Structure of DNA

The structure of DNA was found by Rosalind Franklin when she used x-ray crystallography to study the genetic material. DNA consists of a phosphate group, a sugar, and a nitrogenous base. DNA is helical, double-stranded macromolecule with bases projecting into the interior of the molecule. These two strands are always complementary in sequence.

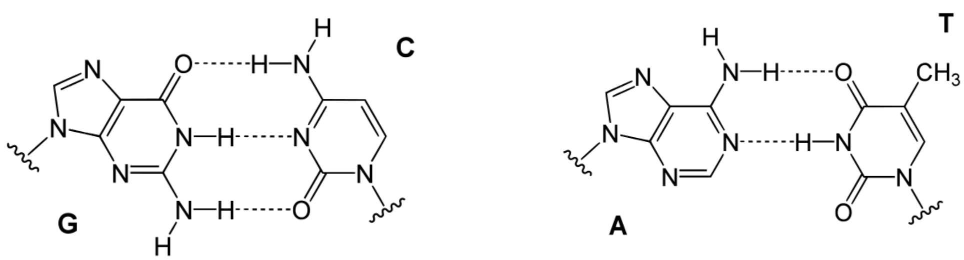
1. The outer edges of DNA are formed by alternating deoxyribose sugar molecules and phosphate groups, which make up the sugar-phosphate backbone.

2. The two strands run in opposite directions, one going in a 3' to 5' direction and the other going in a 5' to 3' direction.

3. A nucleoside and a phosphate group make up a nucleotide. The bond between the deoxyribose sugar of the nucleoside and the phosphate group is a 3'-5' phosphodiester linkage. DNA is composed of subunits called nucleotides. A nucleotide is made up of a sugar (deoxyribose), a phosphate group, and one of four nitrogenous bases: adenine (A), thymine (T), guanine (G) or cytosine (C).

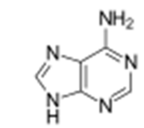
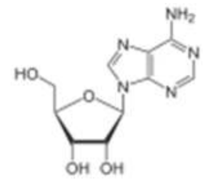
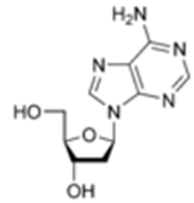
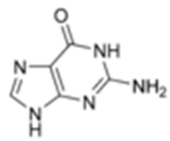
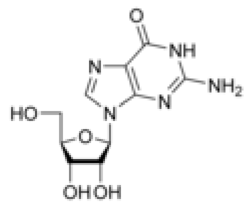
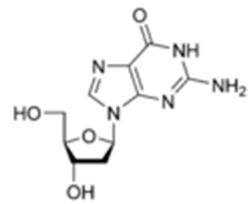
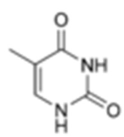
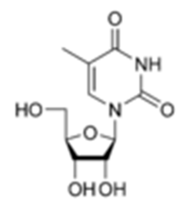
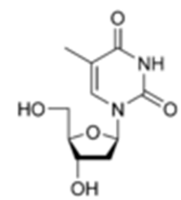
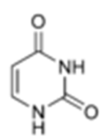
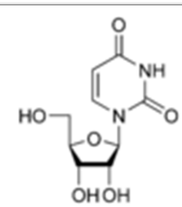
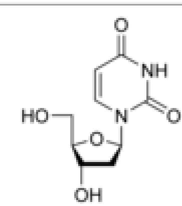
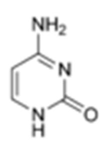
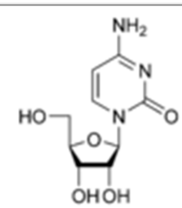
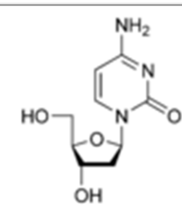
4. The nitrogenous bases are positioned inside the helix structure like "rungs on a ladder," due to the hydrophobic effect, and stabilized by hydrogen bonding. The H-bonds are formed between the base pairs of the anti-parallel strands. C and T bases, which have just one ring, are called pyrimidines, while A and G bases, which have two rings, are called purines.

5. The base in the first strand forms a H-bond only with a specific base in the second strand. Those two bases form a base-pair (H-bond interaction that keeps strands together and form double helical structure). The base–pairs in DNA are adenine-thymine (A-T) and cytosine-guanine (C-G). Such interactions provide us an understanding that nitrogen-containing bases are located inside of the DNA double helical structure, while sugars and phosphates are located outside of the double helical structure.



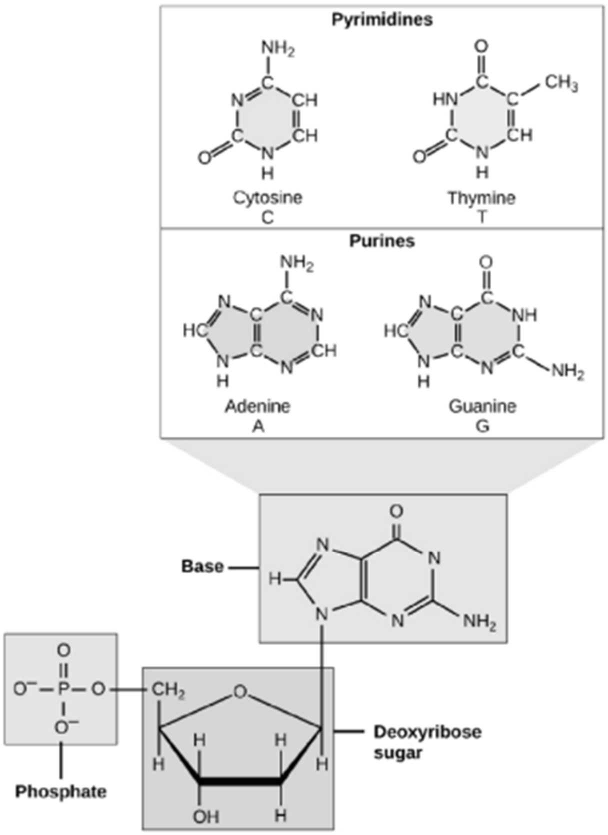
6. The component consisting of the base and the sugar is known as the nucleoside. DNA contains deoxyadenosine (deoxyribose sugar bonded to adenine), deoxyguanosine (deoxyribose sugar bonded to guanine), deoxycytidine (deoxyribose sugar bonded to cytosine), and deoxythymidine (deoxyribose sugar bonded to thymine).

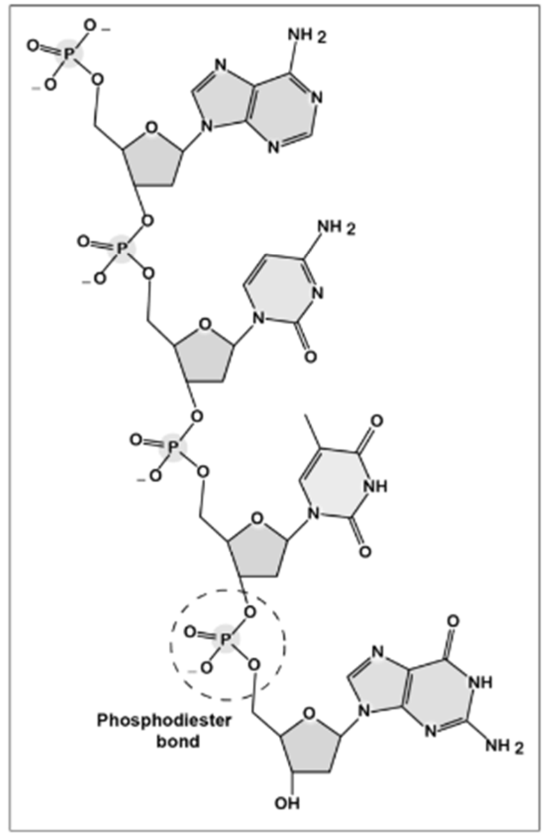
7. The linkage of the bonds between the bases to the sugar is known as the beta-N-Glycosidic linkage. In purines, this occurs between the N-9 and C-1' and in pyrimidines this occurs between the N-1 and C-1'.

Nitrogenous base	**Nucleoside**	**Deoxynucleoside**
 Adenine	 Adenosine A	 Deoxyadenosine dA
 Guanine	 Guanosine G	 Deoxyguanosine dG
 Thymine	 5-Methyluridine m^5U	 Deoxythymidine dT
 Uracil	 Uridine U	 Deoxyuridine dU
 Cytosine	 Cytidine C	 Deoxycytidine dC

9. The bases, located inside the double helix, are stacked. Stacking bases interact with each other through the Van der Waals forces. Although the energy associated with a Van der Waals interaction is relatively small, in a helical structure, a large number of atoms are intertwined in such interactions and the net sum of the energy is quite substantial.

10. The distance between two neighboring bases that are perpendicular to the main axis is 3.4 Å. The DNA structure is repetitive. There are ten bases per turn that is the structure repeats after 34 Å, so every base has a 36° angle of rotation. The radius of the double helix is approximately 10 Å.





A, B and Z DNA

A-DNA

The A-form of DNA is found at 75% relative humidity in the presence of Na^+, K^+ or Cs^+ ions. It contains eleven base pairs as compared to ten base pairs of B-DNA which tilt from the axis of helix by 20.2°. Due to this displacement the depth of major groove increases and that of minor groove decreases. The A-form is metastable and quickly turns to the D-form.

B-DNA

Structure of B-form of DNA has been proposed by Watson and Crick. It is present in every cell at a very high relative humidity (92%) and low concentration of ions. It has antiparallel double helix, rotating clockwise (right hand) and made up of sugar- phosphate back bone combined with base pairs or purine-pyrimidine.

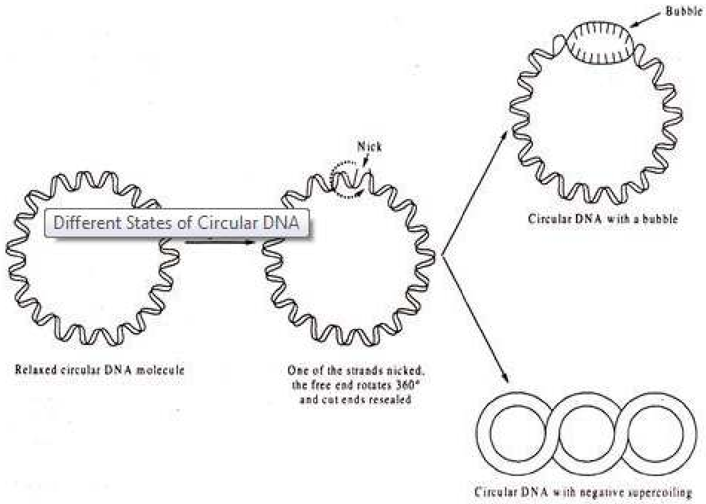
Z-DNA

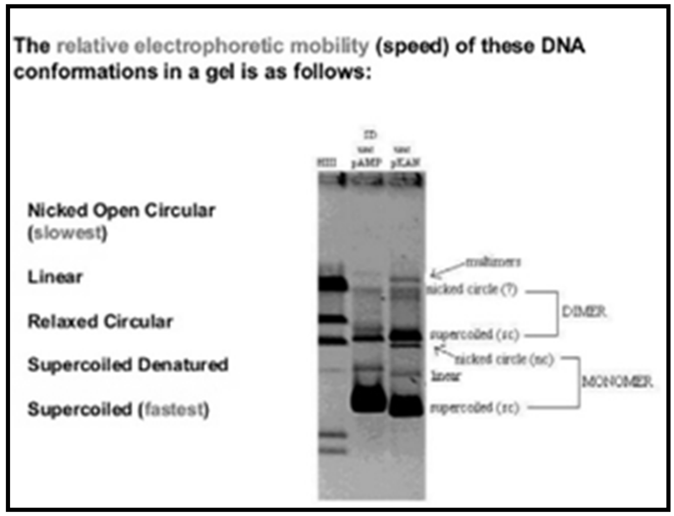
In 1979, Rich and coworkers at MIT (U.S.A.) obtained Z-DNA by artificially synthesizing d (C-G) 3 molecules in the form of crystals. They proposed a left handed (synistral) double helix model with zig-zag sugar-phosphate back bone running in antiparallel direction. Therefore, this DNA has been termed as Z-DNA. The Z-DNA has been found in a large number of living organisms including mammals, protozoans and several plant species.

	A-DNA	B-DNA	Z-DNA
Helix turn	Right handed	Right handed	Left handed
Helical diameter	26 Å	20 Å	18 Å
Height of helical turns (helical pitch)	28.6 Å	34Å	44Å
Number of base pairs per helical turn	11.6	10	12 (6 dimers)
Helical twist per base pair	31^0	36^0	9^0 or 51^0
Distance between each base pair (helical rise/base pair)	2.9 Å	3.4 Å	7.4 Å
Base tilt to the normal helical axis	20^0	6^0	7^0
Major grove	Narrow and deep	Wide and deep	Flat major groves
Minor grove	Wide and shallow	Narrow and deep	Narrow and deep
Ribose sugar conformation	C3' endo	C2'endo	C2' endo for pyrimidine and C3' endo for purine
Glycosidic bond conformation	Anti-	Anti-	Anti- for pyrimidine and Syn- for purine

Circular and Super Helical DNA

Almost in all the prokaryotes and a few viruses, the DNA is organised in the form of closed circle. The two ends of the double helix get covalently sealed to form a closed circle. Thus, a closed circle contains two unbroken complementary strands. Sometimes one or more nicks or breaks may be present on one or both strands, for example DNA of phage PM2. Besides some exceptions, the covalendy closed circles are twisted into super helix or super coils and is associated with basic proteins but not with histones found with all eukaryotic DNA.





Single Stranded (ss) DNA

Almost all the organisms contain double stranded DNA except a few viruses such as bacteriophage ϕ × 174 which consists of single stranded circular DNA. It becomes double stranded only at the time of replication.

The differences of ssDNA from the dsDNA

(a) The dsDNA absorbs wavelength 2600 Å of ultra violet light constantly from 0 to 80°C, thereafter rise sharply, whereas in ssDNA absorption of UV light increases steadily from 20° to 90°C.

(b) The dsDNA resists the action of formaline due to closed reactive site, while the ss DNA does not resist it due to exposed reactive sites.

(c) Base pair composition in dsDNA is equal i.e. A=T and G=C, in ssDNA the composition of A, T, G, C is in proportion of 1:1.33:0.98:0.75.

(d) The dsDNA always remains in linear helical form, while the ssDNA remains in circular form; however, it becomes double stranded only during replication (i.e. replicative form).

Watson, Crick, and Rosalind Franklin

In the early 1950s, American biologist James Watson and British physicist Francis Crick came up with their famous model of the DNA double helix. They were the first to cross the finish line in this scientific "race," with others such as Linus Pauling (who discovered protein secondary structure) also trying to find the correct model.

Rather than carrying out new experiments in the lab, Watson and Crick mostly collected and analyzed existing pieces of data, putting them together in new and insightful ways. Some of their most crucial clues to DNA's structure came from Rosalind Franklin, a chemist working in the lab of physicist Maurice Wilkins.

Franklin was an expert in a powerful technique for determining the structure of molecules, known as X-ray crystallography. When the crystallized form of a molecule such as DNA is exposed to X-rays, some of the rays are deflected by the atoms in the crystal, forming a diffraction pattern that gives clues about the molecule's structure.

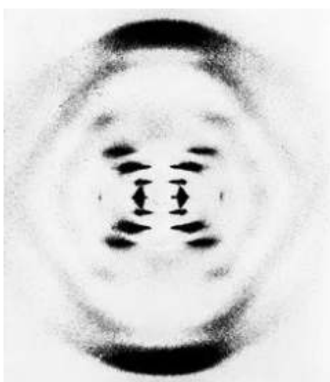


Figure: X-ray diffraction image of B DNA.

Franklin's crystallography gave Watson and Crick important clues to the structure of DNA. Some of these came from the famous "image 51," a remarkably clear and striking X-ray diffraction image of DNA produced by Franklin and her graduate student. To Watson, the X-shaped diffraction pattern of Franklin's image immediately suggested a helical, two-stranded structure for DNA.

Watson and Crick brought together data from a number of researchers (including Franklin, Wilkins, Chargaff, and others) to assemble their celebrated model of the 3D structure of DNA. In 1962, James Watson, Francis Crick, and Maurice Wilkins were awarded the Nobel Prize in Medicine. Unfortunately, by then Franklin had died, and Nobel prizes are not awarded posthumously.

Watson and Crick's model of DNA

J.D.Watson and F.H.C. Crick (1953) combined the physical and chemical data, and proposed a double helix model for DNA molecule. This model is widely accepted. The structure of DNA, as represented in Watson and Crick's model, is a double-stranded, antiparallel, right-handed helix.

Sugar-phosphate backbone and nitrogenous bases

The sugar-phosphate backbones of the DNA strands make up the outside of the helix, while the nitrogenous bases (Adenine, Guanine, Cytosin and Thymine) are found on the inside and form hydrogen-bonded pairs that hold the DNA strands together.

Base pairing

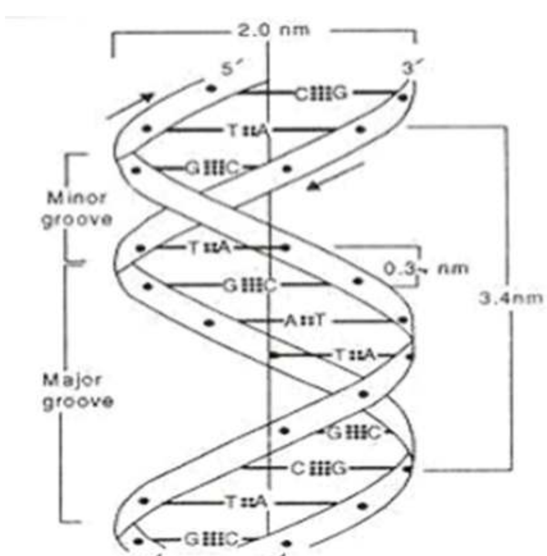
In Watson and Crick's model, the two strands of the DNA double helix are held together by hydrogen bonds between nitrogenous bases on opposite strands. Each pair of bases lies flat, forming a "rung" on the ladder of the DNA molecule.

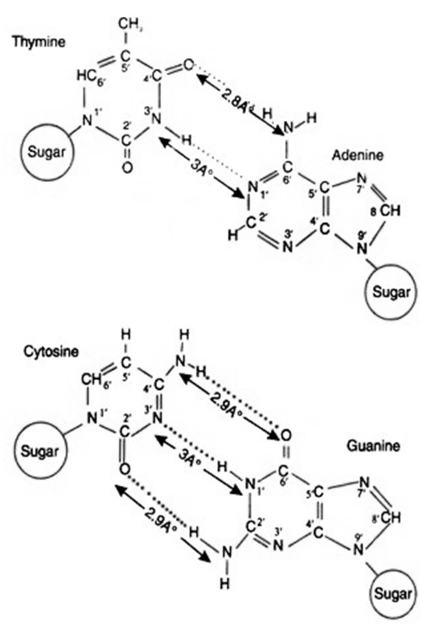
Base pairs aren't made up of just any combination of bases. Instead, if there is an A found on one strand, it must be paired with a T on the other (and vice versa). Similarly, a G found on one strand must always have a C for a partner on the opposite strand. These A-T and G-C associations are known as complementary base pairs.

Base pairing explains Chargaff's rules, that is, why the A always equals that of T, and C equals that of G. DNA from any cell of all organisms should have a 1:1 ratio (base Pair Rule) of pyrimidine and purine bases.

Where there is an A in one strand, there must be a T in the other, and the same is true for G and C. Because a large purine (A or G) is always paired with a small pyrimidine (T or C), the diameter of the helix is uniform, coming in at about 20 Å. Adjacent bases are separated 0.34 nm or by 3.4 Å along the axis. The length of a complete turn of helix is 3.4 nm or 34 Å i.e. there are 10bp per turn.

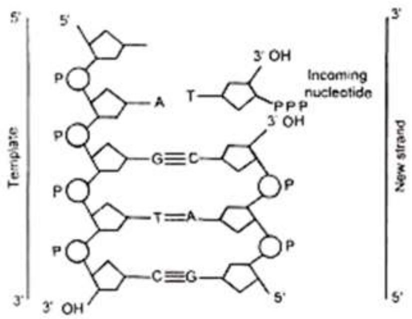
Although Watson and Crick's original model proposed that there were two hydrogen bonds between the bases of each pair, but actually G and C form an additional bond (such that A-T pairs form two hydrogen bonds total, while G-C pairs form three).





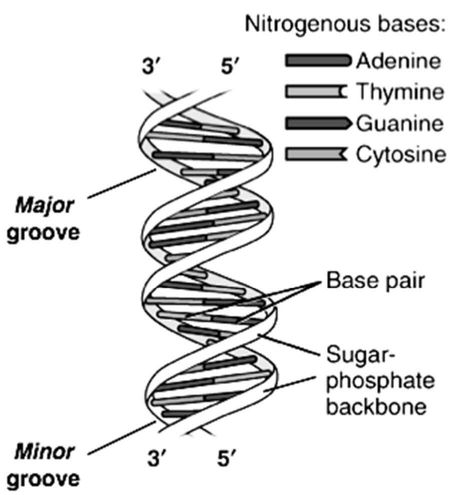
Antiparallel orientation

Double-stranded DNA is an antiparallel molecule, meaning that it's composed of two strands that run alongside each other but point in opposite directions. In a double-stranded DNA molecule, the 5' end (phosphate-bearing end) of one strand aligns with the 3' end (hydroxyl-bearing end) of its partner, and vice versa.



Right-handed helix

In Watson and Crick's model, the two strands of DNA twist around each other to form a right-handed helix. All helices have a handedness, which is a property that describes how their grooves are oriented in space.



The twisting of the DNA double helix and the geometry of the bases creates a wider gap (called the major groove) and a narrower gap (called the minor groove) that run along the length of the molecule, as shown in the figure above. These grooves are important binding sites for proteins that maintain DNA and regulate gene activity.

Biological Importance of DNA:

1. Hereditary material

The genetic information stored in the nucleotide sequence of DNA helps in synthesis of specific proteins or polypeptides and transmit the information to daughter cells or offsprings. Thus, DNA is called as molecular blueprint or thread of life.

2. Autocatalytic role DNA

DNA undergoes replication (self-duplication) in the S-phase of cell cycle. During the process each DNA strand of a double helix can act as template for the synthesis of daughter strand.

3. Heterocatalytic role

During transcription any one strand of DNA acts as template for the synthesis of RNA. This is called the heterocatalytic role of RNA.

4. Variations

DNA undergoes recombination its meiosis and occasional mutation (changes in nucleotide sequences) which creates variations in population and ultimately contributes to evolution.

5. Growth metabolism and differentiation

DNA controls cellular metabolism, growth, and differentiation.

6. DNA finger printing (-DNA typing or profiling)

Each individual carries specific short nucleotide repeats which are called as minisatellites or VNTRs (Variable Number of Tandem Repeats). The VNTRs of two individuals are variable and forms the basis of DNA fingerprinting. This technique is used to identify criminals, determine paternity, verification of immigrant etc.

7. Recombinant DNA technology (Genetic engineering)

It involves the artificial cleaving and rejoining DNA sequences from two or more organisms to create recombinant DNA. This technology is employed for production of genetically modified organisms (GMOs), genetically modified foods (GMFs), vaccines, hormones, enzymes, clones etc. It is also used for construction of probes (short polynucleotide chain attached to a radioactive or fluorescent marker) for diagnosis of diseases und curing hereditary diseases by replacing a faulty gene with a normal gene (gene therapy), formation of clones etc.