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| **Lab 2: Nucleic acid structure** |
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| **YEAR 3-SEMSTER 1** |

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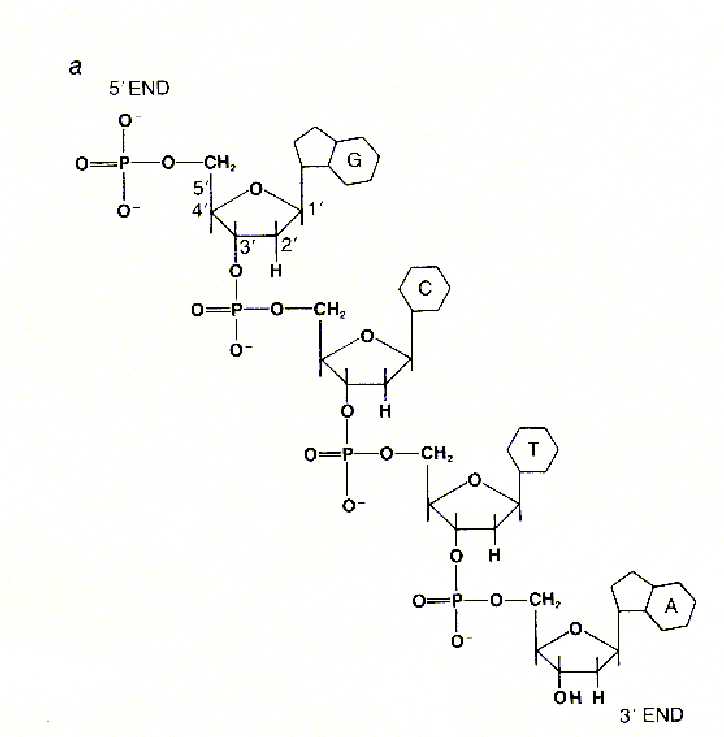
Authored by: Fatima

Lab 2: Nucleic acid structure

DNA structure

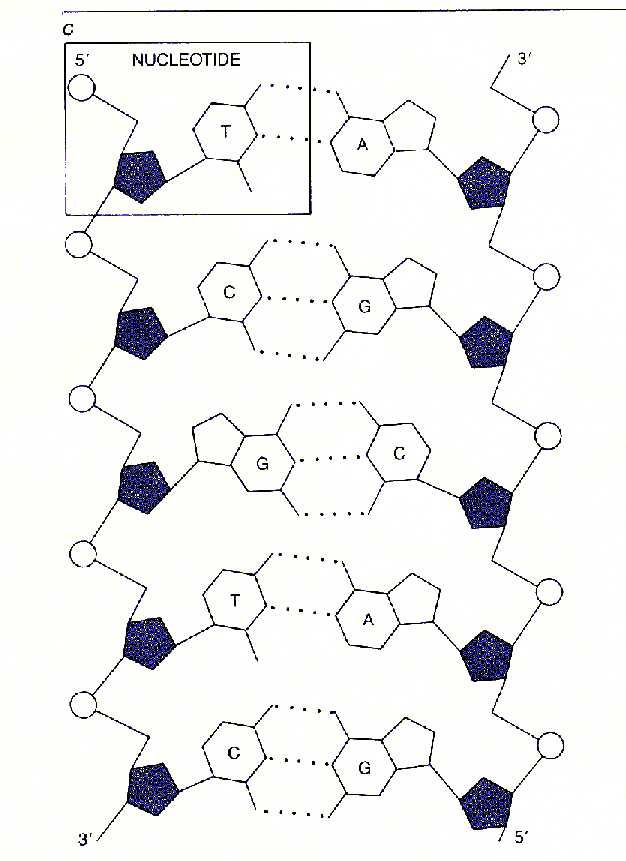
DNA is usually a double-helix and has two strands running in opposite directions. (There are some examples of viral DNA which are single-stranded). Each chain is a polymer of subunits called nucleotides (hence the name **polynucleotide**).

Each strand has a backbone made up of (deoxy-ribose) sugar molecules linked together by phosphate groups. The 3' C of a sugar molecule is connected through a phosphate group to the 5' C of the next sugar. This linkage is also called 3'-5' phosphodiester linkage. All DNA strands are read from the 5' to the 3' end where the 5' end terminates in a phosphate group and the 3' end terminates in a sugar molecule.



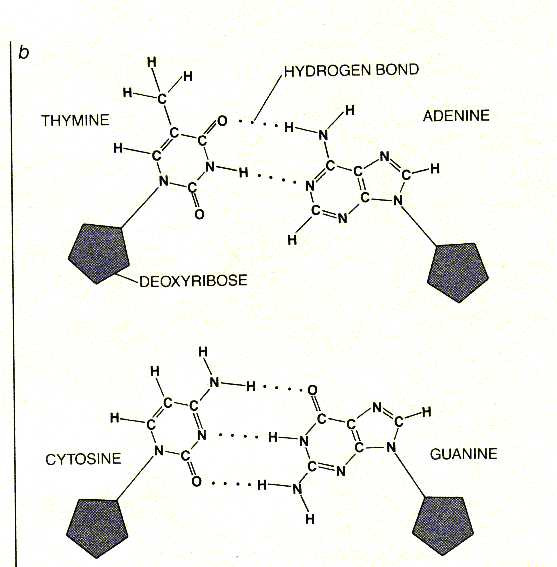
Each sugar molecule is covalently linked to one of 4 possible bases (**A**denine, **G**uanine, **C**ytosine and **T**hymine). A and G are double-ringed larger molecules (called **purines**); C and T are single-ringed smaller molecules (called **pyrimidines**).

In the double-stranded DNA, the two strands run in opposite directions and the bases pair up such that A always pairs with T and G always pairs with C. The A-T base-pair has 2 hydrogen bonds and the G-C base-pair has 3 hydrogen bonds. The G-C interaction is therefore stronger (by about 30%) than A-T, and A-T rich regions of DNA are more prone to thermal fluctuations.

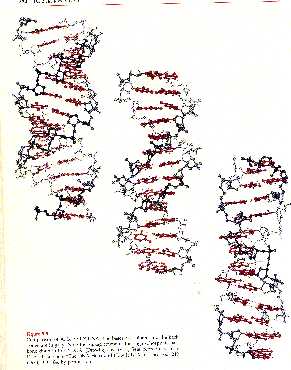


The bases are oriented perpendicular to the helix axis. They are hydrophobic in the direction perpendicular to the plane of the bases (cannot form hydrogen bonds with water). The interaction energy between two bases in a double-helical structure is therefore a combination of hydrogen-bonding between complementary bases, and hydrophobic interactions between the neighboring stacks of base-pairs.

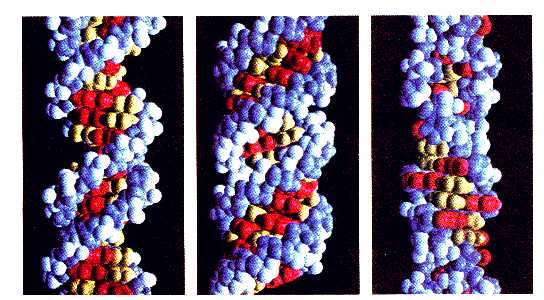
Even in the single-stranded state, the bases prefer to be stacked (like the steps of a spiral staircase if the bases are identical) and a single-stranded chain can also have regions of helical conformation.

The backbone of polynucleotides are highly charged (1 unit negative charge for each phosphate group; 2 negative charges per base-pair). 

The most common DNA structure in solution is the B-DNA. Under conditions of applied force or twists in the DNA, or under low hydration conditions, it can adopt several helical conformations, referred to as the A-DNA, Z-DNA, S-DNA...



Shown in picture above are three crystallized states of DNA, the A-DNA (left), B-DNA (middle) and Z-DNA (right). The A-form crystallizes under low hydration conditions and is not normally found for DNA in the cell. It is, however, the structure adopted by double-stranded regions in RNA as well as the transient double-helix between DNA and RNA during transcription.  Both A- and B-DNA are right-handed helices whereas Z-DNA is a left-handed helix and is commonly found in regions of DNA that have an alternating purine-pyrimidine (e.g. 5'-CGCGCGCG-3' or 5'-CGCGCATGC-3') sequences.



Here, the B-DNA is on the left and the A-DNA is in the middle. The blue and white atoms are the sugar-phosphate backbone atoms, the red are G-C base-pairs and the yellow are A-T base-pairs. The B-DNA picture shows very clearly the 'grooves' in between the backbones that also spiral around the DNA structure; the grooves in B-DNA come in two sizes, the minor groove and the major groove.

A DNA molecule is not a rigid, static structure as x-ray diffraction pictures might suggest, and the crystallographic parameters shown above are average parameters. In reality, each of these structures are under constant thermal fluctuations, which result in local twisting, stretching, bending, and unwinding of the double-strands. Also, certain sequences lead to permanent bends or kinks in the direction of the helix. These local (sequence-specific) fluctuations are essential for the recognition of specific binding sites along the DNA molecule where proteins involved in replication, transcription, regulation of gene expression, or DNA-damage repair can bind.

