THE NUCLEIC ACIDS

Unit 1. Nucleic acids: Structure and Function

Nucleic Acids

- Polymers composed of monomer units known as **nucleotides**
- Information storage
  - DNA (deoxyribonucleic acid)
- Protein synthesis
  - RNA (ribonucleic acid)
- Energy transfers
  - ATP (adenosine tri-phosphate) and NAD (nicotinamide adenine dinucleotide)

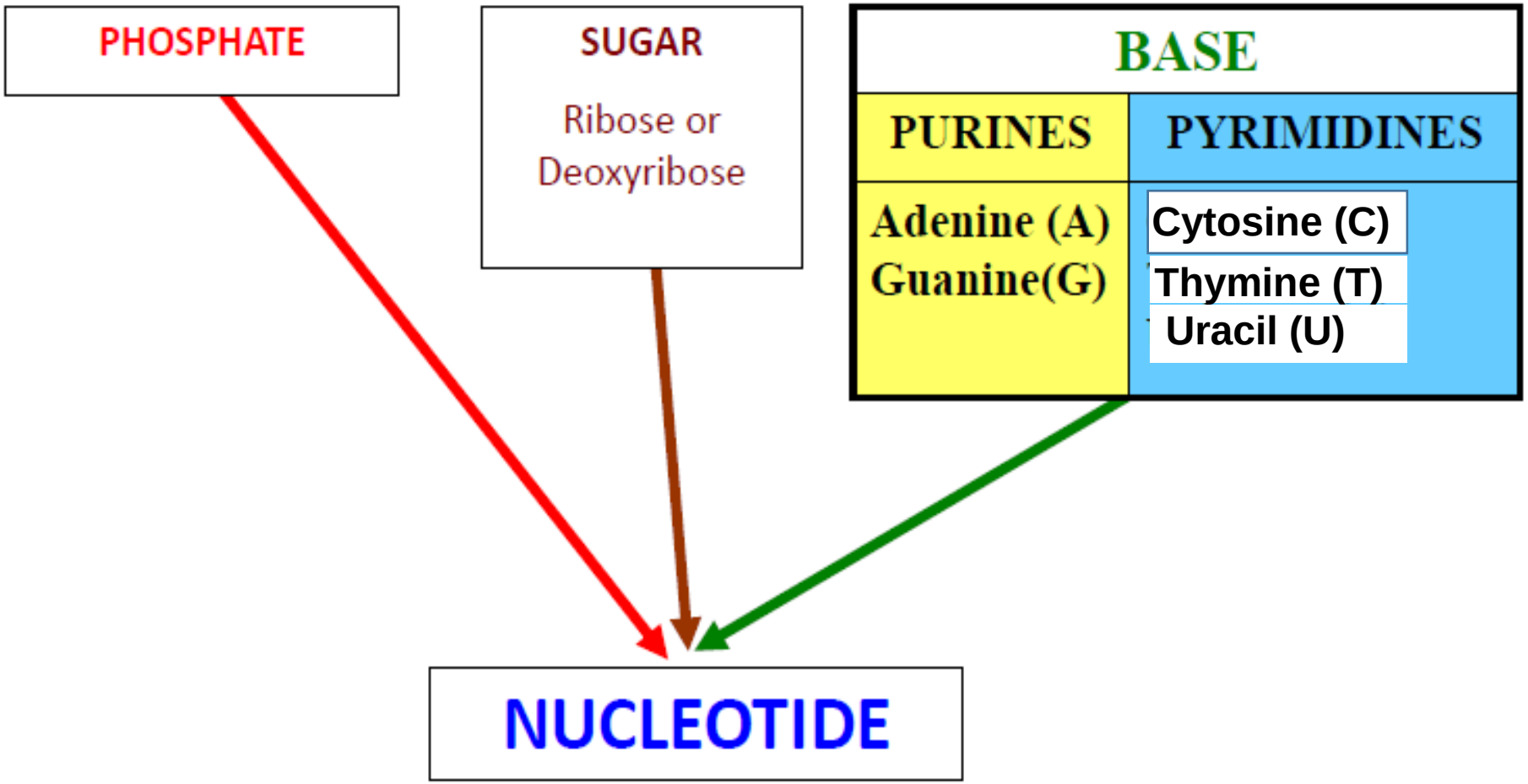
Biological Functions of Nucleic Acid

- DNA is the chemical basis of heredity and may be regarded as the reserve of genetic information.
- The proteins are synthesized by various RNA molecules in the cell but the message for the synthesis of a particular protein is present in DNA.
- DNA is exclusively responsible for maintaining the identity of different species of organisms over millions of years.

The Structure of Nucleic Acids

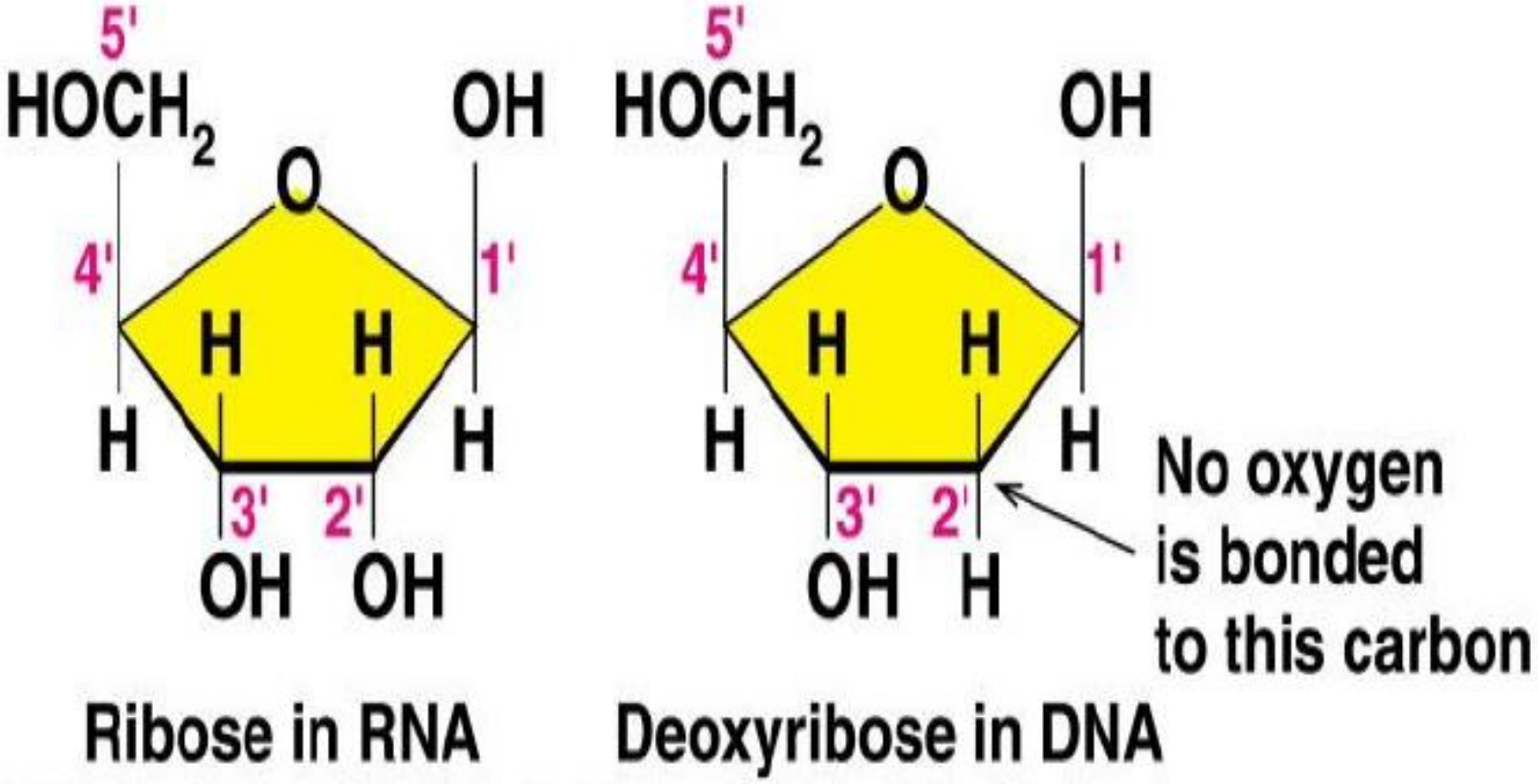
- Nucleic acids are polymers called **polynucleotides**
- Each polynucleotide is made of monomers called **nucleotides**
- Each nucleotide consists of a nitrogenous base, a pentose sugar, and a phosphate group

NUCLEOTIDE STRUCTURE



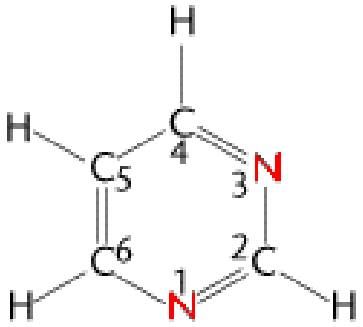
Sugar of nucleic acids

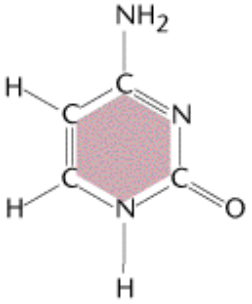
Pentose sugars in RNA and DNA

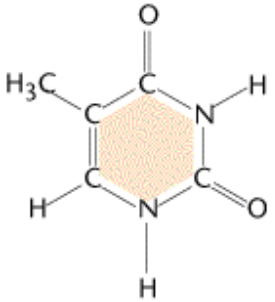


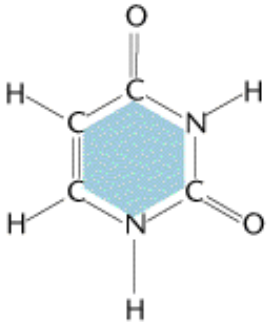
Nitrogenous bases in nucleic acids

Pyrimidine bases

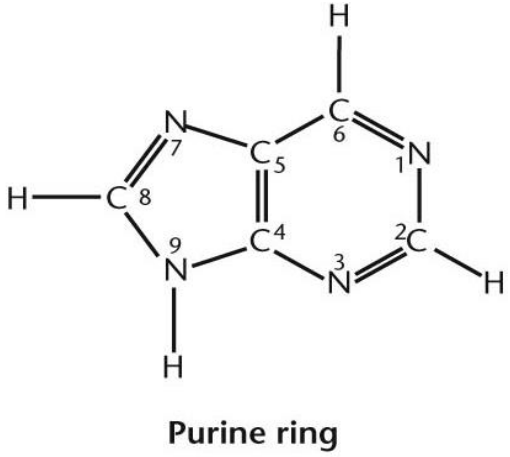


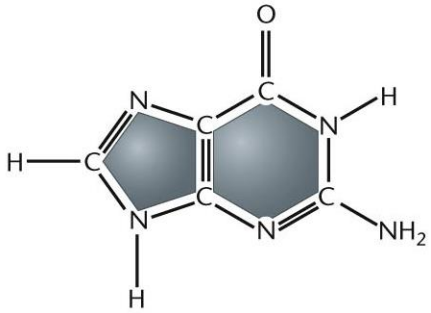


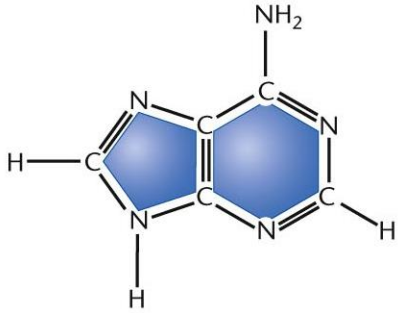




Purine bases

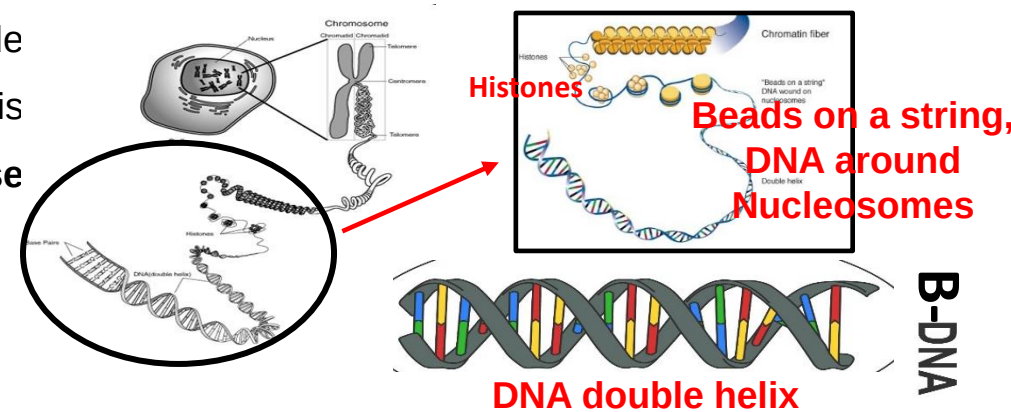


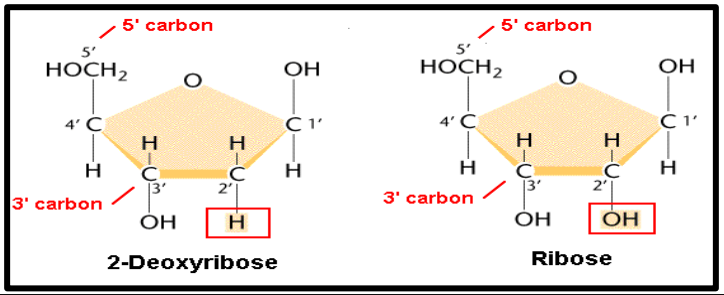


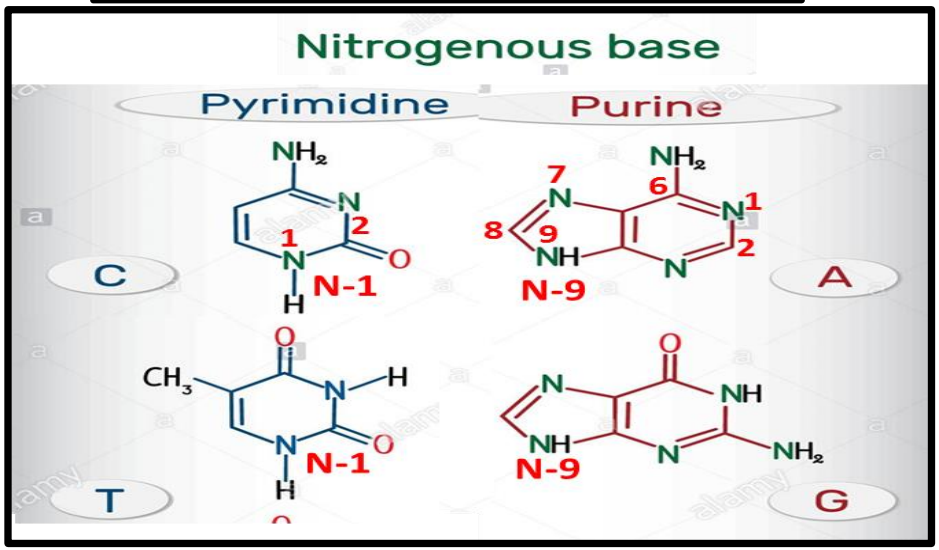


DNA (stores genetic information in the form of genes)

- ✓ **Deoxyribonucleic acid:** deoxyribonucleotide monomers; “Deoxy” because “**one oxygen**” is removed from the –**O**H of **carbon no. 2** of **ribose** sugar and making it deoxyribose.
- ✓ **Double helical (double helix)** with two poly deoxyribonucleotide chain / two polynucleotide chains.
- ✓ B-DNA; A-DNA; Z-DNA form present in cell at different cellular environment condition. ……B-DNA is a common form that exist at neutral pH and physiological salt concentration.
- ✓ Nitrogenous bases…….. Adenine (A) , Guanine (G) are purine form….9 membered ring); Cytosine (C) and Thymine (T) pyrimidine form….. 6 membered ring).
- ✓ Presence of phosphate group





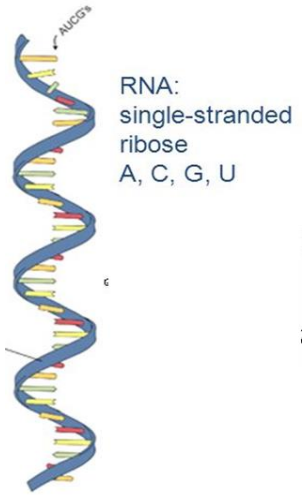


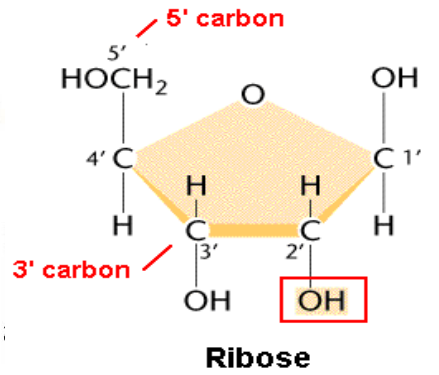
RNA (involved in protein synthesis process)

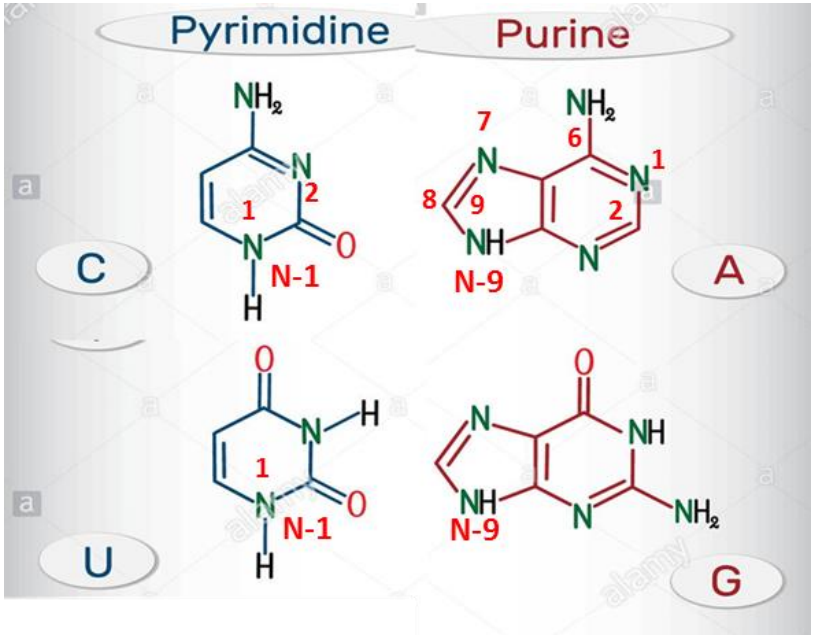
- ✓ **Ribonucleic acid**; ribonucleotide monomers; having **ribose** sugar
- ✓ **Non-helical and Single stranded** with one polyribonucleotide chain / or simply you can say, one polynucleotide chain.
- ✓ All three types of RNA are involved in protein synthesis process but assigned specific roles.

Ribosomal-RNA (rRNA); Transfer-RNA (tRNA); and Messenger RNA (mRNA) each assigned or involved in different role in protein synthesis process.

- ✓ **mRNA** carries **genetic code messages** from DNA, and **which is decoded to** protein information with the help of rRNA and tRNA.
- ✓ **Nitrogenous bases**…….. Adenine (A) , Guanine (G) are purine form….9 membered ring); Cytosine (C) and **Uracil (U)** pyrimidine form….. 6 membered ring)
- ✓ Presence of phosphate group

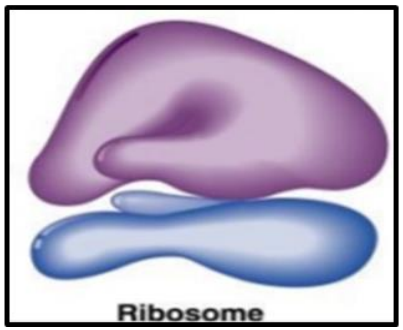






1. Ribosomal RNA: rRNA along with proteins forms the ribosomes which is the site of protein synthesis. Some of them have catalytic activity and coenzyme functions as well

1. Ribosomal RNA (rRNA)

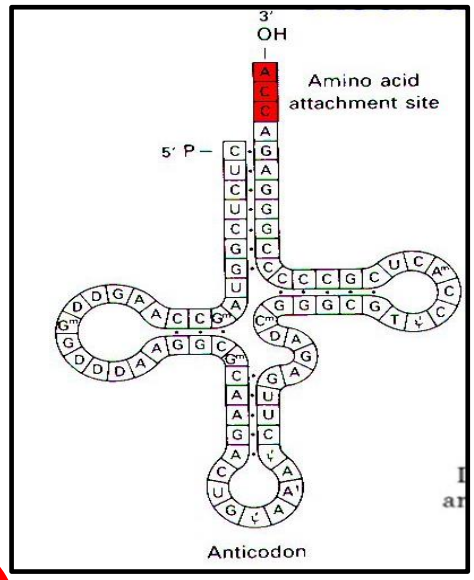


1. **Ribosomal RNA (rRNA):** **Major component of ribosomes where mRNA is translated to protein.**

75% of total RNA of the cell.

2. Transfer RNA (tRNA): tRNA transfers the amino acids from the cytoplasm to the site of protein synthesis.

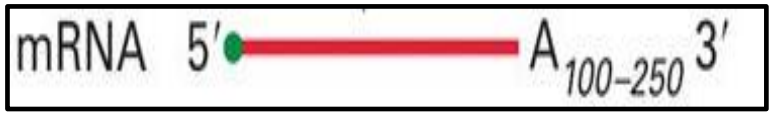
Transfer RNA (tRNA)



Transfer RNA (tRNA): carries amino acids in an activated form to the ribosome for peptide bond formation, in a sequence dictated by the mRNA template. There is at least one kind of tRNA for each of the 20 amino acids. tRNA is transcribed from different segments of DNA.

10-15% of the total RNA of the cell

3. Messenger RNA (mRNA): mRNA is a complementary copy of selected regions of the DNA. It carries the genetic message from the nucleus to the cytoplasm and acts as the template for protein synthesis.



- **Messenger RNA (mRNA): Transcribed from specific segment of DNA which represents a specific gene or genetic unit.**
- **5-10% of the total RNA of the cell**

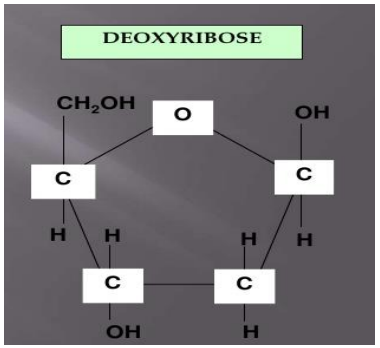
Structural composition of DNA and RNA

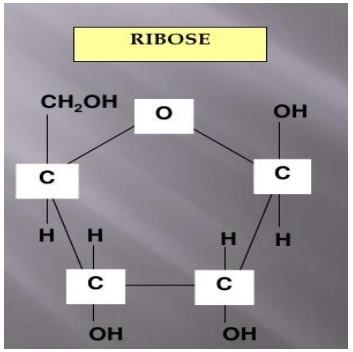
1. Phosphate group → **Phosphoric acid**

2. Sugar / monosaccharide →

DNA has **Deoxyribose**

RNA has **Ribose**



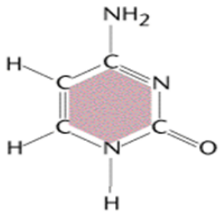


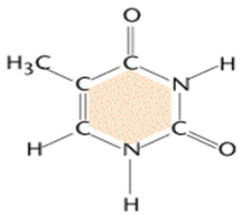
3. Nitrogenous bases (Pyrimidine and Purine bases) →

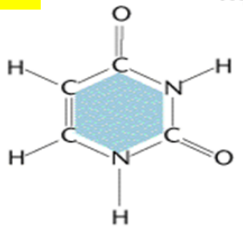
DNA has Adenine (A); Guanine (G); Cytosine (C); and **Thymine (T)**

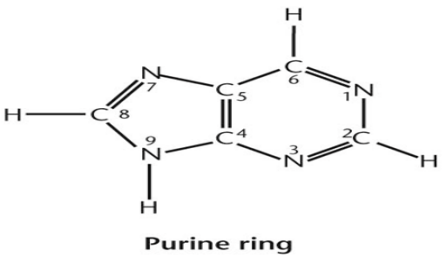
RNA has Adenine (A); Guanine (G); Cytosine (C); and **Uracil (T)**

Pyrimidine bases

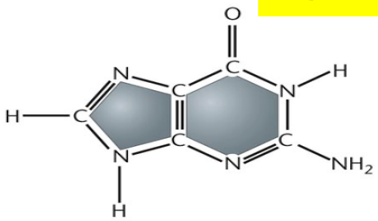


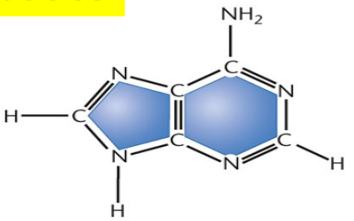




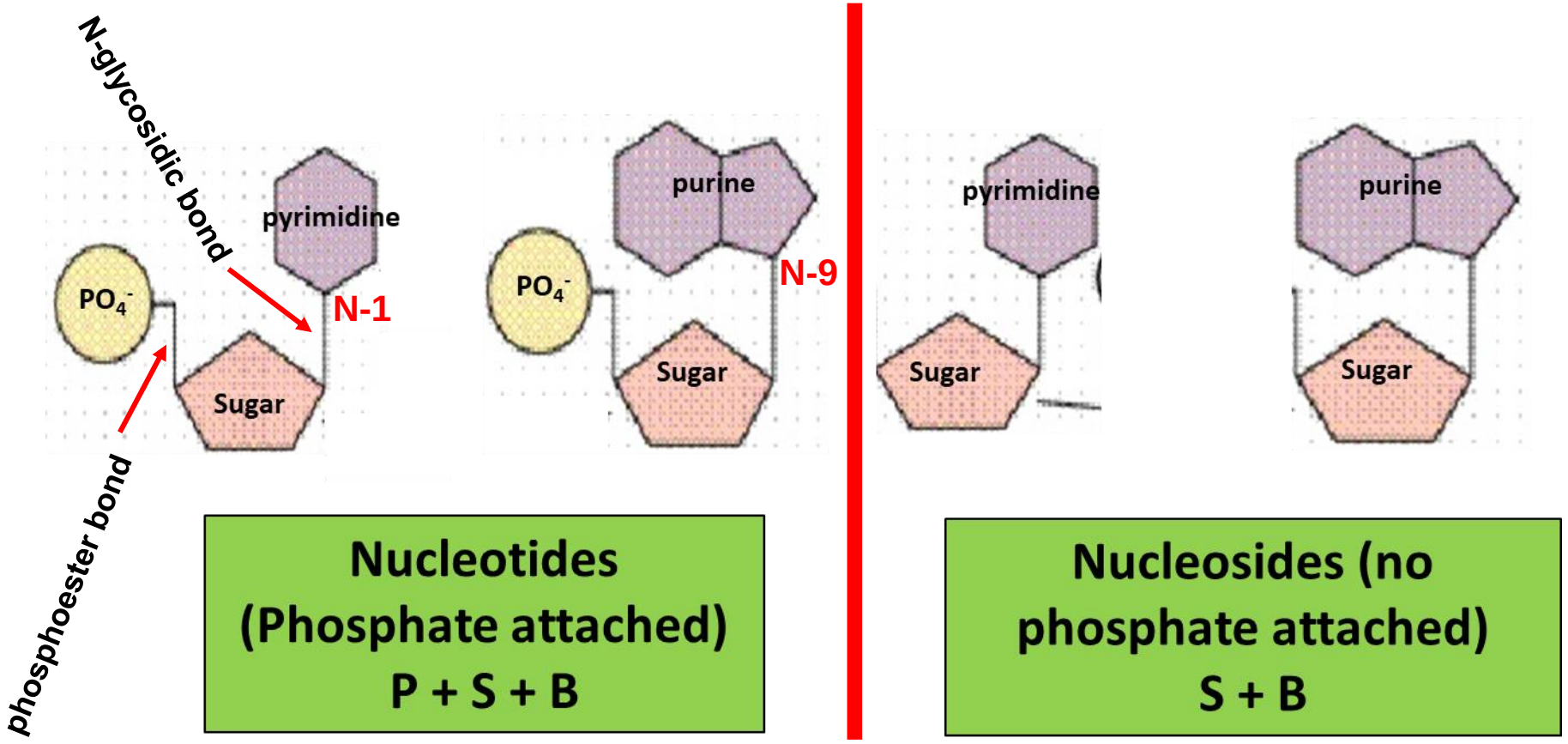


Purine bases

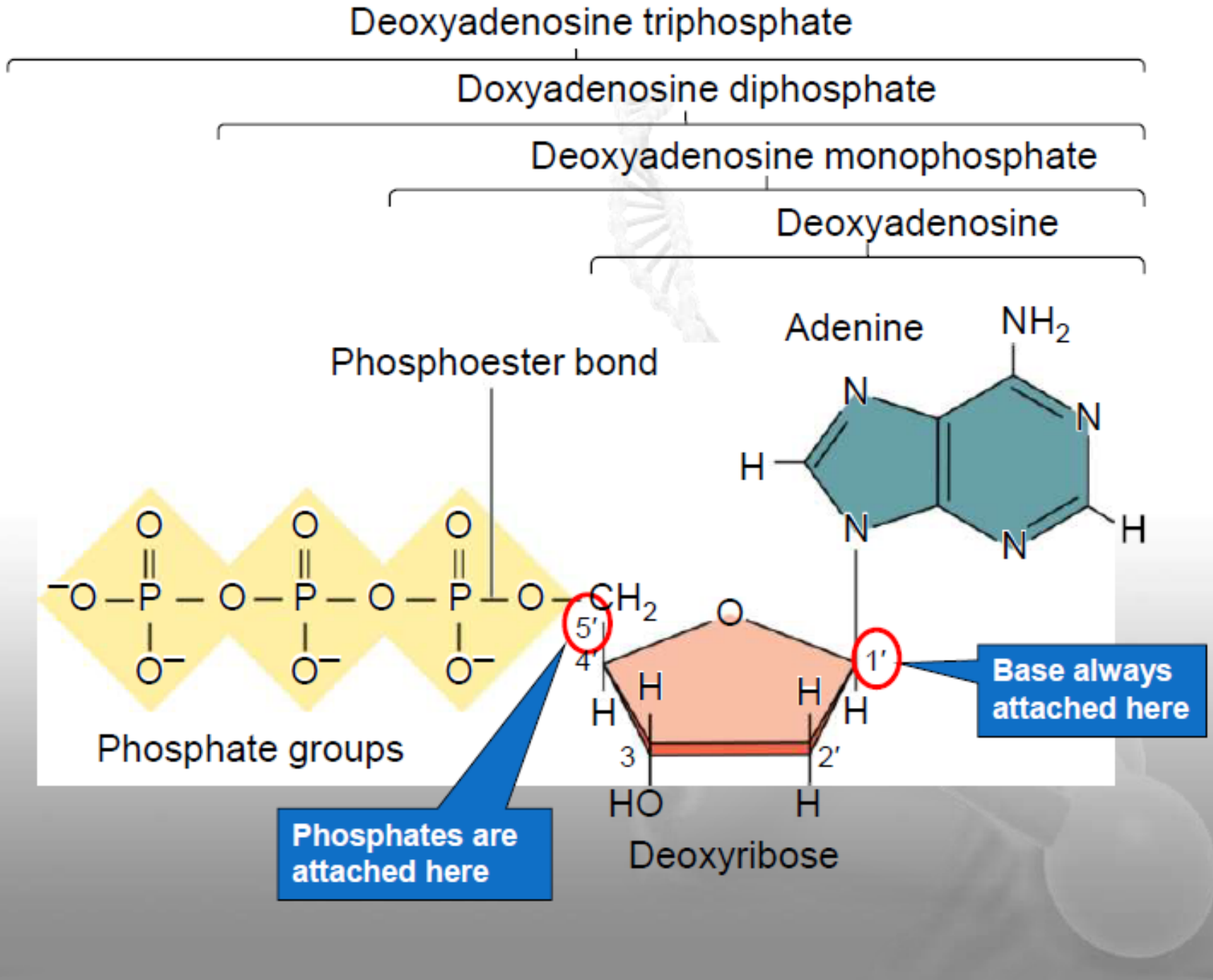




What is a nucleotide?

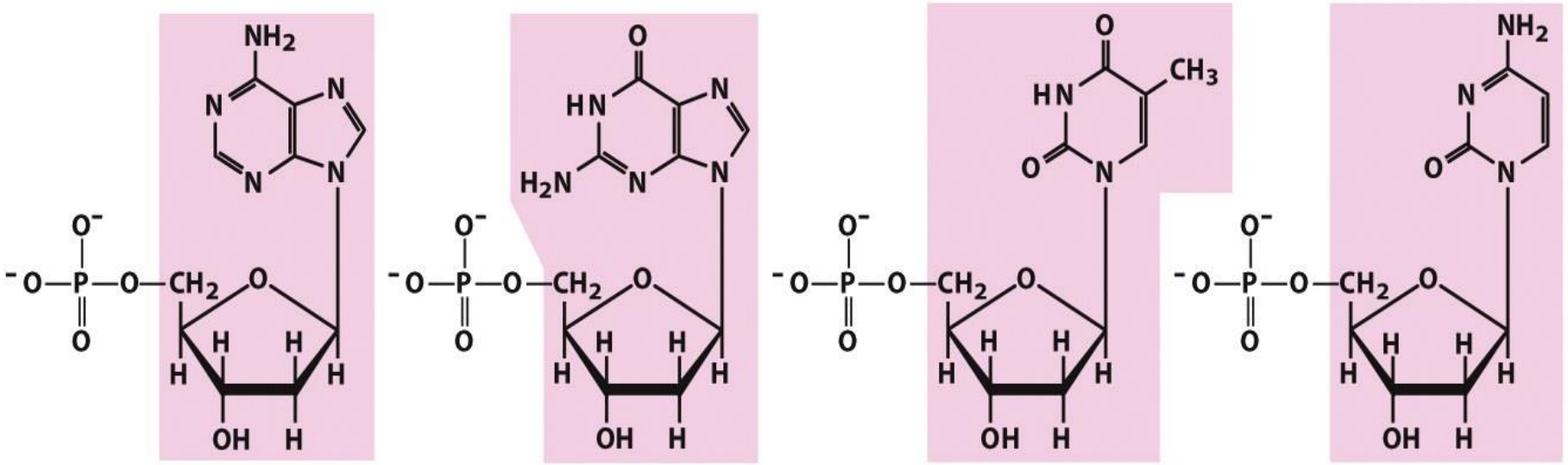


- Linkage between **sugar and base** is called **N-glycosidic bond**. In **Pyrimidine, N-1** is involved in bonding with sugar. **In purine, N-9** is involved in **bonding with sugar**.
- Linkage between **sugar and phosphate** is called **phosphoester bond**.


Deoxyadenosine triphosphate
Doxyadenosine diphosphate
Deoxyadenosine monophosphate
Deoxyadenosine
Adenine
NH2
Phosphoester bond
N
N
H
N
N
H
O
O
O
−O—P—O—P—O—P—O—CH2
O−
O−
O−
5′
4′
1′
H
H
H
H
O
3
2′
HO
H
Phosphate groups
Base always attached here
Phosphates are attached here
Deoxyribose

Nomenclature of nucleotides and nucleosides

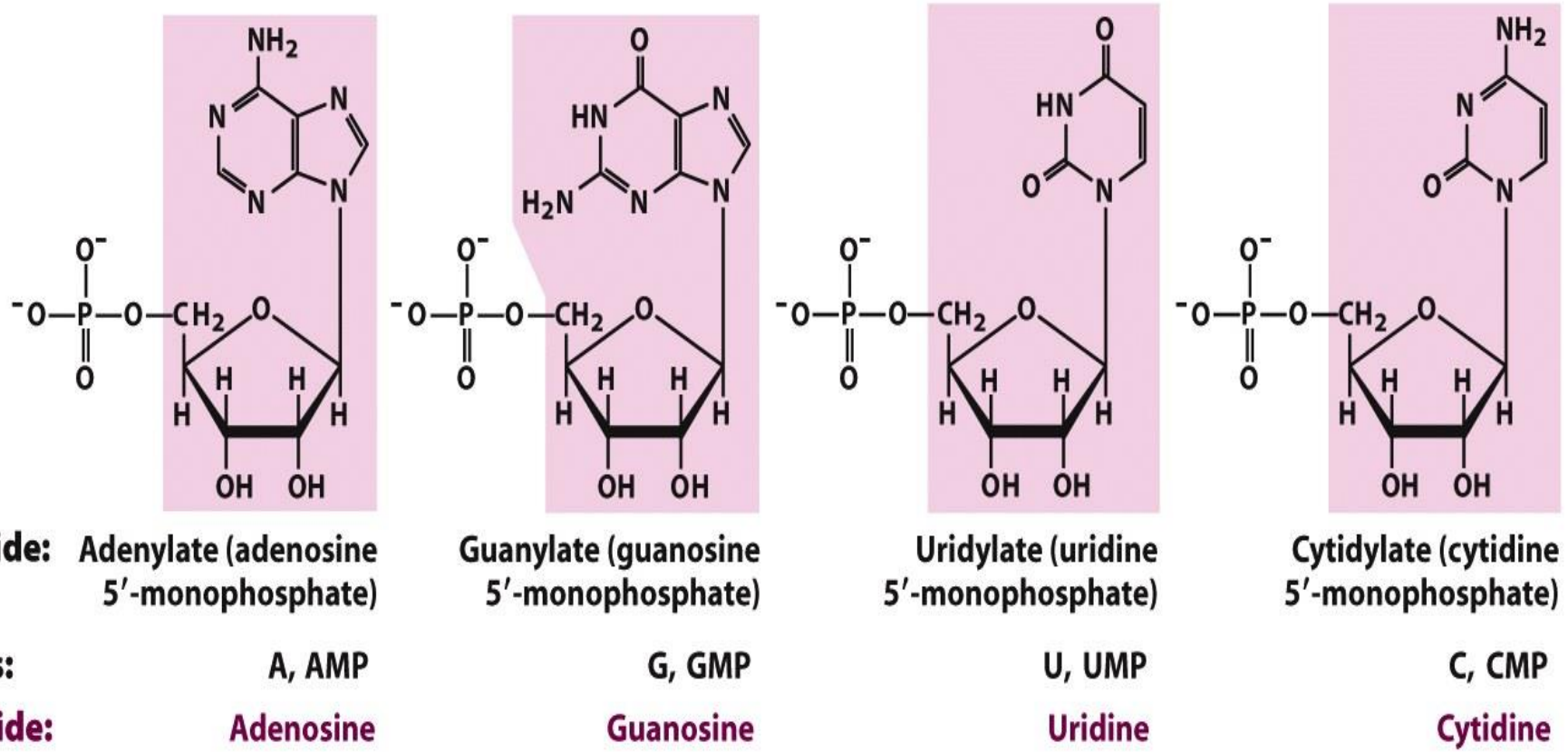
- **Deoxyribonucleotides- monomeric units of DNA**



Nucleotide:	Deoxyadenylate (deoxyadenosine 5′-monophosphate)	Deoxyguanylate (deoxyguanosine 5′-monophosphate)	Deoxythymidylate (deoxythymidine 5′-monophosphate)	Deoxycytidylate (deoxycytidine 5′-monophosphate)
Symbols:	A, dA, dAMP	G, dG, dGMP	T, dT, dTMP	C, dC, dCMP
Nucleoside:	Deoxyadenosine	Deoxyguanosine	Deoxythymidine	Deoxycytidine

Nomenclature of nucleotides and nucleosides

- **Ribonucleotides- monomeric units of RNA**



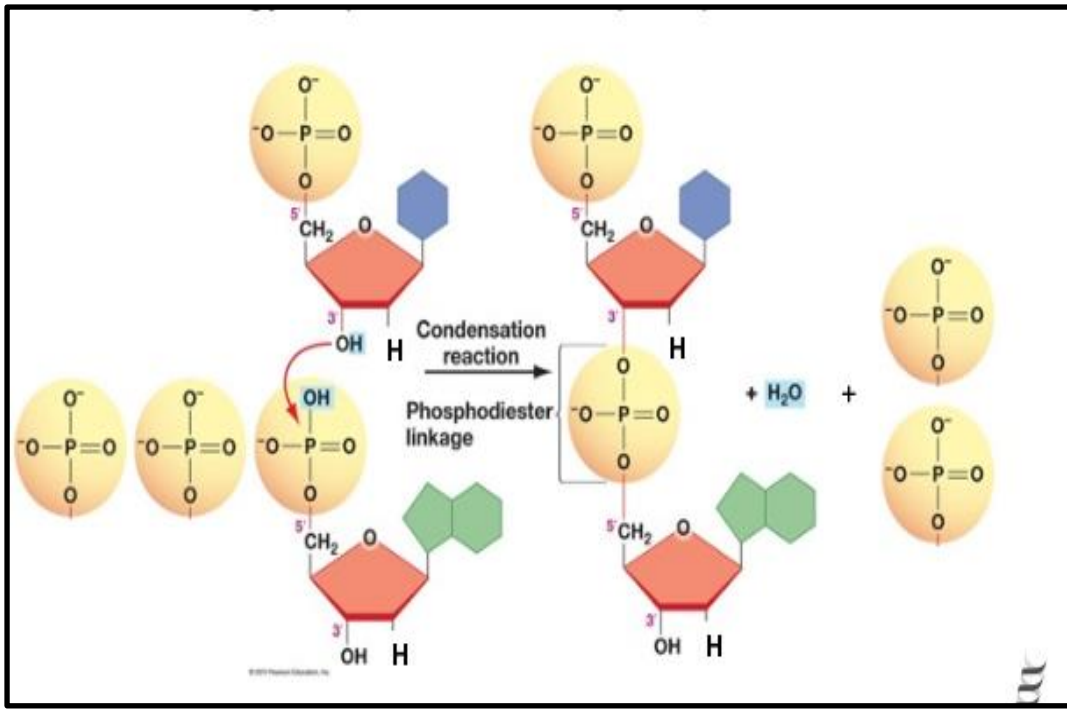
Base	Nucleosides	Nucleotides
RNA		
Adenine (A)	Adenosine (A)	Adenosine 5'-monophosphate (AMP)
Guanine (G)	Guanosine (G)	Guanosine 5'-monophosphate (GMP)
Cytosine (C)	Cytidine (C)	Cytidine 5'-monophosphate (CMP)
Uracil (U)	Uridine (U)	Uridine 5'-monophosphate (UMP)
DNA		
Adenine (A)	Deoxyadenosine (A)	Deoxyadenosine 5'-monophosphate (dAMP)
Guanine (G)	Deoxyguanosine (G)	Deoxyguanosine 5'-monophosphate (dGMP)
Cytosine (C)	Deoxycytidine (C)	Deoxycytidine 5'-monophosphate (dCMP)
Thymine (T)	Deoxythymidine (T)	Deoxythymidine 5'-monophosphate (dTMP)

How is one polynucleotide chain made?

3'-5' Phosphodiester linkage, formed by condensation reaction by removal of water molecule

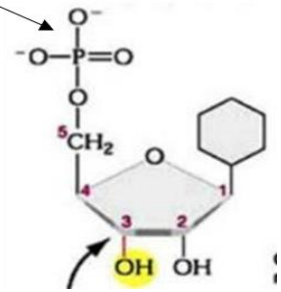
Enzyme that catalyze this condensation reaction is **DNA ligase**

Nucleotides are joined to each other in a polynucleotide chain through **3'-hydroxyl of deoxyribose or ribose of one nucleotide** and the **phosphate attached to the 5'-carbon of another nucleotide through C-O link. Two C-O links are present in phosphodiester bond**

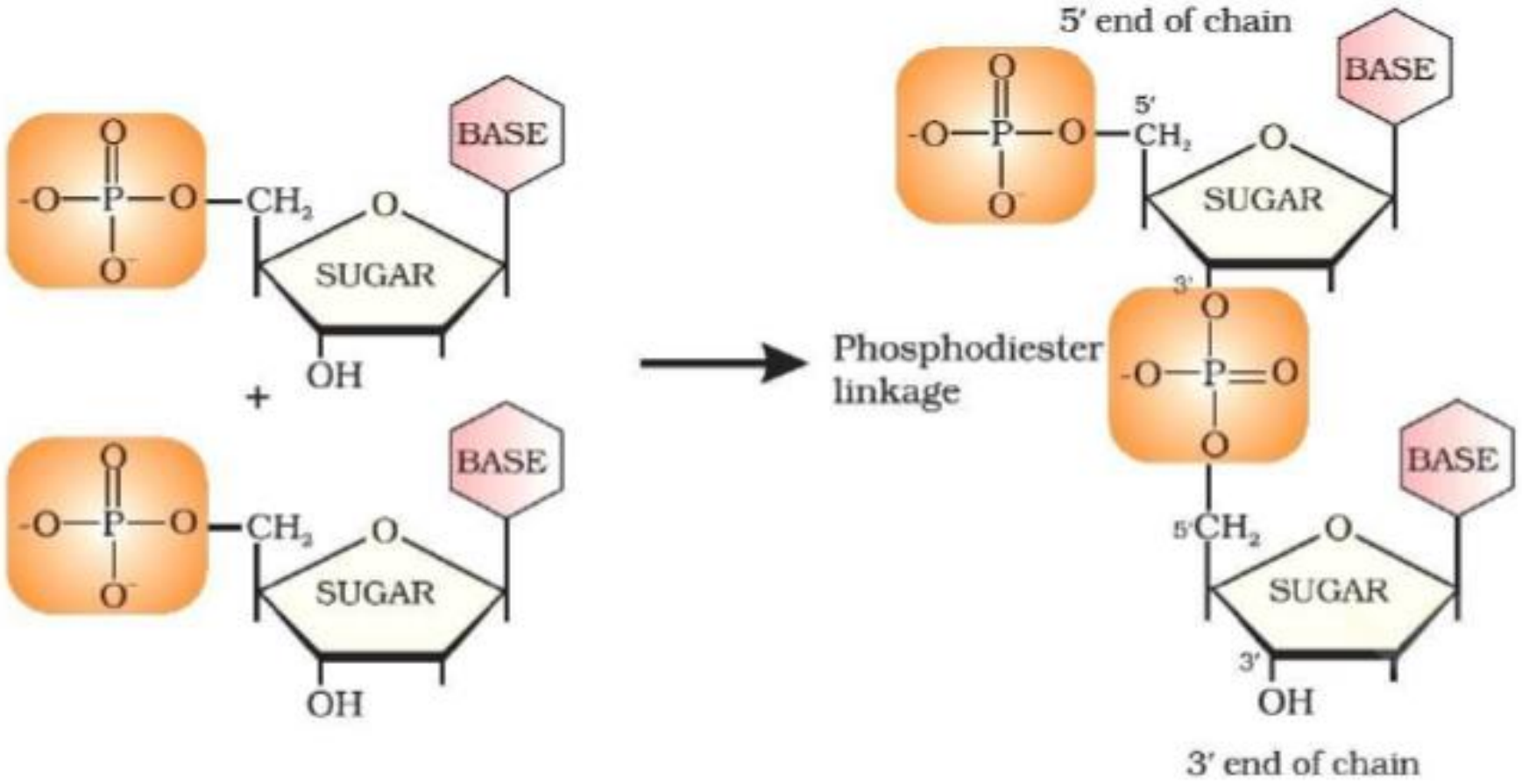


$5'\text{-}PO_4^{2-}$ ——— 3'-OH

Direction of polynucleotide synthesis is in **"5'-3' direction".**



- Nucleotides are joined together by phosphodiester linkage between 5′ and 3′ carbon atoms of the pentose sugar.

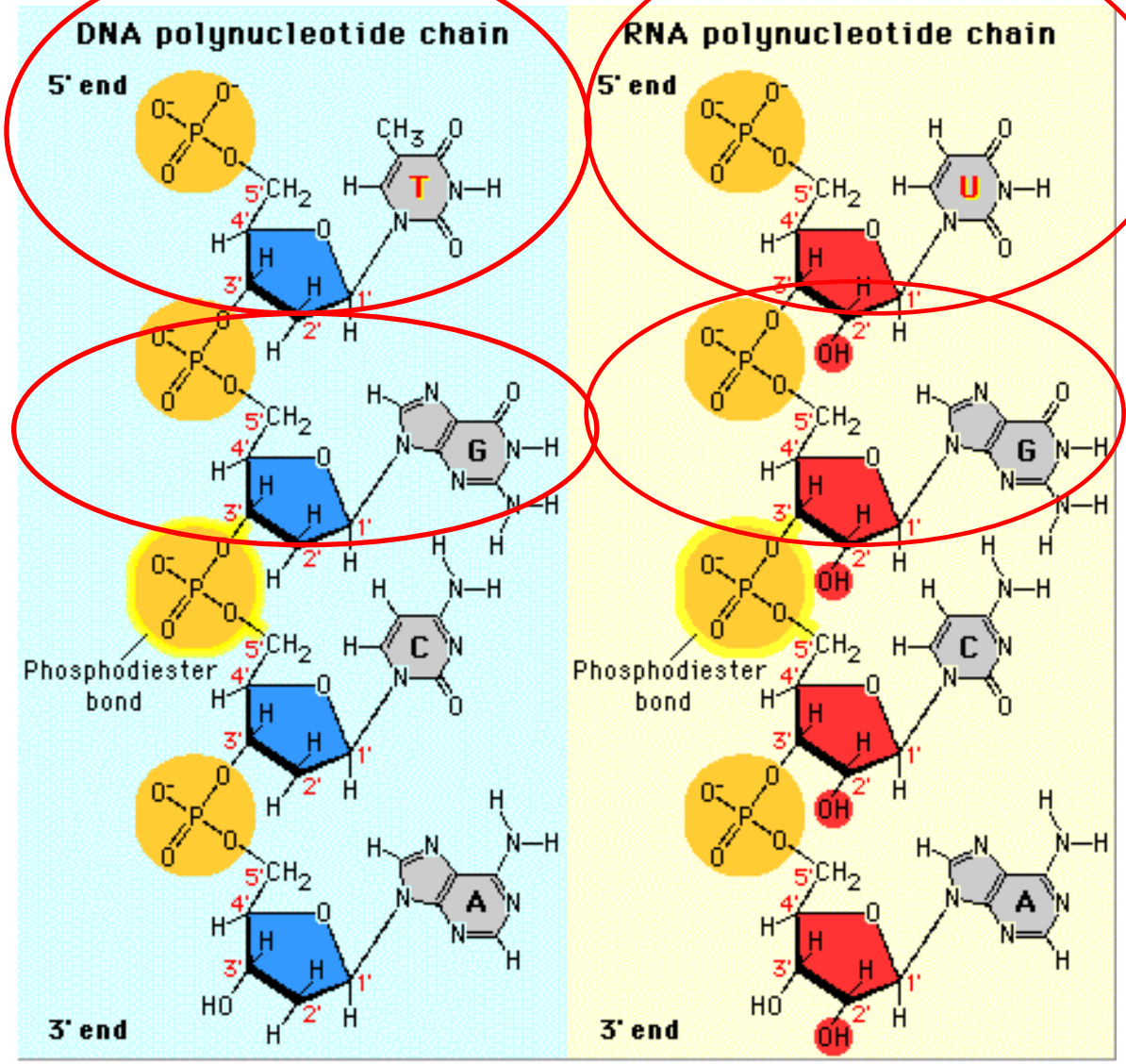


Primary Structure of Nucleic Acids

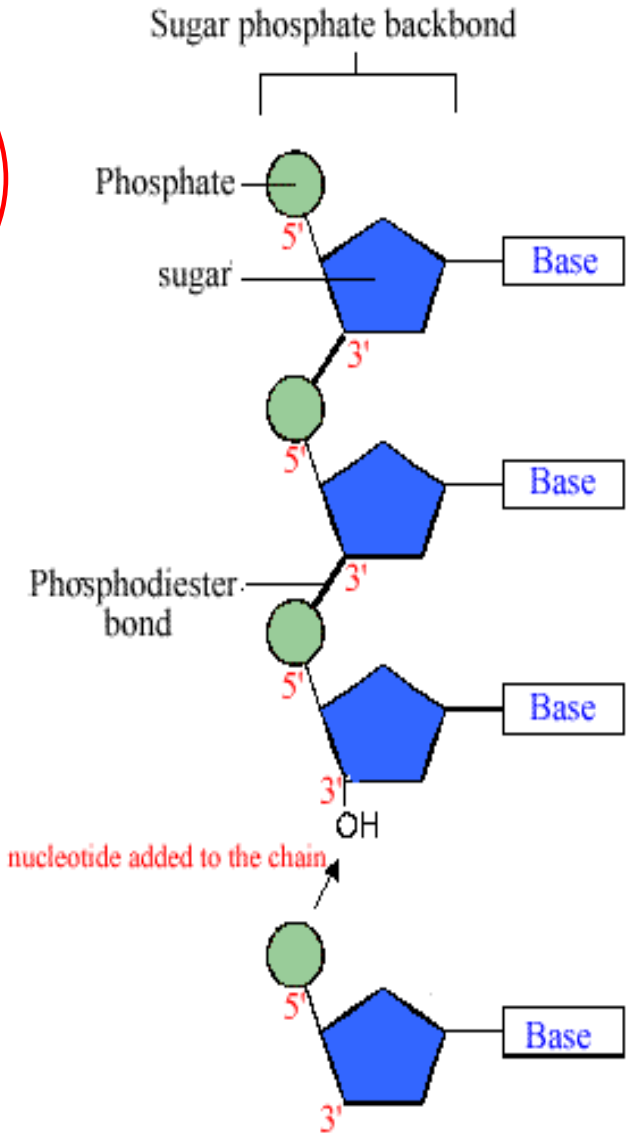
Structure of polynucleotide chain

DNA

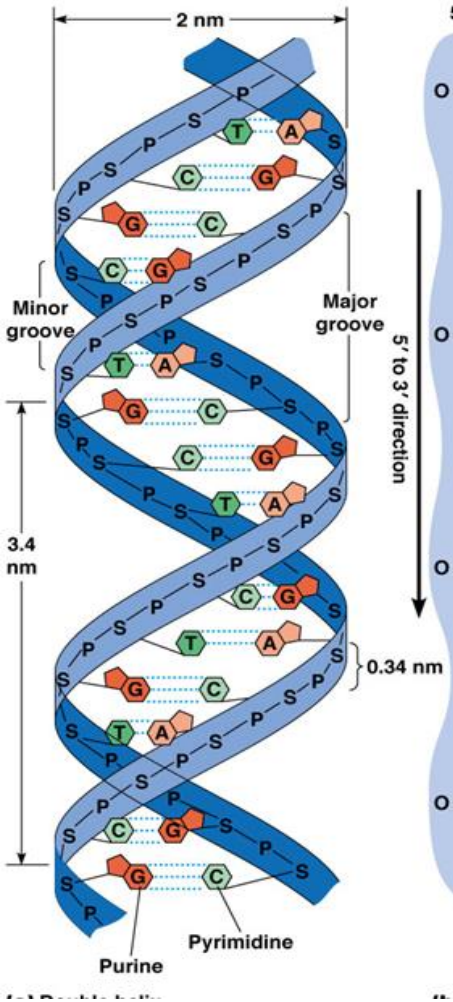
RNA



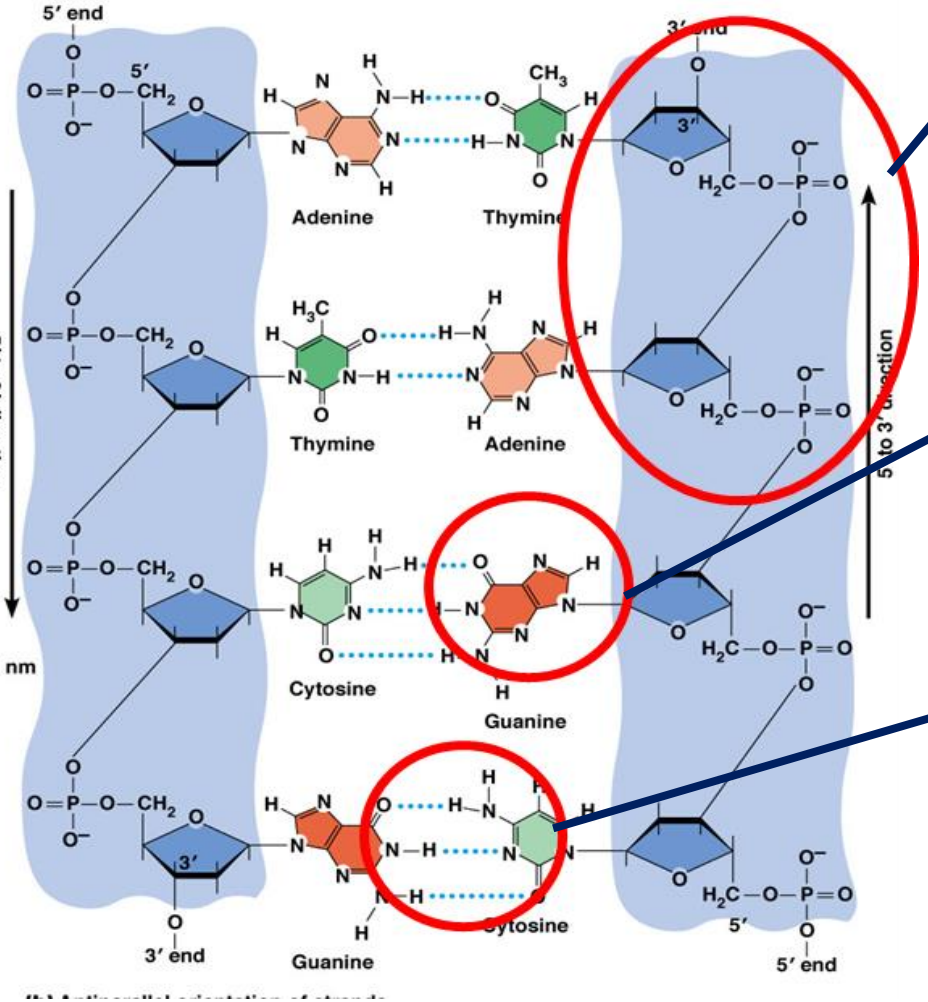
Polynucleotide chain skeleton structure:



Watson and Crick model of B-DNA : DNA is made up of two strands of polynucleotides



A) DNA double helix



B) Antiparallel orientation ……. 5’-3’ direction and 3’-5’ direction ……of polynucleotide chains held together by hydrogen bonds between bases

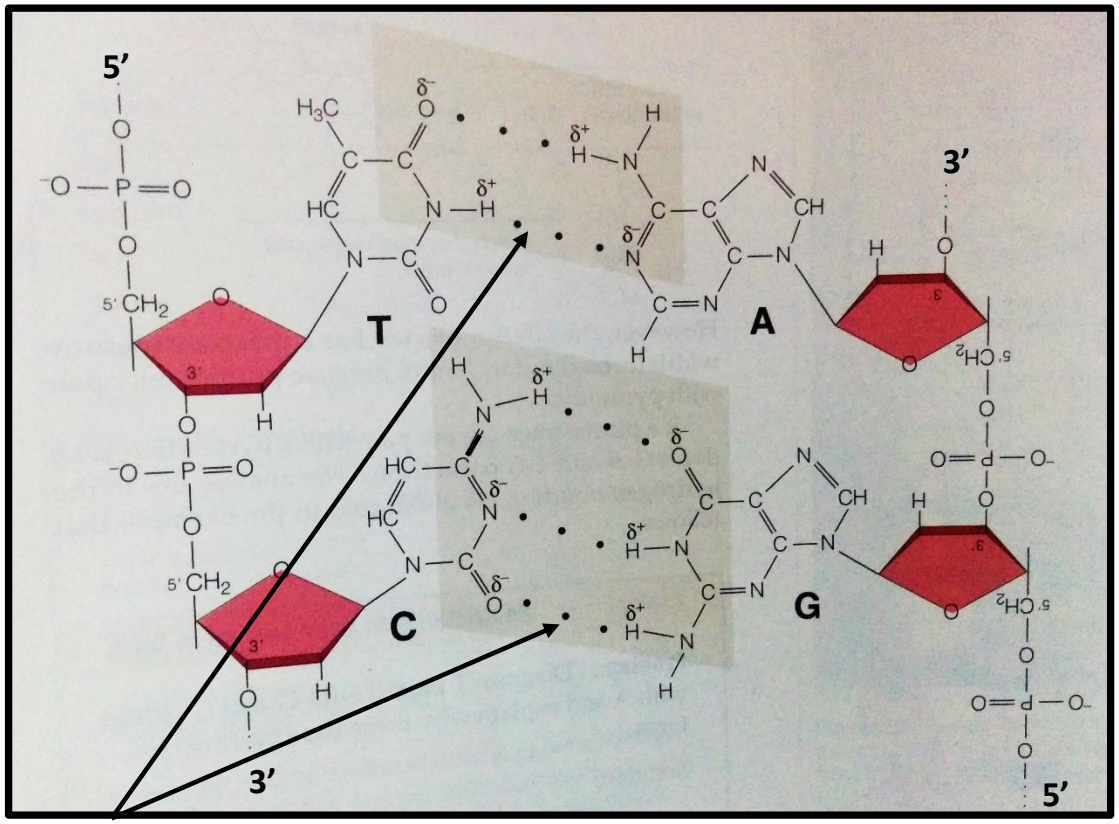
- **Phosphate**
- **deoxyribose** (in blue shade) forms the backbone of the DNA double helix.

- **Nitrogenous bases** (Guanine, Adenine, Thymine, Cytosine) face towards inside of the double helix.

- Two polynucleotide strands are stabilized by hydrogen bonds (blue dashed line) between the bases. **Adenine pairs with thymine with two H-bonds, and Guanine pairs with cytosine with three H-bonds**

How two polynucleotide chains are held together in DNA to form double helix.

- **Through Hydrogen bonds** between the bases held together the two polynucleotide chains.
- Specific base pair: **purine-pyrimidine** base pair or a **pyrimidine-purine base pair**.
- **Thymine** pair with **Adenine** with two Hydrogen bonds (T=A).
- **Cytosine pair with Guanine** with three hydrogen bonds.



Hydrogen bonds

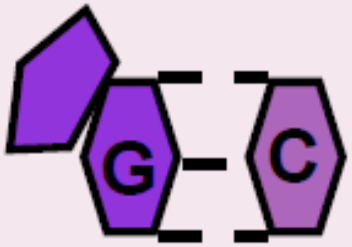
Complementary base pairing Rule

Adenine always base pairs with Thymine (or Uracil if RNA) -----

Double bond

Cytosine always base pairs with Guanine---------- triple bond

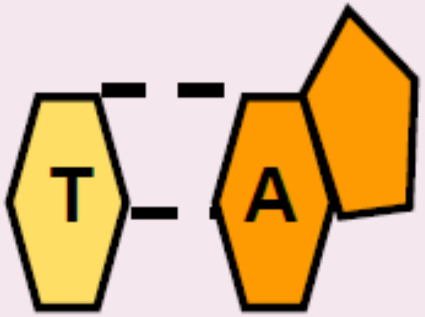
Purines **Pyramidines**



Adenine ◆——————→ Thymine

Adenine ◆——————→ Uracil

Guanine ◆——————→ Cytosine



DNA IS MADE OF TWO STRANDS OF POLYNUCLEOTIDE

- The sister strands of the DNA molecule run in opposite directions (**antiparallel**)
- They are joined by the bases
- Each base is paired with a specific partner:

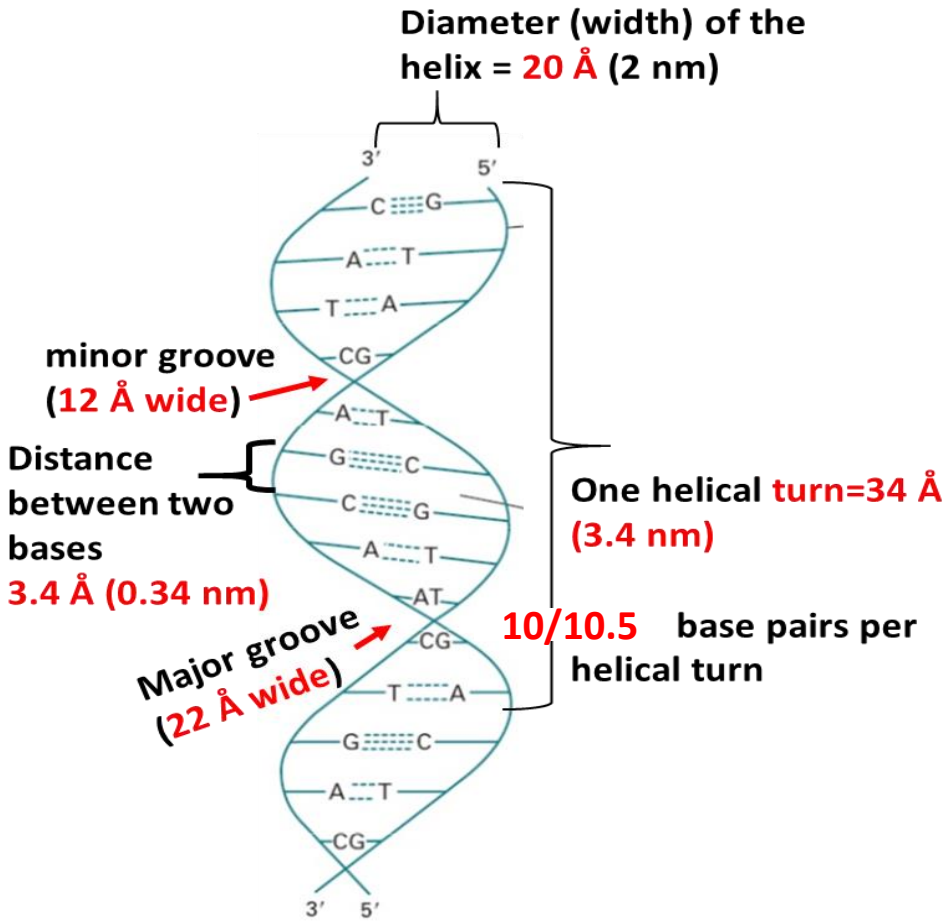
A is always paired with **T**

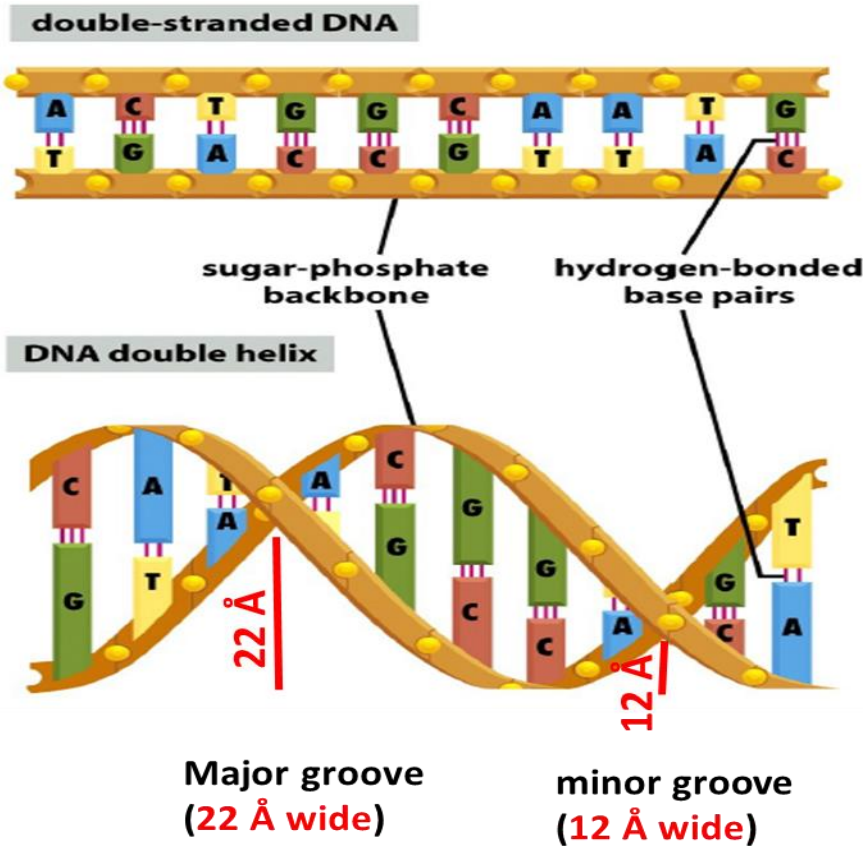
G is always paired with **C**

Purine with Pyrimidine

- Thus the sister strands are **complementary** but **not** identical
- The bases are joined by **hydrogen bonds**, individually weak but collectively strong.

Watson and Crick B-DNA structural measurements





- The two strands are antiparallel, i.e., one strand runs in the 5 ' to 3 ' direction while the other runs in 3' to 5 ' direction.
- The DNA helix, the hydrophilic deoxyribose-phosphate backbone of each chain is on the outside of the molecule, whereas the hydrophobic bases are stacked inside.

Different types of DNA and their structural measurements

- Under different conditions such as relative humidity and salt concentration, alternative forms of DNA has been detected.
- Found only under specific conditions not normally present in cells.
- Differ from each other primarily in the degree and direction of helical winding & in the stacking of the bases.
- **B-DNA** is the most common form of DNA that exist in normal cells.

Feature	B-DNA	A-DNA	Z-DNA
Type of helix	Right-handed	Right-handed	Left-handed
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Topology of major groove	Wide, deep	Narrow, deep	Flat
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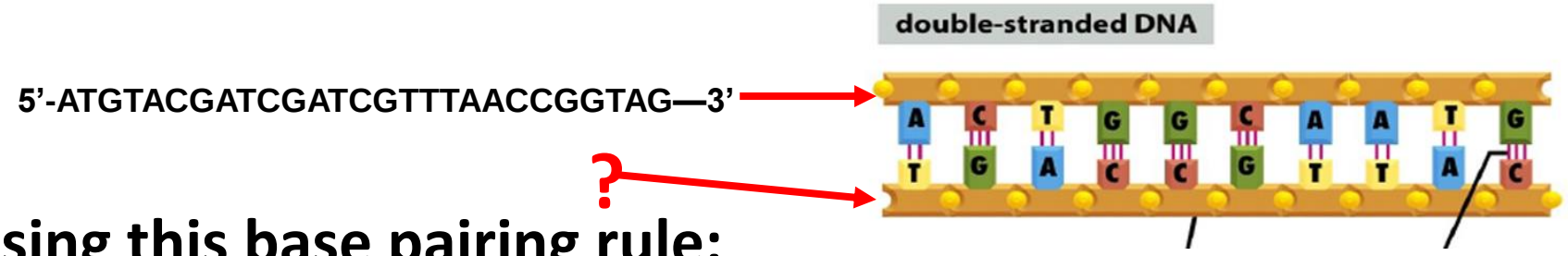
Concept of complementary nucleotide sequences

One of the DNA strand has a sequence

5’-ATGTACGATCGATCGTTTAACCGGTAG—3’. What is its complementary sequence?



Using this base pairing rule:

A pairs with T …….or T pairs with A

C pairs with G ……or C pairs with G

That is, In DNA, if we know the sequence of one DNA strand , the sequence in other DNA strand can be known on the basis of base pairing rule. The sequence on the other strand is called as complementary sequence.

Chargaff's base pairing rules

Chargaff's rules state that DNA from any cell of any organism should have a 1:1 stoichiometric ratio (base pair rule) of pyrimidine and purine bases and more specifically, **the amount of guanine should be equal to cytosine and the amount of adenine should be equal to thymine.**

- **Adenine (A) pairs with Thymine (T)**
- **Guanine (G) pairs with Cytosine (C)**

1) There is equal amount of **Guanine and Cytosine** or **Thymine and Adenine** in DNA double helix. (**A+G/T+C= constant**)

Example ….. a) If there are total 100 G's, then there will be also 100 C's

b) In percentage values; **% of A= % of T or;**

% of G= % of C

2) If Total **GC** in DNA **= X %,** then **% G = X/2** and **% of C=X/2** or AT content = Y%, then **% A = Y/2 and % T = Y/2.**

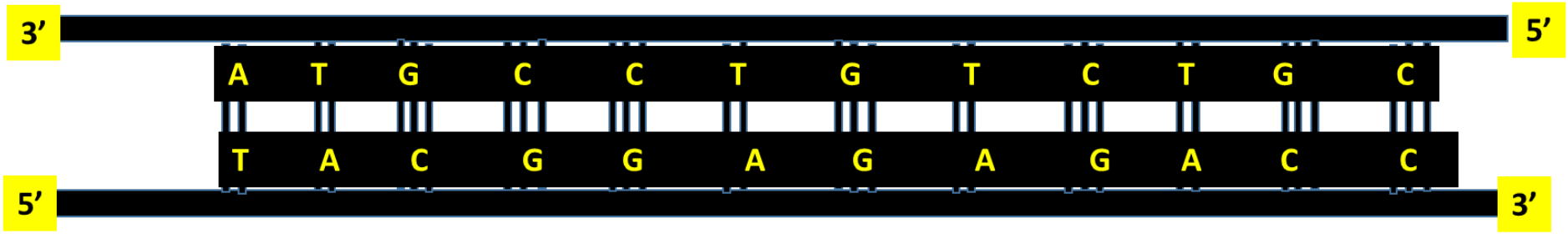
3) But **A+T** is not equal to **G+C**; or

A+T : G+C ratio differs from organism to organism

RNA

❖ **RNA is single stranded and does not obey Chargaff's base pairing rule.**

Have a look of DNA molecule below and answer few question before understanding Chargaff's rules



If A pairs with T and G pairs with C;

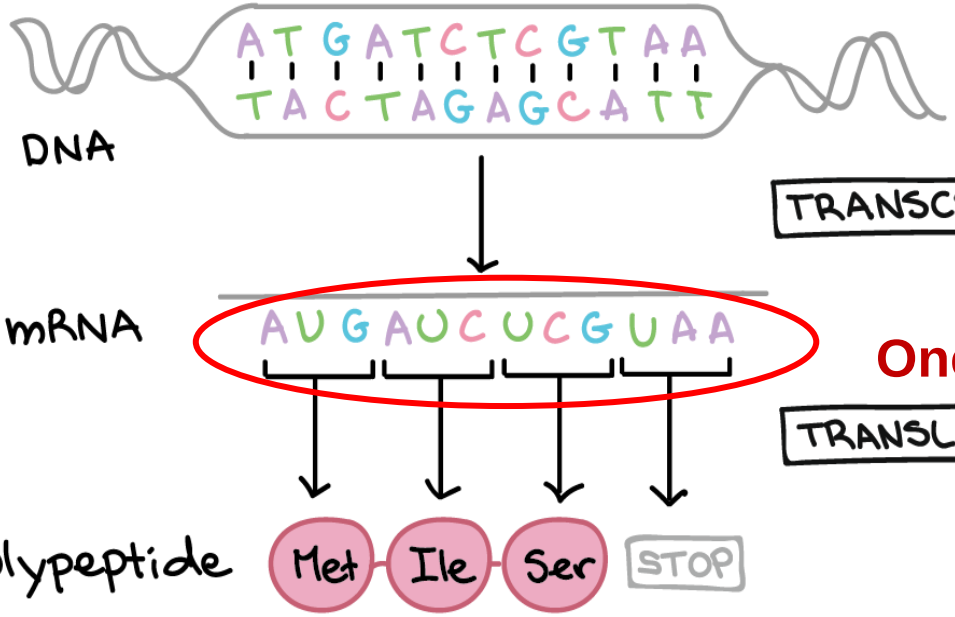
1) Total "A" in above DNA molecule = 5

Then total "T" will be ?

2) Total G = 7, then total C will be?

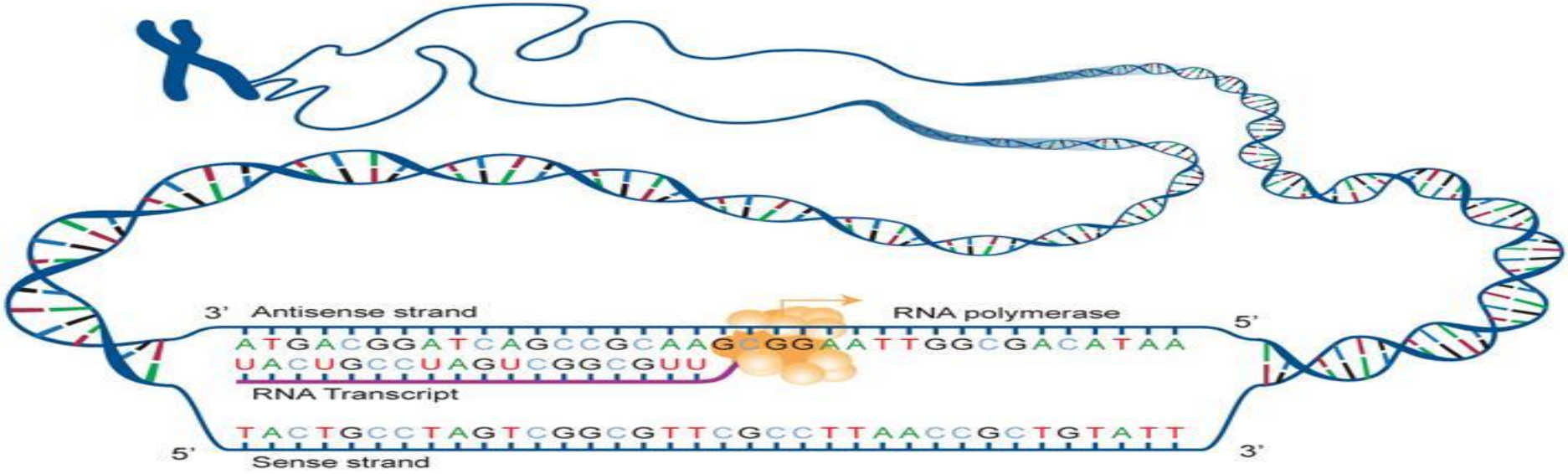
3) If total **deoxyribonucleotides** in above DNA molecule is 24; how many nucleotide pairs will you get?

Concept of Sense and antisense strands of DNA



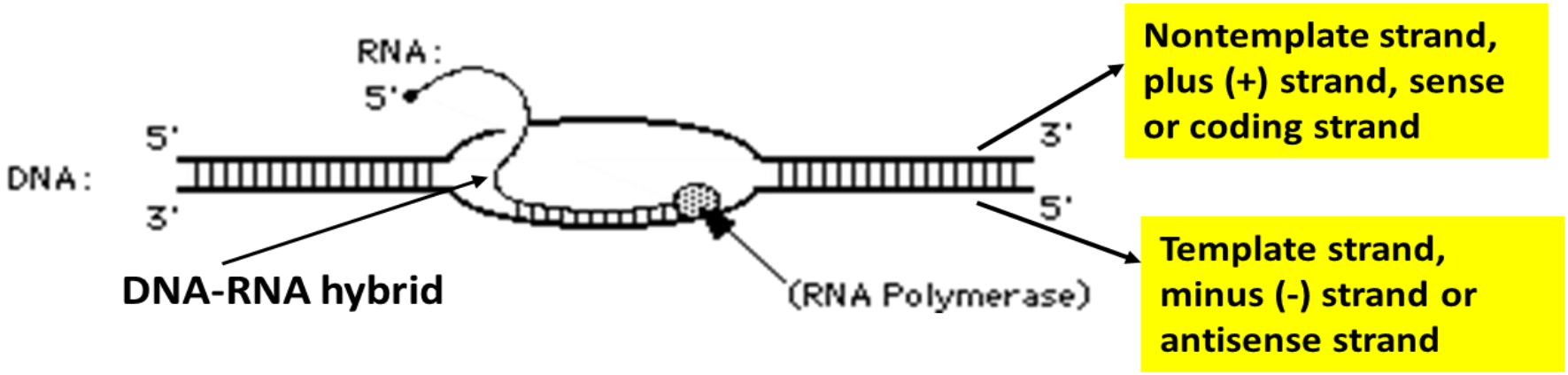
Protein-coding genes

Codons, read in triplet.
One triplet for one amino acid



Sense and antisense strands of DNA

- Both the strands of DNA do not take part in controlling heredity and metabolism. Only one of them does so. The DNA strand which functions as template for RNA synthesis is known **as template strand, minus (-) strand or antisense or noncoding strand.**
- Its complementary strand is named **nontemplate strand, plus (+) strand, sense and coding strand**. The latter name is given because by convention DNA genetic code is written according to its sequence.
- The term antisense is also used in wider prospective for any sequence or strand of DNA (or RNA) which is complementary to mRNA.



For example; If 5‘-GCATTCGGCTAGTAAC-3′ is DNA Nontemplate, Sense (+) or Coding Strand

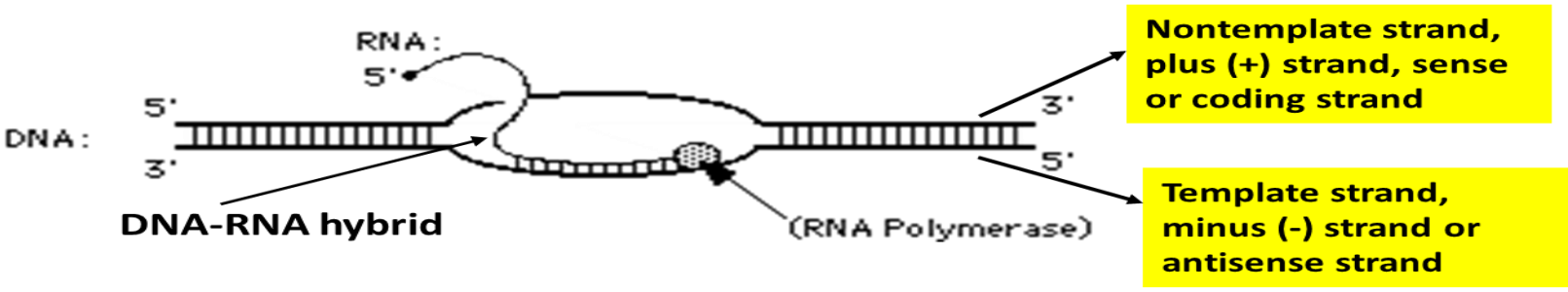
3′-CGTAAGCCGATCATTG-5′ is DNA Template, Antisense, or Noncoding or (-) Strand

Then, 5′- GCAUUCGGCUAGUAAC -3′ is mRNA transcript.

5’- GCATTCGGCTAGTAAC -3′ DNA Nontemplate

5′-GCAUUCGGCUAGUAAC -3′ mRNA transcript

- Thus, mRNA transcript matches with the non-template strand of DNA (+ strand or coding strand) where any “T” will be replaced with “U”. U is uracil and T is thymine as RNA has uracil in place of thymine.



RNA STRUCTURE AND FUNCTIONS

Ribonucleic acid (RNA)

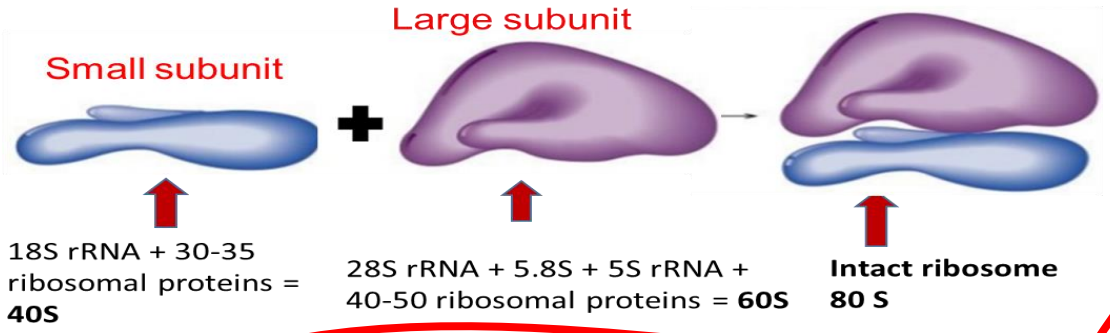
- Different types of RNAs- their structure and functions

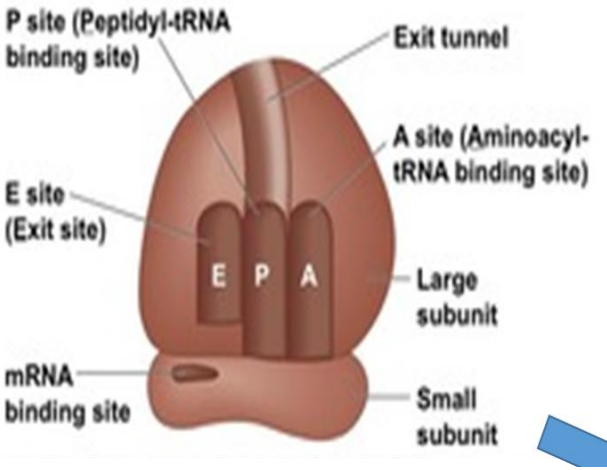
Ribosomal RNA (rRNA)…. Component of Ribosomes

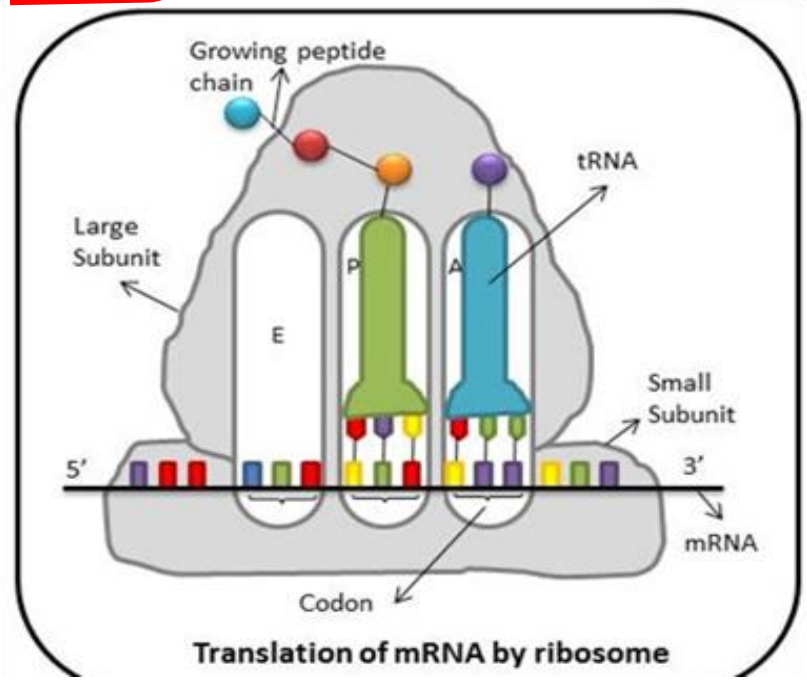
Ribosomes:80S; made up of large subunit and small subunit

Small subunit: 40S; 18S rRNA + 30-35 proteins

Large subunit: 60S; 28S rRNA + 5.8S rRNA + 5S rRNA + 40-50 ribosomal proteins







Three important sites in 60S large subunit are:

A-site: aminoacyl tRNA binding site

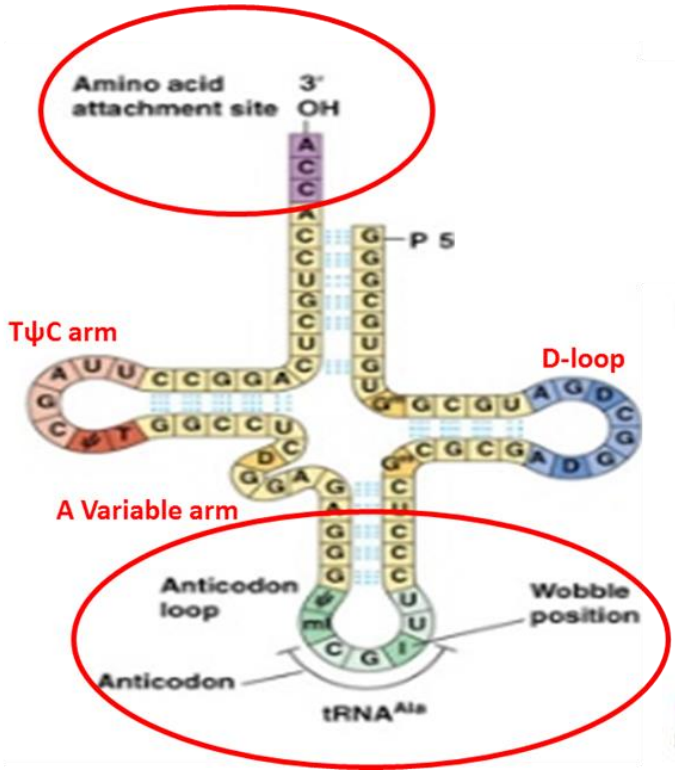
P-site: peptidyl tRNA binding site

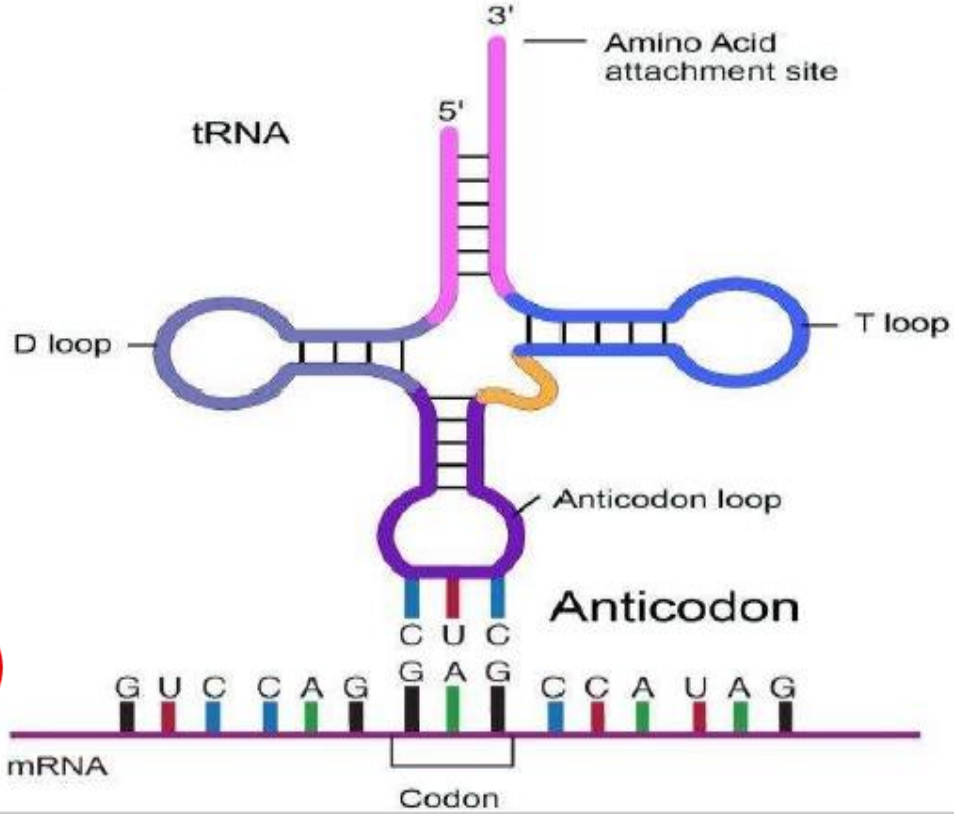
E-site: free tRNA with no amino acid or outgoing tRNA. "E" for exit.

Transfer RNA (tRNA)- has clover leaf –stem loop structure

- Carry amino acids to the ribosome
- Its anticodons attaches with codons of mRNA

tRNA length……80 nucleotides.

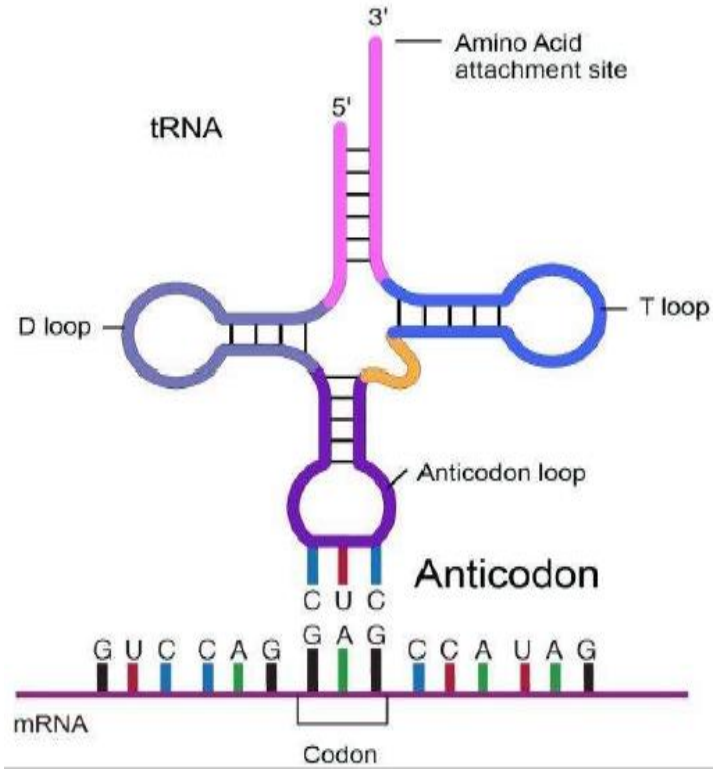




- They transfer the amino acids from cytoplasm to the protein synthesizing machinery, hence the name t RNA.

➢ Amino acid binding site-

- It is site for amino acid attachment and therefore, **each tRNA represent a single amino acid to which it covalently binds.**
- Each tRNA is named **after the amino acid it carries**. For example, if tRNA carries amino acid tyrosine it is written as $tRNA^{Tyr}$. Sometimes there are more than one tRNA for an amino acid, then it is denoted as $tRNA_1^{Try}$ and $tRNA_2^{Try}$.
- A minimum of 32 tRNAs are required to translate all 61 codons.

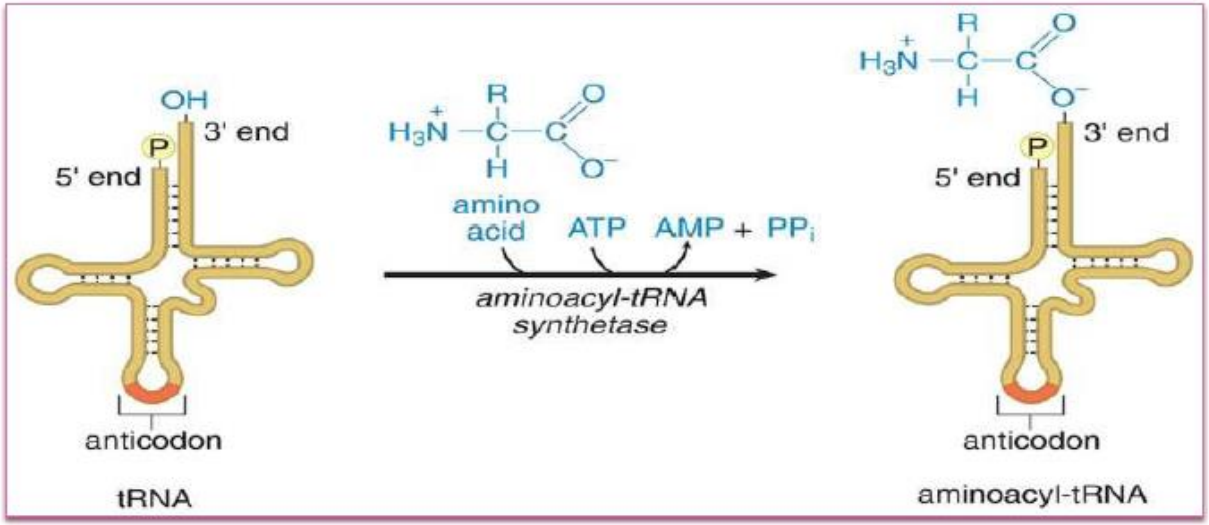


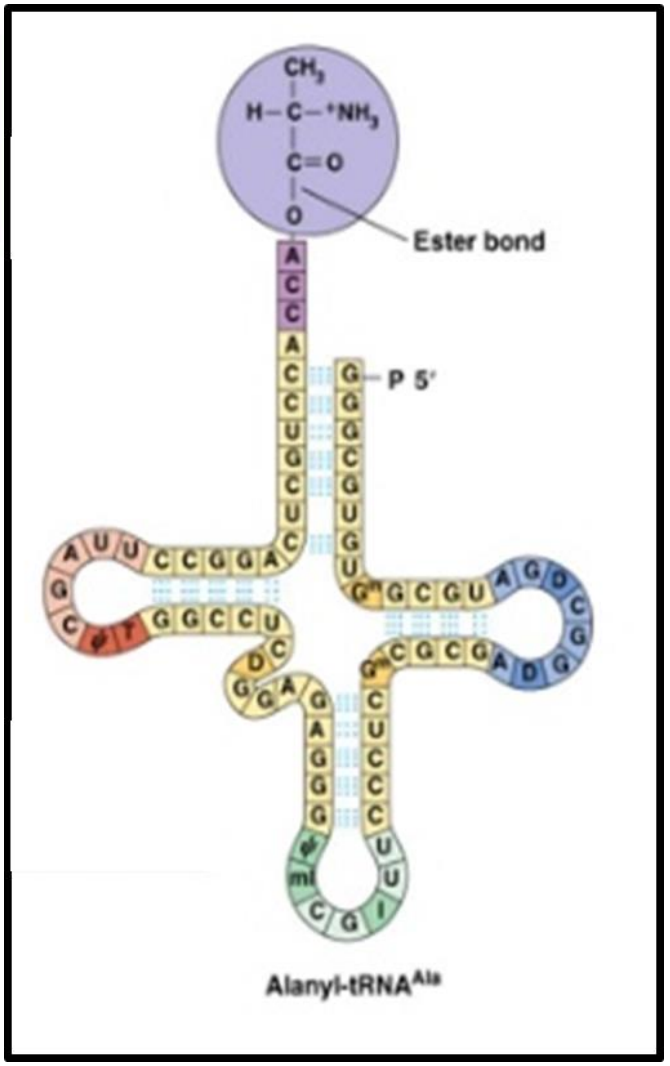
➢ Anticodon site –

- It has an **anticodon site** for **codon recognition site** that binds to a **specific sequence present on the messenger RNA** chain through hydrogen bonding.
- The **codon and anticodon** form base pairs with each other through hydrogen bonding.

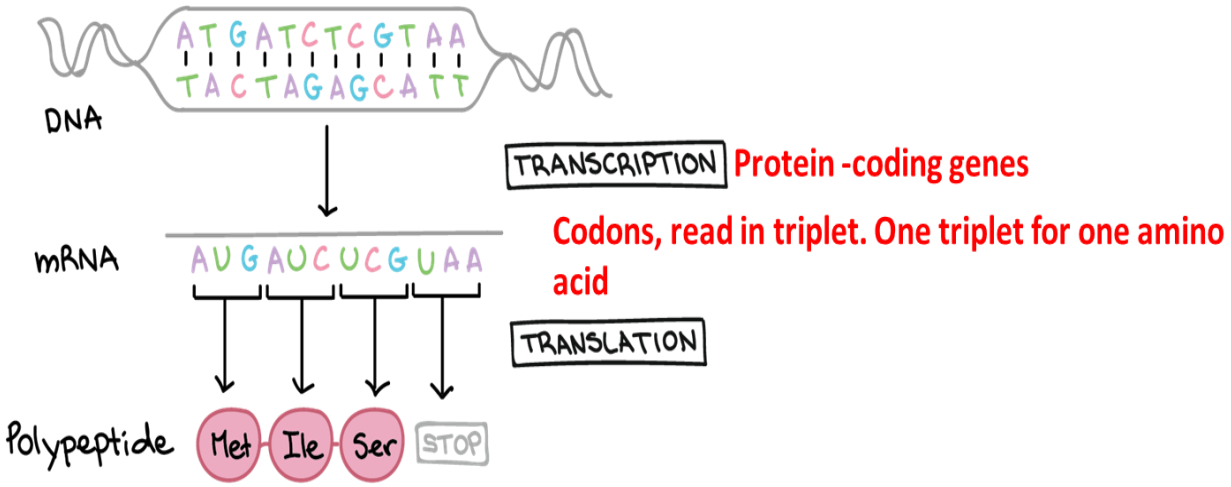
Activation of tRNA or tRNA charging or aminoacylation

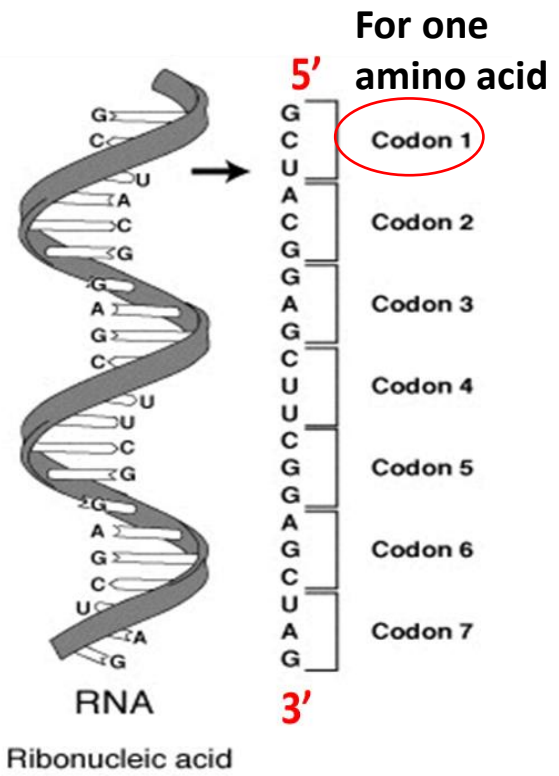
- Attachment of amino acid with t RNA
- Formation of aminoacyl t RNA
- Aminoacyl t RNA binds with mRNA





Messenger RNA (single stranded Nucleic Acid)

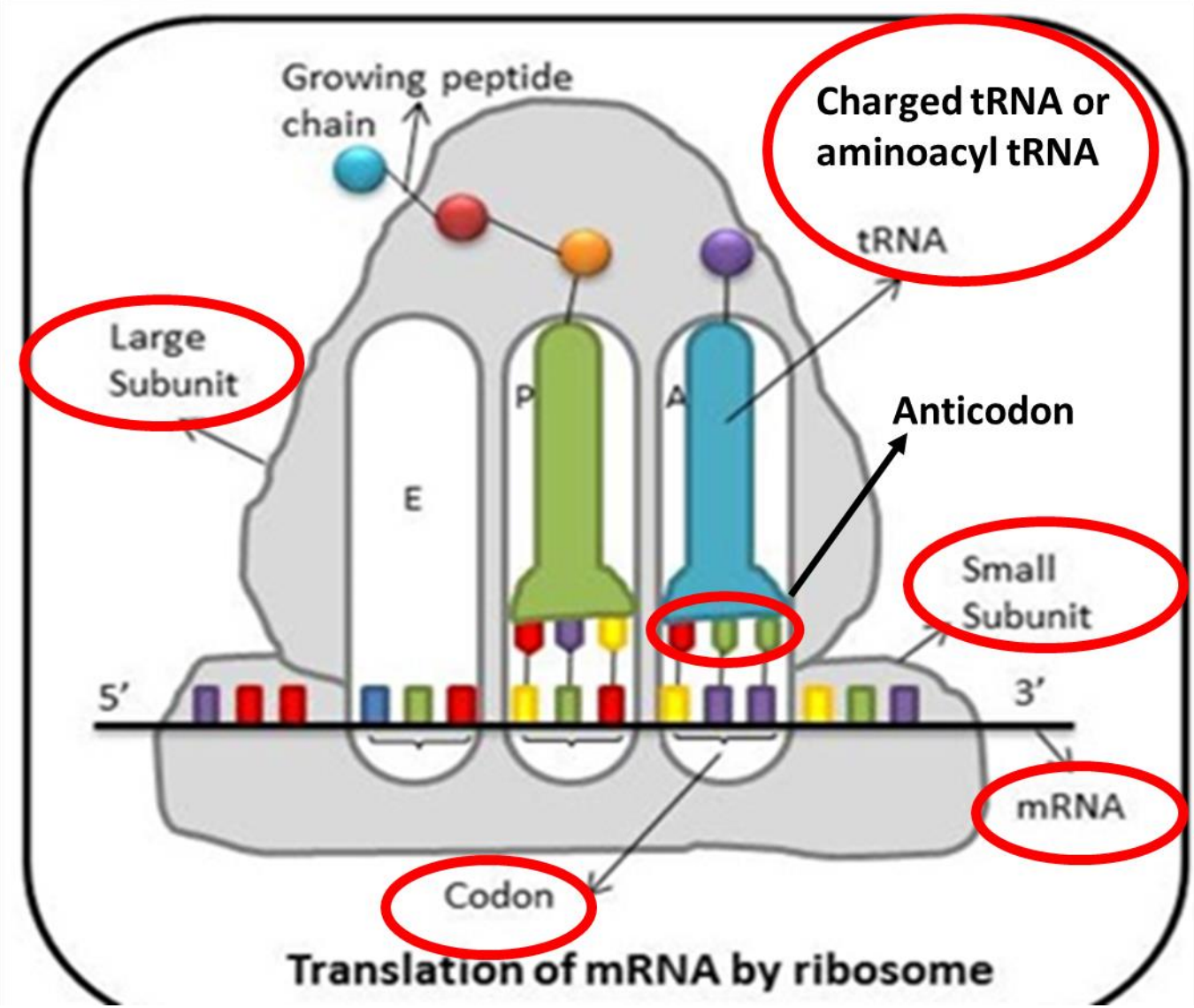




- Messenger RNA is a linear molecule transcribed from one strand of DNA; **the process known as transcription using RNA polymerase II.**
- It carries the base sequence complementary to DNA template strand.
- The base sequence of mRNA is in the form of **consecutive triplet codons specifies for specific amino acids** and translated to proteins.
- Ribosomes translate these triplet codons into amino acid sequence of polypeptide chain.
- **Length of mRNA molecules** depends upon the length of polypeptide chain its codes for.

In RNA "URACIL (U)" is present, in place of Thymine (T)

rRNA, tRNA and mRNA mediates protein synthesis process…..Translation



Sample questions

1. The human genome size is 3.1 billion base pairs **(3.1 x 10^9 base pairs),** is entirely a B-helix. **How long is the DNA in human cell**?

2) A "B- DNA" molecule has total 600 nucleotides.

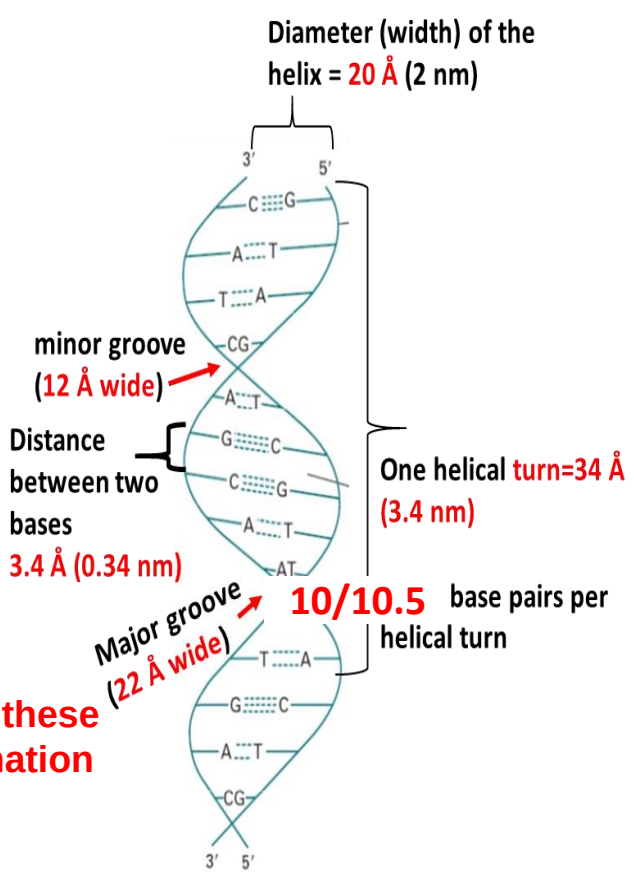
a) How many nucleotide pairs are present?

b) What is the length of given DNA molecule?

c) How many turns are there in a given DNA?

d) If the given B-DNA attains, a Z-form, what will be the length of DNA.

Using these information



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Type of helix	Right-handed	Right-handed	Left-handed
Helical diameter (nm)	2.37	2.55	1.84
Rise per base pair (nm)	0.34	0.29	0.37
Distance per complete turn (pitch) (nm)	**3.4**	**3.19**	**4.44**
Number of base pairs per complete turn	10	11	12
Topology of major groove	Wide, deep	Narrow, deep	Flat
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Sample questions

1. **Analysis of a molecule of DNA found it to contain 200 adenine bases which is 20% of the total number of bases in the strand. How many phosphate groups are present in given DNA molecule?**

a) 200
b) 400
c) 800
d) 1000

2. Which of the following options are the pyrimidine bases found in DNA?

a) Uracil and thymine
b) Thymine and cytosine
c) Adenine and thymine
d) Cytosine and uracil

3. A piece of DNA was analyzed and 15% of its nucleotides were adenine. What percentage would be uracil?

a) 0 %
b) 15 %
c) 30 %
d) 35 %

4. Analysis of a sample of DNA found that 20% of the bases were adenine. What percentage of the bases would be pyrimidines?

a) 20 %
b) 30 %
c) 60 %
d) 50 %

5. Which of the following statements about double-stranded DNA is false?

a) The two strands have an antiparallel orientation.
b) The helix has two grooves called the major groove and the minor groove.
c) The bases are on the outside of the helix
d) The strands are formed by nucleotides linked together via phosphodiester bonds

6. Which of the following components must all free nucleotides contain?

a) 3' OH group
b) 1' OH group
c) 2' H group
d) 5' OH group

7. In humans, DNA exists as double-stranded helices of complimentary strands with the _____ on the outside of the helix and the _____ on the inside of the helix.

a) Hydrogen bonds . . . nucleotides
b) Nucleotides . . . hydrogen bonds
c) Sugar-phosphate chains . . . nitrogenous bases
d) Nitrogenous bases . . . sugar-phosphate chains

8. Which of the following statements is false about the double helix of B-DNA (the most commonly found form of DNA)?

a) The two strands run opposite to each other.
b) There is a complete turn of the helix at approximately every 10 base pairs.
c) The adenine and thymine bases are connected by two hydrogen bonds, and the cytosine and guanine are connected by three.
d) The 5' end contains an −OH group, and the 3' end has a free phosphate group.

9. What is the name of a deoxynucleotide in which the base is thymine?
I. Deoxythymidine monophosphate
II. Deoxythymidine diphosphate
III. Deoxythymine monophosphate
IV. Deoxythymine diphosphate

A. I and II
B. III and IV
C. I, II, and III
D. I, II, III, and IV

10. The sequence of nucleotides in non template, coding (+) strand of DNA is

5’ATGGTTCAAG3’

I. What would be the mRNA sequence?
II. What would be the sequence of antisense stand of DNA
III. What would be length of DNA in B, A and Z form?
IV. What would be the number of turns in B, A and Z forms, respectively.

Sample questions

Q.1) If GC content of a DNA molecule is 60%, what are the percentages of the four bases (G,C,T and A)?

Q. 2) If in one strand of a double stranded DNA the rate of occurrence of G is 4 times of A in consecutive 11 base pairs. So how many G will be there in 121 base pairs of a DNA duplex? [Consider C=T in one strand].

Answer:

Q 3. A sample of DNA of 90,000 nucleotides contains 20% Guanine. How many other bases are present and in what percent (explanation required for your calculations)?

?

Sample questions

Q.1) Write the complementary sequence of the given sequence below, if this sequence is present in one strand of DNA.

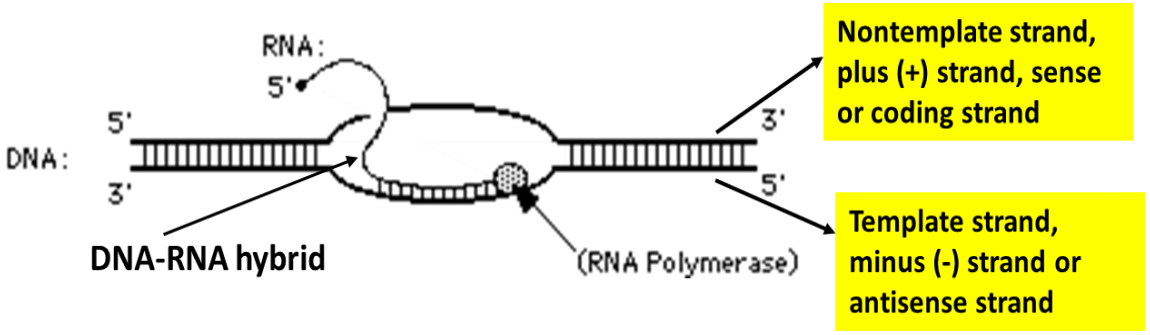
5'- GCTAGCTAAACCTTAAGGGCATTTCCG-3'…… (One strand of DNA)

Q.2) What will be the mRNA sequence , if the above strand is a sense strand?

Q.3) What will be the length of the above DNA strand, considering it as B-DNA form?

Q.4) Compare the length of the above B- DNA form with length of A-form and Z-form with the same sequence of bases?

What concept you will require to solve the above questions?



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