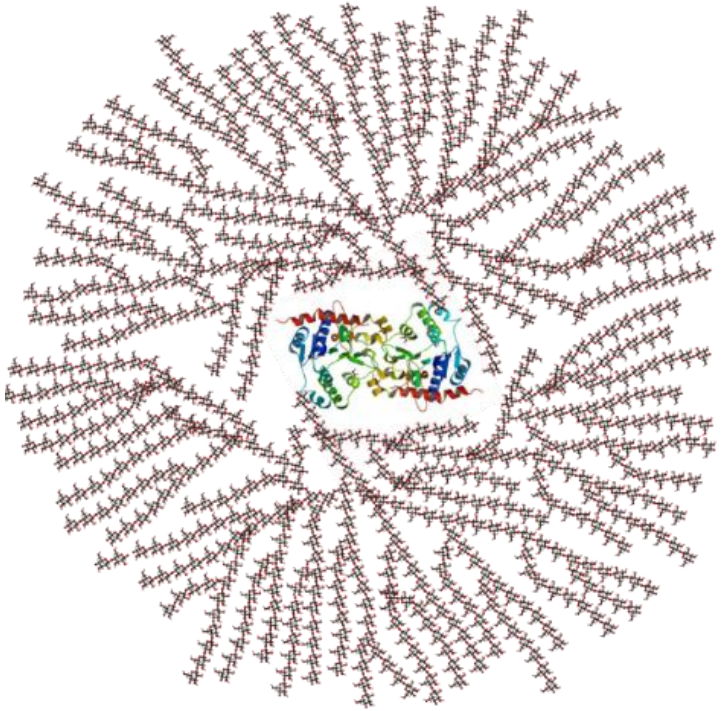
Biomolecules: Structures, functions and interactions



Assoc. Prof. Chadamas Sakonsinsiri, Ph.D.

Email: schadamas@kku.ac.th

Department of Biochemistry, Faculty of Medicine, Khon Kaen University

MD567712 Cells and Molecular Biology

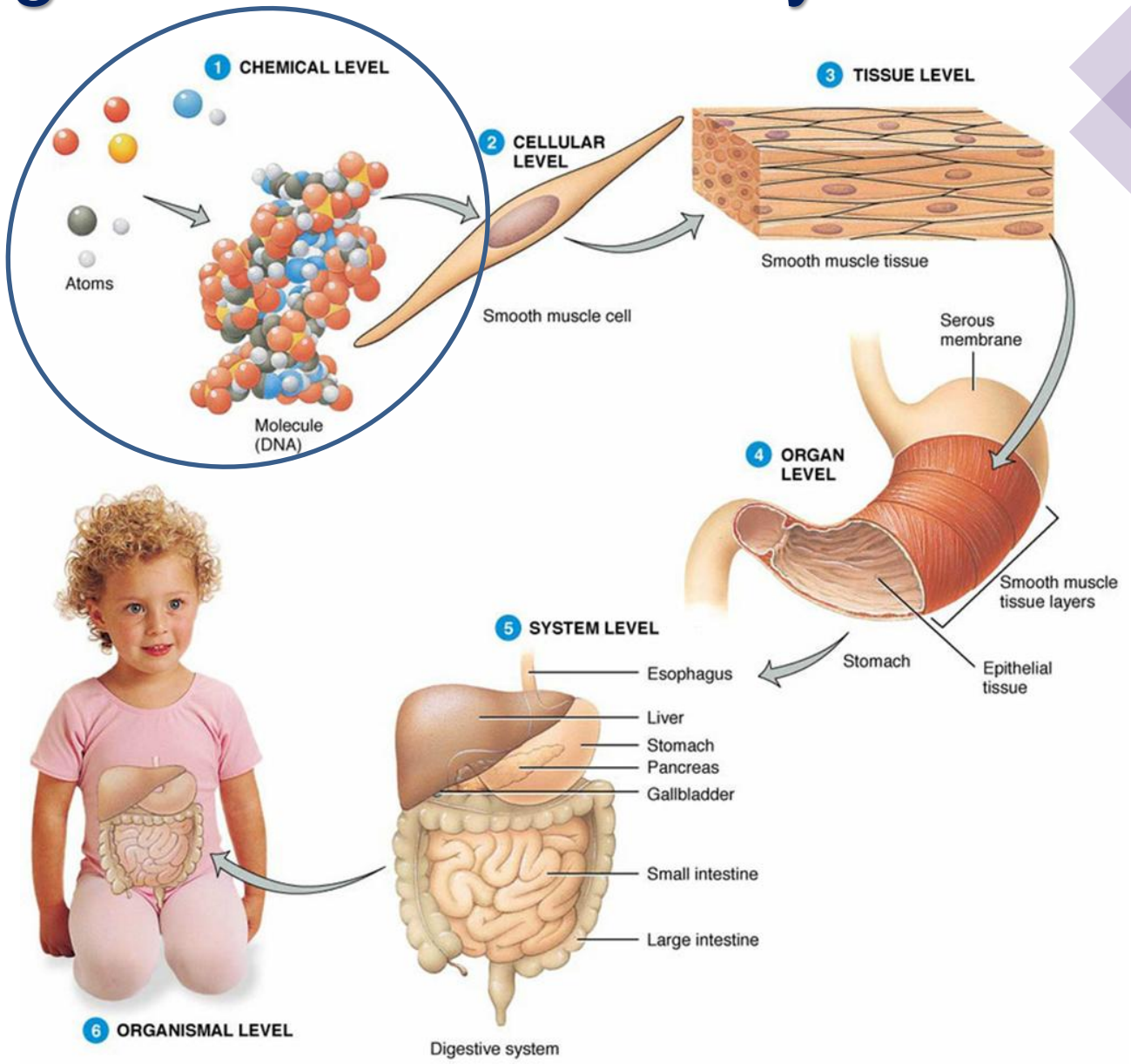
Outline

- Biomolecules (carbohydrates, lipids, proteins, nucleic acids): structures and functions
- Chemical bonding & molecular interactions
- Stereochemistry of biomolecules

The levels of organization in the body

Four major classes of biomolecules/macromolecules:

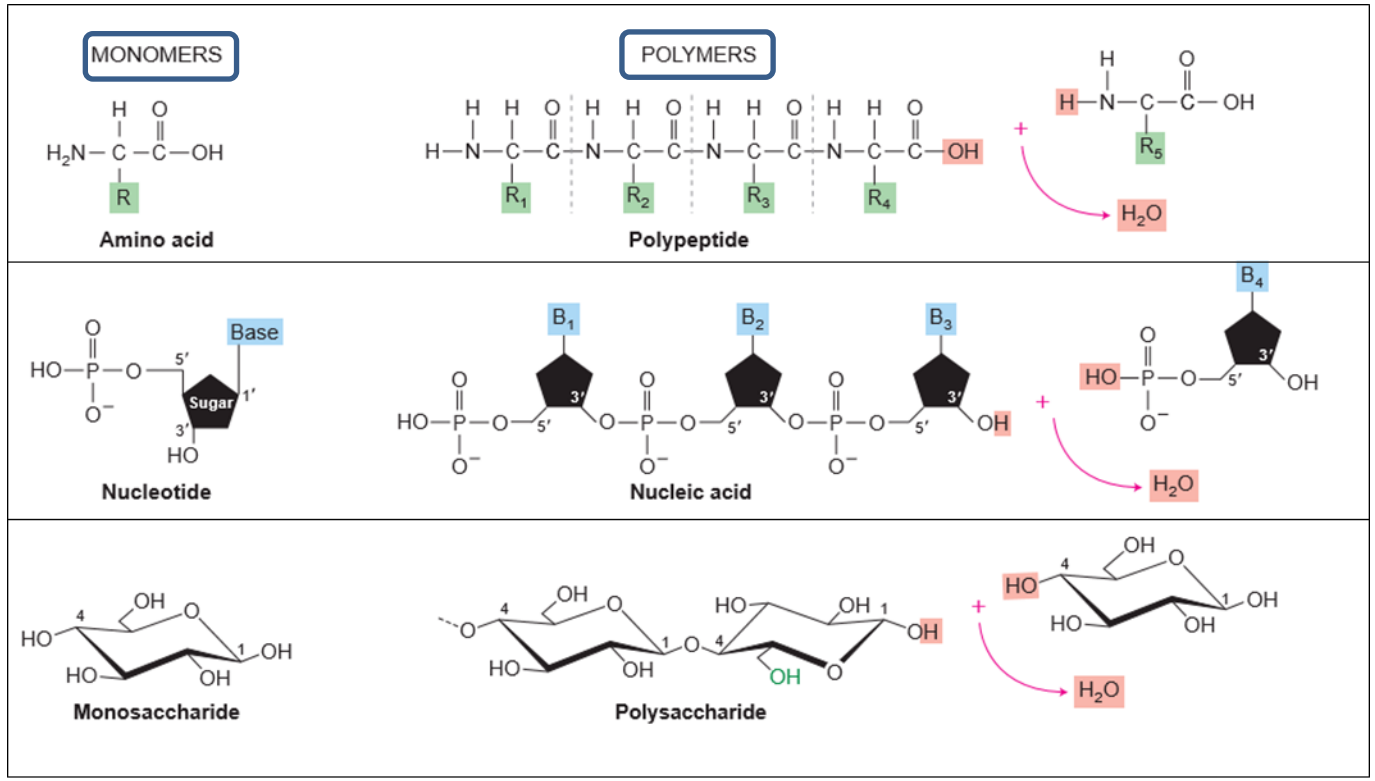
- Proteins
- Nucleic acids
- Carbohydrates
- Lipids

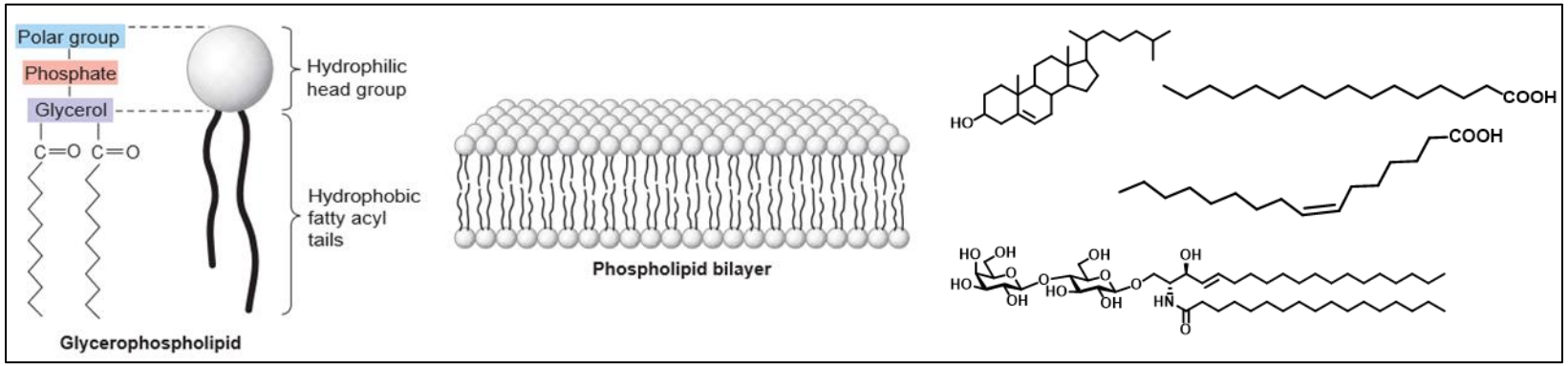


http://ssds-science.weebly.com/cells-tissue-organ-organ-system.html

Biomolecules - an overview

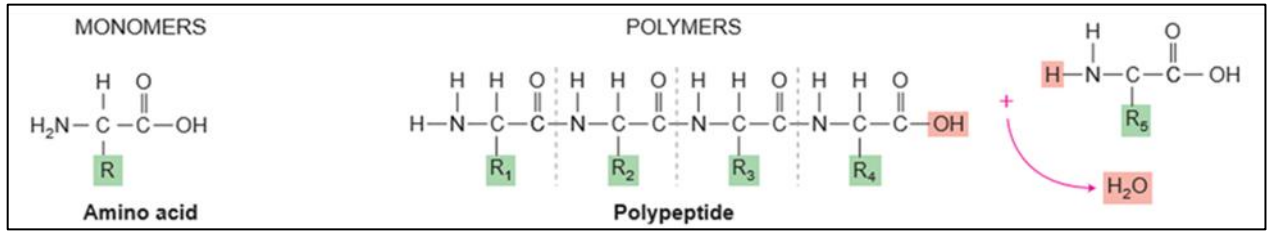
- **Proteins**
  - Polypeptides
  - Amino acids
  - Peptide bonds
- **Nucleic acids (DNA & RNA)**
  - Polynucleotides
  - Nucleotide (base, sugar and phosphate)
  - Phosphodiester bonds
- **Carbohydrates**
  - Polysaccharides
  - Oligosaccharides (Disaccharides)
  - Monosaccharides
  - Glycosidic bonds
- **Lipids**
  - Diverse structures
  - Insoluble in water, hydrophobic, nonpolar
  - Soluble in organic solvents
  - Made up mostly of hydrocarbon chains





Proteins

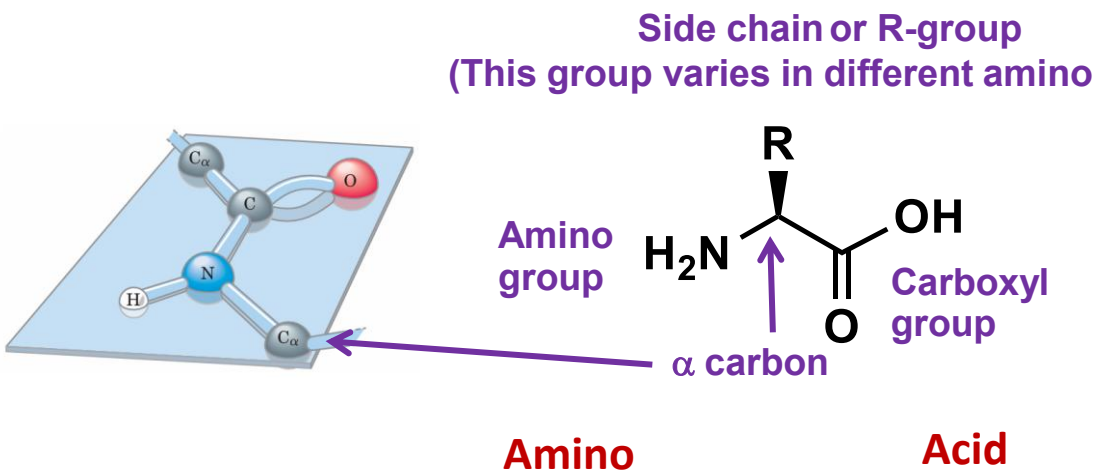
Roles of Proteins:

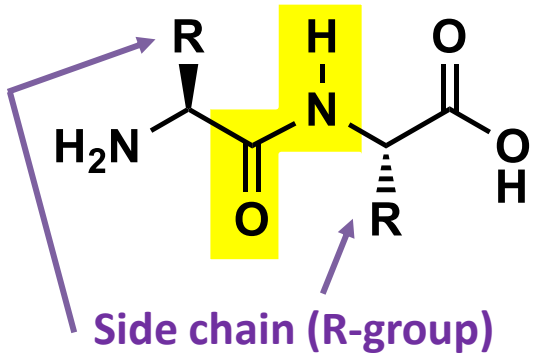


- Catalysts
- Transport of vitamins, minerals, oxygen and fuels
- Receptors
- Cytoskeleton

Primary Structure

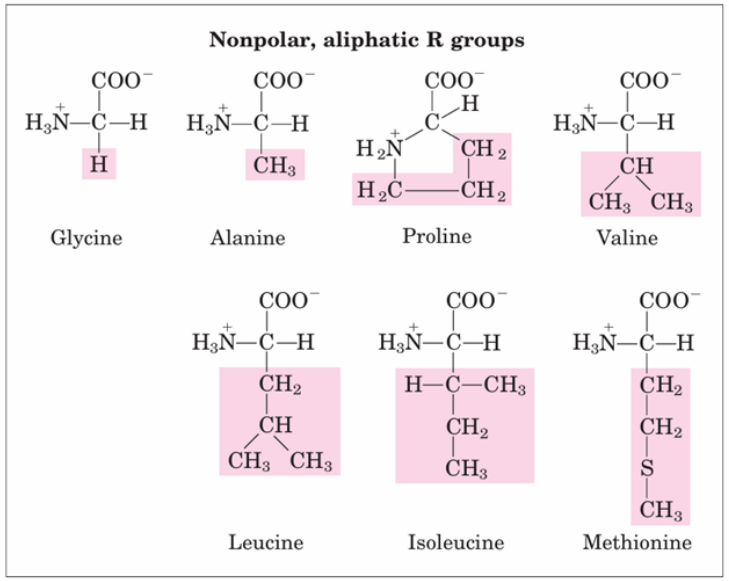
Amino acids: building blocks of proteins linked by amide bonds (peptide bonds)

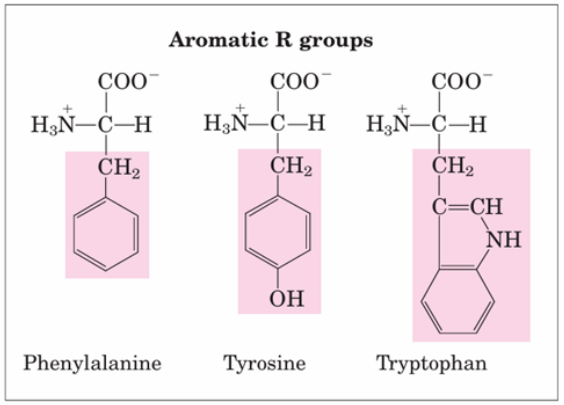


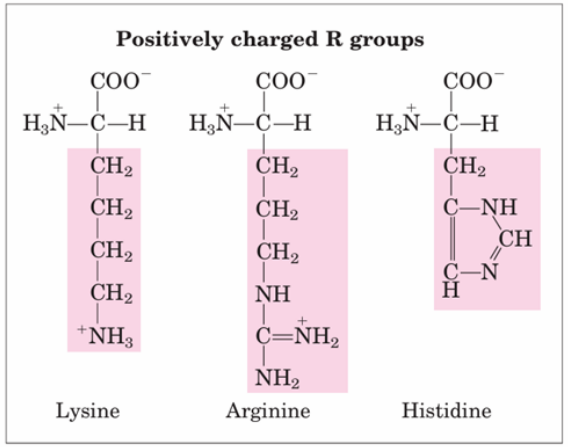


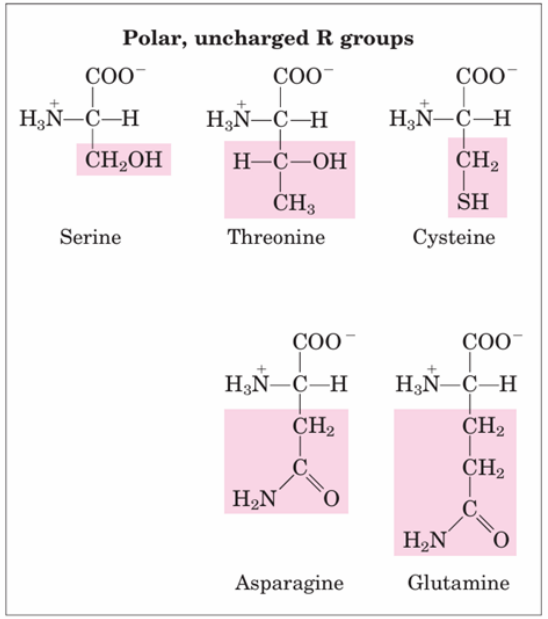
Two amino acids liked by a peptide bond (yellow)

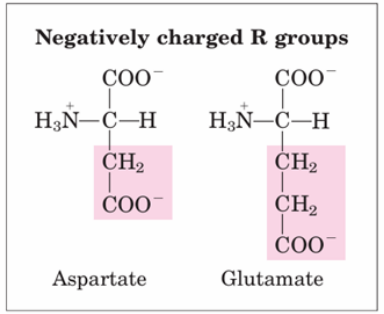
The structural formulas show the state of ionization that would predominate at pH 7.0. The shaded portions are the R groups.











Abbreviations for amino acids

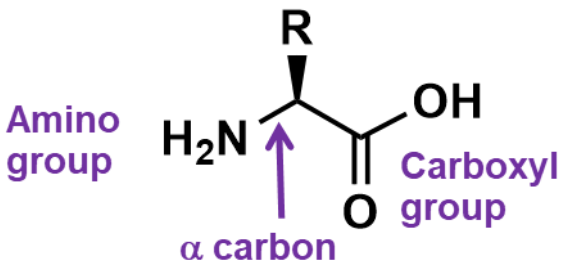
Amino acid	Three-letter abbreviation	One-letter abbreviation
Alanine	Ala	A
Arginine	Arg	R
Asparagine	Asn	N
Aspartic Acid	Asp	D
Cysteine	Cys	C
Glutamine	Gln	Q
Glutamic Acid	Glu	E
Glycine	Gly	G
Histidine	His	H
Isoleucine	Ile	I
Leucine	Leu	L
Lysine	Lys	K
Methionine	Met	M
Phenylalanine	Phe	F
Proline	Pro	P
Serine	Ser	S
Threonine	Thr	T
Tryptophan	Trp	W
Tyrosine	Tyr	Y
Valine	Val	V
Asparagine or aspartic acid	Asx	B
Glutamine or glutamic acid	Glx	Z

1 2 3 4 5 6 7

Example: Ile – Ala – His – Thr – Tyr – Gly – Pro

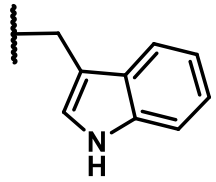
IAHTYGP

UV absorption spectra of the aromatic amino acids and bovine serum albumin

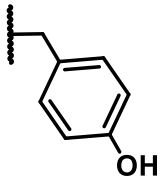


Side chain

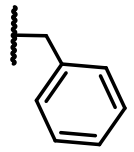
Tryptophan (Trp)

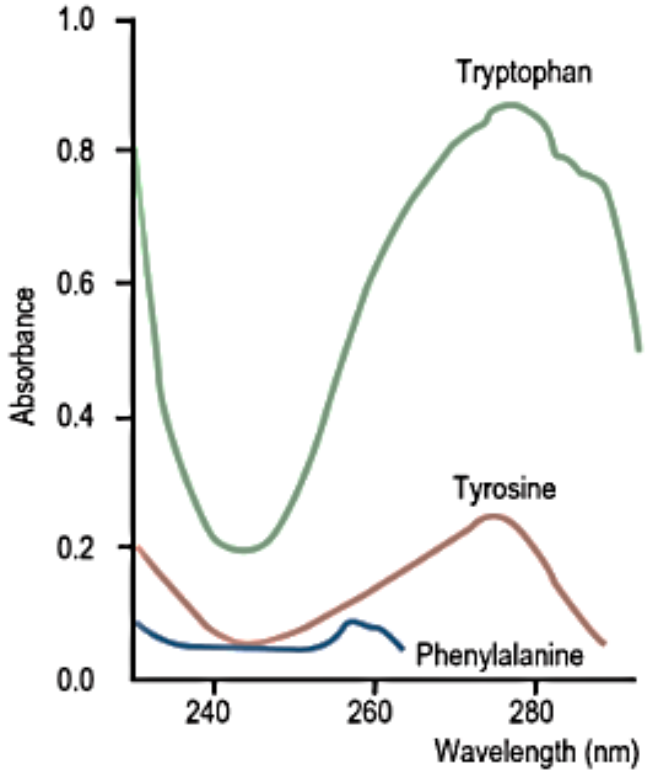


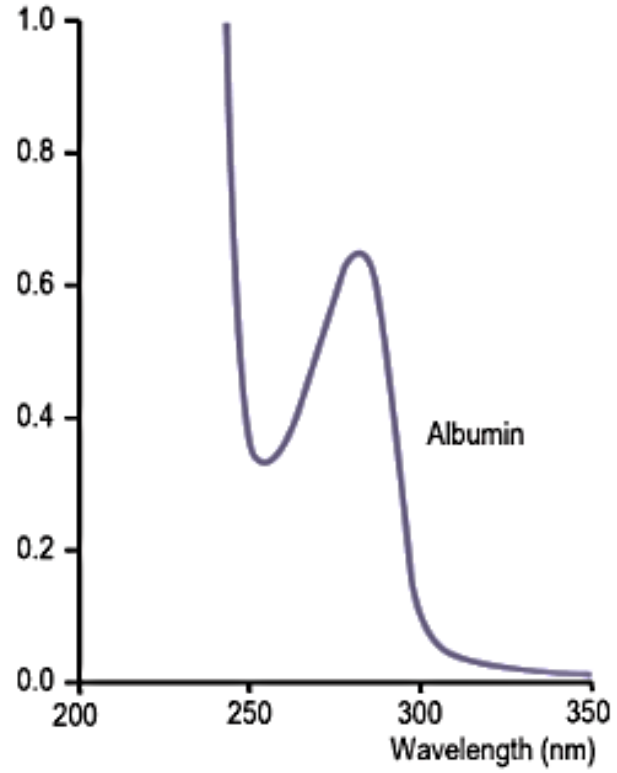
Tyrosine (Try)



Phenylalanine (Phe)



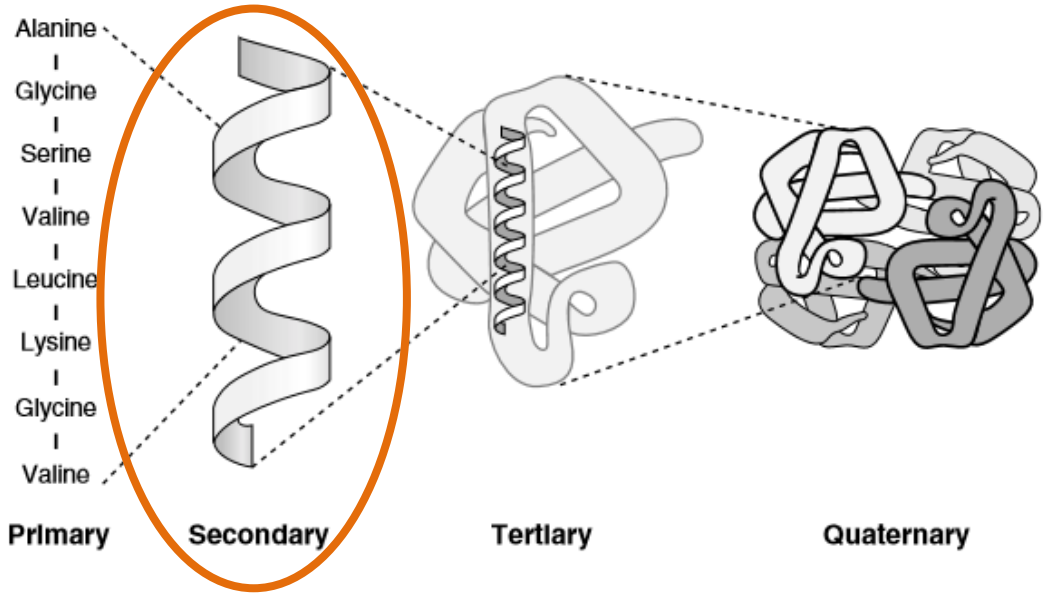


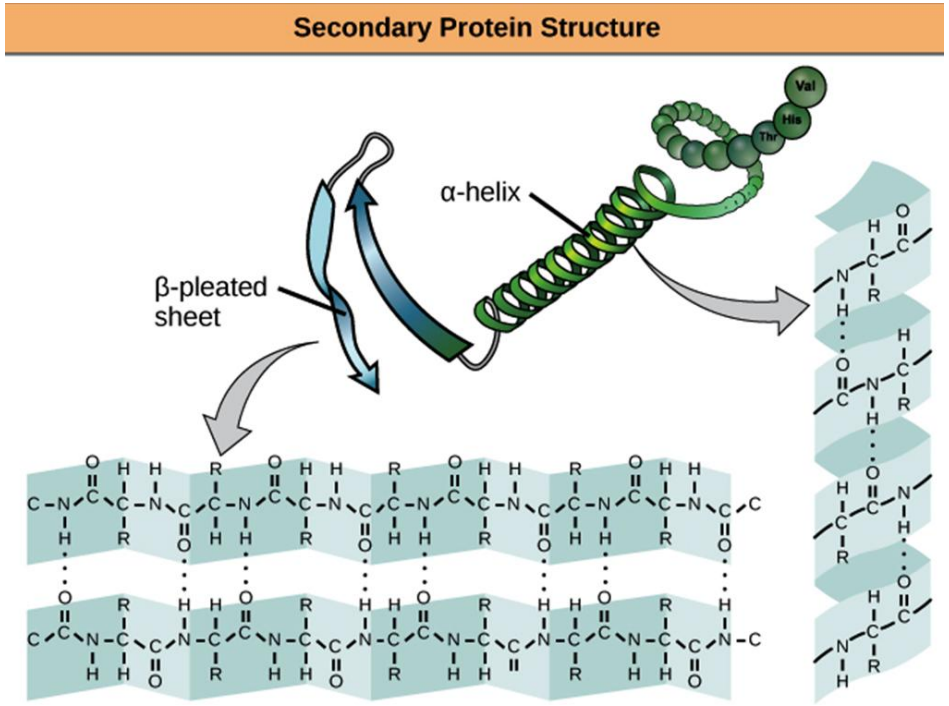


Aromatic amino acids are amino acids that have a ring structure (called an aromatic ring) in their side chain (R group)

Medical Biochemistry, 4th Edition , Ed. John Baynes, Marek Dominiczak, 2014, Elsevier limited.

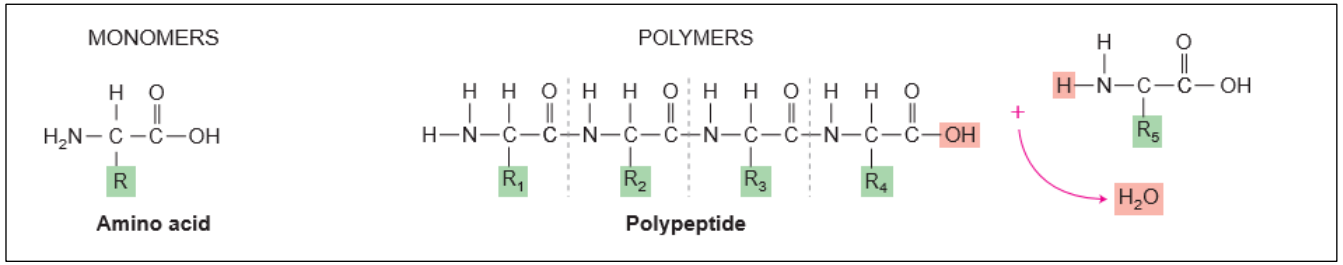
Levels of structure in a protein

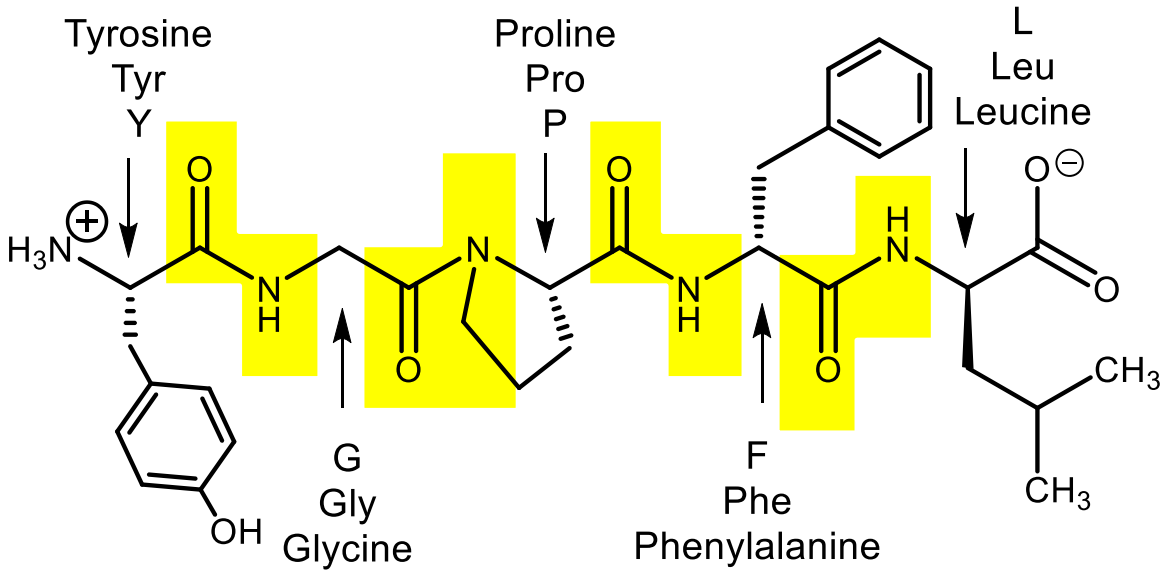




- **Primary structure**: the linear arrangement (sequence) of amino acids in a peptide chain, where each amino acid is connected by a peptide bond.
- **Secondary structure** : Local folding of the polypeptide chain into structures such as α-helices and β-sheets, stabilized by hydrogen bonds between backbone atoms.
- **Tertiary structure**: The overall three-dimensional shape of a single polypeptide chain, formed by further folding and stabilized by various non-covalent interactions between the side chains (R groups) of amino acids.
- **Quaternary**: The specific arrangement and interaction of multiple polypeptide subunits in a protein composed of more than one chain, stabilized by non-covalent interactions.

Primary structures

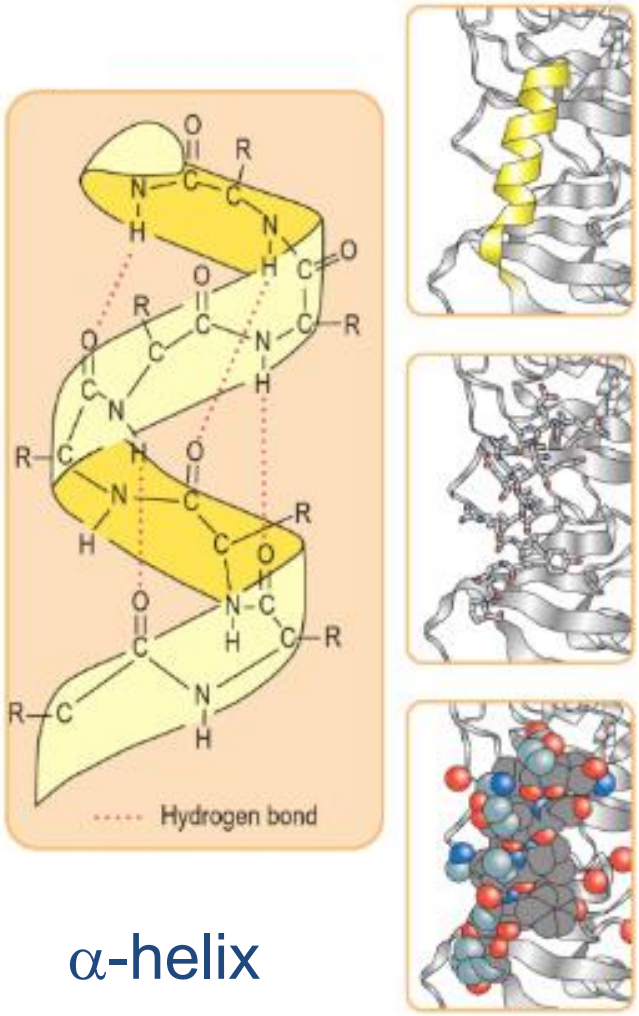




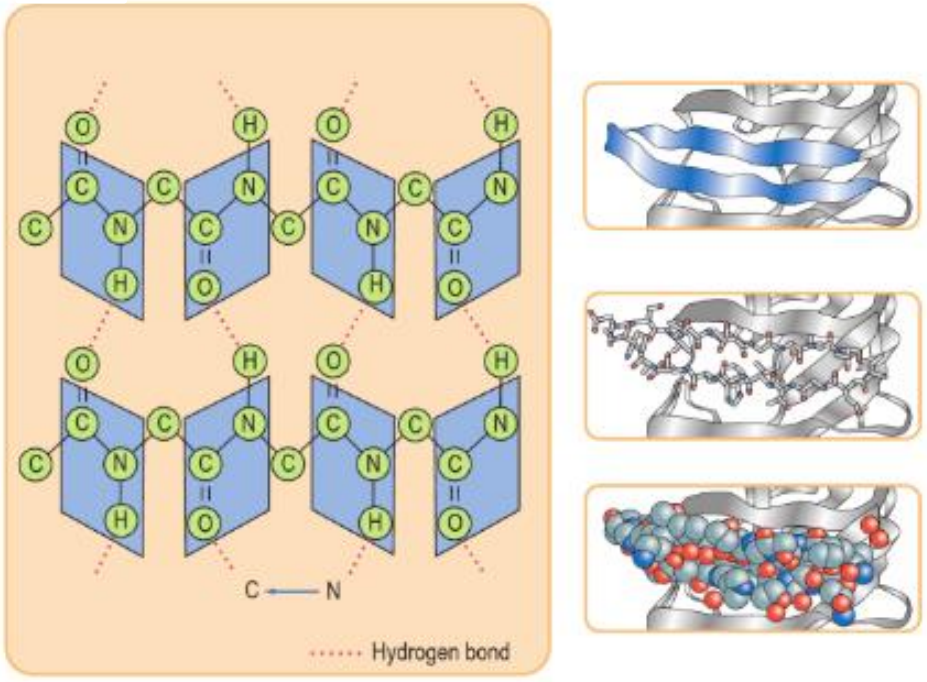
N-terminal residue: Tyr — Gly — Pro — Phe — Leu : C-terminal residue

Secondary structures

"the spatial arrangement of the primary structure determined by H-bonding"



α-helix



β-pleated sheet

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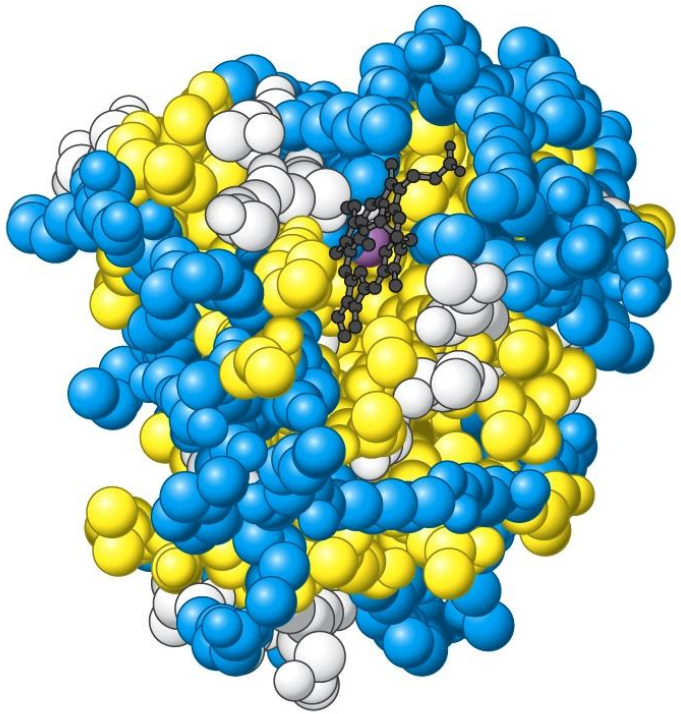
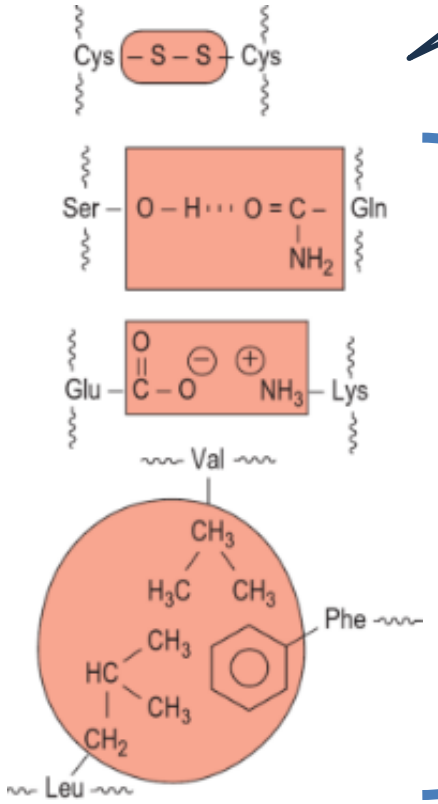
Tertiary structures



Myoglobin; **yellow: hydrophobic AAs**, blue: charged AAs

- Specifies the spatial arrangement of the secondary structure.
- Is determined by multiple interactions include:
  - Disulfide bonds
  - H-bonds
  - Ionic bonds
  - Hydrophobic interactions



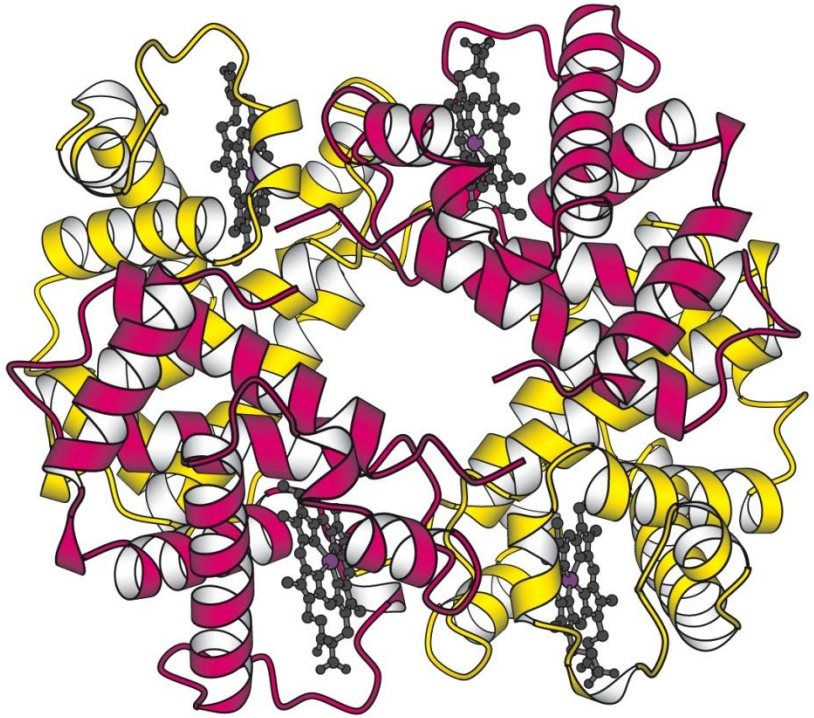
Peptide bonds (covalent bonds) & H-bonds (non-covalent)

Covalent interactions

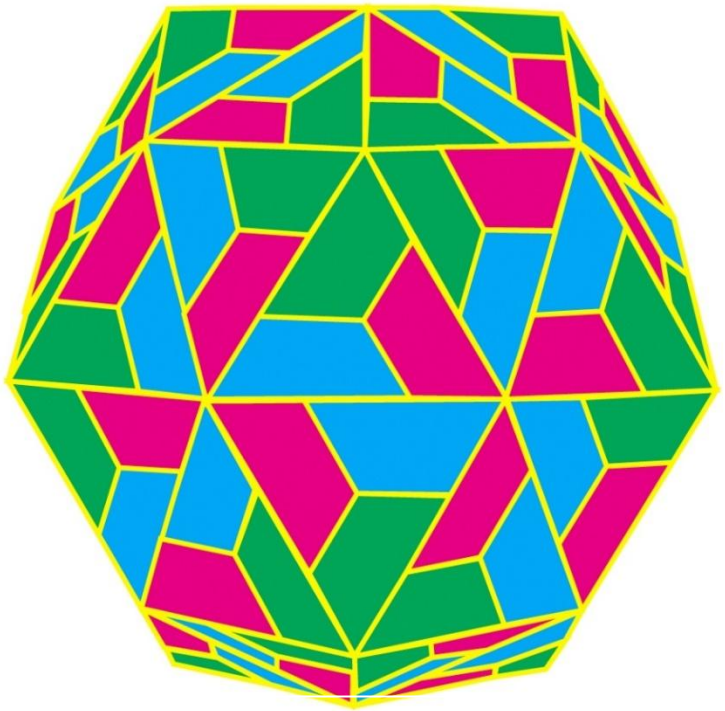
Non-Covalent interactions

Quaternary structures

Several subunits held together by non-covalent bonds

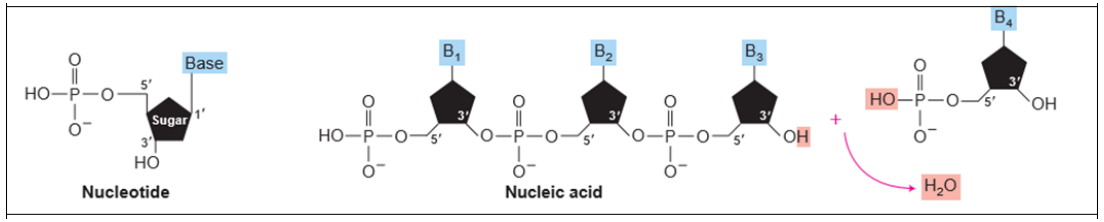


$\alpha_2\beta_2$ **tetramer of Hb**

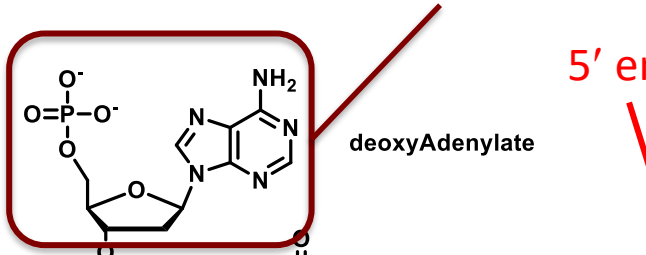


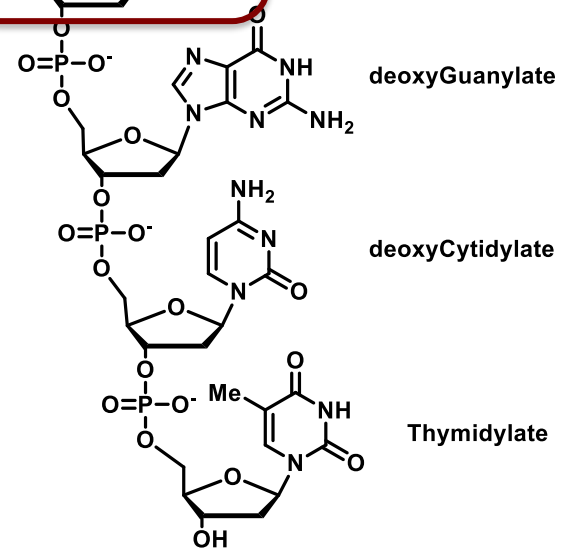
60 copies of each 4 subunits of rhinovirus coat proteins

Nucleic acids



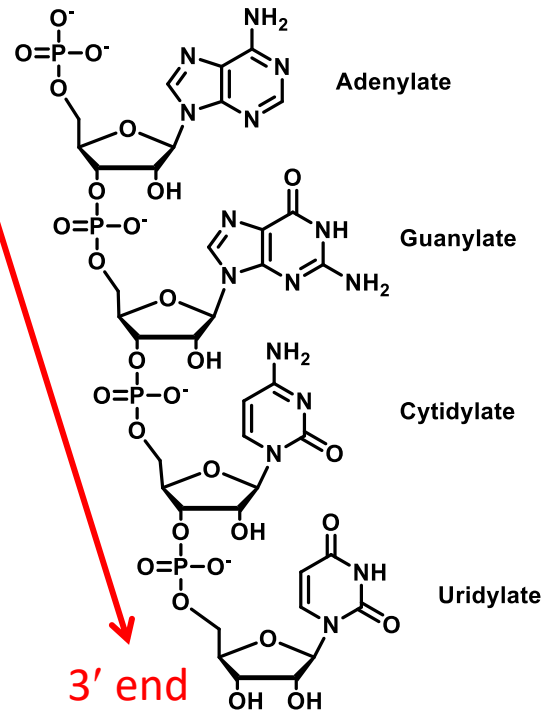
Nucleotide





DeoxyriboNucleic Acid DNA

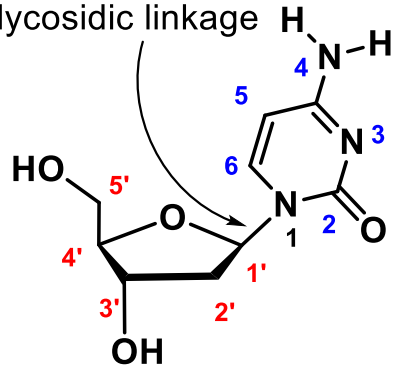
5′ end



3′ end

RiboNucleic Acid RNA

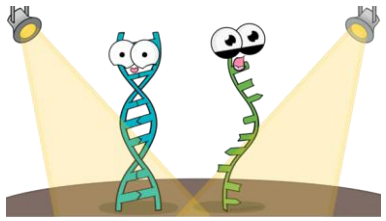
β-glycosidic linkage



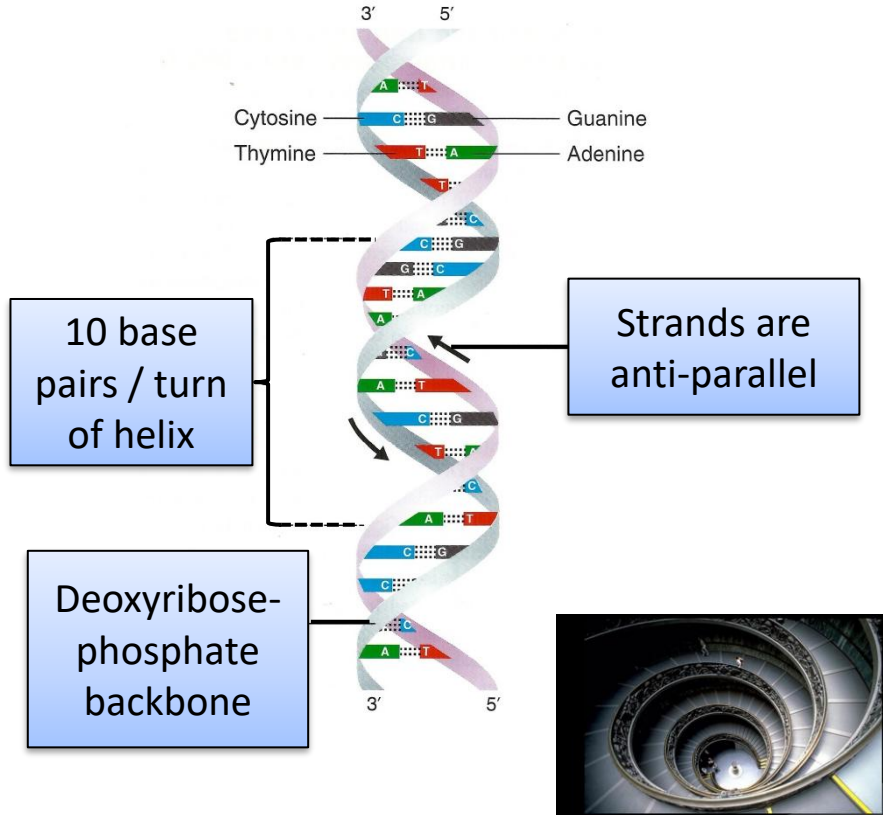
Nucleoside

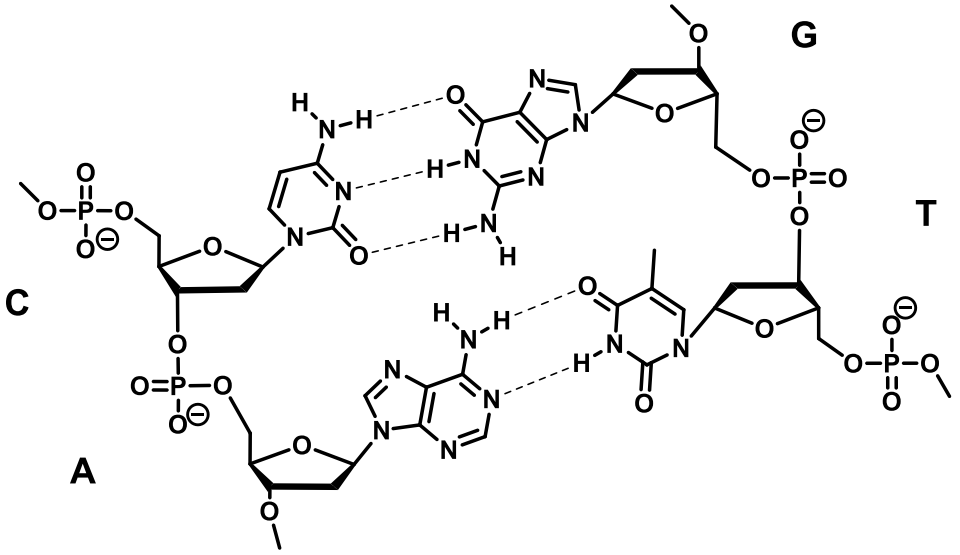
Functions:
Genetic information storage (DNA) and transmission (RNA)

- Nucleic acids: DNA and RNA
- A nucleotide comprises three parts: i) ribose or deoxyribose; ii) a nitrogenous bases/nucleobase (purines or pyrimidines) and a phosphate group
- DNA has deoxyribose and adenine (A), guanine (G), cytosine (C) and thymine (T)
- RNA contains ribose and A, G, C and uracil (U)
- Positions on the base are numbered 1, 2, 3, etc; on the sugar: 1', 2', 3', 4', 5'.



Watson-Crick base pairs and double helix

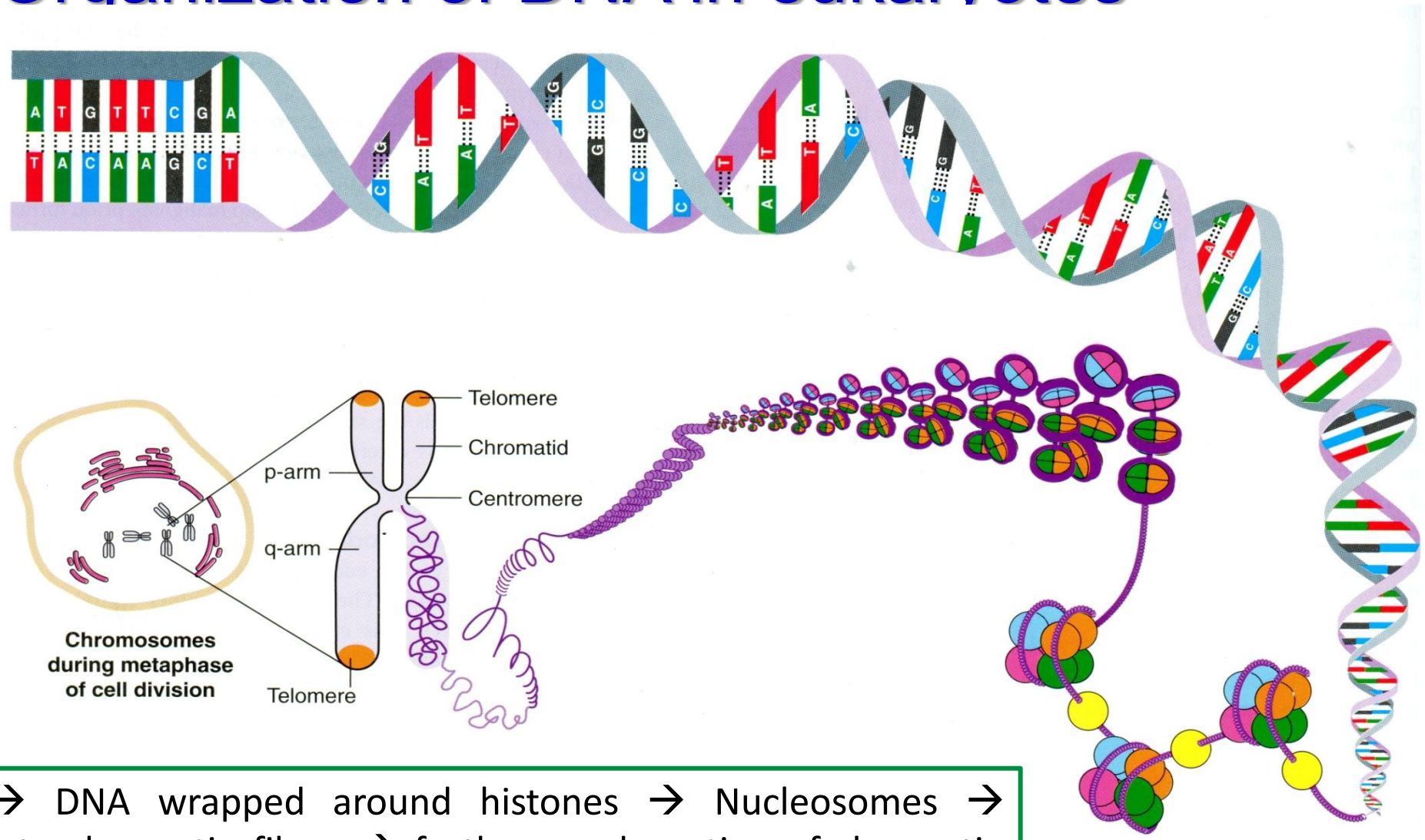




- The two strands in DNA, running anti-parallel, are held together by H-bonds between complementary bases (A=T, C ≡ G)
- High G-C content makes the DNA more stable ➡ T_m (Melting temperature)
- Hydrophobic interactions and Van der Waals interactions from stacked arrangement of base pairs

Medical biochemistry at a glance, 3rd ed., J.G. Salway, John Wiley & Sons, Ltd., 2012

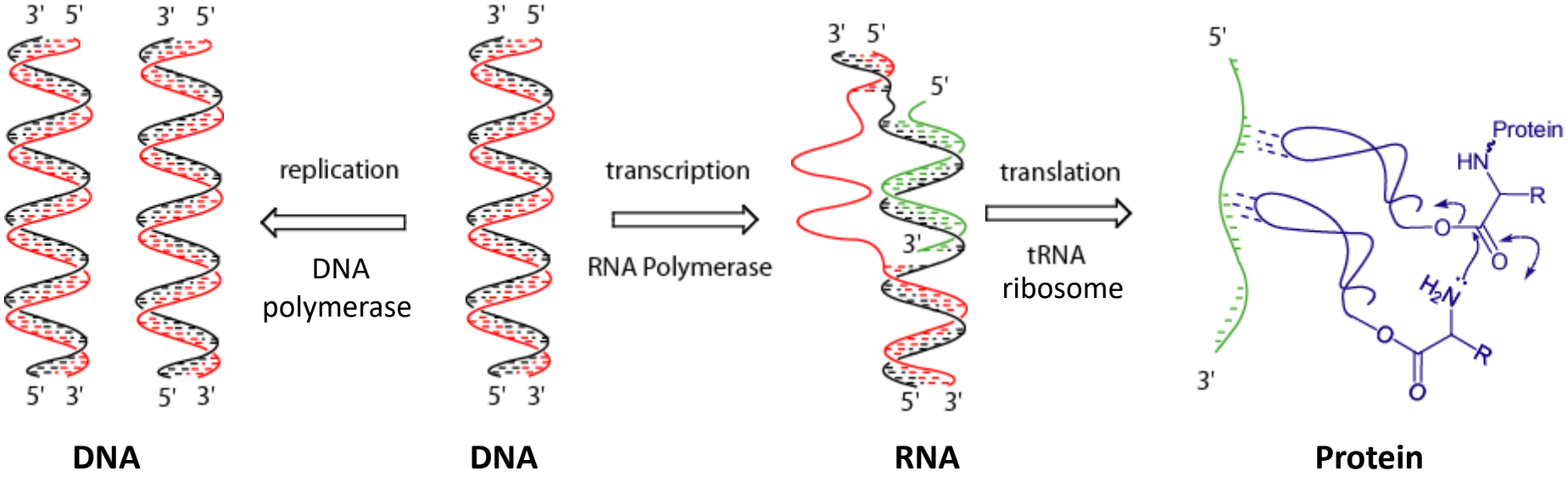
Organization of DNA in eukaryotes



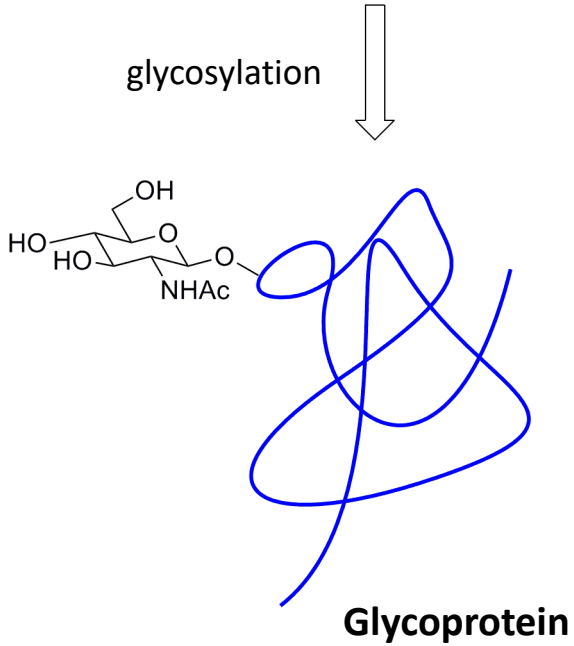
DNA double helix → DNA wrapped around histones → Nucleosomes → Nucleosomes coiled into chromatin fibers → further condensation of chromatin → Chromosome

Medical biochemistry at a glance, 3rd ed., J.G. Salway, John Wiley & Sons, Ltd., 2012

Central dogma of molecular biology

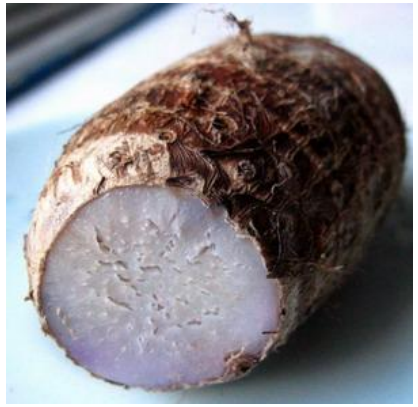


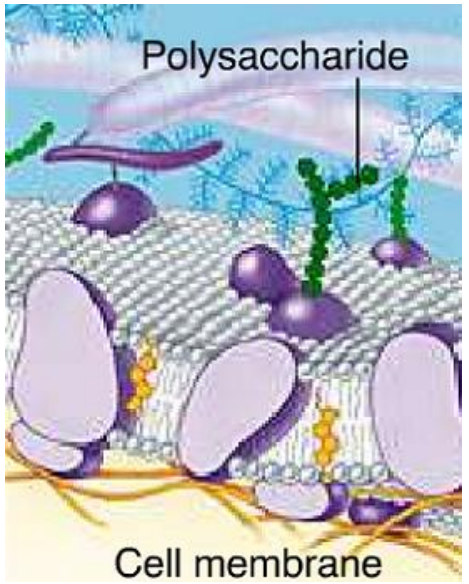
- Describes the flow of genetic information **from DNA to proteins**
- DNA is transcribed in the nucleus to make a complementary RNA strand
- RNA is exported from the nucleus into the cytoplasm where it is translated to make a protein.
- The protein may then be modified further, for example by glycosylation (attaching sugars) to give a glycoprotein.
- DNA is used for **information storage – carries the genetic information**
- RNA, Proteins and Glycoproteins are used for **information transfer and catalysis**

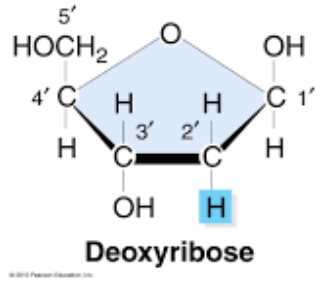


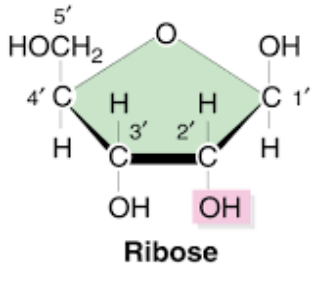
Glycoprotein

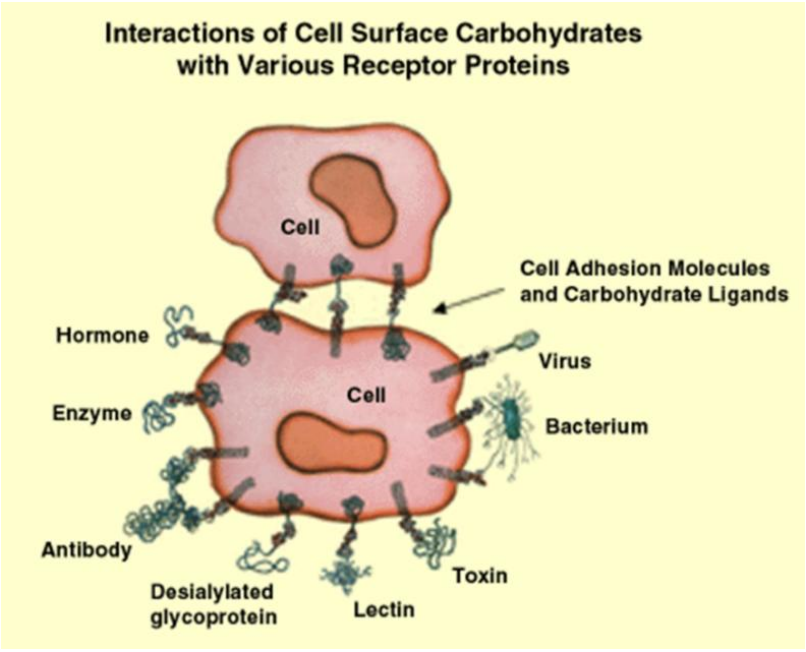
Carbohydrates

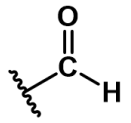




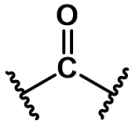








Aldehyde



Ketone

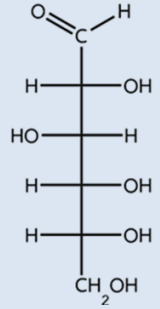
—OH

Alcohol
Hydroxyl group

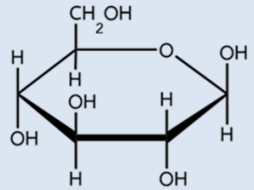
Definition: Polyhydroxy aldehydes or Polyhydroxy ketones

Carbohydrates

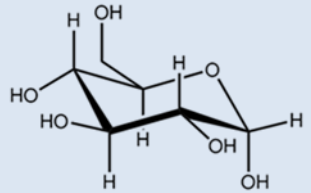
Structures



Fischer projection



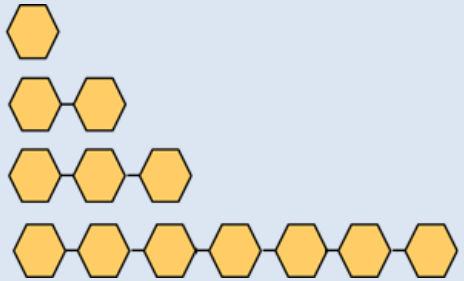
Haworth projection



Conformation

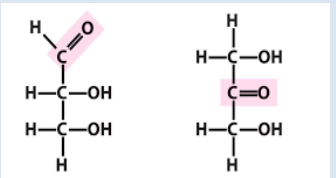
Number of sugar units

- Monosaccharide
- Disaccharide
- Oligosaccharide
- Polysaccharide



(homopolysaccharide/heteropolysaccharide)

Functional groups



Aldehyde — An aldose

Ketone — A ketose

Number of C atoms

Triose – 3 C

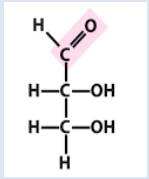
Tetrose – 4 C

Pentose – 5 C

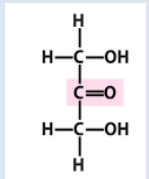
Hexose – 6 C

Heptose – 7 C

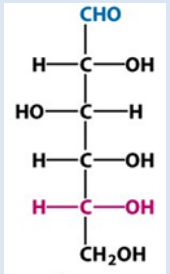
Both functional groups and number of C atoms



Triose
Aldose
Aldotriose



Triose
Ketose
Ketotriose



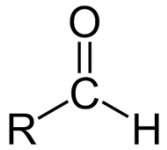
Hexose
Aldose
Aldohexose

...ose

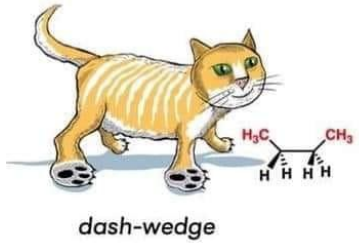
to systematically name sugars.

Monosaccharides – classified by functional groups

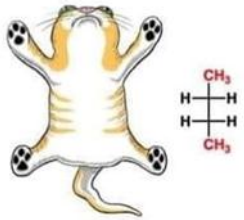
Aldoses: contain an aldehyde group (–CHO) at the end of the molecule.



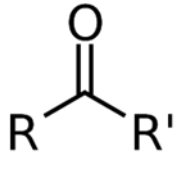
Aldehyde



dash-wedge



Fischer



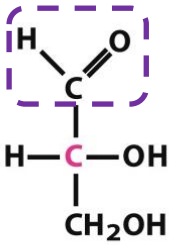
Ketone

Ketoses: contain a **ketone group** (C=O) usually at the second carbon.

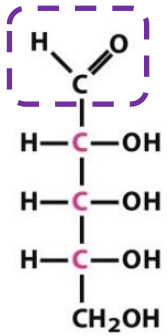
D-Aldoses

Fischer projection

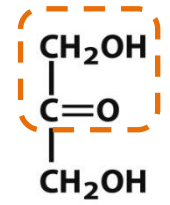
D-Ketoses



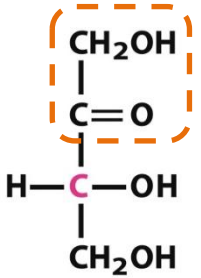
D-Glyceraldehyde



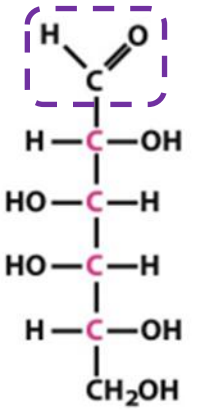
D-Ribose



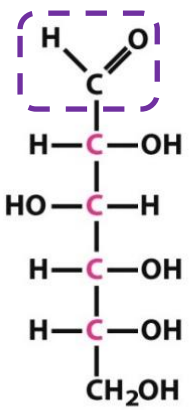
Dihydroxyacetone



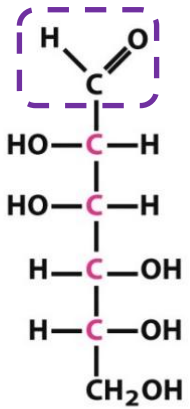
D-Erythrulose



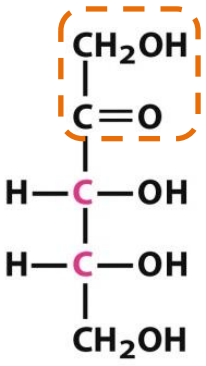
D-Galactose



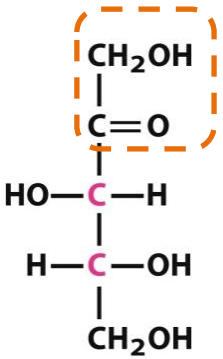
D-Glucose



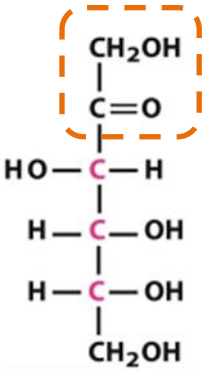
D-Mannose



D-Ribulose



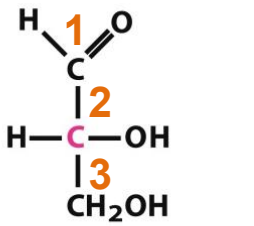
D-Xylulose



D-Fructose

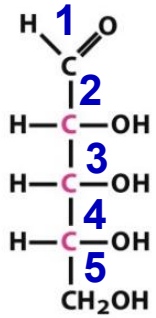
Monosaccharides – classified by number of carbons

Monosaccharides are classified based on the number of carbons in the molecule as trioses (3 C), tetroses (4 C), pentoses (5 C), and hexoses (6 C).



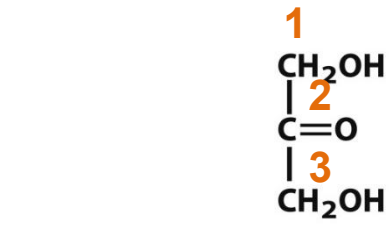
Triose

D-Glyceraldehyde



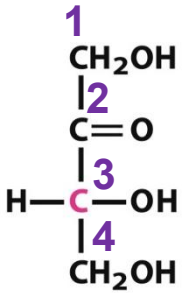
D-Ribose

Pentose



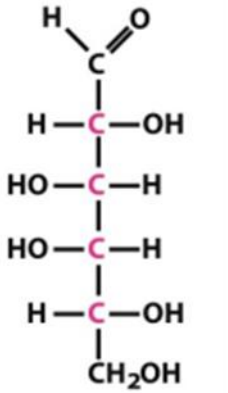
Triose

Dihydroxyacetone



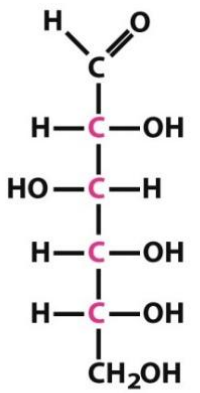
D-Erythrulose

Tetrose



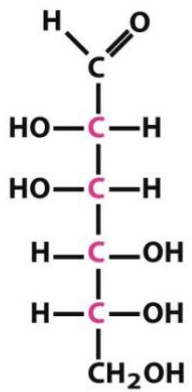
Hexose

D-Galactose



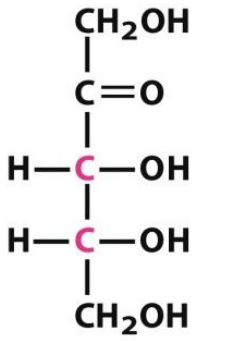
D-Glucose

Hexose



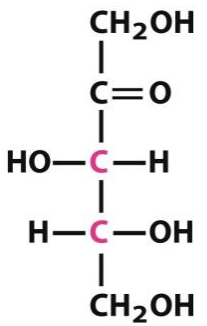
D-Mannose

Hexose



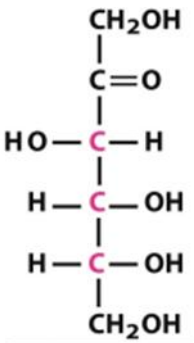
Pentose

D-Ribulose



D-Xylulose

Pentose



D-Fructose

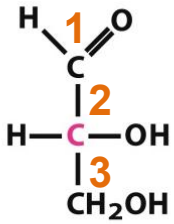
Hexose

Monosaccharides – classified by both functional groups and number of carbons

Example:

- **Glucose**: an aldohexose (6-carbon sugar with an aldehyde group)
- **Fructose**: a ketohexose (6-carbon sugar with a ketone group)

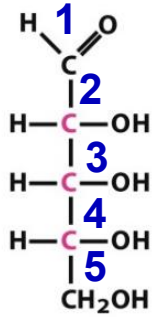
D-Aldoses



D-Glyceraldehyde

Triose

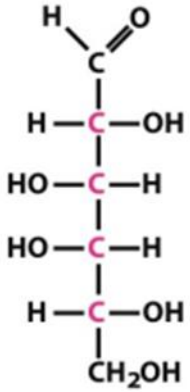
Aldotriose



D-Ribose

Pentose

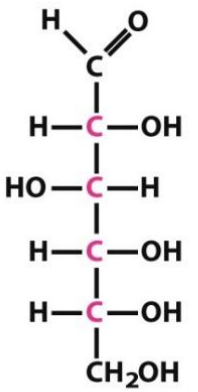
Aldopentose



D-Galactose

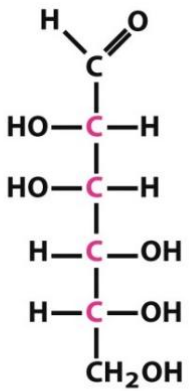
Hexose

Aldohexose



D-Glucose

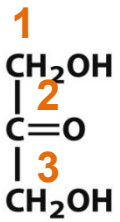
Hexose



D-Mannose

Hexose

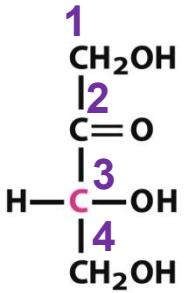
D-Ketoses



Dihydroxyacetone

Triose

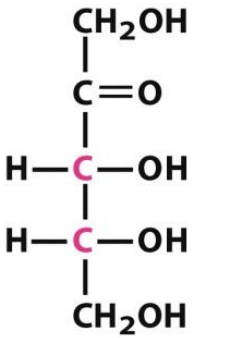
Ketotriose



D-Erythrulose

Tetrose

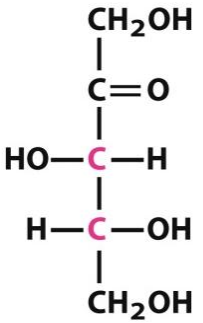
Ketotetrose



D-Ribulose

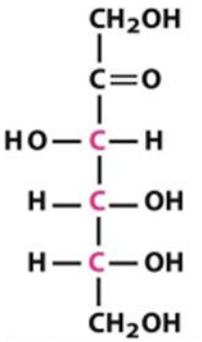
Pentose

Ketopentose



D-Xylulose

Pentose

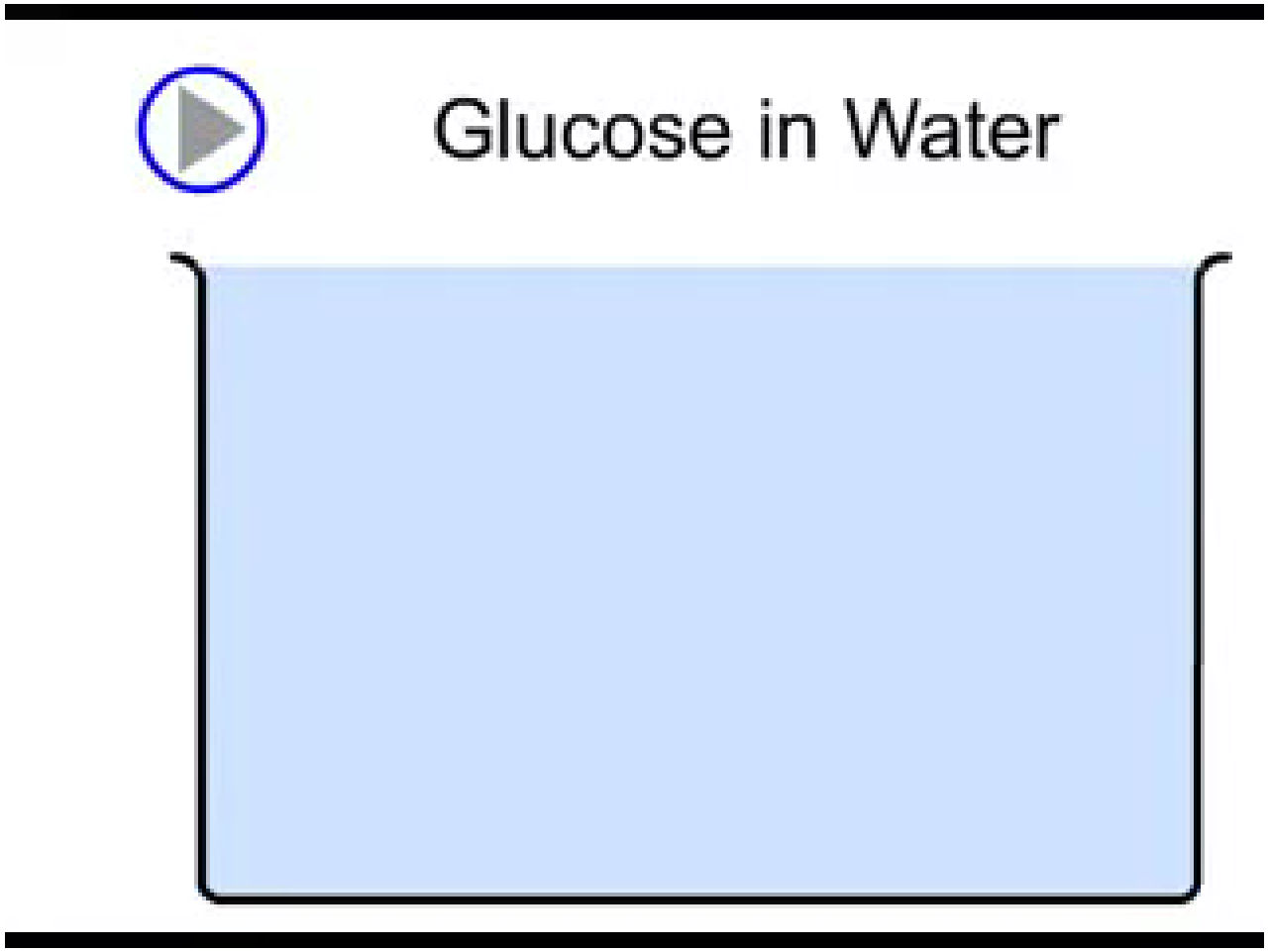


D-Fructose

Hexose

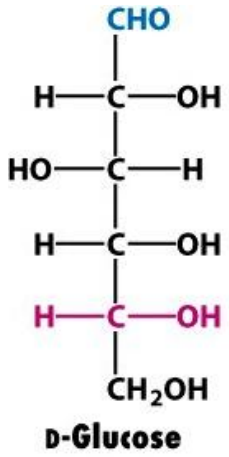
Ketohexose

Intramolecular cyclization of monosaccharides

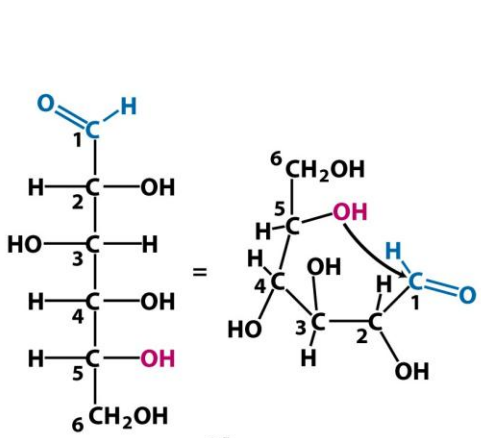


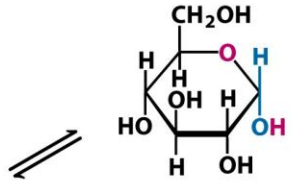
https://www.youtube.com/watch?v=5H8SKas45Rk

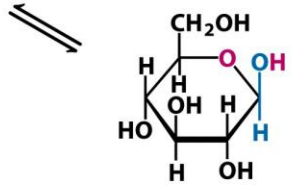
Cyclic structures of monosaccharides

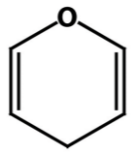


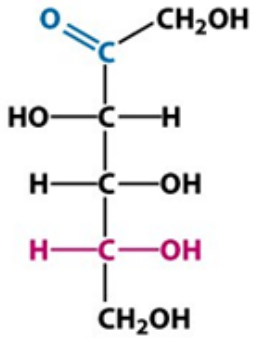
D-Glucose


D-Glucose
(open-chain form)

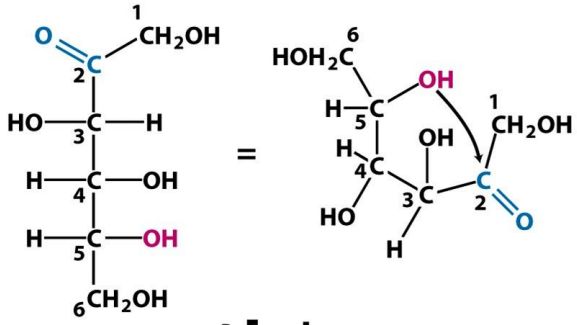

α-D-Glucopyranose

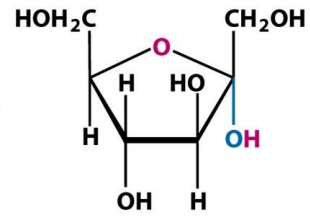

β-D-Glucopyranose


Pyran

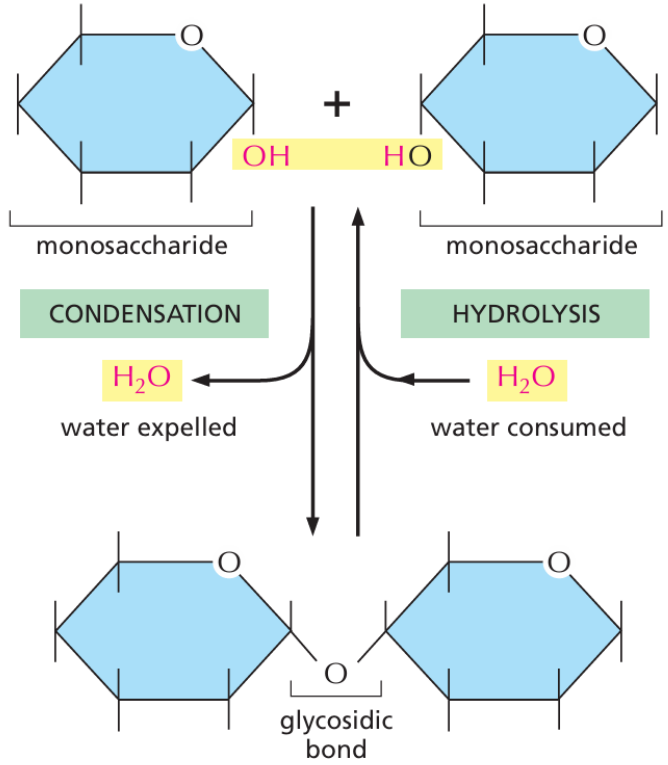


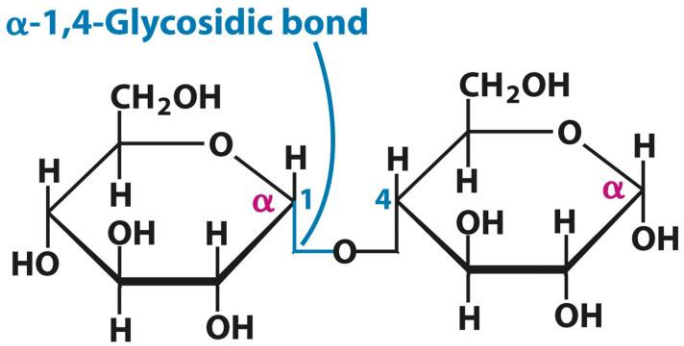
D-Fructose


D-Fructose
(open-chain form)


α-D-Fructofuranose
(a cyclic form of fructose)


Furan

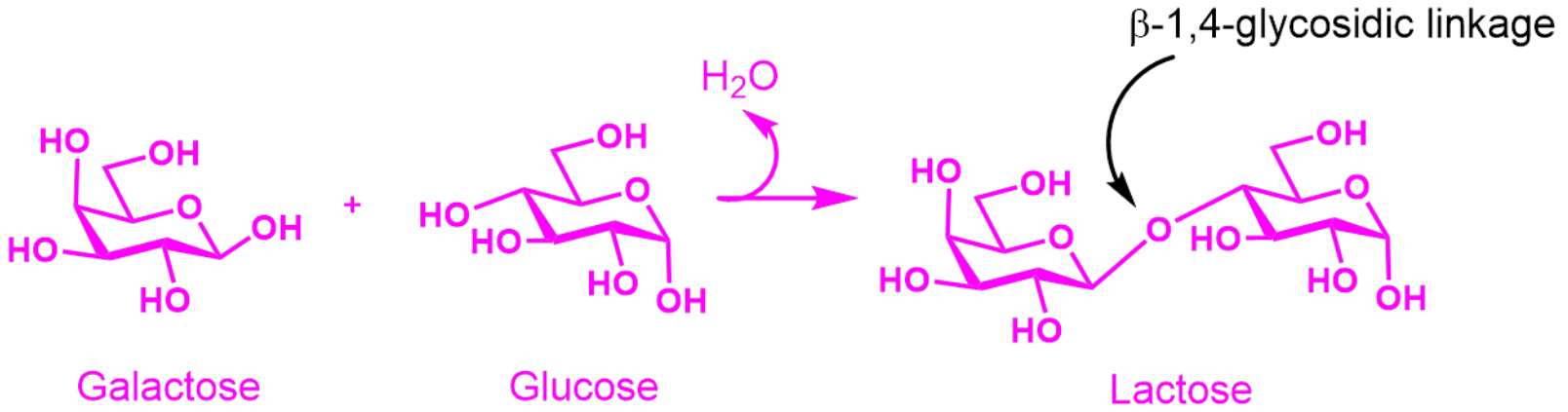




A disaccharide

Disaccharides

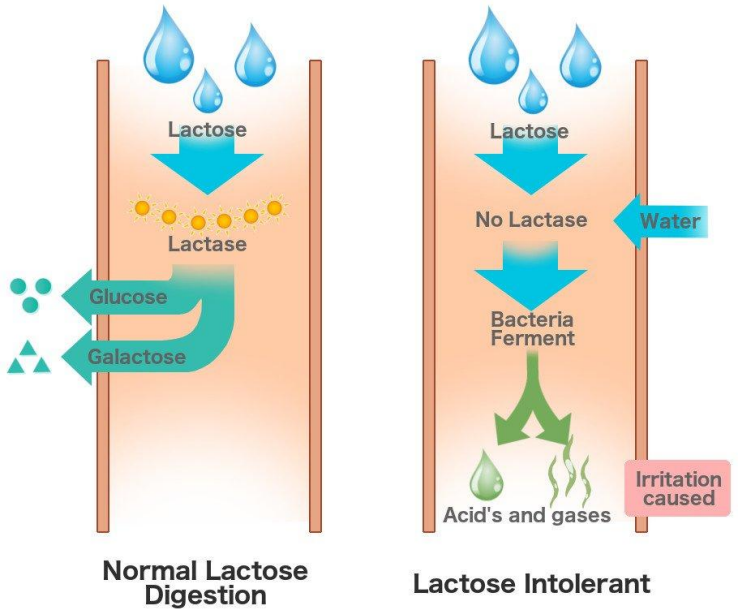
Linked by glycosidic linkages (α-, β-bonds)

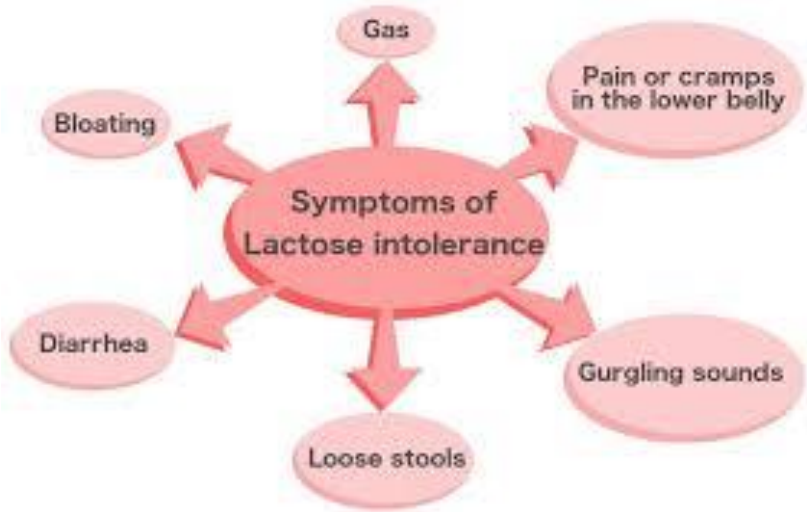


Sugar	Maltose	Sucrose	Lactose
Monosaccharide	Glucose + Glucose	Glucose + Fructose	Galactose + Glucose
Linkage	α-1,4	α-1,2	β-1,4
Source	In plant	In plant	In milk
Enzyme	Maltase	Invertase	Lactase

Lactose intolerance

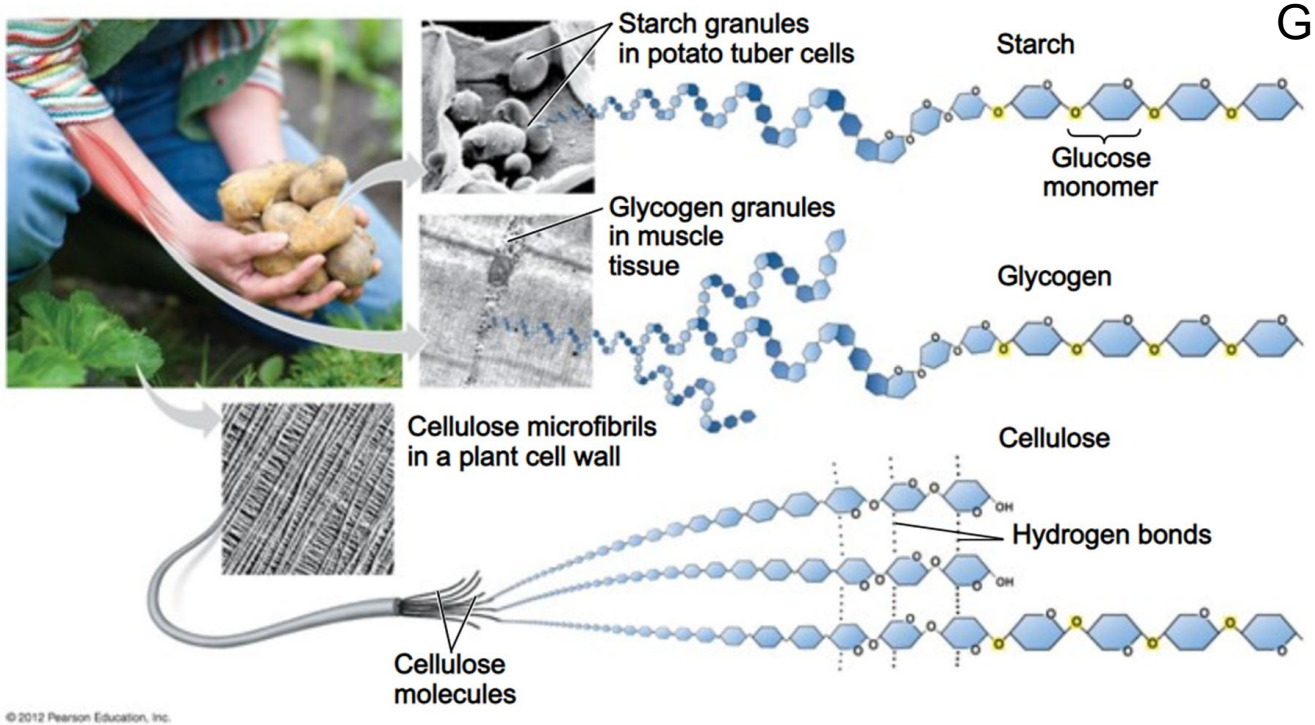
- Caused by the lack of lactase
- Leads to difficulty digesting milk sugar (lactose)
- Triggered by consuming cow's milk or dairy products
- Common in children and older adults
- **Symptoms:** Bloating, abdominal pain, gas and flatulence, nausea, diarrhea, etc.



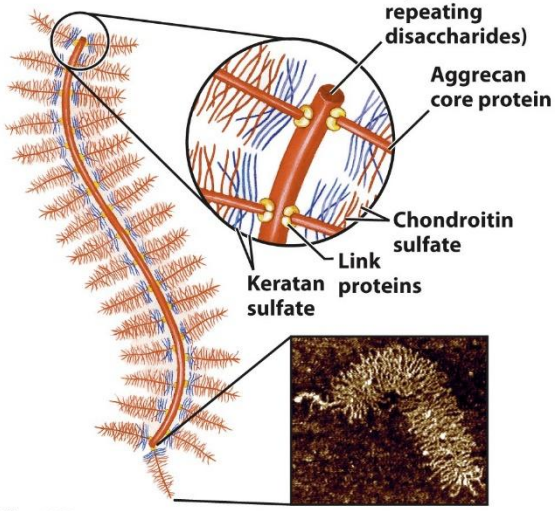


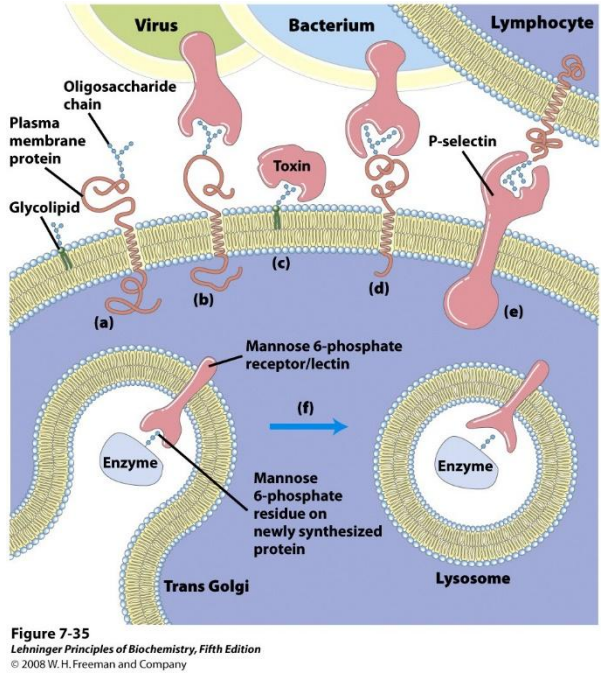
Oligosaccharides & Polysaccharides

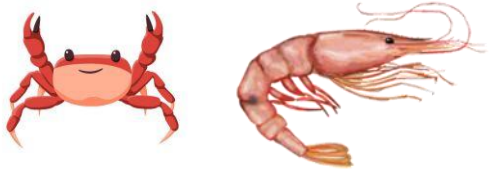
Short & long chain of sugar units

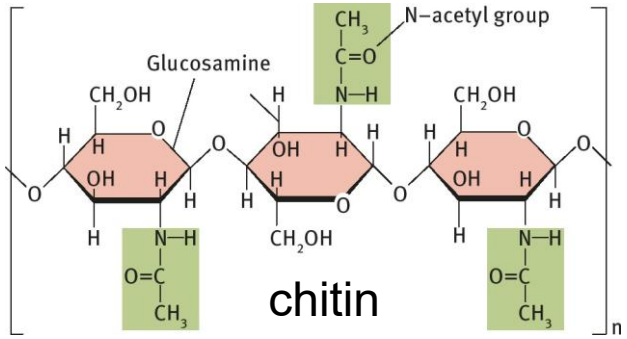


Glycosaminoglycan

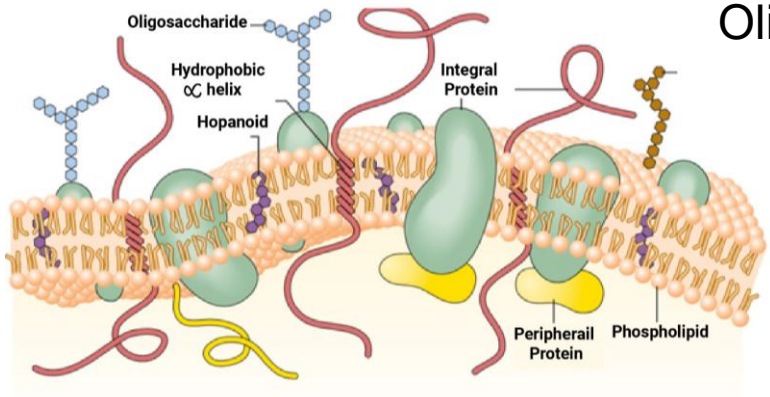








Oligosaccharide

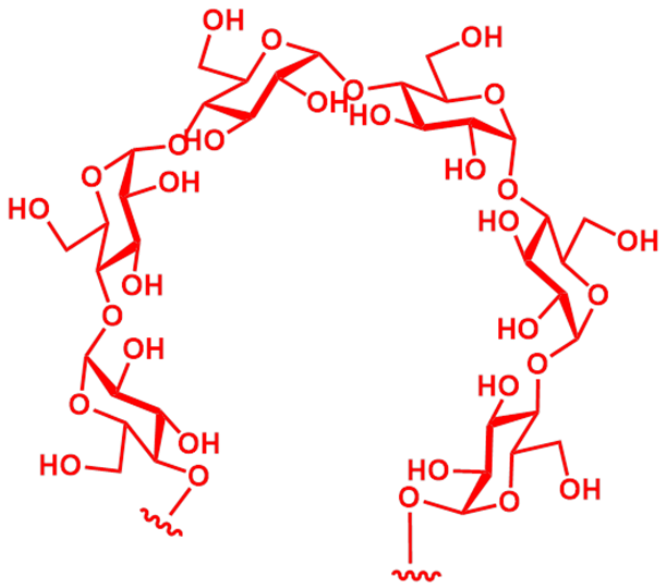


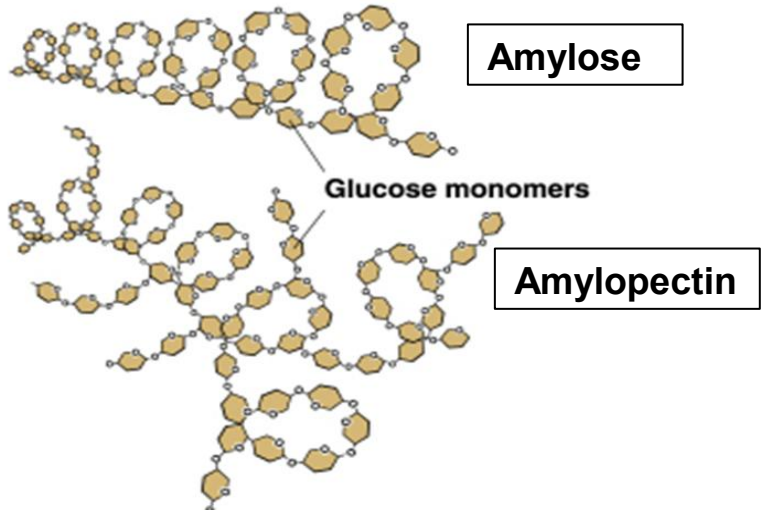
Polysaccharides: Amylose and cellulose

Anomeric configuration can have a dramatic effect on oligosaccharide properties

Amylose (in starch) and cellulose are both 1,4-linked glucose polymers

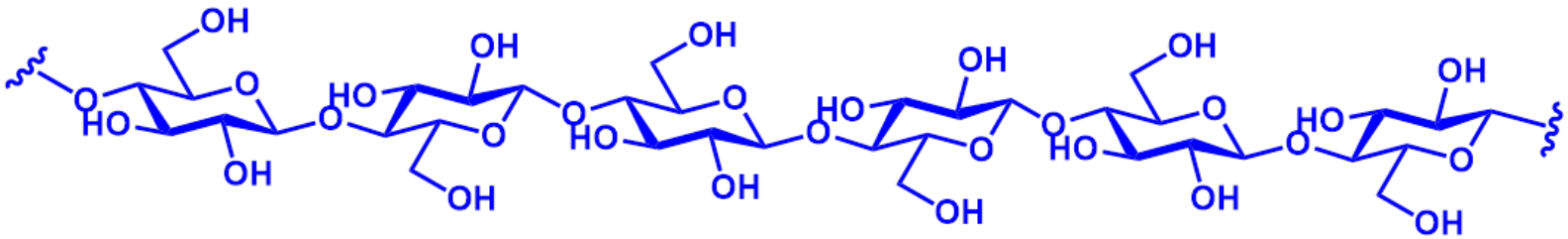
- Amylose forms soluble helices
- Cellulose has an extended conformation that H-bonds to other cellulose molecules to form insoluble fibres





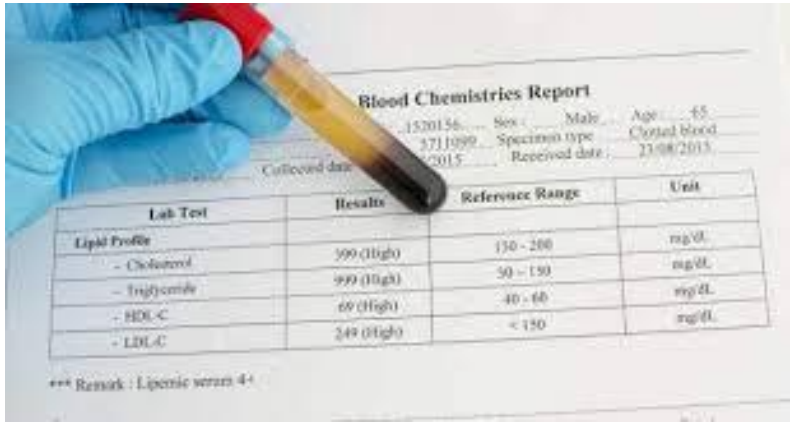
Amylose (poly-α-1,4-D-glucopyranose)

Cellulose (poly-β-1,4-D-glucopyranose)



Humans cannot digest cellulose because they lack the necessary enzymes to break down its β-1,4-glycosidic bonds.

Lipids

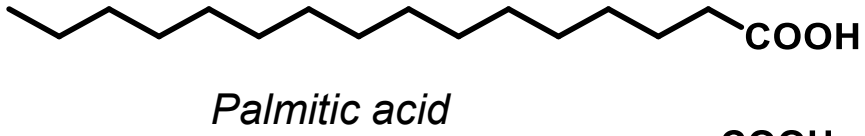

Blood Chemistries Report
Lab Test
Results
Reference Range
Unit
Lipid Profile
- Cholesterol
- Triglyceride
- HDL-C
- LDL-C
*** Remark : Lipemic serum 4+


CHOLESTEROL
Level
NORMAL
HIGH
LOW
ALARMING

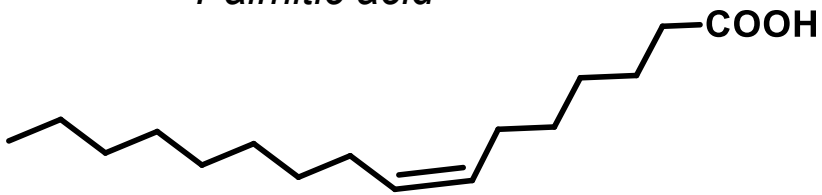

LDL
HDL

Lipids

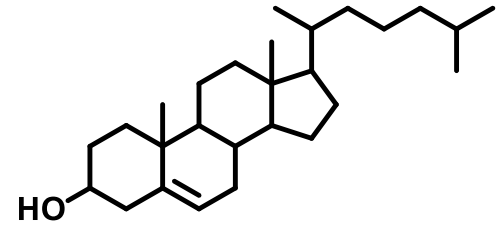
- Lipids are fatty acids (FAs), waxy, or oily organic substances.
- Common types: fats, phospholipids, waxes, and steroids.
- Lipids are found primarily in three components in the body:
  - Plasma
  - Adipose tissues
  - Biological membranes



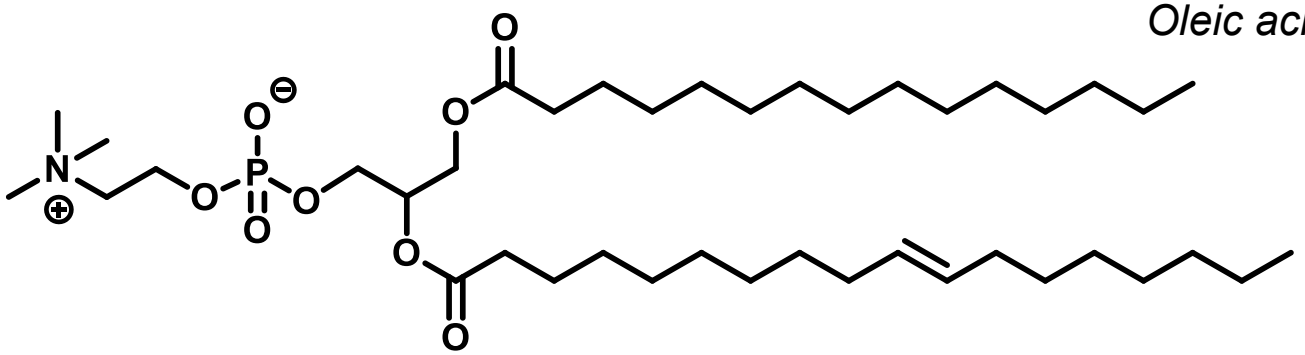
Palmitic acid



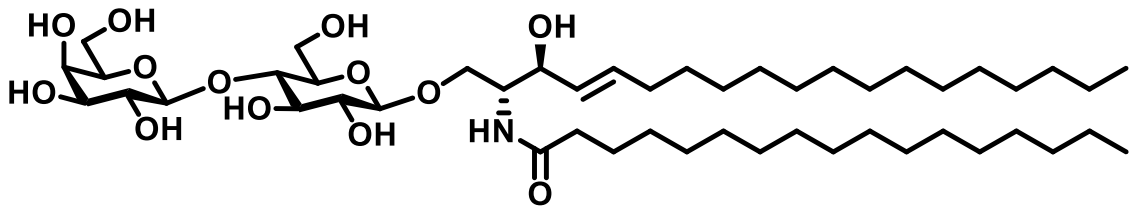
Oleic acid



Cholesterol



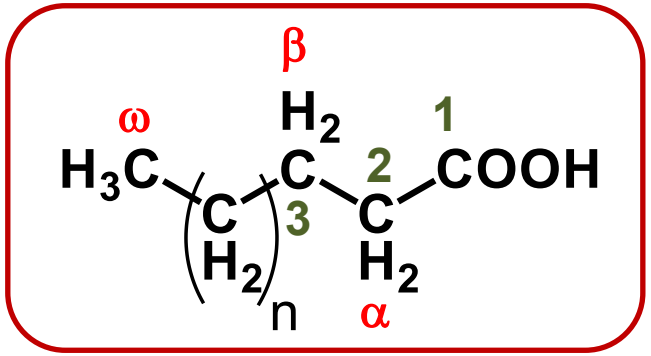
Phosphatidylcholine



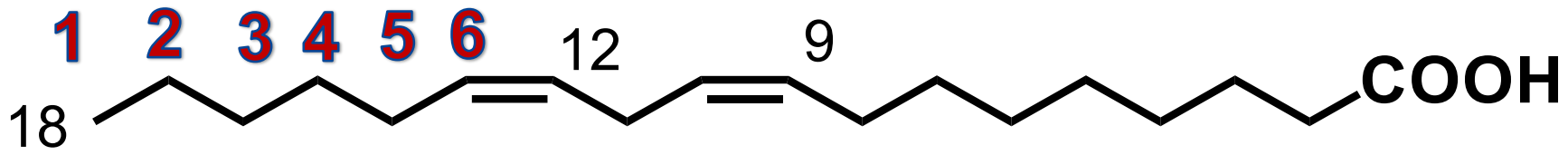
Glycosphingolipid

ω-3 & ω-6 Fatty acids

The double-bonded carbon atom counted from the methyl terminal end of chain

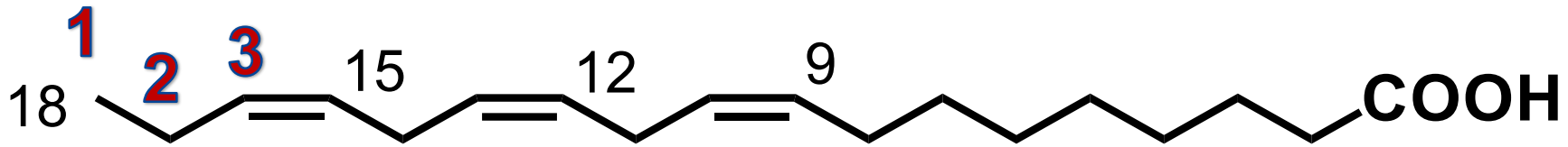


ω-6



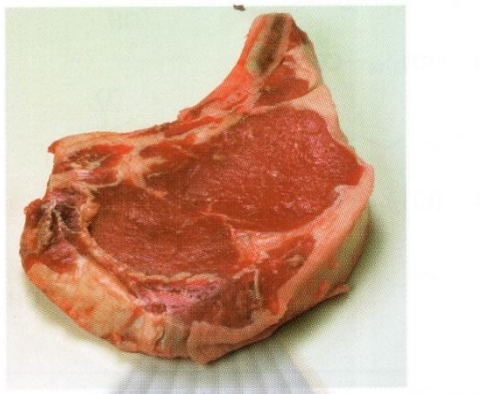
Linoleic acid

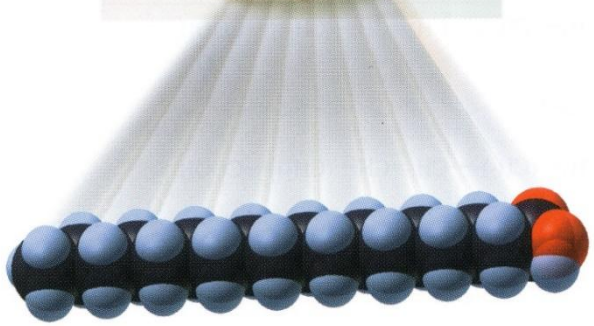
ω-3



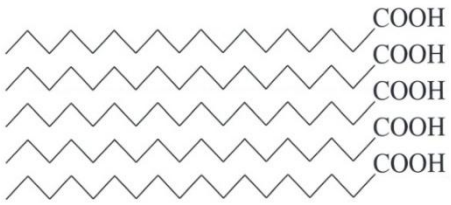
Linolenic acid

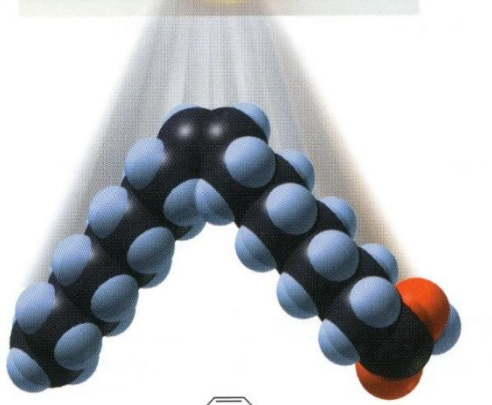
Melting points of some fatty acids



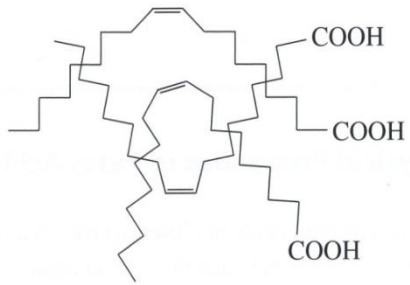


Stearic acid, mp 69°C





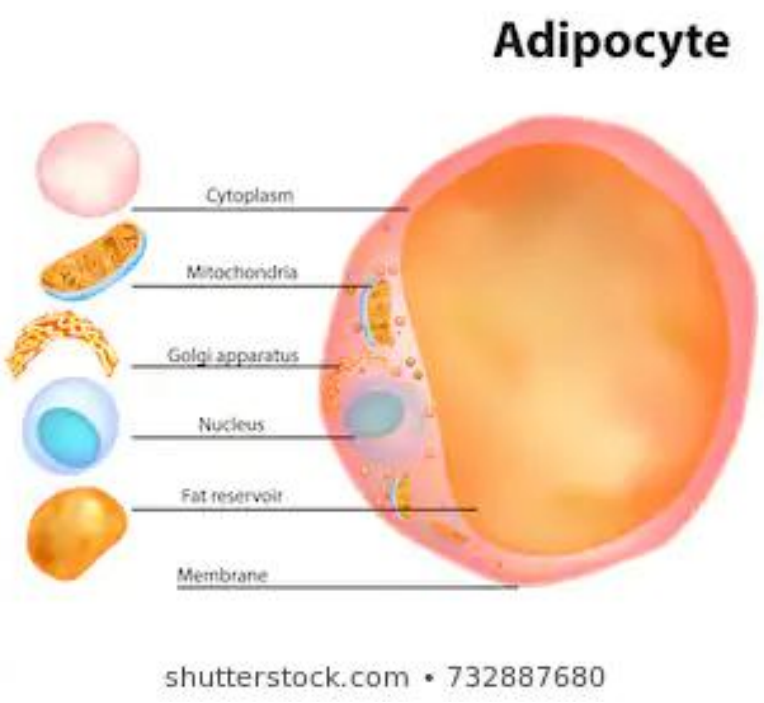
Oleic acid, mp 13°C

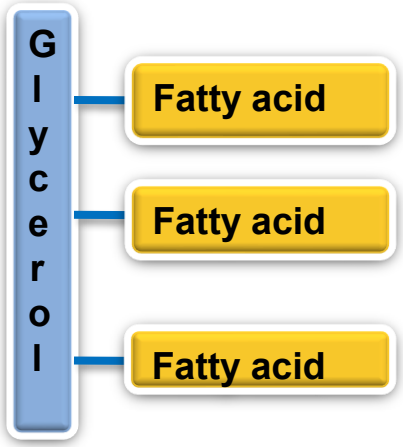


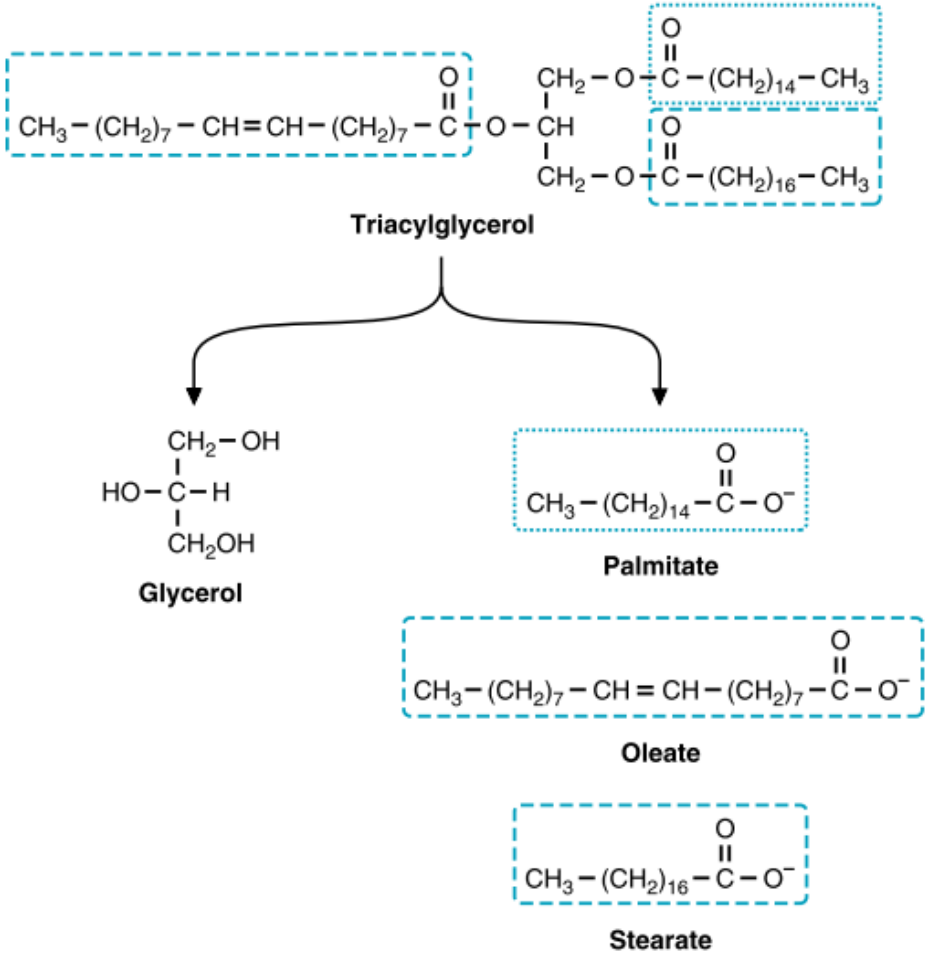
Why does the cis-double bond lower the melting point of unsaturated fatty acids?

The *cis*-double bond creates a kink in the fatty acid chain, preventing tight packing. This weakens intermolecular forces, resulting in a lower melting point.

Triacylglycerol or triglycerides



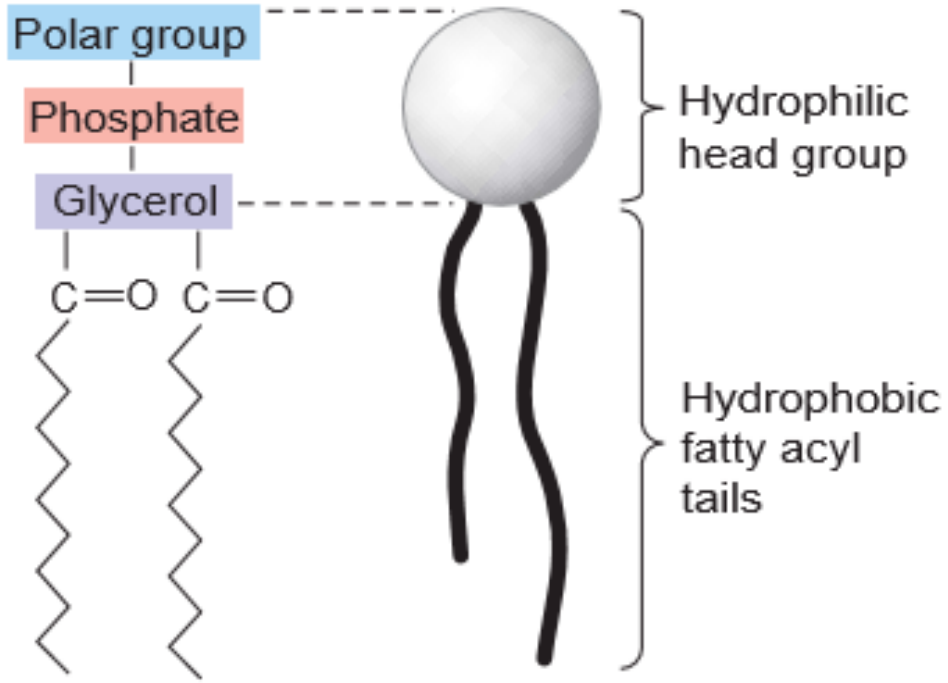




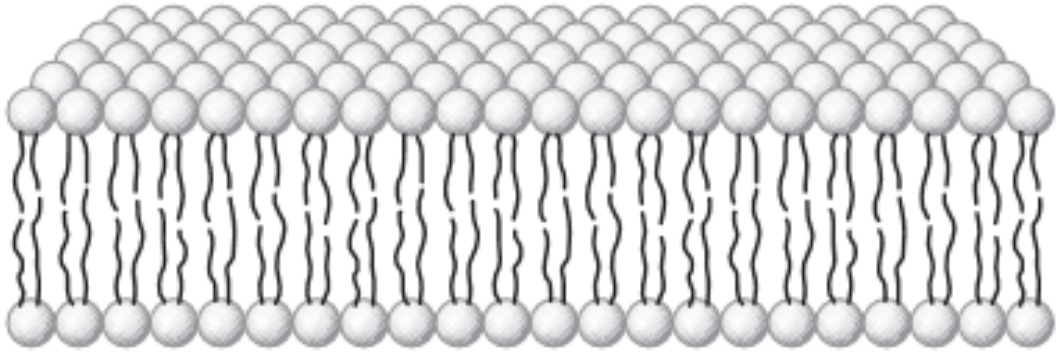
- are the main storage forms of fatty acids
- 3 fatty acids + 1 glycerol
- rarely contain the same fatty acid at all three positions and are therefore called mixed triacylglycerols

Phospholipids

"the main lipid constituents of biological membranes"

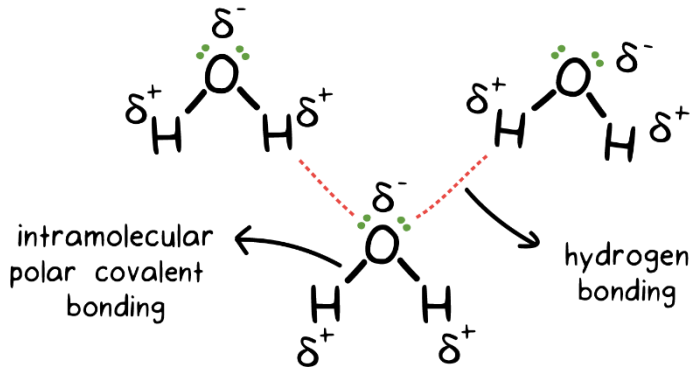


Glycerophospholipid



Phospholipid bilayer

Chemical bonding

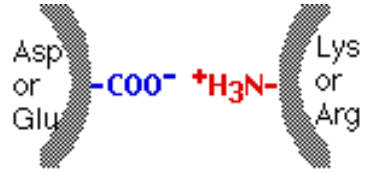


- Covalent bonds:
  - The strongest types of bonds
  - Formed by sharing electrons between adjacent atoms (ex. C-C, H-O, S-S, peptide bonds, glycosidic bonds)

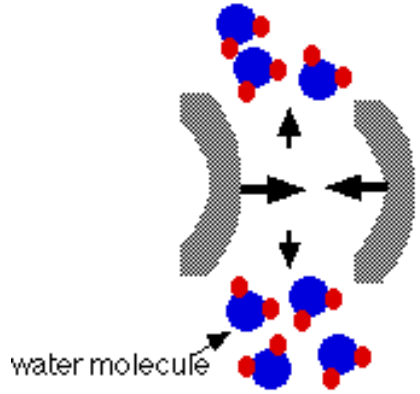
- Non-covalent bonds:
  - Electrostatic interactions

  (Charge-charge/Ionic interactions)
  - Hydrogen bonding
  - Van der Waals forces
  - Hydrophobic interactions

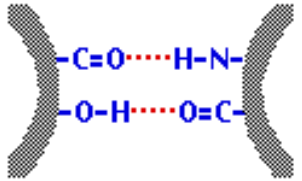
} Weak



Ionic Interactions

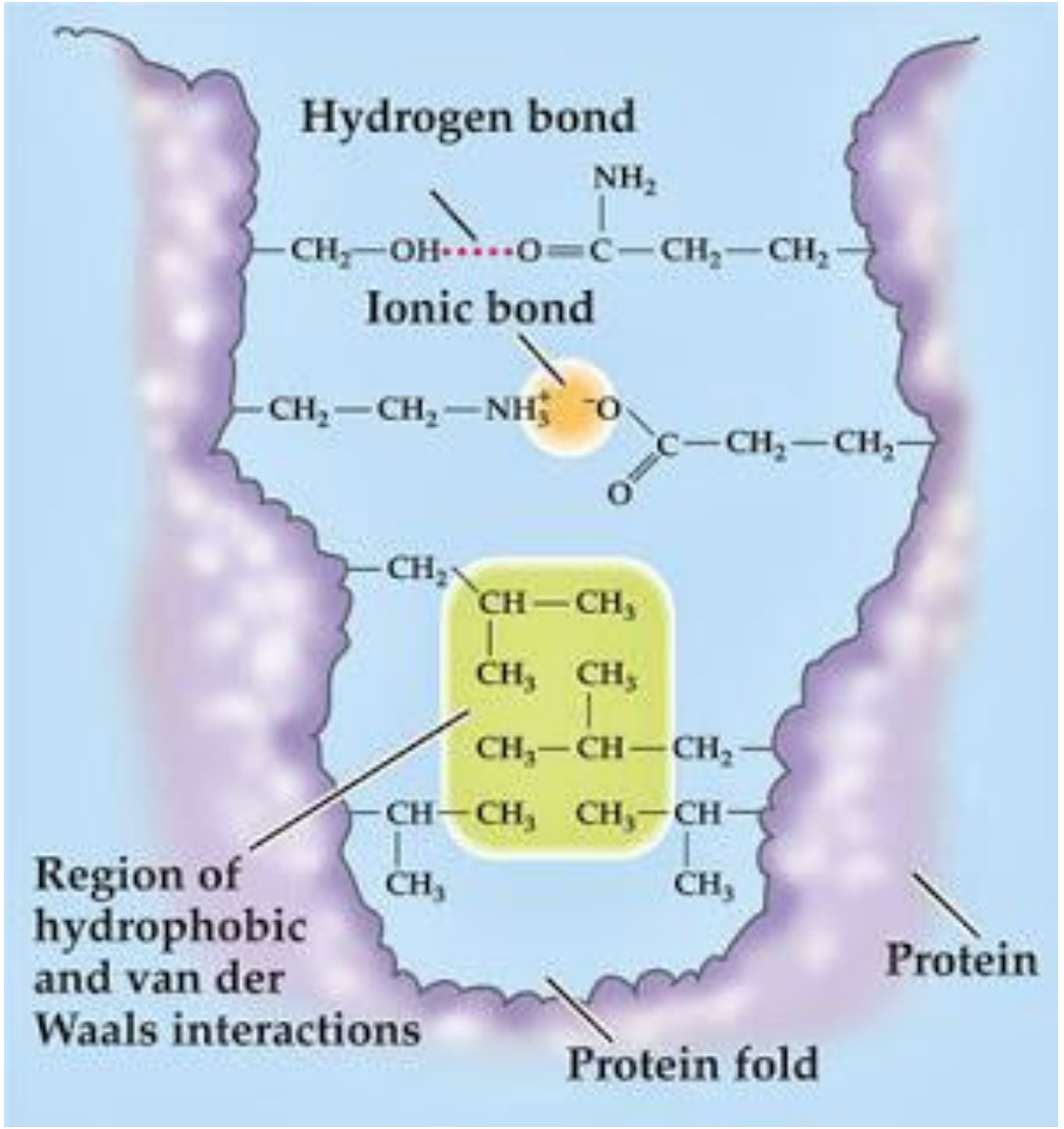


Hydrophobic Interactions

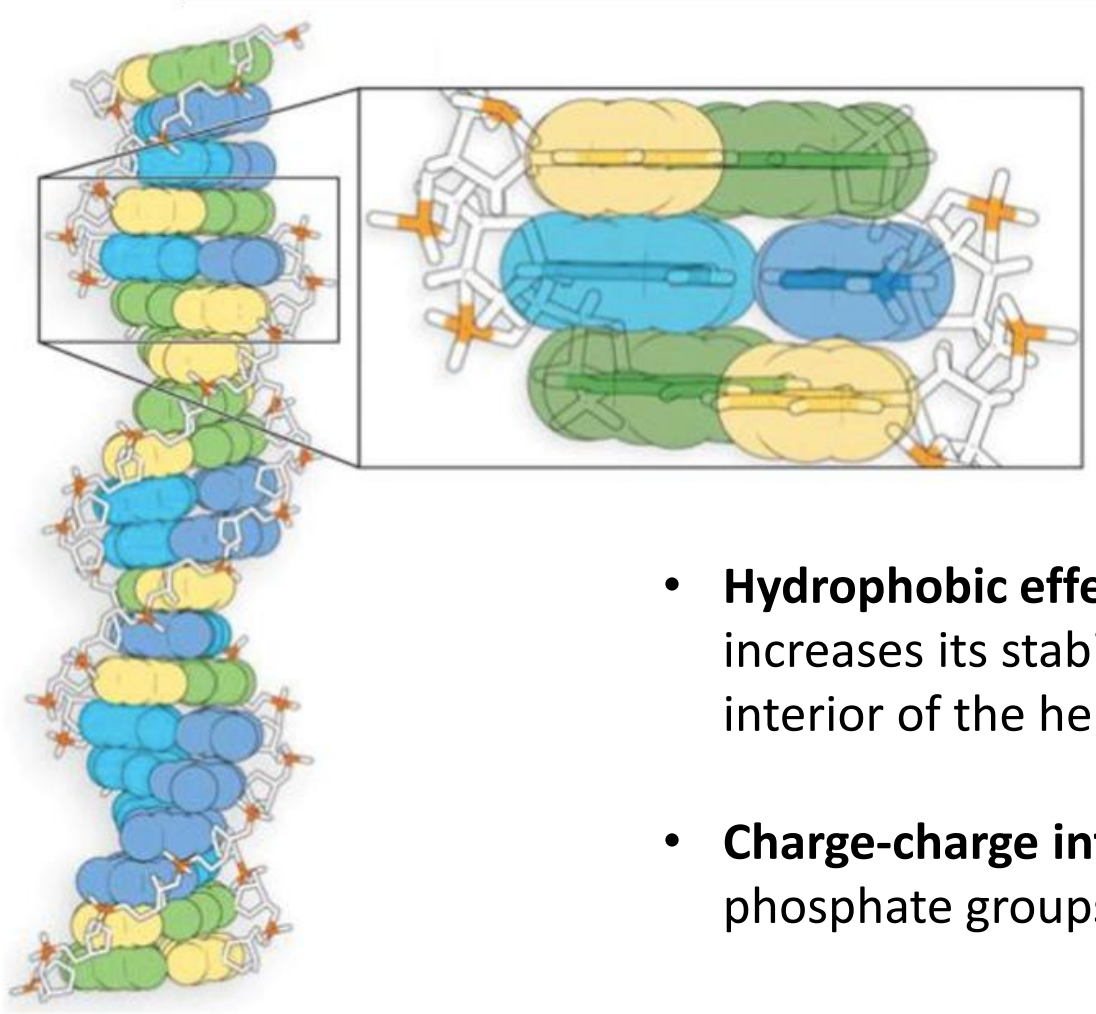


Hydrogen Bonds

Non-covalent interactions in proteins



Non-covalent interactions in DNA

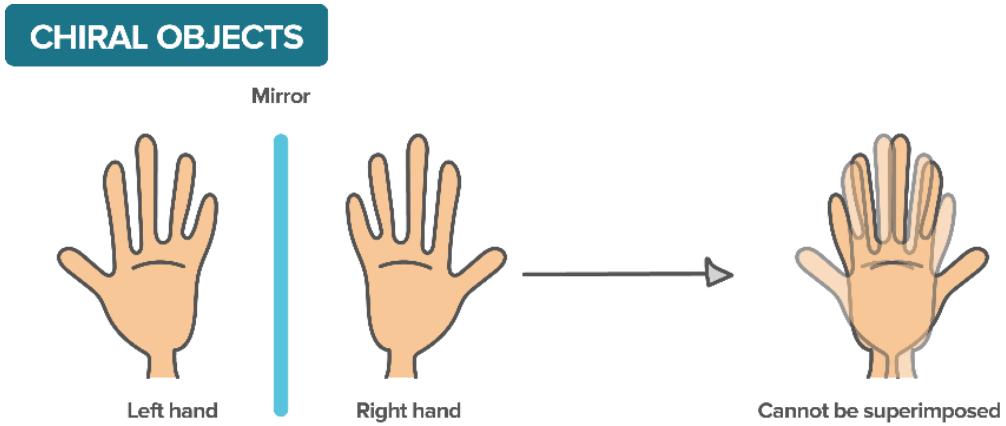


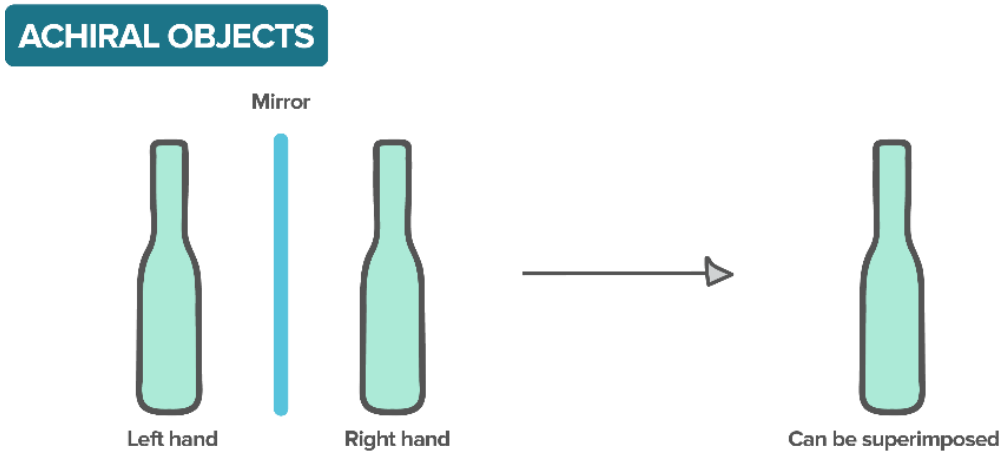
Various weak forces stabilize the double helix

- **Hydrogen bonds:** between base pairs
- **Stacking interactions (or also known as Van der Waals interactions):** between bases as they sit on top of one another
- **Hydrophobic effects:** by burying the bases in the interior of the helix increases its stability; having the hydrophobic bases clustered in the interior of the helix keeps it away from the surrounding water
- **Charge-charge interactions:** electrostatic repulsion of negative charged phosphate groups is decreased by cations (e.g., Mg^{2+})

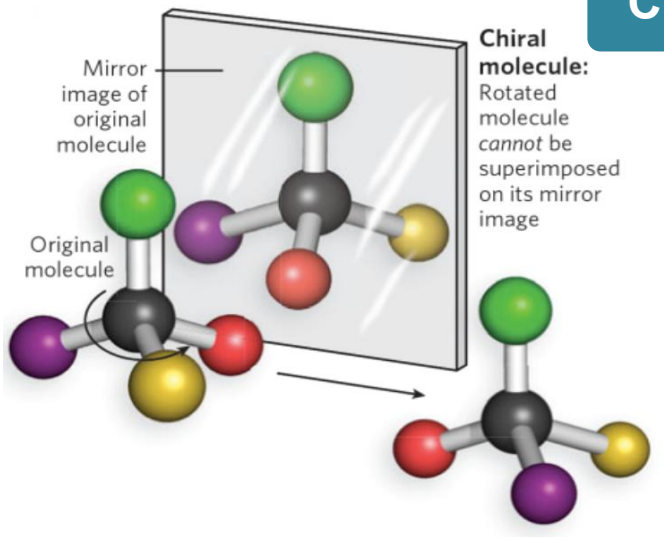
Molecular Biology: Principles and Practice, Michael M. Cox, Jennifer Doudna, Michael O'Donnell, 1st Ed. 2012, W.H. Freeman and Company

Stereochemistry

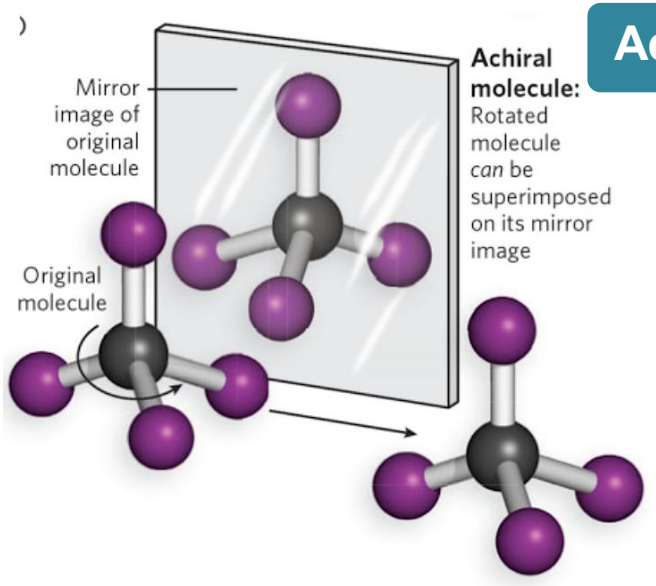




Chiral molecules



Achiral molecules



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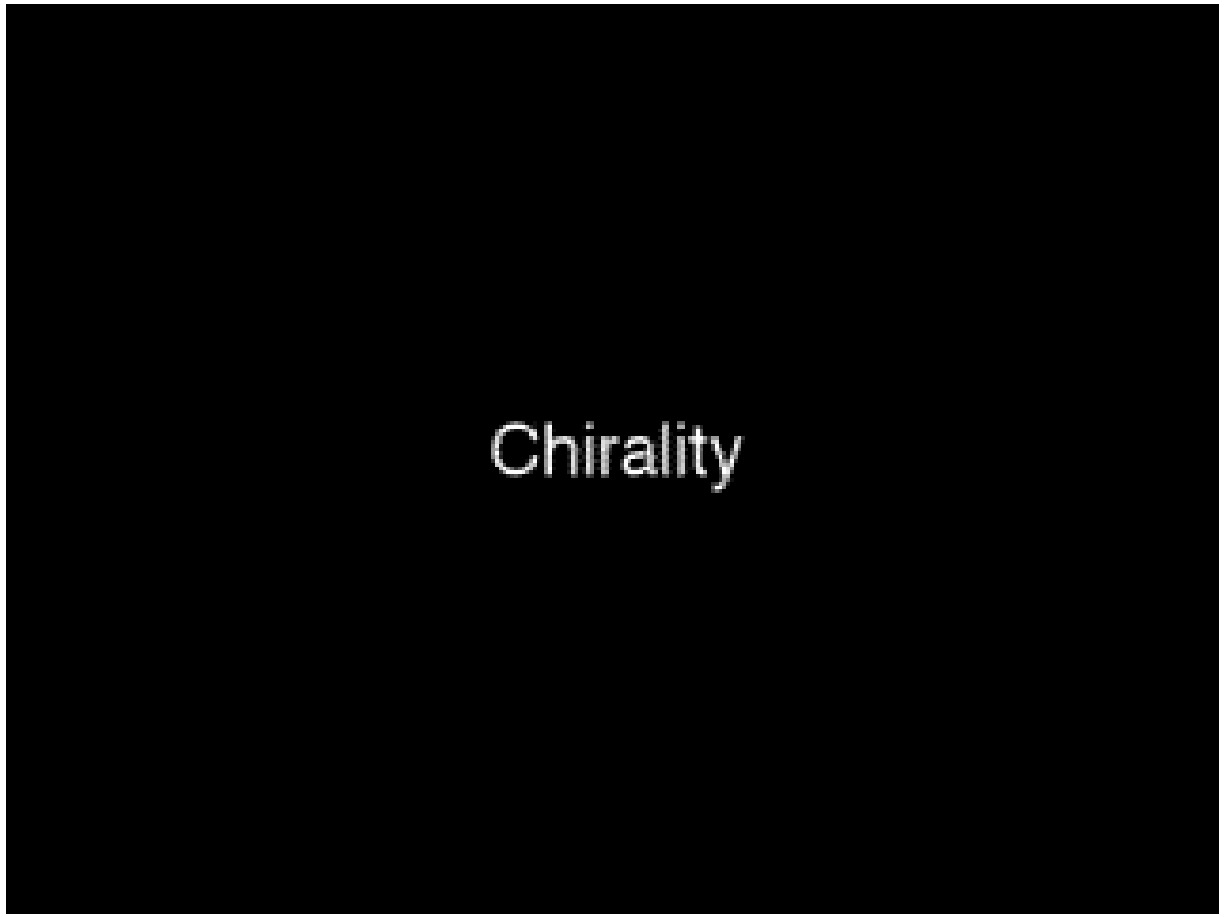
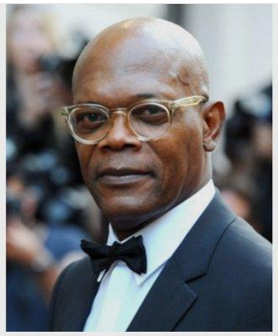
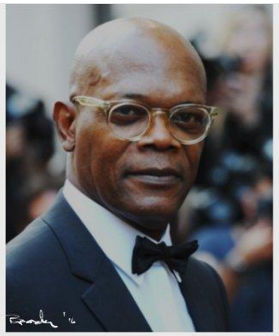
Molecular Biology: Principles and Practice, Michael M. Cox, Jennifer Doudna, Michael O'Donnell, 1st Ed. 2012, W.H. Freeman and Company


Chirality

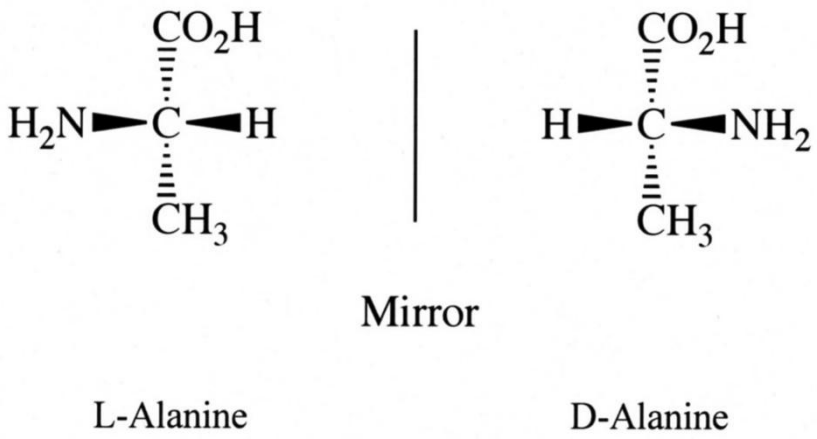
The L and D isomers (enantiomers) of amino acids



Samuel-**L**-Jackson



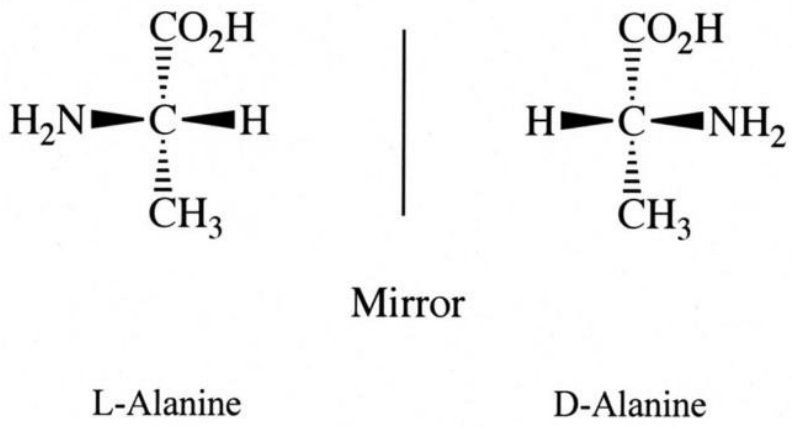
Samuel-**D**-Jackson

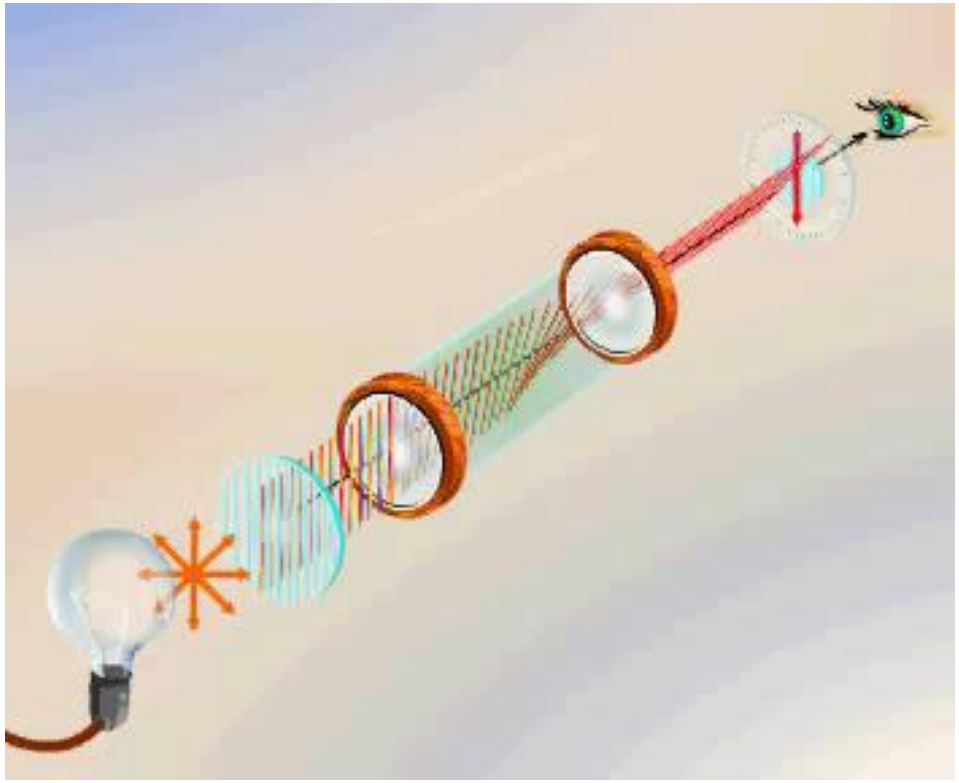


- Chiral carbon atom (α-carbon or Cα); asymmetric carbon
- Chiral molecules; optically active (can rotate planed-polarized light in the opposite direction); enantiomers; mirror images
- D for *dextro* or right; L for *levo* for left
- L-form in nature

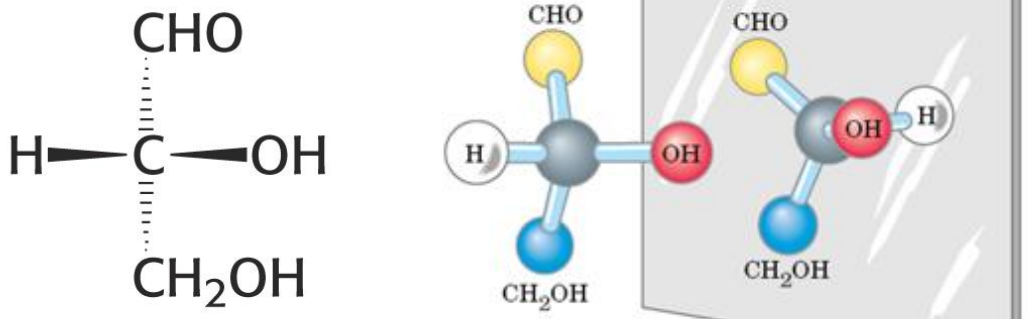
Chiral compounds (Enantiomers) are optically active:
Capable of rotating the plane of polarized light

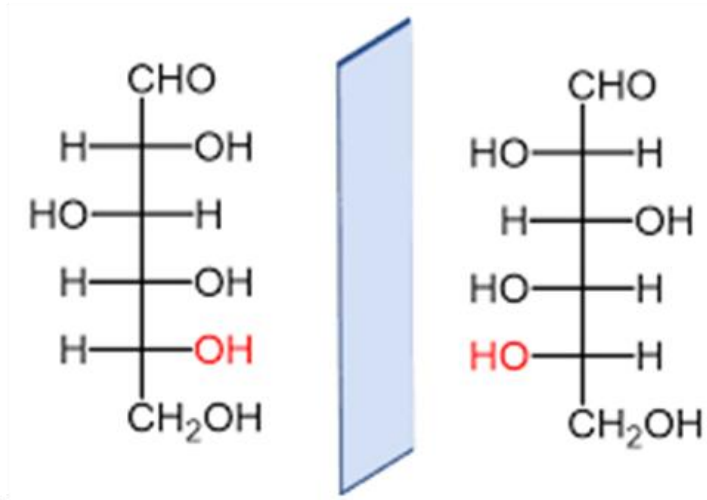
Enantiomers rotate the plane of polarized light in the opposite of direction



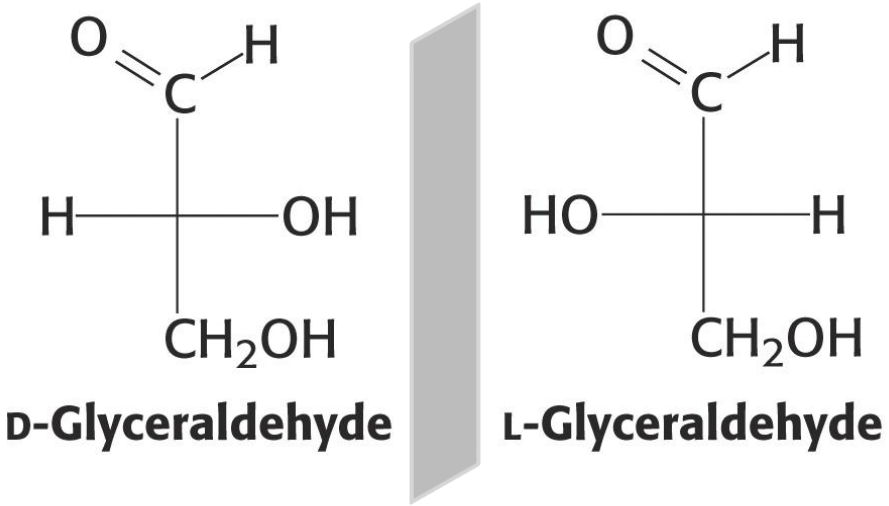


The L and D isomers (enantiomers) of monosaccharides





D-glucose L-glucose



The predominant form in nature is the D-form

	Carbohydrate	Lipid	Protein	Nucleic acid
Building block/monomer	Monosaccharide (D-form)	Non-polymer No building block	Amino acid (L-form)	Nucleotide (sugar, base and phosphate)
Intramolecular interaction	Covalent bonds between atoms (*e.g.*, C-H, C-O) Glycosidic linkages between monosaccharides	Covalent bonds between atoms (*e.g.*, C-H, C-O)	Covalent bonds between atoms (*e.g.*, C-H, N-H) Peptide bonds between amino acids	Covalent bonds between atoms (*e.g.*, C-H, N-H) Phosphodiester bonds between nucleotides
Intermolecular interaction	H-bonds (*e.g.*, in cellulose)	Hydrophobic interactions	H-bonds, hydrophobic interactions, Electrostatic interactions etc.	H-bonds, hydrophobic interactions
Structure	Mono-, di-, oligo-, polysaccharides	Diverse	Primary, secondary, tertiary and quaternary structures	Nucleosides, nucleotides, polynucleotides
Examples	Glucose, lactose, starch, cellulose, glucose-6-phosphate	Fatty acids, triacyglycerols, phospholipids	Peptide chains, myoglobin, hemoglobin	DNAs, RNAs
Biological functions	Energy storage, structural components, cell-cell communication	Energy storage, structural components, cell membrane components	Catalysts, transport of vitamins, minerals, oxygen and fuels, receptors, cytoskeleton	Genetic information storage (DNA) and transmission (RNA)

Main references and further readings

- Stryer et al. Biochemistry, 9th ed., Macmillan Learning, 2019
- Nelson et al. Lehninger Principles of Biochemistry. 8th ed. W. H. Freeman and Company, 2021
- Bayners and Donminiczak Medical Biochemistry, 6th ed., Elsevier Health, 2022
- http://blausen.com/en/video/optically-active/
- https://www.youtube.com/watch?v=3WZZXPOsPNI

schadamas@kku.ac.th