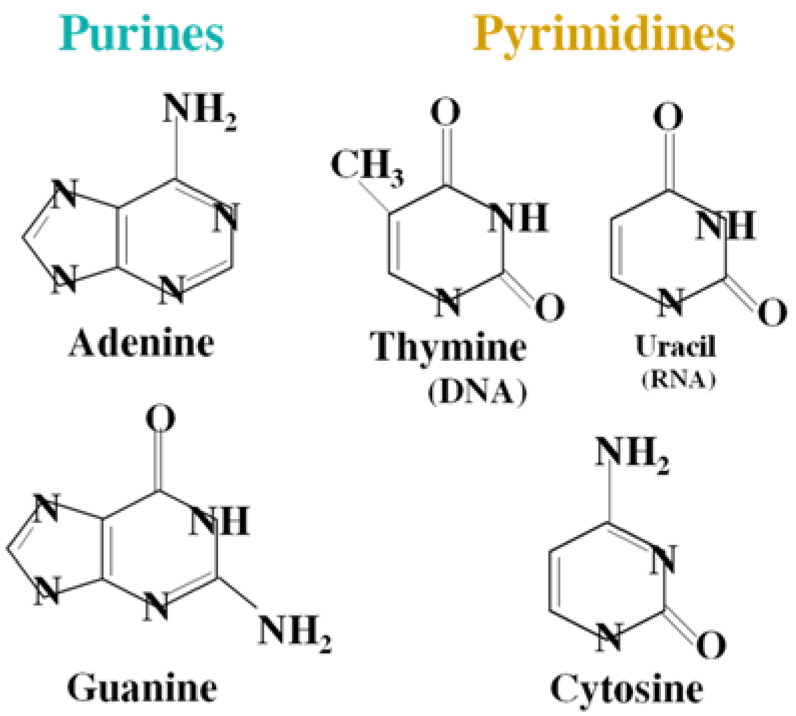
Lecture 26: Overview of deoxyribonucleic acid (DNA) and ribonucleic acid (RNA) structure

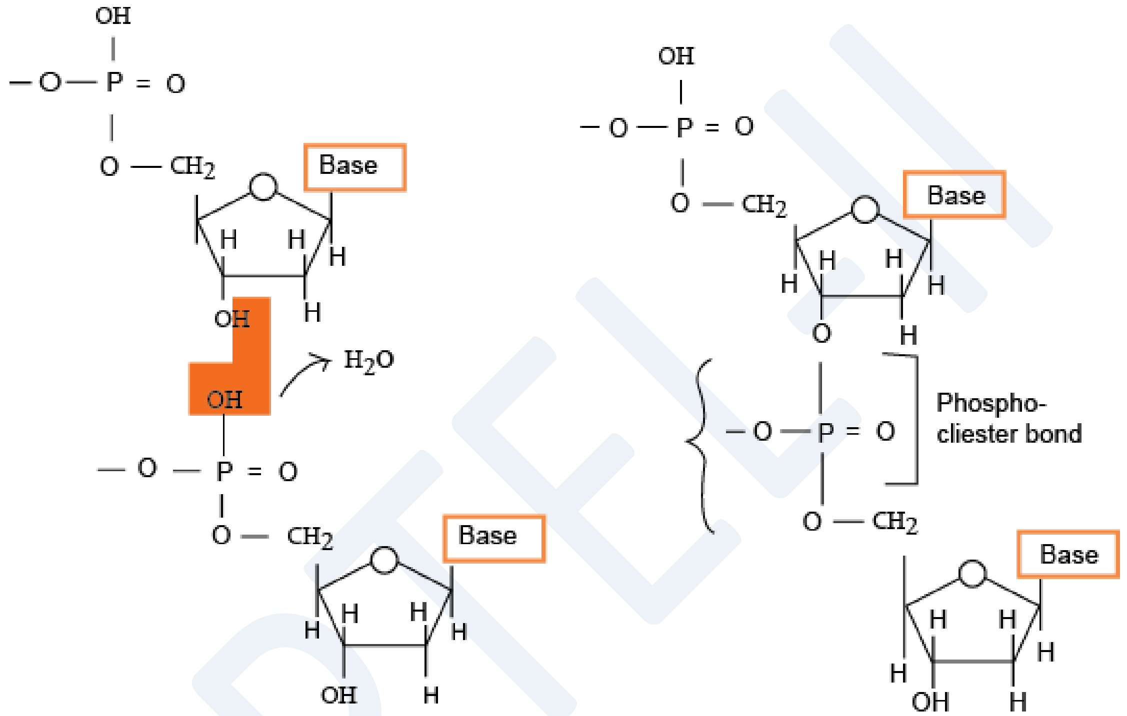
Nucleic acids play an important role in the storage and expression of genetic information. They are divided into two major classes: **deoxyribonucleic acid (DNA)** functions solely in information storage, while **ribonucleic acids (RNAs)** are involved in most steps of gene expression and protein biosynthesis. All nucleic acids are made up from **nucleotide** components, which consist of a nitrogenous base, a sugar and a phosphate residue. A sugar and a nitrogenous base without the phosphate group is called as a **nucleoside**. The nitrogenous bases are classified into two types:-

- Fused 5 & 6 membered rings (heterocyclic) called as **Purines** eg.: Adenine (A) and Guanine (G).
- Six membered rings called as the **Pyrimidines** eg: Thymine (T), Cytosine (C) and Uracil (U).

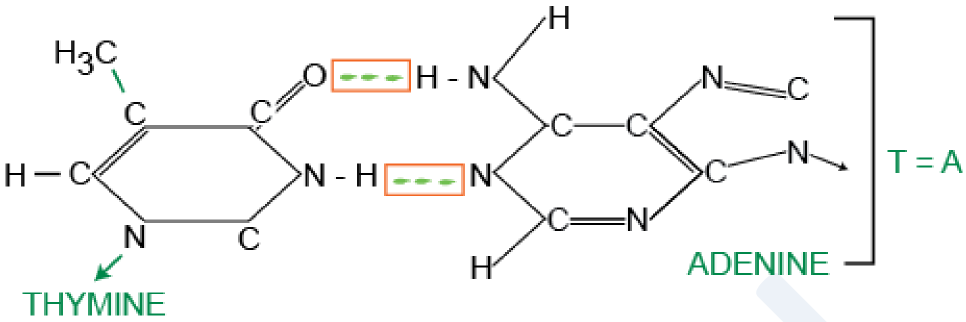
Free purines and pyrimidines are weakly basic and are thus called bases.

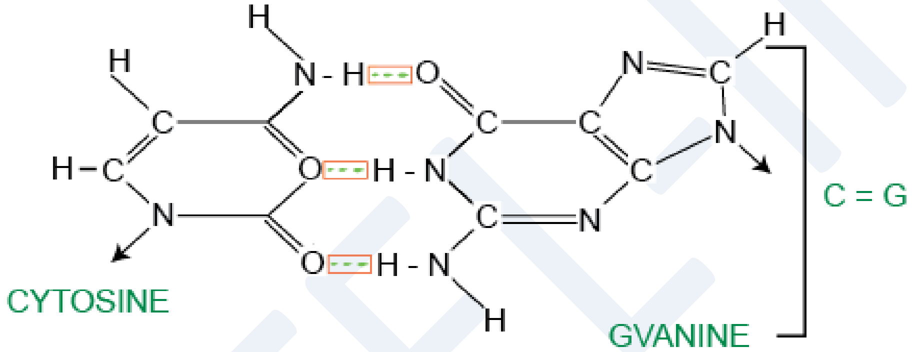


In a nucleotide the base is joined to 1' carbon of pentose by an N-β- glycosyl bond and a phosphate is esterified to 5' carbon. Phosphate of 5' carbon reacts with –OH group attached to 3' ribose sugar carbon. During this bond formation a water molecule is removed. This process is continued to make a polynucleotide with one end 3' sugar carbon attached -OH free (called 3' end) and at other end 5' sugar carbon attached phosphate free (called 5' end).



Structure: Using the methods of X- Ray diffraction, Rosalind Franklin and Maurice Wilkins showed that DNA produces a characteristic X- Ray diffraction pattern from which James Watson and Francis Crick deduced the double helical model of DNA structure showing two polynucleotide chains running in opposite directions and coiled around each other. Erwin Chargoff's findings published in 1949 was of great help in solving base-pairing mystery. He showed that even though different organisms have different amounts of DNA, percentage of adenine always equals thymine and percentage of guanine equals cytosine. This was possible only when adenine (A) pairs with thymine (T) and guanine (G) pairs with cytosine (C) in the double helix. Within the DNA double helix, adenine forms two hydrogen bonds with thymine on the opposite strand and guanine forms three hydrogen bonds with cytosine on the opposite strand. For discovery of DNA structure, Francis Crick, James Watson and Maurice Wilkins awarded Nobel Prize in Physiology and Medicine (1962).





The Nobel Prize in Physiology or Medicine 1962

Nobel Prize Award Ceremony

Francis Crick

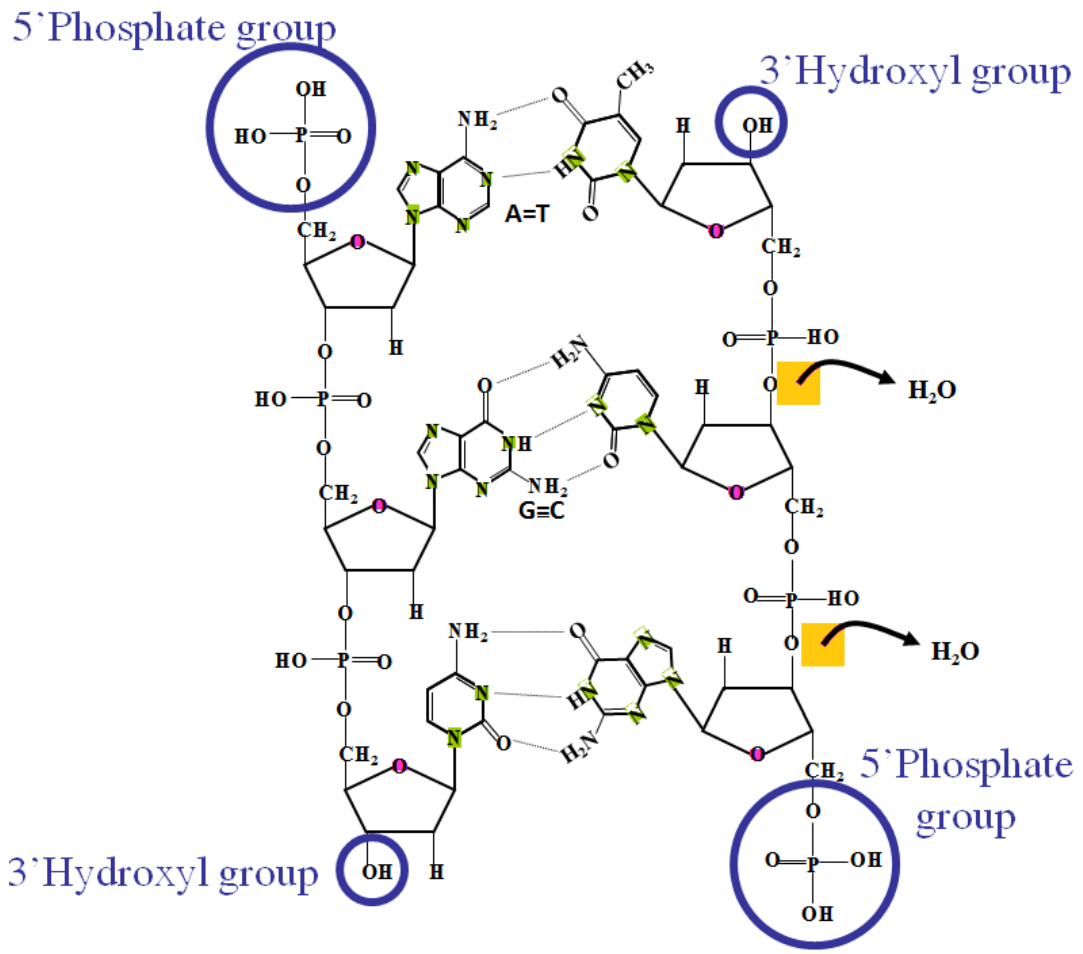
James Watson

Maurice Wilkins

Francis Harry Compton Crick | James Dewey Watson | Maurice Hugh Frederick Wilkins

The Nobel Prize in Physiology or Medicine 1962 was awarded jointly to Francis Harry Compton Crick, James Dewey Watson and Maurice Hugh Frederick Wilkins *"for their discoveries concerning the molecular structure of nucleic acids and its significance for information transfer in living material".*

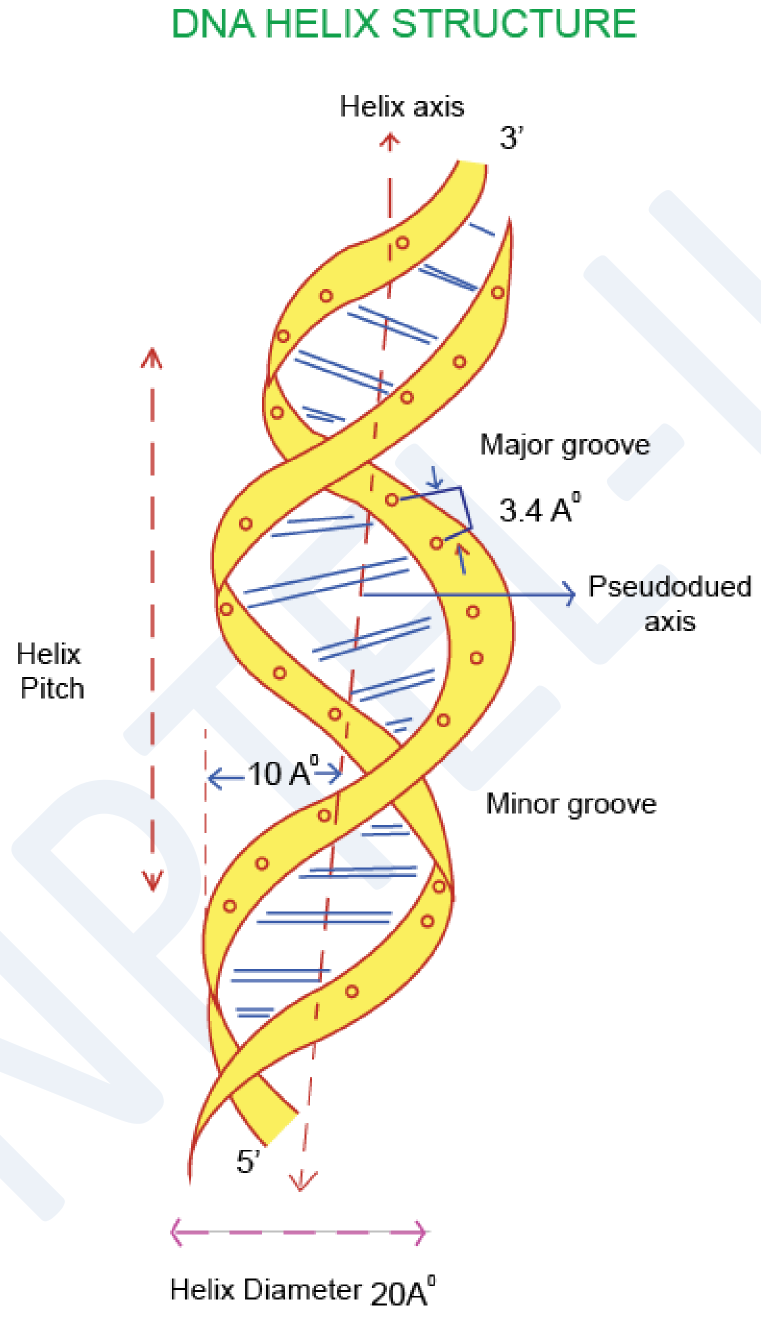
Taken from http://www.nobelprize.org/nobel_prizes/medicine/laureates/1962/index.html



The Watson and Crick structure of DNA (B-DNA) has following features:-

1) It consists of two antiparallel polynucleotide strands that wind about a common axis with a right handed twist to form a double helix.
2) The diameter of a double helix will be around 20 Å.
3) Each base is hydrogen bonded to a base on opposite strand (A with T and G with C) to form a planar base pair and the planes of these base pairs are nearly perpendicular to the helix axis.
4) The ideal B DNA helix has 10 base pairs per turn and the helix rotates 36° per base pair.
5) The helix has a pitch (the distance raised by common axis in a complete turn) of 34 Å. So the per base pair raise in common axis will be 3.4 Å.
6) The double helix has major and minor grooves.

Fibres of DNA assume the so called B- Conformation, when the counter ion is an alkali metal such as Na^+ and the relative humidity is >92%. It is the most stable structure for a random sequence of DNA and is therefore the standard point of reference.



The primary structure of DNA is simple covalent structure and is actually the nucleotide sequence. Secondary structure on the other hand represents any regular, stable structure taken up by some or all of the nucleotides in a nucleic acid. The further coiling and complex folding of large chromosomes within eukaryotic chromatin and bacterial nucleic acids are generally considered tertiary structures.

DNA can exist in 3 forms A, B & Z. Although only B- DNA and Z-DNA have been directly observed in functional organism. The conformation that DNA adopts depends on the hydration level, DNA sequence, the amount and direction of supercoiling, chemical modification of bases, type and concentration of metal ions as well as the presence of polyamines in the solution.

B form of DNA is most stable structures under physiological conditions.

A form is generally observed in partially dehydrated samples of DNA while in the cell it may be produced in hybrid pairings of DNA and RNA strands as well as in enzyme – DNA duplex complexes. DNA is still arranged in right handed double helix but the helix is wider and the number of base pairs per helical turn is 11 rather than 10 in B- DNA. The plane of Base pairs in A- DNA is tilted about 20° with respect to helix axis. These structural changes deepen the major groove while making minor groove shallower. The reagents used to promote crystallization of DNA tend to dehydrate it and thus most short DNA molecules tend to crystallize in the A form.

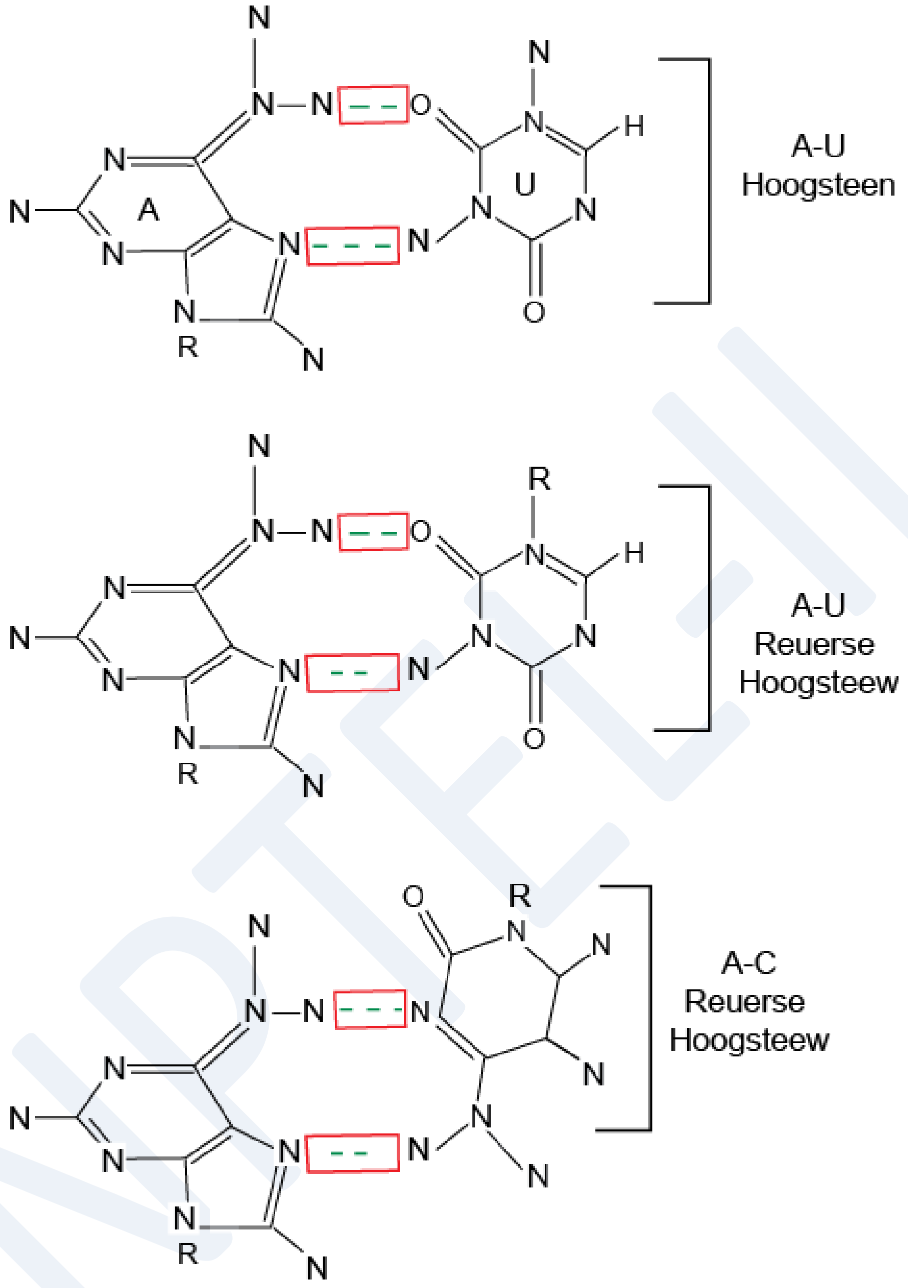
Z form on the other hand shows left handed helical rotation. There are 12 base pairs per helical turn and the structure appears more slender and elongated. DNA backbone takes a zig-zag appearance and that is the reason, why Z-DNA also known as zig-zag DNA. Sequences in which pyrimidine alternate with purines tend to form Z helices much more readily. In the left helices the purine residues flip to the syn conformation alternating with pyrimidines in the anti conformation.

Some Unusual structures

Bends occur in DNA helix wherever four or more adenosine residues appear sequentially in one strand. This bending may be important in binding of some proteins to DNA.

Some unusual structures involve three or even four DNA strands. As nucleotides participating in a Watson- Crick base pair can form a number of additional hydrogen bonds. The N- 7, O^6 and N^6 of purines, the atoms that participate in hydrogen bonding of triplex DNA are often referred to as Hoogsteen position and the non Watson – Crick pairing is called Hoogsteen pairing.

Hoogs Teen Base- Pairing



The triplexes are most stable at low pH, and are readily formed within long sequences containing only purines in a given strand. Tetraplex structures may also form in DNA sequences with a very high proportion of guanosine residues.

Another DNA structure called H- DNA is found in a polypyrimidine or polypurine tract that also incorporates a mirror repeat. Two of the three strands in H- DNA triplex helix contain pyrimidines and the third contains purines.

Solution of native DNA is highly viscous at pH 7.0 and room temperature (25°C). When such a solution is subjected to extremes of pH or temperature above 80°C its viscosity decreases sharply due to disruption of hydrogen bonds and base stacking leading to unwinding of DNA double helix to form two single strands.

Due to base interaction the DNA shows decreased UV absorption relative to that of a solution with same concentration of free nucleotides. This is called as hypochromic effect. Denaturation produces opposite effect leading to an increase in absorption called as hyperchromic effect.

Incubation of DNA at low pH (≈3) causes selective removal of the purine bases, resulting in a derivative called apurinic acid which is highly unstable.

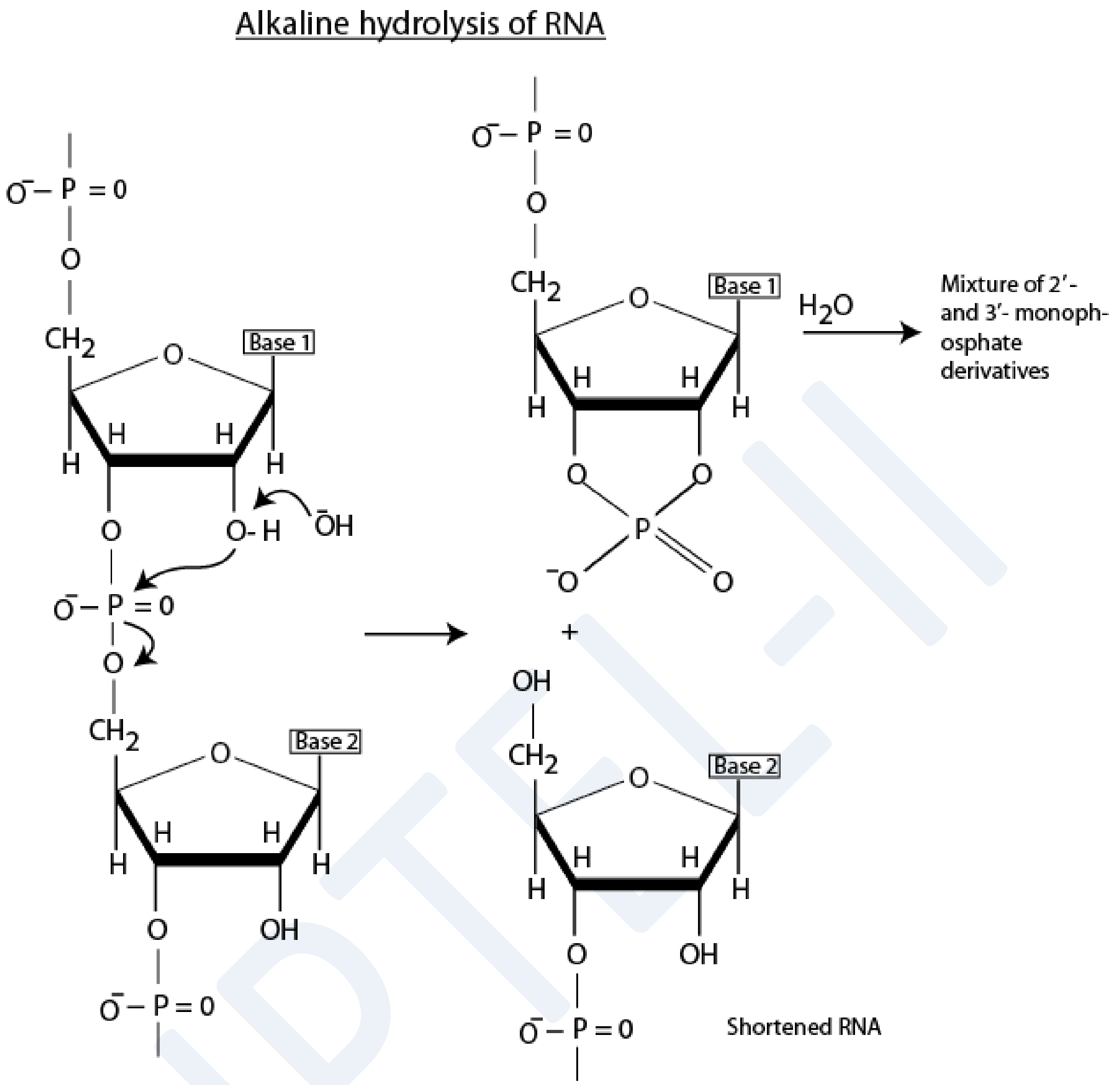
RNA (Ribonucleic acid):

Ribonucleic acid or RNA is the second major nucleic acid in cells, serves as genetic messenger, passing the information stored in DNA to other parts of cell for protein synthesis. In some cases as retro-viruses RNA is found as genetic material. Like DNA it is also a long unbranched polymer consisting of nucleotides joined by phosphodiester bonds in 5' to 3' direction. RNA differs from DNA in two respects…

1) Uracil (U) is found in RNA in place of Thymine (T).

2) The sugar units in RNA are ribose rather than deoxyribose (in DNA).

In addition to 3' - 5', a 2' - 5' linkage is also possible for RNA. This 2' – 5' linkage is important in the removal of introns and joining of exons for the formation of mature RNA during RNA splicing. Due to the presence of an OH group at C-2 , RNA is hydrolysed more rapidly under alkaline conditions. This OH group is directly involved in the formation of 2',3'- monophosphate nucleotides which are further hydrolysed to yield a mixture of 2' and 3' nucleoside monophosphate. This may be the reason why DNA is employed for storing the genetic information and not RNA.



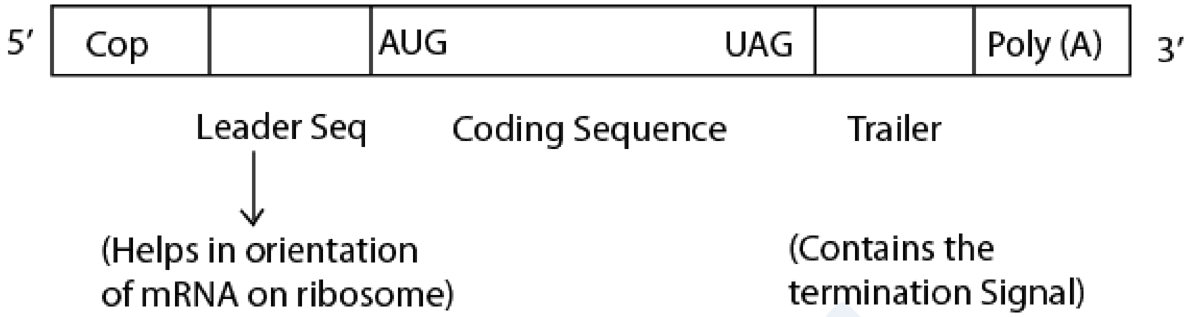
Wherever complimentary sequences are present in RNA, the predominant double stranded structure is an A form right handed double helix. Z form helices have been made in laboratory under very high salt concentration or high temperature conditions. B form of RNA has not been observed.

Due to unknown reasons, RNA duplexes are more stable than DNA duplexes. At neutral pH denaturation of a double helical RNA often requires a temperature 20°C or more than that for DNA.

Three major forms of RNA exist in any living cell…

1) **mRNA:** The process of transcription results the synthesis of mRNA from DNA. These mRNAs carries genetic information of DNA from nucleus to cytoplasm

(ribosome), the sites of protein synthesis. It can be monocistronic as in eukaryotes or polycistronic in prokaryotes.



Eukaryotic mRNA Molecule

2) **tRNA:** At the time of protein synthesis these RNAs recognises the coded genetic information of mRNA and brings specific amino acids at the site of growing poly peptide chain. There is at least one tRNA for each amino acid.
3) **rRNA:** It is synthesised in nucleolus. In cytoplasm ribosomal RNA and protein combine together to form a nucleoprotein called a ribosome.

   These are the most abundant form of RNA and counts about 80% of total cellular RNA.

Some Other functions of nucleotides…….

1) Nucleoside triphosphate (especially ATP) provides chemical energy to drive a wide variety of cellular reactions.
2) They serve as precursor for nucleic acid synthesis (phosphodiester linkage, phosphoanhydride linkage).
3) Adenine nucleotides are components of major enzyme cofactors.
4) Some nucleotides are regulatory molecules like cyclic AMP.