

NUCLEIC ACIDS

LECTURE IV

Eric Mbindo Njunju

Bsc; Msc

OCCURRENCE

Two types of nucleic acids are present in all mammalian cells including humans. They are DNA-deoxy ribonucleic acid and RNA-ribonucleic acid. DNA is present in the nucleus and mitochondria. RNA is present in the nucleus and cytoplasm.

Nucleic acids are also present in bacteria, viruses and plants

MEDICAL AND BIOLOGICAL IMPORTANCE

1. Nucleic acids serve as genetic material of living organisms including humans.
2. Nucleic acids are involved in the storage, transfer and expression of genetic information.
3. Nucleic acids contain all the necessary information required for the formation of an individual or organism.
4. Nucleic acids determine physical fitness of an individual to life.
5. Some nucleic acids act as enzymes and coenzymes. For example, RNA, acts as catalyst and RNA is coenzyme for telomerase which seals ends of chromosomes.
6. DNA exhibits structural polymorphism. It assumes several forms depending on certain conditions. Several DNA variants are known.
7. Some RNAs without protein products are found in mammals, yeast and bacteria. They are involved in cellular functions.
8. Human Genome Project (HGP) was completed in 2000. It is considered as a major achievement of man after landing on the moon. It is useful for finding causes of several diseases whose causes are unknown. It may also lead to development of new therapeutics as well as diagnostics.

Chemical nature of nucleic acids

Nucleic acids are acidic substances containing nitrogenous bases, sugar and phosphorus. Both DNA and RNA are polynucleotides. They are polymers of nucleotides.

Phosphodiester linkage

In polynucleotides, nucleotides are joined together by phosphodiester linkage. Diester linkage of phosphate joins 3' OH and 5' OH belonging two separate sugars (Fig).

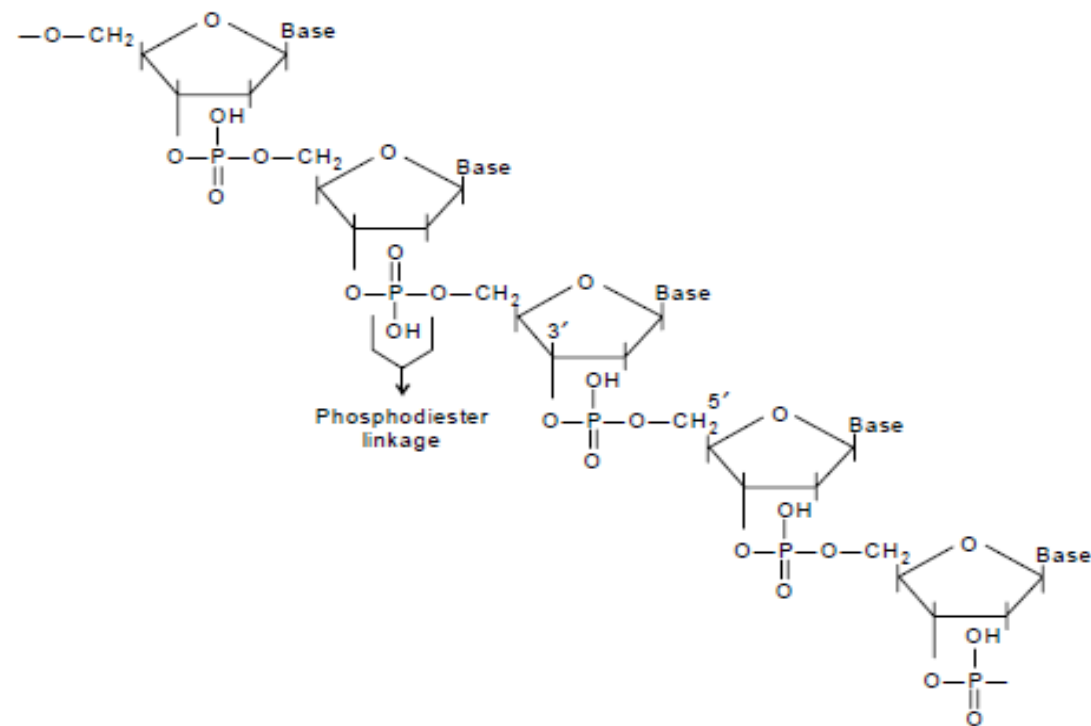
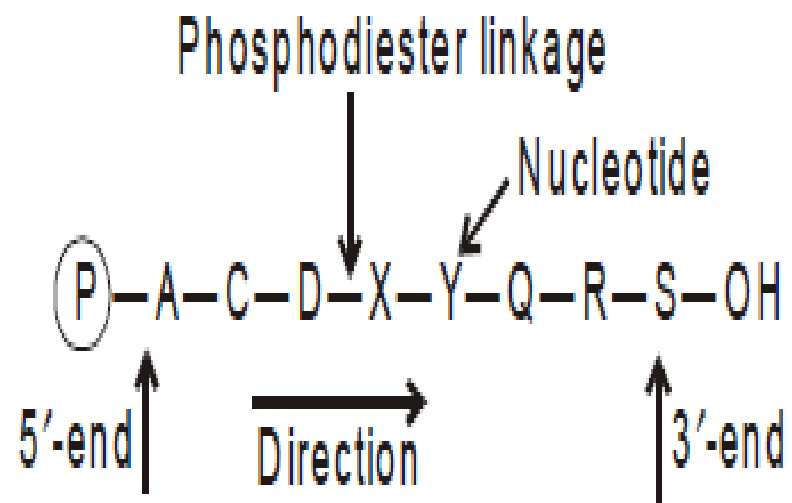


Fig: Structure of a polynucleotide

Nucleic acid structure

Primary structure of nucleic acids

Nucleotide sequence of a polynucleotide is known as primary structure of nucleic acid. The primary structure confers individuality to polynucleotide chain. A polynucleotide chain has direction. They are represented in $5' \rightarrow 3'$ direction only. However, the phosphodiester linkage runs in $3' \rightarrow 5'$ direction. Each polynucleotide chain has two ends. The $5'$ end carrying phosphate is shown on the left hand side and $3'$ end carrying unreacted hydroxyl is shown on the right hand side (Fig). Primary structures of DNA and RNA exist in single stranded DNA and RNA organisms.



Primary structure of nucleic acid. Letters A, C, D, X, Y, Q, R, S are nucleotides

Short-hand representation of polynucleotides

Since polynucleotides consist of various bases, sugars and phosphates, writing a segment of polynucleotide showing structures of bases, sugars with attached phosphates is awkward or highly inconvenient. So, short hand or compact representation of polynucleotides has been proposed. In compact nomenclature or polynucleotide letters A, G, C and T represent nitrogenous bases adenine, guanine, cytosine and thymine, respectively. A vertical line represents sugar back bone. The branches of vertical lines with numerals 3' and 5' represent hydroxyl bearing carbon atoms of sugar. A branch at the middle of the vertical line represents hydroxyl bearing 3rd carbon atom of sugar.

Another branch at the bottom of vertical line represents hydroxyl or phosphate bearing 5th carbon atom of sugar (Fig). The more compact representation of the same molecule is PAPCPGPTPA.

Since primary structure is the sequence of nucleotides still more compact representation of the same molecule is ACGTA. In this primary structure, letters A, G, C, T stand for nucleotides and sequence is written from left to right. Therefore, in DNA and RNA, letters A, G, C, T stand for nucleotides and sugar is deoxy ribose if the polynucleotide is a segment of DNA and sugar is ribose, if it is an RNA segment.

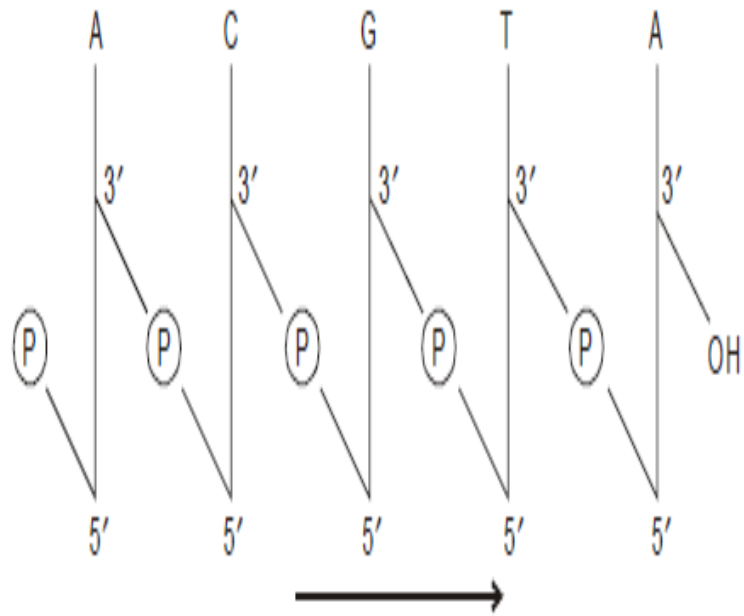


Fig: Short hand representation of a polynucleotide segment. Note the direction of polynucleotide chain and phosphodiester linkage

Structure of DNA

E. Chargaff and his colleagues extensively studied base composition of DNA. Their studies provided valuable information on the structure of DNA.

Characteristics of DNA base composition

1. In DNA, number of adenine residues is equal to the number of thymine residues *i.e.*, $A = T$. Further number of guanine residues is equal to number of cytosine residues *i.e.*, $G = C$. As corollary sum of purine residues is equal to sum of pyrimidine residues $A + G = C + T$.
2. DNAs from different tissues of same species have same base composition.
3. Base composition of DNA varies from one species to another species.
4. DNAs from closely related species have similar base composition.
5. DNAs of widely different species have different base composition.
6. DNA base composition of a species is not affected by age, nutritional state and environment.

In 1953, Watson and Crick proposed precise three dimensional model of DNA structure based on model building studies, base composition and X-ray diffraction studies.

This model is popularly known as DNA double helix.

Using this model, they also suggested a precise mechanism for the transfer of genetic information to daughter cells from parent cells.

Salient features of double helix

1. Two polynucleotide chains are coiled around a central axis in the form of right handed double helix. It represents secondary structure of DNA. It is present in double stranded DNA containing organisms (Fig).

2. Each polynucleotide chain is made up of 4 types of nucleotides. They are adenylate, guanylate, thymidylate and cytidylate.
3. Each polynucleotide chain has direction or polarity. Further each polynucleotide chain has 5' phosphorylated and 3' hydroxyl end.
4. The back bone of each strand consists of alternating sugar and phosphates. The bases project inwards and they are perpendicular to the central axis (Fig).
5. The two strands run in opposite direction, i.e., they are anti-parallel.
6. The strands are complementary to each other. Base composition of one strand is complementary to the opposite strand. If adenine appears in one strand thymine is found in the opposite strand and vice versa. Where ever guanine is found in one strand cytosine is present in the opposite strand and vice versa (Fig).
7. Base pairing: Bases of opposite strands are involved in pairing. Pairing occurs through hydrogen bonding and it is specific. Adenine of one strand pairs with thymine of opposite strand through two hydrogen bonds. Guanine of one strand pairs with cytosine of opposite strand. Three hydrogen bonds between GC pair makes it stronger than AT pair (Fig).

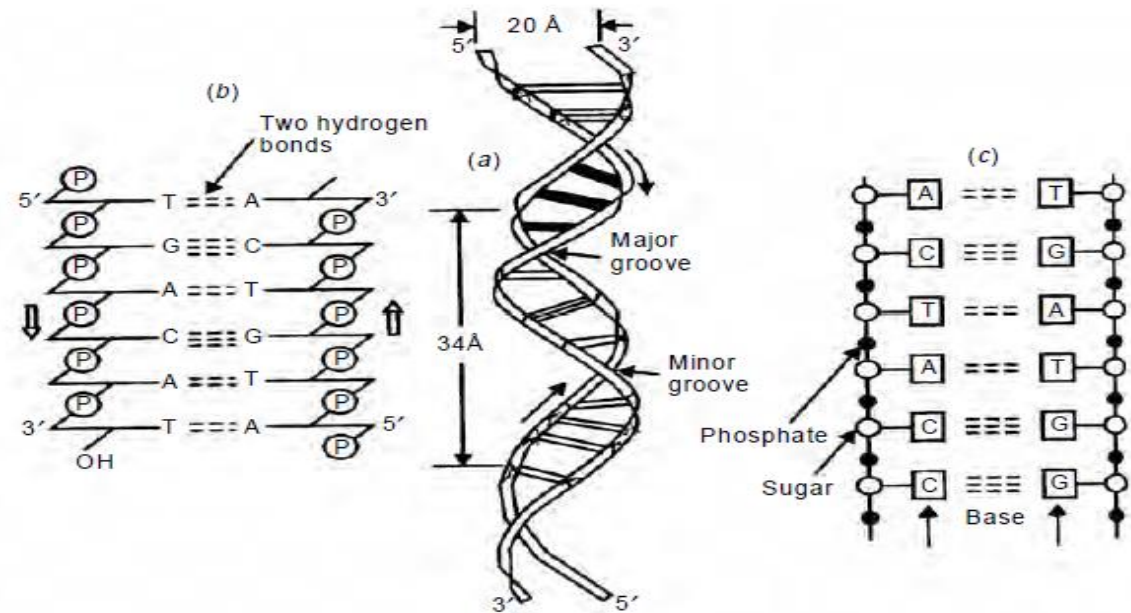


Fig:

(a) DNA double helix

(b) Base pairing among complementary bases of opposite strands

(c) Alternating sugar and phosphate form back bone of strand. Bases project inwards and perpendicular to central axis

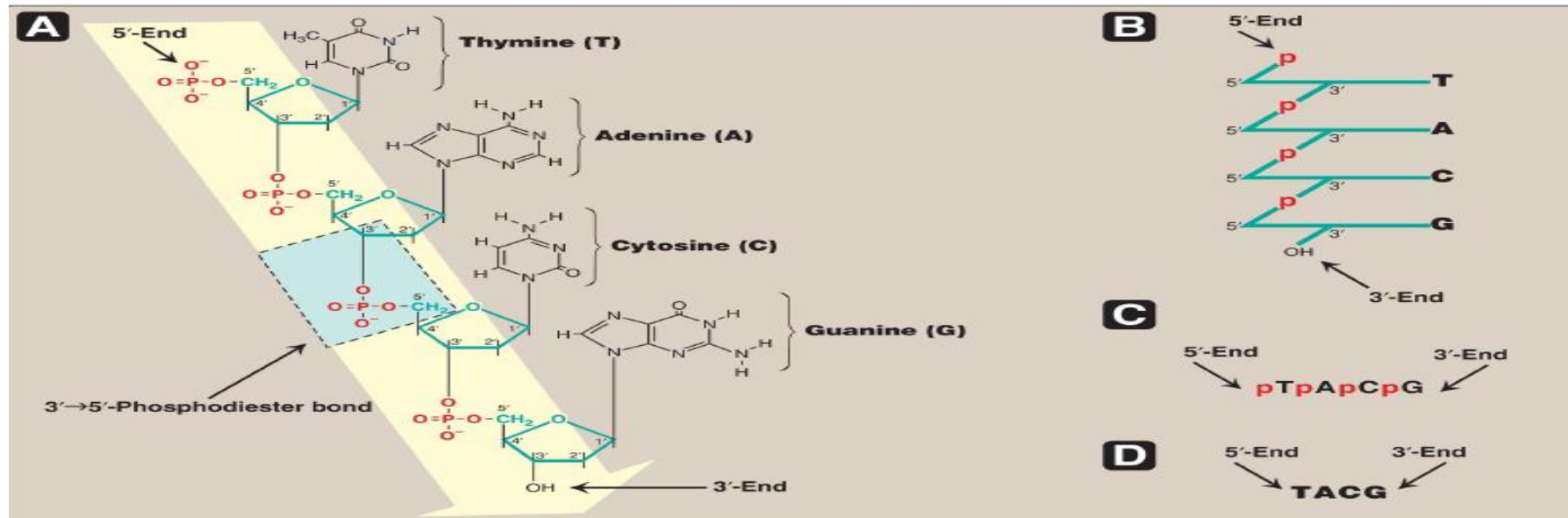


Fig: DNA with the nucleotide sequence shown written in the 5'→3' direction. A 3'→5'-phosphodiester bond is shown highlighted in the blue box, and the deoxyribose-phosphate backbone is shaded in yellow. B. DNA written in a more stylized form, emphasizing the deoxyribose-phosphate (p) backbone. C. A simpler representation of the nucleotide sequence. D. The simplest (and most common) representation. [Note: The nucleotide base sequence is assumed to be written in the 5'→3' direction unless otherwise indicated.]

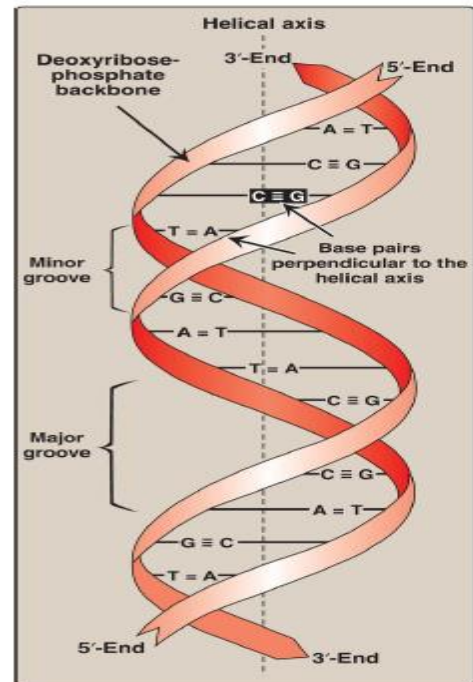


Fig: DNA double helix, illustrating some of its major structural features •

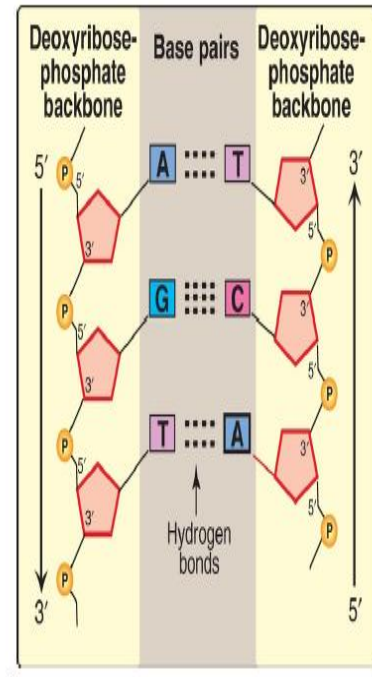


Fig: Two complementary DNA sequences. T = thymine; A = adenine; C= cytosine; G = guanine.

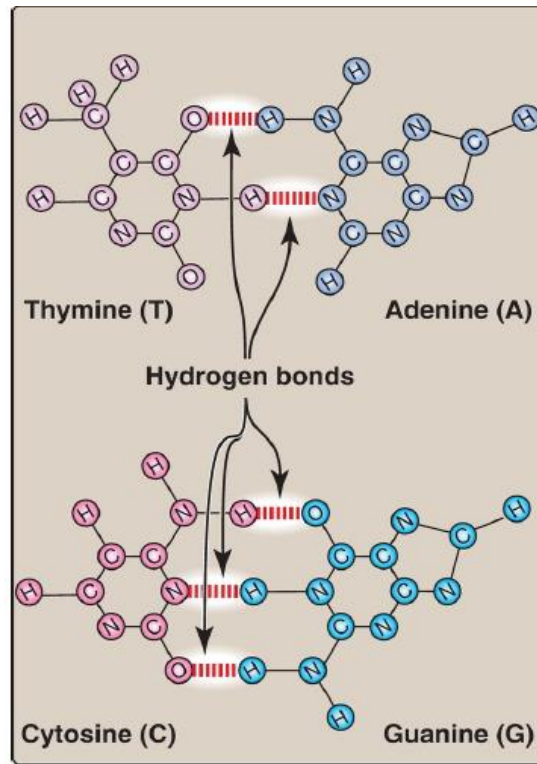


Fig: Hydrogen bonds between complementary bases

8. Complementarity of strands and base pairing are the outstanding features of Watson-Crick model. Specific base pairing immediately suggests a copying mechanism for DNA.

9. The large number of hydrogen bonds along entire length of DNA makes DNA molecule highly stable.

10. Major and minor grooves are present on double helix. They arise because glycosidic bonds of base pairs are not opposite to each other.
11. The base pairs are stacked and 3.4 \AA apart. The pitch of the helix (one turn) is 34 \AA and accommodates ten base pairs.
12. Apart from hydrogen bonding, the double helix is stabilized by hydrophobic attraction between bases.
13. The width of double helix is 20.
14. Watson-Crick model is known as B-DNA. Majority of the nuclear DNA is in B-form.

THANK YOU