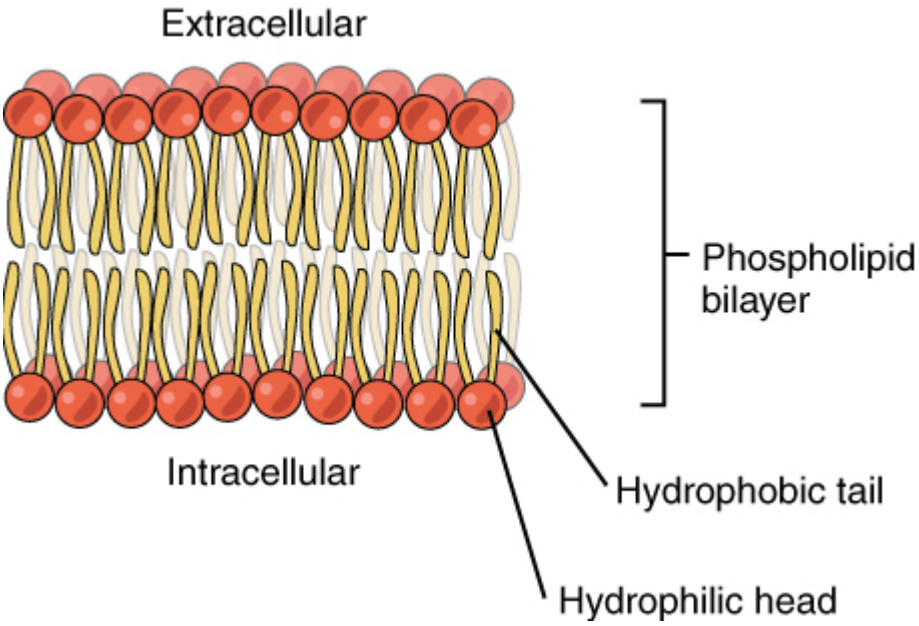


Figure 2. Phospholipid Bilayer. *The phospholipid bilayer consists of two adjacent sheets of phospholipids, arranged tail to tail. The hydrophobic (water fearing) tails associate with one another, forming the interior of the membrane. The hydrophilic (water loving) polar heads contact the fluid inside and outside of the cell.*

The cell membrane consists of two adjacent layers of phospholipids. The lipid tails of one layer face the lipid tails of the other layer, meeting at the interface of the two layers. The phospholipid heads face outward, one layer exposed to the interior of the cell and one layer exposed to the exterior (Figure 2). Because the phosphate groups are polar and hydrophilic, they are attracted to water in the intracellular fluid. **Intracellular fluid (ICF)** is the fluid interior of the cell. The phosphate groups are also attracted to the extracellular fluid. **Extracellular fluid (ECF)** is the fluid environment outside the enclosure of the cell membrane. **Interstitial fluid (IF)** is the term given to extracellular fluid not contained within blood vessels. Because the lipid tails are hydrophobic, they meet in the inner region of the membrane, excluding watery intracellular and extracellular fluid from this space.

The cell membrane has many proteins, as well as other lipids (such as cholesterol), that are associated with the phospholipid bilayer. An important feature of the membrane is that it remains relatively fluid; the lipids and proteins in the cell membrane are not rigidly locked in place but can move. This feature explains the 'fluid' component of the fluid mosaic model.

Membrane Proteins: The lipid bilayer forms the basis of the cell membrane, but it is peppered throughout with various proteins, representing the 'mosaic' part of the fluid mosaic model. Two different types of proteins that are commonly associated with the cell membrane are the integral proteins and peripheral protein (Figure 3). As its name suggests, an **integral protein** is a protein that is embedded in the membrane. A channel protein is an example of an integral protein that selectively allows particular materials, such as certain ions, to pass into or out of the cell.

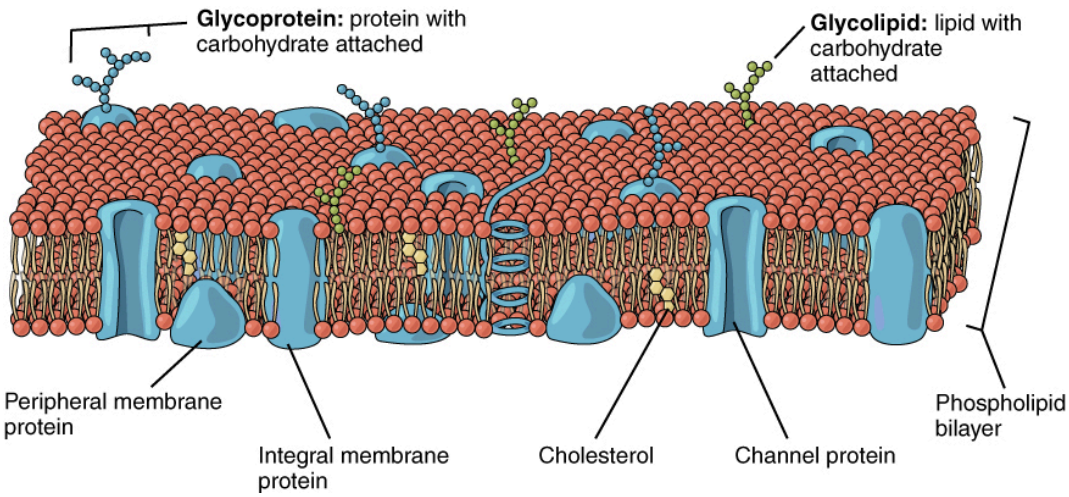


Figure 3. Cell Membrane. *The cell membrane of the cell is a phospholipid bilayer containing many different molecular components, including proteins and cholesterol, some with carbohydrate groups attached.*

Some integral membrane proteins are glycoproteins. A **glycoprotein** is a protein that has carbohydrate molecules attached, which extend into the extracellular matrix. The attached carbohydrate tags on glycoproteins aid in cell recognition. The carbohydrates that extend from membrane proteins and even from some membrane lipids collectively form the glycocalyx. The **glycocalyx** is a fuzzy-appearing coating around the cell formed from glycoproteins and other carbohydrates attached to the cell membrane. The glycocalyx can have various roles. For example, it may have molecules that allow the cell to bind to another cell, it may contain receptors for hormones, or it might have enzymes to break down nutrients. The glycocalyces found in a person's body are products of that person's genetic makeup. They give each of the individual's trillions of cells the "identity" of belonging in the person's body. This identity is the primary way that a person's immune defense cells "know" not to attack the person's own body cells, but it also is the reason organs donated by another person might be rejected.

Peripheral proteins are typically found on the inner or outer surface of the lipid bilayer but can also be attached to the internal or external surface of an integral protein. These proteins typically perform a specific function for the cell. Some peripheral proteins on the surface of intestinal cells, for example, act as digestive enzymes to break down nutrients to sizes that can pass through the cells and into the bloodstream.

Part 2: Transport across the Cell Membrane:

One of the great wonders of the cell membrane is its ability to regulate the concentration of substances inside the cell. These substances include ions such as Ca^{2+}, Na^{+}, K^{+}, and Cl^{-}; nutrients including sugars, fatty acids, and amino acids; and waste products, particularly carbon dioxide (CO_2), which must leave the cell.

The membrane's lipid bilayer structure provides the first level of control. The phospholipids are tightly packed together, and the membrane has a hydrophobic interior. This structure causes the membrane to be selectively permeable. A membrane that has **selective permeability** allows only substances meeting certain criteria to pass through it unaided. In the case of the cell membrane, only relatively small, nonpolar materials can move through the lipid bilayer (remember, the lipid tails of the membrane are nonpolar). Some examples of these are other lipids, oxygen and carbon dioxide gases, and alcohol. However, water-soluble materials—like glucose, amino acids, and electrolytes—need some assistance to cross the membrane because they are repelled by the hydrophobic tails of the phospholipid bilayer. All substances that move through the membrane do so by one of two general methods, which are categorized based on whether or not energy is required. **Passive transport** is the movement of substances across the membrane using their own kinetic energy, without the expenditure of chemical energy. In contrast, **active transport** is the movement of substances across the membrane using energy from the hydrolysis of adenosine triphosphate (ATP).

Passive Transport: In order to understand how substances move passively across a cell membrane, it is

necessary to understand concentration gradients and diffusion. A **concentration gradient** is the difference in concentration of a substance across a space. Molecules (or ions) will spread from where they are more concentrated to where they are less concentrated until they are equally distributed in that space. (When molecules move in this way, they are said to move down their concentration gradient.) **Diffusion** is the movement of particles from an area of higher concentration to an area of lower concentration. A couple of common examples will help to illustrate this concept. Imagine being inside a closed bathroom. If a bottle of perfume were sprayed, the scent molecules would naturally diffuse from the spot where they left the bottle to all corners of the bathroom, and this diffusion would go on until no more concentration gradient remains. Another example is a spoonful of sugar placed in a cup of tea. Eventually the sugar will diffuse throughout the tea until no concentration gradient remains. In both cases, if the room is warmer or the tea hotter, diffusion occurs even faster as the molecules are bumping into each other and spreading out faster than at cooler temperatures. Having an internal body temperature around 37.5° C thus also aids in diffusion of particles within the body.

Whenever a substance exists in greater concentration on one side of a semipermeable membrane than on the other side, such as the cell membranes, any substance that can move down its concentration gradient across the membrane will do so. Consider substances that can easily diffuse through the lipid bilayer of the cell membrane, such as the gases oxygen (O_2) and CO_2. O_2 generally diffuses into cells because it is more concentrated outside of them, and CO_2 typically diffuses out of cells because it is more concentrated inside of them. In both these examples the molecules rely on their own kinetic energy to move, so neither of these examples requires any chemical energy (from the hydrolysis of ATP) output from the cell. The movement of molecules across a cell membrane without the expenditure of cellular energy is referred to as **passive transport**, or **diffusion** (Figure 4)

Before moving on, you need to review the gases that can diffuse across a cell membrane. Because cells rapidly use up oxygen during metabolism, there is typically a lower concentration of O_2 inside the cell than outside. As a result, oxygen will diffuse from the interstitial fluid into the cytoplasm within the cell. On the other hand, because cells produce CO_2 as a byproduct of metabolism, CO_2 concentrations rise within the cytoplasm; therefore, CO_2 will move from the cell into the interstitial fluid, where its concentration is lower. Both these molecules are small and nonpolar, which means they can easily interact with the hydrophobic core of a lipid bilayer and move between the molecules to get from one side to the other. This mechanism of small, nonpolar molecules slipping between the lipid tails of a cell membrane from the side where they are more concentrated to the side where they are less concentrated is a form of passive transport called simple diffusion (Figure 4).

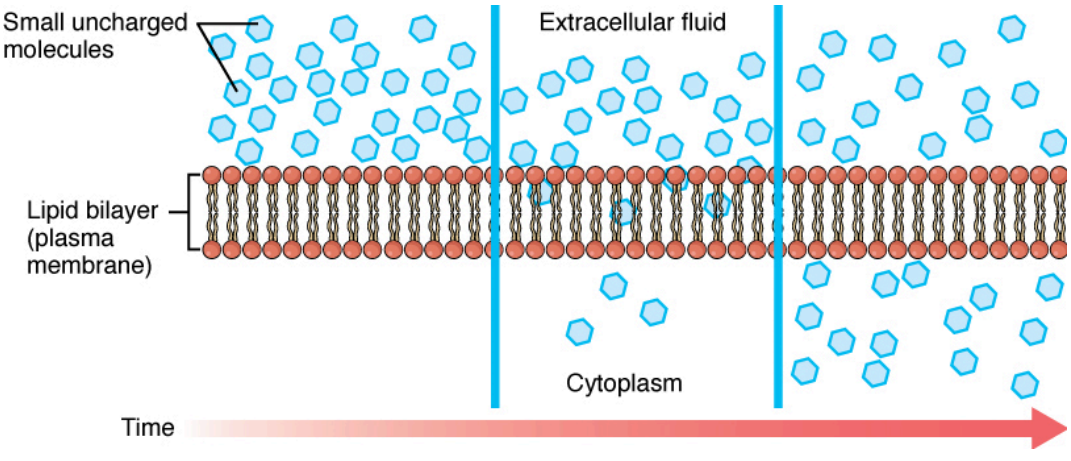


Figure 4. Simple Diffusion across the Cell (Plasma) Membrane. *The structure of the lipid bilayer allows small, uncharged substances such as oxygen and carbon dioxide, and hydrophobic molecules such as lipids, to pass through the cell membrane, down their concentration gradient, by simple diffusion.*

Large polar or ionic molecules, which are hydrophilic, cannot easily cross the phospholipid bilayer. Charged

atoms or molecules of any size cannot cross the cell membrane via simple diffusion as the charges are repelled by the hydrophobic tails in the interior of the phospholipid bilayer. Solutes dissolved in water on either side of the cell membrane will tend to diffuse down their concentration gradients, but because most substances cannot pass freely through the lipid bilayer of the cell membrane, their movement is restricted to protein channels and specialized transport mechanisms in the membrane. **Facilitated diffusion** is the diffusion process used for those substances that cannot cross the lipid bilayer due to their size, charge, and/or polarity (Figure 5). A common example of facilitated diffusion is the movement of glucose into the cell, where it is used to make ATP. Although glucose can be more concentrated outside of a cell, it cannot cross the lipid bilayer via simple diffusion because it is both large and polar.

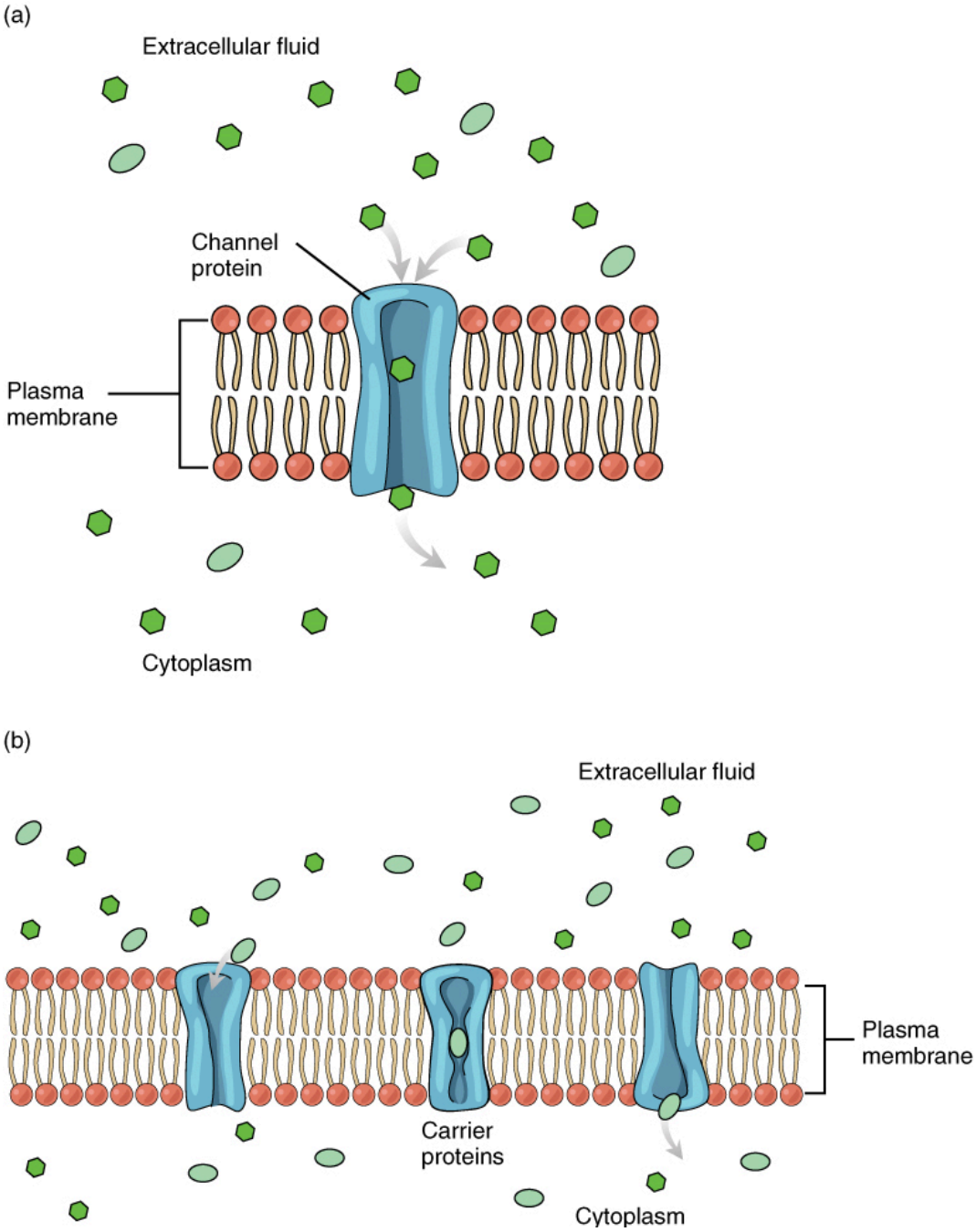


Figure 5. Facilitated Diffusion. *(a) Facilitated diffusion of substances crossing the cell (plasma) membrane takes place with the help of proteins such as channel proteins and carrier proteins. Channel proteins are less selective than carrier proteins, and usually mildly discriminate between their cargo based on size and charge. (b) Carrier proteins are more selective, often only allowing one particular type of molecule to cross.*

To resolve this, a specialized carrier protein called the glucose transporter will transfer glucose molecules into the cell to facilitate its inward diffusion. Glucose and other relatively large polar molecules typically bind to transport proteins that change shape to allow the molecules into the cell by a process known as **carrier-mediated facilitated diffusion**.

The use of a protein that acts as a channel through which an ion or small polar molecule can move down its concentration gradient is referred to as **channel-mediated facilitated diffusion**. For example, sodium ions (Na^+) are highly concentrated outside of cells, these electrolytes are charged and cannot pass through the nonpolar lipid bilayer of the membrane. Their diffusion is facilitated by membrane proteins that form sodium channels (or "pores"), so that Na+ ions can move down their concentration gradient from outside the cells to inside the cells.

There are many other solutes that must undergo facilitated diffusion to move into a cell, such as amino acids, or to move out of a cell, such as wastes. Because facilitated diffusion is a passive process, it **does not** require chemical energy expenditure by the cell.

Very small polar molecules, including water, can cross a phospholipid bilayer via simple diffusion due to their small size. The rate at which water can move across cell membranes is increased by the presence of membrane proteins called aquaporins that form channels through which water molecules (but not solutes) can pass. **Osmosis** refers to the passive movement of water across a semipermeable membrane (Figure 6). Osmosis across a cell membrane therefore includes the movement of water molecules by either simple diffusion or facilitated diffusion or both.

The movement of water across a cell membrane cannot be always easily regulated by cells, so it is important that cells are exposed to an environment in which the concentration of solutes outside of the cells (in the extracellular fluid) is equal to the concentration of solutes inside the cells (in the cytoplasm). Two solutions that have the same concentration of solutes are said to be **isotonic** (equal tension). When cells and their extracellular environments are isotonic, the concentration of water molecules is the same outside and inside the cells, and the cells maintain their normal shape (and function).

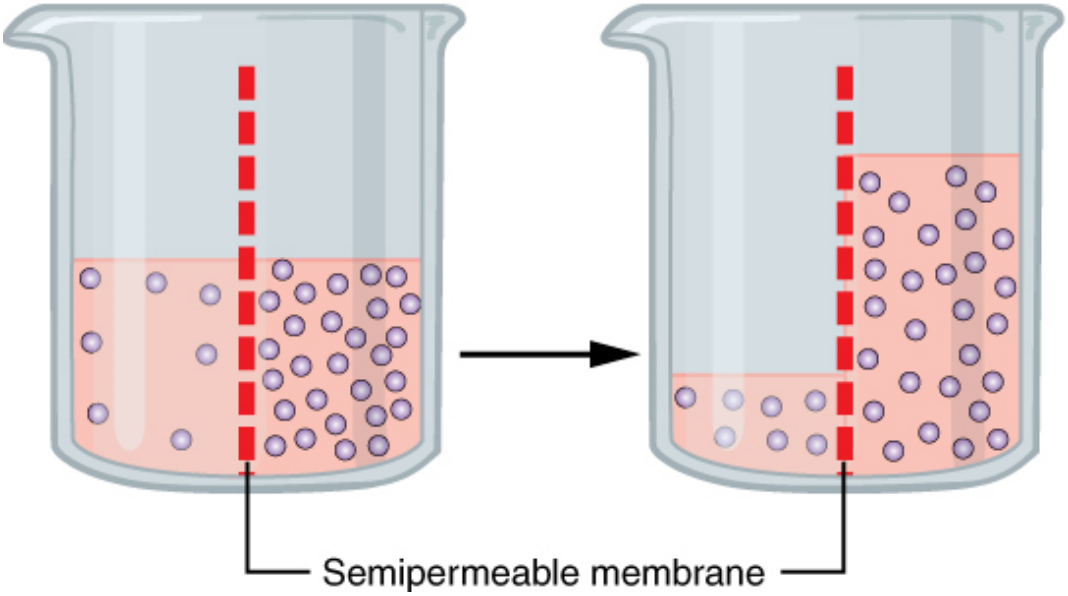


Figure 6. Osmosis. *Osmosis is the diffusion of water through a semipermeable membrane down its concentration gradient. If a membrane is permeable to water, though not to a solute, water will equalize its own concentration by diffusing to the side of lower water concentration (and thus the side of higher solute concentration). In the beaker on the left, the solution on the right side of the membrane is hypertonic relative to the solution on the left side of the membrane.*

Osmosis occurs when there is an imbalance of solutes outside of a cell versus inside the cell. A solution that has a higher concentration of solutes than another solution is said to be **hypertonic**, and water molecules tend

to diffuse into a hypertonic solution (Figure 7). Cells in a hypertonic solution will shrivel as water leaves the cell via osmosis. In contrast, a solution that has a lower concentration of solutes than another solution is said to be **hypotonic**, and water molecules tend to diffuse out of a hypotonic solution.

Cells in a hypotonic solution will take on too much water and swell, with the risk of eventually bursting. A critical aspect of homeostasis in living things is to create an internal environment in which all of the body's cells are in an isotonic solution. Various organ systems, particularly the kidneys, work to maintain this homeostasis.

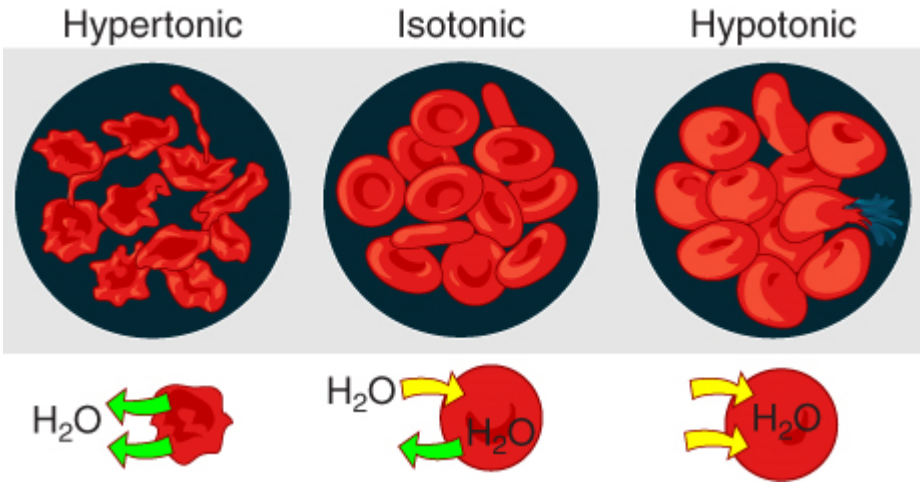


Figure 7. Concentration of Solutions. *A hypertonic solution has a solute concentration higher than another solution. An isotonic solution has a solute concentration equal to another solution. A hypotonic solution has a solute concentration lower than another solution. The figure shows erythrocytes in solutions that are hypertonic, isotonic, or hypotonic relative to cytosol.*

Active Transport: For all of the transport methods described above, the cell does not need to use chemical energy because substrates are moving down their concentration gradients (from high to low concentration) Membrane proteins that aid in the passive transport of substances do so without the hydrolysis of ATP. During active transport, the energy released from ATP hydrolysis is required to move a substance across a membrane, often with the help of carrier proteins, and usually against the concentration gradient of the substance being moved.

One of the most common types of active transport involves proteins that serve as pumps. The word "pump" probably conjures up thoughts of using energy to pump up the tire of a bicycle or a basketball. Similarly, chemical energy from ATP is required for these membrane proteins to transport substances—molecules or ions—across the membrane, usually against their concentration gradients (from an area of low concentration to an area of high concentration).

The **sodium-potassium pump**, which is also called Na^+/K^+ ATPase, transports sodium out of a cell while moving potassium into the cell both against their gradients. The Na^+/K^+ pump is an important ion pump found in the membranes of many types of cells. These pumps are particularly abundant in nerve cells, which are constantly pumping out sodium ions and pulling in potassium ions to maintain an electrical gradient across their cell membranes. An **electrical gradient** is a difference in electrical charge across a space. In the case of nerve cells, for example, the electrical gradient exists between the inside and outside of the cell, with the inside being negatively-charged relative to the outside. The negative electrical gradient is maintained because each Na^+/K^+ pump moves three Na+ ions out of the cell and two K+ ions into the cell for each ATP molecule that is hydrolyzed (Figure 8). This process is so important for nerve cells that it accounts for the majority of their ATP usage.

Active transport pumps can also work together with other active or passive transport systems to move substances across the membrane. For example, the sodium-potassium pump maintains a high concentration of sodium ions outside of the cell. Therefore, if the cell needs sodium ions, all it has to do is open a passive sodium channel, as the concentration gradient of the sodium ions will drive them to diffuse into the cell. In

this way, the action of an active transport pump (the sodium-potassium pump) powers the passive transport of sodium ions by creating a concentration gradient. When active transport of one substance is used to power the transport of another substance in this way, it is called **secondary active transport**, to distinguish it from **primary active transport** mechanisms that use the chemical energy released from ATP to directly drive the movement of an ion or molecule.

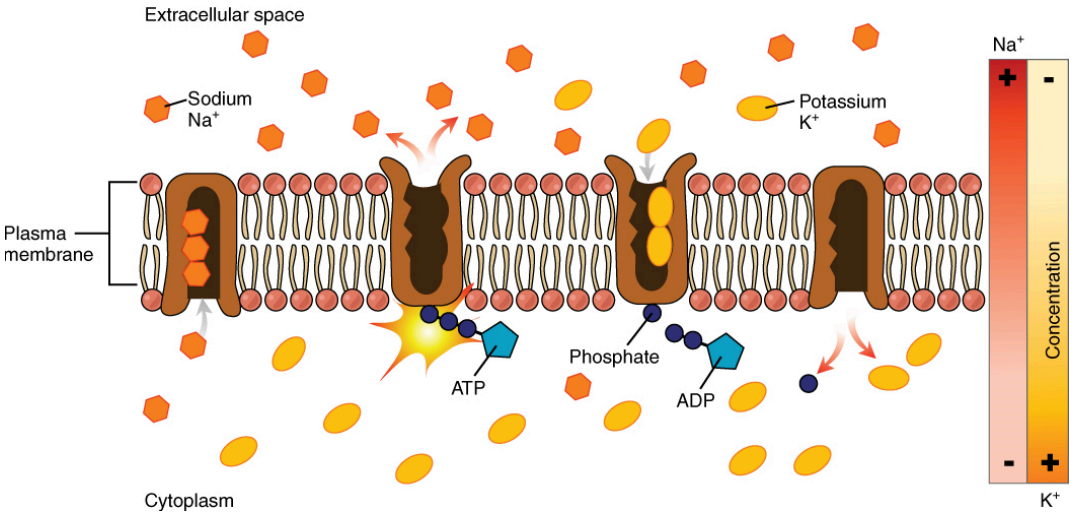


Figure 8. Sodium-Potassium Pump. *The sodium-potassium pump is found in many cell (plasma) membranes. Powered by ATP hydrolysis, the pump moves sodium and potassium ions in opposite directions, each against its concentration gradient. In a single cycle of the pump, three sodium ions are extruded from and two potassium ions are imported into the cell.*

Other forms of active transport do not involve membrane carriers. **Endocytosis** (bringing "into the cell") is the process of a cell ingesting material by enveloping it in a portion of its cell membrane, and then pinching off that portion of membrane (Figure 9). Once pinched off, the portion of membrane and its contents becomes an independent, intracellular vesicle. A **vesicle** is a membranous sac—a spherical and hollow organelle bounded by a lipid bilayer membrane. Endocytosis often brings materials into the cell that must to be broken down or digested. **Phagocytosis** ("cell eating") is the endocytosis of large particles. Many immune cells engage in phagocytosis of invading pathogens. Like little Pac-men, their job is to patrol body tissues for unwanted matter, such as invading bacterial cells, phagocytize them, and digest them. In contrast to phagocytosis, **pinocytosis** ("cell drinking") brings fluid containing dissolved substances into a cell through membrane vesicles.

Phagocytosis and pinocytosis take in large portions of extracellular material, and they are typically not highly selective in the substances they bring in. Cells regulate the endocytosis of specific substances via receptor-mediated endocytosis**. Receptor-mediated endocytosis** is endocytosis by a portion of the cell membrane that contains many receptors that are specific for a certain substance. Once the surface receptors have bound sufficient amounts of the specific substance, the cell will endocytose the part of the cell membrane containing the complex. Iron, a required component of hemoglobin, is endocytosed by red blood cells in this way. Iron is bound to a protein called transferrin in the blood. Specific transferrin receptors on red blood cell surfaces bind the iron-transferrin molecules, and the cell endocytoses the complex.

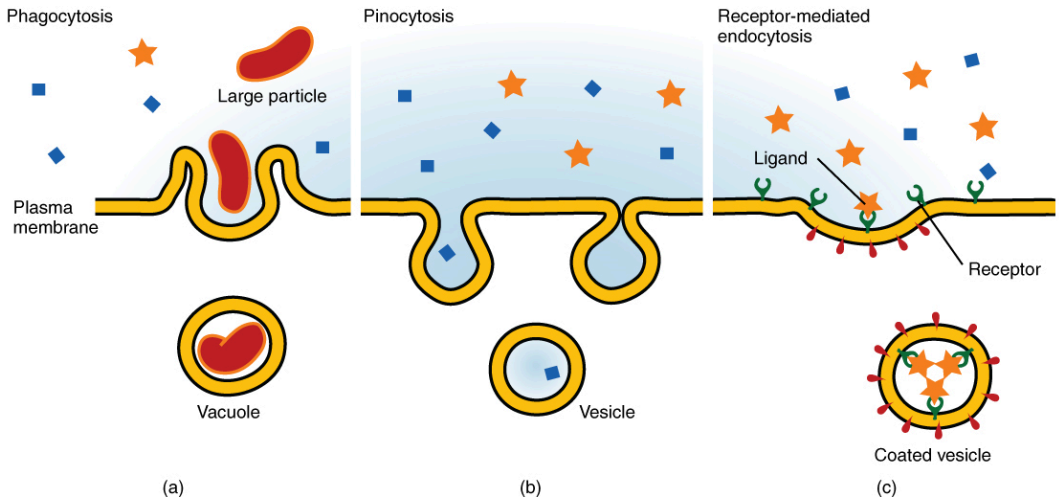


Figure 9. Three Forms of Endocytosis. *Endocytosis is a form of active transport in which a cell envelopes extracellular materials using its cell membrane. (a) In phagocytosis, which is relatively nonselective, the cell takes in a large particle. (b) In pinocytosis, the cell takes in small particles in fluid. (c) In contrast, receptor-mediated endocytosis is quite selective. When external receptors bind a specific ligand, the cell responds by endocytosing the ligand.*

In contrast with endocytosis, **exocytosis** (taking "out of the cell") is the process of a cell exporting material using vesicular transport (Figure 10). Many cells manufacture substances that must be secreted, like a factory manufacturing a product for export. These substances are typically packaged into membrane-bound vesicles within the cell. When the vesicle membrane fuses with the cell membrane, the vesicle releases its contents into the interstitial fluid. The vesicle membrane then becomes part of the cell membrane. Cells of the stomach and pancreas produce and secrete digestive enzymes through exocytosis (Figure 11). Endocrine cells produce and secrete hormones that are sent throughout the body, and certain immune cells produce and secrete large amounts of histamine, a chemical important for immune responses.

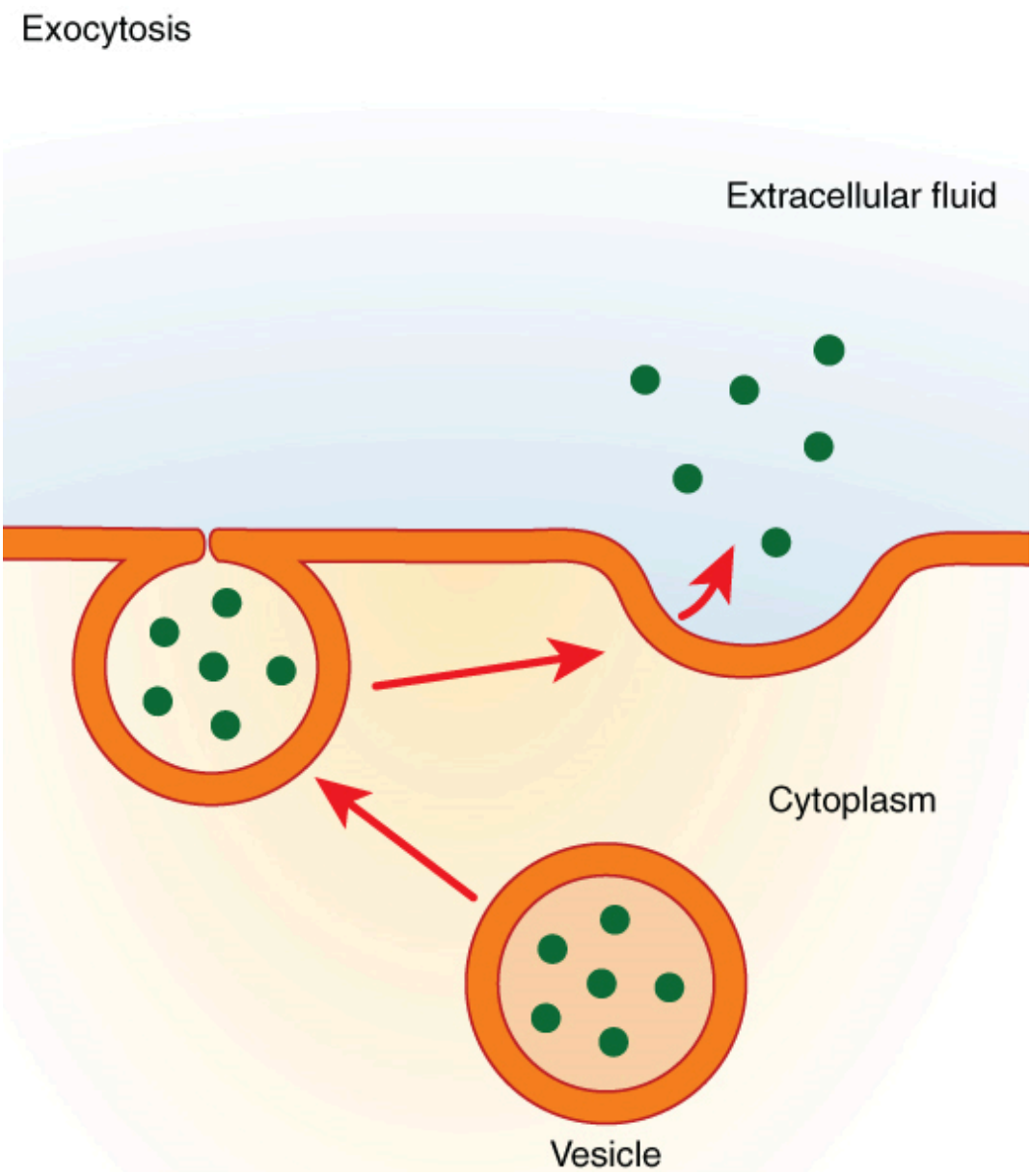


Figure 10. Exocytosis. *Exocytosis is much like endocytosis in reverse. Material destined for export is packaged into a vesicle inside the cell. The membrane of the vesicle fuses with the cell membrane, and the contents are released into the extracellular space.*

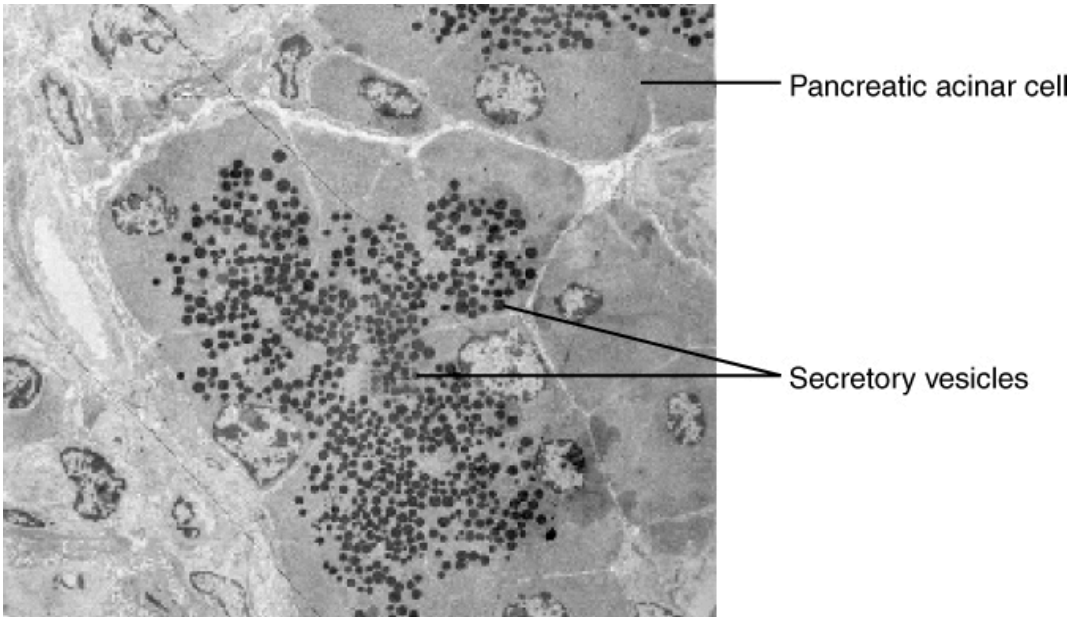


Figure 11. Pancreatic Cells' Enzyme Products. *The pancreatic acinar cells produce and secrete many enzymes that digest food. The tiny black granules in this electron micrograph are secretory vesicles filled with enzymes that will be exported from the cells via exocytosis. LM × 2900. (Micrograph provided by the Regents of University of Michigan Medical School © 2012)*

Watch this Amoeba Sisters video to learn more about cell transport! Direct link: https://youtu.be/Ptmlvtei8hw

Watch this CrashCourse video on membranes and transport! Direct link: https://youtu.be/dPKvHrD1eS4

Check out the Khan Academy membranes and transport section to find out more. Direct link: https://www.khanacademy.org/science/biology/membranes-and-transport

Unit 6: Tissue Structure and Functions

Unit outline

Part 1. Tissue: a higher level of organization

- Definition of tissue
- Importance of tissues

Part 2. Epithelial tissue

- Structure
- Function
- Types of epithelial tissue

Part 3. Connective tissue

- Structure
- Function
- Types of connective tissue

Part 4. Muscle tissue

- Structure
- Function
- Classification of muscle tissue

Part 5. Nervous tissue

- Structure
- Function

Learning Objectives

At the end of this unit, you should be able to:

I. Define tissue and describe the importance of tissue level organization to an organism.

II. Describe the structure and function of epithelial, connective, muscle, and nervous tissue.

III. Explain the relationships between structure and function of tissues.

Learning Objectives and Guiding Questions

At the end of this unit, you should be able to complete all the following tasks, including answering the guiding questions associated with each task.

I. Define tissue and describe the importance of tissue level organization to an organism.

1. What is a tissue?
2. What is the main benefit to humans of having tissue level organization?

II. Describe the structure and function of epithelial, connective, muscle, and nervous tissue.

1. Describe the general structure of each of the following:
    - Epithelial tissue
    - Connective tissue
    - Muscle tissue
    - Nervous tissue
2. Describe the general function of each of the following:
    - Epithelial tissue
    - Connective tissue
    - Muscle tissue
    - Nervous tissue
3. Compare and contrast the structure of the three types of connective tissue (proper, supportive connective tissue, and liquid connective tissue).
4. Compare and contrast the structure of the three types of stratified epithelium (stratified squamous epithelium, stratified cuboidal epithelium, and stratified columnar epithelium).

III. Explain the relationships between structure and function of tissues.

1. Use annotated diagrams to describe the structure and function of each of the seven main types of epithelial tissue (including pseudostratified columnar epithelium).
2. Compare and contrast the structure and function of:
    - Simple squamous epithelium and stratified squamous epithelium
    - Simple squamous epithelium and simple columnar epithelium
    - Simple squamous epithelium and simple cuboidal epithelium
    - Simple cuboidal epithelium and simple columnar epithelium
    - Simple cuboidal epithelium and stratified cuboidal epithelium
3. Create a table stating:
    - The matrix composition,
    - The cellular types,
    - The main function(s), and

- Specific examples

...of each of the following types of connective tissue:

- Fluid connective tissue
- Loose connective tissue
- Dense connective tissue
- Cartilage
- Bone

2. Compare and contrast the three types of muscle tissue by discussing each of the following characteristics:

   - The structure of each of the three types of muscle tissue
   - How each type of muscle tissue is controlled (i.e., whether voluntary control is available or not)
   - The function(s) of each of the three types of muscle tissue

3. Name and describe both of the two main cell types in the nervous tissue. In your description, include:

   - Their general cellular morphology (i.e., their shape)
   - Their main function(s)

4. What is the relationship between the structure and the function of the following tissues?

   - Simple squamous epithelium
   - Stratified squamous epithelium
   - Fluid connective tissue
   - Loose connective tissue
   - Dense connective tissue
   - Cartilage
   - Bone
   - Nervous tissue

The body contains at least 200 distinct cell types. These cells contain essentially the same internal structures, yet they vary enormously in shape and function. The different types of cells are not randomly distributed throughout the body; rather they occur in organized layers, a level of organization referred to as tissue.

Part 1: Tissue: a higher level of organization

The term **tissue** is used to describe a group of cells found together in the body. The cells within a tissue share a common embryonic origin. Microscopic observation reveals that the cells in a tissue share morphological features and are arranged in an orderly pattern that achieves the tissue's functions. From the evolutionary perspective, tissues appear in more complex organisms. For example, multicellular protists, ancient eukaryotes, do not have cells organized into tissues. Having tissue level organization increases the efficiency of the body as different shapes and internal structures are better suited to carry out different functions. Having different tissues for different functions allows for a greater speed of activity and a greater effectiveness in performing the various activities.

Although there are many types of cells in the human body, they are organized into four broad categories of tissues: epithelial, connective, muscle, and nervous. Each of these categories is characterized by specific functions that contribute to the overall health and maintenance of the body. A disruption of the structure is a sign of injury or disease. Such changes can be detected through **histology**, the microscopic study of tissue appearance, organization, and function.

The Four Types of Tissues

Epithelial tissue, also referred to as epithelium, refers to the sheets of cells that cover exterior surfaces of the body, lines internal cavities and passageways, and forms certain glands. Connective tissue, as its name implies, binds the cells and organs of the body together and functions in the protection, support, and integration of all parts of the body. Muscle tissue is excitable, responding to stimulation and contracting to provide movement, and occurs as three major types: skeletal (voluntary) muscle, smooth muscle, and cardiac muscle in the heart. Nervous tissue is also excitable, allowing the propagation of electrochemical signals in the form of nerve impulses that communicate between different regions of the body (Figure 1).

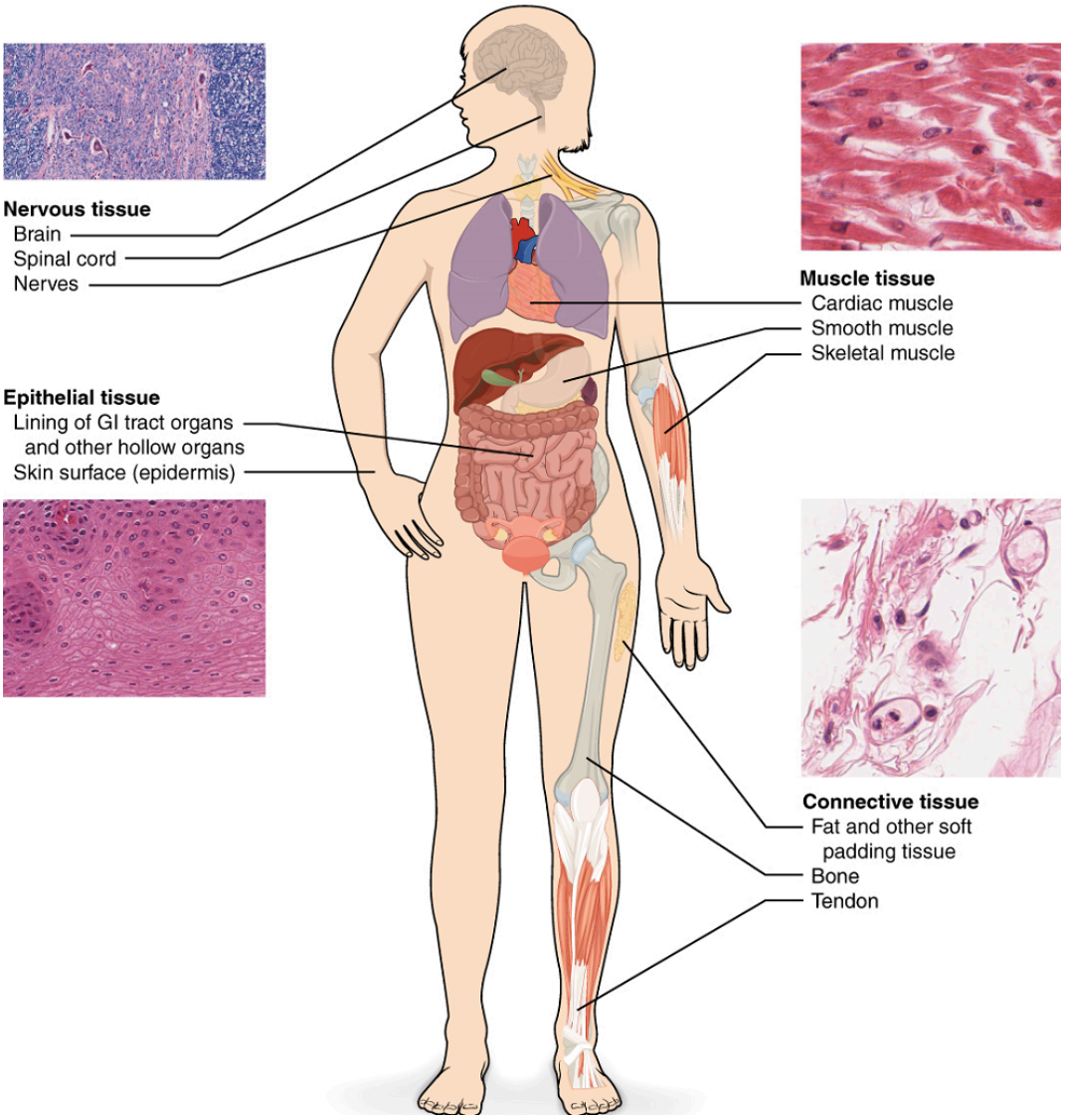


Figure 1. Four Types of Tissue: Body. *The four types of tissues are exemplified in nervous tissue, stratified squamous epithelial tissue, cardiac muscle tissue, and connective tissue in small intestine. Clockwise from nervous tissue, LM × 872, LM × 282, LM × 460, LM × 800. (Micrographs provided by the Regents of University of Michigan Medical School © 2012)*

The next level of organization is the organ, where several types of tissues come together to form a working unit. Just as knowing the structure and function of cells helps you in your study of tissues, knowledge of tissues will

help you understand how organs function. The epithelial and connective tissues are discussed in detail in this chapter. Muscle and nervous tissues will be discussed only briefly in this section.

Part 2: Epithelial Tissue

Most epithelial tissues are essentially large sheets of cells covering all the surfaces of the body exposed to the outside world, and lining the outside of organs and the body cavities. Epithelium also forms much of the glandular tissue of the body. Skin is not the only area of the body exposed to the outside. Other areas include the airways, the digestive tract, as well as the urinary and reproductive systems, all of which are lined by an epithelium. Hollow organs and body cavities that do not connect to the exterior of the body, which includes, blood vessels and serous membranes, are lined by endothelium (plural = endothelia), which is a type of epithelium.

General Structure of Epithelial Tissue

All epithelia share some important structural and functional features. This tissue is highly cellular, with little or no extracellular material present between cells. The epithelial cells exhibit polarity with differences in structure and function between the exposed or **apical** facing surface of the cell and the **basal** surface close to the underlying body structures. Particular structures found in some epithelial cells are an adaptation to specific functions. Certain organelles are segregated to the basal sides, whereas other organelles and extensions, such as cilia, when present, are on the apical surface. The **basal lamina**, a mixture of glycoproteins and collagen, provides an attachment site for the epithelium, separating it from underlying connective tissue. The basal lamina attaches to a **reticular lamina**, which is secreted by the underlying connective tissue, forming a **basement membrane** that helps hold it all together.

Epithelial tissues are nearly completely avascular. For instance, no blood vessels cross the basement membrane to enter the tissue, and nutrients must come by diffusion or absorption from underlying tissues or the surface. Many epithelial tissues are capable of rapidly replacing damaged and dead cells. Sloughing off of damaged or dead cells is a characteristic of surface epithelium and allows our airways and digestive tracts to rapidly replace damaged cells with new cells.

General Functions of Epithelial Tissue: Epithelial tissues provide the body's first line of protection from physical, chemical, and biological wear and tear. The cells of an epithelium act as gatekeepers of the body controlling permeability and allowing selective transfer of materials across a physical barrier. All substances that enter the body must cross an epithelium. Some epithelia often include structural features that allow the selective transport of molecules and ions across their cell membranes.

Many epithelial cells are capable of secretion and release mucous and specific chemical compounds onto their apical surfaces. The epithelium of the small intestine releases digestive enzymes, for example. Cells lining the respiratory tract secrete mucous that traps incoming microorganisms and particles. A glandular epithelium contains many secretory cells.

Classification of Epithelial Tissues: Epithelial tissues are classified according to the shape of the cells and number of the cell layers formed (Figure 2). Cell shapes can be squamous (flattened and thin), cuboidal (boxy, as wide as it is tall), or columnar (rectangular, taller than it is wide). Similarly, the number of cell layers in the tissue can be one—where every cell rests on the basal lamina—which is a simple epithelium, or more than one, which is a stratified epithelium and only the basal layer of cells rests on the basal lamina. Pseudostratified (pseudo- = "false") describes tissue with a single layer of irregularly shaped cells that give the appearance of more than one layer. Transitional describes a form of specialized stratified epithelium in which the shape of the cells can vary.

Simple Epithelium: The shape of the cells in the single cell layer of simple epithelium reflects the functioning of those cells. The cells in **simple squamous epithelium** have the appearance of thin scales. Squamous cell nuclei tend to be flat, horizontal, and elliptical, mirroring the form of the cell. Simple squamous epithelium, because of the thinness of the cell, is present where rapid passage of chemical compounds is observed. The alveoli of lungs where gases diffuse, segments of kidney tubules, and the lining of capillaries are also made of simple squamous epithelial tissue.

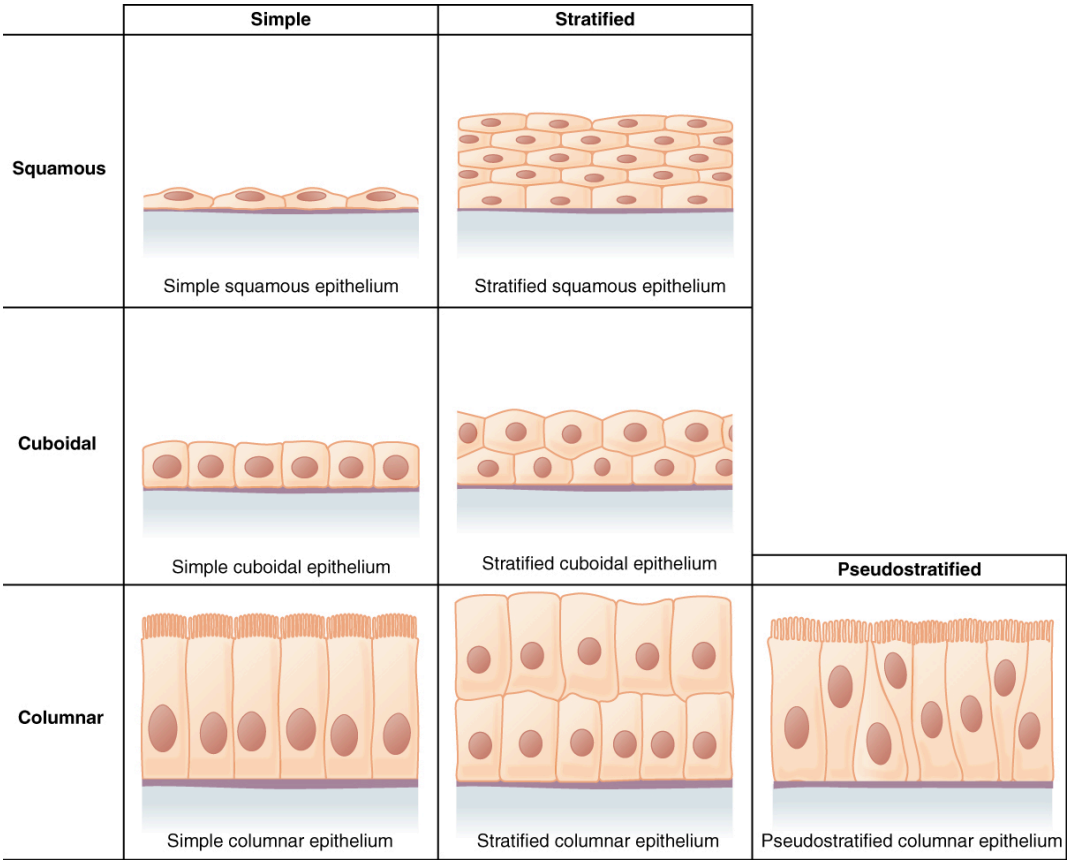


Figure 2. Types of Epithelial Tissue. *Simple epithelial tissue is organized as a single layer of cells and stratified epithelial tissue is formed by several layers of cells. Pseudostratified epithelial tissue is a single layer of cells that appear to be multiple layers because of the position of their nuclei. Epithelial tissue is further defined by the shape of the apical layer of cells in the tissue.*

In **simple cuboidal epithelium**, the nucleus of the box-like cells appears round and is generally located near the center of the cell. These epithelia are active in the secretion and absorptions of molecules. Simple cuboidal epithelia are observed in the lining of the kidney tubules and in the ducts of glands (Figure 3).

In **simple columnar epithelium**, the nucleus of the tall column-like cells tends to be elongated and located in the basal end of the cells (Figure 3). Like the cuboidal epithelia, this epithelium is active in the absorption and secretion of molecules. Simple columnar epithelium forms the lining of some sections of the digestive system and parts of the female reproductive tract. Ciliated columnar epithelium is composed of simple columnar epithelial cells with cilia on their apical surfaces. These epithelial cells are found in the lining of the fallopian tubes and parts of the respiratory system, where the beating of the cilia helps remove particulate matter.

Pseudostratified columnar epithelium is a type of epithelium that appears to be stratified but instead consists of a single layer of irregularly shaped and differently sized columnar cells. In pseudostratified epithelium, nuclei of neighboring cells appear at different levels rather than clustered in the basal end (Figure 3). The arrangement gives the appearance of stratification; but in fact, all the cells are in contact with the basal lamina, although some do not reach the apical surface. Pseudostratified columnar epithelium is found in the respiratory tract, where some of these cells have cilia.

Stratified Epithelium: A stratified epithelium consists of several stacked layers of cells. This epithelium protects against physical and chemical wear and tear. The stratified epithelium is named by the shape of the most apical layer of cells, closest to the free space**.**

Stratified squamous epithelium is the most common type of stratified epithelium in the human body. The apical cells are squamous, whereas the basal layer contains either columnar or cuboidal cells. The top layer may be covered with dead cells filled with keratin. Mammalian skin is an example of this dry, keratinized, stratified squamous epithelium. The lining of the mouth cavity is an example of an nonkeratinized, stratified squamous

epithelium. **Stratified cuboidal epithelium** and **stratified columnar epithelium** can also be found in certain glands and ducts, but are uncommon in the human body (Figure 3).

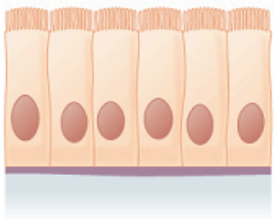
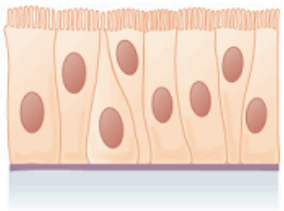
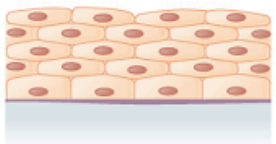
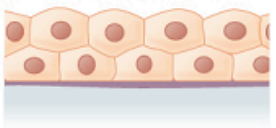
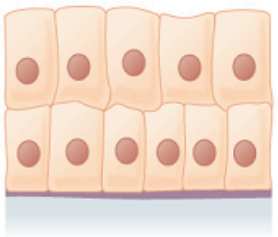
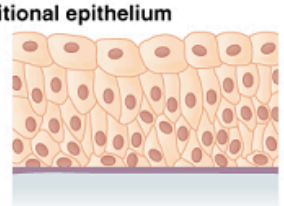
Cells	Location	Function
Simple squamous epithelium 	Air sacs of lungs and the lining of the heart, blood vessels, and lymphatic vessels	Allows materials to pass through by diffusion and filtration, and secretes lubricating substance
Simple cuboidal epithelium 	In ducts and secretory portions of small glands and in kidney tubules	Secretes and absorbs
Simple columnar epithelium 	Ciliated tissues are in bronchi, uterine tubes, and uterus; smooth (nonciliated tissues) are in the digestive tract, bladder	Absorbs; it also secretes mucous and enzymes
Pseudostratified columnar epithelium 	Ciliated tissue lines the trachea and much of the upper respiratory tract	Secretes mucus; ciliated tissue moves mucus
Stratified squamous epithelium 	Lines the esophagus, mouth, and vagina	Protects against abrasion
Stratified cuboidal epithelium 	Sweat glands, salivary glands, and the mammary glands	Protective tissue
Stratified columnar epithelium 	The male urethra and the ducts of some glands	Secretes and protects
Transitional epithelium 	Lines the bladder, uretha, and the ureters	Allows the urinary organs to expand and stretch

Figure 3. Summary of Epithelial Tissue Types. *Different types of epithelial tissue serve different functions and are found in different locations in the body.*

Watch this CrashCourse video to learn more about epithelial histology. Direct link: https://youtu.be/lUe_RI_m-Vg

Part 3: Connective tissue

General structure of connective tissue

As may be obvious from its name, one of the major functions of connective tissue is to connect tissues and organs. Unlike epithelial tissue, which is composed of cells closely packed with little or no extracellular space in between, connective tissue cells are dispersed in a matrix. The matrix usually includes a large amount of extracellular material produced by the connective tissue cells that are embedded within it. The matrix plays a major role in the functioning of this tissue. The major component of the matrix is a ground substance often crisscrossed by protein fibers. This ground substance is usually a fluid, but it can also be mineralized and solid, as in bones. Connective tissues come in a vast variety of forms, yet they typically have in common three characteristic components: cells, large amounts of amorphous ground substance, and protein fibers. The amount and structure of each component correlates with the function of the tissue, from the rigid ground substance in bones supporting the body to the inclusion of specialized cells; for example, a phagocytic cell that engulfs pathogens and also rids tissue of cellular debris.

Functions of Connective Tissues

Connective tissues perform many functions in the body, but most importantly, they support and connect other tissues; from the connective tissue sheath that surrounds muscle cells, to the tendons that attach muscles to bones, and to the skeleton that supports the positions of the body. Protection is another major function of connective tissue, in the form of fibrous capsules and bones that protect delicate organs and, of course, the skeletal system. Specialized cells in connective tissue defend the body from microorganisms that enter the body. Transport of fluid, nutrients, waste, and chemical messengers is ensured by specialized fluid connective tissues, such as blood and lymph. Adipose cells store surplus energy in the form of fat and contribute to the thermal insulation of the body.

Classification of Connective Tissue

The three broad categories of connective tissue are classified according to the characteristics of their ground substance and the types of fibers found within the matrix (Table 1). **Connective tissue proper** includes **loose connective tissue** and **dense connective tissue**. Both tissues have a variety of cell types and protein fibers suspended in a viscous ground substance. Dense connective tissue is reinforced by bundles of fibers that provide tensile strength, elasticity, and protection. In loose connective tissue, the fibers are loosely organized, leaving large spaces in between. **Supportive connective tissue** – **bone** and **cartilage** – provide structure and strength to the body and protect soft tissues. A few distinct cell types and densely packed fibers in a matrix characterize these tissues. In bone, the matrix is rigid and described as calcified because of the deposited calcium salts. In **fluid connective tissue** – **lymph** and **blood** – various specialized cells circulate in a watery fluid containing salts, nutrients, and dissolved proteins.

Table 1: Connective tissue examples

Connective tissue proper	Supportive connective tissue	Fluid connective tissue
Loose connective tissue	Cartilage	
Areolar	Hyaline	Blood
Adipose	Fibrocartilage	
Reticular	Elastic	
Dense connective tissue	Bones	
Regular	Compact bone	Lymph
Irregular	Cancellous bone	

Connective Tissue Proper

Fibroblasts are present in all connective tissue proper (Figure 4). Fibroblast is most abundant cell in connective tissue proper. Fibrocytes, adipocytes, and mesenchymal cells are fixed cells, which means they remain within the connective tissue. Other cells move in and out of the connective tissue in response to chemical signals. Macrophages, mast cells, lymphocytes, plasma cells, and phagocytic cells are found in connective tissue proper but are actually part of the immune system protecting the body.

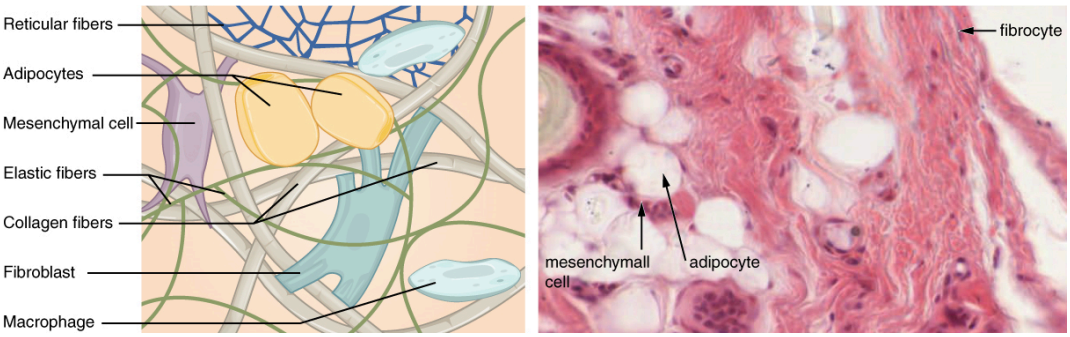


Figure 4. Connective Tissue Proper. *Fibroblasts produce this fibrous tissue. Connective tissue proper includes the fixed cells fibrocytes, adipocytes, and mesenchymal cells. LM × 400. (Micrograph provided by the Regents of University of Michigan Medical School © 2012)*

Adipocytes are cells that store lipids as droplets that fill most of the cytoplasm. The **mesenchymal cell** is a multipotent adult stem cell. These cells can differentiate into any type of connective tissue cells needed for repair and healing of damaged tissue. The **macrophage** is a large type of blood cell, which enters the connective tissue matrix from the blood vessels. The macrophage cells are an essential component of the immune system, which is the body's defense against potential pathogens and degraded host cells. The **mast cell** found in connective tissue proper, when irritated or damaged, release histamine which causes vasodilation and increased blood flow at a site of injury or infection, along with itching, swelling, and redness you recognize as an allergic response.

Three main types of fibers are secreted by fibroblasts: collagen fibers, elastic fibers, and reticular fibers.

Collagen fibers, while flexible, have great tensile strength, resist stretching, and give ligaments and tendons their characteristic resilience and strength. These fibers hold connective tissues together, even during the movement of the body. **Elastic fibers** after being stretched or compressed will return to its original shape. Elastic fibers are prominent in elastic tissues found in skin and the elastic ligaments of the vertebral column. **Reticular fibers** are narrow and are arrayed in a branching network. They are found throughout the body, but are most abundant in the reticular tissue of soft organs, such as liver and spleen, where they anchor and provide structural support to the **parenchyma** (the functional cells, blood vessels, and nerves of the organ). All of these fiber types are embedded in ground substance, a clear, viscous, colorless matrix made of polysaccharides and proteins, forming the extracellular matrix.

Loose Connective Tissue

Loose connective tissue is found between many organs where it acts both to absorb shock and bind tissues together. It allows water, salts, and various nutrients to diffuse through to adjacent or imbedded cells and tissues.

Adipose tissue consists mostly of fat storage cells, with little extracellular matrix (Figure 5). A large number of capillaries allow rapid storage and mobilization of lipid molecules. Fat contributes mostly to lipid storage and can serve as insulation from cold temperatures and mechanical injuries.

Areolar tissue shows little specialization. It contains all the cell types and fibers previously described and is distributed in a random, web-like fashion. It fills the spaces between muscle fibers, surrounds blood and lymph vessels, and supports organs in the abdominal cavity. Areolar tissue underlies most epithelia and represents the connective tissue component of epithelial membranes, which are described further in a later section.

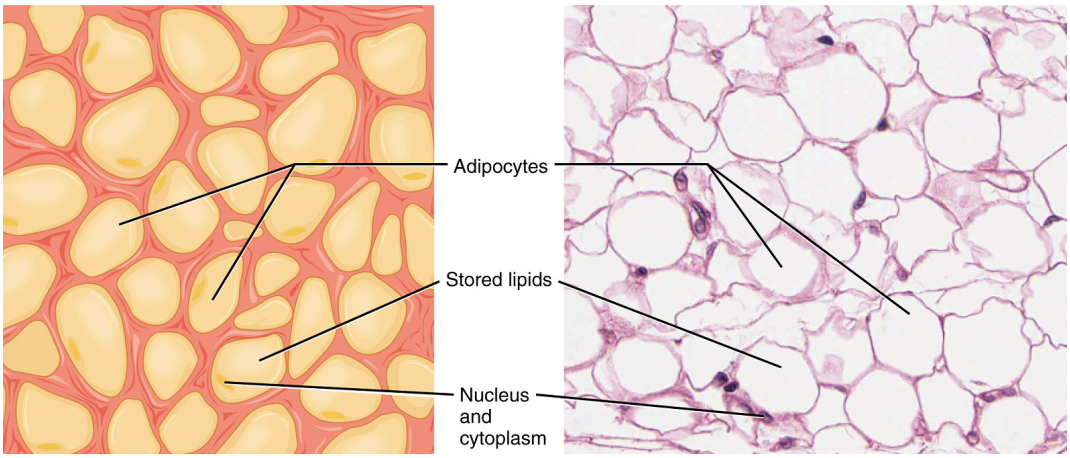


Figure 5. Adipose Tissue. *This is a loose connective tissue that consists of fat cells with little extracellular matrix. It stores fat for energy and provides insulation. LM × 800. (Micrograph provided by the Regents of University of Michigan Medical School © 2012)*

Reticular tissue is a mesh-like, supportive framework for soft organs such as lymphatic tissue, the spleen, and the liver (Figure 6). Reticular cells produce the reticular fibers that form the network onto which other cells attach. It derives its name from the Latin reticulus, which means “little net.”

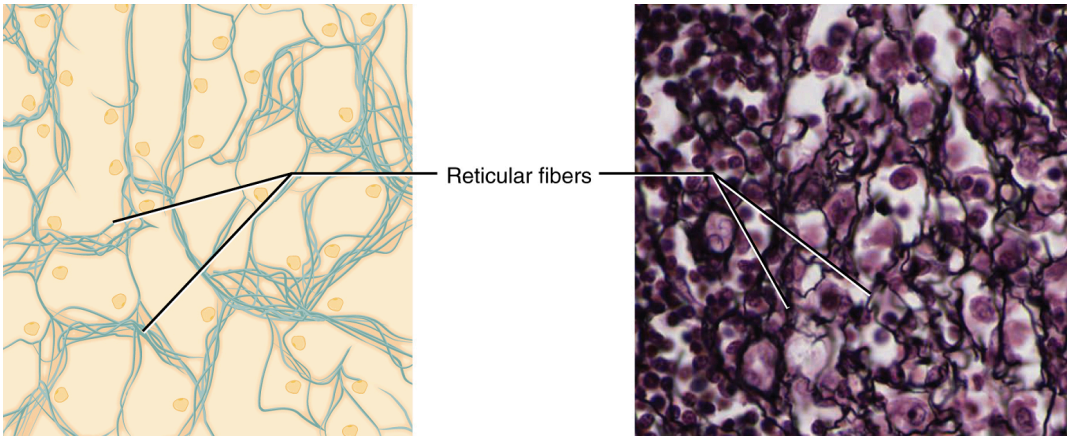


Figure 6. Reticular Tissue. *This is a loose connective tissue made up of a network of reticular fibers that provides a supportive framework for soft organs. LM × 1600. (Micrograph provided by the Regents of University of Michigan Medical school2012)*

Dense Connective Tissue

Dense connective tissue contains more collagen fibers than does loose connective tissue. As a consequence, it displays greater resistance to stretching. There are two major categories of dense connective tissue: **regular** and **irregular**. Dense regular connective tissue fibers are parallel to each other, enhancing tensile strength and resistance to stretching in the direction of the fiber orientations. Ligaments and tendons are made of dense regular connective tissue, but in ligaments not all fibers are parallel. Dense regular elastic connective tissue contains elastin fibers in addition to collagen fibers, which allows the ligament to return to its original length after stretching. The ligaments in the vocal folds and between the vertebrae in the vertebral column are elastic.

In dense irregular connective tissue, the direction of fibers is random. This arrangement gives the tissue greater strength in all directions and less strength in one particular direction. In some tissues, fibers crisscross and form a mesh. In other tissues, stretching in several directions is achieved by alternating layers where fibers run in the same orientation in each layer, and it is the layers themselves that are stacked at an angle. The dermis of the skin is an example of dense irregular connective tissue rich in collagen fibers. Dense irregular elastic connective tissue give arterial walls the strength and the ability to regain original shape after stretching (Figure 7).

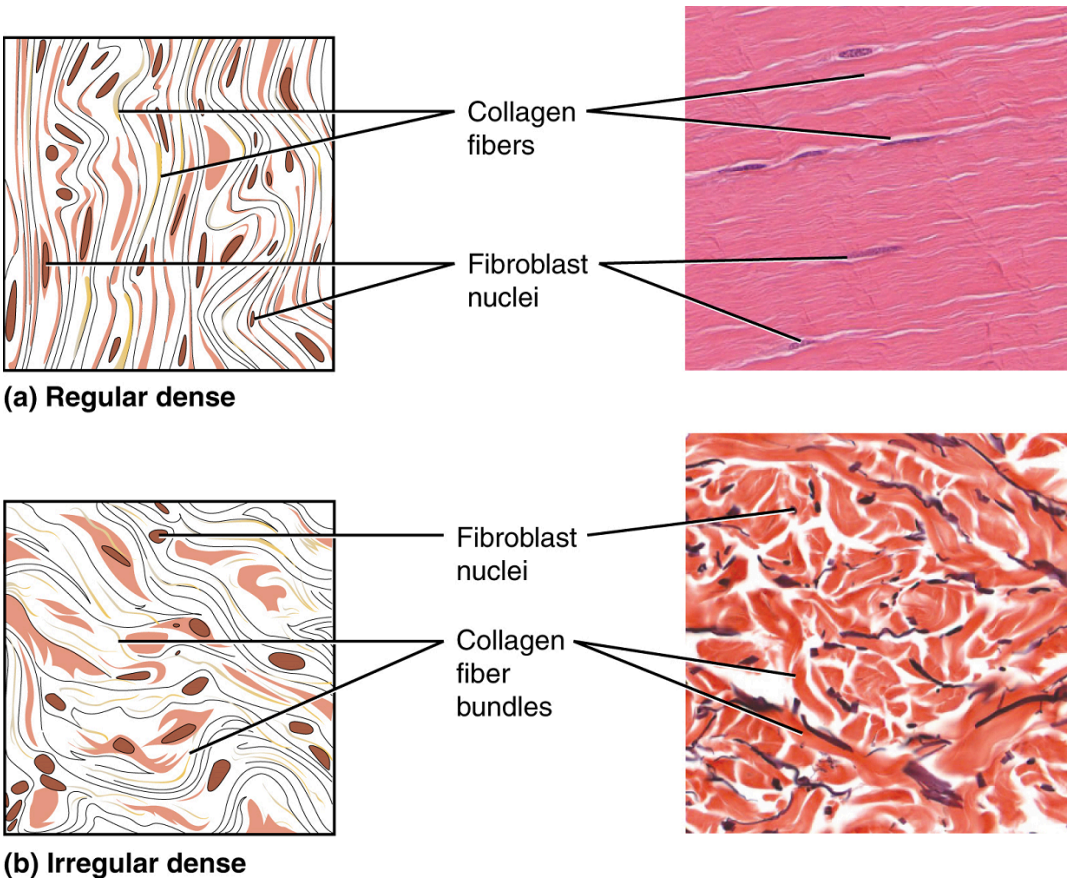


Figure 7. Dense Connective Tissue. *(a) Dense regular connective tissue consists of collagenous fibers packed into parallel bundles. (b) Dense irregular connective tissue consists of collagenous fibers interwoven into a mesh-like network. From top, LM × 1000, LM × 200. (Micrographs provided by the Regents of University of Michigan Medical School © 2012)*

Supportive Connective Tissues

Two major forms of supportive connective tissue, cartilage and bone, allow the body to maintain its posture and protect internal organs.

Cartilage

The distinctive appearance of cartilage is due to polysaccharides, which bind with ground substance proteins to form the extracellular matrix. Embedded within the cartilage matrix are **chondrocytes**, or cartilage cells, and the space they occupy are called **lacunae** (singular = lacuna). A layer of dense irregular connective tissue, the perichondrium, encapsulates the cartilage. Cartilaginous tissue is avascular, thus all nutrients need to diffuse through the matrix to reach the chondrocytes. This is a factor contributing to the very slow healing of cartilaginous tissues.

The three main types of cartilage tissue are hyaline cartilage, fibrocartilage, and elastic cartilage (Figure 8). **Hyaline cartilage**, the most common type of cartilage in the body, contains short and dispersed collagen fibers in the matrix. Both strong and flexible, the hyaline cartilage is found in the rib cage and nose and covers bones where they meet to form moveable joints. It makes up a template of the embryonic skeleton before bone formation. A plate of hyaline cartilage at the ends of bone allows continued growth until adulthood. **Fibrocartilage** is tough because it has thick bundles of collagen fibers dispersed through its matrix. The knee and jaw joints and the intervertebral discs are examples of fibrocartilage. **Elastic cartilage** contains elastic fibers as well as collagen. This tissue gives rigid support as well as elasticity. Tug gently at your ear lobes, and notice that the lobes return to their initial shape. The external ear contains elastic cartilage.

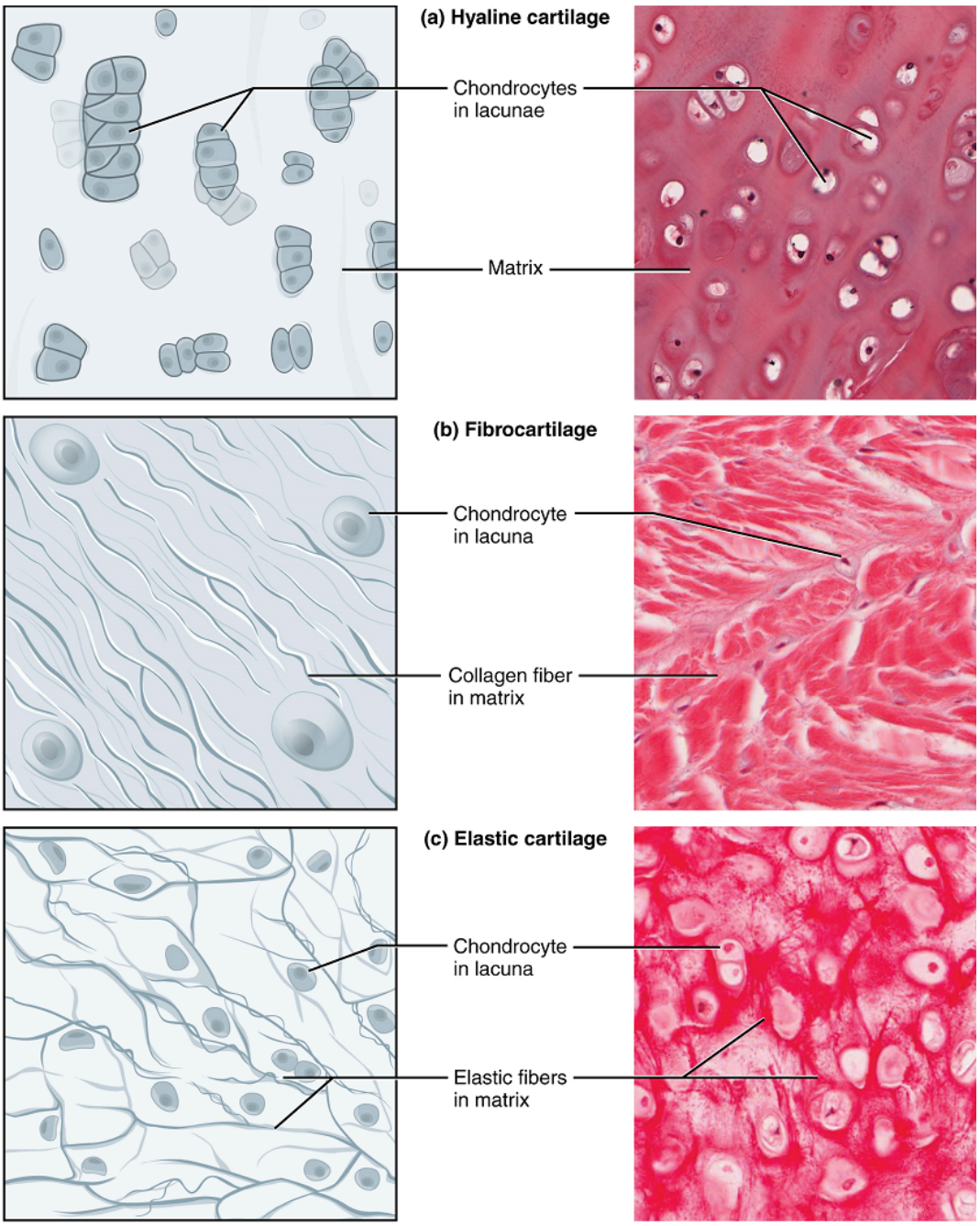


Figure 8. Types of Cartilage. *Cartilage is a connective tissue consisting of collagenous fibers embedded in a firm matrix of chondroitin sulfates. (a) Hyaline cartilage provides support with some flexibility. The example is from dog tissue. (b) Fibrocartilage provides some compressibility and can absorb pressure. (c) Elastic cartilage provides firm but elastic support. From top, LM × 300, LM × 1200, LM × 1016. (Micrographs provided by the Regents of University of Michigan Medical School © 2012)*

Bone

Bone is the hardest connective tissue. It provides protection to internal organs and supports the body. Bone's rigid extracellular matrix contains mostly collagen fibers embedded in a mineralized ground substance containing hydroxyapatite, a form of calcium phosphate. Both components of the matrix, organic and inorganic, contribute to the unusual properties of bone. Without collagen, bones would be brittle and shatter easily. Without mineral crystals, bones would flex and provide little support. Osteocytes, bone cells like chondrocytes, are located within lacunae. The histology of transverse tissue from long bone shows a typical arrangement of osteocytes in concentric circles around a central canal. Bone is a highly vascularized tissue. Unlike cartilage, bone tissue can recover from injuries in a relatively short time.

Cancellous bone ("trabecular bone" or "spongy bone") looks like a sponge under the microscope and contains

empty spaces between trabeculae, or arches of bone proper. It is lighter than compact bone and found in the interior of some bones and at the end of long bones. Compact bone is solid and has greater structural strength.

Fluid Connective Tissue

Blood and **lymph** are fluid connective tissues. Cells circulate in a liquid extracellular matrix. The formed elements circulating in blood are all derived from hematopoietic stem cells located in bone marrow (Figure 9). Erythrocytes, red blood cells, transport oxygen and some carbon dioxide. Leukocytes, white blood cells, are responsible for defending against potentially harmful microorganisms or molecules. Platelets are cell fragments involved in blood clotting.

Some white blood cells have the ability to cross the endothelial layer that lines blood vessels and enter adjacent tissues. Nutrients, salts, and wastes are dissolved in the liquid matrix and transported through the body.

Lymph contains a liquid matrix and white blood cells. Lymphatic capillaries are extremely permeable, allowing larger molecules and excess fluid from interstitial spaces to enter the lymphatic vessels. Lymph drains into blood vessels, delivering molecules to the blood that could not otherwise directly enter the bloodstream. In this way, specialized lymphatic capillaries transport absorbed fats away from the intestine and deliver these molecules to the blood.

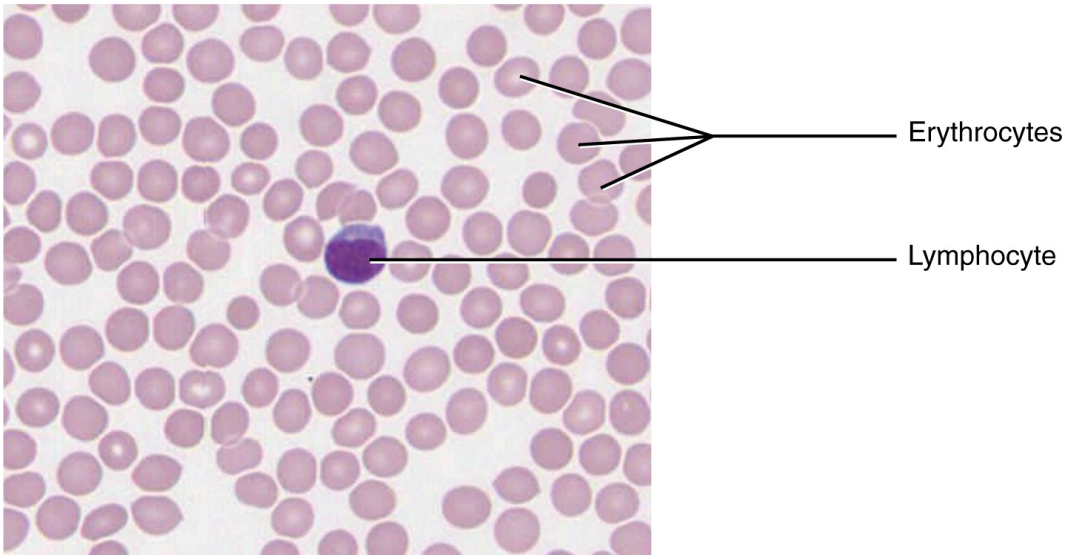


Figure 9. Blood: A Fluid Connective Tissue. *Blood is a fluid connective tissue containing erythrocytes and various types of leukocytes that circulate in a liquid extracellular matrix. LM × 1600. (Micrograph provided by the Regents of University of Michigan Medical School © 2012)*

Part 4: Muscle Tissue

Muscle tissue is characterized by properties that allow movement. Muscle cells are excitable; they respond to a stimulus. They are contractile, meaning they can shorten and generate a pulling force. When attached between two movable objects, in other words, bones, contractions of the muscles cause the bones to move. Some muscle movement is voluntary, which means it is under conscious control. For example, a person decides to open a book and read a chapter on anatomy. Other movements are involuntary, meaning they are not under conscious control, such as the contraction of your pupil in bright light. Muscle tissue is classified into three types according to structure and function: **skeletal**, **cardiac**, and **smooth** (Table 2).

Table 2: Comparison of structure and properties of muscle tissue types

Tissue	Histology	Function	Location
Skeletal	Long cylindrical fiber; striated; many peripherally-located nuclei	Voluntary movement; thermogenesis; organ protection	Attached to bones; found around entrance points to body (e.g. mouth, anus)
Cardiac	Short, branched fibers; striated; single central nucleus	Contracts to pump blood	Heart walls
Smooth	Short, spindle-shaped fibers; no evident striation; single nucleus	Involuntary movement; moves material through digestive tract and ducts; regulates blood flow in arteries	Walls of major organs and passageways

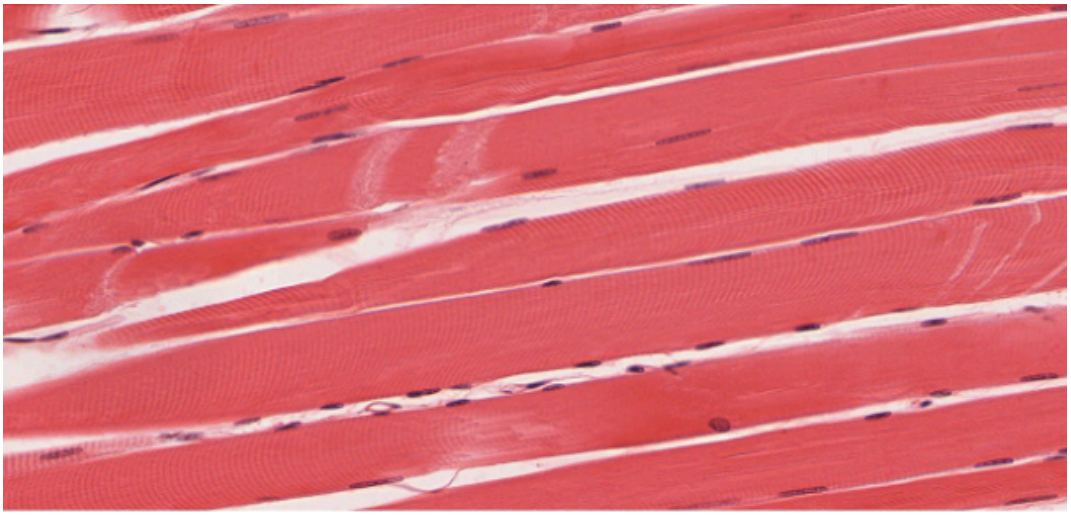
Skeletal muscle

Skeletal muscle is attached to bones and its contraction makes possible locomotion, facial expressions, posture, and other voluntary movements of the body. Forty percent of your body mass is made up of skeletal muscle. Skeletal muscles generate heat as a byproduct of their contraction and thus participate in thermal homeostasis. Shivering is an involuntary contraction of skeletal muscles in response to perceived lower than normal body temperature.

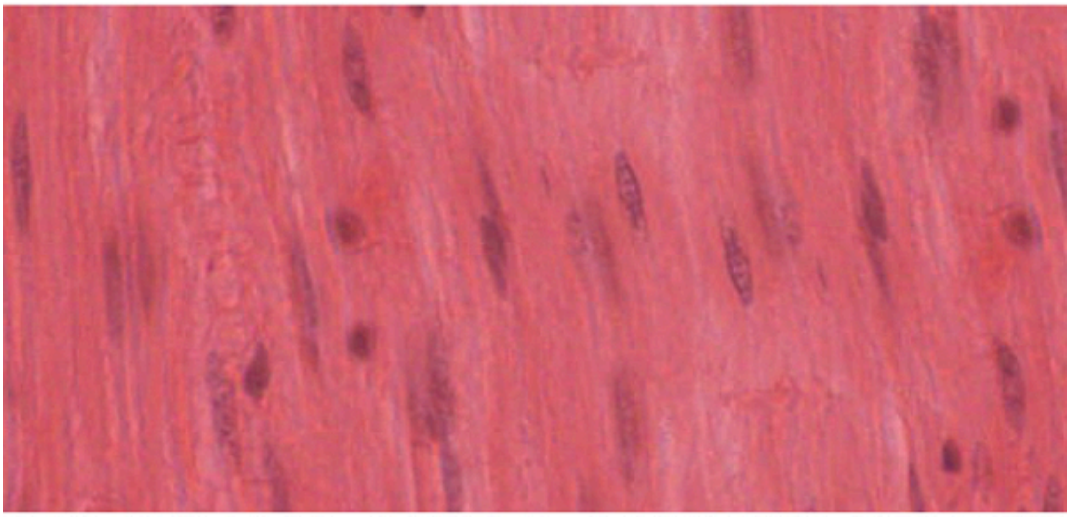
The muscle cells, **muscle fibers** or **myocytes**, and their numbers remain relatively constant throughout life. Skeletal muscle tissue is arranged in bundles surrounded by connective tissue. Under the light microscope, muscle cells appear striated with many nuclei squeezed along the membranes (Figure 10a). The **striation** is due to the regular alternation of the contractile proteins actin and myosin, along with the structural proteins that couple the contractile proteins to connective tissues. The cells are multinucleated as a result of the fusion of the many myoblasts that fuse to form each long muscle fiber.

Cardiac muscle

Cardiac muscle forms the contractile walls of the heart. The cells of cardiac muscle, known as cardiomyocytes, also appear striated under the microscope. Unlike skeletal muscle fibers, cardiomyocytes are single cells typically with a single centrally located nucleus.



(a)



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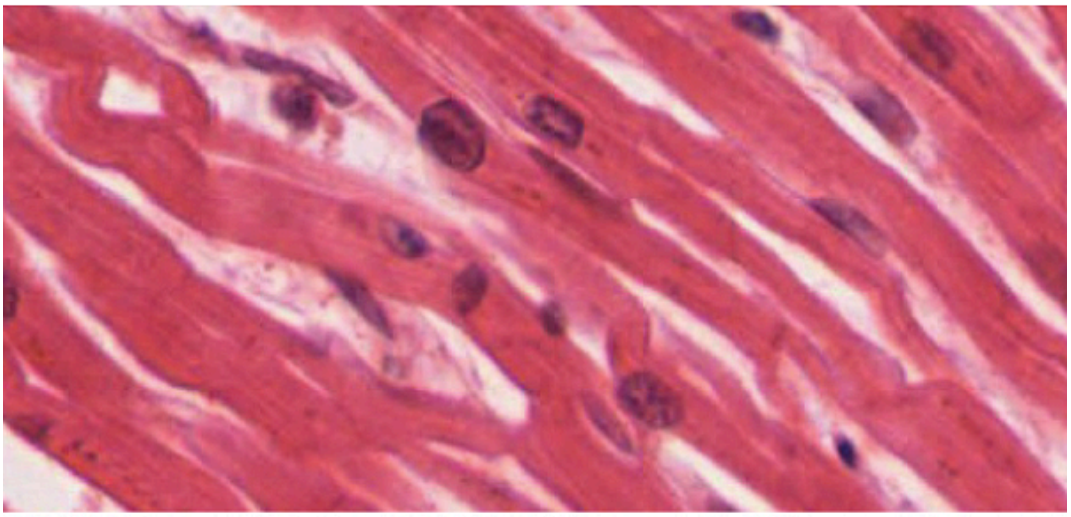


(c)

Figure 10. Muscle Tissue. *(a) Skeletal muscle cells have prominent striation and nuclei on their periphery. (b) Smooth muscle cells have a single nucleus and no visible striations.(c) Cardiac muscle cells appear striated and have a single nucleus. From top, LM × 1600, LM × 1600, LM × 1600. (Micrographs provided by the Regents of University of Michigan Medical School © 2012)*

A principal characteristic of cardiomyocytes is that they contract on their own intrinsic rhythms without any external stimulation. Cardiomyocyte attach to one another with specialized cell junctions called intercalated discs. Attached cells form long, branching cardiac muscle fibers that are (Figure 10c), essentially, a mechanical and electrochemical syncytium allowing the cells to synchronize their actions. The cardiac muscle pumps blood through the body and is under involuntary control.

Smooth muscle tissue contraction is responsible for involuntary movements in the internal organs. It forms the contractile component of the digestive, urinary, and reproductive systems as well as the airways and arteries. Each cell is spindle shaped with a single nucleus and no visible striations (Figure 10b).

Watch this CrashCourse video on tissues to learn more about muscle tissue. Direct link: https://youtu.be/i5tR3csCWYo

Part 5: Nervous Tissue

Nervous tissue is characterized as being excitable and capable of sending and receiving electrochemical signals that provide the body with information. Two main classes of cells make up nervous tissue: the **neuron** and **neuroglia** (Figure 11). Neurons propagate information via electrochemical impulses, called action potentials, which are biochemically linked to the release of chemical signals. Neuroglia play an essential role in supporting neurons and modulating their information propagation.

Neurons display distinctive morphology, well suited to their role as conducting cells, with three main parts. The cell body includes most of the cytoplasm, the organelles, and the nucleus. Dendrites branch off the cell body and appear as thin extensions. A long “tail,” the axon, extends from the neuron body and can be wrapped in an insulating layer known as **myelin**, which is formed by accessory cells. The synapse is the gap between nerve cells, or between a nerve cell and its target, for example, a muscle or a gland, across which the impulse is transmitted by chemical compounds known as neurotransmitters.

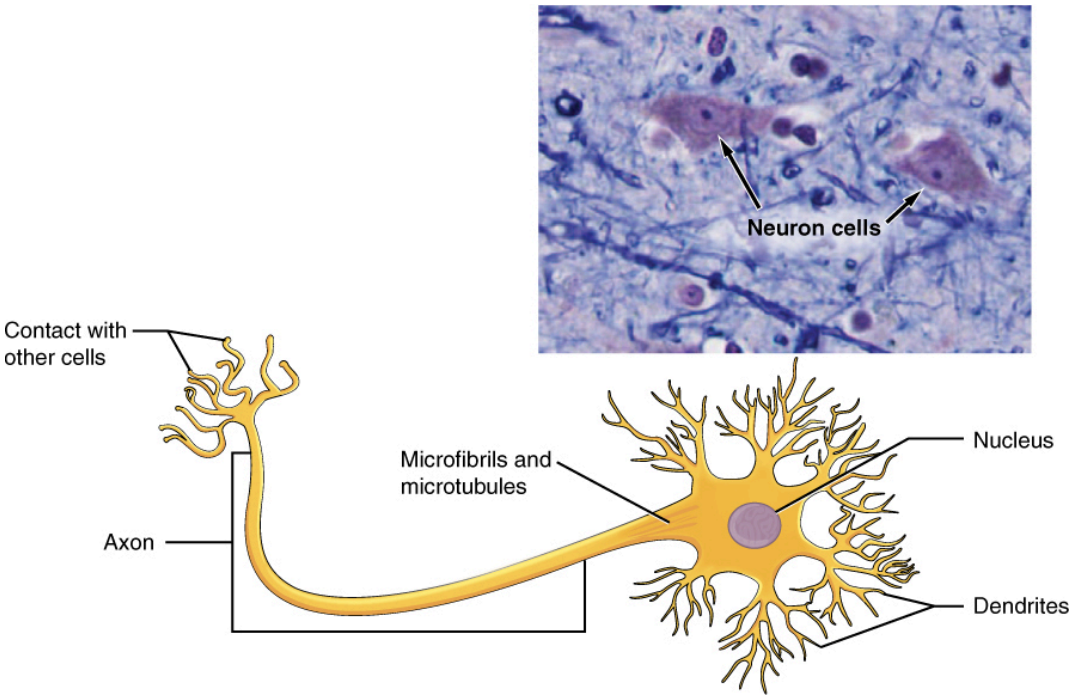


Figure 11. The Neuron. *The cell body of a neuron, also called the soma, contains the nucleus and mitochondria. The dendrites transfer the nerve impulse to the soma. The axon carries the action potential away to another excitable cell. LM × 1600. (Micrograph provided by the Regents of University of Michigan Medical School © 2012)*

The second class of neural cells comprises the neuroglia or glial cells (Figure 12), which have been characterized as having a simple support role. The word "glia" comes from the Greek word for glue. Recent research is shedding light on the more complex role of neuroglia in the function of the brain and nervous system.

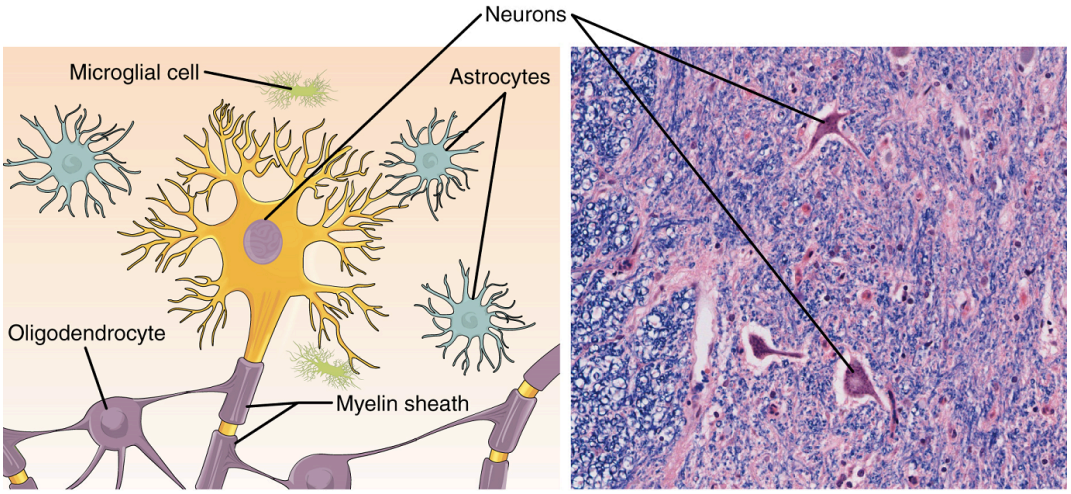


Figure 12. Nervous Tissue. *Nervous tissue is made up of neurons and neuroglia. The cells of nervous tissue are specialized to transmit and receive impulses. LM × 872. (Micrograph provided by the Regents of University of Michigan Medical School © 2012)*

The presence of the nervous tissue throughout the body and its organization allow it to receive, integrate and provide information to the entire body. This ensures that appropriate responses can occur among all body systems within an intact organism, both under normal conditions as well as during times of stress.

Unit 7: Body Structure

Unit Outline

Part 1: Body Systems

- Organs and organ systems of the human body

Part 2: Anatomical Terminology

- The anatomical position
- Directional terms used in human anatomy
- Body planes
- Body cavities and serous membranes
    - Subdivisions of the posterior and anterior cavities
    - Abdominopelvic regions and quadrants
    - Membranes of the anterior body cavity

Learning Objectives

At the end of this unit, you should be able to:

I. Define the terms organ, organ system and organism.

II. Name the eleven organ systems of the human body, identify the major organs, and give a major function of each system.

III. Define and demonstrate the anatomical position.

IV. Locate the anterior (ventral) and posterior (dorsal) surfaces for the body, hands and feet.

V. Define the directional terms used in human anatomy.

VI. Define sagittal, frontal, and transverse planes, and distinguish between midsagittal (median) and parasagittal planes.

VII. Specify and describe the limits of the body cavities.

VIII. Describe how the abdominopelvic region is divided into either nine regions or four quadrants.

Learning Objectives and Guiding Questions

At the end of this unit, you should be able to complete all the following tasks, including answering the guiding questions associated with each task.

I. Define the terms organ, organ system and organism.

II. Name the eleven organ systems of the human body, identify the major organs, and give a major function of each system.

1. Create a table specifying the eleven organ systems of the human body, the major organs found in each organ system, and at least one major function of each organ system.

III. Define and demonstrate the anatomical position.

1. Sketch a human body in standard anatomical position.
2. Use complete sentences to clearly describe the location of each of the following components of the human body when in standard anatomical position:
    - Feet
    - Upper limbs
    - Trunk
    - Head

IV. Locate the anterior (ventral) and posterior (dorsal) surfaces of the human body, hands, and feet.

1. Clearly define each of the following terms:
    - Anterior
    - Posterior
    - Ventral
    - Dorsal
2. Explain why 'anterior' and 'ventral' can be used interchangeably to describe relative locations in the human body.
3. Explain why 'posterior' and 'dorsal' can be used interchangeably to describe relative locations in the human body.
4. Identify the direction (ventral or dorsal) in which the palms face when in standard anatomical position, and thus identify which side of the hand (palm or back) of the hand is the ventral side of the hand, and which is the dorsal side.
5. Compare the anatomy of the foot to the anatomy of the hand to identify which side of the foot (sole or back) is the ventral side of the foot, and which is the dorsal side.
6. Sketch each of the following, and on each diagram clearly indicate the anterior (ventral) and posterior (dorsal) surfaces:
    - A human body
    - A human hand
    - A human foot
7. Use complete sentences to describe how to identify the anterior (ventral) and posterior (dorsal) surfaces of each of the following:

- The human body
- The human hand
- The human foot

V. Define the directional terms used in human anatomy.

1. Define each of the following terms and provide one complete sentence that correctly uses each term to describe the relative position of two or three body structures (as appropriate).

    - Superior
    - Inferior
    - Medial
    - Lateral
    - Intermediate
    - Peripheral
    - Central
    - Proximal
    - Distal
    - Deep
    - Superficial
    - Anterior
    - Posterior
    - Cranial
    - Caudal

2. Distinguish between the terms prone and supine.

VI. Define sagittal, frontal, and transverse planes, and distinguish between midsagittal (median) and parasagittal planes.

1. Explain why a body structure is often cut into thin sections before viewing.
2. Define each of the following:

    - Sagittal plane
    - Midsagittal (median) plane
    - Parasagittal plane
    - Frontal (coronal) plane
    - Transverse plane

VII. Specify and describe the limits of the body cavities.

1. Sketch a diagram of the human body showing the relative locations of all the following body cavities:

    - Dorsal body cavity
    - Ventral body cavity
    - Cranial cavity
    - Vertebral cavity
    - Thoracic cavity

- Abdominal cavity
- Pelvic cavity
- Abdominopelvic cavity

2. For each of the following cavities, specify whether there is a physical body structure separating them or not. If there is a major body structure separating them, name that structure.

   - Dorsal and ventral body cavities
   - Cranial and vertebral cavities
   - Thoracic and abdominal cavities
   - Abdominal and pelvic cavities
   - Abdominal and vertebral cavities

3. For each of the following cavities, name all the organs found within that cavity:

   - Cranial cavity
   - Vertebral cavity
   - Thoracic cavity
   - Abdominal cavity
   - Pelvic cavity

4. For each of the following cavities, name any organ systems that are (mostly) contained within that cavity:

   - Cranial cavity
   - Vertebral cavity
   - Thoracic cavity
   - Abdominal cavity
   - Pelvic cavity

5. Define each of the following terms, using only a single short sentence for each:

   - Parietal serosa
   - Visceral serosa
   - Serous fluid
   - Parietal pericardium
   - Visceral pericardium
   - Parietal peritoneum
   - Visceral peritoneum
   - Parietal pleurae *(NB: "pleurae" means "more than one pleura"; why are there multiple pleurae?)*
   - Visceral pleurae

6. Briefly describe the general function of serosa and the serous fluid in the human body.

VIII. Describe how the abdominopelvic region is divided into either nine regions or four quadrants.

1. Specify the locations of each of the following nine abdominopelvic regions:

   - Right hypochondriac

- Epigastric
- Left hypochondriac
- Right lumbar
- Umbilical
- Left lumbar
- Right iliac
- Hypogastric
- Left iliac

2. Describe the location of each of the following abdominopelvic quadrants:

   - Right upper quadrant
   - Left upper quadrant
   - Right lower quadrant
   - Left lower quadrant

3. Specify the location(s), within the nine abdominopelvic regions, of each of the following organs:

   - Liver
   - Gall bladder
   - Spleen
   - Stomach
   - Small intestine
   - Caecum
   - Appendix
   - Ascending colon
   - Transverse colon
   - Descending colon
   - Urinary bladder

Part 1: Body Systems

An **organ** is an anatomically distinct structure of the body composed of two or more tissue types. Each organ performs one or more specific physiological functions. An **organ system** is a group of organs that work together to perform major functions or meet physiological needs of the body.

The human body contains eleven distinct organ systems (Figure 1 and Figure 2). Assigning organs to organ systems can be imprecise since organs that "belong" to one system can also have functions integral to another system. In fact, most organs contribute to more than one system.

The organism level is the highest level of anatomical organization. An **organism** is a living being that has a cellular structure and that can independently perform all physiologic functions necessary for life. In multicellular organisms, including humans, all cells, tissues, organs, and organ systems of the body work together to maintain the life and health of the organism.

Part 2: Anatomical Terminology

Anatomists and health care providers use terminology that can be bewildering to the uninitiated. However, the purpose of this language is not to confuse, but rather to increase precision and reduce medical errors. For example, is a scar "above the wrist" located on the forearm two or three inches away from the hand? Or is

it at the base of the hand? Is it on the palm-side or back-side? By using precise anatomical terminology, we eliminate ambiguity. Anatomical terms derive from Ancient Greek and Latin words. Because these languages are no longer used in everyday conversation, the meaning of their words does not change.

Anatomical terms are made up of roots, prefixes, and suffixes. The root of a term often refers to an organ, tissue, or condition, whereas the prefix or suffix often describes the root. For example, in the disorder hypertension, the prefix "hyper-" means "high" or "over," and the root word "tension" refers to pressure, so the word "hypertension" refers to abnormally high blood pressure.

Anatomical Position: To further increase precision, anatomists standardize the way in which they view the body. Just as maps are normally oriented with north at the top, the standard body "map," or anatomical position, is that of the body standing upright, with the feet parallel, at shoulder width apart and with toes forward. The upper limbs are held out to each side, and the palms of the hands face forward (Figure 3). Using this standard position reduces confusion. It does not matter how the body being described is oriented, the terms are used as if it is in anatomical position. For example, a scar in the "anterior (front) carpal (wrist) region" would be present on the palm side of the wrist. The term "anterior" would be used even if the hand were palm down on a table.

A body that is lying down is described as either prone or supine. **Prone** describes a face-down orientation, and **supine** describes a face up orientation. These terms are sometimes used in describing the position of the body during specific physical examinations or surgical procedures.

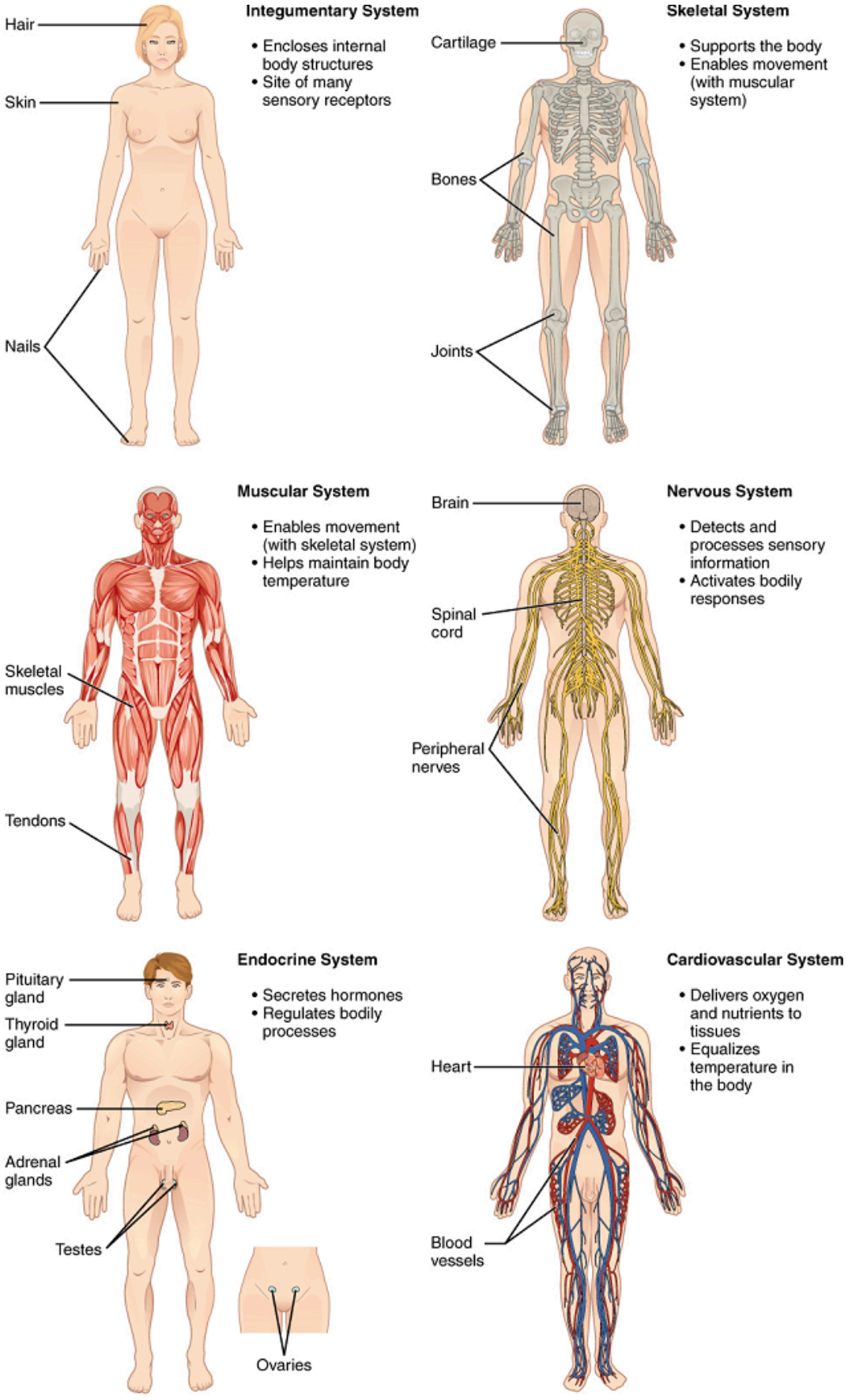


Figure 1. Organ Systems of the Human Body. *Organs that work together are grouped into organ systems.*

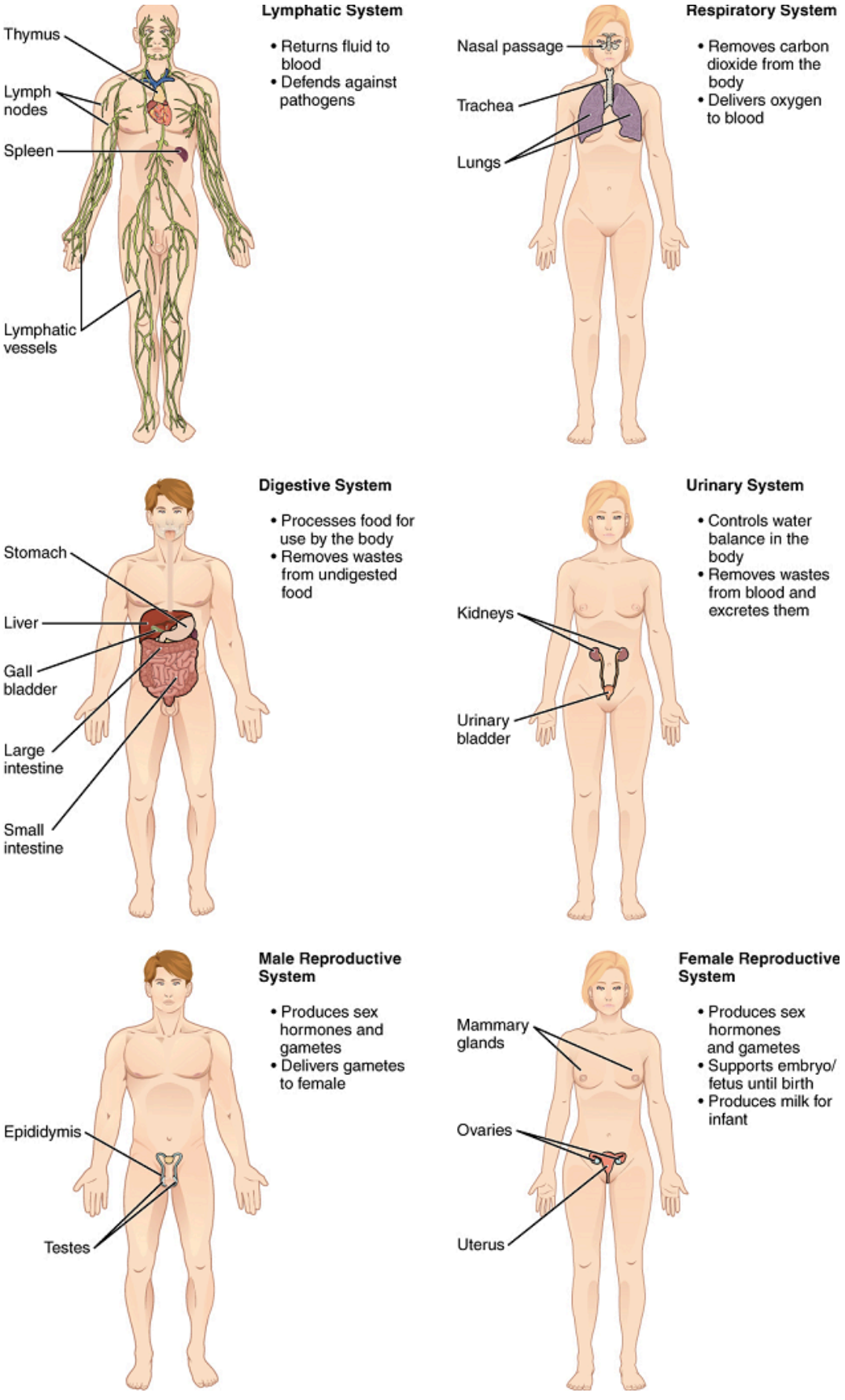


Figure 2. Organ Systems of the Human Body (continued). *Organs that work together are grouped into organ systems.*

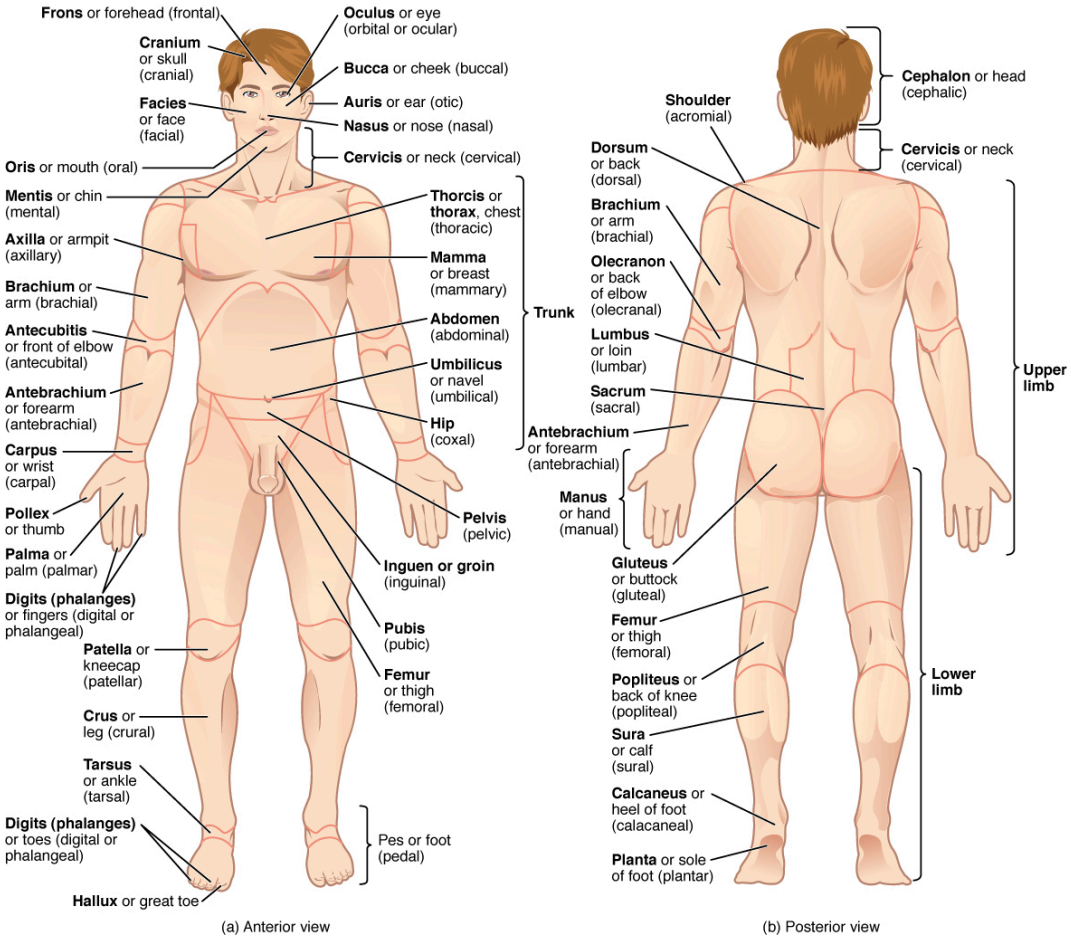


Figure 3. Regions of the Human Body. *The human body is shown in anatomical position in an (a) anterior (ventral) view and a (b) posterior (dorsal) view. The regions of the body are labeled in boldface.*

Regional Terms: The human body's numerous regions have specific terms to help increase precision (Figure 3). Notice that the term "brachium" or "arm" is reserved for the "upper arm" and "antebrachium" or "forearm" is used rather than "lower arm." Similarly, "femur" or "thigh" is correct, and "leg" or "crus" is reserved for the portion of the lower limb between the knee and the ankle. You will be able to describe the body's regions using the terms from the figure.

Directional Terms: Certain directional anatomical terms appear throughout this and any other anatomy textbook (Figure 4). These terms are essential for describing the relative locations of different body structures. For instance, an anatomist might describe one band of tissue as "inferior to" another or a physician might describe a tumor as "superficial to" a deeper body structure. Commit these terms to memory to avoid confusion when you are studying or describing the locations of particular body parts.

- **Anterior** (or ventral) describes the front or direction toward the front of the body. The toes are anterior to the foot.
- **Posterior** (or dorsal) describes the back or direction toward the back of the body. The popliteus is posterior to the patella.
- **Superior** (or **cranial**) describes a position above or higher than another part of the body proper. The orbits are superior to the oris.
- **Inferior** (or **caudal**) describes a position below or lower than another part of the body proper; near or toward the tail (in humans, the coccyx, or lowest part of the spinal column). The pelvis is inferior to the abdomen.
- **Lateral** describes the side or direction toward the side of the body. The thumb (pollex) is lateral to the digits.

- **Medial** describes the middle or direction toward the middle of the body. The hallux is the medial toe.

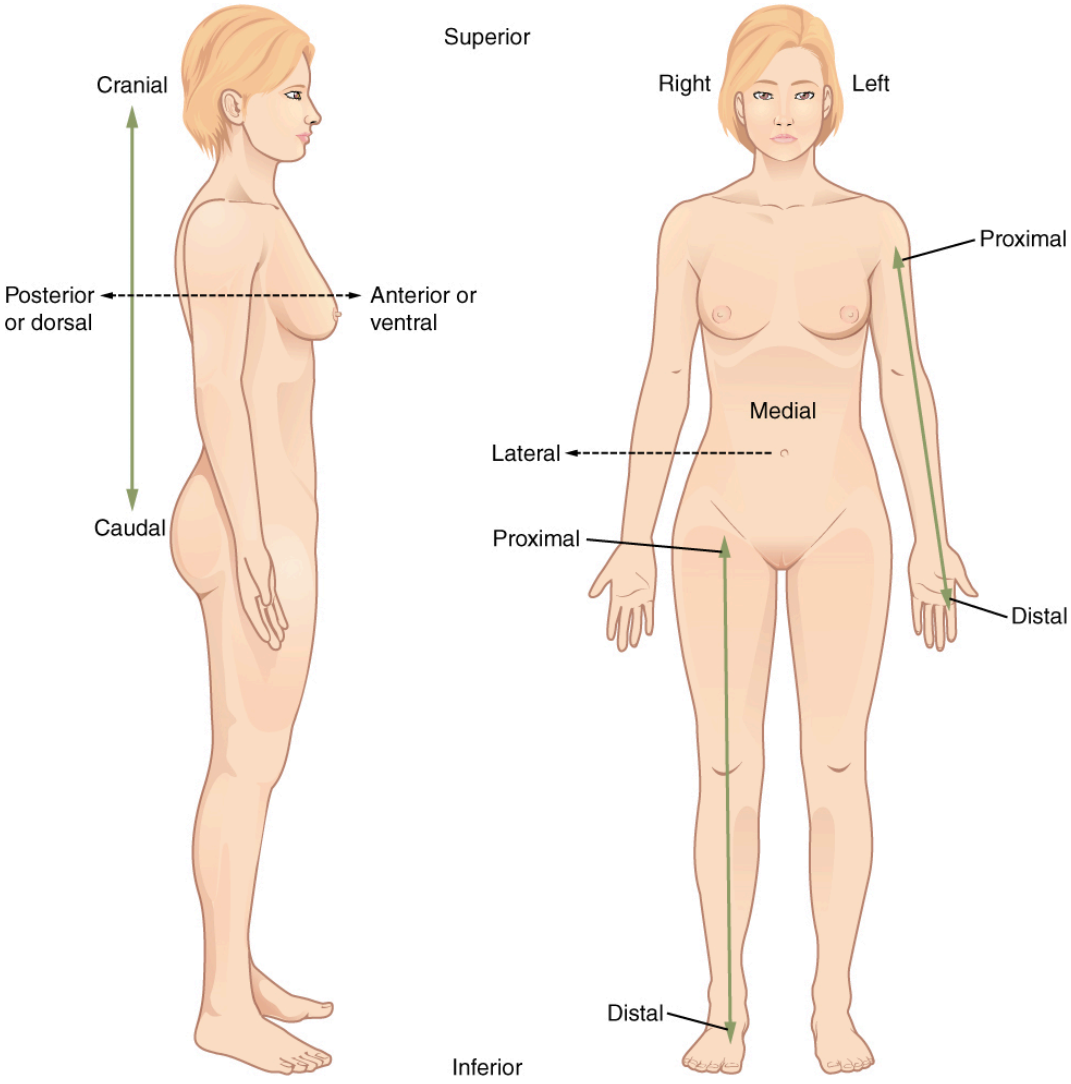


Figure 4. Directional Terms Applied to the Human Body. *Paired directional terms are shown as applied to the human body.*

- **Intermediate** describes a position between a more medial and a more lateral structure. The middle finger is intermediate between the ring and index fingers.
- **Proximal** describes a position in a limb that is nearer to the point of attachment or the trunk of the body. The brachium is proximal to the antebrachium.
- **Distal** describes a position in a limb that is farther from the point of attachment or the trunk of the body. The crus is distal to the femur.
- **Central** describes a position towards the middle (centre) of a structure or organ system. The central nervous system is contained within the skull and vertebral column.
- **Peripheral** describes a position towards the outer edge (periphery) of a structure or organ system. The peripheral nervous system is found outside the skull and vertebral column.
- **Superficial** describes a position closer to the surface of the body. The skin is superficial to the bones.
- **Deep** describes a position farther from the surface of the body. The brain is deep to the skull.

Body Planes: Sectioning, or cutting, is frequently used in the study of Anatomy. The body can be sectioned in various ways to produce a **plane**, this is a two-dimensional surface of a three-dimensional structure that has

been cut. A body structure is often cut into thin sections before macroscopic viewing to allow visualization of the structure's interior and assist with identification of local disease or infiltration as these pathologies may not be obvious when observing the surface anatomy alone. Modern medical imaging devices enable clinicians to obtain "virtual sections" of living bodies. We call these scans. Body sections and scans can be correctly interpreted, however, only if the viewer understands the plane along which the section was made. A plane is an imaginary two-dimensional surface that passes through the body. There are three planes commonly referred to in anatomy and medicine (Figure 5).

- A **sagittal plane** is a plane that divides the body or an organ vertically into right and left sides. If this vertical plane runs directly down the middle of the body, it is called the **midsagittal** or **median** plane. If it divides the body into unequal right and left sides, it is called a **parasagittal** plane or (less commonly) a longitudinal section.
- A **frontal plane** is a plane that divides the body or an organ into an anterior (front) portion and a posterior (rear) portion. A frontal plane is often referred to as a coronal plane ("corona" is Latin for "crown").
- A **transverse plane** is a plane that divides the body or organ horizontally into upper and lower portions. Transverse planes produce images referred to as cross sections.

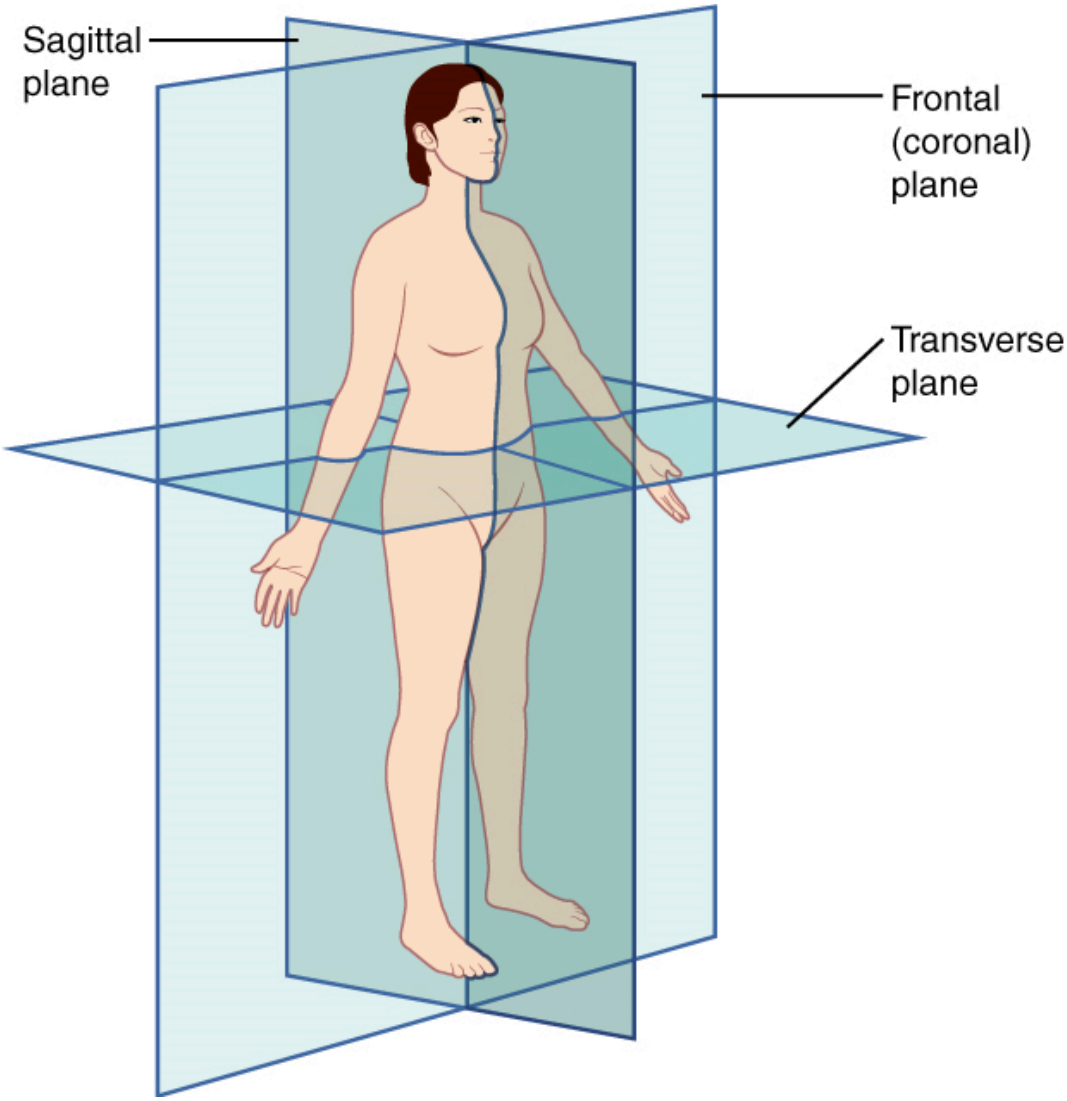


Figure 5. Planes of the Body. *The three planes most commonly used in anatomical and medical imaging are the sagittal, frontal (or coronal), and transverse plane.*

Body Cavities and Serous Membranes: The body maintains its internal organization by means of membranes, sheaths, and other structures that separate compartments. The dorsal (posterior) cavity and the ventral (anterior) cavity are the largest body compartments (Figure 6). These cavities contain and protect delicate internal organs, and the ventral cavity allows for significant changes in the size and shape of the organs as they perform their functions. The lungs, heart, stomach, and intestines, for example, can expand and contract without distorting other tissues or disrupting the activity of nearby organs.

Subdivisions of the Posterior (Dorsal) and Anterior (Ventral) Cavities: The posterior (dorsal) and anterior (ventral) cavities are each subdivided into smaller cavities. In the posterior (dorsal) cavity, the **cranial cavity** houses the brain, and the **spinal cavity** (or vertebral cavity) encloses the spinal cord. Just as the brain and spinal cord make up a continuous, uninterrupted structure, the cranial and spinal cavities that house them are also continuous. The brain and spinal cord are protected by the bones of the skull and vertebral column and by cerebrospinal fluid, a colorless fluid produced by the brain, which cushions the brain and spinal cord within the posterior (dorsal) cavity.

The anterior (ventral) cavity has two main subdivisions: the thoracic cavity and the abdominopelvic cavity (Figure 6). The **thoracic cavity** is the more superior subdivision of the anterior cavity, and it is enclosed by the rib cage. The thoracic cavity contains the lungs and the heart, which is located in the mediastinum. The diaphragm forms the floor of the thoracic cavity and separates it from the more inferior abdominopelvic cavity. The **abdominopelvic cavity** is the largest cavity in the body. Although no membrane physically divides the abdominopelvic cavity, it can be useful to distinguish between the abdominal cavity, the division that houses the digestive organs, and the pelvic cavity, the division that houses the organs of reproduction.

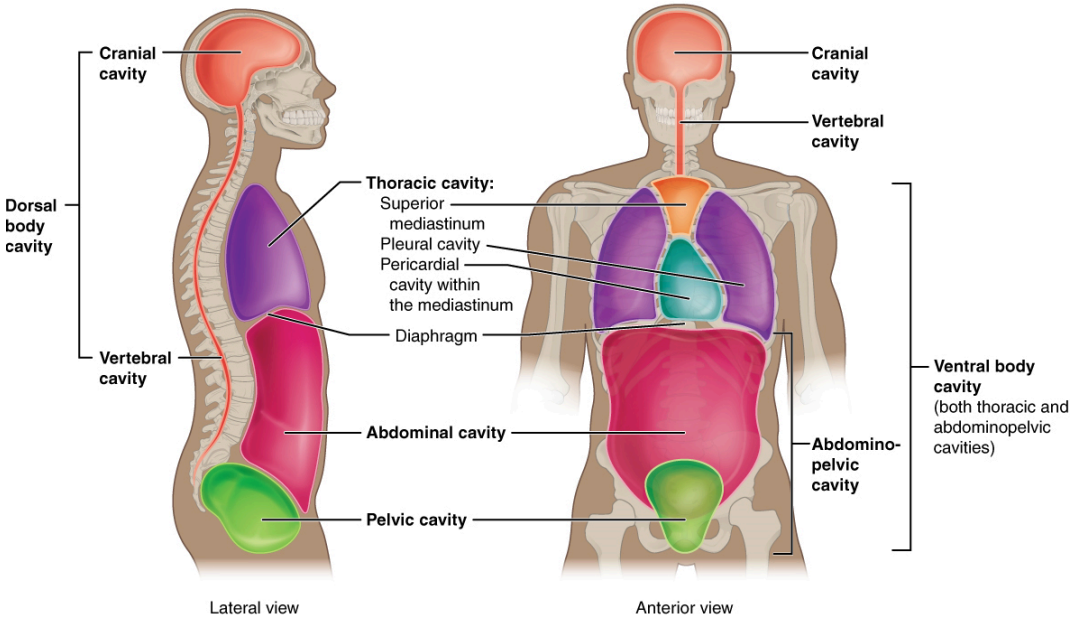


Figure 6. Dorsal and Ventral Body Cavities. *The ventral cavity includes the thoracic and abdominopelvic cavities and their subdivisions. The dorsal cavity includes the cranial and spinal cavities.*

Abdominopelvic Regions and Quadrants: To promote clear communication, for instance about the location of a patient's abdominal pain or a suspicious mass, health care providers typically divide up the abdominopelvic cavity into either nine regions or four quadrants (Figure 7).

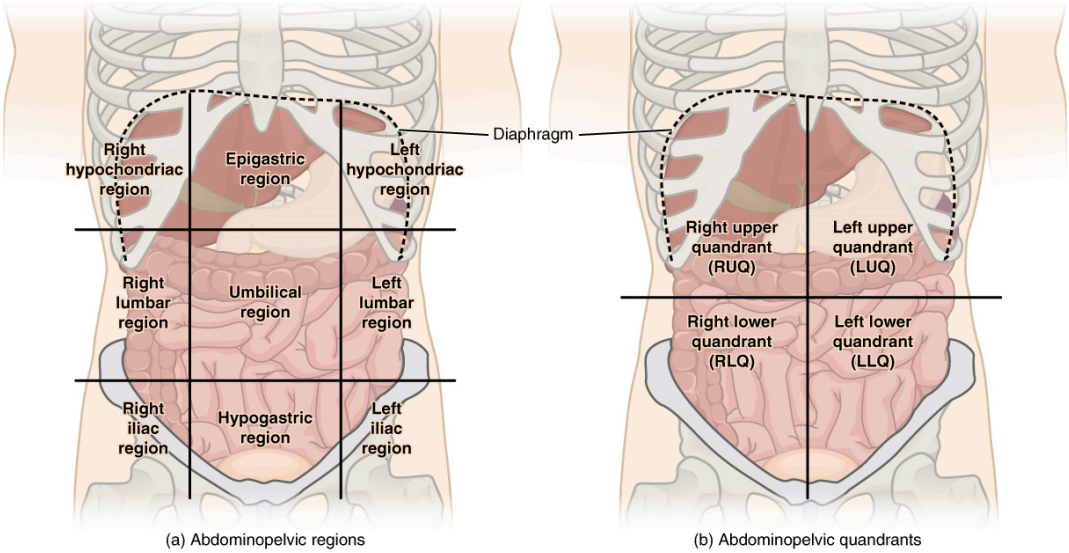


Figure 7. Regions and Quadrants of the Abdominopelvic Cavity. *There are (a) nine abdominopelvic regions and (b) four abdominopelvic quadrants in the peritoneal cavity.*

The more detailed regional approach subdivides the cavity with one horizontal line immediately inferior to the ribs and one immediately superior to the pelvis, and two vertical lines drawn as if dropped from the midpoint of each clavicle (collarbone). There are nine resulting regions. The simpler quadrants approach, which is also commonly used in medicine, subdivides the cavity with one horizontal and one vertical line that intersect at the patient's umbilicus (navel).

These regions can be used to identify the location of abdominal organs more precisely. For example:

- The right hypochondriac region contains the gall bladder and part of the liver, and the right kidney
- The epigastric region contains part of the liver and part of the stomach
- The left hypochondriac region contains part of the spleen and part of the stomach, and the left kidney
- The right lumbar region contains most of the ascending colon
- The umbilical region contains the transverse colon and part of the small intestine
- The left lumbar region contains most of the descending colon
- The right iliac region contains the appendix and caecum
- The hypogastric region contains the lower small intestine, the distal sigmoid colon and anus, and the urinary bladder, as well as the uterus and ovaries in females and the prostate in males
- The left iliac region contains the proximal sigmoid colon

Membranes of the Anterior (Ventral) Body Cavity: A **serous membrane** (also referred to a serosa) is one of the thin membranes that cover the walls and organs in the thoracic and abdominopelvic cavities. The parietal layers of the membranes line the walls of the body cavity (pariet- refers to a cavity wall). The visceral layer of the membrane covers the organs (the viscera). Between the parietal and visceral layers is a very thin, fluid-filled serous space, or cavity (Figure 8).

There are three serous cavities and their associated membranes. The **pleura** is the serous membrane that surrounds the lungs in the pleural cavity; the **pericardium** is the serous membrane that surrounds the heart in the pericardial cavity; and the **peritoneum** is the serous membrane that surrounds several organs in the abdominopelvic cavity.

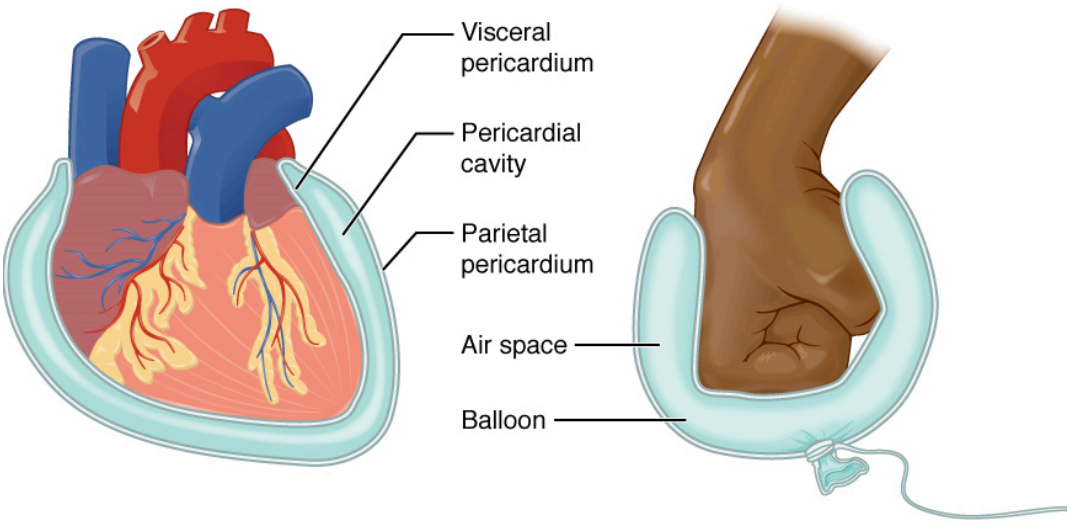


Figure 8. Serous Membrane. *Serous membrane lines the pericardial cavity and reflects back to cover the heart—much the same way that an underinflated balloon would form two layers surrounding a fist.*

The serous membranes form fluid-filled sacs, or cavities, that cushion and reduce friction on internal organs when they move, such as when the lungs inflate or the heart beats. Both the parietal and visceral serosa secrete the thin, slippery serous fluid located within the serous cavities.

The pleural cavity reduces friction between the lungs and the body wall. Likewise, the pericardial cavity reduces friction between the heart and the wall of the pericardium. The peritoneal cavity reduces friction between the abdominal and pelvic organs and the body wall. Therefore, serous membranes provide additional protection to the viscera they enclose by reducing friction that could lead to inflammation of the organs.

Unit 8: Homeostasis

Unit Outline

Part 1: Homeostasis

- Definition
- Conditions maintained by homeostasis
- Internal environment
- Stressors

Part 2: Feedback loops

- Components of a general feedback loop
- Negative feedback examples
- Positive feedback examples

Learning Objectives

At the end of this unit, you should be able to:

I. Explain the importance of homeostasis to physiology and specify three conditions that are maintained by homeostatic processes.

II. Describe the **internal environment** of the human body.

III. Define the term **stressor.**

IV. Define a feedback loop. Explain what is meant by negative and positive feedback systems and describe their role in homeostasis.

Learning Objectives and Guiding Questions

At the end of this unit, you should be able to complete all the following tasks, including answering the guiding questions associated with each task.

I. Explain the importance of homeostasis to physiology and specify three conditions that are maintained by homeostatic processes.

1. Write a definition of homeostasis.
2. State the **three** conditions that are maintained by homeostasis and for each, describe **at least one** consequence to human physiology if that condition deviates from the normal range.

II. Describe the **internal environment** of the human body.

1. Define **internal environment**.
2. Draw an annotated diagram *(a diagram with explanatory labels)* showing extracellular fluid, intracellular fluid, plasma, interstitial fluid and lymph. Be sure to include a label that defines the internal environment.
3. On your diagram, add annotations to describe how substances move between fluid compartments.

III. Define the term **stressor**

1. Write a definition of a stressor.
2. Describe two examples of internal stressors (originate within the body).
3. Describe two examples of external stressors (originate from the external environment).

IV. Define a feedback loop. Explain what is meant by negative and positive feedback systems and describe their role in homeostasis.

1. Write definitions for set point and normal range as they pertain to homeostasis.
2. Draw a flow chart to describe a generalized negative feedback loop including all of the following components: stimulus, receptor, control centre, effector, response. Annotate your flow chart with a description of the role of each of these components in the functioning of a feedback loop.
3. Use appropriate terminology to clearly distinguish between **positive feedback mechanisms** and **negative feedback mechanisms**. *(**Important:** do **NOT** use "shorthand" descriptions for this! Make sure you use appropriate and precise terminology, and complete sentences.)*
4. Use all the terms from question 2, above, along with the specific body structures representing each (where appropriate), to describe in detail:
    - One physiological negative feedback mechanism used in the human body.
    - One physiological positive feedback mechanism used in the human body.
5. Positive feedback mechanisms are likely to continue out of control, and are often associated with disease states. Using your example of a physiological positive feedback mechanisms from the previous question, explain how the positive feedback loop is shut down once the function is served.

Part 1: Homeostasis

Homeostasis refers to a relatively stable set of conditions within an organism's **internal environment**. Within the human body, maintaining a healthy environment for living cells requires maintaining appropriate conditions in the extracellular fluids – including the interstitial fluid and blood plasma – for each living cell to be

able to function properly. The constancy of an internal environment is important in allowing chemical reactions to take place at rates necessary to maintain the body.

Conditions maintained by homeostasis

There are **three important conditions** that must be met in order for the chemical reactions in the body to occur at the rates necessary for homeostasis. The first condition is that there must be a **proper concentration of gases, nutrients, water and salts**. The gases involved are oxygen, which is necessary for the process of cellular respiration which produces energy for the body, and carbon dioxide, which is a waste product of this process, but also must be present in certain amounts for other processes to occur normally. Nutrients provide reactants, enzymes, cofactors and energy for chemical reactions while water and salts determine the fluid balance, electrolyte balance and the pH of the body.

The second important condition for homeostasis is an **optimum temperature** that is about 37°C. The rates of chemical reactions are temperature dependent, occurring slower at cooler temperatures and faster at warmer temperatures. Additionally, the shapes of proteins (remember that proteins fulfill many roles in the body including providing structure, muscle contraction, and enzymatic function, among others) are temperature dependent – if they overheat they may dissociate and be rendered non-functional.

The third and final condition is an **optimum pressure**, for example, blood pressure. The concentrations of various substances in the body and the rates at which these substances move through the body are both dependent on blood pressure. Blood pressure is influenced by the volume of blood in the cardiovascular system, the diameter of the blood vessels and the strength of cardiac muscle contraction.

The Internal Environment

Homeostasis is maintained within the internal environment of the body. The human body is composed of cells surrounded by extracellular material which is mostly fluid. Cells are responsible for controlling bodily activities and also controlling the composition of the material that surrounds them. The **internal environment** is the environment in which cells are found and is thus defined as the fluid inside the body, but outside of cells.

The fluid inside the cells in the body is the **intracellular fluid**, also called cytoplasm (cytosol and the fluid inside organelles). Intracellular fluid makes up approximately 2/3 of the total body fluids.

The fluid outside the cells in the body is the **extracellular fluid**. The internal environment is thus equivalent to the extracellular fluid. Extracellular fluid is found in blood (i.e. plasma), in tissues (i.e. interstitial fluid), in the lymphatic system (i.e. lymph), in joints (i.e. synovial fluid), in the eyes (i.e. aqueous and vitreous humors) and in the central nervous system (i.e cerebrospinal fluid). Extracellular fluid amounts to about 1/3 of the fluids in the body as a whole.

The three main fluid types within the extracellular compartment are plasma, interstitial fluid and lymph. **Plasma** is the liquid portion of blood and functions to move red and white blood cells, platelets, nutrient molecules, gases, electrolytes and wastes throughout the circulatory system. Materials are exchanged at capillary beds where the blood vessel walls are thin enough to allow materials to move between the blood and the tissues.

The fluid that surrounds living cells within tissues is called **interstitial fluid**, which has a unique composition relative to both intracellular fluid and blood plasma. Components of plasma move into the tissues, thus the interstitial fluid is partly derived from the plasma of blood. Interstitial fluid is also in contact with cells and is thus partly derived from the intracellular fluid.

Interstitial fluid must be returned to the circulatory system in order to maintain appropriate pressure within the cardiovascular system and for waste materials from the cells to be removed. However, the interstitial fluid is under lower pressure than the plasma in the capillaries and so only 85% of the interstitial fluid is returned directly back to the circulatory system at the capillaries (mostly as a result of the osmotic gradient, the higher concentration of solutes inside the capillaries "sucks" the water back in). The remaining 15% is returned indirectly through the vessels of another system called the lymphatic system. The fluid in these vessels, now called **lymph**, is derived from tissue fluid but is different from it in composition. Lymph is collected into larger lymphatic vessels that eventually drain into veins close to the heart.

Although the extracellular and intracellular compartments are distinct from one another, there is a continual exchange of materials between them. Cells must receive nutrients, have waste materials taken away and exchange gases. Refer to Unit 5, Cell Membrane Transport to review how substances move between intracellular and extracellular compartments.

Stressors

A constant internal environment is not easily maintained. The internal environment is continually subjected to disturbances that unless counteracted, would quickly cause a new set of conditions in the body that could result in illness or death. A **stressor** is any stimulus that causes an imbalance in the internal environment. Stressors may be factors external to the body or from within the body itself.

Examples of **external stressors** are a lack of environmental oxygen, which may occur at high altitudes or extreme environmental temperatures, such as excessive heat in a desert or excessive cold in the Arctic. Examples of **internal stressors** are rapid changes in blood pressure-hemorrhaging can cause a drop in pressure while unpleasant thoughts may raise blood pressure, or changes in levels of nutrients such as an increase or decrease in blood glucose levels.

Part 2: Feedback loops

Maintaining homeostasis requires that the body continuously monitor its internal conditions. From body temperature to blood pressure to levels of certain nutrients, each physiological condition has a particular set point. A **set point** is the physiological value around which the normal range fluctuates. A **normal range** is the restricted set of values that is optimally healthful and stable. For example, the set point for normal human body temperature is approximately 37°C (98.6°F), however, physiological body temperature tends to fluctuate within a few degrees above and below that set point depending on factors such as activity, digestive function, stress, etc. Control centers in the brain and other parts of the body monitor and react to deviations from homeostasis using negative feedback. **Negative feedback is** a mechanism that reverses a deviation from the set point. Therefore, negative feedback maintains body parameters within their normal range. The maintenance of homeostasis by negative feedback goes on throughout the body at all times, and an understanding of negative feedback is thus fundamental to an understanding of human physiology.

Negative Feedback: Feedback systems have five basic components (Figure 1). A **sensor**, also referred to a receptor, detects when the **stressor/stimulus** produces a deviation in a physiological value away from the set point. This change in value is reported to the control center. The **control center** is the component in a feedback system that compares the value to the normal range. If the value deviates too much from the set point, then the control center activates an effector. An **effector** is the component in a feedback system that produces a **response,** which in the case of a negative feedback loop causes a return of the physiological value to its normal range.

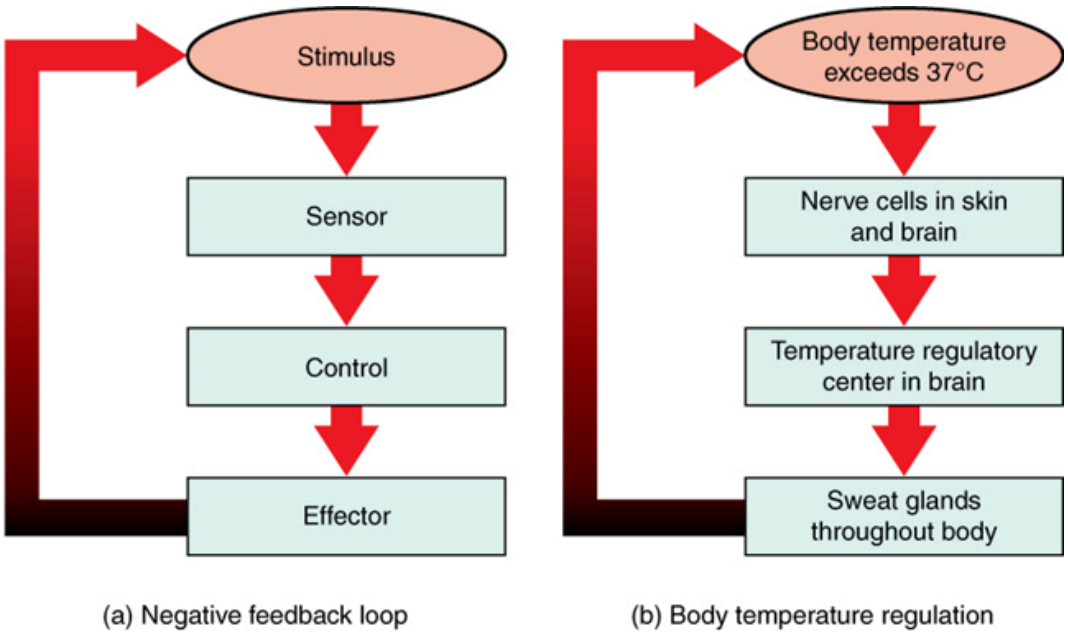


Figure 1. Negative Feedback Loop. *In a negative feedback loop, a stimulus—a deviation from a set point—is resisted through a physiological process that returns the body to homeostasis. (a) A typical negative feedback loop in the body has four basic anatomical parts. (b) Body temperature is regulated by negative feedback.*

For example, in the control of blood glucose, specific endocrine cells (**receptors**) in the pancreas detect excess glucose (**stimulus**) in the bloodstream. These pancreatic beta cells (**control center**) respond to the increased level of blood glucose by releasing the hormone insulin into the bloodstream. The insulin signals skeletal muscle fibers, fat cells (adipocytes), and liver cells (**effectors**) to take up the excess glucose (**response**), removing it from the bloodstream. As glucose concentration in the bloodstream drops, the decrease in concentration — the actual negative feedback (outcome) — is detected by pancreatic beta cells, and insulin release stops. This helps to prevent blood sugar levels from continuing to drop below the normal range.

Humans have a similar temperature regulation feedback system that works by promoting either heat loss or heat gain (Figure 1b). When the brain's temperature regulation center in the hypothalamus receives data from the sensors indicating that the body's temperature exceeds its normal range, it stimulates a cluster of brain cells referred to as the thermoregulatory center. This stimulation has three major effects:

- Blood vessels in the skin begin to dilate allowing more blood from the body core to flow to the surface of the skin allowing the heat to radiate into the environment.
- As blood flow to the skin increases, sweat glands are activated to increase their output. As the sweat evaporates from the skin surface into the surrounding air, it takes heat with it.
- The depth of respiration increases, and a person may breathe through an open mouth instead of through the nasal passageways. This further increases heat loss from the lungs.

In contrast, activation of the thermoregulatory center by exposure to cold reduces blood flow to the skin, and blood returning from the limbs is diverted into a network of deep veins. This arrangement traps heat closer to the body core and restricts heat loss. If heat loss is severe, the hypothalamus triggers an increase in random signals to skeletal muscles, causing them to contract and producing shivering. The muscle contractions of shivering release heat while using up ATP. The brain triggers the thyroid gland in the endocrine system to release thyroid hormone, which increases metabolic activity and heat production in cells throughout the body. The hypothalamus also signals the adrenal glands to release epinephrine (adrenaline), a hormone that causes the breakdown of glycogen into glucose, which can be used as an energy source. The breakdown of glycogen into glucose also results in increased metabolism and heat production.

Watch this OpenStax College video to learn more about water content in the body. Direct link: https://youtu.be/vB7tSHqR1eY

Watch this Crash Course video to learn more about homeostasis! Direct link: https://youtu.be/uBGl2BujkPQ

Positive Feedback: Positive feedback intensifies a change in the body's physiological condition rather than reversing it. Positive feedback loops employ the same five basic components as negative feedback loops, with the difference that a deviation from the normal range results in more change, and the system moves farther away from the normal range. Positive feedback in the body is normal only when there is a definite end point. Childbirth, blood clotting and micturition are some examples of physiological positive feedback loops (there are a number of other examples in immunity, in female reproductive cycles and at the level of cellular function).

Childbirth at full term is an example of a situation in which the maintenance of the existing body state is not desired. Enormous changes in the mother's body are required to expel the baby at the end of pregnancy. And the events of childbirth, once begun, must progress rapidly to a conclusion or the life of the mother and the baby are at risk. The extreme muscular work of labor and delivery are the result of a positive feedback system (Figure 2).

The first contractions of labor (the stimulus) push the baby toward the cervix (the lowest part of the uterus). The cervix contains stretch-sensitive nerve cells that monitor the degree of stretching (the sensors). These nerve cells send messages to the brain, which in turn causes the pituitary gland at the base of the brain (the control center) to release the hormone oxytocin into the bloodstream. Oxytocin causes stronger contractions of the smooth muscles in of the uterus (the effectors), pushing the baby further down the birth canal. This causes even greater stretching of the cervix (the response). The cycle of stretching, oxytocin release, and increasingly more forceful contractions stops only when the baby is born. At this point, the stretching of the cervix halts, stopping the release of oxytocin.

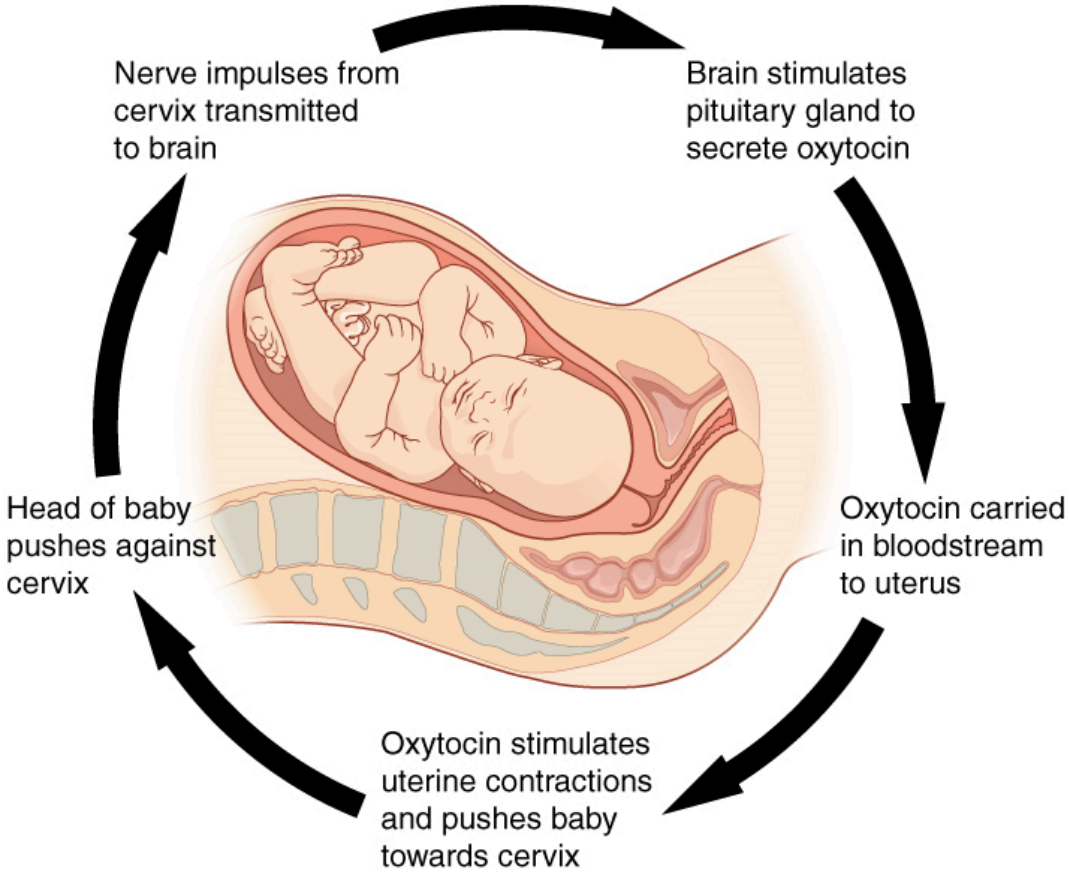


Figure 2. Positive Feedback Loop. *Normal childbirth is driven by a positive feedback loop. A positive feedback loop results in a change in the body's status, rather than a return to homeostasis.*

A second example of positive feedback centers on reversing extreme damage to the body. Following a penetrating wound, the most immediate threat is excessive blood loss. Less blood circulating means reduced blood pressure and reduced perfusion (penetration of blood) to the brain and other vital organs. If perfusion is severely reduced, vital organs will shut down and the person will die. The body responds to this potential catastrophe by releasing substances in the injured blood vessel wall that begin the process of blood clotting. As each step of clotting occurs, it stimulates the release of more clotting substances. This accelerates the processes of clotting and sealing off the damaged area. Clotting is contained in a local area based on the tightly controlled availability of clotting proteins. This is an adaptive, life-saving cascade of events.

NERVOUS REGULATION AND INTEGRATION

Unit 9: The Nervous System

Unit Outline

Part 1: The Anatomical and Functional Organization of the Nervous System

- Anatomical Divisions
- Functional Divisions

Part 2: Nervous Tissue

- Neurons
- Glial cells
- Myelin

Part 3: The Central Nervous System

- The Brain
- The Spinal Cord
- The Meninges
- The Ventricular System and Cerebrospinal Fluid Circulation

Part 4: The Peripheral Nervous System

- Ganglia
- Nerves
- The Somatic Nervous System
- The Autonomic Nervous System

Part 5: Neuronal Signalling

- Ion channels and the Resting Membrane Potential
- Generation of an Action Potential
- Propagation of Action Potentials
- Neurotransmission

Learning Objectives

At the end of this unit, you should be able to:

I. Describe the organization of the nervous system and explain the functions of its principal components.

II. Describe the structure of the following: neuron, glia, ganglion, nerve, gray matter, tract, white matter, sensory neuron, motor neuron.

III. Name, locate and describe the functions of the main areas of the human brain.

IV. Describe the structure and explain the functions of the spinal cord.

V. Describe the components of a reflex arc and explain how a reflex arc works.

VI. Describe the function of the autonomic nervous system (ANS) and compare the specific functions of the parasympathetic and sympathetic divisions of the ANS.

VII. Describe the resting membrane potential of a neuron and explain how it is maintained.

VIII. Explain how a neuronal action potential is generated.

IX. Explain how neuronal action potentials travel down the axon.

X. Explain the process of neurotransmission, and name three different neurotransmitters.

Learning Objectives and Guiding Questions

At the end of this unit, you should be able to complete all the following tasks, including answering the guiding questions associated with each task.

I. Describe the organization of the nervous system and explain the functions of its principal components.

1. Draw a flow chart demonstrating the relationships between, and stating the main function of each of the following components of the nervous system:
    - Central nervous system
    - Peripheral nervous system
    - Sensory neurons
    - Motor neurons
    - Somatic nervous system
    - Autonomic nervous system
    - Sympathetic nervous system
    - Parasympathetic nervous system
2. Are the twelve cranial nerves considered part of the central nervous system, or the peripheral nervous system? Explain how you know.
3. Are the dorsal root ganglia considered part of the central or peripheral nervous system? Explain how you know.

II. Describe the structure of the following: neuron, glia, ganglion, nerve, gray matter, tract, white matter, sensory neuron, motor neuron.

1. Name the parts of a typical neuron and describe their functions.
2. Compare and contrast the location, structure, and function of:
    - Neurons and glia
    - Nerves and tracts
    - White matter and nerves
    - White matter and gray matter
    - Nerves and ganglia
    - Ganglia and gray matter
    - Sensory and motor neurons

III. Name, locate and describe the functions of the main areas of the human brain.

1. Describe the general anatomy of the brain, including the location of the lobes.
2. Where in the brain would you find the cell bodies of neurons? Where would you find their axons? Describe how you can tell just by looking at a (cut) brain with the naked eye.
3. Describe the location and function of each of the following areas of the human brain:
    - Cerebrum
    - Diencephalon
    - Thalamus
    - Hypothalamus
    - Brain stem
    - Midbrain
    - Pons
    - Medulla oblongata
    - Cerebellum
4. What are the names of the three meninges, and where are they located?
5. What are the names of the four ventricles, and where are they located?
6. Describe the path taken by cerebrospinal fluid through the brain.

IV. Describe the structure and explain the functions of the spinal cord.

1. Where in the spinal cord would you find the cell bodies of neurons? Where would you find their axons? Describe how you can tell just by looking at a (cut) spinal cord with the naked eye.
2. What are some of the functions of the spinal cord?

V. Describe the components of a reflex arc and explain how a reflex arc works.

1. Describe the events that take place from the moment the knee is tapped to the moment when the leg extends during the patellar reflex, including the role of each of the structures involved.

VI. Describe the function of the autonomic nervous system (ANS) and compare the specific functions of the parasympathetic and sympathetic divisions of the ANS.

1. Compare the sympathetic and parasympathetic nervous system based on the:
    - Physiological situation to which they respond
    - Location and neurotransmitter of the central (preganglionic) neuron

- Location and neurotransmitter of the ganglionic neuron

VII. Describe the resting membrane potential of a neuron and explain how it is maintained.

1. Describe the gating mechanism of ligand-gated, voltage-gated, mechanically-gated and leakage ion channels.
2. What is the typical resting membrane potential of an animal cell, and what factors contribute to it?

VIII. Explain how a neuronal action potential is generated.

1. Draw a fully annotated figure plotting membrane potential vs. time as an action potential passes a specific location in an axon's membrane. Include in your annotations labels explaining the main mechanisms that underlie each shift in membrane potential.

IX. Explain how neuronal action potentials travel down the axon.

1. Compare the mechanism by which nerve impulses are conducted in unmyelinated and myelinated axons.

X. Explain the process of neurotransmission, and name three different neurotransmitters.

1. Create an annotated diagram (or series of diagrams) showing how neurons communicate with each other:
2. Describe the mechanism by which an action potential travels from the cell body to the axon terminals of a neuron.
3. Describe the mechanisms that return a neuron to its resting state (resting membrane potential) once an action potential has passed.
4. Describe the intracellular events that occur in a neuron once an action potential reaches a synaptic end bulb.
5. Describe how an excitatory neurotransmitter causes an action potential to be produced in a postsynaptic cell.
6. Name at least three specific neurotransmitters: one from the cholinergic system, one amino acid that acts as a neurotransmitter, and one neuropeptide.
7. What factor(s) determines whether a neurotransmitter has an excitatory or inhibitory effect on a cell exposed to that neurotransmitter?

Part 1: Anatomical and Functional Organization of the Nervous System

The picture you have in your mind of the nervous system probably includes the **brain**, the nervous tissue contained within the cranium, and the **spinal cord**, the extension of nervous tissue within the vertebral column. That suggests it is made of two organs—and you may not even think of the spinal cord as an organ—but the nervous system is a very complex structure. Within the brain, many different and separate regions are responsible for many different and separate functions. It is as if the nervous system is composed of many organs that all look similar and can only be differentiated using tools such as the microscope or electrophysiology. In comparison, it is easy to see that the stomach is different than the esophagus or the liver, so you can imagine the digestive system as a collection of specific organs.

Anatomical Divisions

The nervous system can be divided into two major regions: the central and peripheral nervous systems. The **central nervous system (CNS)** is the brain and spinal cord, and the **peripheral nervous system (PNS)** is everything else (Figures 1 and 2). The brain is contained within the cranial cavity of the skull, and the spinal cord is contained within the vertebral cavity of the vertebral column. It is a bit of an oversimplification to say that the CNS is what is inside these two cavities and the peripheral nervous system is outside of them, but that is one way to start to think about it. In actuality, there are some elements of the peripheral nervous system that are within the cranial or vertebral cavities. The peripheral nervous system is so named because it is on the periphery—meaning beyond the brain and spinal cord. Depending on different aspects of the nervous system, the dividing line between central and peripheral is not necessarily universal.

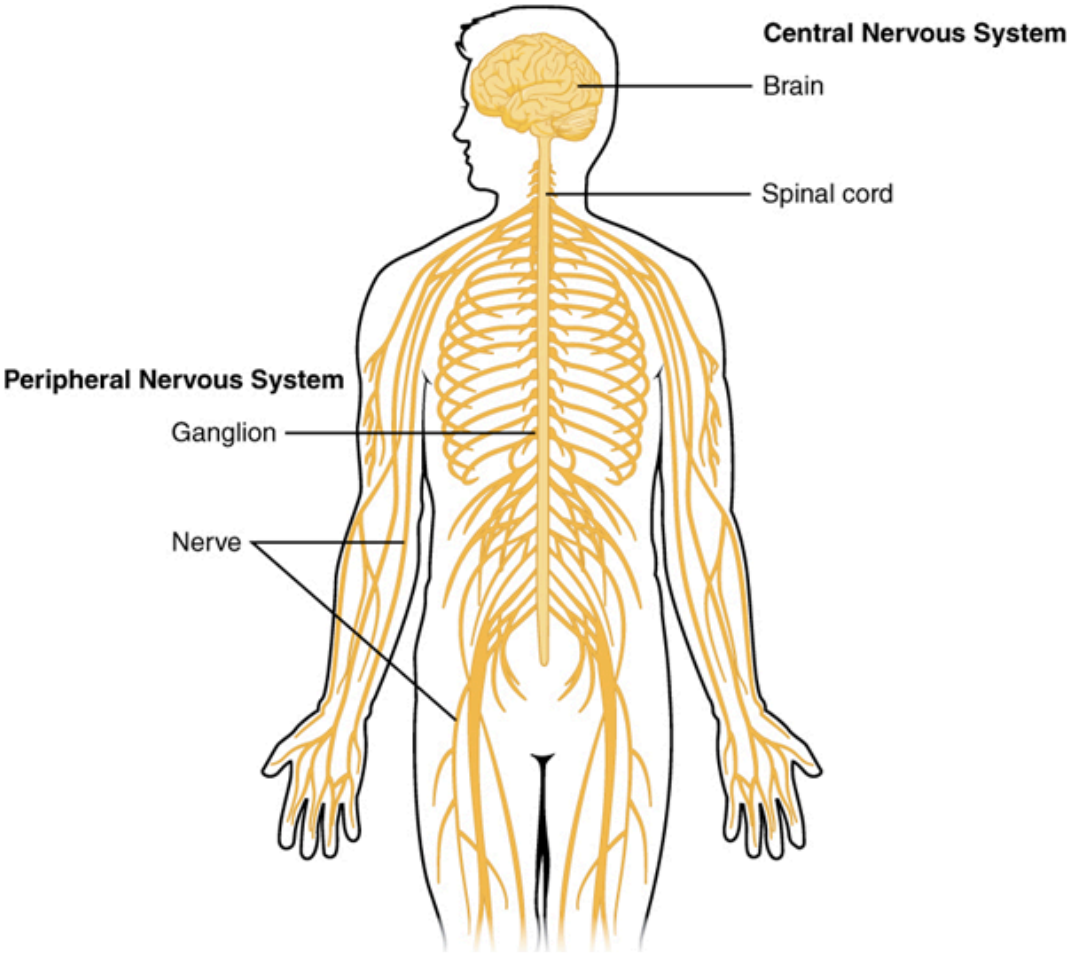


Figure 1. Central and Peripheral Nervous System. *The structures of the PNS are referred to as ganglia and nerves, which can be seen as distinct structures. The equivalent structures in the CNS are not obvious from this overall perspective and are best examined in prepared tissue under the microscope.*

Nervous tissue, present in both the CNS and PNS, contains two basic types of cells: neurons and glial (or neuroglial) cells. A **glial cell** is one of a variety of cells that provide a framework of tissue that supports the neurons and their activities. The **neuron** is the more functionally important of the two, in terms of the communicative function of the nervous system. To describe the functional divisions of the nervous system, it is important to understand the structure of a neuron. Neurons are cells and therefore have a **soma**, or cell body, but they also have extensions of the cell; each extension is generally referred to as a **process**. There is one important process that every neuron has called an **axon**, which is the fiber that connects a neuron with its target. Another type of process that branches off from the soma is the dendrite.

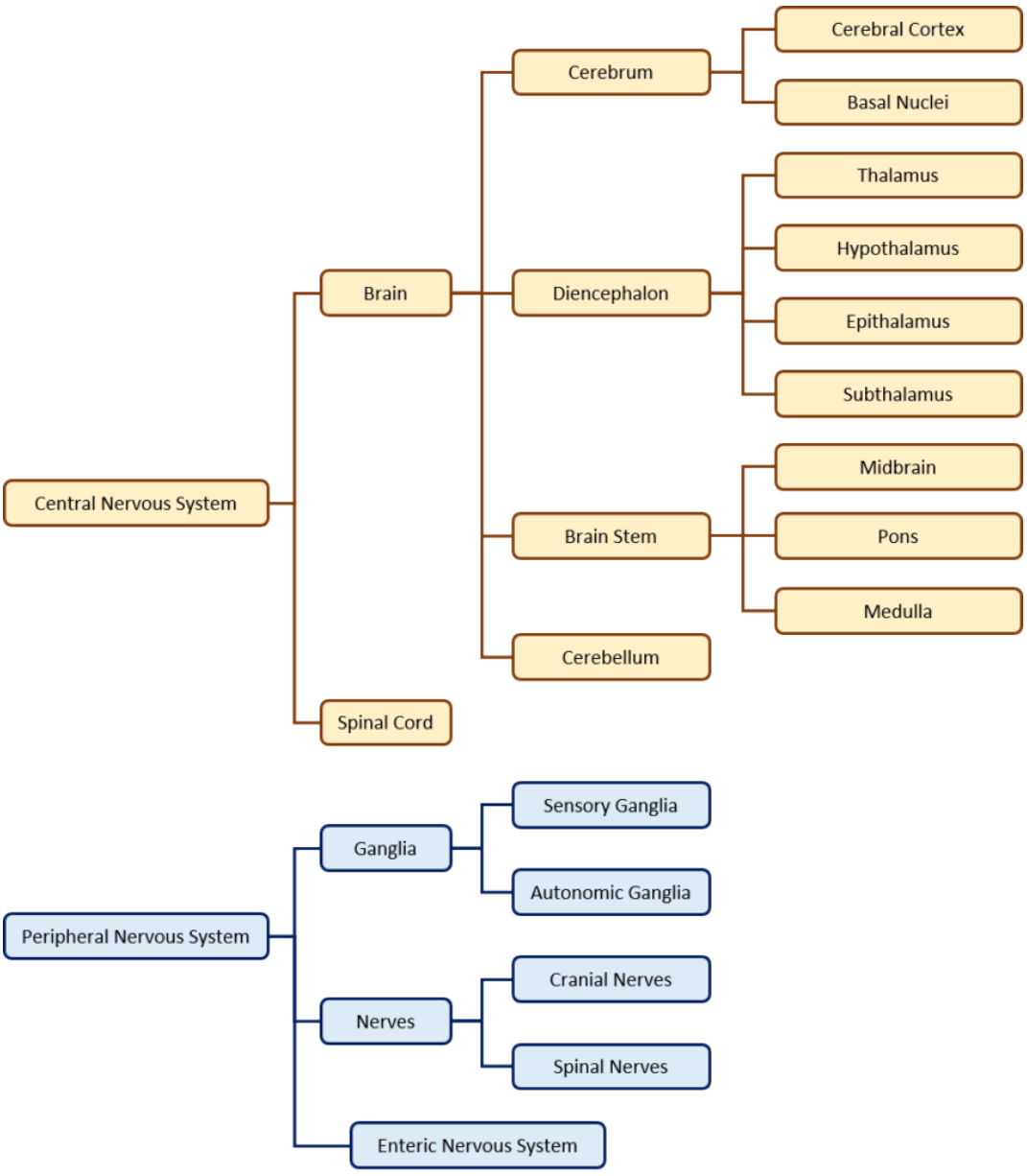


Figure 2. The Anatomical Organization of the Nervous System.

Dendrites are responsible for receiving most of the input from other neurons. Looking at nervous tissue, there are regions that predominantly contain cell bodies and regions that are largely composed of just axons.

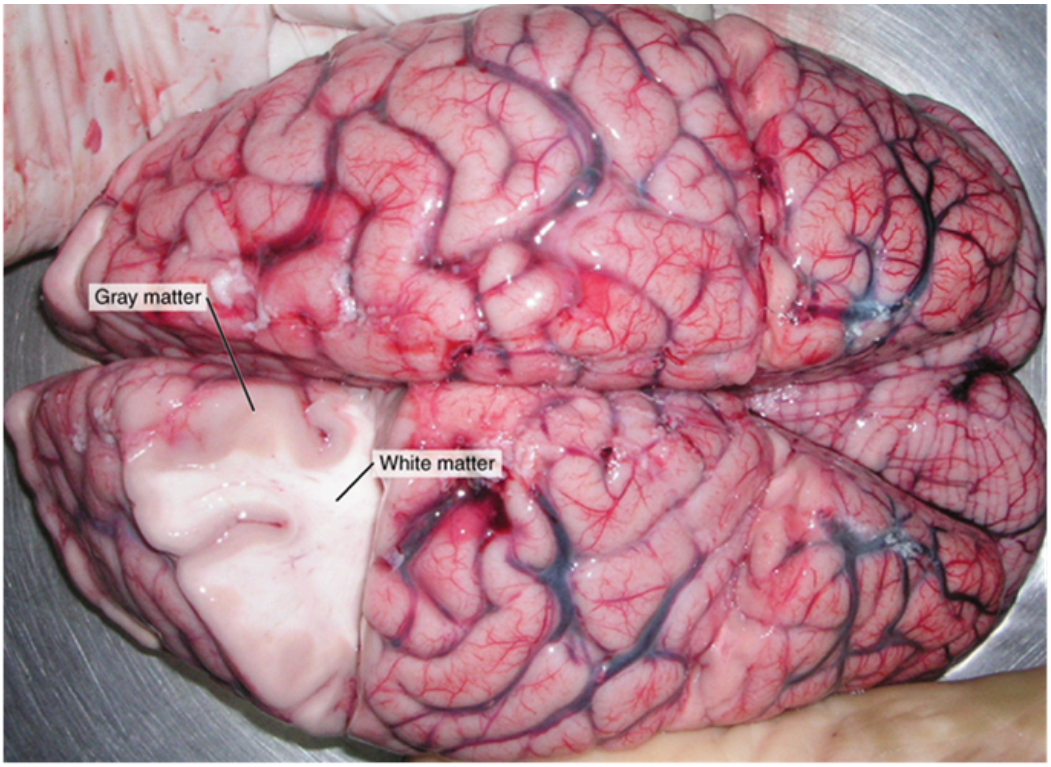


Figure 3. Gray Matter and White Matter. *A brain removed during an autopsy, with a partial section removed, shows white matter surrounded by gray matter. Gray matter makes up the outer cortex of the brain. (credit: modification of work by "Suseno"/ Wikimedia Commons)*

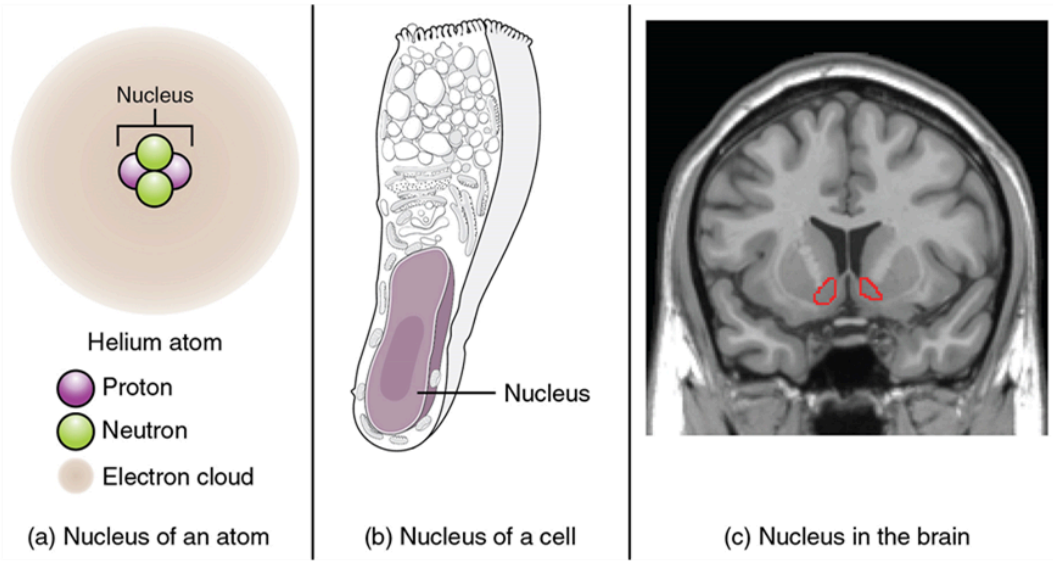


Figure 4. What Is a Nucleus? *(a) The nucleus of an atom contains its protons and neutrons. (b) The nucleus of a cell is the organelle that contains DNA. (c) A nucleus in the CNS is a localized center of function with the cell bodies of several neurons, shown here circled in red. (credit c: "Was a bee"/Wikimedia Commons)*

These two regions within nervous system structures are often referred to as **gray matter** (the regions with many cell bodies and dendrites) or **white matter** (the regions with many axons). The colors ascribed to these regions are what would be seen in "fresh," or unstained, nervous tissue (Figure 3). Gray matter is not necessarily gray. It can be pinkish because of blood content, or even slightly tan, depending on how long the tissue has been preserved. But white matter is white because axons are insulated by a lipid-rich substance called **myelin**. Lipids

can appear as white ("fatty") material, much like the fat on a raw piece of chicken or beef. Actually, gray matter may have that color ascribed to it because next to the white matter, it is just darker—hence, gray.

The distinction between gray matter and white matter is most often applied to central nervous tissue, which has large regions that can be seen with the unaided eye. When looking at peripheral structures, often a microscope is used and the tissue is stained with artificial colors. That is not to say that central nervous tissue cannot be stained and viewed under a microscope, but unstained tissue is most likely from the CNS—for example, a frontal section of the brain or cross section of the spinal cord.

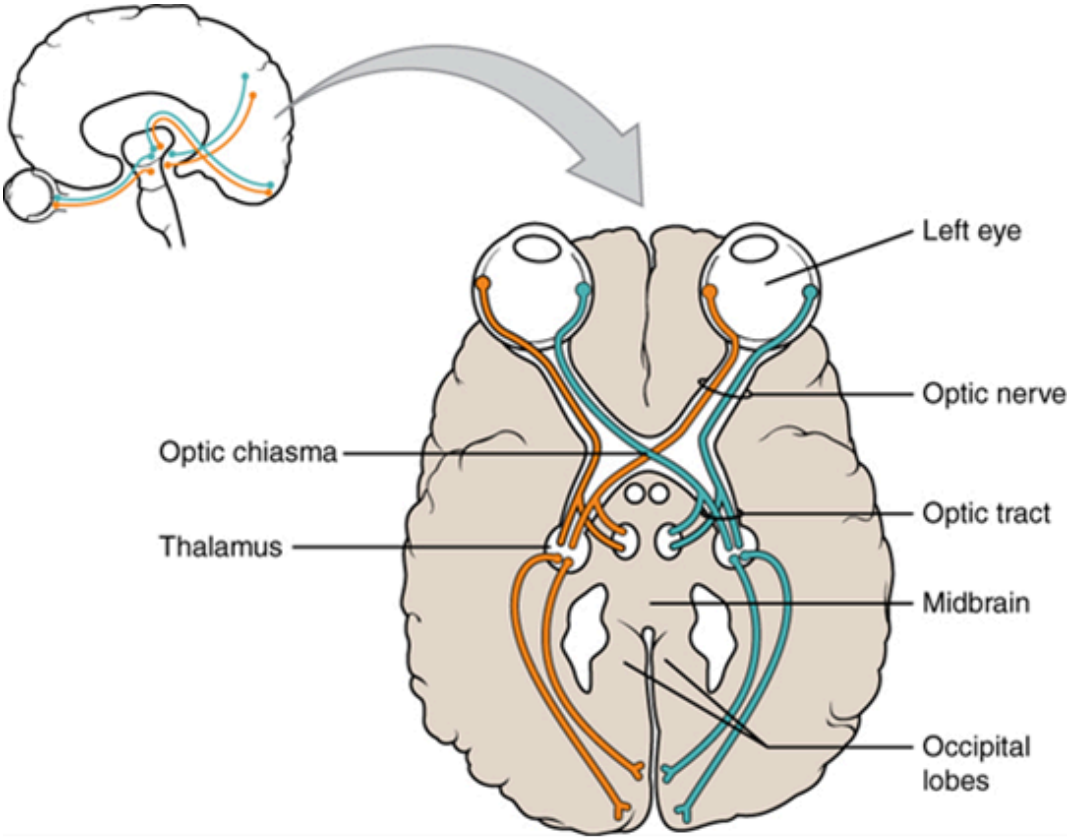


Figure 5. Optic Nerve Versus Optic Tract. *This drawing of the connections of the eye to the brain shows the optic nerve extending from the eye to the chiasm, where the structure continues as the optic tract. The same axons extend from the eye to the brain through these two bundles of fibers, but the chiasm represents the border between peripheral and central.*

Regardless of the appearance of stained or unstained tissue, the cell bodies of neurons or axons can be located in discrete anatomical structures that need to be named. Those names are specific to whether the structure is central or peripheral. A localized collection of neuron cell bodies in the CNS is referred to as a **nucleus**. In the PNS, a cluster of neuron cell bodies is referred to as a **ganglion**. The term nucleus has a few different meanings within anatomy and physiology. It is the center of an atom, where protons and neutrons are found; it is the center of a cell, where the DNA is found; and it is a center of some function in the CNS (Figure 4). There is also a potentially confusing use of the word ganglion (plural = ganglia) that has a historical explanation. In the central nervous system, there is a group of nuclei that are connected together and were once called the basal ganglia before "ganglion" became accepted as a description for a peripheral structure. Some sources refer to this group of nuclei as the "basal nuclei" to avoid confusion.

Table 1: Structures of the Central and Peripheral Nervous System

	CNS	PNS
Group of neuron cell bodies (i.e., gray matter)	Nucleus	Ganglion
Bundle of axons (i.e., white matter)	Tract	Nerve

Terminology applied to bundles of axons also differs depending on location. A bundle of axons, or fibers, found in the CNS is called a **tract** whereas the same thing in the PNS would be called a **nerve**. There is an important point to make about these terms, which is that they can both be used to refer to the same bundle of axons. When those axons are in the PNS, the term is nerve, but if they are CNS, the term is tract. The most obvious example of this is the axons that project from the retina into the brain. Those axons are called the optic nerve as they leave the eye, but when they are inside the cranium, they are referred to as the optic tract. There is a specific place where the name changes, which is the optic chiasm, but they are still the same axons (Figure 5). A similar situation outside of science can be described for some roads. For example, you might know of a street named Canada Way in the city of Burnaby. If you travel south long enough on this road, eventually you will leave Burnaby and enter the city of New Westminster. In New Westminster, Canada Way changes its name to Eighth Street. That is the idea behind the naming of the retinal axons. In the PNS, they are called the optic nerve, and in the CNS, they are the optic tract. Table 1 helps to clarify which of these terms apply to the central or peripheral nervous systems.

Functional Divisions

There are two ways to consider how the nervous system is divided functionally. First, the basic functions of the nervous system are sensation, integration, and response. Secondly, control of the body can be somatic or autonomic—divisions that are largely defined by the structures that are involved in the response (Figure 6). There is also a region of the peripheral nervous system that is called the enteric nervous system that is responsible for a specific set of the functions within the realm of autonomic control related to gastrointestinal functions.

Basic Functions: Sensation, Integration, and Response

The nervous system is involved in receiving information about the environment around us (sensation) and generating responses to that information (motor responses). The nervous system can be divided into regions that are responsible for **sensation** (sensory functions) and for the **response** (motor functions). But there is a third function that needs to be included. Sensory input needs to be integrated with other sensations, as well as with memories, emotional state, or learning (cognition). Some regions of the nervous system are termed **integration** or association areas. The process of integration combines sensory perceptions and higher cognitive functions such as memories, learning, and emotion to produce a response.

The first major function of the nervous system is **sensation**—receiving information about the environment to gain input about what is happening outside the body (or, sometimes, within the body). The sensory functions of the nervous system register the presence of a particular event in the external or internal environment, known as a **stimulus**. The senses we think of most are the "big five": taste, smell, touch, sight, and hearing. The stimuli for taste and smell are both chemical substances (molecules, compounds, ions, etc.), touch is physical or mechanical stimuli that interact with the skin, sight is light stimuli, and hearing is the perception of sound,

which is a physical stimulus similar to some aspects of touch. There are actually more senses than just those, but that list represents the major senses. Those five are all senses that receive stimuli from the outside world, and of which there is conscious perception. Additional sensory stimuli might be from the internal environment (inside the body), such as the stretch of an organ wall or the concentration of certain ions in the blood.

Stimuli that are received by sensory structures are communicated to the nervous system where that information is processed. This is called **integration**. Stimuli are compared with, or integrated with, other stimuli, memories of previous stimuli, or the state of a person at a particular time. This leads to the specific response that will be generated. Seeing a baseball pitched to a batter will not automatically cause the batter to swing. The trajectory of the ball and its speed will need to be considered. Maybe the count is three balls and one strike, and the batter wants to let this pitch go by in the hope of getting a walk to first base. Or maybe the batter's team is so far ahead, it would be fun to just swing away.

The nervous system produces a **response** on the basis of the stimuli perceived by sensory structures. An obvious response would be the movement of muscles, such as withdrawing a hand from a hot stove, but there are broader uses of the term. The nervous system can cause the contraction of all three types of muscle tissue. For example, skeletal muscle contracts to move the skeleton, cardiac muscle is influenced as heart rate increases during exercise, and smooth muscle contracts as the digestive system moves food along the digestive tract. Responses also include the neural control of glands in the body as well, such as the production and secretion of sweat by the eccrine and merocrine sweat glands found in the skin to lower body temperature.

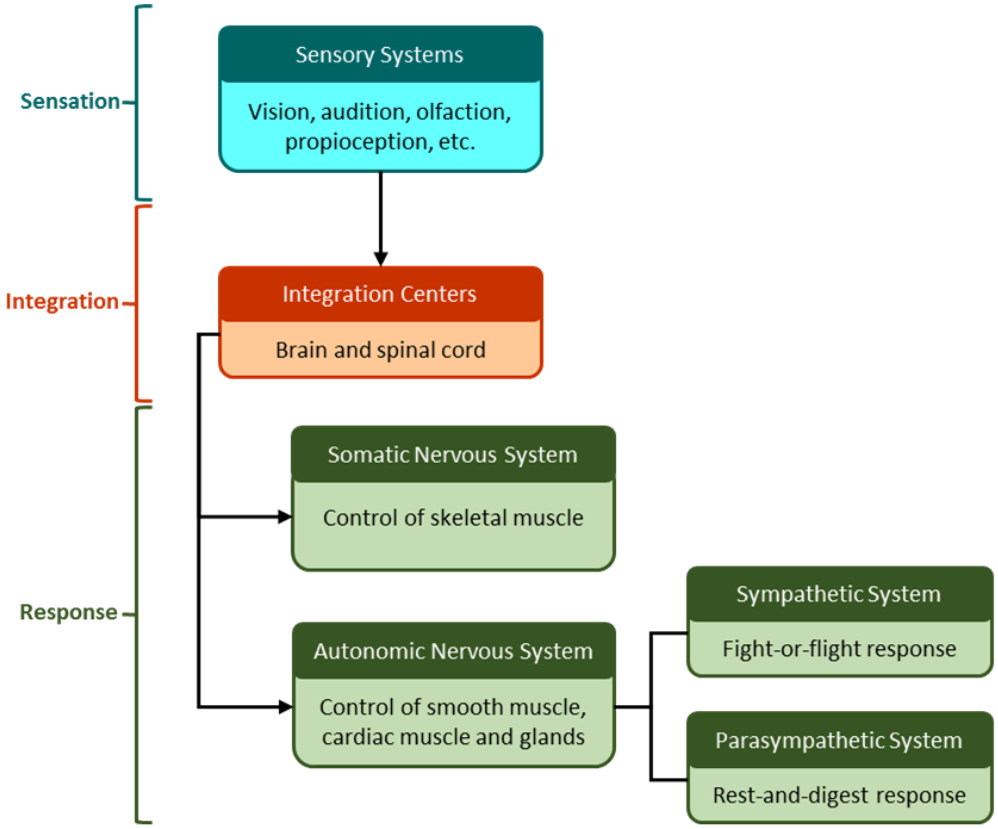


Figure 6. The Functional Organization of the Nervous System. *The diagram represents the divisions of the nervous system involved in each of the basic functions: sensation (receiving and processing information from the external and internal environment), integration (comparing the sensory input with stored information and with other sensory inputs in order for the body to react appropriately) and response (most commonly, a motor command generated by the somatic nervous system or the autonomic nervous system).*

Responses can be divided into those that are voluntary or conscious (contraction of skeletal muscle) and those that are involuntary (contraction of smooth muscles, regulation of cardiac muscle, activation of glands). Voluntary responses are governed by the somatic nervous system and involuntary responses are governed by the autonomic nervous system, which are discussed in the next section.

Somatic, Autonomic and Enteric Nervous Systems

The nervous system can be divided into two parts mostly on the basis of a functional difference in responses. The **somatic nervous system (SNS)** is responsible for conscious perception and voluntary motor responses. Voluntary motor response means the contraction of skeletal muscle, but those contractions are not always voluntary in the sense that you have to want to perform them. Some somatic motor responses are reflexes, and often happen without a conscious decision to perform them. If your friend jumps out from behind a corner and yells "Boo!" you will be startled and you might scream or leap back. You didn't decide to do that, and you may not have wanted to give your friend a reason to laugh at your expense, but it is a reflex involving skeletal muscle contractions. Other motor responses become automatic (in other words, unconscious) as a person learns motor skills (referred to as "habit learning" or "procedural memory").

The **autonomic nervous system (ANS)** is responsible for involuntary control of the body, usually for the sake of homeostasis (regulation of the internal environment). Sensory input for autonomic functions can be from sensory structures tuned to external or internal environmental stimuli. The motor output extends to smooth and cardiac muscle as well as glandular tissue. The role of the autonomic system is to regulate the organ systems of the body, which usually means to control homeostasis. Sweat glands, for example, are controlled by the autonomic system. When you are hot, sweating helps cool your body down. That is a homeostatic mechanism. But when you are nervous, you might start sweating also. That is not homeostatic, it is the physiological response to an emotional state.

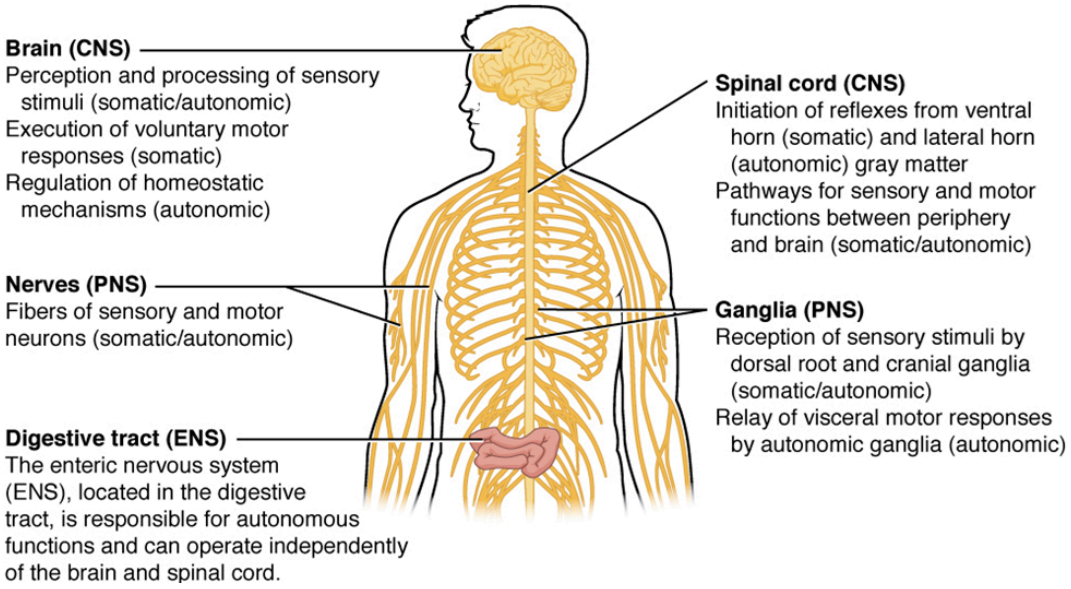


Figure 7. Somatic, Autonomic, and Enteric Structures of the Nervous System. *Somatic structures include the spinal nerves, both motor and sensory fibers, as well as the sensory ganglia (posterior root ganglia and cranial nerve ganglia). Autonomic structures are found in the nerves also, but include the sympathetic and parasympathetic ganglia. The enteric nervous system includes the nervous tissue within the organs of the digestive tract.*

There is another division of the nervous system that describes functional responses. The **enteric nervous system (ENS)** is responsible for controlling the smooth muscle and glandular tissue in your digestive system. It is a large part of the PNS, and is not dependent on the CNS. It is sometimes valid, however, to consider the enteric system to be a part of the autonomic system because the neural structures that make up the enteric system are a component of the autonomic output that regulates digestion (Figure 7). There are some differences between the two, but for our purposes here there will be a good bit of overlap.

Watch this Crash Course video for an overview of the nervous system! Direct link: https://youtu.be/qPix_X-9t7E

Part 2: Nervous Tissue

Nervous tissue is composed of two types of cells, neurons and glial cells. Neurons are the primary type of cell that most anyone associates with the nervous system. They are responsible for the computation and communication that the nervous system provides. They are electrically active and release chemical signals to target cells. Glial cells, or glia, are known to play a supporting role for nervous tissue. Ongoing research pursues an expanded role that glial cells might play in signaling, but neurons are still considered the basis of this function. Neurons are important, but without glial support they would not be able to perform their function.

Neurons

Neurons are the cells considered to be the basis of nervous tissue. They are responsible for the electrical signals that communicate information about sensations, and that produce movements in response to those stimuli, along with inducing thought processes within the brain. An important part of the function of neurons is in their structure, or shape. The three-dimensional shape of these cells makes the immense numbers of connections within the nervous system possible.

Parts of a Neuron

As you learned in the first section, the main part of a neuron is the cell body, which is also known as the soma (soma = "body"). The cell body contains the nucleus and most of the major organelles. But what makes neurons special is that they have many extensions of their cell membranes, which are generally referred to as processes. Neurons are usually described as having one, and only one, axon—a fiber that emerges from the cell body and projects to target cells (Figure 8). That single axon can branch repeatedly to communicate with many target cells. It is the axon that propagates the nerve impulse, which is communicated to one or more cells. The other processes of the neuron are dendrites (Figure 8), which receive information from other neurons at specialized areas of contact called synapses. The dendrites are usually highly branched processes, providing locations for other neurons to communicate with the cell body. Information flows through a neuron from the dendrites, across the cell body, and down the axon. This gives the neuron a polarity—meaning that information flows in this one direction.

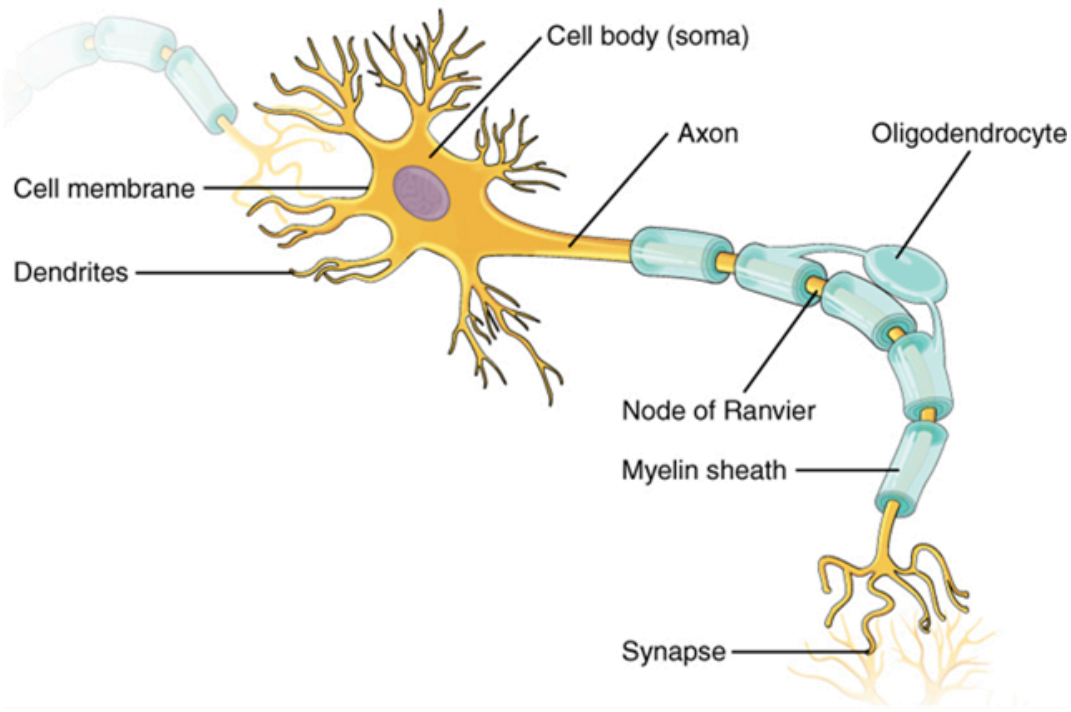


Figure 8. Parts of a Neuron. *The major parts of the neuron are labeled on a multipolar neuron from the CNS.*

Where the axon emerges from the cell body, there is a special region referred to as the axon hillock. This is a tapering of the cell body toward the axon fiber. Within the axon hillock, the cytoplasm changes to a solution of limited components called axoplasm. Because the axon hillock represents the beginning of the axon, it is also referred to as the initial segment.

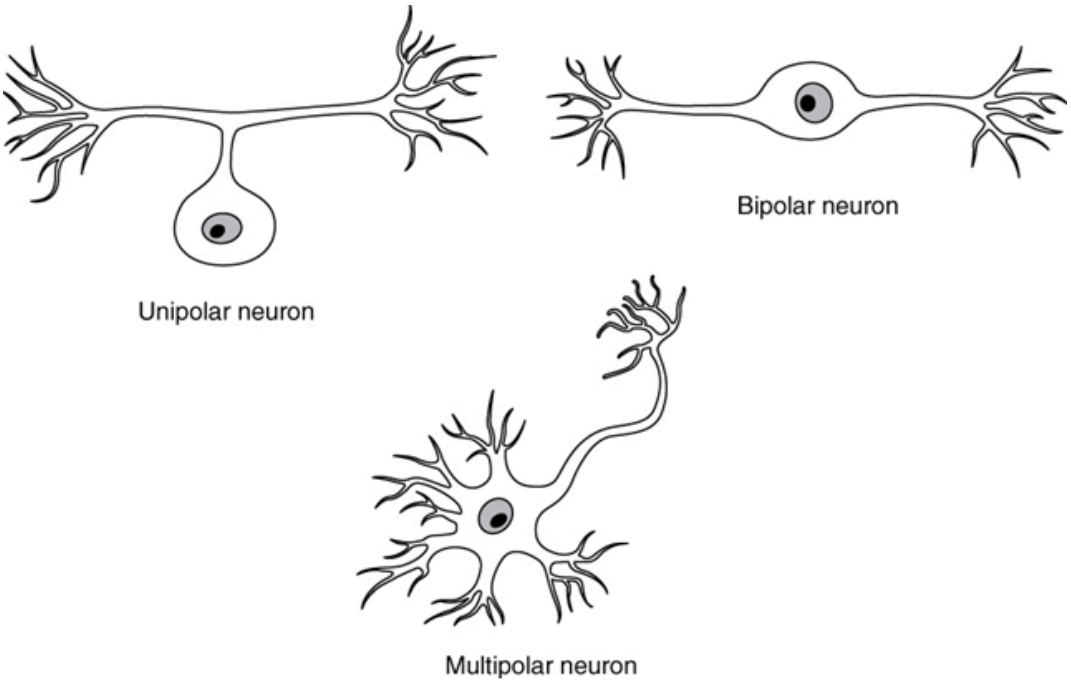


Figure 9. Neuron Classification by Shape. *Unipolar cells have one process that includes both the axon and dendrite. Bipolar cells have two processes, the axon and a dendrite. Multipolar cells have more than two processes, the axon and two or more dendrites.*

Many axons are wrapped by an insulating substance called myelin, which is actually made from glial cells.

Myelin acts as insulation much like the plastic or rubber that is used to insulate electrical wires. A key difference between myelin and the insulation on a wire is that there are gaps in the myelin covering of an axon. Each gap is called a node of Ranvier and is important to the way that electrical signals travel down the axon. The length of the axon between each gap, which is wrapped in myelin, is referred to as an axon segment. At the end of the axon is the axon terminal, where there are usually several branches extending toward the target cell, each of which ends in an enlargement called a synaptic end bulb. These bulbs are what make the connection with the target cell at the synapse.

Types of Neurons

There are many neurons in the nervous system—a number in the trillions. And there are many different types of neurons. They can be classified by many different criteria. The first way to classify them is by the number of processes attached to the cell body. Using the standard model of neurons, one of these processes is the axon, and the rest are dendrites. Because information flows through the neuron from dendrites or cell bodies toward the axon, these names are based on the neuron's polarity (Figure 9).

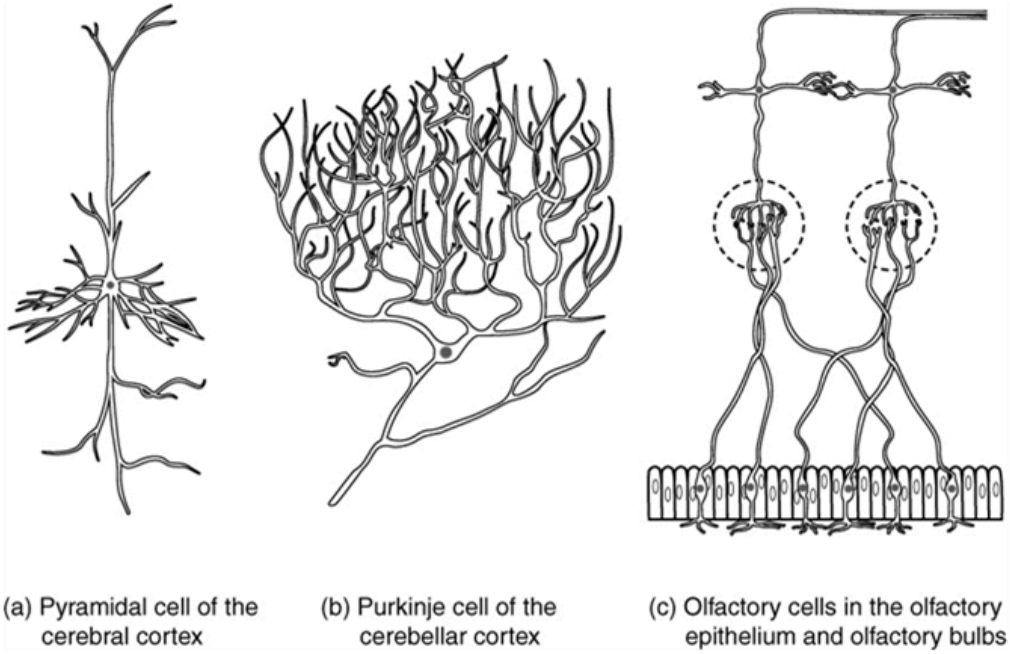


Figure 10. Other Neuron Classifications. *Three examples of neurons that are classified on the basis of other criteria. (a) The pyramidal cell is a multipolar cell with a cell body that is shaped something like a pyramid. (b) The Purkinje cell in the cerebellum was named after the scientist who originally described it. (c) Olfactory neurons are named for the functional group with which they belong.*

Neurons can also be classified on the basis of where they are found, who found them, what they do, or even what chemicals they use to communicate with each other. Some neurons referred to in this section on the nervous system are named on the basis of those sorts of classifications (Figure 10). For example, a multipolar neuron that has a very important role to play in a part of the brain called the cerebellum is known as a Purkinje (commonly pronounced per-KIN-gee) cell. It is named after the anatomist who discovered it (Jan Evangilista Purkinje, 1787–1869).

Glial Cells

Glial cells, or neuroglia or simply glia, are the other type of cell found in nervous tissue. They are considered to be supporting cells, and many functions are directed at helping neurons complete their function for communication. The name glia comes from the Greek word that means "glue," and was coined by the German pathologist Rudolph Virchow, who wrote in 1856: "This connective substance, which is in the brain, the spinal cord, and the special sense nerves, is a kind of glue (neuroglia) in which the nervous elements are planted." Today, research into nervous tissue has shown that there are many deeper roles that these cells play. And research may find much more about them in the future.

Table 2: Glial Cell Types by Location and Basic Function

CNS glia	PNS glia	Basic function
Astrocyte	Satellite cell	Support
Oligodendrocyte	Schwann cell	Insulation, myelination
Microglia	–	Immune surveillance, phagocytosis
Ependymal cell	–	Creating cerebrospinal fluid

There are six types of glial cells (Table 2). Four of them are found in the CNS (Figure 11) and two are found in the PNS (Figure 12). For reference, Table 2 outlines some common characteristics and functions of the various glial cell types, but the specific names and roles of the glial cell types are not examinable material in this course.

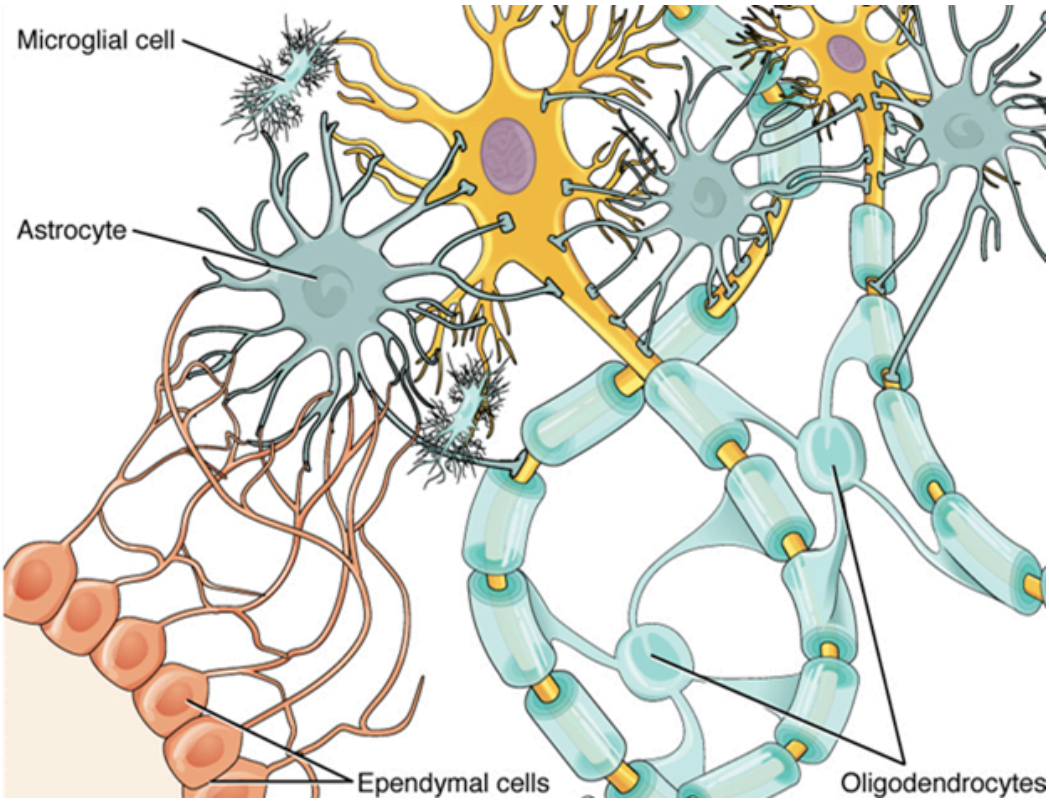


Figure 11. Glial Cells of the CNS. *The CNS has astrocytes, oligodendrocytes, microglia, and ependymal cells that support the neurons of the CNS in several ways.*

Myelin

The insulation for axons in the nervous system is provided by glial cells: oligodendrocytes in the CNS, and Schwann cells in the PNS. Whereas the manner in which either cell is associated with the axon segment, or segments, that it insulates is different, the means of myelinating an axon segment is mostly the same in the two situations. Myelin is a lipid-rich sheath that surrounds the axon and by doing so creates a myelin sheath that facilitates the transmission of electrical signals along the axon. The lipids are essentially the phospholipids of the glial cell membrane. Myelin, however, is more than just the membrane of the glial cell. It also includes important proteins that are integral to that membrane. Some of the proteins help to hold the layers of the glial cell membrane closely together.

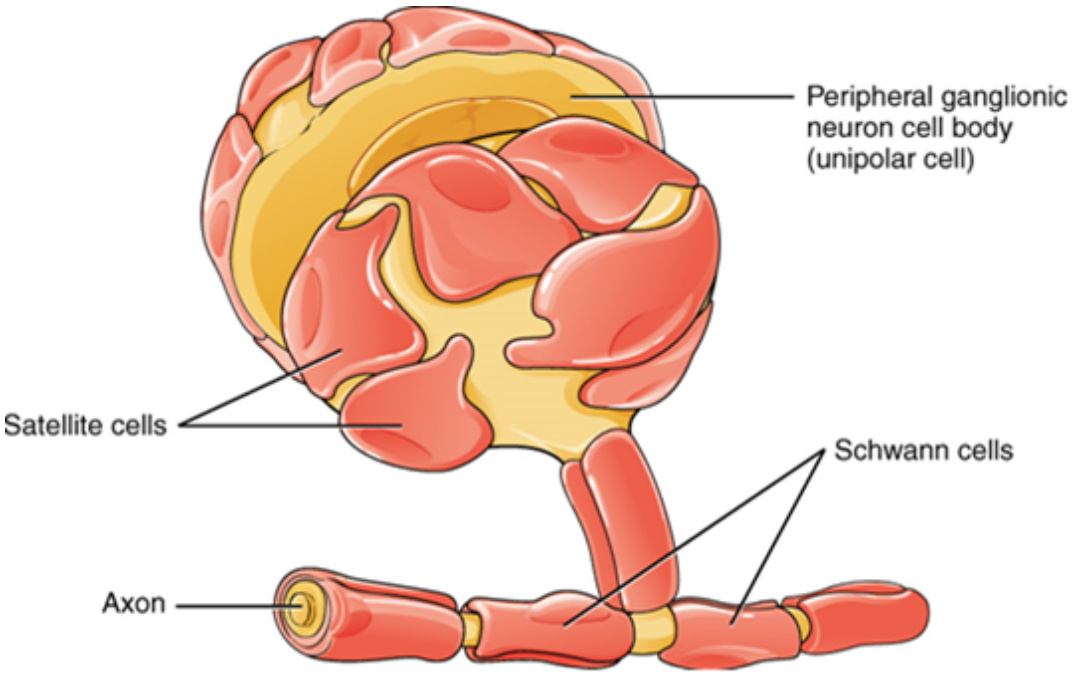


Figure 12. Glial Cells of the PNS. *The PNS has satellite cells and Schwann cells.*

Part 3: The Central Nervous System

The brain and the spinal cord are the central nervous system, and they represent the main organs of the nervous system. The spinal cord is a single structure, whereas the adult brain is described in terms of four major regions: the cerebrum, the diencephalon, the brain stem, and the cerebellum. A person's conscious experiences are based on neural activity in the brain. The regulation of homeostasis is governed by a specialized region in the brain. The coordination of reflexes depends on the integration of sensory and motor pathways in the spinal cord.

The Cerebrum

The iconic grey mantle of the human brain, which appears to make up most of the mass of the brain, is the **cerebrum** with two distinct halves, a right and left **cerebral hemisphere** (Figure 13). Many of the higher neurological functions, such as memory, emotion, and consciousness, are the result of cerebral function. The cerebrum comprises of a continuous, wrinkled and thin layer of grey matter that wraps around both hemispheres, the **cerebral cortex,** and several deep nuclei. A **gyrus** (plural = gyri) is the ridge of one of those wrinkles, and a **sulcus** (plural = sulci) is the groove between two gyri. The pattern of these folds of tissue indicates specific regions of the cerebral cortex (Figure 14).

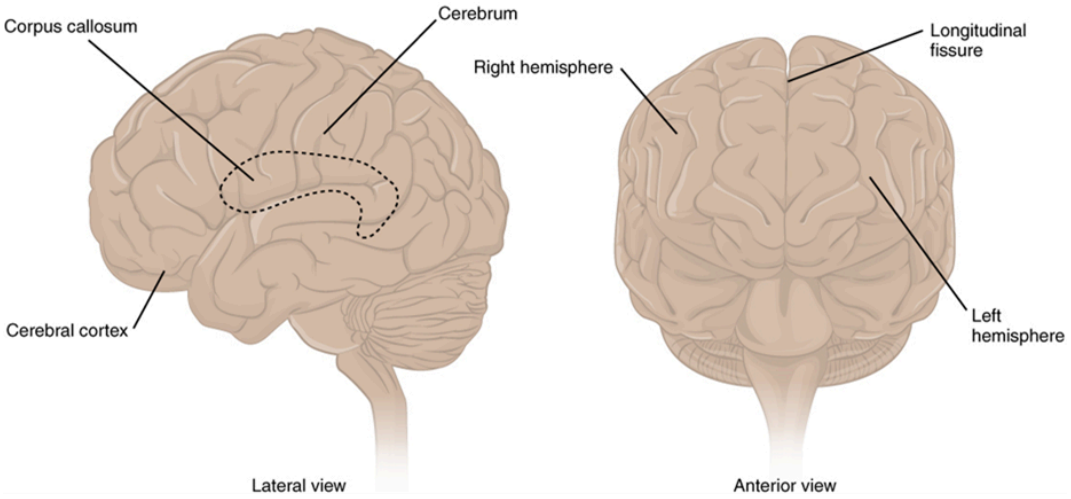


Figure 13. The Cerebrum. *The cerebrum is a large component of the CNS in humans, and the most obvious aspect of it is the folded surface called the cerebral cortex. Deep within the cerebrum, the white matter of the corpus callosum provides the major pathway for communication between the two hemispheres of the cerebral cortex.*

Different regions of the cerebral cortex can be associated with particular functions, a concept known as localization of function. In the early 1900s, a German neuroscientist named Korbinian Brodmann performed an extensive study of the microscopic anatomy (cytoarchitecture) of the cerebral cortex and divided the cortex into 52 separate regions on the basis of the histology of the cortex. His work resulted in a system of classification known as Brodmann's areas, which is still used today to describe the anatomical distinctions within the cortex The results from Brodmann's work on the anatomy align very well with the functional differences within the cortex. For example, Areas 17 and 18 in the occipital lobe are responsible for primary visual perception. That visual information is complex, so it is processed in the temporal and parietal lobes as well.

Beneath the cerebral cortex are sets of nuclei known as **basal nuclei** that augment cortical processes (Figure 15). Some of the basal nuclei in the forebrain, for example, serve as the primary location for acetylcholine production, which modulates the overall activity of the cortex, possibly leading to greater attention to sensory stimuli. Alzheimer's disease is associated with a loss of neurons in the cholinergic basal forebrain nuclei. Some other basal nuclei control the initiation of movement. For example, while a student is sitting in a classroom listening to a lecture, the basal nuclei will keep an urge to jump up and scream from actually happening. (The basal nuclei are also referred to as the basal ganglia, although that is potentially confusing because the term ganglia is typically used for peripheral structures.)

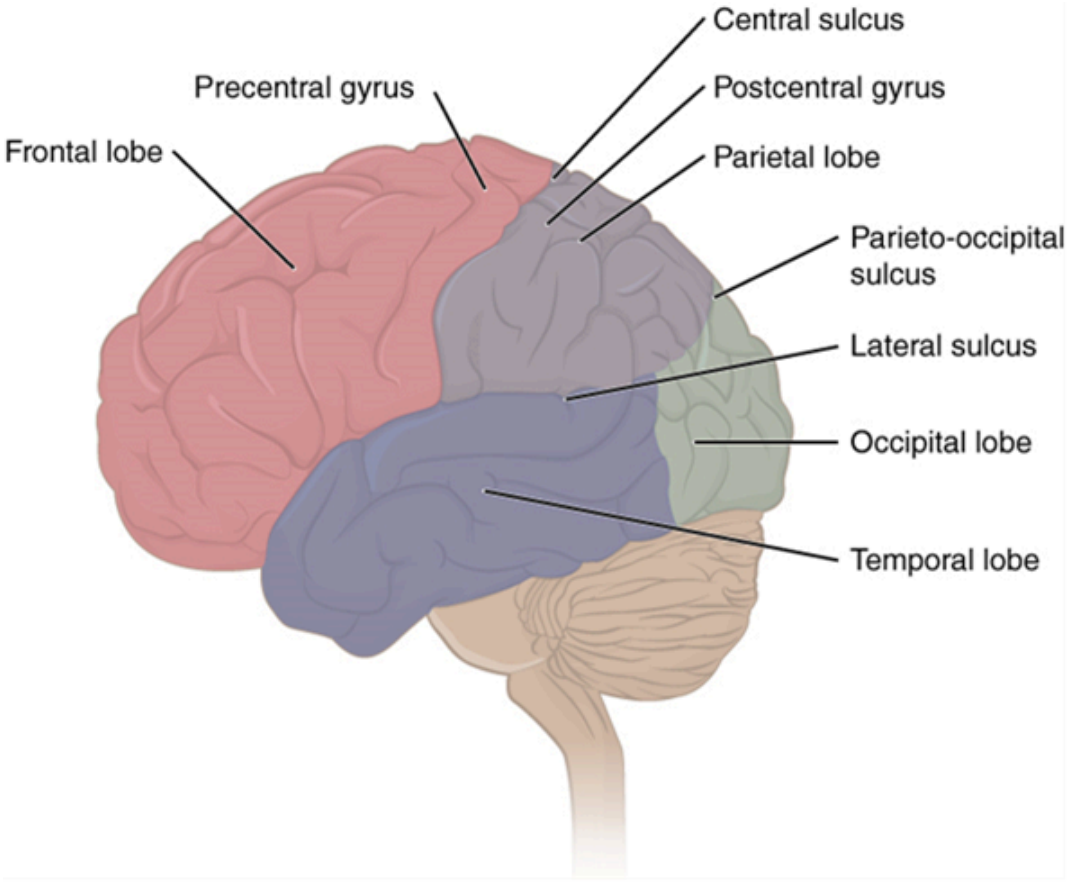


Figure 14. Lobes of the Cerebral Cortex. *The cerebral cortex is divided into four lobes. Extensive folding increases the surface area available for cerebral functions. (The names of the main sulci are provided but they are not required as examinable material in this course.)*

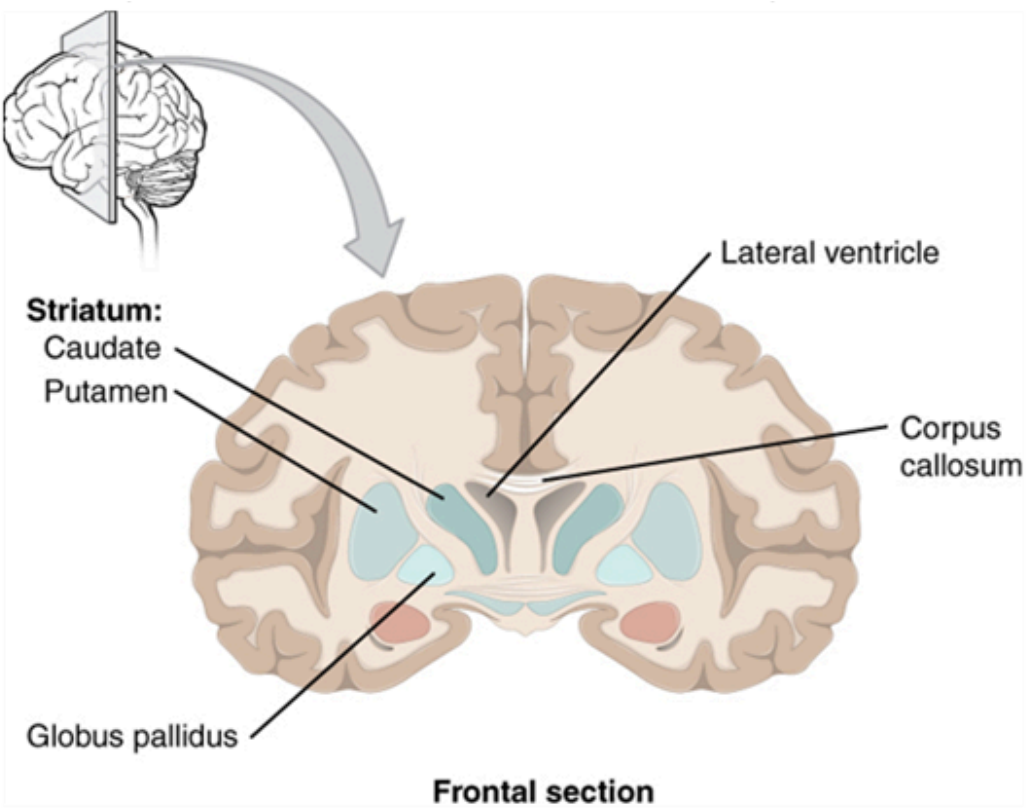


Figure 15. Frontal Section of Cerebral Cortex and Basal Nuclei. *The major components of the basal nuclei, shown in a frontal section of the brain, are the caudate (just lateral to the lateral ventricle), the putamen (inferior to the caudate and separated by the large white-matter structure called the internal capsule), and the globus pallidus (medial to the putamen). (The names of these nuclei are not required as examinable material in this course.)*

The Diencephalon

The word diencephalon translates to "through brain." It is the connection between the cerebrum and the rest of the nervous system, with one exception. The rest of the brain, the spinal cord, and the PNS all send information to the cerebrum through the diencephalon. Output from the cerebrum passes through the diencephalon. The single exception is the system associated with **olfaction**, or the sense of smell, which connects directly with the cerebrum.

The diencephalon is deep beneath the cerebrum and constitutes the walls of the third ventricle. The diencephalon can be described as any region of the brain with "thalamus" in its name. The two major regions of the diencephalon are the thalamus itself and the hypothalamus (Figure 16). There are other structures, such as the **epithalamus**, which contains the pineal gland, and the **subthalamus**, which includes the subthalamic nucleus, one of the basal nuclei.

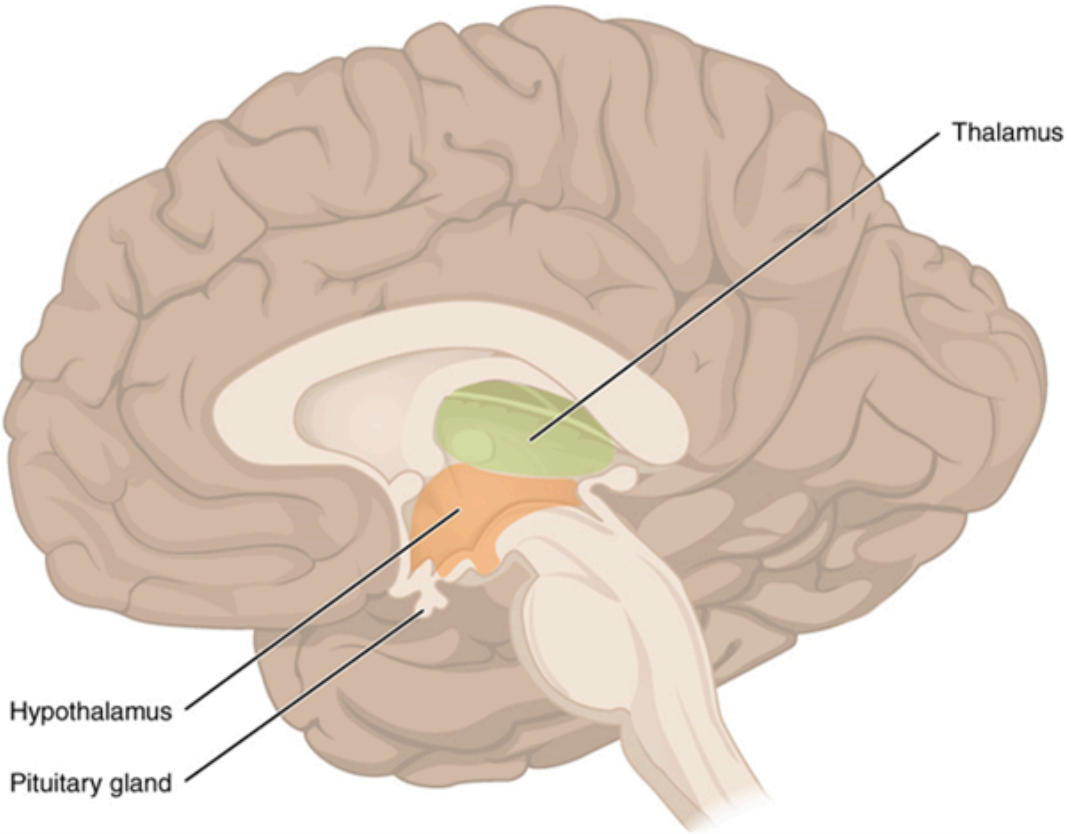


Figure 16. The Diencephalon. *The diencephalon is composed primarily of the thalamus and hypothalamus, which together define the walls of the third ventricle. The thalami are two elongated, ovoid structures on either side of the midline that make contact in the middle. The hypothalamus is inferior and anterior to the thalamus, culminating in a sharp angle to which the pituitary gland is attached.*

Thalamus

The thalamus is a collection of nuclei that relay information between the cerebral cortex and the periphery, spinal cord, or brain stem. All sensory information, except for the sense of smell, passes through the thalamus before processing by the cortex. Axons from the peripheral sensory organs, or intermediate nuclei, synapse in the thalamus, and thalamic neurons project directly to the cerebrum. It is a requisite synapse in any sensory pathway, except for olfaction. The thalamus does not just pass the information on, it also processes that information. For example, the portion of the thalamus that receives visual information will influence what visual stimuli are important, or what receives attention. The cerebrum also sends information down to the thalamus, which usually communicates motor commands.

Hypothalamus

Inferior and slightly anterior to the thalamus is the hypothalamus, the other major region of the diencephalon. The hypothalamus is a collection of nuclei that are largely involved in regulating homeostasis. The hypothalamus is the executive region in charge of the autonomic nervous system and the endocrine system through its regulation of the anterior pituitary gland. Other parts of the hypothalamus are involved in memory and emotion as part of the limbic system.

The Brain Stem

The midbrain and hindbrain (composed of the pons and the medulla) are collectively referred to as the brain stem (Figure 17). The structure emerges from the ventral surface of the forebrain as a tapering cone that connects the brain to the spinal cord. Attached to the brain stem, but considered a separate region of the adult brain, is the cerebellum. The midbrain coordinates sensory representations of the visual, auditory, and somatosensory perceptual spaces. The pons is the main connection with the cerebellum. The pons and the medulla regulate several crucial functions, including the cardiovascular and respiratory systems.

The cranial nerves connect through the brain stem and provide the brain with the sensory input and motor output associated with the head and neck, including most of the special senses. The major ascending and descending pathways between the spinal cord and brain, specifically the cerebrum, pass through the brain stem.

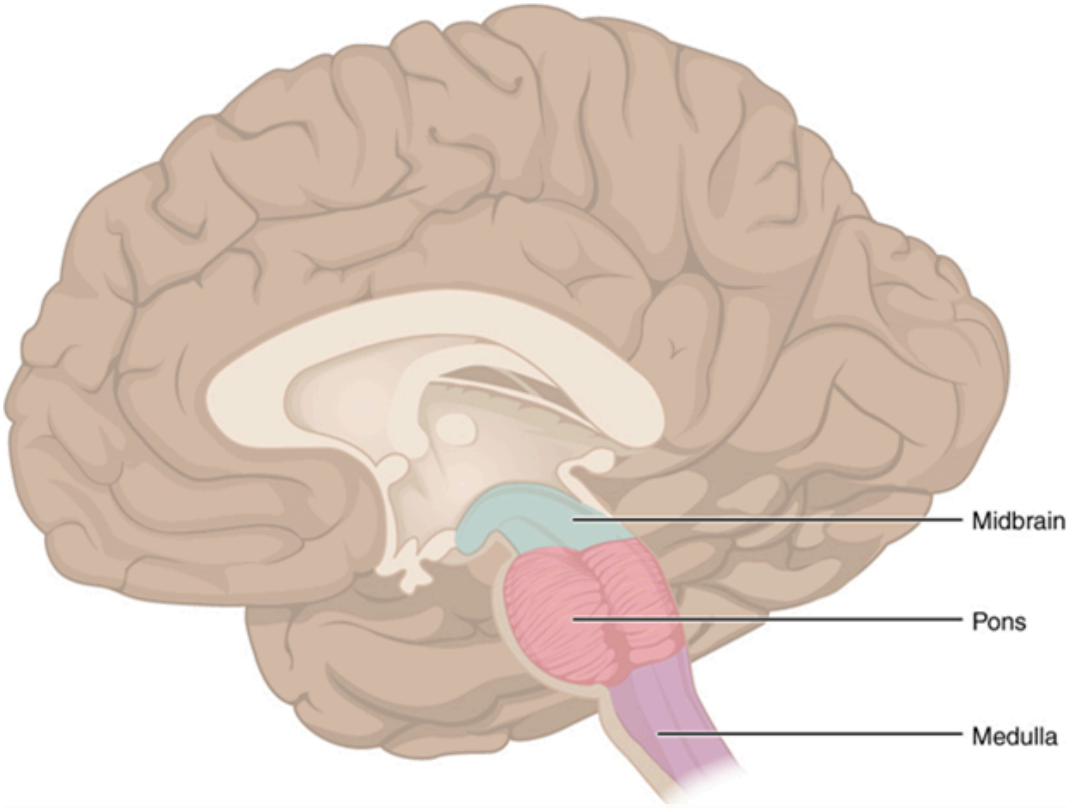


Figure 17. The Brain Stem. *The brain stem includes three regions: the midbrain, the pons, and the medulla.*

Midbrain

One of the original regions of the embryonic brain, the midbrain is a small region between the thalamus and pons. The cerebral aqueduct passes through the center of the midbrain, such that these regions are the roof and floor of that canal.

The midbrain includes four bumps known as the colliculi (singular = colliculus), which means “little hill” in

Latin. The **inferior colliculus** is the inferior pair of these enlargements and is part of the auditory brain stem pathway. Neurons of the inferior colliculus project to the thalamus, which then sends auditory information to the cerebrum for the conscious perception of sound. The **superior colliculus** is the superior pair and combines sensory information about visual space, auditory space, and somatosensory space. Activity in the superior colliculus is related to orienting the eyes to a sound or touch stimulus. If you are walking along the sidewalk on campus and you hear chirping, the superior colliculus coordinates that information with your awareness of the visual location of the tree right above you. That is the correlation of auditory and visual maps. If you suddenly feel something wet fall on your head, your superior colliculus integrates that with the auditory and visual maps and you know that the chirping bird just relieved itself on you. You want to look up to see the culprit, but do not.

Pons

The word pons comes from the Latin word for bridge. It is visible on the anterior surface of the brain stem as the thick bundle of white matter attached to the cerebellum. The pons is the main connection between the cerebellum and the brain stem.

Medulla

The gray matter of the midbrain and pons continues into the medulla, also known as medulla oblongata. This diffuse region of gray matter throughout the brain stem, known as the **reticular formation**, is related to sleep and wakefulness, general brain activity and attention. The medulla contains autonomic nuclei with motor neurons that control the rate and force of heart contraction, the diameter of blood vessels and the rate and depth of breathing, among other essential physiological processes.

The Cerebellum

The cerebellum, as the name suggests, is the "little brain." It is covered in gyri and sulci like the cerebrum, and looks like a miniature version of that part of the brain (Figure 18). The cerebellum integrates motor commands from the cerebral cortex with sensory feedback from the periphery, allowing for the coordination and precise execution of motor activities, such as walking, cycling, writing or playing a musical instrument.

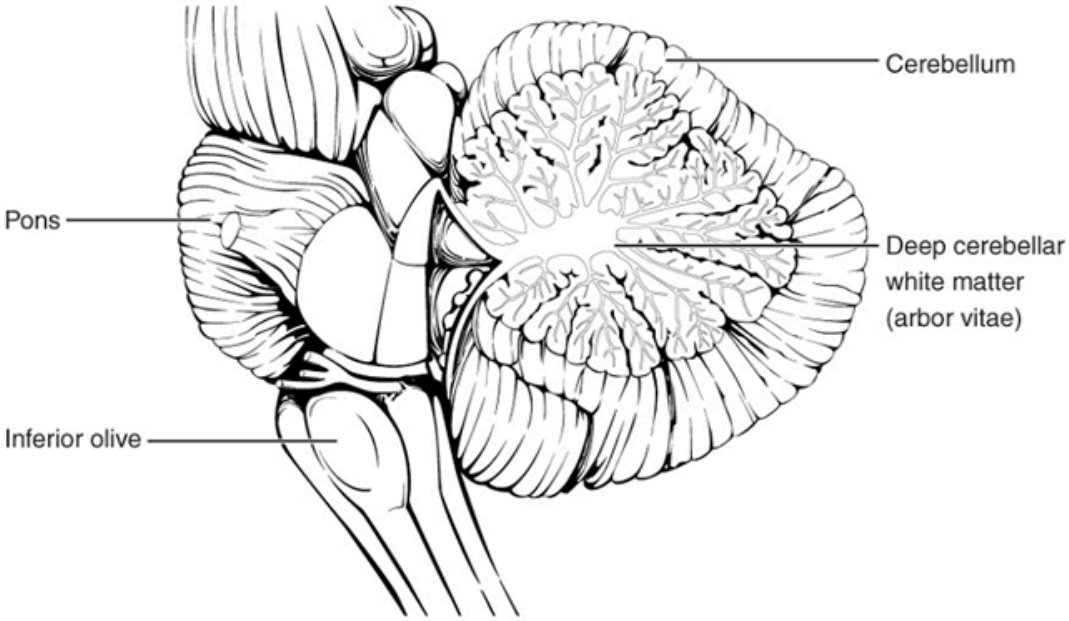
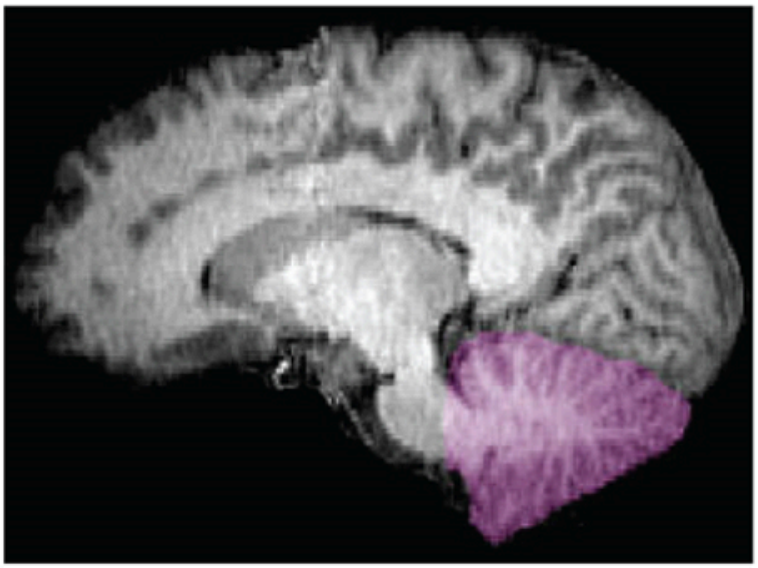


Figure 18. The Cerebellum. *The cerebellum is situated on the posterior surface of the brain stem. Descending input from the cerebellum enters through the large white matter structure of the pons. Ascending input from the periphery and spinal cord enters through the fibers of the inferior olive. Output goes to the midbrain, which sends a descending signal to the spinal cord.*



The Spinal Cord

Whereas the brain develops out of expansions of the neural tube into primary and then secondary vesicles, the spinal cord maintains the tube structure and is only specialized into certain regions.

The length of the spinal cord is divided into regions that correspond to the regions of the vertebral column. The name of a spinal cord region corresponds to the level at which spinal nerves pass through the intervertebral foramina. Immediately adjacent to the brain stem is the cervical region, followed by the thoracic, then the lumbar, and finally the sacral region (Figures 24 and 25).

Gray Horns

In cross-section, the gray matter of the spinal cord has the appearance of an ink-blot test, with the spread of

the gray matter on one side replicated on the other—a shape reminiscent of a bulbous capital "H." As shown in Figure 19, the gray matter is subdivided into regions that are referred to as horns.

The **posterior horn** is responsible for sensory processing. The **anterior horn** sends out motor signals to the skeletal muscles. The **lateral horn**, which is only found in the thoracic, upper lumbar, and sacral regions, is the central component of the sympathetic division of the autonomic nervous system.

Some of the largest neurons of the spinal cord are the multipolar motor neurons in the anterior horn. The fibers that cause contraction of skeletal muscles are the axons of these neurons. The motor neuron that causes contraction of the big toe, for example, is located in the sacral spinal cord. The axon that has to reach all the way to the belly of that muscle may be a meter in length. The neuronal cell body that maintains that long fiber must be quite large, possibly several hundred micrometers in diameter, making it one of the largest cells in the body.

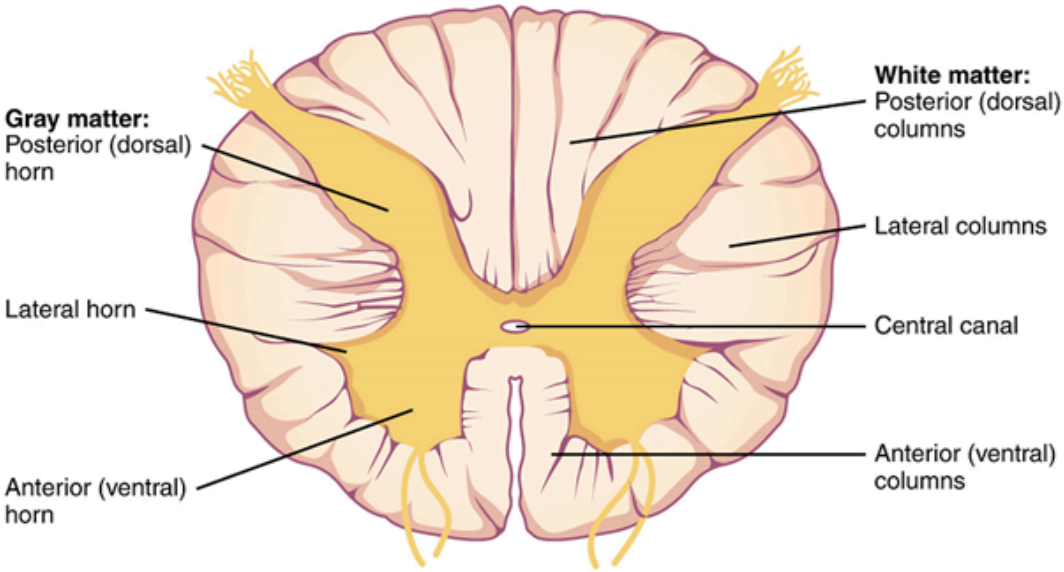
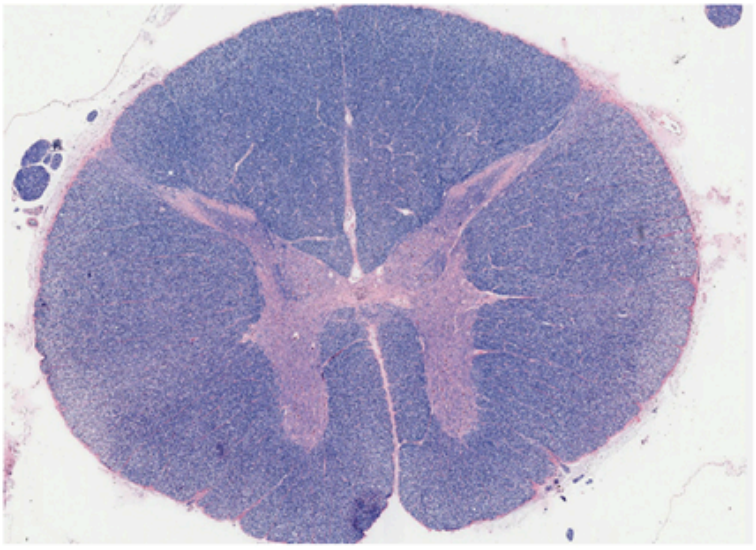


Figure 19. Cross-section of Spinal Cord. *The cross-section of a thoracic spinal cord segment shows the posterior, anterior, and lateral horns of gray matter, as well as the posterior, anterior, and lateral columns of white matter. LM × 40. (Micrograph provided by the Regents of University of Michigan Medical School © 2012)*



White Columns

Just as the gray matter is separated into horns, the white matter of the spinal cord is separated into columns. **Ascending tracts** of nervous system fibers in these columns carry sensory information up to the brain, whereas **descending tracts** carry motor commands from the brain.

Watch this Crash Course video for an overview of the central nervous system! (Direct link: https://youtu.be/q8NtmDrb_qo)

The Meninges

The outer surface of the CNS is covered by a series of membranes composed of connective tissue called the meninges, which protect the brain. The dura mater is a thick fibrous layer and a strong protective sheath over the entire brain and spinal cord. It is anchored to the inner surface of the cranium and vertebral cavity. The arachnoid mater is a membrane of thin fibrous tissue that forms a loose sac around the CNS. Beneath the arachnoid is a thin, filamentous mesh called the arachnoid trabeculae, which looks like a spider web, giving this layer its name. Directly adjacent to the surface of the CNS is the pia mater, a thin fibrous membrane that follows the convolutions of gyri and sulci in the cerebral cortex and fits into other grooves and indentations (Figures 20).

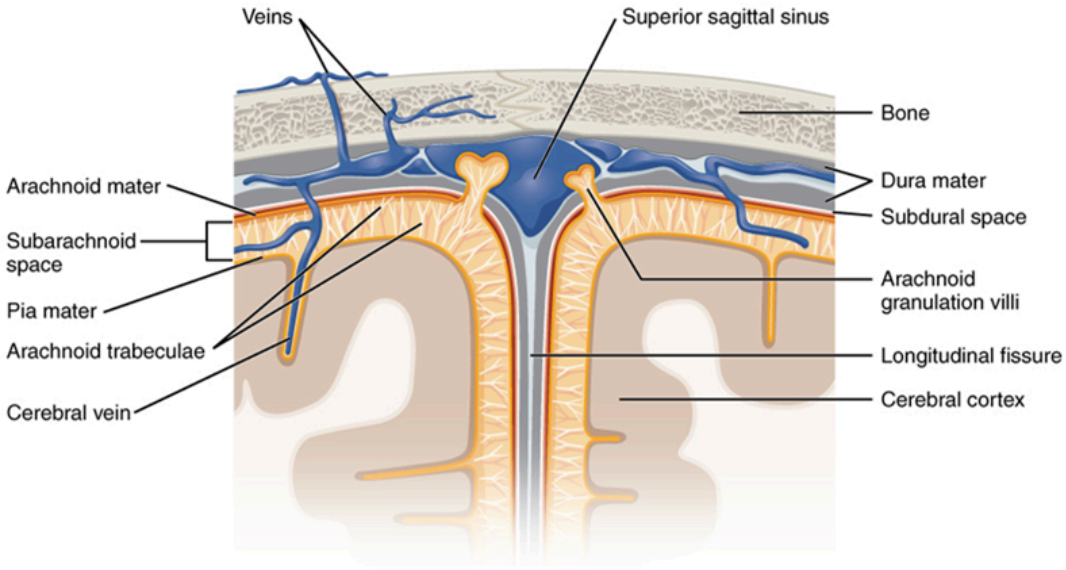


Figure 20. Meningeal Layers of Superior Sagittal Sinus. *The layers of the meninges in the longitudinal fissure of the superior sagittal sinus are shown, with the dura mater adjacent to the inner surface of the cranium, the pia mater adjacent to the surface of the brain, and the arachnoid and subarachnoid space between them. An arachnoid villus is shown emerging into the dural sinus to allow CSF to filter back into the blood for drainage.*

The Ventricular System and Cerebrospinal Fluid Circulation

Cerebrospinal fluid (CSF) circulates throughout and around the CNS. CSF is produced in special structures to perfuse through the nervous tissue of the CNS and is continuous with the interstitial fluid. Specifically, CSF circulates to remove metabolic wastes from the interstitial fluids of nervous tissues and return them to the blood stream. The **ventricles** are the open spaces within the brain where CSF circulates. In some of these spaces, CSF is produced by filtering of the blood that is performed by a specialized membrane known as a choroid plexus. The CSF circulates through all of the ventricles to eventually emerge into the subarachnoid space where it will be reabsorbed into the blood.

There are four ventricles within the brain, all of which developed from the original hollow space within the neural tube, the central canal. The first two are named the lateral ventricles and are deep within the cerebrum. These ventricles are connected to the third ventricle by two openings called the interventricular foramina. The third ventricle is the space between the left and right sides of the diencephalon, which opens into the cerebral aqueduct that passes through the midbrain. The aqueduct opens into the fourth ventricle, which is the space between the cerebellum and the pons and upper medulla (Figure 21).

The ventricular system opens up to the subarachnoid space from the fourth ventricle. The single median aperture and the pair of lateral apertures connect to the subarachnoid space so that CSF can flow through the ventricles and around the outside of the CNS. Cerebrospinal fluid is produced within the ventricles by a type of specialized membrane called a choroid plexus. Ependymal cells (a type of glial cell; see Figure 11) surround blood capillaries and filter the blood to make CSF. The fluid is a clear solution with a limited amount of the constituents of blood. It is essentially water, small molecules, and electrolytes. Oxygen and carbon dioxide are dissolved into the CSF, as they are in blood, and can diffuse between the fluid and the nervous tissue.

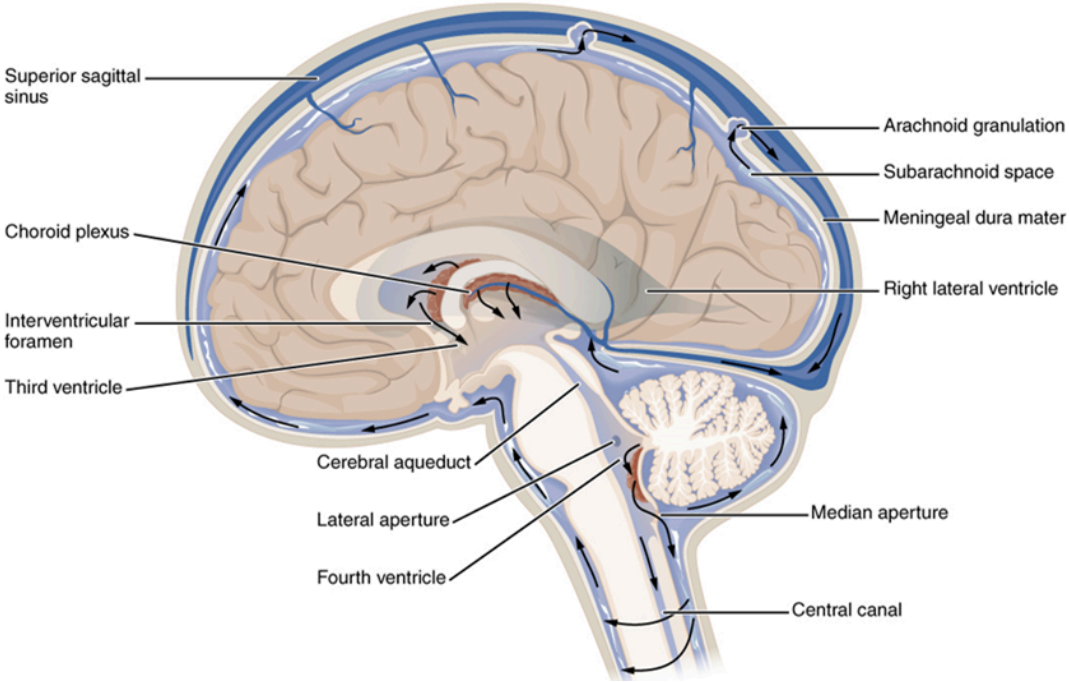


Figure 21. Cerebrospinal Fluid Circulation. *The choroid plexus in the four ventricles produce CSF, which is circulated through the ventricular system and then enters the subarachnoid space through the median and lateral apertures. The CSF is then reabsorbed into the blood at the arachnoid granulations, where the arachnoid membrane emerges into the dural sinuses.*

Cerebrospinal Fluid Circulation

The choroid plexuses are found in all four ventricles. Observed in dissection, they appear as soft, fuzzy structures that may still be pink, depending on how well the circulatory system is cleared in preparation of the tissue. The CSF is produced from components extracted from the blood, so its flow out of the ventricles is tied to the pulse of cardiovascular circulation.

From the lateral ventricles, the CSF flows into the third ventricle, where more CSF is produced, and then

through the cerebral aqueduct into the fourth ventricle where even more CSF is produced. A very small amount of CSF is filtered at any one of the plexuses, for a total of about 500 milliliters daily, but it is continuously made and pulses through the ventricular system, keeping the fluid moving. From the fourth ventricle, CSF can continue down the central canal of the spinal cord, but this is essentially a cul-de-sac, so more of the fluid leaves the ventricular system and moves into the subarachnoid space through the median and lateral apertures.

Within the subarachnoid space, the CSF flows around all of the CNS, providing two important functions. As with elsewhere in its circulation, the CSF picks up metabolic wastes from the nervous tissue and moves it out of the CNS. It also acts as a liquid cushion for the brain and spinal cord. By surrounding the entire system in the subarachnoid space, it provides a thin buffer around the organs within the strong, protective dura mater. The arachnoid granulations are outpocketings of the arachnoid membrane into the dural sinuses so that CSF can be reabsorbed into the blood, along with the metabolic wastes. From the dural sinuses, blood drains out of the head and neck through the jugular veins, along with the rest of the circulation for blood, to be reoxygenated by the lungs and wastes to be filtered out by the kidneys (Table 3).

Table 3: Components of Cerebrospinal Fluid Circulation

	Lateral ventricles	Third ventricle	Cerebral aqueduct	Fourth ventricle	Central canal	Subarachnoid space
Location	Cerebrum	Diencephalon	Midbrain	Between pons/ upper medulla oblongata and cerebellum	Spinal cord	External to entire CNS
Blood vessel structure	Choroid plexus	Choroid plexus	None	Choroid plexus	None	Arachnoid granulations

Part 4: The Peripheral Nervous System

The PNS is not as contained as the CNS because it is defined as everything that is not the CNS. Some peripheral structures are incorporated into the other organs of the body. In describing the anatomy of the PNS, it is necessary to describe the common structures, the nerves and the ganglia, as they are found in various parts of the body. Many of the neural structures that are incorporated into other organs are features of the digestive system; these structures are known as the enteric nervous system and are a special subset of the PNS.

Ganglia

A ganglion is a group of neuron cell bodies in the periphery. Ganglia can be categorized, for the most part, as either sensory ganglia or autonomic ganglia, referring to their primary functions. The most common type of sensory ganglion is a **dorsal root ganglion**. These ganglia are the cell bodies of neurons with axons that are sensory endings in the periphery, such as in the skin, and that extend into the CNS through the dorsal nerve root.

The other major category of ganglia, those of the autonomic nervous system, will be examined later in this chapter.

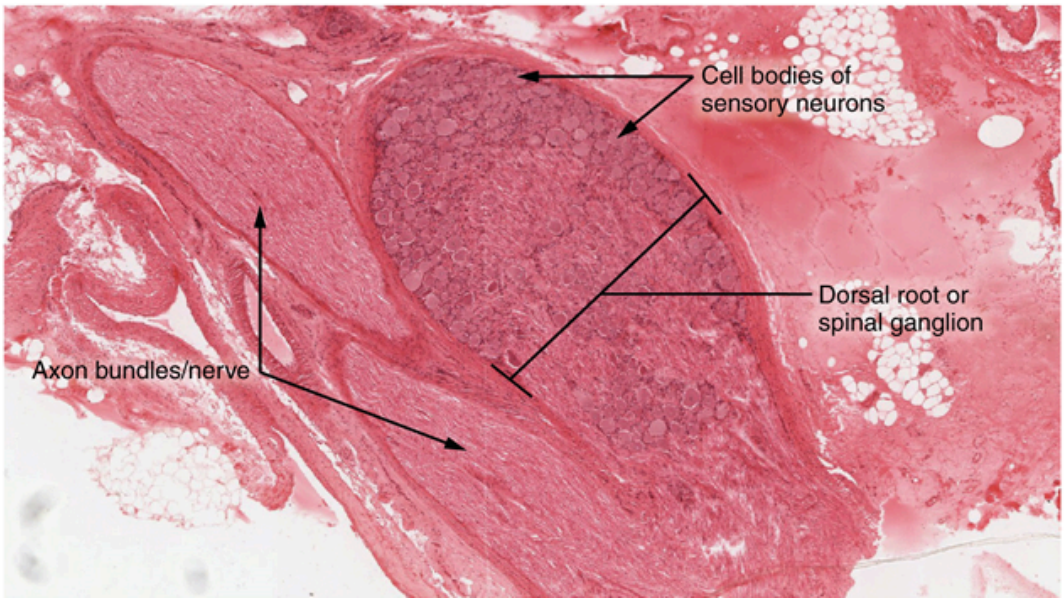


Figure 22. Dorsal Root Ganglion. *The cell bodies of sensory neurons, which are unipolar neurons by shape, are seen in this photomicrograph. Also, the fibrous region is composed of the axons of these neurons that are passing through the ganglion to be part of the dorsal nerve root (tissue source: canine). LM × 40. (Micrograph provided by the Regents of University of Michigan Medical School © 2012)*

Nerves

Bundles of axons in the PNS are referred to as nerves. These structures in the periphery are different than the central counterpart, called a tract. Nerves are composed of more than just nervous tissue. They have connective tissues invested in their structure, as well as blood vessels supplying the tissues with nourishment. Nerves are associated with the region of the CNS to which they are connected, either as cranial nerves (12 pairs) connected to the brain or spinal nerves (31 pairs) connected to the spinal cord.

The cranial nerves are primarily responsible for the sensory and motor functions of the head and neck, although one of these nerves, the vagus, targets organs in the thoracic and abdominal cavities as part of the parasympathetic nervous system. They can be classified as sensory nerves, motor nerves, or a combination of both, meaning that the axons in these nerves originate out of sensory ganglia external to the cranium or motor nuclei within the brain stem.

All of the spinal nerves are combined sensory and motor axons that separate into two nerve roots. The sensory axons enter the spinal cord as the dorsal nerve root. The motor fibers, both somatic and autonomic, emerge as the ventral nerve root. The dorsal root ganglion for each nerve is an enlargement of the spinal nerve.

The Somatic Nervous System

The somatic nervous system is traditionally considered a division within the peripheral nervous system. However, this misses an important point: somatic refers to a functional division, whereas peripheral refers to an anatomic division. The somatic nervous system is responsible for our conscious perception of the environment and for our voluntary responses to that perception by means of skeletal muscles. Peripheral sensory neurons receive input from environmental stimuli, but the neurons that produce motor responses originate in the central nervous system. The distinction between the structures of the peripheral and central nervous systems and the functions of the somatic and autonomic systems can most easily be demonstrated through a simple **reflex**, an automatic response that the nervous system produces in response to specific stimuli. The neurons and neural pathways responsible for a reflex action constitute the **reflex arc**. One of the simplest reflex acts is the **stretch reflex,** by which the nervous system responds to the stretching of a muscle (the stimulus) with contraction of that same muscle (the response). This response protects the muscle from over-stretching, but more importantly, it has a crucial role in maintaining posture and balance. The **patellar reflex** (or knee-jerk reflex) is an example of stretch reflex and it occurs through the following steps (Figure 23):

- Tapping of the patellar tendon with a hammer causes the stretching of muscle fibers in the quadriceps muscle, which stimulates sensory neurons innervating those fibers.
- In the sensory neuron, a nerve impulse (action potential) is generated, which travels along the sensory nerve fiber from the muscle, through the dorsal root ganglion, to the spinal cord.
- The sensory neuron stimulates a motor neuron in the ventral horn of the spinal cord.
- That motor neuron sends a nerve impulse (action potential) along its axon.
- This impulse reaches the quadriceps muscle, causing its contraction and the extension of the leg (a kick).

The sensory neuron can also activate an interneuron (e.g., Figure 23), which inhibits the motor neuron responsible for the contraction of the antagonistic muscle to quadriceps (i.e. hamstring).

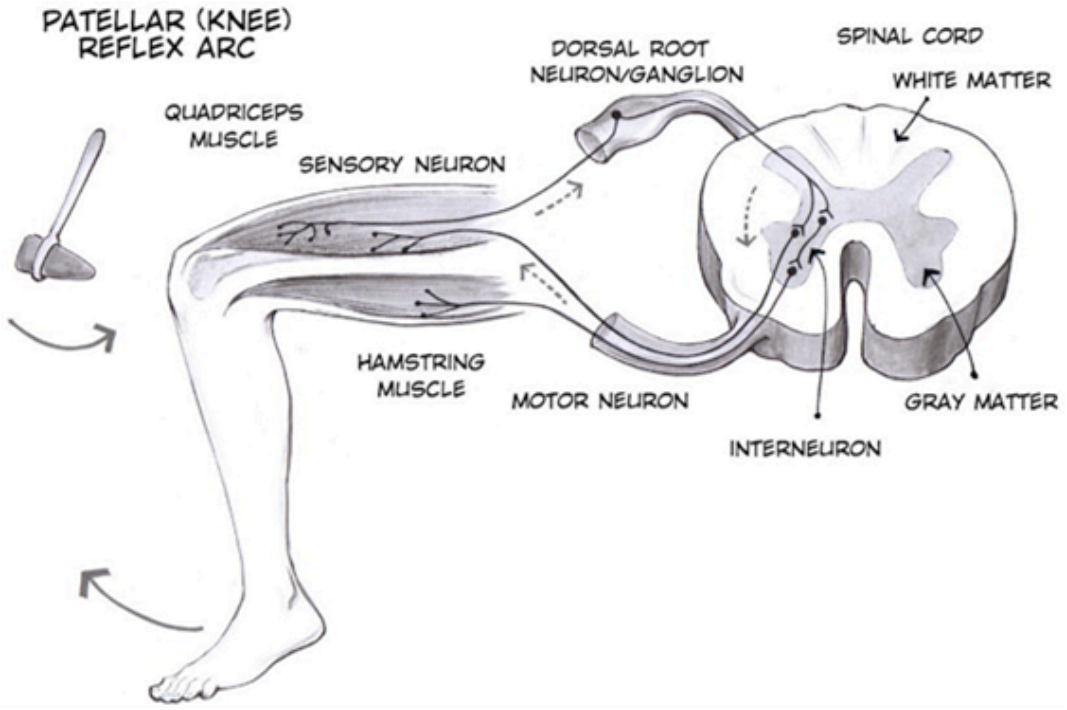


Figure 23. The Patellar Reflex. *The stimulus (stretching of the quadriceps muscle caused by tapping on the tendon) triggers a nerve impulse in a sensory neuron, which synapses with and stimulated a motor neuron, leading to the contraction of the quadriceps. (credit: www.backyardbrains.com/experiments/Musclekneejerk, protected under Creative Commons License)*

Another example of a simple spinal reflex is the **withdrawal reflex,** which occurs, for example, when you touch a hot stove and pull your hand away. This reflex occurs through a similar sequence of steps:

- Sensory receptors in the skin sense extreme temperature and the early signs of tissue damage.
- In a sensory neuron, a nerve impulse (action potential) is generated, which travels along the sensory nerve fiber from the skin, through the dorsal root ganglion, to the spinal cord.
- The sensory neuron stimulates a motor neuron in the ventral horn motor of the spinal cord.
- That motor neuron sends a nerve impulse (action potential) along its axon.
- This impulse reaches the biceps brachii, causing contraction of the muscle and flexion of the forearm at the elbow to withdraw the hand from the hot stove.

The basic withdrawal reflex includes sensory input (the painful stimulus), central processing (the synapse in the spinal cord), and motor output (activation of a ventral motor neuron that causes contraction of the biceps brachii). As seen for the patellar reflex, the withdrawal reflex can also include inhibition of the antagonistic muscle (triceps brachii in our example). Another possible motor output of the withdrawal reflex is cross

extension: counterbalancing movement on the other side of the body by stimulation of the extensor muscles in the contralateral limb.

The somatic nervous system also controls voluntary movement and more complex motor functions. For example, reading of this text starts with visual sensory input to the retina, which then projects to the thalamus, and on to the cerebral cortex. A sequence of regions of the cerebral cortex process the visual information, starting in the primary visual cortex of the occipital lobe, and resulting in the conscious perception of these letters. Subsequent cognitive processing results in understanding of the content. As you continue reading, regions of the cerebral cortex in the frontal lobe plan how to move the eyes to follow the lines of text. The output from the cortex causes activity in motor neurons in the brain stem that cause movement of the extraocular muscles through the third, fourth, and sixth cranial nerves. This example also includes sensory input (the retinal projection to the thalamus), central processing (the thalamus and subsequent cortical activity), and motor output (activation of neurons in the brain stem that lead to coordinated contraction of extraocular muscles).

The Autonomic Nervous System

The autonomic nervous system is often associated with the "fight-or-flight response," which refers to the preparation of the body to either run away from a threat or to stand and fight in the face of that threat. To suggest what this means, consider the (very unlikely) situation of seeing a lioness hunting out on the savannah. Though this is not a common threat that humans deal with in the modern world, it represents the type of environment in which the human species thrived and adapted. The spread of humans around the world to the present state of the modern age occurred much more quickly than any species would adapt to environmental pressures such as predators. However, the reactions modern humans have in the modern world are based on these prehistoric situations. If your boss is walking down the hallway on Friday afternoon looking for "volunteers" to come in on the weekend, your response is the same as the prehistoric human seeing the lioness running across the savannah: fight or flight.

Most likely, your response to your boss—not to mention the lioness—would be flight. Run away! The autonomic system is responsible for the physiological response to make that possible, and hopefully successful. Adrenaline starts to flood your circulatory system. Your heart rate increases. Sweat glands become active. The bronchi of the lungs dilate to allow more air exchange. Pupils dilate to increase visual information. Blood pressure increases in general, and blood vessels dilate in skeletal muscles. Time to run. Similar physiological responses would occur in preparation for fighting off the threat.

This response should sound a bit familiar. The autonomic nervous system is tied into emotional responses as well, and the fight-or-flight response probably sounds like a panic attack. In the modern world, these sorts of reactions are associated with anxiety as much as with response to a threat. It is engrained in the nervous system to respond like this. In fact, the adaptations of the autonomic nervous system probably predate the human species and are likely to be common to all mammals, and perhaps shared by many animals. That lioness might herself be threatened in some other situation

However, the autonomic nervous system is not just about responding to threats. Besides the fight-or-flight response, there are the responses referred to as "rest and digest." If that lioness is successful in her hunting, then she is going to rest from the exertion. Her heart rate will slow. Breathing will return to normal. The digestive system has a big job to do. Much of the function of the autonomic system is based on the connections within an autonomic, or visceral, reflex.

As we have seen, the nervous system can be divided into two functional parts: the somatic nervous system and the autonomic nervous system. The major differences between the two systems are evident in the responses that each produces. The somatic nervous system causes contraction of skeletal muscles. The autonomic nervous system controls cardiac and smooth muscle, as well as glandular tissue. The somatic nervous system is associated with voluntary responses (though many can happen without conscious awareness, like breathing), and the autonomic nervous system is associated with involuntary responses, such as those related to homeostasis.

The autonomic nervous system regulates many of the internal organs through a balance of two aspects, or

divisions. In addition to the endocrine system, the autonomic nervous system is instrumental in homeostatic mechanisms in the body. The two divisions of the autonomic nervous system are the **sympathetic division** and the **parasympathetic division**. The sympathetic system is associated with the **fight-or-flight response**, and parasympathetic activity is referred to by the epithet of **rest and digest**. At each target effector, dual innervation determines activity. For example, the heart receives connections from both the sympathetic and parasympathetic divisions. One causes heart rate to increase, whereas the other causes heart rate to decrease.

Sympathetic Division of the Autonomic Nervous System

To respond to a threat—to fight or to run away—the sympathetic system causes divergent effects as many different effector organs are activated together for a common purpose. More oxygen needs to be inhaled and delivered to skeletal muscle. The respiratory, cardiovascular, and musculoskeletal systems are all activated together. Additionally, sweating keeps the excess heat that comes from muscle contraction from causing the body to overheat. The digestive system shuts down so that blood is not absorbing nutrients when it should be delivering oxygen to skeletal muscles. To coordinate all these responses, the connections in the sympathetic system diverge from a limited region of the CNS to a wide array of ganglia that project to the many effector organs simultaneously. The complex set of structures that compose the output of the sympathetic system make it possible for these disparate effectors to come together in a coordinated, systemic change.

The sympathetic division of the autonomic nervous system influences the various organ systems of the body through connections emerging from the thoracic and upper lumbar spinal cord. It is referred to as the **thoracolumbar system** to reflect this anatomical basis. A **central neuron** in the lateral horn of any of these spinal regions projects to ganglia adjacent to the vertebral column through the ventral spinal roots. The majority of ganglia of the sympathetic system belong to a network of **sympathetic chain ganglia** that runs alongside the vertebral column. The ganglia appear as a series of clusters of neurons linked by axonal bridges. A diagram that shows the connections of the sympathetic system is somewhat like a circuit diagram that shows the electrical connections between different receptacles and devices (Figure 24, wherein the “circuits” of the sympathetic system are intentionally simplified).

An axon from the central neuron that projects to a sympathetic ganglion is referred to as a **preganglionic fiber** or neuron, and represents the output from the CNS to the ganglion. Because the sympathetic ganglia are adjacent to the vertebral column, preganglionic sympathetic fibers are relatively short, and they are myelinated. A **postganglionic fiber**—the axon from a ganglionic neuron that projects to the target effector—represents the output of a ganglion that directly influences the organ. Compared with the preganglionic fibers, postganglionic sympathetic fibers are long because of the relatively greater distance from the ganglion to the target effector. These fibers are unmyelinated. (Note that the term “postganglionic neuron” may be used to describe the projection from a ganglion to the target. The problem with that usage is that the cell body is in the ganglion, and only the fiber is postganglionic. Typically, the term neuron applies to the entire cell.)

One type of preganglionic sympathetic fiber does not terminate in a ganglion. These are the axons from central sympathetic neurons that project to the **adrenal medulla**, the interior portion of the adrenal gland. These axons are still referred to as preganglionic fibers, but the target is not a ganglion. The adrenal medulla releases signaling molecules into the bloodstream, rather than using axons to communicate with target structures.

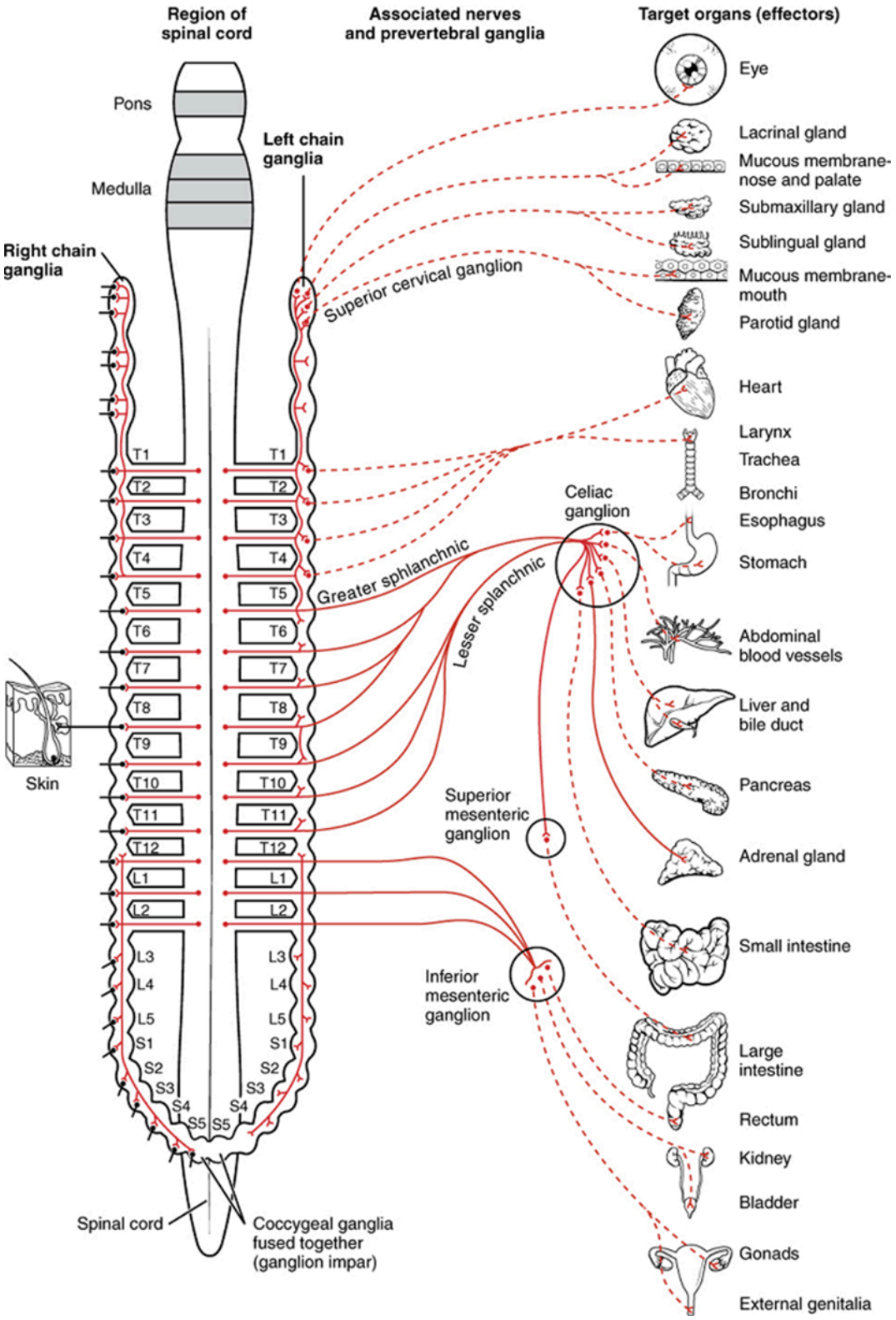


Figure 24. The Sympathetic Division of the Autonomic Nervous System. *Neurons from the lateral horn of the spinal cord (preganglionic nerve fibers – solid lines)) project to the chain ganglia on either side of the vertebral column or to collateral (prevertebral) ganglia that are anterior to the vertebral column in the abdominal cavity. Axons from these ganglionic neurons (postganglionic nerve fibers – dotted lines) then project to target effectors throughout the body. (The names of specific ganglia and nerves, as well as their target organs, are not examinable material in this course.)*

The projections of the sympathetic division of the autonomic nervous system diverge widely, resulting in a broad influence of the system throughout the body. As a response to a threat, the sympathetic system would increase heart rate and breathing rate and cause blood flow to the skeletal muscle to increase and blood

flow to the digestive system to decrease. Sweat gland secretion should also increase as part of an integrated response. All of those physiological changes are going to be required to occur together to run away from the hunting lioness, or the modern equivalent. This divergence is seen in the branching patterns of preganglionic sympathetic neurons—a single preganglionic sympathetic neuron may have 10–20 targets. An axon that leaves a central neuron of the lateral horn in the thoracolumbar spinal cord will pass through the white ramus communicans and enter the sympathetic chain, where it will branch toward a variety of targets. At the level of the spinal cord at which the preganglionic sympathetic fiber exits the spinal cord, a branch will synapse on a neuron in the adjacent chain ganglion. Some branches will extend up or down to a different level of the chain ganglia. Other branches will pass through the chain ganglia and project through one of the splanchnic nerves to a collateral ganglion. Finally, some branches may project through the splanchnic nerves to the adrenal medulla. All of these branches mean that one preganglionic neuron can influence different regions of the sympathetic system very broadly, by acting on widely distributed organs.

Parasympathetic Division of the Autonomic Nervous System

When not responding to an immediate threat, the parasympathetic system is generally more active than the sympathetic system. Many of the same effectors in the body are innervated by both divisions of the autonomic nervous system, but activation of each division tends to have opposing effects. Sympathetic system activation tends to increase activity in the respiratory, cardiovascular, and musculoskeletal systems while reducing activity in the digestive system. Parasympathetic system activation on the other hand tends to *decrease* activity in the respiratory, cardiovascular, and musculoskeletal systems while *increasing* activity in the digestive, urinary, and reproductive systems. Generally speaking, the activity of the many organs that receive input from both systems is dependent on whether neurons of the parasympathetic or sympathetic system are releasing more of their neurotransmitter onto each organ at a given time.

The parasympathetic division of the autonomic nervous system is named because its central neurons are located on either side of the thoracolumbar region of the spinal cord (para- = “beside” or “near”). The parasympathetic system can also be referred to as the **craniosacral system** (or outflow) because the preganglionic neurons are located in nuclei of the brain stem and the lateral horn of the sacral spinal cord.

The connections, or “circuits,” of the parasympathetic division are similar to the general layout of the sympathetic division with a few specific differences (Figure 25). The preganglionic fibers from the cranial region travel in cranial nerves, whereas preganglionic fibers from the sacral region travel in spinal nerves. The targets of these fibers are terminal ganglia, which are located near – or even within – the target organ. The postganglionic fiber projects from the terminal ganglia a short distance to the effector. These ganglia are often referred to as intramural ganglia when they are found within the walls target effector, or to the specific target tissue within the organ. Comparing the relative lengths of axons in the parasympathetic system, the preganglionic fibers are long and the postganglionic fibers are short because the ganglia are close to – and sometimes within – the target effectors.

Watch this Crash Course video for an overview of the autonomic nervous system! (Direct link: https://youtu.be/71pCilo8k4M)

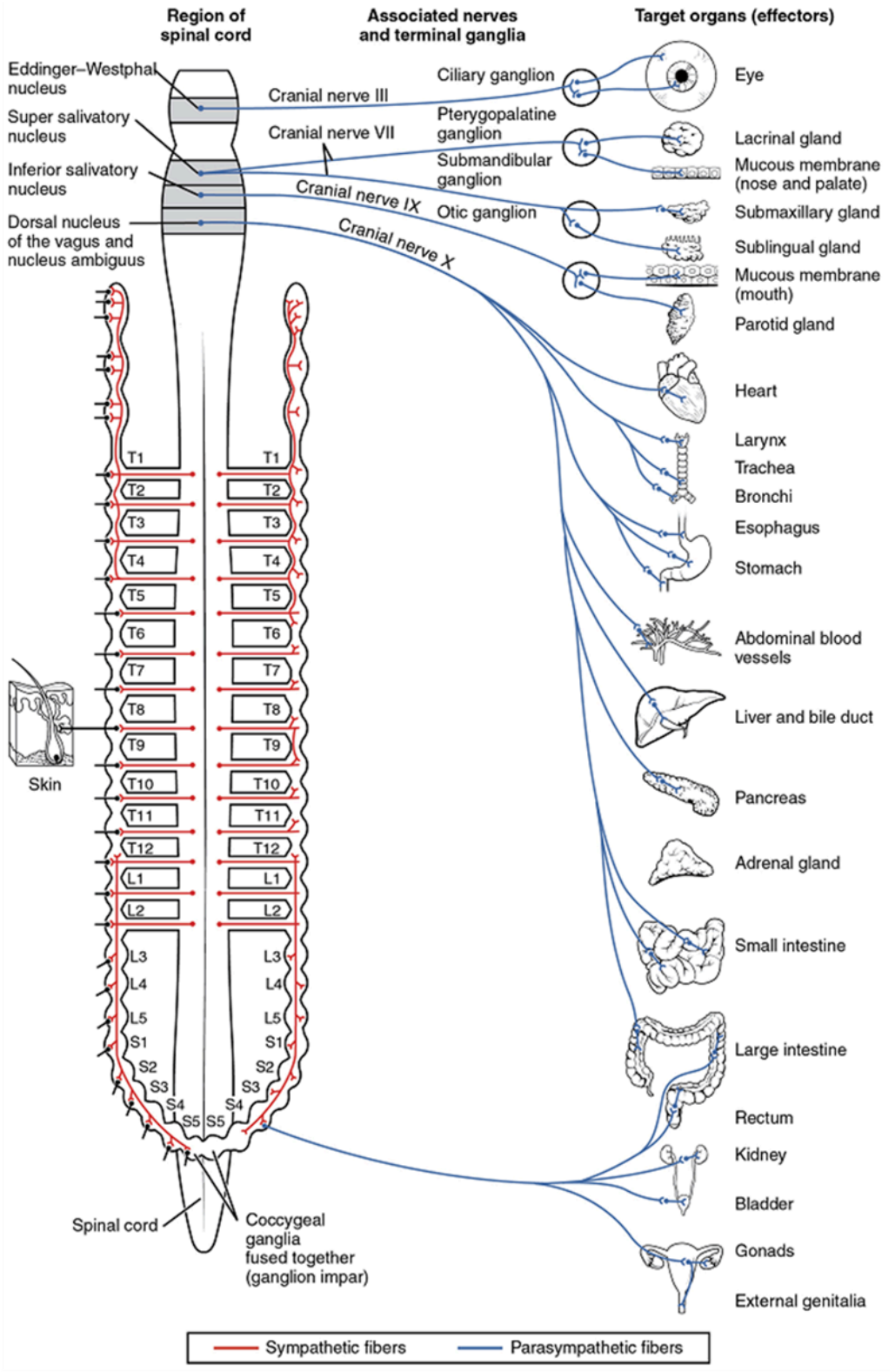


Figure 25. The Parasympathetic Division of the Autonomic Nervous System. *Neurons from brain-stem nuclei, or from the lateral horn of the sacral spinal cord, project to terminal ganglia near or within the various organs of the body. Axons from these ganglionic neurons then project the short distance to those target effectors. (The names of specific ganglia and nerves, as well as their target organs, are not examinable material in this course.)*

Chemical Signaling in the Autonomic Nervous System

Where an autonomic neuron connects with a target, there is a synapse. The electrical signal of the action

potential causes the release of a signaling molecule, which will bind to receptor proteins on the target cell. Synapses of the autonomic system are classified as either **cholinergic**, meaning that **acetylcholine (ACh)** is released, or **adrenergic**, meaning that **norepinephrine** is released. The terms cholinergic and adrenergic refer not only to the signaling molecule that is released but also to the class of receptors that each binds.

The term adrenergic should remind you of the word adrenaline, which is associated with the fight-or-flight response described at the beginning of the chapter. Adrenaline and epinephrine are two names for the same molecule. The adrenal gland (in Latin, ad- = "on top of"; renal = "kidney") secretes adrenaline. The ending "-ine" refers to the chemical being derived, or extracted, from the adrenal gland. A similar construction from Greek instead of Latin results in the word epinephrine (epi- = "above"; nephr- = "kidney"). In scientific usage, epinephrine is preferred in the United States, whereas adrenaline is preferred in Great Britain, because "adrenalin" was once a registered, proprietary drug name in the United States. Though the drug is no longer sold, the convention of referring to this molecule by the two different names persists. Similarly, norepinephrine and noradrenaline are two names for the same molecule.

All preganglionic fibers, both sympathetic and parasympathetic, release ACh. The postganglionic parasympathetic fibers also release ACh. Postganglionic sympathetic fibers release norepinephrine, except for fibers that project to sweat glands and to blood vessels associated with skeletal muscles, which release ACh.

Signaling molecules can belong to two broad groups. Neurotransmitters are released at synapses, whereas hormones are released into the bloodstream. These are simplistic definitions, but they can help to clarify this point. Acetylcholine can be considered a neurotransmitter because it is released by axons at synapses. The adrenergic system, however, presents a challenge. Postganglionic sympathetic fibers release norepinephrine, which can be considered a neurotransmitter. But the adrenal medulla releases epinephrine and norepinephrine into circulation, so they should be considered hormones.

Part 5: Neuronal Signalling

Having looked at the components of nervous tissue, and the basic anatomy of the nervous system, next comes an understanding of how nervous tissue is capable of communicating within the nervous system. Before getting to the nuts and bolts of how this works, an illustration of how the components come together will be helpful (summarized in Figure 26).

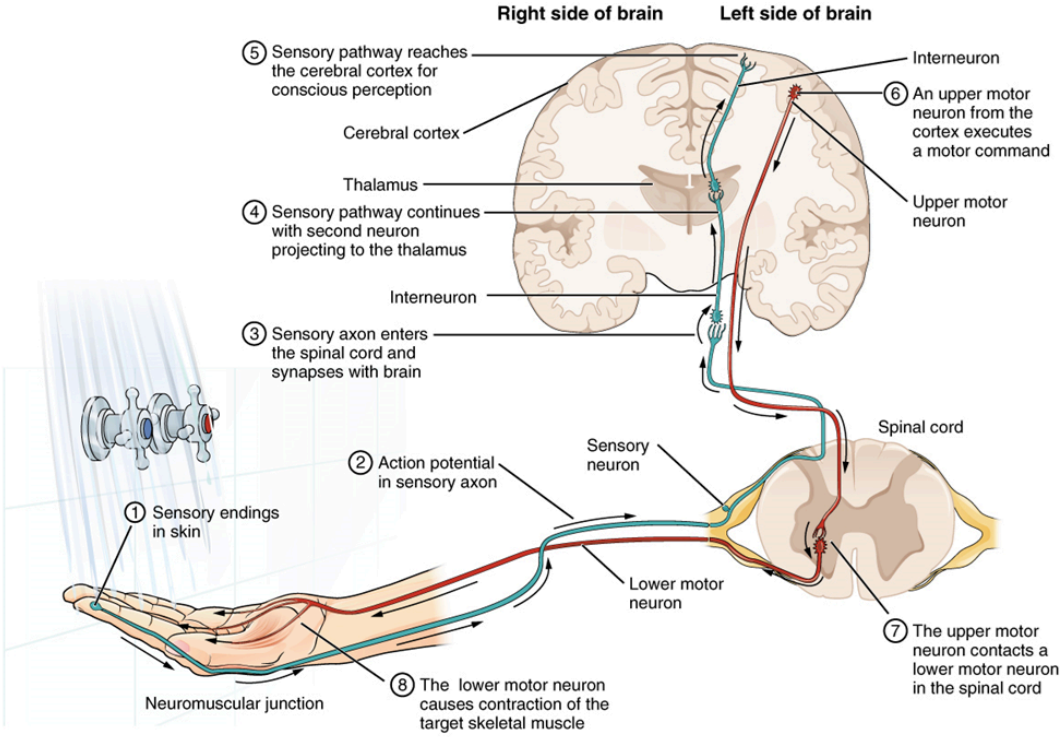


Figure 26. Testing the Water. *(1) The sensory neuron has endings in the skin that sense a stimulus such as water temperature. The strength of the signal that starts here is dependent on the strength of the stimulus. (2) The graded potential from the sensory endings, if strong enough, will initiate an action potential at the initial segment of the axon (which is immediately adjacent to the sensory endings in the skin). (3) The axon of the peripheral sensory neuron enters the spinal cord and contacts another neuron in the gray matter. The contact is a synapse where another graded potential is caused by the release of a chemical signal from the axon terminals. (4) An action potential is initiated at the initial segment of this neuron and travels up the sensory pathway to a region of the brain called the thalamus. Another synapse passes the information along to the next neuron. (5) The sensory pathway ends when the signal reaches the cerebral cortex. (6) After integration with neurons in other parts of the cerebral cortex, a motor command is sent from the precentral gyrus of the frontal cortex. (7) The upper motor neuron sends an action potential down to the spinal cord. The target of the upper motor neuron is the dendrites of the lower motor neuron in the gray matter of the spinal cord. (8) The axon of the lower motor neuron emerges from the spinal cord in a nerve and connects to a*

muscle through a neuromuscular junction to cause contraction of the target muscle.

Imagine you are about to take a shower. You have turned on the faucet to start the water as you prepare to get in the shower. After a few minutes, you expect the water to be a temperature that will be comfortable to enter. So you put your hand out into the spray of water. What happens next depends on how your nervous system interacts with the stimulus of the water temperature and what you do in response to that stimulus.

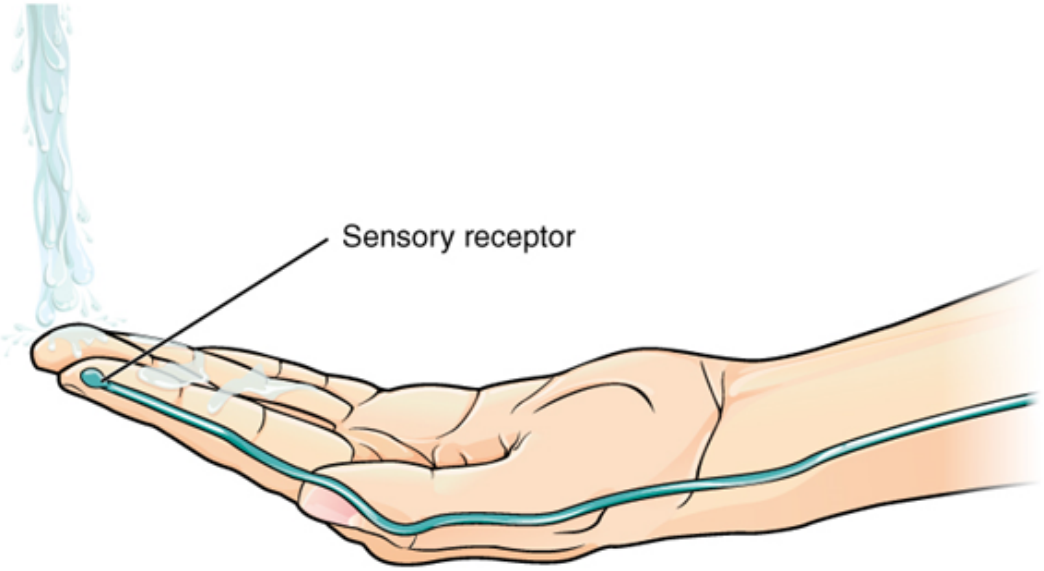


Figure 27. The Sensory Input. *Receptors in the skin sense the temperature of the water.*

Found in the skin of your fingers or toes is a type of sensory receptor that is sensitive to temperature, called a **thermoreceptor**. When you place your hand under the shower (Figure 27), the cell membrane of the thermoreceptors changes its electrical state (voltage). The amount of change is dependent on the strength of the stimulus (how hot the water is). This is called a **graded potential**. If the stimulus is strong, the voltage of the cell membrane will change enough to generate an electrical signal that will travel down the axon.

The voltage at which such a signal is generated is called the **threshold**, and the resulting electrical signal is called an **action potential**. In this example, the action potential travels—a process known as **propagation**—along the axon from the axon hillock to the axon terminals and into the synaptic end bulbs. When this signal reaches the end bulbs, it causes the release of a signaling molecule called a **neurotransmitter**.

The neurotransmitter diffuses across the short distance of the synapse and binds to a receptor protein of the target neuron. When the molecular signal binds to the receptor, the cell membrane of the target neuron changes its electrical state and a new graded potential begins. If that graded potential is strong enough to reach threshold, the second neuron generates an action potential at its axon hillock. The target of this neuron is another neuron in the **thalamus** of the brain, the part of the CNS that acts as a relay for sensory information. At another synapse, neurotransmitter is released and binds to its receptor. The thalamus then sends the sensory information to the **cerebral cortex**, the outermost layer of gray matter in the brain, where conscious perception of that water temperature begins. Within the cerebral cortex, information is processed among many neurons, integrating the stimulus of the water temperature with other sensory stimuli, with your emotional state (you just aren't ready to wake up; the bed is calling to you), memories (perhaps of the lab notes you have to study

before a quiz). Finally, a plan is developed about what to do, whether that is to turn the temperature up, turn the whole shower off and go back to bed, or step into the shower. To do any of these things, the cerebral cortex has to send a command out to your body to move muscles (Figure 28).

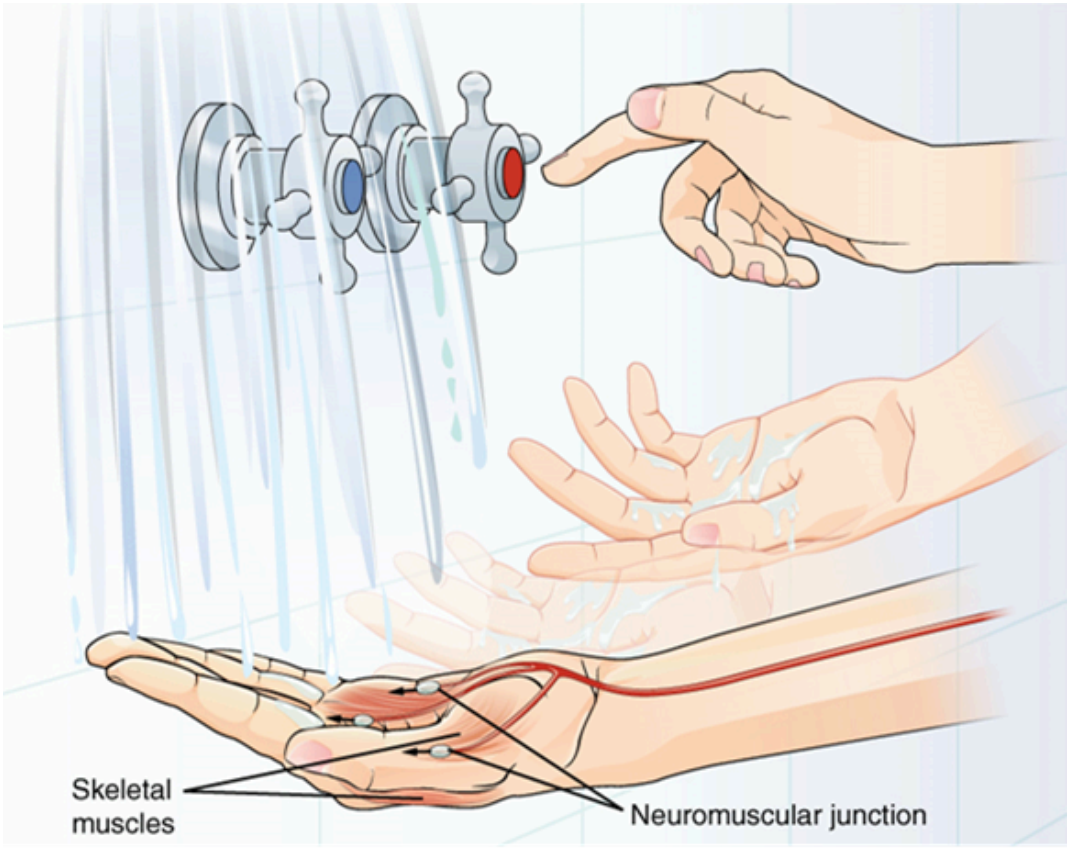


Figure 28. The Motor Response. *On the basis of the sensory input and the integration in the CNS, a motor response is formulated and executed.*

A region of the cortex is specialized for sending signals down to the spinal cord for movement. The **upper motor neuron** is in this region, called the primary **motor cortex**, which has an axon that extends all the way down the spinal cord. At the level of the spinal cord at which this axon makes a synapse, a graded potential occurs in the cell membrane of a **lower motor neuron**. This second motor neuron is responsible for causing muscle fibers to contract. In the manner described in the chapter on muscle tissue, an action potential travels along the motor neuron axon into the periphery. The axon terminates on muscle fibers at the neuromuscular junction. Acetylcholine is released at this specialized synapse, which causes the muscle action potential to begin, following a large potential known as an end plate potential. When the lower motor neuron excites the muscle fiber, it contracts. All of this occurs in a fraction of a second, but this story is the basis of how the nervous system functions.

Ion Channels and the Resting Membrane Potential

The functions of the nervous system—sensation, integration, and response—depend on the functions of the neurons underlying these pathways. To understand how neurons are able to communicate, it is necessary to describe the role of an **excitable membrane** in generating these signals. The basis of this communication is the action potential, which demonstrates how changes in the membrane can constitute a signal. Looking at the way these signals work in more variable circumstances involves a look at graded potentials, which will be covered in the next section.

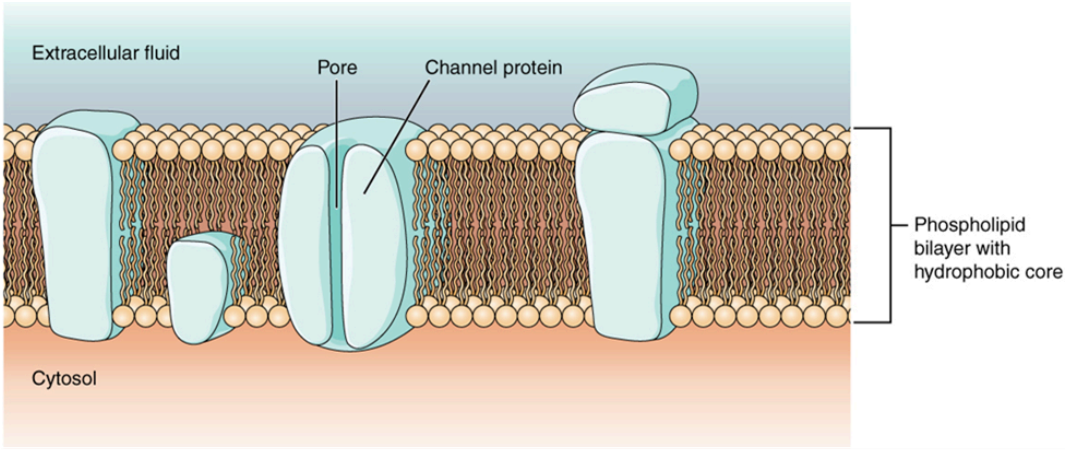


Figure 29. Cell Membrane and Transmembrane Proteins. *The cell membrane is composed of a phospholipid bilayer and has many transmembrane proteins, including different types of channel proteins that serve as ion channels.*

Most cells in the body make use of charged particles, ions, to build up a charge across the cell membrane. Cells make use of the cell membrane to regulate ion movement between the extracellular fluid and cytosol. As you learned in the chapter on cells, the cell membrane is primarily responsible for regulating what can cross the membrane and what stays on only one side. The cell membrane is a phospholipid bilayer, so only substances that can pass directly through the hydrophobic core can diffuse through unaided. Charged particles, which are hydrophilic by definition, cannot pass through the cell membrane without assistance (Figure 29). Transmembrane proteins, specifically channel proteins, make this possible. Several passive ion channels, as well as active transport pumps, are necessary to generate a transmembrane potential and an action potential. Ion channels are pores that allow specific charged particles to cross the membrane in response to an existing concentration gradient.

Of special interest is the carrier protein referred to as the sodium/potassium pump that moves sodium ions (Na^+) out of a cell and potassium ions (K^+) into a cell, thus regulating ion concentration on both sides of the cell membrane. The sodium/potassium pump requires energy in the form of adenosine triphosphate (ATP), so it is also referred to as an ATPase. As was explained in the cell chapter, the concentration of Na^+ is higher outside the cell than inside, and the concentration of K^+ is higher inside the cell than outside. That means that this pump is moving the ions against the concentration gradients for sodium and potassium, which is why it requires energy. In fact, the pump basically maintains those concentration gradients.

Ion channels do not always freely allow ions to diffuse across the membrane. Some are opened by certain events, meaning the channels are **gated**.

A **ligand-gated channel** opens because a signaling molecule, a ligand, binds to the extracellular region of the channel. This type of channel is also known as an ionotropic receptor because when the ligand, known as a neurotransmitter in the nervous system, binds to the protein, ions cross the membrane changing its charge (Figure 30).

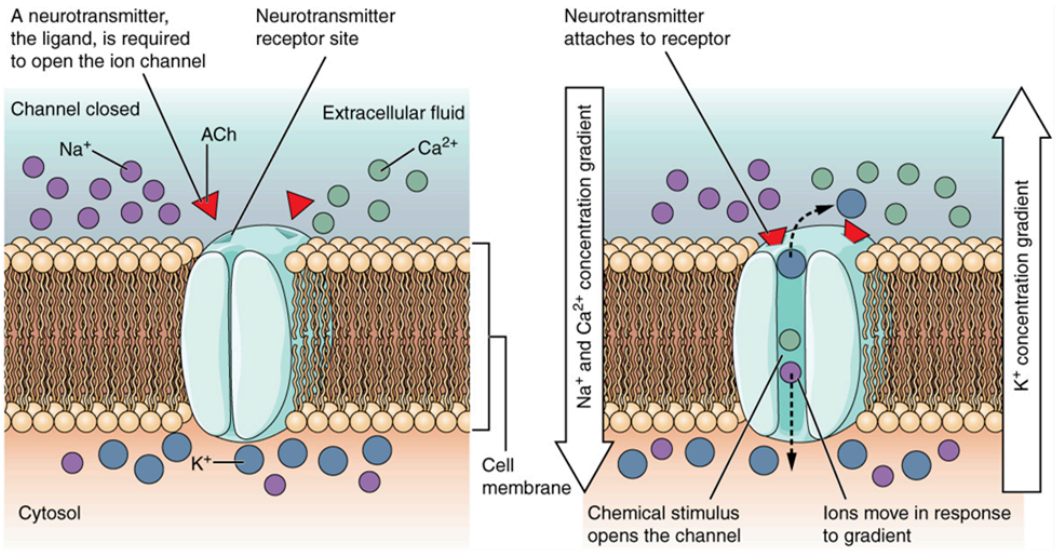


Figure 30. Ligand-Gated Channels. *When the ligand, in this case the neurotransmitter acetylcholine, binds to a specific location on the extracellular surface of the channel protein, the pore opens to allow select ions through. The ions, in this case, are cations of sodium, calcium, and potassium.*

A **mechanically gated channel** opens because of a physical distortion of the cell membrane. Many channels associated with the sense of touch (somatosensation) are mechanically gated. For example, as pressure is applied to the skin, these channels open and allow ions to enter the cell. Similar to this type of channel would be the channel that opens on the basis of temperature changes, as in testing the water in the shower (Figure 31).

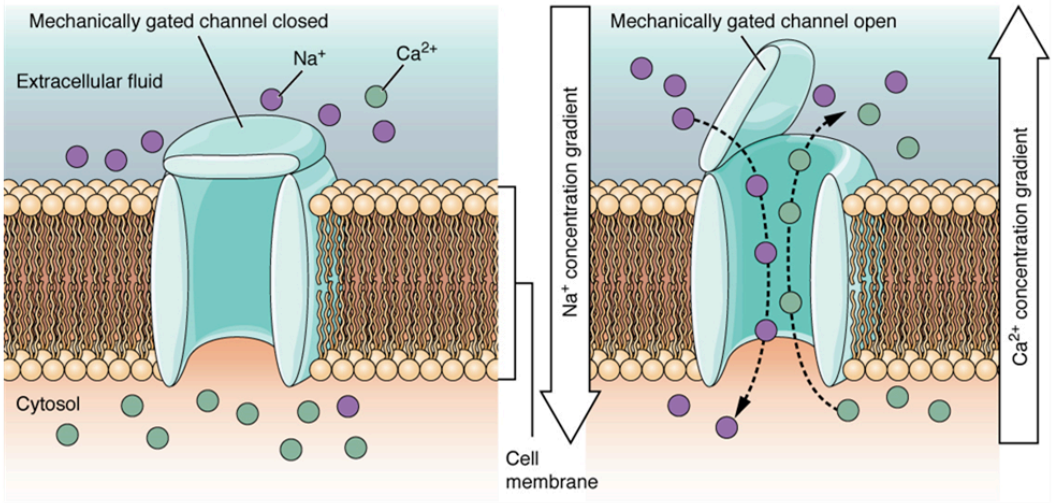


Figure 31. Mechanically Gated Channels. *When a mechanical change occurs in the surrounding tissue, such as pressure or touch, the channel is physically opened. Thermoreceptors work on a similar principle. When the local tissue temperature changes, the protein reacts by physically opening the channel.*

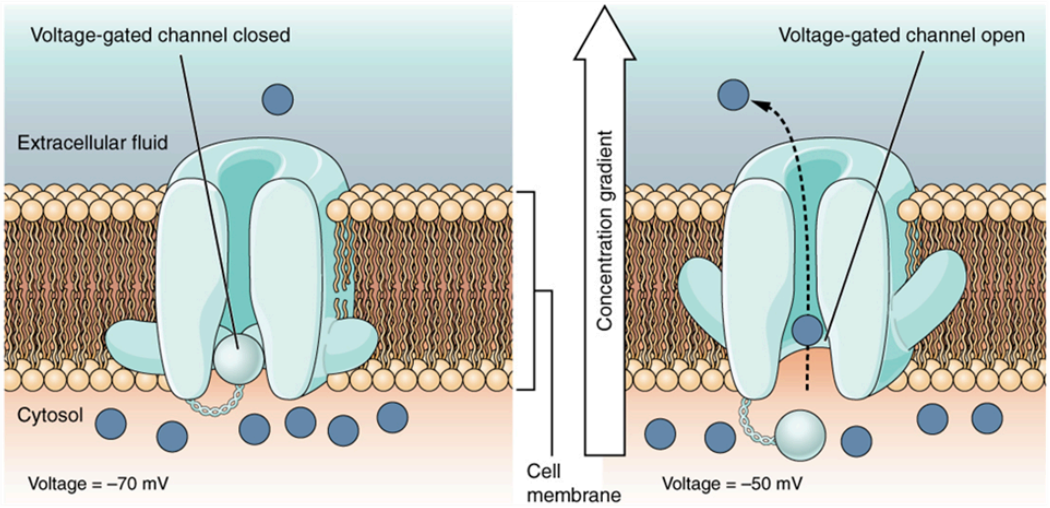


Figure 32. Voltage-Gated Channels. *Voltage-gated channels open when the transmembrane voltage changes around them. Amino acids in the structure of the protein are sensitive to charge and cause the pore to open to the selected ion.*

A **voltage-gated channel** is a channel that responds to changes in the electrical properties of the membrane in which it is embedded. Normally, the inner portion of the membrane is at a negative voltage. When that voltage becomes less negative, the channel begins to allow ions to cross the membrane (Figure 32).

A **leakage channel** is randomly gated, meaning that it opens and closes at random, hence the reference to leaking. There is no actual event that opens the channel; instead, it has an intrinsic rate of switching between the open and closed states. Leakage channels contribute to the resting transmembrane voltage of the excitable membrane (Figure 33).

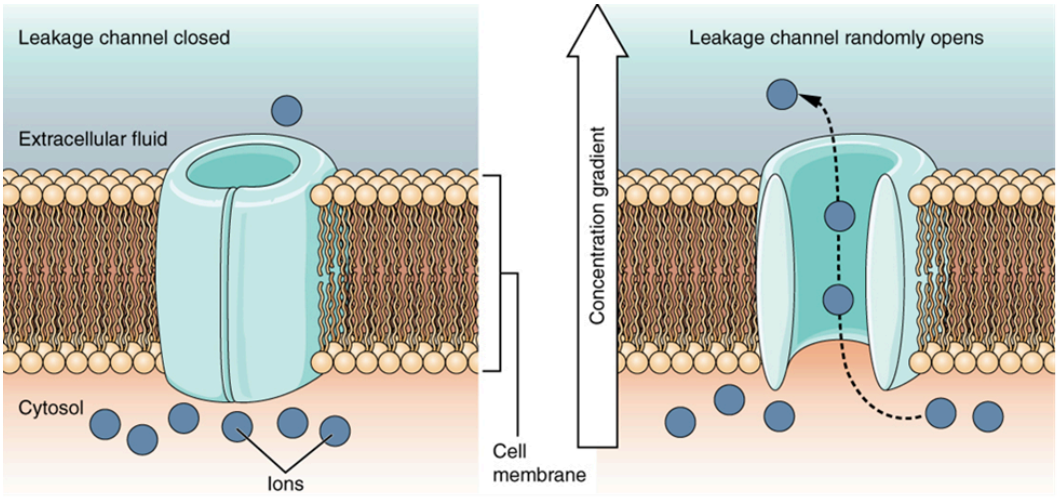


Figure 33. Leakage Channels. *In certain situations, ions need to move across the membrane randomly. The particular electrical properties of certain cells are modified by the presence of this type of channel.*

The electrical state of the cell membrane can have several variations. These are all variations in the **membrane potential**. A potential is a distribution of charge across the cell membrane, measured in millivolts (mV). The standard is to compare the inside of the cell relative to the outside, so the membrane potential is a value representing the charge on the intracellular side of the membrane based on the outside being zero, relatively speaking (Figure 34).

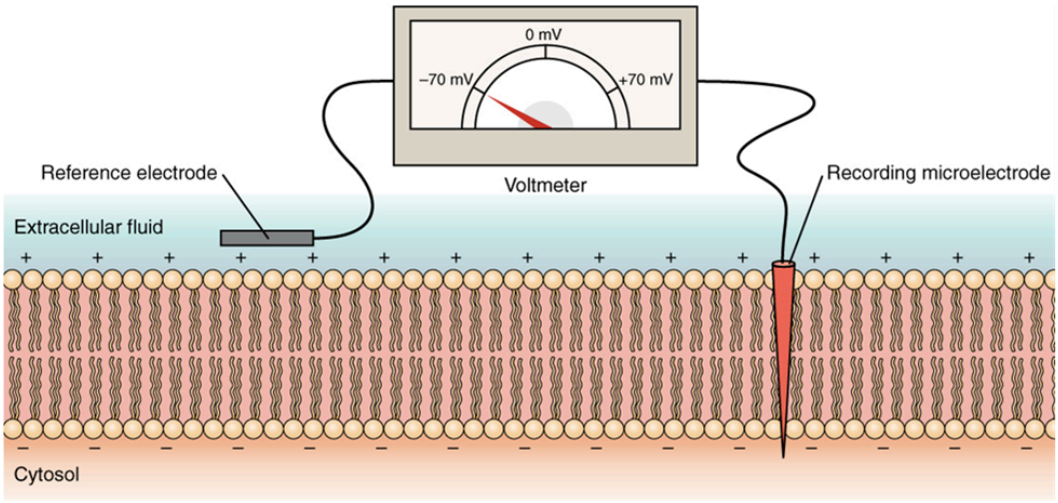


Figure 34. Measuring Charge across a Membrane with a Voltmeter. *A recording electrode is inserted into the cell and a reference electrode is outside the cell. By comparing the charge measured by these two electrodes, the transmembrane voltage is determined. It is conventional to express that value for the cytosol relative to the outside.*

The concentration of ions in extracellular and intracellular fluids is largely balanced, with a net neutral charge. However, a slight difference in charge occurs right at the membrane surface, both internally and externally. It is the difference in this very limited region that has all the power in neurons (and muscle cells) to generate electrical signals, including action potentials.

Before these electrical signals can be described, the resting state of the membrane must be explained. When the cell is at rest, and the ion channels are closed (except for leakage channels which randomly open), ions are distributed across the membrane in a very predictable way. The concentration of Na^+ outside the cell is 10 times greater than the concentration inside. Also, the concentration of K^+ inside the cell is greater than outside. The cytosol contains a high concentration of anions, in the form of phosphate ions and negatively charged proteins. Large anions are a component of the inner cell membrane, including specialized phospholipids and proteins associated with the inner leaflet of the membrane (leaflet is a term used for one side of the lipid bilayer membrane). The negative charge is localized in the large anions.

With the ions distributed across the membrane at these concentrations, the difference in charge is measured at -70 mV, the value described as the **resting membrane potential**. The exact value measured for the resting membrane potential varies between cells, but -70 mV is the most commonly recorded value. This voltage would actually be much lower except for the contributions of some important proteins in the membrane. Leakage channels K^+ channels allow K^+ to slowly move out of the cells. To a much lesser extent, leakage Na^+ channels allow Na^+ to slowly move into the cell. The constant activity of the Na^+/K^+ pump maintains the ion gradients. This may appear to be a waste of energy, but each has a role in maintaining the membrane potential.

Generation of an Action Potential

Resting membrane potential describes the steady state of the cell, which is a dynamic process that is balanced by ion leakage and ion pumping. Without any outside influence, it will not change. To get an electrical signal started, the membrane potential has to change.

This starts with a channel opening for Na^+ in the membrane. Because the concentration of Na^+ is higher outside the cell than inside the cell by a factor of 10, ions will rush into the cell that are driven largely by the concentration gradient. Because sodium is a positively charged ion, it will change the relative voltage immediately inside the cell relative to immediately outside. The resting potential is the state of the membrane at a voltage of -70 mV, so the sodium cation entering the cell will cause it to become less negative. This is known as **depolarization**, meaning the membrane potential moves toward zero.

The concentration gradient for Na^+ is so strong that it will continue to enter the cell even after the membrane potential has become zero, so that the voltage immediately around the pore begins to become positive. The

electrical gradient also plays a role, as negative proteins below the membrane attract the sodium ion. The membrane potential will reach +30 mV by the time sodium has entered the cell.

As the membrane potential reaches +30 mV, other voltage-gated channels are opening in the membrane. These channels are specific for the potassium ion. A concentration gradient acts on K^+, as well. As K^+ starts to leave the cell, taking a positive charge with it, the membrane potential begins to move back toward its resting voltage. This is called **repolarization**, meaning that the membrane voltage moves back toward the -70 mV value of the resting membrane potential.

Repolarization returns the membrane potential to the -70 mV value that indicates the resting potential, but it actually overshoots that value. Potassium ions reach equilibrium when the membrane voltage is below -70 mV, so a period of **hyperpolarization** occurs while the K^+ channels are open. Those K^+ channels are slightly delayed in closing, accounting for this short overshoot.

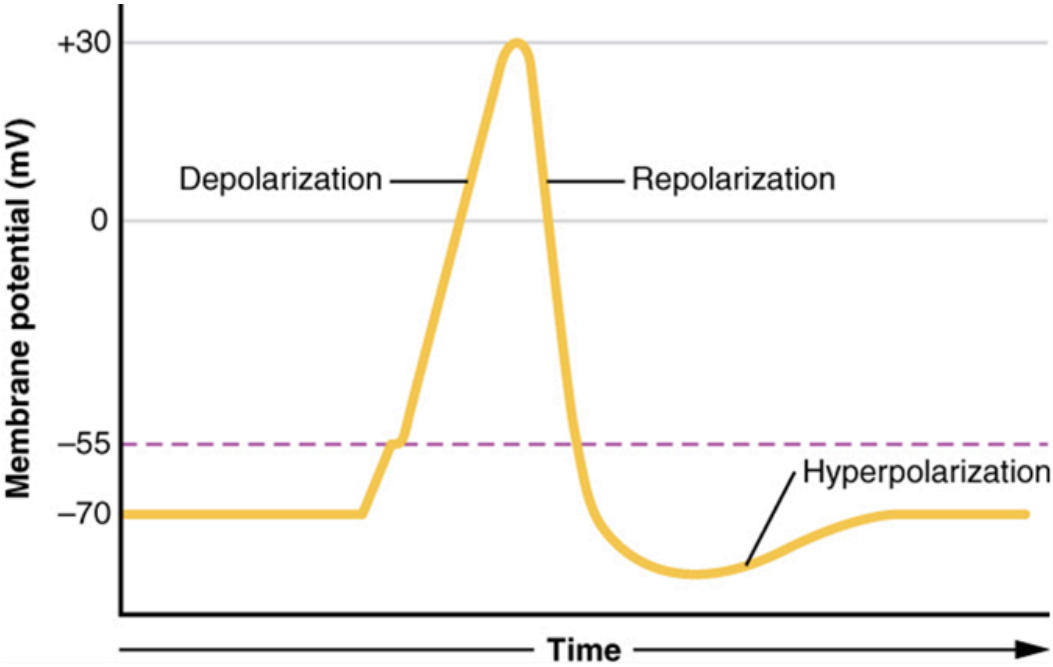


Figure 35. Graph of Action Potential. *Plotting voltage measured across the cell membrane against time, the action potential begins with depolarization, followed by repolarization, which goes past the resting potential into hyperpolarization, and finally the membrane returns to rest.*

Watch this Crash Course video to learn more about the action potential! Direct link: https://youtu.be/OZG8M_ldA1M

What has been described here is the action potential, which is presented as a graph of voltage over time (Figure

35). It is the electrical signal that nervous tissue generates for communication. The change in the membrane voltage from -70 mV at rest to +30 mV at the end of depolarization is a 100-mV change. That can also be written as a 0.1-V change. To put that value in perspective, think about a battery. An AA battery that you might find in a television remote has a voltage of 1.5 V, or a 9-V battery (the rectangular battery with two posts on one end) is, obviously, 9 V. The change seen in the action potential is one or two orders of magnitude less than the charge in these batteries. In fact, the membrane potential can be described as a battery. A charge is stored across the membrane that can be released under the correct conditions. A battery in your remote has stored a charge that is "released" when you push a button.

The question is, now, what initiates the action potential? The description above conveniently glosses over that point. But it is vital to understanding what is happening. The membrane potential will stay at the resting voltage until something changes. The description above just says that a Na^+ channel opens. Now, to say "a channel opens" does not mean that one individual transmembrane protein changes. Instead, it means that one kind of channel opens. There are a few different types of channels that allow Na^+ to cross the membrane. A ligand-gated Na^+ channel will open when a neurotransmitter binds to it and a mechanically gated Na^+ channel will open when a physical stimulus affects a sensory receptor (like pressure applied to the skin compresses a touch receptor). Whether it is a neurotransmitter binding to its receptor protein or a sensory stimulus activating a sensory receptor cell, some stimulus gets the process started. Sodium starts to enter the cell and the membrane becomes less negative.

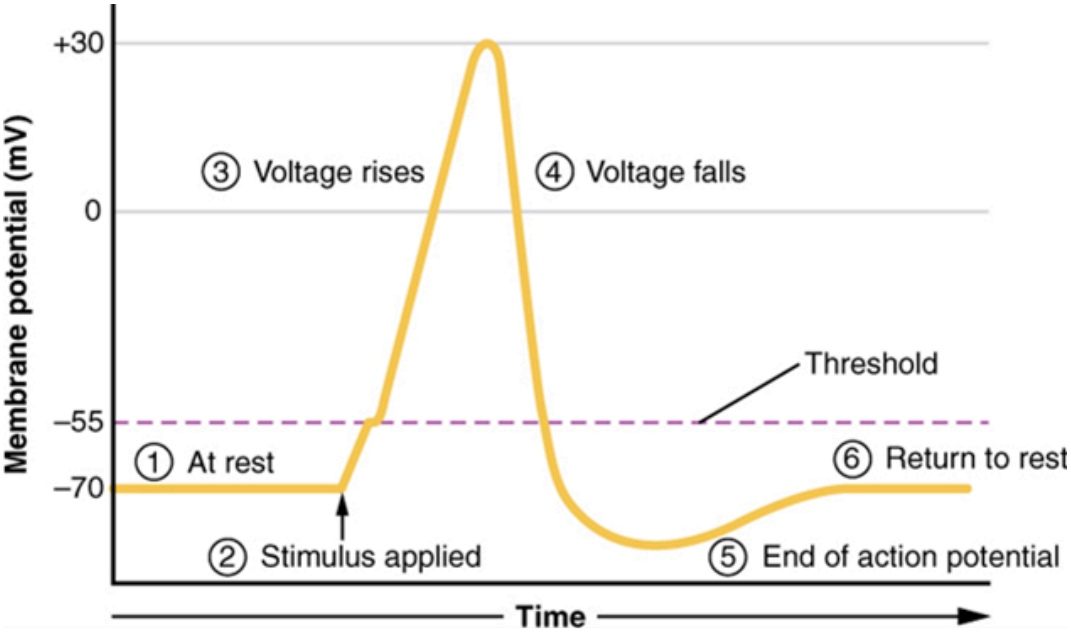


Figure 36. Stages of an Action Potential. *Plotting voltage measured across the cell membrane against time, the events of t6he action potential can be related to specific changes in the membrane voltage. (1) At rest, the membrane voltage is -70 mV. (2) The membrane begins to depolarize when an external stimulus is applied. (3) The membrane voltage begins a rapid rise toward +30 mV. (4) The membrane voltage starts to return to a negative value. (5) Repolarization continues past the resting membrane voltage, resulting in hyperpolarization. (6) The membrane voltage returns to the resting value shortly after hyperpolarization.*

A third type of channel that is an important part of depolarization in the action potential is the voltage-gated Na^+ channel. The channels that start depolarizing the membrane because of a stimulus help the cell to depolarize from -70 mV to -55 mV. Once the membrane reaches that voltage, the voltage-gated Na^+ channels

open. This is what is known as the threshold. Any depolarization that does not change the membrane potential to -55 mV or higher will not reach threshold and thus will not result in an action potential. Also, any stimulus that depolarizes the membrane to -55 mV or beyond will cause a large number of channels to open and an action potential will be initiated.

Because of the threshold, the action potential can be likened to a digital event—it either happens or it does not. If the threshold is not reached, then no action potential occurs. If depolarization reaches -55 mV, then the action potential continues and runs all the way to +30 mV, at which K^+ causes repolarization, including the hyperpolarizing overshoot. Also, those changes are the same for every action potential, which means that once the threshold is reached, the exact same thing happens. A stronger stimulus, which might depolarize the membrane well past threshold, will not make a "bigger" action potential. Action potentials are "all or none." Either the membrane reaches the threshold and everything occurs as described above, or the membrane does not reach the threshold and nothing else happens. All action potentials peak at the same voltage (+30 mV), so one action potential is not bigger than another. Stronger stimuli will initiate multiple action potentials more quickly, but the individual signals are not bigger. Thus, for example, you will not feel a greater sensation of pain, or have a stronger muscle contraction, because of the size of the action potential because they are not different sizes.

As we have seen, the depolarization and repolarization of an action potential are dependent on two types of channels (the voltage-gated Na^+ channel and the voltage-gated K^+ channel). The voltage-gated Na^+ channel actually has two gates. One is the activation gate, which opens when the membrane potential crosses -55 mV. The other gate is the inactivation gate, which closes after a specific period of time—on the order of a fraction of a millisecond. When a cell is at rest, the activation gate is closed and the inactivation gate is open. However, when the threshold is reached, the activation gate opens, allowing Na+ to rush into the cell. Timed with the peak of depolarization, the inactivation gate closes. During repolarization, no more sodium can enter the cell. When the membrane potential passes -55 mV again, the activation gate closes. After that, the inactivation gate re-opens, making the channel ready to start the whole process over again.

The voltage-gated K^+ channel has only one gate, which is sensitive to a membrane voltage of -50 mV. However, it does not open as quickly as the voltage-gated Na^+ channel does. It might take a fraction of a millisecond for the channel to open once that voltage has been reached. The timing of this coincides exactly with when the Na^+ flow peaks, so voltage-gated K^+ channels open just as the voltage-gated Na^+ channels are being inactivated. As the membrane potential repolarizes and the voltage passes -50 mV again, the channel closes—again, with a little delay. Potassium continues to leave the cell for a short while and the membrane potential becomes more negative, resulting in the hyperpolarizing overshoot. Then the channel closes again and the membrane can return to the resting potential because of the ongoing activity of the non-gated channels and the Na^+/K^+ pump. All of this takes place within approximately 2 milliseconds (Figure 36). While an action potential is in progress, another one cannot be initiated. That effect is referred to as the **refractory period**.

Propagation of Action Potentials

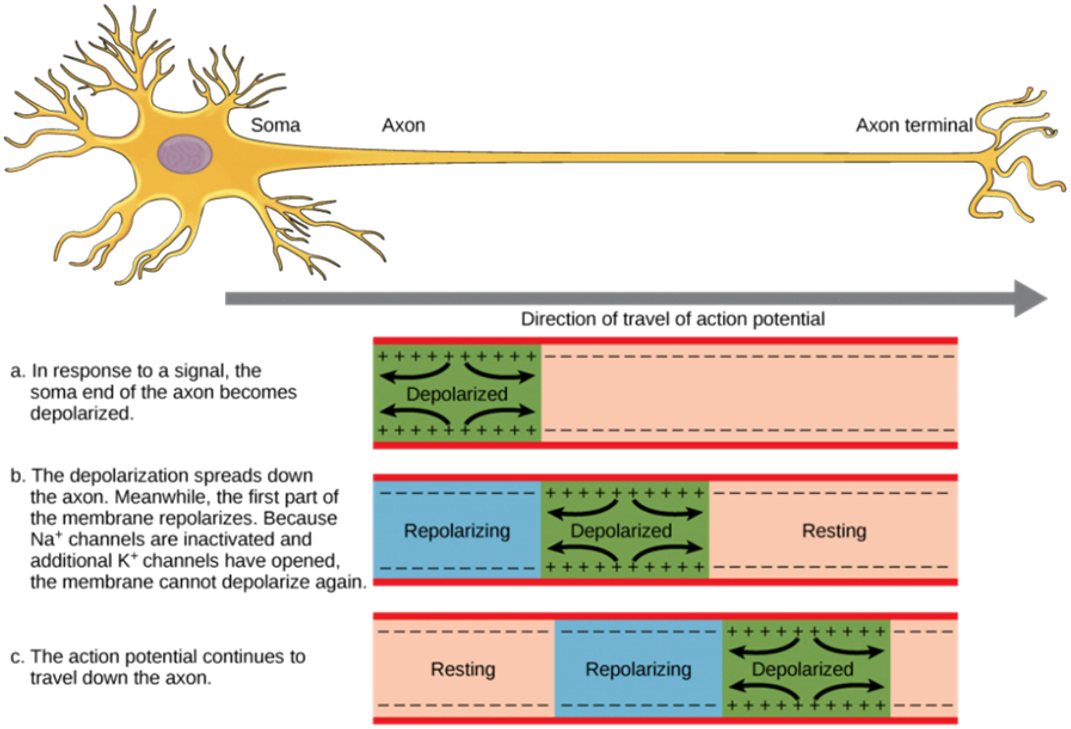


Figure 37. Propagation of an Action Potential Along an Unmyelinated Axon.

The action potential is initiated at the beginning of the axon, at what is called the initial segment. There is a high density of voltage-gated Na^+ channels so that rapid depolarization can take place here. Going down the length of the axon, the action potential is propagated because more voltage-gated Na^+ channels are opened as the depolarization spreads. This spreading occurs because Na^+ enters through the channel and moves along the inside of the cell membrane. As the Na+ moves, or flows, a short distance along the cell membrane, its positive charge depolarizes a little more of the cell membrane. As that depolarization spreads, new voltage-gated Na^+ channels open and more ions rush into the cell, spreading the depolarization a little farther (Figure 37).

Because voltage-gated Na^+ channels are inactivated at the peak of the depolarization, they cannot be opened again for a brief time—the absolute refractory period. Because of this, depolarization spreading back toward previously opened channels has no effect. The action potential must propagate toward the axon terminals; as a result, the polarity of the neuron is maintained, as mentioned above.

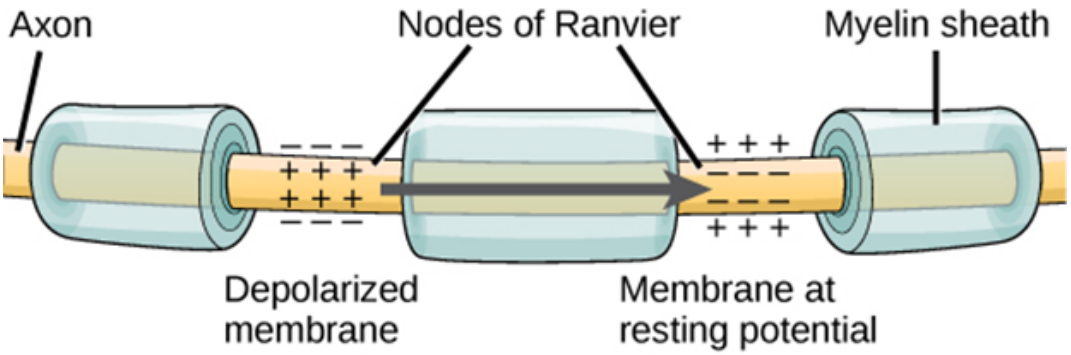


Figure 38. Propagation of an Action Potential Along a Myelinated Axon. *Nodes of Ranvier are gaps in myelin coverage along axons. Nodes contain voltage-gated K^+ and Na^+ channels. Action potentials travel down the axon by jumping from one node to the next. This diagram shows the nodes of Ranvier and the internodal (myelinated) segments with approximately the same length. This is not accurate: in real axons, the segments with myelin are about one thousand times longer than the nodes!*

Propagation, as described above, applies to unmyelinated axons. When myelination is present, the action potential propagates differently (Figure 38). Sodium ions that enter the cell at the initial segment start to spread along the length of the axon segment, but there are no voltage-gated Na^+ channels until the first node of Ranvier. Because there is not constant opening of these channels along the axon segment, the depolarization spreads at an optimal speed. The distance between nodes (1-3 mm) is the optimal distance to keep the membrane still depolarized above threshold at the next node. As Na^+ spreads along the inside of the membrane of the axon segment, the charge starts to dissipate. If the node were any farther down the axon, that depolarization would have fallen off too much for voltage-gated Na^+ channels to be activated at the next node of Ranvier. If the nodes were any closer together, the speed of propagation would be slower.

Propagation along an unmyelinated axon is referred to as **continuous conduction**; along the length of a myelinated axon, it is **saltatory conduction**. Continuous conduction is slow because there are always voltage-gated Na^+ channels opening, and more and more Na^+ is rushing into the cell. Saltatory conduction is faster because the action potential basically jumps from one node to the next (saltare = "to leap"), and the new influx of Na^+ renews the depolarized membrane. Along with the myelination of the axon, the diameter of the axon can influence the speed of conduction. Much as water runs faster in a wide river than in a narrow creek, Na^+-based depolarization spreads faster down a wide axon than down a narrow one. This concept is known as resistance and is generally true for electrical wires or plumbing, just as it is true for axons, although the specific conditions are different at the scales of electrons or ions versus water in a river.

Neurotransmission

The electrical changes taking place within a neuron, as described in the previous section, are similar to a light switch being turned on. A stimulus starts the depolarization, but the action potential runs on its own once a threshold has been reached. The question is now, "What flips the light switch on?" Temporary changes to the cell membrane voltage can result from neurons receiving information from the environment, or from the action of one neuron on another. These special types of potentials influence a neuron and determine whether an action potential will occur or not. Many of these transient signals originate at the **synapse**, the connection between electrically active cells.

There are two types of synapses: chemical synapses and electrical synapses. In a chemical synapse, a chemical signal—namely, a neurotransmitter—is released from one cell and it affects the other cell. In an electrical synapse, there is a direct connection between the two cells so that ions can pass directly from one cell to the next. If one cell is depolarized in an electrical synapse, the joined cell also depolarizes because the ions pass between the cells. Chemical synapses involve the transmission of chemical information from one cell to the next. This section will concentrate on the chemical type of synapse.

An example of a chemical synapse is the neuromuscular junction described in the chapter on muscle tissue. In the nervous system, there are many more synapses that are essentially the same as the neuromuscular junction. All synapses have common characteristics, which can be summarized in this list:

- presynaptic element
- neurotransmitter (packaged in vesicles)
- synaptic cleft
- receptor proteins
- postsynaptic element
- neurotransmitter elimination or re-uptake

Synaptic transmission (or neurotransmission) takes place through the following steps (Figure 39):

- An action potential reaches the axon terminal.
- The change in voltage causes voltage-gated Ca^{2+} channels in the membrane of the synaptic end bulb to open.
- The concentration of Ca^{2+} increases inside the end bulb, and Ca^{2+} ions associate with proteins in the outer surface of neurotransmitter vesicles facilitating the merging of the vesicle with the presynaptic membrane. The neurotransmitter is then released through exocytosis into the small gap between the cells, known as the **synaptic cleft**.
- Once in the synaptic cleft, the neurotransmitter diffuses the short distance to the postsynaptic membrane and can interact with neurotransmitter receptors. Receptors are specific for the neurotransmitter, and the two fit together like a key and lock. One neurotransmitter binds to its receptor and will not bind to receptors for other neurotransmitters, making the binding a specific chemical event.
- The interaction of the neurotransmitter with the receptor can result in depolarization or hyperpolarization of the postsynaptic cell membrane, leading to excitation of the postsynaptic cell (and possibly the generation of a new action potential) or inhibition, respectively.
- The neurotransmitter is removed from the synaptic cleft by diffusion, due to the action of enzymes that break it down chemically or by transporters in the presynaptic cell membrane.

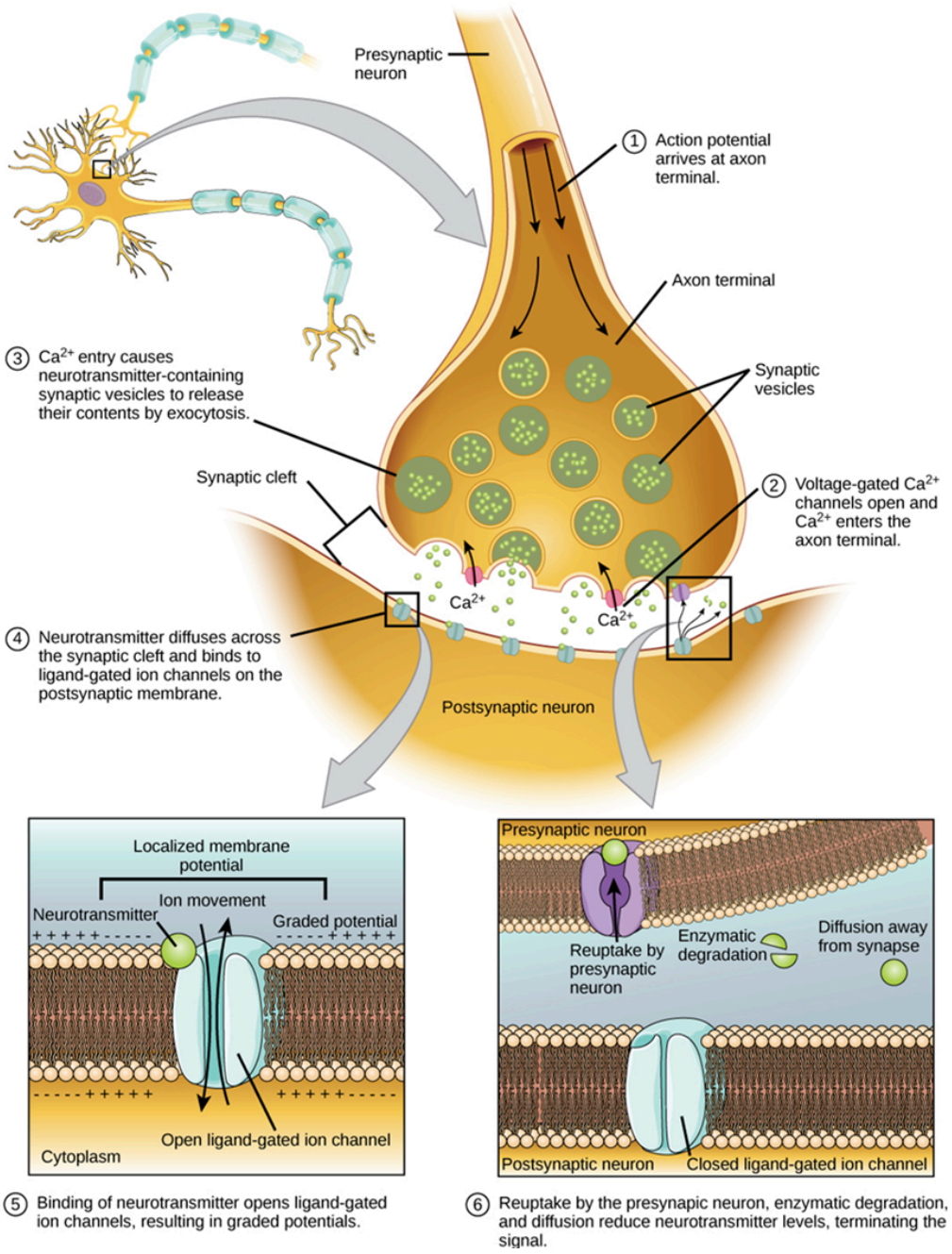


Figure 39. Synaptic Transmission. *The pre-synaptic neuron signals a postsynaptic neuron by releasing neurotransmitter across the synaptic cleft.*

Neurotransmitter Systems

There are several systems of neurotransmitters that are found at various synapses in the nervous system (Figure 40). In this course, you are not required to know all the neurotransmitters, but only to be able to provide one example of a neurotransmitter from each of the systems below.

- **Amino acids**: This includes glutamate (Glu), GABA (gamma-aminobutyric acid, a derivative of glutamate), and glycine (Gly).
- **Biogenic amines**: This is a group of neurotransmitters that are enzymatically made from amino acids. For

example, the neurotransmitter serotonin is made from tryptophan. Other biogenic amines are made from tyrosine, and include dopamine, norepinephrine, and epinephrine. The chemical epinephrine (epi- = "on"; "-nephrine" = kidney) is also known as adrenaline (renal = "kidney"), and norepinephrine is sometimes referred to as noradrenaline. The adrenal gland produces epinephrine and norepinephrine to be released into the blood stream as hormones.

- **Cholinergic system**: It is the system based on acetylcholine. This includes the neuromuscular junction as an example of a cholinergic synapse, but cholinergic synapses are found in other parts of the nervous system. They are in the autonomic nervous system, as well as distributed throughout the brain.
- **Neuropeptides:** These are neurotransmitter molecules made up of chains of amino acids connected by peptide bonds. This is what a protein is, but the term protein implies a certain length to the molecule. Some neuropeptides are quite short, such as met-enkephalin, which is five amino acids long. Others are long, such as beta-endorphin, which is 31 amino acids long. Neuropeptides are often released at synapses in combination with another neurotransmitter, and they often act as hormones in other systems of the body, such as vasoactive intestinal peptide (VIP) or substance P.

The effect of a neurotransmitter on the postsynaptic element is entirely dependent on the receptor protein. First, if there is no receptor protein in the membrane of the postsynaptic element, then the neurotransmitter has no effect. The depolarizing or hyperpolarizing effect is also dependent on the receptor. For example, when acetylcholine binds to a type of receptor called nicotinic receptor, the postsynaptic cell is depolarized. This is because the receptor is a cation channel and positively charged Na^+ will rush into the cell. However, when acetylcholine binds to another type of receptor called muscarinic receptor, of which there are several variants, it might cause depolarization or hyperpolarization of the target cell.

On the other hand, the amino acid neurotransmitters, glutamate, glycine, and GABA, are almost exclusively associated with just one effect. Glutamate is considered an excitatory amino acid, but only because Glu receptors in the adult cause depolarization of the postsynaptic cell. Glycine and GABA are considered inhibitory amino acids, again because their receptors cause hyperpolarization.

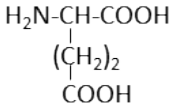
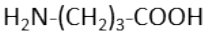
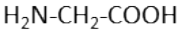
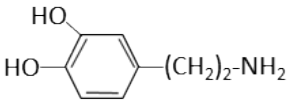
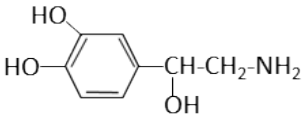
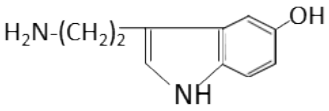
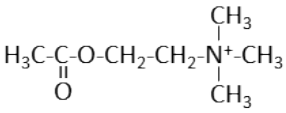
Amino Acids		
Glutamate		**Main excitatory neurotransmitter**
GABA		**Main inhibitory neurotransmitter of the brain**
Glycine		**Inhibitory neurotransmitter of the spinal cord**
Biogenic Amines		
Dopamine		**Wanting, motivation, motor control**
Norepinephrine		**Wakefulness, sympathetic response**
Serotonin		**Satisfaction, arousal**
Cholinergic System		
Acetylcholine		**Muscle contraction, memory**
Neuropeptides		
	Amino Acid Sequences	
Met-Enkephalin	Tyr-Gly-Gly-Phe-Met	**Endorphins (endogenous opioids) have analgesic (i.e. pain reduction) and pleasure-inducing effects.**
Beta-Endorphin	Tyr-Gly-Gly-Phe-Met-Thr-Ser-Glu-Lys-Ser-Gln-Thr-Pro-Leu-Val-Thr-Leu-Phe-Lys-Asn-Ala-Ile-Ile-Lys-Asn-Ala-Tyr-Lys-Lys-Gly-Glu	

Figure 40. Examples of Neurotransmitters. *Shown are some examples of major transmitters, their chemical structures and some of their functions.*

Unit 10: Sensory Systems

Unit Outline

Part 1: Overall Organization of the Sensory Systems

- Sensory receptors
- Sensory modalities
- Somatosensation

Part 2: Gustation

Part 3: Olfaction

Part 4: Audition and Balance

Part 5: Vision

Learning Objectives

Parts 1-3: Overall Organization of the Sensory Systems, Gustation, Olfaction

At the end of this part of this unit, you should be able to:

I. List the five main categories of sense receptors in the body based on the types of stimuli they respond to.

II. Describe the structure and function of cutaneous sensors and proprioceptors.

III. Describe the structure and function of the olfactory system.

IV. Describe the structure and function of the gustatory system.

Part 4: Audition and Balance

At the end of this part of this unit, you should be able to:

I. Describe the structure and functions of the external, middle and inner ear.

II. Describe the physiology of hearing.

III. Describe the physiology of static and dynamic balance.

Part 5: Vision

At the end of this part of this unit, you should be able to:

I. Identify the location and explain the function of each of the main components of the human eye.

II. Describe the formation of an image on the retina.

III. Describe the overall distribution and functions of the two main types of photoreceptors in the retina.

IV. Describe the pathway of the nervous impulses from the photoreceptors of the retina to the brain.

V. Describe the location, structure and functions of the lacrimal apparatus.

Learning Objectives and Guiding Questions

Parts 1-3: Overall Organization of the Sensory Systems, Gustation, Olfaction

At the end of this part of this unit, you should be able to complete all the following tasks, including answering the guiding questions associated with each task.

I. List the five main categories of sense receptors in the body based on the types of stimuli they respond to.

1. Specify the five categories of sense receptors found in the human body. For each category, state the stimuli they are capable of detecting and specify their location(s) in the human body.

II. Describe the structure and function of cutaneous sensors and proprioceptors.

1. Describe the location, structure and function of:
    - Cutaneous sensors
    - Proprioceptors

III. Describe the structure and function of the olfactory system.

1. Describe the location, structure and function of olfactory receptors.
2. Describe the pathway by which information about chemicals detected by olfactory receptors is transmitted to the cerebrum.

IV. Describe the structure and function of the gustatory system.

1. Describe the location, structure and function of gustatory receptors.
2. What are the five primary tastes?
3. Describe the pathway by which information about molecules detected by gustatory receptors is transmitted to the cerebrum.

Part 4: Audition and Balance

At the end of this part of this unit, you should be able to complete all the following tasks, including answering the guiding questions associated with each task.

I. Describe the structure and functions of the external, middle and inner ear.

1. Draw a fully-labelled diagram showing the anatomy of the external, middle and inner ear. Add annotations to each label describing the function of each anatomical component.
2. Name the three auditory ossicles. For each ossicle, use complete sentences to describe its location, structure (shape and tissue type) and function.
3. One opening from the middle ear leads to the mastoid antrum. List and describe (in words) the structure and function of the four other openings of the middle ear. Which one(s) have tissue covering them, and which do not; which can be opened, and which cannot? Why?
4. Describe how a throat infection can lead to the infection of the middle ear.
5. Use correct anatomical terms to specify in detail the route that could be taken by a pathogen (e.g. a bacterium) from the throat to the mastoid air cells.
6. Draw a fully-labelled diagram showing the structure and relative locations of the following components. Add annotations to each label briefly describing the contents and function of each component.

    - Bony labyrinth
    - Membranous labyrinth
    - Cochlea
    - Semicircular canals
    - Vestibule
    - Utricle
    - Saccule
    - Semicircular ducts
    - Cochlear duct
    - Oval window
    - Round window

7. Draw a fully-labelled diagram of the cochlea in *cross section*, including the following components. Add annotations to each label briefly describing the function of each component.

    - Cochlear duct
    - Scala tympani
    - Scala vestibuli
    - Organ of Corti
    - Tectorial membrane
    - Basilar membrane
    - Vestibular membrane
    - Spiral ganglion
    - Endolymph
    - Perilymph
    - Hair cells

8. Draw a fully-labelled diagram of an unwound *longitudinal section* of the cochlea, including the following components. Add annotations to each label briefly describing the function of each component.

    - Cochlear duct
    - Scala tympani

- Scala vestibuli
- Organ of Corti
- Tectorial membrane
- Basilar membrane
- Vestibular membrane
- Helicotrema
- Endolymph
- Perilymph
- Oval window
- Round window

II. Describe the physiology of hearing.

1. Describe in detail (in words, although you may wish to create diagrams to help you) the pathway taken by each the following, travelling from the external environment to an appropriate location to stimulate receptor cells.

    - A high-frequency audible sound
    - A low-frequency audible sound
    - A sound outside of the hearing range

2. Describe in detail the mechanism by which a sound wave travelling through the cochlea stimulates hair cells, and the mechanism by which those receptors then stimulate a neuron of the cochlear branch of the vestibulocochlear nerve to fire an action potential.

III. Describe the physiology of static and dynamic balance.

1. Draw a fully-labelled diagram showing the location and anatomical features of each of the following structures. Add annotations to your diagram briefly describing the function of each component of the structures.

    - A crista ampullaris
    - A macula

2. Compare and contrast the location, structure, and function of the receptor cells in the cristae ampullaris and those of the maculae.
3. Compare and contrast the mechanisms by which the following pairs of cells are stimulated to release neurotransmitters:

    - A hair cell in an Organ of Corti and a hair cell in a macula
    - A hair cell in a macula and a hair cell in a crista ampullaris
    - A hair cell in an Organ of Corti and a rod cell in a retina
    - A hair cell in an Organ of Corti and a motor neuron
    - A hair cell in a crista ampullaris and a motor neuron

4. Describe in detail (in words, although you may wish to create diagrams to help you) the neural pathways taken by information arising in the cochlea and in the vestibular apparatus to reach the brain. (Which parts of these two pathways are similar, and which are different?)
5. Draw one fully-labelled diagram showing the neural pathways taken by information from

sensory receptors in the cochlea, vestibular apparatus, retina, olfactory epithelium, and taste bud. Clearly indicate on your diagram any structures in the brain that these pathways share.

6. Compare and contrast the causes of, effects of conduction deafness and sensorineural deafness.
7. Given what you now know about the physiology of the ear, state whether each of the following could cause tinnitus and/or deafness and/or balance impairments. In each case, explain your reasoning in detail.

    - Buildup of ear wax
    - Perforation of the tympanic membrane
    - Degeneration of the cochlear branch of the vestibulocochlear nerve
    - Degeneration of the vestibular branch of the vestibulocochlear nerve
    - Degeneration of the vestibulocochlear nerve
    - Degeneration of the primary auditory cortex
    - Degeneration of the thalamus
    - Degeneration of the cerebellum
    - Otitis media
    - Otitis interna (labyrinthitis)

Part 5: Vision

At the end of this part of this unit, you should be able to complete all the following tasks, including answering the guiding questions associated with each task.

I. Identify the location and explain the function of each of the main components of the human eye.

1. Draw an annotated diagram showing the human eye in cross-section, clearly identifying the following components and listing (using one sentence only) the function of each:

    - Fibrous tunic
    - Vascular tunic
    - Neural tunic
    - Sclera
    - Cornea
    - Ciliary body
    - Iris
    - Pupil
    - Retina
    - Macula lutea
    - Optic disc
    - Fovea
    - Conjunctiva
    - Optic nerve
    - Lens
    - Suspensory ligaments
    - Aqueous humor
    - Vitreous humor

II. Describe the formation of an image on the retina.

1. Describe the formation of an image on the retina. Include in your description an explanation of where, how, and under what conditions each occur at the eye:
    - The behaviour of light rays upon reaching and moving through the eye (refraction)
    - Accommodation of the lens
    - The behaviour of the pupil when focusing (dilation vs. constriction)
    - Adaptation of the pupil to light intensity (dilation vs. constriction)
    - Convergence of the eyes

III. Describe the overall distribution and functions of the two main types of photoreceptors in the retina.

1. Specify the two main types of photoreceptors in the retina. Clearly describe and distinguish between these two photoreceptor types by comparing their:
    - Distribution across the retina
    - Cellular structure (overall shape and any specialized cell components)
    - Function in the eye in terms of what type and intensity of light they detect

IV. Describe the pathway of the nervous impulses from the photoreceptors of the retina to the brain.

1. Draw an annotated diagram describing in detail the afferent pathways involved in moving information from the photoreceptors of both retinas to neurons in the cortex of the brain. Your diagram should at least include all of these labels:
    - Left eye
    - Right eye
    - Left/right/temporal/nasal visual field
    - Temporal retina
    - Nasal retina
    - Rod
    - Ganglion cell
    - Fovea
    - Cone
    - Bipolar cell
    - Optic disc
    - Optic chiasma
    - Optic nerve
    - Optic tract
    - Primary visual cortex
    - Optic radiation
    - Midbrain
    - Thalamus
2. Explain why the left side of the brain interprets images from the right side of the visual fields, and vice versa.

V. Describe the location, structure and functions of the lacrimal apparatus.

1. Use correct anatomical terms in complete sentences to describe the location of the lacrimal apparatus.
2. Draw an annotated diagram showing the location and function of the lacrimal apparatus.

Part 1: Overall Organization of the Sensory Systems

A major role of sensory receptors is to help us learn about the environment around us, or about the state of our internal environment. Stimuli from varying sources, and of different types, are received and changed into the electrochemical signals of the nervous system. This occurs when a stimulus changes the cell membrane potential of a sensory cell. The stimulus can cause the sensory cell to produce an action potential which is relayed into the central nervous system (CNS), where it is integrated with other sensory information—or sometimes higher cognitive functions—to become a conscious perception of that stimulus. The central integration in the CNS may then lead to a motor response.

Describing sensory function with the term sensation vs. perception is a deliberate distinction. Sensation is the activation of sensory receptor cells at the level of the stimulus. Perception is the central processing of sensory stimuli into a meaningful pattern. Perception is dependent on sensation, but not all sensations are perceived. Receptors are the cells or structures that detect sensations. A receptor cell is changed directly by a stimulus. A transmembrane protein receptor is a protein in the cell membrane which mediates a physiological change in a cell, most often through the opening of ion channels or changes in the cell signaling processes. Transmembrane receptors are activated by chemicals called ligands. For example, a molecule in food can serve as a ligand for taste receptors. Other transmembrane proteins, which are not accurately called receptors, are sensitive to mechanical or thermal changes. Physical changes in these proteins increase ion flow across the membrane, and can generate an action potential or a graded potential in the sensory neurons.

Sensory Receptors: Stimuli in the environment activate specialized receptor cells in the peripheral nervous system. Different types of stimuli are sensed by different types of receptor cells. Receptor cells can be classified into types on the basis of three different criteria: cell type, position, function. Receptors can be classified structurally on the basis of cell type and their position in relation to stimuli they sense. They can also be classified functionally on the basis of the **transduction** of stimuli, or how a mechanical stimulus, light, or chemical changes the cell membrane potential.

Structural Receptor Types: The cells that interpret information about the environment can either be: (1) a neuron that has a **free nerve ending,** with dendrites embedded in tissue that receives a sensation; (2) a neuron that has an **encapsulated ending** in which the sensory nerve endings are encapsulated in connective tissue that enhances their sensitivity; or (3) a specialized **receptor cell**, which has distinct structural components that interpret a specific type of stimulus (Figure 1). The pain and temperature receptors in the dermis of the skin are examples of neurons that have free nerve endings. Also located in the dermis of the skin are lamellated corpuscles, neurons with encapsulated nerve endings that respond to pressure and touch. The cells in the retina that respond to light stimuli are an example of a specialized receptor, in this case a **photoreceptor**.

Another way to classify receptors is based on the location of the stimuli to which they respond. An **exteroceptor** is a receptor that is located near a stimulus in the external environment, such as the somatosensory receptors that are located in the skin. An **interoceptor** is one that interprets stimuli from internal organs and tissues, such as the receptors that sense the increase in blood pressure in the aorta or carotid sinus. Finally, a **proprioceptor** is a receptor located near a moving part of the body, such as a muscle, which interprets the positions of the tissues as they move.

Functional Receptor Types: A third classification of receptors is based on how the receptor transduces

stimuli into changes in membrane potential. Stimuli are of three general types. Some stimuli are ions and macromolecules that affect transmembrane receptor proteins when these chemicals diffuse across the cell membrane. Some stimuli are physical variations in the environment that affect receptor cell membrane potentials. Other stimuli include the electromagnetic radiation from visible light. For humans, the only electromagnetic energy that is perceived by our eyes is visible light. Other organisms have sensory receptors that humans lack, such as the heat sensors of snakes, the ultraviolet light sensors of bees, or the magnetic receptors in migratory birds.

Receptor cells can be further categorized on the basis of the type of stimuli they respond to. Chemical stimuli can be interpreted by a **chemoreceptor** which detects chemical stimuli that arise from the external environment, such as the compounds that determine an object's taste or smell, or from the internal environment to monitor physiologically important parameters or the presence of damage. **Osmoreceptors**, for example, respond to solute concentrations of body fluids. The sensation of pain is primarily the result of the presence of chemicals released as a result of tissue damage or other intense stimuli through **nociceptors**.

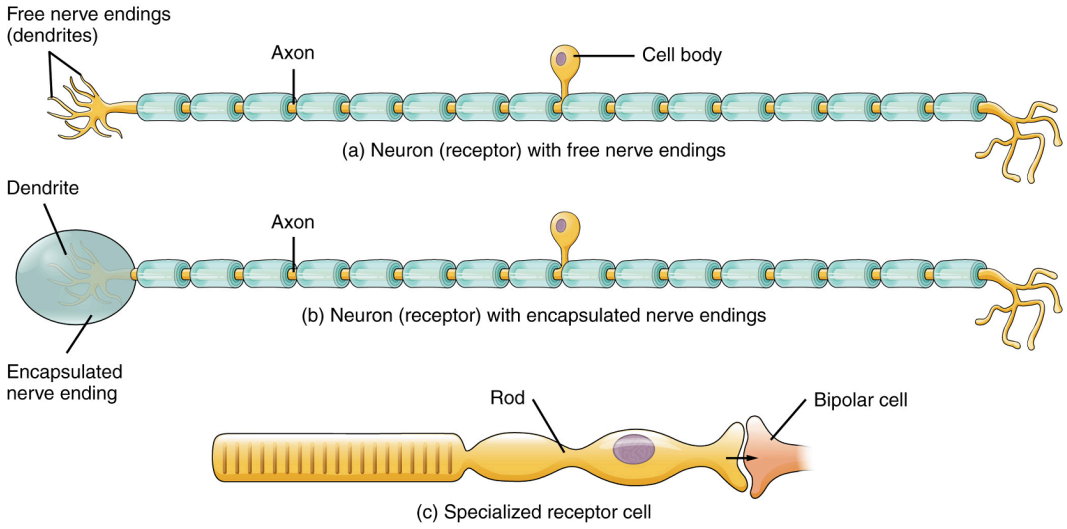


Figure 1. Receptor Classification by Cell Type. *Receptor cell types can be classified on the basis of their structure. Sensory neurons can either have (a) free nerve endings or (b) encapsulated endings. Photoreceptors in the eyes, such as rod cells, are examples of (c) specialized receptor cells. These cells release neurotransmitters onto a bipolar cell, which then synapses with the optic nerve neurons.*

Physical stimuli such as pressure and vibration, as well as the sensation of sound and body position (balance), are interpreted through **mechanoreceptors**. A physical stimulus which has its own type of receptor is temperature, sensed through **thermoreceptors** which are sensitive to temperatures either above (warmth/heat) or below (coolness/cold) normal body temperature.

Finally, highly specialized receptor cells called **photoreceptors** are used to detect light. They are found in the retina of the eye.

Sensory Modalities: Ask anyone what the senses are, and they are likely to list taste, smell, touch, hearing and sight. However, these are not all of the senses. The most obvious omission from this list is balance. Also, what is colloquially referred to as touch is a collection of senses that include pressure, vibration, stretch, and hair follicle position, on the basis of the type and location of mechanoreceptors that perceive these stimuli. Other often-overlooked senses include temperature perception by thermoreceptors and pain perception by nociceptors.

Within the realm of physiology, senses can be classified as either general or specific. A **general sense** is one that is distributed throughout the body and has receptor cells within the structures of other organs. Mechanoreceptors in the skin, muscles, or the walls of blood vessels are examples of receptor cells which function in this type of sense. General senses often contribute to the sense of touch, or to **proprioception** and

kinesthesia (body movement), or to a visceral sense, which is most important to autonomic functions. A **special sense** is one that has a specific organ devoted to it, namely the eye, inner ear, tongue, or nose.

Each sense is referred to as a **sensory modality**. Modality refers to the way information is encoded, which is similar to the idea of transduction. The main sensory modalities can be described on the basis of how each is transduced. The chemical senses are taste and smell. The general sense which is usually referred to as touch includes chemical sensation in the form of nociception, or pain. Pressure, vibration, muscle stretching and the movement of hair by an external stimulus are all sensed by mechanoreceptors. Hearing and balance are also achieved through the actions of mechanoreceptors in sense organs. Finally, vision involves the activation of photoreceptors.

Listing all the different sensory modalities, which can number as many as 17, involves separating the major senses into more specific categories, or **submodalities**, of the larger sense. An individual sensory modality represents the sensation of a specific type of stimulus.

Somatosensation: Somatosensation is the group of sensory modalities which is associated with touch, proprioception and interoception. These modalities include pressure, vibration, light touch, tickle, itch, temperature, pain and kinesthesia. Somatosensation is considered a general sense because somatosensory receptors are not associated with a specialized organ, but are instead spread throughout the body in a variety of organs. Many of these receptors are located in the skin and are referred to as **cutaneous receptors**. However, somatosensory receptors are also found in muscles, tendons, joint capsules, ligaments and in the walls of visceral organs.

Two types of somatosensory signals are transduced by free nerve endings: pain and temperature. These two modalities use thermoreceptors and nociceptors to transduce temperature and pain stimuli, respectively. Thermoreceptors are stimulated when local temperatures differ from body temperature. Some thermoreceptors are sensitive to just cold and others to just heat. Nociception is the sensation of potentially damaging stimuli, leading to pain. Mechanical, chemical or thermal stimuli beyond a set threshold will elicit painful sensations. Stressed or damaged tissues release chemicals which activate receptor proteins in the nociceptors. For example, the sensation of heat associated with spicy foods involves capsaicin, the active molecule in hot peppers. Capsaicin molecules bind to a particular type of transmembrane ion channel in nociceptors which is sensitive to temperatures above 37°C. The dynamics of capsaicin binding with this transmembrane ion channel is unusual in that the molecule remains bound for a long time. During this time, the ability of other stimuli to elicit pain sensations through the activated nociceptor will be diminished. For this reason, capsaicin can be used as a topical analgesic, such as in the product Icy Hot™.

If you drag your finger across a textured surface, the skin of your finger will vibrate. These low-frequency vibrations are sensed by mechanoreceptors called Merkel cells, also known as type I cutaneous mechanoreceptors. Merkel cells are located in the stratum basale of the epidermis. Deep pressure and vibration are transduced by lamellated (Pacinian) corpuscles, which are encapsulated receptors found deep in the dermis, or in the subcutaneous tissue. Light touch is transduced by the encapsulated nerve endings known as tactile (Meissner) corpuscles. Follicles are also wrapped in a plexus of nerve endings known as the hair follicle plexus. These nerve endings detect the movement of hair at the surface of the skin, such as when an insect is walking along the skin. Stretching of the skin is transduced by stretch receptors known as bulbous corpuscles. Bulbous corpuscles are also known as Ruffini corpuscles, or type II cutaneous mechanoreceptors.

Other somatosensory receptors are found in the joints and muscles, the proprioceptors. Stretch receptors monitor the stretching of tendons, muscles and the components of joints. Have you ever stretched your muscles before or after exercise and noticed that you can only stretch so far before your muscles spasm back to a less stretched state? This spasm is a reflex which is initiated by stretch receptors to avoid muscle tearing. These stretch receptors can also prevent the over-contraction of a muscle. In skeletal muscle tissue, these stretch receptors are called muscle spindles. Golgi tendon organs similarly transduce the stretch levels of tendons. Bulbous corpuscles are also present in joint capsules, where they measure stretch in the components of the skeletal system within the joint.

The main types of nerve endings, their locations and the stimuli they transduce are presented in Table 1.

Table 1: Mechanoreceptors of Somatosensation

Name	Historical (eponymous) name	Location(s)	Stimuli
Free nerve endings	–	Dermis, cornea, tongue, joint capsules, visceral organs	Pain, temperature, mechanical deformation
Mechanoreceptors	Merkel's discs	Epidermal-dermal junction, mucosal membranes	Low frequency vibration (5-15 Hz)
Bulbous corpuscle	Ruffini's corpuscle	Dermis, joint capsultes	Stretch
Tactile corpuscle	Meissner's corpuscle	Papillary dermis, especially in the fingertips and lips	Light touch, vibrations below 50 Hz
Lamellated corpuscle	Pacinian corpuscle	Depp dermis, subcutaneous tissue	Deep pressure, high-frequency vibration (~250 Hz)
Hair follicle plexus	–	Wrapped around hair follicles in the dermis	Movement of hair
Muscle spindle	–	In line with skeletal muscle fibers	Muscle contraction & stretch
Tendon stretch organ	Golgi tendon organ	In line with tendons	Stretch of tendons

Part 2: Gustation

Only a few recognized submodalities exist within the sense of taste, or gustation. Until the mid-1980s, only four tastes were recognized: sweet, salty, sour and bitter. Further research led to recognition of the fifth taste: umami. Umami is a Japanese word which means "delicious taste," and is often translated to mean savory. Very recent research has suggested that there may also be a sixth taste for fats, or lipids.

Gustation is the special sense associated with the tongue. The surface of the tongue, along with the rest of the oral cavity, is lined by a stratified squamous epithelium. Raised bumps called **papillae** (singular = papilla) contain the structures for gustatory transduction (Figure 2). Within the papillae are **taste buds** which contain specialized **gustatory receptor cells** for the transduction of taste stimuli. These receptor cells are sensitive to the chemicals contained within ingested foods.

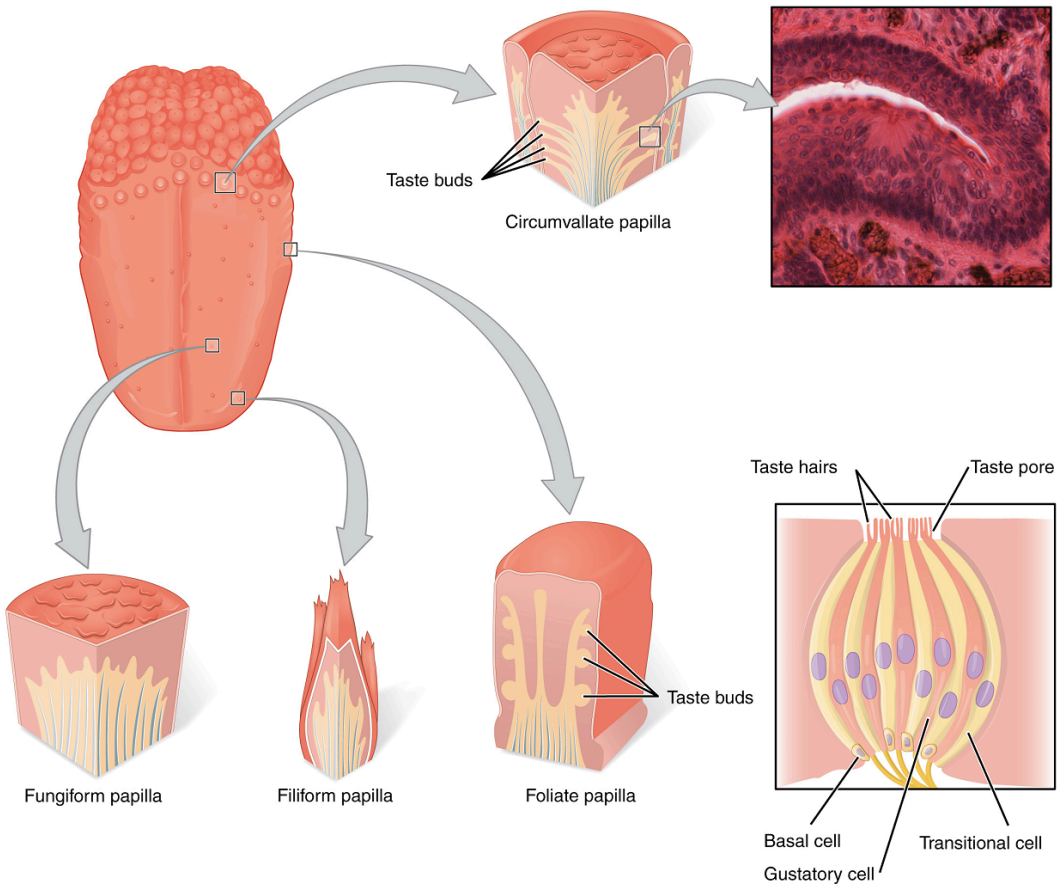


Figure 2. The Tongue. *The tongue is covered with small bumps, called papillae, which contain taste buds that are sensitive to chemicals in ingested food or drink. Different types of papillae are found in different regions of the tongue. The taste buds contain specialized gustatory receptor cells that respond to chemical stimuli dissolved in the saliva. These receptor cells activate sensory neurons that are part of the facial and glossopharyngeal nerves. LM × 1600. (Micrograph provided by the Regents of University of Michigan Medical School © 2012)*

Once the gustatory cells are activated by taste molecules through a change in the membrane potential (usually a depolarization causing a graded potential), these cells release neurotransmitters onto the dendrites of sensory neurons. These neurons are part of the facial and glossopharyngeal cranial nerves, as well as a component of the vagus nerve dedicated to the gag reflex. The facial nerve connects with taste buds in the anterior third of the tongue. The glossopharyngeal nerve connects with taste buds in the posterior two thirds of the tongue and the pharynx. The vagus nerve connects with taste buds in the extreme posterior of the tongue and the pharynx. Sensory neurons in these cranial nerves carry gustatory information to the solitary nucleus of the medulla oblongata, where they synapse with other neurons carrying the information to the thalamus. Axons from thalamic neurons then project to the primary gustatory cortex of the cerebrum, where taste is processed and consciously perceived. Other pathways also bring the information to the limbic system and hypothalamus, which are involved in emotional responses elicited by tasting food. Finally, the information passing through the medulla oblongata also triggers reflexes which contribute to digestion by increasing the secretion of saliva and gastric juices.

Part 3: Olfaction

Like taste, the sense of smell, or olfaction, is responsive to chemical stimuli. The olfactory receptor neurons are located in a small region of the walls of the superior nasal cavity (Figure 3). This region is referred to as the **olfactory epithelium** and contains bipolar sensory neurons. Each **olfactory sensory neuron** has dendrites that extend from the apical surface of the epithelium into the mucus lining the cavity. As airborne molecules are inhaled through the nose, they pass over the olfactory epithelial region and dissolve into the mucus. These **odorant molecules** bind to proteins that keep them dissolved in the mucus and help transport them to the olfactory dendrites. The odorant–protein complex binds to a receptor protein within the cell membrane of an

olfactory dendrite. These receptors are G protein–coupled, and will produce a graded potential in the olfactory sensory neurons.

The axon of an olfactory sensory neuron extends from the basal surface of the epithelium, through an opening in the skull, and into the brain. The group of axons called the olfactory tract connect to the **olfactory bulb** on the ventral surface of the frontal lobe. From there, the axons split to travel to several brain regions. Some travel to the cerebral cortex, specifically to the primary olfactory cortex located in the temporal lobe. Others project to structures within the limbic system and hypothalamus, where smells become associated with long-term memory and emotional responses. This is how certain smells trigger emotional memories, such as the smell of food associated with one's birthplace. Smell is the one sensory modality which does not synapse in the thalamus before connecting to the cerebral cortex. This intimate connection between the olfactory system and the cerebral cortex is one reason why smell can be a potent trigger of memories and emotion.

The nasal epithelium, including the olfactory neurons, can be harmed by airborne toxic chemicals. Therefore, the olfactory neurons are regularly replaced within the nasal epithelium, and the axons of the new neurons must find their appropriate connections in the olfactory bulb. These new axons grow along the axons that are already in place in the cranial nerve.

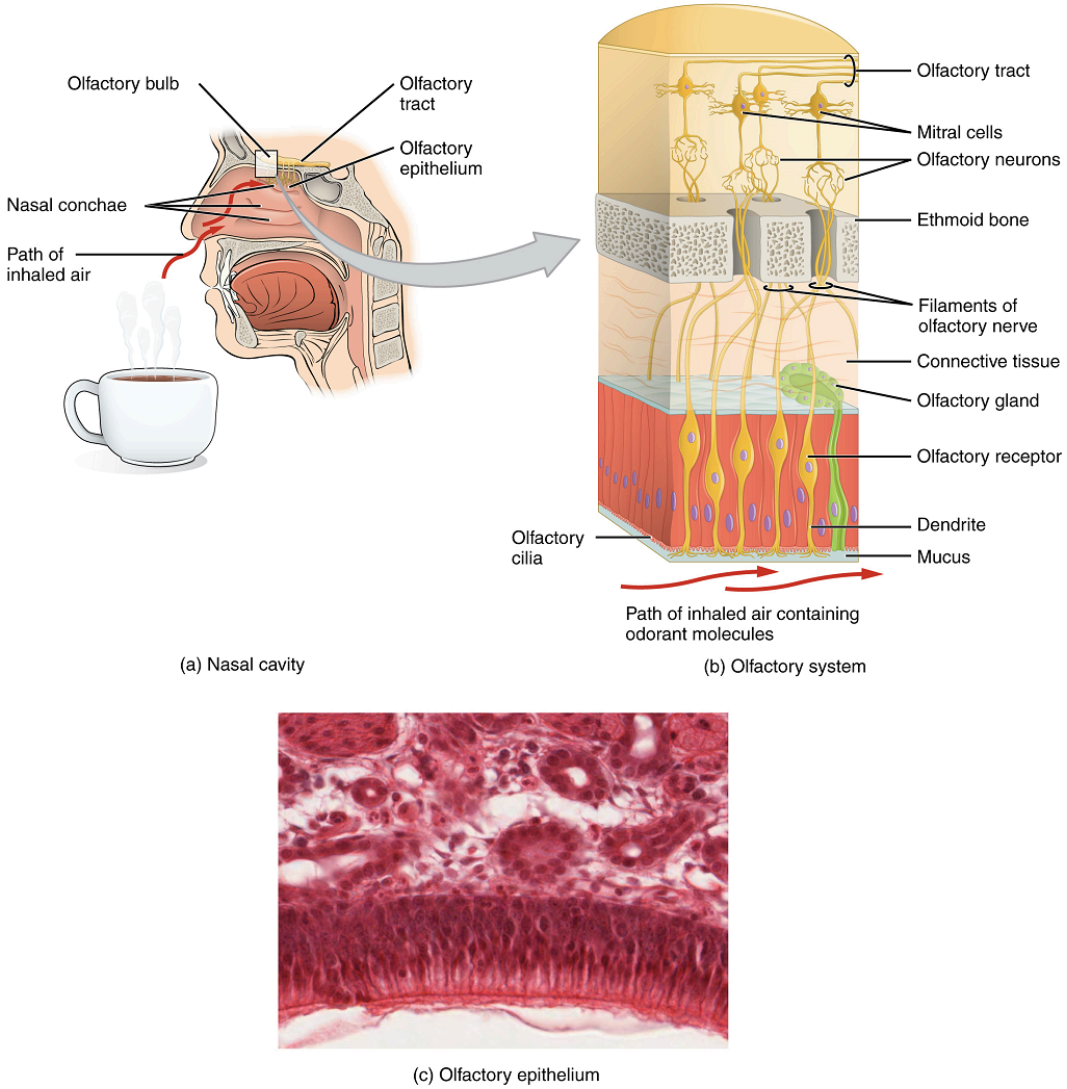


Figure 3. The Olfactory System. *(a) The olfactory system begins in the peripheral structures of the nasal cavity. (b) The olfactory receptor neurons are within the olfactory epithelium. (c) Axons of the olfactory receptor neurons project through the cribriform plate of the ethmoid bone and synapse with the neurons of the olfactory bulb (tissue source: simian). LM × 812. (Micrograph provided by the Regents of University of Michigan Medical School © 2012)*

Watch this Crash Course video for an overview of taste and smell! Direct link: https://youtu.be/mFm3yA1nslE

Part 4: Audition and Balance

Audition: Hearing, or audition, is the transduction of sound waves into a neural signal which is made possible by the structures of the ear (Figure 4). The large, fleshy structure on each lateral aspect of the head is known as the auricle. Some sources also refer to this structure as the pinna, although this term is more appropriate for a structure that can be moved, such as the external ear of a cat. The C-shaped curves of the auricle direct sound waves toward the auditory canal. The canal enters the skull through the external auditory meatus of the temporal bone. At the end of the auditory canal is the tympanic membrane, or eardrum, which vibrates once it is struck by sound waves. The auricle, auditory canal and **tympanic membrane** are collectively referred to as the **external ear**. The **middle ear** consists of a space spanned by three small bones called the **auditory ossicles**. The three ossicles are the **malleus**, **incus** and **stapes**, which are Latin names that roughly translate into hammer, anvil and stirrup, respectively. The malleus is attached to the tympanic membrane and articulates with the incus. The incus, in turn, articulates with the stapes. The stapes covers an opening (the oval window) leading into the **inner ear**, where the sound waves will be transduced into a neural signal. The outer and middle ear are responsible for directing sound waves towards the inner ear; interference with this conduction of sound waves through the outer and middle ear can cause **conductive deafness** if the sound waves fail to reach the inner ear.

The middle ear is connected to the pharynx through the Eustachian tube, which helps equilibrate air pressure across the tympanic membrane. This tube is normally closed but will pop open when the muscles of the pharynx contract during swallowing or yawning. The middle ear is also connected to the mastoid antrum, an air space in the mastoid process of the temporal bone. The middle ear has one more opening covered by a membrane called the round window, which connects with the inner ear.

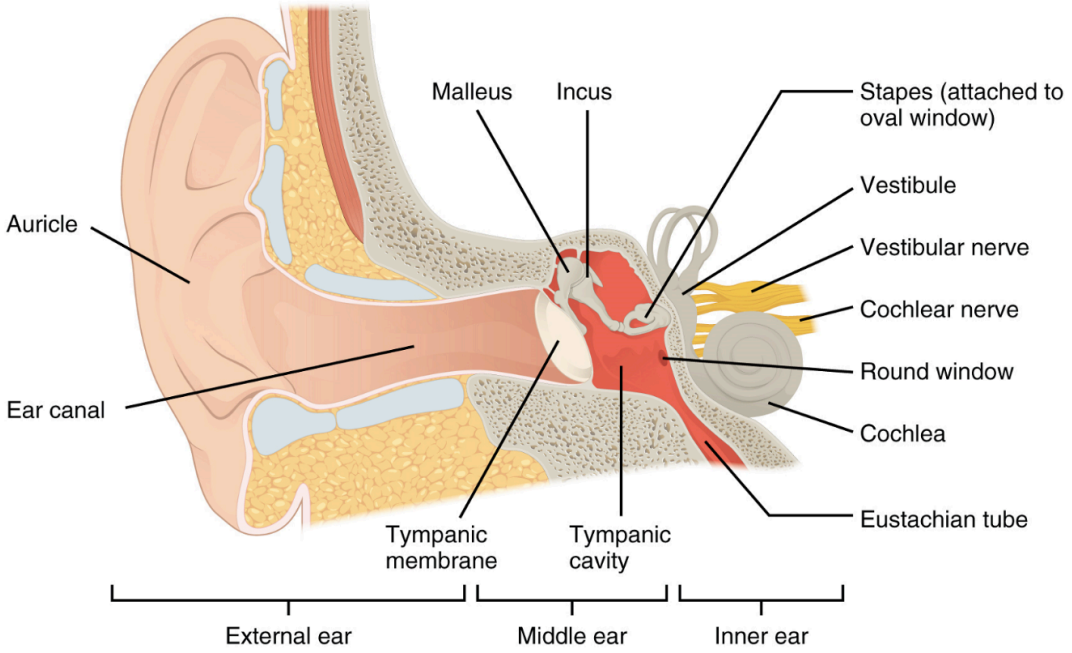


Figure 4. Structures of the Ear. *The external ear contains the auricle, ear (auditory) canal and tympanic membrane. The middle ear contains the auditory ossicles and is connected to the pharynx via the Eustachian tube. The inner ear contains the cochlea and vestibule, which contain sensory organs involved in audition and equilibrium, respectively.*

The inner ear is often described as a bony labyrinth, as it is composed of a series of canals embedded within the temporal bone. It has two separate regions, the **cochlea** and the **vestibule**, which are responsible for audition (hearing) and equilibrium (balance), respectively. The neural signals from these two regions are relayed to the brainstem through separate fiber bundles. However, these two distinct bundles travel together from the inner ear to the brainstem as the vestibulocochlear nerve. Sound is transduced into neural signals within the cochlear region of the inner ear, which contains the sensory neurons of the spiral ganglia. These ganglia are located within the spiral-shaped cochlea of the inner ear. The cochlea is attached to the stapes through the **oval window**. Interference in the mechanisms responsible for transducing sound pressure waves to neural signals, or in the passage of information along the cochlear branch of the vestibulocochlear nerve, can result in **sensorineural deafness**, where a sound wave may reach the inner ear but not ultimately be perceived.

The oval window is located at the beginning of a fluid-filled tube within the cochlea called the **scala vestibuli**. The fluid within it is perilymph. The scala vestibuli runs along, and above, the **cochlear duct** (scala media), which is the central cavity of the cochlea containing sound-transducing neurons. At the uppermost tip of the cochlea, the scala vestibuli curves over the top of the cochlear duct. The perilymph-filled tube, now called the **scala tympani**, returns to the base of the cochlea, this time travelling under the cochlear duct. The scala tympani ends at the **round window**, covered by a membrane that contains the fluid within the scala. As vibrations of the ossicles travel through the oval window, the fluid of the scala vestibuli and scala tympani moves in a wave-like motion. The frequency of the fluid waves matches the frequencies of the sound waves (Figure 5). The membrane covering the round window will bulge out or pucker in with the movement of the fluid within the scala tympani.

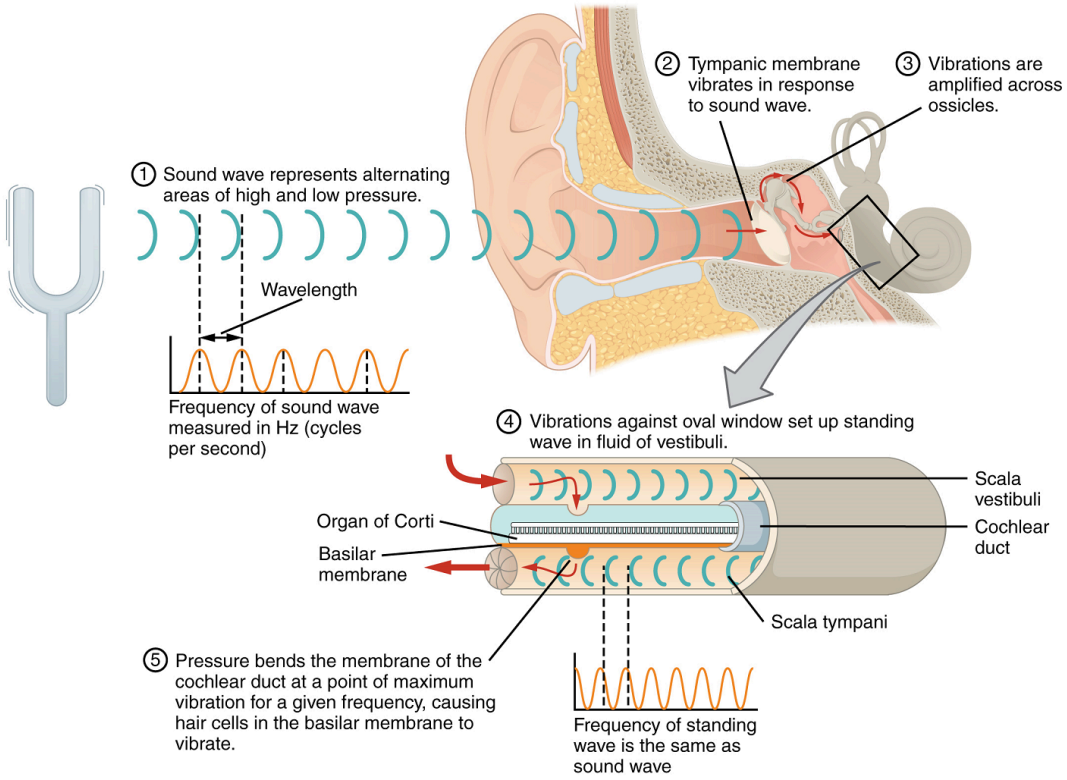


Figure 5. Transmission of Sound Waves to Cochlea. *A sound wave causes the tympanic membrane to vibrate. This vibration is amplified as it moves across the malleus, incus and stapes. The amplified vibration is picked up by the oval window causing pressure waves in the fluid of the scala vestibuli and scala tympani. The complexity of the pressure waves is determined by the changes in amplitude and frequency of the sound waves entering the ear.*

A cross-sectional view of the cochlea shows that the scala vestibuli and scala tympani run along both sides of the cochlear duct (Figure 6). The scala vestibuli is separated from the cochlear duct by the **vestibular membrane**, and the scala tympani is separated from the cochlear duct by the **basilar membrane**. The cochlear duct is a fluid-filled cavity containing endolymph. The cochlear duct contains the **organ of Corti**, which tranduces the wave motion of the two scalae into neural signals. The organ of Corti lies on top of the basilar membrane along the length of the cochlear duct. As the fluid waves move through the scala vestibuli and scala tympani, the basilar membrane moves at a specific spot, depending on the frequency of the waves. Higher frequency waves move a region of the vestibular membrane, then basilar membrane which is close to the base of the cochlea. Lower frequency waves move a region of the vestibular membrane, then basilar membrane which is near the tip of the cochlea.

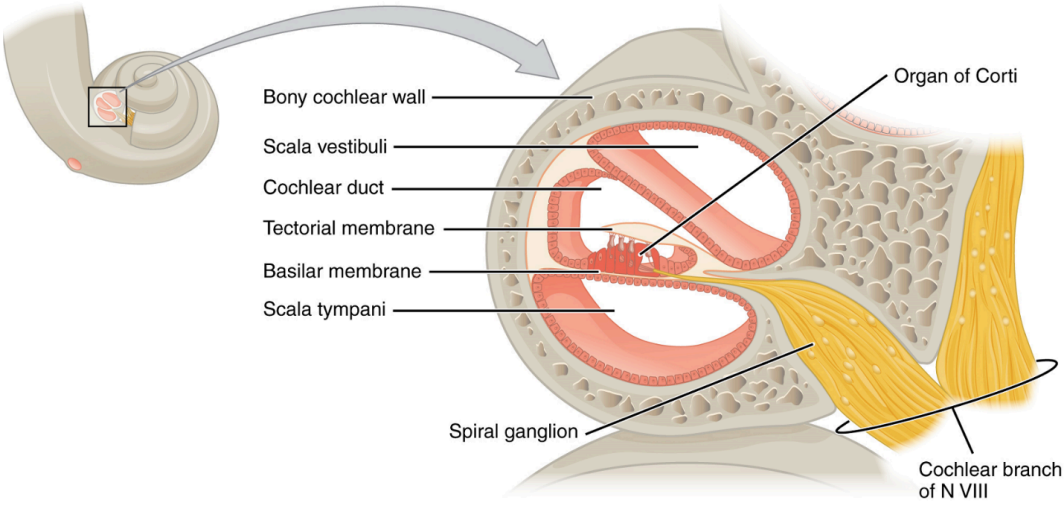


Figure 6. Cross Section of the Cochlea. *The three major spaces within the cochlea are highlighted. The scala tympani and scala vestibuli lie on either side of the cochlear duct. The organ of Corti, containing the mechanoreceptor hair cells, is adjacent to the scala tympani, where it sits atop the basilar membrane.*

The organ of Corti contains **hair cells**, which are named for the hair-like **stereocilia** extending from the cell's apical surfaces (Figure 7). There are two main types of hair cells: the inner hair cells and the outer hair cells. Only the inner hair cells serve as hearing receptors. The stereocilia are an array of microvilli-like structures arranged from tallest to shortest. Protein fibers tether adjacent hairs together within each array, such that the array will bend in response to movements of the basilar membrane. The stereocilia extend up from the hair cells to the overlying gel-like **tectorial membrane**. When the pressure waves of endolymph in the cochlear duct vibrate the basilar membrane, the hair cells move as well. These vibrations bend the stereocilia either toward or away from the tallest member of each array of stereocilia. In inner hair cells, when the stereocilia bend toward the tallest member of their array, tension in the protein tethers opens ion channels in the cell membrane. This will further depolarize the cell membrane, exciting the sensory neurons innervating the hair cells and triggering nerve impulses which travel down the afferent nerve fibers of the cochlear branch of the vestibulocochlear nerve. When the stereocilia bend toward the shortest member of their array, the tension on the tethers slackens and the ion channels close. When no sound is present, and the stereocilia are standing straight, a small amount of tension still exists on the tethers, keeping the membrane potential of the hair cell slightly depolarized. The sterocilia of outer hair cells also bend back and forth in response to the vibrating basilar membrane. However, unlike inner hair cell, they do not serve as sensory receptors, but instead modulate the stiffness of the basilar membrane. This helps inner hair cells be more responsive to certain sounds or protects these cells from potentially damaging sounds.

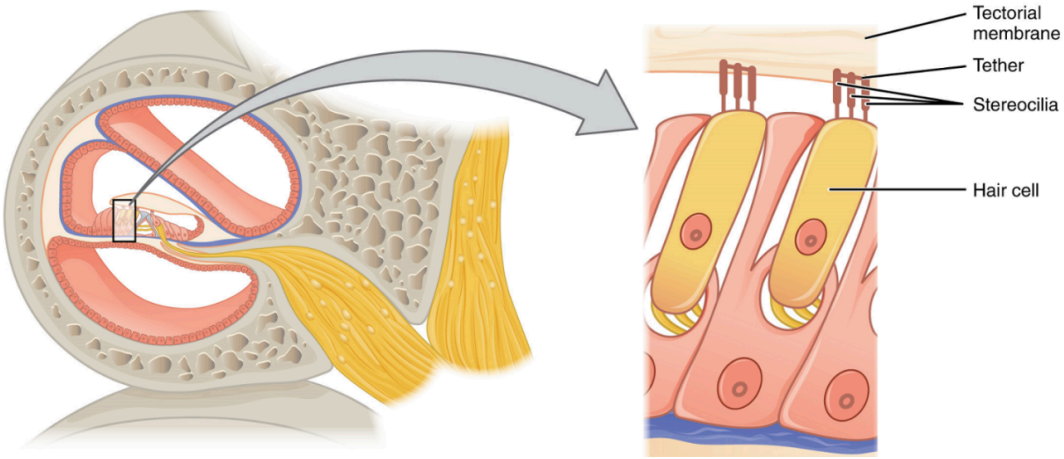


Figure 7. Inner Hair Cell. *The inner hair cell is a mechanoreceptor with an array of stereocilia emerging from its apical surface. The stereocilia are tethered together by proteins that open ion channels when the array is bent toward the tallest member of their array, and closed when the array is bent toward the shortest member of their array.*

Perilymph, the fluid inside the scala vestibuli, helicotrema and scala tympani, is similar in composition to cerebrospinal fluid. In contrast, endolymph, the fluid in the cochlear duct, contains a relatively high concentration of potassium ions (K^+). The depolarization which occurs when stereocilia bend is largely the result of K^+ ions (and Ca^{2+} ions) rushing into the hair cells from the surrounding endolymph through ion channels.

As stated above, a given region of the basilar membrane will only move if the incoming sound is at a specific frequency. Hair cells of the organ of Corti which move in this region will also only respond to sounds of this specific frequency. Therefore, as the frequency of a sound changes, different hair cells of the organ of Corti are activated along the basilar membrane. The cochlea encodes auditory stimuli for frequencies between 20 and 20,000 Hz, which is the range of sound that human ears can detect. The unit of Hertz (Hz) measures the frequency of sound waves in terms of cycles produced per second. Frequencies as low as 20 Hz are detected by hair cells at the apex, or tip, of the cochlea. Frequencies in the higher ranges of 20,000 KHz are detected by hair cells at the base of the cochlea, close to the round and oval windows (Figure 8). Most auditory stimuli contain a mixture of sounds at a variety of frequencies and intensities (represented by the amplitude of the sound wave). The hair cells along the length of the cochlear duct, which are each sensitive to a particular frequency, allow

the cochlea to separate auditory stimuli by frequency, just as a prism separates visible light into its component colours. Sounds outside of the ear's hearing range do reach into the cochlear duct and are thus no perceived by the inner hair cells of the organ of Corti.

The sensory pathway for audition travels along the vestibulocochlear nerve, which synapses with neurons in the cochlear nuclei of the medulla oblongata. Within the brainstem, input from either ear is combined to extract location information from the auditory stimuli. Whereas the initial auditory stimuli received at the cochlea strictly represent the frequency—or pitch—of the stimuli, the locations of sounds can be determined by comparing information arriving at both ears.

Auditory processing continues on to the midbrain. Axons from the midbrain then project to the thalamus and the superior colliculus. The medial geniculate nucleus of the thalamus receives the auditory information and then projects that information to the primary auditory cortex in the temporal lobe of the cerebral cortex, involved in the conscious awareness of sound. The superior colliculus receives input from the visual and somatosensory systems, as well as the ears, to initiate stimulation of the muscles that turn the head and neck toward the auditory stimulus.

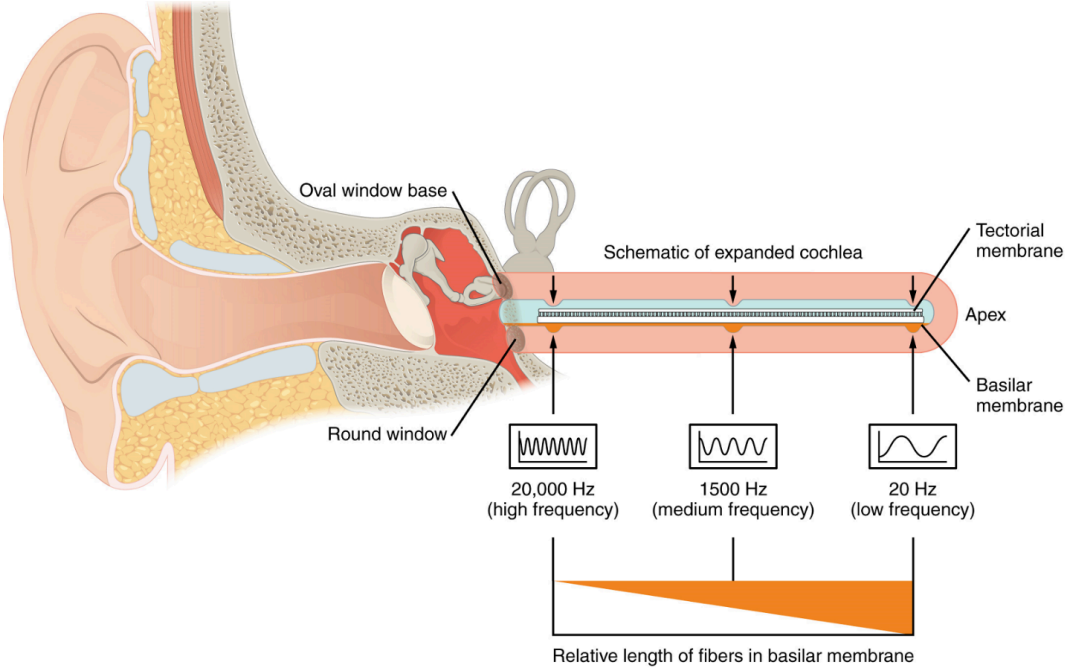


Figure 8. Frequency Coding in the Cochlea. *The standing sound wave generated in the cochlea by the movement of the oval window deflects the basilar membrane on the basis of the frequency of sound. Therefore, inner hair cells at the base of the cochlea are activated only by high frequencies, whereas those at the apex of the cochlea are activated only by low frequencies.*

Balance: Along with audition, the inner ear is responsible for encoding information about equilibrium, the sense of balance (equilibrium). A similar type of mechanoreceptor—a hair cell with stereocilia—senses head position, head movement, and whether our bodies are in motion. These cells are located within the vestibule of the inner ear. Head position and linear acceleration (static equilibrium) is sensed by the **utricle** and **saccule**, whereas rotational movement of the head (dynamic equilibrium) is sensed by the **semicircular ducts**. The neural signals generated in the **vestibular ganglion** are transmitted through the vestibular branch of the vestibulocochlear nerve to the brainstem and cerebellum.

The utricle and saccule are both largely composed of macula tissue (plural = maculae). The macula is composed of hair cells surrounded by support cells. The stereocilia of the hair cells extend into a viscous gel called the otolithic membrane (Figure 9). On top of the otolithic membrane is a layer of calcium carbonate crystals, called otoliths. The otoliths essentially make the otolithic membrane top-heavy. The otolithic membrane moves separately from the macula in response to head movements. Tilting the head causes the

otolithic membrane to slide over the macula in the direction of gravity. The moving otolithic membrane, in turn, bends the sterocilia, causing some hair cells to depolarize, as others hyperpolarize. The exact position of the head is interpreted by the brain based on the pattern of hair-cell depolarization.

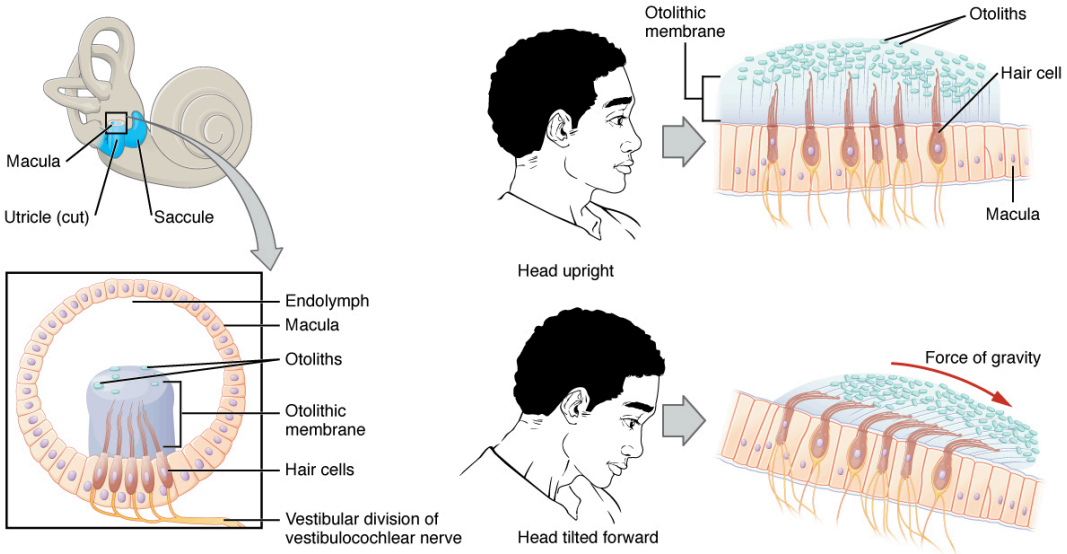


Figure 9. Linear Acceleration Coding by Maculae. *The maculae are specialized for sensing linear acceleration, such as when gravity acts on the tilting head, or if the head starts moving in a straight line. The difference in inertia between the hair cell stereocilia and the otolithic membrane in which they are embedded leads to a shearing force that causes the stereocilia to bend in the direction of that linear acceleration.*

The semicircular canals are three ring-like extensions of the vestibule. One is oriented in the horizontal plane, whereas the other two are oriented in the vertical plane. The anterior and posterior vertical canals are oriented at approximately 45 degrees relative to the sagittal plane (Figure 10). Within each canal is an additional compartment called the semicircular duct. While the semicircular canals are filled with perilymph, the semicircular ducts within are filled with endolymph. The base of each semicircular canal is an enlarged region known as the **ampulla**. Each ampulla contains a sense organ of balance named crista ampullaris, which responds to rotational movement, such as turning the head while saying “no.” This sense organ contains hair cells, with stereocilia on the apical side. The stereocilia extend into the **cupula**, a jelly-like structure which attaches to the top of the ampulla. As the head rotates in a plane parallel to the semicircular duct, the fluid lags, deflecting the cupula in the direction opposite to the head movement. Some ampullae of the canals are oriented horizontally and others are oriented vertically. By comparing the relative movements of both the horizontal and vertical ampullae, the vestibular system can detect the direction of most head movements within three-dimensional (3-D) space.

Balance is coordinated through the vestibular system, the nerves of which are composed of axons from the vestibular ganglion that carries information from the utricle, saccule and semicircular ducts. The system contributes to controlling head and neck movements in response to vestibular signals. An important function of the vestibular system is coordinating eye and head movements to maintain visual attention. Most of the axons terminate in the vestibular nuclei of the medulla oblongata.

Some axons project from the vestibular ganglion directly to the cerebellum, with no intervening synapse in the vestibular nuclei. The cerebellum is primarily responsible for initiating movements on the basis of equilibrium information.

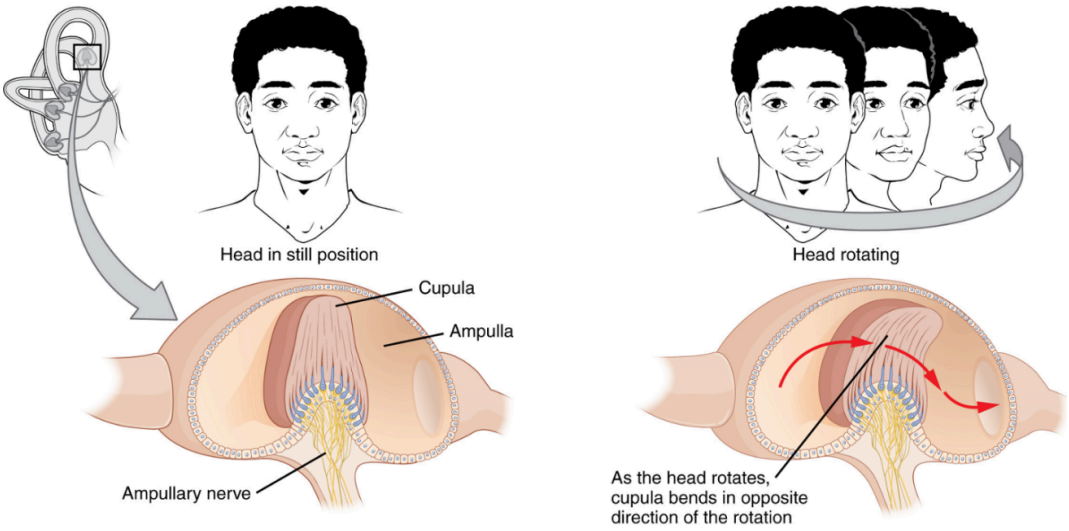


Figure 10. Rotational Coding by Semicircular Ducts. *Rotational movement of the head is encoded by the hair cells in the base of the semicircular ducts. As one of the ducts moves in an arc with the head, the internal fluid moves in the opposite direction, causing the cupula and stereocilia to bend. The movement of two ducts within a plane results in information about the direction in which the head is moving, and activation of all the ducts can give a very precise indication of head movement in three dimensions.*

Neurons in the vestibular nuclei project their axons to targets in the brainstem. One target is the reticular formation, which influences respiratory and cardiovascular functions in relation to body movements. A second target of the axons of neurons in the vestibular nuclei is the spinal cord, which initiates the spinal reflexes involved with posture and balance. To assist the visual system, fibers of the vestibular nuclei project to the oculomotor, trochlear and abducens nuclei to influence signals sent along the cranial nerves. Finally, the vestibular nuclei project to the thalamus to join the proprioceptive pathway, allowing conscious perception of equilibrium.

Watch this Crash Course video for an overview of hearing and balance! Direct link: https://youtu.be/Ie2j7GpC4JU

Part 5: Vision

Vision is the special sense of sight that is based on the transduction of light stimuli received through the eyes. The eyes are located within either orbit in the skull. The bony orbits surround the eyeballs, protecting them and anchoring the soft tissues of the eye (Figure 11). The eyelids, with lashes at their leading edges, help to protect the eye from abrasions by blocking particles that may land on the surface of the eye. The inner surface of each lid is a thin membrane known as the **palpebral conjunctiva**. The conjunctiva extends over the white areas of the eye (the sclera), connecting the eyelids to the eyeball. Tears are produced by the **lacrimal gland**, located

beneath the lateral edges of the nose on each side of the nose. Tears produced by this gland flow through the **lacrimal duct** to the medial corner of the eye, where the tears flow over the conjunctiva, washing away foreign particles.

Movement of the eye within the orbit is accomplished by the contraction of six **extraocular muscles** which originate from the bones of the orbit and insert into the surface of the eyeball (Figure 12).

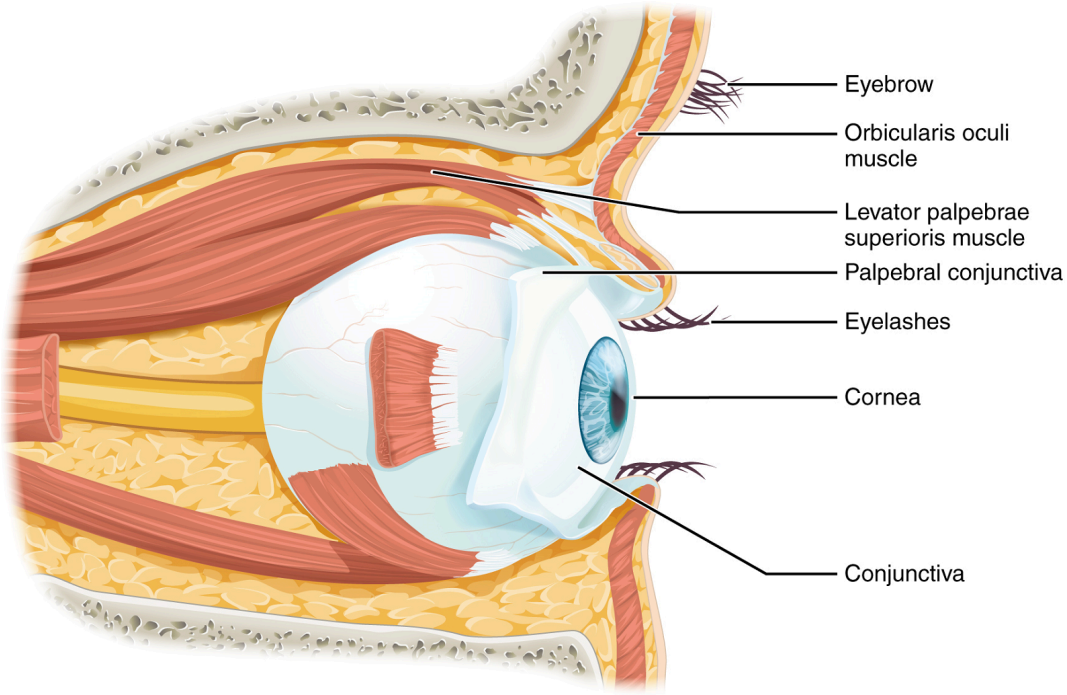


Figure 11. The Eye in the Orbit. *The eye is located within the orbit and surrounded by soft tissues that protect and support its function. The orbit is surrounded by cranial bones of the skull.*

The eye itself is a hollow sphere composed of three layers of tissue (tunics). The outermost layer is **the fibrous tunic**, which includes the white **sclera** and clear **cornea**. The sclera accounts for five sixths of the surface of the eye, most of which is not visible, though humans are unique compared with many other species in having so much of the "white of the eye" visible (Figure 13). The transparent cornea covers the anterior tip of the eye and allows light to enter the eye. The middle layer of the eye is the **vascular tunic**, which is mostly composed of the choroid, ciliary body and iris. The **choroid** is a layer of highly vascularized connective tissue that provides a blood supply to the eyeball. The choroid is posterior to the **ciliary body**, a muscular structure that is attached to the lens by **zonule fibers** (suspensory ligaments). These two structures bend the lens, allowing it to focus light on the back of the eye.

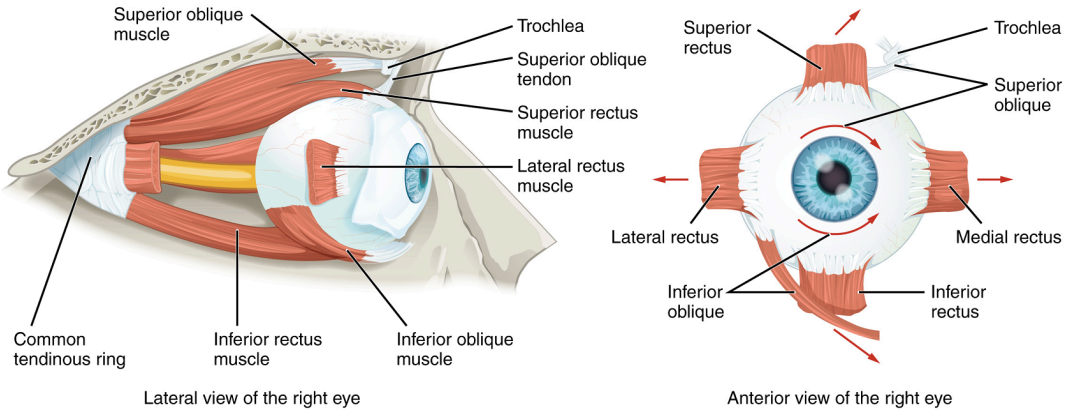


Figure 12. Extraocular Muscles. *The extraocular muscles move the eye within the orbit.*

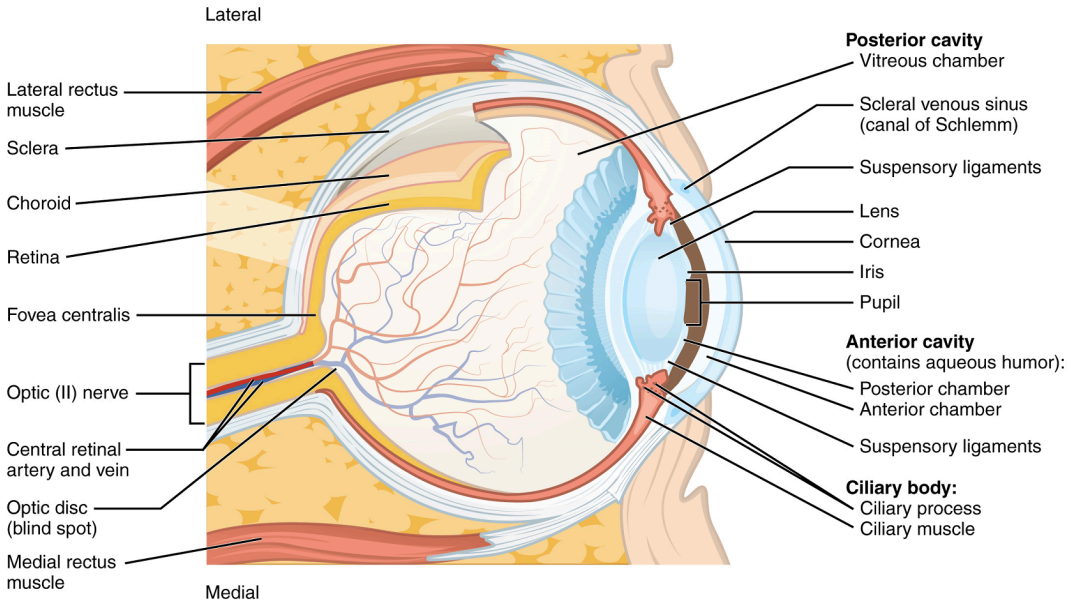


Figure 13. Structure of the Eye. *The sphere of the eye can be divided into anterior and posterior cavities. The wall of the eye is composed of three layers: the fibrous tunic, vascular tunic and neural tunic. Within the neural tunic is the retina, with three layers of cells and two synaptic layers in between. The centre of the retina has a small indentation known as the fovea.*

Overlaying the ciliary body, and visible in the anterior eye, is the iris—the colored part of the eye. The iris is composed of two smooth muscles –the circular *sphincter pupillae* and the radial *dilator pupillae* which open and close the **pupil**, the hole at the centre of the eye that allows light to enter. The sphincter pupillae contracts in response to parasympathetic nervous system activation, contracting the pupil, whereas the dilator pupillae contracts in response to sympathetic nervous system activation, dilating the pupil. The iris generally constricts the pupil in response to bright light and dilates the pupil in response to dim light, to regulate the amount of light reaching the innermost layer of the eye. This innermost layer is the **neural tunic**, or **retina**, which contains the nervous tissue responsible for photoreception.

The eye is also divided into two cavities: the anterior cavity (chamber) and the posterior cavity (chamber). The anterior cavity is the space between the cornea and lens, including the iris and ciliary body. It is filled with a watery fluid called the **aqueous humor**. The posterior cavity is the space behind the lens that extends to the posterior side of the interior eyeball, where the retina is located. The posterior cavity is filled with a more viscous fluid called the **vitreous humor**.

The retina is composed of several layers and contains specialized cells for the initial processing of visual stimuli. The photoreceptors (rods and cones) change their membrane potential when stimulated by light energy. The change in membrane potential alters the amount of neurotransmitter that the photoreceptor cells release onto **bipolar cells** in the **outer synaptic layer**. It is the bipolar cell in the retina that connects a photoreceptor to a **ganglion cell** in the **inner synaptic layer**. There, **amacrine cells** additionally contribute to retinal processing before an action potential is produced by the ganglion cells. The axons of ganglion cells, which lie in the innermost layer of the retina, collect at the **optic disc** and leave the eye as the **optic nerve** (see Figure 13). Because these axons pass through the retina, there are no photoreceptors at the very back of the eye, where the optic nerve begins. This creates a “blind spot” in the retina, and a corresponding blind spot in our visual field.

Note that the photoreceptors in the retina (rods and cones) are located behind the axons, ganglion cells, bipolar cells and retinal blood vessels. A significant amount of light is absorbed by these structures before the light reaches the photoreceptor cells. However, at the exact centre of the retina is a small area known as the **macula lutea** with a small depression in the middle called the **fovea**. At the fovea, the retina lacks the supporting cells and blood vessels, and only contains photoreceptors. The fovea is where the least amount of incoming light is absorbed by other retinal structures (see Figure 13). Therefore, **visual acuity**, or the sharpness

of vision, is greatest at the fovea. As one moves in either direction from this central point of the retina, visual acuity drops significantly. In addition, each photoreceptor cell of the fovea is connected to a single ganglion cell. Therefore, this ganglion cell does not have to integrate inputs from multiple photoreceptors, which reduces the accuracy of visual transduction. Toward the edges of the retina, several photoreceptors converge on ganglion cells (through the bipolar cells) up to a ratio of 50 to 1. The difference in visual acuity between the fovea and peripheral retina is easily evidenced by looking directly at a word in the middle of this paragraph. The visual stimulus in the middle of the field of view falls on the fovea and is in the sharpest focus. Without moving your eyes off that word, notice that words at the beginning or end of the paragraph are not in focus. The images in your peripheral vision are focused on the peripheral retina, and have vague, blurry edges and words that are not as clearly identified. As a result, a large part of the neural function of the eyes is concerned with moving the eyes and head so that important visual stimuli are centered on the fovea. Finally, there is a high concentration of cones (rather than rods) in the fovea, which allow the detection of different colours as described below.

Light falling on the retina causes chemical changes to pigment molecules in the photoreceptors, ultimately leading to a change in the activity of the ganglion cells. Photoreceptor cells have two parts, the **inner segment** and the **outer segment** (Figure 14). The inner segment contains the nucleus and other common organelles of a cell, whereas the outer segment is a specialized region in which photoreception takes place. There are two types of photoreceptors—rods and cones—which differ in the shape of their outer segment.

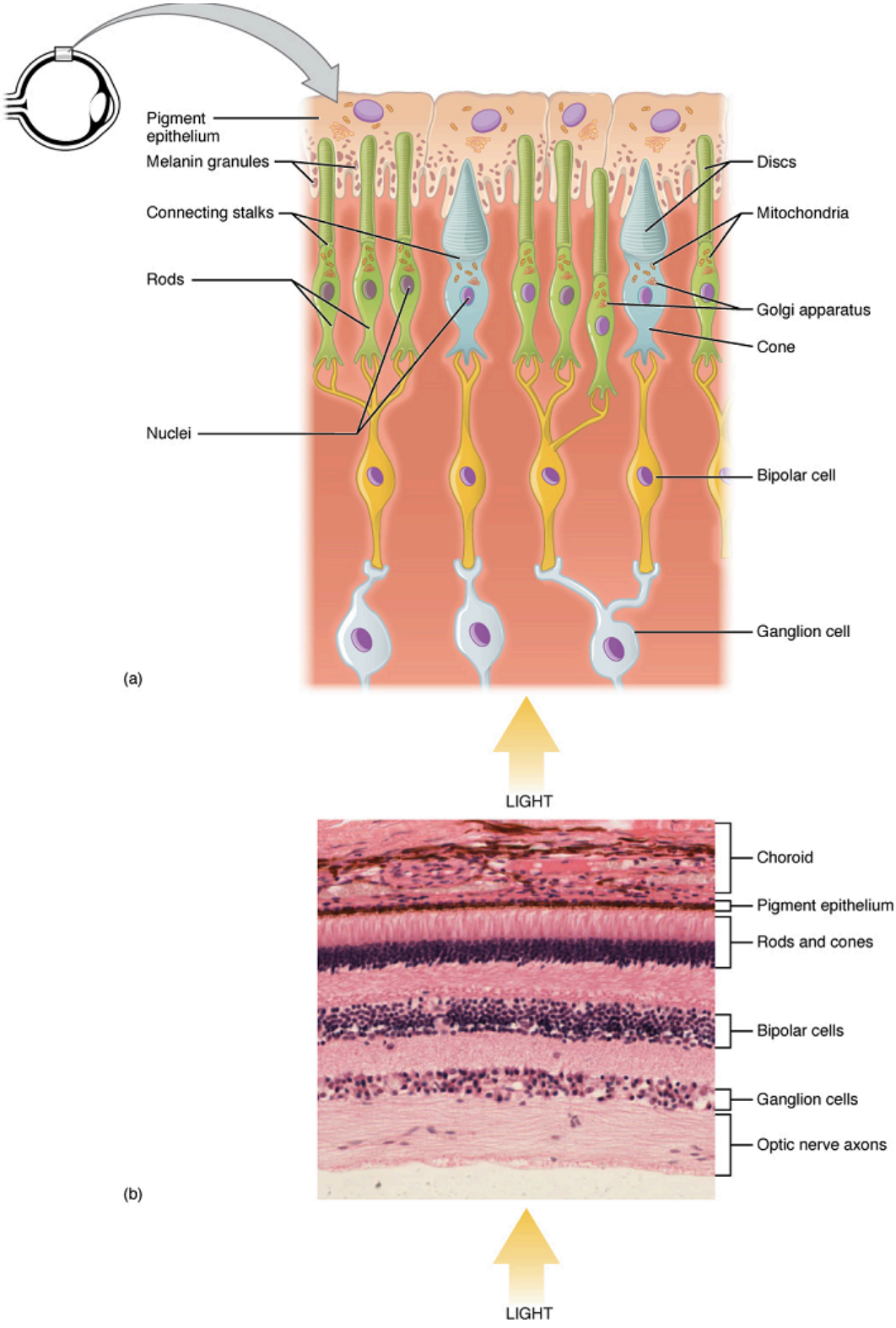


Figure 14. Photoreceptors. *(a) All photoreceptors have inner segments containing the nucleus and other important organelles and outer segments with membrane arrays containing the photosensitive opsin molecules. Rod outer segments are long columnar shapes with stacks of membrane-bound discs that contain the rhodopsin pigment. Cone outer segments are short, tapered shapes with folds of membrane in place of the discs in the rods. (b) Tissue of the retina shows a dense layer of nuclei of the rods and cones. LM × 800. (Micrograph provided by the Regents of University of Michigan Medical School © 2012)*

The rod-shaped outer segments of the **rod photoreceptor** contain a stack of membrane-bound discs that contain the photosensitive pigment **rhodopsin**. The cone-shaped outer segments of the cone photoreceptor contain their photosensitive pigments in infoldings of the cell membrane. There are three **cone**

photopigments, called **opsins**, which are each sensitive to a particular wavelength of light. The wavelength of visible light determines its colour. The pigments in human eyes are specialized in perceiving three different primary colours: red, green and blue.

At the molecular level, visual stimuli cause changes in the photopigment molecule that lead to changes in the membrane potential of the photoreceptor cell. A single unit of light is called a **photon**, which is described in physics as a packet of energy with properties of both a particle and a wave. The energy of a photon is represented by its wavelength, with each wavelength of visible light corresponding to a particular colour. Visible light is electromagnetic radiation with a wavelength between 380 and 720 nm. Wavelengths of electromagnetic radiation longer than 720 nm fall into the infrared range, whereas wavelengths shorter than 380 nm fall into the ultraviolet range. Light with a wavelength of 380 nm is blue whereas light with a wavelength of 720 nm is dark red. All other colours fall between red and blue at various points along the wavelength scale.

Opsin pigments are actually transmembrane proteins that contain a cofactor known as **retinal**. Retinal is a hydrocarbon molecule related to vitamin A. When a photon hits retinal, the long hydrocarbon chain of the molecule is biochemically altered. This process is called **photoisomerization**. Before interacting with a photon, retinal's flexible double-bonded carbons are in the *cis* conformation. This molecule is referred to as 11-*cis*-retinal. A photon interacting with the molecule causes the flexible double-bonded carbons to change to the *trans* conformation, forming all-*trans*-retinal, which has a straight hydrocarbon chain (Figure 15).

The shape change of retinal in the photoreceptors initiates visual transduction in the retina. Activation of retinal and the opsin proteins result in the activation of a G protein. The G protein changes the membrane potential of the photoreceptor cell, causing a slight hyperpolarization, and the cell then releases less neurotransmitter into the outer synaptic layer of the retina. Until the retinal molecule is changed back to the 11-*cis*-retinal shape, the opsin cannot respond to light energy, a process called bleaching. When a large group of photopigments is bleached, the retina will send information as if opposing visual information is being perceived. After a bright flash of light, the afterimages are usually seen in negative. The photoisomerization is reversed by a series of enzymatic changes so that the retinal responds to more light energy.

The opsins are sensitive to limited wavelengths of light. Rhodopsin, the photopigment in rods, is most sensitive to light at a wavelength of 498 nm. The three colour opsins have peak sensitivities of 564 nm, 534 nm and 420 nm, corresponding roughly to the primary colours of red, green and blue (Figure 16). The absorbance of rhodopsin in the rods is much more sensitive than in the cone opsins; specifically, rods are sensitive enough to be excited in low-light conditions, whereas cones are sensitive to brighter conditions. In normal sunlight, rhodopsin will be constantly bleached while the cones are active. In a darkened room, there is not enough light to activate cone opsins, and vision is entirely dependent on rods. Rods are so sensitive to light that a single photon can result in an action potential from a rod's corresponding ganglion cell.

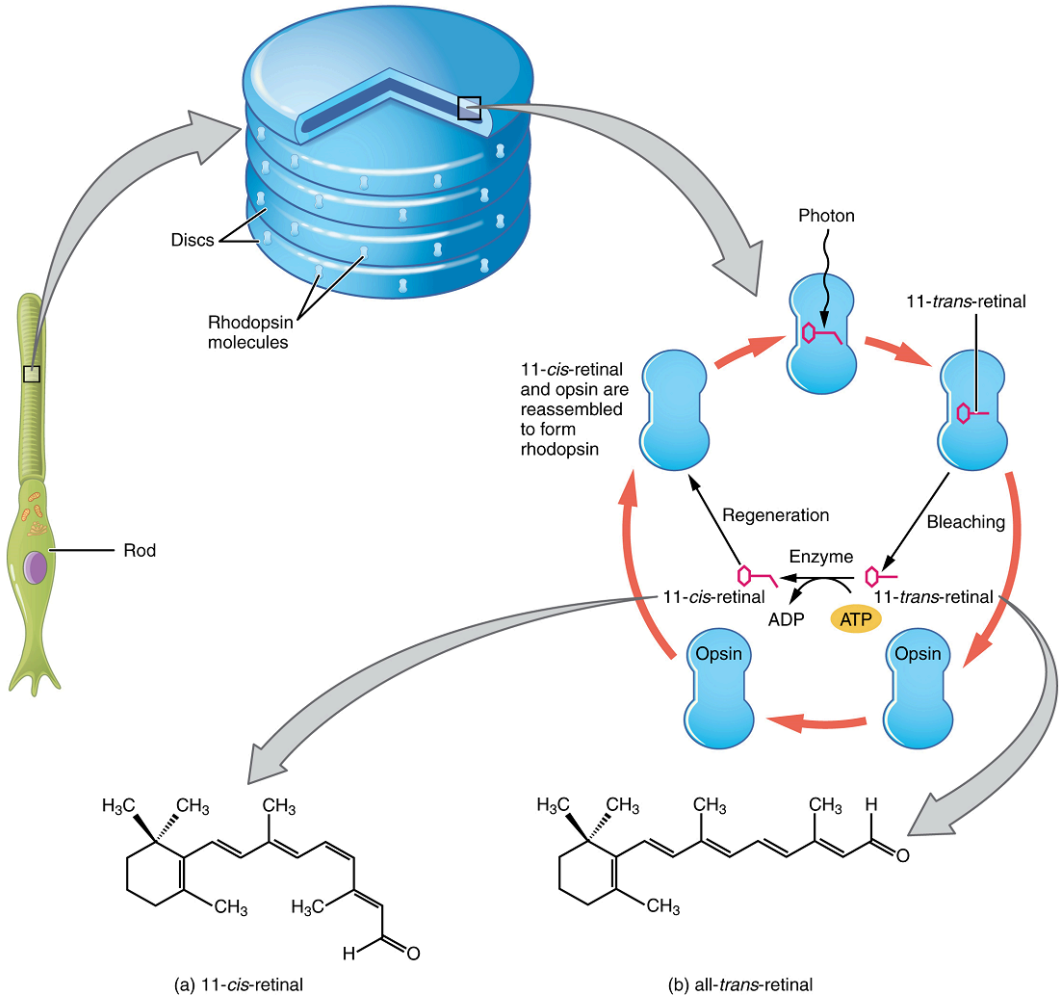


Figure 15. Retinal Isomers. *The retinal molecule has two isomers, (a) one before a photon interacts with it and (b) one that is altered through photoisomerization.*

The three types of cone opsins, being sensitive to different wavelengths of light, provide us with colour vision. By comparing the activity of the three different types of cones, the brain can extract colour information from visual stimuli. For example, a bright blue light that has a wavelength of approximately 450 nm would activate the "red" cones minimally, the "green" cones marginally, and the "blue" cones predominantly. The relative activation of the three different cones is calculated by the brain, which perceives the colour as blue. However, cones cannot react to low-intensity light, and rods do not sense the colour of light. Therefore, our low-light vision is—in essence—in grayscale. In other words, in a dark room, everything appears as a shade of gray. If you think that you can see colours in the dark, it is most likely because your brain knows what colour something is and is relying on that memory.

Focusing Light on the Retina: To see an object in sharp focus and in colour, the light rays from that object must travel to the fovea of the retina. This is largely accomplished through a combination of contractions or relaxations of the appropriate extraocular muscles, as well as the accommodation of the lens.

The extraocular muscles allow for greater or lesser **convergence** of the eyeballs, so that both eyeballs can be directed at the same point in space. When looking at a distant object, both eyes are pointed roughly parallel to each other. As the eyeballs lie at a fixed distance from each other, when focusing on a nearby object the eyes must rotate medially to direct both eyes towards the object being viewed. The closer the object, the greater the degree of convergence required.

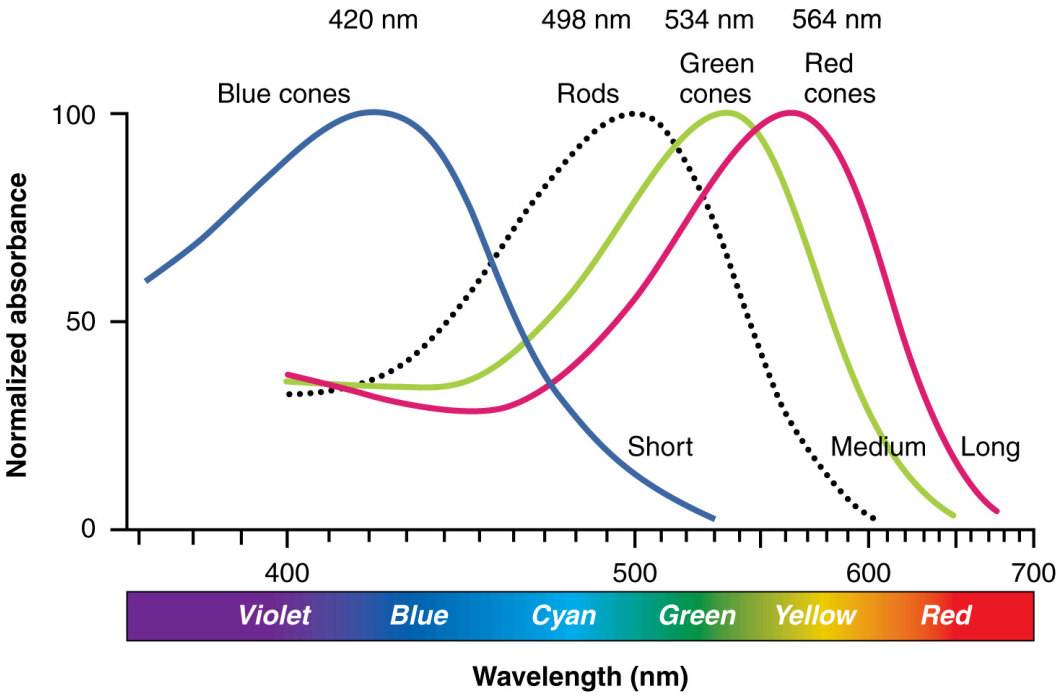


Figure 16. Comparison of Colour Sensitivity of Photopigments. *Comparing the peak sensitivity and absorbance spectra of the four photopigments suggests that they are most sensitive to particular wavelengths.*

When light rays pass from one medium (e.g. air) to another (e.g. water), they tend to bend, or "refract". This **refraction** of light allows light rays entering the eye to be pulled closer together to meet at the fovea. The **cornea** is responsible for the majority of refraction occurring as light rays enter the eyeball, but the cornea itself is not adjustable, so this refraction is constant and cannot be used to focus on objects at different distances. However, additional refraction occurs as the light passes through the **lens**, and the shape and thickness of the lens can be modified to control the degree of refraction (Figure 17). This change in shape of the lens to produce more or less refraction of incoming light rays is known as **accommodation**, and is accomplished by the contraction or relaxation of the circular ciliary muscle in the ciliary body to which the suspensory ligaments are attached. When the ciliary muscle contracts, it allows the suspensory ligaments to loosen and the lens to bulge. When the ciliary muscle relaxes, it pulls the suspensory ligaments taut, pulling the lens flat.

In addition to their role regulating the total amount of light striking the retina, the pupillary muscles also participate in allowing focused vision by limiting the amount of light hitting the edges of the lens specifically. When viewing a distant object, the lens is relatively flat, so there are relatively equivalent changes in light direction at the edges relative to the centre. However, when viewing a nearby object the lens bulges and light entering near the edges could result in a distorted or blurry image as a result of spherical aberration. Constricting the pupil by contracting the sphincter pupillae muscle and relaxing the dilator pupillae muscle covers the edge of the lens with the iris, eliminating this distortion. When viewing a distant object the sphincter pupillae muscle tends to relax and the dilator pupillae contracts, thus dilating the pupil.

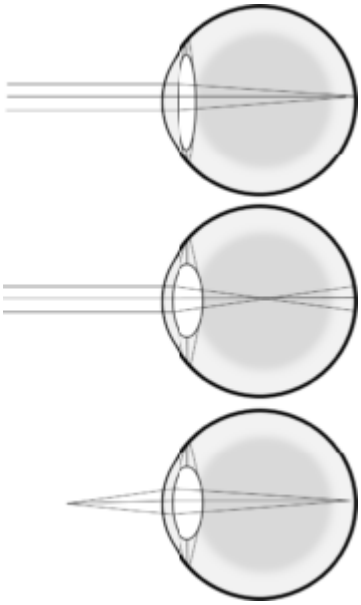


Figure 17. Accommodation of the Lens. *For distant vision, the lens is relatively flat to reduce refraction to a minimum (top image). If the lens were to bulge as shown in the middle image, it would cause too much refraction, changing the direction of the incoming light rays too much, so they would focus in front of the retina and could not be focused. For viewing nearby objects, however, the light rays need to be refracted more than rays coming from distant objects. A bulging lens allows focusing on nearby objects (bottom image). Although there is extensive refraction by the cornea, this refraction is constant and so is not shown in these images.*

Watch this Crash Course video for an overview of vision! Direct link: https://youtu.be/o0DYP-u1rNM

The Visual Pathway: Once any sensory cell transduces a stimulus into a nerve impulse, the impulse has to travel along axons to reach the CNS. In many of the special senses, the axons leaving the sensory receptors have a topographical arrangement, meaning that the location of the sensory receptor relates to the location of the axon in the nerve. For example, in the retina, axons from ganglion cells in the fovea are located at the centre of the optic nerve, where they are surrounded by axons from the more peripheral ganglion cells.

The axons from the medial retina of the left eye cross over to the right side of the brain at the optic chiasm. However, within each eye, the axons projecting from the lateral side of the retina do not decussate. For example, the axons from the lateral retina of the right eye project back to the right side of the brain. Therefore, the left

field of view of each eye is processed on the right side of the brain, whereas the right field of view of each eye is processed on the left side of the brain (Figure 18).

A unique clinical presentation that relates to this anatomic arrangement is the loss of lateral peripheral vision, known as bilateral hemianopia. This is different from "tunnel vision" because the superior and inferior peripheral fields are not lost. Visual field deficits can be disturbing for a patient, but in this case, the cause is not within the visual system itself. A growth of the pituitary gland presses against the optic chiasm and interferes with signal transmission. However, the axons projecting to the same side of the brain are unaffected. Therefore, the patient loses the outermost areas of their field of vision and cannot see objects to their right and left.

Extending from the optic chiasm, the axons of the visual system are referred to as the **optic tract** instead of the optic nerve. The optic tract has three major targets, two in the diencephalon and one in the midbrain. The majority of the connections of the optic tract are to the thalamus—specifically, the **lateral geniculate nucleus**. Axons from this nucleus then project to the visual cortex of the cerebrum, located in the occipital lobe. Another target of the optic tract are the superior colliculi, which are visual reflex centres in the midbrain.

In addition, a very small number of ganglion cell axons project from the optic chiasm to the hypothalamus. These ganglion cells are photosensitive, in that they respond to the presence or absence of light. Unlike photoreceptors, however, these photosensitive ganglion cells cannot be used to perceive images. By simply responding to the absence or presence of light, these ganglion cells can send information about day length. The perceived proportion of sunlight to darkness establishes the **circadian rhythm** of our bodies, allowing certain physiological events to occur at approximately the same time every day.

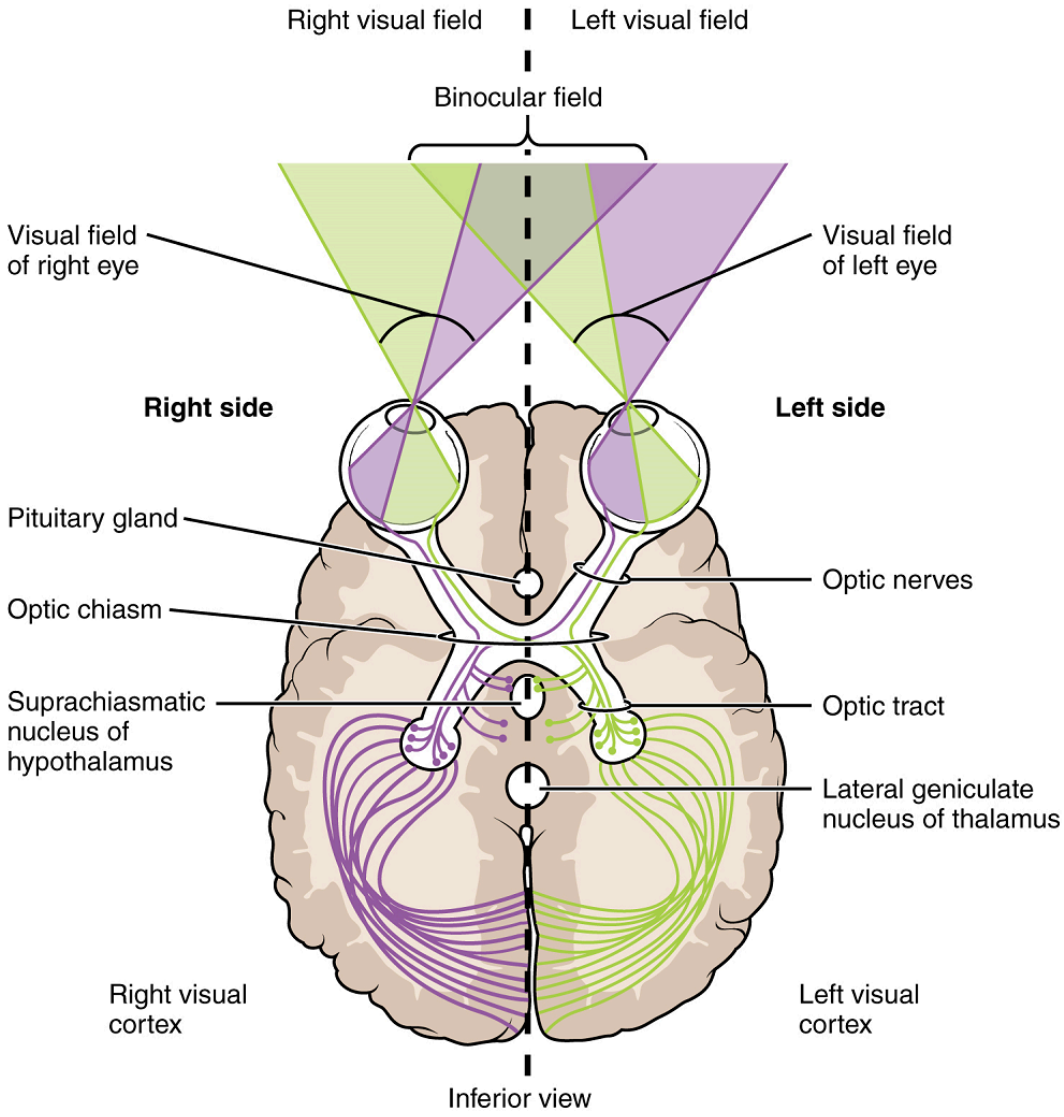


Figure 18. Segregation of Visual Field Information at the Optic Chiasm. *Contralateral visual field information from the lateral retina projects to the ipsilateral brain, whereas ipsilateral visual field information has to decussate at the optic chiasm to reach the opposite side of the brain.*

The topographic relationship between the retina and the visual cortex is maintained throughout the visual pathway. The visual field is projected onto the two retinae, as described above, with sorting at the optic chiasm. The right peripheral visual field falls on the medial portion of the right retina and the lateral portion of the left retina. The right medial retina then projects across the midline through the optic chiasm. This results in the right visual field being processed in the left visual cortex. Likewise, the left visual field is processed in the right visual cortex (Figure 18). Though the chiasm is helping to sort right and left visual information, superior and inferior visual information is maintained topographically in the visual pathway. Light from the superior visual field falls on the inferior retina, and light from the inferior visual field falls on the superior retina. This topography is maintained such that the superior region of the visual cortex processes the inferior visual field and vice versa. Therefore, the visual field information is inverted and reversed as it enters the visual cortex—up is down, and left is right. However, the cortex processes the visual information such that the final conscious perception of the visual field is correct. The topographic relationship is evident in that information from the foveal region of the retina is processed in the centre of the primary visual cortex. Information from the peripheral regions of the retina are correspondingly processed toward the edges of the visual cortex.

SUPPORT AND MOVEMENT

Unit 11: The Integumentary System

Unit outline

Part 1: Layers of the skin

- Epidermal layers and function
- Dermal layers and function
- Hypodermis

Part 2: Accessory structures of the skin

- Hair
- Nails
- Sweat glands
- Sebaceous glands

Part 3: Functions of the skin

Learning Objectives

At the end of this unit, you should be able to:

I. Identify and describe the components of the integumentary system.

II. Identify and describe the five layers of the epidermis of the skin, including the location and function of keratinocytes and melanocytes.

III. Specify the function(s) of epidermal derivatives, including hair, sebaceous glands, sudoriferous glands, ceruminous glands, nails.

IV. Describe five major functions of the integumentary system.

Learning Objectives and Guiding Questions

At the end of this unit, you should be able to complete all the following tasks, including answering the guiding questions associated with each task.

I. Identify and describe the components of the integumentary system.

1. List and identify all the organs and accessory structures of the integumentary system.
2. Define “organ”. Explain why the skin specifically would fit your definition of an organ.
3. For the two layers of the dermis, state their proper anatomical name and the specific tissue type of which each is primarily composed.
4. Identify the accessory structures of the skin that are embedded in each of the two layers of the dermis.
5. Draw an annotated diagram of the skin, clearly showing:
    - The epidermal and dermal layers of the skin, and the hypodermis
    - The type(s) of tissue of that comprise each of the above layers indicated above (*hint: refer back to the Tissue Structure topic)*
    - The layer(s) of the skin that contain(s) blood vessels
    - The layer(s) of the skin that contain(s) nervous structures

II. Identify and describe the five layers of the epidermis of the skin, including the location and function of keratinocytes and melanocytes.

1. Draw an annotated diagram of the epidermis of thick skin, clearly showing the five layers of the epidermis and specifying the distinguishing physical characteristics of each layer.
2. Identify which layer in the diagram you created above would be missing from thin skin.
3. Specify the two main types of cells found in the epidermis, and which important chemical each of them produce. Briefly explain how each of those chemicals provide protection to underlying tissues.

III. Specify the function(s) of epidermal derivatives, including hair, sebaceous glands, sudoriferous glands, ceruminous glands, nails.

1. List the main function(s) served in human by the hairs of the:
    - Scalp
    - Eyelids
    - Nostrils
    - Rest of the body
2. What is the main function(s) of nails, and what about their structure allows them to perform that function(s)?
3. Complete the following table regarding integumentary glands:

Gland name	Location(s) in the body	Product contents	Product function(s)
Eccrine sudoriferous gland			
Apocrine sudoriferous gland			
Ceruminous gland			
Sebaceous gland			

IV. Describe five major functions of the integumentary system.

1. Explain the mechanisms by which the integumentary system carries out each of the following functions:
    - Protection
    - Body temperature regulation
    - Sensation
    - Synthesis of vitamin D
    - Excretion

What do you think when you look at your skin in the mirror? Do you think about cleaning and caring for it, adding a tattoo, or maybe a body piercing? Or do you think about the fact that the skin belongs to one of the body's most essential and dynamic systems: the integumentary system? The **integumentary system** refers to the skin and its accessory structures, and it is responsible for much more than your outward appearance. In the adult human body, the skin makes up about 16 percent of body weight and covers an area of 1.5 to 2 m^2. In fact, the skin and accessory structures are the largest organ system in the human body. As such, the skin protects your inner organs and it is in need of daily care and protection to maintain its health. This chapter will introduce the structure and functions of the integumentary system.

Part 1: Layers of the Skin

Although you may not typically think of the skin as an organ, it is in fact made of tissues that work together as a single structure to perform unique and critical functions. The skin and its accessory structures provides the body with overall protection as part of the integumentary system. The skin is made of multiple layers of cells and tissues, which are held to underlying structures by connective tissue (Figure 1). The deeper layer of skin is well vascularized (has numerous blood vessels). It also has numerous sensory and nerve fibers ensuring communication to and from the brain.

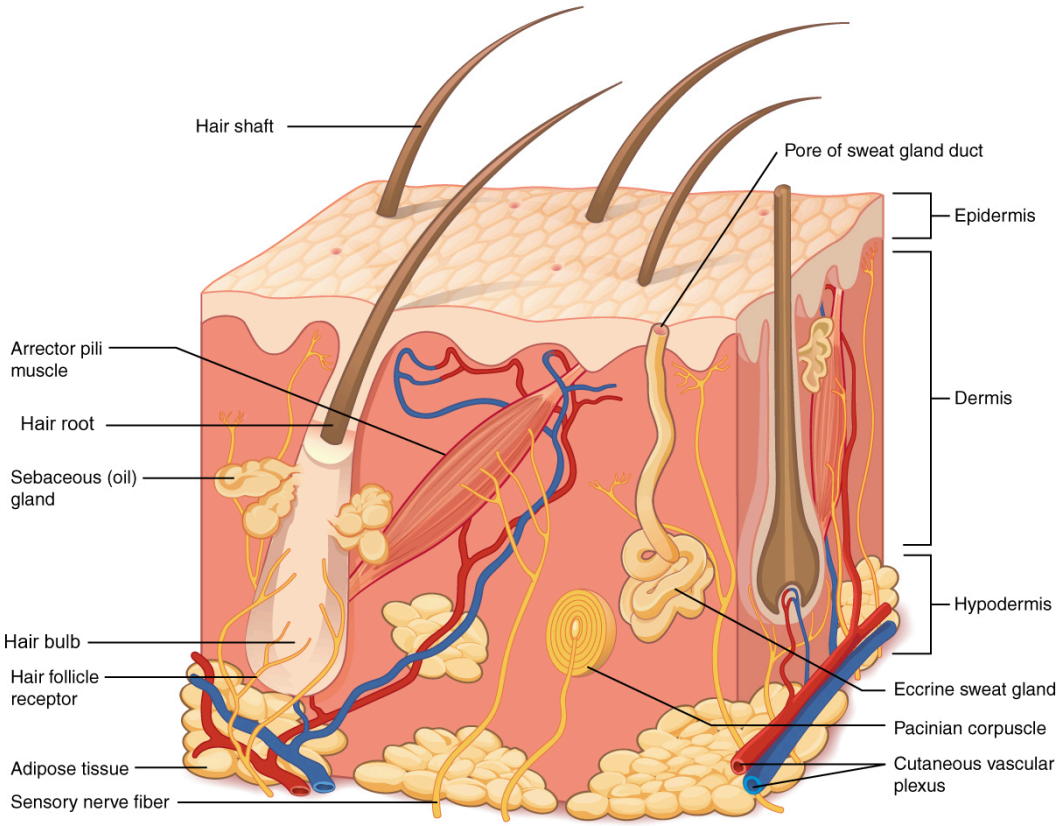


Figure 1. Layers of Skin. *The skin is composed of two main layers: the epidermis, made of closely packed epithelial cells, and the dermis, made of connective tissue that houses blood vessels, hair follicles, sweat glands, and other structures. Deep to the dermis of the skin lies the hypodermis, which is composed mainly of loose connective and fatty tissues.*

Watch this CrashCourse video to learn more about the integumentary system! Direct link: https://youtu.be/Orumw-PyNjw

The Epidermis: The **epidermis** (Figures 2 & 3) is composed of keratinized, stratified squamous epithelium. Like all epithelium, it is avascular and does not have any blood vessels within it. Most of the skin is classified as thin skin, and has four visible layers of cells (Figure 2). From deep to superficial, these layers are the stratum basale, stratum spinosum, stratum granulosum, and stratum corneum. Thick skin is found only on the palms of the hands and the soles of the feet. It has a fifth layer, called the stratum lucidum, located between the stratum corneum and the stratum granulosum (Figures 3 & 4).

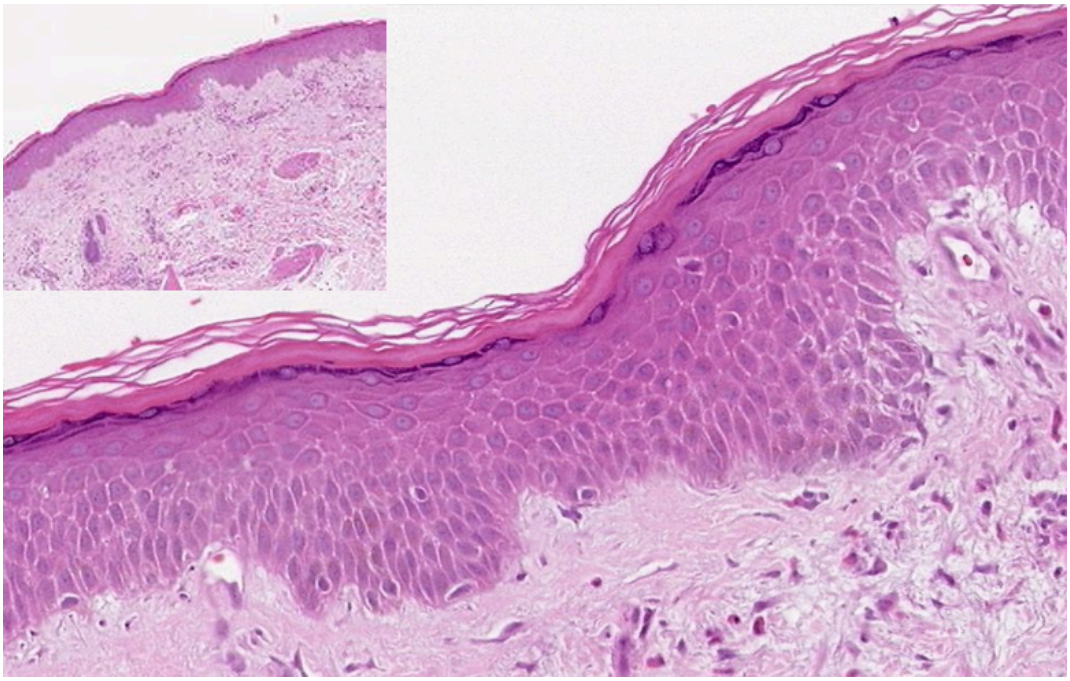


Figure 2. Cross-section of Thin Skin. *The epidermis of thin skin consists of four visibly distinct layers of epithelial cells called keratinocytes. The pale connective tissue deep to the densely-packed keratinocytes is the dermis. Note the difference between the thickness of the epithelial layer of thin skin and that of the thick skin in the subsequent Figure. (Micrographs obtained from Bio-Atlas at the Jake Gittlen Laboratories for Cancer Research © 2013 The Pennsylvania State University.)*

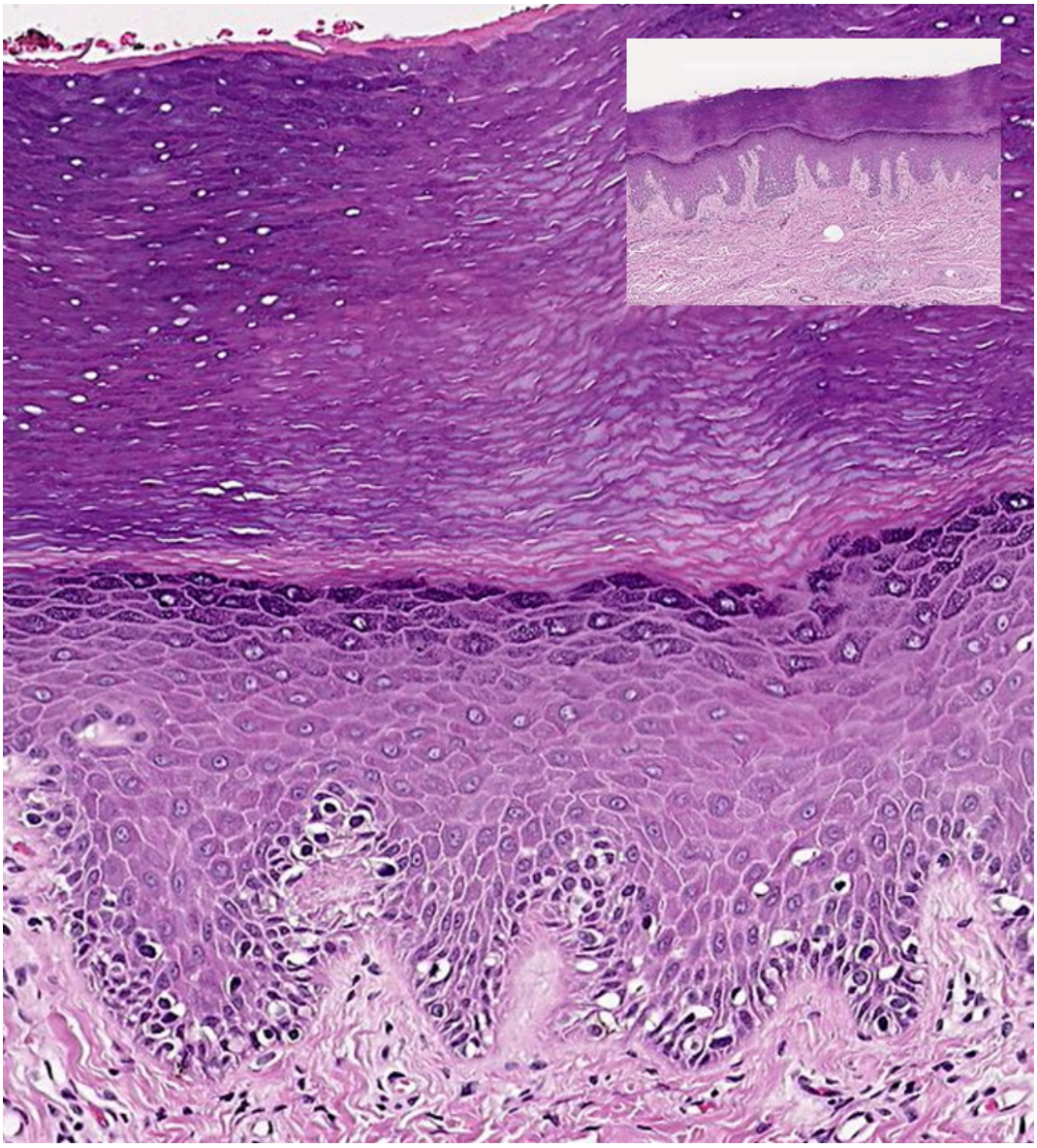


Figure 3. Cross-section of Thick Skin. *The epidermis of thick skin consists of five visibly distinct layers of epithelial cells called keratinocytes. The pale connective tissue deep to the densely-packed keratinocytes is the dermis. Note the difference between the thickness of the epithelial layer of thick skin and that of the thin skin in the previous Figure. (Micrographs obtained from Bio-Atlas at the Jake Gittlen Laboratories for Cancer Research © 2013 The Pennsylvania State University.)*

The dominant cells in the epidermis are called keratinocytes. A **keratinocyte** is a cell that manufactures and stores the protein keratin. **Keratin** is an intracellular fibrous protein that gives hair, nails, and skin their hardness and water-resistant properties. By the time the keratinocytes reach the stratum corneum they are dead and regularly slough away, being replaced by cells from the deeper layers (Figure 4).

1. Stratum Basale: The **stratum basale** (also called the stratum germinativum) is the deepest epidermal layer and attaches the epidermis to the basal lamina, below which lie the layers of the dermis. The cells in the stratum basale bond to the dermis via intertwining collagen fibers that make up the basement membrane. A finger-like projection, or fold, known as the **dermal papilla** (plural = dermal papillae) is found in the superficial portion of the dermis. Dermal papillae increase the strength of the connection between the epidermis and dermis; the greater the folding, the stronger the connection made (Figure 6).

The stratum basale is a single layer of cells primarily made of basal cells. A **basal cell** is a cuboidal-shaped stem cell that is a precursor of the keratinocytes of the epidermis. All of the keratinocytes are produced from this single layer of cells, which are constantly going through growth (mitosis) to produce new cells.

As new cells are formed, the existing cells are pushed superficially away from the stratum basale. Two other

cell types are found dispersed among the basal cells in the stratum basale. The first is a **Merkel cell**, which functions as a receptor and is responsible for stimulating sensory nerves that the brain perceives as touch. These cells are especially abundant on the surfaces of the hands and feet. The second is a **melanocyte**, a cell that produces the pigment melanin. **Melanin** gives hair and skin its color, and also helps protect the living cells of the epidermis from ultraviolet (UV) radiation damage.

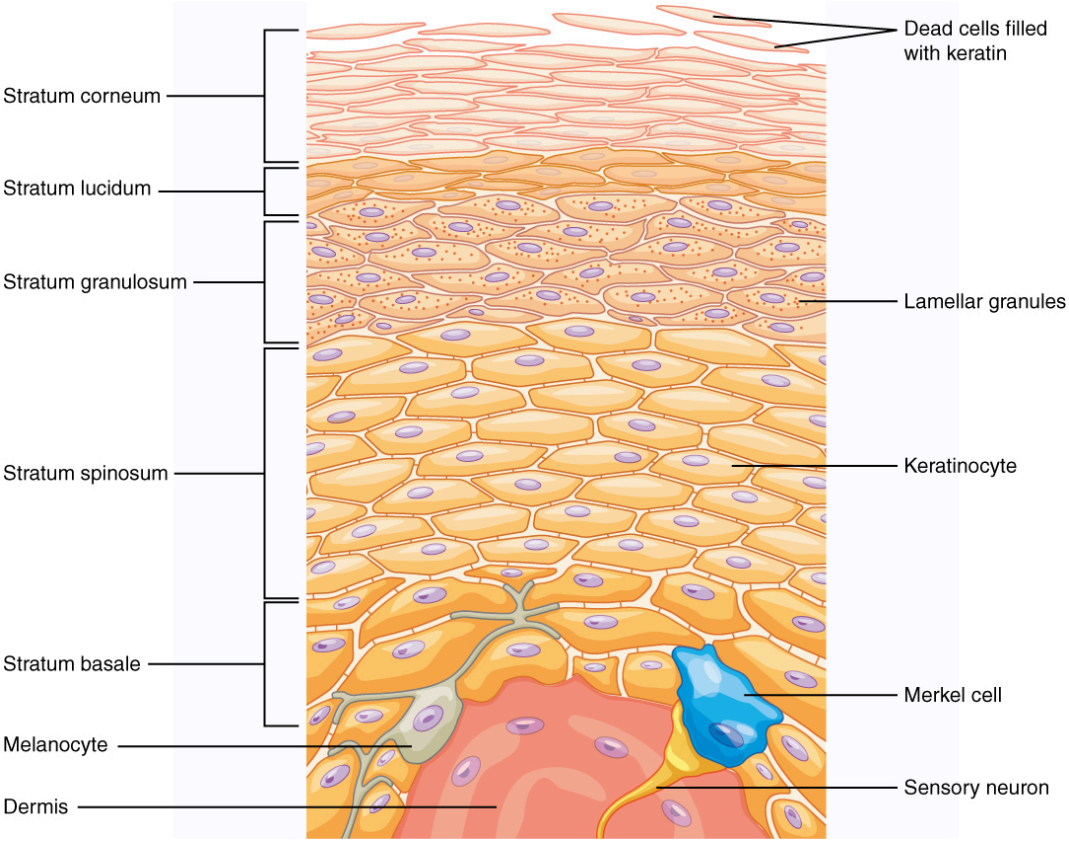


Figure 4. Layers of the Epidermis. *The epidermis of thick skin has five layers: stratum basale, stratum spinosum, stratum granulosum, stratum lucidum, and stratum corneum.*

In a growing fetus, fingerprints form where the cells of the stratum basale meet the papillae of the underlying dermal layer (papillary layer), resulting in the formation of the ridges on your fingers that you recognize as fingerprints. Fingerprints are unique to each individual and are used for forensic analyses because the patterns do not change with the growth and aging processes.

2. Stratum Spinosum: As the name suggests, the **stratum spinosum** is spiny in appearance due to the protruding cell processes that join the cells via a structure called a **desmosome**. The desmosomes interlock with each other and strengthen the bond between the cells. It is interesting to note that the "spiny" nature of this layer is an artifact of the staining process. Unstained epidermis samples do not exhibit this characteristic appearance. The stratum spinosum is composed of eight to 10 layers of keratinocytes, formed as a result of cell division in the stratum basale (Figures 4 & 5). Interspersed among the keratinocytes of this layer is a type of dendritic cell called the Langerhans cell, which functions as a macrophage by engulfing bacteria, foreign particles, and damaged cells that occur in this layer.

The keratinocytes in the stratum spinosum begin the synthesis of keratin and release a water-repelling glycolipid that helps prevent water loss from the body, making the skin relatively waterproof. As new keratinocytes are produced atop the stratum basale, the keratinocytes of the stratum spinosum are pushed into the stratum granulosum.

3. Stratum Granulosum: The **stratum granulosum** has a grainy appearance due to further changes to the

keratinocytes as they are pushed from the stratum spinosum. The cells (three to five layers deep) become flatter, their cell membranes thicken, and they generate large amounts of the proteins keratin, which is fibrous, and **keratohyalin**, which accumulates as granules within the cells (Figures 4 & 5). These two proteins make up the bulk of the keratinocyte mass in the stratum granulosum and give the layer its grainy appearance. The nuclei and other cell organelles disintegrate as the cells die, leaving behind the keratin, keratohyalin, and cell membranes that will form the stratum lucidum, the stratum corneum, and the accessory structures of hair and nails.

4. Stratum Lucidum: The **stratum lucidum** is a smooth, seemingly translucent layer of the epidermis located just above the stratum granulosum and below the stratum corneum. This thin layer of cells is found only in the thick skin of the palms, soles, and digits. The keratinocytes that compose the stratum lucidum are dead and flattened (Figures 4 & 5). These cells are densely packed with **eleiden**, a clear protein, derived from keratohyalin, which gives these cells their transparent (i.e., lucid) appearance and provides a barrier to water.

5. Stratum Corneum: The **stratum corneum** is the most superficial layer of the epidermis and is the layer exposed to the outside environment (Figure 4). The increased keratinization (also called cornification) of the cells in this layer gives it its name. There are usually 15 to 30 layers of cells in the stratum corneum.

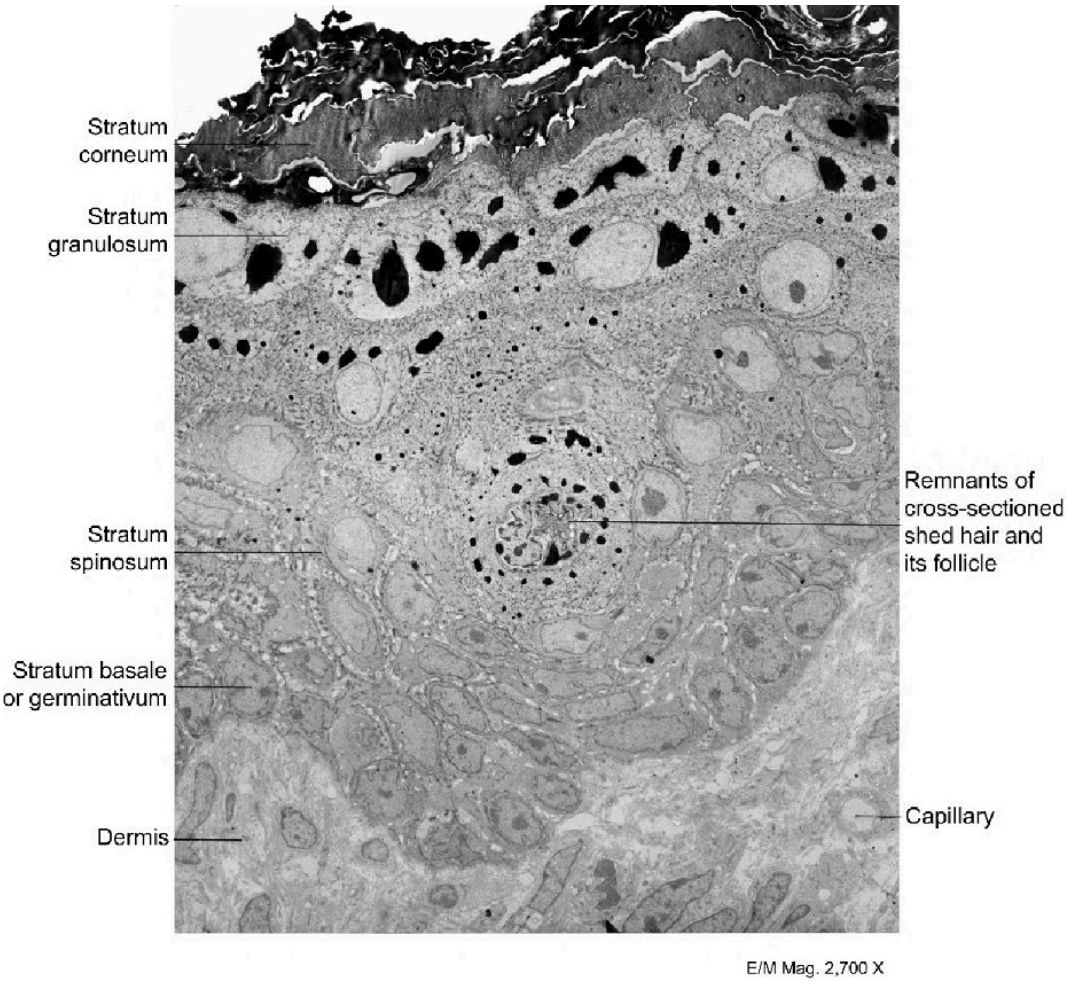


Figure 5. Cells of the Epidermis. *The cells in the different layers of the epidermis originate from basal cells located in the stratum basale, yet the cells of each layer are distinctively different. EM × 2700. (Micrograph provided by the Regents of University of Michigan Medical School © 2012)*

This dry, dead layer helps prevent the penetration of microbes and the dehydration of underlying tissues, and provides a mechanical protection against abrasion for the more delicate, underlying layers. Cells in this layer are shed periodically and are replaced by cells pushed up from the stratum granulosum (or stratum lucidum in the case of the palms and soles of feet). The entire layer is replaced during a period of about 4 weeks. Cosmetic

procedures, such as microdermabrasion, help remove some of the dry, upper layer and aim to keep the skin looking “fresh” and healthy.

Dermis: The **dermis** might be considered the “core” of the integumentary system (derma- = “skin”), as distinct from the epidermis (epi- = “upon” or “over”) and hypodermis (hypo- = “below”). It contains blood and lymph vessels, nerves, and other structures, such as hair follicles and sweat glands. The dermis is made of two layers of connective tissue that compose an interconnected mesh of elastin and collagenous fibers, produced by fibroblasts (Figure 6).

1. Papillary Layer: The papillary layer is made of loose, areolar connective tissue, which means the collagen and elastin fibers of this layer form a loose mesh. This superficial layer of the dermis projects into the stratum basale of the epidermis to form finger-like dermal papillae (Figure 6). Within the papillary layer are fibroblasts, a small number of fat cells (adipocytes), and an abundance of small blood vessels.

In addition, the papillary layer contains phagocytes, defensive cells that help fight bacteria or other infections that have breached the skin. This layer also contains lymphatic capillaries, nerve fibers, and touch receptors called the tactile (Meissner) corpuscles.

2. Reticular Layer: Underlying the papillary layer is the much thicker reticular layer, composed of dense, irregular connective tissue. This layer is well vascularized and has a rich sensory and nerve supply. The reticular layer appears reticulated (net-like) due to a tight meshwork of fibers. Elastin fibers provide some elasticity to the skin, enabling movement. Collagen fibers provide structure and tensile strength, with strands of collagen extending into both the papillary layer and the hypodermis. In addition, collagen binds water to keep the skin hydrated.

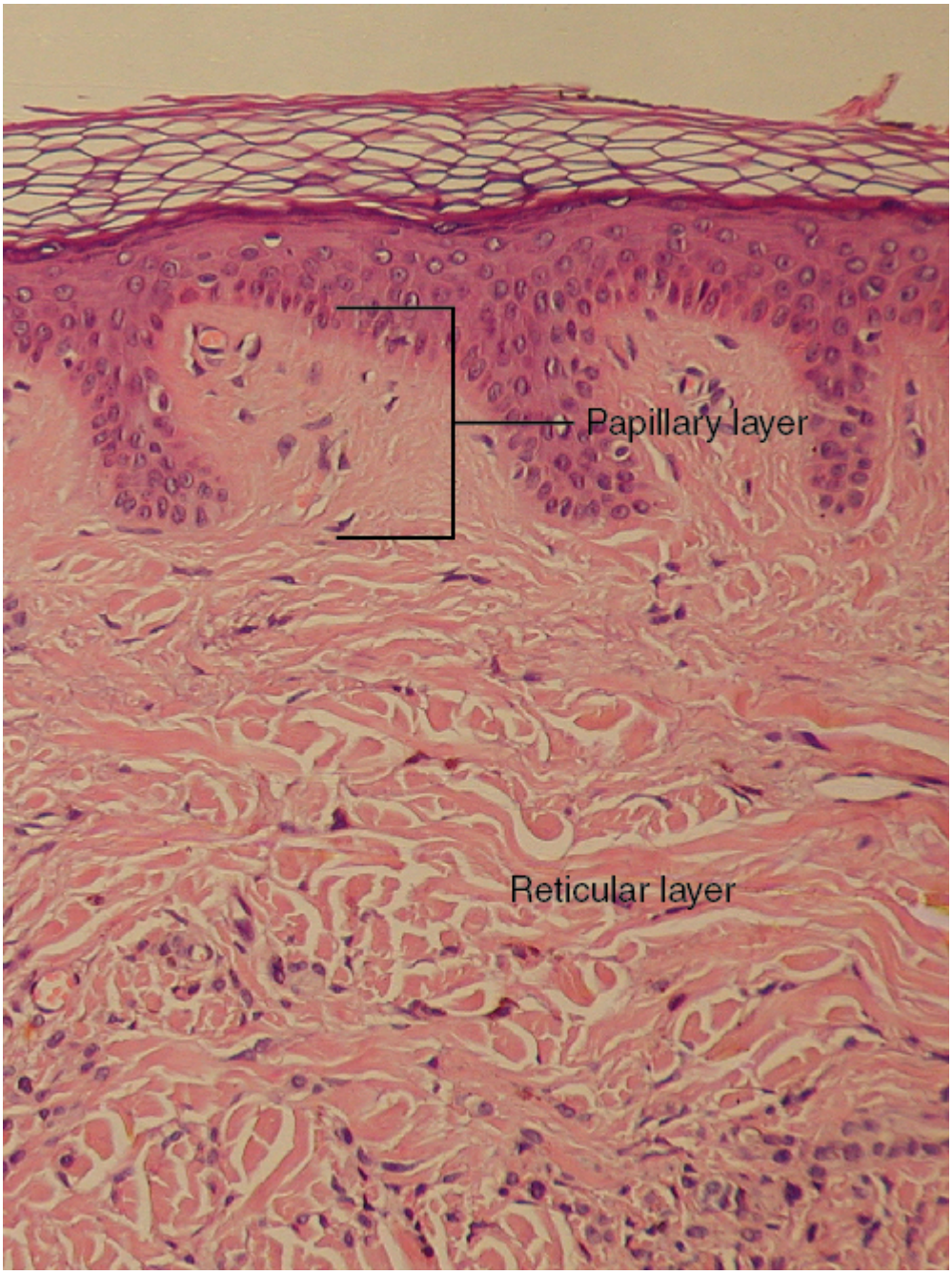


Figure 6. Layers of the Dermis. *This stained slide shows the two components of the dermis—the papillary layer and the reticular layer. Both are made of connective tissue with fibers of collagen extending from one to the other, making the border between the two somewhat indistinct. The dermal papillae extending into the epidermis belong to the papillary layer, whereas the dense collagen fiber bundles below belong to the reticular layer. LM × 10. (credit: modification of work by "kilbad"/Wikimedia Commons)*

Hypodermis: The **hypodermis** (also called the subcutaneous layer or superficial fascia) is a layer directly below the dermis and serves to connect the skin to the underlying fascia (fibrous tissue) of the bones and muscles. It is not considered a part of the skin, although the border between the hypodermis and dermis can be difficult to distinguish. The hypodermis consists of well-vascularized, loose, areolar connective tissue and adipose tissue, which functions as a mode of fat storage and provides insulation and cushioning for the integument.

Pigmentation: The color of skin is influenced by a number of pigments, including melanin, carotene, and hemoglobin. Recall that melanin is produced by cells called melanocytes, which are found scattered throughout the stratum basale of the epidermis. The melanin is transferred into the keratinocytes via a cellular vesicle called a melanosome (Figure 7).

Dark-skinned individuals produce more melanin than those with pale skin. Exposure to the UV rays of the

sun or a tanning salon causes melanin to be manufactured and built up in keratinocytes, as sun exposure stimulates keratinocytes to secrete chemicals that stimulate melanocytes. The accumulation of melanin in keratinocytes results in the darkening of the skin, or a tan. This increased melanin accumulation protects the DNA of epidermal cells from UV ray damage. In contrast, too much melanin can interfere with the production of vitamin D, an important nutrient involved in calcium absorption.

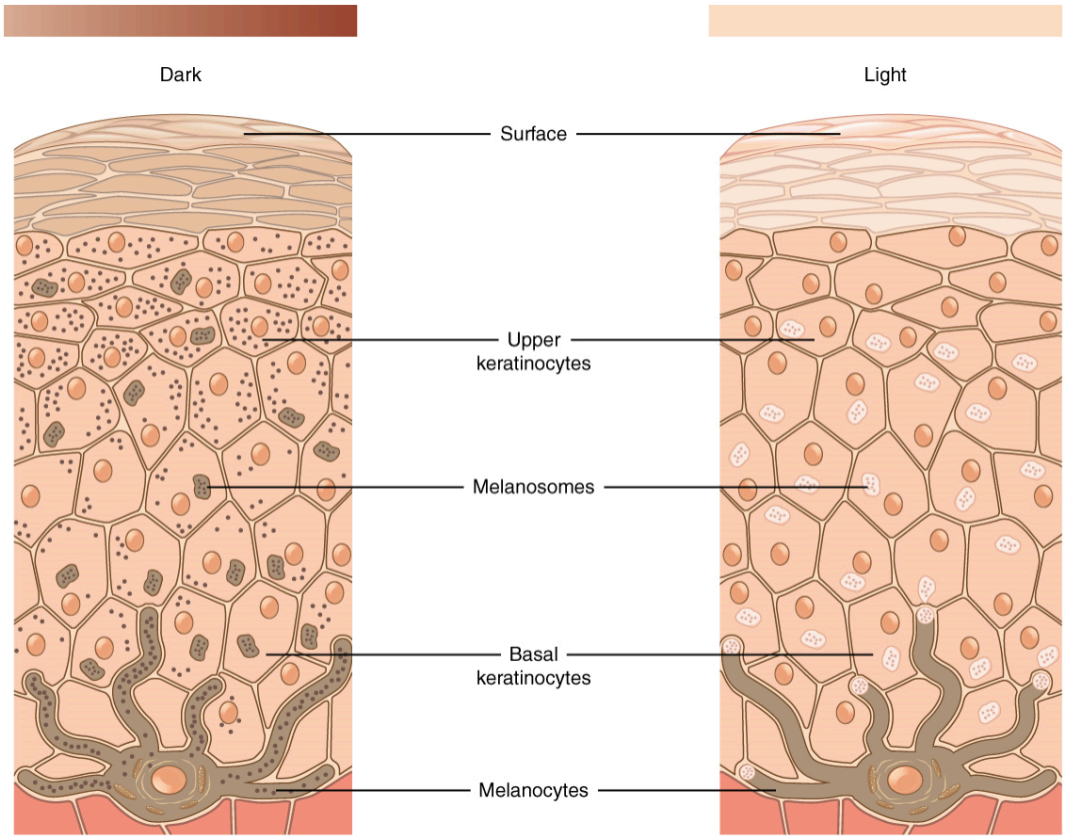


Figure 7. Skin Pigmentation. *The relative coloration of the skin depends of the amount of melanin produced by melanocytes in the stratum basale and taken up by keratinocytes.*

It requires about 10 days after initial sun exposure for melanin synthesis to peak, which is why pale-skinned individuals tend to suffer sunburns of the epidermis initially. Dark-skinned individuals can also get sunburns, but are more protected than are pale-skinned individuals. Melanosomes are temporary structures that are eventually destroyed by fusion with lysosomes; this fact, along with melanin-filled keratinocytes in the stratum corneum sloughing off, makes tanning impermanent.

Too much sun exposure can eventually lead to wrinkling due to the destruction of the cellular structure of the skin, and in severe cases, can cause sufficient DNA damage to result in skin cancer. When there is an irregular accumulation of melanocytes in the skin, freckles appear.

Moles are larger masses of melanocytes, and although most are benign, they should be monitored for changes that might indicate the presence of cancer (Figure 8).

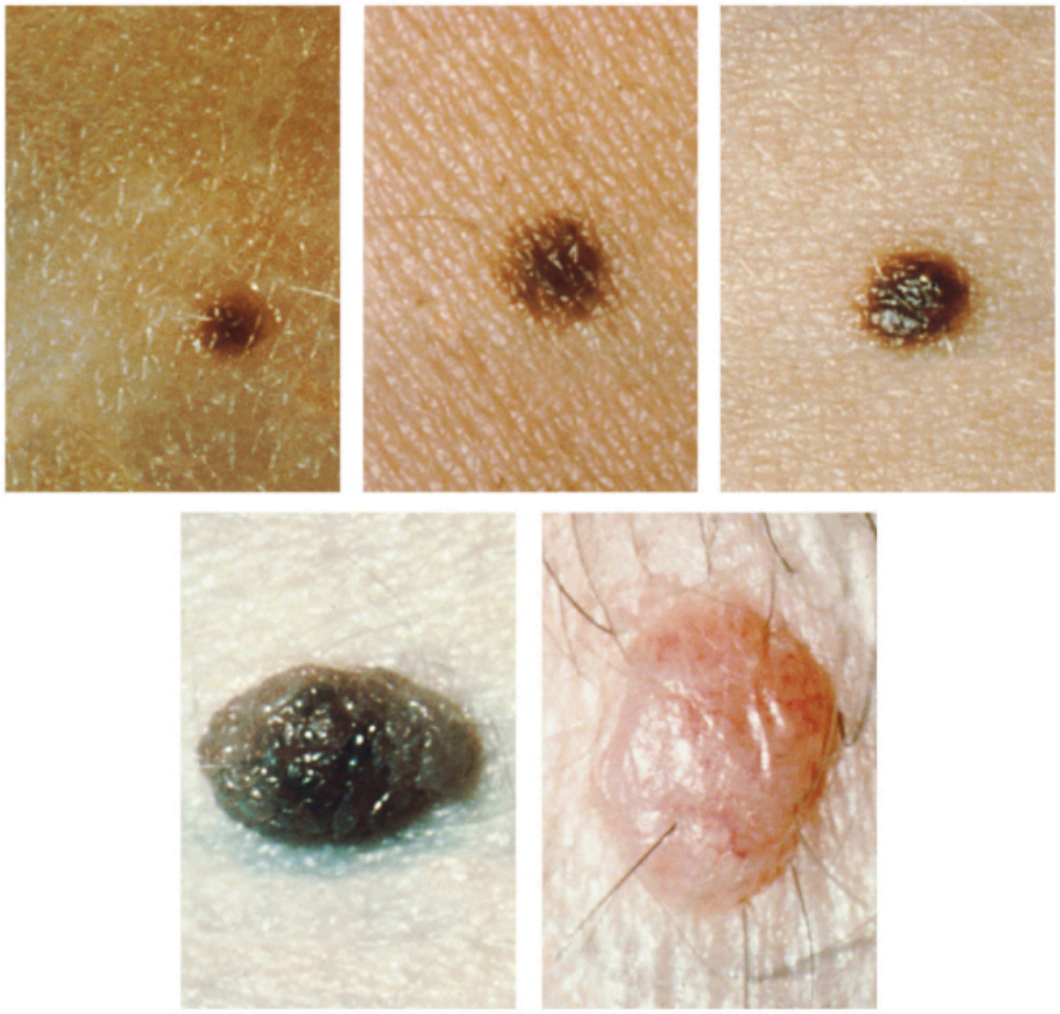


Figure 8. Moles. *Moles range from benign accumulations of melanocytes to melanomas. These structures populate the landscape of our skin. (credit: the National Cancer Institute)*

Part 2: Accessory Structures of the Skin

Accessory structures of the skin include hair, nails, sweat glands, and sebaceous glands. These structures embryologically originate from the epidermis and can extend down through the dermis into the hypodermis.

Hair: Hair is a keratinous filament growing out of the epidermis. It is primarily made of dead, keratinized cells. Strands of hair originate in an epidermal penetration of the dermis called the hair follicle (Figures 9 & 10).

Watch this CrashCourse video to learn more about the accessory structures! Direct link: https://youtu.be/EN-x-zXXVwQ

The hair shaft is the part of the hair not anchored to the follicle, and much of this is exposed at the skin's surface. The rest of the hair, which is anchored in the follicle, lies below the surface of the skin and is referred to as the

hair root. The hair root ends deep in the dermis at the hair bulb (which is the deep end of the hair follicle). The root includes a layer of actively growing basal cells called the hair matrix. The hair bulb surrounds the hair papilla, which is made of connective tissue and contains blood capillaries and nerve endings from the dermis (Figure 9).

Just as the basal layer of the epidermis forms the layers of epidermis that get pushed to the surface as the dead skin on the surface sheds, the basal cells of the hair bulb divide and push cells outward in the hair root and shaft. The external hair is completely dead and composed entirely of keratin. For this reason, hair does not have sensation. Furthermore, you can cut your hair or shave without damaging the hair structure because the cut is superficial. Most chemical hair removers also act superficially; however, electrolysis and plucking both attempt to destroy the hair bulb so hair cannot grow.

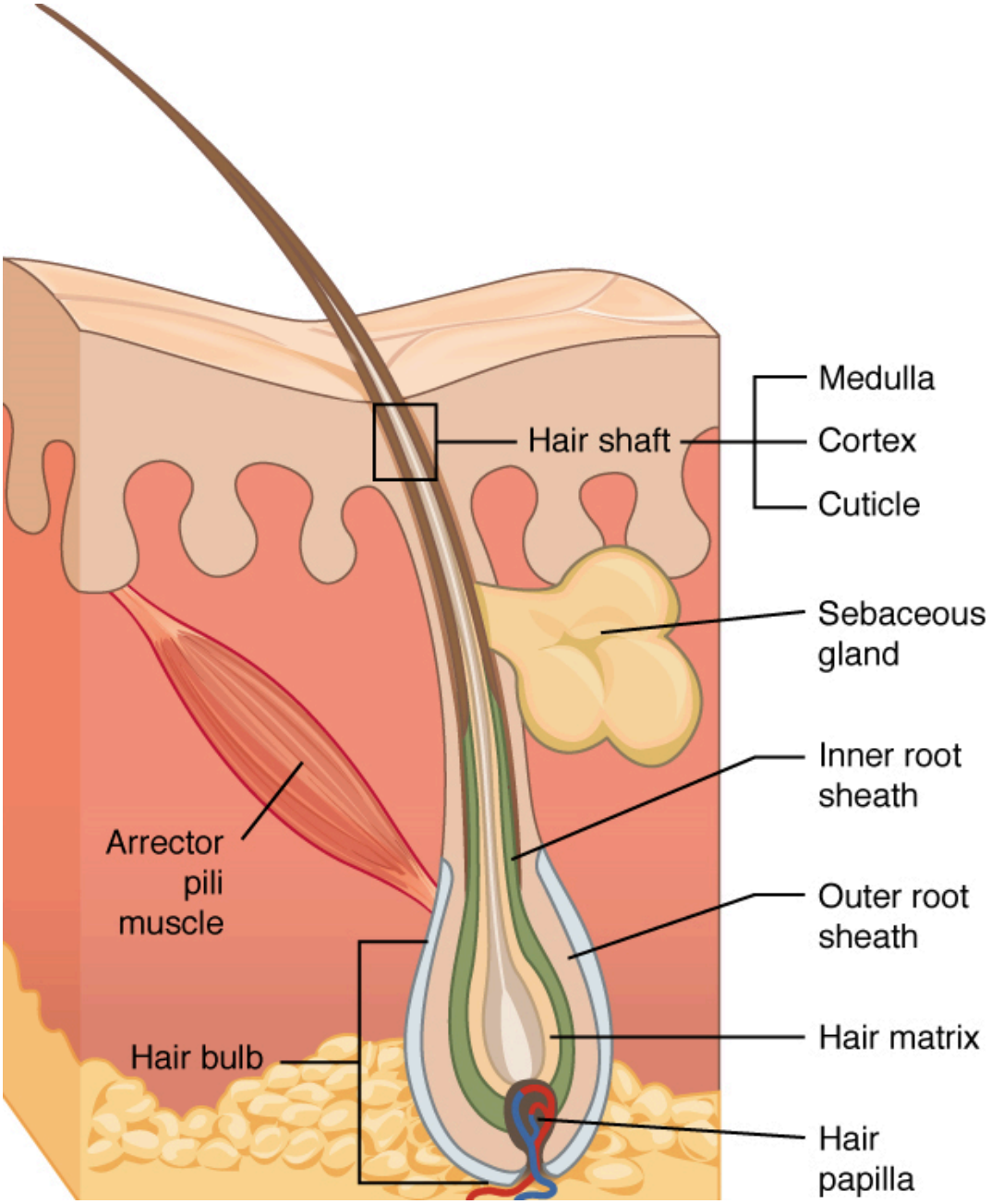


Figure 9. Hair. *A cross-section of a hair follicle, showing the hair bulb and papilla.*

Hair serves a variety of functions in the human body, including protection, sensory input, and communication. For example, hair on the head protects the skull from the sun. The hair in the nose and ears, and around the eyes (eyelashes) defends the body by trapping and excluding dust particles that may contain allergens and microbes. Hair of the eyebrows prevents sweat and other particles from dripping into and bothering the eyes. Hair also has a sensory function due to sensory innervation by a hair root plexus surrounding the base of each hair follicle.

Hair is extremely sensitive to air movement or other disturbances in the environment, much more so than the skin surface. This feature is also useful for the detection of the presence of insects or other potentially damaging substances on the skin surface. Each hair root is connected to a smooth muscle called the **arrector pili** that contracts in response to nerve signals from the nervous system, making the external hair shaft "stand up" (Figure 9). The primary purpose for this would be to trap a layer of air to add insulation, but in humans the hairs are too far away from each other to be effective as insulation. The erection of the hair shafts in response to low body temperature nevertheless persists in humans and is visible as "goose bumps".

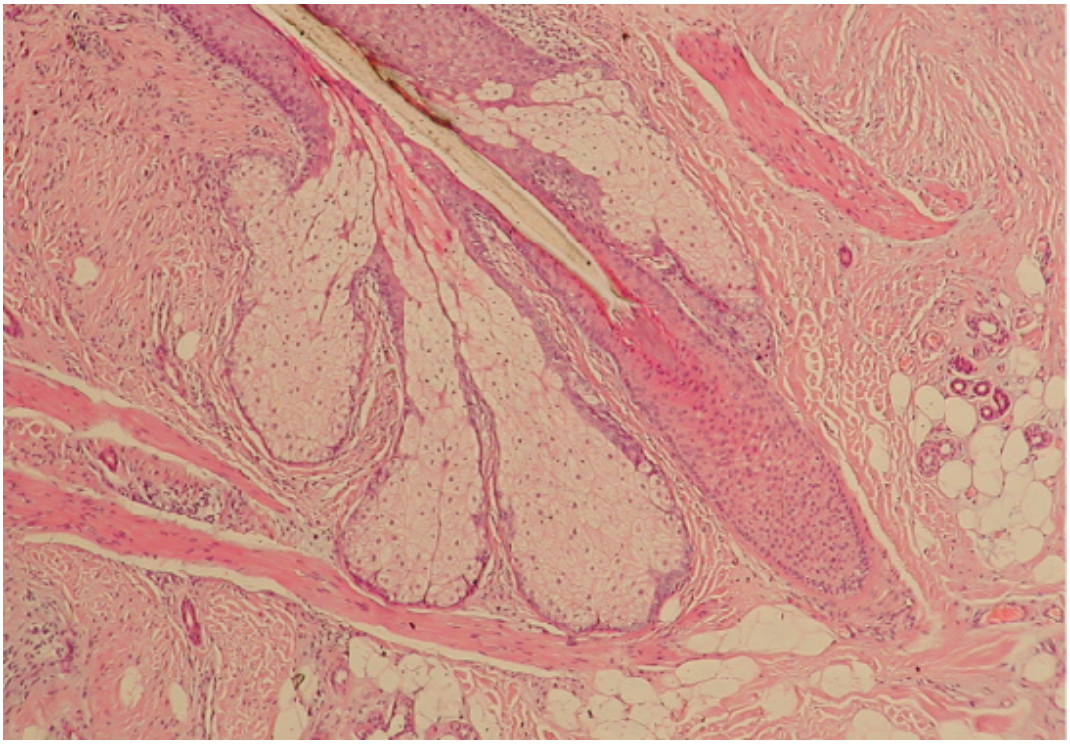


Figure 10. Hair Follicle. *The slide shows a cross-section of a hair follicle. Basal cells of the hair matrix in the center differentiate into cells of the inner root sheath. Basal cells at the base of the hair root form the outer root sheath. LM × 4. (credit: modification of work by "kilbad"/Wikimedia Commons)*

Hair grows and is eventually shed and replaced by new hair. On average, 50 hairs are lost and replaced per day. Hair loss occurs if there is more hair shed than what is replaced and can happen due to hormonal or dietary changes. Hair loss can also result from the aging process, or the influence of hormones.

Similar to the skin, hair gets its color from the pigment melanin, produced by melanocytes in the hair papilla. Different hair color results from differences in the type of melanin, which is genetically determined. As a person ages, the melanin production decreases, and hair tends to lose its color and becomes gray and/or white.

Nails: The nail bed is a specialized structure of the epidermis that is found at the tips of our fingers and toes. The **nail body** is formed on the **nail bed**, and protects the tips of our fingers and toes as they are the farthest extremities and the parts of the body that experience the maximum mechanical stress (Figure 11). In addition, the nail body forms a back-support for picking up small objects with the fingers. The nail body is composed of densely packed dead keratinocytes. The nail body forms at the **nail root**, which has a matrix of proliferating cells from the stratum basale that enables the nail to grow continuously.

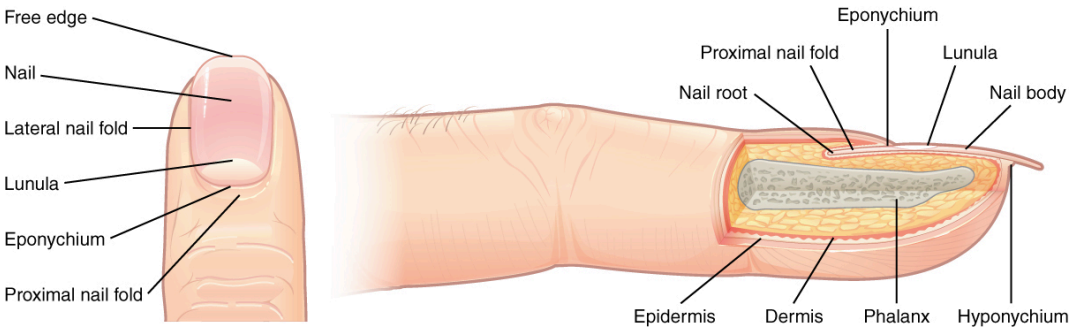


Figure 11. Nails. *The nail is an accessory structure of the integumentary system.*

Sweat Glands: When the body becomes warm, **sudoriferous glands** produce sweat to cool the body. Sweat glands develop from epidermal projections into the dermis and are classified as merocrine glands; that is, the secretions are excreted by exocytosis through a duct without affecting the cells of the gland. There are two main types of sweat glands, each secreting slightly different products.

An **eccrine sweat gland** is type of gland that produces a hypotonic (relative to blood plasma) sweat for thermoregulation. These glands are found all over the skin's surface, but are especially abundant on the palms of the hand, the soles of the feet, and the forehead (Figure 12).

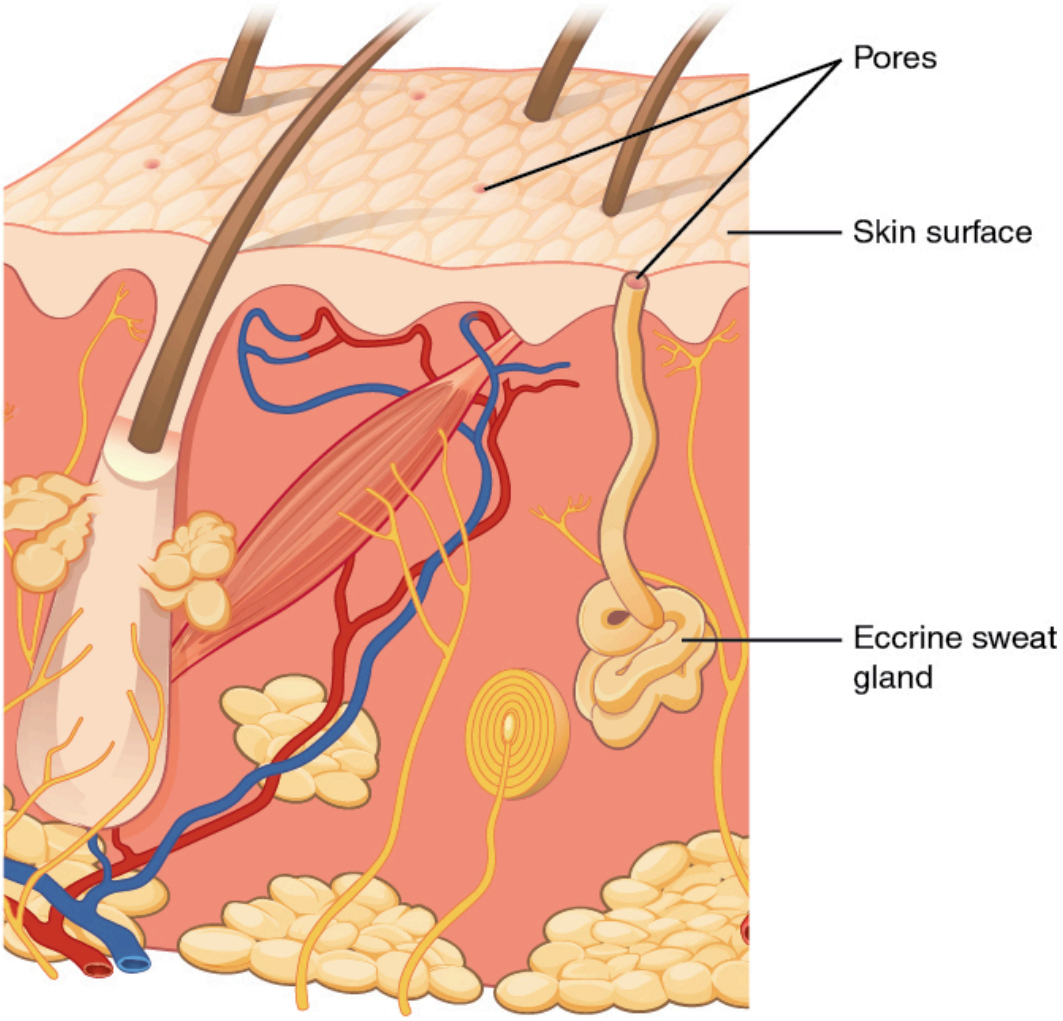


Figure 12. Eccrine Gland. *Eccrine glands are coiled glands in the dermis that release sweat that is mostly water.*

They are coiled glands lying deep in the dermis, with the duct rising up to a pore on the skin surface, where the sweat is released. This type of sweat, released by exocytosis, is composed mostly of water, with some salt, antibodies, traces of metabolic waste, and dermicidin, an antimicrobial peptide. Eccrine glands are a primary component of thermoregulation in humans and thus help to maintain homeostasis.

An **apocrine sweat gland** is usually associated with hair follicles in densely hairy areas, such as the armpits and anogenital regions. Apocrine sweat glands are larger than eccrine sweat glands and lie deeper in the dermis, sometimes even reaching the hypodermis, with the duct normally emptying into the hair follicle. In addition to water and salts, apocrine sweat includes organic compounds that make the sweat thicker and subject to bacterial decomposition and subsequent smell. The release of this sweat is under both nervous and hormonal control, and plays a role in the poorly understood human pheromone response. Most commercial antiperspirants use an aluminum-based compound as their primary active ingredient to stop sweat. When the antiperspirant enters the sweat gland duct, the aluminum-based compounds precipitate due to a change in pH and form a physical block in the duct, which prevents sweat from coming out of the pore.

There are several different types of modified apocrine glands that have become specialized to serve particular functions. One example is the **mammary gland**, which allows mammals to produces and secretes milk (a mixture of water, salt, and organic compounds) in appropriate concentrations to nourish growing offspring. Another example is the **ceruminous gland**, which is found in the external auditory meatus (ear canal) and secretes a pigmented mixture of lipids and proteins that combines with the sebum secreted from sebaceous glands (see below) and dead keratinocytes to form cerumen (earwax). This sticky substance is used to trap small foreign bodies (e.g. dirt, small insects) and help prevent damage to the tympanic membrane (eardrum).

Sebaceous Glands: A **sebaceous gland** is a type of oil gland that is found all over the body and helps to lubricate and waterproof the skin and hair. Most sebaceous glands are associated with hair follicles (Figures 9 & 10). They generate and excrete sebum, a mixture of lipids, onto the skin surface, thereby naturally lubricating the dry and dead layer of keratinized cells of the stratum corneum, keeping it pliable. The fatty acids of sebum also have antibacterial properties, and prevent water loss from the skin in low-humidity environments. The secretion of sebum is stimulated by hormones, many of which do not become active until puberty. Thus, sebaceous glands are relatively inactive during childhood.

Part 3: Functions of the Integumentary System

The skin and accessory structures perform a variety of essential functions, such as protecting the body from invasion by microorganisms, chemicals, and other environmental factors; preventing dehydration; acting as a sensory organ; modulating body temperature and electrolyte balance; and synthesizing vitamin D. The underlying hypodermis has important roles in storing fats, forming a “cushion” over underlying structures, and providing insulation from cold temperatures.

Protection: The skin protects the rest of the body from the basic elements of nature such as wind, water, and UV sunlight. It acts as a protective barrier against water loss, due to the presence of layers of keratin and glycolipids in the stratum corneum. It also is the first line of defense against abrasive activity due to contact with grit, microbes, or harmful chemicals. Sweat excreted from sweat glands deters microbes from over-colonizing the skin surface by generating dermicidin, which has antibiotic properties.

Sensory Function: The fact that you can feel an ant crawling on your skin, allowing you to flick it off before it bites, is because the skin, and especially the hairs projecting from hair follicles in the skin, can sense changes in the environment. The hair root plexus surrounding the base of the hair follicle senses a disturbance, and then transmits the information to the central nervous system (brain and spinal cord), which can then respond by activating the skeletal muscles of your eyes to see the ant and the skeletal muscles of the body to act against the ant.

The skin acts as a sense organ because the epidermis, dermis, and the hypodermis contain specialized sensory nerve structures that detect touch, surface temperature, and pain. These receptors are more concentrated on the tips of the fingers, which are most sensitive to touch, especially the **tactile (Meissner)**

corpuscle (Figure 13), which responds to light touch, and the **lamellated (Pacinian) corpuscle**, which responds to vibration.

Merkel cells, seen scattered in the stratum basale, are also touch receptors. In addition to these specialized receptors, there are sensory nerves connected to each hair follicle, pain and temperature receptors scattered throughout the skin, and motor nerves innervate the arrector pili muscles and glands. This rich innervation helps us sense our environment and react accordingly.

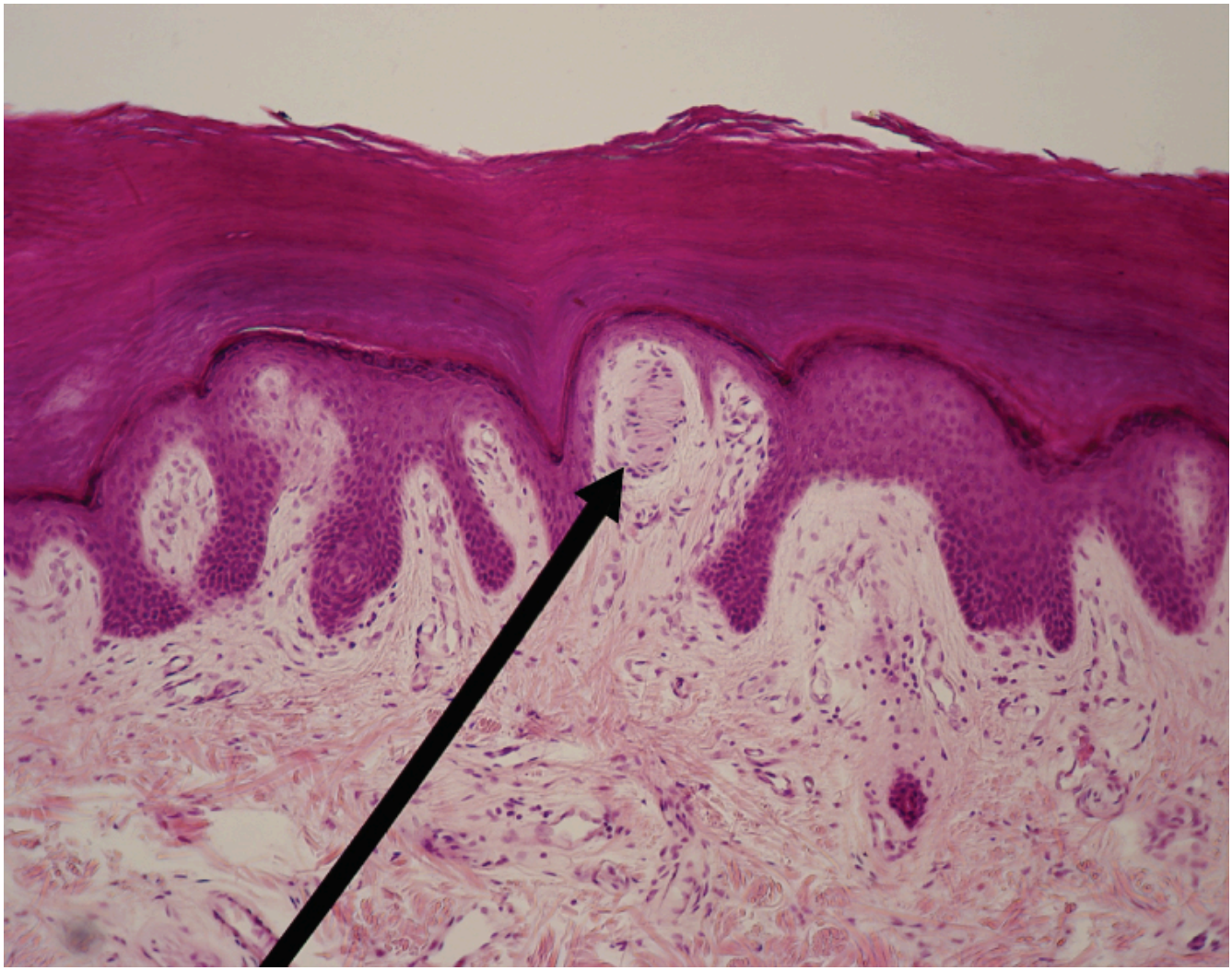


Figure 13. Light Micrograph of a Tactile (Meissner) Corpuscle. In this micrograph of a skin cross-section, you can see a tactile (Meissner) corpuscle (arrow), a type of touch receptor located in a dermal papilla adjacent to the basement membrane and stratum basale of the overlying epidermis. LM × 100. (credit: "Wbensmith"/Wikimedia Commons)

Thermoregulation: The integumentary system helps regulate body temperature through its tight association with the nervous system. The nervous system is continuously monitoring body temperature and initiating appropriate motor responses. Recall that sweat glands, accessory structures to the skin, secrete water, salt, and other substances to cool the body when it becomes warm.

Even when the body does not appear to be noticeably sweating, approximately 500 mL of sweat (insensible perspiration) are secreted a day. If the body becomes excessively warm due to high temperatures, vigorous activity (Figure 14ac), or a combination of the two, sweat glands will be stimulated by the sympathetic nervous system to produce large amounts of sweat, as much as 0.7 to 1.5 L per hour for an active person. When the sweat evaporates from the skin surface, the body is cooled as body heat is dissipated.

In addition to sweating, arterioles in the dermis dilate so that excess heat carried by the blood can dissipate

through the skin and into the surrounding environment (Figure 14b). This accounts for the skin redness that many people experience when exercising.

When body temperatures drop, the arterioles constrict to minimize heat loss, particularly in the ends of the digits and tip of the nose. This reduced circulation can result in the skin taking on a whitish hue. Although the temperature of the skin drops as a result, passive heat loss is prevented, and internal organs and structures remain warm. If the temperature of the skin drops too much (such as environmental temperatures below freezing), the conservation of body core heat can result in the skin actually freezing, a condition called frostbite.

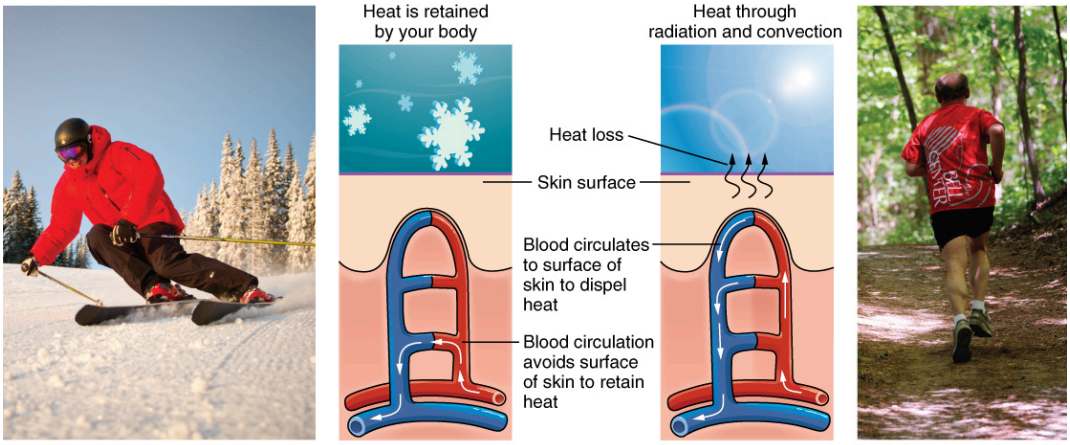


Figure 14. Thermoregulation. *During strenuous physical activities, such as skiing (a) or running (c), the dermal blood vessels dilate and sweat secretion increases (b). These mechanisms prevent the body from overheating. In contrast, the dermal blood vessels constrict to minimize heat loss in response to low temperatures (b). (credit a: "Trysil"/flickr; credit c: Ralph Daily)*

Other Functions of the Skin: The epidermal layer of human skin synthesizes vitamin D when exposed to UV radiation. In the presence of sunlight, a precursor of vitamin D is synthesized from a derivative of the cholesterol in the skin. Further biochemical reactions in the liver and kidney produce then calcitriol, the active chemical form of the vitamin, which has important roles in the absorption of calcium from the small intestine In present day society, vitamin D is added as a supplement to many foods, including milk and orange juice, compensating for the need for sun exposure.

The skin is also a minor component of the excretory system, which is used to remove metabolic waste products from the body. Most metabolic waste products are removed from the body via the urinary and respiratory systems. However, the skin does release in sweat some of the metabolic waste products that are found in blood plasma, albeit at relatively low concentrations.

Unit 12: The Skeletal System

Unit outline

Bone Tissue and the Skeletal System

Part 1: The Functions of the Skeletal System

- Support, movement, and protection
- Mineral storage, energy storage, and hematopoiesis

Part 2: Bone Classification

Part 3: Bone Structure

- Gross anatomy of bone
- Bone cells and tissues
- Compact and spongy bone
- Blood and nerve supply

Part 4: Bone Formation and Development

- Cartilage templates
- Intramembranous ossification
- Endochondral ossification
- How bones grow in length
- How bones grow in diameter
- Bone remodeling

Part 5: Fractures

- Types of fractures

Divisions of the Skeletal System

- The axial skeleton
- The appendicular skeleton

The Axial Skeleton

Part 1: The Skull

- Development of the skull
- Anterior view of the skull
- Lateral view of the skull
- Bones of the brain case
- Facial bones of the skull
- The bones of the middle ear

- The hyoid bone

Part 2: The Vertebral Column

- Regions of the vertebral column
- General structure of a vertebra
- Regional modifications of vertebrae
- Cervical vertebrae

Part 3: The Thoracic Cage

The Appendicular Skeleton

Part 1: The Pectoral Girdle

Part 2: Bones of the Upper Limb

Part 3: The Pelvic Girdle and Pelvis

- Comparison of a female and male pelvis

Part 4: Bones of the Lower Limb

Learning Objectives

At the end of this unit, you should be able to:

I. Describe the functions of the skeletal system and the five basic shapes of human bones.

II. Describe the structure and histology of the skeletal system.

III. Define and identify the following parts of a long bone: diaphysis, epiphysis, metaphysis, articular cartilage, periosteum, medullary cavity, and endosteum.

IV. Compare the composition and function of compact bone versus spongy bone.

V. Define ossification, compare intramembranous ossification with endochondral ossification, describe how a long bone grows in length and width, and specify how various factors might affect the rate of ossification and, by extension, the height of a mature individual.

VI. Describe four types of bone fractures.

VII. Specify the components of the axial and appendicular skeletons, describe the general function of each skeleton, and name and describe the principle components of the axial skeleton.

VIII. Describe the structure and function of a typical vertebra and explain how these differ in the case of the atlas and axis.

IX. Describe the components and functions of the pectoral girdle and the pelvic girdle.

X. Specify all bones and structures in the human skeleton covered in this Unit.

XI. Describe the differences between the pelvis of a human female and that of a human male.

XII. Describe the major differences between the skeleton of an infant and that of an adult.

Learning Objectives and Guiding Questions

At the end of this unit, you should be able to complete all the following tasks, including answering the guiding questions associated with each task.

I. Describe the functions of the skeletal system and the five basic shapes of human bones.

1. Specify the ways that the skeletal system functions in the human body.
2. The main common functions of all components of the human skeletal system are "protection" and "support". Based on the material that follows in this Unit, select several examples of individual components (including both bone and cartilage examples) and describe how they serve each of these two functions.
3. Name, describe, and provide one example of each of the five different shapes of human bones.

II. Describe the structure and histology of the skeletal system.

1. Based on previously covered material and the information in this Unit, describe each of the different cell types found in cartilage and bone. For each cell type, identify:
    - Where in the body, and from which type of cell, it arose.
    - Where it normally resides in the body, as specifically as possible.
    - What its main function is, and how (briefly) it serves that function.
    - What happens to the cell if the matrix that surrounds it calcifies.
2. Based on previously covered material and the information in this Unit, compare and contrast the components of cartilage matrix and bone matrix, explaining the differences in the physical characteristics of cartilage and bone.
3. From what tissue type do bones and cartilage arise during early development? What other mature tissues arise from the same fetal tissue type?

III. Define and identify the following parts of a long bone: diaphysis, epiphysis, metaphysis, articular cartilage, periosteum, medullary cavity, and endosteum.

1. Create a fully-labelled diagram of a typical long bone, showing the main external and internal features and identifying all the main tissue types found in a long bone.

IV. Compare the composition and function of compact bone versus spongy bone.

1. Compare and contrast compact bone and spongy bone, in terms of the following characteristics:

- The tissue type and cell type found in each type of bone.
- The arrangement of tissue and/or cells in each type of bone.
- The location of each within a bone.
- The function of each type of bone.

2. Use annotated diagrams to compare and contrast the internal structure of an osteon with that of a trabecula.

V. Define ossification, compare intramembranous ossification with endochondral ossification, describe how a long bone grows in length and width, and specify how various factors might affect the rate of ossification and, by extension, the height of a mature individual.

1. Explain in detail the processes of:
    - Intramembranous ossification
    - Endochondral ossification
    - Growth in length of a long bone
    - Growth in width of a long bone
2. Compare and contrast the processes of intramembranous ossification and endochondral ossification.
3. Compare and contrast the processes of endochondral ossification and lengthwise growth of a long bone.
4. Compare and contrast the processes of intramembranous ossification and widthwise growth of a long bone.
5. The height of an individual is largely determined by the rate of ossification prior to physical maturity. Briefly explain why this is so.
6. Based on information provided in this and other Units, briefly describe the effects you would expect to see, if any, on the height of an individual under the following conditions, and briefly explain your reasoning for each.
    - Hypersecretion of growth hormone during development
    - Hyposecretion of growth hormone during development
    - Premature onset of puberty
    - Late onset of puberty
    - Shorter than average parents
    - Taller than average parents
    - Excessive caloric intake during development
    - Malnutrition during development

VI. Describe four types of bone fractures.

1. Compare and contrast the common causes and appearance of:
    - Closed (simple) vs. open (compound) fractures
    - Comminuted *vs* closed fractures
    - Greenstick *vs* closed fractures
    - Comminuted *vs* greenstick fractures

2. Can a fracture be classified as two of the above types at the same time? In other words, are any of the following fracture types possible? In each case, explain why or why not.
    - A closed open fracture
    - A closed comminuted fracture
    - A closed greenstick fracture
    - An open comminuted fracture
    - An open greenstick fracture

VII. Specify the components of the axial and appendicular skeletons, describe the general function of each skeleton, and name and describe the principle components of the axial skeleton.

1. List all the components of the axial skeleton.
2. List all the components of the appendicular skeleton.
3. Write one sentence that clearly describes and differentiates between the axial and appendicular skeletons.
4. Specify the main functions of the axial skeleton, and that of the appendicular skeleton. Explain how the overall shape of each skeleton is appropriate to its primary function.
5. Describe the location of the following:
    - Xiphoid process of the sternum
    - Mastoid process of the temporal bone
6. Describe in general terms the location and function of the following:
    - Hyoid bone
    - Incus, malleus, and stapes
    - Atlas
    - Axis

VIII. Describe the structure and function of a typical vertebra and explain how these differ in the case of the atlas and axis.

1. Sketch a diagram of a typical vertebra, clearly showing and labelling all the following components:
    - Body
    - Vertebral foramen
    - Transverse processes
    - Spinous process
2. Sketch a diagram of the atlas and of the axis, clearly showing and labelling the following components, where applicable:
    - Body
    - Vertebral foramen
    - Transverse processes
    - Spinous process
    - Dens

IX. Describe the components and functions of the pectoral girdle and the pelvic girdle.

1. List the bones that make up in the pectoral girdle. Identify each as being part of the appendicular or axial skeleton.
2. List the bones and cartilage that make up the pelvic girdle. Identify each as being part of the appendicular or axial skeleton.
3. Compare and contrast the location, structure, and function of the pectoral girdle and the pelvic girdle. What about them is similar? What differs?

X. Specify all bones and structures in the human skeleton covered in this Unit.

1. Locate and identify the following bones in a diagram of a human skeleton:
    - Frontal bone
    - Parietal bone
    - Temporal bone
    - Occipital bone
    - Mandible
    - Maxilla
    - Cervical vertebrae
    - Thoracic vertebrae
    - Lumbar vertebrae
    - Sacrum
    - Coccyx
    - True ribs
    - False ribe
    - Floating ribs
    - Sternum
    - Clavicle
    - Scapula
    - Humerus
    - Radius
    - Ulna
    - Carpals
    - Metacarpals
    - Phalanges
    - Hip bone
    - Femur
    - Patella
    - Tibia
    - Fibula
    - Tarsals
    - Metatarsals
2. Sketch a human skeleton from memory. Label all the large long bones, and all the visible cartilages. Check your sketch against your textbook and worksheet to see if you've missed anything.
3. By external examination (look and feel), determine the location of your own:

- Phalanges
- Metacarpals and metatarsals
- Carpals and tarsals
- Humerus and femur
- Patella
- Ulna, radius, tibia, and fibula
- True ribs, false ribs, and floating ribs
- Sternum
- Clavicle and scapula
- Iliac crest of the hip bone
- Maxilla and mandible
- Frontal bone and occipital bone
- Sacrum
- Spinous process of a vertebra

XI. Describe the differences between the pelvis of a human female and that of a human male.

1. Describe the differences between an average male pelvis and an average female pelvis.
2. Why are male and female pelves generally shaped differently? For each sex difference noted in the question above, briefly explain the functional relevance of that sex difference specifically.

XII. Describe the major differences between the skeleton of an infant and that of an adult.

1. Describe the difference in tissue composition (relative amounts of different tissue types) of the skeleton of a child and that of an adult.
2. Explain why the skeleton of a newborn contains more bones than that of an adult, by naming two examples of bones that are formed by fully fusing two or more pieces of bone tissue.
3. Describe the difference in relative body proportions between the skeleton of an infant and that of an adult.
4. Describe the differences between the skull of a newborn and that of an adult.

Bone Tissue and the Skeletal System: Your skeleton is a structure of living tissue that grows, repairs, and renews itself. The bones within it are dynamic and complex organs that serve a number of important functions, including some necessary to maintain homeostasis.

The skeletal system forms the rigid internal framework of the body. It consists of the bones, cartilages, and ligaments. Bones support the weight of the body, allow for body movements, and protect internal organs. Cartilage provides flexible strength and support for body structures such as the thoracic cage, the external ear, and the trachea and larynx. At joints of the body, cartilage can also unite adjacent bones or provide cushioning between them. Ligaments are the strong connective tissue bands that hold the bones at a moveable joint together and serve to prevent excessive movements of the joint that would result in injury. Providing movement of the skeleton are the muscles of the body, which are firmly attached to the skeleton via connective tissue structures called tendons. As muscles contract, they pull on the bones to produce movements of the body. Thus, without a skeleton, you would not be able to stand, run, or even feed yourself!

Each bone of the body serves a particular function, and therefore bones vary in size, shape, and strength based on these functions. For example, the bones of the lower back and lower limb are thick and strong to

support your body weight. Similarly, the size of a bony landmark that serves as a muscle attachment site on an individual bone is related to the strength of this muscle. Muscles can apply very strong pulling forces to the bones of the skeleton. To resist these forces, bones have enlarged bony landmarks at sites where powerful muscles attach. This means that not only the size of a bone, but also its shape, is related to its function. Bones are also dynamic organs that can modify their strength and thickness in response to changes in muscle strength or body weight. Thus, muscle attachment sites on bones will thicken if you begin a workout program that increases muscle strength. Similarly, the walls of weight-bearing bones will thicken if you gain body weight or begin pounding the pavement as part of a new running regimen. In contrast, a reduction in muscle strength or body weight will cause bones to become thinner. This may happen during a prolonged hospital stay, following limb immobilization in a cast, or going into the weightlessness of outer space. Even a change in diet, such as eating only soft food due to the loss of teeth, will result in a noticeable decrease in the size and thickness of the jaw bones.

Part 1: The Functions of the Skeletal System

Bone, or osseous tissue, is a hard, dense connective tissue that forms most of the adult skeleton, the support structure of the body. In the areas of the skeleton where bones move (for example, the ribcage and joints), cartilage, a semi-rigid form of connective tissue, provides flexibility and smooth surfaces for movement. The skeletal system is the body system composed of bones and cartilage and performs the following critical functions for the human body:

- supports the body
- facilitates movement
- protects internal organs
- produces blood cells
- stores and releases minerals and fat

Support, Movement and Protection: The most apparent functions of the skeletal system are the gross functions—those visible by observation. Simply by looking at a person, you can see how the bones support, facilitate movement, and protect the human body.

Just as the steel beams of a building provide a scaffold to support its weight, the bones and cartilage of your skeletal system compose the scaffold that supports the rest of your body. Without the skeletal system, you would be a limp mass of organs, muscle, and skin.

Bones also facilitate movement by serving as points of attachment for your muscles. While some bones only serve as a support for the muscles, others also transmit the forces produced when your muscles contract. From a mechanical point of view, bones act as levers and joints serve as fulcrums (Figure 1). Unless a muscle spans a joint and contracts, a bone is not going to move.

Figure 1. Bones Support Movement. *Bones act as levers when muscles span a joint and contract. (credit: Benjamin J. DeLong)*

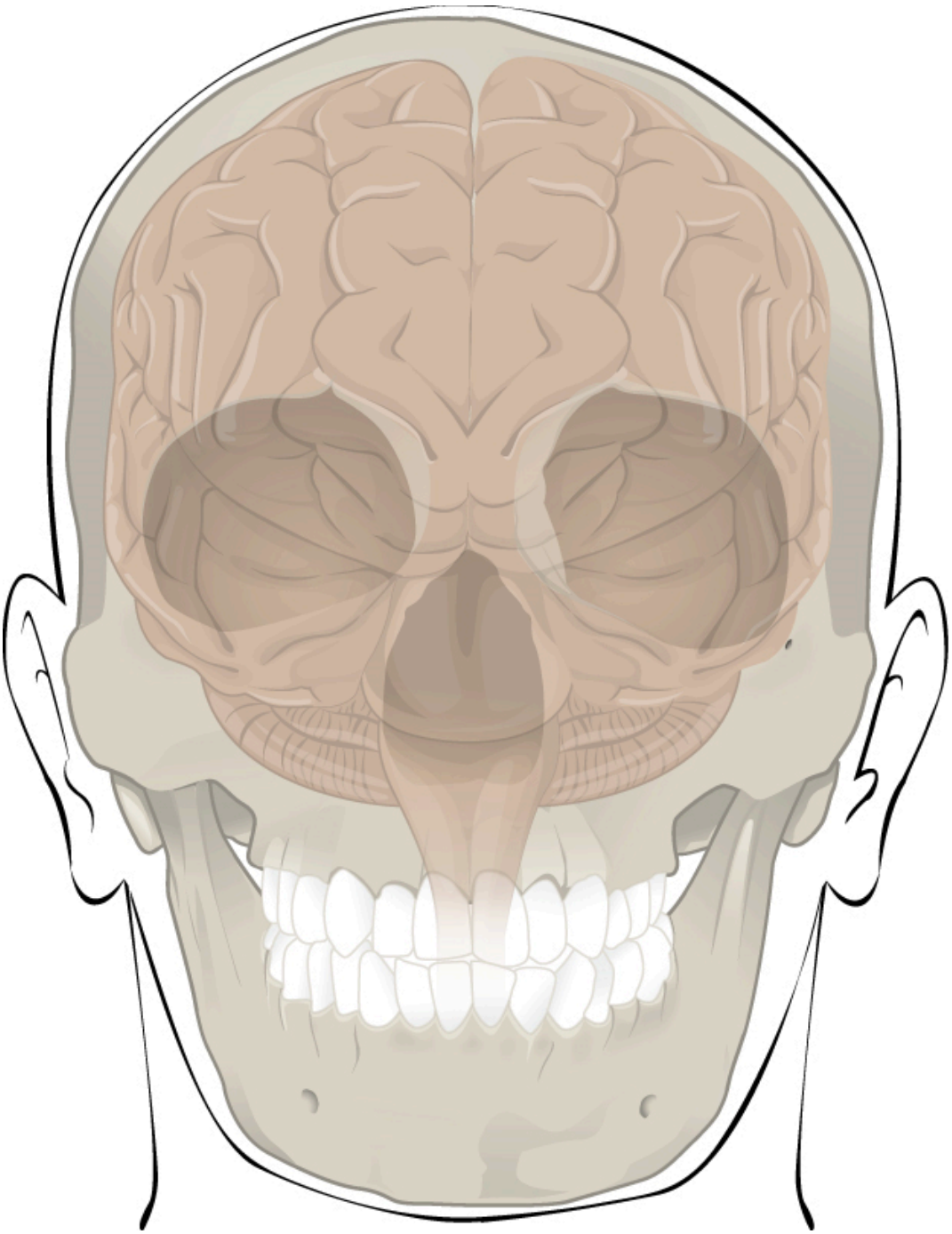


Figure 2. Bones Protect the Brain. *The cranium completely surrounds and protects the brain from non-traumatic injury.*

Bones also protect internal organs from injury by covering or surrounding them. For example, your ribs protect your lungs and heart, the bones of your vertebral column (spine) protect your spinal cord, and the bones of your cranium (skull) protect your brain (Figure 2).

Mineral Storage, Energy Storage, and Hematopoiesis: On a metabolic level, bone tissue performs several critical functions. For one, the bone matrix acts as a reservoir for a number of minerals important to the functioning of the body, especially calcium, and phosphorus. These minerals, incorporated into bone tissue, can be released back into the bloodstream to maintain levels needed to support physiological processes. Calcium

ions, for example, are essential for muscle contractions and controlling the flow of other ions involved in the transmission of nerve impulses.

Bone also serves as a site for fat storage and blood cell production. The softer connective tissue that fills the interior of most bone is referred to as bone marrow (Figure 3). There are two types of bone marrow: yellow marrow and red marrow. Yellow marrow contains adipose tissue; the triglycerides stored in the adipocytes of the tissue can serve as a source of energy. Red marrow is where hematopoiesis—the production of blood cells—takes place. Red blood cells, white blood cells, and cell fragments called platelets are all produced in the red marrow.

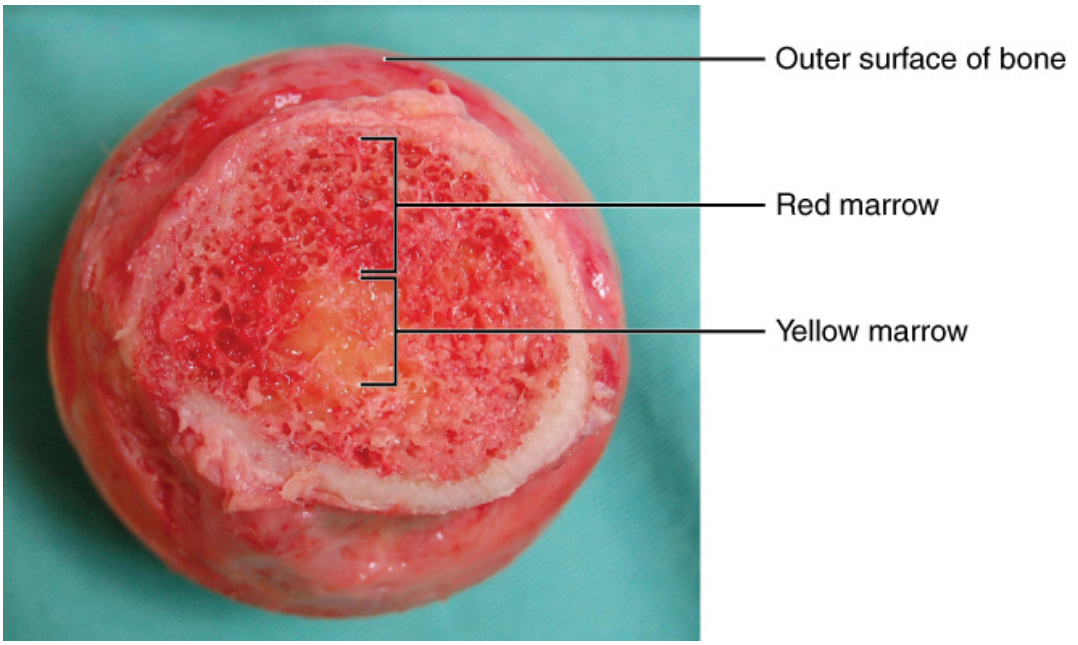


Figure 3. Head of the Femur Showing Red and Yellow Marrow. *The head of the femur contains both yellow and red marrow. Yellow marrow stores fat. Red marrow is responsible for hematopoiesis. (credit: modification of work by "stevenfruitsmaak"/Wikimedia Commons)*

Part 2: Bone Classification

The 206 bones that compose the adult skeleton can be divided into five categories based on their shapes (Figure 4). Their shapes and their functions are related such that each categorical shape of bone has a distinct function.

Long Bones: A long bone is one that is cylindrical in shape, with a diameter smaller than its height. Keep in mind, however, that the term describes the shape of a bone, not its size. Long bones are found in the arms (humerus, ulna, and radius) and legs (femur, tibia, and fibula), as well as in the fingers (metacarpals and phalanges) and toes (metatarsals and phalanges). Long bones function as levers; they move when muscles contract.

Short Bones: A short bone is one that is cube-like in shape, being approximately equal in length, width, and thickness. The only short bones in the human skeleton are in the carpals of the wrists and the tarsals of the ankles. Short bones provide stability and support as well as some limited motion.

Flat Bones: The term "flat bone" is somewhat of a misnomer because, although a flat bone is typically thin, it is also often curved. Examples include the cranial bones of the skull, the scapulae (shoulder blades), the sternum (breastbone), and the ribs. Flat bones serve as points of attachment for muscles and often protect internal organs.

Irregular Bones: An irregular bone is one that does not have any easily characterized shape and therefore does not fit any other classification. These bones tend to have more complex shapes, like the vertebrae that support the spinal cord and protect it from compressive forces. Many facial bones, particularly the ones containing sinuses, are classified as irregular bones.

Sesamoid Bones: A sesamoid bone is a small, round bone that, as the name suggests, is shaped like a sesame seed. These bones form in tendons (the sheaths of tissue that connect bones to muscles) where a great deal of pressure is generated in a joint. The sesamoid bones protect tendons by helping them overcome compressive forces. Sesamoid bones vary in number and placement from person to person but are typically found in tendons associated with the feet, hands, and knees. The patellae (singular = patella) are the only sesamoid bones found in common with every person. Table 1 reviews bone classifications with their associated features, functions, and examples.

Table 1: Bone Classification by Shape

Bone classification	Features	Function(s)	Examples
Long	Cylinder-like shape, longer than it is wide	Leverage	Femur, tibia, fibula, metatarsals, humerus, ulna, radius, metacarpals, phalanges
Short	Cube-like shape, approximately equal in length, width, and thickness	Provide stability & support while allowing for some motion	Carpals, tarsals
Flat	Thin and curved	Points of attachment for muscles; protectors of internal organs	Sternum, ribs, scapulae, cranial bones
Irregular	Complex shape	Protect internal organs	Vertebrae, facial bones
Sesamoid	Small and round; embedded in tendons	Protect tendons from compressive forces	Patellae

Part 3: Bone Structure

Bone tissue (osseous tissue) differs greatly from other tissues in the body. Bone is hard and many of its functions depend on that characteristic hardness. Later discussions in this chapter will show that bone is also dynamic in that its shape adjusts to accommodate stresses. This section will examine the gross anatomy of bone first and then move on to its histology.

Gross Anatomy of Bone: The structure of a long bone allows for the best visualization of all of the parts of a bone (Figure 5). A long bone has two parts: the **diaphysis** and the **epiphysis**. The diaphysis is the tubular shaft that runs between the proximal and distal ends of the bone. The hollow region in the diaphysis is called the **medullary cavity**, which is filled with yellow marrow. The walls of the diaphysis are composed of dense and hard **compact bone**. The wider section at each end of the bone is called the **epiphysis** (plural = epiphyses), which is filled with spongy bone. Red marrow fills the spaces in the spongy bone.

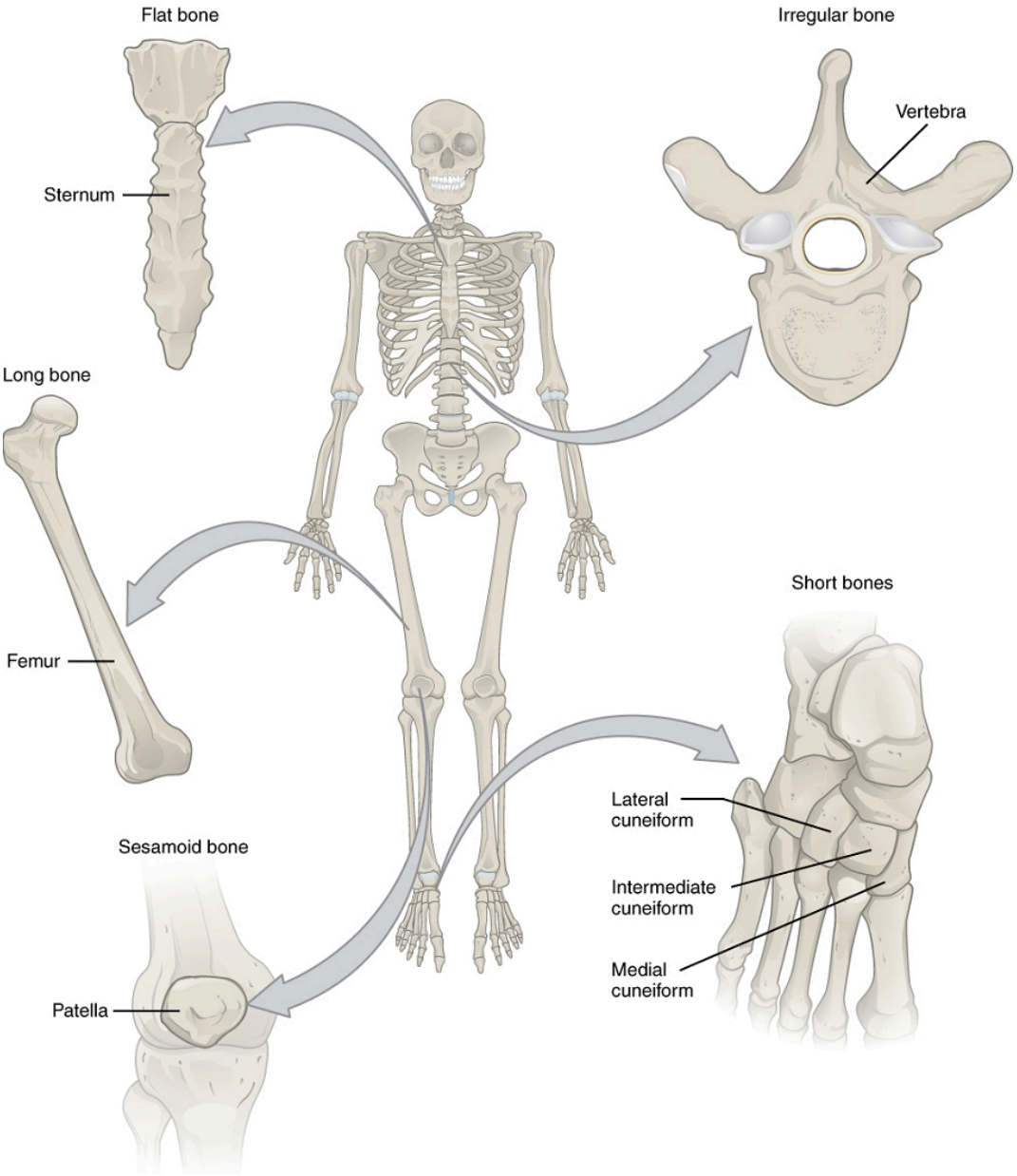


Figure 4. Classifications of Bones. *Bones can be classified according to their shape.*

Each epiphysis meets the diaphysis at the metaphysis, the narrow area that contains **the epiphyseal plate** (growth plate), a layer of hyaline (transparent) cartilage in a growing bone. When the bone stops growing in early adulthood (approximately 18–21 years), the cartilage is replaced by osseous tissue and the epiphyseal plate becomes an epiphyseal line.

The medullary cavity has a delicate membranous lining called the **endosteum** (end- = "inside"; oste- = "bone"), where bone growth, repair, and remodeling occur. The outer surface of the bone is covered with a fibrous membrane called the **periosteum** (peri– = "around" or "surrounding"). The periosteum contains blood vessels, nerves, and lymphatic vessels that nourish compact bone. Tendons and ligaments also attach to bones at the periosteum. The periosteum covers the entire outer surface except where the epiphyses meet other bones to form joints (Figure 6). In this region, the epiphyses are covered with **articular cartilage**, a thin layer of cartilage that reduces friction and acts as a shock absorber.

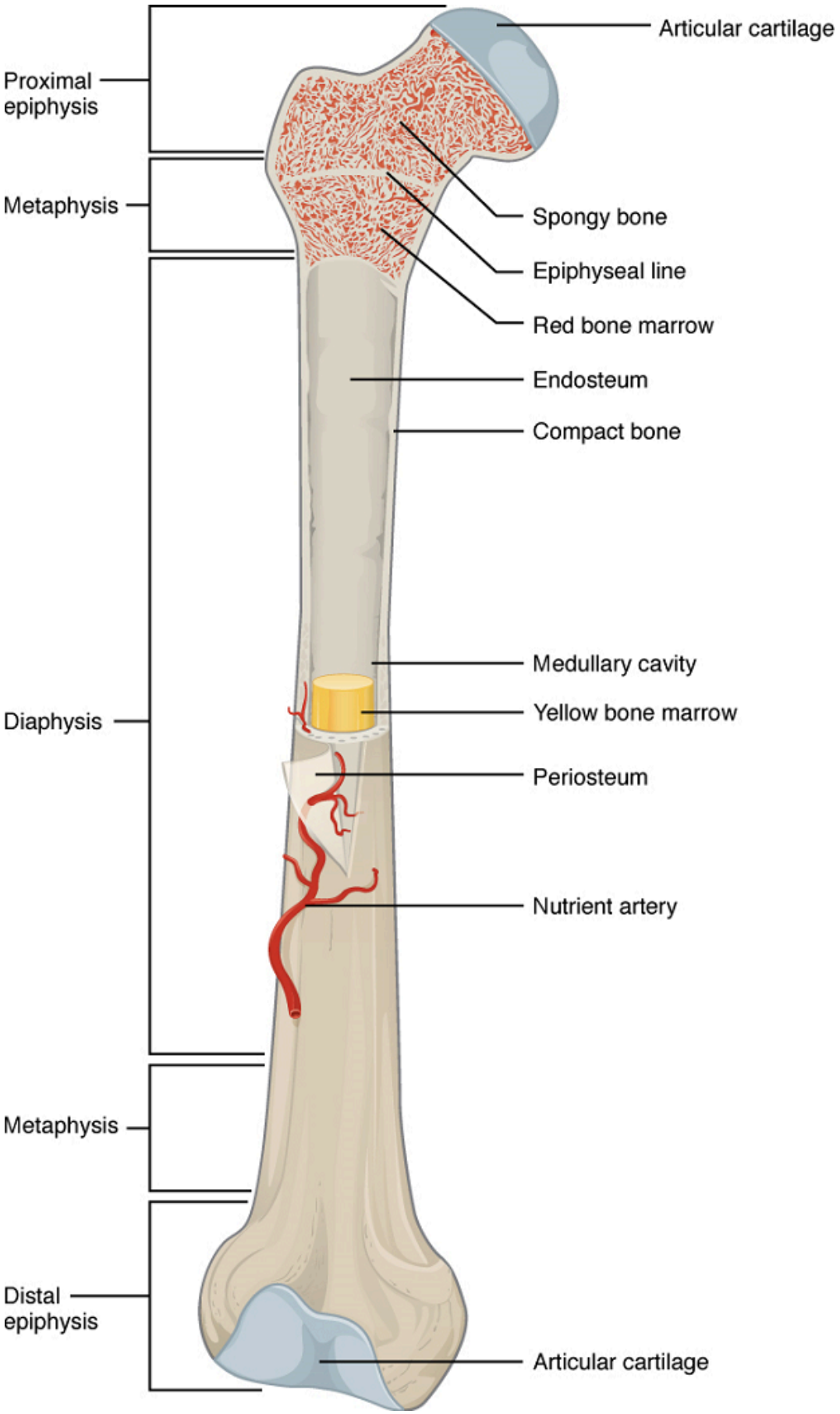


Figure 5. Anatomy of a Long Bone. *A typical long bone shows the gross anatomical characteristics of bone.*

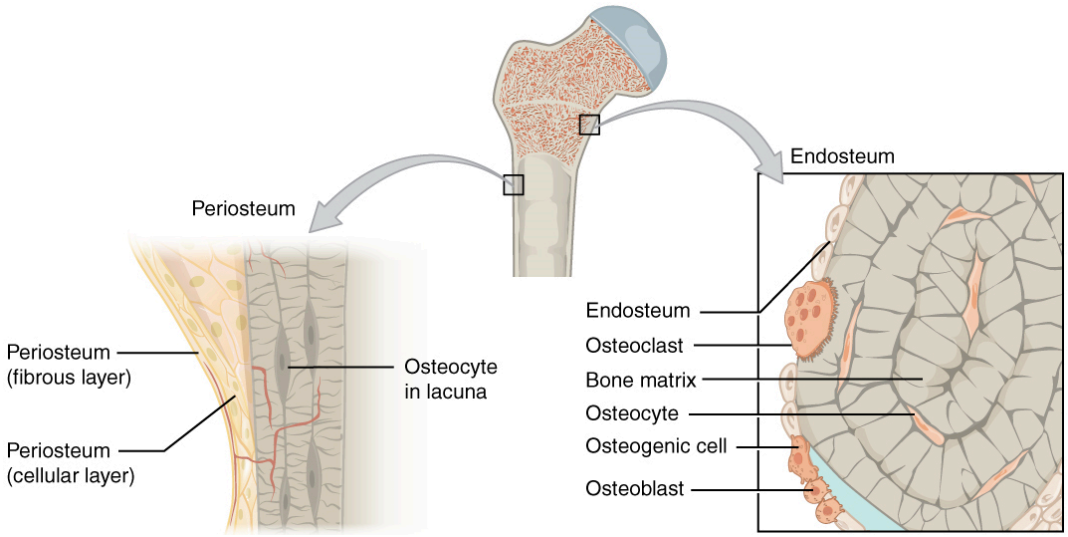


Figure 6. Periosteum and Endosteum. *The periosteum forms the outer surface of bone, and the endosteum lines the internal surfaces of bone, like the medullary cavity.*

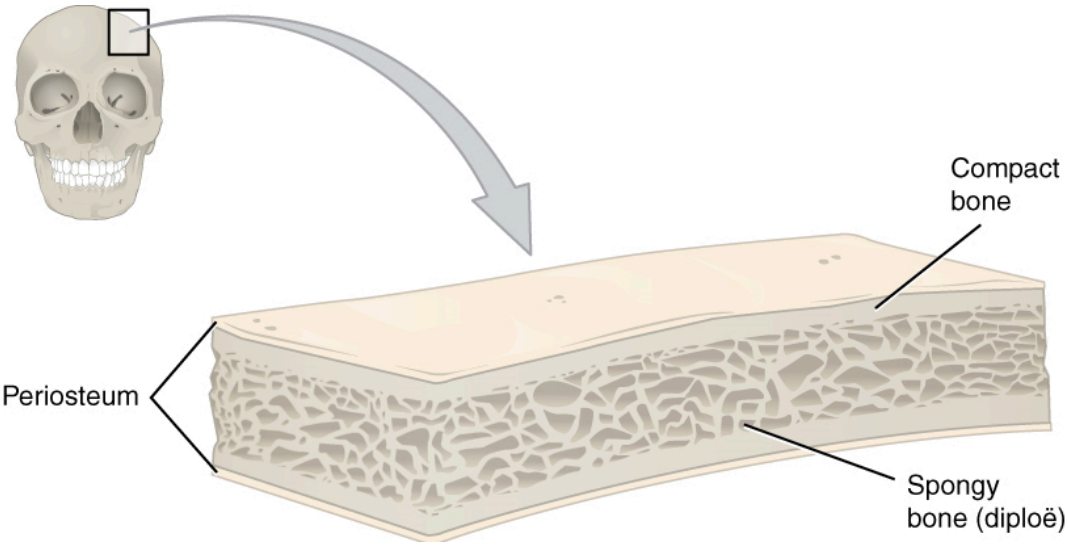


Figure 7. Anatomy of a Flat Bone. *This cross-section of a flat bone shows the spongy bone (diploë) lined on either side by a layer of compact bone.*

Flat bones, like those of the cranium, consist of a layer of **diploë** (spongy bone), lined on either side by a layer of compact bone (Figure 7). The two layers of compact bone and the interior spongy bone work together to protect the internal organs. If the outer layer of a cranial bone fractures, the brain is still protected by the intact inner layer.

Bone Cells and Tissue: Bone contains a relatively small number of cells entrenched in a matrix of collagen fibers that provide a surface for inorganic salt crystals to adhere. These salt crystals, made of a substance called hydroxyapatite, form when calcium phosphate and calcium carbonate combine with other inorganic salts and solidify, (i.e. calcify) on the collagen fibers. The crystals give bones their hardness and strength, while the collagen fibers give them flexibility so that they are not brittle.

Although bone cells compose a small amount of the bone volume, they are crucial to the function of bones. Four types of cells are found within bone tissue: osteoblasts, osteocytes, osteogenic cells, and osteoclasts (Figure 8).

The **osteoblast** is the bone cell responsible for forming new bone and is found in the growing portions of bone, including the periosteum and endosteum. Osteoblasts, which do not divide, synthesize and secrete the

collagen matrix and calcium salts. As the secreted matrix surrounding the osteoblast calcifies, the osteoblast become trapped within it; as a result, it changes in structure and becomes an **osteocyte**, the primary cell of mature bone and the most common type of bone cell. Each osteocyte is located in a space called a **lacuna** and is surrounded by bone matrix. Osteocytes maintain the mineral concentration of the matrix. Like osteoblasts, osteocytes lack mitotic activity. They can communicate with each other and receive nutrients via long cytoplasmic processes that extend through **canaliculi** (singular = canaliculus), channels within the bone matrix.

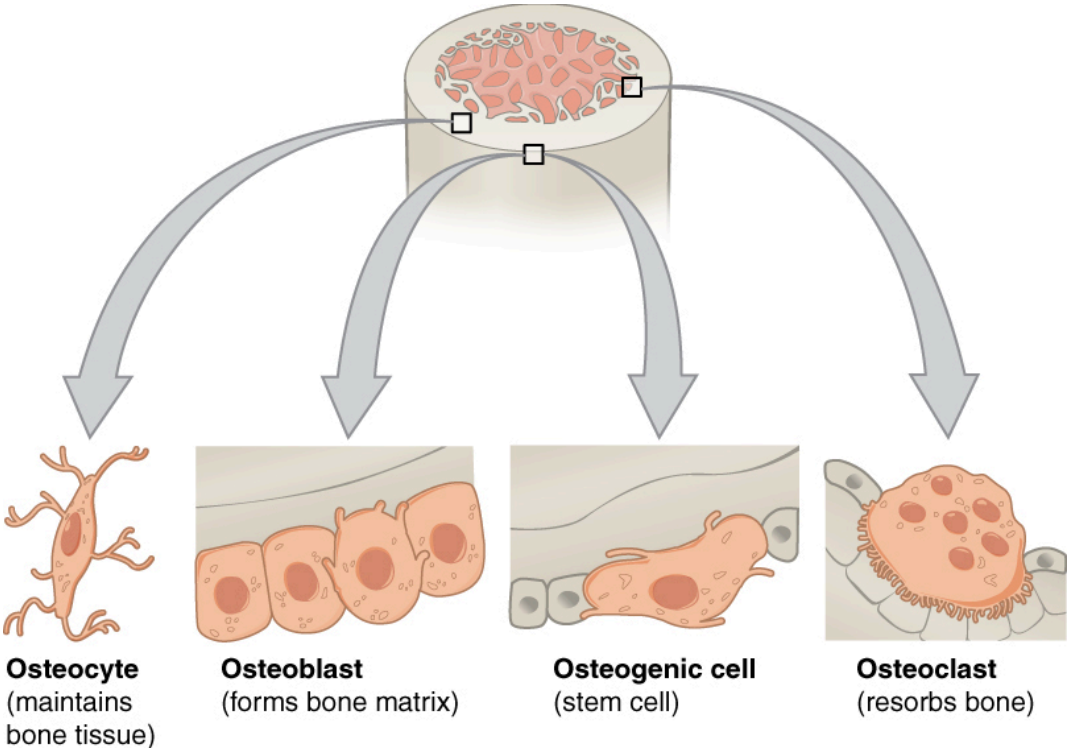


Figure 8. Bone Cells. *Four types of cells are found within bone tissue. Osteogenic cells are undifferentiated and develop into osteoblasts. When osteoblasts get trapped within the calcified matrix, their structure and function changes, and they become osteocytes. Osteoclasts develop from monocytes and macrophages and differ in appearance from other bone cells.*

If osteoblasts and osteocytes are incapable of mitosis, then how are they replenished when old ones die? The answer lies in the properties of a third category of bone cells—the **osteogenic cell**. These osteogenic cells are undifferentiated with high mitotic activity and they are the only bone cells that divide. Immature osteogenic cells are found in the deep layers of the periosteum and the marrow. They differentiate and develop into osteoblasts.

The dynamic nature of bone means that new tissue is constantly formed, and old, injured, or unnecessary bone is dissolved for repair or for calcium release. The cell responsible for bone resorption, or breakdown, is the **osteoclast**. They are found on bone surfaces, are multinucleated, and originate from monocytes and macrophages, two types of white blood cells, not from osteogenic cells. Osteoclasts are continually breaking down old bone while osteoblasts are continually forming new bone. The ongoing balance between osteoblasts and osteoclasts is responsible for the constant but subtle reshaping of bone. Table 2 reviews the bone cells, their functions, and locations.

Table 2: Bone Cells

Cell type	Function	Location
Osteogenic cells	Develop into osteoblasts	Deep layers of the periosteum and the marrow
Osteoblasts	Bone formation	Growing portions of bone, including periosteum and endosteum
Osteocytes	Maintain mineral concentration of matrix	Entrapped in matrix (in lacunae)
Osteoclasts	Bone resorption	Bone surfaces and at sites of old, injured, or unneeded bone

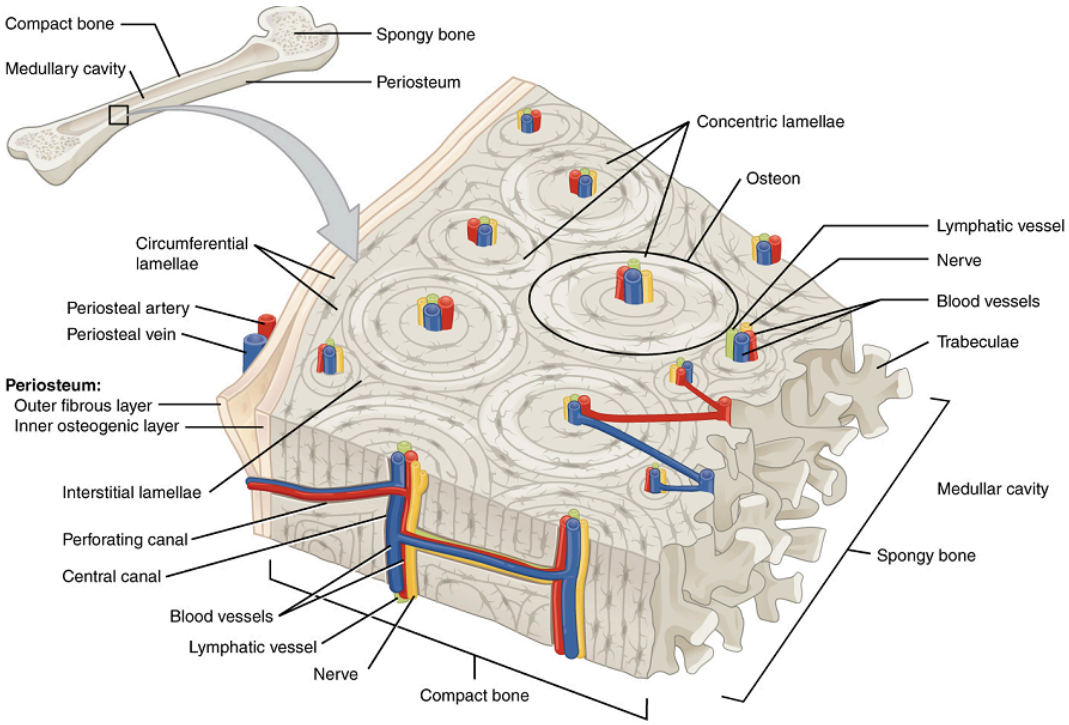
Compact and Spongy Bone: The differences between compact and spongy bone are best explored via their histology. Most bones contain compact and spongy osseous tissue, but their distribution and concentration vary based on the bone's overall function. Compact bone is dense so that it can withstand compressive forces, while spongy (cancellous) bone has open spaces and supports shifts in weight distribution.

1. Compact Bone: Compact bone is the denser, stronger of the two types of bone tissue (Figure 9). It can be found deep to the periosteum and in the diaphyses of long bones, where it provides support and protection.

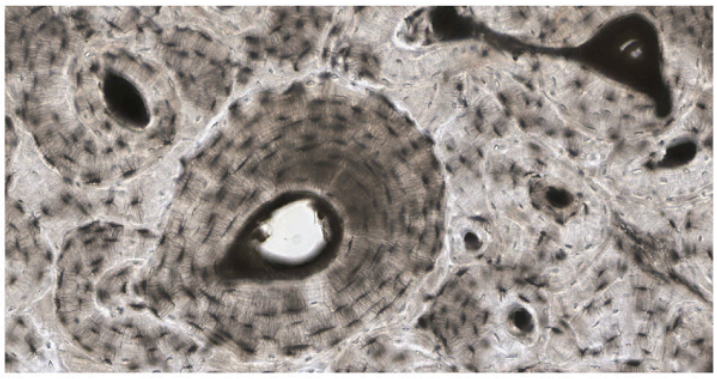
The microscopic structural unit of compact bone is called an **osteon**, or Haversian system. Each osteon is composed of concentric rings of calcified matrix called lamellae (singular = lamella). Running down the center of each osteon is the **central canal**, or Haversian canal, which contains blood vessels, nerves, and lymphatic vessels. These vessels and nerves branch off at right angles through a **perforating canal**, also known as Volkmann's canals, to extend to the periosteum and endosteum.

The osteocytes are located inside spaces called lacunae (singular = lacuna), found at the borders of adjacent lamellae. As described earlier, canaliculi connect with the canaliculi of other lacunae and eventually with the central canal. This system allows nutrients to be transported to the osteocytes and wastes to be removed from them.

2. Spongy (Cancellous) Bone: Like compact bone, **spongy bone,** also known as cancellous bone, contains osteocytes housed in lacunae, but they are not arranged in concentric circles. Instead, the lacunae and osteocytes are found in a lattice-like network of matrix spikes called **trabeculae** (singular = trabecula) (Figure 10). The trabeculae may appear to be a random network, but each trabecula forms along lines of stress to provide strength to the bone. The spaces of the trabeculated network provide balance to the dense and heavy compact bone by making bones lighter so that muscles can move them more easily. In addition, the spaces in some spongy bones contain red marrow, protected by the trabeculae, where hematopoiesis occurs.



(a)



(b)

Figure 9. Compact Bone. *(a) This cross-sectional view of compact bone shows the basic structural unit, the osteon. (b) In this micrograph of the osteon, you can clearly see the concentric lamellae and central canals. LM × 40. (Micrograph provided by the Regents of University of Michigan Medical School © 2012)*

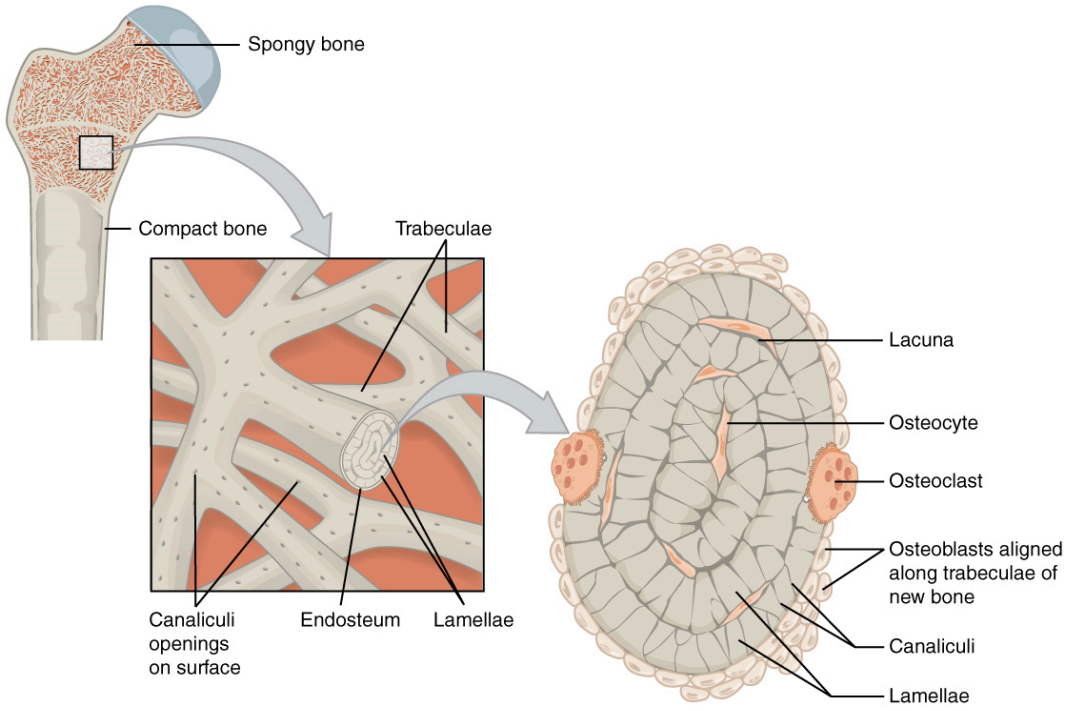


Figure 10. Spongy Bone. *Spongy bone is composed of trabeculae that contain the osteocytes. Red marrow fills the spaces in some bones.*

Blood and Nerve Supply: The spongy bone and medullary cavity receive nourishment from arteries that pass through the compact bone. The arteries enter through the **nutrient foramen** (plural = foramina), a small opening in the diaphysis (Figure 11). The osteocytes in spongy bone are nourished by blood vessels of the periosteum that penetrate spongy bone and blood that circulates in the marrow cavities. As the blood passes through the marrow cavities, it is collected by veins, which then pass out of the bone through the foramen.

In addition to the blood vessels, nerves follow the same paths into the bone where they tend to concentrate in the more metabolically active regions of the bone. The nerves sense pain, and it appears the nerves also play roles in regulating blood supplies and in bone growth, hence their concentrations in metabolically active sites of the bone.

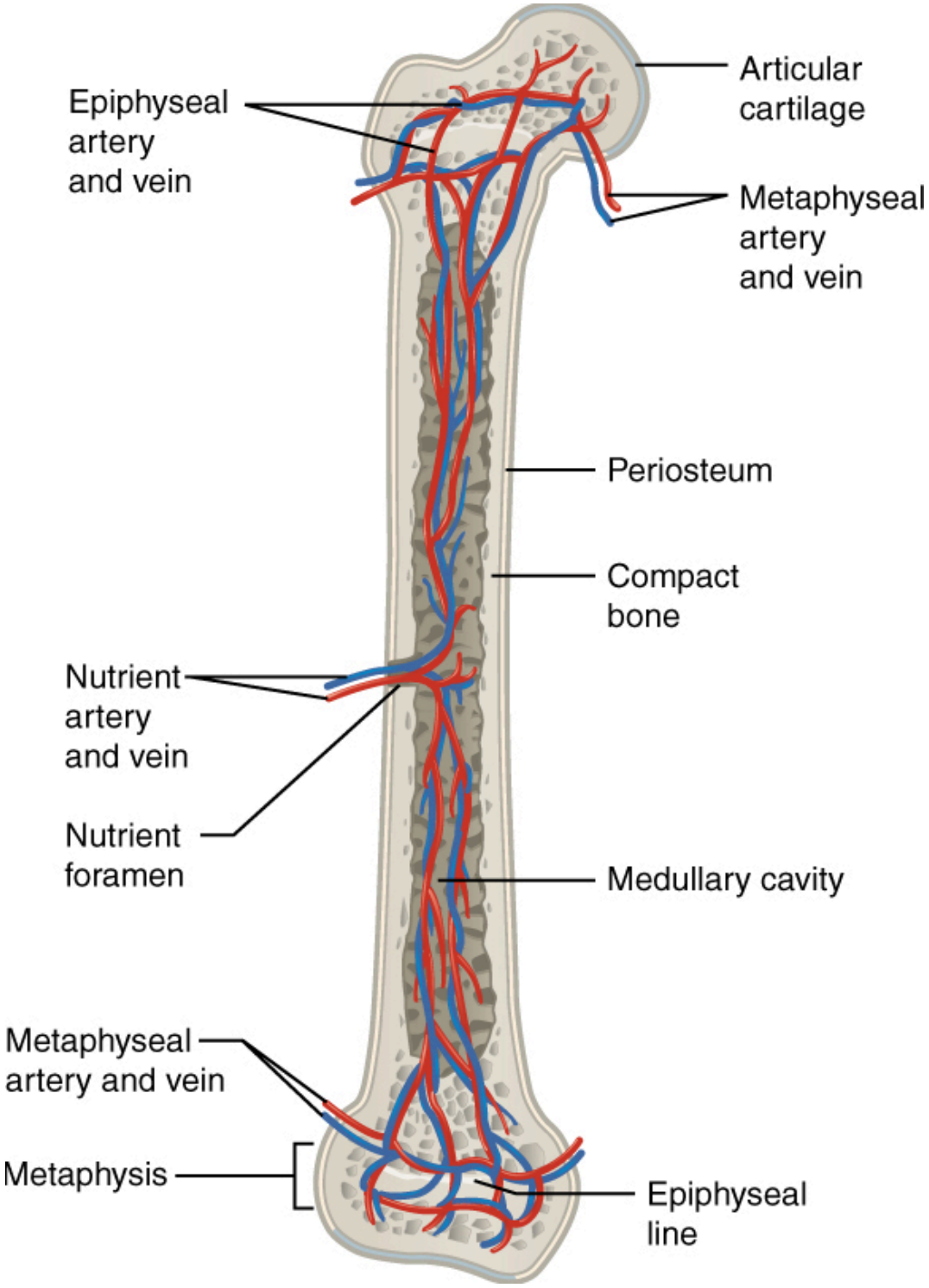


Figure 11. Blood and Nerve Supply to Bone. *Blood vessels and nerves enter the bone through the nutrient foramen.*

Part 4: Bone Formation and Development

In the early stages of embryonic development, the embryo's skeleton consists of fibrous membranes and hyaline cartilage. By the sixth or seventh week of embryonic life, the actual process of bone development, **ossification** (osteogenesis), begins. There are two osteogenic pathways—intramembranous ossification and endochondral ossification—but bone is the same regardless of the pathway that produces it.

Cartilage Templates: Bone is a replacement tissue; that is, it uses a model tissue on which to lay down its mineral matrix. For skeletal development, the most common template is cartilage. During fetal development, a framework is laid down that determines where bones will form. This framework is a flexible, semi-solid cartilage matrix produced by chondroblasts. As the matrix surrounds and isolates chondroblasts, they are called chondrocytes. Unlike most connective tissues, cartilage is avascular, meaning that it has no blood vessels supplying nutrients and removing metabolic wastes. All of these functions are carried on by diffusion through the matrix. This is why damaged cartilage does not repair itself as readily as most tissues do.

Throughout fetal development and into childhood growth and development, bone forms on the cartilaginous matrix. By the time a fetus is born, most of the cartilage has been replaced with bone. Some additional cartilage will be replaced throughout childhood, and some cartilage remains in the adult skeleton.

Intramembranous Ossification: During **intramembranous ossification**, compact and spongy bone develops directly from sheets of mesenchymal (undifferentiated) connective tissue. The flat bones of the face, most of the cranial bones, and the clavicles (collarbones) are initially formed via intramembranous ossification.

The process begins when mesenchymal cells in the embryonic skeleton gather together and begin to differentiate into specialized cells (Figure 12a). Some of these cells will form capillaries, while others will become osteogenic cells and then osteoblasts. Although they will ultimately be spread out by the formation of bone tissue, early osteoblasts appear in a cluster called an **ossification center**.

The osteoblasts secrete **osteoid**, uncalcified matrix, which calcifies (hardens) within a few days as mineral salts are deposited on it, thereby entrapping the osteoblasts within. Once entrapped, the osteoblasts become osteocytes (Figure 12b). As osteoblasts transform into osteocytes, osteogenic cells in the surrounding connective tissue differentiate into new osteoblasts.

Osteoid (unmineralized bone matrix) secreted around the capillaries results in a trabecular matrix, while osteoblasts on the surface of the spongy bone become the periosteum (Figure 12c). The periosteum then creates a protective layer of compact bone superficial to the trabecular bone. The trabecular bone crowds nearby blood vessels, which eventually condense into red marrow (Figure 12d).

Intramembranous ossification begins *in utero* during fetal development and continues on into adolescence. At birth, the skeleton is not fully ossified. Most joints of the skull, for example, are more mobile in an infant than an adult to allow the skull to deform during passage through the birth canal. The flat bones of the cranium continue to grow throughout childhood, ultimately being separated by narrow immobile joints called sutures. Each clavicle also initially (at about 6 weeks of embryonic age) forms by intramembranous ossification from two primary ossification centres that fuse together *in utero* to form a single bone with cartilage at both ends. This cartilage later ossifies to form the mature clavicles with articular cartilage on either end (usually in an individual's early twenties). The last bones to ossify via intramembranous ossification are the flat bones of the face, which reach their adult size at the end of the adolescent growth spurt. The mandible in an infant, for example, consists of two separate bones (left and right), connected by a joint called a symphysis. This mandibular symphysis is fully ossified within the first year of life, permanently fusing the left and right bones to form the mandible.

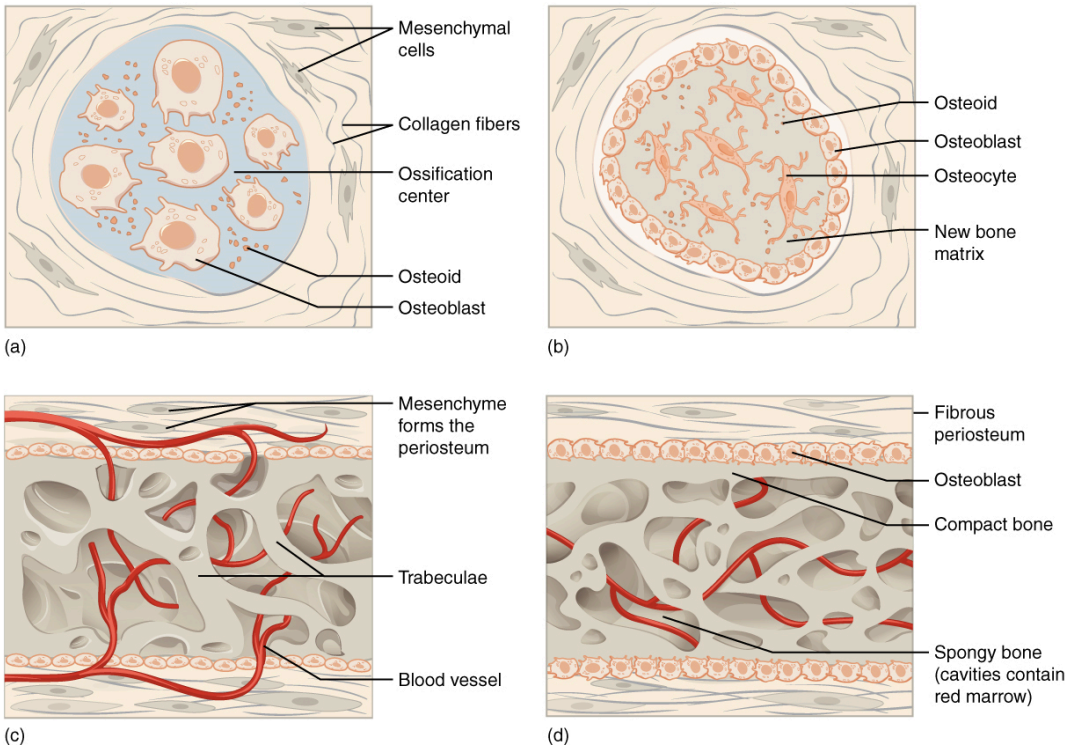


Figure 12. Intramembranous Ossification. *Intramembranous ossification follows four steps. (a) Mesenchymal cells group into clusters, and ossification centers form. (b) Secreted osteoid traps osteoblasts, which then become osteocytes. (c) Trabecular matrix and periosteum form. (d) Compact bone develops superficial to the trabecular bone, and crowded blood vessels condense into red marrow.*

Endochondral Ossification: In **endochondral ossification**, bone develops by replacing hyaline cartilage. Cartilage does not become bone, but instead serves as a template to be completely replaced by new bone. Endochondral ossification takes much longer than intramembranous ossification. Bones at the base of the skull and long bones form via endochondral ossification.

In a long bone, for example, at about 6 to 8 weeks after conception, some of the mesenchymal cells differentiate into chondrocytes (cartilage cells) that form the cartilaginous skeletal precursor of the bones (Figure 13a). Soon after, the **perichondrium**, a membrane that covers the cartilage, appears (Figure 13b).

As more matrix is produced, the chondrocytes in the center of the cartilaginous model grow in size. As the matrix calcifies, nutrients can no longer reach the chondrocytes. This results in their death and the disintegration of the surrounding cartilage. Blood vessels invade the resulting spaces, not only enlarging the cavities but also carrying osteogenic cells with them, many of which will become osteoblasts (Figure 13c). These enlarging spaces eventually combine to become the medullary cavity (Figure 13d).

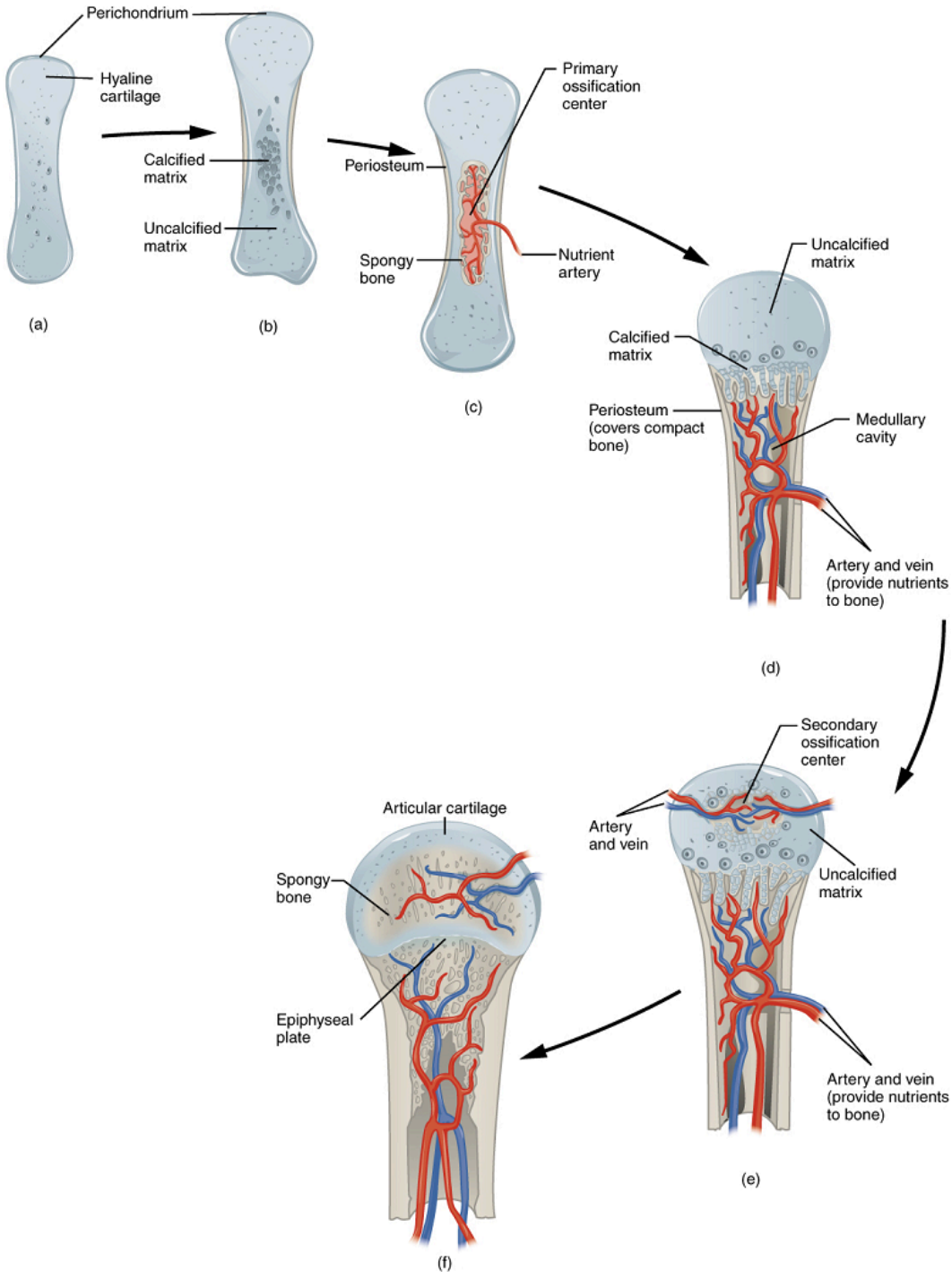


Figure 13. Endochondral Ossification. *Endochondral ossification follows five steps. (a) Mesenchymal cells differentiate into chondrocytes. (b) The cartilage model of the future bony skeleton and the perichondrium form. (c) Capillaries penetrate cartilage. Perichondrium transforms into periosteum. Periosteal collar develops. Primary ossification center develops. (d) Cartilage and chondrocytes continue to grow at ends of the bone. Medullary cavity forms. (e) Secondary ossification centers develop. (f) Cartilage remains at epiphyseal (growth) plate and at joint surface as articular cartilage.*

As the cartilage grows, capillaries penetrate it. This penetration initiates the transformation of the perichondrium into the bone-producing periosteum. Here, the osteoblasts form a periosteal collar of compact bone around the cartilage of the diaphysis. By the second or third month of fetal life, bone cell development and ossification ramps up and creates the **primary ossification center**, a region deep in the periosteal collar where ossification begins (Figure 13c).

While these deep changes are occurring, chondrocytes and cartilage continue to grow at the ends of the bone (the future epiphyses), which increases the bone's length at the same time bone is replacing cartilage

in the diaphyses. By the time the fetal skeleton is fully formed, cartilage only remains at the joint surface as articular cartilage and between the diaphysis and epiphysis as the epiphyseal plate, the latter of which is responsible for the longitudinal growth of bones (Figure 13f). After birth, this same sequence of events (matrix mineralization, death of chondrocytes, invasion of blood vessels from the periosteum, and seeding with osteogenic cells that become osteoblasts) occurs in the epiphyseal regions, and each of these centers of activity is referred to as a **secondary ossification center** (Figure 13e).

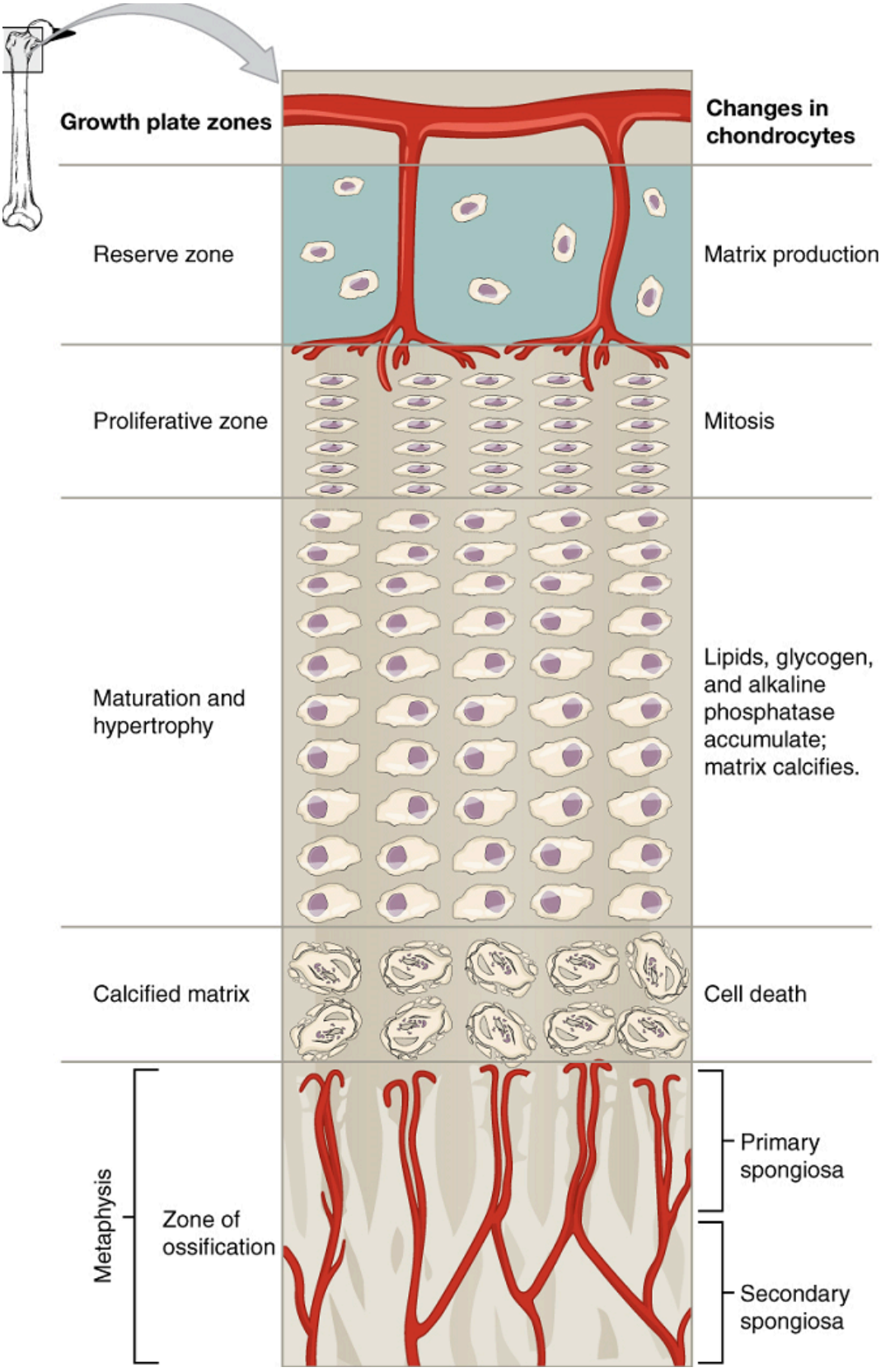


Figure 14. Bone Growth in Length. *The epiphyseal plate is responsible for longitudinal bone growth.*

How Bones Grow in Length: The epiphyseal plate is the area of growth in a long bone. It is a layer of hyaline

cartilage where ossification occurs in immature bones. On the epiphyseal side of the epiphyseal plate, cartilage is formed. On the diaphyseal side, cartilage is ossified, and the diaphysis grows in length. The epiphyseal plate is composed of four zones of cells and activity (Figure 14). The **reserve zone** is the region closest to the epiphyseal end of the plate and contains small chondrocytes within the matrix. These chondrocytes do not participate in bone growth but secure the epiphyseal plate to the osseous tissue of the epiphysis.

The **proliferative zone** is the next layer toward the diaphysis and contains stacks of slightly larger chondrocytes. It makes new chondrocytes (via mitosis) to replace those that die at the diaphyseal end of the plate. Chondrocytes in the next layer, **the zone of maturation and hypertrophy**, are older and larger than those in the proliferative zone. The more mature cells are situated closer to the diaphyseal end of the plate. The longitudinal growth of bone is a result of cellular division in the proliferative zone and the maturation of cells in the zone of maturation and hypertrophy.

Most of the chondrocytes in **the zone of calcified matrix**, the zone closest to the diaphysis, are dead because the matrix around them has calcified. Capillaries and osteoblasts from the diaphysis penetrate this zone, and the osteoblasts secrete bone tissue on the remaining calcified cartilage.

Thus, the zone of calcified matrix connects the epiphyseal plate to the diaphysis. A bone grows in length when osseous tissue is added to the diaphysis.

Bones continue to grow in length until early adulthood. The rate of growth is controlled by hormones, which will be discussed later. When the chondrocytes in the epiphyseal plate cease their proliferation and bone replaces the cartilage, longitudinal growth stops. All that remains of the epiphyseal plate is the now fully ossified epiphyseal line (Figure 15).

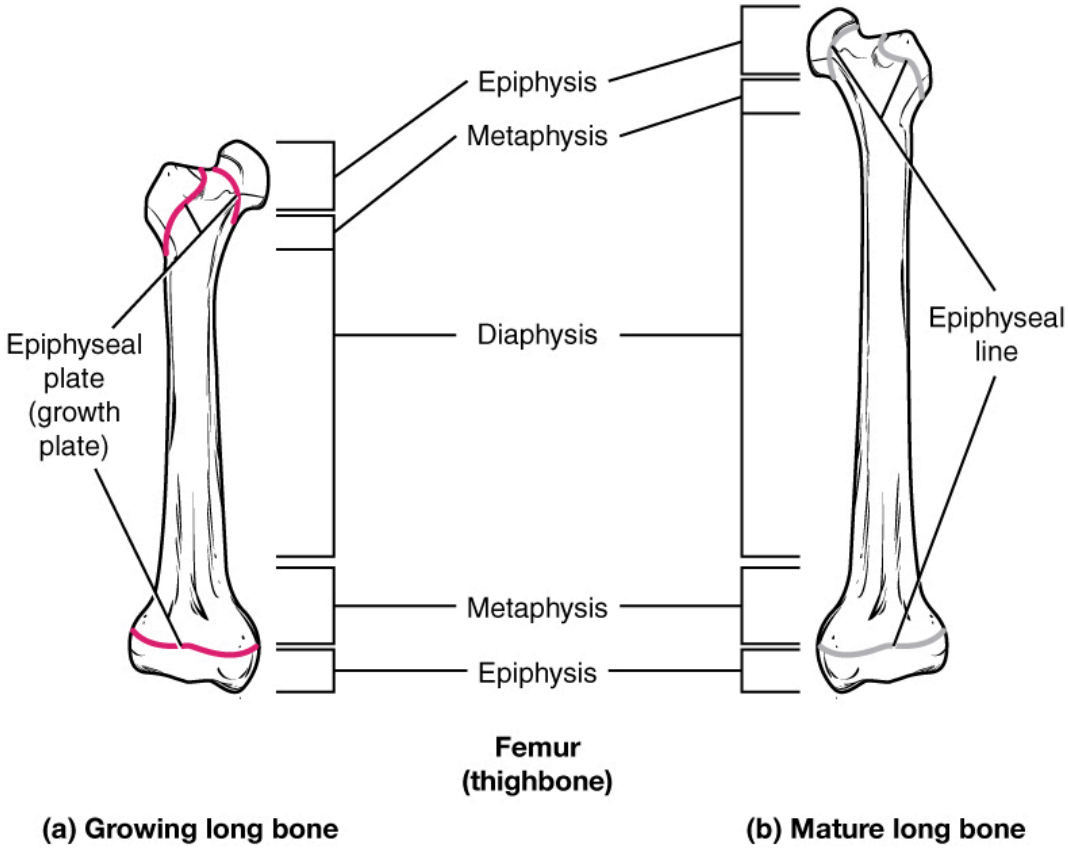


Figure 15. Progression from Epiphyseal Plate to Epiphyseal Line. *As a bone matures, the epiphyseal plate fully ossifies into an epiphyseal line. (a) Epiphyseal plates are visible in a growing bone. (b) Epiphyseal lines are the remnants of epiphyseal plates in a mature bone.*

How Bones Grow in Diameter: While bones are increasing in length, they are also increasing in diameter; growth in diameter can continue even after longitudinal growth ceases. This is called appositional growth.

Osteoclasts resorb old bone that lines the medullary cavity, while osteoblasts, via intramembranous ossification, produce new bone tissue beneath the periosteum. The erosion of old bone along the medullary cavity and the deposition of new bone beneath the periosteum not only increase the diameter of the diaphysis but also increase the diameter of the medullary cavity. This process is called **modeling**.

Bone Remodeling: The process in which matrix is resorbed on one surface of a bone and deposited on another is known as bone modeling. Modeling primarily takes place during a bone's growth. However, in adult life, bone undergoes **remodeling**, in which resorption of old or damaged bone takes place on the same surface where osteoblasts lay new bone to replace that which is resorbed. Injury, exercise, and other activities lead to remodeling. Those influences are discussed later in the unit, but even without injury or exercise, about 5 to 10 percent of the skeleton is remodeled annually just by destroying old bone and renewing it with fresh bone.

Part 5: Fractures

A **fracture** is a broken bone. It will heal whether or not a physician resets it in its anatomical position. If the bone is not reset correctly, the healing process will keep the bone in its deformed position.

Types of Fractures: Fractures are classified by their complexity, location, and other features (Figure 16). Table 3 outlines common types of fractures. Some fractures may be described using more than one term because it may have the features of more than one type (e.g., an open transverse fracture). Of the types pictured in Figure 16 and Table 3, you are only required to understand the details of closed, open, comminuted, and greenstick fractures.

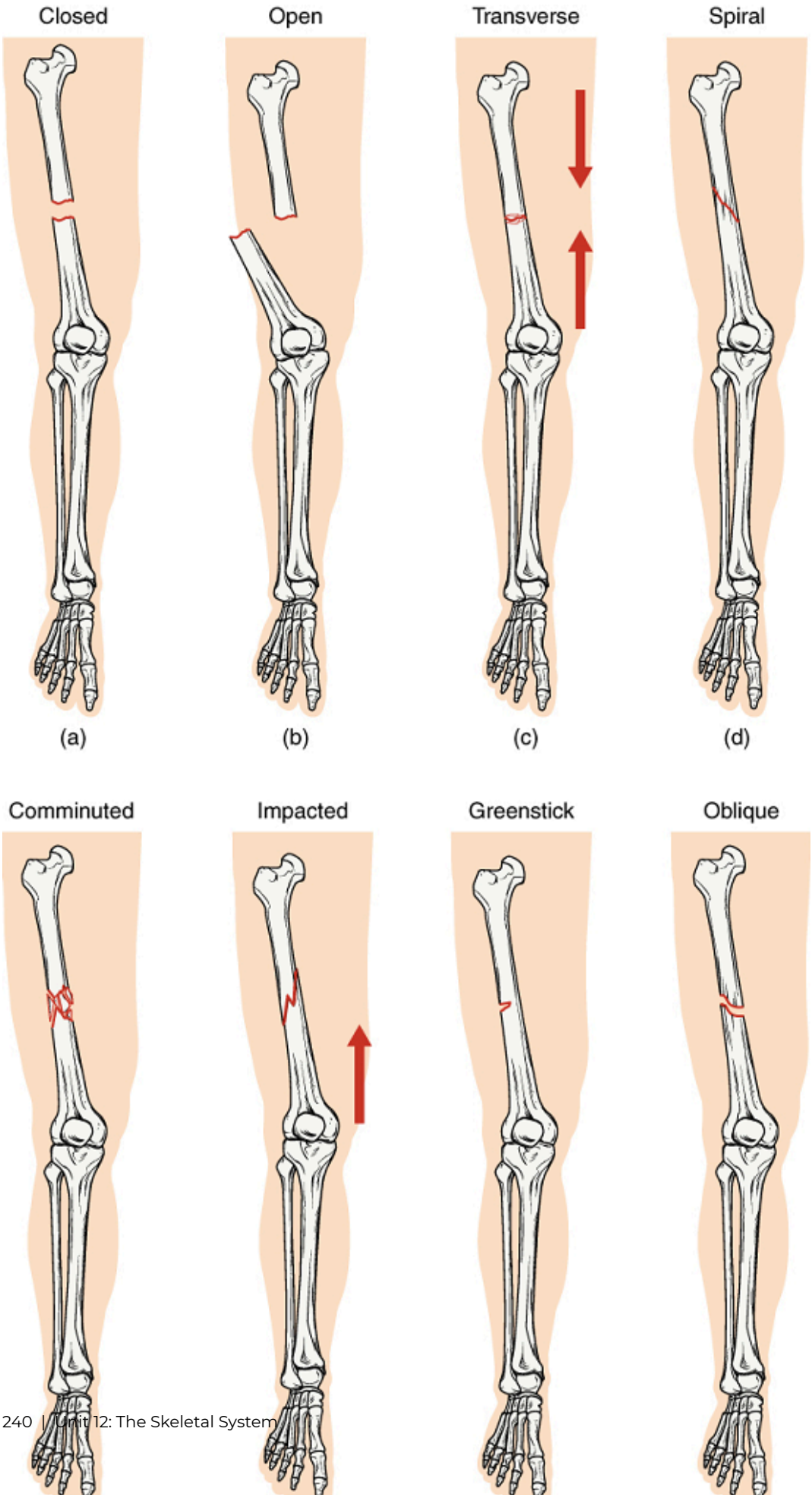


Figure 16. Types of Fractures. *Compare healthy bone with different types of fractures:(a) closed fracture, (b) open fracture, (c) transverse fracture, (d) spiral fracture, (e) comminuted fracture, (f) impacted fracture, (g) greenstick fracture, and (h) oblique fracture.*

Table 3: Types of Fractures

Type of fracture	Description
Transverse	Occurs straight across the long axis of the bone
Oblique	Occurs at an angle that is not 90 degrees
Spiral	Bone segments are pulled apart as a result of a twisting motion
Comminuted	Several breaks result in many small pieces between two large segments
Impacted	One fragment is driven into the other (usually a result of compression)
Greenstick	A partial fracture in which only one side of the bone is broken
Open (compound)	A fracture in which at least one end of the broken bone tears through the skin; carries a high risk of infection
Closed (simple)	A fracture in which the skin remains intact

Divisions of the Skeletal System: The skeletal system includes all of the bones, cartilages, and ligaments of the body that support and give shape to the body and body structures. The **skeleton** consists of the bones of the body. For adults, there are 206 bones in the skeleton. Younger individuals have higher numbers of bones because some bones fuse together during childhood and adolescence to form an adult bone. The skeleton is subdivided into two major divisions – the axial skeleton and the appendicular skeleton.

The Axial Skeleton: The skeleton is subdivided into two major divisions—the axial skeleton and appendicular skeleton. The **axial skeleton** forms the vertical, central axis of the body and includes all bones of the head, neck, chest, and back (Figure 17). It serves to protect the brain, spinal cord, heart, and lungs. It also serves as the attachment site for muscles that move the head, neck, and back, and for muscles that act across the shoulder and hip joints to move their corresponding limbs.

The axial skeleton of the adult consists of 80 bones, including the **skull**, the **vertebral column**, and the **thoracic cage**. The skull is formed by 22 bones. Also associated with the head are an additional seven bones, including the **hyoid bone** and the **ear ossicles** (three small bones found in each middle ear). The vertebral column consists of 24 bones, each called a **vertebra**, plus the **sacrum** and **coccyx**. The thoracic cage includes the 12 pairs of **ribs**, and the **sternum**, the flattened bone of the anterior chest.

The Appendicular Skeleton: The appendicular skeleton includes all bones of the upper and lower limbs, plus the bones that attach each limb to the axial skeleton (Figure 17). There are 126 bones in the appendicular skeleton of an adult. The bones of the appendicular skeleton are covered later in the unit.

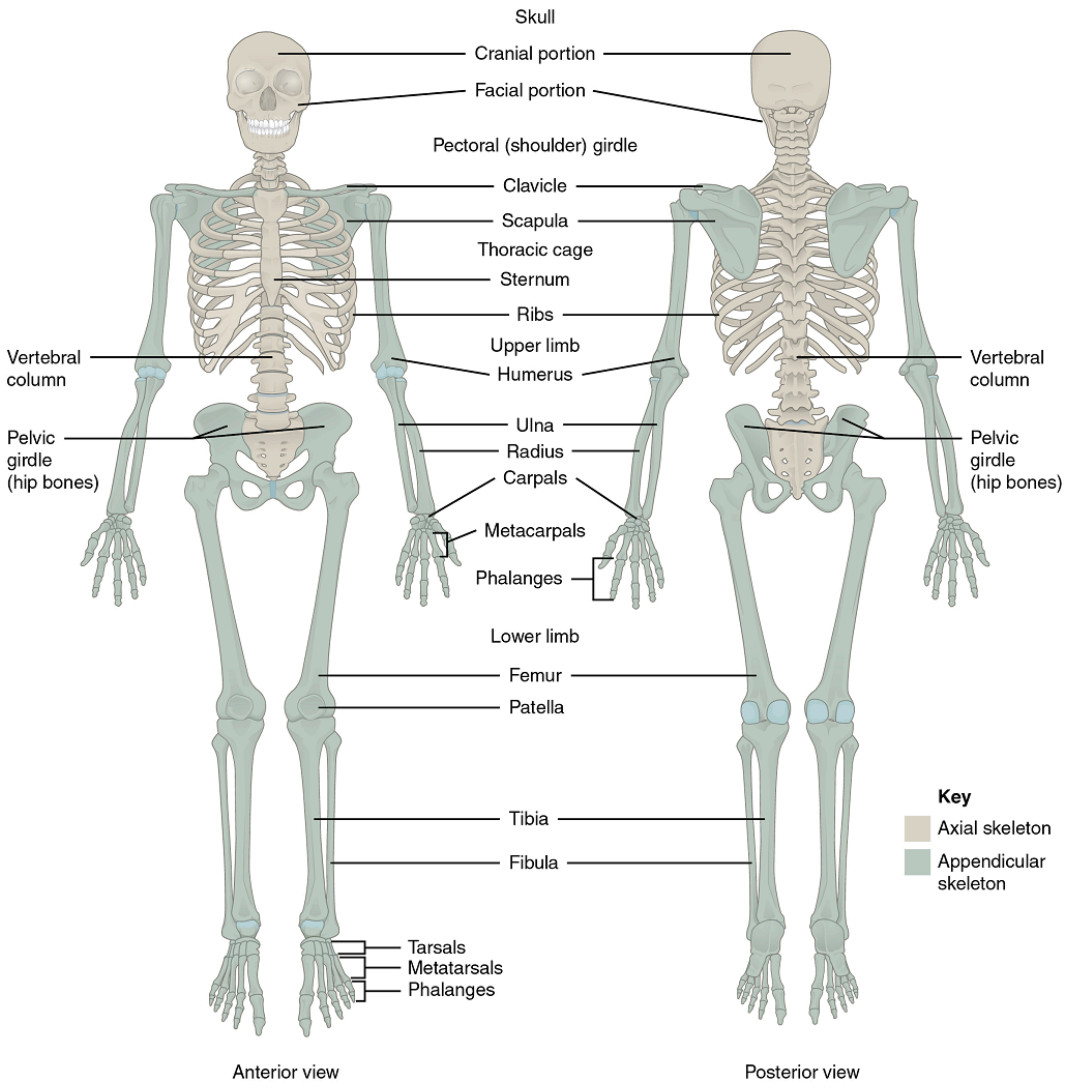


Figure 17. Axial and Appendicular Skeleton. *The axial skeleton supports the head, neck, back, and chest and thus forms the vertical axis of the body. It consists of the skull, vertebral column (including the sacrum and coccyx), and the thoracic cage, formed by the ribs and sternum. The appendicular skeleton is made up of all bones of the upper and lower limbs.*

The Axial Skeleton

Part 1: The Skull

The **cranium** (skull) is the skeletal structure of the head that supports the face and protects the brain. It is subdivided into the **facial bones** and the **brain case**, or cranial vault (Figure 19). The facial bones underlie the facial structures, form the nasal cavity, enclose the eyeballs, and support the teeth of the upper and lower jaws. The rounded brain case surrounds and protects the brain and houses the middle and inner ear structures.

In the adult, the skull consists of 22 individual bones, 21 of which are immobile and united into a single unit. The 22nd bone is the **mandible** (lower jaw), which is the only moveable bone of the skull.

Development of the Skull: As the brain case bones grow in the fetal skull, they remain separated from each other by large areas of dense connective tissue, each of which is called a fontanelle (Figure 18). The fontanelles are the soft spots on an infant's head. They are important during birth because these areas allow the skull to change shape as it squeezes through the birth canal. After birth, the fontanelles allow for continued growth and expansion of the skull as the brain enlarges. The largest fontanelle is located on the anterior head, at the junction of the frontal and parietal bones. The fontanelles decrease in size and disappear by age 2. However, the skull bones remained separated from each other at the sutures, which contain dense fibrous connective tissue that unites the adjacent bones. The connective tissue of the sutures allows for continued growth of the

skull bones as the brain enlarges during childhood growth. This structure also means that, although the size of the cranium increases from birth to adulthood, proportionately it does so less than other parts of the skeleton; the relative size of the cranium in proportion to the rest of the body therefore decreases with age from birth to adulthood.

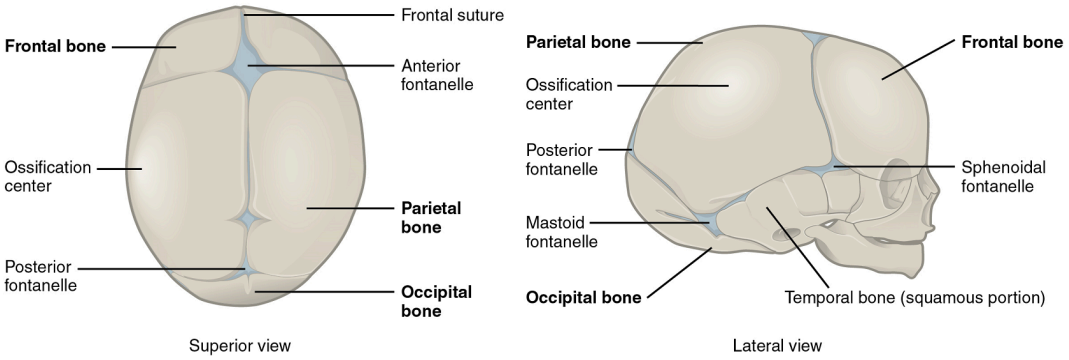


Figure 18. Newborn Skull. *The bones of the newborn skull are not fully ossified and are separated by large areas called fontanelles, which are filled with fibrous connective tissue. The fontanelles allow for continued growth of the skull after birth. At the time of birth, the facial bones are small and underdeveloped, and the mastoid process has not yet formed.*

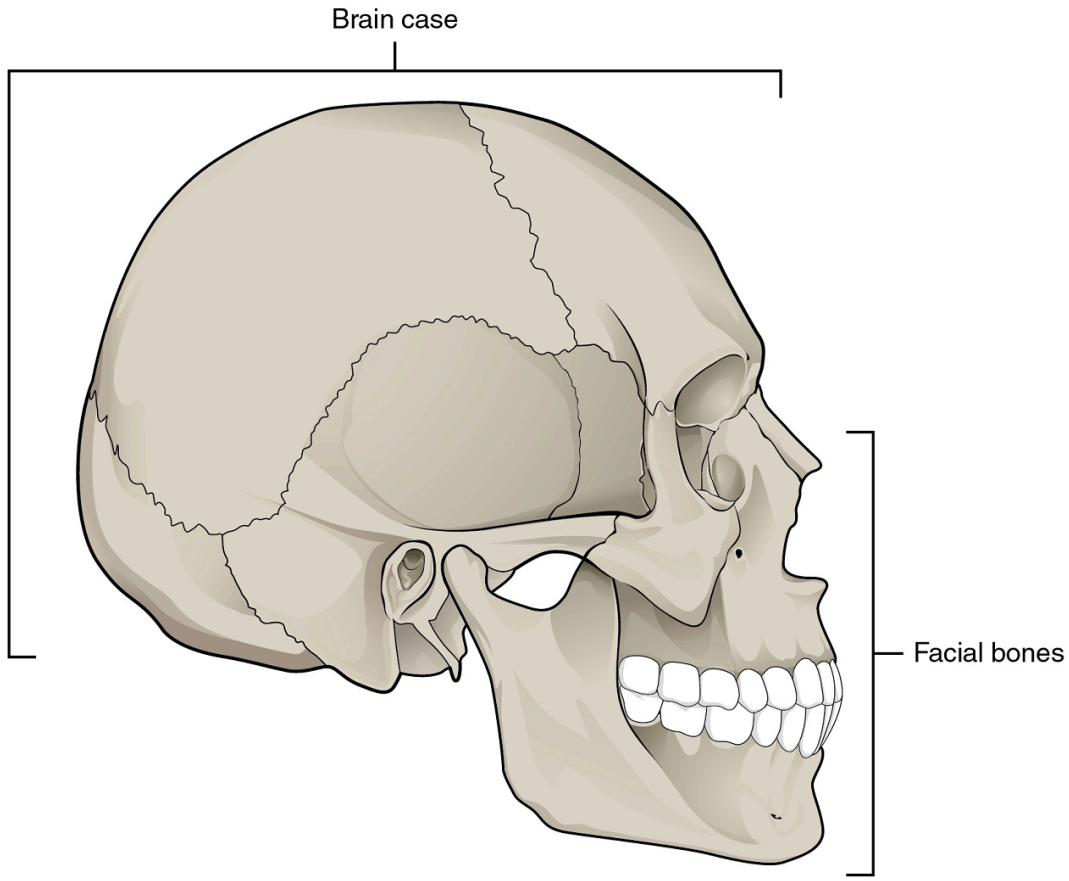


Figure 19. Parts of the Skull. *The skull consists of the rounded brain case that houses the brain and the facial bones that form the upper and lower jaws, nose, orbits, and other facial structures.*

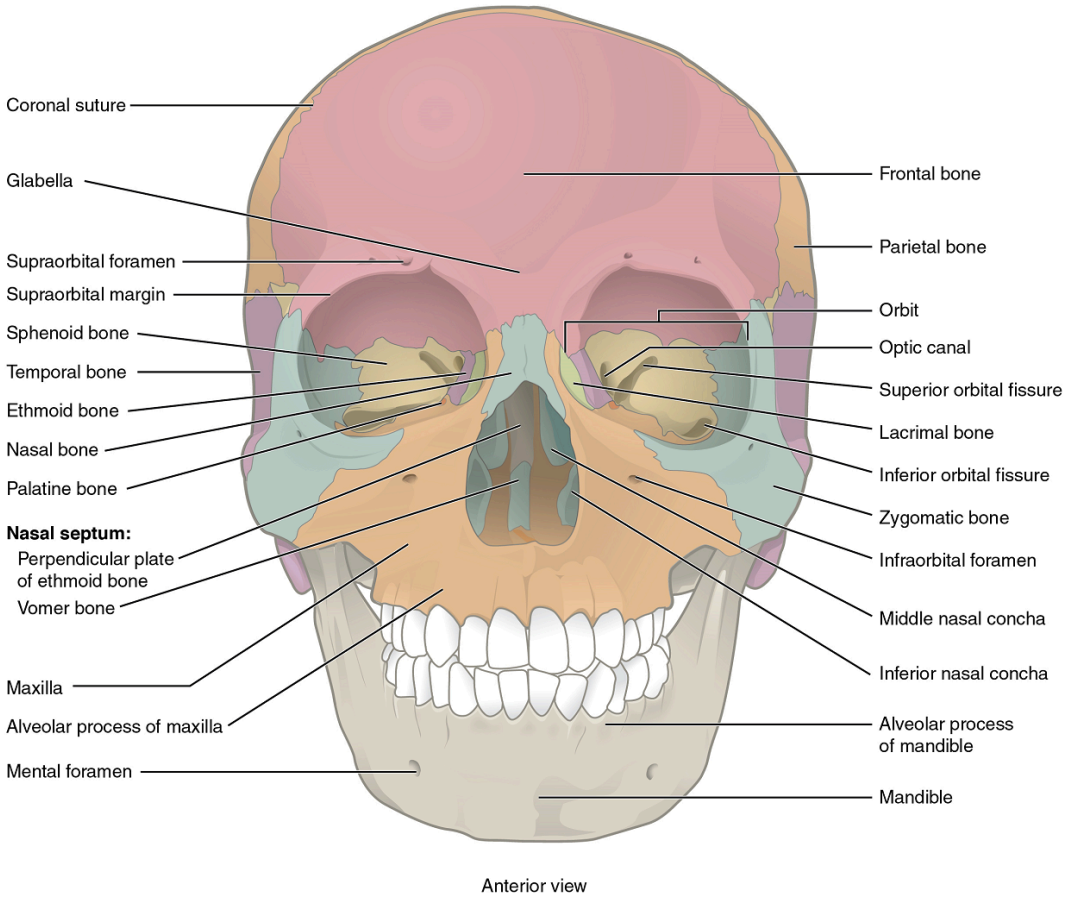


Figure 20. Anterior View of Skull. *An anterior view of the skull shows the bones that form the forehead, orbits (eye sockets), nasal cavity, nasal septum, and upper and lower jaws.*

Bones of the Brain Case: The brain case contains and protects the brain (Figure 19). The interior space that is almost completely occupied by the brain is called the **cranial cavity**.

The brain case consists of eight bones (Figures 20 & 21). These include the paired parietal and temporal bones, plus the unpaired frontal, occipital, sphenoid, and ethmoid bones. For our purposes, we will not be specifying the details of the sphenoid and ethmoid bones.

1. Parietal Bone: The **parietal bone** forms most of the upper lateral side of the skull (Figures 21 & 22). These are paired bones, with the right and left parietal bones joining together at the top of the skull. Each parietal bone is also bounded anteriorly by the frontal bone, inferiorly by the temporal bone, and posteriorly by the occipital bone.

2. Temporal Bone: The **temporal bone** forms the lower lateral side of the skull (Figure 21). Common wisdom has it that the temporal bone (temporal = “time”) is so named because this area of the head (the temple) is where hair typically first turns gray, indicating the passage of time.

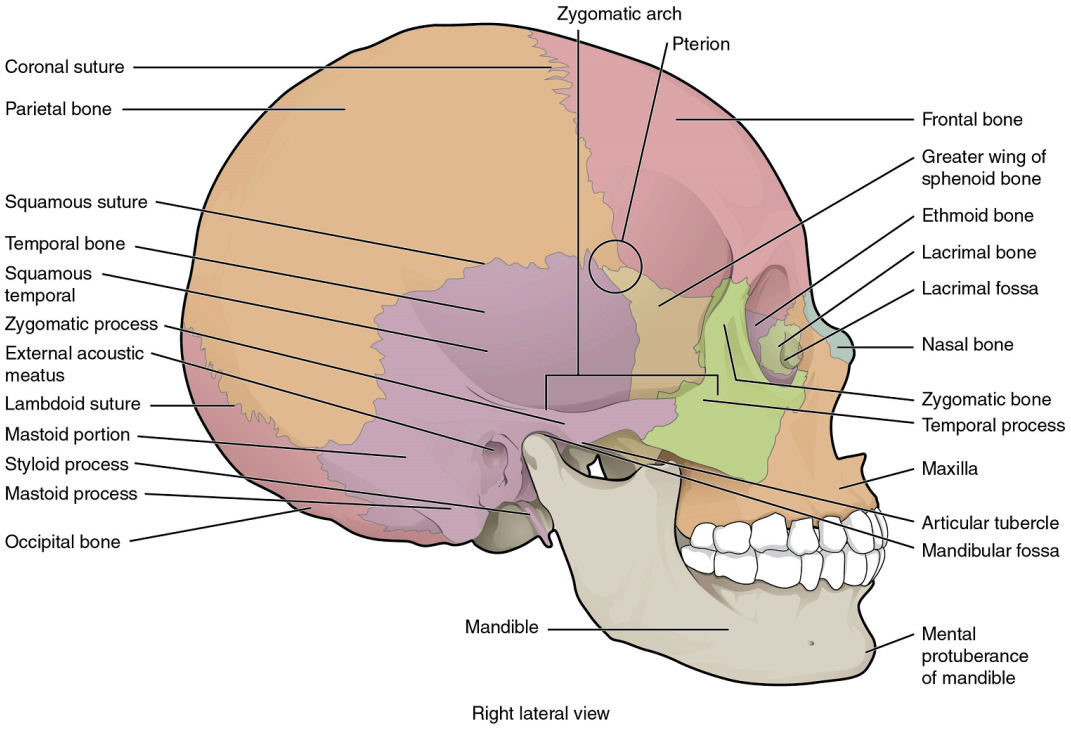


Figure 21. Lateral View of Skull. *The lateral skull shows the large rounded brain case, zygomatic arch, and the upper and lower jaws. The zygomatic arch is formed jointly by the zygomatic process of the temporal bone and the temporal process of the zygomatic bone. The shallow space above the zygomatic arch is the temporal fossa. The space inferior to the zygomatic arch and deep to the posterior mandible is the infratemporal fossa.*

3. Frontal Bone: The frontal bone is the single bone that forms the forehead (Figure 20).

4. Occipital Bone: The **occipital bone** is the single bone that forms the posterior skull and posterior base of the cranial cavity (Figures 21 & 22). On its outside surface, at the posterior midline, is a small protrusion called the **external occipital protuberance**, which serves as an attachment site for a ligament of the posterior neck.

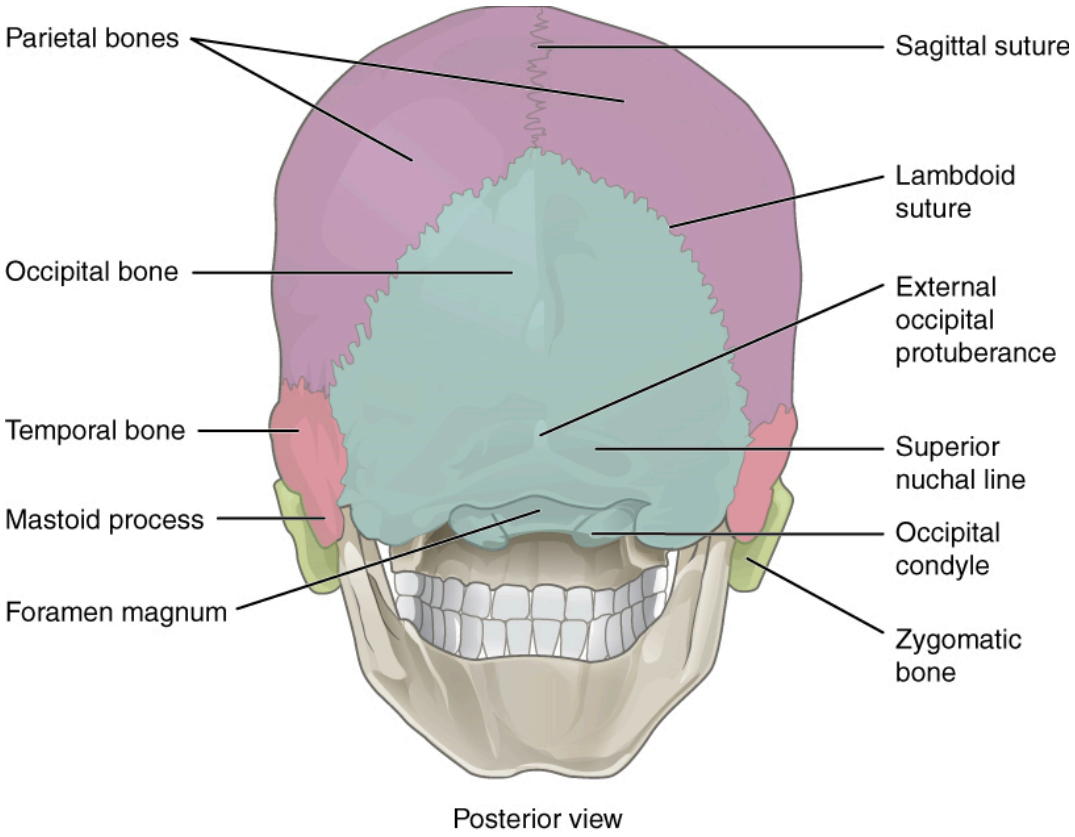


Figure 22. Posterior View of Skull. *This view of the posterior skull shows attachment sites for muscles and joints that support the skull.*

Facial Bones of the Skull: The facial bones of the skull form the upper and lower jaws, the nose, nasal cavity and nasal septum, and the orbit. The facial bones include 14 bones, with six paired bones and two unpaired bones (Figures 20 & 21). We will focus on the maxillary bones and the mandible bone.

1. Maxillary Bone: The **maxillary bone**, often referred to simply as the maxilla (plural = maxillae), is one of a pair that together form the upper jaw, much of the hard palate, the medial floor of the orbit, and the lateral base of the nose (Figures 20 & 21).

2. Mandible: The **mandible** forms the lower jaw and is the only moveable bone of the skull. At the time of birth, the mandible consists of paired right and left bones, but these fuse together during the first year to form the single U-shaped mandible of the adult skull (Figures 20 & 21).

The Bones of the Middle Ear: Three small bones (ossicles) are found on either side of the head in the middle ear. These are the malleus, incus, and stapes, and they function in transferring the vibrations from the eardrum to the inner ear.

The Hyoid Bone: The hyoid bone is an independent bone that does not contact any other bone and thus is not part of the skull (Figure 23). It is a small U-shaped bone located in the upper neck near the level of the inferior mandible, with the tips of the "U" pointing posteriorly. The hyoid serves as the base for the tongue above and is attached to the larynx below and the pharynx posteriorly. The hyoid is held in position by a series of small muscles that attach to it either from above or below. These muscles act to move the hyoid up/down or forward/back. Movements of the hyoid are coordinated with movements of the tongue, larynx, and pharynx during swallowing and speaking.

Part 2: The Vertebral Column

The vertebral column is also known as the spinal column or spine (Figure 24). It consists of a sequence of vertebrae (singular = vertebra), each of which is separated and united by an **intervertebral disc**. Together, the vertebrae and intervertebral discs form the vertebral column. It is a flexible column that supports the head,

neck, and body and allows for their movements. It also protects the spinal cord, which passes down the back through openings in the vertebra.

Regions of the Vertebral Column: The vertebral column originally develops as a series of 33 vertebrae, but this number is eventually reduced to 24 vertebrae, plus the sacrum and coccyx. The vertebral column is subdivided into five regions, with the vertebrae in each area named for that region and numbered in descending order. In the neck, there are seven cervical vertebrae, each designated with the letter "C" followed by its number. Superiorly, the C1 vertebra articulates (forms a joint) with the occipital condyles of the skull. Inferiorly, C1 articulates with the C2 vertebra, and so on. Below these are the 12 thoracic vertebrae, designated T1–T12. The lower back contains the L1–L5 lumbar vertebrae. The single sacrum, which is also part of the pelvis, is formed by the fusion of five sacral vertebrae. Similarly, the coccyx, or tailbone, results from the fusion of four small coccygeal vertebrae. However, the sacral and coccygeal fusions do not start until age 20 and are not completed until middle age.

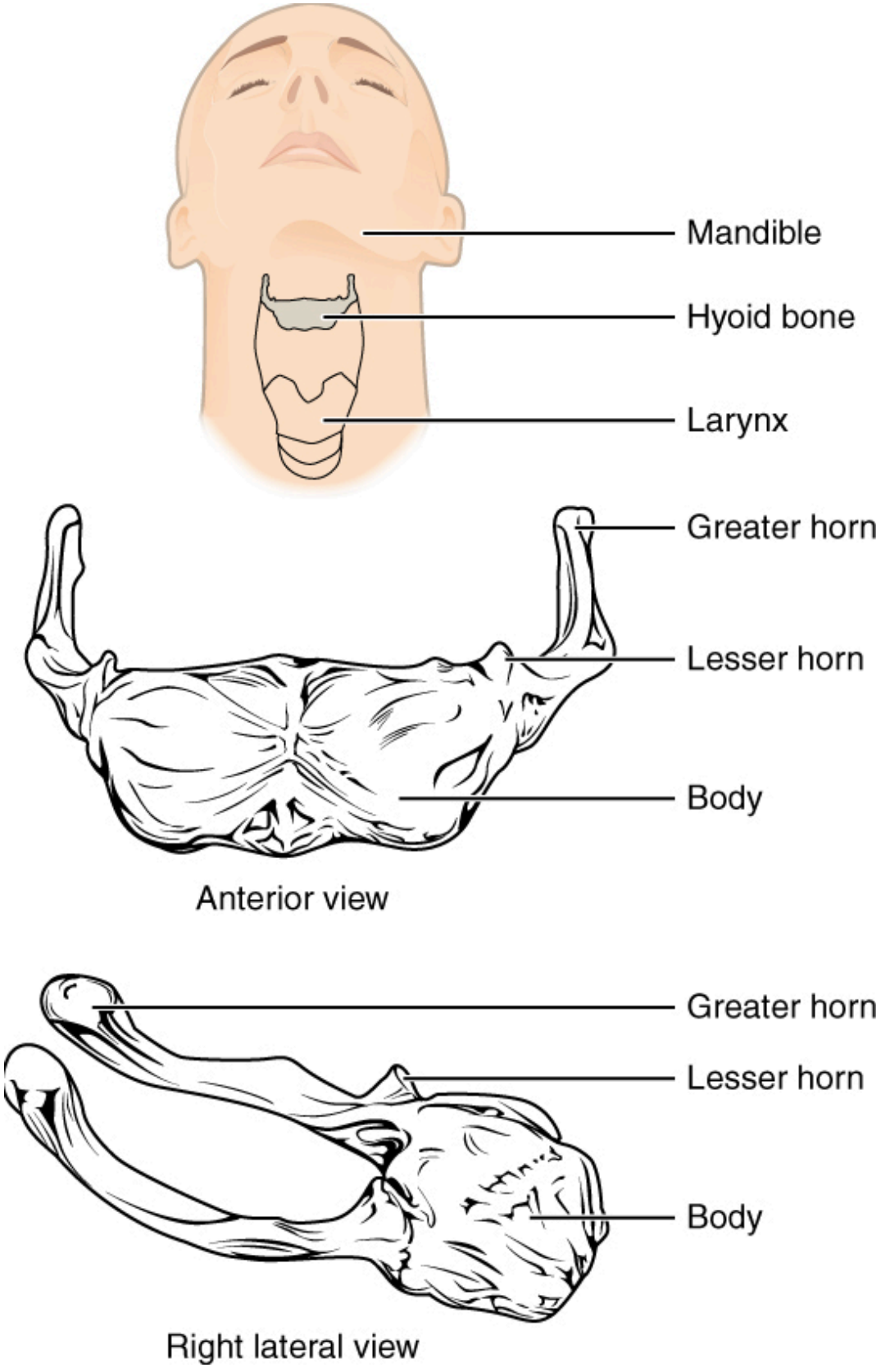


Figure 23. Hyoid Bone. *The hyoid bone is located in the upper neck and does not join with any other bone. It provides attachments for muscles that act on the tongue, larynx, and pharynx.*

Curvatures of the Vertebral Column: The adult vertebral column does not form a straight line, but instead has four curvatures along its length (see Figure 24). These curves increase the vertebral column's strength, flexibility, and ability to absorb shock.

During fetal development, the body is flexed anteriorly into the fetal position, giving the entire vertebral column a single curvature that is concave anteriorly. In the adult, this fetal curvature is retained in two regions of the vertebral column as the **thoracic curve**, which involves the thoracic vertebrae, and the **sacrococcygeal curve**, formed by the sacrum and coccyx.

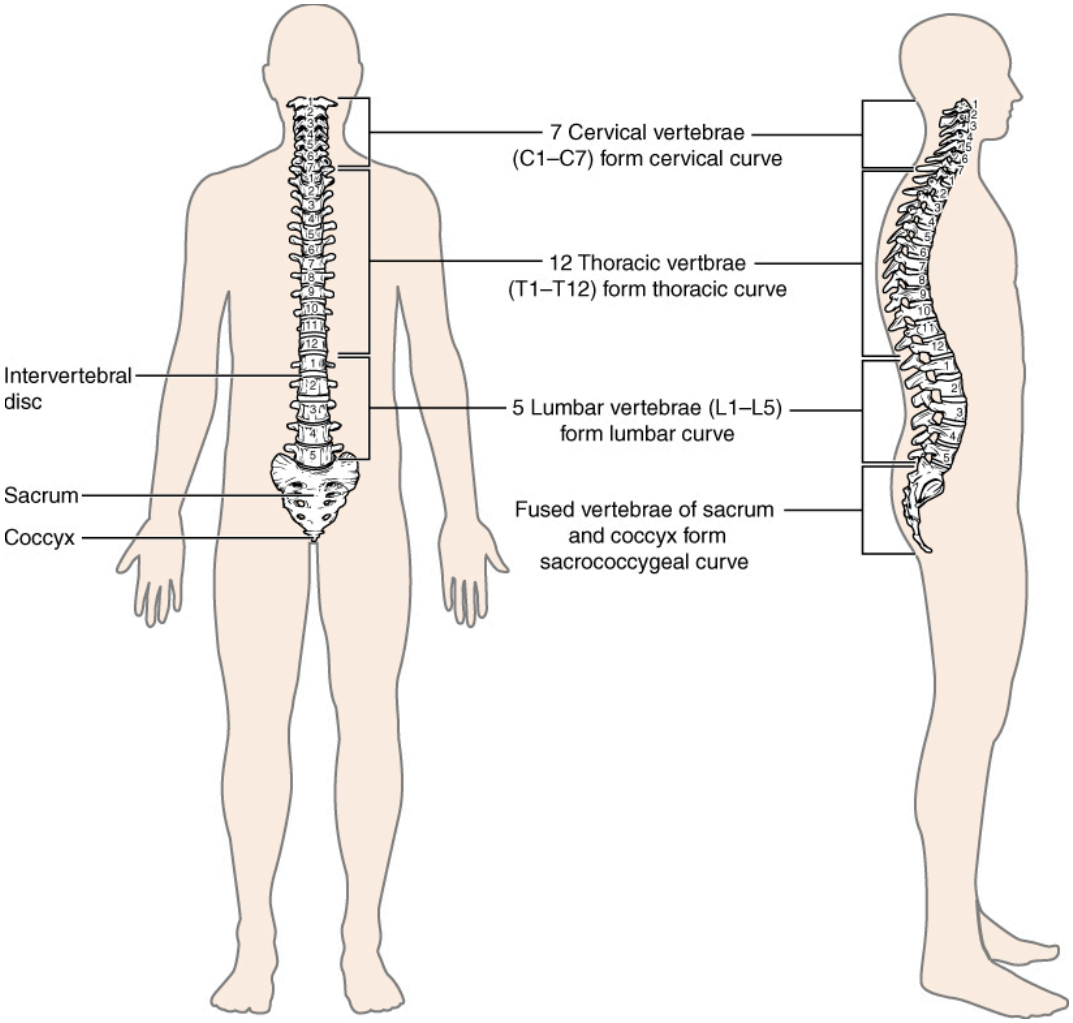


Figure 24. Vertebral Column. *The adult vertebral column consists of 24 vertebrae, plus the sacrum and coccyx. The vertebrae are divided into three regions: cervical C1–C7 vertebrae, thoracic T1–T12 vertebrae, and lumbar L1–L5 vertebrae. The vertebral column is curved, with two primary curvatures (thoracic and sacrococcygeal curves) and two secondary curvatures (cervical and lumbar curves).*

General Structure of a Vertebra: Within the different regions of the vertebral column, vertebrae vary in size and shape, but they all follow a similar structural pattern. A typical vertebra will consist of a body, a vertebral arch, and seven processes (Figure 25).

The **body** is the anterior portion of each vertebra and is the part that supports the body weight. Because of this, the vertebral bodies progressively increase in size and thickness going down the vertebral column. The bodies of adjacent vertebrae are separated and strongly united by an intervertebral disc.

The **vertebral arch** forms the posterior portion of each vertebra.

The large opening between the vertebral arch and body is the **vertebral foramen**, which contains the spinal cord. In the intact vertebral column, the vertebral foramina of all of the vertebrae align to form the **vertebral (spinal) canal**, which serves as the bony protection and passageway for the spinal cord down the back. When

the vertebrae are aligned together in the vertebral column, notches in the margins of the pedicles of adjacent vertebrae together form an **intervertebral foramen**, the opening through which a spinal nerve exits from the vertebral column (Figure 26).

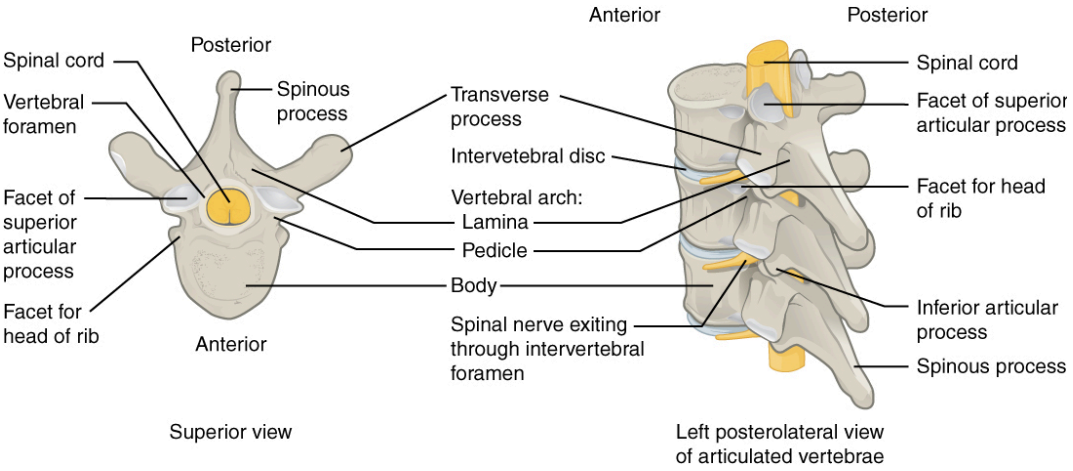


Figure 25. Parts of a Typical Vertebra. *A typical vertebra consists of a body and a vertebral arch. The arch is formed by the paired pedicles and paired laminae. Arising from the vertebral arch are the transverse, spinous, superior articular, and inferior articular processes. The vertebral foramen provides for passage of the spinal cord. Each spinal nerve exits through an intervertebral foramen, located between adjacent vertebrae. Intervertebral discs unite the bodies of adjacent vertebra*

Seven processes arise from the vertebral arch. Each paired transverse process projects laterally and arises from the junction point between the pedicle and lamina. The single **spinous process** (vertebral spine) projects posteriorly at the midline of the back. The vertebral spines can easily be felt as a series of bumps just under the skin down the middle of the back. The transverse and spinous processes serve as important muscle attachment sites. A **superior articular process** extends or faces upward, and an **inferior articular process** faces or projects downward on each side of a vertebrae. The paired superior articular processes of one vertebra join with the corresponding paired inferior articular processes from the next higher vertebra. These junctions form slightly moveable joints between the adjacent vertebrae. The shape and orientation of the articular processes vary in different regions of the vertebral column and play a major role in determining the type and range of motion available in each region.

Regional Modifications of Vertebrae: In addition to the general characteristics of a typical vertebra described above, vertebrae also display characteristic size and structural features that vary between the different vertebral column regions. Thus, cervical vertebrae are smaller than lumbar vertebrae due to differences in the proportion of body weight that each will support. Thoracic vertebrae have sites for rib attachment, and the vertebrae that give rise to the sacrum and coccyx have fused together into single bones. We will focus on the anatomically distinct natures of the first two cervical vertebrae, the atlas and the axis.

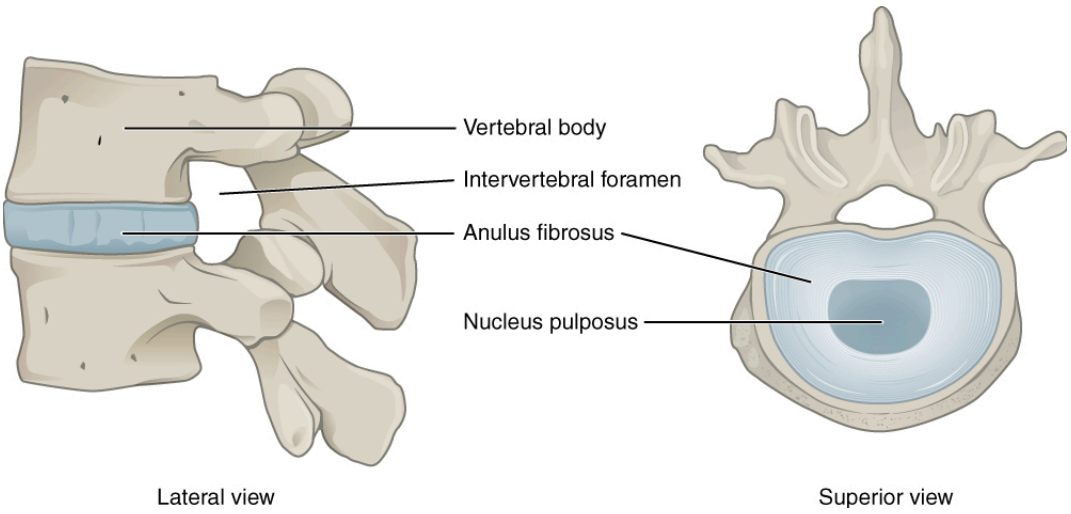


Figure 26. Intervertebral Disc. *The bodies of adjacent vertebrae are separated and united by an intervertebral disc, which provides padding and allows for movements between adjacent vertebrae. The disc consists of a fibrous outer layer called the anulus fibrosus and a gel-like center called the nucleus pulposus. The intervertebral foramen is the opening formed between adjacent vertebrae for the exit of a spinal nerve.*

Cervical Vertebrae: Typical **cervical vertebrae**, such as C4 or C5, have several characteristic features that differentiate them from thoracic or lumbar vertebrae (Figure 27). Cervical vertebrae have a small body, reflecting the fact that they carry the least amount of body weight. Cervical vertebrae usually have a bifid (Y-shaped) spinous process. The transverse processes of the cervical vertebrae are sharply curved (U-shaped) to allow for passage of the cervical spinal nerves. Each transverse process also has an opening called the **transverse foramen**.

The first and second cervical vertebrae are further modified, giving each a distinctive appearance. The first cervical (C1) vertebra is also called the **atlas**, because this is the vertebra that supports the skull on top of the vertebral column (in Greek mythology, Atlas was the god who supported the heavens on his shoulders). The C1 vertebra does not have a body or spinous process. Instead, it is ring-shaped, consisting of an **anterior arch** and a **posterior arch**. The transverse processes of the atlas are longer and extend more laterally than do the transverse processes of any other cervical vertebrae. The superior articular processes face upward and are deeply curved for articulation with the occipital condyles on the base of the skull. The inferior articular processes are flat and face downward to join with the superior articular processes of the C2 vertebra.

The second cervical (C2) vertebra is called the **axis**, because it serves as the axis for rotation when turning the head toward the right or left. The axis resembles typical cervical vertebrae in most respects but is easily distinguished by the **dens** (odontoid process), a bony projection that extends upward from the vertebral body. The dens joins with the inner aspect of the anterior arch of the atlas, where it is held in place by transverse ligament.

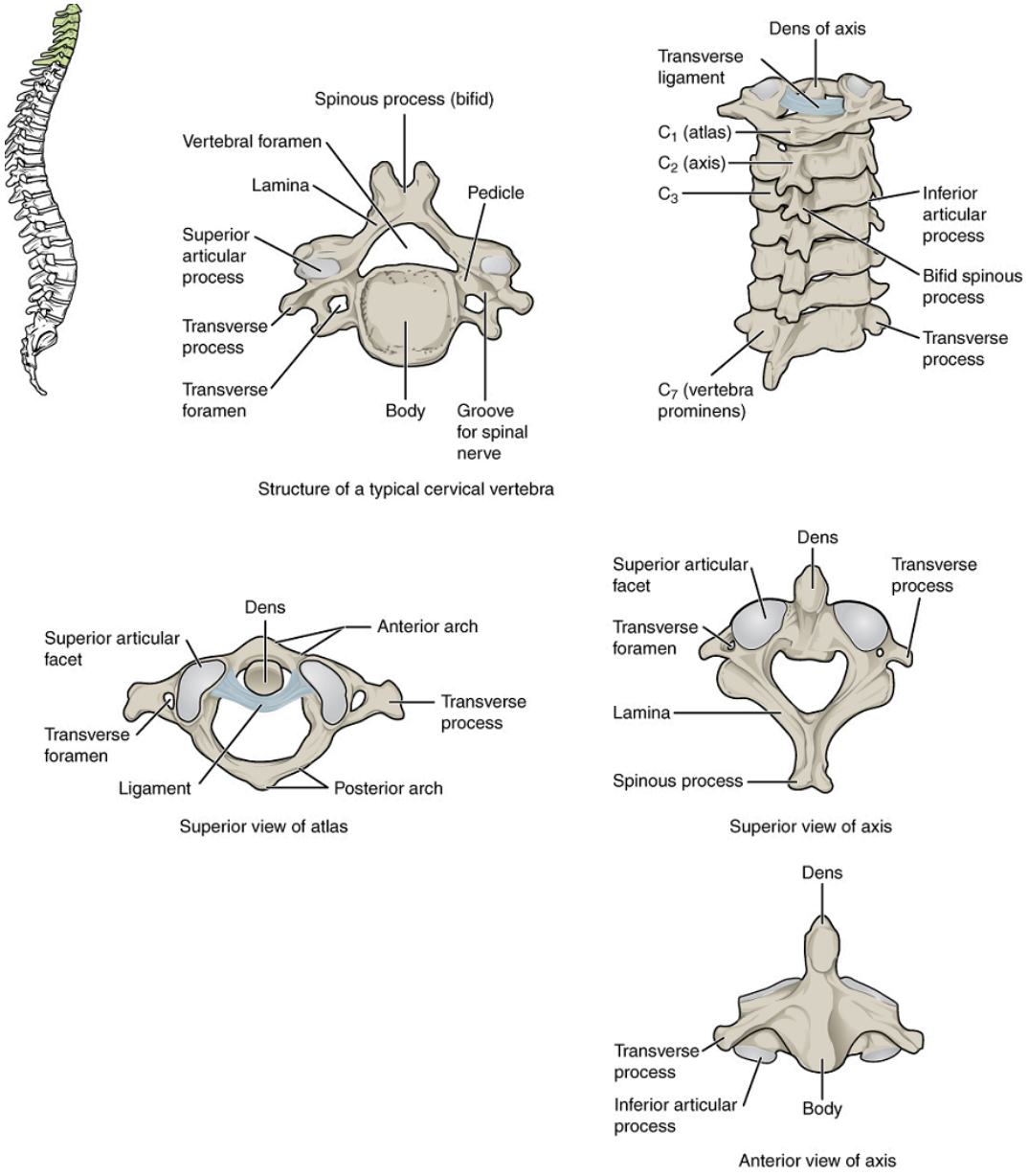


Figure 27. Cervical Vertebrae. *A typical cervical vertebra has a small body, a bifid spinous process, transverse processes that have a transverse foramen and are curved for spinal nerve passage. The atlas (C1 vertebra) does not have a body or spinous process. It consists of an anterior and a posterior arch and elongated transverse processes. The axis (C2 vertebra) has the upward projecting dens, which articulates with the anterior arch of the atlas.*

Part 3: The Thoracic Cage

The thoracic cage (rib cage) forms the thorax (chest) portion of the body. It consists of the 12 pairs of ribs with their costal cartilages and the sternum (Figure 28). The ribs are anchored posteriorly to the 12 thoracic vertebrae (T1–T12). The thoracic cage protects the heart and lungs.

Sternum: The sternum is the elongated bony structure that anchors the anterior thoracic cage. It consists of three parts: the manubrium, body, and xiphoid process.

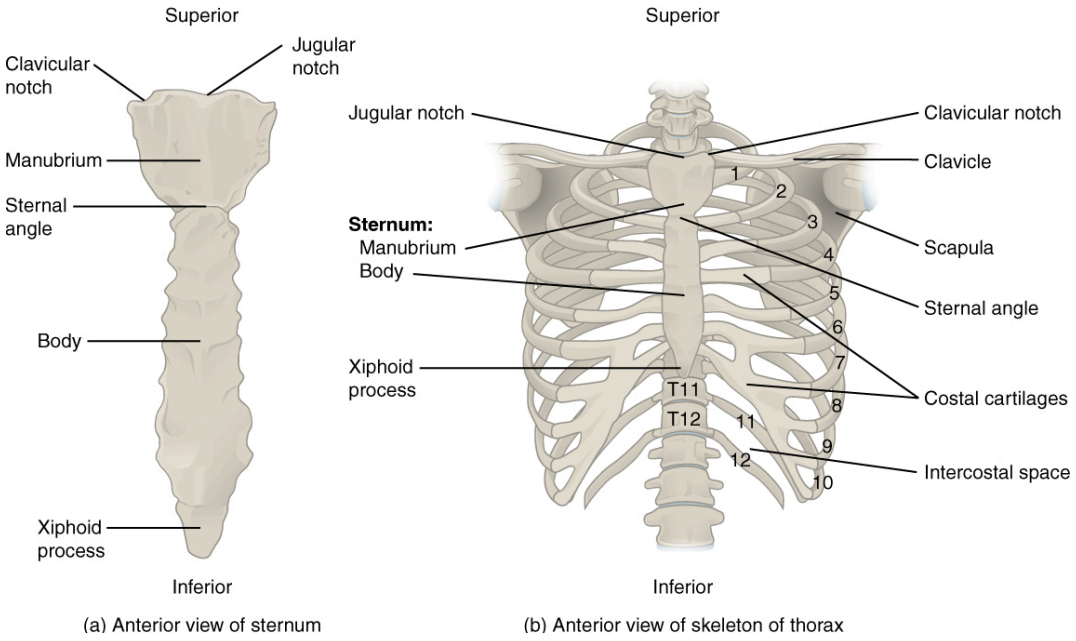


Figure 28. Thoracic Cage. *The thoracic cage is formed by the (a) sternum and (b) 12 pairs of ribs with their costal cartilages. The ribs are anchored posteriorly to the 12 thoracic vertebrae. The sternum consists of the manubrium, body, and xiphoid process. The ribs are classified as true ribs (1–7) and false ribs (8–12). The last two pairs of false ribs are also known as floating ribs (11–12)*

Ribs: Each rib is a curved, flattened bone that contributes to the wall of the thorax. The ribs articulate posteriorly with the T1–T12 thoracic vertebrae, and most attach anteriorly via their costal cartilages to the sternum. There are 12 pairs of ribs. The ribs are numbered 1–12 in accordance with the thoracic vertebrae.

The bony ribs do not extend anteriorly completely around to the sternum. Instead, each rib ends in a costal cartilage. These cartilages are made of hyaline cartilage and can extend for several inches. Most ribs are then attached, either directly or indirectly, to the sternum via their costal cartilage (Figure 28). The ribs are classified into three groups based on their relationship to the sternum.

Ribs 1–7 are classified as **true ribs** (vertebrosternal ribs). The costal cartilage from each of these ribs attaches directly to the sternum. Ribs 8–12 are called **false ribs** (vertebrochondral ribs). The costal cartilages from these ribs do not attach directly to the sternum. For ribs 8–10, the costal cartilages are attached to the cartilage of the next higher rib. Thus, the cartilage of rib 10 attaches to the cartilage of rib 9, rib 9 then attaches to rib 8, and rib 8 is attached to rib 7. The last two false ribs (11–12) are also called **floating ribs** (vertebral ribs). These are short ribs that do not attach to the sternum at all. Instead, their small costal cartilages terminate within the musculature of the lateral abdominal wall.

The Appendicular Skeleton: Attached to the axial skeleton are the limbs, whose 126 bones constitute the appendicular skeleton (Figure 29) These bones are divided into two groups: the bones that are located within the limbs themselves, and the girdle bones that attach the limbs to the axial skeleton. The bones of the shoulder region form the pectoral girdle, which anchors the upper limb to the thoracic cage of the axial skeleton. The lower limb is attached to the vertebral column by the pelvic girdle.

Because of our upright stance, different functional demands are placed upon the upper and lower limbs. Thus, the bones of the lower limbs are adapted for weight-bearing support and stability, as well as for body locomotion via walking or running. In contrast, our upper limbs are not required for these functions. Instead, our upper limbs are highly mobile and can be utilized for a wide variety of activities. The large range of upper limb movements, coupled with the ability to easily manipulate objects with our hands and opposable thumbs, has allowed humans to construct the modern world in which we live.

Part 1: The Pectoral Girdle

The bones that attach each upper limb to the axial skeleton form the pectoral girdle (shoulder girdle). This consists of two bones, the scapula and clavicle (Figure 30).

The **clavicle** (collarbone) is an S-shaped bone located on the anterior side of the shoulder. It is attached on its medial end to the sternum of the thoracic cage, which is part of the axial skeleton. The lateral end of the clavicle articulates (joins) with the scapula just above the shoulder joint. You can easily palpate, or feel with your fingers, the entire length of your clavicle.

The **scapula** (shoulder blade) lies on the posterior aspect of the shoulder. It is supported by the clavicle, which also articulates with the humerus (upper arm bone) to form the shoulder joint. The scapula is a flat, triangular-shaped bone with a prominent ridge running across its posterior surface. This ridge extends out laterally, where it forms the bony tip of the shoulder and joins with the lateral end of the clavicle. By following along the clavicle, you can palpate out to the bony tip of the shoulder, and from there, you can move back across your posterior shoulder to follow the ridge of the scapula. Move your shoulder around and feel how the clavicle and scapula move together as a unit. Both of these bones serve as important attachment sites for muscles that aid with movements of the shoulder and arm. (Figures 30 & 31)

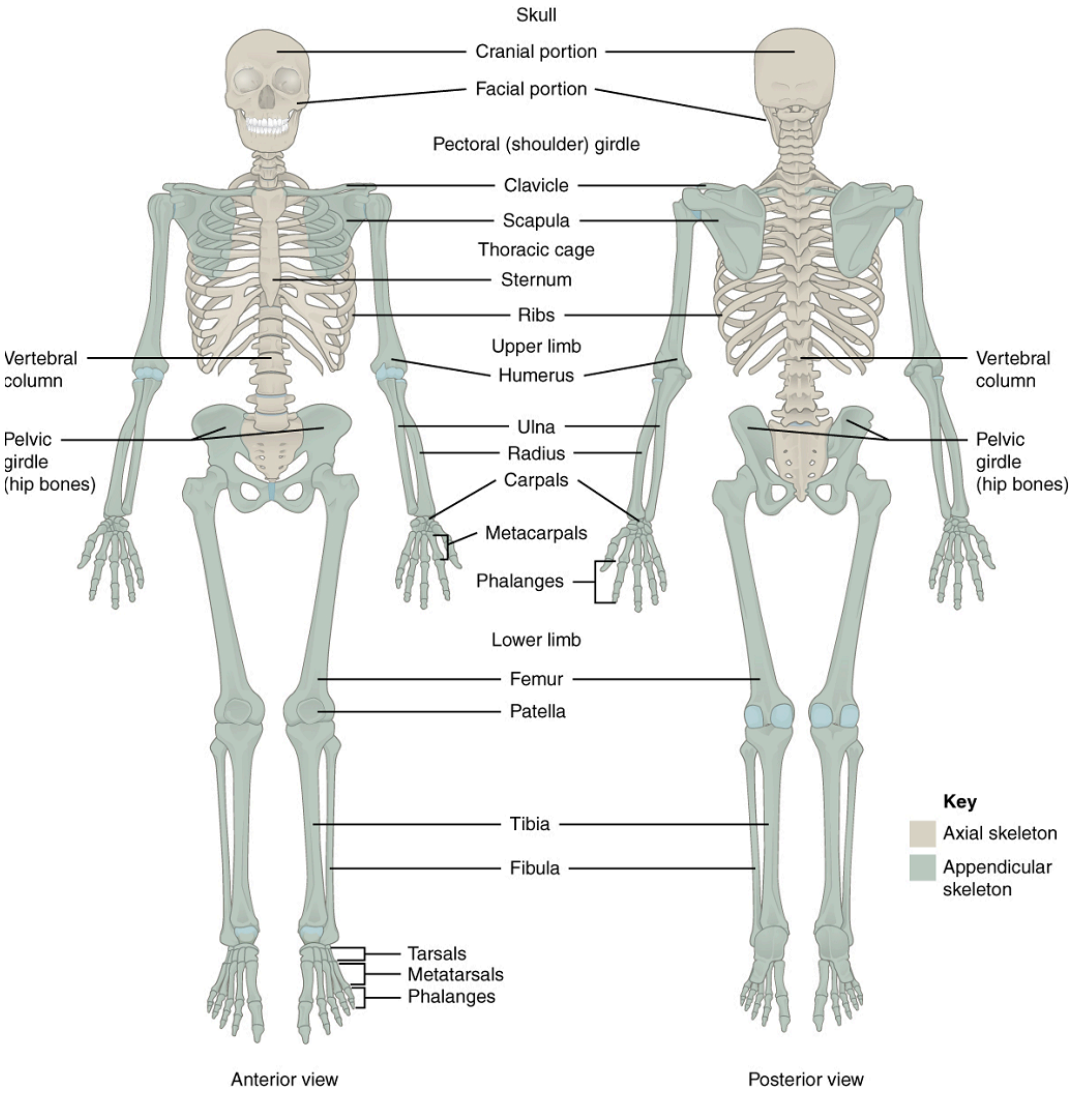


Figure 29. Axial and Appendicular Skeletons. *The axial skeleton forms the central axis of the body and consists of the skull, vertebral column, and thoracic cage. The appendicular skeleton consists of the pectoral and pelvic girdles, the limb bones, and the bones of the hands and feet.*

The right and left pectoral girdles are not joined to each other, allowing each to operate independently. In addition, the clavicle of each pectoral girdle is anchored to the axial skeleton by a single, highly mobile joint. This allows for the extensive mobility of the entire pectoral girdle, which in turn enhances movements of the shoulder and upper limb.

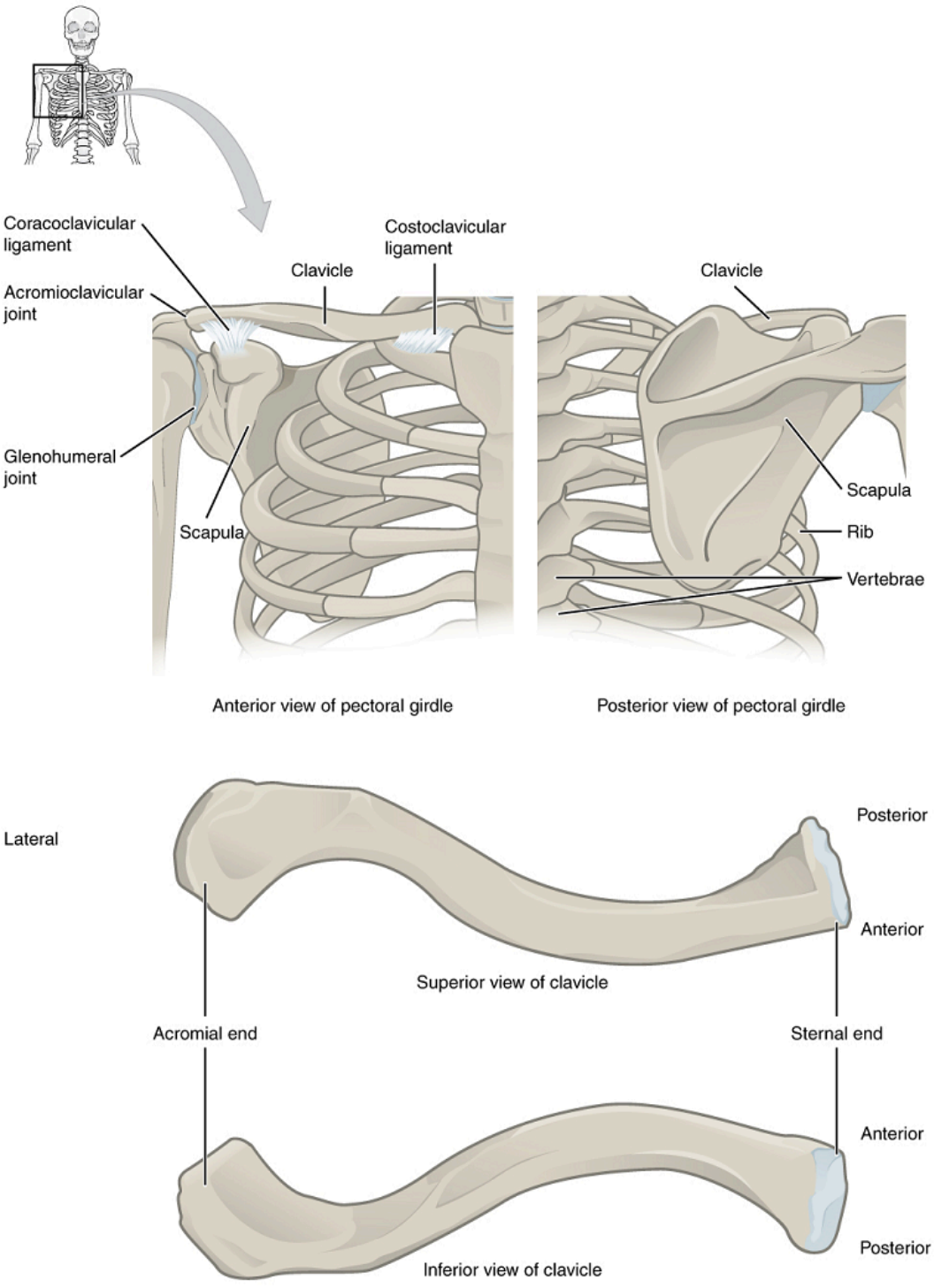


Figure 30. Pectoral Girdle. *The pectoral girdle consists of the clavicle and the scapula, which serve to attach the upper limb to the sternum of the axial skeleton.*

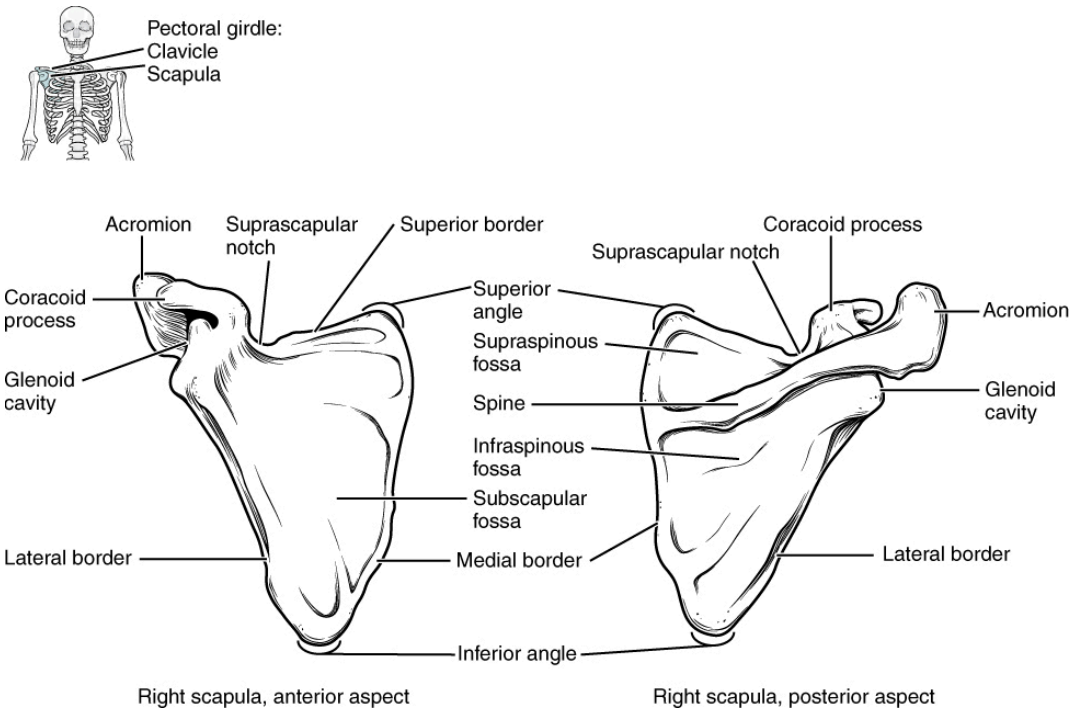


Figure 31. Scapula. *The isolated scapula is shown here from its anterior (deep) side and its posterior (superficial) side.*

Part 2: Bones of the Upper Limb

The upper limb is divided into three regions. These consist of the **arm**, located between the shoulder and elbow joints; the **forearm**, which is between the elbow and wrist joints; and the **hand**, which is located distal to the wrist. There are 30 bones in each upper limb. The **humerus** is the single bone of the upper arm, and the **ulna** (medially) and the **radius** (laterally) are the paired bones of the forearm. The base of the hand contains eight bones, each called a **carpal bone**, and the palm of the hand is formed by five bones, each called a metacarpal bone. The fingers and thumb contain a total of 14 bones, each of which is a **phalanx bone of the hand**. (Figure 29)

Humerus: The humerus is the single bone of the upper arm region (Figure 32). At its proximal end is the head of the humerus. This is the large, round, smooth region that faces medially. The head articulates with the glenoid cavity of the scapula to form the glenohumeral (shoulder) joint. Distally, the humerus becomes flattened and has two articulation areas, which join the ulna and radius bones of the forearm to form the **elbow joint**

Ulna: The ulna is the medial bone of the forearm. It runs parallel to the radius, which is the lateral bone of the forearm (Figure 33). The proximal end of the ulna articulates with the humerus as part of the elbow joint.

Radius: The radius runs parallel to the ulna, on the lateral (thumb) side of the forearm (Figure 33). The head of the radius is a disc-shaped structure that forms the proximal end. The distal end of the radius has a smooth surface for articulation with two carpal bones to form **the radiocarpal joint** or wrist joint (Figure 34 & 35).

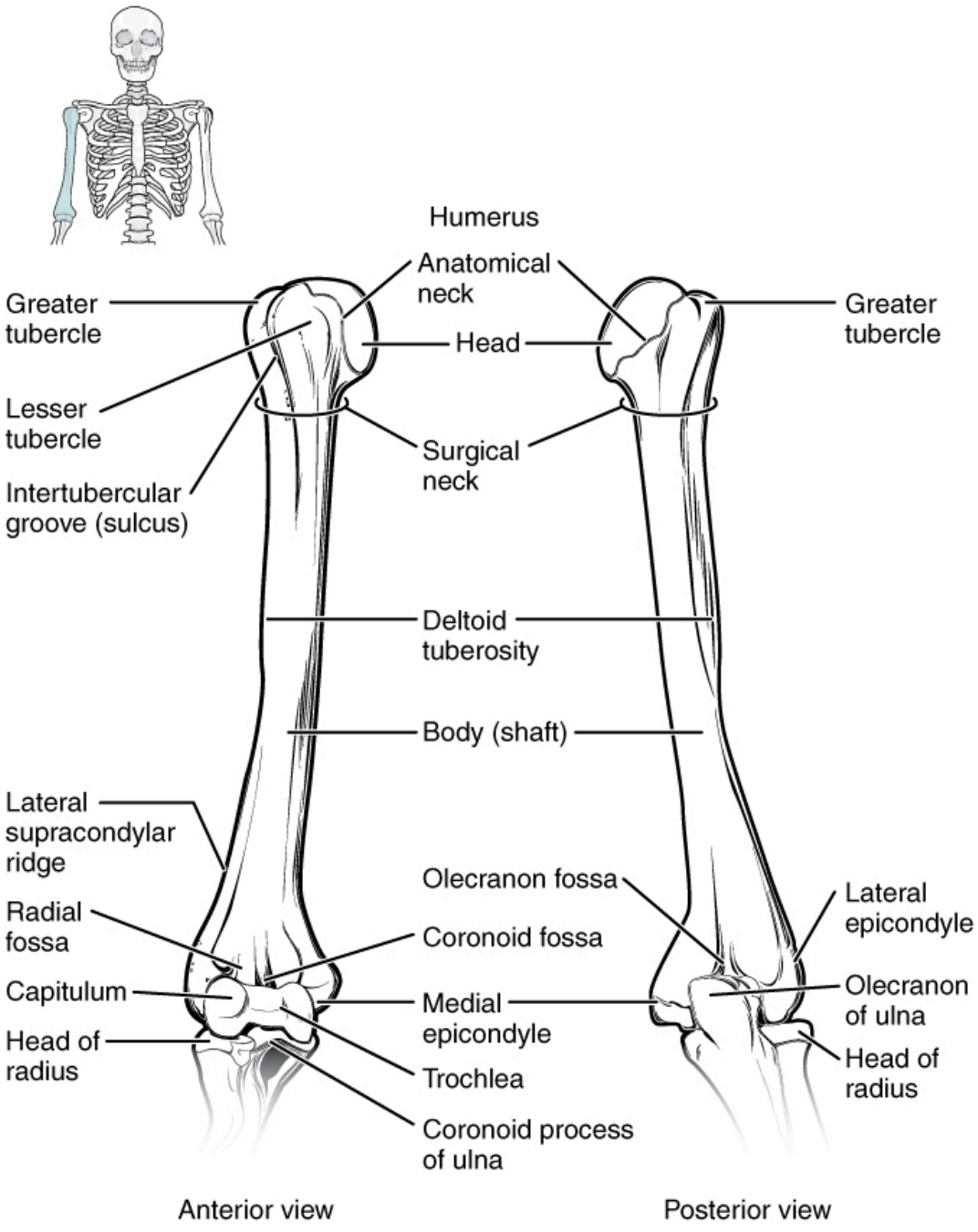


Figure 32. Humerus and Elbow Joint. *The humerus is the single bone of the upper arm region. It articulates with the radius and ulna bones of the forearm to form the elbow joint.*

Carpal Bones: The wrist and base of the hand are formed by a series of eight small carpal bones (Figure 34). The carpal bones are arranged in two rows, forming a proximal row of four carpal bones and a distal row of four carpal bones.

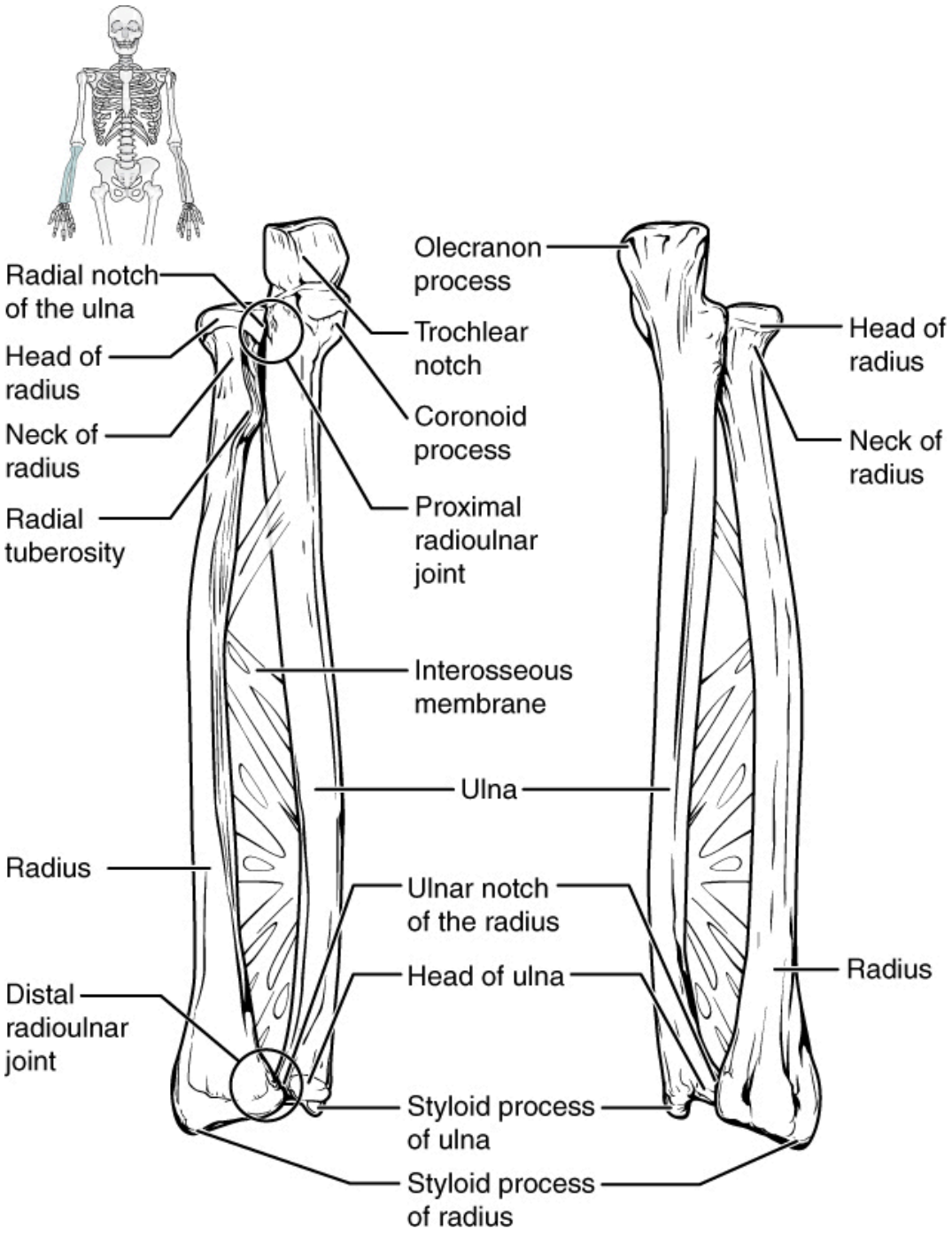


Figure 33. Ulna and Radius. *The ulna is located on the medial side of the forearm, and the radius is on the lateral side. These bones are attached to each other by an interosseous membrane.*

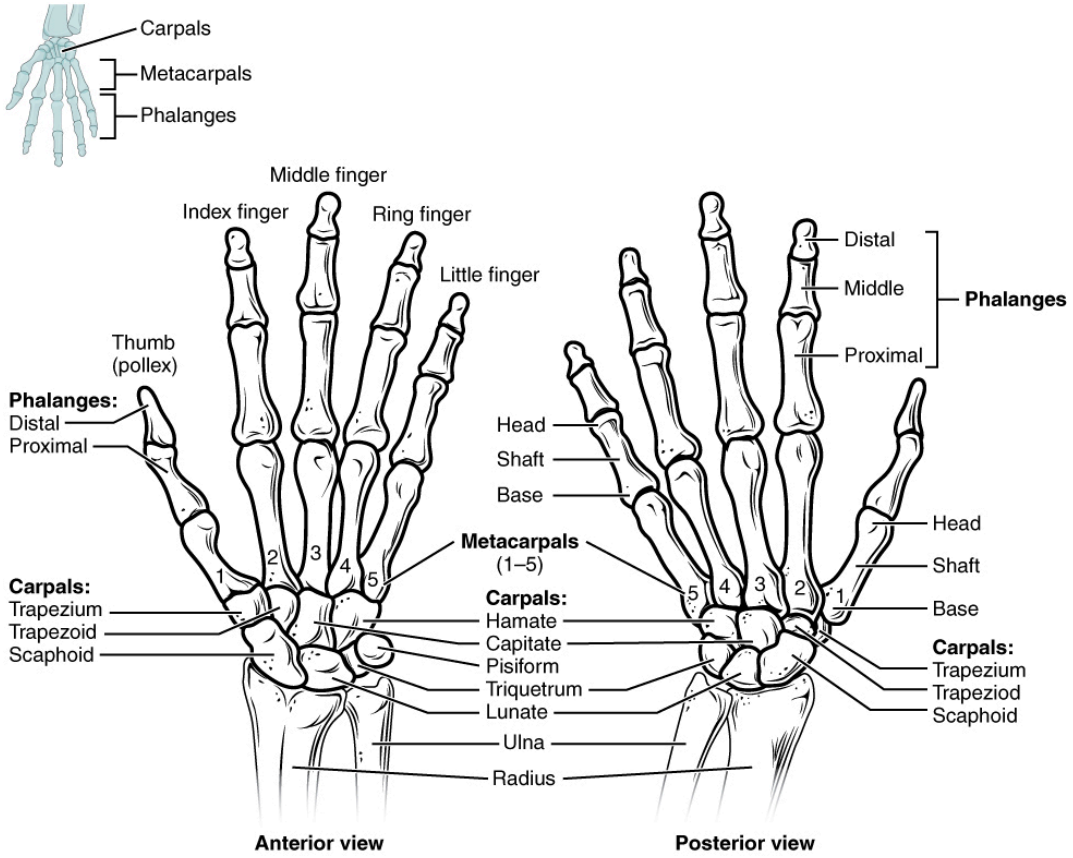


Figure 34. Bones of the Wrist and Hand. *The eight carpal bones form the base of the hand. These are arranged into proximal and distal rows of four bones each. The metacarpal bones form the palm of the hand. The thumb and fingers consist of the phalanx bones.*

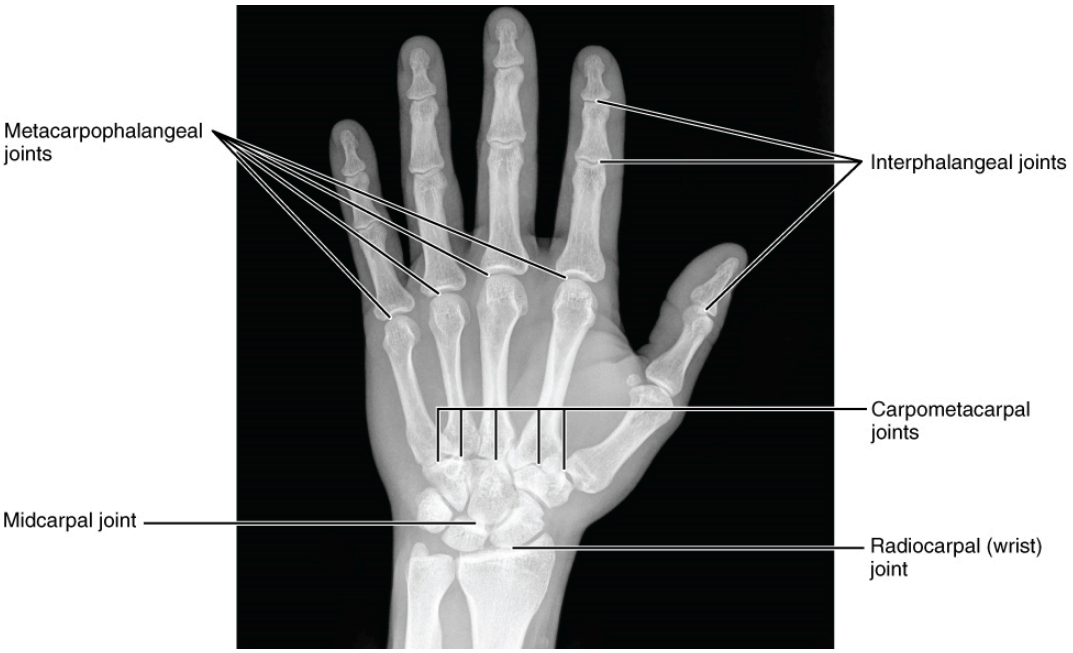


Figure 35. Bones of the Hand. *This radiograph shows the position of the bones within the hand. Note the carpal bones that form the base of the hand. (credit: modification of work by Trace Meek)*

The carpal bones form the base of the hand. This can be seen in the radiograph (X-ray image) of the hand that shows the relationships of the hand bones to the skin creases of the hand (Figure35).

Metacarpal Bones: The palm of the hand contains five elongated metacarpal bones. These bones lie between the carpal bones of the wrist and the bones of the fingers and thumb (Figure 34). The proximal end of each metacarpal bone articulates with one of the distal carpal bones. Each of these articulations is a carpometacarpal joint (Figure 35). The expanded distal end of each metacarpal bone articulates at the metacarpophalangeal joint with the proximal phalanx bone of the thumb or one of the fingers. The distal end also forms the knuckles of the hand, at the base of the fingers. The metacarpal bones are numbered 1–5, beginning at the thumb.

Phalanx Bones: The fingers and thumb contain 14 bones, each of which is called a phalanx bone (plural = phalanges), named after the ancient Greek phalanx (a rectangular block of soldiers). The thumb (pollex) is digit number 1 and has two phalanges, a proximal phalanx, and a distal phalanx bone (Figure 34). Digits 2 (index finger) through 5 (little finger) have three phalanges each, called the proximal, middle, and distal phalanx bones. An **interphalangeal joint** is one of the articulations between adjacent phalanges of the digits (Figure 35).

Part 3: The Pelvic Girdle and Pelvis

The **pelvic girdle** (hip girdle) is formed by a single bone, the **hip bone** or **coxal bone** (coxal = "hip"), which serves as the attachment point for each lower limb. Each hip bone, in turn, is firmly joined to the axial skeleton via its attachment to the sacrum of the vertebral column. The right and left hip bones also converge anteriorly to attach to each other. The bony **pelvis** is the entire structure formed by the two hip bones, the sacrum, and the coccyx that is attached inferiorly to the sacrum (Figure 36).

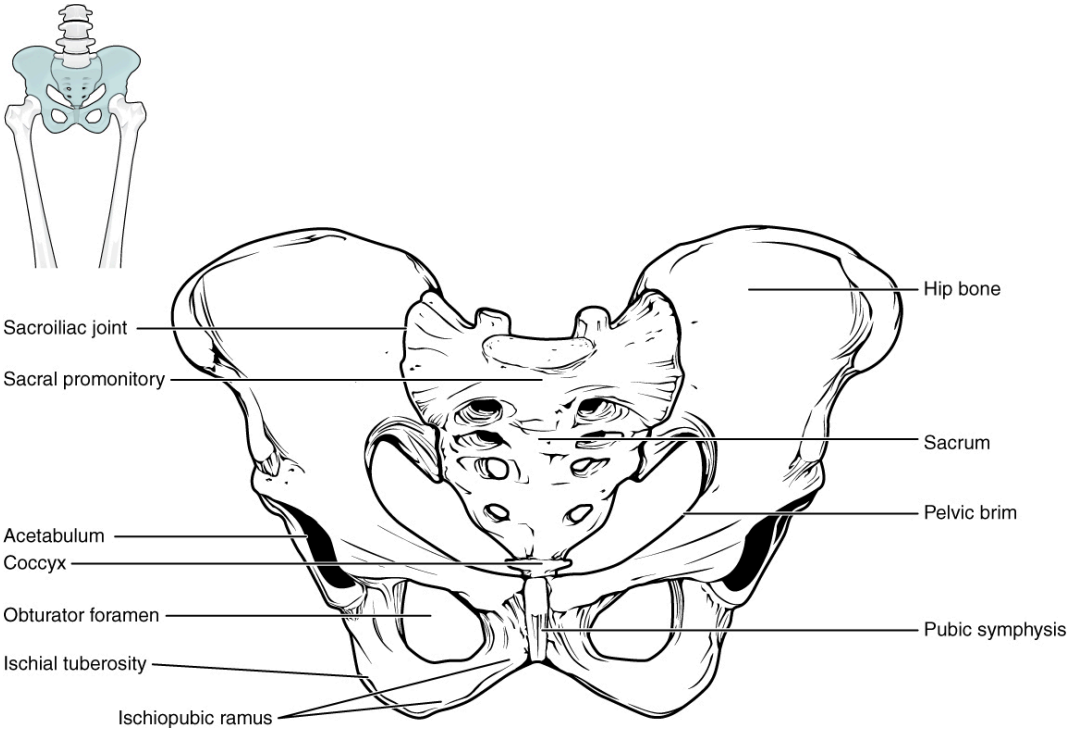


Figure 36. Pelvis. *The pelvic girdle is formed by a single hip bone. The hip bone attaches the lower limb to the axial skeleton through its articulation with the sacrum. The right and left hip bones, plus the sacrum and the coccyx, together form the pelvis.*

Unlike the bones of the pectoral girdle, which are highly mobile to enhance the range of upper limb movements, the bones of the pelvis are strongly united to each other to form a largely immobile, weight-bearing structure. This is important for stability because it enables the weight of the body to be easily transferred laterally from the vertebral column, through the pelvic girdle and hip joints, and into either lower limb whenever the other limb is not bearing weight. Thus, the immobility of the pelvis provides a strong foundation for the upper body as it rests on top of the mobile lower limbs.

Hip Bone: The hip bone, or coxal bone, forms the pelvic girdle portion of the pelvis. The paired hip bones are the large, curved bones that form the lateral and anterior aspects of the pelvis. Each adult hip bone is formed by

three separate bones that fuse together during the late teenage years. These bony components are the ilium, ischium, and pubis (Figure 37). These names are retained and used to define the three regions of the adult hip bone.

The **ilium** is the fan-like, superior region that forms the largest part of the hip bone. It is firmly united to the sacrum at the largely immobile **sacroiliac joint** (Figure 36). The **ischium** forms the posteroinferior region of each hip bone. It supports the body when sitting. The **pubis** forms the anterior portion of the hip bone. The pubis curves medially, where it joins to the pubis of the opposite hip bone at a specialized joint called the **pubic symphysis**.

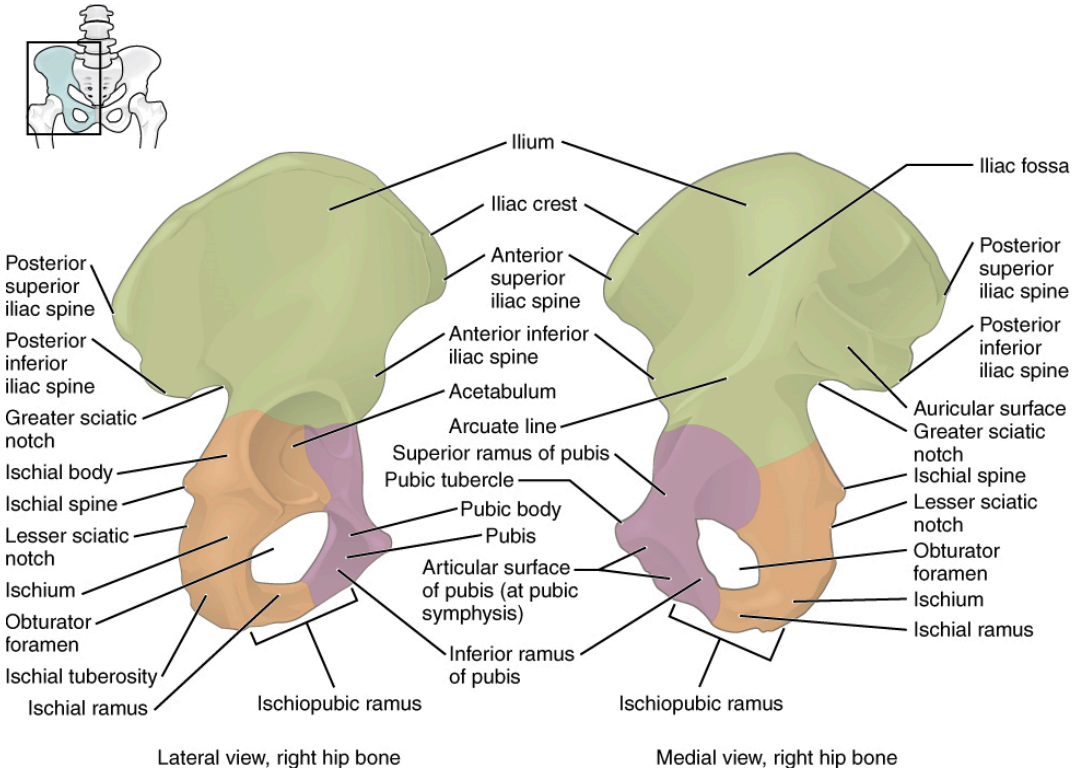


Figure 37. The Hip Bone. *The adult hip bone consists of three regions. The ilium forms the large, fan-shaped superior portion, the ischium forms the posteroinferior portion, and the pubis forms the anteromedial portion.*

Pelvis: The pelvis consists of four bones: the right and left hip bones, the sacrum, and the coccyx (Figure 36). The pelvis has several important functions. Its primary role is to support the weight of the upper body when sitting and to transfer this weight to the lower limbs when standing. It serves as an attachment point for trunk and lower limb muscles, and also protects the internal pelvic organs.

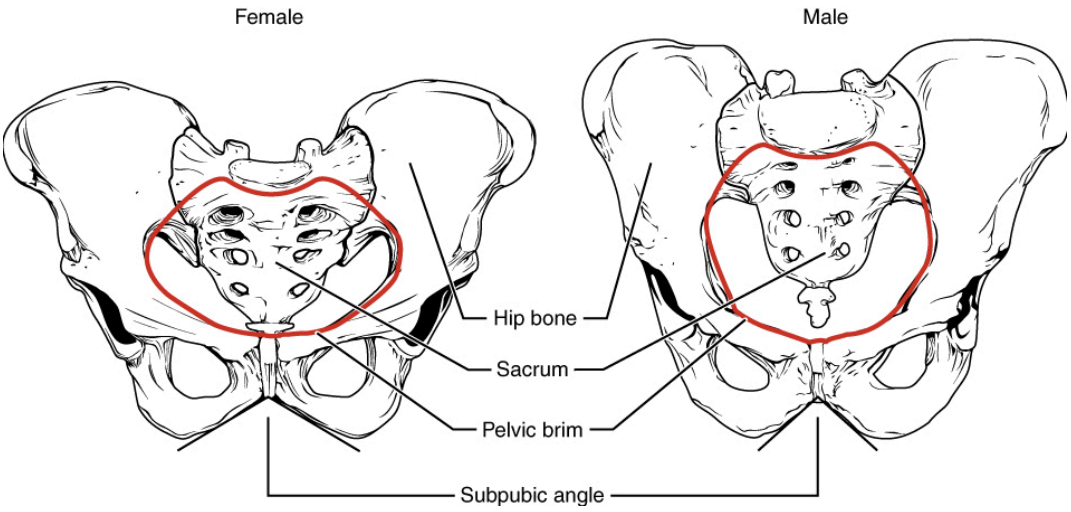


Figure 38. Male and Female Pelves. *The female pelvis is adapted for childbirth and is broader, with a larger subpubic angle, a rounder pelvic brim, and a wider and more shallow lesser pelvic cavity than the male pelvis.*

Comparison of the Female and Male Pelvis: The differences between the adult female and male pelvis relate to function and body size. In general, the bones of the male pelvis are thicker and heavier, adapted for support of the male's heavier physical build and stronger muscles; this average size difference is generally true of other bones of the skeleton as well. The pelvis does show more robust differences between males and females due to its functional relationship to bipedal movement (requiring a relatively narrow pelvis) and birth of infants with large brains (requiring a relatively broad pelvis). Because the female pelvis is adapted for childbirth, it is wider than the male pelvis, as evidenced by the distance between the anterior superior iliac spines (Figure 38). The ischial tuberosities of females are also farther apart, which increases the size of the pelvic outlet. Because of this increased pelvic width, the subpubic angle is larger in females (greater than 80 degrees) than it is in males (less than 70 degrees). The female sacrum is wider, shorter, and less curved, and the sacral promontory projects less into the pelvic cavity, thus giving the female pelvic inlet (pelvic brim) a more rounded or oval shape compared to males. The pelvic cavity of females is also wider and shallower than the narrower, deeper, and tapering lesser pelvis of males. The greater sciatic notch of the male hip bone is narrower and deeper than the broader notch of females. Because of the obvious differences between female and male hip bones, this is the one bone of the body that allows for the most accurate sex determination. Table 4 provides an overview of the general differences between the female and male pelvis.

Table 4: Overview of Differences Between Average Female and Male Pelves

	Female pelvis	Male pelvis
Pelvic weight	Bones are lighter and thinner	Bones are thicker and heavier
Pelvis inlet shape	Round or oval	Heart-shaped
Lesser pelvic cavity shape	Shorter and wider	Longer and narrower
Subpubic angle	Greater than 80 degrees	Less than 70 degrees
Pelvic outlet shape	Rounded and larger	Smaller

Part 4: Bones of the Lower Limb

Like the upper limb, the lower limb is divided into three regions. The **thigh** is that portion of the lower limb located between the hip joint and knee joint. The **leg** is specifically the region between the knee joint and the ankle joint. Distal to the ankle is the **foot**. The lower limb contains 30 bones. These are the femur, patella, tibia, fibula, tarsal bones, metatarsal bones, and phalanges (Figure 29). The **femur** is the single bone of the thigh. The **patella** is the kneecap and articulates with the distal femur. The **tibia** is the larger, weight-bearing bone located

on the medial side of the leg, and the **fibula** is the thin bone of the lateral leg. The bones of the foot are divided into three groups. The posterior portion of the foot is formed by a group of seven bones, each of which is known as a **tarsal bone**, whereas the mid-foot contains five elongated bones, each of which is a **metatarsal bone**. The toes contain 14 small bones, each of which is a **phalanx bone of the foot**.

Femur: The femur, or thigh bone, is the single bone of the thigh region (Figure 39). It is the longest and strongest bone of the body, and accounts for approximately one-quarter of a person's total height. The rounded, proximal end is the head of the femur, which articulates with the acetabulum of the hip bone to form the **hip joint**.

Patella: The patella (kneecap) is the largest sesamoid bone of the body (see Figure 39). A sesamoid bone is a bone that is incorporated into the tendon of a muscle where that tendon crosses a joint. The sesamoid bone articulates with the underlying bones to prevent damage to the muscle tendon due to rubbing against the bones during movements of the joint. The patella is found in the tendon of the quadriceps femoris muscle, the large muscle of the anterior thigh that passes across the anterior knee to attach to the tibia. The patella articulates with the patellar surface of the femur and thus prevents rubbing of the muscle tendon against the distal femur. The patella also lifts the tendon away from the knee joint, which increases the leverage power of the quadriceps femoris muscle as it acts across the knee. The patella does not articulate with the tibia.

Tibia: The tibia (shin bone) is the medial bone of the leg and is larger than the fibula, with which it is paired (Figure 40). The tibia is the main weight-bearing bone of the lower leg and the second longest bone of the body, after the femur. The medial side of the tibia is located immediately under the skin, allowing it to be easily palpated down the entire length of the medial leg.

Fibula: The fibula is the slender bone located on the lateral side of the leg (Figure 40). The fibula does not bear weight. It serves primarily for muscle attachments and thus is largely surrounded by muscles. Only the proximal and distal ends of the fibula can be palpated.

Tarsal Bones: The posterior half of the foot is formed by seven tarsal bones (Figure 43). The most superior tarsal bone, the **talus**, articulates with the tibia and fibula to form the **ankle joint**. Inferiorly, the talus articulates with the **calcaneus** (heel bone), the largest bone of the foot, which forms the heel. Body weight is transferred from the tibia to the talus to the calcaneus, which rests on the ground.

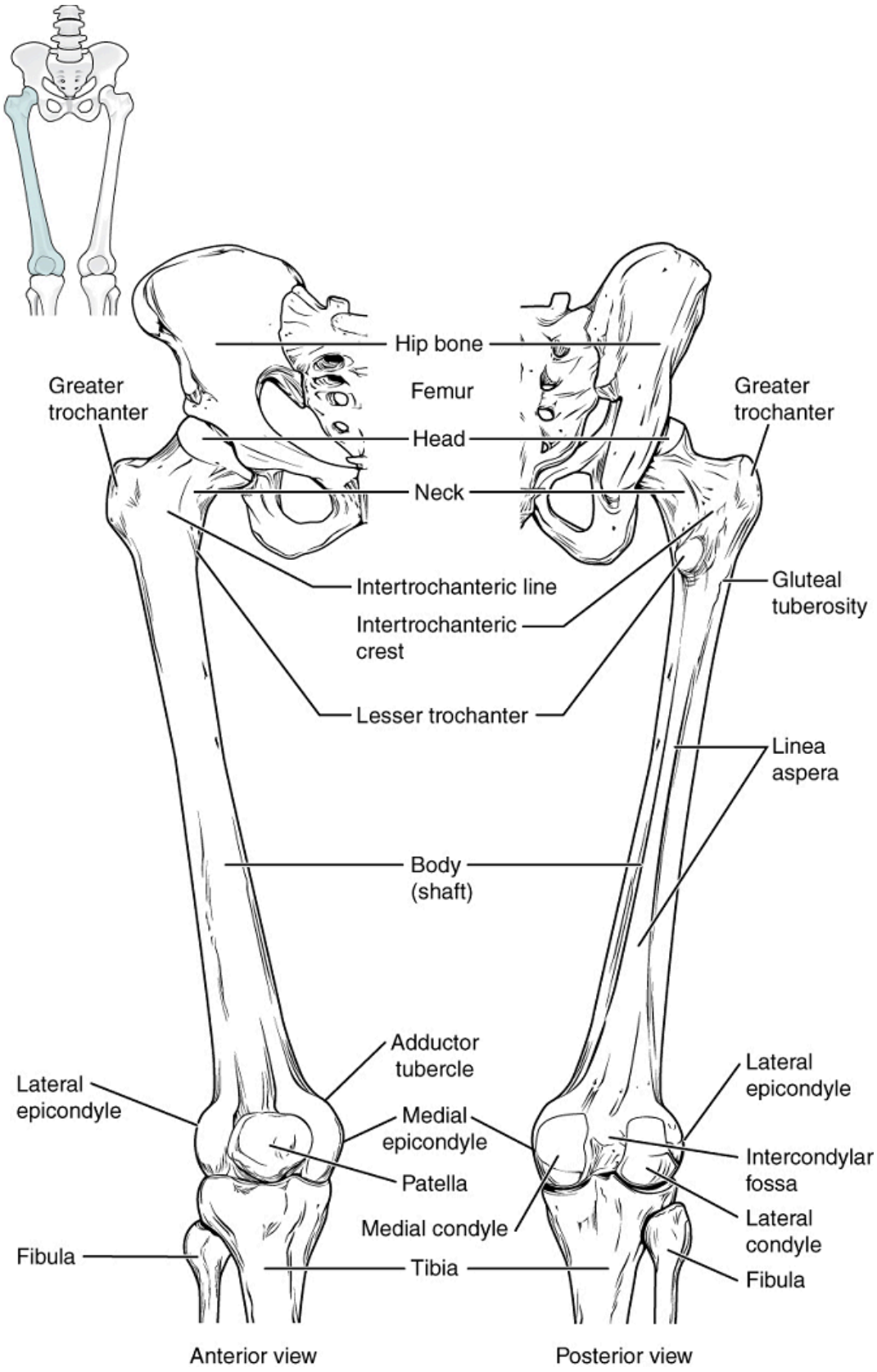


Figure 39. Femur and Patella. *The femur is the single bone of the thigh region. It articulates superiorly with the hip bone at the hip joint, and inferiorly with the tibia at the knee joint. The patella only articulates with the distal end of the femur.*

Metatarsal Bones: The anterior half of the foot is formed by the five metatarsal bones, which are located

between the tarsal bones of the posterior foot and the phalanges of the toes (Figure 41). These elongated bones are numbered 1–5, starting with the medial side of the foot.

Phalanx bones: The toes contain a total of 14 phalanx bones (phalanges), arranged in a similar manner as the phalanges of the fingers (Figure 41). The toes are numbered 1–5, starting with the big toe (**hallux**). The big toe has two phalanx bones, the proximal and distal phalanges. The remaining toes all have proximal, middle, and distal phalanges. A joint between adjacent phalanx bones is called an interphalangeal joint.

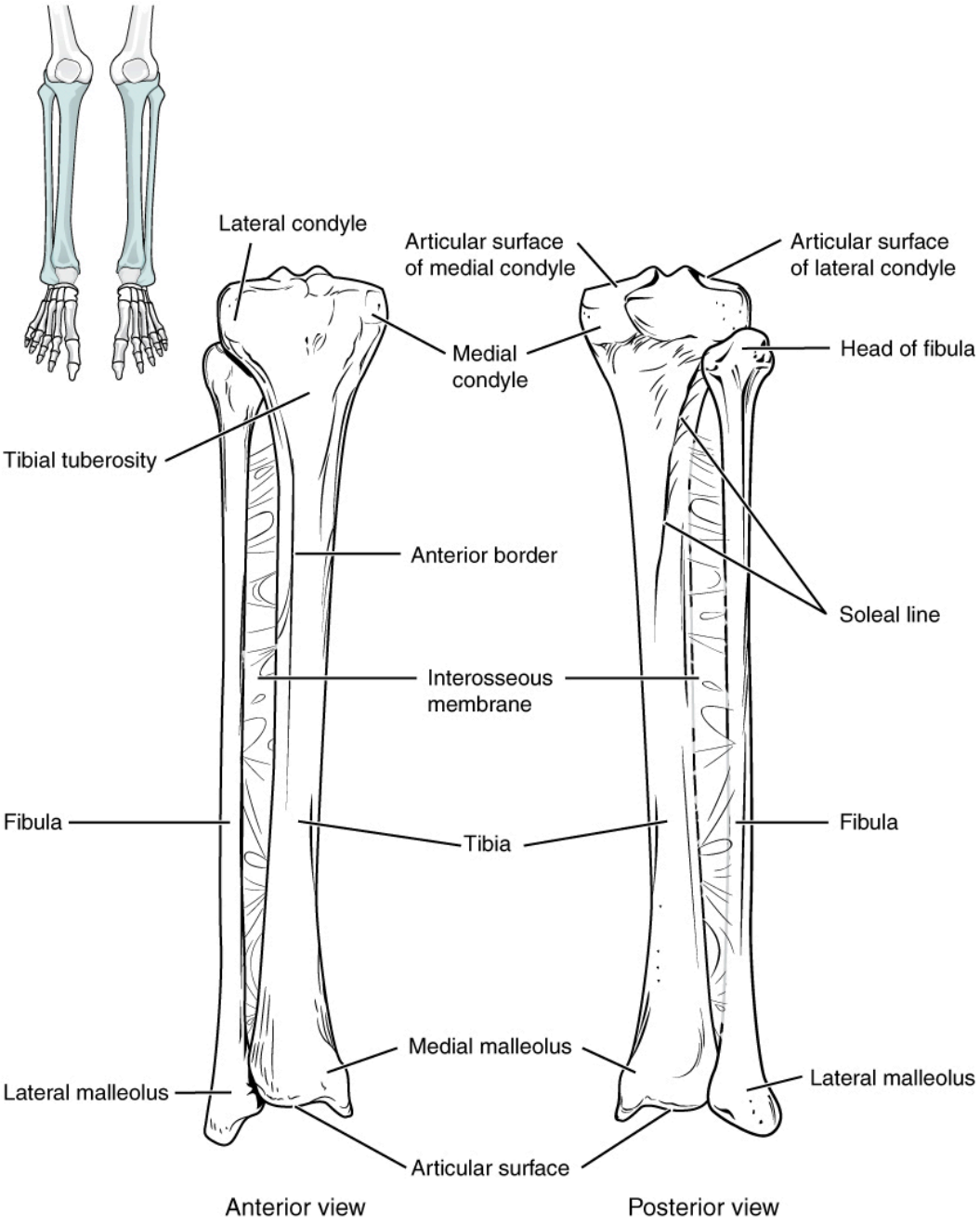


Figure 40. Tibia and Fibula. *The tibia is the larger, weight-bearing bone located on the medial side of the leg. The fibula is the slender bone of the lateral side of the leg and does not bear weight.*

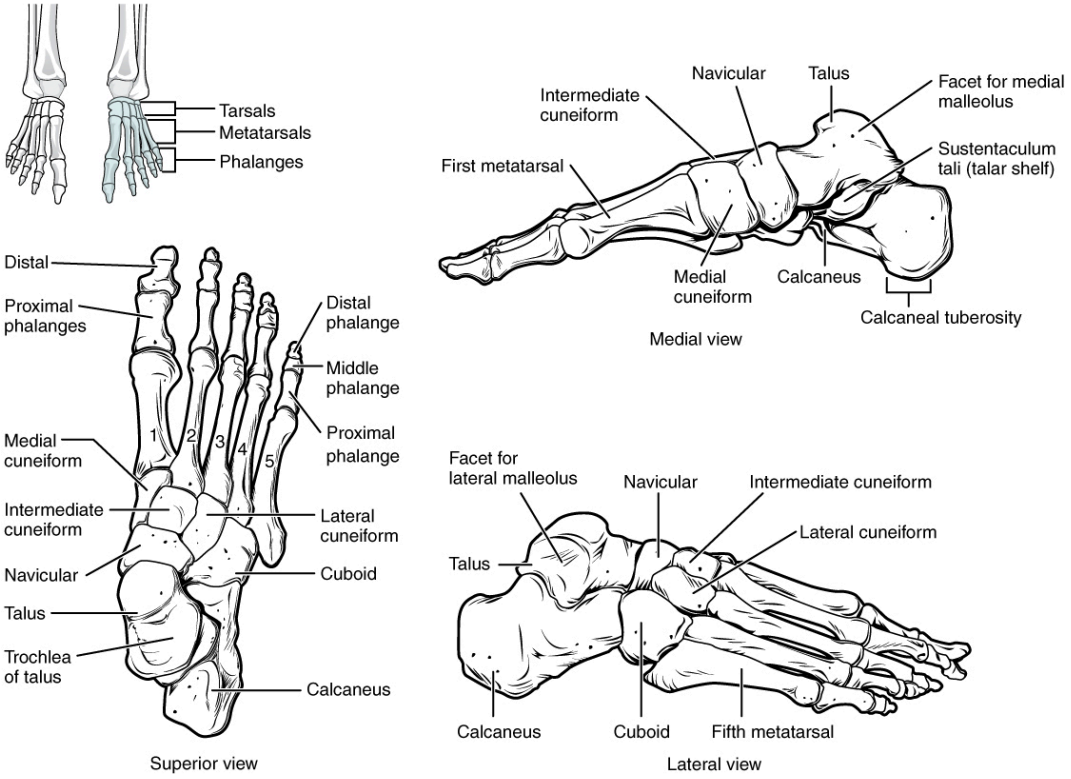


Figure 41. Bones of the Foot. *The bones of the foot are divided into three groups. The posterior foot is formed by the seven tarsal bones. The mid-foot has the five metatarsal bones. The toes contain the phalanges.*

Unit 13: Joints

Unit outline

Joints

Part 1: Overview and Classification of Joints

- Structural classification
- Functional classification

Part 2: Fibrous Joints

- Suture
- Syndesmosis
- Gomphosis

Part 3: Cartilaginous Joints

- Synchondrosis
- Symphysis

Part 4: Synovial Joints

- Structural features of synovial joints
- Additional structures associated with synovial joints
- Types of synovial joints

Learning Objectives

At the end of this unit, you should be able to:

I. Explain what is meant by the terms synarthrotic, diarthrotic, and amphiarthrotic as descriptions of the functional classes of joints.

II. Describe the structures, classifications, functions, and locations of the various types of joints in the human body.

III. Describe the structure of a synovial joint and using the knee joint as an example, specify the functions of each component.

IV. Describe the movements allowed by synovial joints and specify examples of each.

V. Describe the structures and movements allowed by each type of synovial joint and also specify an example of each in the human body.

Learning Objectives and Guiding Questions

At the end of this unit, you should be able to complete all the following tasks, including answering the guiding questions associated with each task.

I. Explain what is meant by the terms synarthrotic, diarthrotic, and amphiarthrotic as descriptions of the functional classes of joints.

1. Define each of the following terms:
    - Synarthrotic joint
    - Diarthrotic joint
    - Amphiarthrotic joint

II. Describe the structures, classifications, functions, and locations of the various types of joints in the human body.

1. For each of the following types of joints, describe its structure (specific material found between the articulating bones), classification as a fibrous, cartilaginous, or synovial joint (based on the material found between the articulating bones), its function (movements allowed), and one specific location in the human body where it is found (between which two specific named bones):
    - Suture
    - Syndesmosis
    - Gomphosis
    - Synchondrosis
    - Symphysis
    - Synovial joint

III. Describe the structure of a synovial joint and using the knee joint as an example, specify the functions of each component.

1. Draw a fully-annotated diagram showing the detailed structure of a human knee joint, including each of the following structures:
    - Articular capsule
    - Synovial membrane
    - Synovial cavity
    - Synovial fluid
    - Articular cartilage
    - Ligaments
    - Tendons
    - Meniscus
    - Bursa
2. Describe the function of each of the following structures:

- Articular capsule
- Synovial membrane
- Synovial cavity
- Synovial fluid
- Articular cartilage
- Ligaments
- Tendons
- Meniscus
- Bursa

3. Compare and contrast the structure and function of synovial capsules and bursae.

IV. Describe the movements allowed by synovial joints and specify examples of each.

1. Using complete sentences, describe and provide one example of each of the following movements, including the names of the structure(s) that move in relation to each other:

    - Gliding movement
    - Angular movement
    - Rotation
    - Circumduction

V. Describe the structures and movements allowed by each type of synovial joint and also specify an example of each in the human body.

1. For each of the following joint types, describe its structure (material found between the articulating bones), specify its function (movements allowed), and specify one clear example of each by correctly naming the two articulating bones of the joint you are describing:

    - Pivot joint
    - Plane joint
    - Hinge joint
    - Saddle joint
    - Condyloid joint
    - Ball-and-socket joint

Part 1: Overview and Classification of Joints

The adult human body has 206 bones, and with the exception of the hyoid bone in the neck, each bone is connected to at least one other bone. **Joints,** or **articulations,** are the location where bones, or bone and cartilage, come together. Many joints allow for movement between the bones. At these joints, the articulating surfaces of the adjacent bones can move smoothly against each other. However, the bones of other joints may be joined to each other by connective tissue or cartilage. These joints are designed for stability and provide for little or no movement. Importantly, joint stability and movement are related to each other. This means that stable joints allow for little or no mobility between the adjacent bones. Conversely, joints that provide the most movement between bones are the least stable. Understanding the relationship between joint structure and function will help to explain why particular types of joints are found in certain areas of the body.

The articulating surfaces of bones at stable types of joints, with little or no mobility, are strongly united to each

other. For example, most of the joints of the skull are held together by fibrous connective tissue and do not allow for movement between the adjacent bones. This lack of mobility is important, because the skull bones serve to protect the brain. Similarly, other joints united by fibrous connective tissue allow for very little movement, which provides stability and weight-bearing support for the body. For example, the tibia and fibula of the leg are tightly united to give stability to the body when standing. At other joints, the bones are held together by cartilage, which permits limited movements between the bones. Thus, the joints of the vertebral column only allow for small movements between adjacent vertebrae, but when added together, these movements provide the flexibility that allows your body to twist, or bend to the front, back, or side. In contrast, at joints that allow for wide ranges of motion, the articulating surfaces of the bones are not directly united to each other. Instead, these surfaces are enclosed within a space filled with lubricating fluid, which allows the bones to move smoothly against each other. These joints provide greater mobility, but since the bones are free to move in relation to each other, the joint is less stable. Most of the joints between the bones of the appendicular skeleton are this freely moveable type of joint. These joints allow the muscles of the body to pull on a bone and thereby produce movement of that body region. Your ability to kick a soccer ball, pick up a fork, and dance the tango depend on mobility at these types of joints.

Joints are classified both structurally and functionally. Structural classifications of joints take into account whether the adjacent bones are strongly anchored to each other by fibrous connective tissue or cartilage, or whether the adjacent bones articulate with each other within a fluid-filled space called a **joint cavity**. Functional classifications describe the degree of movement available between the bones, ranging from immobile, to slightly mobile, to freely moveable joints. The amount of movement available at a particular joint of the body is related to the functional requirements for that joint. Thus immobile or slightly moveable joints serve to protect internal organs, give stability to the body, and allow for limited body movement. In contrast, freely moveable joints allow for much more extensive movements of the body and limbs.

Structural Classification of Joints: The structural classification of joints is based on whether the articulating surfaces of the adjacent bones are directly connected by fibrous connective tissue or cartilage, or whether the articulating surfaces contact each other within a fluid-filled joint cavity. These differences serve to divide the joints of the body into three structural classifications. A **fibrous joint** is where the adjacent bones are united by fibrous connective tissue. At a **cartilaginous joint**, the bones are joined by hyaline cartilage or fibrocartilage. At a **synovial joint**, the articulating surfaces of the bones are not directly connected, but instead come into contact with each other within a joint cavity that is filled with a lubricating fluid. Synovial joints allow for free movement between the bones and are the most common joints of the body.

Functional Classification of Joints: The functional classification of joints is determined by the amount of mobility found between the adjacent bones. Joints are thus functionally classified as a synarthrosis or immobile joint, an amphiarthrosis or slightly moveable joint, or as a diarthrosis, which is a freely moveable joint (arthroun = "to fasten by a joint"). Depending on their location, fibrous joints may be functionally classified as a synarthrosis (immobile joint) or an amphiarthrosis (slightly mobile joint). Cartilaginous joints are also functionally classified as either a synarthrosis or an amphiarthrosis joint. All synovial joints are functionally classified as a diarthrosis joint.

Synarthrosis: An immobile or nearly immobile joint is called a synarthrosis. The immobile nature of these joints provides for a strong union between the articulating bones. This is important at locations where the bones provide protection for internal organs. Examples include the sutures, the fibrous joints between the bones of the skull that surround and protect the brain (Figure 1).

Amphiarthrosis: An **amphiarthrosis** is a joint that has limited mobility. An example of this type of joint is the cartilaginous joint that unites the bodies of adjacent vertebrae. Filling the gap between the vertebrae is a thick pad of fibrocartilage called an intervertebral disc (Figure 2).

Each intervertebral disc strongly unites the vertebrae but still allows for a limited amount of movement between them. However, the small movements available between adjacent vertebrae can sum together along the length of the vertebral column to provide for large ranges of body movements.

Another example of an amphiarthrosis is the pubic symphysis of the pelvis. This is a cartilaginous joint in which the pubic regions of the right and left hip bones are strongly anchored to each other by fibrocartilage. This joint normally has very little mobility. The strength of the pubic symphysis is important in conferring weight-bearing stability to the pelvis.

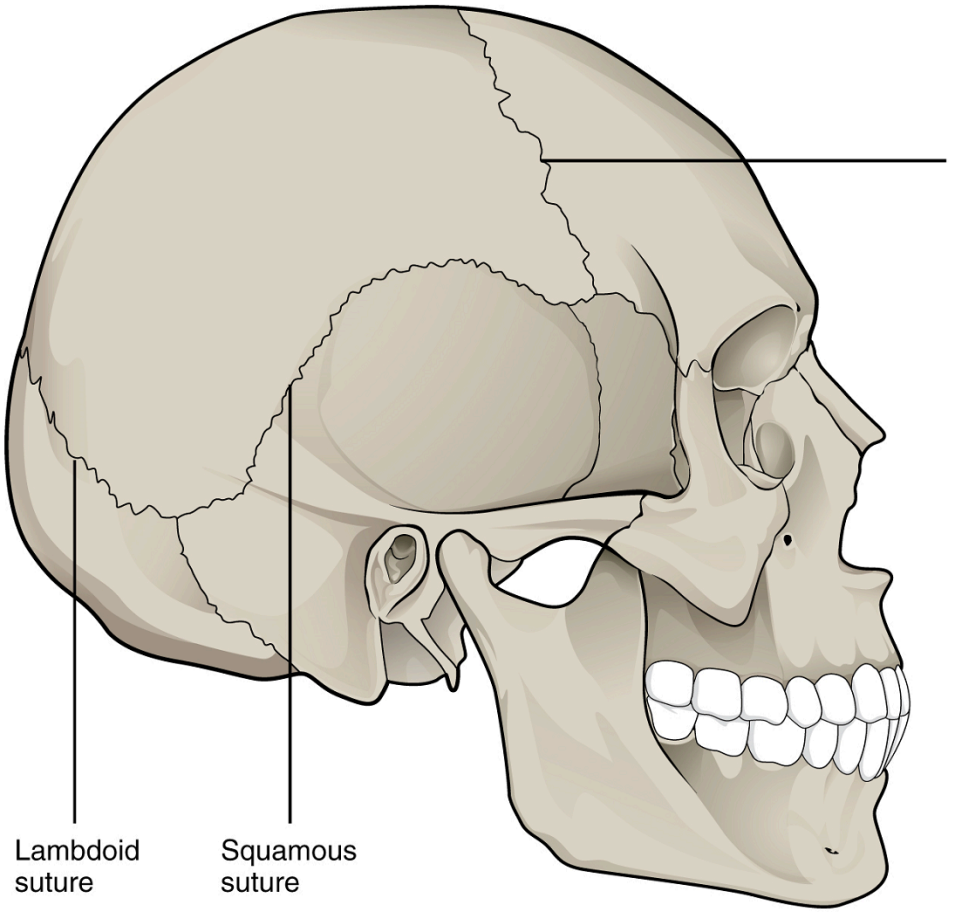


Figure 1. Suture Joints of Skull. *The suture joints of the skull are an example of a synarthrosis, an immobile or essentially immobile joint.*

Diarthrosis: A freely mobile joint is classified as a diarthrosis. These types of joints include all synovial joints of the body, which provide the majority of body movements. Most diarthrotic joints are found in the appendicular skeleton and thus give the limbs a wide range of motion.

This type of multiaxial diarthrotic joint allows for movement along three axes (Figure 3). The shoulder and hip joints are multiaxial joints. They allow the upper or lower limb to move in an anterior-posterior direction and a medial-lateral direction. In addition, the limb can also be rotated around its long axis. This third movement results in rotation of the limb so that its anterior surface is moved either toward or away from the midline of the body.

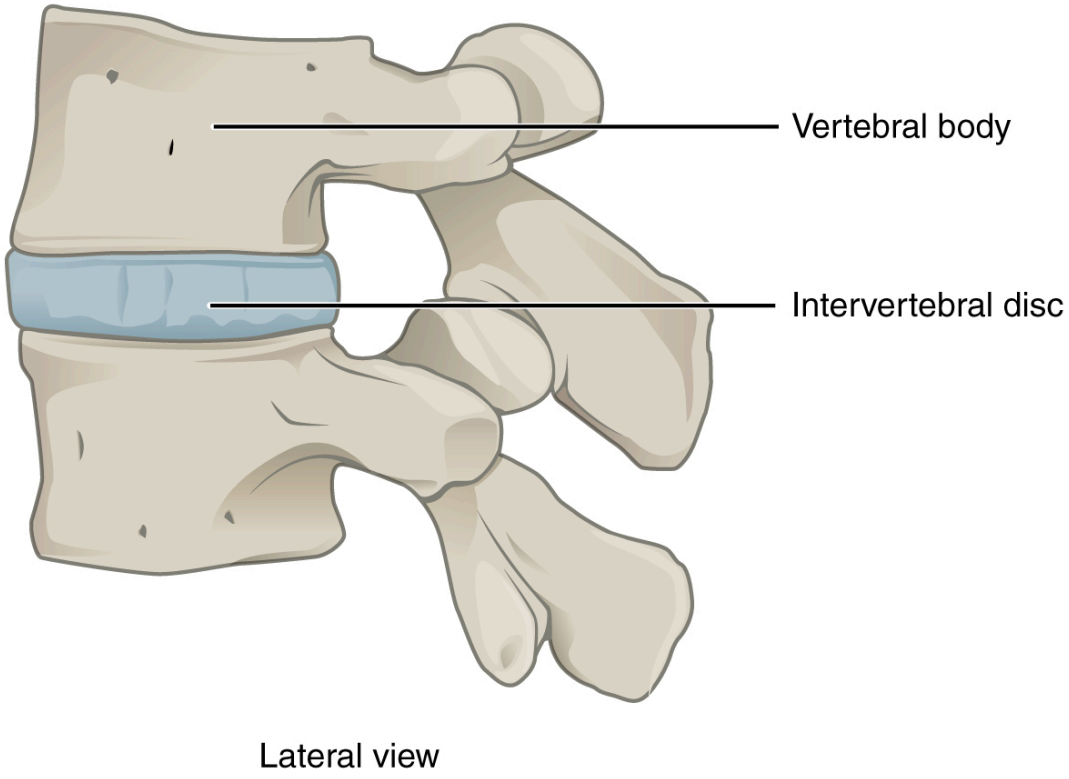


Figure 2. Intervertebral Disc. *An intervertebral disc unites the bodies of adjacent vertebrae within the vertebral column. Each disc allows for limited movement between the vertebrae and thus functionally forms an amphiarthrosis type of joint. Intervertebral discs are made of fibrocartilage and thereby structurally form a symphysis type of cartilaginous joint.*

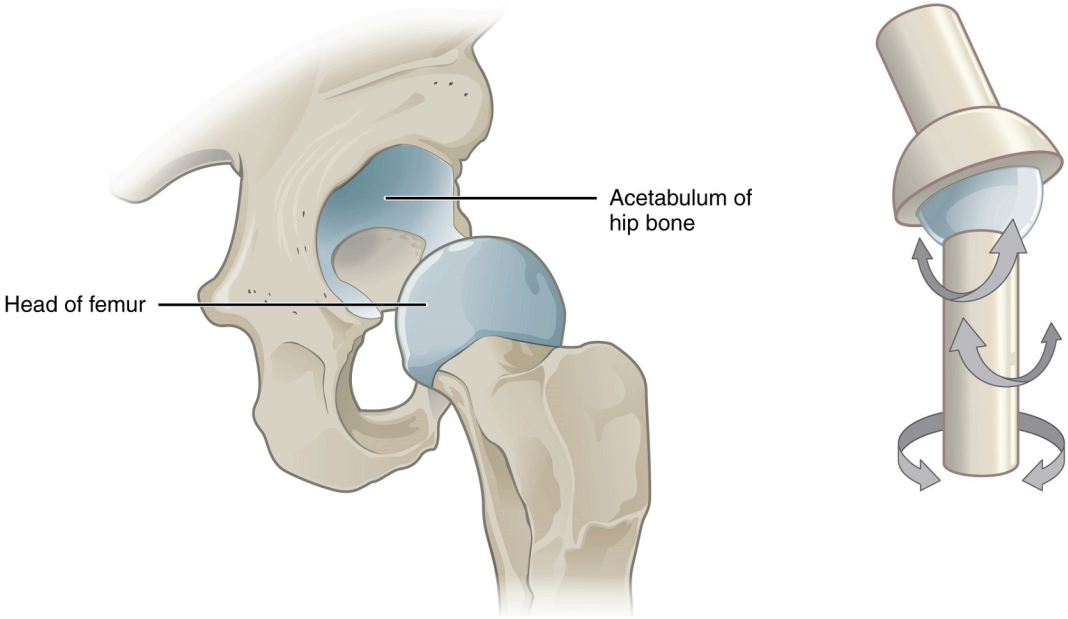


Figure 3. Multiaxial Joint. *A multiaxial joint, such as the hip joint, allows for three types of movement: anterior-posterior, medial-lateral, and rotational.*

Watch this CrashCourse video to learn more about joints! Direct link: https://youtu.be/DLxYDoN634c

Part 2: Fibrous Joints

At a fibrous joint, the adjacent bones are directly connected to each other by fibrous connective tissue, and thus the bones do not have a joint cavity between them (Figure 4). The gap between the bones may be narrow or wide. There are three types of fibrous joints. A suture is the narrow fibrous joint found between most bones of the skull. At a syndesmosis joint, the bones are more widely separated but are held together by a narrow band of fibrous connective tissue called a **ligament** or a wide sheet of connective tissue called an interosseous membrane. This type of fibrous joint is found between the shaft regions of the long bones in the forearm and in the leg. Lastly, a gomphosis is the narrow fibrous joint between the roots of a tooth and the bony socket in the jaw into which the tooth fits.

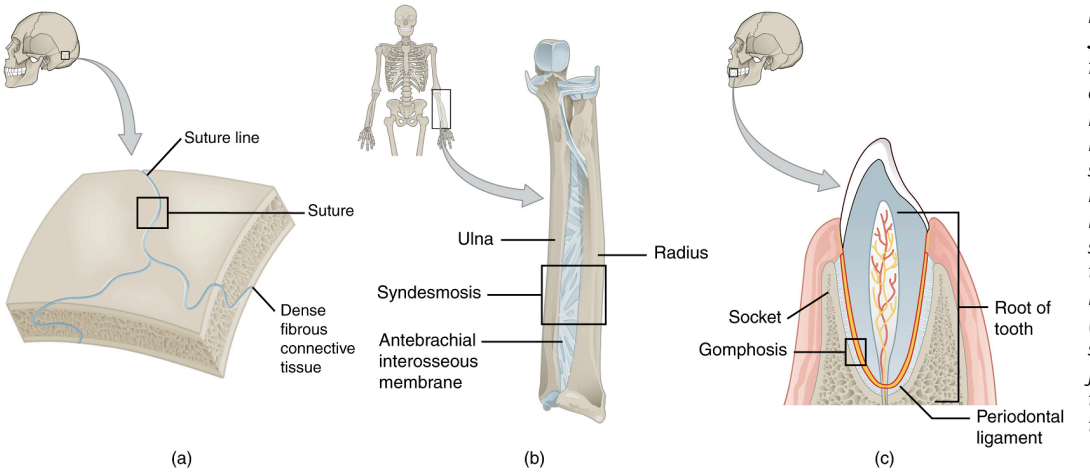


Figure 4. Fibrous Joints. *Fibrous joints form strong connections between bones. (a) Sutures join most bones of the skull. (b) An interosseous membrane forms a syndesmosis between the radius and ulna bones of the forearm. (c) A gomphosis is a specialized fibrous joint that anchors a tooth to its socket in the jaw.*

Suture: All the bones of the skull, except for the mandible, are joined to each other by a fibrous joint called a **suture**. The fibrous connective tissue found at a suture ("to bind or sew") strongly unites the adjacent skull bones and thus helps to protect the brain and form the face. In adults, the skull bones are closely opposed, and fibrous connective tissue fills the narrow gap between the bones. The suture is frequently convoluted, forming a tight union that prevents most movement between the bones (Figure 4a). Thus, skull sutures are functionally classified as a synarthrosis, although some sutures may allow for slight movements between the cranial bones.

At some sutures, the connective tissue will ossify and be converted into bone, causing the adjacent bones to fuse to each other. Examples of fusions between cranial bones are found both early and late in life. At the time of birth, the frontal and maxillary bones consist of right and left halves joined together by sutures, which disappear by the eighth year as the halves fuse together to form a single bone. Late in life, the sagittal, coronal, and lambdoid sutures of the skull will begin to ossify and fuse, causing the suture line to gradually disappear.

Syndesmosis: A **syndesmosis** ("fastened with a band") is a type of fibrous joint in which two parallel bones are united to each other by fibrous connective tissue. The gap between the bones may be narrow, with the

bones joined by ligaments, or the gap may be wide and filled in by a broad sheet of connective tissue called an **interosseous membrane**.

In the forearm, the wide gap between the shaft portions of the radius and ulna bones are strongly united by an interosseous membrane (Figure 4b). Similarly, in the leg, the shafts of the tibia and fibula are also united by an interosseous membrane. In addition, at the distal tibiofibular joint, the articulating surfaces of the bones lack cartilage and the narrow gap between the bones is anchored by fibrous connective tissue and ligaments on both the anterior and posterior aspects of the joint. Together, the interosseous membrane and these ligaments form the tibiofibular syndesmosis.

The syndesmoses found in the forearm and leg serve to unite parallel bones and prevent their separation. However, a syndesmosis does not prevent all movement between the bones, and thus this type of fibrous joint is functionally classified as an amphiarthrosis. In the leg, the syndesmosis between the tibia and fibula strongly unites the bones, allows for little movement, and firmly locks the talus bone in place between the tibia and fibula at the ankle joint. This provides strength and stability to the leg and ankle, which are important during weight bearing. In the forearm, the interosseous membrane is flexible enough to allow for rotation of the radius bone during forearm movements. Thus, in contrast to the stability provided by the tibiofibular syndesmosis, the flexibility of the antebrachial interosseous membrane allows for the much greater mobility of the forearm.

Gomphosis: A **gomphosis** ("fastened with bolts") is the specialized fibrous joint that anchors the root of a tooth into its bony socket within the maxillary bone (upper jaw) or mandible bone (lower jaw) of the skull. A gomphosis is also known as a peg-and-socket joint. Spanning between the bony walls of the socket and the root of the tooth are numerous short bands of dense connective tissue, each of which is called a **periodontal ligament** (see Figure 4c). Due to the immobility of a gomphosis, this type of joint is functionally classified as a synarthrosis.

Part 3: Cartilaginous Joints

As the name indicates, at a cartilaginous joint, the adjacent bones are united by cartilage, a tough but flexible type of connective tissue.

These types of joints lack a joint cavity and involve bones that are joined together by either hyaline cartilage or fibrocartilage (Figure 5). There are two types of cartilaginous joints. A synchondrosis is a cartilaginous joint where the bones are joined by hyaline cartilage. Also classified as a synchondrosis are places where bone is united to a cartilage structure, such as between the anterior end of a rib and the costal cartilage of the thoracic cage. The second type of cartilaginous joint is a symphysis, where the bones are joined by fibrocartilage.

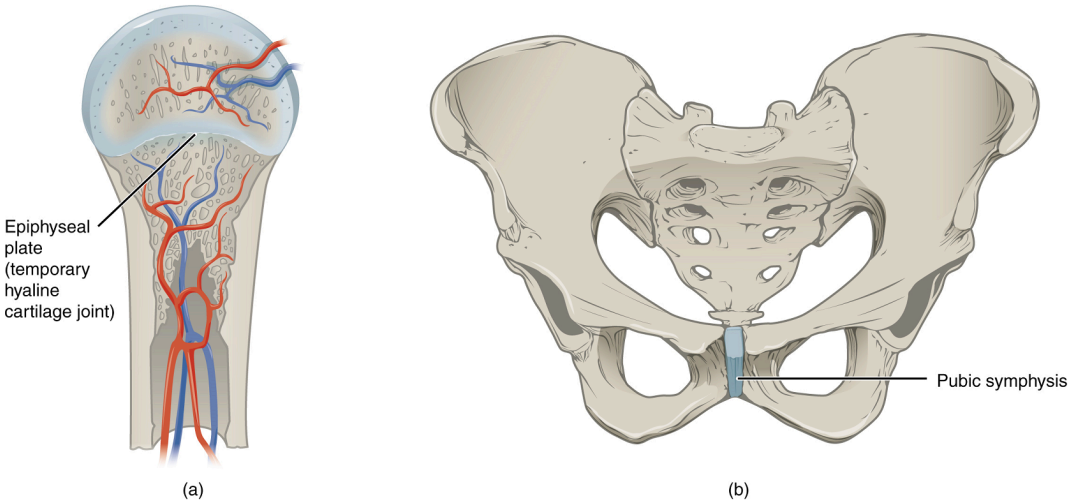


Figure 5. Cartilaginous Joints. *At cartilaginous joints, bones are united by hyaline cartilage to form a synchondrosis or by fibrocartilage to form a symphysis. (a) The hyaline cartilage of the epiphyseal plate (growth plate) forms a synchondrosis that unites the shaft (diaphysis) and end (epiphysis) of a long bone and allows the bone to grow in length. (b) The pubic portions of the right and left hip bones of the pelvis are joined together by fibrocartilage, forming the pubic symphysis.*

Synchondrosis: A **synchondrosis** ("joined by cartilage") is a cartilaginous joint where bones are joined together by hyaline cartilage, or where bone is united to hyaline cartilage. A synchondrosis may be temporary or permanent. A temporary synchondrosis is the epiphyseal plate (growth plate) of a growing long bone. The epiphyseal plate is the region of growing hyaline cartilage that unites the diaphysis (shaft) of the bone to the epiphysis (end of the bone). Bone lengthening involves growth of the epiphyseal plate cartilage and its replacement by bone, which adds to the diaphysis. For many years during childhood growth, the rates of cartilage growth and bone formation are equal and thus the epiphyseal plate does not change in overall thickness as the bone lengthens. During the late teens and early 20s, growth of the cartilage slows and eventually stops. The epiphyseal plate is then completely replaced by bone, and the diaphysis and epiphysis portions of the bone fuse together to form a single adult bone. Once this occurs, bone lengthening ceases. For this reason, the epiphyseal plate is considered to be a temporary synchondrosis. Because cartilage is softer than bone tissue, injury to a growing long bone can damage the epiphyseal plate cartilage, thus stopping bone growth and preventing additional bone lengthening.

Growing layers of cartilage also form synchondroses that join together the ilium, ischium, and pubic portions of the hip bone during childhood and adolescence. When body growth stops, the cartilage disappears and is replaced by bone, forming synostoses and fusing the bony components together into the single hip bone of the adult. Similarly, the sacral vertebrae fuse together to form the adult sacrum.

Examples of permanent synchondroses are found in the thoracic cage. One example is the first sternocostal joint, where the first rib is anchored to the manubrium by its costal cartilage. (The articulations of the remaining costal cartilages to the sternum are all synovial joints.) Additional synchondroses are formed where the anterior end of the other 11 ribs is joined to its costal cartilage. Unlike the temporary synchondroses of the epiphyseal plate, these permanent synchondroses retain their hyaline cartilage and thus do not ossify with age. Due to the lack of movement between the bone and cartilage, both temporary and permanent synchondroses are functionally classified as a synarthrosis.

Symphysis: A cartilaginous joint where the bones are joined by fibrocartilage is called a **symphysis** ("growing together"). Fibrocartilage is very strong because it contains numerous bundles of thick collagen fibers, thus giving it a much greater ability to resist pulling and bending forces when compared with hyaline cartilage. This gives symphyses the ability to strongly unite the adjacent bones but can still allow for limited movement to occur. Thus, a symphysis is functionally classified as an amphiarthrosis.

The gap separating the bones at a symphysis may be narrow or wide. An example in which the gap between the bones is narrow is the pubic symphysis, where the pubic portions of the right and left hip bones of the pelvis are joined together by fibrocartilage across a narrow gap.

The intervertebral symphysis is a wide symphysis located between the bodies of adjacent vertebrae of the vertebral column. Here a thick pad of fibrocartilage called an intervertebral disc strongly unites the adjacent vertebrae by filling the gap between them. The width of the intervertebral symphysis is important because it allows for small movements between the adjacent vertebrae. In addition, the thick intervertebral disc provides cushioning between the vertebrae, which is important when carrying heavy objects or during high-impact activities such as running or jumping.

Part 4: Synovial Joints

Synovial joints are the most common type of joint in the body (Figure 6). A key structural characteristic for a synovial joint that is not seen at fibrous or cartilaginous joints is the presence of a joint cavity. This fluid-filled space is the site at which the articulating surfaces of the bones contact each other. Also, unlike fibrous or cartilaginous joints, the articulating bone surfaces at a synovial joint are not directly connected to each other with fibrous connective tissue or cartilage. This gives the bones of a synovial joint the ability to move smoothly against each other, allowing for increased joint mobility.

Structural Features of Synovial Joints: Synovial joints are characterized by the presence of a joint cavity. The walls of this space are formed by the **articular capsule**, a fibrous connective tissue structure that is attached to

each bone just outside the area of the bone's articulating surface. The bones of the joint articulate with each other within the joint cavity.

Friction between the bones at a synovial joint is prevented by the presence of the **articular cartilage**, a thin layer of hyaline cartilage that covers the entire articulating surface of each bone. However, unlike at a cartilaginous joint, the articular cartilages of each bone are not continuous with each other. Instead, the articular cartilage acts like a Teflon® coating over the bone surface, allowing the articulating bones to move smoothly against each other without damaging the underlying bone tissue. Lining the inner surface of the articular capsule is a thin **synovial membrane**. The cells of this membrane secrete **synovial fluid** (synovia = "a thick fluid"), a thick, slimy fluid that provides lubrication to further reduce friction between the bones of the joint. This fluid also provides nourishment to the articular cartilage, which does not contain blood vessels. The ability of the bones to move smoothly against each other within the joint cavity, and the freedom of joint movement this provides, means that each synovial joint is functionally classified as a diarthrosis.

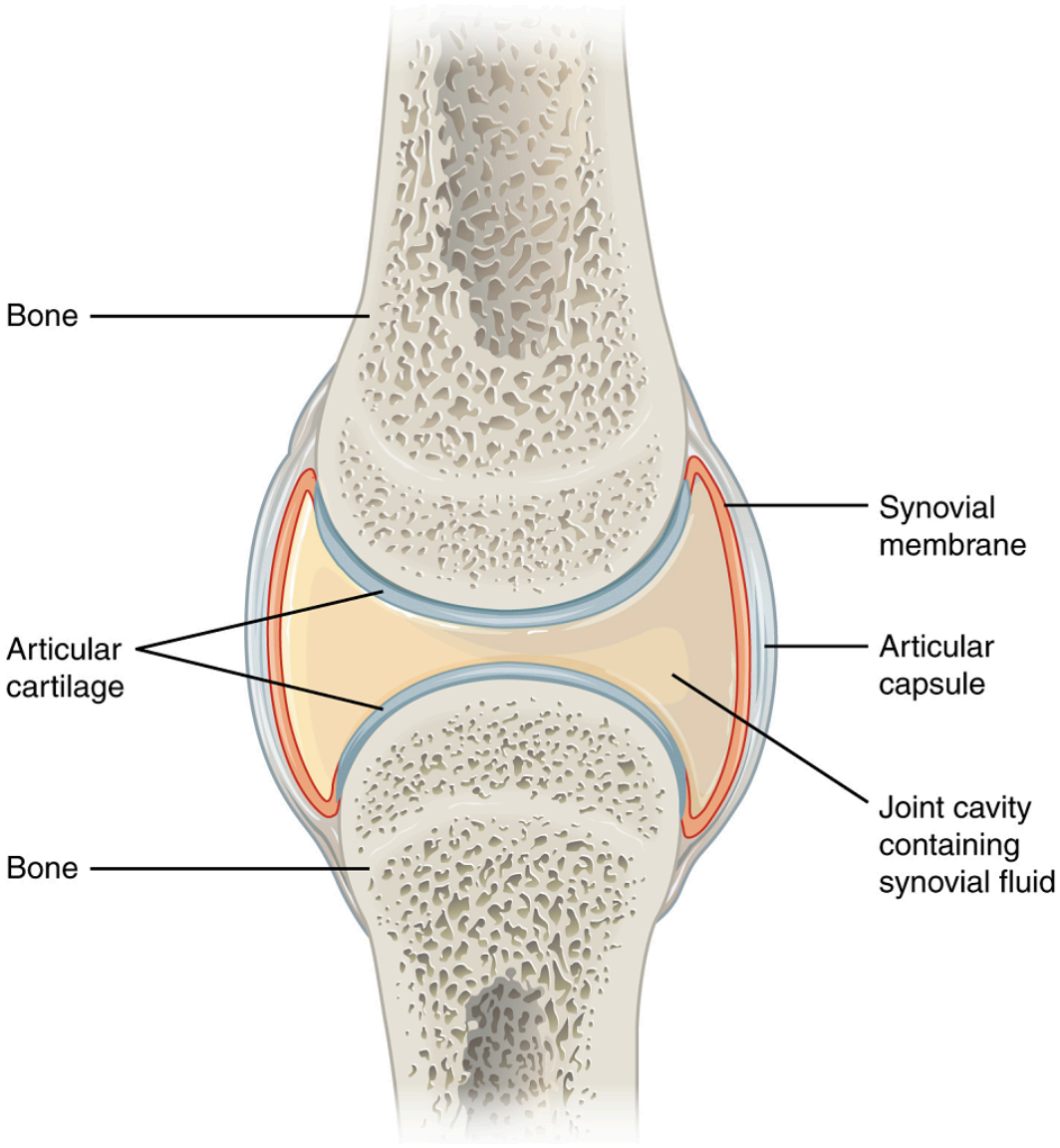


Figure 6. Synovial Joints. *Synovial joints allow for smooth movements between the adjacent bones. The joint is surrounded by an articular capsule that defines a joint cavity filled with synovial fluid. The articulating surfaces of the bones are covered by a thin layer of articular cartilage. Ligaments support the joint by holding the bones together and resisting excess or abnormal joint motions.*

Outside of their articulating surfaces, the bones are connected together by **ligaments,** which are strong bands of fibrous connective tissue. These strengthen and support the joint by anchoring the bones together and

preventing their separation. Ligaments allow for normal movements at a joint, but limit the range of these motions, thus preventing excessive or abnormal joint movements.

At many synovial joints, additional support is provided by the muscles and their tendons that act across the joint. A **tendon** is the dense connective tissue structure that attaches a muscle to bone. As forces acting on a joint increase, the body will automatically increase the overall strength of contraction of the muscles crossing that joint, thus allowing the muscle and its tendon to serve as a "dynamic ligament" to resist forces and support the joint. This type of indirect support by muscles is very important at the shoulder joint, for example, where the ligaments are relatively weak.

Additional Structures Associated with Synovial Joints: A few synovial joints of the body have a fibrocartilage structure located between the articulating bones. This is called an **articular disc**, which is generally small and oval-shaped, or a **meniscus**, which is larger and C-shaped. These structures can serve several functions, depending on the specific joint. In some places, an articular disc may act to strongly unite the bones of the joint to each other. Examples of this include the articular discs found at the sternoclavicular joint or between the distal ends of the radius and ulna bones. At other synovial joints, the disc can provide shock absorption and cushioning between the bones, which is the function of each meniscus within the knee joint. Finally, an articular disc can serve to smooth the movements between the articulating bones, as seen at the temporomandibular joint. Some synovial joints also have a fat pad, which can serve as a cushion between the bones.

Additional structures located outside of a synovial joint serve to prevent friction between the bones of the joint and the overlying muscle tendons or skin. A **bursa** (plural = bursae) is a thin connective tissue sac filled with lubricating liquid. They are located in regions where skin, ligaments, muscles, or muscle tendons can rub against each other, usually near a body joint (Figure 7). Bursae reduce friction by separating the adjacent structures, preventing them from rubbing directly against each other.

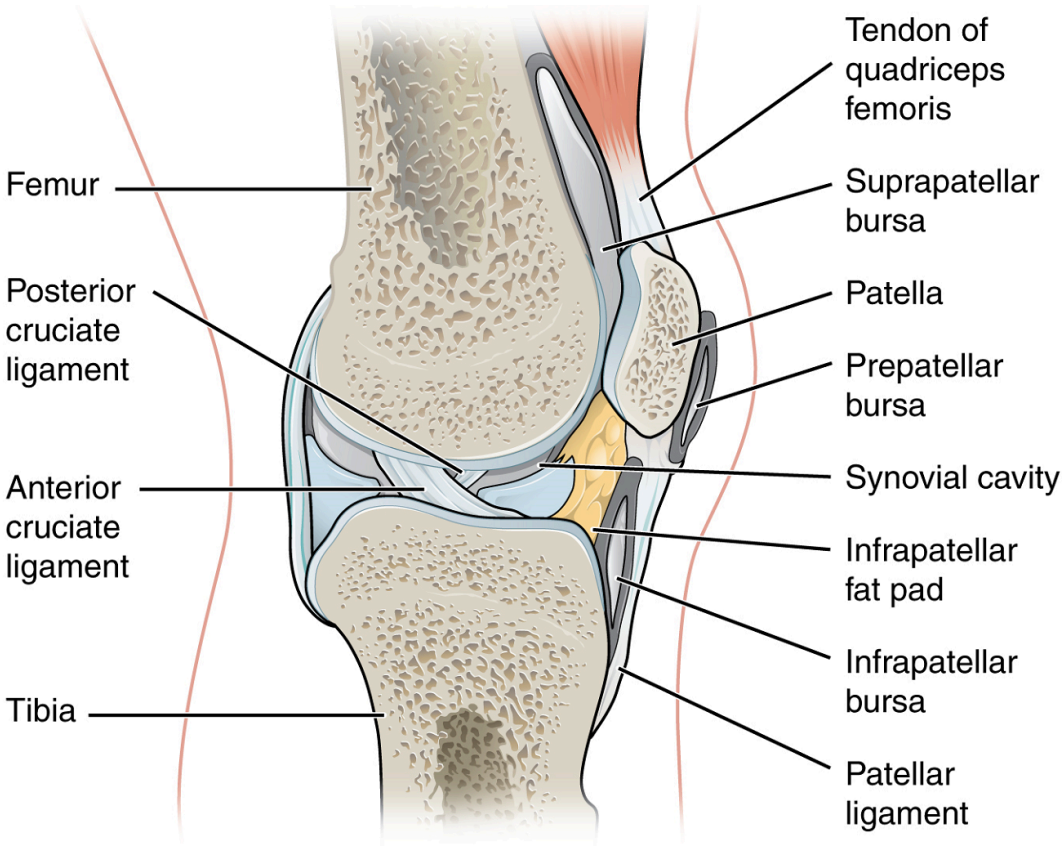


Figure 7. Bursae. *Bursae are fluid-filled sacs that serve to prevent friction between skin, muscle, or tendon and an underlying bone. Three major bursae and a fat pad are part of the complex joint that unites the femur and tibia of the leg.*

Types of Synovial Joints: Synovial joints are subdivided based on the shapes of the articulating surfaces of the bones that form each joint. The six types of synovial joints are pivot, hinge, condyloid, saddle, plane (gliding), and ball-and socket-joints (Figure 8).

1. Pivot Joint: At a **pivot joint**, a rounded portion of a bone is enclosed within a ring formed partially by the articulation with another bone and partially by a ligament (Figure 8a). The bone rotates within this ring. Since the rotation is around a single axis, pivot joints are functionally classified as a uniaxial joint. An example of a pivot joint is the atlantoaxial joint, found between the C1 (atlas) and C2 (axis) vertebrae. Here, the upward projecting dens of the axis articulates with the inner aspect of the atlas, where it is held in place by a ligament. Rotation at this joint allows you to turn your head from side to side. A second pivot joint is found at the **proximal radioulnar joint**. Here, the head of the radius is largely encircled by a ligament that holds it in place as it articulates with the radial notch of the ulna. Rotation of the radius allows for forearm movements.

2. Hinge Joint: In a **hinge joint**, the convex end of one bone articulates with the concave end of the adjoining bone (Figure 8b). This type of joint allows only for angular movements – bending and straightening motions along a single axis – and thus hinge joints are functionally classified as uniaxial joints. A good example is the elbow joint, with the articulation between the humerus and the ulna. Other hinge joints of the body include the knee, ankle, and interphalangeal joints between the phalanx bones of the fingers and toes.

3. Condyloid Joint: At a **condyloid joint** (ellipsoid joint), the shallow depression at the end of one bone articulates with a rounded structure from an adjacent bone or bones (Figure 8e). The knuckle (metacarpophalangeal) joints of the hand between the distal end of a metacarpal bone and the proximal phalanx bone are condyloid joints. Another example is the radiocarpal joint of the wrist, between the shallow depression at the distal end of the radius bone and three of the carpal bones. In this case, the articulation area has a more oval (elliptical) shape. Functionally, condyloid joints are biaxial joints that allow for two planes of angular movement. One movement involves the bending and straightening of the fingers or the anterior-posterior movements of the hand. The second movement is a side-to-side movement, which allows you to spread your fingers apart and bring them together, or to move your hand in a medial-going or lateral-going direction.

4. Saddle Joint: At a saddle joint, both of the articulating surfaces for the bones have a saddle shape, which is concave in one direction and convex in the other (Figure 8c). This allows the two bones to fit together like a rider sitting on a saddle. Saddle joints are functionally classified as biaxial joints. The primary example is the first carpometacarpal joint, between the trapezium (a carpal bone) and the first metacarpal bone at the base of the thumb. This joint provides the thumb the ability for angular movement away from the palm of the hand along two planes. Thus, the thumb can move within the same plane as the palm of the hand, or it can jut out anteriorly, perpendicular to the palm. This movement of the first carpometacarpal joint is what gives humans their distinctive “opposable” thumbs. The sternoclavicular joint is also classified as a saddle joint.

5. Plane Joint: At a **plane joint** (gliding joint), the articulating surfaces of the bones are flat or slightly curved and of approximately the same size, which allows for predominantly gliding movement where the bones slide back and forth against each other (Figure 8d). The motion at this type of joint is usually small and tightly constrained by surrounding ligaments. It is worth noting that based only on their shape, plane joints have the ability to allow multiple movements, including rotation. Thus, plane joints can be functionally classified as a multiaxial joint. However, not all of these movements are available to every plane joint due to limitations placed on it by ligaments or neighboring bones. Thus, depending upon the specific joint of the body, a plane joint may exhibit only a single type of movement or several movements. Plane joints are found between the carpal bones (intercarpal joints) of the wrist or tarsal bones (intertarsal joints) of the foot, between the clavicle and acromion of the scapula (acromioclavicular joint), and between the superior and inferior articular processes of adjacent vertebrae (zygapophysial joints).

6. Ball-and-Socket Joint: The joint with the greatest range of motion is the **ball-and-socket joint**. At these joints, the rounded head of one bone (the ball) fits into the concave articulation (the socket) of the adjacent bone (Figure 8f). The hip joint and the glenohumeral (shoulder) joint are the only ball-and-socket joints of

the body. At the hip joint, the head of the femur articulates with the acetabulum of the hip bone, and at the shoulder joint, the head of the humerus articulates with the glenoid cavity of the scapula.

Ball-and-socket joints are classified functionally as multiaxial joints. The femur and the humerus are able to effect angular movements in both anterior-posterior and medial-lateral directions and they can also rotate around their long axis. These multiaxial joints also allow for a complex movement called circumduction. In this instance, the distal end of the bone moves in a circle while the proximal end remains relatively stationary. Circumduction of the arm and leg are possible at ball-and-socket joints.

The shallow socket formed by the glenoid cavity allows the shoulder joint an extensive range of motion. In contrast, the deep socket of the acetabulum and the strong supporting ligaments of the hip joint serve to constrain movements of the femur, reflecting the need for stability and weight-bearing ability at the hip.

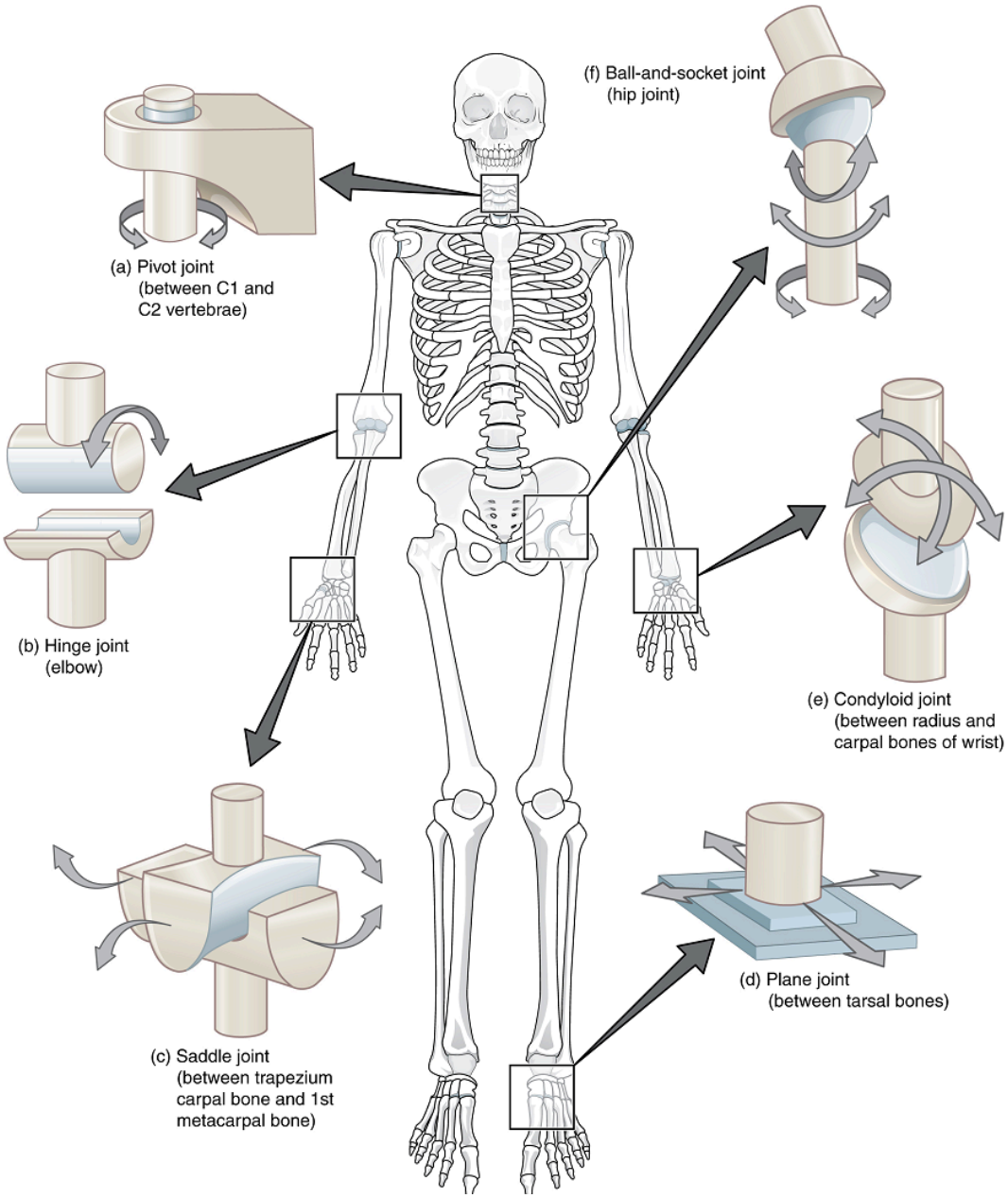


Figure 8. Types of Synovial Joints. *The six types of synovial joints allow the body to move in a variety of ways. (a) Pivot joints allow for rotation around an axis, such as between the first and second cervical vertebrae, which allows for side-to-side rotation of the head. (b) The hinge joint of the elbow works like a door hinge. (c) The articulation between the trapezium carpal bone and the first metacarpal bone at the base of the thumb is a saddle joint. (d) Plane joints, such as those between the tarsal bones of the foot, allow for limited gliding movements between bones. (e) The radiocarpal joint of the wrist is a condyloid joint. (f) The hip and shoulder joints are the only ball-and-socket joints of the body.*

Unit 14: Biomechanics

Unit Outline

Part 1: Skeletal muscle anatomy

- Attachments to skeleton
- Muscular antagonism
- Muscles without attachments to the skeleton

Part 2: Lever systems

- General characteristics
- First-class levers
- Second-class levers
- Third-class levers

Learning Objectives

At the end of this unit, you should be able to:

I. Describe how muscles attach to bones to produce movement.

II. Describe the principle of muscular antagonism in movement, using the forearm as an example.

III. Define the following terms: lever, fulcrum, resistance, effort.

IV. Describe three types of levers and give an example of each type in the human body.

V. Explain the biomechanical principles and functioning of a lever system.

Learning Objectives and Guiding Questions

At the end of this unit, you should be able to complete all the following tasks, including answering the guiding questions associated with each task.

I. Describe how muscles attach to bones to produce movement.

1. Use one complete sentence to describe the function of a tendon (See Unit 6).
2. State the specific tissue type of which tendons are composed (See Unit 6).
3. Describe the location of and relationship between the origin and the insertion of a muscle, to explain how muscles move bones.

II. Describe the principle of muscular antagonism in movement, using the forearm as an example.

1. Define the terms 'agonist' and 'antagonist' as they pertain to specific movements and muscles.
2. Using the elbow joint as a specific example, explain how antagonistic pairs of muscles produce a movement about a joint.

III. Define the following terms: lever, fulcrum, resistance, effort.

1. Draw an annotated diagram of a lever system. Your diagram should show where along a lever each major component acts, along with single-sentence definitions for each of these terms:
    - Lever
    - Fulcrum
    - Resistance
    - Effort

IV. Describe three types of levers and give an example of each type in the human body.

1. Draw annotated diagrams of each of the three classes of levers, showing the major components of a lever system as well as the location where the effort and resistance are applied. Provide one specific example of each class of lever found in the human body.
2. Draw an annotated diagram of each of the following movements, describing each as a lever system. Each diagram should include labels identifying the main components (bone, muscle, joint, force), both as part of a lever system (using the terms lever, fulcrum, resistance, effort) and by their correct anatomical name (for bones and muscles).
    - Bending the elbow (flexion at the elbow).
    - Starting with the head tilted forward, tilt the head upwards (extension of the head).
    - Standing on your toes (extension at the ankle).
3. Clearly indicate the following on each diagram from the question above:
    - The exact location where the resistance is applied to the lever
    - The exact location where the effort is applied to the lever
    - The resistance arm
    - The effort arm
4. Draw annotated diagrams to demonstrate whether each of the three classes of levers can be a power lever, a speed lever, both, or neither.

V. Explain the biomechanical principles and functioning of a lever system.

1. Using the flexion of the forearm as an example, explain how a lever system is used to move body parts or maintain the posture of body parts.
2. Describe one mechanical disadvantage and two mechanical advantages of the insertion of the

biceps brachii being near the elbow joint.

3. Calculate the relationships between forces and distances in a lever system using particular examples.
4. Draw a straight horizontal line representing a forearm. This line shows the distance from the elbow joint to a weight held in the hand (length = 35 cm). Draw an arrow at one end of the line representing the elbow joint, and a square at the opposite end of the line representing the weight to be lifted. The weight will be lifted through the actions of the biceps brachii muscle. Assuming the distance between the elbow joint and the insertion point of the biceps brachii is 5 cm, add a circle to your horizontal line at the location where the biceps brachii inserts onto the radius. *Note: what matters here is the location of the insertion point of a muscle onto a bone, not the location or orientation of the muscle itself.*
5. Then, report the following for the lever system described above:

    a. The length of the resistance arm, in cm
    b. The length of the effort arm, in cm
    c. The effort exerted by the biceps brachii, if the resistance is:

        - 1 kg
        - 10 kg
        - 25 kg

    d. The effort exerted by the biceps brachii to lift a resistance of 10 kg, if the distance between the elbow joint and the insertion point of the biceps brachii remains the same (5 cm), but the total length of the forearm is:

        - 25 cm
        - 35 cm
        - 50 cm

    e. The effort exerted by the biceps brachii to lift a resistance of 10 kg, if the total length of the forearm remains the same (35 cm) but the distance between the elbow joint and the insertion point of the biceps brachii is:

        - 1 cm
        - 5 cm
        - 7 cm
        - 28 cm

6. Using your diagram and your results from the above calculations, explain the following:

    - Whether more or less effort is required to move the weight in the hand, when the biceps brachii's insertion point is relatively close to the elbow vs. further away.
    - Whether the weight in the hand moves a greater or lesser distance when the same amount of effort is exerted by the biceps brachii, but the effort arm varies in length.
    - Whether the weight in the hand would move faster or slower when the same amount of effort is exerted by the biceps brachii over the same period of time, but the effort arm varies in length.

Part 1: Skeletal Muscle Anatomy

Interactions of Skeletal Muscles, Their Fascicle Arrangement, and Their Lever Systems: To move the skeleton, the tension created by the contraction of the fibers in most skeletal muscles is transferred to the tendons. The tendons are strong bands of dense, regular connective tissue that connect muscles to bones. The bone connection is why this muscle tissue is called skeletal muscle.

Interactions between Skeletal Muscles in the Body: To pull on a bone, that is, to change the angle at its synovial joint, which essentially moves the skeleton, a skeletal muscle must be attached to a fixed part of the skeleton. The moveable end of the muscle which attaches to the bone being pulled is called the muscle's **insertion**, whereas the end of the muscle attached to a fixed (stabilized) bone is called the **origin**.

Although a number of muscles may be involved in an action, the principal muscle involved is called the **prime mover**, or **agonist**. To lift a cup, a muscle called the biceps brachii is the prime mover; however, because this muscle can be assisted by the brachialis, the brachialis is called a **synergist** in this action (Figure 1). A synergist can also be a **fixator** which stabilizes the bone that is the attachment for the prime mover's origin.

A muscle with the opposite action of the prime mover is called an **antagonist**. Antagonists play two important roles in muscle function: (1) they maintain body or limb position, such as holding the arm out or standing erect; and (2) they control rapid movement as in shadow boxing without landing a punch, and thereby check the motion of a limb.

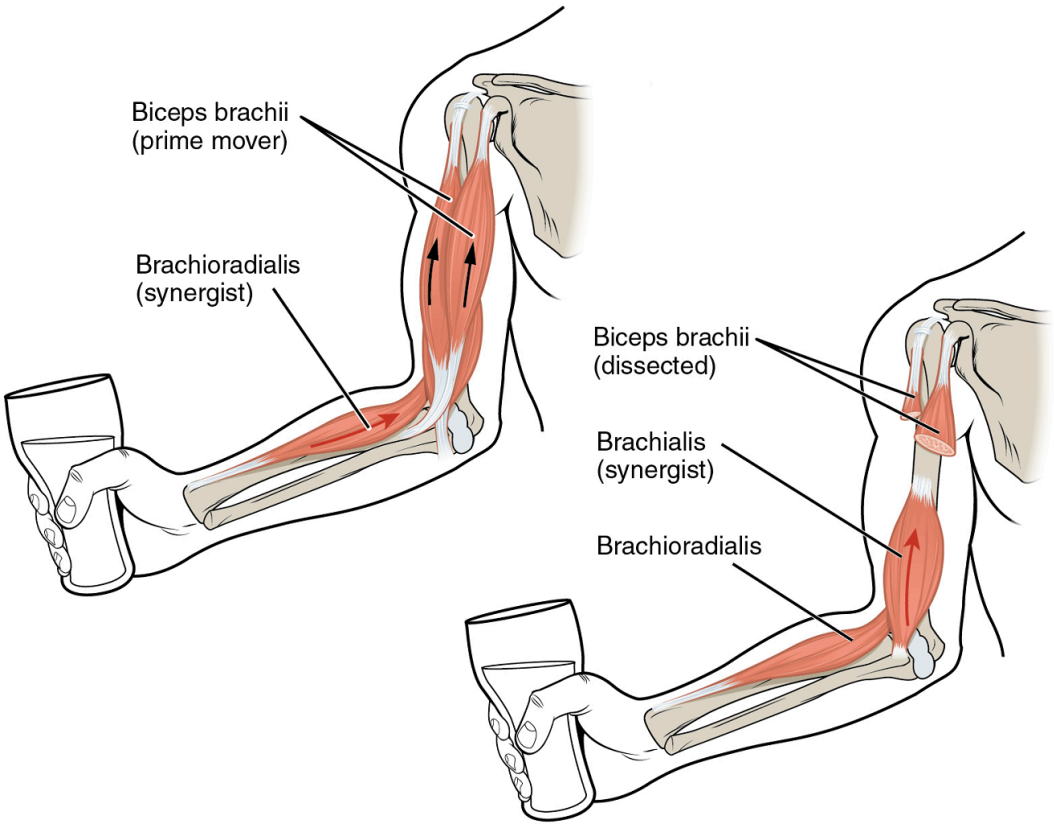


Figure 1. Prime Movers and Synergists. *The biceps brachii flexes the lower arm. The brachoradialis, in the forearm, and brachialis, located deep to the biceps brachii in the upper arm, are both synergists that aid in this motion.*

For example, to extend the knee, a group of four muscles called the quadriceps femoris in the anterior compartment of the thigh is activated. These muscles would be called the agonists of knee extension. However, to flex the knee, an opposite or antagonistic set of muscles called the hamstrings is activated. Flexing the knee involves the hamstrings muscles as the agonists and the quadriceps femoris muscles as the antagonists. As you can see, the terms agonist and antagonist are associated with a particular movement, and these terms can be reversed for opposing movements. See Table 1 for a list of some common agonists and antagonists.

Table 1: Select Agonist and Antagonist Skeletal Muscle Pairs

Agonist	Antagonist	Movement
Biceps brachii (in anterior compartment of arm)	Triceps brachii (in posterior compartment of arm)	The biceps brachii flexes the forearm, whereas the triceps brachii extends it
Hamstrings (group of three muscles in the posterior compartment of thigh)	Quadriceps femoris (group of four muscles in anterior compartment of thigh)	The hamstrings flex the leg, whereas the quadriceps femoris extend it
Flexor digitorum superficialis and flexor digitorum profundus (in anterior compartment of forearm)	Extensor digitorum (in posterior compartment of forearm)	The flexor digitorum superficialis & profundus flex the fingers and hand at the wrist, whereas the extensor digitorum extends the fingers and hand at the wrist

Some skeletal muscles do not pull on the skeleton to cause movements. For example, the muscles that produce facial expressions have their insertions and origins in the skin, and particular muscles contract to form a smile or frown, form sounds or words, or raise the eyebrows. There are also such skeletal muscles in the tongue, as well as in the external urinary and anal sphincters that allow for voluntary regulation of urination and defecation, respectively. Another example is the diaphragm, which contracts and relaxes to change the volume of the pleural cavities without moving the skeleton.

Part 2: Lever Systems

Skeletal muscles do not work by themselves. Muscles are arranged in pairs based on their functions. For muscles attached to the bones of the skeleton, the connection determines the force, speed and range of movement. These characteristics depend on one another and can explain the general organization of the muscular and skeletal systems.

The skeleton and muscles act together to move the body. Have you ever used the back of a hammer to remove a nail from wood? The handle acts as a lever and the head of the hammer acts as a fulcrum, the fixed point that the force is applied to when you pull back or push down on the handle. The effort applied to this system is the pulling or pushing on the handle to remove the nail, which is the resistance to the movement of the handle in the system. The resistance is also sometimes called the load. Our musculoskeletal system works in a similar manner, with bones being stiff levers and the articular endings of the bones—encased in synovial joints—acting as fulcrums. The resistance would be an object or body part being moved, or any resistance to a movement (e.g. your head when you are lifting it). The effort, or applied force, comes from contracting particular skeletal muscles.

The characteristics and operation of a particular lever system are mainly determined by distances and forces. The two opposing forces are the effort and resistance. There are two main distances to consider: (1) the effort arm, which is the distance from the fulcrum to the insertion point of the skeletal muscle delivering most of the effort, and (2) the resistance arm, which is the distance between the fulcrum and the bulk of the resistance.

In order for movement to occur (e.g. when lifting a weight in your hand), the effort produced by one or several muscles needs to overcome the resistance. When the lever system is balanced, the two opposing forces applied at their respective distances from the fulcrum work to maintain a body posture or carry a particular weight without moving it. Thus, in a balanced lever system, the effort times the effort arm is equal to the resistance times the resistance arm. This is the basic formula used to calculate relationships between forces and distances in a lever system:

Effort x Effort arm = Resistance x Resistance arm

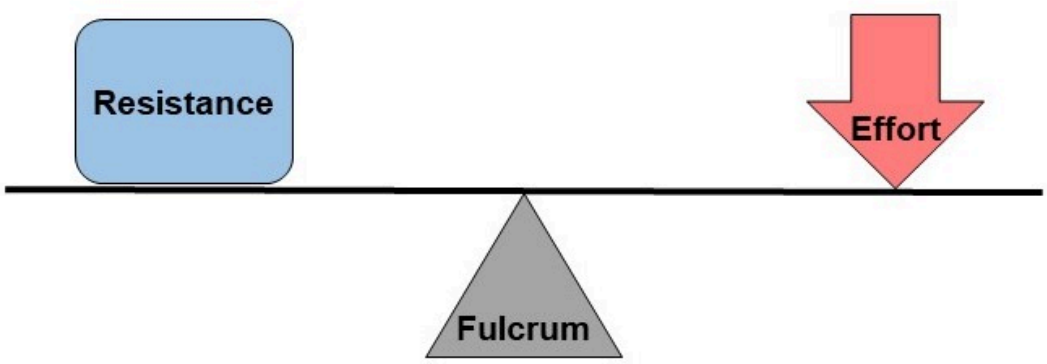
Lever systems that can move heavy loads over short distances using little effort are referred to as “power levers”. Conversely, lever systems that can quickly move light loads over large distances using a large amount of effort are referred to as “speed levers”. The location of the insertion point of a muscle (or muscles) delivering the effort relative to the resistance determines whether a lever system operates as a power lever or speed lever. For example, a lever system with a muscle insertion point close to the joint (fulcrum) and a resistance far away from the joint will move a particular object relatively fast over a large distance with a great range of motion. However,

the muscle(s) involved need(s) to deliver a large effort for the movement to occur. Another lever system with a resistance close to the fulcrum which is supported by a muscle (or muscles) inserting far away from the fulcrum will require a small effort to support or move the resistance. However, the resistance will only be moved over a short distance and slowly.

There are several types of lever systems in the body, identified as either first-class, second-class or third-class levers.

First-class levers are the simplest types of lever, where the two forces, the effort and the resistance, are applied on opposite sides of the fulcrum (Figure 2). In the body, the best example of a first-class lever is the way your head is raised off your chest (Figure 3). The posterior neck muscles produce the effort, the facial skeleton is the resistance, and the atlanto-occipital joint behaves as the fulcrum.

Figure 2. First-class lever.



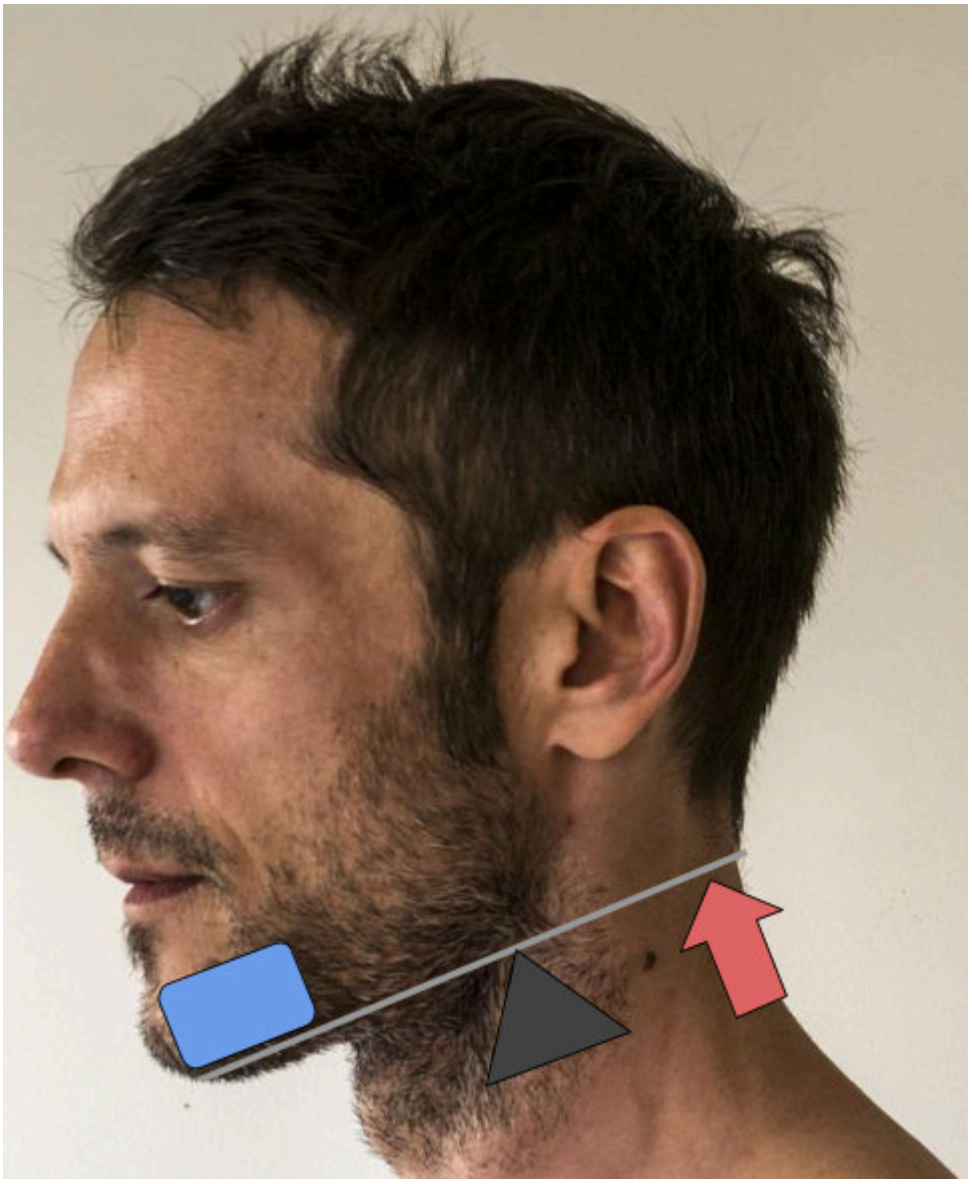
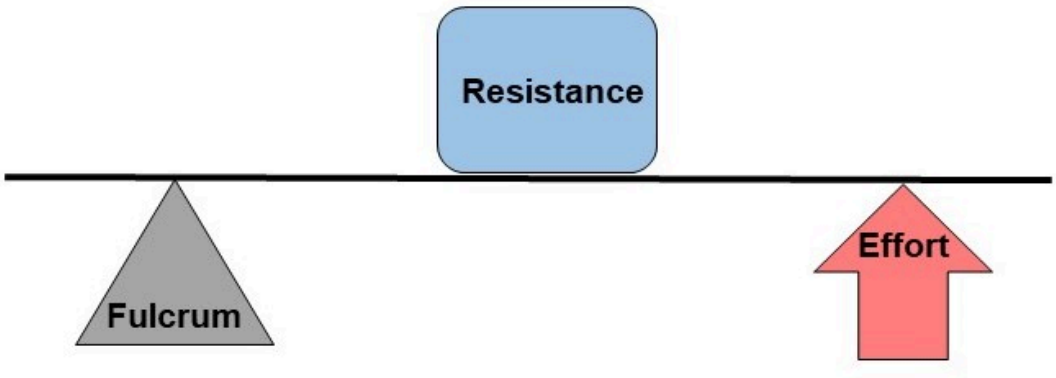


Figure 3. First-class lever as seen in the body. *(credit: sarahmckinnon/ flickr.com, original image: celtibere/ pixabay.com)*

Second-class levers have the resistance between the effort and the fulcrum (Figure 4). The effort is closer to the resistance than the fulcrum, which allows a large resistance to be moved by a small amount of effort. However, this means that the resistance will be moved at a relatively slow pace, and can only be moved a short distance. Any time you stand up on your toes, as shown in Figure 5, you are using a second-class lever. The weight of your body acts as the resistance, your calf muscles produce the effort, and the joints in the balls of your feet act as fulcrums.

Figure 4.
Second-class lever.



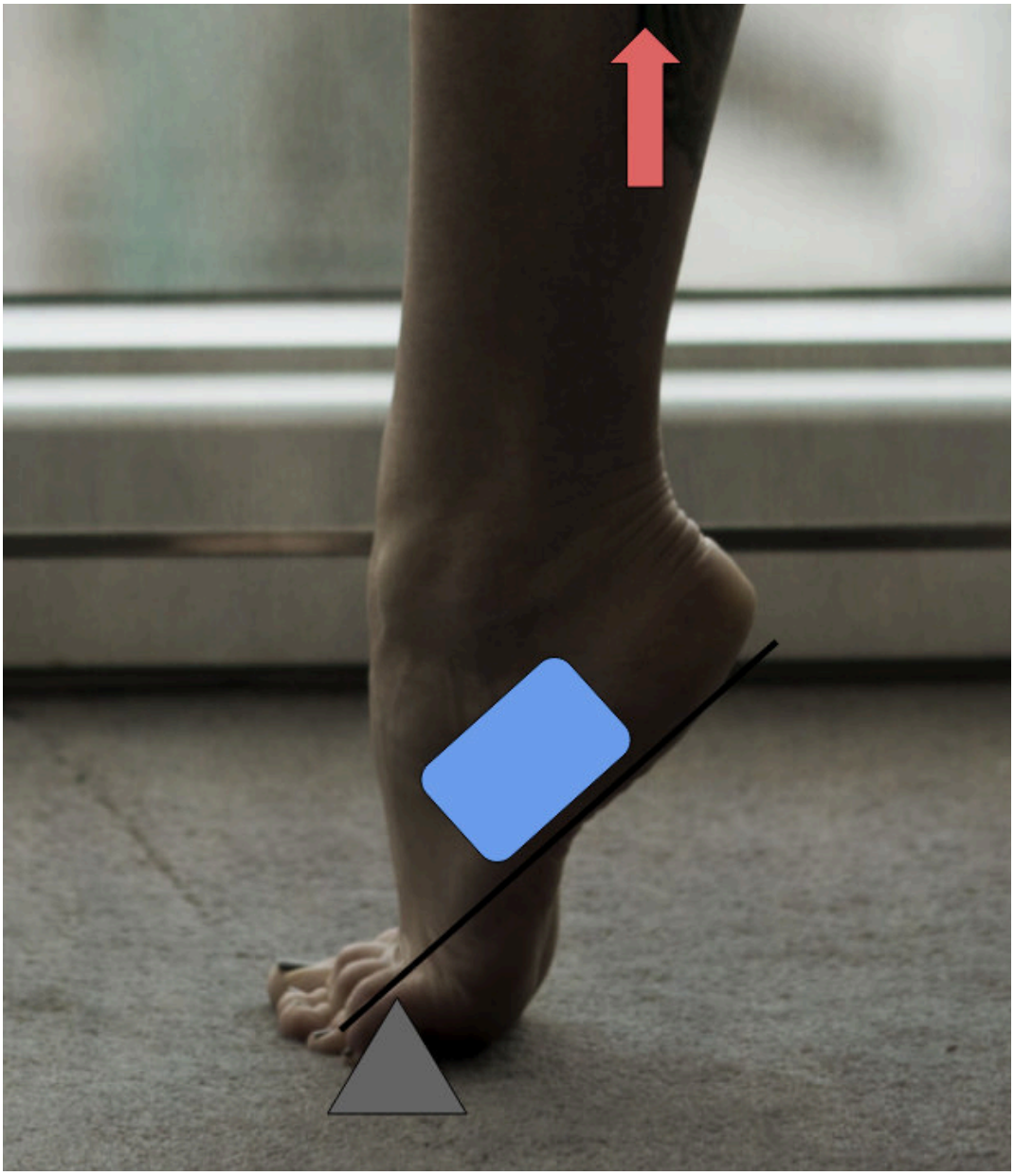
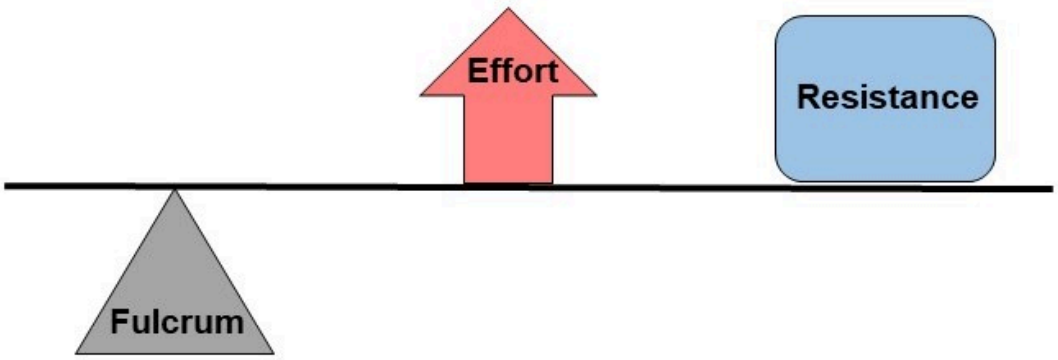


Figure 5. Second-class lever. *(credit: sarahmckinnon/ flickr.com, original image: thenarratographer/ flickr.com)*

Third-class levers are the most common type of levers in your body (Figure 6). The effort is applied between the fulcrum and the resistance, which allows the resistance to be moved relatively quickly over large distances. When you lift your hand by flexing your biceps brachii, you are using a third-class lever. The elbow joint acts as the fulcrum, the biceps brachii produces the effort, and the weight of your hand is the resistance being lifted (Figure 7).

Figure 6. Third-class Lever.



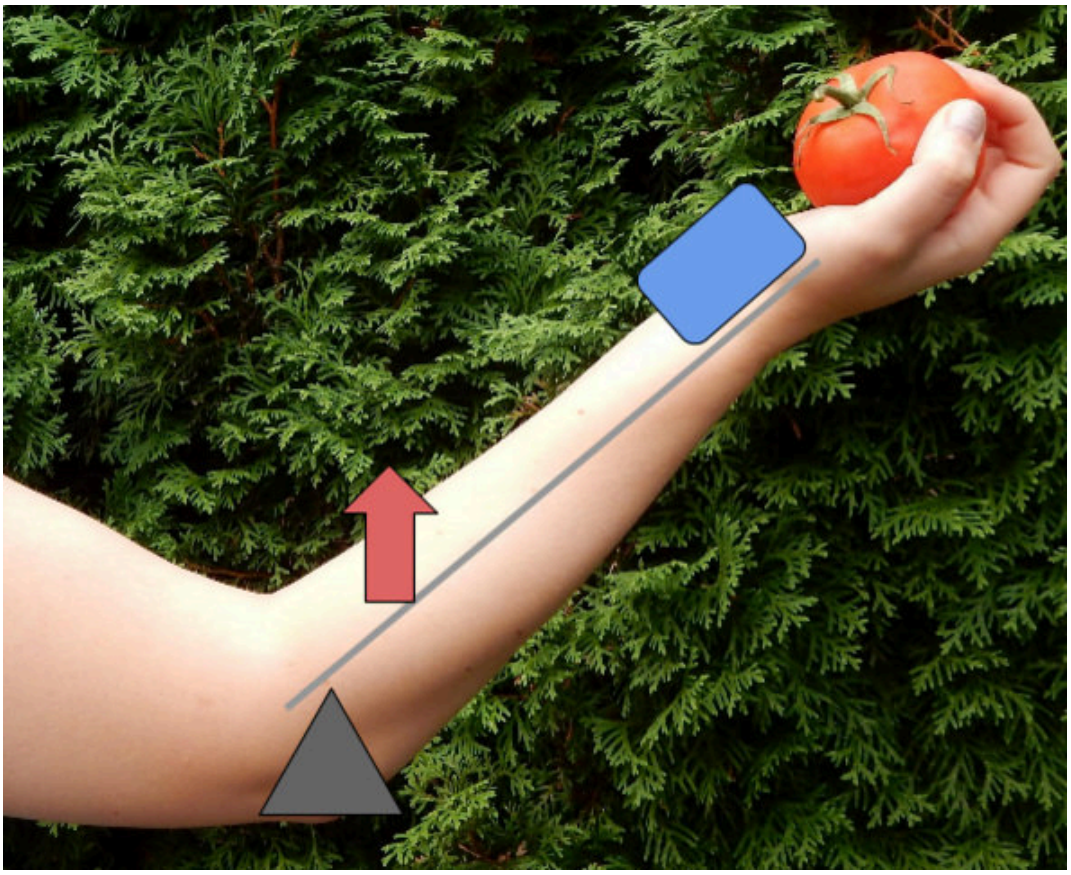


Figure 7. Third-class lever. *(credit: sarahmckinnon/ flickr.com)*

Unit 15: Muscle Anatomy and Movement

Unit outline

Part 1: Muscle Tissue

- Overview of Muscle Tissue
- Skeletal Muscle
- Skeletal Muscle Fibers
- The Sarcomere

Part 2: Types of Movement

- Flexion and Extension
- Hyperextension
- Abduction and Adduction
- Circumduction
- Rotation
- Supination and Pronation
- Plantar flexion and Dorsiflexion
- Protraction and Retraction
- Depression and Elevation

Part 3: The Muscular System

- Naming Skeletal Muscles
- Axial Muscles of the Head, Neck, and Back
    - Muscles that move the Head
    - Muscles of the Posterior Neck and the Back
- Muscles of abdominal wall and Thorax
    - Muscles of the abdomen
    - Muscles of the thorax
        - Diaphragm
        - Intercostal muscles
- Muscles of the pectoral girdle and upper limbs
    - Muscles that position the pectoral girdle
    - Muscles that move the humerus
    - Muscles that move the forearm
- Appendicular Muscles of the Pelvic Girdle and Lower Limbs
    - Muscles that move the thigh

- Gluteal region muscles that move the femur

Learning Objectives

At the end of this unit, you should be able to:

I. Describe the levels of muscle organization: fascia, fascicles, muscle fibres.

II. Describe the following structures of a muscle cell: sarcolemma, sarcoplasm, nuclei, mitochondria, sarcoplasmic reticulum, transverse tubules, myofibrils, myofilaments, sarcomere.

III. Describe the following structures of a sarcomere: Z line, I band, A band, H zone, M line.

IV. Describe the basic structure of the thick and thin filaments and their primary protein components.

V. Specify four factors which determine the type of movement accomplished by a muscle.

VI. Specify some of the criteria used in the naming of muscles.

VII. Describe, using specific examples, 16 types of movements characteristic of skeletal muscle contractions.

Learning Objectives and Guiding Questions

At the end of this unit, you should be able to complete all the following tasks, including answering the guiding questions associated with each task.

I. Describe the levels of muscle organization: fascia, fascicles, muscle fibres.

II. Describe the following structures of a muscle cell: sarcolemma, sarcoplasm, nuclei, mitochondria, sarcoplasmic reticulum, transverse tubules, myofibrils, myofilaments, sarcomere.

1. Define the following terms:
    - Fascia
    - Fascicle
    - Epimysium
    - Perimysium
    - Endomysium

- Muscle fiber
- Muscle cell
- Tendon

2. Explain why skeletal muscle fibers appear to have striations.
3. Describe the location and general structure of each of the following:

- Sarcolemma
- Sarcoplasm
- Sarcoplasmic reticulum
- Sarcomere
- Myofilaments
- Myofibrils
- Transverse tubules

III. Describe the following structures of a sarcomere: Z line, I band, A band, H zone, M line.

1. Draw and fully label a diagram showing two adjacent, relaxed sarcomeres. Your diagram must include (labelled!):

- Z line
- I band
- A band
- H zone
- M line
- Sarcomere width

2. Draw and fully label a diagram showing one fully contracted sarcomere. Your diagram must include labels:

- Z line
- I band
- A band
- H zone
- M line
- Sarcomere width

IV. Describe the basic structure of the thick and thin filaments and their primary protein components.

1. Draw a diagram showing and identifying the major structural components of:

- A single myosin molecule
- A single thick filament
- A single thin filament

V. Specify four factors which determine the type of movement accomplished by a muscle.

1. Define “origin” and “insertion” as these terms pertain to skeletal muscles.
2. Describe how the locations of the origin(s) and insertion(s) of a skeletal muscle affect the

movement produced when that muscle contracts.

3. Describe one specific example of a skeletal muscle that participates in multiple different movements, and then explain how it is possible for a skeletal muscle to participate in multiple different movements.
4. Describe how the movement produced by contraction of a skeletal muscle is influenced by the structure of a joint about which the muscle moves the bone on which it inserts.
5. Describe how tension in ligaments, tendons, and skeletal muscles can limit the range of motion available when a skeletal muscle contracts.

VI. Specify some of the criteria used in the naming of muscles.

1. List, and provide an example for each of, at least seven criteria used to name skeletal muscles.

VII. Describe, using specific examples, 16 types of movements characteristic of skeletal muscle contractions.

1. Clearly define each of the following terms.
    - Flexion
    - Extension
    - Rotation
    - Circumduction
    - Abduction
    - Adduction
    - Elevation
    - Depression
    - Protraction
    - Retraction
    - Eversion
    - Inversion
    - Plantarflexion
    - Dorsiflexion
    - Pronation
    - Supination
2. Clearly describe (including an example of the body part being moved) and distinguish between each of the following pairs of terms:
    - Flexion and extension
    - Adduction and abduction
    - Eversion and inversion
    - Protraction and retraction
    - Rotation and circumduction
    - Plantarflexion and dorsiflexion
    - Elevation and depression
    - Pronation and supination
3. For each of the angular movement terms listed below, describe in detail at least one specific

example of each in the human body. Each example should include the correct anatomical names for the agonist(s), antagonist(s), and joint(s) involved, as well as the origin(s) and insertion(s) of the muscles involved.

- Flexion
- Extension
- Abduction
- Adduction
- Plantarflexion
- Dorsiflexion

4. For each of the complex movements listed below, describe in detail at least one specific example of each in the human body. Each example should include the correct anatomical names for the agonist(s), antagonist(s), and joint(s) involved, as well as the origin(s) and insertion(s) of the muscles involved.

- Rotation
- Circumduction
- Pronation
- Supination
- Eversion
- Inversion
- Elevation
- Depression
- Protraction
- Retraction

Part 1: Muscle Tissue

When most people think of muscles, they think of the muscles that are visible just under the skin, particularly of the limbs. These are skeletal muscles, so-named because most of them move the skeleton. But there are two other types of muscle in the body, with distinctly different jobs. Cardiac muscle, found in the heart, is concerned with pumping blood through the circulatory system. Smooth muscle is concerned with various involuntary movements, such as having one's hair stand on end when cold or frightened, or moving food through the digestive system. This chapter will examine the structure and function of these three types of muscles.

Overview of Muscle Tissues: Muscle is one of the four primary tissue types of the body, and the body contains three types of muscle tissue: skeletal muscle, cardiac muscle, and smooth muscle (Figure 1). All three muscle tissues have some properties in common; they all exhibit a quality called **excitability** as their plasma membranes can change their electrical states (from polarized to depolarized) and send an electrical wave called an action potential along the entire length of the membrane. While the nervous system can influence the excitability of cardiac and smooth muscle to some degree, skeletal muscle completely depends on signaling from the nervous system to work properly. On the other hand, both cardiac muscle and smooth muscle can respond to other stimuli, such as hormones and local stimuli.

The processes of muscle contraction (shortening) and relaxation (return to its resting length) will be studied in the next chapter. A muscle can return to its original length when relaxed due to a quality of muscle tissue called **elasticity**. It can recoil back to its original length due to elastic fibers. Muscle tissue also has the quality

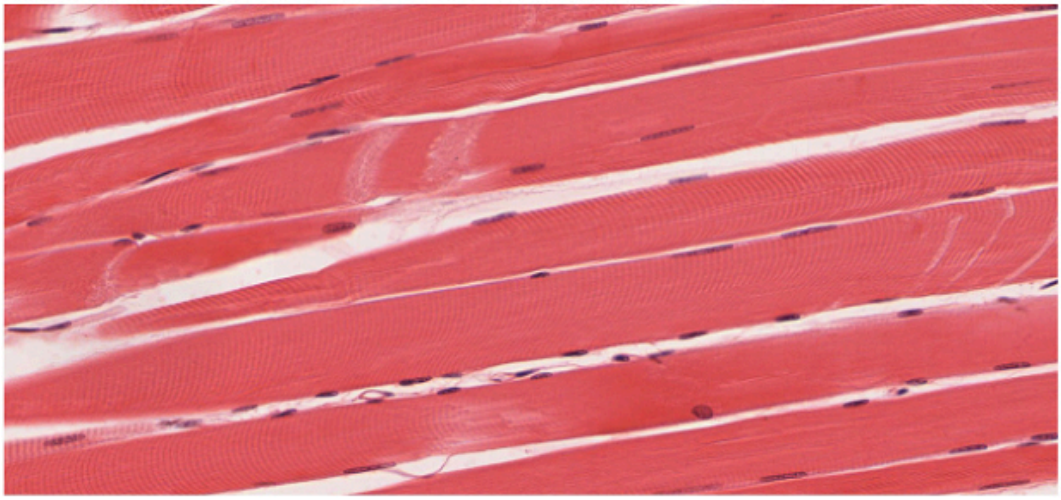
of **extensibility**; it can stretch or extend. **Contractility** allows muscle tissue to pull on its attachment points and shorten with force.

Differences among the three muscle types include the microscopic organization of their contractile proteins—**actin** and **myosin**. The actin and myosin proteins are arranged very regularly

in the cytoplasm of individual muscle cells (referred to as fibers) in both skeletal muscle and cardiac muscle, which creates a pattern, or stripes, called **striations**. The striations are visible with a light microscope under high magnification (Figure 1). **Skeletal muscle** fibers are multinucleated structures that compose the skeletal muscle. **Cardiac muscle** fibers each have one to two nuclei and are physically and electrically connected to each other so that the entire heart contracts as one unit (called a **syncytium**).

Because the actin and myosin are not arranged in such regular fashion in **smooth muscle**, the cytoplasm of a smooth muscle fiber (which has only a single nucleus) has a uniform, nonstriated appearance (resulting in the name smooth muscle). However, the less organized appearance of smooth muscle should not be interpreted as less efficient.

Smooth muscle in the walls of arteries is a critical component that regulates blood pressure necessary to push blood through the circulatory system; and smooth muscle in the skin, visceral organs, and internal passageways is essential for moving all materials through the body.



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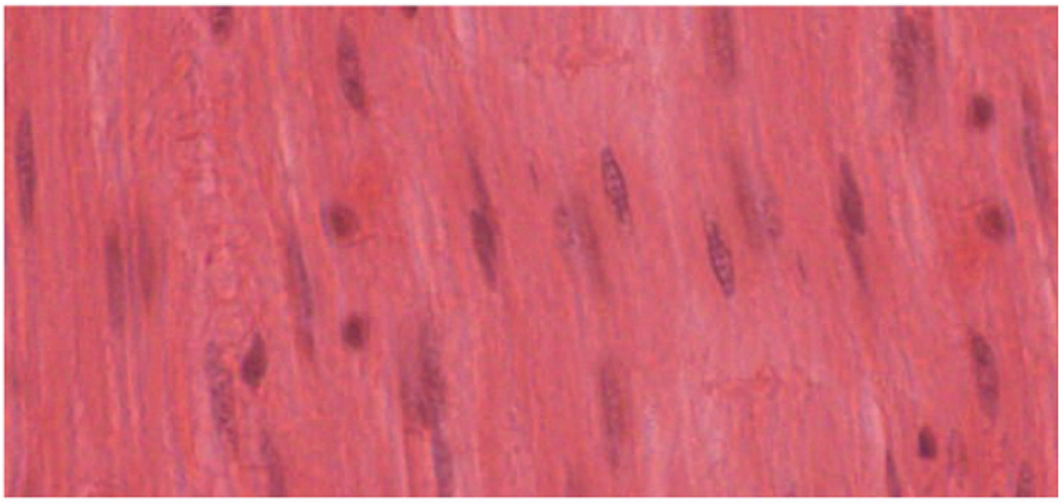

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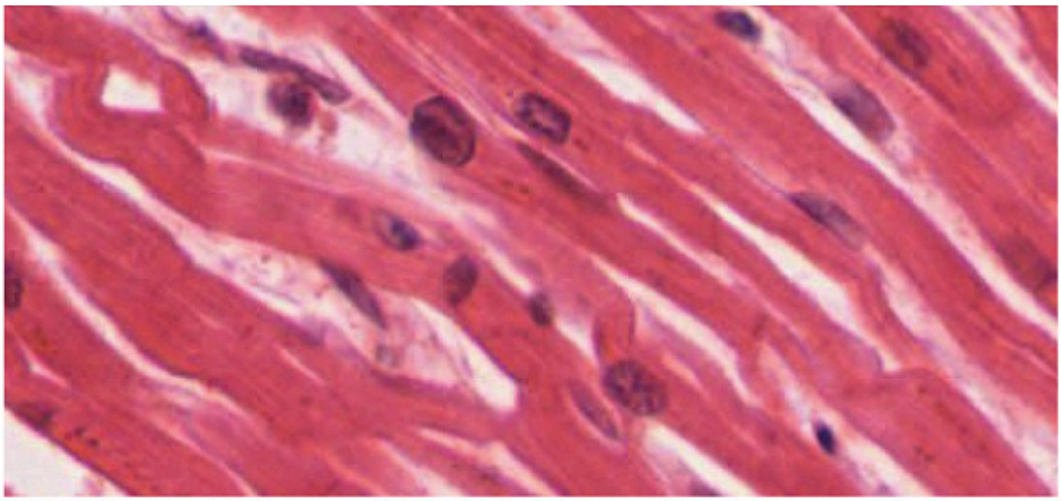

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Figure 1. The Three Types of Muscle Tissue. *The body contains three types of muscle tissue: (a) skeletal muscle, (b) smooth muscle, and (c) cardiac muscle. From top, LM × 1600, LM × 1600, LM × 1600. (Micrographs provided by the Regents of University of Michigan Medical School © 2012)*

Skeletal Muscle: The best-known feature of skeletal muscle is its ability to contract and cause movement. Skeletal muscles act not only to produce movement but also to stop movement, such as resisting gravity to maintain posture. Small, constant adjustments of the skeletal muscles are needed to hold a body upright or balanced in any position. Muscles also prevent excess movement of the bones and joints, maintaining skeletal stability and preventing skeletal structure damage or deformation. Joints can become misaligned or dislocated entirely by pulling on the associated bones; muscles work to keep joints stable. Skeletal muscles are located throughout the body at the openings of internal tracts to control the movement of various substances. These muscles allow functions, such as swallowing, urination, and defecation, to be under voluntary control. Skeletal muscles also protect internal organs (particularly abdominal and pelvic organs) by acting as an external barrier or shield to external trauma and by supporting the weight of the organs.

Skeletal muscles contribute to the maintenance of homeostasis in the body by generating heat. Muscle contraction requires energy, and when ATP is broken down, heat is produced. This heat is very noticeable during exercise, when sustained muscle movement causes body temperature to rise, and in cases of extreme cold, when shivering produces random skeletal muscle contractions to generate heat.

Each skeletal muscle is an organ that consists of various integrated tissues. These tissues include the skeletal muscle fibers, blood vessels, nerve fibers, and connective tissue. Each skeletal muscle has three layers of connective tissue (called “mysia”) that enclose it and provide structure to the muscle as a whole, and also compartmentalize the muscle fibers within the muscle (Figure 2). Each muscle is wrapped in a sheath of dense, irregular connective tissue called the **epimysium**, which allows a muscle to contract and move powerfully while maintaining its structural integrity. The epimysium also separates muscle from other tissues and organs in the area, allowing the muscle to move independently.

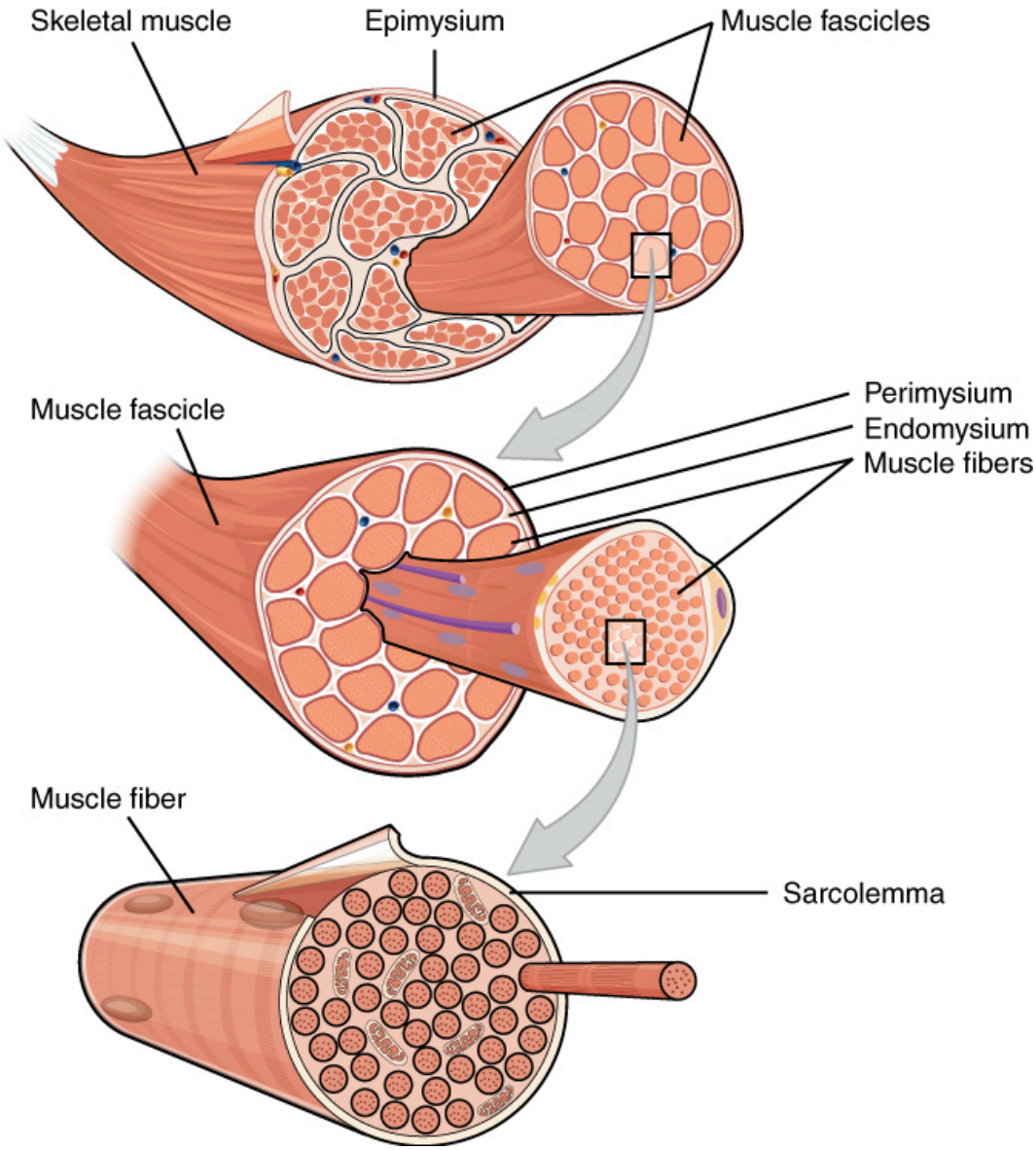


Figure 2. The Three Connective Tissue Layers. *Bundles of muscle fibers, called fascicles, are covered by the perimysium. Muscle fibers are covered by the endomysium.*

Inside each skeletal muscle, muscle fibers are organized into individual bundles, each called a **fascicle**, by a middle layer of connective tissue called the **perimysium**. This fascicular organization is common in muscles of the limbs; it allows the nervous system to trigger a specific movement of a muscle by activating a subset of muscle fibers within a bundle, or fascicle of the muscle. Inside each fascicle, each muscle fiber is encased in a thin connective tissue layer of collagen and reticular fibers called the **endomysium**. The endomysium contains the extracellular fluid and nutrients to support the muscle fiber. These nutrients are supplied via blood to the muscle tissue.

In skeletal muscles that work with tendons to pull on bones, the collagen in the three tissue layers (the mysia) intertwines with the collagen of a tendon. At the other end of the tendon, it fuses with the periosteum coating the bone. The tension created by contraction of the muscle fibers is then transferred though the mysia, to the tendon, and then to the periosteum to pull on the bone for movement of the skeleton.

Every skeletal muscle is also richly supplied by blood vessels for nourishment, oxygen delivery, and waste removal. In addition, every muscle fiber in a skeletal muscle is supplied by the axon branch of a somatic motor

neuron, which signals the fiber to contract. Unlike cardiac and smooth muscle, the only way to functionally contract a skeletal muscle is through signaling from the nervous system.

Skeletal Muscle Fibers: Because skeletal muscle cells are long and cylindrical, they are commonly referred to as muscle fibers. Skeletal muscle fibers can be quite large for human cells, with diameters up to 100 µm and lengths up to 30 cm (11.8 in) in the Sartorius of the upper leg. During early development, embryonic myoblasts, each with its own nucleus, fuse with up to hundreds of other myoblasts to form the multinucleated skeletal muscle fibers. Multiple nuclei mean multiple copies of genes, permitting the production of the large amounts of proteins and enzymes needed for muscle contraction.

Some other terminology associated with muscle fibers is rooted in the Greek sarco, which means "flesh." The plasma membrane of muscle fibers is called the **sarcolemma**, the cytoplasm is referred to as **sarcoplasm**, and the specialized smooth endoplasmic reticulum, which stores, releases, and retrieves calcium ions (Ca++) is called the **sarcoplasmic reticulum (SR) (**Figure 3). As will soon be described, the functional unit of a skeletal muscle fiber is the sarcomere, a highly organized arrangement of the contractile myofilaments **actin** (thin filament) and **myosin** (thick filament), along with other support proteins.

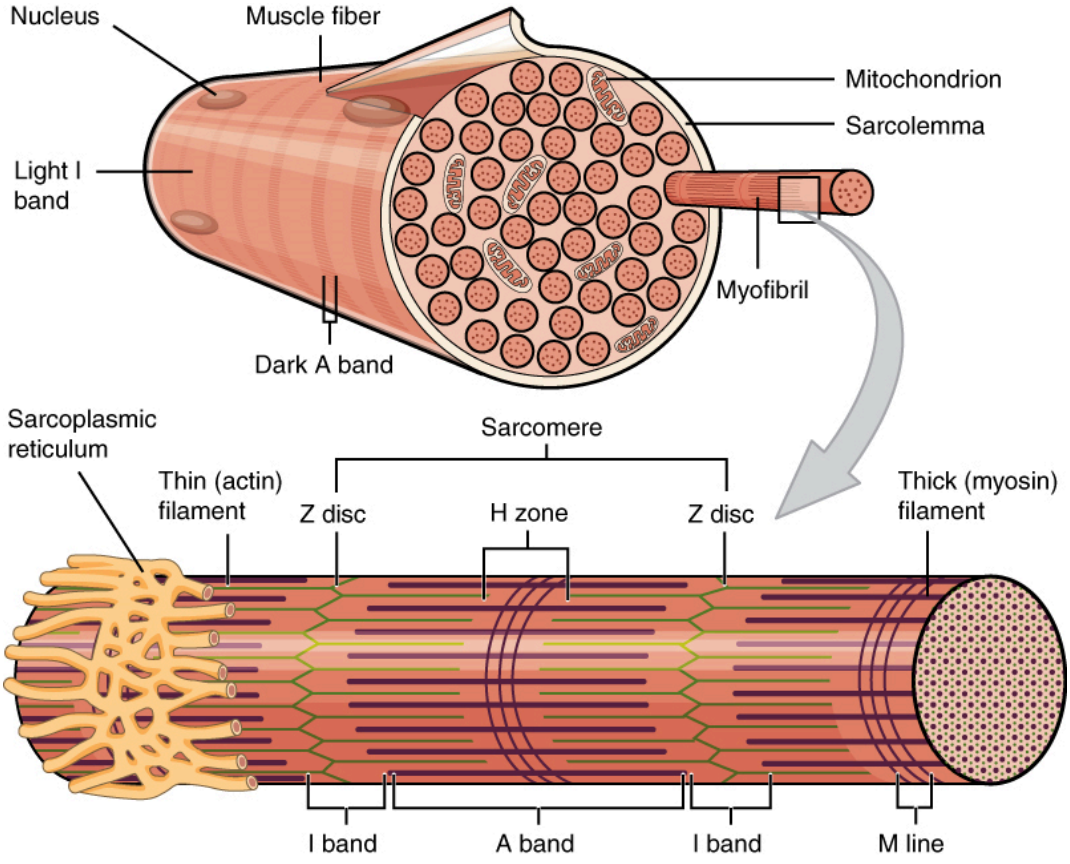


Figure 3. Muscle Fiber. *A skeletal muscle fiber is surrounded by a plasma membrane called the sarcolemma, which contains sarcoplasm, the cytoplasm of muscle cells. A muscle fiber is composed of many fibrils, which give the cell its striated appearance.*

The Sarcomere: The striated appearance of skeletal muscle fibers is due to the arrangement of the myofilaments of actin and myosin in sequential order from one end of the muscle fiber to the other. Each packet of these microfilaments and their regulatory proteins, **troponin** and **tropomyosin** (along with other proteins) is called a **sarcomere**.

Watch this video to learn more about macro- and microstructures of skeletal muscles. Direct link: https://youtu.be/XoP1diaXVCI

Watch this CrashCourse video to find out more about skeletal muscle structure. Direct link: https://youtu.be/Ktv-CaOt6UQ

The sarcomere is the functional unit of the muscle fiber. The sarcomere itself is bundled within the myofibril that runs the entire length of the muscle fiber and attaches to the sarcolemma at its end. As myofibrils contract, the entire muscle cell contracts. Because myofibrils are only approximately 1.2 μm in diameter, hundreds to thousands (each with thousands of sarcomeres) can be found inside one muscle fiber.

Each sarcomere is around 2 μm in length with a cylinder-like arrangement and is bordered by structures called Z-discs (also called Z-lines, because pictures are two-dimensional), to which the actin myofilaments are anchored (Figure 4). Because the actin and its troponin-tropomyosin complex (projecting from the Z-discs toward the center of the sarcomere) form strands that are thinner than the myosin, it is called the **thin filament** of the sarcomere. Likewise, because the myosin strands and their multiple heads (projecting from the center of the sarcomere, toward but not all to way to, the Z-discs) have more mass and are thicker, they are called the **thick filament** of the sarcomere.

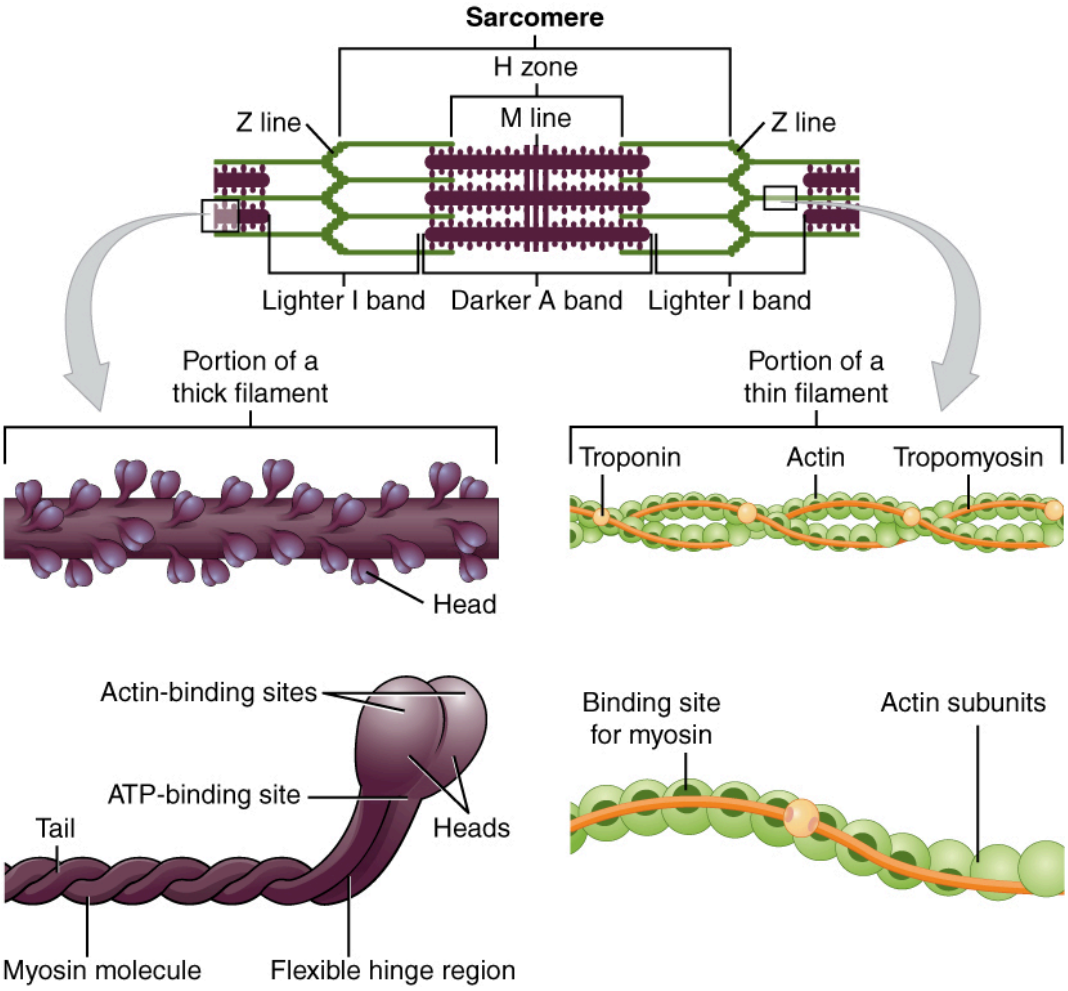


Figure 4. The Sarcomere. *The sarcomere, the region from one Z-line to the next Z-line, is the functional unit of a skeletal muscle fiber.*

Part 2: Types of Body Movement

Synovial joints allow the body a tremendous range of movements. Each movement at a synovial joint results from the contraction or relaxation of the muscles that are attached to the bones on either side of the articulation. The type of movement that can be produced at a synovial joint is determined by four factors:

- **Orientation of the muscle**. Each muscle is attached at an origin and an insertion. The origin of the muscle is its attachment to the bone that will remain relatively stable when that muscle contracts. It is the bone to which the muscle is anchored. The other end of the muscle will be its insertion, which is its attachment to the bone which will move when that muscle contracts. The orientation of the muscle – which bone it is anchored to and which bone it inserts in, will determine the movement.
- **Action of other muscles** that may insert and/or originate on the same bone(s) that when any particular muscle contracts, the bone will be moved in a particular direction, different from the direction any single muscle may produce. It is not uncommon to see the same muscle being involved in two or more different movements.
- **Type of joint** between the bones. There are a number of different types of joints between bones. Only the synovial joint, allows for any significant movement. Each specific joint is limited in the movement it can provide because of the shape of the ends of the bones in the joint, and because of the tension in the ligaments holding the bones together.
- **Muscle tension**. This is a limitation that works in a similar manner to tension in the ligaments. An example

of the role of muscle tension is demonstrated when touching one's toes with the knees straight. The movement is restricted by the tension of the hamstring muscles.

While the ball-and-socket joint gives the greatest range of movement at an individual joint, in other regions of the body, several joints may work together to produce a particular movement. Overall, each type of synovial joint is necessary to provide the body with its great flexibility and mobility. There are many types of movement that can occur at synovial joints (Table 1). Movement types are generally paired, with one being the opposite of the other. Body movements are always described in relation to the anatomical position of the body: upright stance, with upper limbs to the side of body and palms facing forward.

Table 1: Movements of the Joints

Type of Joint	Movement	Examples
Pivot	Uniaxial joint; allows rotational movement	Atlantoaxial joint (C1-C2 vertebrae articulation); proximal radioulnar joint
Hinge	Uniaxial joint; allows flexion/extension movements	Knee; elbow; ankle; interphalangeal joints of fingers and toes
Condyloid	Biaxial joint; allows flexion/extension, abduction/adduction, and circumduction movements	Metacarpophalangeal (knuckle) joints of fingers; radiocarpal joint of wrist; metatarsophalangeal joints of toes
Saddle	Biaxial joint; allows flexion/extension, abduction/adduction, and circumduction movements	First carpometacarpal joint (carpometacarpal joint of the thumb); sternoclavicular joint
Plane	Multiaxial joint; allows inversion/eversion of the foot, flexion/extension and lateral flexion of the vertebral column	intertarsal joints of foot; superior-inferior articular process articulations between vertebrae
Ball-and-socket	Multiaxial joint; allows flexion/extension, abduction/adduction, circumduction, and medial/lateral rotation movements	Shoulder joint, hip joint

Flexion and Extension: Flexion and **extension** are movements that take place within the sagittal plane and involve anterior or posterior movements of the body or limbs. For the vertebral column, flexion (anterior flexion) is an anterior (forward) bending of the neck or body, while extension involves a posterior-directed motion, such as straightening from a flexed position or bending backward. Lateral flexion is the bending of the neck or body toward the right or left side. These movements of the vertebral column involve both the symphysis joint formed by each intervertebral disc, as well as the plane type of synovial joint formed between the inferior articular processes of one vertebra and the superior articular processes of the next lower vertebra.

In the limbs, flexion decreases the angle between the bones (bending of the joint), while extension increases the angle and straightens the joint. For the upper limb, all anterior-going motions are flexion and all posterior-going motions are extension. These include anterior-posterior movements of the arm at the shoulder, the forearm at the elbow, the hand at the wrist, and the fingers at the metacarpophalangeal and interphalangeal joints. For the thumb, extension moves the thumb away from the palm of the hand, within the same plane as the palm, while flexion brings the thumb back against the index finger or into the palm. These motions take place at the first carpometacarpal joint. In the lower limb, bringing the thigh forward and upward is flexion at the hip joint, while any posterior-going motion of the thigh is extension. Note that extension of the thigh beyond the anatomical (standing) position is greatly limited by the ligaments that support the hip joint. Knee flexion is the bending of the knee to bring the foot toward the posterior thigh, and extension is the straightening of the knee. Flexion and extension movements are seen at the hinge, condyloid, saddle, and ball-and-socket joints of the limbs (Figure 5a-d).

Hyperextension is the abnormal or excessive extension of a joint beyond its normal range of motion, thus resulting in injury. Similarly, **hyperflexion** is excessive flexion at a joint. Hyperextension injuries are common at hinge joints such as the knee or elbow. In cases of "whiplash" in which the head is suddenly moved backward and then forward, a patient may experience both hyperextension and hyperflexion of the cervical region.

Abduction and Adduction: Abduction and **adduction** motions occur within the coronal plane and involve medial-lateral motions of the limbs, fingers, toes, or thumb. Abduction moves the limb laterally away from the midline of the body, while adduction is the opposing movement that brings the limb toward the body or across the midline. For example, abduction is raising the arm at the shoulder joint, moving it laterally away from the body, while adduction brings the arm down to the side of the body. Similarly, abduction and adduction at the wrist moves the hand away from or toward the midline of the body. Spreading the fingers or toes apart is also abduction, while bringing the fingers or toes together is adduction. For the thumb, abduction is the anterior movement that brings the thumb to a 90°perpendicular position, pointing straight out from the palm. Adduction moves the thumb back to the anatomical position, next to the index finger. Abduction and adduction movements are seen at condyloid, saddle, and ball-and-socket joints (Figure 5e).

Circumduction: Circumduction is the movement of a body region in a circular manner, in which one end of the body region being moved stays relatively stationary while the other end describes a circle. It involves the sequential combination of flexion, adduction, extension, and abduction at a joint. This type of motion is found at biaxial condyloid and saddle joints, and at multiaxial ball-and-sockets joints (Figure 5e).

Rotation: Rotation can occur within the vertebral column, at a pivot joint, or at a ball-and-socket joint. Rotation of the neck or body is the twisting movement produced by the summation of the small rotational movements available between adjacent vertebrae. At a pivot joint, one bone rotates in relation to another bone. This is a uniaxial joint, and thus rotation is the only motion allowed at a pivot joint. For example, at the atlantoaxial joint, the first cervical (C1) vertebra (atlas) rotates around the dens, the upward projection from the second cervical (C2) vertebra (axis). This allows the head to rotate from side to side as when shaking the head "no." The proximal radioulnar joint is a pivot joint formed by the head of the radius and its articulation with the ulna. This joint allows for the radius to rotate along its length during pronation and supination movements of the forearm.

Rotation can also occur at the ball-and-socket joints of the shoulder and hip. Here, the humerus and femur rotate around their long axis, which moves the anterior surface of the arm or thigh either toward or away from the midline of the body. Movement that brings the anterior surface of the limb toward the midline of the body is called medial (internal) rotation. Conversely, rotation of the limb so that the anterior surface moves away from the midline is lateral (external) rotation (Figure 5f). Be sure to distinguish medial and lateral rotation, which can only occur at the multiaxial shoulder and hip joints, from circumduction, which can occur at either biaxial or multiaxial joints.

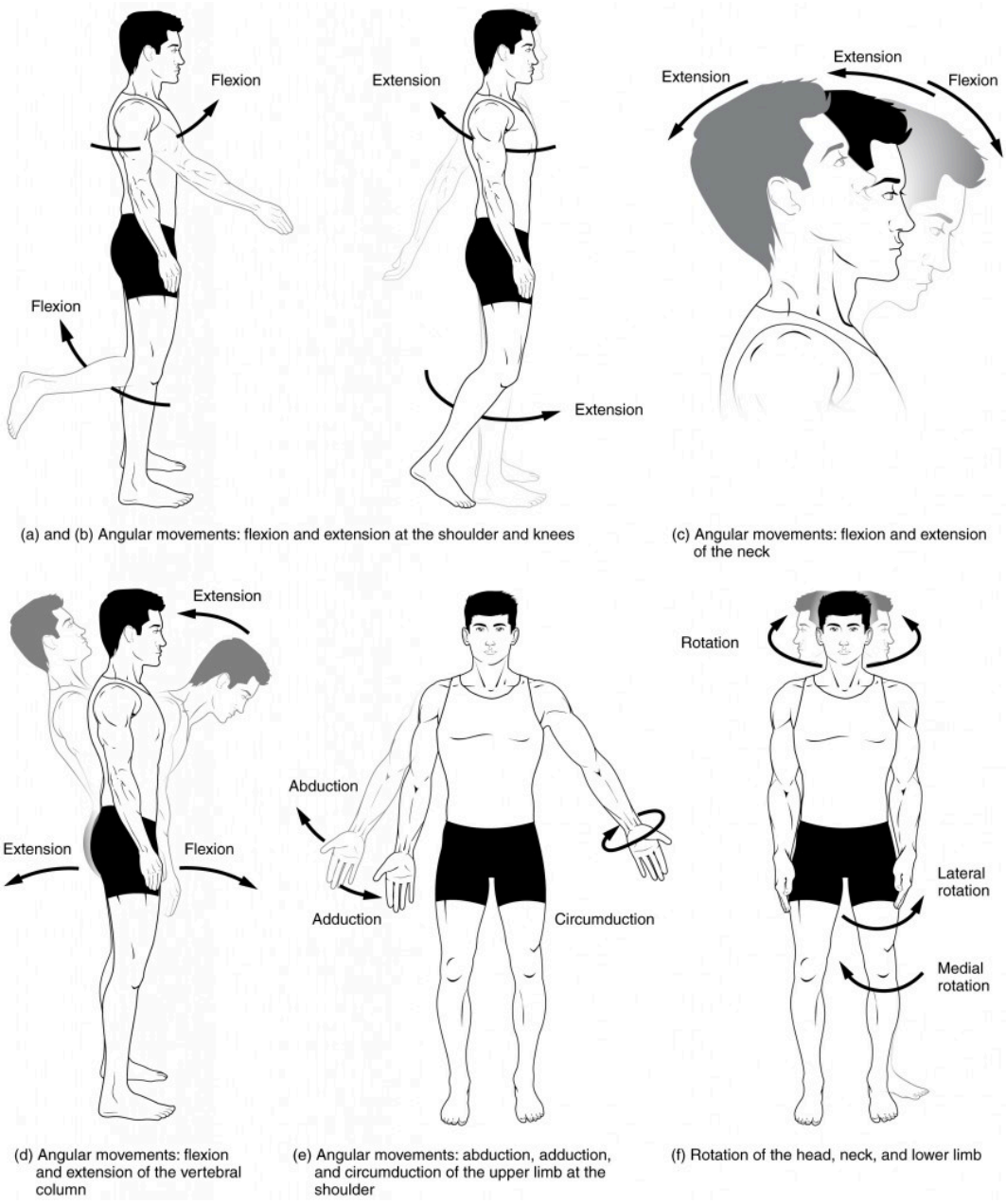


Figure 5. Movements of the Body, Part 1. *Synovial joints give the body many ways in which to move. (a)–(b) Flexion and extension motions are in the sagittal (anterior–posterior) plane of motion. These movements take place at the shoulder, hip, elbow, knee, wrist, metacarpophalangeal, metatarsophalangeal, and interphalangeal joints. (c)–(d) Anterior bending of the head or vertebral column is flexion, while any posterior-going movement is extension. (e) Abduction and adduction are motions of the limbs, hand, fingers, or toes in the coronal (medial–lateral) plane of movement. Moving the limb or hand laterally away from the body, or spreading the fingers or toes, is abduction. Adduction brings the limb or hand toward or across the midline of the body, or brings the fingers or toes together. Circumduction is the movement of the limb, hand, or fingers in a circular pattern, using the sequential combination of flexion, adduction, extension, and abduction motions. Adduction/abduction and circumduction take place at the shoulder, hip, wrist, metacarpophalangeal, and metatarsophalangeal joints. (f) Turning of the head side to side or twisting of the body is rotation. Medial and lateral rotation of the upper limb at the shoulder or lower limb at the hip involves turning the anterior surface of the limb toward the midline of*

the body (medial or internal rotation) or away from the midline (lateral or external rotation).

Supination and Pronation: Supination and pronation are movements of the forearm. In the anatomical position, the upper limb is held next to the body with the palm facing forward. This is the **supinated position** of the forearm. In this position, the radius and ulna are parallel to each other. When the palm of the hand faces backward, the forearm is in the **pronated position**, and the radius and ulna form an X-shape.

Supination and pronation are the movements of the forearm that go between these two positions. **Pronation** is the motion that moves the forearm from the supinated (anatomical) position to the pronated (palm backward) position. This motion is produced by rotation of the radius at the proximal radioulnar joint, accompanied by movement of the radius at the distal radioulnar joint. The proximal radioulnar joint is a pivot joint that allows for rotation of the head of the radius. Because of the slight curvature of the shaft of the radius, this rotation causes the distal end of the radius to cross over the distal ulna at the distal radioulnar joint. This crossing over brings the radius and ulna into an X-shape position. **Supination** is the opposite motion, in which rotation of the radius returns the bones to their parallel positions and moves the palm to the anterior facing (supinated) position. It helps to remember that supination is the motion you use when scooping up soup with a spoon (Figure 6g).

Dorsiflexion and Plantar Flexion: Dorsiflexion and plantar flexion are movements at the ankle joint, which is a hinge joint. Lifting the front of the foot, so that the top of the foot moves toward the anterior leg is dorsiflexion, while lifting the heel of the foot from the ground or pointing the toes downward is plantar flexion. These are the only movements available at the ankle joint (Figure 6h).

Inversion and Eversion: Inversion and eversion are complex movements that involve the multiple plane joints among the tarsal bones of the posterior foot (intertarsal joints) and thus are not motions that take place at the ankle joint. **Inversion** is the turning of the foot to angle the bottom of the foot toward the midline, while **eversion** turns the bottom of the foot away from the midline. The foot has a greater range of inversion than eversion motion. These are important motions that help to stabilize the foot when walking or running on an uneven surface and aid in the quick side-to-side changes in direction used during active sports such as basketball, racquetball, or soccer (Figure 6i).

Protraction and Retraction: **Protraction** and **retraction** are anterior-posterior movements of the scapula or mandible. Protraction of the scapula occurs when the shoulder is moved forward, as when pushing against something or throwing a ball. Retraction is the opposite motion, with the scapula being pulled posteriorly and medially, toward the vertebral column. For the mandible, protraction occurs when the lower jaw is pushed forward, to stick out the chin, while retraction pulls the lower jaw backward. (Figure 6j.)

Depression and Elevation: Depression and elevation are downward and upward movements of the scapula or mandible. The upward movement of the scapula and shoulder is elevation, while a downward movement is depression. These movements are used to shrug your shoulders. Similarly, elevation of the mandible is the upward movement of the lower jaw used to close the mouth or bite on something, and depression is the downward movement that produces opening of the mouth (Figure 6k).

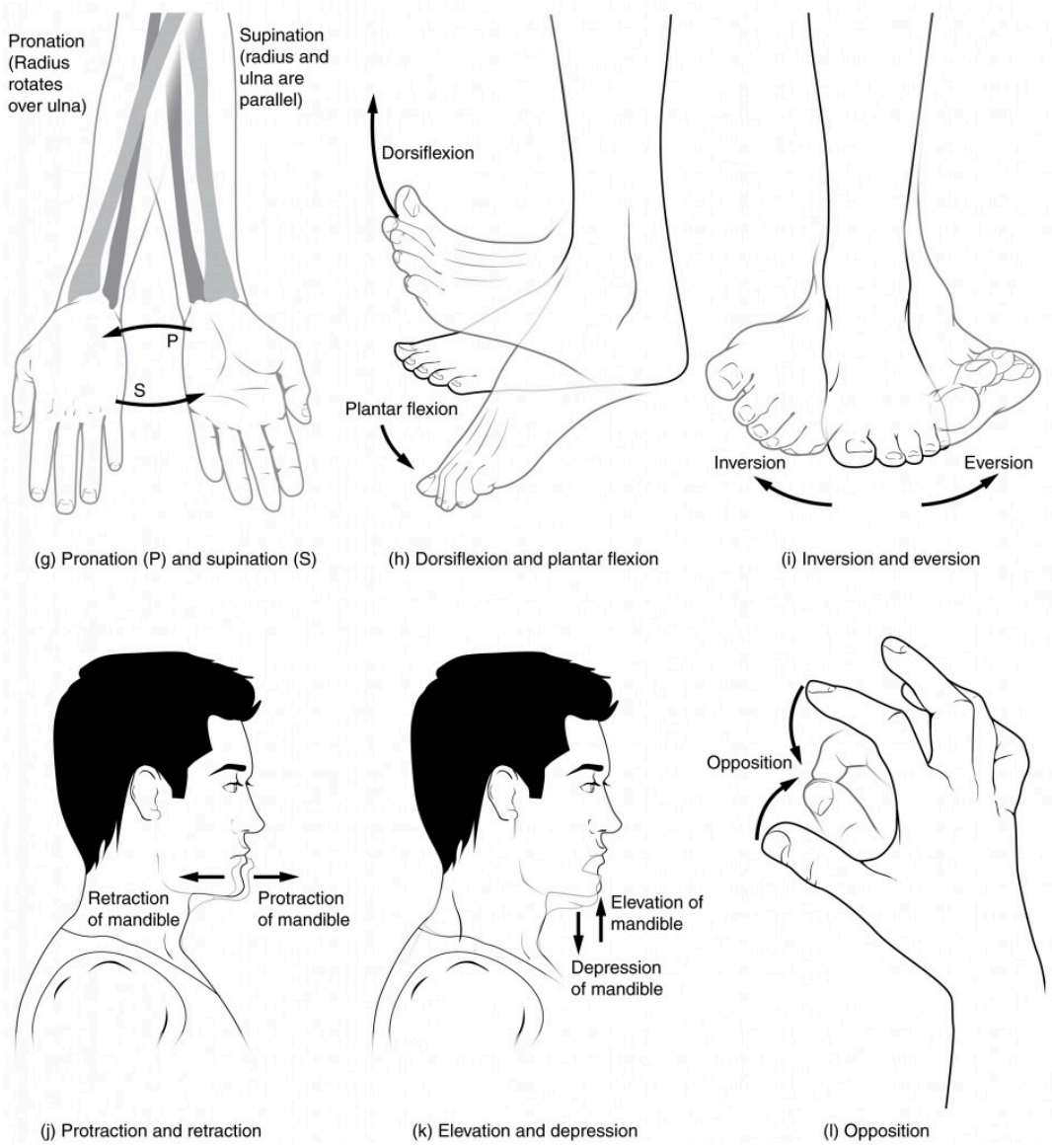


Figure 6. Movements of the Body, Part 2. *(g) Supination of the forearm turns the hand to the palm forward position in which the radius and ulna are parallel, while forearm pronation turns the hand to the palm backward position in which the radius crosses over the ulna to form an "X." (h) Dorsiflexion of the foot at the ankle joint moves the top of the foot toward the leg, while plantar flexion lifts the heel and points the toes. (i) Eversion of the foot moves the bottom (sole) of the foot away from the midline of the body, while foot inversion faces the sole toward the midline. (j) Protraction of the mandible pushes the chin forward, and retraction pulls the chin back. (k) Depression of the mandible opens the mouth, while elevation closes it. (l) Opposition of the thumb brings the tip of the thumb into contact with the tip of the fingers of the same hand and reposition brings the thumb back next to the index finger.*

Part 3: The Muscular System

Think about the things that you do each day—talking, walking, sitting, standing, and running—all of these activities require movement of particular skeletal muscles. Skeletal muscles are even used during sleep. The diaphragm is a sheet of skeletal muscle that has to contract and relax for you to breathe day and night. If you recall from your study of the skeletal system and joints, body movement occurs around the joints in the body. The focus of this chapter is on skeletal muscle organization. The system to name skeletal muscles will be explained; in some cases, the muscle is named by its shape, and in other cases it is named by its location or attachments to the skeleton. If you understand the meaning of the name of the muscle, often it will help you remember its location and/or what it does. This chapter also will describe how skeletal muscles are arranged to accomplish movement, and how other muscles may assist, or be arranged on the skeleton to resist or carry out the opposite movement. The actions of the skeletal muscles will be covered in a regional manner, working from the head down to the toes.

Naming Skeletal Muscles: The Greeks and Romans conducted the first studies done on the human body in Western culture. The educated class of subsequent societies studied Latin and Greek, and therefore the early pioneers of anatomy continued to apply Latin and Greek terminology or roots when they named the skeletal muscles. The large number of muscles in the body and unfamiliar words can make learning the names of the muscles in the body seem daunting, but understanding the etymology can help. Etymology is the study of how the root of a particular word entered a language and how the use of the word evolved over time. Taking the time to learn the root of the words is crucial to understanding the vocabulary of anatomy and physiology. When you understand the names of muscles it will help you remember where the muscles are located and what they do (Figure 7, Table 2, Table 3, Table 4). Pronunciation of words and terms will take a bit of time to master, but after you have some basic information; the correct names and pronunciations will become easier.

Table 2: Understanding a Muscle Name from its Latin Roots

Example	Word	Latin Root 1	Latin Root 2	Meaning	Translation
	abductor	ab = away from	duct = to move	moves away from	
abductor digiti minimi	digiti	digitus = digit		refers to a finger or toe	A muscle that moves the little finger/toe away
	minimi	minimus = minimal, tiny		little	
	adductor	ad = towards	duct = to move	moves towards	
adductor digiti minimi	digiti	digitus = digit		refers to a finger or toe	A muscle that moves the little finger/toe toward
	minimi	minimus = minimal, tiny		little	

Anatomists name the skeletal muscles according to a number of criteria, each of which describes the muscle in some way. These include naming the muscle after its shape, the direction of its muscle fibers, its size compared to other muscles in the area, its location in the body or the location of its attachments to the skeleton, how many origins it has, or its action. Often, a muscle's name will refer to several of these characteristics (Table 3). You should be able to list the criteria and provide an example of each in the name of a muscle.

The shapes of some muscles are very distinctive and the names, **deltoid** for the Greek letter delta (which looks like a triangle), reflect their shape. The direction of the muscle fibers and fascicles of a muscle can be used to name muscles by describing their orientation relative to the longitudinal axis of the body or of a limb, such as the **rectus** (straight) abdominis, or the **oblique** (at an angle) muscles of the abdomen.

For the buttocks, the size of the muscles influences the names: gluteus **maximus** (largest), gluteus **medius** (medium), and the gluteus **minimus** (smallest). Names are also given to muscles that indicate length—**brevis** (short), or **longus** (long). Some muscle names are used indicate the number of muscles in a group. One example of this is the quadriceps, a group of four muscles located on the anterior (front) thigh.

The skeletal muscle's anatomical location or its relationship to a particular bone often determines its name. Some muscles are named after their relative anatomical position: **lateralis**, **medialis**, **dorsi** ("dorsal"), **anterior**, and **posterior**.

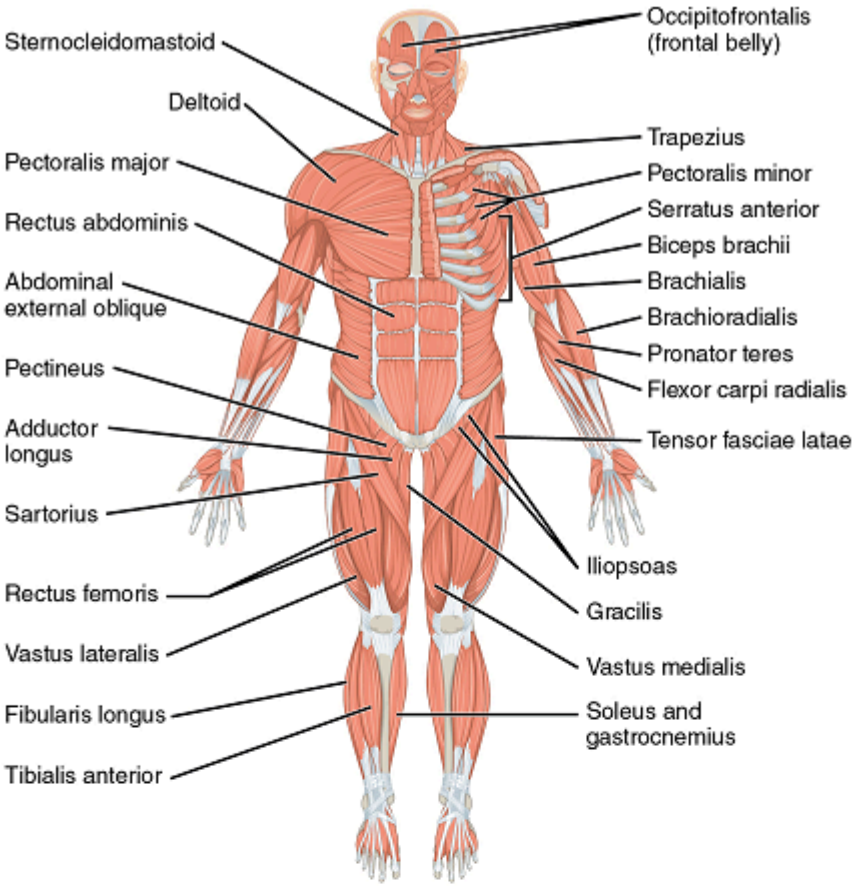
The location of a muscle's attachment can also appear in its name. When the name of a muscle is based on

the attachments, the origin is always named first. For instance, the **sternocleidomastoid** muscle of the neck has a dual origin on the sternum ("sterno") and clavicle ("cleido"), and inserts on the mastoid process of the temporal bone. Other muscle names can provide information as to how many origins a particular muscle has, such as the biceps brachii. The prefix **bi** indicates that the muscle has two origins, and tri indicates three origins.

The last feature by which to name a muscle is its action. When muscles are named for the movement they produce, one can find action words in their name.

Table 3: Muscle Naming Criteria

Criteria	Descriptions	Meaning	Example
Shape	Orbicularis	Orbit (ring)	Orbicularis oculi
	Deltoid	Triangle	Deltoid
Orientation	Rectus	Straight	Rectus femoris
	Oblique	At an angle	Abdominis external oblique
Size	Brevis	Short	Adductor brevis
	Longissimus/longus	Long	Adductor longus
	Maximus	Largest	Gluteus maximus
	Medius	Medium	Gluteus medius
	Minimus	Smallest	Gluteus minimus
Anatomical position	Medialis	Medial (Along the midline)	Vastus medialis
	Lateralis	Lateral (Away from midline)	Vastus lateralis
	Dorsi	Dorsal (back)	Latissimus dorsi
	Anterior	Forward	Tibialis anterior
	Posterior	Rear	Tibialis posterior
	Adbominis	abdomen	Abdominis external oblique
	Bone name	various	Rectus femoris (along femur) Frontalis (on top of frontal bone)
Number of origins	Bi-, tri-		Biceps brachii
Origin/Insertion location on skeleton	Names of bones or parts of bones	various	Sternocleidomastoid (origins: sternum, clavicle; insertion: mastoid process)
Actions	Muscle actions		Adductor longus



Major muscles of the body. Right side: superficial; left side: deep (anterior view)

Figure 7. Overview of the Muscular System. *On the anterior and posterior views of the muscular system above, superficial muscles (those at the surface) are shown on the right side of the body while deep muscles (those underneath the superficial muscles) are shown on the left half of the body. For the legs, superficial muscles are shown in the anterior view while the posterior view shows both superficial and deep muscles.*

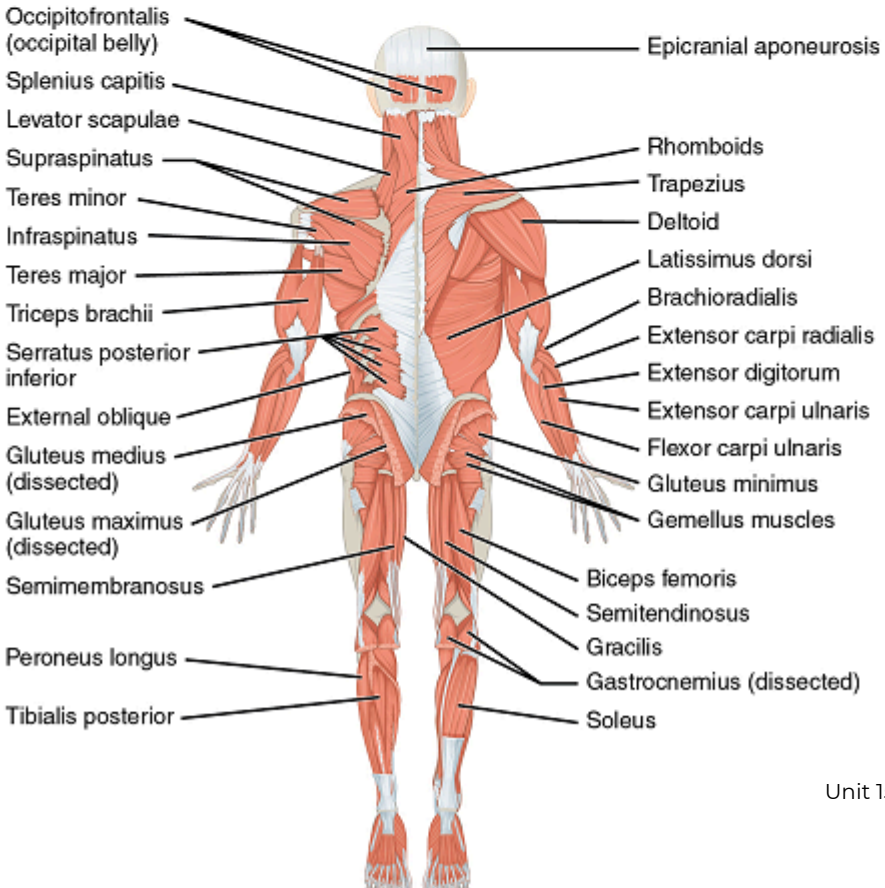


Table 4: Some Mnemonic Devices for Latin Roots

Example	Latin or Greek Translation	Mnemonic Device
ad-	to; toward	ADvance toward your goal
ab-	away from	Aliens ABduct you away from home
sub-	under	SUBmarines move under water
-ductor	something that moves	A conDUCTOR makes a train move
anti-	against	If you are ANTIsocial, you are against engaging in social activities
epi-	on top of	She is the EPItome of goodness
apo-	to the side of	An APOstrophe separates parts of a contraction from each other
longissimus	longest	"Longissimus" is longer than the word "long"
longus	long	LONGus
brevis	short	BRief
maximus	large	MAXIMUm size
minimus	tiny; little	MINIMUm size
medius	between large and tiny	Of MEDIUm size
rectus	straight	A situation is considered RECTified when it is straightened out
multi	many	A rainbow is MULTIcoloured
uni-	one	A UNIcorn has one horn
bi- (Latin root) or di- (Greek root)	two	You can DIvide something into two pieces; BIcycles have two wheels
tri-	three	To TRIple your money, you multiply it by three
quad-	four	QUADruplets are four children born at one birth
externus	outside	EXTERNal
internus	inside	INTERNal

Axial Muscles of the Head, Neck, and Back: The skeletal muscles are divided into **axial** (muscles of the trunk and head) and **appendicular** (muscles of the arms and legs) categories. This system reflects the bones of the skeleton system, which are also arranged in this manner. The axial muscles are grouped based on location, function, or both. Some of the axial muscles may seem to blur the boundaries because they cross over to the appendicular skeleton. The first grouping of the axial muscles you will review includes the muscles of the head and neck, then you will review the muscles of the vertebral column, and finally you will review the oblique and rectus muscles.

Muscles That Move the Head: The head, attached to the top of the vertebral column, is balanced, moved, and rotated by the neck muscles. When these muscles act unilaterally, the head rotates. When they contract bilaterally, the head flexes or extends. The major muscle that laterally flexes and rotates the head is the **sternocleidomastoid**. In addition, both muscles working together are the flexors of the head. Place your fingers on both sides of the neck and turn your head to the left and to the right. You will feel the movement originate there. This muscle divides the neck into anterior and posterior triangles when viewed from the side (Figure 8).

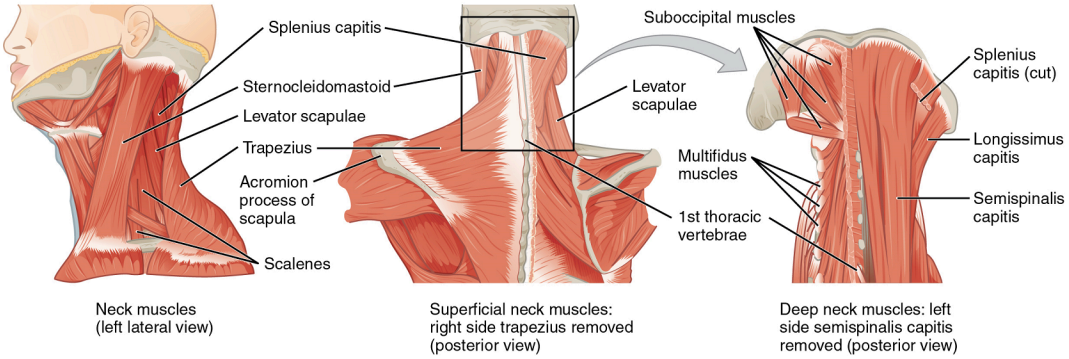


Figure 8. Posterior and Lateral Views of the Neck. *The superficial and deep muscles of the neck are responsible for moving the head, cervical vertebrae, and scapulae.*

Muscles of the Posterior Neck and the Back: The posterior muscles of the neck are primarily concerned with head movements, like extension. The back muscles stabilize and move the vertebral column, and are grouped according to the lengths and direction of the fascicles.

The **erector spinae group** forms the majority of the muscle mass of the back and it is the primary extensor of the vertebral column. It controls flexion, lateral flexion, and rotation of the vertebral column, and maintains the lumbar curve. The erector spinae comprises the iliocostalis (laterally placed) group, the longissimus (intermediately placed) group, and the spinalis (medially placed) group.

Axial Muscles of the Abdominal Wall, and Thorax: It is a complex job to balance the body on two feet and walk upright. The muscles of the vertebral column, thorax, and abdominal wall extend, flex, and stabilize different parts of the body's trunk. The deep muscles of the core of the body help maintain posture as well as carry out other functions. The brain sends out electrical impulses to these various muscle groups to control posture by alternate contraction and relaxation. This is necessary so that no single muscle group becomes fatigued too quickly. If any one group fails to function, body posture will be compromised.

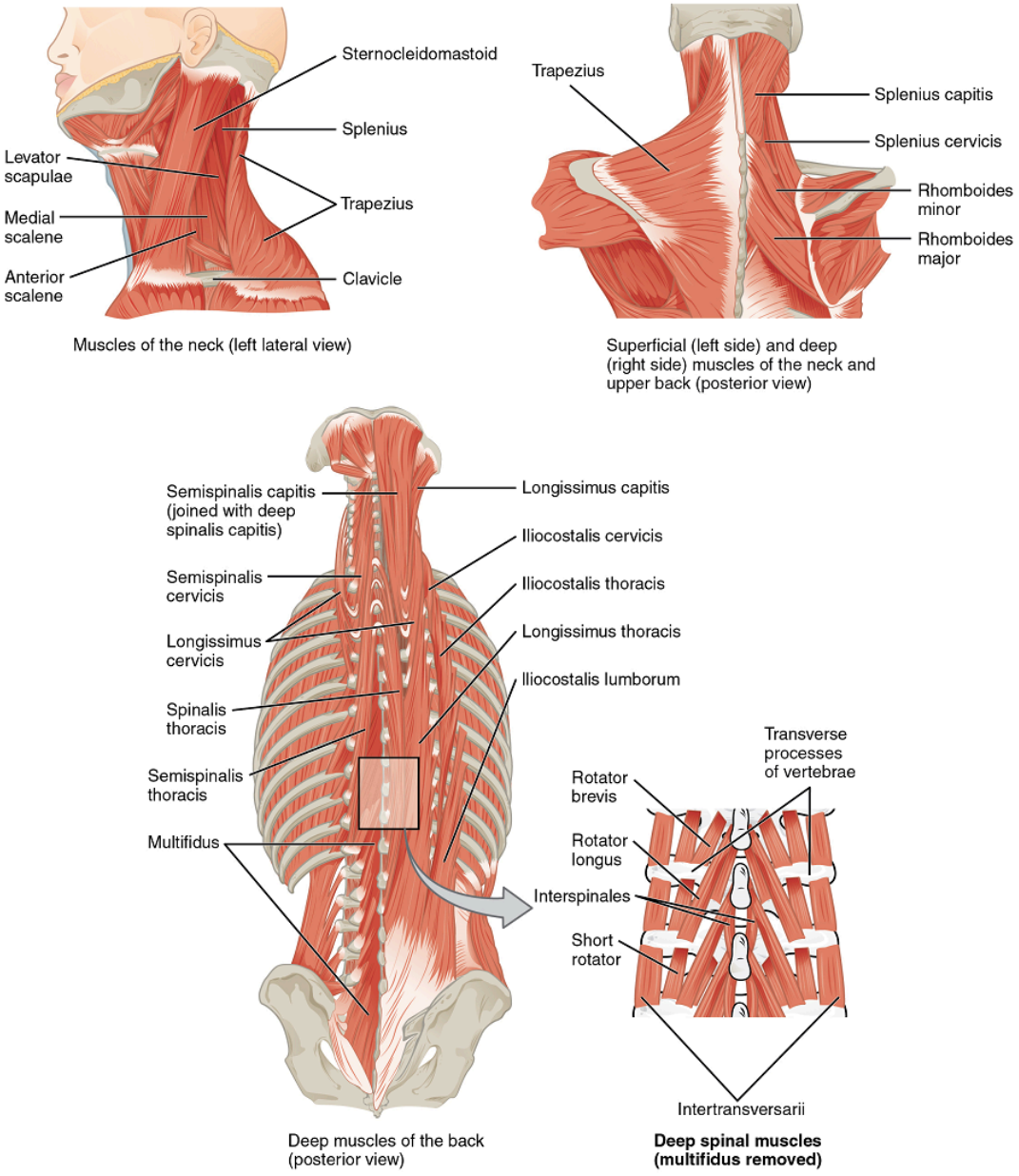


Figure 9. Muscles of the Neck and Back. *The large, complex muscles of the neck and back move the head, shoulders, and vertebral column.*

Muscles of the Abdomen: There are four pairs of abdominal muscles that cover the anterior and lateral abdominal region and meet at the anterior midline. These muscles of the anterolateral abdominal wall can be divided into four groups: the external obliques, the internal obliques, the transversus abdominis, and the rectus abdominis (Figure 10).

The external obliques, internal obliques, and transversus abdominis are three flat skeletal muscles in the antero-lateral wall of the abdomen. This arrangement of three bands of muscles in different orientations allows various movements and rotations of the trunk. The three layers of muscle also help to protect the internal abdominal organs in an area where there is no bone.

The linea alba is a white, fibrous band that is made of the bilateral rectus sheaths that join at the anterior midline of the body. These enclose the **rectus abdominis** muscles (a pair of long, linear muscles, commonly called the "sit-up" muscles) that originate at the pubic crest and symphysis, and extend the length of the body's trunk to insert on the sternum and ribs 5 to 7. These muscles flex the abdomen, as in the motion or bending

forward or doing a sit-up exercise. Each muscle is segmented by three transverse bands of collagen fibers called the tendinous intersections. This results in the look of "six-pack abs," as each segment hypertrophies on individuals at the gym who do many sit-ups.

The posterior abdominal wall is formed by the lumbar vertebrae, parts of the ilia of the hip bones, psoas major and iliacus muscles, and quadratus lumborum muscle. This part of the core plays a key role in stabilizing the rest of the body and maintaining posture.

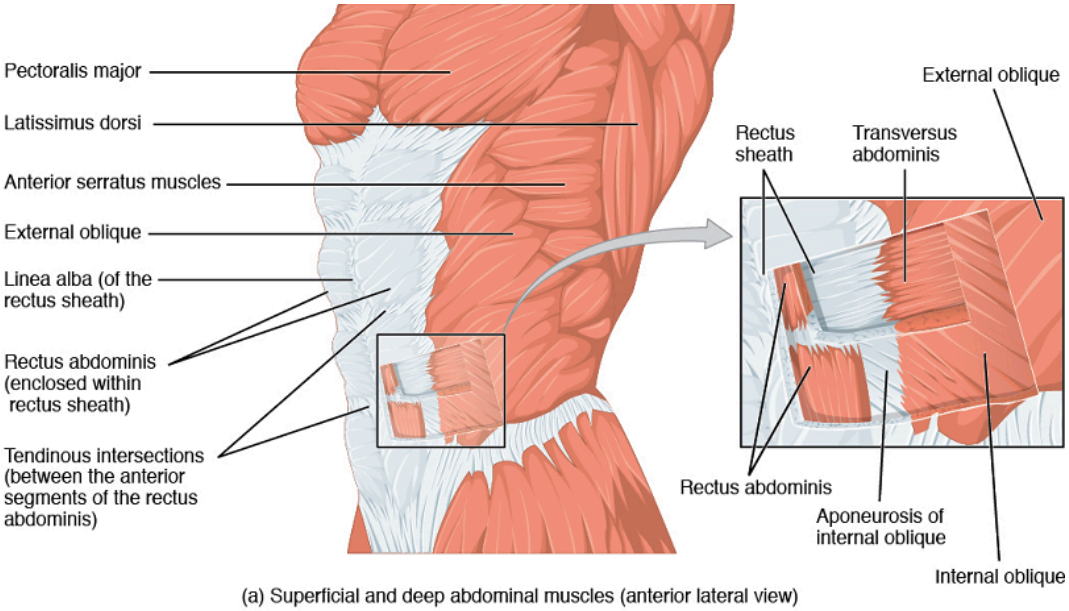
Muscles of the Thorax: The muscles of the chest serve to facilitate breathing by changing the size of the thoracic cavity. When you inhale, your chest rises because the cavity expands. Alternately, when you exhale, your chest falls because the thoracic cavity decreases in size.

***The Diaphragm*:** The change in volume of the thoracic cavity during breathing is due to the alternate contraction and relaxation of the **diaphragm** (Figure 11). It separates the thoracic and abdominal cavities, and is dome-shaped at rest. The superior surface of the diaphragm is convex, creating the elevated floor of the thoracic cavity. The inferior surface is concave, creating the curved roof of the abdominal cavity.

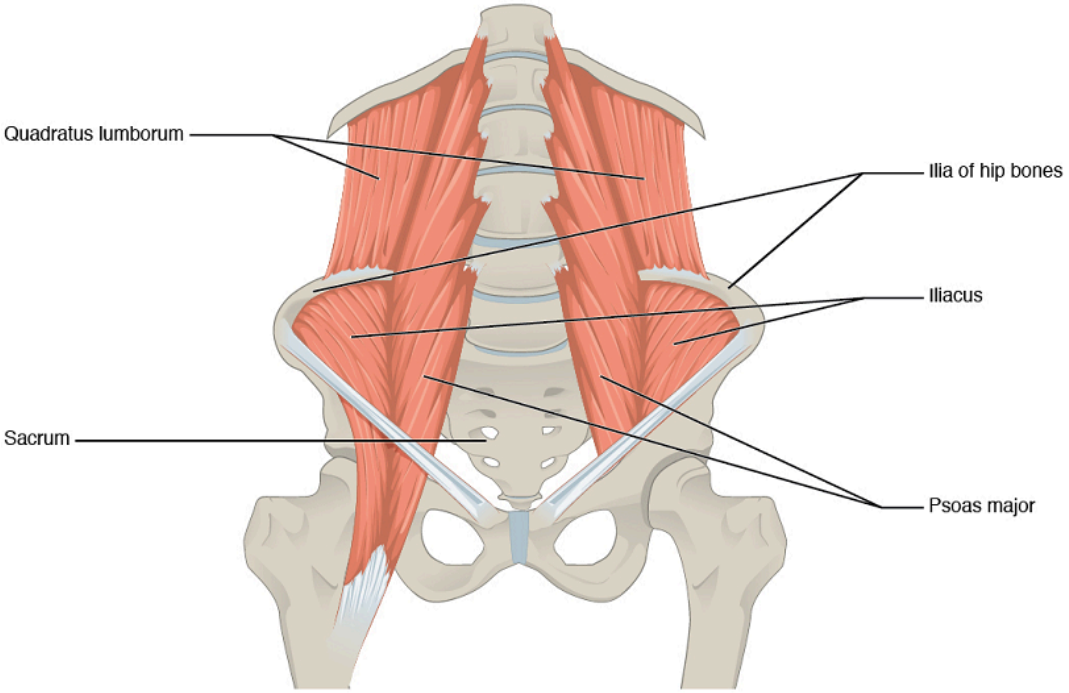
Defecating, urination, and even childbirth involve cooperation between the diaphragm and abdominal muscles (this cooperation is referred to as the "Valsalva maneuver"). You hold your breath by a steady contraction of the diaphragm; this stabilizes the volume and pressure of the peritoneal cavity. When the abdominal muscles contract, the pressure cannot push the diaphragm up, so it increases pressure on the intestinal tract (defecation), urinary tract (urination), or reproductive tract (childbirth).

The inferior surface of the pericardial sac and the inferior surfaces of the pleural membranes (parietal pleura) fuse onto the central tendon of the diaphragm. To the sides of the tendon are the skeletal muscle portions of the diaphragm, which insert into the tendon while having a number of origins including the xiphoid process of the sternum anteriorly, the inferior six ribs and their cartilages laterally, and the lumbar vertebrae and 12th ribs posteriorly.

The diaphragm also includes three openings for the passage of structures between the thorax and the abdomen. The inferior vena cava passes through the **caval opening**, and the esophagus and attached nerves pass through the esophageal hiatus. The aorta, thoracic duct, and azygous vein pass through the aortic hiatus of the posterior diaphragm.



(a) Superficial and deep abdominal muscles (anterior lateral view)



(b) Posterior abdominal muscles (anterior view)

Figure 10. Muscles of the Abdomen. *(a) The anterior abdominal muscles include the medially located rectus abdominis, which is covered by a sheet of connective tissue called the rectus sheath. On the flanks of the body, medial to the rectus abdominis, the abdominal wall is composed of three layers. The external oblique muscles form the superficial layer, while the internal oblique muscles form the middle layer, and the transverses abdominus forms the deepest layer. (b) The muscles of the lower back move the lumbar spine but also assist in femur movements.*

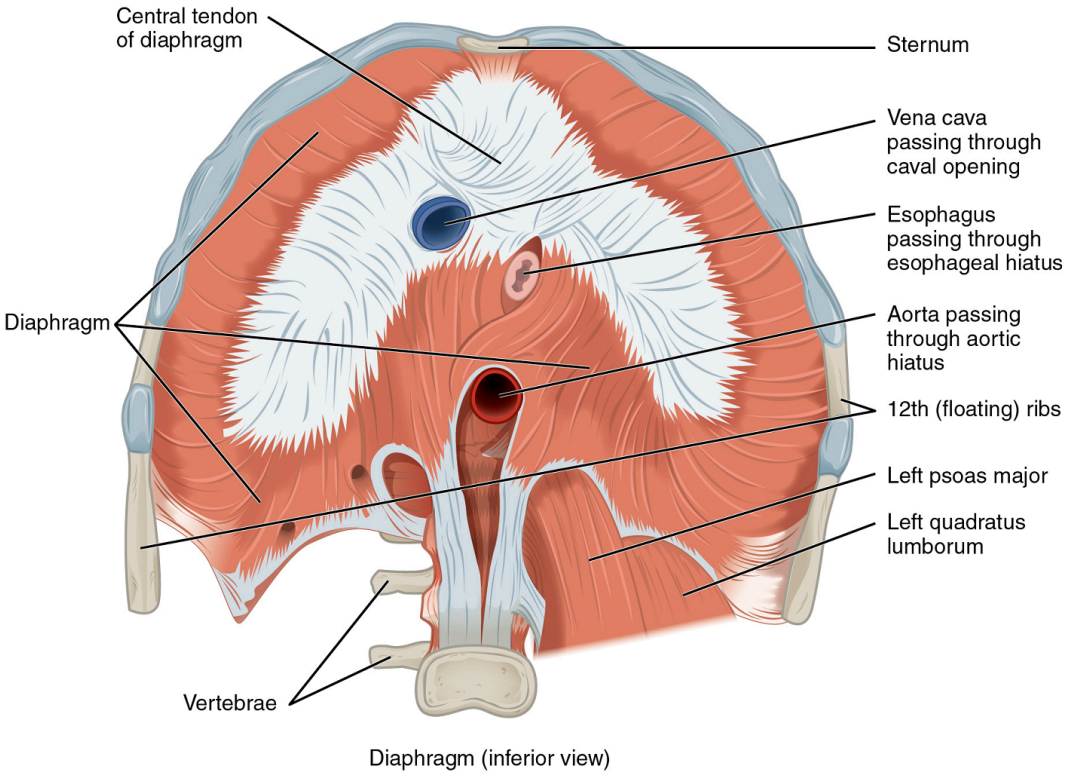


Figure 11. Muscles of the Diaphragm. *The diaphragm separates the thoracic and abdominal cavities.*

***The Intercostal Muscles*:** There are three sets of muscles, called intercostal muscles, which span each of the intercostal spaces. The principal role of the intercostal muscles is to assist in breathing by changing the dimensions of the rib cage (Figure 12).

The 11 pairs of superficial **external intercostal** muscles aid in inspiration of air during breathing because when they contract, they raise the rib cage, which expands it. The 11 pairs of **internal intercostal** muscles, just under the externals, are used for expiration because they draw the ribs together to constrict the rib cage. The **innermost intercostal** muscles are the deepest, and they act as synergists for the action of the internal intercostals.

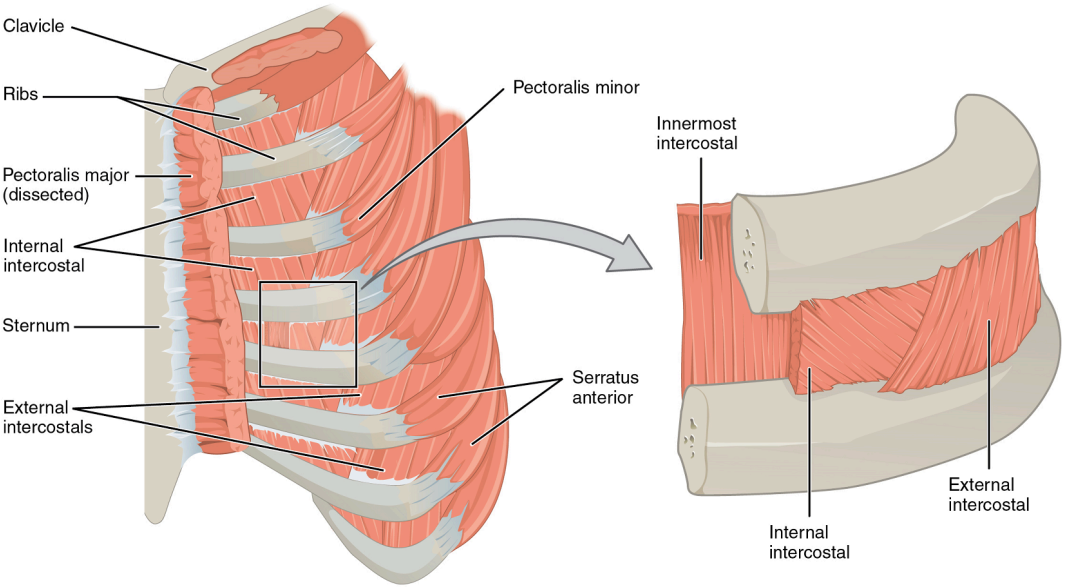


Figure 12. Intercostal Muscles. *The external intercostals are located laterally on the sides of the body. The internal intercostals are located medially near the sternum. The innermost intercostals are located deep to both the internal and external intercostals.*

Muscles of the Pectoral Girdle and Upper Limbs: Muscles of the shoulder and upper limb can be divided into four groups: muscles that stabilize and position the pectoral girdle, muscles that move the arm, muscles that move the forearm, and muscles that move the wrists, hands, and fingers. The pectoral girdle, or shoulder girdle, consists of the lateral ends of the clavicle and scapula, along with the proximal end of the humerus, and the muscles covering these three bones to stabilize the shoulder joint. The girdle creates a base from which the head of the humerus, in its ball-and-socket joint with the glenoid fossa of the scapula, can move the arm in multiple directions.

Muscles that position the pectoral girdle are located either on the anterior thorax or on the posterior thorax (Figure 13). Among the most important of these is the **trapezius**, located in the posterior thorax that originate on the skull and upper vertebral column and insert on the clavicle and scapula. The trapezius are capable of diverse movements such as elevation and depression of the scapula (shrugging shoulders), moving the scapula together, and tilting the head backward.

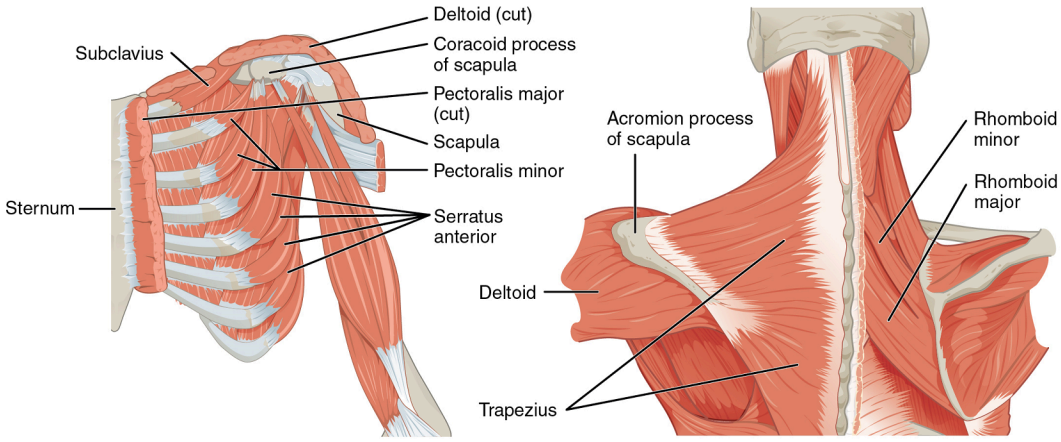


Figure 13. Muscles That Position the Pectoral Girdle. *The muscles that stabilize the pectoral girdle make it a steady base on which other muscles can move the arm. Note that the pectoralis major and deltoid, which move the humerus, are cut here to show the deeper positioning muscles.*

Muscles that move the humerus: Similar to the muscles that position the pectoral girdle, muscles that cross the shoulder joint and move the humerus bone of the arm include both axial and scapular muscles (Figure 14 and Table 5). The two axial muscles are the **pectoralis major** and the **latissimus dorsi**. The **pectoralis major** is thick and fan-shaped, covering much of the superior portion of the anterior thorax. The broad, triangular **latissimus dorsi** is located on the inferior part of the back, where it inserts into a thick connective tissue sheath called an aponeurosis.

The rest of the shoulder muscles originate on the scapula. The anatomical and ligamental structure of the shoulder joint and the arrangements of the muscles covering it, allows the arm to carry out different types of movements. The **deltoid**, the thick muscle that creates the rounded lines of the shoulder is the major abductor of the arm, but it also facilitates flexing and medial rotation, as well as extension and lateral rotation. Named for its location, the **supraspinatus** (superior to the spine of the scapula) abducts the arm. The thick and flat **teres major** extends the arm, and assists in adduction and medial rotation of it. The long teres minor laterally rotates and extends the arm. Finally, the **coracobrachialis** flexes and adducts the arm (Table 5)

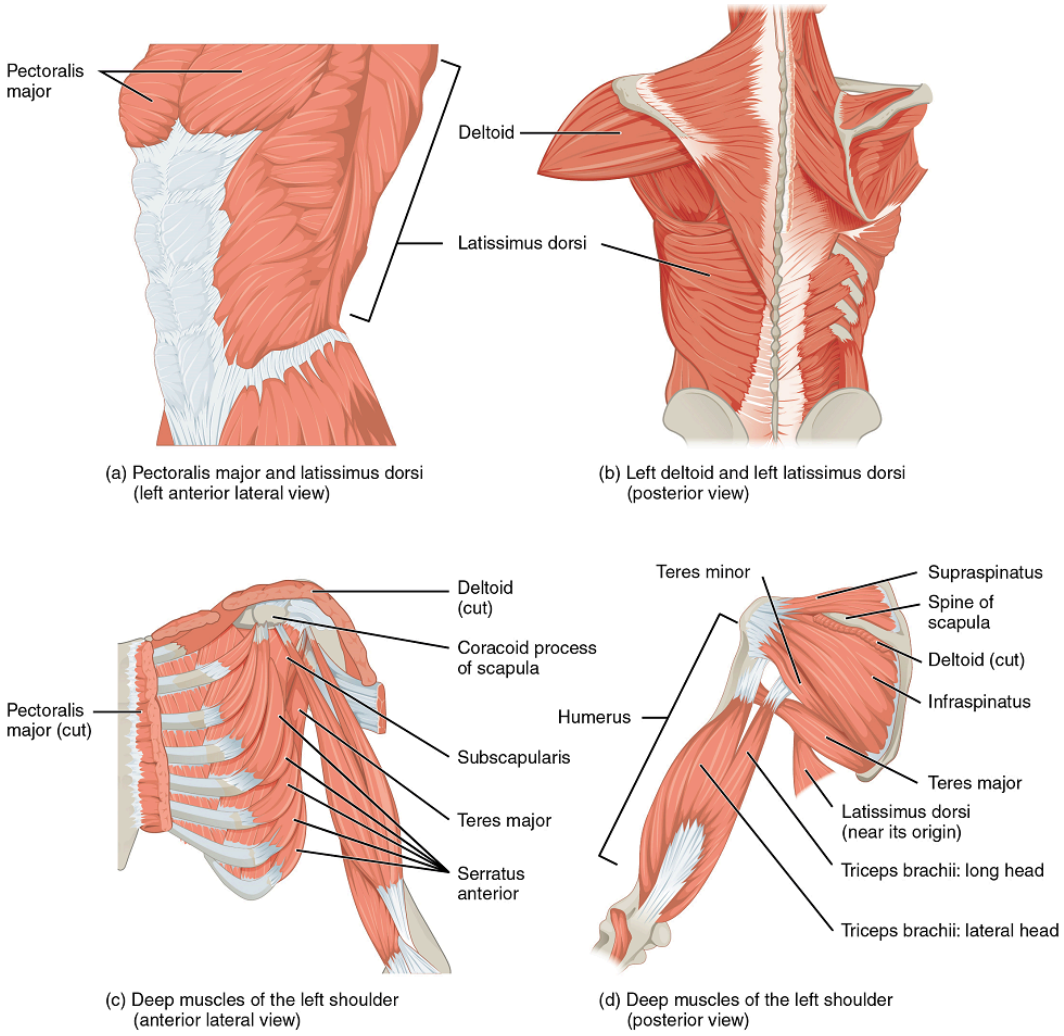


Figure 14. Muscles That Move the Humerus. *(a, c) The muscles that move the humerus anteriorly are generally located on the anterior side of the body and originate from the sternum (e.g., pectoralis major) or the anterior side of the scapula (e.g., subscapularis). (b) The muscles that move the humerus superiorly generally originate from the superior surfaces of the scapula and/or the clavicle (e.g., deltoids). The muscles that move the humerus inferiorly generally originate from middle or lower back (e.g., latissiumus dorsi). (d) The muscles that move the humerus posteriorly are generally located on the posterior side of the body and insert into the scapula (e.g., infraspinatus).*

The tendons of the deep subscapularis, supraspinatus, infraspinatus, and teres minor connect the scapula to the humerus, forming the rotator cuff (musculotendinous cuff), the circle of tendons around the shoulder joint. When baseball pitchers undergo shoulder surgery it is usually on the rotator cuff, which becomes pinched and inflamed, and may tear away from the bone due to the repetitive motion of bring the arm overhead to throw a fast pitch.

Table 5: Muscles that move the humerus

Movement	Target	Target motion direction	Prime mover	Origin	Insertion
Axial muscles					
Brings elbows together; moves elbow up (as during an uppercut punch)	Humerus	Flexion; adduction; medial rotation	Pectoralis major	Clavicle, sternum, cartilage of certain ribs (1-6 or 1-7); aponeurosis of external oblique muscle	Greater tubercle of humerus
Moves elbow back (as in elbowing someone behind you); spreads elbows apart	Humerus, scapula	Humerus:extension, adduction and medial rotation; Scapula: depression	Latissimus dorsi	Thoracic vertebrae (T7-T12); Lumbar vertebrae; lower ribs (9-12);iliac crest	Intertubercular sulcus of humerus
Scapular muscles					
Lifts arms at shoulder	Humerus	Abduction; flexion; extension; medial and lateral rotation	Deltoid	Trapezius; Clavicle; Acromion spine of scapula	Deltoid tuberosity of humerus
Rotates elbow outwards, as during a tennis swing	Humerus	Abduction	Supraspinatus	Supraspinous fossa of scapula	Greater tubercle of humerus
Rotate elbow outward	Humerus	Extension; Adduction	Teres major	Posterior surface of scapula	Intertubercular sulcus of humerus
Moves elbow up and across body, as when putting hand on chest.	Humerus	Flexion; adduction	Caracobrachialis	Corachoid process of scapula	Medial surface of humerus shaft

Muscles That Move the Forearm: The forearm, made of the radius and ulna bones, has four main types of action at the hinge of the elbow joint: flexion, extension, pronation, and supination. The forearm flexors include the **biceps brachii** and **brachioradialis**. The major extensor is the **triceps brachii**.

The **biceps brachii** and **brachioradialis** flex the forearm. The two-headed **biceps brachii** crosses the shoulder and elbow joints to flex the forearm, also taking part in supinating the forearm at the radioulnar joints and flexing the arm at the shoulder joint. The brachioradialis can flex the forearm quickly or help lift a load slowly. These muscles and their associated blood vessels and nerves form the anterior compartment of the arm (anterior flexor compartment of the arm) (Figure 15 and Table 6).

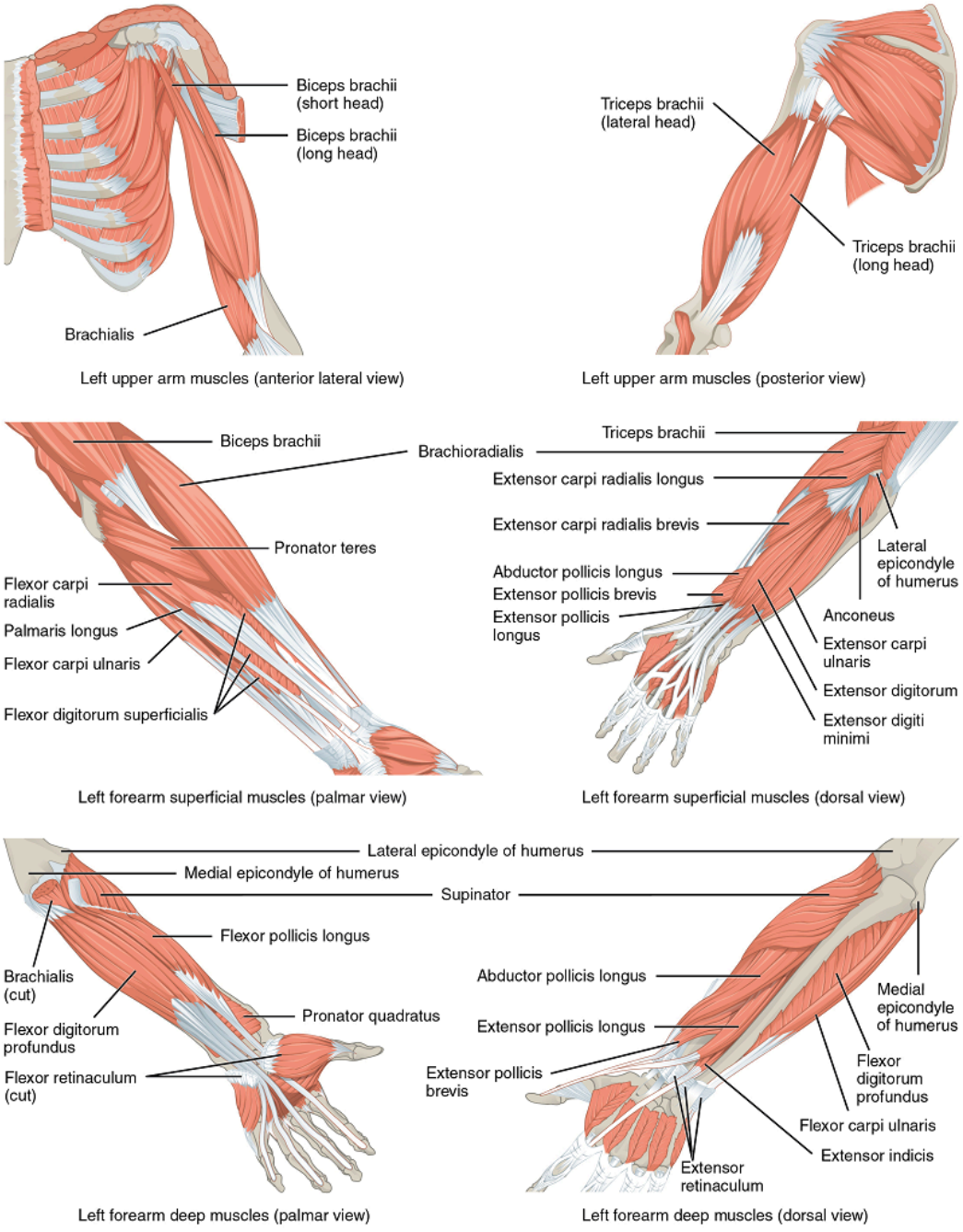


Figure 15. Muscles That Move the Forearm. *The muscles originating in the upper arm flex, extend, pronate, and supinate the forearm. The muscles originating in the forearm move the wrists, hands, and fingers.*

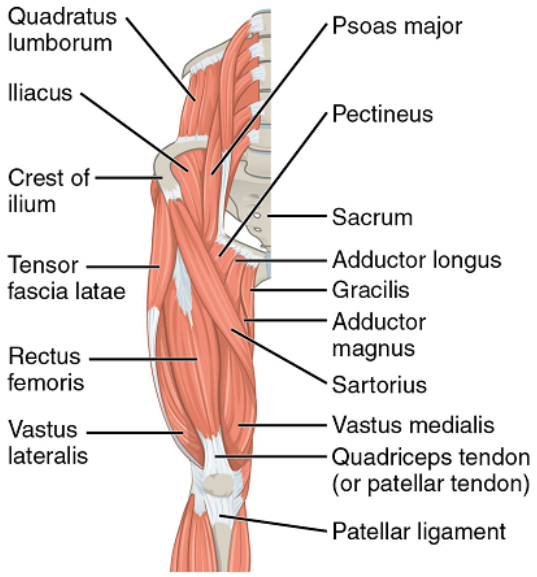
Table 6: Muscles that move the forearm

Movement	Target	Target motion direction	Prime mover	Origin	Insertion
Anterior muscles (flexion)					
Performs a bicep curl; also allows palm of hand to point toward body while flexing	Forearm	Flexion; supination	Biceps brachii	Scapula: coracoid process and tubercle above glenoid cavity	Radial tuberosity
Assists and stabilizes elbow while performing a bicep curl	Forearm	Flexion	Brachioradialis	Lateral supracondylar ridge at distal end of humerus	Base of styloid process of radius
Posterior muscle (extension)					
Extends forearm, as during a punch	Forearm	Extension	Triceps brachii	Infraglenoid tubercle of scapula; posterior shaft of humerus; posterior humeral shaft distal to radial groove	Olecranon process of ulna

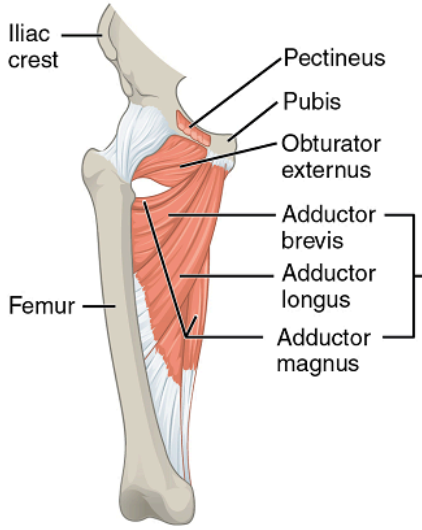
Appendicular Muscles of the Pelvic Girdle and Lower Limbs: The appendicular muscles of the lower body position and stabilize the **pelvic girdle**, which serves as a foundation for the lower limbs. Comparatively, there is much more movement at the pectoral girdle than at the pelvic girdle. There is very little movement of the pelvic girdle because of its connection with the sacrum at the base of the axial skeleton. The pelvic girdle is less range of motion because it was designed to stabilize and support the body.

Muscles of the Thigh: What would happen if the pelvic girdle, which attaches the lower limbs to the torso, were capable of the same range of motion as the pectoral girdle? For one thing, walking would expend more energy if the heads of the femurs were not secured in the acetabula of the pelvis. The body's center of gravity is in the area of the pelvis. If the center of gravity were not to remain fixed, standing up would be difficult as well. Therefore, what the leg muscles lack in range of motion and versatility, they make up for in size and power, facilitating the body's stabilization, posture, and movement.

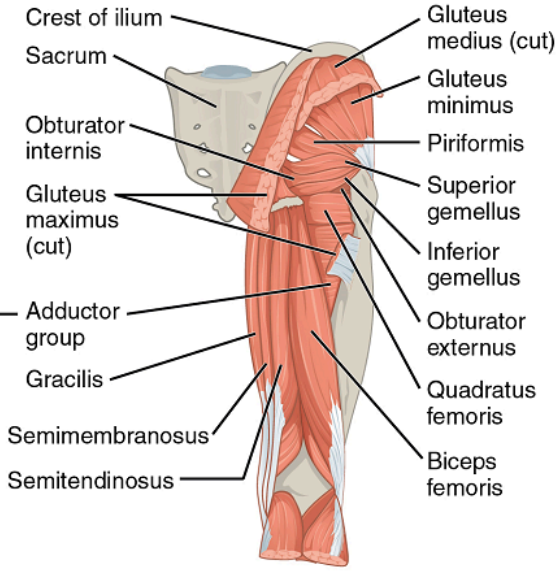
Gluteal Region Muscles That Move the Femur: Most muscles that insert on the femur (the thigh bone) and move it, originate on the pelvic girdle. **The psoas major** and **iliacus** make up the **iliopsoas group**. Some of the largest and most powerful muscles in the body are the gluteal muscles or **gluteal group**. The **gluteus maximus** is the largest and deep to the gluteus maximus is the **gluteus medius** (Figure 16 and Table 7).



Superficial pelvic and thigh muscles of right leg (anterior view)



Deep pelvic and thigh muscles of right leg (anterior view)



Pelvic and thigh muscles of right leg (posterior view)

Figure 16. Hip and Thigh Muscles. *The large and powerful muscles of the hip that move the femur generally originate on the pelvic girdle and insert into the femur. The muscles that move the lower leg typically originate on the femur and insert into the bones of the knee joint. The anterior muscles of the femur extend the lower leg but also aid in flexing the thigh. The posterior muscles of the femur flex the lower leg but also aid in extending the thigh. A combination of gluteal and thigh muscles also adduct, abduct, and rotate the thigh and lower leg.*

Table 7: Gluteal region muscles that move the femur

Movement	Target	Target motion direction	Prime mover	Origin	Insertion
Iliopsoas group					
Raises knee at hip, as if performing a knee attack; assists lateral rotators in twisting thigh (and lower leg) outward; assists with bending over, maintaining posture.	Femur	Thigh: flexion and lateral rotation; torso: flexion	Psoas major Iliacus	Psoas major: Lumbar vertebrae; and thoracic vertebra T12; Iliacus: iliac fossa, iliac crest and lateral sacrum	Lesser trochanter of femur
Gluteal group					
Lowers knee and moves thigh back, as when getting ready to kick a ball	Femur	Extension	Gluteus maximus	Dorsal ilium; sacrum; coccyx	Gluteal tuberosity of femur; iliotibial tract
Opens thighs, as when doing a split	Femur	Abduction	Gluteus medius	Lateral surface of ilium	Greater trochanter of femur

Thigh Muscles That Move the Femur, Tibia, and Fibula: Deep fascia in the thigh separates it into medial, anterior, and posterior compartments (Figure 16 and Table 8). The major muscle in the medial compartment of the thigh is the strap-like **gracilis** that adducts the thigh in addition to flexing the leg at the knee.

The muscles of the anterior compartment of the thigh flex the thigh and extend the leg. This compartment contains the **quadriceps femoris group**, which actually comprises four muscles that extend and stabilize the knee. The most important of these is the **rectus femoris**, located on the anterior aspect of the thigh, The tendon common to all four is the **quadriceps tendon** (patellar tendon), which inserts into the **patella** and continues below it as the patellar ligament. The **patellar ligament** attaches to the tibial tuberosity. In addition to the quadriceps femoris, the **sartorius** is a band-like muscle that extends from the anterior superior iliac spine to the medial side of the proximal tibia. This versatile muscle flexes the leg at the knee and flexes, abducts, and laterally rotates the leg at the hip. This muscle allows us to sit cross-legged.

The posterior compartment of the thigh includes muscles that flex the leg and extend the thigh. The three long muscles on the back of the knee are the **hamstring group**, which flexes the knee. These are the **biceps femoris**, **semitendinosus**, and **semimembranosus**. The tendons of these muscles form the popliteal fossa, the diamond-shaped space at the back of the knee.

Muscles That Move the Feet and Toes: Similar to the thigh muscles, the muscles of the leg are divided by deep fascia into compartments, although the leg has three: anterior, lateral, and posterior (Figure 17 and Table 9).

The muscles in the anterior compartment of the leg: the **tibialis anterior**, a long and thick muscle on the lateral surface of the tibia, the extensor hallucis longus, deep under it, and the extensor digitorum longus, lateral to it, all contribute to raising the front of the foot when they contract. The fibularis tertius, a small muscle that originates on the anterior surface of the fibula, is associated with the extensor digitorum longus and sometimes fused to it, but is not present in all people. Thick bands of connective tissue called the superior extensor retinaculum (transverse ligament of the ankle) and the inferior extensor retinaculum, hold the tendons of these muscles in place during dorsiflexion.

Table 8. Thigh Muscles That Move the Femur, Tibia, and Fibula

Movement	Target	Target motion direction	Prime mover	Origin	Insertion
Medial compartment of thigh					
Moves back of lower legs up toward buttocks, as when kneeling; assists in opening thighs	Femur; tibia/fibula	Tibia/fibula: flexion; thigh: adduction	Gracilis	Inferior ramus; body of pubis; ischial ramus	Medial surface of tibia
Anterior compartment of thigh: Quadriceps femoris group					
Moves lower leg out in front of body, as when kicking; assists in raising the knee	Femur; tibia/fibula	Tibia/fibula: extension; thigh: flexion	Rectus femoris	Anterior inferior iliac spine; superior margin of acetabulum	Patella; tibial tuberosity
Moves lower leg out in front of body, as when kicking	Tibia/fibula	Extension	Vastus lateralis	Greater trochanter; intertrochanteric line; linea aspera	Patella; tibial tuberosity
Moves lower leg out in front of body, as when kicking	Tibia/fibula	Extension	Vastus medialis	Linea aspera; intertrochanteric line	Patella; tibial tuberosity
Moves lower leg out in front of body, as when kicking	Tibia/fibula	Extension	Vastus intermedius	Proximal femur shaft	Patella; tibial tuberosity
Moves back of lower legs up and back toward the buttocks, as when kneeling; assists in moving thigh diagonally upward and outward as when mounting a bike	Femur; tibia/fibula	Tibia: flexion; thigh: flexion, abduction, lateral rotation	Sartorius	Anterior superior iliac spine	Medial aspect of proximal tibia
Posterior compartment of thigh: Hamstring group					
Moves back of lower legs up and back toward the buttocks, as when kneeling; moves thigh down and back; twists the thigh (and lower leg) outward	Femur; tibia/fibula	Tibia/fibula: flexion; thigh: extension, lateral rotation	Biceps femoris	Ischial tuberosity; linea aspera; distal femur	Head of fibula; lateral condyle of tibia
Moves back of lower legs up toward buttocks, as when kneeling; moves thigh down and back; twists the thigh (and lower leg) inward	Femur; tibia/fibula	Tibia/fibula: flexion; thigh: extension, medial rotation	Semitendinosus	Ischial tuberosity	Upper tibial shaft
Moves back of lower legs up and back toward the buttocks as when kneeling; moves thigh down and back; twists the thigh (and lower leg) inward	Femur; tibia/fibula	Tibia/fibula: flexion; thigh: extension, medial rotation	Semi-membranosus	Ischial tuberosity	Medial condyle of tibia; lateral condyle of femur

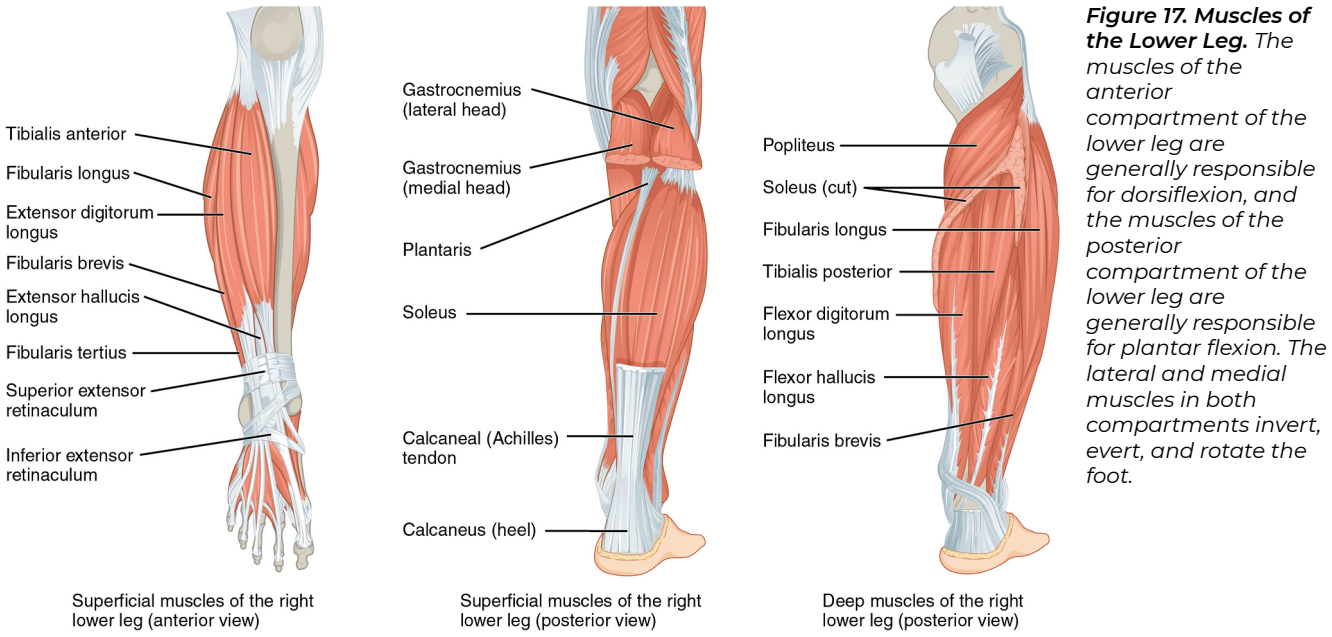


Figure 17. Muscles of the Lower Leg. *The muscles of the anterior compartment of the lower leg are generally responsible for dorsiflexion, and the muscles of the posterior compartment of the lower leg are generally responsible for plantar flexion. The lateral and medial muscles in both compartments invert, evert, and rotate the foot.*

The lateral compartment of the leg includes two muscles: the fibularis longus (peroneus longus) and the fibularis brevis (peroneus brevis). The superficial muscles in the posterior compartment of the leg all insert onto the calcaneal tendon (Achilles tendon), a strong tendon that inserts into the calcaneal bone of the ankle. The muscles in this compartment are large and strong and keep humans upright. The most superficial and visible muscle of the calf is the **gastrocnemius**. Deep to the gastrocnemius is the wide, flat **soleus**. The plantaris runs obliquely between the two; some people may have two of these muscles, whereas no plantaris is observed in about seven percent of other cadaver dissections. The plantaris tendon is a desirable substitute for the fascia lata in hernia repair, tendon transplants, and repair of ligaments. There are four deep muscles in the posterior compartment of the leg as well: the popliteus, flexor digitorum longus, flexor hallucis longus, and tibialis posterior.

Movement	Target	Target motion direction	Prime mover	Origin	Insertion
Anterior compartment of leg					
Raises the sole of the foot off the ground, as when preparing to foot-tap; bends the inside of the foot upwards, as when catching your balance while falling laterally toward the opposite side as the balancing foot	Foot	Dorsiflexion; inversion	Tibialis anterior	Lateral condyle and upper tibial shaft; interosseous membrane	Interior surface of medial cuneiform; First metatarsal bone
Raises the sole of the foot off the ground, as when preparing to foot-tap; extends the big toe	Foot; big toe	Foot: dorsiflexion; big toe: extension	Extensor hallucis longus	Anteromedial fibula shaft; interosseous membrane	Distal phalanx of big toe
Raises the sole of the foot off the ground, as when preparing to foot-tap; extends toes	Foot; toes 2–5	Foot: dorsiflexion; toes: extension	Extensor digitorum longus	Lateral condyle of tibia; proximal portion of fibula; interosseous membrane	Middle and distal phalanges of toes 2–5
Lateral compartment of leg					
Lowers the sole of the foot to the ground, as when foot-tapping or jumping; bends the inside of the foot downwards, as when catching your balance while falling laterally toward the same side as the balancing foot	Foot	Plantar flexion and eversion	Fibularis longus	Upper portion of lateral fibula	First metatarsal; medial cuneiform
Lowers the sole of the foot to the ground, as when foot-tapping or jumping; bends the inside of the foot downward, as when catching your balance while falling laterally toward the same side as the balancing foot	Foot	Plantar flexion and eversion	Fibularis (peroneus) brevis	Distal fibula shaft	Proximal end of fifth metatarsal
Posterior compartment of leg: Superficial muscles					
Lowers the sole of the foot to the ground, as when foot-tapping or jumping; assists in moving the back of the lower legs up and back toward the buttocks	Foot; tibia/ fibula	Foot: plantar flexion; tibia/fibula: flexion	Gastrocnemius	Medial and lateral condyles of femur	Posterior calcaneus
Lowers the sole of the foot to the ground, as when foot-tapping or jumping; maintains posture while walking	Foot	Plantar flexion	Soleus	Superior tibia; fibula; interosseous membrane	Posterior calcaneus
Lowers the sole of the foot to the ground, as when foot-tapping or jumping; assists in moving the back of the lower legs up and back toward the buttocks	Foot; tibia/ fibula	Foot: plantar flexion; tibia/fibula: flexion	Plantaris	Posterior femur above lateral condyle	Calcaneus or calcaneus tendon
Lowers the sole of the foot to the ground, as when foot-tapping or jumping	Foot	Plantar flexion	Tibialis posterior	Superior tibia and fibula; interosseous membrane	Several tarsals and metatarsals 2–4
Posterior compartment of leg: Deep muscles					
Moves the back of the lower legs up and back toward the buttocks; assists in rotation of the leg at the knee and thigh	Tibia/ fibula	Tibia/fibula: flexion thigh and lower leg: medial and lateral rotation	Popliteus	Lateral condyle of femur; lateral meniscus	Proximal tibia
Lowers the sole of the foot to the ground, as when foot-tapping or jumping; bends the inside of the foot upward and flexes toes	Foot; toes 2–5	Foot: plantar flexion and inversion toes: flexion	Flexor digitorum longus	Posterior tibia	Distal phalanges of toes 2–5
Flexes the big toe	Big toe; foot	Big toe: flexion foot: plantar flexion	Flexor hallucis longus	Midshaft of fibula; interosseous membrane	Distal phalanx of big toe

Table 9. Muscles That Move the Feet and Toes

Unit 16: Muscle Physiology

Unit Outline

Part 1: The two required precedents of skeletal muscular contraction

- The neuromuscular junction
- Excitation-contraction coupling

Part 2: Skeletal muscle fiber contraction and relaxation

- The Sliding Filament Model of contraction
- ATP and muscle contraction
- Sources of ATP: Creatine phosphate metabolism, the anaerobic pathway, and aerobic cellular respiration
- Relaxation of a skeletal muscle
- Muscle tone
- Exercise and muscle performance
- Muscle atrophy

Part 3: Cardiac muscle tissue

- Gap junctions and desmosomes
- Electric coupling
- The functional syncytium

Part 4: Smooth muscle tissue

Learning Objectives

At the end of this unit, you should be able to:

I. Describe the anatomy of a neuromuscular junction.

II. Explain the process of muscle contraction.

III. Describe the physiology of muscle relaxation.

IV. Describe the concept of muscle tone as it pertains to skeletal muscle.

V. Define the following terms: paralysis, muscular dystrophy, muscular atrophy, muscular hypertrophy.

VI. Describe the microscopic anatomy (histology) of cardiac muscle.

VII. Describe the mechanism of contraction in cardiac muscle. Describe in detail how a cardiac muscle contracts by describing the events that occur within the cardiac muscle starting from the depolarization of the plasma membrane of a cardiac muscle cell and ending with cross-bridge formation.

VIII. Describe the functional significance of self-excitatory cardiac muscle cells.

IX. Describe the microscopic anatomy of smooth muscle.

X. Explain the mechanism of contraction and relaxation in smooth muscle.

XI. Describe the neural, hormonal and chemical factors that regulate contraction of smooth muscle.

XII. Define the process and anatomical basis of peristalsis.

Learning Objectives and Guiding Questions

At the end of this unit, you should be able to complete all the following tasks, including answering the guiding questions associated with each task.

I. Describe the anatomy of a neuromuscular junction.

1. Draw a fully-labelled diagram showing a neuromuscular junction. Add annotations explaining the events that occur when a nerve impulse (or "action potential") arrives at the synaptic end bulb, until the time the sarcolemma of the muscle cell is depolarized.

II. Explain the process of muscle contraction.

1. Describe the physiology of muscle contraction, including the roles of the following components: calcium ions (Ca^{2+}), troponin, tropomyosin, myosin, actin, ATP.
2. Describe the generation of a muscle action potential, including the roles of acetylcholine (ACh) and sodium (Na^{+}) ions.
3. Draw and fully label a diagram showing one fully contracted sarcomere. Your diagram must include the following **labelled** structures:
    - Z line
    - A band
    - M line
    - I band
    - H zone
    - Sarcomere width
4. Complete your diagram above by annotating it. For each of the labelled structures above, add notes that state and *explain how* that particular structure is different (or not) in a fully contracted vs. a fully relaxed sarcomere:
5. Explain the roles of calcium ions in muscle contraction, including their involvement in:

- The release of acetylcholine (ACh) from a motor neuron
- The binding of myosin to actin

6. Draw a fully-annotated diagram describing how an action potential in a muscle fiber causes the release of calcium ions from the sarcoplasmic reticulum to the sarcoplasm.
7. Describe the the role of each of the following in the process of muscle contraction: calcium ions, troponin, tropomyosin, myosin, actin, and ATP.

III. Describe the physiology of muscle relaxation.

1. Describe the events that must occur for a contracted muscle to relax. Include in your description the events that must occur at:

    - The neuromuscular junction
    - The sarcomere
    - The sarcoplasmic reticulum membrane

2. Describe the functions of ATP in a muscle cell, including its roles in muscle contraction, in muscle relaxation, and in maintaining the muscle cell in its resting (relaxed) state.
3. List and describe in general terms the three pathways by which a muscle fiber can produce ATP.
4. Compare and contrast the three pathways by which a muscle fiber can produce ATP, in terms of:

    - The source of the phosphate group attached to ADP to produce ATP
    - The name of the substrate (starting molecule) required
    - The number of ATP molecules generated per molecule of substrate
    - The speed at which ATP can be generated
    - Whether myoglobin is useful for each pathway

IV. Describe the concept of muscle tone as it pertains to skeletal muscle.

1. Define the term “muscle tone”.
2. What is the physiological purpose of this phenomenon?

V. Define the following terms: paralysis, muscular dystrophy, muscular atrophy, muscular hypertrophy.

1. Define the term “paralysis”.
2. Briefly describe the major differences between flaccid paralysis and spastic paralysis.
3. Describe the common characteristic of the group of muscle diseases known as “muscular dystrophies”.
4. Define the following terms:

    - Muscular atrophy
    - Muscular hypertrophy

VI. Describe the microscopic anatomy (histology) of cardiac muscle.

1. Describe the structure and location within a cardiac muscle cell of each of the following:

- Intercalated discs
- Sarcomeres
- T-tubules
- Sarcoplasmic reticulum

VII. Describe the mechanism of contraction in cardiac muscle.

1. Describe in detail how a cardiac muscle contracts by describing the events that occur within the cardiac muscle starting from the depolarization of the plasma membrane of a cardiac muscle cell and ending with cross-bridge formation.
2. Which pathway is used to produce ATP in cardiac cells?
3. Compare and contrast the contraction of a skeletal muscle cell with that of a cardiac muscle cell by comparing and contrasting:

    - How the basic heartbeat is controls vs. how skeletal muscle contraction is initiated.
    - How contraction of multiple neibouring muscle cells is coordinated and synchronized within cardiac muscle vs. within skeletal muscle.
    - The source of the calcium ions required to promote and sustain muscle contraction in a cardiac muscle cell vs. a skeletal muscle cell.

4. Compare and contrast the contraction of a smooth muscle cell with that of a cardiac muscle cell.

VIII. Describe the functional significance of self-excitatory cardiac muscle cells.

1. Describe the difference in the excitation of a pacemaker cell with that of other cardiac muscle fiber cells

IX. Describe the microscopic anatomy of smooth muscle.

1. Describe the structure, location within a smooth muscle cell, and the function of each of the following:

    - Caveolae
    - Sarcoplasmic reticulum
    - Myofilaments
    - Intermediate filaments
    - Dense bodies

X. Explain the mechanism of contraction and relaxation in smooth muscle.

1. Describe the location and function within a smooth muscle cell of each of the following:

    - Calcium ions
    - Calmodulin
    - Dense bodies
    - Gap junctions
    - Calcium ion pumps

2. Describe in detail how a smooth muscle contracts by describing the events that occur within the

smooth muscle from the generation of an action potential in one smooth muscle cell to contraction of the entire smooth muscle.

3. Compare and contrast the contraction of a skeletal muscle cell with that of a smooth muscle cell by comparing and contrasting:
    - The intracellular location and function of calmodulin vs. troponin and tropomyosin
    - How the opening of calcium channels is controlled in a smooth muscle cell vs. in a skeletal muscle cell
    - The source of the calcium ions required to promote and sustain muscle contraction in a smooth muscle cell vs. a skeletal muscle cell
    - The types of chemicals normally used to trigger contraction in a smooth muscle cell vs. in a skeletal muscle cell

XI. Describe the neural and hormonal factors that regulate contraction of smooth muscle.

1. For each of the following neurotransmitters, describe their effect and mechanism of action on a smooth muscle cell (i.e., contraction or relaxation):
    - Acetylcholine, on a smooth muscle cell in the wall of a respiratory duct
    - Norepinephrine, on a smooth muscle cell in the wall of a respiratory duct
    - Norepinephrine, on a smooth muscle cell in the wall of a blood vessel
2. Provide examples of conditions which would result in an increase in $[Ca^{2+}]$ and therefore stimulate smooth muscle contraction.
3. For each of the following hormones, describe their effect, mechanism of action and physiological significance on a smooth muscle cell (i.e., contraction or relaxation):
    - Cholecystokinin, on the smooth muscle around the hepatopancreatic sphincter
    - Gastrin, on the smooth muscle in the stomach wall
    - Oxytocin, on the smooth muscle in the uterine wall

XII. Define the process and anatomical basis of peristalsis.

1. Define the term ‘peristalsis’.
2. Describe how sheets of smooth muscle are arranged in the wall of a hollow organ or vessel to allow peristalsis.
3. Describe the function of peristalsis in the human body.

Part 1: The Two Required Precedents of Skeletal Muscular Contraction

Two requirements must be met in order for skeletal muscular contraction to occur. First, there must be in place a neuromuscular junction.

The Neuromuscular Junction is the site where a motor neuron’s terminal meets a muscle fiber (the equivalent of a single muscle cell, as recalled from Unit 15, Muscle Anatomy and Movement). The neuromuscular junction is where the muscle fiber first responds to signaling by the motor neuron. Every skeletal muscle fiber must be activated, or stimulated, by a nerve ending at the neuromuscular junction so that a change in membrane potential occurs.

Watch this video to learn more about what happens at the neuromuscular junction. Direct link: https://youtu.be/HulbYOoFieA

Excitation signals from the neuron are the only way to functionally activate the fiber to contract; they generate an electrical current, called an *action potential*, in the sarcolemma (plasma membrane) of the muscle fiber.

The action potential thus generated is linked to contraction, which is why the second requirement for skeletal muscular contraction is referred to as excitation-contraction coupling.

Excitation-Contraction Coupling: All living cells have membrane potentials, or electrical gradients across their membranes. The inside of the membrane is usually around -70 mV, relative to the outside. This is referred to as a cell's resting membrane potential. Neurons and muscle cells can use their membrane potentials to generate electrical signals. They do this by controlling the movement of charged particles, called ions, across their membranes to create electrical currents. This is achieved by opening and closing specialized proteins in the membrane called ion channels. Although the currents generated by ions moving through these channel proteins are very small, they form the basis of both neural signaling and muscle contraction.

Both neurons and skeletal muscle cells are electrically excitable, meaning that they are able to generate action potentials. An action potential is a special type of electrical signal that can travel along a cell membrane as a wave. This allows a signal to be transmitted quickly and faithfully over long distances.

Although the term **excitation-contraction coupling** confuses or scares some students, it comes down to this: for a skeletal muscle fiber to contract, its membrane must first be "excited"—in other words, it must be stimulated to fire an action potential. The muscle fiber action potential, which sweeps along the sarcolemma as a wave, is "coupled" to the actual contraction through the release of calcium ions from the **sarcoplasmic reticulum**(SR).

In skeletal muscle, this sequence begins with signals from the somatic motor division of the nervous system. In other words, the "excitation" step in skeletal muscles is always triggered by signaling from the nervous system (Figure 1).

Signaling begins when a **neuronal action potential** travels along the axon of a motor neuron, and then along the individual branches of the axon, terminating at individual neuromuscular junctions. Membrane potential changes cause calcium channels in the membrane of the neuron to open, allowing calcium ions to diffuse into the neuron's cytosol. This influx of Ca^{2+} causes vesicles in the neuron to fuse with its plasma membrane, releasing their contents – the neurotransmitter Acetylcholine (ACh) – into the space between the neuron and the muscle fiber, called the synaptic cleft. It is the exocytotic release of acetylcholine from these vesicles that is ultimately calcium-ion dependent.

Thus, the associated axon terminal at *each* neuromuscular junction releases **Acetylcholine (ACh).** The acetylcholine molecules diffuse across a minute space called the synaptic cleft and bind to acetylcholine receptors located within the **motor end-plate** of the sarcolemma on the other side of the synapse. Once acetylcholine binds, a channel in the acetylcholine receptor (called a **ligand-gated ion channel)** opens and positively charged ions can pass through into the muscle fiber, causing it to **depolarize**, meaning that the membrane potential of the muscle fiber becomes less negative (closer to zero, and this continues so that there is a temporary reversal of charge with the inside of the membrane briefly positive relative to the outside).

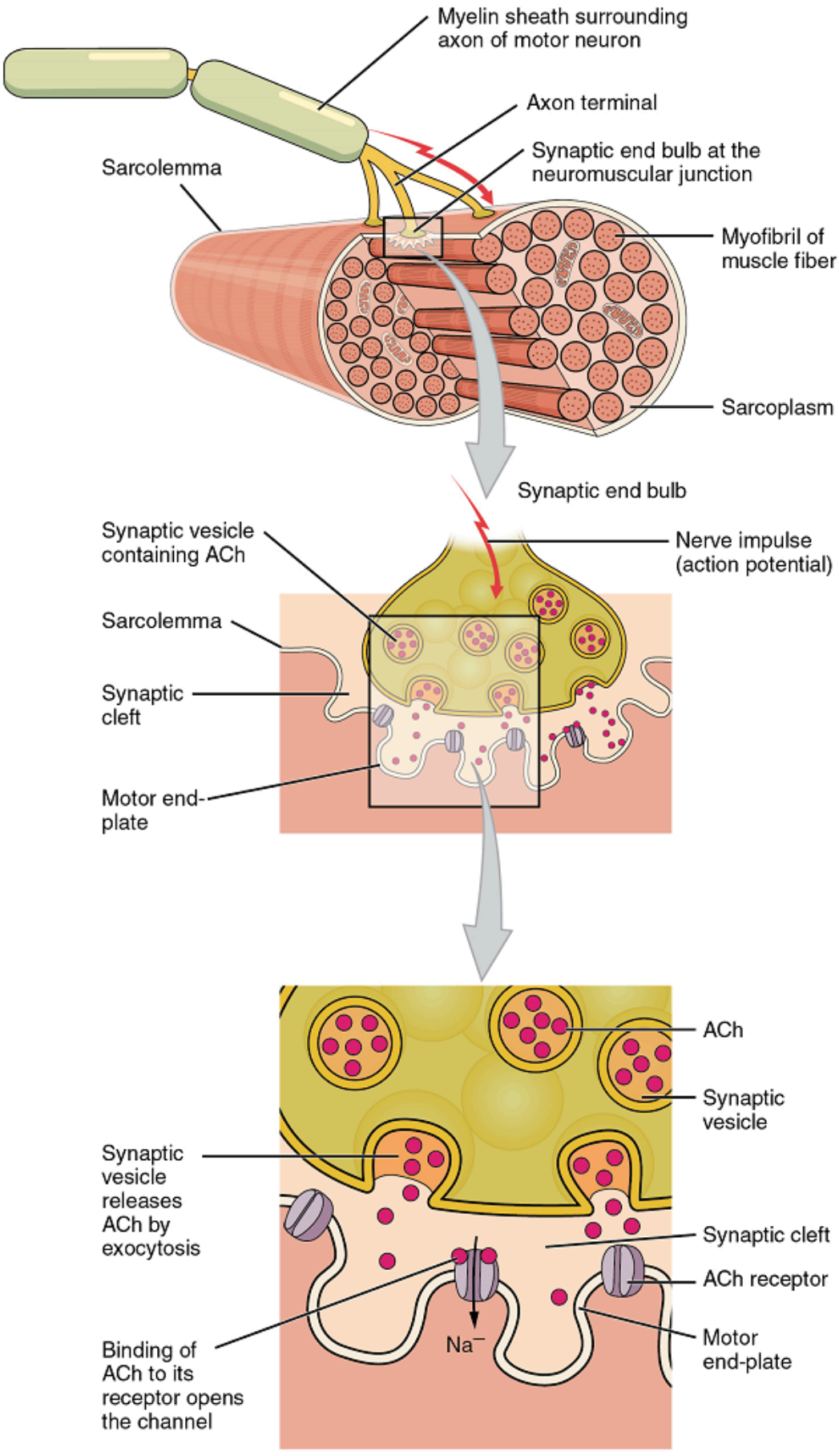


Figure 1. Motor End-Plate and Innervation. *At the neuromuscular junction, the axon terminal releases acetylcholine. The motor end-plate is the location of the acetylcholine-receptor s in the muscle fiber sarcolemma. When acetylcholine molecules are released, they diffuse across a minute space called the synaptic cleft and bind to the receptors.*

As the membrane depolarizes, another set of ion channels called **voltage-gated sodium channels** are triggered to open. Sodium ions enter the muscle fiber, and an action potential rapidly spreads (or "fires") along the entire membrane to initiate excitation-contraction coupling.

Things happen very quickly in the world of excitable membranes (just think about how quickly you can snap your fingers as soon as you decide to do it). Immediately following depolarization of the membrane, it repolarizes, re-establishing the negative membrane potential. Meanwhile, the acetylcholine in the synaptic cleft is degraded by the enzyme acetylcholinesterase (AChE) so that the acetylcholine can no longer bind to an acetylcholine receptor, thereby avoiding unwanted extended muscle excitation and contraction.

Propagation of an action potential along the sarcolemma is *still part of the excitation portion* of excitation-contraction coupling; it is this excitation that triggers the release of calcium ions from its storage in the cell's **sarcoplasmic reticulum**. For the action potential to reach the membrane of the SR, there are periodic invaginations that run deep within the sarcolemma, called transverse tubules (**T-tubules**). A T-tubule along with SR membranes on either side of it is referred to as a **triad** (Figure 2). Triads surround and enclose the cylindrical structure known as a **myofibril**, which contains actin and myosin.

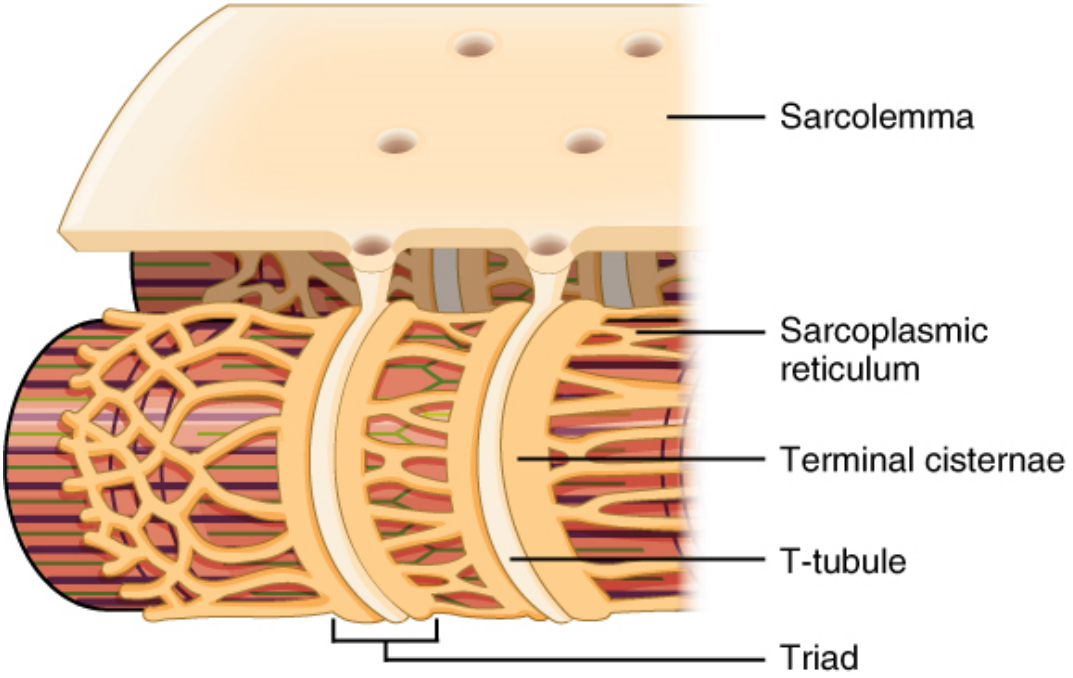


Figure 2. The T-tubule. *Narrow T-tubules permit the conduction of electrical impulses. The SR functions to regulate intracellular levels of calcium. Two terminal cisternae (where enlarged SR connects to the T-tubule) and one T-tubule comprise a triad—a "threesome" of membranes, with those of SR on two sides and the T-tubule sandwiched between them.*

T-tubules thus carry the action potential into the interior of the cell. The action potential triggers the opening of calcium channels in the membrane of adjacent SRs, causing calcium ions to diffuse out of the SR and into the sarcoplasm. *It is the arrival of Ca^{2+} in the sarcoplasm that initiates contraction of the muscle fiber by its contractile units, or sarcomeres.*

Part 2: Skeletal Muscle Fiber Contraction and Relaxation

Once again, the **sequence of events** that result in the contraction of an individual muscle fiber begins with an electrical signal – an action potential – travelling down a motor neuron innervating the muscle fiber. Calcium's role in initiating the release of acetylcholine from the synaptic end bulb has already been described.

When acetylcholine reaches the muscle fiber's sarcolemma, it binds to closed acetylcholine -gated ion channels there that now open as a result. In the area where these ion channels open, the sarcolemma of the

muscle fiber will depolarize as positively charged sodium ions (Na^+) enter, triggering an action potential that spreads to the rest of the sarcolemma. The whole sarcolemma will depolarize, including the T-tubules.

Embedded in the walls of the T-tubules of skeletal muscle fibers are voltage-sensitive proteins that are connected to calcium channels in the membrane of the adjacent sarcoplasmic reticulum (SR). When the action potential travels along each T-tubule, the voltage-sensitive proteins there change shape, pulling on the calcium channels of the SR and opening them. This allows Ca^{2+} ions to be released from their storage in the SR (where their concentration is higher), out to the cytosol (sarcoplasm) of the muscle fiber. The Ca^{2+} ions then initiate contraction, which is sustained by ATP (Figure 3).

Troponin and tropomyosin are the two major proteins that regulate skeletal muscle contraction via Ca^{2+} ions binding. Tropomyosin is a long, rod-like molecule which shields (blocks) the myosin-binding sites on actin. Troponin, which has a binding site for Ca^{2+}, is a globular protein whose role is to keep the longer, tropomyosin in its place.

Upon binding of Ca^{2+} to troponin, troponin changes its conformation (overall three-dimensional shape) and loses its hold on tropomyosin, thereby exposing the myosin-binding sites on actin.

Therefore, as long as calcium ions remain in the sarcoplasm to bind to troponin, which in turn keeps the myosin-binding sites on actin "unshielded," and as long as ATP is available to drive the cross-bridge cycling and the pulling of actin strands by myosin, the muscle fiber will continue to shorten to an anatomical limit.

Muscle contraction usually stops when signaling from the motor neuron ends, which repolarizes the sarcolemma and T-tubules, and closes the voltage-gated calcium channels in the SR. Calcium ions are then pumped back into the SR, which causes the tropomyosin to reshield (or re-cover) the binding sites on the actin strands. A muscle also can stop contracting when it runs out of ATP and becomes fatigued (Figure 4).

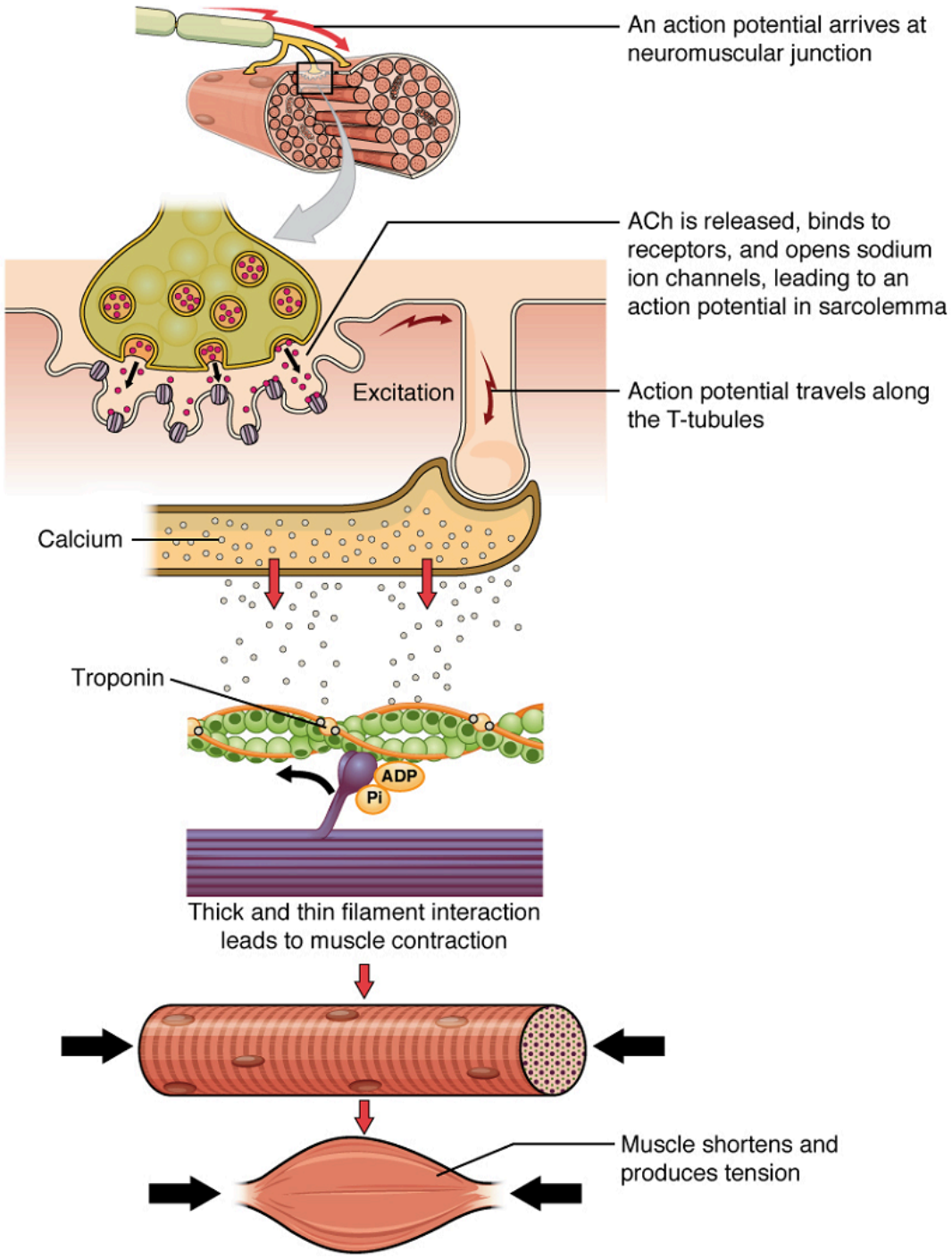


Figure 3. Contraction of a Muscle Fiber. *A cross-bridge forms between actin and the myosin heads triggering contraction. As long as Ca^{2+} ions remain in the sarcoplasm to bind to troponin, and as long as ATP is available, the muscle fiber will continue to shorten.*

The molecular events of muscle fiber shortening occur within the fiber's sarcomeres (Figure 5). The contraction of a striated muscle fiber occurs as the sarcomeres, linearly arranged within myofibrils, shorten as myosin heads pull on the actin filaments.

The region where thick and thin filaments overlap has a dense appearance, as there is little space between the filaments. This zone, where thin and thick filaments overlap, is very important to muscle contraction, as it is the site where filament movement starts. Thin filaments, anchored at their ends by the Z-discs, do not extend completely into the central region that only contains thick filaments, which are themselves anchored at their

bases at a spot called the M-line. A myofibril is composed of many sarcomeres running along its length; thus, myofibrils and muscle cells shorten (contract) as the sarcomeres contract.

Watch this video to learn more about the role of calcium. Direct link: http://openstaxcollege.org/l/calciumrole

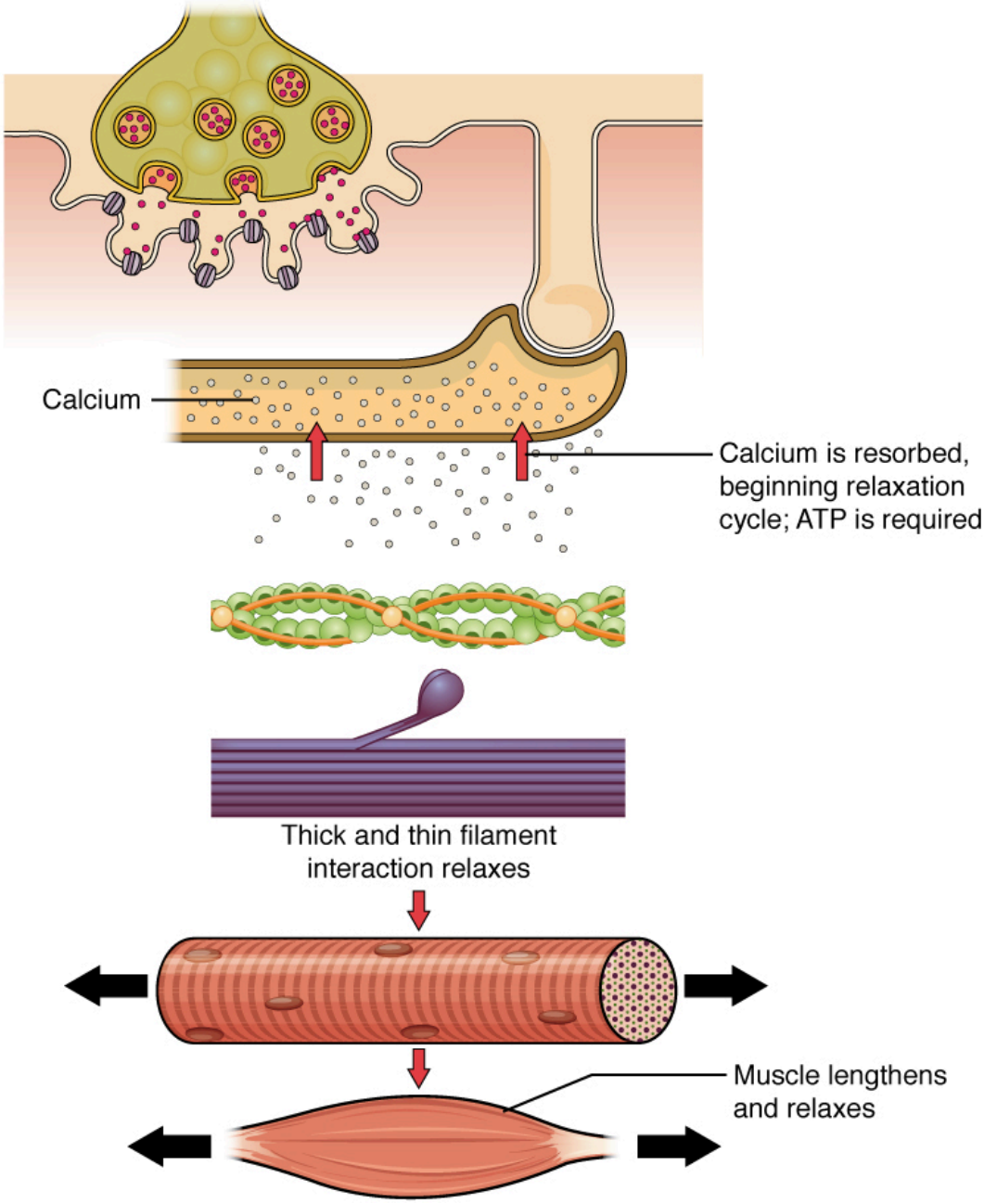


Figure 4. Relaxation of a Muscle Fiber. *Calcium ions are pumped back into the SR, which causes the tropomyosin to reshield the binding sites on the actin strands. A muscle may also stop contracting when it runs out of ATP and becomes fatigued.*

The Sliding Filament Model of Contraction: When signaled by a motor neuron, a skeletal muscle fiber contracts as the thin filaments are pulled and then slide past the thick filaments within the fiber's sarcomeres. This process is known as the sliding filament model of muscle contraction (Figure 5). The sliding can only occur when myosin-binding sites on the actin filaments are exposed by a series of steps that begins with Ca^{2+} entry into the sarcoplasm.

Recall that to initiate muscle contraction, tropomyosin has to expose the myosin-binding site on an actin filament to allow cross-bridge formation between the actin and myosin microfilaments. The first step in the process of contraction is for Ca^{2+} to bind to troponin so that tropomyosin can slide away from the binding sites on the actin strands. This allows the myosin heads to bind to these exposed binding sites and form cross-bridges. The thin filaments are then pulled by the myosin heads to slide past the thick filaments toward the center of the sarcomere. But each head can only pull a very short distance before it has reached its limit and must be "re-cocked" before it can pull again, a step that requires ATP.

ATP and Muscle Contraction: For thin filaments to continue to slide past thick filaments during muscle contraction, myosin heads must pull the actin at the binding sites, detach, re-cock, attach to more binding sites, pull, detach, re-cock, etc. This repeated movement is known as the cross-bridge cycle.

Each cross-bridge cycle requires energy, which is provided for by ATP.

Cross-bridge formation occurs when the myosin head attaches to the actin while adenosine diphosphate (ADP) and inorganic phosphate (Pi) are still bound to myosin (Figure 6a,b). Pi is then released, causing myosin to form a stronger attachment to actin, after which the myosin head moves toward the M-line, pulling the actin along with it, and releasing the ADP. As actin is pulled, the filaments move approximately 10 nm toward the M-line. This movement is called the **power stroke,** as movement of the thin filament occurs at this step (Figure 6c). In the absence of ATP, the myosin head will not detach from actin.

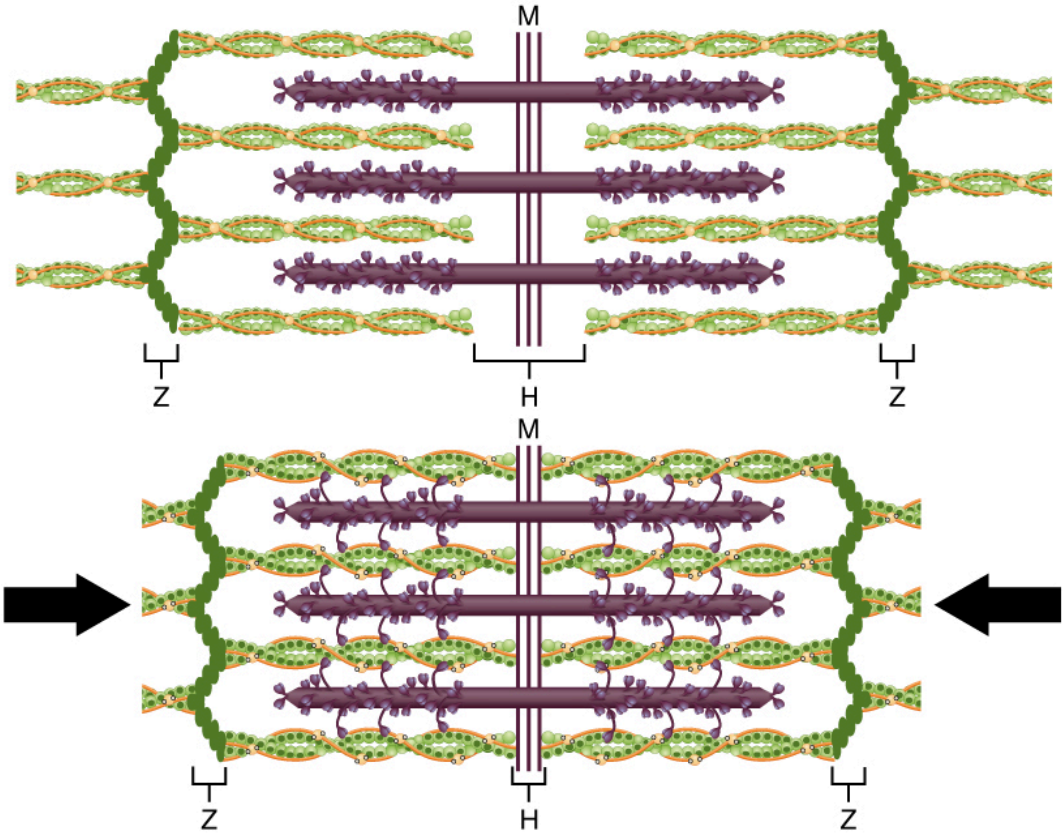


Figure 5. The Sliding Filament Model of Muscle Contraction. *When a sarcomere contracts, the Z lines move closer together, and the I band (only the portion of actin filaments not overlapping with myosin filaments) becomes smaller. The A band (the length of the myosin filaments) stays the same width. At full contraction, the thin and thick filaments overlap.*

One part of the myosin head attaches to the binding site on the actin, but the head has another binding site for ATP. ATP binding causes the myosin head to detach from the actin (Figure 6d).

After this occurs, ATP is converted to ADP and Pi by the intrinsic ATPase activity of myosin. The energy released during ATP hydrolysis changes the angle of the myosin head into a cocked position (Figure 6e). When the myosin head is cocked, it is said to be in a *high-energy configuration* and is capable of further movement as long as ATP is available.

Note that each thick filament of roughly 300 myosin molecules has multiple myosin heads, and many cross-bridges form and break continuously during muscle contraction. Multiply this by all of the sarcomeres in one myofibril, all the myofibrils in one muscle fiber, and all of the muscle fibers in one skeletal muscle, and you can understand why so much energy (ATP) is needed to keep skeletal muscles working. In fact, it is the loss of ATP that results in the **rigor mortis** observed soon after someone dies. With no further ATP production possible, there is no ATP available for myosin heads to detach from the actin-binding sites, so the cross-bridges stay in place, causing the rigidity in the skeletal muscles.

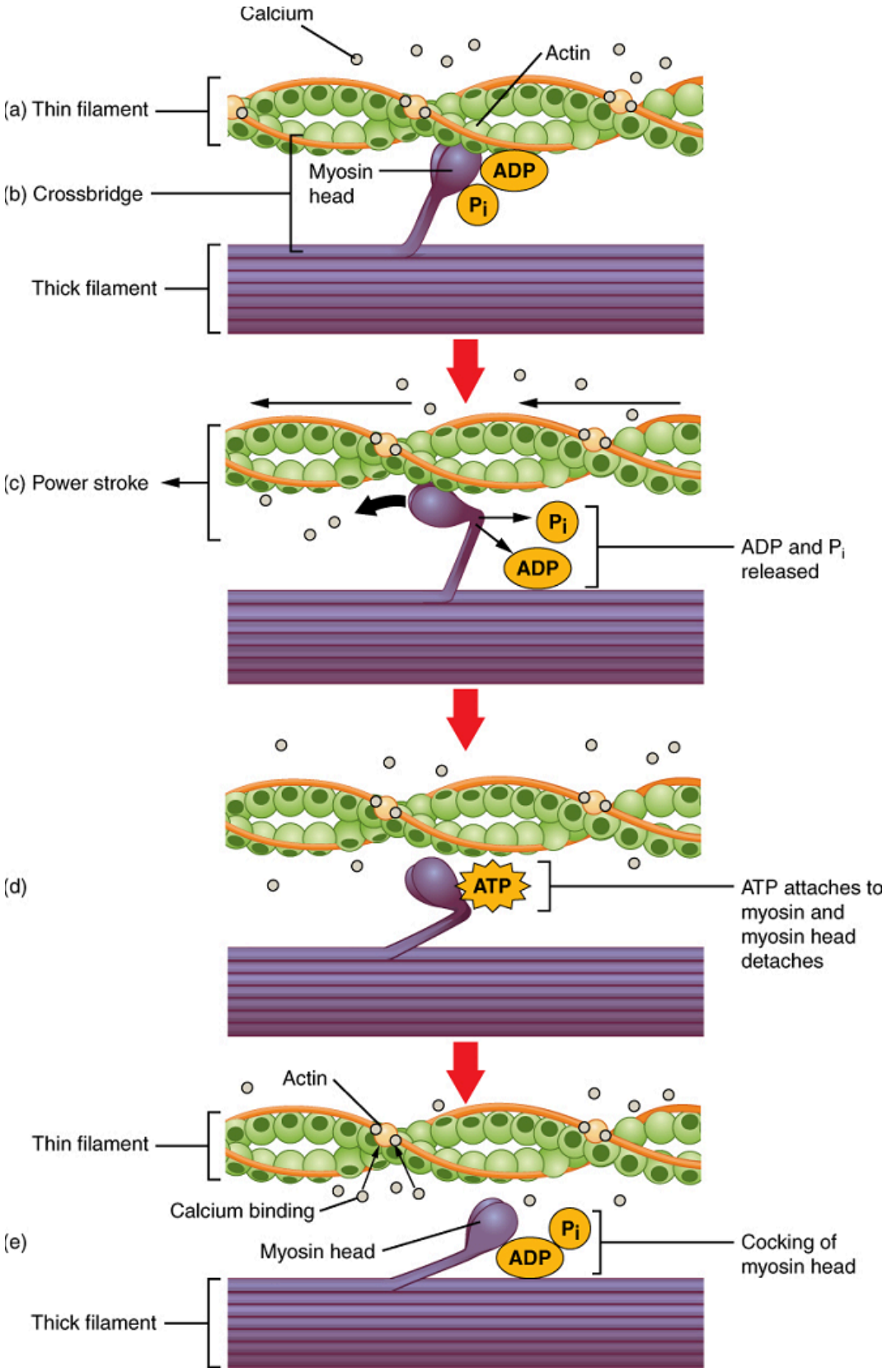
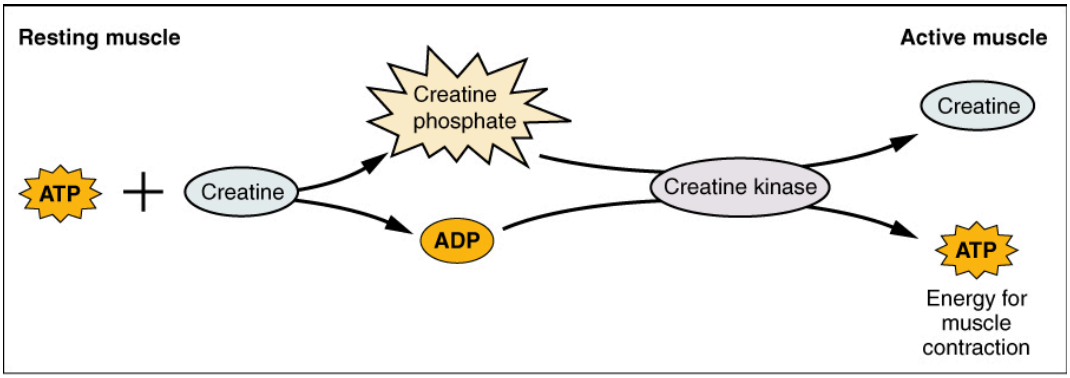


Figure 6. Skeletal Muscle Contraction. *(a) The active site on actin is exposed as calcium binds to troponin. (b) The myosin head is attracted to actin, and myosin binds actin at its actin-binding site, forming the cross-bridge. (c) During the power stroke, the phosphate generated in the previous contraction cycle is released. This results in the myosin head pivoting toward the center of the sarcomere, after which the attached ADP is released. (d) A new molecule of ATP attaches to the myosin head, causing the cross-bridge to detach. (e) The myosin head hydrolyzes ATP to ADP and phosphate, which returns the myosin to the cocked position.*

Sources of ATP: ATP supplies the energy for muscle contraction to take place. In addition to its direct role in the cross-bridge cycle, ATP also provides the energy for the active-transport utilizing Ca^{2+} pumps housed in the SR membranes. Muscle contraction does not occur without sufficient amounts of ATP. The amount of ATP stored in muscle is very low, only sufficient to power a few seconds worth of contractions.

Therefore, as it is broken down, ATP must be regenerated and replaced quickly to allow for sustained contraction: ATP can be regenerated through three mechanisms: creatine phosphate metabolism, anaerobic pathway (glycolysis and lactic acid formation) and aerobic cellular respiration.

(a) Creatine phosphate is a molecule that can store energy in its phosphate bonds. In a resting muscle, excess ATP transfers its energy to creatine, producing ADP and creatine phosphate. This acts as an energy reserve that can be used to quickly create more ATP. When the muscle starts to contract and needs energy, creatine phosphate transfers its phosphate back to ADP to form ATP and creatine. This reaction is catalyzed by the enzyme creatine kinase and occurs very quickly; thus, creatine phosphate-derived ATP powers the first few seconds of muscle contraction. However, creatine phosphate can only provide approximately 15 seconds worth of energy, at which point another energy source has to be used (Figure 7).



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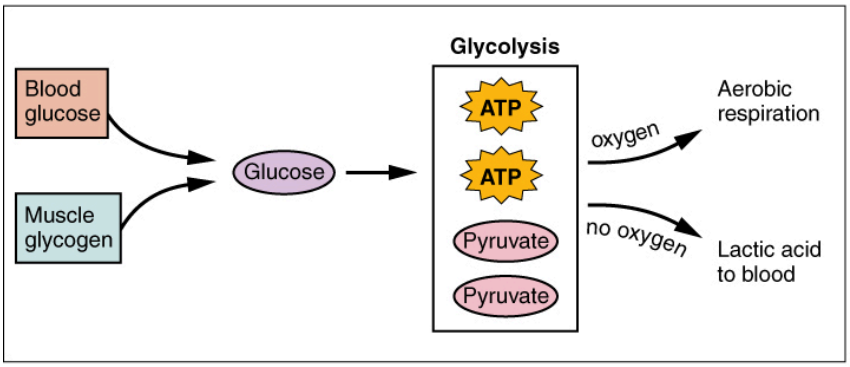

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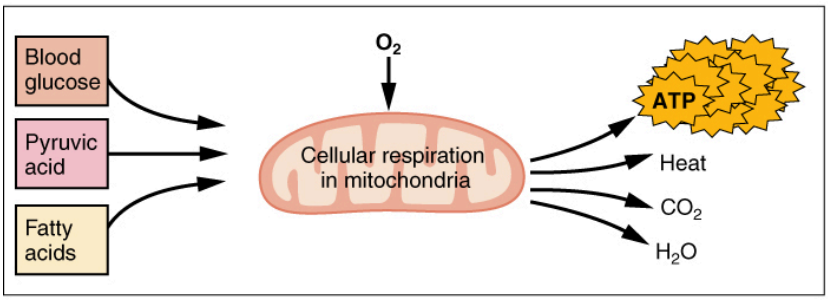

(c)

Figure 7. Muscle Metabolism. *(a) Some ATP is stored in a resting muscle. As contraction starts, it is used up in seconds. More ATP is generated from creatine phosphate for about 15 seconds. (b) Each glucose molecule produces two ATP and two molecules of pyruvic acid, which can be used in aerobic respiration or converted to lactic acid. If oxygen is not available, pyruvic acid is converted to lactic acid, which may contribute to muscle fatigue. This occurs during strenuous exercise when high amounts of energy are needed but oxygen cannot be sufficiently delivered to muscle. (c) Aerobic respiration is the breakdown of glucose in the presence of oxygen (O2) to produce carbon dioxide, water, and ATP. Approximately 95 percent of the ATP required for resting or moderately active muscles is provided by aerobic respiration, which takes place in mitochondria.*

(b) The Anaerobic Pathway: As the ATP produced by creatine phosphate is depleted, muscles turn to glycolysis as an ATP source. **Glycolysis** is an anaerobic (non-oxygen-dependent) process that breaks down glucose (sugar) to produce ATP. Because glycolysis cannot generate ATP as quickly as creatine phosphate, the switch to glycolysis results in a slower rate of ATP availability to the muscle. The sugar used in glycolysis can be provided by blood glucose or by metabolizing glycogen that is stored in the muscle. The breakdown of one glucose molecule produces two ATP and two molecules of **pyruvic acid**, which can be used either in aerobic respiration if sufficient oxygen is available, or when oxygen levels are low, converted to **lactic acid** (Figure 7b).

The lactic acid so produced may contribute to muscle fatigue. This conversion allows the recycling of the coenzyme NAD^+ from NADH, which is needed for glycolysis to continue. This occurs during strenuous exercise when high amounts of energy are needed but oxygen cannot be sufficiently delivered to muscle. Glycolysis itself cannot be sustained for very long (approximately one minute of muscle activity), but it is useful in facilitating short bursts of high-intensity output. This is because glycolysis does not utilize glucose very efficiently, producing a net gain of two ATPs per molecule of glucose, and the end product of lactic acid.

(c) Aerobic cellular respiration is the breakdown of glucose or other nutrients in the presence of oxygen to produce carbon dioxide, water, and ATP. Approximately 95 percent of the ATP required for resting or moderately active muscles is provided by aerobic respiration, which takes place in mitochondria. The inputs for aerobic respiration include glucose circulating in the bloodstream, pyruvic acid, and fatty acids. Aerobic respiration is much more efficient than anaerobic glycolysis, producing approximately 32 to 34 ATPs per molecule of glucose versus two (net) from glycolysis. However, aerobic respiration cannot be sustained without a steady supply of O_2 to the skeletal muscle (Figure 7c). To compensate, muscles store small amount of excess oxygen in a protein called myoglobin, allowing for more efficient muscle contractions and less fatigue. Aerobic training also increases the efficiency of the circulatory system so that O_2 can be supplied to the muscles for longer periods of time.

Relaxation of a Skeletal Muscle: Relaxing skeletal muscle fibers, and ultimately, the skeletal muscle, begins with the motor neuron, which stops releasing its chemical signal, acetylcholine, into the synapse at the neuromuscular junction. The muscle fiber will repolarize, which closes the gates in the SR where Ca^{2+} was being released. ATP-driven pumps will move Ca^{2+} out of the sarcoplasm back into the SR. Ca^{2+} no longer binds to troponin, resulting in the "reshielding" of the myosin-binding sites on the thin filaments by tropomyosin, which is now once again held in its place by troponin. Without the ability to form cross-bridges between the thin and thick filaments, the muscle fiber loses its tension and relaxes.

Muscle Tone: Skeletal muscles are rarely completely relaxed, or flaccid. Even if a muscle is not producing movement, it is contracted a small amount to maintain its contractile proteins and produce muscle tone. This continuous partial contraction of a muscle that causes the muscle to resist passive stretch while at rest is referred to as **muscle tone**. The tension produced by muscle tone allows muscles to continually stabilize joints and maintain posture.

Muscle tone is accomplished by a complex interaction between the nervous system and skeletal muscles that results in the activation of a few motor units at a time, most likely in a cyclical manner. In this manner, muscles never fatigue completely, as some motor units can recover while others are active.

The absence of the low-level contractions that lead to muscle tone is referred to as hypotonia or atrophy, and can result from damage to parts of the central nervous system, such as the cerebellum, or from loss of innervations to a skeletal muscle, as in poliomyelitis. Hypotonic muscles have a flaccid appearance and display functional impairments, such as weak reflexes or flaccid paralysis, where a person loses the ability to move affected muscles of the body. Conversely, excessive muscle tone is referred to as hypertonia, accompanied by hyperreflexia (excessive reflex responses), often the result of damage to upper motor neurons (found in the cerebral cortex and brainstem) of the central nervous system. Hypertonia can present with muscle rigidity (as seen in Parkinson's disease) or spasticity, a phasic change in muscle tone, where a limb will "snap" back from passive stretching (as seen in some strokes). Severe cases of this condition can lead to a specific type of paralysis, called spastic paralysis.

Exercise and Muscle Performance: Physical training alters the appearance of skeletal muscles and can produce changes in muscle performance. Conversely, a lack of use can result in decreased performance and muscle appearance. Although muscle cells can change in size, new cells are not formed when muscles grow. Instead, structural proteins are added to muscle fibers in a process called **hypertrophy**, so cell diameter increases. The reverse, when structural proteins are lost and muscle mass decreases, is called **atrophy**. Age-related muscle atrophy is called **sarcopenia**. Cellular components of muscles can also undergo changes in response to changes in muscle use.

Muscle Atrophy: Although atrophy due to disuse can often be reversed with exercise, muscle atrophy can also be the result of any of a number of genetic diseases, called **muscular dystrophy**, that result in increasing weakness of muscles and loss of muscle tissue over time. Although there are medications that can slow muscle degeneration and reduce damage to dying muscle cells, the atrophy due to muscular dystrophy is irreversible. Muscle atrophy with age, referred to as **sarcopenia**, is also irreversible. This is a primary reason why even highly trained athletes succumb to declining performance with age. This decline is noticeable in athletes whose sports require strength and powerful movements, such as sprinting, whereas the effects of age are less noticeable in endurance athletes such as marathon runners or long-distance cyclists. As muscles age, muscle fibers die, and they are replaced by connective tissue and adipose tissue (Figure 8). Because those tissues cannot contract and generate force as muscle can, muscles lose the ability to produce powerful contractions. The decline in muscle mass causes a loss of strength, including the strength required for posture and mobility. This may be caused by a reduction in FG fibers that hydrolyze ATP quickly to produce short, powerful contractions. Muscles in older people sometimes possess greater numbers of SO fibers, which are responsible for longer contractions and do not produce powerful movements. There may also be a reduction in the size of motor units, resulting in fewer fibers being stimulated and less muscle tension being produced.

Sarcopenia can be delayed to some extent by exercise, as training adds structural proteins and causes cellular changes that can offset the effects of atrophy. Increased exercise can produce greater numbers of cellular mitochondria, increase capillary density, and increase the mass and strength of connective tissue.

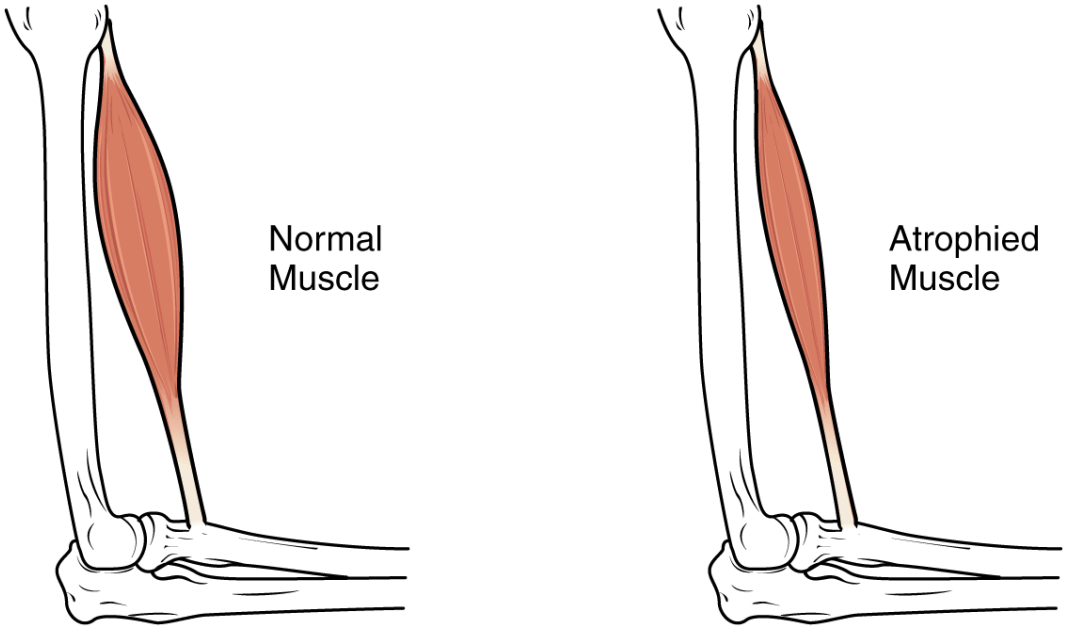

Figure 8. Atrophy. *Muscle mass is reduced as muscles atrophy with disuse.*

The effects of age-related atrophy are especially pronounced in people who are sedentary, as the loss of muscle cells is displayed as functional impairments such as trouble with locomotion, balance, and posture. This can lead to a decrease in quality of life and medical problems, such as joint problems because the muscles that stabilize

bones and joints are weakened. Problems with locomotion and balance can also cause various injuries due to falls.

Part 3: Cardiac Muscle Tissue

Cardiac muscle tissue is only found in the heart. Highly coordinated contractions of cardiac muscle pump blood into the vessels of the circulatory system. Similar to skeletal muscle, cardiac muscle is striated and organized into sarcomeres, possessing the same banding organization as skeletal muscle (Figure 9). However, cardiac muscle fibers are shorter than skeletal muscle fibers and usually contain only one nucleus, which is located in the central region of the cell. Cardiac muscle fibers, similarly to skeletal muscle fibers, also possess many mitochondria and myoglobin, as ATP is produced primarily through aerobic metabolism. Cardiac muscle fiber cells are also extensively branched and are connected to one another at their ends by intercalated discs. An intercalated disc allows the cardiac muscle cells to contract in a wave-like pattern so that the heart can work as a pump.

Intercalated discs are part of the sarcolemma and contain two structures important in cardiac muscle contraction: gap junctions and desmosomes. A **gap junction** forms channels between adjacent cardiac muscle fibers that allow the depolarizing current produced by cations to flow from one cardiac muscle cell to the next. This joining is called **electric coupling (as opposed to excitation-contraction coupling)**, and in cardiac muscle it allows the quick transmission of action potentials and the coordinated contraction of the entire heart. This network of electrically connected cardiac muscle cells creates a functional unit of contraction called a **syncytium**. The remainder of the intercalated disc is composed of desmosomes. A **desmosome** is a cell structure that anchors the ends of cardiac muscle fibers together so the cells do not pull apart during the stress of individual fibers contracting (Figure 10).

Contractions of the heart (heartbeats) are controlled by specialized cardiac muscle cells called pacemaker cells that directly control heart rate. Although cardiac muscle cannot be consciously controlled, the pacemaker cells respond to signals from the autonomic nervous system to increase or decrease heart rate. The pacemaker cells can also respond to various hormones with the effect of modulating heart rate and thus also controlling blood pressure.

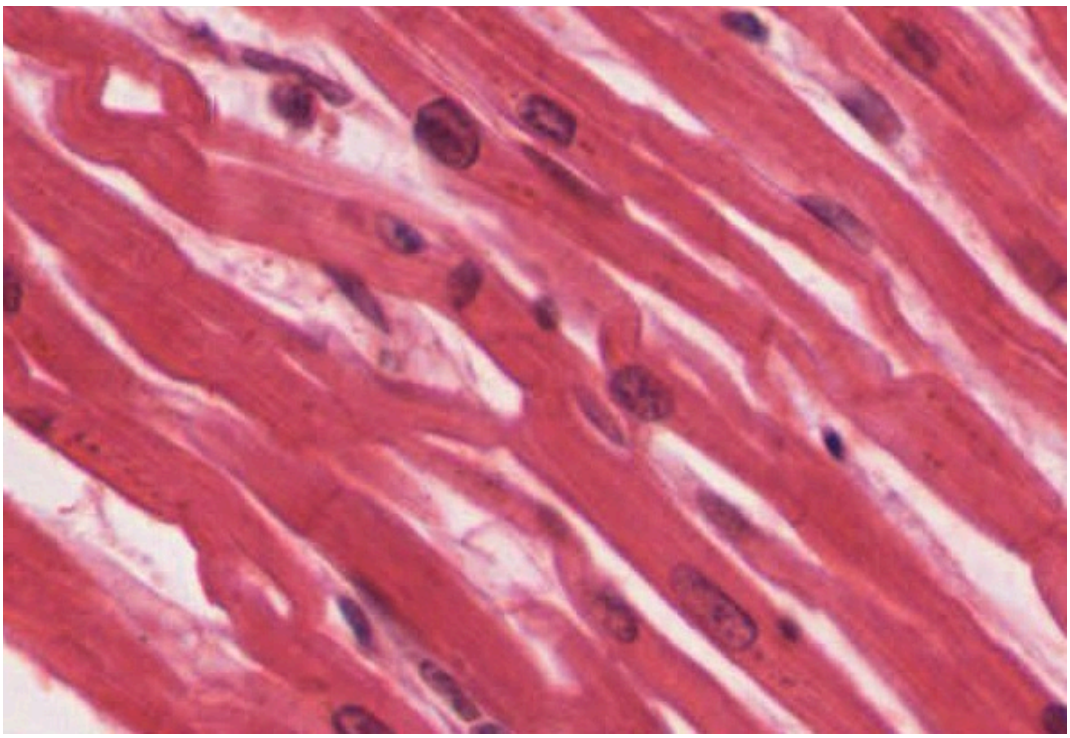

Figure 9. Cardiac Muscle Tissue. *Cardiac muscle tissue is only found in the heart. LM × 1600. (Micrograph provided by the Regents of University of Michigan Medical School © 2012)*

The **functional syncytium** (the wave of contraction that allows the heart to work as a unit) begins with the pacemaker cells. This group of cells is self-excitable and able to depolarize to threshold and fire action potentials on their own, a feature called **autorhythmicity**; they do this at set intervals which determine heart rate. Because they are connected with gap junctions to surrounding muscle fibers and the specialized fibers of the heart's conduction system, the pacemaker cells are able to transfer the depolarization to the other cardiac muscle fibers in a manner that allows the heart to contract in a coordinated manner.

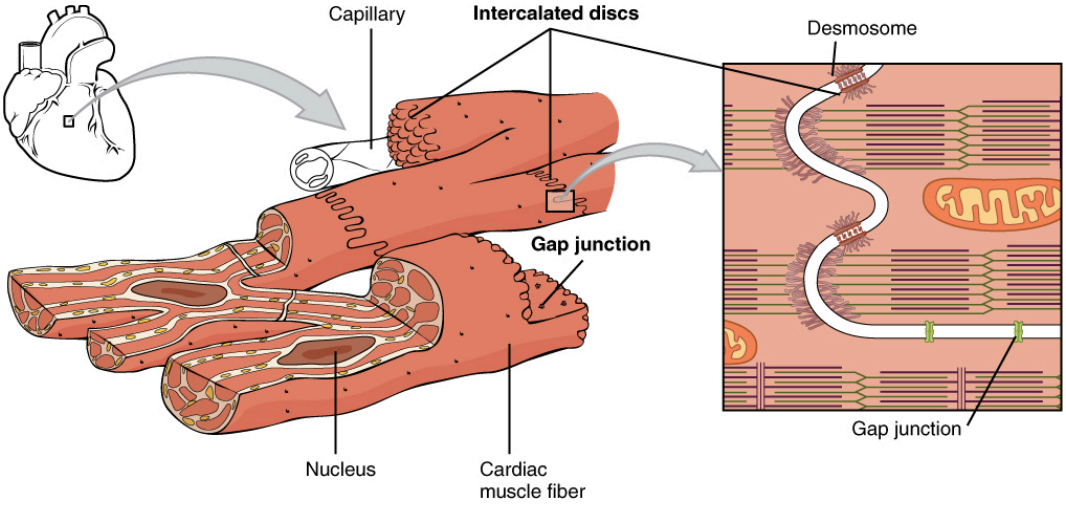

Figure 10. Cardiac Muscle. *Intercalated discs are part of the cardiac muscle sarcolemma and they contain gap junctions and desmosomes.*

In cardiac cells, unlike skeletal muscles, extracellular Ca^{2+} is required to initiate release of calcium from the sarcoplasmic reticulum (SR). The SR in cardiac muscle fibers is simpler than that of skeletal muscle fibers, lacking terminal cisterns, and there is no direct physical link between proteins in the T-tubule and proteins in the SR membrane, so depolarization of the T-tubule membrane cannot directly cause Ca^{2+} release from the SR. Instead, cardiac muscle cells have voltage-gated calcium channels in the sarcolemma and along the T-tubules that open when the membrane is depolarized, allowing Ca^{2+} to enter the cardiac muscle fiber from the extracellular fluid. This calcium then causes the opening of calcium-gated calcium channels in the SR membrane that release *additional* Ca^{2+} into the sarcoplasm. This mechanism allows cardiac muscle to have a relatively long-lasting depolarization "plateau" in its fibers. This sustained depolarization (and Ca^{2+} entry) provides for a longer contraction than is produced by an action potential in skeletal muscle.

Part 4: Smooth Muscle Tissue

Smooth muscle (Figure 11), so named because the cells do not have striations, is present in the walls of hollow organs like the urinary bladder, uterus, stomach, intestines, and in the walls of passageways, such as the arteries and veins of the circulatory system, and the tracts of the respiratory, urinary, and reproductive systems. Smooth muscle is also present in the eyes, where it functions to change the size of the iris and alter the shape of the lens. It is also present in the skin where it causes hair to stand erect in response to cold temperature or fear.

Smooth muscle fibers are spindle-shaped (wide in the middle and tapered at both ends, somewhat like a football) and have a single nucleus; they range from about 30 to 200 μm (thousands of times shorter than skeletal muscle fibers), and they produce their own connective tissue, endomysium. Although they do not have striations and sarcomeres, smooth muscle fibers do have thick and thin filaments composed of myosin and actin contractile proteins. These thin filaments are anchored by dense bodies. A **dense body** is analogous to the Z-discs of skeletal and cardiac muscle fibers and is tethered, or fastened, to the sarcolemma. Calcium ions are supplied by the sarcoplasmic reticulum (SR) in the fibers and by sequestration from the extracellular fluid through membrane indentations called **caveolae**.

Because smooth muscle cells do not contain troponin, cross-bridge formation is not regulated by the troponin-tropomyosin complex but instead by the regulatory protein **calmodulin**. In a smooth muscle fiber,

external calcium ions passing through opened calcium channels in the sarcolemma, and additional Ca^{2+} released from SR, bind to calmodulin. The Ca^{2+}-calmodulin complex then activates an enzyme called myosin (light chain) kinase, which, in turn, activates the myosin heads by phosphorylating them (converting ATP to ADP and Pi, with the Pi attaching to the head). The myosin heads can then attach to actin-binding sites and pull on the thin filaments. The thin filaments are anchored to the dense bodies, which also have cord-like intermediate filaments attached to them. In fact, intermediate filaments appear as a network throughout the sarcoplasm and are connected to each other through dense bodies. Thus, as the thin filaments slide past the thick filaments, they pull on the dense bodies, which in turn pull on the network of intermediate filaments throughout the sarcoplasm. This arrangement causes the entire muscle fiber to contract in a manner which sees its ends being pulled toward the center, causing the midsection to bulge inward, like a corkscrew (Figure 12).

Although smooth muscle contraction relies on the presence of calcium ions, smooth muscle fibers have a much smaller diameter than skeletal muscle cells. Smooth muscle fibers have a limited calcium-storing SR but have calcium channels in the sarcolemma (similar to cardiac muscle fibers) that open during the action potential along the sarcolemma. The influx of extracellular calcium ions, which diffuse into the sarcoplasm to reach the calmodulin, accounts for most of the Ca^{2+} that triggers contraction of a smooth muscle cell.

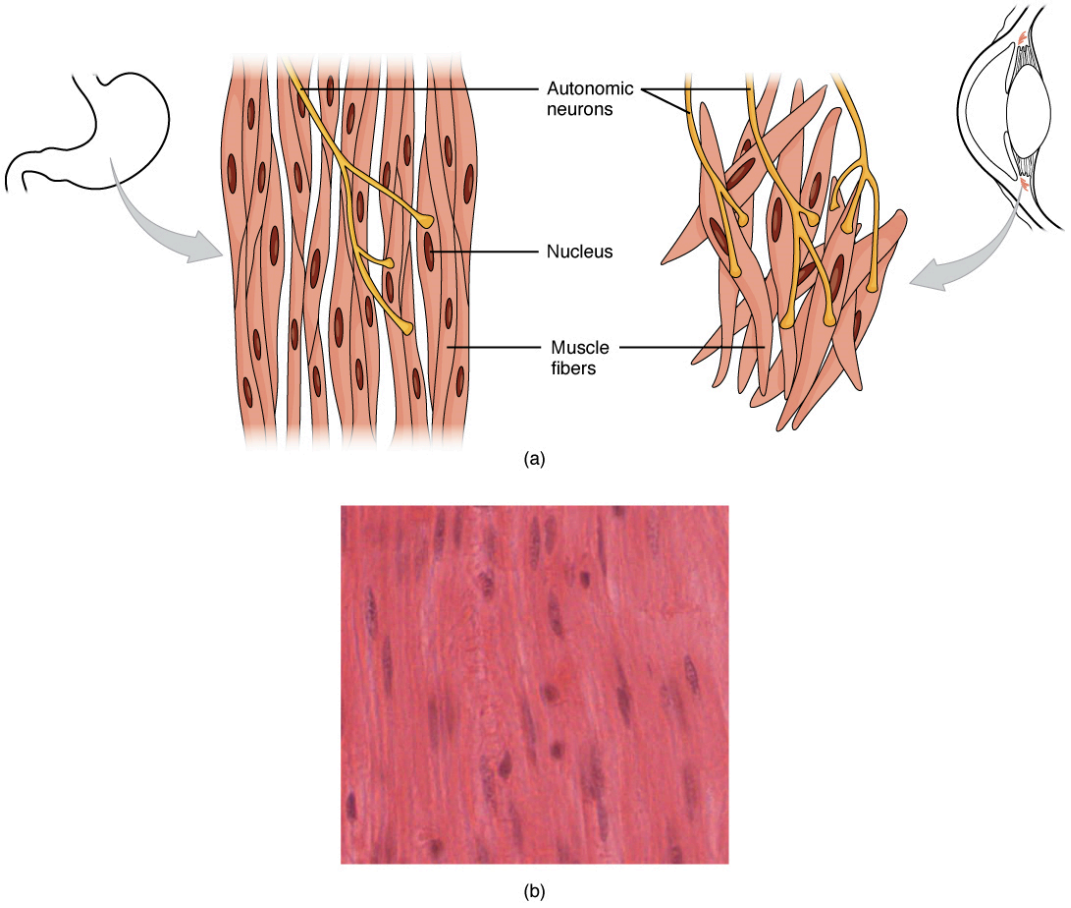

Figure 11. Smooth Muscle Tissue. *Smooth muscle tissue is found around organs in the digestive, respiratory, reproductive tracts and the iris of the eye. LM × 1600. (Micrograph provided by the Regents of University of Michigan Medical School © 2012)*

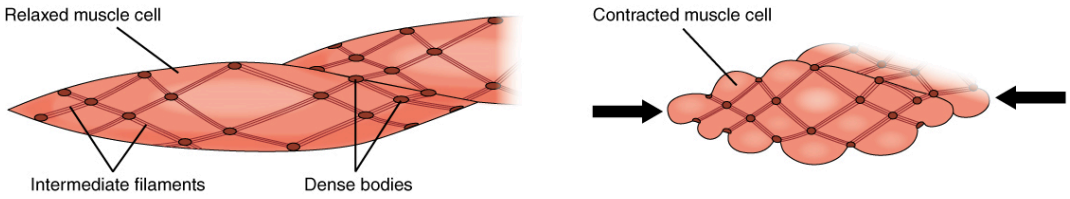

Figure 12. Muscle Contraction. *The dense bodies and intermediate filaments are networked through the sarcoplasm, which cause the muscle fiber to contract.*

Muscle contraction continues until ATP-dependent calcium pumps actively transport calcium ions back into the SR and out of the cell. However, a low concentration of calcium remains in the sarcoplasm to maintain muscle tone. This remaining calcium keeps the muscle slightly contracted, which is important in certain tracts and around blood vessels.

Because most smooth muscles must function for long periods without rest, their power output is relatively low, but contractions can continue without using large amounts of energy. Some smooth muscle can also maintain contractions even as Ca^{2+} is removed and myosin kinase is inactivated/dephosphorylated. This can happen because a subset of cross-bridges between myosin heads and actin, called **latch-bridges**, keep the thick and thin filaments linked together for a prolonged period, and without the need for ATP. This allows for the maintaining of muscle "tone" in smooth muscle that lines arterioles and other visceral organs with very little energy expenditure.

Smooth muscle is not under voluntary control; thus, it is called involuntary muscle. The triggers for smooth muscle contraction include hormones, neural stimulation by the autonomic nervous system, and local factors (e.g. localized histamine release, pH levels etc).

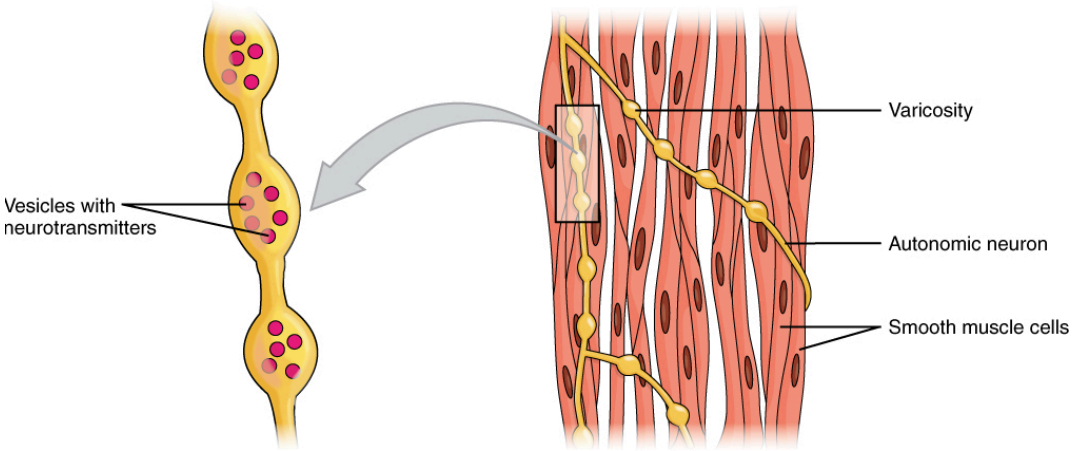

Figure 13. Motor Units. *A series of axon-like swelling, called varicosities or "boutons," from autonomic neurons form motor units through the smooth muscle.*

Different autonomic nerves release various neurotransmitters onto smooth muscle. For example, some nerves release acetylcholine that causes contraction of smooth muscle around some respiratory ducts and thus constriction of these airways. Other nerves release norepinephrine that causes relaxation of smooth muscle and thus widening of the airways. The same neurotransmitter can even cause opposite effects depending partly on the tissue where it acts and/or the variant of neurotransmitter receptor on target cells. Although norepinephrine causes relaxation of smooth muscle and thus widening of some airways, it also causes contraction of smooth muscle and thus constriction of most blood vessels. Autonomic neurons innervating smooth muscle release their neurotransmitters from swellings along their axons, called varicosities, that tend

to result in less specific localization of the released neurotransmitter than at a neuromuscular junction (Figure 13).

Several hormones also affect the activity of smooth muscle, either by encouraging contraction or relaxation. For example, in the digestive system, cholecystokinin induces relaxation of the smooth muscle around the hepatopancreatic sphincter causing it to open. Conversely, gastrin stimulates contraction of smooth muscle in the stomach to enhance the churning activity of the stomach. Within the reproductive system, oxytocin stimulates uterine smooth muscle contraction to facilitate childbirth.

Smooth muscle arranged in layers around a hollow organ generally produces slow, steady contractions known as **peristalsis** that allow substances, such as food in the digestive tract, to move through the body. One layer of smooth muscle is parallel to the longitudinal axis of the lumen and the other layer is wrapped around the lumen in a circular fashion. A third layer of longitudinal muscle (ureters) or obliquely arranged muscle (stomach) is present in some organs. This action and arrangement of smooth muscle layers, causes mixing and/or unidirectional propulsion of materials through the lumen. Movement of substances through lumens by peristalsis occurs in some organs (uterus, urinary bladder, esophagus, stomach, small and large intestines) and ducts (ureters, uterine tubes, vas deferens, bile ducts).

In summary, smooth muscle is found throughout the body around various organs and tracts. Smooth muscle cells have a single nucleus, and are spindle-shaped. Smooth muscle cells are nonstriated, but their sarcoplasm is filled with actin and myosin, along with dense bodies in the sarcolemma to anchor both thin filaments as well as a network of intermediate filaments, which during contraction, are together involved in pulling the sarcolemma toward the fiber's middle, shortening it in the process.