Biochemistry

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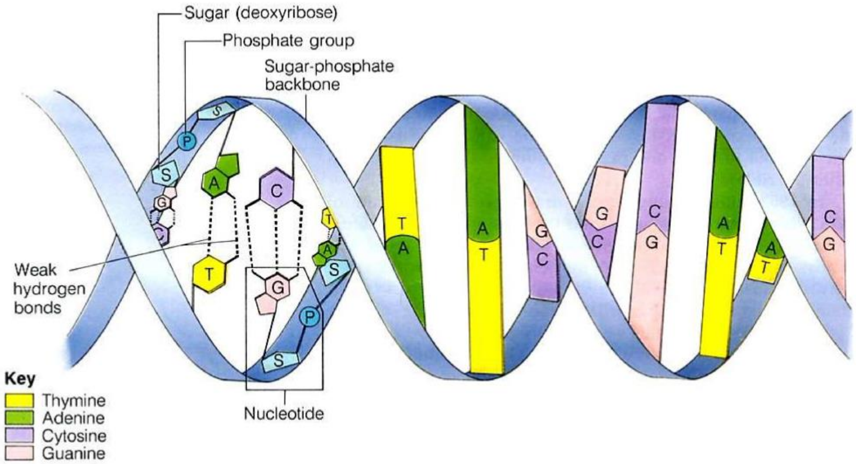
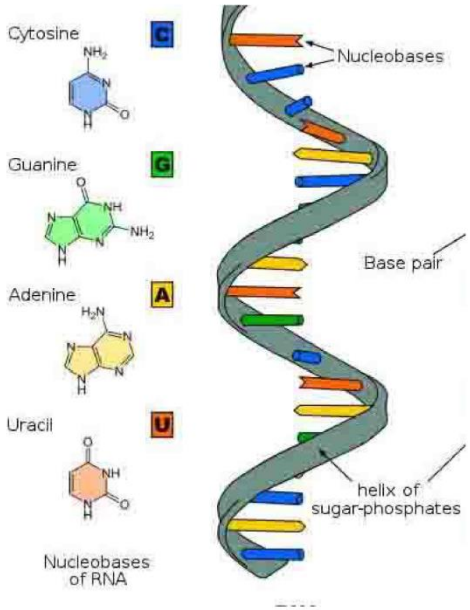
Nucleic Acids

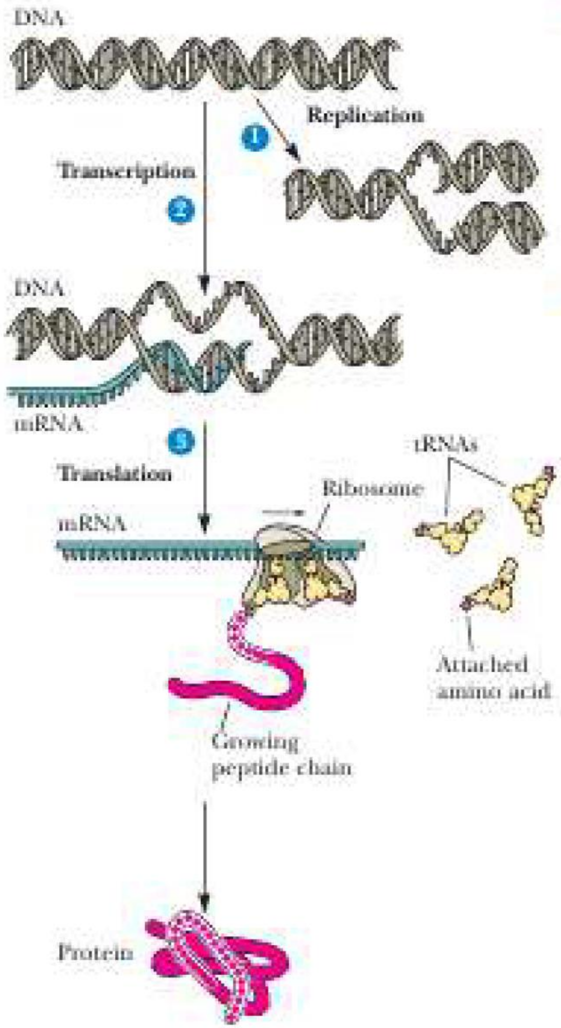


DNA

DNA =deoxyribonucleic acid
RNA = Ribonucleic acid



RNA



1 Replication
DNA replication yields two DNA molecules identical to the original one, ensuring transmission of genetic information to daughter cells with exceptional fidelity.

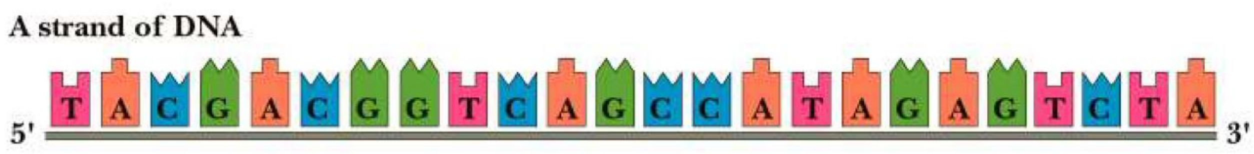
2 Transcription
The sequence of bases in DNA is recorded as a sequence of complementary bases in a single-stranded mRNA molecule.

3 Translation
Three-base codons on the mRNA corresponding to specific amino acids direct the sequence of building a protein. These codons are recognized by tRNAs (transfer RNAs) carrying the appropriate amino acids. Ribosomes are the "machinery" for protein synthesis.

DNA – storage of genetic material

RNA – mRNA (messenger) – transport of information from DNA to ribosomes
rRNA (ribosomal) – structure and function of ribosomes
tRNA (transport) – adapter molecules during protein synthesis
etc.

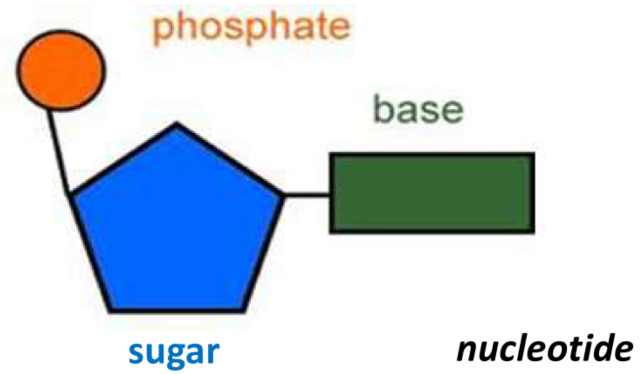
Nucleic Acids - Sequence

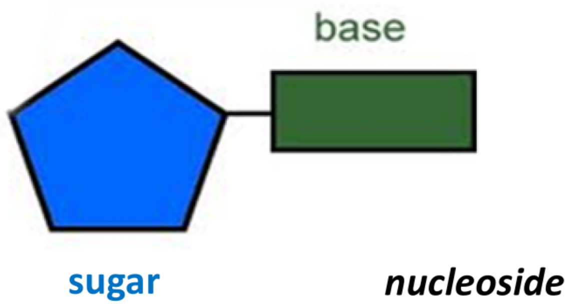


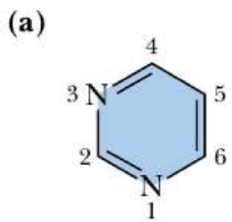
Nucleic Acids - Nucleotides

Nucleic acid – polymer
Nucleotide – monomer

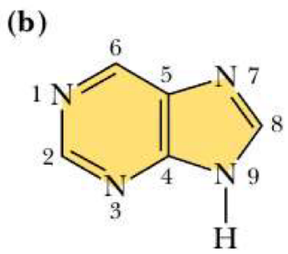
Structure of monomer
- heterocyclic base
- 5-chain sugar (pentose)
- phosphate





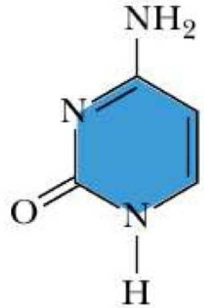


The pyrimidine ring

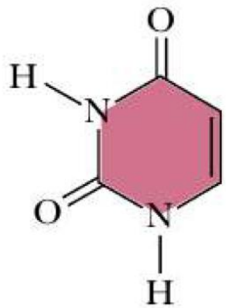


The purine ring system

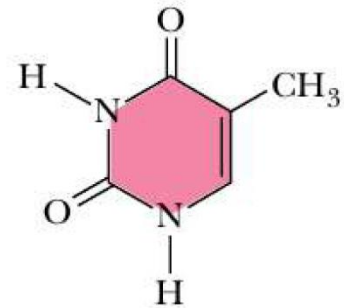
Nucleic Acids - Bases



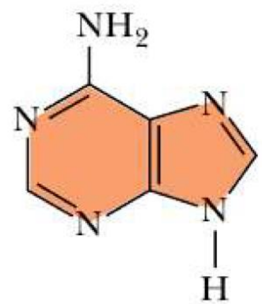
Cytosine
(2-oxy-4-amino pyrimidine)



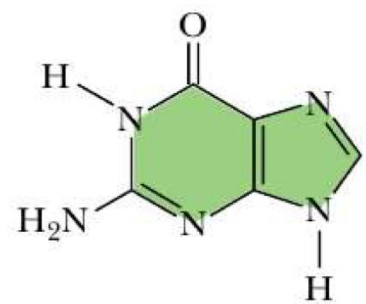
Uracil
(2-oxy-4-oxy pyrimidine)



Thymine
(2-oxy-4-oxy 5-methyl pyrimidine)

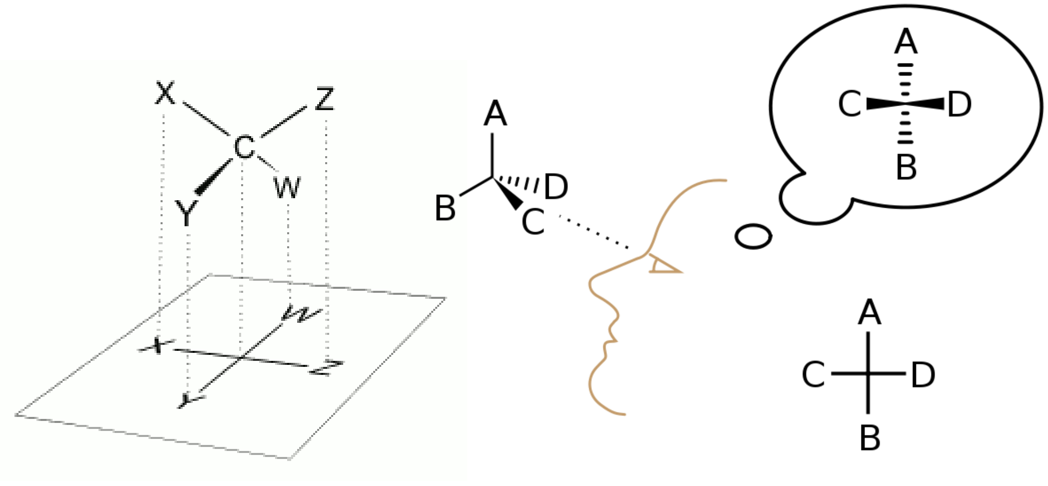


Adenine
(6-amino purine)

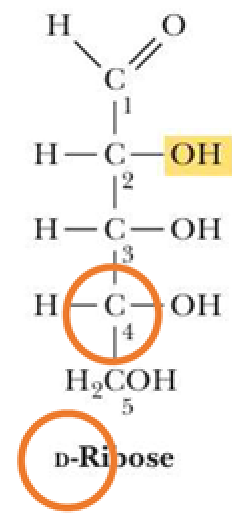


Guanine
(2-amino-6-oxy purine)

Fischer projection of carbohydrates (sugars)

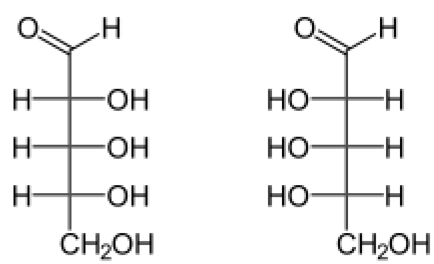


Fischer projection of aldo-pentoses



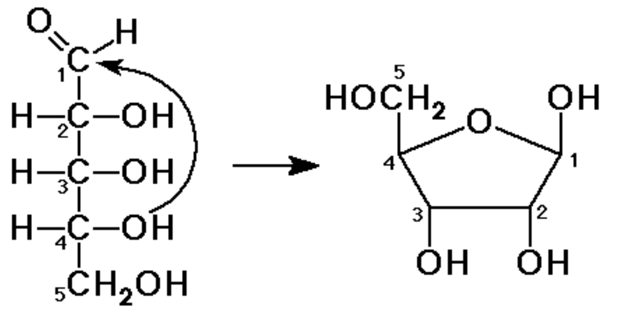
For carbohydrates carbon chain is depicted vertically with C1 (for aldoses) carbon on top

D means that OH at number C4 is on the right (L – will be on the left)



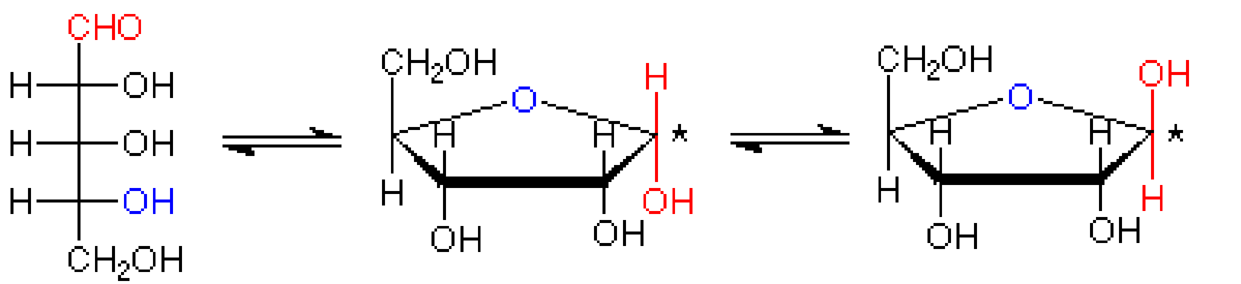
D-Ribose L-Ribose

Cyclization



D-ribose β-D-ribofuranose

* anomeric carbon

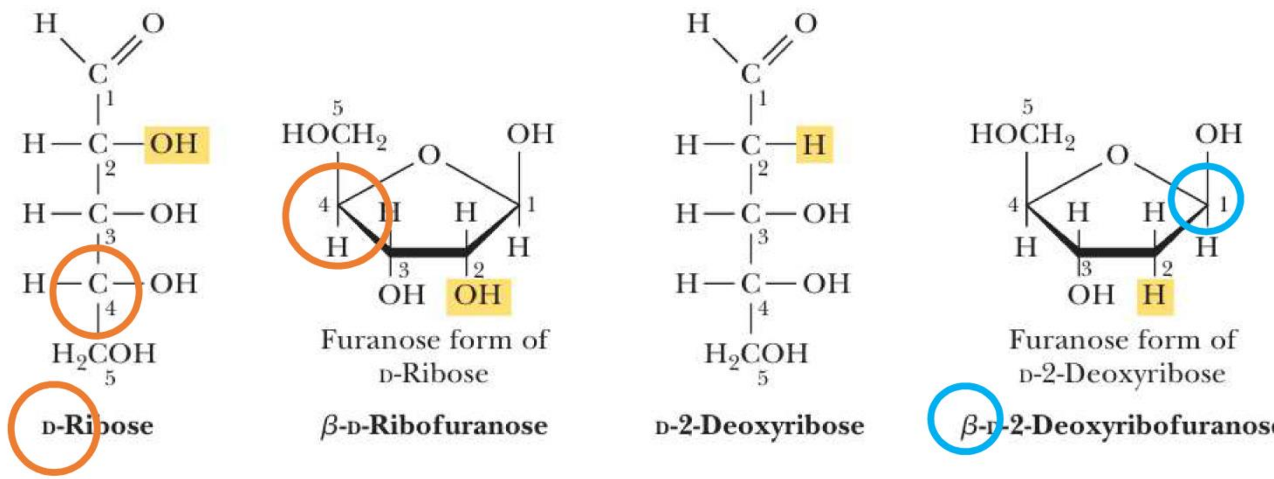


D-ribose

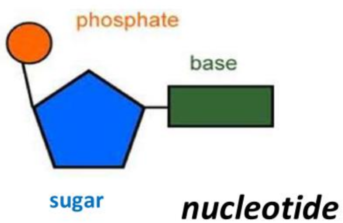
α-D-ribose
OH at anomeric carbon down

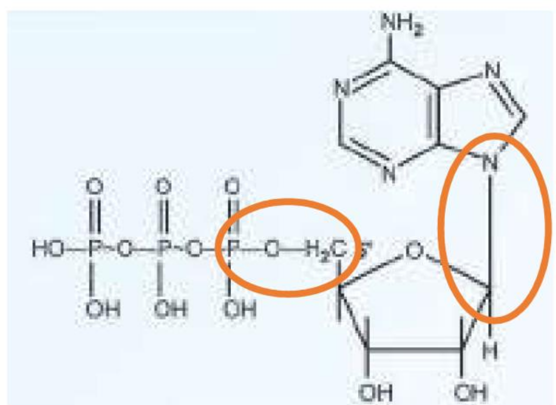
β-D-ribose
OH at anomeric carbon up

Nucleic Acids - Sugars



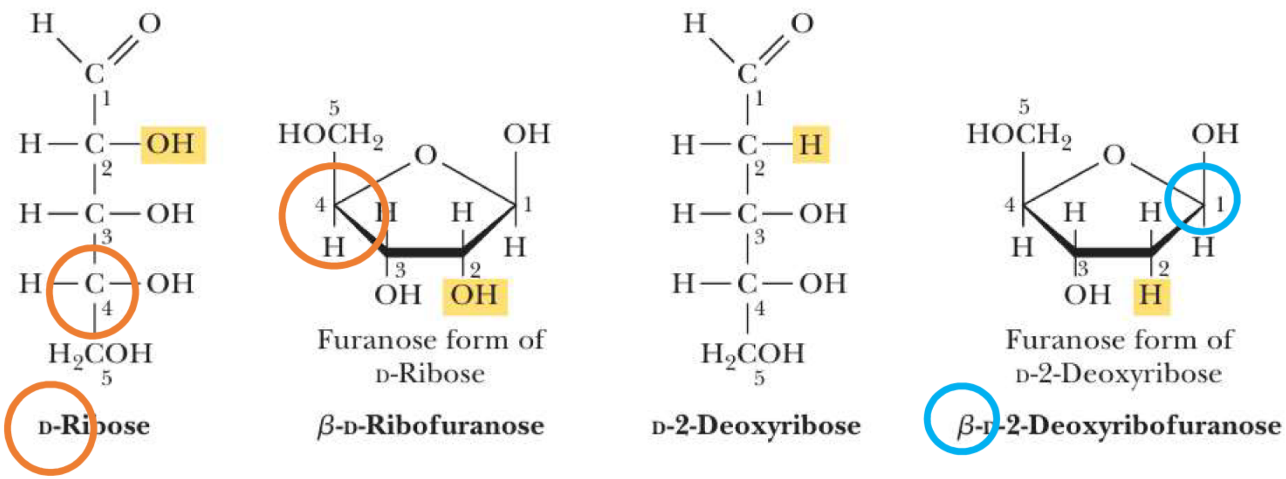
Nucleic Acids – Intranucleotide bonds



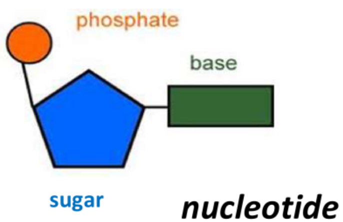


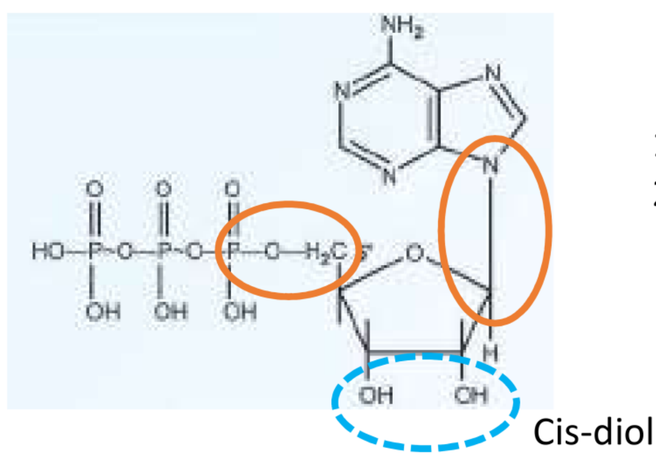
1. Ester bond
2. N-glycosidic bond

Nucleic Acids - Sugars



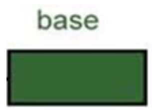
Nucleic Acids – Intranucleotide bonds

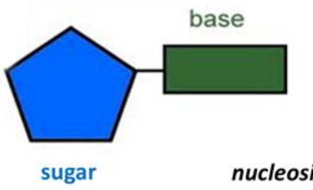




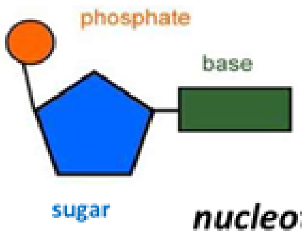
1. Ester bond
2. N-glycosidic bond

Base	*Nucleoside*	*Nucleotide*	*Nucleic acid*
Purines			
Adenine	Adenosine	Adenylate	RNA
	Deoxyadenosine	Deoxyadenylate	DNA
Guanine	Guanosine	Guanylate	RNA
	Deoxyguanosine	Deoxyguanylate	DNA
Pyrimidines			
Cytosine	Cytidine	Cytidylate	RNA
	Deoxycytidine	Deoxycytidylate	DNA
Thymine	Thymidine or deoxythymidine	Thymidylate or deoxythymidylate	DNA
Uracil	Uridine	Uridylate	RNA



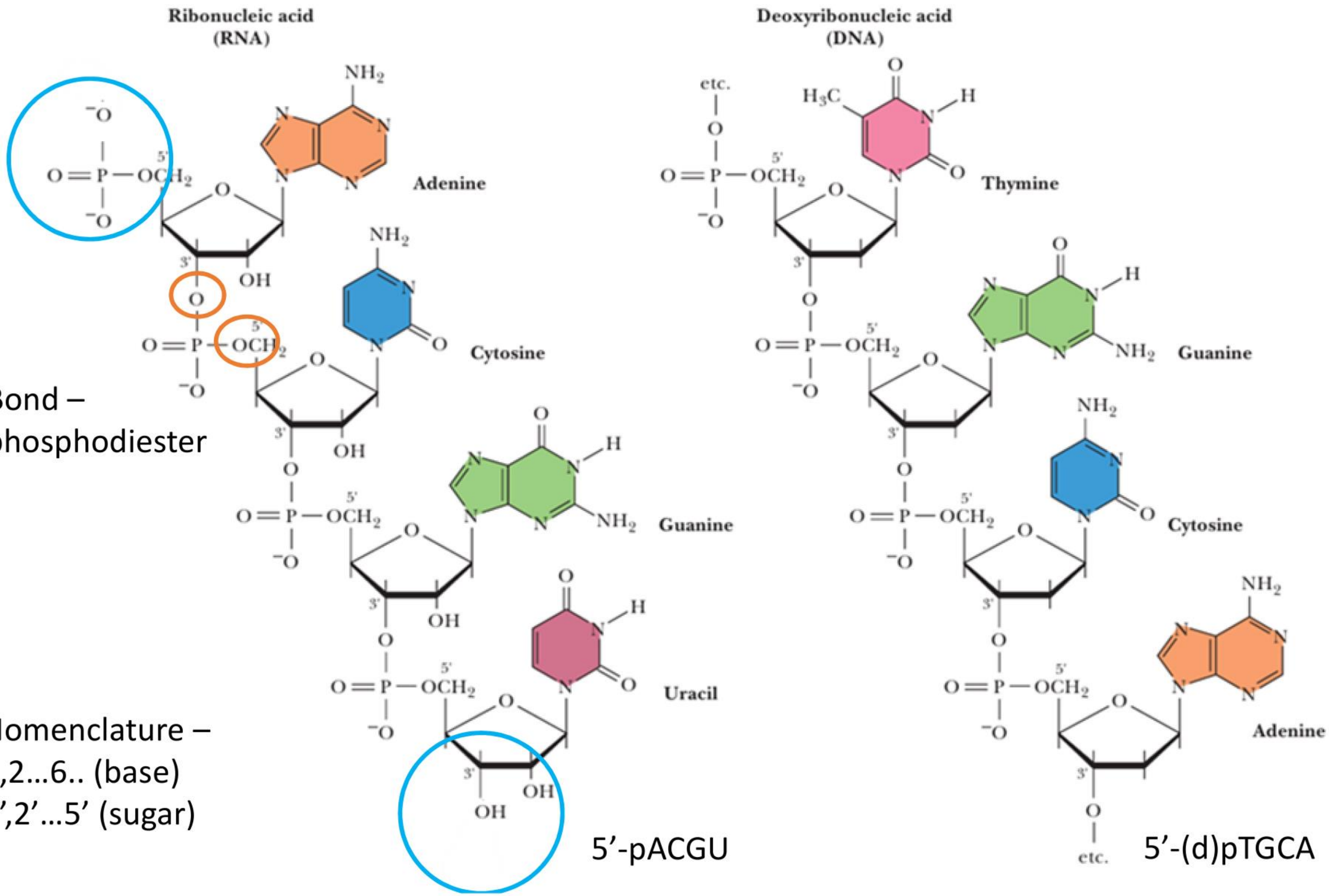


nucleoside



nucleotide

Nucleic Acids - Chain



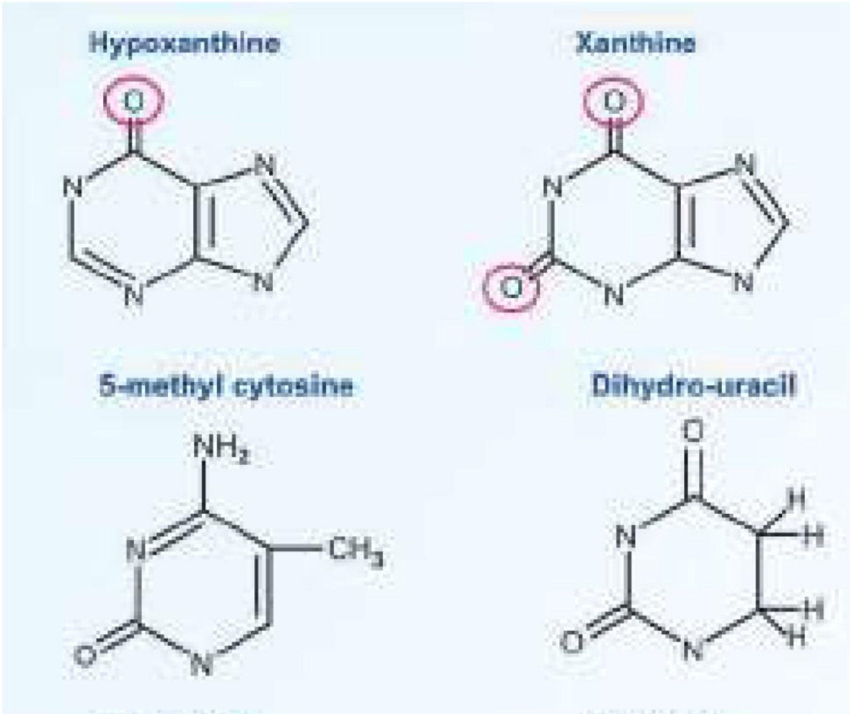
Bond –
phosphodiester

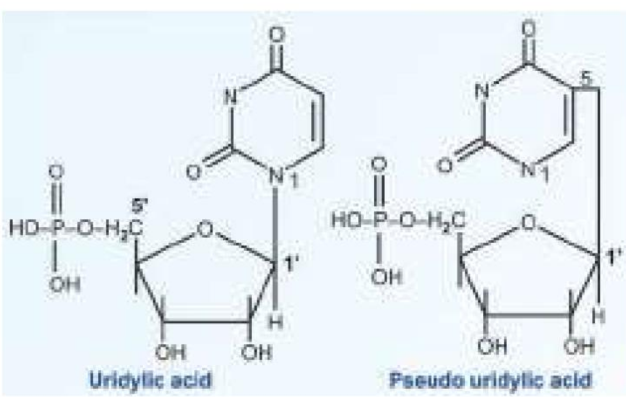
Nomenclature –
1,2…6.. (base)
1’,2’…5’ (sugar)

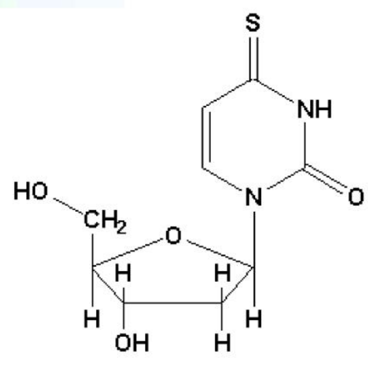
5’-pACGU

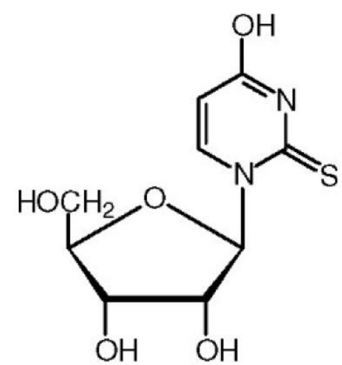
5’-(d)pTGCA

Nucleic Acids –
Minor nucleobases



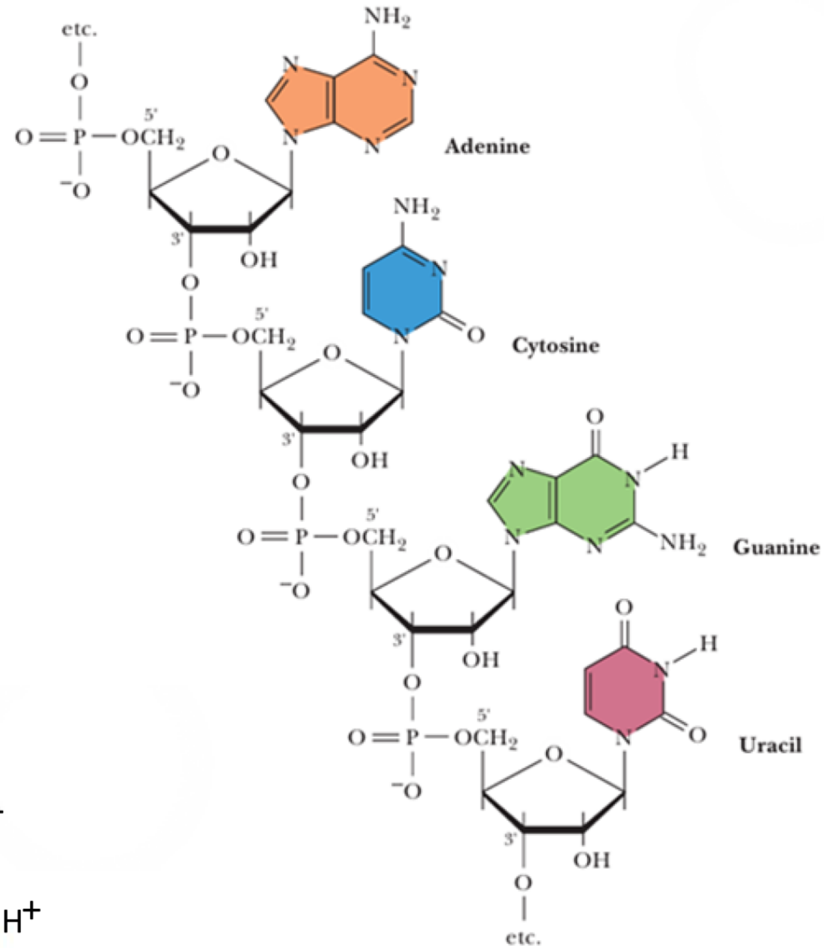



4-Thiouridine


2-thiouridine

Nucleic Acids – Charge

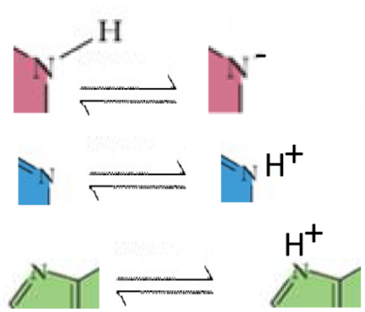
pK phosphate = 2-3
(negative charge)



What can have charge?
(pK for free nucleotides)

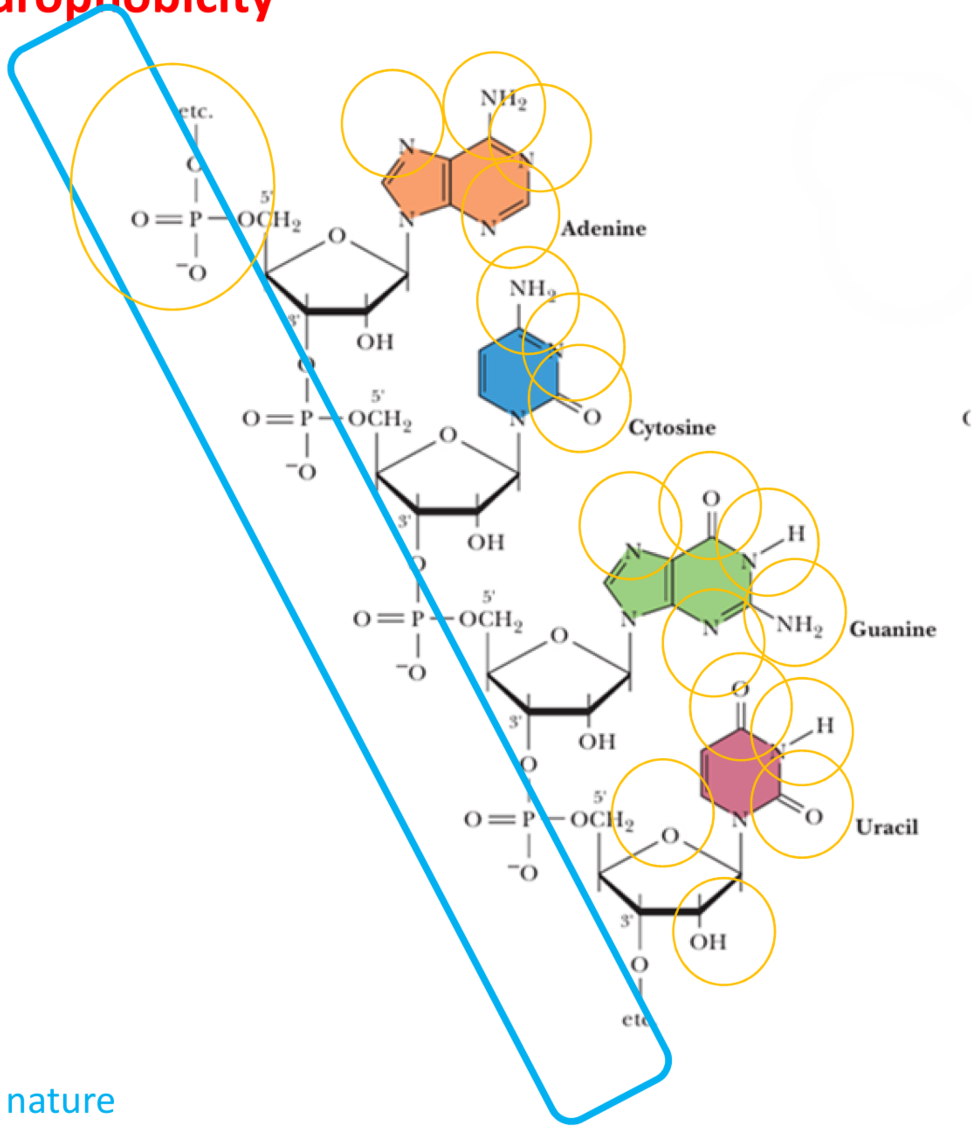
pK(T N3) 9.68
pK(U N3) 9.25

pK(C N3) 4.2
pK(G N7) 2.2



Nucleobases are uncharged

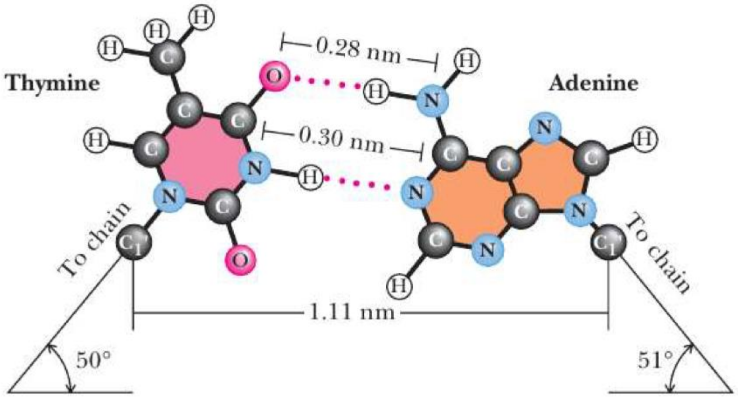
Nucleic Acids – hydrophobicity

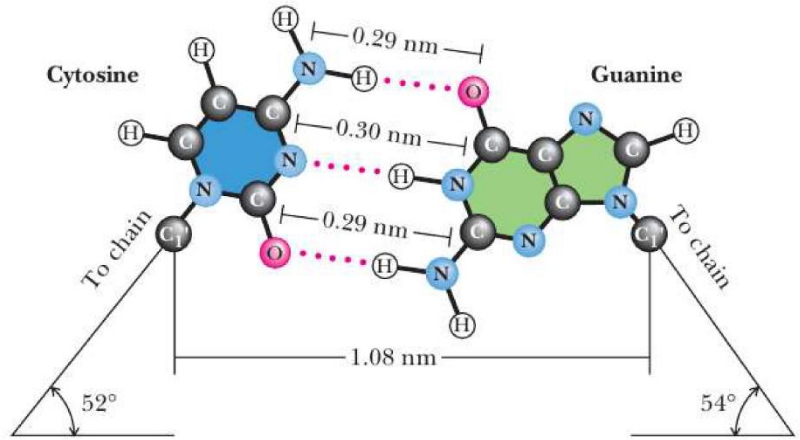


Hydrophilic centers
(polar or charged or
hydrogen bonding)

Nucleic acid – polyanionic nature

Nucleic Acids – Watson Crick base pairing

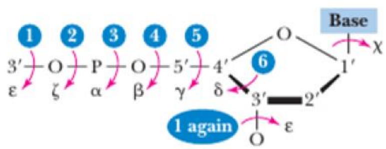




Purine-pyrimidine pairing (H-bonds)

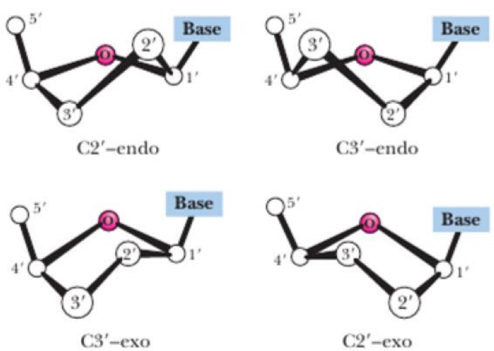
Nucleic Acids – degrees of freedom

(a) The six degrees of freedom in the sugar–PO_4 backbone:



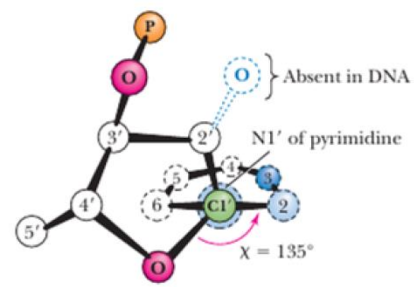
Rotation about bonds 1, 2, 3, 4, 5, and 6 correspond to 6 degrees of freedom designated α, β, γ, δ, ε, and ζ as indicated.

(b) Four puckered conformations of furanose rings:



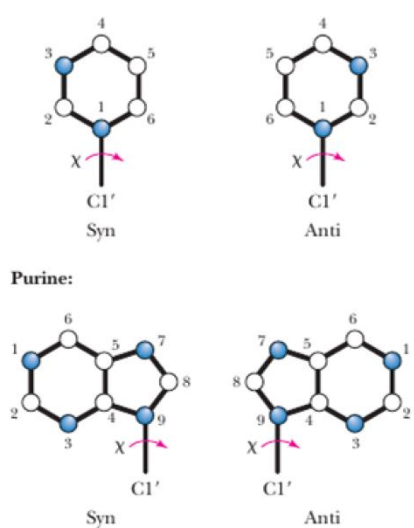
+twists!

(c) Free rotation about C1′–N glycosidic bond (7th degree of freedom):

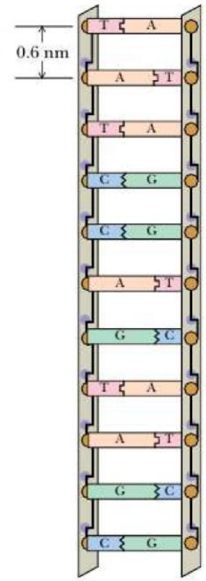


Pyrimidine:

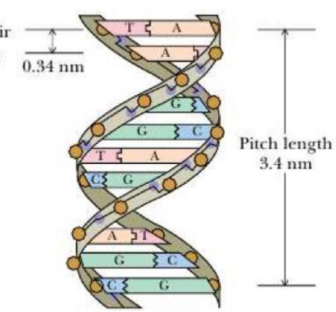
Purine:



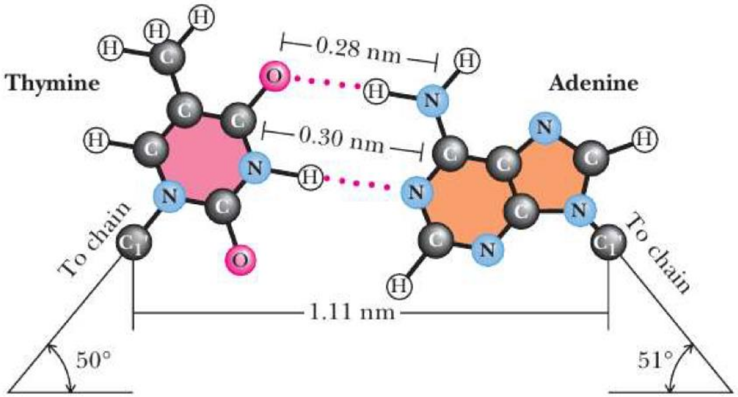
(a) Ladder

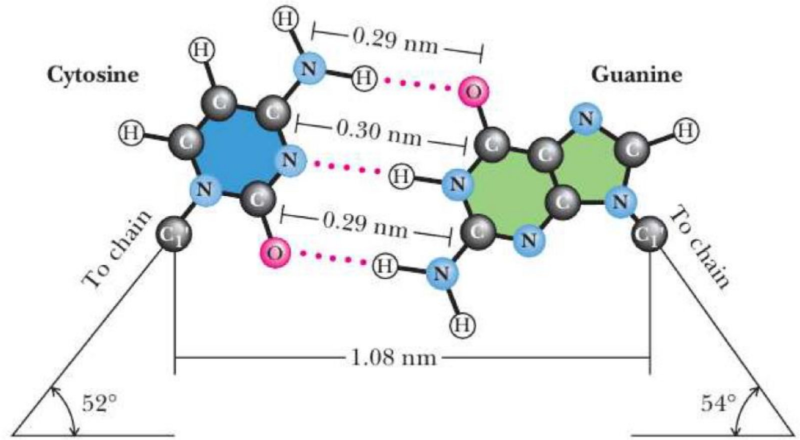


(b) Helix



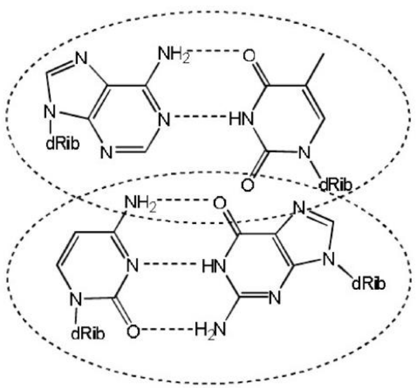
Nucleic Acids – Watson Crick base pairing

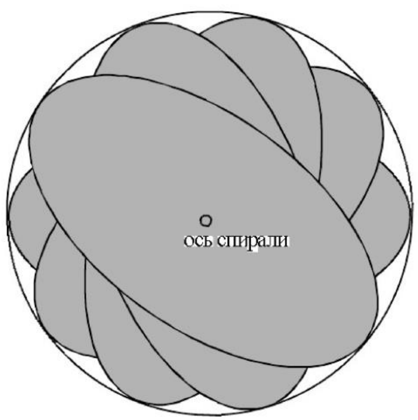


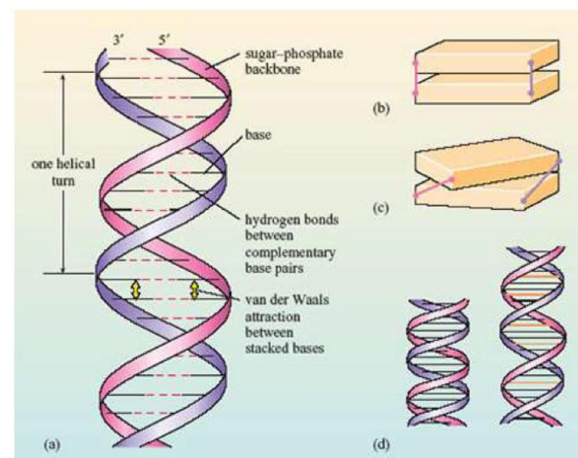


Purine-pyrimidine pairing (H-bonds)

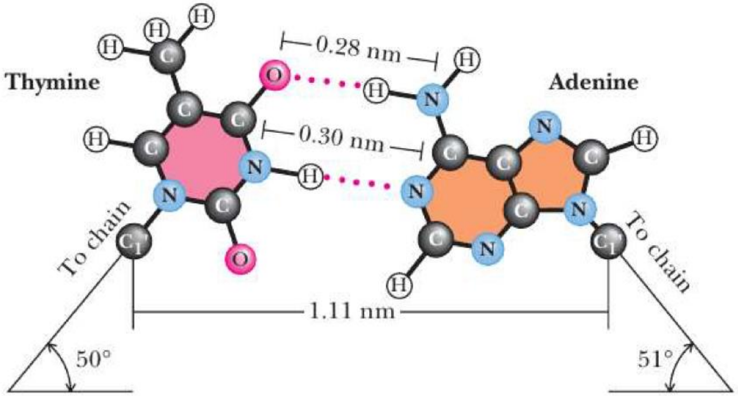
Base stacking (planar) – Hydrophobic + dipole-dipole interactions (van der Wals)

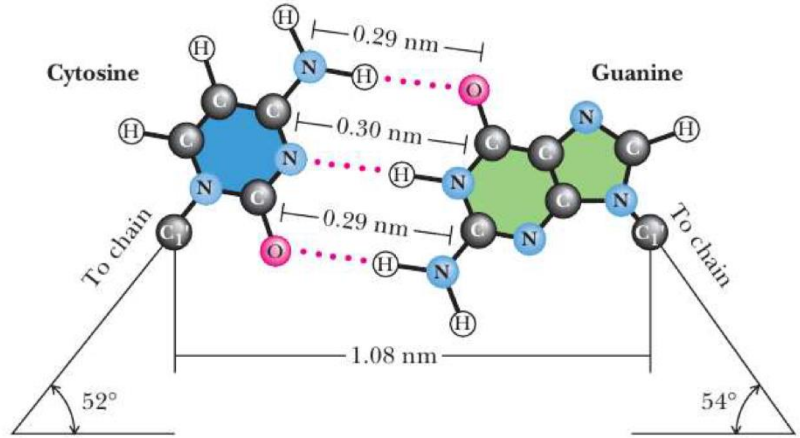


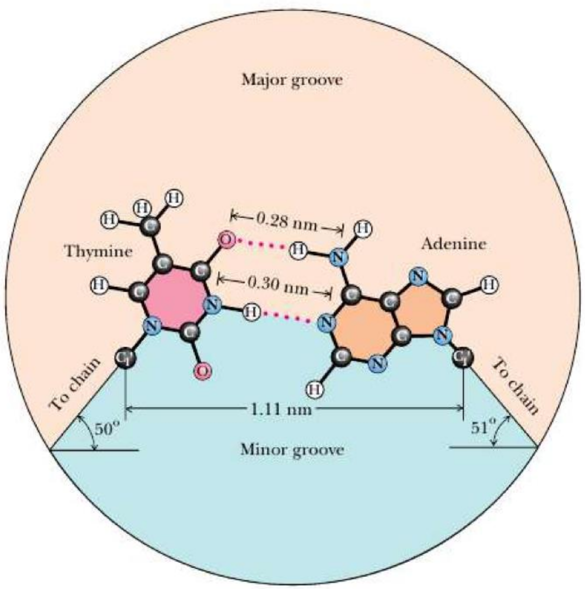


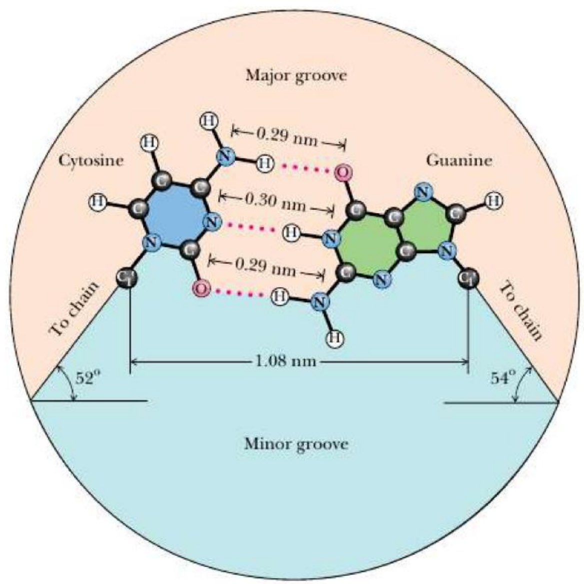


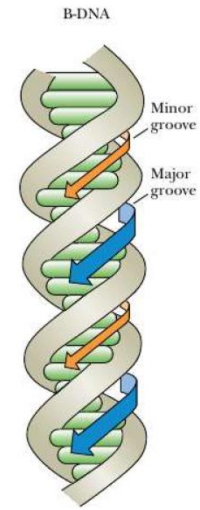
Nucleic Acids – Watson Crick base pairing (grooves)



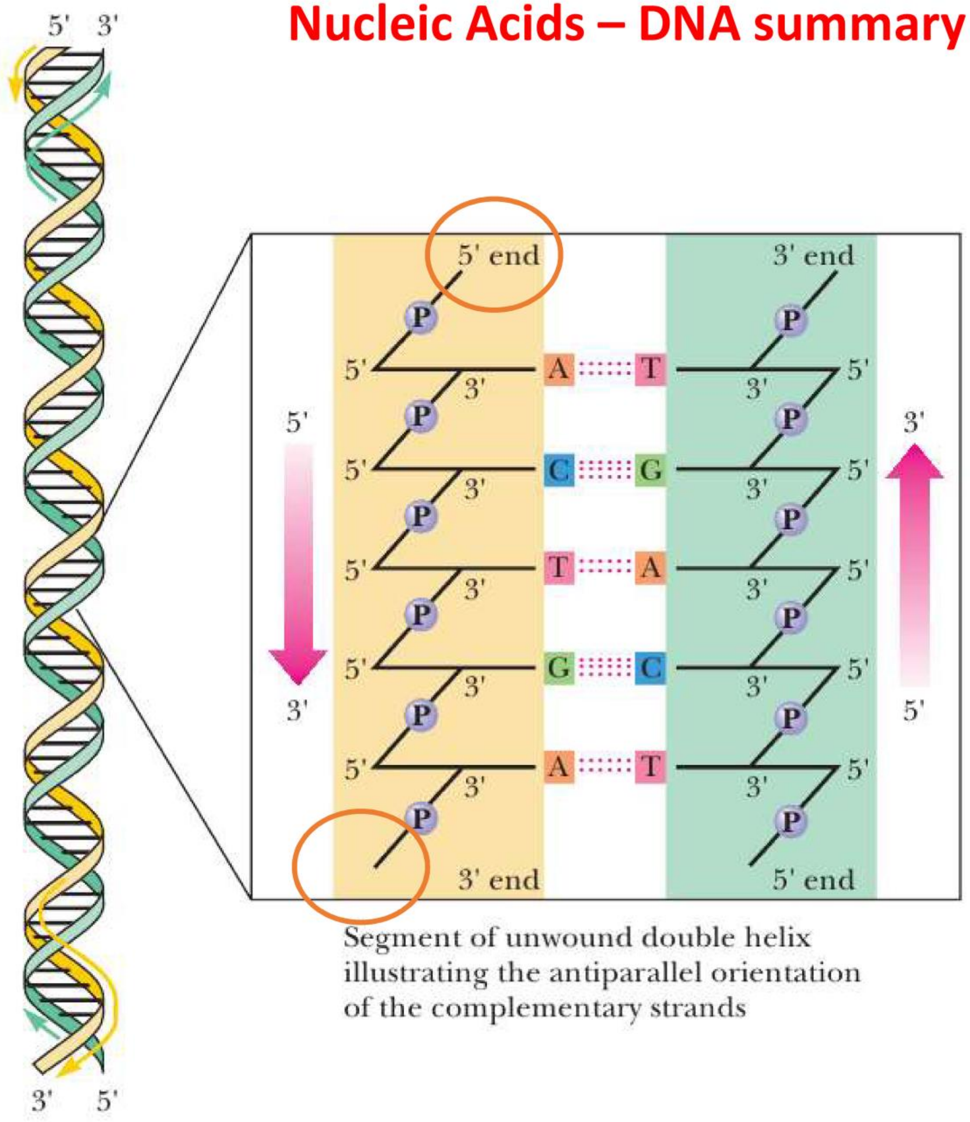








Nucleic Acids – DNA summary

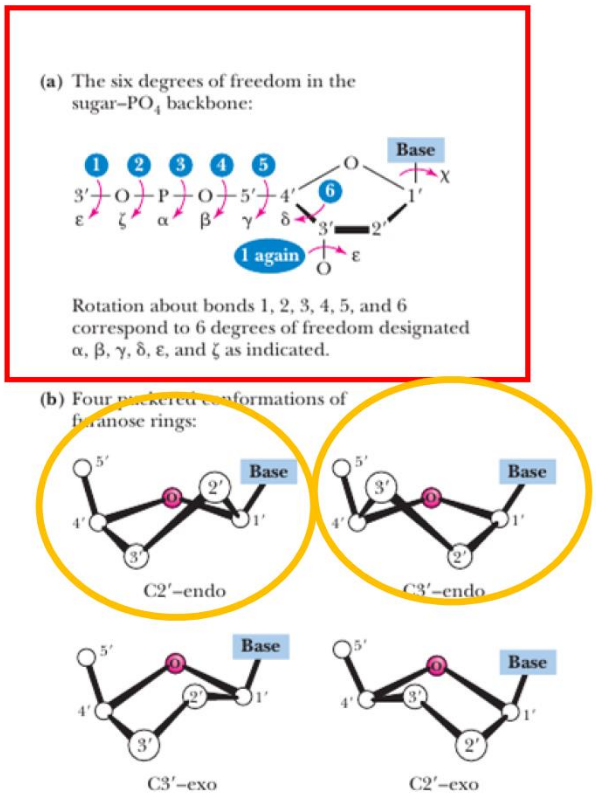


Segment of unwound double helix illustrating the antiparallel orientation of the complementary strands

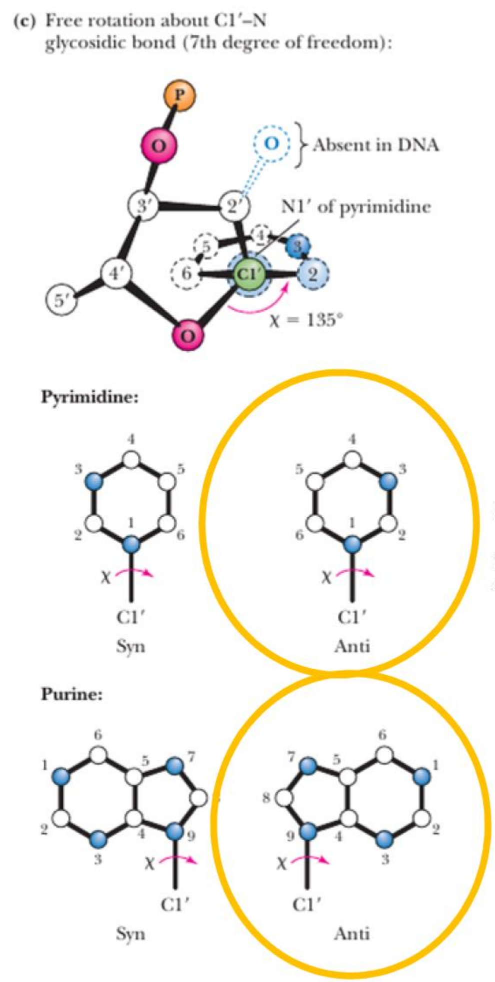
DNA

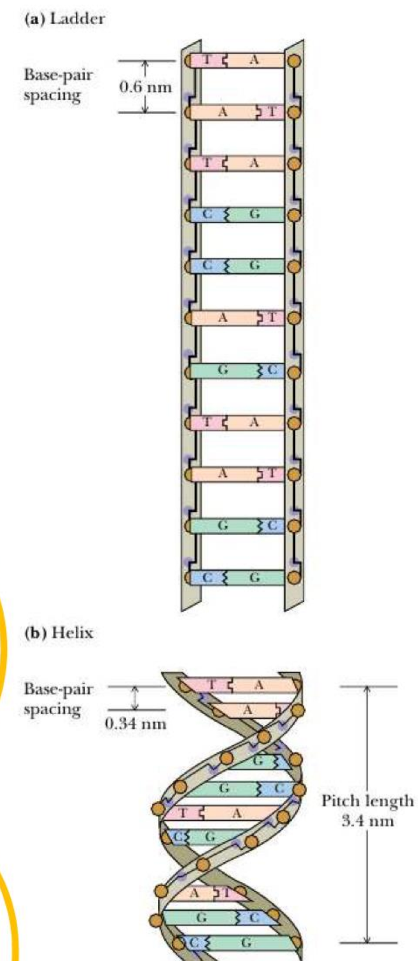
1. Irregularity
2. Antiparallel orientation
3. Complementarity
4. (Secondary structure)

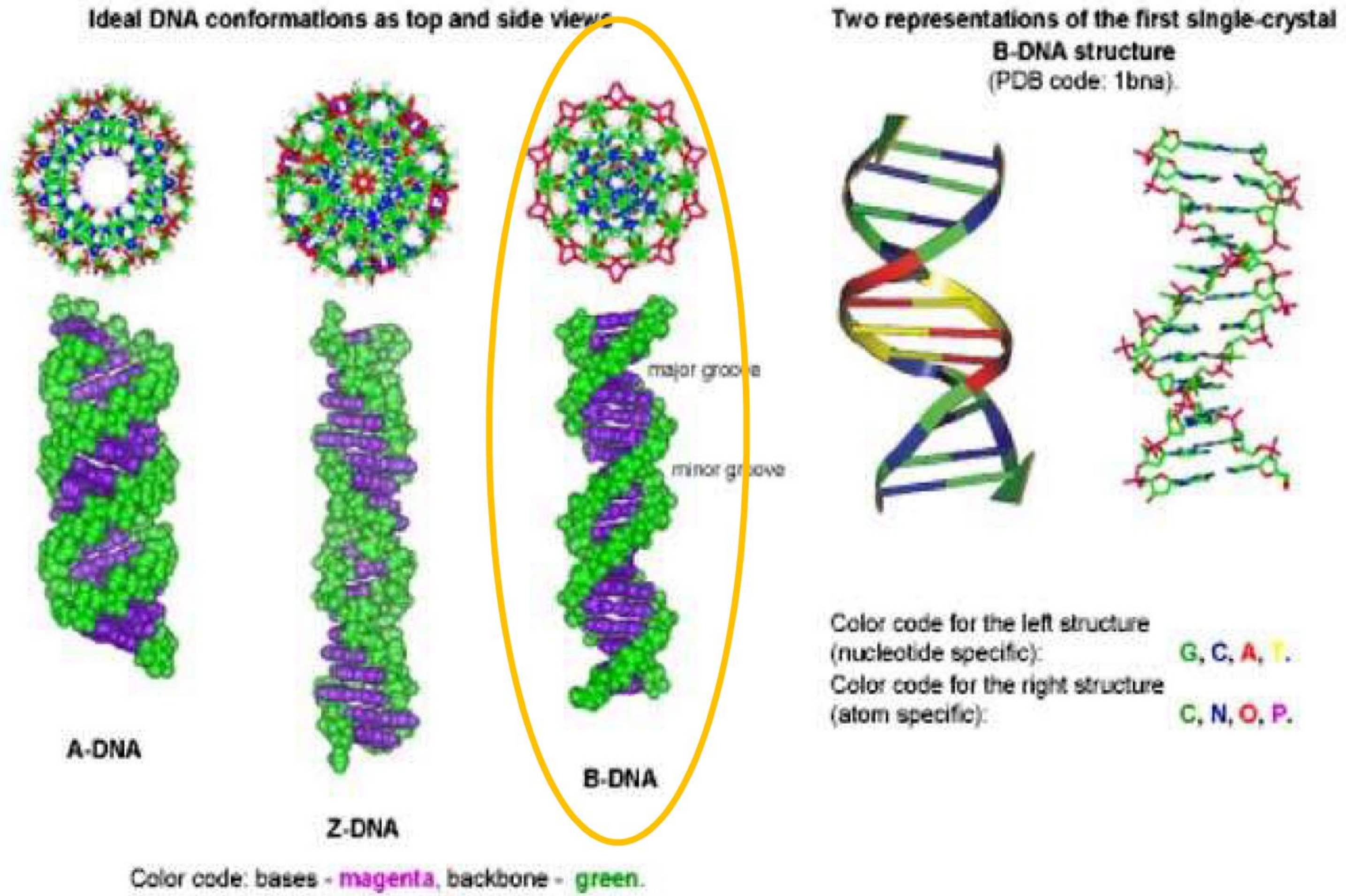
Nucleic Acids – degrees of freedom



+twists!







A, B, C – right handed spirals

Z - left

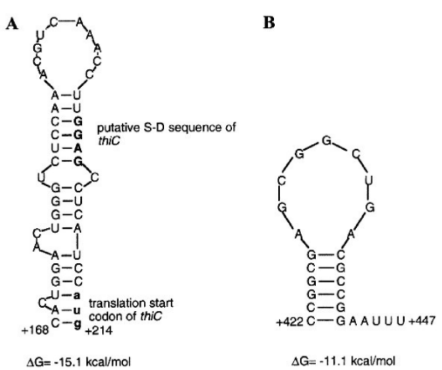
Nucleic Acids – RNA vs DNA

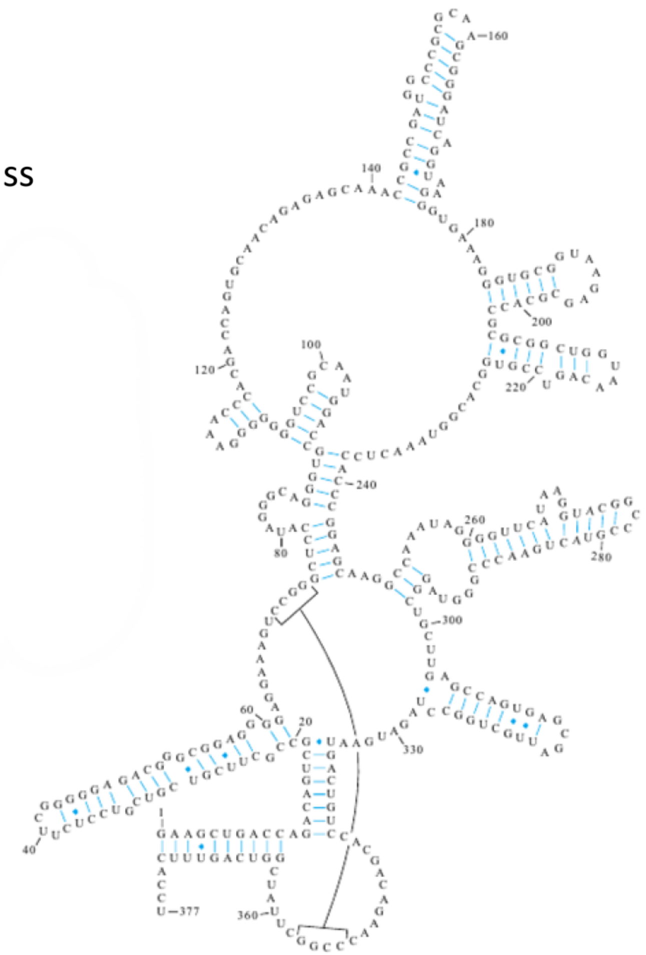
	DNA	RNA
Pentose	Deoxyribose	Ribose
Bases	A T G C	A U G C
Structure	99.99% ds	99.99% ss

Single stranded DNA (ss) is usually circular, double-stranded DNA is majorly (not always) linear

RNA – high degree of secondary structure

Clear preference for hairpins

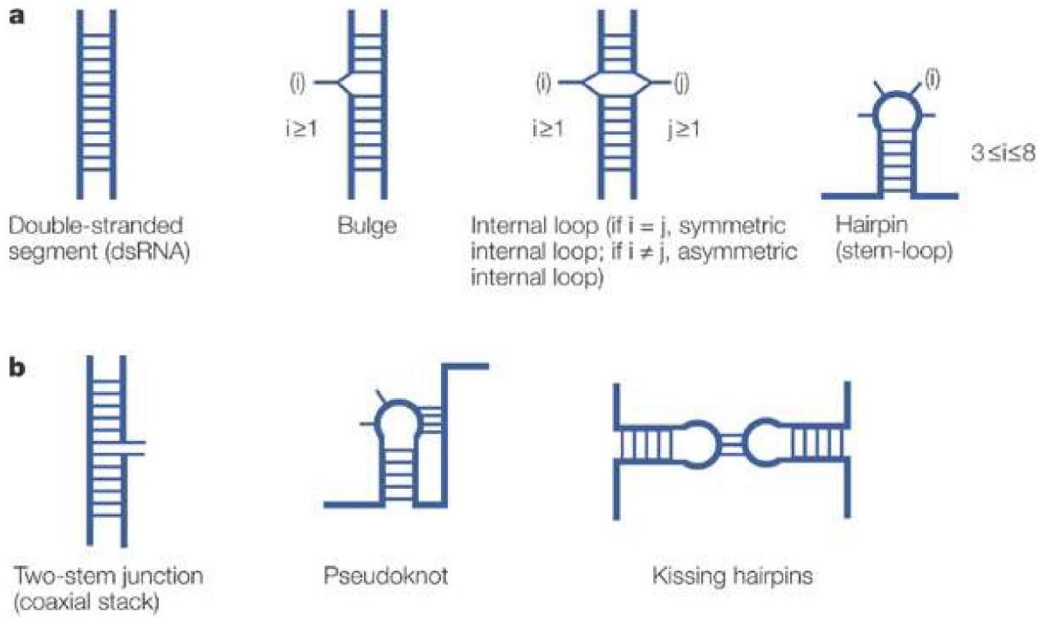




Component of RNAse P

	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

Nucleic Acids – RNA secondary structures (usually within 1 molecule)



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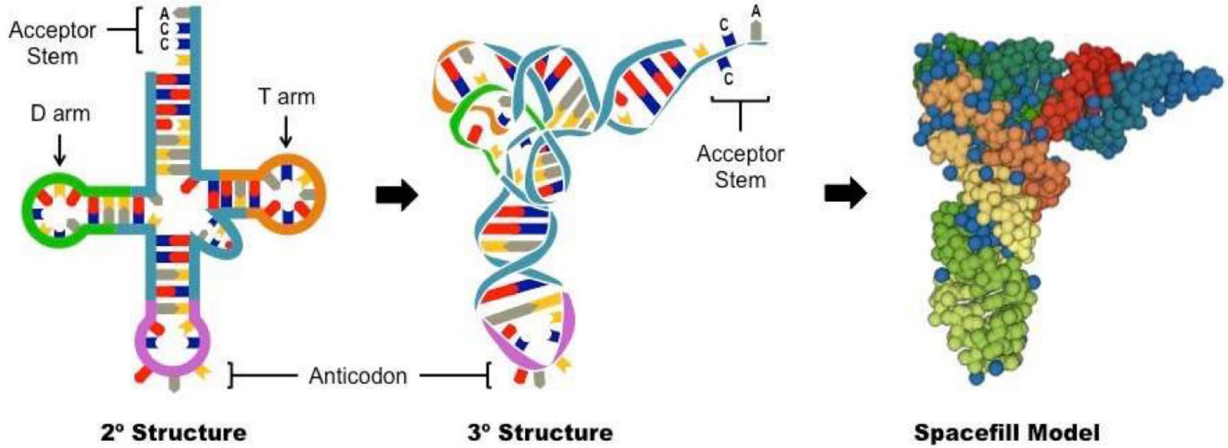
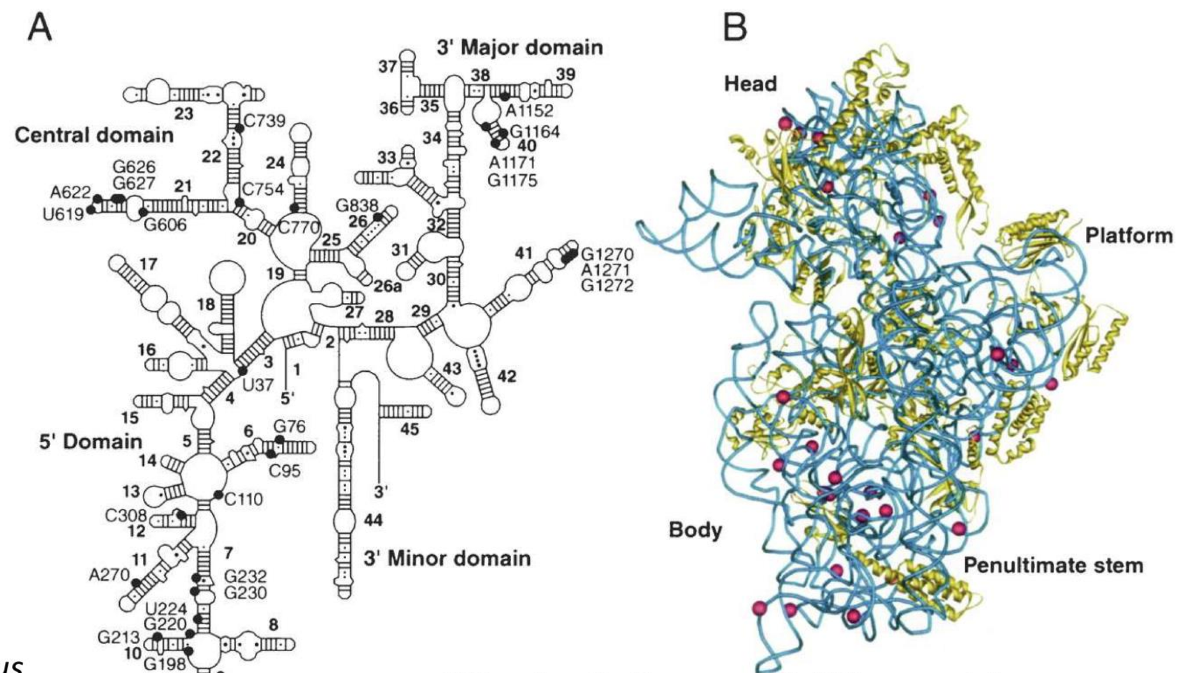


tRNA

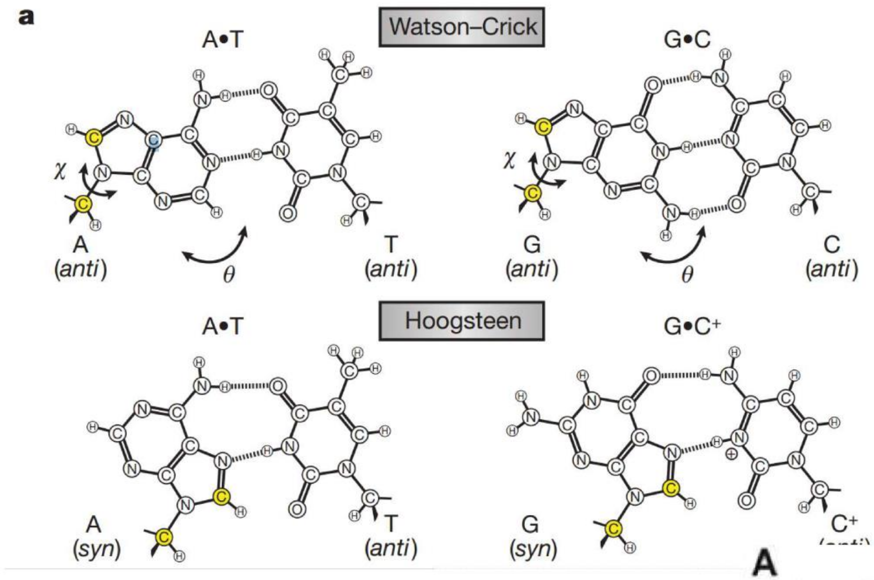


rRNA

16S rRNA T.Thermophilus

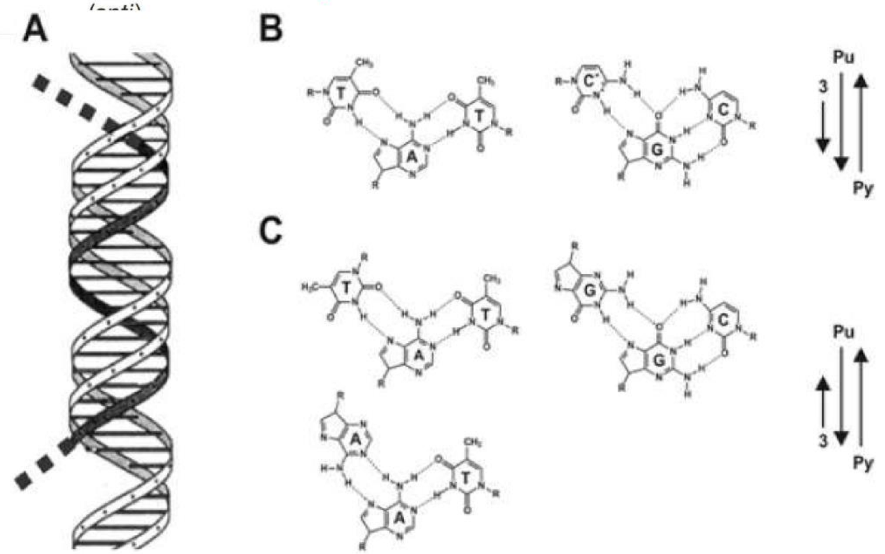
30S subunit ribosome of T.Thermophilus

Nucleic Acids – non-Watson-Crick interations

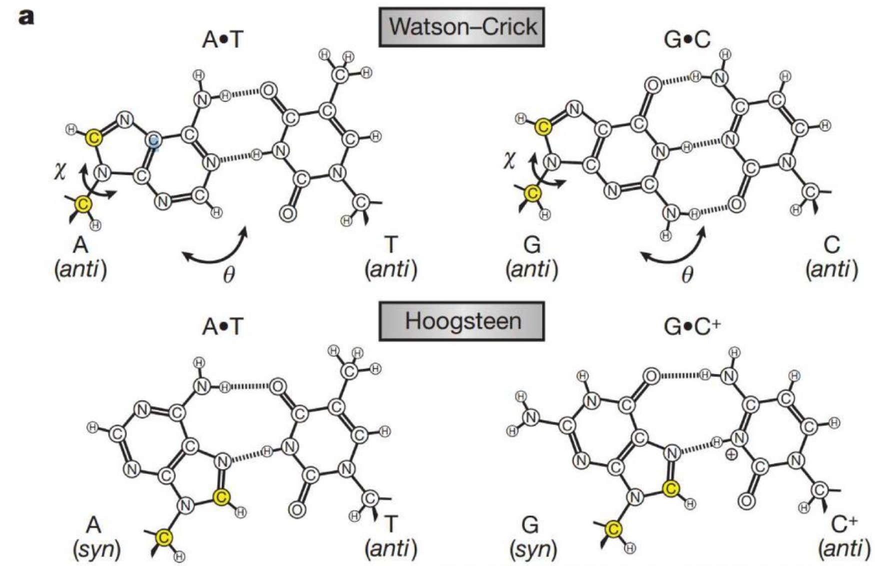


1. Predominately on homo-purinic Stretches in duplex
2. Usually third chain is homopurinic or homopyrimidinic

Triplexes



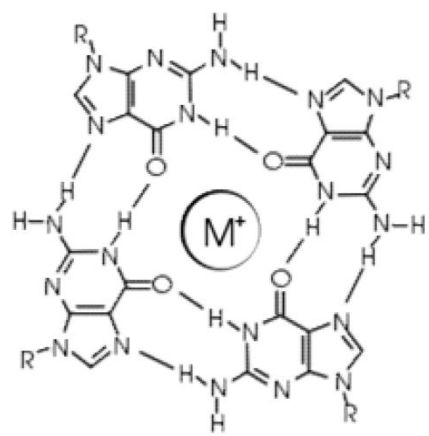
Nucleic Acids – non-Watson-Crick interations

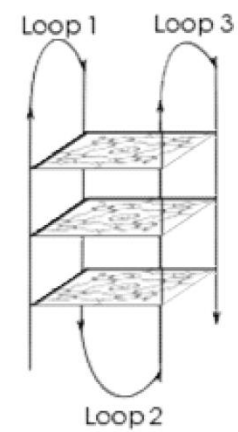


Quadruplex
(ala telomeric repeats)

Stability is almost as complementary

Also found in promotors (biological function)





Quadruplexes are formed at stretches with very high proportion of G residues

Nucleic Acids – Stability

1. Watson-crick interactions determine complementary interactions

2. Secondary structure is determined majorly by base stacking and other weak VDW interactions

3. Double helix is destabilized by negative charge (phosphate repulsion) and is stabilized therefore by the presence of metal ions (Mg^{2+}, K^+, Na^+) or proteins (histones – positively charged proteins)

4. Transition from one form to another can be forced by isruption of weak noncovalent interactions – high temperatures, low salt conditions, change of pH, chaotropic agents (disrupting H-bonds) such as DMSO, urea, formamide.