



Biopolymers

Chem. 563

bio polymers

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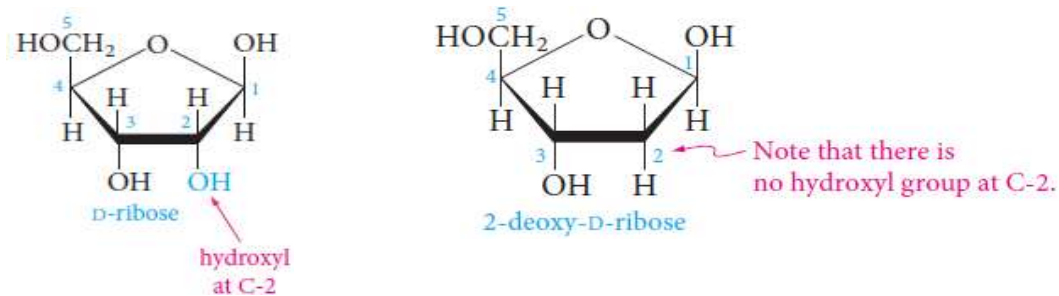
NUCLEIC ACIDS

DNA, the double helix, and the genetic code

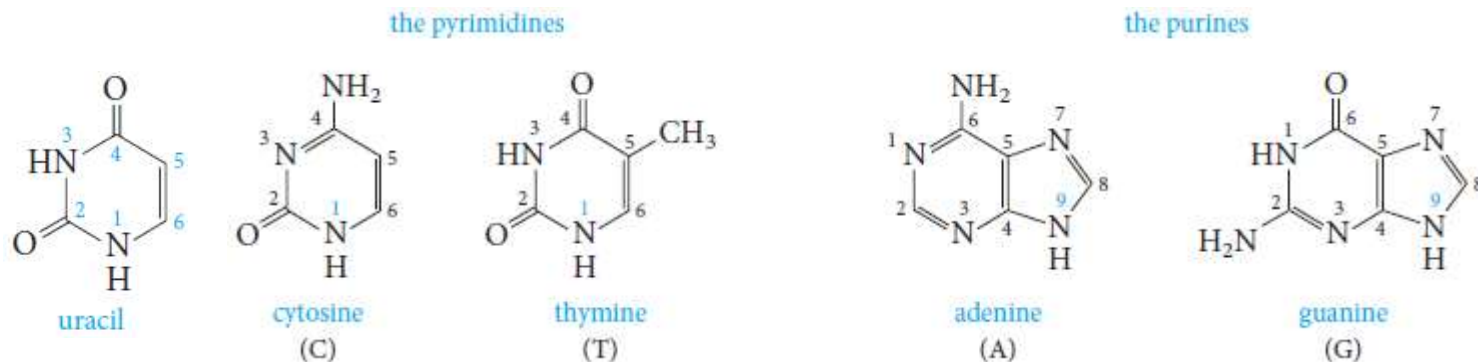
- Nucleoproteins, which are conjugated proteins, may be separated into nucleic acids and proteins in aqueous sodium chloride.
- The name “nuclein,” which was coined by Miescher in 1869 to describe products isolated from nuclei in pus, was later changed to nucleic acid.
- Pure nucleic acid was isolated by Levene in the early 1900s.
- He showed that either D-ribose or D-deoxyribose was present in what are now known as ribonucleic acid (RNA) and deoxyribonucleic acid (DNA).
- There are two major types of nucleic acids: deoxyribonucleic acid (DNA) and ribonucleic acid (RNA).
- The name nucleic acid is derived from the fact that they are acidic, containing a phosphoric acid moiety, and are found in the nuclei of cells.

The General Structure of Nucleic Acids

- **Nucleic acids** are high polymers consisting of a pentose sugar containing a heterocyclic base and a phosphate moiety.
- RNA contains the pentose ribose while DNA contains the pentose deoxyribose.



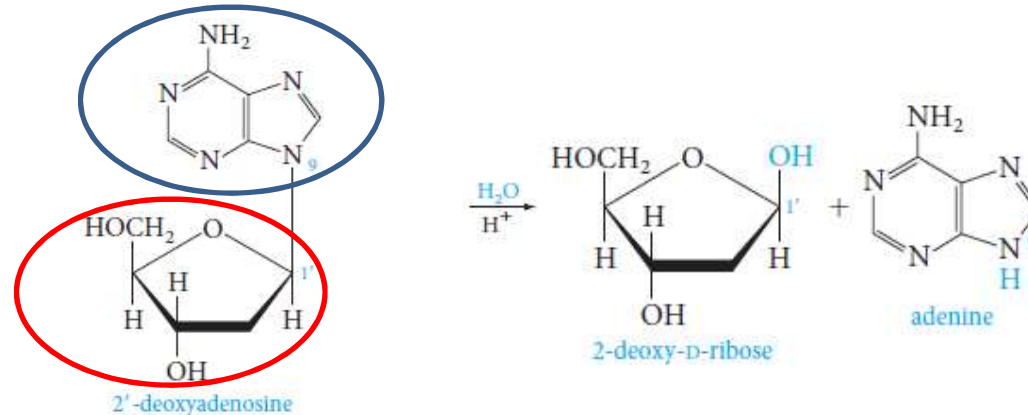
- The sugars also contain a pyrimidine or purine base present on the 1-carbon replacing the hydroxyl group with a base.



- Both DNA and RNA contain adenine and guanine.
- Uracil is found only in RNA.
- thymine or methyluracil is found only in DNA.

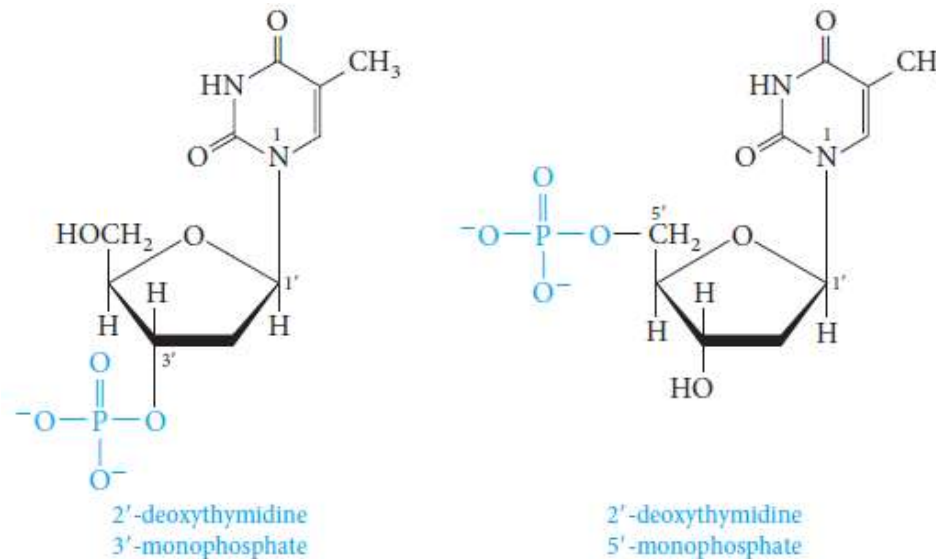
The General Structure of Nucleic Acids

- The combination of the pentose sugar and a purine or pyrimidine base is called a **nucleoside**.



- Nucleotides** are phosphate esters of nucleosides.

A hydroxyl group in the sugar part of a nucleoside is esterified with phosphoric acid. In DNA nucleotides, either the 5' or the 3' hydroxyl group of 2-deoxy-d-ribose is esterified.



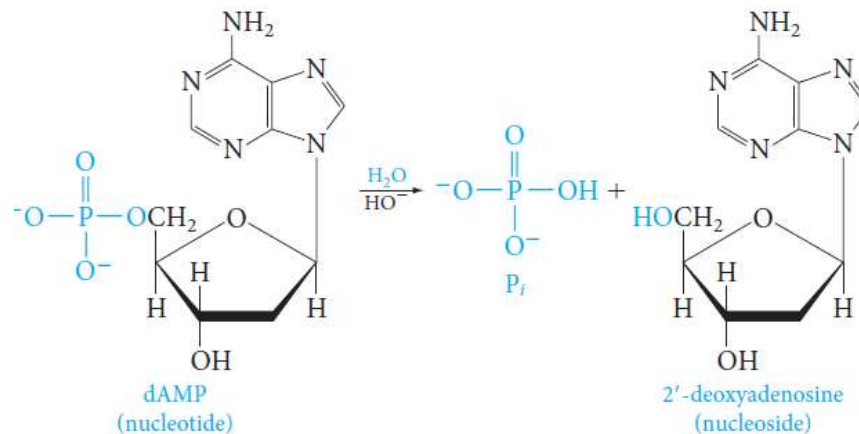
The General Structure of Nucleic Acids

- Nucleotides are named as the 3'- or 5'-monophosphate esters of a nucleoside,
- These names are frequently abbreviated as in Table 18.1.
- In these abbreviations, letter d stands for 2-deoxy-d-ribose, the next letter refers to the heterocyclic base, and MP stands for monophosphate.

Table 18.1 The Common 2-Deoxyribonucleotides

Base	Monophosphate name	Abbreviation
cytosine (C)	2'-deoxycytidine 5'-monophosphate	dCMP
thymine (T)	2'-deoxythymidine 5'-monophosphate	dTMP
adenine (A)	2'-deoxyadenosine 5'-monophosphate	dAMP
guanine (G)	2'-deoxyguanosine 5'-monophosphate	dGMP

- Nucleotides can be hydrolyzed by aqueous base (or by enzymes) to nucleosides and phosphoric acid.

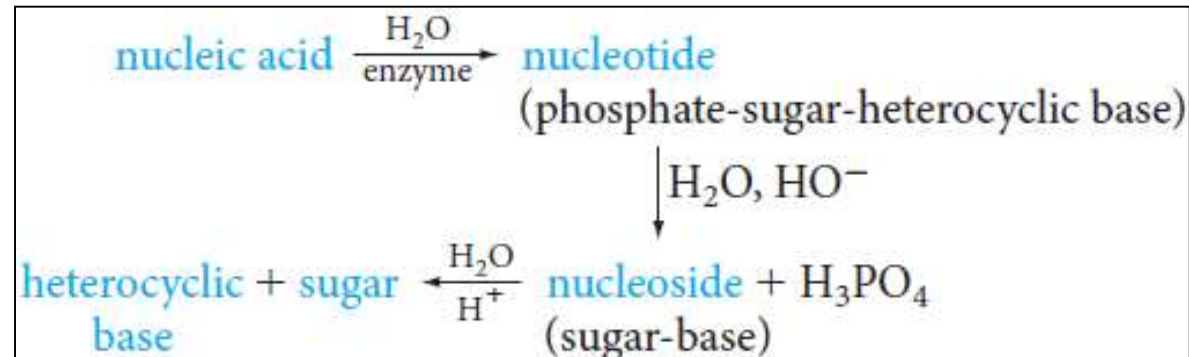


The General Structure of Nucleic Acids

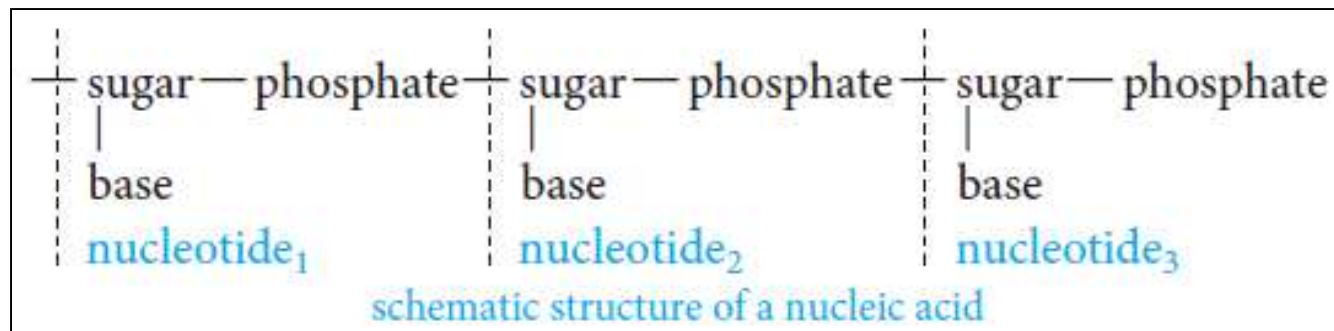
- Two important 5'-nucleotides of adenine are:
 - adenosine-5'-diphosphate (ADP) and
 - adenosine-5'-triphosphate (ATP).
- The hydrolysis of ATP to ADP is important in biological energy transfer with a net Gibbs free energy of about 8.4 kcal/mol (or about 35 kJ/mol). The energy to “drive” this reaction comes from carbohydrates by the process of glycolysis.
- ATP acts as a storage site for energy released during conversion of carbohydrates to carbon dioxide and water.
- ATP, ADP, and AMP are referred to as “high energy” materials with the phosphate linkages being the sites of high energy.

The General Structure of Nucleic Acids

- Hydrolysis of nucleic acids gives nucleotides, which are the building blocks of nucleic acids, just as amino acids are the building blocks of proteins.



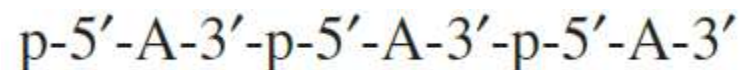
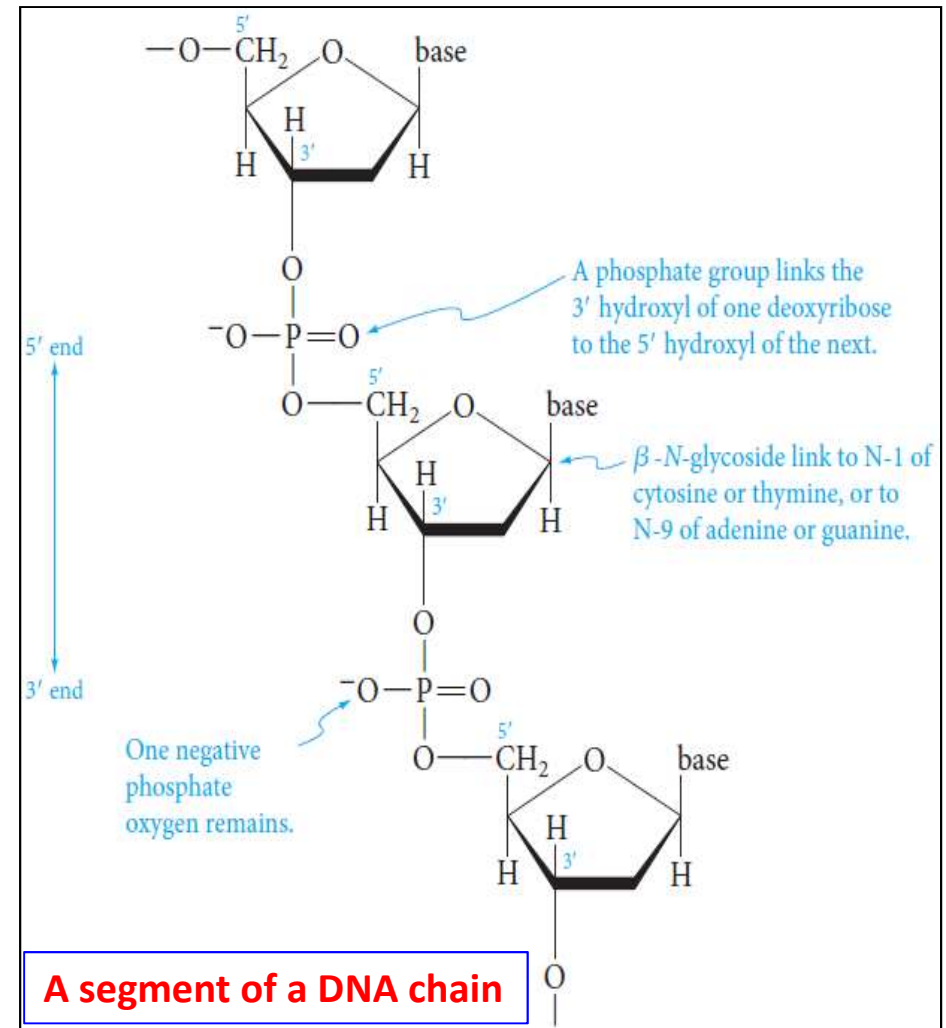
- The overall structure of the nucleic acid itself is a macromolecule with a backbone of sugar molecules connected by phosphate links and with a base attached to each sugar unit.



- **Nucleic acids** are polynucleotides attached by the phosphate moieties through the 3' and 5' sites on the pentose.

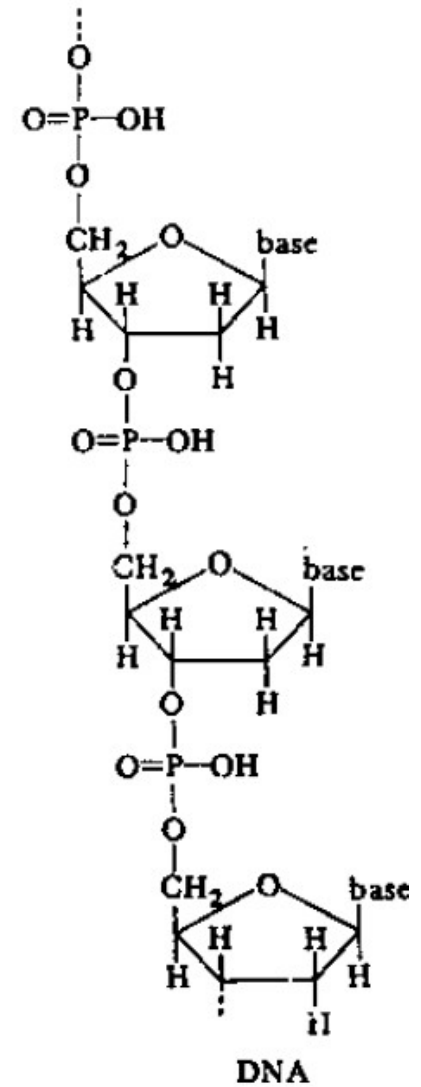
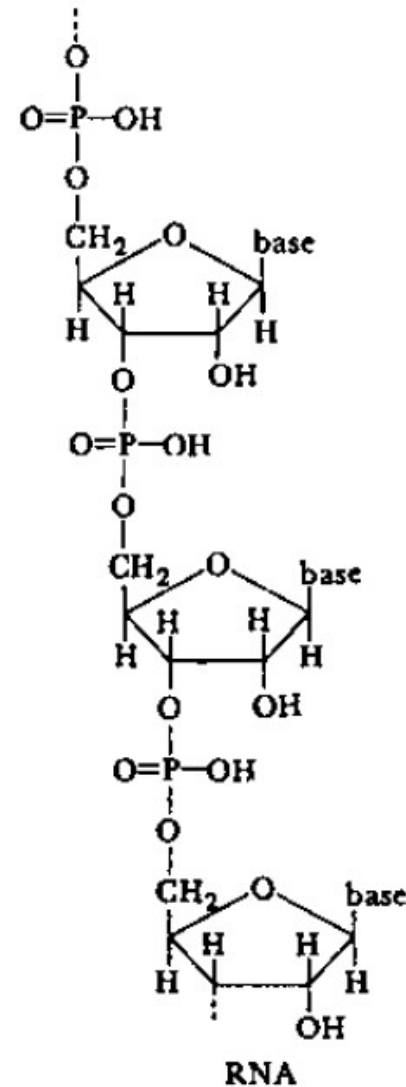
The Primary Structure of deoxyribonucleic acid (DNA)

- The 3' hydroxyl of one ribose unit is linked to the 5' hydroxyl of the next ribose unit by a phosphodiester bond.
- The heterocyclic base is connected to the anomeric carbon of each deoxyribose unit by a β -N-glycosidic bond.
- There are no remaining hydroxyl groups on any deoxyribose unit.
- Each phosphate, however, still has one acidic proton that is usually ionized at pH 7, leaving a negatively charged oxygen.
- If this proton were present, the substance would be an acid; hence the name nucleic acid.
- The two ends of a DNA are not alike-one containing an unreacted 5' phosphate and the other an unreacted 3' hydroxyl group.



The Primary Structure of Ribonucleic Acids (RNA)

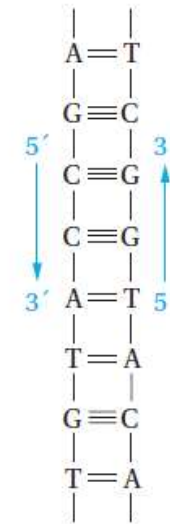
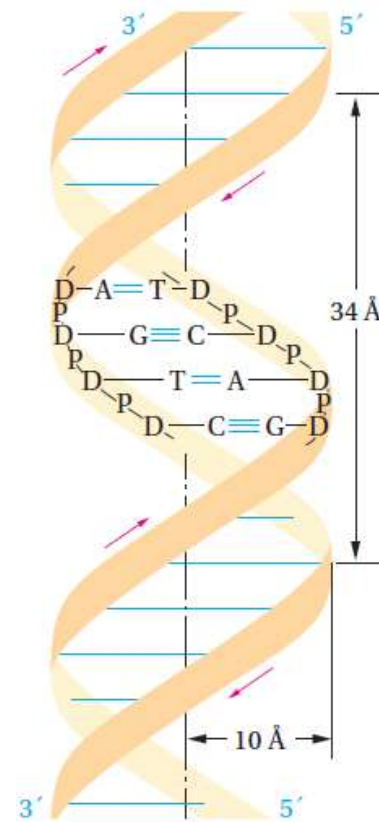
- Ribonucleic acids (RNA) differ from DNA in three important ways:
 - (1) The sugar is d-ribose;
 - (2) uracil replaces thymine as one of the four heterocyclic bases;
 - (3) most RNA molecules are single stranded, although helical regions may be present by looping of the chain back on itself.



Secondary DNA Structure; the Double Helix

- In 1953, when Watson and Crick, working together in Cambridge, England, proposed the double helix model for DNA.
- They received simultaneous supporting x-ray data for their proposal from Rosalind Franklin and Maurice Wilkins in London.
- The important features of their model follow:
 1. DNA consists of two helical polynucleotide chains coiled around a common axis.
 2. The helices are right-handed, and the two strands run in opposite directions with regard to their 3' and 5' ends.
 3. The purine and pyrimidine bases lie *inside* the helix, in planes perpendicular to the helical axis; the deoxyribose and phosphate groups form the outside of the helix.
 4. The two chains are held together by purine–pyrimidine base pairs connected by hydrogen bonds. *Adenine is always paired with thymine, and guanine is always paired with cytosine.*
 5. The diameter of the helix is 20 Å. Adjacent base pairs are separated by 3.4 Å and oriented through a helical rotation of 36°. There are therefore 10 base pairs for every turn of the helix (360°), and the structure repeats every 34 Å.
 6. There is no restriction on the sequence of bases along a polynucleotide chain. The exact sequence carries the genetic information.

Secondary DNA Structure; the Double Helix



A = T pairs have two hydrogen bonds

G ≡ C pairs have three hydrogen bonds

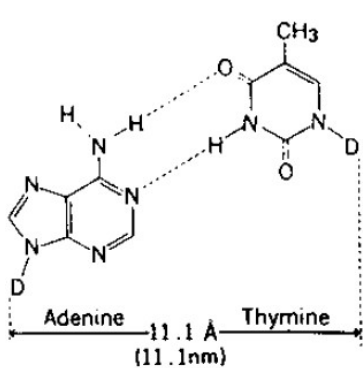
D = deoxyribose
P = phosphate
A = adenine
T = thymine
G = guanine
C = cytosine

Model and schematic representations of the DNA double helix.

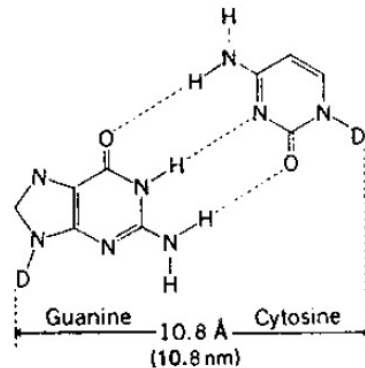
The space-filling model at the left shows the base pairs in the helix interior, in planes perpendicular to the main helical axis. The center drawing shows the structure more schematically, including the dimensions of the double helix. At the far right is a schematic method for showing base pairing in the two strands.

Secondary DNA Structure; the Double Helix

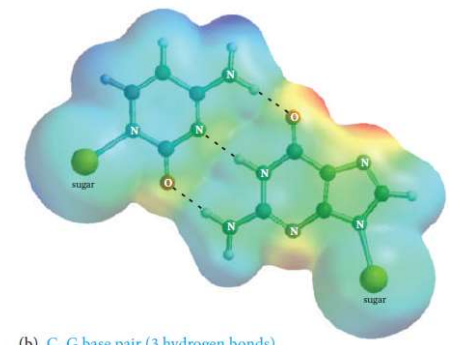
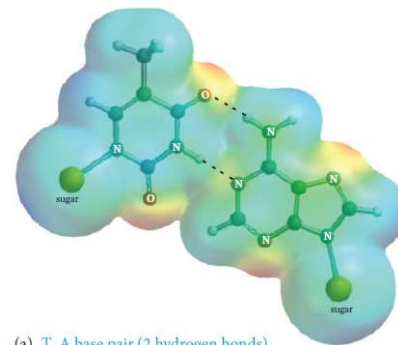
- **Watson and Crick correctly deduced that DNA existed as a double stranded helix** in which a pyrimidine base on one chain or strand was hydrogen-bonded to a purine base on the other chain.
- The bases are said to be complementary because coupling in helical double strands only occurs between certain base pairs, such as G with C.



two hydrogen bonds



three hydrogen bonds



- This (difference in H-bond) results in a difference in the twisting resulting from the presence of the AT or GC units and combinations of these units result in structures that are unique to the particular combination.

Secondary DNA Structure; the Double Helix

- The stability of the DNA is due to both internal and external hydrogen bonding as well as ionic and other bonding.
 - 1) The internal hydrogen bonding between the complementary purine-pyrimidine base pairs.
 - 2) The external hydrogen bonding occurs between the polar sites along exterior sugar and phosphate moieties and water molecules.
 - 3) Ionic bonding occurs between the negatively charged phosphate groups situated on the exterior surface of the DNA and electrolyte cations such as Mg^{+2} .
 - 4) The core consists of the base pairs, which, along with being hydrogen bonded, stack together through hydrophobic interactions and van der Waals forces.
- The AT and CG base pairs are oriented in such a manner so that the sugar-phosphate backbones of the two twined chains are in opposite or antiparallel directions with one end starting at the 5' and ending at the 3' and the starting end of the other across from the 5' end being a 3' end and opposite the other 3' end is a 5' end.
- Thus, *the two chains “run” in opposite directions.*

Secondary DNA Structure; the Double Helix

- Double-stranded DNA takes on one of three secondary structures called A, B, and Z.
- The major form is the B structure existing almost exclusively in water-based solutions.
- Helical twisting results in a stacking where the average distance between the stacked bases is 0.34 nm with a sugar to sugar distance of 0.6 nm with the helix repeating about every 10 base pairs with a pitch of 0.34 nm
- Helical conformations of DNA can be classified into three general families, called the A-, B-, and Z-forms.
- B-DNA, the predominant form, is the regular right-handed helix of Watson and Crick, with the base pairs essentially perpendicular to the helix axis.
- In the A-form, base pairs may be tilted by as much as 20° to the helix axis, and the sugar rings are puckered differently from the way they are in the B-form.
- Z-form, we see a 180° rotation of some of the bases about the C-N glycosidic bond, resulting in a *left*-handed helix.

- For the A form, the pitch or distance required to complete one helical turn is about 0.246 nm with one turn requiring about 11 base pairs.
- The base pairs are no longer nearly perpendicular to the helix axis as in the case for B DNA, but rather are tilted 19° with respect to the axis.

Successive base pairs occur every 0.23 nm in comparison to 0.33 nm for the B form of DNA. The A form is thicker and not as long for the same number of base pairs.

While dehydrated DNA can assume an A conformation under physiological conditions, it is unclear if “natural” DNA assumes this form.

In fact, the A form is typical for short chained DNA chains in the crystalline form since here much of the DNA is dehydrated. The major groove is deepened while the minor groove is shallower for the A form.

The A and B forms are called right handed forms or to have a right handed helical sense.

The Z form of DNA is a left-handed form. It is slimmer and elongated with a rise per base pair of 0.38 nm, about 12 base pairs per turn with a pitch of about 0.456 nm.

Certain nucleotide sequences fold into left-handed Z helices more readily than do others; this includes alternating CG sequences. This is evidence that suggests that some natural DNA exists in the Z form.

In solution, DNA is a dynamic, flexible molecule. It undergoes elastic motions on a nanosecond time scale most closely related to changes in the rotational angles of the bonds within the DNA backbone. The net result of these bendings and twistings is that DNA assumes a roughly globular or spherical tertiary shape. The overall structure of the DNA surface is not that of a reoccurring “barber pole” but rather because of the particular base sequence composition each sequence will have its own characteristic features of hills, valleys, bumps, etc.

As the two strands in a double helix separate, they act as a template for the construction of a complementary chain. This process occurs enzymatically with each nucleotide being introduced into the growing chain through matching it with its complementary base on the existing chain. Thus, two identical strands are produced when one double-helix combination replicates.

Secondary DNA Structure; the Double Helix

- The particular overall conformation adopted by a DNA molecule depends in part on the actual base sequence.
- For example, synthetic DNAs made of alternating purine–pyrimidine units have different conformations from DNAs made of blocks of purine bases followed by blocks of pyrimidine bases.
- Also, A-T and G-C base pairing with different H-bonds from that originally proposed by Watson and Crick has been observed.

- These variations in details of DNA structures lead to DNA molecules with bends, hairpin loops, supercoils, single-stranded loops, and even cruciforms in which single intrastrand H-bonded loops are extruded from the double helix.
- These structural changes add flexibility to the way DNA molecules are able to recognize and interact with other cellular components to perform their functions.

Ribonucleic Acids; RNA

- The transcription product of DNA is always single-stranded RNA.
- The single strand generally assumes a right-handed helical conformation mainly caused by base-stacking interactions also present in the DNA.
- The order of interaction is purine–purine >> purine–pyrimidine > pyrimidine–pyrimidine.
- The purine–purine interaction is so strong that a pyrimidine separating two purines is often displaced from the stacking order to allow the interaction between the two purines to occur. Base pairing is similar to that of the DNA except that uracil generally replaces thymine. For coupled RNA the two strands are antiparallel as in DNA.
- Where complementary sequences are present, the predominant double-stranded structure is an A form right-handed double helix. Many RNAs are combinations of complementary two-stranded helices, single-stranded segments, as well as other complex structures.

There are four kinds of RNA.

Messenger RNA (mRNA) varies greatly in size from about 75 units to over 3000 nucleotide units giving a molecular weight of 25,000 to one million. It is present at a percentage of about 2% of the total RNA in a cell.

Transfer RNA (tRNA) has about 73–94 nucleotides with a corresponding molecular weight range of 23,000–30,000. It is present in the cell at a level of about 16%. The most abundant RNA, 82%, is the **ribose RNA (rRNA)**, which has several groupings of molecular weight with the major ones being about 35,000 (about 120 nucleotide units), 550,000 (about 1550 units) and 1,100,000 (about 2900 units). Eukaryotic cells contain an additional type called small **nuclear RNA (snRNA)**.

tRNA generally contains 73–94 nucleotides in a single chain, a majority of the bases are hydrogen-bonded to one another. Hairpin curves promote complementary stretches of base bonding giving regions where helical double stranding occurs. The usual overall structure can be represented as a cloverleaf with each cloverleaf containing four of these helical double stranded units. One of the loops acts as the acceptor stem that serves as the amino acid–donating moiety in protein synthesis.

rRNA is a part of the protein synthesizing machinery of cells, ribosomes. Ribosomes contain two subunits called “small” and “large” with ribosomal RNAs being part of both of these units. rRNAs contain a large amount of intrastrand complementary sequences and are generally highly folded. Interestingly, there is a similarity between the folded structures of rRNA from many different sources even though the primary structure, base sequence, is quite varied. Thus, there appears to be preferred folding patterns for rRNAs.

mRNA, is the carrier of messages that are encoded in genes to the sites of protein synthesis in the cell where this message is translated into a polypeptide sequence. Because mRNA is a transcribed copy of the genetic unit, it is sometimes referred to as being the “DNA-like RNA.” mRNA is made during transcription, an enzymatic sequence in which a specific RNA sequence is “copied” from a gene site. rRNA and tRNA are also made by transcription of DNA sequences but unlike mRNA, they are not subsequently translated to form proteins.

Actual reproduction steps involving DNA and RNA often occur in concert with protein where the protein can act as a clamp or vice holding the various important members involved with the particular reproduction step in place. Thus, the protein complex acts as an assembly line tunnel or doughnut with the reactants present within the interior.