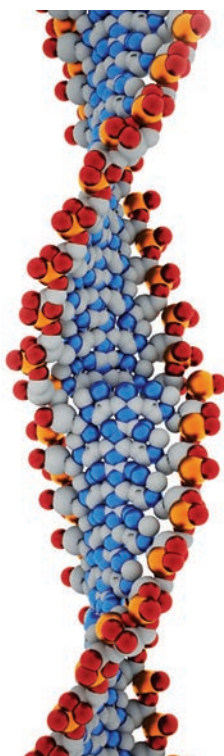


The Swiss scientist Friedrich Miescher who discovered DNA in 1869 and also suggested that they may play a role in heredity.



### Learning objectives

After studying this unit the students will be able to

- Explain the role played by nucleic acids in an organism
- Relate DNA with inheritance of traits from ancestors
- Describe the structural differences between bases, nucleosides and nucleotides.
- Explain the Chargaff's rule
- Elaborate the structure of DNA and RNA
- Differentiate the DNA from RNA

### Introduction

We might have heard people saying, "It is in your genes?", "like mother, like daughter". Many physical traits like skin colour, curly or straight hair etc... are inherited from our parents or grandparents. We also inherit talent in special fields such as art, music, etc from then. How are these characters inherited? This is through the agents of inheritance called DNA.

Nucleic acids were first discovered by Friedrich Miescher in 1869 and were named as nuclein as they were found

in the nuclei of leukocytes (pus cells) from discarded surgical bandages. The functions of nucleic acids were left undiscovered until early 1900.

## 7.1 Significance of Nucleic acids

- Nucleic acids are the molecular repositories (store houses / reserve bank) of genetic inheritance, i.e they have the ability to store and transmit information from one generation to the next.
- Ultimately, every macromolecule (proteins and RNAs) of the cell is the product of information that has been stored in the nucleotide sequences of the genes.
- Certain nucleotides like ribozymes have catalytic activities.
- Certain purine and pyrimidine analogs are used for treating cancer and AIDS.

## 7.2 Composition

Nucleic acids are very long, thread-like polymers, made up of a linear array of monomers called nucleotides held together by phosphodiester bridges. Nucleotides have three characteristic components (i) Base (ii) Sugar (iii) Phosphate group.

### 7.2.1 Common Bases of Nucleic acids

The bases of nucleic acids are heterocyclic, containing aromatic ring in their structures. They may be monocyclic pyrimidines or bicyclic purines.

### i. Pyrimidine bases

- Pyrimidines are six-membered heterocyclic aromatic rings containing two nitrogen atoms (Figure 7.1) Pyrimidine ring is numbered in the clock-wise fashion. The common naturally occurring pyrimidines are cytosine, uracil, and thymine (5-methyluracil) (Figure 7.2). Cytosine and thymine are the pyrimidines typically found in DNA, whereas cytosine and uracil are common in RNA.

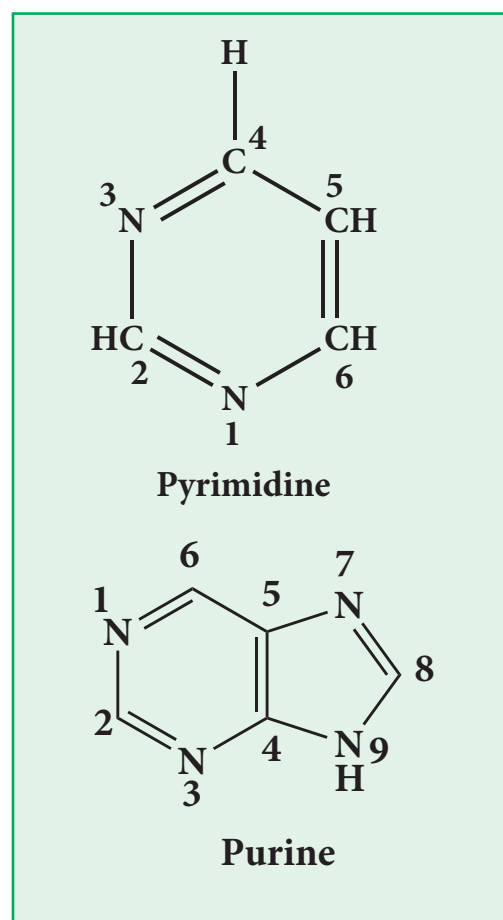


Figure 7.1. Structure of Purine and Pyrimidine

### Properties of Pyrimidine bases

1. Pyrimidines are basic in nature. They are less soluble in water.

2. They absorb UV light at 260 nm. This property is used to detect and estimate DNA and RNA in biological solutions.
3. They are capable of forming hydrogen bonds with purine nucleotides in nucleic acids.
4. They exhibit keto–enol tautomerism.

## ii. Purine bases

Purine is a bicyclic ring formed by fusion of pyrimidine ring with imidazole ring. Purine ring is numbered in the anti-clockwise fashion. Adenine (6-amino purine) and guanine (2-amino-6-oxy purine), the two common purines, are found in both DNA and RNA (Figure 7.2 ). Other naturally occurring purine derivatives include hypoxanthine, xanthine, and uric acid. Hypoxanthine and xanthine are found only rarely as constituents of RNA, while they are intermediates (compounds formed in the synthetic pathway) in the synthesis of nucleic acids. Uric acid is the catabolic end product of nucleic acids.

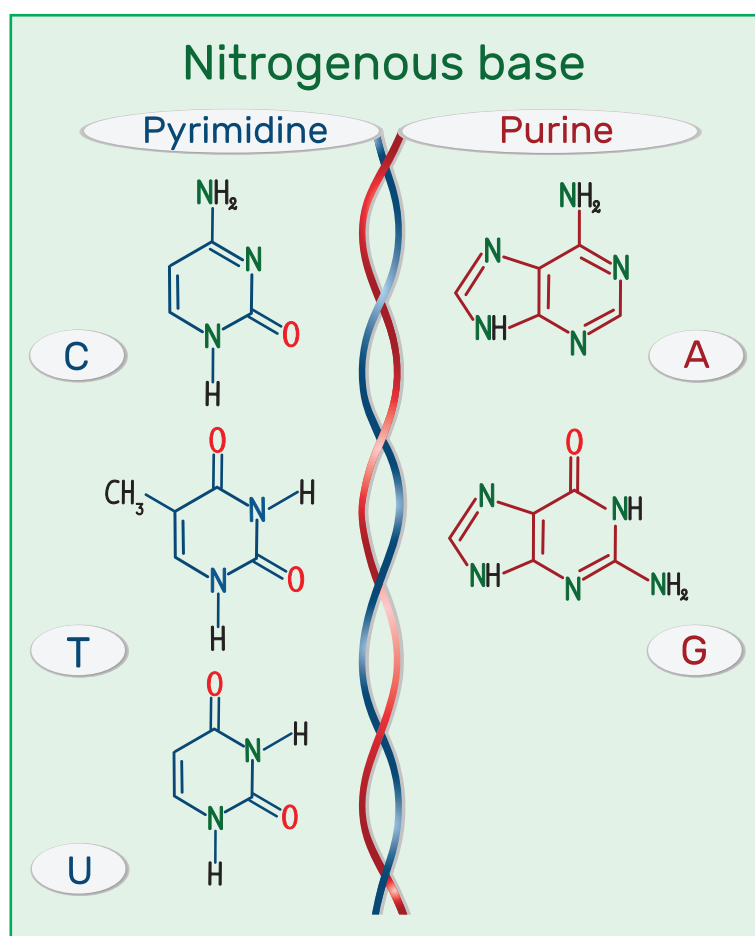


Figure 7.2. Structure of Purine and Pyrimidine bases

## Properties of Purine bases

1. Purines are basic in nature. They are sparingly soluble in water.
2. They also absorb UV light at 260 nm. This property is used to detect and estimate DNA and RNA in biological solutions.
3. They are capable of forming hydrogen bonds with pyrimidine nucleotides in nucleic acids.
4. They exhibit keto –enol tautomerism.

### 7.2.2 Sugars

There are two types of sugars present in nucleic acids. They are ribose and deoxyribose (Fig.7.3). Based on the sugar moiety present in the nucleic acids, they are classified as Deoxy ribonucleic acid (DNA) and Ribonucleic acid (RNA). DNA is present in the nucleus, mitochondria and chloroplasts. RNA is present in the nucleus, nucleolus, ribosome and cytoplasm. Ribose and deoxy ribose have differences in their properties. Deoxy ribose is less reactive in nature, when compared to ribose.

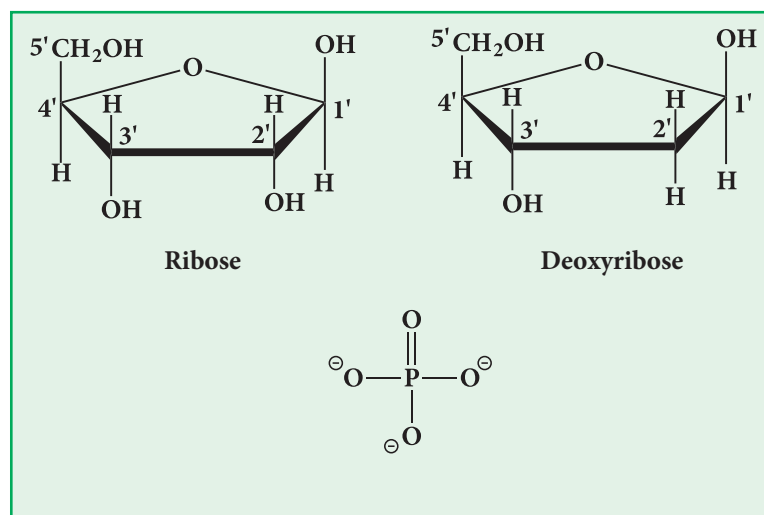


Figure 7.3 Structure of ribose, deoxy ribose and phosphate

### 7.2.3 Phosphate

Phosphoric acid forms phospho-diester linkage between nucleosides. Based on the number of phosphate group present in the nucleotide, they are classified as monophosphates, diphosphates and triphosphates.

### 7.3 Nucleosides

A nucleoside is composed of purine or pyrimidine base and a pentose sugar. In the case of purine nucleoside, the sugar is attached to N-9 of the purine ring, whereas in pyrimidine nucleoside, the sugar is attached to the N-1 of the pyrimidine ring. This type of linkage is N-glycosidic linkage (Fig. 7.4).

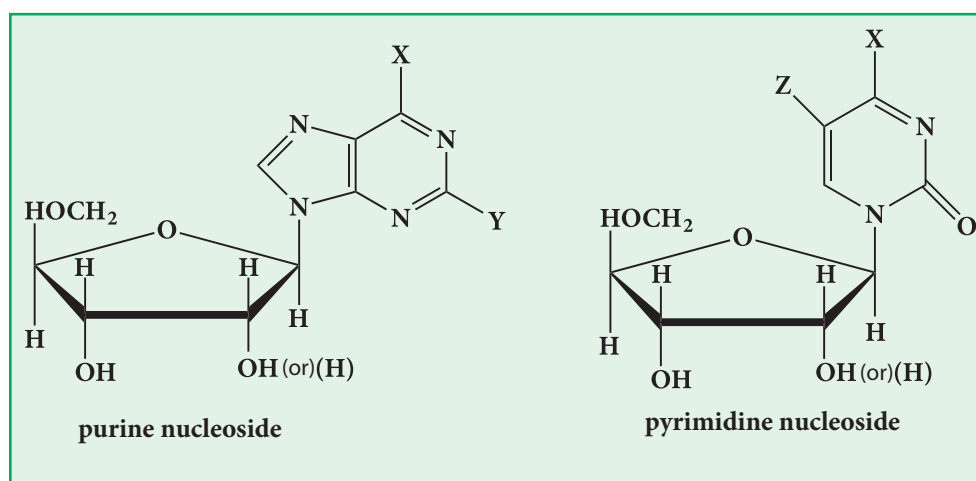


Figure 7.4 Structure of a nucleoside

### 7.4 Nucleotides

Nucleotides are phosphorylated forms of nucleosides. Phosphorylation (addition of phosphate group) occurs generally in the 5'OH group of the ribose or deoxy ribose sugar. A nucleotide with one phosphate group is called as monophosphate of the respective nucleoside. For example, the monophosphate of adenosine is called as Adenosine Mono Phosphate. If two phosphate groups are attached to the sugar moiety at the 5'OH group, it is called as diphosphate. eg. Cytidine Diphosphate. A nucleotide containing three phosphate groups is called as triphosphate eg. Adenosine Triphosphate (Fig. 7.5). The corresponding nucleosides and nucleotides are listed in Table 7.11 (Bases, their nucleosides and nucleotides).

#### Functions

- Nucleotides are the energy currency of the cells (ATP).
- They actively take part in metabolism as hydrogen donors, phosphate group donors and methyl group donors.
- They form the structural components of some co-enzymes (NAD and FAD).

**Table 7.1 Bases, their nucleosides and nucleotides**

Name of the base	Sugar	Nucleoside	No. of Phosphate Groups	Nucleotide
Adenine	Ribose	Adenosine	1	AMP
			2	ADP
			3	ATP
	Deoxyribose	Deoxy Adenosine	1	dAMP
			2	dADP
			3	dATP
Guanine	Ribose	Guanosine	1	GMP
			2	GDP
			3	GTP
	Deoxyribose	Deoxy Guanosine	1	dGMP
			2	dGDP
			3	dGTP
Cytosine	Ribose	Cytidine	1	CMP
			2	CDP
			3	CTP
	Deoxyribose	Deoxy Cytidine	1	dCMP
			2	dCDP
			3	dCTP
Uracil	Ribose	Uridine	1	UMP
			2	UDP
			3	UTP
	Deoxyribose	Deoxy Uridine	1	dUMP
			2	dUDP
			3	dUTP
Thymine	Ribose	Thymidine	1	TMP
			2	TDP
			3	TTP
	Deoxyribose	Deoxy Thymidine	1	dTMP
			2	dTDP
			3	dTTP

- Nucleotides like cAMP (cyclic AMP) and cGMP (cyclic GMP) act as second messengers involved in hormonal signaling pathways.

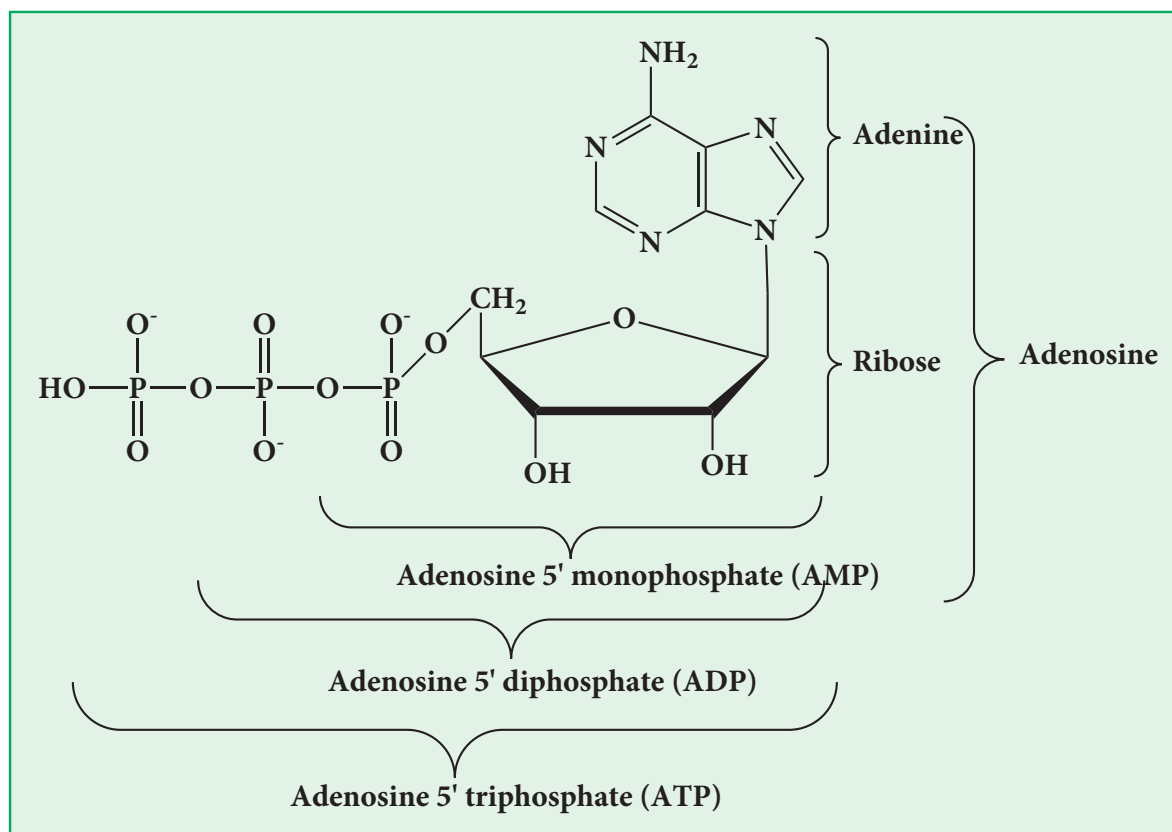


Figure 7.5 Structure of a nucleotide



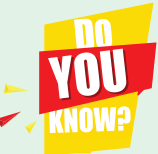
Nucleosides generally do not have physiological role. However, adenosine is an exemption with biological activity. It acts as a local hormone and is involved in many different biological effects like blood vessel dilation. Supraventricular tachycardia, a heart condition characterized by rapid heart beat is treated with intravenous injections of adenosine. Adenosine promotes sleepiness. Caffeine, a chemical found in tea and coffee brings wakefulness by blocking the binding of adenosine to its receptors.

Oligonucleotides are polymers which yield two to ten residues of mononucleotides on hydrolysis. Two nucleotides join together to form dinucleotides. Example for biologically important dinucleotides are NAD and FAD, which act as co-enzymes.


Polynucleotides are polymers that yield more than ten nucleotides on hydrolysis. Polynucleotides have directions. If the first nucleotide of the sequence has 5' triphosphate free and 3' OH group bonded to the next nucleotide, then the direction of the polynucleotide is 5' to 3'. If the first nucleotide in the sequence has 3' OH group free, then it is said to be from 3' to 5' direction.

## 7.5 Structure of DNA


In 1953, J.D. Watson and F.H.C. Crick proposed a precise three dimensional model of DNA structure based on model building studies, base composition and X-ray diffraction studies carried out by Maurice Wilkins and Rosalind Franklin. This model is popularly known as the DNA double helix (Figure 7.6).




The Nobel prize in Physiology or Medicine (1962) was awarded jointly to Francis Harry Compton Crick, James Dewey Watson and Maurice Hugh Fredrick Wilkins “for discoveries concerning the molecular structure of nucleic acids”



**Francis Harry Compton Crick**



**James Dewey Watson**



**Maurice Hugh Fredrick Wilkins**

### 7.5.1 Different forms of DNA

There are three forms of DNA – A, B and Z DNA. The characteristics of each form of DNA is listed in the table given below.

**Table 7.2 Properties of major forms of DNA**

Particulars	A DNA	B DNA	Z DNA
Helix	Right handed	Right handed	Left handed
Base pairs per turn	~11	~10.5	~12
Helical Diameter (nm)	2.6	2.0	1.8
Helical length (nm)	2.6	3.4	3.7
Shape	Broadest	Intermediate	Narrowest
Major Groove	Wide, deep	Narrow, deep	Flat
Minor Groove	Narrow, shallow	Broad, shallow	Narrow, deep





Synthetic analogs of purines, pyrimidines, nucleosides and nucleotides or sugar moiety have numerous application in clinical medicine. Oncologists employ 5- fluoro - or 5 iodouracil, and 8-azaguanine for treatment of cancer. The purine analog allopurinol is used in treatment of hyperuricemia and gout. Azathioprine is employed during organ transplantation to suppress immunologic rejection.

### 7.5.2 Salient features of the structure of DNA

The B form DNA, also known as the Watson- Crick DNA is the most stable and prevalent form of DNA. The important structural features of B- DNA are :

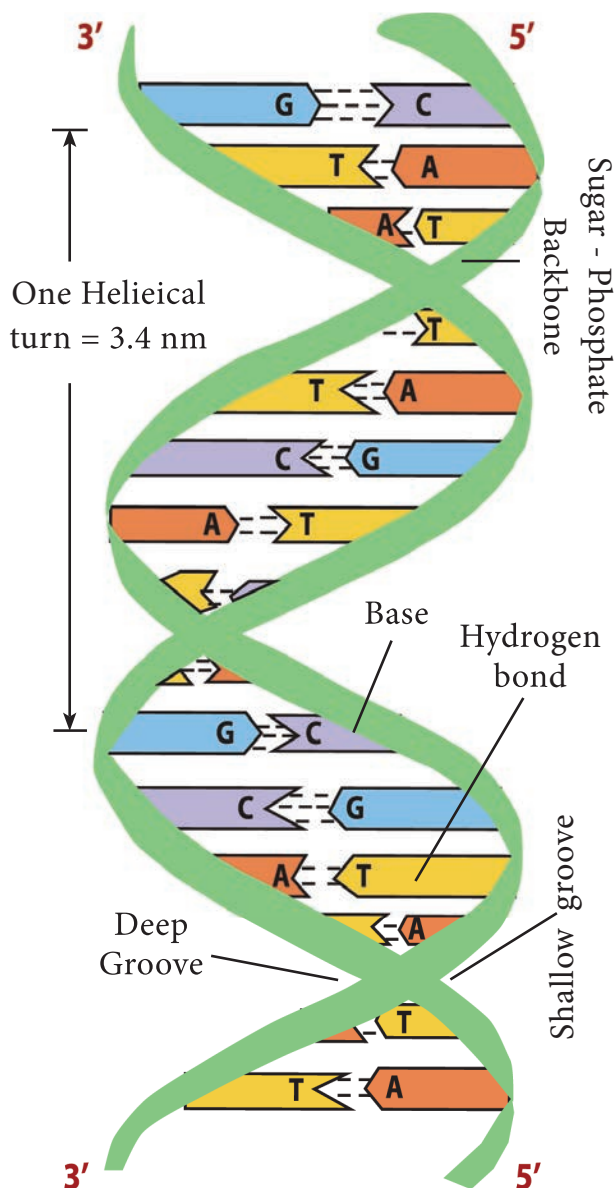
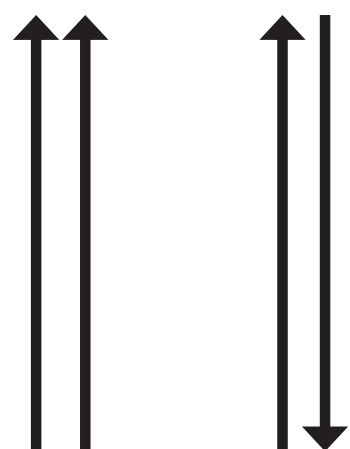


Figure. 7.6 Structure of DNA

1. There are two polynucleotide chains in the DNA spirally twisted around each other to form a right handed double helix.



Parallel      Anti-parallel

2. The sugar-phosphate backbones remain on the outside, while the core of the helix contains the purine and pyrimidine bases.
3. The diameter of DNA is 2 nm or 20 Å. The length of a complete turn of helix is 3.4 nm or 34 Å i.e. there are ~10.5bp per turn.
4. The DNA helix has a shallow groove called minor groove (-1.2nm) and a deep groove called major groove (-2.2nm). Proteins interact with DNA through the minor and major grooves without disrupting the DNA strands.

5. Each polynucleotide chain is made up of four different bases. The purine bases present in DNA are adenine and guanine and the pyrimidine bases present are thymine and cytosine. The sequence of purine and pyrimidine carry the genetic information whereas the sugar and phosphate groups perform the structural role.
6. Each polynucleotide chain has direction or polarity. Further, each polynucleotide chain has 5' phosphorylated and 3' hydroxyl ends.
7. The two strands run in opposite direction (i.e.) they are antiparallel.
8. The two strands are held together by hydrogen bonds (base pairing) between the purine and pyrimidine bases of the opposite strands.

Watson and Crick deduced the rules of base pairing (Fig. 7.7). They are:

- The purine adenine (A) always pairs with the pyrimidine thymine (T).
- The purine guanine (G) always pairs with the pyrimidine cytosine (C).

Base pairing is achieved through hydrogen bonding.

Therefore, if adenine appears in one strand, thymine is found in the opposite strand and vice versa. When guanine is found in one strand, cytosine is present in

the opposite strand and vice versa. So, Base sequence of one strand is complementary to the opposite strand. For example, If the sequence 5'ATGGACC3' is present in one strand, the complementary strand will be having the sequence, 3'TACCTGG5'.

There are two hydrogen bonds between A and T and three hydrogen bonds between G and C.

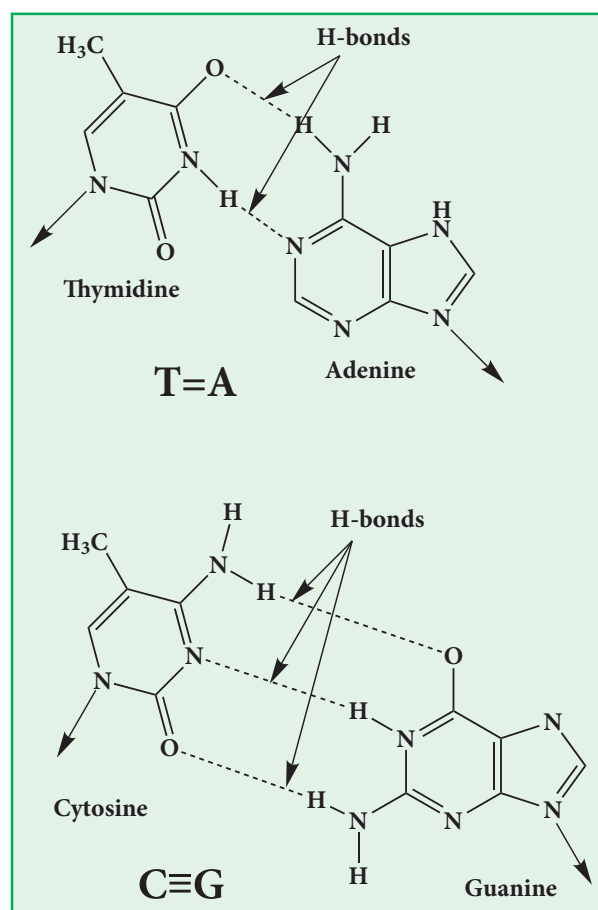


Figure. 7.7 Nucleotide base pairing

9. Base composition of DNA obeys Chargaff's rule.

### Chargaff's rule

Erwin Chargaff, a scientist

analyzed the chemical composition of DNA isolated from different species and found that irrespective of the source, the molar concentration of Adenine always equals Thymine and the molar concentration of Guanine always equals Cytosine.  $A=T$  and  $G=C$ . Therefore,  $A + T = G + C$  and the ratio of  $A+T / G+C = 1.0$ , which means that the total number of purine bases = the total number of pyrimidine bases.

## 7.6 Denaturation of DNA

At high temperatures ( $95^{\circ}\text{C}$ ), the double helical structure of DNA melts due to disruption of base pairing that results in two single strands. This is called as Denaturation of DNA. The temperature at which it does so is called as Melting temperature ( $T_m$ ). AT rich regions melt faster than GC rich regions. Therefore,  $T_m$  is dependent upon the composition of DNA. During denaturation, the absorption of DNA at 260nm increases. This property of DNA is called as hyperchromicity. If the temperature is brought down, the single strands rejoin to form double stranded regions. This is called as annealing or renaturing of DNA (Fig. 7.8). This property of DNA is exploited in Polymerase Chain Reaction.

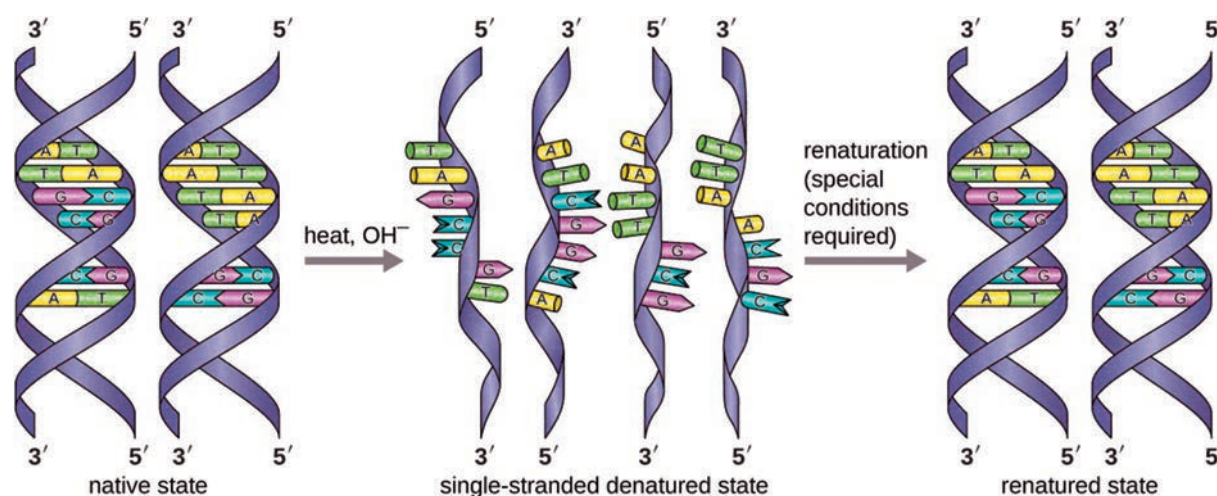


Figure. 7.8 Denaturation and renaturation of DNA

## 7.7 Griffith's experiment to identify the genetic material

Frederick Griffith conducted experiments in 1928 with *Streptococcus pneumoniae*, which was the milestone for discovery of DNA as the genetic material. There are two different strains of *Streptococcus pneumoniae*, one with smooth shiny colonies called the S strain, while the other with rough colonies (R). The difference is due to the presence of mucous coat in S strain bacteria, whereas the R strain bacteria lacked them. Because of the presence of the mucous coat, S strain is lethal, while R strain is not lethal.

Griffith injected both S and R strains to two different groups of mice separately. The group which was infected with the S strain developed pneumonia and died while that infected with the R strain stayed alive.

Next, Griffith heat-killed the S strain bacteria and injected into mice, but the mice stayed alive, which suggests that heat killed S- strain are avirulent (inefficient to cause the disease). Then, he mixed the heat-killed S and live R strains and injected into the mice. The mice died. In addition, he found living S strain bacteria in dead mice (Fig. 7.9). This suggests that some transforming principle is present in the S form that has mediated the transformation of R form to S form. Later, the experiments conducted by Avery, Macleod and McCarty in 1944 showed that the transforming principle is DNA, which carries the genetic information from one generation to another.

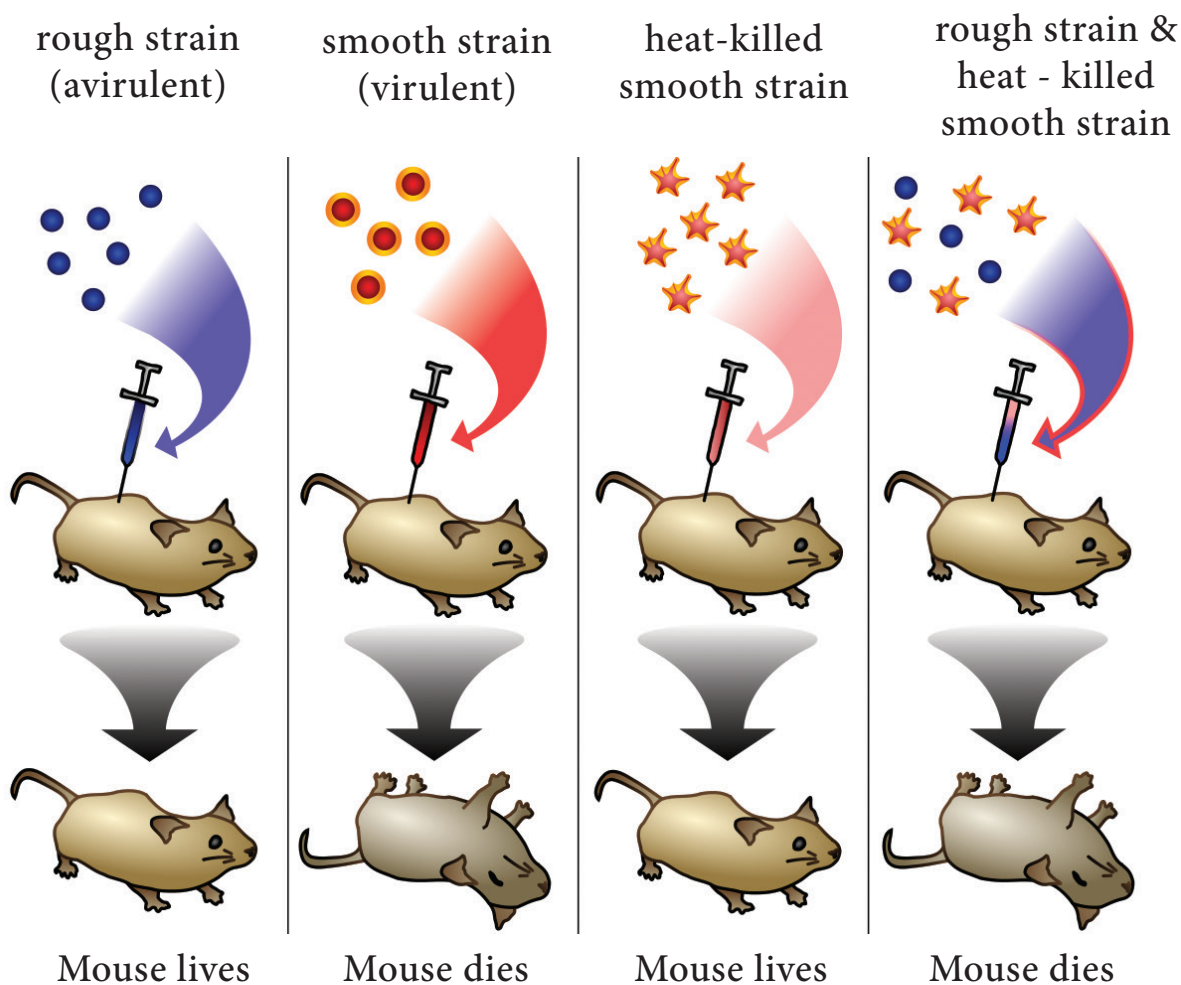


Figure. 7.9 Griffith's Experiment to identify genetic material

### Functions of DNA

1. DNA is the genetic material of all living organisms except for RNA viruses like HIV. It is the greatest super chip and enormous data can be stored in high density.
2. DNA inside the zygote contains all the information required for developing into an individual organism.
3. DNA inherited from their parents is responsible for the characteristic features of an individual, i.e. shape of the eyes, ears, nose, colour of the skin, height, longevity, ability





to withstand stress, certain congenital diseases like diabetes and hypertension.

4. DNA is the source of information for the synthesis of all cellular proteins. The segment of DNA that contains information for a protein is known as gene.

## 7.8 Ribonucleic acids (RNA)

RNAs, the second most abundant form of nucleic acids inside the cell are single-stranded and composed of nucleotides with ribose as their sugar. The major role of RNA is in protein synthesis as it aids in transfer of information from nucleus to cytosol, decoding, and synthesis of proteins. RNA nucleotides contain three components.

- Nitrogenous Base
- Ribose Sugar
- Phosphate Group

The nitrogenous bases include adenine (A), guanine (G), cytosine (C) and uracil (U).

Eventhough RNA is single-stranded, it has the ability to form three-dimensional structures like hairpin loops by base pairing within the strand. Adenine pairs with uracil ( $A=U$ ) and guanine pairs with cytosine ( $G\equiv C$ ). Chargaff's rule is not followed by RNA.

### 7.8.1 Types of RNA

There are three major types of RNAs in all prokaryotic and eukaryotic cells. They are (1). Messenger RNA (mRNA). (2). Transfer RNA (tRNA) (3). Ribosomal RNA (rRNA). They differ

from each other by size, shape, formation and stability.

#### i. Messenger RNA

They are named so because they carry the information from nucleus to cytosol. It accounts for 1-5% of cellular RNA. They do not have specific secondary structure like helices. They are single stranded linear molecules. They consist of 1000-10,000 nucleotides. They have a free or phosphorylated 3' and 5' end. They have different life span ranging from few minutes to days.

Prokaryotic mRNA is different from eukaryotic mRNA. Prokaryotic mRNAs are polycistronic, that is they code for many proteins. While eukaryotic mRNAs are monocistronic and contain exons (expressed sequences) and introns (intervening sequences). Eukaryotic mRNAs are capped at 5' end by methylated guanosine triphosphate. Capping protects mRNA from nuclease attack. At 3' end, a polymer of adenylate (polyA) is found as tail. Poly A tail protects mRNA from nuclease attack.

Intrastrand base pairing among complementary bases allows folding of the linear molecule. As a result, hairpin or loop like secondary structure is formed.

#### Functions

1. mRNA is a direct carrier of genetic information from the nucleus to cytoplasm.
2. It contains information required for the synthesis of protein molecules.

#### ii. Transfer RNA

It accounts for 10-15% of total cell RNA. Usually they consist of 50-100 nucleotides. They are single stranded

molecules. They contain unusual bases such as methylated adenine, thymine, dihydrouracil and pseudouridine. These unusual bases are unique to tRNA. Intra-chain base pairing is observed with many base pairs, while some bases are not involved in base pairing, resulting in loops and arms formation in tRNA. These foldings in the primary structure generate a clover-leaf secondary structure (Figure 7.10).

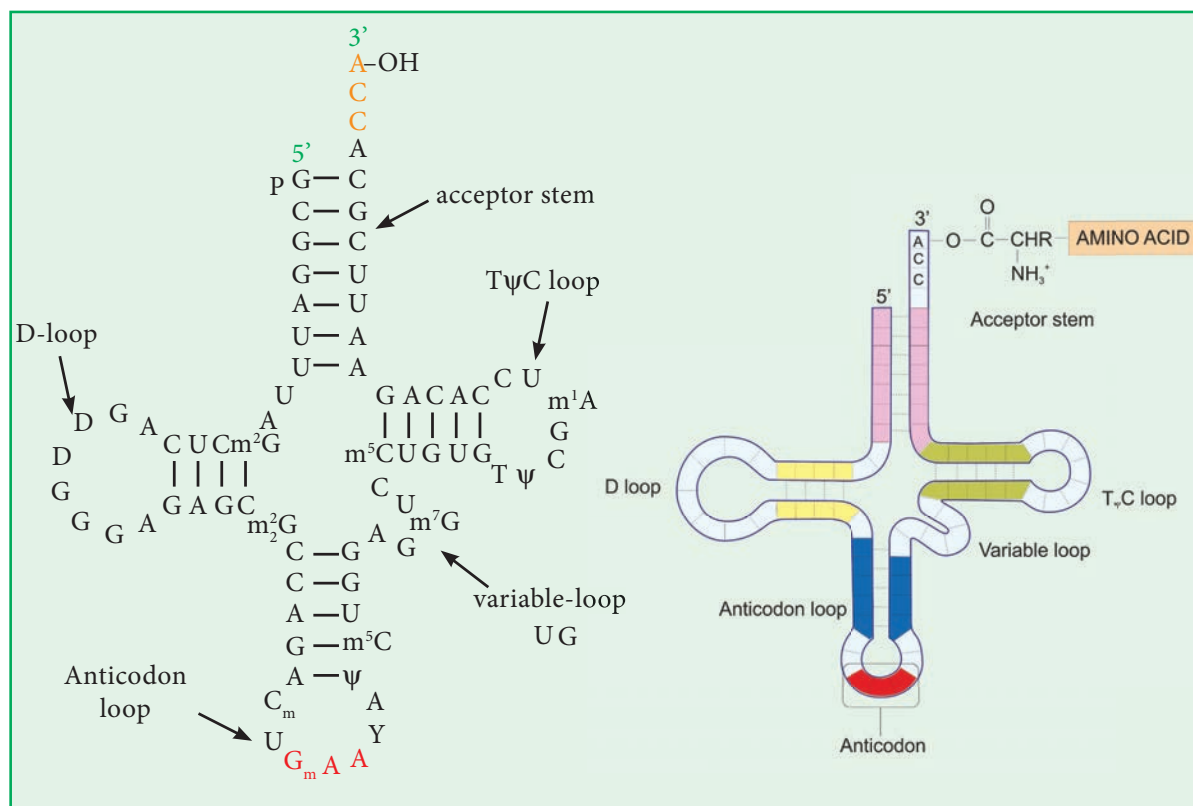


Figure 7.10 Structure of tRNA

The important features of the clover-leaf structure are,

1. An acceptor arm with base sequence “CCA” is present at the 3' end. The hydroxyl group of adenosine moiety of tRNA is responsible for getting amino acylated.
2. An anticodon arm which recognises codon on mRNA is present.
3. A TψC loop which contains an unusual base pseudouracil.
4. A D - arm which contains many dihydrouracil residues.

### Functions

1. It is the carrier of amino acids to the site of protein synthesis.
2. There is at least one t-RNA molecule to each of 20 amino acids required for protein synthesis.

### iii. Ribosomal RNA

Ribosomal RNA accounts for 80% of the total cellular RNA. It is present in ribosomes in combination with proteins. It is known as ribonucleoprotein. The length

of rRNA ranges from 100-600 nucleotides. rRNA molecules have a secondary structure. Intra-strand base pairing between complementary bases often generate double helical segments or loops.

### Functions

1. They are required for the formation of ribosomes.
2. They are involved in the initiation of protein synthesis.



Apart from these RNAs, there are also a heterogeneous group of RNAs present in the nucleus called as hnRNA and small non-coding RNAs of approximately 22 nucleotide length called as micro RNA or miRNAs.

## 7.9 Differences between DNA and RNA

S. No.	DNA	RNA
1	Sugar moiety is Deoxy ribose	Sugar moiety is Ribose
2	The bases present are Adenine, Thymine, Guanine and Cytosine. Uracil is not present.	The bases present are Adenine, Uracil, Guanine and Cytosine. Thymine is rarely present.
3	Double stranded molecules	Single stranded molecules
4	Obeys Chargaff's rule	Does not obey Chargaff's rule
5	Bases are not modified	Bases are modified
6	It is stable and not hydrolysed easily by alkalis	It is unstable and hydrolysed easily by alkalis
7	DNA content is constant in all the cells except during cell division	Varies from cell to cell
8	The life time of DNA is comparatively high.	RNA is short lived.
9	No natural DNA is catalytic	RNA can be catalytic
10	Present in the nucleus, mitochondria and chloroplast	Present in the nucleus, mitochondria, nucleolus, ribosomes and cytosol.



## EVALUATION



### I Choose the correct answer

1. The genetic material in higher organisms is
  - a. mRNA
  - b. rRNA
  - c. DNA
  - d. Protein
2. \_\_\_\_\_ ring is numbered in the clock wise direction.
  - a. Pyrimidine
  - b. Purine
  - c. Thiamine
  - d. All the above
3. Which nucleotide sequence has a high  $T_m$ ?
  - a. AAATTT
  - b. GGGCCC
  - c. AAGTTC
  - d. GGATTC
4. Purine and Pyrimidine bases absorb at \_\_\_\_\_ nm.
  - a. 260
  - b. 280
  - c. 300
  - d. 650
5. Which of the following contains base, sugar and phosphate in its structure?
  - a. Adenine
  - b. Adenosine
  - c. AMP
  - d. Deoxy adenosine
6. \_\_\_\_\_ acts as second messenger in hormonal signaling pathways.
  - a. AMP
  - b. ADP
  - c. cAMP
  - d. ATP
7. Which of the following form of DNA has 11 base pairs per turn?
  - a. A DNA
  - b. B DNA
  - c. C DNA
  - d. Z DNA
8. Which is the stable form of DNA?
  - a. A DNA
  - b. B DNA
  - c. C DNA
  - d. Z DNA





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## II Give short answers (Two marks)

1. Who discovered nucleic acid? When and how?
2. Write down the composition of nucleic acids.
3. Name the common bases present in nucleic acids.
4. What is a nucleotide? Give examples.
5. Write shortly on the sugars present in the nucleic acid.
6. Give the nucleosides and nucleotides of adenine.
7. What is a dinucleotide? Give examples.
8. Write about the directionality of nucleotides.
9. State Chargaff's rules.
10. Give the rules of base pairing.
11. What is the complementary strand for 5'GTAATTGC3'?
12. What are the major types of RNA?

## III Give short answers (Three marks)

1. What are bases? How are they classified? Give example for each group.
2. List the properties of pyrimidine bases.
3. Write short notes on purine bases.
4. What are Oligo nucleotides Give examples?
5. Enumerate the functions of nucleotides.
6. Outline the differences between A, B and Z DNA.
7. List down the functions of DNA.
8. Write about the characteristic features of mRNA.
9. What are ribosomal RNAs? Give an account on them.

## IV Answer the following questions in elaborate manner (Five marks)

1. List the Significance and functions of nucleic acid.
2. Detail on the bases, their types and properties.
3. Write an essay on the composition of nucleic acids.

4. Draw a neat labelled diagram and explain the salient features of Watson-Crick Structure of DNA.
5. Outline the experiment carried out by Griffith to identify the genetic material.
6. With a neat illustration, explain the structure of t-RNA.
7. Give the differences between DNA and RNA.

### Activity

The students may be asked to prepare a three dimensional structure of DNA or to prepare a chart explaining the structure of DNA.

## SUMMARY

Nucleic acids are the molecular repositories of genetic inheritance. Every macro molecules of the cell is the product of the information that has been stored in the nucleotide sequences of genes. Nucleic acids are long threadlike polymers made up of monomers called nucleotides held together by phospho diester bridges. Nucleotides have three components namely base, sugar and a phosphate group.

The bases are either monocyclic pyrimidines (cytosine, uracil and thymine) or the bicyclic purines (adenine and guanine). There are two types of sugars are present in nucleic acid. They are ribose and deoxyribose. When the sugar is ribose it is called ribonucleic acid (RNA) and if the sugar is deoxy ribose it is called Deoxyribonucleic acid (DNA). The phosphate groups are used to connect the nucleotides with each other. Depending upon the number of phosphate groups they can be classified as monophosphates, diphosphates and triphosphates.

DNA is the genetic material of all living organisms except RNA viruses like HIV. The B form DNA, also known as the Watson-crick DNA, is the most stable and prevalent form of DNA. The two antiparallel strands of DNA are complementary to each others. The diameter of DNA is 2nm and helical length is 3.4nm. It has ~10.5basepairs per turn of the helix. It has three different forms namely A-DNA, B-DNA and Z-DNA. There are three major types of RNA are known. They are messenger RNA (mRNA), transfer RNA (tRNA) and ribosomal RNA (rRNA).

They differ from each other by size, shape, formation and stability. The mRNA is a direct carrier of genetic information from nucleic acid to cytoplasm. tRNA is the carrier of amino acids to the site of protein synthesis. rRNA are required for the formation of ribosomes.



## CONCEPT MAP

