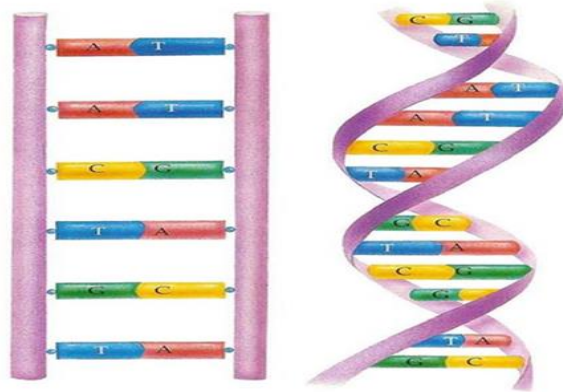


# Molecular biology and bacterial genetics

البايولوجي الجزيئي ووراثة الاحياء المجهرية

## Lec 2



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## he Structure of DNA

DNA, though relatively simple in structure, has an elegance and beauty unsurpassed by other large molecules. It is useful to consider the structure of DNA at three levels of increasing complexity, known as the (i) primary, (ii) secondary, and (iii) tertiary structures of DNA. The primary structure of DNA refers to its nucleotide structure and how the nucleotides are joined together. The secondary structure refers to DNA's stable three-dimensional configuration, the helical structure worked out by Watson and Crick. The tertiary structures are the complex packing arrangements of double-stranded DNA in chromosomes.

### primary structure of DNA:

The Primary Structure of DNA consists of a string of nucleotides joined together by phosphodiester linkages

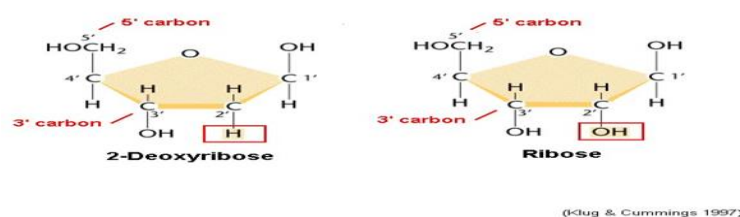
- **nucleotides**

DNA has a relatively simple structure: it is a polymer, a chain made up of many repeating units linked together. As already mentioned, the repeating units of DNA are nucleotides, each comprising three parts: (1) a sugar, (2) a phosphate, and (3) a nitrogen-containing base.(table 1).

	Phosphate	Sugar	Base	
			Purines	Pyrimidines
DNA	Present	Deoxyribose	Guanine (G) Adenine (A)	Cytisine (C) Thymine (T)
RNA	Present	Ribose	Guanine (G) Adenine (A)	Cytosine (C) Uracil (U)

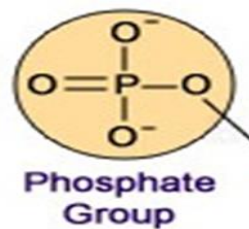
(Table 1): the components of nucleotides

### 1- The Pentose Sugars The sugars of nucleic acids—called pentose sugars—have five carbon atoms



The sugars of DNA and RNA are slightly different in structure. RNA's ribose sugar has a hydroxyl group attached to the 2'-carbon atom, whereas DNA's sugar, called deoxyribose, has a hydrogen atom at this position and contains one oxygen atom fewer overall. This difference gives rise to the names ribonucleic acid (RNA) and deoxyribonucleic acid (DNA).

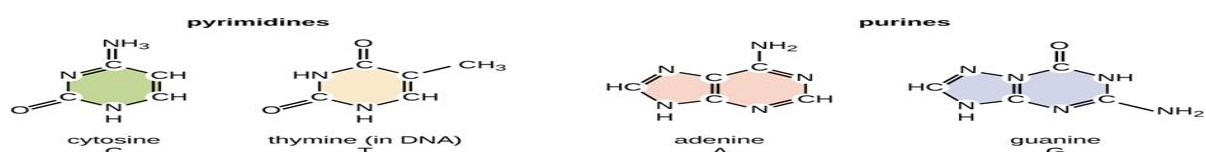
**2-The Phosphate Group** The third component of a nucleotide is the phosphate group, which consists of a phosphorus atom bonded to four oxygen atoms. Phosphate groups are found in every nucleotide and frequently carry a negative charge, which makes DNA acidic. The phosphate is always bonded to the 5'-carbon atom of the sugar in a nucleotide.



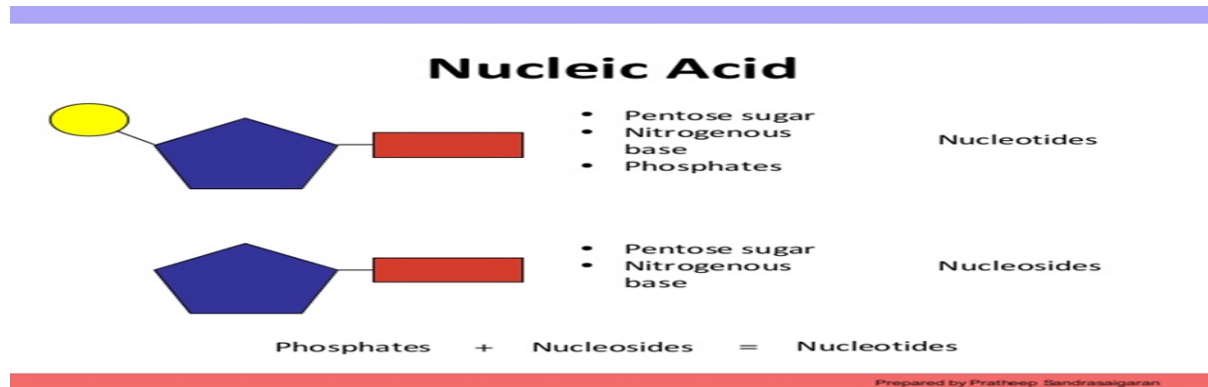
**3-The Nitrogenous Bases** The third component of a nucleotide is its nitrogenous base, which may be of two types—a purine or a pyrimidine. Each purine consists of a six-sided ring attached to a five-sided ring, whereas each pyrimidine consists of a six-sided ring only. DNA and RNA both contain two purines, adenine and guanine (A and G), which differ in the positions of their double bonds and in the groups attached to the six-sided ring. There are three pyrimidines found in nucleic acids: cytosine (C), thymine (T), and uracil (U). Cytosine is present in both DNA and RNA; however, thymine is restricted to DNA, and uracil is found only in RNA.

The four bases in DNA are:

Adenine(A)    Guanine (G)    Thymine(T)    Cytosine (C)



- **The Nucleic Acids** Nucleic acids are made by joining nucleotides in a repetitive way into long, chainlike polymers, In DNA, each base is chemically linked to one molecule of the sugar deoxyribose, forming a compound called a nucleoside. When a phosphate group is also attached to the sugar, the nucleoside becomes a nucleotide, thus a nucleotide is a nucleoside+phosphate. as shown in figure below:



- **Polynucleotide Chains**

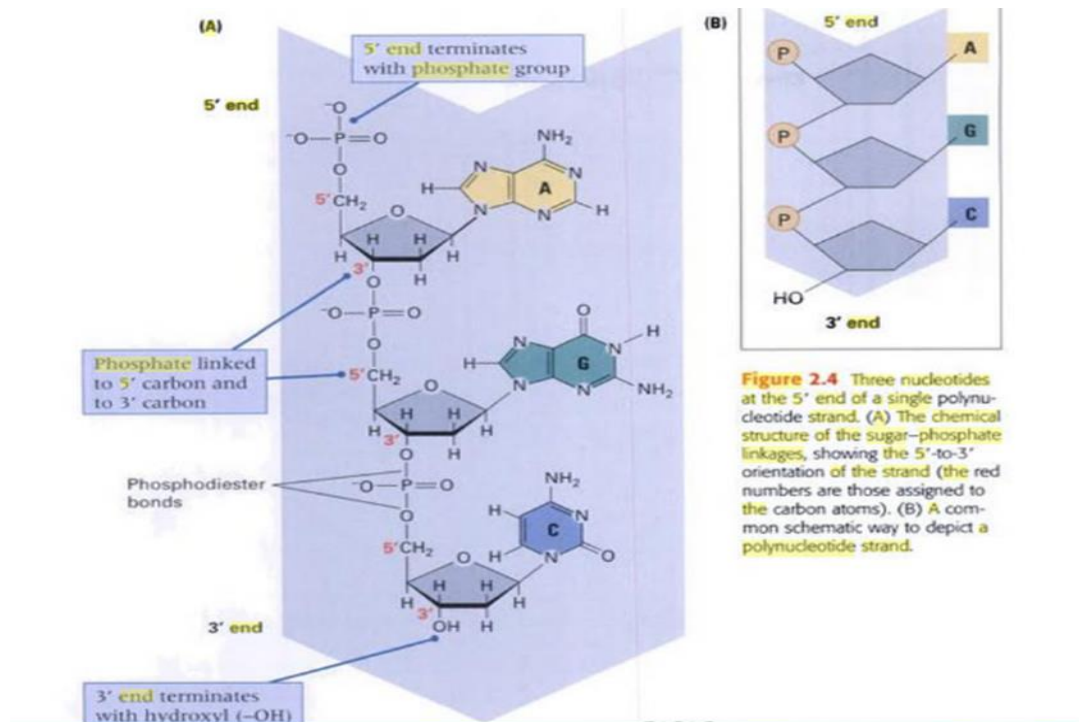
In terms of biochemistry, a DNA strand is a polymer ( a large molecule built from repeating units).

In nucleic acids, such as DNA and RNA, the nucleotides are joined to form a polynucleotide chain, in which the phosphate attached to the 5' carbon of one sugar is linked to the hydroxyl group attached to the 3' carbon of the next sugar in line.

### **Polarity**

An important characteristic of the polynucleotide strand is its direction, or polarity. At one end of the strand a phosphate group is attached only to the 5'-carbon atom of the sugar in the nucleotide. This end of the strand is therefore referred to as the 5' end. The other end of the strand, referred to as the 3' end, has an OH group attached to the 3'-carbon atom of the sugar. RNA nucleotides also are connected by phosphodiester linkages to form similar polynucleotide

strands. The asymmetry of the ends of a DNA strand implies that each strand has a polarity determined by which end bears the 5' phosphate and which end bears the 3' hydroxyl.



**Figure 2.4** Three nucleotides at the 5' end of a single polynucleotide strand. (A) The chemical structure of the sugar-phosphate linkages, showing the 5'-to-3' orientation of the strand (the red numbers are those assigned to the carbon atoms). (B) A common schematic way to depict a polynucleotide strand.

Figure 4: Three nucleotides at the 5' end of a single polynucleotides strand. (A) the chemical structure of the sugar phosphate linkages, showing the 5' to 3' orientation of the strand. (B) a common schematic way to depict a polynucleotide strand.

The nomenclature of the nucleoside and nucleotide derivatives of the DNA bases is summarized in following table.

Base	Nucleoside	Nucleotide
Adenine (A)	Deoxyadenosine	Deoxyadenosine-5' monophosphate (dAMP) diphosphate (dADP) triphosphate (dATP)
Guanine (G)	Deoxyguanosine	Deoxyguanosine-5' monophosphate (dGMP) diphosphate (dGDP) triphosphate (dGTP)
Thymine (T)	Deoxythymidine	Deoxythymidine-5' monophosphate (dTMP) diphosphate (dTDP) triphosphate (dTTP)
Cytosine (C)	Deoxycytidine	Deoxycytidine-5' monophosphate (dCMP) diphosphate (dCDP) triphosphate (dCTP)

## The Secondary Structures of DNA

The secondary structure of DNA refers to its three-dimensional configuration—its fundamental helical structure. DNA's secondary structure can assume a variety of configurations, depending on its base sequence and the conditions in which it is placed.

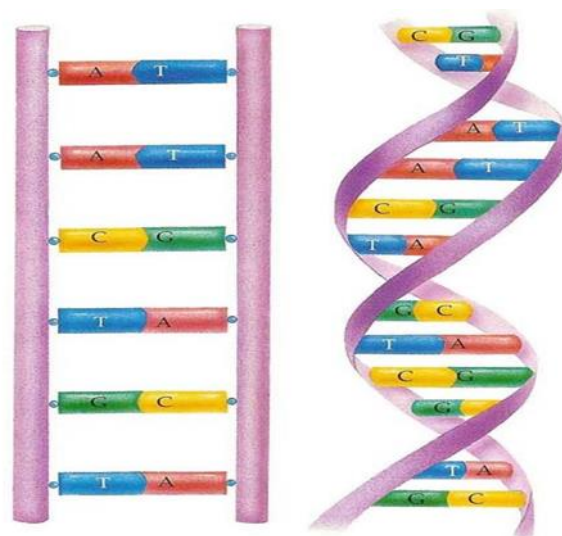
**The Double Helix:** A fundamental characteristic of DNA's secondary structure is that it consists of two polynucleotide strands wound around each other—it's a double helix

The bases in double helix are paired complementary. At any position on the parried strands of a DNA molecule, the complement of A is T , and the complement of G is C. The complementary pairing means that each base along one strand of the DNA is matched with a base in the opposite position on the other strand. The complementary pairing is also called Watson-Crick pairing. The individual strands as single-stranded DNA and to the double helix as double-stranded DNA or duplex DNA

- 1- A fundamental characteristic of DNA's secondary structure is that it consists of two polynucleotide strands wound around each other—it's a double helix
- 2- The two polynucleotide strands run in opposite directions—they are antiparallel, which means that the 5' end of one strand is opposite the 3' end of the second
- 3- The diameter of the helix could only be kept constant at about 2 nm or 20 Å (10 angstrom units = 1 nanometer) if one purine and one pyrimidine base made up each rung. Two purines per rung would be too big, and two pyrimidines would be too small.
- 4- The base pairs in DNA are stacked about 0.34 nm apart, with 10 base pairs per turn (360 ) of the double helix occupying a distance of 3.4 nm or 34 Å.
- 5- The strands are held together by two types of molecular forces. Hydrogen bonds link the bases on opposite strands (Figure 4.18). These bonds are relatively weak compared with the covalent phosphodiester bonds that connect the sugar and phosphate groups of adjoining nucleotides

In 1953 James Watson and Francis Crick at Cambridge University proposed the first essentially correct three-dimensional structure of the DNA molecule. In the Watson-Crick structure, DNA consists of two long chains of subunits, each twisted around the other to form a double stranded helix.

Watson and Crick deduced the basic structure of DNA by using three pieces of information: (i) X-ray diffraction data, (ii) the structures of the bases, and (iii) Chargaff's findings that, in most DNA samples, the mole fraction of guanine equals that of cytosine, as well as the mole fraction of adenine equals that of thymine. The Watson-Crick structure is a pair of oppositely oriented, antiparallel, DNA strands that wind around one another in a right-handed helix. That is, the strands wrap clockwise moving down the axis away from an observer. Base pairs A-T and G-C lie on the interior of the helix and the phosphate groups on the outside.



### Chargaff's rules:

A few years before Watson and Crick proposed their essentially correct three dimensional structure of DNA as a double helix; Erwin Chargaff developed a chemical technique to measure the amount of each base present in DNA. As we describe this technique, we will let the molar concentration of any base be



represented by the symbol for the base in square brackets; for example, [A] denotes the molar concentration of adenine. Chargaff used his technique to measure the [A], [T], [G], and [C] content of the DNA from a variety of sources. He found that the base composition of the DNA, defined as the present G+C, differs among species but is constant in all cells of an organism and within a species.

Chargaff also observed certain regular relationships among the molar concentrations of the different bases. These relationships are now called Chargaff's rules:

- The amount of adenine equals that of thymine:  $[A]=[T]$ .
- The amount of guanine equals that of cytosine:  $[G]=[C]$ .
- The amount of the purine bases equals that of the pyrimidine bases:

$$[A]+[G]=[T]+[C].$$

### **Base pairing and base stacking**

In the standard structure (Watson and Crick), which is called the Bform of DNA, each chain make one complete turn every  $34\text{\AA}$  the helix is right handed. The bases are spaced at  $3.4\text{\AA}$ , so there are (10) bases per helical turn in each strand and (10) base pairs per turn of the double helix.

The diameter of the helix is 2 nm, spiralling of the nucleotide strands creates major and minor grooves in the helix, features that are important for the binding of some DNA-binding proteins that regulate the expression of genetic information. The two grooves spiralling along outside of the double helix are not symmetrical; one groove, called the major groove, is larger than the other, which is called the minor groove. Proteins that interact with double-stranded DNA often have regions that make contact with the base pairs by fitting into the major groove, into the minor groove or into both grooves.



## The double helix has minor and major grooves

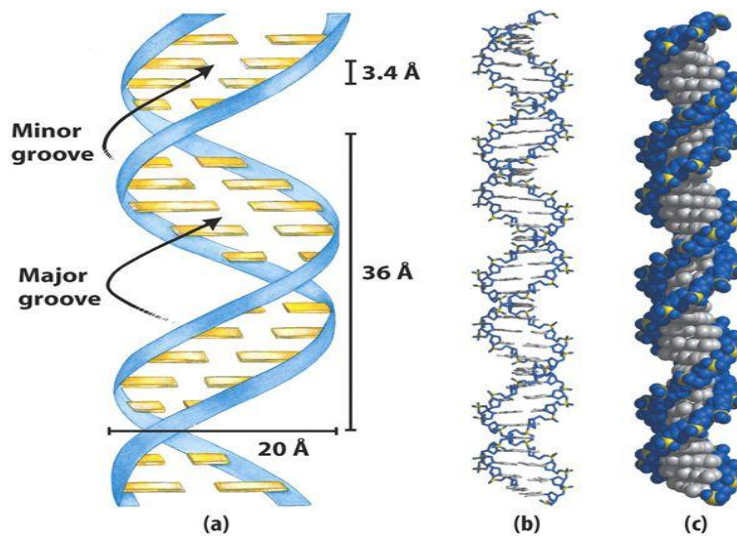


figure 5:major and minor grooves of DNA.

The strand feature base pairing, in which each base is paired to a complementary base in the other strand by hydrogen bonds which provide one type of force holding the strands together.(figure 6).

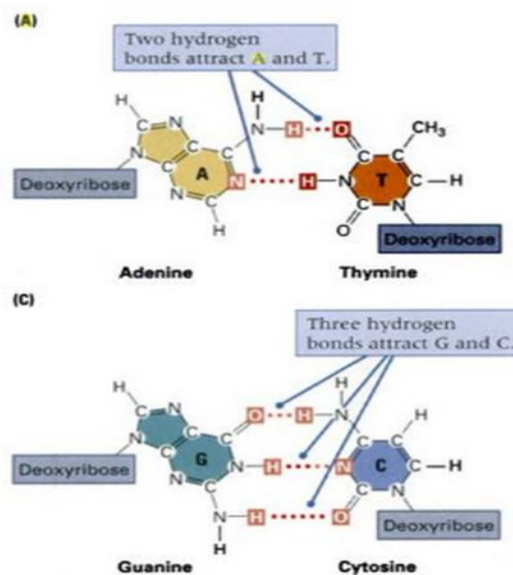


Figure6: base pairing hydrogen bonds.

The paired bases are planar, parallel to one another, and perpendicular to the long axis of the double helix. This feature of double stranded DNA is known as base stacking. The upper and lower faces of each nitrogenous base are relatively flat and nonpolar (uncharged). These surfaces are said to be hydrophobic because they bind poorly to water molecules, which are very polar.

- ✓ The three-dimensional structure of DNA that Watson and Crick described is termed the B-DNA structure
  - ✓ Another secondary structure that DNA can assume is the A-DNA structure. Like B-DNA, A-DNA is an alpha (right-handed) helix, but it is shorter and wider than B-DNA and its bases are tilted away from the main axis of the molecule.
  - ✓ A radically different secondary structure called Z-DNA forms a left-handed helix. In this form, the sugar phosphate backbones zigzag back and forth, giving rise to the name Z-DNA (for zigzag). Some regions can even form helices in which the strands twist to the left. Z-DNA structures can arise under physiological conditions when particular base sequences are present, such as stretches of alternating C and G sequences. Parts of some active genes form Z-DNA, suggesting that Z-DNA may play a role in regulating gene transcription.
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- Sequences that are methylated typically show low levels of transcription while sequences lacking methylation are actively being transcribed. Methylation can also affect the three-dimensional structure of the DNA molecule.