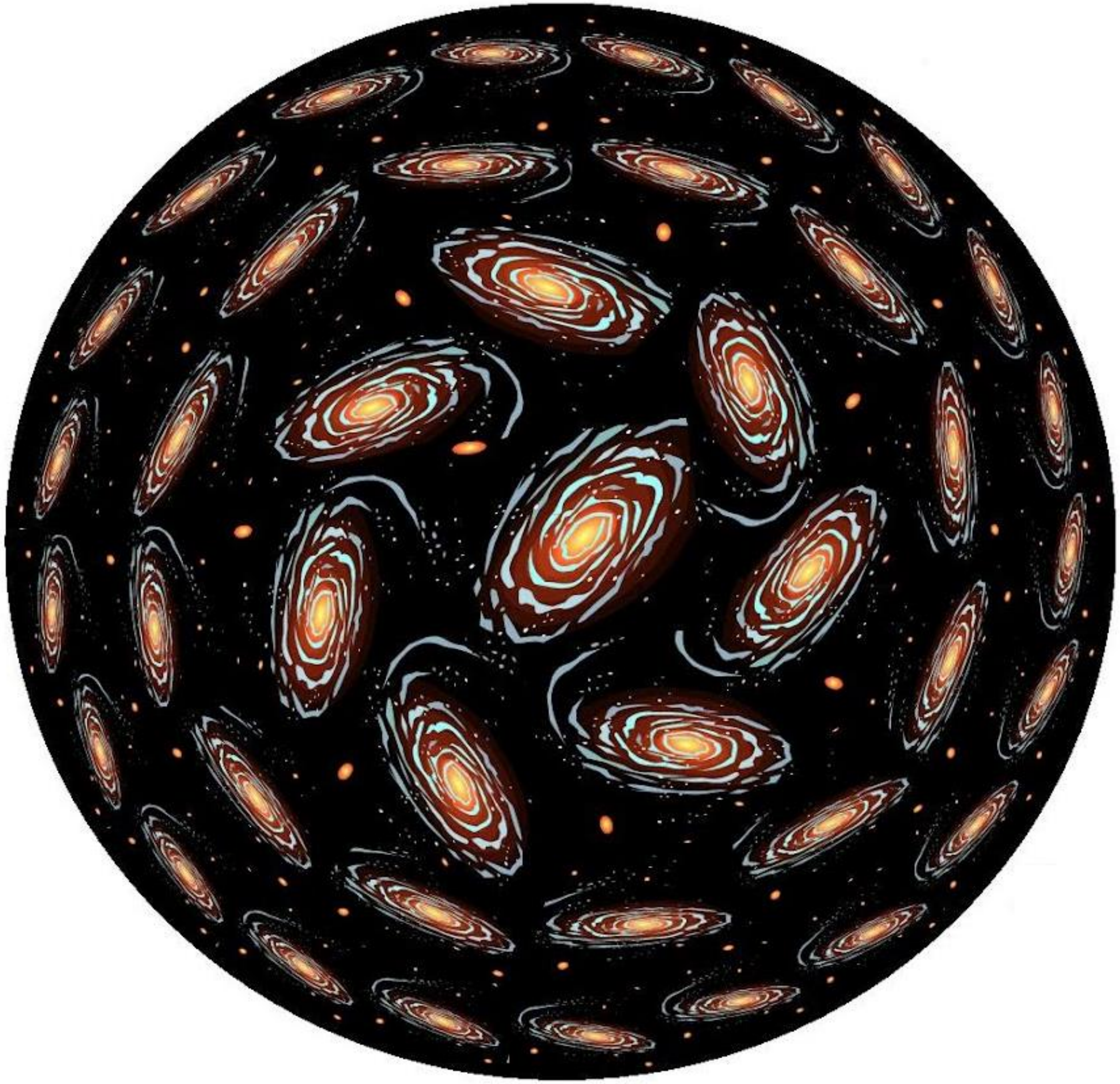
The Chemical Basis of Life



The Nature of Biological Molecules

- The atoms that make up a molecule are joined together by covalent bonds in which pairs of electrons are shared between pairs of atoms.

- The energy required to cleave covalent bonds is relatively large, making these bonds stable under most conditions.

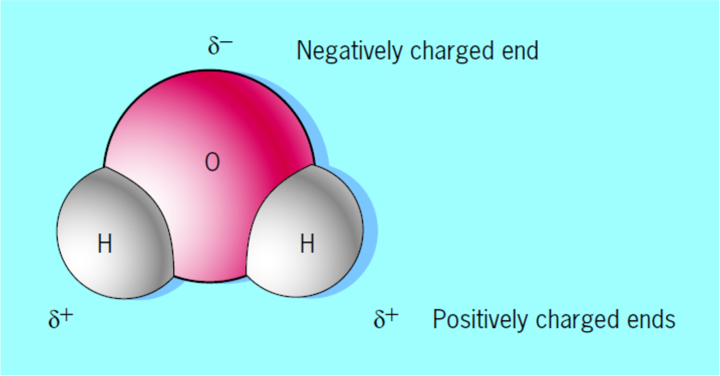
- When atoms of the same element bond to one another, as in H_2, the electron pairs of the outer shell are equally shared between the two bonded atoms.

- When two unlike atoms are covalently bonded, however, the positively charged nucleus of one atom exerts a greater attractive force on the outer electrons than the other.

- Consequently, the shared electrons tend to be located more closely to the atom with the greater attractive force, that is, the more electronegative atom.

- Water's single oxygen atom attracts electrons much more forcefully than do either of its hydrogen atoms.

- As a result, the O—H bonds of a water molecule are said to be polarized, such that one of the atoms has a partial negative charge and the other a partial positive charge.



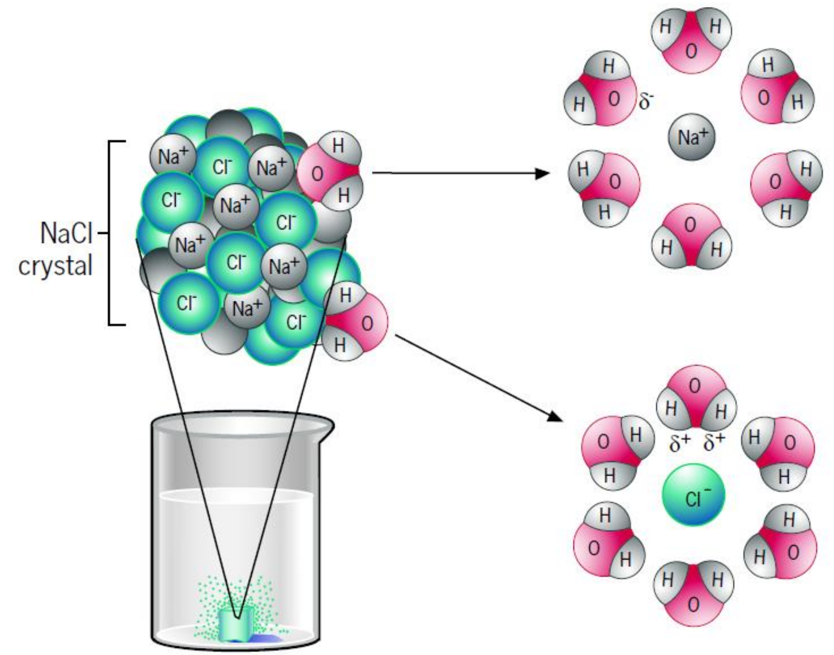
- Molecules, such as water, that have an asymmetric distribution of charge (or dipole) are referred to as polar molecules.

- Polar molecules of biological importance contain one or more electronegative atoms, usually O, N, and/or S. Molecules that lack electronegative atoms and strongly polarized bonds, such as molecules that consist entirely of carbon and hydrogen atoms, are said to be nonpolar.

- Some atoms are so strongly electronegative that they can capture electrons from other atoms during a chemical reaction.
- As a result, these atoms are transformed into charged ions.
- **Covalent bonds** are strong bonds between the atoms that make up a molecule.
- Interactions between molecules (or between different parts of a large biological molecule) are governed by a variety of weaker linkages called noncovalent bonds.
- Noncovalent bonds do not depend on shared electrons but rather on attractive forces between atoms having an opposite charge.
- Even though individual noncovalent bonds are weak, when large numbers of them act in concert, their attractive forces are additive.

- Attraction between fully charged components is called an **ionic bond**.

- Ionic bonds within a salt crystal may be quite strong. However, if a crystal of salt is dissolved in water, each of the individual ions becomes surrounded by water molecules.

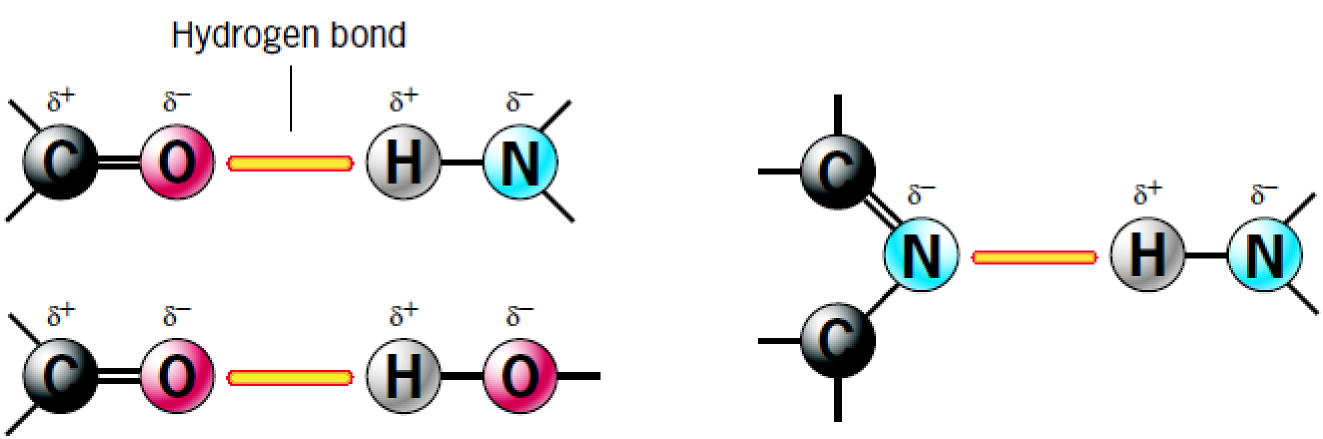


- The strength of ionic bonds in a cell is generally weak (about 3 kcal/mol) due to the presence of water, but deep within the core of a protein, where water is often excluded, such bonds can be much stronger.

- When a hydrogen atom is covalently bonded to an electronegative atom, particularly an oxygen or a nitrogen atom, the single pair of shared electrons is greatly displaced toward the nucleus of the electronegative atom, leaving the hydrogen atom with a partial positive charge.

- As a result, the bare, positively charged nucleus of the hydrogen atom can approach near enough to an unshared pair of outer electrons of a second electronegative atom to form an attractive interaction.

- This weak attractive interaction is called a **hydrogen bond.**

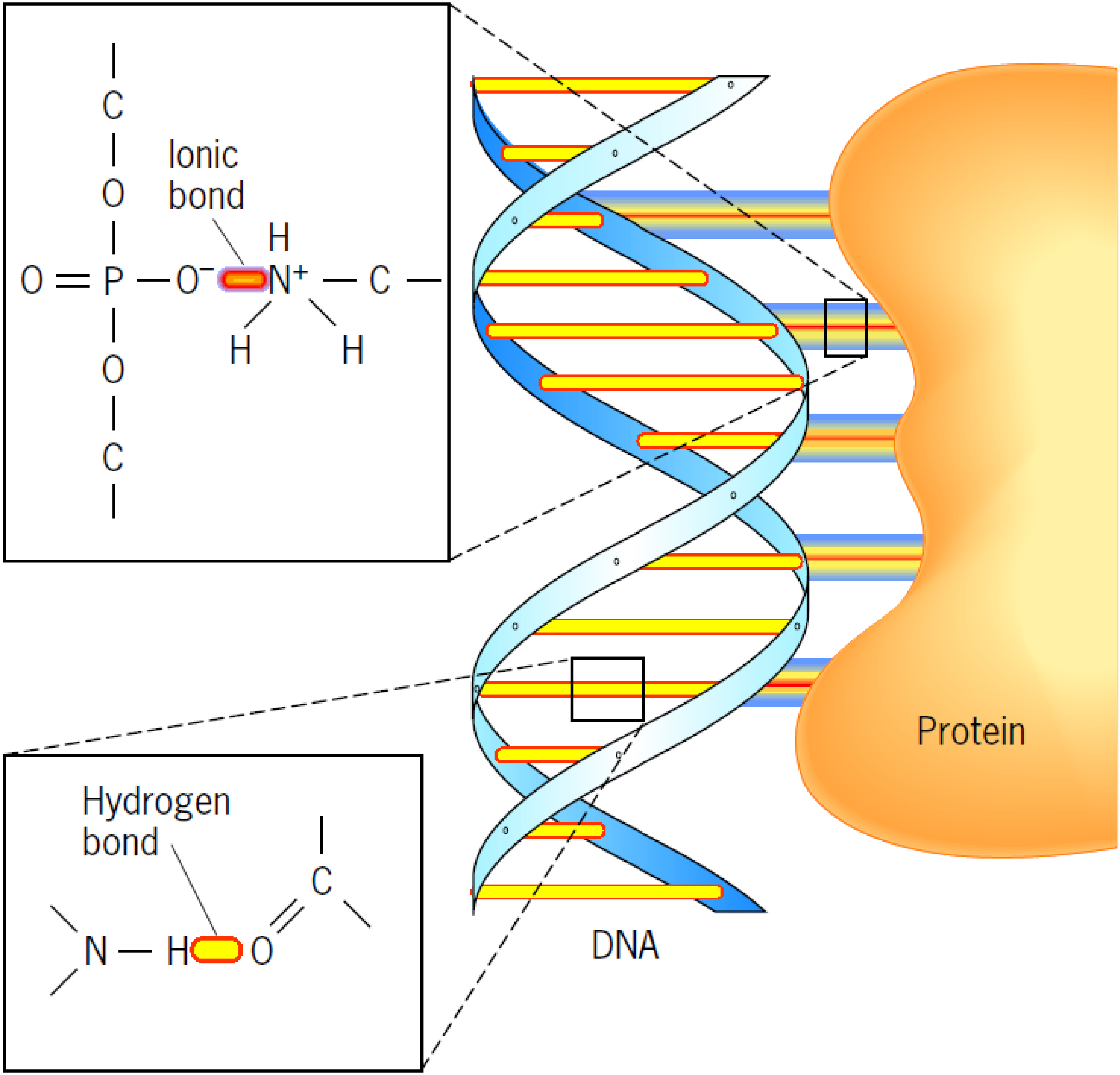


- Hydrogen bonds occur between most polar molecules and are particularly important in determining the structure and properties of water.

- Hydrogen bonds also form between polar groups present in large biological molecules, as occurs between the two strands of a DNA molecule.

- Because their strength is additive, the large number of hydrogen bonds between the strands makes the DNA duplex a stable structure.

- However, because individual hydrogen bonds are weak (2–5 kcal/mol), the two strands can be partially separated to allow enzymes access to individual strands of the DNA molecule.


C
O
Ionic
bond
H
O = P — O⁻ N⁺ — C —
H
H
O
C
Hydrogen
bond
C
N — H O
DNA
Protein

- Because of their ability to interact with water, polar molecules, such as sugars and amino acids, are said to be hydrophilic, or "water loving."

- Nonpolar molecules, such as steroid or fat molecules, are essentially insoluble in water because they lack the charged regions that would attract them to the poles of water molecules.

- When nonpolar compounds are mixed with water, the nonpolar, hydrophobic ("water fearing") molecules are forced into aggregates, which minimizes their exposure to the polar surroundings.

- This association of nonpolar molecules is called a **hydrophobic interaction.**

- In addition to hydrophobic interaction, hydrophobic groups can form weak bonds with one another based on electrostatic attractions.

- Electron distributions of covalent bonds that make up a nonpolar molecule are not always symmetric.

- Consequently, at any given time, the electron density may happen to be greater on one side of an atom.

- These transient asymmetries in electron distribution result in momentary separations of charge (dipoles) within the molecule.

- If two molecules with transitory dipoles are very close to one another and oriented in the appropriate manner, they experience a weak attractive force, called a **van der Waals force**, that bonds them together.

- Life on Earth is totally dependent on water, and water may be essential to the existence of life anywhere in the universe.

- Even though it contains only three atoms, a molecule of water has a unique structure that gives the molecule extraordinary properties.

  - Water is a highly asymmetric molecule with the O atom at one end and the two H atoms at the opposite end.

  - Each of the two covalent bonds in the molecule is highly polarized.

  - All three atoms in a water molecule are adept at forming hydrogen bonds.

- Each molecule of water can form hydrogen bonds with as many as four other water molecules, producing a highly interconnected network of molecules.

- The bulk of an organism is water. If the water is evaporated away, most of the remaining dry weight consists of molecules containing atoms of carbon.

- The chemistry of life centers around the chemistry of the carbon atom.

- The compounds produced by living organisms are called biochemicals.

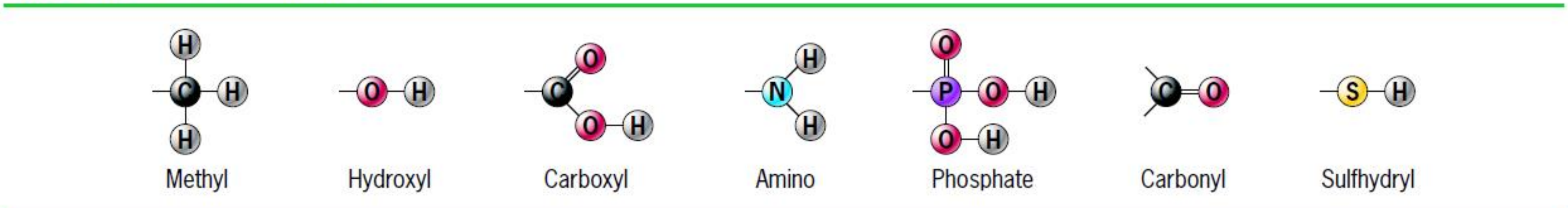
- Both the size and electronic structure of carbon make it uniquely suited for generating large numbers of molecules.

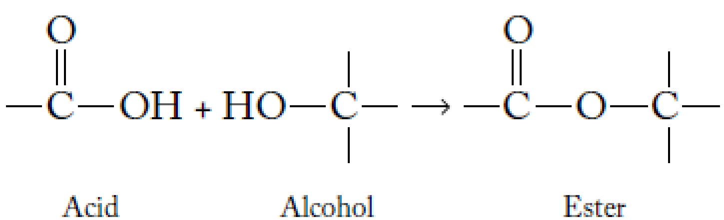
- In contrast, silicon, which is just below carbon in the periodic table and also has four outer-shell electrons, is too large for its positively charged nucleus to attract the outer-shell electrons of neighboring atoms with sufficient force to hold such large molecules together.

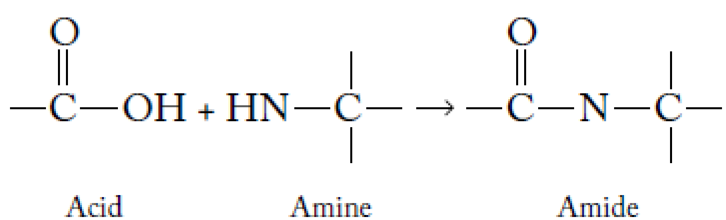
- Functional groups are particular groupings of atoms that often behave as a unit and give organic molecules their physical properties, chemical reactivity, and solubility in aqueous solution.

- Two of the most common linkages between functional groups are ester bonds, which form between carboxylic acids and alcohols, and amide bonds, which form between carboxylic acids and amines.

Table 2.2 ***Functional Groups***

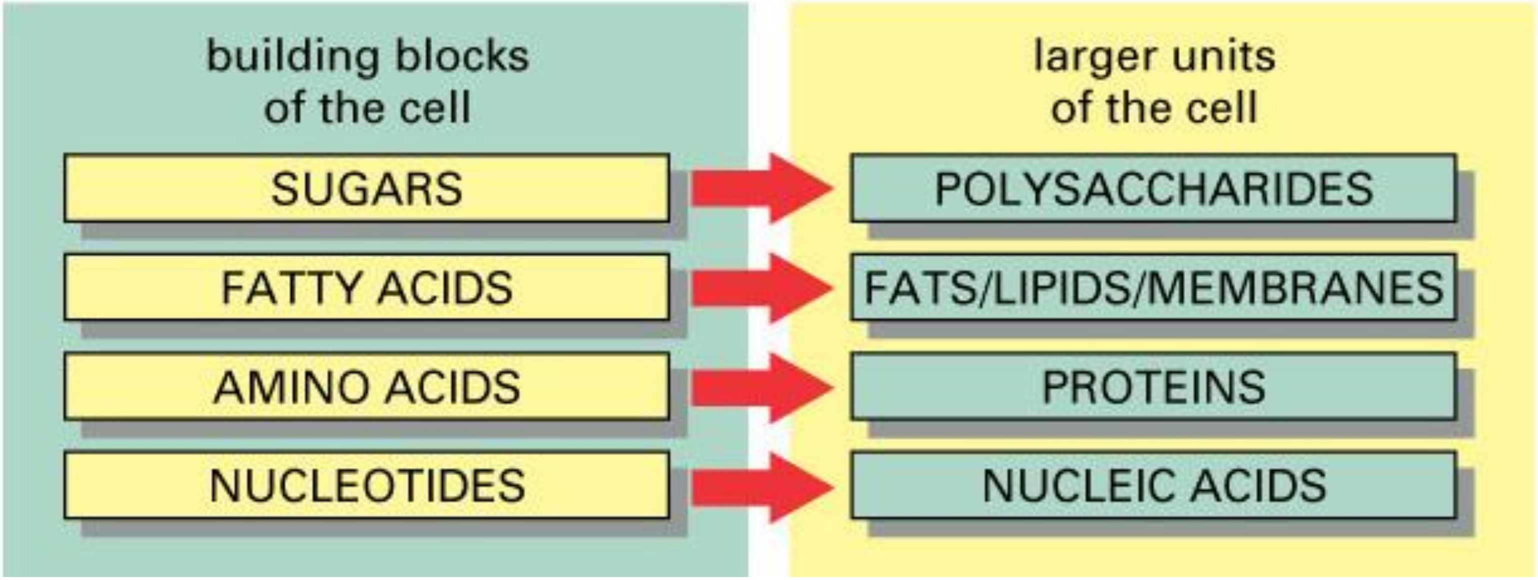






- The molecules that form the structure and carry out the activities of cells are huge, highly organized molecules called macromolecules, which contain anywhere from dozens to millions of carbon atoms.

- The presence of macromolecules, more than any other characteristic, endows organisms with the properties of life and sets them apart chemically from the inanimate world.



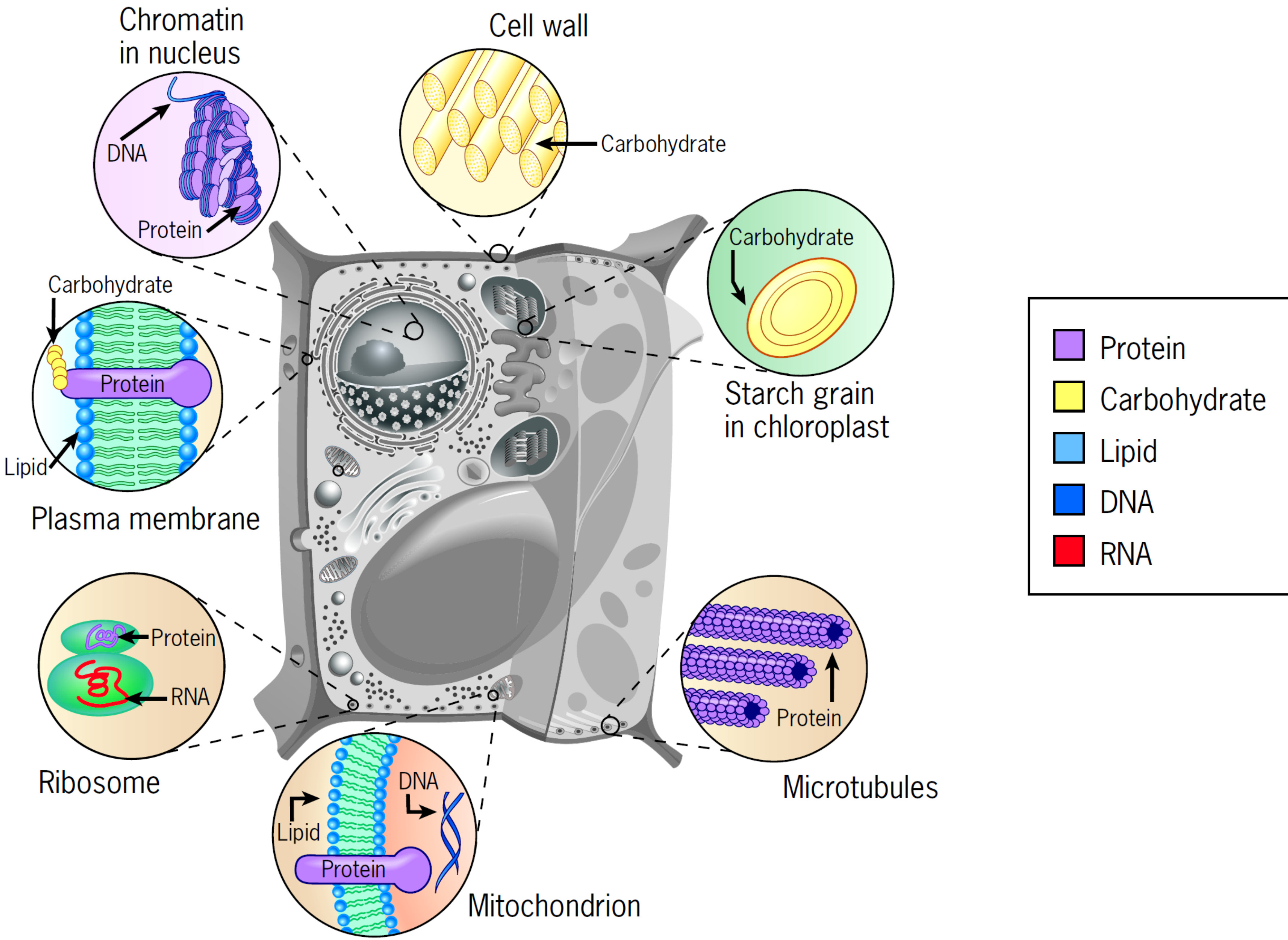
- Biological macromolecules can be divided into four major categories: proteins, nucleic acids, polysaccharides, and lipids.

- The first three types are polymers composed of a large number of low-molecular-weight building blocks, or monomers.

- These macromolecules are constructed from monomers by a process of polymerization.

- Most of the macromolecules within a cell have a short lifetime compared with the cell itself; with the exception of the cell's DNA, they are continually broken down and replaced by new macromolecules.

- These include sugars, which are the precursors of polysaccharides; amino acids, which are the precursors of proteins; nucleotides, which are the precursors of nucleic acids; and fatty acids, which are incorporated into lipids.


Chromatin in nucleus
DNA
Protein
Cell wall
Carbohydrate
Carbohydrate
Starch grain in chloroplast
Carbohydrate
Protein
Lipid
Plasma membrane
Protein
RNA
Ribosome
Lipid
DNA
Protein
Mitochondrion
Protein
Microtubules
Protein
Carbohydrate
Lipid
DNA
RNA

- **Carbohydrates** include simple sugars (or monosaccharides) and all larger molecules constructed of sugar building blocks.

- Carbohydrates function primarily as stores of chemical energy and as durable building materials for biological construction.

- Most sugars have the general formula $(CH_2O)_n$ and can be describe as polyhydroxy aldehydes or ketones.

- The sugars of importance in cellular metabolism have values of n that range from 3 to 7.

- Sugars containing three carbons are known as trioses, those with four carbons as tetroses, those with five carbons as pentoses, those with six carbons as hexoses, and those with seven carbons as heptoses.

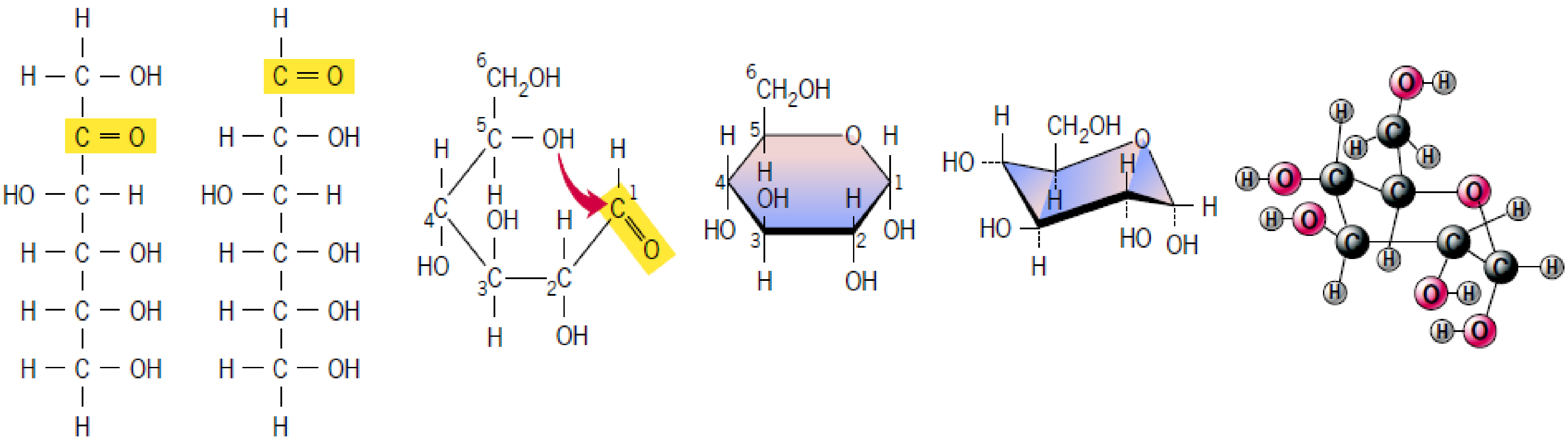
- Each sugar molecule consists of a backbone of carbon atoms linked together in a linear array by single bonds.

- Each of the carbon atoms of the backbone is linked to a single hydroxyl group, except for one that bears a carbonyl (C=O) group.

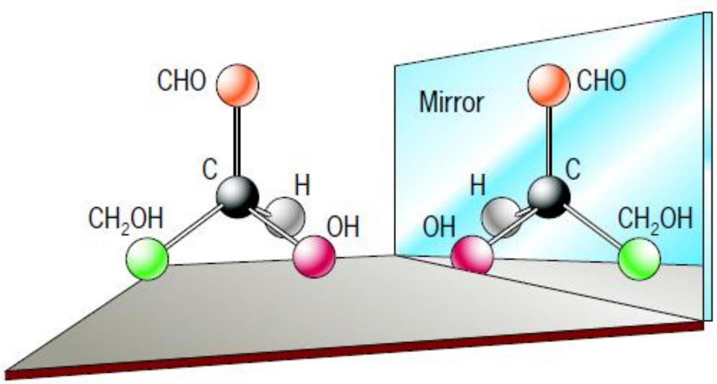
- If the carbonyl group is located at an internal position (to form a ketone group), the sugar is a ketose, such as fructose,

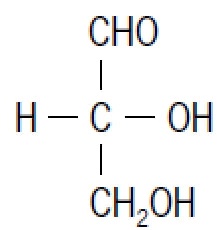
- If the carbonyl is located at one end of the sugar, it forms an aldehyde group and the molecule is known as an aldose, such as glucose.

- Because of their large numbers of hydroxyl groups, sugars tend to be highly water soluble.

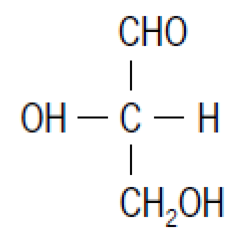


D-Fructose (a) | D-Glucose (b) | D-Glucose (Ring Formation) (c) | α-D-Glucose (Haworth projection) (d) | α-D-Glucose (Chair form) (e) | α-D-Glucose (Ball-and-stick chair) (f)



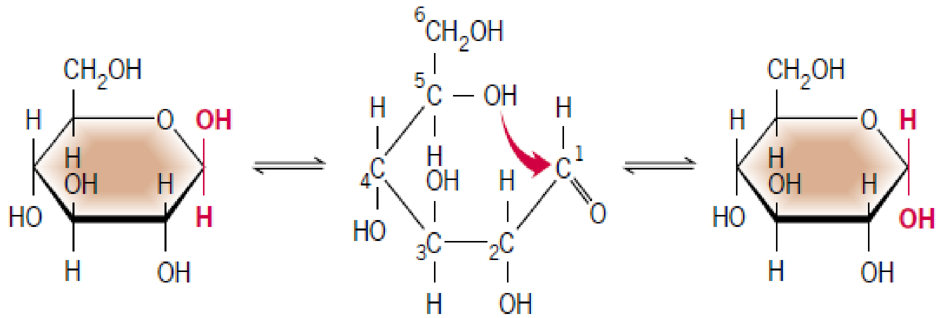


D-Glyceraldehyde



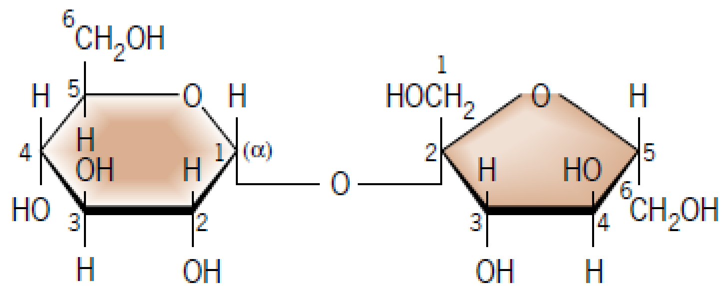
L-Glyceraldehyde

❖ Sugars can be joined to one another by covalent glycosidic bonds to form larger molecules.



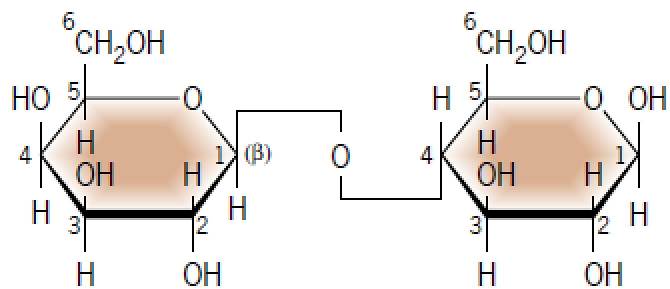
β-D-Glucopyranose α-D-Glucopyranose

Sucrose



(a)

Lactose

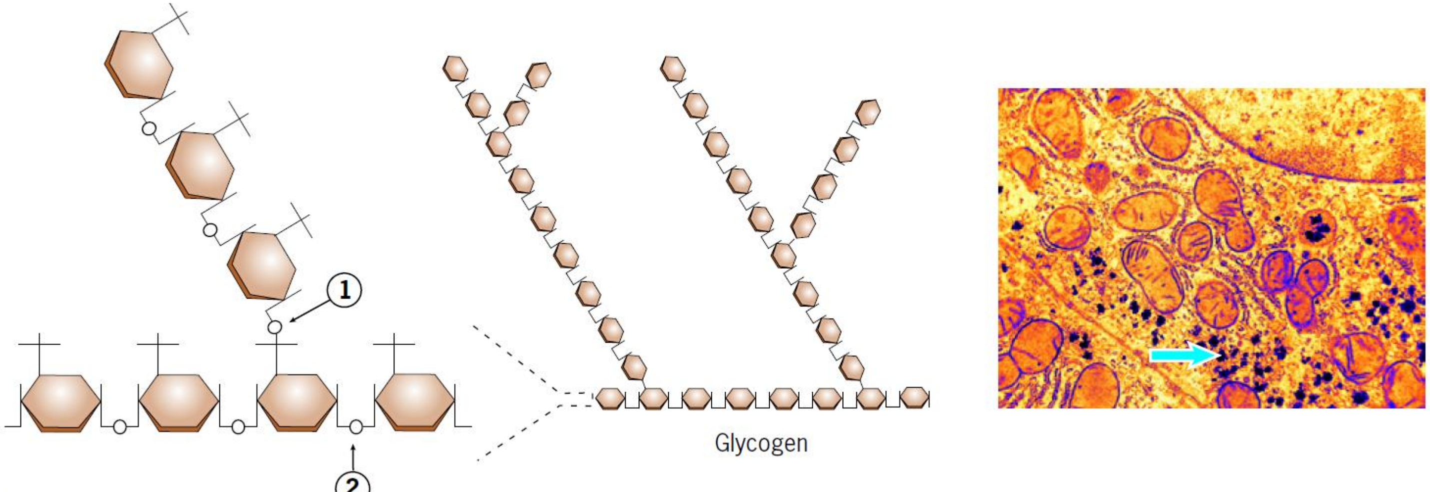


- Sugars may also be linked together to form small chains called oligosaccharides.

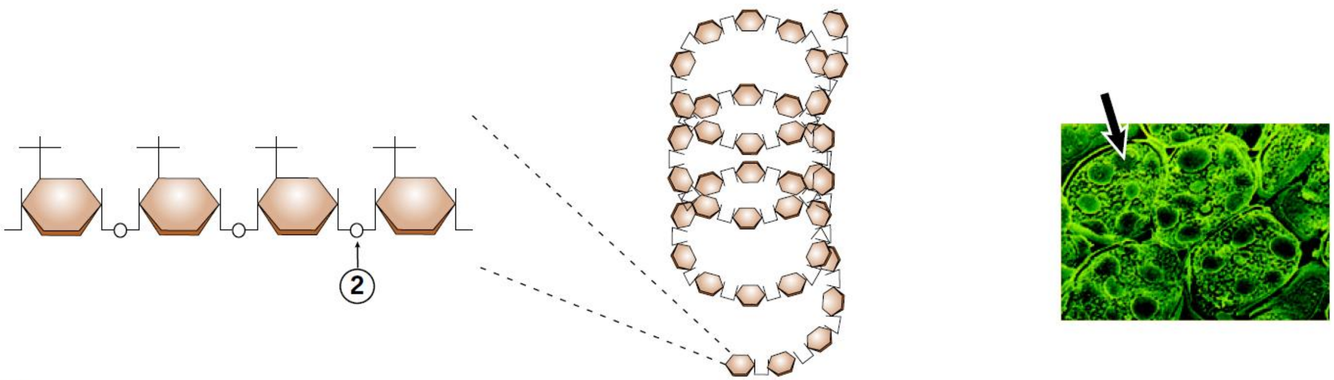
- Most often such chains are found covalently attached to lipids and proteins, converting them into glycolipids and glycoproteins, respectively.

- Oligosaccharides are particularly important on the glycolipids and glycoproteins of the plasma membrane, where they project from the cell surface.

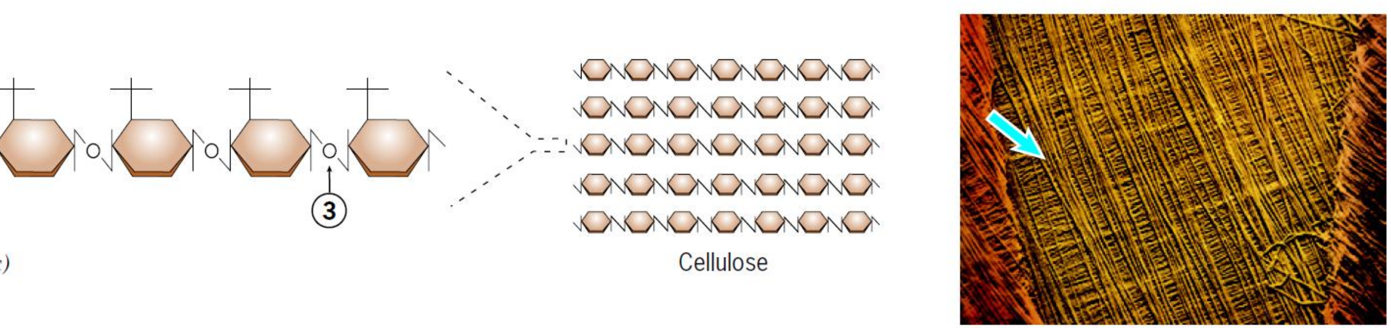
- A polymer of sugar units joined by glycosidic bonds call polysaccharides.



(a)



(b)



(c)

- Glycogen is a branched polymer containing only one type of monomer: glucose.
- Most of the sugar units of a glycogen molecule are joined to one another by $\alpha(1 \rightarrow 4)$ glycosidic bonds.
- Branch points contain a sugar joined to three neighboring units rather than to two, as in the unbranched segments of the polymer.
- The extra neighbor, which forms the branch, is linked by an $\alpha(1 \rightarrow 6)$ glycosidic bond.
- Glycogen serves as a storehouse of surplus chemical energy in most animals.
- Most plants bank their surplus chemical energy in the form of starch, which like glycogen is also a polymer of glucose.

- Starch is actually a mixture of two different polymers, amylose and amylopectin.

- Amylose is an unbranched, helical molecule whose sugars are joined by (1 → 4) linkages , whereas amylopectin is branched but less than glycogen.

- Starch is stored as densely packed granules, or starch grains, which are enclosed in membranebound organelles (plastids) within the plant cell.

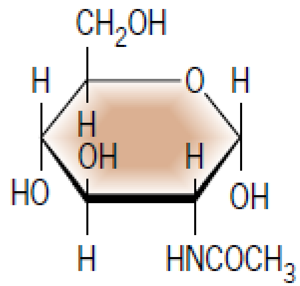
- Whereas some polysaccharides constitute easily digested energy stores, others form tough, durable structural materials.

- Cotton and linen, for example, consist largely of cellulose, which is the major component of plant cell walls.

- Like glycogen and starch, cellulose consists solely of glucose monomers; its properties differ dramatically from these other polysaccharides because the glucose units are joined by β (1 →4) linkages rather than α (1 →4) linkages .

❖Not all biological polysaccharides consist of glucose monomers.

❖Chitin is an unbranched polymer of the sugar N-acetylglucosamine.



N-Acetylglucosamine

❖Another group of polysaccharides that has a more complex structure is the glycosaminoglycans (or GAGs).

❖Unlike other polysaccharides, they have the structure —A—B—A—B—, where A and B represent two different sugars.

❖**Lipids** are a diverse group of nonpolar biological molecules whose common properties are their ability to dissolve in organic solvents, such as chloroform or benzene, and their inability to dissolve in water.

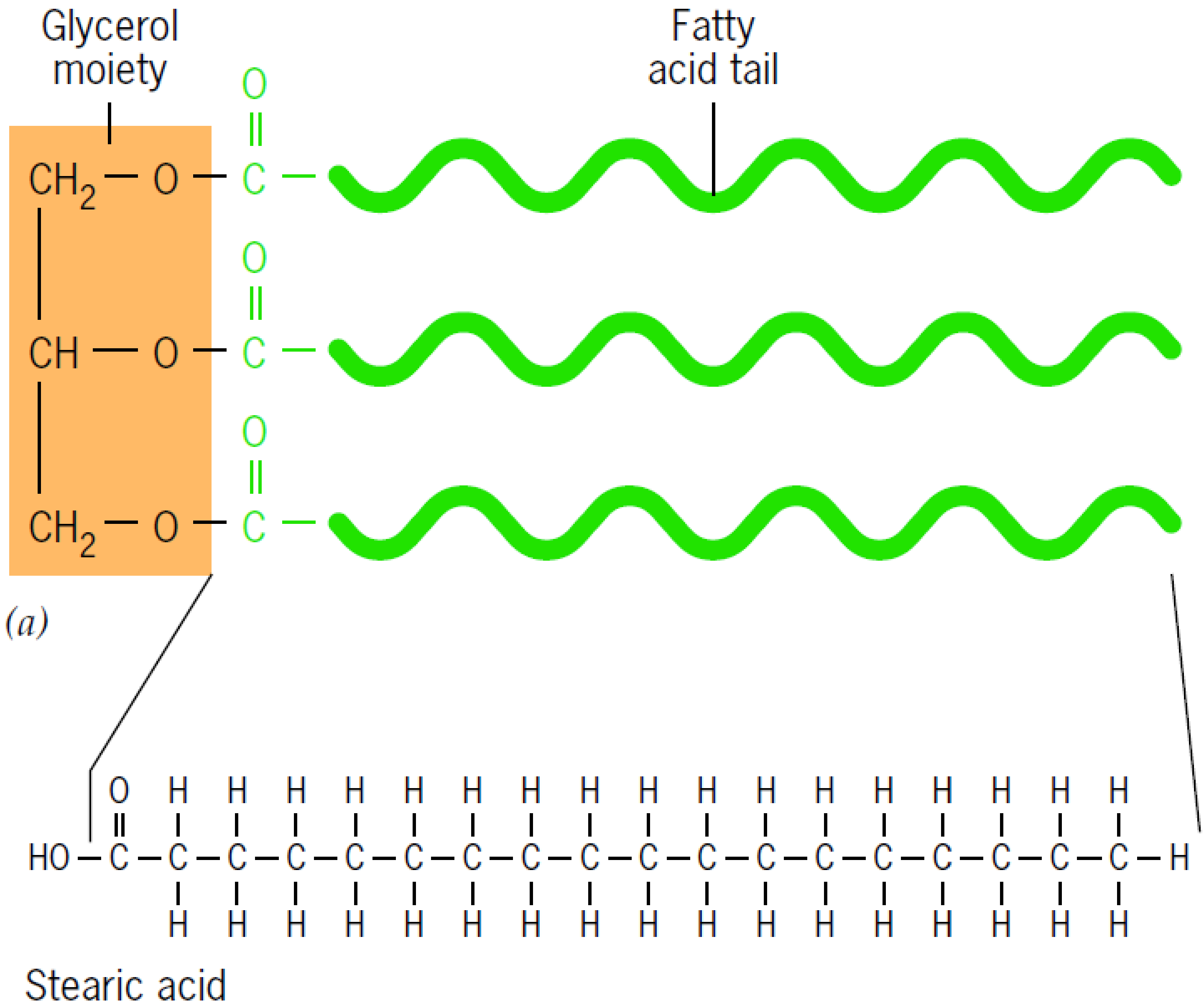
- Lipids of importance in cellular function include fats, steroids, and phospholipids.

- Fats consist of a glycerol molecule linked by ester bonds to three fatty acids; the composite molecule is termed a triacylglycerol.

- Fatty acids are long, unbranched hydrocarbon chains with a single carboxyl group at one end.

- The hydrocarbon chain of fatty acids hydrophobic, whereas the carboxyl group (—COOH), which bears a negative charge at physiological pH, is hydrophilic.

- Molecules having both hydrophobic and hydrophilic regions are said to be amphipathic; such molecules have unusual and biologically important properties.


Glycerol moiety
Fatty acid tail
CH2 — O — C —
CH — O — C —
CH2 — O — C —
O
O
O
(a)
HO — C — C — C — C — C — C — C — C — C — C — C — C — C — C — C — C — C — C — H
Stearic acid

- Fatty acids differ from one another in the length of their hydrocarbon chain and the presence or absence of double bonds.

- Fatty acids present in cells typically vary in length from 14 to 20 carbons.

- Fatty acids that lack double bonds, such as stearic acid, are described as saturated; those possessing double bonds are unsaturated.

- Naturally occurring fatty acids have double bonds in the cis configuration.

- Fats that are liquid at room temperature are described as oils. Oils usually consists of unsaturated fatty acids.

- Fats are very rich in chemical energy; a gram of fat contains over twice the energy content of a gram of carbohydrate

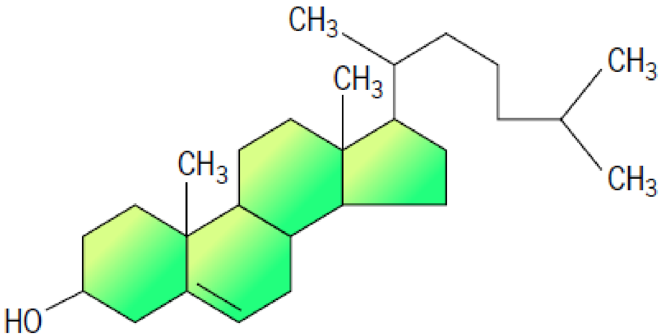
- Steroids are built around a characteristic four ringed hydrocarbon skeleton.

- One of the most important steroids is cholesterol, a component of animal cell membranes and a precursor for the synthesis of a number of steroid hormones, such as testosterone, progesterone, and estrogen.

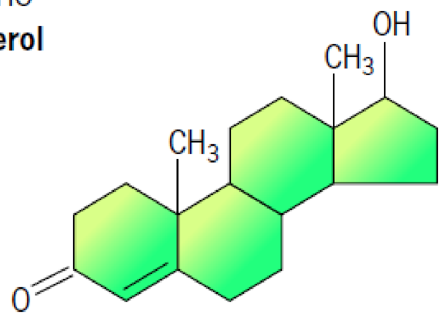
- Phospholipid molecule resembles a triacylglycerol, but has only two fatty acid chains rather than three.

- The third hydroxyl of the glycerol backbone is covalently bonded to a phosphate group, which in turn is covalently bonded to a small polar group, such as choline.

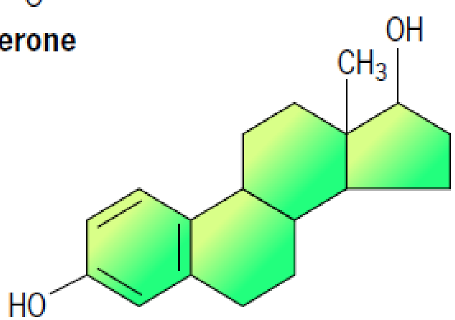
- Thus, unlike fat molecules, phospholipids contain two ends that have very different properties.



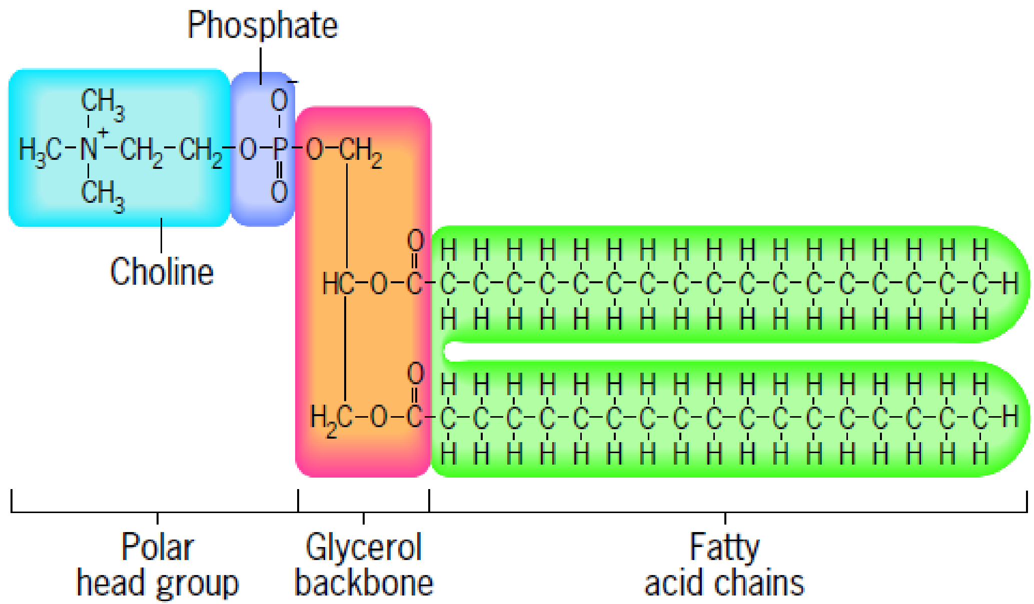
Cholesterol



Testosterone



Estrogen



- **Proteins** are the macromolecules that carry out virtually all of a cell’s activities; they are the molecular tools and machines that make things happen.

- As enzymes, proteins vastly accelerate the rate of metabolic reactions;

- as structural cables, proteins provide mechanical support both within cells and outside their perimeters;

- as hormones, growth factors, and gene activators, proteins perform a wide variety of regulatory functions;

- as membrane receptors and transporters, proteins determine what a cell reacts to and what types of substances enter or leave the cell;

- as contractile filaments and molecular motors, proteins constitute the machinery for biological movements.

- Among their many other functions, proteins act as antibodies, serve as toxins, form blood clots, absorb or refract light , and transport substances from one part of the body to another.

- Each protein, has a unique and defined structure that enables it to carry out a particular function.

- Most importantly, proteins have shapes and surfaces that allow them to interact selectively with other molecules.

- Proteins are polymers made of amino acid monomers. Twenty different amino acids are commonly used in the construction of proteins.

- All amino acids have a carboxyl group and an amino group, which are separated from each other by a single carbon atom, the α-carbon.

- With the exception of glycine, the α-carbon of amino acids bonds to four different groups so that each amino acid can exist in either a D or an L form .

- Amino acids used in the synthesis of a protein on a ribosome are always L-amino acids.

- The "selection" of L-amino acids must have occurred very early in cellular evolution and has been conserved for billions of years.

- During the process of protein synthesis, each amino acid becomes joined to two other amino acids, forming a long, continuous, unbranched polymer called a polypeptide chain.

- The "average" polypeptide chain contains about 450 amino acids.

- The longest known polypeptide, found in the muscle protein titin, contains more than 30,000 amino acids.

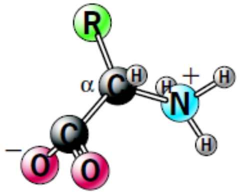
- Once incorporated into a polypeptide chain, amino acids are termed residues.

- The residue on one end of the chain, the N-terminus, contains an amino acid with a free (unbonded) α-amino group, whereas the residue at the opposite end, the C-terminus, has a free α-carboxyl group.

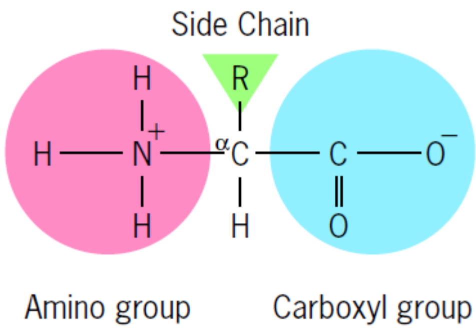
- In addition to amino acids, many proteins contain other types of components that are added after the polypeptide is synthesized.

- These include carbohydrates (to form glycoproteins), metal-containing groups (to form metalloproteins) and organic groups (e.g., flavoproteins).

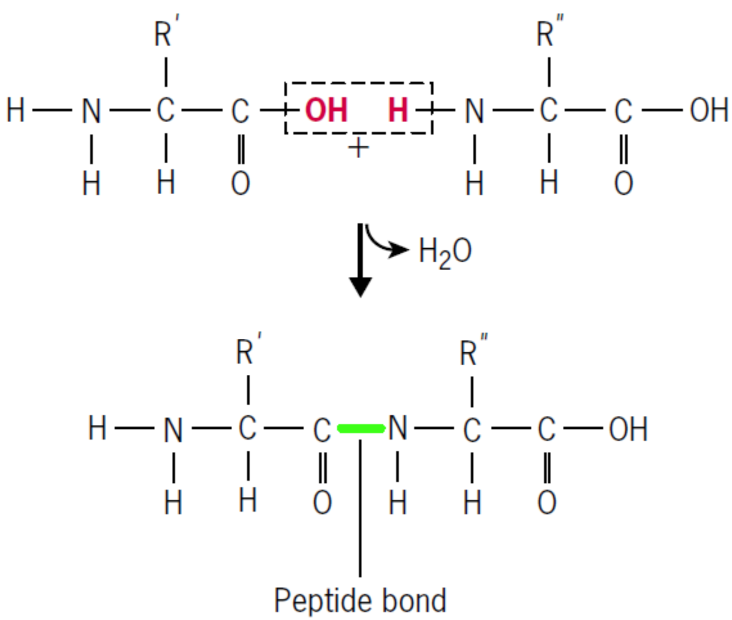
- The side chain or R group , bonded to the α-carbon, is highly variable among the 20 building blocks, and it is this variability that ultimately gives proteins their diverse structures and activities.


R
α C H
H + H
N
H
C
− O O

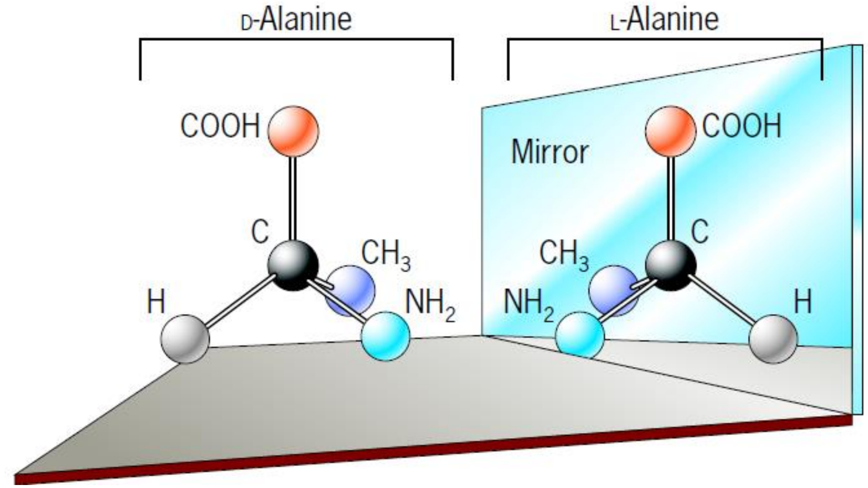
(a)

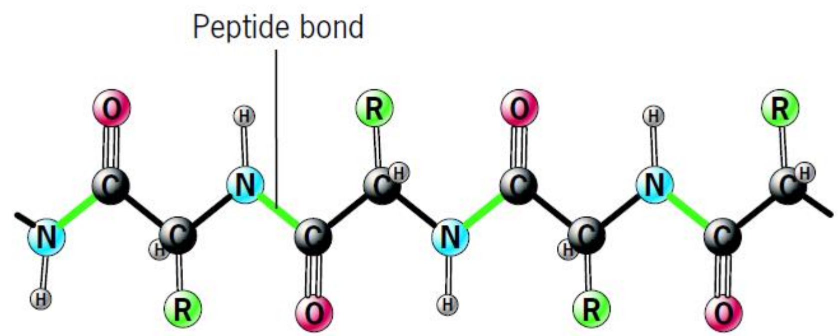

Side Chain
R
H
H N+ αC C O−
H H O
Amino group
Carboxyl group

(b)

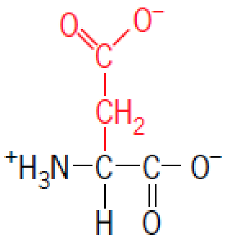

R′ R″
H N C C OH H N C C OH
H H O + H H O
H_2O
R′ R″
H N C C N C C OH
H H O H H O
Peptide bond

(c)

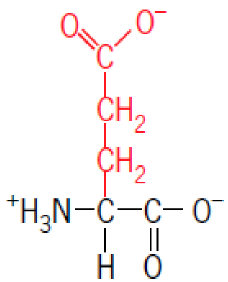

D-Alanine
L-Alanine
COOH
C
CH_3
H
NH_2
Mirror
COOH
C
CH_3
NH_2
H


Peptide bond

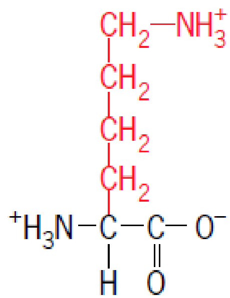
Polar charged



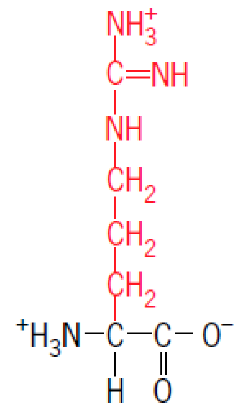
Aspartic acid
(Asp or D)



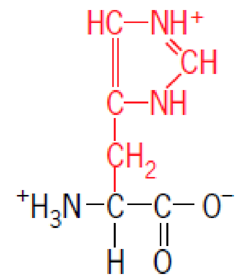
Glutamic acid
(Glu or E)



Lysine
(Lys or K)



Arginine
(Arg or R)

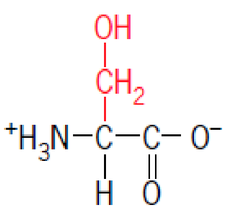


Histidine
(His or H)

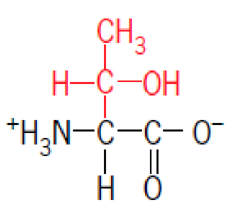
Properties of side chains (R groups):

Hydrophilic side chains act as acids or bases which tend to be fully charged (+ or –) under physiologic conditions. Side chains form ionic bonds and are often involved in chemical reactions.

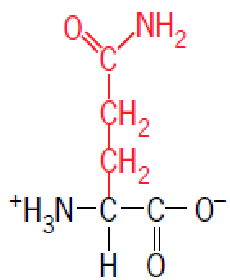
Polar uncharged



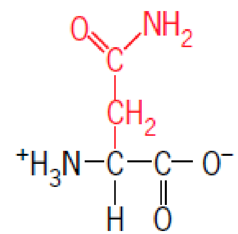
Serine
(Ser or S)



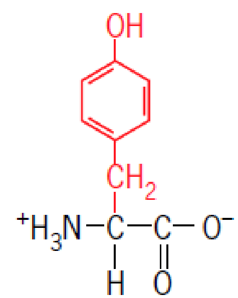
Threonine
(Thr or T)



Glutamine
(Gln or Q)



Asparagine
(Asn or N)

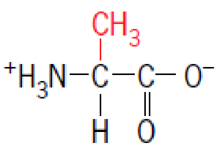


Tyrosine
(Tyr or Y)

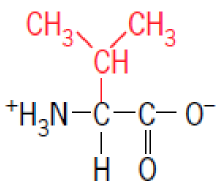
Properties of side chains:

Hydrophilic side chains tend to have partial + or – charge allowing them to participate in chemical reactions, form H-bonds, and associate with water.

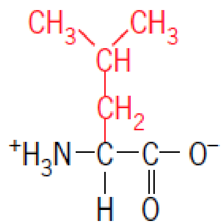
Nonpolar



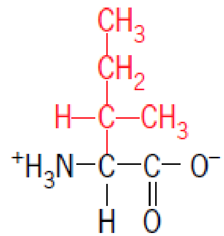
Alanine
(Ala or A)



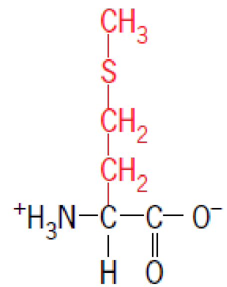
Valine
(Val or V)



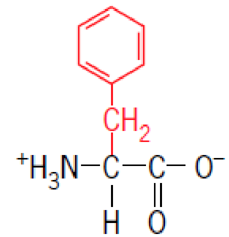
Leucine
(Leu or L)



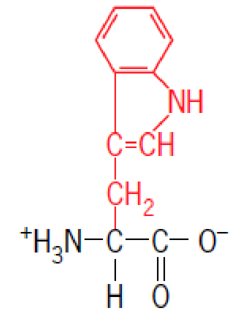
Isoleucine
(Ile or I)



Methionine
(Met or M)



Phenylalanine
(Phe or F)

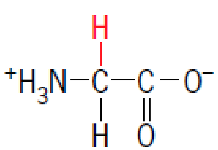


Tryptophan
(Trp or W)

Properties of side chains:

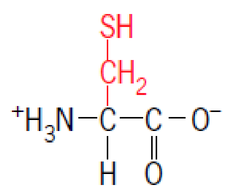
Hydrophobic side chain consists almost entirely of C and H atoms. These amino acids tend to form the inner core of soluble proteins, buried away from the aqueous medium. They play an important role in membranes by associating with the lipid bilayer.

Side chains with unique properties



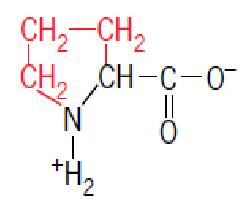
Glycine
(Gly or G)

Side chain consists only of hydrogen atom and can fit into either a hydrophilic or hydrophobic environment.Glycine often resides at sites where two polypeptides come into close contact.



Cysteine
(Cys or C)

Though side chain has polar, uncharged character, it has the unique property of forming a covalent bond with another cysteine to form a disulfide link.



Proline
(Pro or P)

Though side chain has hydrophobic character, it has the unique property of creating kinks in polypeptide chains and disrupting ordered secondary structure.

- Polar, charged. Amino acids of this group include aspartic acid, glutamic acid, lysine, and arginine.

- These four amino acids contain side chains that become fully charged; that is, the side chains contain relatively strong organic acids and bases.

- They are able to form ionic bonds with other charged species in the cell.

- Histidine is also considered a polar, charged amino acid, though in most cases it is only partially charged at physiologic pH.

- Polar, uncharged. The side chains of these amino acids have a partial negative or positive charge and thus can form hydrogen bonds with other molecules including water.

- These amino acids, asparagine , glutamine , threonine, serine, and tyrosine. are often quite reactive.

- Nonpolar. The side chains of these amino acids are hydrophobic and are unable to form electrostatic bonds or interact with water.
- The amino acids of this category are alanine, valine, leucine, isoleucine, tryptophan, phenylalanine, and methionine.
- They vary primarily in size and shape, which allows one or another of them to pack tightly into a particular space within the core of a protein, associating with one another as the result of van der Waals forces and hydrophobic interactions.
- The other three amino acids—glycine, proline, and cysteine—have unique properties that separate them from the others.
- Owing to its lack of a side chain, glycine residues provide a site where the backbones of two polypeptides (or two segments of the same polypeptide) can approach one another very closely.

- Proline is unique in having its -amino group as part of a ring (making it an imino acid).

- Proline is a hydrophobic amino acid that does not readily fit into an ordered secondary structure, such as an helix, often producing kinks or hinges.

- Cysteine contains a reactive sulfhydryl (—SH) group and is often covalently linked to another cysteine residue, as a disulfide (—SS—) bridge.

- The structure of most proteins is completely defined and predictable.

- Each amino acid in one of these giant macromolecules is located at a specific site within the structure, giving the protein the precise shape and reactivity required for the job at hand.

- Protein structure can be described at several levels of organization, each emphasizing a different aspect and each dependent on different types of interactions.

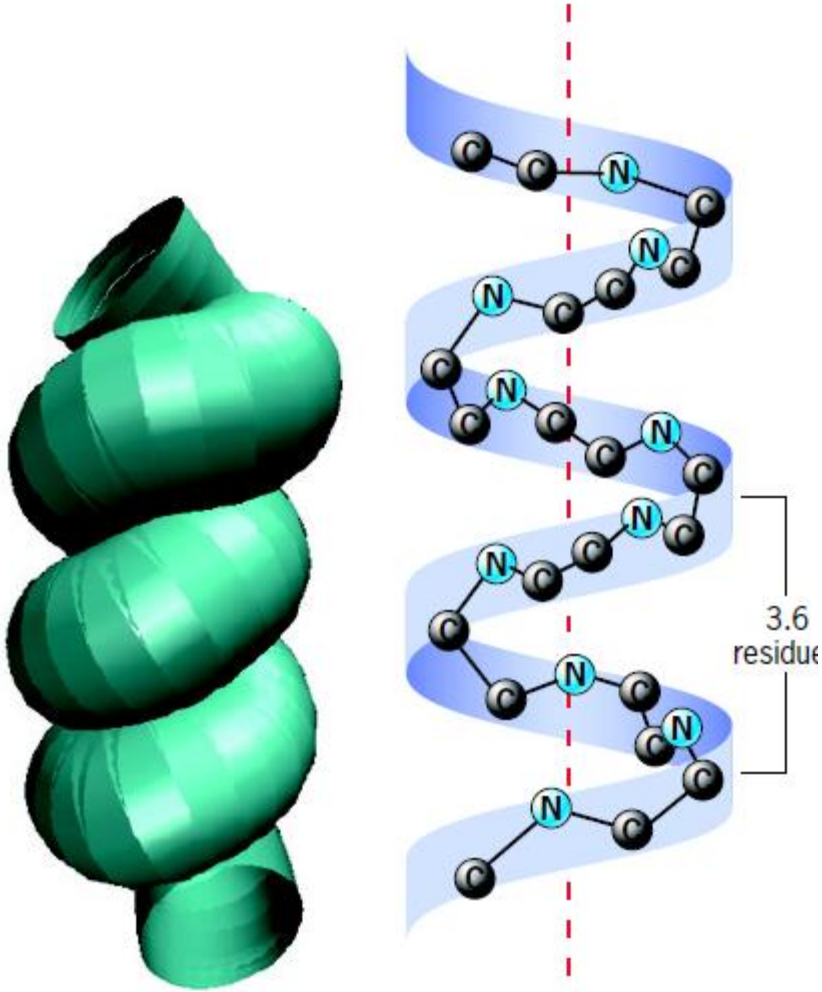
- Customarily, four such levels are described: primary, secondary, tertiary, and quaternary.

- The primary structure of a polypeptide is the specific linear sequence of amino acids that constitute the chain.

- Secondary structure describes the conformation of portions of the polypeptide chain. Alpha(α)-helix and beta (β)-pleated sheet are the most common secondary structures.

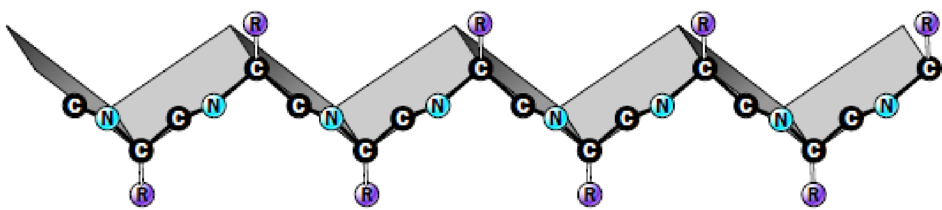
- α-helix, first discovered in the protein keratin found in hair and later in various oxygen-binding proteins, such as myoglobin and hemoglobin.

- Silk is composed of a protein containing an extensive amount of β-sheet; silk fibers are thought to owe their strength to this architectural feature.

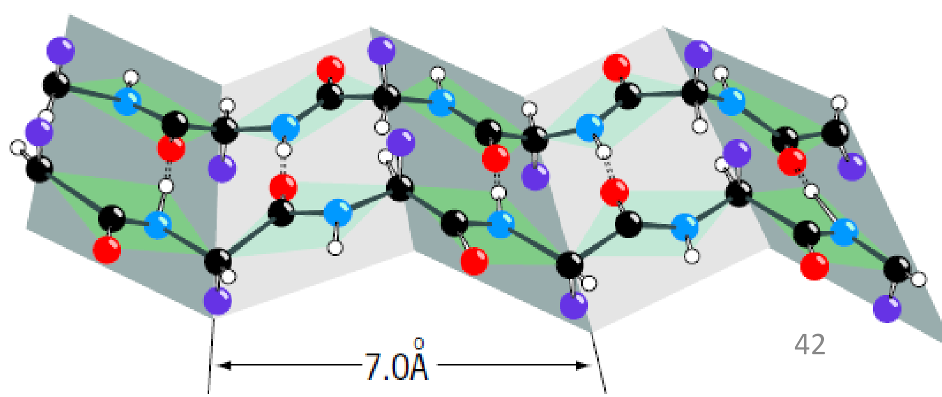


(a) (b)

(a)



(b)



- Those portions of a polypeptide chain not organized into an α-helix or a β-sheet may consist of hinges, turns, loops, or finger-like extensions.
- Often, these are the most flexible portions of a polypeptide chain and the sites of greatest biological activity.
- The next level above secondary structure is tertiary structure, which describes the conformation of the entire polypeptide.
- Secondary structure is largely limited to a small number of conformations, but tertiary structure is virtually unlimited.
- The detailed tertiary structure of a protein is usually determined using the technique of X-ray crystallography.
- Most proteins can be categorized on the basis of their overall conformation as being either fibrous proteins, which have an elongated shape, or globular proteins, which have a compact shape.

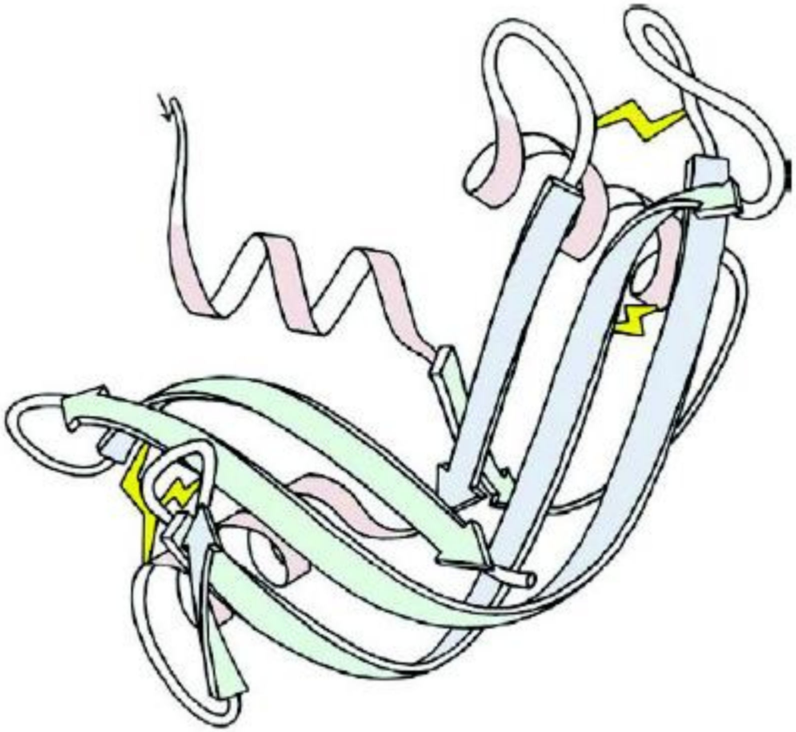


Figure 2.32 **A ribbon model of ribonuclease.** The regions of α helix are depicted as spirals and β strands as flattened ribbons with the arrows indicating the N-terminal → C-terminal direction of the polypeptide. Those segments of the chain that do not adopt a regular secondary structure (i.e., an α helix or β strand) consist largely of loops and turns. Disulfide bonds are shown in yellow. (HAND DRAWN BY JANE S. RICHARDSON.)

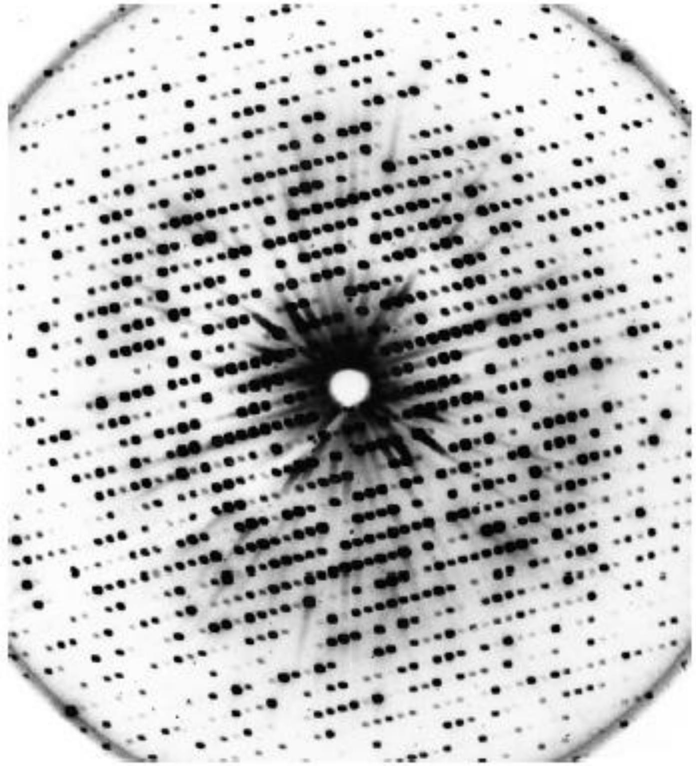


Figure 2.33 **An X-ray diffraction pattern of myoglobin.** The pattern of spots is produced as a beam of X-rays is diffracted by the atoms in the protein crystal, causing the X-rays to strike the film at specific sites. Information derived from the position and intensity (darkness) of the spots can be used to calculate the positions of the atoms in the protein that diffracted the beam, leading to complex structures such as that shown in Figure 2.34. (COURTESY OF JOHN C. KENDREW.)

- Most eukaryotic proteins are composed of two or more spatially distinct modules, or domains, that fold independent of one another. The different domains of a polypeptide often represent parts that function in a semi-independent manner.

- Whereas many proteins composed of only one polypeptide chain, most are made up of more than one chain, or subunit.

- The subunits may be linked by covalent disulfide bonds, but most often they are held together by noncovalent bonds as occur typically between hydrophobic “patches” on the complementary surfaces of neighboring polypeptides.

- Proteins composed of subunits are said to have quaternary structure.

- The unfolding or disorganization of a protein is termed denaturation, and it can be brought about by a variety of agents, including detergents, organic solvents, radiation, heat, and compounds such as urea and guanidine chloride, all of which interfere with the various interactions that stabilize a protein’s tertiary structure.

- Protein misfolding can have deadly consequences: In April 1996 a paper was published in the medical journal Lancet that generated widespread alarm in the populations of Europe.

- The paper described a study of 10 persons afflicted with Creutzfeld-Jakob disease (CJD), a rare, fatal disorder that attacks the brain, causing a loss of motor coordination and dementia.

- The cases described in the 1996 Lancet paper had been acquired the disease from contaminated beef that the infected individuals had eaten years earlier.

- The contaminated beef was derived from cattle raised in England that had contracted a neurodegenerative disease that caused the animals to lose motor coordination and develop demented behavior. The disease became commonly known as “mad cow disease.”

- How can the same disease be both inherited and infectious?

- The answer to this question has emerged gradually over the past several decades, beginning with observations by D. Carleton Gajdusek in the 1960s on a strange malady that once afflicted the native population of Papua, New Guinea.

- Gajdusek showed that these islanders were contracting a fatal neurodegenerative disease—which they called “kuru”—during a funeral ritual in which they ate the brain tissue of a recently deceased relative.

- Autopsies of the brains of patients who had died of kuru showed a distinct pathology, referred to as spongiform encephalopathy, in which certain brain regions were riddled with microscopic holes (vacuolations), causing the tissue to resemble a sponge.

- In 1982, Stanley Prusiner of the University of California, San Francisco, published a paper suggesting that, unlike viruses, the infectious agent responsible for CJD lacked nucleic acid and instead was composed solely of protein. He called the protein a prion.

- The prion protein was shown to be encoded by a gene (called PRNP) within the cell's own chromosomes.

- The gene is expressed within normal brain tissue and encodes a protein designated PrP^C (standing for prion protein cellular) that resides at the surface of nerve cells.

- The precise function of PrPC remains a mystery. A modified version of the protein (designated PrPSc, standing for prion protein scrapie) is present in the brains of humans with CJD.

- Unlike the normal PrPC, the modified version of the protein accumulates within nerve cells, forming aggregates that kill the cells.

- In their purified states, PrP^{C} and PrP^{Sc} have very different physical properties.

- PrP^{C} remains as a monomeric molecule that is soluble in salt solutions and is readily destroyed by protein-digesting enzymes.

- In contrast, PrP^{Sc} molecules interact with one another to form insoluble fibrils that are resistant to enzymatic digestion.

- Based on these differences, one might expect these two forms of the PrP protein to be composed of distinctly different sequences of amino acids, but this is not the case.

- The two forms can have identical amino acid sequences, but they differ in the way the polypeptide chain folds to form the three-dimensional protein molecule.

- Apparently, the appearance of the abnormal protein in the body starts a chain reaction in which normal protein molecules in the cells are gradually converted to the misshapen prion form.

- CJD is a rare disease caused by a protein with unique infective properties.

- Alzheimer’s disease (AD), on the other hand, is a common disorder that strikes as many as 10 percent of individuals who are at least 65 years of age and perhaps 40 percent of individuals who are 80 years or older.

- Persons with AD exhibit memory loss, confusion, and a loss of reasoning ability.

- CJD and AD share a number of important features. Both are fatal neurodegenerative diseases that can occur in either an inherited or sporadic form.

- Like CJD, the brain of a person with Alzheimer’s disease contains fibrillar deposits of an insoluble material referred to as amyloid.

- In both diseases, the fibrillar deposits result from the self-association of a polypeptide composed predominantly of β-sheet.

- Nucleic acids are macromolecules constructed out of long chains (strands) of monomers called nucleotides.

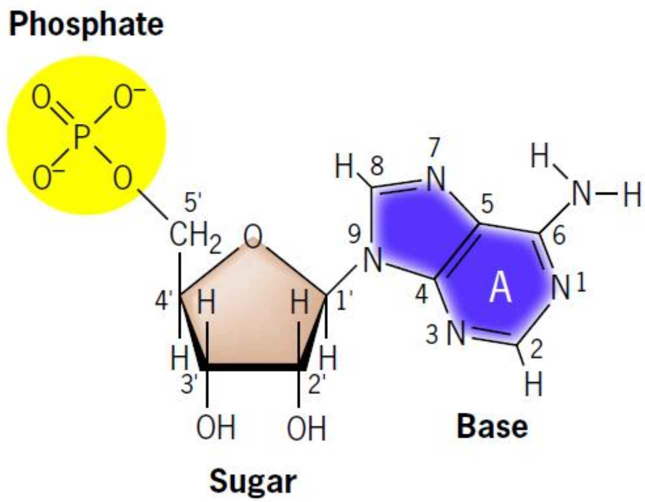
- Nucleic acids function primarily in the storage and transmission of genetic information, but they may also have structural or catalytic roles.

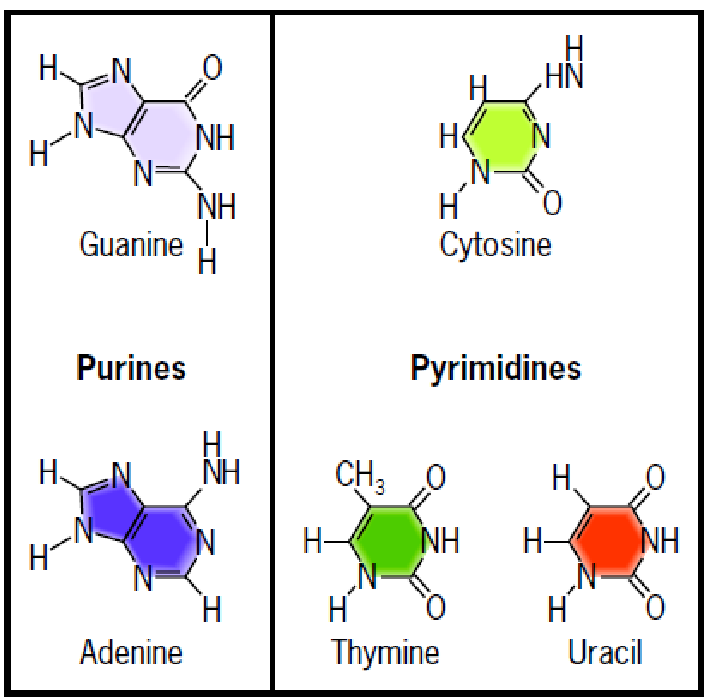
- There are two types of nucleic acids found in living organisms, deoxyribonucleic acid (DNA) and ribonucleic acid (RNA).

- DNA serves as the genetic material of all cellular organisms, though RNA carries out that role for many viruses.

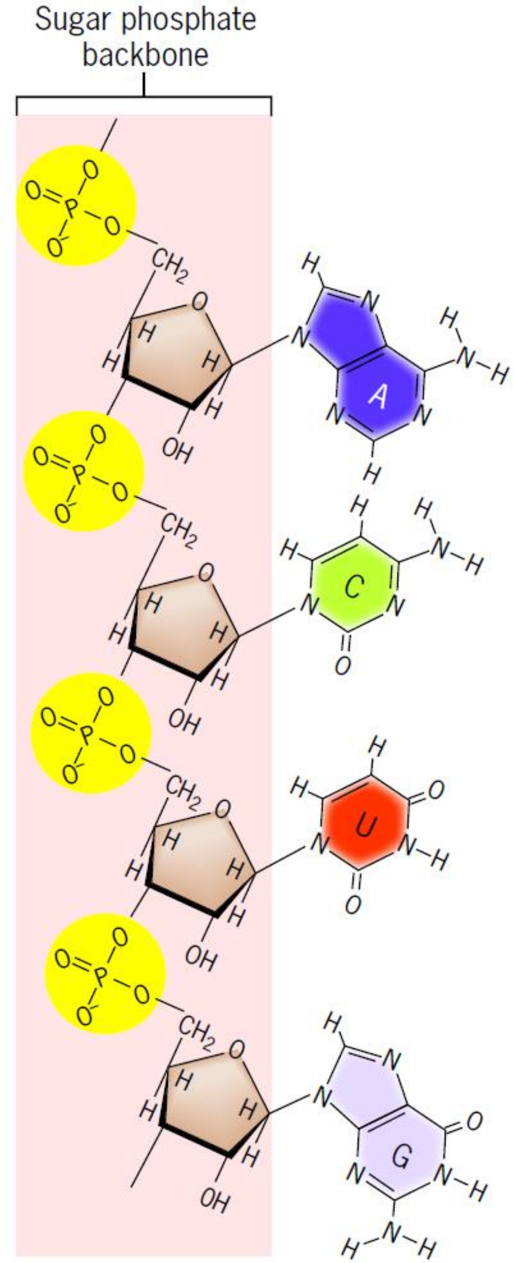
- In cells, information stored in DNA is used to govern cellular activities through the formation of RNA messages.

- Each nucleotide in a strand of RNA consists of three parts: (1) a five-carbon sugar, ribose; (2) a nitrogenous base; and (3) a phosphate group.

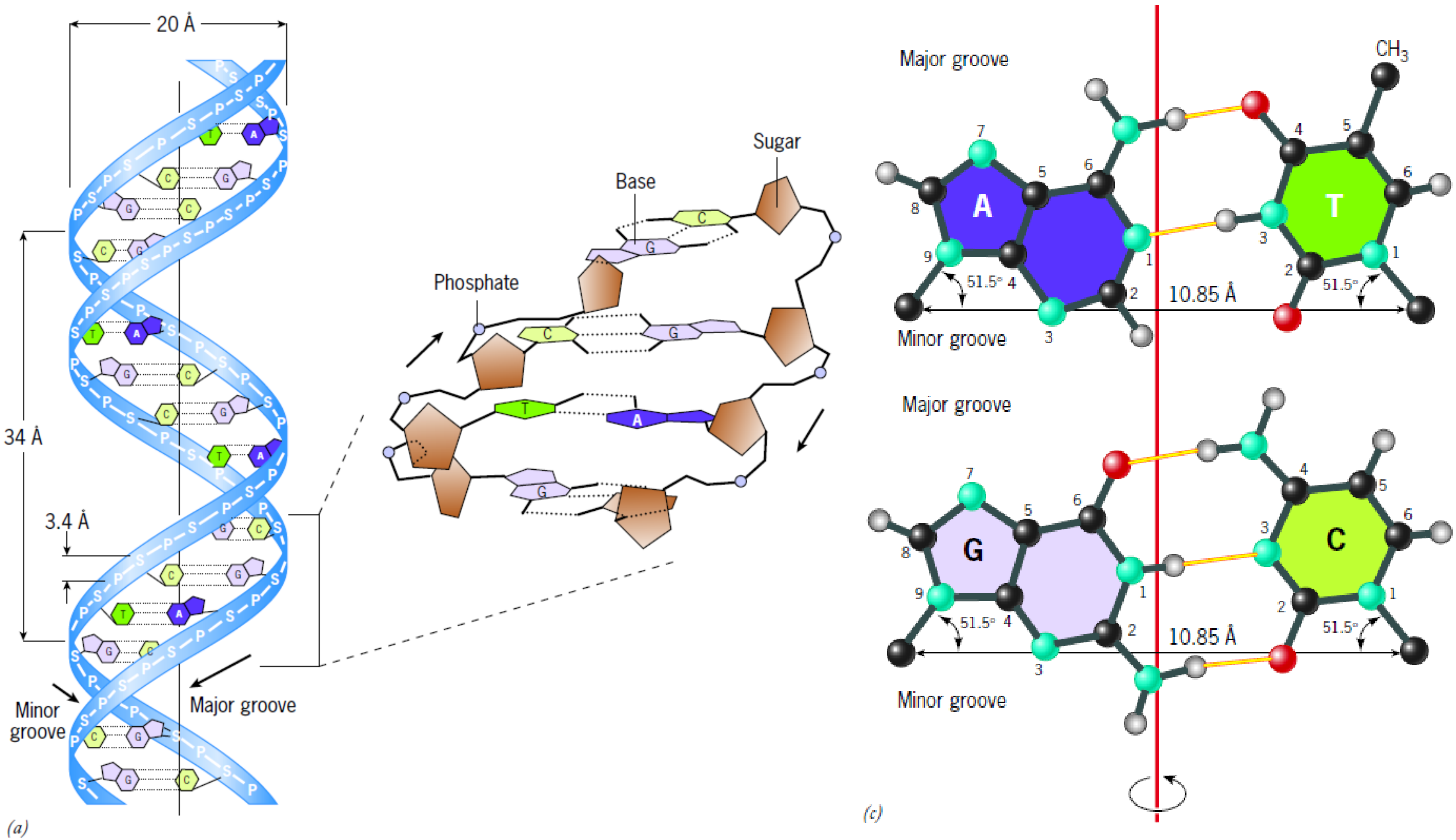

Phosphate
Sugar
Base
A
OH
OH

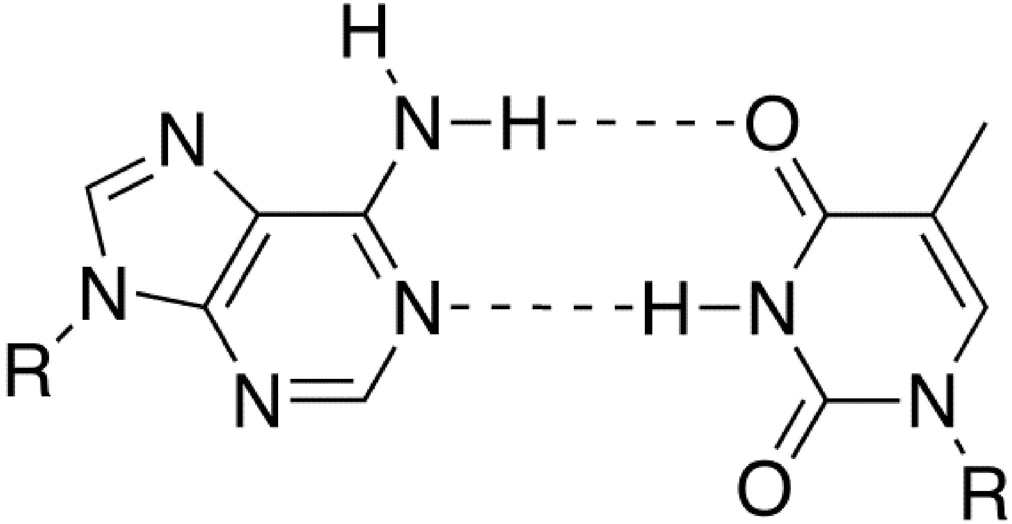

Guanine
Purines
Adenine
Cytosine
Pyrimidines
Thymine
Uracil

(a)

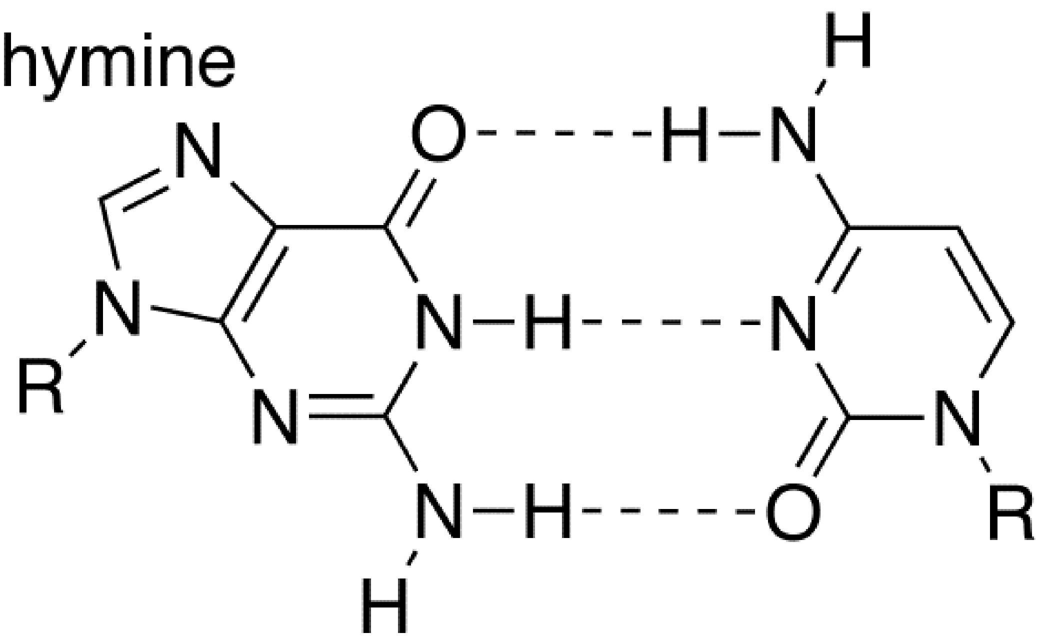

Sugar phosphate backbone
A
C
U
G

(b)


20 Å
34 Å
3.4 Å
Minor groove
Major groove
(a)
Phosphate
Base
Sugar
Major groove
Minor groove
CH3
A
T
G
C
51.5°
10.85 Å
(c)



Adenine Thymine



Guanine Cytosine

- The sugar and nitrogenous base together form a nucleoside, so that the nucleotides of an RNA strand are also known as ribonucleoside monophosphates.

- A strand of RNA (or DNA) contains four different types of nucleotides distinguished by their nitrogenous base.

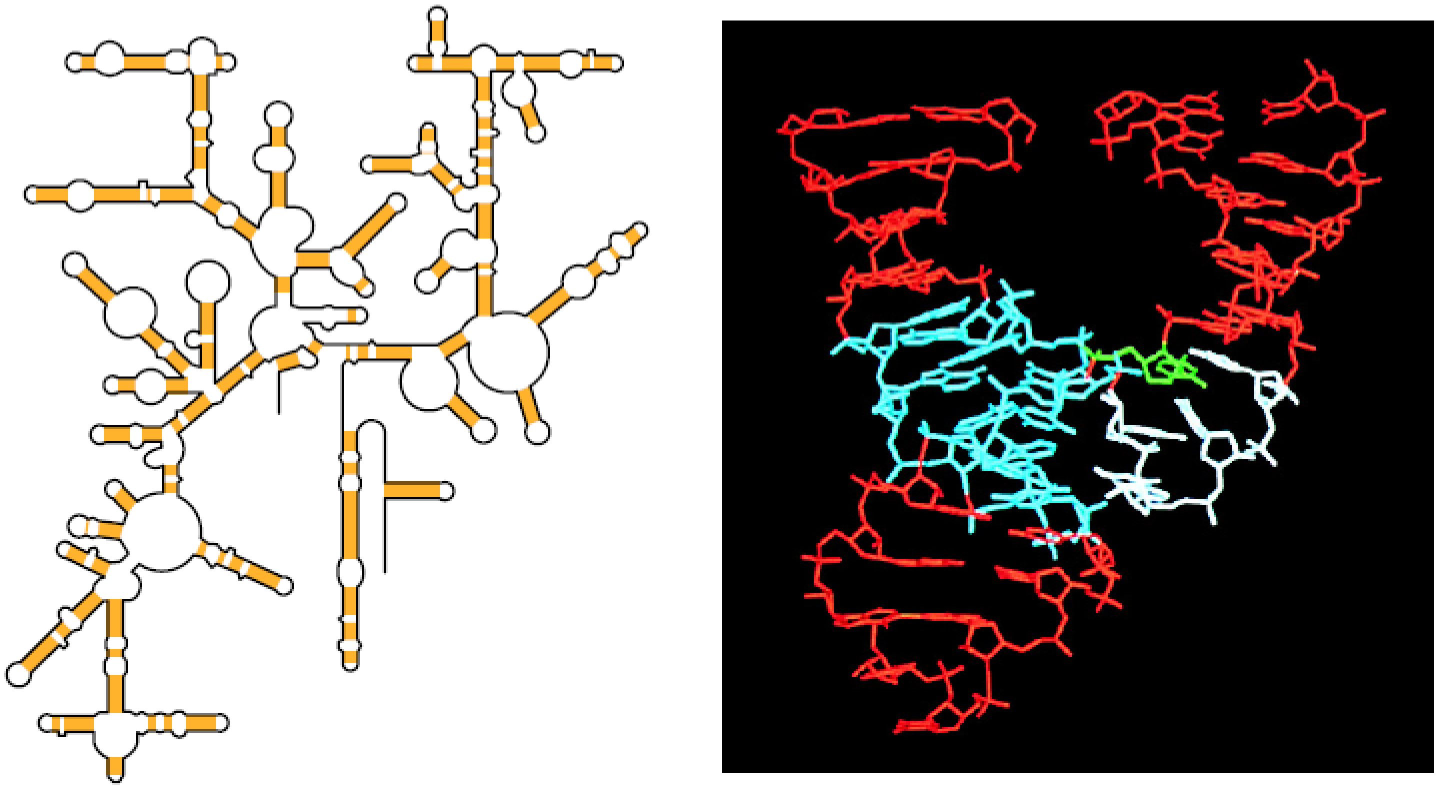
- Two types of bases occur in nucleic acids: pyrimidines and purines.

- Pyrimidines are smaller molecules, consisting of a single ring; purines are larger, consisting of two rings.

- RNAs contain two different purines, adenine and guanine, and two different pyrimidines, cytosine and uracil.

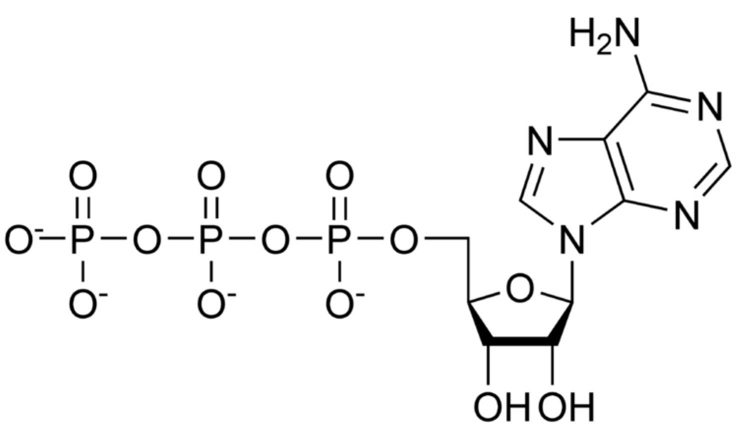
- In DNA, uracil is replaced by thymine, a pyrimidine with an extra methyl group attached to the ring .

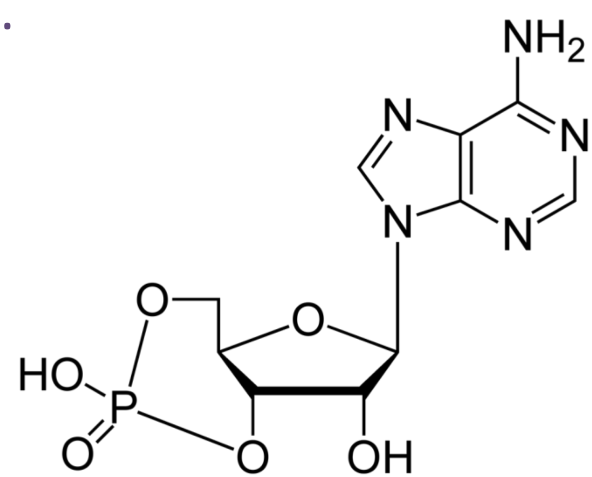
❖ Although RNAs consist of a continuous single strand, they often fold back on themselves to produce molecules having extensive double-stranded segments and complex three-dimensional structures.



(a) (b)

- ❖ Nucleotides are not only important as building blocks of nucleic acids, they also have important functions in their own right.
- ❖ Most of the energy being put to use at any given moment in any living organism is derived from the nucleotide adenosine triphosphate (ATP).
- ❖ Guanosine triphosphate (GTP) is another nucleotide of enormous importance in cellular activities.
- ❖ GTP binds to a variety of proteins (called G proteins) and acts as a switch to turn on their activities.
- ❖ cAMP is important for signalling pathways.





Synopsis

- Covalent bonds hold atoms together to form molecules. Covalent bonds are stable partnerships formed when atoms share their outershell electrons, each participant gaining a filled shell.

- If electrons in a bond are shared unequally by the component atoms, the atom with the greater attraction for electrons (the more electronegative atom) bears a partial negative charge, whereas the other atom bears a partial positive charge.

- Molecules that lack polarized bonds have a nonpolar, or hydrophobic, character, which makes them insoluble in water.

- Molecules that have polarized bonds have a polar, or hydrophilic, character, which makes them water soluble.

- Polar molecules of biological importance contain atoms other than just carbon and hydrogen, usually O, N, S, or P.

Synopsis

- Noncovalent bonds are formed by weak attractive forces between positively and negatively charged regions within the same molecule or between two nearby molecules.

- Noncovalent bonds play a key role in maintaining the structure of biological molecules and mediating their dynamic activities.

- Noncovalent bonds include ionic bonds, hydrogen bonds, and van der Waals forces.

- Ionic bonds form between fully charged positive and negative groups; hydrogen bonds form between a covalently bonded hydrogen atom (which bears a partial positive charge) and a covalently bonded nitrogen or oxygen atom (which bears a partial negative charge); van der Waals forces form between two atoms exhibiting a transient charge due to a momentary asymmetry in the distribution of electrons around the atoms.

Synopsis

- Water has unique properties on which life depends.

- The covalent bonds that make up a water molecule are highly polarized. As a result, water is an excellent solvent capable of forming hydrogen bonds with virtually all polar molecules.

- Water is also a major determinant of the structure of biological molecules and the types of interactions in which they can engage.

- Most biological processes are acutely sensitive to pH because changes in hydrogen ion concentration alter the ionic state of biological molecules.

- Cells are protected from pH fluctuations by buffers—compounds that react with hydrogen or hydroxyl ions.

Synopsis

- Carbon atoms play a pivotal role in the formation of biological molecules.

- Each carbon atom is able to bond with up to four other atoms, including other carbon atoms.

- This property allows the formation of large molecules whose backbone consists of a chain of carbon atoms.

- Molecules consisting solely of hydrogen and carbon are called hydrocarbons.

- Most of the molecules of biological importance contain functional groups that include one or more electronegative atoms, making the molecule more polar, more water soluble, and more reactive.

Synopsis

- Biological molecules are members of four distinct types: carbohydrates, lipids, proteins, and nucleic acids.

- Carbohydrates include simple sugars and larger molecules (polysaccharides) constructed of sugar monomers.

- Carbohydrates function primarily as a storehouse of chemical energy and as durable building materials for biological construction.

- Simple biological sugars consist of a backbone of three to seven carbon atoms, with each carbon linked to a hydroxyl group except one, which bears a carbonyl.

- Sugars are linked to one another by glycosidic bonds to form disaccharides, oligosaccharides, and polysaccharides.

- In animals, sugar is stored primarily as the branched polysaccharide glycogen, which provides a readily available energy source. In plants, glucose reserves are stored as starch, which is a mixture of unbranched amylose and branched amylopectin.

Synopsis

- Lipids are a diverse array of hydrophobic molecules having widely divergent structures and functions.

- Fats consist of a glycerol molecule esterified to three fatty acids.

- Fatty acids differ in chain length and the number and position of double bonds (sites of unsaturation).

- Fats are very rich in chemical energy; a gram of fat contains over twice the energy content of a gram of carbohydrate.

- Steroids are a group of lipids containing a characteristic four-ringed hydrocarbon skeleton. Steroids include cholesterol as well as numerous hormones that are synthesized from cholesterol.

- Phospholipids are phosphate-containing lipid molecules that contain both a hydrophobic end and a hydrophilic end and play a pivotal role in the structure and function of cell membranes.

Synopsis

- Proteins are macromolecules of diverse function consisting of amino acids linked by peptide bonds into polypeptide chains.

- Included among the diverse array of proteins are enzymes, structural materials, membrane receptors, gene regulatory factors, hormones, transport agents, and antibodies.

- The order in which the 20 different amino acids are incorporated into a protein is encoded in the sequence of nucleotides in DNA.

- The structure of a protein can be described at four levels of increasing complexity.

- Primary structure is described by the amino acid sequence of a polypeptide; secondary structure by the three-dimensional structure (conformation) of sections of the polypeptide backbone; tertiary structure by the conformation of the entire polypeptide; and quaternary structure by the arrangement of the subunits if the protein consists of more than one polypeptide chain.

Synopsis

- Nucleic acids are primarily informational molecules that consist of strands of nucleotide monomers.

- Each nucleotide in a strand consists of a sugar, phosphate, and nitrogenous base.

- The nucleotides are linked by bonds between the 3 hydroxyl group of the sugar of one nucleotide and the 5 phosphate group of the adjoining nucleotide.

- Both RNA and DNA are assembled from four different nucleotides; nucleotides are distinguished by their bases, which can be a pyrimidine (cytosine or uracil/thymine) or a purine (adenine or guanine).

- DNA is a double-stranded nucleic acid, and RNA is generally single stranded, though the single strand is often folded back on itself to form double-stranded sections.