LECTURE NO. SEVEN

DNA STRUCTURE

Nucleotide:

DNA **is a** polymer containing chains of nucleotide monomers. Each nucleotide contains a **sugar, a** base and a phosphate group. The sugar is 2'-deoxyribose which has five **carbons** named 1' (prime) 2' etc. There are four types of base: adenine and guanine **have** two carbon-nitrogen rings and are purines; thymine and cytosine have a single ring and are pyrimidines. The bases are attached to the 1' carbon of the deoxyribose. A sugar plus a base is termed a nucleoside. A nucleotide has one, two or three phosphate groups attached to the 5' carbon of the sugar. Nucleotides occur as individual molecules or polymerized as DNA or RNA.

DNA Polynucleotides:

Nucleotide triphosphates of the four bases are joined to form DNA polynucleottde chains. Two phosphates are lost during polymerization and the nucleotides **are** joined by the remaining phosphate. A phosphodiester bond forms between the 5' phosphate of one nucleotide and the 3' hydroxyl of the next nucleotide. The polynucleotide has a free 5' phosphate at one end (5' end) and a free 3' OH (3' end) at the other end. The sequence of bases encodes the genetic information. It can be read 5'—»3' or 3'—>5'. Polynucleotides are extremely long. It is possible to have 4" different sequences.

The double helix:

DNA molecules are composed of two polynucleotide strands wrapped around each other to form a double helix. The sugar-phosphate part of the molecule forms a backbone. The bases face inwards and are stacked on top of each other. The two polynucleotide chains run in opposite directions. The double helix is right-handed and executes a turn every 10 bases. The helix has a major groove which mediates interactions with proteins. Variant DNA structures have been identified including Z DNA which has a left-handed helix.

Complementary base pairing:

Hydrogen bonds between bases on the two DNA strands stabilize the double helix. The available space between the strands restricts the bases that can interact such mat a purine always interacts with a pyrimidine. Thus, A interacts only with T and G only with C. This is called complementary base pairing. The restriction on base pairing means that the sequence of bases on the two strands are related to each other, such that the sequence of one determines and predicts the sequence of the other. This allows genetic information to be preserved during replication of the DNA and expression of the genes.

RNA structure:

Disruption of the hydrogen bonds between the bases by heat or chemicals or by the action of enzymes causes the strands of the double helix to separate.

In RNA thymine is replaced by uracil and 2-deoxyribose by ribose. RNA normally exists as a single polynucleotide strand however, short stretches of base pairing may occur between complementary sequences.

Nucleotides

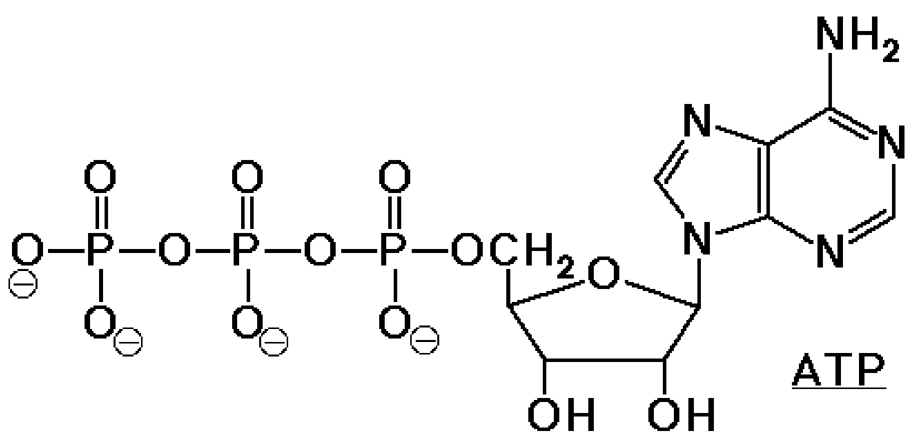
The ability of DNA to carry the genetic information required by a cell to reproduce itself is closely related to the structure of DNA molecules. DNA is a polymer and consists of a long chain of monomers called nucleotides. The DNA molecule is said to be a polynucleotide. Each nucleotide has three parts: a sugar, a nitrogen containing ring-structure called a base, and a phosphate group. The sugar present in DNA is a five carbon pentose called 2'-deoxyribose in which the -OH group on carbon 2 of ribose is replaced by hydrogen (Fig. 1). The carbon atoms in the sugar are numbered 1-5. The numbers are given a dash 0 referred to as prime to distinguish them from the numbers of the atoms in the base. The numbering is important because it indicates where other components of the nucleotide are attached to the sugar.

Nucleotides contain one of four bases: **adenine,** guanine, thymine or cytosine (Fig. 2). These are complex molecules containing carbon and nitrogen ring structures. Adenine and guanine contain two carbon-nitrogen rings and are known as purines. Cytosine and thymine contain a single ring and are called pyrimidines. The bases are attached to the sugar by a bond between the I' carbon of the sugar and a nitrogen at position 9 of the purines or position 1 of the pyrimidines. A sugar plus a base is called a nucleoside (Fig. 3a).

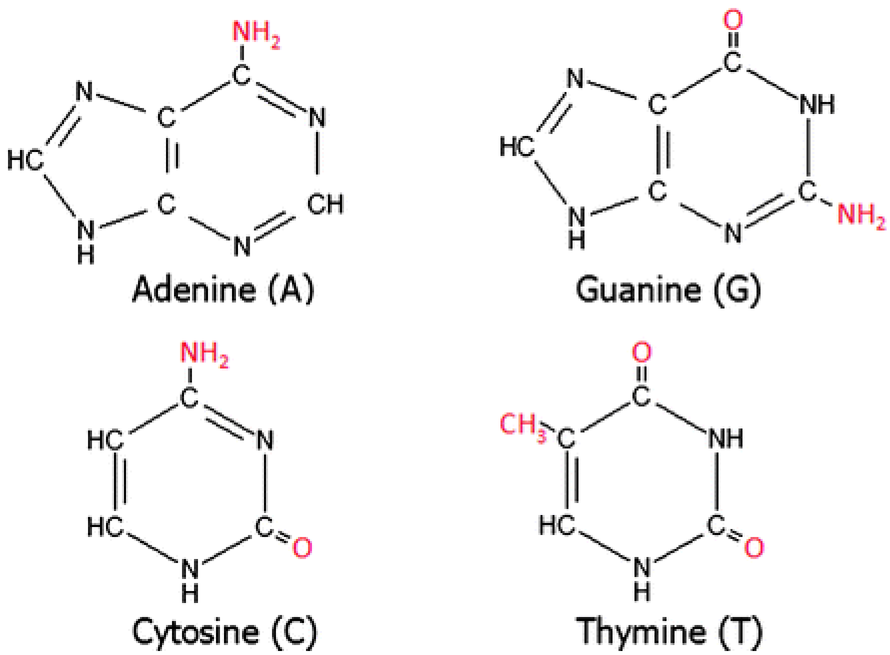
Nucleotides contain phosphate groups (PO,) attached to the 5' carbon of the sugar (Fig. 3b). *A.* nucleoside is called a nucleotide when a phosphate group is attached, the attachment can consist of one, two or three phosphate groups joined together. The phosphate groups are called a, p and -y, with a directly attached to the sugar. Nucleotides may exist in cells as individual molecules (nucleotide triphosphates play an important role in cells as the carriers of energy used to power enzymatic reactions) or polymerized as nucleic acids (DNA or RNA).

DNA polynucleotides:

Nucleotide triphosphates are joined together to give polynucleotides. There are **polynucteotides—** four used to synthesize DNA polynucleotides, 2'-deoxyadenosine S'-triphosphate (dATP or A), 2'-deoxythyrnidine S'-triphosphate (dTTP or T), 2'-deoxycytosine S'-triphosphate (dCTP or C) and 2-deoxyguanosine S'-triphosphate (dGTP or G). The P and •y phosphates are lost during polymerization and the nucleotide units are joined together by the remaining phosphate. The 5' phosphate of one nucleotide forms a bond with the 3' carbon of the next nucleotide eliminating the -OH group on the 3' carbon during the reaction. The bond is called a *3'-5'* **phosphodiester bond** (C-O-P) *(Fig. 4).* The polynudeoode chain has a free 5' triphosphate at one end known as the 5' end and a free 3' hydroxyl group at the other end called the 3' end. This distinction gives the DNA polynucleotide polarity so that a DNA molecule can be described as running 5'-»3' or 3'-»5'.

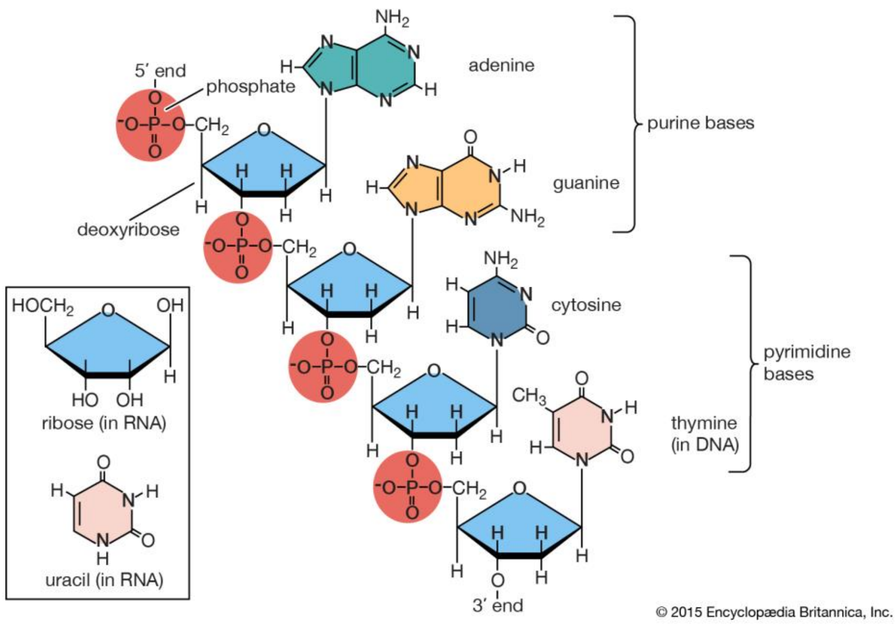


It is the sequence of the bases in the DNA polynucleotide that encodes the genetic information. This sequence is always written in the 5'-»3' direction (polymerase enzymes copy DNA molecules in this direction). Polynucleotides can be extremely long with no apparent limit to the number of nucleotides and no restrictions on the sequence of the nucleotides. The maximum number of possible base sequences for a polynucleotide is 4" , where n is the number of nucleotides. This is an enormous number. For example, a polynucleotide containing just six bases could be arranged as 4*' = 4096 different sequences.



The double helix:

DNA molecules have a very distinct and characteristic three-dimensional structure known as the double helix (Fig. 5). The structure of DNA was discovered in 1953 by Watson and Crick working in Cambridge using X-ray diffraction pictures taken by Franklin and Wilkins. DNA exists as two polynucleotide chains wrapped around each other to form the double helix. The sugar-phosphate part of the molecule forms a spine or backbone which is on the outside of the helix. The bases, which are flat molecules, face inwards towards the center of the helix and are stacked on top of each other like a pile of plates.



X-ray diffraction pictures of the double helix show repeated patterns of bands that reflect the regularity of the structure of the DNA. The double helix executes a turn every 10 base pairs. The pitch of the helix is 34A so the spacing between bases is 3.4A. The diameter of the helix is 20A. The double helix is said to be 3 anti-parallel. One of the strands runs in the 5'-»3' direction and the other 3'-»5' direction. Only antiparallel polynucleotides form a stable helix. The double helix is not absolutely regular and when viewed from die outside a major groove and a minor groove can be seen. These are important for interaction with proteins, for replica tion of the DNA and for expression of the genetic information. The double helix is right-handed. This means that if the double helix were a spiral staircase and you were climbing up, the sugar-phosphate backbone would be on your right.

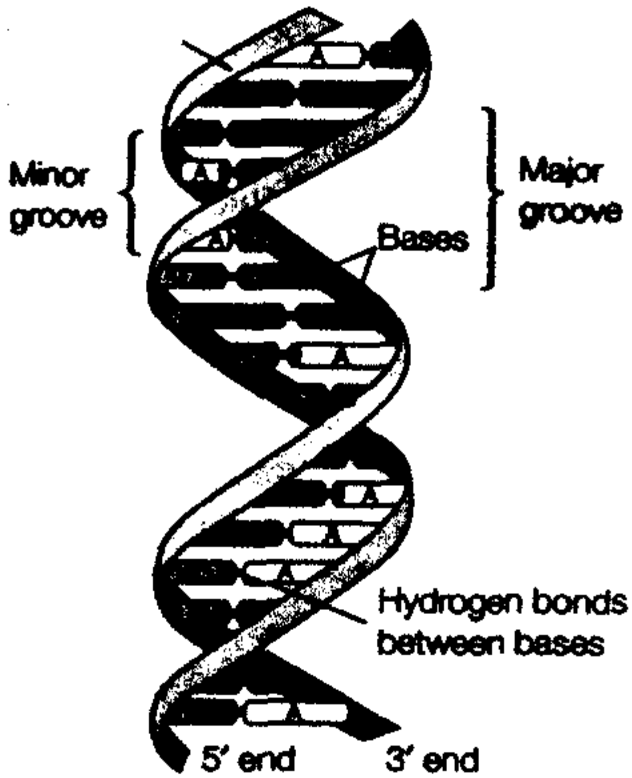
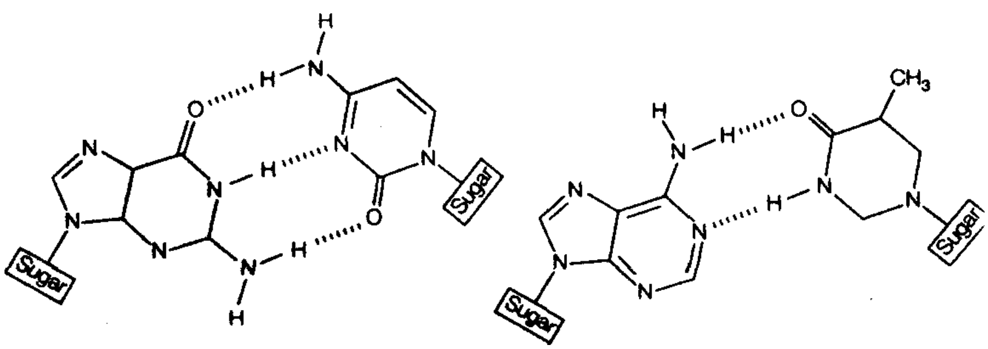


Fig. 5. The double helix.

A number of variant forms of DNA occur when crystals of the molecule are formed under different conditions. The form present in cells is called the B fonn. Another form called die A form has a slightly more compact structure. Other forms that exist are C, D, E and Z, which is striking because it exists as a left-handed helix. Regions in chromosomes containing nonstandard structures such as Z-DNA have recently been identified.

Complementary base pairing:

The bases of the two polynucleotide chains interact with each other. The space between the polynucleotides is such diat a two-ring purine interacts with a single-ring pyrimidme. Thus, thymine always interacts with adenine and guanine with cytosine. Hydrogen bonds form between die bases and help to stabilize die interaction. Two bonds form between A and T and three between G and C. Thus, G-C bonds are stronger dian A-T bonds. The way in which the bases form pairs between the two DNA strands is known as



&Wlkr: Cytosine *Aderune : Thyrtnne*

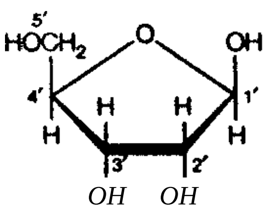
Fig. 6. Complementary haw pairing. Hydrogen bonds are shown as dashed lines.

complementary base pairing and is of fundamental importance (Fig. 6). Combinations other than G-C and A-T do not work because they are too large or too small to fit inside the helix or they do not align correctly to allow hydrogen bond formation. Because G must always bond to C and A to T the sequences of the two strands are related to each other and are said to be complementary with the sequence of one strand predicting and determining the sequence of the other. This means that one strand can be used to replicate the other. This is a vital mechanism for retaining genetic information and passing it on to other cells following cell division. Complementary base pairing is also essential for the expression of genetic information and is central to me way DNA sequences are transcribed into mRNA and translated into protein.

The double helix is stabilized by hydrogen bonds between the base pairs, These can be disrupted by heat and some chemicals. This results in separation of me double helix into two strands and the molecule is said to be denatured. In cells enzymes can separate the strands of the double helix for the purposes of copying the DNA and for expression of the genetic information.

RNA structure:

The structure of RNA is similar to that of DNA but a number of important differences exist. In RNA ribose replaces 2'-deoxyribose and me base thymine is replaced by another base, uracil, which can also base pair with adenine (Fig. 7)' In addition, RNA molecules normally exist as a single polynucleotide strand and do not form a double helix. However, it is possible for base pairing to occur between complementary parts of the same RNA strand resulting in short double -stranded regions.



Ribose

*Fig.*7. Structures of ribose.