University of Jordan
Faculty of Medicine

Medical Committee
The University of Jordan

Introduction to

BIOCHEMISTRY

Lecture #: (.....8.....)

■ Sheet ☐ Slides ☐ Other

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Date: .June – 30th – 2013.....

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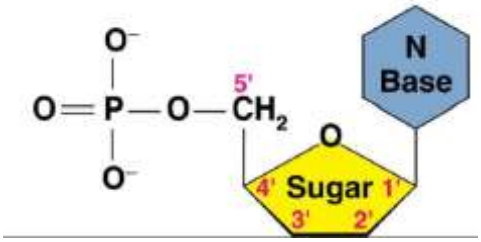
Price: .....

Designed by Waseem Bilal

Nucleic Acids: Molecules that carries information for growth and production of cells, and they are Polymers of "Nucleotides" (the monomers).01

Nucleotide consists of:



1)N-Base

2)Pentose Sugar

3)Phosphate Group

Nucleic Acids: DNA or RNA

RNA: Everywhere in the Cell

DNA: In nucleus (mainly), mitochondria and chloroplasts in plants.

The bond between N-Base & Sugar:

It is Glycosidic bond of (β) type. →remember how to Indicate (β) or (α)

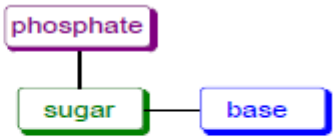
It is between the anomeric **Carbon** (in sugar) & **N-Base**

***What are the "Nucleosides"??**

NUCLEOSIDE= NEOCLUTIDE-PHOSPHATE GROUP

So nucleoside is a nucleotide **WITHOUT** phosphate group

nucleoside



nucleotides

***How can I name a nucleoside??**

-For Purines **((Adenine & Guanine)):** we add "-osine" →"Adenosine"

-For Pyrimidines **((Cytosine, Thymine and Uracil)):** we add "-idine"→"Thymidine"

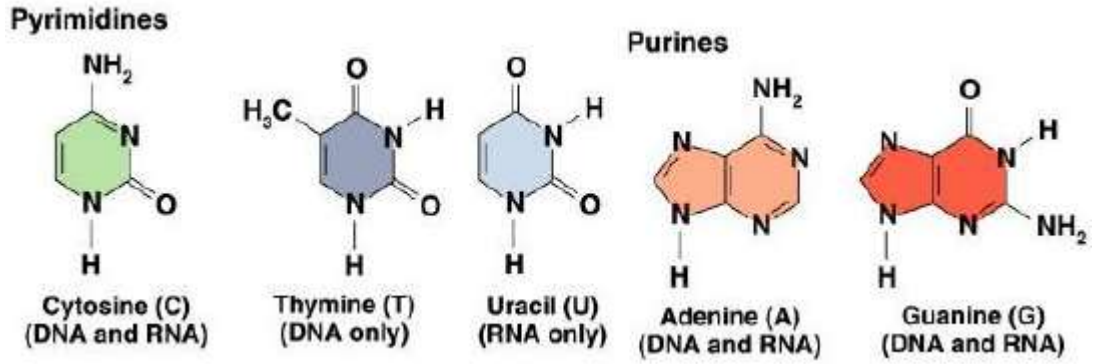
***How can I name a nucleotide??**

-Name it as nucleoside then add (mono, di or tri phosphate)→"Adenosine triphophate"

-Or we add "-ylate" instead of "mono Phosphate"

The Bond between 2 nucleotides: it is Phospho diester bond

Structures of Purines and Pyrimidines: (we should be familiar with them)



-There are some bases "non-coding" bases:

-These bases are related to Purines and Pyrimidines.

-These N-Bases may be related to genetic coding and sometimes not related.

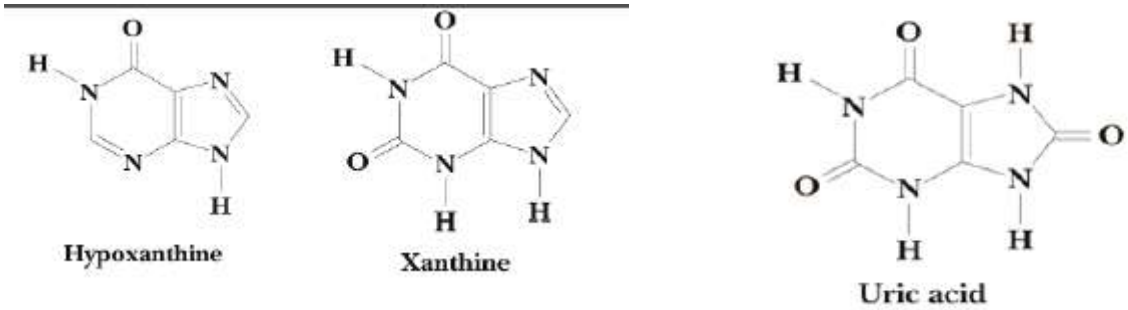
*These bases may be produced by methylation of N-Bases.

Like: Cytosine→5-methylcytosine

*Methylation of nucleotides in DNA plays a role in regulation of DNA replication.

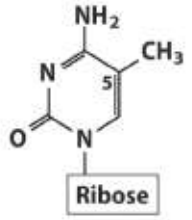
*Sometimes these nucleotides are linked to tRNA.

These three Nucleotides are intermediate in Purine metabolism

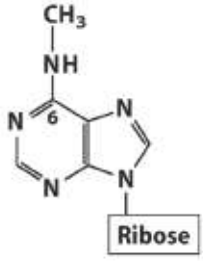


* Uric acid concentration Increasing due to a problem in the pathway of Purine metabolism……and this may lead to Capillary clotting (especially in joints near big toe and hands.

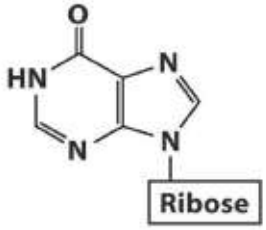
***Other examples:**



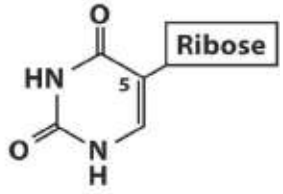
5-Methylcytidine



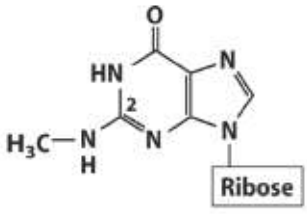
N^6-Methyladenosine



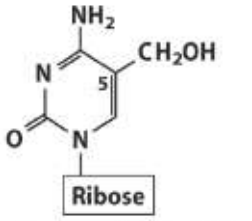
Inosine



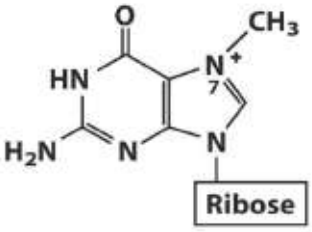
Pseudouridine



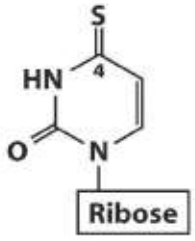
N^2-Methylguanosine



5-Hydroxymethylcytidin

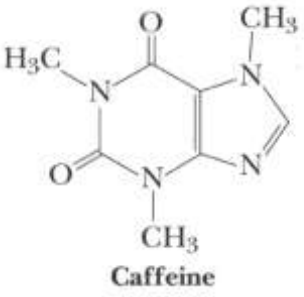


7-Methylguanosine



4-Thiouridine

<u>In Addition to:</u> N4methylcytosine ((cytidine))



Caffeine

Caffeine (**1,3,7trimethylxanthine**):

***Why Caffeine makes us awake??**

→due to its structure (similar to adenosine)….that binds to its neural receptors to promote sleeping….so Caffeine works as Inhibitor for these receptors.

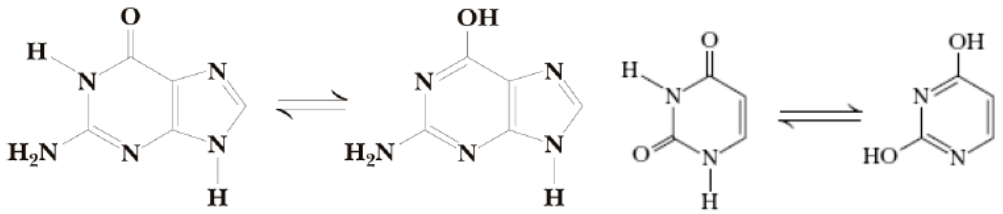
***ATP→Adenosine triphosphate**

***ADP→Adenosine diphosphate**

***AMP→Adenosine monophosphate**

Properties of Pyrimidines & Purines

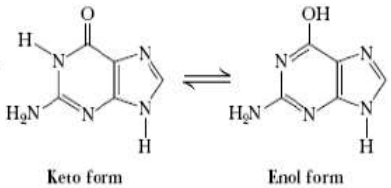
- 1. Keto-enol tautomerism:
  - ✓ Tautomers are constitutional isomers of organic compounds that readily interconvert by a chemical reaction
  - ✓ Commonly: migration of a hydrogen atom/proton, accompanied by a switch of a single bond & adjacent double bond
  - ✓ The keto tautomer (lactam), whereas the enol form (lactim)
  - ✓ lactam form vastly predominates at neutral pH (pKa values for ring nitrogen atoms 1 & 3 in uracil are greater than 8)

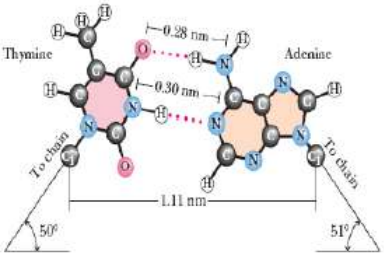


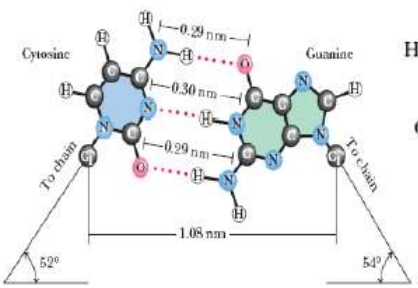
Remember: When PH reaches pKa of a substance, then this substance will dissociate (H)……so if pKa was above PH→it will not dissociate the proton…and if pKa was below PH so it is surely dissociated.

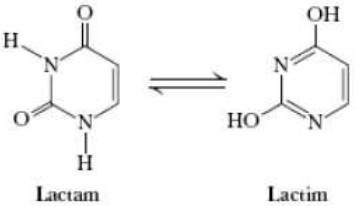
***The Keto (lactam) form is more common due to its pKa→pKa is high so it will control the association of (H).(PH in body is around 7)**

- 2. Acid/base dissociations:
  - ✓ E.g; Uracil, Cytosine, Guanine
- Important in determining if nitrogens are H-bond donors/ acceptors (double helix formation)
- Important functional groups participating in H-bond formation:
  - ✓ Amino groups, Ring Ns, Os





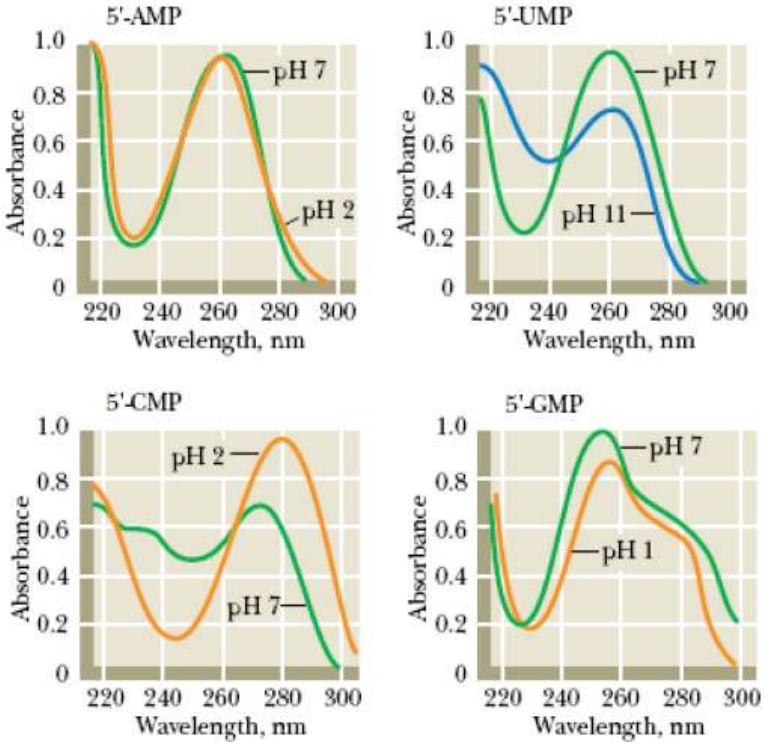




Proton Dissociation Constants (pK_a Values) for Nucleotides			
Nucleotide	pK_a Base-N	pK_1 Phosphate	pK_2 Phosphate
5′-AMP	3.8 (N-1)	0.9	6.1
5′-GMP	9.4 (N-1)	0.7	6.1
	2.4 (N-7)		
5′-CMP	4.5 (N-3)	0.8	6.3
5′-UMP	9.5 (N-3)	1.0	6.4

-So: this keto form is important because it helps in control the association of (H) in the double helix structure of DNA. (Control hydrogen bonding in base paring) because each nucleotide has a specific pKa value at one of its Nitrogens

- **3. Strong absorbance of UV light:**
  - ✓ **A consequence of being aromatic**
  - ✓ **Particularly useful in quantitative & qualitative analysis of nucleotides & nucleic acids**



*This absorbance helps us to detect what is the Nucleotide and its quantity.

→For(U) & (A): the peak is around 260 nm.

→For (C): the peak is around 280 nm.

→For (G): the peak is around 255 nm.

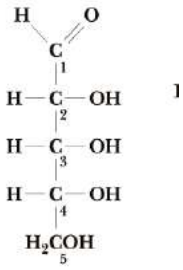
*So we can detect what is the nucleotide then we can use factors to get the concentration of that nucleotide. →convert absorbance to concentration.

Pentoses in Nucleotides

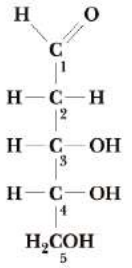
***How to differentiate between Carbon in N-Base & that in the sugar??**

→(') is for the carbon in CHO not N-Base

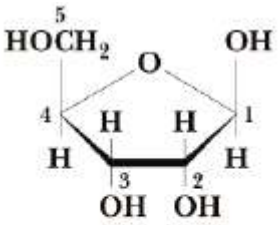
- D-ribose (in RNA)
- 2-deoxy-D-ribose (in DNA)
- Sugars icreases solubility (compared to free bases)
- The position of the carbohydrate is followed by a ′ (prime)
- stereochemistry is β



D-Ribose

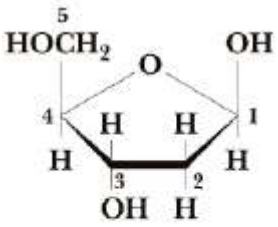


D-2-Deoxyribose



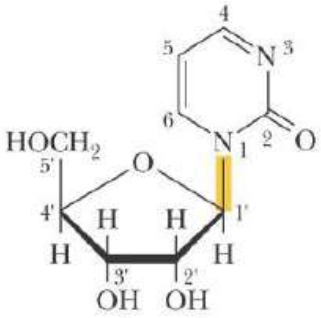
Furanose form of D-Ribose

β-D-Ribofuranose

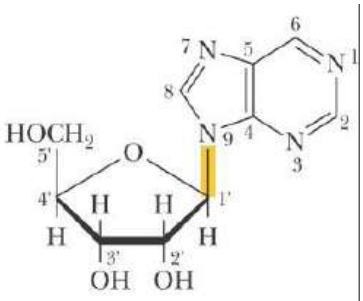


Furanose form of D-2-Deoxyribose

β-D-2-Deoxyribofuranose



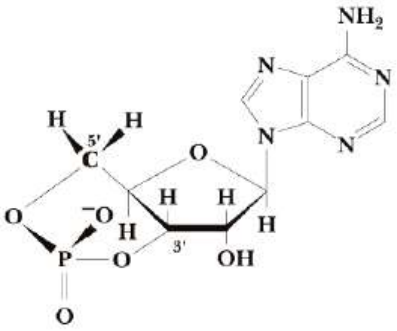
β-N_1-glycosidic bond in pyrimidine ribonucleosides



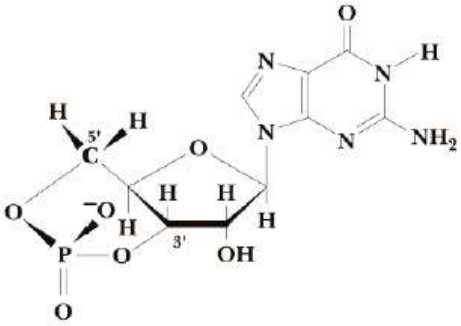
β-N_9-glycosidic bond in purine ribonucleosides

Functions of nucleotides

- Nucleoside 5'-triphosphates are carriers of energy
- Cyclic nucleotides are signal molecules & regulators of cellular metabolism & reproduction
- ATP is central to energy metabolism
- GTP drives protein synthesis
- CTP drives lipid synthesis
- UTP drives carbohydrate metabolism



3',5'-Cyclic AMP

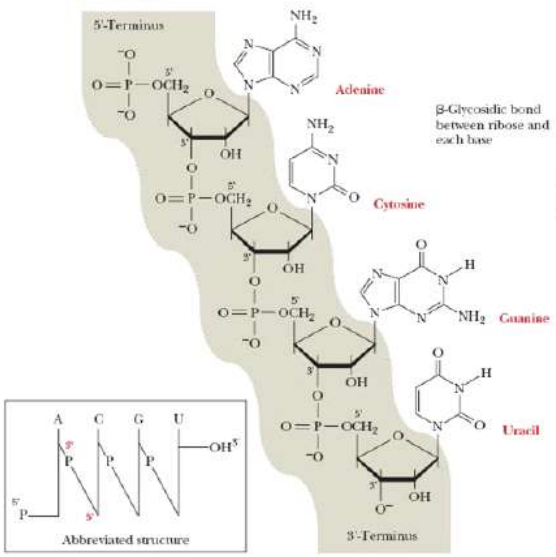


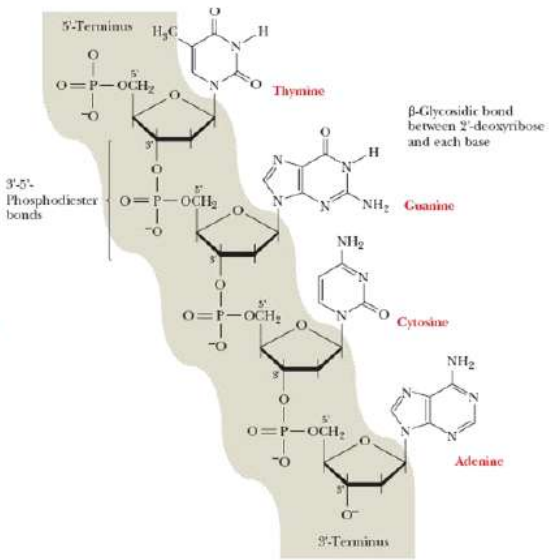
3',5'-Cyclic GMP

-When phosphate is connected to carbon (3) →Cyclic form of nucleotides like:cAMP and cGMP as second messenger

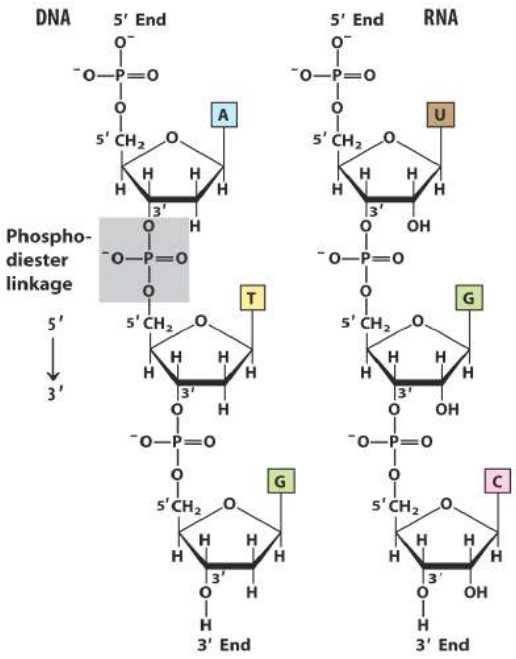
Polymerization

- Leads to nucleic acids. Linkage is repeated (3′,5′-phosphodiester bond)





- *Phosphodiester* bond: connects the 5′-hydroxyl group of one nucleotide to the 3′-hydroxyl group of the next one
- Formed by Polymerase & Ligase activities
- Phosphate pKa ≈ 0
- Nucleic acids are negatively charged



*So we must have free 5' at beginning and free 3' at the end

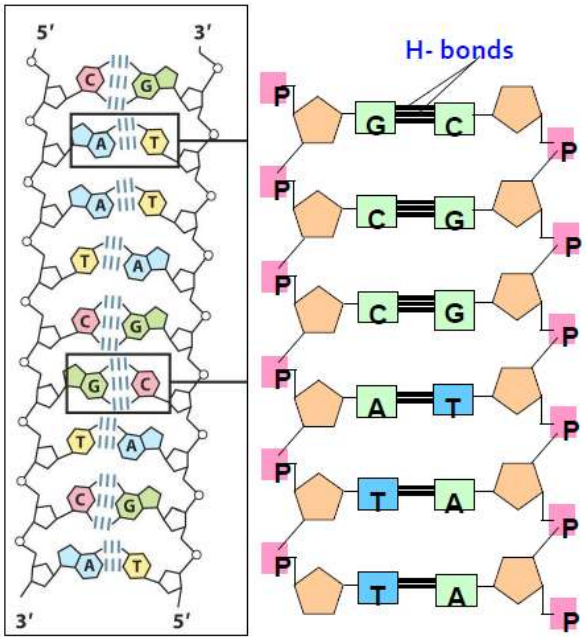
*Phosphate pKa is 0 →always acidic regardless the value of pH (dissociated).

Classes of nucleic acids:

- DNA - one type, one purpose:
  - ✓ A single DNA molecules in virus and bacteria
  - ✓ Eukaryotic cells have many diploid chromosomes mainly in nucleus, but also mitochondria & chloroplasts
- RNA - 3 (or 4) types, 3 (or 4) purposes
  - ✓ Ribosomal RNA - the basis of structure & function of ribosomes
  - ✓ Messenger RNA - carries the message
  - ✓ Transfer RNA - carries the amino acids
  - ✓ Small nuclear RNA
  - ✓ Small non-coding RNAs

.

- Diameter: 2 nm
- Length: 1.6 million nm (*E. coli*)
- Compact and folded (*E. coli* cell is only 2000 nm long)
- Antiparallel double helix
- Backbone vs. side chains
- Specific base-pairing
  - ✓ Chargaff's rules (A=T & C=G)
- Strands are joined by the bases (complementary)
- Stable (H-bonds)



***E.coli is a reference in bacterial cells.**

***DNA is circular in eukaryotes.**

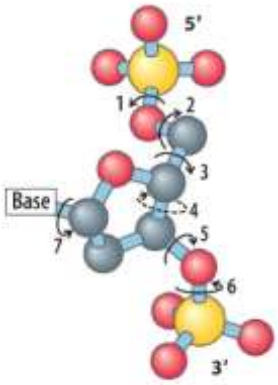
***N-Base is the different in nucleotides.**

***Side chain is the N-Base and the sugar with phosphate group is the back bone.**

***hydrogen bonding is weak but number of H-bonding is high →stability**

***DNA structure has flexibility due to rotations around bonds in the nucleotides.**

***purines form hydrogen bonds to pyrimidines, with adenine bonding only to thymine in two hydrogen bonds, and cytosine bonding only to guanine in three hydrogen bonds (in DNA).**



DNA Primary Structure → → →

((Here: Numbers, types and sequence of nucleotides is important))

- A biopolymer that consists of a backbone of alternating units of 2-deoxy-D-ribose and phosphate

- Primary Structure: the sequence of bases along the pentose-phosphodiester backbone of a DNA molecule
  - ✓ By convention, from left to right, & from the 5′-end to the 3′-end
  - ✓ System of notation single letter (A,G,C,U and T)
  - ✓ More abbreviated notations: d(GACAT); pdApdCpdGpdT pdACGT

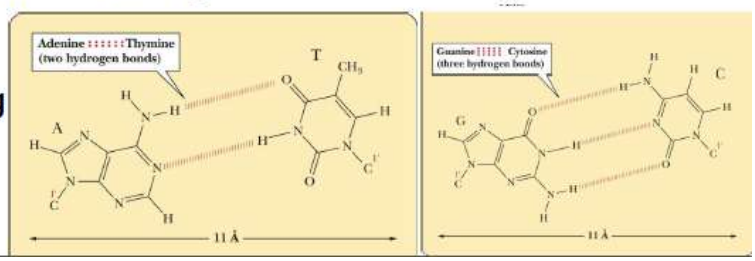
DNA secondary structure:

- Secondary structure: the ordered arrangement of nucleic acid strands

- Double helix model (James Watson and Francis Crick): a type of 2° structure of DNA molecules in which two antiparallel polynucleotide strands are coiled in a right-handed manner about the same axis

- Base Pairing: T-A (2 H-bonds) & G-C (3 H-bonds)

- Minor vs. major grooving

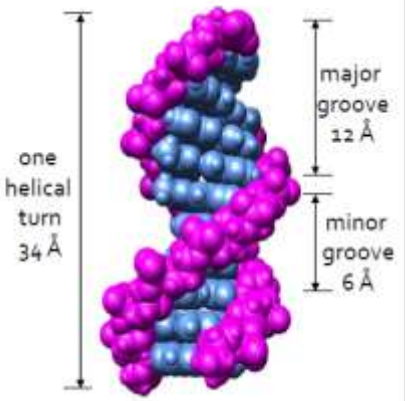


***this grooving makes it soluble in water.**

Please check slide 21*

Classes Of DNA → → →

- B-DNA
  - Considered the physiological form
  - A right-handed helix, diameter 11 Å
  - 10 base pairs per turn (34Å)
- A-DNA
  - A right-handed helix, but thicker than B-DNA
  - 11 base pairs per turn of the helix
  - Has not been found *in vivo*
- Z-DNA
  - A left-handed double helix
  - May play a role in gene expression



B-DNA is the form that we know (in nucleus)…A-DNA is thicker than B-DNA.

- Base stacking
  - Bases are very nearly planar, hydrophobic & interact by hydrophobic interactions
  - In B-DNA, each base rotated by 32° compared to the next and (base pairing vs. maximum overlap)
  - Bases exposed to the minor groove come in contact with water
  - Many bases adopt a *propeller-twist* in which base pairing distances are less optimal but base stacking is more optimal and water is eliminated from minor groove contacts

***in double helix..Bases on top of each other are very nearly…and there is hydrophobic interactions between them…and base paring (hydrogen bonding) in this case are not in their perfect binding manner due to base stacking….and this called "Propeller-twist".**

***base pairing: N bases are opposite to each other.**

***base staking : N bases are above each other.**