DNA STRUCTURE

Introduction-Historical Resume of Nucleic acid discovery

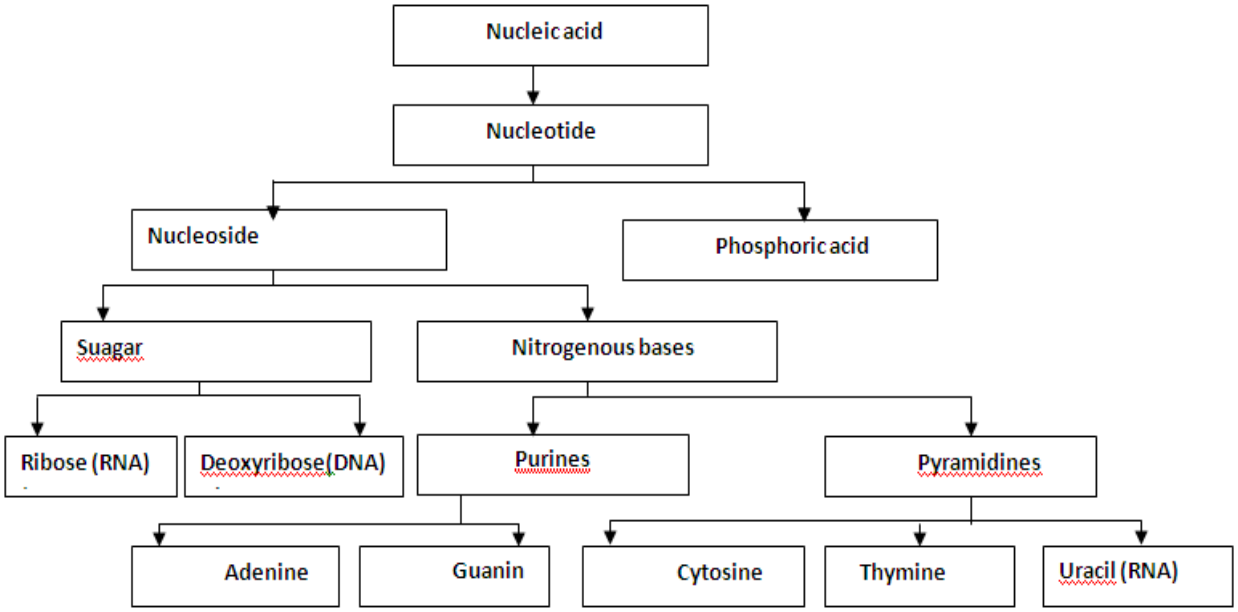
- In 1869 Frederick Miescher (a 25 year old Swiss scientist) isolated nuclei from white blood corpuscles and the materials contain unknown phosphate rich substance named as nuclein.
- 1899 Altmann found that nuclein had acid properties and termed nucleic acid
- 1910, a Russian Biochemist Levene recognized the 5 carbon ribose sugar and deoxyribose in the nucleic acid.
- 1928, Frederick Griffth suggested that the transforming factor of an organism is nucleic acid with the help of his transformation experiments in *Streptococcus pneumoniae.*
- 1931, P.A Levine identified two types of nucleic acid DNA and RNA.
- 1940s W T Astbury started the X-ray crystallographic studies for the detection of 3D structure of DNA.
- 1940s Erwin Chargaff proved that the specific relationship between two bases in DNA and published Chrgaff's equivalence rule.
- 1944, Osward Avery, Colin McLeord, MaClyan MaCarty proved that the inheritance factor of an organism is DNA and which is the only genetic material of an organism.
- 1950s Maurice Wilkins and Rosalind Franklin discovered the superior X ray diffraction photographs of a DNA double helix.
- 1952, Alfred Hershey and Martha Chase demonstrated that, even in T_4 bacteriophage (smallest virus) DNA is the genetic material and which is entered the host *E.coli* cell.
- Linnus Pauling suggested that the nitrogenous bases projected outward from sugar phosphate backbone.
- 1953, James Dewey Watson and Francis Harry Campton Crick constructed the double helical model for DNA. They were awarded the Nobel Prize in 1962 in Physiolology/Medicine for that.

Nucleic Acids

- The nucleic acids are molecular repositories for genetic information and are collectively referred to as the molecules of heredity. The structure of every protein and every cell constituent is a product of information programmed in to the nucleotide sequence of a cell's nucleic acids
- Nucleic acids are biologically occurring polynucleotides in which the nucleotide residues are linked in a specific sequence by phosphodiester bonds. The two types of nucleic acids are deoxyribonucleic acid (DNA) which is double stranded and ribonucleic acid (RNA) which is single stranded.
- The nucleic acids are the hereditary determinants of living organisms. They are the macromolecules present in most living cells either in the Free State or bound to protein as nucleoproteins.
- A nucleic acid is a biopolymer composed of high molecular weight monomeric nucleotides as their repeating units.
- The nucleic acid contains carbon, hydrogen, oxygen, nitrogen and phosphorous. Nitrogen and phosphorous are the predominant compound in the nucleic acid that constitutes about 15 and 10 % respectively.

Structural Components of Nucleic acids and their geometries

- The nucleic acid consists of the following components



Nucleotides

- Nucleotides are energy rich compounds that derive metabolic processes in all cells. They also serve as chemical signals, key links in cellular systems that respond to hormones and other extracellular signals, and are structural components of enzyme cofactors and metabolic intermediates.
- The Nucleotide contains three components.

1. Phosphoric acid
2. Pentose sugar
3. Nitrogenous (nitrogen contain) bases } Nucleoside

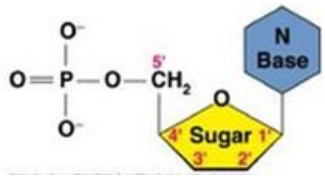


Figure: General geometry of a nucleotide

1. Phosphoric acid

- It is an inorganic acid having the chemical formula H_3PO_4.
- It contains three monovalent hydroxyl groups and a divalent oxygen atom, all linked to the pentavalent phosphorous atom.

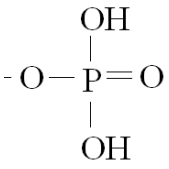


Fig: Phosphoric acid

Nucleoside

- Nucleosides are compounds in which nitrogenous bases (purines and pyramidines) are conjugated to the pentose sugar (ribose or deoxy ribose by a β- glycosidic linkage.
- The β- glycosidic linkage involves theC-1 of sugar and the hydrogen atom of N-9 (in the case of purines) or N-1 (in the case of pyramidines) by elimination of water molecules.
- Hence the purine nucleosides are N- 9 glycosides and the pyramidine nucleosides are N-1 glycosides.
- Purine nucleosides are hydrolysed by acid whereas pyrimidine nucleosides are hydrolysed only by the treatment of acid.
- The nucleosides are generally named for the particular purine or pyrimidine present.
- Nucleosides containing ribose are called ribonucleosides, whereas nucleotide containing deoxyribose are called deoxyribonucleosides

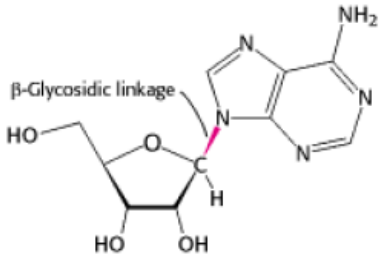


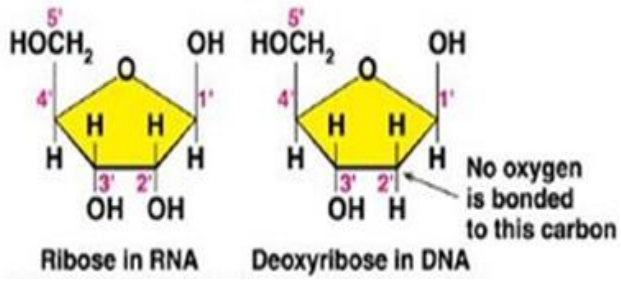
Figure: structure of a nucleoside

Table: The nucleosides

Base	Sugar	Nucleoside	Common name
Ribonucleosides			
Adenine	Ribose	Adenine ribonucleoside	Adenosine
Guanine	Ribose	Guanine ribonucleoside	Guanosine
Cytosine	Ribose	Cytosine ribonucleoside	Cytidine
Thymine	Ribose	Thymine ribonucleoside	Thymidine
Uracil	Ribose	Uracil ribonucleoside	Uridine
Deoxy ribose			
Adenine	Deoxy Ribose	Adenine deoxyribonucleoside	DeoxyAdenosine
Guanine	Deoxy Ribose	Guanine deoxyribonucleoside	DeoxyGuanosine
Cytosine	Deoxy Ribose	Cytosine deoxyribonucleoside	DeoxyCytidine
Thymine	Deoxy Ribose	Thymine deoxyribonucleoside	DeoxyThymidine
Uracil	Deoxy Ribose	Uracil deoxyribonucleoside	DeoxyUridine

2. Pentose Suagr –Structure of Ribose and deoxyribose moieties

- Pentose sugar is a 5 carbon compound present in nucleic acid.
- The pentose sugar present in DNA is called Deoxyribose and RNA is called Ribose.
- Both ribose and deoxyribose present nucleic acid are in the furanose form and are of β-configuration.
- The carbon atoms of sugars are designated by primed numbers. i.e., C-1', C-2', C-3' etc.
- D ribose is the parent sugar while deoxyribose is a derivative in which OH group on C2 has been replaced by an H atom.
- The pentose sugar is either in their aldehyde form (straight chain) or in their ketoform (closed five membered ring, β - furanose)
- The pentose ring is not planar but occurs in different conformations in the pentose ring skeleton is called as ribose puckering **(Note: Give detail information, refer ribose puckering at the end.)**



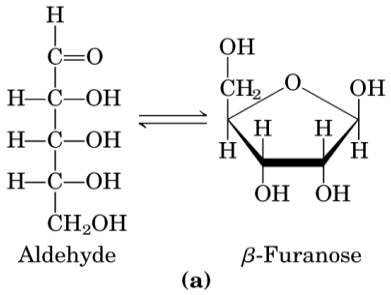


Figure: pentose Sugar **Aldehyde and Furanose form of pentose sugar**

3. Nitrogenous bases

- A nitrogenous base is an organic compound that gives its property as a base to the lone pair of electrons of a nitrogen atom.
- The nitrogenous bases are classified in to two.
  1. Major Nitrogenous base
  2. Minor (Modified) Nitrogenous base

I. Major Nitrogenous base

- There are two types of nitrogenous bases found in all nucleic acid- pyrimidine and purine.

Pyrimidine

- Pyrimidine is a heterocyclic aromatic organic compound containing two nitrogen atoms at positions 1 and 3 of the six-member ring.
- A pyrimidine has many properties. It has two N atoms. As the number of nitrogen atoms in the ring structure increases the pi electrons become less energetic and nucleophilic aromatic substitution reaction will take place more easily.

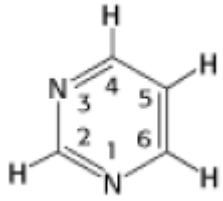


Figure: Structure of Pyrimidine

Pyrimidine Derivatives

The common types of purines present in nucleic acids are

1. Uracil
2. Thymine
3. Cytosine

1. Uracil

- Its molecular formula is $C_4 H_4 O_2N_2$
- It is found in RNA and is a white, crystalline pyrimidine base with molecular weight 112.1 dalton and melting point is 338^0 C
- It has two oxygen atom at C-2' and C-4 of the pyrimidine.

2. Thymine

- Its molecular formula is $C_5 H_6O_2N_2$
- It is first isolated from thymus hence named as thymine.
- It is present in DNA and the molecular weight is 126.13 dalton.
- Thymine contains a methyl group at C-5' henece it is called 5-methyluracil
- One of the common mutations of DNA involves two adjacent thymines in presence of ultraviolet light, may form thymine dimers, causing "kinks" in the DNA molecule that disturb normal DNA function.

3. Cytosine

- Its molecular formula is $C_5 H_6ON_3$
- It is a white crystalline substance present both DNA and RNA
- Its molecular weight is around 111.12 dalton and melting point is $320\text{-}325^0$C
- The structure of cytosine, the C-4 atom contains an amino group and C-2 contains an oxygen group**.**

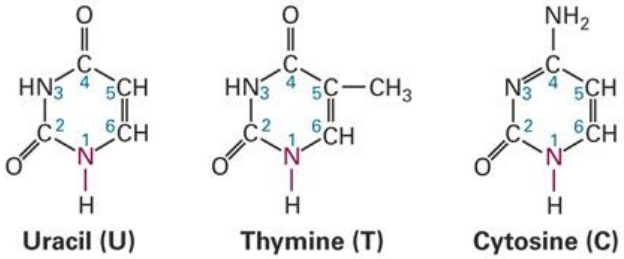


Figure: Major pyrimidine derivatives

Purines

- A purine is a heterocyclic aromatic organic compound, consisting of a pyrimidine ring fused to an imidazole ring.
- Purines are biochemically significant components in a number of important biomolecules, such as ATP, GTP, cyclic AMP, NADH, and coenzyme A.

- The most important purines are Adenine and Guanine

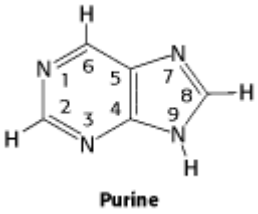


Figure: Structure of Purine

1. Adenine

- Adenine is a purine derivative with a variety of roles in structural biology including cellular respiration, in the form of both the energy-rich adenosine triphosphate (ATP) and the cofactors nicotinamide adenine dinucleotide (NAD) and flavin adenine dinucleotide (FAD), and protein synthesis, as a chemical component of DNA and RNA.
- The molecular formula of Adenine is $C_5 H_5N_5$ and it is present in both DNA and RNA.
- It is a white crystalline purine base with molecular weight 135.15 dalton and melting point 360- 365^0C
- The structure of Adenine contains an amino group at the C-6 position of the pyrimidine ring.

2. Guanine

- The molecular formula of Adenine is $C_5 H_5ON5$ and it is present in both DNA and RNA
- It is a colorless, insoluble crystalline substance with molecular weight 151.15 dalton.
- It was first isolated from excreta of sea birds, known as guano, bird manure hence it is named as guanine.
- The pyrimidine part of Guanine consists of an amino group at the C-2 positions and oxygen at C-6 position.

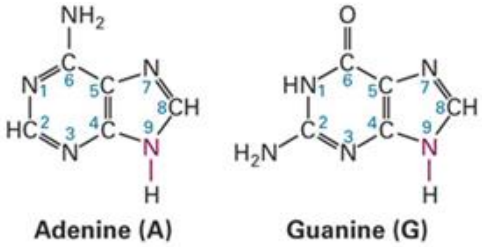


Figure: Major pyrimidine derivatives

II. Minor (Modified) nitrogenous base

- The minor nitrogenous bases present in nucleic acids are called Modified bases. They are two types.

1. Modified purines

2. Modified pyrimidines

Modified Purine

- The purines are chemically or enzymatic ally modified to produce modified purine.

- Some of the purine bases are present in RNA especially transfer RNA.
- Methylation is a common type of modification in purine, especially adinine, and it occurring in the genetic material of microorganisms.
- The most important modified purines are Xanthine, Hypoxanthine, Uric acid, etc.

Modified Pyrimidines

- The modified pyrimidines are also present in nucleic acid and they are having some functional role in the Nucleic acid metabolism.
- The most important modified pyrimidines are Methylcytosine (Component of plant genome),Psuedouracil, Dihydrouracil etc.

Tautomerism in Nitrogenous Bases

- Certain compounds can exist in two structural isomeric forms which are mutually interconvertable and exist in dynamic equilibrium are called tautomers and the phemnomenon is termed as tautomerism.i.e., Tautomers are isomers of a compound which differ only in the position of the protons and electrons
- The tautomers containing the carbonyl group (=CO) is designated as keto or lactam form and the compounds containing a hydroxyl group (-OH) attached to a doubly bonded carbon is called as enol or lactim form. This kind of tautomerism is called Keto –enol or Lactam- Lactim tautomerism.

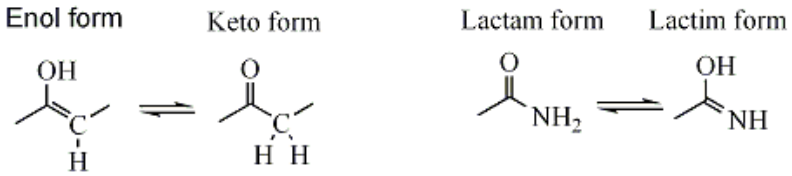


Figure- Keto enol tautomerism.

- The tautomerism is common in nitrogenous bases. It is common in both purines and pyrimidines.
- Oxygen containing nitrogenous bases such as Uracil, Thymine and Cytosine and guanine exist in keto enol (Lactam –Lactim) forms.
- The lactam form (keto form) is physiologically more important and which is predominate at neutral and acidic pH values than lactim form.

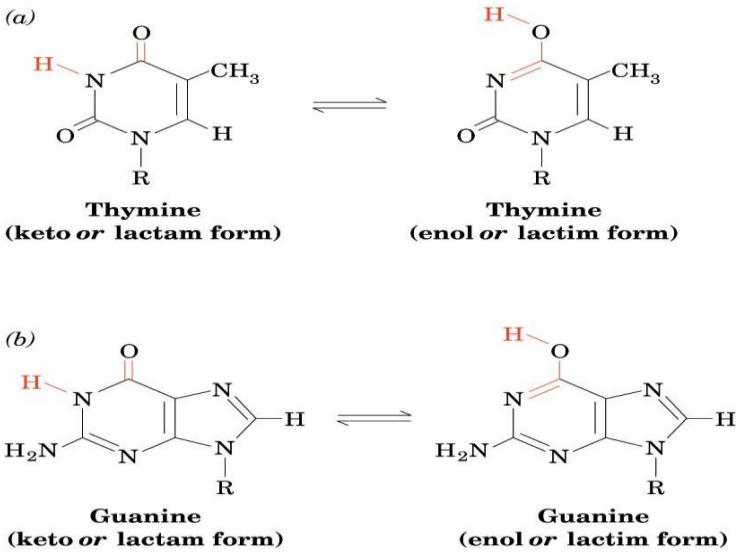


Figure: Keto –enol (lactam –lactim) tautomerism in purine and pyrimidine bases

GLYCOSIDIC BOND

- One of the most important types of force which stabilize the nucleic acid is Glycosisdic linkage.
- In DNA the glcosidic bond is refers to the nitrogen-carbon linkage between the 9' nitrogen of purine bases or 1' nitrogen of pyrimidine bases and the 1' carbon of the sugar group.
- The base moiety is attached to the polynucleotide chain of DNA via glycosidic bond and it is a covalent bond.

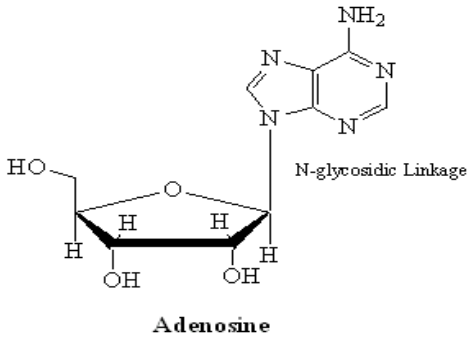


Figure: Glycosidic Linkage

- The purine and pyrimidine bases in cells are linked to carbohydrate are termed as nucleosides. The nucleosides are coupled to D-ribose or 2'-deoxy-D-ribose through a β-N-glycosidic bond between the anomeric carbon of the ribose and the N9 of a purine or N1 of a pyrimidine.
- The rotation of glycosidic bonds is due to steric clash between base and sugar.
- The relative orientation of the base with respect to the ribose units is describes by right handed rotation (torsion angle) about this bond. The torsion angle is denoted by χ.
- In the case of Glycosidic bond, there are two types of torsion angles.
  1. Syn and 2. Anti.
- Primidine posses only anti, the steric interfernec between ribose and the C2' substituent of pyrimidine.
- But the torsion angle of purines is either syn or anti
- The angle is assigned a value of 0^0 for the cis conformation of bonds O^1- C^1 and N^9-C^8.In the case of pyrimidines, the rotation angle is measured with reference to orientation of the O^1- C^1 and N^1-C^6.

ROTATIONAL ISOMERS

In nucleic acid, the bases can exist in 2 distinct orientations about the N-glycosidic bond. These conformations are called as rotational isomers.

There are two types of rotational isomers present in the nucleotide. These are designated as

1. Syn
2. Anti

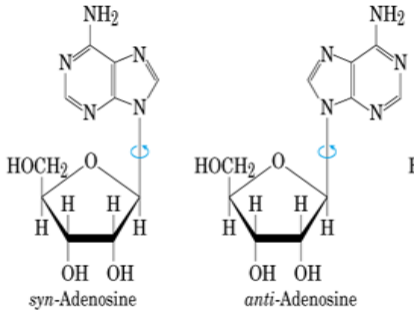


Figure: Rotational isomers of Adenosine nucleoside

Features of rotational isomers

Anti

- ✓ anti ($+180^o$ <= χ <= $+90^o$) and (-90^o <= χ <= -180^o)
- ✓ Base extended out from the sugar.

Syn

- ✓ syn (-90^o <= χ <= $+90^o$)
- ✓ Base sitting above the ring.
- ✓ More compact;
- ✓ Sterically disfavored.
- ✓ Particularly for pyrimidines

- The torsion angle about the N-glycosidic bond (N-C1') that links the base to the sugar is denoted by the symbol χ which is the same as the notation used to denote side-chain torsion angles in polypeptides χ (i) denotes the torsion angle in the i th nucleotide unit.
- The sequence of atoms chosen to define this angle is O4'-C1'-N9-C4 for purine and O4'-C1'-N1-C2 for pyrimidine derivatives. Thus when $\chi = 0°$ the O4'-C1' bond is eclipsed with the N9-C4 bond for purine and the N1-C2 bond for pyrimidine derivatives. The definitions of torsion angles of the N-glycosidic bond are illustrated below.

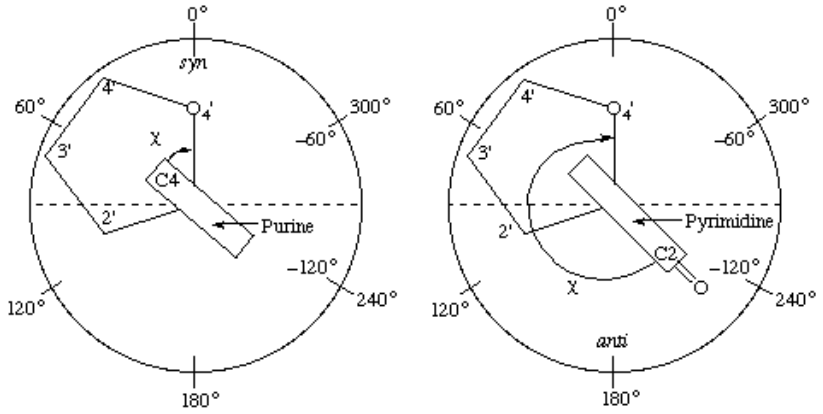


Figure: Diagrammatic represeniation of the N-glycosidic bond torsion angle χ and the syn and anti regions for purine and pyrimidine derivatives

STABILIZING ORDERED FORMS OF DNA- TRANSFORMATION FROM ONE FORM TO ANOTHER

- There are some variants of double helical DNA which are regarded as the major stabilizing ordered forms. The most important types of such verities are A-DNA, B-DNA, Z-DNA, C-DNA, D-DNA etc.

1. B-DNA

- Most of the DNA in bacterial or eukaryotic genome is in the classic Watson and –Crick form called B form.
- The B form is the most stable structure for a random sequence DNA molecule and it is based on typical Watson- Crick Pairing.

Features of the Watson-Crick base pair

1. The permitted hydrogen bonds are: adenine with thymine (2 bonds); and, cytosine with guanine (3 bonds).
2. The dimensions of the 2 permitted base-pairs are similar, i.e. the C1'-C1' distance is nearly identical in both cases.
3. The beta-glycosidic bond is attached on the same edge of the base pair. This has implications for the structure of B-DNA.
4. Although some of the atoms in the purine and pyrimidine bases are involved in hydrogen bonds, there is still potential for further hydrogen bonding. This potential is particularly important for sequence specific protein binding.
5. The Watson-Crick base-pair is a planar structure.
6. The beta glycosidic bonds point in opposite directions. As a result, both chains can contain both purines and pyrimidines and the backbones of the two chains run in opposite directions.

Features of BDNA

- It is an antiparallel double helix.
- It is a right-handed helix.
- The base-pairs are perpendicular to the axis of the helix.
- The axis of the helix passes through the centre of the base pairs.
- Each base pair is rotated by 36 degrees from the adjacent base pair.
- The base-pairs are stacked 0.34 nm apart from one another.
- The double helix repeats every 3.4 nm, i.e. the pitch of the double helix is 3.4 nm.

- B-DNA has two distinct grooves: a MAJOR groove; and, a MINOR groove. These grooves form as a consequence of the fact that the beta-glycosidic bonds of the two bases in each base pair are attached on the same edge. However, because the axis of the helix passes through the centre of the base pairs, both grooves are similar in depth.
- The other features of the BDNA have tabulated.

2. A-DNA

- When the native B DNA is dehydrated under suitable conditions A DNA will Form. i.e., The relative humidity is reduced to 92 to 75 % and Na^+, K^+, and Cs^+ ions are present in the medium.
- In the solutions DNA assumes normal B form But under dehydration condition it assume A form. This is because of the phosphate groups in the A DNA bind fewer water molecules than that do phosphate in B DNA
- A DNA is right handed double helix made up of antiparallel strands held together by Watson –Crick Pairing .The other feature of A DNA is tabulated below.
- The helix of A DNA is wider and shorter than that of B DNA.
- The base pairs are tilted rather than normal to the helix axis.
- The ribose puckering in ADNA is C3 endo, i.e., C3 is arranged out of plane formed by the other 4 atoms of the furanose ring of sugar.But in B DNA the ribose puckering is C2 endo in nature.
- The minor groove is practically nonexistent in A DNA.

3. Z-DNA

- Z DNA is the more radical departure from B DNA and is characterized by a left handed helical rotation.
- It was discovered by Rich, Nordheim and Wang in 1984. They found that a hexanucleotide, CGCGCG forms a duplex of antiparellel strands held together by Watson –Crick base pairing. They found that this double helix was left handed and phosphates in the DNA backbone were Zigzag manner. Hence this new form termed as Z DNA.
- Another remarkable characteristic of Z DNA is that in Z DNA, the repeating sugar residues have alternating orientation and it is dinucleotide unit. Where as in B DNA this feature is a mononucleotide unit.
- Z DNA contain only one deep helical groove and the other features are tabulated below,

Comparison of different forms of DNA

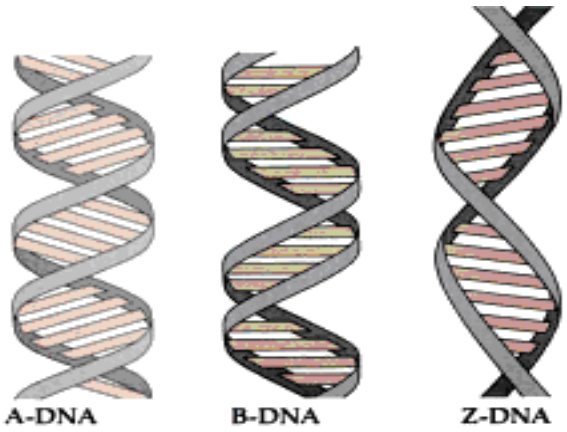


Figure: Stabilizing ordered forms of DNA

S.No.	Characteristics	A-DNA	B-DNA	Z-DNA
1.	**Conditions**	75% relative humidity, Na^+, K^+, Cs^+, ions	92% Relative humidity: Low ion Strength	Very high salt Concentration
2	**Shape**	Broadest	Intermediate	Narrowest
3.	**Helix Sense**	Right handed	Right handed	Left handed
4.	**Helix Diameter**	25.5 A^o	23.7 A^o	18.4 A^o
5.	**Rise per base pair**	2.3 A^o	3.4 A^o	3.8 A^o
6.	**Base pair per turn of helix**	11	10.4	12
7.	**Helix pitch**	25.30 A^o	35.36 A^o	45.60 A^o
8.	**Rotation per base pair**	+ 32.72 ^{o}	+34.61 ^{o}	-60 ^{o}
9.	**Base pair tilt**	19 ^{o}	1 ^{o}	9 ^{o}
11.	**Glycosisdic bond**	anti	anti	Anti for C, T Syn for A, G
12.	**Major groove**	Narrow and very deep	Wide and quite deep	Flat
13.	**Minor groove**	Very broad and shallow	Narrow and quite deep	Very narrow and deep
14.	**Ribose puckering**	C3 edo form	C2 endo form	Purines: -C3'-endo forms; Pyrimidines:-C2'-endo forms

BASE PAIRING TYPES

Two factors are mainly responsible for the stability of the DNA double helix:

(a) Base pairing between complementary strands and (b) stacking between adjacent bases.

Base pairing

- Two nucleotides on opposite complementary DNA strands that are connected via hydrogen bonds are called a base pair.
- Each type of base on one strand forms a bond with just one type of base on the other strand. This is called complementary base pairing.

- Here, purines form hydrogen bonds to pyrimidines, with A bonding only to T, and C bonding only to G.
- There are two types of Base pairing
  1. Watson- Crick pairing (Normal)
  2. Non watson Crick (unusual)

Watson Crick Pairing

- This is based on the Chargaff rule of equivalence and Base pair rule

Base Pairing Principle:

- Base pairing rule states that adenine and thymine (A - T) and guanine and cytosine (G - C) are complementary bases. The purine adenine (A) always pairs with the pyrimidine thymine/Uracil (T in the case of DNA and U in the case of RNA) by two hydrogen bonds and the pyrimidine cytosine (C) always pairs with the purine guanine (G) by three hydrogen bonds.
- The base pairing is called complementary because there are specific geometry requirements in the formation of hydrogen bonds between the heterocylic amines.
- Heterocyclic amine base pairing is an application of the hydrogen bonding principle.

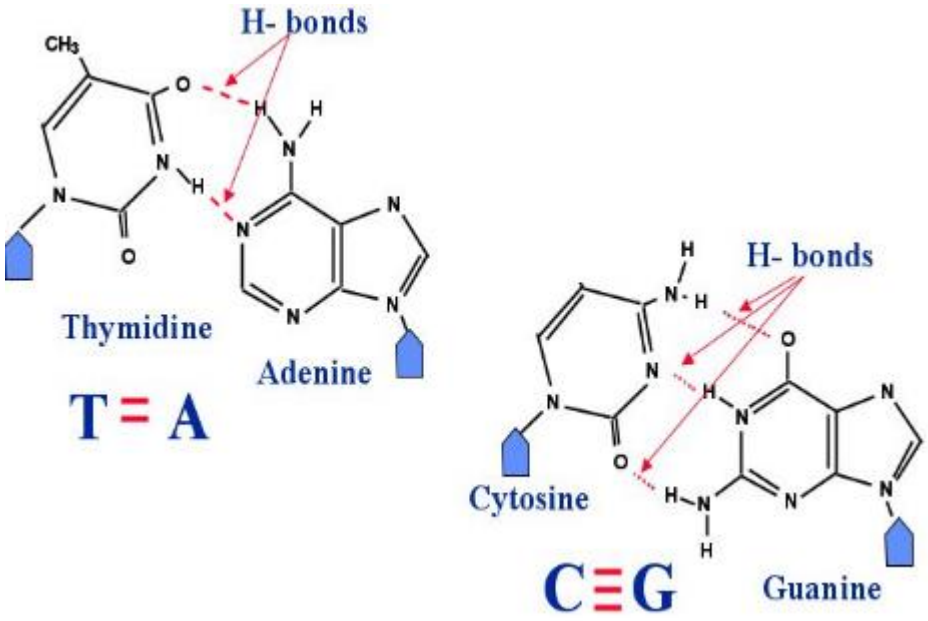


Figure: Watson Crick pairing of bases

Factors influencing Base pairing

- Pairing of bases always occurs between adenine and thymine and between guanine and cytosine.ie. A 6-amino purine will always bond with a 6- keto pyrimidine , and 6- ketopurine with 6- aminopyrimidine.
- The most important factors influencing base pairing are
  1. Steric factor
  2. Hydrogen bonding factors

1. Steric Factors

- The distances between the glycosidic bonds are the same for both the base pairs

- The glycosidic bonds of all nucleotide are arranged in an identical manner with respect to the axis of the helix
- The glycosidic bond that are attached to a base pair always $10.58A^{0.}$ A purine – pyrimidine base pair fits perfectly in this space. But there is no space for two purines. Whereas there is enough space for two pyrimidines so that they would be far apart to form hydrogen bonds, which is a rare happening.
- Because of steric reasons one member of a base pair in a DNA helix must be purine and other should be a complementary pyrimidines.

2. Hydrogen bonding factor

- The hydrogen atoms in purine and pyrimidine bases have well defined positions. Adenine cannot pair with cytosine because there would be two hydrogen atoms near one of the bonding positions and none at other. Similarly guanine cannot pair with thymine.
- So adenine forms two hydrogen bonds with thymine where as guanine forms three with cytosine. Hence GC bond is stronger bond than AT bond.

2. Non Watson Crick pairing- Hoogsteen pairing

- Several unusual DNA structures involve three or even four DNA strands. These structural variations are important events in DNA metabolism (replication, recombination, transcription)
- Nucleotides participating in a Watson-Crick base pair can form a number of additional hydrogen bonds, particularly with functional groups present in the major groove.
- For example, a cytidine residue (if protonated) can pair with the guanosine residue GC of a nucleotide pair, and a thymidine can pair with the adenosine of an AT pair
- The N^{-7}, O^6, and N^6 of purines, the atoms that participate in the hydrogen bonding of triplex DNA, are often referred to as Hoogsteen positions, and the non-Watson-Crick pairing is called Hoogsteen pairing, after Karst Hoogsteen, who in 1963 first recognized these unusual pairings.
- Hoogsteen pairing allows the formation of triplex DNAs.

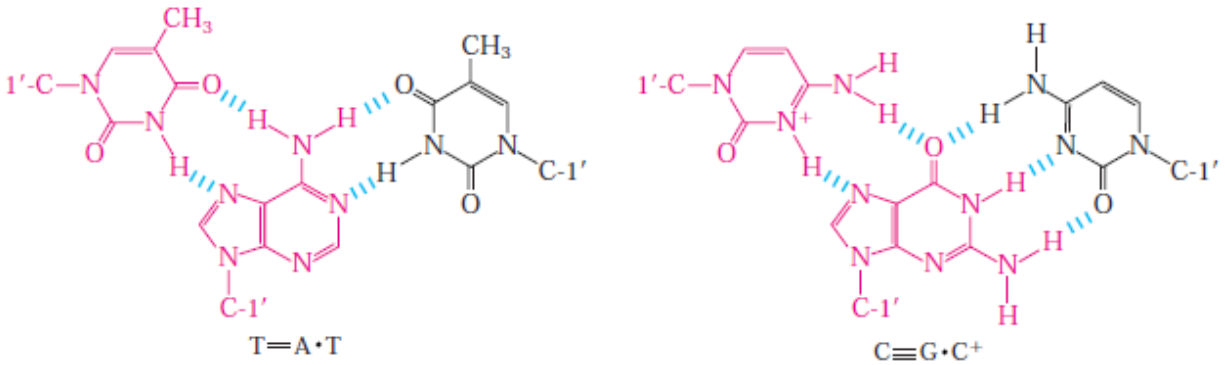


Figure: Hoogstein Pairing

BASE STACKING

- Stacking refers to a stacked arrangement of aromatic molecules adopted due to inter atomic interactions.
- The most common example of a stacked system is found for consecutive base pairs in DNA.
- The stability of a duplex nucleic acid is due to interactions that result from base stacking.

- The most important type of base stacking is called vertical nitrogen base stacking. Vertical nitrogen base stacking is a significant stabilizing interaction of DNA and RNA 3-D structures, which plays a major role in their folding and complexation.
- Base stacking refers to the interaction between nearest-neighbor nucleotides along the same strand.
- This is a very complex interaction that depends on Van der Waals forces, electostatic dipole forces between bases, and solvation effects, i.e. whether the DNA base is better bound to water, rather than to the adjacent base.
- DNA base stacking is a type of aromatic stacking. Aromatic stacking refers both to the geometry of face-to-face juxtaposition of two aromatic molecules so that the pi-systems are in direct contact, and to the forces that favor this geometry energetically.
- Bases in DNA are in near-maximal face-to-face contact. Electrostatic interactions account for the large differences in stacking efficiency of DNA bases depending on the neighboring base.

Mechanism of Base Stacking

Controlling forces

1. Hydrogen bonding
2. Forces due to pi-pi interaction
3. Electrostatic dipole between the bases
4. Solvation effects

- The base stacking occurs between adjacent nucleotides and adds to the stability of the molecular structure.
- The nitrogenous bases of the nucleotides are made from either purine or pyrimidine rings, consisting of aromatic rings.
- Within the DNA molecule, the aromatic rings are positioned nearly perpendicular to the length of the DNA strands. Thus, the faces of the aromatic rings are arranged parallel to each other, allowing the bases to participate in aromatic interactions.
- The polynucleotide chain of DNA has a ‘gap’ between each base and the surfaces of the bases have few polarized bonds and hydrophobicity.
- As a result the new conformation is attained by reducing exposure of the base surfaces to the aqueous environment, which is achieved by the bases moving closer together.
- In this conformation, the backbone is ‘tilted’ by an angle of 30° from horizontal, as shown in Figure below.
- Tilting the backbone in this way brings the planar rings of adjacent base pairs to a position where they lie vertically one above the other, an arrangement that maximizes hydrophobic interactions and maximizes van der Waals attractive forces between them
- Through aromatic interactions, the pi bonds, extending from atoms participating in double bonds, overlap with pi bonds of adjacent bases. This is a type of non-covalent chemical bond.
- Though a non-covalent bond is weaker than a covalent bond, the sum of all pi stacking interactions within the double-stranded DNA molecule creates a large net stabilizing energy.

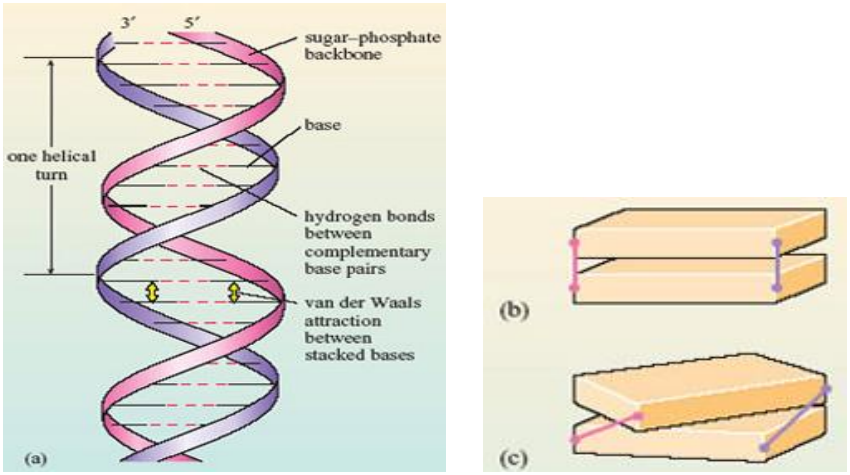


Figure: (a) Simple 'strands' diagram of the DNA duplex with the base pairing(b). Figure in which each base pair is shown as a single block spanning the duplex and the sugar-phosphate backbones are represented by solid lines.

(c).Diagram showing how stacking results in the bases interacting and twisting, such that the backbone angle is 30°.

Table: Base stacking energies for various adjacent base pairs.

Dinucleotide pair (5′–3′)–(3′–5′)	**Stacking energy per stacked pair / kJ mol−1**
(GC)–(GC)	−61.0
(AC)–(GT)	−44.0
(TC)–(GA)	−41.0
(CG)–(CG)	−41.3
(GG)–(CC)	−34.6
(AT)–(AT)	−27.5
(TG)–(CA)	−27.5
(TA)–(TA)	−16.0