BIOCHEMISTRY

BCH 201

Chemical elements in Biomolecules

- All living matter contains C, H, O, N, P and S

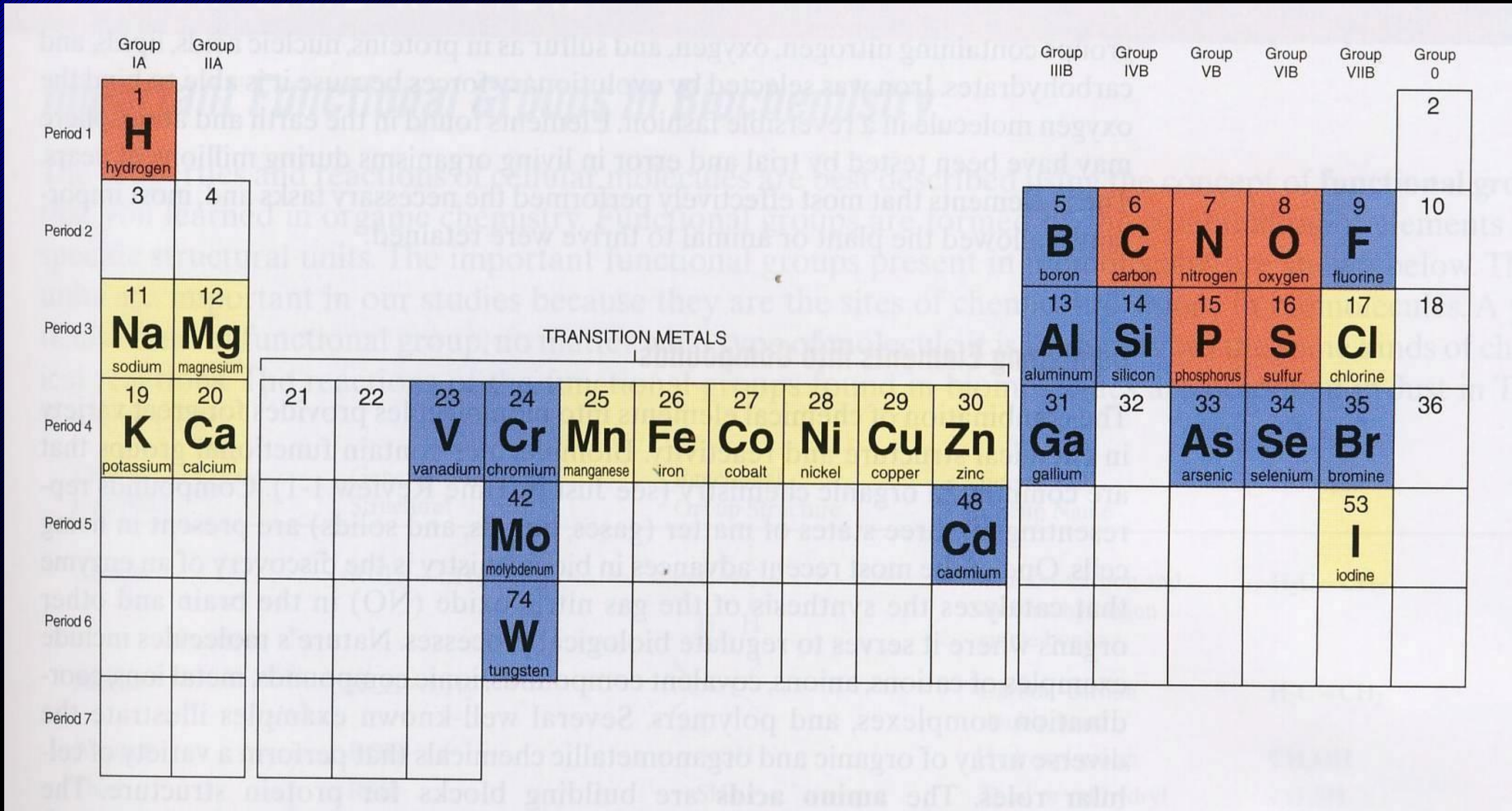
- 28% of chemical elements occurs in plants and animals

- Divided into 3 categories :

1. Found in bulks & essential for life (92% of dry weight of living things)

. Trace Quantities in most organism (Calcium, Mg, Fe, I, Fe etc)

3. 2Trace 2element 2in 2some 2organism 2(arsenic, 2Bromine, molybdenum & vanadium)



- Elements in red (present in bulk in living cells – essential for life)
- Elements Yellow are trace elements (very likely essential)
- Elements in blue are presents in some organisms and may be essential

Combining elements into compounds

- Combination of these elements :

  → Variety of chemical structure & reactivity

- Compound representing all three states of matters (gases, liquid and solids) are present in living cells :

  • *Gas : Nitric Oxide (NO) in the brain – for biological regulation*

  • *Liquid : H_2O in the blood circulation*

  • *Solids : Glycoprotein, protein etc.*

Biological Macromolecules

- There are 3 major classes :

1. Carbohydrate (Polysaccharide)

. Nucleic Acids

3. Lipid

4. Proteins

Carbohydrate

Carbohydrate

- An important class of biomolecules
- make up highest percentage of biomass than any other biomolecules
- Carbohydrate :

`Carbon’ + ` Hydrate’ (In which the ratio of C : H : O is 1 : 2 : 1)

→ Impirical formula : $(CHO)_n$

- Compounds that have reactive aldehyde or ketone functional group or multiple hydroxyl groups

- There are 3 major classes of Carbohydrate : Monosaccharide, Oligosaccharide and polysaccharide

Saccharide (means `Sugar’ in Greek)

- So ;

Monosaccharide : simple sugar – single polyhydroxyl aldehyde or ketone unit (the most abundant monosaccharide in nature is the 6-carbon sugar… D-glucose)

Oligosaccharide : Oligo (`few' in Greek) – consist of short chains of monosaccharide units joined together by covalent bonds (the most abundant are disaccharide)

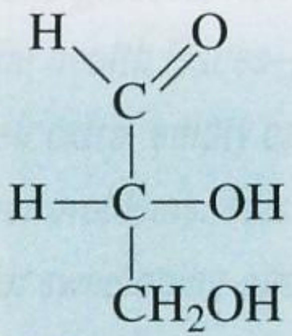
Polysaccharide 2: 2Consist 2of 2long 2chain 2 2having 2hundred 2or thousands of monosaccharide units. Eg. Cellulose (have linear chains), glycogen (have branched chain)

Common mono & disaccharide have names ending with the suffix -*ose*

Families of monosaccharide

Aldose

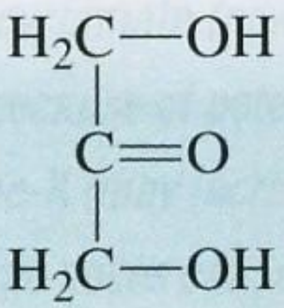
(Carbonyl group is at the 2end 2of 2Carbon chain)



Glyceraldehyde
(aldose)

Ketose

(Carbonyl group is at any other position)



Dihydroxyacetone
(ketose)

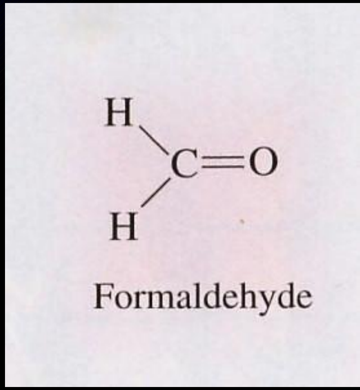
-In Details :

Monosaccharide : A compound with single aldehyde or ketone unit with multiple Hydroxyl (OH) group

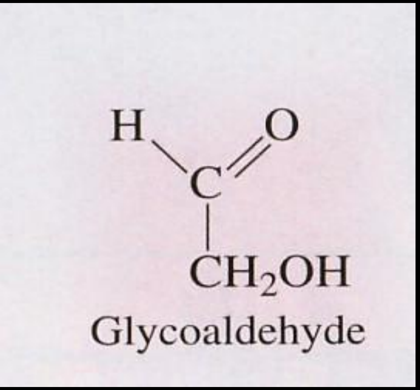
→ empirical formula : $(CHO)_n$

whereby n ≠ 3

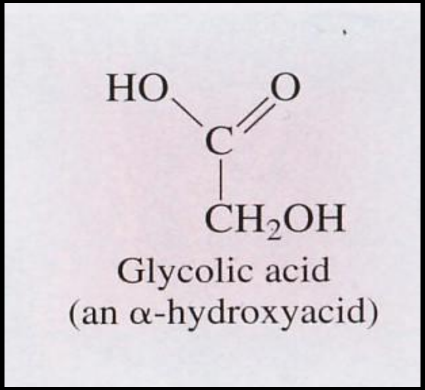
& / n = 1 @



If the n is = 1 then it will be formaldehyde (a poison)



When n = 2, it will become glycoaldehyde (biological important is nknown)



An intermediate in plant & microbial metabolism (used in skin cream)

- The smallest compound for monosaccharide is trioses (n = 3)

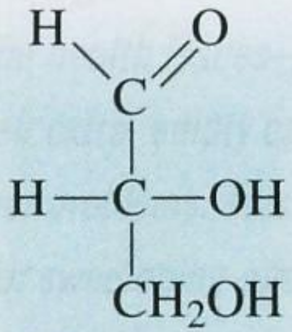
So, if n = 4 ; tetrose

n = 5 ; pentose

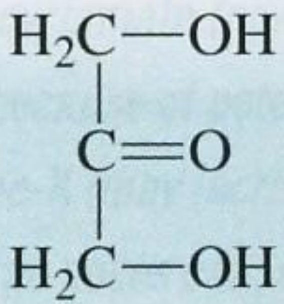
n = 6 ; hexose

n = 7 ; heptose

- There are 2 kind of trioses :

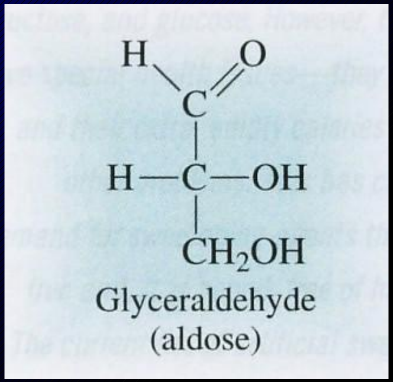


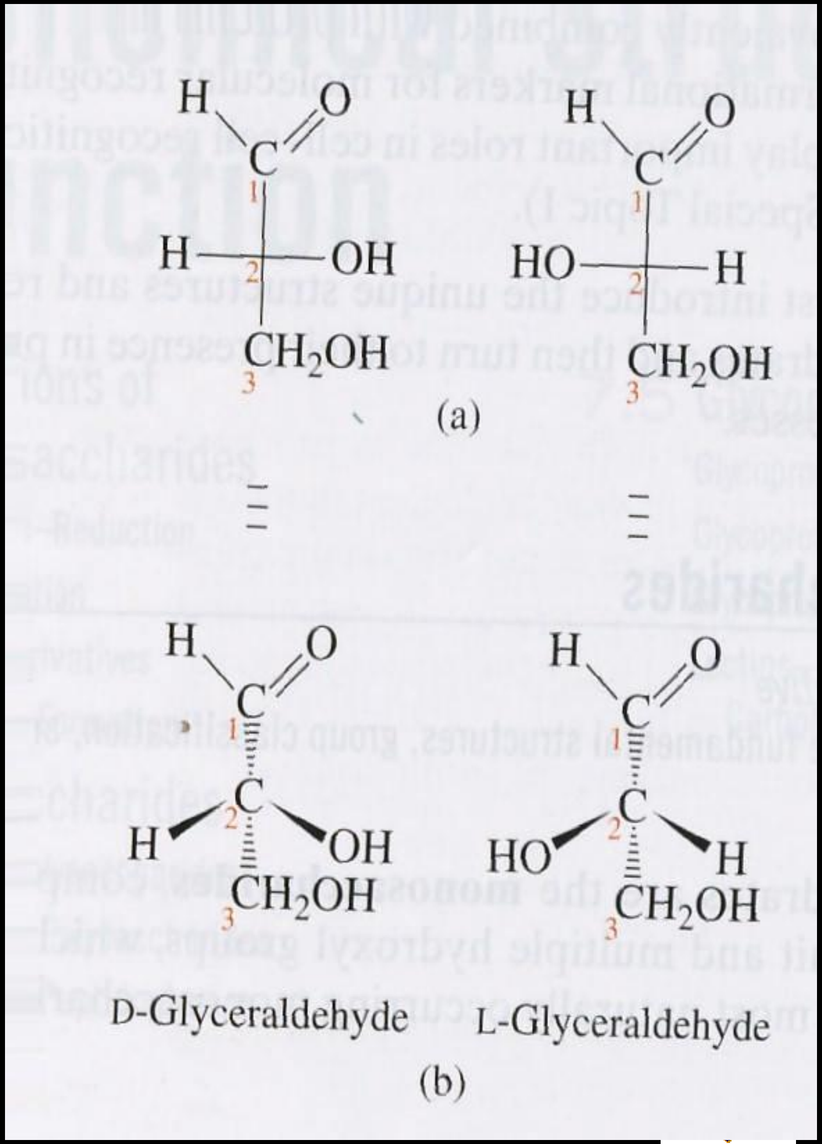
Glyceraldehyde
(aldose)



Dihydroxyacetone
(ketose)

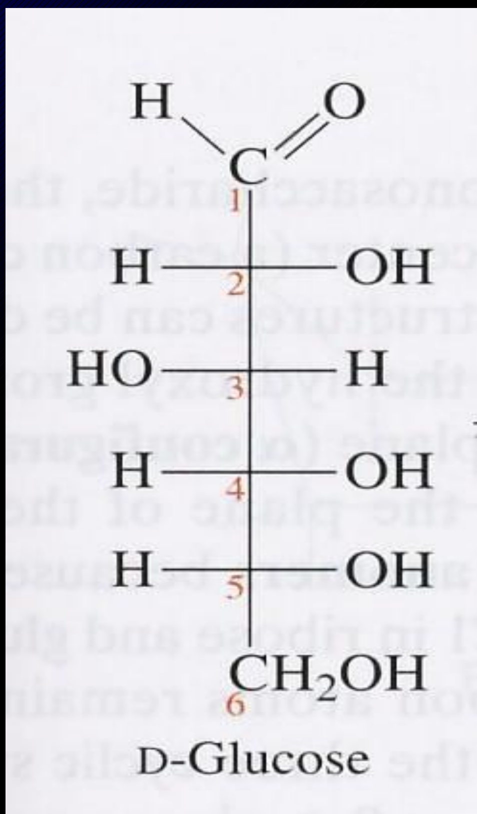
- The structure of small monosaccharide were drawn based on \`Fischer Projection' (straight chains diagram)



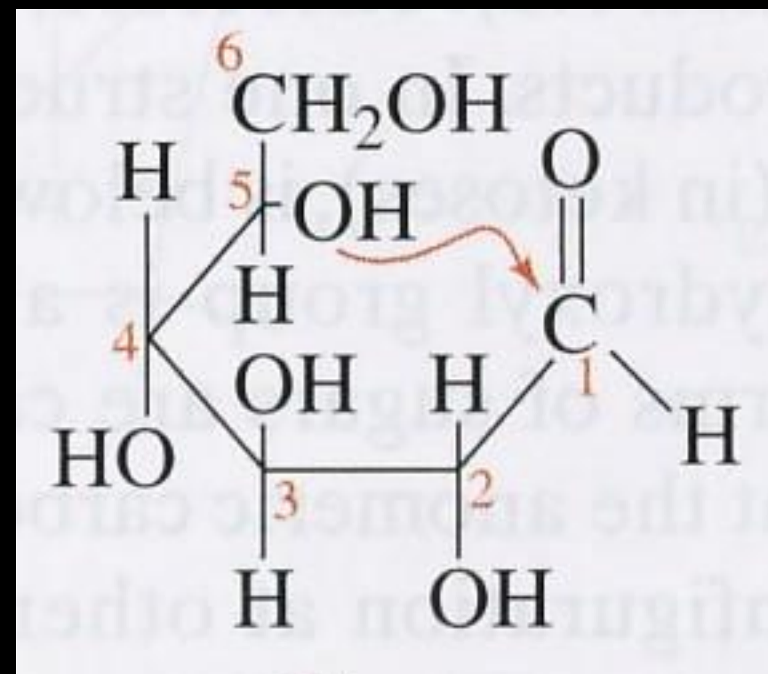


Can exist in two stereoisomers (enantiomers)

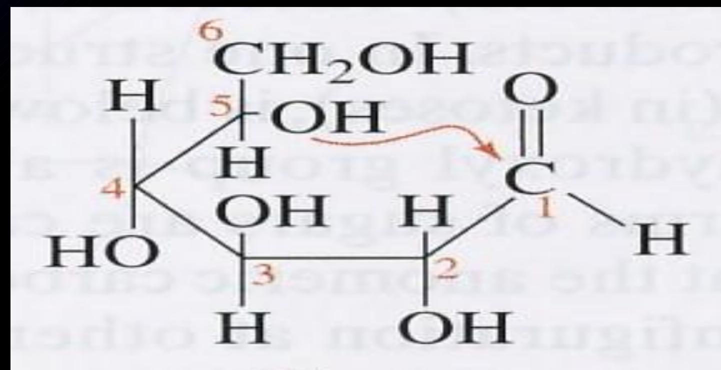
- However, monosaccharide with 5C or more spend most of their time in solution as `Cyclic’ structure (Haworth Projection) , for example Glucose (6C) :

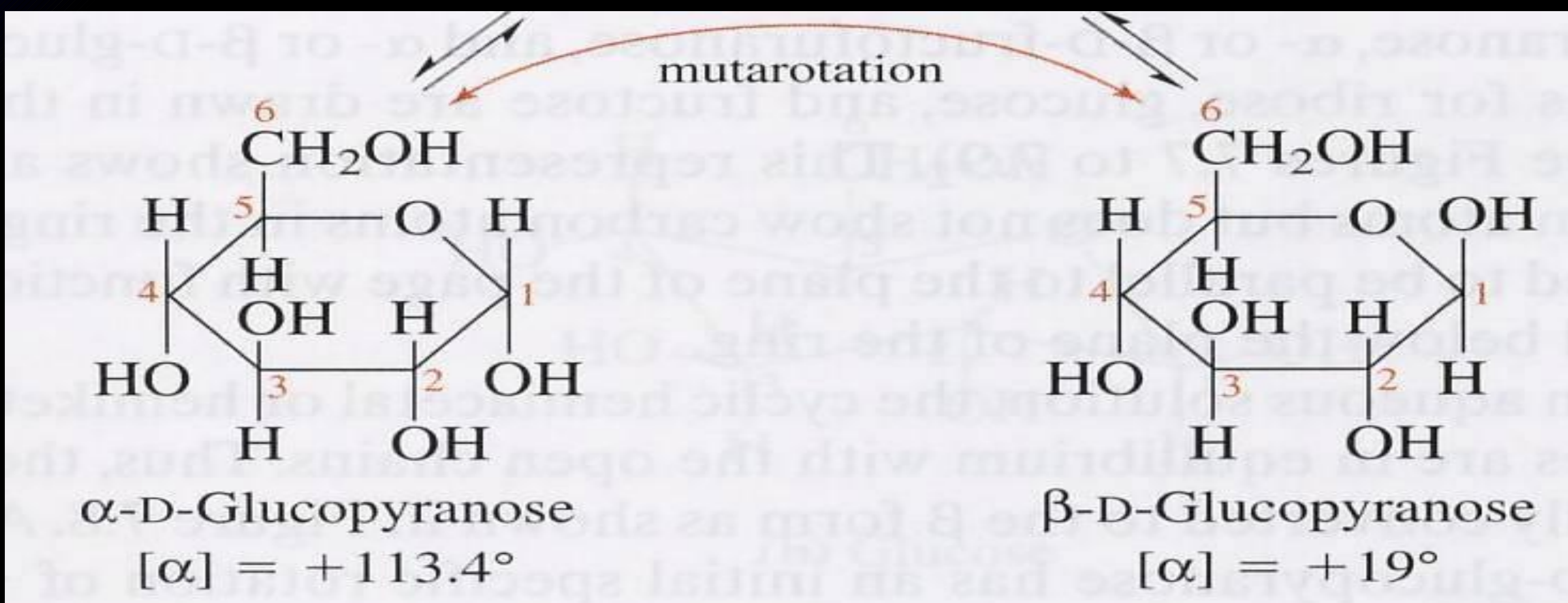


Carbonyl & OH reacted among 2themselves 2(in the same molecule)



And during cyclization of glucose, it can can be either D-Glucose of L-Glucose : *mutarotation* phenomena

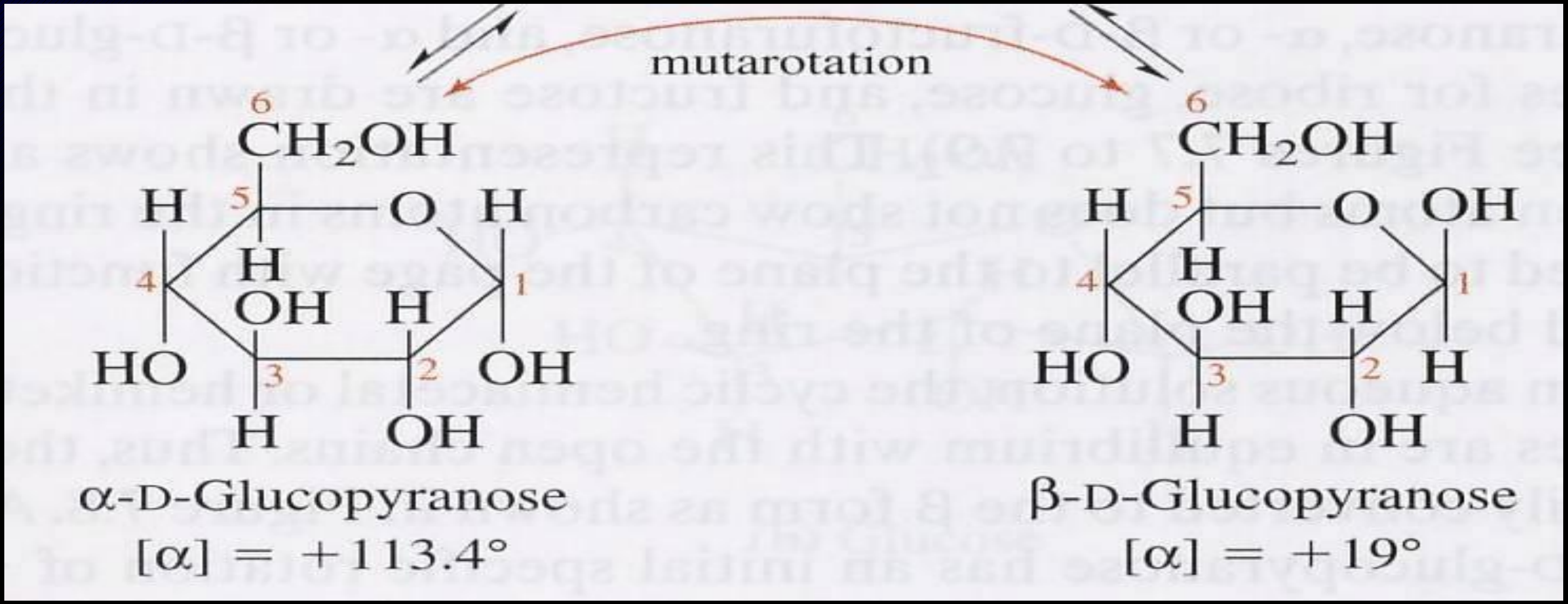




Examples of monosaccharides

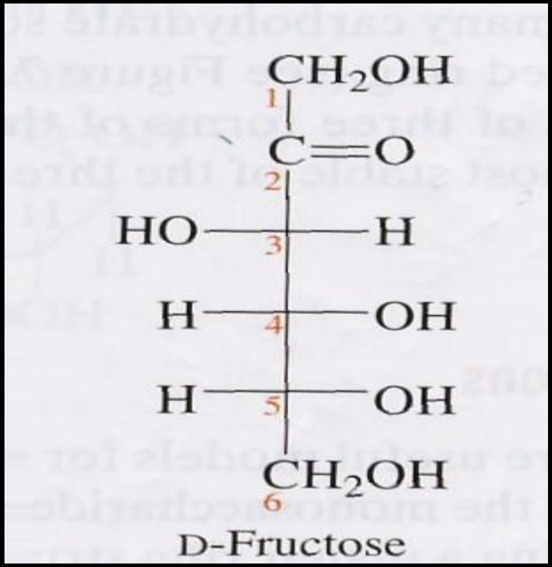
a. Glucose

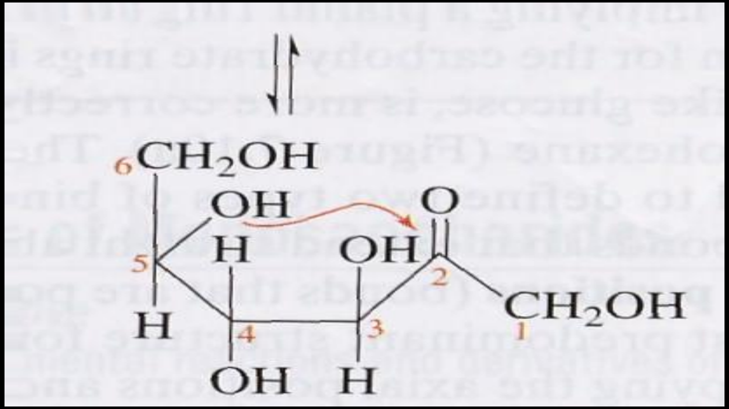
- A aldohexose

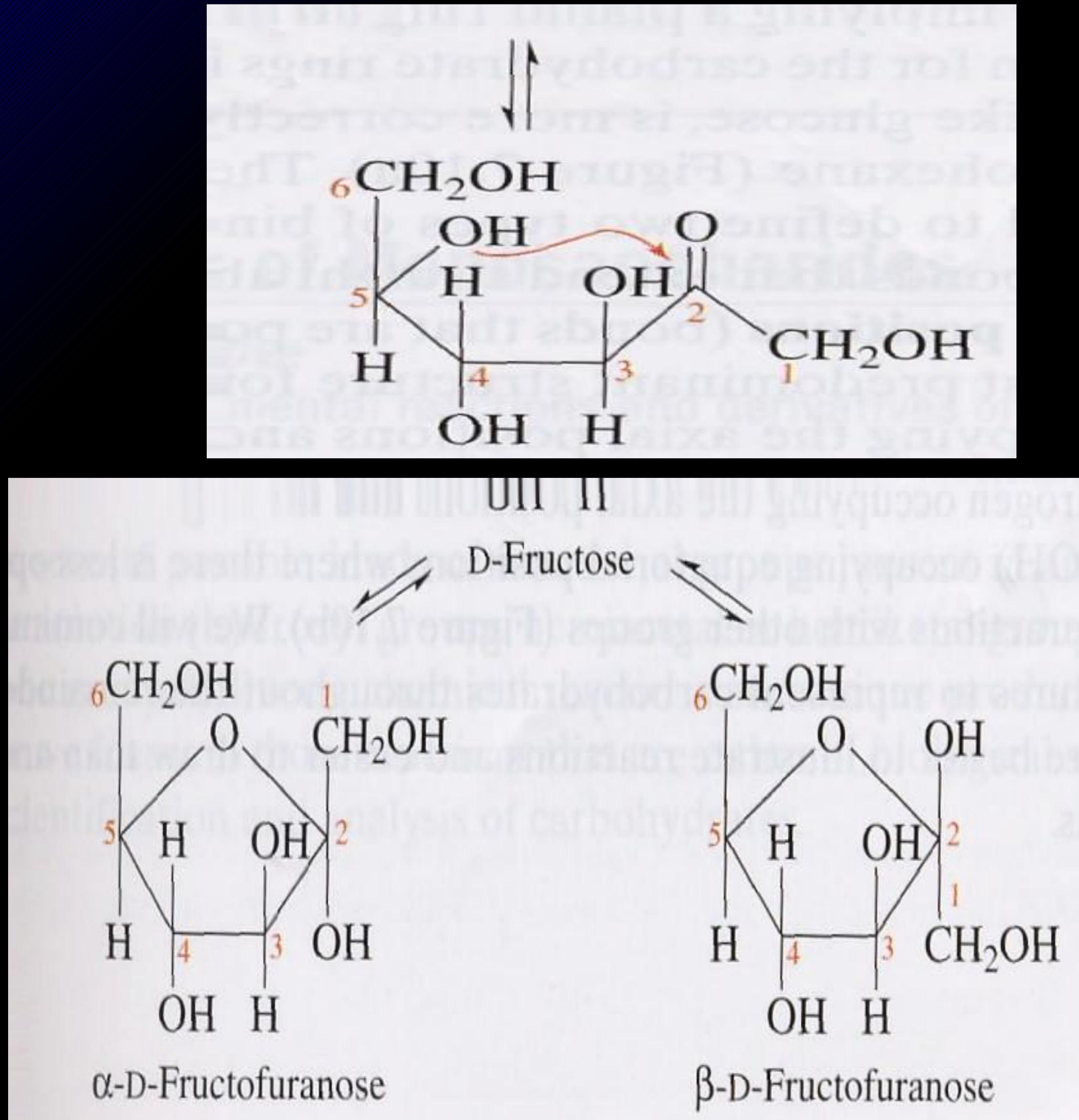


b. Fructose

- A ketohexose







Cyclization of D-Fructose

Examples of Disaccharide

- Consist of 2 monosaccharide covalently bound to each other

- 2In 2most 2disaccharide, 2the 2covalent 2bond 2that 2join 2the 2two monosaccharide units is called a *glycosidic bond*

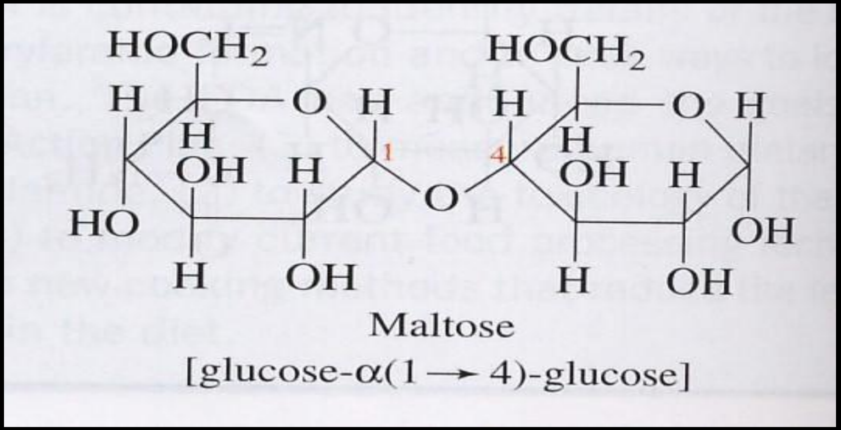
- The most common disaccharide are : sucrose, lactose and maltose

Common disaccharides and their structural properties

Name	Monosaccharide Components	Type of Glycosidic Linkage
Maltose	Glucose, glucose	$\alpha(1 \rightarrow 4)$
Cellobiose	Glucose, glucose	$\beta(1 \rightarrow 4)$
Lactose	Galactose, glucose	$\beta(1 \rightarrow 4)$
Sucrose	Glucose, fructose	$\alpha,\beta(1 \rightarrow 2)$

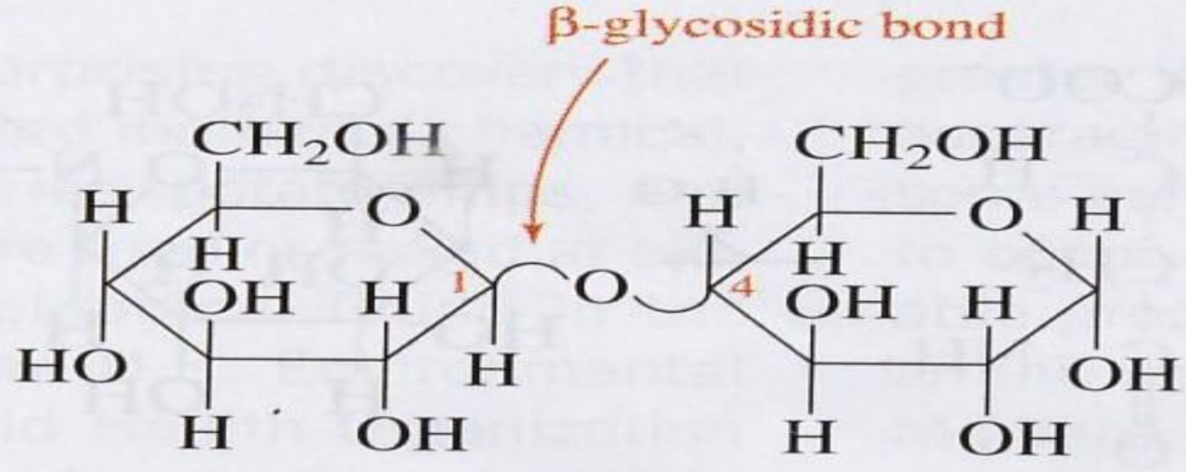
Maltose

- 2 2The 2simplest, 2consist 2of 2two 2D-glucose 2residues 2joined 2by glycosidic linkage α(1 □ 4)



- Is a reducing sugar (contain one potential carbonyl group)

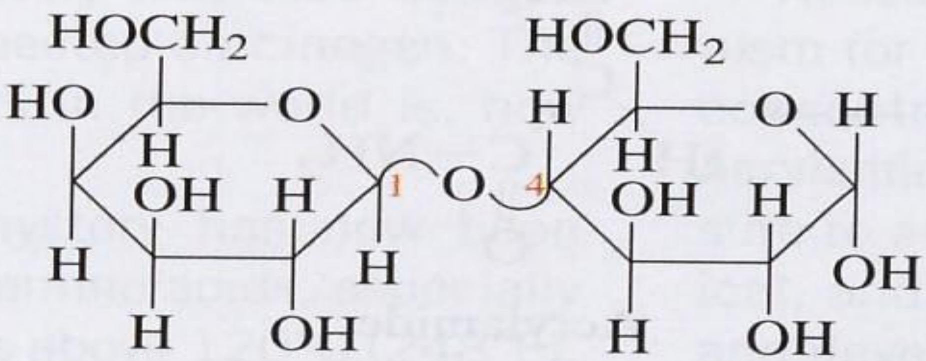
* Cellobiose also contains two D-Glucose residues, but they are joined in β(1 □ 4) linkage



Cellobiose
[glucose-β(1 → 4)-glucose]

Lactose

- Occurs in milk, also a reducing sugar
- Consist of D-galactose and D-glucose with b(1□ 4) linkage



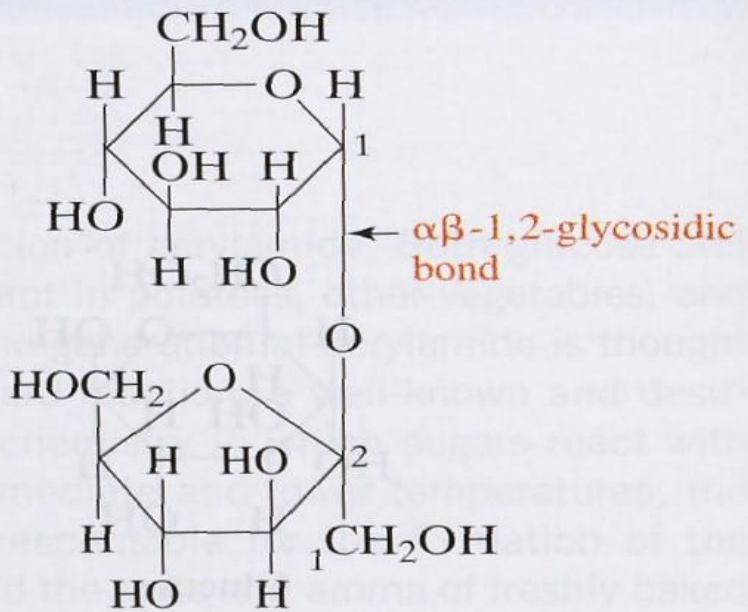
Lactose

[galactose-β(1 → 4)-glucose]

- Cannot be absorbed from intestine into the bloodstream unless it is first hydrolized into its monosaccharide units

Sucrose

- Cane sugar (Gula putih)
- Disaccharide of glucose & fructose viaαβ(1 □ 2) glycosidic bond
- Produced by many plants but NOT in animals



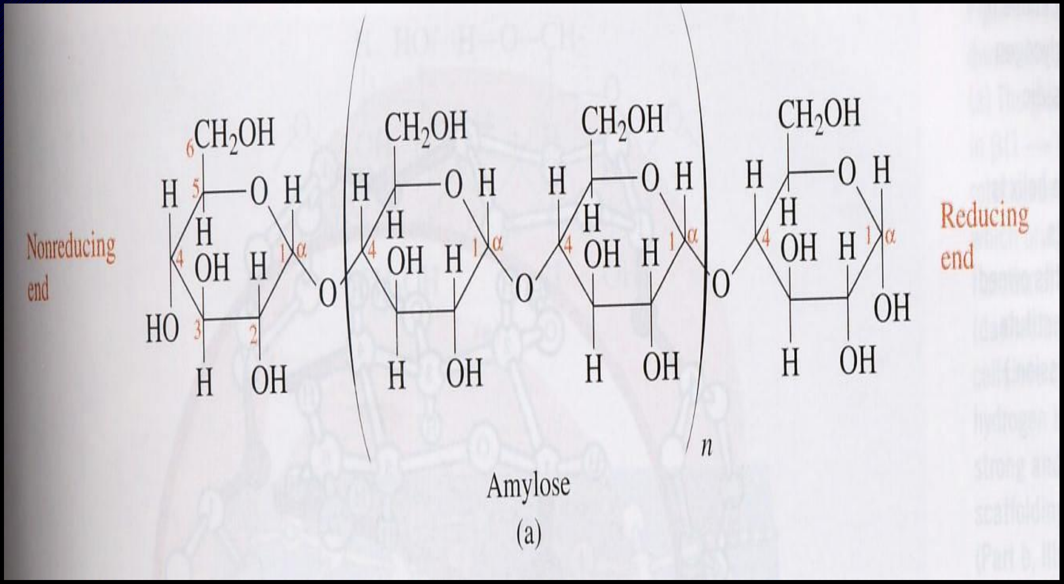
Sucrose [glucose-α, β (1→2)-fructose]

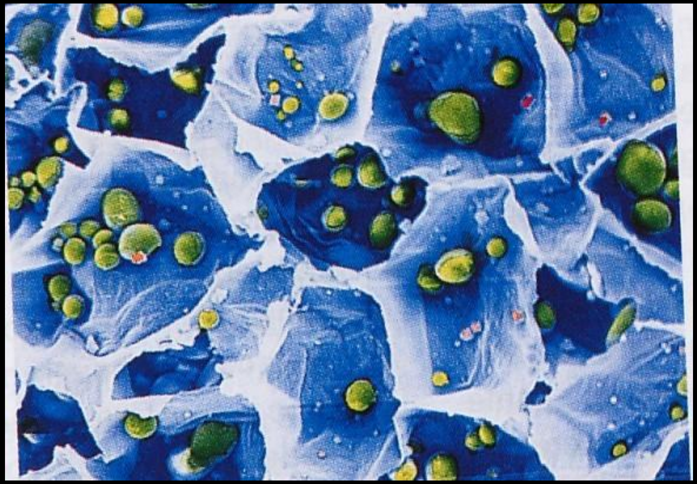
Examples of Polysaccharide

Consist of :

Homo-polysaccharide (consist of single type of monomer)

Eg. Starch (only contain D-glucose units)





Starch granule (green) in plant cell chloroplast

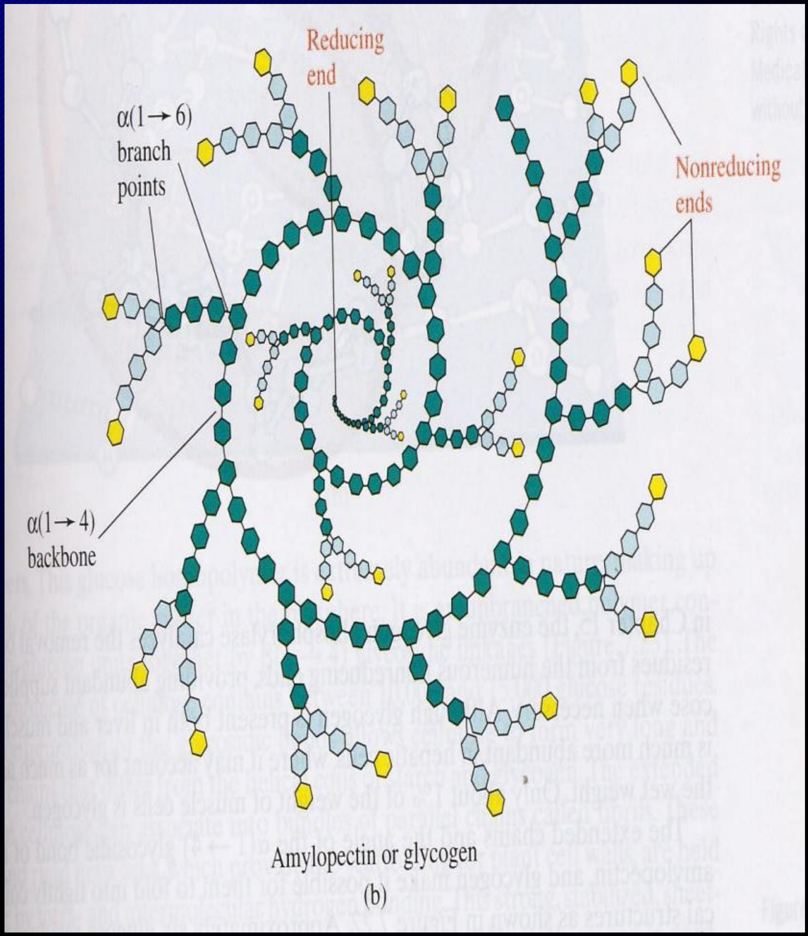
Hetero-polysaccharide (consist of two or different kind of monomer)

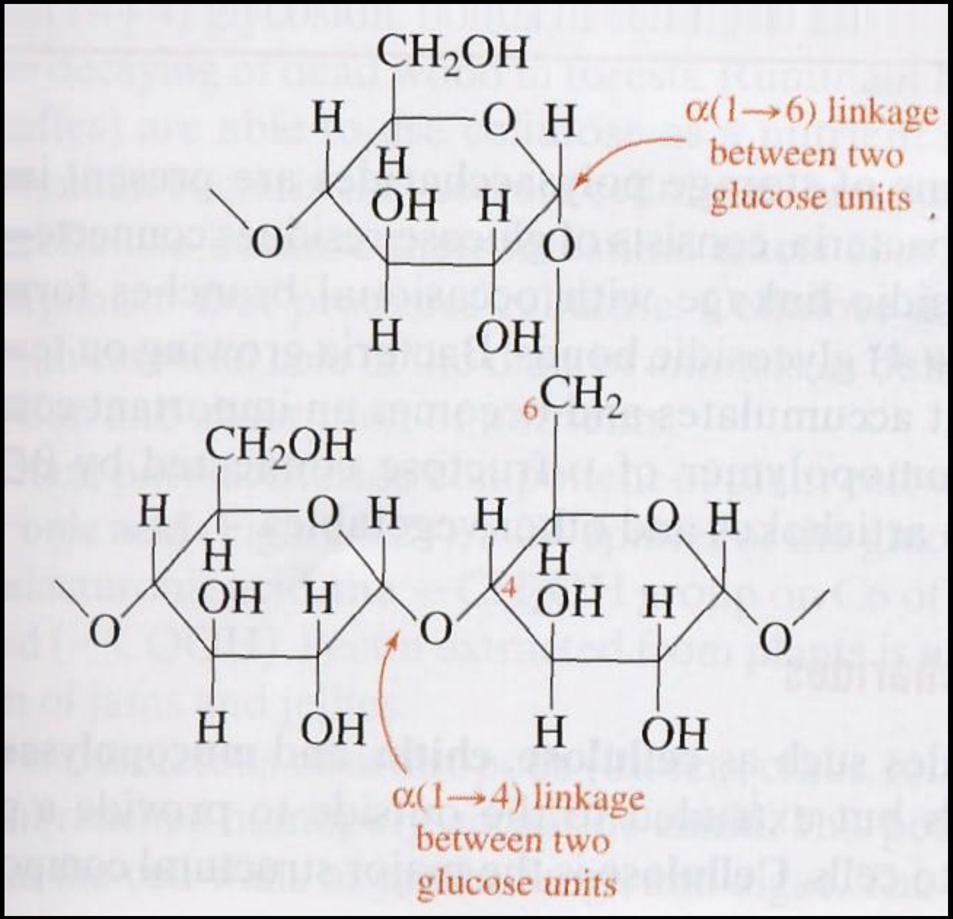
Eg. Glycogen

- the main storage polysaccharide of animal cells (es. in liver)

2- 2Polysaccharide 2of 2D-glucose α(1 □ 4) 2linkage 2with branches of D-glucose α(1 □ 6) lingkage

Glycogen granules (pink) in liver cells)





The structure of glycogen

The function of Carbohydrate

a. Energy metabolism :

- Monosaccharide : as an immediate fuel molecule
- Polysaccharide : Chemical storage for future energy (both plants & animals)

b. Structural & Function : Microstructure of bacterial cell wall/plant cell wall, connective tissues (tendon etc)

c. Component of nucleic acids : Ribose & Deoxyribose

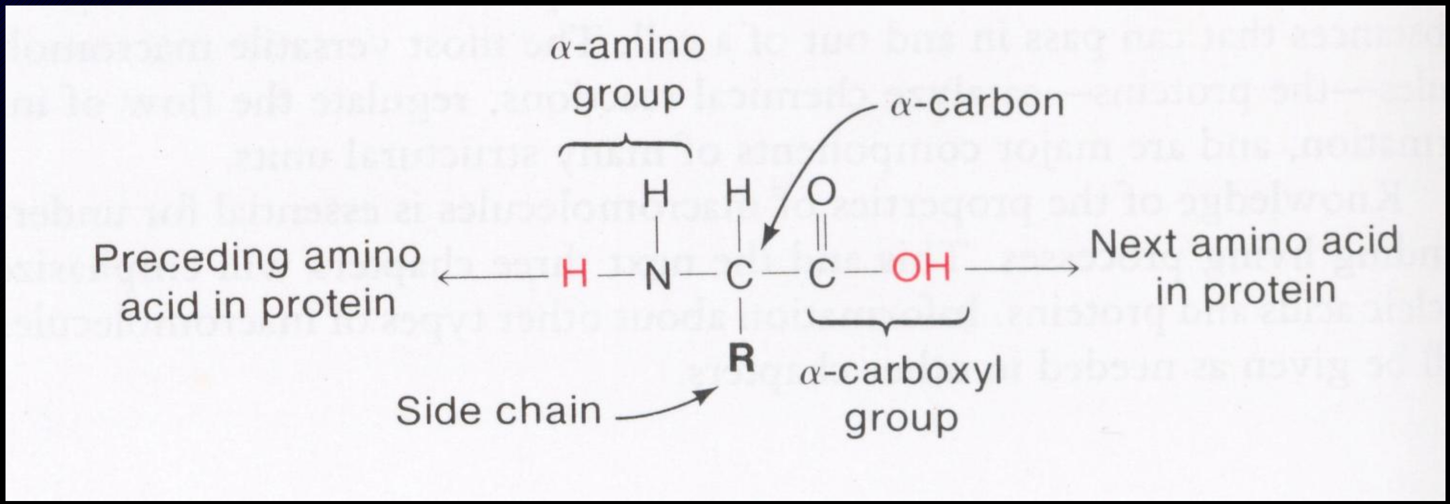
d. Imformation marker for molecular recognition : Glycoprotein, glycolipid etc

Protein

Protein

- A polymer of amino acids (a polypeptide)

- General structure of amino acid :



- Each amino acid in polypeptide is connected with peptide bond result of the chemical reaction between amino group of one amin acid with carboxyl group of another)

- Amino acids are joined together by peptide bond to form a polypeptide chain

- More than 15 peptide bonds (approx.) : a protein

- 2 ends of every protein : Amino group (-NH2) & Carboxyl group (-COOH)

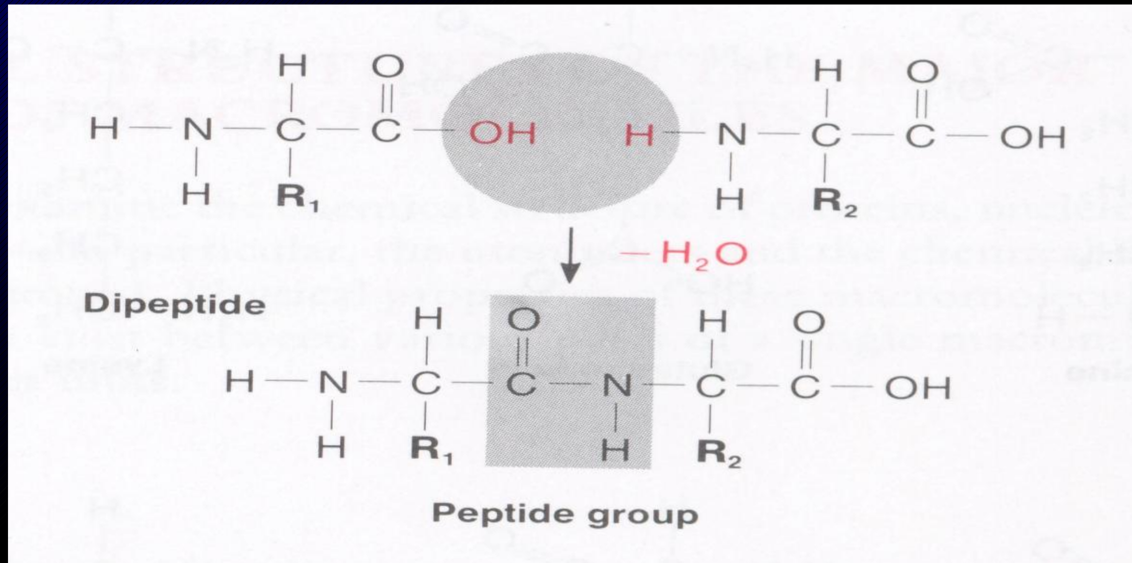
→ Known as N terminal & C terminal

- the central chain, without the R group (side chain) is called : The Polypeptide backbone

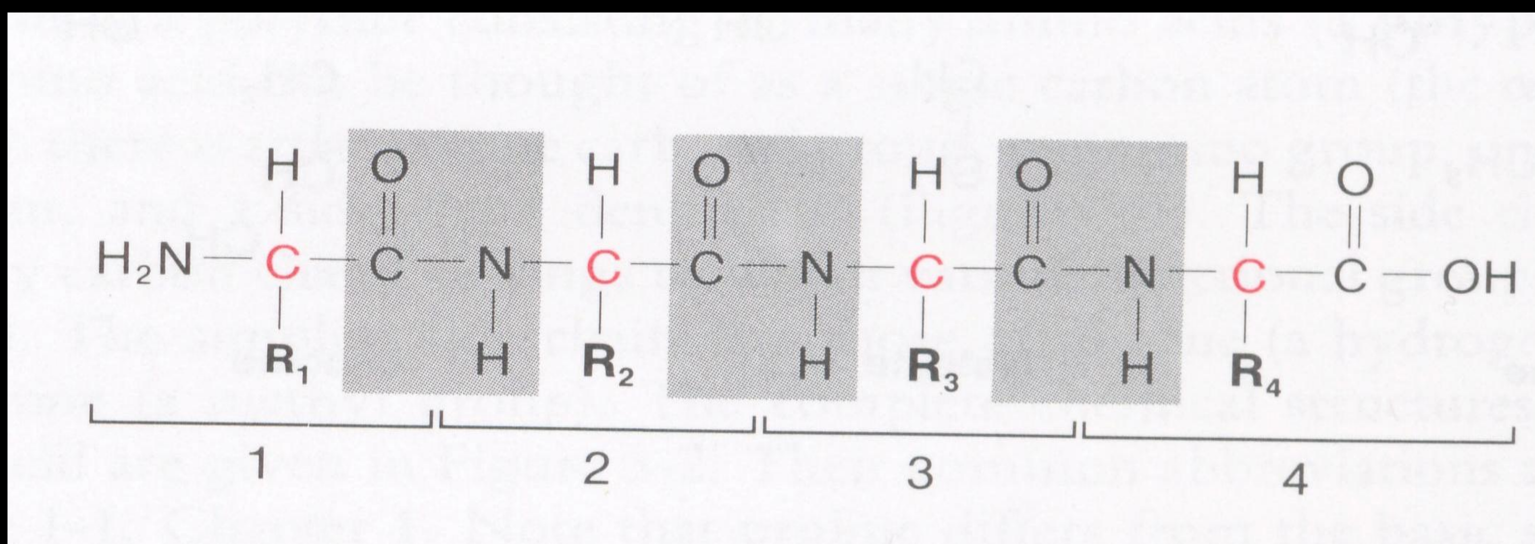
- When 20 different amino acid are arranged in a polypeptide = 20 amino acid sequence

- Determining of these sequences = protein sequencing (a ve important technique in protein chemistry)

* Fred Sanger was awarded a Nobel Prize in 1958 for his sequencing work on insulin polypeptide



- There are approx. 20 important aa. Some are acidic & som
are basic



What do proteins do ?

- Enzymes
- Signalling
- Transport & storage
- Structure & Movement
- Nutrition (Casien & Ovalbumin)
- Immunity

Classes of protein

1 - Structural protein : Keratin, Collagen (give support to cells)
2 - Dynamic protein : Hormone, enzyme (for catalytic purpose)

- Based on the structure, protein can be divided to :

  * Fibrin : Blood clotting
  * Fibrous : Myosin (from muscle)
  * Globular : Half sphere form/structure ± eg. Enzyme

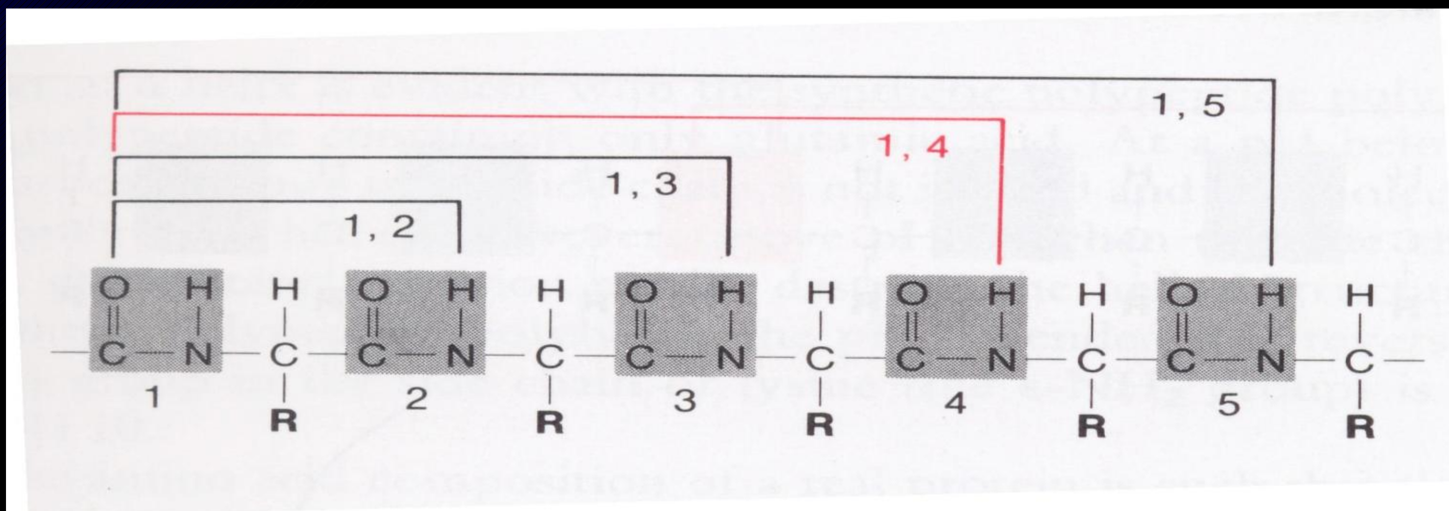
- Size : Varied - depending on functions

- 1 amino acid = 110 Daltons

- Most protein are highly folded

Hydrogen bond & the α-helix

- Hydrogen bonds easily form between the H of the N-H group (1s
acid amino) and the O of the carbonyl group (4th amino acid)



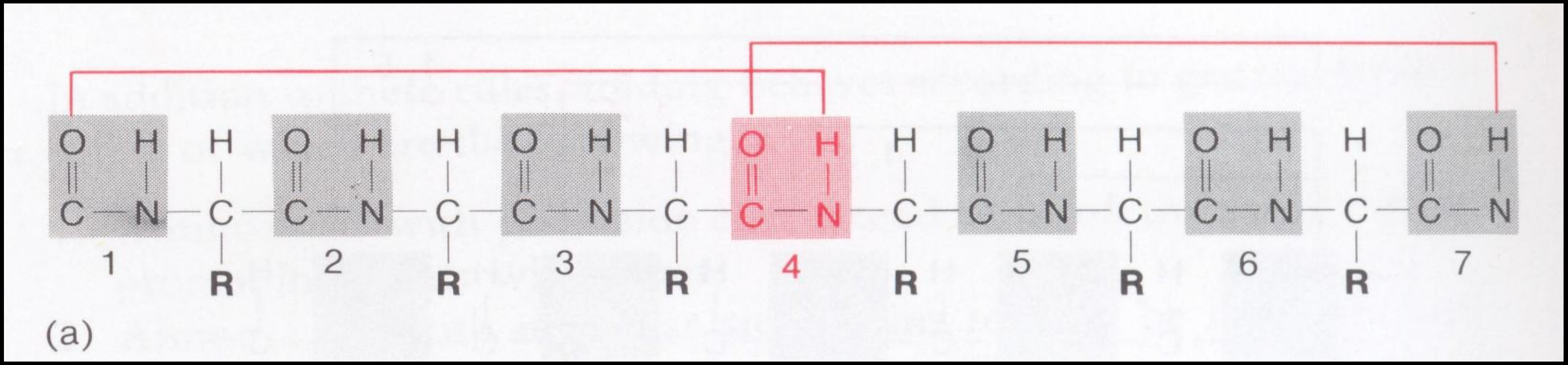
- A large number of protein contain region having a repeat distar
of 5.5A : such repeats implies that some order is present in
region

- Linus Pauling & Robert Corey (1951) described this phenomena as the α-helic structure of protein

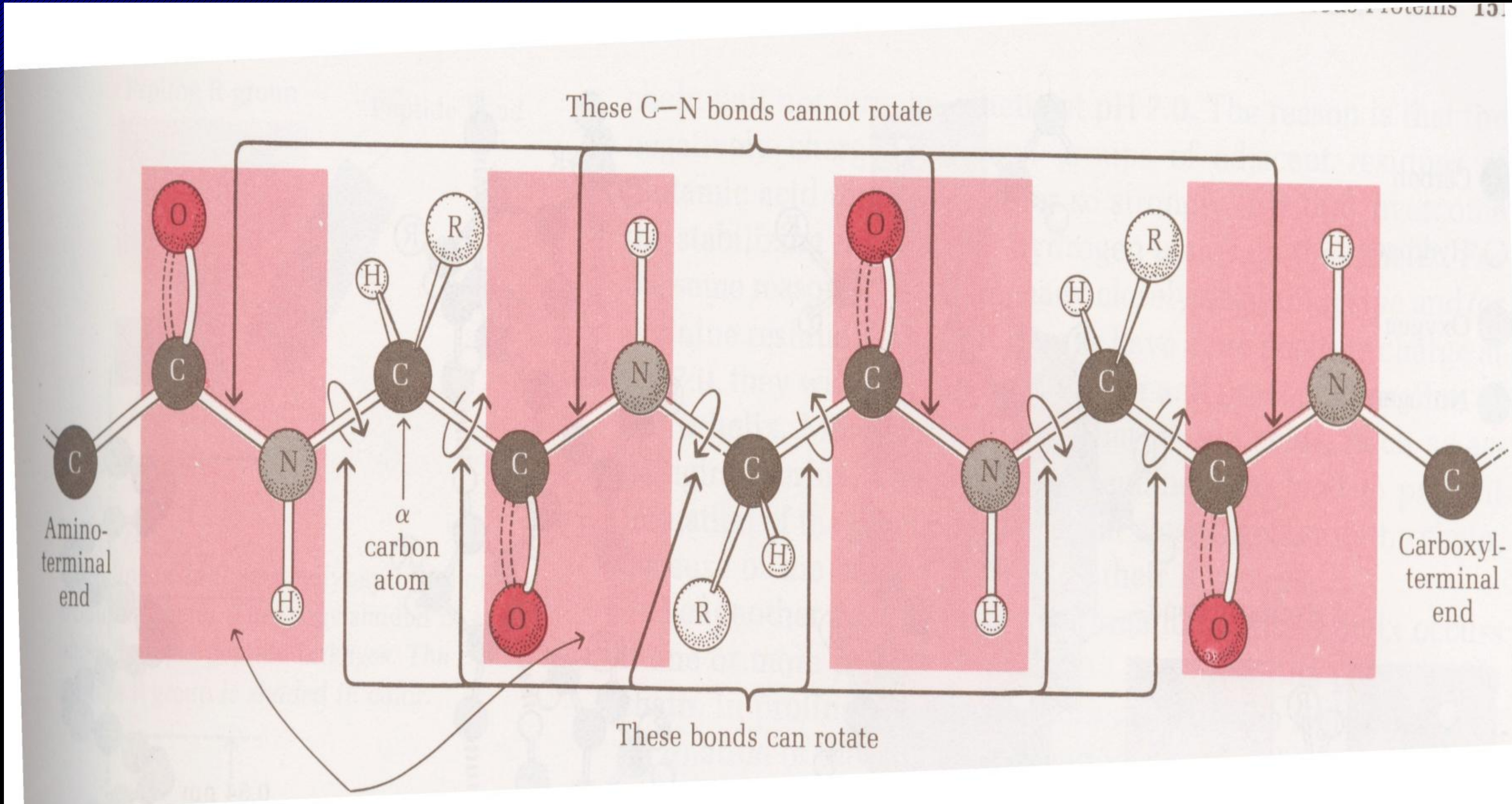
http://osulibrary.orst.edu/specialcollections/coll/pauling/dna/papers/paulingcorey1.htm

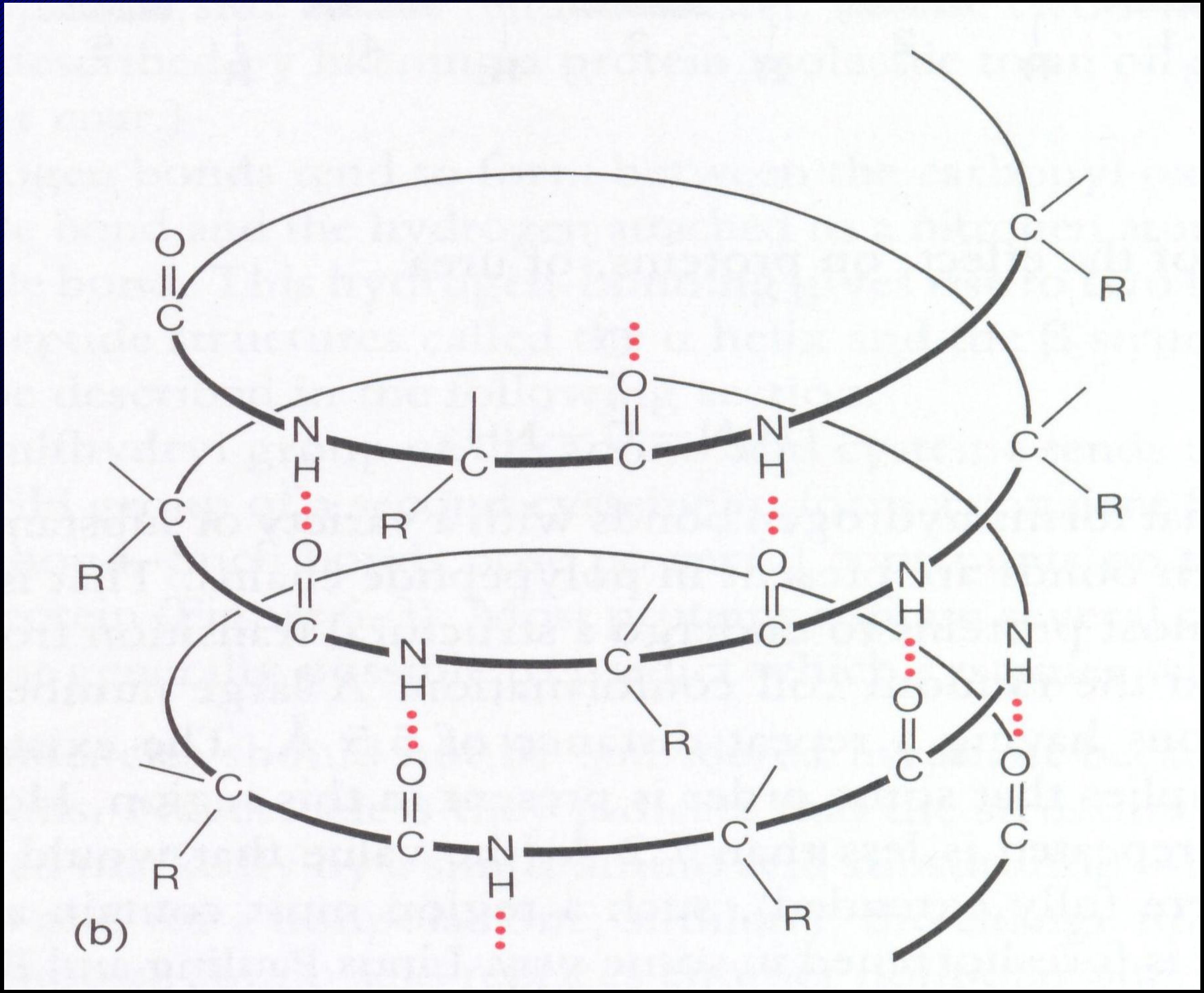
→ The polypeptide chain follows a helical path that is stabilized by Hydrogen bonding between peptide groups

- Each peptide group is Hydrogen bonded to 2 other peptide groups : one three units ahead and three unit behind the ch direction (picture)

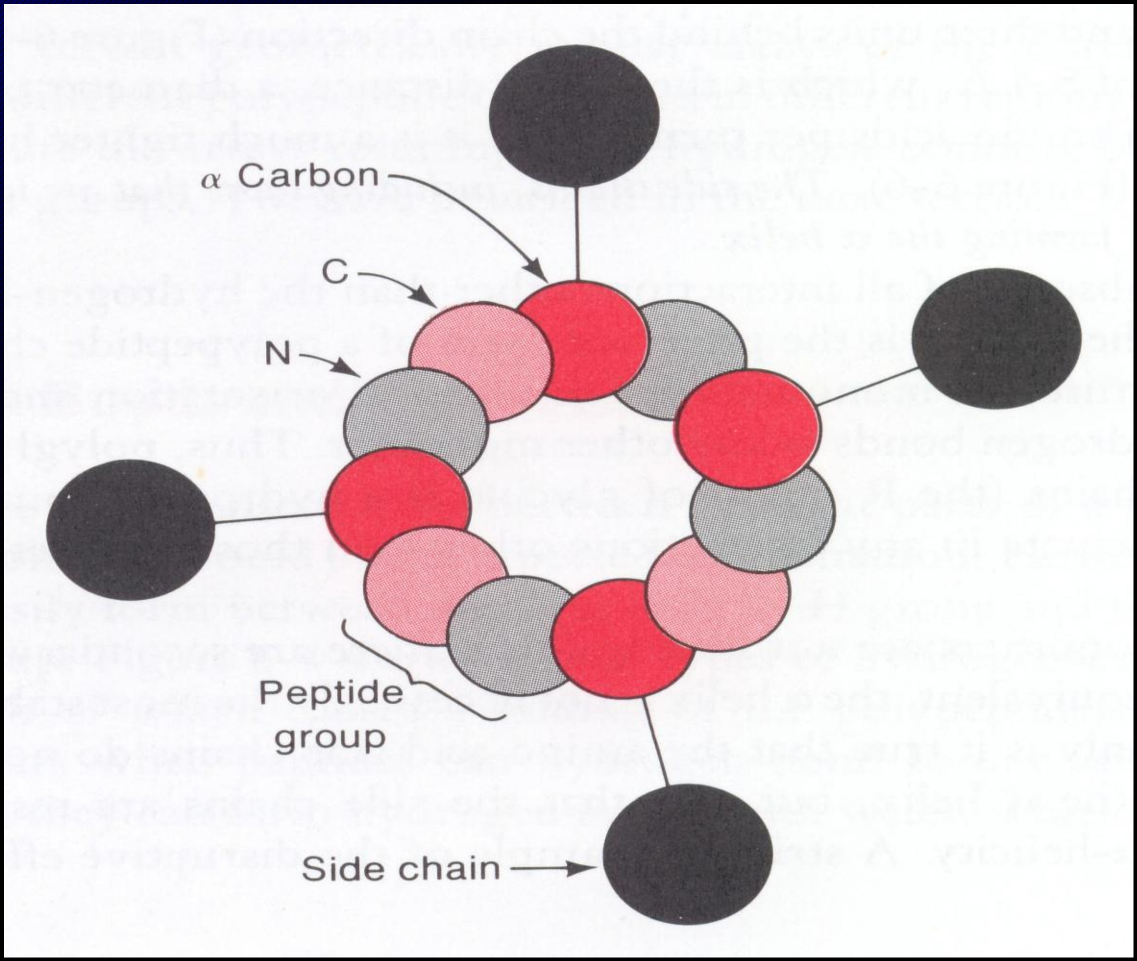


The 2 Hydrogen bond in which peptide group 4 (red) is enganged. The side chains (R) including those that are ionized , do not participate in forming the α-helix


These C—N bonds cannot rotate
Amino-
terminal
end
α
carbon
atom
Carboxyl-
terminal
end
These bonds can rotate



α-helix drawn in 3 dimension : showing how the Hydrogen bonds stabilize the structure


α Carbon
C
N
Peptide group
Side chain

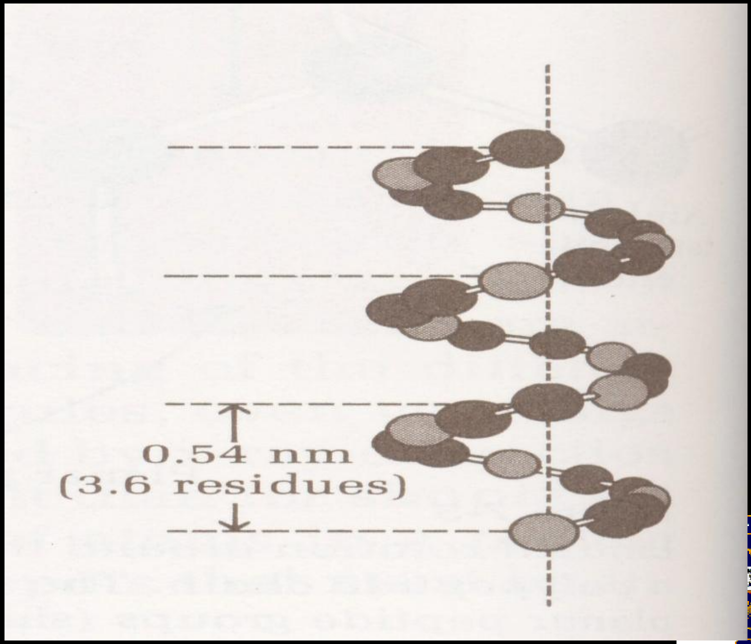
- Character of α-helix structure of polypeptide :

i. The region will form a rod-like structure

ii. Every round of a helix will have 3.6 amino acid residue

iii. The side chain (R) will not involve in the formation

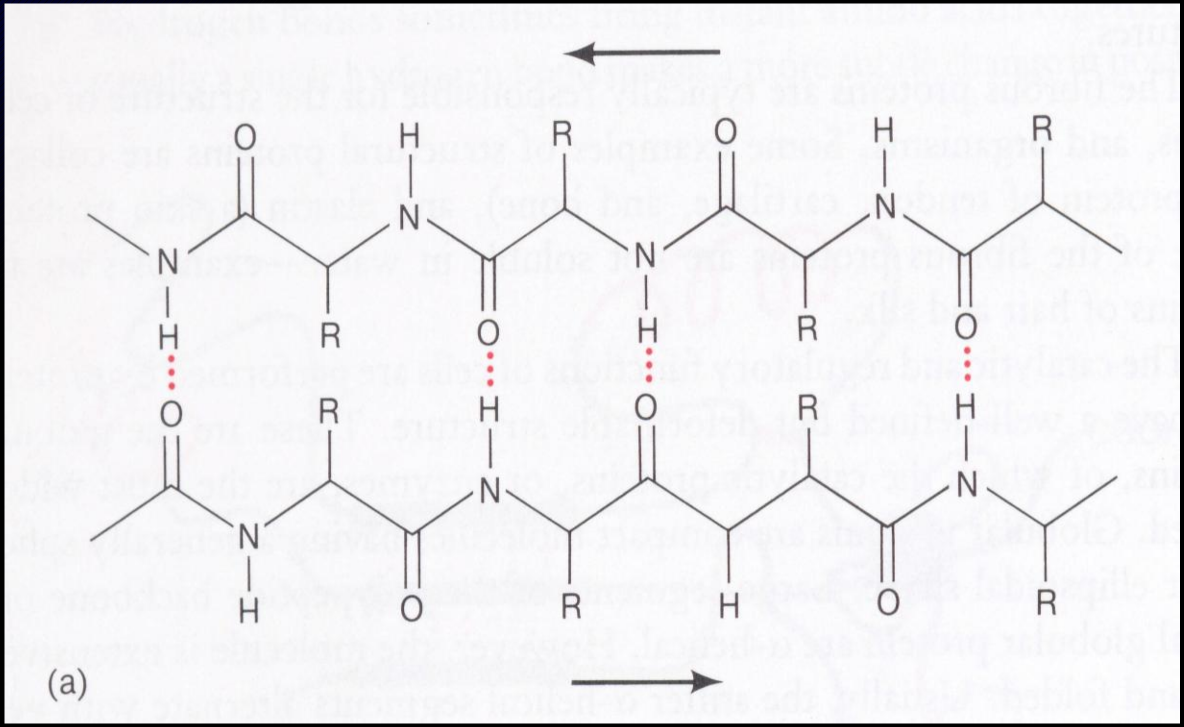
iv. Hydrogen bonding can be erupted by using strong denaturant chemicals such as Urea etc..



β-structure

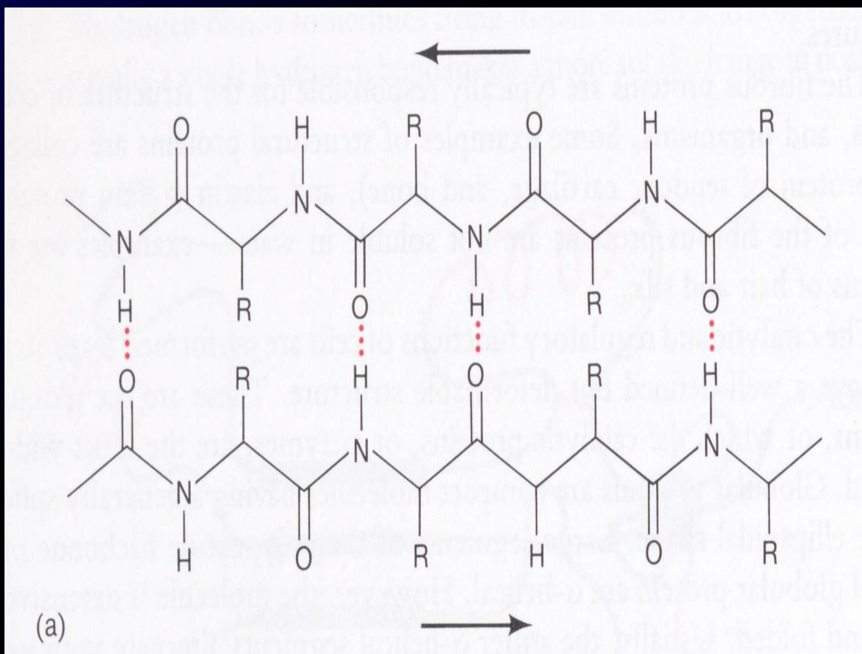
- Another common hydrogen-bonded conformation in polypeptide

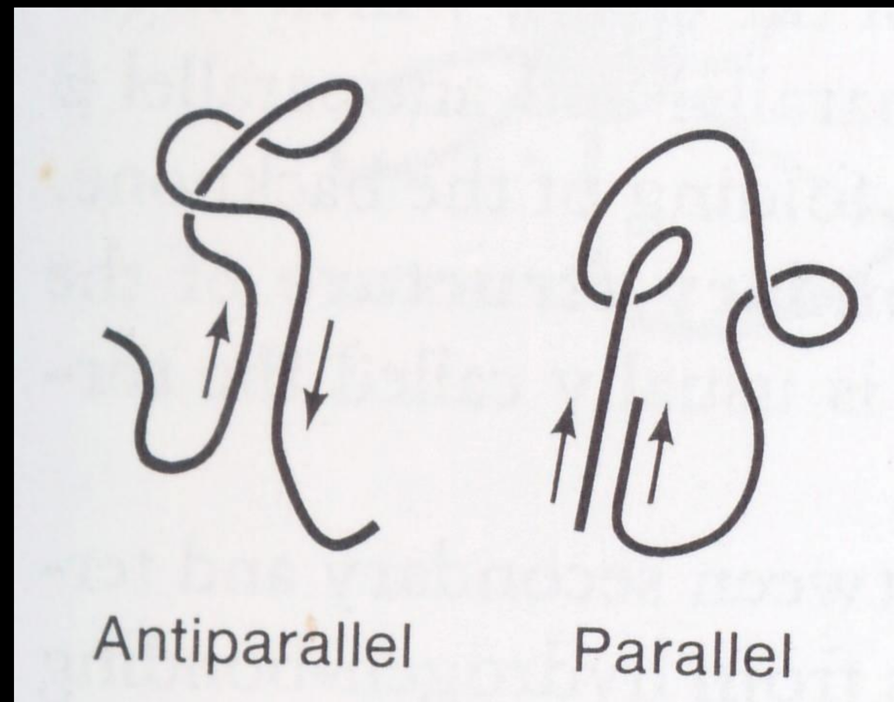
- The molecule is completely extended and hydrogen bonds fo between peptide group of polypeptide segments lying adjacent & parallel with one another. Side chains lie alternately above & below the main chain



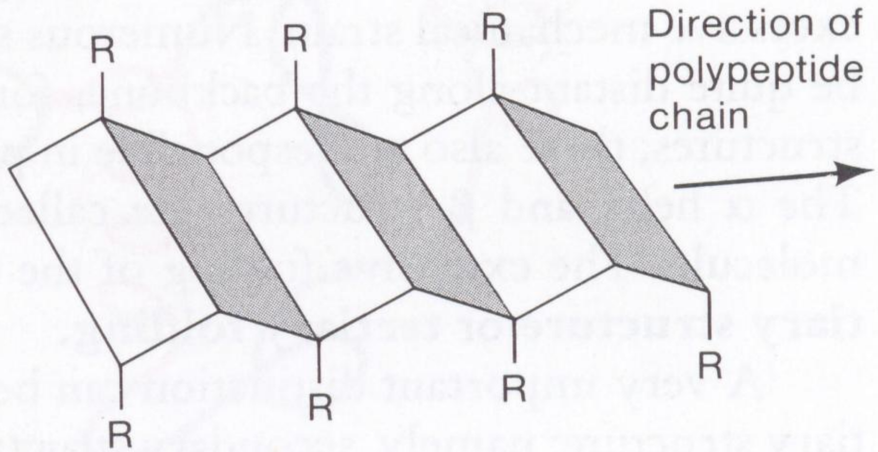
- 2 regions of nearly extended chain are hydrogen bonded (red dots) in an antiparallel array (arrows)

- β structure can be form by 2 segments of a polypeptide chain (2 chains) & based on their orientation, it can produce either paralle or anti parallel





- When many polypeptide interact in this way, a pleated structure results called the β-pleated sheet (picture)



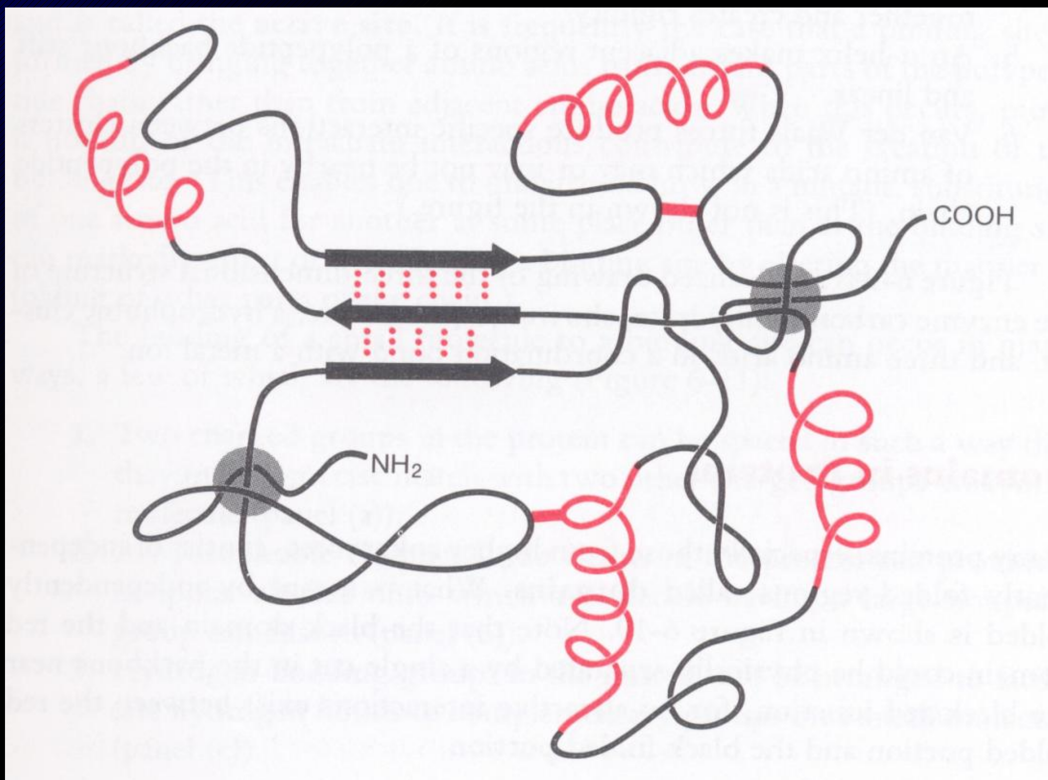
(c) β-pleated structure

Level of protein structure

- Primary structure : Polymer of amino acids without any extra interaction

- Secondary structure : Having 2 kind of interactions (hydrog bonds) between amino acids in a polypeptide

- Tertiary structure : Not only α structure & β pleated, but also include other kind of interactions that will provide a very stal structure for the protein (in a single polypeptide) : an ideal protei



Heavy black arrows : β-structure

- Red dots joining the arrows : hydrogen bonds

- 2 Heavy red line : disulfide bonds

- 2 shaded areas : hydrophobic clusters

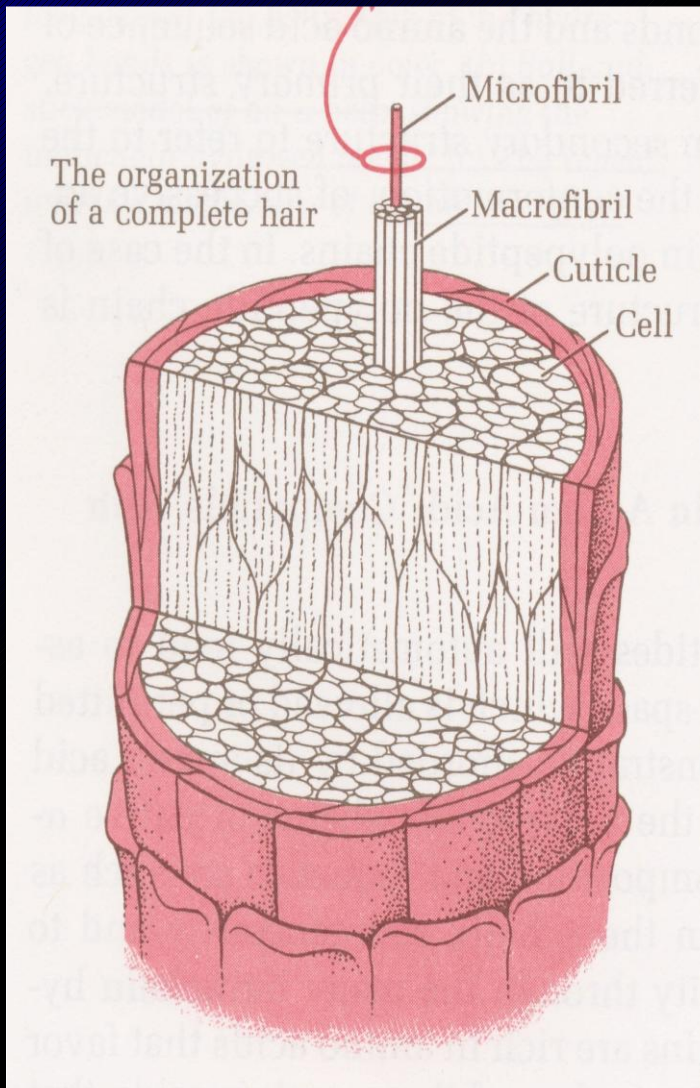
- Quaternary structure : Is a cumulative of interactions betwe
more than a subunit of protein (has to be more than 1 subunits)

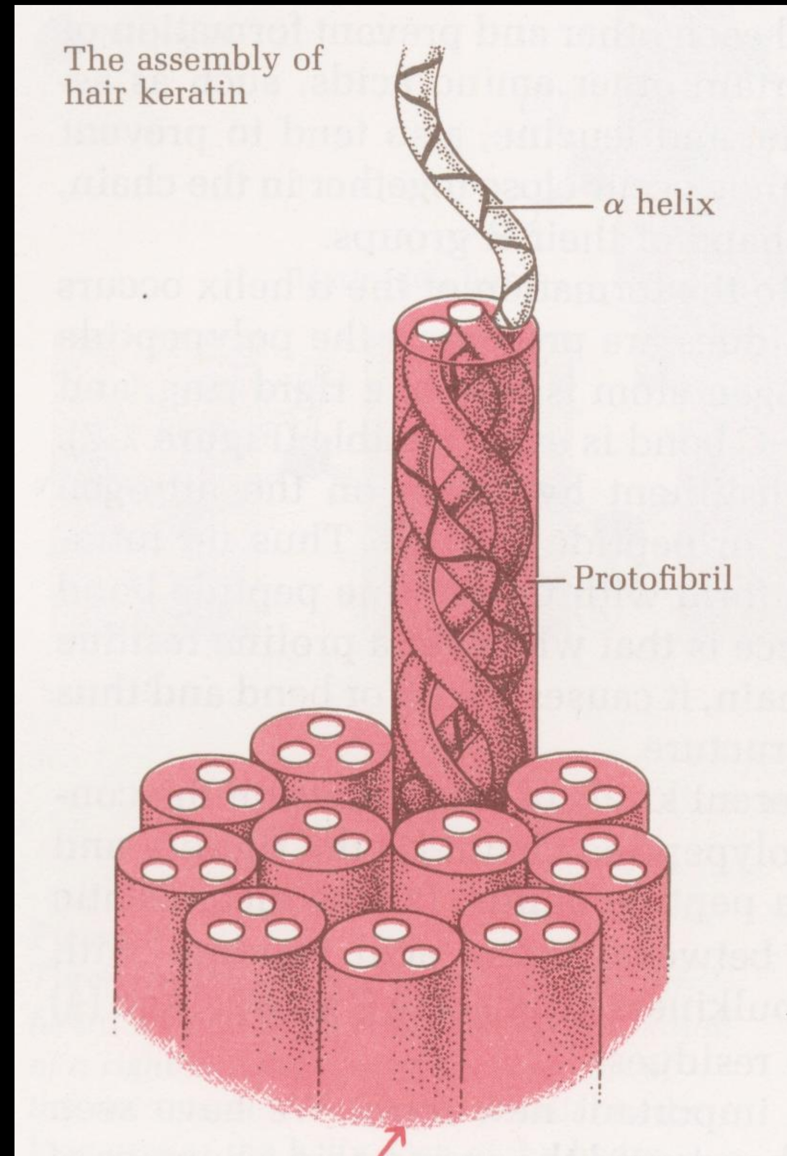
Fibrous and Globular Proteins

- Very few proteins contain pure α-helix @ β-structure
- Normally regions having each structure are found within a prote
- Protein in which most of the polypeptide chain are arrangec long strand or sheets

→ Fibrous protein

Example : α-keratins (major fibrous protein that provide external protection to vertebrate - hair, wool, nails, claw,skin etc)


The organization of a complete hair
Microfibril
Macrofibril
Cuticle
Cell


The assembly of hair keratin
α helix
Protofibril

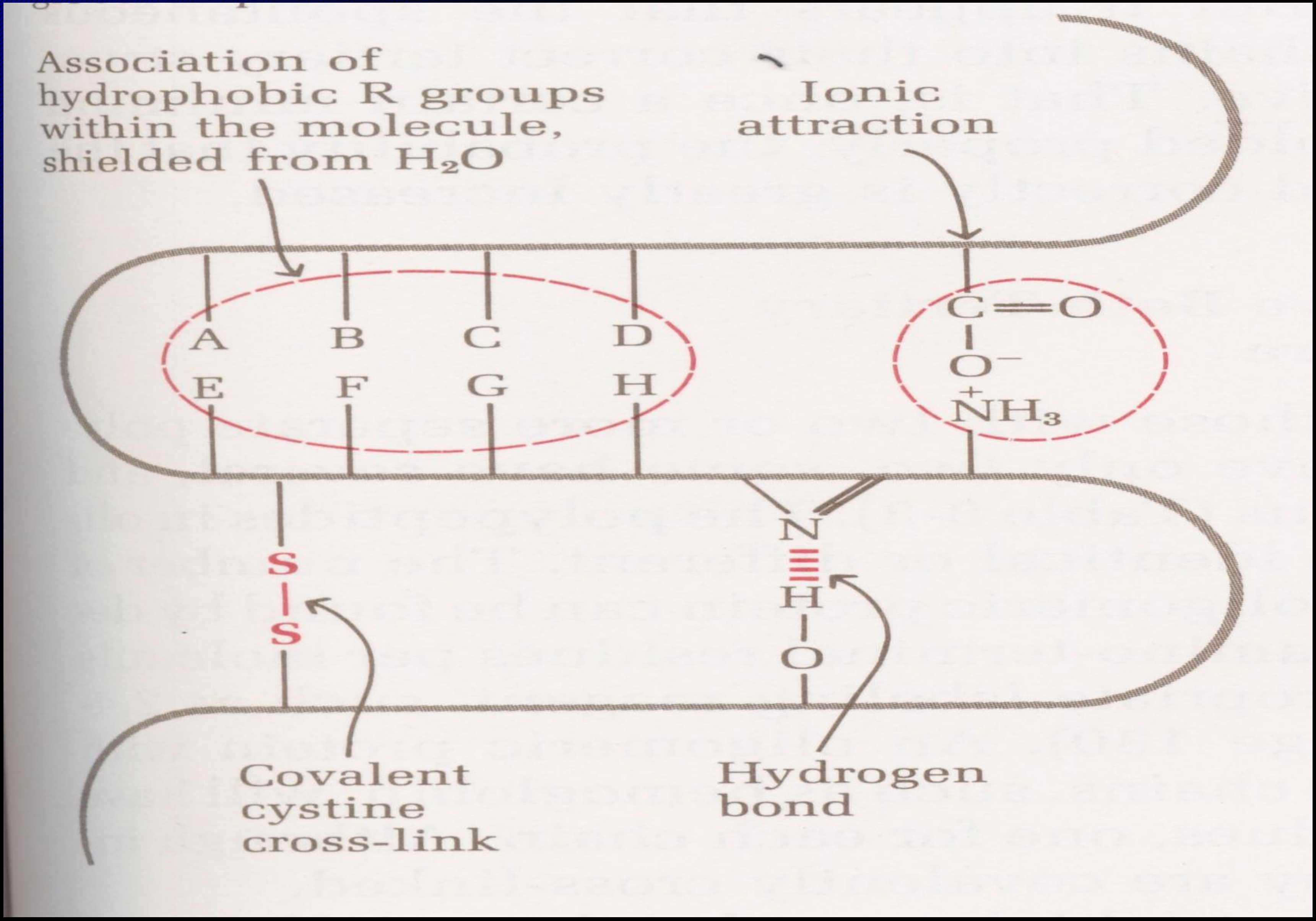
- 4 different forces stabilize the tertiary structure of globular protein

  i. Hydrogen bonding between R groups of residues in adjacent loops of the chain

  ii. Ionic attraction between oppositely charged R groups

  iii. Hydrophobic interactions

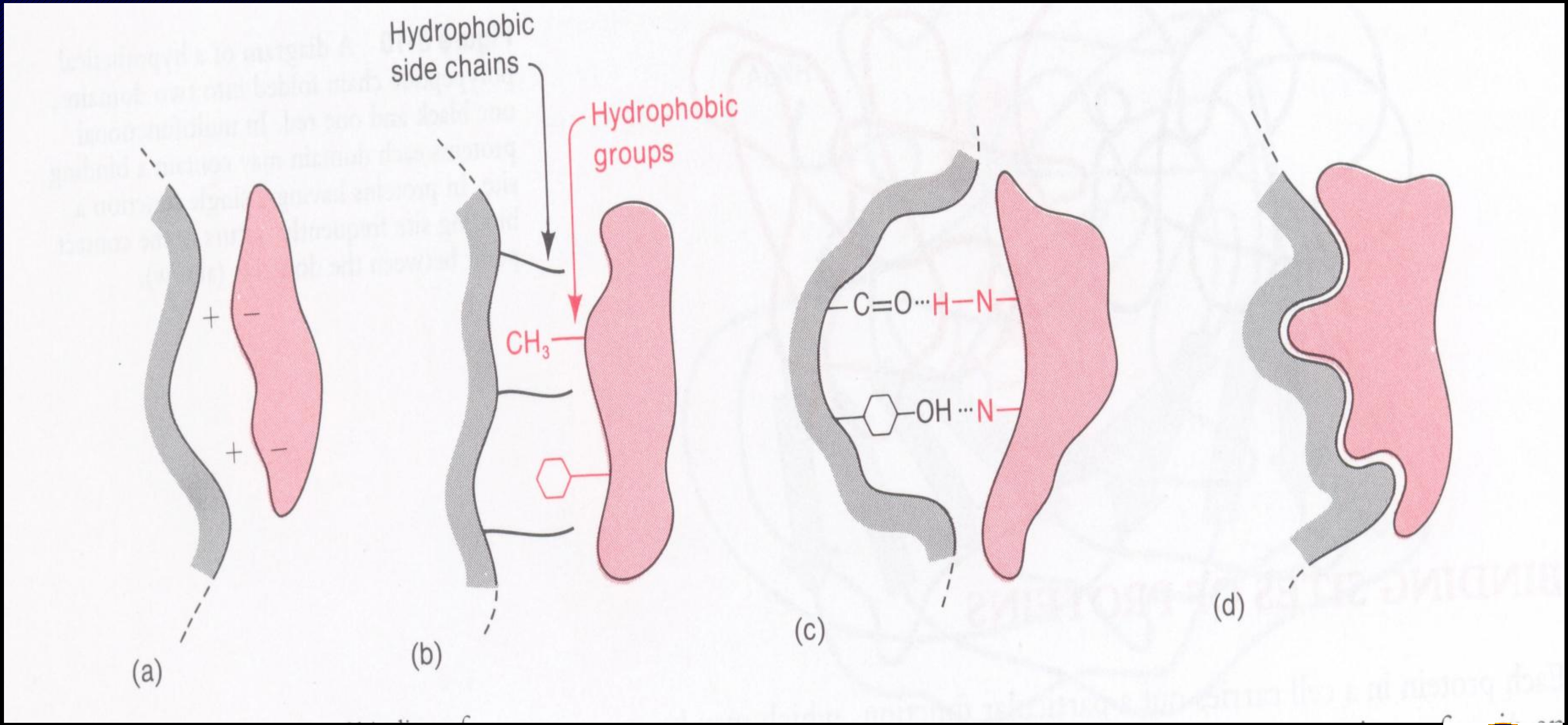
  iv. Covalent cross-linkages (via intrachain cystein residues)



Factors maintaining the 3° structure of globular protein

- In an enzyme, a Ábinding site' = an Áactive site'

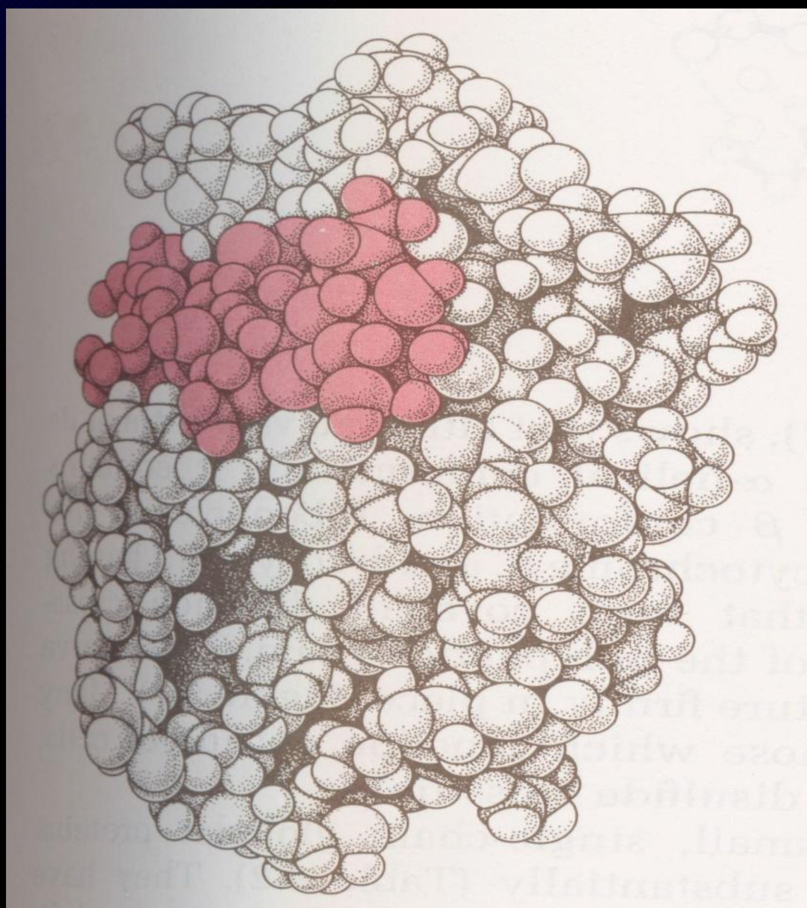
- 4 types of binding of small molecule (red) to the binding site of a protein (shaded)



) Electrostatic b)Hydrophobic c)Hydrogen bond d) Van Der Waal

- There are also protein which its polypeptide chains are tightl folded into a spherical or globular shape

→ Globular protein



Example of globular protein : Lysozyme molecule with its tightly bound polysaccharide substrate (color)

Proteins with subunits

- Why important protein always exist in the form of subunits ?

i. Subunits are an economical way to utilize DNA

ii. The activity of multisubunit proteins is very efficiently and rapidly switched on & off

ipid

Lipid

- Best known for their role in energy metabolism

- In most organism, the principle molecules for long term ene storage are the non-polar lipid called FATS.

- The fatty acid, main components of the non-polar lipids are important energy molecules especially in the heart, brain anc adipose tissues

- The Polar Lipids which contain some Nitrogen and Phosph are important components of Biological membrane

- Steroid class of lipid is represented by Cholesterol which is foun in membranes and also serve as a precursor for many hormones

Lets look into the structure of Fatty Acids¼¼¼¼¼

Fatty Acids

- A fatty acid has a structure of R-COOH (whereby R = long Hydrocarbon Chain ; the most common length are C_{16} & C_{18})

- These structural features give them a split personality : One end Polar & sometimes ionic (the COOH group) whereas the opposite end (the H-C chain) has non-polar properties

→ Amphiphilic molecule

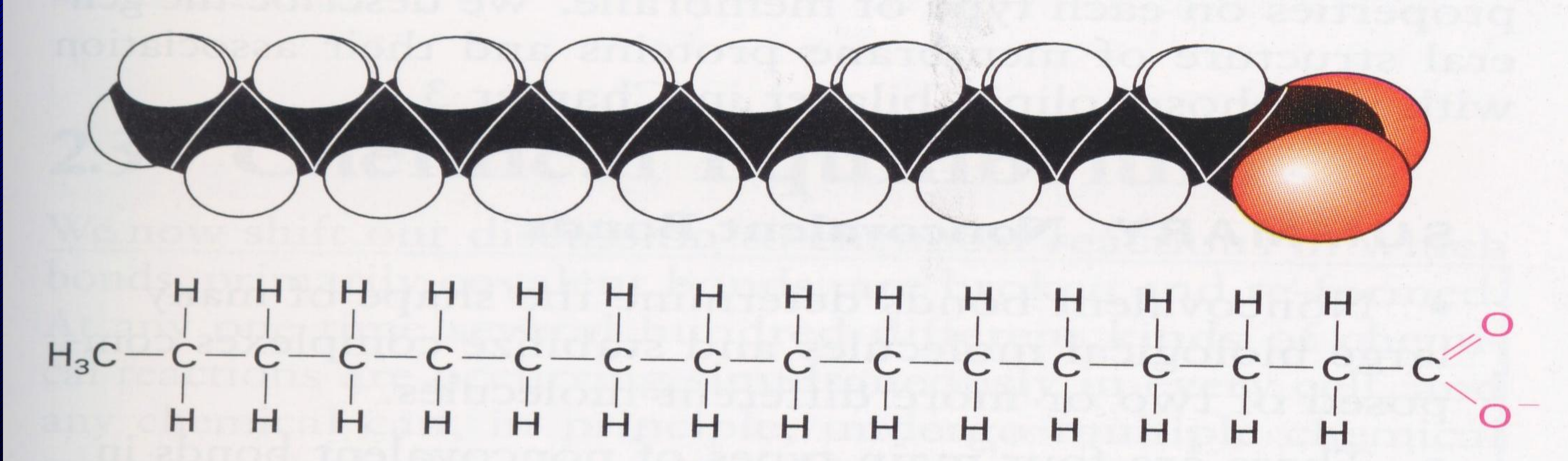
- Fatty acid rarely found in a free form in the cells and tissues, but most often in fats (triacylglycerols and other lipids)

- Types of Fatty Acids :

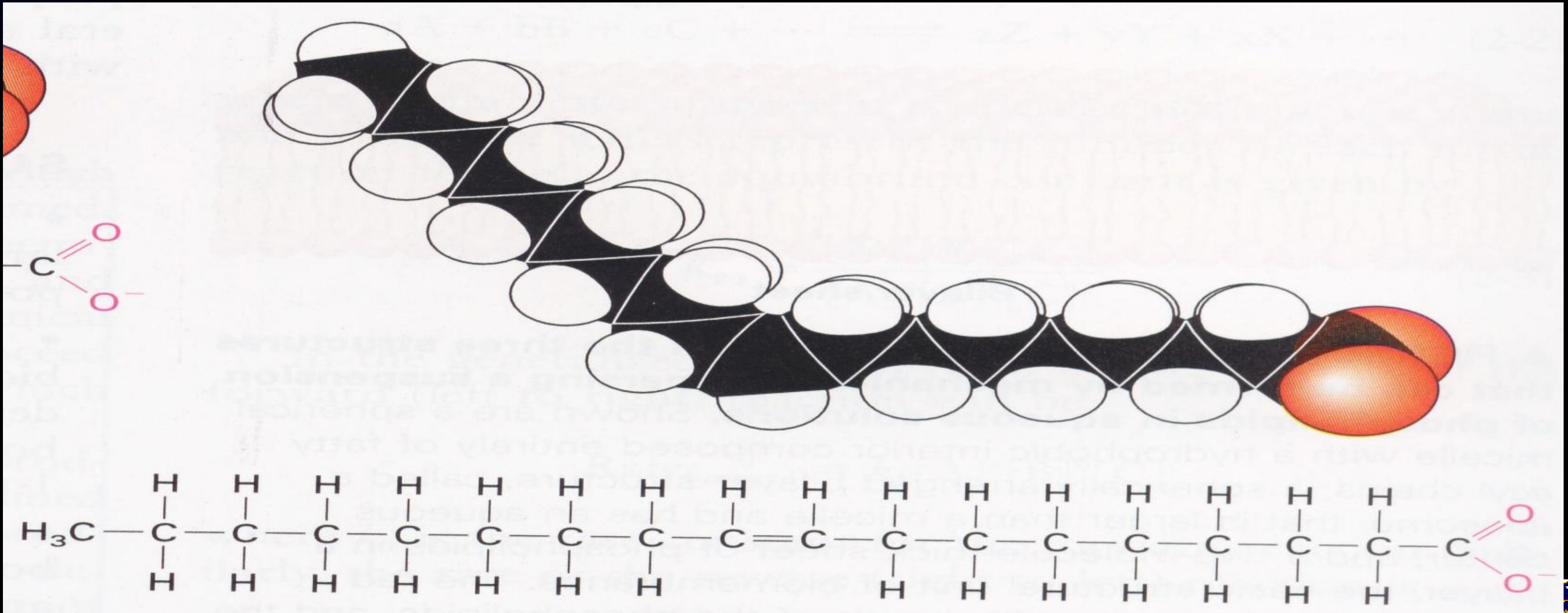
i. Saturated Fatty Acid : Consists of C-C single bond

ii. Un-Saturated Fatty Acid : Consists One or More C=C double bond

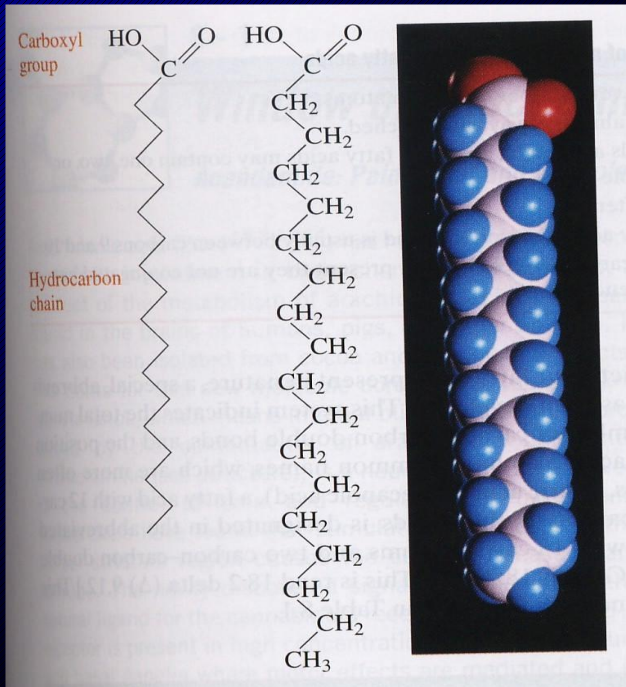
* Those with 2 or more double bonds : Poly-Unsaturated Fatty Ac



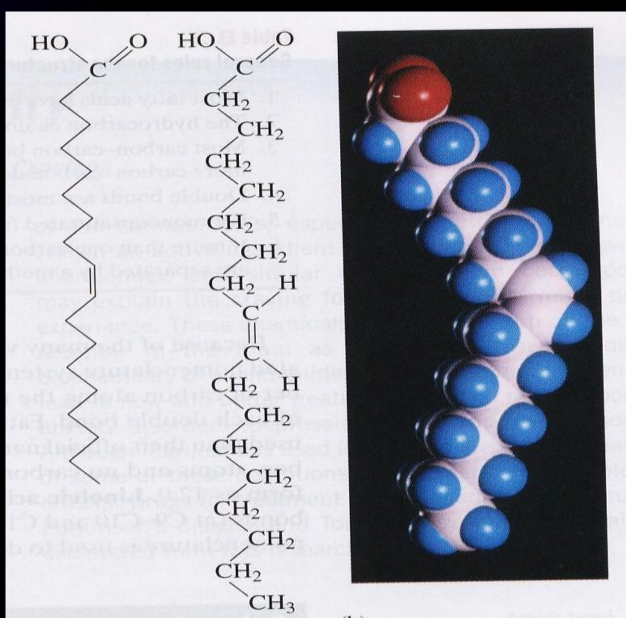
Palmitate
(ionized form of palmitic acid)



Oleate
(ionized form of oleic acid)



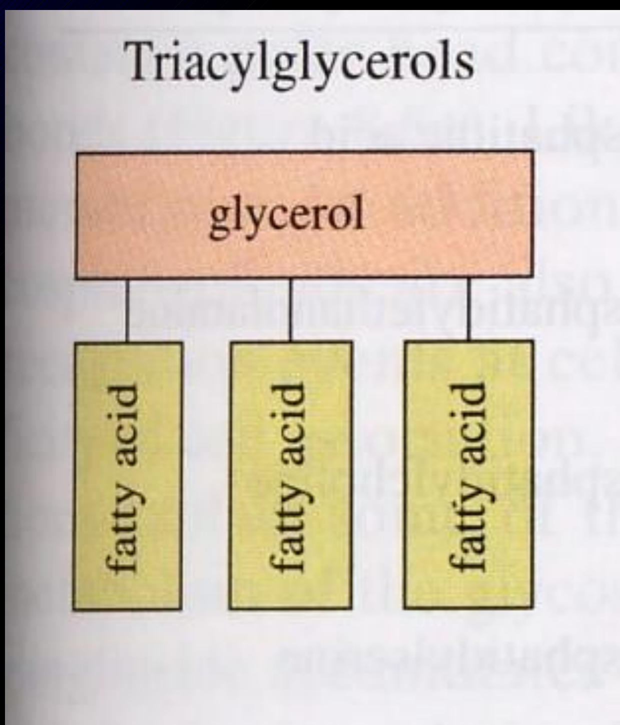
A saturated fatty acids (Octadecanoic acid) ± zig zag line represent the H-C chain ; a structure showing all C & H atoms and space filling models showing the actual shape of each molecule



An Un-saturated fatty acids (9-Octadecenoic acid) ± zig zag line represent the H-C chain ; a structure showing all C & H atoms and space filling models showing the actual shape of each molecule

Non-Polar Lipid

- Almost all fatty acids present in nature are found as constituents
non-polar lipid called triacylglycerol
- Triacylglycerol isolated from animal tissues are called FATS and
are solid at room temperature because they contain predom
antly
saturated fatty acids



- Triacylglycerol mixture from plant seeds are termed oil and contain mainly unsaturated fatty acid

- Table in the next slide will compare the fatty acid content in plant and animal sources

* TAG (Triacylglycerol/Triglyceride):
It has 3 molecule of fatty acid (acyl group) attached to a glycerol molecule

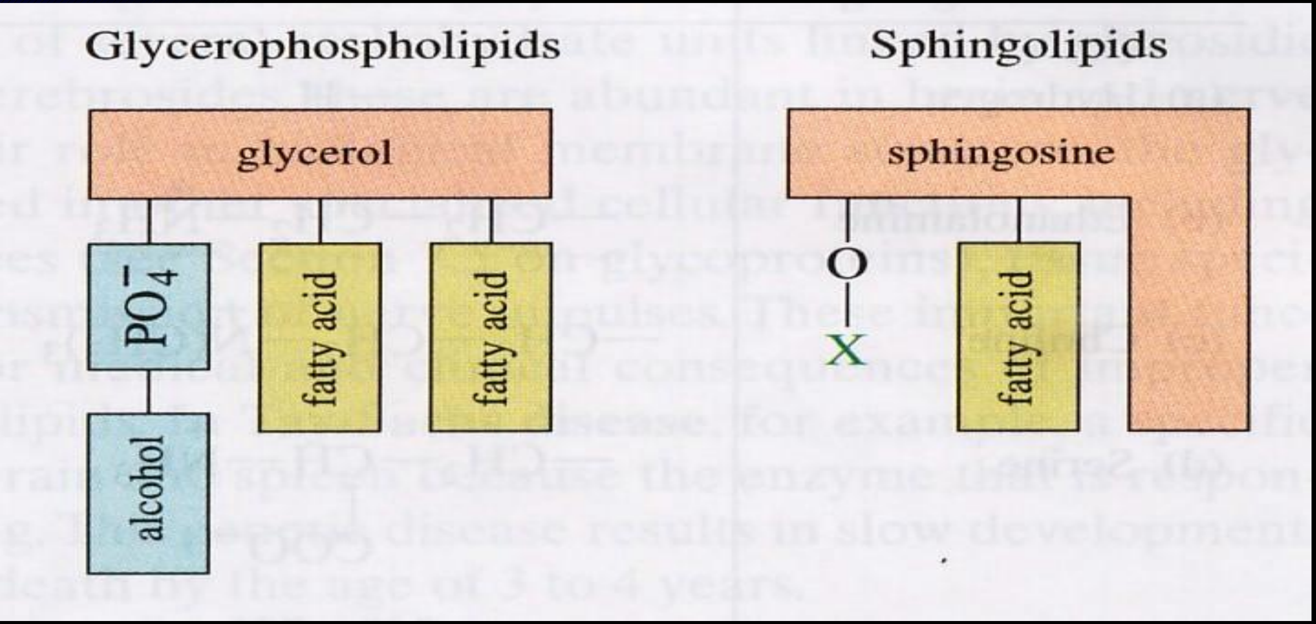
	Fatty Acids				
	Saturated				*Unsaturated*
Source	C_4–C_{12}	C_{14}	C_{16}	C_{18}	$C_{16} + C_{18}$
Canola oil	—	—	5	1	94
Olive oil	2	2	13	3	80
Butter	10	11	29	10	40
Beef fat	2	2	29	21	46
Coconut oil	60	18	11	2	8
Corn oil	—	2	10	3	85
Palm oil	—	2	40	6	52
Nutmeg oil	7	90	3	—	—
Peanut oil	—	5	8	3	84
Soybean oil	—	2	10	3	85
Sunflower oil	—	—	6	3	91

Fatty acid content of common oil and fats. The fatty acids a present in triacylglycerol form. The number represent percentage of each fatty acid in an oil

Polar Lipid

- The polar class of lipid, represented by the very hydrophob triacylglycerols serve as a storage molecules for metabolic fuel

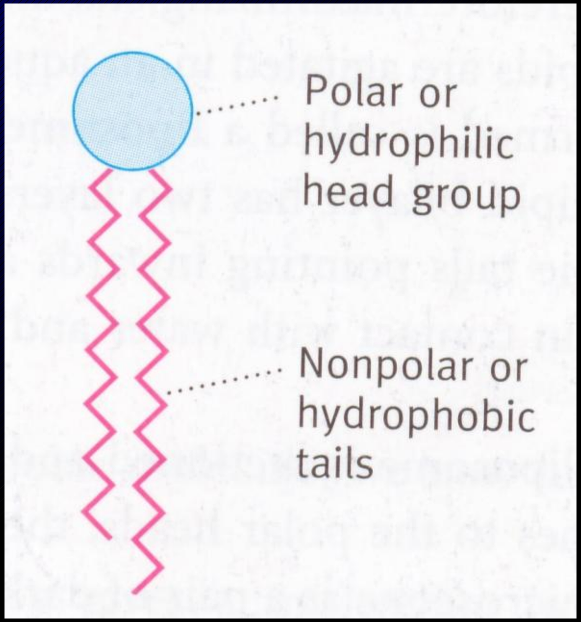
- 2 types of polar lipid :



Sphingolipids : component of the membrane in the brain and nervous system (nerve membrane)

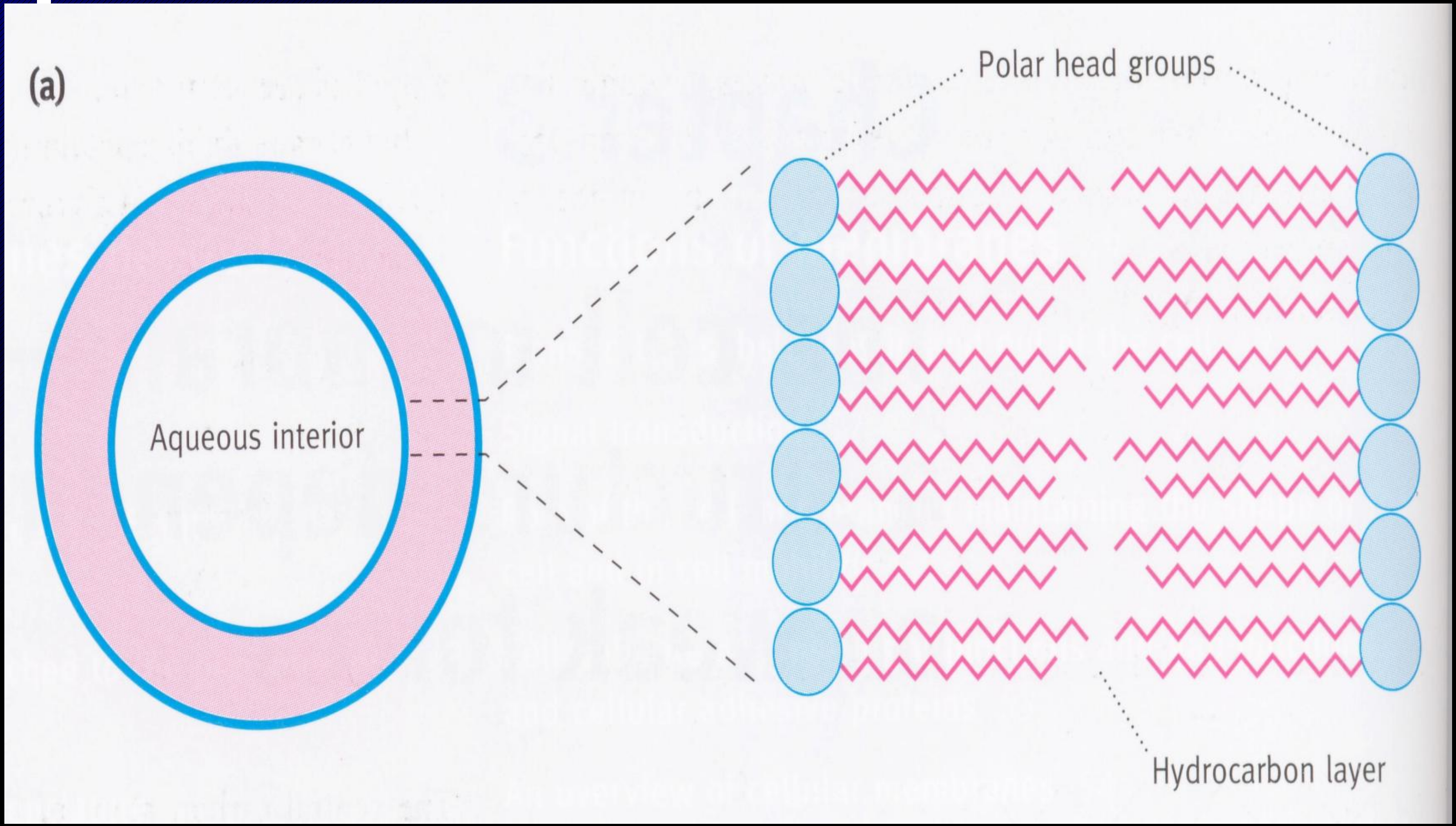
Glycerophopholipids : Important component in the biological membrane structure

- Consist of membrane polar lipid : With polar head & two hydrophobic tails

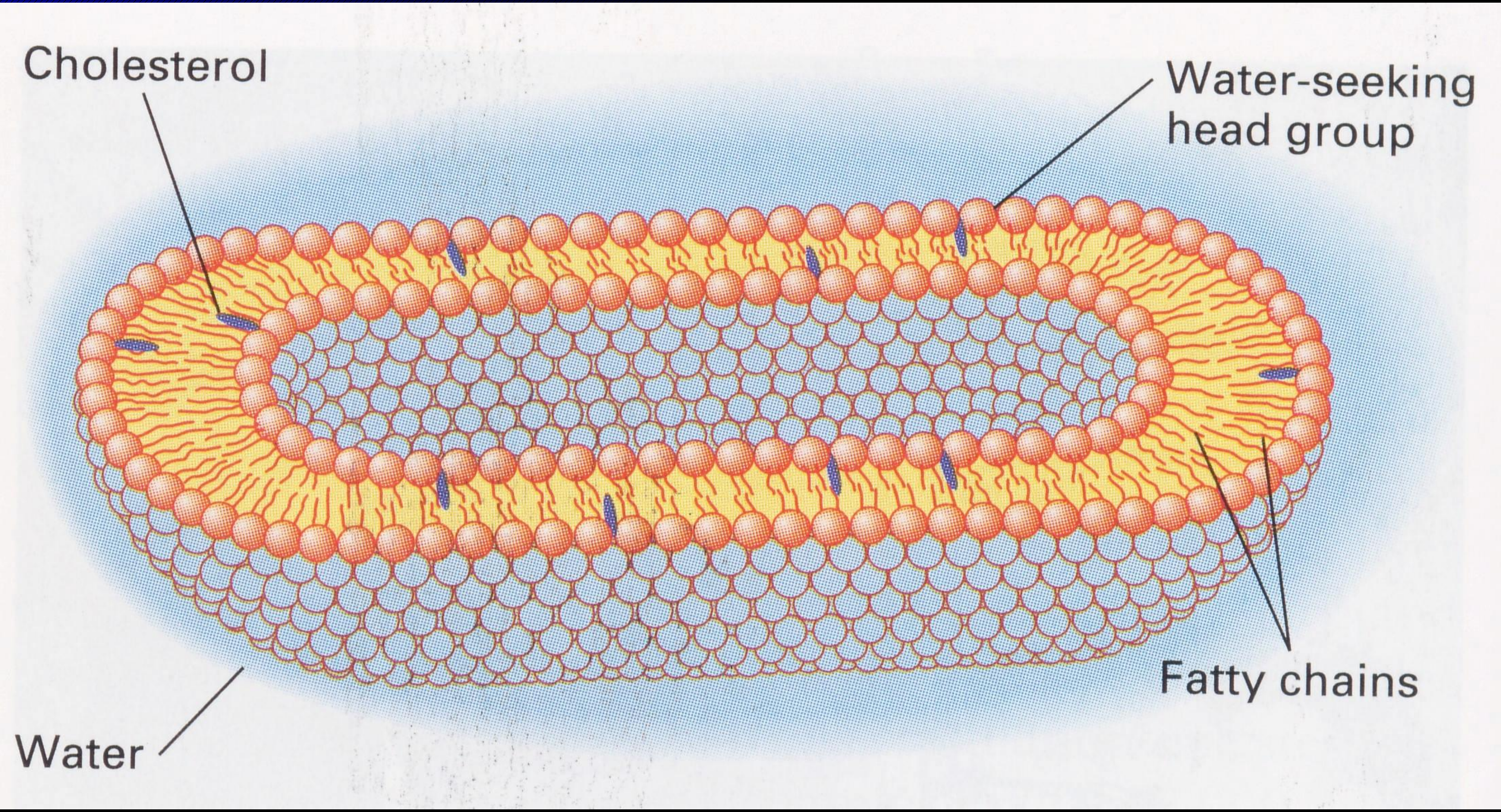


- There are many different types of membrane lipid (this will justify their different function on the different membrane surface)

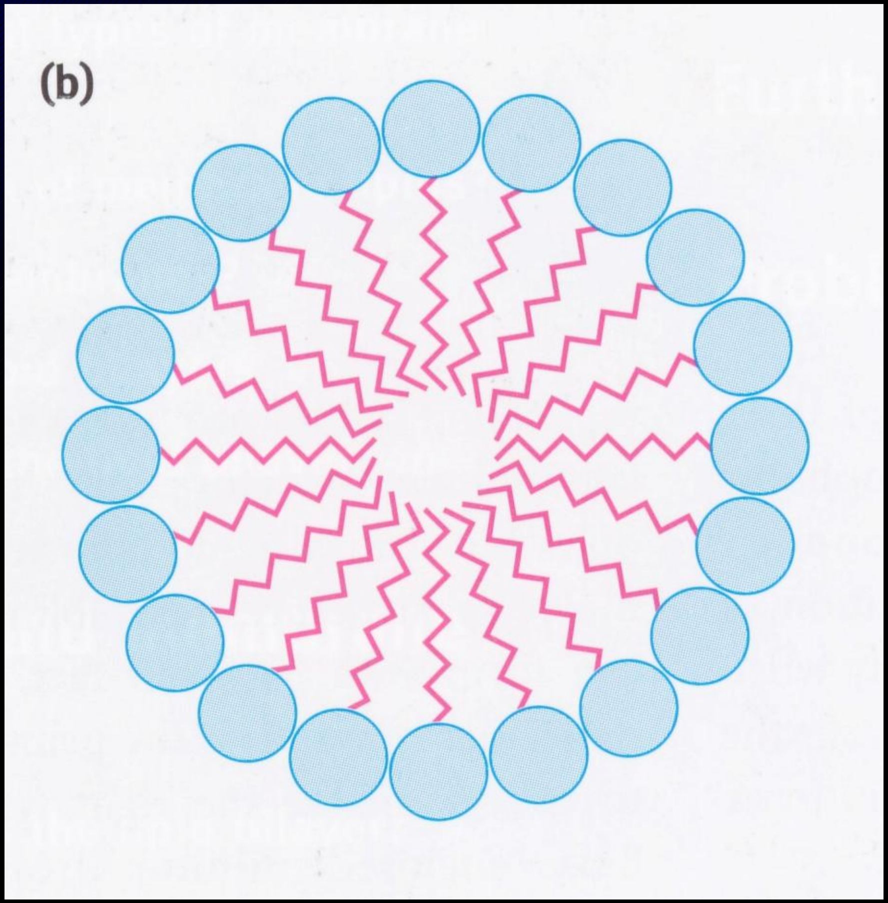
- eg. Cerebrosides/gangliosides in brain and phospholipids in the bilayer membrane of many kind of organeles



A synthetic liposome made of a lipid bilayer structure



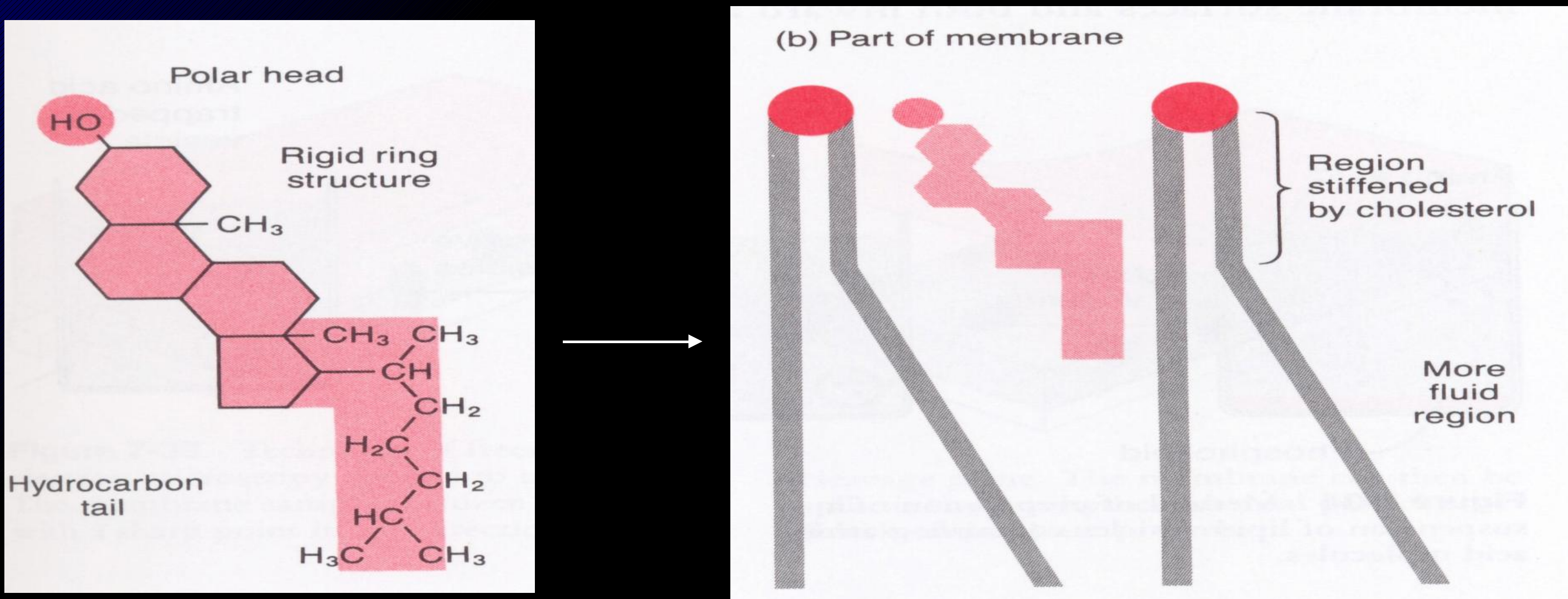
Plasma membrane - 2 layered phospholipid



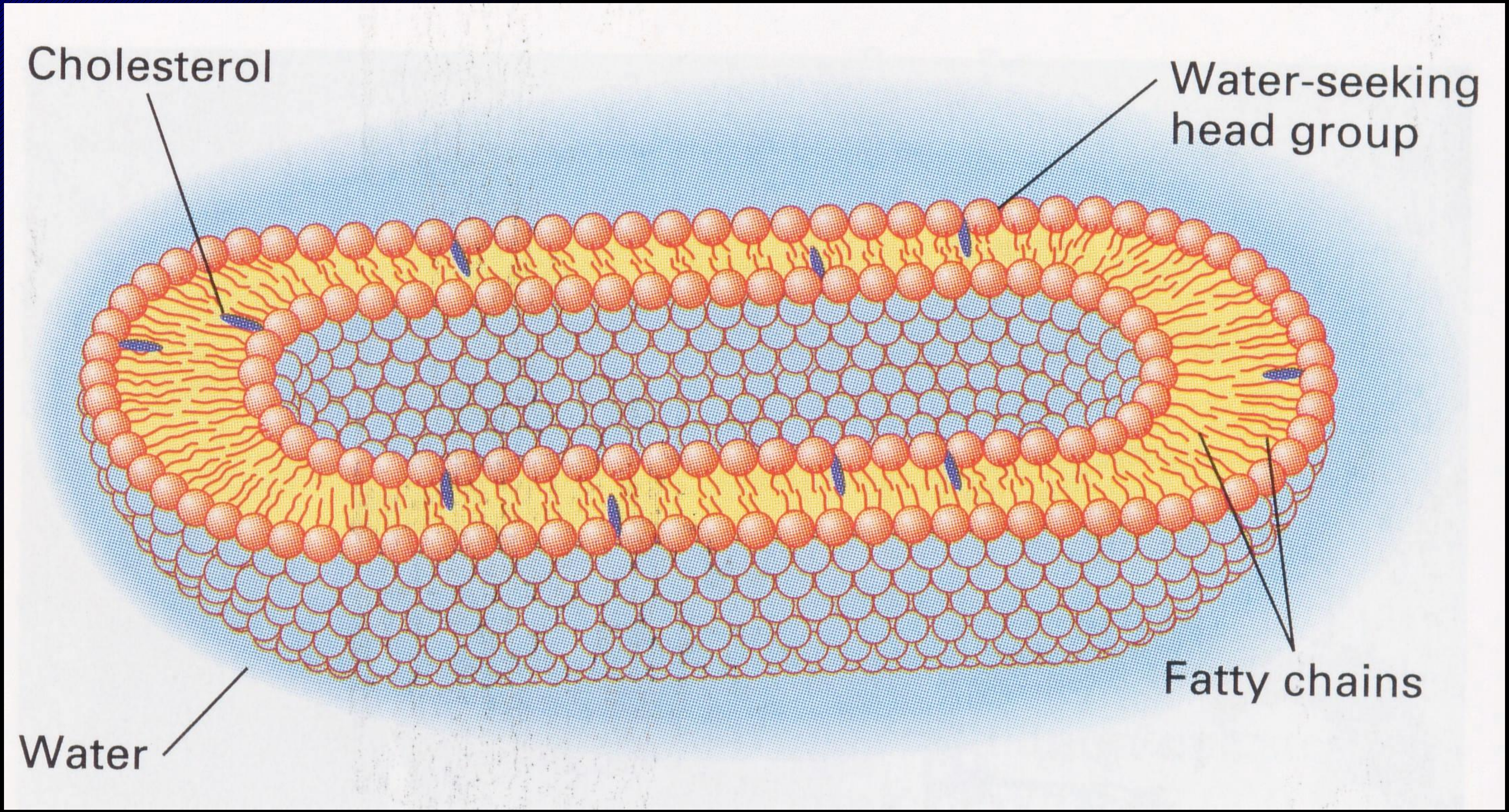
A Ámicelle’ : Solid cylindrical structure taken up by amphiphatic molecule

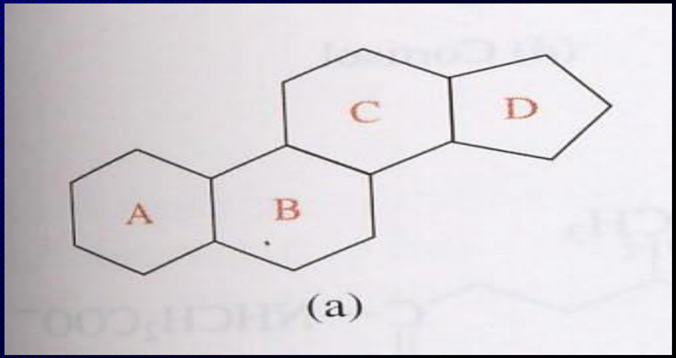
* Cholesterol (amphiphatic molecule)

- Is not classified as a lipid BUT it is one component of the membrane : An animal steroids



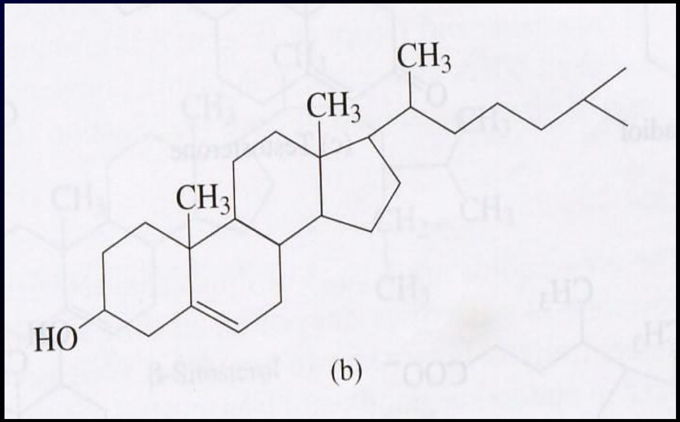
- It provide rigidity to the fatty layer & acts as a Áfluidity buffer’
- Inserted between the membrane lipid & prevent close packing of the hydrocarbon chains and thereby lower the melting point


Cholesterol
Water-seeking
head group
Fatty chains
Water



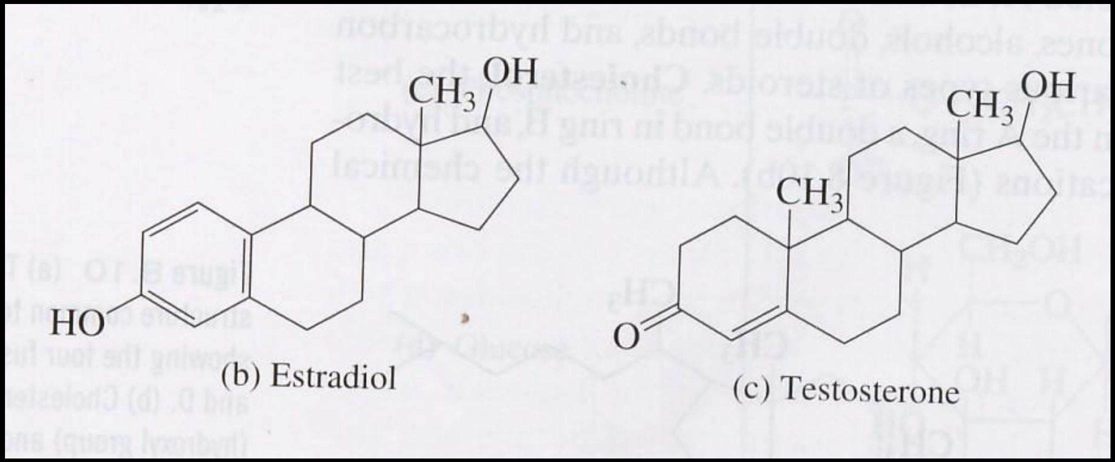
(a)

The molecular structure common to all steroids showing the 4 fused rings : A, B, C and D.



(b)

Cholesterol has polar head (OH group) and non-polar tail (H-C skeleton)



(b) Estradiol

(c) Testosterone

Nucleic Acid

DNA : Deoxyribonucleic Acid

- Is the single most important molecule in living cells and contain all of the information that specifies cellular properties

- Firstly isolated in 1868 by Johann Friedrich Miescher, a young Swiss medical student in Germany

→ An acidic structure from pepsin treated puss cells : Named it as ‘Nuclein’

- The nuclein contain P & N (two elements that only

- Miescher reported his finding in 1869 but only been published in 1871 :

  * His finding have not have been anticipated

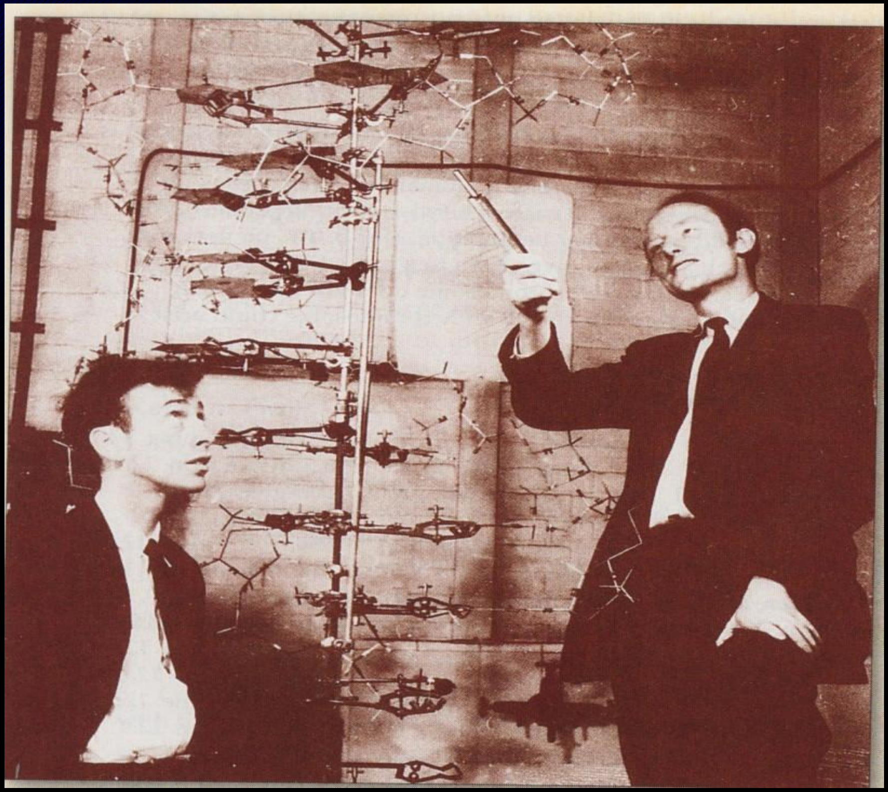
  * There is no knowledge to link this new substance to inheritance

- Frederick Griffith (in 1928) showed that the hereditary material is transferable in bacteria Streptococcus pneumoniae

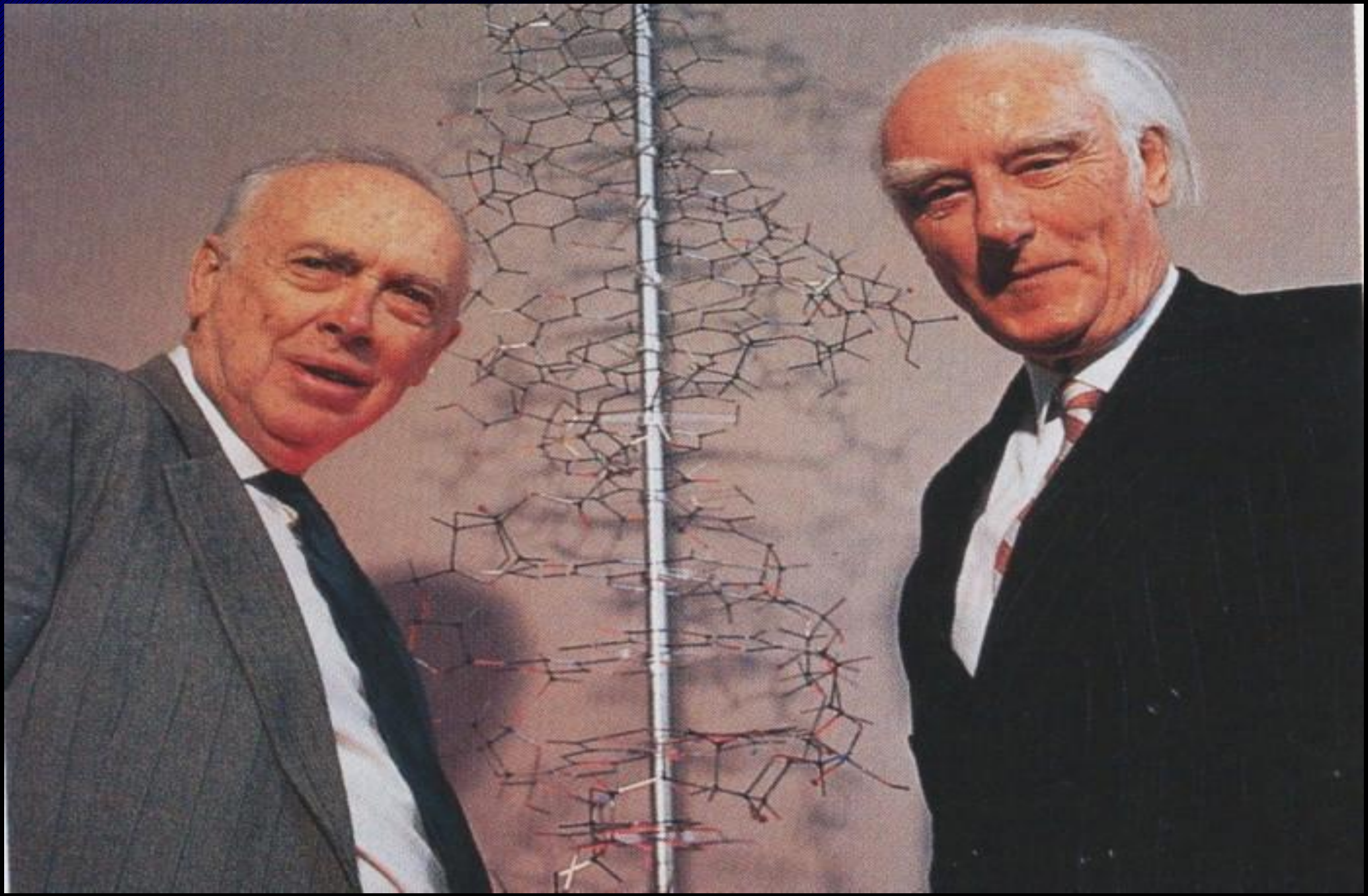
- The role of this substance in storing & transferring genetic information ONLY been established in 1944 (Avery, MacLeod & McCarthy's experiment)

- 2nd prove showed that DNA (not protein) is responsible for inheritance : Hershey & Chase (1952)

¼.and double helix DNA was only being discovered in 1953 (Watson & Crick)



James Watson & Francis Crick posing in 1853 by their newly unveiled structural model of DNA



James D. Watson (left) & Francis H.C. Crick (right)

Nature of the chemical subunits in DNA & RNA

- Nucleic acid : Composed of repeating subunits called Ánucleotide'

- Each nucleotide composed of :

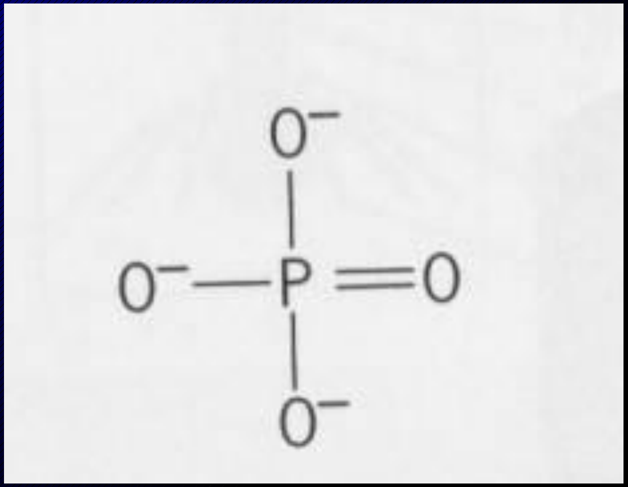
i. Phosphate group

ii. 5-Carbon sugar : 2-deoxyribose (DNA) @ ribose (RNA)

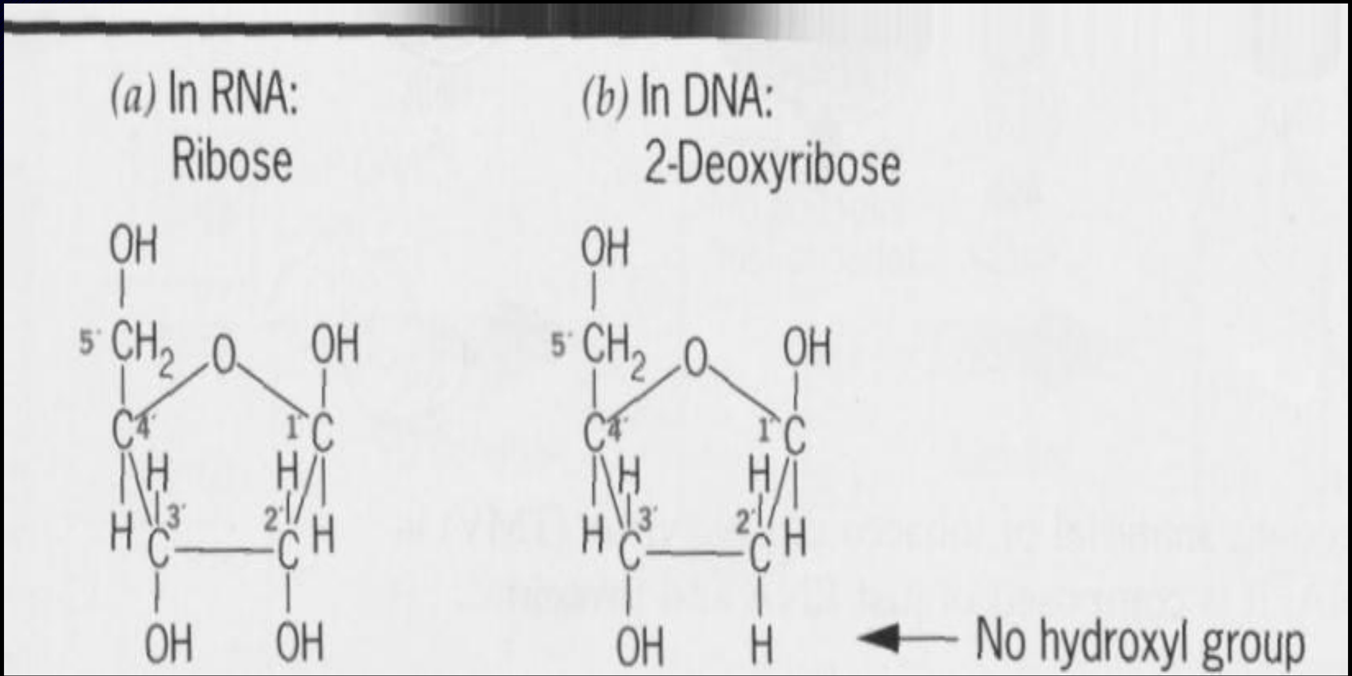
iii. Cyclic Nitrogen - containing compound called ÁA Base'

⟶ Purine [Adenine & Guanine] - double base ring

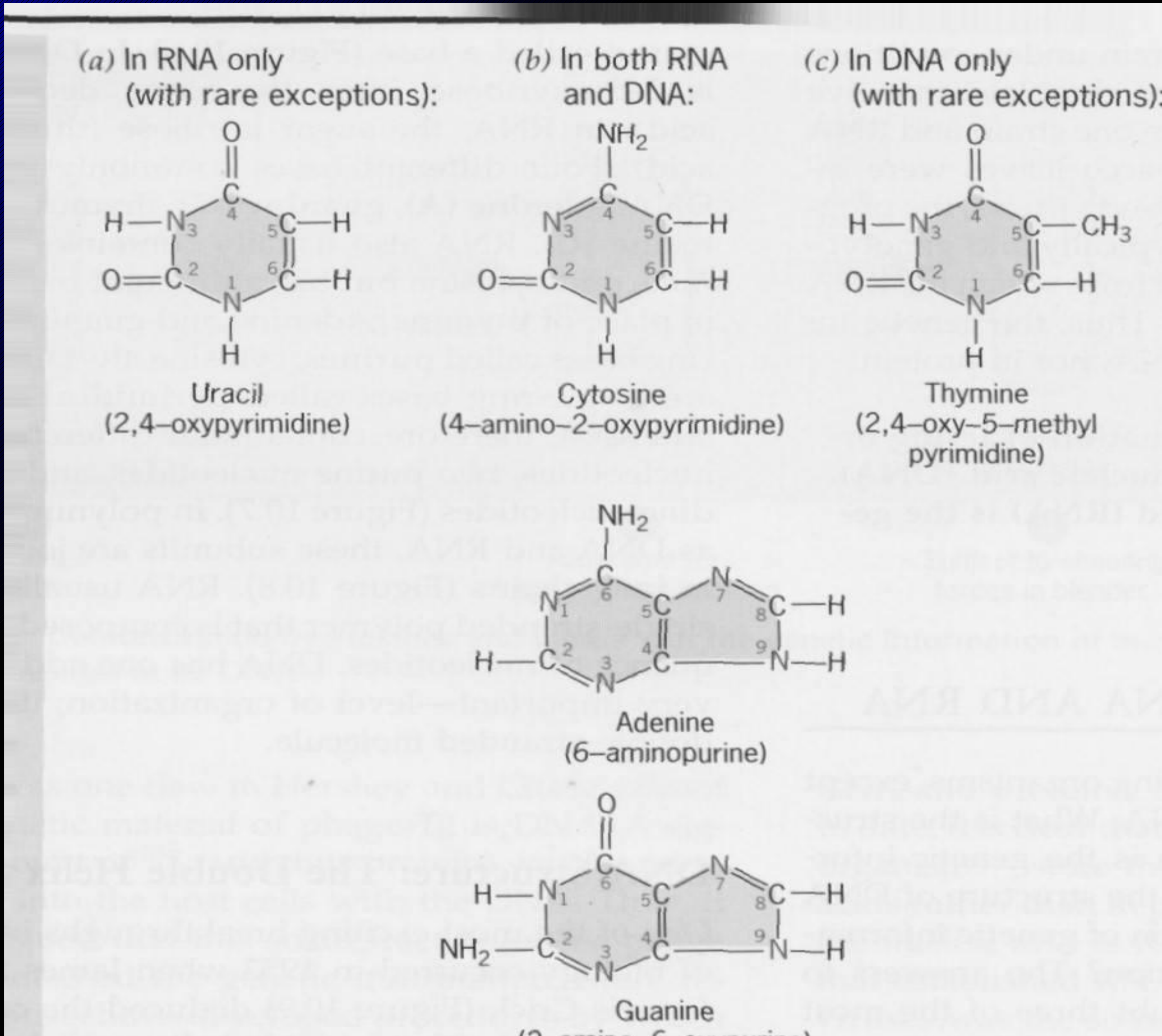
⟶ Pirimidine [Cytosine & Thymine (DNA)/Uracil (RNA) - single ring base]



Phosphate group



5-Carbon Sugar



Cyclic Nitrogen

- In DNA & RNA, these subunits are joined together in long chain : polynucleotide

DNA : Double strand RNA : single strand

- Nucleoside : Combination of a base and a sugar without a phosphate

- Nucleotides are nucleosides that have one, two or three phosphate groups esterified at the 5’ hydroxyl (OH)

* Nucleoside triphosphate are used in the synthesis of nucleic acids. However, the also serve many other function in the cells : ATP (energy carrier), GTP (intracellular signaling & energy reservoir)

TABLE 4-1 Naming Nucleosides and Nucleotides

		Bases		
	Purines		Pyrimidines	
	Adenine (A)	Guanine (G)	Cytosine (C)	Uracil (U) Thymine [T]
Nucleosides in RNA	Adenosine	Guanosine	Cytidine	Uridine
Nucleosides in DNA	Deoxyadenosine	Deoxyguanosine	Deoxycytidine	Deoxythymidine
Nucleotides in RNA	Adenylate	Guanylate	Cytidylate	Uridylate
Nucleotides in DNA	Deoxyadenylate	Deoxyguanylate	Deoxycytidylate	Thymidylate
Nucleoside monophosphates	AMP	GMP	CMP	UMP
Nucleoside diphosphates	ADP	GDP	CDP	UDP
Nucleoside triphosphates	ATP	GTP	CTP	UTP
Deoxynucleoside mono-, di-, and triphosphates	dAMP, etc.			

DNA structure : The double helix

- One of the most exciting breakthrough in history

- In 1953, Watson & Crick deduced the correct DNA structure based on 2 major kinds of evidence :

i. The work of Erwin Chargaff & collegues at University of Columbia in late 1940 :

a. DNA specimens isolated from different tissues of the same species have th same base composition

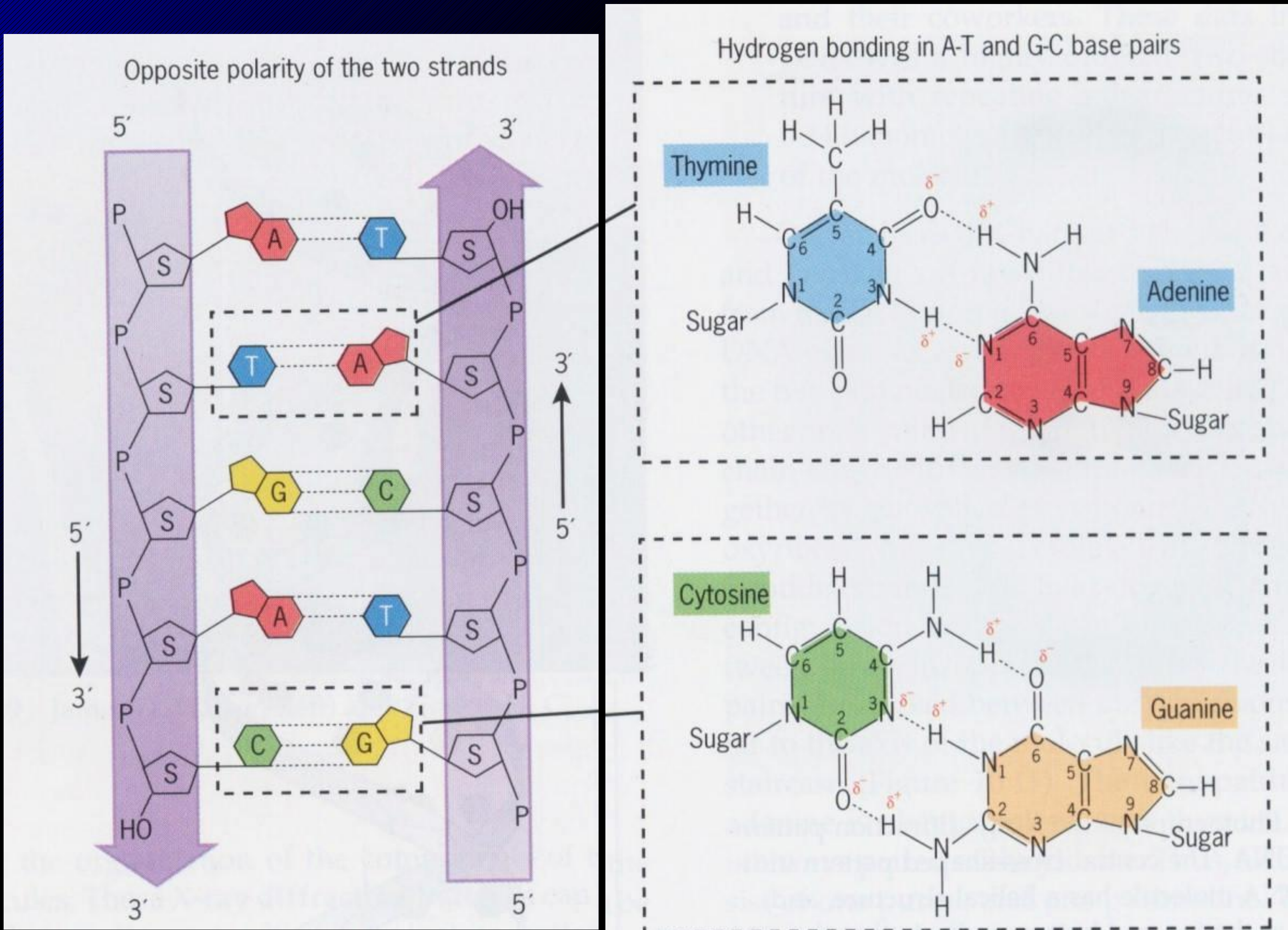
b. The base composition of DNA varies from one species to another

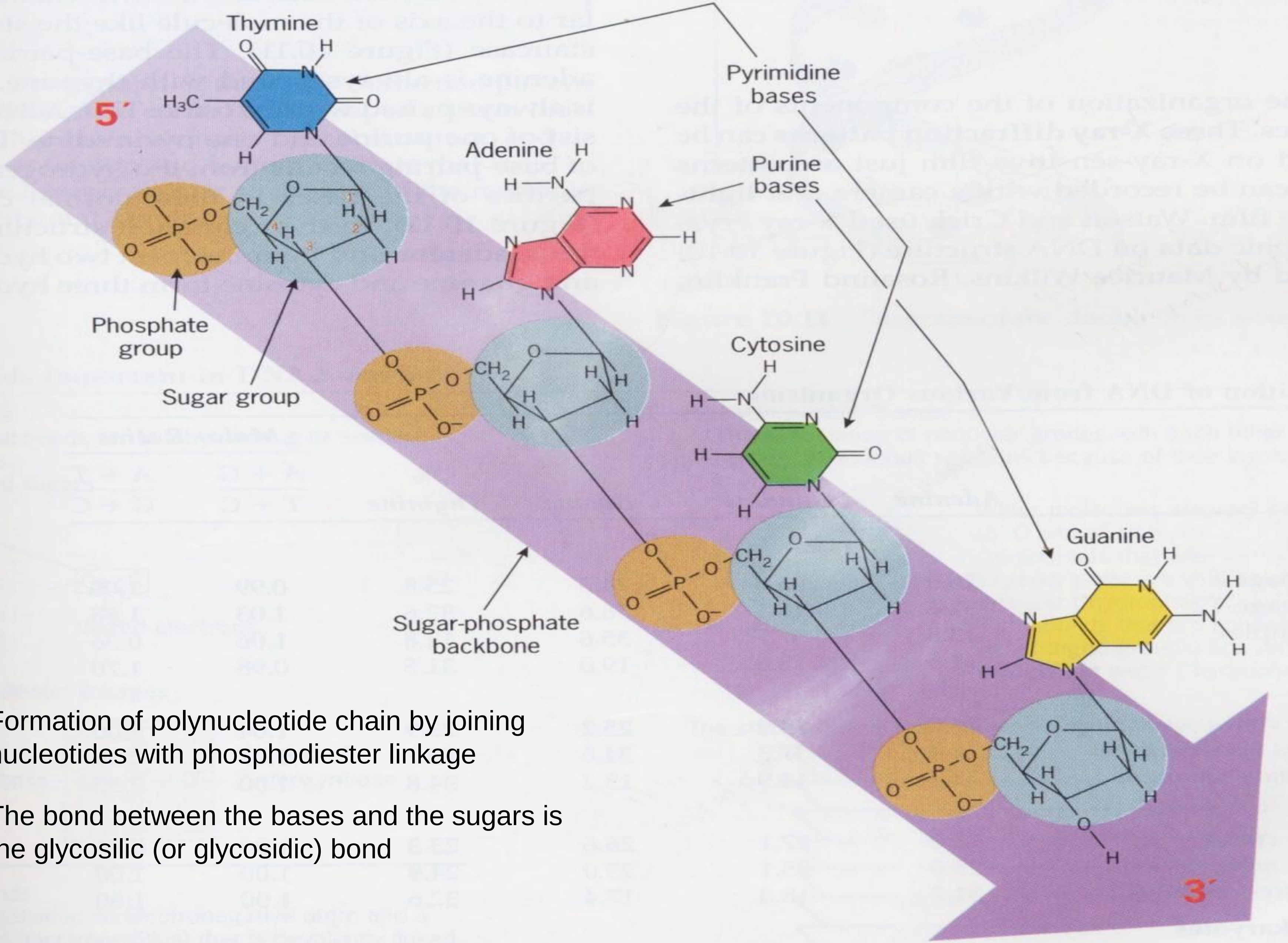
c. The base composition of DNA in a given species does not change with age of the organism, its nutritional state, or changes in its environment

d. The number of Adenine residue in all DNAs, regardless of the species, is equal to the number of thymine residues (A = T)¼and the same goes with (C = G)

The [T] was equal to the [A] and the [C] was always eq
to the [G]

[pyrimidines (T + C)] = [purines (G + A)]


Opposite polarity of the two strands
5′
3′
P
S
OH
A
T
G
C
HO
Hydrogen bonding in A-T and G-C base pairs
Thymine
Adenine
Cytosine
Guanine
Sugar
H
C
N
O
δ⁻
δ⁺

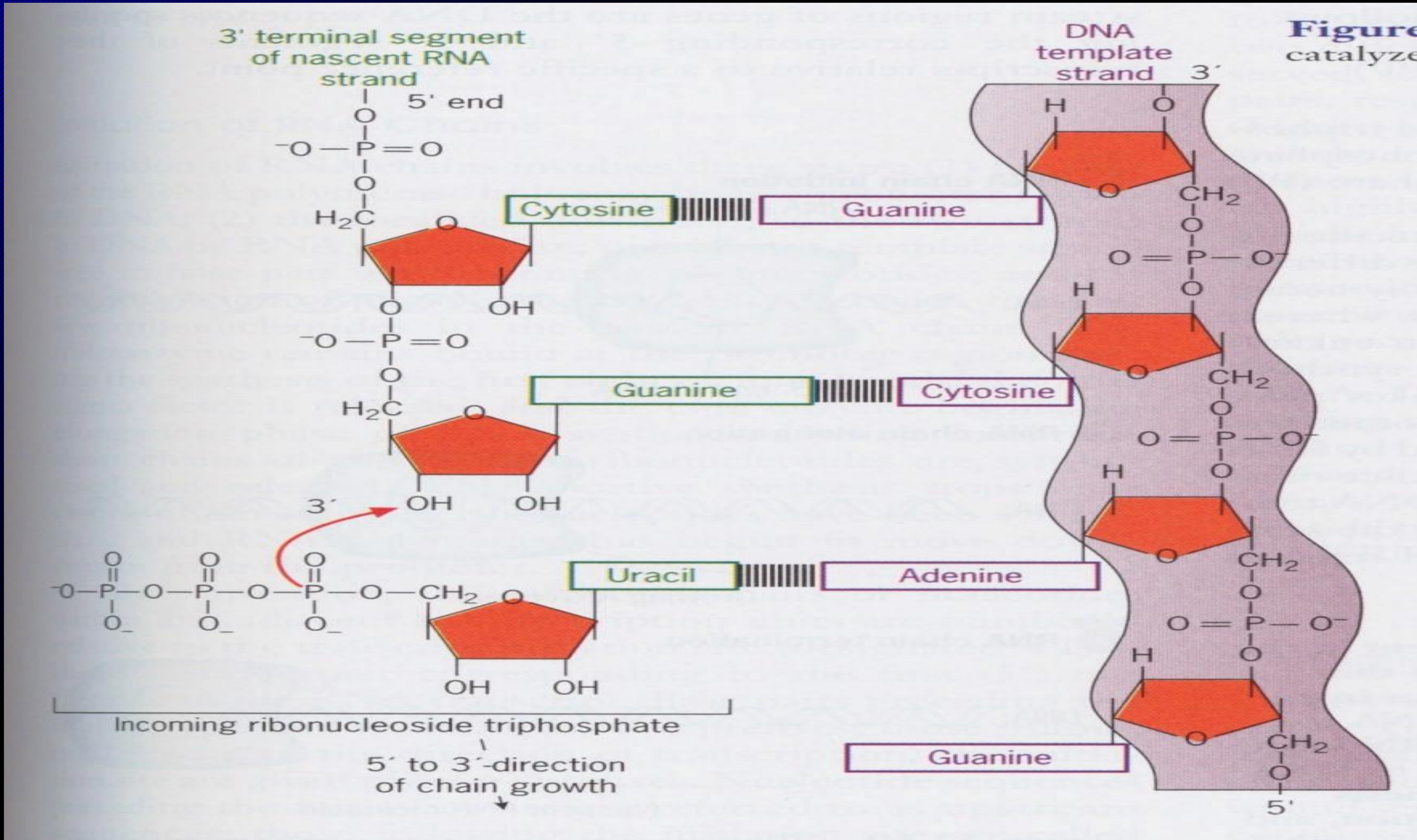


Formation of polynucleotide chain by joining nucleotides with phosphodiester linkage

The bond between the bases and the sugars is the glycosilic (or glycosidic) bond

RNA : Structure and characteristics

- RNA : Ribonucleic Acid
- A typical cell contains about 10x as much RNA a DNA !
- A single stranded polynucleotide (with the exception of the RNA of one phage and a few viruses)
- Uses ÁRibose’ sugar instead of ÁDeoxyribose’



The RNA chain elongation reaction catalized by RNA Polymerase

Thank You