Contents

5 Organic Compounds	Carbon
	Functional Groups
	Carbohydrates
	Lipids
	Steroids
	Proteins
	Enzymes
	Nucleotide-based Molecules
	DNA
	RNA
	ATP
	NAD & FAD
6 Eukaryotic Cell	Nonmembranous Organelles
	Ribosomes
	Membranous Organelles
	Membrane Cycling
	Nucleus
	Endosymbiotic Theory
	Plant Cell Specializations
7 Cell Membrane and Membrane Transport	Membrane Structure
	Passive Transport
	Diffusion
	Facilitated Diffusion
	Osmosis
	Tonicity
	Active Transport
	Endocytosis & Exocytosis
8 Prokaryotes	Bacteria
	Bacteria & Human Disease
	Use & Abuse of Antibiotics
	Bacterial Reproduction
	Plasmids

9 Energy, Chemical Reactions, Enzymes	Energy
	Laws of Thermodynamics
	Energy Transfer in Chemical Reactions
	Catabolic Reactions
	Anabolic Reactions
	Energy & ATP
	Enzymes
10 Redox Reactions & Metabolic Pathways	Oxidation – Reduction Reactions
	Energy Extraction in Cells
	Introduction to Cellular Respiration
	Glycolysis
	Krebs Cycle
	Electron Transport Chain
	Fermentation Pathways
	Other Nutrient Sources
	Anabolic Pathways
11 DNA Replication and Cell Division	Cell Cycle
	DNA Structure
	DNA Replication
	Mitosis
	Meiosis
	Genetic Diversity in Humans
	Fertilization
12 Mendelian Genetics	Vocabulary Words
	Karyotype
	Chromosome Structure
	Mechanism of Inheritance
	Punnett Square
13 Gene Expression & Protein Synthesis	DNA Structure (review)
	Genetic Code
	RNA Structure (review)
	tRNA
	Ribosomes
	Protein Synthesis

14 Evolution and Natural Selection	Darwin
	Other Scientists' Contributions
	Fossils
	Meaning of Evolution
	Some Proofs of Evolution
15 Mutations	Genetic Disorders & Sickle-Cell Anemia
	Cancer

LECTURE 1: INTRODUCTION TO BIOLOGY

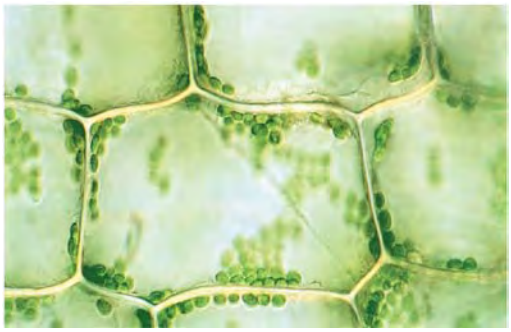
Biology is the scientific study of life. Biologists study the diversity of life in its many different forms, from microscopic bacteria to complex animals. But what is life? There is no short answer to that question. The best biologists can do is define life in terms of a list of characteristics possessed by living things. Yet some of these characteristics are also true of nonliving things. For example, movement- water is not living yet water moves: growth – fire is non living but it can grow. One approach to understanding living from nonliving is that living things share five basic properties elaborated on below.

Characteristics of living things

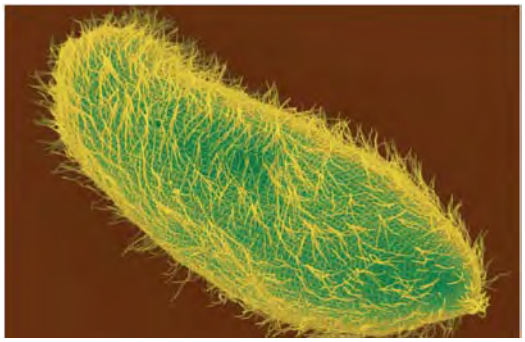
1. All living things are composed of either one cell or many cells. Details of the structure and function of cells are covered in **Lectures 6 & 7**. The study of living organisms has led scientists to formulate a **Modern Cell Theory** which states that

A. **Every living organism is made up of one or more cells.**
B. **The smallest living organisms are single cells, and cells are the functional units of multicellular organisms.**
C. **All cells arise from preexisting cells.**
D. **Life evolved once, about 3.5 billion years ago, and all organisms alive today represent a continuous line of descent from those first cells.**

Examples of Cells



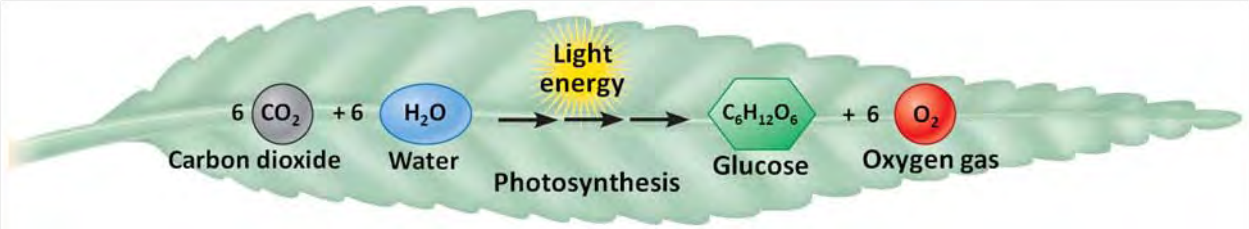
Plant Cell



Paramecium – unicelled organism

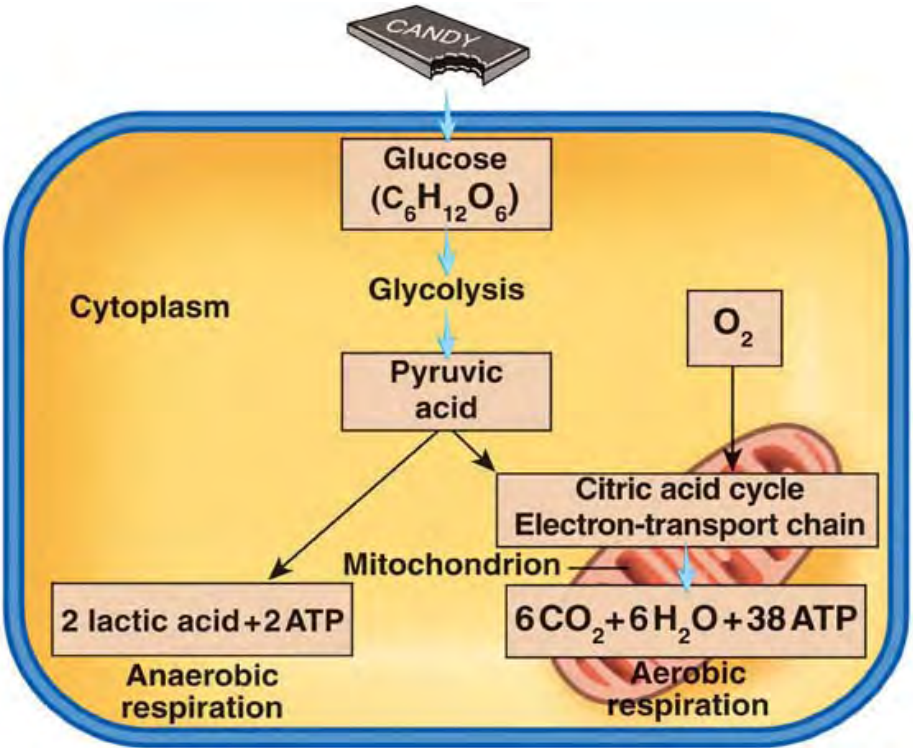
2. All living things use energy. Energy and metabolic pathways are discussed in more detail in **Lecture 9**. All organisms need energy to grow, move, and even think. Almost all organisms get energy from the sun - either directly in the case of photosynthetic plants or, in the case of heterotrophs, by eating the plants or by eating organisms that have eaten the plants.

Photosynthesis (summary of)



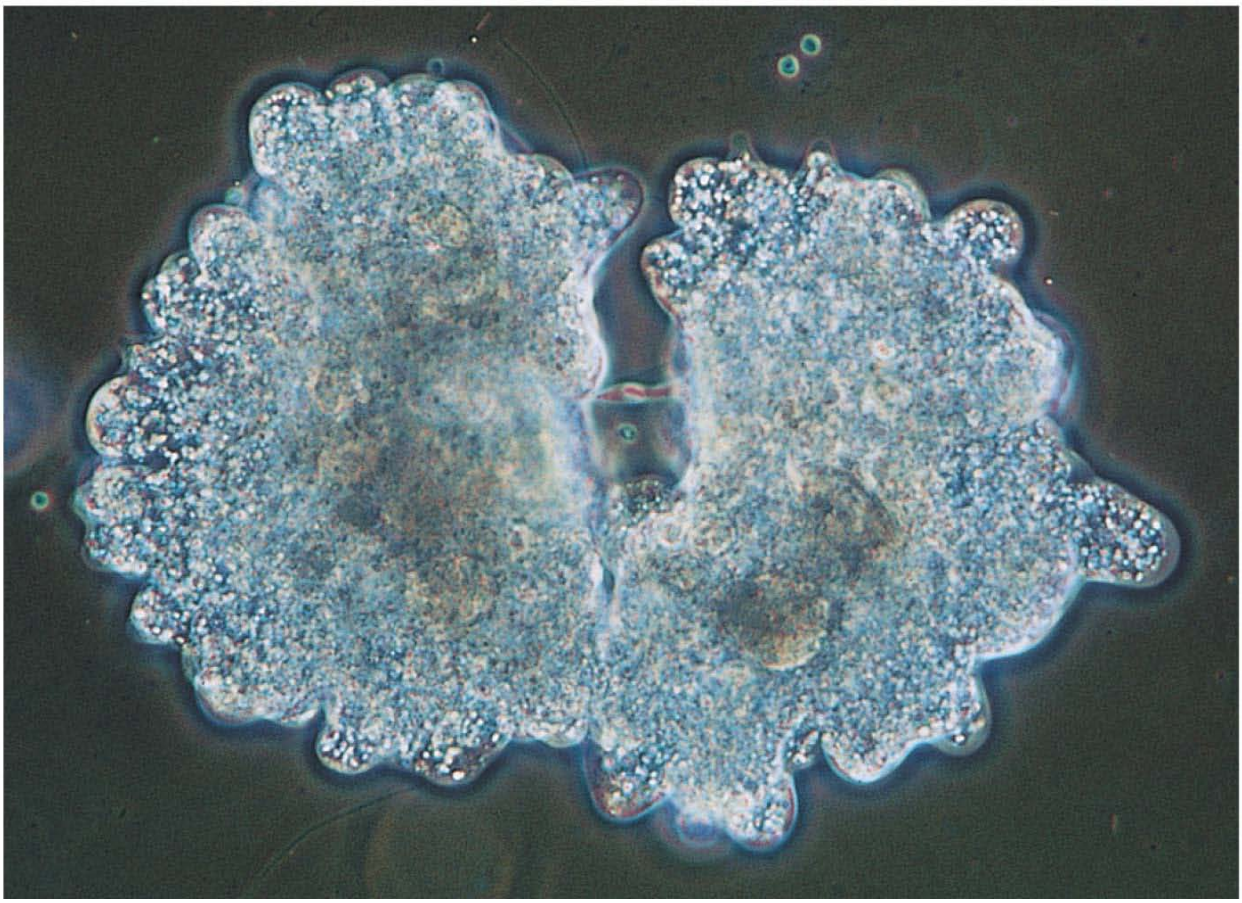
Using light energy, plants rearrange the atoms in carbon dioxide and water to synthesize glucose or other organic molecules and release oxygen.

Cellular Respiration (summary of)



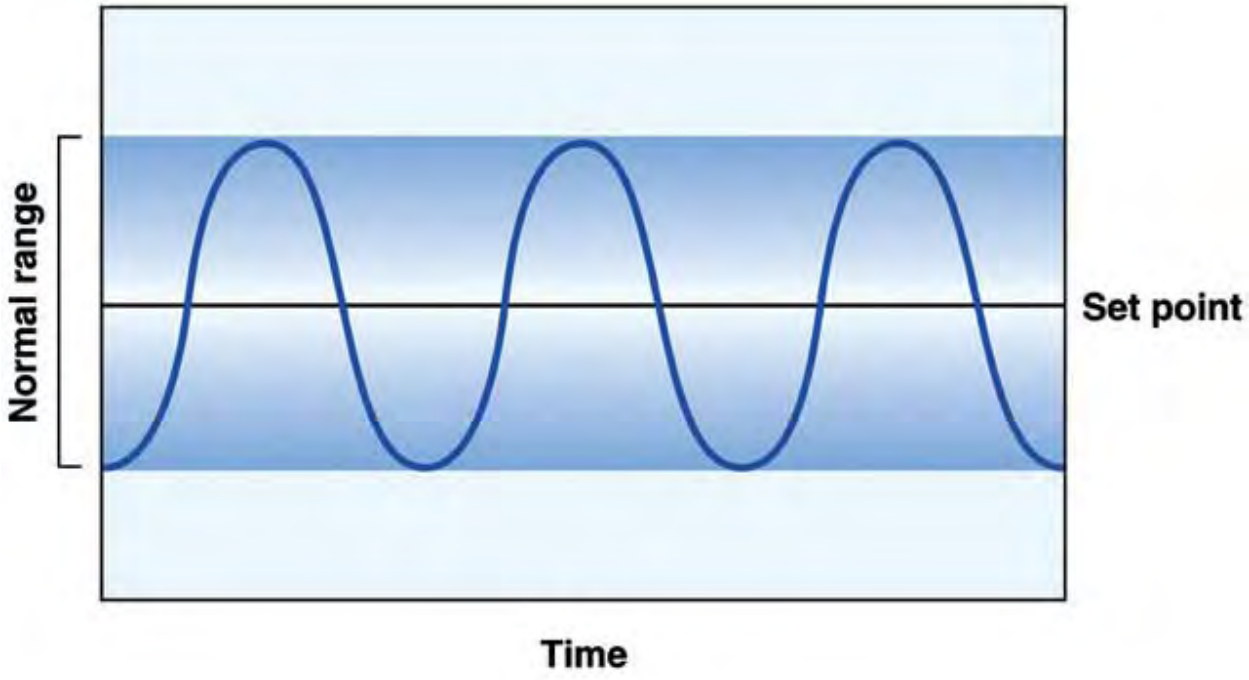
Cells break down glucose and other organic molecules, releasing the energy stored in the bonds of these molecules and use it to make ATP.

3. All living things have the potential to grow and reproduce. Reproduction is discussed in more detail in **Lecture 10**. For example, bacteria reproduce by binary fission and animals by the production of specialized reproductive cells such as sperm and ovum (in humans). Even if organisms don't actually produce offspring (many bees and ants are sterile) they still possess cells that divide and grow. The goal in all cases is to pass on the parental DNA to the offspring or to daughter cells.



This shows a single-celled amoeba producing a genetically identical offspring cell through asexual reproduction. All the genetic information from the parent cell must be passed on to the other cell. This is heredity.

4. All living things must maintain homeostasis. While the environment always varies a lot, organisms act to maintain their internal conditions relatively constant. This maintenance is called **Homeostasis** and it is maintained by a variety of mechanisms. For example, humans and other warm-blooded animals need to have a stable body temperature. One main reason for needing to maintain temperature relatively close to its set point is discussed in **Lecture 8**:- Enzymes are extremely important proteins that are necessary for catalyzing all cellular chemical reactions but they operate best at an optimum temperature.

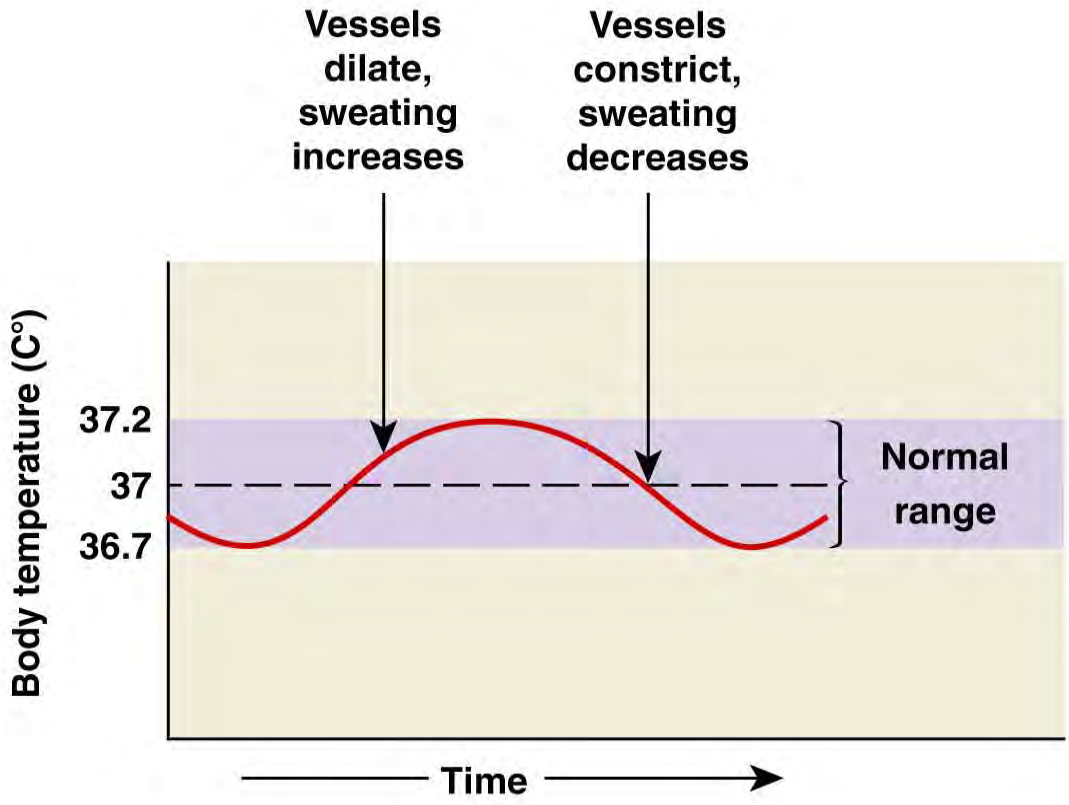


Temperature, pH, and blood glucose, are just a few of the many variables that must be maintained within a fairly narrow range in the human body for it to remain in homeostasis.

Using the example of body temperature mentioned before: – the average body temperature is 98.6^{0}F but it can vary down or up within a degree or two and still be homeostatic. However any major change in either direction will set in motion a series of events that will attempt to return body temperature to within its normal range.

If body temperature rises as occurs with exercise, sweating and vasodilation will occur. Vasodilation is the dilation of blood vessels which increases delivery of blood to the skin thereby cooling the blood. The evaporation of sweat from the body's surface also removes significant heat.

On the other hand, if body temperature drops as occurs in cold weather, then vasoconstriction and shivering occur. Vasoconstriction decreases the blood supply to the skin conserving heat. Cold also initiates shivering (involuntary muscle contractions) where energy is consumed and the byproduct of those pathways is the release of some energy as heat.



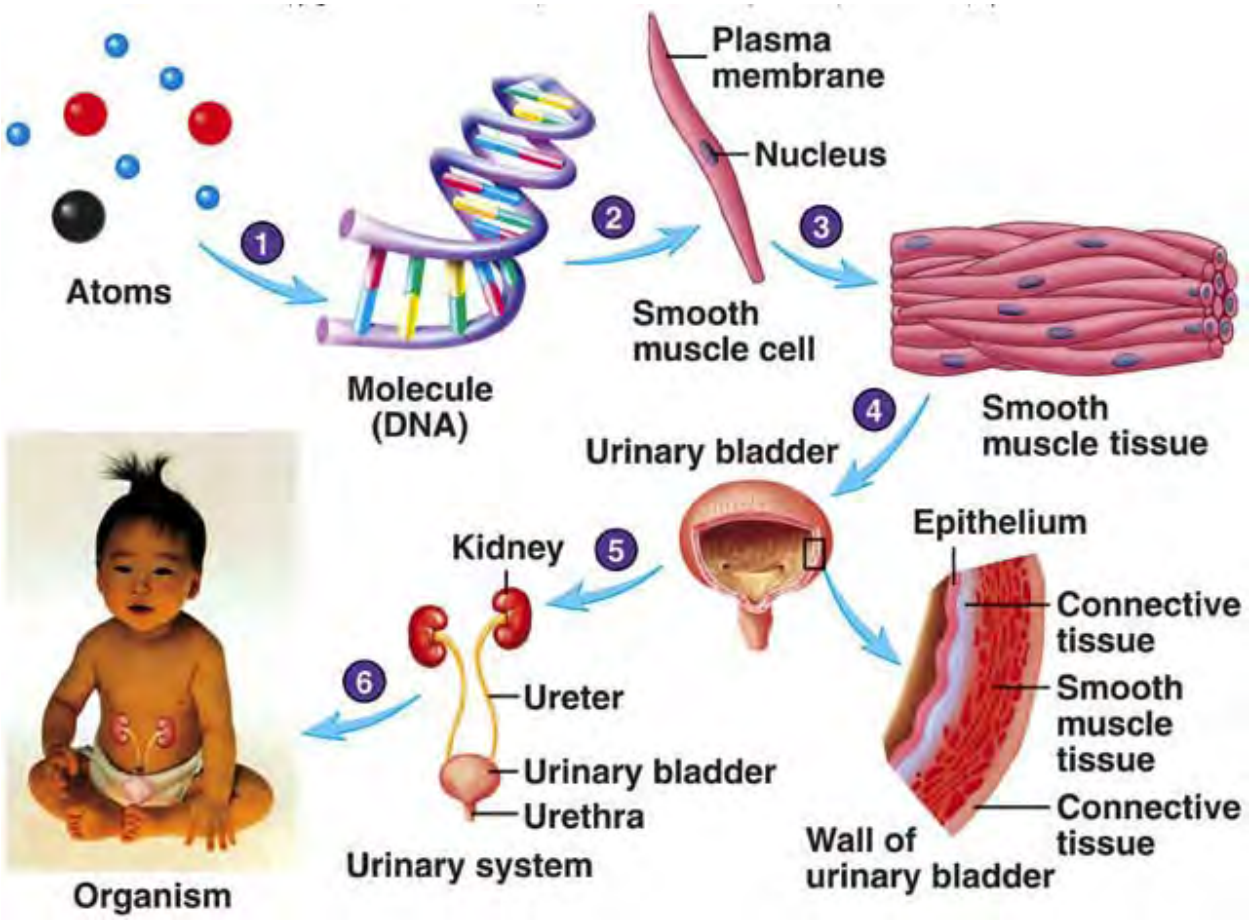
This is type of mechanism is a typical **negative feedback mechanism** so called because any deviation from the normal range sets in motion reactions that will return the variable to normal values, thereby **negating** the change.

5. Living organisms are organized. Living things are highly organized. No nonliving thing comes close to a living thing in terms of organizational complexity. There is a hierarchy of complexity in any one cell – a cell is the smallest level of organization that can be considered to be alive.

Levels of Organization

Atoms are the basic building blocks of matter; atoms combine to form **molecules.** The next level of organization within a cell is an **organelle** such as a mitochondrion or a ribosome, each of which have a specific function within the cell.

With multicellular organisms such as an animal or plant, there is increasing complexity and organization beyond the level of the cell. Cells with a similar structure and function are grouped together into **tissues.** Different tissues are combined into **organs** (heart, brain) and organs are part of **organs systems** such as the cardiovascular system or the brain. Multiple organ systems function together in the **organism.**



There are also some levels of organization beyond the level of organism.

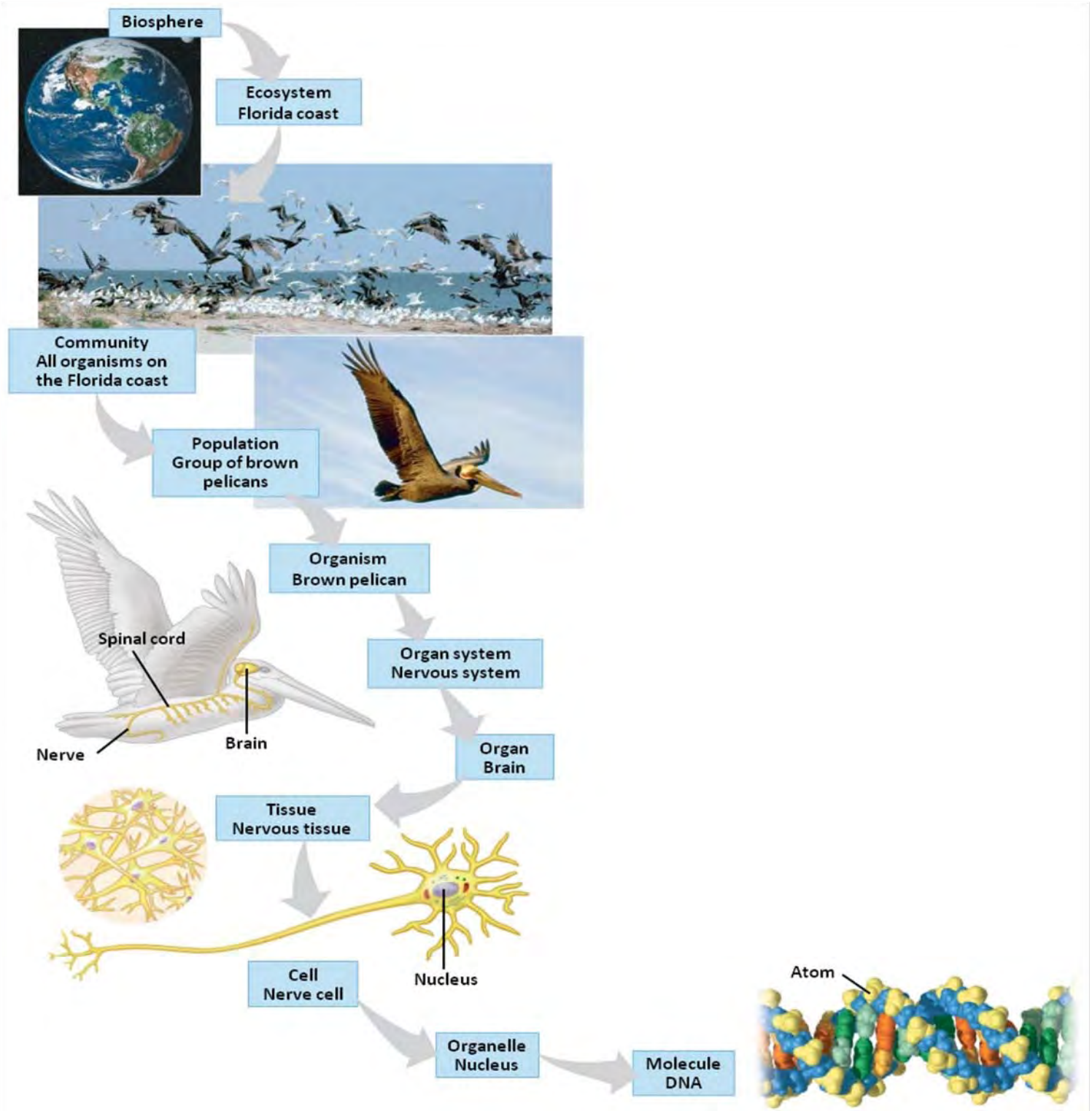
A **population** is a group of the same type of organism living together – for example, all the squirrels living in Fairmount Park.

A **community** refers to all the populations of species living in a particular area. This would include all the chipmunks, birds, trees, etc, as well as the squirrels, in Fairmount Park.

An **ecosystem** includes the community as well as the physical environment. Now the water, rocks, soil etc are included.

The **Biosphere** is that part of the earth inhabited by living organisms. It includes both the living and nonliving components.

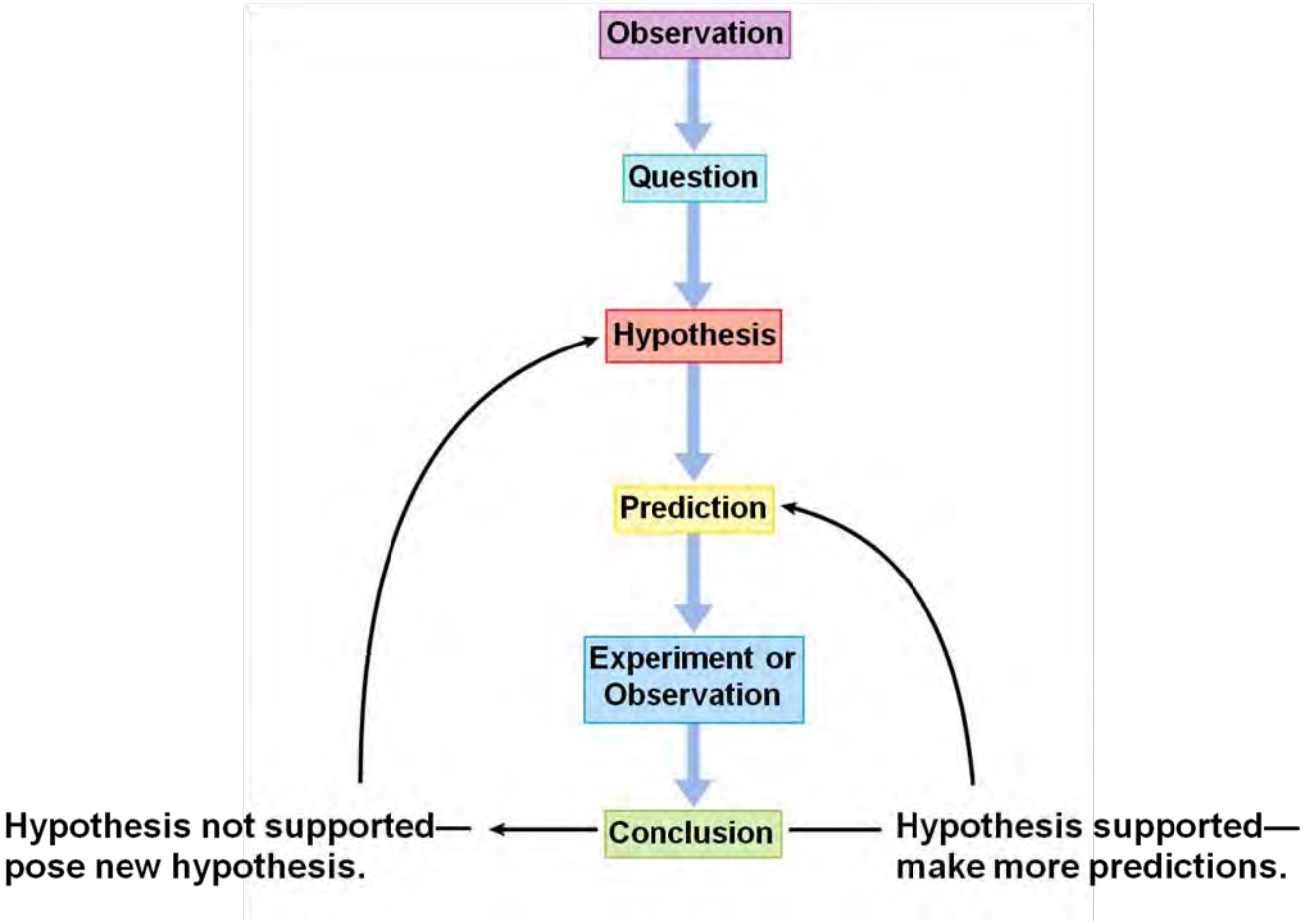
All these levels of organization for an organism known as the brown pelican can be seen on the next page.


Biosphere
Ecosystem
Florida coast
Community
All organisms on
the Florida coast
Population
Group of brown
pelicans
Organism
Brown pelican
Spinal cord
Nerve
Brain
Organ system
Nervous system
Organ
Brain
Tissue
Nervous tissue
Cell
Nerve cell
Nucleus
Organelle
Nucleus
Molecule
DNA
Atom

SCIENCE AND THE SCIENTIFIC METHOD

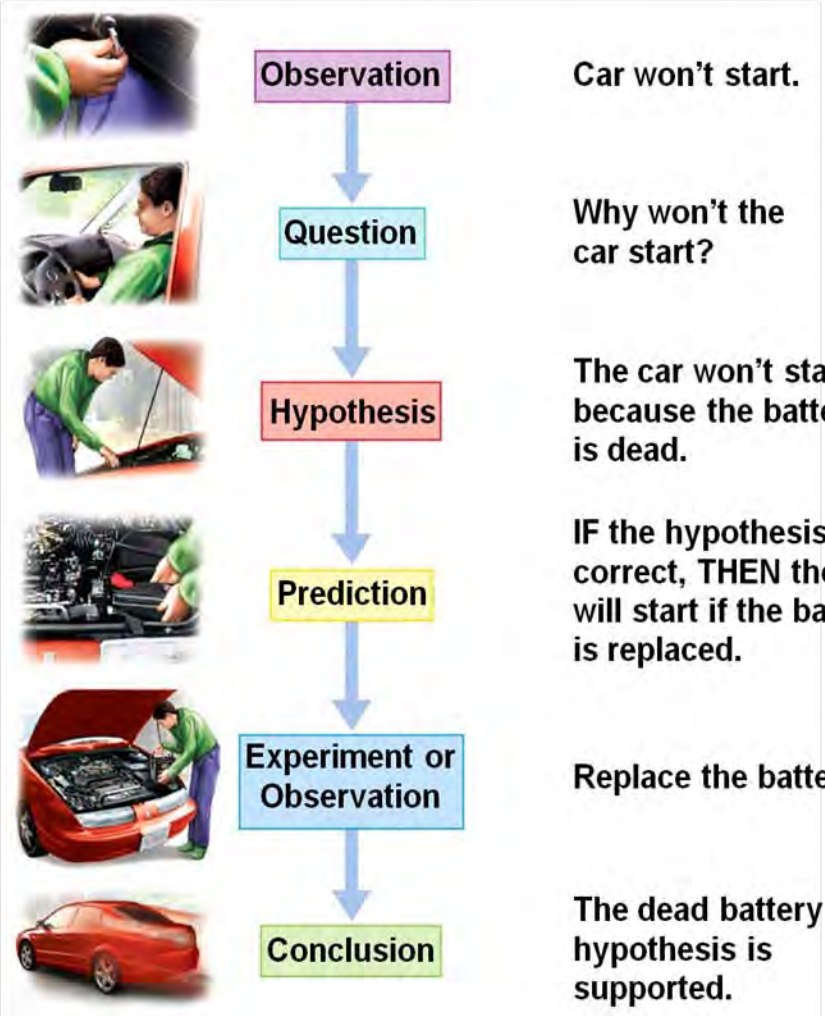
WHAT IS SCIENCE?

Science is a process – a way of understanding the natural world. The Harvard biologist E.O. Wilson defines science as "the organized systematic enterprise that gathers knowledge about the world and condenses the knowledge into testable laws and principles." Science is also a body of knowledge about the natural world. This knowledge is considered empirical because it is based on experience and observations that are rational, able to be tested, and the results are the same with repeated testing. This process of examination and discovery is based on the scientific method, the steps of which are outlined below.



An **observation** is made generating a **question**. A **hypothesis** is a tentative, testable explanation for the **observation**. A scientist will make a rational **prediction** and then test that prediction by conducting an **experiment**. He or she will arrive at a **conclusion**.

We often use the scientific method to solve every day problems. Let's say you make the observation that the car won't start.



In the above example note that if the car doesn't start when the battery is replaced, then a new hypothesis must be proposed and the steps of the scientific method are run through again.

Some principles that underlie scientific inquiry are worth mentioning.

1. All events can be traced to *natural* causes. Scientists search for natural explanations for observed phenomena and do not rely on the supernatural.

2. Natural laws such as the law of gravity or the interaction of atoms are the same everywhere in the universe. For example, humans have only been on the earth for a short period of time (in evolutionary terms). They were not around for the origin of the earth but scientists have arrived at explanations for the origin of the earth based on their belief in the universality of natural laws.

3. People perceive natural events in similar ways. One person may find a work of art beautiful while another finds it reprehensible. These are subjective opinions. Science tries to be objective; the vast majority of scientists should see the results of an experiment in the same way. Consequently science is unable to answer ethical questions that are based on value systems such as whether it is ethical to use embryonic stem cells for research. Scientists can explain the origin of stem cells or arrive at conclusions about their abilities based on research but they cannot say whether the research is moral.

Controls

Simple experiments usually involve observing and testing the effect of a single factor on an observation – that single factor is the **variable**. For the experiment to be valid other possible causes or variables must be ruled out. Consequently, if possible, **controls** are a part of the experiment's design. A **control** experiment is a replicate of the experiment with the variable being studied omitted.

On the next page is a classic experiment conducted in the 1600s by Francesco Redi. At this time most people believed that maggots (immature flies) appeared spontaneously on rotting meat. That is, it was understood that nonliving matter (the dead meat) gave rise to living matter (maggots) – this was known as **spontaneous generation**. Redi conducted the following experiment using the scientific method.

As much as possible everything is the same in the 2 jars except that one is open (**the control jar**) and gauze covers the experimental jar.

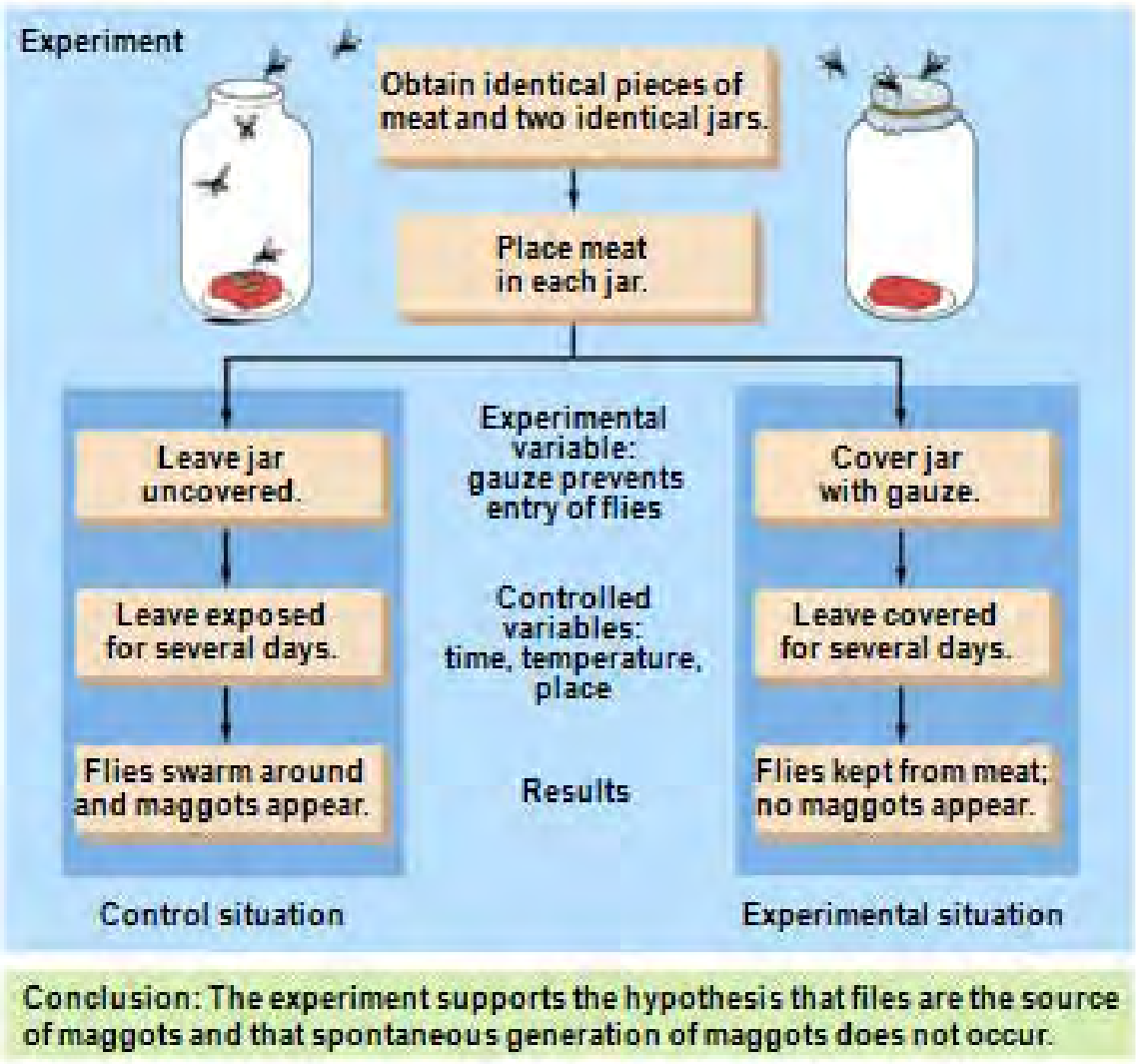
Observation: Flies swarm around meat left in the open; maggots appear on meat.

Question: Where do maggots on the meat come from?

Hypothesis: Flies produce the maggots.

Prediction: If the hypothesis is correct, then keeping the flies away from the meat will prevent the appearance of maggots.

Below are the steps of the experiment Redi conducted and the conclusion he reached based on his observations.



THE MEANING OF "THEORY" IN SCIENCE.

The word "theory" in everyday speech means an educated guess or a hunch – an unproven idea that may or may not be true. But "theory" has a very different meaning in science and this has led to some unfortunate misunderstandings.

In science, **a theory is an explanation of important natural phenomena** such as the Big Bang theory or the Theory of Evolution. A scientific theory is far from being an educated guess. **It is an explanation that is developed through extensive research that has been subjected to rigorous testing and experimentation with results that are reproducible.** Scientists are reluctant to use the word "fact" because a basic premise of science is that it is always open to new evidence and therefore can be modified.

Science is based on **REASONING**.

When a scientific conclusion is reached as a result of making many observations that support it and none that contradict it, this method is called **Inductive Reasoning** and it is how scientific theories are formed. On the other hand a scientific theory itself can be used to support **Deductive Reasoning** which is the process of generating hypotheses based on well-supported generalizations.

Cell theory discussed in **Lecture 1** can be used to demonstrate these 2 types of reasoning. Scientists have examined huge numbers of living organisms and each time they have observed that the organism is made up of cells (sometimes just one cell, sometimes many cells) so a **Cell Theory** is formed stating that all living things are made from cells. This is **inductive reasoning**.

Then if a new organism is discovered, scientists can use the established **Cell Theory** to assume that this organism will also be made of one or more cells – **deductive reasoning**.

LECTURE 2:BIOLOGICAL CLASSIFICATIONS

There are millions of different kinds of organisms on earth and a whole branch of biology is concerned with naming and classifying them. This is the science of **taxonomy.**

More than 2000 years ago the Greek philosopher Aristotle categorized living things as either plants or animals. This system of classification has been revised and modified throughout the centuries and today we have a system of naming based on the work of Carl von Linne (1707-1778), a Swedish naturalist who introduced the two-part scientific name that is still used today.

Scientists internationally have agreed that the name of an organism will be in Latin – a language that is not currently spoken in any country. The two-part name, (for example in humans – *Homo Sapiens*) designates the **genus and the species**. The **genus** includes a number of species that are very closely related and a **species** is loosely defined as populations of organisms that can potentially interbreed. (This biological definition of species works better for animals than for plants and other kingdoms.) The genus name appears first followed by the species name and by convention the names are italicized.

More than two categories are necessary to classify all living things and the Linnaean classification system now includes 8 major categories:

DOMAIN

KINGDOM

PHYLUM

CLASS

ORDER

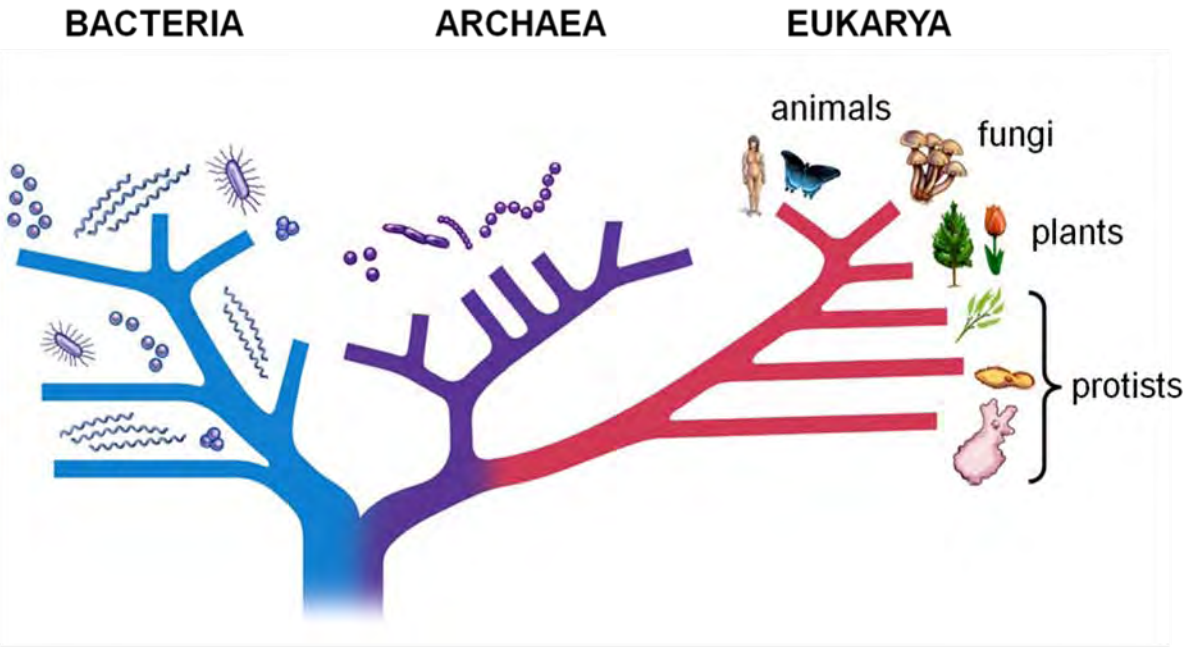
FAMILY

GENUS

SPECIES

THE THREE DOMAINS

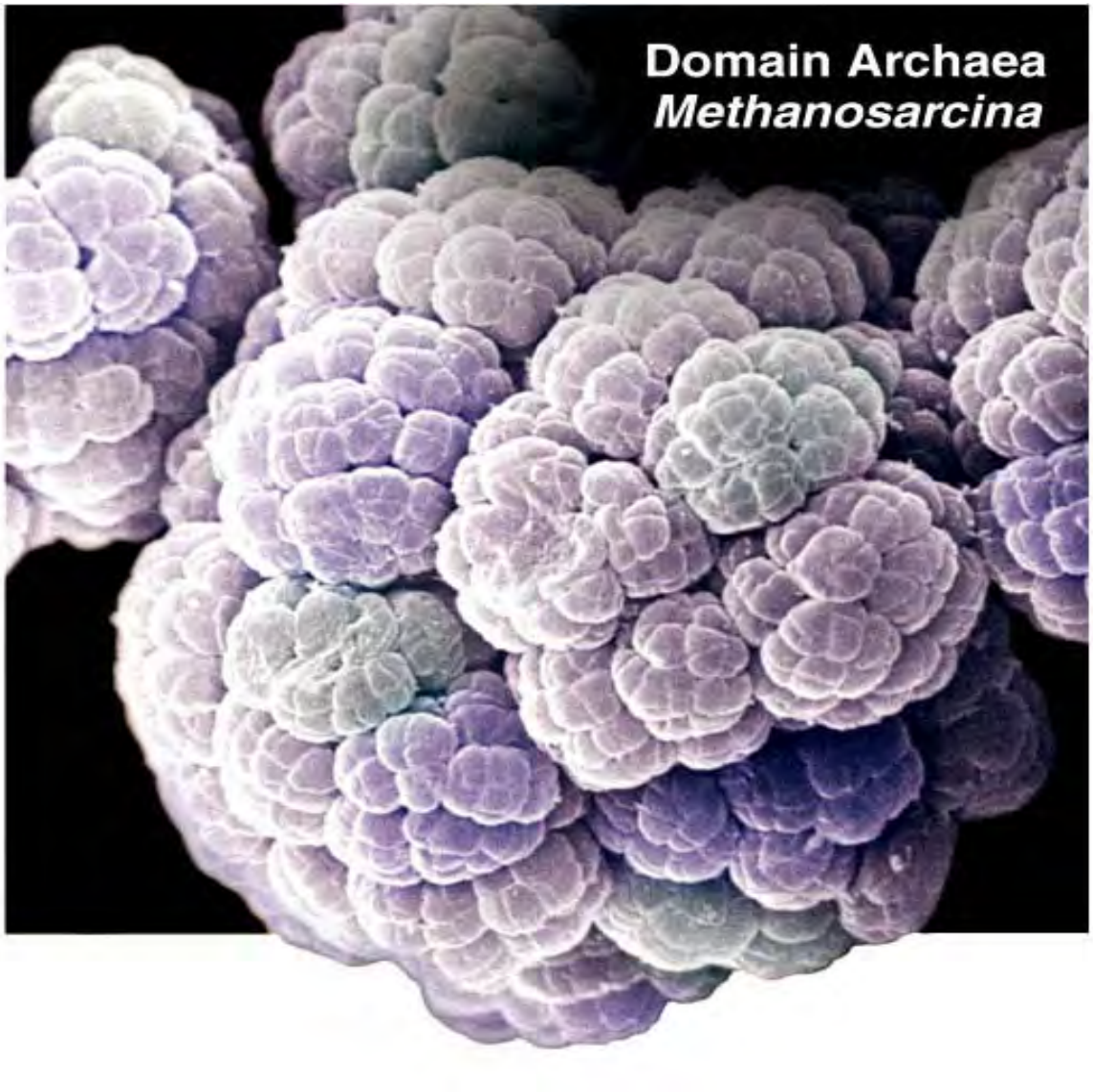
THE TREE OF LIFE



At the bottom of the evolutionary tree is the "universal ancestor" – the organism that gave rise to all other organisms. All organisms that have been identified so far fit in one of the 3 domains. The domains contain several kingdoms but those for the domains Bacteria and Archaea are a work in progress. In the domain Eukarya each kingdom contains several phyla, each phyla contains several classes and so on as discussed in the next few pages.

BACTERIA arose from the first self-replicating cells and are the most abundant organisms on earth. They are prokaryotic (no membrane- enclosed nucleus or organelles), asexual, single-celled organisms that are very diverse metabolically. There is ongoing debate among taxonomists about the details of classification within this domain. (More about bacteria in **Lecture 8**)

ARCHAEA are similar structurally to bacteria in that they are also prokaryotic, asexual, single-celled organisms. But they differ from bacteria in ways that are significant enough to warrant a separate domain. Archaea do not have peptidoglycans in their cell walls as bacteria do, and they have very unusual lipids and ribosomal RNA that differs from bacteria. Archaea actually have some genes and metabolic pathways which are more closely related to eukaryotes. Some archaea are extremophiles – living in extreme environments such as the Arctic but archaea also occupy a wide variety of habitats, especially the earth's oceans. Again the debate about kingdoms is ongoing.



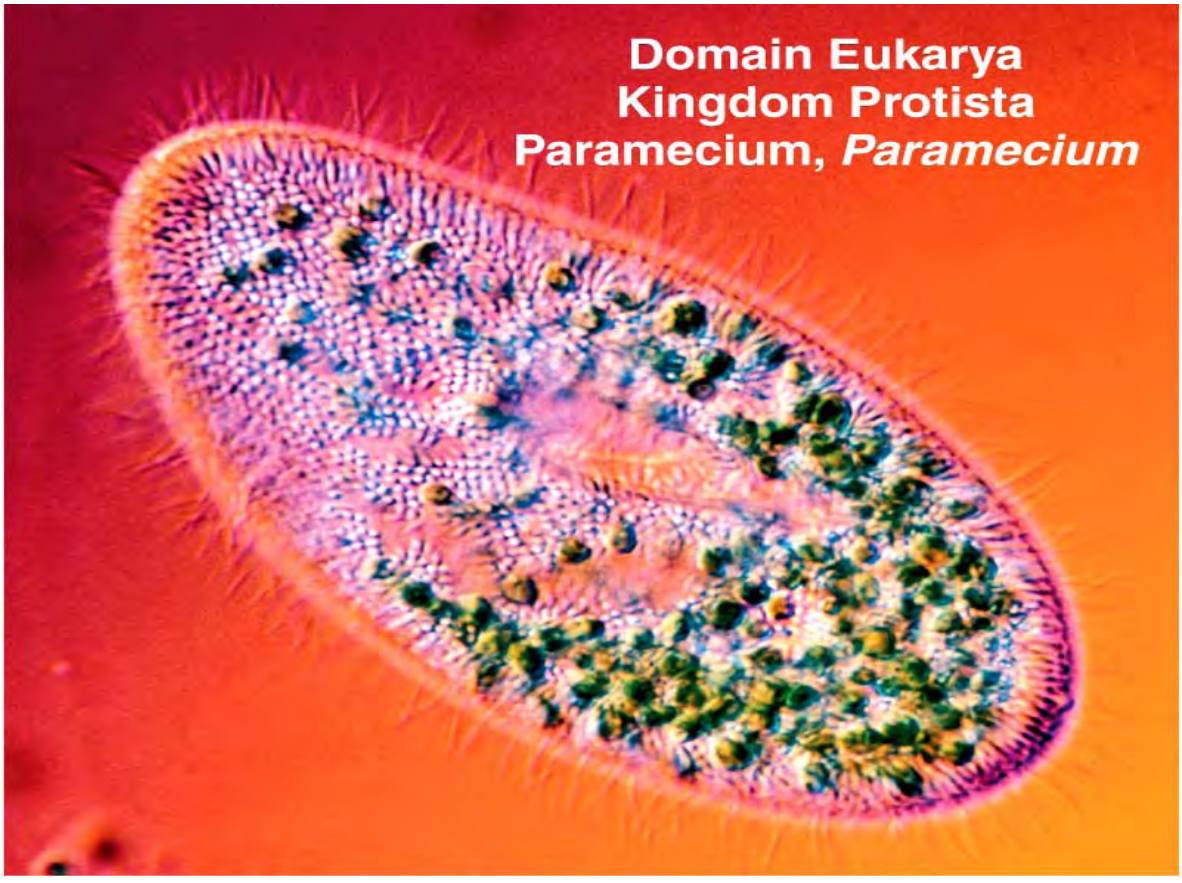
EUKARYA

The Eukarya domain includes all eukaryotic organisms. (Cells of eukaryotic organisms contain membranous organelles and the DNA is located in a membranous nucleus.) This domain consists of **FOUR KINGDOMS** as can be seen on the Tree of Life on page 1: **PROTISTS, PLANTS, FUNGI, AND ANIMALS**.

Below is a short summary of the major characteristics of each group.

PROTISTS are a miscellaneous group of organisms that includes any eukaryote that does not meet the definition of plant, animal, or fungus. Most protists are **single-celled**. They have diverse modes of nutrition including ingestion and absorption, and some can photosynthesize. They also have a variety of ways of reproducing. A few protists are multicellular, for example, seaweed.

A paramecium - a single-celled protist that you may have seen before

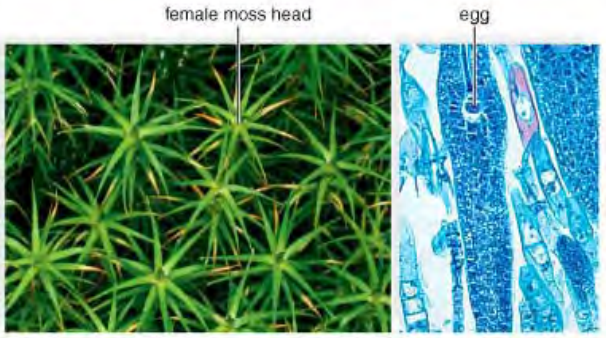


PLANTS are multicellular eukaryotes that everyone is familiar with. They have tremendous variety in size, from being as small as 1 millimeter to being 300+ feet tall. They live mainly on land although some species have returned to the ocean.

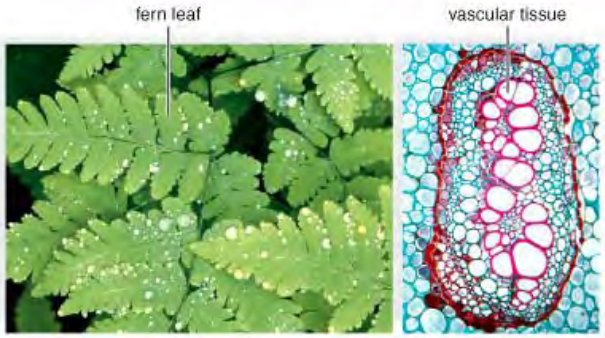
Plants have the ability to make their own food via **photosynthesis**. The green color of plants is from the presence of chlorophyll, a pigment that enables plants to capture energy from the sun and combine it with carbon dioxide and water to make glucose and other organic compounds. Chloroplasts are the cellular organelles where photosynthesis takes place. Plants, then, are autotrophic (self-feeders) but they also make energy available for almost all other organisms that don't have the ability to photosynthesize. Humans, for example, are heterotrophic. They get energy by eating plants or eating animals that have eaten plants.

Plants are also distinguished by their inability to move which makes being autotrophic a necessity as they cannot go somewhere else to acquire food.

Like protists, plants also have a complex reproduction cycle with alternation of generations and haploid and diploid states; the details are not included here.



a. In nonvascular plants (e.g., mosses), multicellular embryos are protected and nourished within the structures that produce an egg.

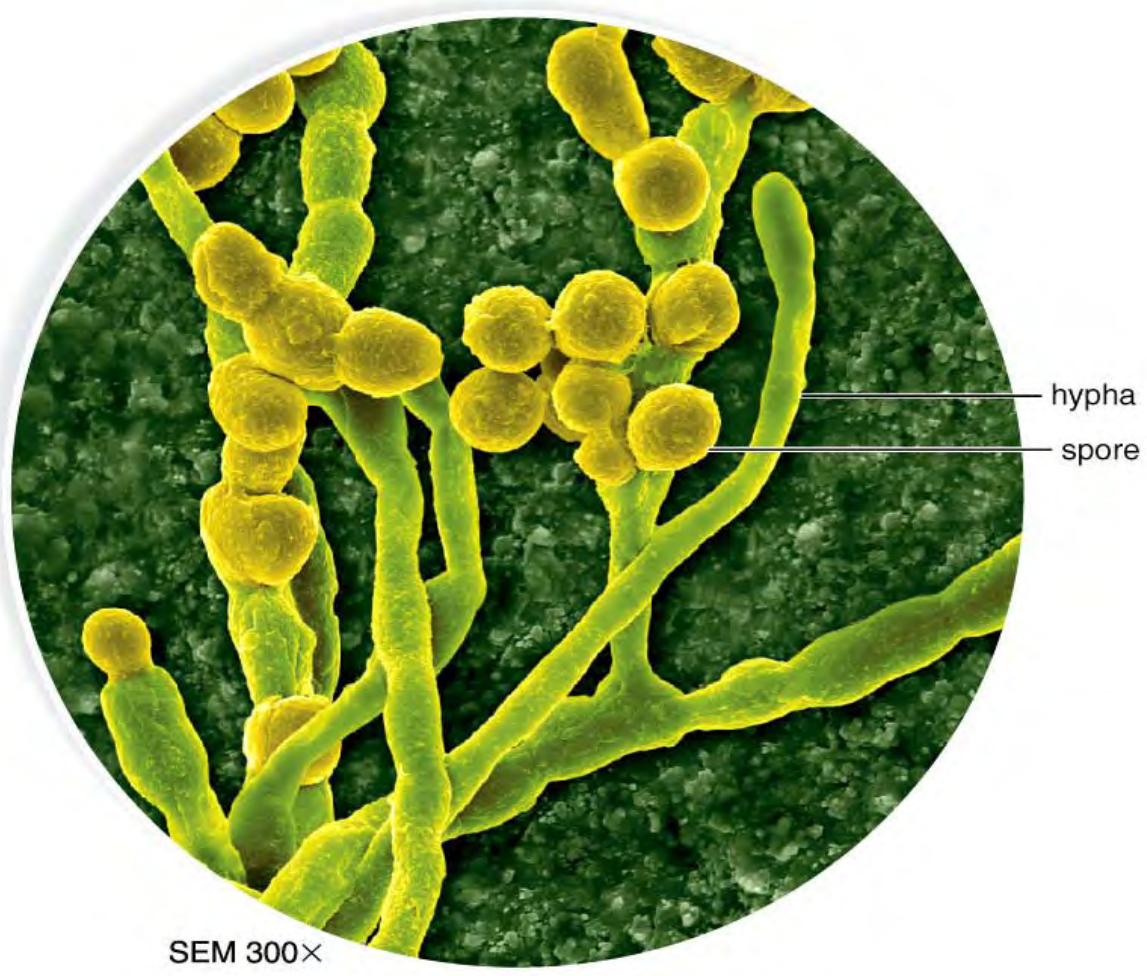


b. In seedless vascular plants (e.g., ferns), vascular tissue conducts water and organic nutrients within its roots, stems, and leaves.

c. In gymnosperms (e.g., conifers), seeds produced in seed cones disperse offspring away from the parent plant.

d. In angiosperms, flowers produce seeds protected by fruits, which aid in the dispersal of offspring.

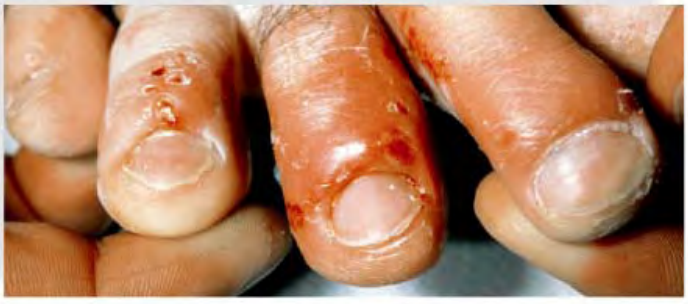
Fungi are multicellular eukaryotes that were once classified as plants because they are also immobile, and some disperse spores that are similar to plant seeds. They also have complex reproduction that can be sexual or asexual. But they are actually very different organisms. They do not have chlorophyll and so cannot photosynthesize and, like animals, are dependent on other organisms for food (**heterotrophic**). Most of the functional part of fungi is made up of hyphae – a thin, stringy material which grows over and into a food source. Fungi secrete chemicals that break down food into small molecules which are then absorbed by the hyphae.

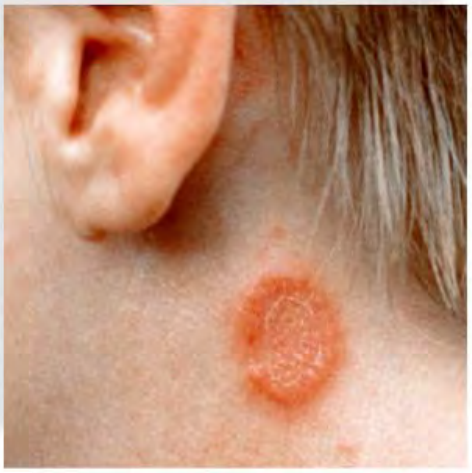


b. Specialized fungal hyphae that bear spores

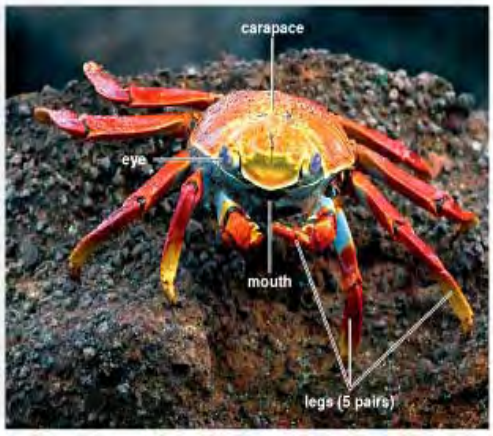
Fungi interact with other species sometimes forming symbiotic relationships. They have many important functions; they are important decomposers, their fermentation processes make wine, beer and bread (see yeast in **Lecture 9**).

However, they can also cause plant and animal diseases. Below is a picture of human diseases caused by fungal infections.

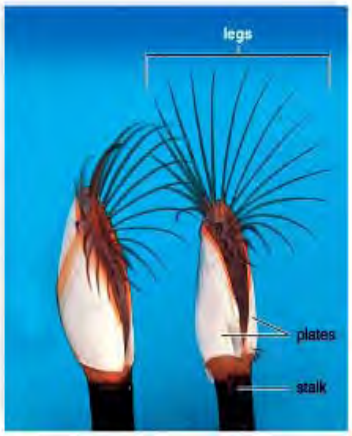




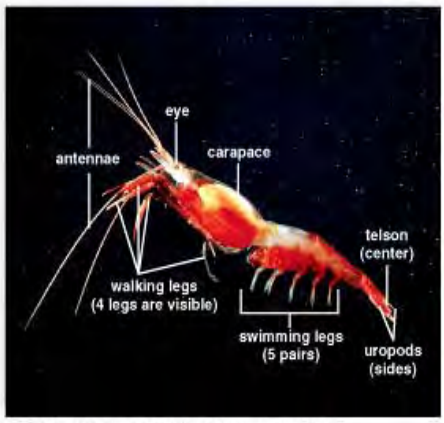
Animals are defined by a list of characteristics. These varied organisms are multicellular, eukaryotic, heterotrophic, motile, and they mostly reproduce sexually. Yet there is still significant diversity within the kingdom. Most people think of mammals, birds, reptiles, fish, frogs etc when they think of animals. These are the **vertebrates** – animals with a backbone – but they only make up about 4% of the animal kingdom. The vast majority of animals are **invertebrates** which include sponges, anemones, worms, snails, clams, insects and crustaceans (crabs, lobsters, shrimp etc).



a. Sally lightfoot crab, *Grapsus grapsus*

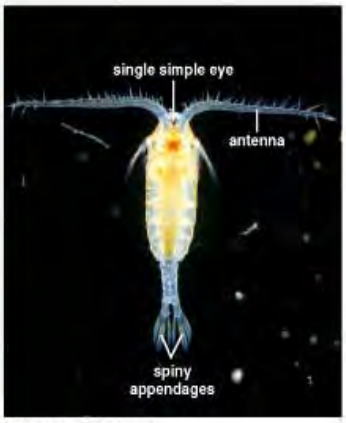


b. Gooseneck barnacles, *Lepas anatifera*



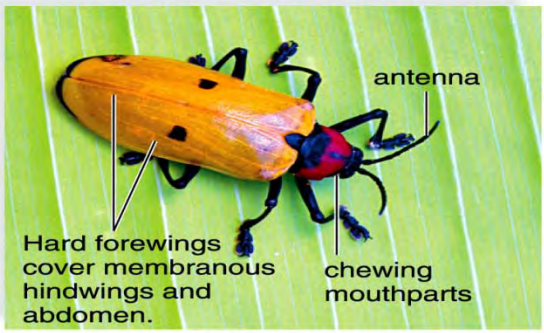
c. Red-backed cleaning shrimp, *Lysmata grasbhami*

d. Pillbug, *Armadillidium vulgare*



e. Copepod, *Diaptomus*

Leafhopper, order *Homoptera*



Beetle, order *Coleoptera*

LECTURE 3:INTRODUCTION TO CHEMISTRY

Any study of biology, the study of life, requires a little knowledge of chemistry. Organisms are chemical machines so to understand their structure and function requires a basic understanding of atoms, molecules, etc.

Introduction

We will look at:

Matter
Elements
Periodic Table
Atoms & Molecules
Chemical Bonds
Inorganic Molecules

Chemistry is the science of the structure and interaction of **MATTER.**
Any substance in the universe that has mass and occupies space is matter.
Consequently, **All living (and nonliving) things consist of matter**.

Matter is defined as anything that occupies space and has mass.
The terms mass and weight are sometimes used interchangeably but
–**Mass** is the ***amount*** of matter in any object.
–**Weight** is the force of gravity acting on matter.

For example, whether an organism is here on earth or on the moon will not change the amount of matter but it will change the weight since the force of gravity is greater on earth than on the moon.

All forms of matter are made up of chemical elements

CHEMICAL ELEMENTS

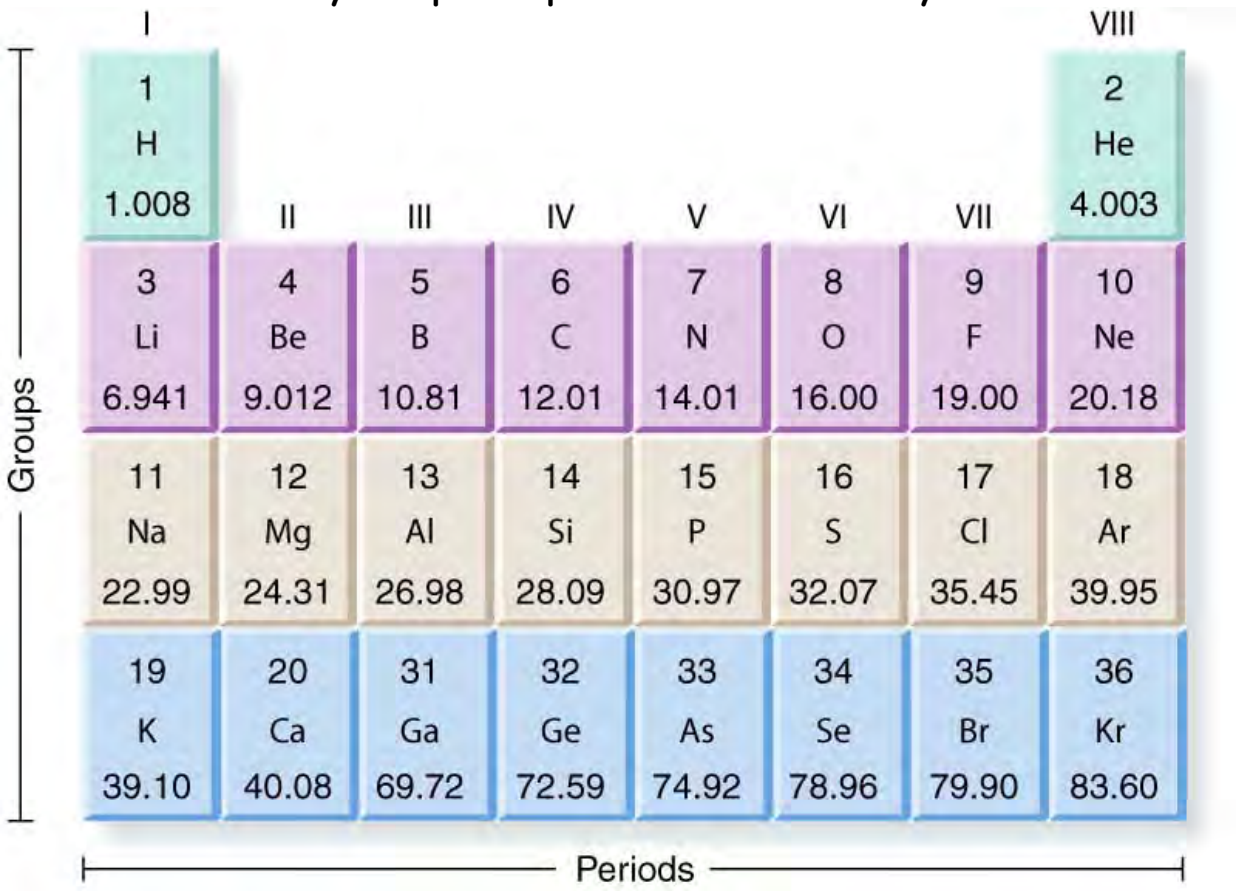
•Elements are the building blocks of the universe and are substances that cannot be split into simpler substances by ordinary means. Each element has its own name and properties.

•Each chemical element is represented by a symbol which is usually the first or first two letters of the element's name (sometimes the Latin name).

•For example: Naming sodium (Latin name - natrium) – S is used for sulfur and N for nitrogen so sodium is represented by the symbol Na.

• **92** elements occur naturally and are represented on the **PERIODIC TABLE**

For clarity this partial periodic table shows only 26 elements.



Most living organisms only require about 20 – 30 elements. Just 26 of the naturally occurring elements are in the human body and only **4 elements form 96-98% of the body. These elements are**

CARBON (C) HYDROGEN (H) OXYGEN (O) NITROGEN (N)

Other important elements in living organisms in much smaller amounts include:
Phosphorus (P) Sulfur (S) Sodium (Na) Chlorine (Cl) Potassium (K) Calcium (Ca) Iron (Fe) Magnesium (Mg) Iodine (I)

ATOMS and ATOMIC STRUCTURE

Atoms are the **smallest units of elements** and each element is made up of only one type of atom. Atoms consist of many types of subatomic particles but the ones of interest to us are **protons, neutrons, & electrons**.
Below is some information about each of these subatomic particles.

•**Protons** are located in the nucleus (the center) of the atom. Each proton is a positively charged particle and has an atomic mass weight (amu) of 1.

•**Neutrons** are also located in the nucleus, also have an amu of 1, but have no charge.

•**Electrons** are never in the nucleus. Instead they make up an electron cloud which may be divided into different energy levels. Electrons are negatively charged and they are so small that they are considered to have no weight.

Subatomic Particles			
Particle	**Electric Charge**	**Atomic Mass**	**Location**
Proton	+1	1	Nucleus
Neutron	0	1	Nucleus
Electron	−1	0	Electron shell

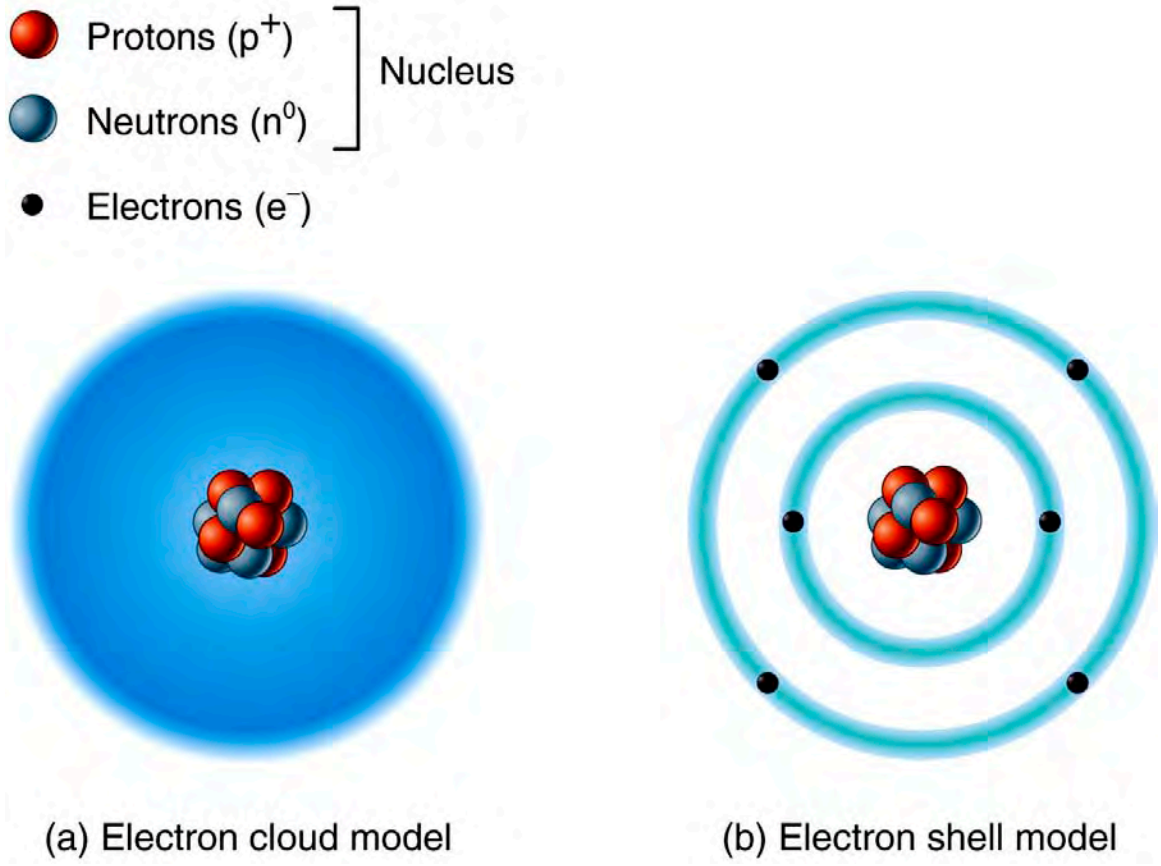
Electron Shells

Electrons move around the nucleus of the atom in **orbits** but it is easier to visualize them as moving in circles called **electron shells**. They try to stay as close to the nucleus as possible but each electron shell can hold only a limited number of electrons obeying the **Octet Rule:-**

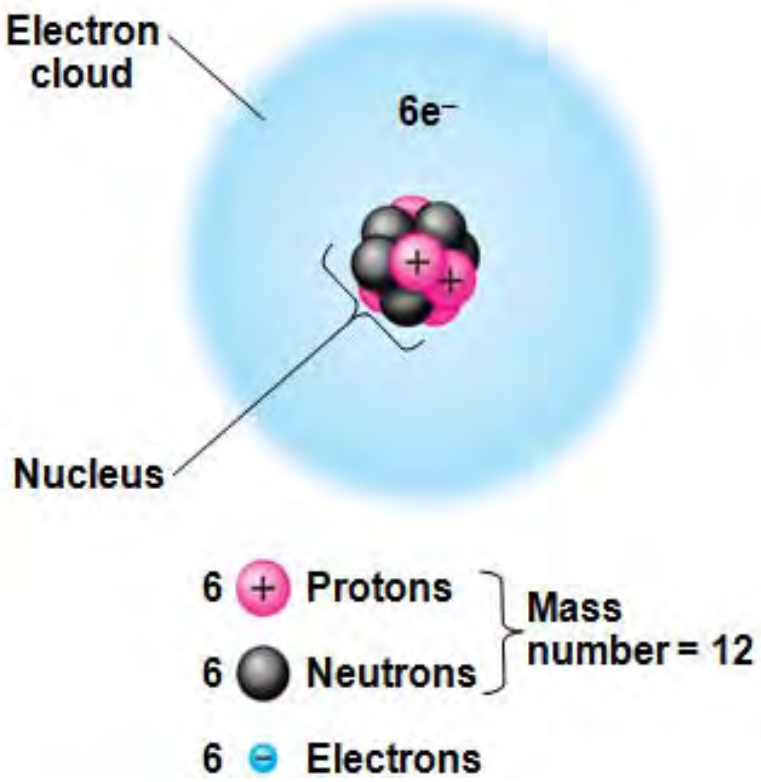
The first shell can hold only **2** electrons and must be filled before electrons can move on to the second shell. The second and subsequent shells can hold **8** electrons (octet) or more. Note that the outer shell is referred to as the **valence shell**.

In any atom the number of electrons = number of protons. Therefore each atom is electrically neutral.
As you will see electrons determine the chemical behavior of an atom.

TWO WAYS TO REPRESENT AN ATOM



REPRESENTATION OF A TYPICAL CARBON ATOM



Each element has 2 numbers associated with it on the periodic table.

1. Atomic number = number of protons in the nucleus of an atom. Atoms of different elements have a different number of protons in the nucleus. The atomic number for an atom of each element can be found on the periodic table.

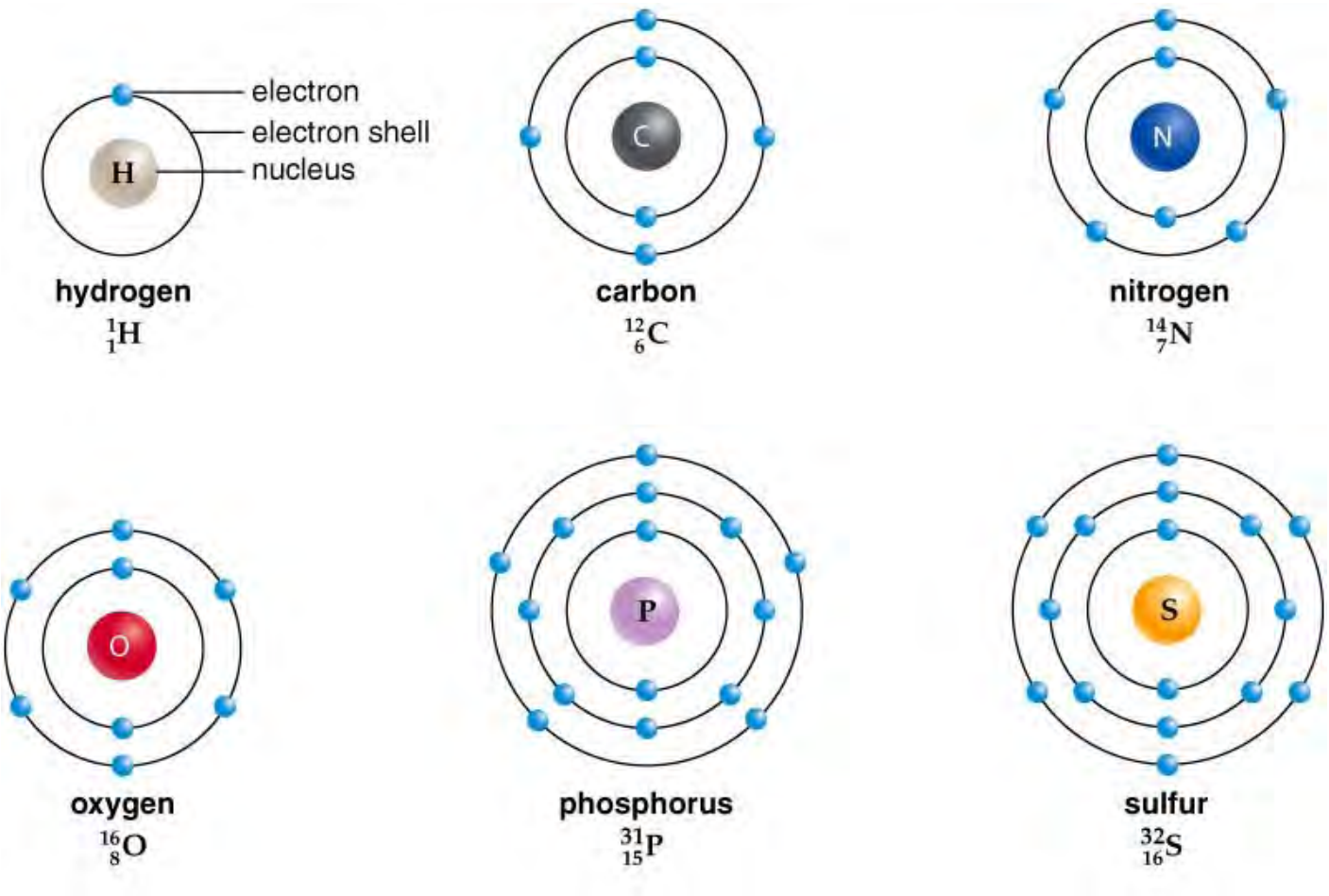
Atomic # = 6 in above atom of carbon.

2. Mass number is the sum of the masses of the subatomic particles in the atom but since electrons have such small mass, the mass number is the number of protons and neutrons in the nucleus of the atom.

Mass # = 12 in above atom of carbon.

Atomic mass/weight is the average mass/weight of all the atoms of the element including the different **isotopes** (see page 7) of an element that exist. (Note – the terms atomic mass and atomic weight are used interchangeably but the more precise term is **atomic mass**. Atomic weight reflects the effect of gravity.

SAMPLE REPRESENTATIONS OF COMMON ATOMS OF ELEMENTS

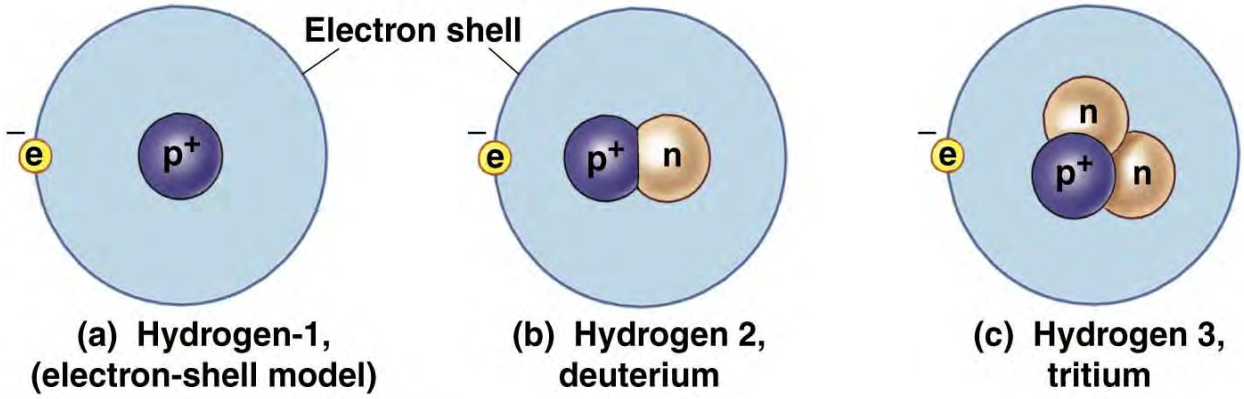


Lower number is the atomic number. The higher number is the mass number. The letter is the symbol for the element.

Remember if you know an atom's atomic number you know how many protons it has. Since the number of electrons in an atom equals the number of protons, you also know the number of electrons.

Isotopes are atoms of an element with a different number of neutrons and therefore have a different atomic mass/weight because each neutron has a mass of 1 amu. **Isotopes** of an element have the same properties as other atoms of that element since only the neutron number changes. However radioactive isotopes are unstable & can be a serious health threat. Isotopes of certain elements are used in medical imaging procedures or used to treat cancer.

Isotopes of hydrogen



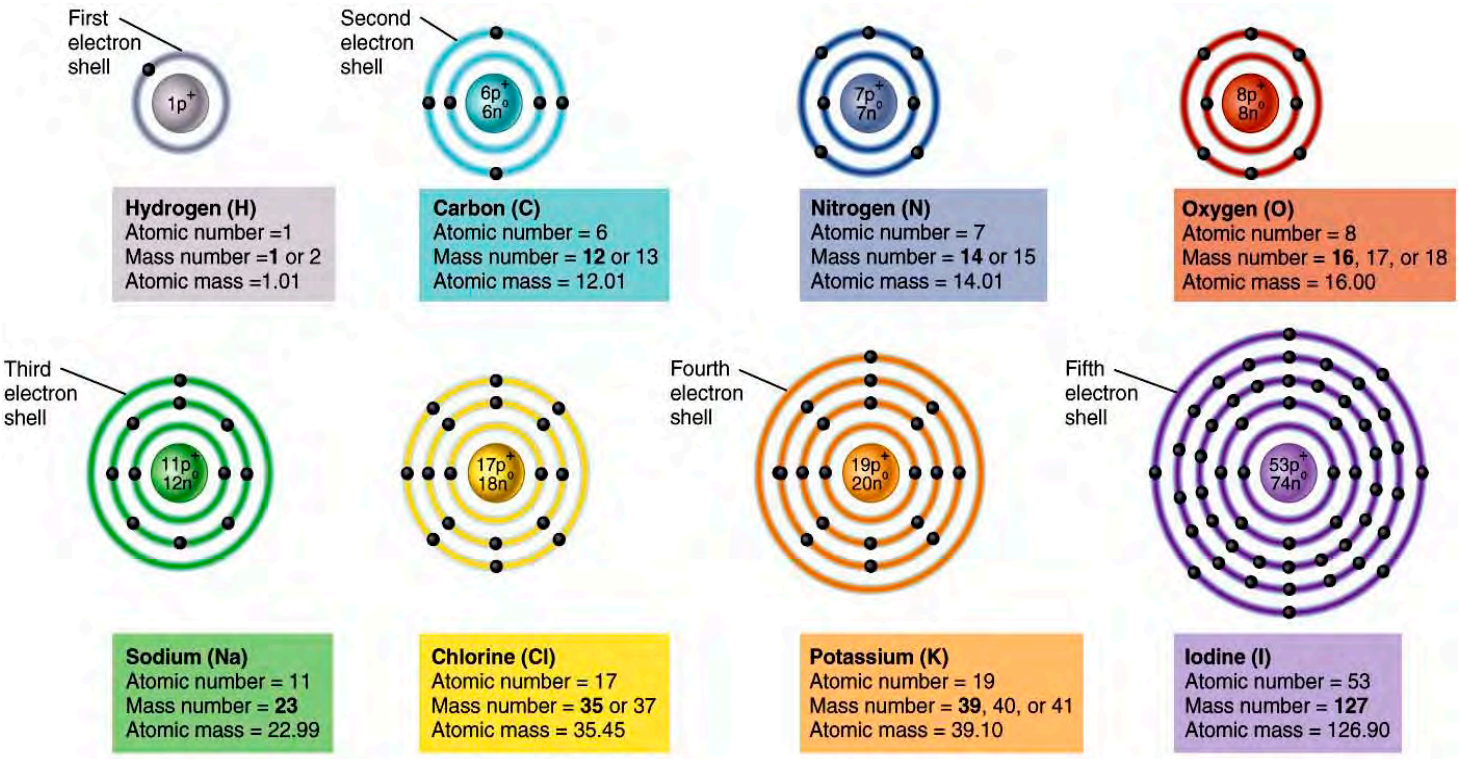
(a) Hydrogen-1, (electron-shell model)

(b) Hydrogen 2, deuterium

(c) Hydrogen 3, tritium

Hydrogen is the smallest atom. It has an atomic number of 1 and a mass number of 1 – there is only 1 proton and no neutrons in the nucleus of the majority of hydrogen atoms so mass = 1. However a small number of hydrogen atoms have 1 neutron as well as 1 proton (mass = 2) and a small number of hydrogen atoms have 2 neutrons as well as 1 proton (mass = 3)…..these "variations" are isotopes of hydrogen. Remember all atoms of hydrogen have only 1 proton.

The mass number of hydrogen can change when the number of neutrons change but the number of protons will remain the same….if the number of protons change the atom would no longer be a hydrogen atom.



Above are several important elements in living systems. All of these elements have isotopes as is evidenced by the different mass numbers.

Atomic number = number of protons in an atom
Mass number = number of protons and neutrons in an atom (boldface indicates most common isotope
Atomic mass = average mass of all stable atoms of that element (in Daltons or amus)

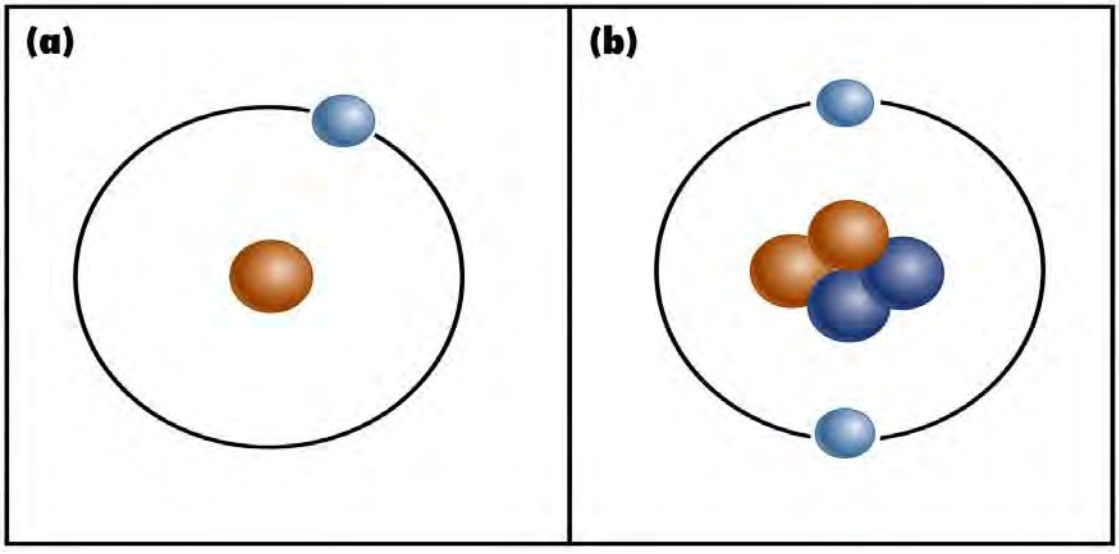
IONS, MOLECULES, & NOBLE GASES

An **ion** is an atom that has acquired an electrical charge by either losing or gaining an electron. An atom that **loses** an electron loses a negative charge and therefore will become a positively charged ion because now it will have one more positive charge than negative charge and is known as a **Cation**. Ex. Na^+. An atom that gains an electron will become a negatively charged ion known as an **Anion** Ex. Cl^-.

Atoms combine to form **Molecules.** For example, a molecule of water, H_2O, contains 2 atoms of hydrogen and an atom of oxygen. A molecule of glucose, $C_6H_{12}O_6$ has 6 atoms of carbon, 12 atoms of hydrogen, and 6 atoms of oxygen. Usually the formation of molecules occurs by the sharing of electrons (discussed later).

However atoms of some elements are stable and do not react. These atoms already have a complete **valence shell or outer energy level**. These elements are **inert gases** sometimes referred to as **Noble gases.**
For example, **Helium** has an atomic number of 2 which means it has 2 atoms and therefore 2 electrons. This means that the outer (valence) shell is complete. Another example of an inert gas is **Neon** with an atomic # of 10:- 2 electrons in the first shell and 8 in the second which is now complete.

Most atoms reach a stable state when they have 8 electrons in their valence shell and will form bonds with other atoms in order for this to happen (remember the octet rule). Below is an atom of hydrogen (a) which will react and form molecules while helium (b) is stable and will not react.



CHEMICAL BONDS

Atoms will **bond** with other atoms to fulfill their outer or valence shell requirements with orbiting electrons – to have 2 electrons if the atom only has one shell or 8 electrons if the atoms are larger. Whether **electrons** are shared, donated, or acquired, determines the types of bonds formed.

1. Ionic Bonds

Positively and negatively charged ions attract each other to form an ionic bond such as in the formation of **Sodium Chloride (NaCl)—table salt.**

Here you see that Sodium gives up an electron to achieve stability and becomes a sodium ion Na^+. Chlorine accepts the electron becoming a stable ion, Cl-. The negatively charged ion is attracted to the positively charged ion and a bond is formed. **See page 11.** This type of bond is called an Ionic bond. Ionic compounds generally exist as solids as in table salt.

An ionic compound that dissociates in water into positive & negative ions is called an **Electrolyte** – such a solution can conduct an electric current.

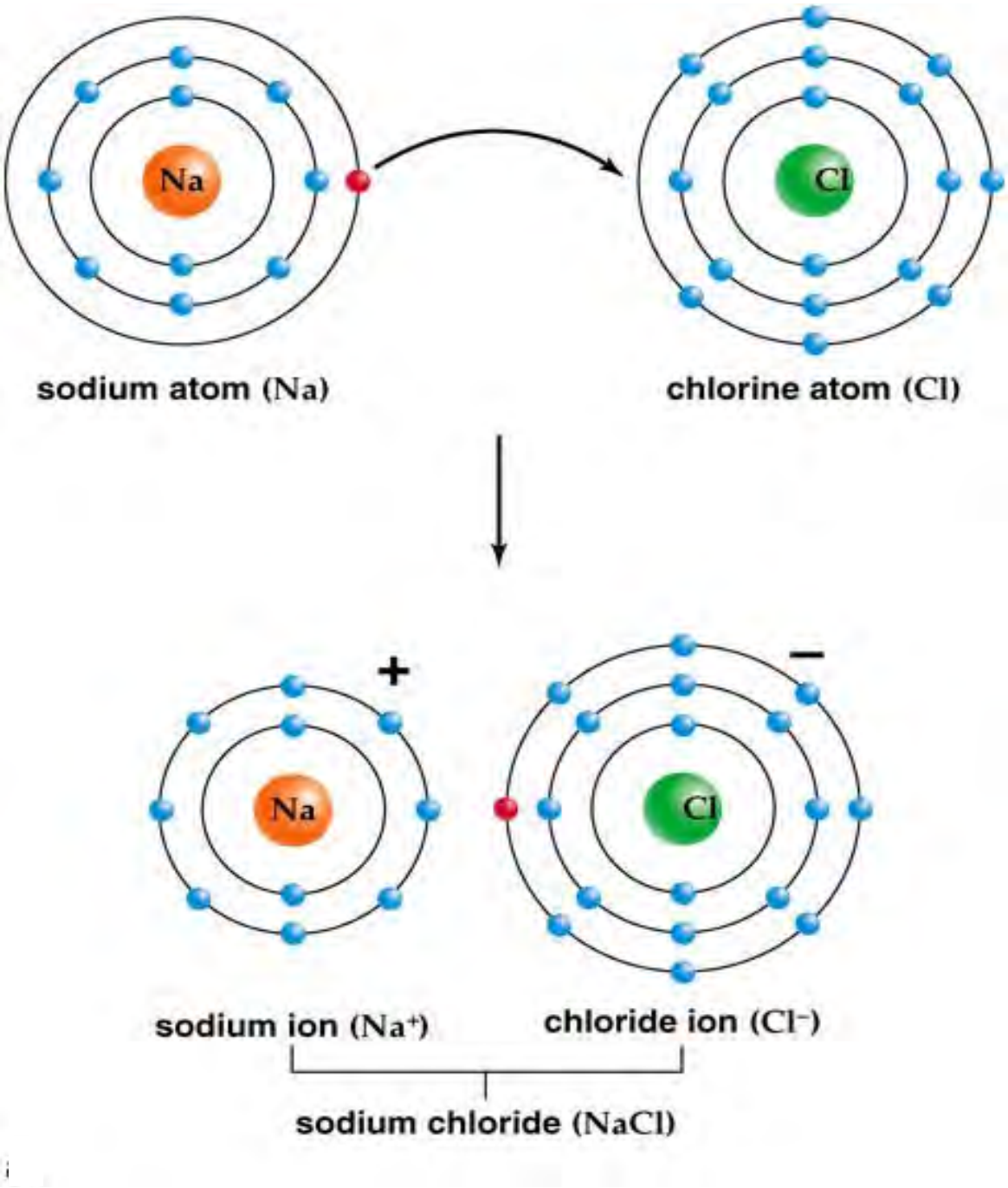
2. Covalent Bonds

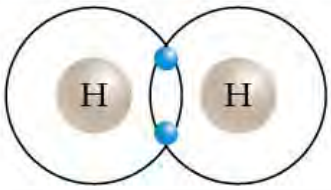
Covalent bonds are the most common bonds in the human body. Atoms with incomplete outer valence shells will share electrons forming covalent bonds. Electrons spend most of the time between the 2 atomic nuclei. Two key properties of covalent bonds that make them ideal for building molecules are 1) they are very strong, sharing lots of energy and 2) they are directional, i.e. bonds form between specific atoms rather than there being just a generalized attraction. Bonds can be single, double, or triple.

Single bond = share 1pair E.g. H_2
Double bond = share 2 pair E.g. O_2
Triple bond = share 3 pair E.g. N_2, Chlorine

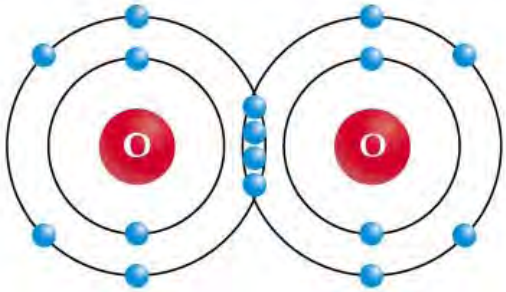
Covalent bonds also form between atoms of different elements as in CH_4
Examples of these bonds can be found on **page 12**.

FORMATION OF AN IONIC BOND

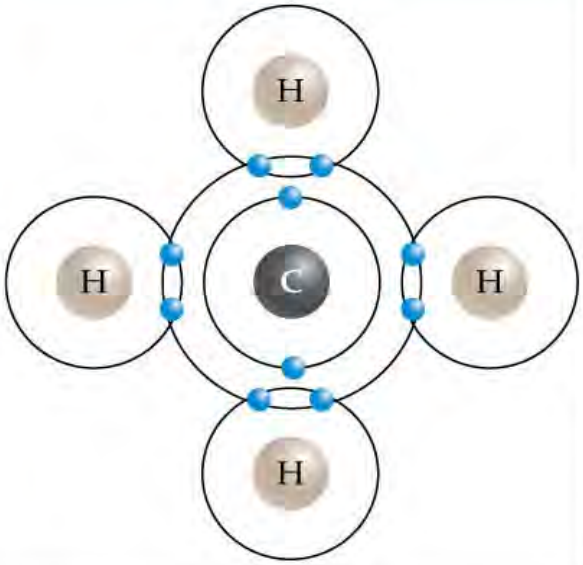
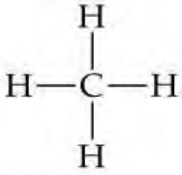


Electron Model	Structural Formula	Molecular Formula
	H—H	H_2

a. Hydrogen gas

	O=O	O_2

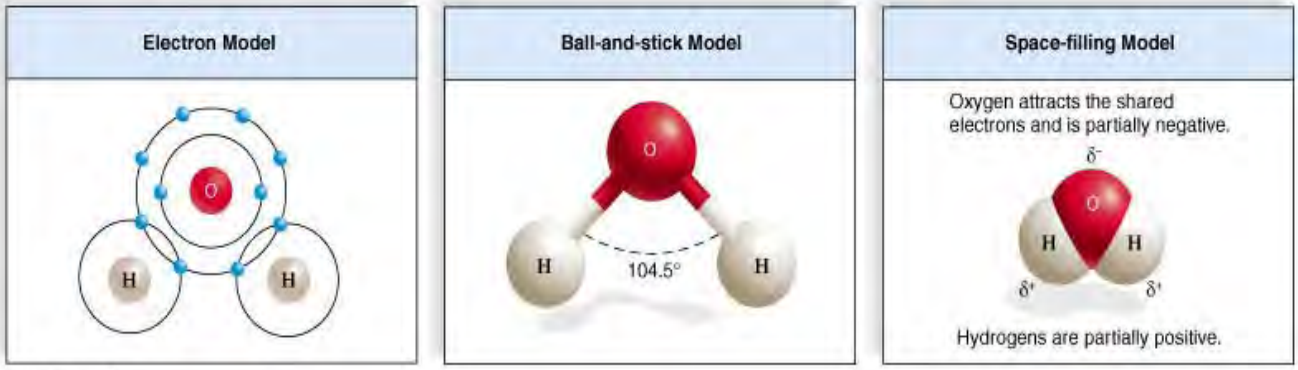
b. Oxygen gas

		CH_4

c. Methane

3. Polar Covalent Bonds

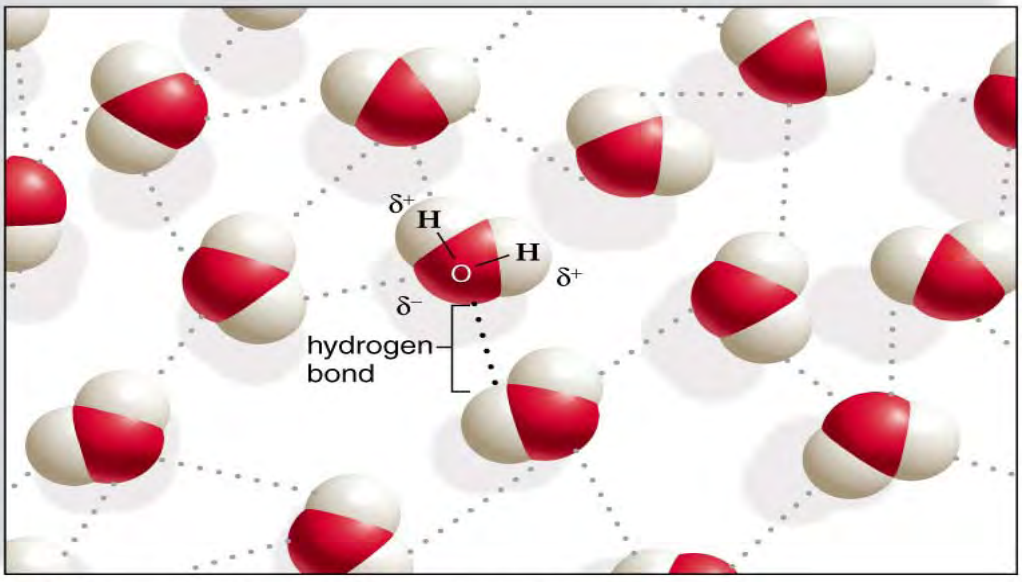
In water molecules electrons are shared covalently, but they are shared unequally. An atom of oxygen has 8 electrons and just shares 2 electrons while each hydrogen atom shares its only electron with oxygen. The electrons from both hydrogen atoms will spend more time around the larger oxygen than around their own nuclei so there is a slight imbalance of electrical charge in the water molecule. This is called **polarity**.



a. Water (H_2O)

4. Hydrogen Bond

Each water molecule is now polar having a slight negative charge at the oxygen end and a slight positive charge at the hydrogen ends. One water molecule is attracted to another water molecule forming a weak bond known as a hydrogen bond. Water and other molecules such as, sugars, proteins, and DNA are polar and the formation of hydrogen bonds within these molecules can stabilize the structures.



b. Hydrogen bonding between water molecules

Compounds

As mentioned earlier, when 2 or more atoms bond together they form a molecule. Some examples are water H_2O, Oxygen (O_2), glucose $C_6H_{12}O_6$.
If the atoms are from different elements, the substance formed is called a **Compound**. Water is a compound because it has 2 different elements.

In other words, a compound is a substance whose molecules are formed from different types of atoms. In chemistry compounds are classified as **inorganic** or **organic**.

Brief Introduction to Inorganic Compounds

Inorganic compounds usually lack carbon and are structurally simple (although there are some exceptions).

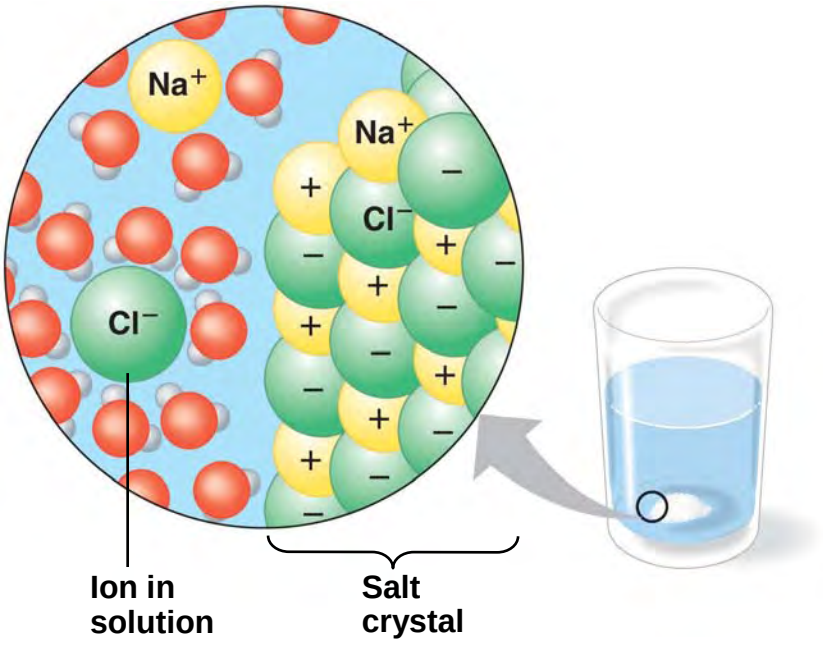
The gases: Oxygen (O_2), and Carbon Dioxide (CO_2), are important inorganic compounds in biology. But the most important inorganic compound in living systems is Water. All living things must have water. This topic is discussed in some detail in Lecture 4.

WATER.

As described in **Lecture 3**, each water molecule is polar and this polarity and the consequent hydrogen bond formation is the characteristic that gives water its unusual properties and makes it indispensible to living systems.

Some characteristics of water are listed below:

1. Water is an excellent solvent.
For example, NaCl (sodium chloride) dissolves in water. Na+ is attracted to the negatively charged oxygen atoms in a water molecule and Cl- is attracted to the positively charged hydrogen ions in a water molecule. The Na+ and Cl- ions get pulled apart (dissolve) in water.



Water works as a solvent here because sodium chloride carries an electrical charge. What generally makes water an **excellent solvent** is its ability to form hydrogen bonds with other molecules. Other polar molecules as well as all ions are attracted by water molecules.

TABLE 2–3 Important Electrolytes That Dissociate in Body Fluids

Electrolyte		Ions Released
NaCl (sodium chloride)	$\longrightarrow$	$Na^+ + Cl^-$
KCl (potassium chloride)	$\longrightarrow$	$K^+ + Cl^-$
$CaPO_4$ (calcium phosphate)	$\longrightarrow$	$Ca^{2+} + PO_4^{2-}$
$NaHCO_3$ (sodium bicarbonate)	$\longrightarrow$	$Na^+ + HCO_3^-$
$MgCl_2$ (magnesium chloride)	$\longrightarrow$	$Mg^{2+} + 2Cl^-$
Na_2HPO_4 (disodium phosphate)	$\longrightarrow$	$2Na^+ + HPO_4^{2-}$
Na_2SO_4 (sodium sulfate)	$\longrightarrow$	$2Na^+ + SO_4^{2-}$

Other attributes of water include:

2. Participates in Chemical Reactions
The solvent properties of water allow water to be the medium in which most **chemical reactions** occur and water itself participates in many chemical reactions. See **Lecture 8**.

3. Transports
Because so many substances dissolve in water, it is an **excellent form of transport** in living systems.

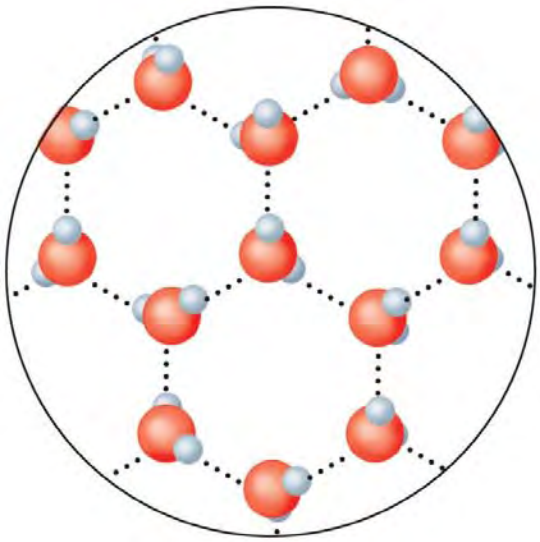
4. Water has a high heat of vaporization and a high heat capacity.
Heat of vaporization refers to the amount of heat required to convert 1 gram of liquid water to a gaseous state.

Unlike other substances water absorbs a great amount of heat energy before it will vaporize – **it has a high heat of vaporization**. Why? Because water molecules are attracted to one another and form hydrogen bonds so "resist" breaking off into a gaseous state.
This is important in maintaining a stable body temperature in humans.
The evaporation of perspiration from the skin carries away a large amount of heat so sweating is an effective way to stay cool.

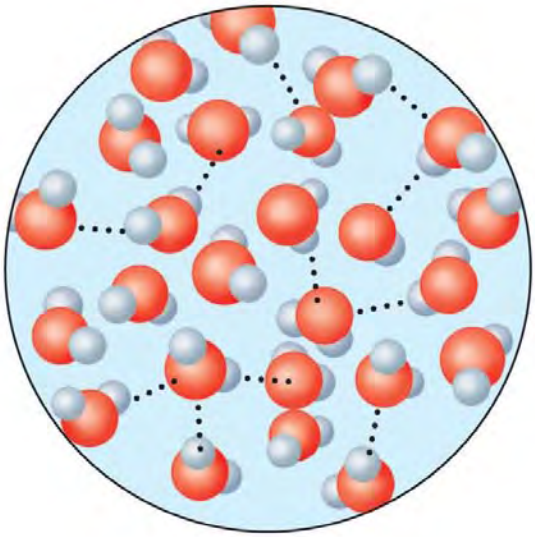
5. Water has a high specific heat. This refers to the amount of heat required to raise the temperature of 1 gram of water by 1 degree Centigrade. Again, unlike other substances, because of hydrogen bonding water must absorb a lot of heat before it increases its molecular motion. (Temperature is a measure of the rate at which molecules are moving.) Because of these bonds water resists temperature changes and because we are mostly water (~ 60%), we are also able to resist temperature changes. A good comparison is the ocean and sand in summer: the ocean water temperature changes very slowly unlike the sand although both are subjected to the same heat from the sun.

6. Water can also exist as a solid.
When water freezes, each molecule forms a stable hydrogen bond with four neighboring water molecules resulting in a three-dimensional crystal. There is space between the water molecules, therefore ice is less dense than water and will float providing a barrier for the water below. The deeper water will stay warmer and this is important for protecting marine life.

Hydrogen bonds are stable in ice.



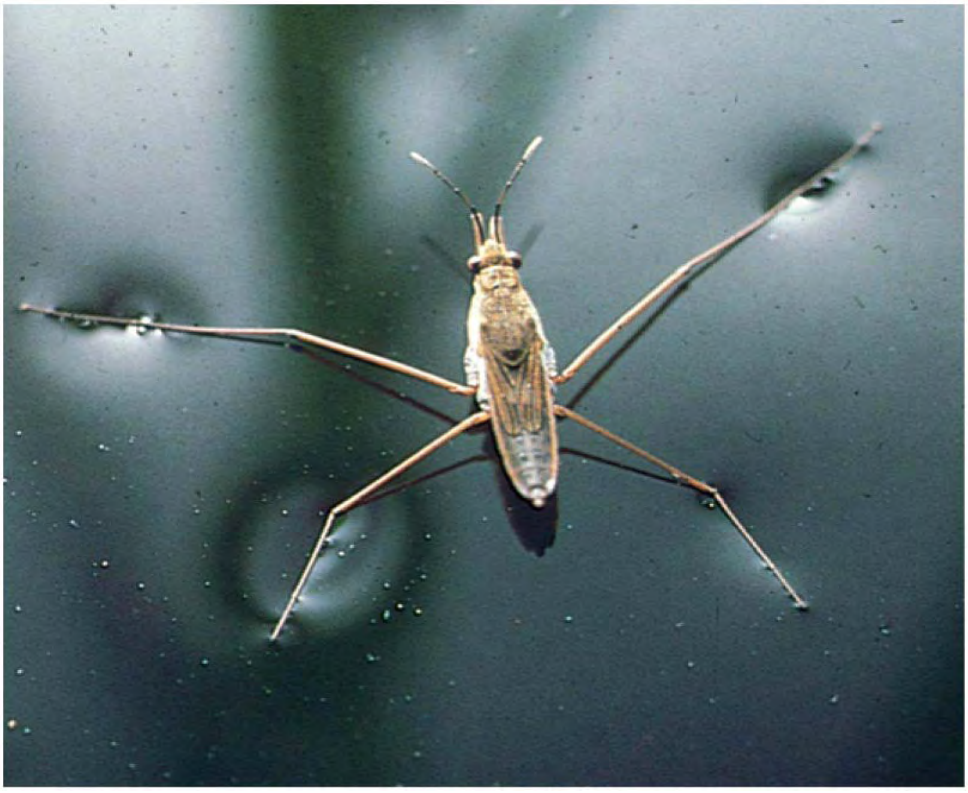
Hydrogen bonds repeatedly break and re-form in liquid.



7. Cohesion, Surface Tension, and Adhesion

The hydrogen bonds that form between water molecules give water molecules **cohesion**. Cohesion is what gives water **surface tension** which is a measure of how difficult it is to break the surface of liquid – lightweight insects can actually walk on water.

And the polarity of water allows water to adhere (**gives adhesion**) to polar surfaces. For example, this allows water to move up the vascular tubes in plants, from roots to leaves.



INORGANIC ACIDS, BASES, & SALTS

Acids, bases, and salts always dissociate into ions if they are dissolved in water.

ACIDS release hydrogen ions when they dissociate (separate) in water or in another substance.
(Note – a hydrogen ion (H^+) is a hydrogen atom that has lost an electron; therefore a hydrogen ion is a proton.)

For example, HCL (hydrochloric acid) dissociates into its ionic compounds:-

$$HCL \text{ ----------> } H^+ + Cl^-$$

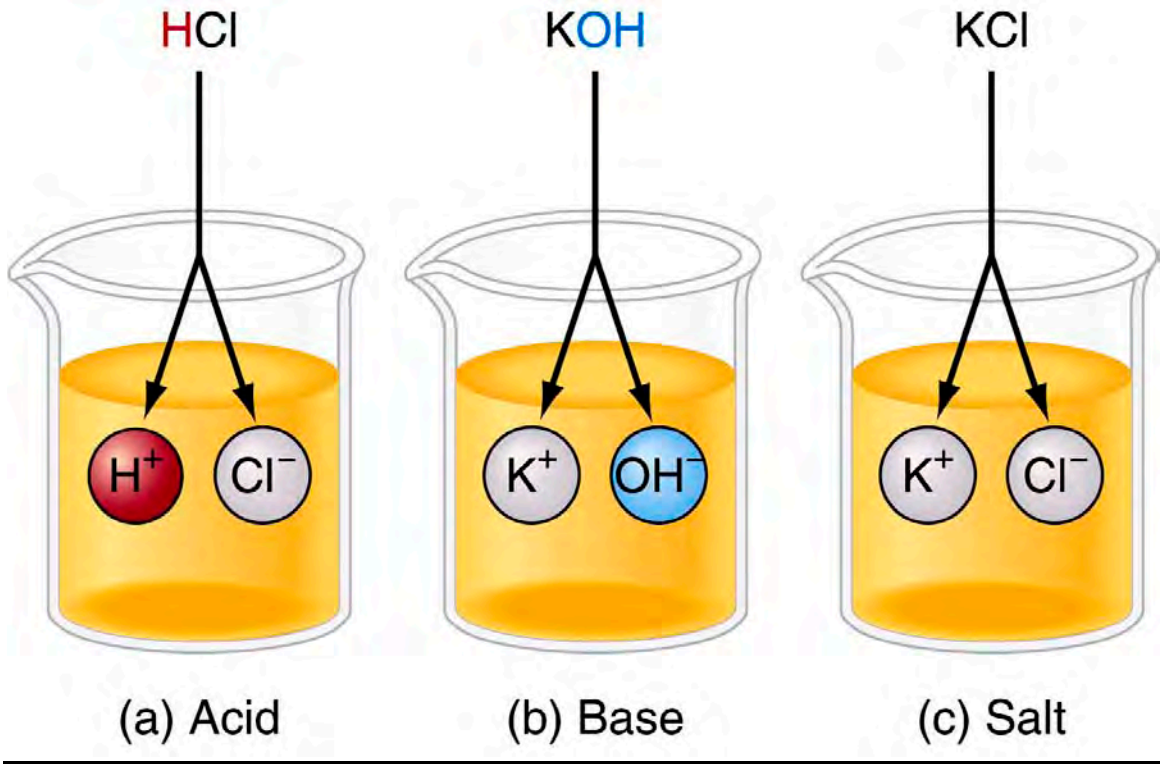
BASES are substances that accept hydrogen ions (or protons) in a solution.
A base dissociates in solution releasing a hydroxide ion (OH^-).
A hydroxide ion accepts a hydrogen ion forming water.

$$NaOH \text{ ---------} \rightarrow Na^+ + OH^-$$

$$H^+ + OH^- \text{ ----------} \rightarrow H_2O$$

SALTS also release ions in solution but these ions are neither hydrogen ions nor hydroxide ions. Salts are produced by mixing solutions of appropriate acids and bases.
In neutralization reactions, the acid and base react to form a salt and water.

$$HCL + NaOH \text{ ----------} \rightarrow NaCl + H_2O$$


HCl
KOH
KCl
H+
Cl−
K+
OH−
K+
Cl−
(a) Acid
(b) Base
(c) Salt

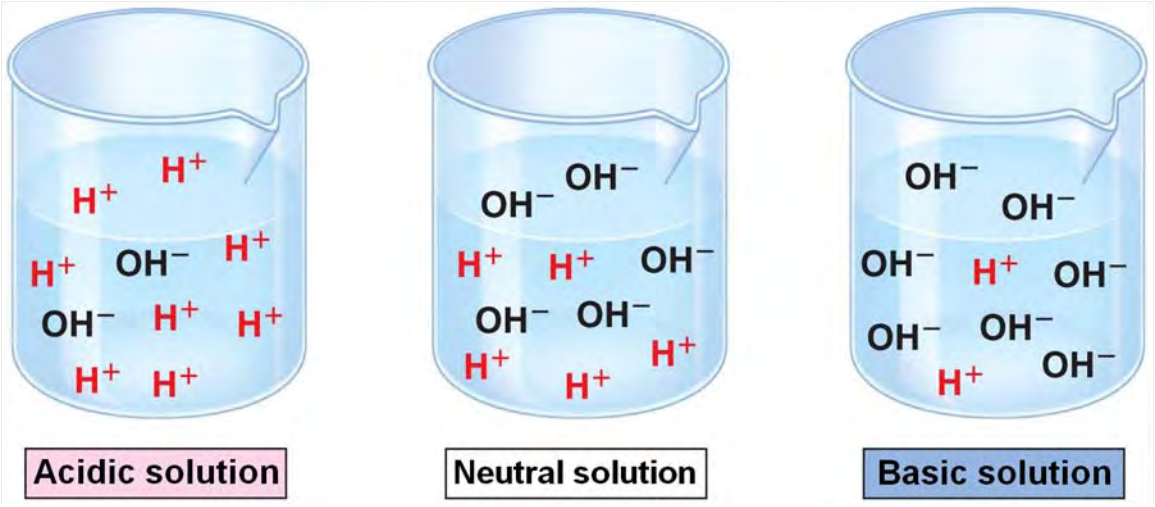
Concept of pH

pH scale runs from 0 to 14 and measures the concentration of H+ in moles/liter. The H stands for hydrogen and p is thought of as power.

A solution with a **pH of 7 is neutral**. Distilled water has a pH of 7 meaning that the concentration of the ions, OH- and H+, are equal.

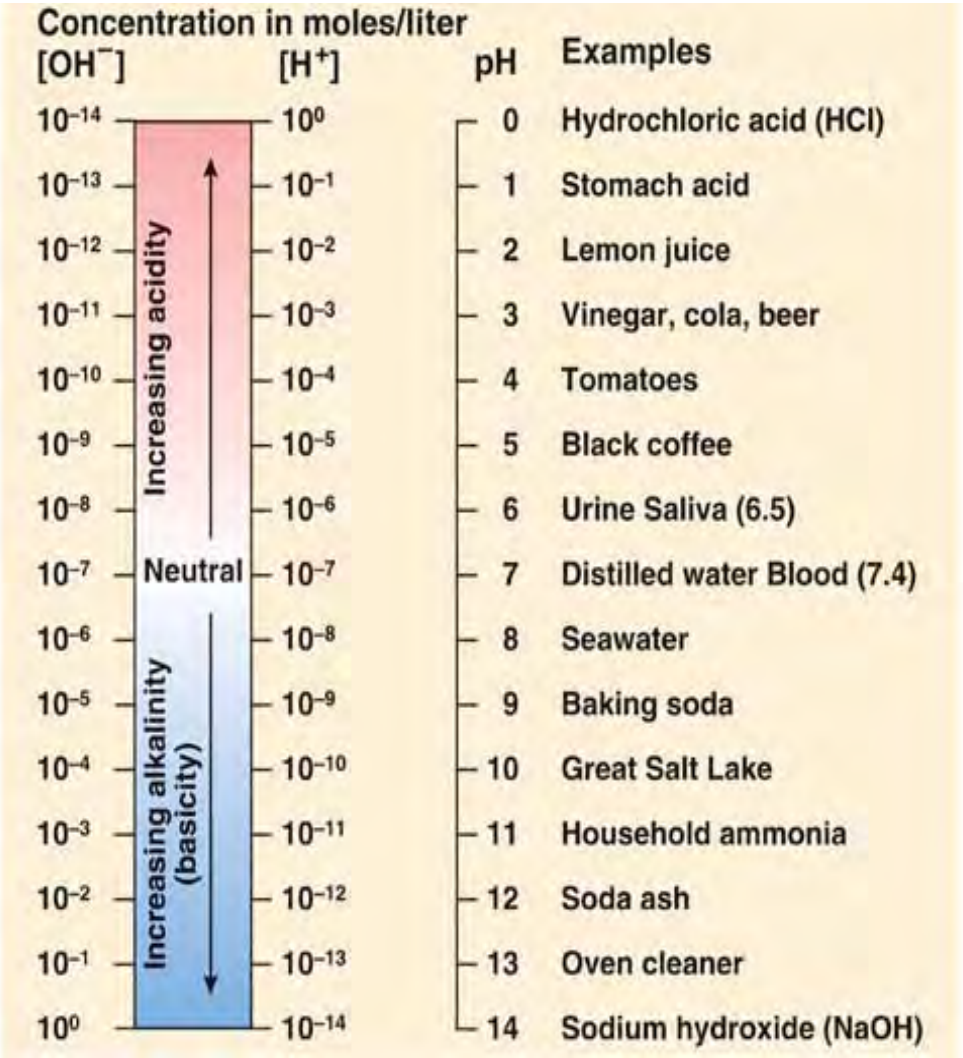
A solution with a **pH below 7 is acidic**. It has an excess of hydrogen ions.

A solution with a pH **above 7 is basic or alkaline**. It has an excess of hydroxide ions.



Each number on the pH scale represents the exponent (without the minus sign) of the hydrogen ion concentration expressed in moles of hydrogen ions (H^+) per liter of solution.
Note: A mole of a compound is the number of grams of that compound equal to its molecular mass.

A difference of one unit on the pH scale represents a tenfold change in acidity or alkalinity. For example, a solution with a pH of 4 contains 0.0001 (10^{-4}) moles of hydrogen ions per liter, while a solution with a pH of 3 contains 0.001 (10^{-3}) moles of hydrogen ions per liter. The number, 0.001 ($10^{-3)}$ is 10 times greater than 0.0001 (10^{-4}). Therefore a solution with a pH of 4 contains 10 times less free hydrogen ions (H+) than a solution with a pH of 3 that is, it is 10 times less acidic.



BUFFER SYSTEMS

Buffers convert strong acids to weak acids and strong bases to weak bases. Buffer solutions maintain a constant pH even when small amounts of acid or small amounts of base are added. Basically, buffers systems contribute H^+ or OH^- as needed to keep the pH of the solution stable.

HCl is a strong acid; that is, it is about 100% ionized (H^+ and Cl^-) in solution.

If a strong acid is added to a buffer solution it is changed to a weak acid.

$HCL + NaHCO^2$ ----------→ $H^2CO^3 + NaCl$

Here a strong acid (hydrochloric acid) is added to a weak base and the result is a weak acid (carbonic acid) and a salt – the strong acid has been buffered.

Buffers and a stable pH are very important to living systems. A good example that demonstrates the importance of this is the example of enzymes (**Lecture 9**). Enzymes are the proteins responsible for catalyzing chemical reactions, and are very sensitive to pH. If an enzyme is put in a solution with a pH that is too acidic, the enzyme will change shape making it unable to function. This is because the ions that are abundant in the acidic solution (lots of H^+) interfere with the enzyme's chemical bonds.

Cell membranes are also very sensitive to changes in pH. The pH in a human cell is usually close to neutral ~ 7. The pH of human blood is about 7.4.

The pH of some other solutions are listed on page 9.

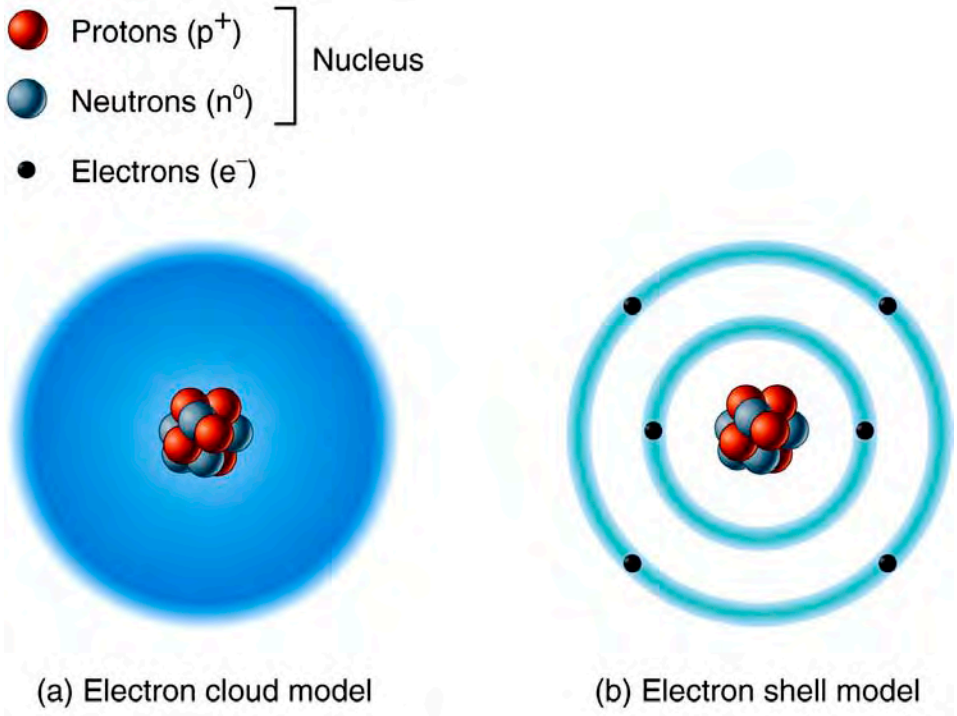
LECTURE 5: ORGANIC COMPOUNDS

Unlike **inorganic compounds** talked about in **Lectures 3 and 4**, **organic compounds** always contain carbon bonded to hydrogen and usually contain **covalent** bonds.

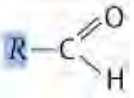
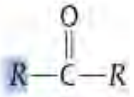
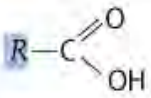
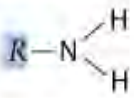
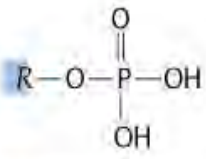
Nearly all molecules in living organisms are made of chains of carbon atoms. The carbon-based building blocks of life are simple and universal and in this lecture we will discuss the four building blocks (carbon-containing) that form almost all biological structures.

These four classes of carbon-containing molecules are:
Carbohydrates
Lipids
Proteins
Nucleotide-based molecules

Because all these building blocks contain carbon we will review the structure of carbon.



Because carbon has 4 electrons in its valence shell which can be seen on the figure on page 1, carbon can form bonds with 4 other atoms. Most of the classes of organic compounds that form the building blocks of living organisms are based on long chains of carbon and hydrogen (hydrocarbon chains). These molecules can have many different shapes: rings, straight chains, branched chains, etc and many functional groups can attach to carbon skeleton- see chart below.

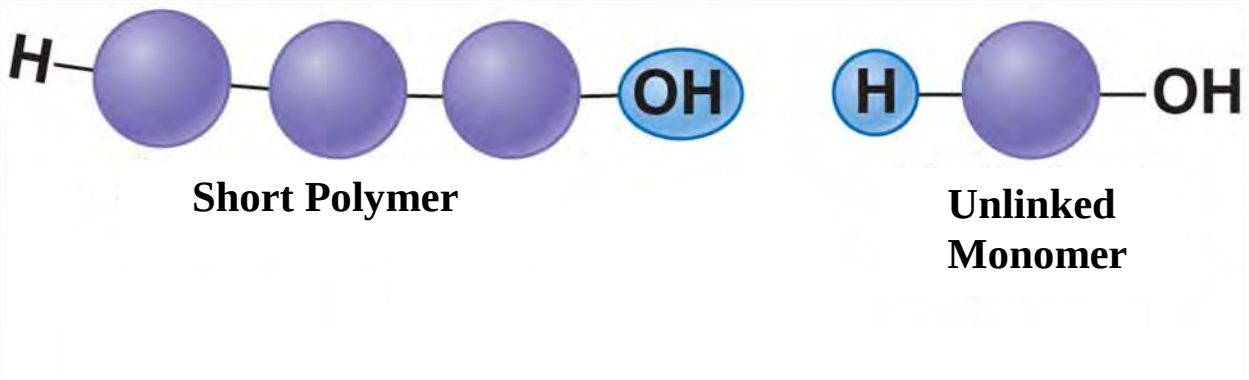
Functional Groups			
Group	**Structure**	**Compound**	**Significance**
Hydroxyl		Alcohol as in ethanol	Polar, forms hydrogen bond Present in sugars, some amino acids
Carbonyl		Aldehyde as in formaldehyde	Polar Present in sugars
		Ketone as in acetone	Polar Present in sugars
Carboxyl (acidic)		Carboxylic acid as in acetic acid	Polar, acidic; Present in fatty acids, amino acids
Amino		Amine as in tryptophan	Polar, basic, forms hydrogen bonds Present in amino acids
Sulfhydryl		Thiol as in ethanethiol	Forms disulfide bonds Present in some amino acids
Phosphate		Organic phosphate as in phosphorylated molecules	Polar, acidic; Present in nucleotides, phospholipids

R = remainder of molecule

Some terminology:

Very large organic molecules are called **macromolecules**.
A single building block of a macromolecule is called a monomer and if all **monomers** joined together in a large molecule are the same or similar, then the term **polymer** is used. See below.

Isomers have same molecular formulas but different structures (glucose & fructose are both $C_6H_{12}O_6$.- see page 5.)



Short Polymer

Unlinked Monomer

FOUR CLASSES OF MACROMOLECULES

CARBOHYDRATES

Diverse group of substances formed from carbon, hydrogen, and oxygen, usually in the ratio of 1:2:1

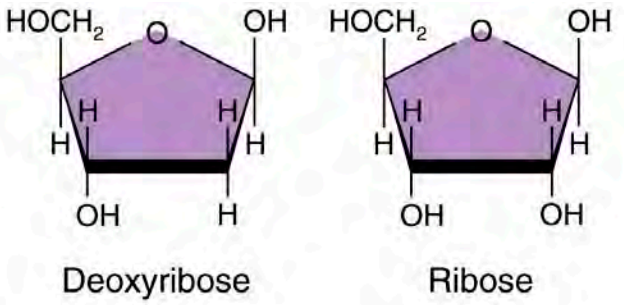
There are 3 sizes of carbohydrate molecules:

A. Monosaccharides

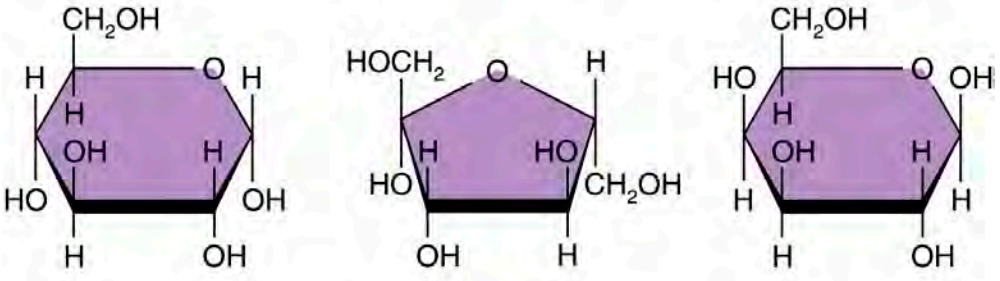
These are called simple sugars and contain 3 to 7 carbon atoms
There are **5 monosaccharides** you should be familiar with:

1. Glucose 2.Fructose 3.Galactose (all hexoses – 6 carbon sugars)

4. Ribose 5.Deoxyribose (all pentoses – 5 carbon sugars)



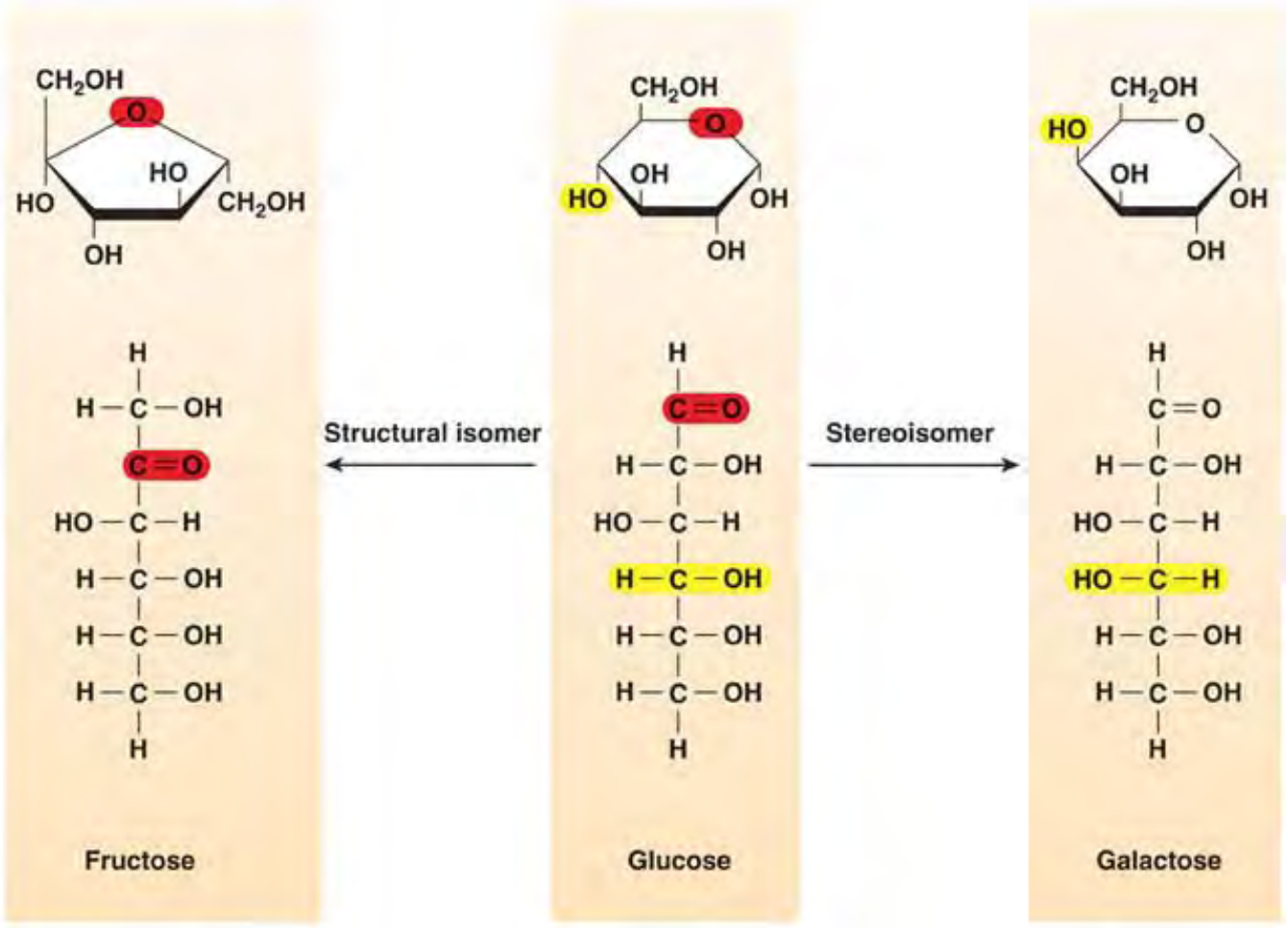
(a) Pentoses



(b) Hexoses

□

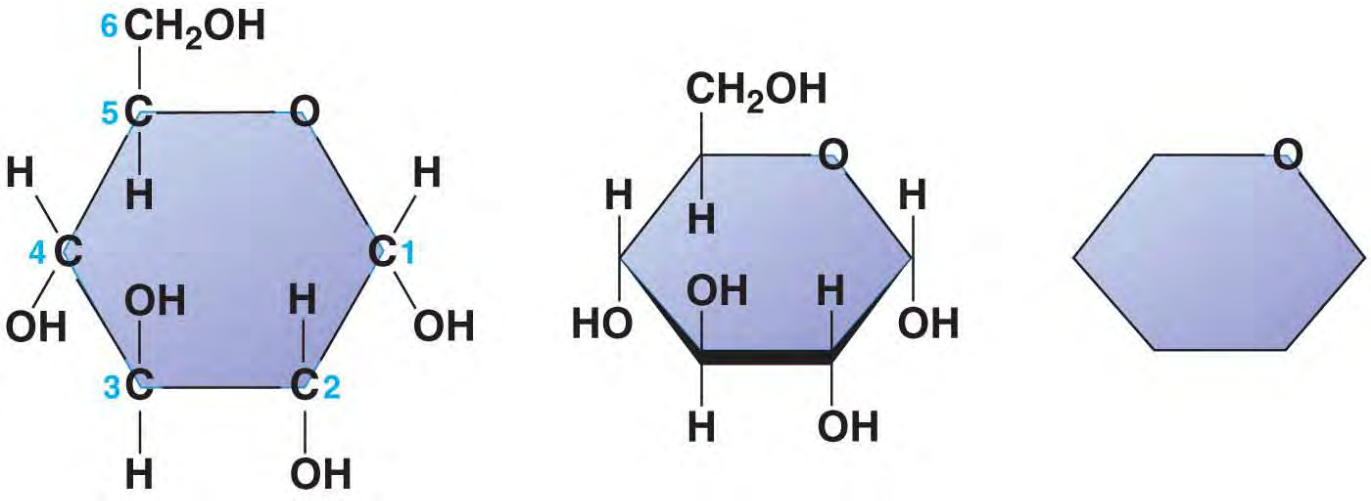
Fructose and Galactose are isomers of glucose.



The molecular formula for glucose is $C_6 H_{12} O_6$

Fructose and Galactose are isomers of glucose i.e. they have the same molecular formula but the atoms are arranged differently.

GLUCOSE is a very important molecule in living systems and is a monomer of the disaccharides and polysaccharides described next.



A **B** **C**

Three representations of glucose

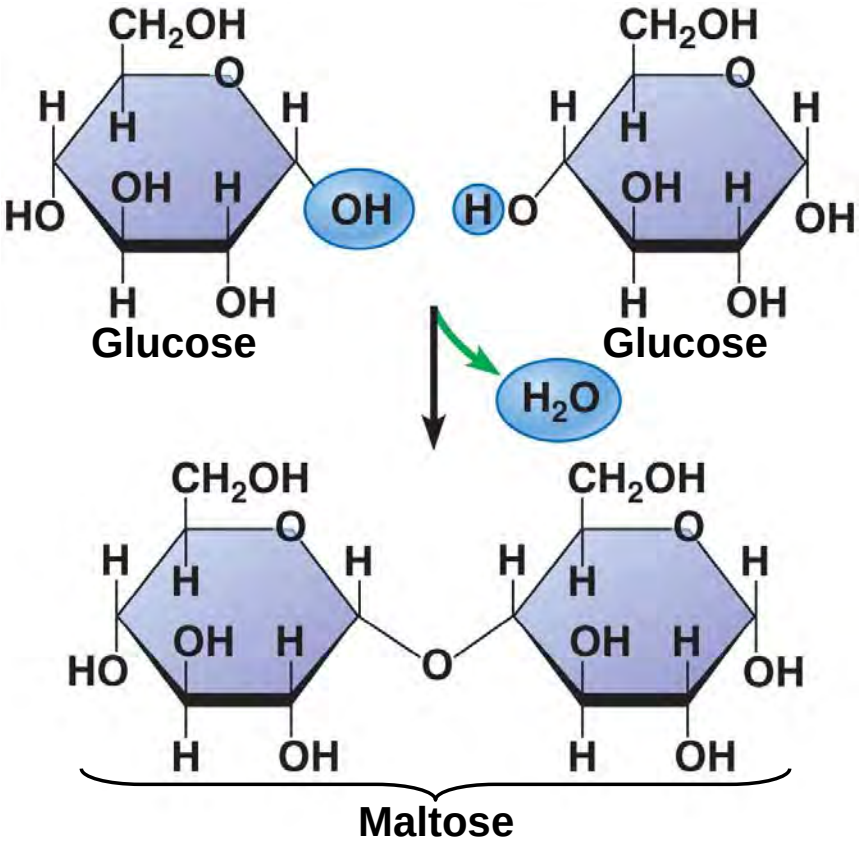
A. Structural formula with all atoms written in

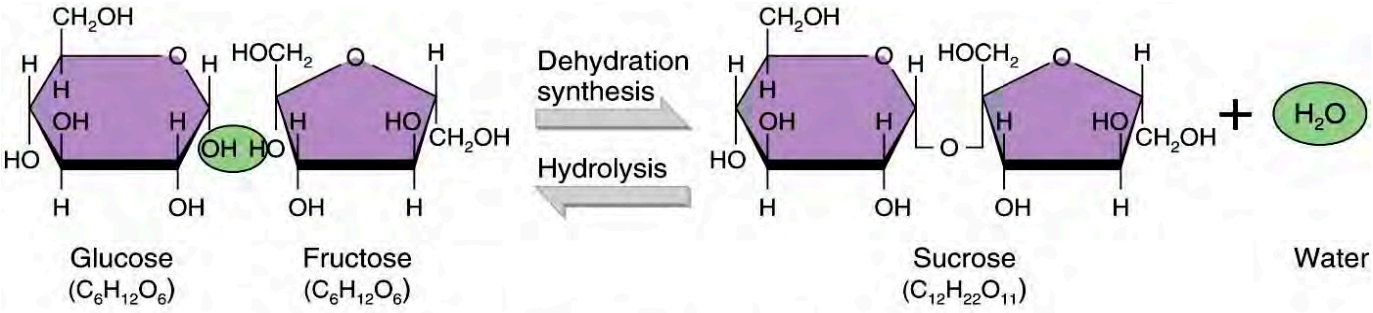
B. Abbreviated formula with the ring carbons omitted

C. Simplified structure

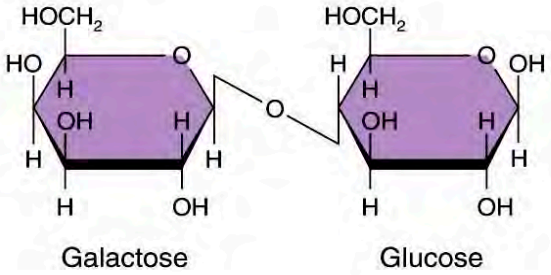
B. Disaccharides

Disaccharides are formed by combining 2 monosaccharides in a dehydration synthesis reaction (see **Lecture 8**)

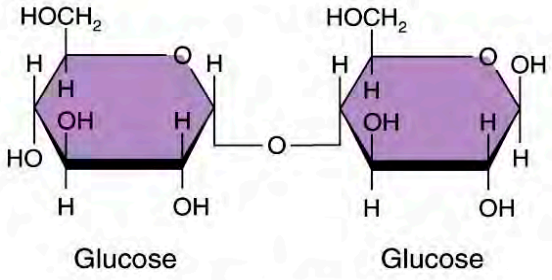




(a) Dehydration synthesis and hydrolysis of sucrose



(b) Lactose



(c) Maltose

3 important disaccharides:

Sucrose formed by combining glucose and fructose

Maltose formed by combining glucose and glucose

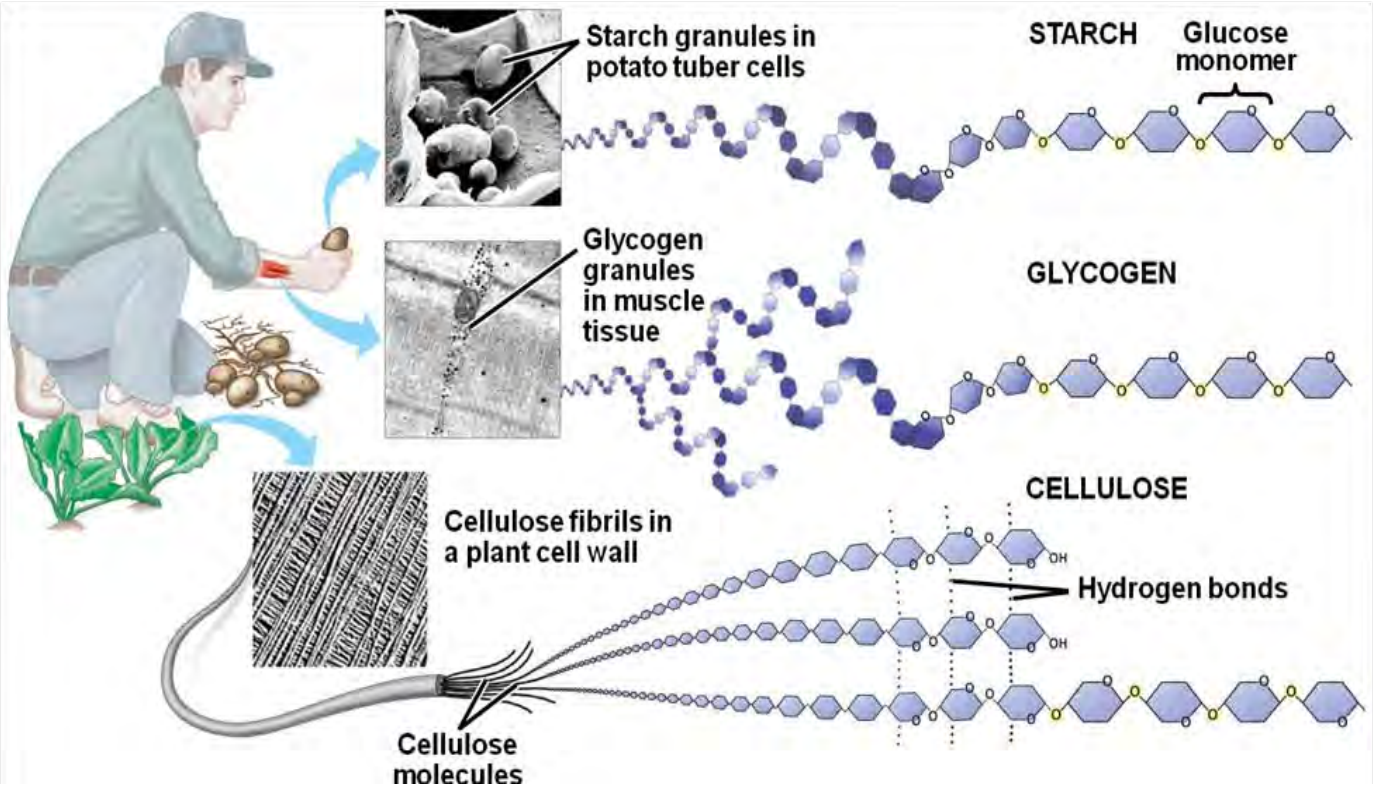
Lactose formed by combining glucose and galactose

C. Polysaccharides

Polysaccharides contain 10s or 100s of monosaccharides joined by **dehydration synthesis** reactions.
Glycogen, starch, and cellulose are all polymers of glucose molecules.

Glycogen is an important polysaccharide in animals, including humans, and is a chain of hundreds of glucose molecules. Glycogen is a storage carbohydrate and is found in liver & skeletal muscle cells. When blood sugar (glucose) levels drop, liver cells hydrolyze glycogen (break apart by the addition of H_2O) to release glucose into the blood.

Starch and Cellulose are the most abundant polysaccharides in plants. Again, one of the functions in plants is energy storage (rice, potatoes, and grains). The bonding between the glucose units of cellulose are slightly different than in the other 2 polysaccharides and humans do not have the necessary enzymes to break these bonds. Other animals such as cows and sheep have these enzymes and can extract energy from cellulose.



Functions of Carbohydrates

1. As stated above, all 3 forms of carbohydrates mentioned here are important energy sources.

2. Carbohydrates also serve as a **storage** form of chemical energy. For example, humans store some glucose as glycogen in liver cells. As mentioned on the previous page, this polysaccharide can be broken down (by **hydrolysis** reactions) to release glucose monomers into the bloodstream when blood glucose is low.

3. Carbohydrates provide carbon for the synthesis of cell components.

4. Carbohydrates also form some structural components of cells.

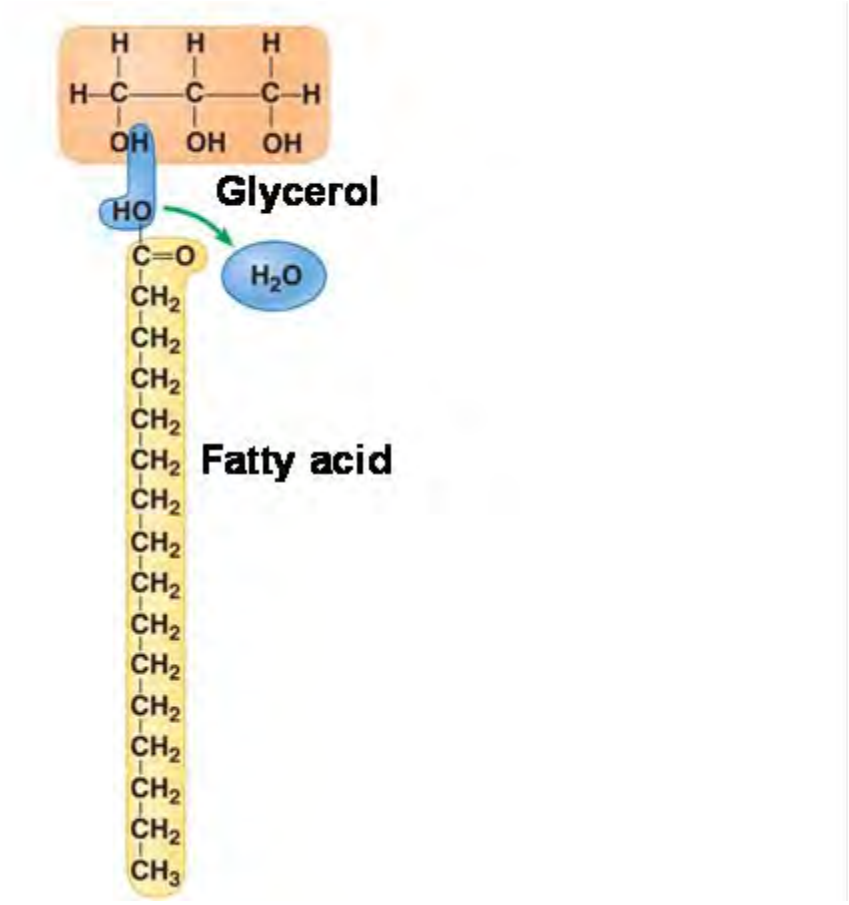
LIPIDS/FATS

Lipids are formed from carbon, hydrogen, and a little oxygen usually at one end. They are compounds that are insoluble in water but soluble in nonpolar solvents and are sometimes referred to as hydrophobic.

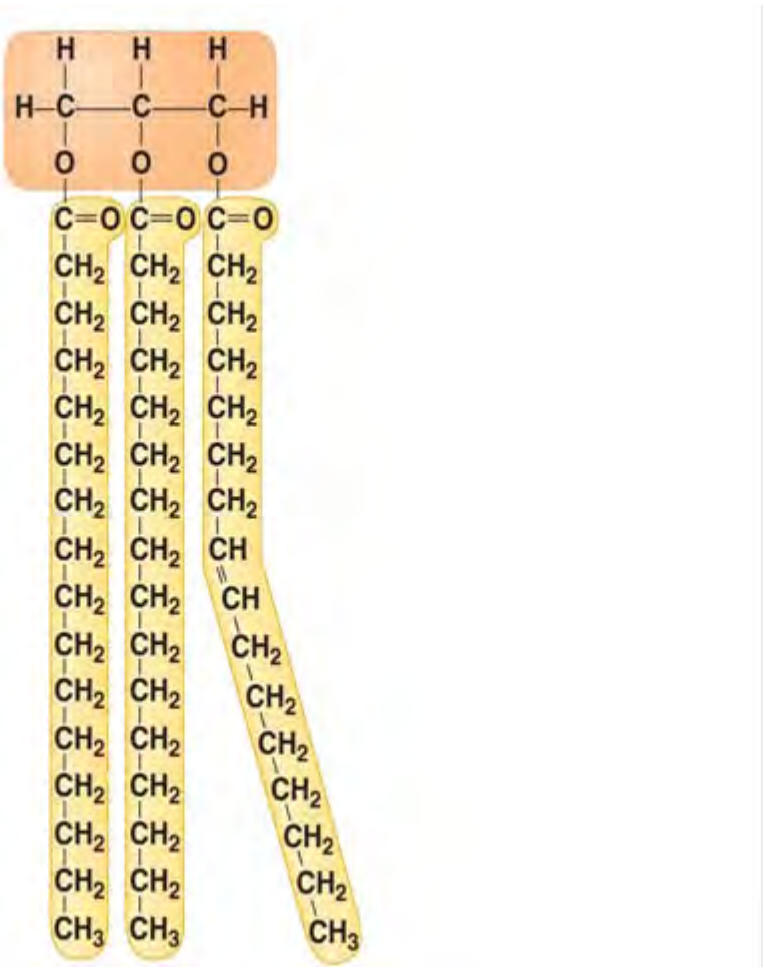
There are several types of lipids.

A. Triglycerides

95% of lipids in the body are in the form of triglycerides which are composed of a single glycerol molecule and 3 **fatty acid** molecules. (Again by dehydration reactions).



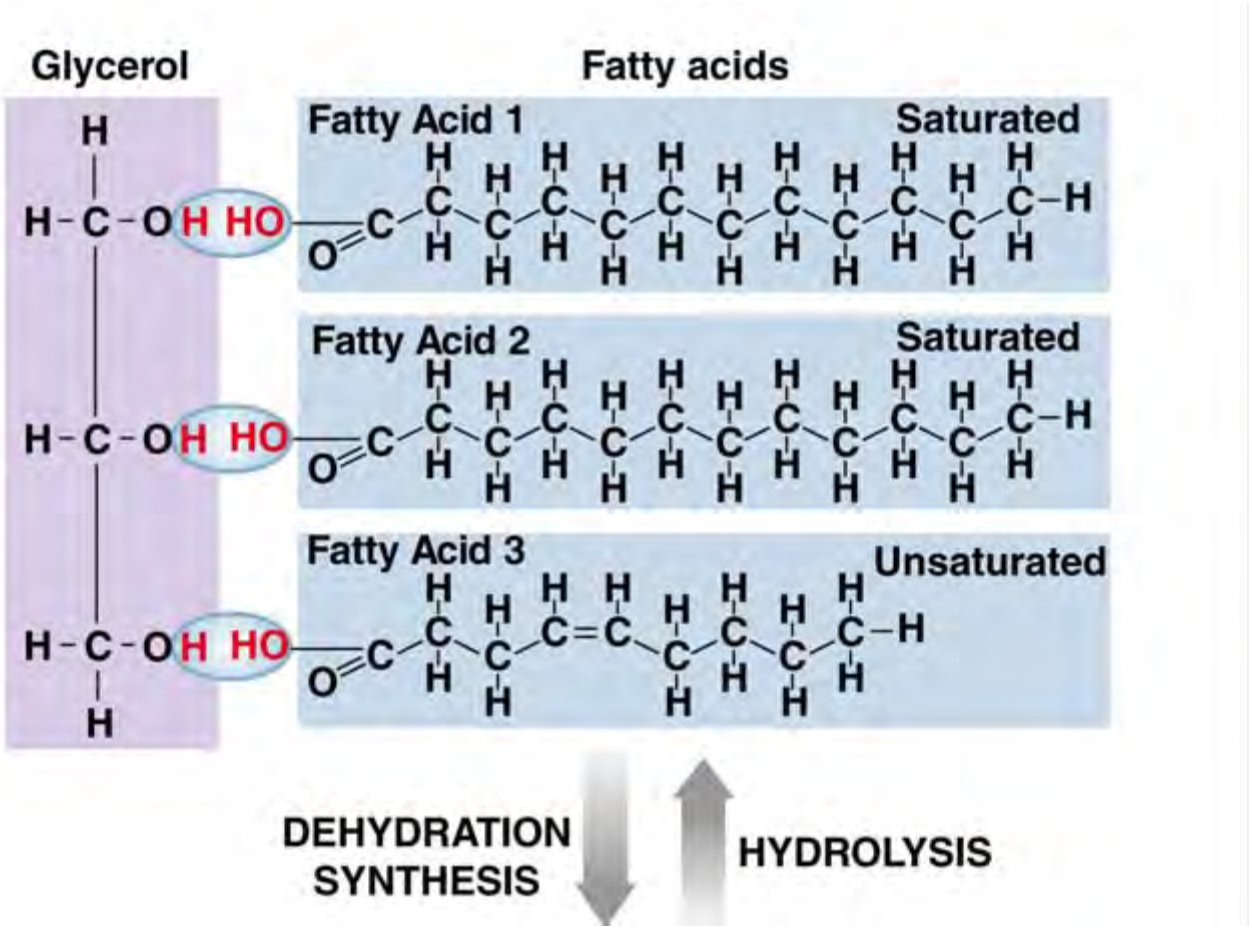
A monoglyceride: one fatty acid is attached to a glycerol (an alcohol) molecule by a dehydration synthesis reaction.



A triglyceride: three fatty acids attached to a glycerol molecule.

•Saturated fats

Saturation is determined by the number of single or double bonds in a fatty acid. Two of the fatty acids above are saturated – each carbon forms single covalent bonds with other carbon and hydrogen atoms. In the third fatty acid, not all the carbons are "saturated" with hydrogen, so carbon forms a double bond and the fat is unsaturated- this one is **monounsaturated- one double bond**. More than one double bond means that the fat is **polyunsaturated**. The next image should clarify this.



Trans or partially hydrogenated fats are created by the process of hydrogenation whereby they are artificially changed to unhealthy fatty acids. These types of fatty acids are commonly found in commercially baked goods and in fried foods. Their consumption may have many adverse effects on the human body such as an increase in cholesterol and triglyceride levels which increases the risk of cardiovascular disease.

Function of triglycerides is to store energy. Triglycerides are stored in our adipose tissue and elsewhere throughout the body. This is the most efficient storage form as one gram of lipid contains more than twice the energy (calories) as one gram of carbohydrate or protein.
Fat or adipose tissue is also very important in providing insulation and therefore helps maintain a stable body temperature.

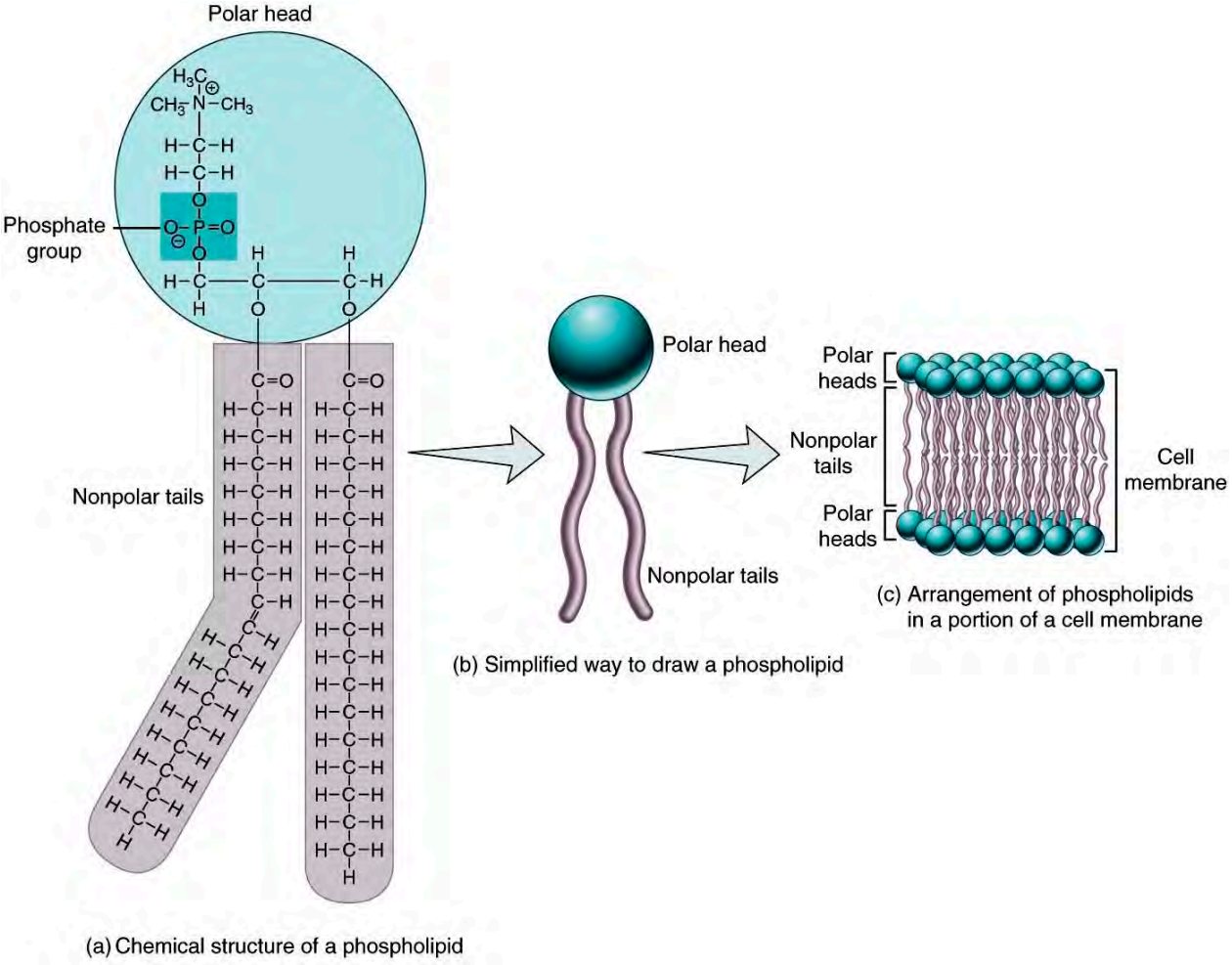
B. Phospholipids

These molecules have a similar composition to triglycerides; they have a glycerol backbone and 2 fatty acids but attached to the third carbon in glycerol is a phosphate group ($PO4^{-3}$).

Composition: the portion of the molecule that has the phosphate is known as the polar head which forms hydrogen bonds with water and is **hydrophilic**.
The 2 nonpolar fatty acid tails interact only with lipids and are **hydrophobic**.

Phospholipid molecules are **amphipathic** (molecules with polar & nonpolar parts)

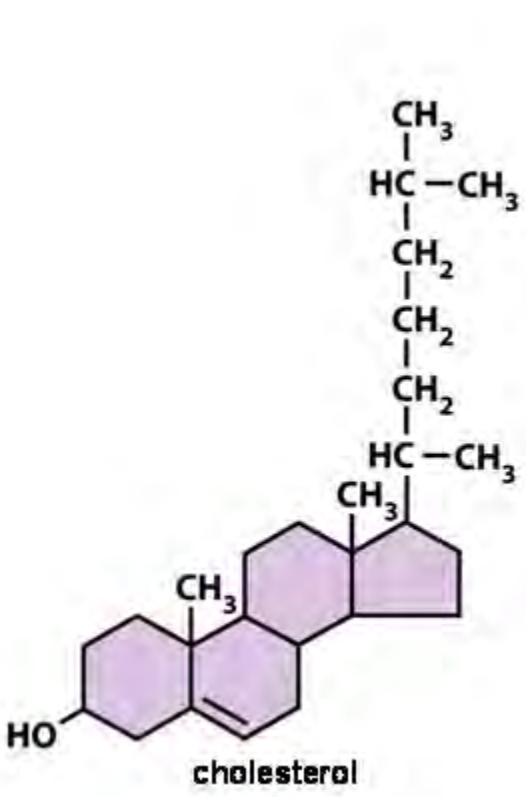
Function: The major function of phospholipids is their role in the cell membrane which in all cases is a double row of phospholipids.



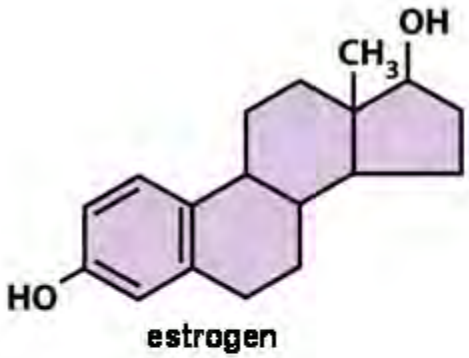
C.Steroids

Steroids are formed from 4 rings of carbon atoms joined together. Different steroids have different functional groups attached.

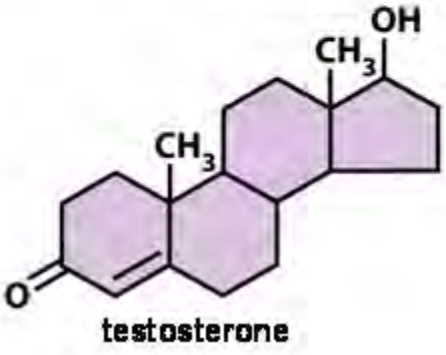
Cholesterol is the most abundant steroid in the human body. It is necessary for cell membrane structure and is used by the body to produce other important steroids such as bile salts, cortisol, vitamin D, and the sex hormones testosterone and estrogen.



cholesterol



estrogen



testosterone

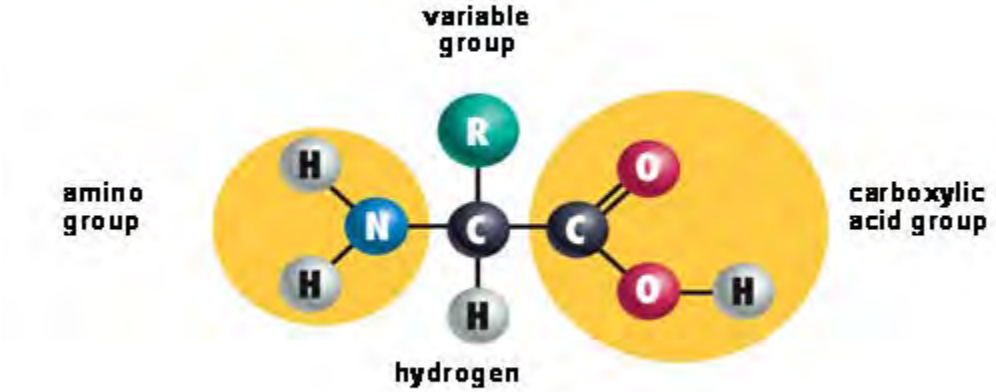
Other important lipids in the human body include **Lipoproteins** which are a means of transporting lipids in the watery environment of the blood. Examples include HDLs and LDLs which transport cholesterol and triglycerides in the bloodstream.

Vitamins A, D, E & K are all fat soluble.

3. PROTEINS

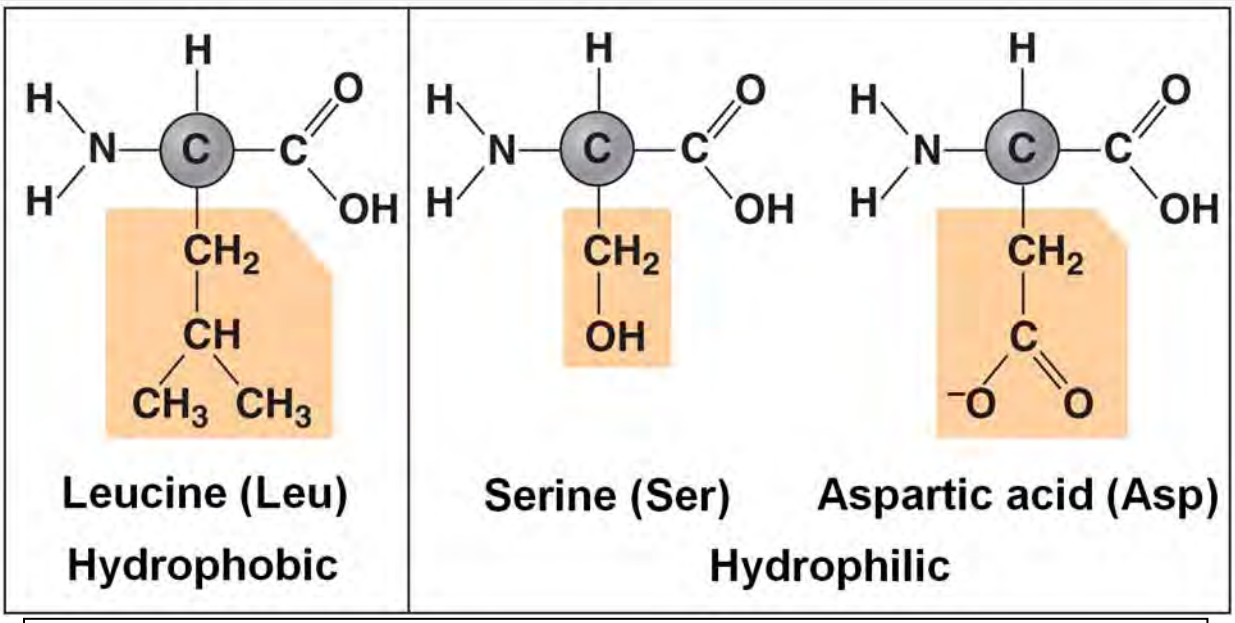
Proteins contain carbon, hydrogen, oxygen, and nitrogen (and sulfur in some cases) and are constructed from combinations of 20 amino acids.
Note that here an amino acid is the monomer; a polypeptide or protein is a polymer.

Amino Acid Structure



Central Carbon atom which forms 4 covalent bonds with:-

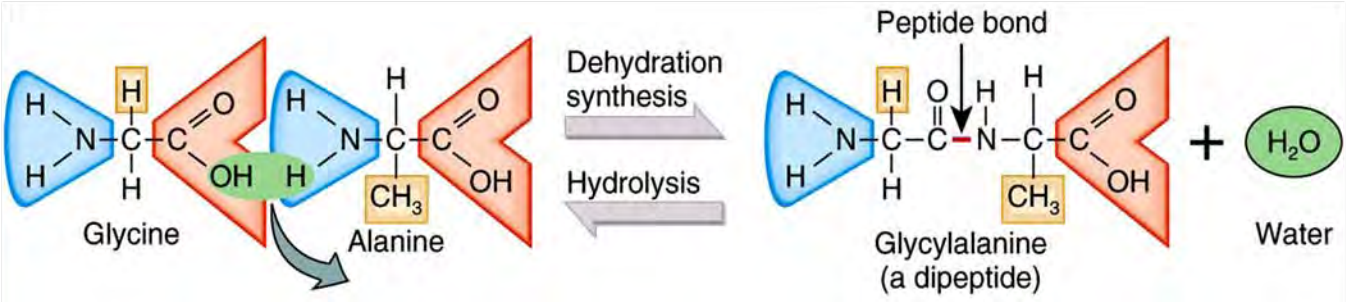
- **H, a hydrogen atom**
- **Amino group (NH_2)**
- **Carboxyl group (COOH)**
- **Side chains (R groups) which vary between amino acids**



EXAMPLES OF SOME AMINO ACIDS SHOWING DIFFERENT SIDE CHAINS

Dipeptides are formed from 2 amino acids joined by a covalent bond called a peptide bond. **Polypeptides and proteins** are formed from 10 to 2000 amino acids. The chemical reaction linking amino acids is, once again, a dehydration synthesis reaction.

Formation of a peptide bond



Levels of structural organization in proteins

The first level of protein structure is the **primary structure** and is simply the order in which amino acids are joined together to form a protein chain.

Secondary structures result when hydrogen bonding occurs between the amino hydrogen of one amino acid and an oxygen in another amino acid in the primary chain. The chain may form a helix or a pleated sheet.

Tertiary structures form when functional groups of the side chains react with one another.

Some proteins even have a **quaternary structure** which means that there are 2 or more coiled, folded chains interacting.

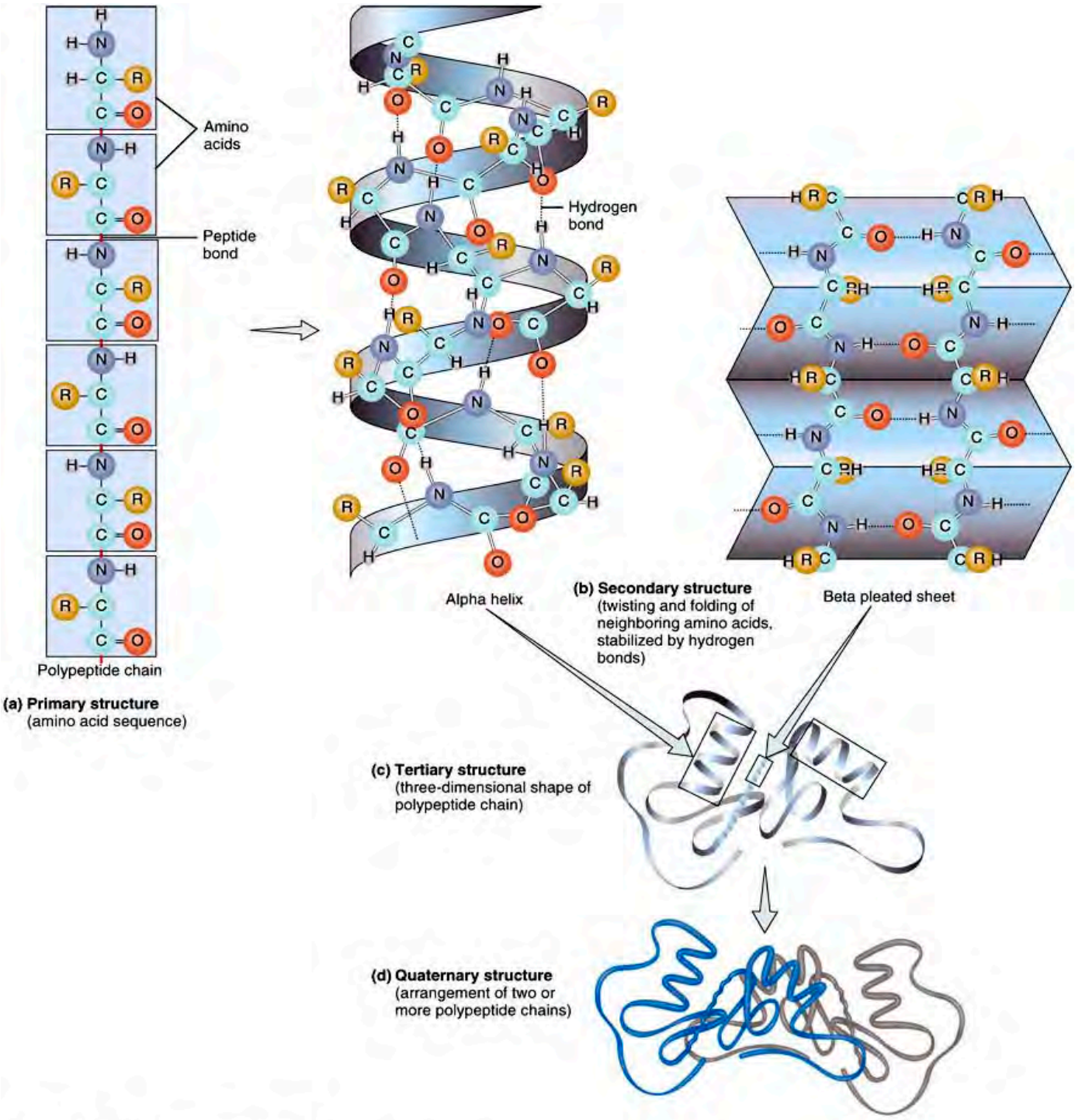


Figure 02.22 Tortora - PAP 12/e

Hemoglobin is a good example of a protein that has a quaternary structure

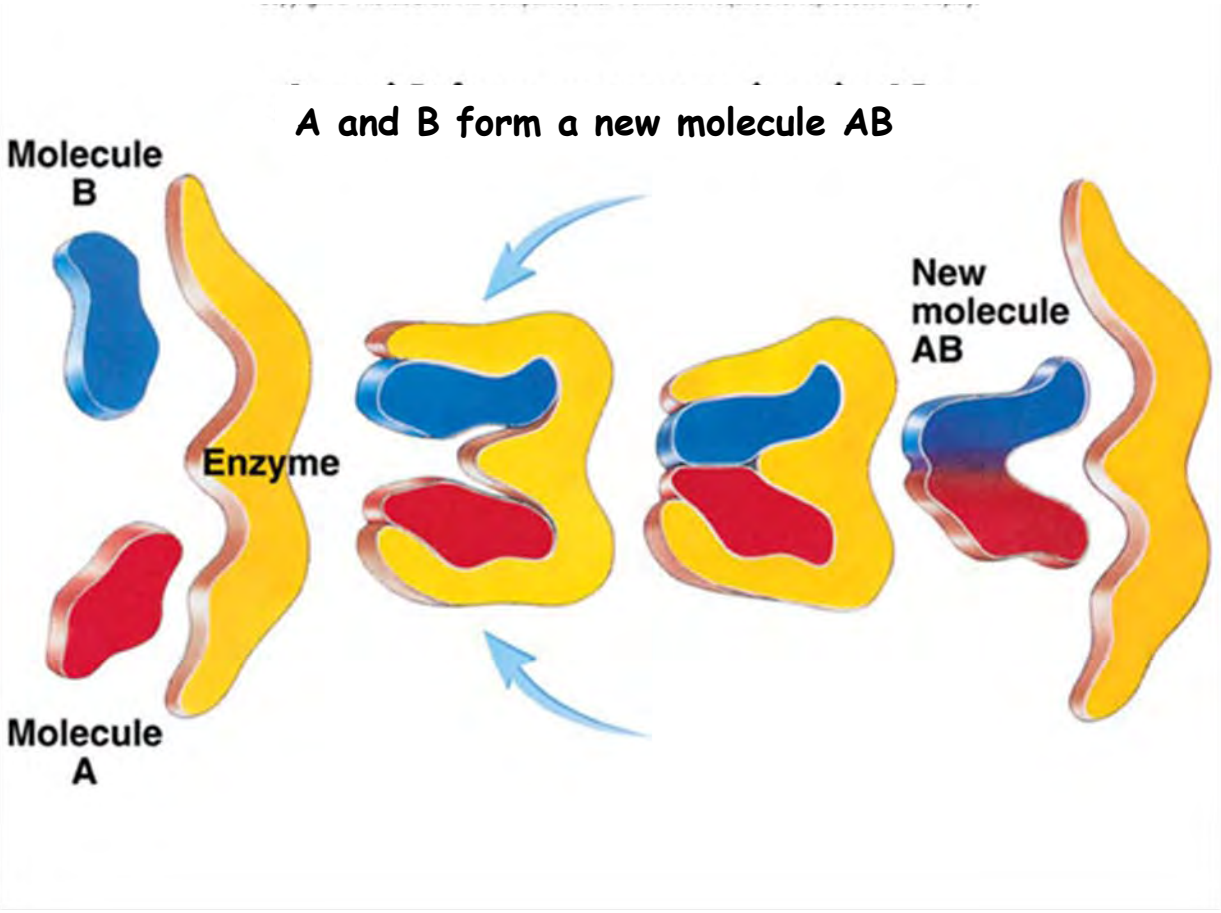
Proteins can perform many different functions because there are large numbers of different proteins. The number of different proteins the body can produce with different combinations of the **20 amino acids** can be compared to the number of words in the English language all made from some combination of only 26 letters.

Functions of Proteins are many and varied. Some examples include:

Enzymes

The importance of the structure of proteins as described earlier can be emphasized by looking at how enzymes work. Enzymes are biological catalysts. They are necessary for all the essential chemical reactions that go on in the cell. Almost all enzymes are proteins and to do their "work" they must maintain the proper structure so that the appropriate substrates will fit. More on enzymes in **Lecture 9**.

Note that Enzymes usually end in suffix -ase and are often named for the types of chemical reactions they catalyze. Enzymes are highly specific very efficient, and under nuclear control.



Other functions of proteins include:

•**Structural**:- Collagen in skin, Keratin in hair, nails, horns, hooves

b.

•**Energy** – Proteins are also metabolized for energy. **See Lecture 9**

•**Regulatory** – Most hormones are proteins and, of course, enzymes are regulatory

•**Contractile** – Muscle cells are filled with proteins. Other cell movements are also dependent on proteins.

•**Immunological** – Antibodies which have tremendous diversity, are proteins

•**Transport** – LDLs and HDLs mentioned earlier

•**Osmotic Pressure** – Important component in maintaining osmotic pressure in the Blood, for example. (Osmotic Pressure – see lecture)

•**Buffers** – the importance of buffers was described in **Lecture 4**. Proteins can act as buffers by releasing a hydrogen ion (H^+) when a solution is too basic or absorbing H^+ when a solution is too acidic.

Denaturation of Proteins

Denaturation, which is literally a change in the nature of a protein, occurs when the bonds in the peptide chain, particularly in the secondary, tertiary, or quaternary structure, are broken. This can occur when the proteins are subjected to a different pH, a severe change in temperature, or treated with specific chemicals among other things.

When a protein has been denatured it is unable to perform its specific function. If enough proteins are denatured, this can mean the death of the cell or even the death of the organism.

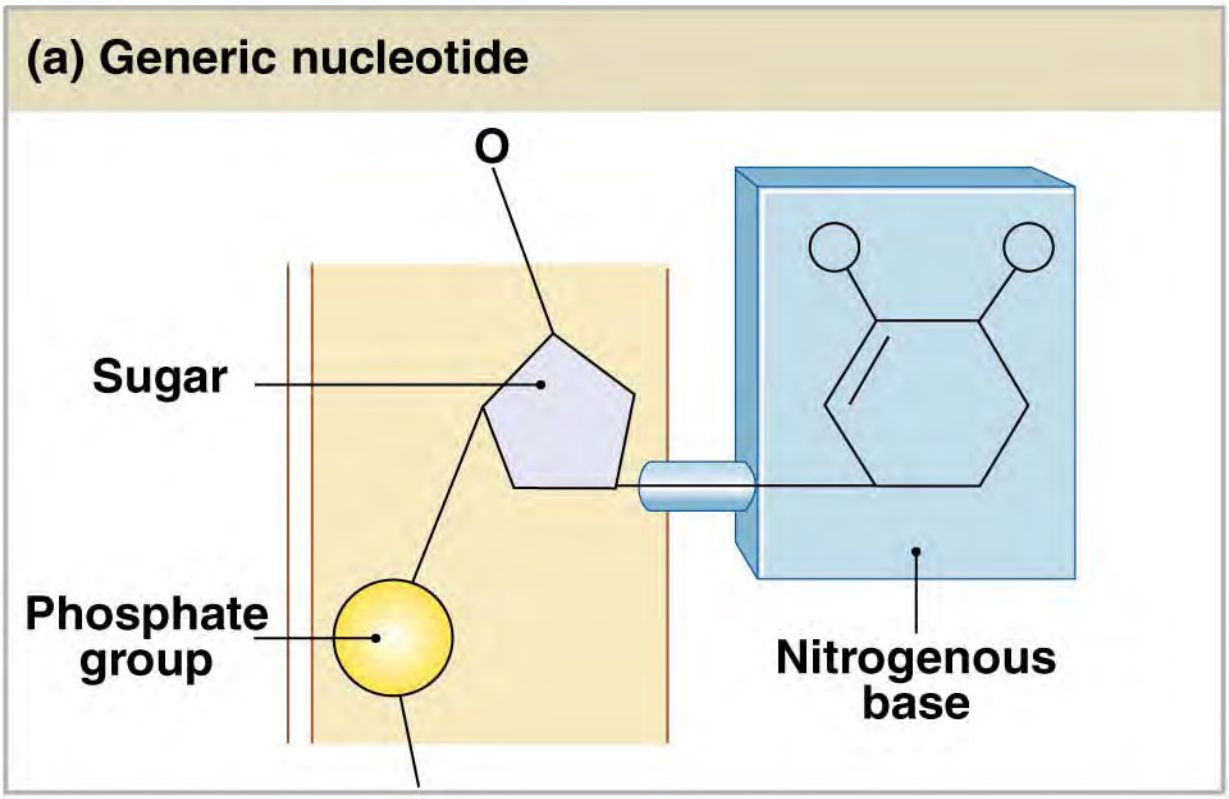
---

4. NUCLEOTIDE-BASED MOLECULES

Nucleotide-based molecules contain carbon, hydrogen, oxygen, nitrogen, and phosphorous and, as their name suggests, are made of nucleotides.

Nucleotides have 3 components as shown below:

A 5-carbon sugar, a phosphate group, and a nitrogenous base

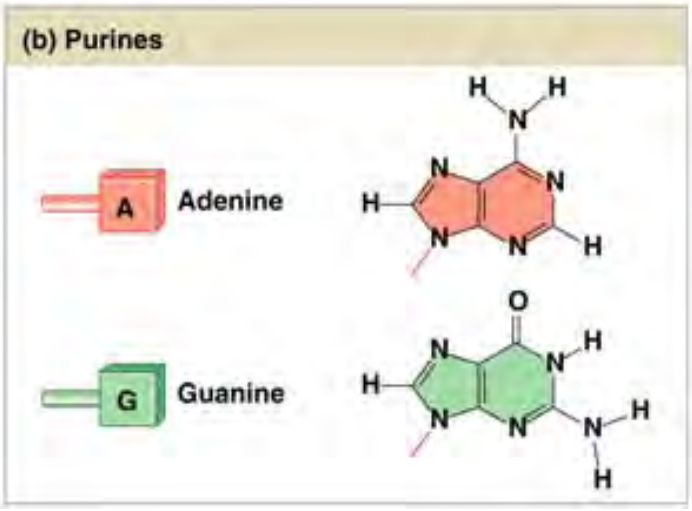


The sugars are pentoses, either ribose or deoxyribose (described under carbohydrates).

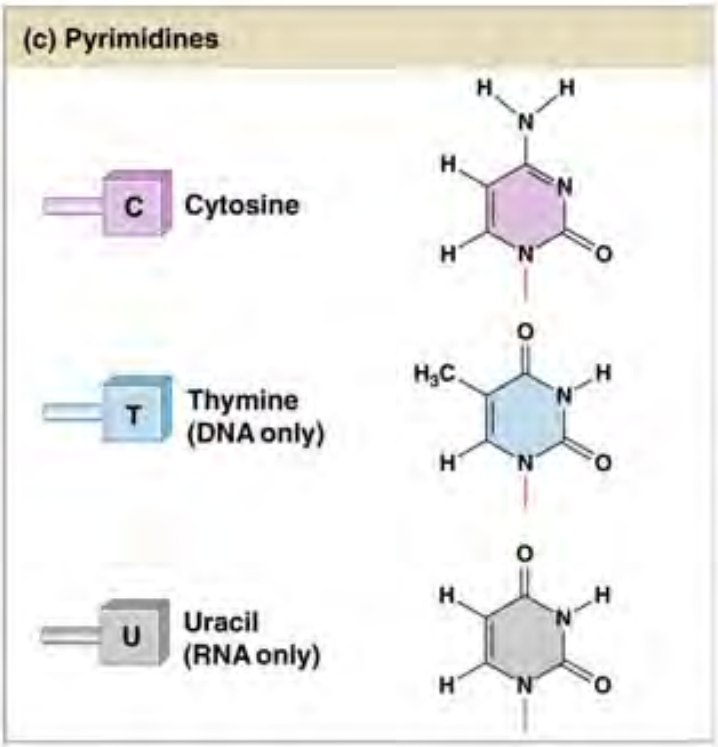
Phosphate is usually a phosphate group (PO_4).

There are 5 nitrogenous bases described on the next page.

Adenine and Guanine are larger, double-ring bases called purines.



Cytosine, Thymine and Uracil are smaller, single-ring bases called pyrimidines

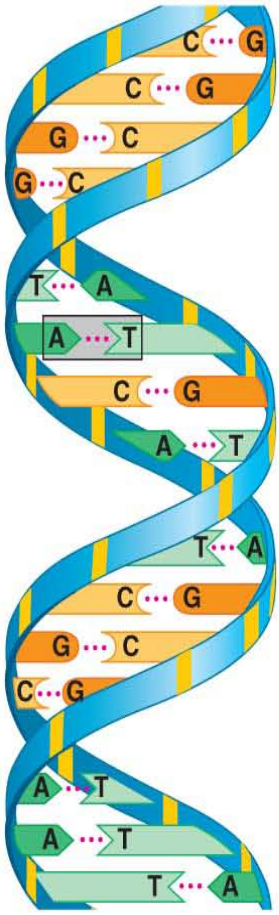


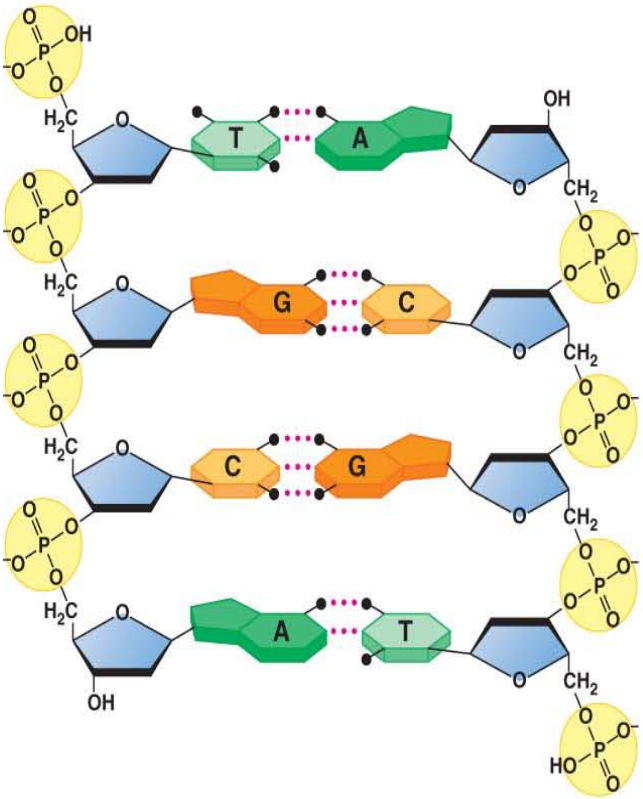
There are 5 important nucleotide-based molecules considered here:

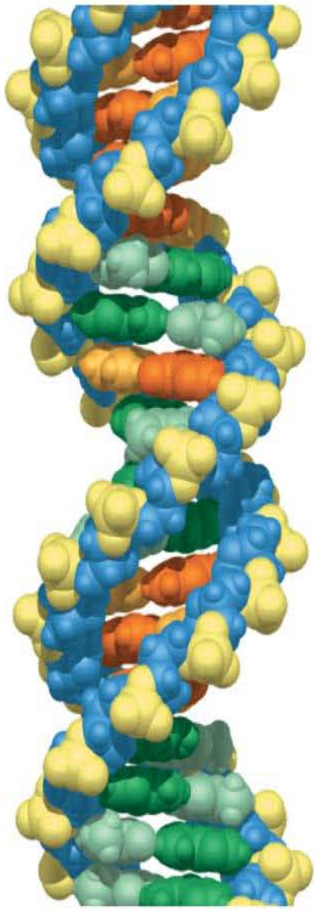
DNA, RNA, ATP, NAD, FAD All contain C, H, O, N, & P.

DNA & RNA are Nucleic Acids, i.e. they are polymers of nucleotides.

1. DNA is a huge molecule. It consists of 2 strands (chains of nucleotides) which are held together by hydrogen bonds. The 2 strands are entwined in the form of a double helix. DNA contains the genetic material. All cells have DNA (some lose it as the cells specialize but all cells have DNA when formed). In eukaryotic cells the DNA is stored in the nucleus. In prokaryotic cells the DNA is in the cytoplasm. A gene is a segment of DNA that codes for a protein. The code is a sequence of nucleotides such as "TACCGGTAGCCATACAAGGTA" could be a very small gene.





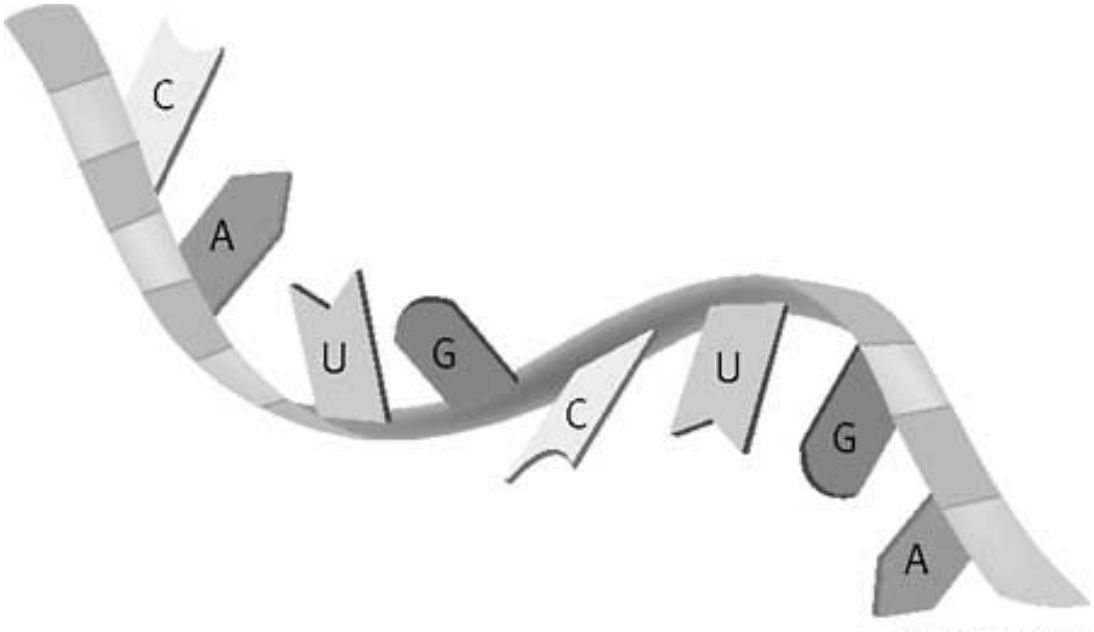


2. RNA is also a nucleic acid but has some important structural differences from DNA.

1. DNA is double stranded; RNA is single stranded;
2. DNA contains deoxyribose; RNA contains ribose; (hence the names)
3. DNA contains the nitrogenous bases **adenine, *thymine,* guanine, cytosine**.
   RNA contains the nitrogenous bases **adenine, *uracil*, guanine, cytosine.**
4. DNA is double stranded; RNA is single stranded.
5. DNA is large and in a eukaryotic cell it remains in the nucleus.
   RNA is much smaller and can leave the nucleus of the cell.

There are 3 types of RNA:
–messenger RNA, ribosomal RNA, transfer RNA

Each type has a specific function and will be discussed in more detail in **Lecture 12**

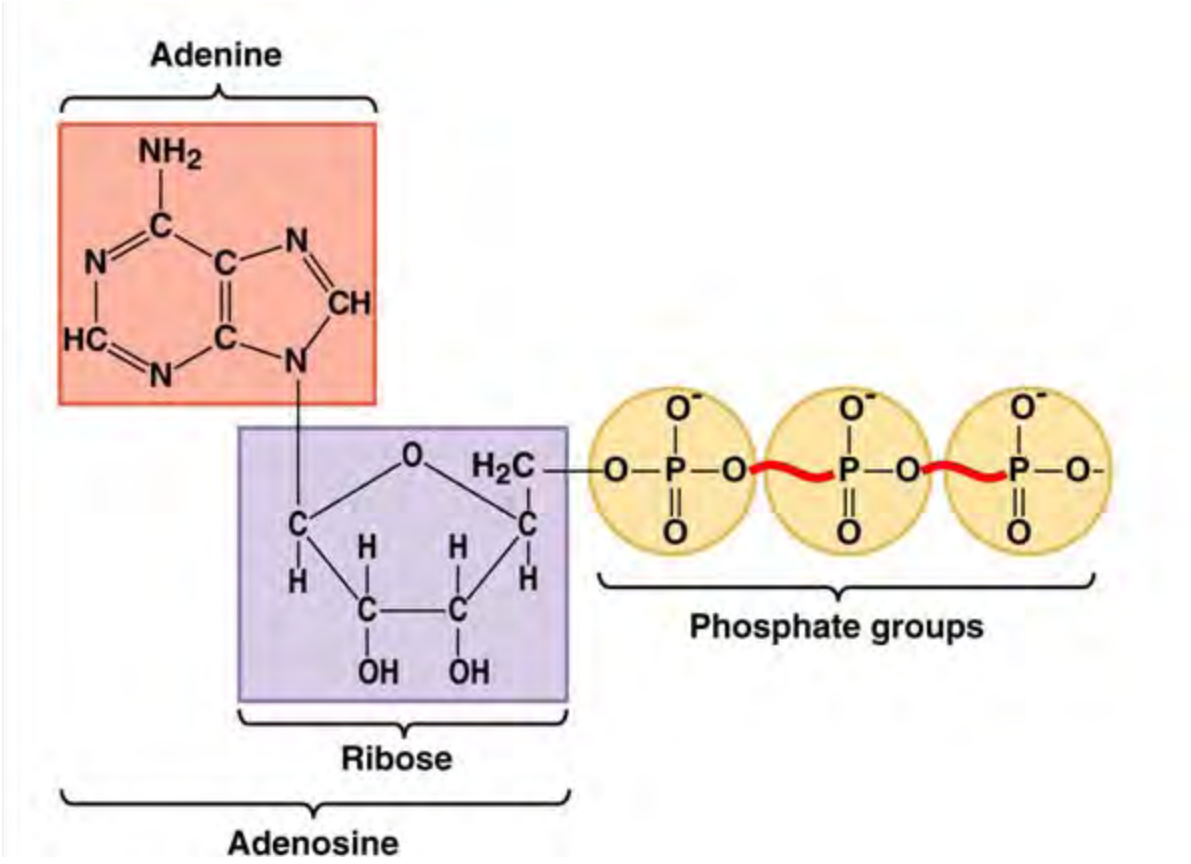


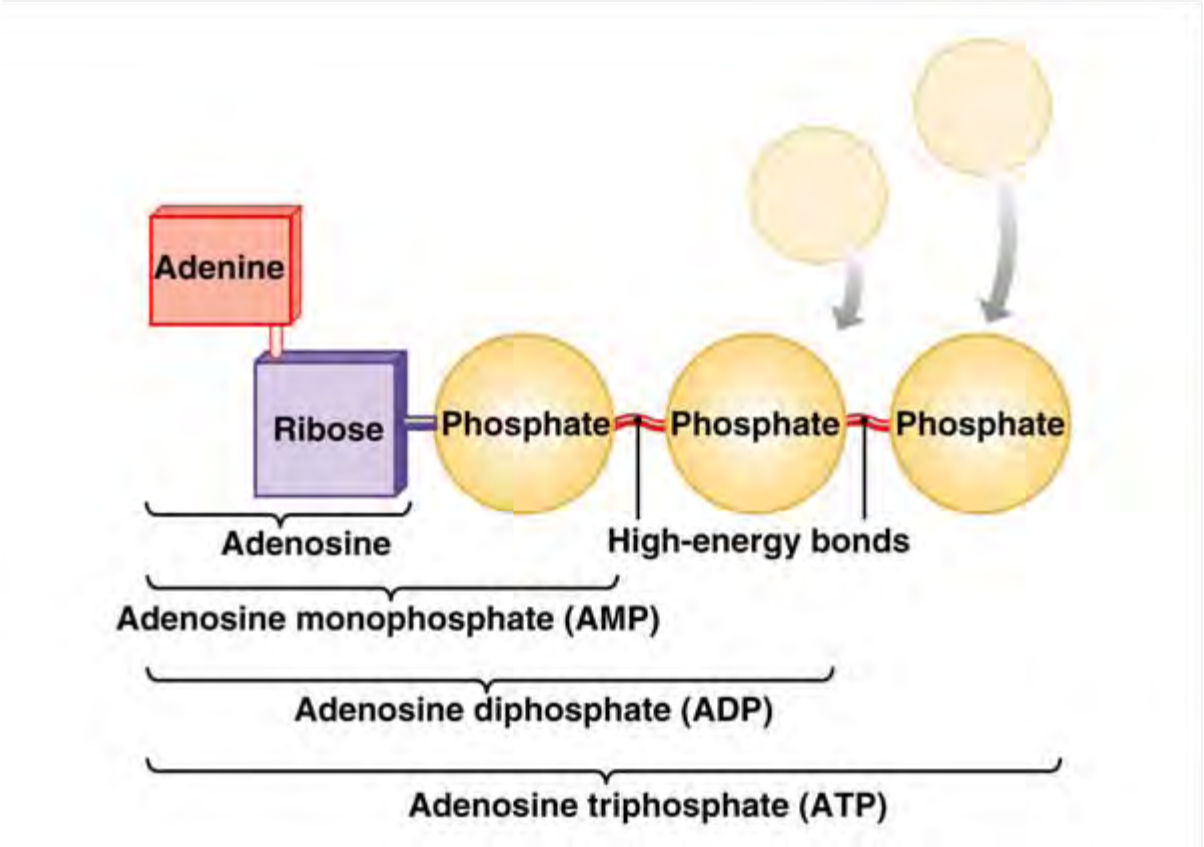
3. Adenosine Triphosphate (ATP)

ATP consists of **3** phosphate groups attached to adenine (the nitrogenous base) & 5-carbon sugar (ribose)

As discussed earlier, carbohydrates, lipids, and proteins store energy in their bonds – energy that is necessary for the cell to use to do work. ATP transfers this energy released in exergonic reactions to ATP. The cell uses the energy in ATP to perform muscle contractions and other types of movement, to drive cell division, and many other tasks.

Hydrolysis of ATP (removal of terminal phosphate group by the enzyme ATPase releases this energy.





ATP is an unstable molecule and is constantly being broken down to ADP to release the energy stored in the high-energy bonds. Then the reaction is reversed using energy from other molecules and reforming the high-energy bond.

ADP + phosphate + energy ←----→ ATP + H_2O

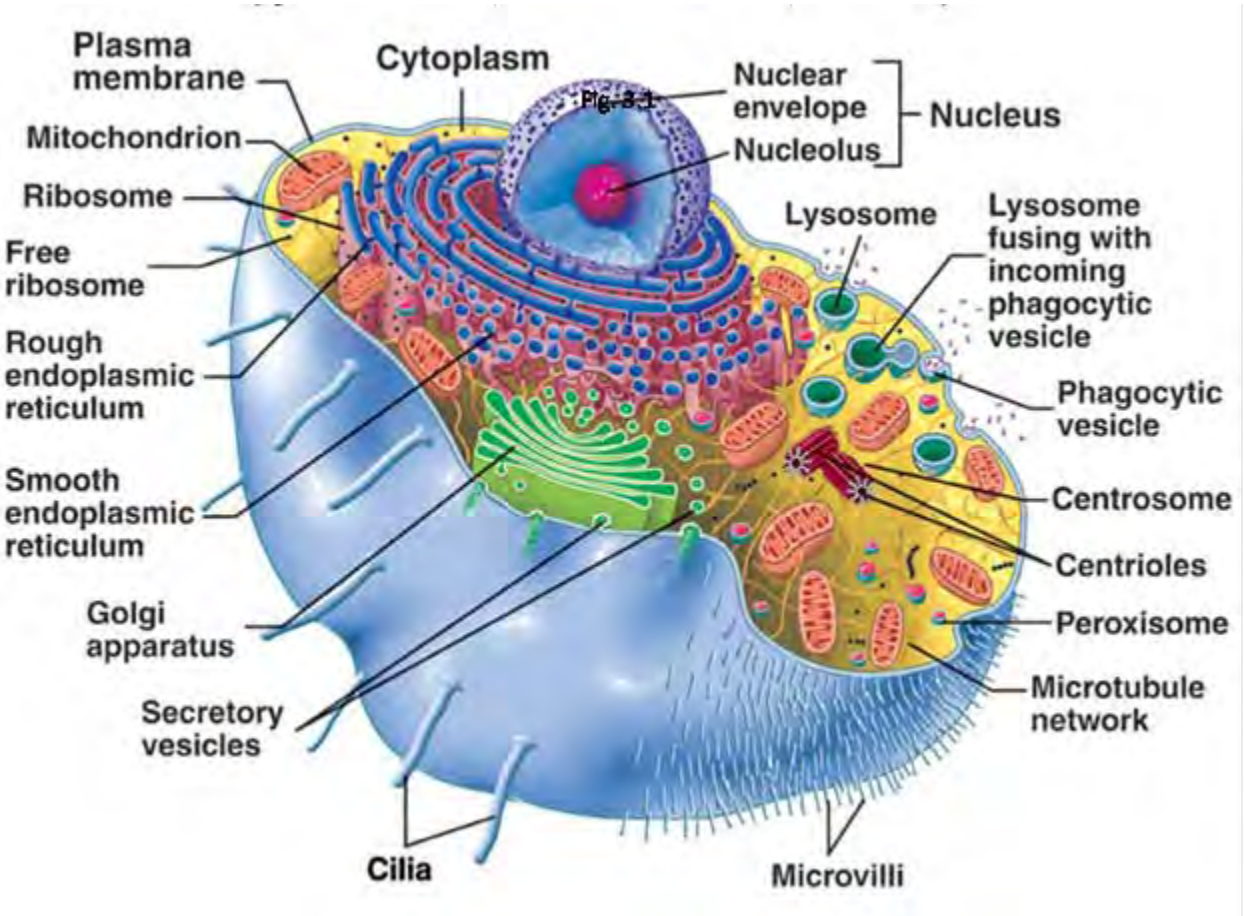
4 & 5 NAD and FAD

Nicotinamide Adenine Dinucleotide and Flavin Adenine Dinucleotide are coenzymes used to transport hydrogen atoms (hydrogen ions/protons & electrons in metabolic pathways. See **Lecture 9**.

LECTURE 6: THE EUKARYOTIC CELL

All organisms are made of cells. Cells can differ greatly even within a single organism yet all cells consist of a cell membrane, genetic instructions in the form of DNA and cytoplasm.
Eukaryotic cells, (cells with a nucleus) occur in plants, animals, fungi, and protists but here a "generic" animal cell will be considered, followed by specializations that occur in a plant cell. Although plant and animal cells have a lot of diversity, they also have a basic similarity of architecture that will be reviewed here.

The cell membrane (also known as a plasma membrane) is a very thin, structure that separates the cell from the external environment. Its structure and function will be discussed in detail in **Lecture 7**.



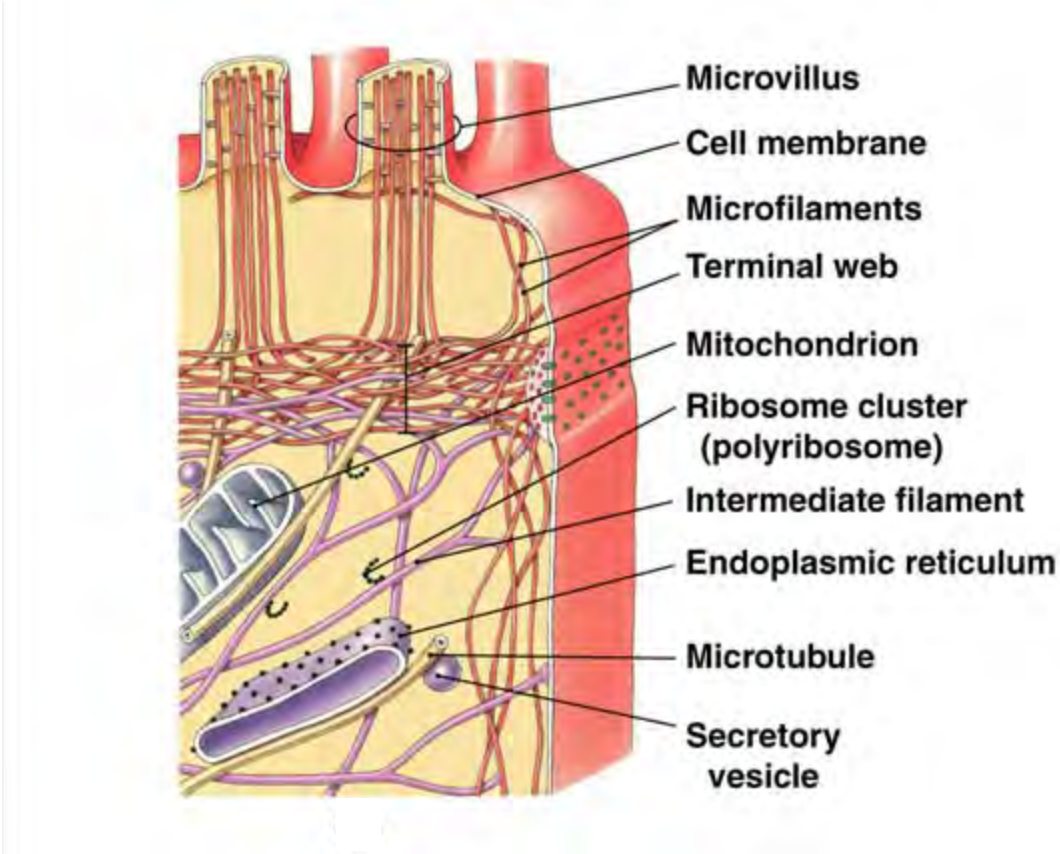
All cells contain **cytoplasm** which consists of all the material and structures that lie inside the plasma membrane but outside the nucleus.
The fluid portion of the cytoplasm is called the **cytosol** and is comprised of water, salts, ions, organic molecules, and more.
The second component of the cytoplasm are the organelles. These organelles are of 2 general kinds: **Nonmembranaous organelles and Membranous organelles**

NONMEMBRANOUS ORGANELLES.

Nonmembranous organelles lack membranes & are in direct contact with cytoplasm

1. **Cytoskeleton** is a network of protein filaments throughout the cytosol whose functions include: - cell support and shape, cell & organelle movement, and cell division.

The Cytoskeletal Filaments

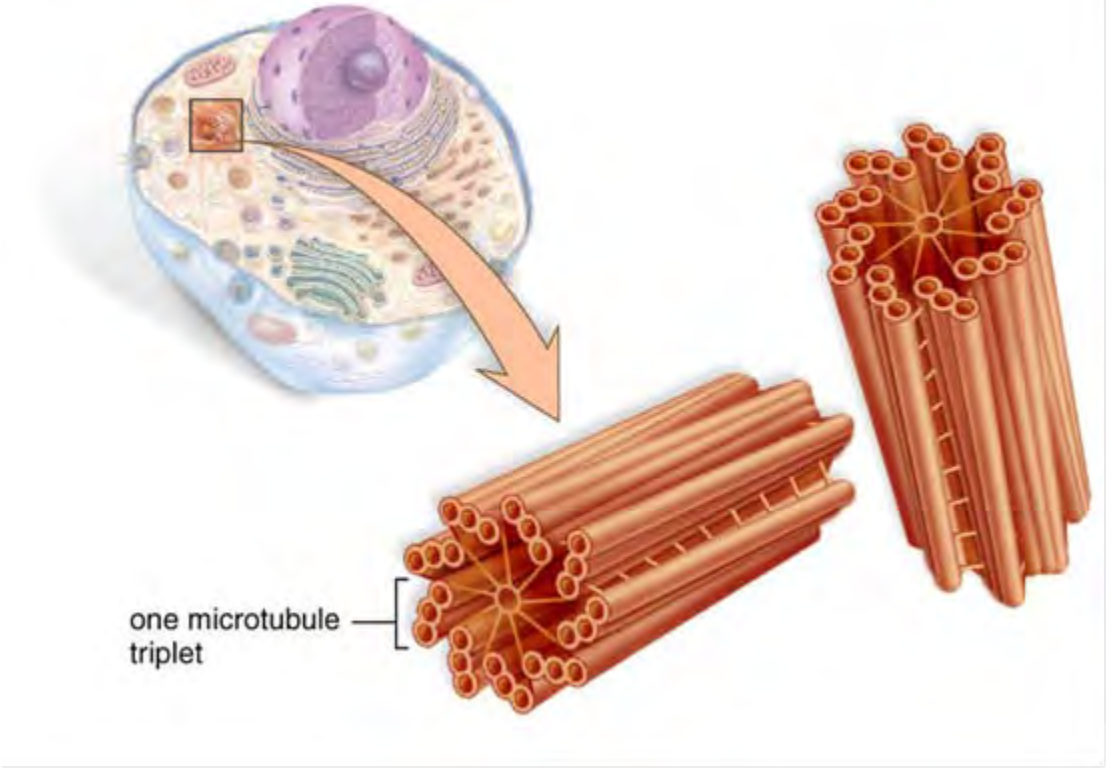


The cytoskeleton is composed of 3 types of proteins which are continually being reorganized.

1). Microfilaments are the thinnest filaments. They are involved in locomotion & cell division and support microvilli.

2). Intermediate filaments can be composed of several different proteins. They anchor organelles, support the cell especially in areas subjected to mechanical stress, and help attach cells to one another.

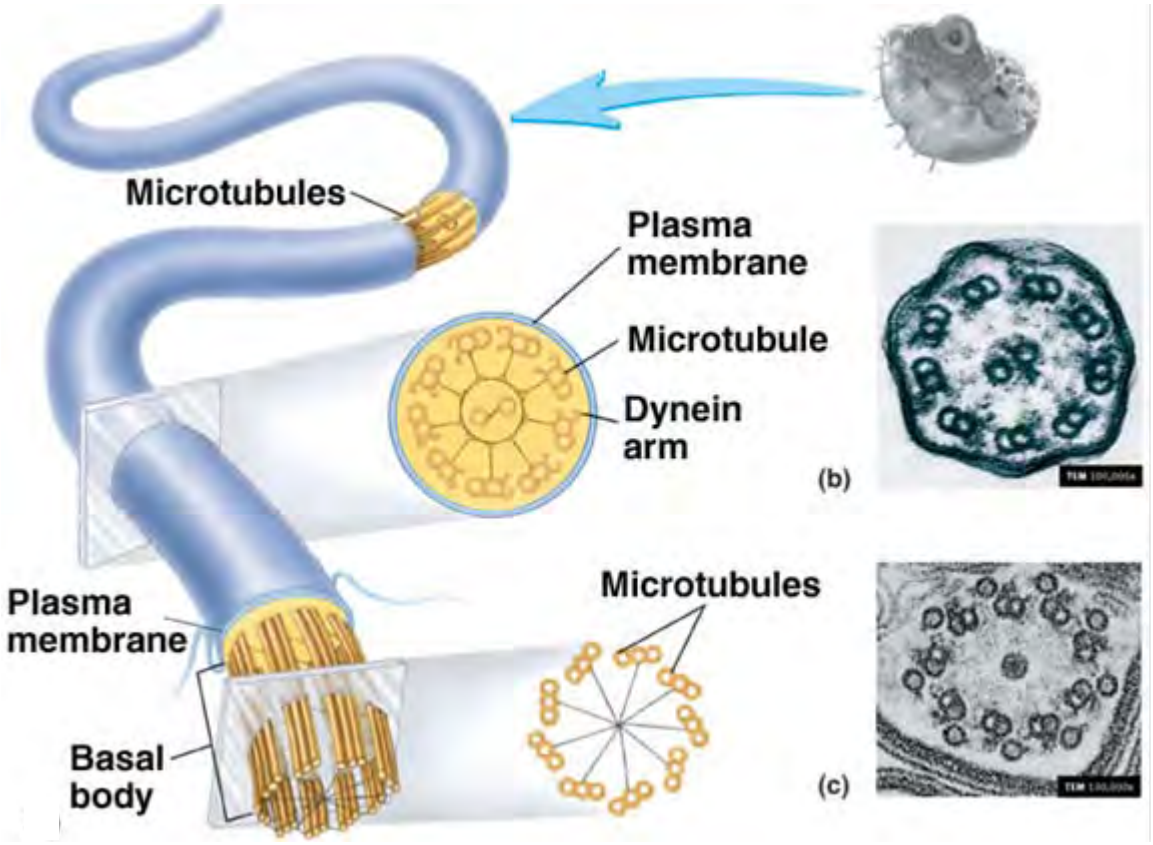
3). Microtubules are large cylindrical structures (composed of the protein tubulin). The assembly of microtubules begins in an organelle called the **centrosome** which is found near the nucleus
The centrosome has 2 **centrioles** which lie at 90 degrees to each other, and are composed of 9 clusters of 3 microtubules (9+0 array). The centrosome has a pericentriolar area for the formation of mitotic spindles and microtubules which are the dominant components of cilia & flagella.



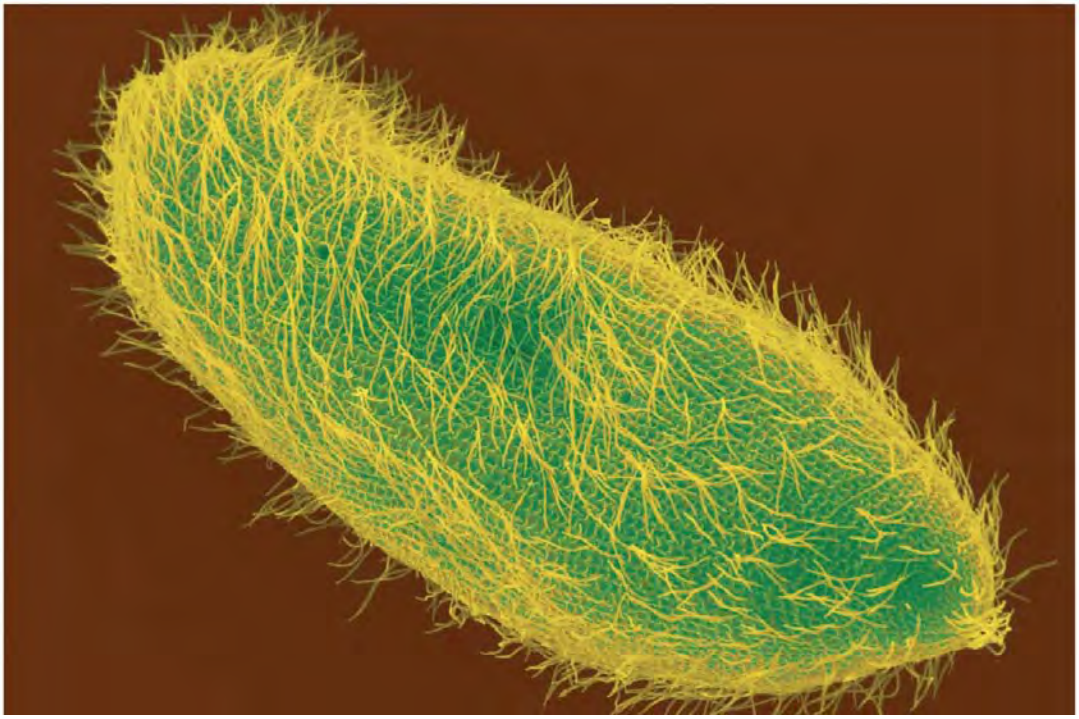
Cilia and Flagella

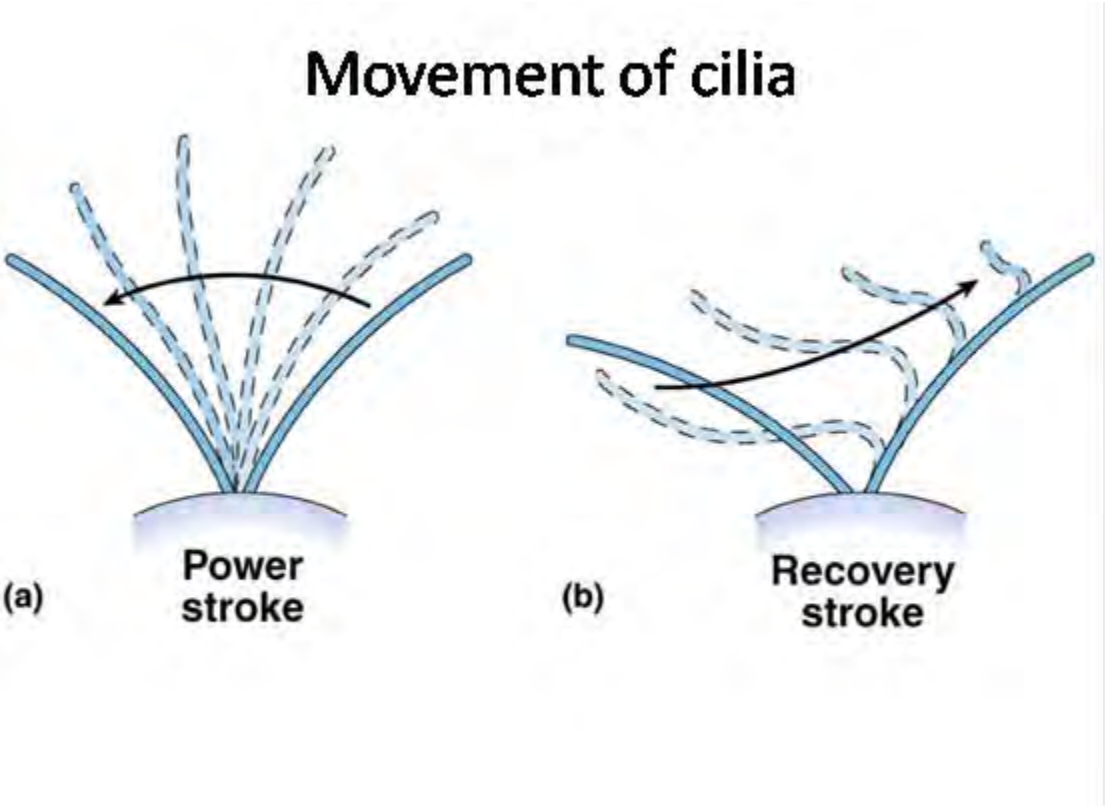
Structure
Each **cilium** (singular) is made up of 20 microtubules arranged in 9 pairs surrounding a pair in the center. Each cilium is attached to a basal body which is similar to a centriole and responsible for initiating the assembly of both cilia and flagella.
Cilia line airways and the uterine tubes and beat in an oar like fashion with a power stroke and a recovery stroke. Their coordinated movements sweep particles of mucus along the respiratory tract and the oocyte along the fallopian tube.
Some unicellular organisms such as a paramecium use cilia to swim through water.

Flagella are longer than cilia but are similar in structure. Flagella wiggle in a wavelike pattern usually propelling sperm (animal) forward.



A PARAMECIUM WITH CILIA

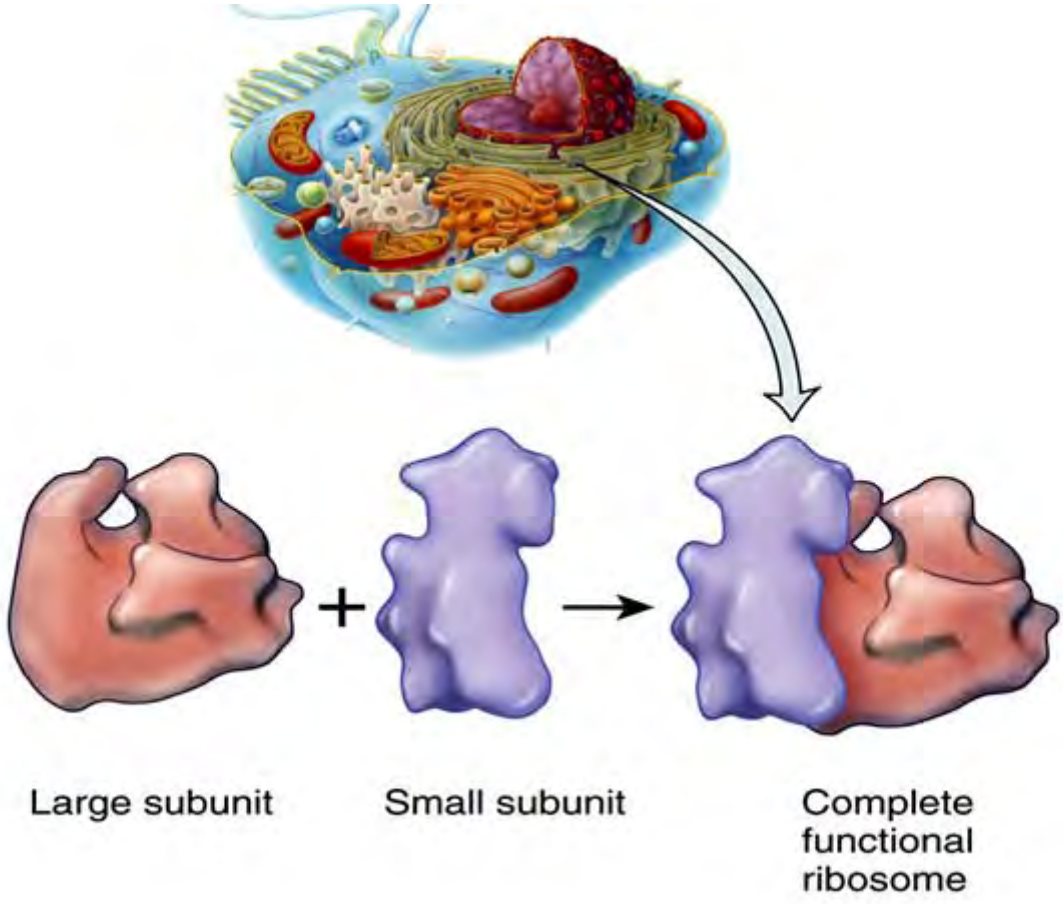




Ribosomes

Ribosomes are found in all cells and even in mitochondria. They are very small two-part organelles made of ribosomal RNA & proteins. They are made in the nucleolus (located in the nucleus) and assembled in the cytoplasm. Each ribosome has a large and small subunit.

There are two types of ribosomes
1) Free ribosomes which are loose in the cytosol and synthesize proteins for use within the cell.
2) Membrane-bound ribosomes which are attached to endoplasmic reticulum or the nuclear membrane and synthesize proteins needed for the plasma membrane or for export from the cell.
Inside mitochondria, ribosomes synthesize mitochondrial proteins



MEMBRANOUS ORGANELLES

Membranous organelles form functional, organized, compartments within the cytoplasm. This means that the cell runs more efficiently. Metabolic pathways have their components grouped together; waste products can be separated from the rest of the cell etc.

Endoplasmic Reticulum

This is an extensive network of membranes forming flattened sacs or tubules called cisterns. The membranes may be continuous with the nuclear membrane.

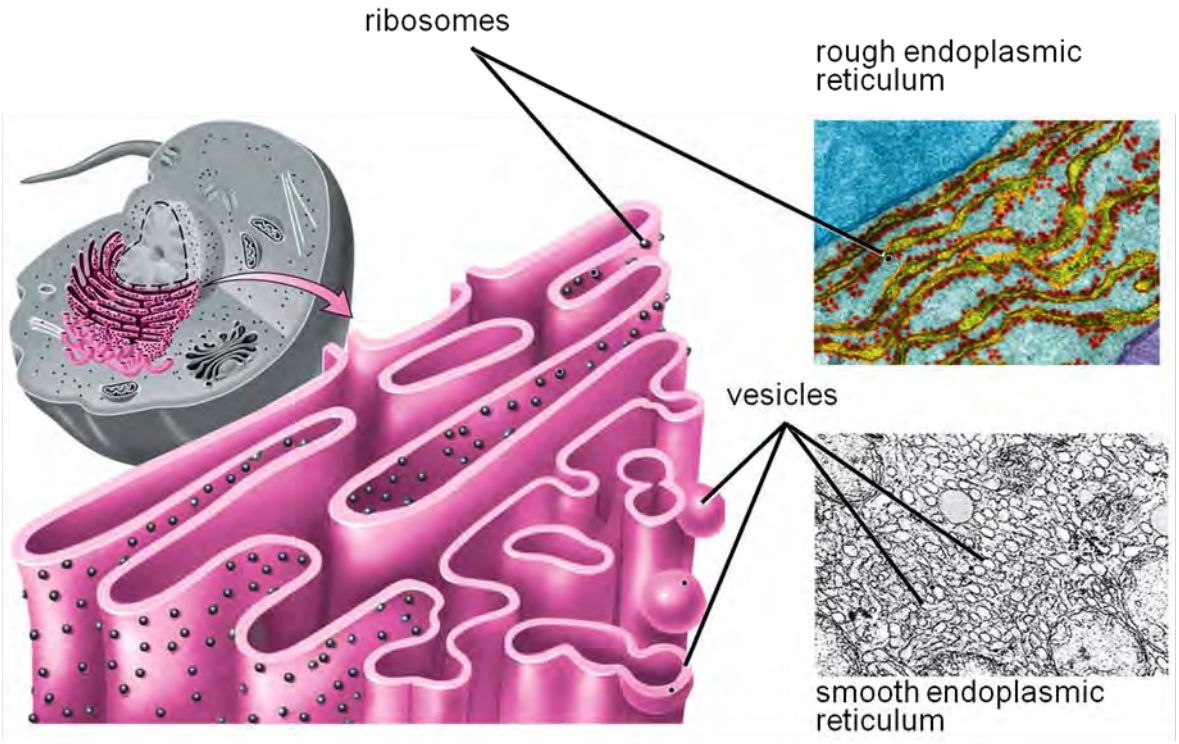
Rough ER (RER) is continuous with nuclear envelope & covered with attached ribosomes. It synthesizes, processes, and packages proteins which may be exported from the cell or to other organelles or the cell membrane.

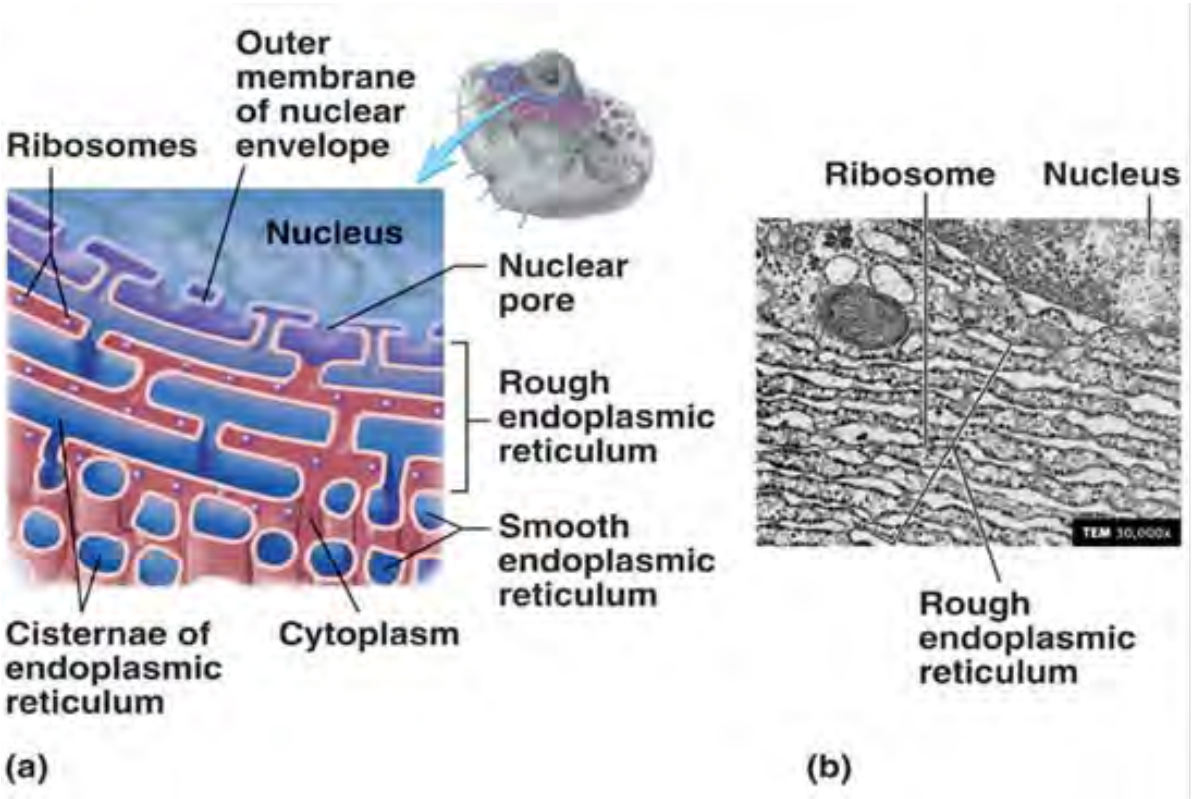
Smooth ER (SER) have no attached ribosomes and have a few different functions. Some smooth ER synthesize phospholipids, steroids, and fats. Other smooth ER detoxify harmful substances such as alcohol.

Both Smooth & Rough Endoplasmic Reticulum exist in most eukaryotic cells but some specialized cells may have greater amounts of one or other type. For example, cells that produce a large amount of protein such as pancreatic cells, will have large amounts of RER while cells that produce large amounts of lipids, such as cells that synthesize steroid hormones, will have large amounts of SER.

Golgi Complex

The golgi complex consists of sets of 3-20 flattened, curved membranous sacs called cisterns. It is often thought of as the packaging and shipping center of the cell because it processes & packages proteins produced by rough ER.
Proteins pass from rough ER to the golgi complex in transport vesicles. Processed proteins pass from entry cistern to medial cistern to exit cistern in transfer vesicles. Finished proteins exit Golgi as secretory, membrane, or storage vesicles such as a lysosome.


ribosomes
rough endoplasmic reticulum
vesicles
smooth endoplasmic reticulum


Outer membrane of nuclear envelope
Ribosomes
Nucleus
Nuclear pore
Rough endoplasmic reticulum
Smooth endoplasmic reticulum
Cisternae of endoplasmic reticulum
Cytoplasm
(a)
Ribosome
Nucleus
Rough endoplasmic reticulum
(b)

Lysosomes

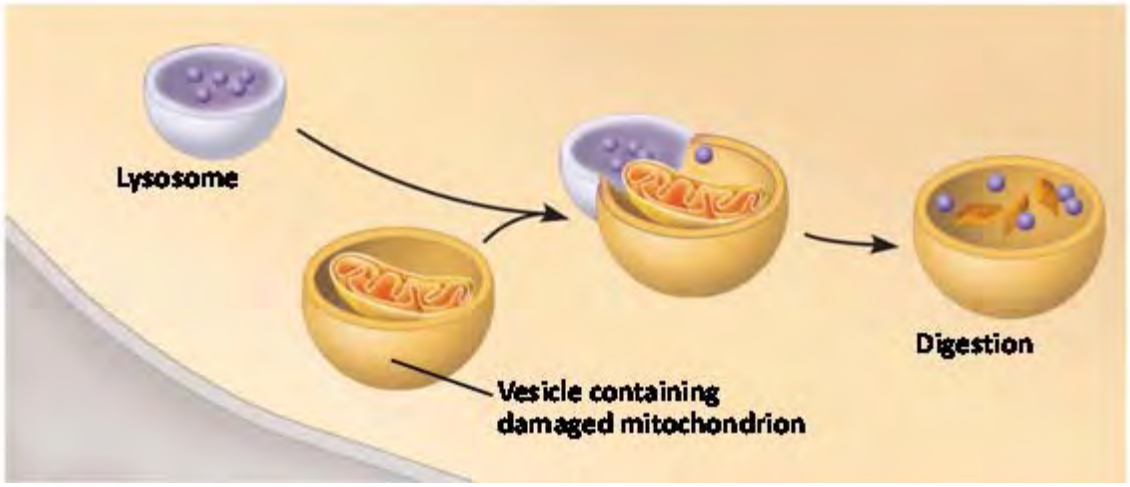
–Are membranous vesicles which are formed in the Golgi complex. They are filled with digestive enzymes and have several functions:

Digesting foreign substances

Recycling organelles

Released by sperm during fertilization

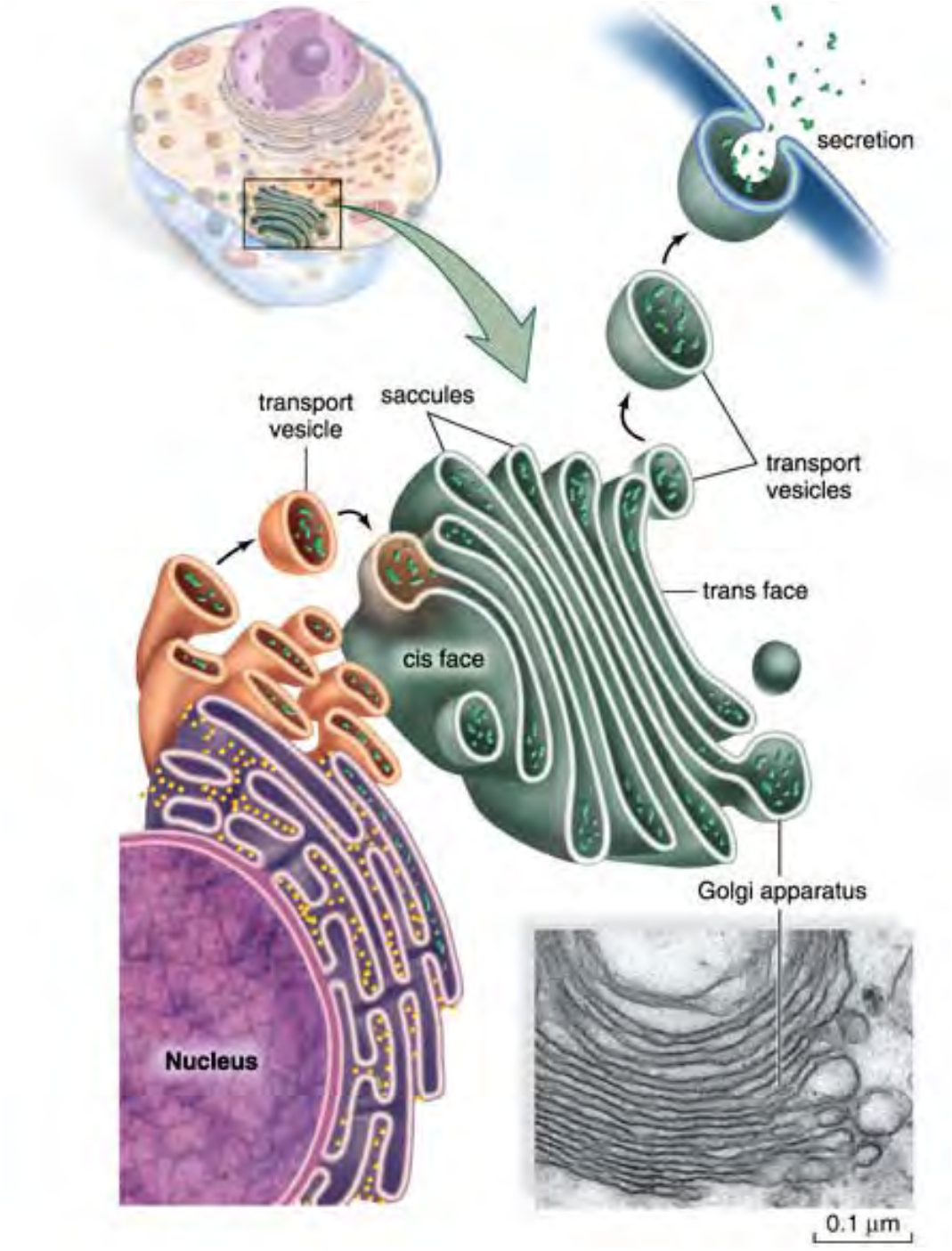
Lysosomal damage after death causing cellular breakdown



Peroxisomes are another type of membranous vesicle formed by division of preexisting peroxisomes. They contain enzymes that oxidize organic material and function in the normal metabolic breakdown of amino acids and fatty acids. They also oxidize toxic substances such as alcohol and formaldehyde and contain catalase which decomposes H_2O_2

Membrane Cycling within the Cell

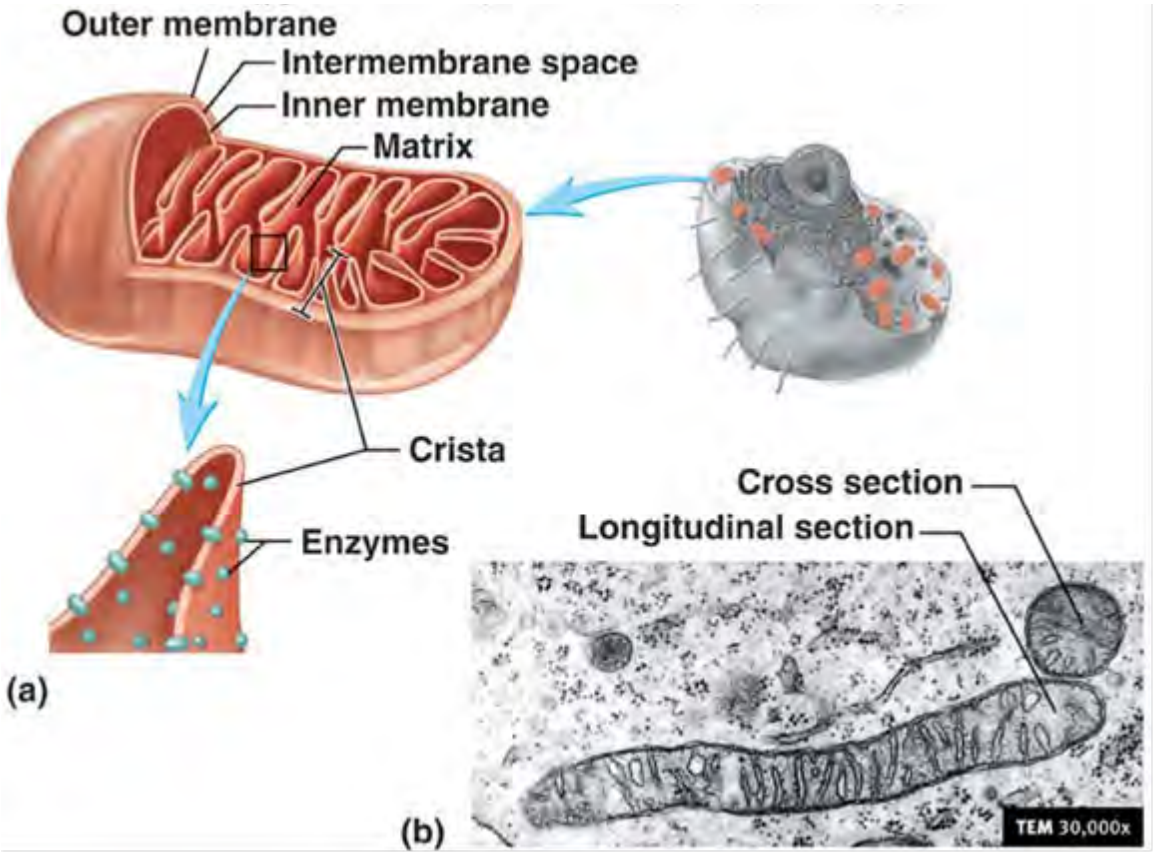
All cell and organelle membranes are phospholipid bilayers and there is a constant exchange of membrane between the organelles and the membrane itself as demonstrated by the diagram below showing the export of a protein from the cell.



Mitochondria
These are double membrane organelles with a central cavity known as the **matrix.** Between the two membranes is the **intermembranous space** which plays an important role in the synthesis of ATP.
The inner membrane folds are known as **cristae** which provide a large surface area for the chemical reactions of cellular respiration.

Function
Mitochondria are the organelles most responsible for the cell's ability to obtain energy from nutrients by generating ATP. They are known as the "powerhouses of the cell".
Mitochondria have their own DNA and are able to self-replicate. Cells may have more than 1000 mitochondria. Their numbers increase with the need for ATP. Exercising muscle cells can have large numbers of mitochondria.

–Mitochondria are only inherited from the mother.

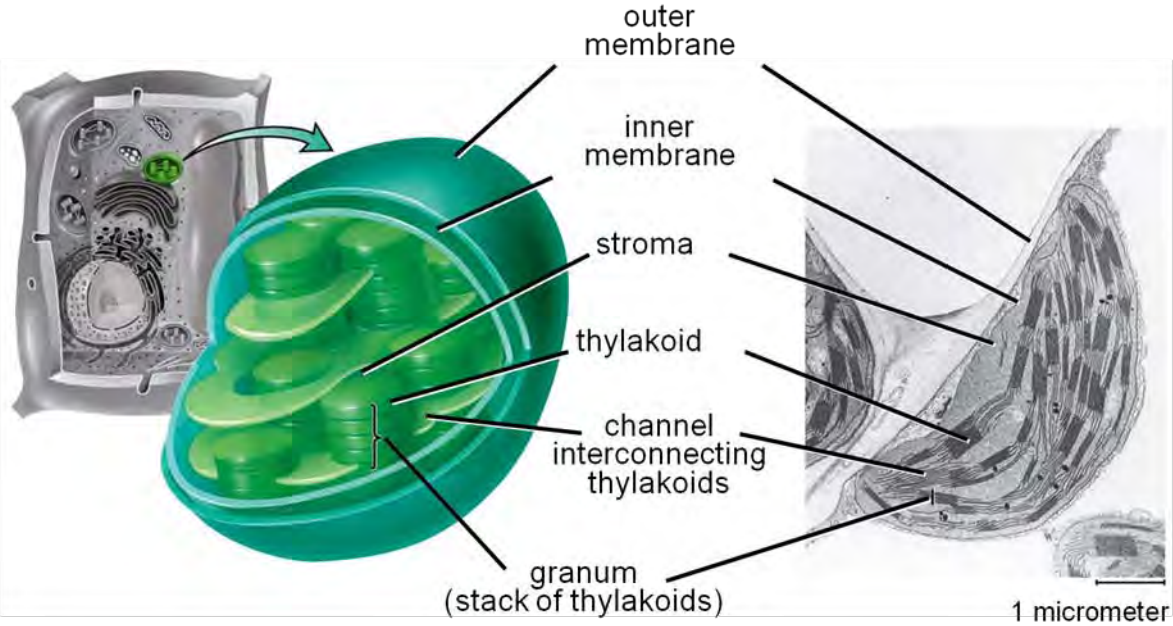


Chloroplasts

Chloroplasts have a structure similar to mitochondria with their own DNA, and a double membrane. Here the inner membrane encloses spaces filled with a fluid called the **stroma** and an extensive array of saclike structures called **thylakoids**.

Chlorophyll, a pigment that can absorb energy from the sun, thereby allowing photosynthesis to take place, is found within the thylakoids.

The chief function of chloroplasts is the capture of energy from the sun and its conversion to chemical energy – the source of energy for most other organisms.

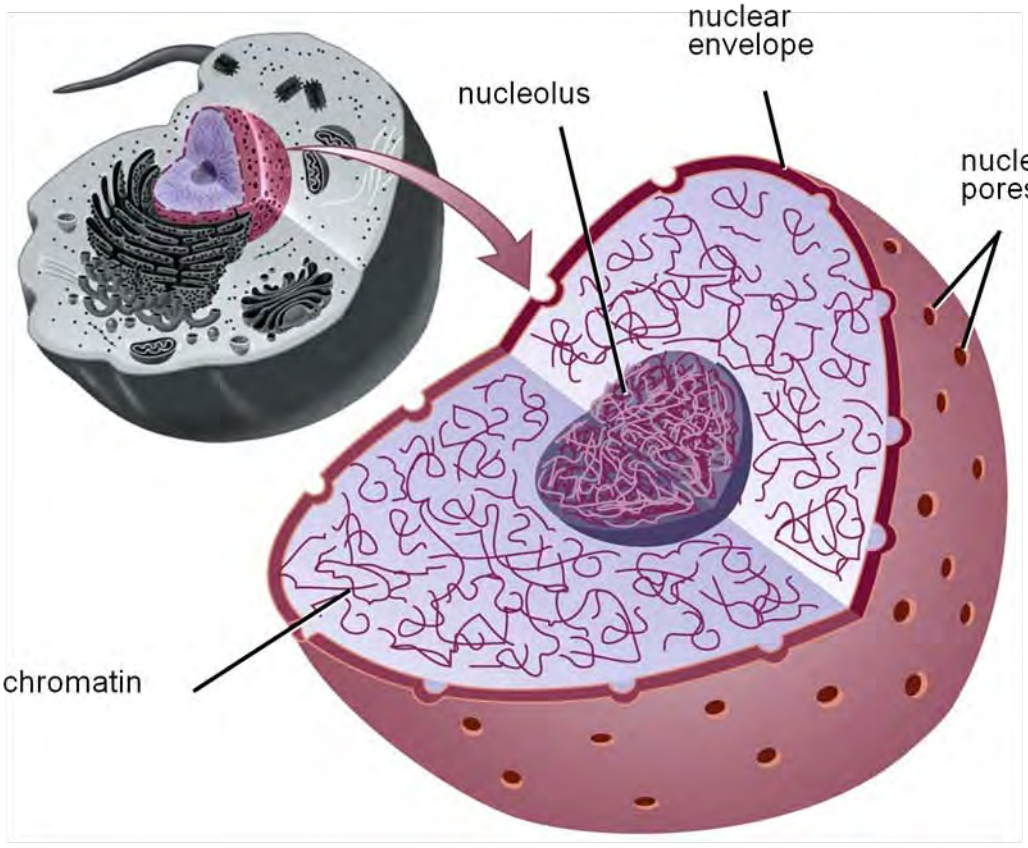


Nucleus

This large organelle with a double membrane called the nuclear envelope is usually the most prominent feature of a eukaryotic cell. The outer membrane is continuous with the rough ER. The double membrane is perforated by water-filled nuclear pores which control the movement of substances between the cytoplasm and the nucleus.

Within the nucleus is most of the cell's genetic information in the form of genes. A **gene** is a segment of DNA that codes for a protein. For example, humans have more than twenty thousand genes distributed along 23 pairs of **chromosomes** – all of which are located within the nucleus. Chromosomes are only visible when a cell is dividing. When a cell is not dividing the chromosomes assume a looser arrangement of DNA, proteins, and some RNA, called **chromatin**.

Nucleoli (sing. Nucleolus) are spherical, dark bodies within the nucleus (no membrane) and are the site of ribosome assembly



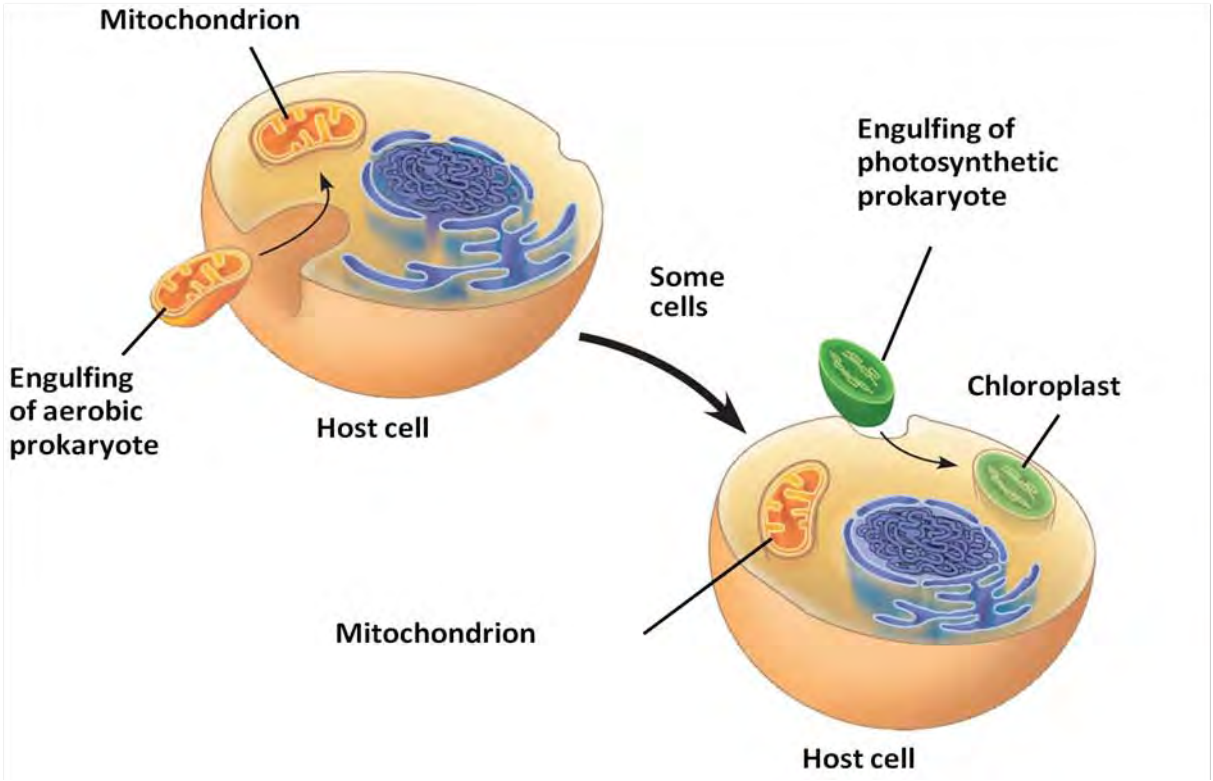
Endosymbiotic Theory

The question "How did eukaryotic cells get filled up with so many organelles?" has been partially answered by the explanation that, millions of years ago, different types of prokaryotes may have come to live inside a larger host cell forming a symbiotic relationship and eventually becoming a single, more complex organism. Small prokaryotes capable of performing photosynthesis may have been incorporated into a larger cell providing chemical energy for the cell and becoming what is now termed a **chloroplast**.

A similar scenario may also explain the origin of the **mitochondrion** and even the **nucleus**.

Part of the scientific evidence for this theory includes:

a) the presence of DNA and ribosomes in these organelles
b) the fact that all three have double membranes indicating that the process of endocytosis may have been the mechanism that brought these prokaryotes into the cell.

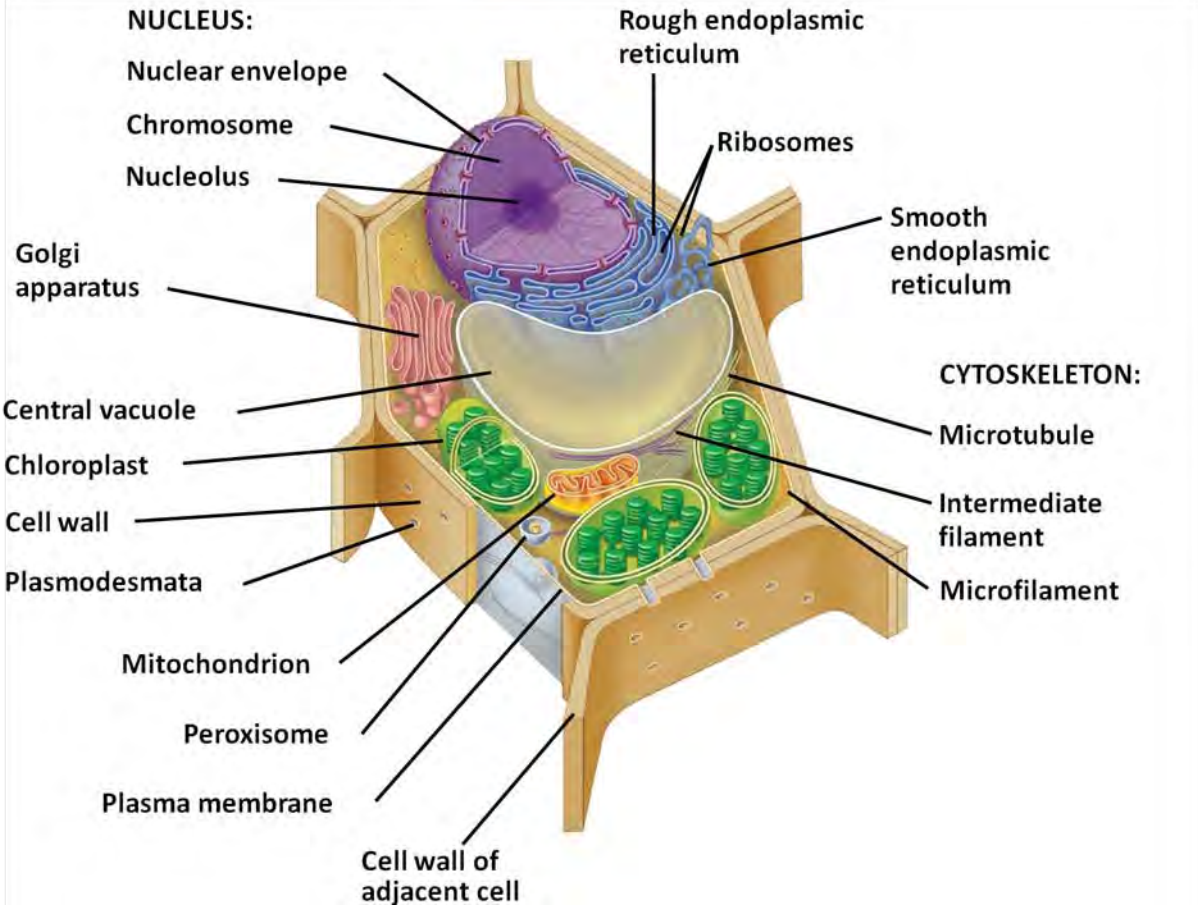


THINGS THAT ARE SPECIAL ABOUT PLANT CELLS

Most organelles and structures discussed so far are common to both plant and animal cells but plant cells have a few specializations. First of all plant cells are the only cells that have **chloroplasts** page 12. The presence of the pigment, **chlorophyll,** gives plants their green color.

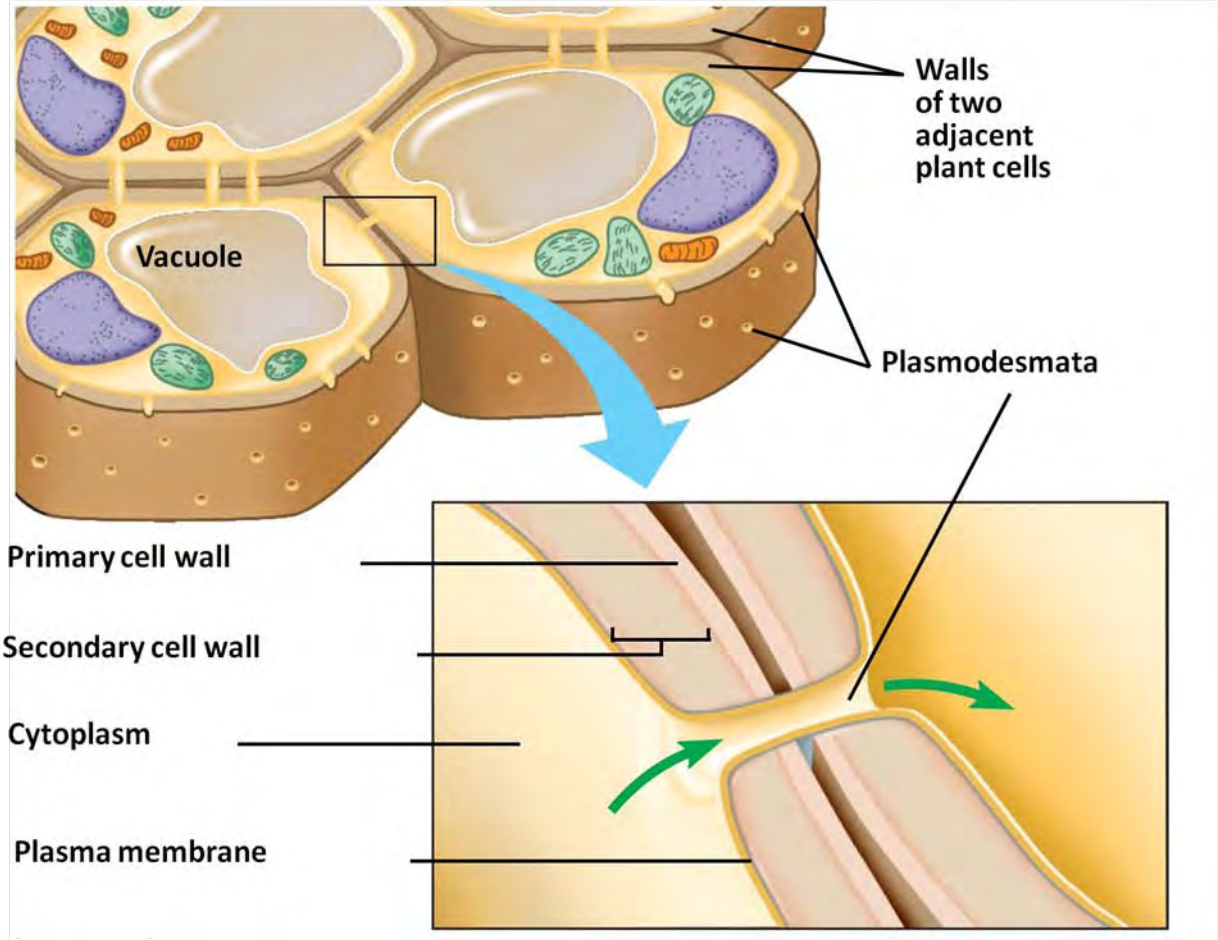
Most plant cells contain a large **vacuole**. This is a storage compartment for large amounts of water and other materials such as sugar, ions, pigments, waste, and sometimes poisons. The vacuole when it is full of fluid also serves the purpose of expanding the cell membrane to increase surface area creating turgor pressure. **Turgor pressure** allows stems and other plant parts to stand upright and is especially important in nonwoody plants.

Diagram of a plant cell



Plant cells walls protect the plant cell. These walls are composed primarily of **cellulose**, a polysaccharide. Primary cell walls are laid down when the plant is still growing and adjacent cell walls are "glued" together. Some plants develop a secondary cell wall constructed from a complex molecule called **lignin** which gives the plant strength and rigidity.

As can be seen below, the cell wall is porous allowing water and solutes to move between plant cells. It also has larger channels called **plasmodesmata** which allow larger molecules to move from one cell to the next.



LECTURE 7: CELL MEMBRANE AND TRANSPORT

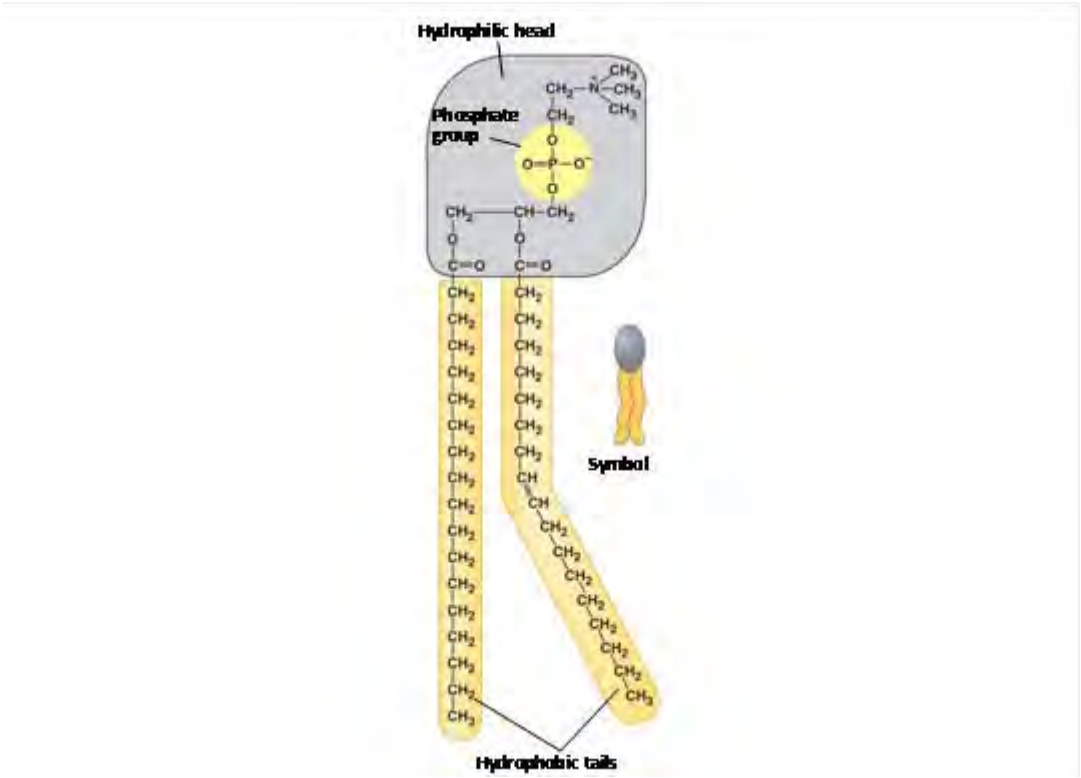
The cell membrane or plasma membrane is the structure that encloses all cells and separates the contents of the cell from the external environment. It is a selectively or differentially permeable membrane that regulates the flow of materials into and out of the cell and is involved in cells communicating with other cells or with the external environment.

Composition of the Plasma Membrane: lipid bilayer interspersed with proteins.

The Lipid Bilayer The cell membrane is primarily a lipid bilayer made of 3 lipid components: **1) Phospholipids 2) Cholesterol 3) Glycolipids**

1. Phospholipids

The **phospholipids** are by far the most numerous lipids in the membrane. Phospholipids are amphipathic (see **Organic compounds**) and are oriented so that the fatty acid, nonpolar tails are on the inside and the phosphate-containing heads face the watery environment on the inside and on the outside. This lipid bilayer acts as a barrier to the entry or exit of charged or polar substances.

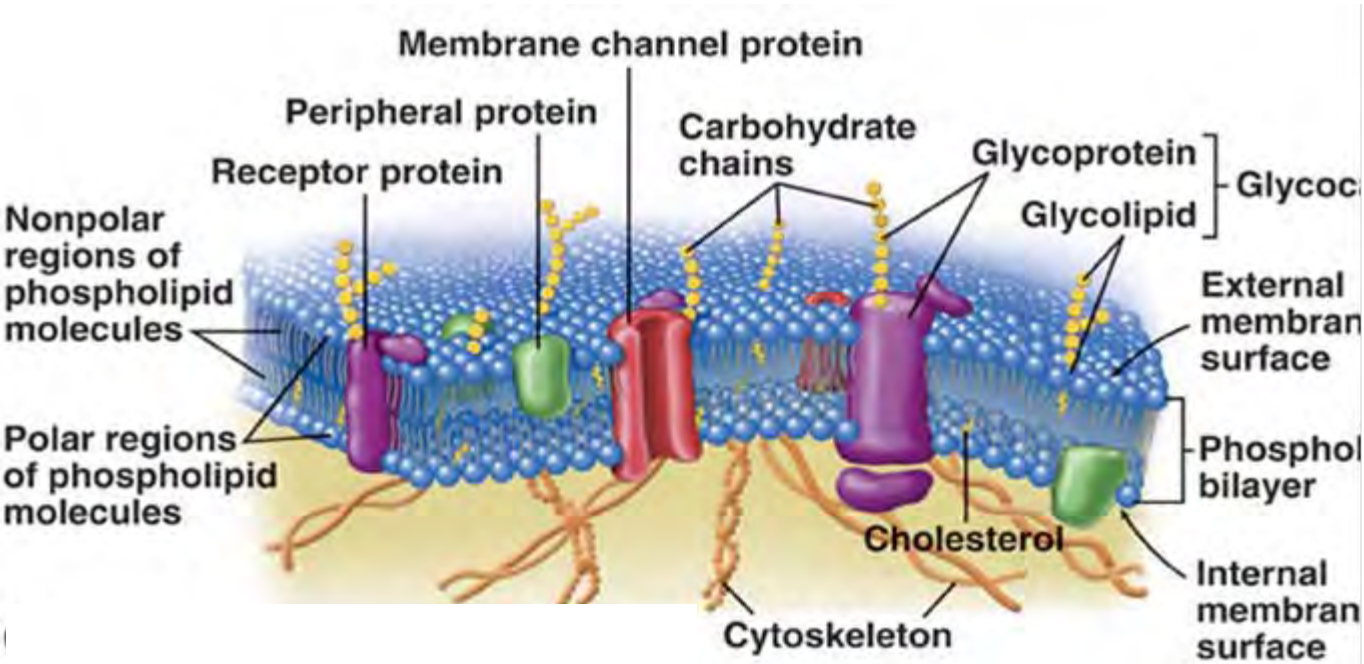


2) Cholesterol

Cholesterol is a small lipid molecule interspersed among the phospholipids. Cholesterol molecules help keep the membrane at the optimum fluidity so that it doesn't become too rigid in cold temperatures or too liquid in hot ones. Cholesterol also helps prevent small molecules passing through the membrane by attaching to phosholipid tails.

3) Glycolipids

These are carbohydrate chains of monosaccharides some of which are attached to membrane lipids and form part of the **glycocalyx** (discussed shortly).

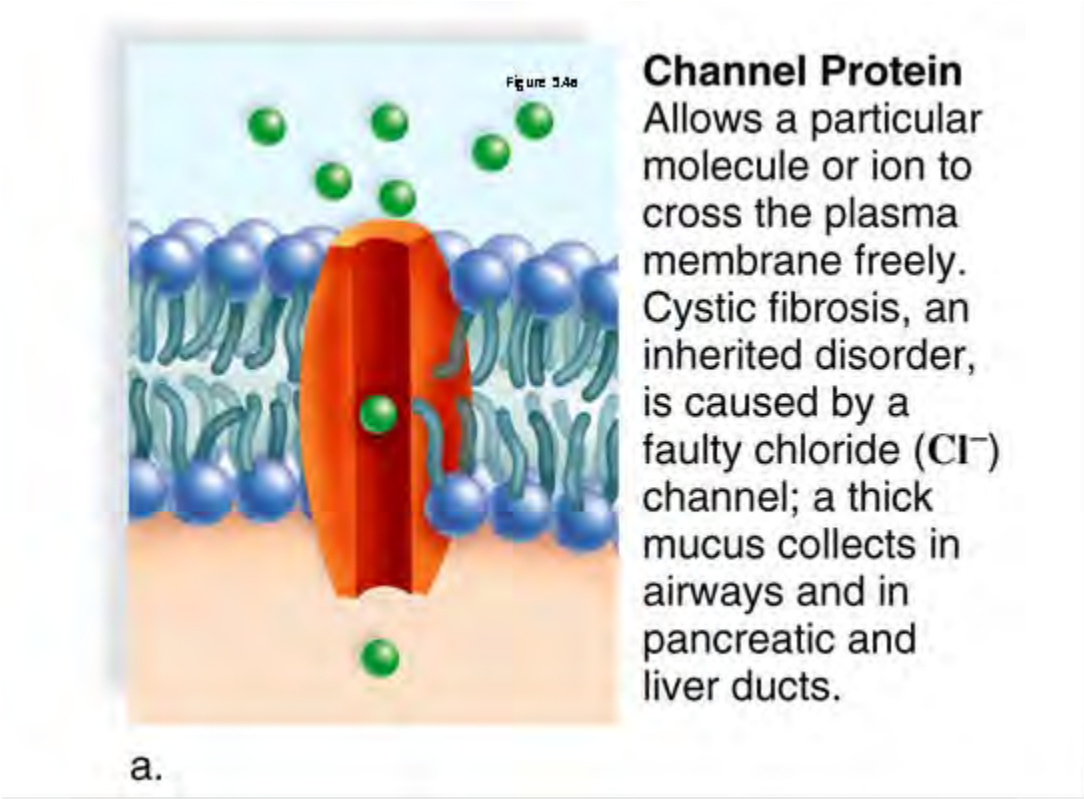


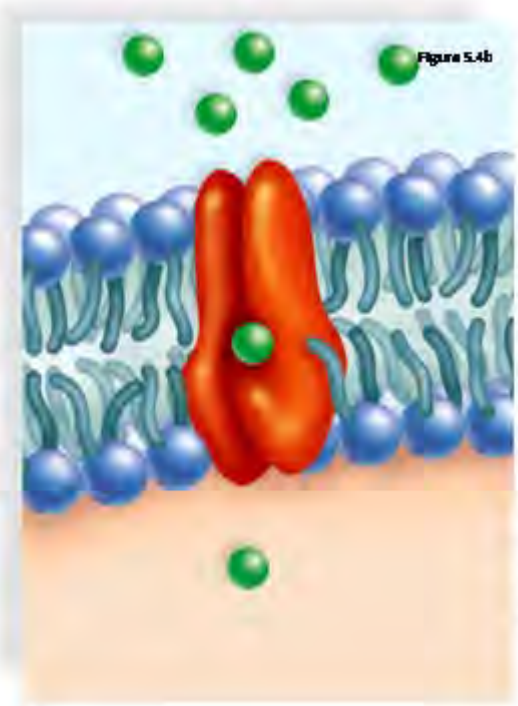
Proteins in Cell Membrane

From the image of a cell membrane on the previous page, it is clear that while lipids are the most numerous molecules in the cell membrane, there are also large numbers of proteins embedded within the membrane (integral) or lying on the phospholipid bilayer (peripheral).

Peripheral proteins support the plasma membrane, anchor integral proteins, and form attachments between cells.

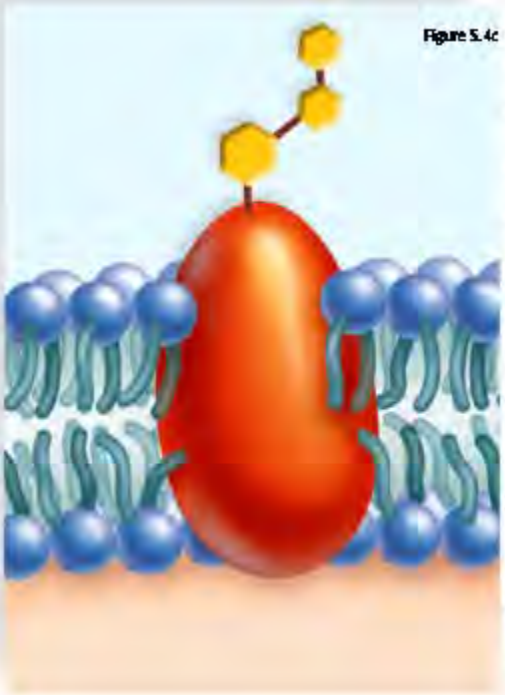
Integral proteins have many different shapes and functions some of which are listed below.





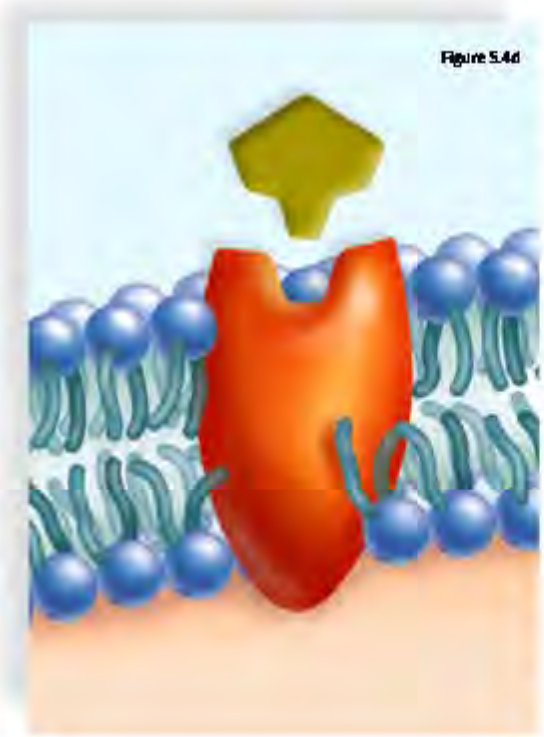
Carrier Protein
Selectively interacts with a specific molecule or ion so that it can cross the plasma membrane. The inability of some persons to use energy for sodium-potassium (Na^+–K^+) transport has been suggested as the cause of their obesity.

b.



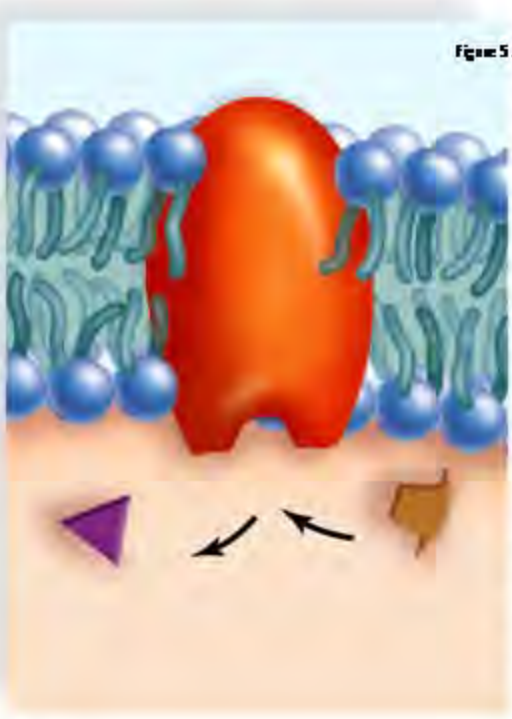
Cell Recognition Protein
The MHC (major histocompatibility complex) glycoproteins are different for each person, so organ transplants are difficult to achieve. Cells with foreign MHC glycoproteins are attacked by white blood cells responsible for immunity.

c.



Receptor Protein
Is shaped in such a way that a specific molecule can bind to it. Pygmies are short, not because they do not produce enough growth hormone, but because their plasma membrane growth hormone receptors are faulty and cannot interact with growth hormone.

d.



Enzymatic Protein
Catalyzes a specific reaction. The membrane protein, adenylate cyclase, is involved in **ATP** metabolism. Cholera bacteria release a toxin that interferes with the proper functioning of adenylate cyclase; sodium ions and water leave intestinal cells, and the individual may die from severe diarrhea.

e.

Fluid Mosaic Model

Membranes are fluid structures. Lipids and proteins move easily and continuously within the cell membrane. This allows actions to occur within the cell membrane such as the insertion of new proteins, and it allows cell movement, growth and division, and the formation of junctions.
This model of the cell membrane is described as the **Fluid mosaic model**.

Glycocalyx

Many of the proteins in the cell membrane have carbohydrate groups attached that protrude into the extracellular fluid (ECF). These molecules form a sugary coat around the cell membrane. This coating is known as the glycocalyx and has several functions. It attracts water and allows certain cells to move easily, other cells to adhere to each other, and in some cells the glycocalyx helps with recognition.

Selective Permeability of Membrane
Cell membranes are selectively permeable, allowing the passage of some molecules and not others. The movement of molecules depends on several factors.

Gradients
Several types of gradients exist across the cell membrane:

Concentration gradient – a difference in concentration across the membrane
Electrical gradient – a difference in charge across the membrane
Pressure gradient – a difference in pressure across the membrane

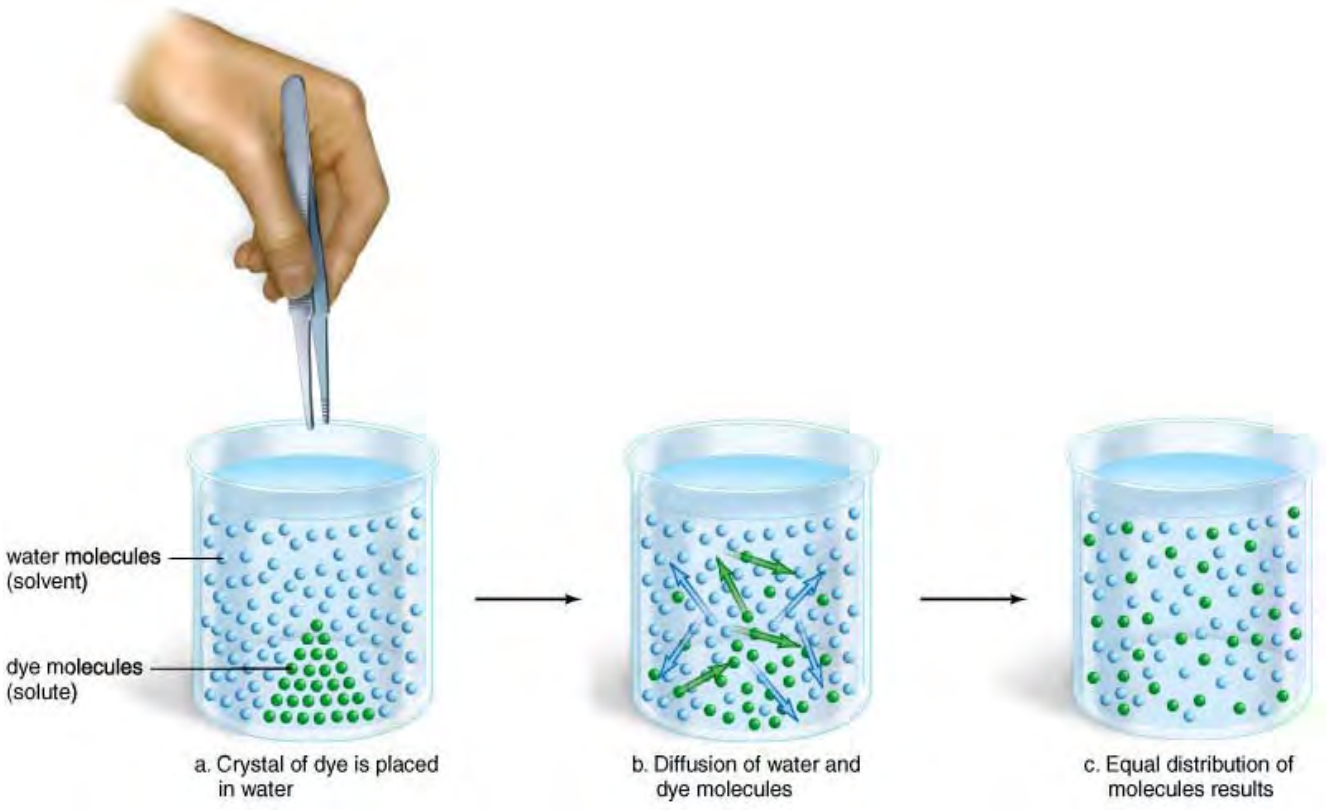
Sometimes the combination of the first two gradients is referred to as the **electrochemical** gradient.
These gradients variously affect movement across the cell membrane.

TYPES OF TRANSPORT THROUGH CELL MEMBRANES

The transport of substances across the cell membrane can be classified as **passive transport**, which does not require energy and is based on the gradients just mentioned **OR active transport** which involves the use of energy in the form of ATP.

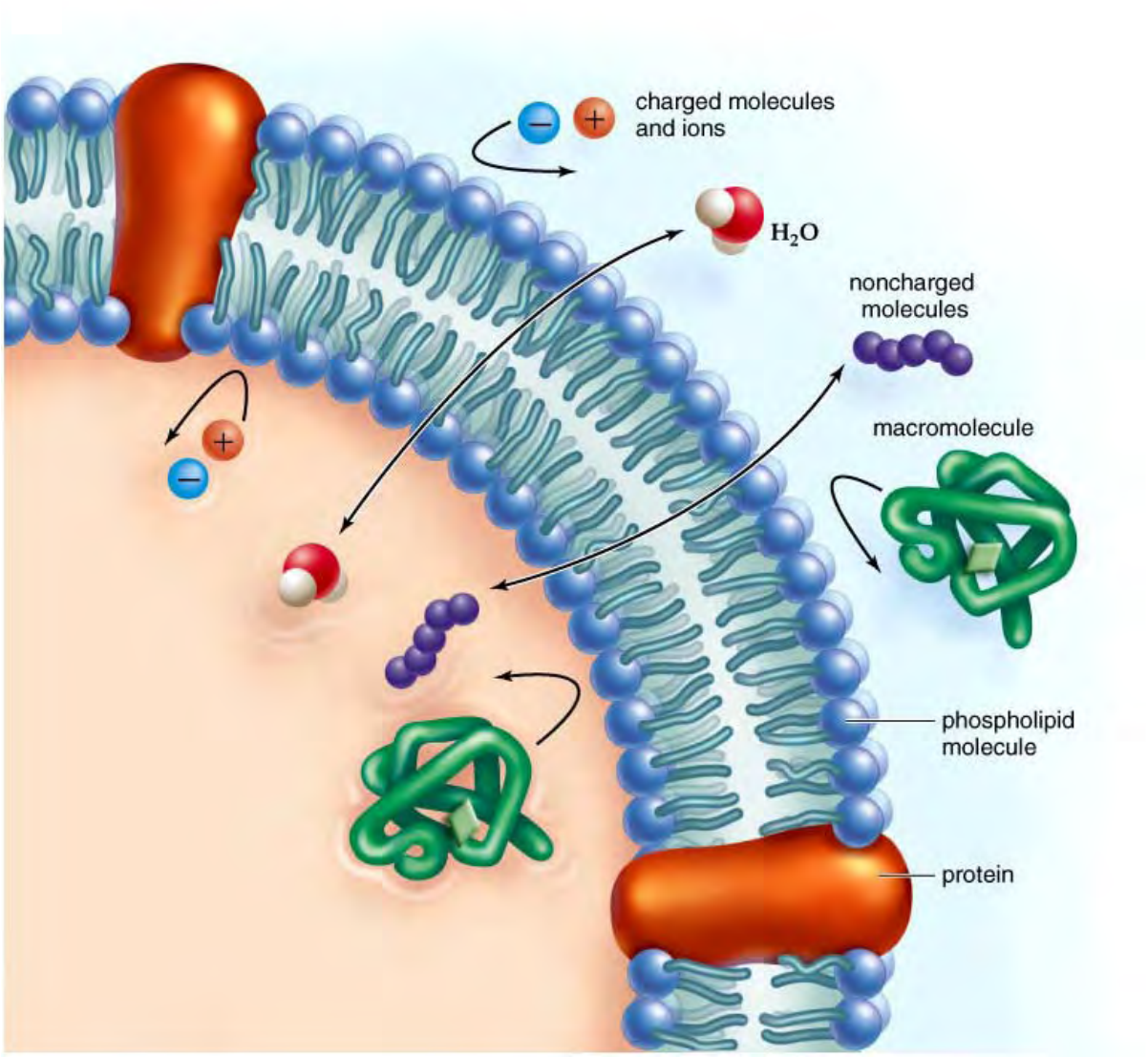
PASSIVE TRANSPORT

1. **Simple Diffusion** is the random movement of molecules from an area of high concentration to low concentration as demonstrated by placing some dye in a beaker of water (see below). It eventually results in an even distribution of the dye throughout the water – a result of the random movement of molecules. Diffusion can occur in solutions and in gases - think of how the smell of coffee in the kitchen can reach your nose in the bedroom.



The lipid bilayer of the cell membrane is permeable to nonpolar, uncharged molecules such as small lipid-soluble molecules and to gases, especially CO_2 and O_2. The lipid bilayer is also permeable to H_2O even though water is a polar molecule as discussed in **Lecture 3**. Cell membranes contain small channels called aquaporins that allow water to pass through down its concentration gradient – either into or out of the cell. Also, water molecules are very small and may be able to pass through between the lipids as they move about in the membrane.

To summarize, small lipid-soluble molecules, water, and oxygen and carbon dioxide move by simple diffusion through the cell membrane



2. **<u>Facilitated Diffusion/ Facilitated Transport</u>** is also based on concentration gradients. A protein is required to "facilitate" the process usually because the molecule is polar or charged and therefore cannot cross directly through the phospholipid bilayer.

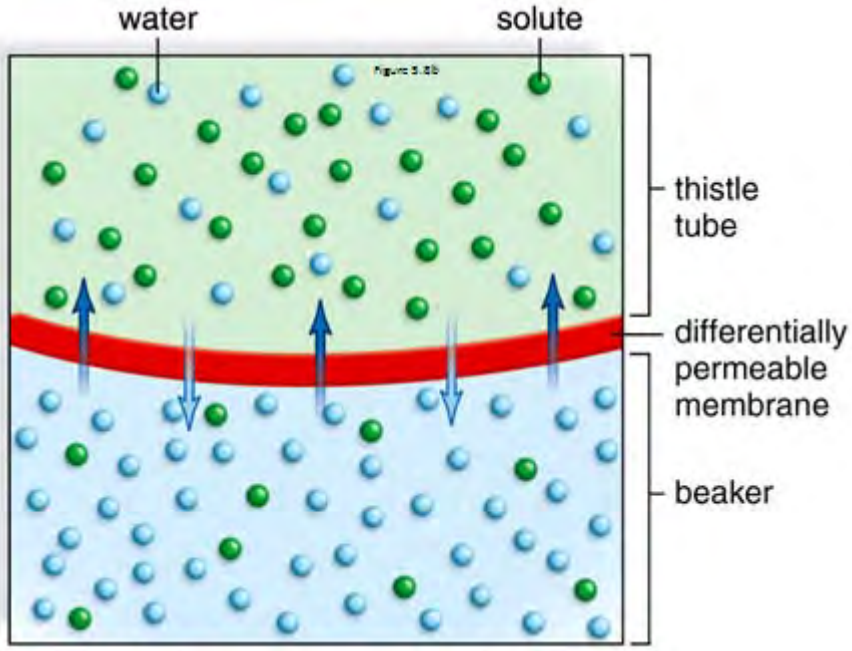
Channel proteins facilitate diffusion. These are usually ion channels for the movement of ions such as K^+, Cl^- , Na^+ Ca^{++} etc. The channels are often specific for one type of ion. Sometimes these channels are gated so that the flow of ions is controlled. **See page 3, fig. a**

Carrier proteins facilitate diffusion too. Sometimes a molecule is too big or too charged to cross the cell membrane and instead will bind to a protein on one side of the membrane. The carrier protein will change shape and the molecule is released on the other side. Good examples of molecules that are transported in this manner are glucose molecules and amino acids. **See page 4, fig. b**

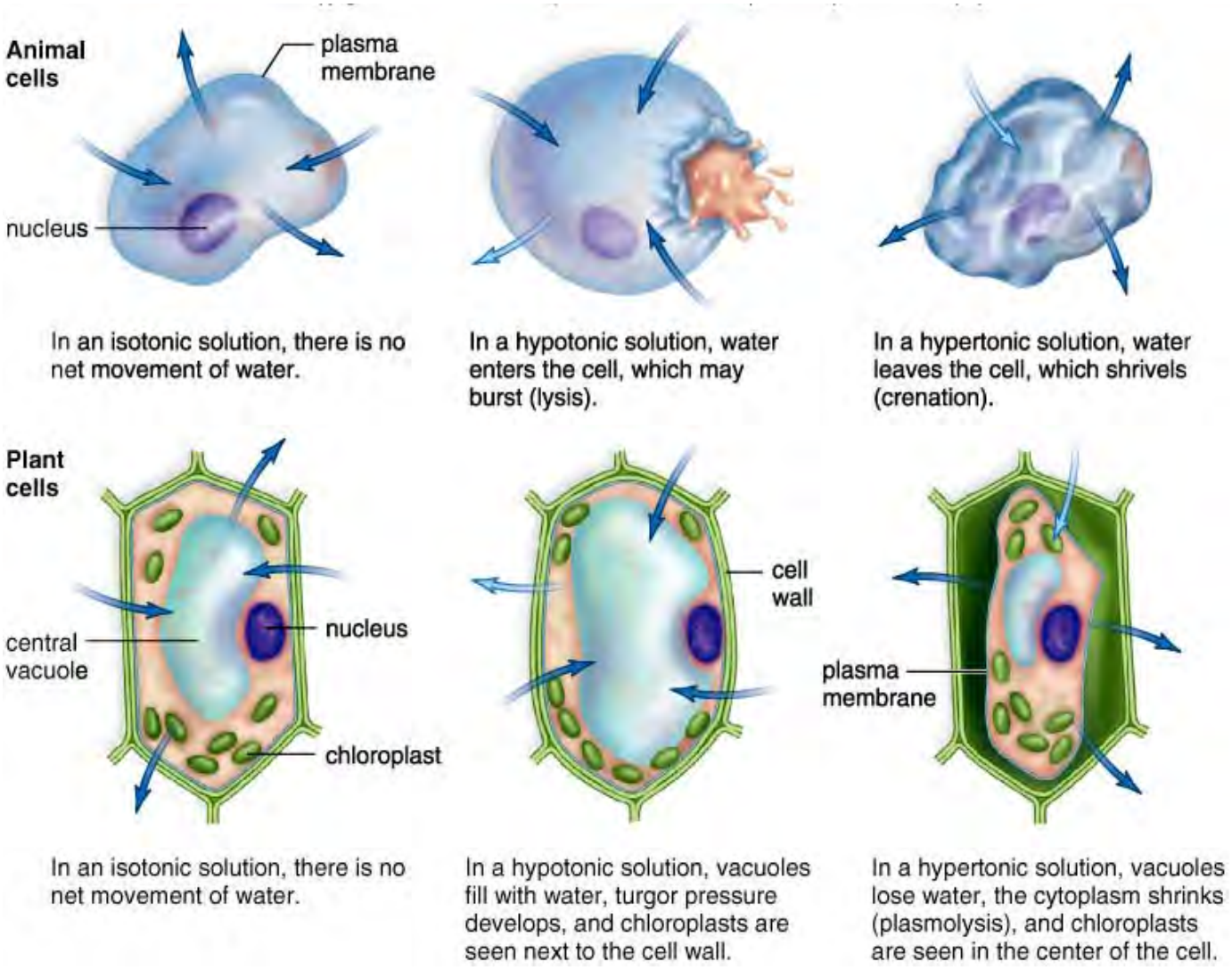
3. Osmosis

Osmosis is a term for the diffusion of water. It is the movement of water down its concentration gradient. It's important to note that this is **movement of water from an area of high water concentration to an area of low water concentration.** This is still a type of diffusion as water diffuses through the lipid bilayer as well as moving via aquaporins as described earlier. **Osmosis** can have important effects on cells. The term **tonicity** is used to compare substances dissolved in water and separated - the cell membrane separates the contents of the cell from the extracellular fluid. **Tonicity** is a relative term.

A **hypertonic solution** has a greater concentration of solutes than the solution it is being compared to.
An **isotonic solution** has the same concentration of solutes as the solution it is being compared to.
A **hypotonic solution** has a lower concentration of solutes than the solution inside it is being compared to.
(As water flows in it creates a force against the membrane - **osmotic pressure**).

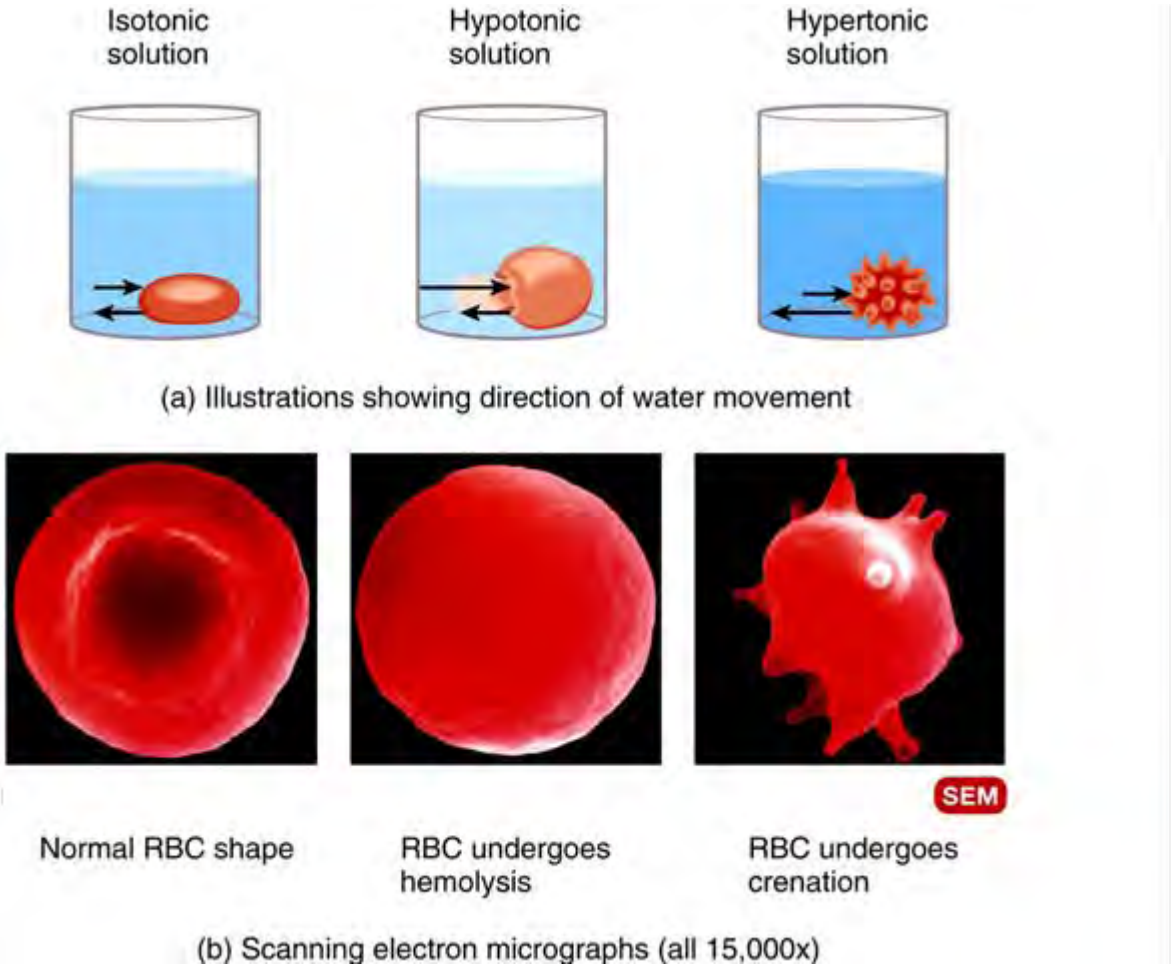


There is a greater concentration of solutes in the thistle tube than in the beaker so water will move down its concentration gradient from the beaker to the thistle tube. Water will actually move both ways across the differentially permeable membrane but more water will move into the solution which has the greater number of solutes and therefore less free water molecules.



Animal cells will not change shape in an isotonic solution, may swell up when placed in a hypotonic solution, and may shrink when placed in a hypertonic solution.

Plant cells, because they are surrounded by a cell wall, develop turgor pressure when placed in a hypotonic solution. The plant cell membrane pulls away from the wall in a hypertonic solution and the vacuole shrinks.



Red blood cells must be maintained in an isotonic solution. In a hypotonic solution they will swell up and may burst (lyse), while in a hypertonic solution red blood cells will shrivel up or undergo crenation.

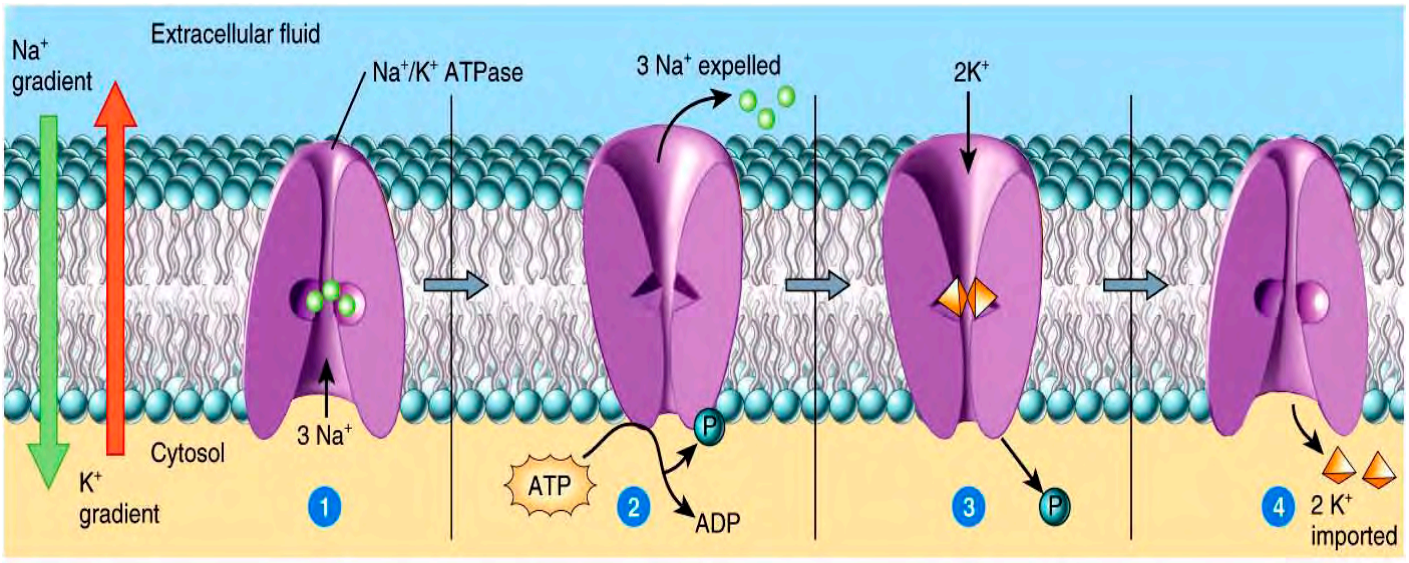
ACTIVE TRANSPORT OR ENERGY-REQUIRING MECHANISMS

Sometimes cells must use energy to move substances into or out of cells. Energy is required if the molecules being moved are very large or being moved against the concentration gradient. When active transport uses energy directly in the form of ATP, the process is called

Primary Active Transport

The proteins involved in primary active transport are often called pumps and a good example of this mechanism is the **sodium-potassium pump**. Animal cells have thousands of these pumps in their cell membranes working to maintain a low concentration of Na+ inside the cell and a higher concentration of K+ outside the cell. This difference in concentration is necessary for a variety of cell functions but especially for nerve cell conduction and muscle cell contraction.

Both sodium and potassium continually leak down their concentration gradients so these pumps work continually to maintain the electrochemical gradient.



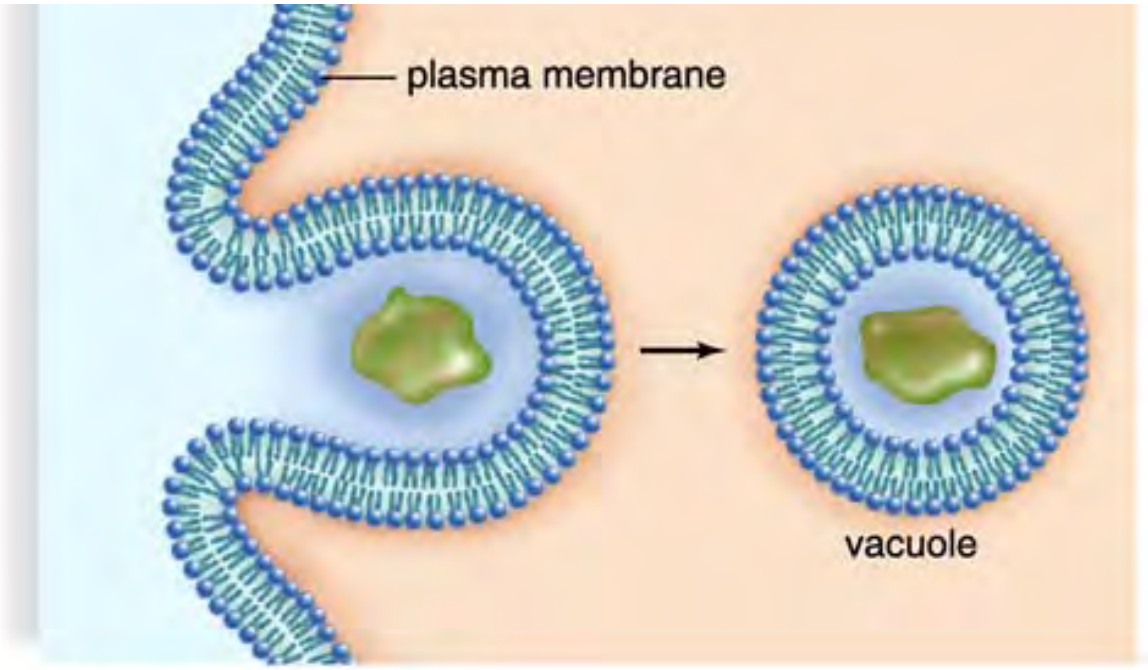
ATP (adenosine triphosphate) is broken down to ADP and P and the energy released is used to power the pump. The enzyme ATPase causes this reaction to occur.

Transport in Vesicles.
Many molecules required by a cell or undergoing export from a cell are too big to get transported even by the previously described active transport mechanisms. In these cases vesicle formation occurs. A vesicle is a small, spherical sac (again a phospholipid bilayer) that transports substances within the cell.
When a substance is being moved into a cell by this method, the vesicle forms from an indentation of the cell membrane. This process is called **Endocytosis.**

There are 3 types of Endocytosis

A) Phagocytosis

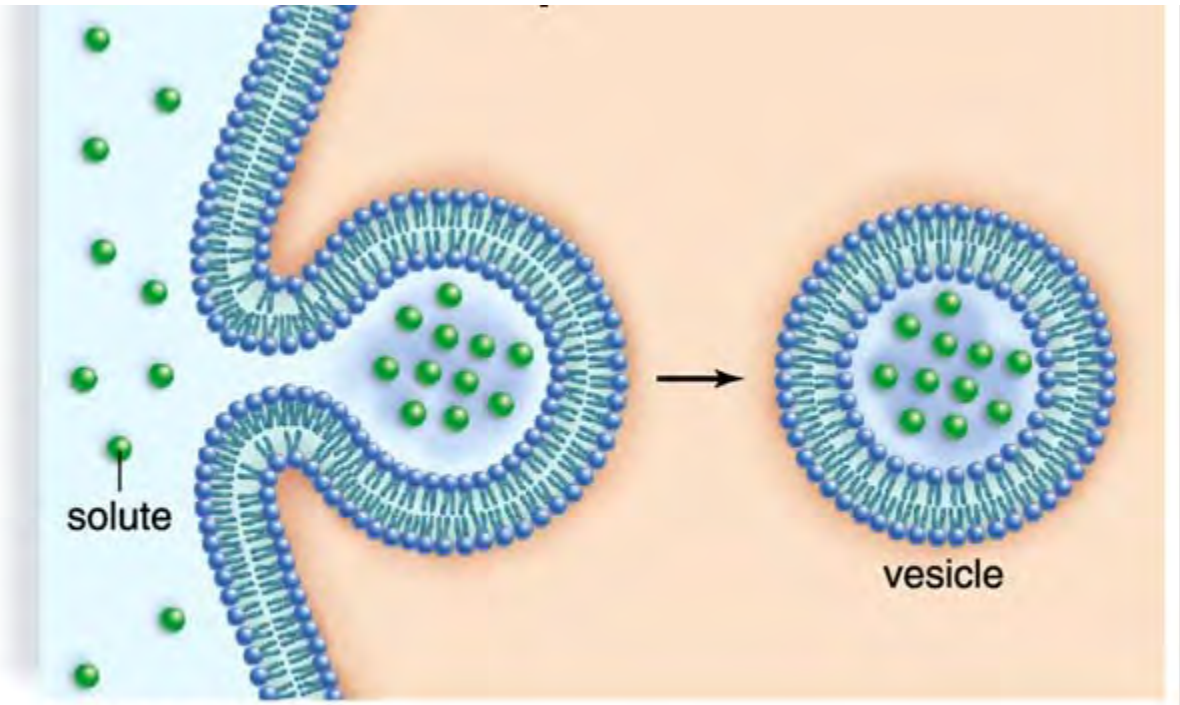
This is the term used when the material being brought into the cell is a bacterial cell, a virus, large particles, or worn-out cells. First, part of the cell membrane extends outwards and surrounds the particle, then fuses to form a vesicle which is moved into the cell. The vesicle's membrane may fuse with a lysosomal membrane so that the lysosomal enzymes can digest the particle.



a. Phagocytosis

B) Pinocytosis

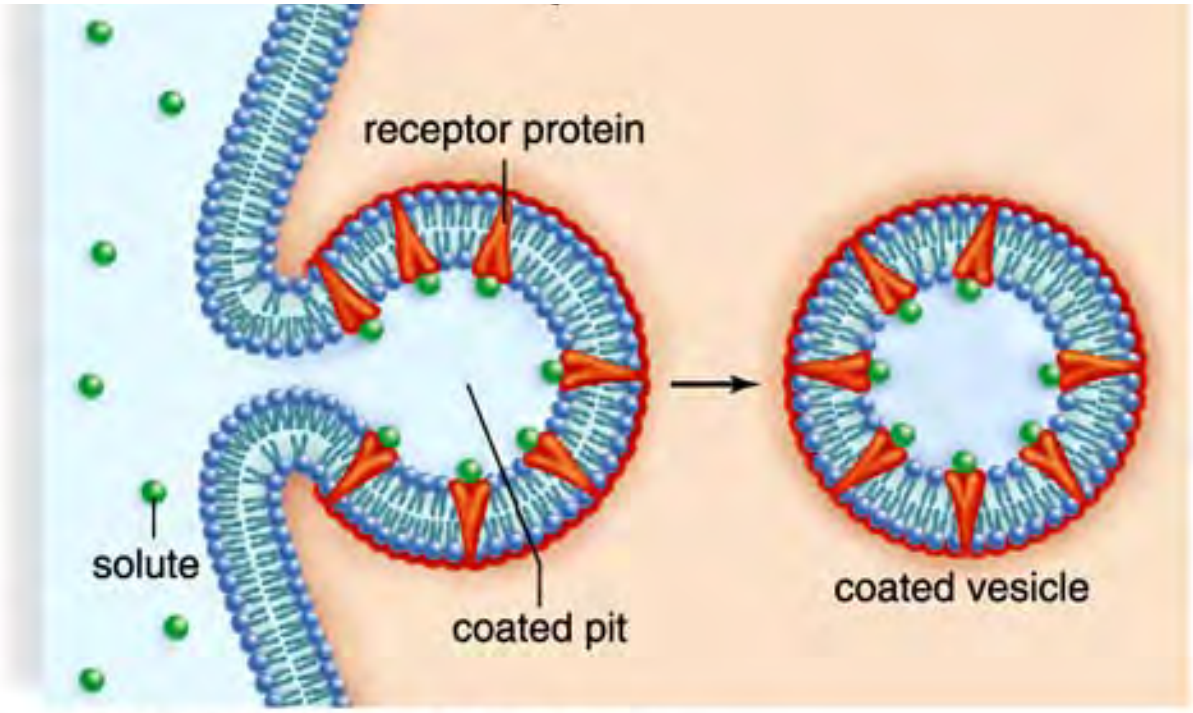
Pinocytosis is similar to endocytosis but the vesicles formed are much smaller. Tiny droplets of extracellular fluid including solutes are brought into the cell.
This process is common in animal cells. For example, egg cells use pinocytosis to take in surrounding nutrients.



b. Pinocytosis

C) Receptor-mediated Endocytosis

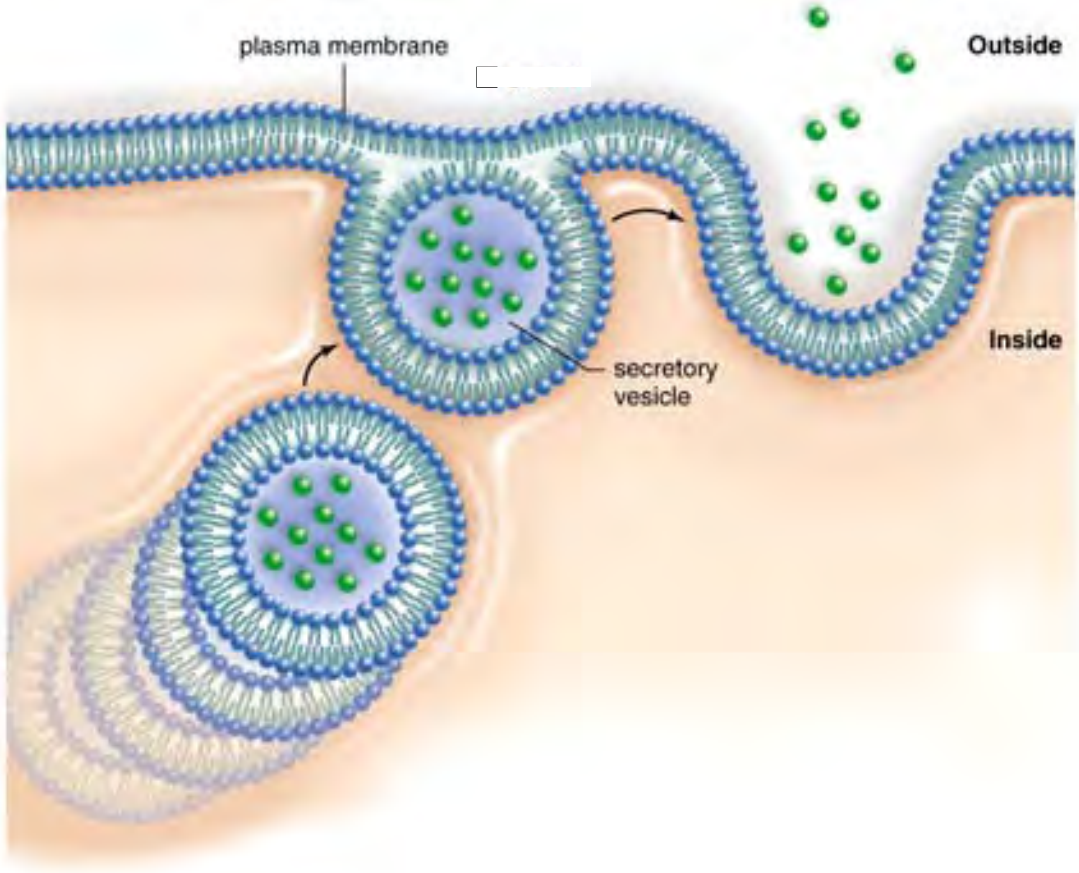
This process is more specific about what is brought into the cell. Here, receptor molecules on the surface bind a specific molecule like cholesterol. Many of the same receptors are located on the same place on the plasma membrane. When the receptors have bound the molecules, the membrane folds inwards forming a vesicle similar to the process in phagocytosis.

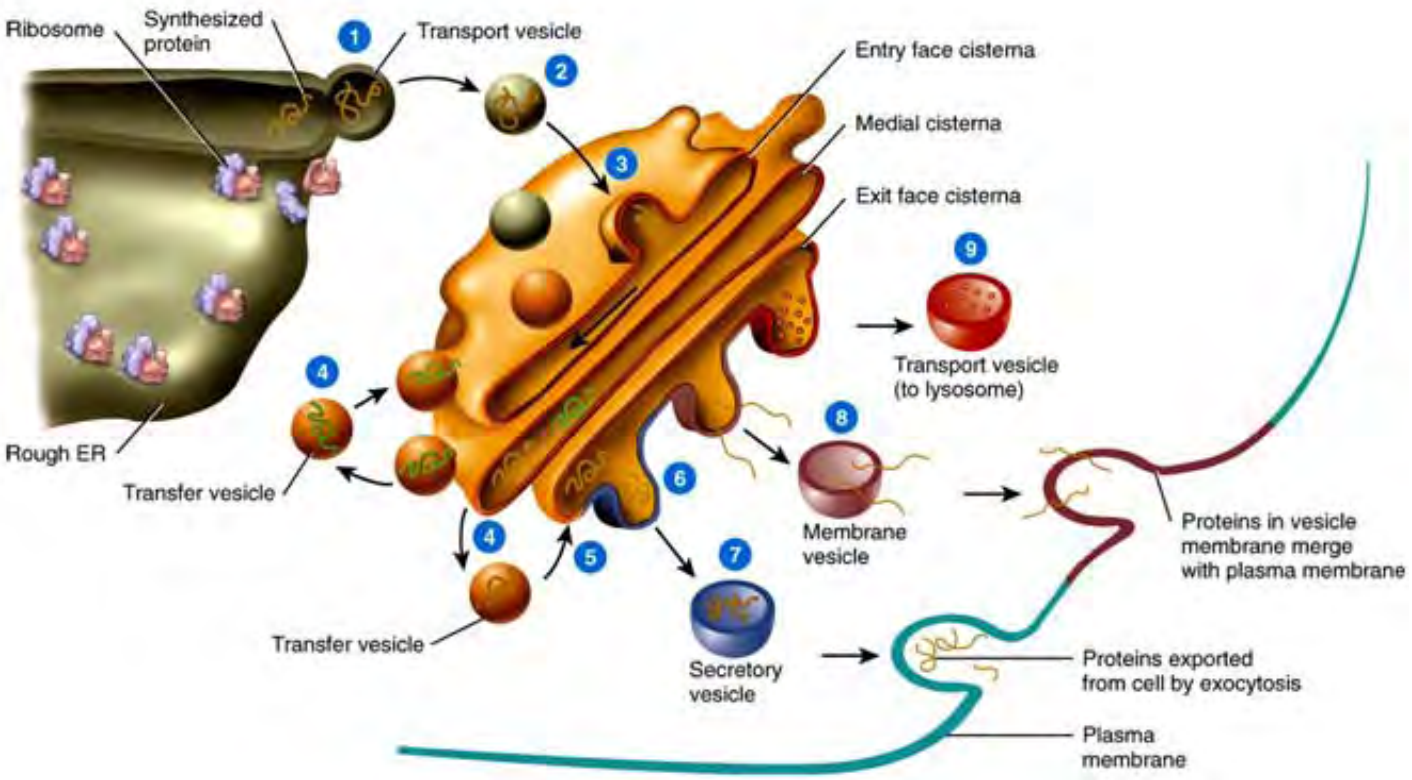


c. Receptor-mediated endocytosis

Exocytosis

The reverse of endocytosis is exocytosis – the movement of substances out of the cell, again by vesicle formation. For example, cells in the pancreas produce the hormone insulin which is too big to move out of the cell through the cell membrane. Instead insulin molecules are packaged in a vesicle which moves through the cytoplasm to the inner surface of the cell's membrane. Both membranes fuse together and the insulin molecules are "dumped" out of the cell.





This illustration shows the formation of proteins on the ribosomes on the rough ER, their passage through the Golgi body, and their export from the cell. Vesicle formation also occurs in the formation and delivery of new membrane and in the making of lysosomes.

LECTURE 8: PROKARYOTES

Every cell falls into one of two basic categories; they are either **prokaryotic** cells or **eukaryotic** cells. Eukaryotic cells or eukaryotes are discussed in **Lecture 3**. The difference between eukaryotes and prokaryotes is that prokaryotic cells do not have a nucleus or membranous organelles and are therefore structurally simpler. The DNA resides in the cytoplasm and is usually in the form of a circular loop.

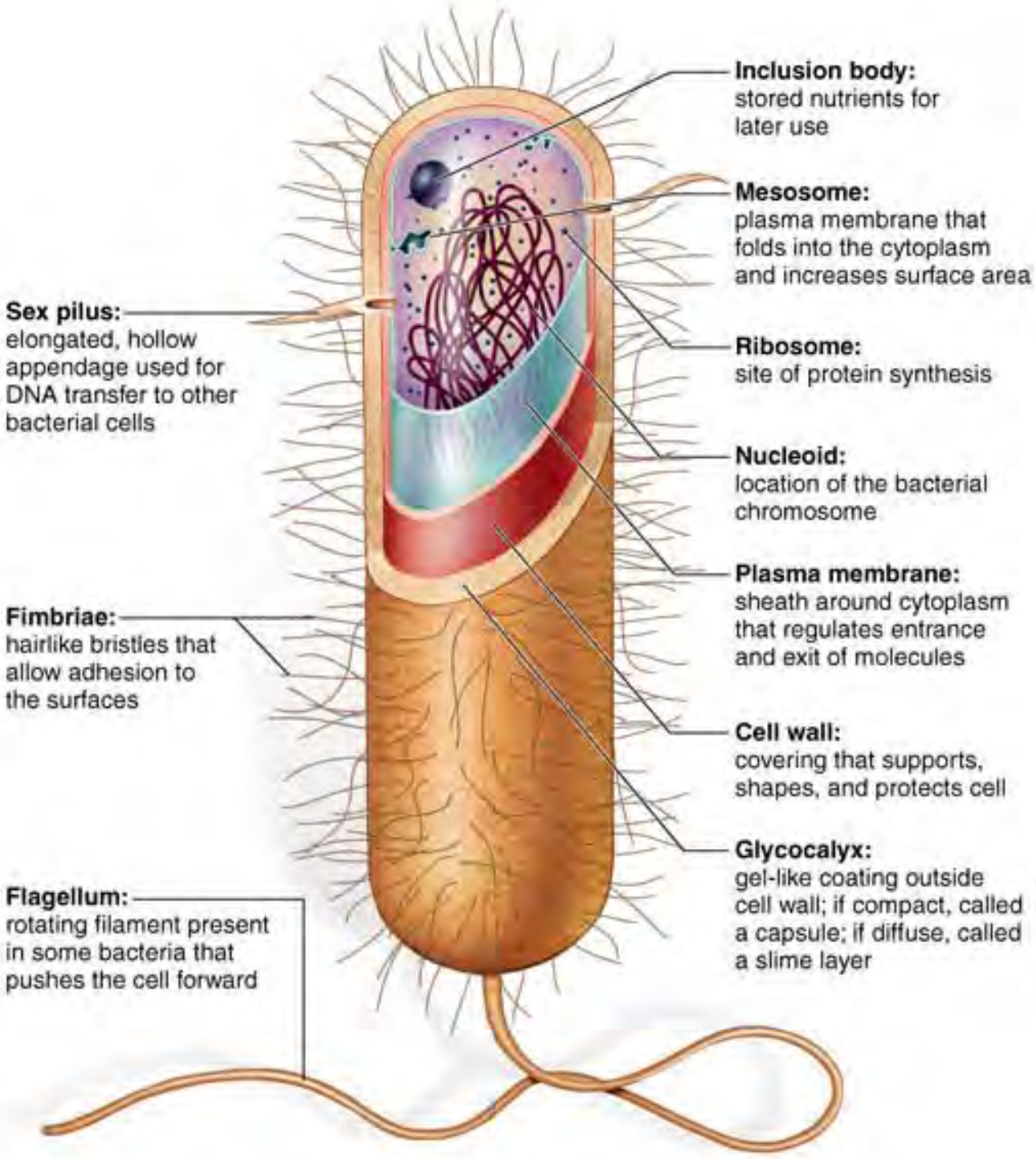
Prokaryotes were the first type of cell to exist on earth and two of the three domains of life – **bacteria and archaea** – are prokaryotes. All prokaryotes are **one-celled organisms** and can only be seen with the aid of a microscope.

All prokaryotes have a cell membrane – the typical phospholipid bilayer enclosing the cytoplasm. Within the cytoplasm is a "nucleoid" region that encloses the DNA, and lots of ribosomes for protein synthesis as well as nutrients and other inclusions.

Most prokaryotes have a cell wall that protects and gives shape to the cell. Some have a slimy outer coat (outside the cell wall) called a **glycocalyx.** This provides protection and helps prokaryotes attach to other structures (such as your teeth). **Fimbriae,** hair like extensions, also help with attachment. Some also have **flagella** which are protein structures that can be longer than the cell itself and help some bacteria move by twisting in a corkscrew fashion.

The 2 domains, **Bacteria and Archaea**, are superficially similar in appearance but under the microscope there are differences in composition of cell walls, plasma membranes, ribosomes, some enzymes and even in the steps of basic pathways.

The evolutionary relationships within Bacteria and Archaea are still a work in progress.


Inclusion body:
stored nutrients for later use
Mesosome:
plasma membrane that folds into the cytoplasm and increases surface area
Sex pilus:
elongated, hollow appendage used for DNA transfer to other bacterial cells
Ribosome:
site of protein synthesis
Nucleoid:
location of the bacterial chromosome
Plasma membrane:
sheath around cytoplasm that regulates entrance and exit of molecules
Fimbriae:
hairlike bristles that allow adhesion to the surfaces
Cell wall:
covering that supports, shapes, and protects cell
Glycocalyx:
gel-like coating outside cell wall; if compact, called a capsule; if diffuse, called a slime layer
Flagellum:
rotating filament present in some bacteria that pushes the cell forward

BACTERIA

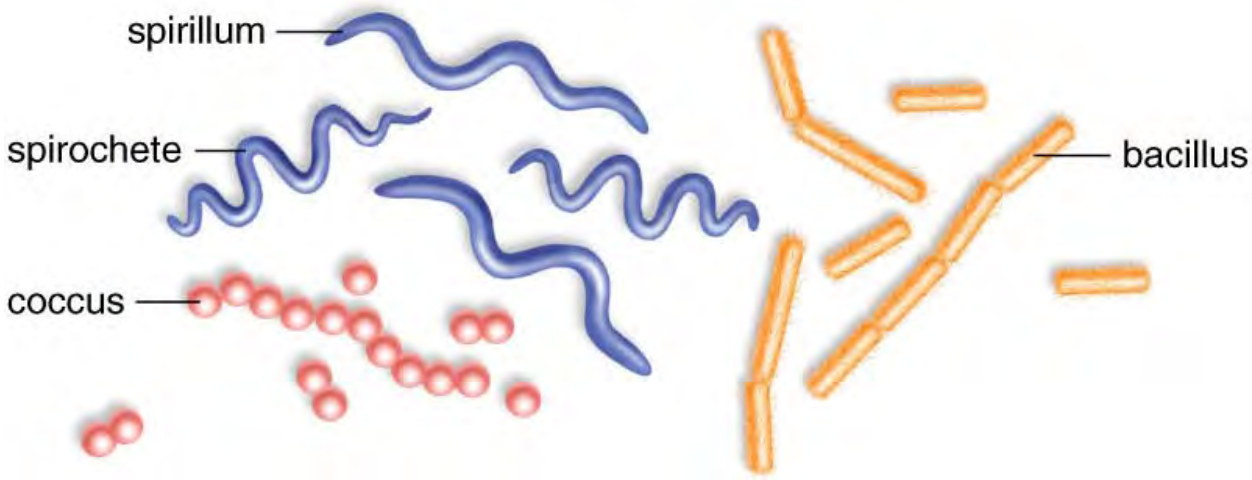
The largest group of prokaryotes is **Bacteria**. It is thought that millions of different species of bacteria exist but only several thousand species have been identified so far. Bacteria are metabolically more diverse than eukaryotes so are able to exist in a wide range of habitats. Some are autotrophic i.e. they can obtain their own energy; some autotrophs are photoautotrophs - able to obtain energy from sunlight; some are chemoautotrophs who obtain energy by oxidizing inorganic substances such as sulfur. But most bacteria are chemoheterotrophs which obtain both carbon atoms and energy from organic molecules.

Bacteria affect our lives in many important ways.
For example: bacteria fix atmospheric nitrogen and make it available for other organisms; they are used to produce many foods such as yogurt, cheeses, and vinegar using fermentation pathways (see **lecture 10**).
Hundreds of species of bacteria grow in and on the human body maintaining the "normal flora" so that pathogenic bacteria have trouble getting a foothold.
Also, in the body bacteria help with digestion, and produce vitamins.

Bacteria are important decomposers, breaking down matter and recycling chemical elements like carbon, nitrogen and sulfur. Bacteria have also been used to break down the hydrocarbons in petroleum and to remediate toxic wastes.

And these microscopic, rapidly-reproducing microorganisms are a critical tool in genetic research and biotechnology. Scientists can cause mutations in bacterial genes which help to determine genetic functions and this knowledge can be used to better understand more complex organisms. Bacteria have also been genetically engineered to produce a whole range of therapeutic proteins such as insulin and growth factors.

Bacteria generally exist in one of 3 shapes: the rod-like bacillus, the spherical coccus which sometimes is found in chains, and the corkscrew-shaped spirrulum.



BACTERIA AND HUMAN DISEASE

Although the vast majority of bacterial species are beneficial to the earth and to humans, a small number of species are **pathogenic** – they have the ability to cause disease. Some of these species are always pathogenic and some only become pathogenic under special circumstances. Tuberculosis, cholera, tetanus, botulism, Lyme disease, some sexually- transmitted diseases, and some food poisonings are just some of the bacterial infections that afflict humans.

How do bacteria cause illness? Some bacteria actually invade human cells and reproduce there. But most bacteria cause damage by secreting toxins which are substances that alter living cells or interfere with biological processes. Different

species of the streptococcal bacterium cause tooth decay, pneumonia, even "flesh-eating" disease. And certain strains of the bacteria that inhabit human intestines, *Escherichia coli* (*E.coli*) are also capable of harm.

Prior to the 1930's it was difficult for doctors to treat bacterial infections but then sulfa drugs were discovered and were the first successful antimicrobial drugs. Their mechanism of action is functioning as competitive inhibitors of enzymes (see **Lecture 9**).

Penicillin was the first **antibiotic** to be manufactured and used widely against bacterial infections. Such antibiotics, which are chemical compounds produced by microorganisms that kill other microorganisms, came into widespread use in the 1940s. Penicillin was produced by a fungus and was accidentally discovered by scientist Alexander Fleming. Since that fortuitous discovery many other antibiotics have been produced. Nowadays many antibiotics are semi synthetic.

The mechanism of action of the various antibiotics involves interfering with the synthesis of bacterial cell walls, or cell membranes, or bacterial enzyme activity.

Unfortunately in the 60 + years of antibiotic use, many bacteria have developed resistant strains. For example, *staphyloccus aureus* infections are resistant to so many antibiotics that people can die from the disease (MRSA).

Humans contribute to this serious problem by their misuse of these critical medications. Sometimes patients request antibiotics for illnesses like the common cold or influenza. These illnesses are caused by viruses and will not respond to antibiotics.

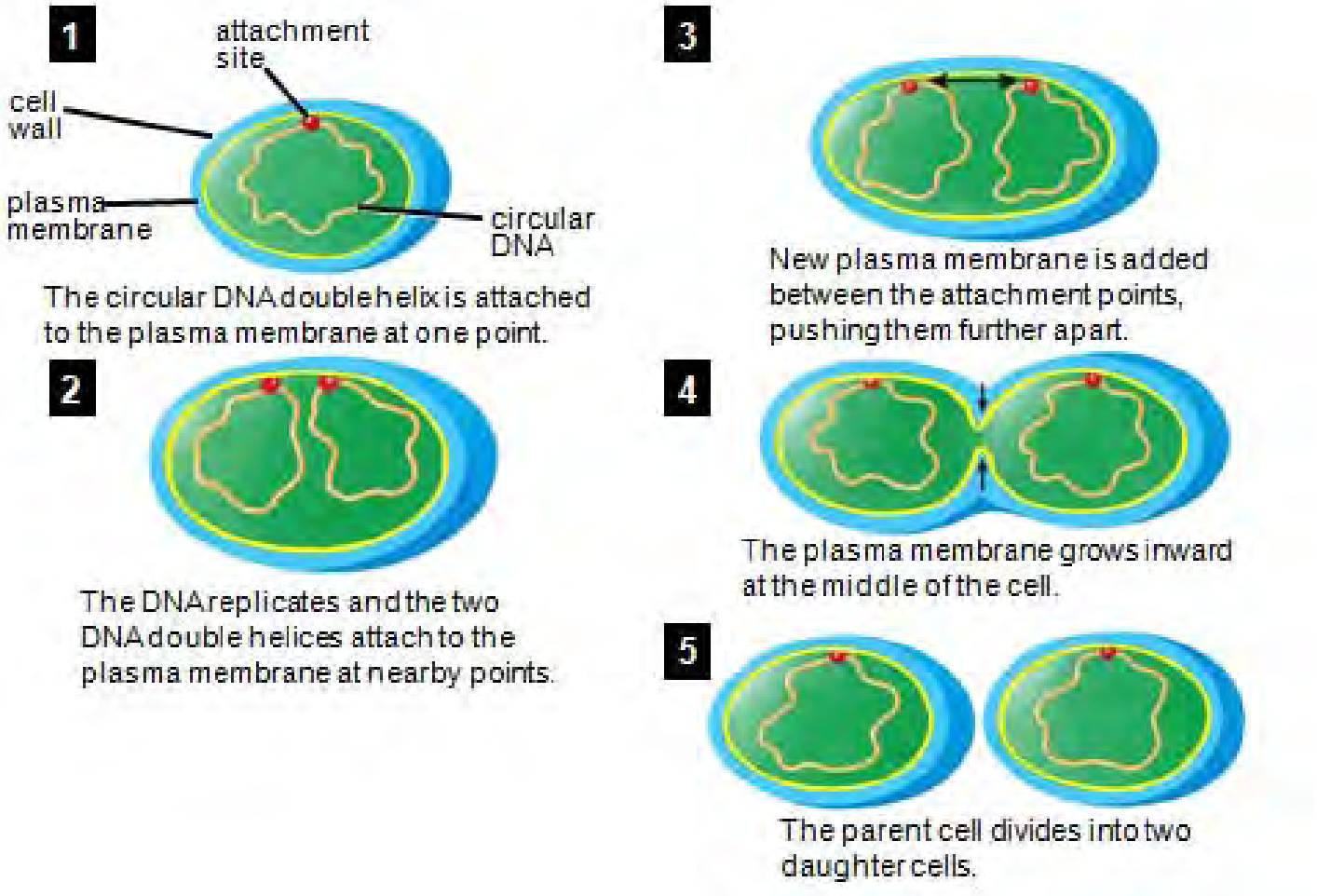
Other patients only take an antibiotic until they feel better. When an antibiotic is appropriately prescribed it should be taken as instructed, until all the medication has been consumed. This way the population of pathogenic bacteria will be greatly reduced and any that are resistant will be small in number and their growth will be held in check by competition from other bacteria.

The use of antibiotics in agriculture is another reason for antibiotic resistance. Their long-term use as additives to food for cattle, pigs, chickens, etc will also lead to selection for resistant strains as well as antibiotics moving through the food chain.

Antibiotics need to be administered appropriately to avoid a return to the days of old when bacterial infections were frequently life-threatening.

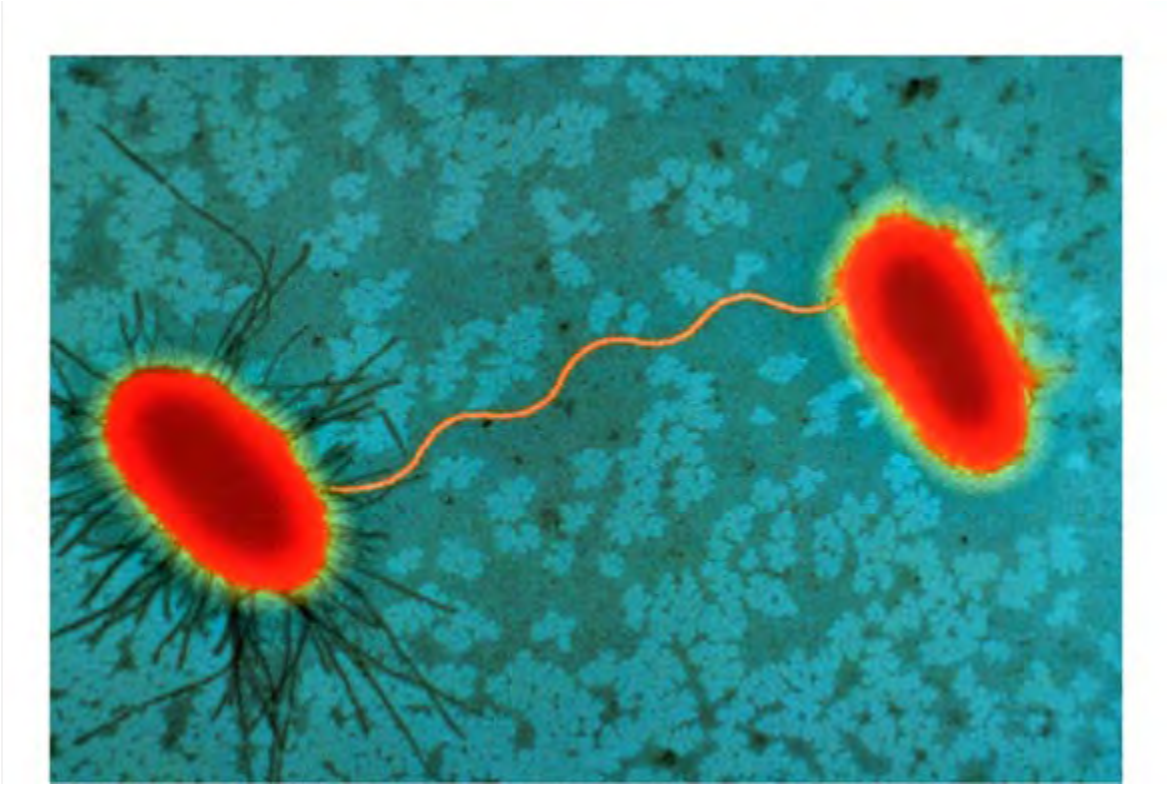
REPRODUCTION OF PROKARYOTES

Most prokaryotes reproduce asexually by binary fission. This is a type of cell division that is much simpler than mitosis (**Lecture 11**). The following figure outlines the steps involved in the replication of DNA, enlargement of the cell, and division into 2 identical daughter cells. Some bacteria can divide every 20 minutes meaning that millions can be produced in a matter of hours.



Plasmids

Besides their main chromosome, many bacteria have additional circular pieces of DNA called **plasmids**. Some of these plasmids contain genes that code for proteins that enable the bacteria to become resistant to antibiotics or change the level of toxicity. These plasmids can be transferred from one bacterial cell to another by a variety of means. One way is by **conjugation**, seen below. Here one donor bacterium develops a sex pilus and in this way can transfer genetic information to another bacterium. For example, genes that code for resistance proteins can be passed on in this way even between bacteria of different species.



LECTURE 9; ENERGY AND CHEMICAL REACTIONS

Energy

For most living things, the ultimate source of energy is the sun. Most organisms including humans cannot extract energy from the sun directly but solar energy can be converted into forms of chemical energy that humans can use.

Energy is defined as the ability to do work and it exists in many forms such as heat, sound, solar, electricity, chemical, and more.

All energy exists in 2 states: potential and kinetic.

Potential energy is stored energy or the capacity to do work that results from an object's position. An apple is a form of stored energy as is water behind a dam or a person on a bike at the top of a hill.

Kinetic energy is the energy of motion. Pushing the pedals on the bike is a form of kinetic energy (a contracting muscle) as is a moving car or a buzzing bee.

Energy in food is measured in calories. A calorie is defined as the amount of energy required to raise 1 gram of water 1 degree Centigrade. Food energy is measured in kilocalories (Calorie written with uppercase C) is defined as the amount of energy required to raise 1 kilogram of water 1 degree Centigrade.

Much of the work of living organisms involves changing potential energy into kinetic energy. For the muscle contractions necessary for pushing the bicycle pedals potential energy in the food eaten must be extracted and converted to kinetic energy.

LAWS OF THERMODYNAMICS

All the energy changes in the universe are governed by 2 laws of thermodynamics:

The First Law of Thermodynamics also called the Law of Conservation of Energy, states that energy can neither be created nor destroyed. However, energy can be converted from one form to another, from the chemical energy stored in the bonds of food to the kinetic energy necessary to push the pedals on the bicycle, for example.

The Second Law of Thermodynamics states that the amount of useful energy always decreases when energy is converted from one form to another. Another way of expressing this law is to state that the amount of energy available for work always decreases. In any energy transformation some of the energy will move to a less useful form although the amount of energy doesn't change. This less useful form or lowest form of energy is usually heat energy which is the most easily dispersed or most difficult form of energy to concentrate. So, although the quantity of energy in the universe is not changing, the quality is.

The tendency for a system to become less orderly or more random is referred to as **Entropy.** The greater the disorder in a system, the greater the entropy.
A simple example of this is your bedroom which will become more and more disorganized unless you are willing to invest some **energy** to restore order. The bedroom will ***not*** move to a state of order by itself.

Above is an example of the second law of thermodynamics. Only $\frac{1}{4}$ of the energy stored in the chemical bonds of gasoline is converted to kinetic energy in moving the car. $\frac{3}{4}$ of the energy moves to a lower form of energy – heat.

All living things require energy to do the work of staying alive. All living things are made of cells and each cell requires energy to maintain order and to do the work of the cell such as secreting a hormone or contracting a muscle.

If all the energy comes from the sun and humans cannot directly harness solar energy directly, how do human cells get energy?

The answer is that other organisms, primarily green plants, capture solar energy for us and with CO_2 and H_2O, convert solar energy into chemical energy and store that energy in the covalent bonds of carbohydrates, fats, and proteins. This process involves a series of chemical reactions called **photosynthesis**

Humans get energy by eating plants or by eating animals that have eaten plants and so have access to the stored chemical energy in the covalent bonds of organic molecules. The process whereby cells extract the energy from the chemical bonds is another series of chemical reactions called **cellular respiration – Lecture 10.**

A LOOK AT ENERGY AND CHEMICAL REACTIONS

Energy Transfer in Chemical Reactions

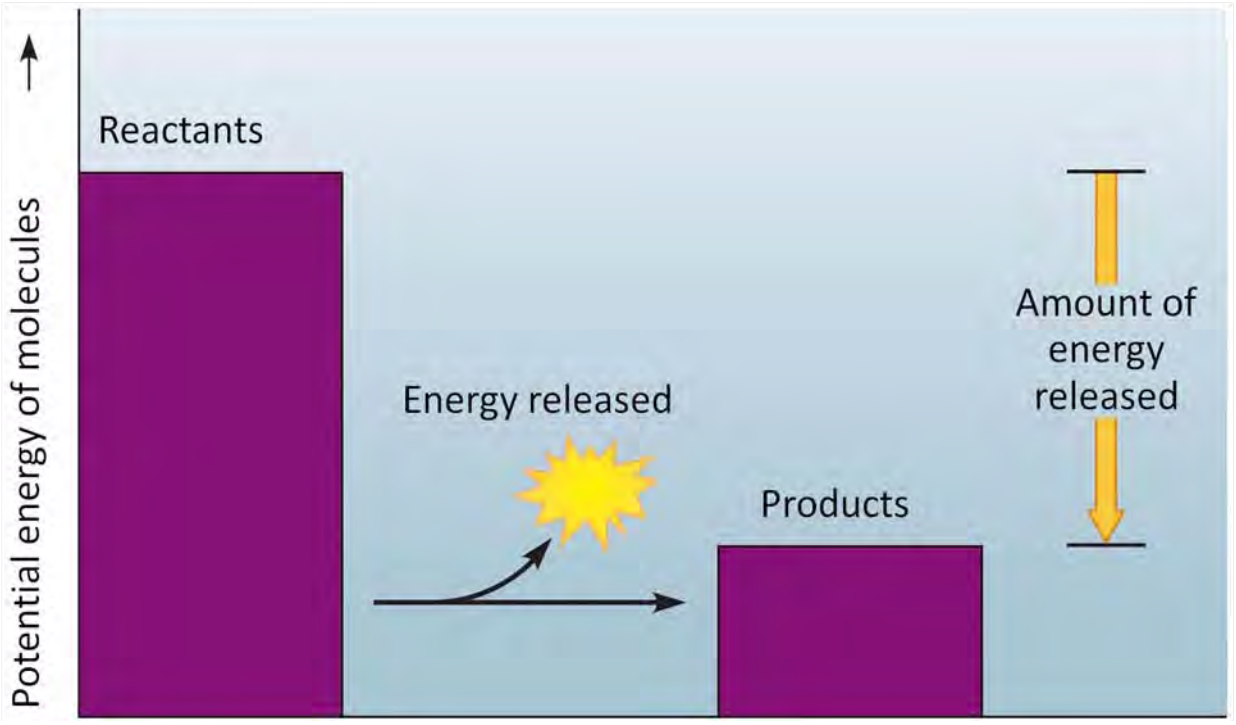
Energy is released and stored in chemical reactions. **Reactants** are the molecules entering into a chemical reaction. When the reactants undergo a chemical change, resulting in new bond formation, the changed reactants are now called **products.**

In the reaction A + B ---→ AB A and B are the reactants, AB the product.

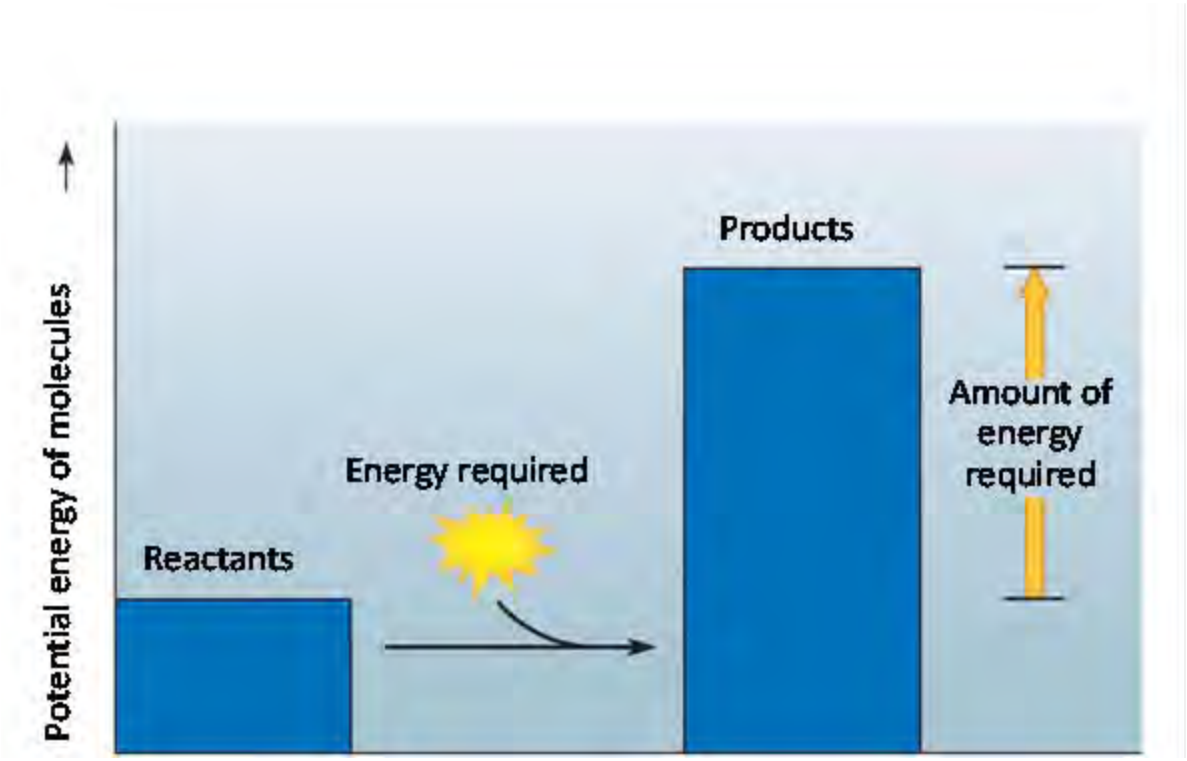
Activation energy

All chemical reactions require activation energy to get started. Activation energy helps break or destabilize chemical bonds, excites electrons, or overcomes repulsion so molecules can get close enough to react. **In summary, activation energy allows the reaction to go.**

Forming new bonds requires energy & breaking old bonds releases energy. **Exergonic reactions** are chemical reactions that release energy. These types of reactions release the energy in the covalent bonds of the reactants. **Cellular respiration (Lecture 10)** is a series of reactions that release energy. **Exergonic reactions release more energy than they absorb.**



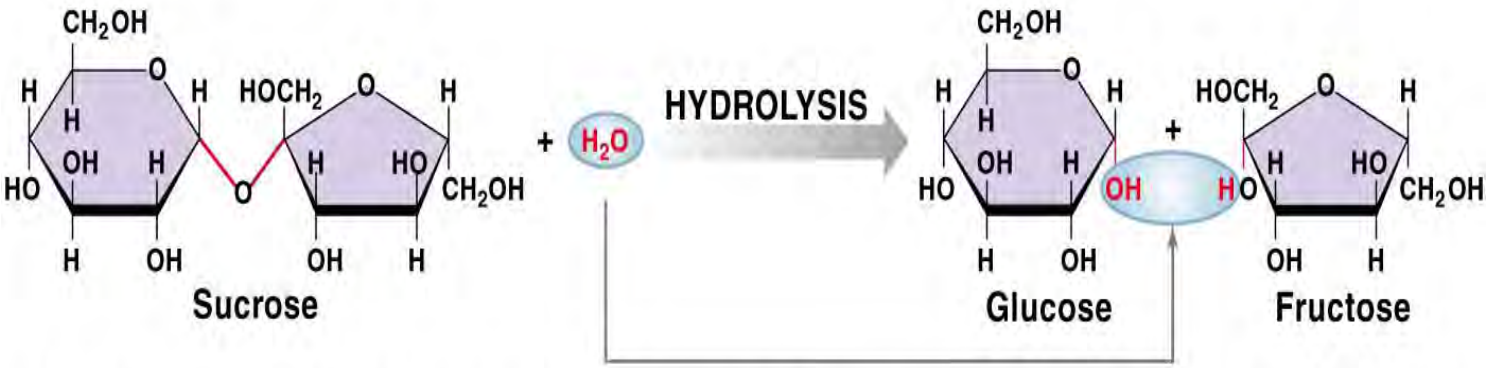
Endergonic reaction requires an input of energy and yield products rich in potential energy. The reactants contain little energy in the beginning, but energy is absorbed from the surroundings and stored in covalent bonds of the products. **Photosynthesis** (mentioned earlier) makes energy-rich sugar molecules using the energy of sunlight.



Exergonic reactions proceed spontaneously. For example, the breakdown of glucose and other organic molecules in cells are exergonic reactions. These are catabolic reactions of which there are several types.

CATABOLIC REACTIONS also called DECOMPOSITION REACTIONS

In catabolic reactions, large molecules are split into smaller atoms, ions, or molecules usually by **Hydrolysis;** the addition of water is involved in the reaction. These reactions are exergonic since they release more energy than they absorb. Good examples are the breakdown of polysaccharides or disaccharides to monosaccharides (see below), triglycerides to glycerol and fatty acids, and protein to amino acids.

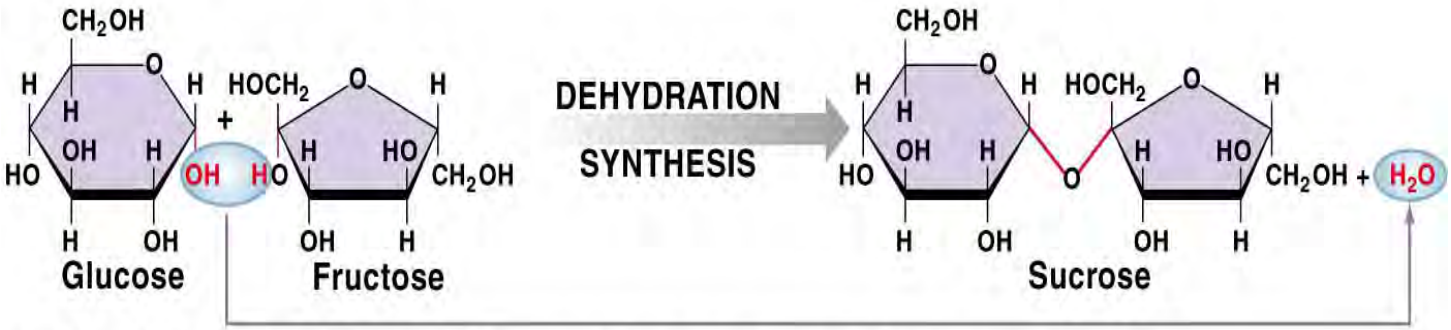


Hydrolysis reverses the steps of dehydration synthesis; a complex molecule is broken down by the addition of a water molecule

Endergonic reactions do not occur spontaneously. In an endergonic reaction, the **product** contains more energy in its chemical bonds that the **reactants**. Reactions which use energy to build complex molecules from simpler molecules are called **anabolic** reactions.

ANABOLIC REACTIONS also called SYNTHESIS REACTIONS

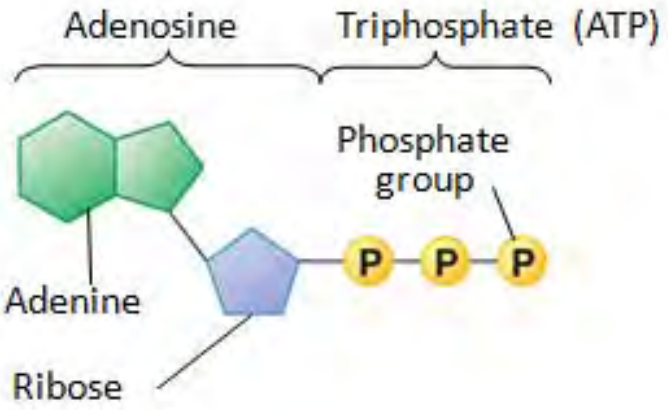
In Anabolic reactions two or more atoms, ions, or molecules combine to form new & larger molecules
These reactions are also called **Dehydration Synthesis or Condensation reactions,** because a molecule of water is removed. They are usually endergonic because the reactions absorb more energy than they release.
Again, good examples are the organic molecules – this time the **joining** of monomers to make a polymer. For example, joining 2 monosaccharides to form a disaccharide as seen below is a dehydration synthesis reaction – note the removal of one molecule of water.



(During dehydration synthesis, two molecules are joined by the removal of a water molecule

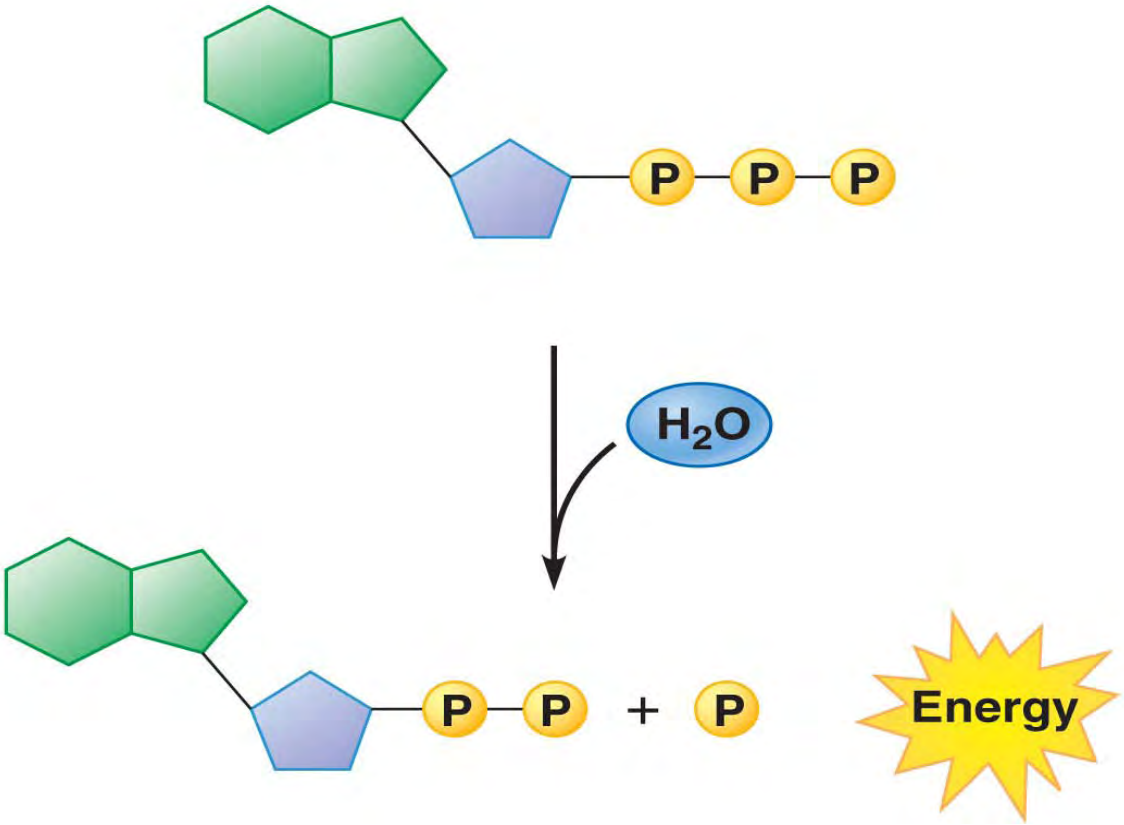
Much of the work that cells do requires energy. But, although the energy from the sun has been changed into the chemical energy in the bonds of food molecules such as carbohydrates, lipids, and proteins, none of this energy can be used directly to fuel chemical reactions in cells. Instead the energy released from these molecules must be captured in the bonds of a nucleotide-based molecule mentioned in **Lecture 5**, called **ATP**.

Adenosine **Tri**phosphate (**ATP**) is a nucleotide based molecule; it has the sugar ribose, the nitrogenous base adenine, and 3 phosphate groups.



The bonds between the phosphate groups are high energy bonds – each bond contains a large amount of energy and is unstable i.e. it will release the energy easily.

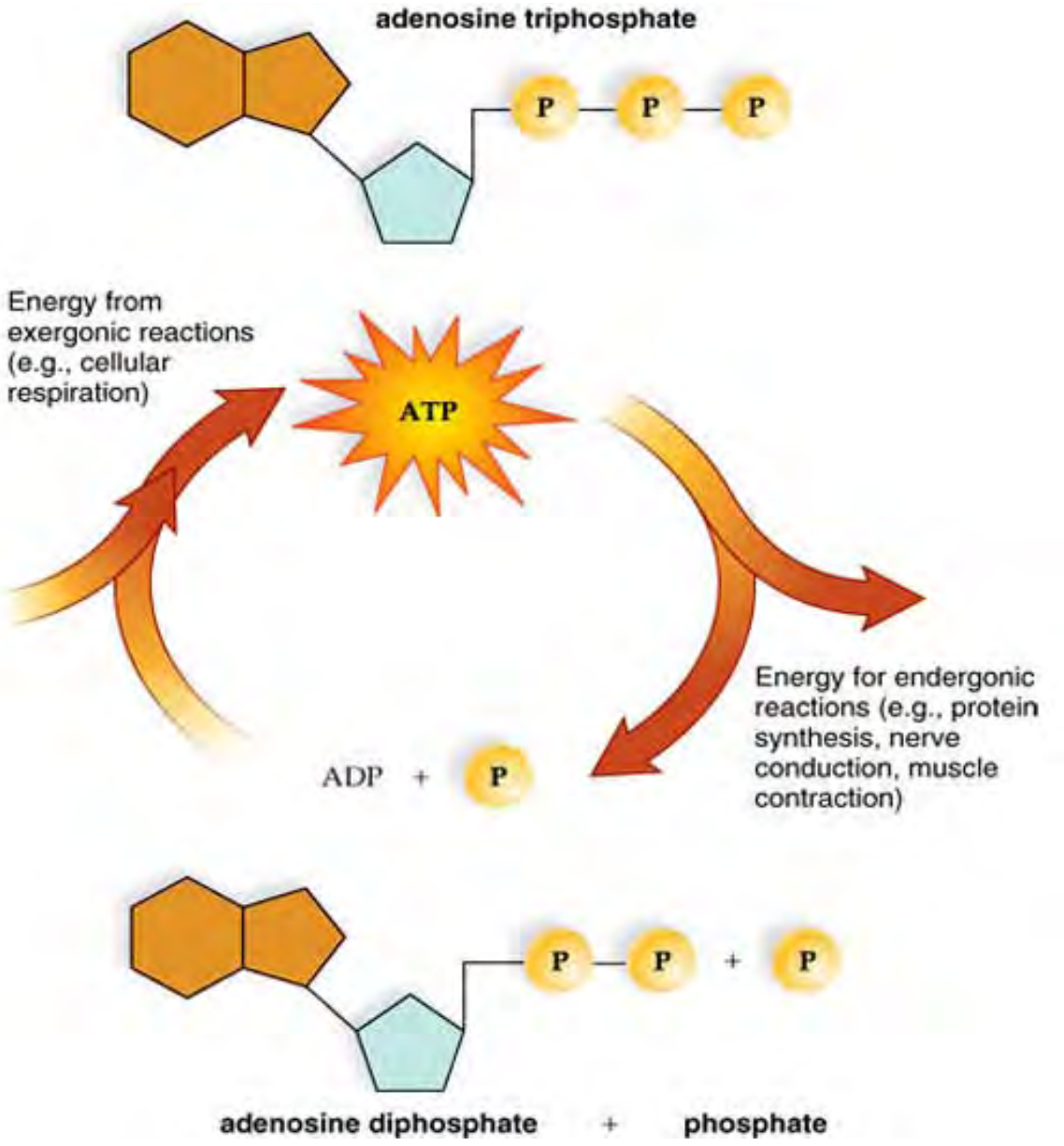
ATP ------→ ADP AND P



When energy is needed in a cell ATP is broken down to ADP and P and the energy is released to do work.

Reactions involving the making and breaking of these bonds take place constantly in cells.

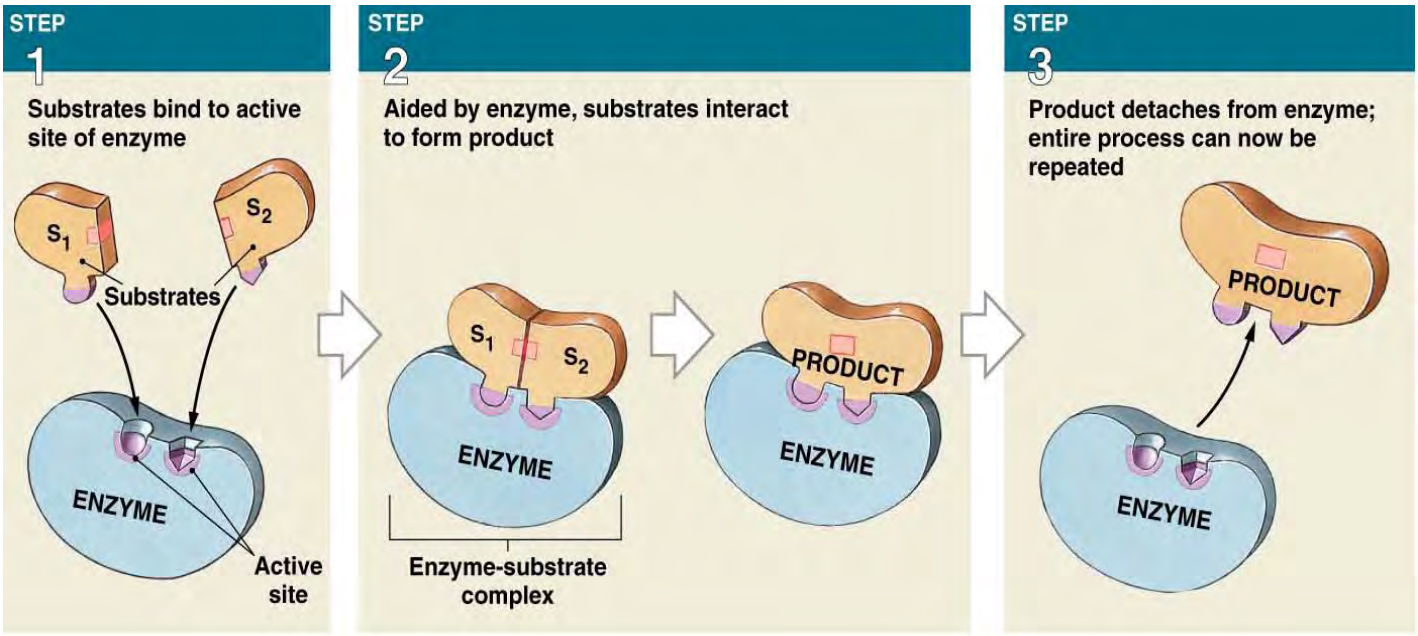
Human metabolism couples exergonic and endergonic reactions, so that the energy released from one reaction will drive the other.



On one side the energy from exergonic reactions such as the breakdown of carbohydrates, fats, or proteins is stored between the last 2 phosphate groups in ATP – stored for a very short period of time. It is quickly used to power reactions that *require* energy such as muscle contraction.

ENZYMES

As stated earlier, chemical reactions require activation energy to get started. For reactions to occur at a speed necessary for life, some help is needed to reduce the activation energy required. This help is provided by very important molecules present in all cells – no organisms can survive without them. These essential molecules are **ENZYMES** – types of protein molecules that catalyze chemical reactions. (A few enzymes are RNA molecules but the enzymes involved in metabolic pathways are protein enzymes.)



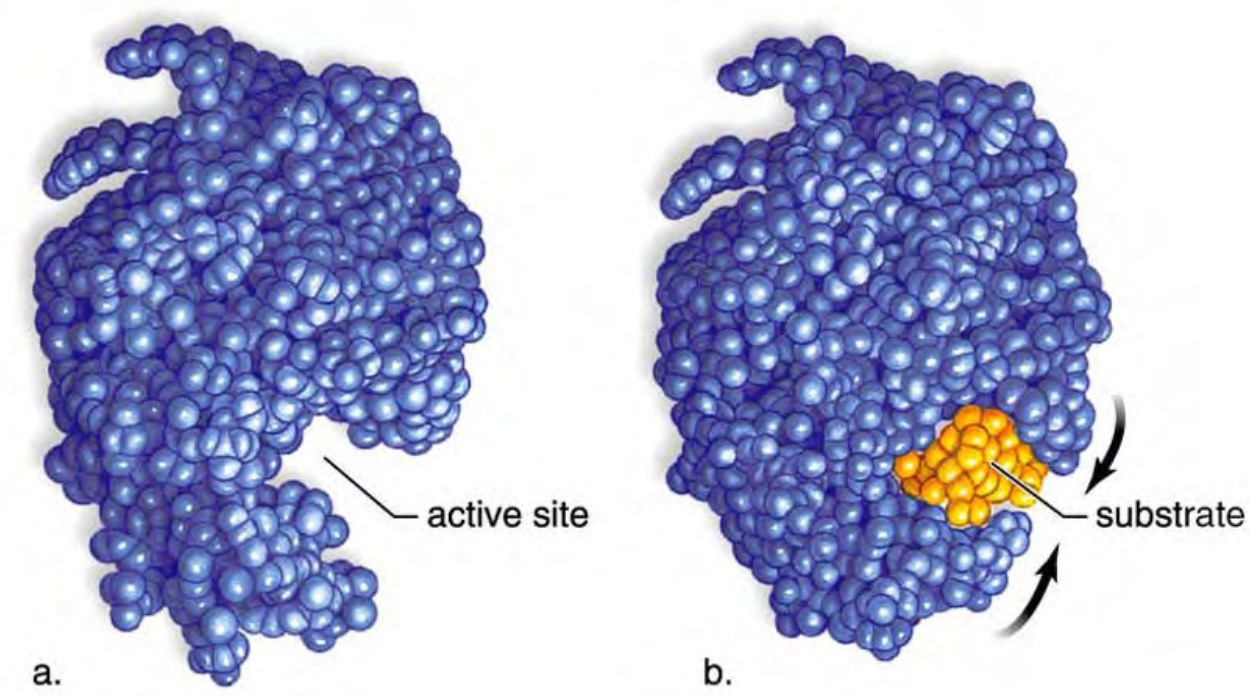
Enzymes bind substrates at active sites, which bring the substrates together.

Take the example of the synthesis of lactose, a disaccharide made from one molecule of glucose and one molecule of galactose. Above, S_1 and S_2 represent glucose and galactose. These reactants bind to the enzyme **lactase*** at active sites that are specific for these substrates. The enzyme – substrate complex adjusts its shape and a bond forms between the substrates and the product lactose is formed.

***Note: Enzyme names often start with part of the product or substrate name and **ase** on the end.

Structure of Enzymes

Enzymes are proteins that have a particular shape, usually globular. They are made of thousands of amino acids but only a few hundred of these are actively involved in binding with the substrate, forming the **active site**. Enzymes are very specific and are usually designed so that they can only bind one particular substrate. The enzyme itself is not permanently changed in the reaction and is used over and over again. Therefore the structure of enzymes is critical and must be maintained for the specific reaction to occur.



Enzymes can work very fast catalyzing up to 100,000 reactions per second.

Factors that affect the structure and activity of enzymes.

As has been stated several times most enzymes are proteins and are therefore subject to denaturation (**Lecture 5**). There are several factors that may affect the activity of an enzyme.

1. Temperature

The white of an egg is primarily albumin which is a protein. The structure of this protein is permanently changed when subjected to excess heat such as when frying. So too will the nature of the majority of proteins be changed by dramatic changes in temperature. At temperatures colder or warmer than an enzyme's normal range the bonds between the amino acids may change thereby changing the shape of the active site and preventing the substrate from binding, stopping the reaction.

Increases in temperature can initially speed up the rate of reaction but when the temperature gets too high it causes denaturation of the protein structure of the enzyme and limits the reaction.

A decrease in temperature will slow down the rate of reaction but if the temperature gets too cold the reaction may stop completely.

2. pH

Enzymes work best within a specific pH range. Most enzymes in the human body, for example, work best at a pH close to 7.

Just as for temperature, changes in pH will also denature the enzyme.

3. Salt conditions

Salt ionizes in a water environment and the ions can interfere with bonding at various places on enzymes.

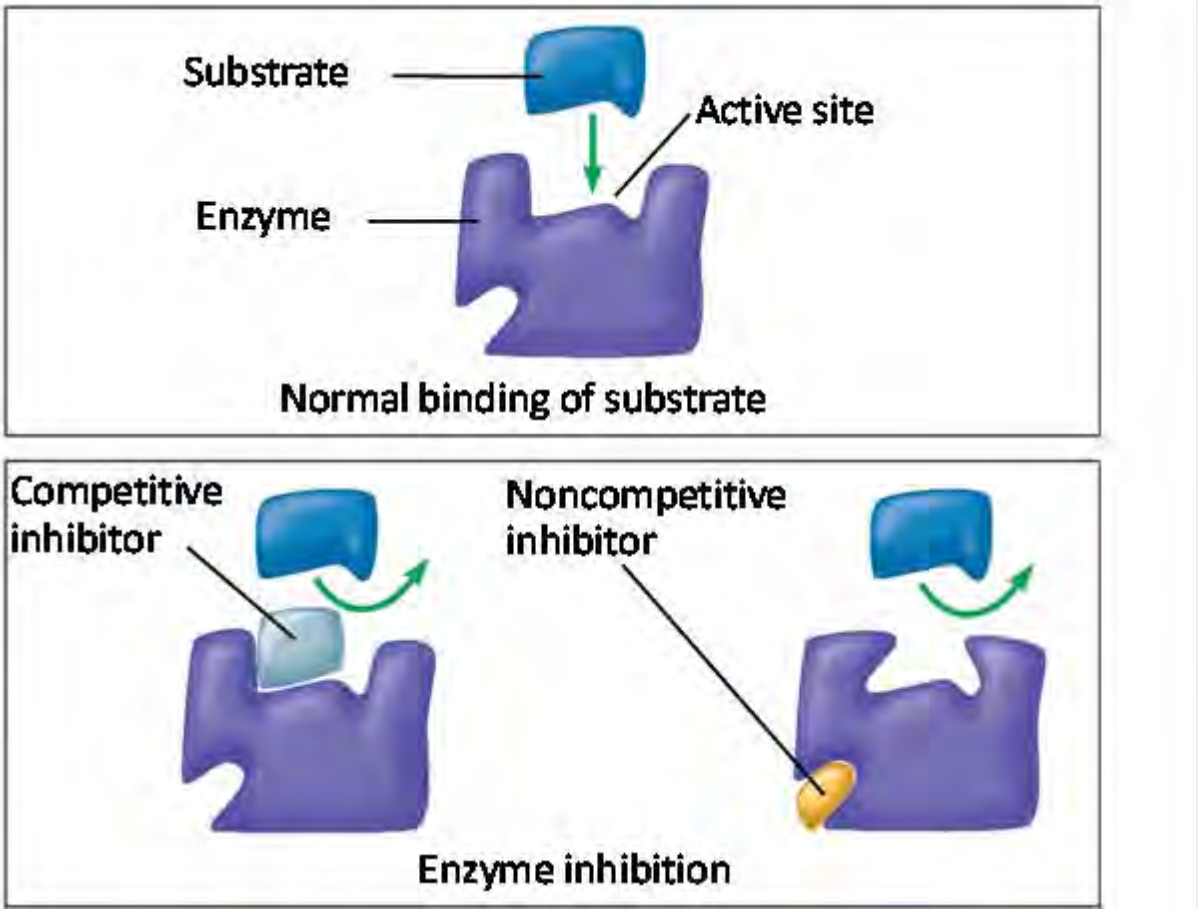
4. Enzyme Helpers

The activity of an enzyme is also affected by **"enzyme helpers" or cofactors.** These are usually vitamins or metal ions such as zinc, copper, or iron that bind to the enzyme and facilitate the reaction. For example, NAD and FAD, important coenzymes in metabolic pathways such as photosynthesis and cellular respiration, are derived from B vitamins.

Regulation of Enzyme Activity

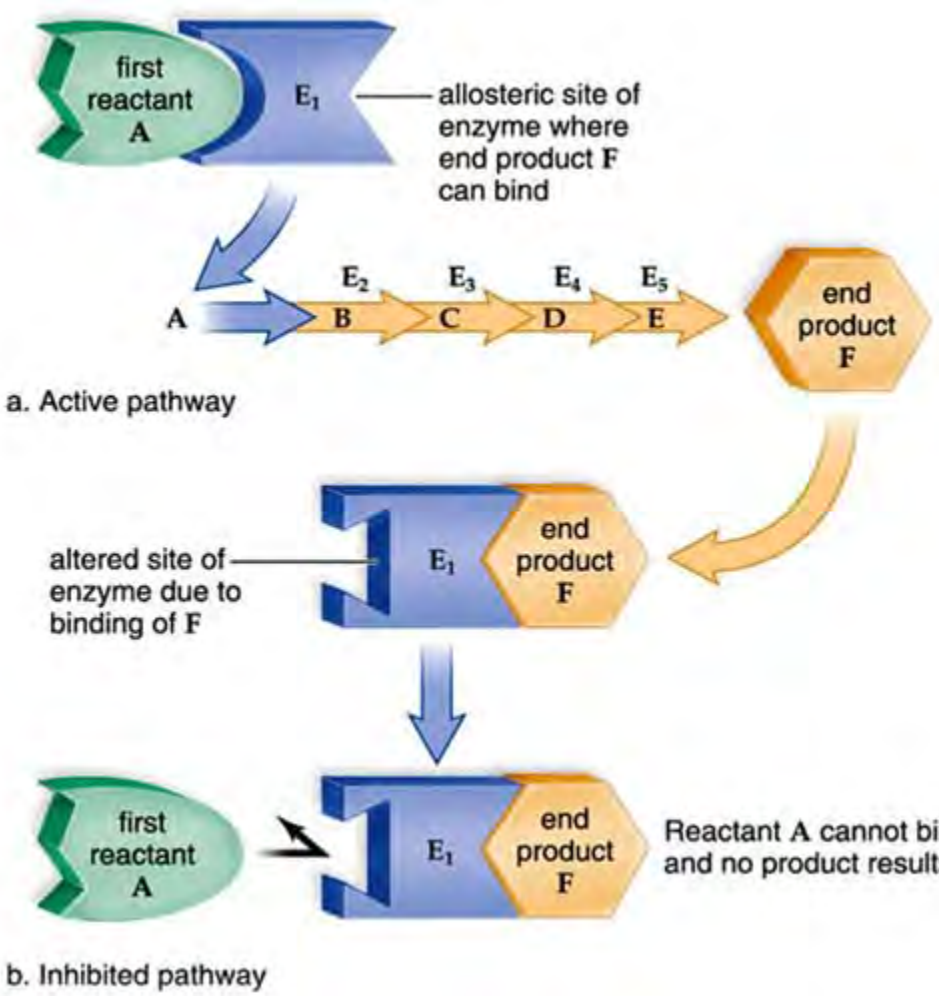
Organisms conserve energy by regulating the activity of enzymes. For example, if a metabolic pathway results in the production of an amino acid the cell will inhibit activity of the pathway by inhibiting an enzyme if the cell already has enough of the product.

How do cells limit enzyme activity?
An inhibitor often competes for the enzyme's active site and thus it blocks the substrate from entering the active site.
These types of inhibitors are called **competitive inhibitors** because they are competing with the substrate for the active site.



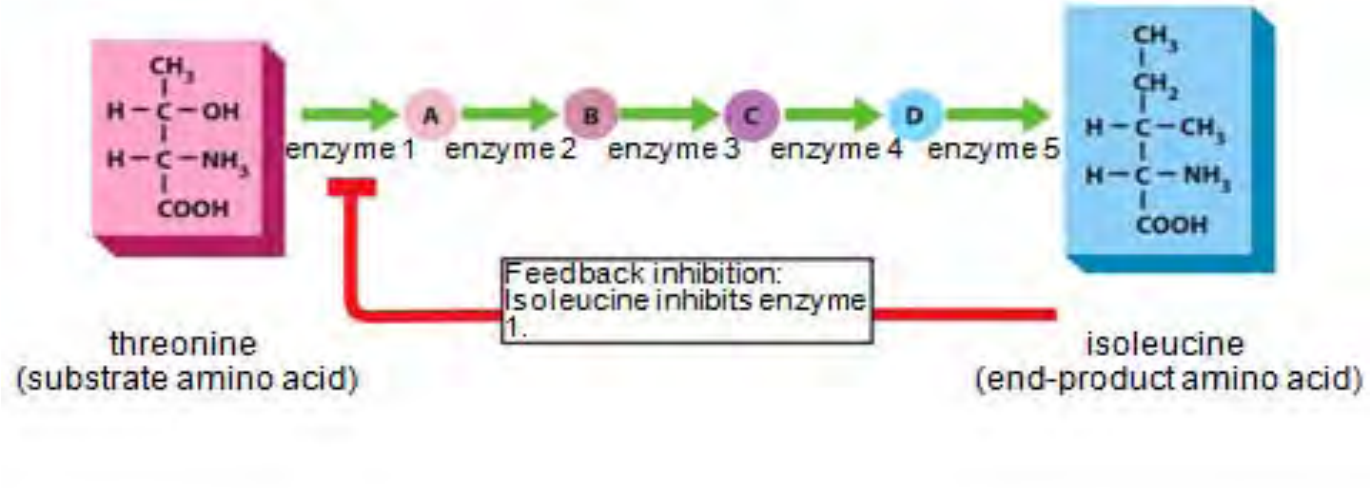
A **non competitive inhibitor** binds to another site on the enzyme but changes the structure of the active site so that the enzyme can no longer bind its substrate. This is sometimes called an **allosteric inhibitor**.

Another method of inhibition occurs when the product of a metabolic pathway itself acts as an inhibitor of the pathway by inhibiting one enzyme in the pathway. This mechanism is called **feedback inhibition**



When enough product F is available, the cell no longer wants to waste energy making more. Production is stopped when F binds to an allosteric site on the enzyme changing the shape of the active site so that the first reactant in the pathway cannot bind and the whole pathway comes to a halt.

Another example of feedback inhibition



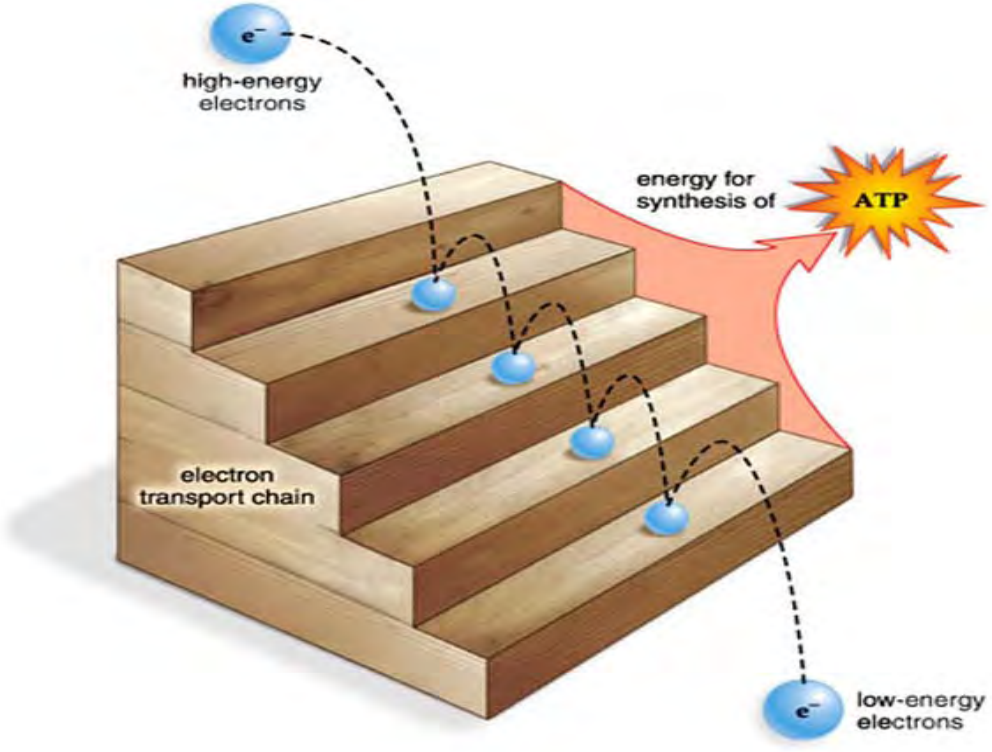
This shows the pathway for blocking the production of isoleucine, the example mentioned at the top of page 14. The metabolic pathway for making isoleucine has 5 steps, each one involving a specific enzyme. If any enzyme in the pathway is blocked the pathway comes to a halt. This diagram shows the inhibition of enzyme 1 so there will be no product A and no next step.

LECTURE 10: METABOLIC PATHWAYS AND REDOX REACTIONS

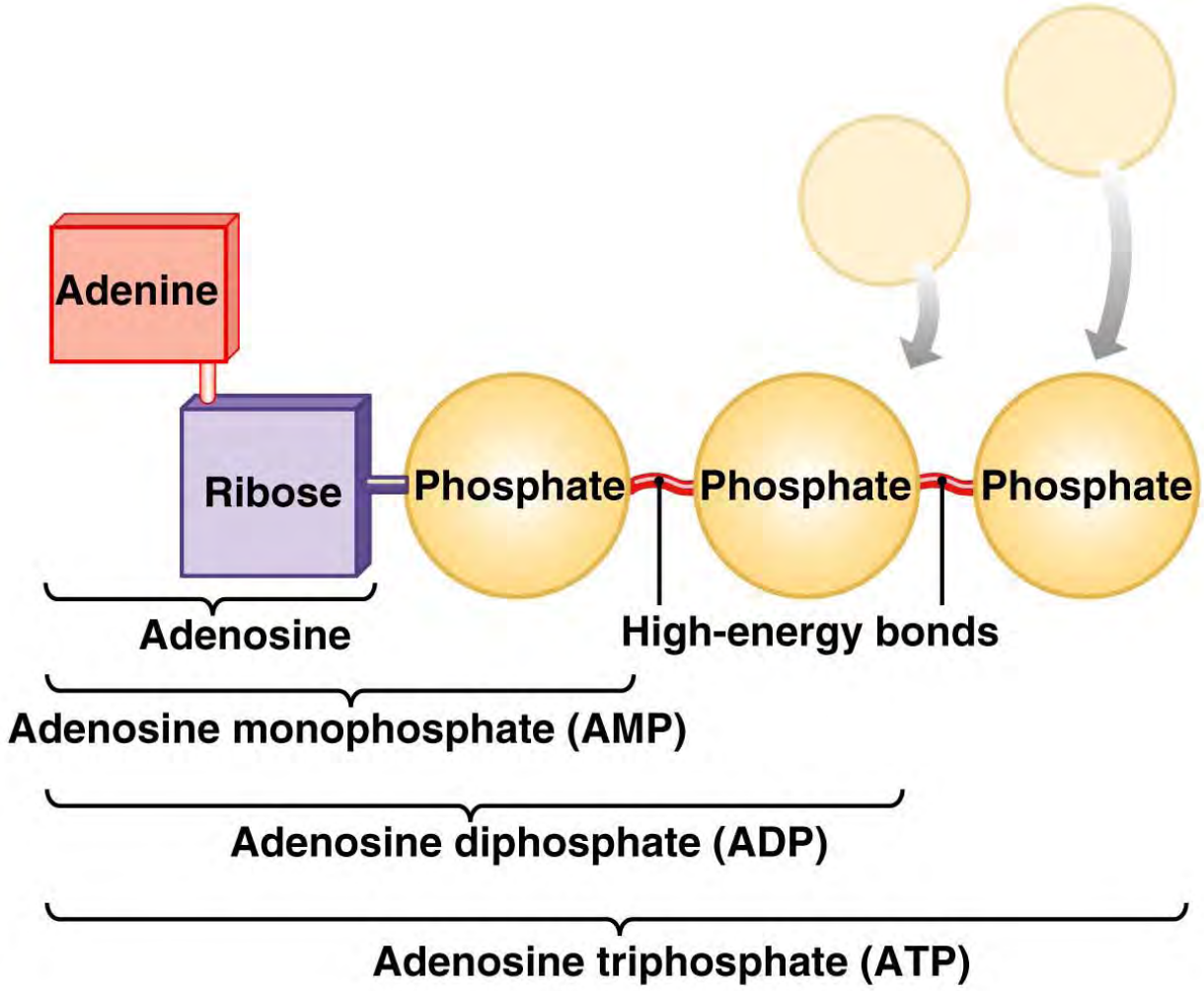
Oxidation Reduction Reactions

A transfer of an electron involves the transfer of the energy of that electron. Some substances attract electrons more strongly than others. When substance A loses an electron to substance B, substance A is said to be **oxidized** and substance B **reduced**. (It doesn't seem to make sense that the substance that gains electrons is considered reduced, but remember that electrons carry negative charges so substances that gain electrons lose some of their positive charge so in that sense they are reduced.)
If one substance is oxidized another must be reduced so this **red**uction-**ox**idation process is sometimes referred to as a **Redox Reaction**.

We see redox reactions occurring all the time. When metal rusts it is oxidized – it has lost electrons to oxygen. When an apple turns brown when cut, the same thing has happened – it has lost electrons to oxygen. In these examples the metal and the apple (or the glucose in the apple) have lost electrons, therefore they have been oxidized and oxygen, which has accepted the electrons, is reduced.
Oxygen is the **oxidizing agent** – it has "pulled" the electrons from the metal and the glucose and become reduced. The molecule that has "donated" the electrons (the metal or the apple) is described as the **reducing agent**.



As the previous image depicts, electrons lose energy as they are "bounced" along in a series of redox reactions. This occurs in cellular respiration. Electron transport chains that function to transfer electrons in this way are very important in cellular respiration where the purpose of metabolic pathways is to extract energy in a series of small steps and use it to form a high energy bond between the last 2 phosphate groups in ATP.



The second high-energy bond between the 2nd and 3rd phosphate groups is the bond that is broken to release energy when a cell needs energy to do work. In all cells, this bond is continually being broken and reformed. All cells are constantly carrying out the following reactions: ATP <--------→ ADP + P Note that the reaction going both ways.

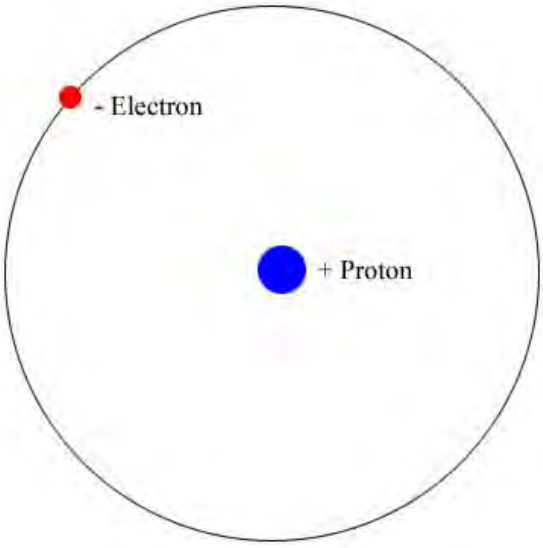
ENERGY EXTRACTION IN CELLS

Cells can get energy from carbohydrates, lipids, and proteins, as mentioned in **Lecture 5**. The most important small molecule from which cells extract energy is the carbohydrate glucose. When summarizing the steps of cellular respiration it is traditional to use glucose as the prototype. At the end of the discussion, how cells extract energy from other organic molecules is summarized.

In a cell, when glucose is broken down in cellular respiration to release the energy stored in its bonds, and uses that energy to phosphorylate ADP to make ATP a series of redox reactions are involved. Remember a cell can only use energy through ATP.

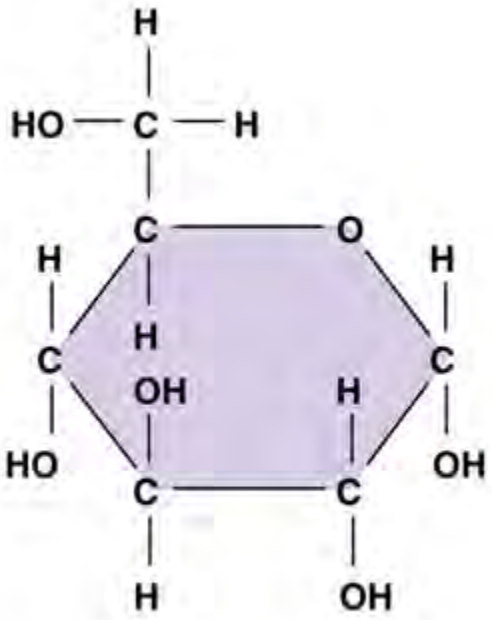
All 6 carbon atoms in glucose donate electrons which are eventually accepted by O_2.**Therefore glucose is oxidized and oxygen is reduced in these reactions.**

Besides oxygen, there are 2 very important **electron acceptors or electron carriers** in cellular respiration: - NAD^+ (nicotinamide adenine dinucleotide) and **FAD** (flavin adenine dinucleotide). Each NAD^+ can accept 2 electrons and a hydrogen ion, becoming **NADH.** Each FAD can accept 2 electrons and 2 hydrogen ions, forming **$FADH_2$. NADH and $FADH_2$ are the reduced forms of these electron carriers.**
Sometimes an electron is bound up in a hydrogen atom but remember that a hydrogen atom is a single electron bound to a proton. In transferring a hydrogen atom a molecule is still transferring an electron.



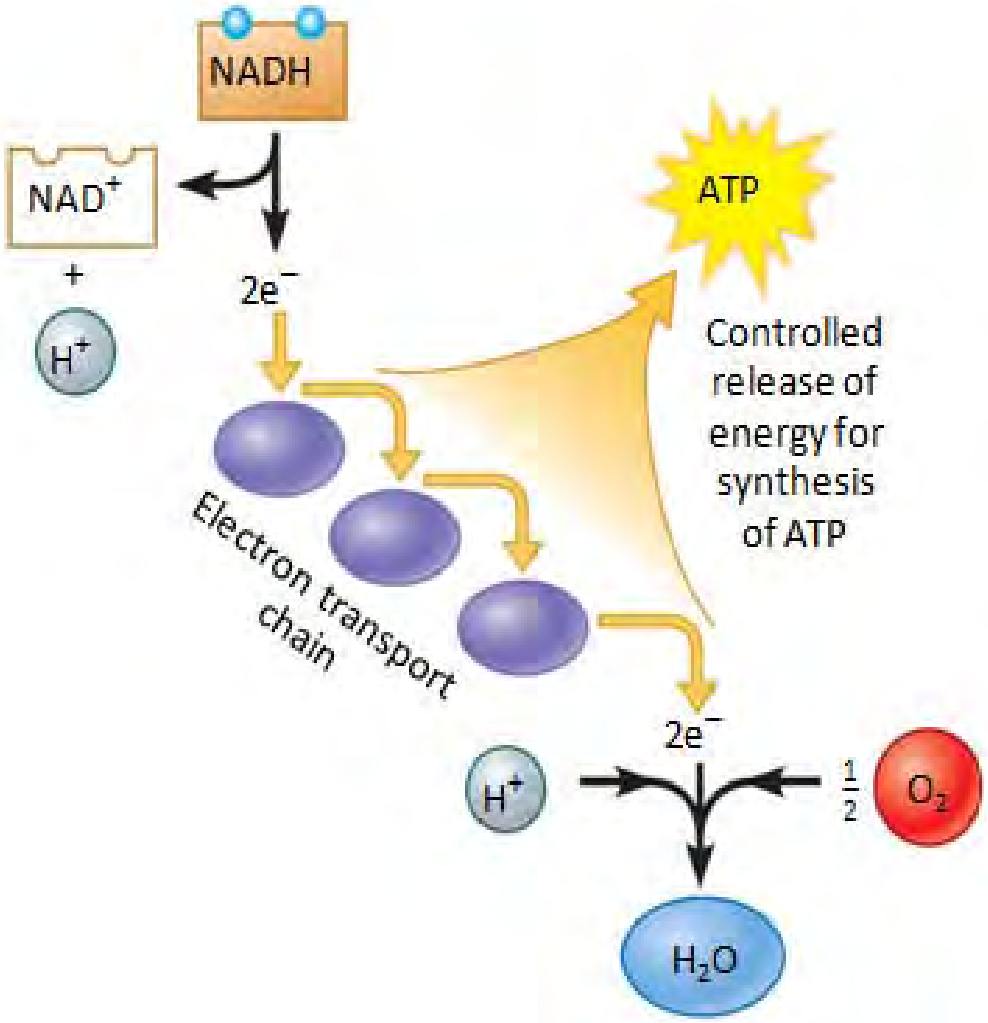
A Hydrogen Atom

There is a lot of energy in the bonds of a glucose molecule.



Think of cellulose, a polymer of glucose, and a major component of wood. When wood is burned, oxidation reactions occur, releasing a large amount of energy as heat energy. Cells also release energy from glucose to form ATP but cells do it differently (although sometimes the term "burning" is used with respect to using calories).

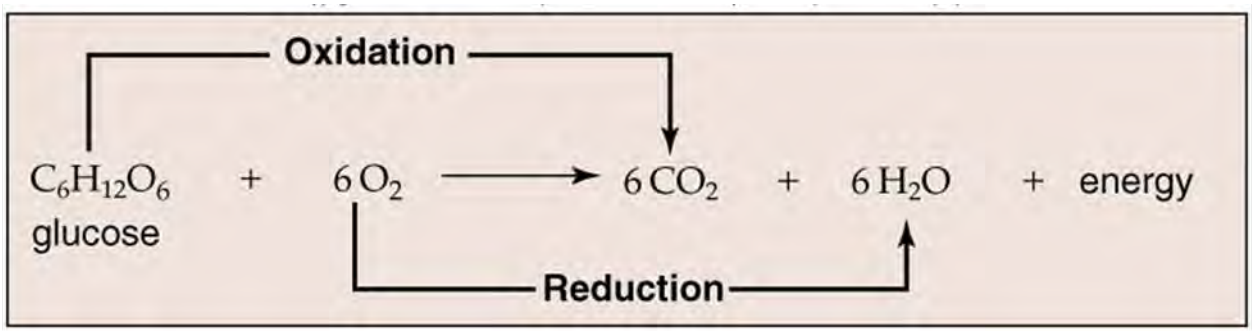
The major difference in cells releasing energy from glucose and the burning of wood for heat energy is this; in burning wood, the energy is released all at once, in cells the reactions occur in small steps which allow cells to capture the energy in small amounts in a very controlled fashion.


NADH
NAD+
+
H+
2e−
ATP
Controlled release of energy for synthesis of ATP
Electron transport chain
2e−
H+
½
O2
H2O

CELLULAR RESPIRATION

As mentioned earlier, cells can metabolize carbohydrates, lipids, and proteins for energy. However it is standard to use the metabolism of glucose (a small carbohydrate) as an example of how cells extract energy from an organic molecule. At the end of this unit we will see how the metabolic pathways of other organic molecules are a variation on the metabolism of glucose.

A summary of the basic chemical reaction shows that cells extract energy from glucose by breaking the bonds between the carbon atoms and transferring the energy from those bonds to the high-energy bonds of ATP.



As you can see this involves a series of redox reactions where hydrogen atoms are removed from glucose and donated to O_2 – in other words, glucose is ***oxidized*** and O_2 is ***reduced***. The energy is used to add phosphate groups (phosphorylate) to ADP to make ATP.

We humans and other animals eat food and digest it in our gastrointestinal tracts. This means that large polymers like carbohydrates and proteins get digested or broken down to smaller monomers like glucose and amino acids. These smaller molecules get absorbed into our bloodstream and delivered to every cell of the body where the molecules either diffuse in or are transported into the cells. Once in the cell the molecules are catabolized further and the energy released is used to make ATP – the only form of energy that cells can actually use.

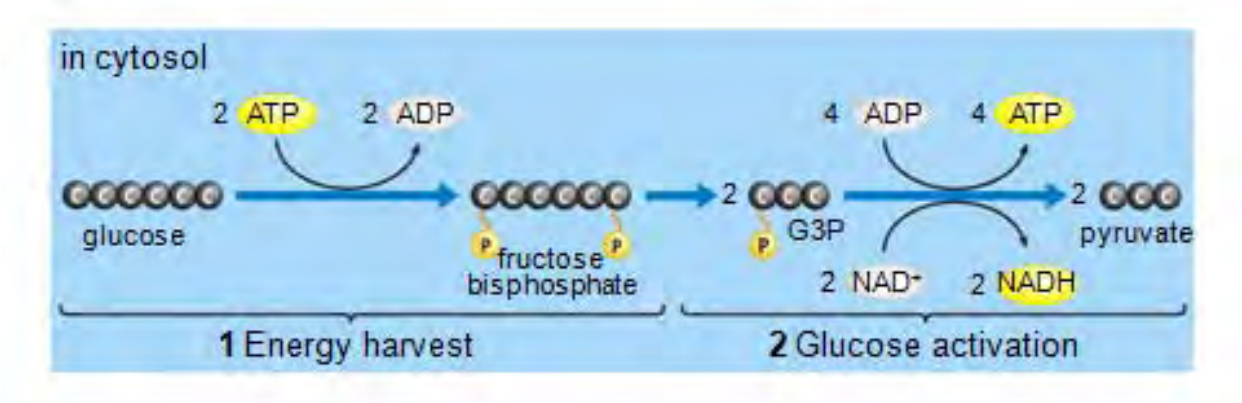
CATABOLISM OF GLUCOSE

The complete catabolism of glucose has 4 basic steps:

1. **Glycolysis**
2. **Preparation or Transition Step**
3. **Citric Acid Cycle**
4. **Electron Transport Chain & Oxidative Phosphorylation**

1. Glycolysis - The word means the splitting (lysis) of glucose and it is the first step all organisms on the planet take in breaking down food molecules and involves a series of **10 reactions.**

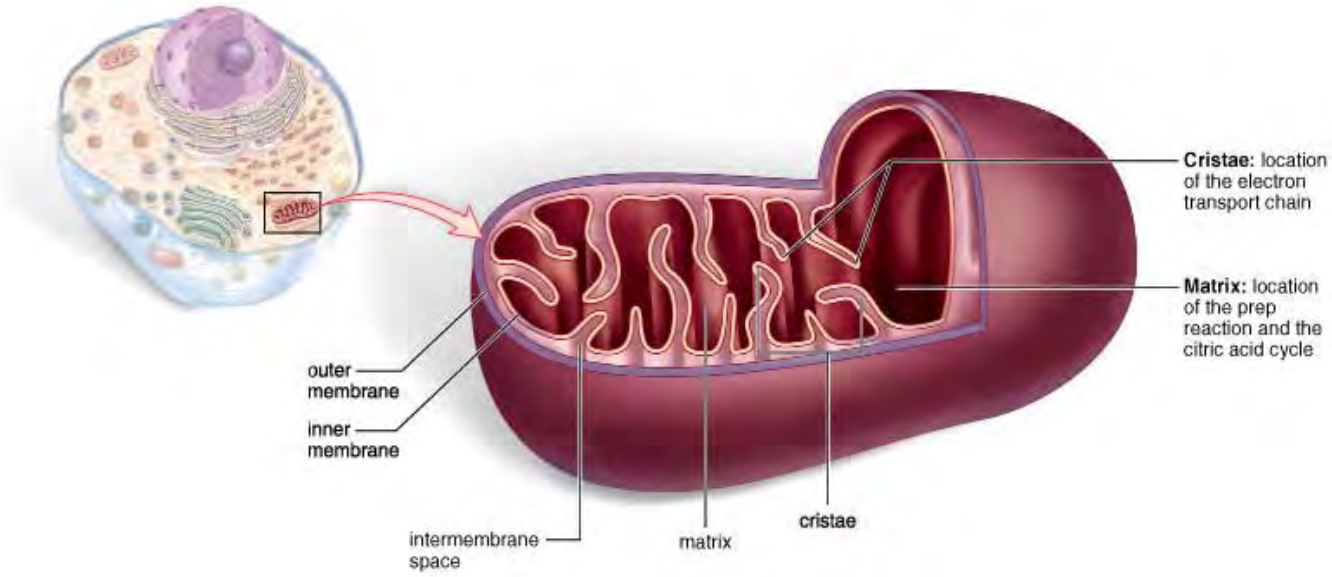
The first reactions use 2 ATP to get the reaction going – really to destabilize the glucose molecule so it can be broken down more easily. The 6- carbon molecule is now split in two and the remaining reactions extract energy and form 4 molecules of ATP and 2 NADP. The original carbon, hydrogen, and oxygen atoms in glucose end up as 2 molecules of pyruvate.



As depicted on the previous page, **at the end of glycolysis the cell has gained 2 ATP molecules** which can be directly used by the cell to do work.

For many single-celled organisms such as yeast and bacteria (or in other cells when oxygen is not available), glycolysis is sufficient to meet energy needs in cells. Also, glycolysis takes place in the cytoplasm of cells so does **not** require any specialized organelles.

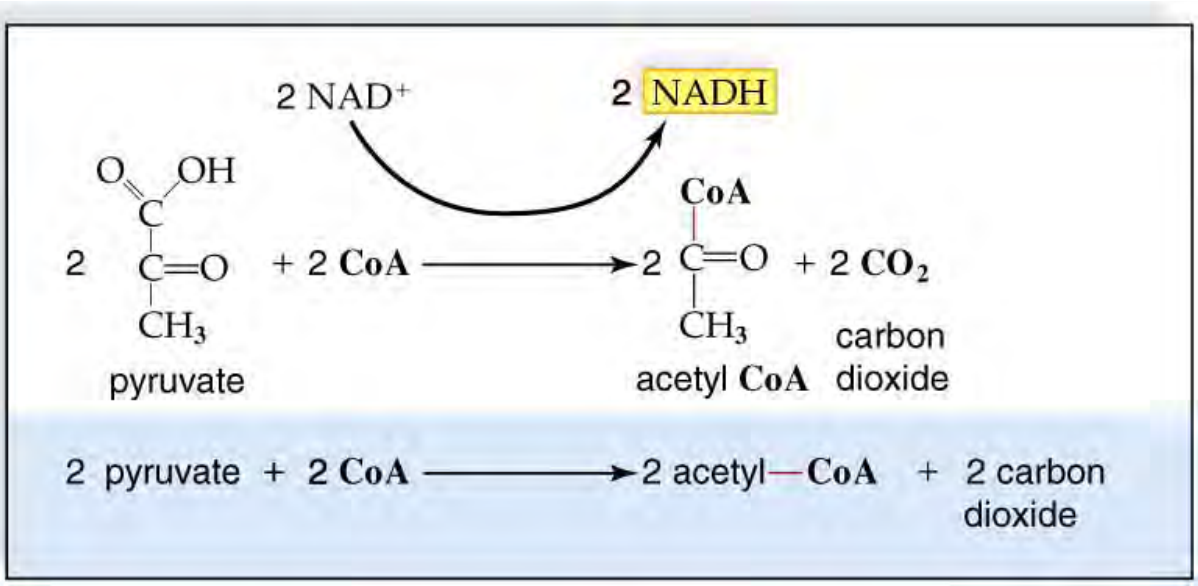
But in humans and other larger organisms much more energy can be extracted from glucose in subsequent pathways. These pathways do require specialized organelles – the mitochondria.



For a review of the structure of the mitochondrion see Lecture 6.

2. Preparation or Transition step.

The end products of glucose, the 2 pyruvate molecules, enter the mitochondria and undergo some modification so that they can enter the Krebs cycle. The two 3-carbon pyruvate molecules pass some of their electrons to NAD+, forming NADH. 2 molecules of CO_2 are formed in the process and will diffuse out of the mitochondria and the cell. A large molecule, Coenzyme A, will attach to the remainder of each of the pyruvate molecules, forming acetyl-CoA. Each acetyl-CoA is now ready to enter the Krebs cycle



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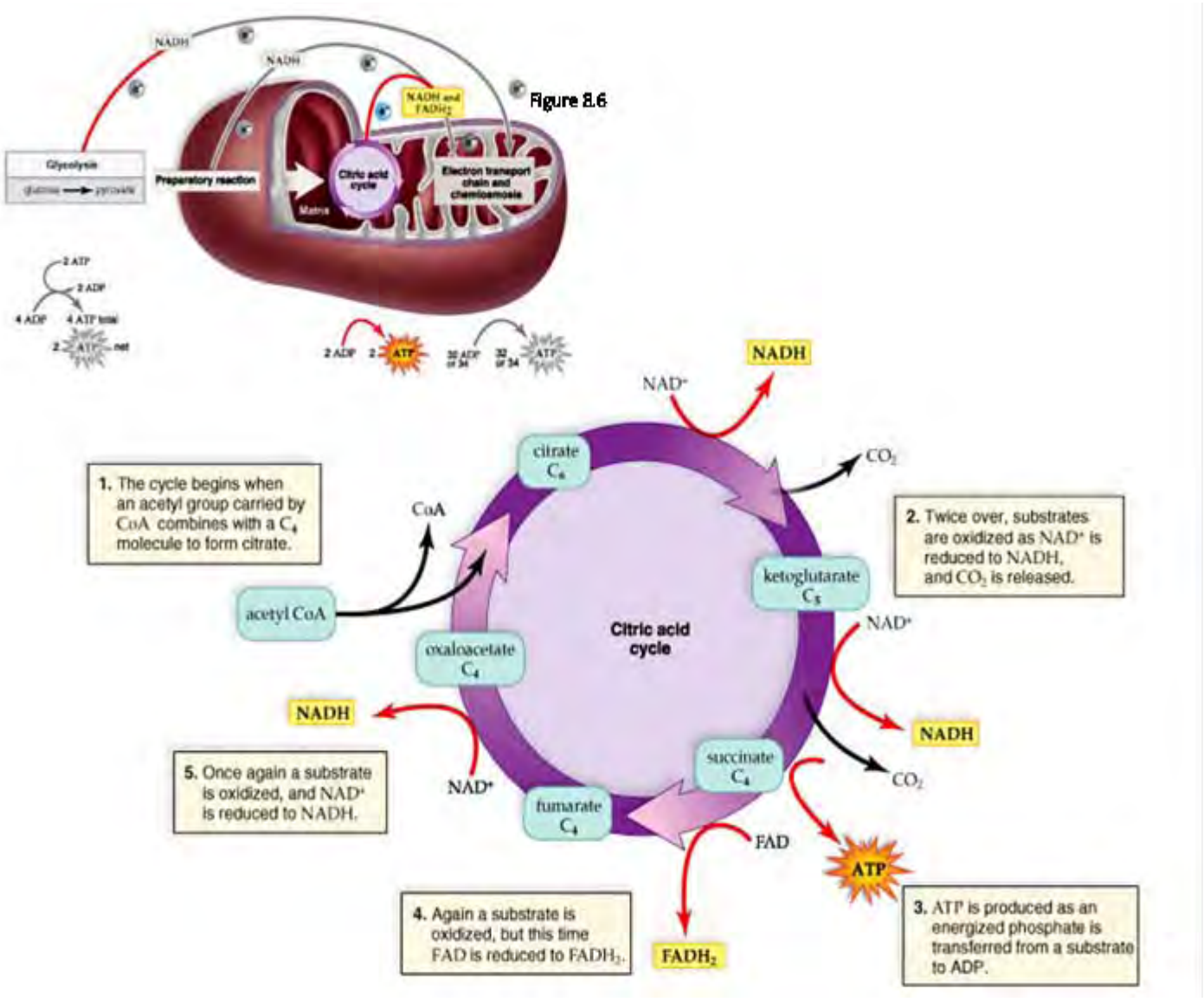
3. Citric Acid (or Krebs) cycle.

Each molecule of acetyl-CoA enters the cycle and binds to oxaloacetate, creating the 6-carbon molecule for which the cycle is named – citric acid (or citrate). As the cycle turns, electrons are donated to NAD+ creating NADH and to FAD creating $FADH_2$, 2 carbon dioxide molecules are released and one molecule of ATP is formed. At the end of the cycle one molecule of oxaloacetate is reformed and the cycle is ready to run again.



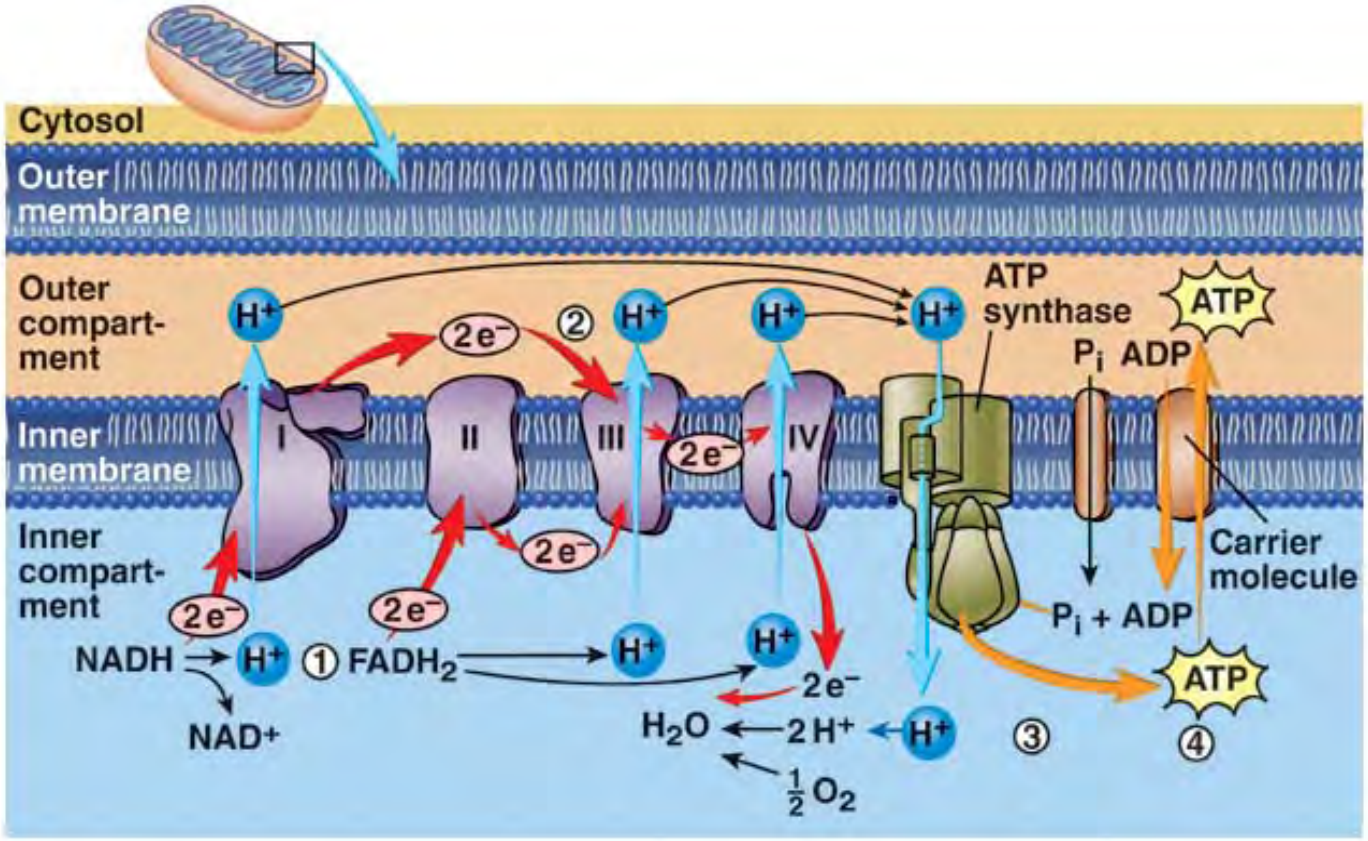
The preparation/transition step and the citric acid cycle (Krebs) take place in the mitochondrial matrix.

So far, in the complete catabolism of one molecule of glucose, the cell has only gained 4 ATP molecules – two in glycolysis and one for each turn of the citric acid cycle.

But a lot of energy was donated to electron carriers NADH and $FADH_2$.

What happens to these high-energy electron carriers?

Embedded in the inner mitochondrial membrane are numerous molecules sequentially arranged to form a "chain" – the electron transport chain. All the electron carriers (NADH and $FADH_2$) generated in glycolysis, the preparation steps, and the citric acid cycles, donate their electrons to molecules in the electron transport chain. The electrons are moved along falling from a high-energy state to a lower energy state. The energy released is used to power proton pumps in the inner mitochondrial membrane which then pump hydrogen ions (H^+) into the intermembrane space (outer compartment).



Hydrogen ions accumulate in this outer compartment (intermembrane space) creating a concentration gradient and an electrical gradient. Hydrogen ions carry a positive charge and when they are pumped out of the mitochondrial matrix it leaves an excess of ions with a negative charge in the matrix and a large difference in concentration of hydrogen ions between the intermembrane space and the matrix. An electrochemical gradient is created and is a source of potential energy.

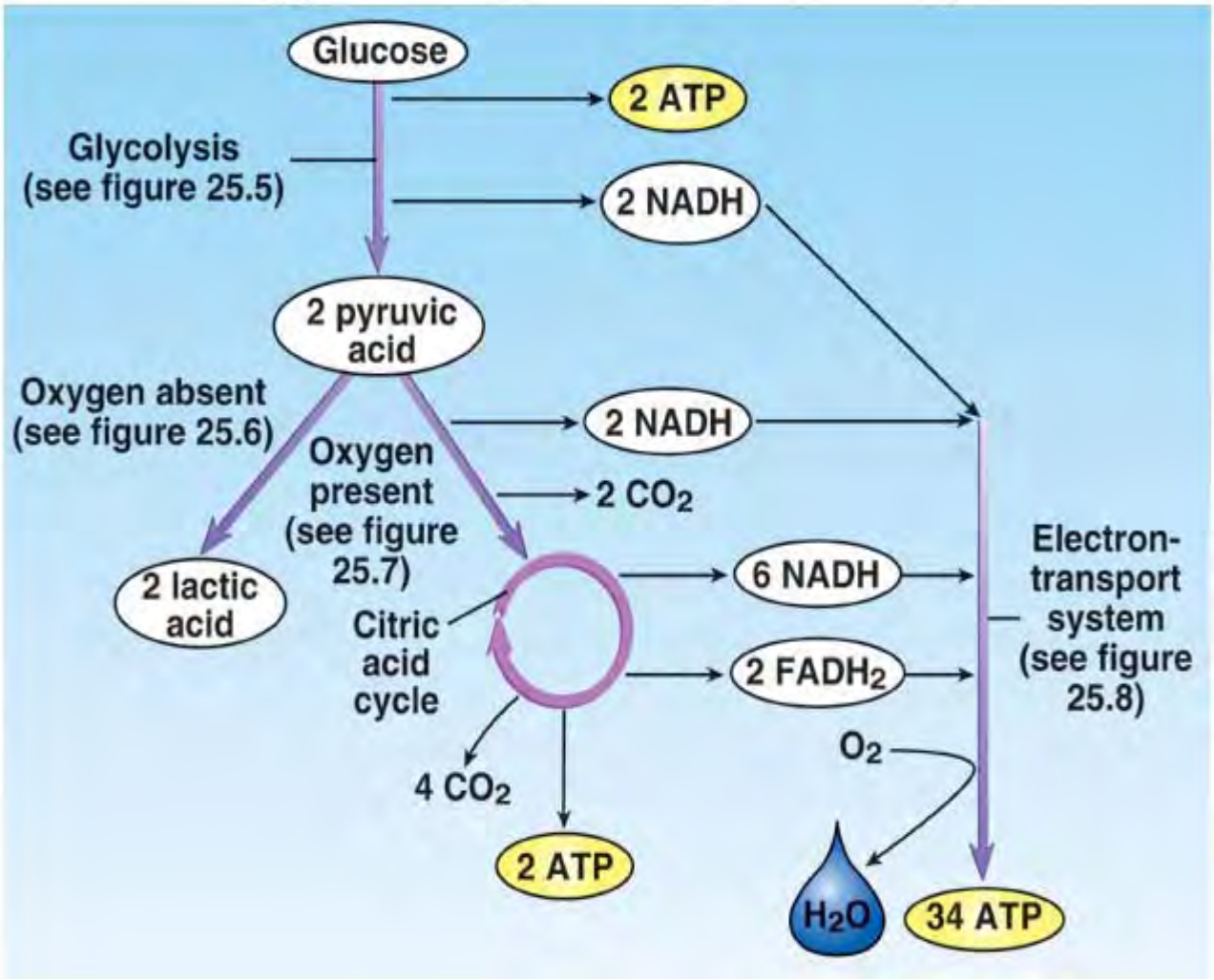
The hydrogen ions or protons that have accumulated in the space cannot move by simple diffusion through the phospholipid bilayer of the inner membrane which separates them from the matrix. However, located in the membrane are hydrogen ion channels which will permit the hydrogen ions to move down their gradient. These channels are linked to an ATP synthase complex and, as the protons are flowing down their gradient into the mitochondrial matrix, the ATP synthase converts the energy from the flow of protons into the chemical energy of ATP. **Chemiosmosis** is the term used to describe this process - how cells link the energy of oxidation reactions to pump hydrogen ions across a membrane, resulting in a gradient that can be used to generate ATP.

In most cells **a total of 34 ATP is generated by this process**. Because the ATP synthesized here is linked to the redox reactions the process is sometimes referred to as **oxidative phosphorylation**. Oxygen must be present to be the final electron acceptor.

Notice that at the end of the electron transport chain the electrons are donated to oxygen (represented in the figure as 1/2 O_2). Oxygen combines with the electrons and hydrogen ions forming H_2O. This is essentially why we need to breathe - the O_2 present in our cells comes from the atmosphere. We breathe it into our lungs where, because it is lipid-soluble, it moves into our bloodstream and is transported to our cells.

Consequently, these pathways that require oxygen are sometimes referred to as **Aerobic Pathways**.

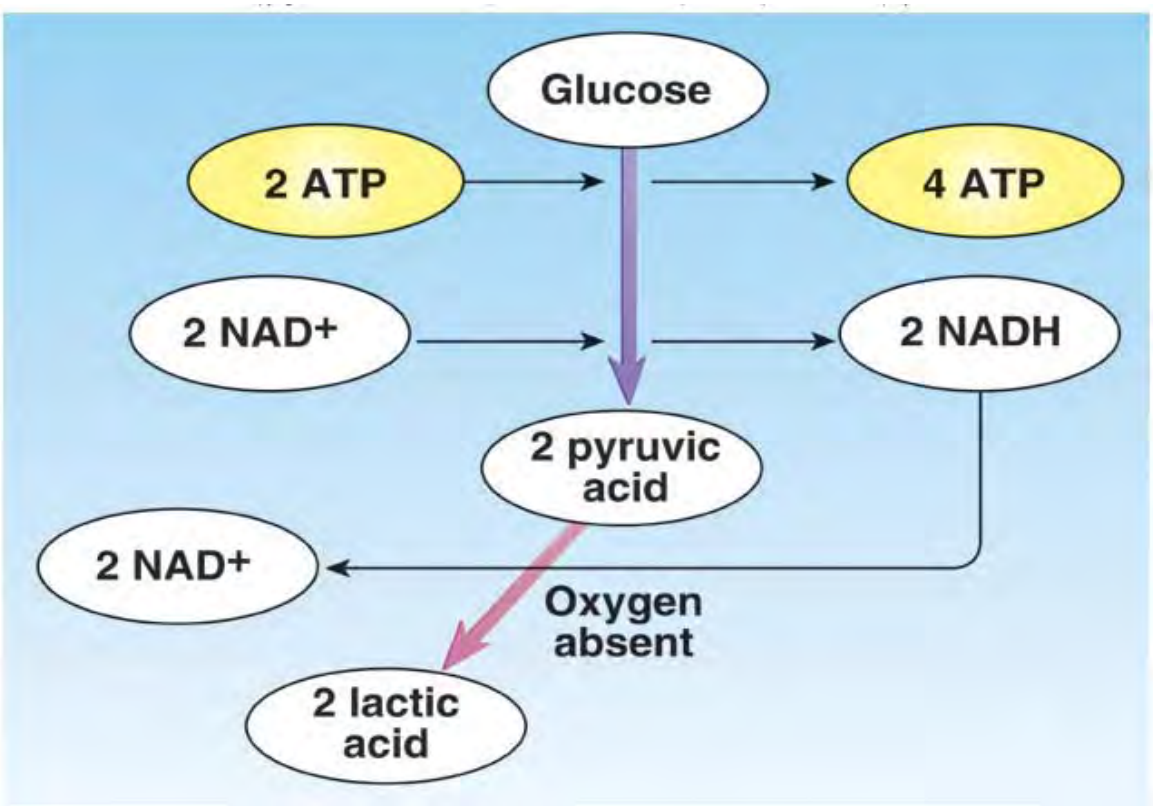
Note that glycolysis is an **Anaerobic Pathway** because it does not require oxygen.



In the presence of oxygen a cell is able to generate 2 ATP in glycolysis, 2ATP in the citric acid cycle, and 34 ATP by oxidative phosphorylation in the electron transport chain.

More on Anaerobic Pathways
If cells such as muscle cells get depleted of O_2, they can still generate some ATP for muscle contraction through glycolysis and fermentation pathways.
Prokaryotes and Yeast cells also use glycolysis and fermentation pathways.

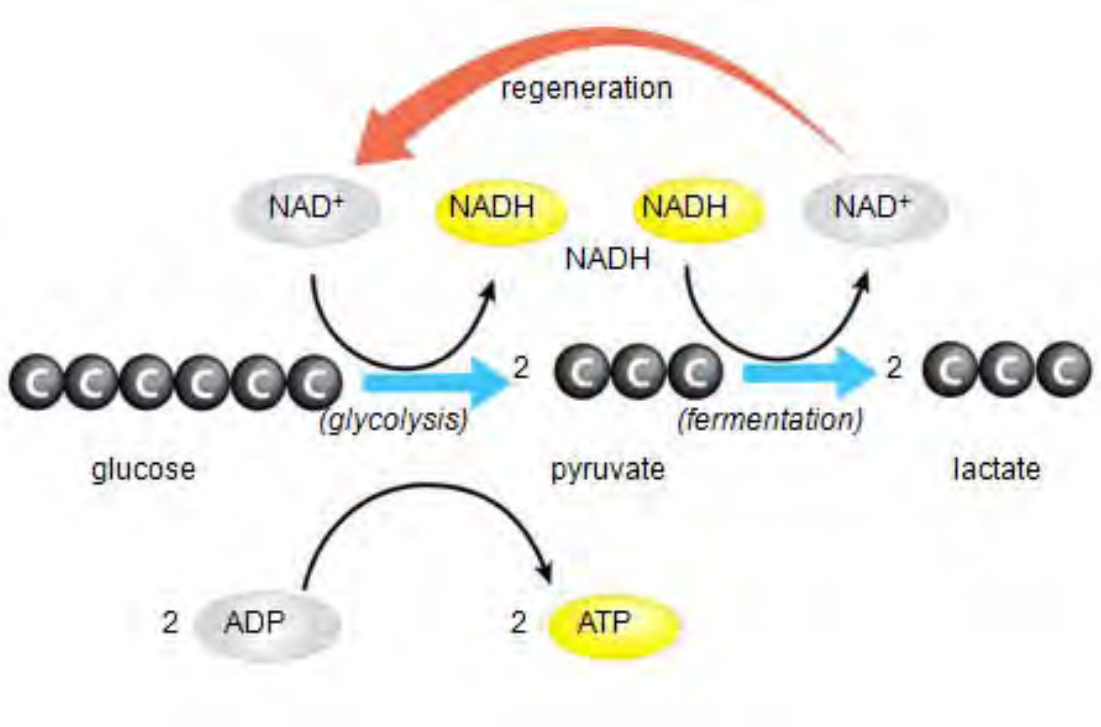
Fermentation Pathways
Fermentation pathways are **anaerobic** and take place in the cytoplasm of the cell. In animal cells that do not have mitochondria such as red blood cells, or in animal cells that have temporarily run out of oxygen, the cells are still able to run glycolysis, generating 2 molecules of ATP for each molecule of glucose. **However, the pathway does not stop at pyruvate. Rather, pyruvate is converted to lactate or lactic acid.**



What is the reason for this "extra" step? It is because cells have a limited supply of NAD^+. Normally, if a cell is metabolizing aerobically, the reduced NADH produced in glycolysis, will donate its electrons to the electron transport chain and go back to its oxidized state (NAD^+) which continues to pick up electrons and keep the pathways running.

If the oxygen supply to a cell is diminished or the cell has no mitochondria (such as a red blood cell) then the supply of NAD+ would rapidly diminish as there would be no place for the NADH to donate its electrons. To prevent this from happening, at the end of glycolysis pyruvate (pyruvic acid) accepts the electrons and becomes (is reduced to) lactate (lactic acid), thereby freeing NAD+ to continue picking up electrons.

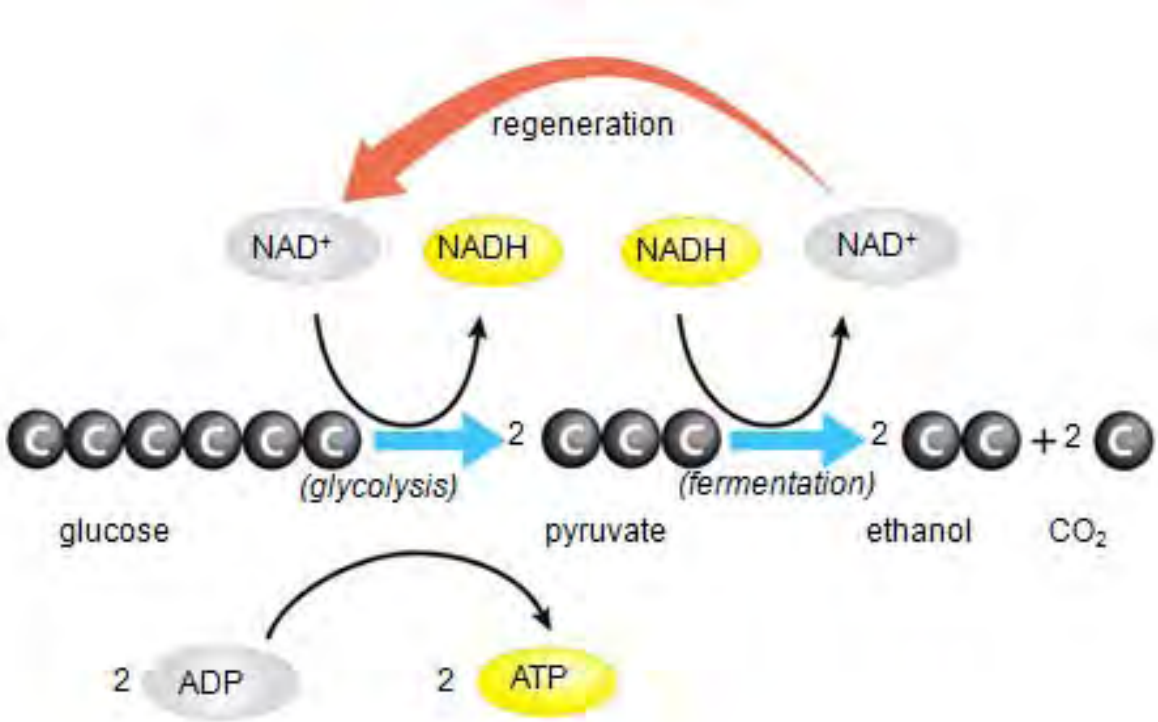
Lactic Acid Fermentation and the Recycling of NAD^+



Many microorganisms live solely by fermentation pathways. Many bacterial cells perform lactic acid fermentation. Think of how milk tastes sour as it ages. This is due to the lactic acid being produced by bacteria as they ferment milk sugars – the same process as human cells use in the absence of oxygen.

ALCOHOL FERMENTATION

Yeast cells utilize a different fermentation pathway – these cells reduce pyruvate to ethanol instead of lactate. Beer, wine, and spirits are produced by yeast cells metabolizing under anaerobic conditions.

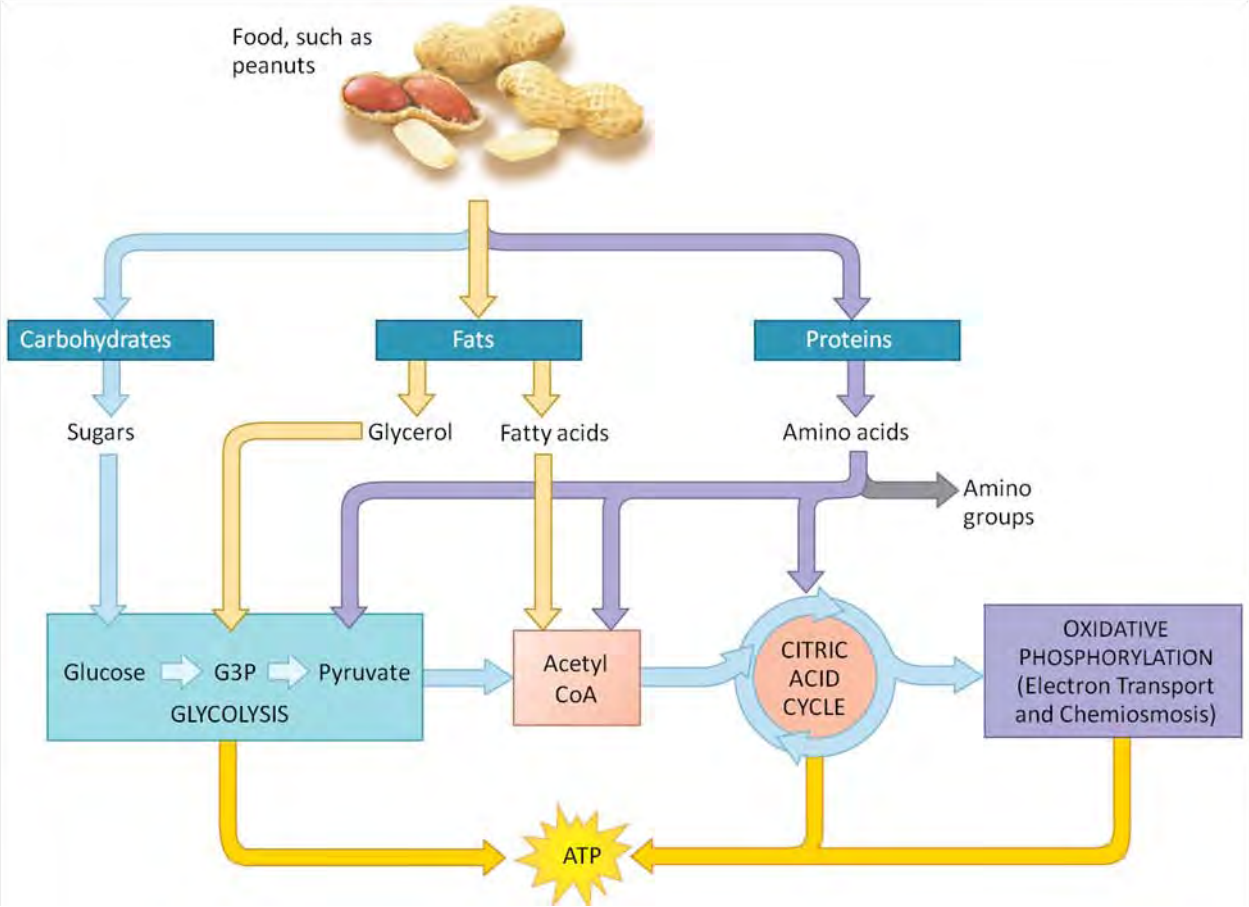


Alcohol Fermentation and the recycling of NAD^+

Notice also that in this fermentation pathway pyruvate is converted to ethanol and CO_2 is released as a by-product. The CO_2 gas is trapped in the process of making beer or bread and is what makes beer or champagne bubble and bread rise.

NUTRIENTS OTHER THAN GLUCOSE ALSO PROVIDE ENERGY

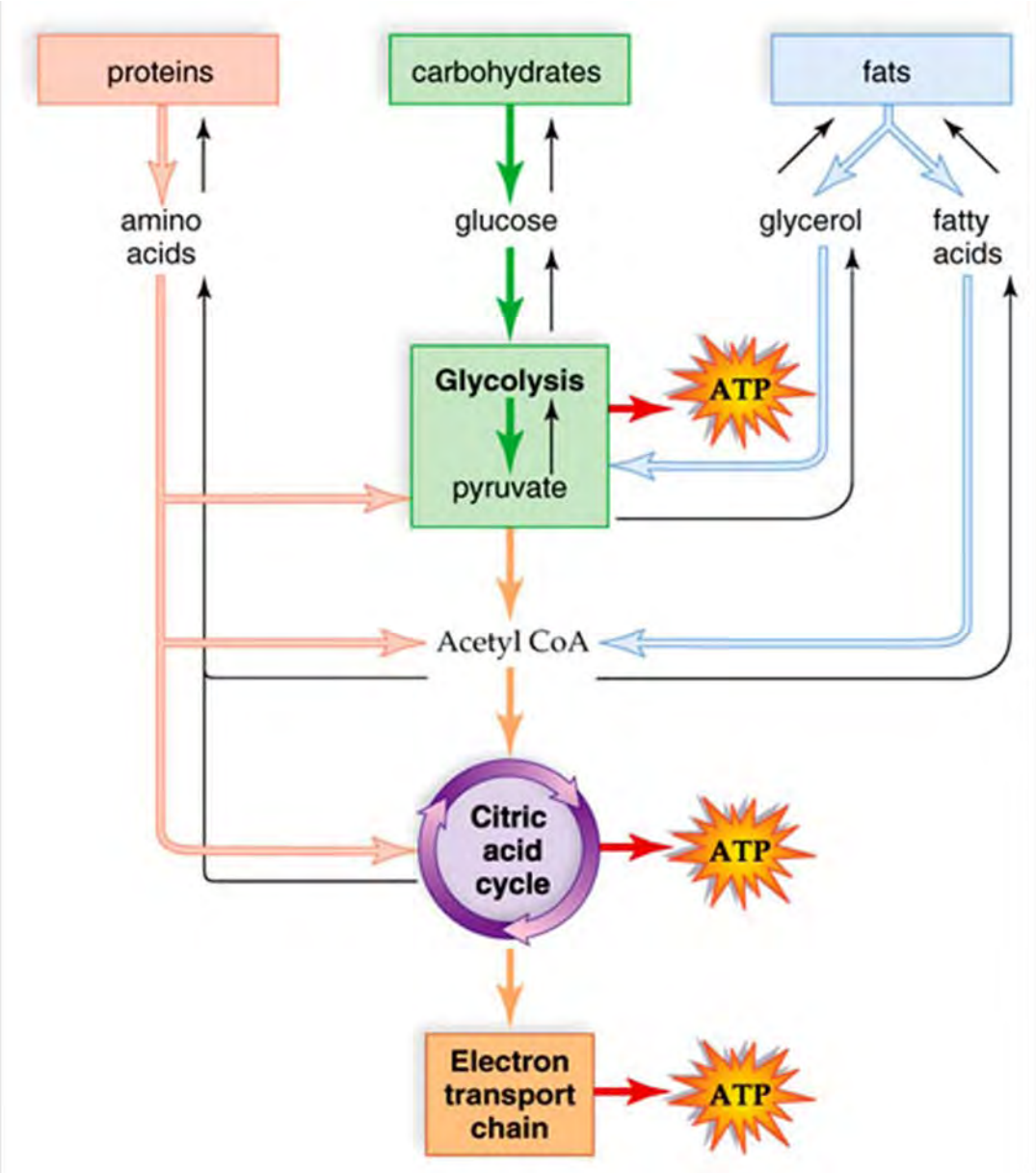
So far only the catabolic pathways for glucose have been considered. But energy can be obtained from fats, proteins, and other carbohydrates. These foods enter the process at different stages as can be seen below.
All carbohydrates first get broken down to glucose, fats to glycerol and fatty acids, and proteins to amino acids. These monomers enter cellular respiration pathways at various points.



A meal, or even one food source like the peanut above, may contain some combination of carbohydrates, lipids, and proteins. The nutrients are modified in some preliminary steps but are then able to enter glycolysis or the Krebs cycle to transfer their energy to ATP.

ANABOLIC PATHWAYS ALSO REQUIRE ENERGY

Cells also need to build molecules and they use the monomers provided by food as the building blocks for larger molecules. For example, in **Lecture 5** the numerous functions of proteins in living systems were discussed and cells build these proteins from the amino acids provided by food. Also cells build glycogen to store glucose in liver cells and an excessive intake of all carbohydrates and proteins means that they get converted to fat and stored for future needs. So there is a continuous **interconversion of nutrient molecules** going on as demonstrated below.



LECTURE 11: DNA REPLICATION AND CELL DIVISION

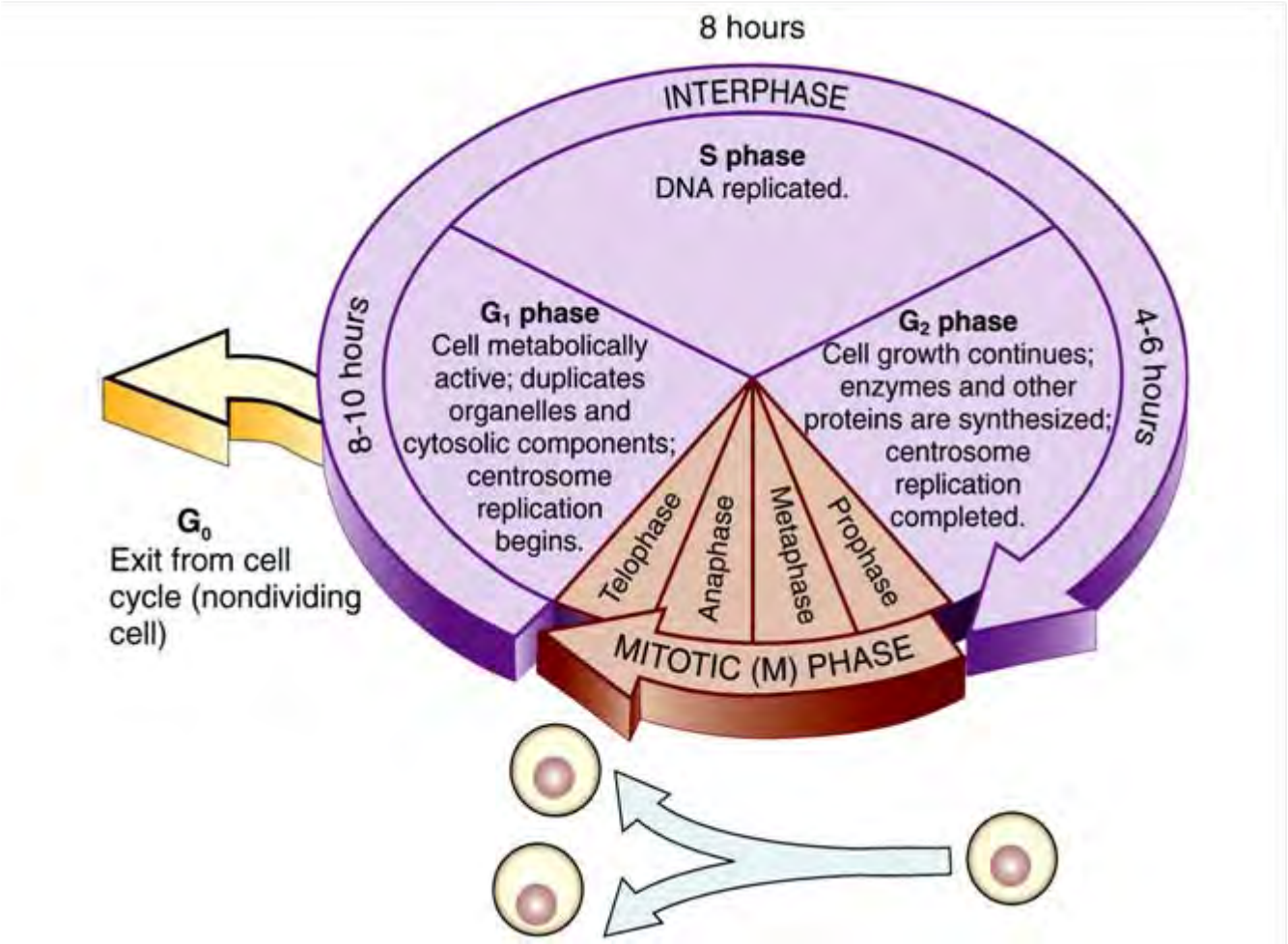
Cellular Reproduction

Most cells undergo cell division in order to reproduce themselves. How cells do this is the topic of this lecture – basically, cells enlarge, divide in two, enlarge, divide in two and so on. Each newly formed cell contains a copy of the genetic information and duplicates of the molecular machinery and materials that the cell will need to function and to divide again.

Each round of growth is called a cell cycle.

All of the cells in a multicellular, eukaryotic organism can be divided into 2 types: **somatic cells** which are the cells that form the body of the organism (including the human body) and **the reproductive cells** which pass on the genetic information to the offspring. These two different types of cells also divide by different processes.

First we will examine the cell cycle and how somatic cells divide.



This simple diagram (on previous page) of a **somatic cell** cycle shows the following sequence for cell division:

- The cycle consists of two stages; **interphase** followed by **mitosis**.

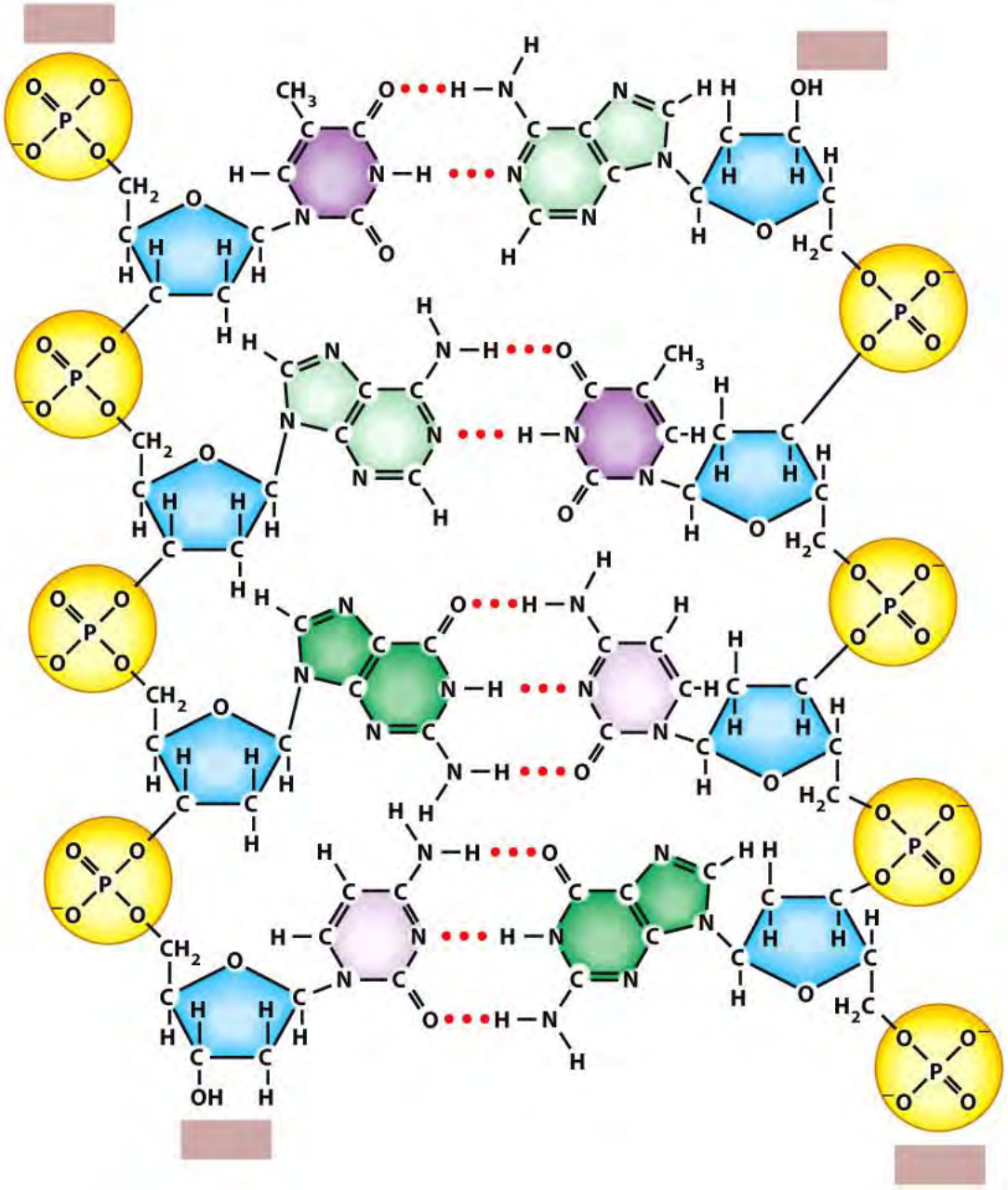
  - **Interphase**: duplication of cell contents
    - **G_1**—growth, increase in cytoplasm
    - **S**—duplication of chromosomes
    - **G_2**—growth, preparation for division

  - **Mitotic phase**: division
    - **Mitosis**—division of the nucleus
    - **Cytokinesis**—division of cytoplasm and the formation of 2 cells

How long the cell cycle takes depends on the type of cell. Some cells do not divide and instead remain in Interphase or what is sometimes referred to as the **Go phase**. Good examples of cells that rarely, if ever, divide are animal nerve cells and skeletal muscle cells.
Other body cells such as skin cells divide rapidly, about once in 24 hours. These cells are continuously moving through the cell cycle.

The **3 phases of interphase (G_1, S, G_2)** as listed above prepare the cell for division by duplicating the hereditary material and all the enzymes and organelles that are necessary for 2 functioning cells. What occurs in G_1 and G_2 is self-explanatory; more detail is needed to understand how the cell duplicates all the genetic material.

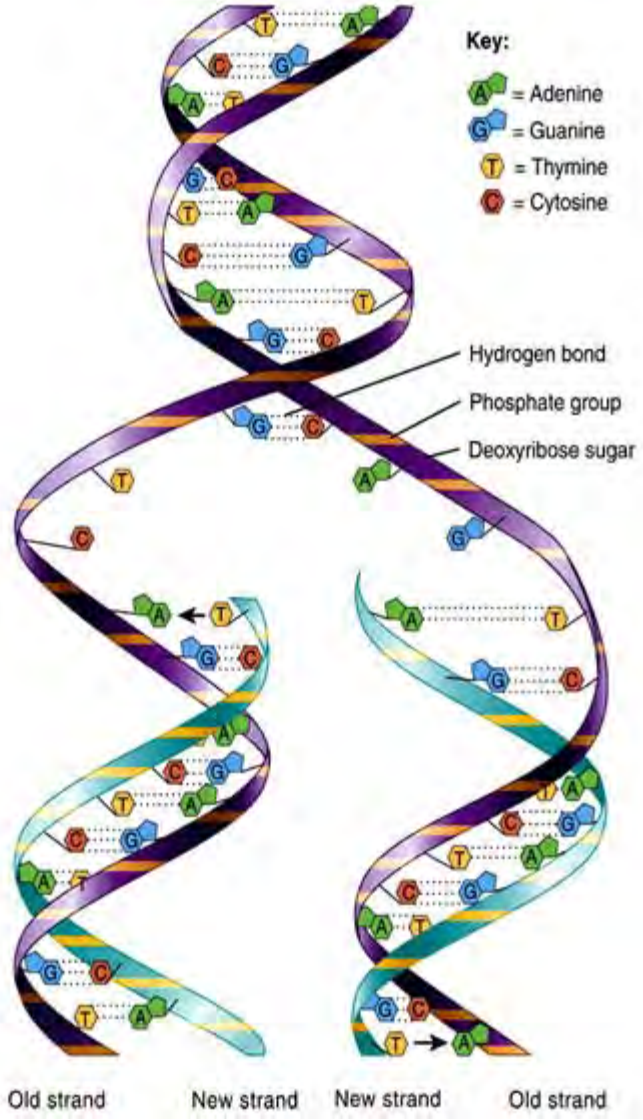
A review of the structure of DNA (the genetic material) shows that DNA is a double stranded helix composed of subunits called nucleotides (a nucleotide is composed of a sugar, a phosphate group, and a nitrogenous base).



The sugars and phosphates that link one nucleotide to the next form the backbone on each side of the double helix, while the bases from each strand pair up in the middle of the helix and are linked by hydrogen bonds. Only "complimentary" base pairs can link together in the helix: adenine with thymine and guanine with cytosine. A-T C-G

DNA REPLICATION

When DNA is replicated before mitosis (or meiosis), the two DNA strands of each double helix unwind. This is accomplished by DNA **helicase** enzymes. Replication begins at one or more sites where there is a specific sequence called a replication origin. The sequence of nucleotides in each newly formed strand is complementary to the sequence on a parental strand. As a result two double helices are synthesized, each consisting of one parental DNA strand plus one newly synthesized **complementary** strand that is an exact copy of the other parental strand.



- The two DNA strands separate
- Each strand is used as a pattern or template to produce a complementary strand, using specific base pairing
- Each new DNA helix has one old strand with one new strand

The synthesized DNA molecules are therefore duplicates of the parental DNA molecule.

DNA Replication occurs in the S phase of the cell cycle.

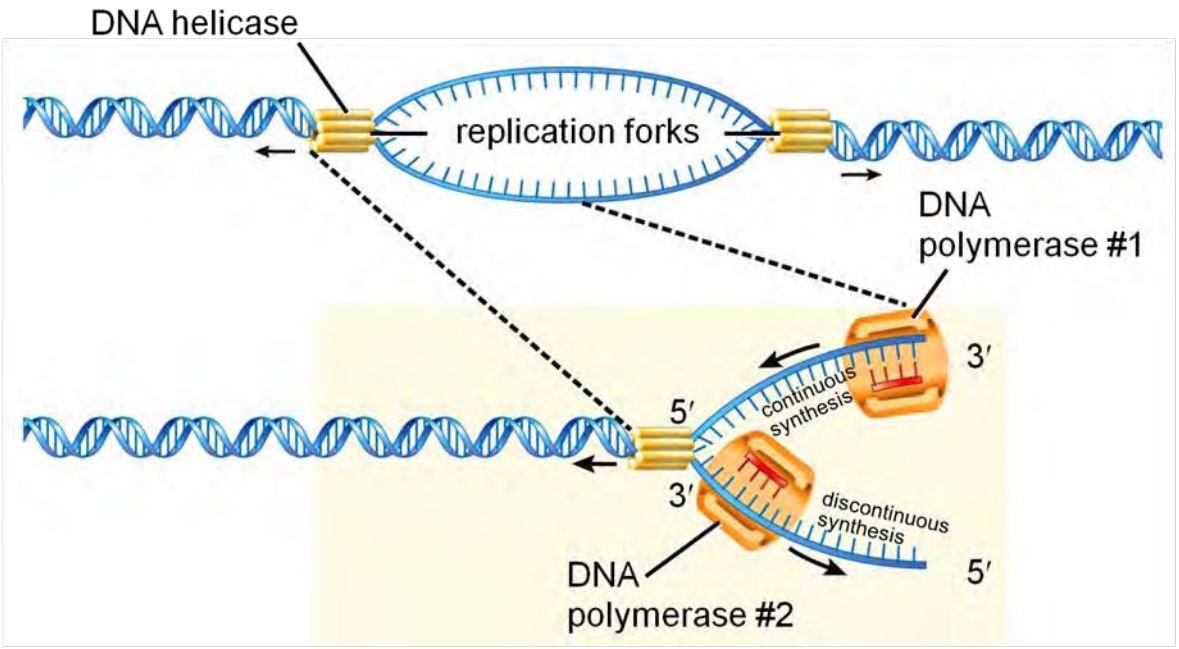
A more detailed drawing of DNA replication is represented in the following 3 images.

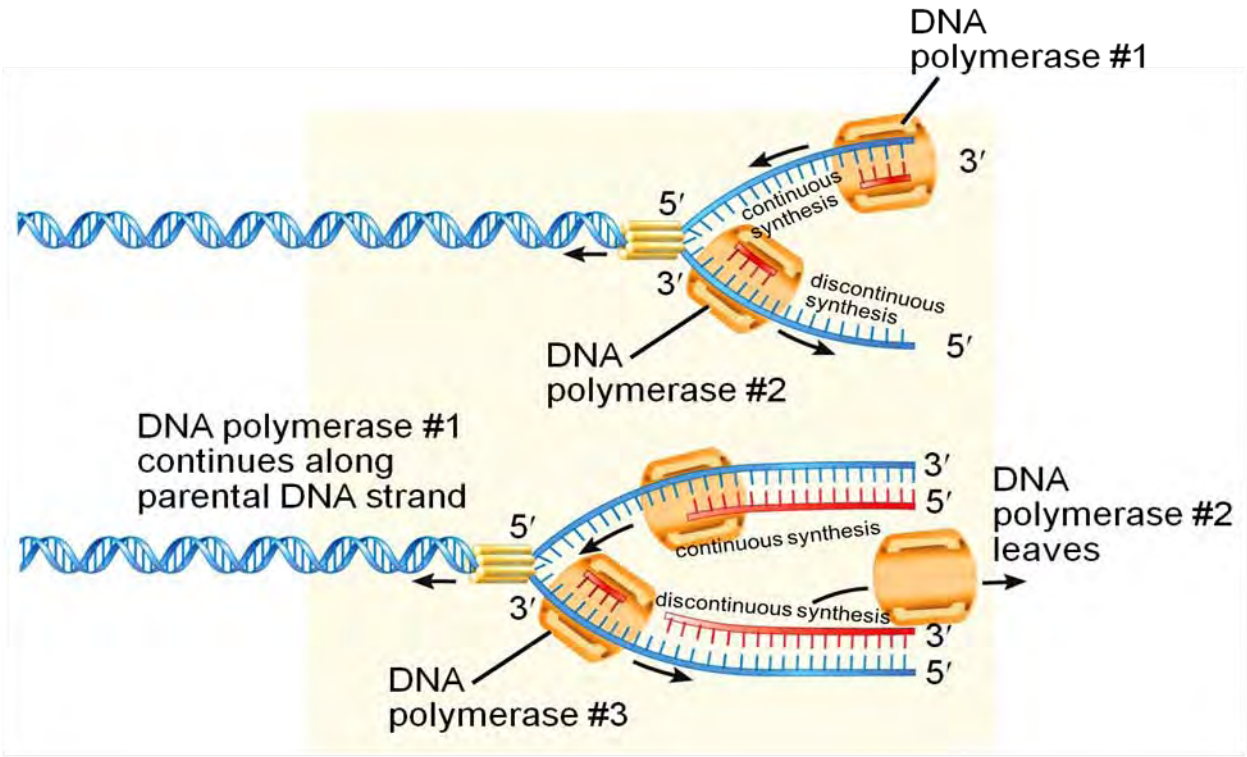
3 of the enzymes involved, a helicase, a polymerase, and a ligase, are demonstrated in the more detailed diagrams.

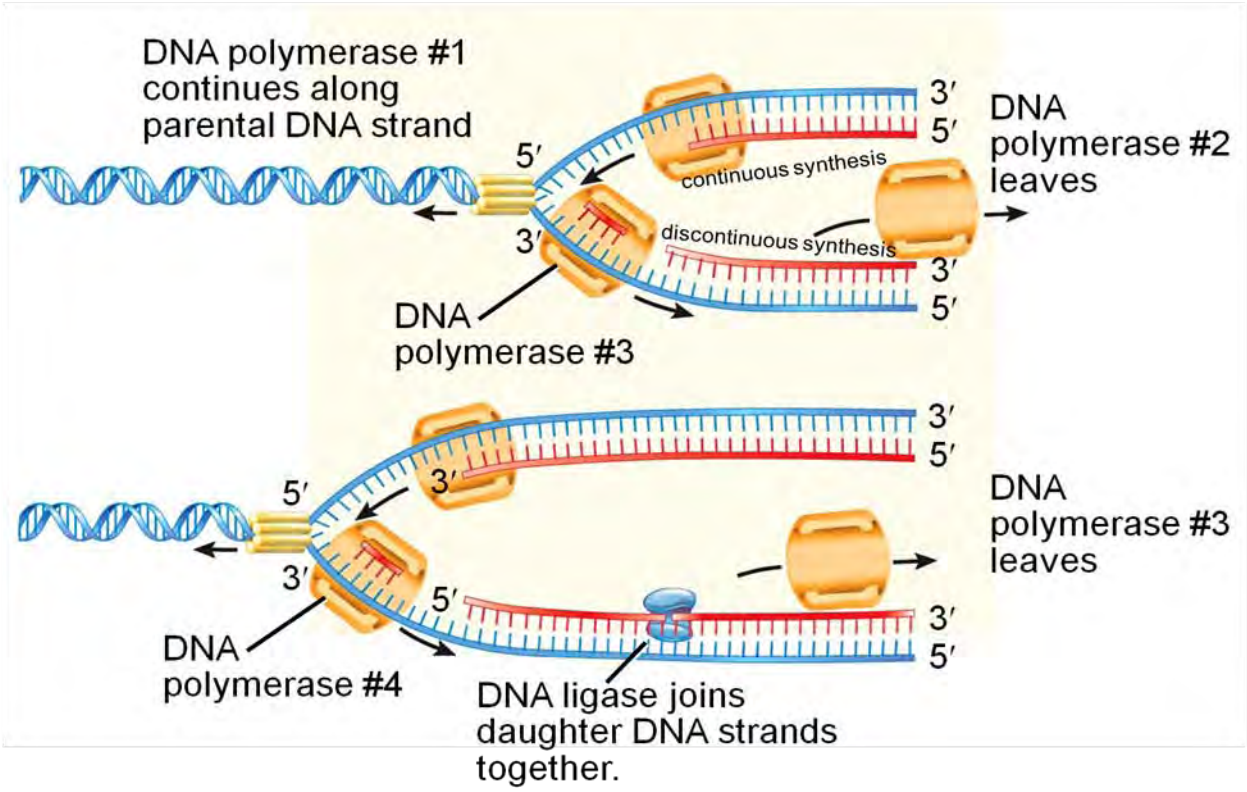
DNA helicase breaks the hydrogen bonds in the original DNA strand – the one that is to be copied.

DNA polymerases move along each strand linking up free nucleotides into new DNA strands. Because DNA strands are oriented in opposite directions one polymerase moves along forming a continuous strand, while the other DNA strand is synthesized in short seqments (**Okazaki fragments**) that are then connected by a DNA **ligase.**

Note that the replication of DNA is semiconservative. One of the strands in the original DNA double helix is conserved in each of the two new strands.


DNA helicase
replication forks
DNA
polymerase #1
3′
continuous
synthesis
5′
3′
discontinuous
synthesis
5′
DNA
polymerase #2

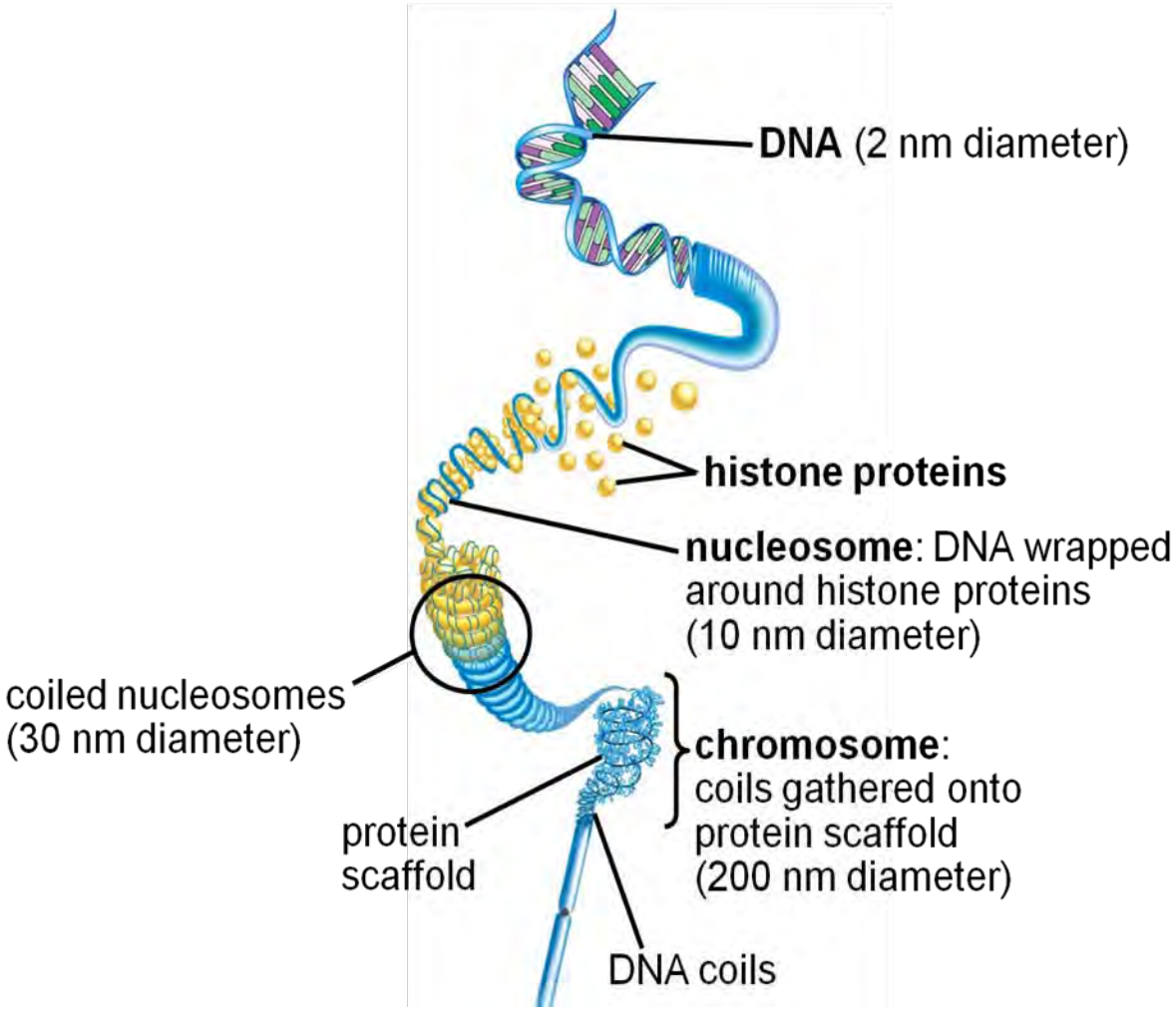

DNA
polymerase #1
3′
5′
continuous
synthesis
3′
discontinuous
synthesis
5′
DNA
polymerase #2
DNA polymerase #1
continues along
parental DNA strand
3′
5′
DNA
polymerase #2
leaves
5′
continuous synthesis
3′
discontinuous synthesis
3′
5′
DNA
polymerase #3


DNA polymerase #1 continues along parental DNA strand
5′
3′
continuous synthesis
discontinuous synthesis
3′
5′
DNA polymerase #2 leaves
DNA polymerase #3
3′
5′
DNA polymerase #3 leaves
5′
3′
3′
5′
3′
5′
DNA polymerase #4
DNA ligase joins daughter DNA strands together.

MITOSIS

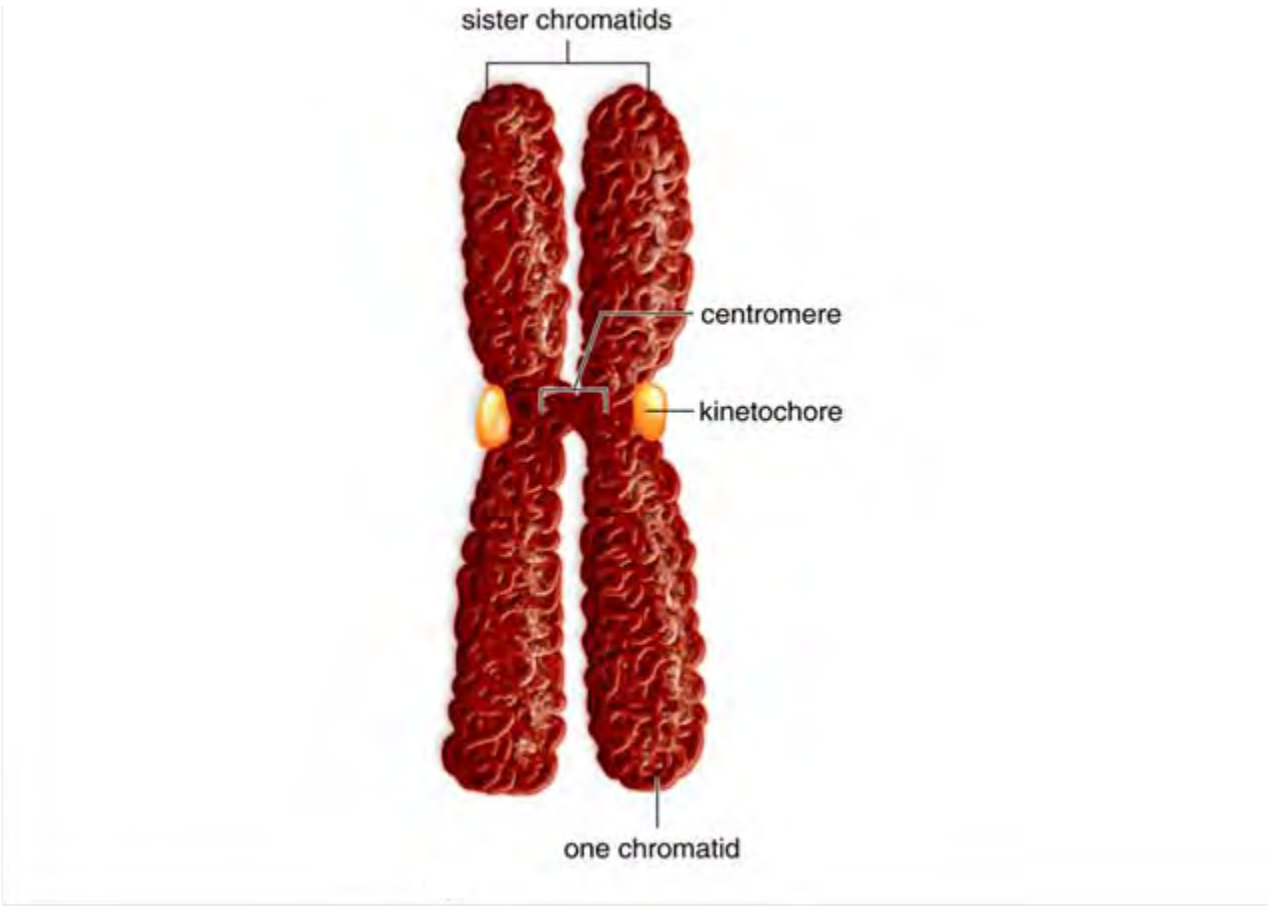
Vocabulary terms used here.

A CHROMOSOME is a gene-carrying structure and is most visible during cell division.
A chromosome consists of DNA wrapped around specific proteins called **histones.**



A **CHROMATID** – when the DNA in a cell has replicated, each replicated chromosome now consists of 2 identical **sister chromatids** connected at a region called the **CENTROMERE**.

KINETCHORES are proteins that form on the centromere of each chromatid and will be the attachment site for the mitotic spindle.



CHROMATIN is the loose arrangement of DNA in the nucleus during most of the life of the cell. In this arrangement the DNA/genes is more accessible to enzymes for transcription and translation of proteins. Chromatin is only condensed into chromosomes when the cell is getting ready to divide. Chromatin can be seen in the first cell of the next diagram.

HAPLOID - having one copy of each chromosome and therefore one copy of each gene.

DIPLOID – having two copies of each chromosome as seen in the karyotype on pg 12.

MITOSIS

At the end of the G_2 phase in the cell cycle the cell has duplicated all it needs (Remember that the entire DNA was replicated in the S phase) to produce 2 new cells. Then the steps of **Mitosis** begin - the details are outlined in the following 4 steps.

- **1. Prophase (sometimes divided into prophase & prometaphase)**
    - Occurs in the cytoplasm
        - Microtubules begin to emerge from centrosomes, forming the spindle
    - In the nucleus
        - Chromosomes coil and become compact
        - Nucleoli disappear
        - -- Spindle microtubules reach chromosomes, where they attach at kinetochores on the centromeres of sister chromatids and chromosomes are moved to the center of the cell through associated protein "motors"
        - the nuclear envelope disappears

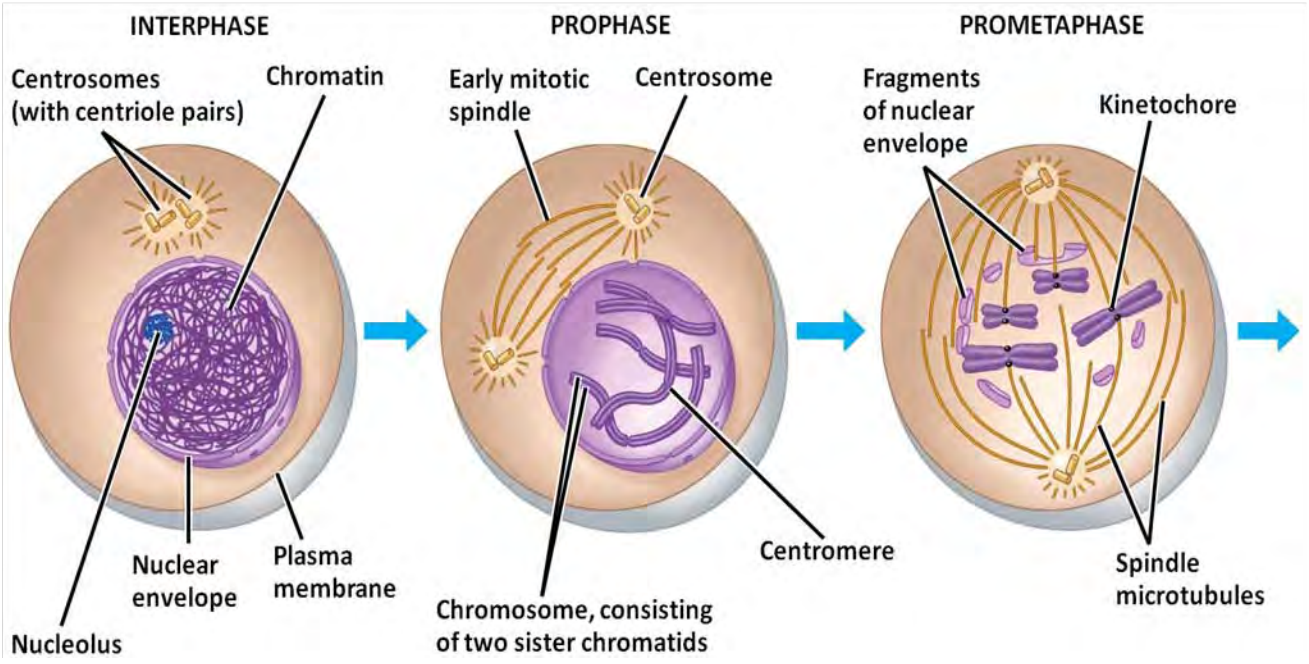
- **2. Metaphase**
    - Chromosomes align at the cell equator
    - Kinetochores of sister chromatids are facing the opposite poles of the spindle

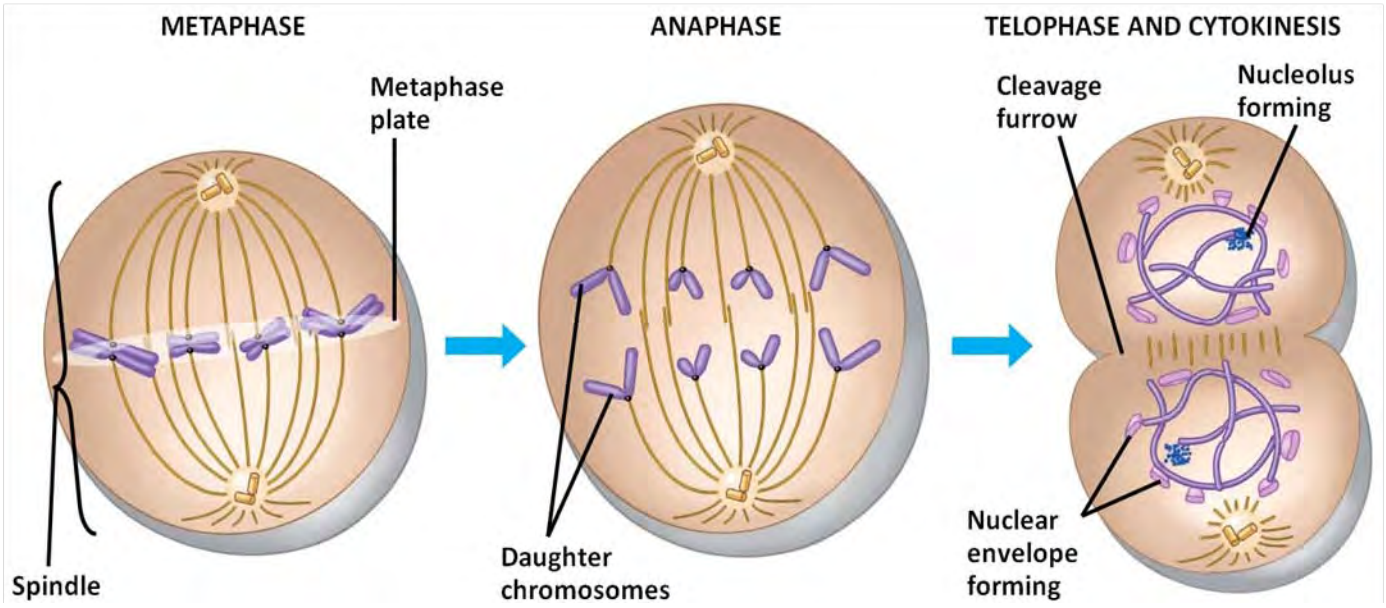
- **3. Anaphase**
    - Sister chromatids separate at the centromeres
    - Daughter chromosomes are moved to opposite poles of the cell
        - Motor proteins move the chromosomes along the spindle microtubules
- **4. Telophase**
    - The cell continues to elongate
    - The nuclear envelope forms around chromosomes at each pole, establishing daughter nuclei
    - Chromatin uncoils
    - Nucleoli reappear and the spindle disappears

- **Cytokinesis**

    Cytoplasm is divided into separate cells

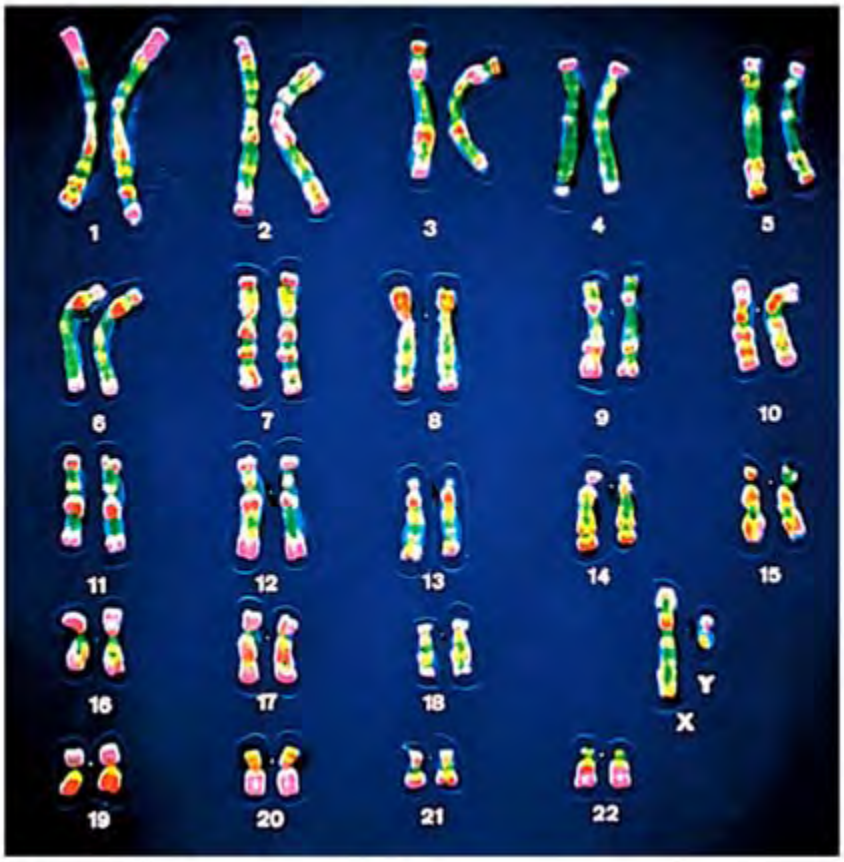
STEPS OF MITOSIS





Mitosis results in the production of 2 identical cells with equal amounts of DNA.

Looking at a **karyotype of a human somatic cell**, there are 23 pairs of chromosomes – 23 from the mother and 23 from the father.



Normal male karyotype with 46 chromosomes.

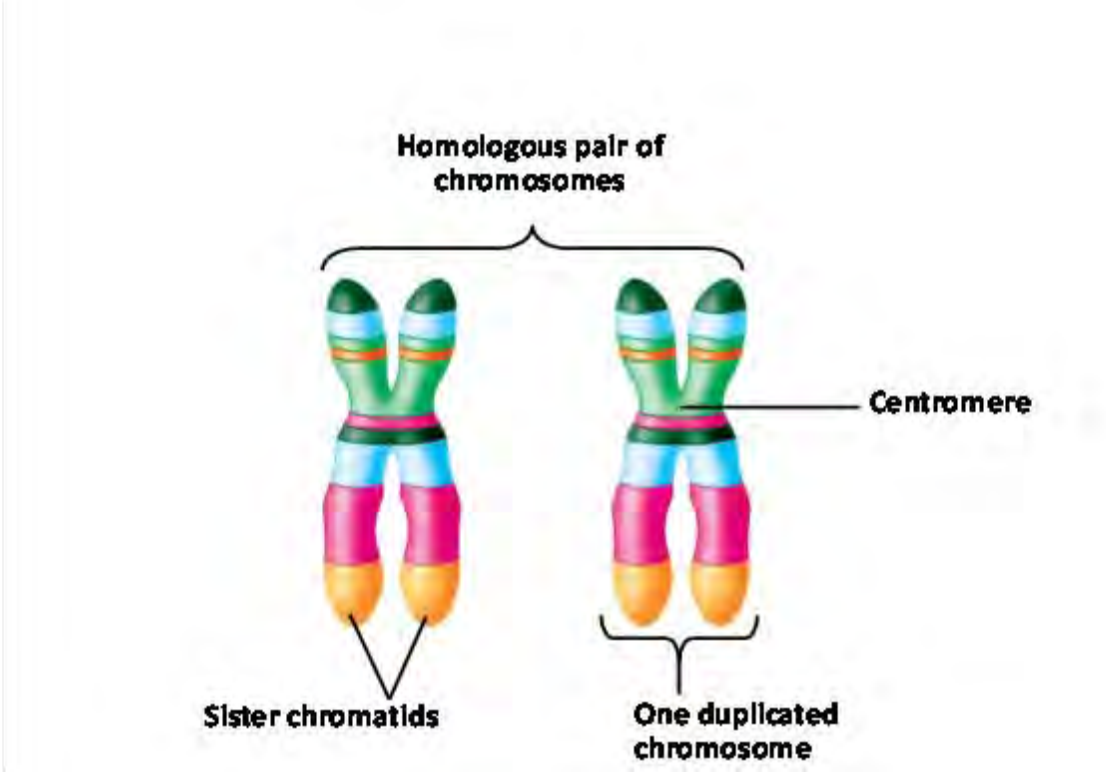
This shows the picture of the normal chromosome content of any somatic cell in a human male. One member of each pair came from this male's mother, one from his father. Chromosomes are only evident when the cell is preparing to divide; during the remainder of interphase the DNA is not compacted into chromosomes, instead it is in a loose arrangement called **chromatin** which makes genes more accessible to enzymes. Each chromosome contains a few thousand genes.

The 2 members of each pair of chromosomes in this picture are **homologous** (except for X and Y). For example, if the gene for eye color is located on chromosome 7 and codes for blue eyes, then the gene at the same location on the other chromosome 7 also codes for eye color but the color may be brown, green, blue, etc.

MEIOSIS

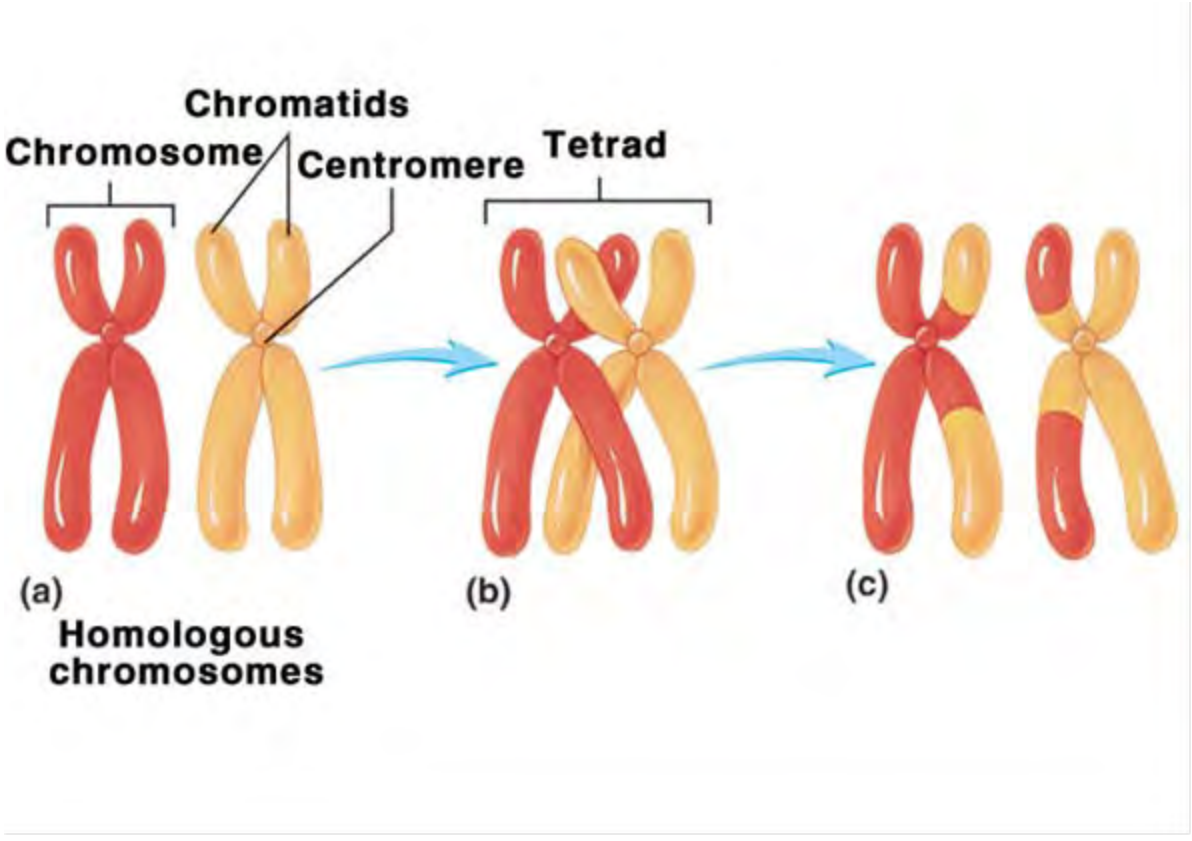
Continuing to use the human chromosomal number as an example, it is clear that when reproductive cells or **gametes (sperm and egg)** are formed, the number of chromosomes passed on needs to be reduced by half. At fertilization, when a sperm with 23 chromosomes combines with an egg with 23 chromosomes, the first cell of a new human is formed – with 46 (23 pairs) of chromosomes.
How does this reduction in the number of chromosomes happen? The answer is a special type of cell division called **Meiosis.**

Meiosis consists of 2 successive nuclear divisions called **Meiosis 1 and Meiosis 11**. Each of these nuclear divisions has the same 4 steps as mitosis but what happens in each phase is quite different, particularly in Meiosis 1.
Note that a cell entering meiosis has 46 duplicated chromosomes. These duplicates are held together at the centromere and are referred to as sister **chromatids** - below **one chromosome pair** has been duplicated, forming 2 pairs of sister chromatids. **Sister chromatids are identical**.

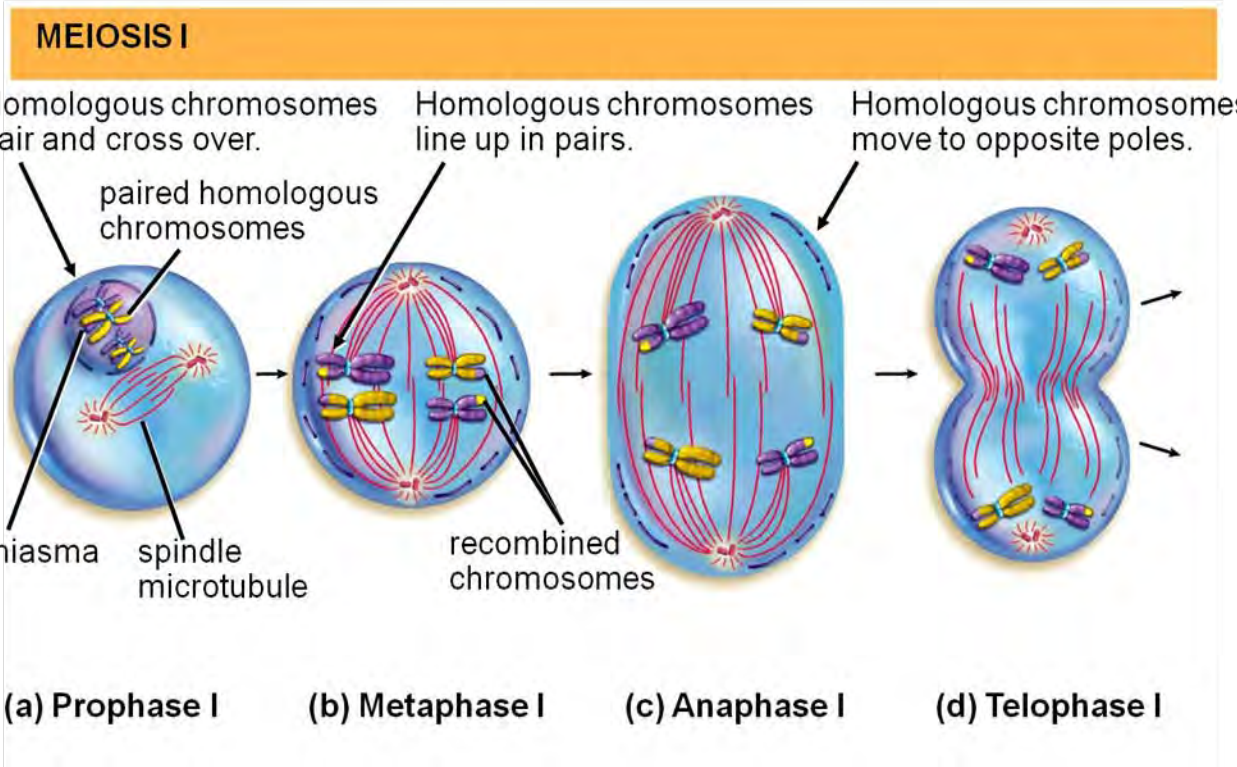


Meiosis 1 – <u>DURING MEIOSIS 1 HOMOLOGOUS CHROMOSOMES SEPARATE</u>

- **Prophase I**
  - Chromosomes coil and become compact
  - **Homologous** chromosomes come together as pairs by **synapsis**
  - Each pair, with four chromatids, is called a **tetrad**
  - Nonsister chromatids exchange genetic material by **crossing over**



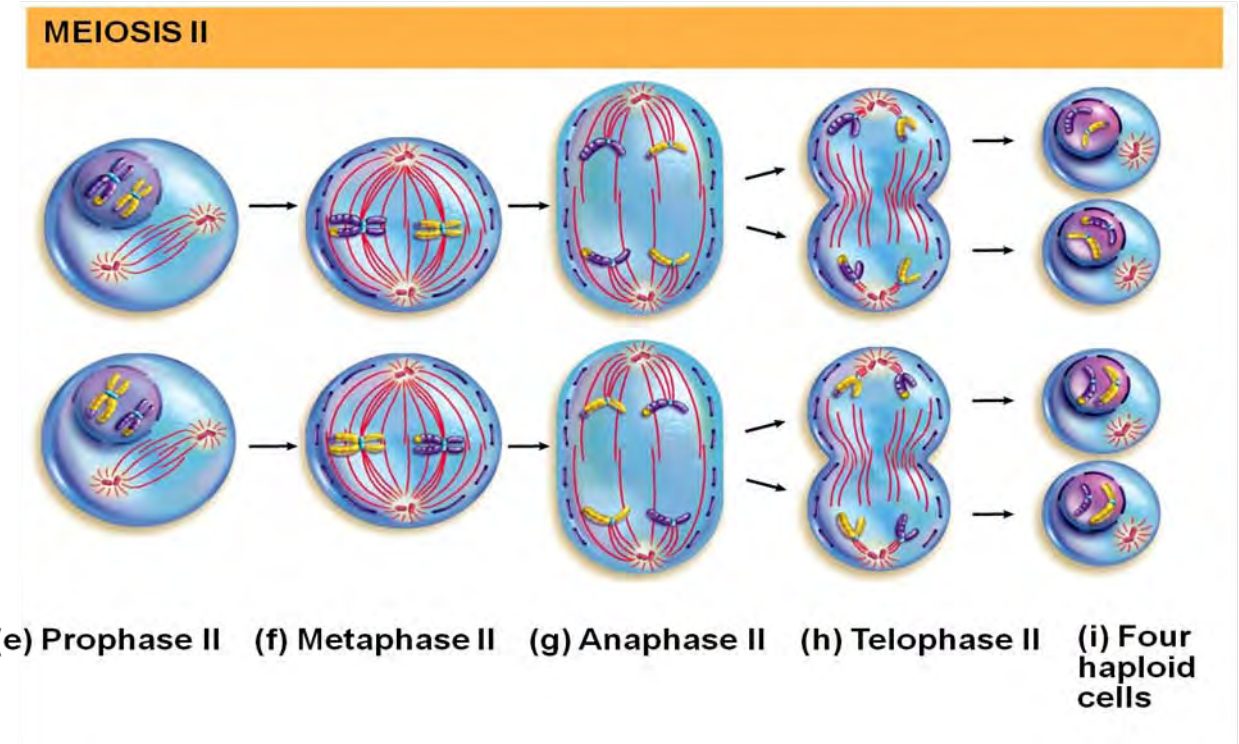
- **Metaphase I**
  - Tetrads align at the cell equator
- **Anaphase I**
  - Homologous pairs separate and move toward opposite poles of the cell
- **Telophase I**
  - Duplicated chromosomes have reached the poles
  - A nuclear envelope forms around chromosomes in some species
  - Each nucleus has the haploid number of chromosomes



At the end of Meiosis 1 two cells are formed. These 2 cells enter Meiosis 11 which follows Meiosis 1 without duplicating the chromosomes.

Meiosis 11 – <u>DURING MEISOIS 11 SISTER CHROMATIDS SEPARATE.</u>

- **Prophase II**
  - Chromosomes coil and become compact
- **Metaphase II**
  - Duplicated chromosomes align at the cell equator
- **Anaphase II**
  - Sister chromatids separate and chromosomes move toward opposite poles
  -
- **<u>Telophase II</u>**
  - <u>Chromosomes have reached the poles of the cell</u>
  - <u>A nuclear envelope forms around each set of chromosomes</u>
  - <u>With cytokinesis, four haploid cells are produced</u>



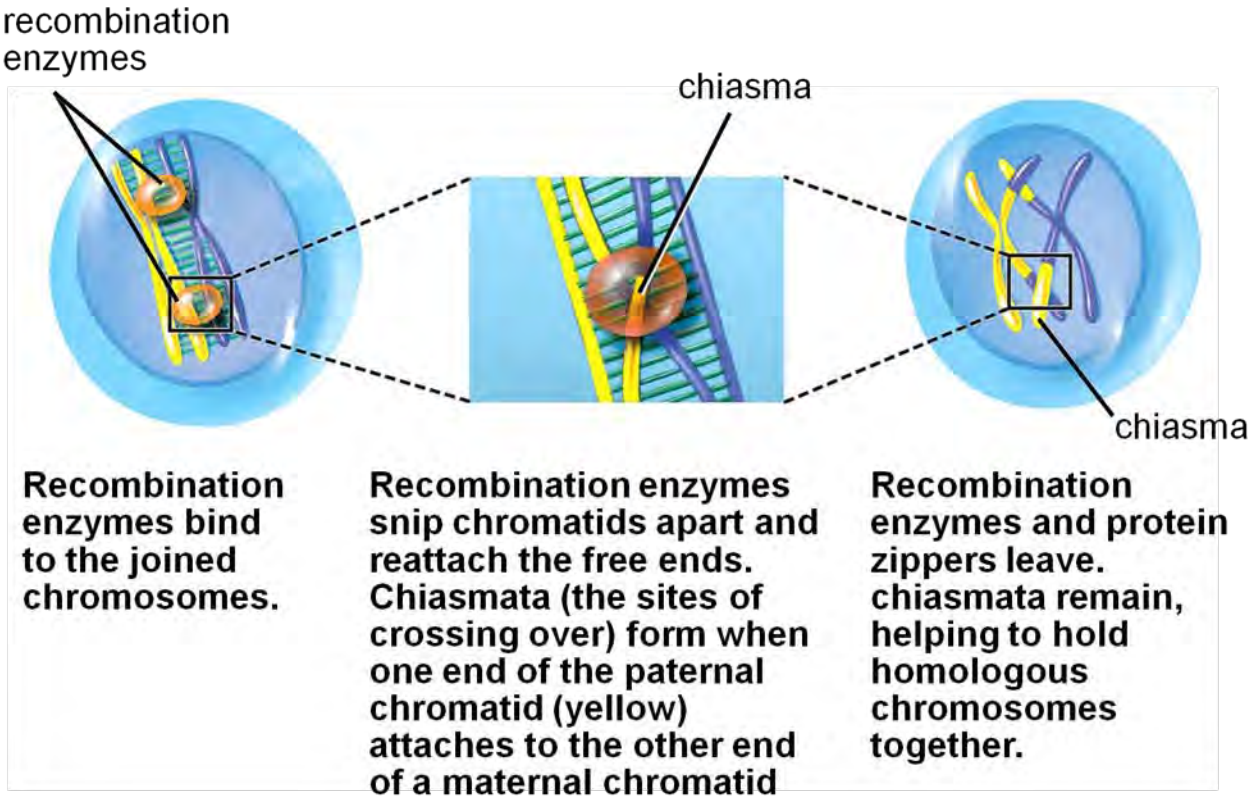
At the end of Meiosis 11 four *haploid* cells are formed. The chromosome number has been halved and each cell (if human) now has 23 chromosomes.

GENETIC DIVERSITY IN HUMANS – GENETIC RECOMBINATION

In humans, meiotic cell division (meiosis) only occurs in the germ cells which are located in the reproductive organs of the male (testes) and the female (ovaries) (Testes and ovaries are also known as the **gonads**.) These germ cells are **diploid**.

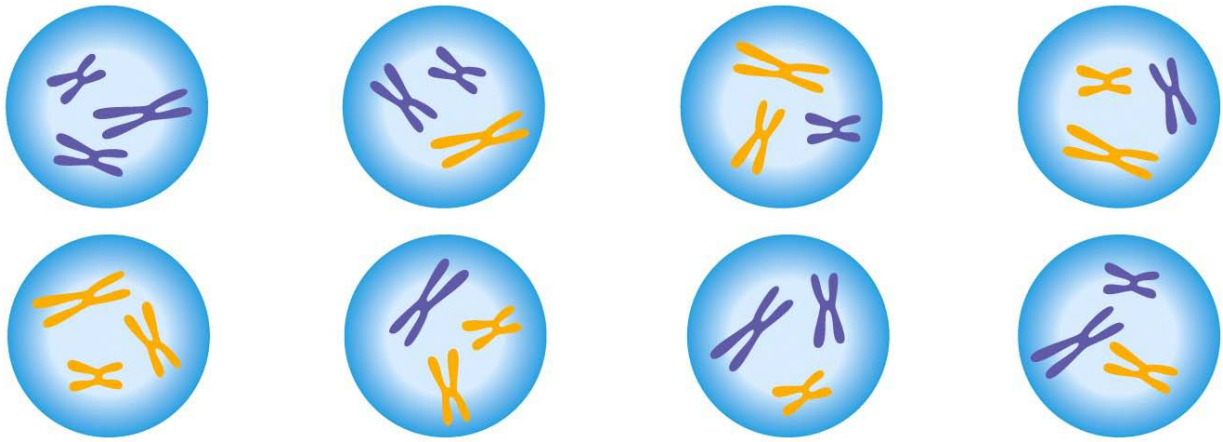
The four cells produced at the end of meiosis are haploid – all other cells of the body are diploid. These four cells are nonidentical. They contain different combinations of genes. How did this RECOMBINATION happen?

1). 1n Meiosis 1 the maternal and paternal chromosomes undergo a process of crossing over during the formation of tetrads. When this occurs the chromosomes that are produced contain genes from both parents – a new combination of genes that probably didn't exist before.



2) Another contribution to genetic diversity is the random distribution of maternal and paternal chromosomes to daughter cells during meiosis 1. When the paired homologues line up at the equator of the cell, which one faces which way is random. A single human cell with 23 pairs of homologous chromosomes can produce gametes with more than 8 million (2^{23}) different combinations of maternal and paternal chromosomes.

This figure shows the 4 possible combinations of chromosomes in mosquitoes which only have 3 pairs of homologous chromosomes and therefore can produce 8 (2^3) possible combinations. The 8 gametes are shown below.



So in the human every sperm and every egg is unique. Although a male may produce about 100 million sperm each day each one carries its own specific assortment of genes. This explains how we have such genetic diversity from one generation to the next, something that is necessary for successful evolution.

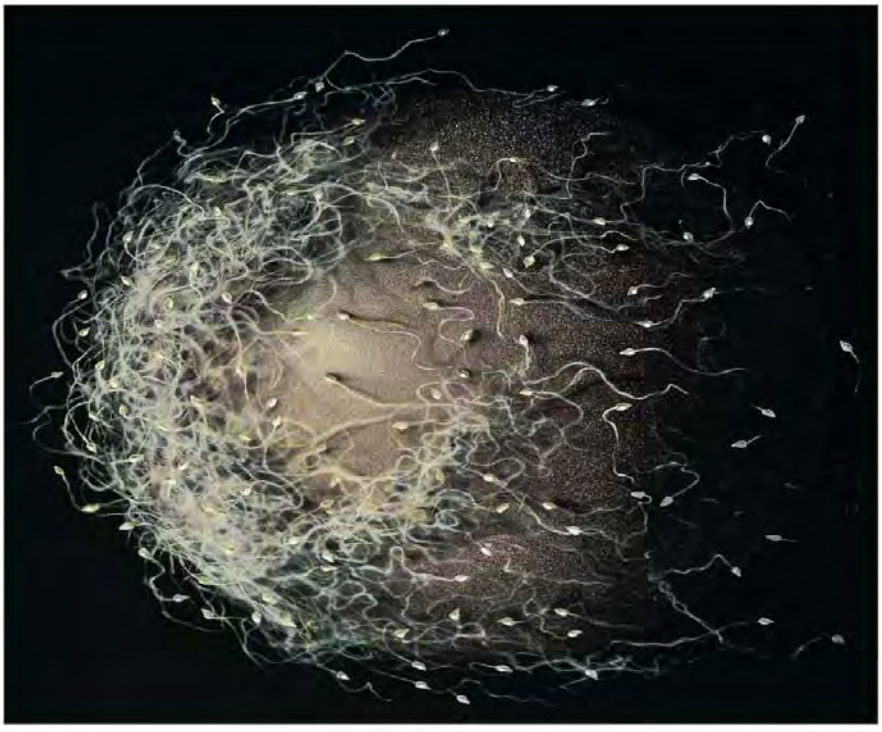
3) Fusion of the 2 gametes to form a diploid cell (during fertilization) furthers genetic variation dramatically so that the chance of having 2 offspring that are genetically identical is nonexistent. The exception is identical twins which form from the same one fertilized cell.

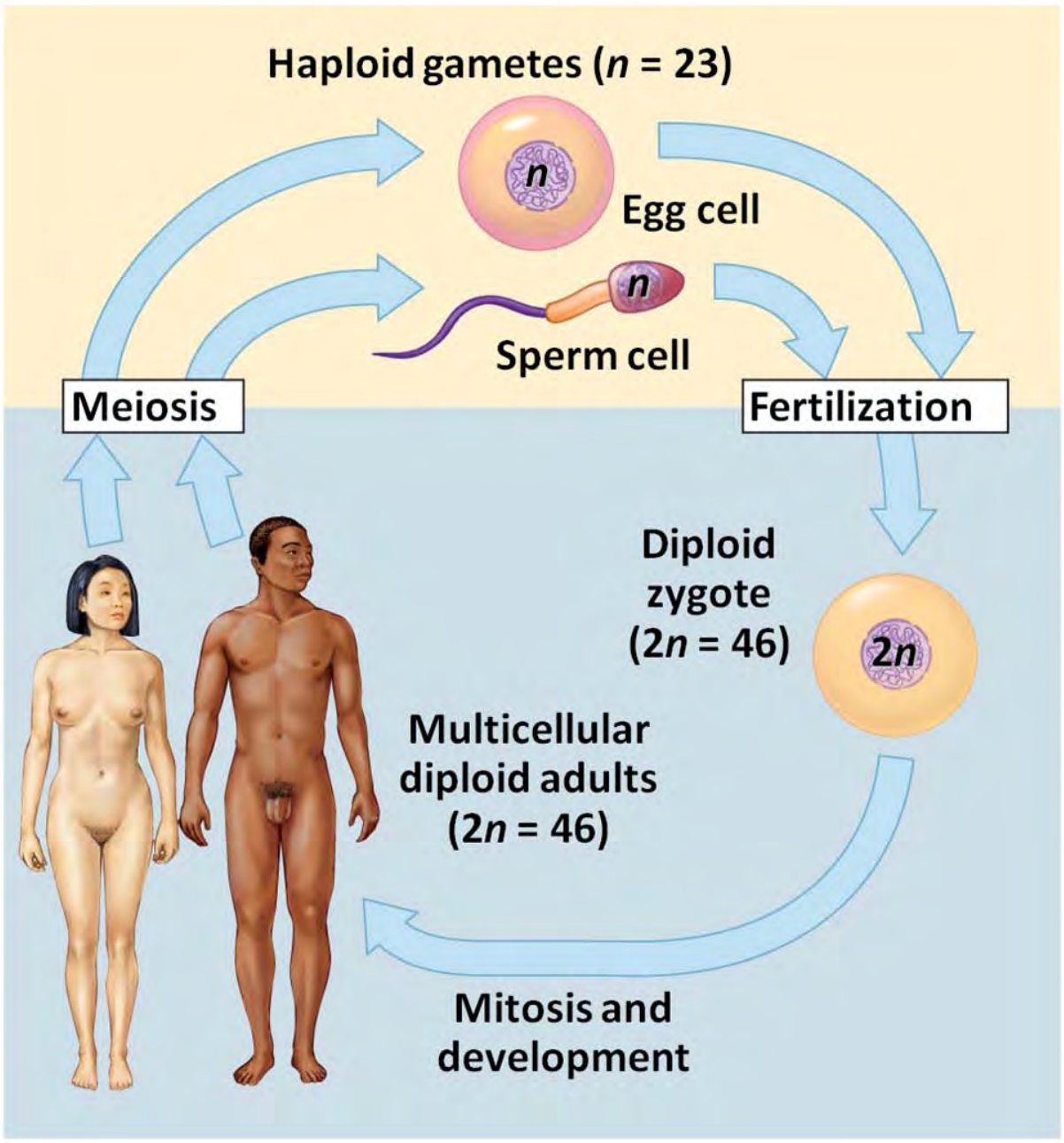
FERTILIZATION

Fertilization takes place when the male sperm carrying 23 chromosomes fertilizes the female ovum (egg) which also contains 23 chromosomes. Thus the first cell of the new human is formed and it is a diploid cell containing 23 chromosomes from the father and 23 chromosomes from the mother. This cell is called a **ZYGOTE.** When the zygote divides to form the trillions of cells to make up the mature organism, the type of cell division that occurs is mitosis.

A summary of human fertilization

During copulation, the male releases semen containing millions of sperm into the female vagina where they swim through the vagina and uterus to the uterine or Fallopian tube where fertilization usually takes place. Hundreds of sperm reach the egg and encircle it releasing enzymes that will weaken the protective barriers around the ovum. **See below**. When the first sperm contacts the egg's surface, the cell membranes of the egg and sperm fuse and the head of the sperm containing the 23 chromosomes is drawn into the cytoplasm of the egg. The two haploid nuclei fuse forming a diploid nucleus that contains all the genetic instructions for a new human being.





The zygote divides by mitosis forming the trillions of cells that make up the human body. As the organism develops the cells **specialize or differentiate** – some become muscle cells, some become nerve cells etc. As stated earlier, mitosis produces identical daughter cells so that all cells contain the same genetic instructions. How, then, is it possible to have different cells? The answer is that not all genes are expressed in all cells. For example skin cells contain the genes for muscle proteins but those genes are not transcribed or translated in skin cells.

LECTURE 12: MENDELIAN GENETICS

To understand genetics it is important to have a good understanding of the steps of meiosis (**Lecture 11**) and a good understanding of the following vocabulary words:

Allele....the gene for each trait can exist in two or more alternative forms

dominant allele....form of a gene that hides the effect of a **recessive allele** in a **heterozygote**

recessive allele....form of a gene whose effect is hidden by the **dominant allele** in a **heterozygote**

multiple allele....more than 2 alleles for a particular trait

Autosome....any **chromosome** other than the sex-determining pair...**sex chromosome**

Chromosome.... a threadlike gene-carrying structure found in the nucleus of all eukaryotic cells and is most visible during mitosis and meiosis. Chromosomes consist of DNA and proteins

Chromosome theory of inheritance....a basic principle in biology stating that genes are located on chromosomes and that the behavior of chromosomes during meiosis accounts for inheritance patterns

Codominance....a condition in heredity in which both alleles in the gene pair of an organism are expressed

Diploid....most higher organisms have **two** copies of each gene in every body (somatic) cell

Gamete....a male or female sex cell with half the chromosomal material (**haploid**). In humans these are the sperm cells in the male and egg cells (ova) in the female

Gene....the unit of heredity {a sequence of DNA (or in some viruses, RNA)} occupying a particular **locus** on the chromosome and passed on to offspring. Genes determine an organism's external appearance, biochemical functioning, behavior and much, much, more.

Gene locus.... the specific location of a particular gene on a chromosome

Genome....all of the genes of an organism

Genotype....the genes of an organism for a particular trait or trait, eg. BB or Aa where A or B (upper case letter) represents the dominant trait and a or b (lower case letter) represents the recessive trait

Haploid....pairs of alleles separate, or segregate, during egg and sperm formation and each gamete will have **one** copy of each gene

Heterozygous....possessing 2 different alleles for a particular trait

Homologous chromosomes are two chromosomes that are similar (but not identical) in size, shape, and genetic content

Homozygous....possessing 2 identical alleles for a particular trait

Hybrid offspring…….of a genetic cross, inherit nonidentical alleles for a trait

Incomplete dominance....a pattern of inheritance in which the offspring shows characteristics intermediate between the two parental characteristics: for example, a red and white flower producing pink offspring

Linkage group....genes that are located on the same chromosome and tend to be inherited together

Mendel's law of segregation: Each organism contains 2 factors for each trait. The factors segregate (separate) during the formation of gametes so that each gamete contains only one factor for each trait. When fertilization occurs, the new organism has 2 factors for each trait, one from each parent.

Mendel's theory of independent assortment: Members of one pair of factors segregate (assort) independently of members of another pair of factors. Therefore, all possible combinations of factors can occur in the gamete.

Monohybrid....a genetic cross involving one trait

Mutation....a change in the composition of DNA, due to either a genetic or a chromosomal alteration

Pedigree….a family tree representing the occurrence of heritable traits in parents and offspring, across as many generations as possible.

Phenotype....the expression of a genotype: enzyme structure, eye color, height, for example

Polygenic inheritance....a pattern of inheritance in which a trait is controlled by several gene pairs that segregate independently

Polyploid (polyploidy)....a condition in which an organism has more than 2 sets of chromosomes

Punnett square....a grid-like graph that enables one to calculate the results of simple genetic crosses by lining genotypes of gametes on the outside margin and their recombination in boxes inside the grid

- **P** parental generation
- **F_1** first-generation offspring
- **F_2** second-generation offspring

Sex-linked gene....unit of heredity, a gene, located on a sex chromosome

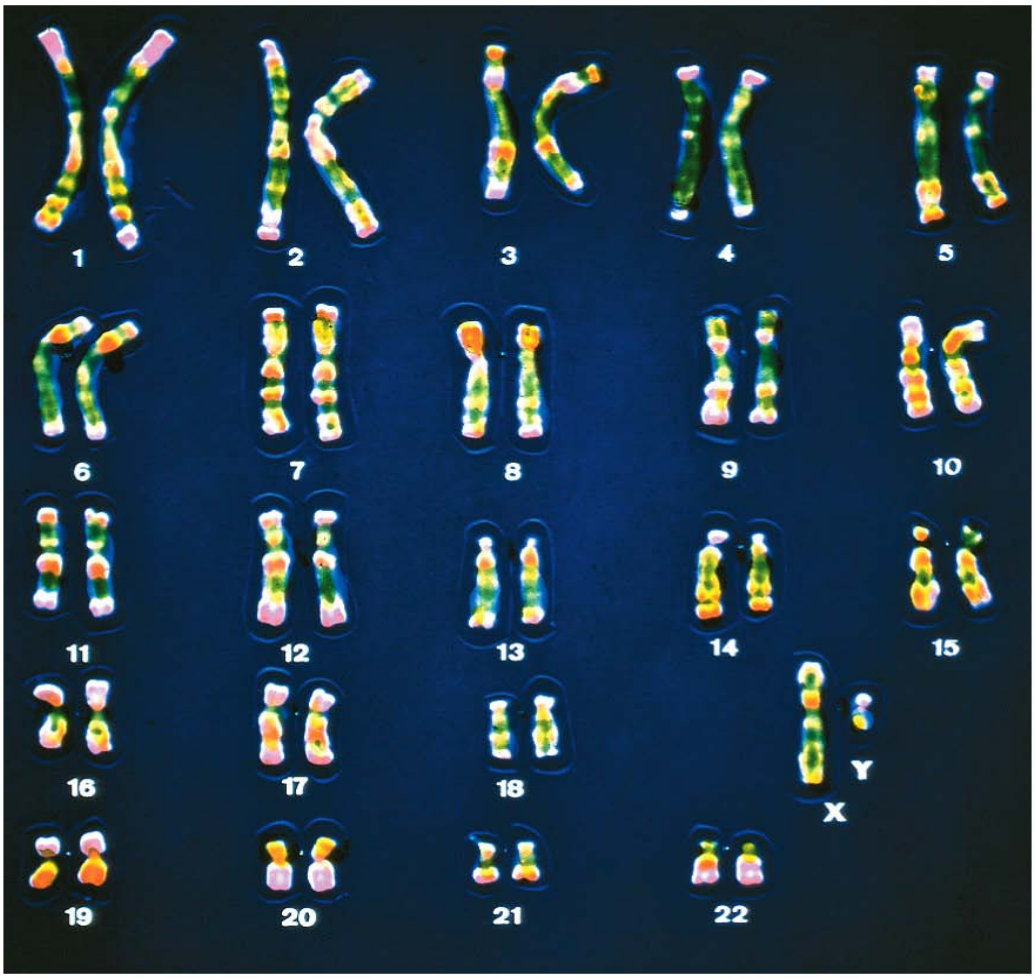
Testcross....a genetic mating in which a possible heterozygote is crossed with an organism homozygous recessive for characteristic(s) in question in order to determine its genotype

True-breeding lineage....what occurs when genetic crosses involve identical alleles for a trait, generation after generation

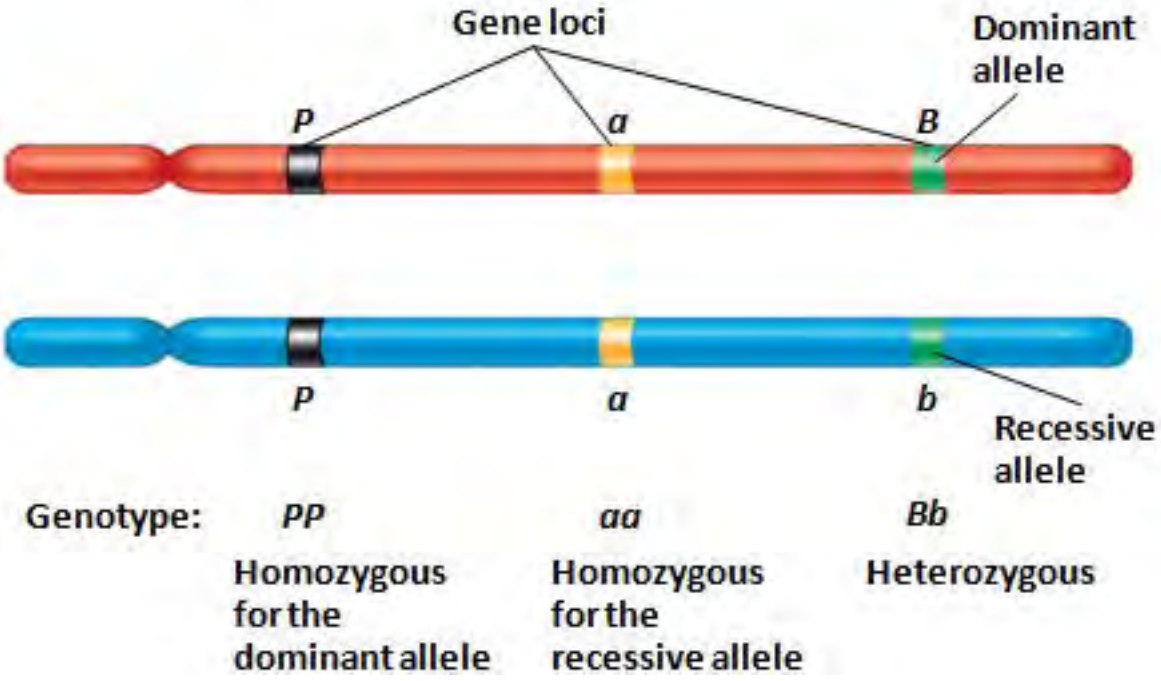
X-linked gene....gene located on the X chromosome that does not control a sexual feature of the organism

Wild type….typical form of a gene as it occurs in nature

A karyotype is a preparation showing the number, sizes, and shapes of all chromosomes.
Below is a human karyotype showing the 46 chromosome – 23 from the mother and 23 from the father. These are present in every cell of the human body (except the sex cells which only have 23). Each pair below is called a homologous pair meaning that it carries similar but not necessarily identical genes. One comes from the mother, the other from the father. There is always one pair of sex chromosomes. Here the male is represented, an x and a y. A female would have 2 x chromosomes.



Representations of chromosomes including gene locations and dominant and recessive terminology.



A chromosome is made of DNA and proteins. Each human chromosome contains several thousand genes. Genes are sections of DNA that code for proteins. Each gene is a series of triplets or codons (3 base pairs) that specifies a particular amino acid.

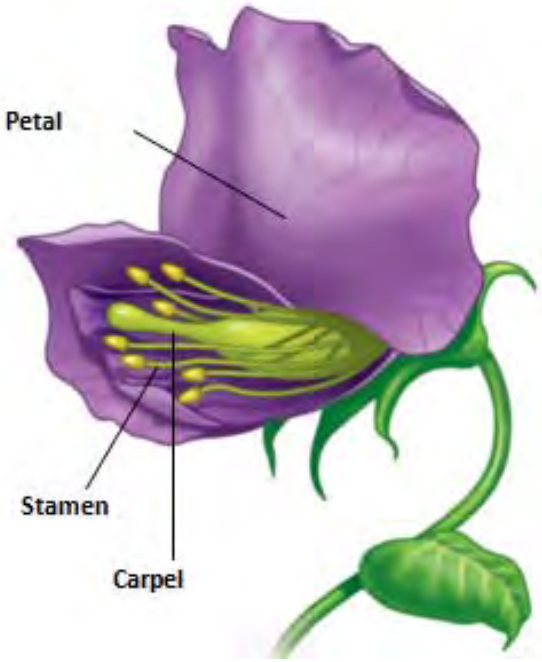
MECHANISM OF INHERITANCE

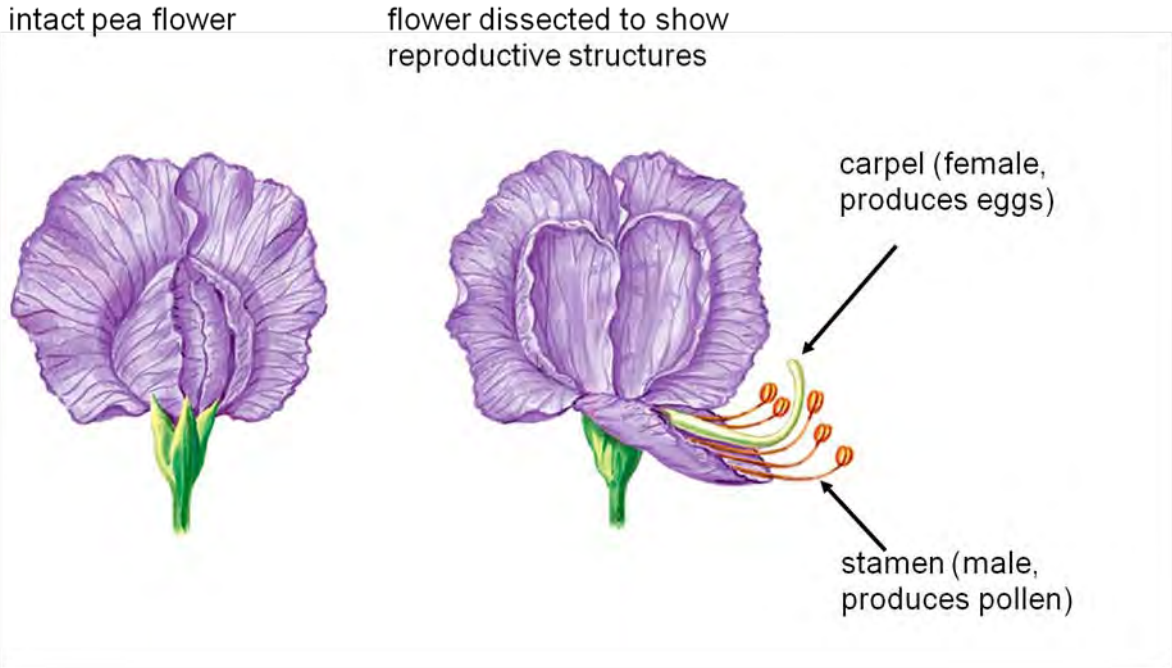
(Note v indicates that the term is defined in the previous list)

Recorded theories of inheritance have been around since the time of the ancient Greeks but only in the 1800s, with a crude understanding of cells and cell division, did scientists realize that new cells arose from old cells. New organisms were understood to develop from parental organisms but it took a clearer understanding of nuclear events before the details of mitosis and meiosis (**Lecture 11**) were worked out.

Ground – breaking contributions to our understanding of genetics were made by an Austrian monk named Gregor Mendel who was able to discover what was going on inside the "black box" of genetics without any sophisticated scientific instruments or any knowledge of genes or chromosomes.

Mendel studied patterns of inheritance using garden pea plants which were good subjects because each plant contains both male and female parts. The female part, called the carpel, contains the stigma, style, and ovules. The male part is the stamen which contains the filament and anthers on which pollen (sperm) is found.

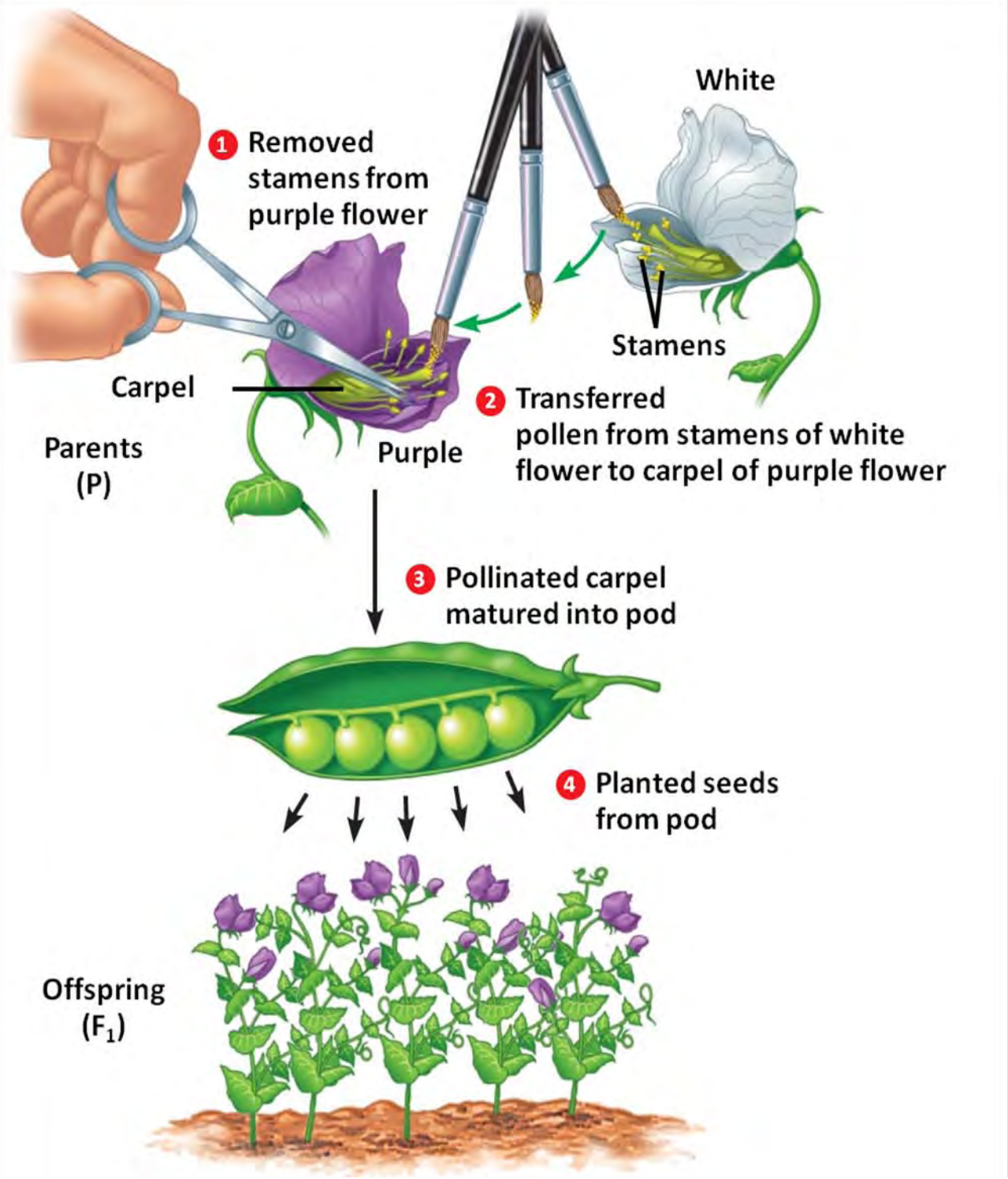




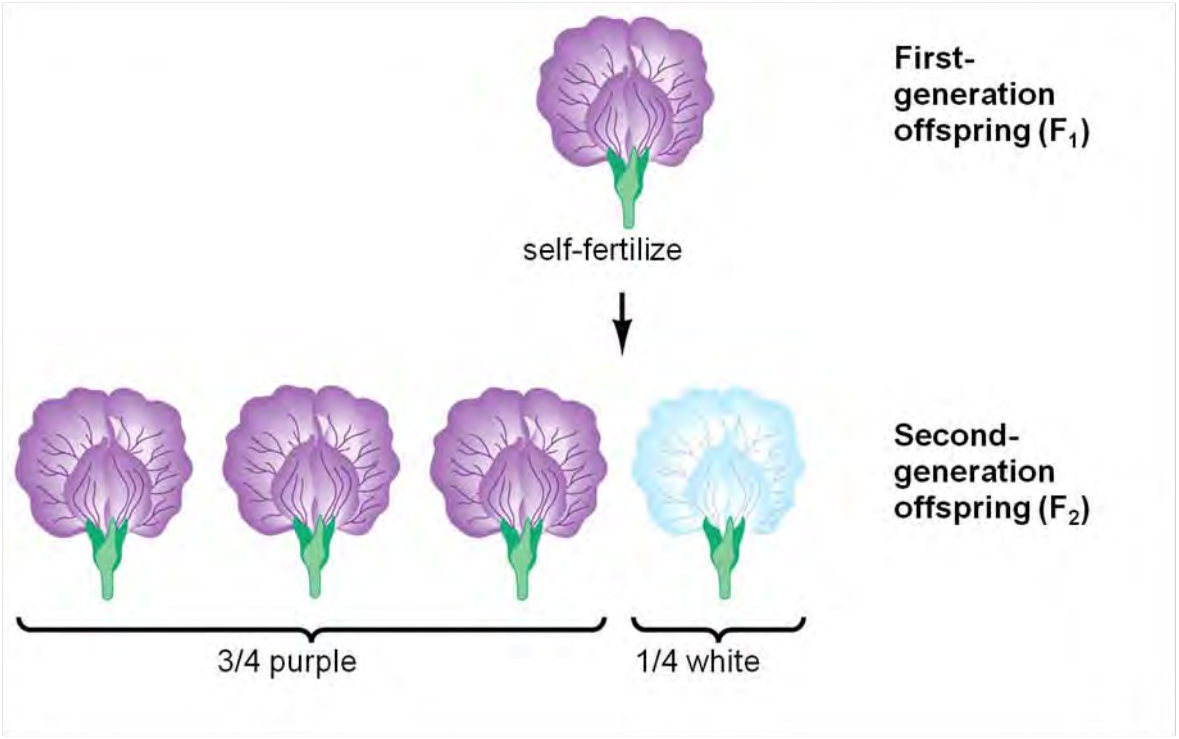
The gametes (**v**) produced within each flower – sperm within pollen grains on the anthers, and eggs within ovules – fuse to produce the embryos within the seeds of new plants. This is **self-fertilization** and after several generations some plants produce offspring which are identical to the parent and are said to be true-breeding (**v**).
Mendel took plants that were true-breeding for several characteristics and **cross-fertilized** them, producing hybrids (**v**).

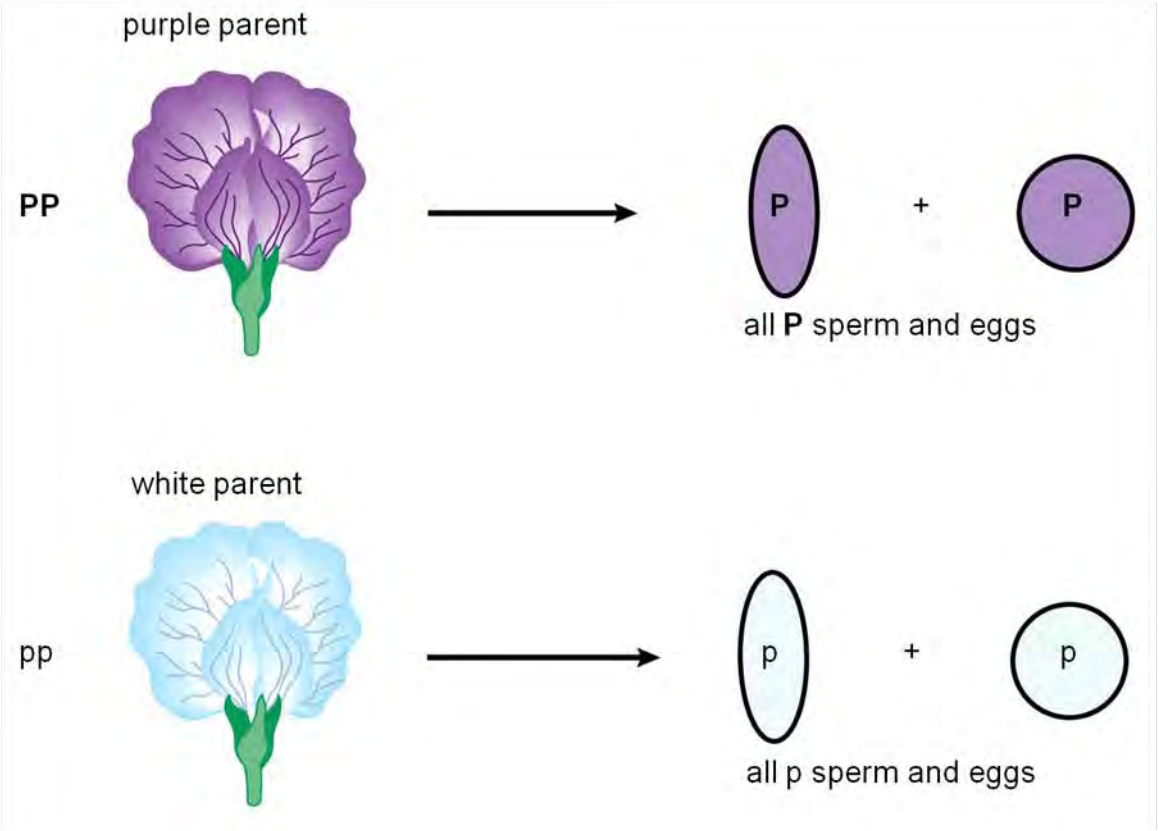
One trait that is easily followed is color and the details of fertilization through parental (P), first generation (F1) and second generations (F2) are on the next pages. Note that it is conventional to use the uppercase letter to denote the dominant trait and the lowercase letter for the recessive trait. For example P = purple p = white

An organism has 2 copies of each trait or gene (usually). An organism with the genotype PP is homozygous dominant, an organism with the genotype Pp is heterozygous, and an organism with the genotype pp is homozygous recessive

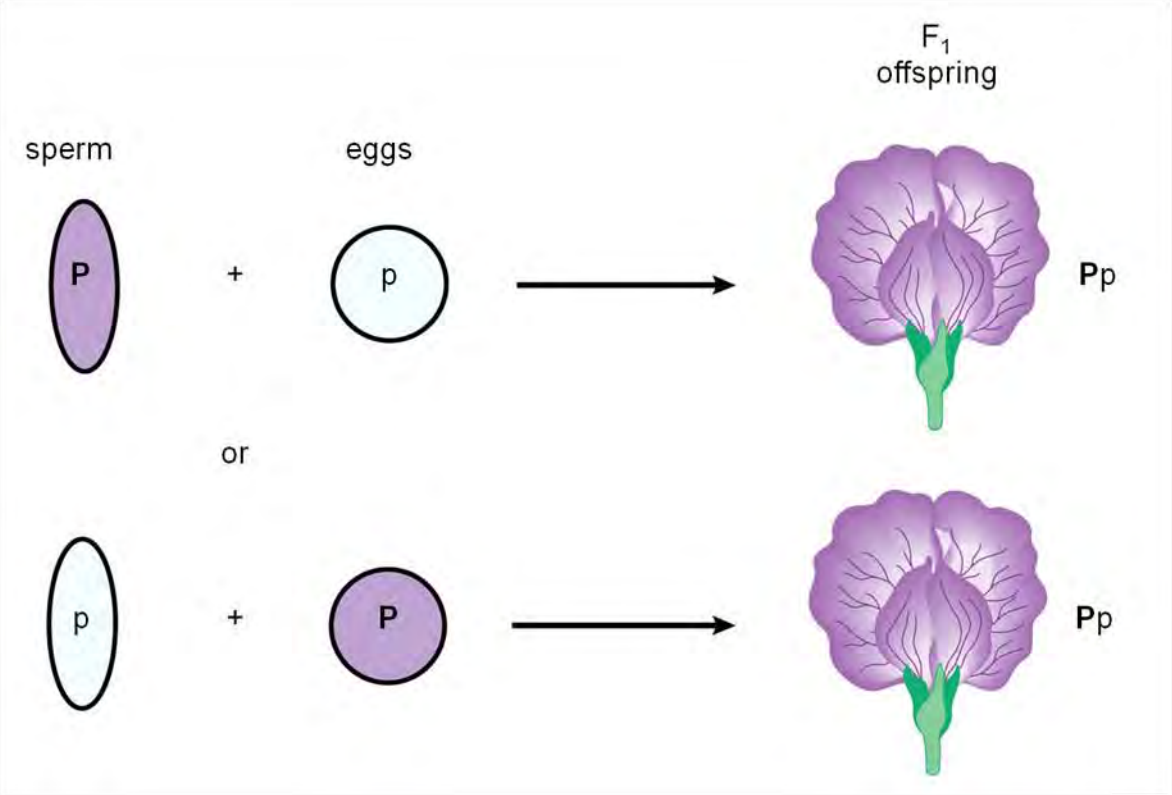


How Mendel cross fertilized plants.

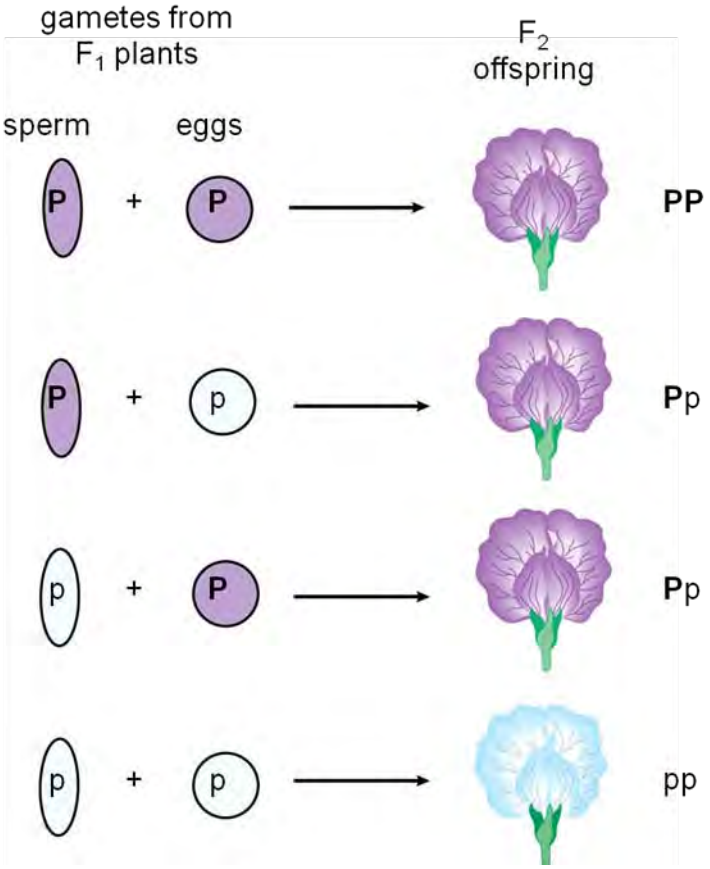

First-generation offspring (F_1)
self-fertilize
Second-generation offspring (F_2)
3/4 purple
1/4 white


purple parent
PP
P
+
P
all P sperm and eggs
white parent
pp
p
+
p
all p sperm and eggs

In the P generation both plants are true breeding so all gametes from the purple plant carry the dominant trait P and all gametes from the white plant carry the recessive trait p.

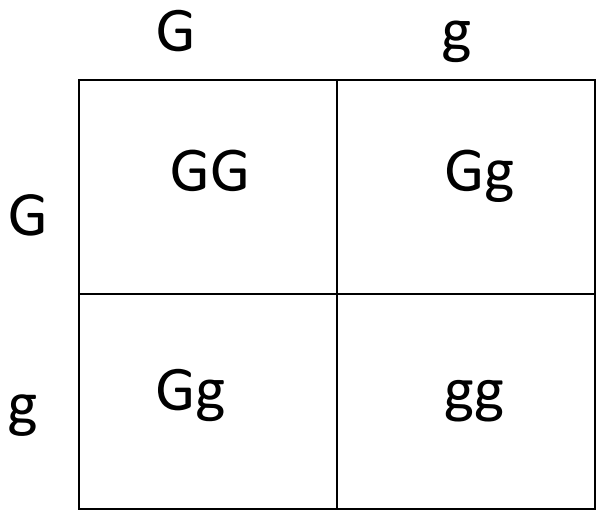


Using a simple Punnett square (v) it is clear that when cross fertilization occurs all offspring will have the genotype (v) Pp and the phenotype (v) purple.



When the F1 generation (all Pp) self fertilize the result is that ¾ of the offspring (F2 generation) will have the genotype Pp and will have the phenotype purple and ¼ will have the genotype pp and have the phenotype white – see Punnett Square on next page.

PUNNETT SQUARE (Example shows crossing 2 heterozygotes -Gg)



GAMETES ON THE OUTSIDE; GENOTYPE OF OFFSPRING INSIDE

On previous pages we looked at the pattern for inheritance of one trait or gene - how it is passed on through generations. Similarly, we can apply this to human genes. We all have 2 copies of each gene – one from our mother and one from our father. (An exception - males have only one copy of each gene for those that are located on the X chromosome.) And the same probabilities apply.

If both parents carry only the dominant form of the gene (GG) then the child will inherit that genotype. But if both parents are heterozygous for a particular gene (Gg, Gg) then the child will have a 25 % chance of having the genotype GG, a 25% chance of having the genotype gg, and a 50% chance of having the genotype Gg. See above.

Recessive traits and disease.
Remember that to express or to display a recessive trait the offspring must have 2 copies of the recessive gene. Many disease traits are recessive and only show up when the child inherits a recessive trait from both parents. For example, if both parents carry a recessive trait for a disease like ***Cystic Fibrosis***, they will not have the disease but there is a 25% chance that a child could have the disease.

The parents' genotype will be **Ss** where **S** stands for normal version of the gene and **s** stands for the mutated version. The Punnett Square above shows the likely

genotypes of offspring from two parents with the genotype Ss. The parents are carriers so the probability of the genotype of the offspring is: 25% will have no mutated gene, 50% will be carriers, and 25% will have the disease.
Remember that these percentages are the probabilities. It is also possible that all offspring could have the disease or no offspring have it.

Sometimes genes have the basic pattern of dominant and recessive as was shown with the gene for color in pea plants but sometimes genes can be **codominant** or **incompletely dominant** or more than one gene influences the same trait. Also, the effect of genes can vary with the environment. Although Mendel's contributions to genetics have been invaluable, there are a lot of instances in the living world where inheritance is more complex and these will not be discussed here.

LECTURE 13 GENE EXPRESSION AND PROTEIN SYNTHESIS

Proteins

Think back to the unit on organic chemistry (**Lecture 5**), specifically the segment on proteins. You will see that their functions in living cells are many and varied. It is not an exaggeration to say that DNA's essential function is to serve as a code for how to build proteins or polypeptides.

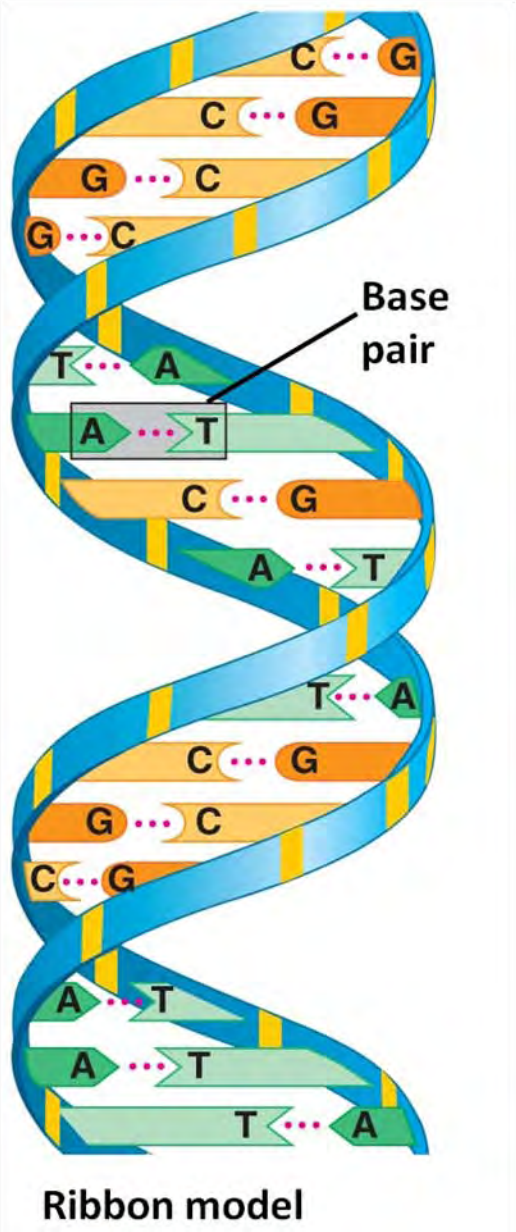
Note: Sometimes the terms **protein and polypeptide** are used interchangeably, each being a combination of amino acids. But sometimes the terms are used more specifically. A protein has a specific function and sometimes one protein is made from several polypeptide chains.

There are hundreds of thousands of proteins; each one is built from some combination of 20 different amino acids. The comparison to the English alphabet is often made where hundreds of thousands of words are constructed from just 26 different letters.

DNA is the molecule that contains the directions for the synthesis of proteins or polypeptides. ***A gene is a sequence of bases in a DNA molecule that carries the information necessary for producing a protein or, in some cases, an RNA molecule***. Different genes have different base sequences, and different proteins have different amino acid sequences. Therefore the sequence of bases in DNA must encode the sequence of amino acids in a protein.

Review of Structure of DNA

The DNA of chromosomes is composed of two strands wound about one another in a double helix. The sugars and phosphates that link one nucleotide to the next form the backbone on each side of the double helix (blue), while the bases from each strand pair up in the middle of the helix. Only specific pairs of bases, called complimentary base pairs, can link together in the helix and are held by hydrogen bonds: **adenine always pairs with thymine and guanine with cytosine**.



Ribbon model

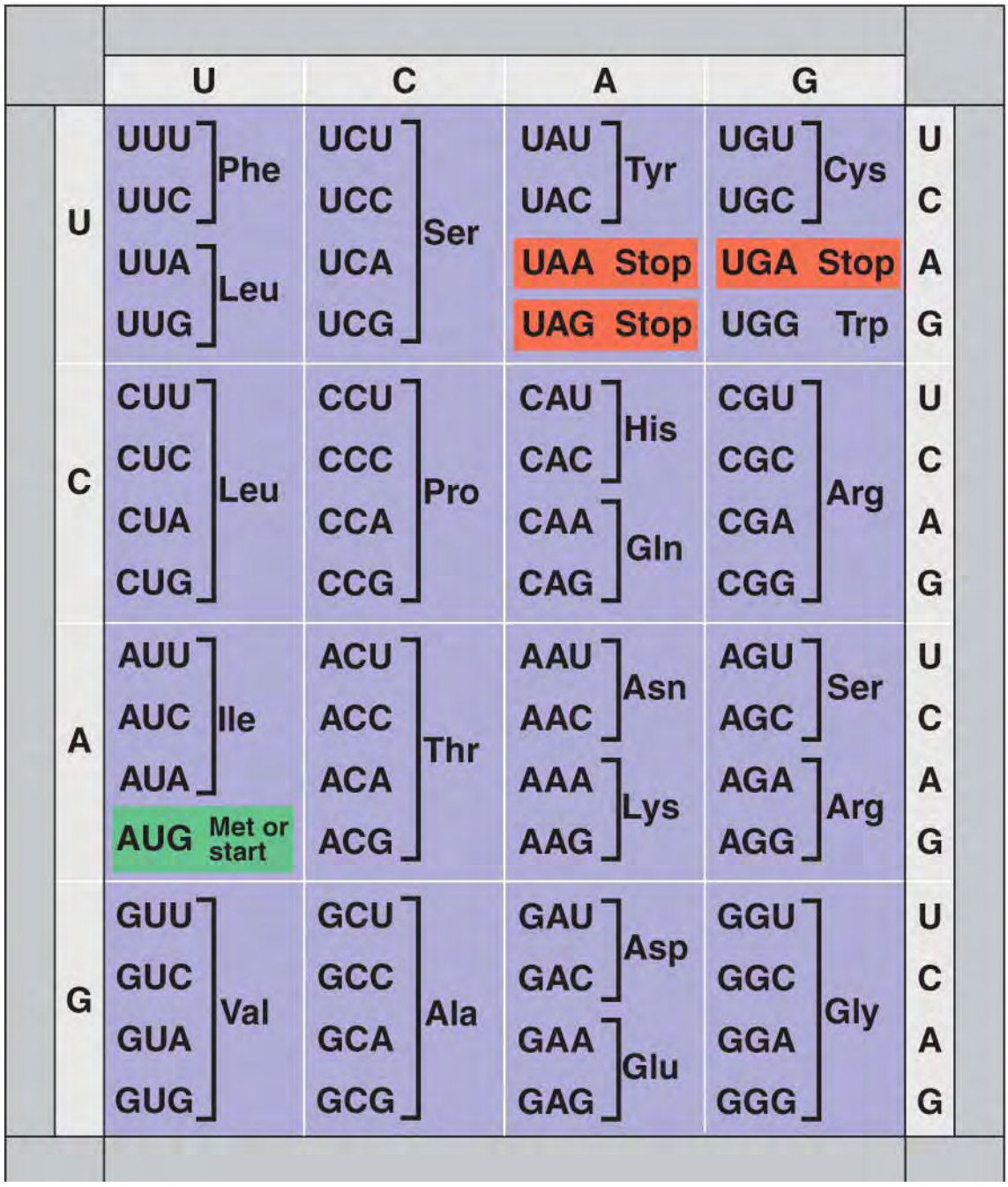
Those 4 base pairs, adenine, thymine, guanine, and cytosine, make up the genetic code. A gene is literally some combination of those 4 bases and could be represented by "ATACCGTACGTTACGGGCCTTATGCCGTGTCAGTGCTAGCTA" although most genes are much longer. So the obvious question is: **How can just 4 different bases (4 different letters, in a way) code for 20 different amino acids?**

If each code word was made up of 1 base then only 4 amino acids would be coded for. If 2 bases are used then there would be only 16 code words (4^2 = 4x4=16) but 20 are needed. But if each code word were made up of 3 bases you would get 64 code words…4^3 = 4x4x4=64 which turns out to be the case. See the genetic code on the next page.

The genetic code is:

- **A. degenerate i.e. most amino acids have more than one codon. Some have 6.**
- **B. unambiguous. Each triplet code has only one meaning.**
- **C. has start and stop signals.**
- **D. is universal**

THE GENETIC CODE



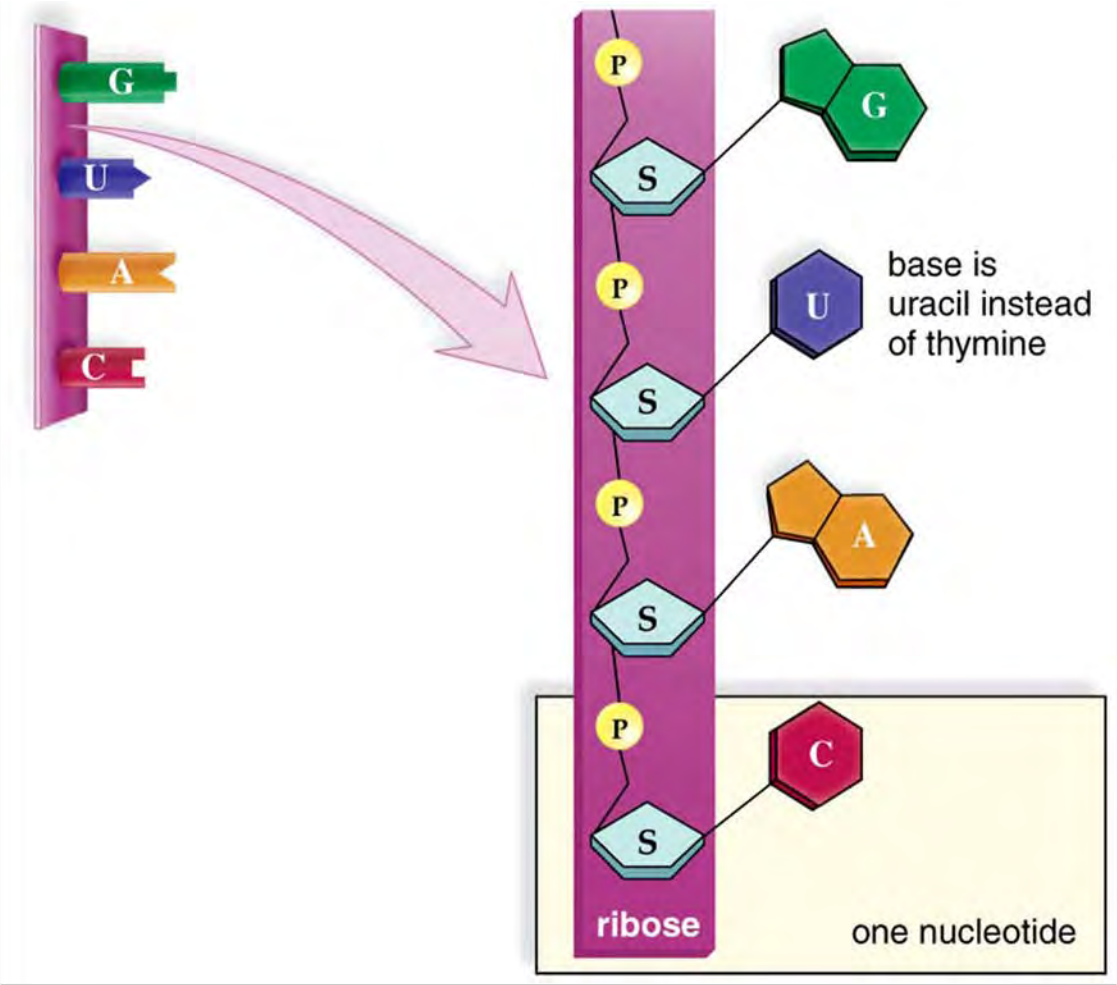
	U	C	A	G	
U	UUU Phe UUC Phe	UCU Ser UCC Ser UCA Ser UCG Ser	UAU Tyr UAC Tyr	UGU Cys UGC Cys	U C
	UUA Leu UUG Leu		UAA Stop UAG Stop	UGA Stop UGG Trp	A G
C	CUU Leu CUC Leu CUA Leu CUG Leu	CCU Pro CCC Pro CCA Pro CCG Pro	CAU His CAC His CAA Gln CAG Gln	CGU Arg CGC Arg CGA Arg CGG Arg	U C A G
A	AUU Ile AUC Ile AUA Ile	ACU Thr ACC Thr ACA Thr ACG Thr	AAU Asn AAC Asn AAA Lys AAG Lys	AGU Ser AGC Ser AGA Arg AGG Arg	U C A G
	AUG Met or start				
G	GUU Val GUC Val GUA Val GUG Val	GCU Ala GCC Ala GCA Ala GCG Ala	GAU Asp GAC Asp GAA Glu GAG Glu	GGU Gly GGC Gly GGA Gly GGG Gly	U C A G

The genetic code is represented by RNA **codons** which are sequences of 3 bases. Note that there are **start (AUG) and stop (UAA & UGA) codons** that signal the beginning and end of protein synthesis as well as codons for the 20 amino acids.

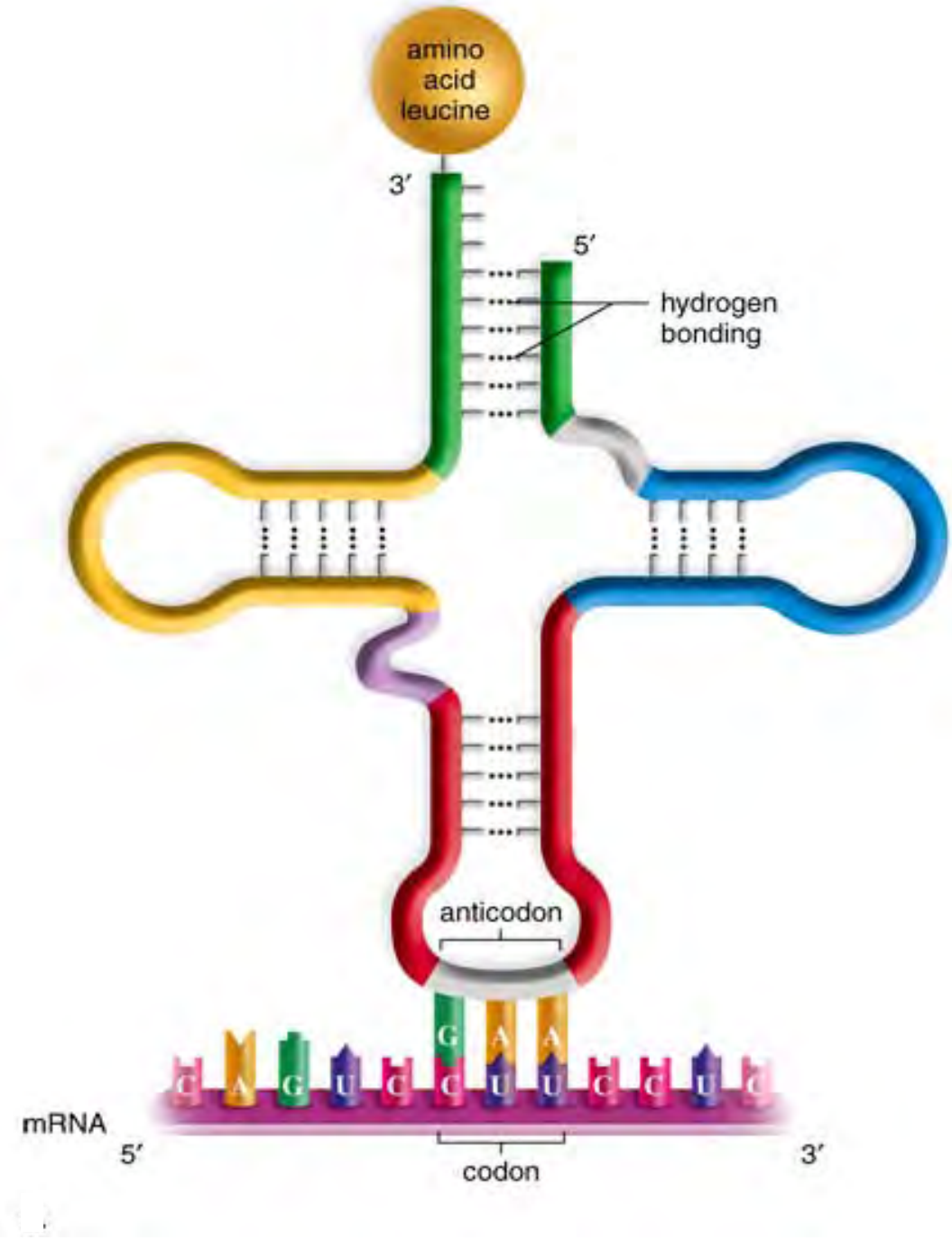
RNA molecules and RIBOSOMES are also necessary for the process of protein synthesis: - a quick review here.

RNA (covered in **lecture 5)**
Remember RNA is a nucleic acid (like DNA) with some important differences. It is small, single – stranded, has uracil (U) instead of thymine (T), ribose instead of deoxyribose, and it can leave the nucleus of the cell.
Involved in protein synthesis are 3 types of RNA:
A) messenger RNA/mRNA,
B) ribosomal RNA/rRNA,
C) transfer RNA/tRNA

A) Messenger RNA



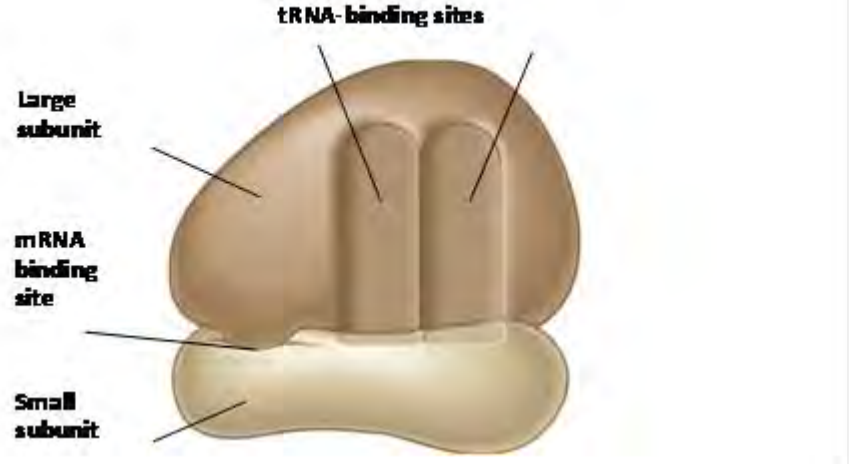
B) Transfer RNA is similar to mRNA but the chain of nucleotides is folded in a 4-leaf clover shape. One end of the tRNA molecule is linked to a specific amino acid, the other end bonds with mRNA as it is moving through the ribosome.



C) Ribosomal RNA is a component of ribosomes which are reviewed next.

Ribosomes (covered in **Lecture 6**)

Ribosomes are composed of 2 subunits – one larger than the other. Both are made of proteins and ribosomal RNA (rRNA). The 2 subunits are separate in the cytoplasm but come together to synthesize proteins. Some ribosomes are free in the cytoplasm and synthesize proteins for use in the cell. Other ribosomes are attached to the rough endoplasmic reticulum (RER) and synthesize proteins that are used in the cell membrane or for export from the cell.



In summary, to synthesize a protein a cell needs:

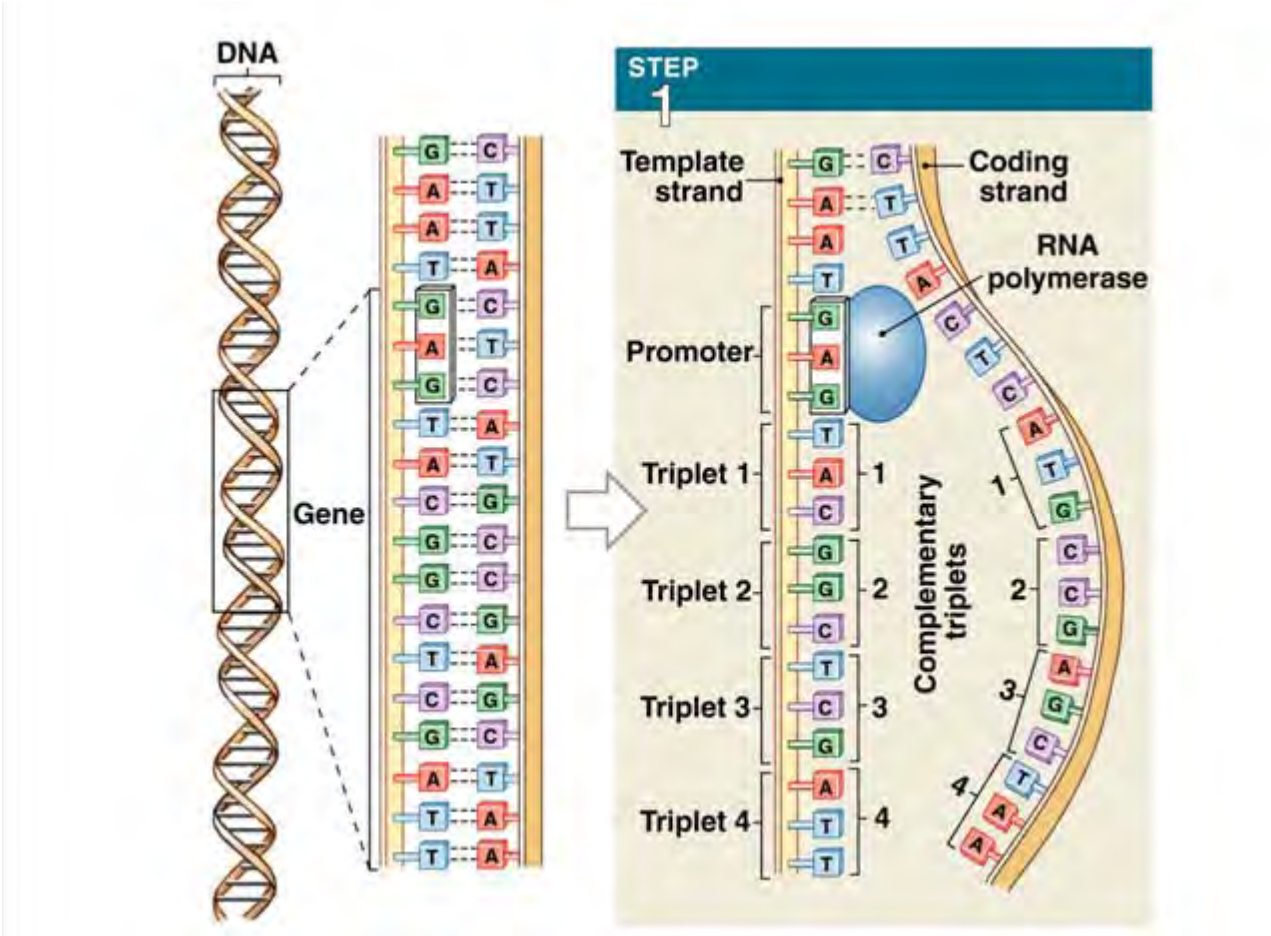
1) **A set of instructions which are segments of DNA called genes located in the nucleus of eukaryotic cells.**
2) **A pool of amino acids which are the building blocks of all proteins and are available in the cytoplasm having been obtained from proteins consumed, or the breakdown and recycling of other molecules in the cell.**
3) **3 different types of RNA and ribosomes as described above.**

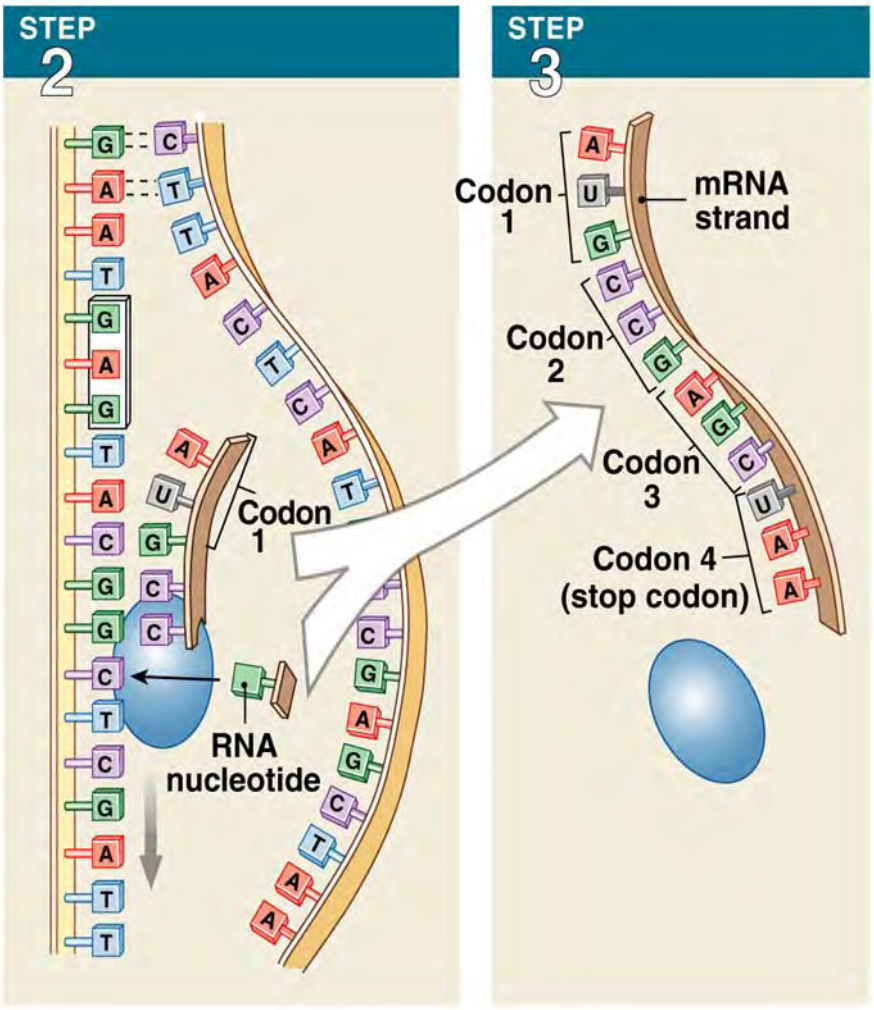
FROM DNA TO PROTEINS: HOW A CELL CONVERTS THE MESSAGE OF ITS DNA INTO PROTEIN VIA TRANSCRIPTION & TRANSLATION.

Simplified steps of Protein Synthesis

Transcription: In the nucleus the DNA strand unwinds at the gene location. An RNA polymerase binds and moves along the template DNA strand and makes a complimentary copy of mRNA. The mRNA strand leaves the nucleus of the cell and enters the cytoplasm.

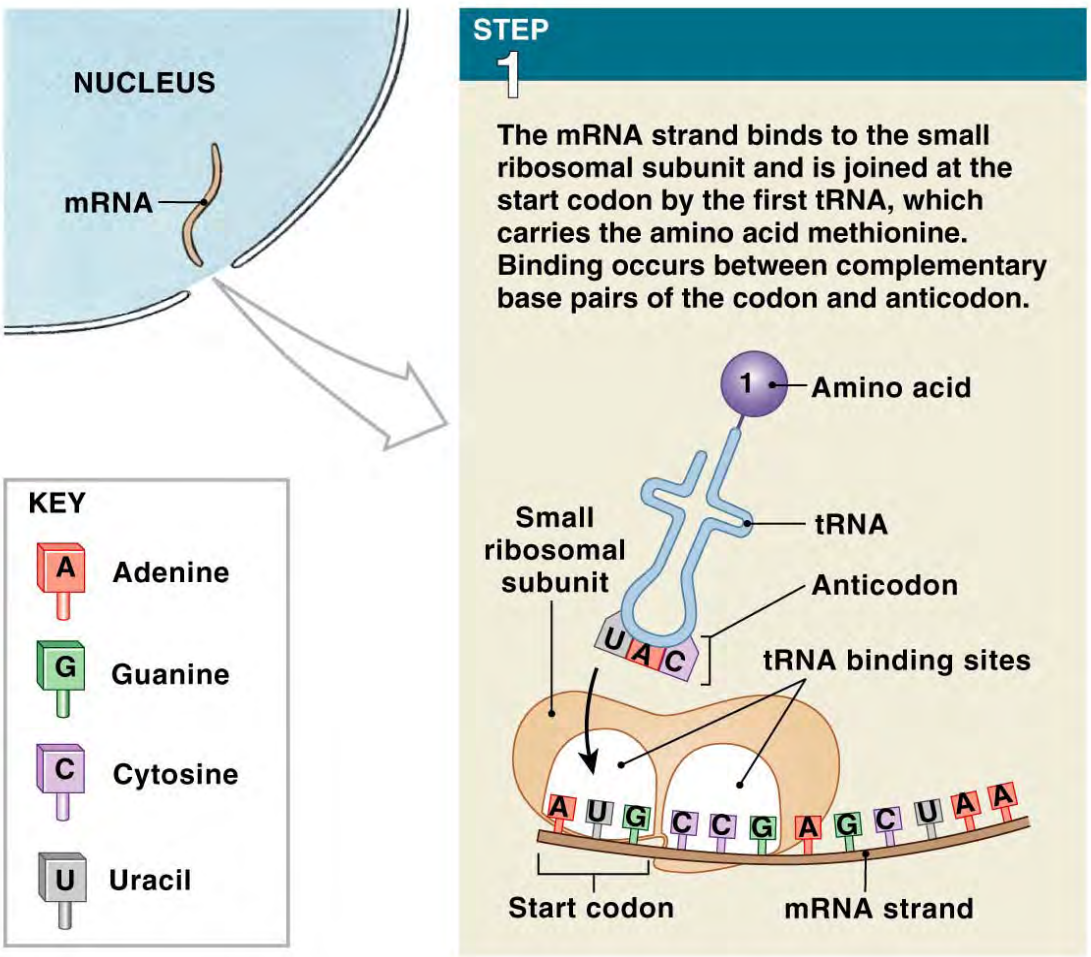
The following figures show the basic steps in the process.
A sequence of 3 bases in DNA is called a triplet, in mRNA a codon, in tRNA an anticodon.




STEP 2
STEP 3
Codon 1
RNA nucleotide
Codon 1
mRNA strand
Codon 2
Codon 3
Codon 4 (stop codon)

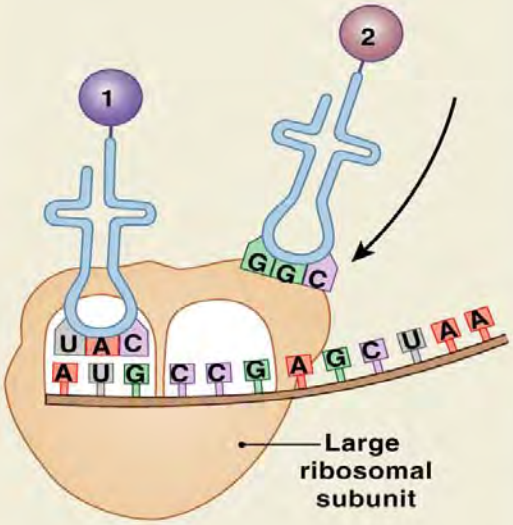
Translation: A small ribosomal subunit binds to the mRNA at the "start" codon. A tRNA with its attached amino acid and the larger ribosomal subunit attach to the small subunit with the mRNA and begin "reading" the mRNA, one codon (3 base pairs) at a time. The complementary tRNA with its amino acid is "pulled" in. A peptide bond forms between the amino acids.

When a "stop" codon is reached, translation is complete and the finished protein is released from the ribosome.



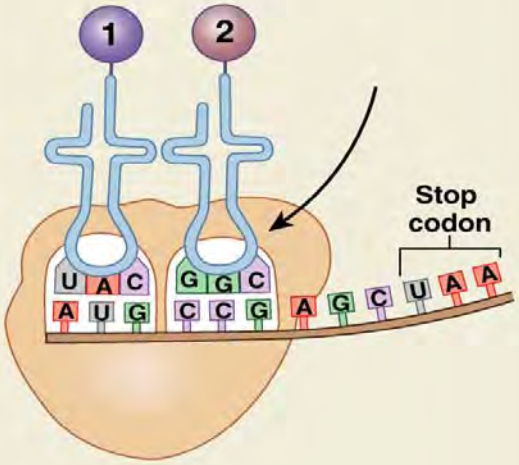
STEP 2

The small and large ribosomal subunits interlock around the mRNA strand.



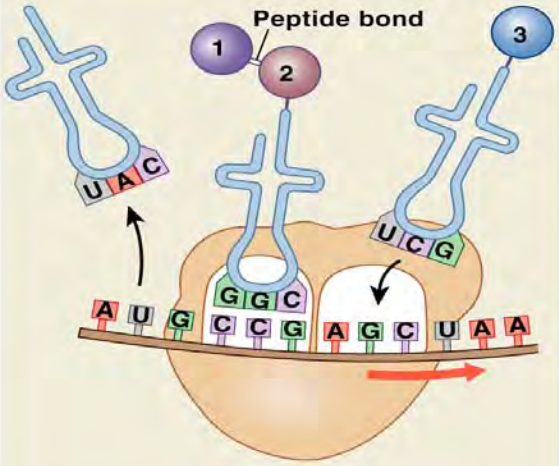
STEP 3

A second tRNA arrives at the adjacent binding site of the ribosome. The anticodon of the second tRNA binds to the next mRNA codon.



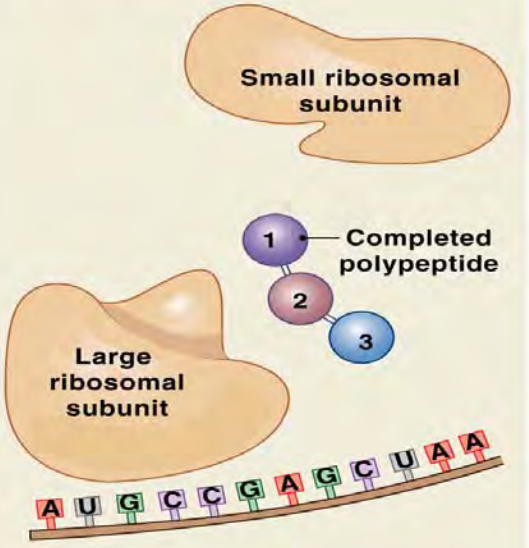
STEP 4

The first amino acid is detached from its tRNA and is joined to the second amino acid by a peptide bond. The ribosome moves one codon farther along the mRNA strand; the first tRNA detaches as another tRNA arrives.



STEP 5

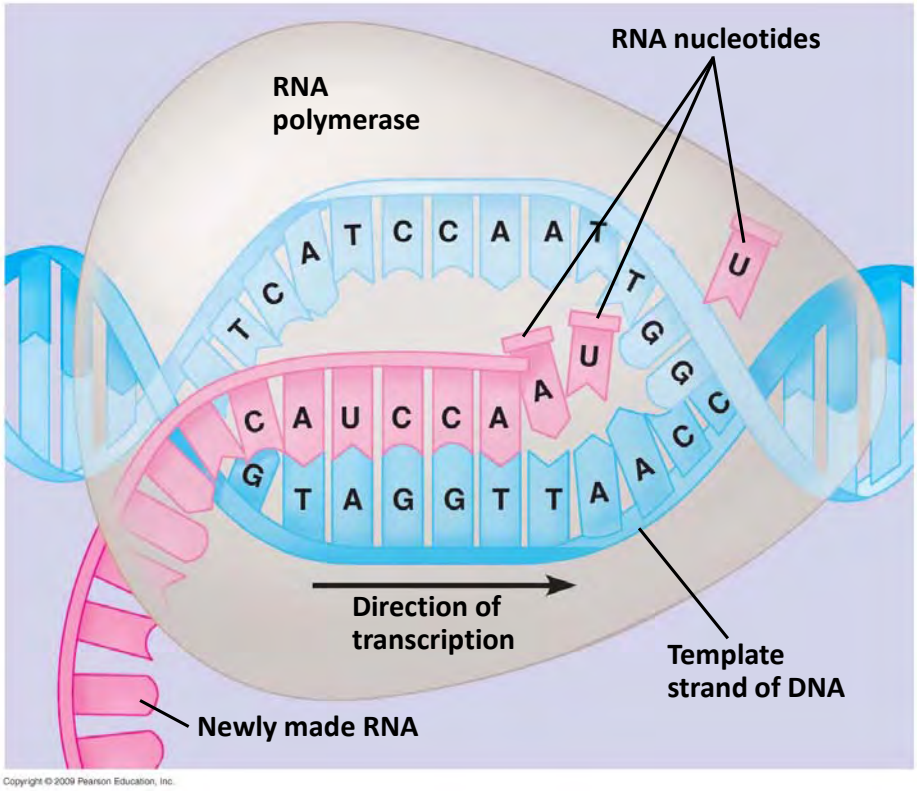
The chain elongates until the stop codon is reached; the components then separate.



A more detailed description of protein synthesis (transcription and translation) is outlined below.

TRANSCRIPTION involves making an mRNA copy of the gene.
A section of the DNA unwinds and the exposed nucleotides form base pairs with RNA nucleotides in the nucleus. (**C pairs with G and A with U**). The enzyme involved is RNA polymerase which binds to a **PROMOTER** site on the DNA. This is a sequence of DNA bases that signals the start of a gene.
Transcription involves 3 processes: Initiation, Elongation, & Termination.

- Stages of transcription
  - **Initiation:** RNA polymerase binds to a **promoter**, where the helix unwinds and transcription starts
  - **Elongation**: RNA nucleotides are added to the chain
  - **Termination**: RNA polymerase reaches a **terminator** sequence on DNA and detaches from the template



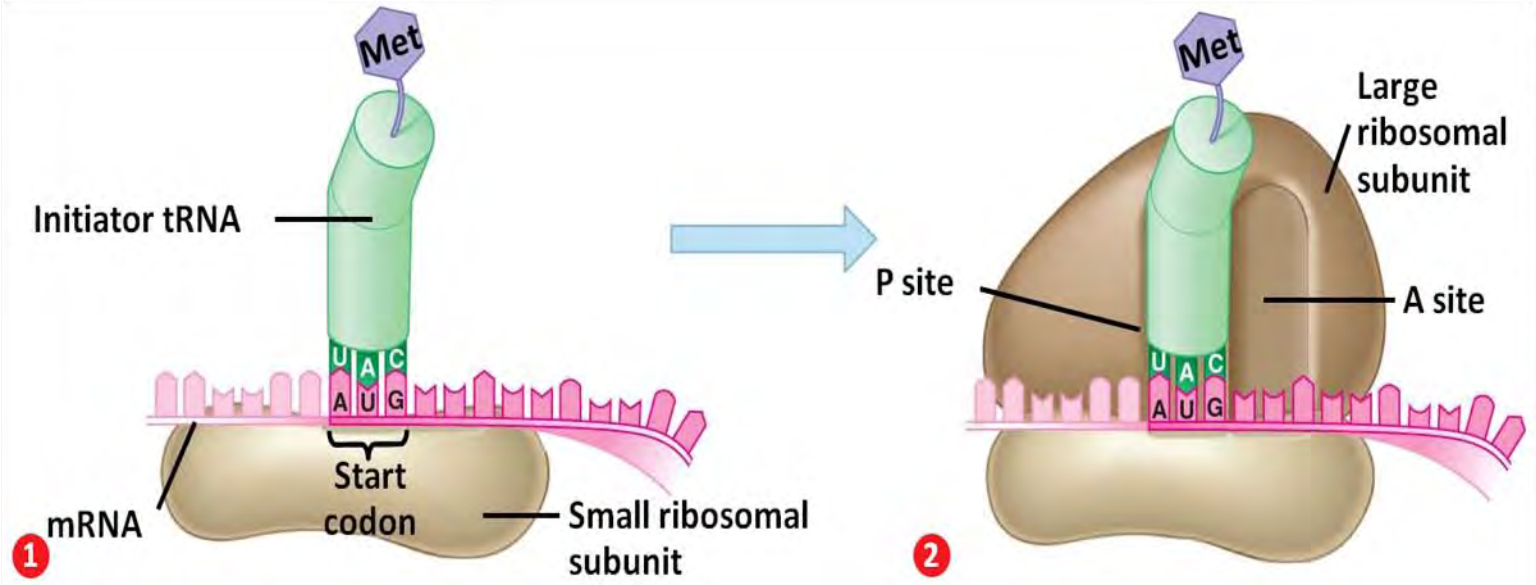
Pre-mRNA is modified in the nucleus and the finished mRNA leaves the nucleus and travels to a ribosome where the information will be translated.

<u>TRANSLATION</u> also involves 3 processes: Initiation, Elongation, & Termination

Initiation involves bringing all the components together.

- **Initiation** occurs in two steps
  1. mRNA binds to a small ribosomal subunit, and the first tRNA binds to mRNA at the start codon
     - The start codon reads AUG and codes for methionine
     - The first tRNA has the anticodon UAC

  2. A large ribosomal subunit joins the small subunit, allowing the ribosome to function
     - The first tRNA occupies the P site, which will hold the growing peptide chain
     - The A site is available to receive the next tRNA



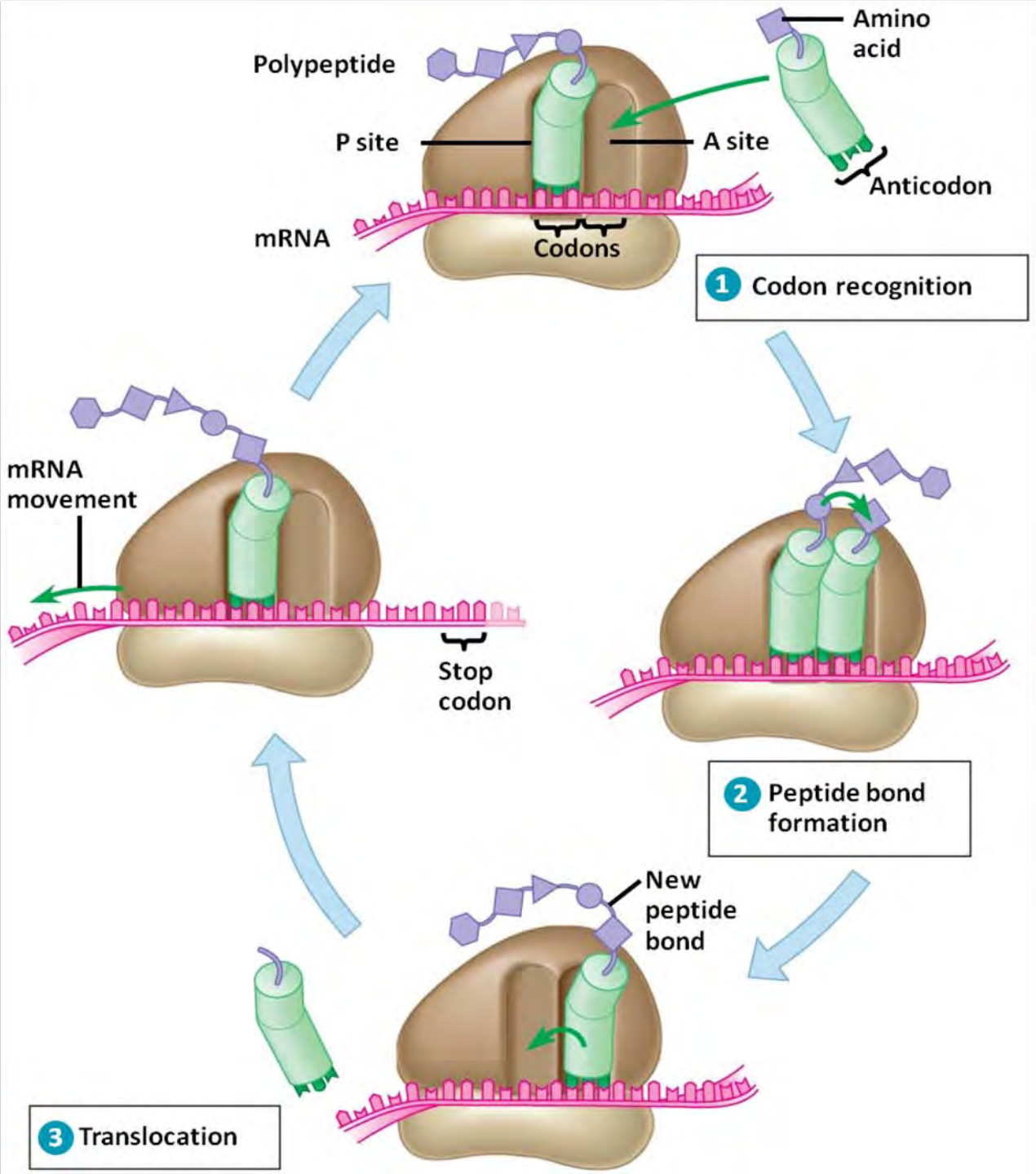
Transfer RNAs (**tRNAs**), carrying their appropriate amino acids, move to the **mRNA**. The **ANTICODONS** of two tRNA molecules base pair with the two codons of mRNA, and the tRNAs bind to the large ribosomal subunit.

3) The large subunit of the ribosome catalyzes the formation of a peptide bond between the amino acids carried by the two tRNA molecules. The "first" amino acid detaches from its tRNA. The chain of two amino acids remains attached to the "second" tRNA.

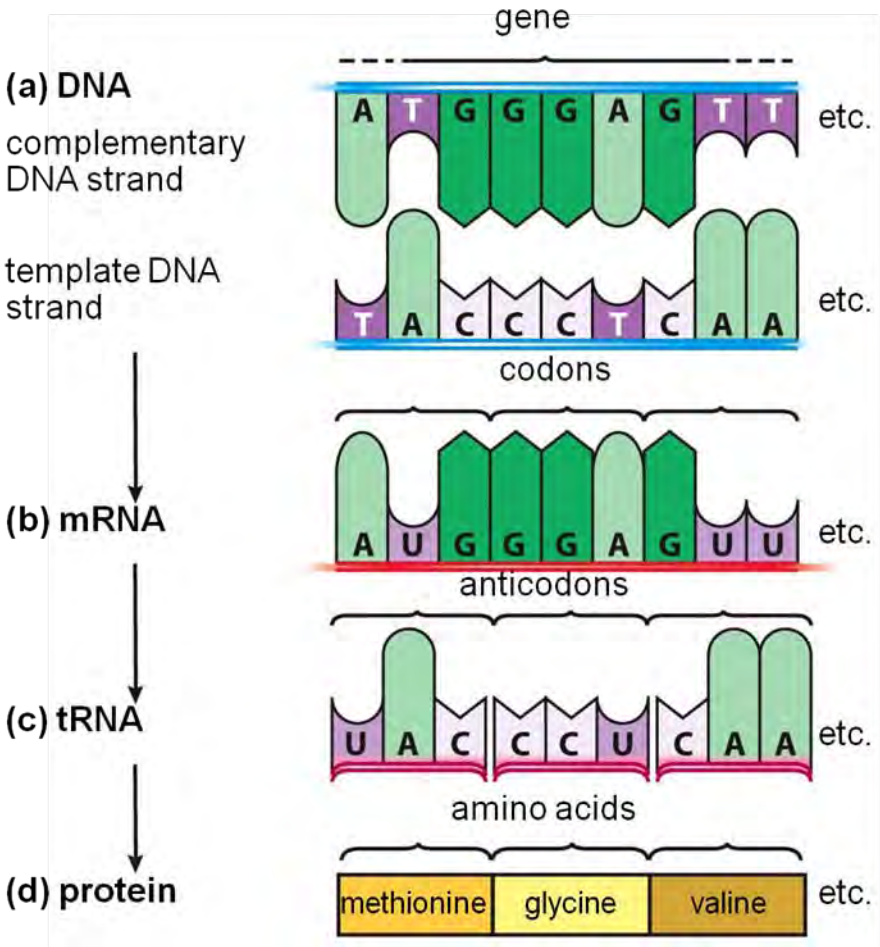
Elongation involves adding amino acids, one at a time.

- Each cycle of elongation has three steps
    1. Codon recognition: next tRNA binds to the mRNA at the A site
    2. Peptide bond formation: joining of the new amino acid to the chain
        - Amino acids on the tRNA at the P site are attached by a covalent bond to the amino acid on the tRNA at the A site Translocation: tRNA is released from the P site and the ribosome moves tRNA from the A site into the P site
    3. Translocation: tRNA is released from the P site and the ribosome moves tRNA from the A site into the P site

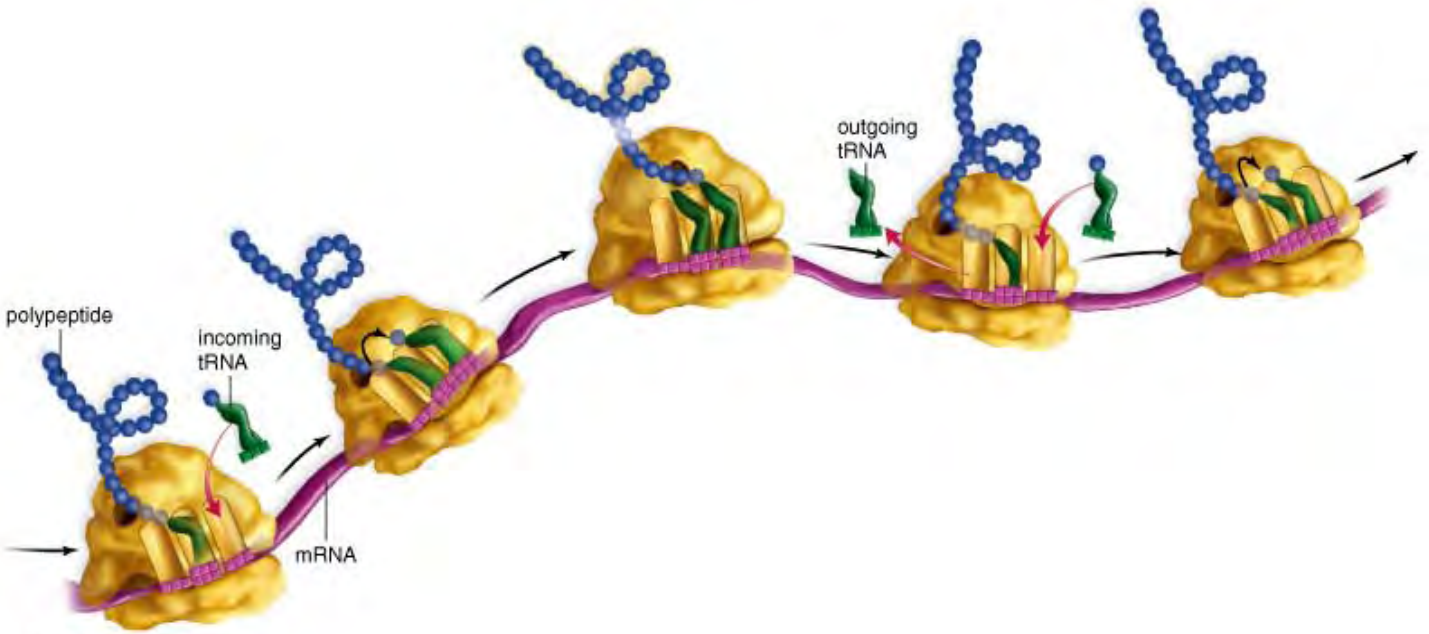
Termination: this process continues until a stop codon is reached, whereupon the mRNA and the newly formed protein leave the ribosome.


Amino acid
Polypeptide
P site
A site
Anticodon
mRNA
Codons
1 Codon recognition
mRNA movement
Stop codon
2 Peptide bond formation
New peptide bond
3 Translocation

NOTE THAT COMPLEMENTARY BASE PAIRING IS INVOLVED IN BOTH PROCESSES: DNA → mRNA in transcription and mRNA →tRNA in translation.

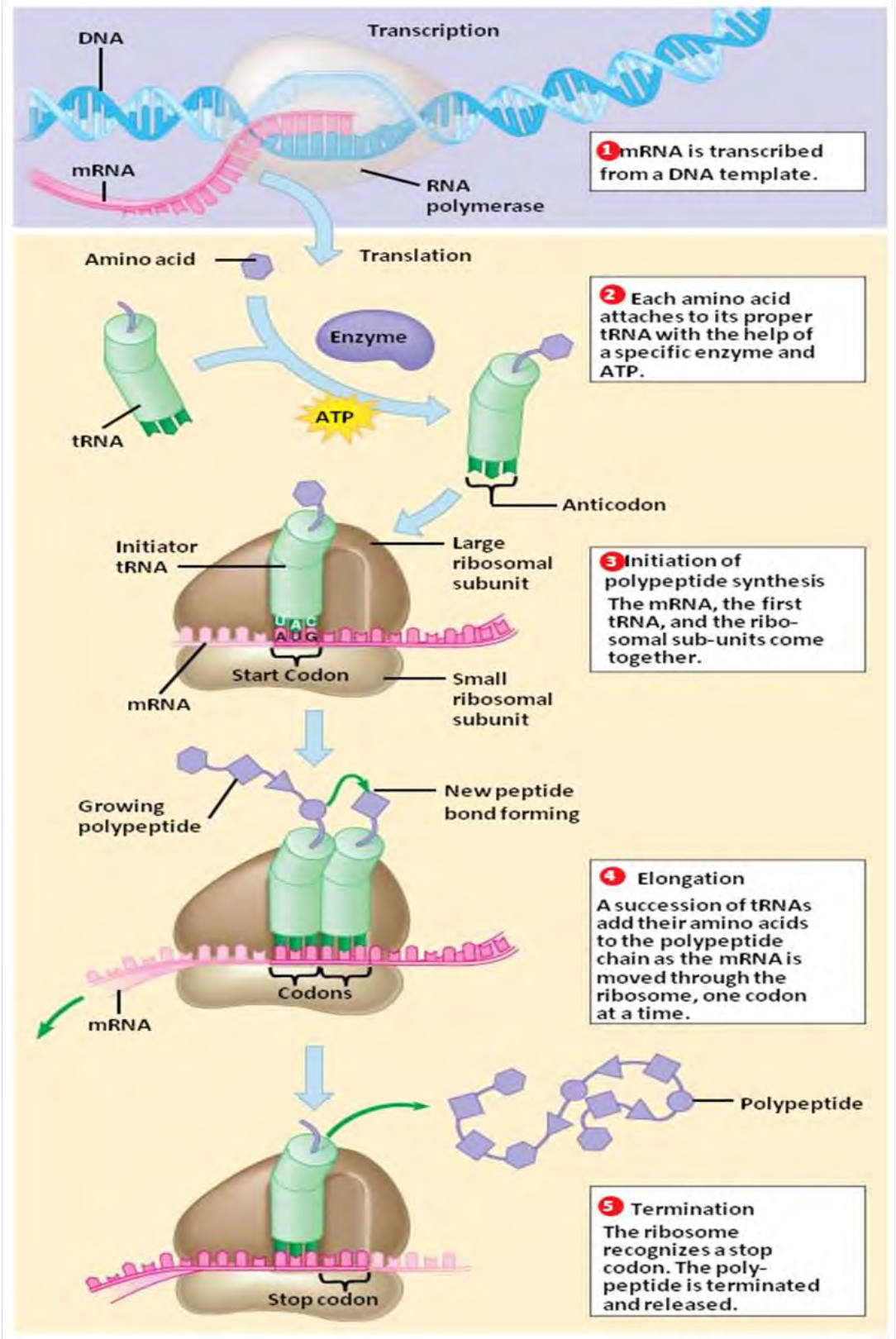


The same mRNA molecule may be translated multiple times as a cell usually needs to make multiple copies of a protein. Therefore many ribosomes may attach to the same RNA molecule, simultaneously making multiple copies of the same protein.



c. Function of ribosomes

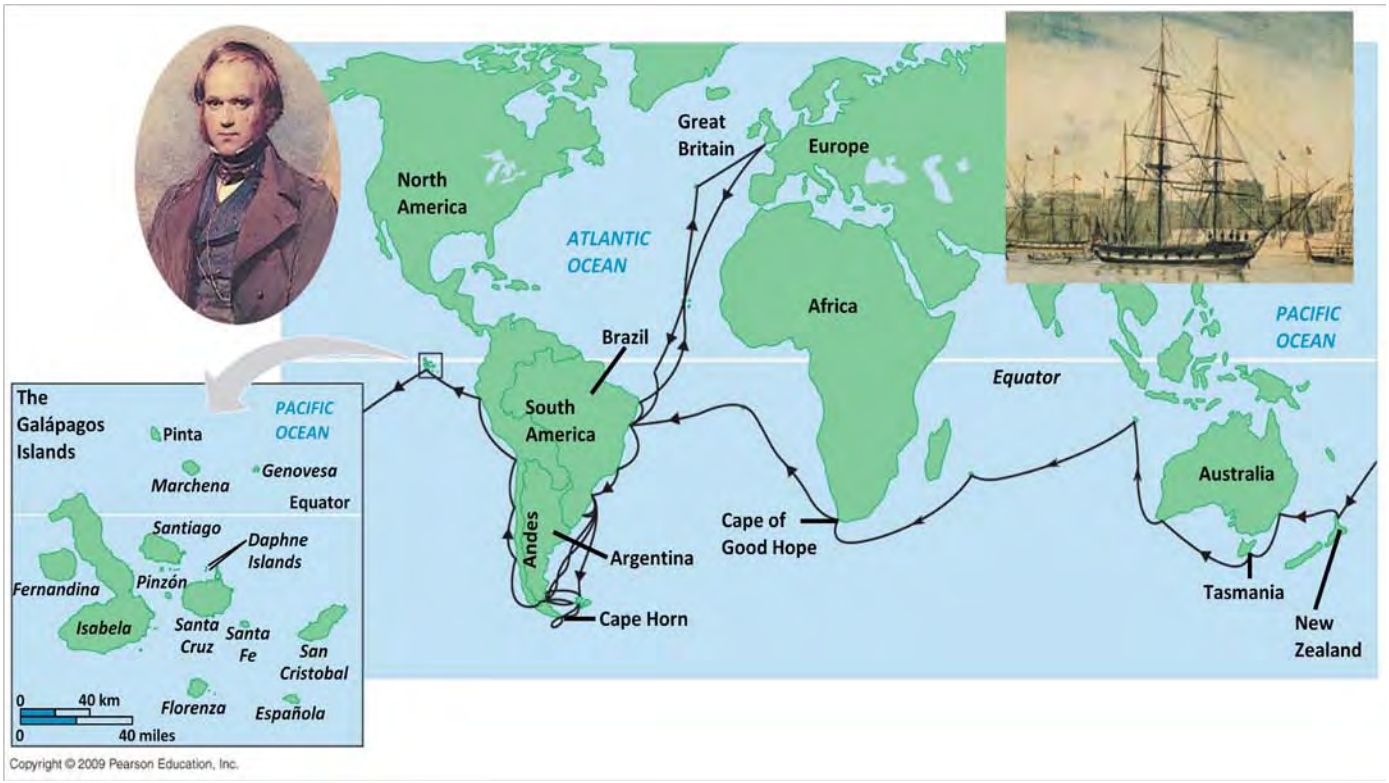
A SUMMARY OF THE PROCESS OF PROTEIN SYNTHESIS



EVOLUTION AND NATURAL SELECTION

To explain the origin and diversity of life on earth, people historically have turned to hypotheses of Creationism...the most common hypothesis being that a divine or supernatural being created each type of organism individually at the beginning of the world, and that all modern organisms are essentially unchanged descendants of those ancestors. As explained in **Lecture 1**, scientists seek **natural rather than supernatural** causes to explain natural events and throughout history scientists have sought natural causes for the origin of species. Yet it was only in the nineteenth century that a truly coherent theory was developed – the **Theory of Evolution.** This theory was published by Charles Darwin and Alfred Russell Wallace, in 1858 and today still forms the foundation of our understanding of the origin and diversity of all living things.

Charles Darwin was born in England to an intellectual family. He studied medicine and then went to Cambridge to study for the ministry. He was always interested in nature and collected rock, animal, and plant specimens from a young age, but it wasn't until he went on a voyage around the world serving as a naturalist aboard the ship HMS Beagle that his collections led to several years of study and contemplation, resulting in the publication of On Origin of Species in 1859.



But Darwin wasn't the first person to question long held beliefs about the natural world.

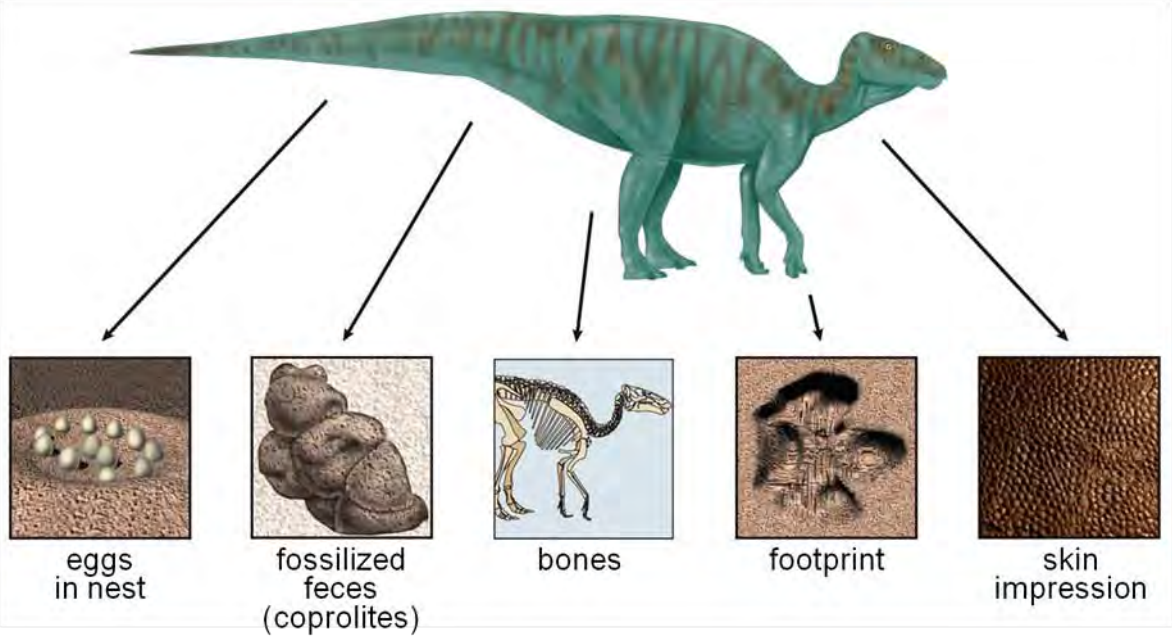
Above is **Aristotle's Ladder of Nature**. Species here are arranged in order of complexity with "inferior" species at the bottom and "superior" ones above, with humans at the top. At this time it was thought that all species were created individually, were "fixed and unchanging". While these ideas persisted for several centuries new views began to emerge beginning in the 1700s.

At this time Europeans were exploring and colonizing large areas of Africa, Asia, and America. Naturalists accompanied the explorers and collected specimens of plants and animals that were previously unknown to Europeans. They also noticed that certain species only inhabited certain areas, yet they closely resembled species in different locations.

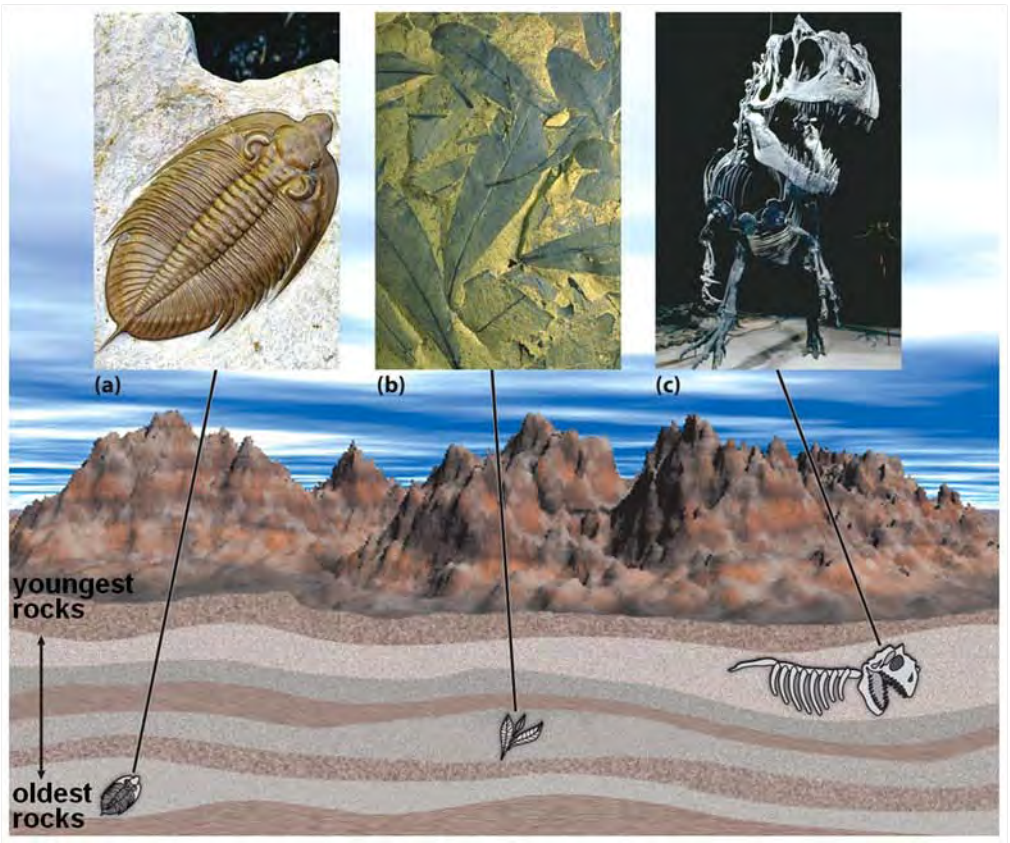
Also at this time deep layers of the earth were being exposed in the construction of canals and railways and several geologists made important observations. Cutting into the earth revealed that the earth's crust was formed in layers with newer layers forming over older layers. William Smith (1769-1839), an English geologist, recognized that certain fossils were always found in certain layers.

Fossils are the preserved remains of organisms that had died long ago. Many fossils are bones, shells, eggs, pollen grains, or their impressions in mud, that have been preserved for at least 10,000 years. It was observed that fossil remains show a progression with the ones on the oldest layers being very different from modern organisms. George Cuvier (1769-1832), a French paleontologist, proposed that successive catastrophes produced the layers of rock that were being exposed – the idea of **Catastrophism**. His work was challenged by the geologist Charles Lyell (1795-1875) and James Hutton (1726-1797) who had realized that the layers of the earth were changed very slowly by the effects of weather and water. Rivers overflowing lay down layers of sediment, volcanoes erupting lay down layers of lava. These slow and gradual processes were called **Uniformitarianism** and challenged the prevailing view of the age of the earth which interpretations of the Old Testament had suggested was just 6000 years. The earth must be much older if rock layers, which are thousands of feet thick, were produced so gradually.

Examples of Fossils



Fossil locations in layers of the earth's crust

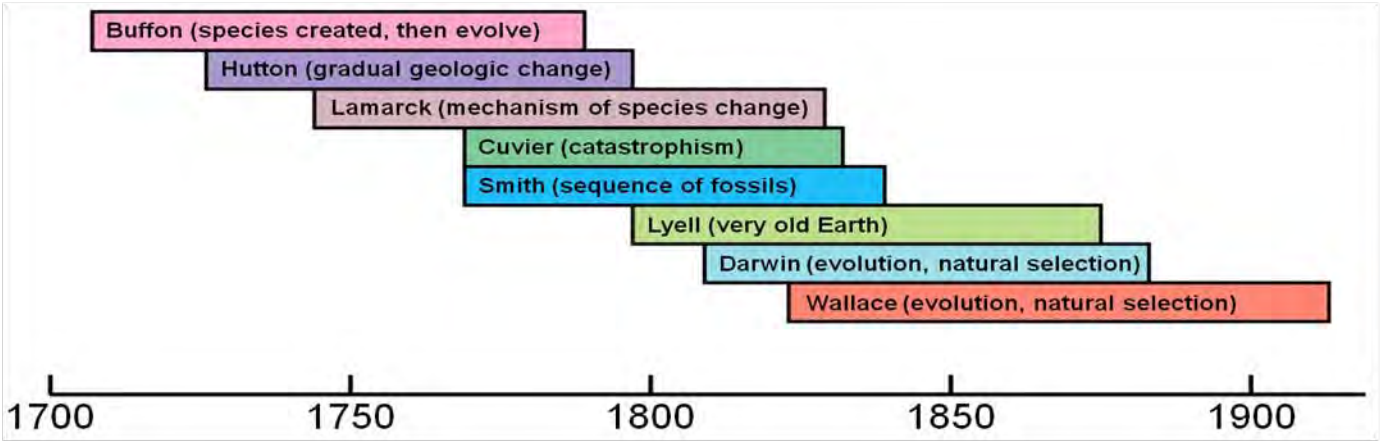


Another hypothesis about the variation in organisms was proposed around this time by a French biologist, Jean Baptiste Lamarck (1744-1829). This was the **Inheritance of Acquired Characteristics** which suggested that organisms **evolved.** Lamarck had the idea that changes in an organism acquired over a lifetime could be passed on to the offspring. He used the example of giraffes, stating that ancestral giraffes had stretched their necks to enable them to reach leaves higher up on trees. Their necks would therefore become slightly longer and this change could be passed on. Now with our understanding of genetics we know that body changes acquired during a lifetime are **not** passed on to children. However Lamarck's idea had a great deal of influence on subsequent evolutionary thought.

So some biologists before Darwin had suggested that organisms could change i.e. **evolve.** As well as Lamarck, Georges Louis LeClerc (1707-1788) a French naturalist suggested that perhaps there were a small number of founding species from which modern species had developed. By the mid-1800s a growing number of scientists had concluded that present-day species had evolved from earlier ones.

But **Charles Darwin and Alfred Russel Wallace** are credited with bringing the theory of evolution into the mainstream of modern science. As previously stated, Darwin had spent 5 years traveling the world and this voyage sowed the seeds for his theory of evolution. These ideas were reinforced by his knowledge of the scientific discoveries that had preceded him. In 1859 Darwin published his ***On Origin of Species by means of Natural Selection*** presenting a logical explanation for the changes that occur in organisms over time.

Wallace, like Darwin, was a naturalist and a collector of specimens and had traveled extensively through Southeast Asia and South America. He arrived at the same conclusions as Darwin about the processes that shaped evolution. But it was the publication of Darwin's book that was controversial and deeply disturbing to many people. Yet Darwin's argument for the theory of evolution by natural selection was so compelling that his views were almost completely accepted within the intellectual community of Great Britain by the 1860s. But, as you are well aware, some people still regard the **Theory of Evolution** not as a body of knowledge solidly grounded in evidence but as a "guess" about the history of life on Earth.



THE MEANING OF EVOLUTION

Evolution is sometimes referred to as the **GUT** theory – **G**rand, **U**nifying **T**heory of biology. Yet, although we live in one of the most educated societies of all time, the theory of evolution is frequently misunderstood. This is probably for 2 reasons. One is that people believe that the theory of evolution is at odds with their religious beliefs, forgetting that scientific inquiry is not involved with faith. And, secondly, the term **theory** itself implies an idea that is unproven or is really just a hypothesis. However in science the term theory **(Lecture 1)** is reserved for a body of knowledge that is supported by evidence and explains some aspect of the natural world. In scientific terminology when the term theory is used, just about all scientists in the world agree with the body of knowledge that supports it.

SO WHAT IS EVOLUTION?

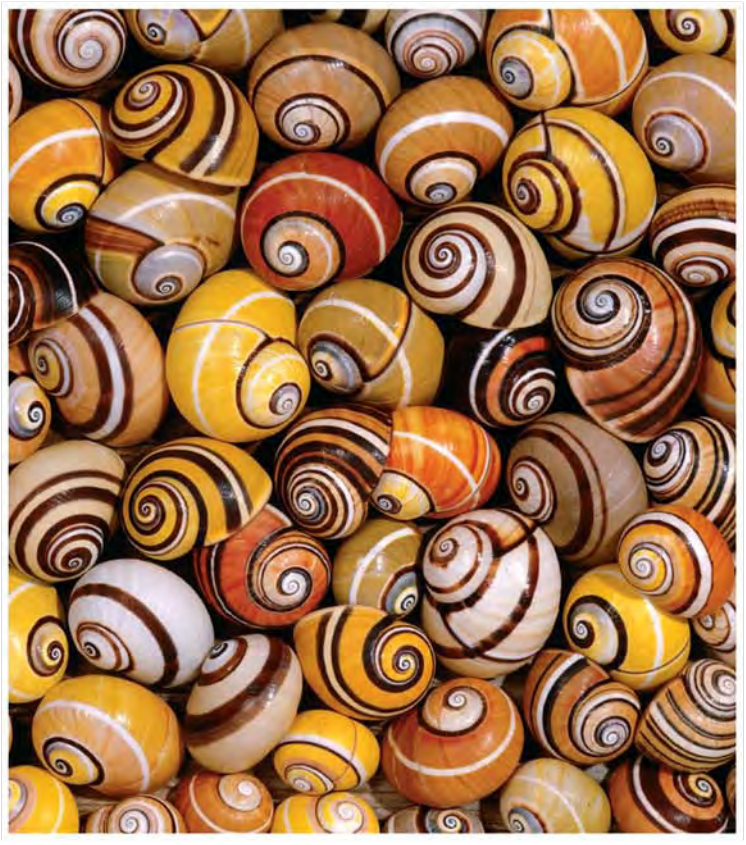
Evolution is a change in the characteristics of a population of organisms that occurs over the course of generations. These changes are heritable changes, that is,changes that occur in the DNA sequence in genes.

The **Theory of Evolution** is stated as:
"All species present on Earth today are descendants of a single common ancestor, and all species represent the product of millions of years of microevolution via natural selection and other modes of evolutionary change." This means that modern animals, plants, fungi, protists, and prokaryotes (classifications are discussed in **Lecture 2**) are related to each other and have been diverging from their common ancestor since the origin of life on earth.

In summary, the theory of evolution states that modern organisms descended, with modification, from preexisting life-forms. It is important to keep in mind that **individuals don't evolve; populations evolve.** Evolution involves change in populations through time. It is actually a change in the **gene pool**, which is the total of all the alleles of genes (all the different forms of a particular gene) of all the individuals in an interbreeding population.

Darwin's Theory of Evolution is based on the understanding that evolution arose as a consequence of three natural processes:

1. There must be variation of traits within a population. If we take a look at the members of any species, even our own, it is obvious that there are striking differences among individuals. It is now known that variations in a natural population arise by random mutations in DNA and, in humans and other animals, by the random assortment of chromosomes during meiosis. Although all the snails below are the same species no two are alike.



2. These variable traits are passed on from parents to offspring. From observations of people, animals, and even plants it was obvious to Darwin that traits are passed on. Animal breeders knew that the offspring of faster or stronger animals were more likely to also have those traits. Farmers used seeds from their more productive plants to grow the next generation. However, it was not until the work of Mendel and subsequent genetic research that the details of the mechanisms of inheritance were understood.

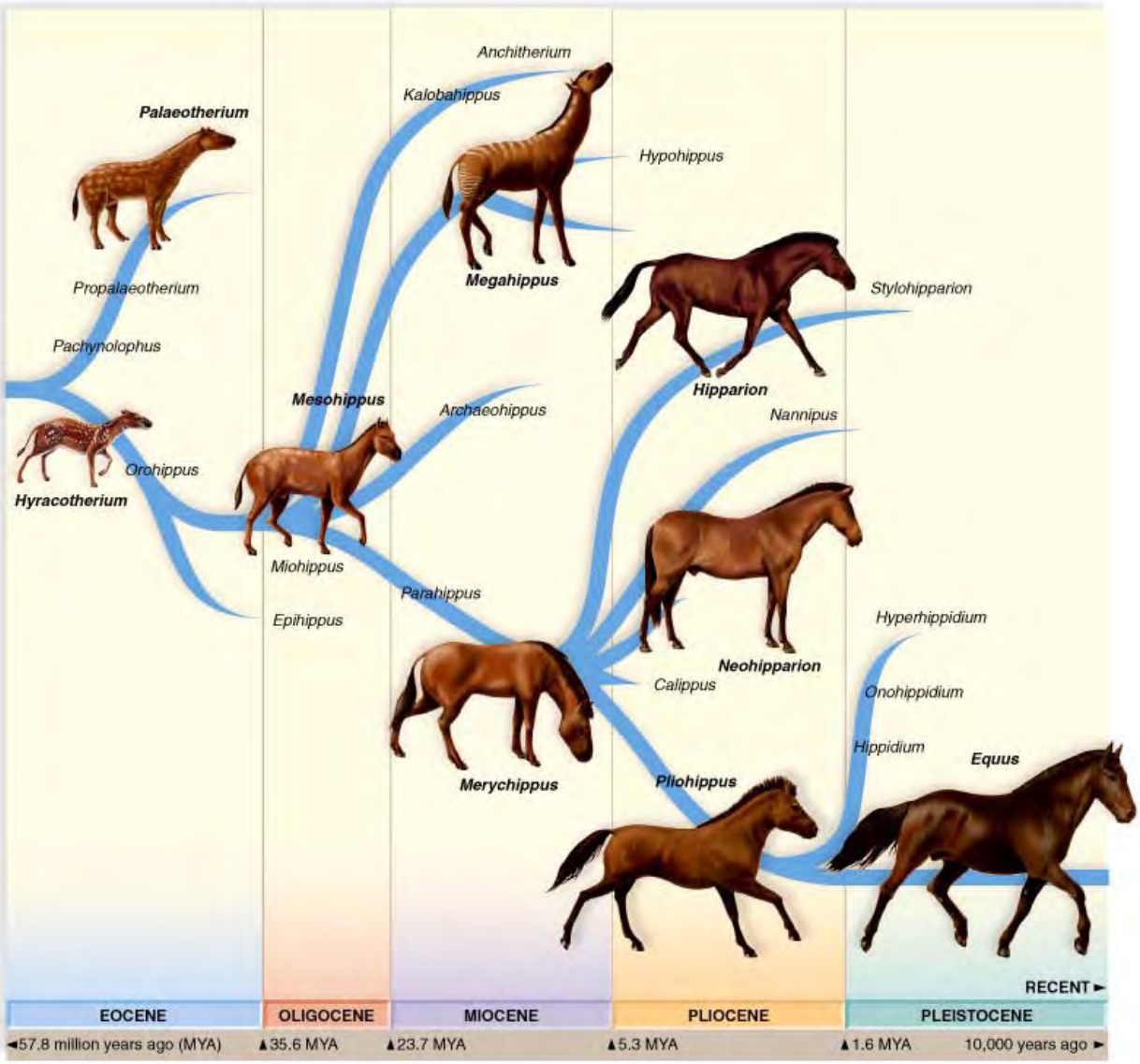
3. Some individuals fail to survive and reproduce. The work of **Thomas Malthus** who studied population growth had a great influence on Darwin. Reproductive rates for organisms, if unimpeded, would clearly produce far more offspring that needed to just replace parents. For example, elephants have a slow reproductive rate yet the number of elephants would multiple many times if each pair of elephants had just 6 offspring. But the number of elephants remains relatively constant so Darwin wondered why this was so.

Clearly, the amount of resources for any particular species is limited so Darwin concluded that **individuals with traits more suited to survival and reproduction in their environment will leave more offspring** – if a rabbit carries a trait that enables it to run faster than other rabbits then it is less likely to get eaten by a fox and will be more likely to reproduce and pass on that trait. Or some animals have traits that make them more likely to be sexually selected for, like large antlers in male red deer which are more attractive to female deer, or white flowers on snapdragons that are more attractive to pollinators. Consequently these organisms within a population have better chances of having more offspring.

SOME PROOFS OF EVOLUTION

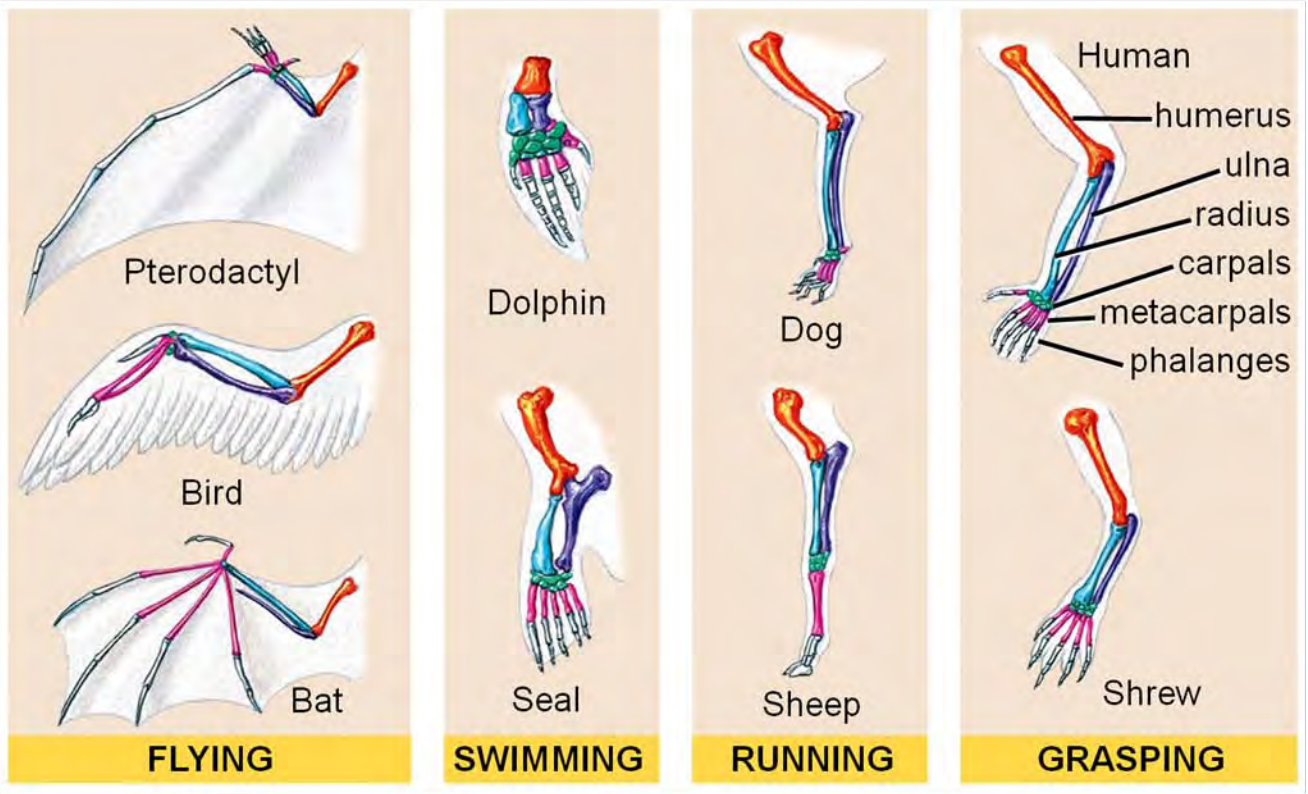
Virtually all biologists today consider evolution to be a fact – Why? - Because of the evidence. A few examples include:

1. The fossil record provides evidence of evolutionary change over time. Below paleontologists, using the fossil record, have been able to construct a time line for evolution of the modern horse.



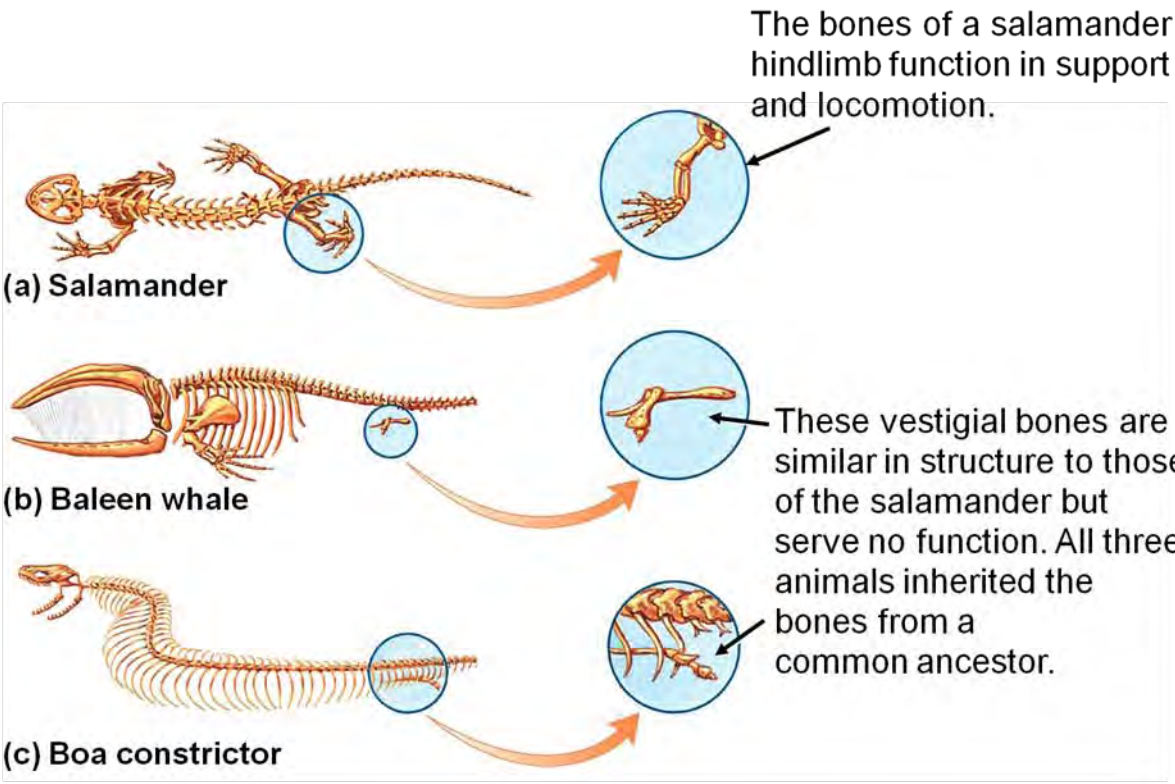
2. Comparative morphology…homologous structures inherited from a common ancestor. A similar forelimb structure is seen in a very diverse group of animals. The different colors of bones highlight the similarities among the various species, clearly demonstrating that they have all descended from a common ancestor.

a. Morphological divergence: these body features have changed in appearance and function depending on the line of descent but they are basically the same bones that have been modified extensively. These features are called **homologous structures**.



b. **Morphological convergence:** Parts of the body features that were not similar become similar because they are adapting to similar environments; these body parts are now called **analogous structures**. The wings of insects and birds are good examples of similar structures that differ anatomically. These structures developed from different original structures and are modified through natural selection – a process called **convergent evolution**.

3. Vestigial structures provide evidence for relatedness of organisms adapted to different environments. Vestigial structures are structures that appear to serve no purpose in the organism.



Examples of Vestigial Structures

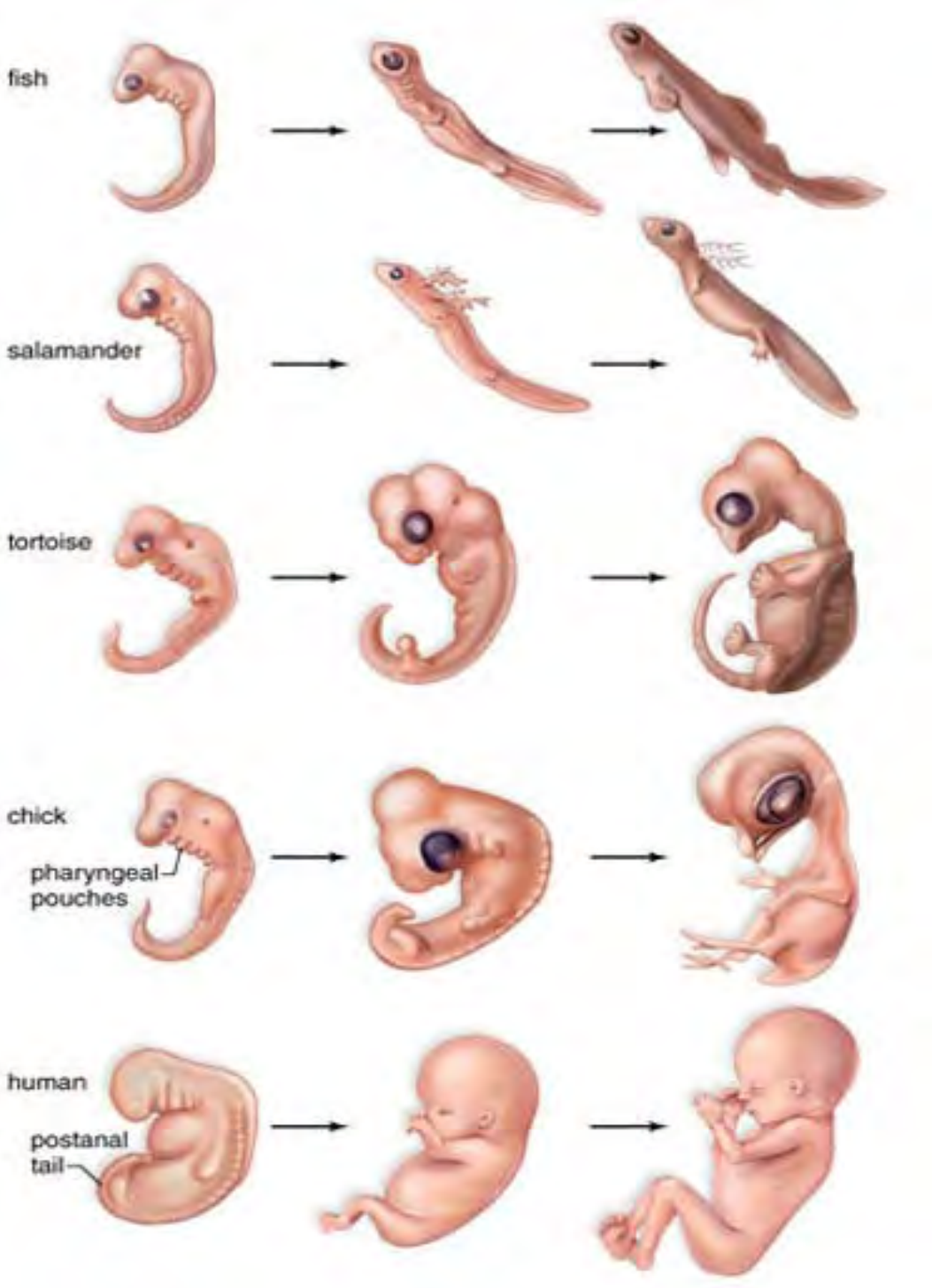
Above are diagrams of the anatomical structure of a salamander, a baleen whale and a boa constrictor – all have hind limb bones that are used only by the salamander, suggesting a common line of descent.

In the human the appendix and wisdom teeth are regarded as vestigial, and we have three little muscles that wiggle our ears that we don't use.

The ostrich is an example of a bird that has wings but doesn't fly.

The best explanation for the presence of these structures is that they are left over from our ancestors.

4. Embryological stages of animals can provide evidence for common ancestry. The embryonic similarities here are obvious. For example, all vertebrate embryos, including the human embryo, have tails and gill pouches but only fish retain the gills and only fish, turtles, and mice retain tails.



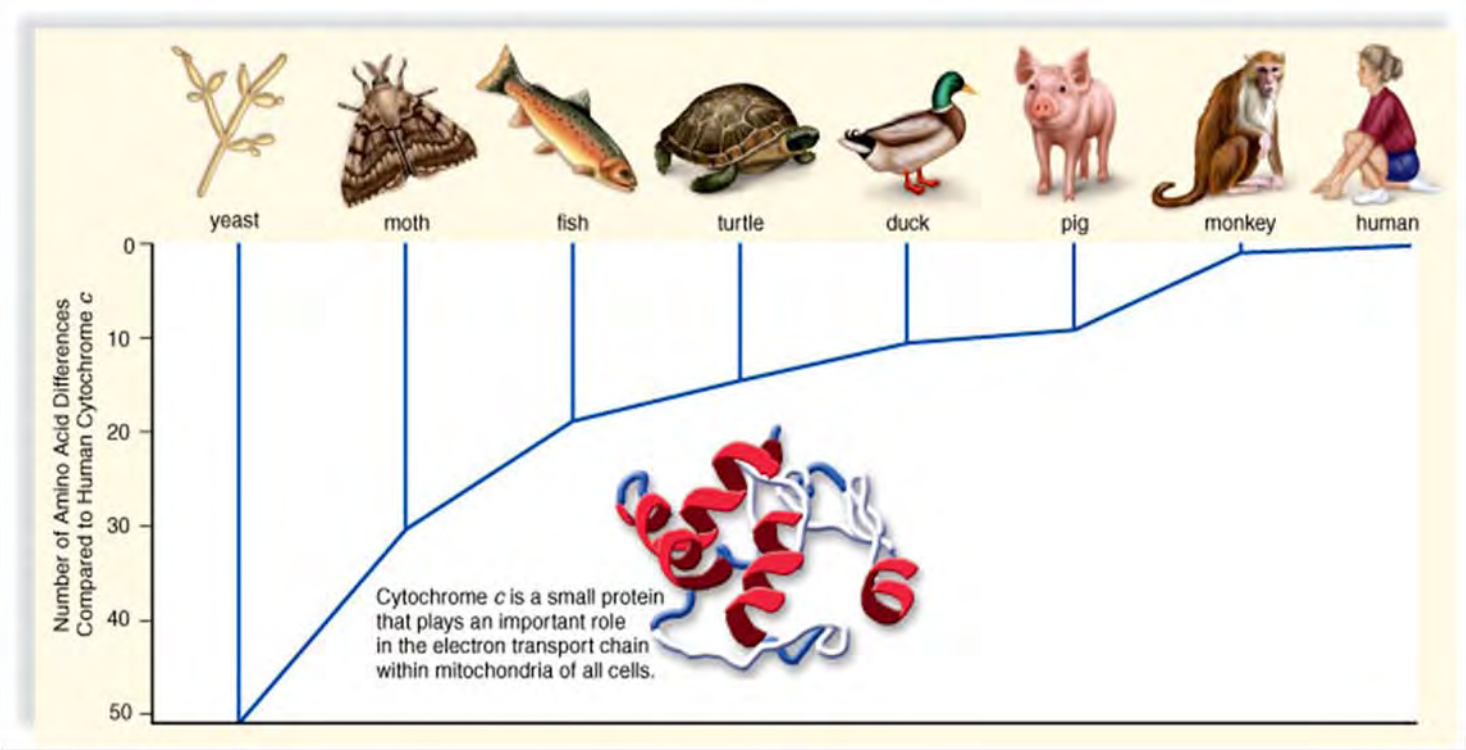
5. Artificial selection demonstrates that organisms may be modified by controlled breeding.

Artificial selection is the breeding of domestic plants and animals to produce offspring that have particular traits. All dogs have descended from the wolf; yet many modern breeds have very little resemblance to a wolf but the two will still readily crossbreed. Darwin had lots of experience with life on a farm and he made the connection between artificial selection and natural selection. If, over the course of a few thousand years, humans by artificial selection could produce so many different breeds of dag, didn't it make sense that over several million years, random mutations and natural selection could produce the huge diversity of living organisms on earth today?

6. Modern biochemical and genetic analyses reveal relatedness among diverse organisms.

It is important to note that with the development of new technologies Darwin's controversial ideas on evolution published in 1859 have only been confirmed and reinforced. For example, scientists are now able to compare DNA between organisms, establishing the fact that all living organisms share the same genetic code; from bacteria to plants and animals the molecular instructions are written with the same "4 letters" – A, T, C, & G.

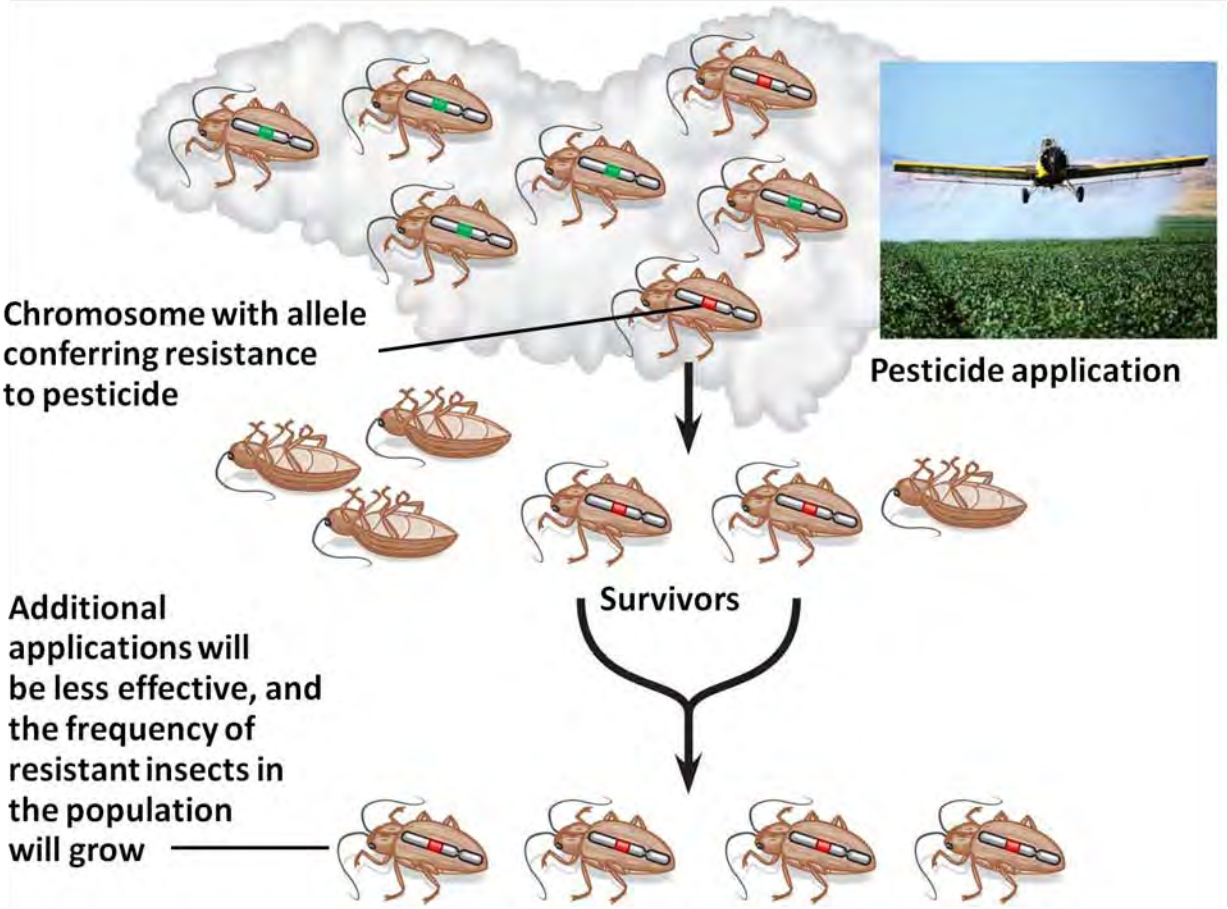
DNA sequences in individual genes can now be compared to establish an organism's place on the evolutionary tree. **A similar DNA sequence suggests a recent common ancestor; a somewhat different sequence suggests a more ancient ancestor.**



Here scientists have compared the DNA sequence for a small protein in mitochondria. The evidence shows that humans and monkeys share a fairly recent common ancestor while humans and yeast share a distant common ancestor.

7. Evolution by natural selection occurs today

Development of pesticide resistance in insects demonstrates evolution by natural selection. Initial use of pesticides favors those few insects that have genes for pesticide resistance; those resistant insects survive and reproduce and with continued use of pesticides, resistant insects flourish and vulnerable insects die so the proportion of resistant insects increases over time.



Pesticide resistance is not the only type of resistance to concern us. The evolution of bacterial resistance to antibiotics is of serious concern. When first discovered penicillin was effective in killing just about all *Staphyloccus aureus* bacteria. Today, more than 90% of certain strains of *S. aureus* are resistant to penicillin. This is evolution at work and it happens in a very short span of evolutionary time!

MUTATIONS

A mutation is defined as a permanent change either in a DNA sequence or in the amount of DNA found in a cell.

All evolution begins with alterations in the genetic message. Genetic changes through mutation and recombination provide the raw material for evolution by natural selection.

Alleles **(Lecture 12)** which are alternative forms of genes or genes that have a change in the sequence of DNA nucleotides, arise by mutation. Say one of these alleles codes for an enzyme that confers some type of evolutionary advantage – makes a stronger muscle protein, for example. The organism with this allele has an advantage and will likely live longer (perhaps because of being able to outrun a predator) and survive to pass on that allele to its offspring.

A single individual has just two alleles for every gene but in a population there may be several alleles of the same gene. For example, if eye color in humans was the result of one gene coding for one protein, it is obvious that there must be several versions of this gene since in the population there are brown, blue, green, gray and several in-between colors of eyes – this gene has several alleles. **New alleles arise by mutation.**

HOW DO MUTATIONS HAPPEN?

As seen in the steps of cell division (mitosis and meiosis – **Lecture 11**), before cells divide the entire DNA must be duplicated so that copies can be passed on to the daughter cells. Most mutations occur during cell division. They arise by accident as the DNA is replicating and, although some are repaired by enzymes, some slip through. Remember that there are billions of base pairs in most genomes so it is understandable that in the copying process mistakes may occur.

Other mutations are caused by environmental factors such as chemicals in cigarette smoke – more about this later.

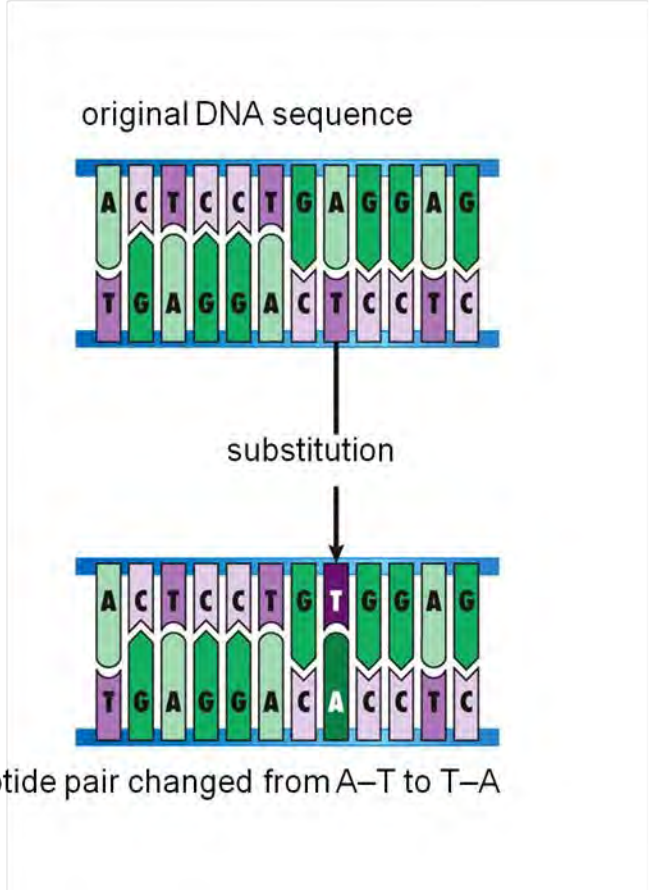
Mutations generally fall into two types: mutations in individual genes known as point mutations and mutations that affect the chromosome structure.

Point Mutations

Many mutations alter a single base pair and there are 3 major types of such mutations.

1) In a **substitution mutation** one base is changed to another at a single point in the DNA

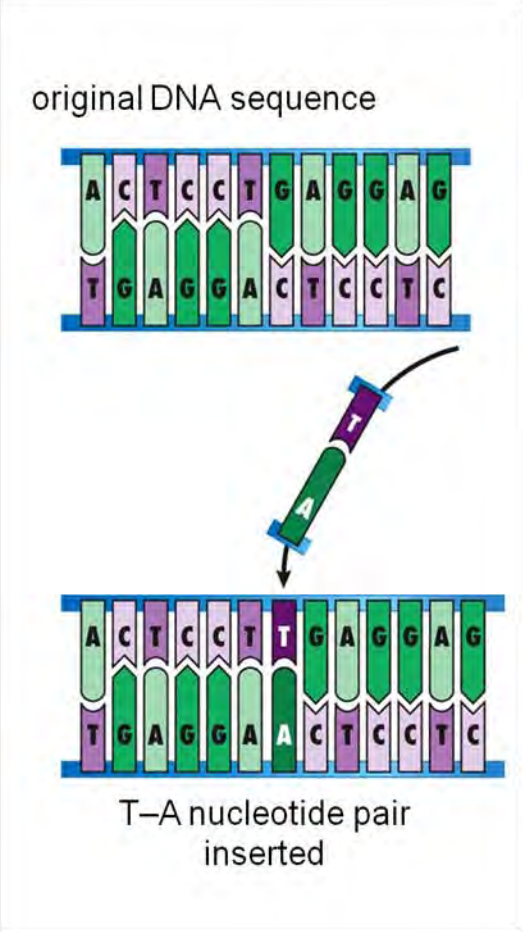
Nucleotide substitution



Above, the exchange of a T for an A may lead to a different amino acid being inserted at a particular place in the protein coded for by this gene.

2 & 3) An **Insertion or Deletion mutation** occurs when a single base is inserted into or deleted from a DNA sequence.

Insertion mutation



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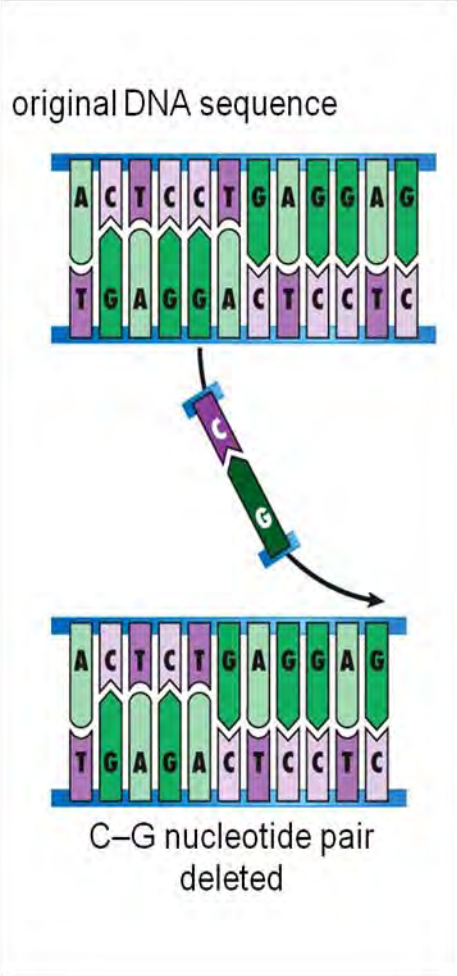
Deletion mutation



These types of mutations are termed **Frameshift Mutations** because they change the sequence of bases from that point until the end of the gene usually resulting in many wrong amino acids and a non functioning protein. Remember DNA bases are read in triplets. In the previous two examples a mutation has occurred so that the triplets following the insertion or deletion will be one letter off and all the amino acids downstream from the mutation will likely be different leading to a malfunctioning protein.

Consequently, point mutations may have any of the following effects:

- Most amino acids have several different codons (**Lecture 13, page 4**) so the mutation may have no effect – for example, if the codon *CCC* is changed to *CCA* or *CCG* the amino acid will still be proline and the protein structure will not change.

- The new amino acid may function in a similar way to the original one and no obvious difference is observed in the function of the protein.

- If the mutation results in a codon that codes for an amino acid with different properties or if the mutation results in a premature stop codon then the protein will not function properly.

SOME IMPORTANT INFORMATION ABOUT MUTATIONS AND EVOLUTION

1. Most mutations in the human genome are neutral.
Although random changes in the DNA sequence are the source of all genetic variation and these mutations give rise to all diversity, most mutations have no effect on the organism because of the long stretches of DNA that do not code for anything. In the human genome only about 1-2 % of the DNA actually codes for proteins or RNA so most mutations are neutral.

2. For a mutation to affect populations it must occur in germ-line cells; in the human these cells will become sperm or eggs (gametes). These germ-line mutations including mutations that occur in gametes, are **heritable** and can be passed on from one generation to the next. Mutations that occur in **somatic** cells (all the cells of the body except the germ-line cells) are not passed on to offspring.

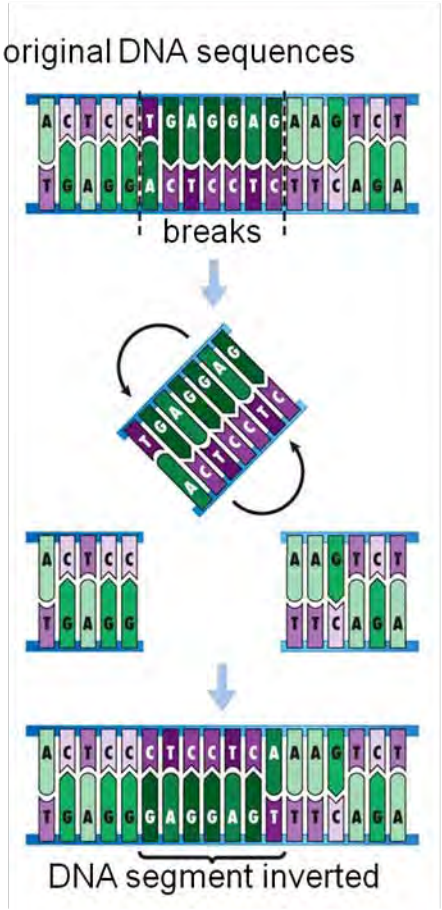
3. In general, mutations occur rarely and are random, yet in large populations of unicellular organisms mutations can spread very rapidly. The spread of a gene conferring antibiotic resistance is a good example of a mutation that can move quickly in a population. Bacteria exist in huge numbers; the number of bacteria in and on the human body vastly outnumbers the number of eukaryotic cells. There are hundreds of trillions of bacterial cells present and some of them reproduce every 15 minutes. This rapid reproductive rate in such a large population ensures that a mutation that is beneficial to the organism such as one that confers resistance to antibiotics will spread rapidly throughout that species of bacteria.

Mutations can also occur at the chromosomal level

Sometimes large parts of the chromosome may be rearranged. Below are two examples of chromosomal mutations.

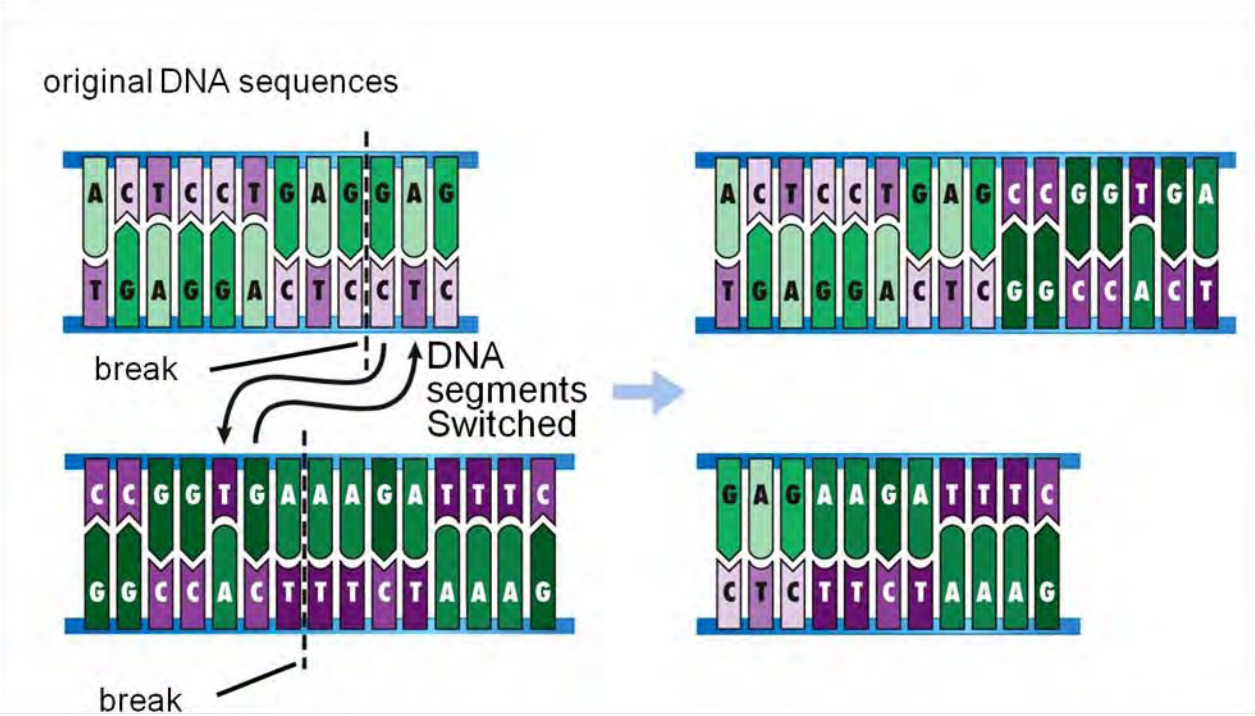
1. Inversion - Here the figure shows a segment of several bases being cut out, inverted, and reinserted but an inversion may be much bigger with a large segment of the chromosome being inverted.

Inversion



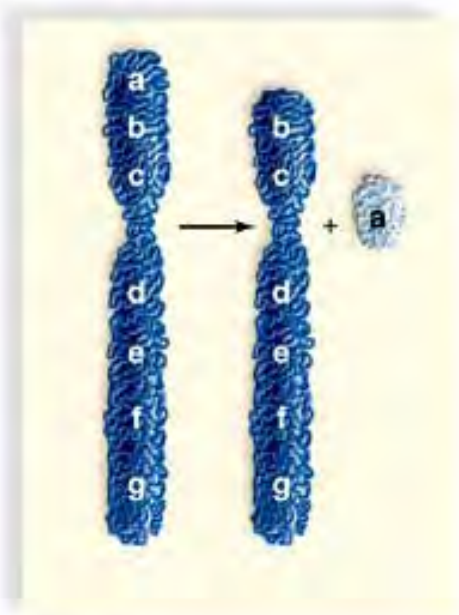
2. Translocation A translocation mutation also involves large segments of DNA. In this case the segments are moved to a different place on a chromosome or removed from one chromosome and attached to another.

Translocation



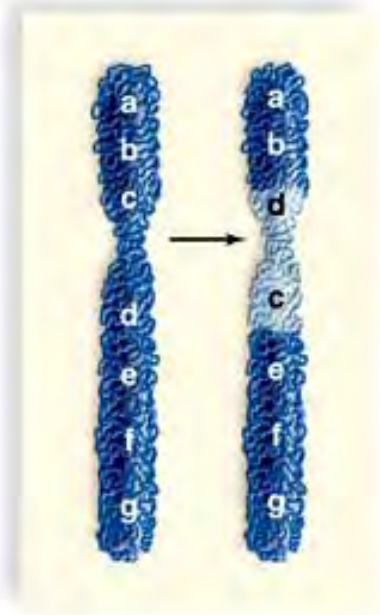
3. Other possibilities
As well the examples of insertion and translocation, sometimes large parts of a chromosome may be deleted or sections are duplicated and sometimes inserted elsewhere.

All of these changes in the structure of a chromosome can result in an alteration in the gene sequence and, consequently, an alteration in the specified protein.



a. Deletion

b. Duplication



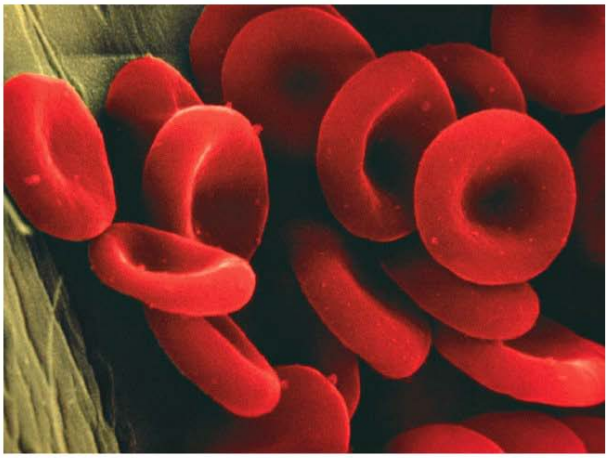
c. Inversion

d. Translocation

GENETIC DISORDERS – FOR EXAMPLE SICKLE-CELL ANEMIA

Heritable illnesses are called genetic disorders. Many are caused by a single dysfunctional gene – a gene that has undergone a mutation. Several different mutations that occur in the gene that codes for hemoglobin, an important protein for transporting oxygen in the blood, have been identified. A good example of a genetic disorder caused by one of these mutations is **Sickle-Cell Anemia**. This disease is caused by a point mutation – a substitution of one nucleotide for another. **See table on next page for some mutations that have been identified in the hemoglobin gene and the precise substitution that occurs in sickle-cell.**

This particular mutation results in a protein that doesn't perform its function normally. The abnormal hemoglobin causes rigid structures when red blood cells are low in oxygen such as during exercise. Individuals who have two copies of the gene have sickle-cell disease meaning that they suffer many painful and life-threatening consequences of these mutated proteins causing red blood cells to sickle and block small capillaries.



(a)

(b)

Table 10-4 Effects of Mutations in the Hemoglobin Gene

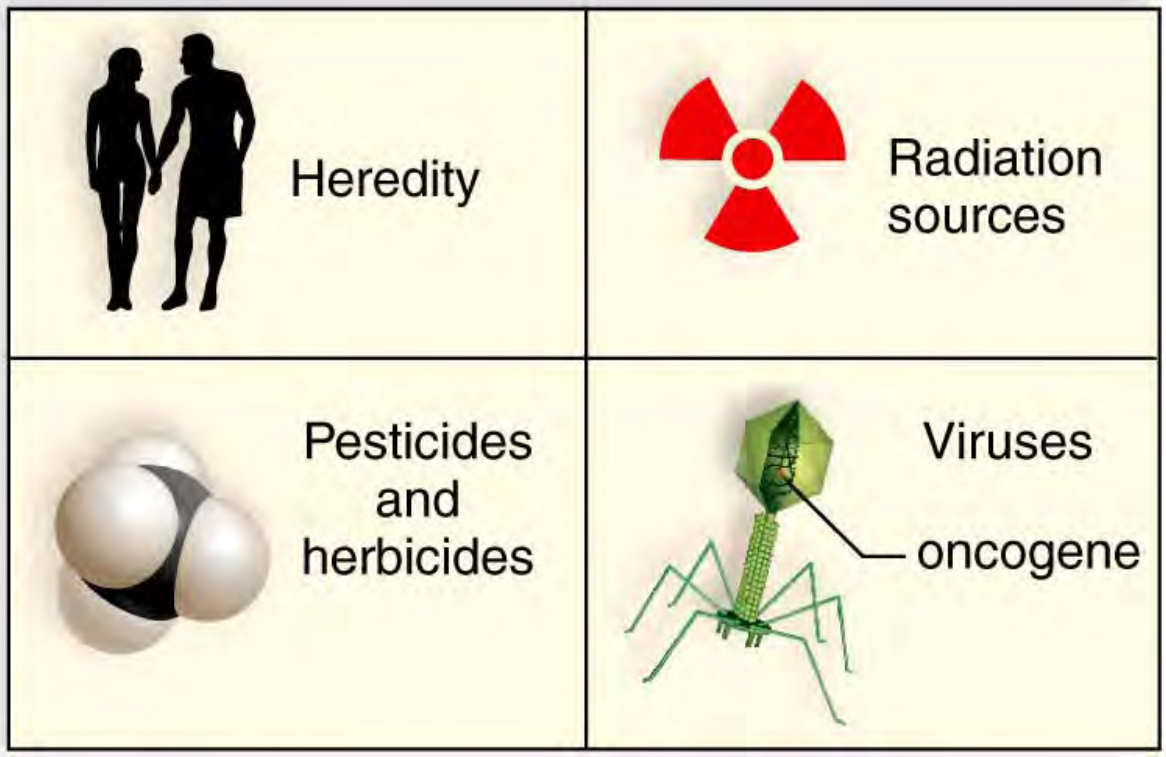
	DNA (template strand)	mRNA	Amino Acid	Properties of Amino Acid	Functional Effect on Protein	Disease
Original codon 6	CTC	GAG	Glutamic acid	Hydrophilic	Normal protein function	None
Mutation 1	CTT	GAA	Glutamic acid	Hydrophilic	Neutral; normal protein function	None
Mutation 2	GTC	CAG	Glutamine	Hydrophilic	Neutral; normal protein function	None
Mutation 3	CAC	GUG	Valine	Hydrophobic	Loses water solubility; compromises protein function	Sickle-cell anemia
Original codon 17	TTC	AAG	Lysine	Hydrophilic	Normal protein function	None
Mutation 4	ATC	UAG	Stop codon	Ends translation after amino acid 16	Synthesizes only part of protein; eliminates protein function	Beta-thalassemia

This table shows how point mutations can have a variety of effects or no effect on the function of the protein hemoglobin.

Many genetic disorders have been identified. Other genetic disorders you may have heard of are Huntington's disease, Marfan's Syndrome or Cystic Fibrosis. The underlying cause is always a mutation.

OTHER CAUSES OF MUTATIONS

In addition to rare mistakes that occur during DNA replication, some environmental conditions can cause mutations in DNA. These include ultraviolet light (sun), nuclear radiation, viruses, and certain chemicals such as components of cigarette smoke, asbestos, benzene and many more. Many of these substances can cause disease in humans. (A mutagen is a substance that can cause DNA to mutate.)



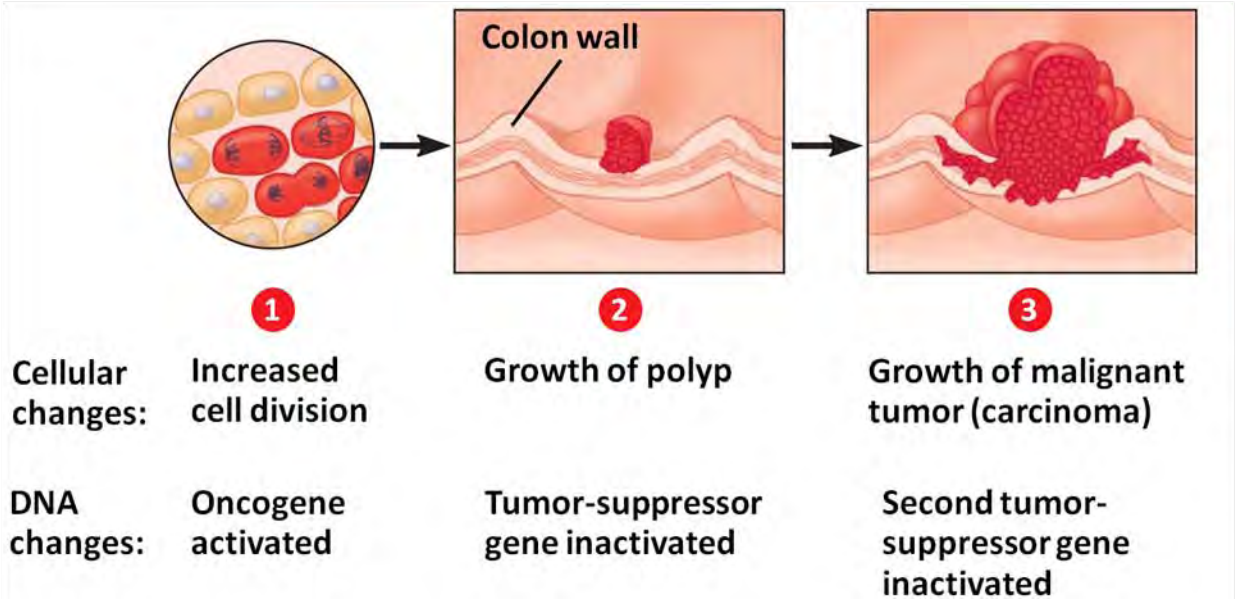
Influences that cause mutated proto-oncogenes (called oncogenes) and mutated tumor suppressor genes

CANCER – a short introduction

Cancer is a good example of a disease caused by some of the various contributors mentioned above - ultraviolet light can cause skin cancer, viruses can cause cervical cancer, and chemicals in cigarette smoke can cause lung cancer to name just a few.

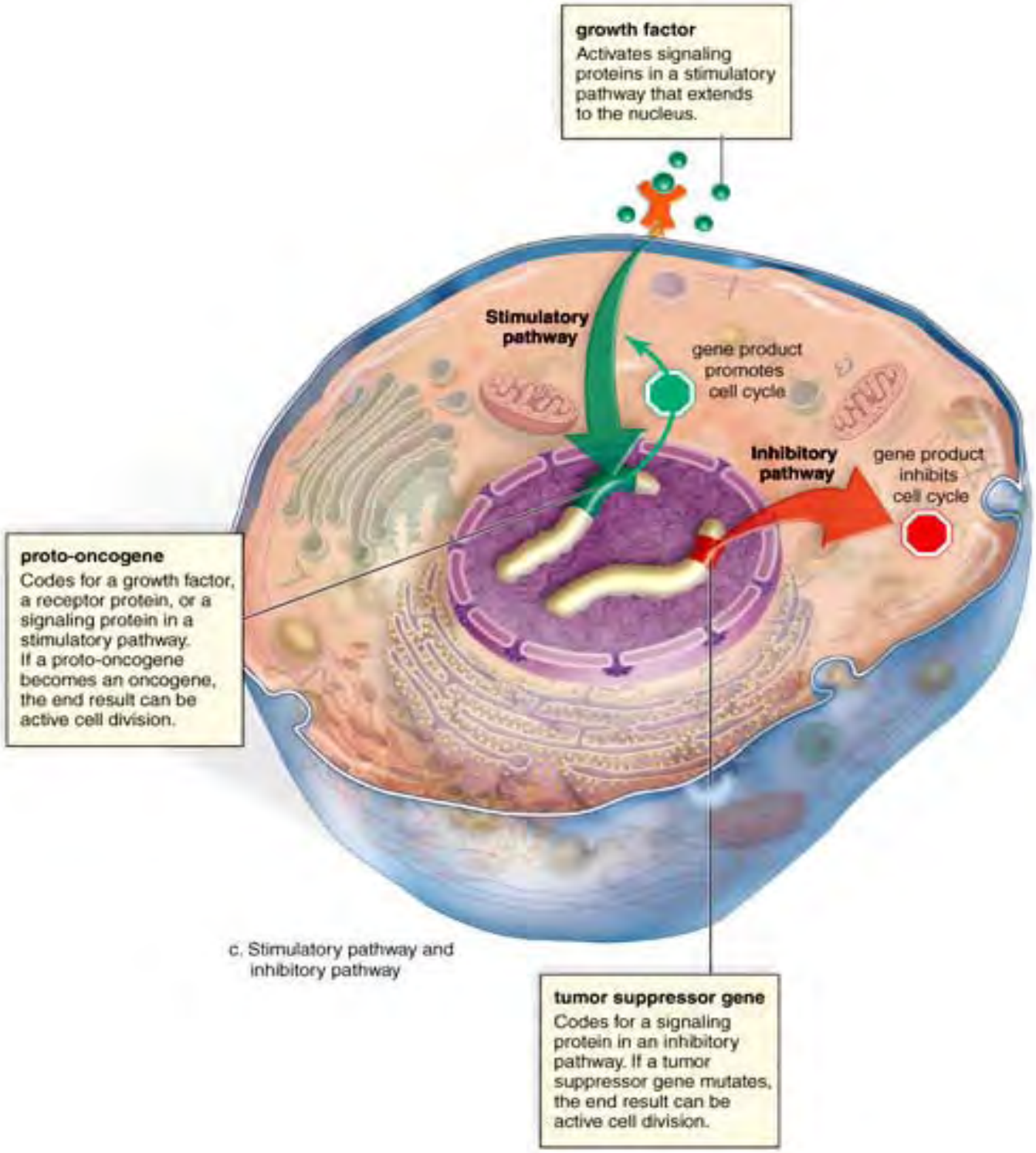
Basically, all cancers are a result of failure of proteins to control the cell cycle **(Lecture 11)**. Consequently, since control is lost, cells keep on dividing and abnormal cells accumulate, often forming tumors. How does this happen? Remember that cell proteins that control the cell cycle are (like all proteins) coded for by genes. Any gene whose protein product promotes mitotic cell division is called a **proto-oncogene**. A mutation may convert a harmless proto-oncogene into an **oncogene** – a gene capable of causing cancer.

Many carcinogens (cancer-causing substances) cause mutations in tumor-suppressor genes such as p53 - mutations of this particular gene are linked to half of all cancers. Whether the mutation is caused by overactive growth factors or inactive tumor suppressor proteins, the result is the same – the proliferation of cell division.



Cancer usually occurs in somatic cells so cannot be passed on to offspring but scientists have identified genes that, if inherited, significantly increase the risk of developing cancer. Two genes that have been identified are BRCA1 and BRCA2.

When these genes function properly they deter cells from dividing uncontrollably but when they are altered by mutations that function is lost and the person has an increased risk of developing breast cancer.

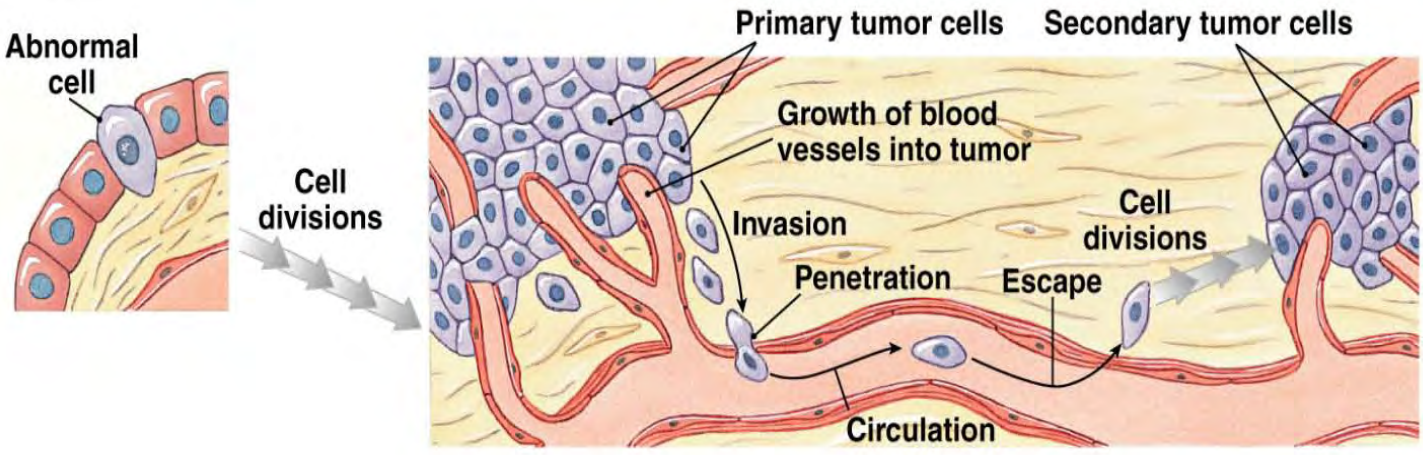


Age also plays a role in the development of cancer. Most people who develop cancer are older and consequently their cellular DNA has been subjected to environmental insults for longer periods of time and is more likely to have mutated.

Another factor related to age is the effectiveness of the immune system. This may decline with age and the person may lose some ability to target and eliminate cancerous cells before they divide. People who have compromised immune systems such as individuals who are undergoing chemotherapy or those who are HIV positive or have AIDS, are also more prone to develop cancer.

Characteristics of cancer cells

Cancerous cells have an abnormal appearance and do not adequately perform the functions of the cell. They also have the ability to metastasize meaning that they can move into the blood stream or lymphatic system and migrate to other parts of the organism where they can leave the blood or lymph and take up residence in other tissues causing secondary growths.



Treatment of Cancer

The following information was found on the CancerQuest website at Emory University and has been abbreviated somewhat.

The treatment given for cancer is variable and dependent on a number of factors including the type, location, and amount of disease and the health status of the patient. Most treatments are designed to either directly kill or remove the cancer cells or to lead to their eventual death by depriving them of signals needed for cell division. Other treatments work by stimulating the body's own defenses against the cancer cells.

Often the different types of treatment are used in combination, either simultaneously or sequentially. The following sections describe some of the most common forms of cancer treatment.

Surgery: Often the first line of treatment for many solid tumors. In cases in which the cancer is detected at an early stage, surgery may be sufficient to cure the patient by removing all cancerous cells. Benign growths may also be removed by surgery.

Radiation: May be used in conjunction with surgery and/or drug treatments. The goal of radiation is to kill the cancer cells directly by damaging them with high energy beams.

Chemotherapy: A term used for a wide array of drugs used to kill cancer cells. Chemotherapy drugs work by damaging the dividing cancer cells and preventing further reproduction. These drugs usually interfere with some part of the cell cycle such as preventing DNA replication or inhibiting the synthesis of microtubules.

Hormonal Treatments: These drugs are designed to prevent cancer cell growth by preventing the cells from receiving signals necessary for their continued growth and division.

Targeted Therapy: This class of drugs is relatively new in the treatment of cancer. They work by targeting specific proteins and processes that are

limited primarily to cancer cells or that are much more prevalent in cancer cells. Inhibition of these processes prevents cancer cell growth and division.

Antibodies: This treatment involves the use of antibodies to target cancer cells. While antibodies are naturally occurring proteins in our bodies, the antibodies used in the treatment of cancer have been manufactured for use as drugs. The antibodies may work by several different mechanisms, either depriving the cancer cells of necessary signals or causing the direct death of the cells. Because of their specificity, antibodies may be thought of as a type of specific inhibitor.

Biological Response Modifiers: These treatments involve the use of naturally occurring, normal proteins that stimulate the body's own defenses against cancer.

Vaccines: The purpose of cancer vaccines is to stimulate the body's defenses against cancer. Vaccines usually contain proteins found on or produced by cancer cells. By administering these proteins, the treatment aims to increase the response of the body against the cancer cells.

Complementary and Alternative Medicines: These treatment methods are not practiced by conventional western medicine. They can include herbal, animal derived, and mind-body approaches to treating cancer. The scientific evidence about the efficacy of these treatments either refutes cancer fighting claims or is inconclusive at the present time.