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PROFESSOR, DEPARTMENT OF ZOOLOGY, NARAJOLE RAJ COLLEGE

DNA

BY

DR. POULAMI ADHIKARY MUKHERJEE
ASSISTANT PROFESSOR
DEPARTMENT OF ZOOLOGY
NARAJOLE RAJ COLLEGE

ZOOLOGY: SEM- III, PAPER- C7T: FUNDAMENTALS OF BIOCHEMISTRY, UNIT 4: NUCLEIC ACIDS



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- + DNA, known as Deoxyribonucleic Acid, is an organic compound that has a unique molecular structure and found in all prokaryotic cells and eukaryotic cells.
- + DNA is a group of molecules that is responsible for carrying and transmitting the hereditary materials or the genetic instructions from parents to offsprings.



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✚ This is also true for viruses as most of these entities have either RNA or DNA as their genetic material. For instance, some viruses may have RNA as their genetic material, while others have DNA as the genetic material. The Human Immunodeficiency Virus (HIV) contains RNA, which is then converted into DNA after attaching itself to the host cell.



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- ✚ Apart from being responsible for the inheritance of genetic information in all living beings, DNA also plays a crucial role in the production of proteins.
- ✚ Nuclear DNA is the DNA contained within the nucleus of every cell in a eukaryotic organism. It codes for the majority of the organism's genomes while the mitochondrial DNA and plastid DNA handles the rest.



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- ✚ The DNA present in the mitochondria of the cell is termed as mitochondrial DNA. It is inherited from the mother to the child.
- ✚ In humans, there are approximately 16,000 base pairs of mitochondrial DNA. Similarly, plastids have their own DNA, and they play an essential role in photosynthesis. DNA is a long polymer and therefore, difficult to isolate



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from cells in an intact form. This is why it is difficult to study its structure.

- ✚ However, in 1953, James Watson and Francis Crick revealed the 'double helix' model of the structure of DNA, based on X-ray diffraction data from Maurice Wilkins and Rosalind Franklin.



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- + This model also reveals a unique property of polynucleotide chains – Base pairing.
- + It refers to the hydrogen bonds that connect the nitrogen bases on opposite DNA strands.
- + This pairing gives rise to complementary strands i.e. if you know the sequence of bases on one strand, you can predict the bases on the other strand.



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✚ Additionally, if each DNA strand acts as a template for synthesis (parent) of a new strand, then the new double-stranded DNA (daughters) produced are identical to the parental DNA strand.



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Salient Features of DNA Double-Helix:

- It consists of two polynucleotide chains where the sugar and phosphate group form the backbone and the nitrogenous bases project inside the helix.
- The two polynucleotide chains have anti-parallel polarity i.e. if one strand has $5' \rightarrow 3'$ polarity, the other strand has $3' \rightarrow 5'$ polarity.



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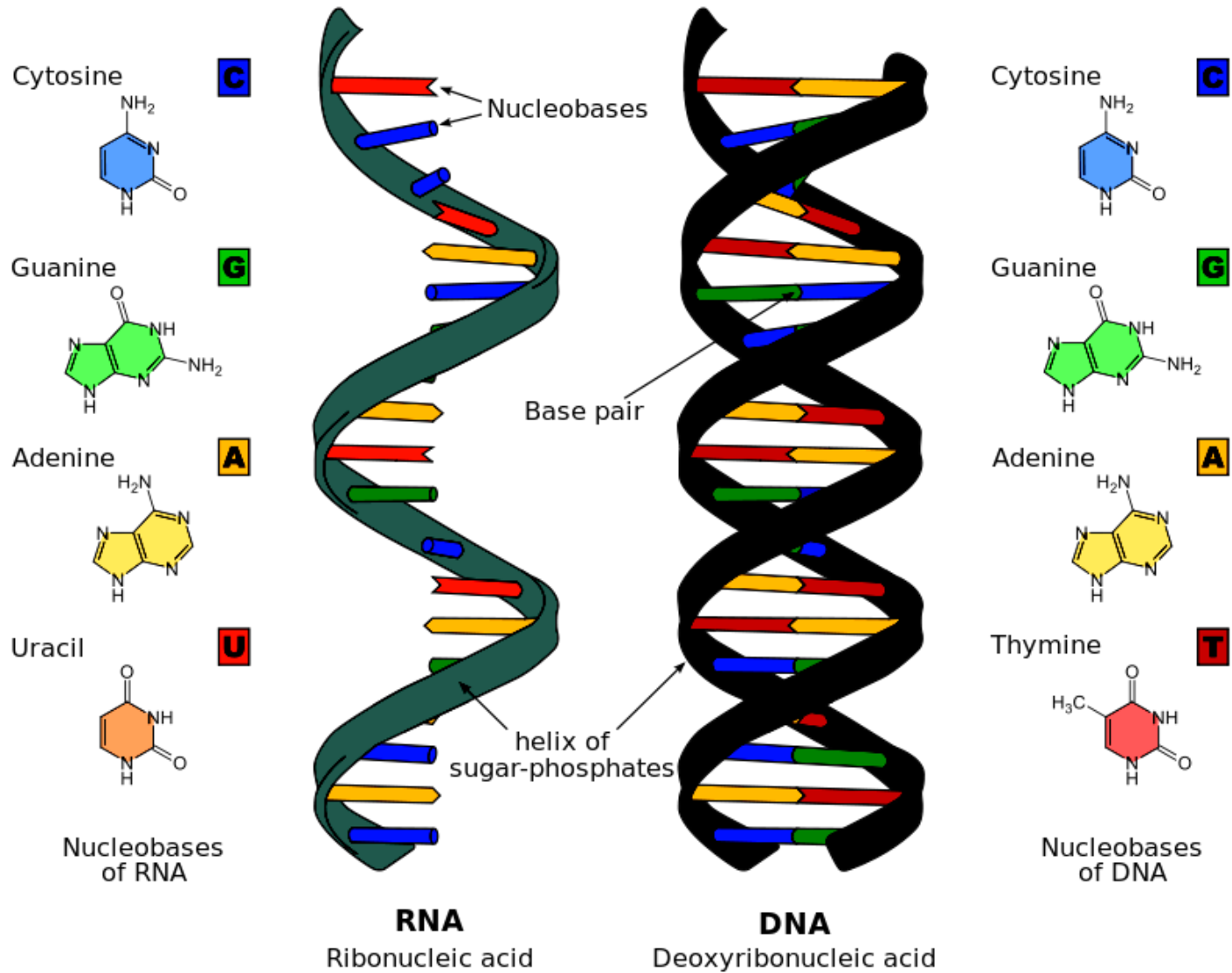
- The bases on the opposite strands are connected through hydrogen bonds forming base pairs (bp). Adenine always forms two hydrogen bonds with thymine from the opposite strand and vice-versa. Guanine forms three hydrogen bonds with cytosine from the opposite strand and vice-versa. Therefore, a purine always pairs with a pyrimidine on the other strand, giving rise to a uniform distance between the two strands of the helix.



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- The two strands coil in a right-handed fashion. Each turn of the helix is 3.4nm (or 34 Angstrom units) consisting of 10 nucleotides. These nucleotides are at a distance of 0.34nm (or 3.4 Angstrom units).
- The helix is stable because of the base pairs that stack over one another and hydrogen bonds that hold the bases together.

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- Prokaryotes like *E. coli*, do not have a defined nucleus. Here, the negatively-charged DNA is held together in large loops by positively-charged proteins in a structure called 'nucleoid'.
- In Eukaryotes, however, the organization of DNA in the nucleus is much more complex and is as follows:



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- The negatively-charged DNA is wrapped around a positively-charged histone octamer i.e. a unit of 8 histone molecules. This forms a 'Nucleosome'.
- Histones are positively-charged proteins that are rich in basic amino acids – arginines and lysines. A typical nucleosome has 200bp of DNA helix.



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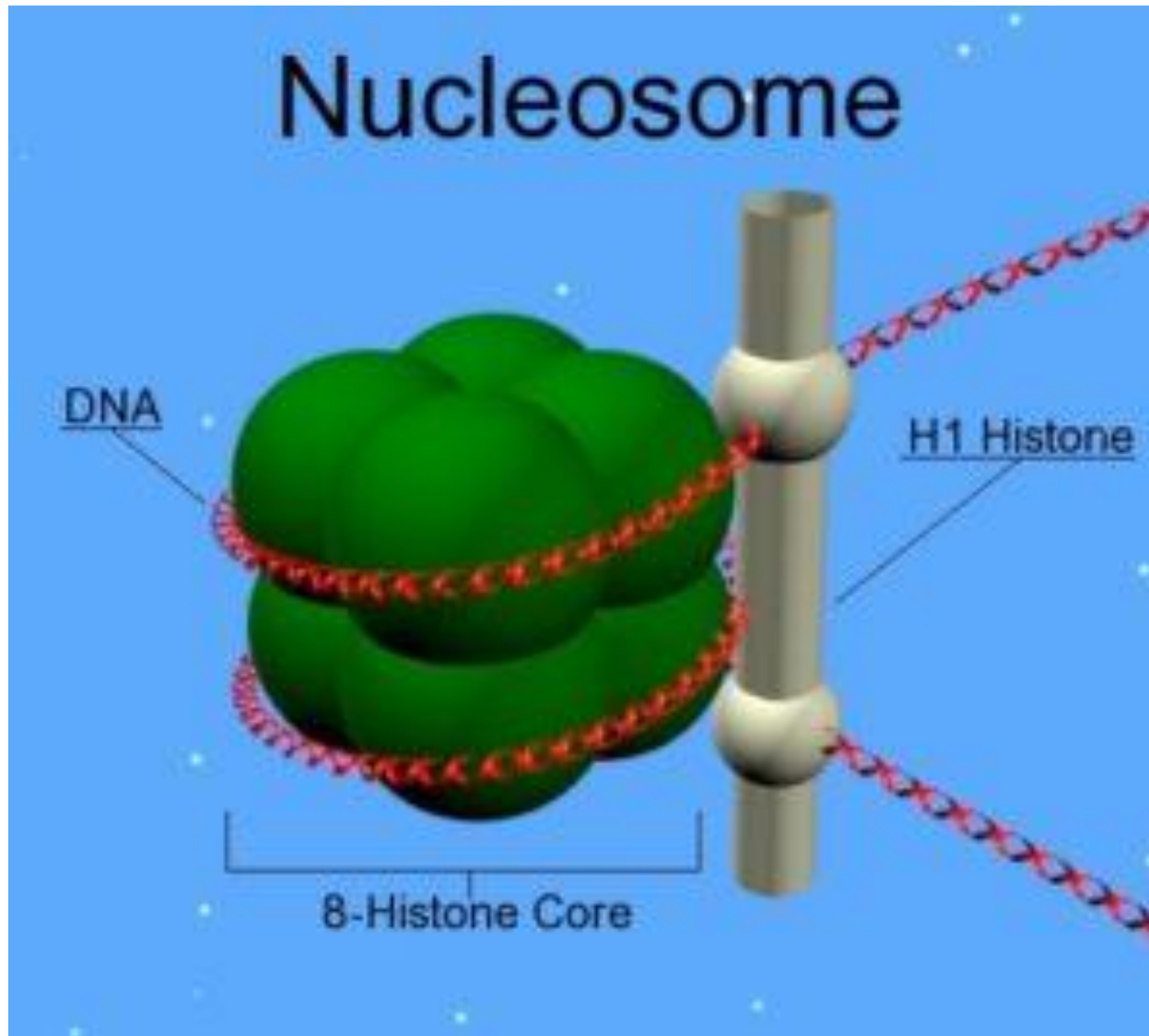
- Many nucleosomes join together to form a thread-like structure – Chromatin in the nucleus.
- The nucleosomes in chromatin appear as ‘beads-on-string’ under the electron microscope.
- The chromatin is packaged to form chromatin fibres, which are further coiled and condensed to form chromosomes.



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- The higher level packaging of chromatin requires another set of proteins – Non-histone Chromosomal (NHC) proteins.
- Euchromatin is the region of chromatin that is loosely packed and therefore stains lightly; whereas Heterochromatin is the densely packed region and therefore stains dark.

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Chargaff's Rule:

Erwin Chargaff, a biochemist, discovered that the number of nitrogenous bases in the DNA was present in equal quantities. The amount of A is equal to T, whereas the amount of C is equal to G.

$$A=T;$$

$$C=G$$



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In other words, the DNA of any cell from any organism should have a 1:1 ratio of purine and pyrimidine bases. The rules of base pairing (or nucleotide pairing) are:

A with T: the purine adenine (A) always pairs with
the pyrimidine thymine (T)

C with G: the pyrimidine cytosine (C) always pairs with
the purine guanine (G)

A=T;

C = G

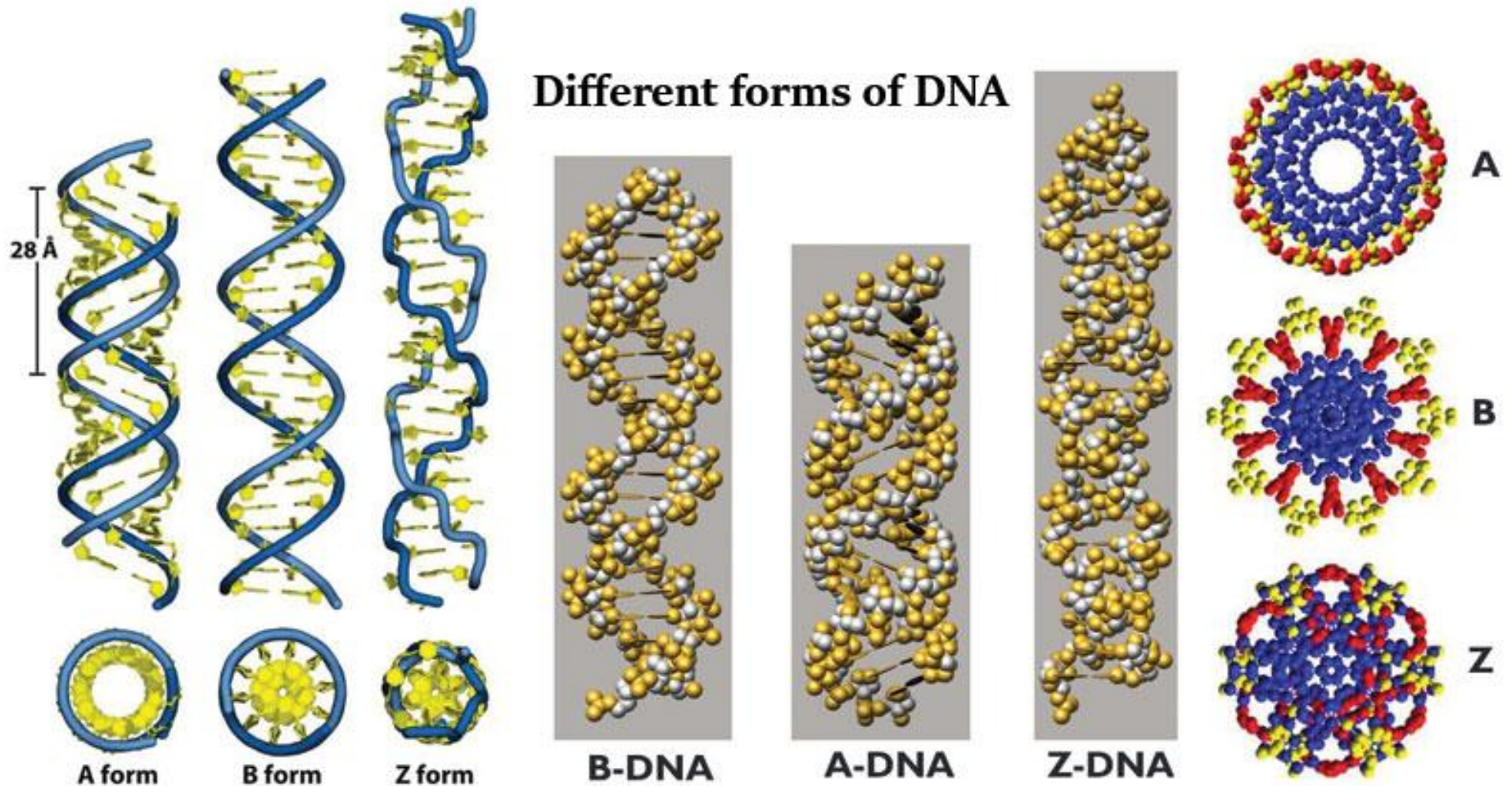


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Different forms of DNA- A form, B form, Z form:

- The right-handed double-helical Watson – Crick Model for B-form DNA is the most commonly known DNA structure.
- In addition to this classic structure, several other forms of DNA have been observed.
- The helical structure of DNA is thus variable and depends on the sequence as well as the environment.

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Why do different forms of DNA exist?

- There is simply not enough room for the DNA to be stretched out in a perfect, linear B-DNA conformation.
- In nearly all cells, from simple bacteria through complex eukaryotes, the DNA must be compacted by more than a thousand fold in order even to fit inside the cell or nucleus.



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- Refined resolution of the structure of DNA, based on X-ray crystallography of short synthetic pieces of DNA, has shown that there is a considerable variance of the helical structure of DNA, based on the sequence.
- For example, a 200-bp piece of DNA can run as if it were more than 1000 bp on an acrylamide gel if it has the right sequence. The double helix is not the same uniform structure.



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The Different Forms of DNA:

B-form DNA:

- B-DNA is the Watson–Crick form of the double helix that most people are familiar.
- They proposed two strands of DNA — each in a right-hand helix — wound around the same axis. The two strands are



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held together by H-bonding between the bases (in anti-conformation).

- The two strands of the duplex are antiparallel and plectonemically coiled. The nucleotides arrayed in a 5' to 3' orientation on one strand align with complementary nucleotides in the 3' to 5' orientation of the opposite strand.
- Bases fit in the double helical model if pyrimidine on one strand is always paired with purine on the other.



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From Chargaff's rules, the two strands will pair A with T and G with C. This pairs a keto base with an amino base, a purine with a pyrimidine. Two H-bonds can form between A and T, and three can form between G and C.

- These are the complementary base pairs. The base-pairing scheme immediately suggests a way to replicate and copy the genetic information.
- 34 nm between bp, 3.4 nm per turn, about 10 bp per turn.



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- 9 nm (about 2.0 nm or 20 Angstroms) in diameter.
- 34° helix pitch; -6° base-pair tilt; 36° twist angle.

A-form DNA:

- The major difference between A-form and B-form nucleic acid is in the conformation of the deoxyribose sugar ring. It is in the C2' endoconformation for B-form, whereas it is in the C3' endoconformation in A-form.



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- A second major difference between A-form and B-form nucleic acid is the placement of base-pairs within the duplex. In B-form, the base-pairs are almost centered over the helical axis but in A-form, they are displaced away from the central axis and closer to the major groove. The result is a ribbon-like helix with a more open cylindrical core in A-form.
- Right-handed helix
- 11 bp per turn; 0.26 nm axial rise; 28° helix pitch; 20° base-pair tilt
- 33° twist angle; 2.3nm helix diameter



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Z-form DNA:

- Z-DNA is a radically different duplex structure, with the two strands coiling in left-handed helices and a pronounced zig-zag (hence the name) pattern in the phosphodiester backbone.
- Z-DNA can form when the DNA is in an alternating purine-pyrimidine sequence such as GCGCGC, and indeed the G and C nucleotides are in different conformations, leading to the zig-zag pattern.
- The big difference is at the G nucleotide.



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- It has the sugar in the C3' endoconformation (like A-form nucleic acid, and in contrast to B-form DNA) and the guanine base is in the synconformation.
- This places the guanine back over the sugar ring, in contrast to the usual anticonformation seen in A- and B-form nucleic acid. Note that having the base in the anticonformation places it in the position where it can readily form H-bonds with the complementary base on the opposite strand.
- The duplex in Z-DNA has to accommodate the distortion of this G nucleotide in the synconformation. The cytosine in the



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adjacent nucleotide of Z-DNA is in the “normal” C2' endo, anticonformation.

- Discovered by Rich, Nordheim & Wang in 1984.
- It has antiparallel strands as B-DNA.
- It is long and thin as compared to B-DNA.
- 12 bp per turn; 0.45 nm axial rise; 45° helix pitch; 7° base-pair tilt
- -30° twist angle; 1.8 nm helix diameter



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Conditions Favoring A-form, B-form, and Z-form of DNA:

- Whether a DNA sequence will be in the A-, B-or Z-DNA conformation depends on at least three conditions.
- The first is the ionic or hydration environment, which can facilitate conversion between different helical forms.
- A-DNA is favored by low hydration, whereas Z-DNA can be favored by high salt.
- The second condition is the DNA sequence: A-DNA is favored by certain stretches of purines (or pyrimidines), whereas Z-



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DNA can be most readily formed by alternating purine-pyrimidine steps.

- The third condition is the presence of proteins that can bind to DNA in one helical conformation and force the DNA to adopt a different conformation, such as proteins which bind to B-DNA and can drive it to either A-or Z forms.
- In living cells, most of the DNA is in a mixture of Aand B-DNA conformations, with a few small regions capable of forming Z-DNA.



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Other rare forms of DNA:

C-DNA

- Formed at 66% relative humidity and in presence of Li^+ and Mg^{2+} ions.
- Right-handed with the axial rise of 3.32\AA per base pair
- 33 base pairs per turn
- Helical pitch $3.32\text{\AA} \times 9.33^\circ = 30.97\text{\AA}$.
- Base pair rotation = 38.58° .
- Has a diameter of 19\AA , smaller than that of A-&B- DNA.
- The tilt of base is 7.8°



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D-DNA

- Rare variant with 8 base pairs per helical turn
- These forms of DNA found in some DNA molecules devoid of guanine.
- The axial rise of 3.03\AA per base pairs
- The tilt of 16.7° from the axis of the helix.

E- DNA

- Extended or eccentric DNA.
- E-DNA has a long helical axis rise and base perpendicular to the helical axis.



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- . Deep major groove and the shallow minor groove.
- . E-DNA allowed to crystallize for a period time longer, the methylated sequence forms standard A-DNA.
- . E-DNA is the intermediate in the crystallographic pathway from B-DNA to A-DNA.



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A comparison table of the structural features of A-DNA, B-DNA and Z-DNA

	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°	36°	9° or 51°
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°	6°	7°
Major groove	Narrow and deep	Wide and deep	Flat major grooves
Minor groove	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



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