Different types of DNA and their discussion

The double helical model of the DNA we all are familiar with was given by Watson and Crick in 1953 and it was based on the X-ray diffraction data obtained by Maurice Wilkins and Rosalind Franklin. This structure came to be called as B-DNA model and it was thought that it is most common form of dsDNA found in the cells.

But with improvements in methods and evolution of experimental approaches we have come to realize that DNA in vivo has many conformations and some of these are double stranded forms and others are triple stranded or quadruple stranded.

We will be discussing the double stranded variants here which includes B-DNA, A-DNA and Z-DNA. A comparative account of all these forms is given in the table below:

	A form	*B form*	*Z form*
Helical sense	Right handed	Right handed	Left handed
Diameter	~26 Å	~20 Å	~18 Å
Base pairs per helical turn	11	10.5	12
Helix rise per base pair	2.6 Å	3.4 Å	3.7 Å
Base tilt normal to the helix axis	20°	6°	7°
Sugar pucker conformation	C-3′ endo	C-2′ endo	C-2′ endo for pyrimidines; C-3′ endo for purines
Glycosyl bond conformation	Anti	Anti	Anti for pyrimidines; syn for purines

Table: Comparison of the basic properties for different forms of the dsDNA.

Right-handed helix is the helix which when observed along its axis spirals in a clockwise fashion away from the observer.

Left-handed helix is the helix which when observed along its axis spirals in a clockwise fashion towards the observer.

Consider the image given below.

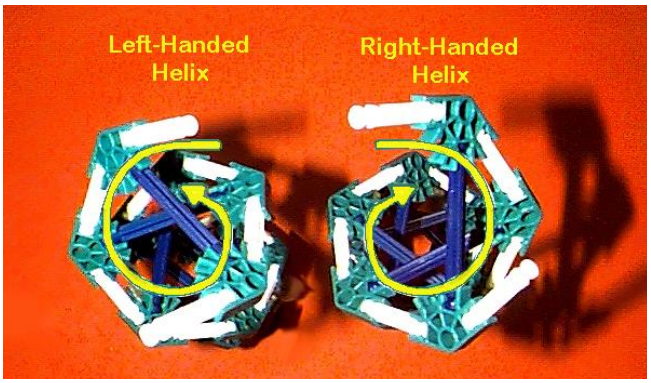

Figure: Helix handedness in the double stranded helix.

Before we discuss about the different forms of DNA, let us discuss why the DNA is helical. This question also becomes important in the light of the fact that double helix is actually an obstacle to many of the DNA`s functions.

As part of the answer, we can consider the fact that helices are very common in the biological macromolecules such as in the protein α-helices. This is due to fact that when asymmetric monomer units stack upon each other they tend to adopt helical structure. In case of DNA, monomers i.e. nucleotides are asymmetric and their stacking upon each other leads to formation of helix e.g. when adenine molecules are added in water they stack upon themselves to form a single stranded helix.

The requirement for keeping the hydrophobic bases away from the water leads to formation of the double helix in which interior is largely hydrophobic with bases being stacked upon each other and exterior is made of hydrophilic sugar-phosphate backbone. To maximize the hydrophobic interactions among themselves the bases are slightly twisted along their axis which also aids in the formation of double helix.

To understand the formation of helix please visit the link for animation tutorial
http://www.oup.com/uk/bioscience/dnatopology

Note: In routine discussion, basic description of the B-DNA derived from fiber diffraction studies is sufficient. But we now know that DNA is not a uniform structure and the double stranded structure can adopt various conformations.

This includes local variations in the helical parameters of B-form of DNA, other helical species of DNA such as Z-form, and alternatives to the double helical structures such as triple stranded DNA and quadruplex DNA.

B-form of DNA: For the basic details mentioned in this section, please refer to the table given in the previous page.

- Its basic structural details were derived from the X-ray diffraction data of DNA fibers at high humidity i.e. >90%.
- Some of the features that distinguish the B-form from other forms are location of base pairs of the helix axis, the near perpendicular orientation of the base pairs relative to the helix axis and distinct major and minor grooves where major groove allows easy access to the bases.
- The helical repeat i.e. base pairs per turn is generally accepted to have average value of 10.5 bp/turn. However, exact value depends on the solution conditions.

In 1980, the structure of the B-DNA was analyzed at atomic resolution using X-ray diffraction of single crystals. This confirmed most of the aspects known from the X-ray diffraction studies. But it also revealed that there are local level sequence-dependent variations in the structure of the DNA. These variations are:

- Distance between base pairs varies from 0.314 to 0.356nm with average value being 0.33nm.
- The DNA base pairs show propeller twist i.e. the DNA base pairs are not exactly perpendicular to the helix axis. The purine and pyrimidine pair are not present in the same plane but are twisted with respect to each other like the blades of the propeller.
- The helical axis is not always straight but can be slightly curved.

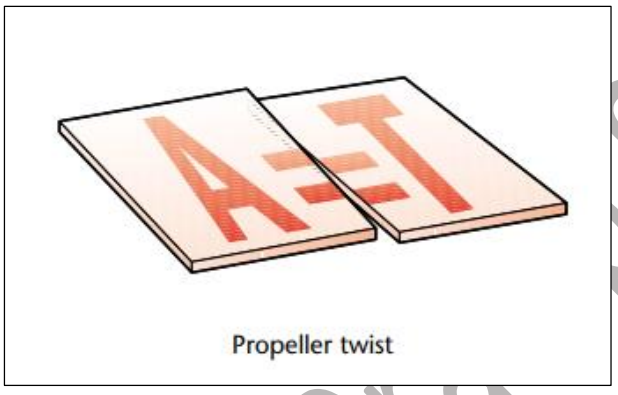

Figure: Propeller twist in A=T base pairs

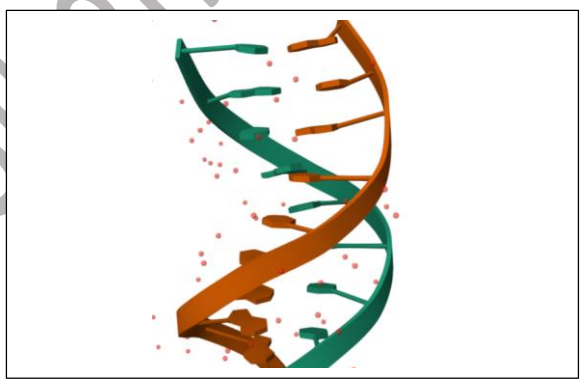

Figure: Propeller twist in dsDNA

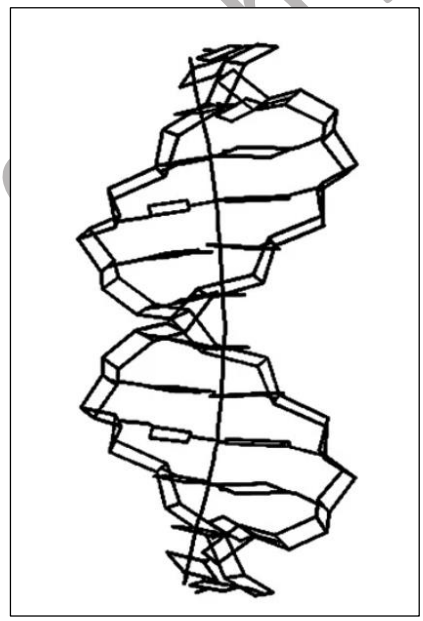

Figure: Intrinsic curve in the DNA helical axis in a sequence dependent manner.

This type of intrinsic curve is seen in DNA when we have in phase A-tracts.

The in phase A-tracts are defined as continuous (4-6) A=T base pairs in the DNA and is in phase with 10bp helical repeat.

This phenomenon was first observed in the DNA isolated from kinetoplast body of *Leishmania tarentolae* because fragments with intrinsic helical curve move slowly in PAGE than the fragment of same size that lacks the intrinsic curve.

If the in phase repeat is 4-6 T=A base pair, then we do not see the intrinsic curve in the dsDNA helical axis.

A related property to is DNA flexibility. This is of two types i.e. isotropic and anisotropic.

Isotropic means the DNA can bend equally in all the directions and anisotropic means that DNA flexibility is in a particular direction due to presence of sequences that act like hinge. Thus, DNA flexibility is also dependent on the DNA sequence.

The origin of sequence dependent DNA bending and flexibility is complex but can be attributed to chemical and stereochemical inhomogeneity of the DNA sequence. DNA bending and flexibility are important in DNA:Protein interactions and it can be understood by the examples given below.

- *E. coli* cAMP receptor protein (CRP) also known as catabolite activator protein (CAP) is expressed when there is carbon source limitation in the cell leading to cAMP level elevation. CRP binds to its target sequences and induces a bend of 90^0 in the DNA which leads to desired effects, usually transcriptional activation because bending of the DNA facilitates the interaction between RNA polymerase and upstream sequences.

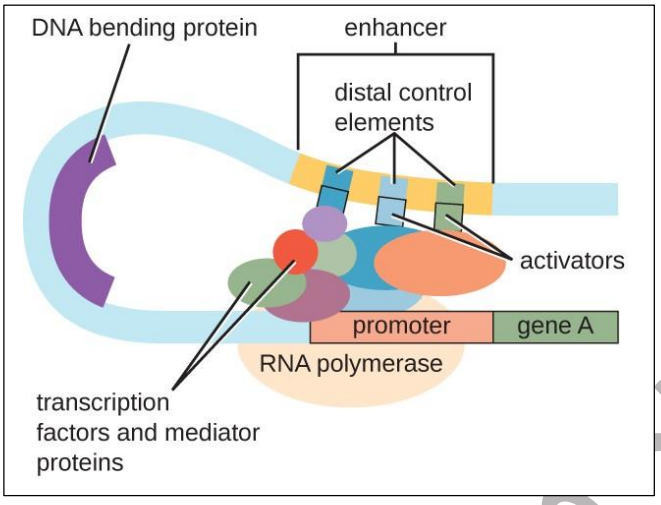

Figure: Role of DNA bending proteins in transcriptional activation.

- The TATA box binding protein (TBP) is a highly conserved eukaryotic transcription factor. It binds at a consensus sequence TATAAAA. When TBP binds to the consensus sequence on the DNA then creates a bend angel of 100^0. If this consensus sequence is changed by substitution to TAAAAAA then bend angle is reduced leading to reduction in the transcriptional activity. This reduction in bend angle is due to greater rigidity in the TAAAAAA sequence by loss of TpA step which provides greater flexibility.

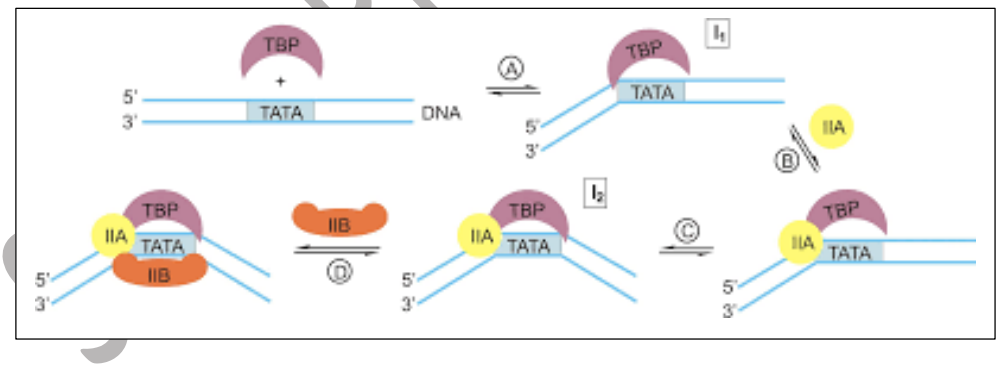

Figure: DNA bending on binding of TBP at TATA site.

- DNA flexibility is also involved wrapping of the DNA around the histone proteins leading to the formation of the nucleosomes.

A-form of DNA: This form of the DNA was first identified from X-ray fiber diffraction studies under low humidity conditions i.e. 75%. In comparison to the B-DNA, A-form helix is broader in diameter (2.6nm) and less twisted due to which it has 11bp/turn.

The bases are tilted and are present well off the helix axis and the major groove is thin and deep while the minor groove is shallow. A major difference between A-form and B-form of DNA is in the sugar pucker i.e. out-of-plane twisting of the furanose rings, in order to minimize the non-bonded interactions between ring substituents.

In B-DNA the ring pucker is C2`-endo while in the A-DNA it is C3`-endo.

Conformation of the A-DNA closely resembles the double helical form of RNA, A-RNA. The occurrence of this form of DNA in vivo is uncertain but it has been proposed that at certain sites such as promoter regions it might be present.

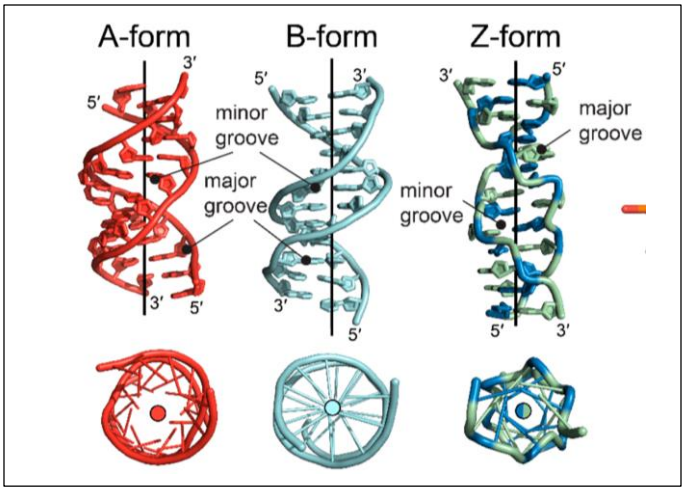

Figure: Different forms of the DNA.

Z-form of DNA: This form of DNA was first speculated from the spectroscopic studies of poly(dG-dC) in 1972. Its presence was confirmed when first DNA molecules were analysed by X-ray crystallography in 1979 and 1980. The molecules analyzed were d(CGCGCG) and d(CGCG) respectively.

The helix in this case is left handed and contains the zigzag backbone. The zigzag pattern of the backbone is responsible for the name i.e. Z-DNA. It is mainly found in the GC rich sequences and can be thought of as a helix of dinucleotide pairs. The latter is derived from the fact that successive base pairs are in alternating conformations. The Z-DNA lacks major groove for practical purposes and has a deep and narrow minor groove.

Other than the GC rich sequences the Z-DNA formation is also favored under certain conditions such as high salt concentration.

The existence of Z-DNA in vivo is still debated but there is proof that left handed forms arise during transcription, gene activation and DNA supercoiling.