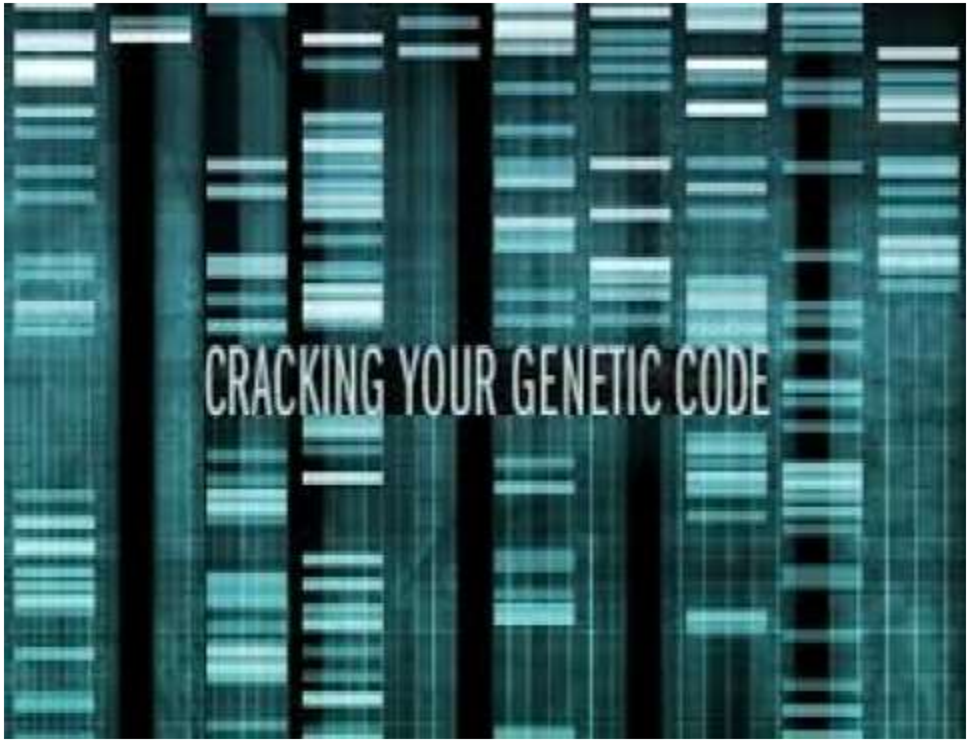
Genetic code

By the end of this chapter you should be able to:

- Identity the chemical components of DNA.
- Assemble the double helix: The structure of DNA.
- Understand the components of amino acids.
- Understand the concept of genetic code.



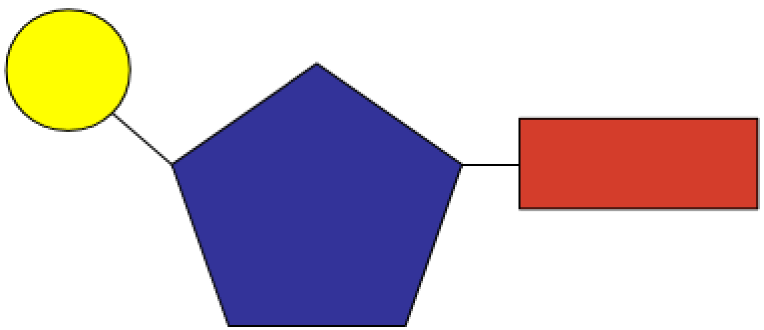
3.1 The chemical components of DNA

Nucleic Acid

- Nucleic acids are produced from nucleotide polymerization.

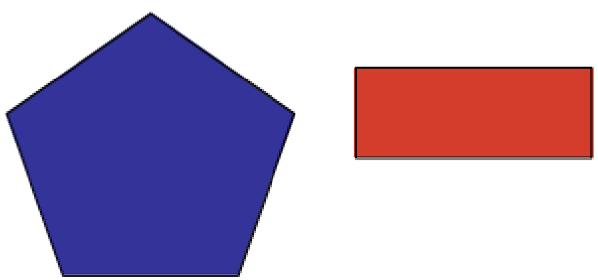
- During synthesis a series of nucleic acid condensation reactions occur between phosphate and sugar groups.

Nucleic Acid



- Pentose sugar
- Nitrogenous base
- Phosphates

Nucleotides

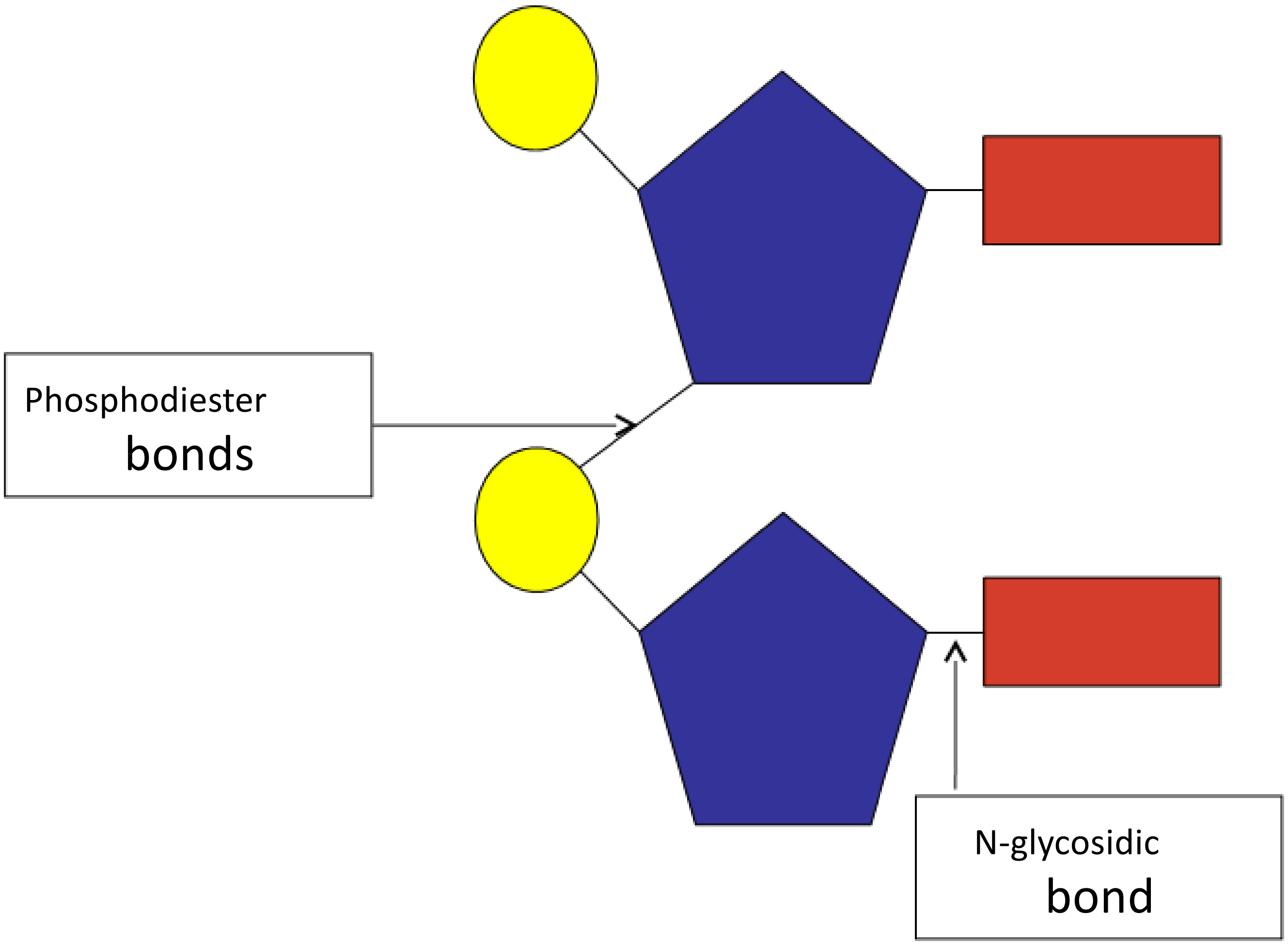


- Pentose sugar
- Nitrogenous base

Nucleosides

Phosphates + Nucleosides = Nucleotides

Nucleic Acid



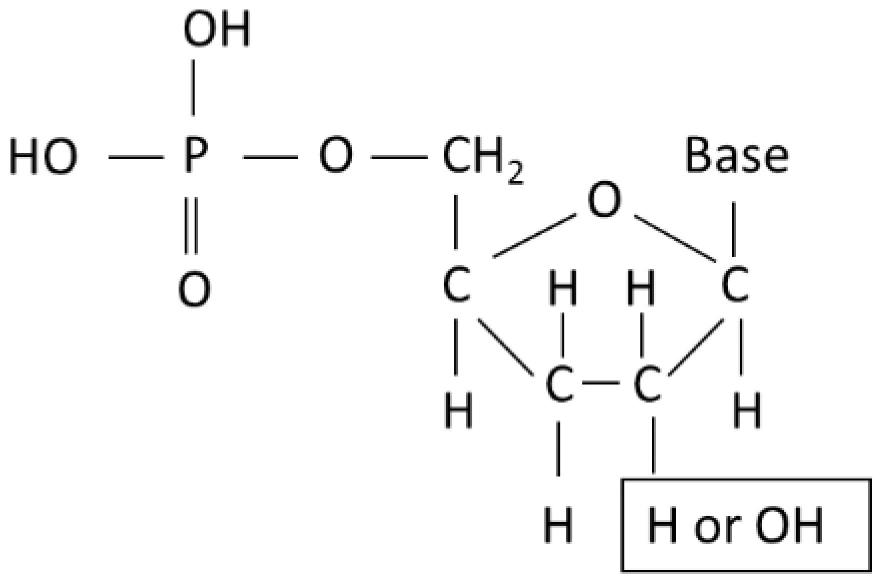
DNA vs RNA

Fig. 6.5 Comparing DNA and RNA.

Feature	DNA	RNA
Sugar	Deoxyribose	Ribose
Base pairing	A–T/G–C	A–U/G–C
Structure	Double helix	Single stranded structures

Diagram adopted from Crash course: Cell Biology and Genetics, 4th ED

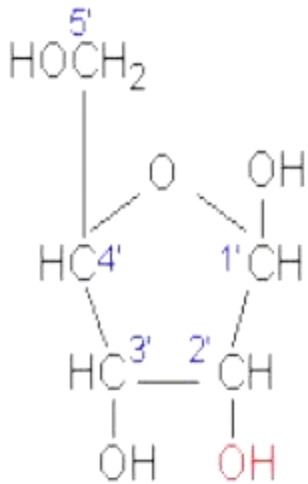
DNA vs RNA
Sugar



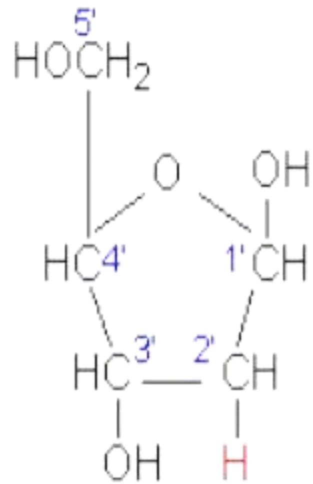
Sugar:
- RNA – ribose (OH)
- DNA – deoxyribose (H)

DNA vs RNA

Sugar



A



B

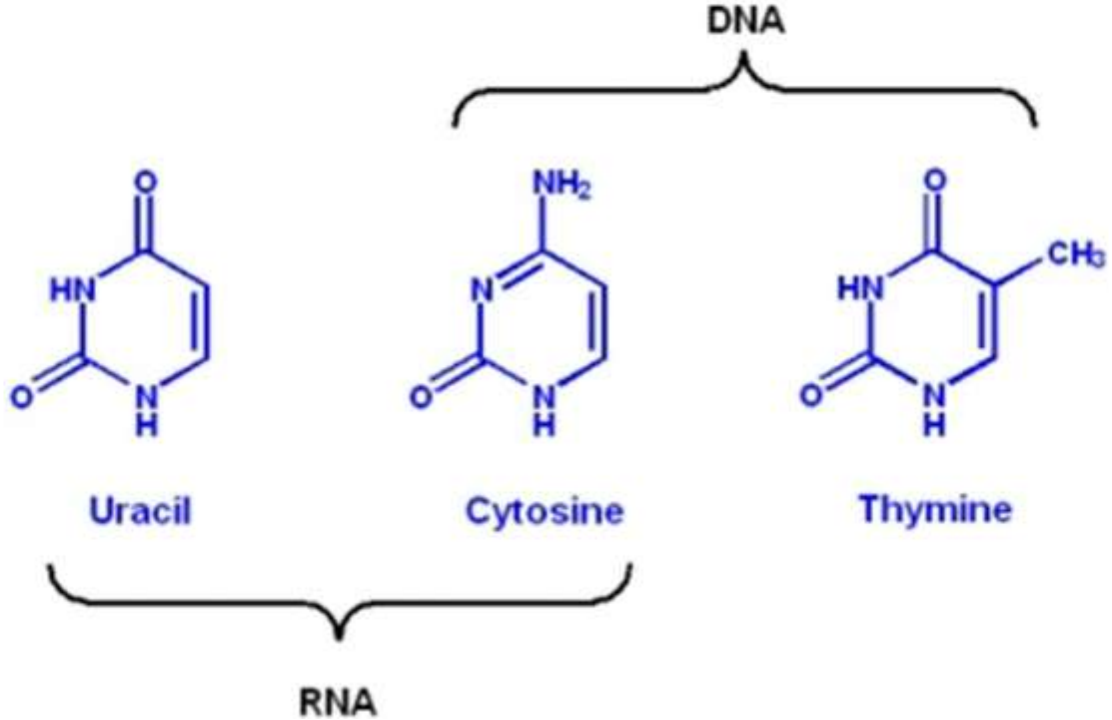
DNA vs RNA
Bases

- The nucleotide bases in nucleic acids contain nitrogen derived from either purines or pyrimidines.

- Purines (Double ring)
  - Adenine
  - Guanine

- Pyrimidines (Single ring)
  - Cytosine
  - Thymine*
  - Uracil*

DNA vs RNA PYRIMIDINES

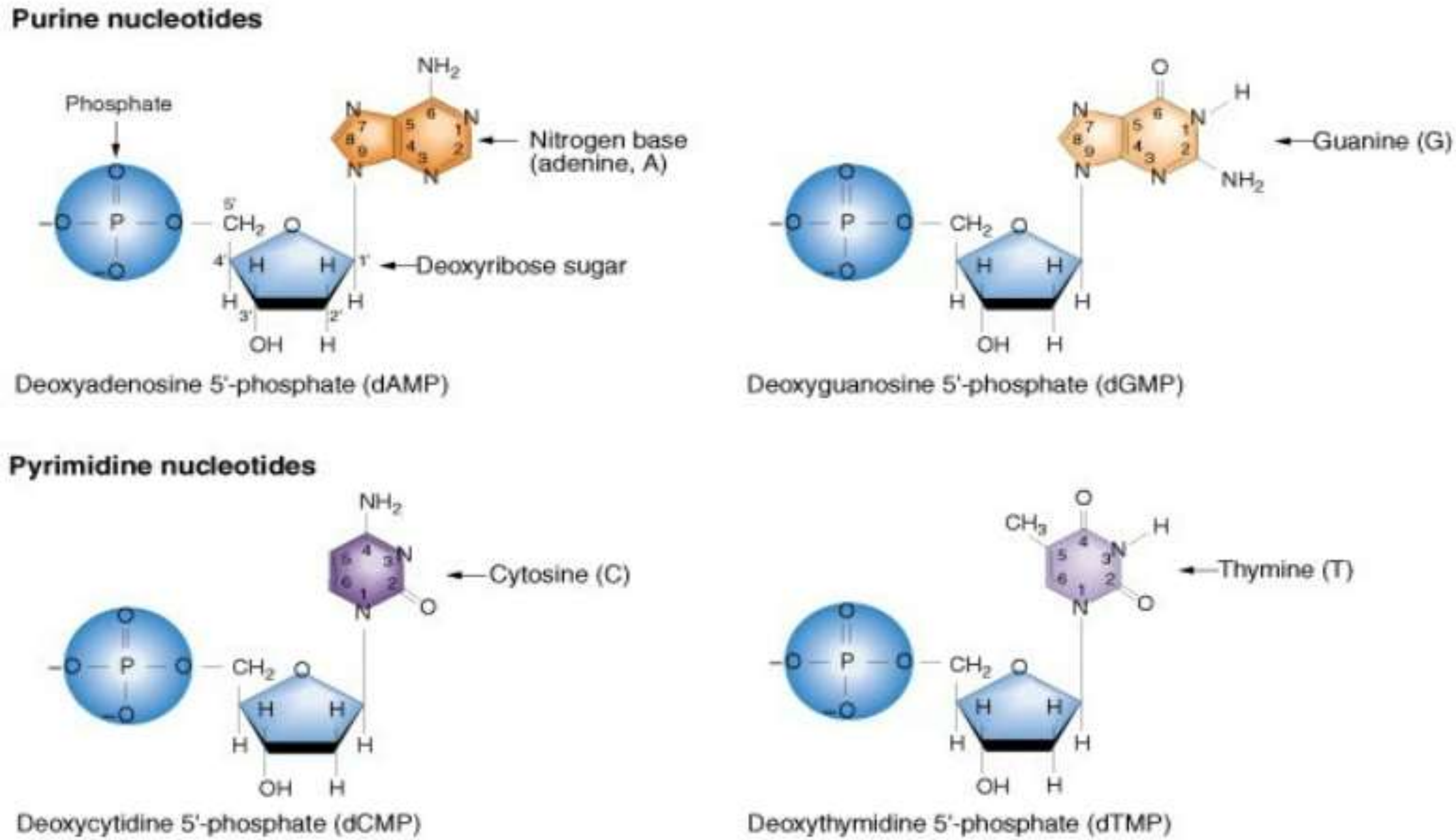


DNA vs RNA
PURINES

Adenine

Guanine

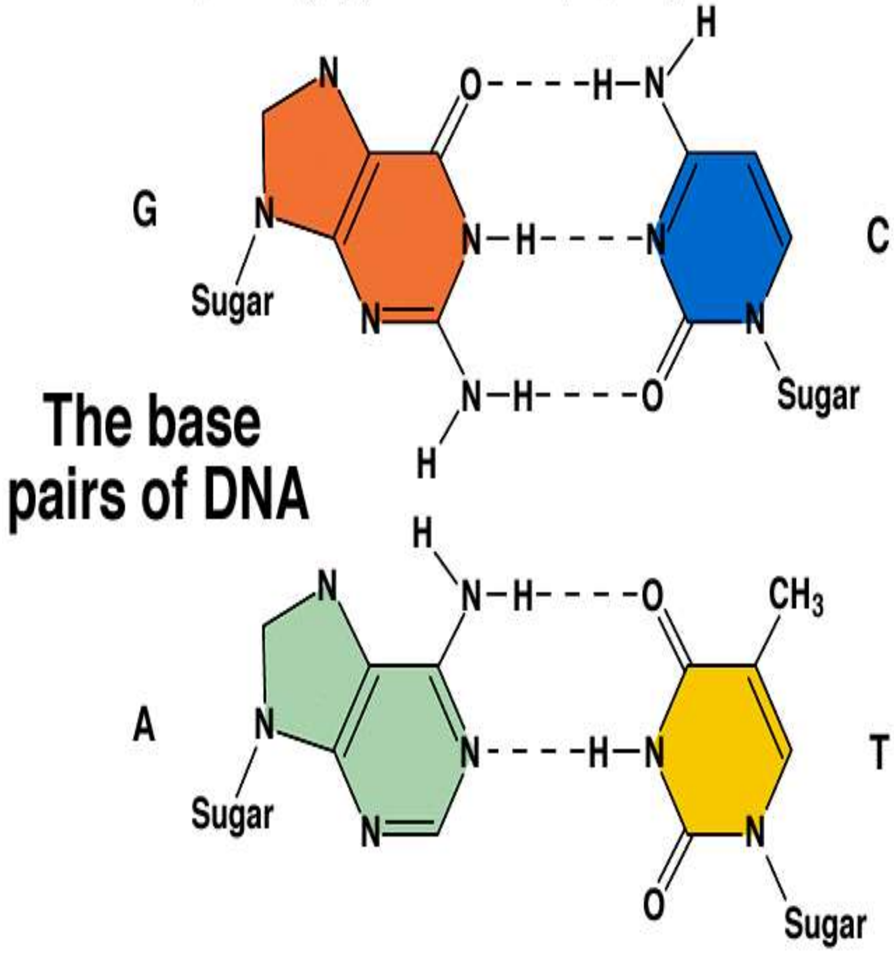
DNA vs RNA Nucleotides

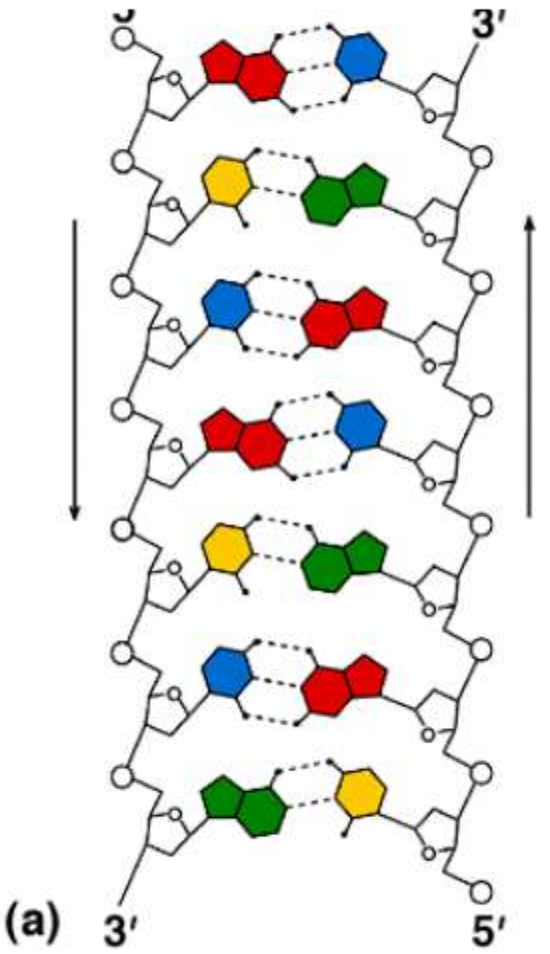


DNA is double helix

- Discovered by Watson and Crick in 1953
  - Base composition analysis of hydrolyzed samples of DNA
  - X-ray diffraction studies of DNA.
- Adenine and thymine pair via two hydrogen bonds between opposing strands.
- Guanine and cytosine pair via three hydrogen bonds.
- Base pairing results in two complementary polynucleotides, which run antiparallel to each other.

DNA is double helix





RNA is Single strand- mRNA

- Messenger RNA
- Carries genetic information from the nucleus into the cytoplasm.
- In eukaryotes, it is derived by splicing the initial RNA transcript (heteronuclear RNA that holds introns)

RNA is Single strand- mRNA

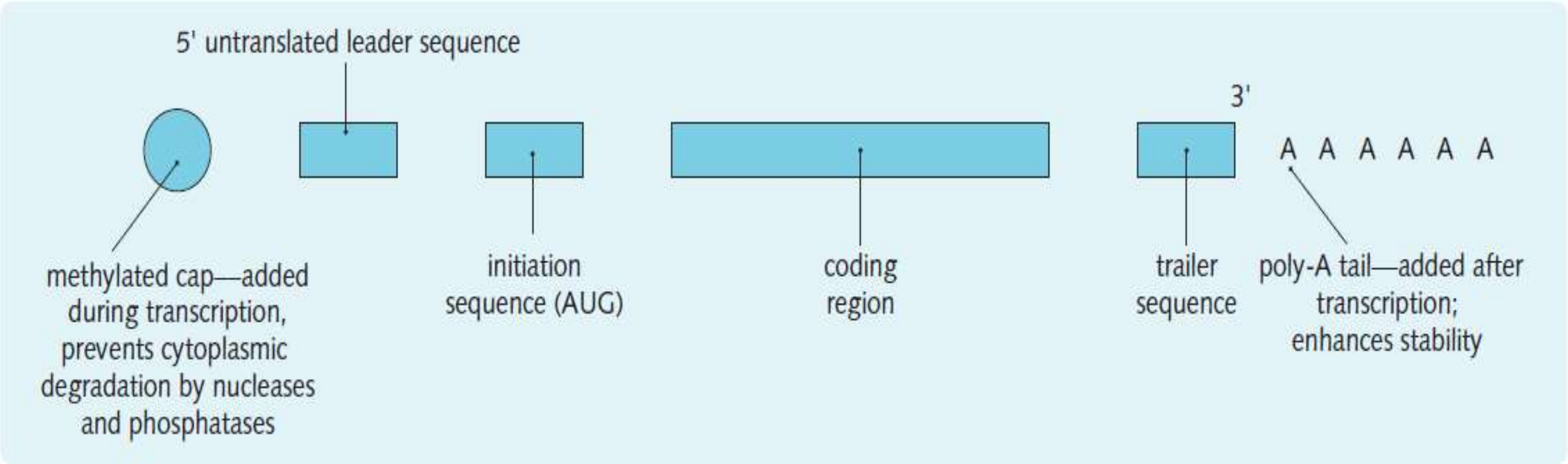
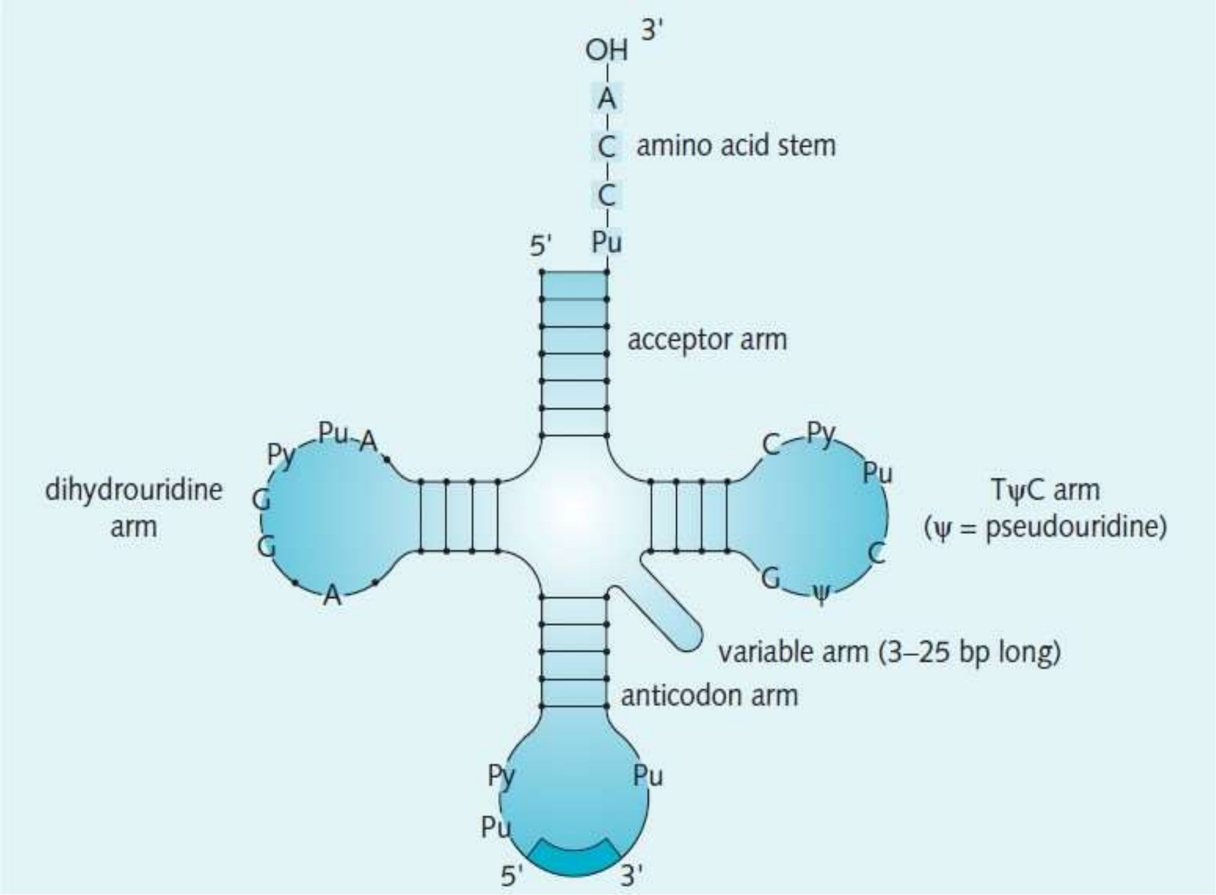


Diagram adopted from Crash course: Cell Biology and Genetics, 4th ED

RNA is Single strand- tRNA

- Transfer RNA
- Linear molecule with an average of 76 nucleotides
- Exhibits extensive intramolecular base pairing, giving it a ‘clover-leaf’-shaped secondary structure
- Carries specific amino acids to the site of protein synthesis.

RNA is Single strand- tRNA



- Terminal CCA group can accept a specific amino acid.
- anticodon arm, recognizes the corresponding mRNA codon.
- Specific base pairing within the five arms helps to maintain the secondary structure.

Diagram adopted from Crash course: Cell Biology and Genetics, 4th ED

3.2 The structure of DNA: double helix

Evidence 1: Base-Composition Studies

- Between 1949 and 1953, Erwin Chargaff and his colleagues used chromatographic methods to separate the four bases in DNA samples from various organisms.

DNA Base-Composition Data

(a) Chargaff's Data*	Molar Proportions[a]			
	1	2	3	4
Organism/Source	A	T	G	C
Ox thymus	26	25	21	16
Ox spleen	25	24	20	15
Yeast	24	25	14	13
Avian tubercle bacilli	12	11	28	26
Human sperm	29	31	18	18

Diagram adopted from William S and Klug. Concept of Genetics, 10th ED

What can be derived from Erwin Chargaff?

- The amount of adenine residues is proportional to the amount of thymine residues in DNA.
- The amount of guanine residues is proportional to the amount of cytosine residues.
- The sum of the purines (A + G) equals the sum of the pyrimidines (C + T).
- The percentage of (G + C) does not necessarily equal the percentage of (A + T).

The Watson–Crick Model

- Two long polynucleotide chains are coiled around a central axis, forming a right-handed double helix.
- The two chains are antiparallel; that is, their C-5’-to-C-3’orientations run in opposite directions.
- The bases of both chains are flat structures lying perpendicular to the axis; they are “stacked” on one another, 3.4 Å (0.34 nm) apart, on the inside of the double helix.

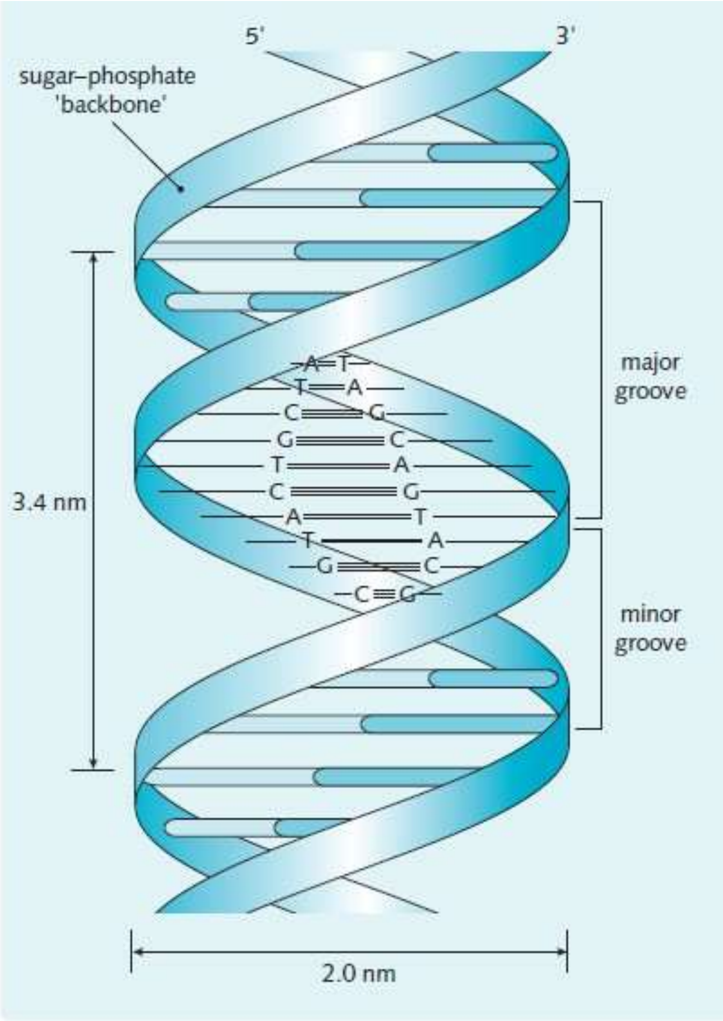


Diagram adopted from Crash course: Cell Biology and Genetics, 4th ED

The Watson–Crick Model

- The nitrogenous bases of opposite chains are paired as the result of the formation of hydrogen bonds
- In DNA, only A -T and G-C pairs occur.
- Each complete turn of the helix is 34 Å (3.4 nm) long; thus, each turn of the helix is the length of a series of 10 base pairs.

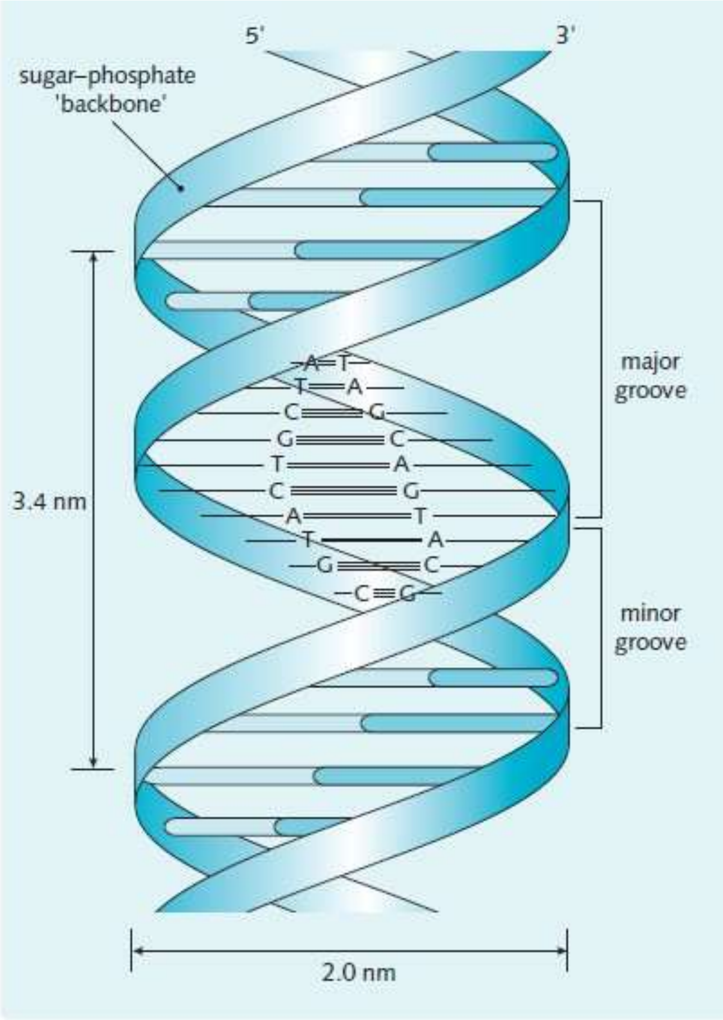


Diagram adopted from Crash course: Cell Biology and Genetics, 4th ED

The Watson–Crick Model

- A larger major groove alternating with a smaller minor groove winds along the length of the molecule.

- The double helix has a diameter of 20 Å (2.0 nm).

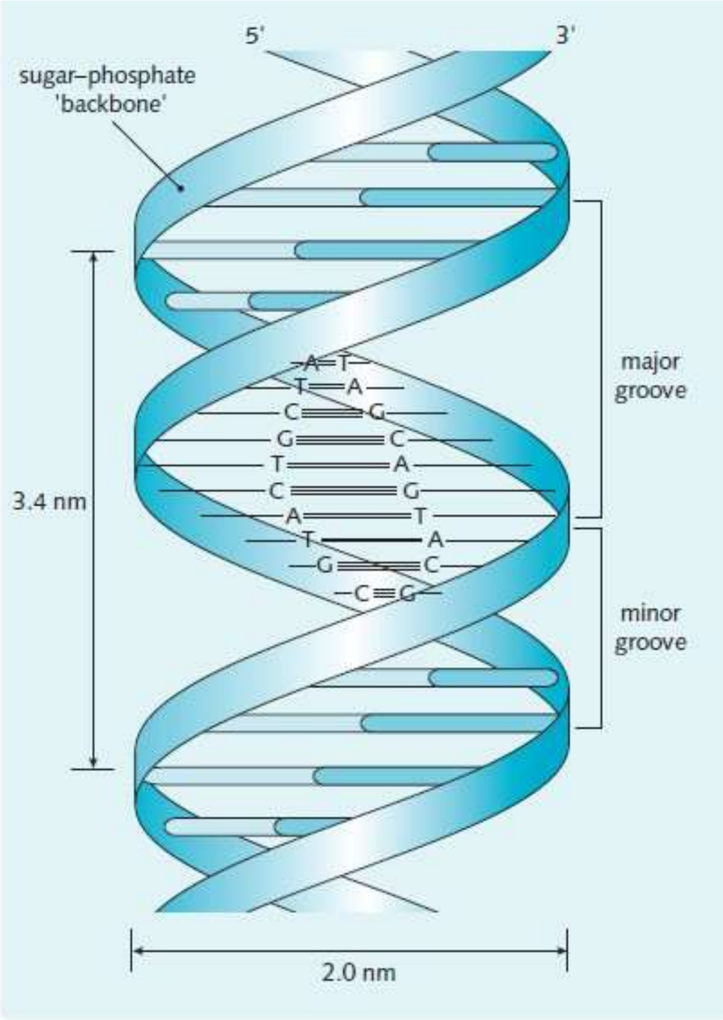


Diagram adopted from Crash course: Cell Biology and Genetics, 4th ED

DNA and Inheritance

- The structure of DNA is a linear sequence of deoxyribonucleotides.
- There are regions within the DNA that contain protein-coding genes.
- How is the information within DNA decoded for translation of proteins?
- Central dogma – flow of information from

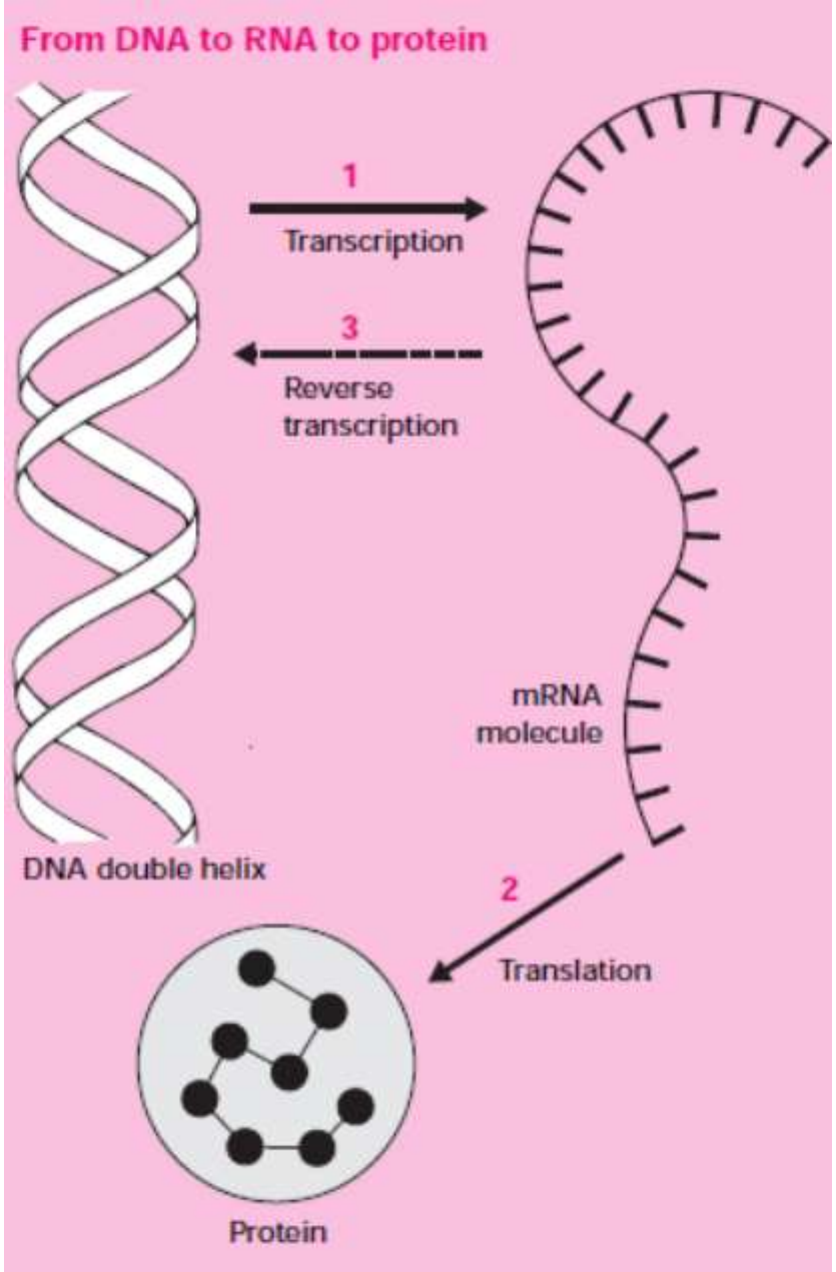


Diagram adopted from
The Facts On File Illustrated Guide to the Human Body: Cells and Genetics

Transcription & translation

- Information present on one of the two strands of DNA is transferred into an RNA complement in a process called transcription.

- Messenger RNA (mRNA) serves as a messenger molecule transporting coded information out of the nucleus.

- mRNAs associate with ribosomes, where translation occurs.

3.3 Components of amino acids

AMINO ACIDS

- Amino acids are the subunits of proteins, and they all have the same basic structure.

  - A central carbon atom (the a carbon)
  - An amino (NH2) group at the a carbon
  - A carboxyl group (COOH)
  - A side group (R).

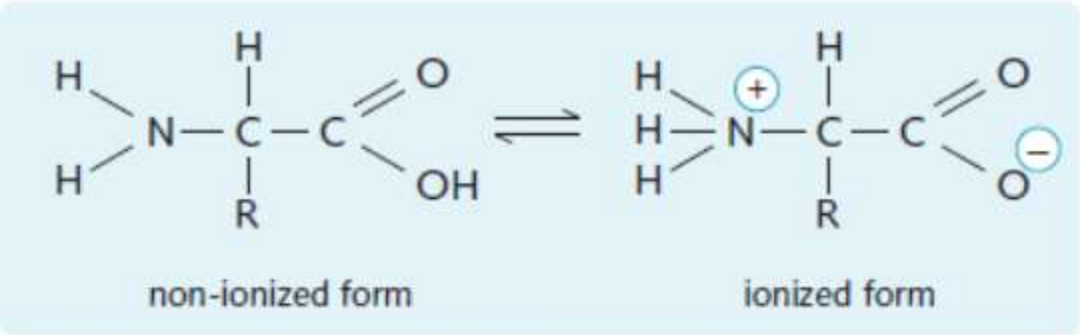


Diagram adopted from Crash course: Cell Biology and Genetics, 4th ED

AMINO ACIDS

- There are 20 naturally occurring amino acids, which differ in their side group.
- All amino acids, except glycine, have an asymmetrical α-carbon atom, giving rise to D or L stereoisomer forms; however, only the L form is found in humans.
- Amino acids form proteins by joining together through peptide bonds.

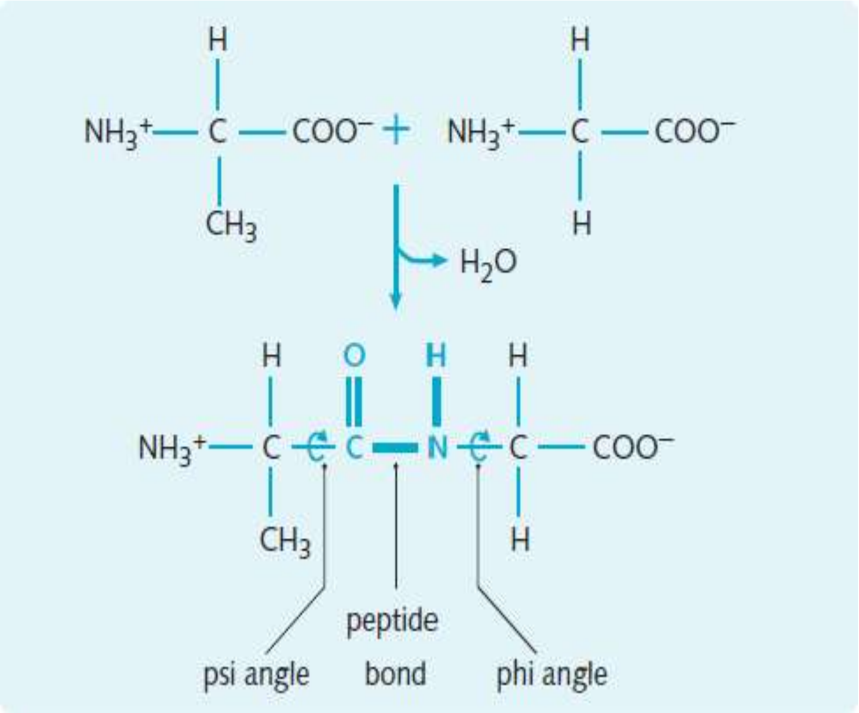


Diagram adopted from Crash course: Cell Biology and Genetics, 4th ED

Amino acids code

Nonpolar and uncharged

A	Ala	Alanine
F	Phe	Phenylalanine
G	Gly	Glycine
I	Ile	Isoleucine
L	Leu	Leucine
M	Met	Methionine
P	Pro	Proline
V	Val	Valine
W	Trp	Tryptophan

Polar and uncharged

C	Cys	Cysteine
N	Asn	Asparagine
Q	Gln	Glutamine
S	Ser	Serine
T	Thr	Threonine
Y	Tyr	Tyrosine

Positively charged (basic)

H	His	Histidine
K	Lys	Lysine
R	Arg	Arginine

Negatively charged (acidic)

D	Asp	Aspartic acid
E	Glu	Glutamic acid

Ambiguous codes

B	Asx	Asparagine or aspartic acid
Z	Glx	Glutamine or glutamic acid

Links between amino-acid residues

- Hydrogen bonds occur between carbonyl (C-O) and amino (N–H) groups.

- Disulphide bridges are covalent bonds between -SH groups of cysteine residues.

- Non-covalent hydrophobic bonds form between two hydrophobic residues.

- Electrovalent (ionic) bonds occur between a negative group of one amino-acid residue and a positive group of another amino-acid residue.

3.4 Genetic code

Deciphering the Code

- Marshall Nirenberg and Heinrich Matthaei at the National Institutes of Health used a precise and logical series of experiments to "crack the code.

- They were among the first to characterize specific coding sequences.

- Made possible by advancements that:
  - Allowed protein synthesis in vitro
  - Synthesizing RNA strands in vitro

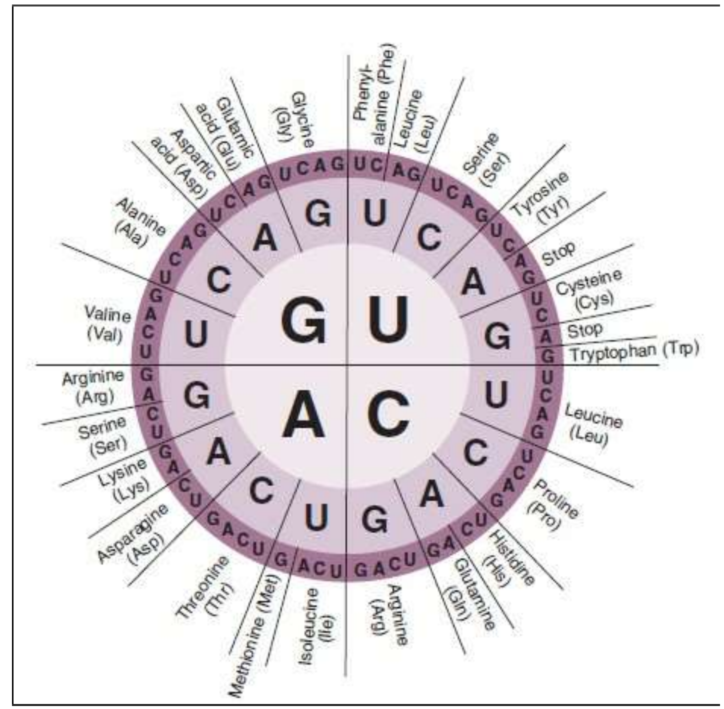


Diagram adopted from Human Genetics concepts and Application 9th ed

8 Characteristics of the Genetic Code

1. Written in linear form of ribonucleotide bases (mRNA).

2. Each word consists of 3 ribonucleotide letters which (**triplet code- codon**) specifies one amino acid.

3. The code is unambiguous- each triplet specifies only a single amino acid.

4. The code is degenerate, given amino acid can be specified by more than one triplet codon.

8 Characteristics of the Genetic Code

5. The code is commaless; Once translation of mRNA begins, the codons are read one after the other with no breaks between them (until a stop signal is reached).

6. The code contains 1 start and 3 stop codons

7. The code is non-overlapping

8. The code is (nearly) universal. With only minor exceptions, a single coding dictionary is used by almost all viruses, prokaryotes, archaea, and eukaryotes.

The Genetic Code Uses Ribonucleotide Bases as "Letters"

- Even though genetic information is stored in DNA, the code that is translated into proteins resides in RNA.

- How only four nucleotides could specify 20 the amino acids?

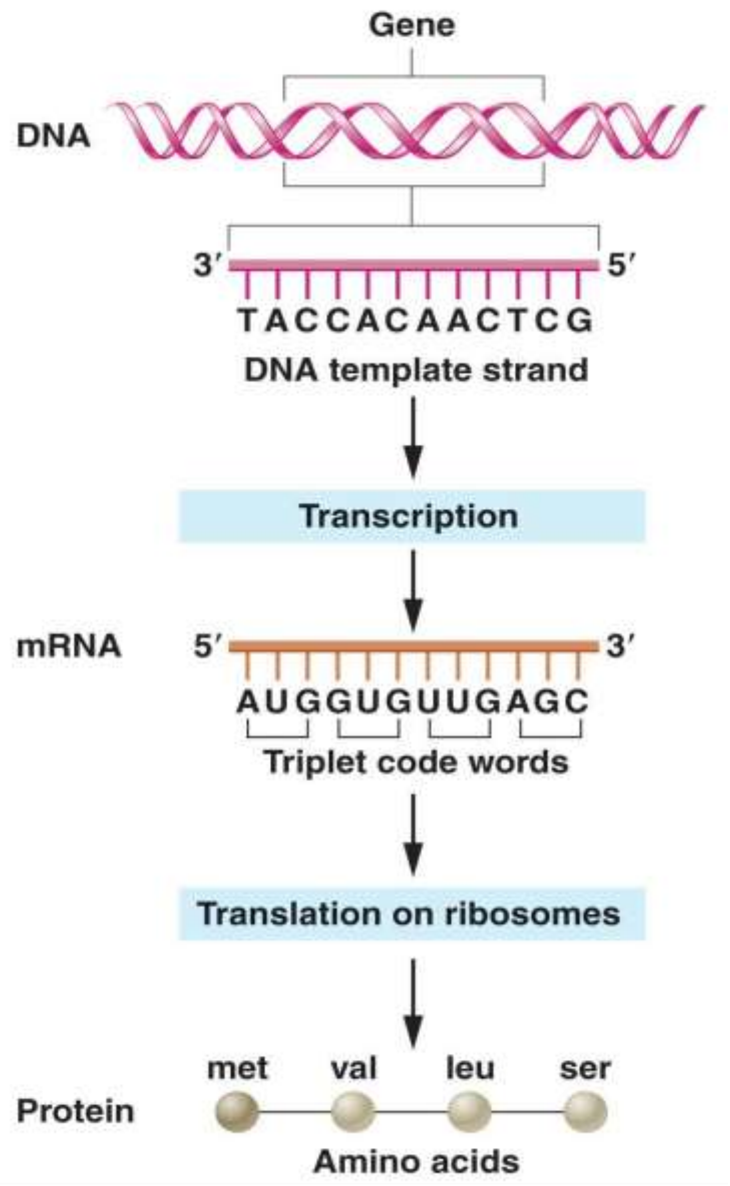


Diagram adopted from William S and Klug. Concept of Genetics, 10th ED

Evidence for the Triplet Code

- How Many RNA Bases Specify One amino acid code; 20 amino acids code?
- If a codon consisted of only one mRNA base?
- Two base, for example, provides only 16 unique code words (4^2). Not enough..!
- A triplet code yields 64 words (4^3) and therefore is sufficient for the 20 amino acids.
- A four-letter code (4^4), which would specify 256 words.

Theory

The code contains 1 start and 3 stop codons

- Chemical analysis eventually showed that the genetic code includes directions for starting and stopping translation.

- The codon AUG signals “start,” and the codons UGA, UAA, and UAG signify “stop.”

The code is (nearly) universal

- All life evolved from a common ancestor, hence all species use the same mRNA codons to specify the same amino acids.

- Do you think there is exceptions to the universality of the genetic code?
  - Mitochondria
  - Certain single-celled eukaryotes (ciliated protozoa)

- These deviations may be tolerated because they do not affect the major repositories of DNA.

The code is unambiguous

- Which codons specify which amino acids?
- Marshall Nirenberg and Heinrich Matthaei experiments.

Table 10.4 Deciphering RNA Codons and the Amino Acids They Specify

Synthetic RNA	Encoded Amino Acid Chain	Puzzle Piece
UUUUUUUUUUUUUUUUUU	Phe-Phe-Phe-Phe-Phe-Phe	UUU = Phe
AAAAAAAAAAAAAAAAAA	Lys-Lys-Lys-Lys-Lys-Lys	AAA = Lys
GGGGGGGGGGGGGGGGGG	Gly-Gly-Gly-Gly-Gly-Gly	GGG = Gly
CCCCCCCCCCCCCCCCCC	Pro-Pro-Pro-Pro-Pro-Pro	CCC = Pro
AUAUAUAUAUAUAUAUAU	Ile-Tyr-Ile-Tyr-Ile-Tyr	AUA = Ile or Tyr
		UAU = Ile or Tyr
UUUAUAUUUAUAUUUAUA	Phe-Ile-Phe-Ile-Phe-Ile	AUA = Ile
		UAU = Tyr

Diagram adopted from Human Genetics concepts and Application 9th ed

The Genetic code

Second Letter

1st letter	U		C		A		G		3rd letter
U	UUU	Phe	UCU		UAU	Tyr	UGU	Cys	U
	UUC		UCC	Ser	UAC		UGC		C
	UUA	Leu	UCA		UAA	Stop	UGA	Stop	A
	UUG		UCG		UAG	Stop	UGG	Trp	G
C	CUU		CCU		CAU	His	CGU		U
	CUC	Leu	CCC	Pro	CAC		CGC	Arg	C
	CUA		CCA		CAA	Gln	CGA		A
	CUG		CCG		CAG		CGG		G
A	AUU		ACU		AAU	Asn	AGU	Ser	U
	AUC	Ile	ACC	Thr	AAC		AGC		C
	AUA		ACA		AAA	Lys	AGA	Arg	A
	AUG	Met	ACG		AAG		AGG		G
G	GUU		GCU		GAU	Asp	GGU		U
	GUC	Val	GCC	Ala	GAC		GGC	Gly	C
	GUA		GCA		GAA	Glu	GGA		A
	GUG		GCG		GAG		GGG		G

Diagram adopted from Internet source

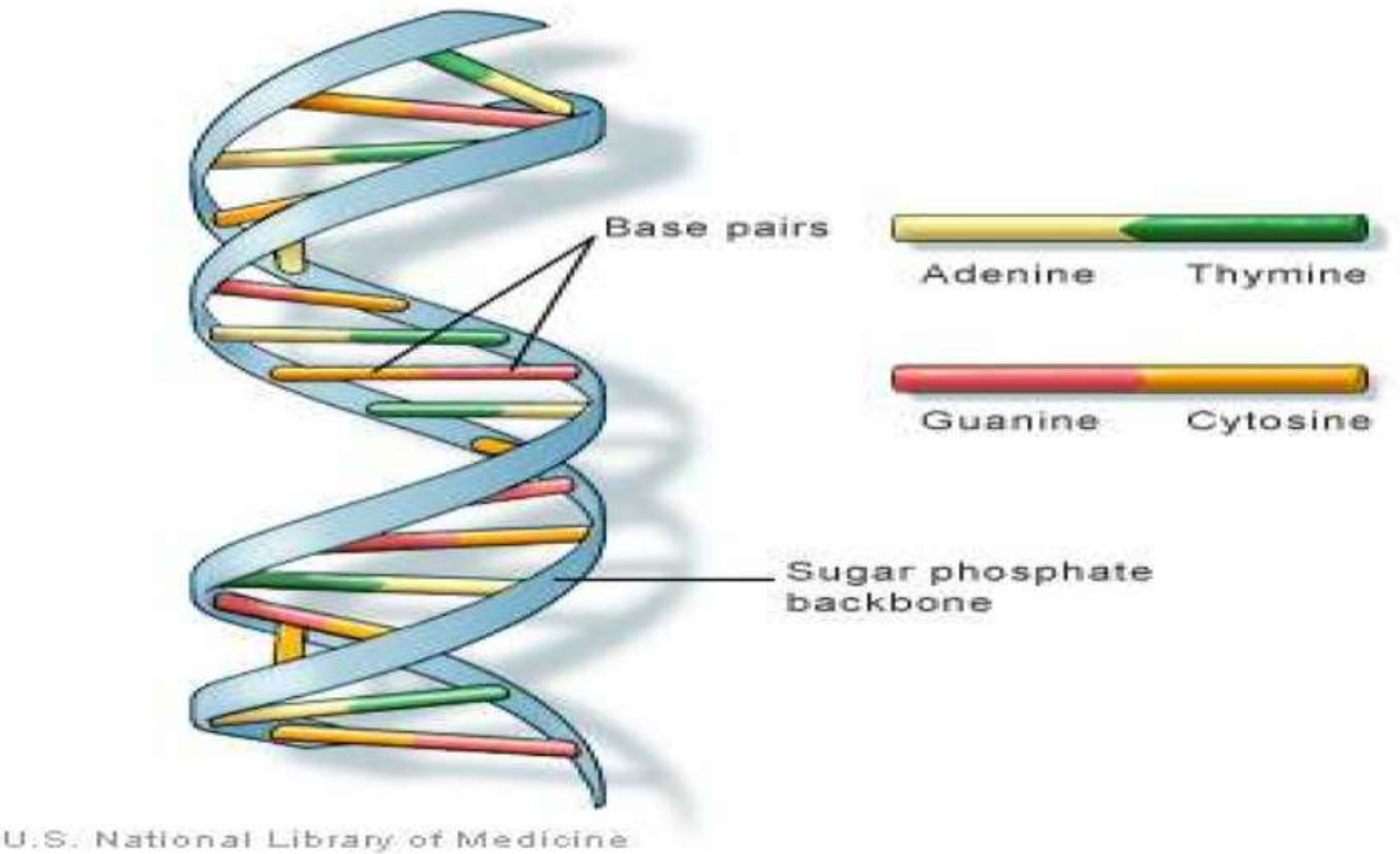
Chemistry of Nucleic Acids

What is Nucleic Acid ?

- Deoxyribonucleic acid (DNA)
- Ribonucleic acid (RNA)
- The chemical basis of hereditary
- They organized into genes, the fundamental units of genetic information.
- Nucleoproteins:
- *Conjugated proteins, presence of non-protein prosthetic group, nucleic acid & attached to one or more molecules of a simple protein,* a basic protein histone or protamine is called nucleoprotein.

Structure of DNA was discovered by James Watson & Francis Crick

DNA double helix with two strands as Proposed by Watson & Crick



Nucleic Acid

- First discovered in the nuclei of cells.
- Huge organic molecules that contains C, H, O, N, & P.
- Nucleic acid is a polymer of NUCLEOTIDE held by 3’ and 5’ phosphate bridges.
- These are of **two** types:
- Deoxyribonucleic acid (DNA)
- Ribonucleic acid (RNA)

Functions of nucleic acids

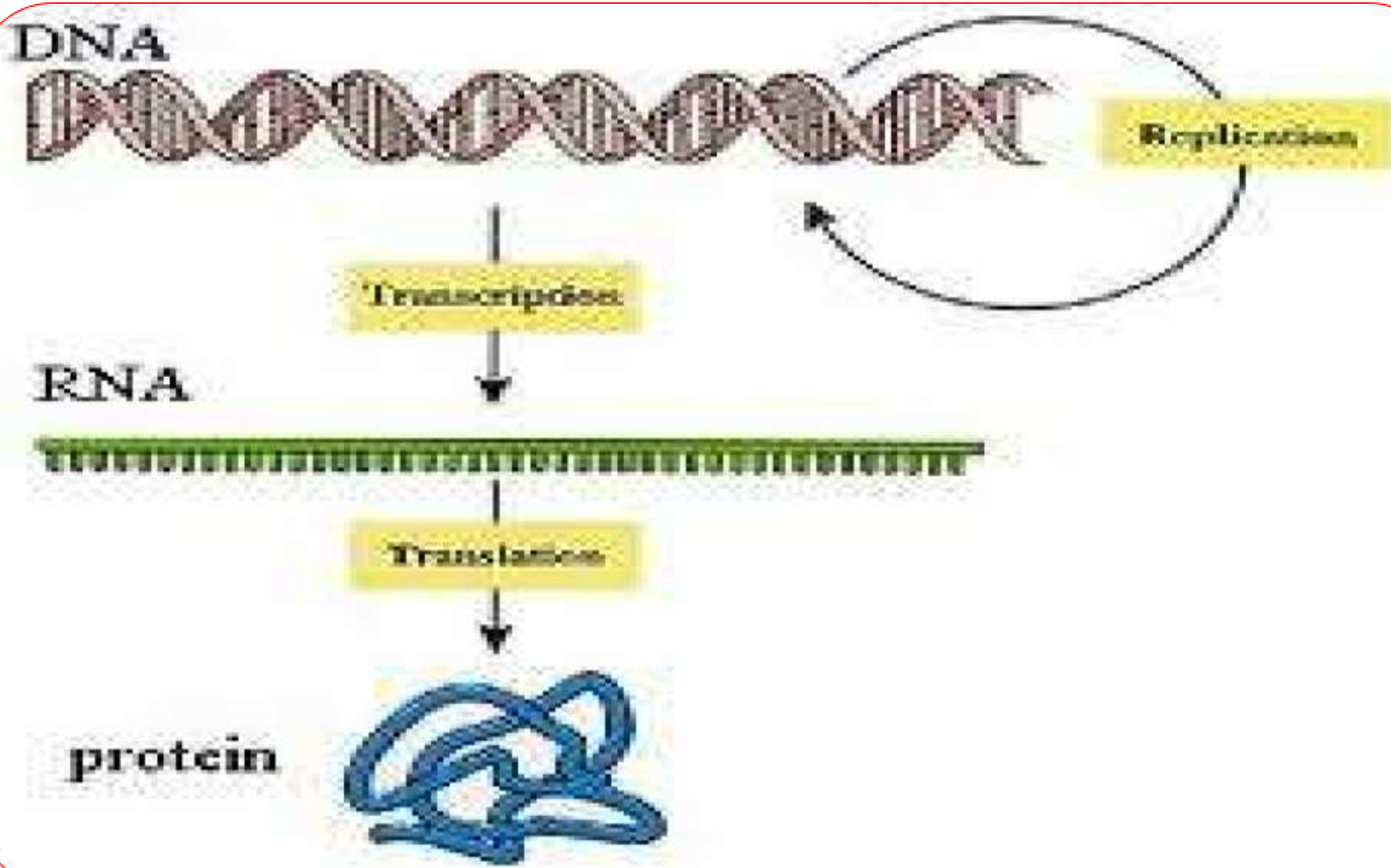
- DNA is the chemical basis of heredity
- Reserve bank of genetic information
- Responsible for maintaining the identity of different species of organisms over millions of years
- Cellular function is under the control of DNA
- The basic information pathway
- DNA directs the synthesis of RNA, which in turn directs protein synthesis

Central dogma of life

DNA ⟶ **RNA** ⟶ **Protein**

- DNA to DNA = Replication
- DNA to RNA = Transcription
- RNA to Protein = Translation

Central dogma of life



Composition of nucleic acids

Nucleic acids

Polymer of

Nucleotides

Nucleosides

Phosphate

Bases
Purines
Pyrimidines

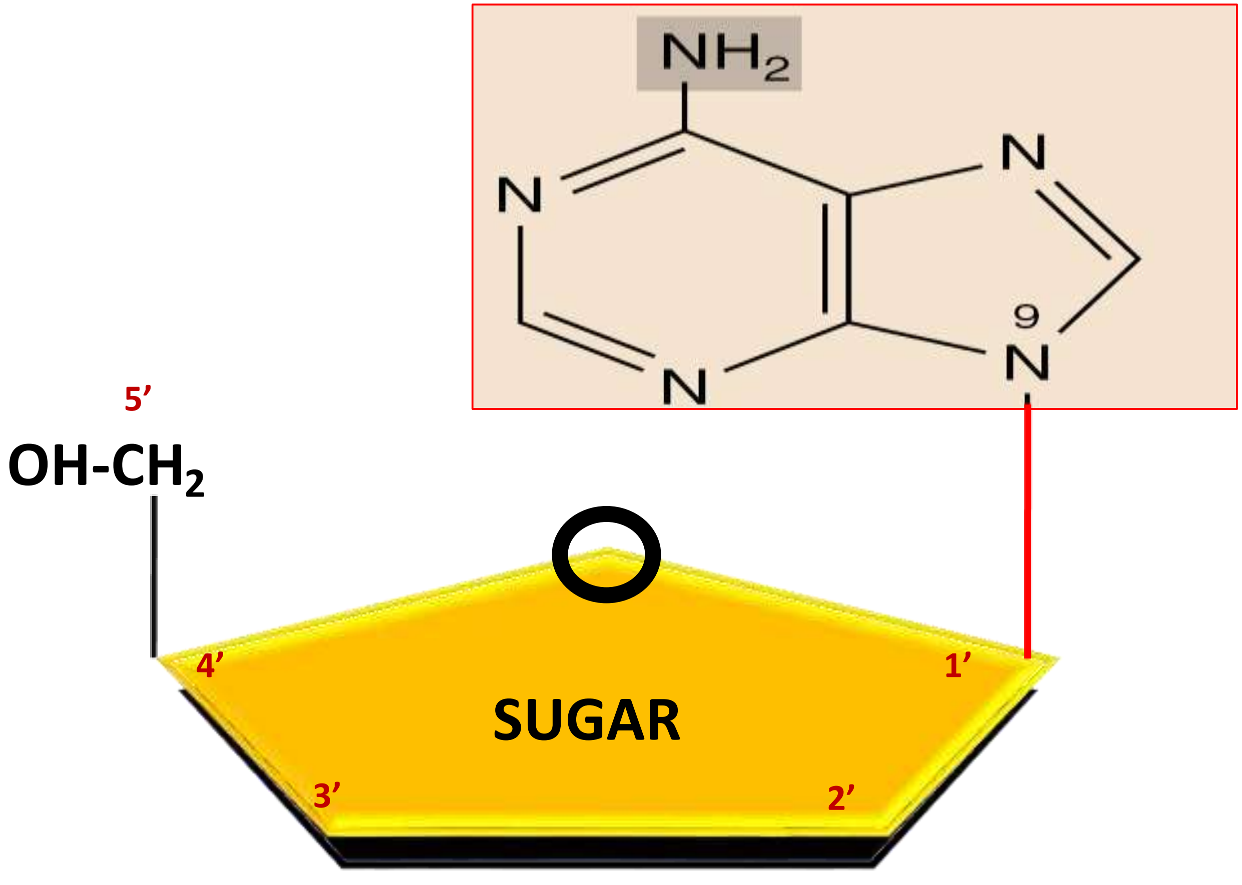
Sugar
Ribose
deoxyribose

Composition Nucleoside

- Nucleosides are composed of nitrogenous base and sugar
- The pentose sugar is either ribose in ribonucleosides or 2-deoxyribose in deoxyribonucleosides
- Glycosid bond:
- The linkage of base & sugar (N-glycosidic bond) for nucleosides involves distinct nitrogen atoms in purine & pyrimidine ring

- In purine nucleosides, nitrogen 9 of purine ring is linked to carbon 1 of pentose sugar.
- In pyrimidine nucleosides, nitrogen 1 of pyrimidine ring is linked to carbon 1 of pentose sugar.
- Nucleosides with purine bases have the suffix - sine, while pyrimidine nucleosides end with - dine.

Nucleoside



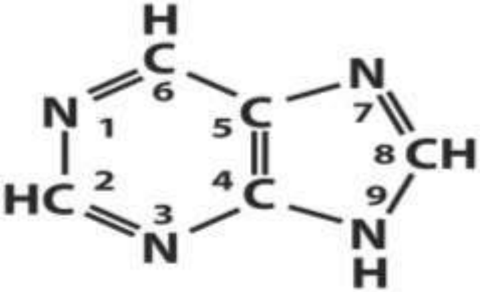
Composition of Nucleotides

- Phosphate esters of nucleosides.
- Nucleotides are composed of nitrogenous base, a pentose sugar and phosphate
- Nucleotide = nucleoside + phosphate
- The esterification occurs at 5^{th} or 3^{rd} hydroxyl group of the pentose sugar
- *Most of the nucleoside phosphates involved in biological function are 5' phosphates.*
- 5' AMP is abbreviated as AMP, but 3' variety is written as 3'-AMP.

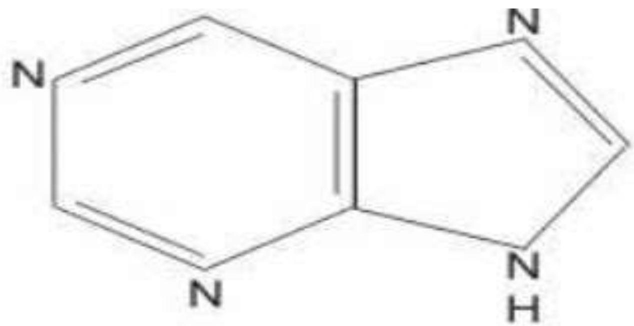
Purines

- Purine bases are nine membered ring structures consisting of pyrimidine ring fused to imidazole ring.
- The atoms of purine ring are numbered in the anticlockwise manner.
- Major bases in nucleic acids: Adenine & Guanine
- Adenine (6-amino purine):
- It contains amino group at 6th position
- Guanine (2-amino 6-oxypurine):
- It contains amino group at 2nd position & oxygen at 6th position.

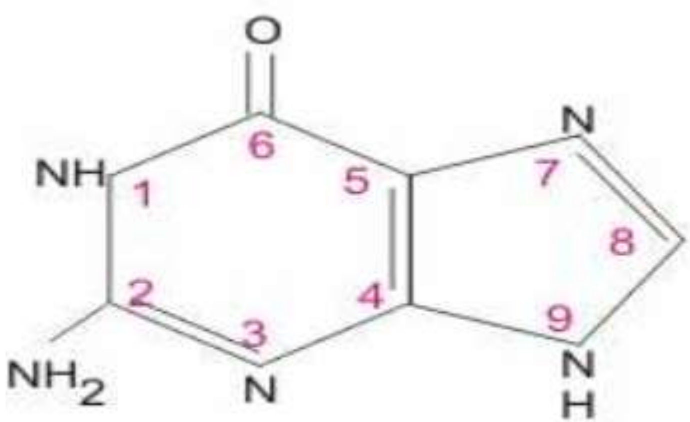
Purine Nucleotides



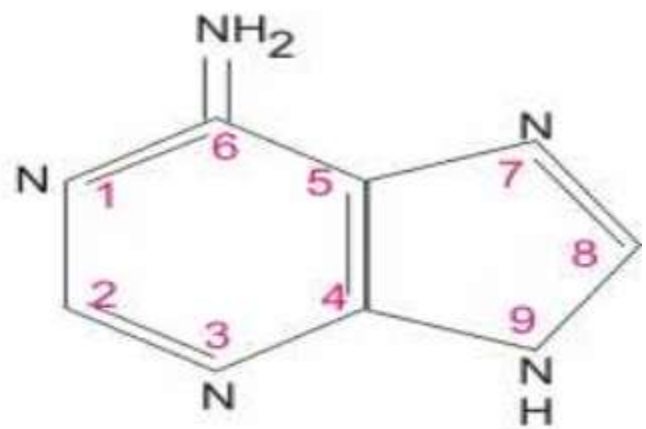
Purine



Purine Molecule



Guanine



Adenine

2-amino-6-oxypurine

6-aminopurine

Minor purines present nucleic acids

- Several minor & unusual bases are often found in DNA & RNA
- These include 5-methylcytosine, N^4-acetylcytosine, N^6 methyl adenine, N^6 dimethyl adenine & N^7 methylguanine
- Importance:
- The unusual bases in nucleic acids help in the recognition of specific enzymes.

Purine bases of plants

- Plants contain certain methylated purines.
- Caffeine (1,3,7-trimethylxanthine):
- It is found in coffee.
- It acts as a stimulant.
- Theophylline (1,3-dimethylxanthine):
- Present in tea leaves.
- It acts as a bronchial smooth muscle relaxant.

Purine analogs

- These have structural similarities to purines.
- They inhibit the enzymes involved in the metabolism of purine nucleotides.
- Allopurinol:
- Inhibits xanthine oxidase & used in the treatment of hyperuricemia (gout).
- 6-mercaptopurine:
- It inhibits purine nucleotide synthesis & used as an anticancer drug.
- Metabolic intermediates:
- These are formed during metabolism of nucleotides
- E.g. hypoxanthine, xanthine & uric acid.

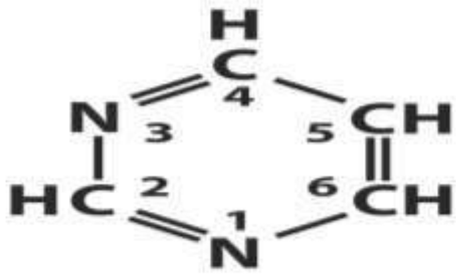
Pyrimidines

- Pyrimidines contain six membered nitrogenous ring.
- The atoms in pyrimidine ring are numbered in clockwise direction.
- Major pyrimidines found in nucleic acids:
- Cytosine
- Uracil
- Thymine

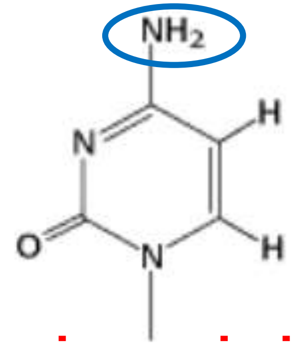
Pyrimidines

- Cytosine: Cytosine is found in both RNA & DNA.
- Cytosine (2-oxy,4-amino pyrimidine) has oxygen at position 2 & amino group at position 4.
- Uracil: Uracil is found only in RNA.
- Uracil (2,6-dioxy-pyrimidine) has oxygens at position 2 & 4
- Thymine:
- Thymine found in DNA and thymine (methyluracil) has oxygen at position 2 & 4, methyl group at position 5

Pyrimidines: Cytosine, Uracil & thymine (CUT)

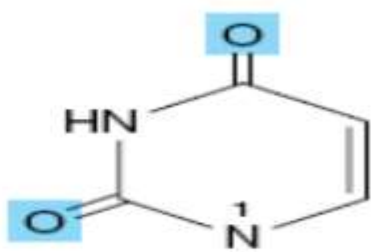


Pyrimidine



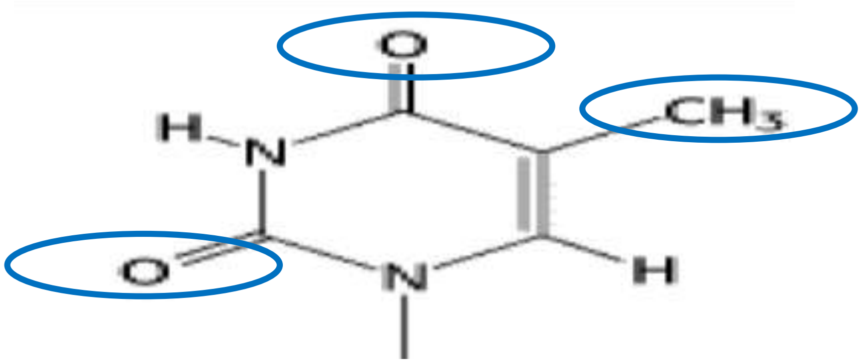
2-oxy-4-aminopyrimidine

Cytosine (C)



2,4-dioxy pyrimidine

Uracil (U)



2,4-dioxy-5-methylpyrimidine

Thymine (T)

Minor (unusual) pyrimidines found in nucleic acids

- Methylcytosine present in DNA & dihydrouracil present in tRNA.
- Pyrimidine analogs:
- These have structural similarities to pyrimidines.
- They act either as inhibitors of enzymes in the metabolism of pyrimidines or interact with nucleic acids.
- 5-fluorouracil:
- It inhibits the enzyme thymidylate synthase.
- It is used in the treatment of cancer.

Minor/Unusual bases

- Specific DNA and RNA contains small quantities of Minor/modified bases also.
- These modifications includes-
- Methylation
- Hydroxymethylation
- Glycosylation
- Alteration of atoms.

Minor/Unusual base

- Modification of Adenine:

  N-methyladenine,

  N_6N_6- dimethyladenine

- Modification of Guanine:

  7-methylguanine

- Modification of Cytosine:

  5-methylcytosine

  5-hydroxymethylcytosine

- Modification of Uracil:

  Dihydroxyuracil

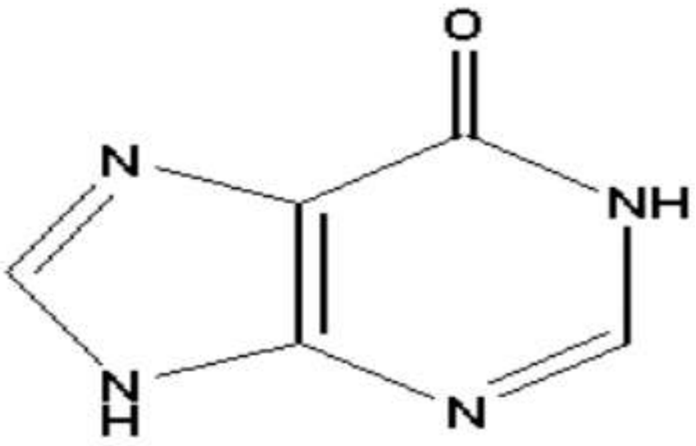
- **Special Bases:**

  Hypoxanthine (6-oxopurine)

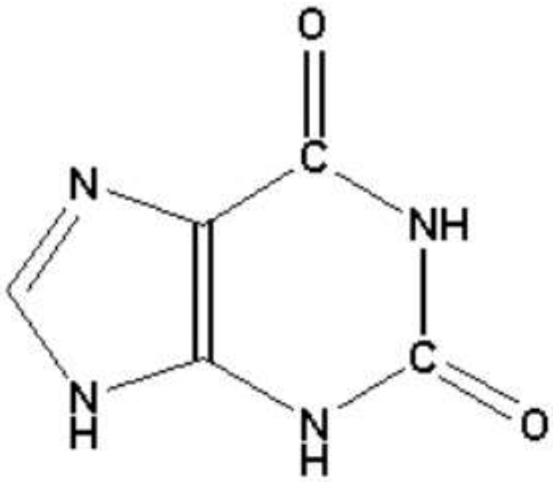
  Xanthine (2,6-dioxopurine)

  Uric acid (2,6,8-trioxopurine)

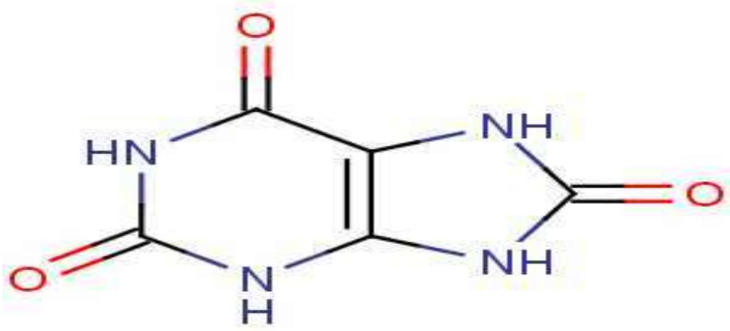
Special Bases



Hypoxanthine



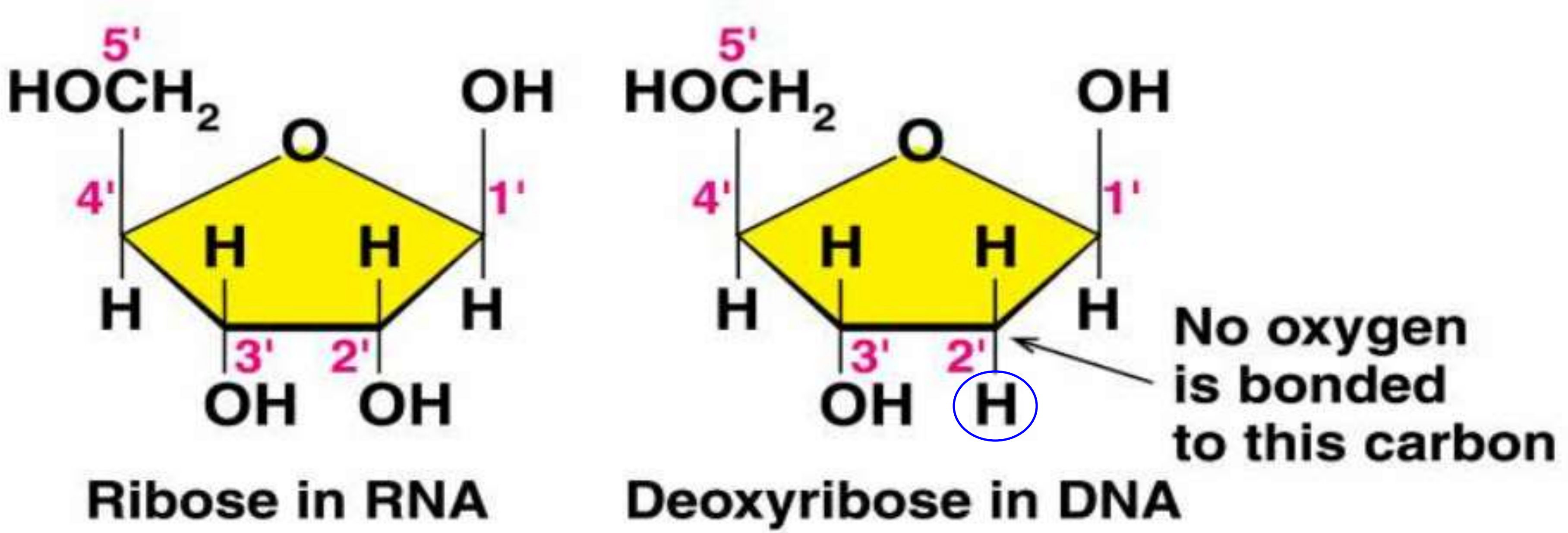
Xanthine



Uric Acid (2,6,8-trioxypurine)

Sugars Present in DNA & RNA

- DNA & RNA are distinguished on the basis of the pentose sugar present.
- DNA contains β-D-2-deoxyribose
- RNA contains β-D-ribose.



Principal Nucleotides

- Ribonucleotides are named as
- Adenine = Adenosine monophosphate (AMP)
- Guanine = Guanosine monophosphate (GMP)
- Cytosine = Cytidine monophosphate (CMP)
- Thymine = Thymidine monophosphate (TMP)
- Uracil = Uridine monophosphate (UMP)
- Deoxyribonucleotides are named as
- Adenine = Deoxyadenosine monophosphate (dAMP)
- Guanine = Deoxyguanosine monophosphate (dGMP)
- Cytosine = Deoxycytidine monophosphate (dCMP)
- Thymine = Deoxythymidine monophosphate (dTMP)
- Uracil = Deoxyuridine monophosphate (dUMP)

Functions of Nucleotides

- Activated precursors of DNA & RNA.
- ATP – Universal currency of energy.
- Required for activation of intermediates in many biosynthetic pathway.
- Carrier of methyl group in the form of SAM
- GTP-involved in protein biosynthesis as source of energy.
- Components of coenzymes: NAD, FAD & CoA.
- Metabolic regulators, e.g. cAMP, cGMP.

Physiological Important Nucleotides

- Nucleotides of Adenine
- Adenosine triphosphate (ATP)
- Adenosine diphosphate (ADP)
- Adenosine monophosphate (AMP)
- Cyclic adenosine monophosphate (cAMP)
- Phospho adenosine phospho sulfate (PAPS)
- S-adenosyl methionine (SAM)

ATP and ADP

- In oxidative phosphorylation,
- ADP is substrate,
- ATP is product
- ATP is universal currency of energy in biological systems.

Nucleotides of Guanine

- Guanosine triphosphate (GTP)
- Guanosine diphosphate (GDP)
- Cyclic guanosine monophosphate (cGMP)
- **GTP and GDP:**
- In Substrate level phosphorylation, GDP & GTP is used
- GTP is required for activation of *adenylate cyclase*.
- Energy source for protein synthesis (GTP)
- Acts as allosteric regulator

Nucleotide of Uracil

- Uridine diphosphate - sugar derivatives (UDP-sugar) acts as sugar donar in….
- UDP-glucose in synthesis of glycogen
- Other UDP-sugar in glycoproteins
- UDP-glucuronate in conjugation reaction

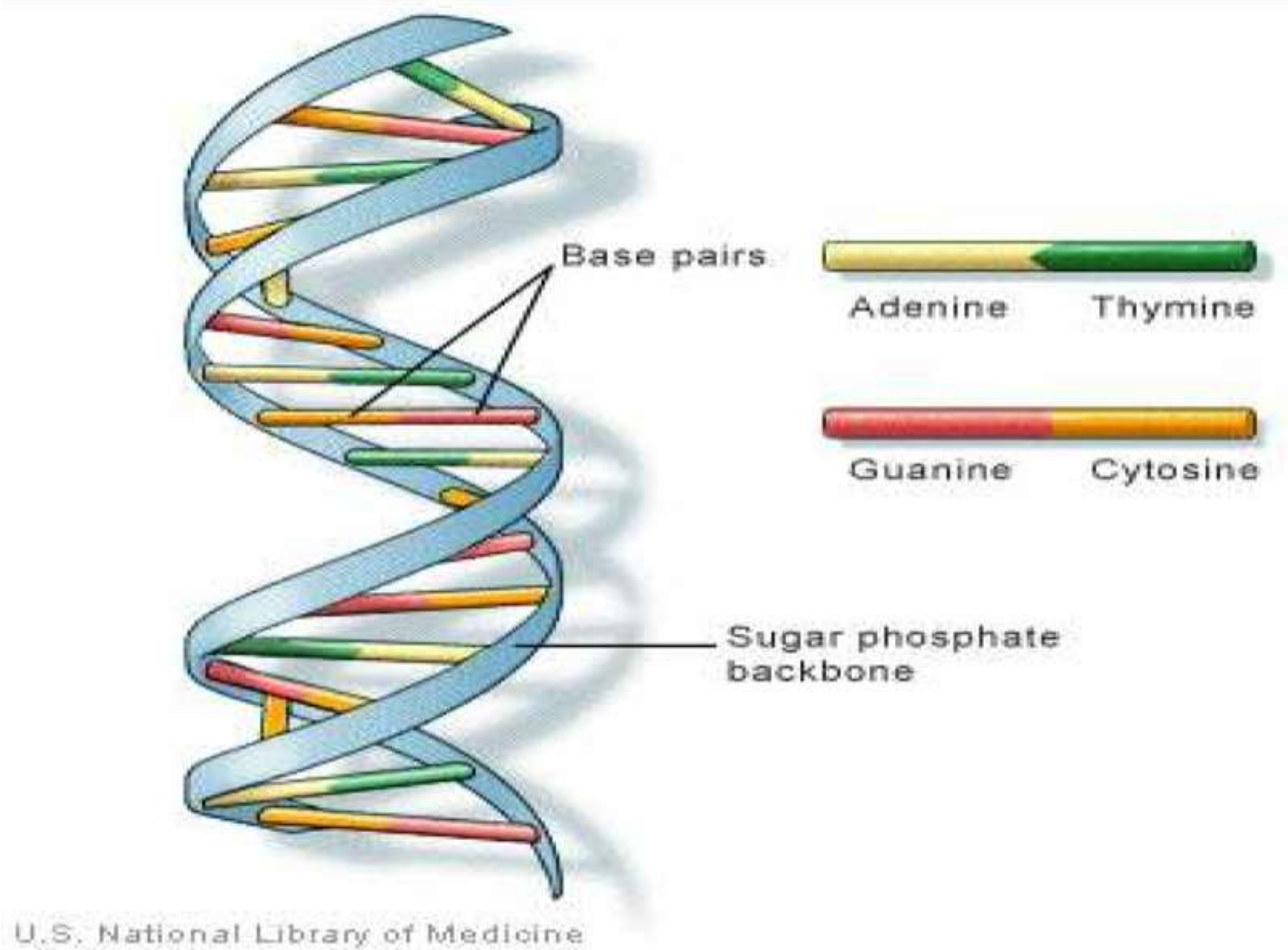
Nucleotide of Cytosine

- CTP is required for synthesis of phosphoglycerides.
- CMP-N-acetylneuraminic acid required for synthesis of glycoproteins.
- CDP-choline involved in the synthesis of sphinogomyelin

Structure of DNA

- DNA is a polymer of deoxyribonucleotides
- Composed of monomeric units namely
- Deoxyadenylate (dAMP)
- Deoxyguanylate (dGMP)
- Deoxycytidylate (dCMP)
- Deoxythymidylate (dTMP)
- The monomeric units held together by 3’5’-phosphodiester bonds as back bone.

DNA structure



Chargaff's rule

- DNA had equal numbers of adenine & thymine residues (A=T) and equal number of guanine & cytosine residues(G=C).
- This is called as *Chargaff's rule of molar equivalence of between purines & pyramidines in DNA structure.*
- RNAs which are usually single stranded, do not obey Chargaff's rule.

DNA double helix

- Double helical structure was proposed by Watson & Crick in 1953.
- The DNA is a right handed double helix.
- It consists of two polydeoxyribonucleotide chains twisted around each other on a common axis of symmetry.
- The chains are paired in an antiparallel manner, that is, the 5'-end of one strand is paired with the 3'-end of the other strand

- 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 width (or diameter) of a double helix is 20A^0(2nm)
- Each turn of helix is 34 A^0 (3.4nm) with 10 pairs of nucleotides, each pair placed at a distance of about 3.4 A^0
- 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.

- The polynucleotide chains are not identical but complementary to each other due to base pairing.
- The two strands are held together by hydrogen bonds.

A = T, G ≡ C

- The hydrogen bonds are formed between a purine & pyrimidine.
- The spatial relationship between the two strands in the helix creates a major (wide) groove and a minor (narrow) groove.

- These grooves provide access for the binding of regulatory proteins to their specific recognition sequences along the DNA chain.
- DNA helix proves Chargaff's.
- The genetic information resides on one of the two strands known as template strand or sense strand.
- The opposite strand is antisense strand.

Modification of bases in DNA

- About 5% of cytosine in eukaryotic DNA is methylated.
- Methylation is catalysed by methylase (DNA methyl transferase)
- Methylation suppresses migration of segment of DNA (which are called as transposons) & increase the tendency of DNA to assume Z form.
- Hypomethylation of DNA is associated with development of cancer.

Conformations of DNA double helix

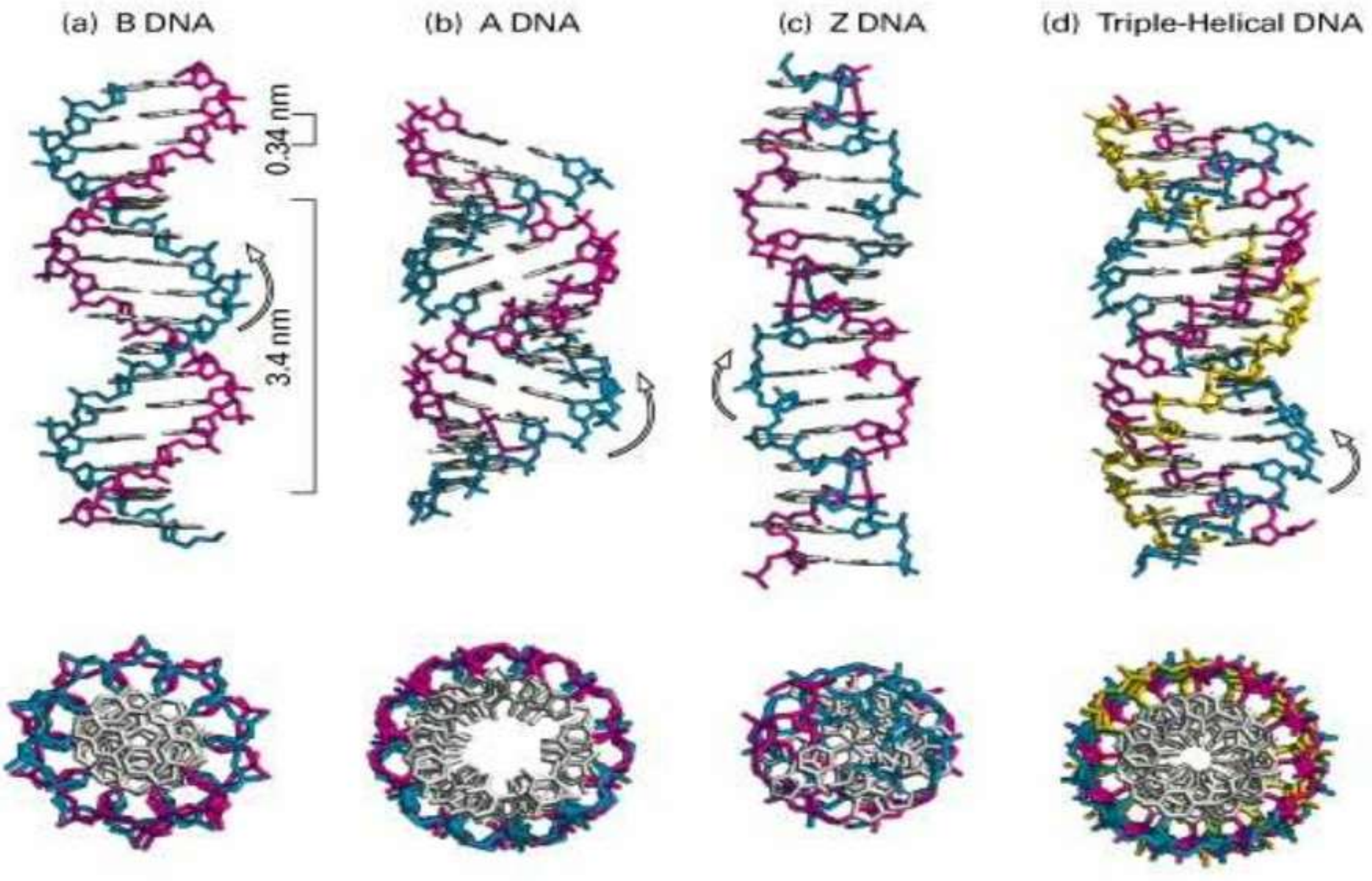
- The double helical structure of DNA exists in 6 forms A,B,C,D,E and Z form.
- Among these, B, A & Z forms are important.
- B-form is most predominant form under physiological conditions.
- A-from is also right-handed helix.
- Contains 11 base pairs.
- There is a tilting of the base pairs by 20^0 away from the central axis.
- Z-form is a left –handed helix and contains 12 base pairs per turn.

- The polynucleotide strands of DNA move in a somewhat zig-zag fashion, hence called as Z-DNA.
- Other types of DNA:
- DNA also exists in certain unusual structures.
- These structure are important for molecular recognition of DNA by proteins & enzymes.

Complementary strands

- The two strands of DNA are not identical but two strands are complementary to each other.
- The complementary results from base pairing.
- Adenine pairs with thymine through two hydrogen bonds.
- Guanine pairs with cytosine through three hydrogen bonds.
- G-C base pairs are more stable than A-T base pairs.
- Complementary base sequence accounts for chargaff's rule.
- It also accounts for each DNA strand acting as a template for the synthesis of its complementary strand during DNA replication.

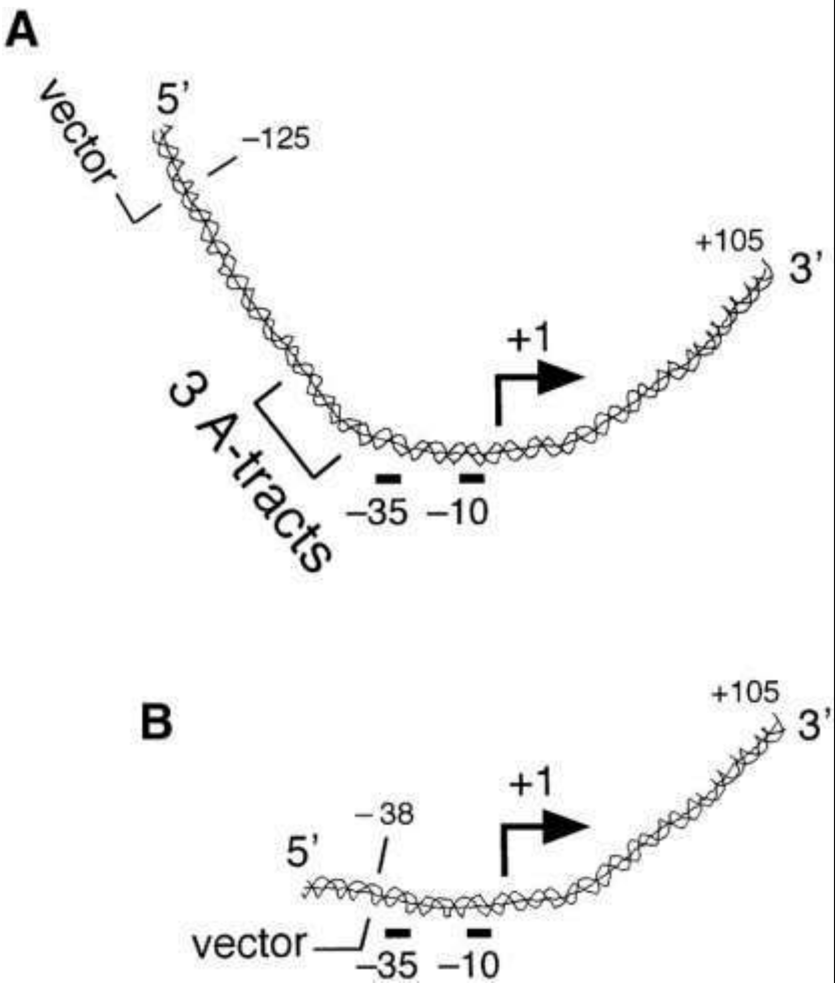
Types of DNA

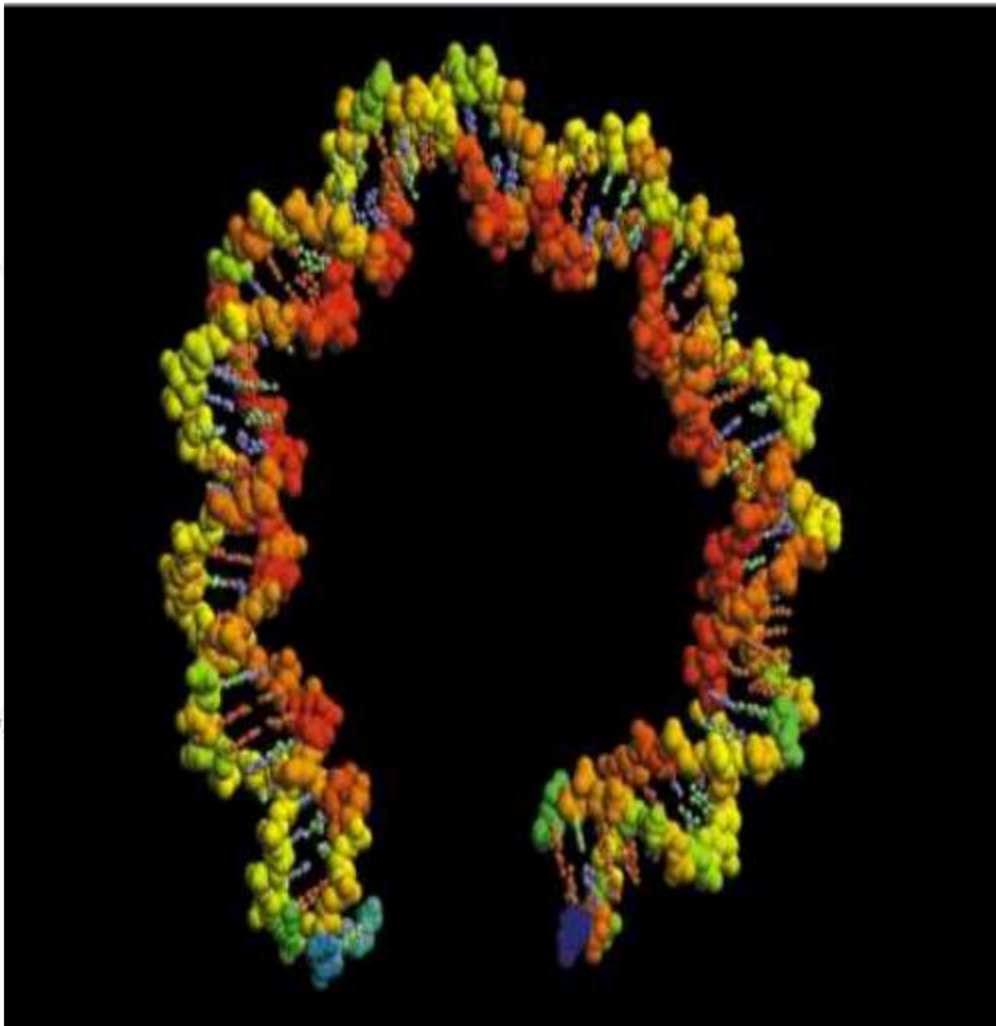


Bent DNA

- Adenine base containing DNA tracts are rigid & straight.
- Bent conformation of DNA occurs when A-tracts are replaced by other bases or a collapse of the helix into minor groove of A-tract.
- Bending in DNA structure is due to photochemical damage or mispairing bases.
- Certain antitumor drugs (e.g.,cisplastin) produce bent structure in DNA.
- Such changed structure can take up proteins that damage the DNA.

Bent DNA

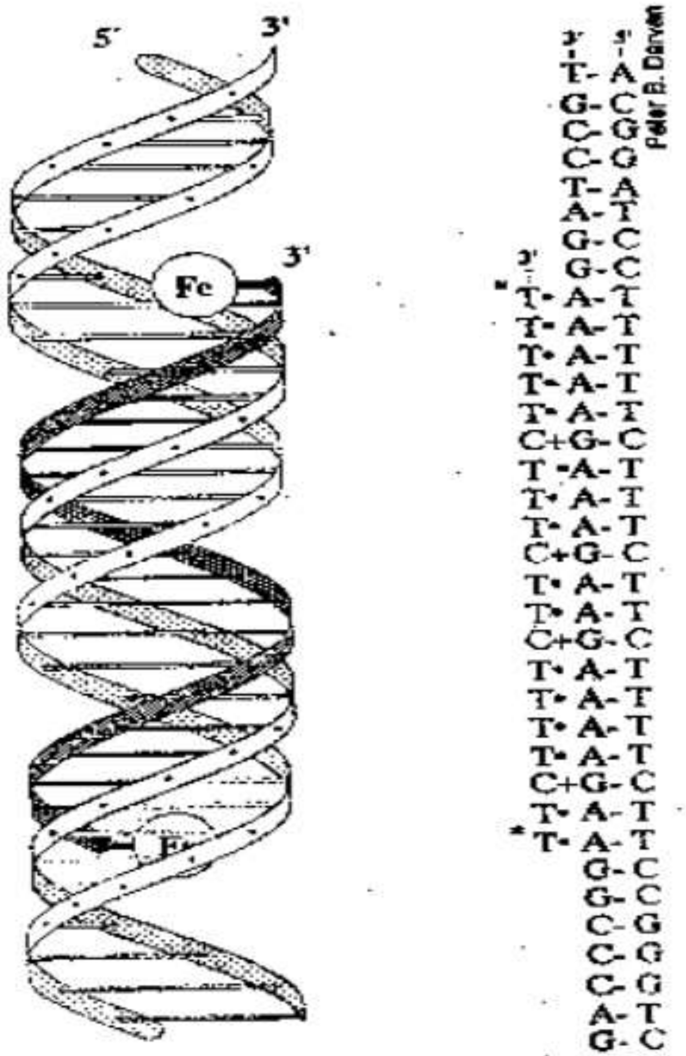


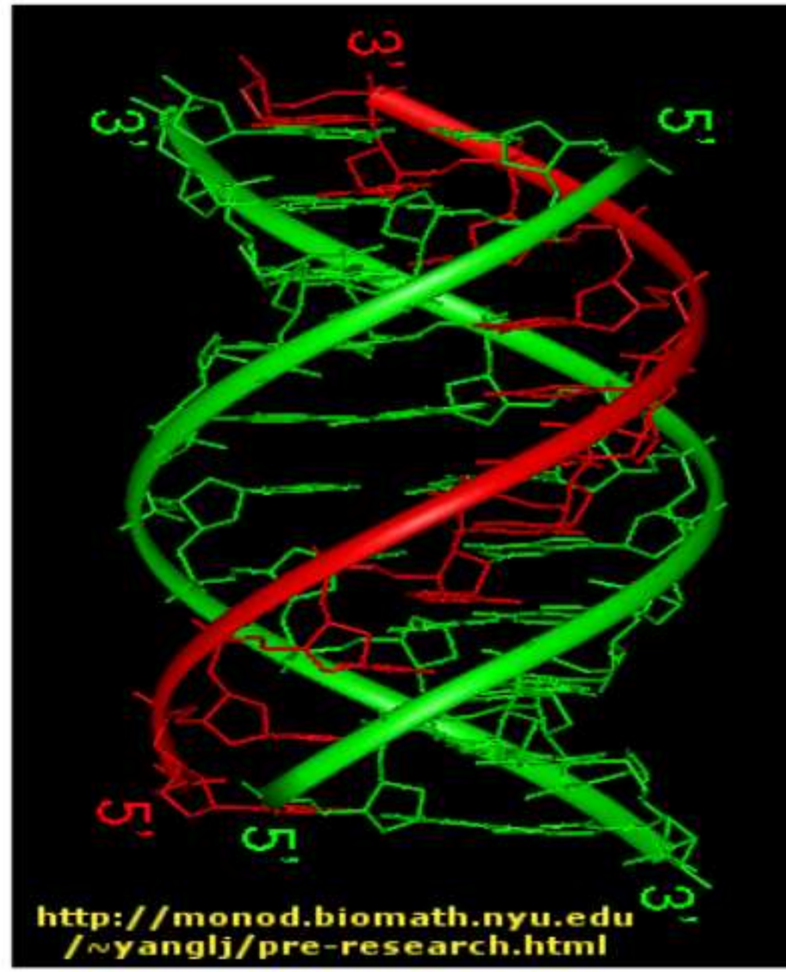


Triple-stranded DNA

- Triple stranded DNA formation may occur due to additional hydrogen bonds between the bases
- Thymine can selectively form two Hoogsteen hydrogen bonds to the adenine of A-T pair to form T-A-T.
- Cytosine can also form two hydrogen bonds with guanine of G-C pairs that results in C-G-C.
- Triple helical structure is less stable than double helix.
- Due to three negatively charged backbone strands in triple helix results in an increased electrostatic repulsion.

Triple-stranded DNA

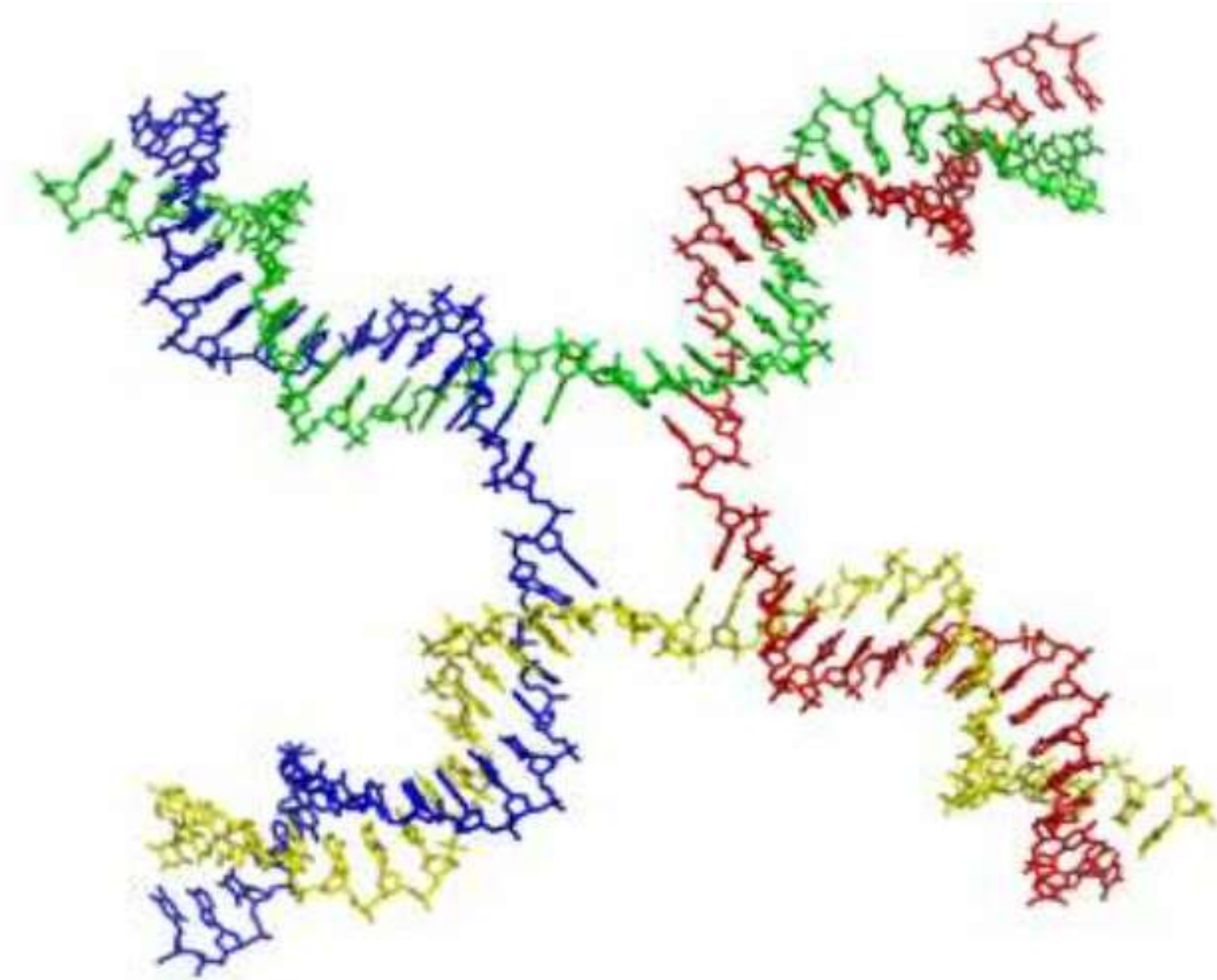




Four-stranded DNA

- Polynucleotides with very high content of guanine can form a tetrameric structure called G-quartets.
- These structures are planar & are connected by Hoogsteen hydrogen bonds.
- Antiparallel four stranded DNA structures referred to as G-tetraplexes.
- The ends of eukaryotic chromosomes namely telomeres are rich in guanine,& forms G-tetraplexes.

Four-stranded DNA



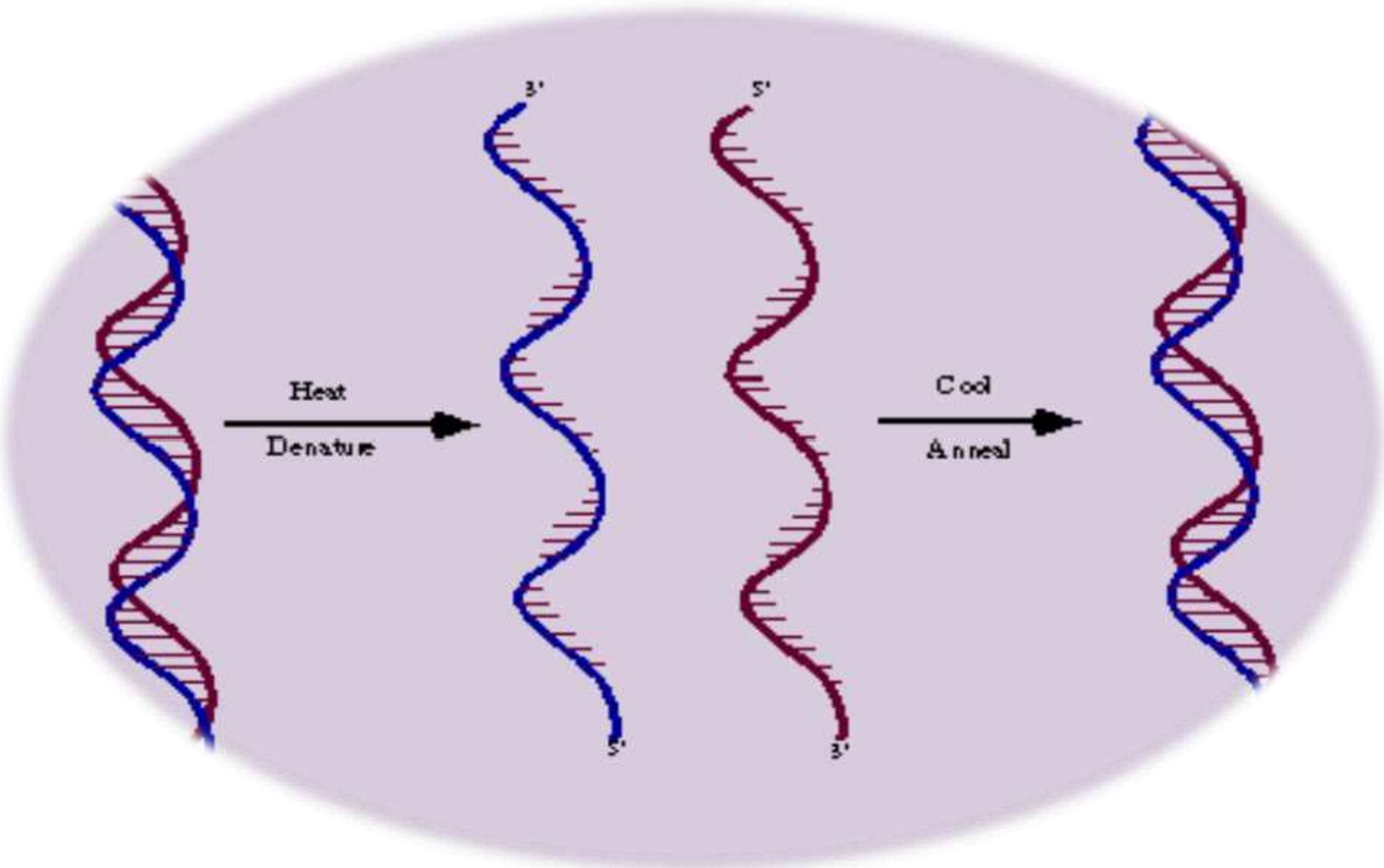
Size of the DNA molecule

- Huge in size
- B-DNA with a thickness of 0.34nm
- Molecular weight of 660 daltons
- Length is expressed in base pairs(bp)
- A kilobase pair 10^3bp, a megabase pair(Mb) is 10^6bp & gigabase pair (Gp) is10^9
- 1kb=1000bp
- 1Mb=1000kb=1,000,000bp
- 1Gb=1000Mb=1,000,000,000bp
- Length varies from species to species
- Length of Human DNA is 2 meters &10µ diameter

Denaturation of DNA

- The two strands of DNA are held together by hydrogen bonds
- Disruption of hydrogen bonds (by change in pH or increase in temperature) results in separation of strands
- The phenomenon of loss of helical structure of DNA is known as denaturation
- Phosphodiester bonds are not broken by denaturation.
- It is measured by absorbance at 260nm.

Denaturation of DNA



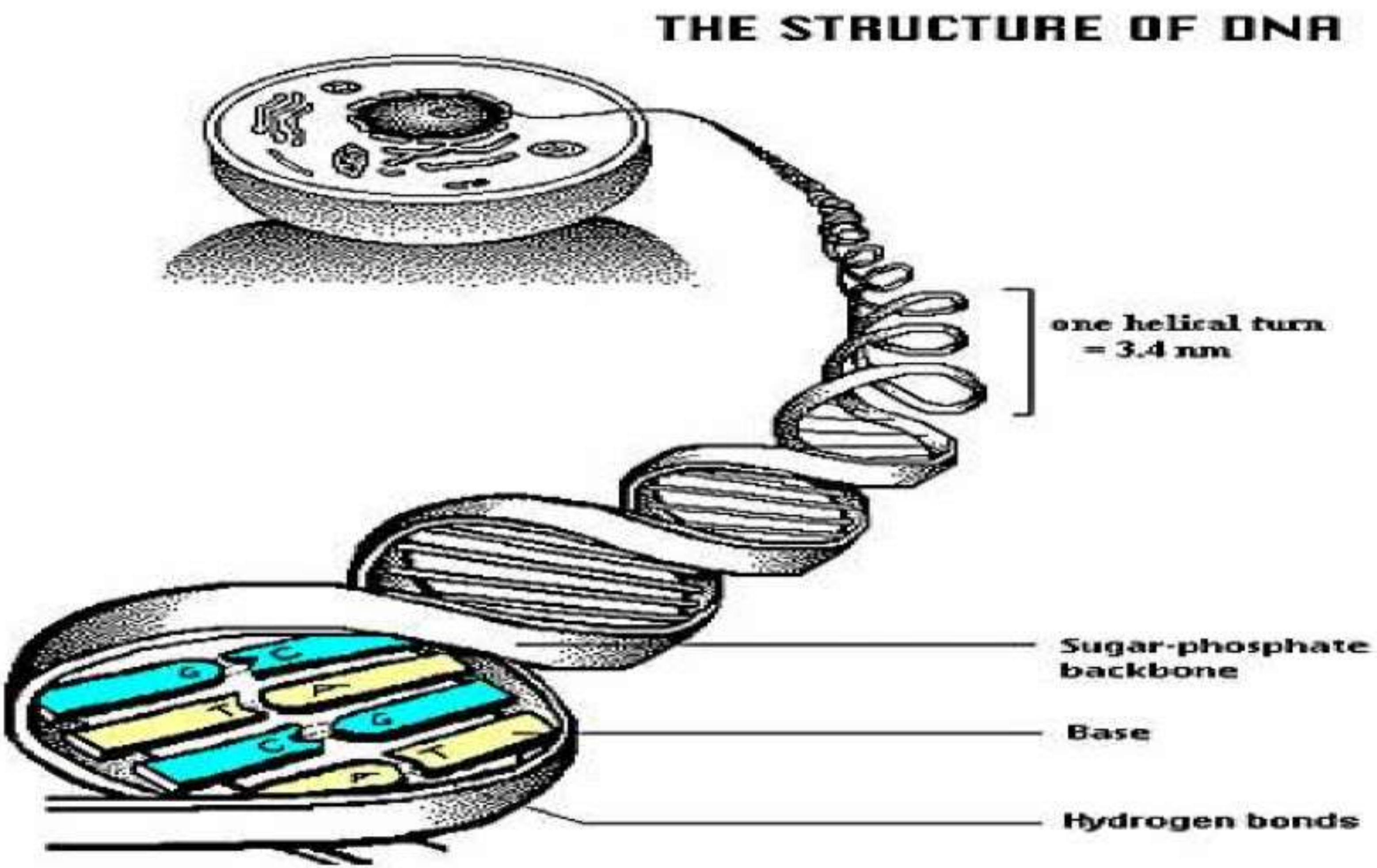
Melting temperature (Tm)

- It is defined as the temperature at which half of the helical structure of DNA is lost.
- G-C base pairs are more stable than A-Tbp.
- Tm is greater for DNAs with high content of GC.
- Formamide destabilizes hydrogen bonds of base pairs.
- This is used in rDNA technology.
- **Renaturation (reannealing):**
- It is a process in which the separated complementary DNA strands can form a double helix.

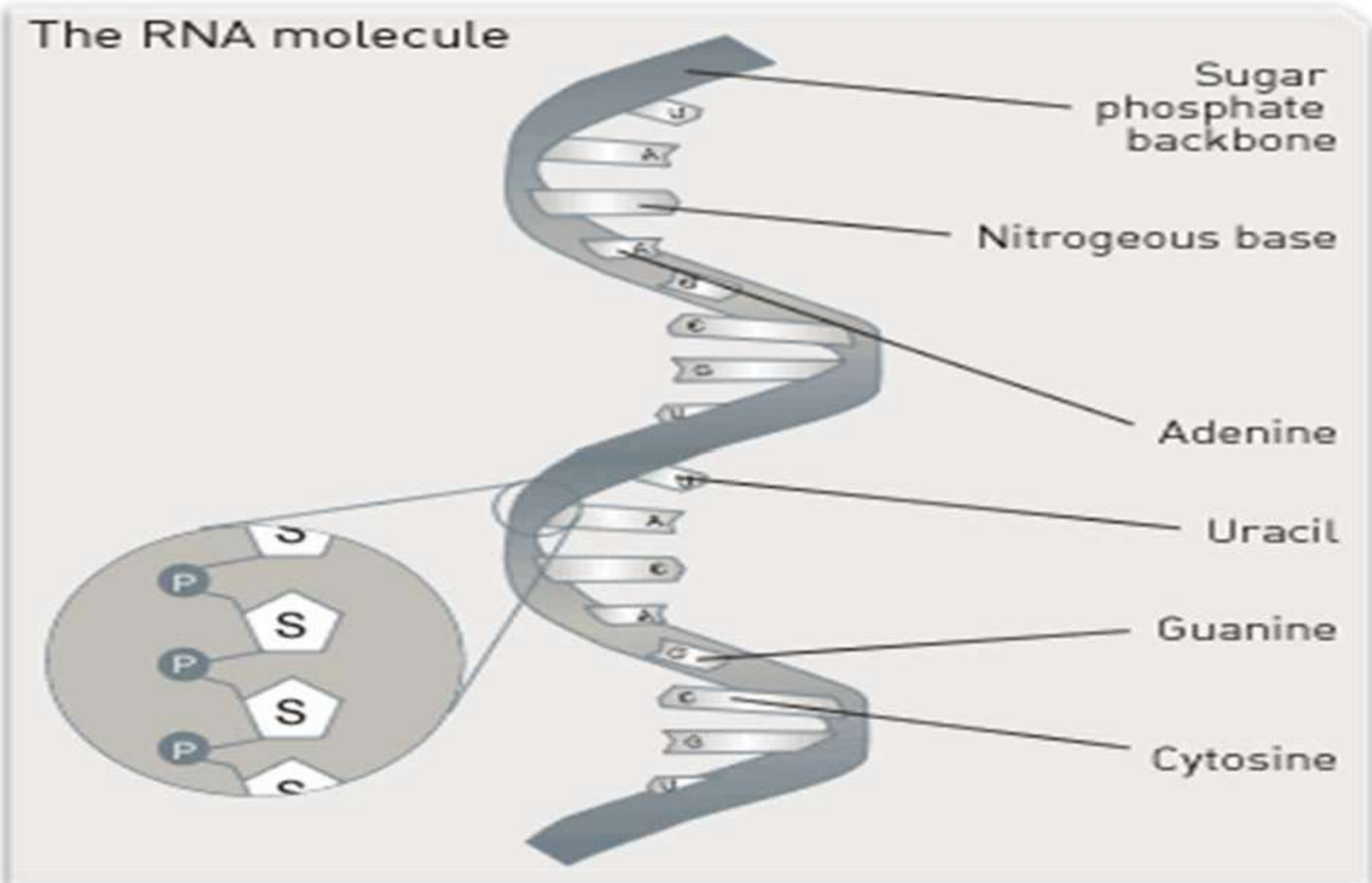
Organization of DNA in cell

- Prokaryotic DNA:
- The DNA is organized as a single chromosome in the form of double stranded circle.
- Packed in the form of nucleoids.
- Eukaryotic DNA:
- DNA is associated with various proteins to form chromatin which then organized into compact structures chromosomes.

Organization of DNA in cell



Structure of RNA



Structure of RNA

- RNA is a polyribonucleotide
- It is single stranded polynucleotide.
- Phosphodiester bond links the nucleotides
- Formed between 3-OH group of one pentose sugar & 5-OH group of another pentose sugar of ribonucleotide.
- Nucleotides found in RNA are
- AMP
- GMP
- CMP
- UMP
- Thymine base absent in RNA
- Minor methylated thymine & dihydrouracil also present.

- Chargaff’s rule- due to single – stranded nature, there is no specific relation between purines & pyramidine content.
- It will not obey the chargaff’s rule.
- Alkali hydrolysis:
- Alkali can hydrolyse RNA to 2’3’-cyclic diesters.
- This is due to presence of OH group at 2’position.
- Orcinol colour reaction:
- RNAs can be identified by orcinol colour reaction due to presence of ribose.

Structures of DNA & RNA

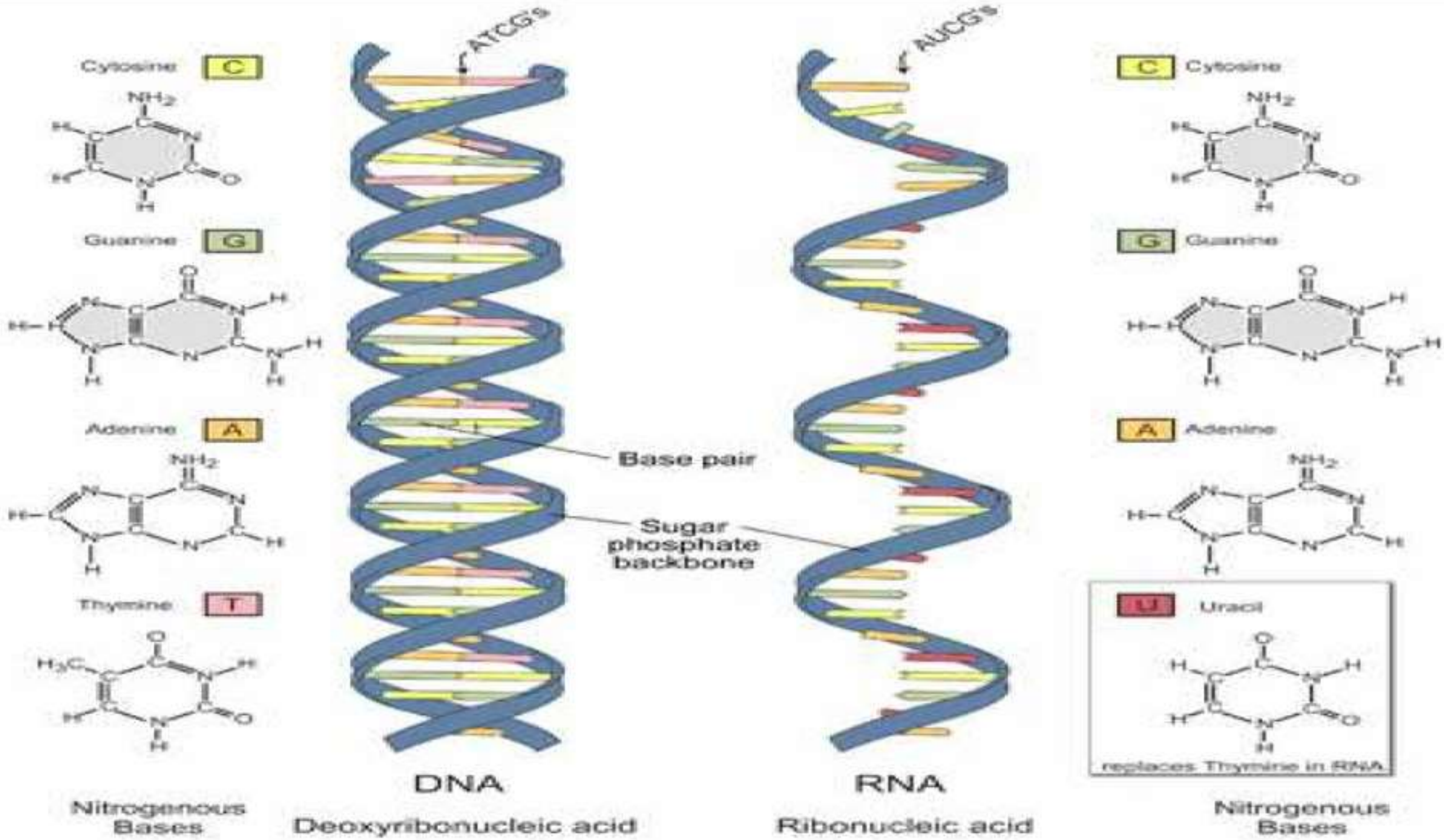


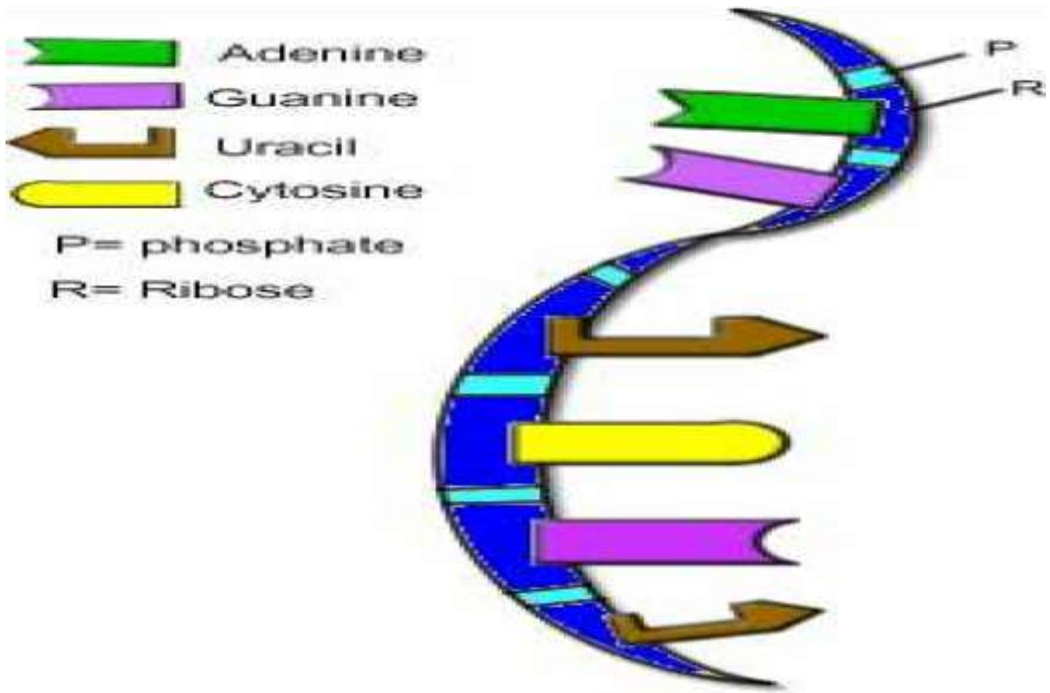
Image adapted from: National Human Genome Research Institute.

Types of RNA

- Three major types:
- Messenger RNA:5-10%
- Transfer RNA:10-20%
- Ribosomal RNA:50-80%
- RNAs are synthesized from DNA
- Involved in protein synthesis.
- Messenger RNA:
- ***mRNA:***
- It carries genetic information from DNA for protein synthesis.
- Precursor form is heterogeneous nuclear RNA(hnRNA).

- ***Structure*:** It contains
- Cap: is an inverted 7-methyl GTP attached to 5'end.
- 5'UTR: (5'untranslated region) is at the 5'end.
- Coding region contains 3 types of codons:
- Initiating codon-is always for AUG for methionine.
- Specific codon-for different amino acids
- Terminating codons-which are UGA, UAA & UAG.

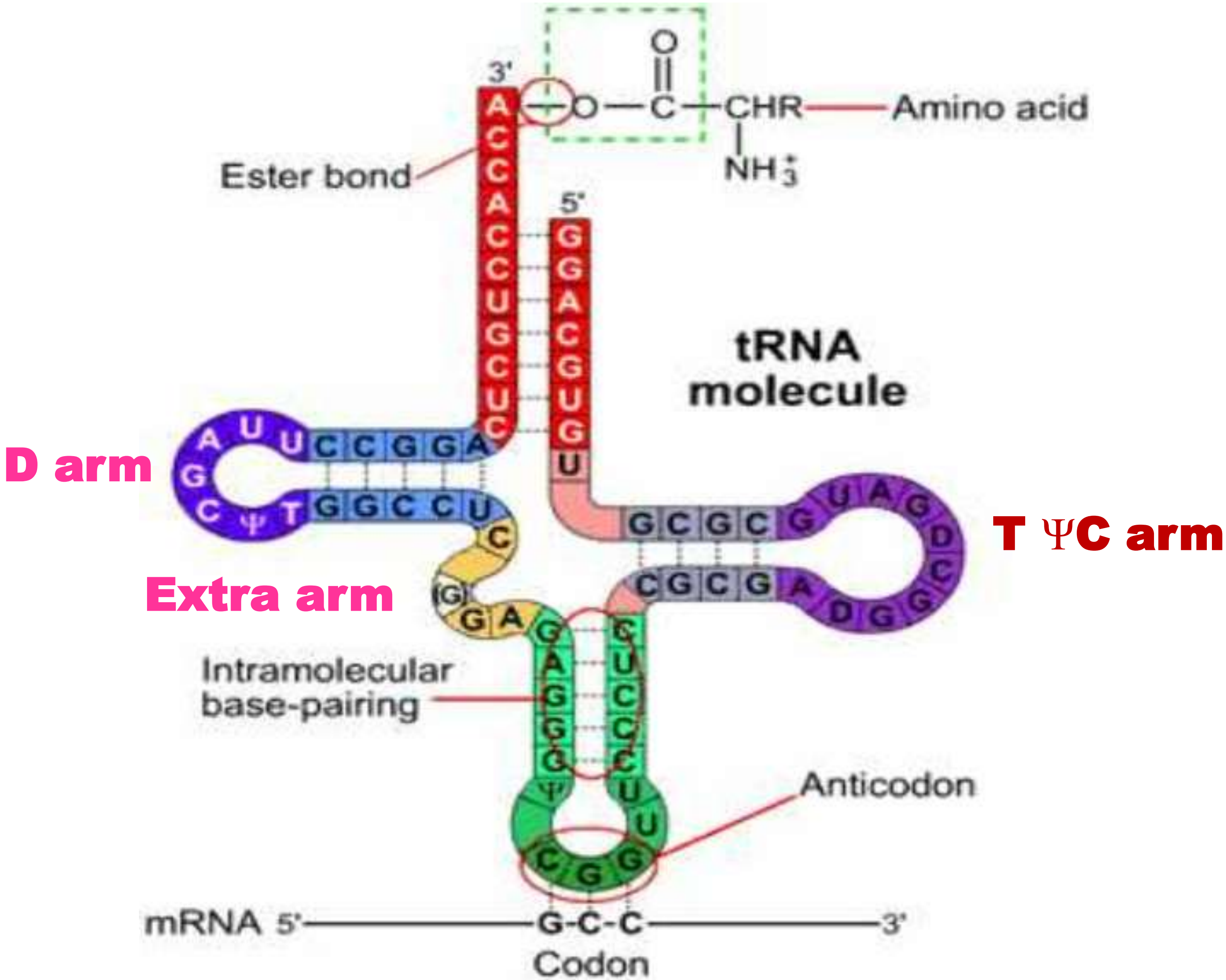
- 3'UTR (3'untranslated region) at 3' end.
- Polyadenylate tail (poly A tail): Consists of 200-300 adenylate residues at the 3' end.
- mRNA accounts for 5 to 10% of total RNA.
- Function: It is required for protein biosynthesis.



Transfer RNA

- Transfer RNA (soluble RNA) contains 71-80 nucleotides.
- Molecular weight-25,000.
- At least 20 species of tRNAs, corresponding to 20 Amino acids.
- Required for protein biosynthesis.
- It contains many unusual bases & nucleosides.
- *Unusual bases present in t RNA are thymine, dihydrouracil, hypoxanthine,1-methyladenine & 2-N dimethyl guanine*

Structure of tRNA



- Unusual nucleosides are formed from the unusual bases,
- Pseudouridine is an unusual nucleoside found in t-RNA.
- ***Structure:***
- Clover leaf structure & it has five arms.
- ***CCA arm:*** cytosine-cytosine-adenine (CCA-arm) present at 3'end. It is an acceptor arm for the attachment of amino acids to form amino acyl tRNA.
- ***D arm:*** contains dihydrouracil.

- T¥C arm: (thymidine-pseudouridine-cytosine arm) contains pseudouridine.
- Anticodon arm: contains of sequence of three bases that are complementary to codon mRNA.
- tRNA is also *called adapter tRNA because it carries specific amino acids on its 3' end corresponding to anticodon at its anticodon arm.*
- Extra arm: also called variable arm.
- Based on length of extra arm-tRNA is classified into
- Class-1 tRNA: Contain short arm (3-5 base pairs)
- Class-2t RNA: Contain long arm (13-20base pairs)

- tRNA accounts for 15-30% of total cellular RNAs.
- tRNA is smaller in size.
- tRNA is synthesized as precursor tRNA.
- Mature form is formed by post transcriptional modifications.
- Functions:
- tRNA is required fro protein synthesis.
- It is required for the transfer of specific amino acids to the site of protein synthesis.
- Also required for incorporation of specific amino acids to the growing polypeptide chain.

Ribosomal RNA

- r-RNA is found in ribosomes.
- Eukaryotic ribosomes are factories of protein synthesis.
- Composed of two major nucleoprotein complexes-60s subunit & 40s subunit
- 60s subunit contains-28s rRNA, 5s rRNA & 5.8s rRNA
- 40s subunit contains-18s rRNA
- Main function is protein biosynthesis.

Cellular RNA & their functions

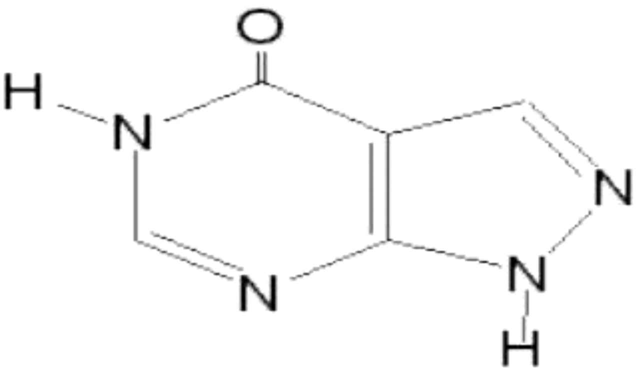
Type of RNA	abbreviation	functions
Messenger RNA	mRNA	**Transfers genetic information to synthe**
Heterogeneous nuclear RNA	hnRNA	**Precursor for mRNA & other RNAs**
Transfer RNA	tRNA	**Transfers amino acid to mRNA for protein biosynthesis.**
Ribosomal RNA	rRNA	**Provides structural frame work for ribosomes.**
Small nuclear RNA	snRNA	**Involved in mRNA processing**
Small nucleolar RNA	snoRNA	**Involved in processing of rRNA molecules.**
Small cytoplasmic RNA	scRNA	**Selection of proteins for export.**
Transfer messenger RNA	tmRNA	**Present in bacteria. adds short peptide tags to proteins to facilitate degradation of incorrectly synthesized proteins.**

Synthetic Analogues of Nucleotides

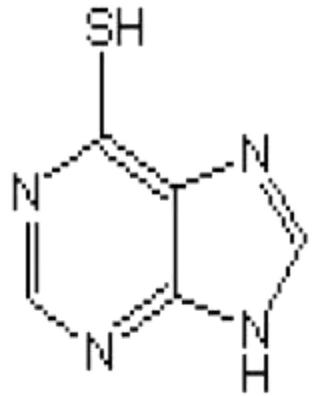
- Chemically synthesized analogues.
- Prepared by altering either the heterocyclic ring or sugar moiety.
- These are used chemotherapeutically to control cancer or infections.
- Allopurinol: used in the treatment of hyperuricemia and gout.
- 5-fluorouracil,6-mercaptopurine,8-guanine, 3-deoxyuridine,5- or 6-azauridine,5- or 6-azacytidine & 5-idouracil are used in treatment of cancer.
- These compounds will block cell proliferation.

- Azathioprine is used to suppress immunological rejection during transplantation.
- Arabinosyladenine is used for treatment of neurological diseases, viral encephalitis.
- Arabinosylcytosine is used in cancer therapy as it interferes with DNA replication.
- Zidovudine or AZT & didanosine are sugar modified synthetic nucleotide analogs, used in the treatment of AIDS

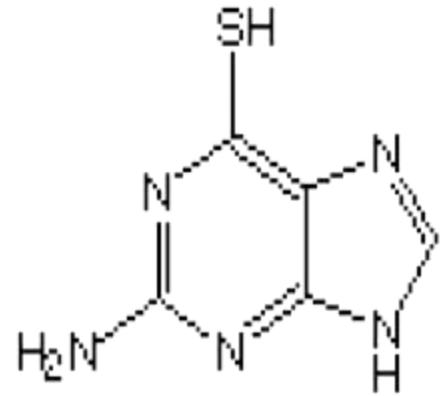
Synthetic Nucleotides



allopurinol



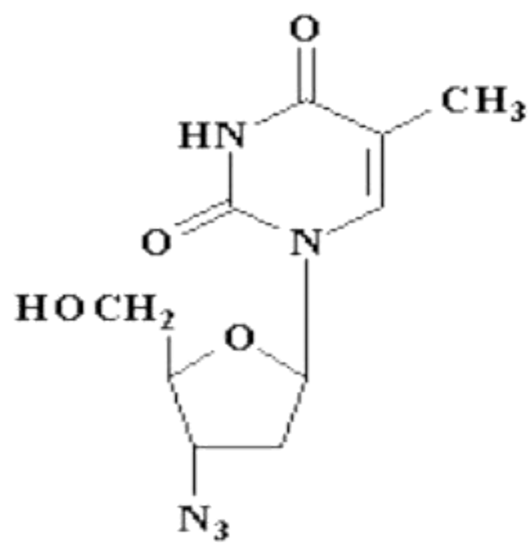
6-mercaptopurine



6-thioguanine

Zidovudine

$C_{10}H_{13}N_5O_4$



Thank you