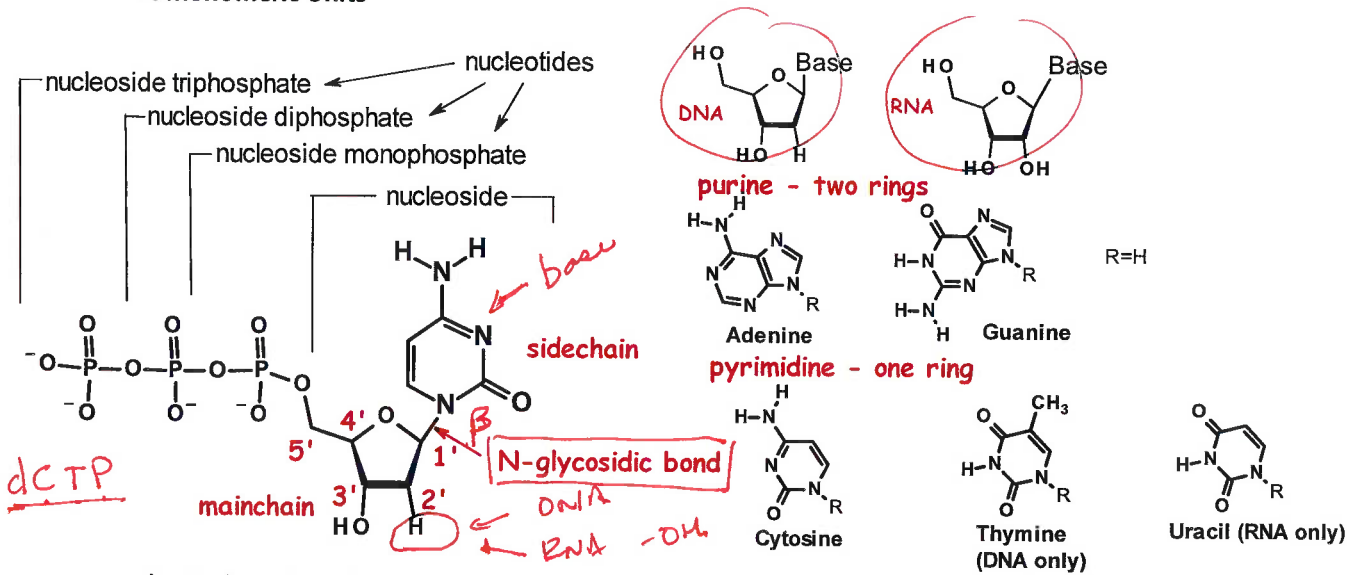


Lecture 34-35: Introduction to Nucleic Acids & Review of Central Dogma.

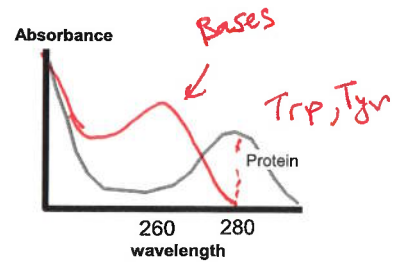
Goals:

- Draw chemical structures of monomeric bases
- Understand labile nature of RNA
- Draw chemical structure of dsDNA
- Identify minor and major groove, including H-bond donors and acceptors
- Distinguish between syn- and anti-base orientation
- Identify exo- and endo ring pucker in ribose.
- DNA supercoiling and how supercoiling affects migration on agarose gels.
- mRNA synthesis – role of promotor
- tRNA structure and charging
- Protein synthesis:
 - Ribosome binding site
 - Start codon
 - Stop codon
 - Initiation, elongation, termination.

1. Monomeric Units



- Nucleoside triphosphates are the building blocks of nucleic acids.
- The base ("sidechain") is connected to the C1' of the sugar ("mainchain") by an N-linked glycosidic bond.
Base + sugar = nucleoside.
Base + sugar + n-phosphates = nucleotide
- The carbon atoms on the sugar are numbered 1' to 5'. The primes distinguish the atoms on the sugar from those on the base.
- DNA differs from RNA in the sugar (deoxyribose versus ribose) and one base.
- Four different monomers, A, G, C, T in DNA. U replaces T in RNA.
- Aromatic rings of bases absorb light at ~260 nm. Beers law applies:
 $A = [C]\epsilon l$



$$E_{DNA} = n_C \epsilon_C + n_G \epsilon_G + n_T \epsilon_T + n_A \epsilon_A$$

(Single stranded)

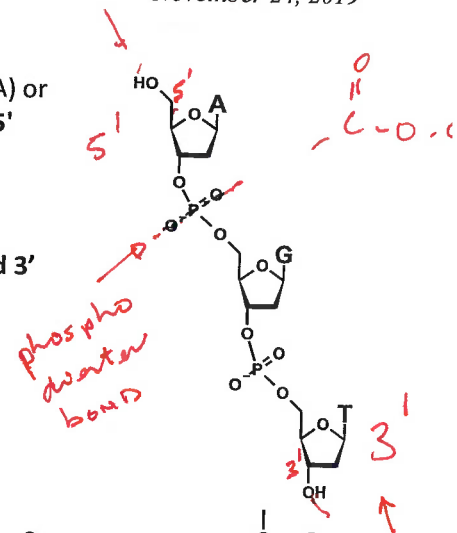
	Nitrogenous Base	Nucleoside	Deoxynucleoside	Deoxynucleoside triphosphate
A				
G	Guanine	Guanosine	Deoxyguanosine (dG)	dGTP
C	Cytosine	Cytidine	Deoxycytidine (dC)	dCTP
T	Thymine	5-methyluridine	Thymidine (dT)	dTTP
U	Uracil	Uridine	Deoxyuridine (dU)	dUTP

dNTP

2. DNA and RNA are Polynucleotides:

- The **phosphodiester backbone** is comprised of deoxyribose (DNA) or ribose (RNA) sugars bridged by phosphates between the **3' and 5'** positions of the sugars.
- The phosphates are always ionized ($pK_a \sim 1$), nucleic acids are **polyanions**.
- Note that the polarity, i.e. $5' \rightarrow 3'$. Be able to identify the **5' and 3' ends**.

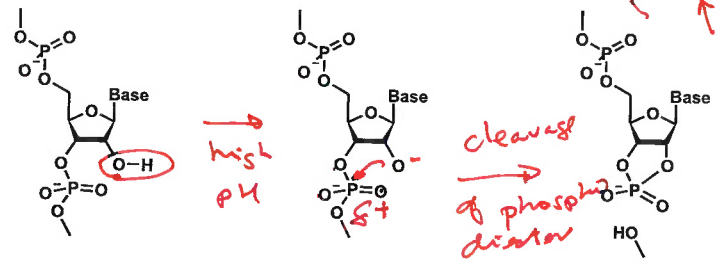
Sequence of nucleotide bases is written in the 5'-3' direction.



3. Chemical Stability.

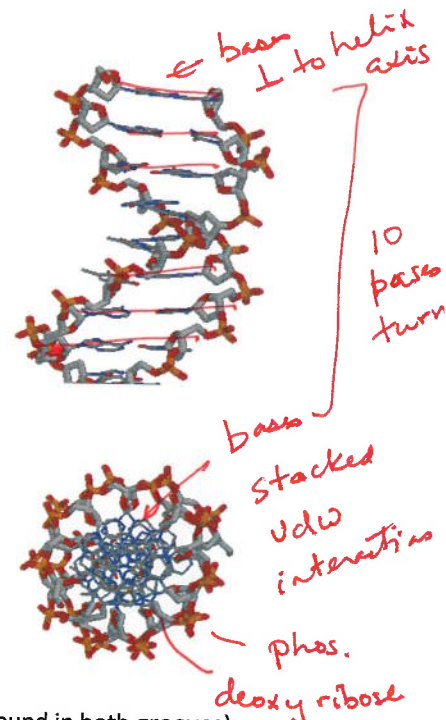
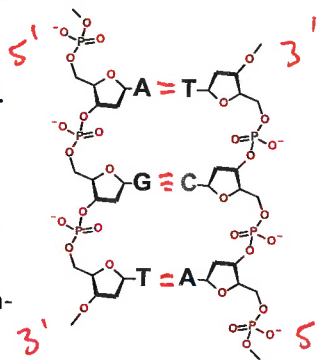
- DNA is stable to acids and bases.
- RNA is readily hydrolyzed at high pH (alkaline hydrolysis) due to 2' OH, the deprotonated 2'-OH attacks the 3' phosphate.

RNA is usually degraded in cells for regulation (regulation of protein levels).



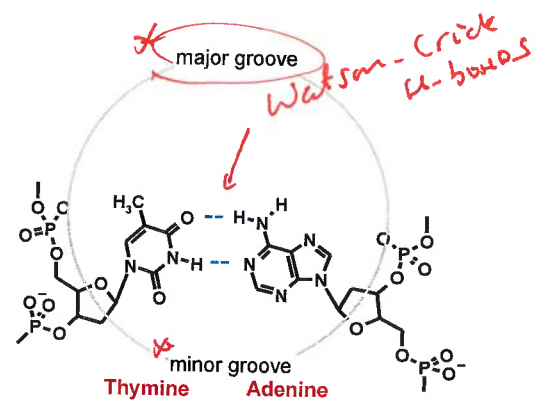
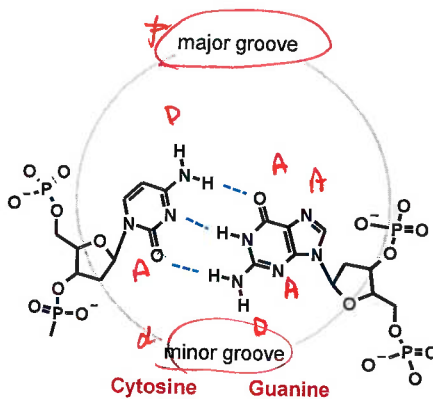
4. Double Helical Structures: B-DNA

- The helix is right-handed; the chains are **antiparallel**.
- Rise 3.4 \AA /base pair; **10 bp/turn**.
- The helix interior is filled with stacked base, phosphates and deoxyriboses on the outside.
- T pairs with A via two "Watson-Crick H-bonds" (see below)
- C pairs with G via three "Watson-Crick hydrogen bonds"
- Opposite strand termed "complimentary strand". Top strand is always written $5' \rightarrow 3'$.
- The spacing between the two phosphate chains in the direction of the helix is not uniform. There is a wider groove (**major groove**) and a narrower groove (**minor groove**). Each basepair has an edge in both grooves.



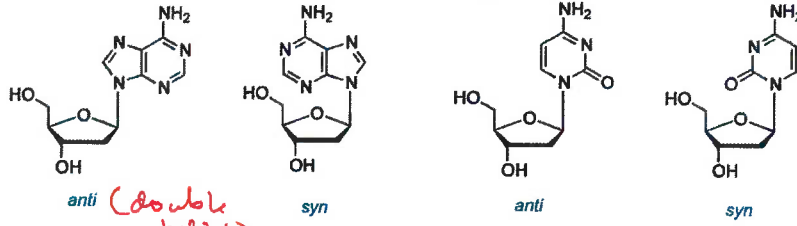
5. Hydrogen Bonds are Responsible for Base Pairing A-T, G-C:

(Watson-Crick (WC) H-bonds as lines, non-WC donors and acceptors are found in both grooves).



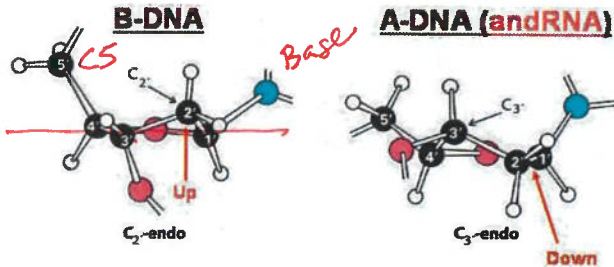
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6. Conformational Geometry of bases – syn and anti:



*

7. Conformational geometry of sugar pucker – endo & exo



endo - above ring
exo - below

8. DNA Topology: Taking a linear double stranded segment of DNA and joining the two ends will make circular DNA. This is referred to as **closed circular, relaxed DNA**. Most circular DNA molecules are **plasmids**, which can replicate autonomously within cells because they have an origin of replication.



*

Supercoiled DNA is generated by:

- i) breaking one phosphodiester bond,
- ii) rotating the DNA 360 degrees,
- iii) rejoining the broken strands.

The 360° twists induce stress in the DNA because it generates poor vdw contacts between bases. This stress is relieved by introducing a twist, or supercoil in the entire circular DNA molecule, restoring good vdw between the bases.

The number of supercoils is the difference between how many times the DNA strands cross each other in the relaxed plasmid and the supercoiled one. In fully relaxed (nicked) DNA this is N/γ , where N is the # of basepairs, γ =bases/turn (10).

