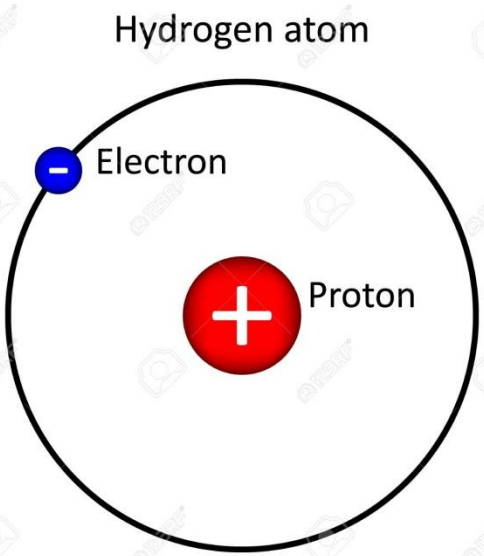
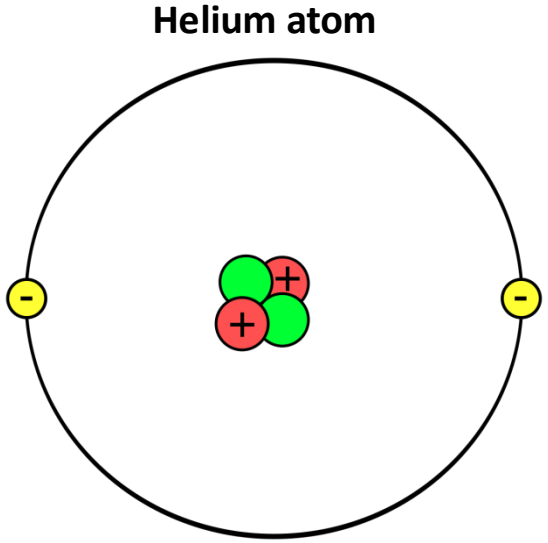
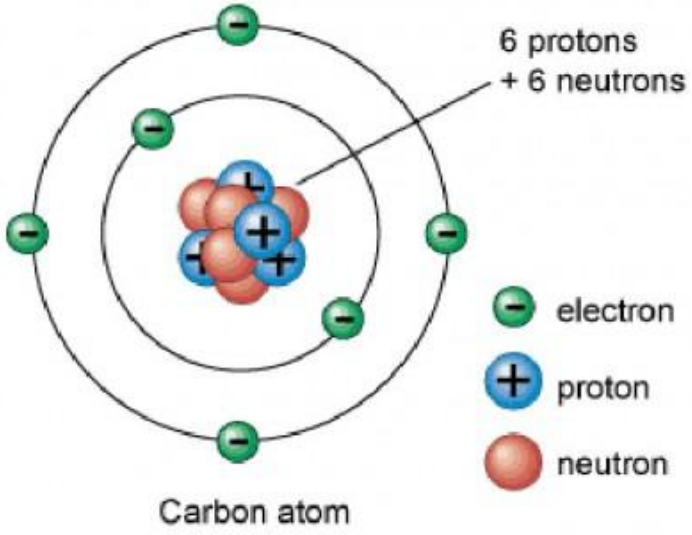
Molecules of life

Atoms

- Physical matter consists of atoms that can associate with each other and form molecules
- Every atom is composed of a nucleus and one or more electrons bound to the nucleus. Nucleus has positive electrostatic charge, electrons have negative electrostatic charge.
- Interactions between nucleus and electrons are governed by laws of quantum mechanics

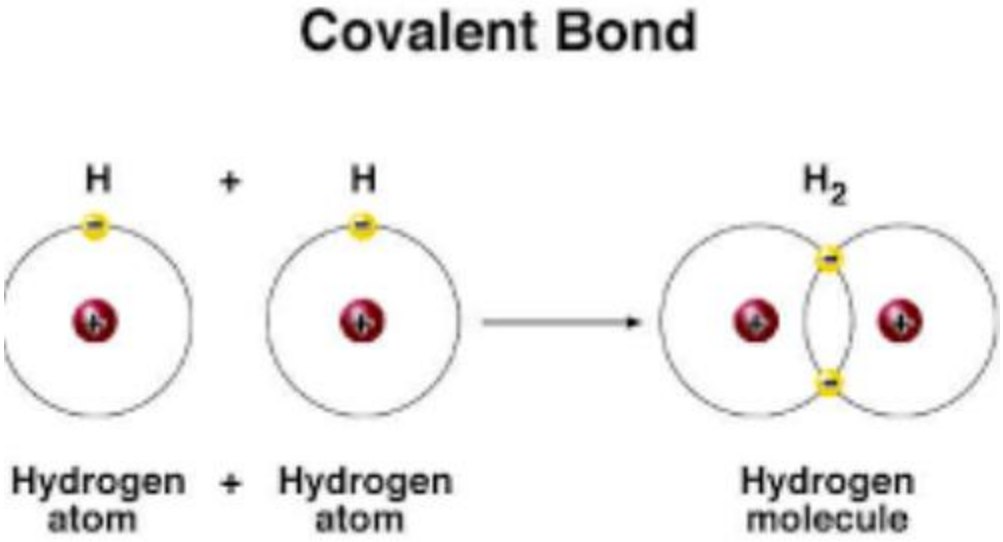

Hydrogen atom
Electron
Proton


Helium atom


6 protons
+ 6 neutrons
electron
proton
neutron
Carbon atom

Covalent bonds

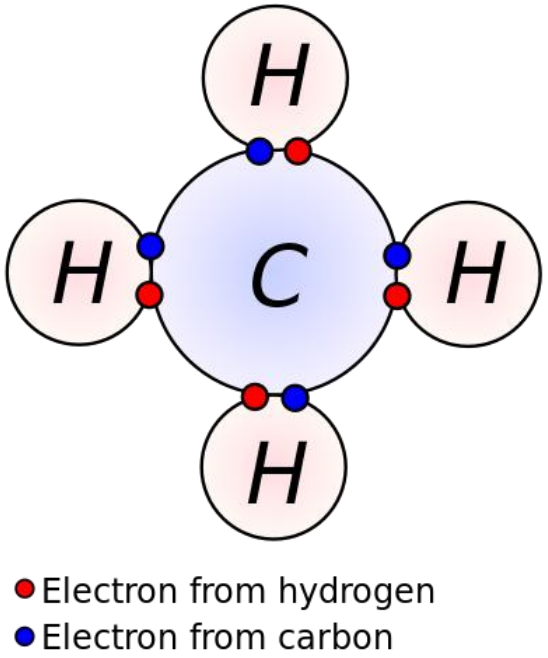
- Sometimes when atoms come close together they can share electrons with each other. This creates a connection between atoms called a **covalent bond** .



Molecules

- A group of two or more atoms connected by covalent bonds constitute a **molecule**.

Example :
a molecule of methane



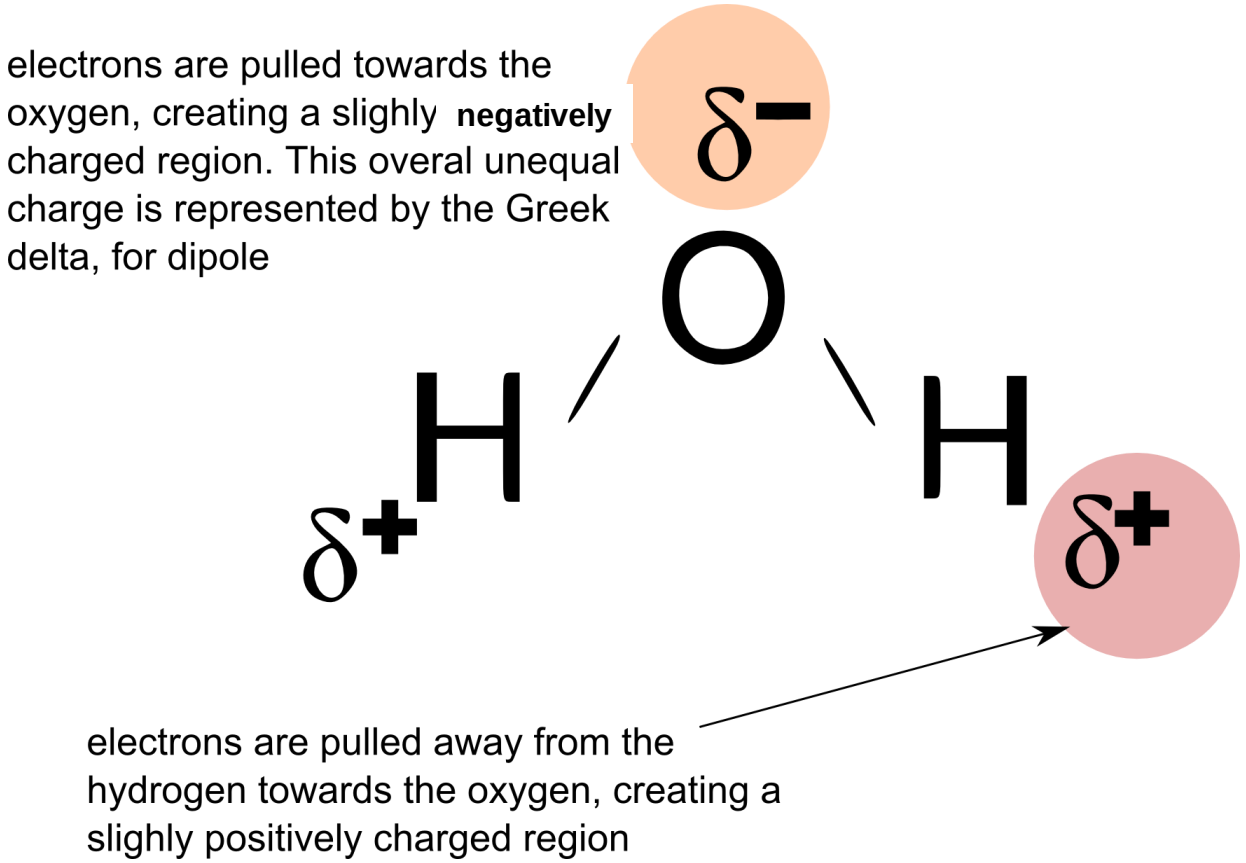
Non-covalent bonds

- A **non-covalent bond** is an interaction between atoms that does not involve the sharing of electron pairs. Non-covalent interactions can occur within a single molecule or between different molecules. Many interactions of biological molecules have non-covalent character.

Water

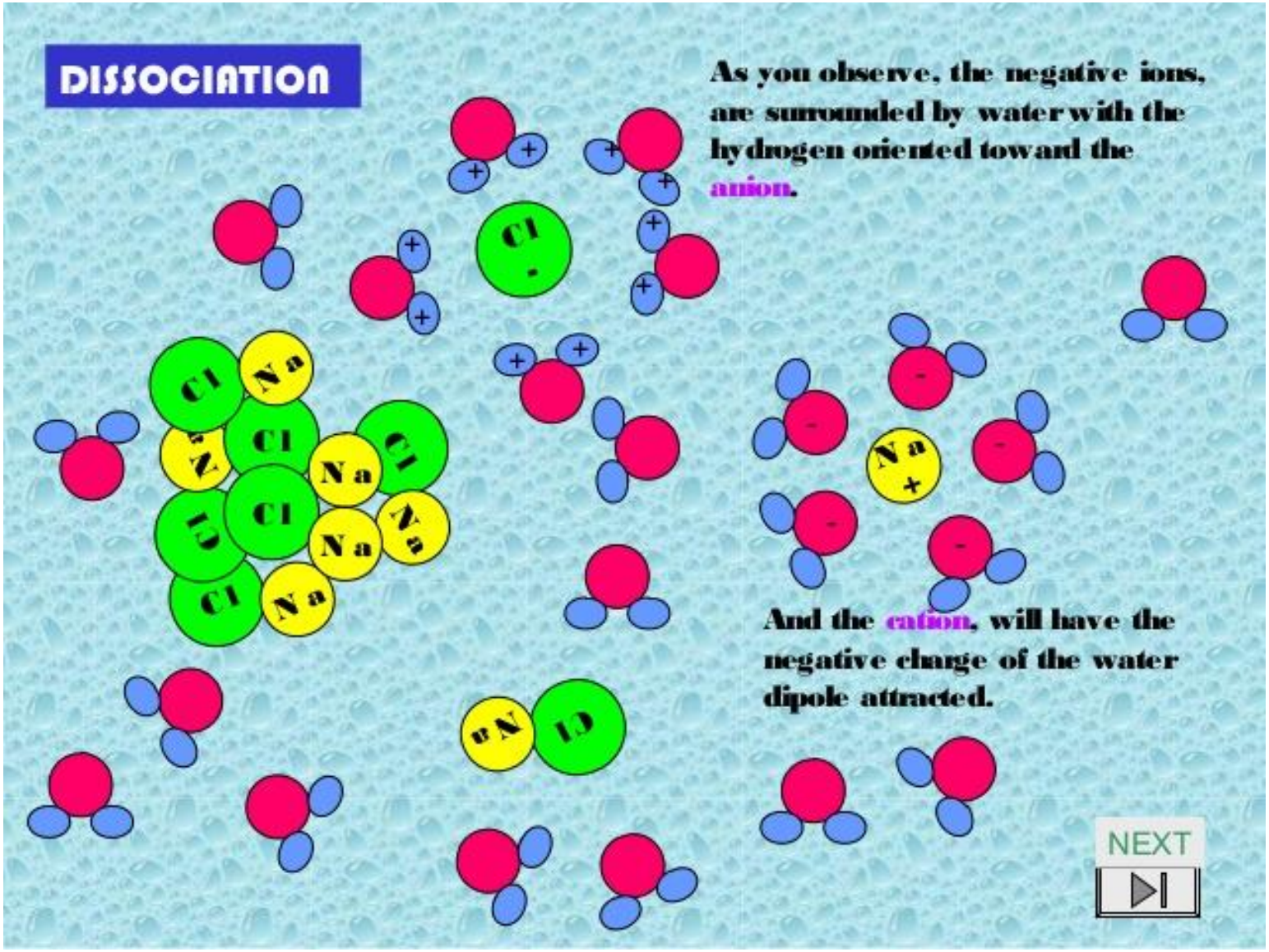
- Water is of major importance to all living things; in some organisms, up to 90% of their body weight comes from water.
- Water is an active matrix of life for cell and molecular biology
- Up to 60% of the human adult body is water.

Water molecule

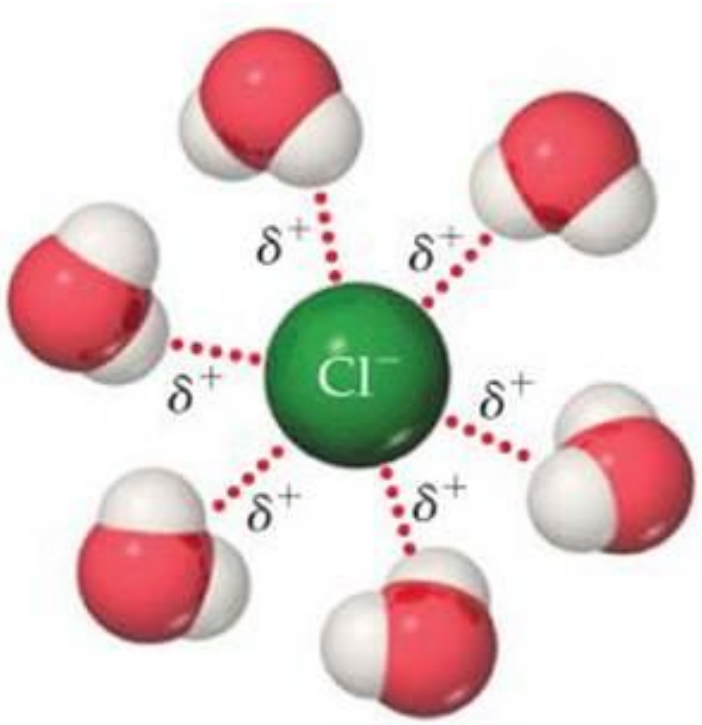


Electrolytic Dissociation

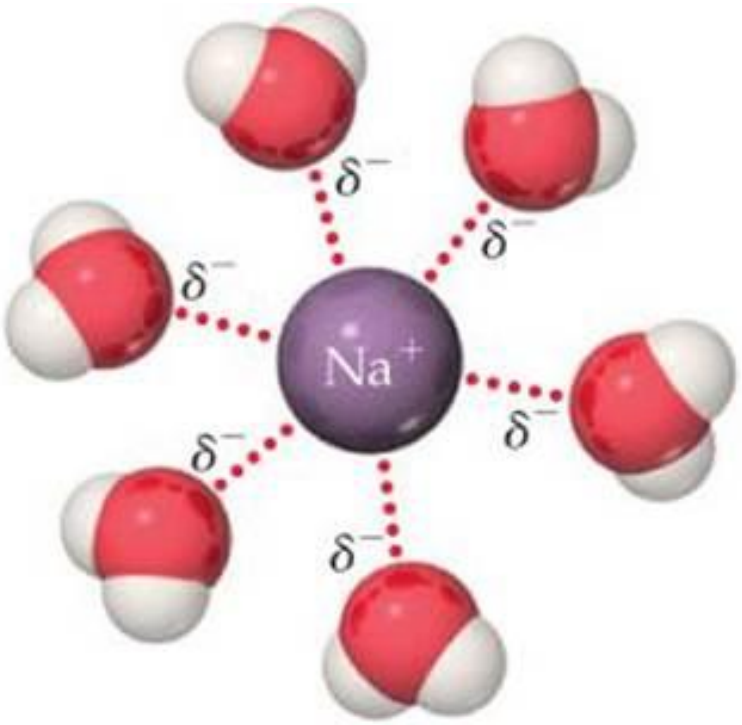
- Many substances will undergo an event called *dissociation* when dissolved in water.
- In electrolytic, or ionic, dissociation, the addition of a water causes molecules or crystals of the substance to break up into *ions* (electrically charged particles).
- The salt can be recovered by evaporation of the solvent.
- Positively charged ions are called *cations*, negatively charged – *anions*.


DISSOCIATION
As you observe, the negative ions, are surrounded by water with the hydrogen oriented toward the anion.
Cl -
Na +
And the cation, will have the negative charge of the water dipole attracted.
NEXT

Ions in water



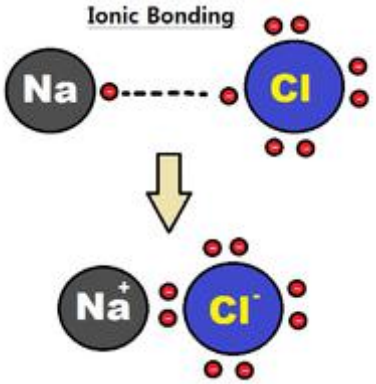
Positive ends of polar molecules are oriented toward negatively charged anion



Negative ends of polar molecules are oriented toward positively charged cation

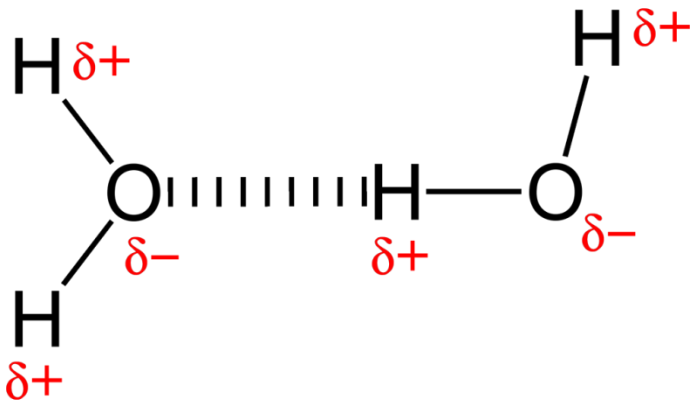
Non-covalent bonds

Ionic bonding - the electrostatic attraction between oppositely charged ions.

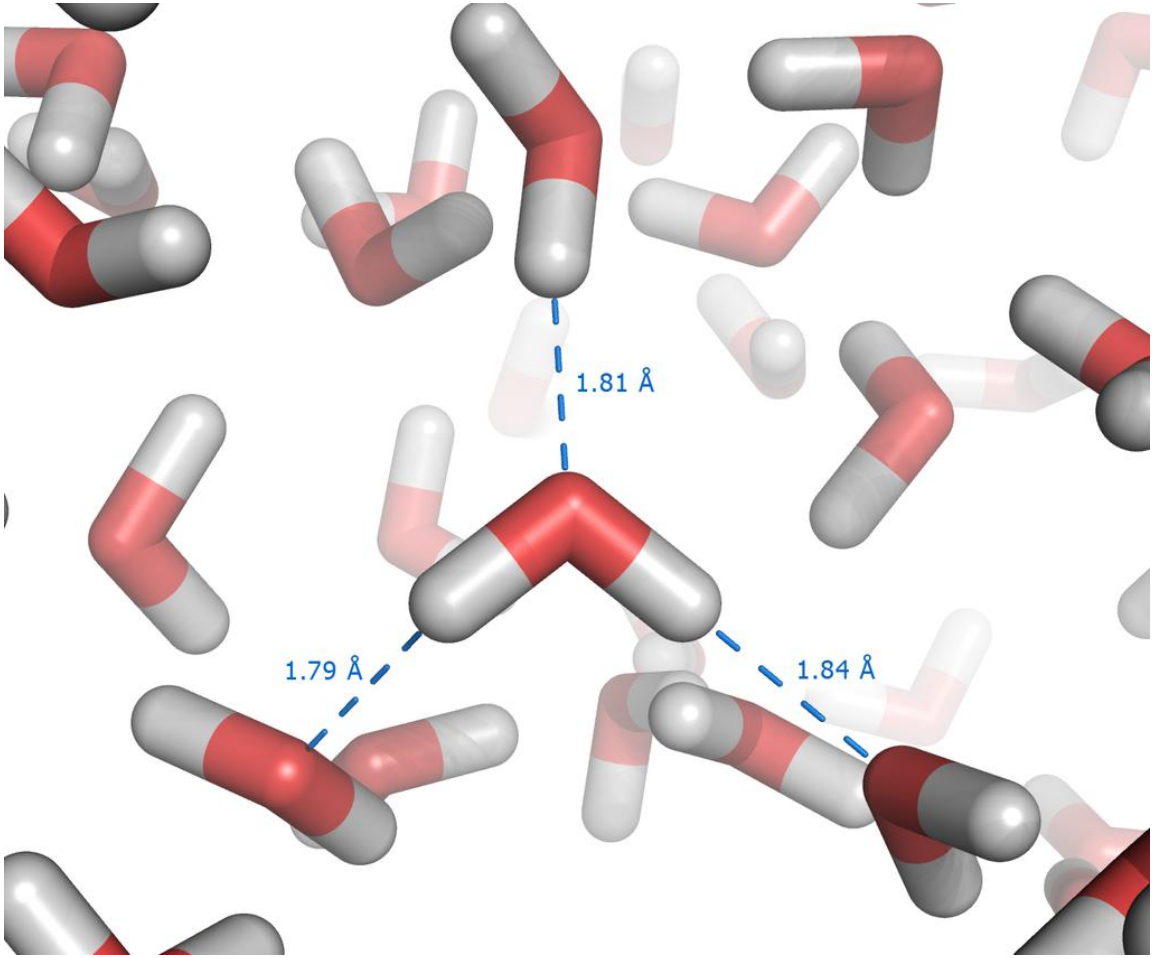


Non-covalent bonds

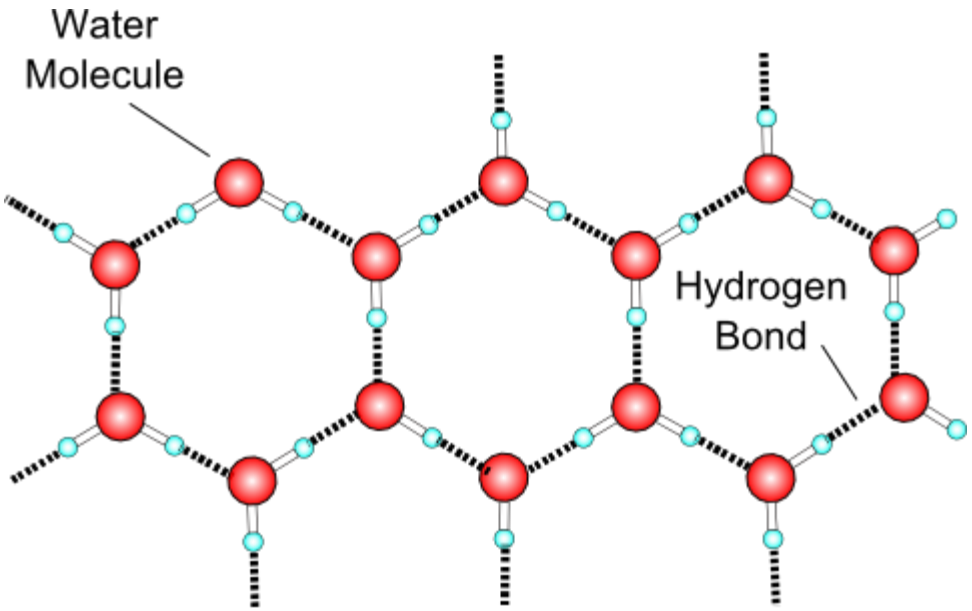
Hydrogen bond - electrostatic attraction between two polar groups. It involves hydrogen (H) atom covalently bound to a highly electronegative atom such as nitrogen (N), oxygen (O), or fluorine (F) .



Dynamic hydrogen bonds between molecules of liquid water



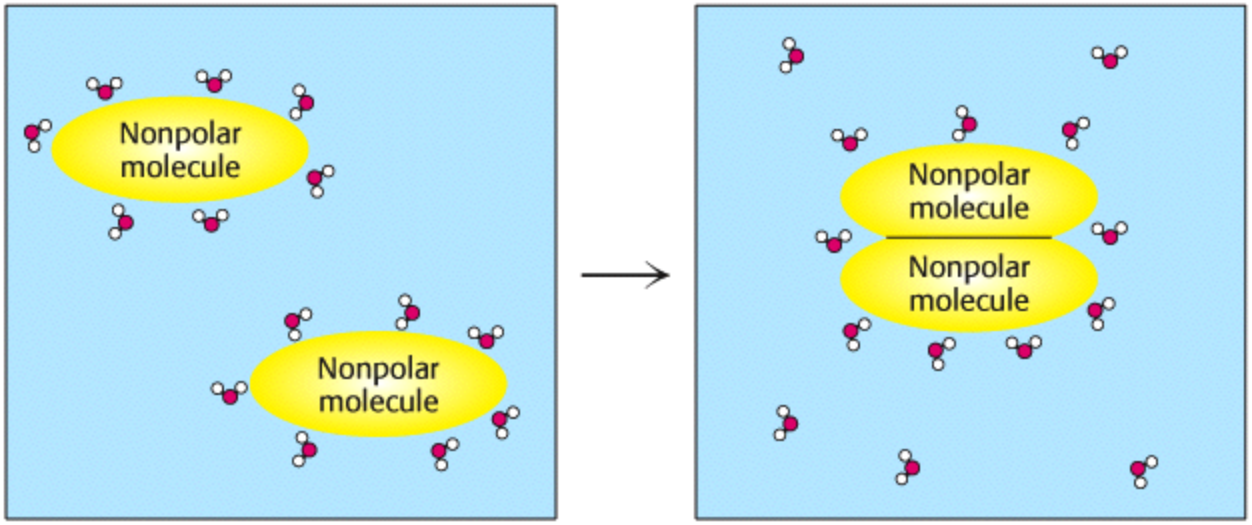
Ice



When temperature of water is decreased
more water molecules stick together with hydrogen bonds.
At 0^{o}C they form a regular pattern, as shown here.

Hydrophobic effect

Non-polar molecules aggregate in aqueous solutions in order to separate from water.



Hydrophobic Effect

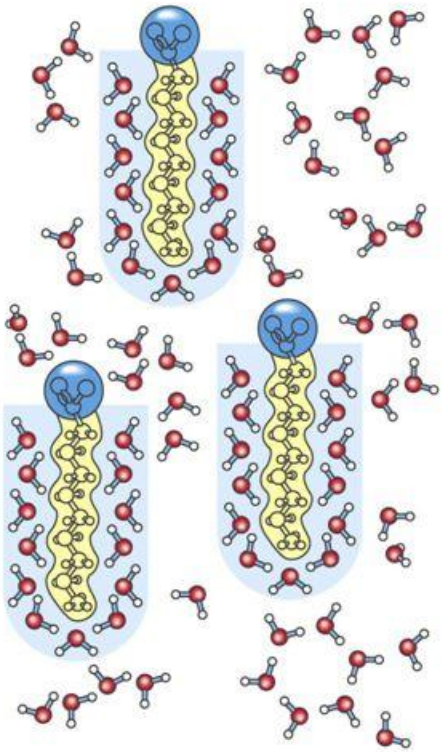


Figure 2-7b part 1
Lehninger Principles of Biochemistry, Fifth Edition

- Lipid molecules disperse in the solution; nonpolar tail of each lipid molecule is surrounded by ordered water molecules
- Lipid aggregates – Water released, surface area reduced

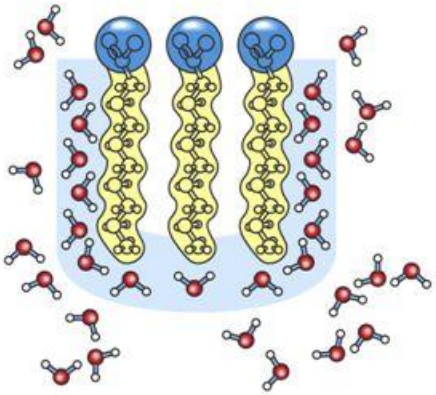
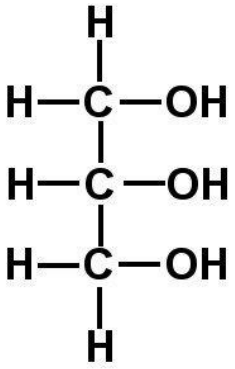


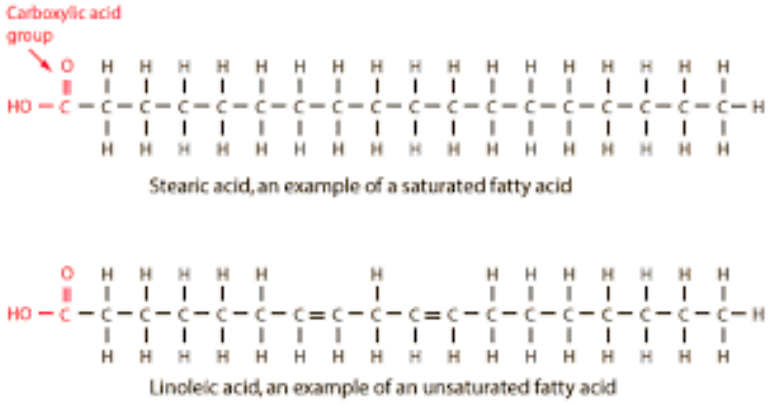
Figure 2-7b part 2
Lehninger Principles of Biochemistry, Fifth Edition

Example of a hydrophobic molecule – triglyceride (fat)



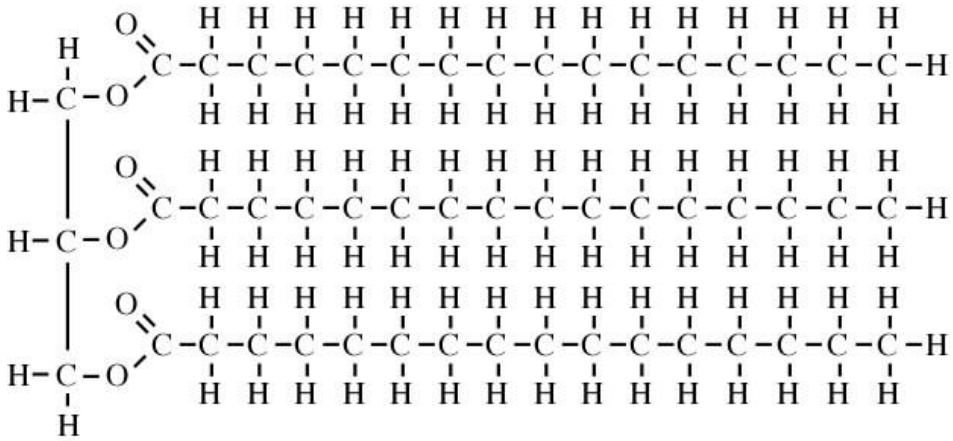
glycerol

+



Fatty acids

=



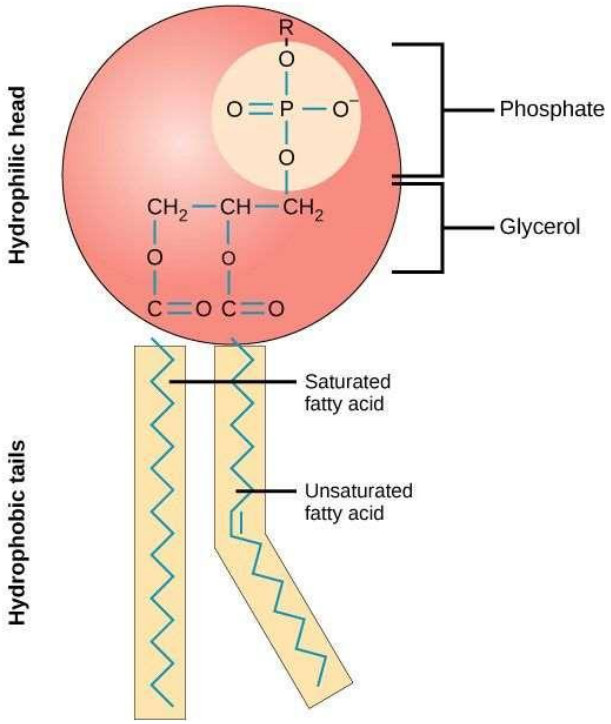
=

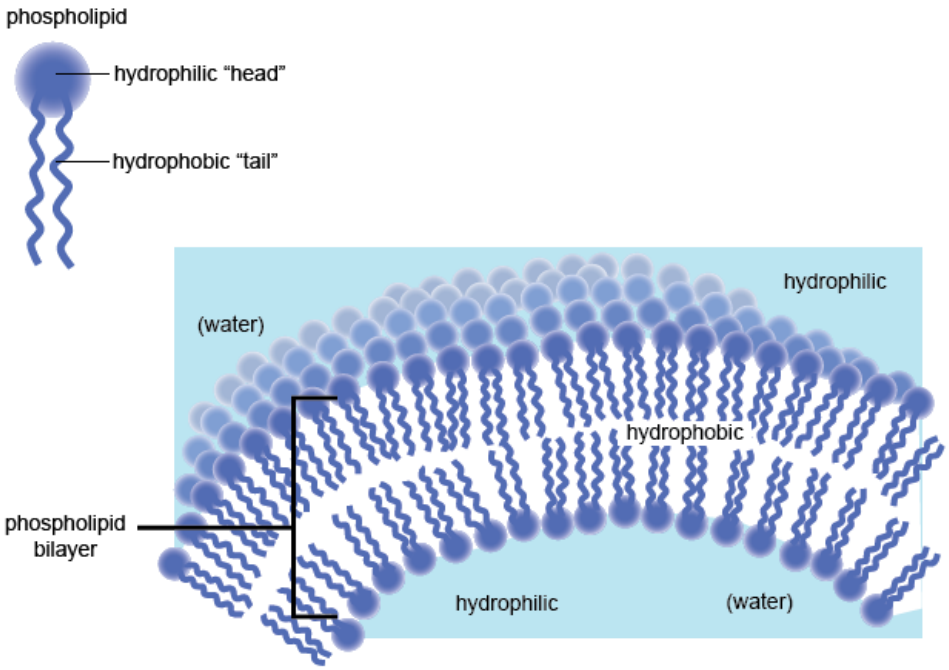
-triglyceride

Cell membrane

- A cell is surrounded by the cell membrane that separates its interior from the outside environment (the extracellular space).
- The cell membrane is the barrier that keeps ions, proteins and other molecules where they are needed and prevents them from diffusing into areas where they should not be.
- Eukariotic cells have internal compartments separated from the rest of the cell by their own membranes

Cell membrane consists of lipid bilayer





- The cell membrane is selectively permeable and able to regulate what enters and exits the cell, thus facilitating the transport of materials needed for survival. The movement of substances across the membrane can be either "passive", occurring without the input of cellular energy, or "active", requiring the cell to expend energy in transporting it. The cell membrane thus works as a selective filter that allows only certain things to come inside or go outside the cell.

PROTEINS

Functions of proteins

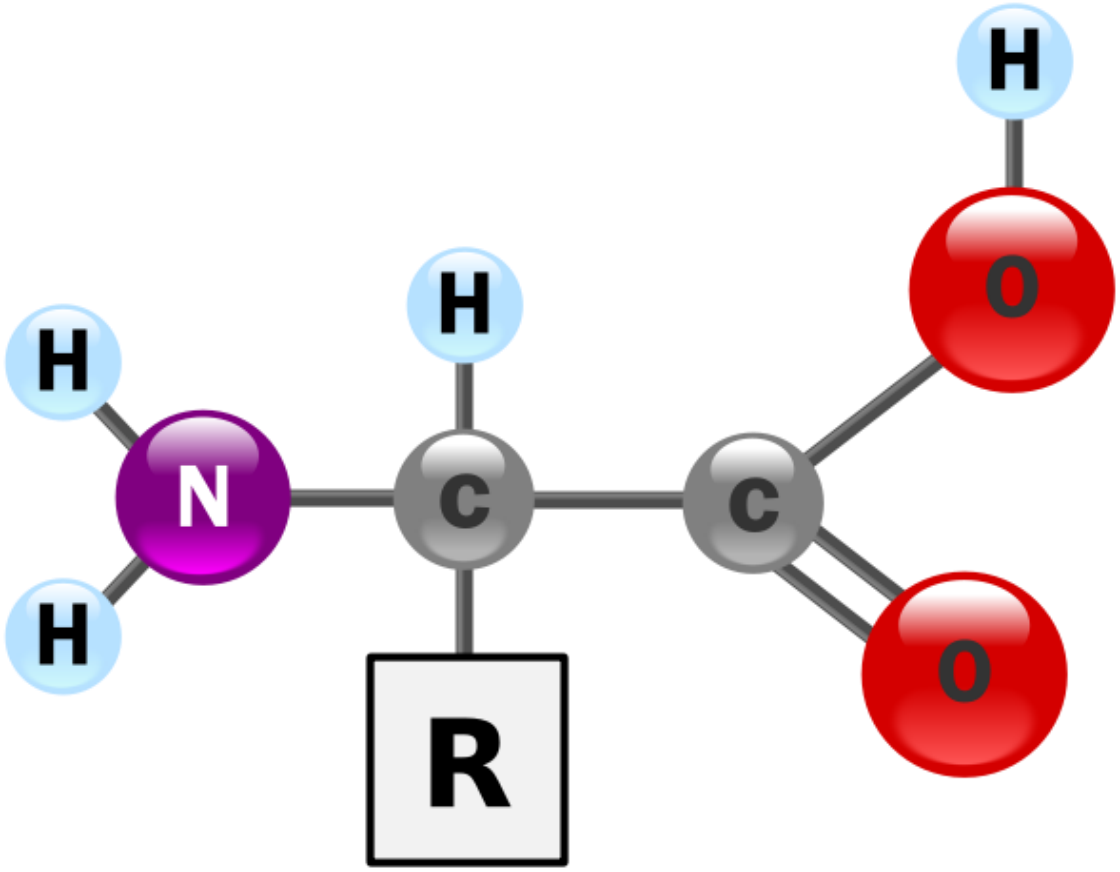
- Proteins are large, complex molecules that play many critical roles in the cell:

1. Enzymes carry out almost all of the thousands of chemical reactions that take place in cells. They also assist with the formation of new molecules by reading the genetic information stored in DNA.
2. Structural component proteins provide structure and support for cells.
3. Transport/storage proteins bind and carry atoms and small molecules within cells and throughout the body

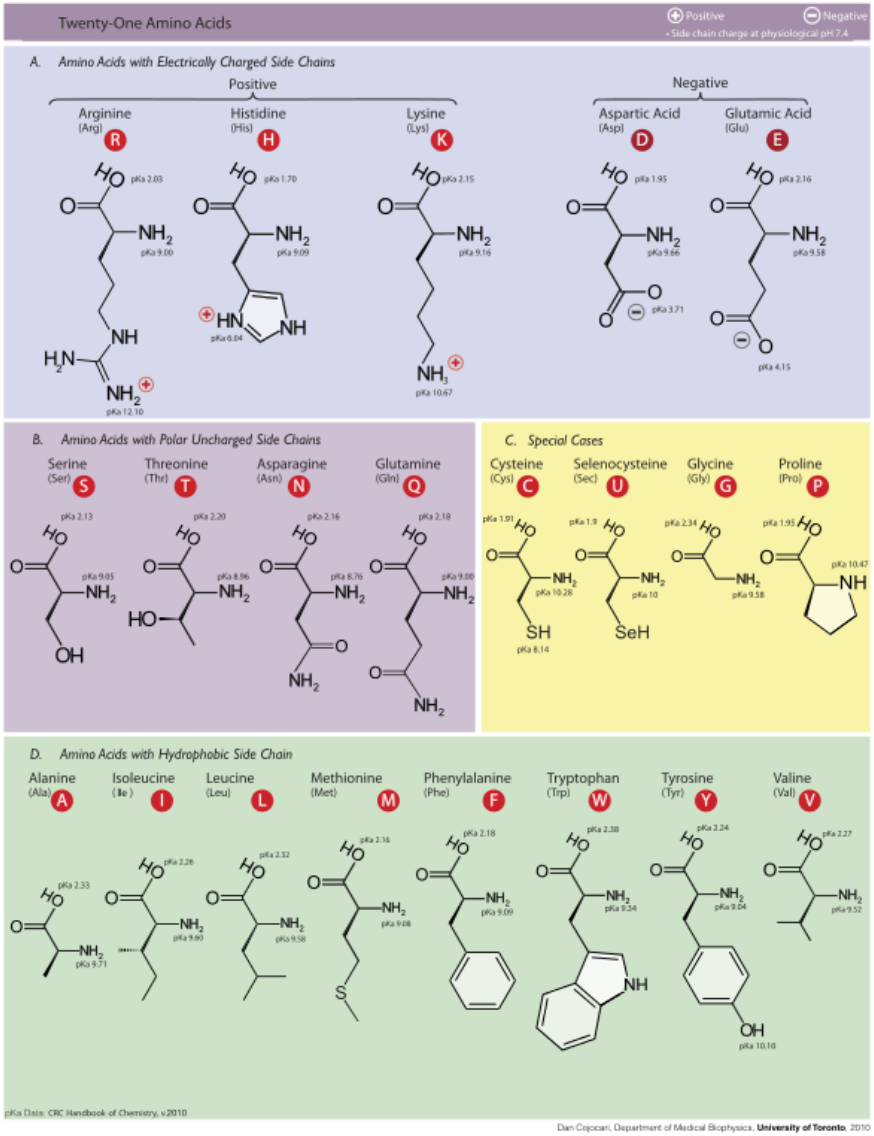
Proteins are composed of amino acids

- Proteins are made up of hundreds or thousands of smaller units called amino acids, which are attached to one another in long chains.
- Amino acids are organic compounds that contain amine (–NH2) and carboxyl (–COOH) functional groups, along with a side chain (R group) specific to each amino acid.
- There are 20 different types of amino acids that can be combined to make a protein.

Amino acid



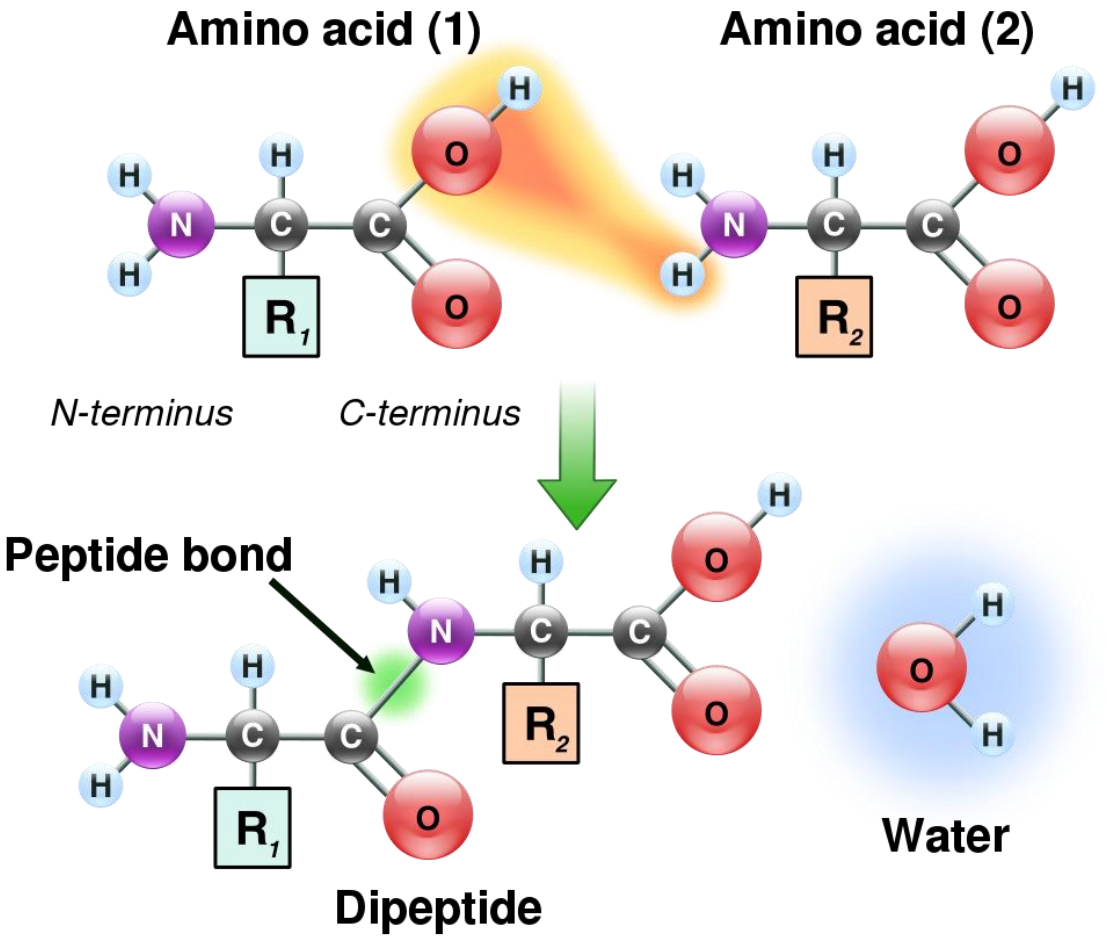
The 20 amino acids (plus selenocysteine)



Peptide bond

- Amino acids could be connected to each other by a special covalent bond called ***peptide bond***.
- In living organisms amino acids are joined by peptide bonds by enzymes which are part of a complex molecular machine called ***ribosome***.
- Peptide bond could be also created in chemical or biochemical experiment

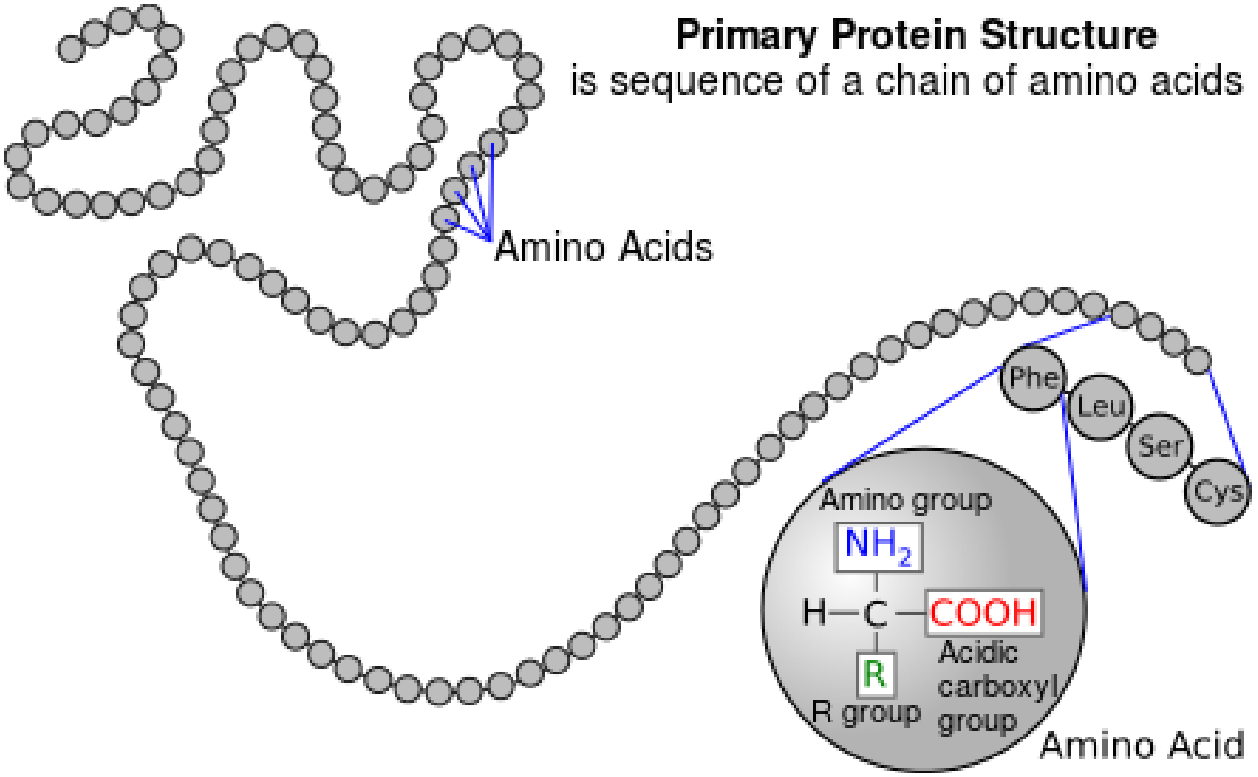
Peptide bond



Peptides

- ***Peptide*** – a molecule consisting of two or more amino acids joined together by peptide bonds.
- Peptides made up of two amino acids are called *di*peptides of three amino acids – *tri*petides, etc. Peptides made up of “many” amino acids are called *poly*ptides
- Peptides have N-terminus and C-terminus

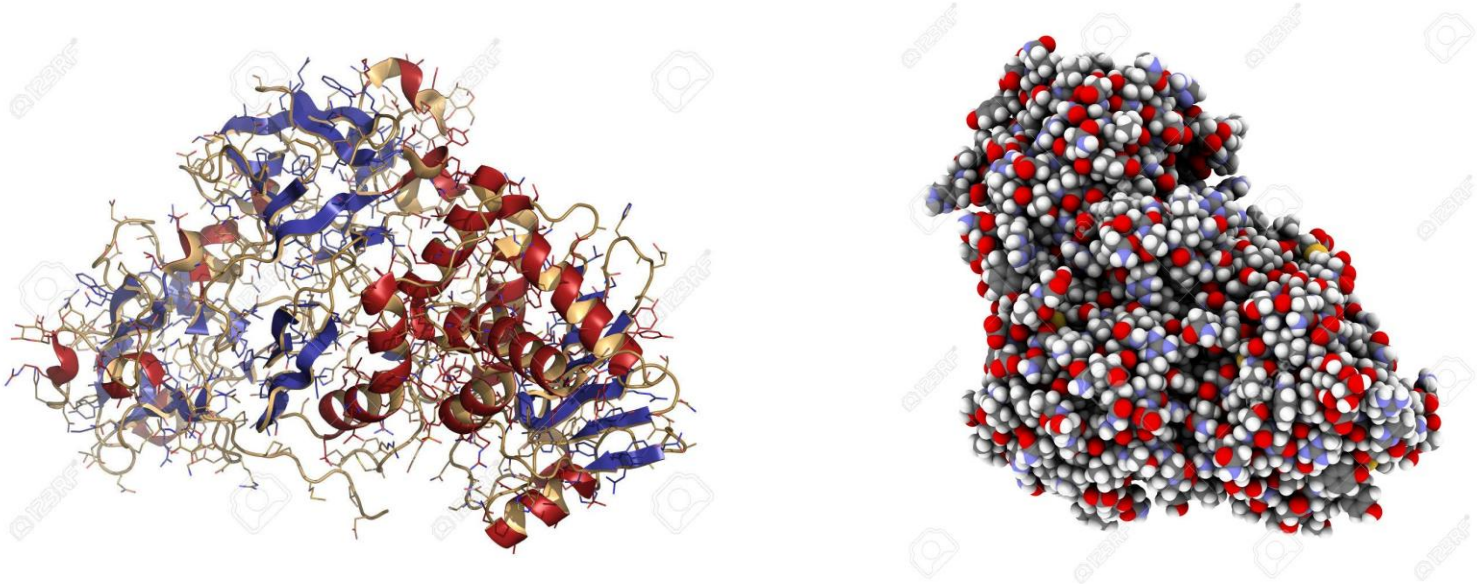
Primary protein structure



Protein primary structure

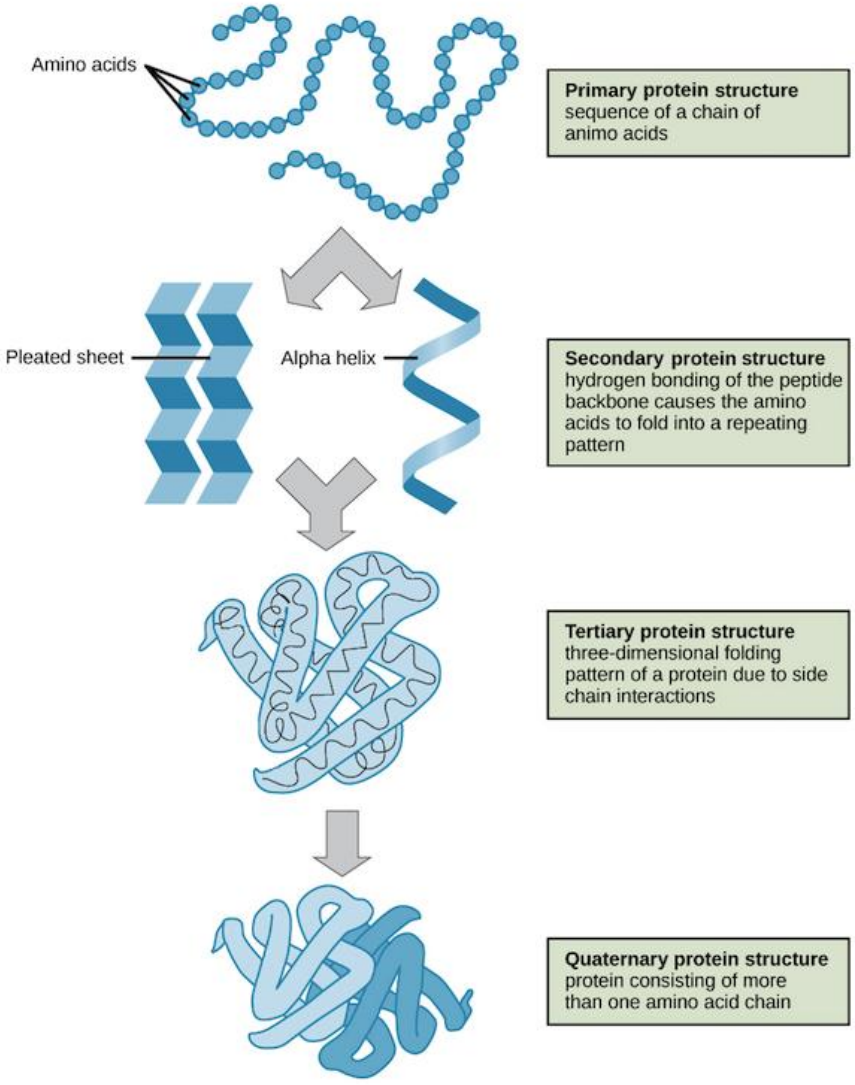
- Protein primary structure is the linear sequence of amino acids in a peptide or protein.
- The sequence of amino acids determines each protein's unique 3-dimensional structure and its specific function.

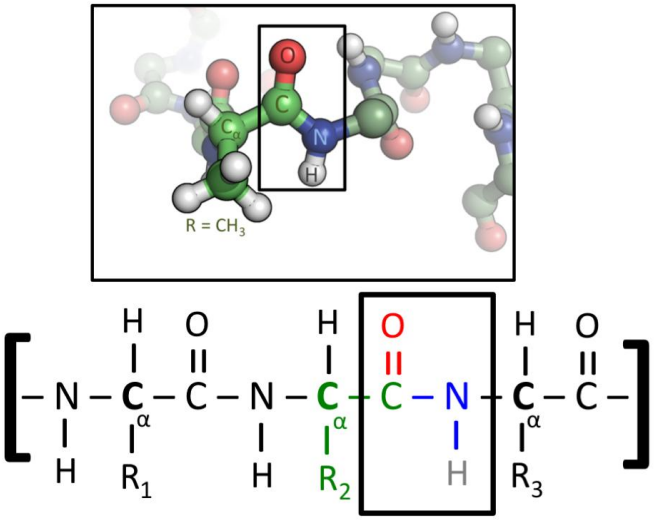
Proteins are very large molecules with complex 3-D organization



3-D structure of ricin – poisonous protein of castor beans

Levels of protein structure





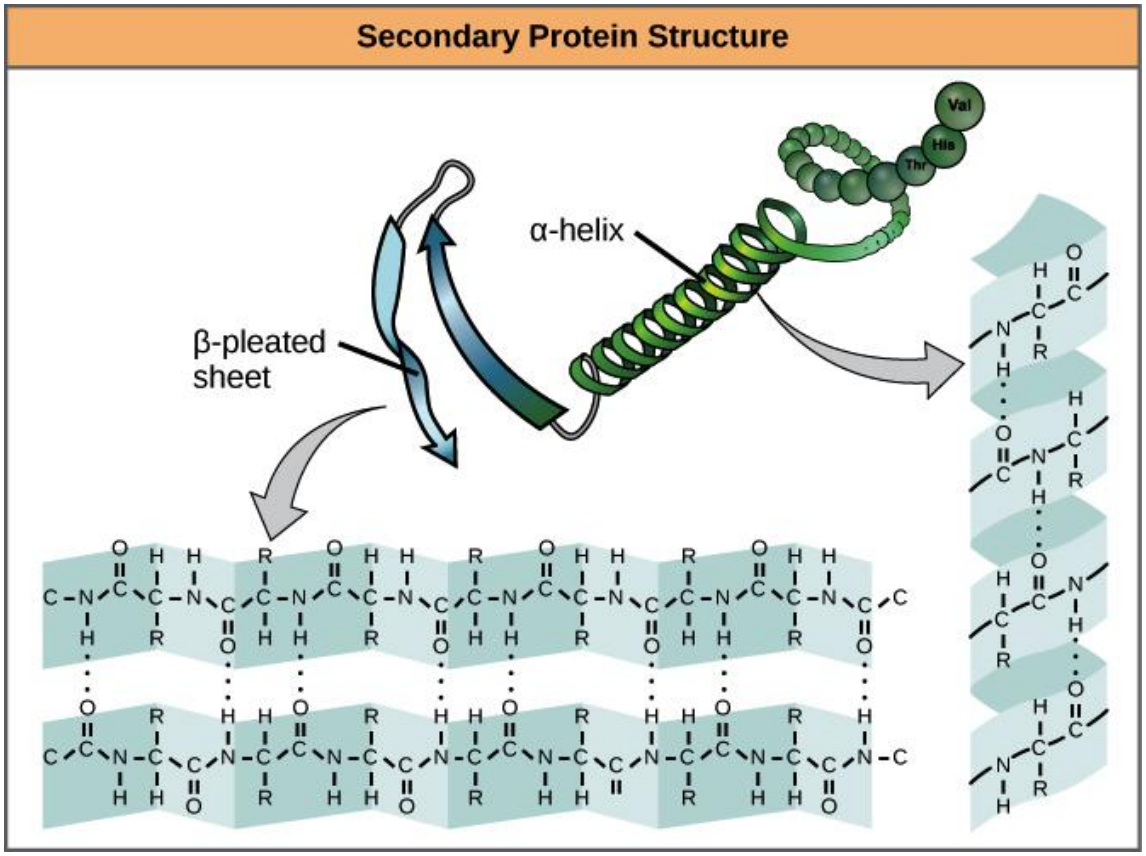
- Peptide bond is a single covalent bond
- Single bonds tend to be very flexible allowing atoms to rotate around the bond. They can also bend and stretch within certain limits without breaking.
- Flexibility of the peptide backbone allows atoms of proteins to find partners in forming non-covalent interactions within the same molecule. These interactions are called ***intramolecular interactions***.

Protein secondary structure

- Protein secondary structure is the three dimensional form of **local segments** of proteins.
- Secondary structure forms as the result of hydrogen bonding of the **peptide backbone**. It causes the amino acids to fold into a repeating pattern

- The two most common secondary structural elements are alpha helices and beta sheets.
- Secondary structure elements typically spontaneously form as an intermediate before the protein folds into its three dimensional tertiary structure.

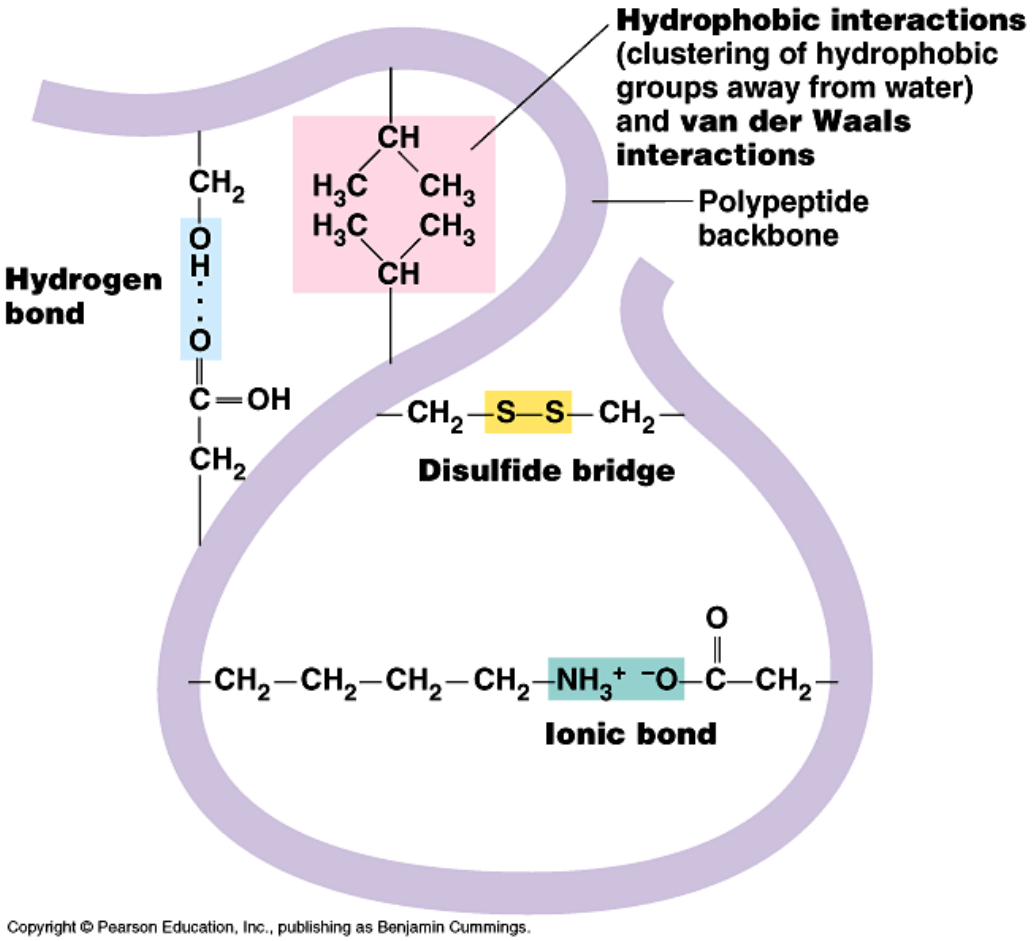
- **In alpha helices hydrogen bonds are formed within the peptide strand, in beta sheets – between peptide strands.**



Protein tertiary structure

- The overall three-dimensional shape of an entire protein molecule is the tertiary structure. The protein molecule will bend and twist in such a way as to achieve maximum stability. Although the three-dimensional shape of a protein may seem irregular and random, it is fashioned by many stabilizing forces due to bonding **interactions between the side-chain groups** of the amino acids.

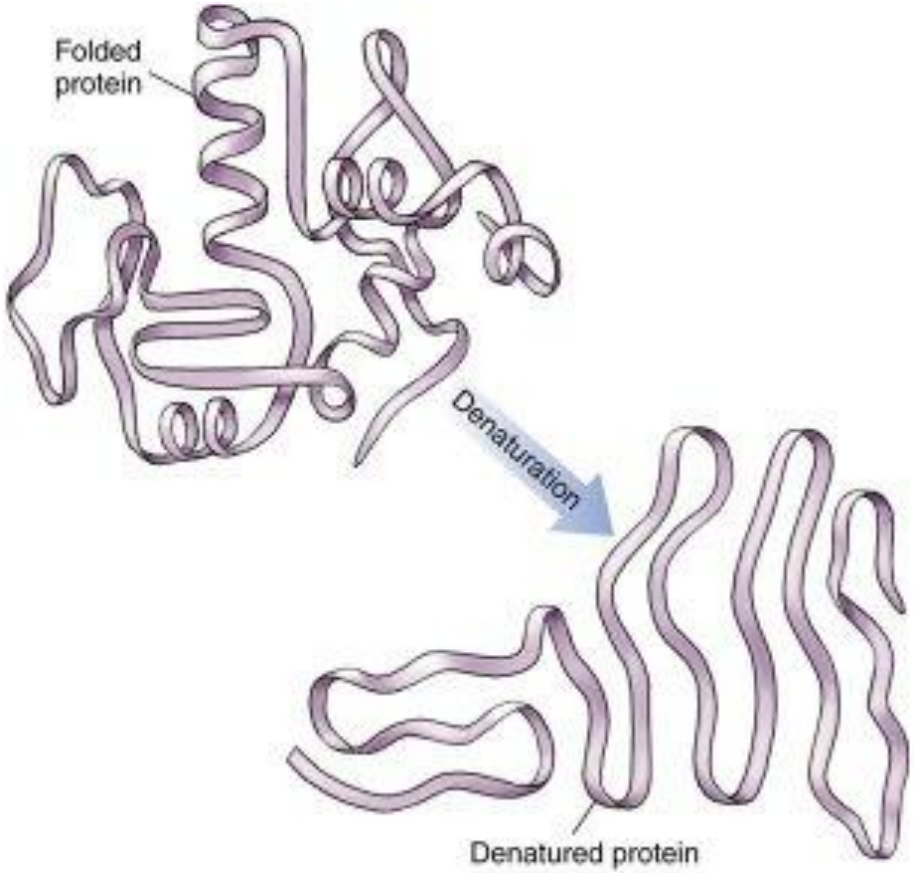
Protein tertiary structure



Protein quaternary structure

- Many proteins are made up of **multiple polypeptide chains**, often referred to as **protein subunits**. These subunits may be the same (as in a homodimer) or different (as in a heterodimer). The quaternary structure refers to how these protein subunits interact with each other and arrange themselves to form a larger aggregate protein complex.
- The final shape of the protein complex is once again stabilized by various interactions, including hydrogen-bonding, disulfide-bridges and ionic bonds.

- Higher levels of protein structure are formed without covalent bonds. Therefore, they are not as stable as peptide covalent bonds which make protein primary structure
- Under external stress like, temperature or action of certain chemical compounds the protein 3-dimentional structure becomes even less stable and can unravel


Folded
protein
Denaturation
Denatured protein

How denaturation occurs at levels of protein structure

- In **quaternary structure** denaturation, protein sub-units are dissociated and/or the spatial arrangement of protein subunits is disrupted.
- **Tertiary structure** denaturation involves the disruption of:

i. Covalent interactions between amino acid side-chains (such as disulfide bridges between cysteine groups)
ii. Non-covalent dipole-dipole interactions between polar amino acid side-chains (and the surrounding solvent)

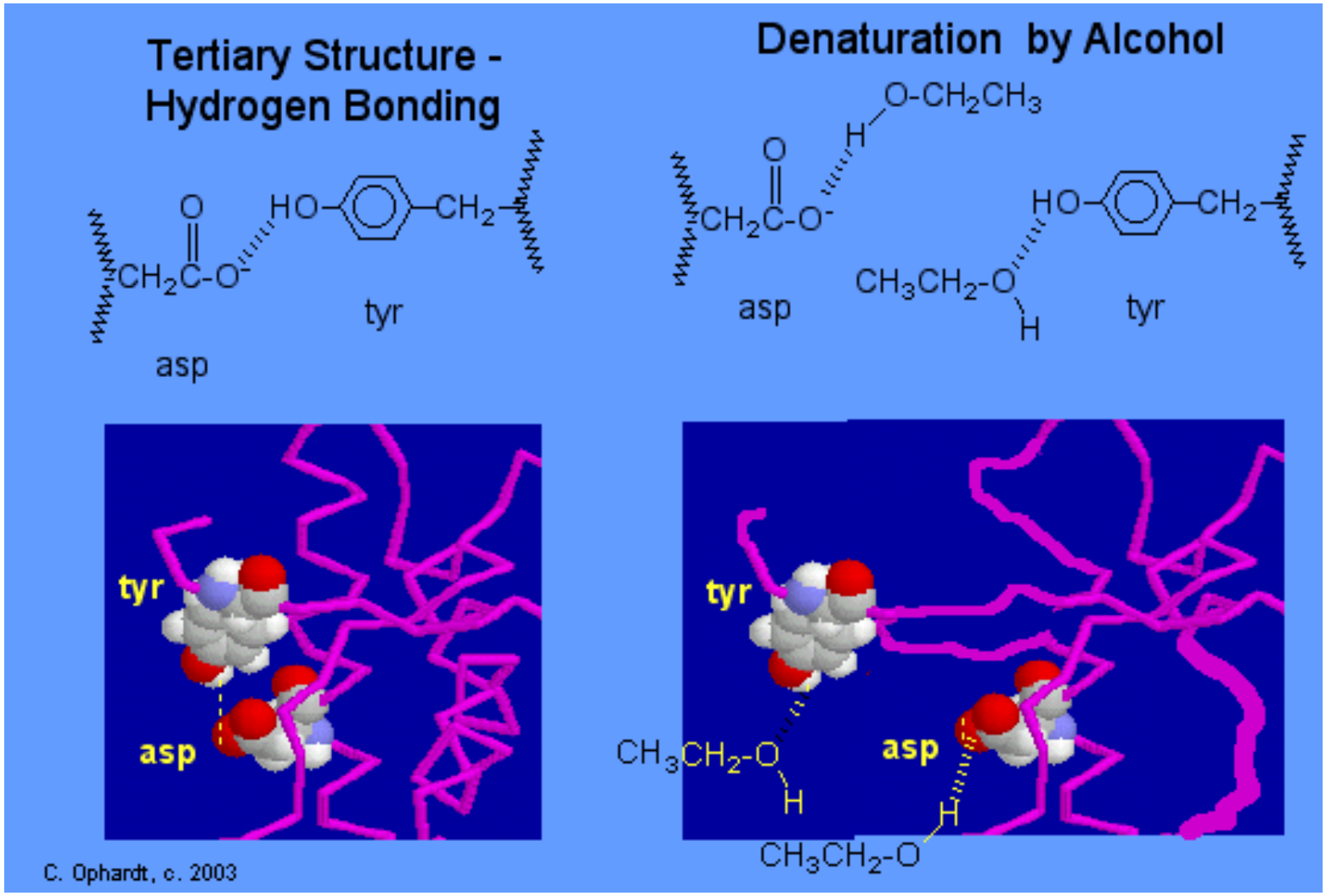
- In **secondary structure** denaturation, proteins lose all regular repeating patterns such as alpha-helices and beta-pleated sheets, and adopt a random coil configuration.
- **Primary structure**, such as the sequence of amino acids held together by covalent peptide bonds, is **not disrupted** by denaturation.

Denaturation usually disrupts the function of a protein.

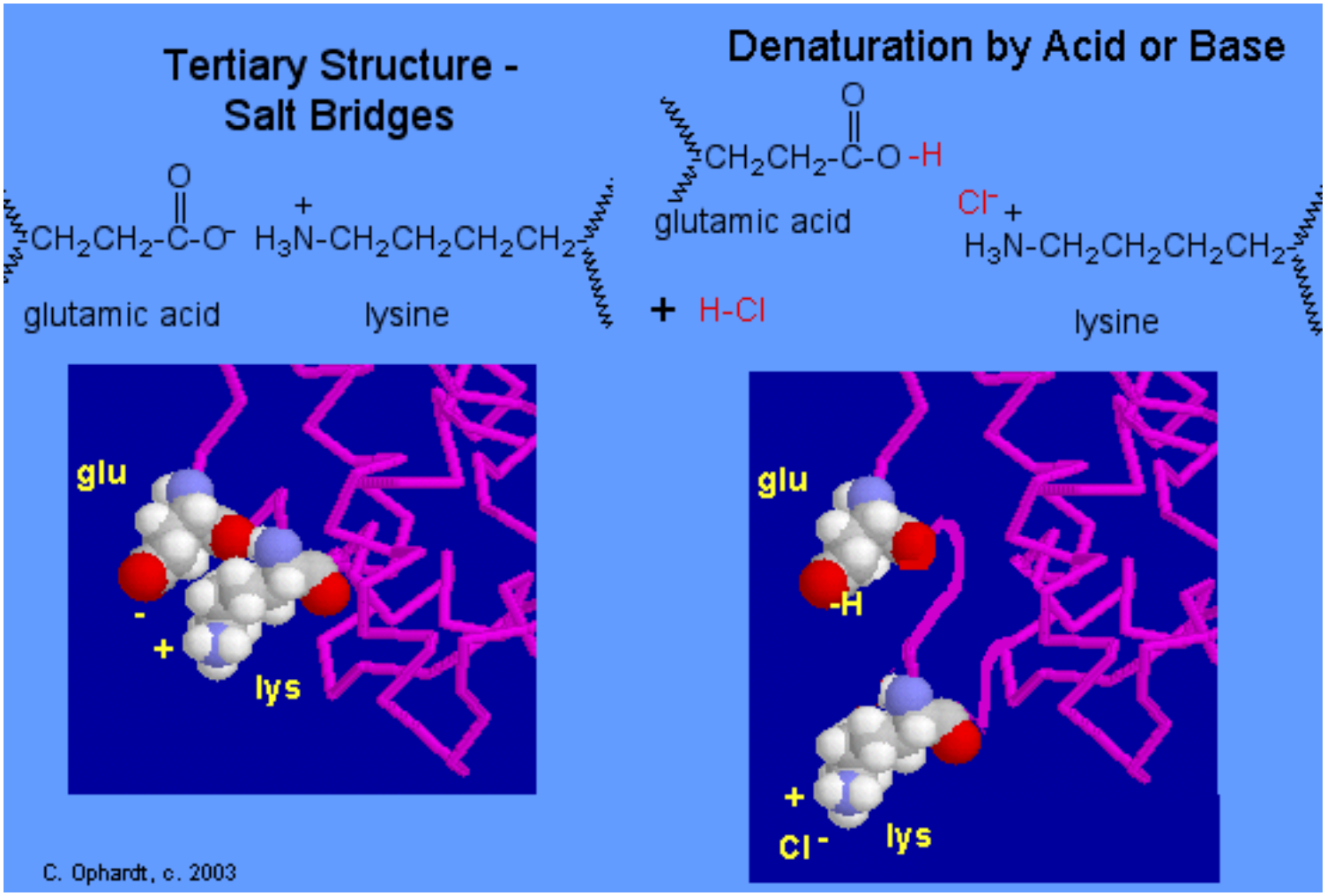
Heat denaturation

- **Heat** can be used to disrupt hydrogen bonds and non-polar hydrophobic interactions. This occurs because heat increases the kinetic energy and causes the molecules to vibrate so rapidly and violently that the bonds are disrupted. The proteins in eggs denature and coagulate during cooking. Other foods are cooked to denature the proteins to make it easier for enzymes to digest them. Medical supplies and instruments are sterilized by heating to denature proteins in bacteria and thus destroy the bacteria.

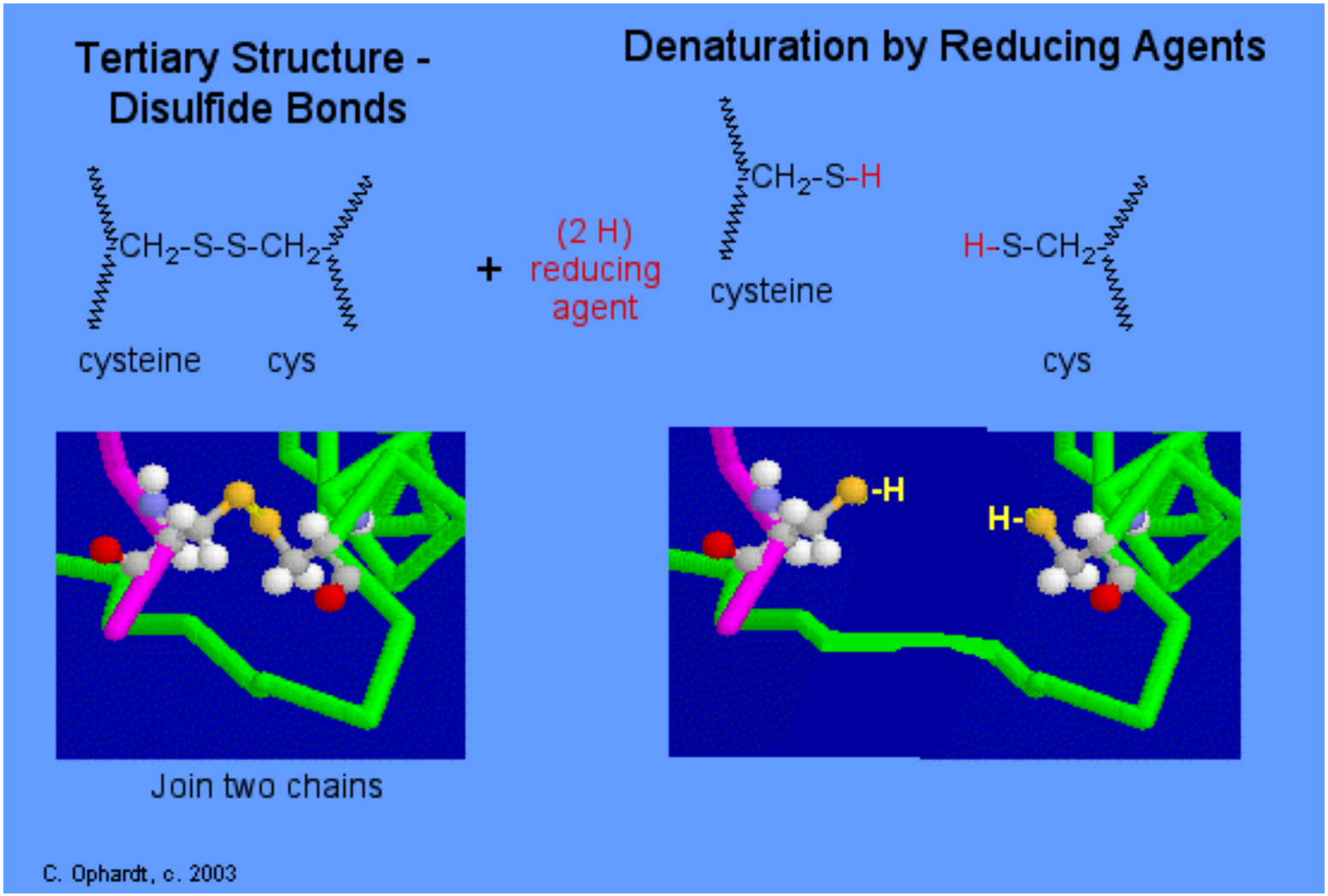
Alcohol Disrupts Hydrogen Bonding:



Acids and Bases Disrupt Salt Bridges:

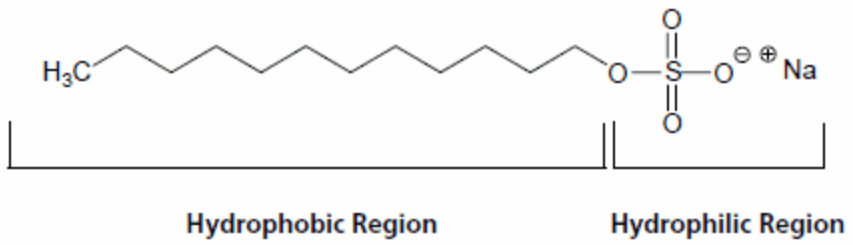


Disruption of disulphide bonds by reducing agents



Detergents disrupt hydrophobic interactions

- Detergents are used in biomedical laboratories for the disruption of cell membranes (cell lysis) and the release of intracellular materials in a soluble form. Detergents break the protein-protein, protein-lipid and lipid-lipid associations, denature proteins.
- Detergents are molecules that contain both hydrophobic groups (their tails) and hydrophilic groups (their heads)



A detergent – Sodium dodecyl sulphate (SDS)

Detergents

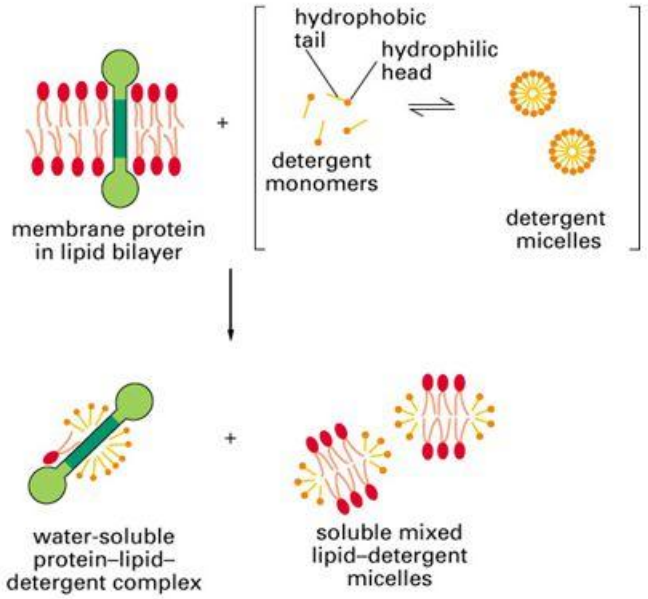
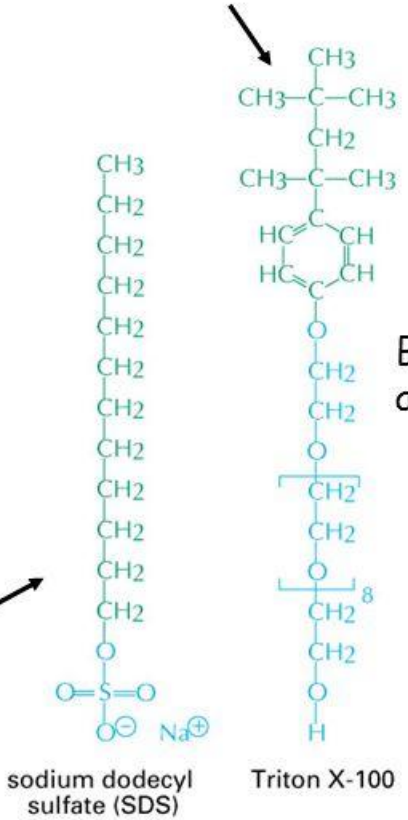


Figure 10–24. Molecular Biology of the Cell, 4th Edition.

Mild nonionic detergent that dissolves membranes without unfolding proteins.

Ionic detergent that dissolves membranes and unfolds proteins.



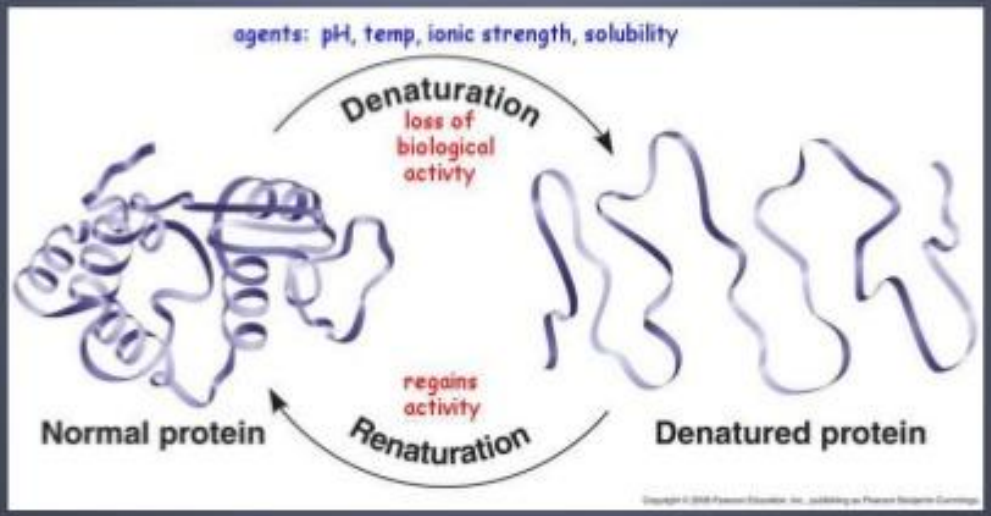
Both are amphipathic

Figure 10–25. Molecular Biology of the Cell, 4th Edition.

Renaturation

- In many cases, denaturation is reversible (the proteins can regain their native state when the denaturing influence is removed). This process is called renaturation. It could be complete or partial.
- Renaturation can completely or partially restore the protein function lost because of denaturation.

- The denatured state does not necessarily equate with complete unfolding of the protein and randomization of conformation.
- Under most conditions, denatured proteins exist in a set of partially folded states that are poorly understood.

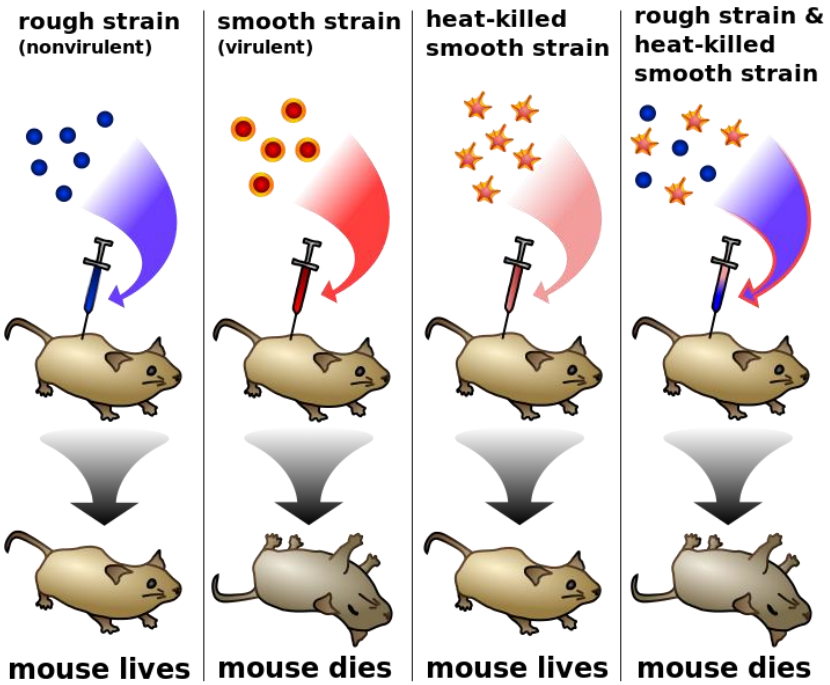


Nucleic Acids

Nucleic acids carry genetic information

- For long time scientists assumed that genetic information is carried by proteins
- In 1928 Griffith reported an experiment suggesting that bacteria are capable of transferring genetic information through a process known as transformation.
- In 1944 Avery, MacLeod and McCarty reported experiment showing that DNA was transforming factor in bacteria.

Griffith experiment



- Griffith experiment indicated that non-pathogenic strain of bacteria could be "transformed" into the lethal strain by a "transforming principle" that was somehow part of the dead pathogenic bacteria.
- Avery, MacLeod and McCarty showed that the “transforming principle” was DNA from the dead bacteria.

Functions of nucleic acids in the cell

- Storage and propagation of genetic information.
- Transcribing and translating of genetic information into protein sequences.
- Structural and catalytic functions.
- Regulatory functions.

The Central Dogma of Molecular Biology

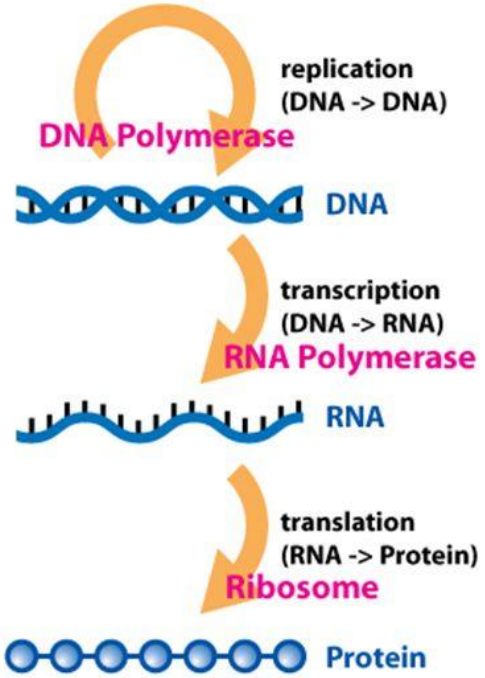
- Information is transferred from DNA to RNA to protein

  DNA -> RNA -> Protein

- Proteins create traits

- This is called **gene expression**

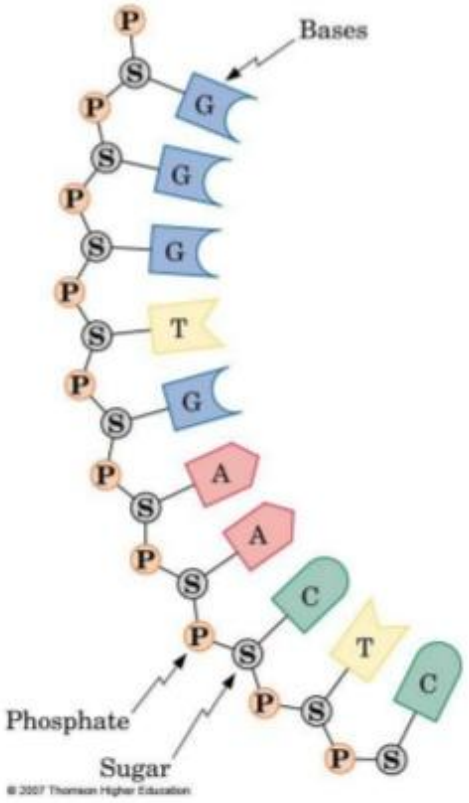
- This process is found in all organisms



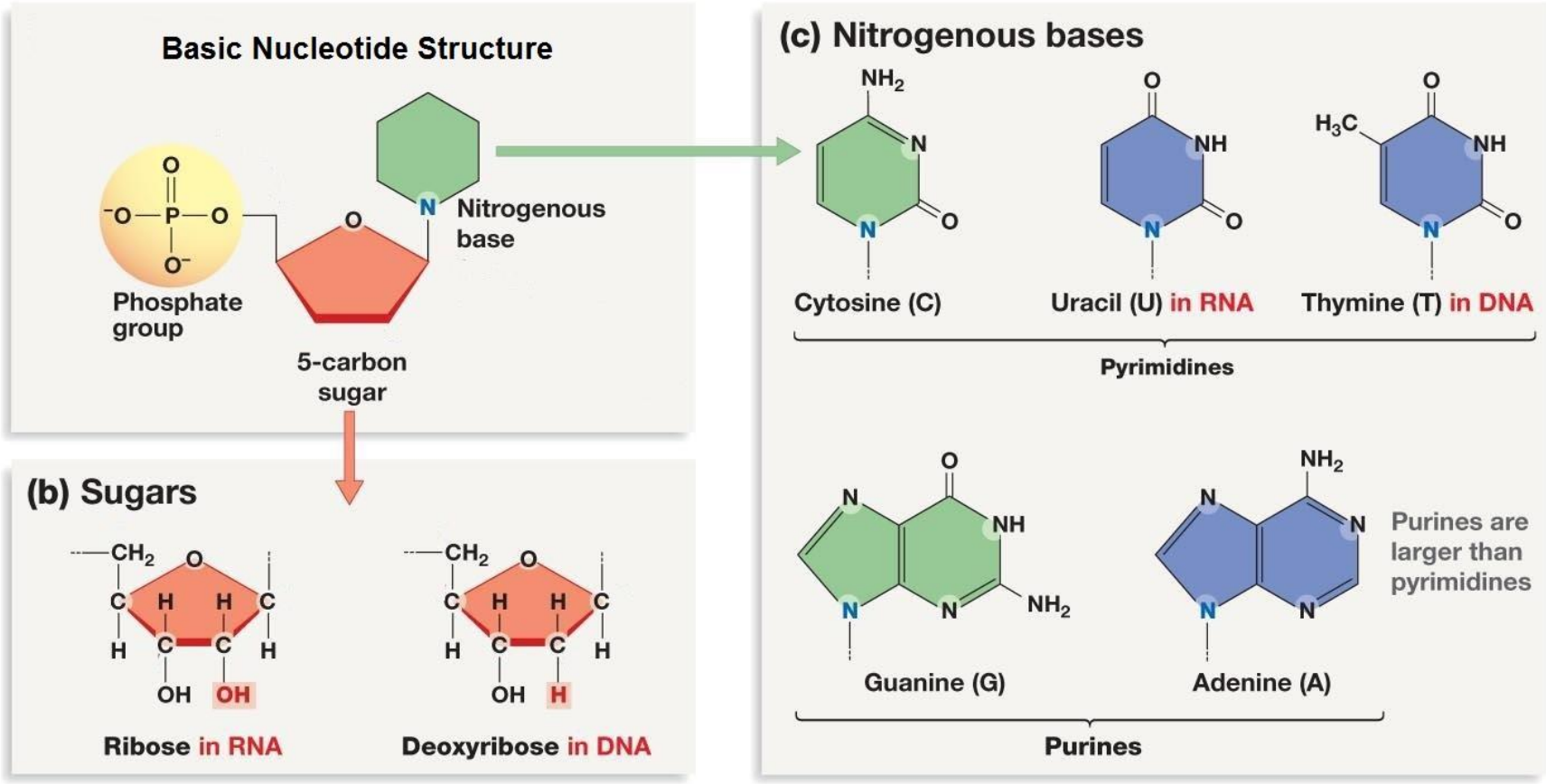
Chemical structure of nucleic acids

- Nucleic acids are biopolymers. They are chains consisting of monomers called nucleotides joined together by phosphodiester bonds

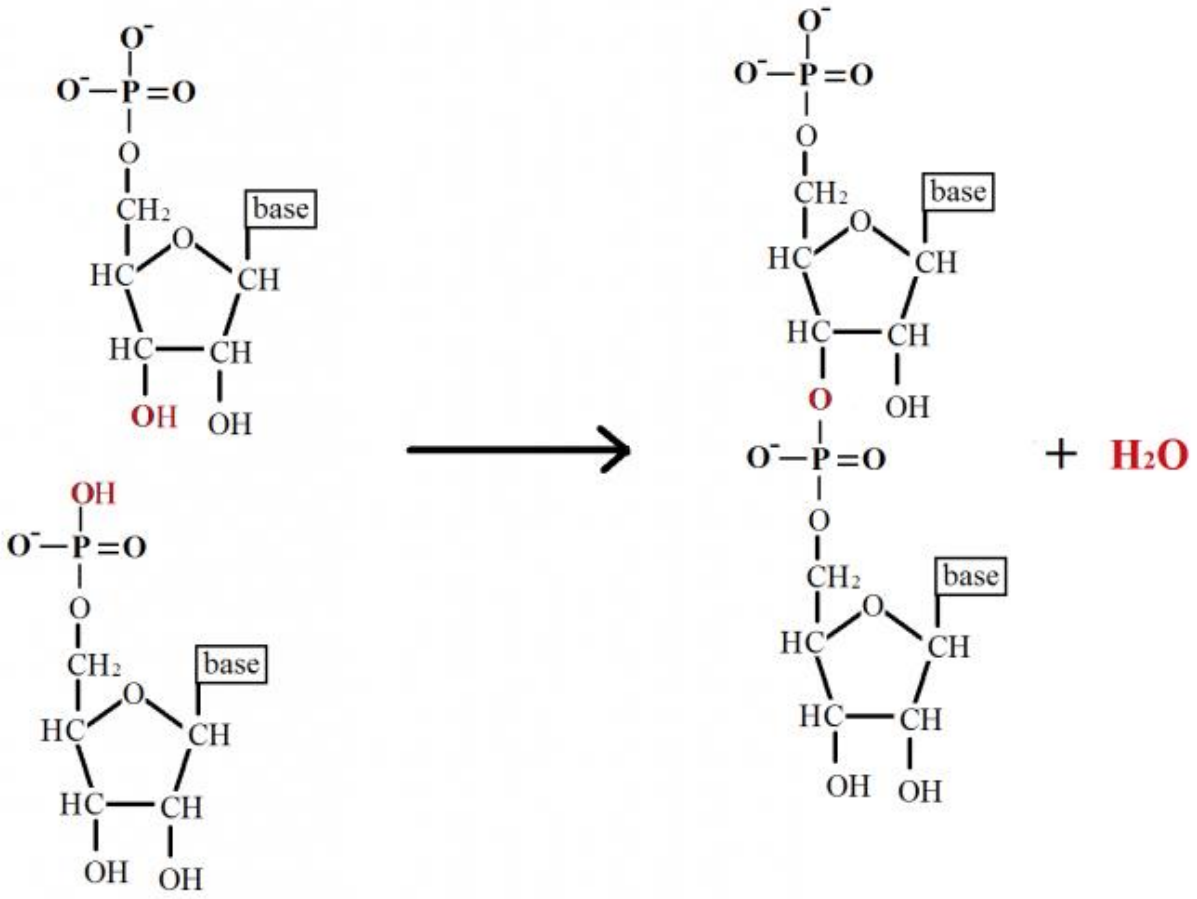
Structure of DNA and RNA



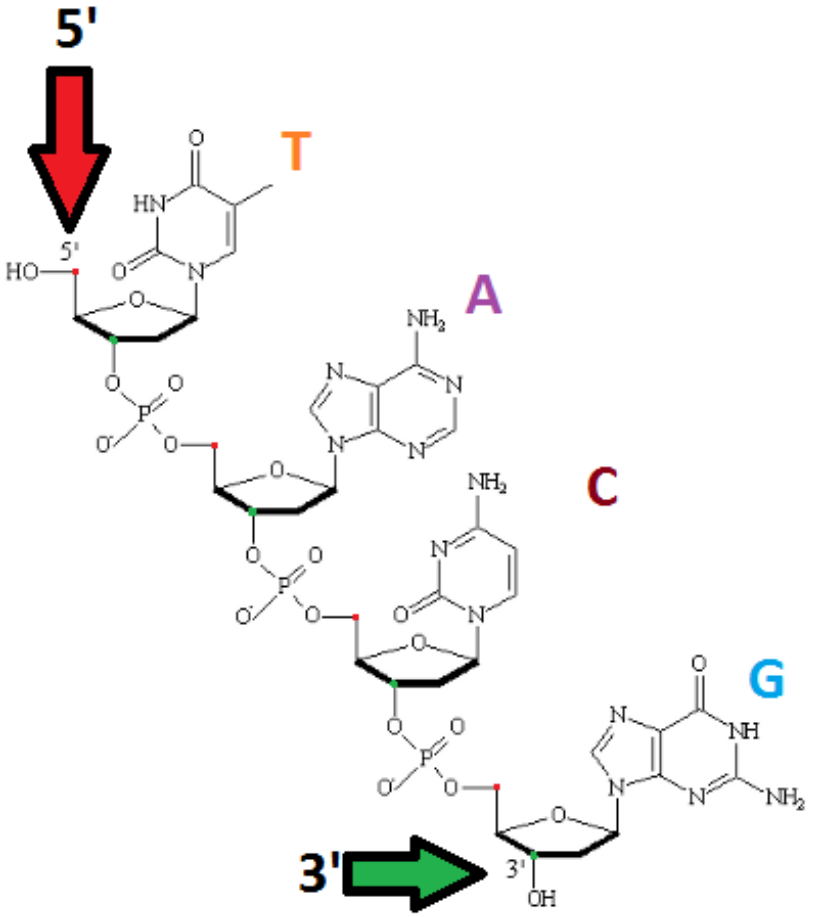
Nucleotides



Phosphodiester bond

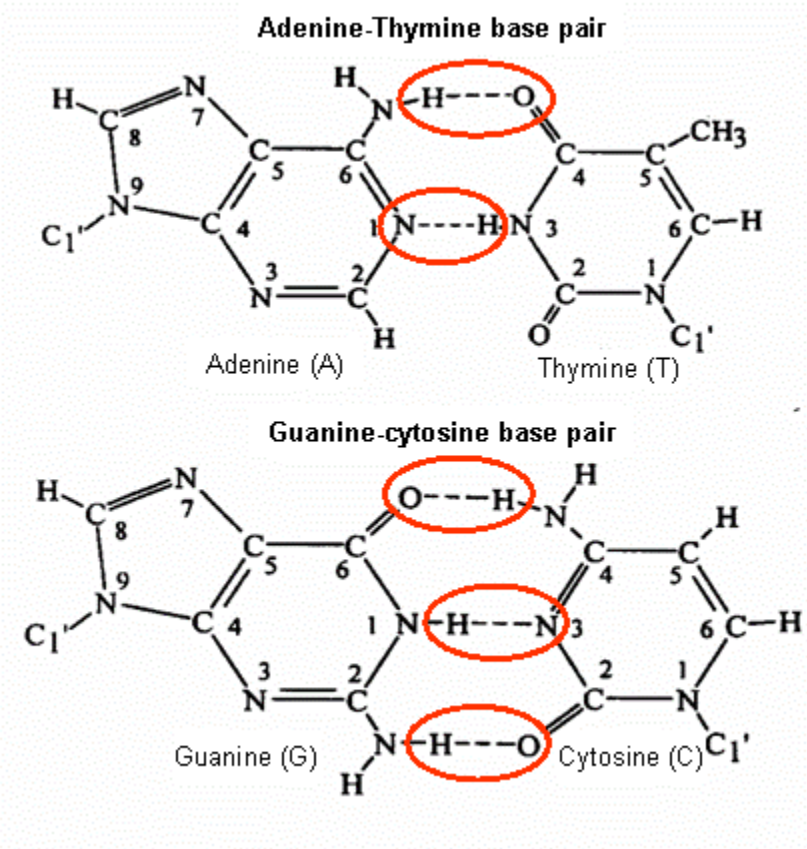


Nucleic acid strand has direction



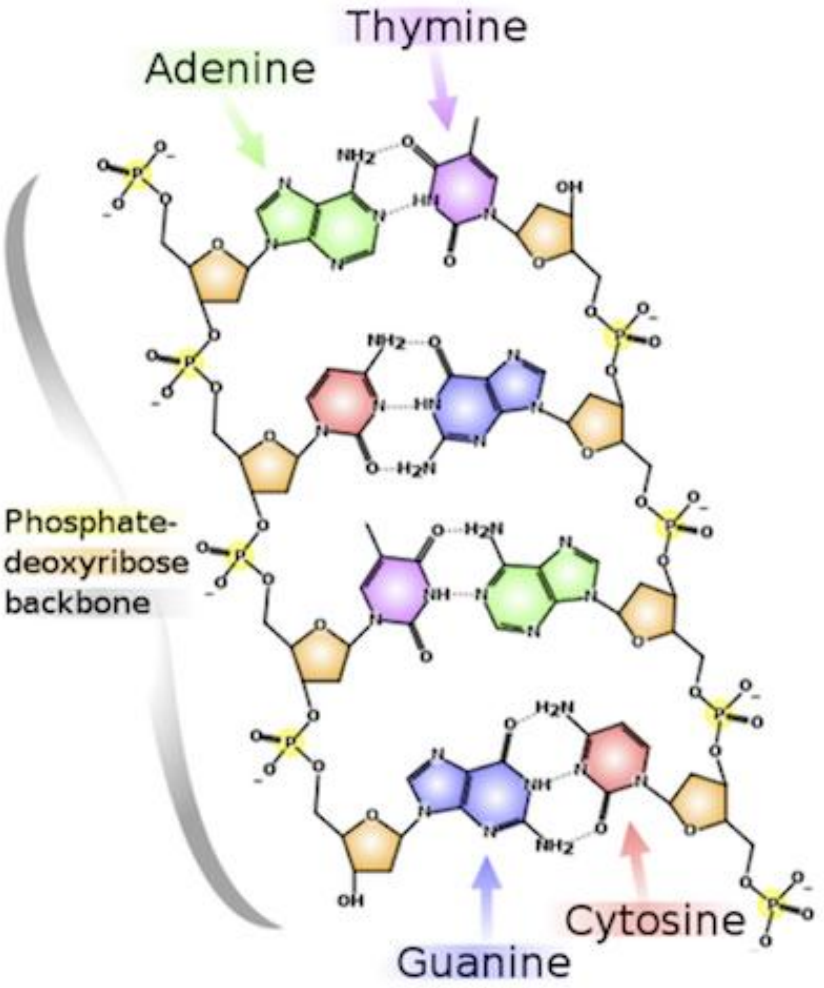
Nucleic Acids
secondary structure

Nitrogenous bases of nucleotides can form hydrogen bonds with each other:

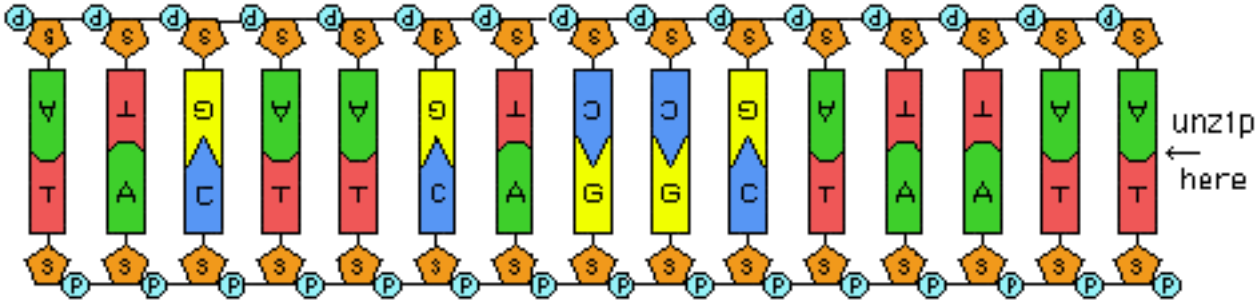


- Nucleic acids have **secondary structure**. They could be single stranded (ssDNA, ssRNA) or double stranded (dsDNA, dsRNA or DNA-RNA hybrid molecules). Double stranded nucleic acid forms when two single stranded molecules with **complementary sequences** meet and hydrogen bonds are formed between the bases of the two strands.

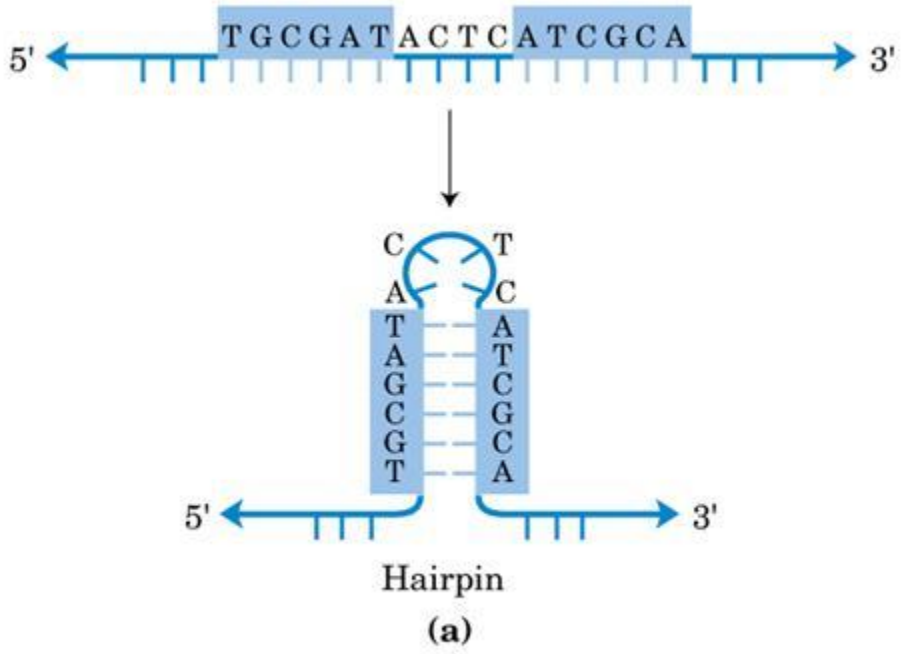
- Complementary nucleic acid strands



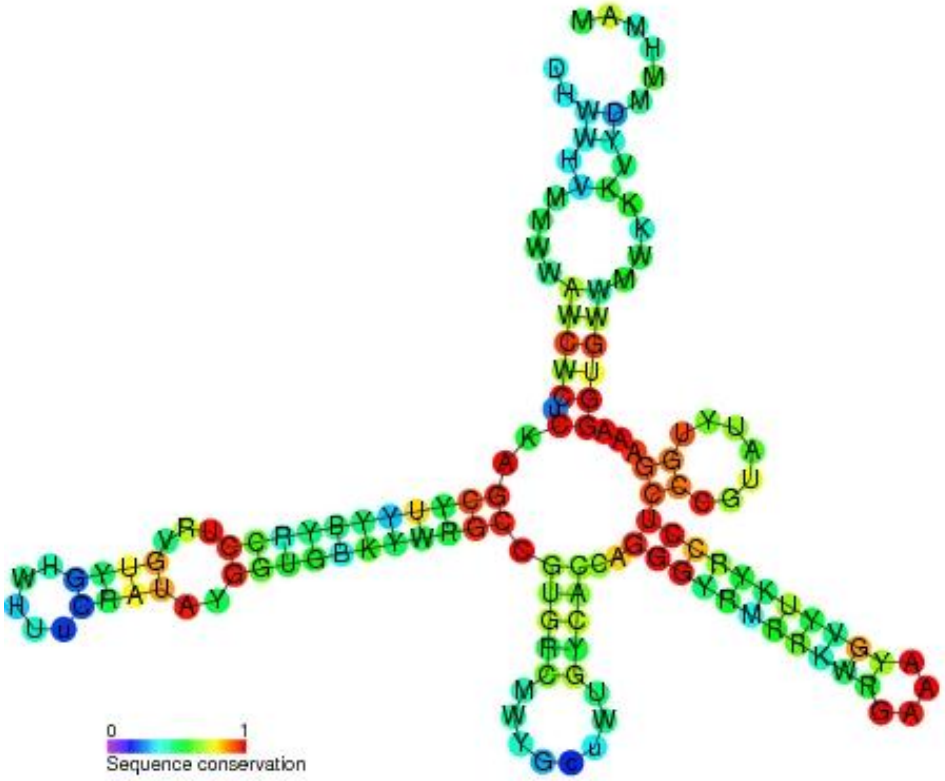
Complementary nucleic acid strands



Sometimes double stranded regions are formed within the same single stranded NA molecule

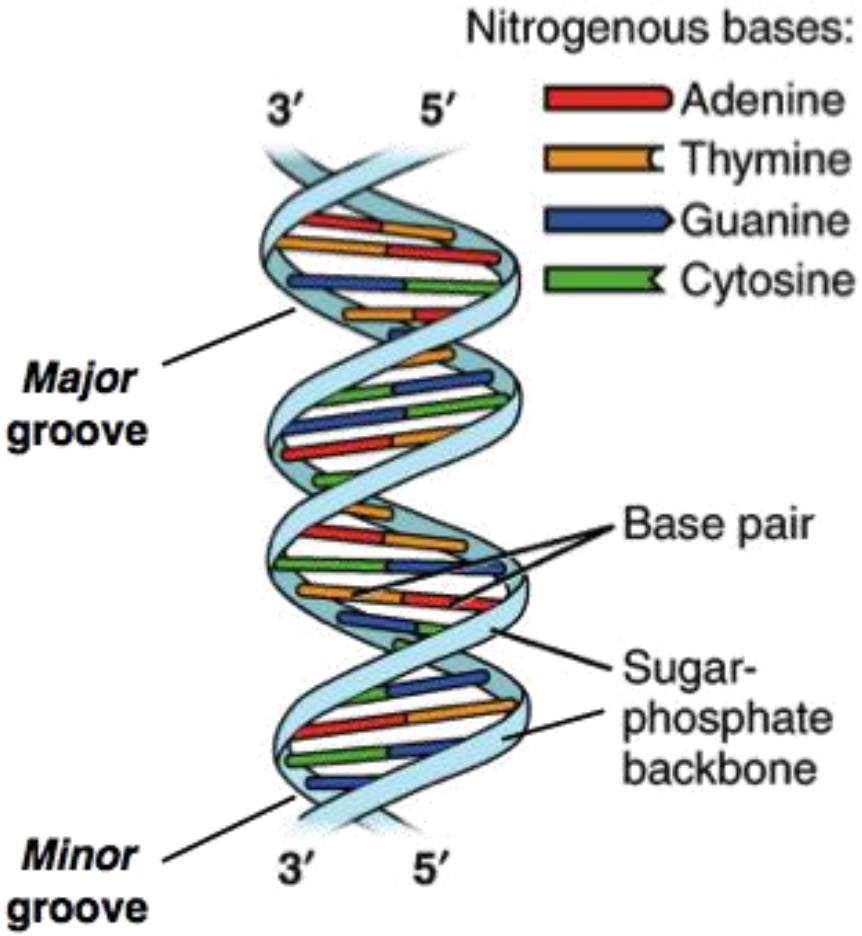


ssNA secondary structure



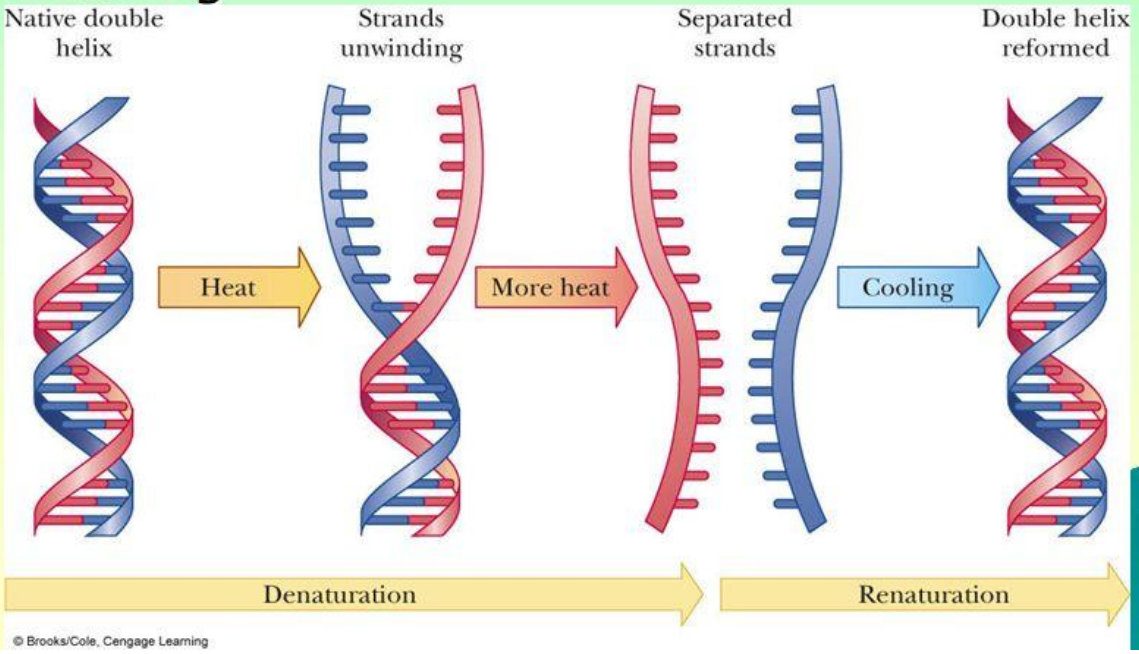
- DNA in living cell exists *mostly* in a double stranded form.
- It’s 3D-shape is a double helix.

DNA double helix

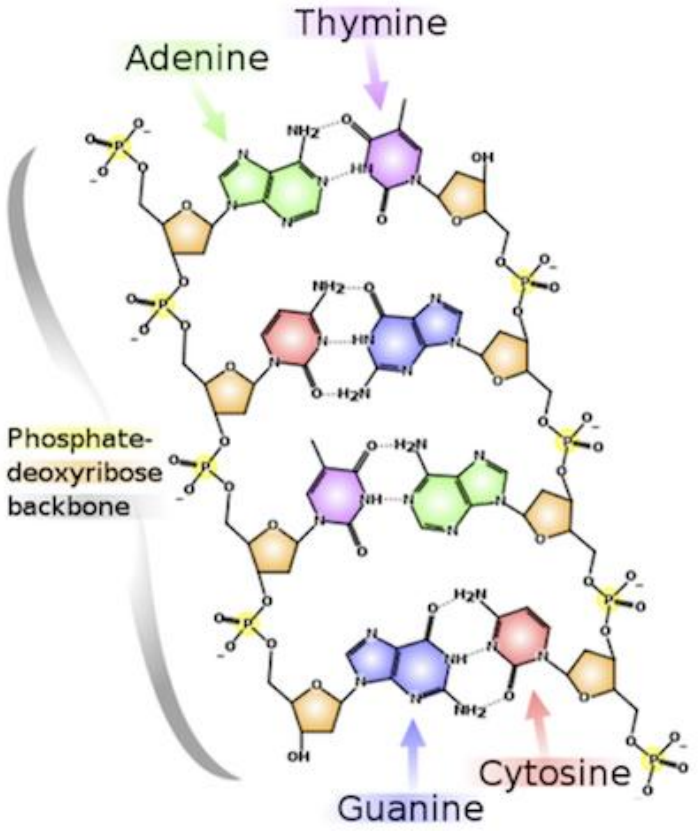


Denaturation of DNA

- Double helix unwinds when DNA is denatured
- Can be re-formed with slow cooling and annealing

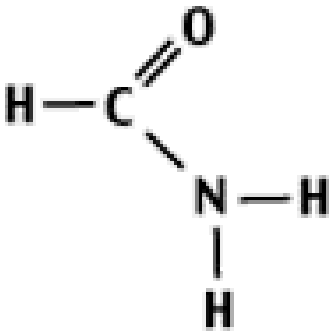


- **G-C pair forms 3 hydrogen bonds while A-T pair forms only 2. Therefore, GC-reach ds-nucleic acid has more heat resistant secondary structure than AT-reach one.**

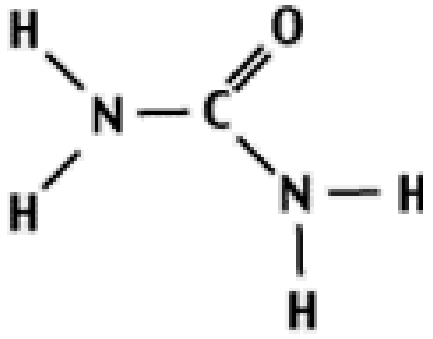


Denaturation of nucleic acids

- Heat
- Chemical agents. Urea or formamide are most commonly used

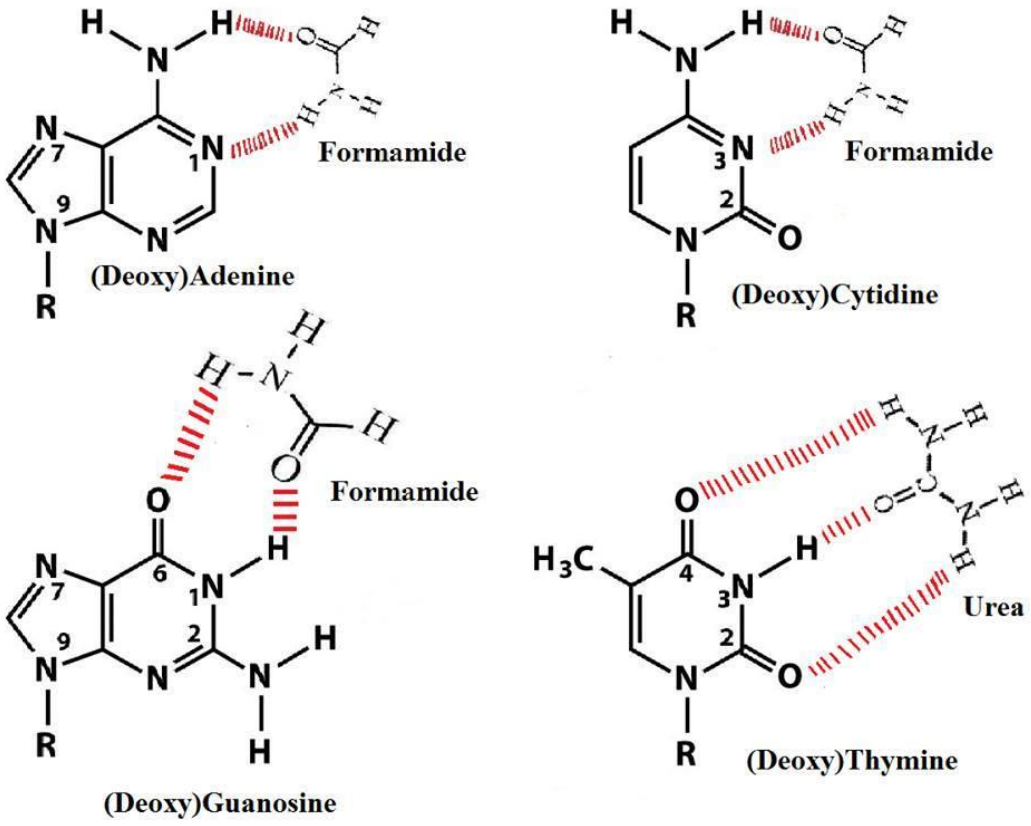


formamide



urea

Urea and formamide interaction with NA bases



Synthesis and degradation of nucleic acids strands

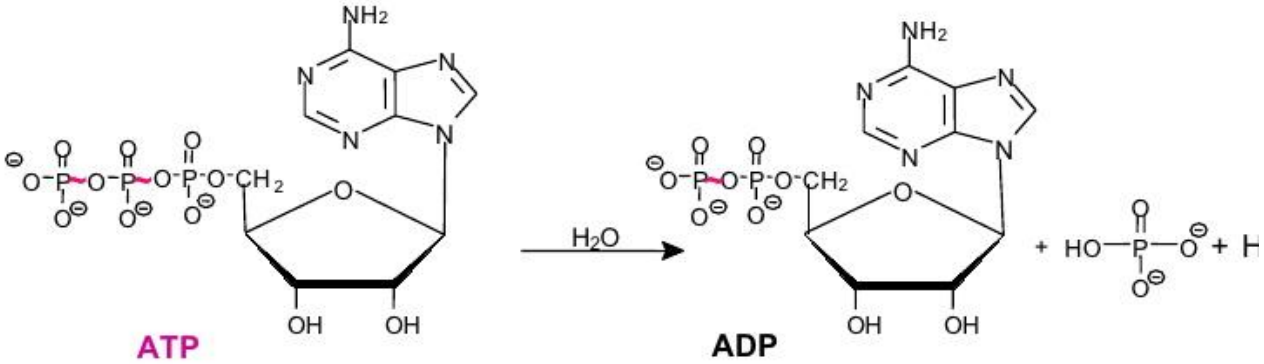
- Polymerized nucleic acid strand has higher free energy than a mixture of monomers
- Therefore nucleic acid could be degraded (hydrolyzed) with no additional energy needed.
- In order to synthesize a nucleic acid strand from monomers additional chemical energy is required. This energy comes in a form of a high-energy (macroergic) phosphate bond.

ATP

The term „high-energy compound“

(also „macroergic compound“ or „energy rich compounds“)

The most important is ATP



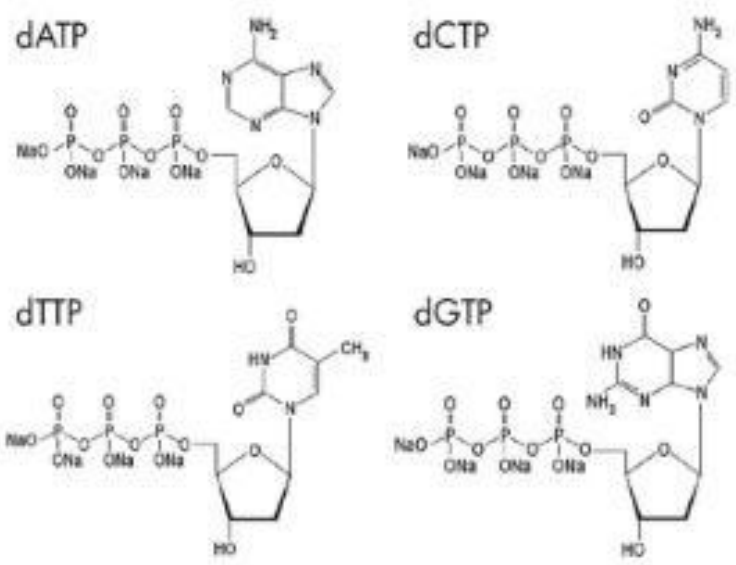
ATP in cells

- Life expectancy of an ATP molecule is about 2 min.
- It must be permanently synthesized
- Momentary content of ATP in a human body is about 100 g, but 60-70 kg is produced daily
- Adenylate kinase maintains the equilibrium between ATP, ADP a AMP

$$ATP + AMP \rightleftarrows 2\ ADP$$

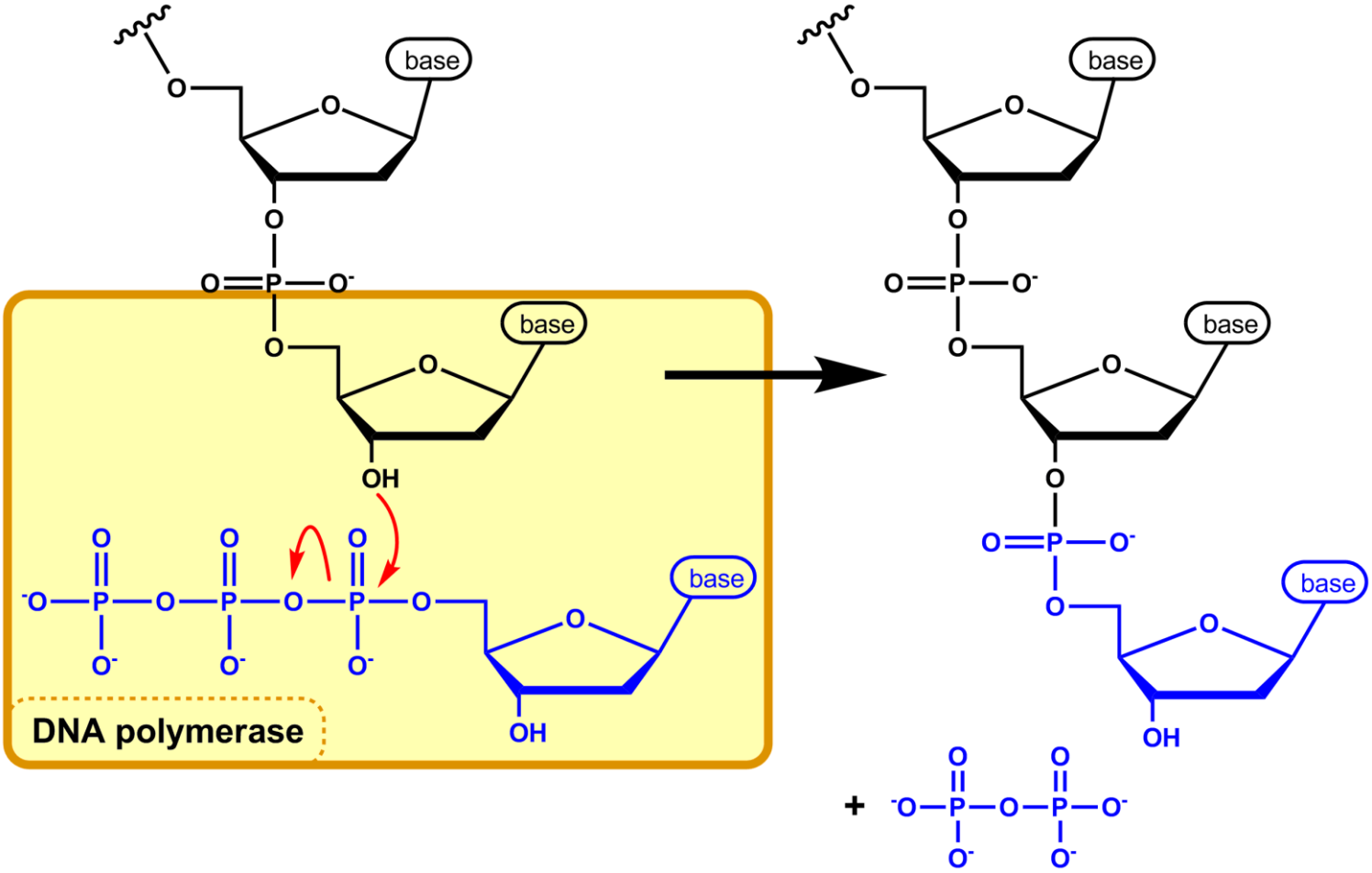
ATP is a universal "fuel" in the cell used in the majority of the reactions that require additional energy

- Any nucleotide or deoxynucleotide could be phosphorylated yielding a triphosphate macro-ergic derivative :



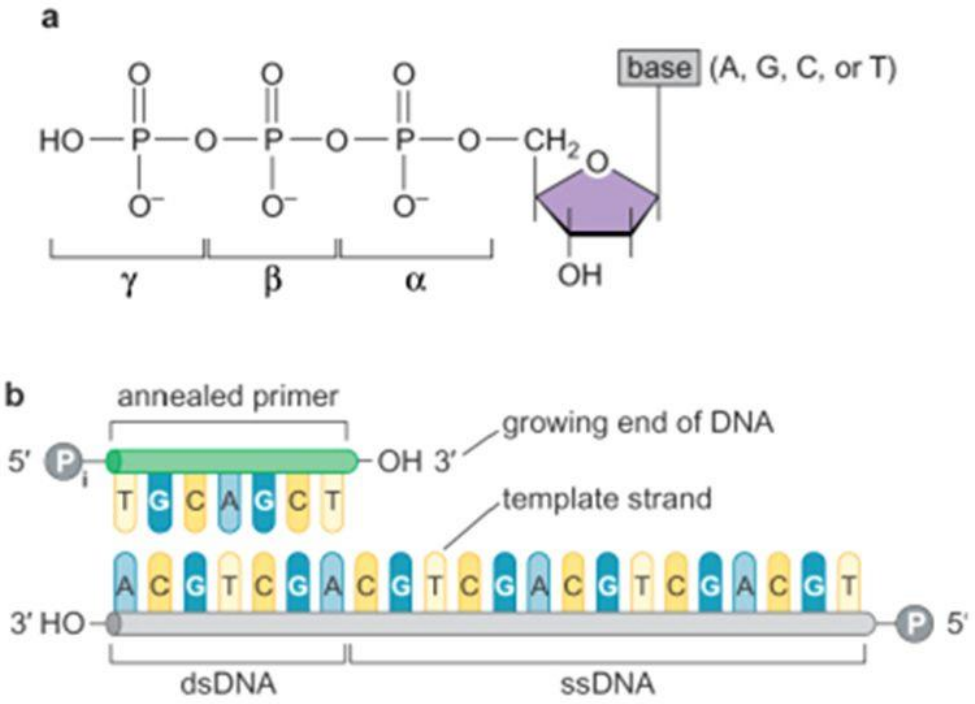
- Specialized enzymes maintain pool of NTP and dNTP in the cell at concentrations needed for new DNA and RNA synthesis.

Addition of new monomer to the growing DNA (RNA) strand



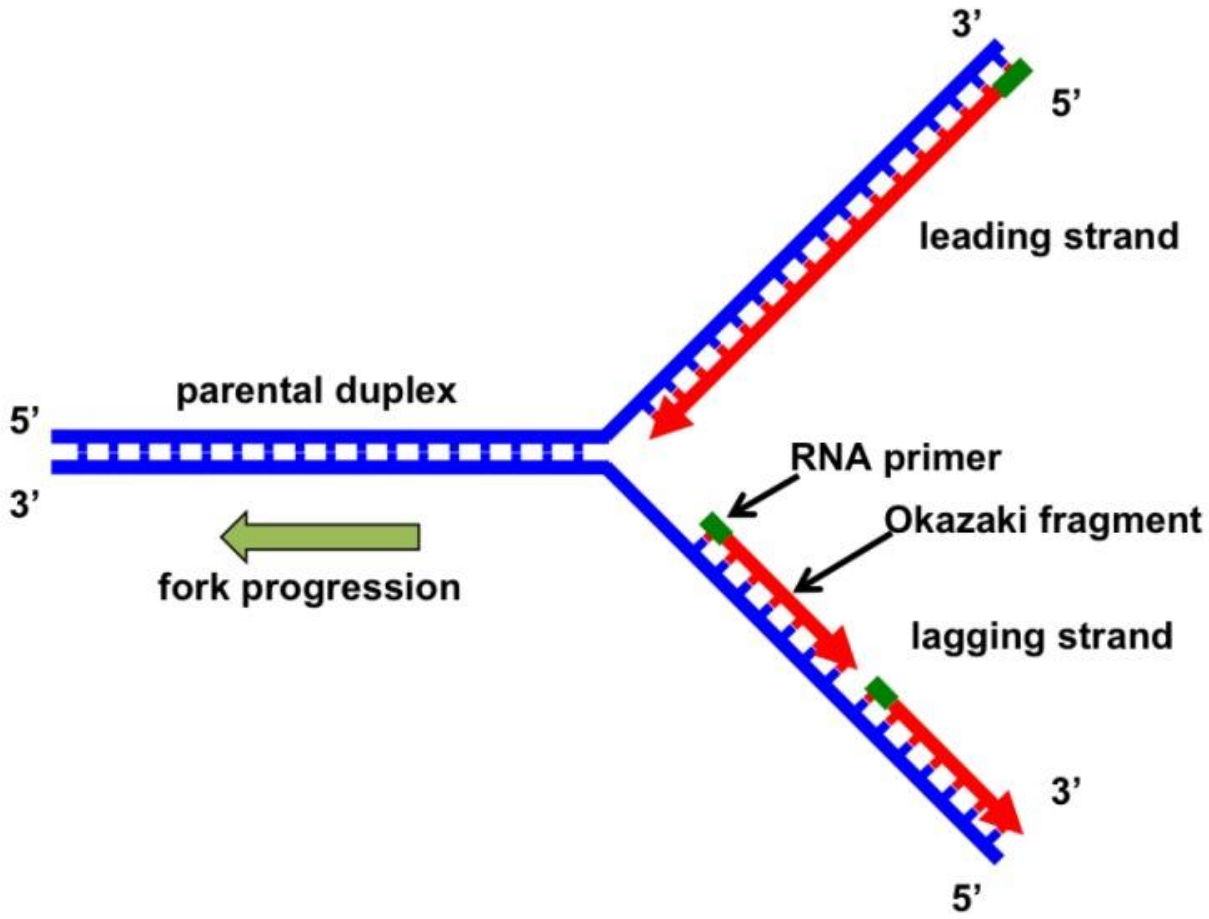
- There are many enzymes that can catalyze polymerization of DNA or RNA strand
- In the processes of DNA replication and transcription into RNA new nucleic acid strand is copied from a template NA that has complimentary sequence to the new strand.
- Some enzymes can extend NA strand without a template

Substrates required for DNA synthesis



Newly synthesized NA strand grows from in the 5' to 3' direction

DNA replication



DNA replication