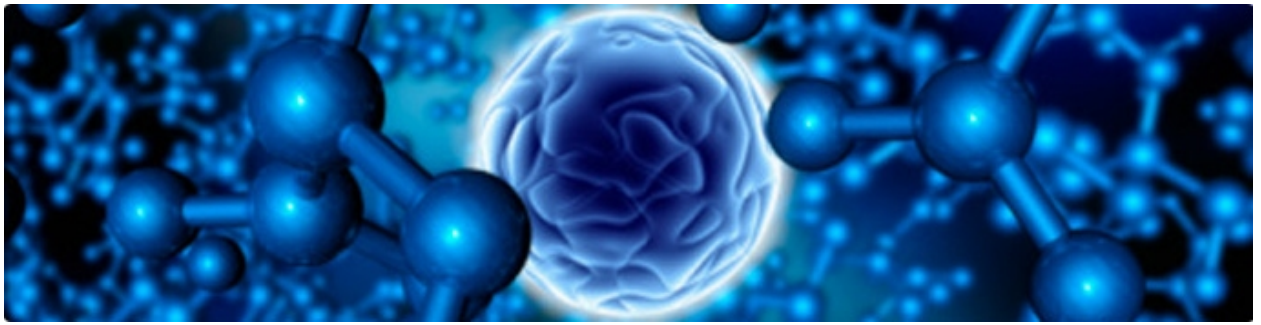
Summer term 2016
Nanobiophysics Module

Introduction to Molecular and Cellular Biology

LECTURE 2:

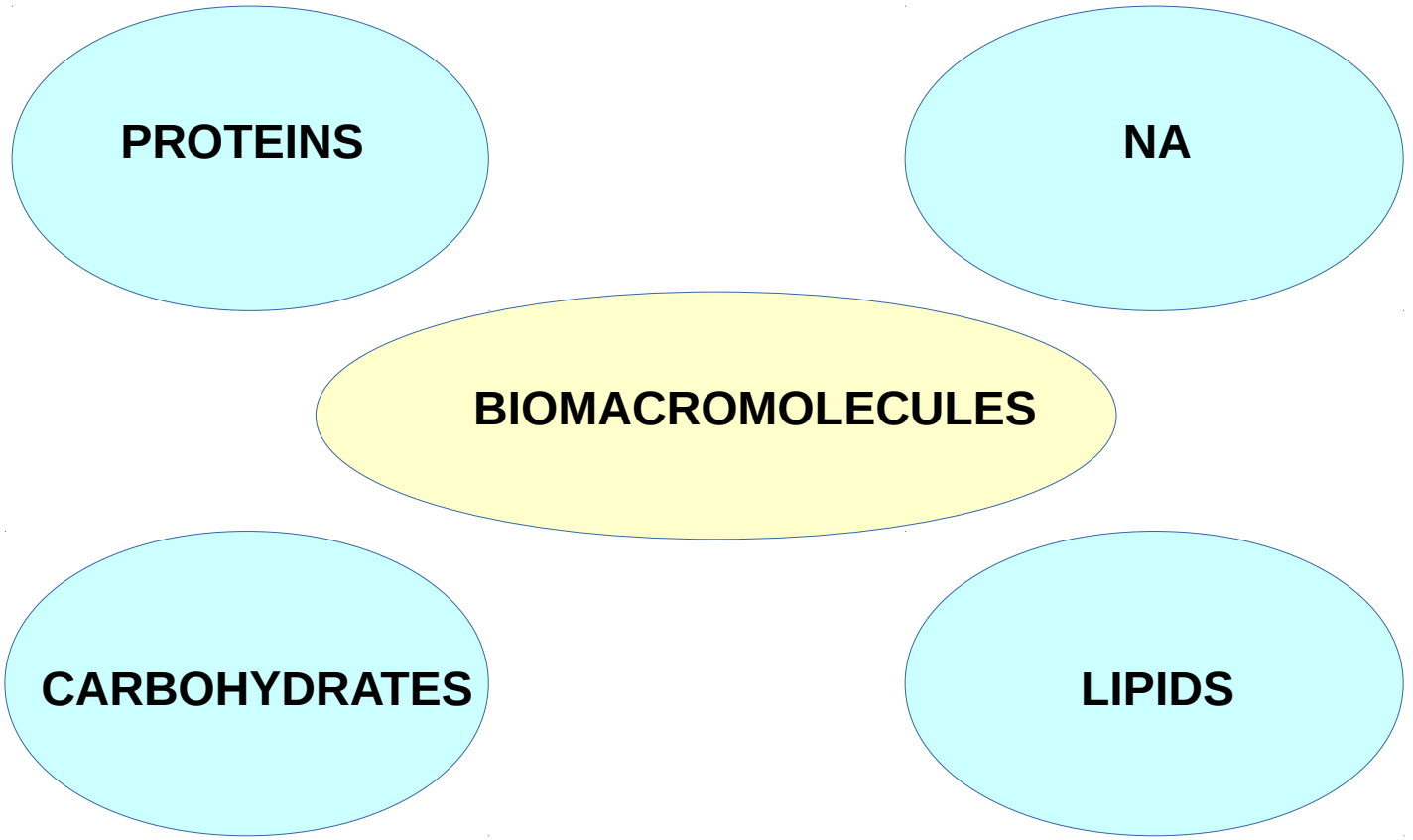
Introduction to cell chemistry and biosynthesis I



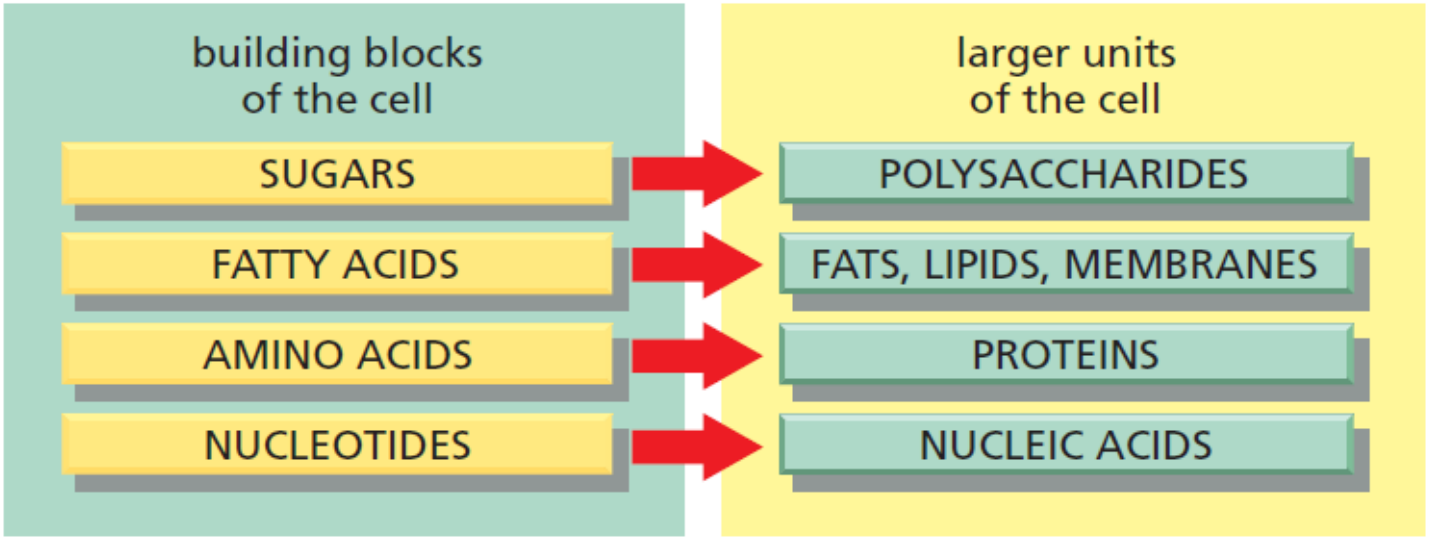
LECTURE 2: INTRODUCTION TO CELL CHEMISTRY AND BIOSYNTHESIS I

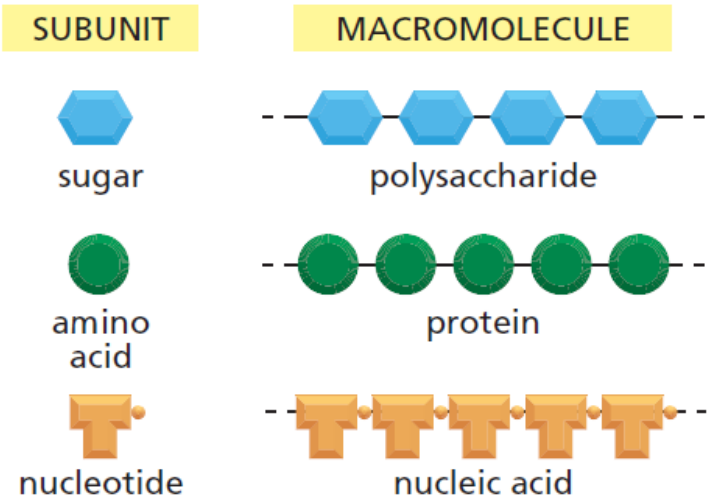
- **Building blocks of biological systems:**
  - **sugars: polysaccharides**
  - **nucleic acids: RNA, DNA**
  - **fatty acids: lipids**
  - **amino acids: proteins**
- **Chemical modifications**
- **Localization of biomolecules**
- **Biomacromolecules in the PDB**

FOUR PRINCIPAL CLASSES OF BIOMACROMOLECULES



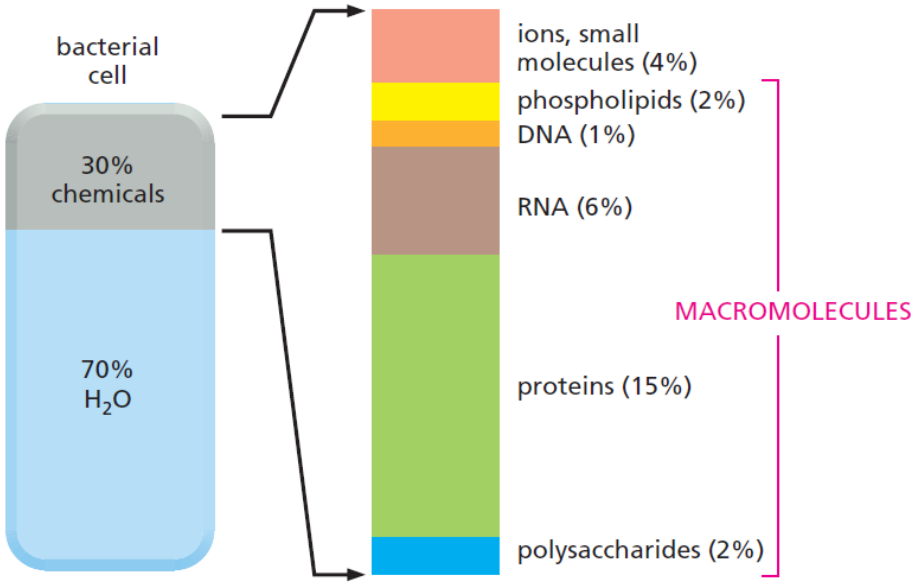
MOLECULES=>MACROMOLECULES





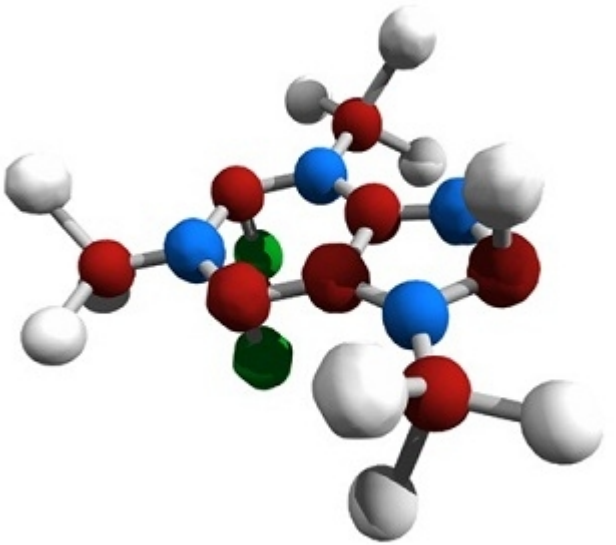
DISTRIBUTION OF MACROMOLECULES

	PERCENTAGE OF TOTAL CELL WEIGHT	NUMBER OF TYPES OF EACH MOLECULE
Water	70	1
Inorganic ions	1	20
Sugars and precursors	1	250
Amino acids and precursors	0.4	100
Nucleotides and precursors	0.4	100
Fatty acids and precursors	1	50
Other small molecules	0.2	~300
Macromolecules (proteins, nucleic acids, polysaccharides, and phospholipids)	26	~3000



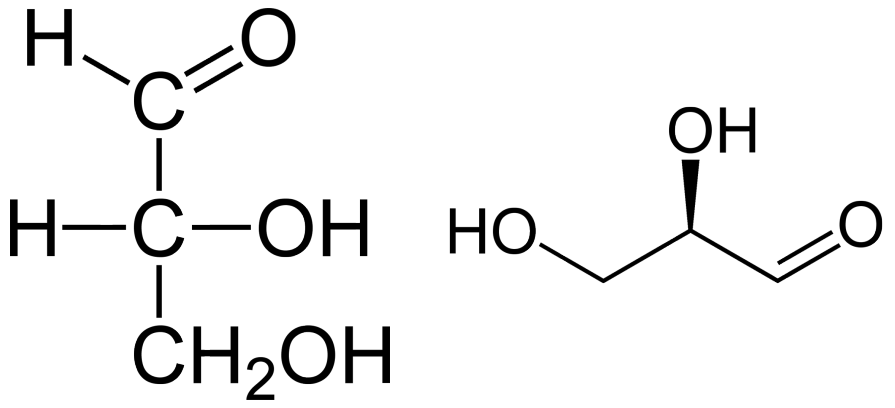
CHARACTERIZATION OF MACROMOLECULES: OUTLINE

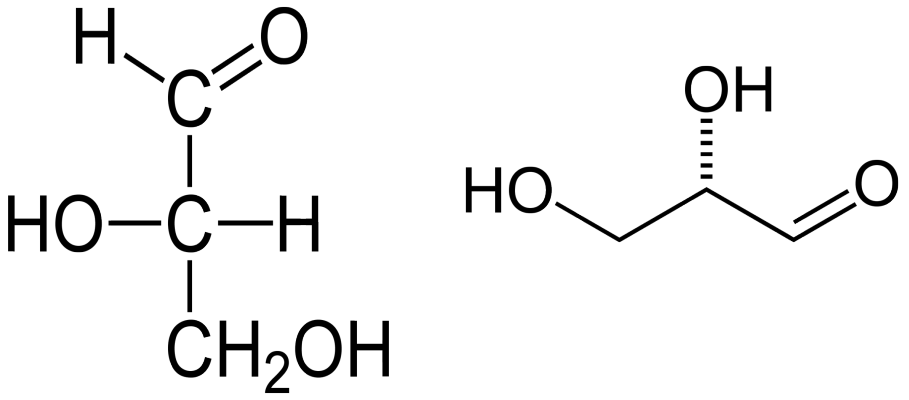
- Chemistry of building blocks molecule
- Chemistry of biomacromolecule
- Structure
- Sources in nature
- Function

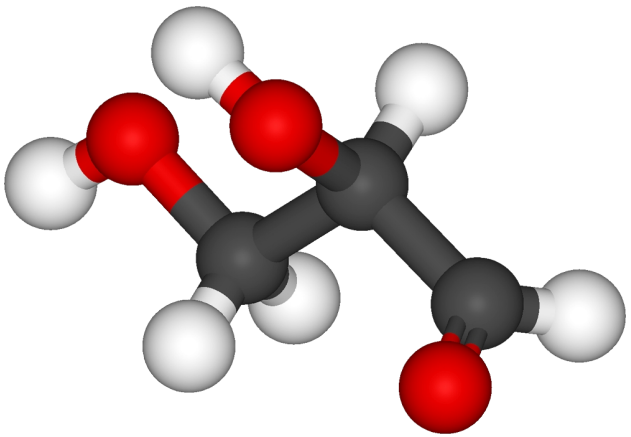


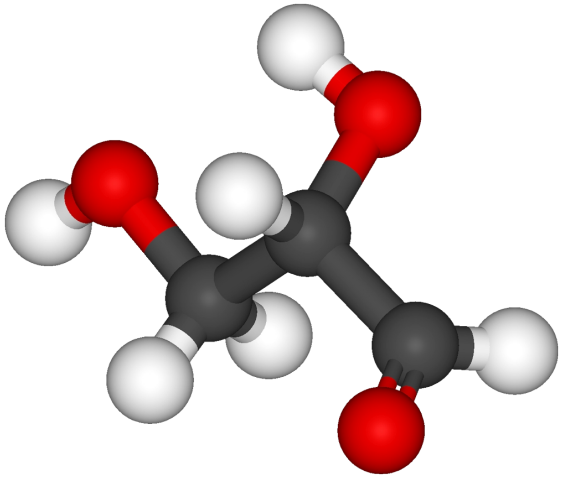
CARBOHYDRATES

Saccharides/carbohydrates: $C_n(H_2O)_m$; polyhydroxy aldehydes/ketones





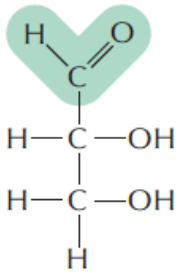
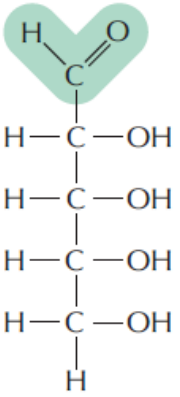
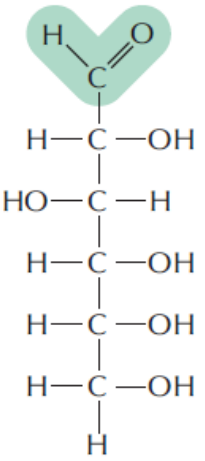
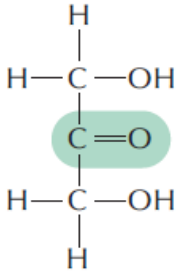
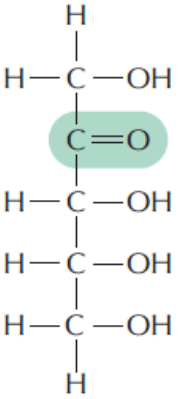
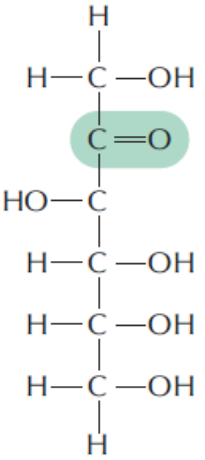




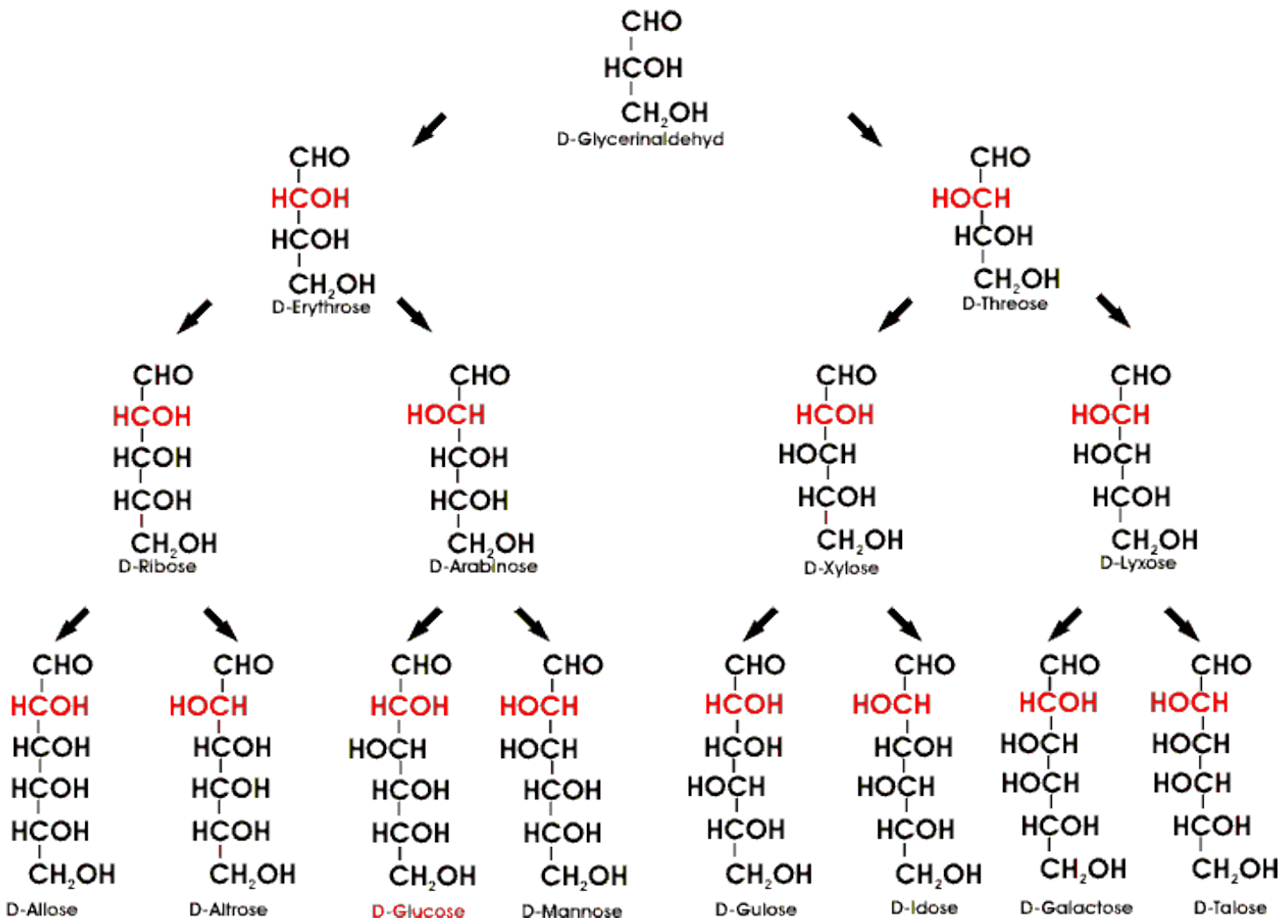
D-glyceraldehyde (R, +)

L-glyceraldehyde (S, -)

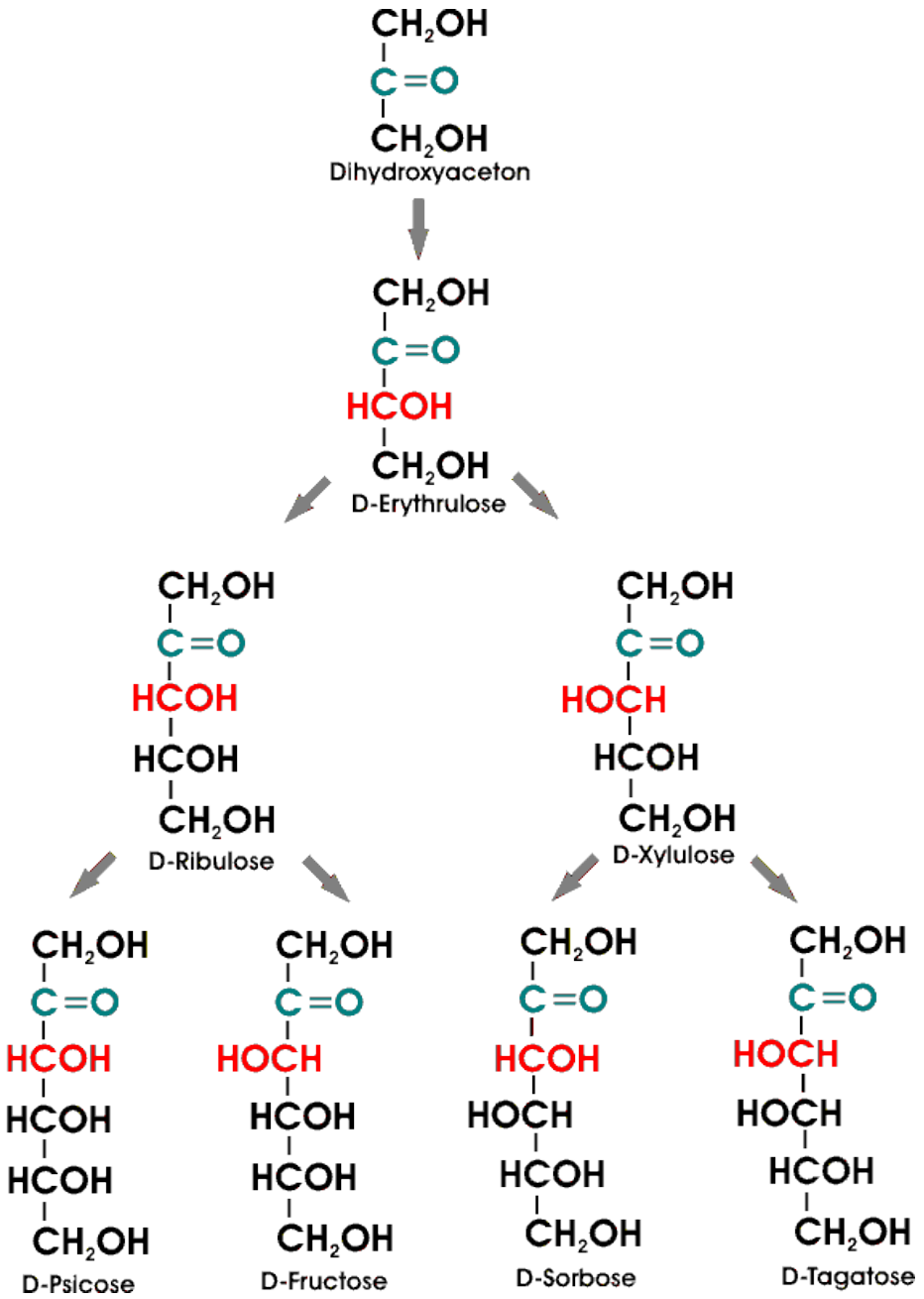
CARBOHYDRATES: ALDOSES/KETOSES

	3-carbon (TRIOSES)	5-carbon (PENTOSES)	6-carbon (HEXOSES)
ALDOSES	 glyceraldehyde	 ribose	 glucose
KETOSES	 dihydroxyacetone	 ribulose	 fructose

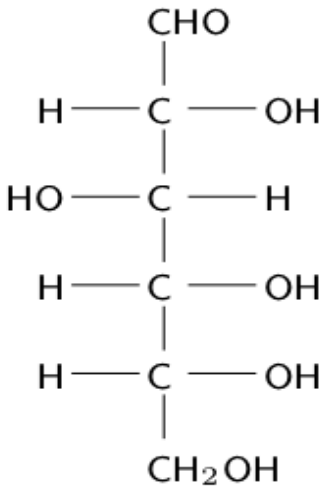
CARBOHYDRATES: ALDOSE TREE

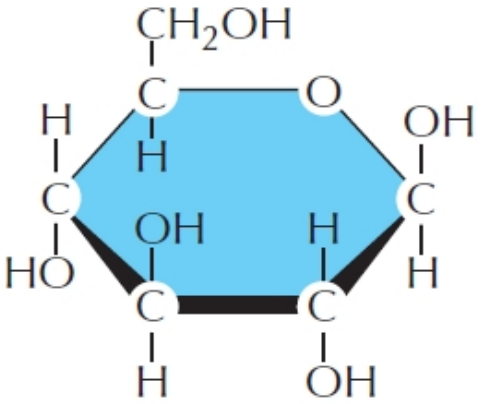


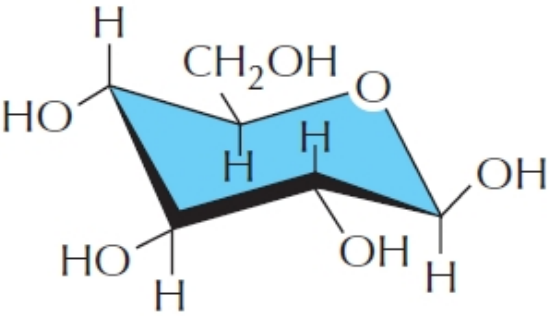
CARBOHYDRATES: KETOSE TREE

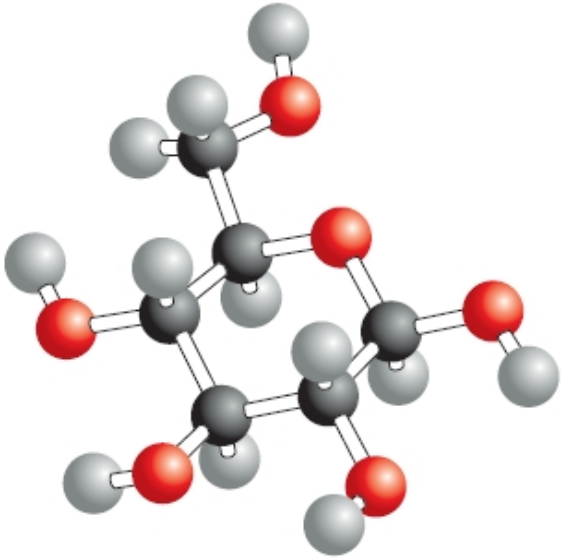


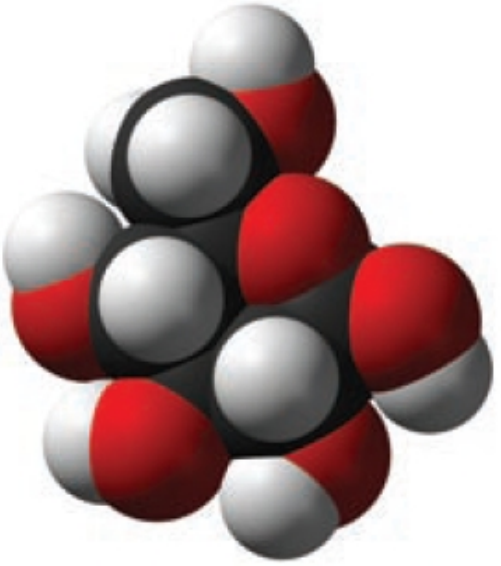
GLUCOSE: DIFFERENT REPRESENTATIONS



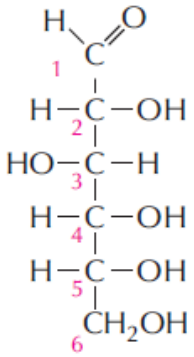


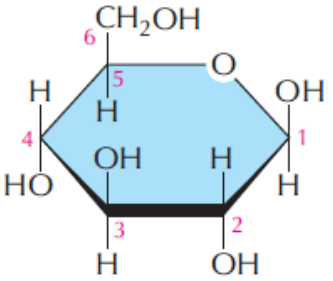






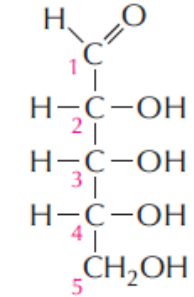
CARBOHYDRATES: CYCLIC FORM

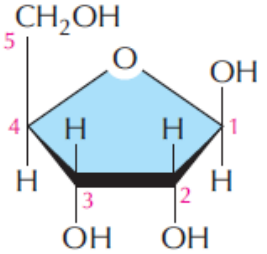




glucose

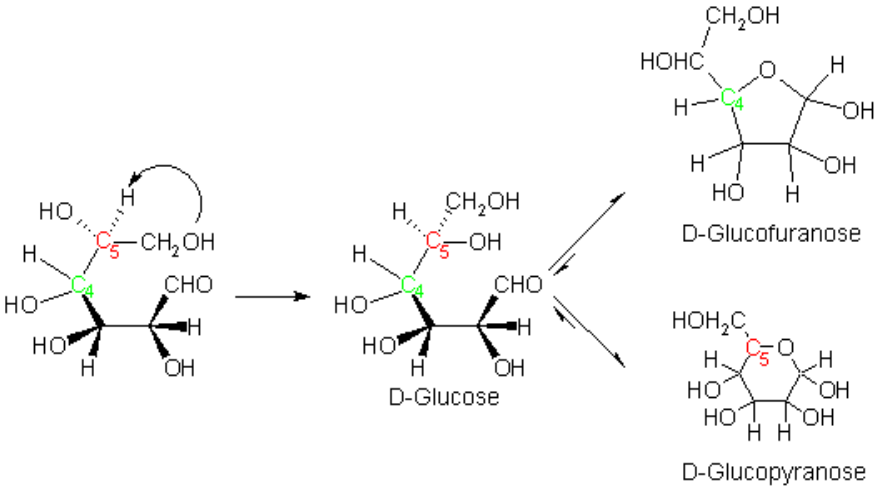
Pyranose



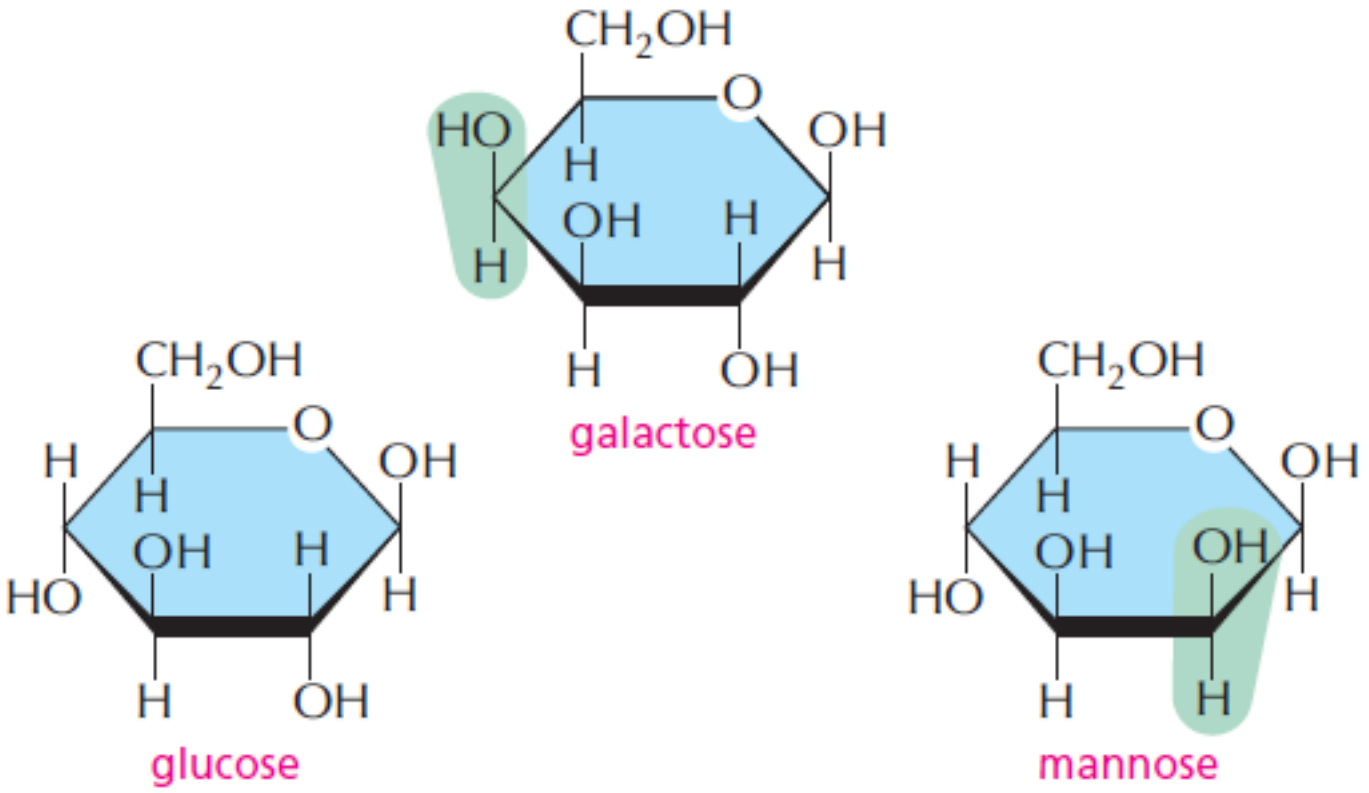


ribose

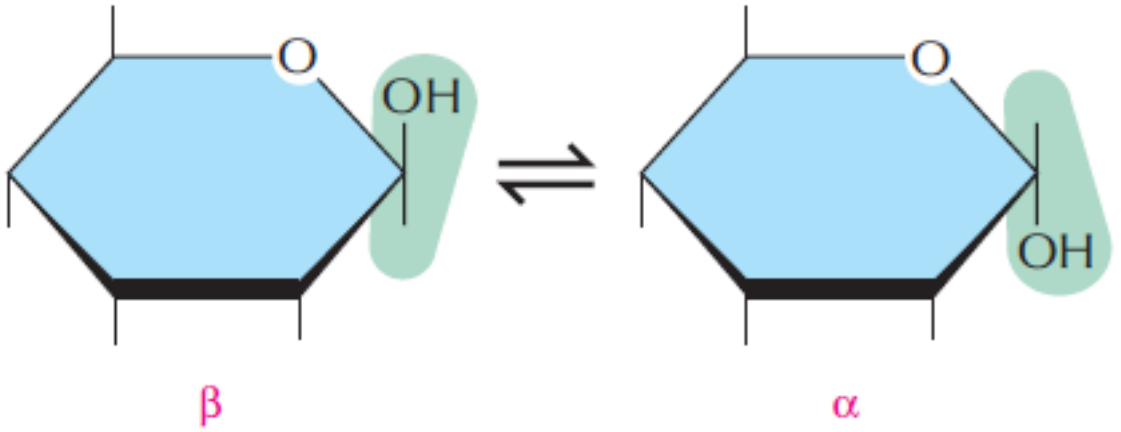
Furanose

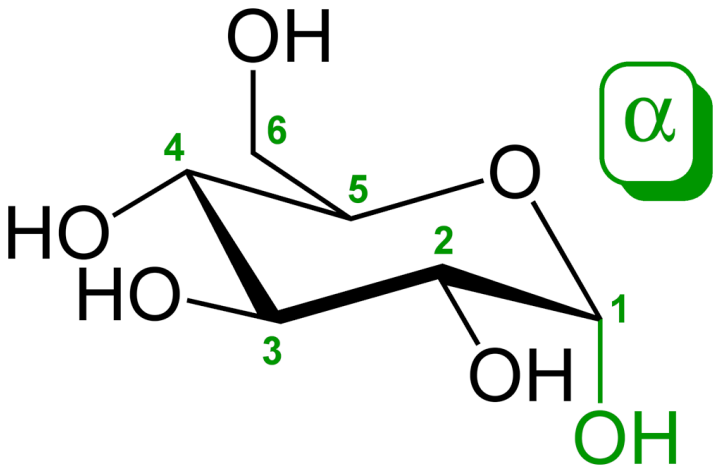


CARBOHYDRATES: DIASTEREOMERS



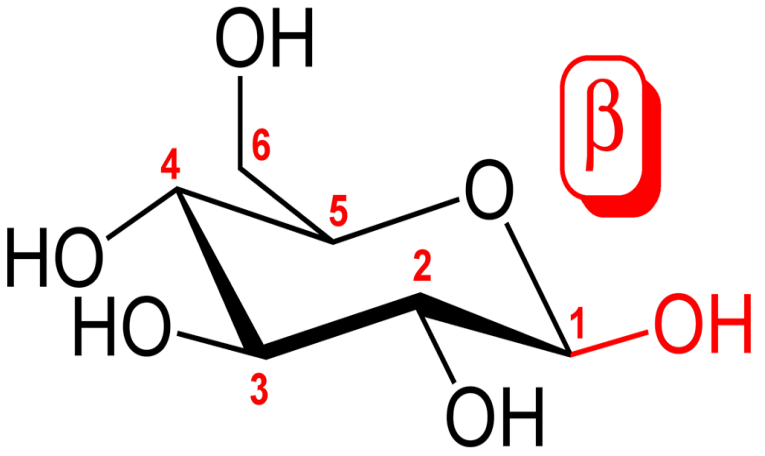
CARBOHYDRATES: α/β-FORMS





α-D-

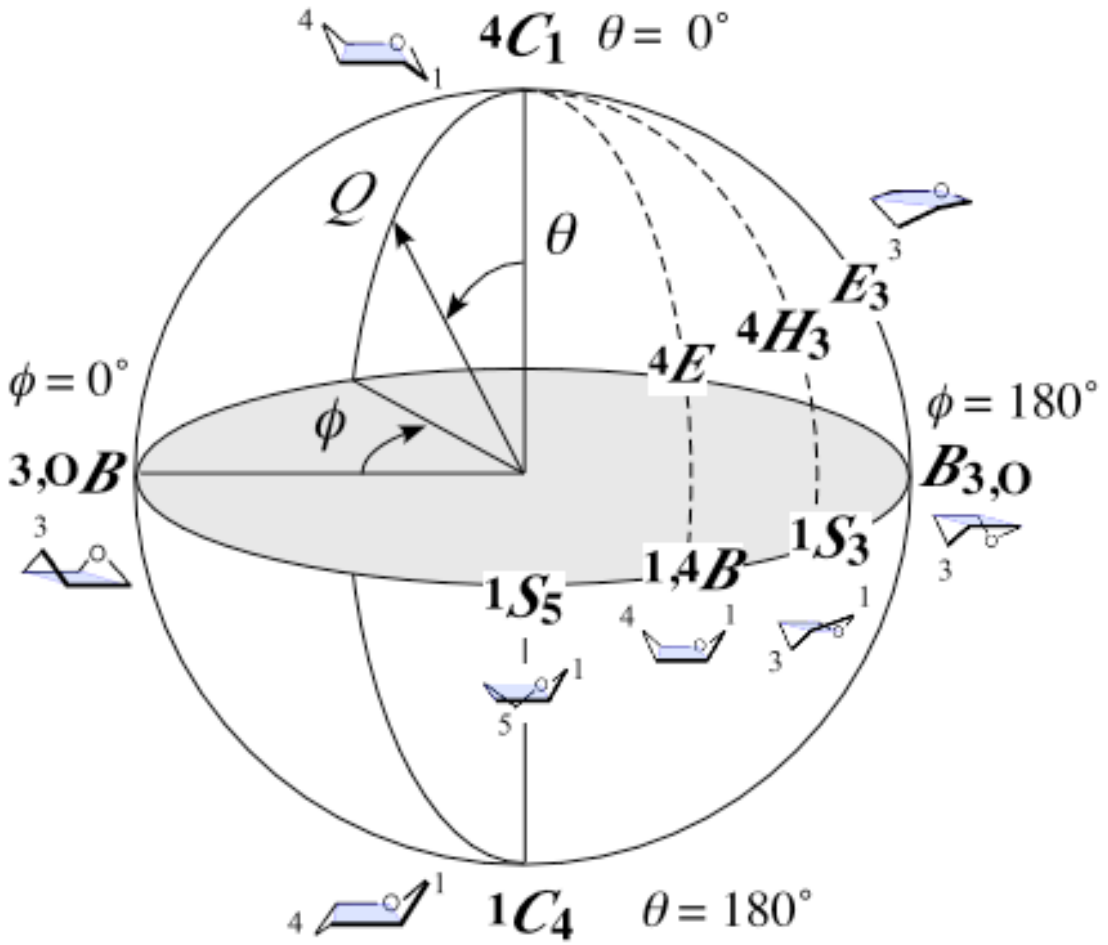
glucopyranose

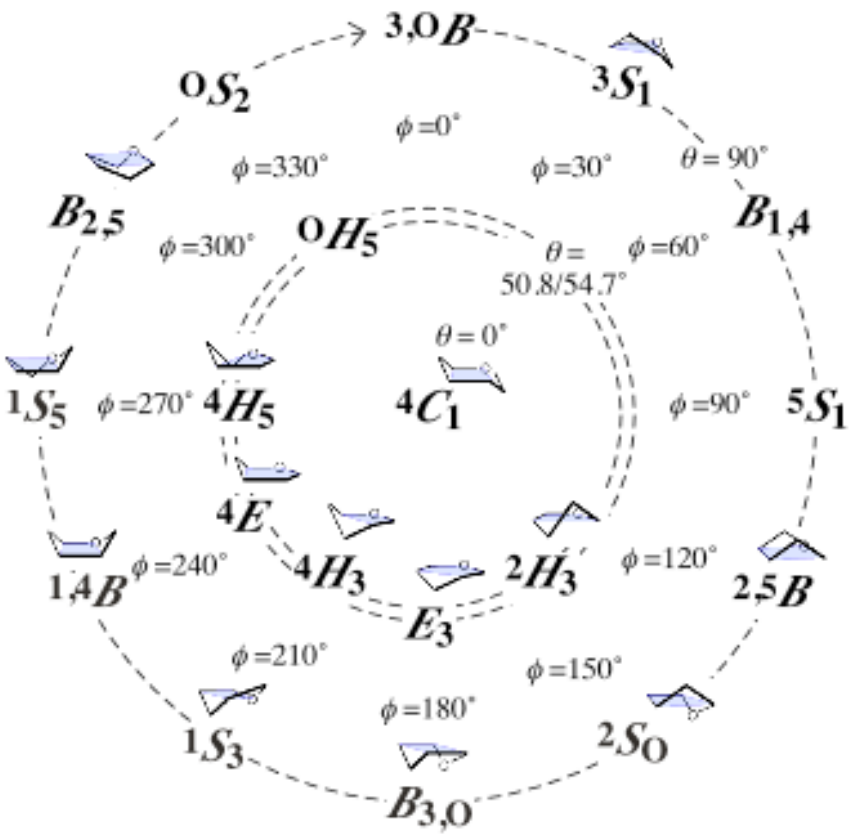


β-D-

glucopyranose

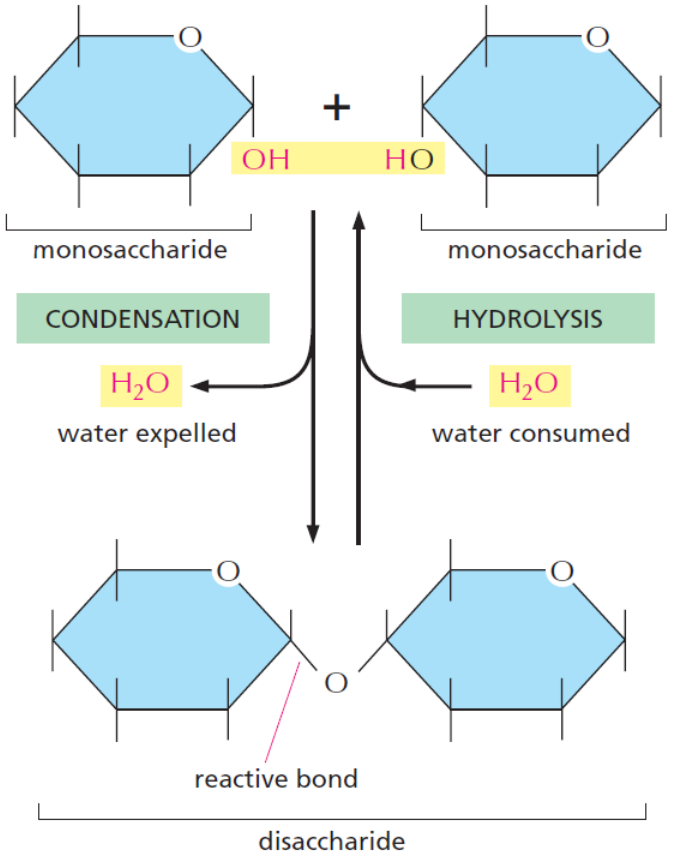
CYCLIC FORMS: PYRANOSE RING CONFORMATIONS

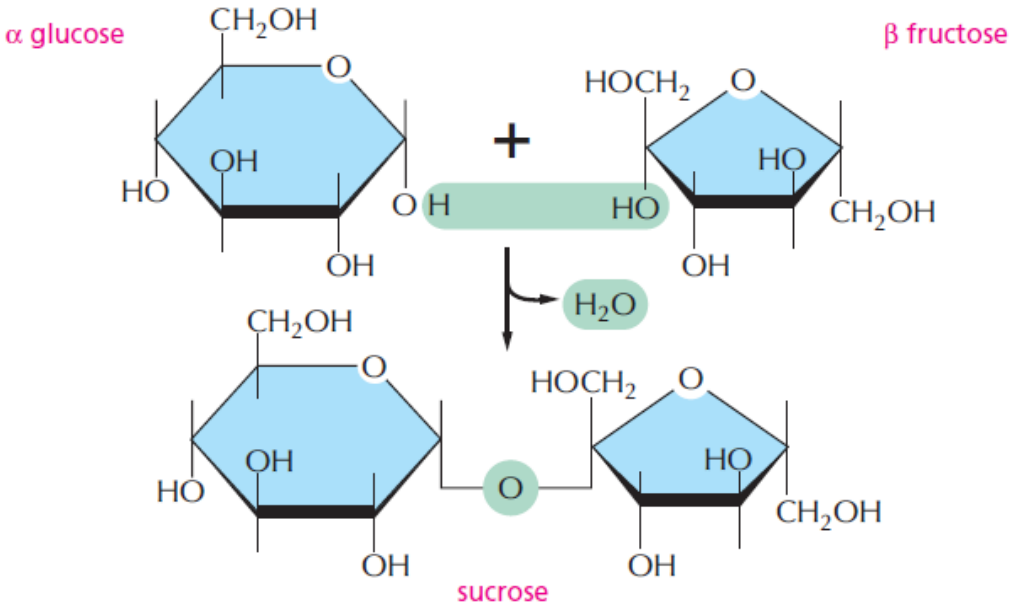




CARBOHYDRATES: OLIGOMERIZATION

- **Polymerization in general: $A_n + A = A_{n+1}$**
- **Reaction of condensation: A-OH + H-B = A-B + H-OH**

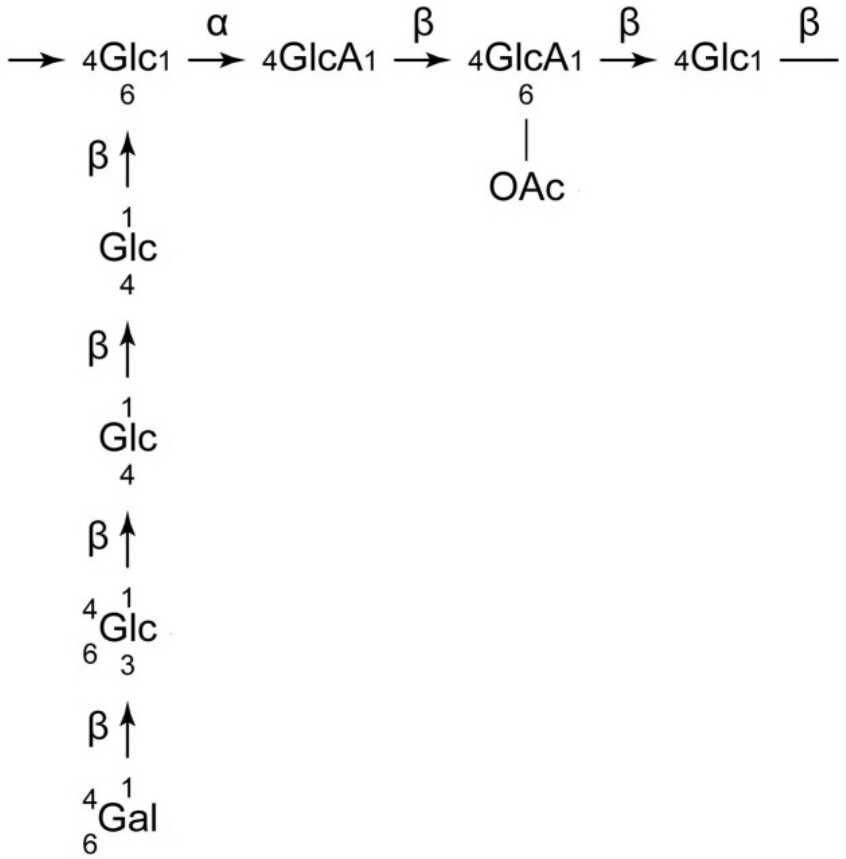


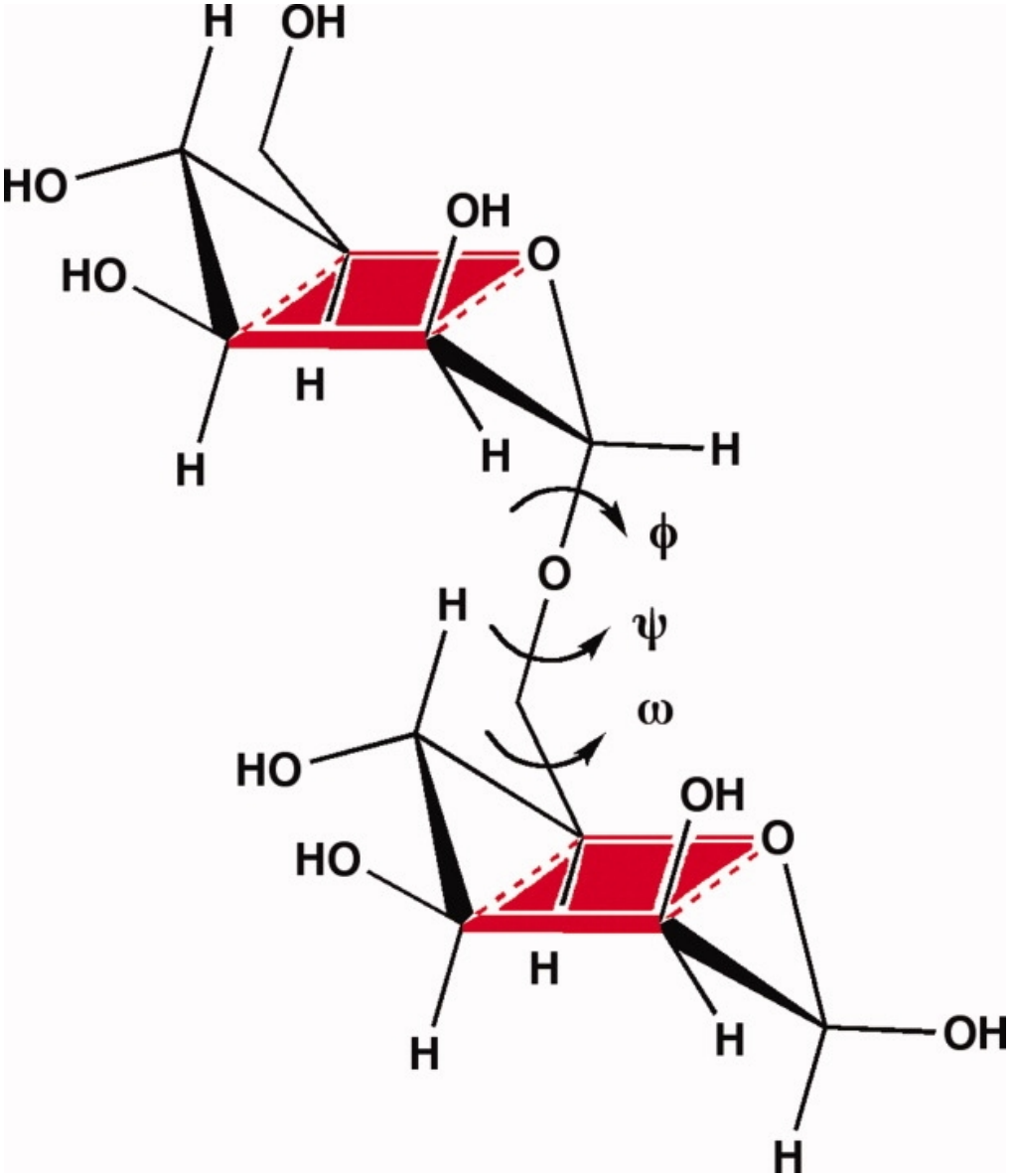


GLYCOSIDIC LINKAGE

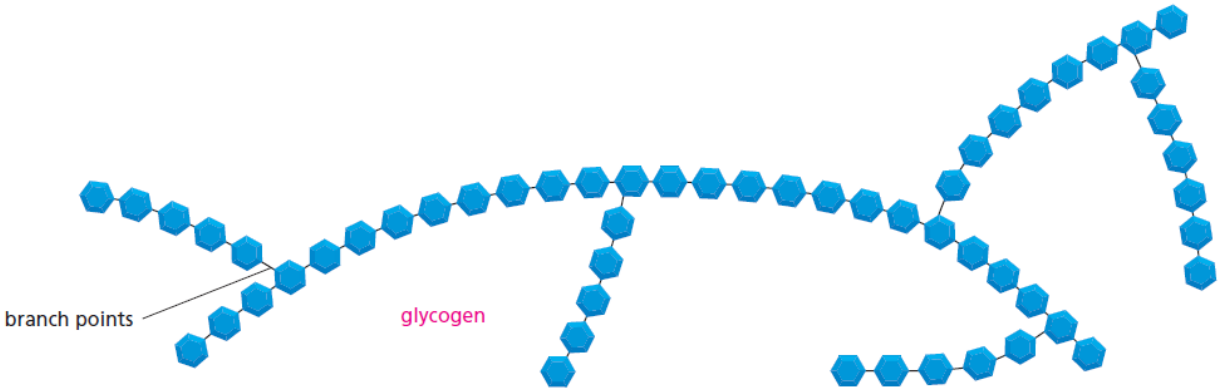
Broad variety of combinations:

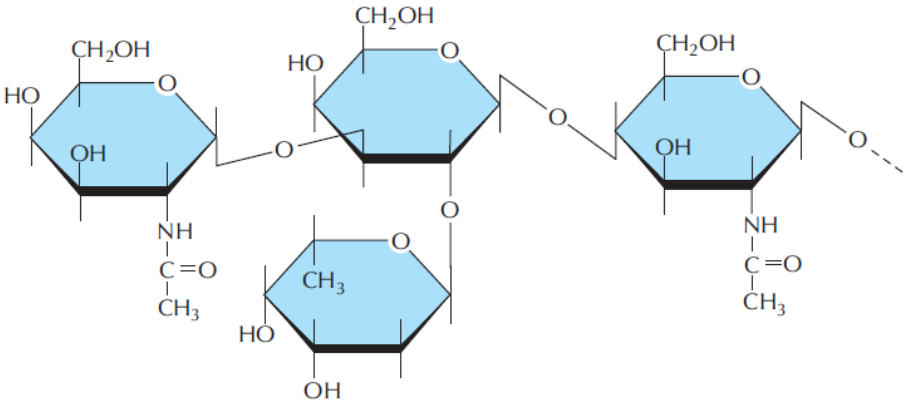
2 Glu => 11 disaccharides

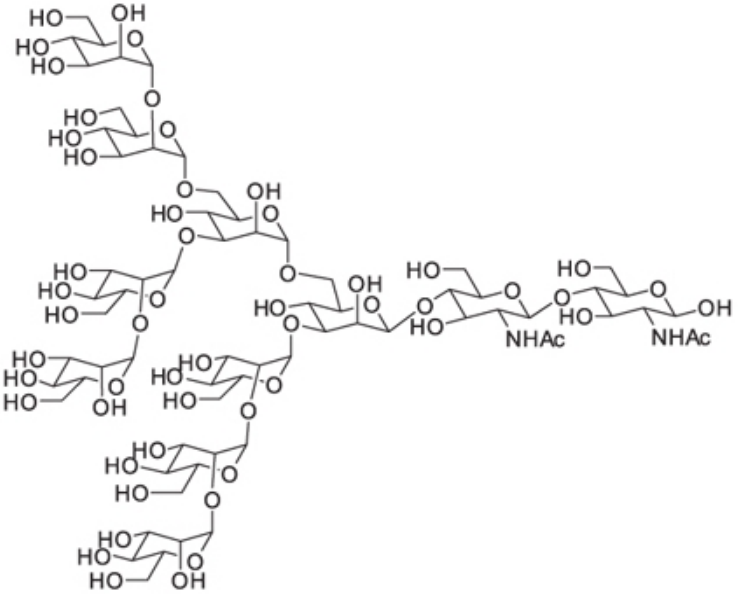




BRANCHED POLYSACCHARIDES

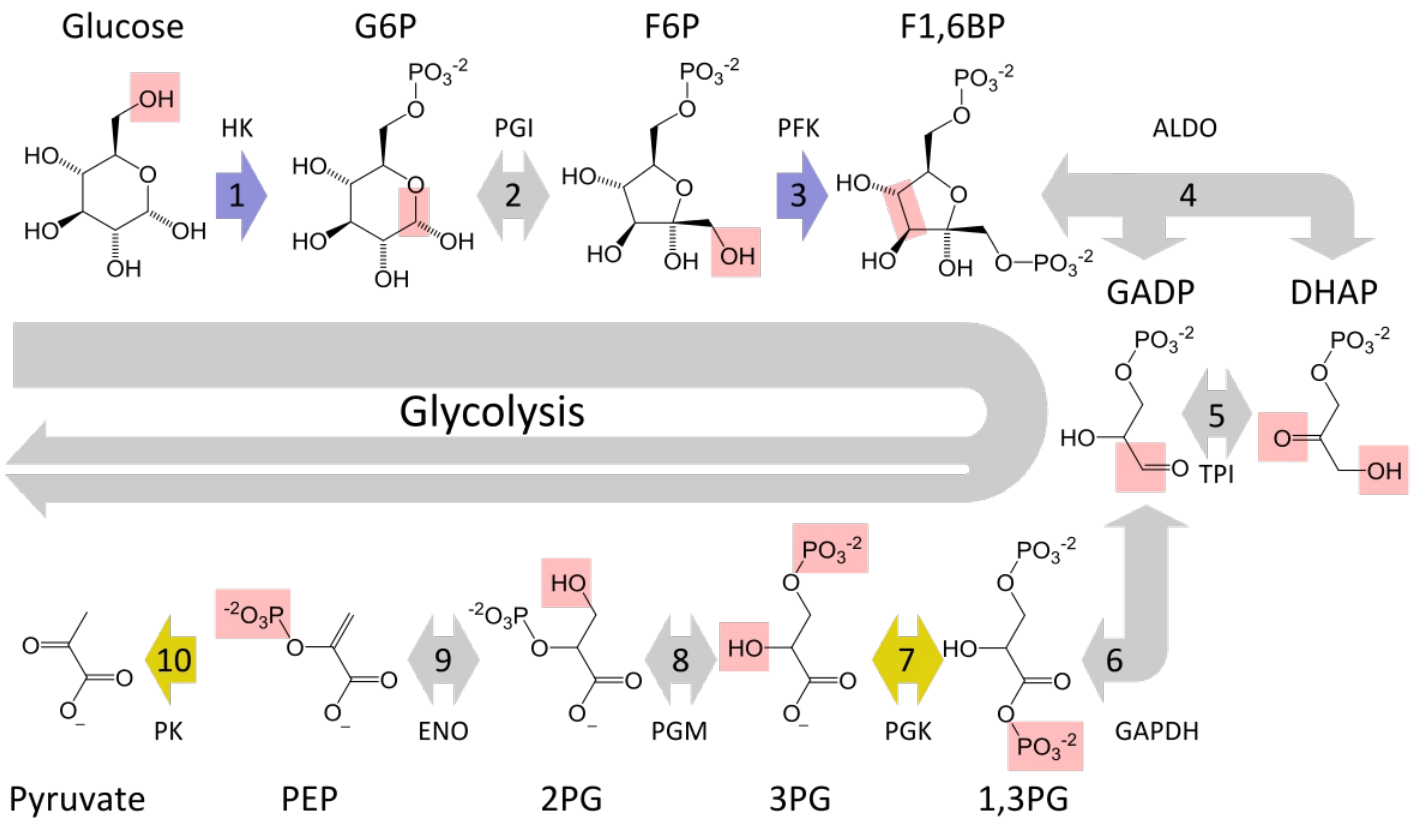


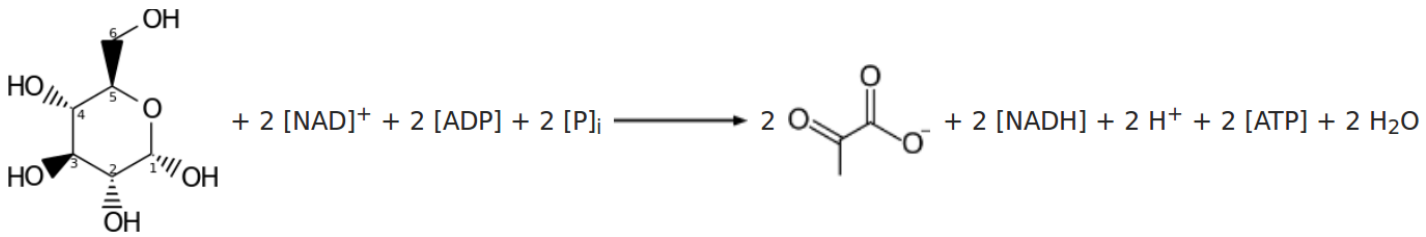




Polysaccharides can be either linear or branched

GLYCOLISIS: GLUCOSE AEROBIC CATABOLISM

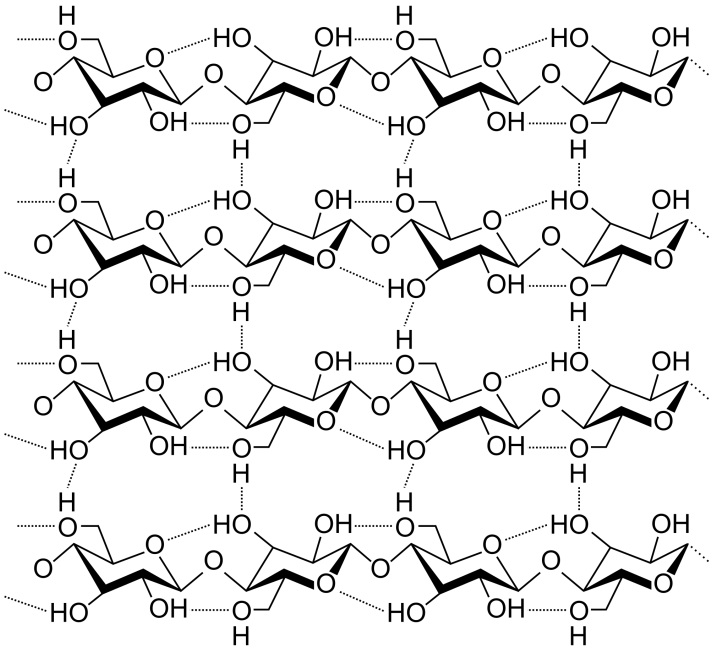




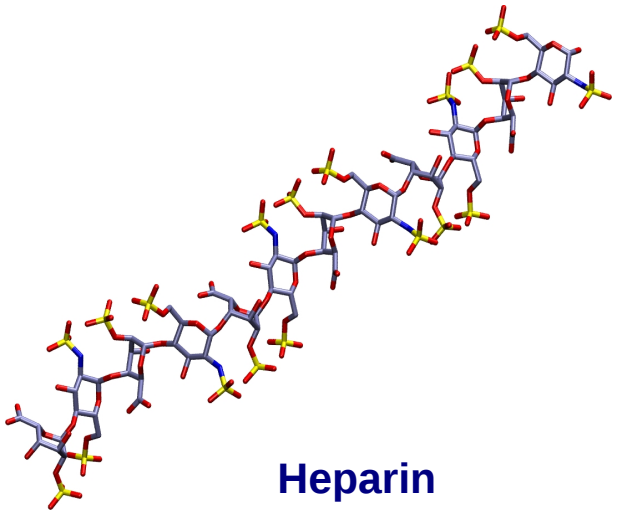
- **In glycolisis, glucose is catabolyzed to pyruvate and energy (NADH, ATP)**
- **Gluconeogenesis is a reverse process**

CARBOHYDRATES FUNCTION

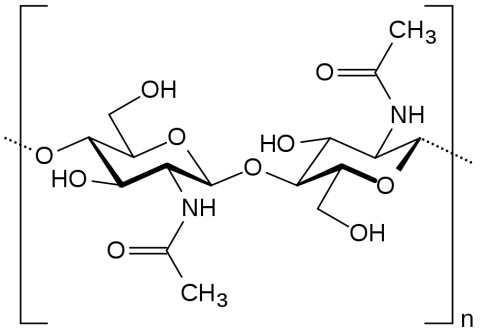
- Production and storage of energy (glycogen)
- Mechanical support (cellulose, chitin)
- Integration in the membranes (glycolipids)
- Signaling (glycosaminoglycans)



Cellulose layers



Heparin



Chitin

NUCLEIC ACIDS: BRIEF HISTORY

- **Friedrich Miescher (1844-1895): discovery of DNA in 1869**

  - leucocytes => protein + unknown molecules

  - existance in acidic and dissolvation in basic conditions

  - HCl => nuclei

  - Not a protein (proteases), not a lipid (ether)

  - C, O, H, P, N

NUCLEIC ACIDS: BRIEF HISTORY

- **Alexander Todd (1907-1997): composition of DNA in 1952**

  - sugar+phosphate+nucleotide

- **James Watson, Francis Crick, Maurice Wilkins, Rosalind Franklin (1953):**

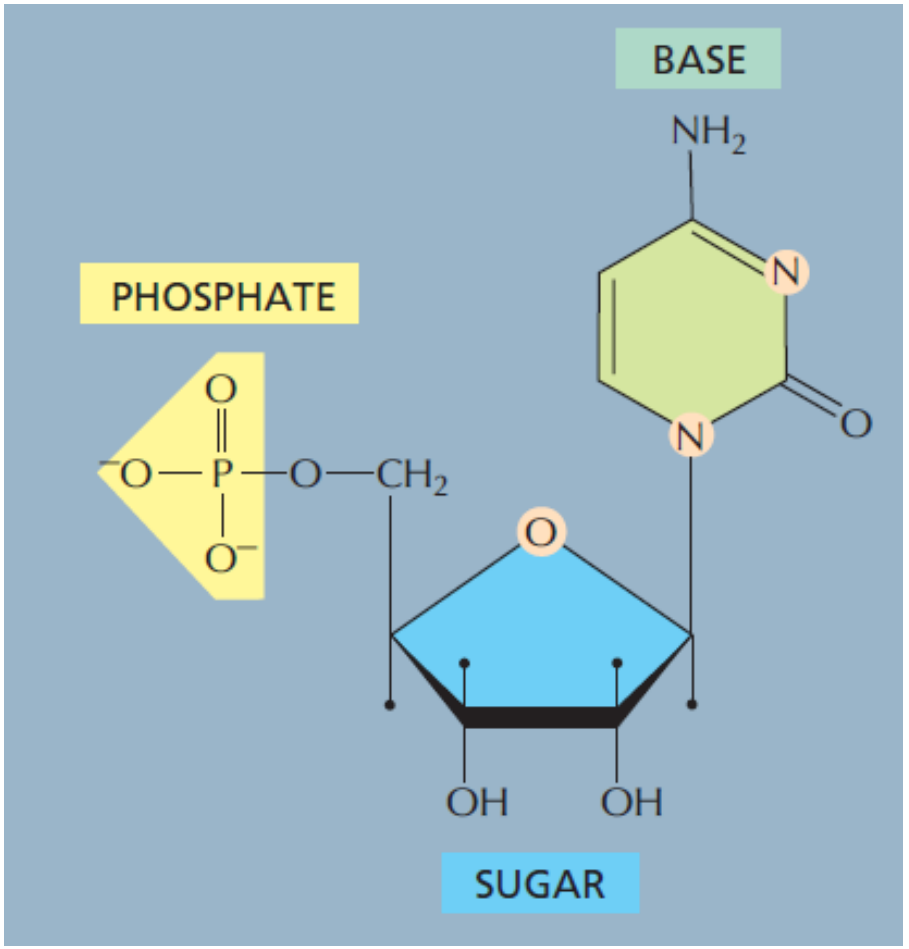
  - model of double-stranded DNA

  - H-bonds between A-T, C-G

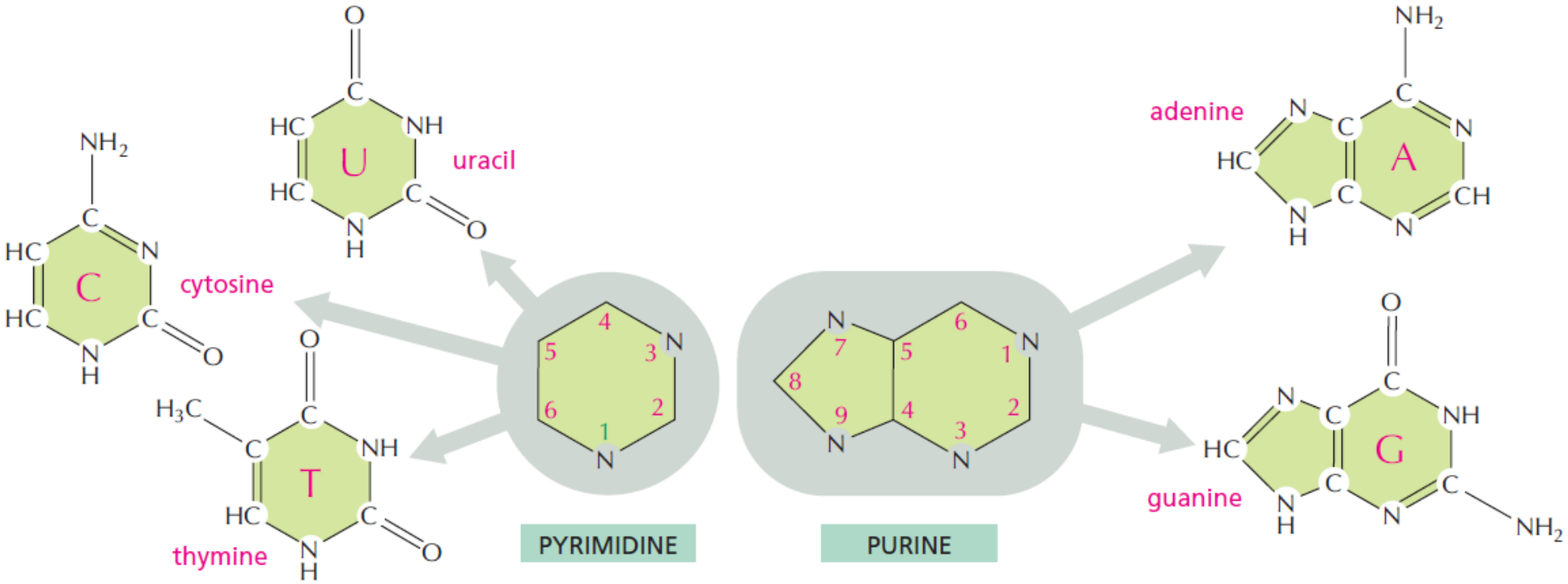
  - potential molecule for genetic information

NUCLEIC ACIDS: BUILDING BLOCKS

- **Base**
- **Sugar**
- **Phosphate**



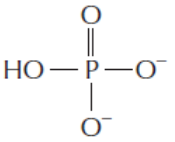
BASES



- **DNA: A, G, C, T**
- **RNA: A, G, C, U**

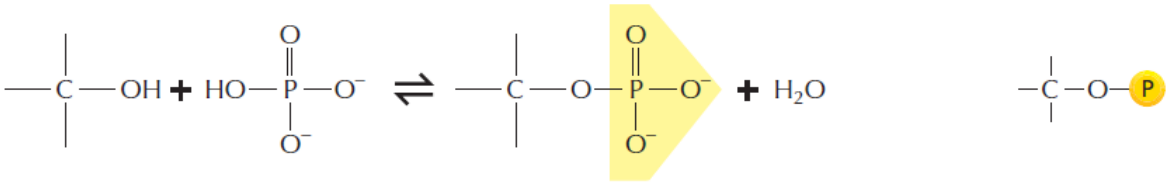
PHOSPHATE

- **Phosphate (ion of H_3PO_4), P_i**



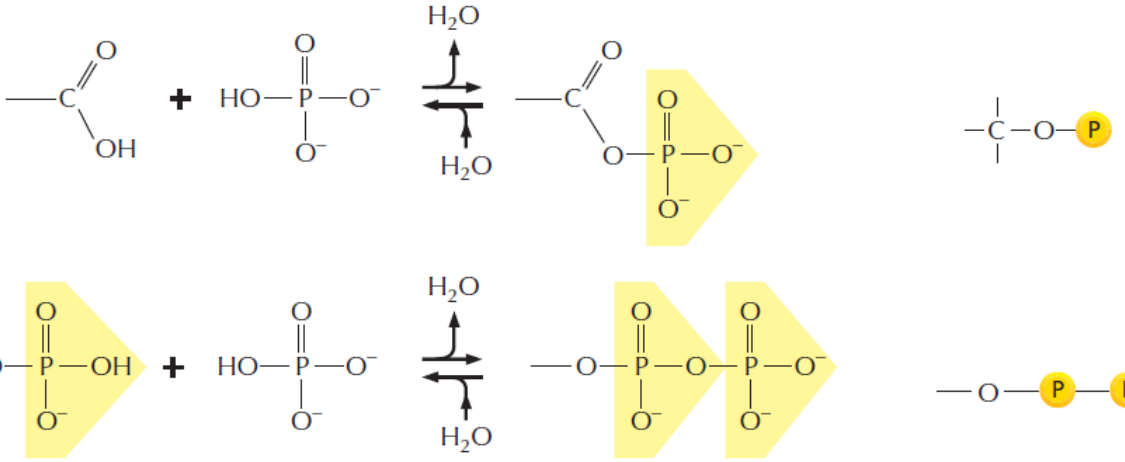
- **Hydroxyl group + P_i =**

phosphate ester

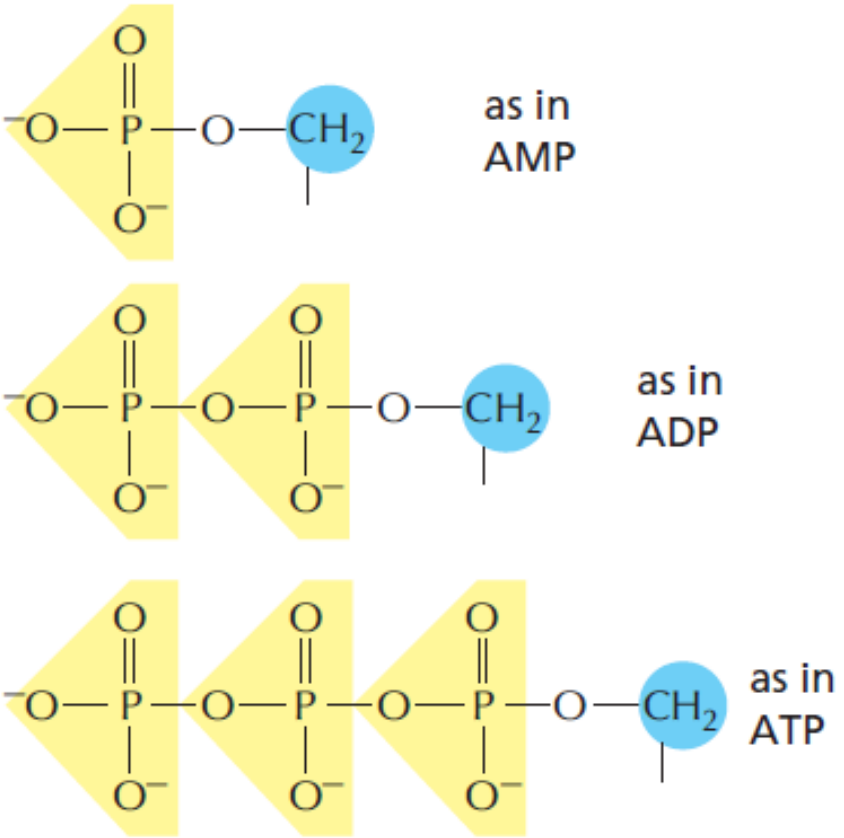


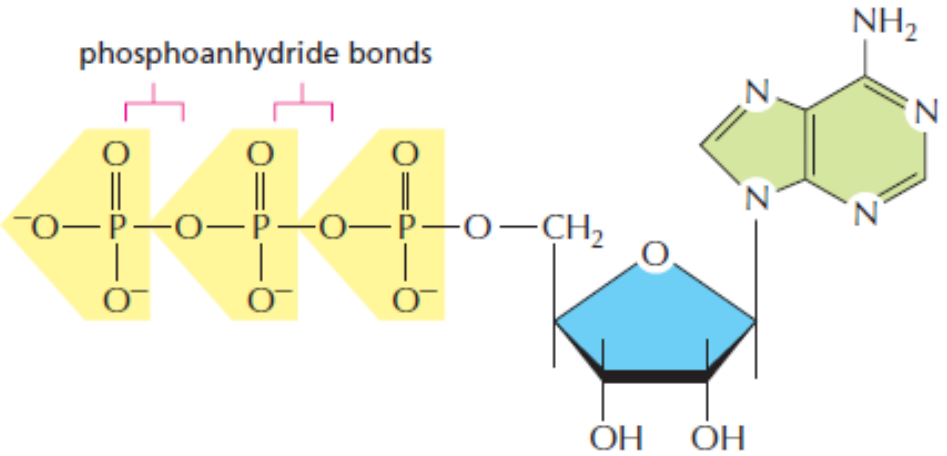
- **Carboxyl group + $(P_i)_n$ =**

anhydrids



PHOSPHATE IN NA

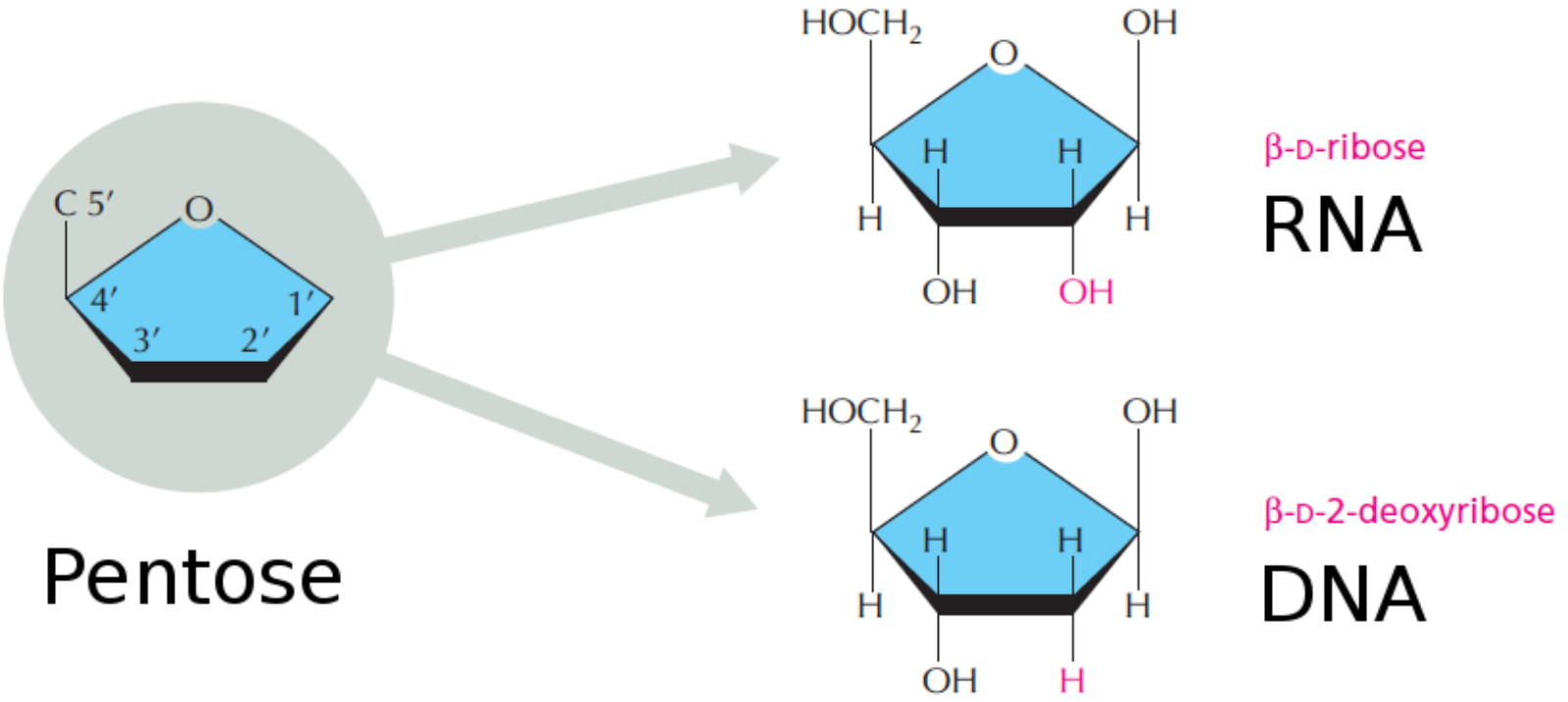




ATP

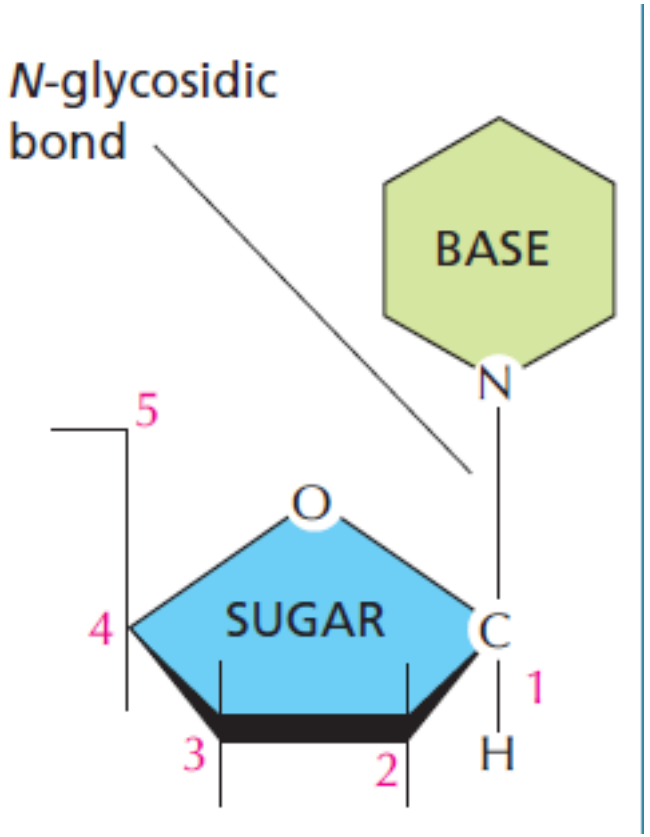
- **Mono-**
- **Di-**
- **Tri-**

SUGAR



- **DNA: deoxyribose (2'-position)**
- **RNA: ribose**

GLYCOSIDIC LINKAGE

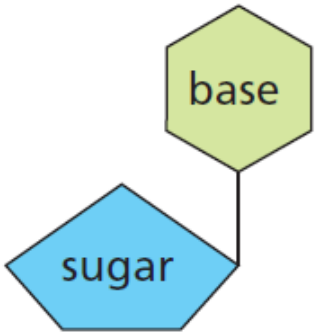


C1-base glycosidic linkage

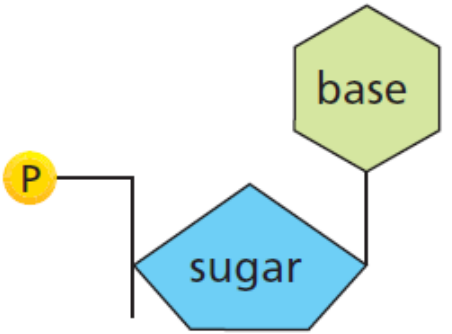
NUCLEOSIDES AND NUCLEOTIDES

BASE	NUCLEOSIDE	ABBR.
adenine	adenosine	A
guanine	guanosine	G
cytosine	cytidine	C
uracil	uridine	U
thymine	thymidine	T

AMP = adenosine monophosphate
dAMP = deoxyadenosine monophosphate
UDP = uridine diphosphate
ATP = adenosine triphosphate



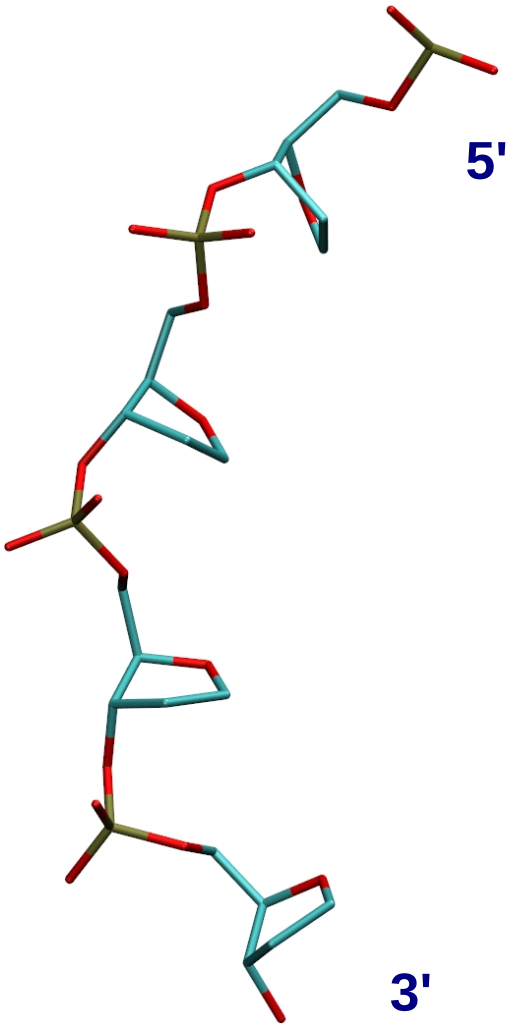
BASE + SUGAR = NUCLEOSIDE



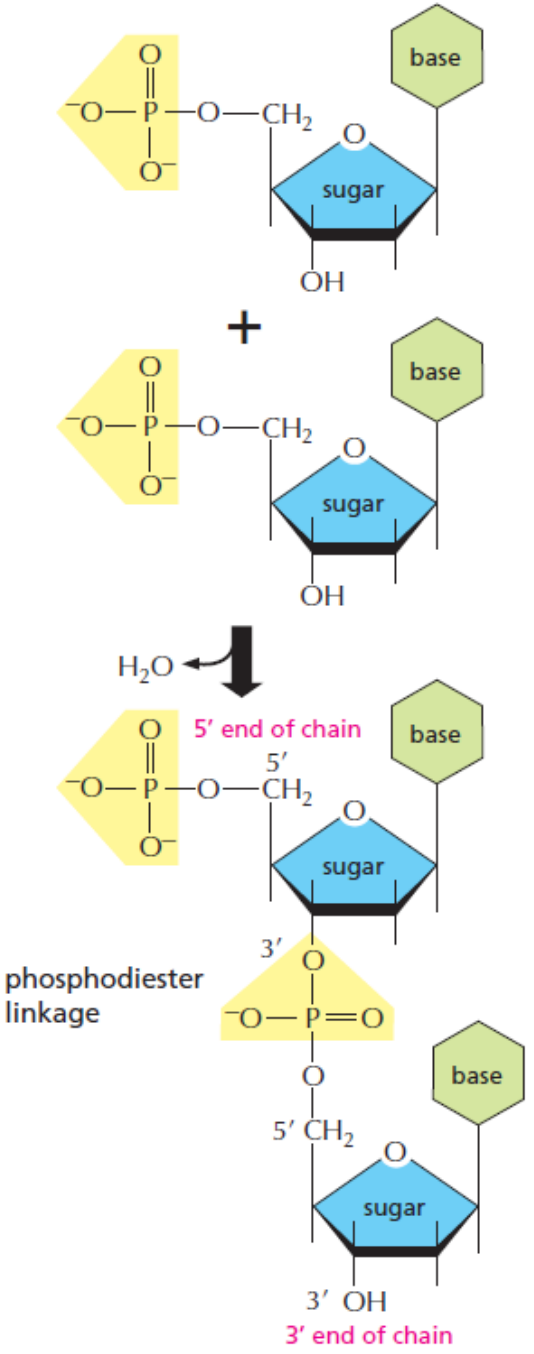
BASE + SUGAR + PHOSPHATE = NUCLEOTIDE

NA BACKBONE

Backbone = Phosphate Group + Deoxyribose



NA POLYMERIZATION

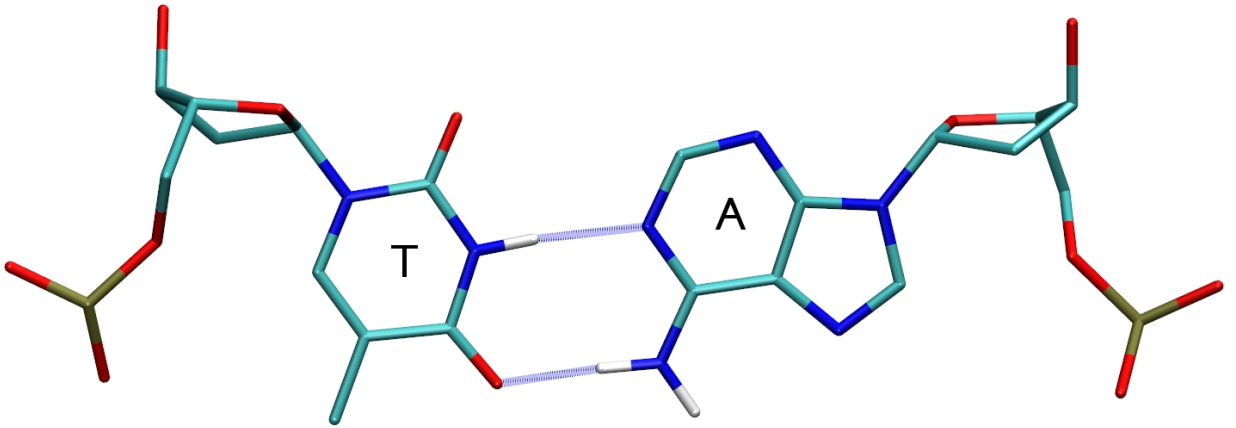


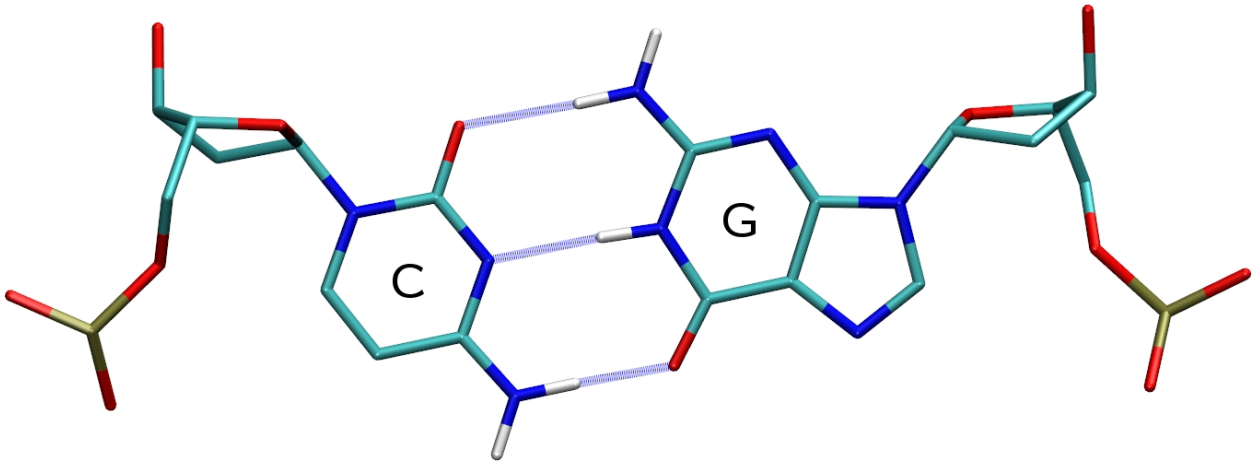
DNA STRUCTURE: COMPLEMENTARITY

- **Complementary pairing**

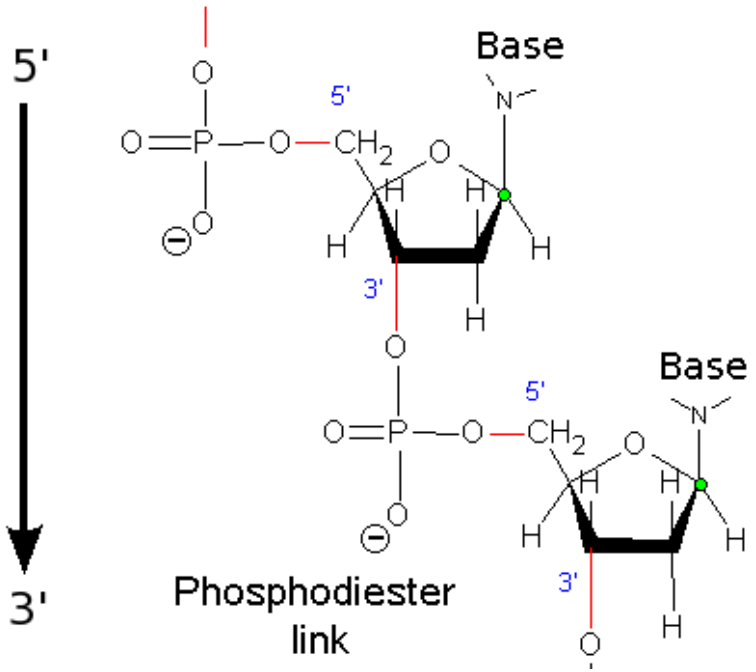
  - A-T (2 hydrogen bonds)

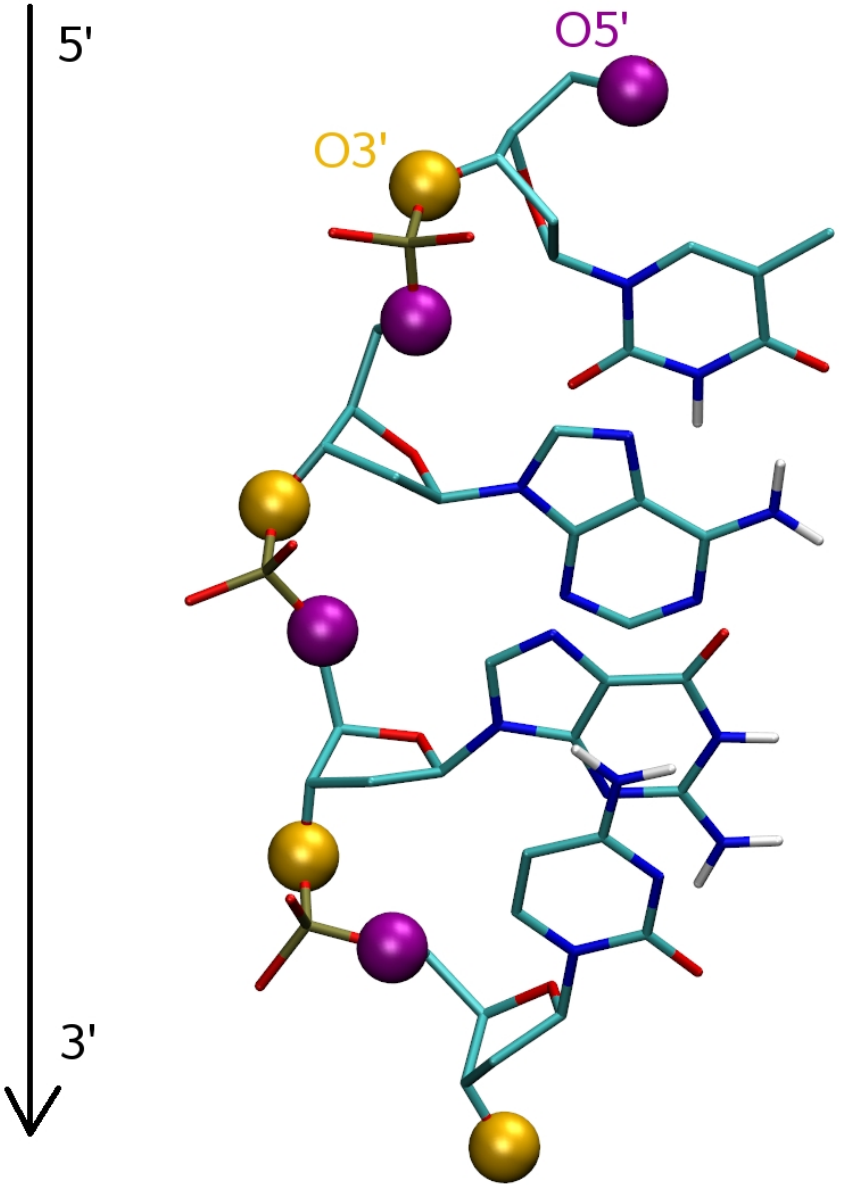
  - C-G (3 hydrogen bonds)



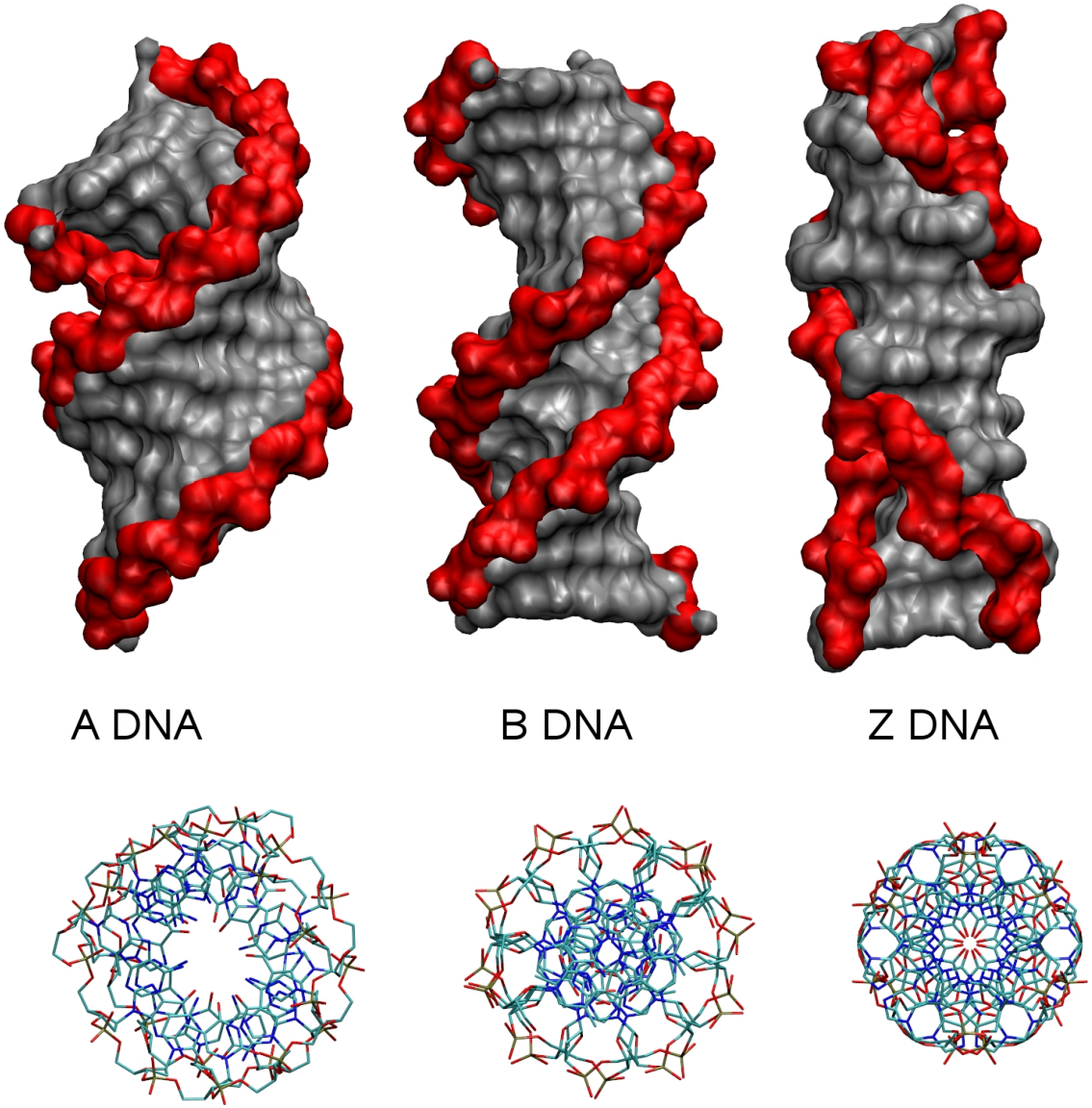


DNA STRUCTURE: SINGLE STRAND



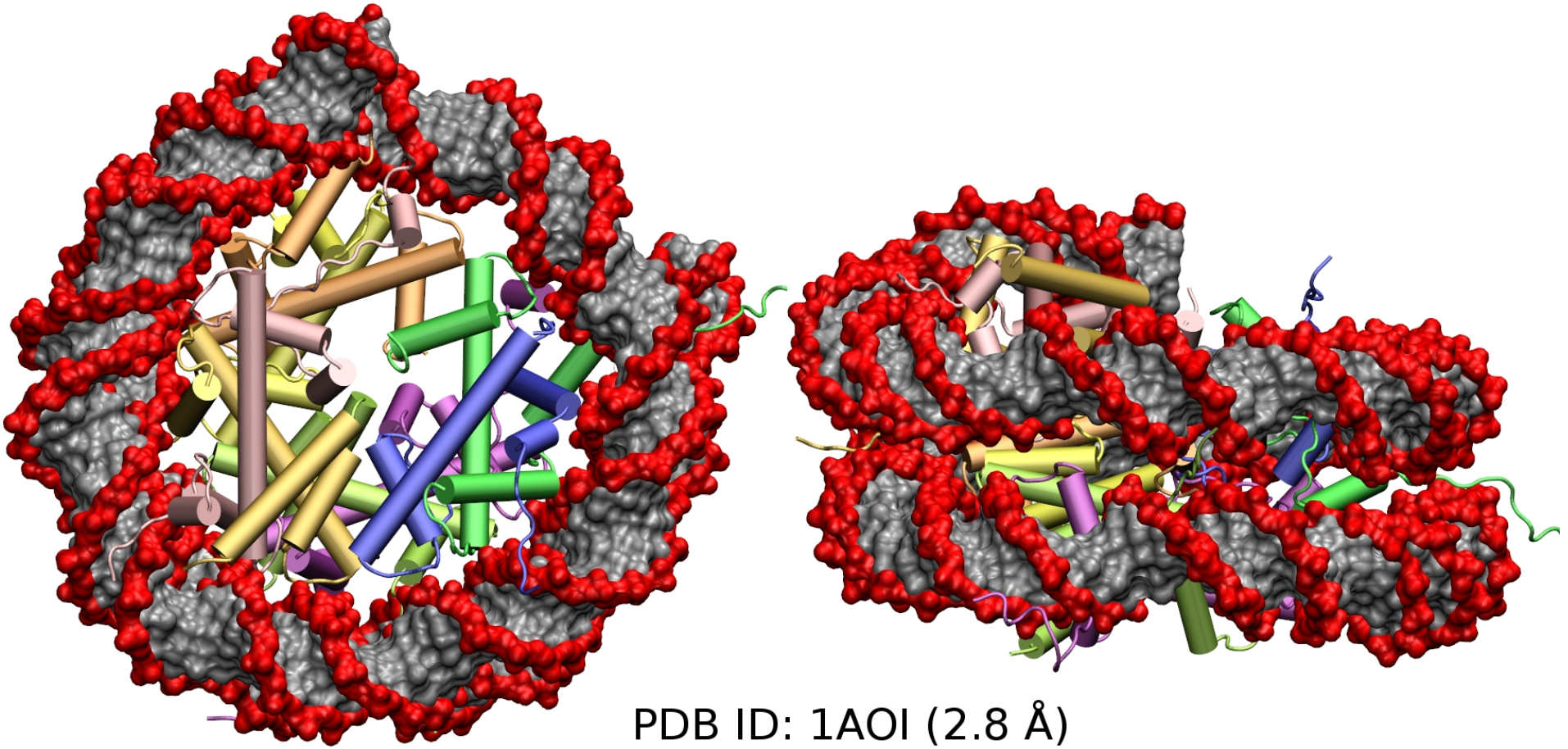


DNA STRUCTURE: DNA HELIX



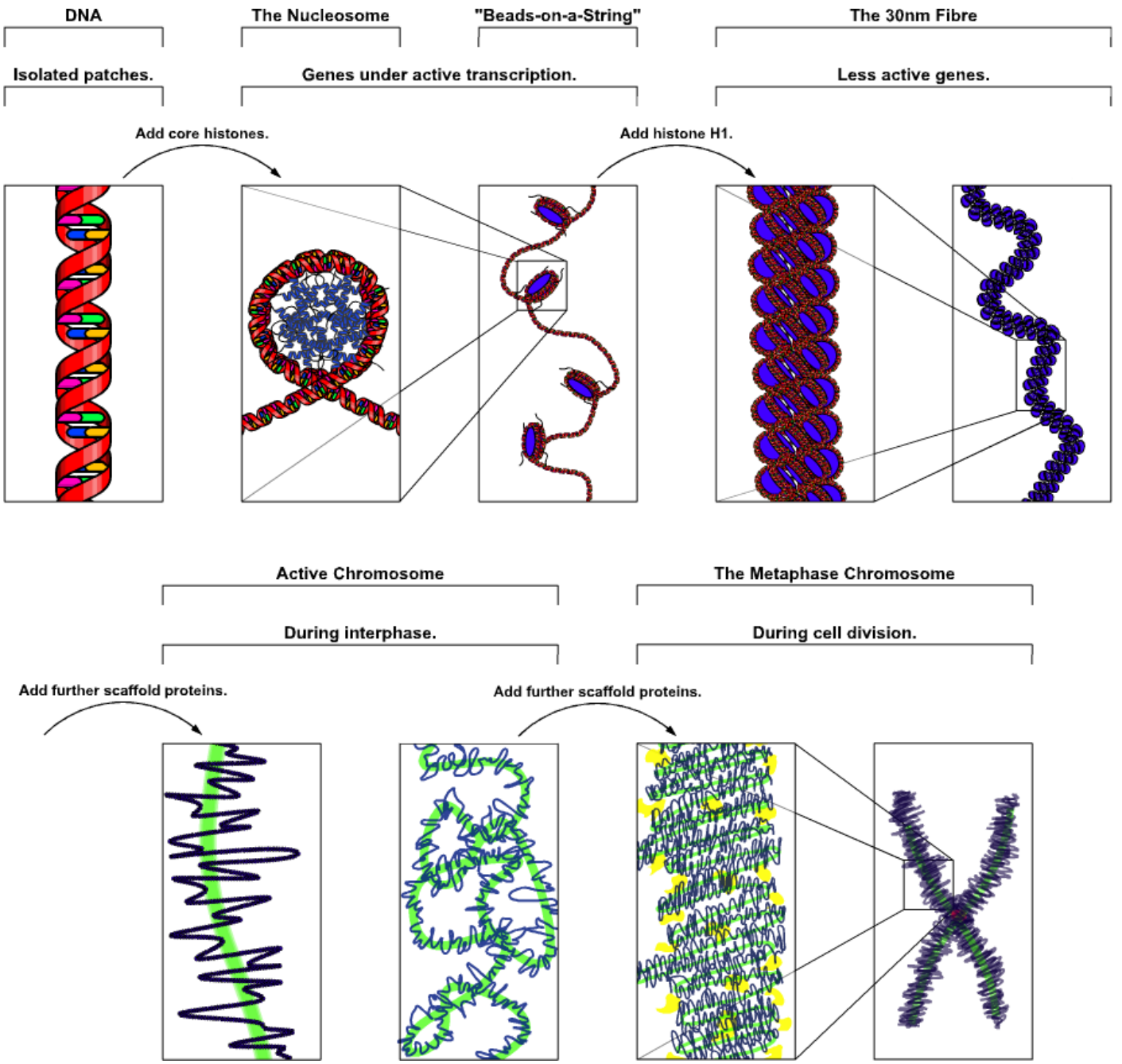
- **Usual structures: A, B, Z double helix**
- **Unusual structures: mismatched pairs, circular, triple, supercoiled etc.**

DNA STRUCTURE: NUCLEOSOME

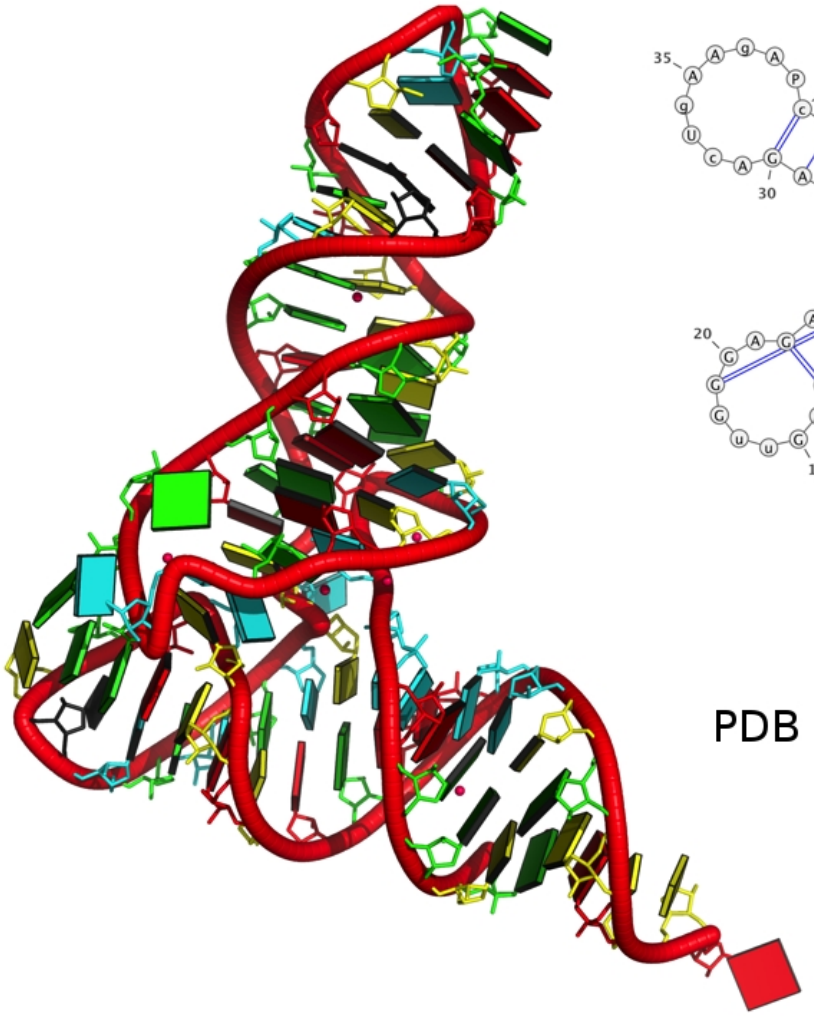


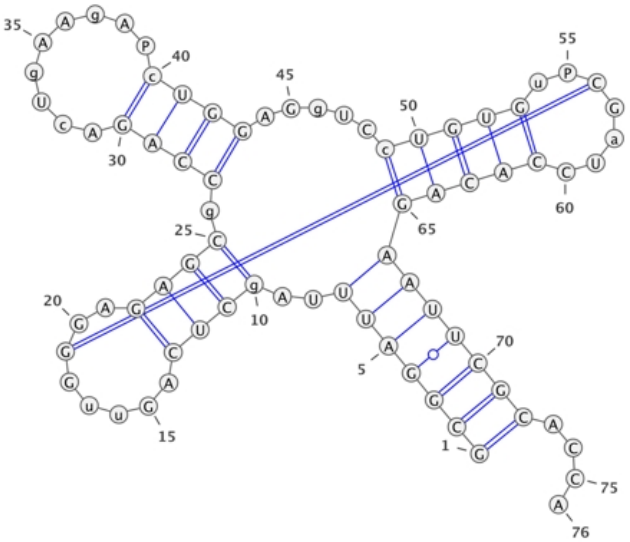
PDB ID: 1AOI (2.8 Å)

DNA STRUCTURE: HIGH ORDERS OF ORGANIZATION



RNA STRUCTURES





PDB ID: 1EHV (1.93 Å)

- **Complementarity: A-U, C-G**
- **High diversity**

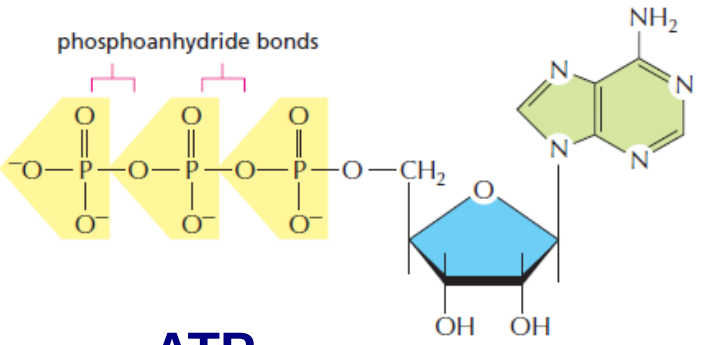
DNA *vs.* RNA

- Deoxyribose
- A, T, G, C
- Double-stranded
- Nucleus, mitochondria
- Less chemically reactive
- Self-replicating
- Mostly in B-form helix, sensitive to UV

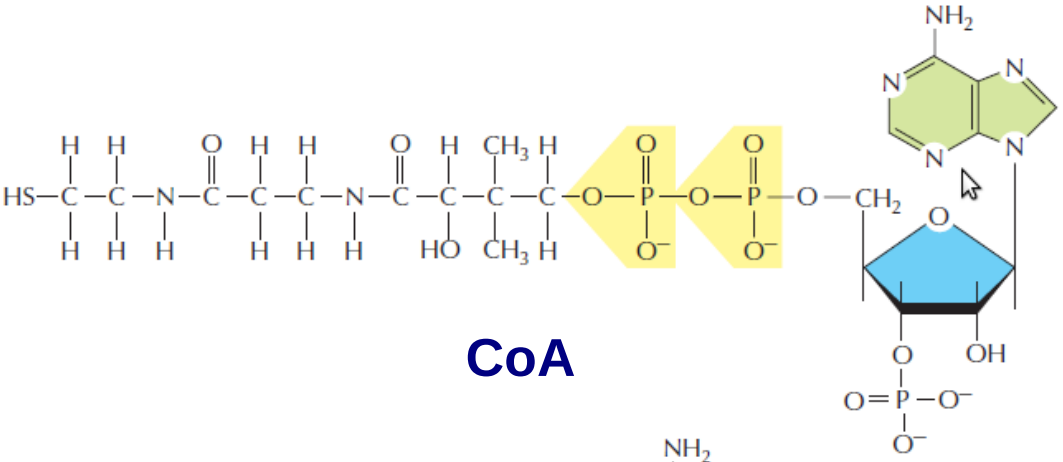
- Ribose
- A, U, G, C
- Single-stranded
- Nucleus, cytoplasm, ribosome
- More chemically reactive
- Synthetized from DNA
- Mostly in A-form helix, more resistant to UV

NA FUNCTION

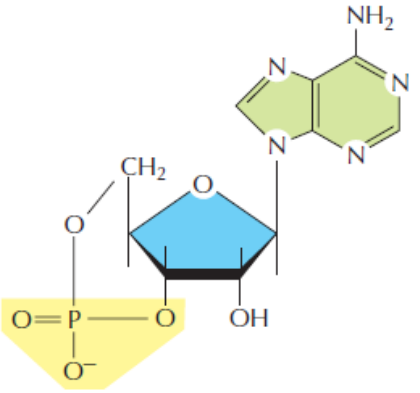
- Genetic information (DNA=>RNA)
- Energy carriers
- Co-factors (RNA in coenzymes, ribosomes)
- Signalling molecules



ATP



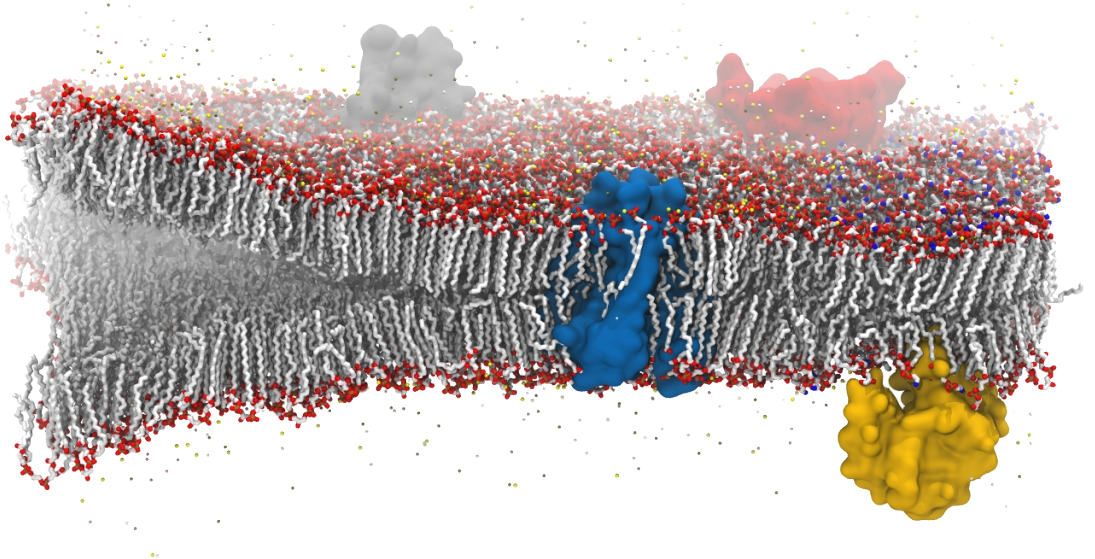
CoA



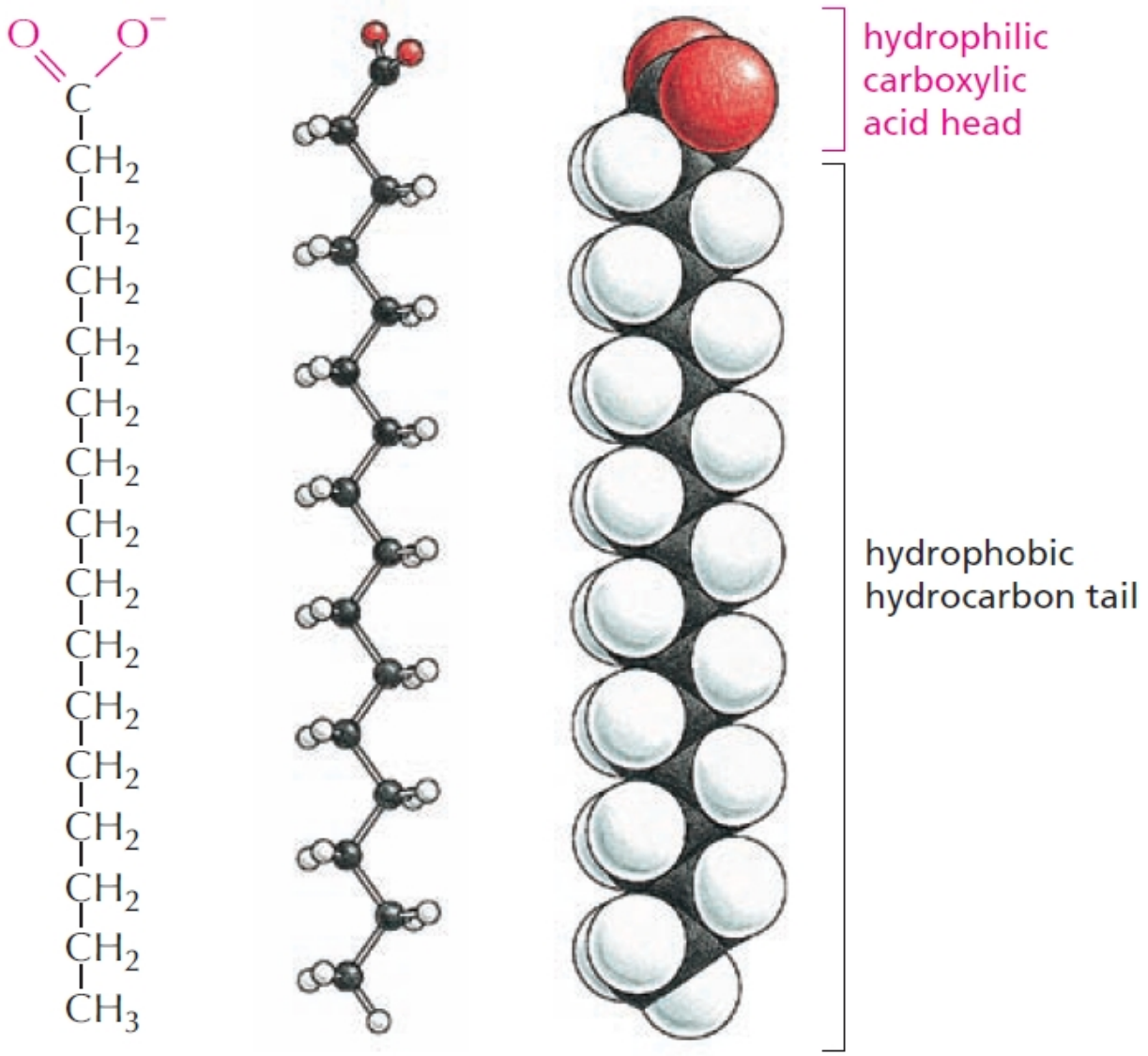
Cyclic AMP

LIPIDS

- Fatty acids
- Glycerolipids
- Glycerophospholipids
- Sphingolipids
- Sterol lipids
- Prenol lipids
- Saccharolipids
- Polyketides

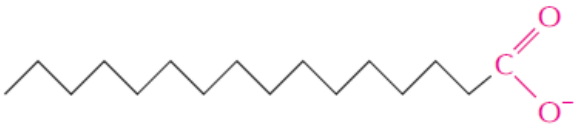


FATTY ACIDS

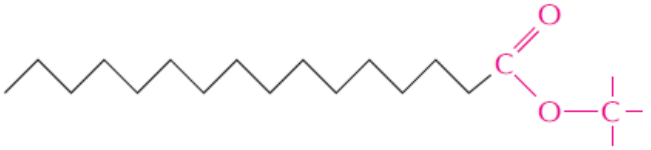


COO^- group can be covalently linked to other molecules

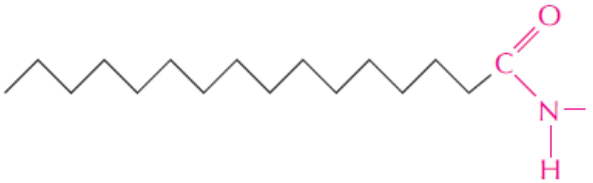
FATTY ACIDS: CARBOXYL GROUP



ionized

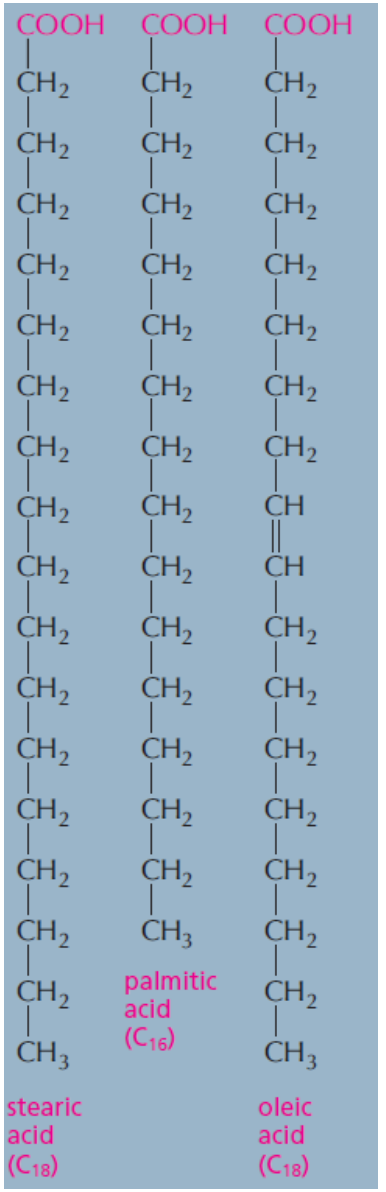


forms esters

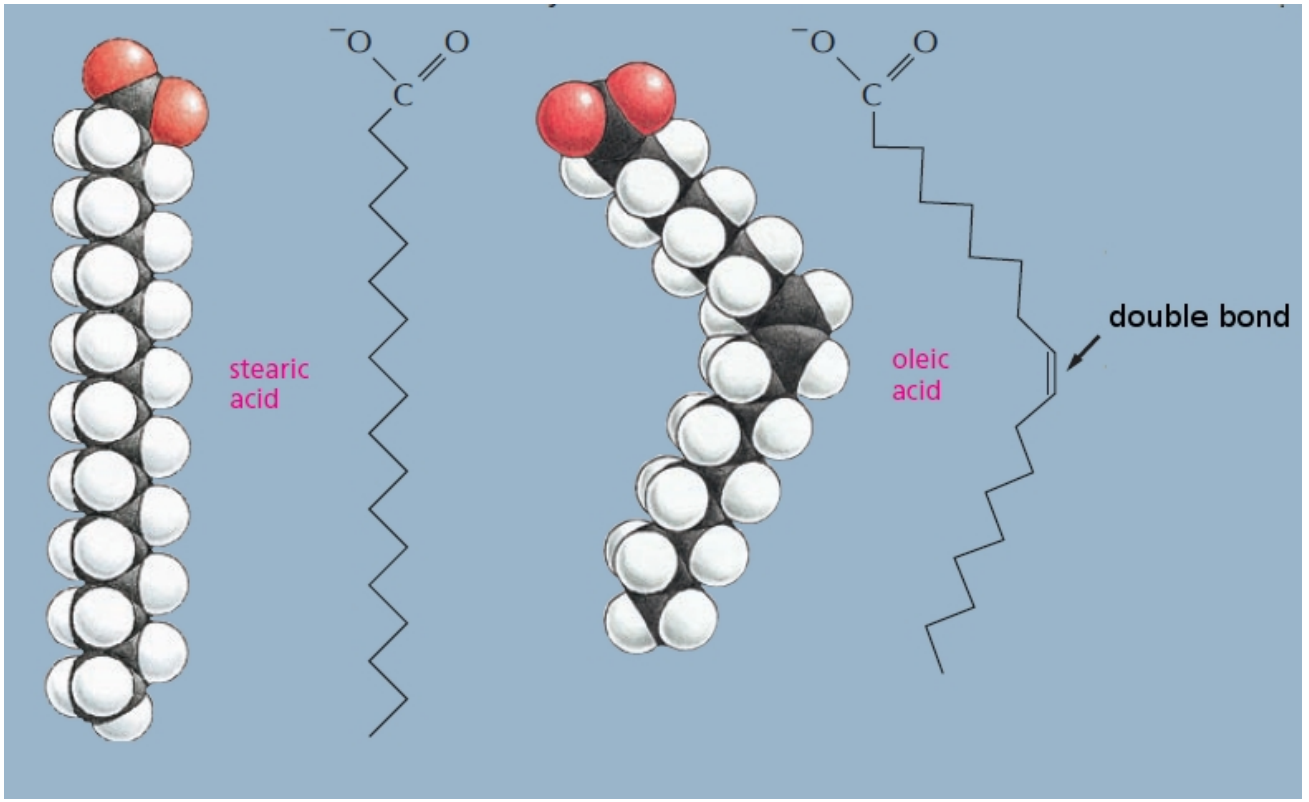


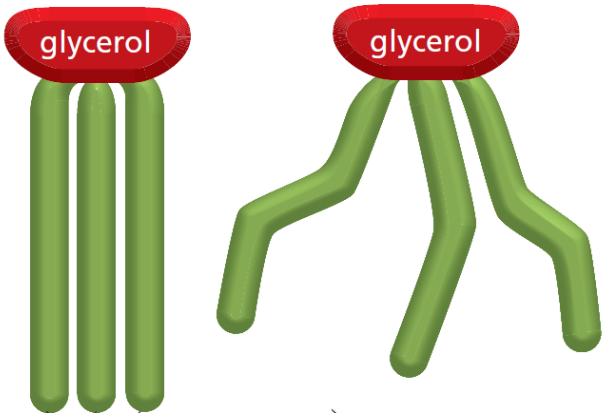
forms amides

COO^- group can be covalently linked to other molecules



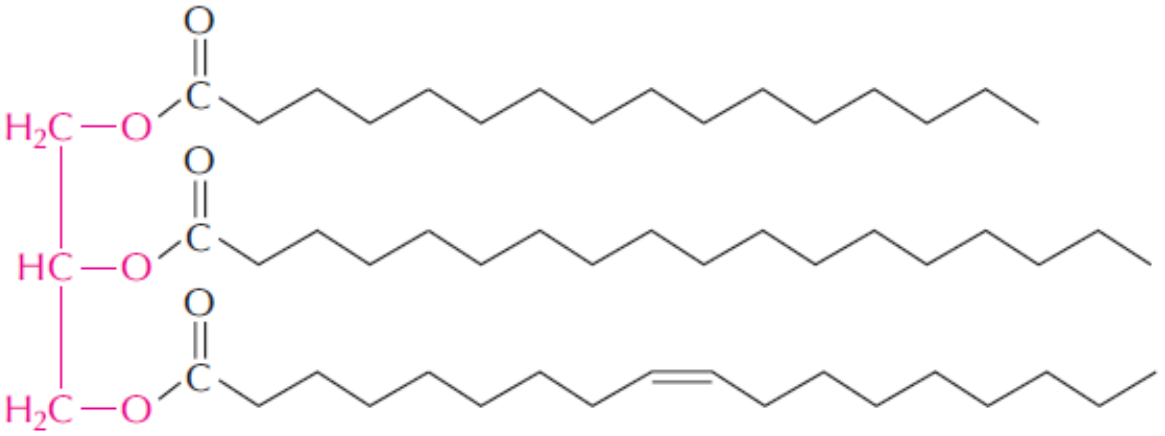
FATTY ACIDS: SATURATION

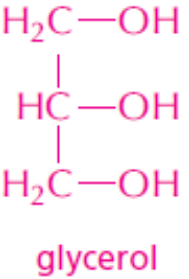




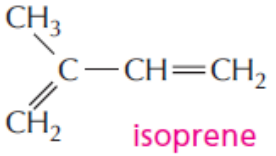
- **Saturated**
- **Unsaturated: more energy, structurally different**

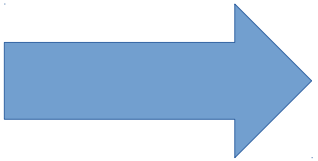
TRIACYLGLYCEROLS

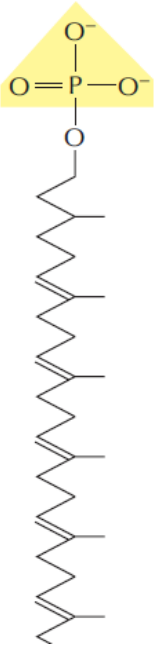




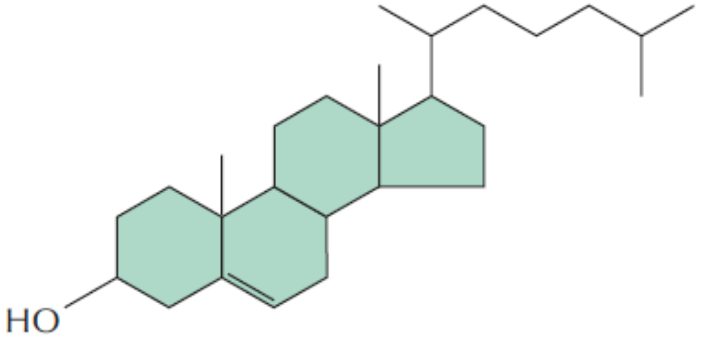
POLYISOPRENOIDS



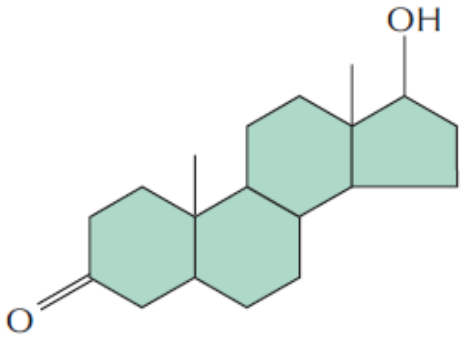




STEROIDS

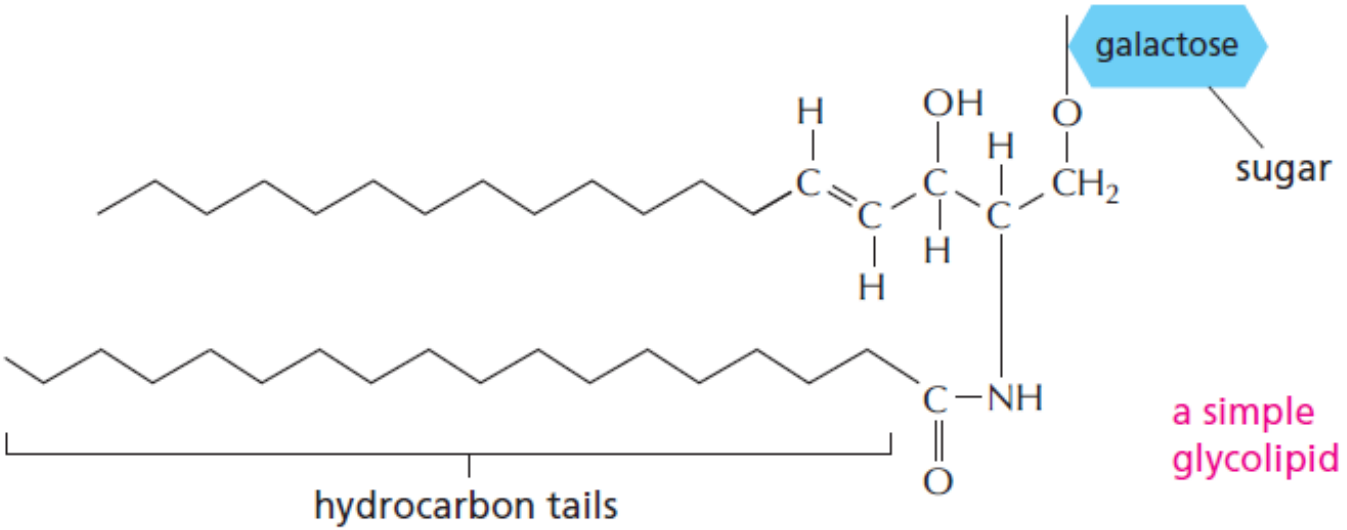


Cholesterol



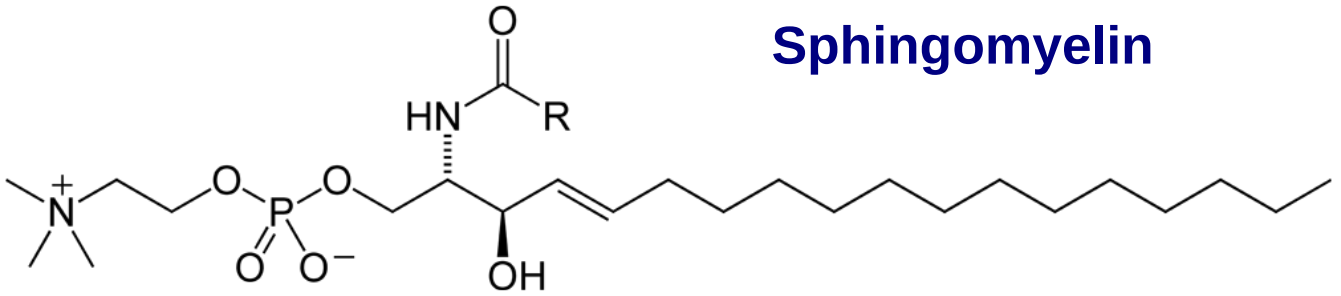
Testosterone

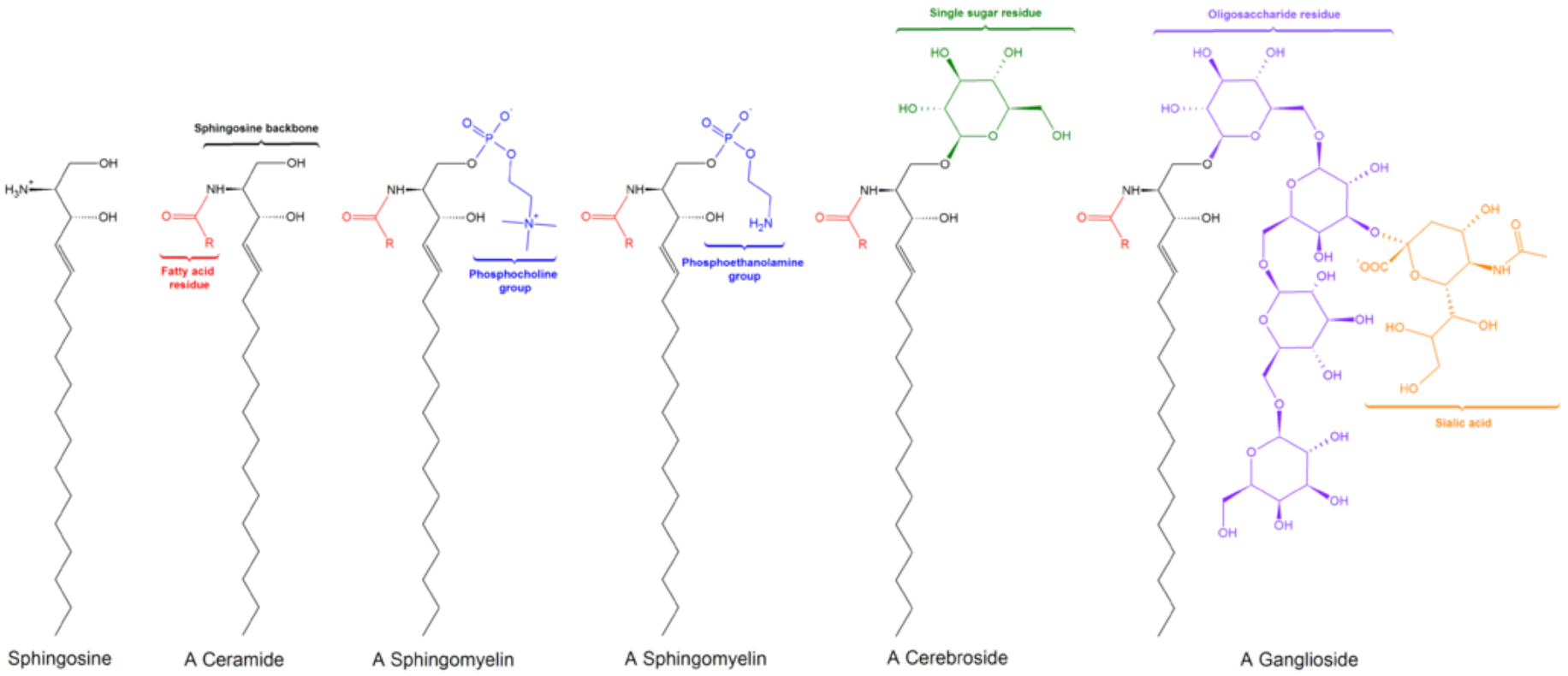
GLYCOLIPIDS



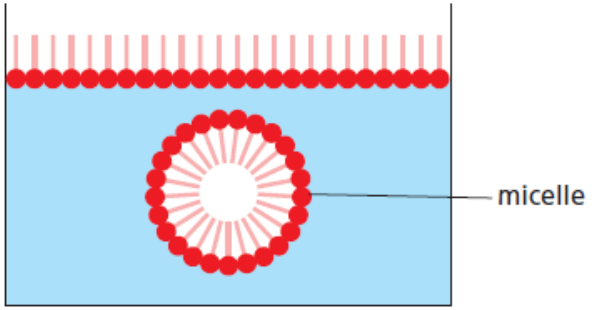
SPHINGOLIPIDS

Sphingomyelin

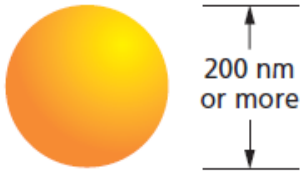




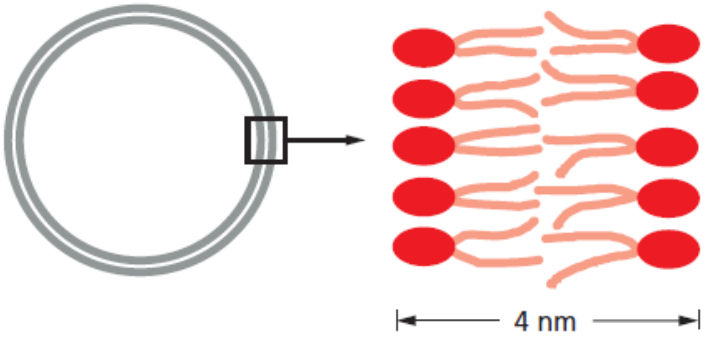
LIPID AGGREGATES



Fatty acids



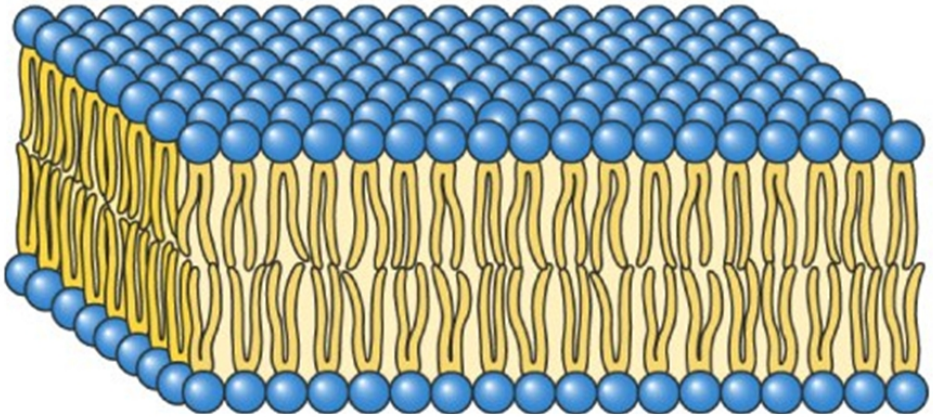
Triacylglycerols



Phospholipids/Glycolipids

LIPIDS FUNCTION

- Energy source (~6 x glucose; 1g ~ 2 g of carbohydrates)
- Energy storage: triglycerides
- Cell membrane structural components: phosphoglycerides, sphingolipids, steroids
- Lipid rafts organization
- Neurons protection (sphingolipids)
- Signaling
- Components of vitamins (A, D, E, K)

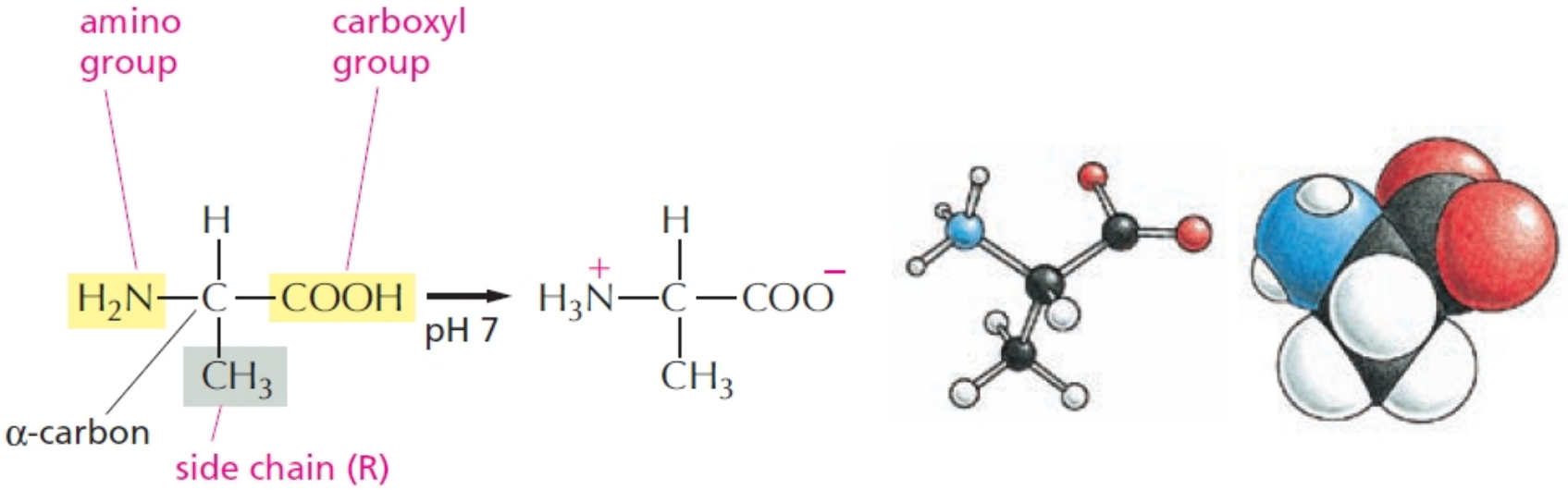


PROTEINS: BRIEF HISTORY

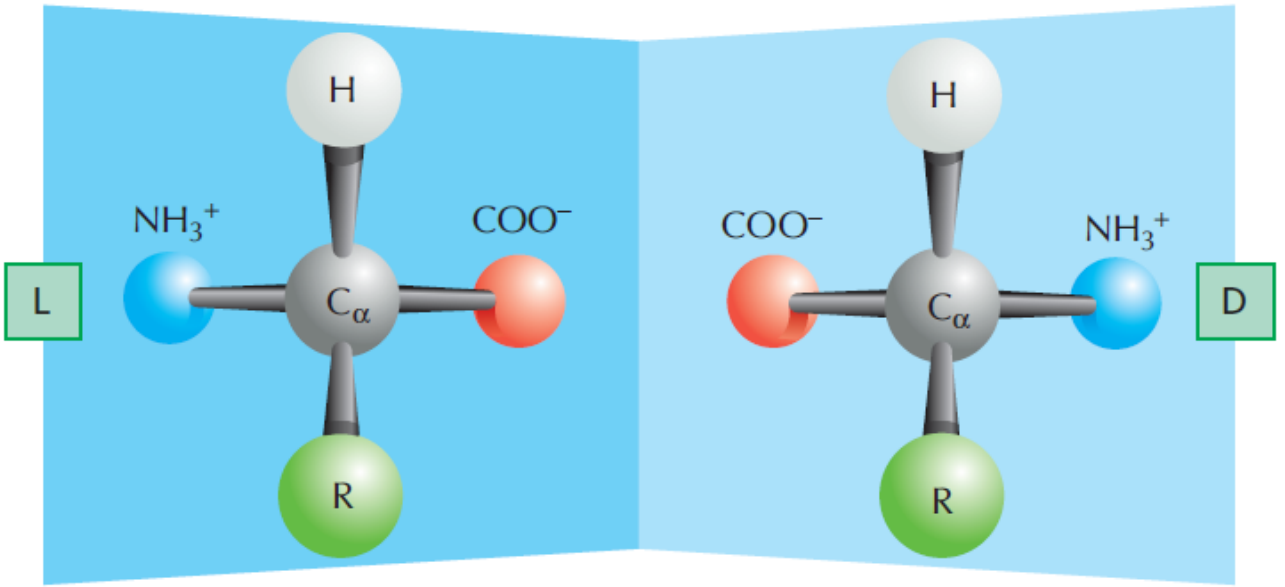
- XVIII centure. Fourcroy: gluten, fibrin, albumin, egg white coagulate and flocculate under heat and acid.
- 1838. Mulder: $C_{400}H_{620}N_{100}O_{120}P_1S_1$
- Berzelius introduces the term 'protein'.
- XX centure, beginning. Hoffmeister, Fischer: protein is a polypeptide.
- 1926. Sumner: urease is a protein.
- 1930s. Pauling: first predictions of secondary structures.
- 1949. Sanger: sequencing.
- 1950s. First extractions of proteins.
- 1958. Perutz and Kendrew: first structures of hemaglobin and myoglobin.

Francois Fourcroy (1755-1809)

AMINO ACIDS



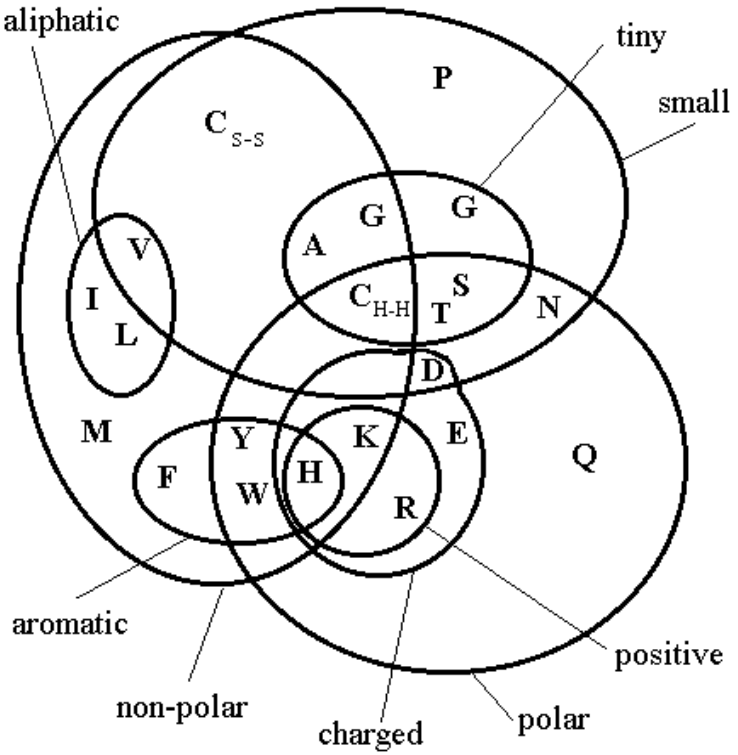
Neutral form **Zwitterion**



In nature L prevail

AMINO ACIDS CLASSIFICATIONS

- **Polarity**
  - **- basic**
  - **- acidic**
  - **- uncharged polar**
  - **- non-polar**
- **Aromaticity/aliphaticity**
  - **- Aromatic (F, Y, W)**
  - **- Aliphatic**
- **Size**
- **Essential (F, V, T, W, M, I, K, H), conditionally essential (R, C, G, Q, P, Y)**

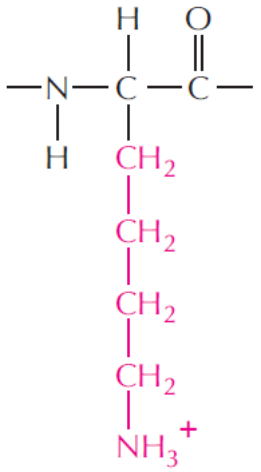


AMINO ACIDS: CHARGED

Positive

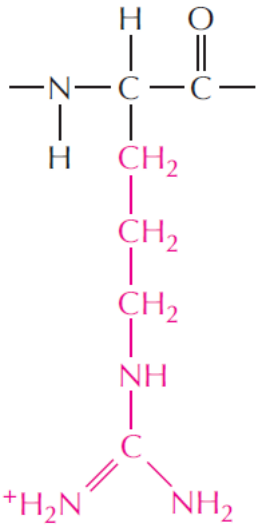
lysine

(Lys, or K)



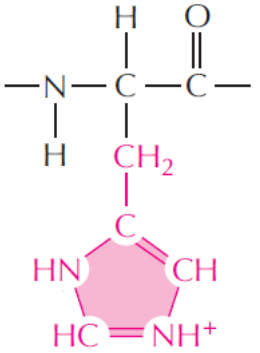
arginine

(Arg, or R)



histidine

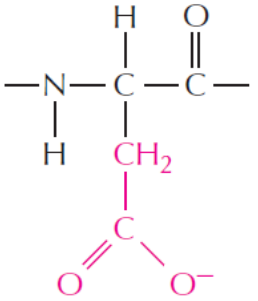
(His, or H)



Negative

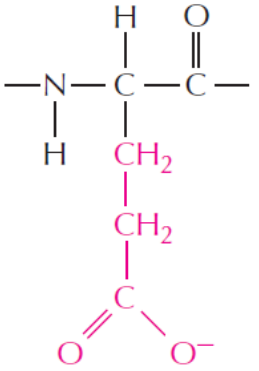
aspartic acid

(Asp, or D)

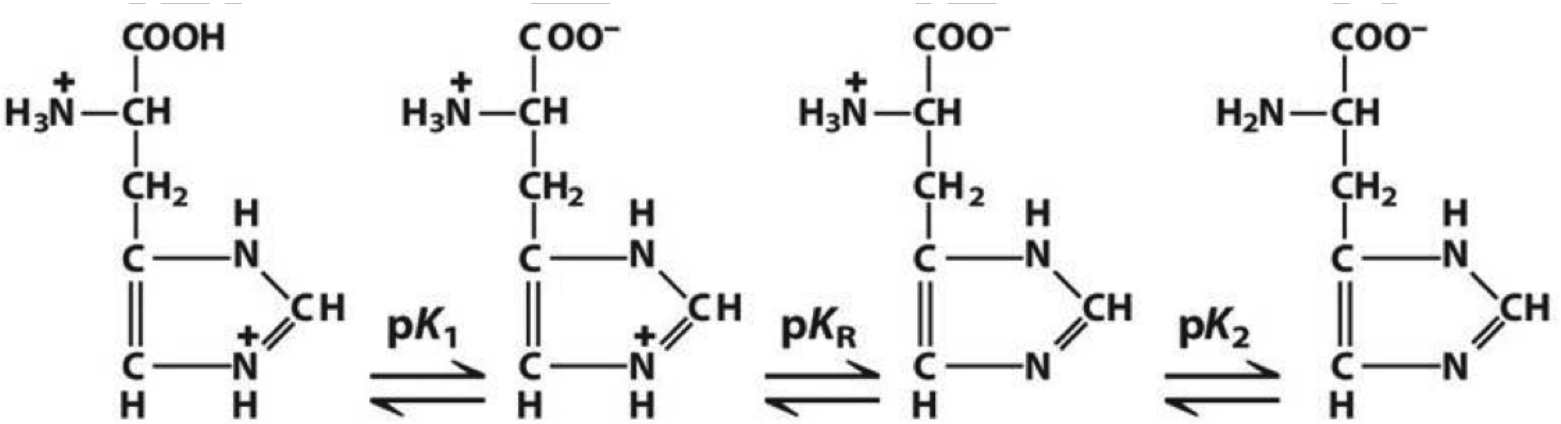


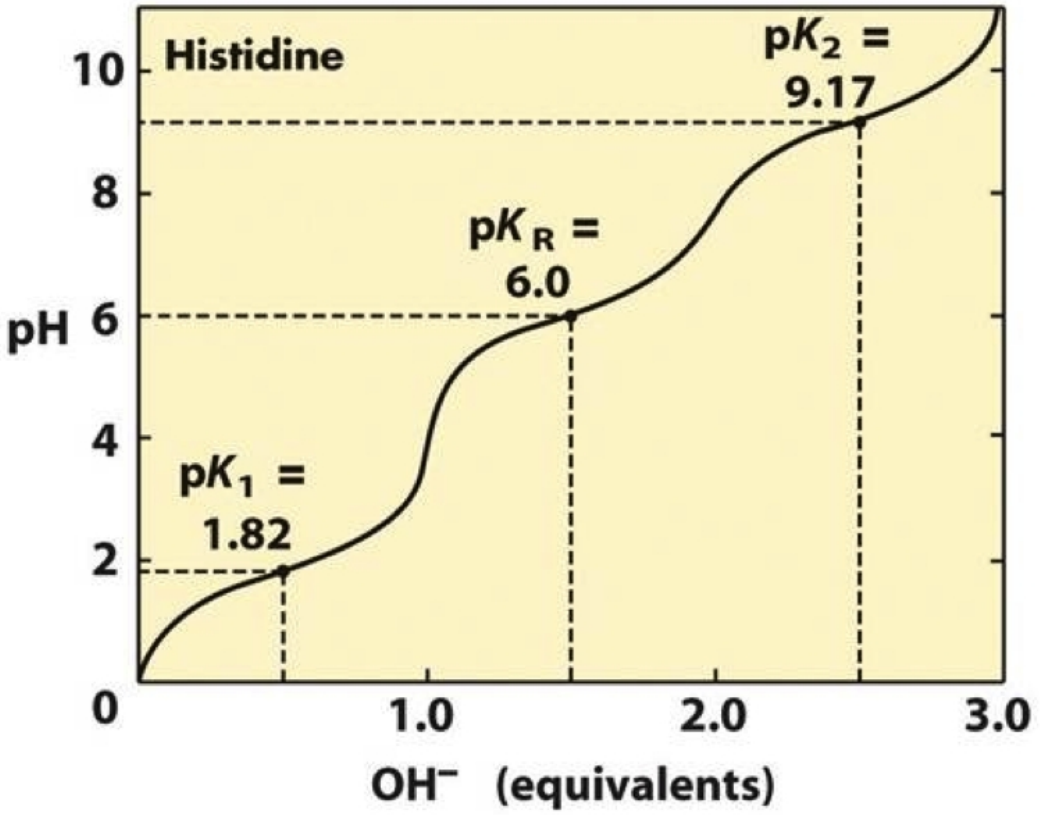
glutamic acid

(Glu, or E)



AMINO ACIDS: HISTIDINE

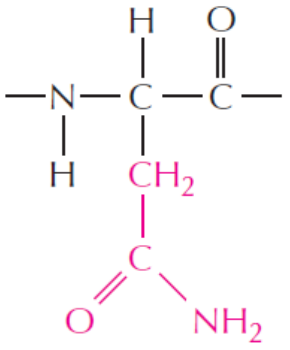




AMINO ACIDS: POLAR

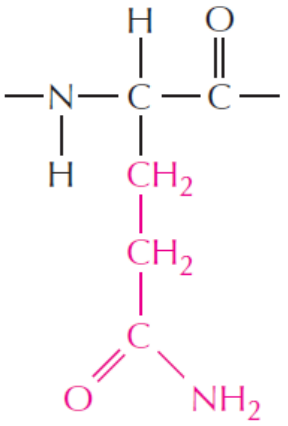
asparagine

(Asn, or N)



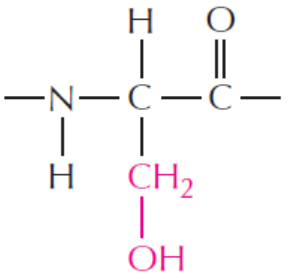
glutamine

(Gln, or Q)



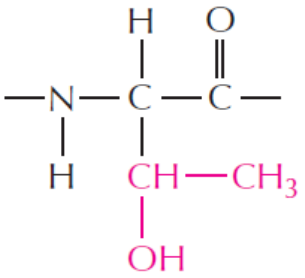
serine

(Ser, or S)



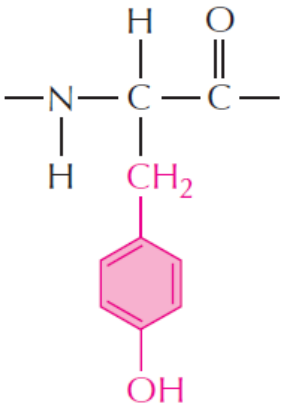
threonine

(Thr, or T)



tyrosine

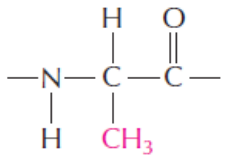
(Tyr, or Y)



AMINO ACIDS: UNPOLAR

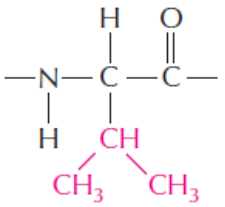
alanine

(Ala, or A)



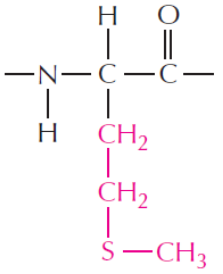
valine

(Val, or V)



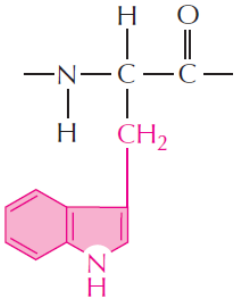
methionine

(Met, or M)



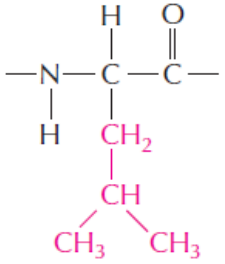
tryptophan

(Trp, or W)



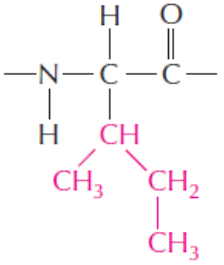
leucine

(Leu, or L)



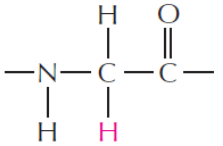
isoleucine

(Ile, or I)



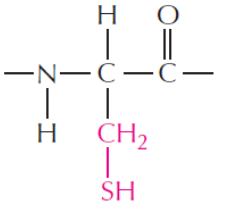
glycine

(Gly, or G)



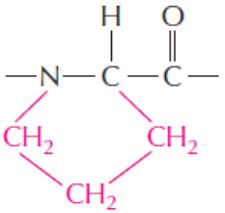
cysteine

(Cys, or C)



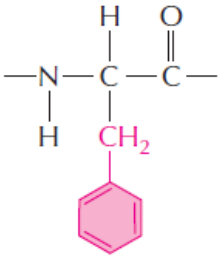
proline

(Pro, or P)

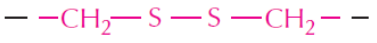


phenylalanine

(Phe, or F)

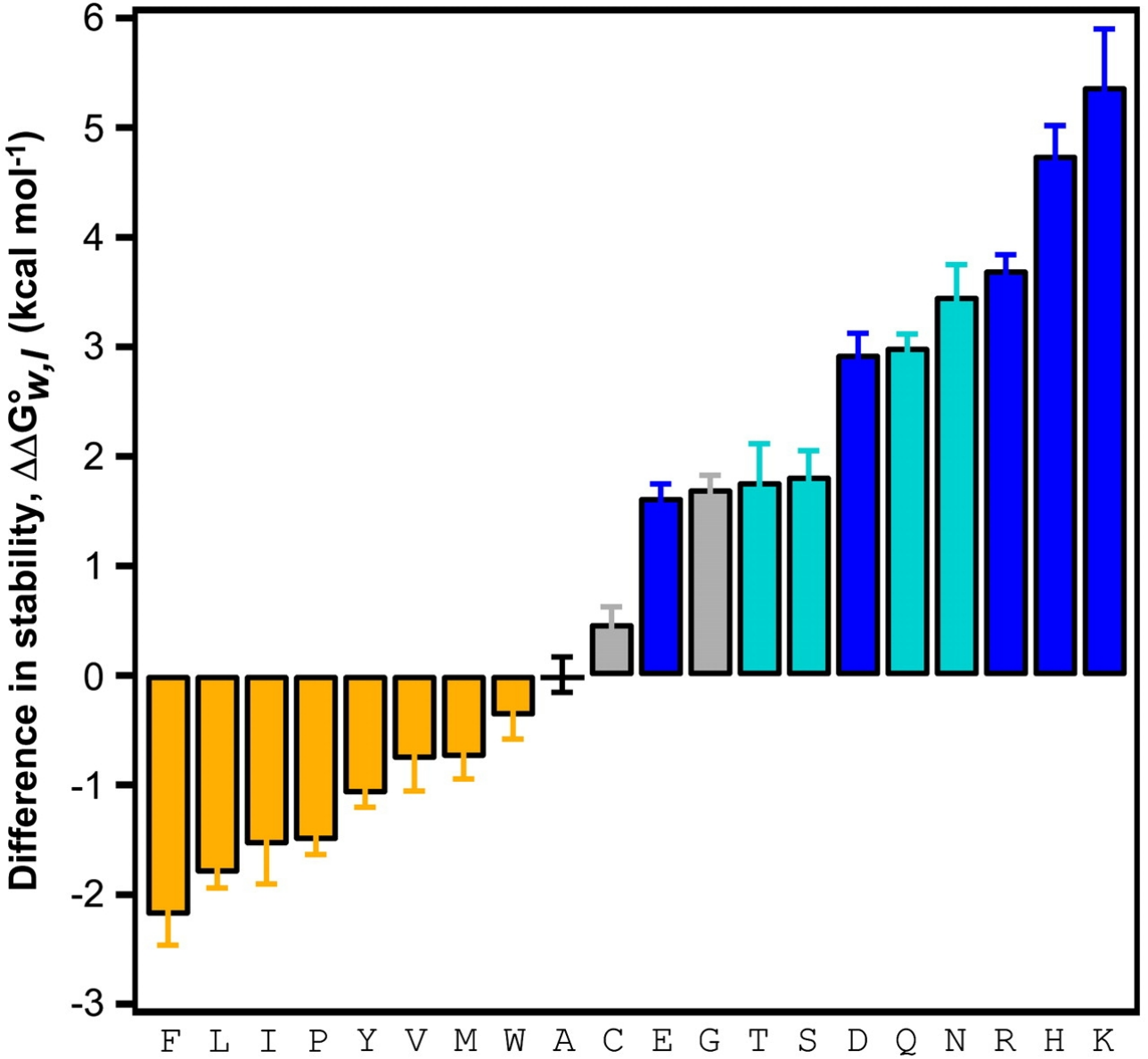


Disulfide bond



Proline is *IMINO*acid

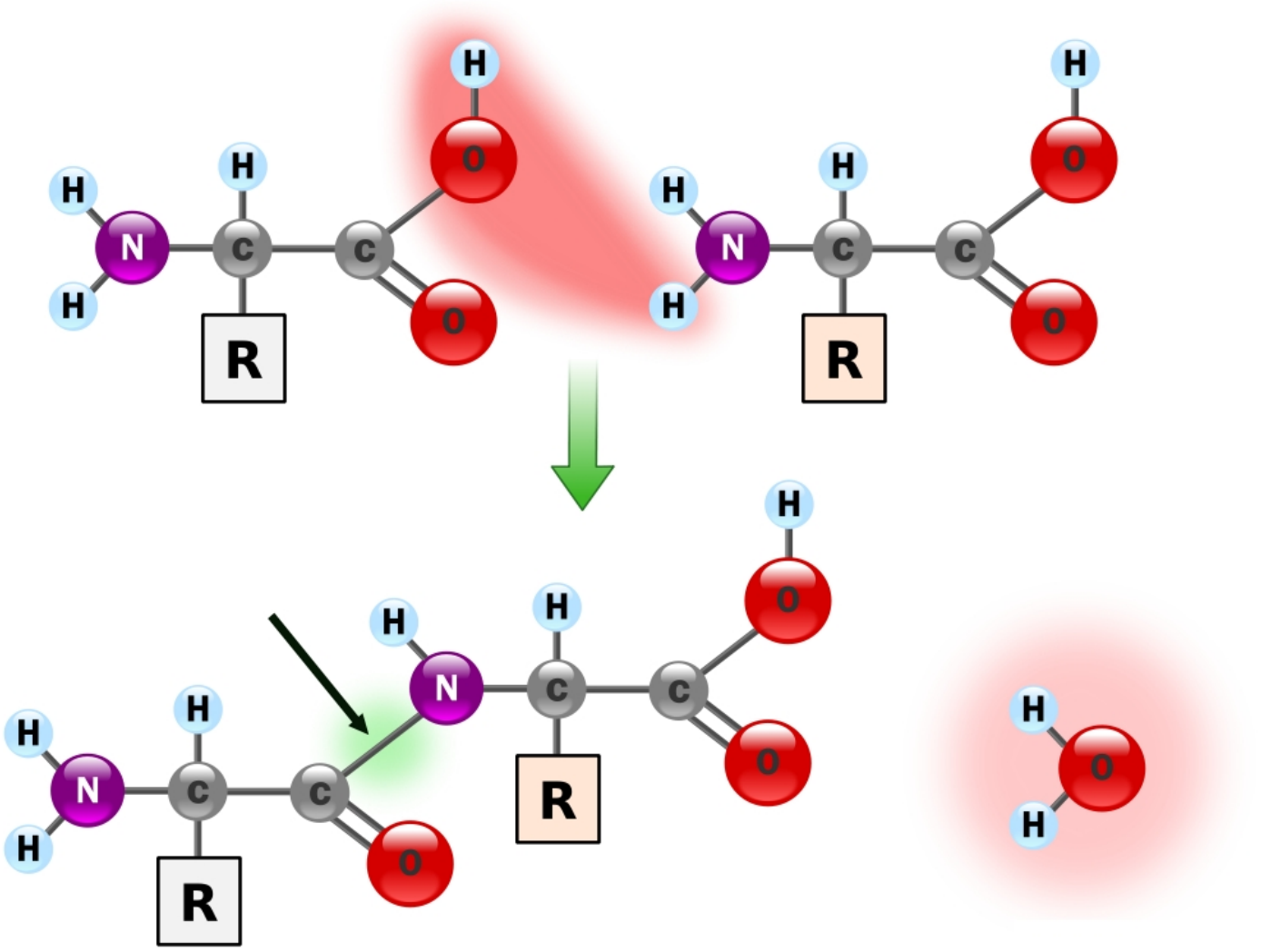
AMINO ACIDS: HYDROPHOBICITY



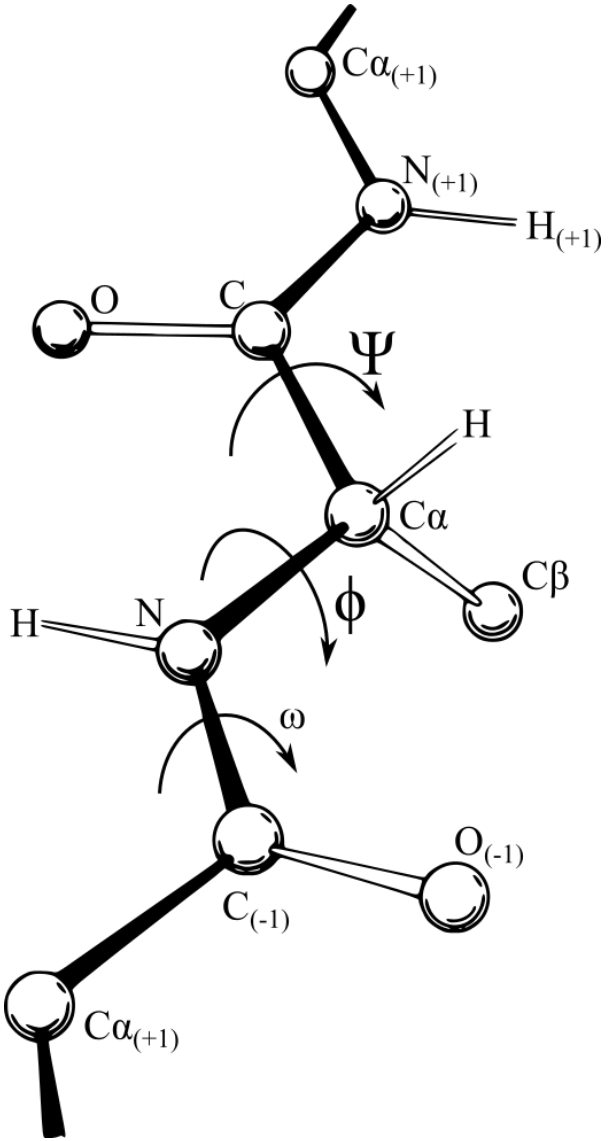
Index of hydrophobicity for amino acids: equilibrium constant between water and nonpolar solvent.

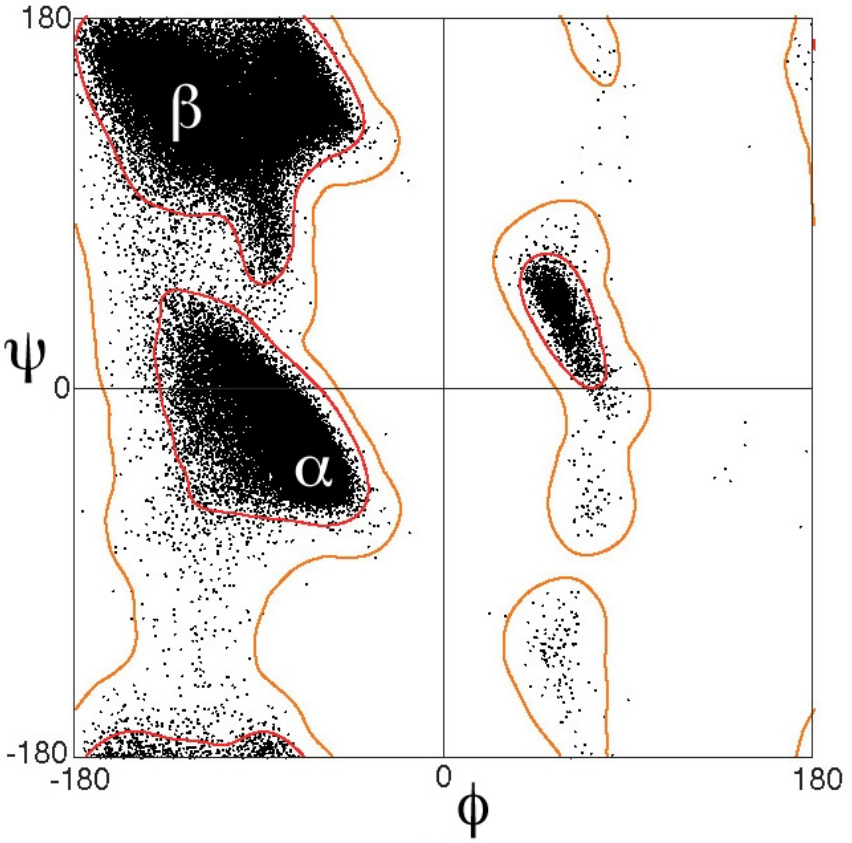
PEPTIDE BOND

Reaction of condensation: AA_1-OH + H-AA_2 = AA_1-AA_2 + H-OH



PEPTIDE BOND STRUCTURAL CHARACTERISTIC: RAMACHANDRAN PLOT



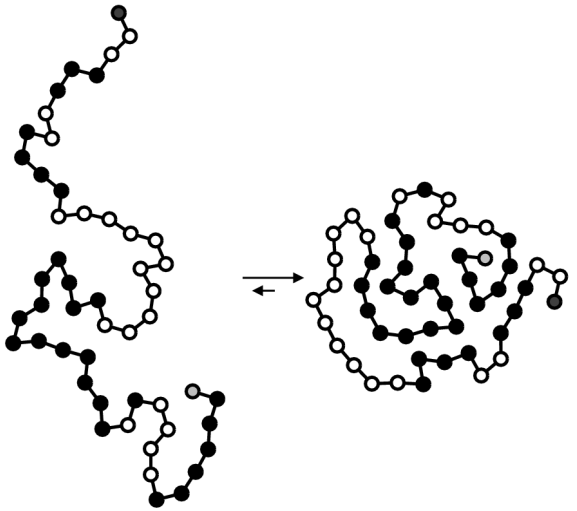


AA-PEPTIDE-PROTEIN

- AA – monomer
- Peptide – oligomer (2-20...40 aa)
- Protein – polymer

PROTEIN STRUCTURE

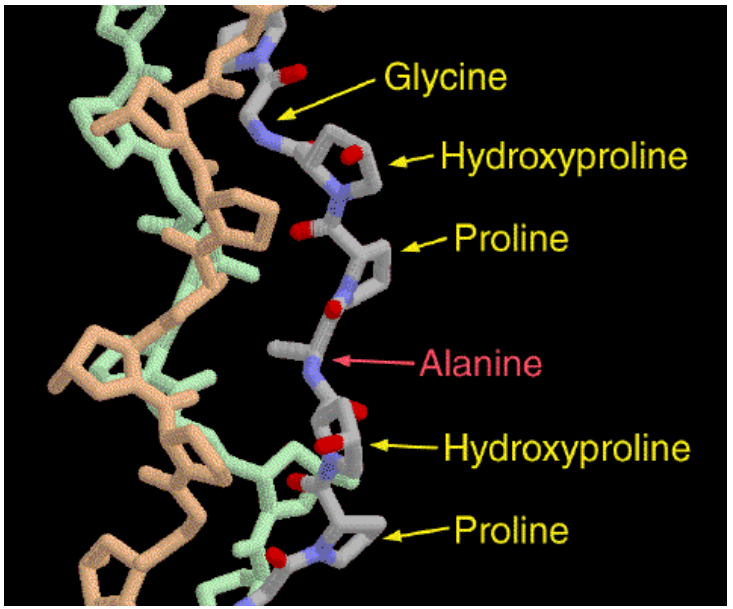
- Primary (sequence)
- Secondary (α-helix, β-sheet, 3_{10}-helix, π-helix)
- Tertiary



CHEMICAL MODIFICATIONS OF PROTEINS

Formation or breakage of covalent bonds in proteins

- **Disulfide bonds**
- **Addition of chemical groups:**
  - **phosphorylation (phosphorylated Tyr)**
  - **glycosylation (glycoproteins)**
  - **methylation (elongated Ala)**
  - **hydroxylation (hydroxy-Pro)**
  - **carboxylation (carboxy-Glu)**
- **Truncation:**
  - **intermolecular cleavage**
  - **self-cleavage**
- **Ubiquitination**
- **Sel introduction (Selenocysteine, seleomethionine)**

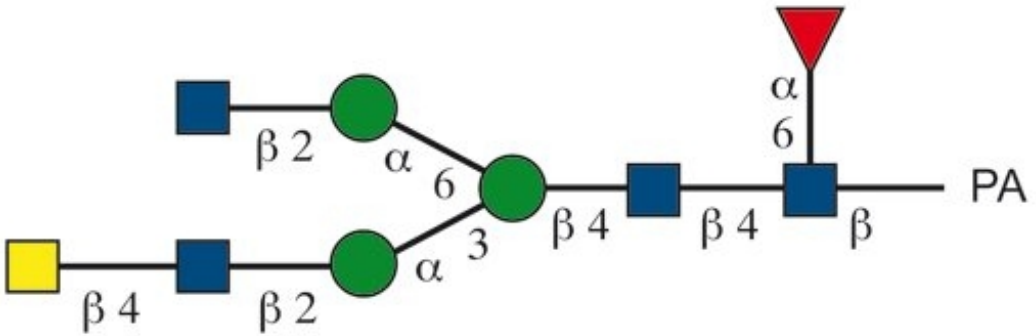


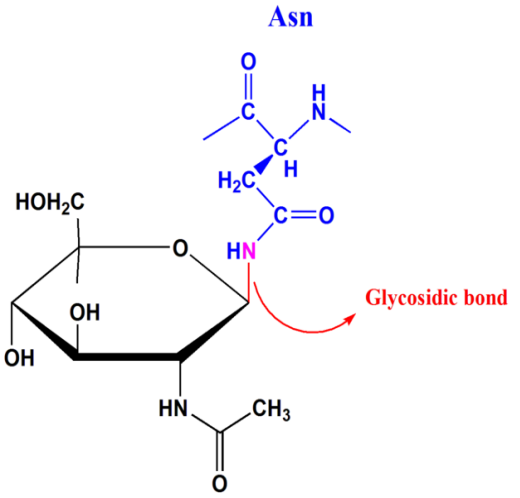
PROTEINS GLYCOSYLATION

Condensation reaction:

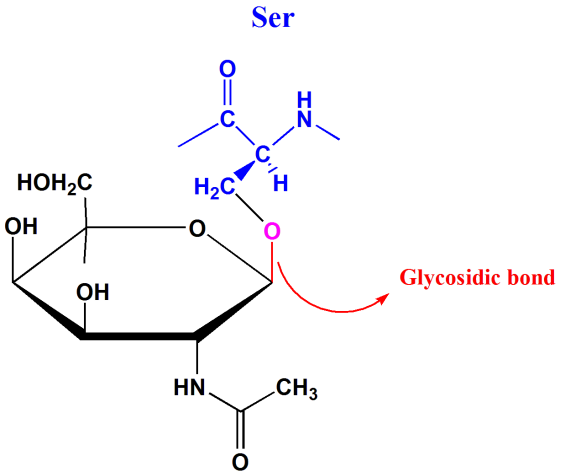
protein + carbohydrate = protein-carbohydrate + H_2O

- **N-glycosylation: Asn**
- **O-glycosylation: Thr, Ser, Tyr, HO-Lys, HO-Pro**





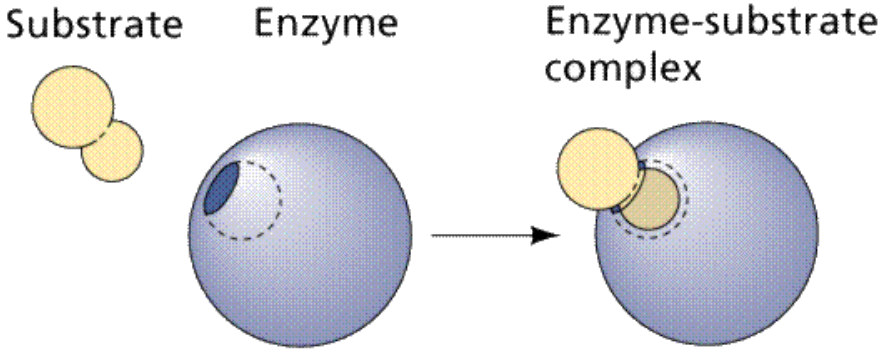
N-linked GlcAC

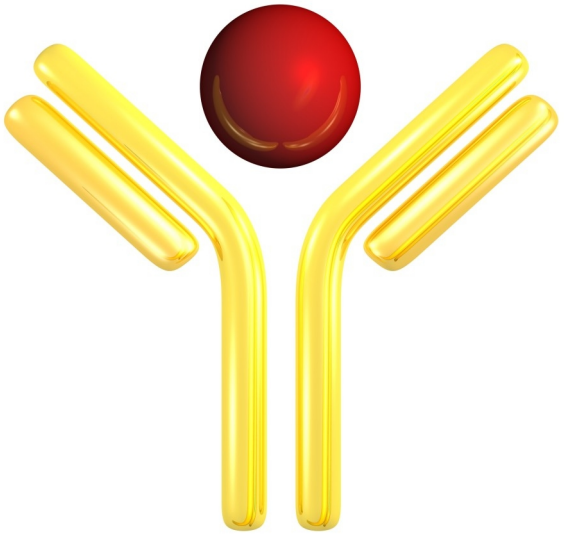


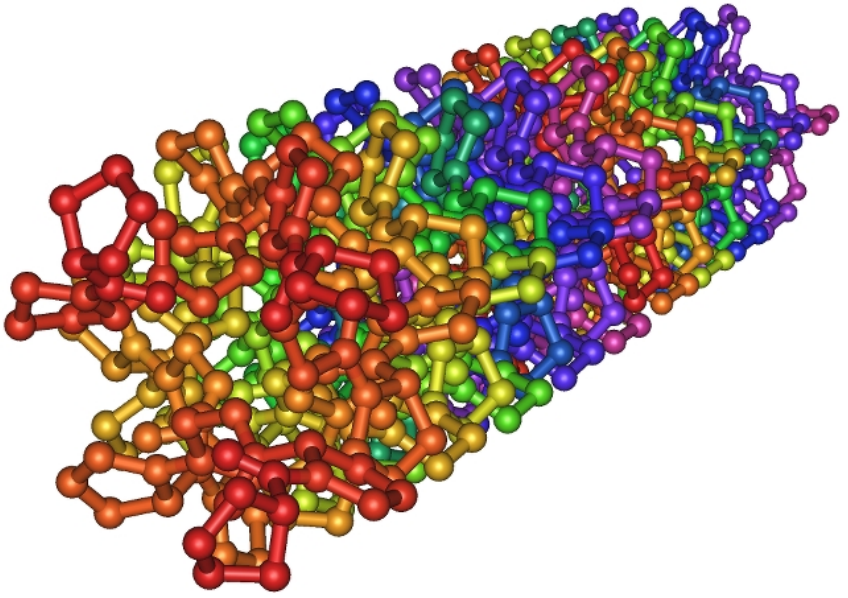
O-linked GalNAC

PROTEINS FUNCTION

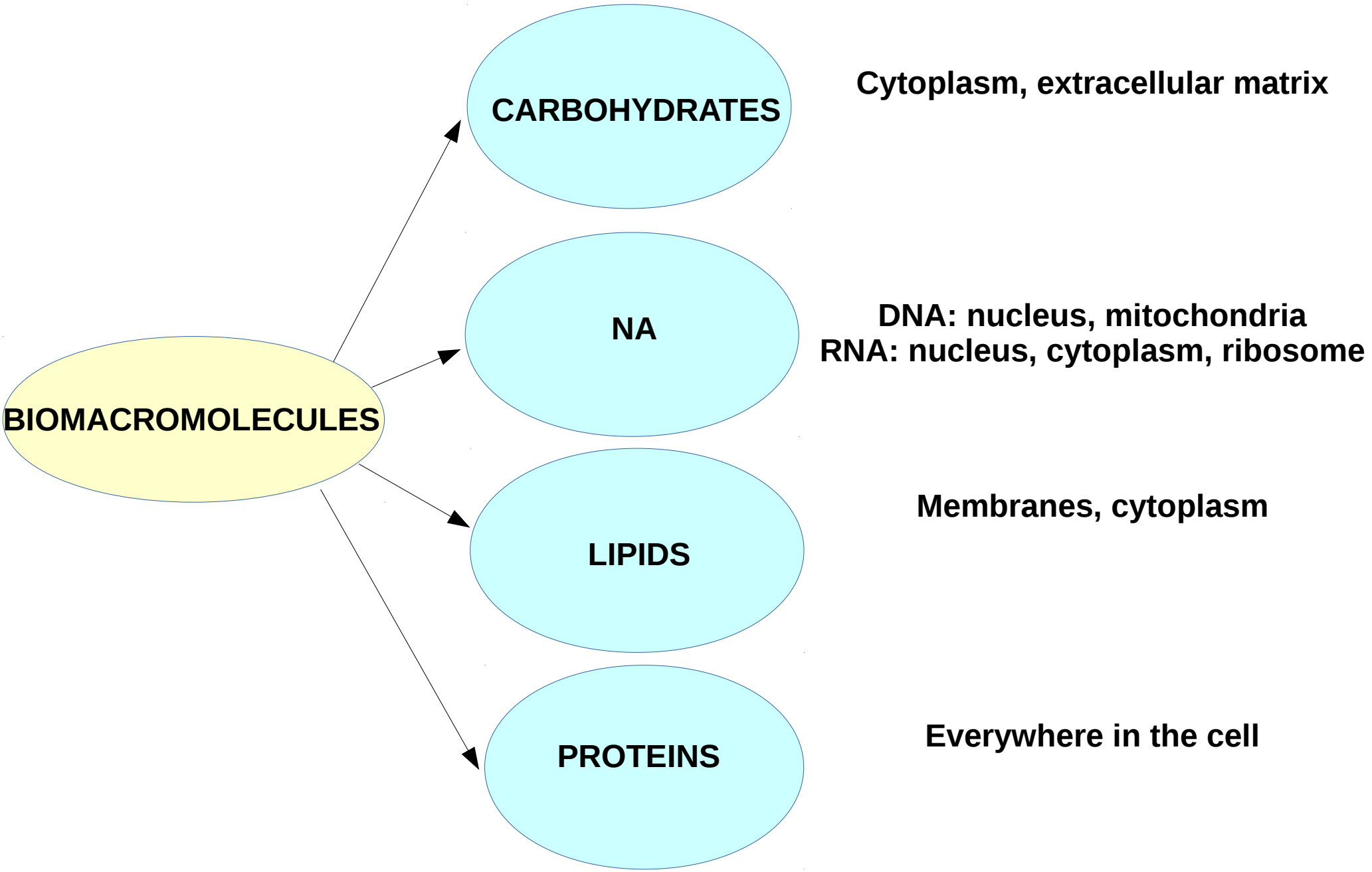
- **Enzymes**
- **Cell signaling and ligand binding**
- **Structural proteins**







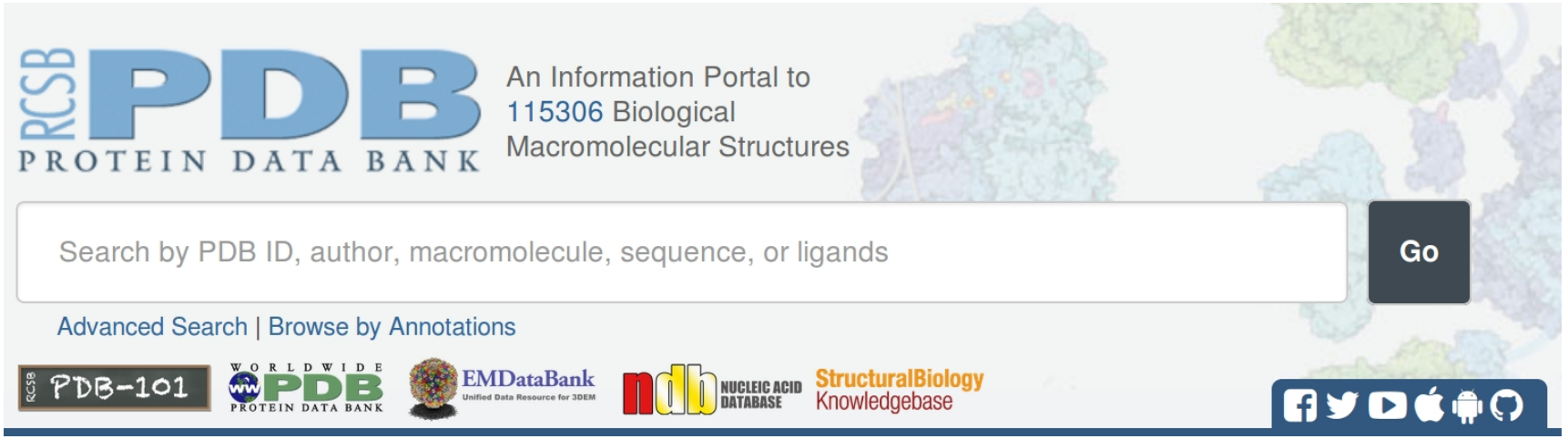
LOCALIZATION OF BIOMACROMOLECULES



BIOMACROMOLECULES IN THE PDB

Total (december 2015): 114526

- **Proteins: 106293 (1059- membrane proteins)**
- **Nucleic acids: 2865**
- **Carbohydrates: ~10^2-10^3**
- **Lipids: ?**



LECTURE 2: INTRODUCTION TO CELL CHEMISTRY AND BIOSYNTHESIS I

- **Building blocks of biological systems:**
  - **sugars: polysaccharides**
  - **nucleic acids: RNA, DNA**
  - **fatty acids: lipids**
  - **amino acids: proteins**
- **Chemical modifications**
- **Localization of biomolecules**
- **Biomacromolecules in the PDB**