NUCLEIC ACID

Nucleic acids:

Nucleic acids are polynucleotides that is long chain like molecules composed of a series of nearly identical building blocks called nucleotides. Each nucleotide consists of a nitrogen containing aromatic base attached to a pentose (five-carbon) sugar, which is in turn attached to a phosphate group.

Nucleic acids are naturally occurring chemical compounds that serve as the primary information carrying molecules in cells. They play an especially important role in directing protein synthesis. nucleic acids which are polymers found in all living cells.

Types of nucleic acids

There are two types of nucleic acids:

- **DNA**
- **RNA**

Deoxyribonucleic Acid(DNA) is found mainly in the nucleus of the cell, while **Ribonucleic Acid(RNA)** is found mainly in the cytoplasm of the cell although it is usually synthesized in the nucleus.

Definition of DNA

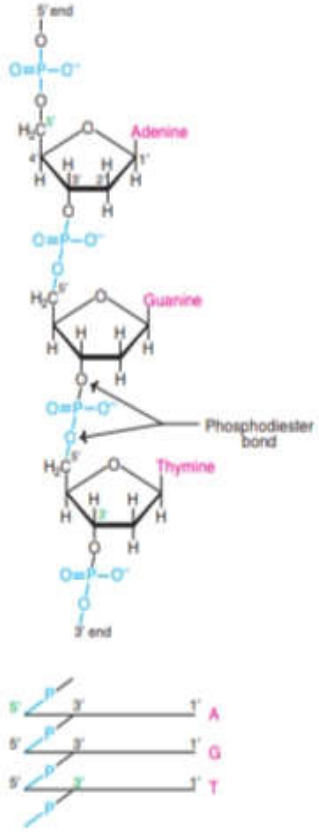
Deoxyribonucleic acid or DNA is a molecule that contains the instructions an organism needs to develop, live and reproduce. These instructions are found inside every cell, and are passed down from parents to their children.

Structure of DNA

DNA is a polymer of deoxyribonucleotides or deoxynucleotides. It is composed of monomeric units namely deoxyadenylate(dAMP), deoxyguanylate (d GMP), deoxycytidylate (d CMP) and deoxythymidylate (d TMP).

Schematic representation of polynucleotides

The monomeric deoxynucleotides in DNA are held together by 3',5'-phosphodiester bridges. DNA or RNA structure is often represented in a short hand form. The horizontal line indicates the carbon chain of sugar with base attached to C1, near the middle of the horizontal line is C3, phosphate linkage while at the other end of the line is C5, phosphate linkage

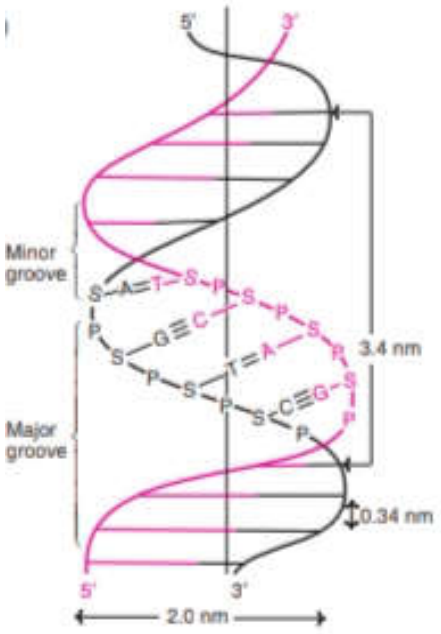


Chargaff's rule of DNA composition

Erwin Chargaff's in late 1940s qualitatively analysed the DNA hydrolysates from different species. He observed that in all the species he studied, DNA had equal numbers of adenine and thymine residues (A=T) and equal numbers of guanine and cytosine residues (G=C). This is known as Chargaff's rule of molar equivalence between the purines and pyrimidines in DNA structure. The significance of Chargaff's rule was not immediately realized. The double helical structure of DNA derives its strength from Chargaff's rule.

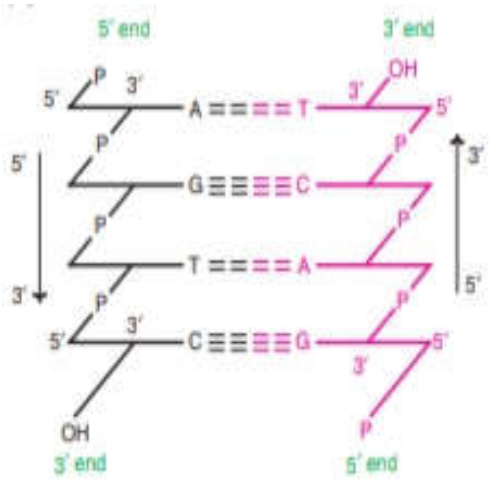
James Watson and Francis Crick Model (DNA DOUBLE HELIX)

The features of Watson-Crick model of DNA are described;

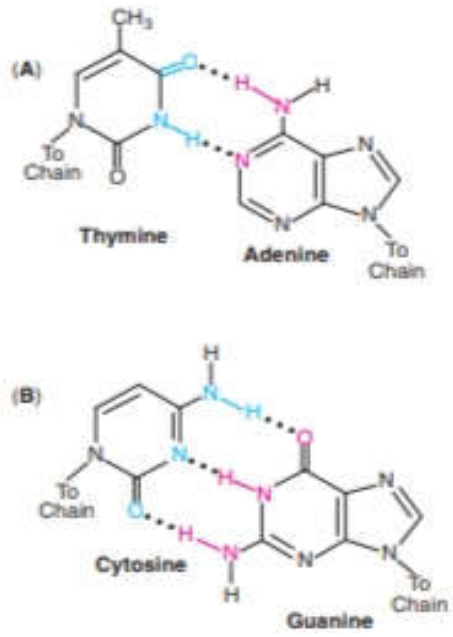


- The DNA is a right handed double helix. It consists of two polydeoxyribonucleotide chains (strand) twisted around each other on a common axis.

- The two strands are antiparallel i.e., one strand runs in the 5' to 3' direction while the other in 3' to 5' direction.
- The width or diameter of a double helix is 20 A^0
- Each turn of the helix is 34 A^0 (3.4nm) with 10 pairs of nucleotides, each pair placed at a distance of about 3.4 A^0
- Each strand of DNA has a hydrophilic deoxyribose phosphate backbone (3'-5' phosphodiester bonds) on the outside (periphery) of the molecule while the hydrophilic bases are stacked inside (core).
- The two polynucleotide chains are not identical but complementary to each other due to base pairing.



- The two strands are held together by hydrogen bonds formed by complementary base pairs. The A-T pair has 2 hydrogen bonds while G-C pair has 3 hydrogen bonds. The G-C is stronger by 50% than A = T.
- The Hydrogen bonds are formed between a purine and a pyrimidine only. If two purines face each other, they would not fit into the allowable space. And two pyrimidines would be too far to form hydrogen bonds. The only base arrangement possible in DNA structure is A-T, T-A, G-C and C-G.



- The complementary base pairing in DNA helix proves Chargaff's rule. The content of adenine equals to that of thymine (A =T) and guanine equals to that of cytosine (G=C).
- The genetic information resides on one of the two strands known as **template strands or sense strand**. The opposite strand is antisense strand. The double helix has (wide) major grooves and (narrow) minor grooves along the phosphodiester backbone. Proteins interact with DNA at these grooves without disrupting the base pairs and double helix.

DNA is a molecule composed of two polynucleotide chains that coil around each other to form a double helix carrying genetic instructions for the development, functioning, growth and reproduction of all known organisms and many viruses. DNA and RNA are nucleic acids. The two DNA strands are known as polynucleotides as they are composed of simpler monomeric units called nucleotides. Each nucleotide is composed

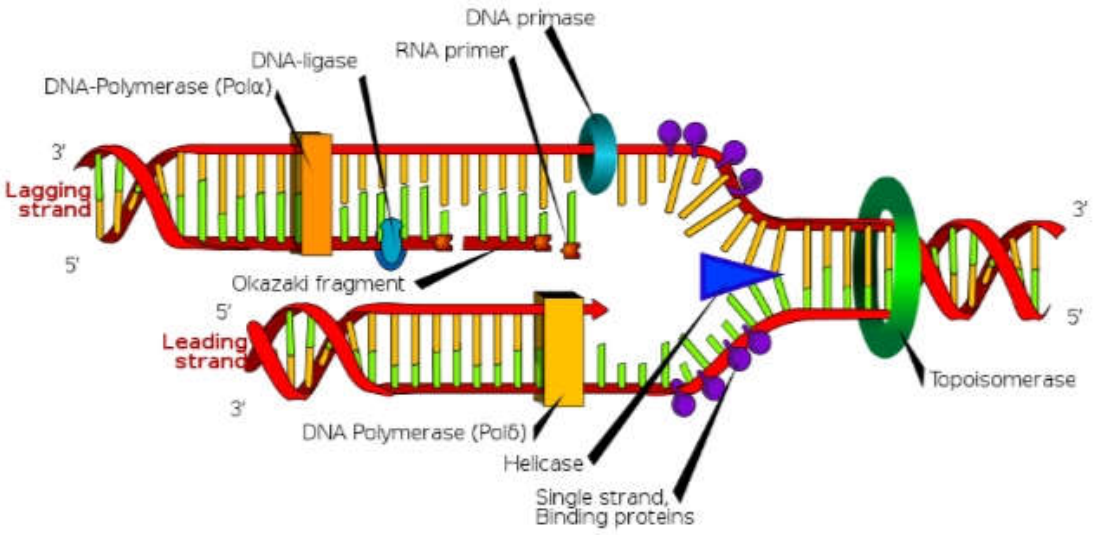
of one of four nitrogen containing nucleobases cytosine C, guanine G, adenine A or thymine T, a sugar called deoxyribose and a phosphate group. The nucleotides are joined to one another in a chain by covalent bonds (known as the phosphodiester linkage) between the sugar of one nucleotide and the phosphate of the next resulting in an alternating sugar phosphate backbone. The nitrogenous bases of the two separate polynucleotide strands are bound together, according to base pairing rules (A with T and C with G), with hydrogen bonds to make double stranded DNA. The complementary nitrogenous bases are divided into two groups, pyrimidines and purines. In DNA, the pyrimidines are thymine and cytosine; the purines are adenine and guanine.

Transcription and translation

A gene is a sequence of DNA that contains genetic information and can influence the phenotype of an organism. Within a gene, the sequence of bases along a DNA strand defines a messenger RNA sequences. The relationship between the nucleotide sequence of genes and the amino acid sequence of proteins is determined by the rules of translation known collectively as the genetic code. The genetic code consists of **codons** formed from a sequence of three nucleotides (e.g. ACT, CAG, TTT).

In transcription, the codons of a gene are copied into messenger RNA by **RNA polymerase.** This RNA copy is then decoded by a ribosome that reads the RNA sequence by base-pairing the messenger RNA to transfer RNA, which carries amino acids. There are 64 possible codons (4^3 combinations). These encode the twenty standard amino acids, giving most amino acids more than one possible codon. There are also three ‘stop’ or ‘nonsense’

codons signifying the end of the coding region, these are the TAA, TGA, and TAG codons.



The double helix is unwound by a helicase and topoisomerase. Next, one DNA polymerase produces the **leading strand** copy. Another DNA polymerase binds to the **lagging strand**. This enzyme makes discontinuous segments called **Okazaki fragments** before DNA ligase joins them together.

Replication

Cell division is essential for an organism to grow but when a cell divides, it must replicate the DNA in its genome so that the two daughter cells have the same genetic information as their parents. The double stranded structure of DNA provides a simple mechanism for DNA replication. Here, the two strands are separated and then each strands complementary DNA sequence is recreated by an enzyme called DNA polymerase. This enzyme makes the complementary strand through complementary base pairing and bonding it onto the original strand. DNA polymerases can only original strand. DNA polymerase can only extend a DNA strand in a 5' to 3' direction, different

mechanisms are used to copy the antiparallel strands of the double helix. In this way, the base on the old strand dictates which base appears on the new strand, and the cell up with a perfect copy of its DNA.

Conformation of DNA double helix

The double helical structure of DNA exists in at least 6 different forms A to E and Z. Among these B, A and Z forms are important. Each turn of the B-form has 10 base pairs at distance of 3.4 nm. The width of the double helix is 2 nm.

The **A-form** is also a right handed helix. It contains 11 base pairs per turn.

The **Z-form** (Z-DNA) is a left handed helix and contains 12 base pairs per turn. The polynucleotide strands of DNA move in a **'zig zag'** fashion, hence the name Z-DNA.

It is believed that transition between different helical forms of DNA plays a significant role in regulating gene expression.

Other types of DNA Structure

It is now recognized that besides double helical structure, DNA also exists in certain unusual structures. It is believed that such structures are important for molecular recognition of DNA by proteins and enzymes. Some selected unusual structures of DNA are briefly described.

Bent DNA

Adenine base containing DNA tracts are rigid and straight. Bent conformation of DNA occurs when A-tracts are replaced by other bases. Bending in DNA structure has also been reported due to photochemical damage or mispairing of bases. Certain antitumor drugs (e.g. cisplatin)

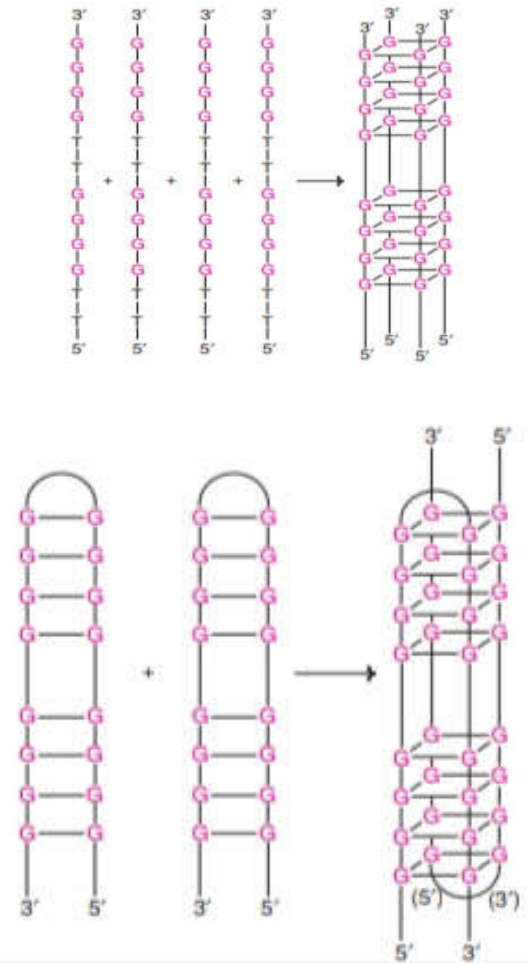
produce bent structure in DNA. Such changed structure can take up proteins that damage the DNA.

Triple-stranded DNA

Triple-stranded DNA formation may occur due to additional hydrogen bonds between the bases. Thus, a thymine can selectively form two **Hoogsteen hydrogen bonds** to the adenine of A-T pair to form **T-A-T.** likewise, a protonated cytosine can also form two hydrogen bonds with guanine of G-C pairs that results in C-G-C. triple helical structure is less stable than double helix. This is due to three negatively charged backbone strands in triple helix results in an increased electrostatic repulsion.

Four-stranded DNA

Polynucleotides with very high contents of guanine can form a novel tetrameric structure called **G-quartets.** These structures are planar and are connected by Hoogsteen hydrogen bonds. Antiparallel four-stranded DNA structures, referred to as **G-tetraplexes** have also been reported.



The ends of eukaryotic chromosomes namely **telomeres** are rich in guanine, and therefore form G-tetraplexes. Telomeres have become the targets for anticancer chemotherapies. G-tetraplexes have been implicated in the recombination of immunoglobin genes, and in dimerization of double-stranded genomic RNA of the immunodeficiency virus(HIV).

Size of DNA molecule

DNA molecules are huge in size. On an average, a pair of DNA with a thickness of 0.34 nm has a molecular weight of 660 daltons.

For the measurement of lengths, DNA double stranded structure is considered and expressed in the form of **base pairs (bp),** A **kilobase pair**

(kb) is 10^3 bp, and a **megabase pair (Mb)** is 10^6 bp and a gigabase (Gb) is 10^9 bp. The kb, Mb and Gb relations may be summarized as follows:

1kb = 1000bp

1Mb = 1000kp = 1,000,000 bp

1Gb = 1000Mb = 1,000,000,000 bp

It may be noted here that the lengths of RNA molecules cannot be expressed in bp, since most of the RNAs are single stranded. The length of DNA varies from species to species and is usually expressed in terms of base pair composition and contour length. Contour length represents the total length of the genomic DNA in a cell. Some examples of organisms with bp and contour lengths are listed.

ʎ phage virus – 4.8×10^4 bp --- contour length 16.5 µm.

Diploid human cell (46 chromosomes) – 6.0×10^9 bp --- contour length 2 meters.

The genomic DNA size is usually much larger the size of the cell or nucleus containing it. The genomic DNA may exist in linear or circular forms. Most DNA in bacteria exist as closed circles. This includes the DNA of bacterial chromosomes and the extra-chromosomal DNA of plastids. Mitochondria and chloroplasts of eukaryotic cells also contain circular DNA. Chromosomal DNAs in higher organisms are mostly linear. Individual human chromosomes contain a single DNA molecule with variable sizes compactly packed. Thus the smallest chromosome contains 34 Mb while the largest one has 263 Mb.

Denaturation of DNA Strands

The two strands of DNA helix are held together by hydrogen bonds. Disruption of hydrogen bonds (by change in PH or increase in temperature) results in the separation of polynucleotide strands. This phenomenon of **loss of helical structure of DNA is known as denaturation.**

The phosphodiester bonds are not broken by denaturation. Loss of helical structure can be measured by increase in absorbance at 260 nm (in a spectro-photometer). The phenomenon of increase in the absorbance of purines and pyrimidines is referred to as **hyperchromicity. Renaturation** is the process in which the separated complementary DNA strands can form a double helix.

Organization of DNA in the cell

- *Organization of prokaryotic DNA*
- *Organization of eukaryotic DNA*

Organization of prokaryotic DNA

In prokaryotic cells, the DNA is organized as a single chromosome in the form of a double stranded circle. These bacterial chromosomes are packed

in the form of nucleoids, by interaction with proteins and certain cations (polyamines).

Organization of eukaryotic DNA

In the eukaryotic cells, the DNA is associated with various proteins to form **chromatin** which then gets organized into compact structures namely **chromosomes.** The DNA double helix is wrapped around the core proteins namely **histones** which are basic in nature. The core is composed of two molecules of histones. Each core with two turns of DNA wrapped around it, is termed as a **nucleosome,** the basic unit of chromatin. Nucleosome are separated by spacer DNA to which histones H_1 is attached. This continuous string form of nucleosomes, representing beads on a string form of chromatin is 10 nm fiber.