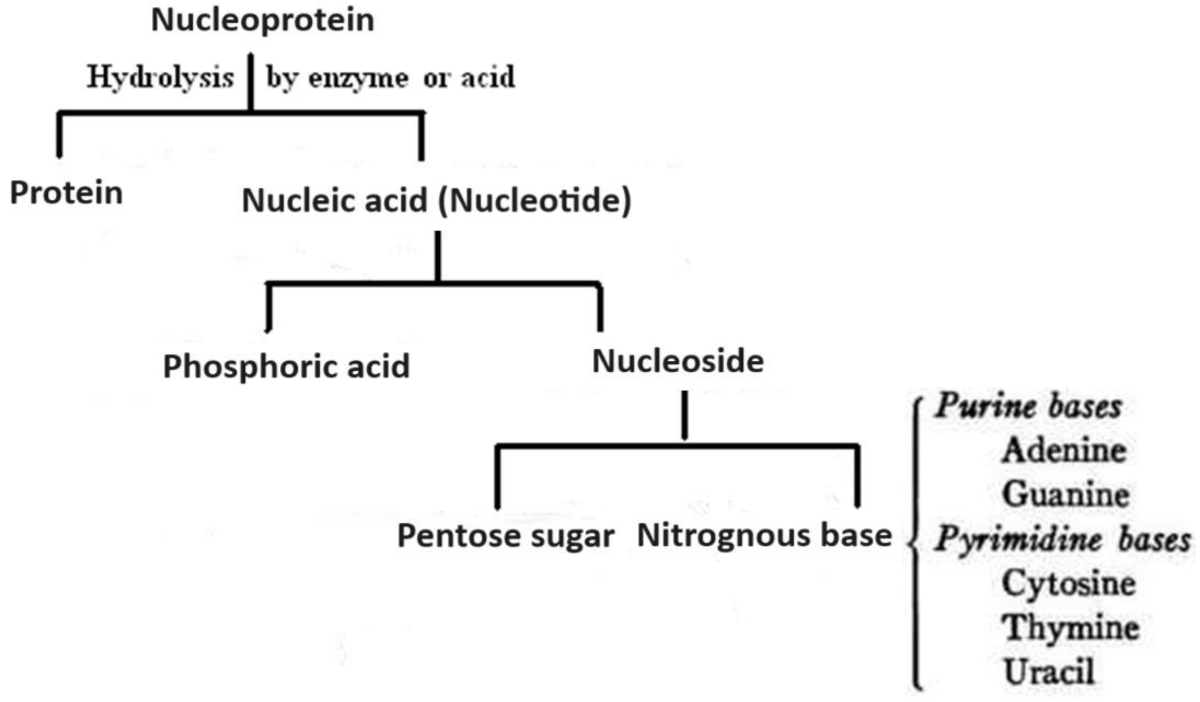
Chapter seven

Nucleic acids

Introduction

Nucleic acids are macromolecules present in all living cells, either in free state or bound to proteins as **nucleoproteins**.

Nucleoproteins are a group of conjugated proteins, the protein part (is usually basic in nature, e.g., protamines and histones containing high concentration of basic amino acids) and the non-protein prosthetic group (nucleic acid). By hydrolysis with acid or enzymes, various compounds are obtained.



Components of nucleic acid:

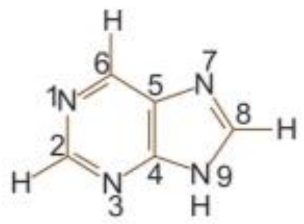
Fundamental components of nucleic acids are the **nitrogenous bases, pentose sugar (ribose or deoxyribose) and phosphoric acid.**

Nitrogenous bases of DNA&RNA:

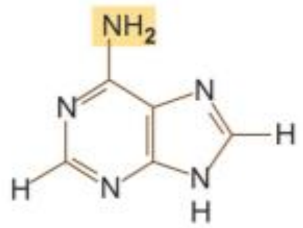
All nitrogenous bases of nucleic acid are derived from two heterocyclic bases purine and pyrimidine.

Purine bases:

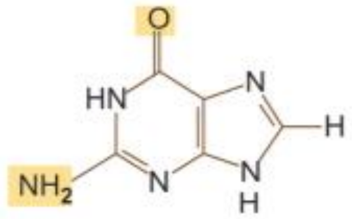
Two principal purine bases **adenine and guanine** are found in DNA and RNA.



Purine ring



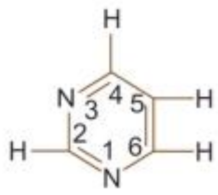
Adenine (6-aminopurine)



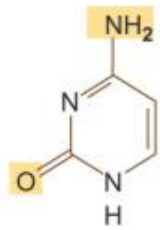
Guanine
(2-amino-6-oxypurine)

Pyrimidine bases:

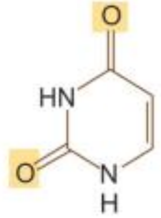
The major pyrimidine bases are **Cytosine, uracil and Thymine**:



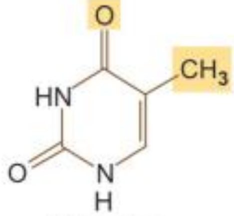
Pyrimidine ring



Cytosine
2-oxy-4-aminopyrimidine



Uracil
(2,4-dioxypyrimidine)

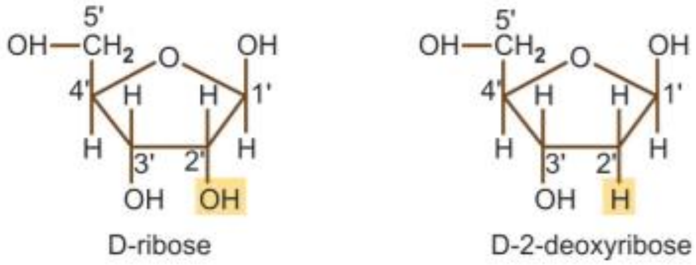


Thymine
(2,4-dioxy, 5-methyl pyrimidine)

Cytosine and uracil are found in RNA and **Cytosine and Thymine** in DNA.

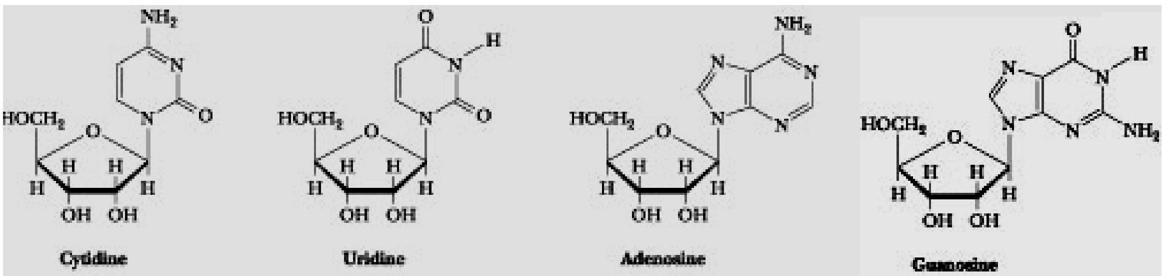
Pentose sugar:

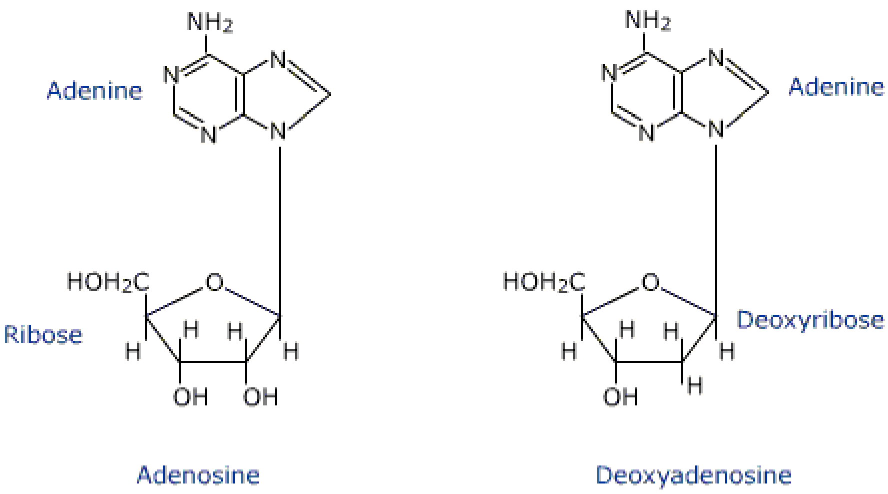
D- Ribose is a sugar that found in RNA, while D-2- Deoxyribose is a sugar that found in DNA, and they are present as the β- furanoside ring structure.



Nucleosides:

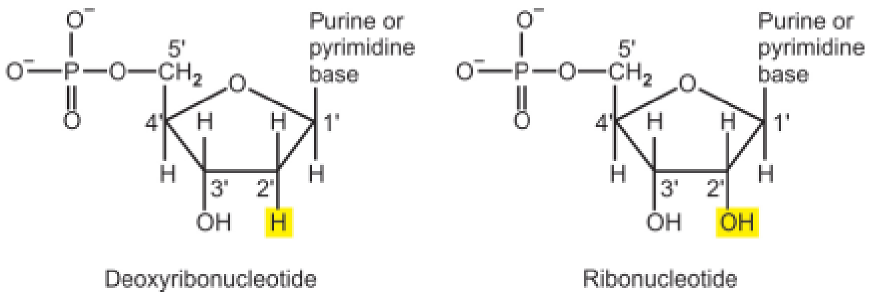
Nucleosides are compounds in which purine or pyrimidine bases linked to a sugar β-D- ribose or β-D- deoxyribose via a β-N-glycosidic linkage. This linkage joins nitrogen-9 of the purine base or nitrogen-1 of the pyrimidine base with C-1 of a sugar. The atoms of the base in nucleoside are given cardinal numbers, whereas the carbon atoms of the sugars are given prime number to distinguish sugar atoms from those of the base. Purine nucleosides have the suffix (-osine) and the pyrimidine nucleosides the suffix (-idine).



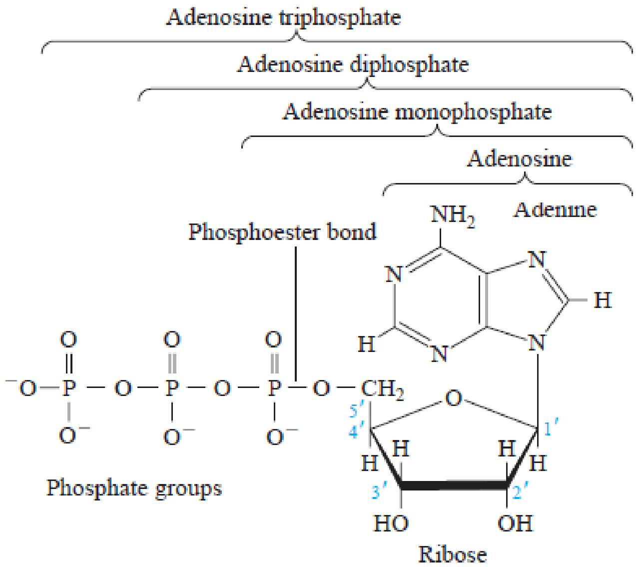


Nucleotides:

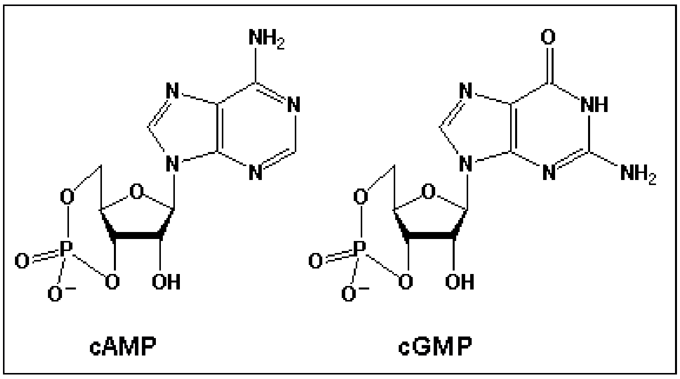
Nucleotides are nucleoside phosphates (phosphorylated nucleoside), in which the phosphate group is attached by an ester linkage to the–OH group of the pentose. The esterification of occurs on the 3^- or 5^- carbon of OH group of the sugar to obtain nucleoside-3^-- monophosphate (NMP). Most of the nucleoside phosphates involved in biological function are 5^- -phosphates. The nucleotides occur either in free form or as subunits in nucleic acids.



If an additional phosphate groups (one or two) is attached to the nucleoside monophosphate, nucleoside diphosphate (NDP) or nucleoside triphosphate (NTP) are formed



Besides, there are cyclic nucleotides where a phosphoric acid esterifies two hydroxyls of the pentose at a same time. Like 3-,5-cyclic Adenosine monophosphate (cAMP) and 3-,5- cyclic Guanine monophosphate (cGMP). Which play a role in various regulatory mechanisms.



Functions of nucleotides:

1- Polymers of nucleotides are the nucleic acids DNA&RNA.

2- Nucleotides play an important source of energy like ATP and GTP.

3- Nucleotides form part of Coenzymes like FAD, NAD, NADP and Coenzyme A.

4- Cyclic nucleotides act as a second messenger in the cell and they have regulatory functions.

5- Nucleotide diphosphate act as carrier molecules like UDP for monosaccharide.

6- Synthetic derivatives of nucleotides act as anticancer drugs like 5-fluorouracil.

Nucleic acids:

Nucleic acids are polymers of nucleotide; they are therefore called polynucleotides. The nucleotides are linked together by phosphodiester bonds between 3' –hydroxyl on the sugar of one nucleotide and the 5'-phosphate on the sugar of another nucleotides to form long chains of nucleotide. One end contains the free phosphate group (5' end) and the other contains the free hydroxyl at 3' end.

The nucleic acid is of two main categories:

1) Deoxyribonucleic acid (DNA) and

2) Ribonucleic acid (RNA).

Deoxyribonucleic acid (DNA)

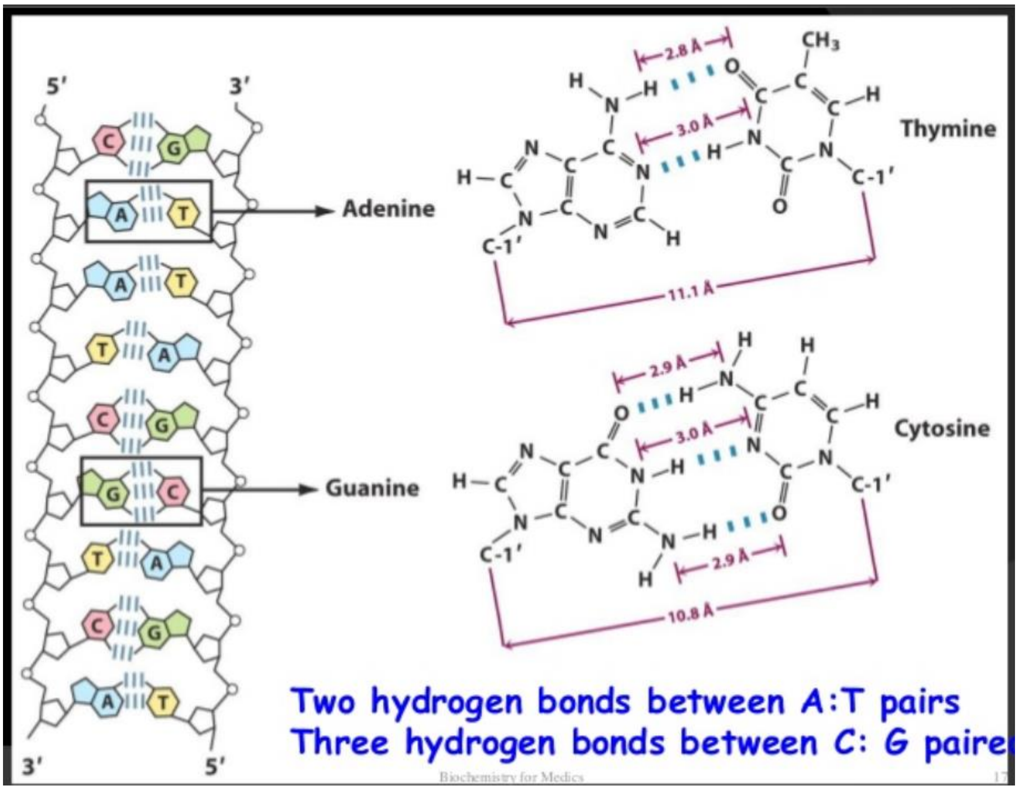
DNA serves as the genetic material for cell both prokaryotes and eukaryotes. DNA is present in nuclei and small amounts (less than 0.1%) are also present in mitochondria and present in chloroplast of plants. Many viruses also contain DNA as their genetic material.

DNA is a very long macromolecule made up of many deoxynucleotides (it may reach millions of nucleotide units). Each nucleotide composed of a nitrogenous base (Adenine, guanine, cytosine and thymine), a sugar (Deoxyribose) and phosphate group.

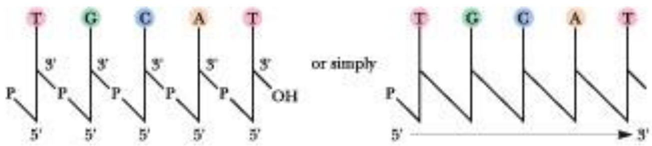
The nucleotides are arranged in chains linked together by a phosphodiester bonds between 5' carbon atom of a deoxyribose of one nucleotide and 3' carbon atom of the next. The chain begins with 5’ and ends with 3'.

The bases of DNA molecule carry genetic information, whereas their sugar and phosphate groups perform a structural role.

The resulting is long, unbranched DNA chain. One end of the chain have a free 5’ -hydroxyl group (5’ - end) and the other end have 3’ -hydroxyl group (3’ - end), then the sequence of DNA is written (5’ →3’).



DNA is formed of

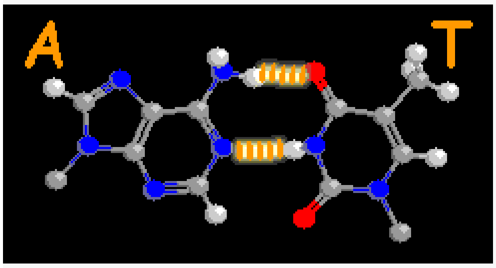
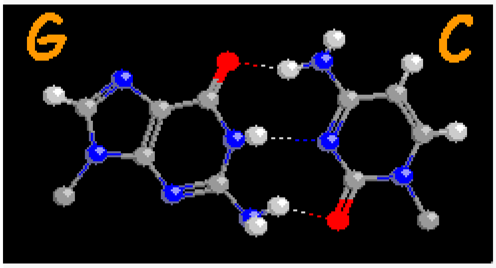


The Watson and Crick DNA Double Helical Structure

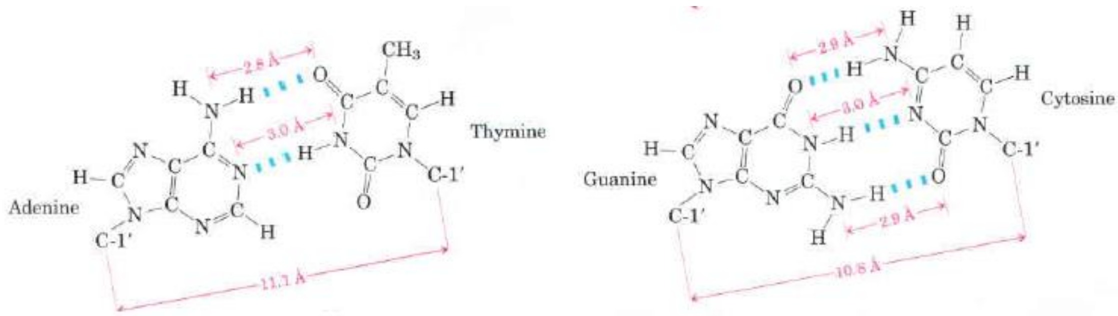
Watson and Crick described that DNA consists of two helical polydeoxyribonucleotide chains coiled a round a common axis. The chains run in opposite direction (anti parallel). The bases are on the inside of the helix, whereas the phosphate are deoxyribose and on the outside. The bases are perpendicular to the helix axis, while the sugars nearly at right angles to the axis.

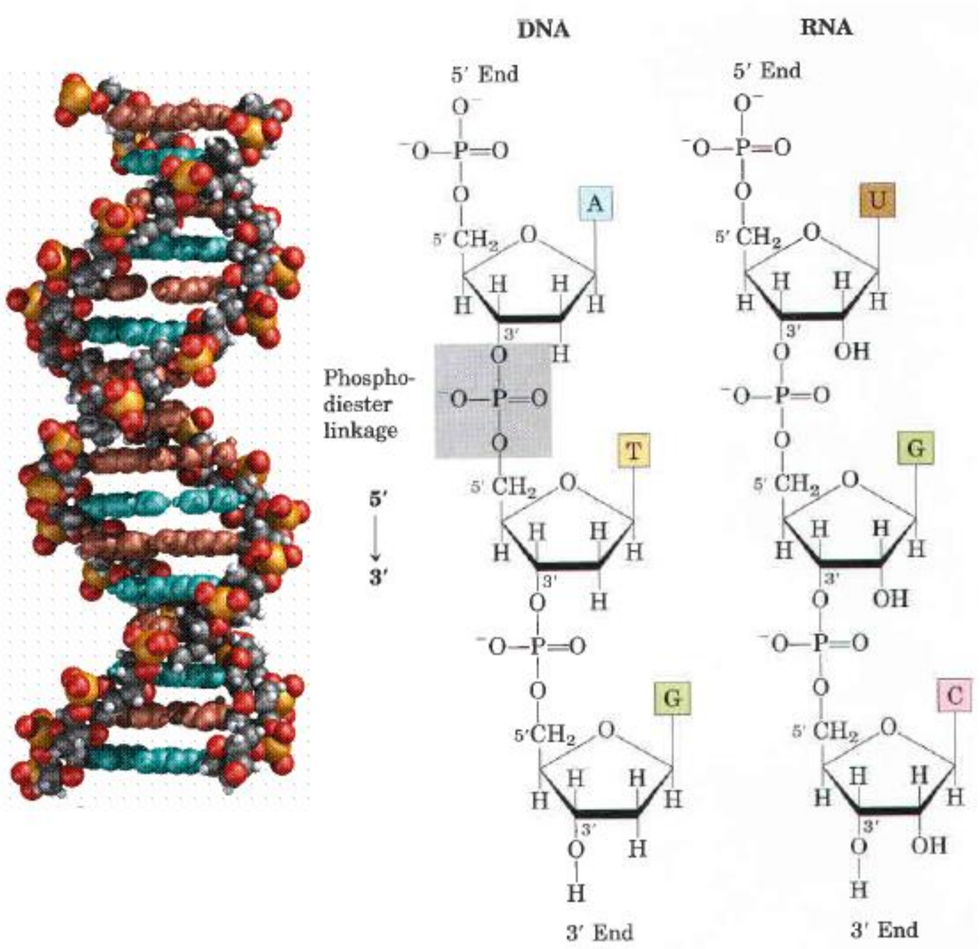
Always the two helixes are complementary to each other. Therefore, the Adenine of one helix (strand) will pair with the Thymine of the opposite helix, while Guanine will pair with Cytosine. The base pairing (A with T; G with C) is called Chargaff's rule, which states the number of purines equal to the number of pyrimidines.

The DNA helixes are held together by hydrogen bonds between the purine and pyrimidine bases. There are two hydrogen bonds between A and T while there are three hydrogen bonds between C and G. The GC bond is therefore stronger than AT bond.

Base pairs in DNA	
	
Adenine-Thymine base pair with two hydrogen bounds. C = Carbon = gray N = Nitrogen = blue O = Oxygen = red	Guanine-Cytosine base pair with three hydrogen bounds

The diameter of the double helix is 2nm (20A°). The helix complexes one turn every ten base pairs. One complete turn is 3.4nm (34A°). In other words, each helix contains 10 nucleotides.





Functions of DNA:

1) Carrying genetic information

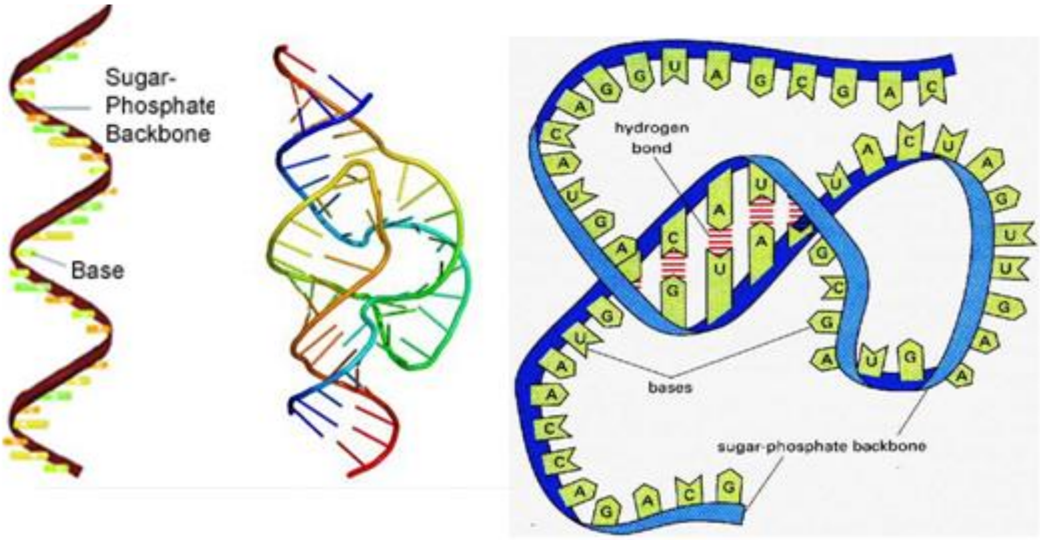
2) DNA controls the production of certain proteins in the cell.

Ribonucleic acids (RNA):

RNA is a single strand of polyribonucleotides of Adenine, Guanine, Cytosine and Uracil, linked by 3-, 5- -phosphodiester bonds. The pentose sugar is ribose.

RNA is found in the nucleolus, ribosomes, mitochondria and cytoplasm. In RNA, Adenine pairs with Uracil via two hydrogen bonds, but Guanine pairs with Cytosine via three hydrogen bonds.

RNA does contain regions of double helical structure that are produced by the formation of hairpin loops. RNA is capable of folding back on itself like a hairpin and thus forms the double stranded pattern.



Differences between RNA and DNA

1. In RNA, the sugar is ribose rather than 2'-deoxyribose of DNA.

2. RNA does not possess thymine except in the rare case. Instead of thymine, RNA contains uracil.

3. In RNA, adenine pairs with uracil rather than thymine.

4. RNA is a single stranded and does not exhibit the equivalence of adenine with uracil and cytosine with guanine

Types of RNA:

There are three types of RNA, and these types differ from each other by size and function. All of these are involved in some aspects in the protein biosynthesis.

1. **Messenger RNA (mRNA) : 5-10%**
2. **Transfer RNA (tRNA) : 10-20%**
3. **Ribosomal RNA (rRNA) : 50-80%**

Besides the three RNAs referred above, other RNAs are also present in the cells. These include heterogeneous nuclear RNA (hnRNA), small nuclear RNA (snRNA), small nucleolar RNA (snoRNA) and small cytoplasmic RNA (scRNA).

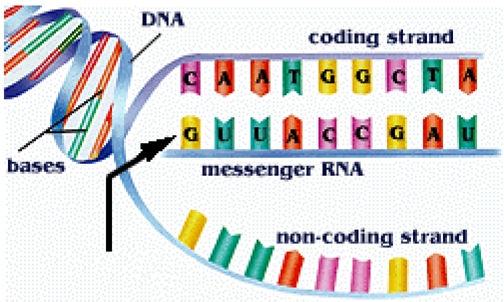
The RNAs are synthesized from DNA, and are primarily involved in the process of protein biosynthesis. The RNAs vary in their structure and function.

Messenger RNA:

The mRNA is a one stranded nucleic acid. It is produced on one of the DNA strands ‘in the nucleus in a process called (transcription). Hence, the base sequence of mRNA is complementary to that of the DNA strand. It encodes the information directing protein synthesis and make up about 21% of RNA in the cell. Formation of mRNA from coding (sense) strand of the DNA is the first step in the transcription It is composed of 400 - 4000 nucleotides.

The main Function of mRNA carries the genetic information from DNA of the nucleus to the cytosol, where it is used as the template for protein synthesis.

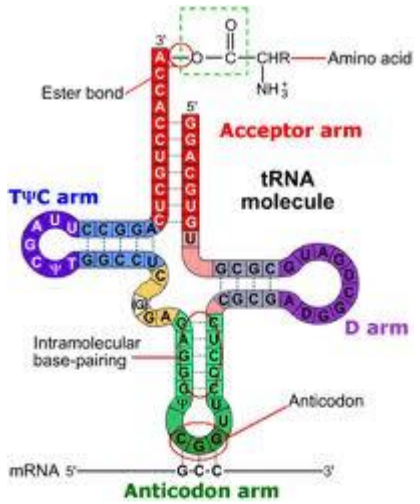
Information is organizing in DNA and in RNA in a sequence of three nucleotides called a codon. Each codon specifies one amino acid from wh ich proteins is made. The sequence of codons on the mRNA strand is called the mRNA language. It indicates the sequence of amino acids for the synthesis of a protein. The mRNA language begins with the codon AUG (initiation codon or starting codon) and ends with UAA, UAG or UGA (stop codons).



Transfer RNA (tRNA):

Transfer RNA (tRNA) molecules vary in length from 74 to 95 nucleotides. All tRNA molecules can form structures that appear like a clover leaf. One end of tRNA contains a three nucleotide sequence called anticodon loop that is complementary to the codon of the mRNA. The other end of the tRNA is covalently attached to a specific amino acid.

There are at least 20 different tRNA molecules one for each of the amino acids that is used in the synthesis of proteins. Many Amino acids have more than tRNA. tRNA carries amino acids in an inactive form to the ribosome for the translations (protein synthesis) of the information in the sequence of nucleotides of the mRNA.



Ribosomal RNA (rRNA):

It is the most stable and abundant form of RNA in living cells (in most cells), rRNA constitutes approximately 80% of the total amount of RNA.

The cytoplasmic ribosomes are the site of protein synthesis i.e. They contain enzymes needed for this process. rRNA is mostly in combination with proteins to form aggregates called as the ribosome. The ribosome has three sites for tRNA to bind. They are the aminoacyl site (abbreviated A-site), the peptidyl site (abbreviated P- site) and the exit site (abbreviated E- site). The function of rRNAs in ribosomes play a significant role in the binding of mRNA to ribosomes and protein synthesis

.