Structure of nucleic acid:

A DNA is composed of 3 components:

1) Aromatic bases (purine and pyrimidine)
2) Ribose sugar
3) Phosphate groups.

I. BASES:
The different placement of H-bond donor (NH2) and acceptor (C=O) give them a unique structural identity and allows them to be the genetic information carriers.

a. PURINES: (adenine and guanine)
The purine rings are composed of carbon and nitrogen into two rings of 5 and 6 members. Adenine and guanine are the two common purine bases found in DNA and RNA. Purines are derived from the nucleotide inosine monophosphate (IMP). Where inosine is the last common intermediate in the cycle.

Adenine: NH2 on C6.
Guanine: NH2 on C2 and C=O (carbonyl) on C6.

b. PYRIMIDINES: (thymine, cytosine and uracil)
These are 6-member rings. Uracil is present in RNA at the place of thymine.
Thymine has a methyl group at C5 along with C=O (carbonyl) at C2 and C4.
Cytosine has an amino (NH2) at C4 and C=O at C2.
The only difference between uracil and thymine is the methyl group on the 5th Carbon.
II. SUGAR:
   a) Ribose sugar of RNA:
      Source: 5-phosphoribosyl pyrophosphate (PRPP) derived from α-D-ribose-5-phosphate. Both purines and pyrimidines are synthesized on β-D-ribose ring.

   b) Deoxy Ribose sugar of DNA:
      When the hydroxyl ion of the 2’ position of β-D-ribose is converted to hydrogen group by the enzyme ribonucleotide reductase, then it is called β-D-deoxyribose sugar.

III. NUCLEOSIDES AND NUCLEOTIDES:
   Nucleosides are the combination of base and sugar and are named adenosine, guanosine, thymidine, cytidine. Whereas the term nucleotide is the used for the combination of base sugar and the phosphate group. The phosphate group is attaches to the sugar at the 5’C, base is attached at the 1’C by the help of glycosidic bond on which the base is free to rotate forming two confirmations namely syn and anti. The anti-confirmation is generally seen in DNA like the B-form DNA whereas the syn form is found in Z-form DNA.

IV. PHOSPHODIESTER BOND:
   The nucleotides are joined by phosphodiester bond from 3’ sugar of one base to 5’ sugar of the next base or vice-versa. So hence it is called 3’ – 5’ phosphodiester bond. This bond is formed with the help of DNA polymerase (RNA polymerase in RNA). Nuclease is the enzyme that cut the DNA by cleaving the phosphodiester bonds.

Structure of Double Stranded DNA:
Watson and crik first proposed the right handed double helix structure. It’s made of two individual strands aligned in anti-parallel fashion. These two strands are held together by H-bonds. The bases are stacked over each other near the cylindrical helix, which provides
considerable stability. The sugar and the phosphate are outside the helix and is known as the backbone of the helix.

The points that helped the development of this model are:

a) Chargaff’s Rules: the amount of adenine is equal to the amount of thymine and the amount of guanine is equal to the amount of cytosine.
b) X-ray diffraction of DNA showed that the genomic shape of DNA is a right-handed helix.

I. Hydrogen bonding:
A hydrogen bond is a short, non-covalent bond between a H-bond donor (nitrogen or oxygen) H-bond acceptor (C=O and N:). The N and O atoms of the H-bond are separated by 2.82 – 2.91 Å in A and T pair with 2 H-bonds and 2.84 – 2.92 in G and C pair with 3 H-bonds. Although H-bonds are directional they can be deformed by stretching and bending.

II. Base stacking:
Aromatic bases are planar so hence stacking is easy. Between the two base pairs there are hydrophobic interactions and Van der Waals forces like dipole-dipole forces and London dispersion forces.

III. Helix parameters:
a) Helix sense: it refers to the rotation of DNA which is generally right handed and left handed in Z-DNA.
b) Residues per turn: the no. of base pairs for one helical turn i.e. 360 degrees of rotation and according to Watson and crick model it is 10 bp per turn.
c) Axial rise: the distance between adjacent bp. Which is 3.4 Å in Watson and Crick model.
d) Helix pitch: the length of one complete helical turn. 34Å in Watson and Crick model.
e) Base pair tilt: angle of planar base pairs with respect to helical axis.
f) Diameter: the distance between the two helices. It is 20Å in Watson and Crick model.
g) Rotation per residue or twist angle: the angle between two adjacent base pairs. And it’s 36 degrees for Watson and Crick model.

IV. B-FORM DNA:
Was originally deduced from X-Ray diffraction analysis of the sodium salt of DNA.
a) It is a right-handed helix.
b) There are about 10.5 bp per turn.
c) There are 2 grooves the minor and the major groove with which the proteins interact.
d) The center of the helix stores the genetic information.
e) Sugar pucker is located on C2’ endo.

V. A-FORM DNA:
Identified from X-Ray diffraction analysis of DNA fibers.
a) It is also a right-handed helix.
b) Grooves are not so prominent as in B- DNA.
c) Bases are tilted up to 20 degrees.
d) Sugar pucker is located on C3’ endo.
e) Double stranded RNA forms an A-like helix.

VI. Z- FORM DNA:
a) It is a left-handed DNA.
b) There are many structural differences between B-DNA and Z-DNA like sugar pockets, tilt of bases, rotation about the glycosidic bond etc.

### Table 6-2 A Comparison of the Structural Properties of A, B, and Z DNAs as Derived from Single-Crystal X-Ray Analysis

<table>
<thead>
<tr>
<th>Helix Type</th>
<th>Overall proportions</th>
<th>Rise per base pair</th>
<th>Helix-packing diameter</th>
<th>Helix rotation sense</th>
<th>Base pairs per helix repeat</th>
<th>Base pairs per turn of helix</th>
<th>Rotation per base pair</th>
<th>Pitch per turn of helix</th>
<th>Tilt of base normals to helix axis</th>
<th>Base-pair mean propeller twist</th>
<th>Helix axis location</th>
<th>Major-groove proportions</th>
<th>Minor-groove proportions</th>
<th>Glycosyl-bond conformation</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Short and broad</td>
<td>2.3 Å</td>
<td>25.5 Å</td>
<td>Right-handed</td>
<td>1</td>
<td>~11</td>
<td>33.6°</td>
<td>24.8 Å</td>
<td>+19°</td>
<td>+18°</td>
<td>Major groove</td>
<td>Extremely narrow but very deep</td>
<td>Very broad but shallow</td>
<td>anti</td>
</tr>
<tr>
<td>B</td>
<td>Longer and thinner</td>
<td>3.32 Å</td>
<td>23.7 Å</td>
<td>Right-handed</td>
<td>1</td>
<td>~10</td>
<td>35.9°</td>
<td>33.2 Å</td>
<td>~1.2°</td>
<td>+16°</td>
<td>Through base pairs</td>
<td>Wide and of intermediate depth</td>
<td>Narrow and of intermediate depth</td>
<td>anti</td>
</tr>
<tr>
<td>Z</td>
<td>Elongated and slim</td>
<td>3.8 Å</td>
<td>18.4 Å</td>
<td>Left-handed</td>
<td>2</td>
<td>12</td>
<td>~60° per 2 bp</td>
<td>45.6 Å</td>
<td>~9°</td>
<td>~0°</td>
<td>Minor groove</td>
<td>Flattened out on helix surface</td>
<td>Extremely narrow but very deep</td>
<td>anti at C, syn at G</td>
</tr>
</tbody>
</table>


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**Denaturation and Renaturation double stranded DNA:**

The stability of DNA is due to H-Bonding and Base Stacking Interactions. Apart from this the helix is solvated with water all around and is always hydrated by the shell of hydration. Denaturation means breaking the bonds of the DNA that can be reversed if out of those conditions.

The conditions for denaturation are:

A) Ph<2 and ph>12 as ionization occurs and the donor acceptor bonds are broken and hence break Watson and Crick H-Bonds as well as base stacking.
B) Acid treatment of DNA leads to depyrimidation and depurination, cleavage of glycosidic bond, and phosphodiester bonds too for strong acids.

C) Increase in temperature disrupts the H-Bonds and the shell of hydration breaks.

Measurement of denaturation:

a) By measuring the increase in absorbance at 260nm called hyperchromicity which results due to the unstacking of the bases.

b) By using enzymes that bind to only one form of DNA either single or the double. Eg: s1 nuclease for single and hydroxyapatite for double stranded DNA.

Renaturation can occur only if the denatured DNA is cooled down slowly.

Triplex DNA:

It is formed by placing another strand in the main groove of the DNA which may adapt an unwound B-DNA like conformation. The 3rd strand must H-Bond with another surface of the duplex leaving the side that is already H-Bonded with the duplex. This process of base pairing is called Hoogsteen base-pairing. The allowed pairs are TAT, CGC, AAT, GGC. The no. of purines must be more in the 3rd strand as they can form more than one H-Bonds. The 3rd strand which is purine rich forms reverse Hoogsteen h-bond in an antiparallel orientation with the purine strand of Watson and crick helix. And if the strand is pyrimidine rich then the Hoogsteen h-bond are formed in a parallel orientation with Watson and crick paired purine strand.