Unit 1. Nucleic acids: Structure and Function

Course code: SC301

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What are Nucleic acids?

Nucleic acids

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

2. 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 tRNA

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

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

5. Energy Transfers-

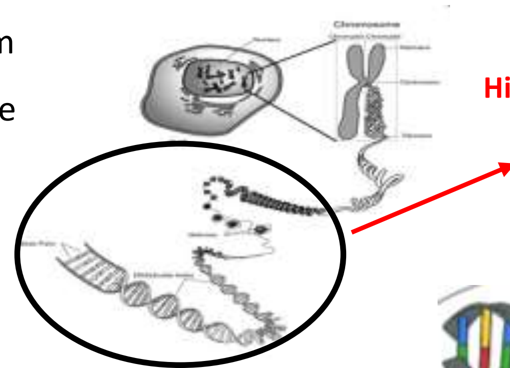
ATP (adenosine triphosphates)

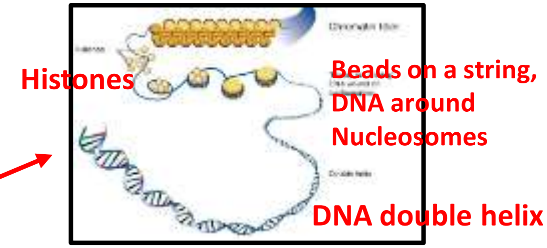
NAD (Nicotinamide adenine dinucleotide)

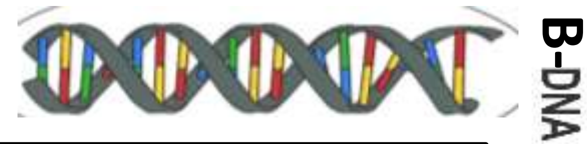
Function and Type of Nucleic acids

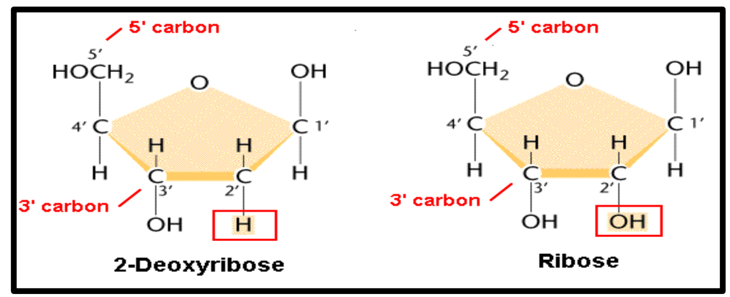
1) DNA…………stores genetic information in the form of genes; found inside the nucleus, packed with histone proteins

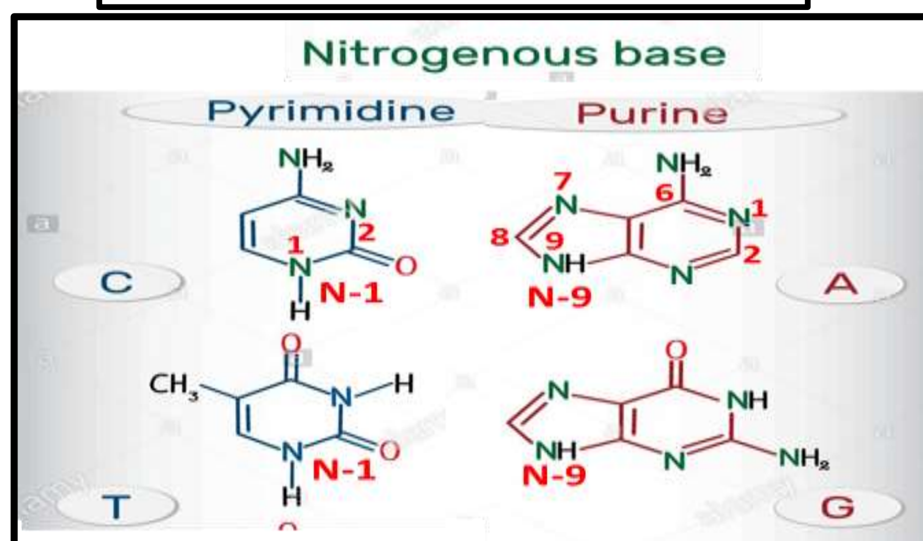
- **Deoxyribonucleic acid**; deoxyribonucleotide monom "Deoxy" because "**one oxygen**" is removed from the **O**H of **carbon no. 2** of **ribose** sugar and making it deoxyribose.
- **Double helical** (**double helix**) with two poly deoxyribonucleotide chain / or simply you can say, two polynucleotide chain.
- **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









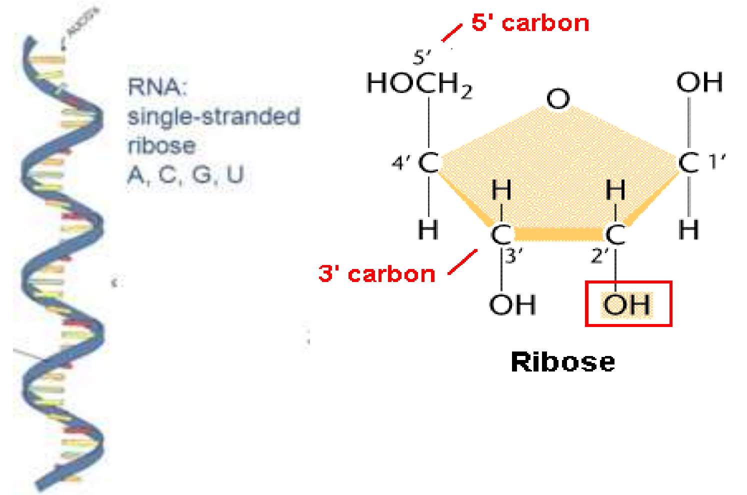


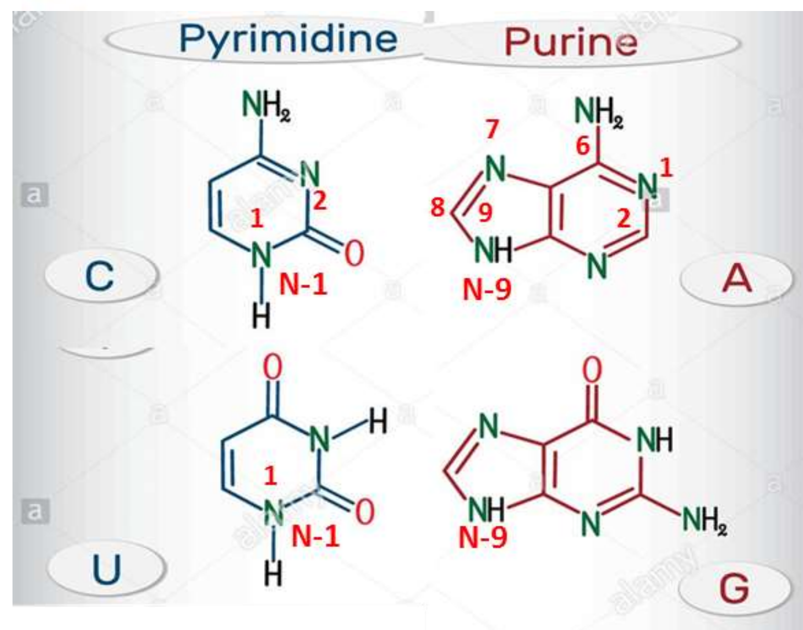
2) RNA…………they are involved in protein synthesis process; all three types of RNA (rRNA; tRNA; mRNA) are assigned specific roles found inside the nucleus and cytoplasm

- ✓ **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.

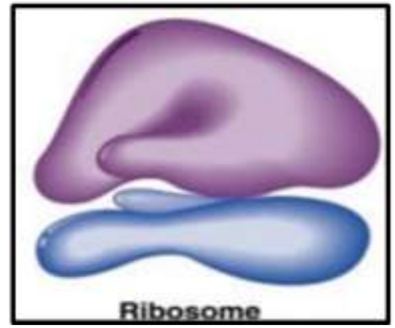
- ✓ **mRNA** carries **genetic code messages** from DNA and **which is decoded to** protein information with the help of rRNA and tRNA.
- ✓ **Nitrogenous bases**…….. Adenine (A) , Guanine (G) are purine form….9 membered ring); Cytosine (C) and Uracil (U) pyrimidine form….. 6 membered ring)
- ✓ Presence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

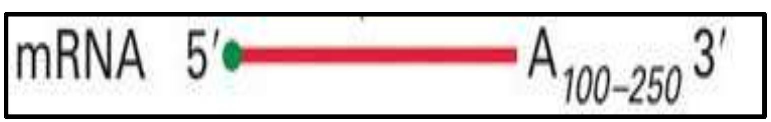


1. **Ribosomal RNA (rRNA): Major component of ribosomes where mRNA is translated to protein.**

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.

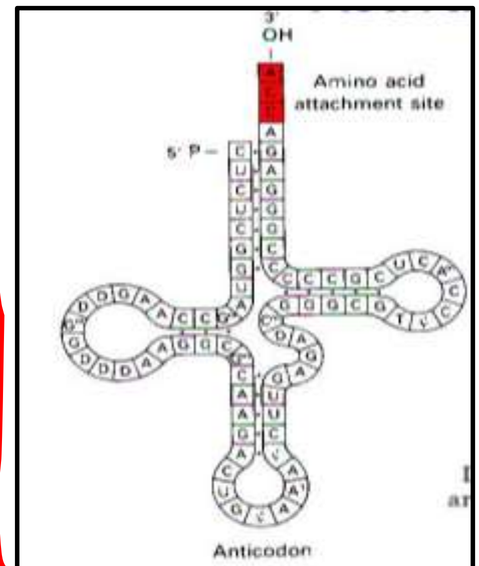
3. Messenger RNA (mRNA): mRNA is a complementary copy of selected regions of the DNA. It carries the genetic message from the nucleus to the cytoplasm and acts as the template for protein synthesis.



3. 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

2. Transfer RNA (tRNA)



2. 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

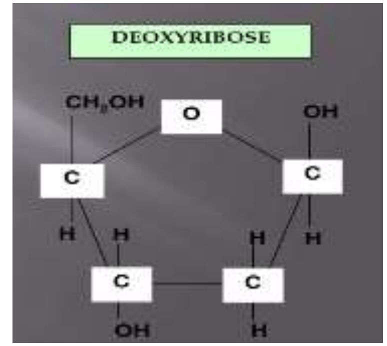
Structural composition of DNA and RNA

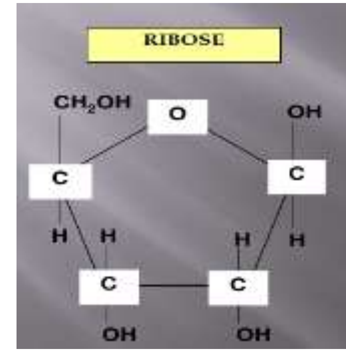
1. Phosphate group

2. Sugar / monosaccharide

DNA has **Deoxyribose**

RNA has **Ribose**

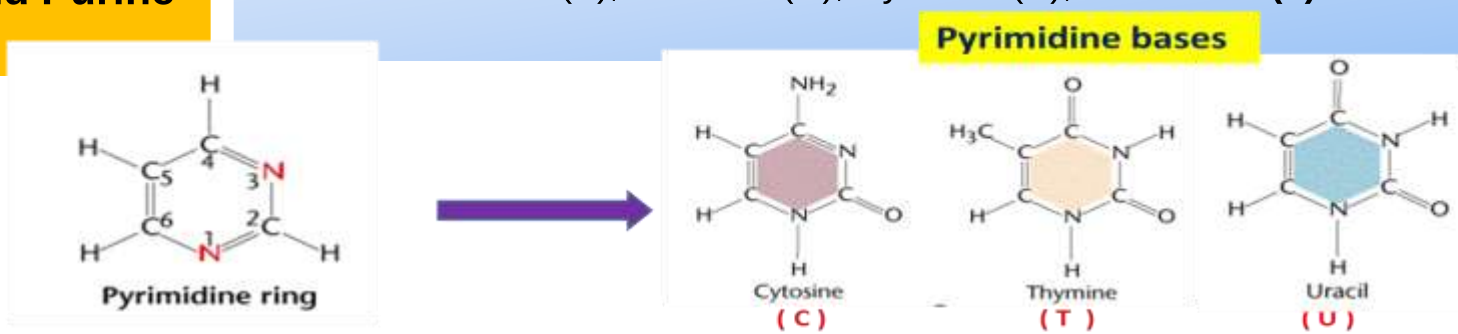


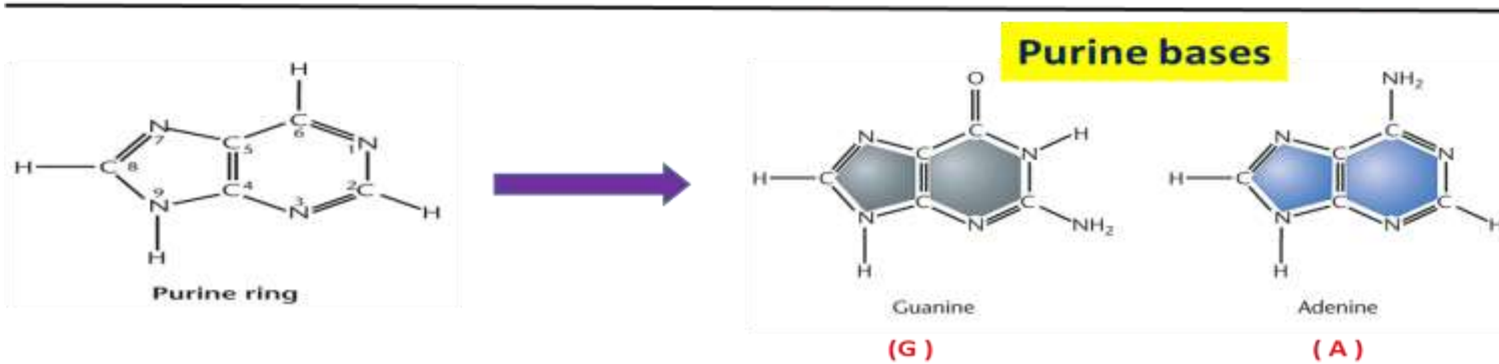


3. Nitrogenous bases (Pyrimidine and Purine bases)

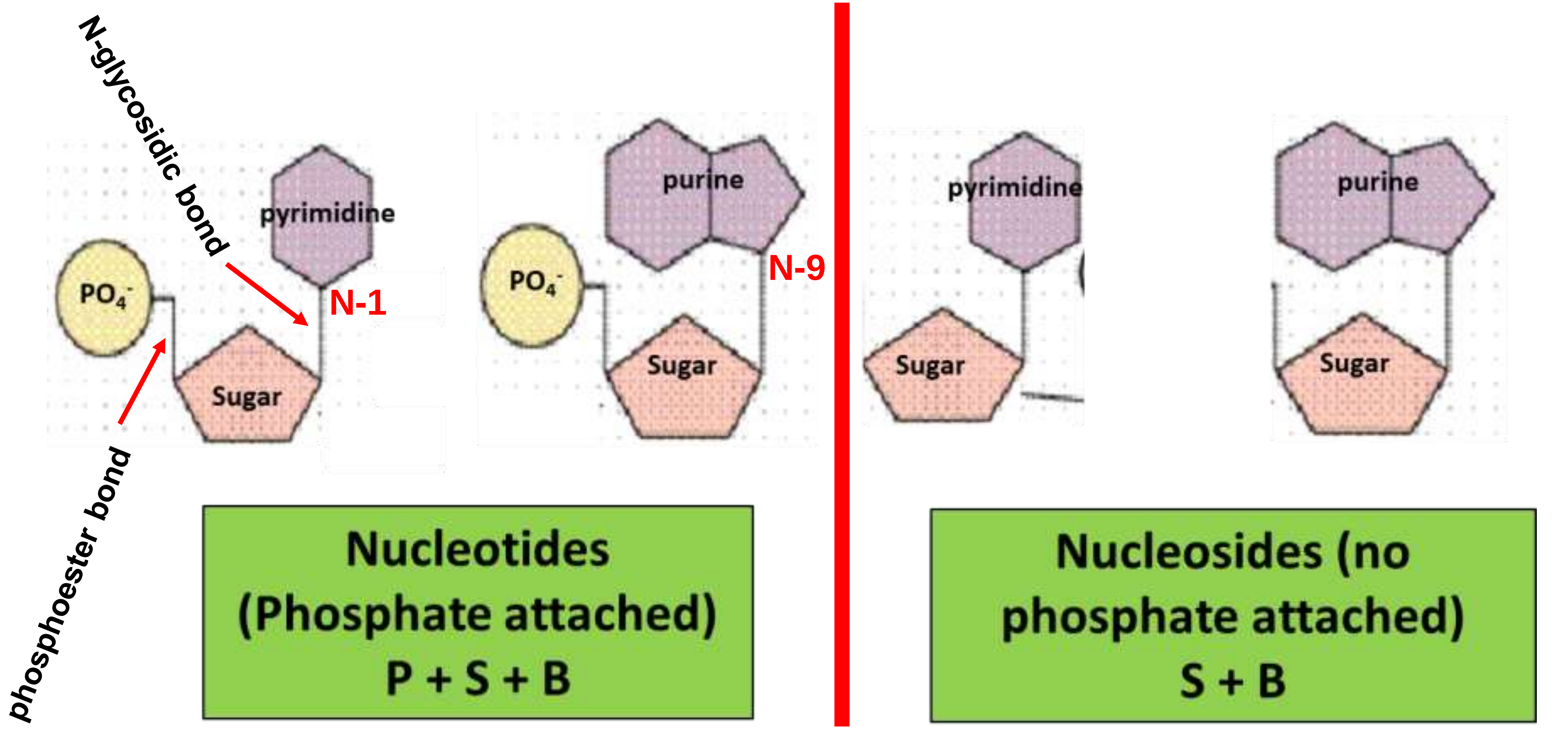
DNA has Adenine (A); Guanine (G); Cytosine (C); and **Thymine (T)**

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





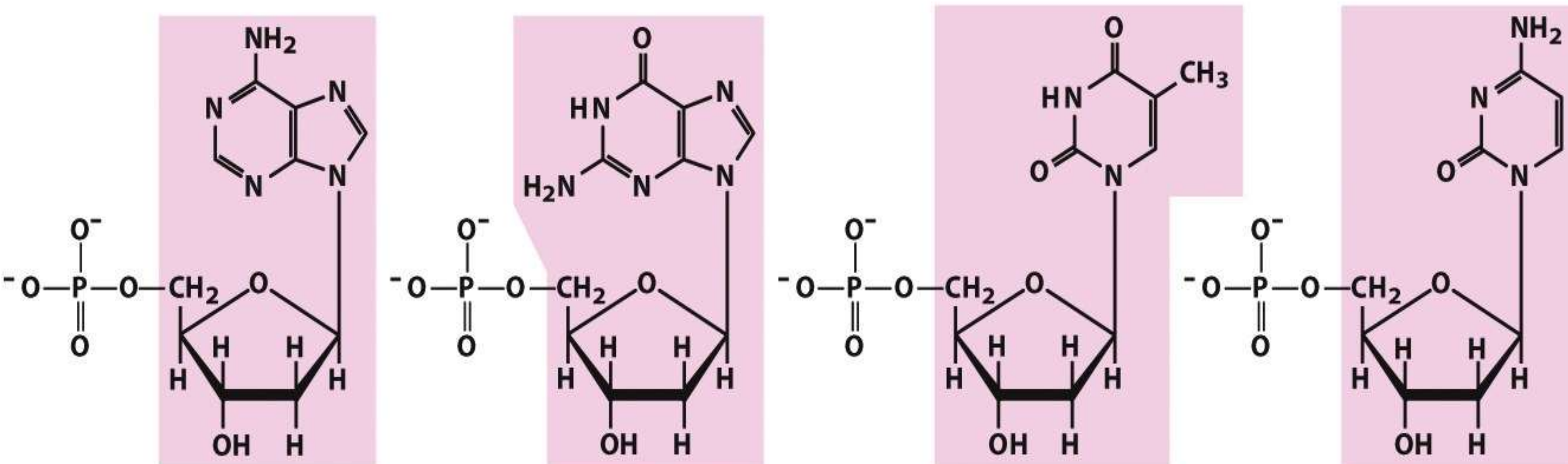
DNA and RNA is a polymer of Nucleotide. What is a nucleotide?



- 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**.

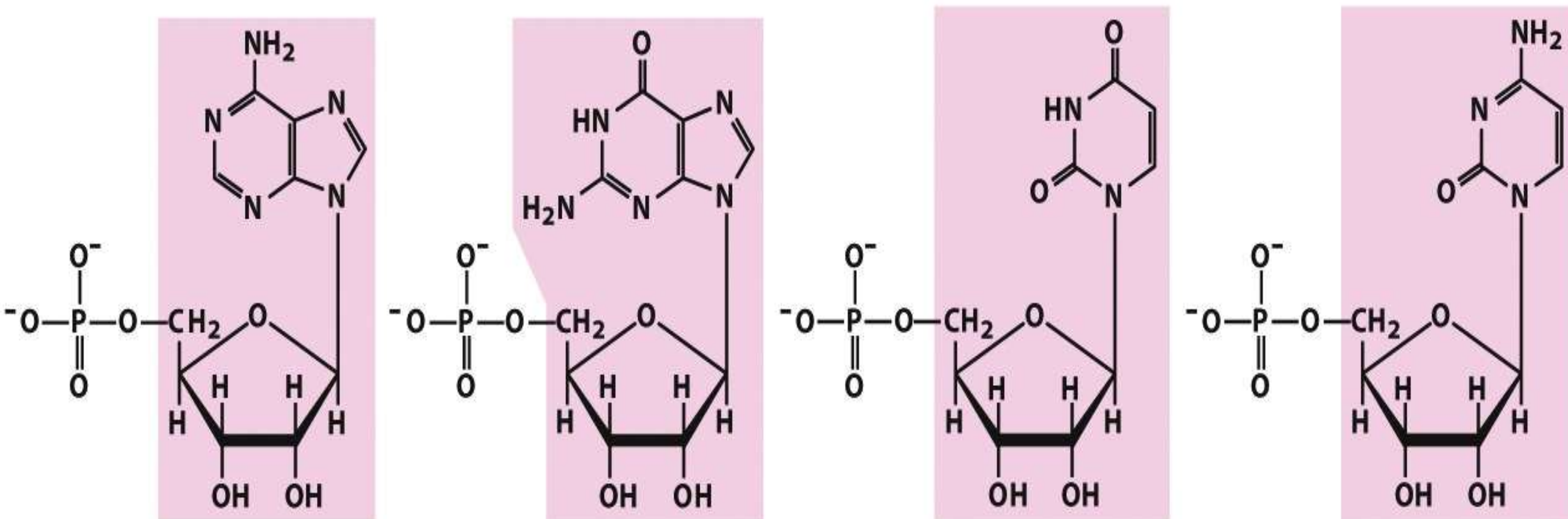
Nomenclature: how nucleotide and nucleosides are named

1. 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

2. Ribonucleotides- monomeric units of RNA



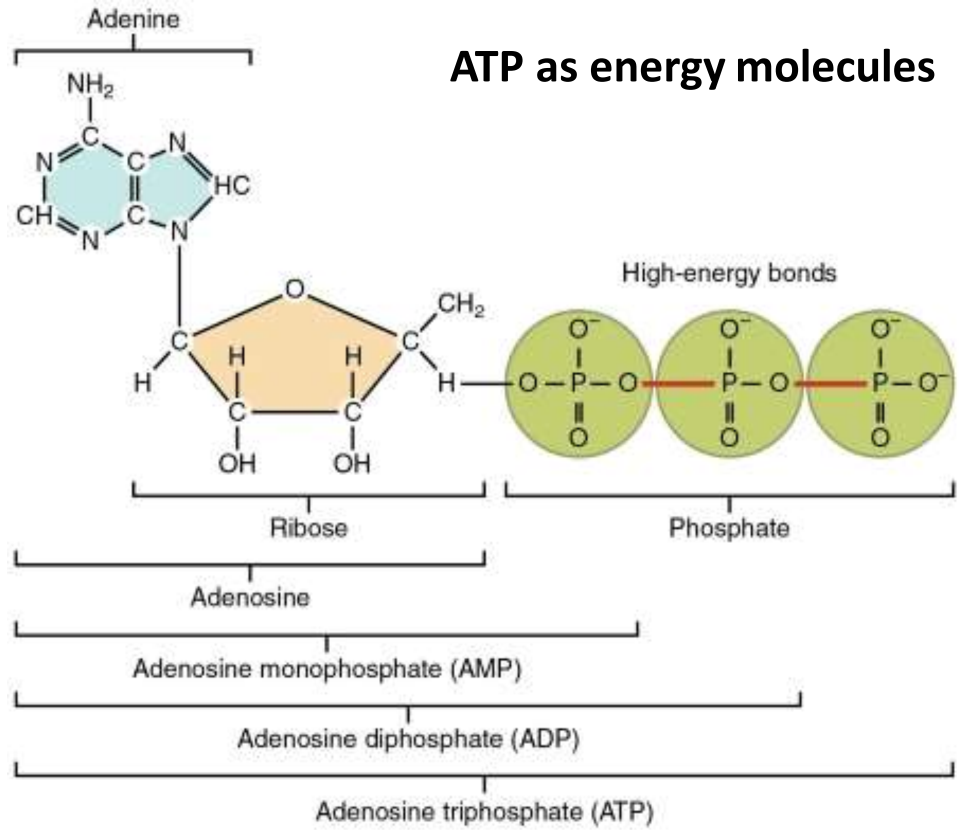
Nucleotide:	Adenylate (adenosine 5′-monophosphate)	Guanylate (guanosine 5′-monophosphate)	Uridylate (uridine 5′-monophosphate)	Cytidylate (cytidine 5′-monophosphate)
Symbols:	A, AMP	G, GMP	U, UMP	C, CMP
Nucleoside:	Adenosine	Guanosine	Uridine	Cytidine

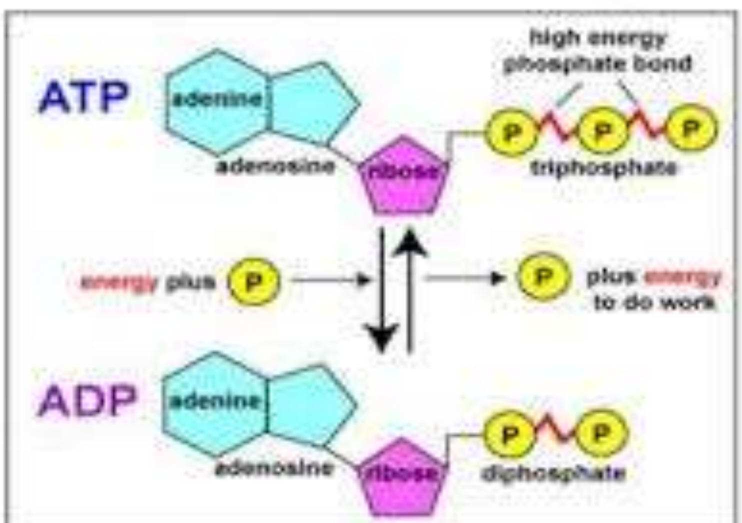
Base	Nucleosides	Nucleotides
RNA		
Adenine (A)	Adenosine (A)	Adenosine 5'-monophosphate (AMP)
Guanine (G)	Guanosine (G)	Guanosine 5'-monophosphate (GMP)
Cytosine (C)	Cytidine (C)	Cytidine 5'-monophosphate (CMP)
Uracil (U)	Uridine (U)	Uridine 5'-monophosphate (UMP)
DNA		
Adenine (A)	Deoxyadenosine (A)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

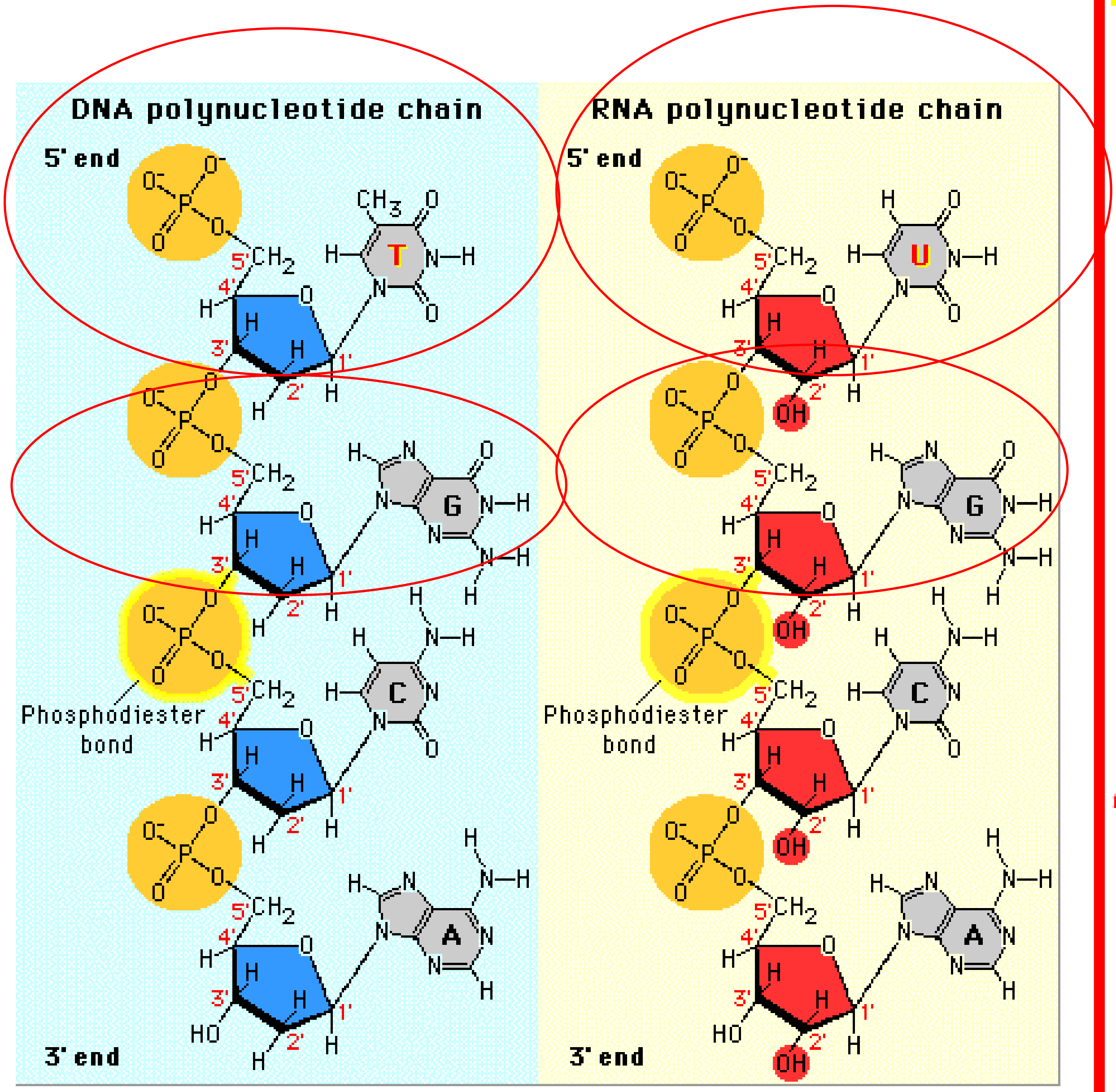
ADP + P to ATP = energy stored

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

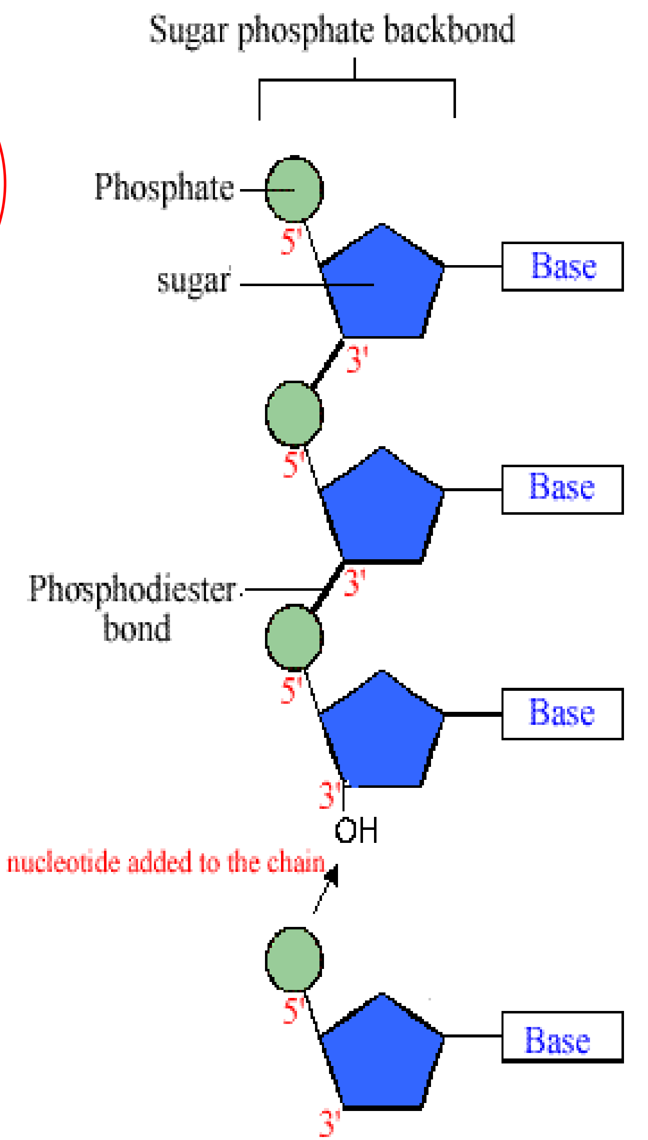
  - $ATP + H_2O \rightarrow ADP + P_i$ $\Delta G = -7.3$ kcal/ mol **(exergonic)**

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

Finally polynucleotide chain has the structure below:



polynucleotide chain skeleton structure:

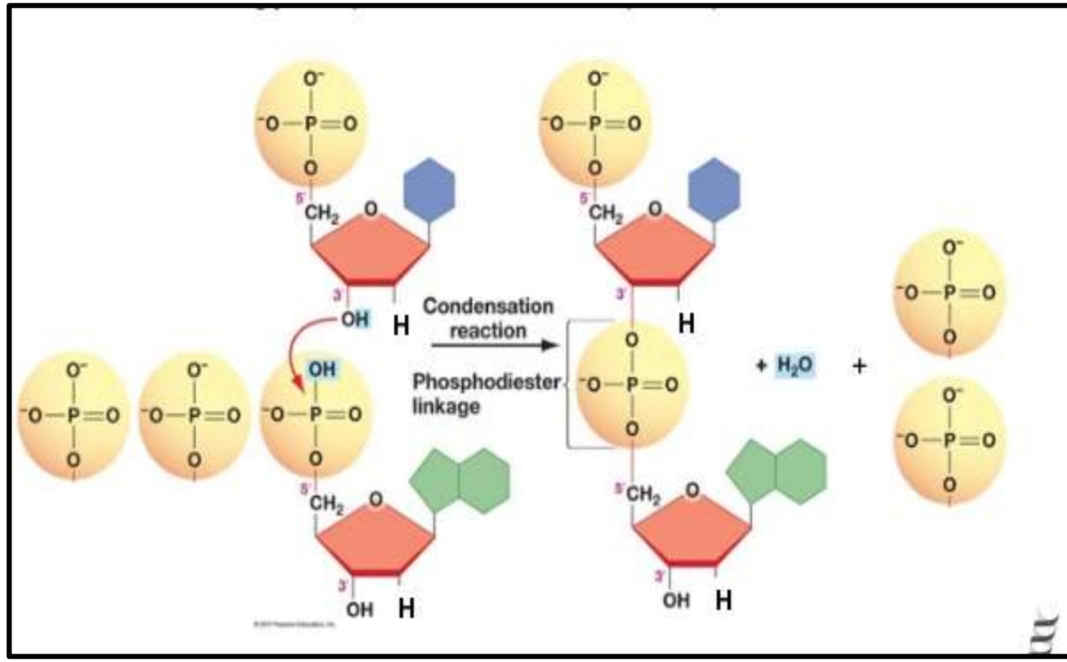


How one polynucleotide chain is made?

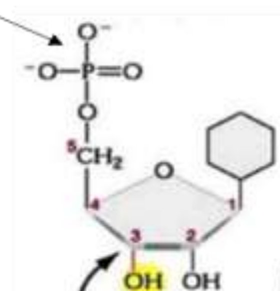
3'-5' Phosphodiester linkage, formed by condensation reaction by removal of water molecule

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**

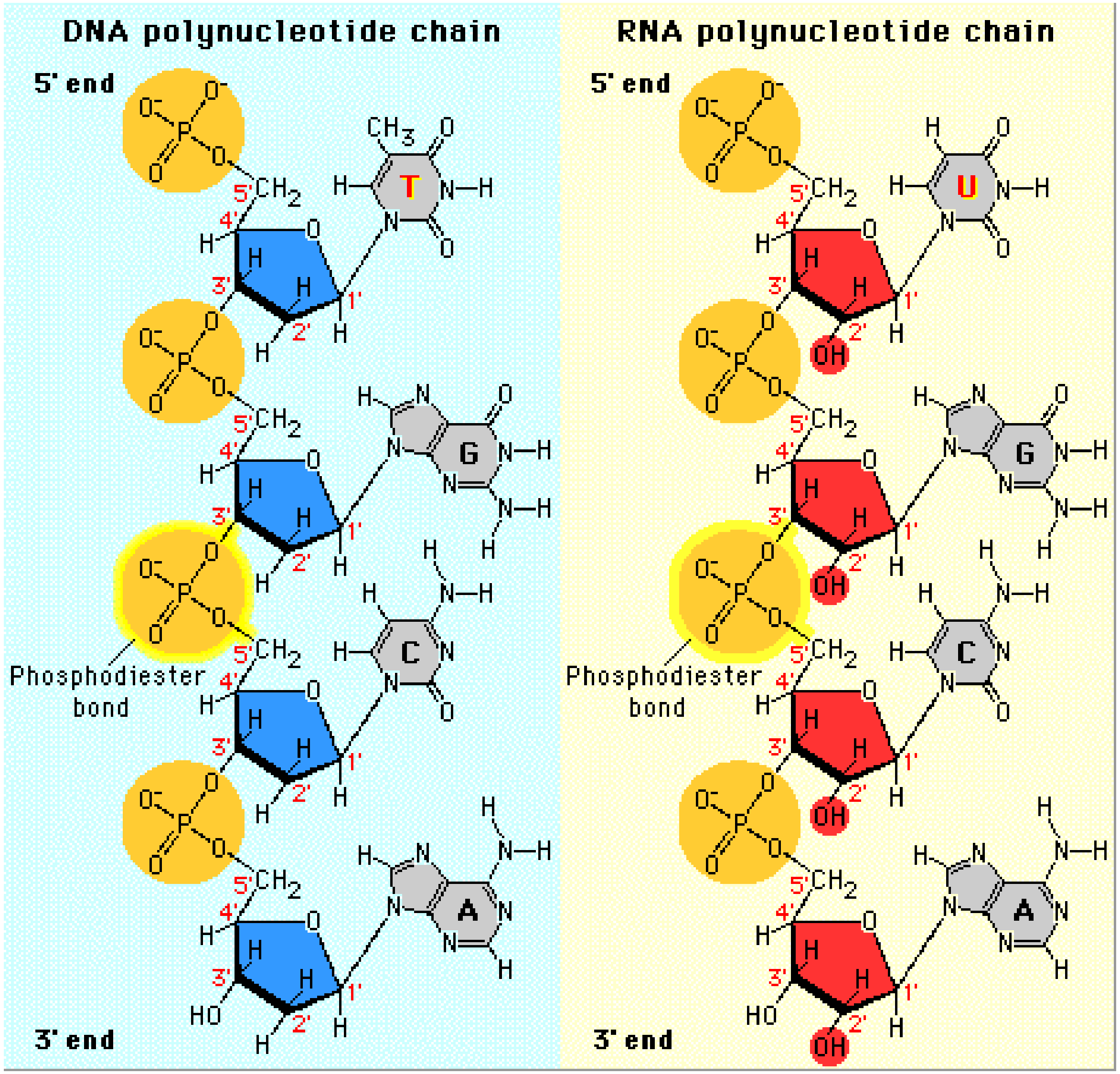


$5'\text{-}PO_4^{2-}$ —— $3'\text{-}OH$

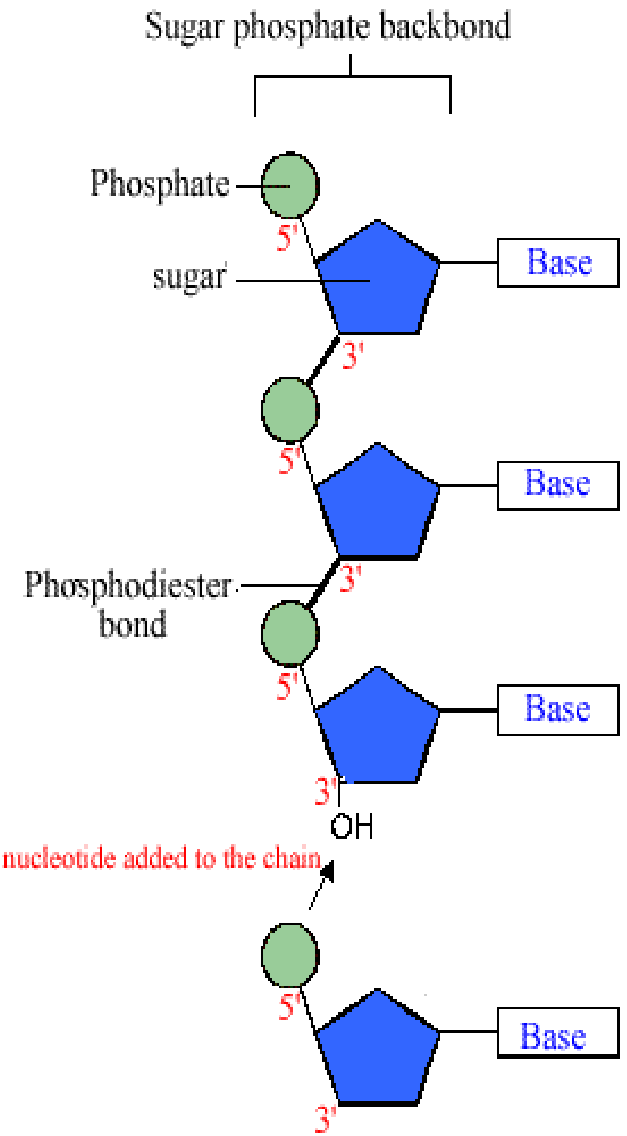


Direction of polynucleotide synthesis is in **“5'-3' direction”.**

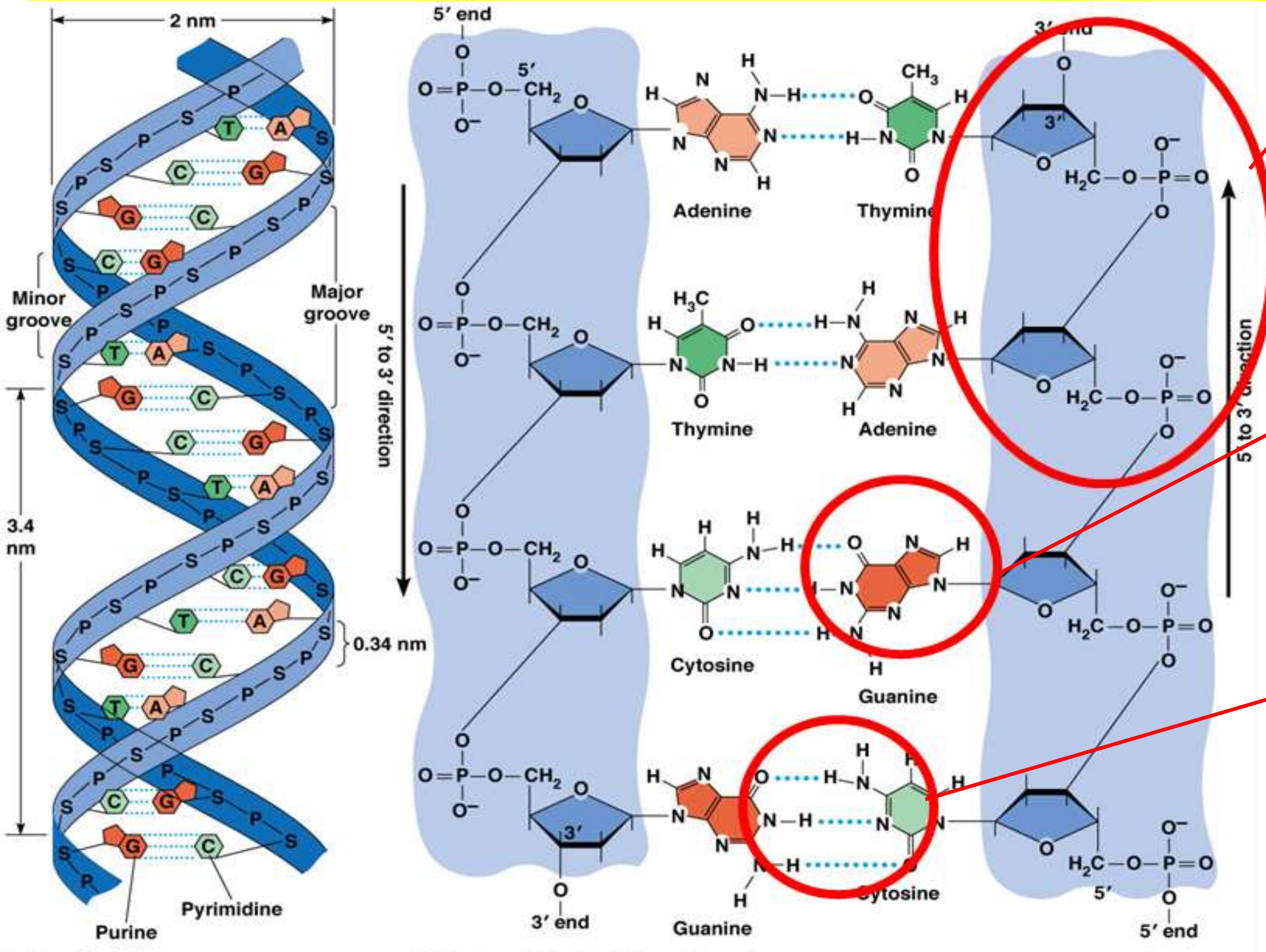
Finally polynucleotide chain has the structure below:



polynucleotide chain skeleton structure:



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



A) DNA double helix

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

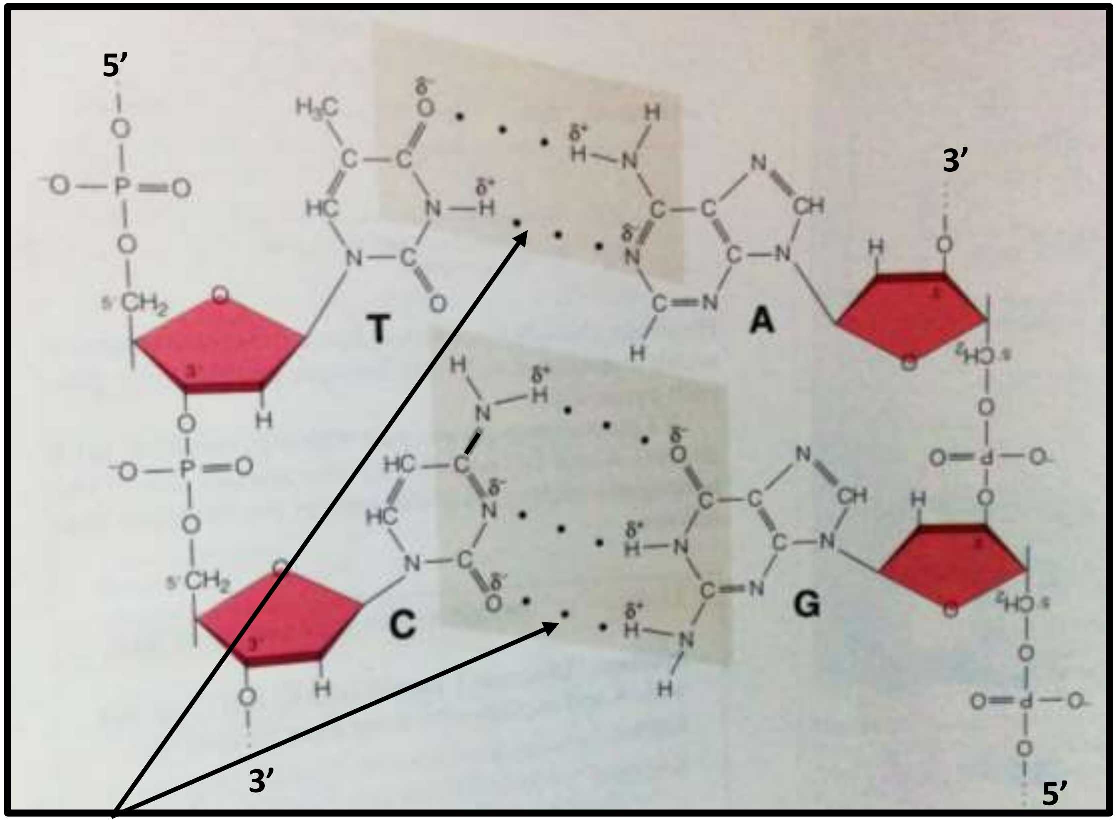
- Phosphate-deoxyribose (in blue shade) forms the backbone of the DNA double helix.
- Nitrogenous bases (Guanine, Adenine, Thymine, Cytosine) face towards inside of the double helix.
- Two polynucleotide strands are stabilized by hydrogen bonds (blue dashed line) between the bases. Adenine pairs with 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.

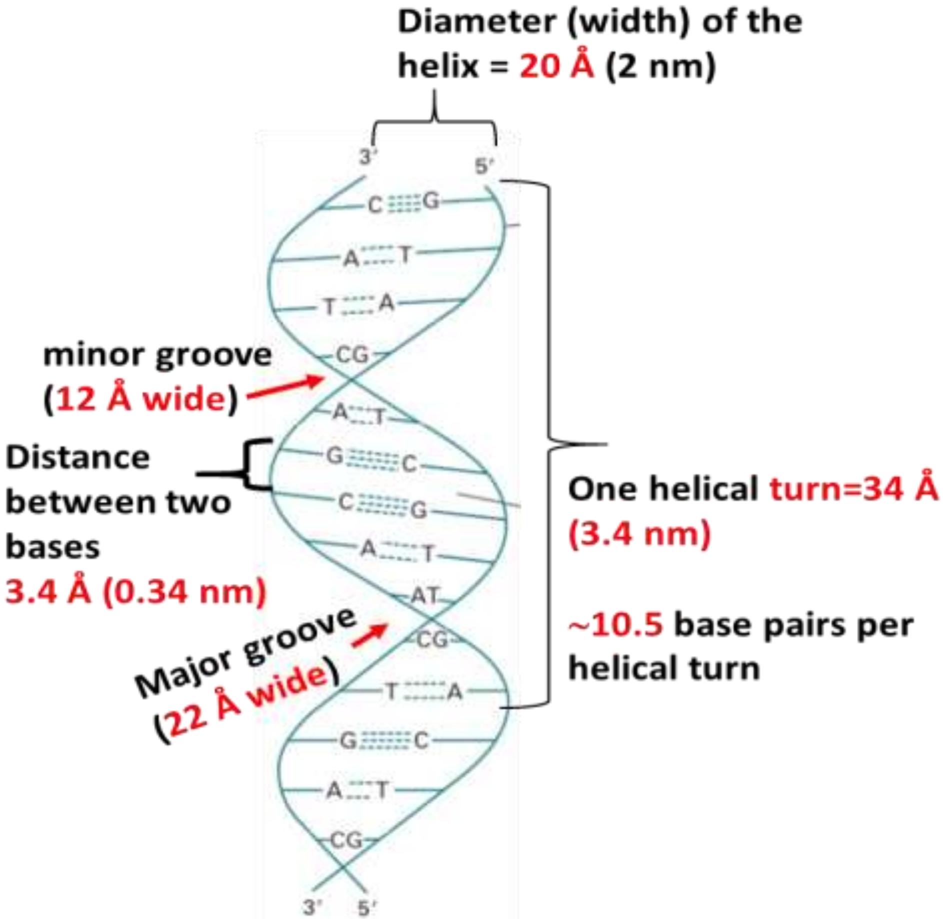
Specific base pair: **purine-pyrimidine** base pair or a **pyrimidine-purine base pair**.

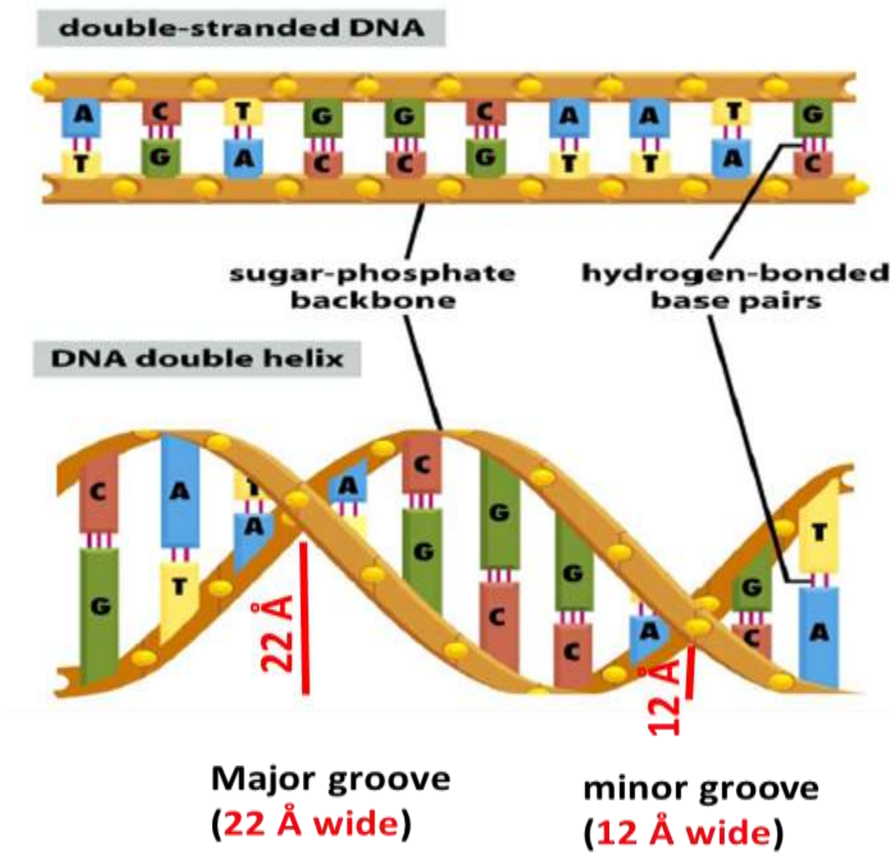
- **Thymine** pair with **Adenine** with two Hydrogen bonds (T=A).
- **Cytosine pair with Guanine** with three hydrogen bonds.



Hydrogen bonds

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

1. Under different conditions such as relative humidity and salt concentration, alternative forms of DNA has been detected.

2. Found only under conditions not normally present in cells.

3. Differ from each other primarily in the degree and direction of helical winding & in the stacking of the bases.

4. 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	3.2	4.5
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 question on structural parameters of DNA…..

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. Assume that B-DNA molecule in a particular chromosome is **50 mm** long. How many **nucleotide pairs** are in this DNA molecule?

3) 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 this information

Feature	B-DNA	A-DNA	Z-DNA
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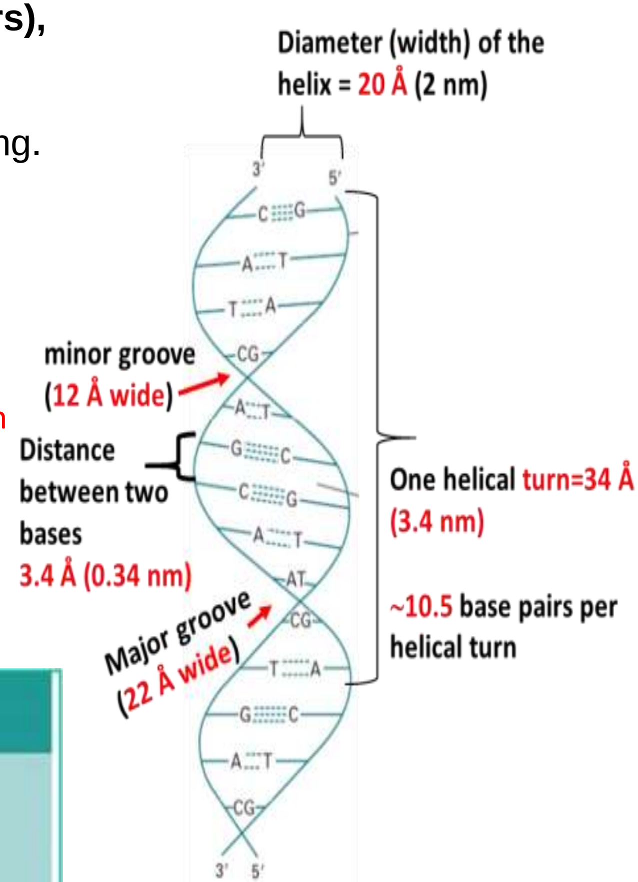


Above 3 Sample questions

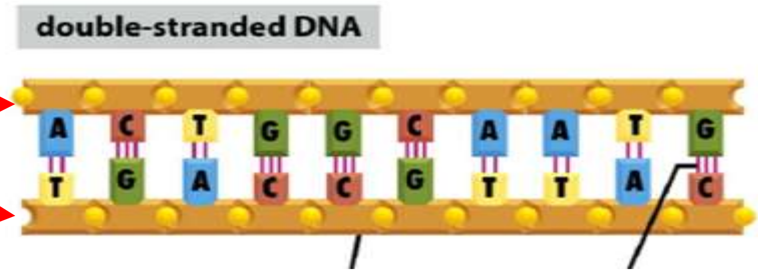
Concept of complementary nucleotide sequences

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

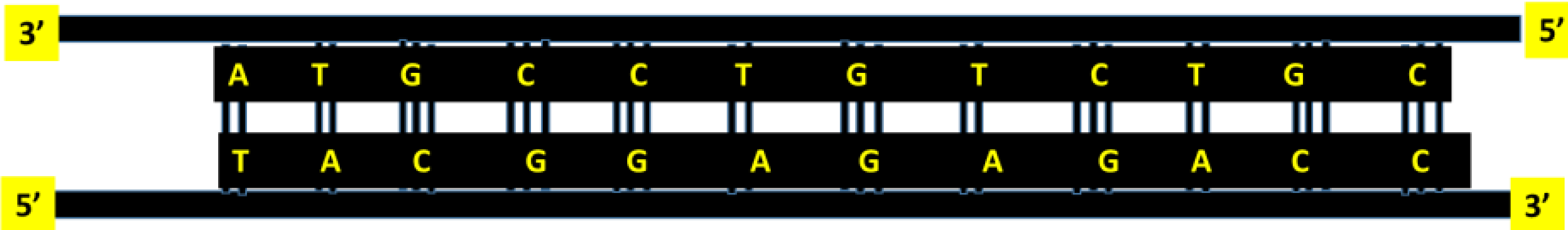
That is, In DNA, if we know the sequence of one DNA strand , the sequence in other DNA strand can be known on the basis of base pairing rule. The sequence on the other strand is called as complementary sequence.

Today's lecture: 17-9-20

Understanding Chargaff's base pairing rule

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, that **the amount of guanine should be equal to cytosine and the amount of adenine should be equal to thymine.**

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?

Chargaff's Base pairing rules

1) Adenine (A) pairs with Thymine (T)

Guanine (G) pairs with Cytosine (C)

2) There is equal amount of **Guanine and Cytosine** or **Thymine and Adenine** in DNA double helix.

Eg ….. 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

3) 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

Based on our understanding on Chargaff's Base pairing rules

1) If "GC", content in DNA of an organism is 60%, then find out the percentage of other bases (A, C, and T)?

Ans: "GC" content means; **G+C = 60%;**

and amount of G = C; in a given DNA molecule (According to Chargaff analysis);

therefore % G= 30 % or % C= 30 %

T= ? And A=?

If, (A+T)+(G+C) = 100 % ;

Then, A+T = 40%;

therefore, A= 20 % and T= 20%

A = 20%
T = 20%
G = 30%
C = 30%

Q.2) 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)?

Ans : **G = 20 % of 90,000 = 18,000**

C = 18,000; 20%

A+T= 90,000-36,000 = 54, 000

A = 27, 000; T = 27,000

To find values

A+T = 100-40 = 60 %
A = 30 %
T = 30%

30% of 90,000 = 27,000
A=27,000 and T = 27, 000

To find percentage and values of A and T

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

Ans.) Two cases arises according to question; **4 'G' sand 1 'A'** , or if **2 'A's, then 8 'G's**

- **Ist case**: If G = 4 times of A, and also C=T, then in 11 bases, **there are 1A, 4G, 3C and 3T** in a single stranded DNA. Considering **11 base pairs, there will 4G in top strand of DNA** and **3G in bottom strand due to G and C complementary rule**. Therefore, in 11 base pairs we have **total 7 'G's**

Therefore, In 121 base pairs, 7x11=77 'G's present.

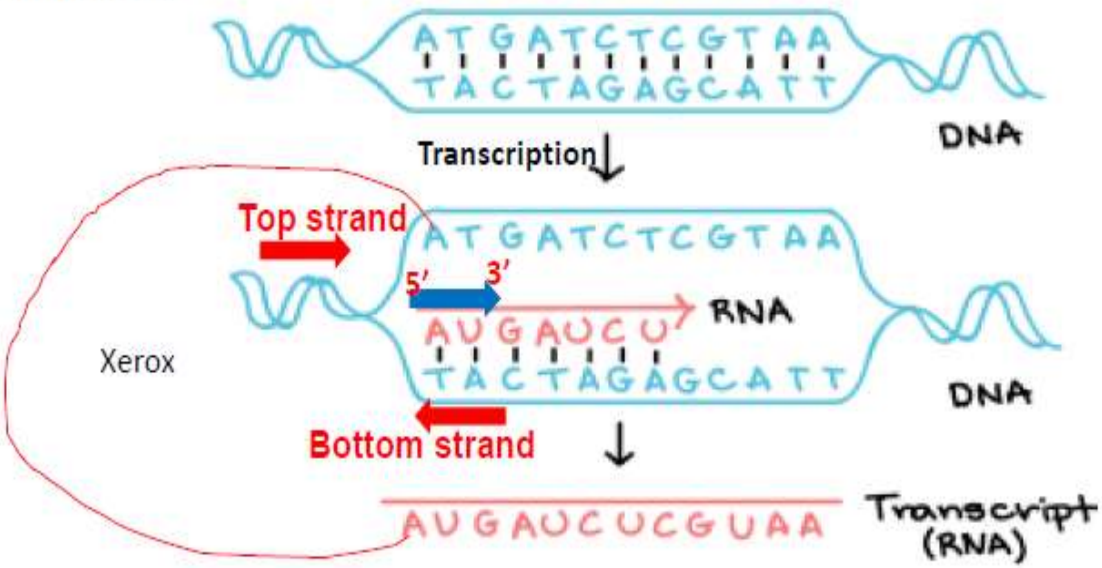
- **IInd case:** not applicable since C=T cannot be maintained according to question

Concept of Sense / non-template / coding and Antisense/ template / coding Strands of a DNA: In context "When there is RNA transcription"

Today's lecture- 21-9-20

- **Writing sequence of mRNA** (carrier of genetic message from DNA)…. Message for amino acids sequence for protein formation.
- Direction of writing the sequence.
- Understanding what is coding / sense /non-template and non-coding / antisense /template strands of DNA.
- Concept of "Triplet codon"

We say, mRNA carries code messages from DNA. How? It is just Xerox of one of the template strand (in image either bottom or top). By process called transcription



DNA;

Double strands or two polynucleotide chains

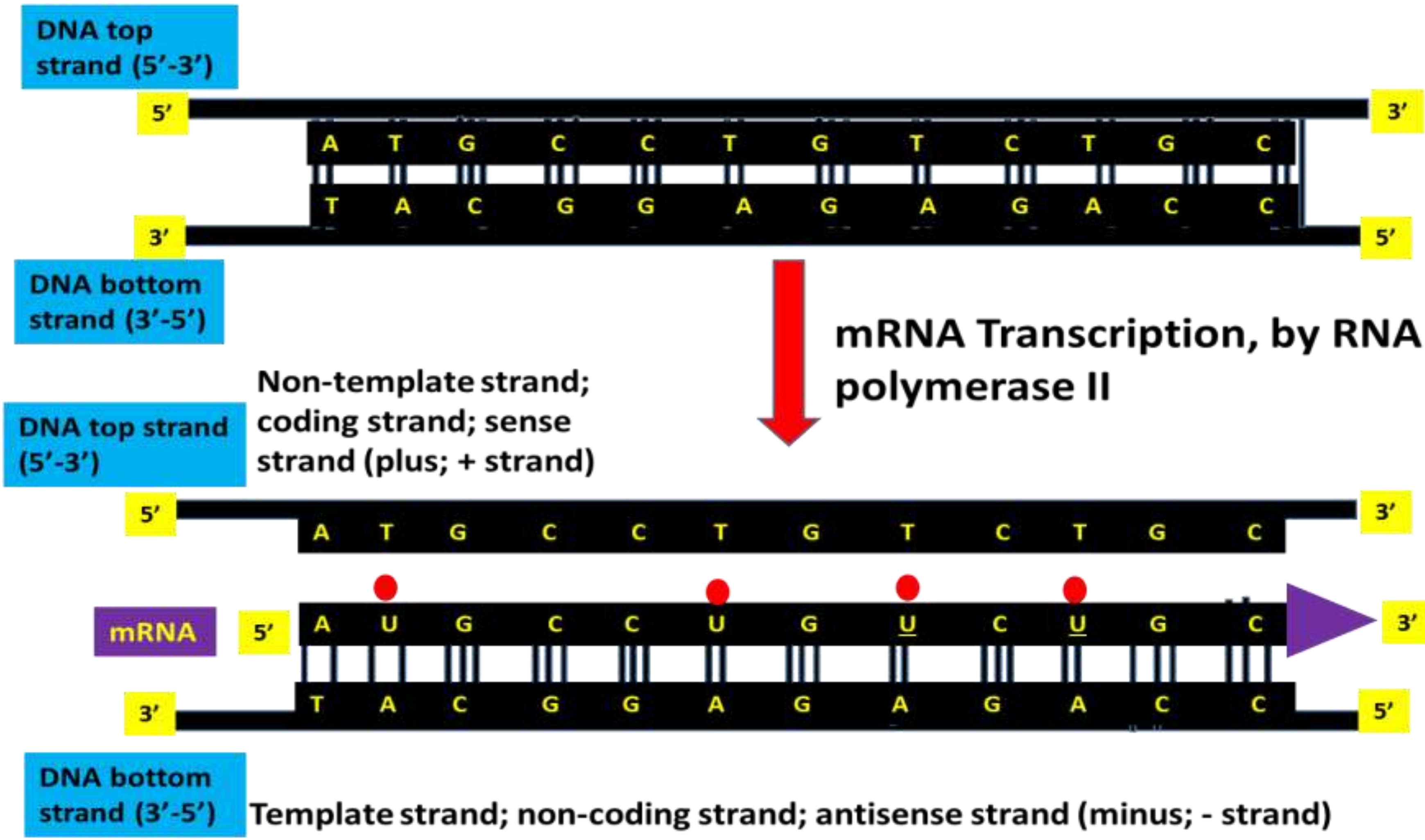
Strands are **read in 5'-3' direction**, because new nucleotide is added to carbon no. 3 –OH group of deoxyribose or ribose sugar

read in 5'-to 3'-direction........5'-AUGAUCUCGUAA-3'...... same or Xerox copy of top strand; difference

is presence of Uracil rather than thymine.

Top strand of DNA " T is replaced with Uracil (U) of RNA.

Concept of Sense/non-template/coding and Antisense/template/coding Strands of a DNA: In context "When there is RNA transcription"

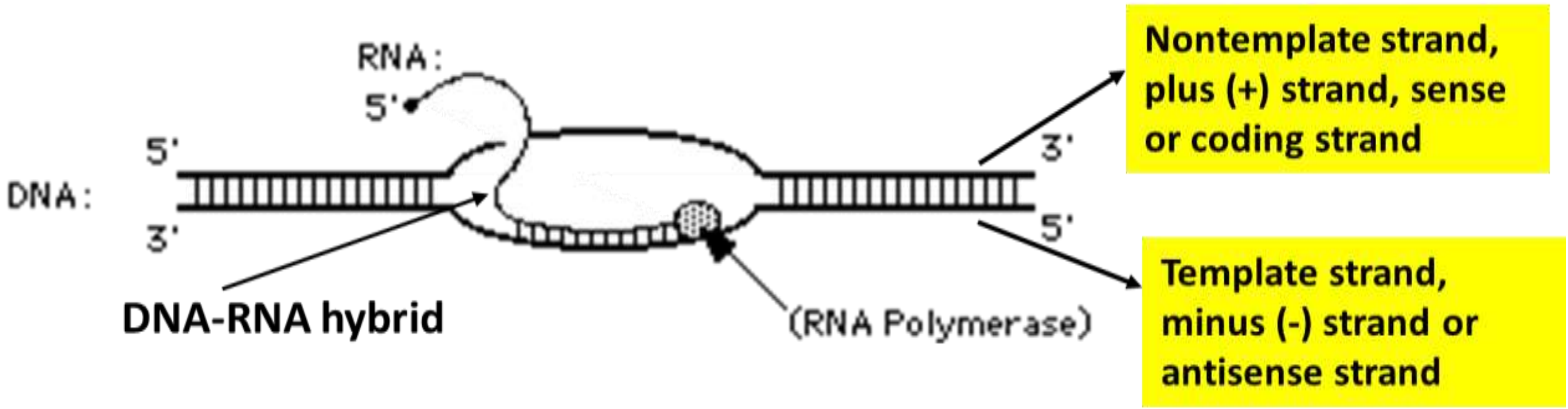


What we can conclude from previous slide of template and non-template concept ?

- Both the strands of DNA do not take part in controlling heredity. Only one of them does so. The DNA strand which functions as template for RNA synthesis is known **as template strand, Non-coding, minus (-) strand or antisense 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.

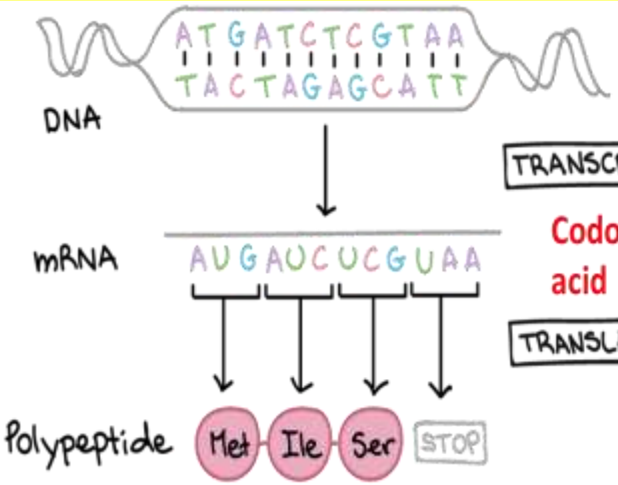
- The term antisense is also used in wider prospective for any sequence or strand of DNA (or RNA) which is complementary to mRNA.



Triplet base / or codon concept….. mRNA

one codon has three bases…so triplet
One codon…..decoded to one amino acid.
Stop codon….. Do not code any amino acid

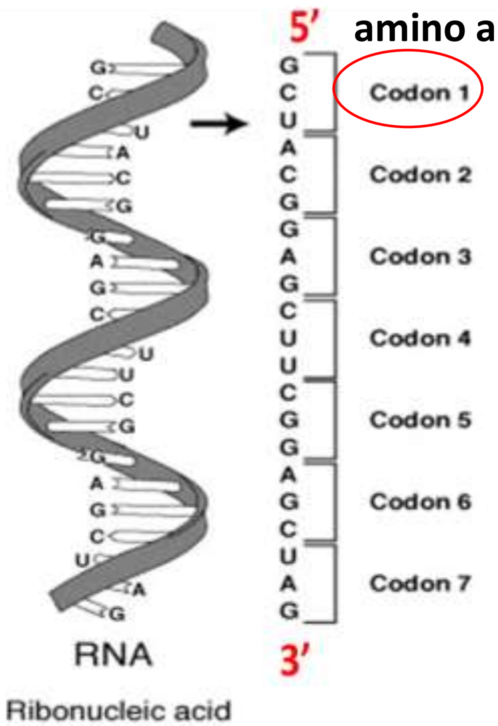
Messenger RNA (single stranded Nucleic Acid) and triplet codon concept



Protein -coding genes

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

For one amino acid



1) Messenger RNA is a linear molecule transcribed from one strand of DNA, **the process known as transcription using RNA polymerase II.**

2) It carries the base sequence complementary to DNA template strand.

3) The base sequence of mRNA is in the form of consecutive triplet codons specifies for specific amino acids and translated to proteins.

4) Ribosomes translate these triplet codons into amino acid sequence of polypeptide chain.

5) **Length of mRNA molecules**: depends upon the length of polypeptide chain it codes for.

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

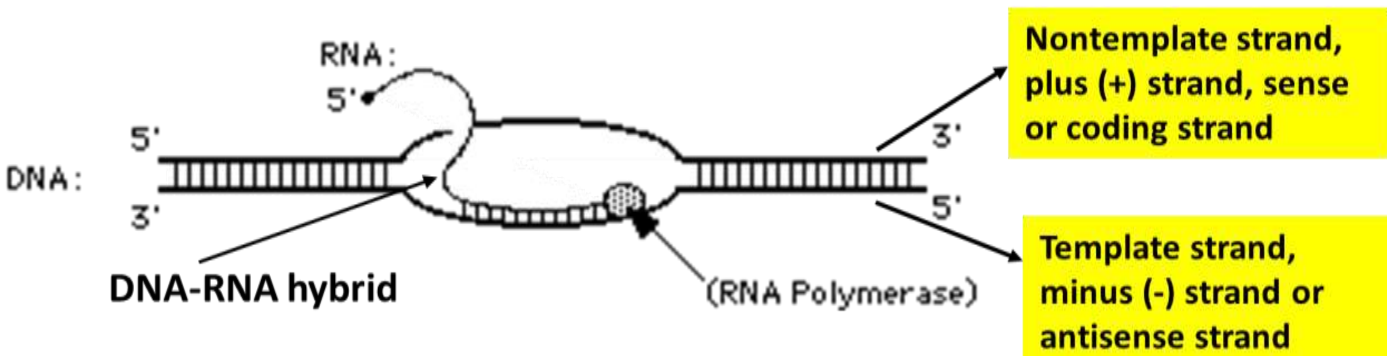
Questions: On the basis of understanding of concept of non-template and template strand

Q.1) If the sequence **5’-GATCGATCGTTTAACCG—3’** used as **a template sequence** of DNA for transcribing mRNA, what will be the mRNA sequence?

Q.2) A segment of DNA is used in mRNA transcription. The sequence of its **non-template strand is 5’-GATCGATCGTTTAACCG—3’. What will be the mRNA transcript sequence?**

Q.3) If mRNA sequence is 5’- AUGAGCAGCUGGUCCAGU-3’; what is its template sequence, its non-template sequence, or what will be non-coding strand sequence and coding strand sequence? (Hint: apply concept of sense and antisense sequence of DNA

Apply the concept from this diagram



Ans.1) 5’-GATCGATCGTTTAACCG—3’……….DNA template

3’-CUAGCUAGCAAAUUGGC—5’…….. mRNA

Or

5’-CGGUUAAACGAUCGAUC-3’ ……mRNA

Keep the direction correctly for mRNA.

Ans.2) 5’-GATCGATCGTTTAACCG—3’……….DNA non-template

5’-GAUCGAUCGUUUAACCG—3’………mRNA (same as non-template only “U” is present in place of “T”

Question: Applying triplet / codon concept

Q.1) The mRNA strand has total 90 ribonucleotides.

A) How many codons will be there? …….*ans.* 90/3= 30 codons

B) How many amino acids will be coded if last codon do not code for amino acids?…… 29 amino acids.

Q.2) If mRNA has 64 codons, how many ribonucleotides present in mRNA? ….. (Hint : 1 codon 3 ribonucleotides because codon is read in triplet).

Sample question

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

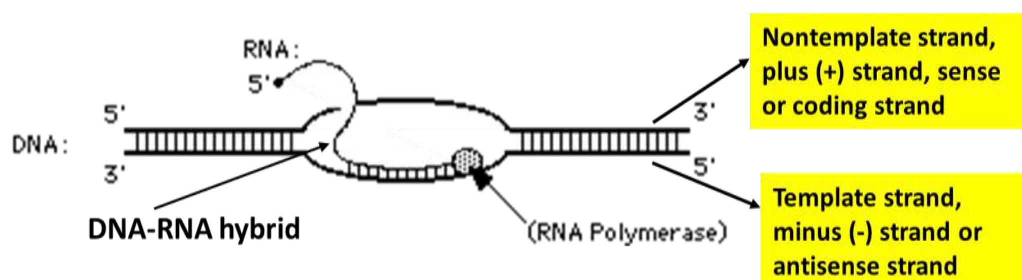
5'- GCTAGCTAAACCTTAAGGGCATTTCCG-3'...... (One strand of DNA)

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 required to solved the above questions?



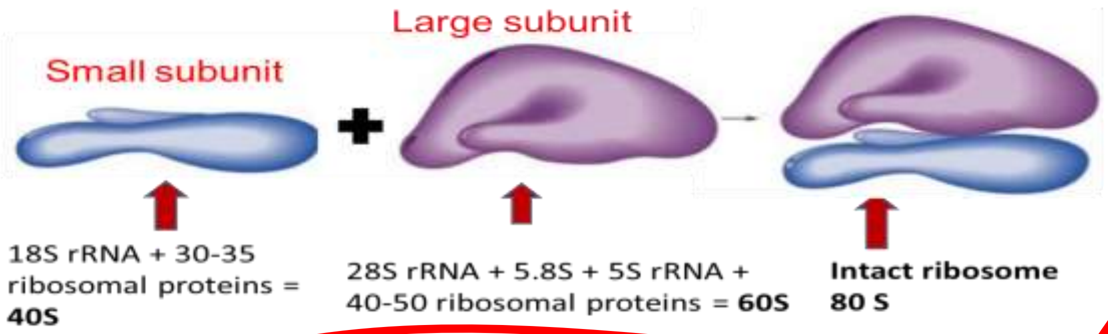
5'-ATGCCCATGC-3'
3'-TACGGGTACG-5'

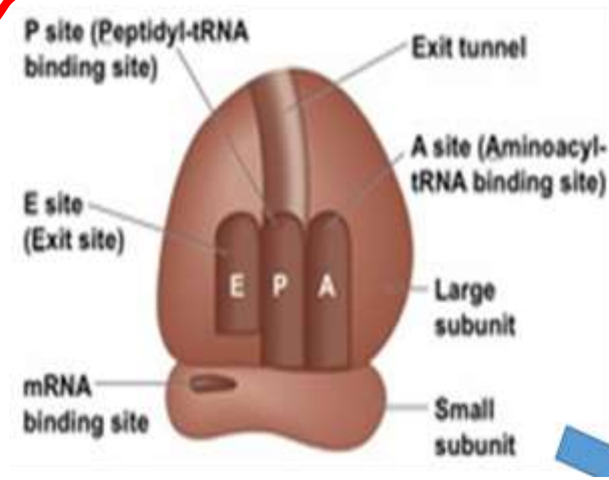
Feature	B-DNA	A-DNA	Z-DNA
Type of helix	Right-handed	Right-handed	Left-handed
Helical diameter (nm)	2.37	2.55	1.84
Rise per base pair (nm)	0.34	0.29	0.37
Distance per complete turn (pitch) (nm)	3.4	3.2	4.5

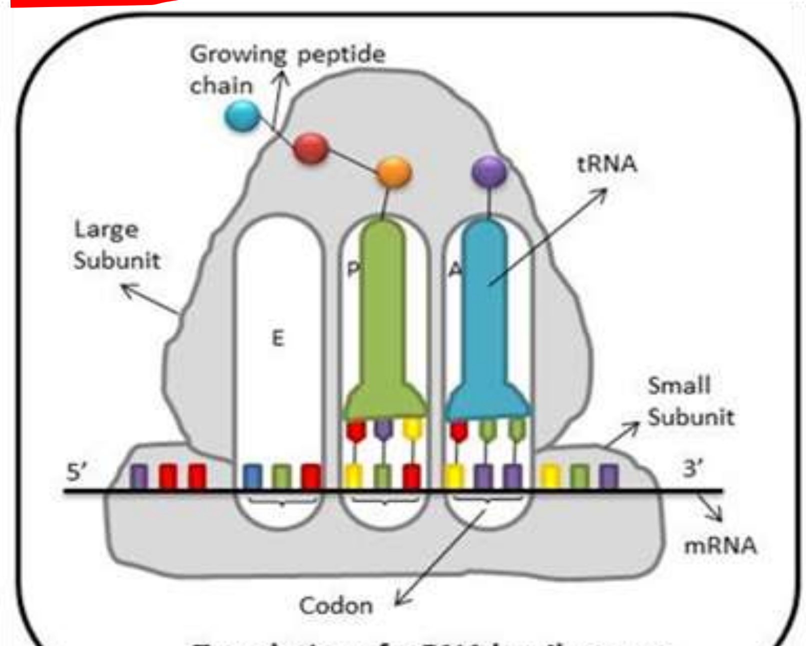
Understanding Ribonucleic Acid and its types

Ribosomal RNA (rRNA)…. Component of Ribosomes

Eukaryotic Ribosomes: 80 S; made up of large subunit and small subunit
Small subunit: 40 S ; 18 S rRNA + 30-35 proteins
Large subunit: 60 S; 28 S rRNA + 5.8 S 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

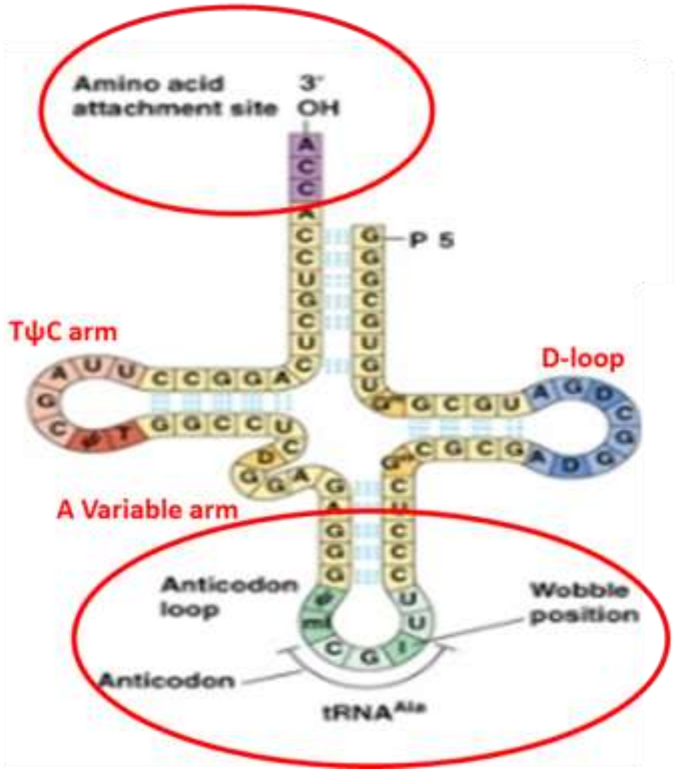
P-site: peptidyl tRNA binding site

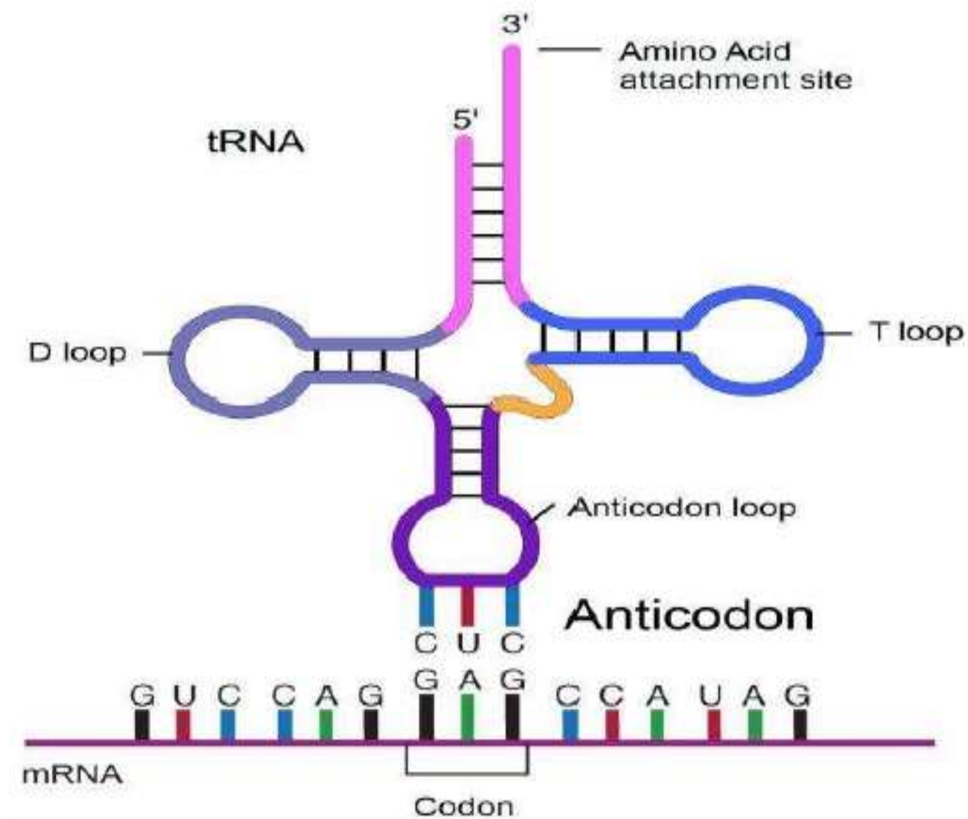
E-site: free tRNA with no amino acid or outgoing tRNA. "E" for exit.

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.



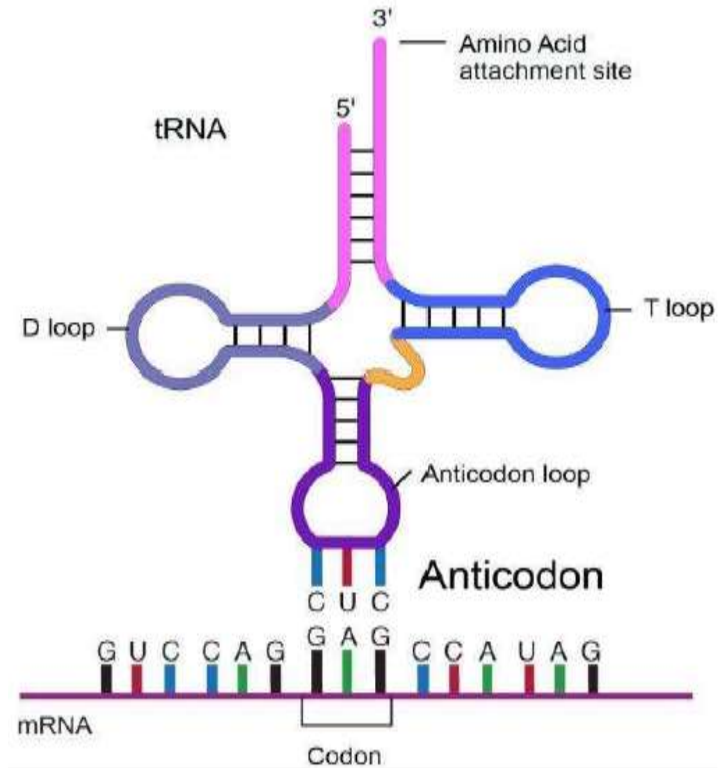


➢ Amino acid binding site-

1) It has sites for amino acid attachment and therefore, **each tRNA represent a single amino acid to which it covalently binds.**

2) 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 $\text{tRNA}_1^{\text{Try}}$ and $\text{tRNA}_2^{\text{Try}}$.

3) A minimum of 32 tRNAs are required to translate all 61 codons.



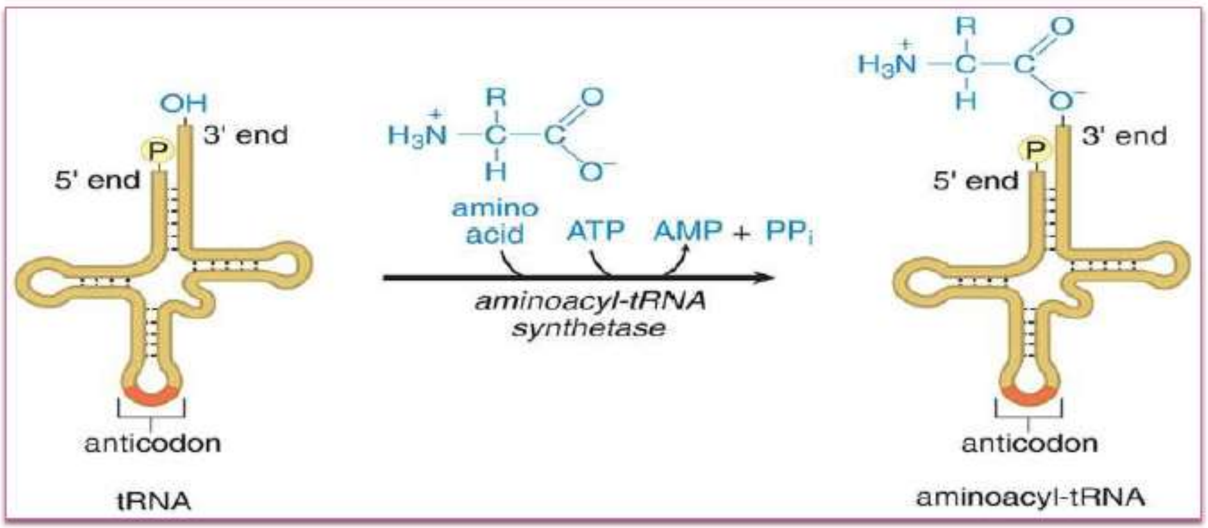
➢ Anticodon site –

1) It has an **anticodon site** for **codon recognition** that binds to a specific **sequence on the messenger RNA** chain through hydrogen bonding.

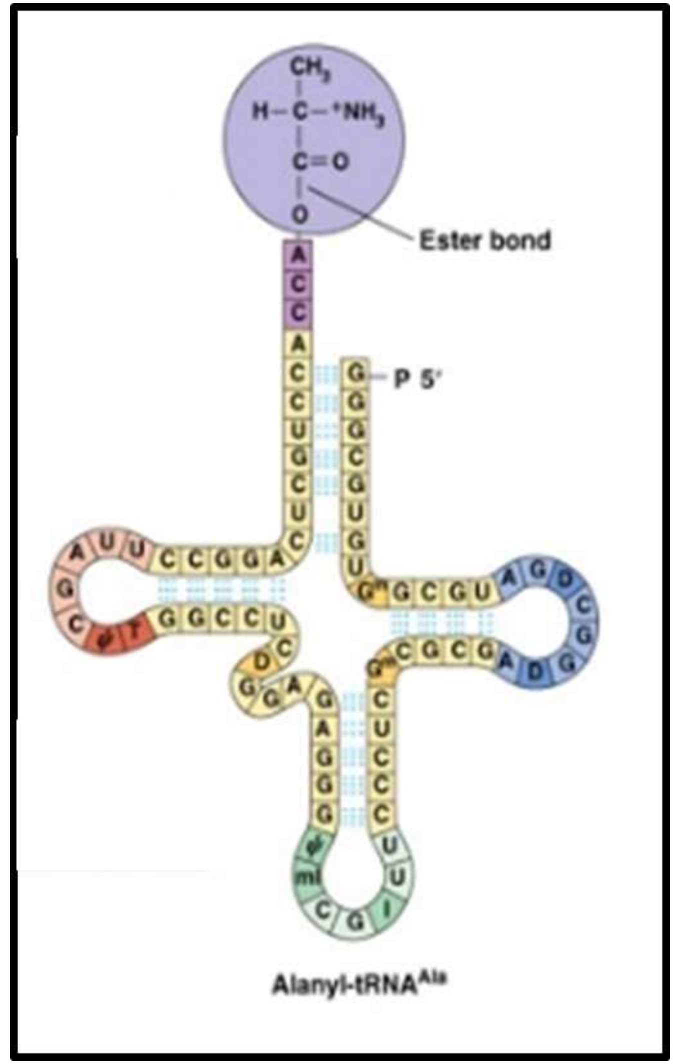
2) The codon and anticodon form base pairs with each other through hydrogen bonding.

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

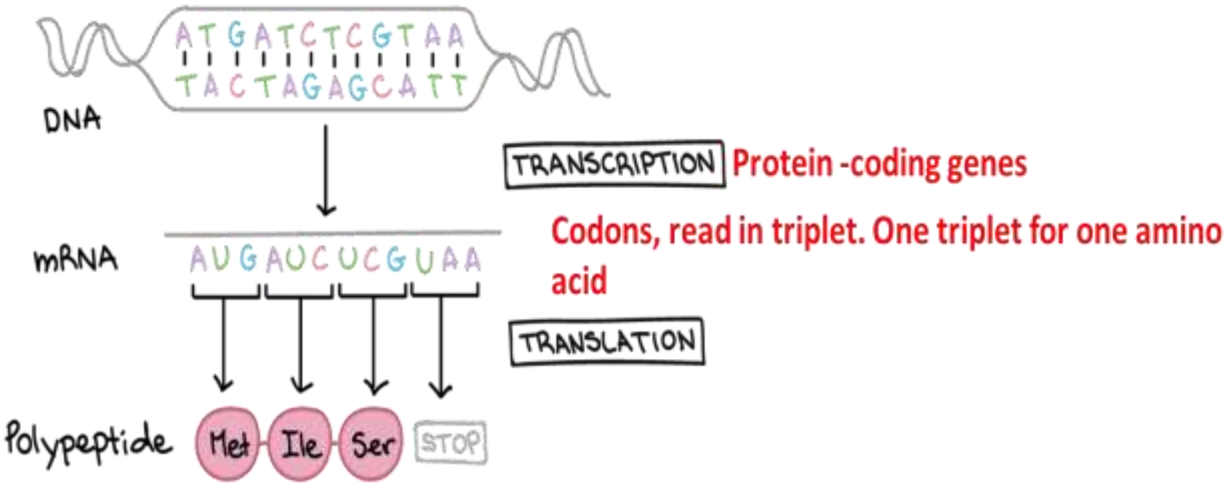


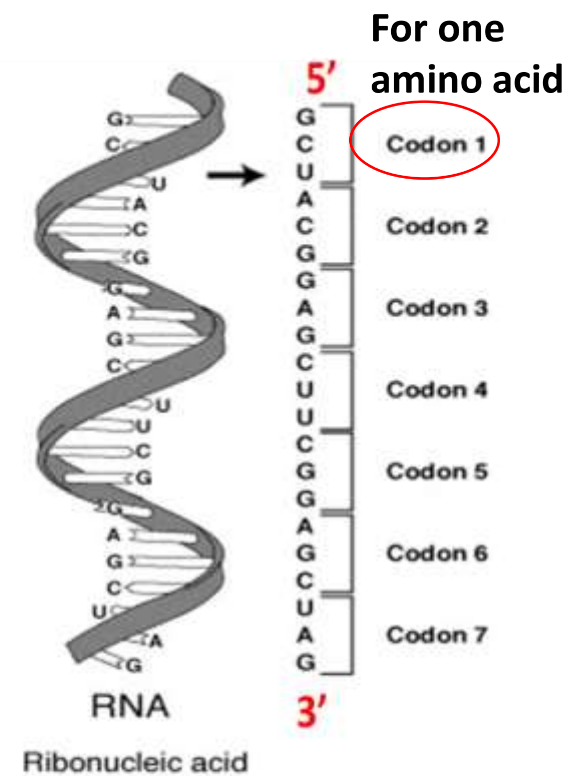
Ester-Bond is formed between free –OH of ribonucleotide (Adenylate) at 3’-end and carboxyl group of alpha carbon of amino acid.



Charged-tRNA or aminoacyl tRNA, carrying amino acid at 3’-end

Messenger RNA (single stranded Nucleic Acid)





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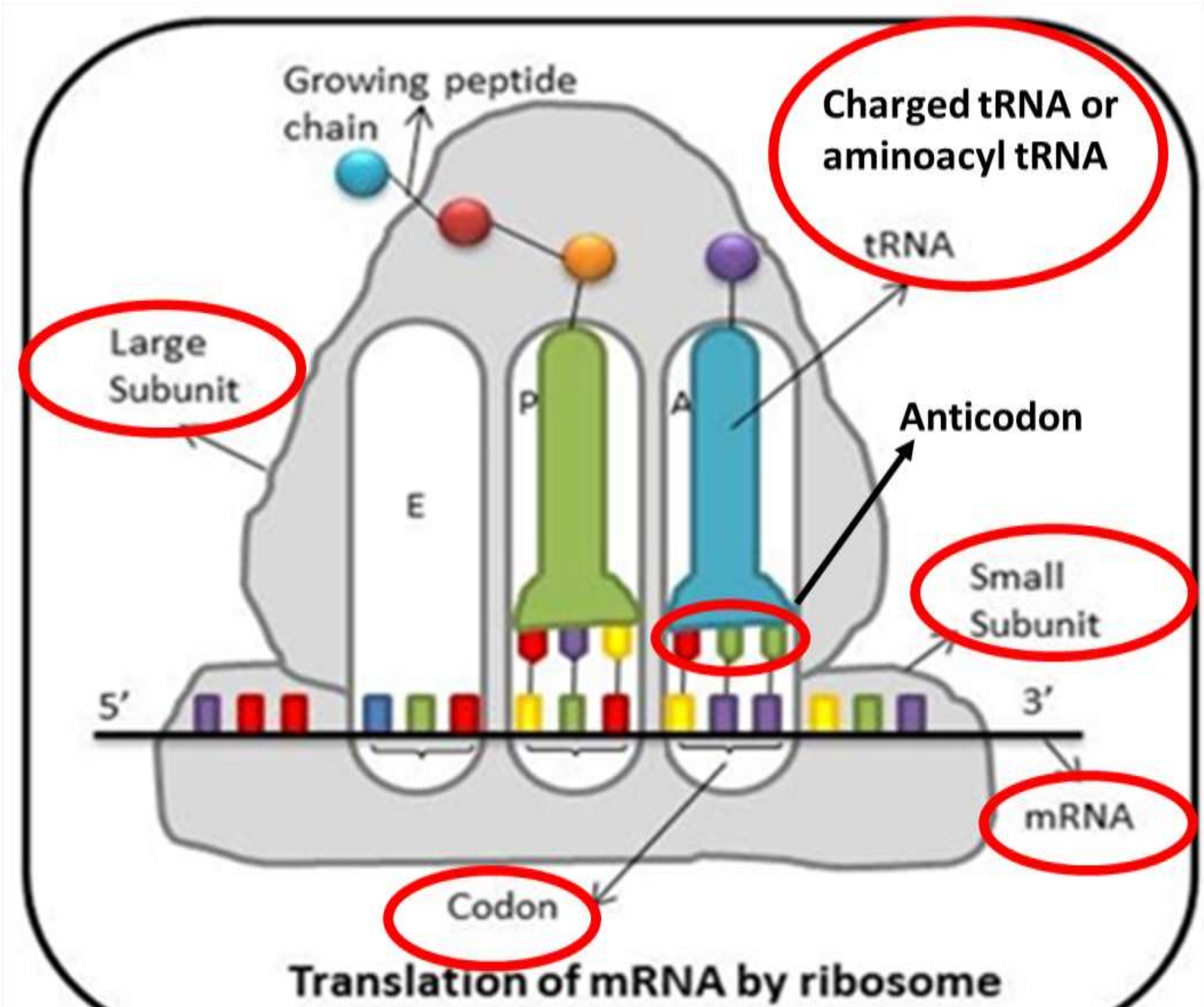
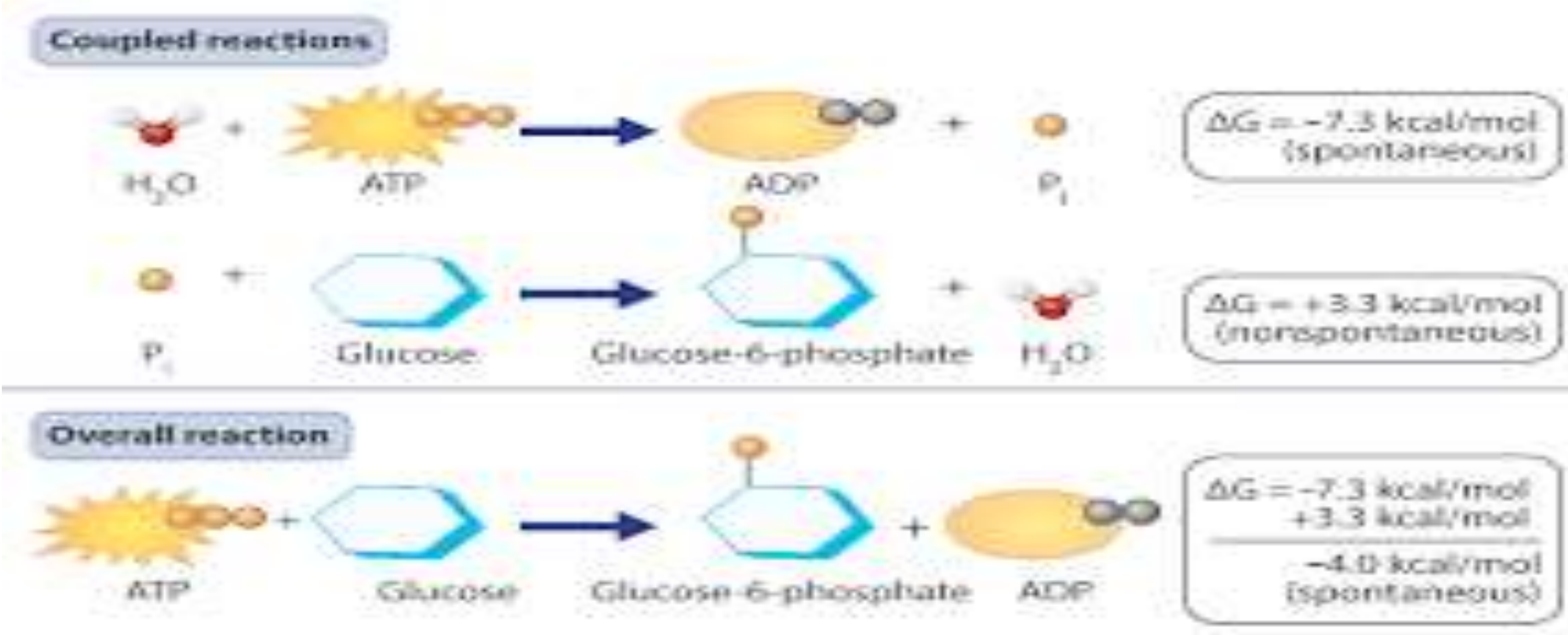
As a whole rRNAs, tRNA and mRNA in protein synthesis process…..Translation



Thank you

Endergonic Reaction to make Glucose-6-phosphate from Glucose in metabolic process glycolysis- Use of ATP for coupled reaction



The phosphorylation of glucose is coupled with ATP hydrolysis.

the addition of an inorganic phosphate group (Pi) to glucose to form glucose-6-phosphate — the first step of glycolysis — is energetically unfavorable ($\Delta G = +3.3$ kcal/mol).

The hydrolysis of ATP into ADP and Pi is energetically favorable (-7.3 kcal/mol).

Coupling the two reactions allows the energy released