THE NUCLEIC ACIDS

Unit 1. Nucleic acids: Structure and Function

What are Nucleic acids?

Nucleic acids

- Nucleic acids are long chain polymers **made up of nucleotide monomers**, store information for cellular growth and reproduction.

- **Two types** of **Nucleic acids-**
- Deoxyribonucleic acid (DNA) and Ribonucleic acid (RNA).
- **DNA types** are **A-DNA; B-DNA and Z-DNA.**
- **RNA types are messenger RNA (mRNA), ribosomal RNA (rRNA), and transfer RNA (tRNA)**

- **DNA**- for information storage, It is **Double stranded** (double helix), contains **deoxyribose** as its sugar unit.

- **RNA**- role in protein synthesis, **Single stranded**, contains **ribose** as its sugar unit.

- **Energy Transfer molecules**

❖ ATP (adenosine triphosphates)

❖ NAD (Nicotinamide adenine dinucleotide)

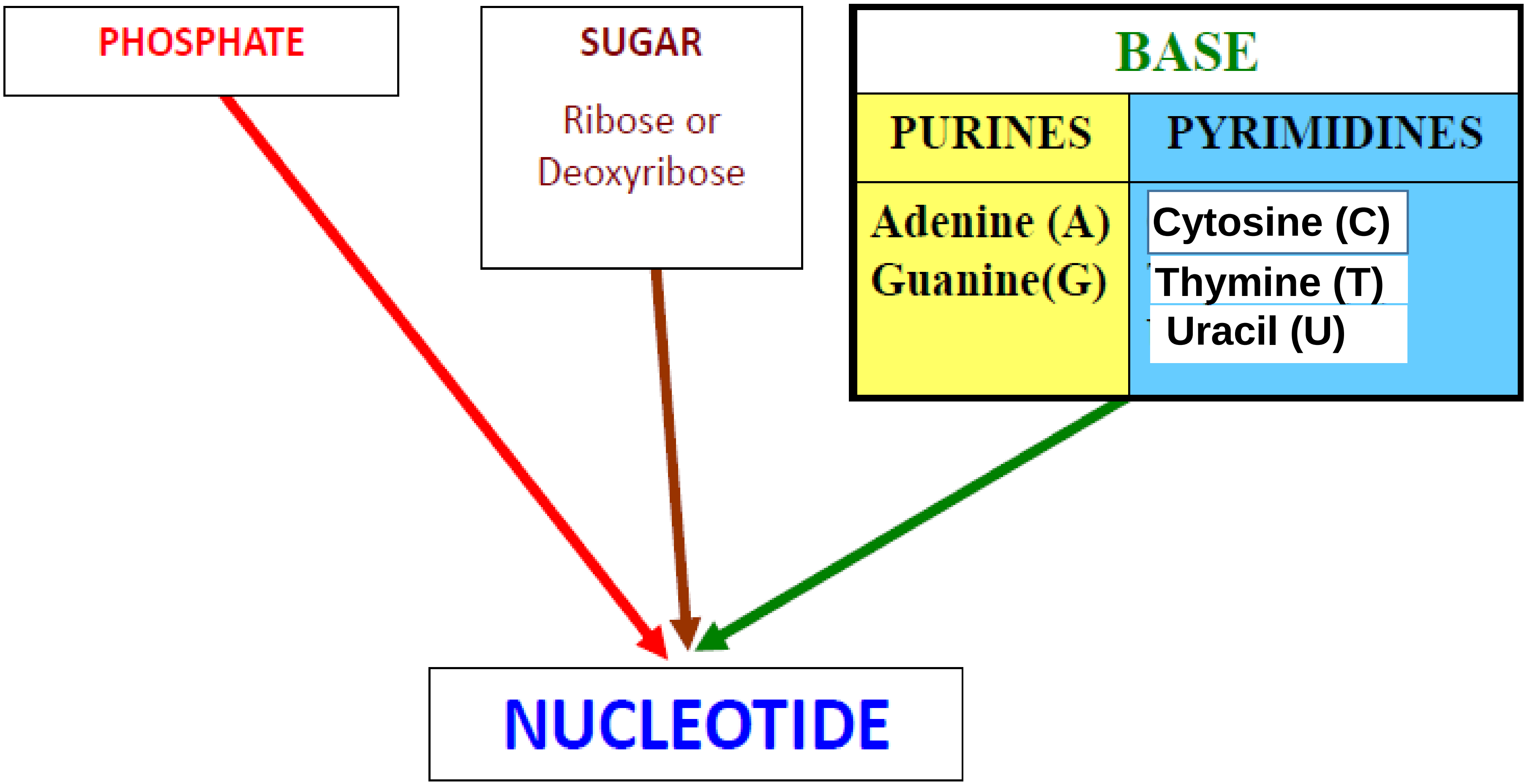
Biological Functions of Nucleic Acid

- 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.

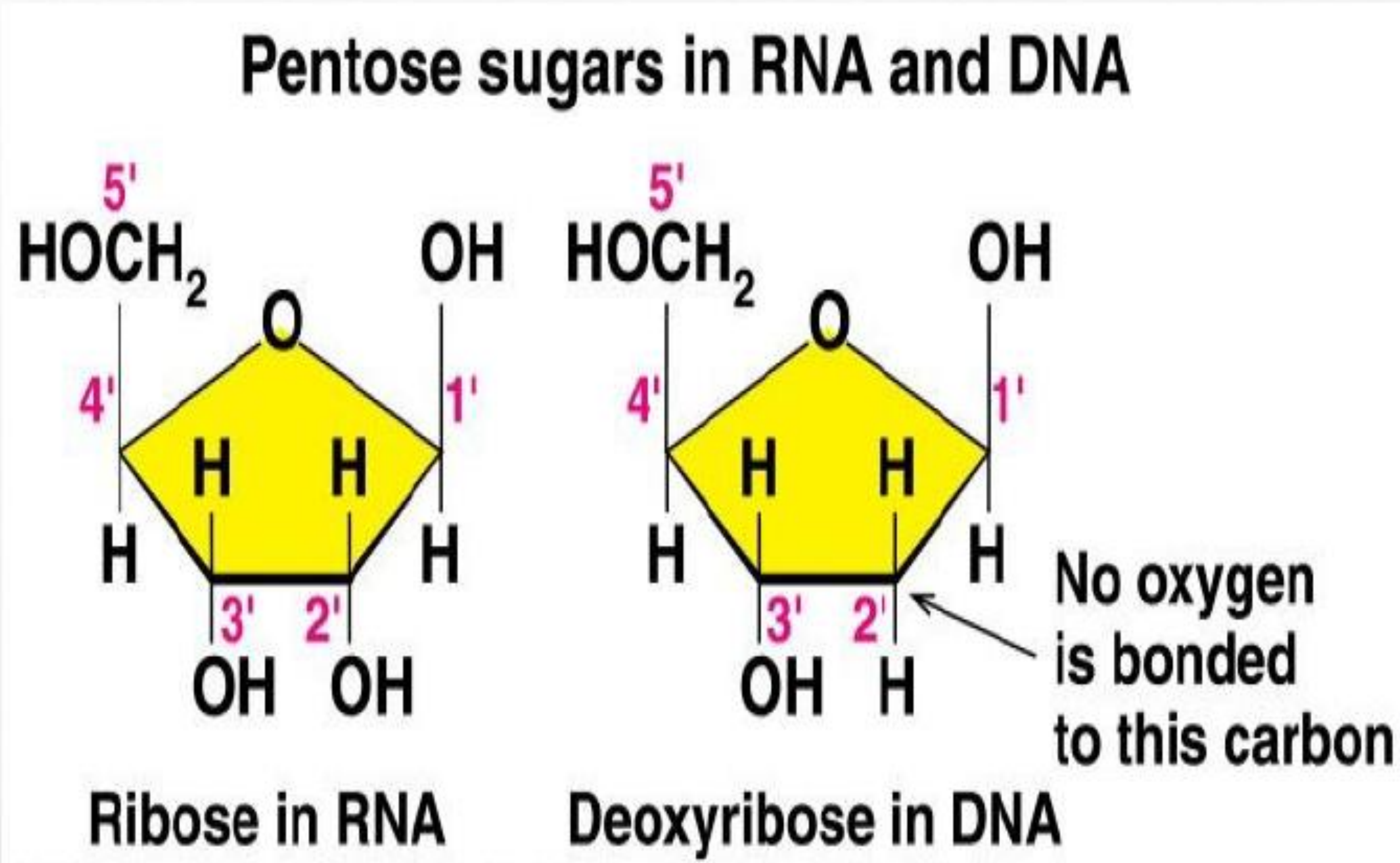
The Structure of Nucleic Acids

- 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

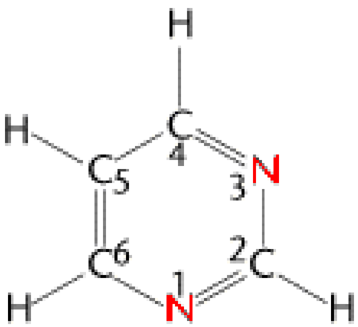


Sugar of nucleic acids

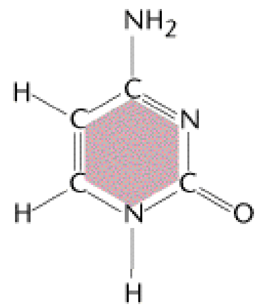


Nitrogenous bases in nucleic acids

Pyrimidine bases

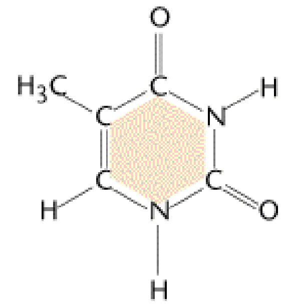


Pyrimidine ring



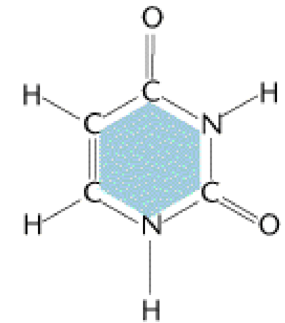
Cytosine

(C)



Thymine

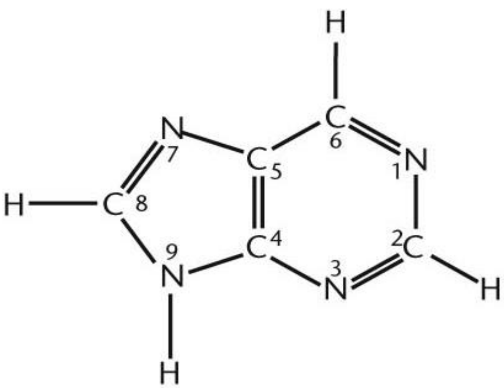
(T)



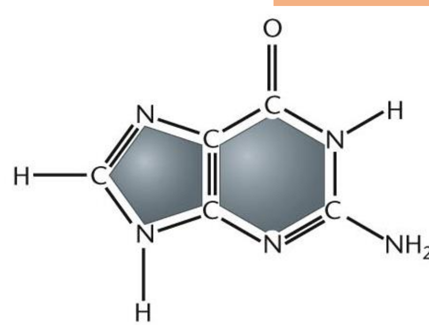
Uracil

(U)

Purine bases

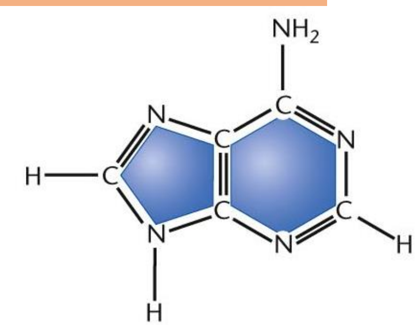


Purine ring



Guanine

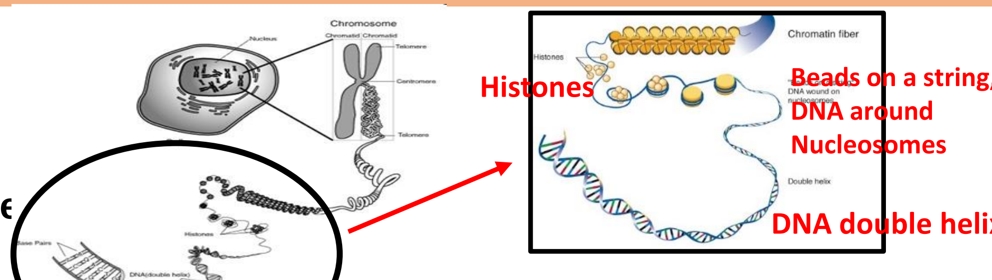
(G)



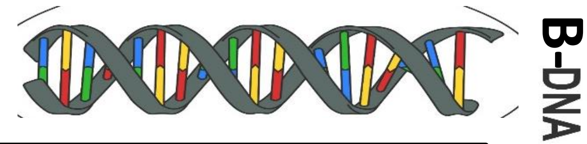
Adenine

(A)

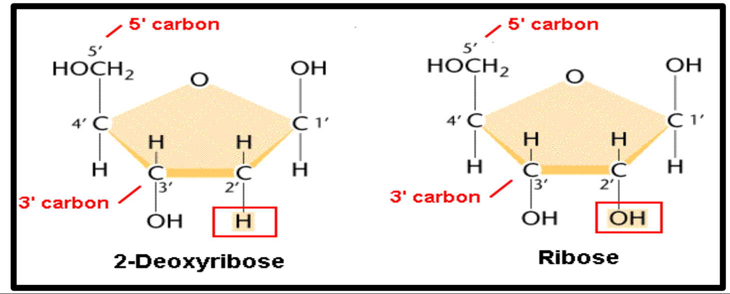
DNA…………stores genetic information in the form of genes; found inside the nucleus, packed with histone proteins



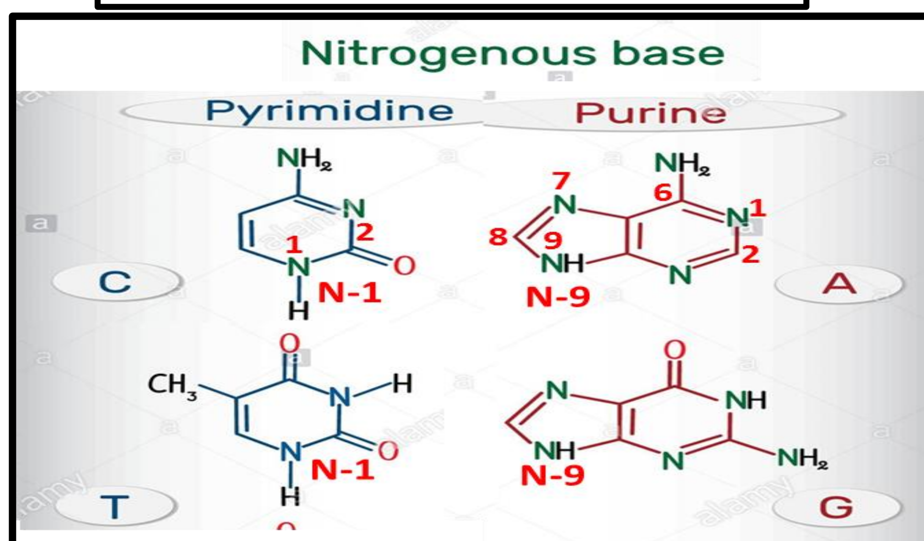
- Deoxyribonucleic acid; deoxyribonucleotide monomers; "Deoxy" because "**one oxygen**" is removed from the –OH of **carbon no. 2** of **ribose** sugar and making it deoxyribose.



- **Double helical (double helix)** with two poly deoxyribonucleotide chain / or simply you can say, 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).

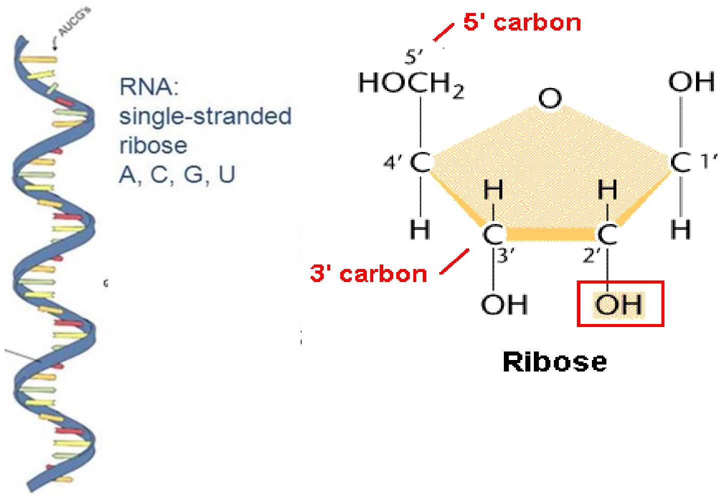
- Presence of phosphate group

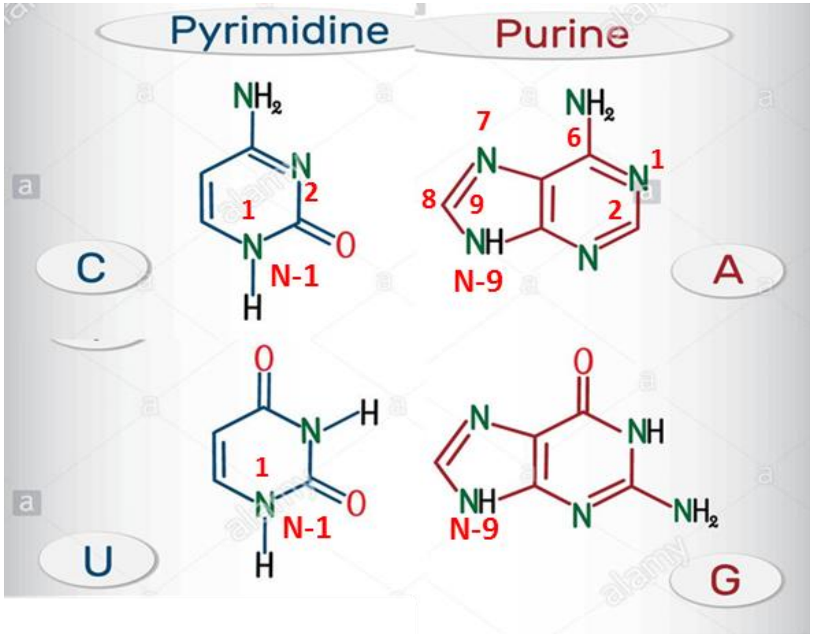
RNA…………they are involved in protein synthesis process; all three types of RNAs (rRNA; tRNA; mRNA) are assigned specific roles found inside the nucleus and cytoplasm

- ✓ **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.

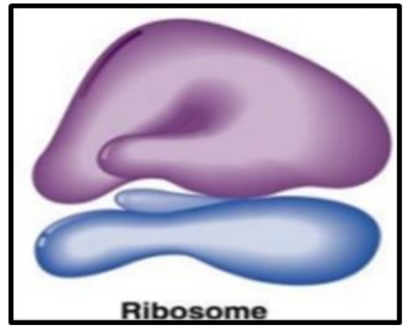
- ✓ **mRNA** carries **genetic code messages** from DNA and **which is decoded to** protein information with the help of rRNA and tRNA.
- ✓ **Nitrogenous bases**…….. Adenine (A) , Guanine (G) are purine form….9 membered ring); Cytosine (C) and **Uracil (U)** pyrimidine form….. 6 membered ring)
- ✓ Presence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

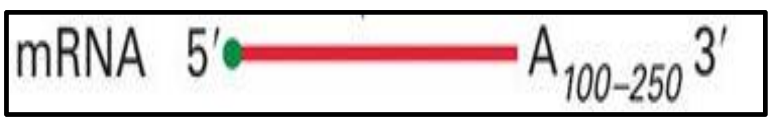


1. **Ribosomal RNA (rRNA): Major component of ribosomes where mRNA is translated to protein.**

75% of total RNA of the cell.

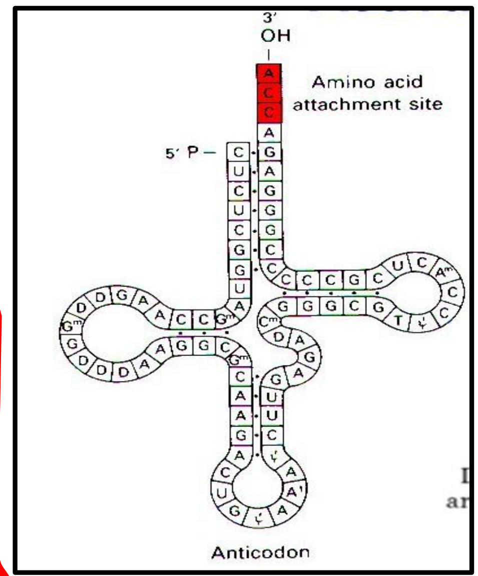
2. Transfer RNA (tRNA): tRNA transfers the amino acids from the cytoplasm to the site of protein synthesis.

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**

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

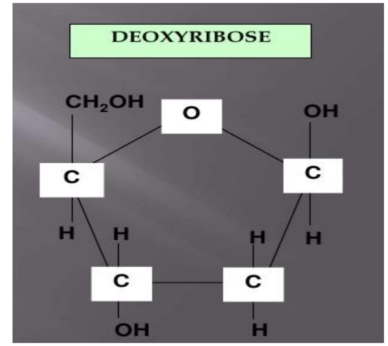
Structural composition of DNA and RNA

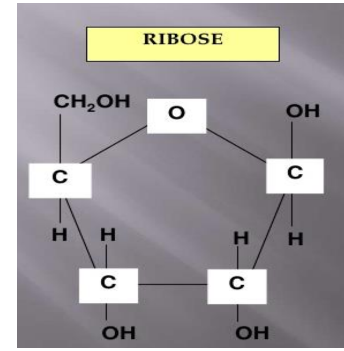
1. Phosphate group — **Phosphoric acid**

2. Sugar / monosaccharide →

DNA has **Deoxyribose**

RNA has **Ribose**



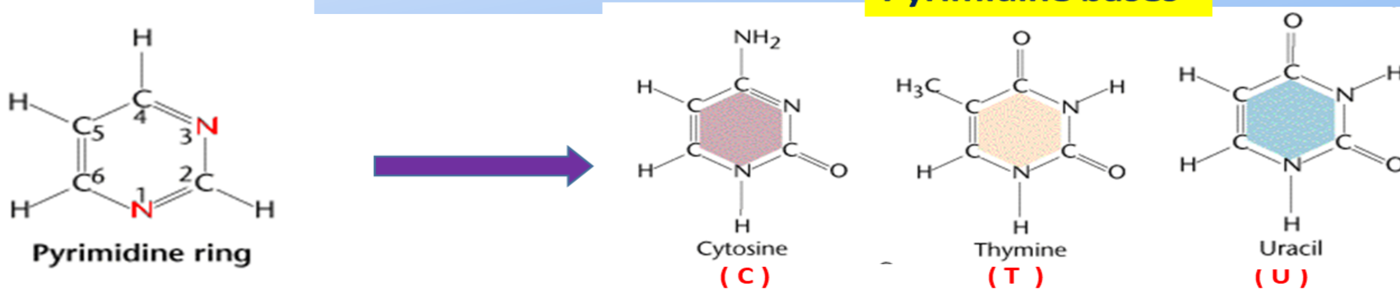


3. Nitrogenous bases (Pyrimidine and Purine bases) →

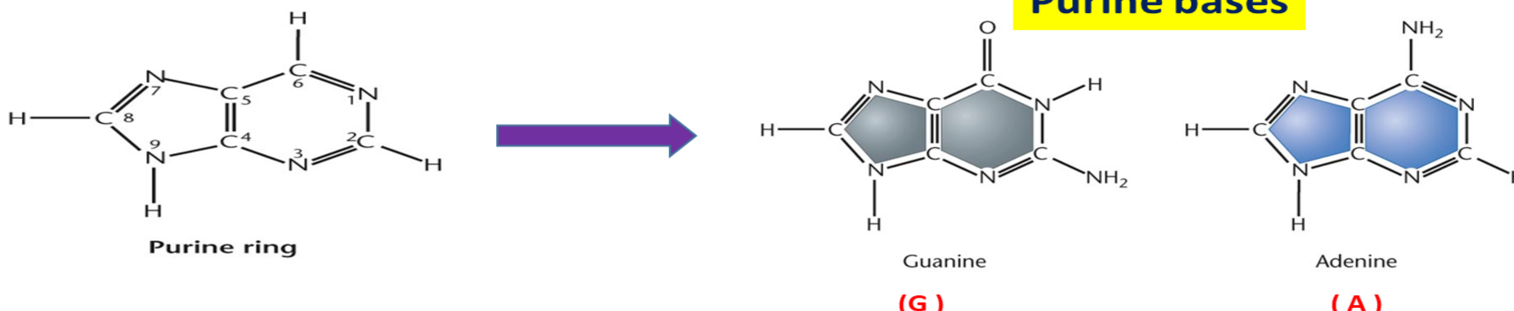
DNA has Adenine (A); Guanine (G); Cytosine (C); and **Thymine (T)**

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

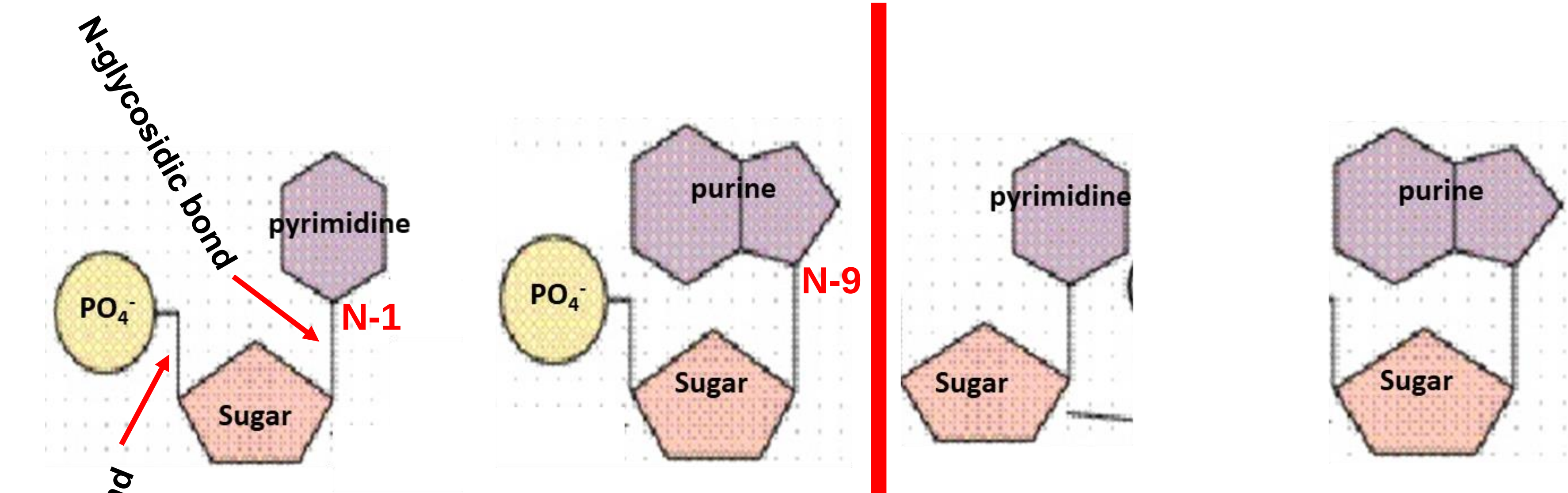
Pyrimidine bases



Purine bases



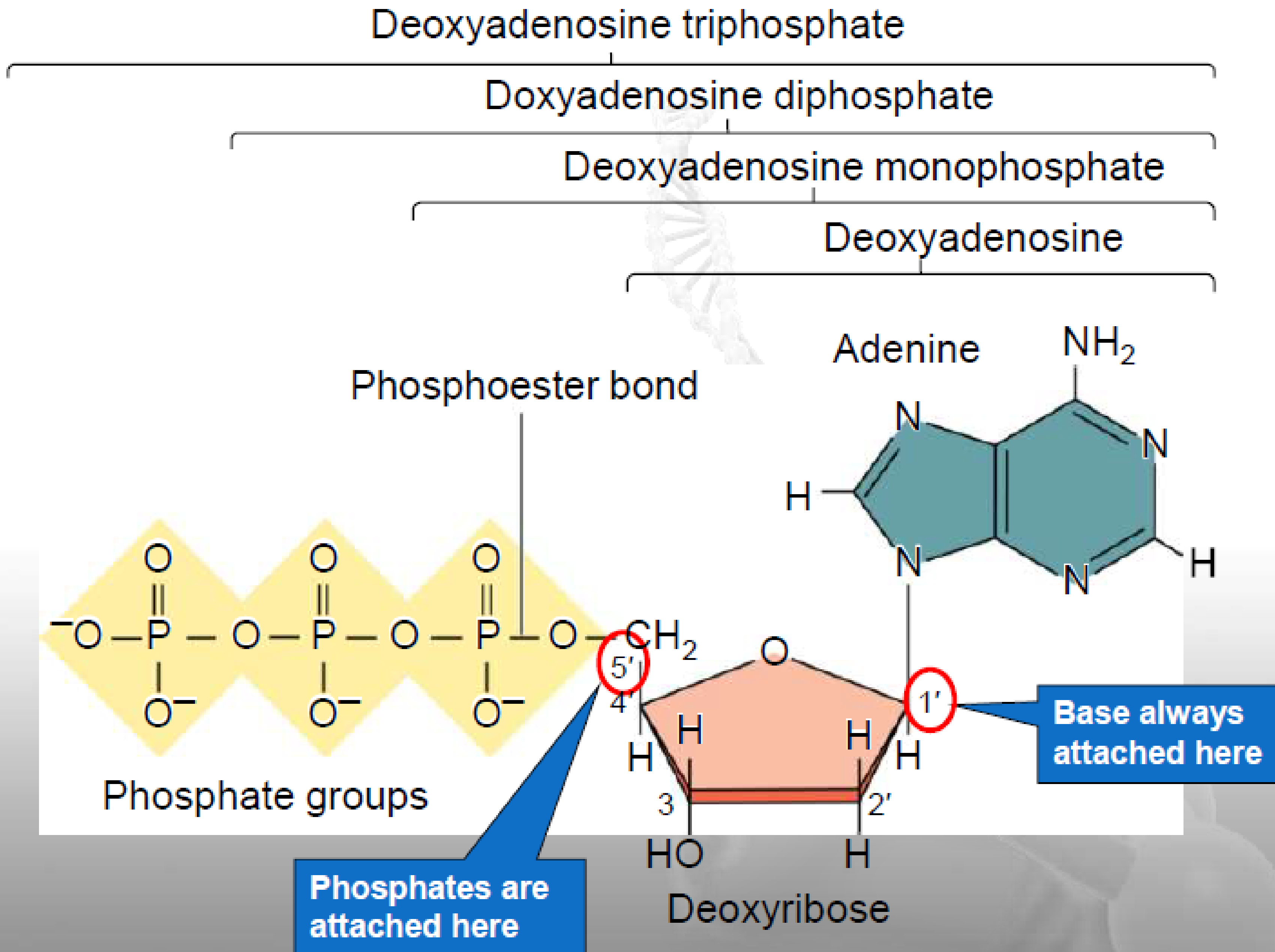
What is a nucleotide?



Nucleotides (Phosphate attached)
P + S + B

Nucleosides (no phosphate attached)
S + B

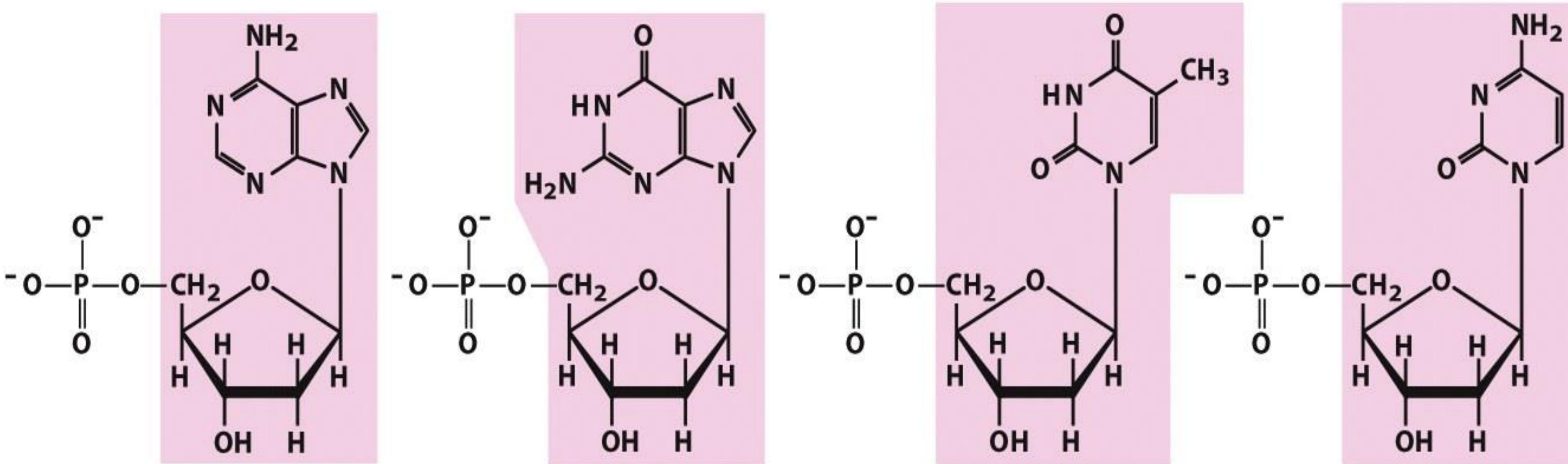
- Linkage between **sugar and base** is called **N-glycosidic bond**. In **Pyrimidine, N-1** is involved in bonding with sugar. **In purine, N-9** is involved in **bonding with sugar**.
- Linkage between **sugar and phosphate** is called **phosphoester bond**.



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′
O
1′
H
H
H
H
3
2′
HO
H
Phosphate groups
Deoxyribose
Base always attached here
Phosphates are attached here

Nomenclature of nucleotides and nucleosides

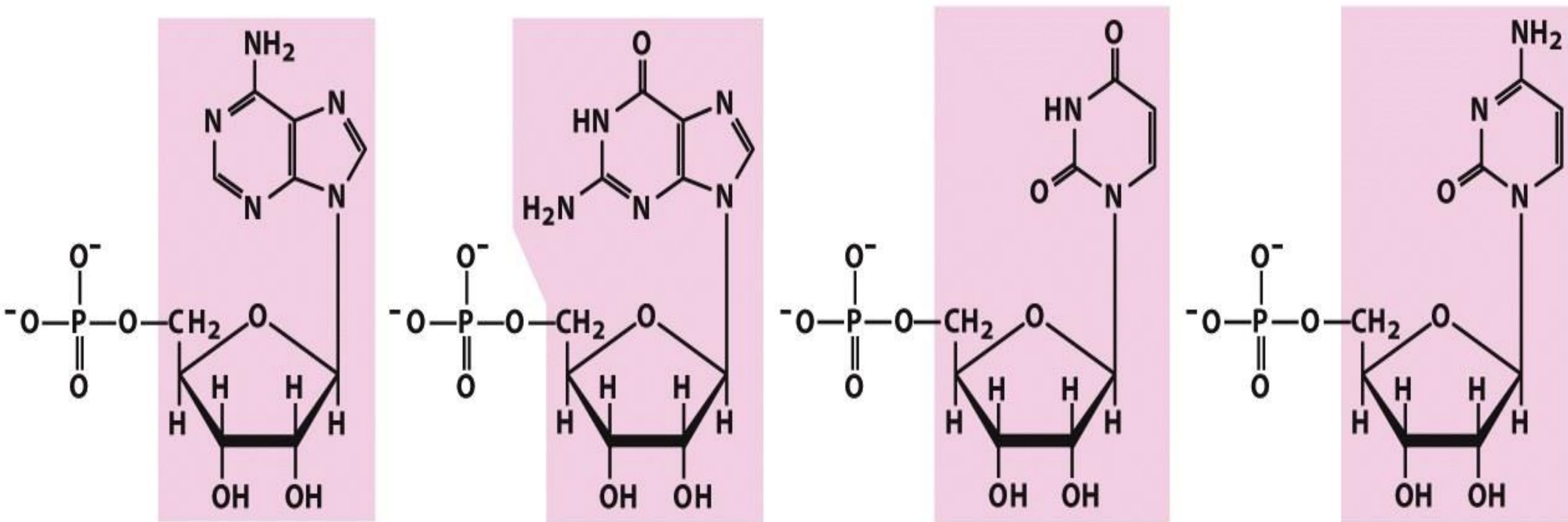
- **Deoxyribonucleotides- monomeric units of DNA**



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**



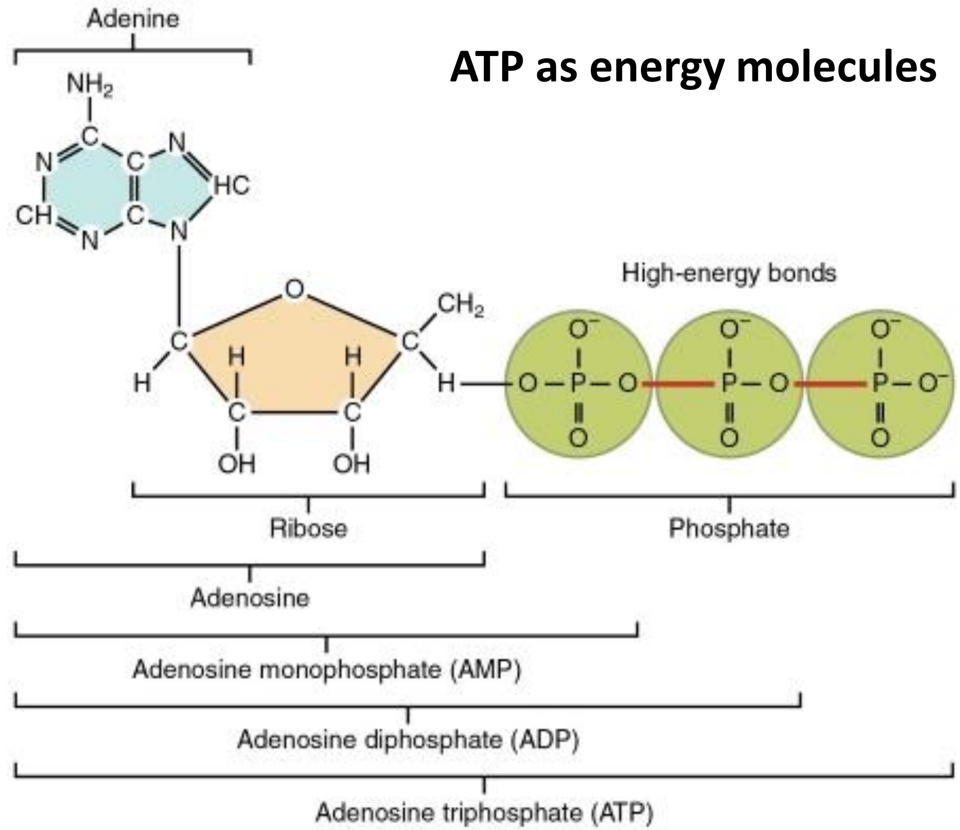
Nucleotide:	Adenylate (adenosine 5′-monophosphate)	Guanylate (guanosine 5′-monophosphate)	Uridylate (uridine 5′-monophosphate)	Cytidylate (cytidine 5′-monophosphate)
Symbols:	A, AMP	G, GMP	U, UMP	C, CMP
Nucleoside:	Adenosine	Guanosine	Uridine	Cytidine

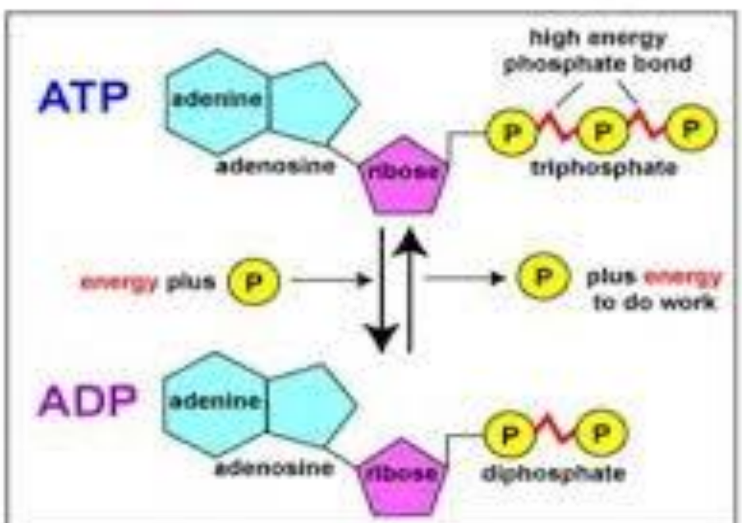
Base	Nucleosides	Nucleotides
RNA		
Adenine (A)	Adenosine (A)	Adenosine 5'-monophosphate (AMP)
Guanine (G)	Guanosine (G)	Guanosine 5'-monophosphate (GMP)
Cytosine (C)	Cytidine (C)	Cytidine 5'-monophosphate (CMP)
Uracil (U)	Uridine (U)	Uridine 5'-monophosphate (UMP)
DNA		
Adenine (A)	Deoxyadenosine (A)	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)

A nucleotide: ATP

- Energy storage for cells
- Many enzymes use ATP
- Provides a way to run reactions that are otherwise **endergonic** (require energy)

ATP as energy molecules





ATP to ADP + P = energy released

ADP + P to ATP = energy stored

- When **hydrolyzed**, ATP produces -7.3 kcal of energy per mole of ATP hydrolyzed

  - $ATP + H_2O \rightarrow ADP + P_i$ $\Delta G = -7.3$ kcal/ mol **(exergonic)**

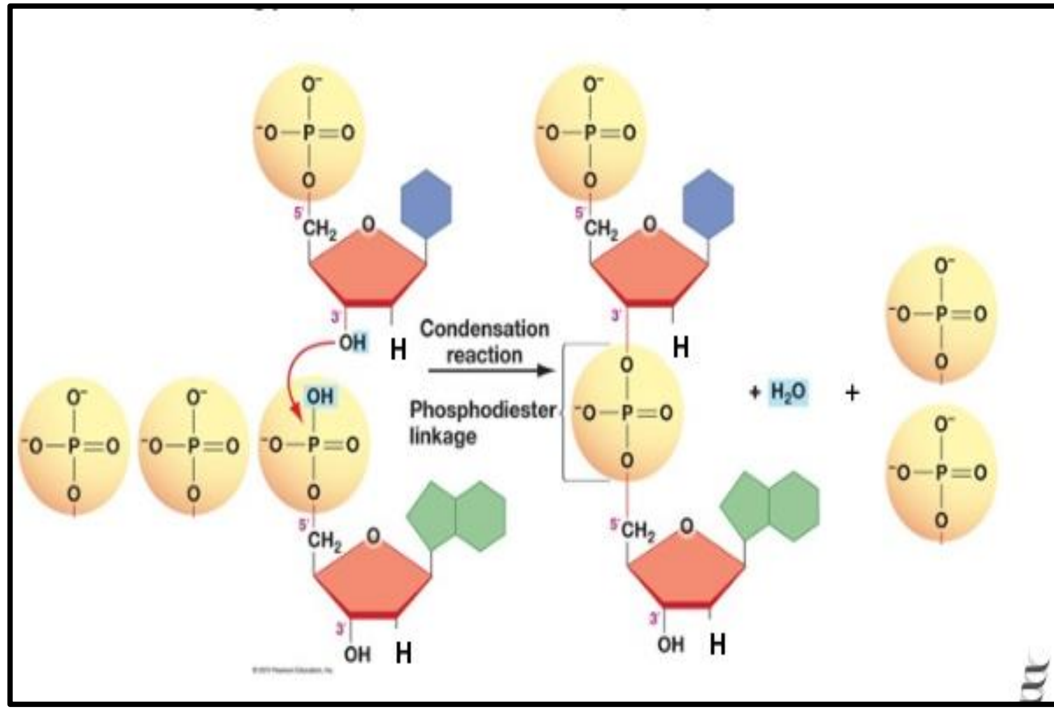
- This -7.3 kcal/ mol of energy can be "coupled" and the reaction can still be **exergonic** (and spontaneous!)

How is one polynucleotide chain made?

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

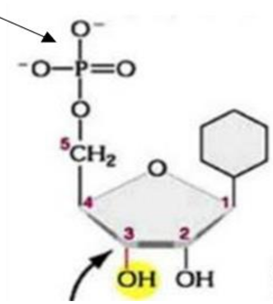
Enzyme that catalyze this condensation reaction is **DNA ligase**

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**

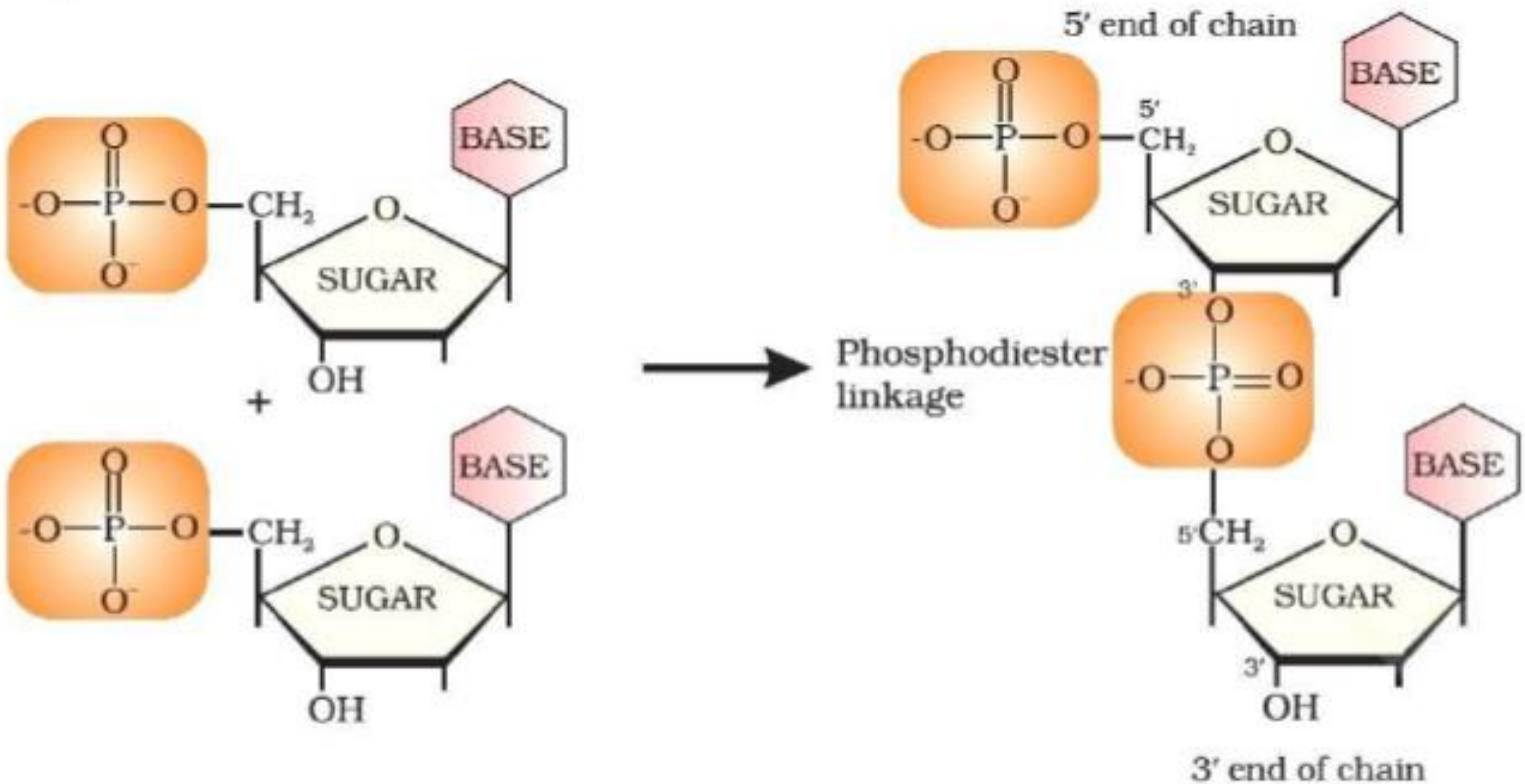


5'-PO_4^{2-} ——— **3'-OH**

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

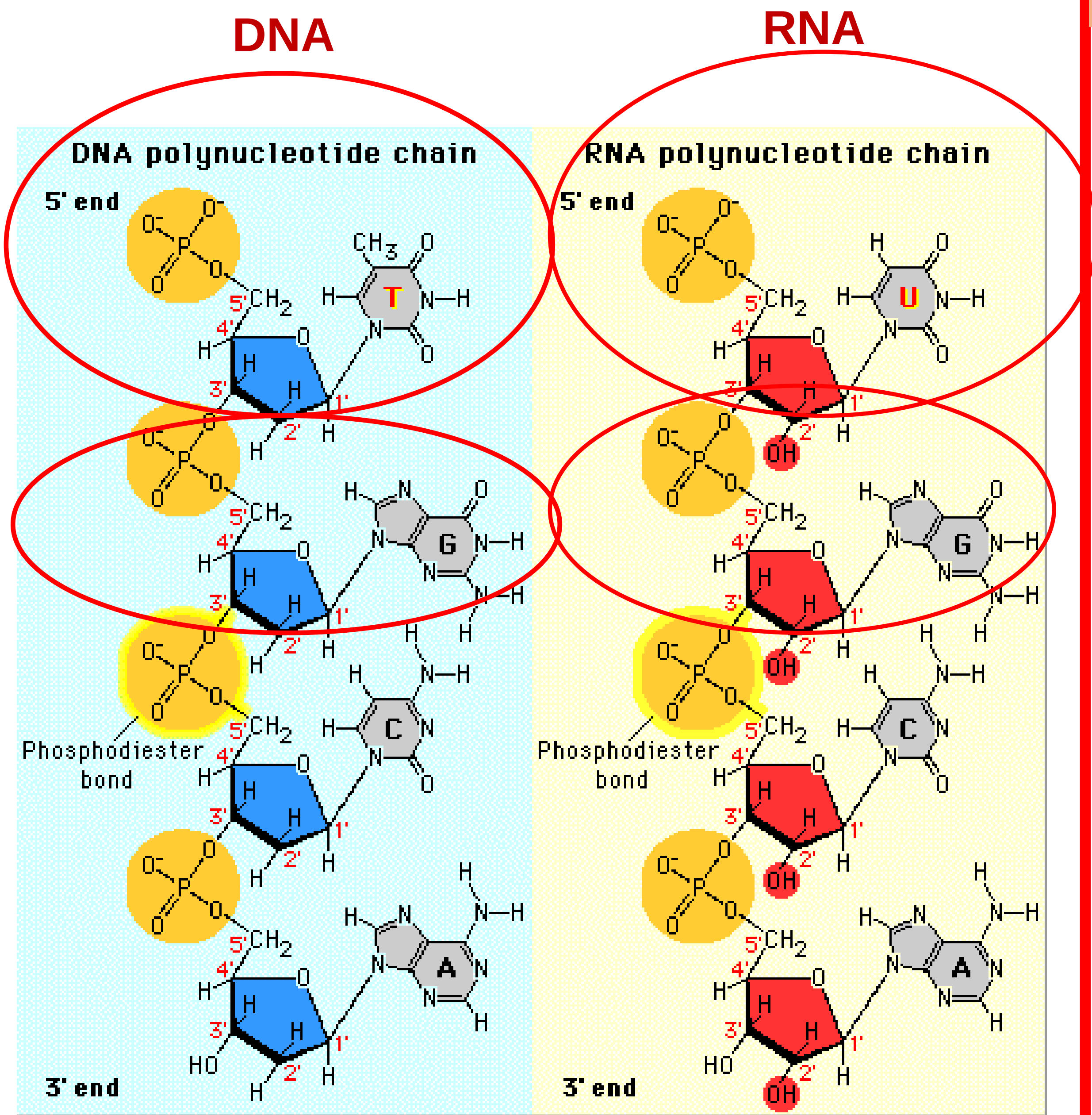


- Nucleotides are joined together by phosphodiester linkage between 5′ and 3′ carbon atoms of the pentose sugar.

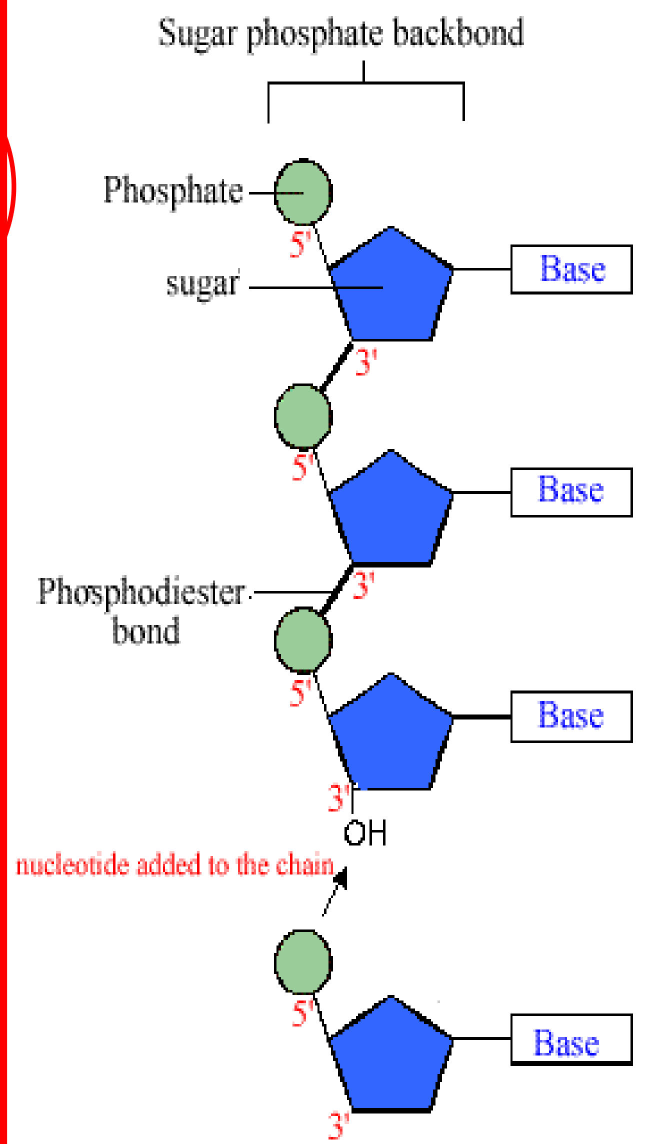


Primary Structure of Nucleic Acids

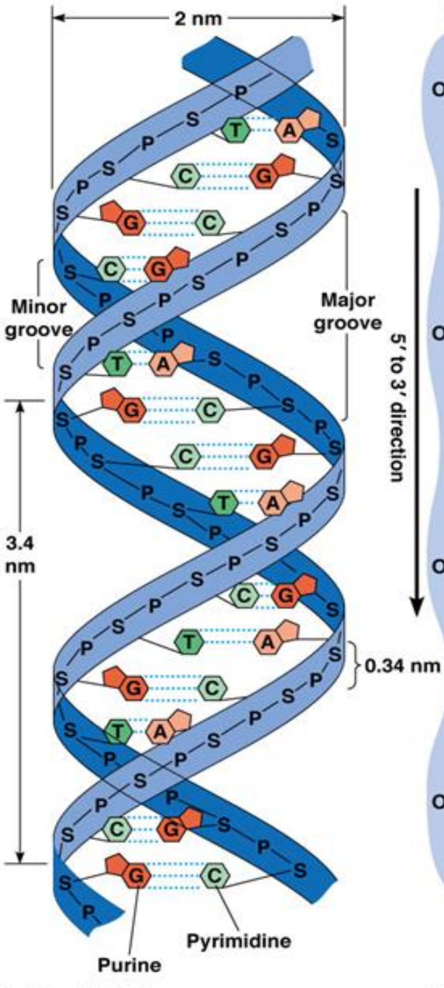
Structure of polynucleotide chain



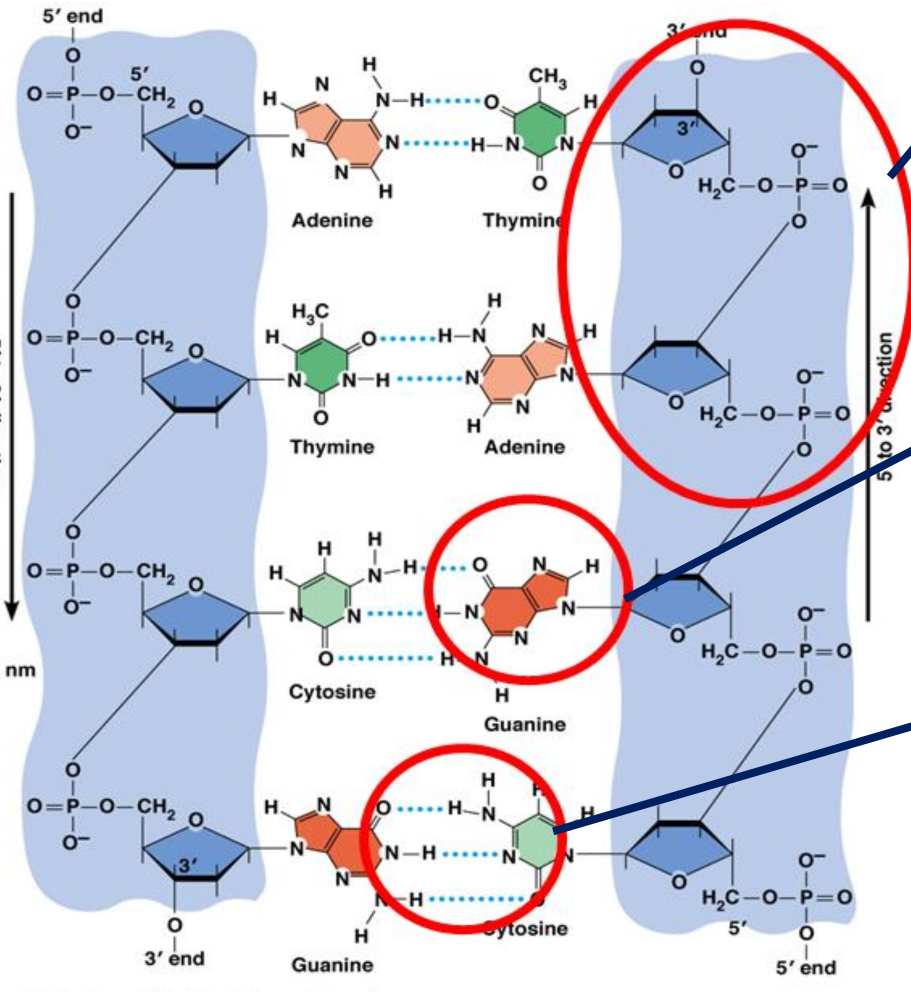
Polynucleotide chain skeleton structure:



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



A) DNA double helix

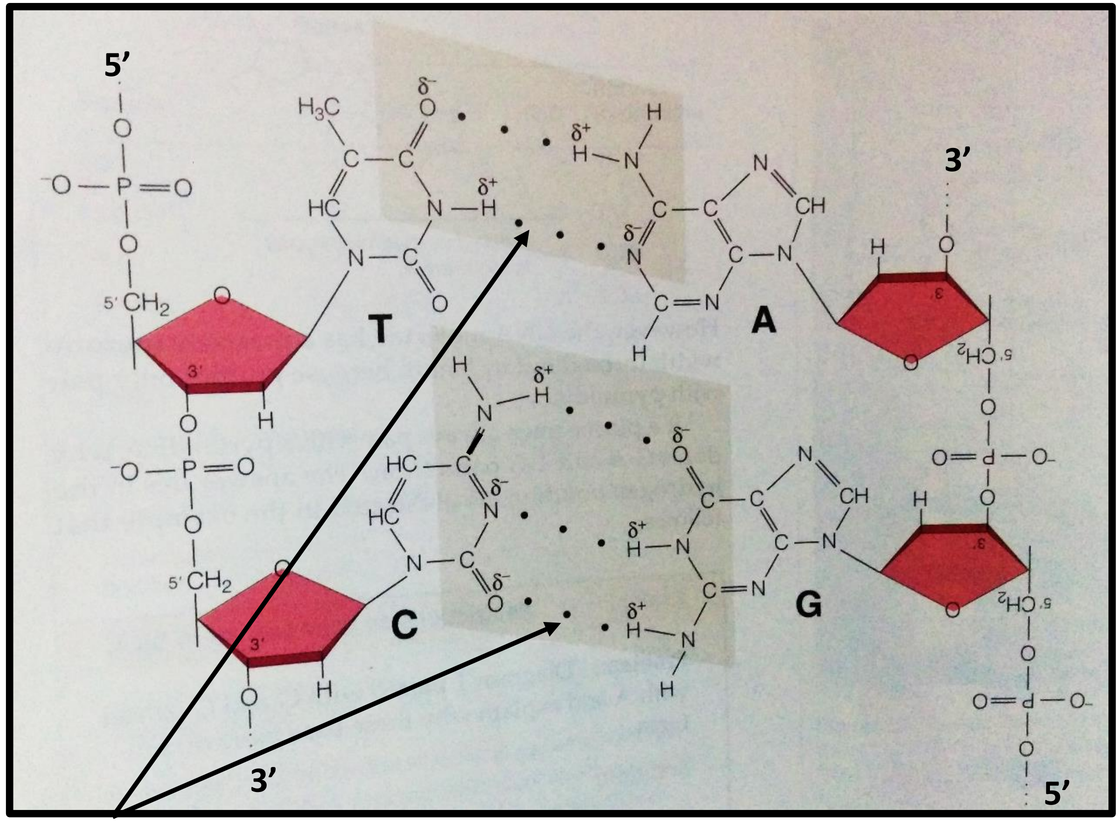


B) Antiparallel orientation ……. 5’-3’ direction and 3’-5’ direction ……of polynucleotide chains held together by hydrogen bonds between bases

- **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

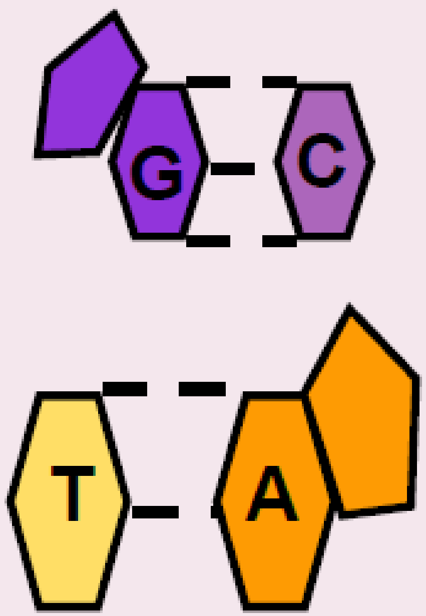
Complementary base pairing Rule

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:

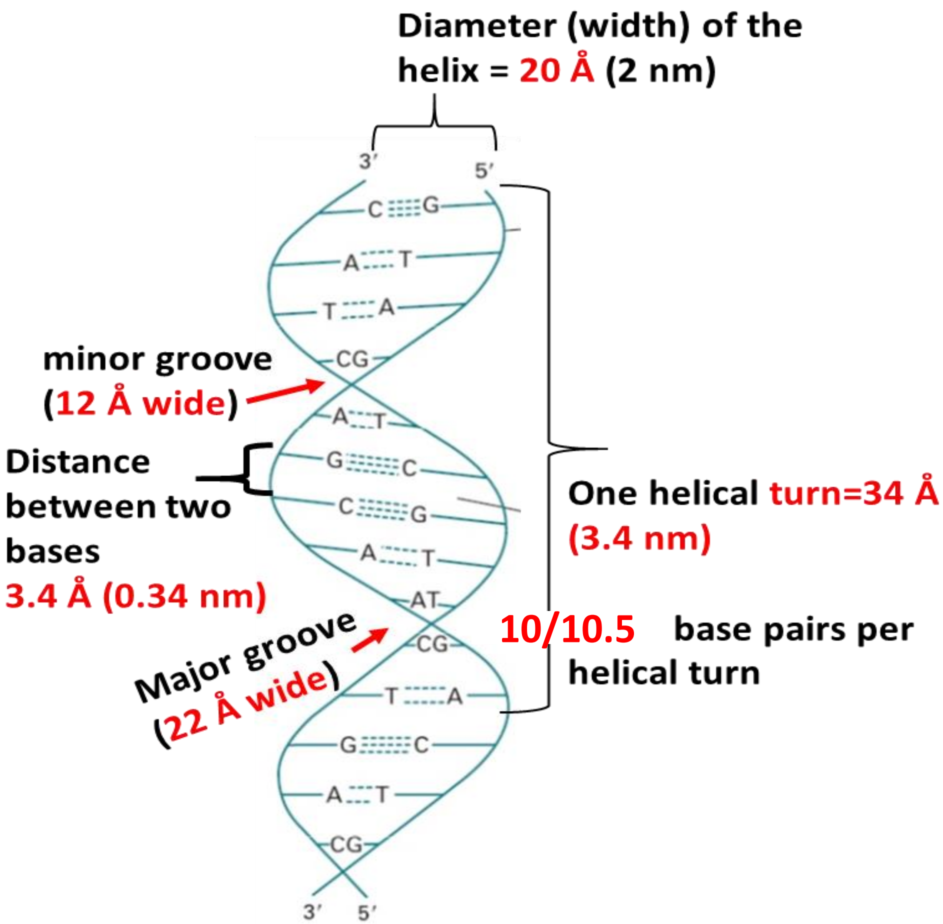
A is always paired with **T**

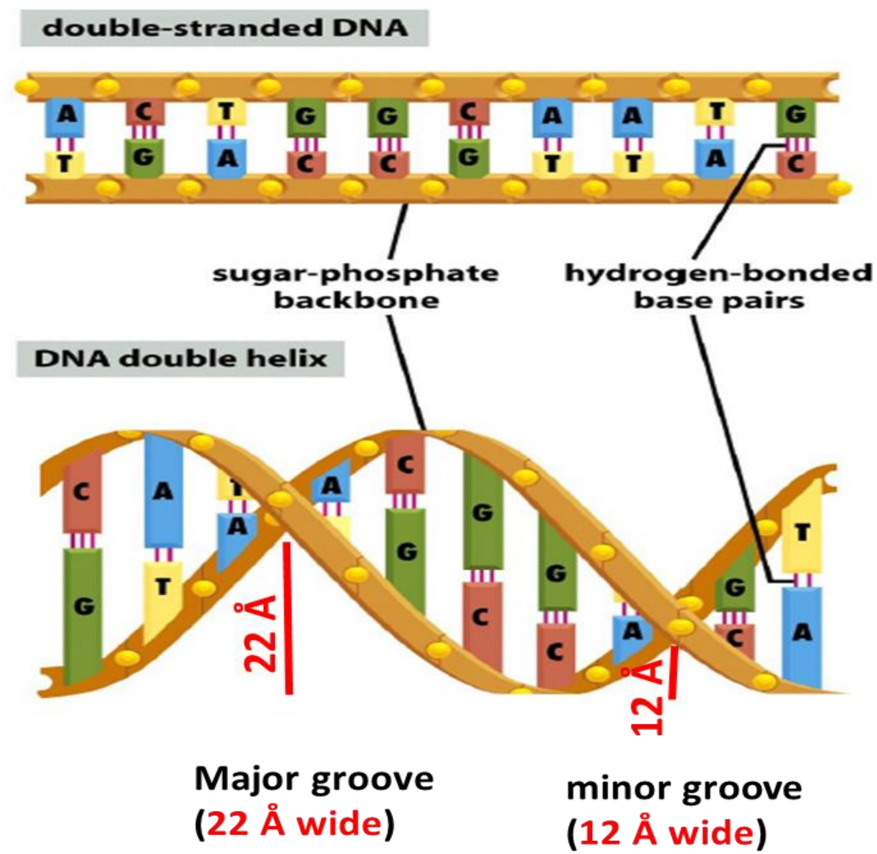
G is always paired with **C**

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
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
Topology of minor groove	Narrow, shallow	Broad, shallow	Narrow, deep

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.

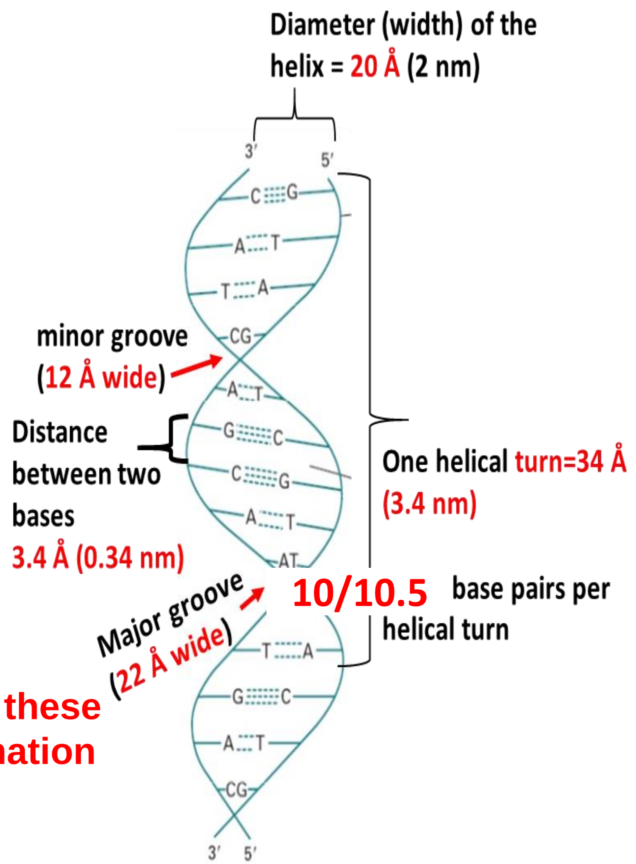
a) How many nucleotide pairs are present?

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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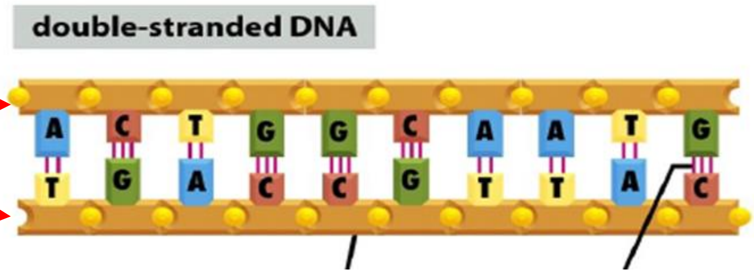
Concept of complementary nucleotide sequences

One of the DNA strand has a sequence

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

5’-ATGTACGATCGATCGTTTAACCGGTAG—3’

?



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 I say total 100 G’s, then there will be also 100 C’s

b) If I say 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.**

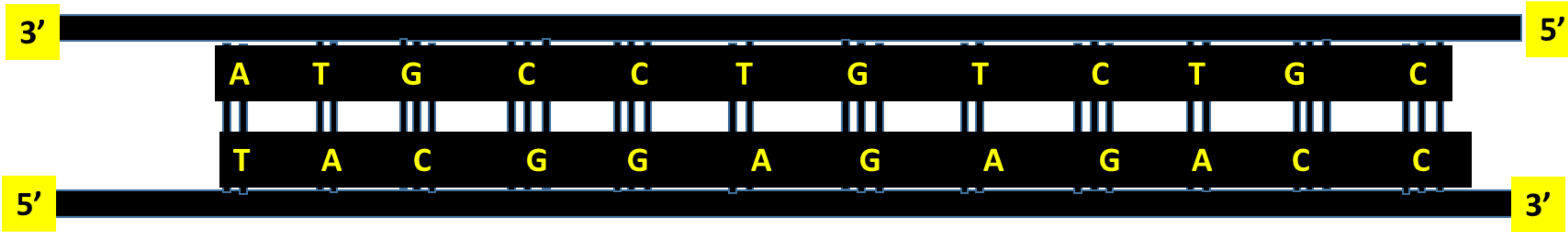
3) But, **A+T** is not equal to **G+C**; or

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;

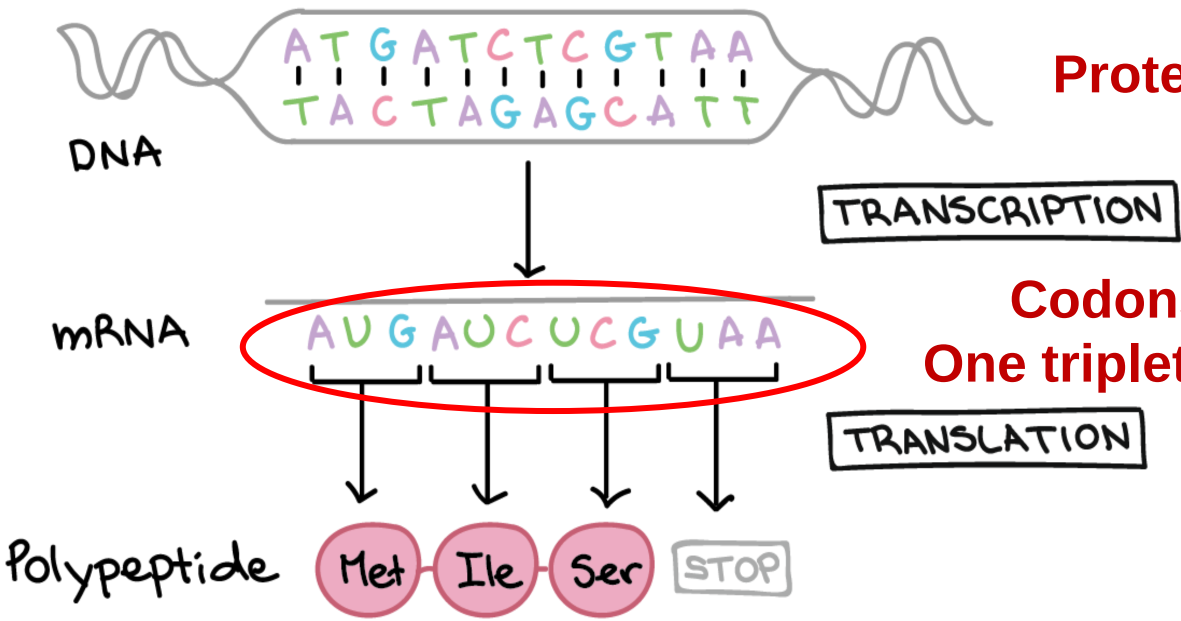
1) Total "A" in above DNA molecule = 5

Then total "T" will be ?

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

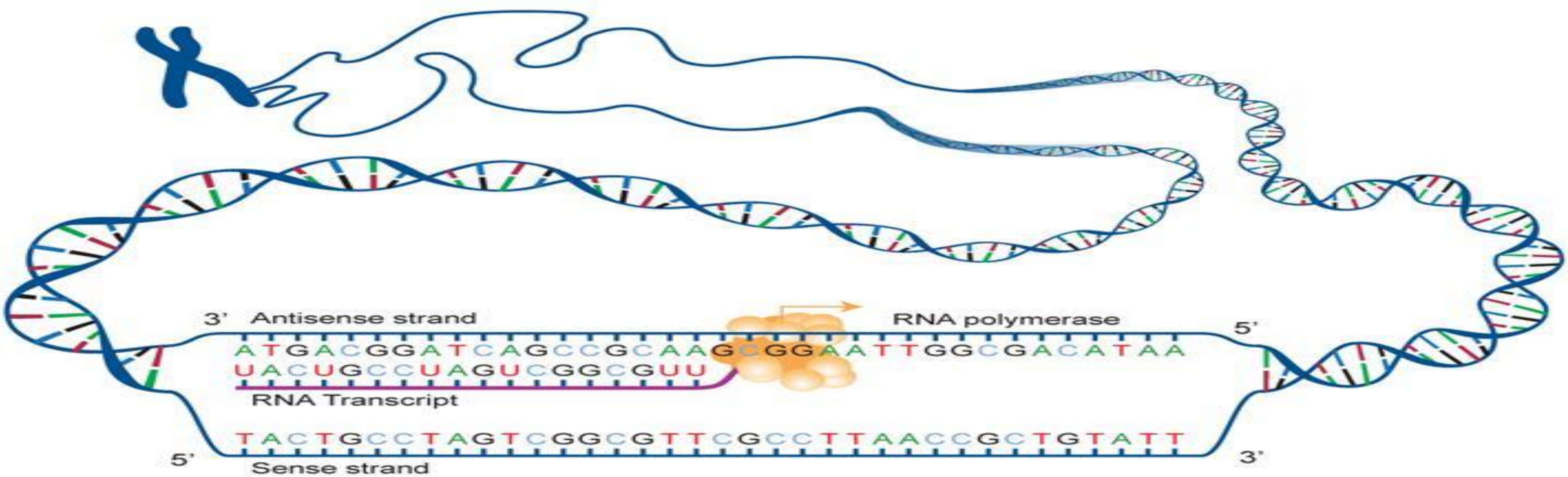
3) If total **deoxyribonucleotides** in above DNA molecule is 24; how many nucleotide pairs will you get?

Concept of Sense and antisense strands of DNA



Protein-coding genes

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

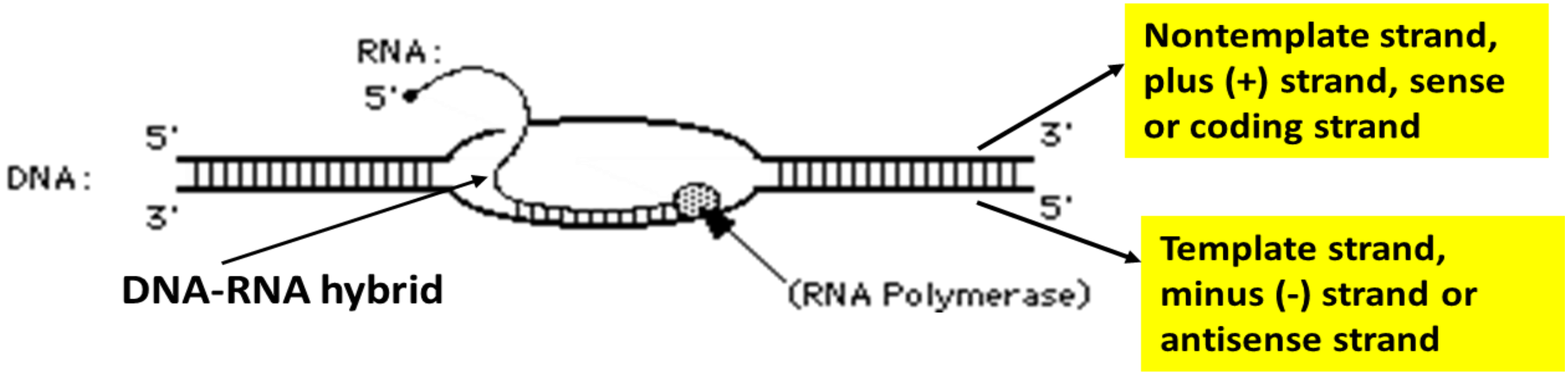


Sense and antisense strands of DNA

- 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

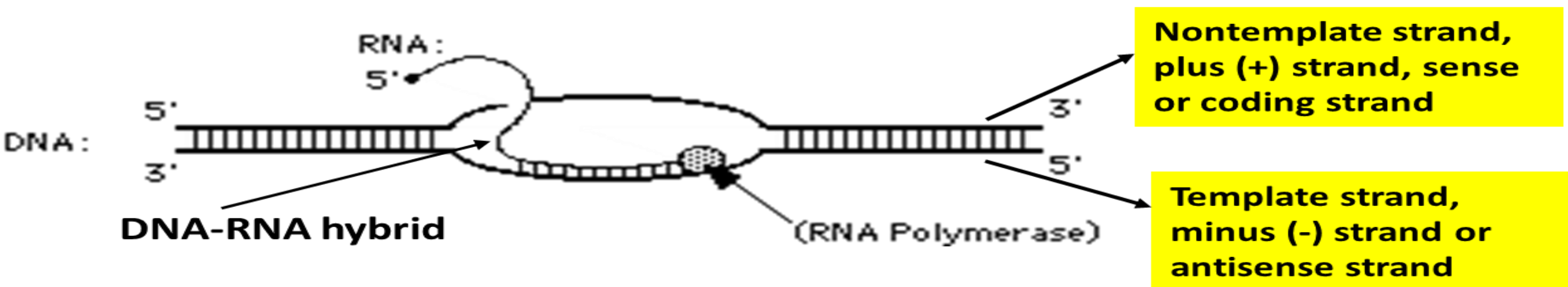
3′-CGTAAGCCGATCATTG-5′ is DNA Template, Antisense, or Noncoding or (-) Strand

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.



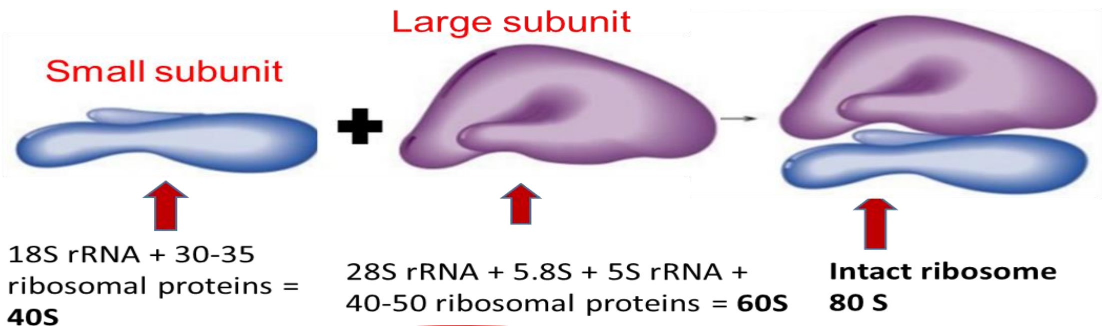
RNA STRUCTURE AND FUNCTIONS

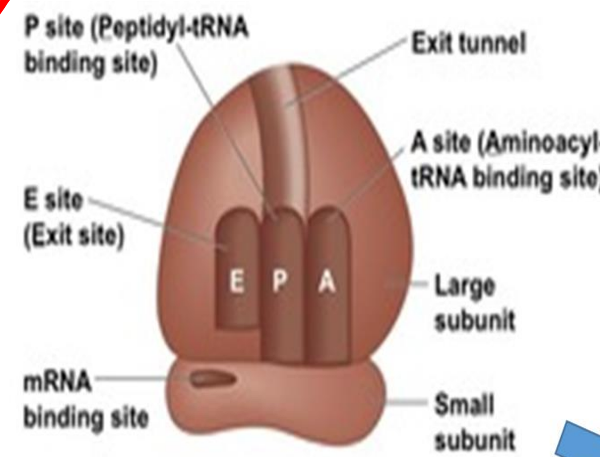
Ribonucleic acid (RNA)

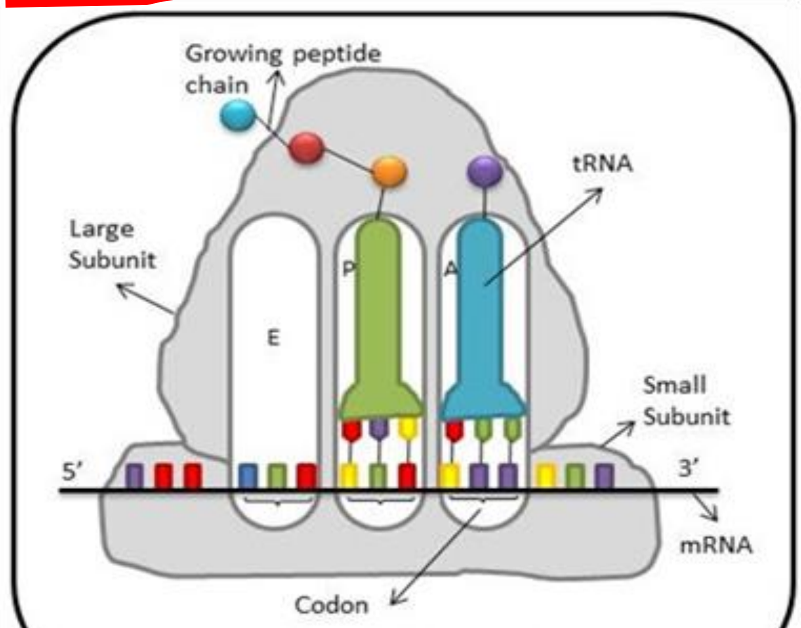
- Different types of RNAs- their structure and functions

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







Translation of mRNA by ribosome

Three important sites in 60S large subunit are:

A-site: aminoacyl tRNA binding site

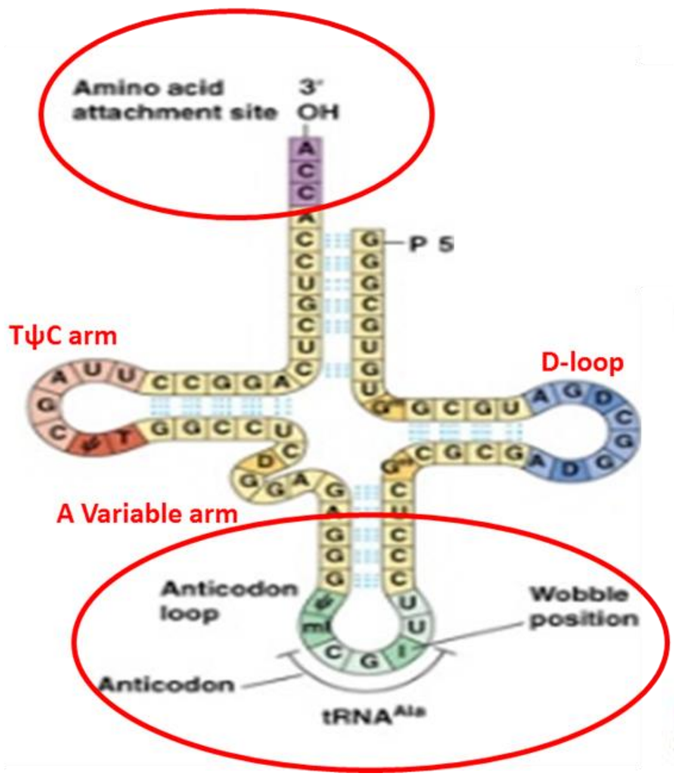
P-site: peptidyl tRNA binding site

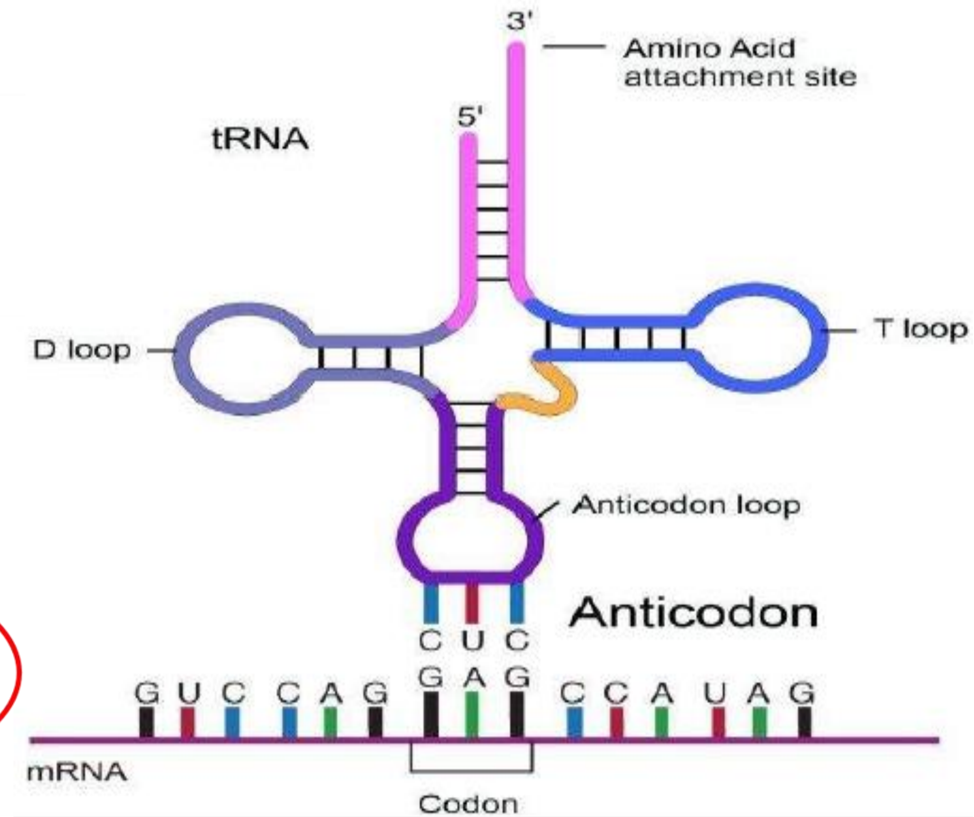
E-site: free tRNA with no amino acid or outgoing tRNA. "E" for exit.

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.

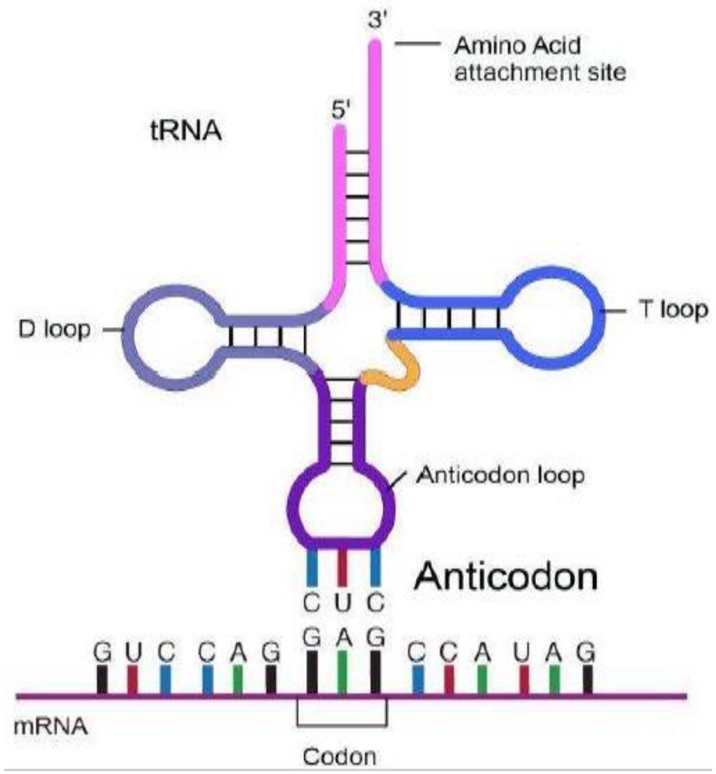




➢ They transfer the amino acids from cytoplasm to the protein synthesizing machinery, hence the name t RNA.

➢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.

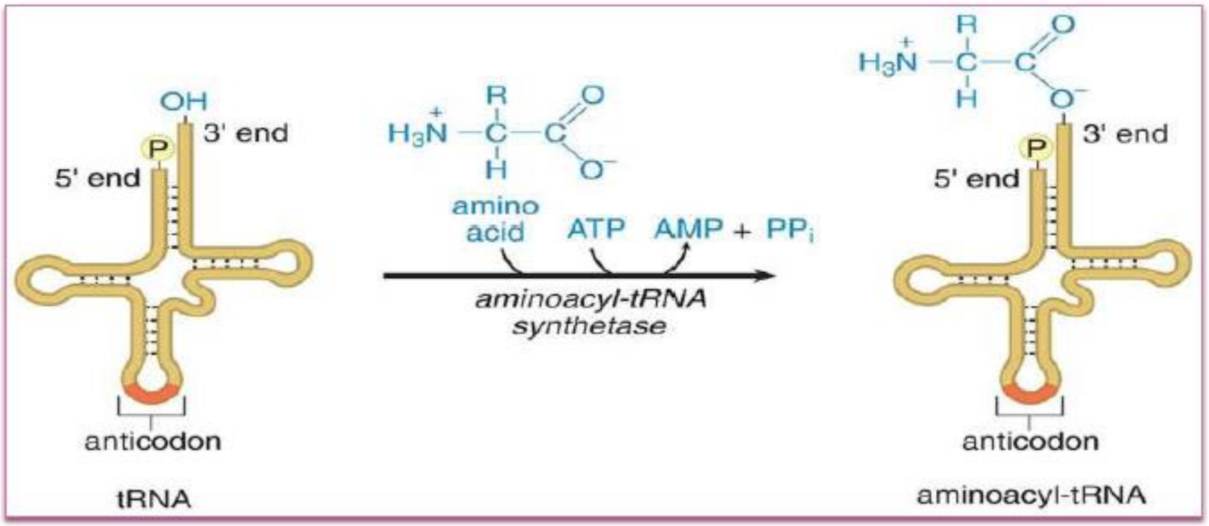


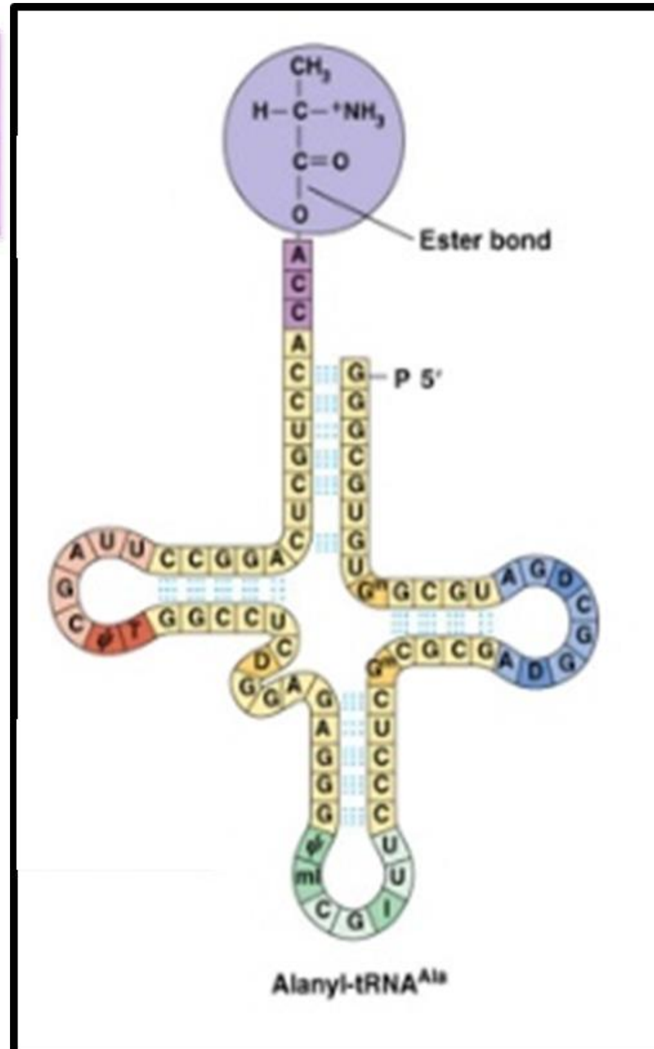
➢Anticodon site –

- 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.

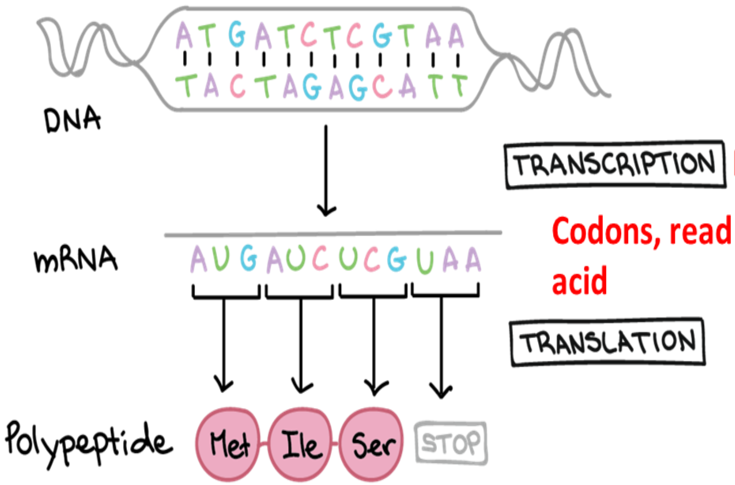
Activation of tRNA or tRNA charging or aminoacylation

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





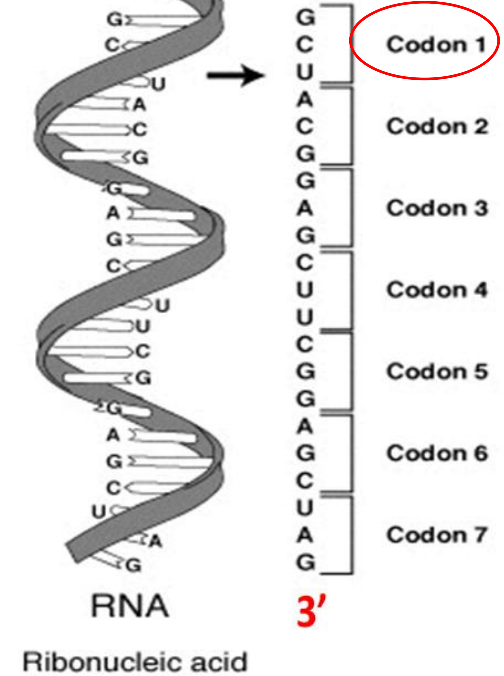
Messenger RNA (single stranded Nucleic Acid)



Protein -coding genes

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

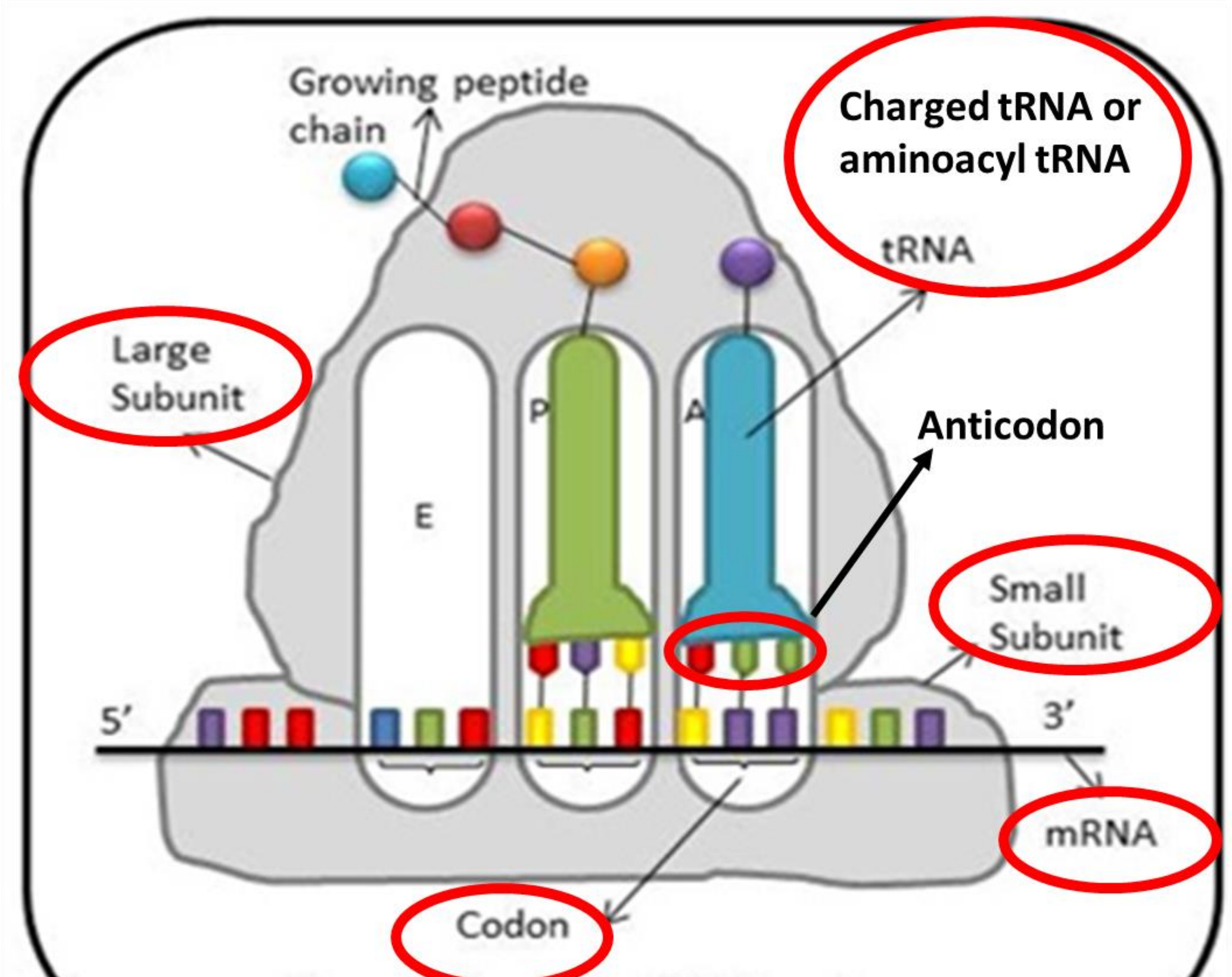
For one amino acid



- 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)

As a whole rRNA, tRNA and mRNA in protein synthesis process…..Translation



Translation of mRNA by ribosome

Sample questions

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

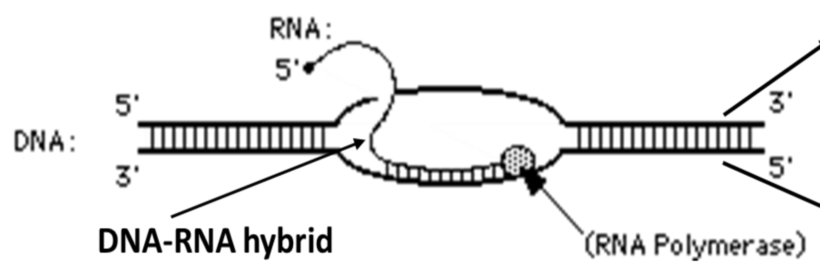
5'- GCTAGCTAAACCTTAAGGGCATTTCCG-3'…… (One strand of DNA)

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?



Nontemplate strand, plus (+) strand, sense or coding strand

Template strand, minus (-) strand or antisense strand

Feature	B-DNA	A-DNA	Z-DNA
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**