Saccharides and polysaccharides

Structure and significance in biochemistry

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Saccharides and polysaccharides

Functions of saccharides

- Source of energy
- Source of basic metabolites
- Signalling
- Mechanical support (bacterial wall)

Saccharides and polysaccharides
Structure and significance in biochemistry

Content

- Structure, basic terms, formulas, stereochemistry, isomers
- Functional groups and their reactivity
- Saccharide chains
- Saccharide classification
- Pathogenetic role of saccharides

Saccharides and polysaccharides: significance in biochemistry and dentistry.

- Structure, basic terms, formulas, stereochemistry, isomers
- Functional groups and their reactivity
- Saccharide chains
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- Pathogenetic role of saccharides

NOTE TO SACCHARIDE TERMINOLOGY

Saccharides
(from the Greek word σάκχαρον (sákkharon), meaning 'sugar')

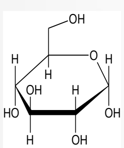
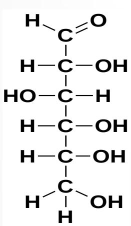
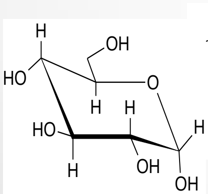
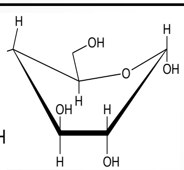
Carbohydrates
synonym to saccharides,
derived from fact that the *empirical formula* of some saccharides appears to contain molecules of water $(C_m(H_2O)_n$. ***However this is not truth. Saccharides contain -H and -OH substituents*** and no molecule of water (explained in the next two slides). In fact, the name **hydrates** describes substances that have **whole** molecules of water in their crystals, e.g. $CaSO_4{\cdot}2H_2O$ or $CuSO_4{\cdot}5H_2O$.

Sugars
is generic name for sweet-tasting, soluble saccharides, many of which are used in food.

Do not confuse the names *carbohydrates* and *hydrocarbons.*
Hydrocarbons are organic compounds consisting entirely of hydrogen and carbon, **e.g. methane, butane or benzene.** It means that saccharides (carbohydrates) are derivatives **of hydrocarbons** containing hydroxyl groups –OH and often also some carbonyl groups –CO-, mainly aldehyde or ketone groups

Conclusion
In terminology of saccharides should be preferred name saccharide over name carbohydrate or sugars

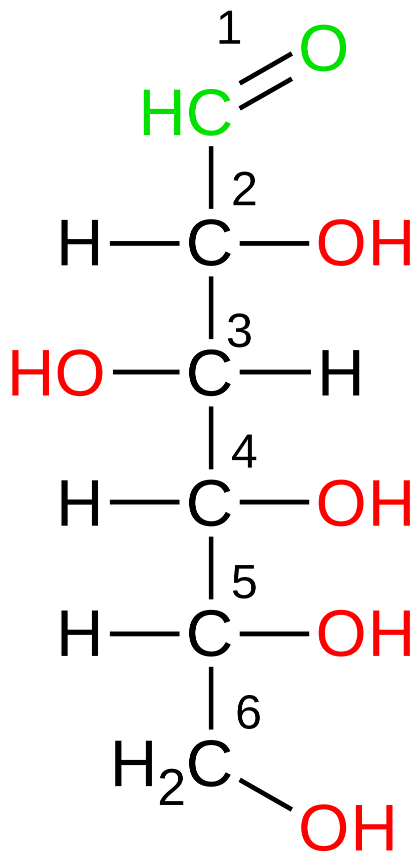
Levels of saccharide structure description

	FORMULA TYPE	DESCRIPTION	LEVEL OF DESCRIPTION
CH_2O	Empirical	Simplest number ratio of atoms	
$C_6H_{12}O_6$	Molecular	Total number of atoms of each element in each molecule of a substance	
CHO-CHOH- CHOH- CHOH- CHOH- CH_2OH	Condensed	Only the binds are drawn which give the order of the atom groups	**Constitution**
  **glucose**	Structural	Relative position of the atoms in a molecule is given that can be changed exclusively by cleaving and forming new chemical bonds.	**Configuration**
  **glucose** *Chair* and *boat* conformation	Conformational	The isomers can be interconverted exclusively by rotation about single bonds only	**Conformation**

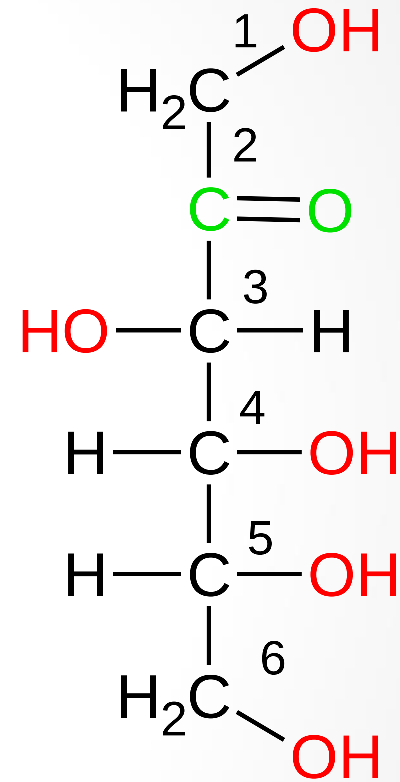
Saccharides (Carbohydrates)

Derivatives of hydrocarbons containing hydroxyl groups –OH and often also some carbonyl groups –CO-, mainly aldehyde or ketone groups.

Carbons atoms are numbered beginning from the reactive end of the molecule (containing aldehyde -CHO or carbonyl -CO- group). Each carbon atom is then numbered in order throughout the whole chain.



Glucose



Fructose

Basic terms describing saccharide structure

D- and L- prefixes

plus and minus optical rotation (+ and -)

trioses, tetroses, pentoses, hexoses

funktional groups

?

homologous series

aldoses and ketoses

α- β- saccharides (anomers)

chiral centre (asymmetric carbon)

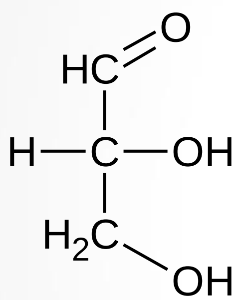
stereoisomers epimers, diastereomers, optical isomers (enantiomers)

Basic terms describing saccharide structure

The terms will be explained in more details on the next slides

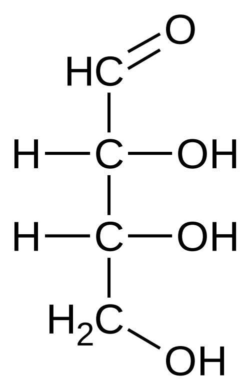
Trioses, tetroses, pentoses, hexoses	Monosaccharides with, respectively, three, four, five, and six carbon atoms	
Functional group	Group of atoms that determine the chemical properties of a compound.	Alcohol group –OH Aldehyde group -CHO Ketone group -CO-
Aldoses and ketoses	Monosaccharide classification according to functional groups	
Chiral centre (asymmetric carbon)	Carbon attached to four different types of atoms or groups of atoms	
Plus and minus optical rotation (+ and -)	Rotation of a plane of monochromatic polarized light after having passed through a sample of an optically active (chiral) substance.(e.g. solution of a saccharide).	Plus and minus indicate direction of the rotation Plus (+) …. clockwise Minus (-)… counterclockwise
D- and L- prefixes	Description the configuration of substituents (e.g. H and OH groups) on the asymmetric carbon furthest from the carbonyl group	
Absolute configuration R and S (rectus and sinister)	Description the configuration of substituents around one single chiral centre (asymmetric carbon)	
Homologous series	Groups of molecules that have the same basic structure, including the same functional group. They only differ in the number of methylene (CH2) groups. The chemical properties of homologous series are similar because they have the same functional group.	
Isomers and stereoisomers	Isomers are molecules with the same <u>molecular</u> formula but with a different structure. Stereoisomers are isomers that differ <u>only</u> in the spatial orientation of their component atoms (in configuration)	
α- β- sacharides (anomers)	Alpha and beta anomers are isomers differing in the position of -OH group resulted during intramolecular reaction of the aldehyde or ketone group with one from the alcohol OH groups of the same molecule.	

Trioses, tetroses, pentoses, hexoses	Monosaccharides with, respectively, three, four, five, and six carbon atoms



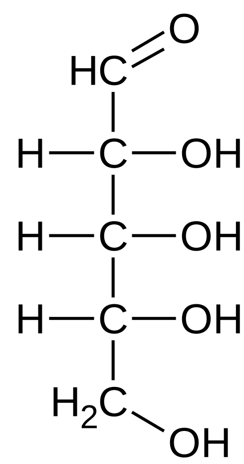
Triose

Glyceraldehyde



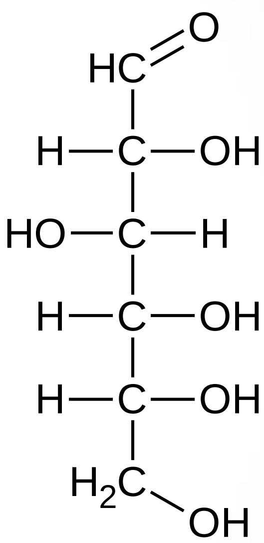
Tetrose

Erythrose



Pentose

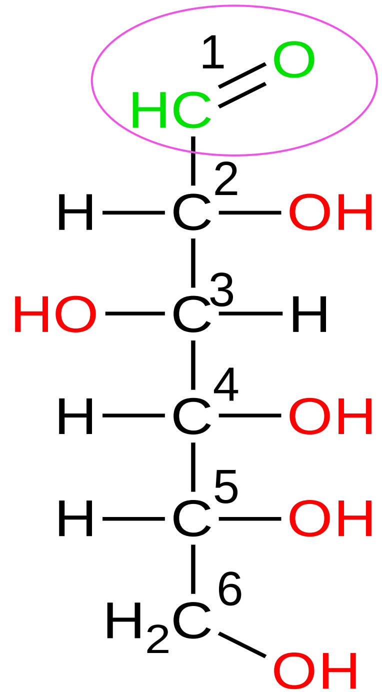
Ribose



Hexose

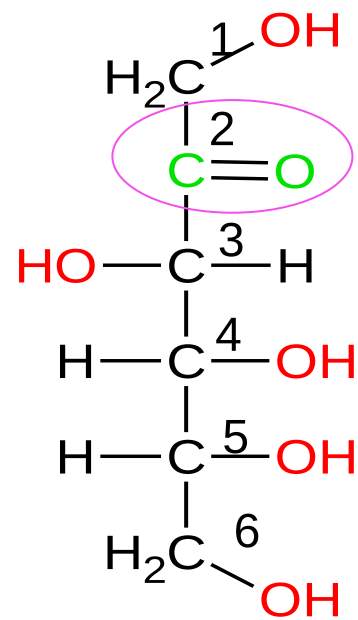
Glucose

Functional group	Group of atoms that determine the chemical properties of a compound.	Alcohol group –OH Aldehyde group -CHO Carbonyl group -CO-
Aldoses and ketoses	Monosaccharides classification according to functional groups	



Aldose

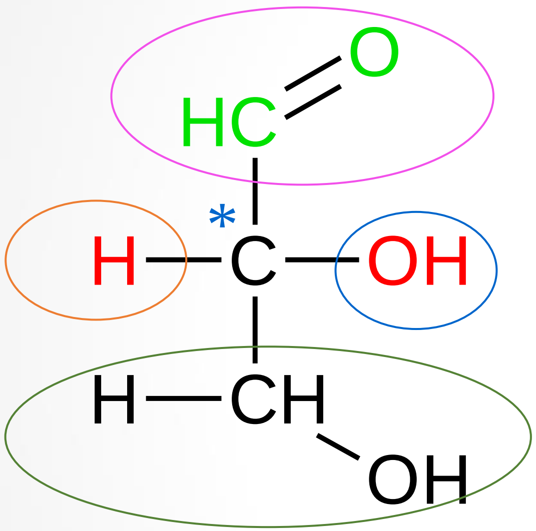
Glucose



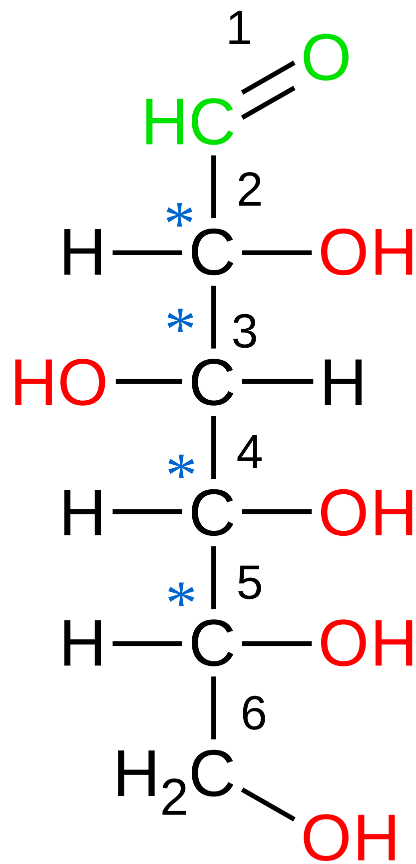
Ketose

Fructose

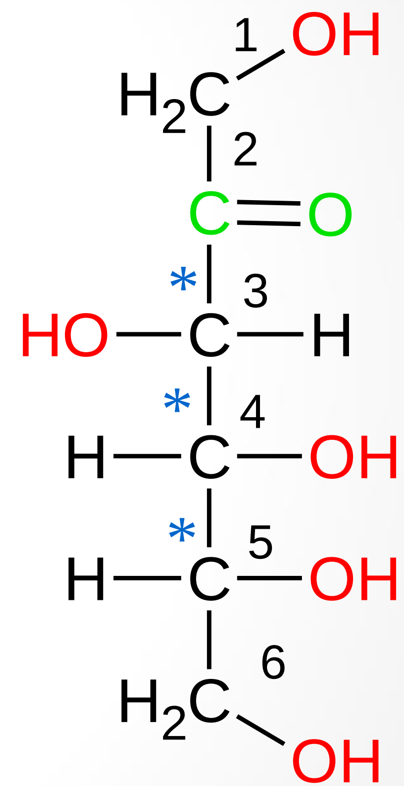
Chiral centre (asymmetric carbon)	Carbon attached to four different types of atoms or groups of atoms	*



Glyceraldehyde



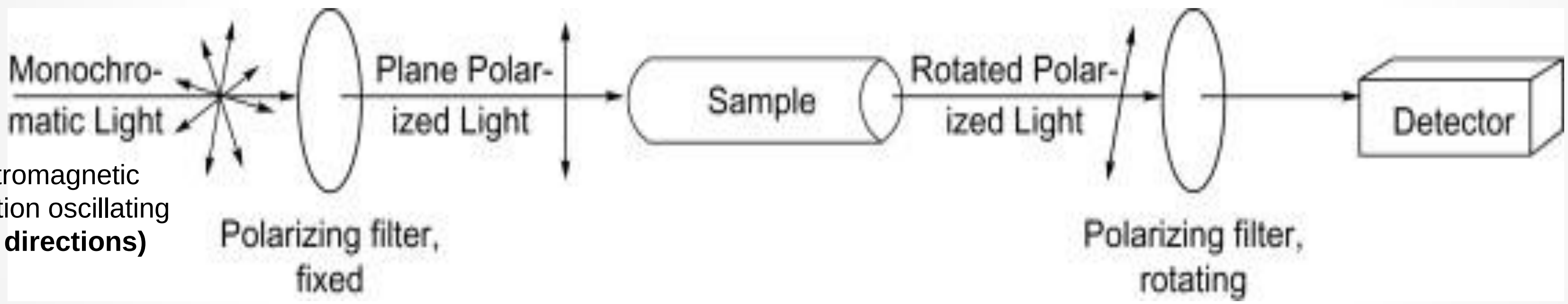
Glucose



Fructose

plus and minus optical rotation (+ and -)	Rotation of a plane of monochromatic polarized light after having passed through a sample of an optically active (chiral) substance.(e.g. solution of a saccharide).	Plus and minus indicate direction of the rotation Plus (+) …. clockwise Minus (-)…. counterclockwise

Polarimeter is an instrument **which measures the angle of rotation** of the polarized light plane



(electromagnetic radiation oscillating **in all directions)**

Robert E. Gawley, Jeffrey Aubé, in Principles of Asymmetric Synthesis (Second Edition), 2012

Absolute configuration R and S (rectus and sinister)	Description the configuration of substituents **around one single** chiral centre (asymmetric carbon)	

How to find absolute configuration „R“ and “S“ at any asymmetric carbon (L glyceraldehyde is used as an example)

Atoms with higher **atomic number** has higher **priority** (C>H, O > C)

Determine the priorities of the substituents around the chiral centre (asymmetric carbon) 1 OH.. 2 HC=O .. .
3 ...CH_2OH,.. 4 H

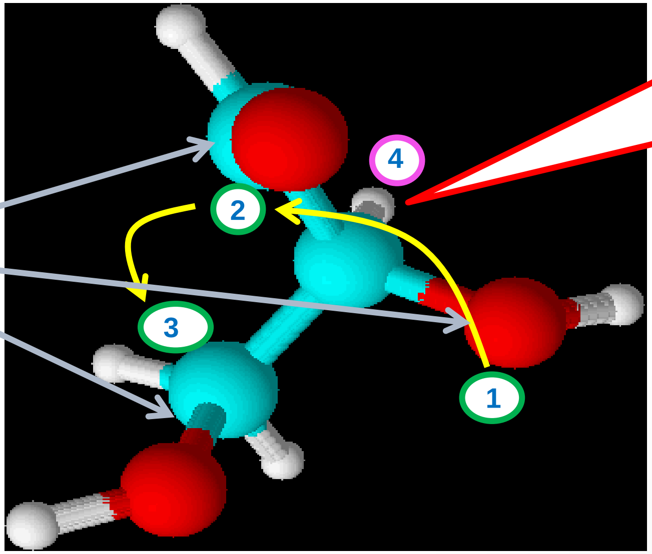
Point the substituent of lowest priority (H) away from the viewer (like you would hold it in your hand). Let remaining three ligands point forward to you and determine the order of priorities from highest to lowest one.

If this sequence goes in the clockwise direction, then the absolute configuration at the stereocenre is „R“ (Latin rectus - right), when is in contrary the counterclockwise, the absolute configuration is „S“ (Latin sinister -left)

Priority 1 2 3 4
high → low

(Carbon of HC=O has higher priority than CH_2OH, because the carbon in aldehyde is considered as atom, binding one H and ***two*** *ligands are occupied by* ***oxygen*** *in contrary to CH_2OH, binding two hydrogen and* ***one oxygen only****.)*

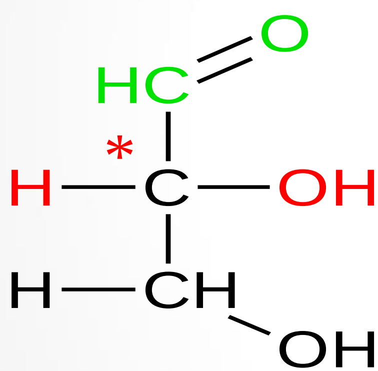
Three ligands point forward to you

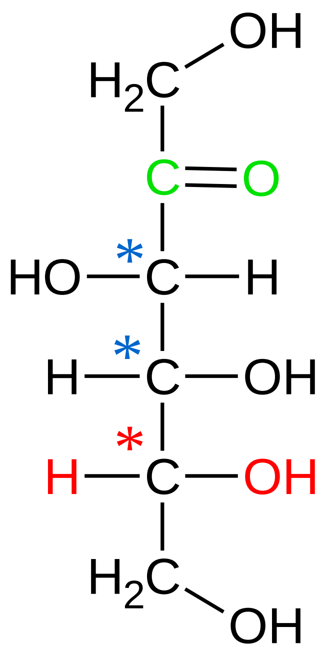


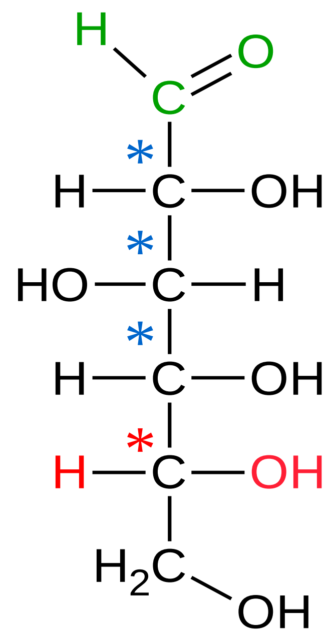
Substituent of lowest priority (H)

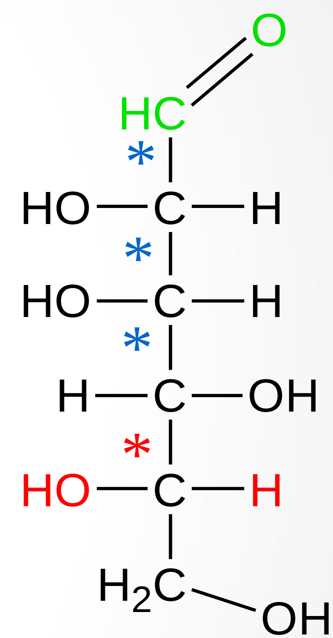
Absolute configuration „S“
(counterclockwise)

D- and L- prefixes	Description the **configuration** of substituents (e.g. H and OH groups) **on the asymmetric carbon furthest from the carbonyl group.** In these Fisher's formulas L - isomers have the hydroxy group attached to the left side, while D - isomers have the hydroxy group on the right side	

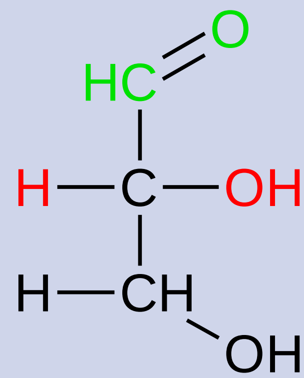
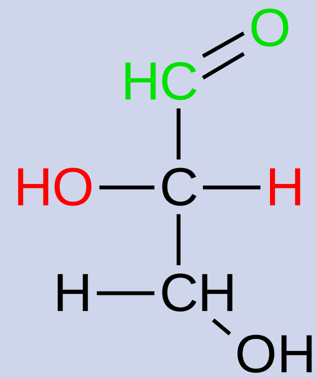
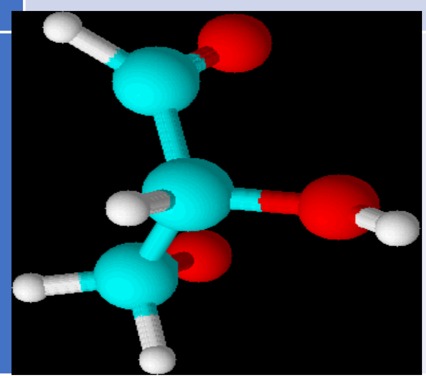
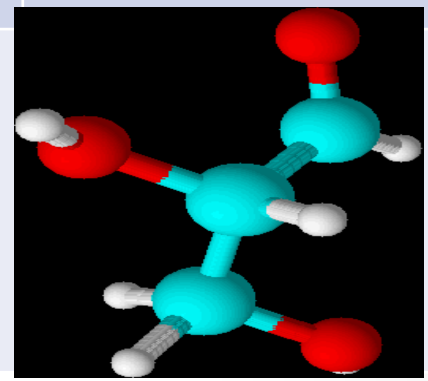








D - Glyceraldehyde **D** - Fructose **D** - Glucose **L** - Mannose

	D-glyceraldehyde **(R) - glyceraldehyde** **(+) - glyceraldehyde**	**L-glyceraldehyde** **(S) - glyceraldehyde** **(-) – glyceraldehyde**
Fischer projection		
Ball-and stick model		

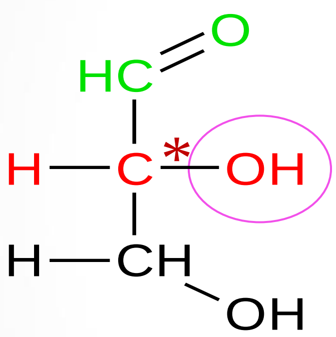
There are two different **glyceraldehydes - D and L**. At first glance, it seems to be no difference between the two formulas. One could say that it would be quite enough to rotate the formula around its vertical axis. <u>But this must not be done.</u> Here we see actually two formulas of two different molecules. And only one of them (isomer D-) is a glucose metabolite. It is necessary to understand Fischer rules on the projection of 3-dimensional molecules into two-dimensional space, such as paper or monitor. ***See next slide - the rules of Fischer projection.***

R and S are terms for absolute configuration.

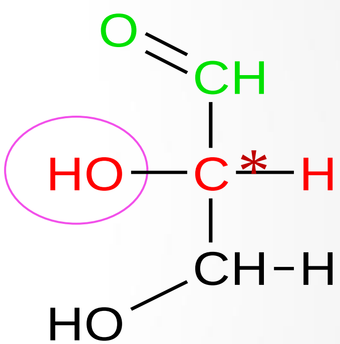
Plus and minus indicate the rotation direction of the plane of polarized light passing through the substance solution.

Fischer projection of a three-dimensional molecule onto a two-dimensional, such as a paper

* Asymmetric (chiral) carbon



D - GLYCERALDEHYDE



L - GLYCERALDEHYDE

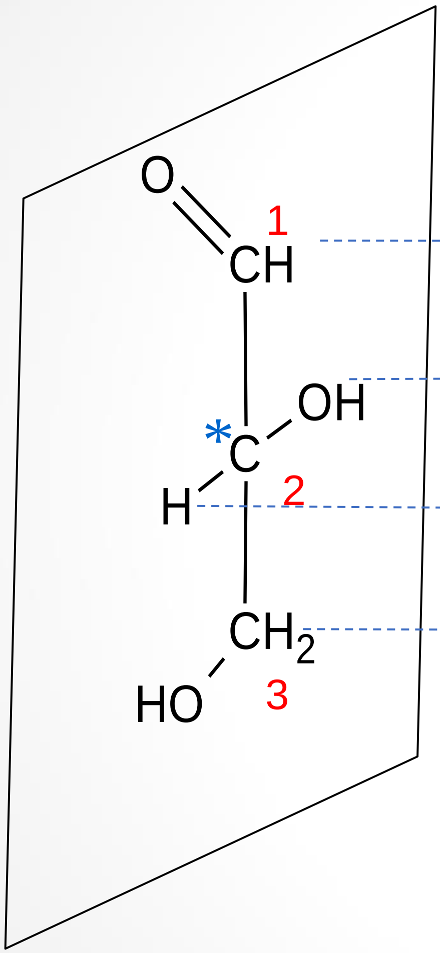
Prof. Hermann Emil Fischer 1852 - 1919

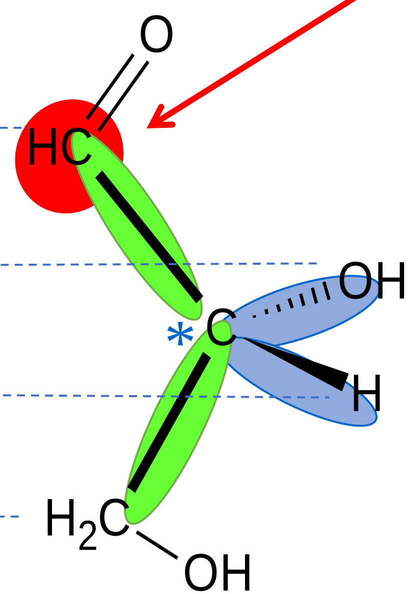
Nobel Prize winner

Fig. from https://www.nobelprize.org/prizes/chemistry/1902/fischer/biographical/

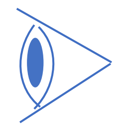
Fischer projection rules

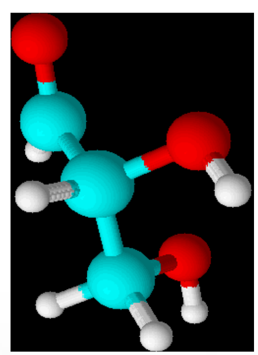
how to project **unequivocally** a 3-dimensional molecules into two-dimensional space, such as a paper

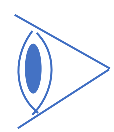




D - glyceraldehyde





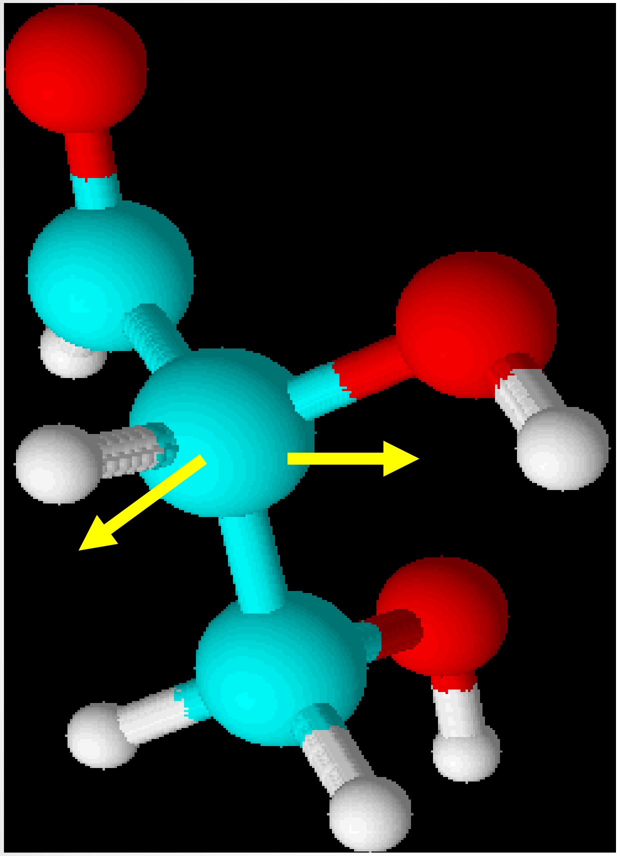


1. The lowest-numbered carbon atom with oxo- group (C-1 in aldoses; C-2 in 2-ketoses,) is drawn at the top, and the rest of the carbon atoms in the chain (here C2 and C3) **are drawn in sequence below the top carbon atom.**

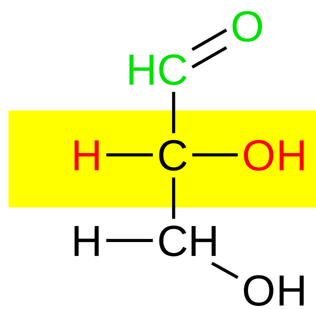
2. Then it is necessary to rotate the chiral carbon so that its bonds to adjacent carbons (here C1 and C3) **point away from the viewer, towards the projection plane**

3. The horizontal left and right bonds of chiral carbon now will be pointed to the viewer and that is the right viewer and that is the right position for the projection and draw the right and left horizontal bonds of H and OH onto the paper.

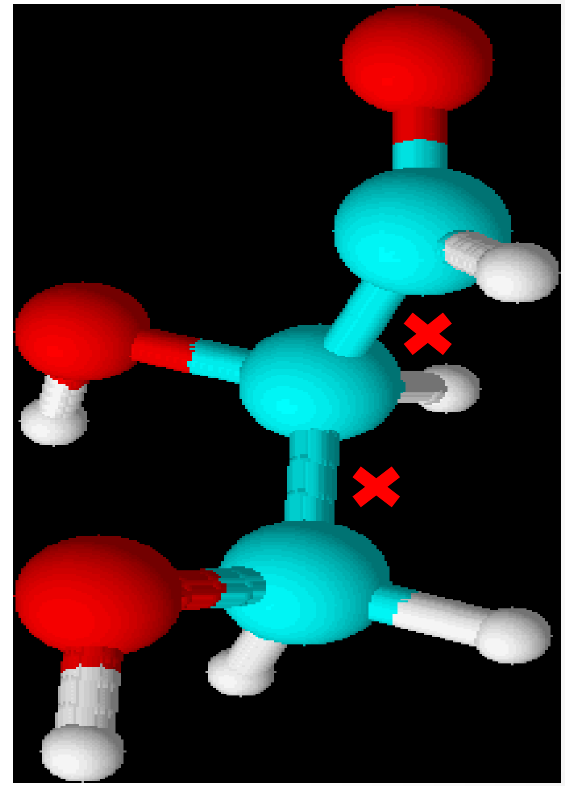
Fischer projection of the three-dimensional structure to two-dimensional paper



D-glyceraldehyde in the
correct position
for Fischer projection
(projection allowed)



Correct Fischer formula

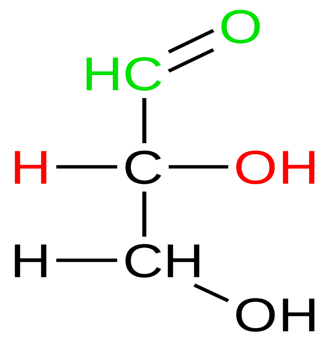


Also D-glyceraldehyde in the
incorrect position
for Fischer projection
(projection not allowed)

D-glyceraldehyde

(R) - glyceraldehyde

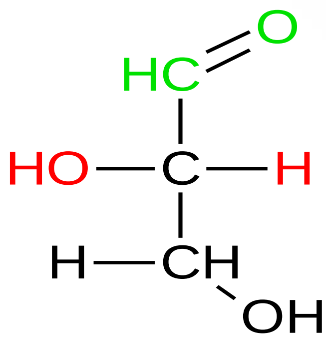
(+) - glyceraldehyde

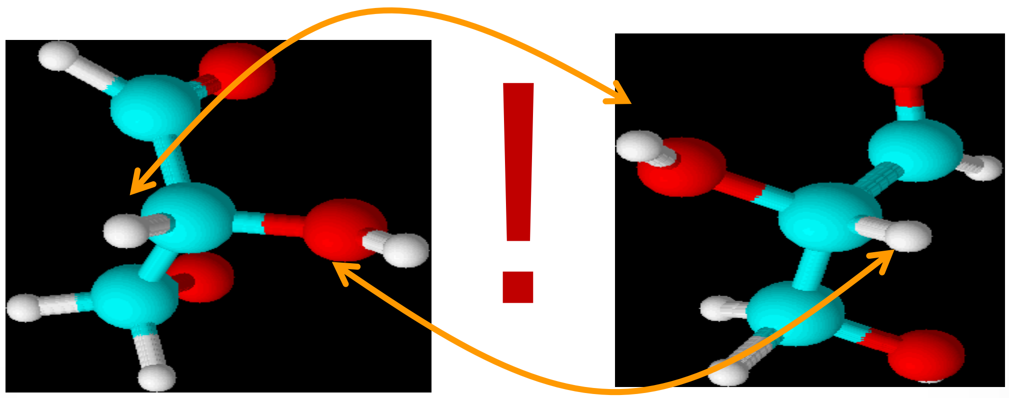


L-glyceraldehyde

(S) - glyceraldehyde

(-) - glyceraldehyde

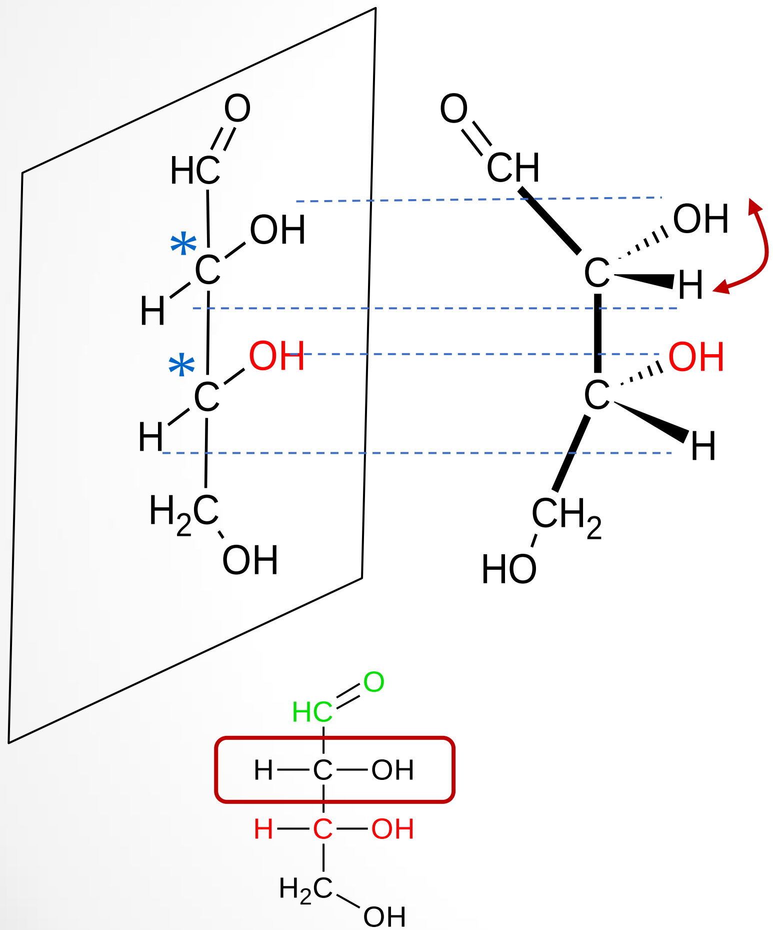




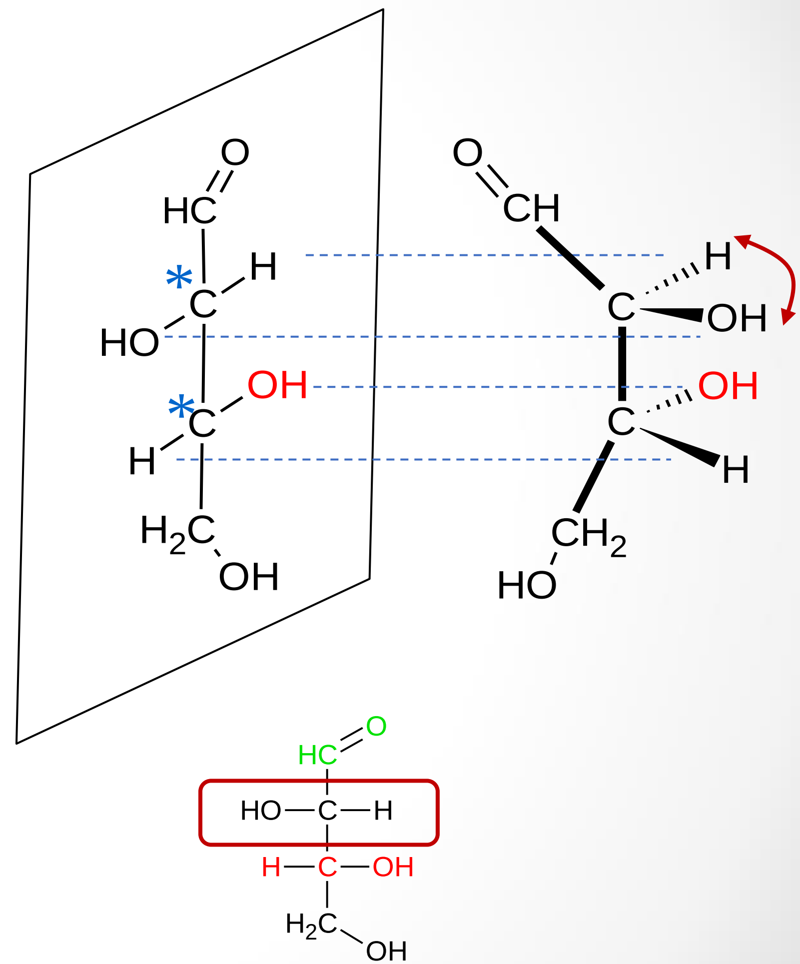
If you want to change D-glyceraldehyde to L-glyceraldehyde, you have to pull out both the substituents H and OH and then to attach them in the opposite positions. Only in this way you will ***change the configuration***. Never by means of any rotation only.

Fischer projection

Fischer projection for a monosaccharides with **more than one chiral carbon.**
Each of the chiral carbons must be evaluated separately according to Fischer's rules



D - Erythrose



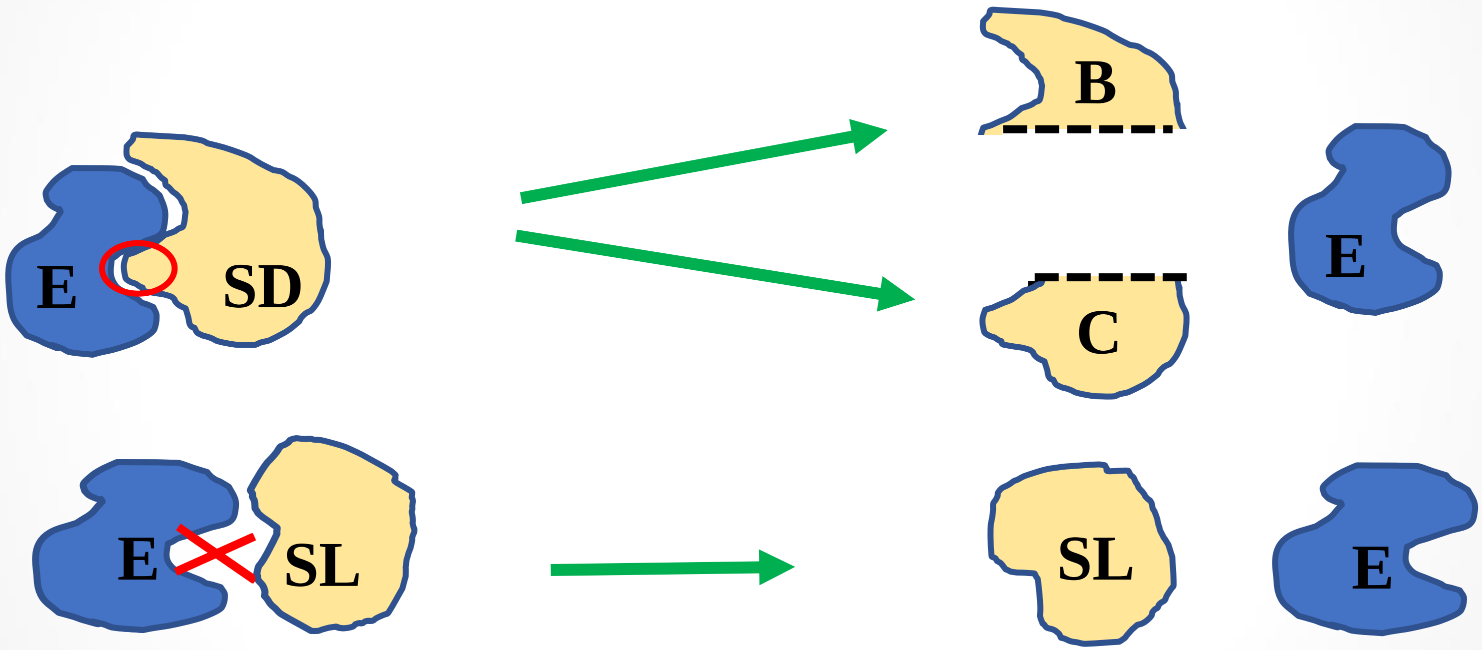
D - Threose

Let say, that an enzyme catalyses
the splitting of substrate S to products A and B

$$S \longrightarrow A + B$$

for example

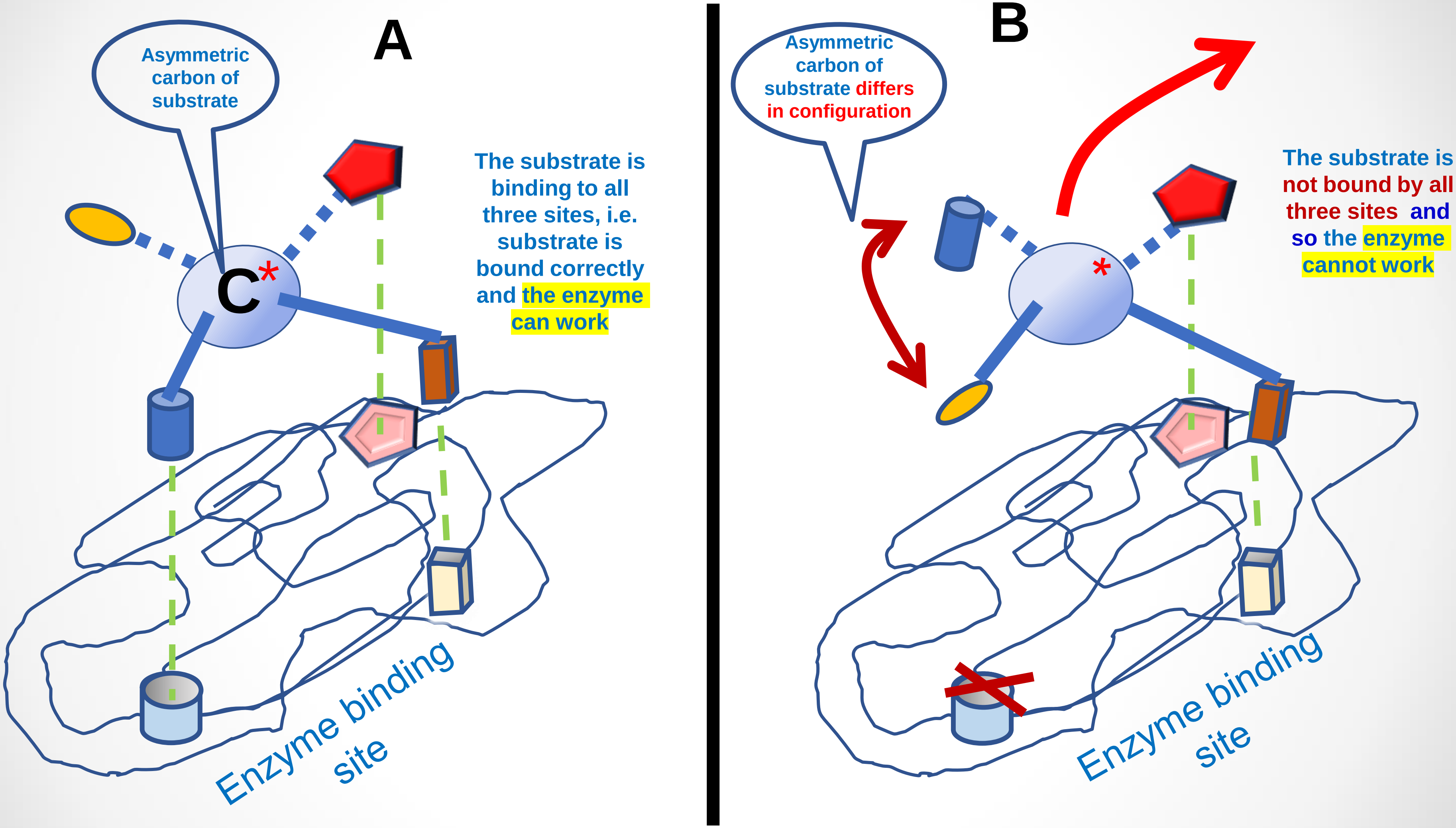
D-fructose-1,6- bisphosphate → D-glyceraldehyde phosphate + dihydroxyacetone phosphate



SD … substrate in D-configuration
SD … substrate in L-configuration

The enzyme must fit very precisely and tightly to the substrate so that the reacting groups of the enzyme and the substrate can react together

Enzyme stereospecifity



Homologous series

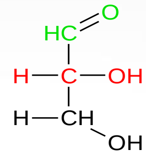
Groups of molecules that have the same basic structure, including the same functional group.

They only differ in the number of some identical groups (e.g. methylen groups $-CH_2-$ of hydrocarbons / methane, ethane, propane ….) or –CHOH- group in the case of saccharides).

The chemical properties of homologous series are similar because they have the same functional groups.

The homologous series of the monosaccharides can be constructed from a triose.

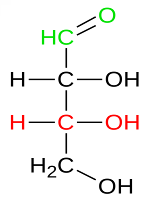
D - Aldoses
(homologous series).



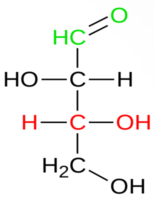
D - Glyceraldehyde

Groups of molecules that have <u>the same basic structure</u>, including the same functional group.

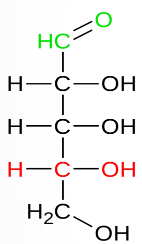
They only <u>differ in the number CHOH groups.</u>



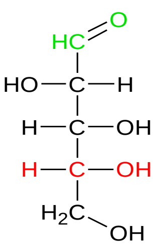
D - Erythrose



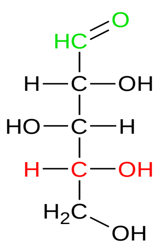
D - Threose



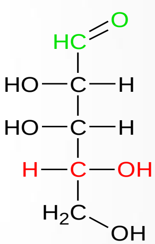
D - Ribose



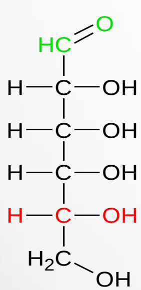
D - Arabinose



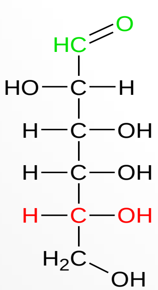
D - Xylose



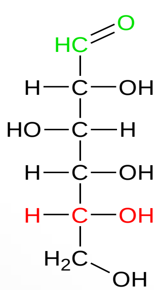
D - Lyxose



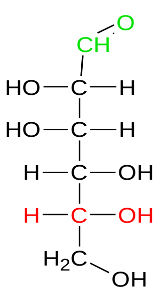
D - Allose



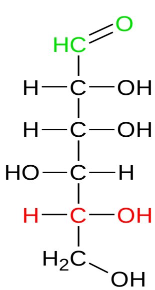
D - Altrose



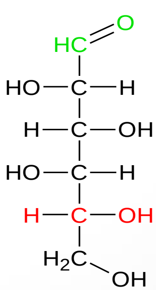
D - Glucose



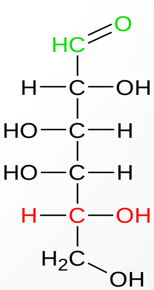
D - Mannose



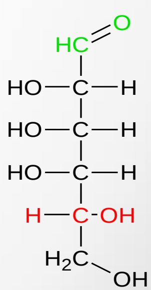
D - Gulose



D - Galactose



D - Idose



D - Talose

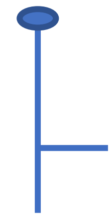
D - Aldoses

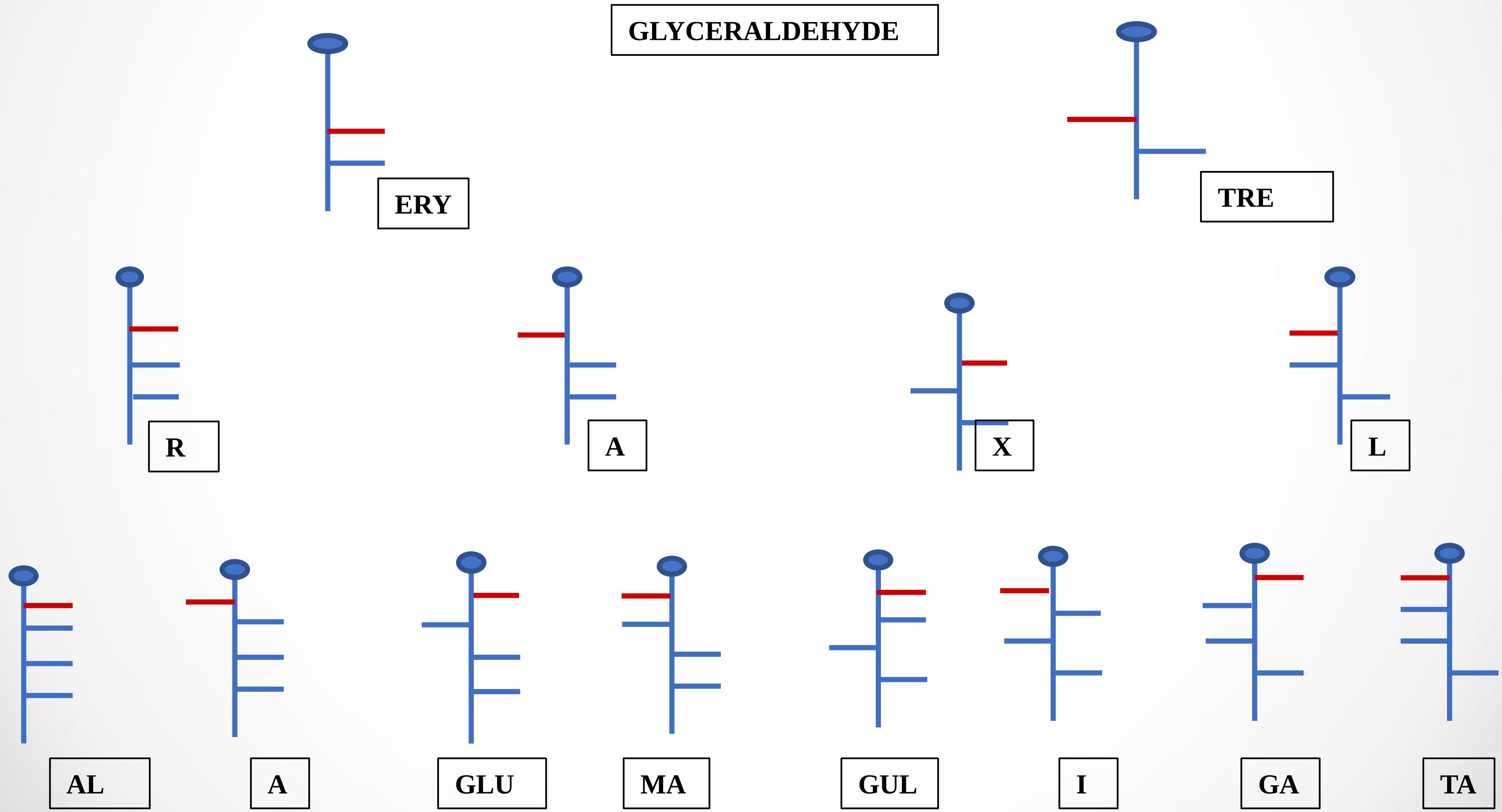
(homologous series).

Method how to construct the homologous series.

Draw the glyceraldehyde. Copy twice the molecule to the next row and then add the **red OH groups to the one and to the other side directly under the aldehyde group .....**

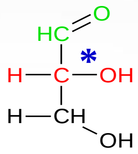
Then copy twice each of the resulting molecules (now whole in blue) and repeat the previous steps with the red OH group… etc.





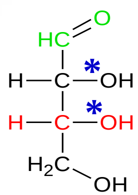
D - Aldoses

(homologous series).

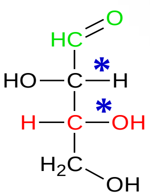


D - Glyceraldehyde

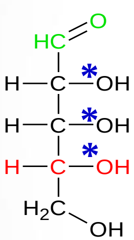
* Asymmetric (chiral) carbons



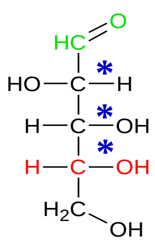
D - Erythrose



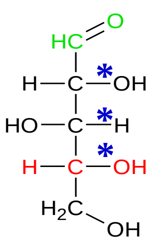
D - Threose



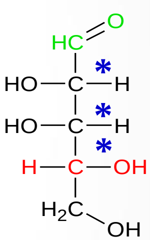
D - Ribose



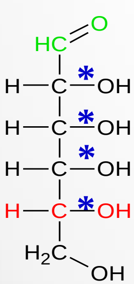
D - Arabinose



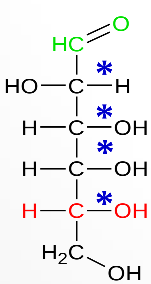
D - Xylose



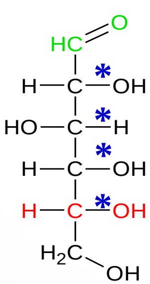
D - Lyxose



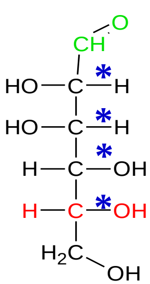
D - Allose



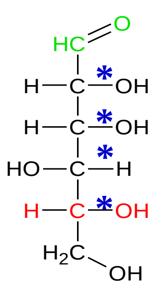
D - Altrose



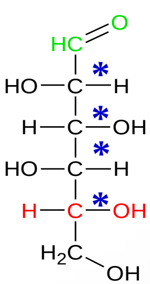
D - Glucose



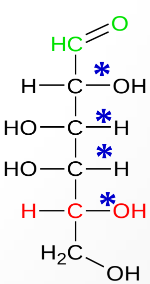
D - Mannose



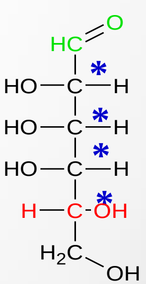
D - Gulose



D - Galactose



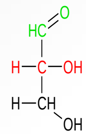
D -Idose



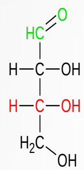
D - Talose

D and corresponding L aldoses

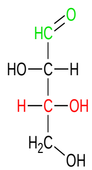
D - Aldoses
(homologous serie).



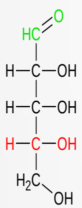
D - Glyceraldehyde



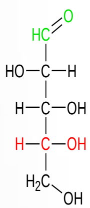
D - Erythrose



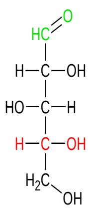
D - Threose



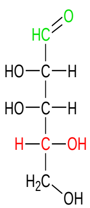
D - Ribose



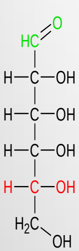
D - Arabinose



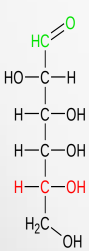
D - Xylose



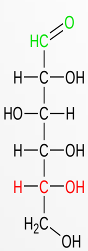
D - Lyxose



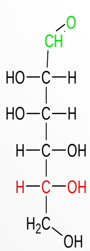
D - Allose



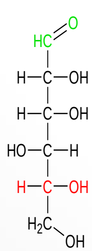
D - Altrose



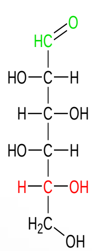
D - Glucose



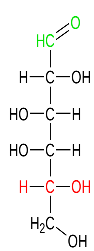
D - Mannose



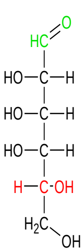
D - Gulose



D - galactose

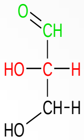


D - Idose

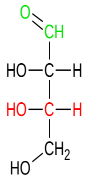


D - Talose

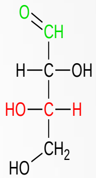
L - Aldoses
(homologous serie).



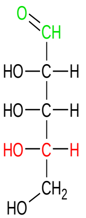
L - Glyceraldehyde



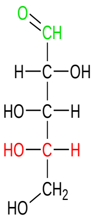
L - Erythrose



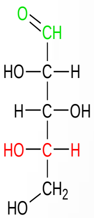
L - Threose



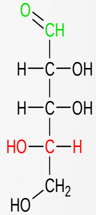
L - Ribose



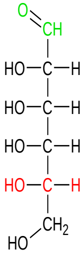
L - Arabinose



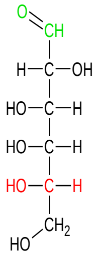
L - Xylose



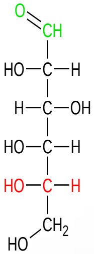
L - Lyxose



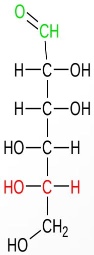
-L - Allose



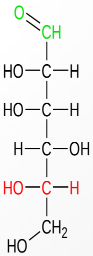
L- Altrose



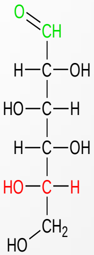
L- Glucose



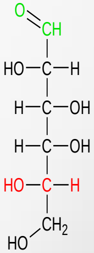
L- Mannose



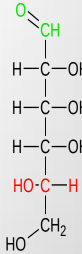
L - Gulose



L - Galactose



L - Idose



L - Talose

Significance of enzyme stereospecifity

D-glucose enters metabolic pathways in the body and is ***an important source of energy.***

L-glucose does not occur naturally in living organisms

Synthetic L- glucose ***cannot be used as a*** **source of energy** because the organisms ***lack the enzymes with appropriate stereospecifity.***

Potential use of the synthetic L-glucose:

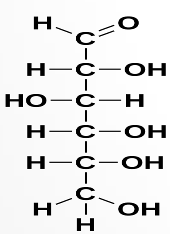
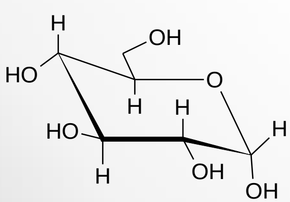
Low-calorie sweetener suitable for diabetics, but it was never marketed due to excessive manufacturing costs.

Laxative for colon-cleansing agent in preparation for colonoscopy

The L-glucose pentaacetate is **stimulater of insulin release**

Isomers

Isomers are molecules with the same molecular formula but with a different constitution, configuration or conformation.

	FORMULA TYPE	DESCRIPTION	LEVEL OF DESCRIPTION
CH_2O	Empirical	Simplest whole number ratio of atoms in a compound	
$C_6H_{12}O_6$	Molecular	Total number of atoms of each element in each molecule of a substance	
CHO-CHOH-CHOH-CHOH-CHOH-CH_2OH	Condensed	Symbols of atoms are listed in order as they appear in the molecule's structure with bond dashes omitted or limited	Constitution
 glucose	Structural	Graphic representation of the molecular structure showing how the atoms are possibly arranged in the real three-dimensional space.	Configuration
 glucose	Confor-mational	The isomers can be interconverted exclusively by rotations about formally single bonds only	Conformation

ISOMERS

Compounds whose molecule has the same number of atoms of each element, but they differ in arrangment of the atoms
They can differ on the level of constitution, configuration or conformation

1.**Structural isomers** (*compounds with the different constitution*)

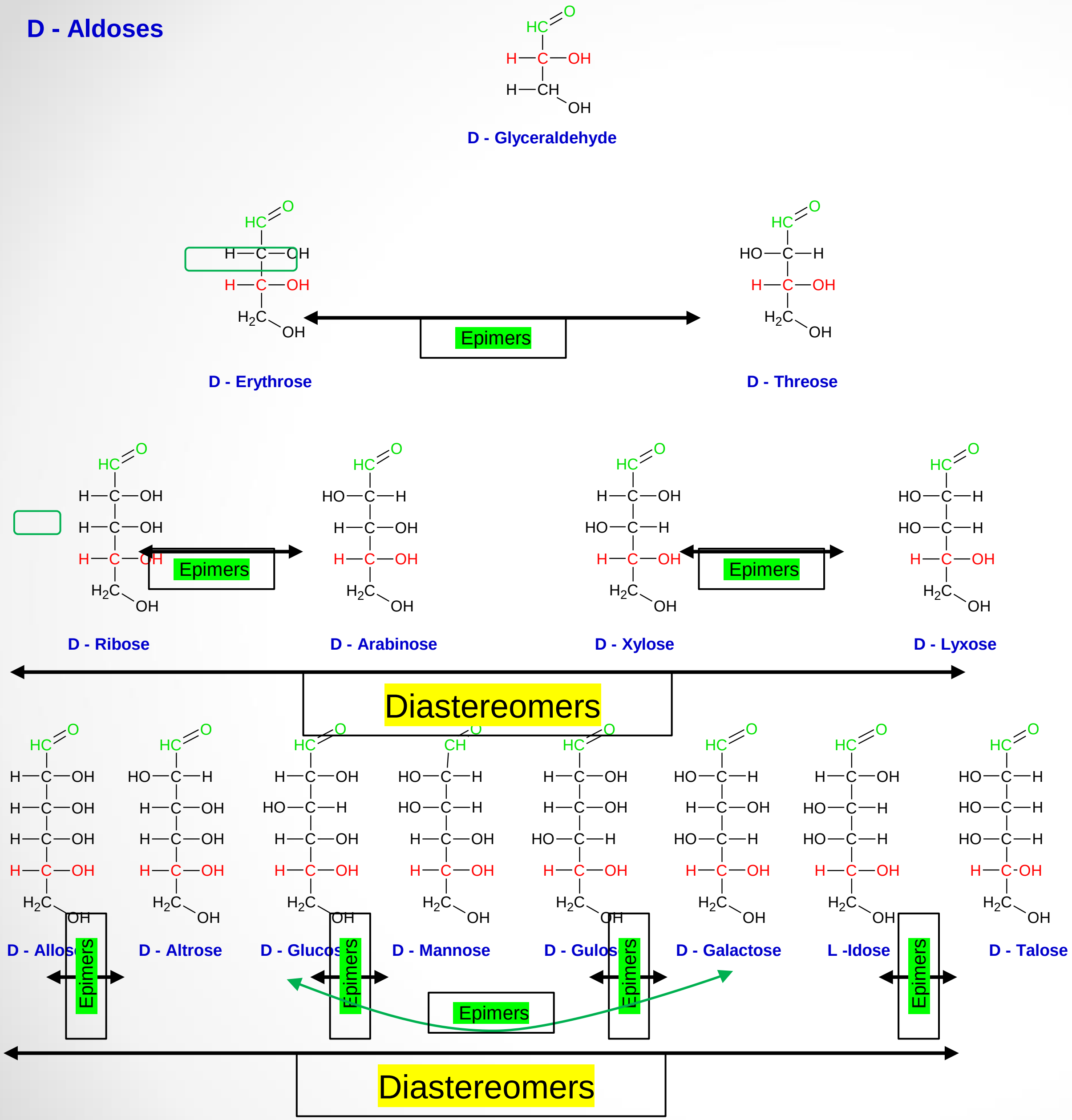
2. **Stereoisomers** (*compounds with the same constitution and different configuration*)

a. Diastereomers
Epimers (and anomers)

b. Optical isomers (enantiomers)

Biochemical note
Many enzymes are stereospecific. They are able to recognise "their" isomer.

D - Aldoses



ISOMERS

compound whose molecule **has the same number of atoms of each element**, but they differ in arrangment of the atoms,.

There are two kinds of isomers:

1) **Structural isomers** ***differ in constitution***, it means in atom distribution inside the molecule, e,g, propan-1-ol and propan-2-ol

2) **Stereoisomers** have the same molecular formula and sequence of bonded atoms (constitution), but differ in the three-dimensional orientations of their atoms in space (in configuration).

   a) ***Diastereomers*** are stereoisomers having different configurations at one or more (but not all) of the equivalent (related) stereocentres and are not mirror images of each other

   e.g. one line in the scheme (the same constitution and different configuration).

   - ***Epimers (and anomers of cyclic saccharides)*** *Special kind of diastereomers differing in configuration on one carbon only (eg glucose and galactose)*

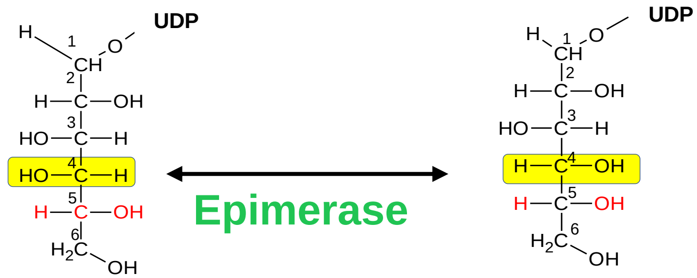
   b) ***Enantiomers = optical antipodes*** *have different configuration at all stereocentres* (Mirror image like right and left hands, e.g. L- and D-glucose)

Biochemical note
Enzyme galactose 4-*epimerase* catalyses interconversion of galactose to glucose.

Biochemical notes

Enzyme UDP - galactose 4-*epimerase* catalyses interconversion of galactose to glucose.

UDP … uridine diphosphate

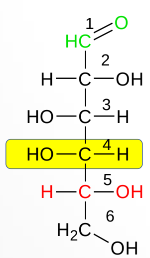


UDP-D-galactose

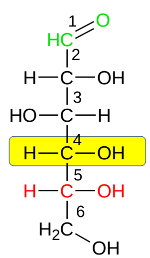
UDP-D-glucose

Epimers

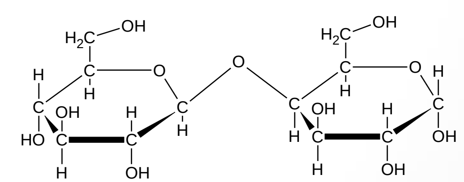
Disaccharide lactose consists of glucose and galactose and acts as an energy-carrier in milk.



D-galactose



D-glucose



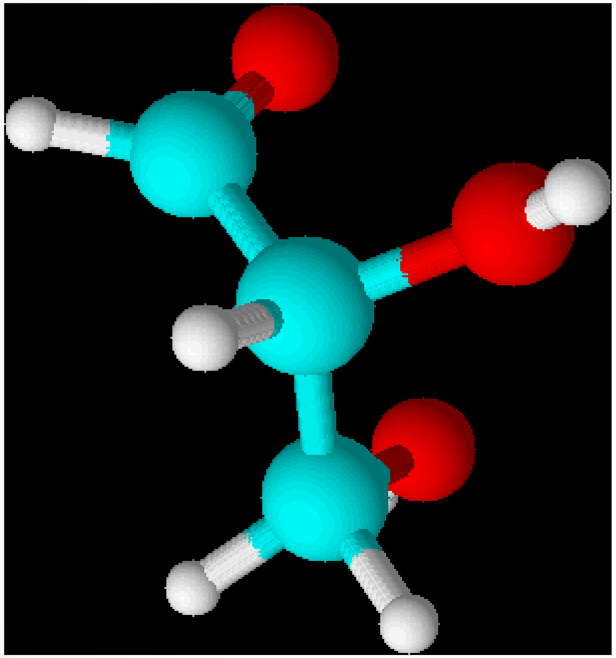
β -D-Galactopyranosyl-(1,4)–α–D-glucopyranose

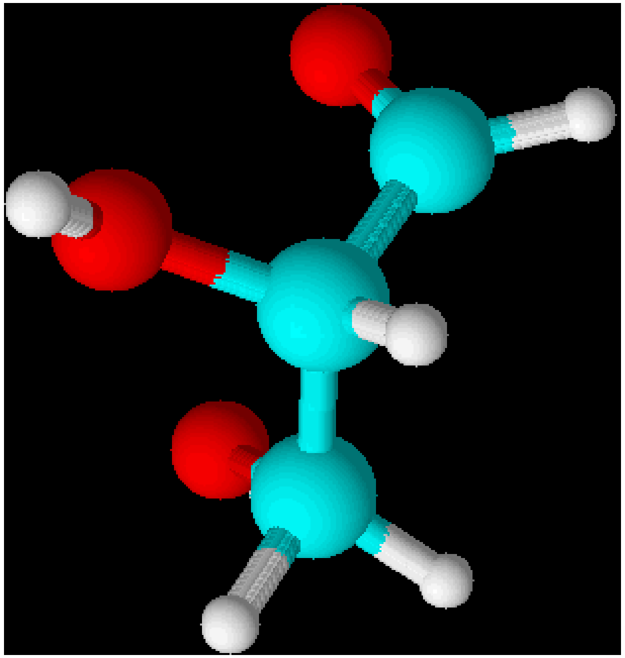
Lactose

Fischer formulas

Haworth formulas

Enantiomers
(optical antipodes,
mirror image).
Special kind of diastereomers which have different configuration <u>at all stereocentres</u>
(mirror image like right and left hand)





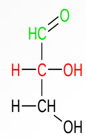
D - Glyceraldehyde

L - Glyceraldehyde

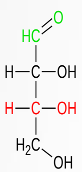
D- and corresponding L-monosaccharides are **enantiomers = optical antipodes.**

They differ in configuration at all stereocentres (mirror images like right and left hands)

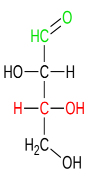
D - Aldoses
(homologous series).



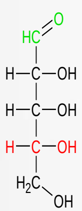
D - Glyceraldehyde



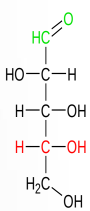
D - Erythrose



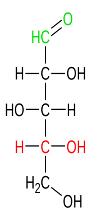
D - Threose



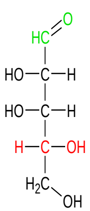
D - Ribose



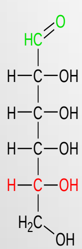
D - Arabinose



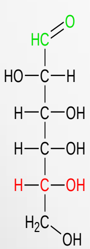
D - Xylose



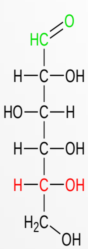
D - Lyxose



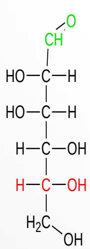
D - Allose



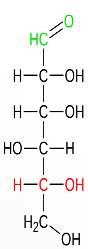
D - Altrose



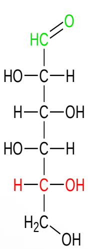
D - Glucose



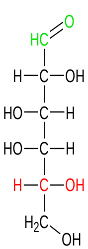
D - Mannose



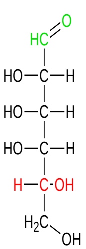
D - Gulose



D - Galactose

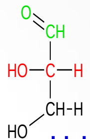


D - Idose

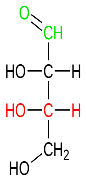


D - Talose

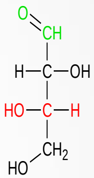
L - Aldoses
(homologous series).



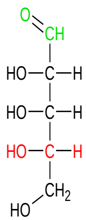
L - Glyceraldehyde



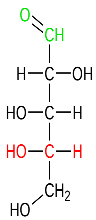
L - Erythrose



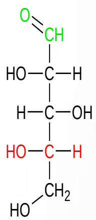
L - Threose



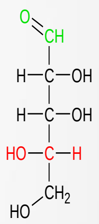
L - Ribose



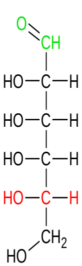
L - Arabinose



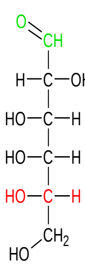
L - Xylose



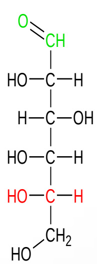
L - Lyxose



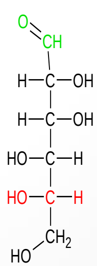
-L - Allose



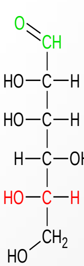
L- Altrose



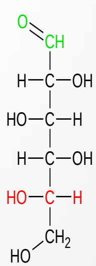
L- Glucose



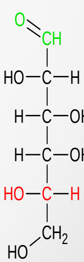
L- Mannose



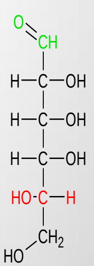
L - Gulose



L - Galactose



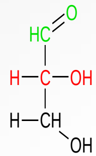
L - Idose



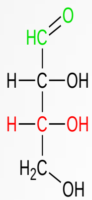
L - Talose

D - Aldoses
(homologous series).

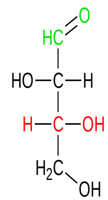
Remember especially



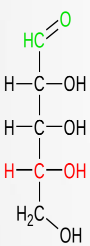
D - Glyceraldehyde



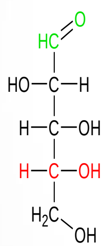
D - Erythrose



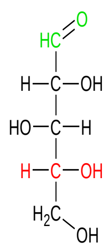
D - Threose



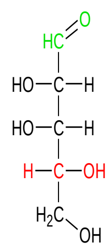
D - Ribose



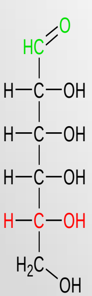
D - Arabinose



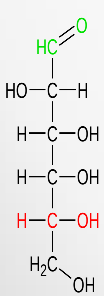
D - Xylose



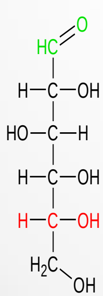
D - Lyxose



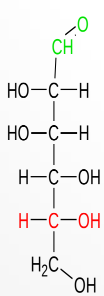
D - Allose



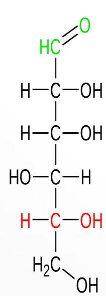
D - Altrose



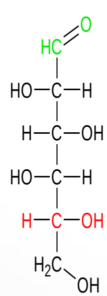
D - Glucose



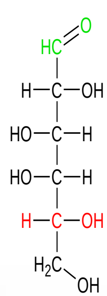
D - Mannose



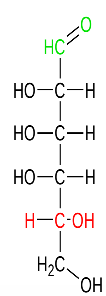
D - Gulose



D - Galactose



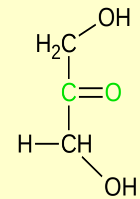
D - Idose



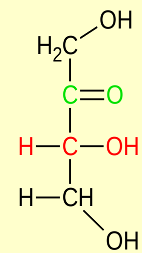
D - Talose

D - Ketoses
(homologous series)

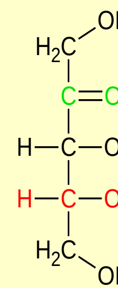
Ketoses have one asymetric carbon less than corresponding aldoses



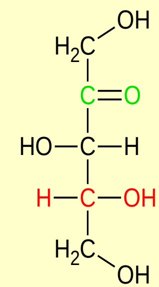
Dihydroxyacetone



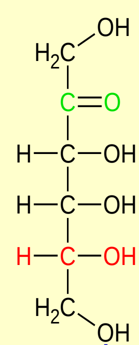
D- Eryhtrulose



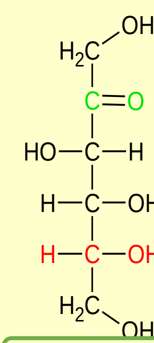
D- Ribulose



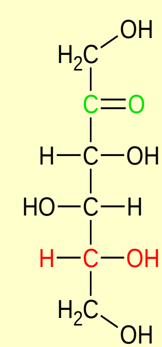
D- Xylulose



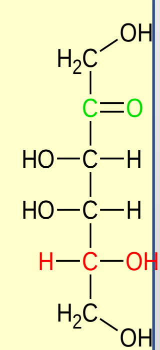
D- Psicose



D- Fructose



D- Sorbose



D- Tagatose

Saccharides and polysaccharides
Structure and significance in biochemistry

- Structure, basic terms, formulas, stereochemistry, isomers
- Functional groups and their reactivity
- Saccharide chains
- Saccharide classification
- Pathogenetic role of saccharides

Functional groups and reactivity of saccharides

Functional groups

hydroxyl group -OH
carbonyl groups (aldehyde and keto groups) - CHO -CO-
carboxylic group - COOH
amine group - NH_2
sulfo group - SO_3H
acetyl group - CO-CH_3

Reactions

oxidation, reduction
esterification (by phosphoric or sulphuric acid)
reaction of oxo group with hydroxyl group (hemiacetal, hemiketal)
reaction of aldehydic group with a free amine group (glycation)
reaction of hemiacetal with hydroxyl or with an amine– glycosidic bond

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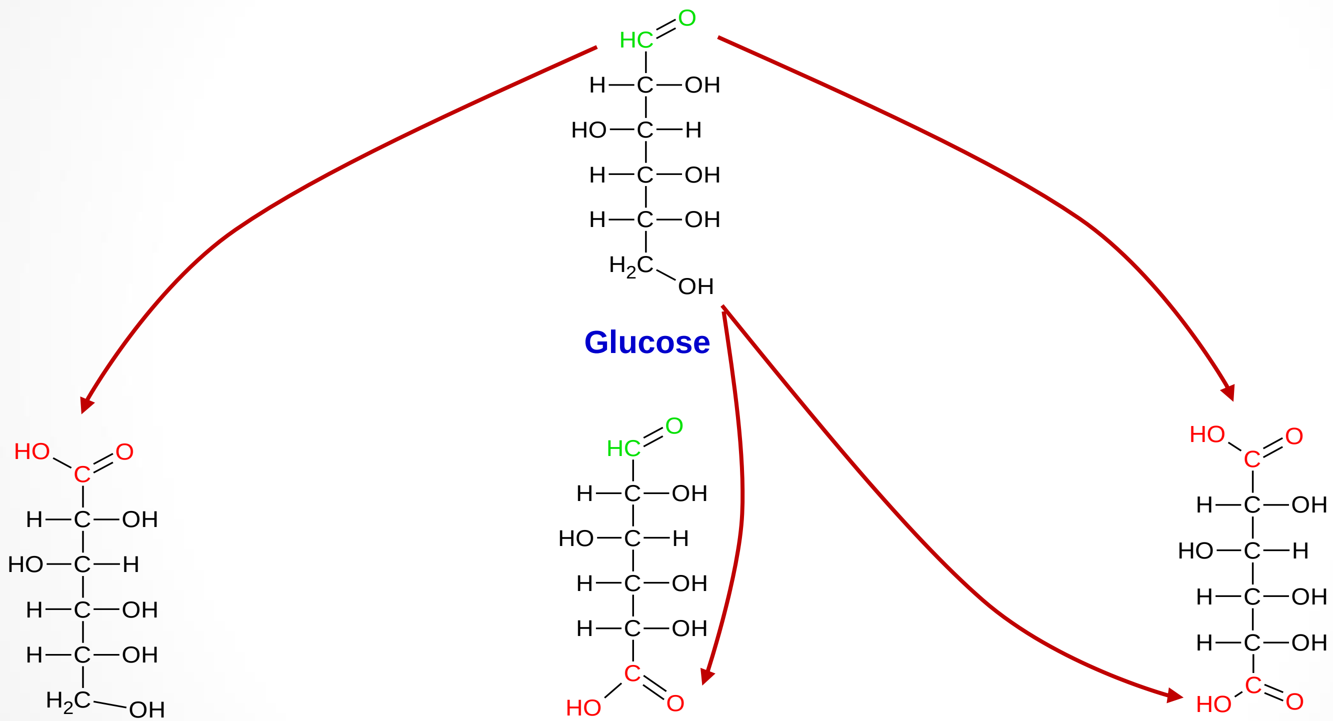
Functional groups and reactivity of saccharides

Biochemical oxidation of saccharide hydroxyl and aldehyde groups



Gluconic acid | Glucuronic acid | Glucaric acid

Aldonic acids | **Uronic acids** | **Aldaric acids**

← **IN GENERAL** →

yellow skin or yellow sclera of the eyes

Biochemical note

Heme metabolite **bilirubin is conjugated** within the hepatocytes **to glucuronic acid**. In this way it is changed into an aqueous soluble form. Conjugation facilitates bilirubin secretion into bile.
Unconjugated (**indirect**) and conjugated (**direct**) bilirubin are important laboratory markers for **differential diagnosis of different kinds of jaundice (obstructive or hepatic one).**

Symptoms - yellow skin or yellow eye scleras

Uronic acids are part of some polysaccharide structure, e.g. Hyaluronic acid, **anticoagulant heparin** and other glycosaminoglycans.

Functional groups and reactivity of saccharides

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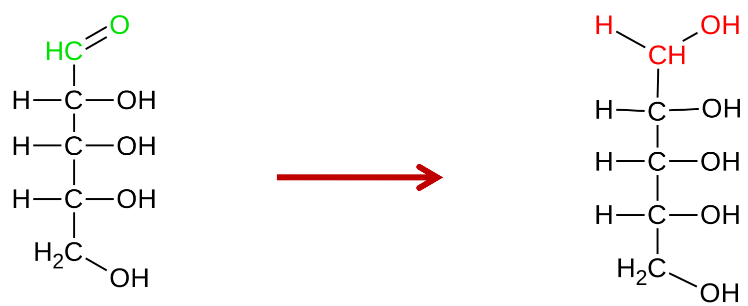
reaction of hemiacetal hydroxyl or with an amine– glycosidic bond

Functional groups and reactivity of saccharides

Biochemical reduction of aldehyde group to hydroxyl

(polyhydric **alcohols**, polyalcohols, alditols or glycitols)

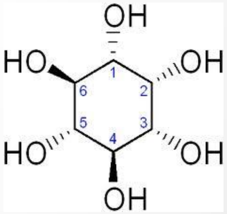


Ribose **Ribitol**

D-Glucitol (sorbitol) … ..sweetener

Mannitol,………………… reduction of fructose, sweetener for diabetics

Inositol derivates …….... cell signalling



Inositol

synthesized from glucose 6-phosphate

Functional groups and reactivity of saccharides

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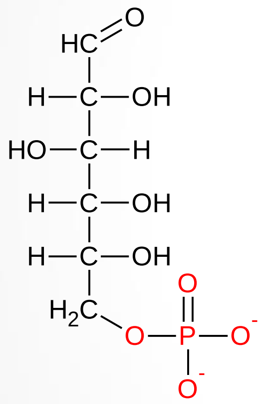
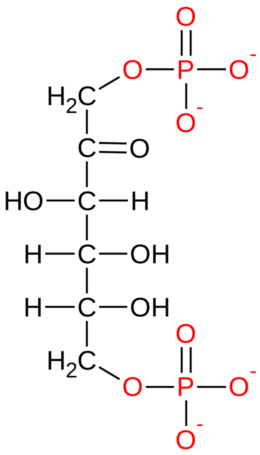
reaction of hemiacetal hydroxyl or with an amine– glycosidic bond

Functional groups and reactivity of saccharides

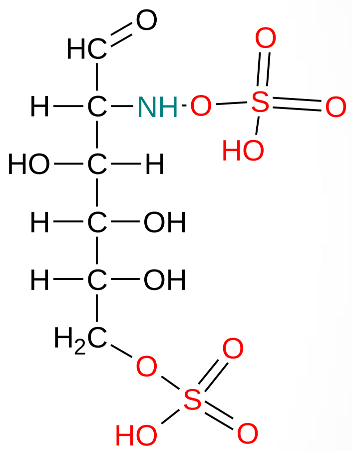
Esterification by phosphoric or sulfuric acid



Glucose-6-phosphate



Fructose – 1,6 - bisphosphate



N-Sulpho-D-glucosamine -6-sulphate

Metabolites of monosacharide metabolism

Glycosaminoglycans in extracellular matrix

Functional groups and reactivity of saccharides

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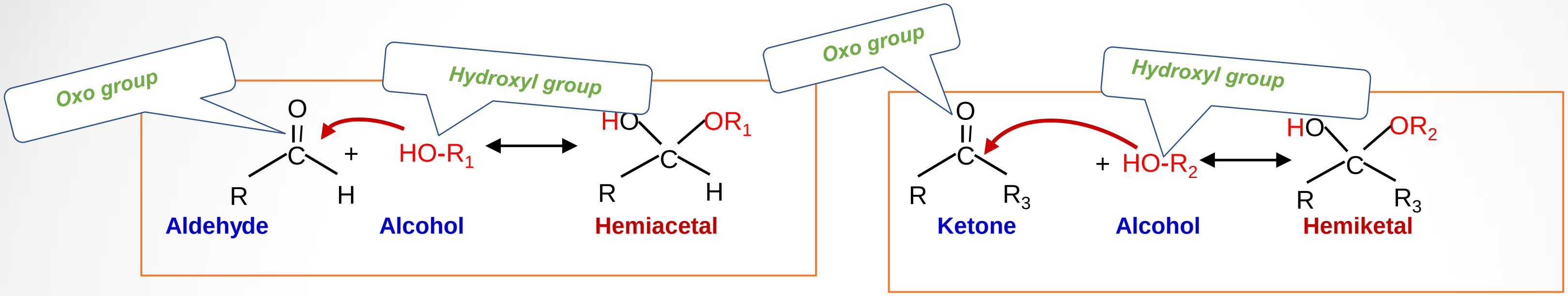
reaction of hemiacetal with hydroxyl or with an amine group – glycosidic bond

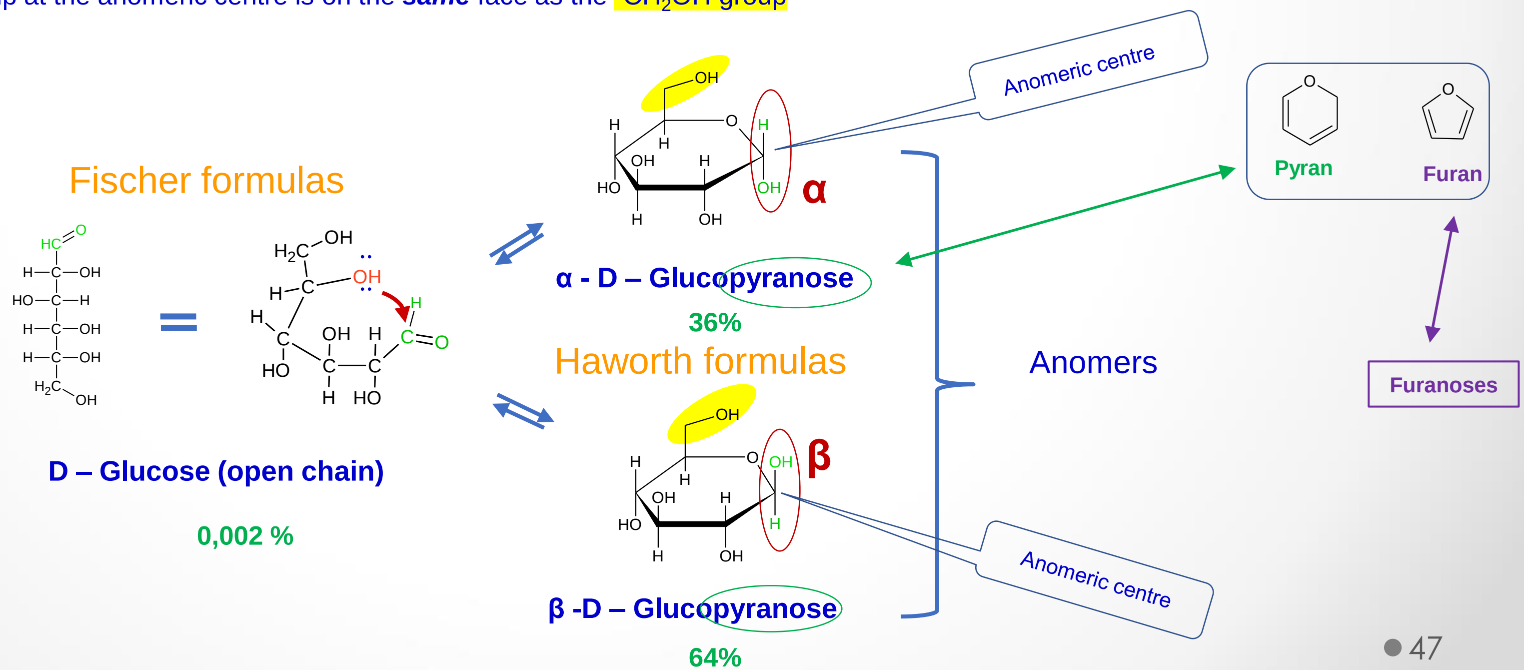
Functional groups and reactivity of saccharides

Reaction of oxo group with hydroxyl group

In general – upon reaction of an alcohol with an aldehyde or with a ketone is formed hemiacetal or hemiketal respectively.



Intramolecular reaction of hydroxyl and oxo group **in a monosaccharide** results to cyclic molecule with **anomeric centre** (carbon) binding H and OH.
The configuration at the anomeric centre is denoted alpha- (α-) or beta- (β-).
In the **α- form** the OH group at the anomeric centre is on the ***opposite*** face to the $-CH_2OH$ group
In the **β- form** the OH group at the anomeric centre is on the ***same*** face as the $-CH_2OH$ group



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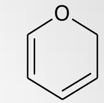
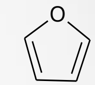
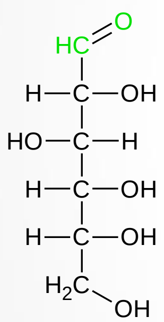

Pyran


Furan

Mutarotation

Once the glucose has dissolved, regardless of the configuration of the starting D-glucose, the solution is gradually shifted toward a mixture of approximately **64% β**-D-glucopyranoside and **36%** α-D-glucopyranose. The concentration of the open form will be **negligible** at equilibrium. *As the ratio of the* α and β *forms changes, the* ***optical rotation*** ***of the mixture changes too***. The plane of polarization light rotates by an angle.

Fischer formula



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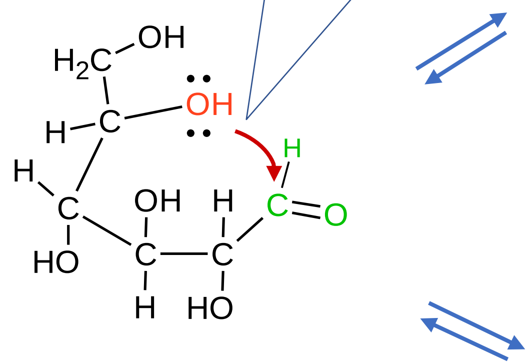
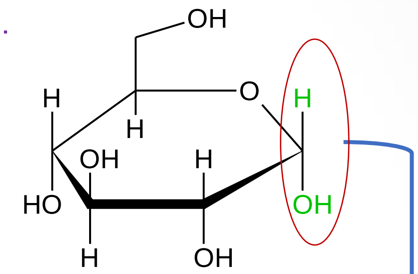
Nucleophilic atack of O on C closes the cycle



D – Glucose (open chain)

0,002 %

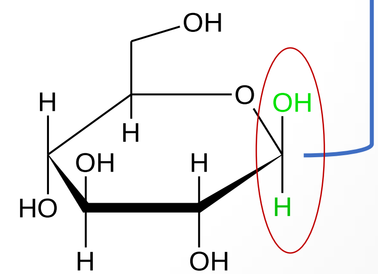


α - D – Glucopyranose

36%

α and β anomers (epimers)

Haworth formulas



β -D – Glucopyranose

64%

Functional groups and reactivity of saccharides

Functional groups

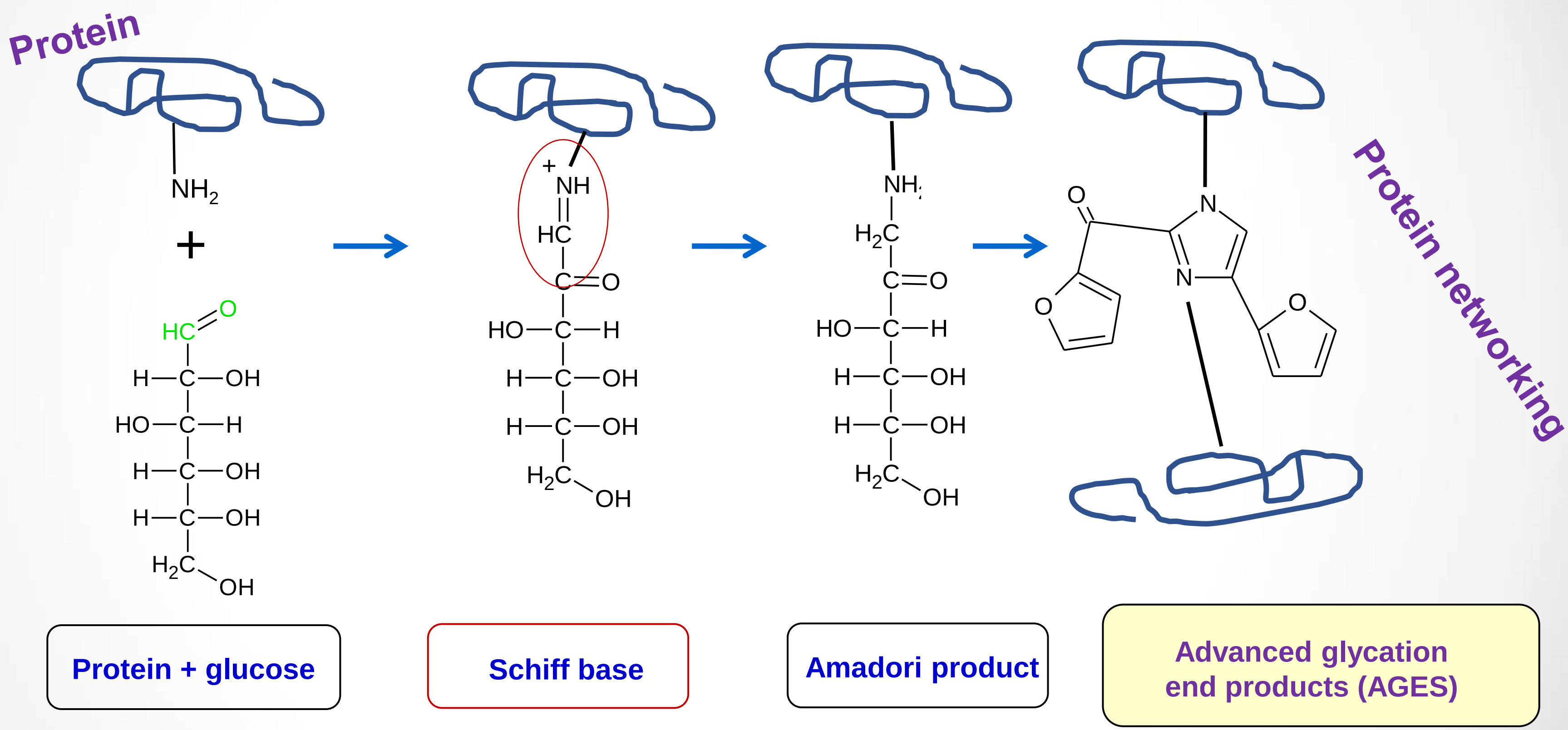
hydroxyl group -OH
carbonyl groups (aldehyde and keto groups) - CHO -CO-
carboxylic group - COOH
amine group - NH_2
sulfo group - SO_3H
acetyl group - $CO\text{-}CH_3$

Reactions

oxidation, reduction
esterification (by phosphoric or sulphuric acid)
reaction of oxo group with hydroxyl group (hemiacetal, hemiketal)
reaction of aldehydic group with a free amine group (**glycation**)
reaction of hemiacetal hydroxyl or with an amine– glycosidic bond

Glycation

Glycation is the reaction of the saccharide aldehyde group with the amino group of a protein. It is a spontaneous uncatalyzed process with pathological consequences, e.g., complications of diabetes mellitus.



! Glycosylation x Glycation !

Glycosylation is ***physiological*** enzyme catalysed posttranslation modification of some proteins (synthesis of glycoproteins).

Functional groups and reactivity of saccharides

Functional groups

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carbonyl groups (aldehyde and keto groups) - CHO -CO-
carboxylic group - COOH
amine group - NH_2
sulfo group - SO_3H
acetyl group - $CO\text{-}CH_3$

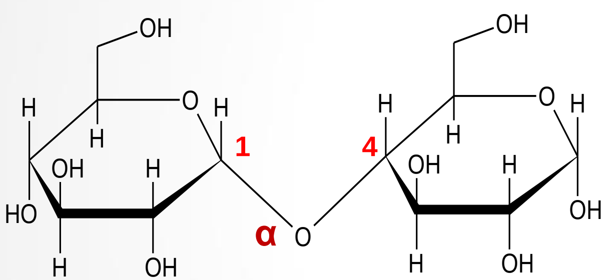
Reactions

oxidation, reduction
esterification (by phosphoric or sulphuric acid)
reaction of oxo group with hydroxyl group (hemiacetal, hemiketal)
reaction of aldehydic group with an amine group (glycation)
reaction of hemiacetal and hemiketal with hydroxyl group of an other molecule resulting to a glycosidic bond

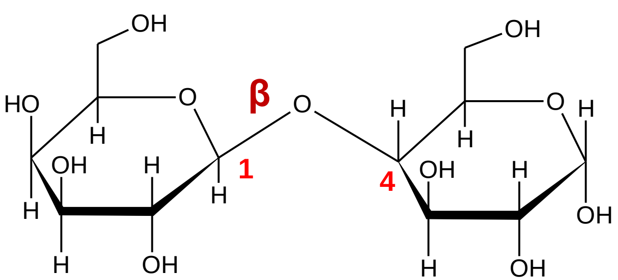
Functional groups and reactivity of saccharides

Reaction of hemiacetal and hemiketal with the hydroxyl or amine of an other molecule

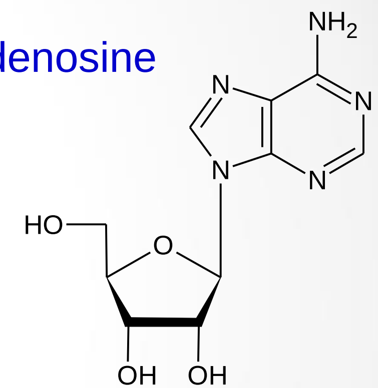
Maltose



Lactose



Adenosine



α -D-glucopyranosyl-(1- 4)-α-D-glucopyranose

β-D-galactopyranosyl-(1- 4)-α-D-glucopyranose

Adenosine

α - glycosidic bond

O - glycosidic bond

β - glycosidic bond

O - glycosidic bond

β - glycosidic bond

N - glycosidic bond

Enzymes distinguish α – and β - glycosidic bonds.

Saccharide classification

1. **MONOSACCHARIDES** — **Simple saccharides and most basic units of saccharide chains**

2. **HOLOGLYCOSIDES** — **Saccharide chains composed of only sacharide units**

   2.1. O*LIGOSACCHARIDES* (2 -10 UNITS) — **Short sacharide chains**

   2.2. *POLYSACCHARIDES* (>10 UNITS) — **Long saccharide chains**

      2.2.1. HOMOPOLYSACCHARIDES (GLYCOGEN, STARCH) — **Saccharide chains composed of only one kind of sacharide units**

      2.2.2. HETEROPOLYSACCHARIDES — **Saccharide chains composed of more then one kind of sacharide units**

      GLYCOSAMINOGLYCANS (MUCOPOLYSACCHARIDES)

      … PROTEOGLYCANS

3. **HETEROGLYCOSIDES (GLYCONE + AGLYCONE)** — **Saccharides composed of sacharide and non-saccharide components (protein, lipid, peptides)**

   3.1. GLYCOPROTEINS (MUCOPROTEINS)

   3.2. GLYCOLİPIDS

   3.3. PEPTIDOGLYCANS (MUROPEPTIDES)

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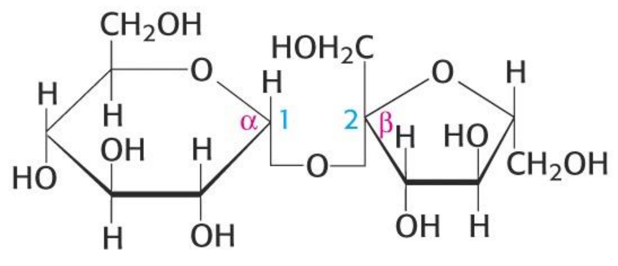
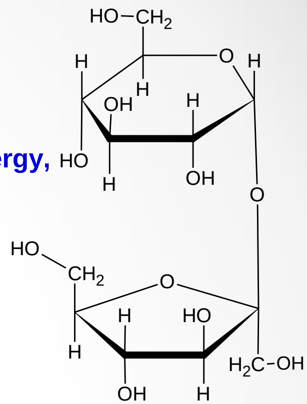
Common disaccharides

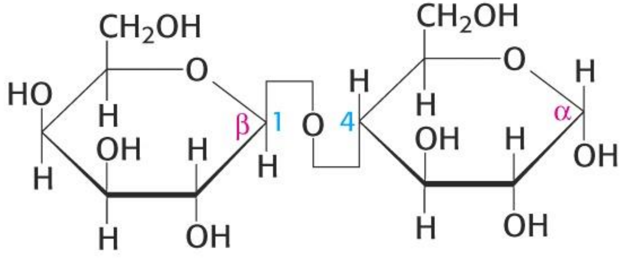


Sucrose
(α-D-Glucopyranosyl-(1→2)-β-D-fructofuranose

Major human makronutrient, source of energy, product of plant photosynthesis

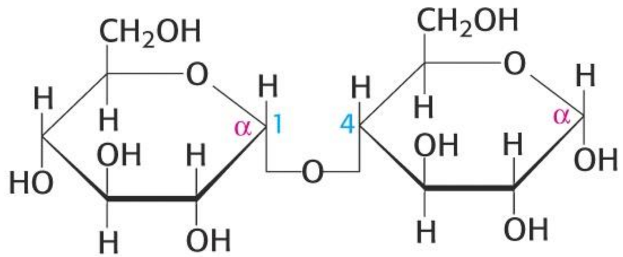


Sucrose



Lactose
(β-D-Galactopyranosyl-(1→4)-α-D-glucopyranose

Milk sugar, source of energy.
Lactose intolerance .. inability to digest lactose (abdominal pains, bloating, nauzea, diarhea)



Maltose
(α-D-Glucopyranosyl-(1→4)-α-D-glucopyranose

Malt sugar, source of energy, product of starch and glycogen hydrolysis, present in beer

Berg J.M., Tymoczko J.L. Clarke N,D, Stryer L., Biochemistry, W.H.Freeman and Company 2002

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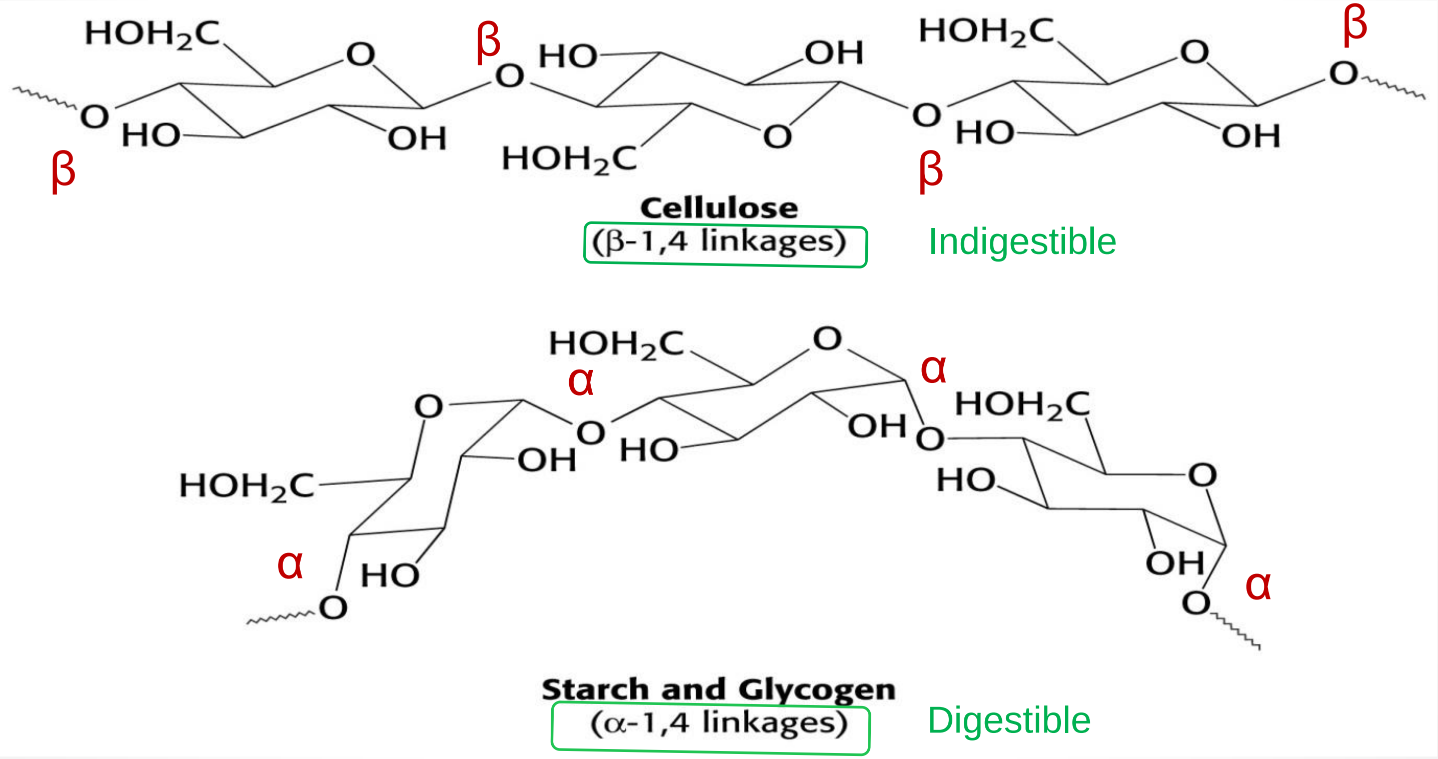
Homopolysaccharides

Glucans	(starch, glycogen, cellulose)
Fructans	(inulin in artichoke) – clearance (glomerular filtration)
Galactans	(agar from seaweeds)



Many enzymes are stereospecific. They are able to recognize "their" isomer. Intestinal amylase distinguishes α and β glycosidic bonds

Figure from Berg J.M., Tymoczko J.L. Clarke N,D, Stryer L., Biochemistry, W.H.Freeman and Company 2002

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Glycosaminoglycans

Long polysaccharide chains from bound disaccharides (from two different alternating monosaccharides – mostly from uronic acid + hexosamine)
Many **negative charges,** strongly **hydrophilic.**

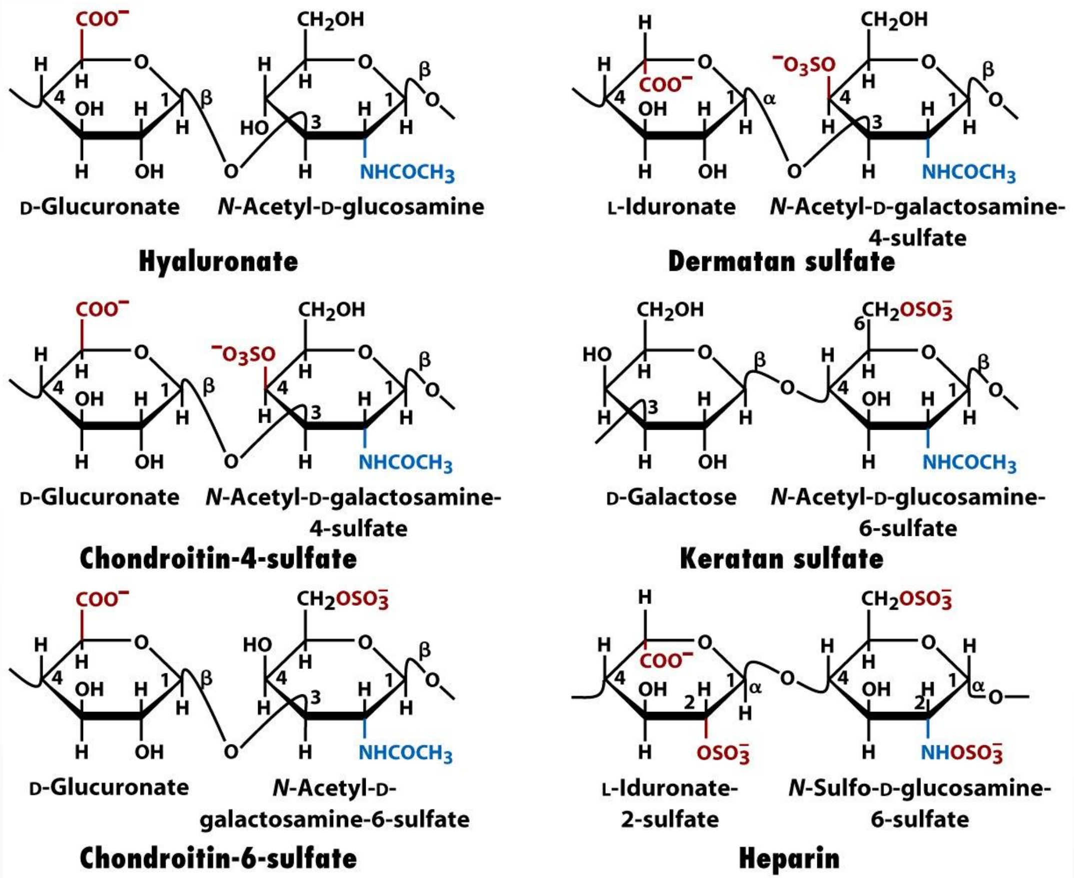

Figure 8-12 Fundamentals of Biochemistry, 2/e

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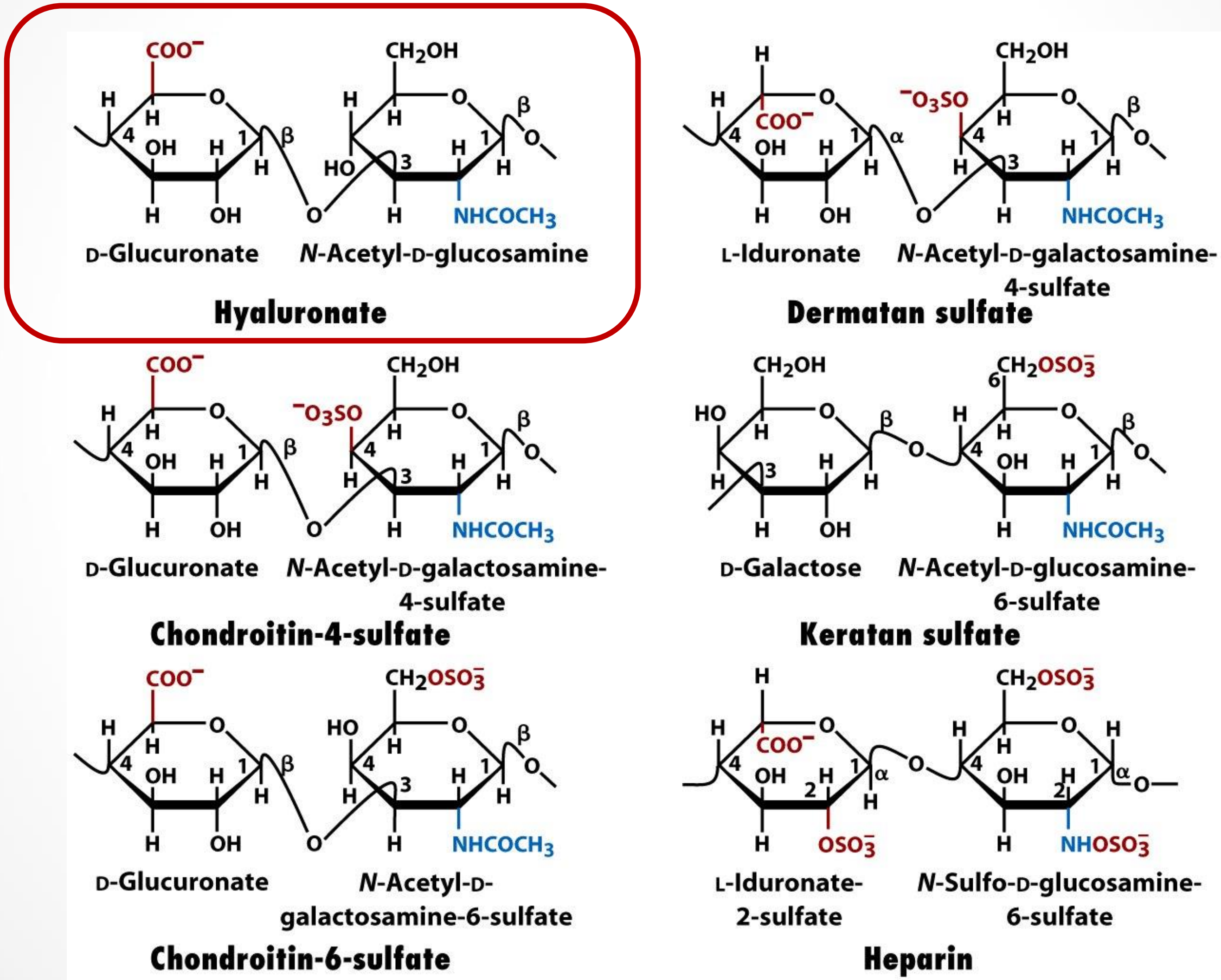
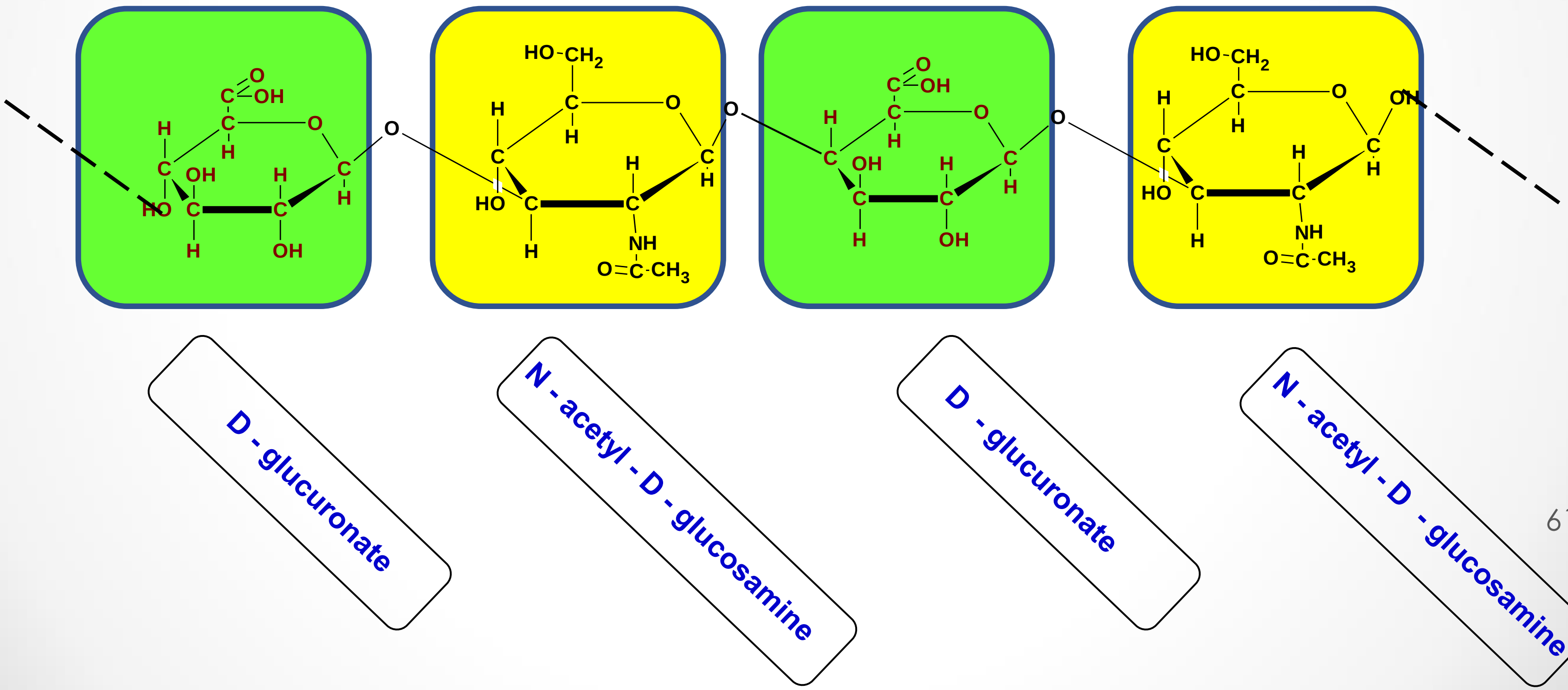


Figure 8-12 Fundamentals of Biochemistry, 2/e

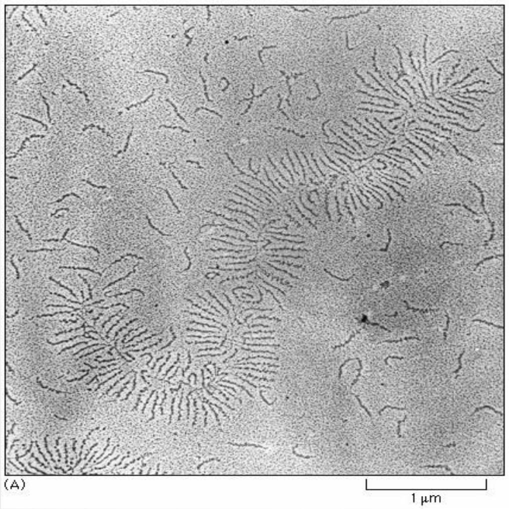
Hyaluronic acid chain

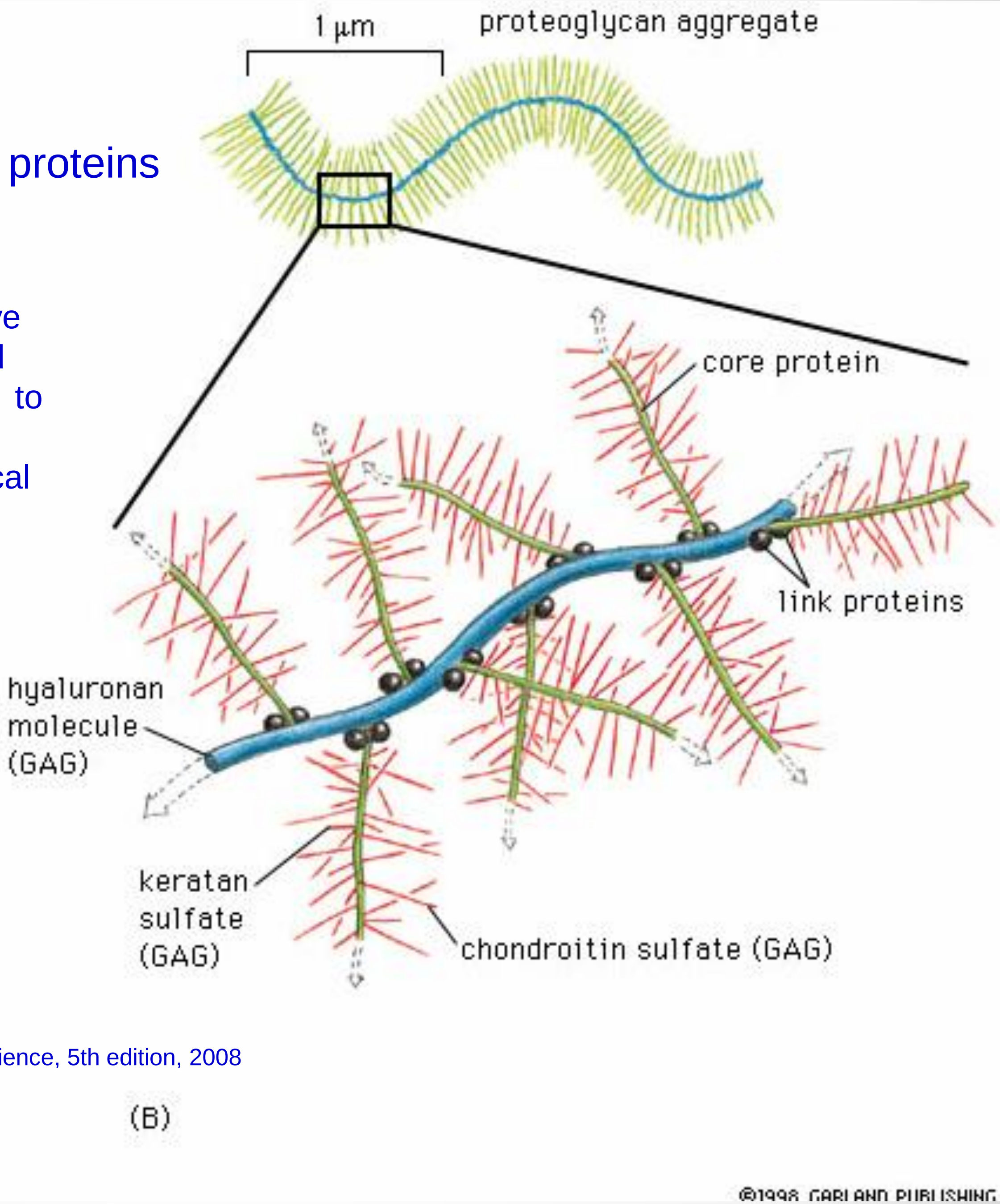


Proteoglycan

Glycosaminoglycans + binding proteins

They are important component of all extracellular matrices in the connective tissues, where provide hydration and swelling pressure to the tissue enabling to withstand compressional forces. Proteoglycans have also many biological functions.





Alberts et al. Molecular Biology of Cell, Garland Science, 5th edition, 2008

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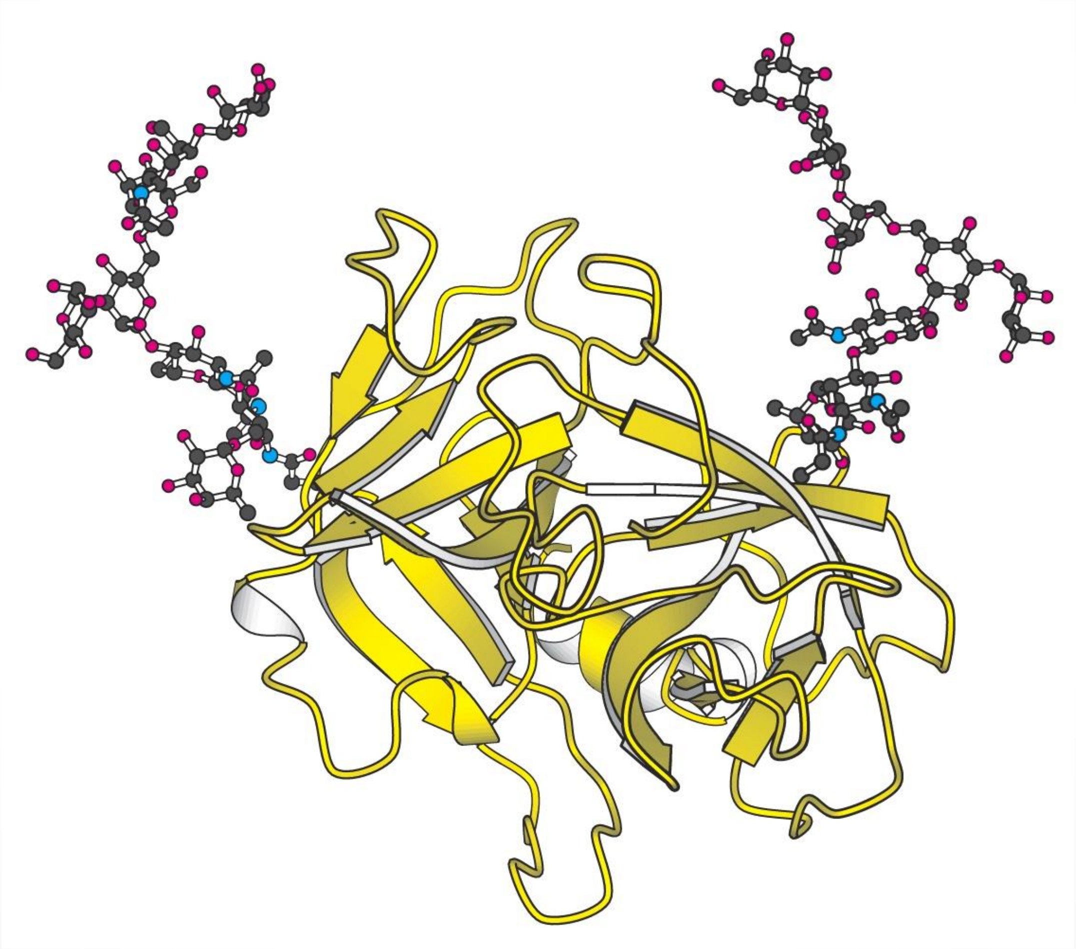
Glycoprotein

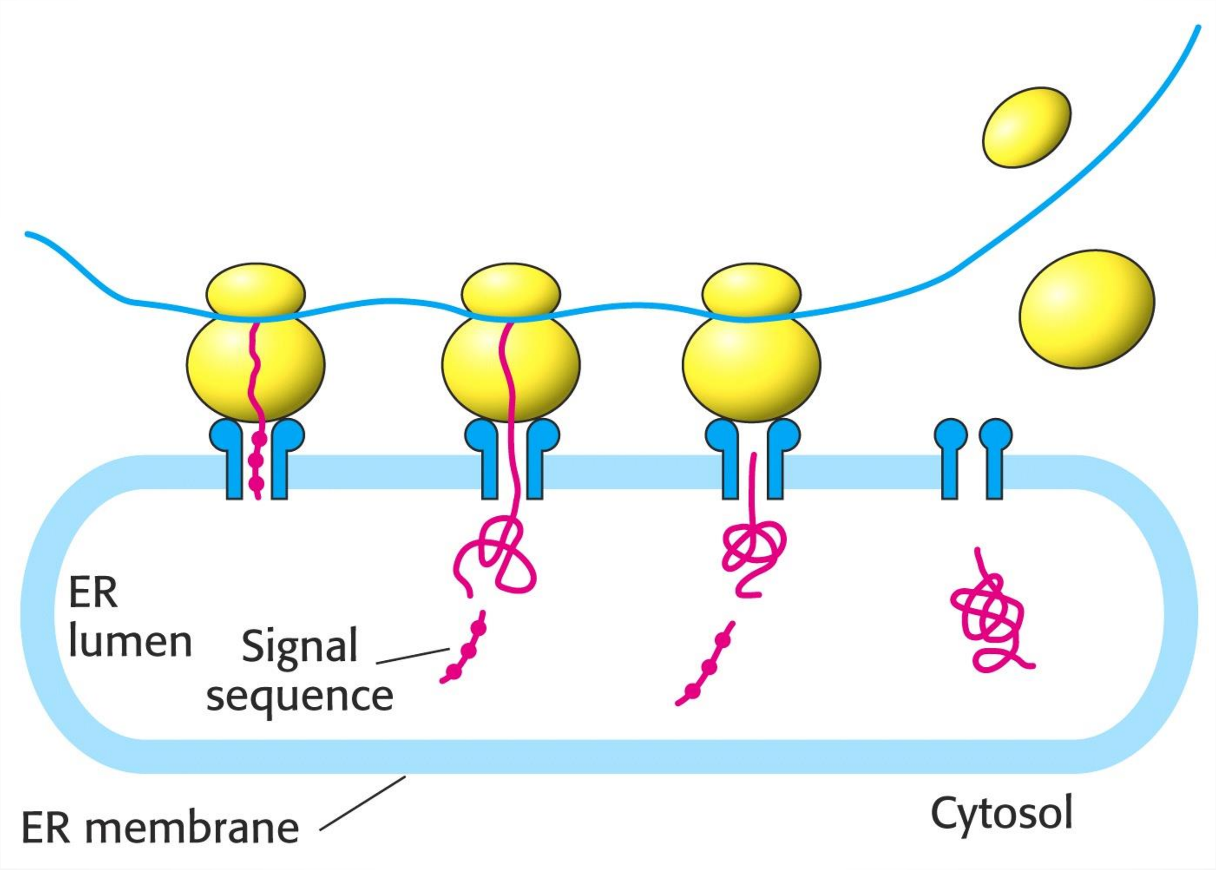
Proteins with covalently attached oligosaccharides



Berg J.M., Tymoczko J.L. Clarke N,D, Stryer L., Biochemistry, W.H.Freeman and Company 2002

Glycoproteins

Oligosaccharides are attached to the protein already during its synthesis (translation).

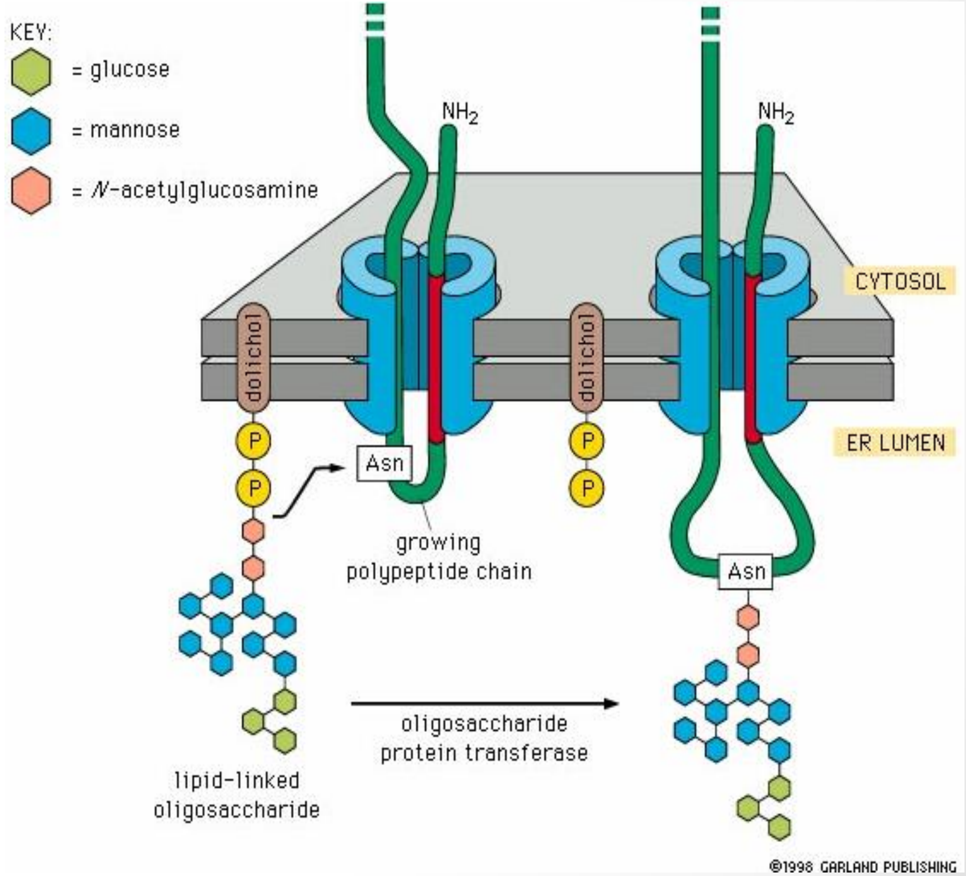


Berg J.M., Tymoczko J.L. Clarke N,D, Stryer L., Biochemistry, W.H.Freeman and Company 2002

Glycoproteins

Glycosylation

.



Oligosaccharides are attached to the protein already during its synthesis (translation). This glycosylation is physiological cotranslation and posttranslational process catalyzed by special enzymes.

Alberts et al. Molecular Biology of Cell, Garland Science, 5th edition, 2002

Glycoproteins

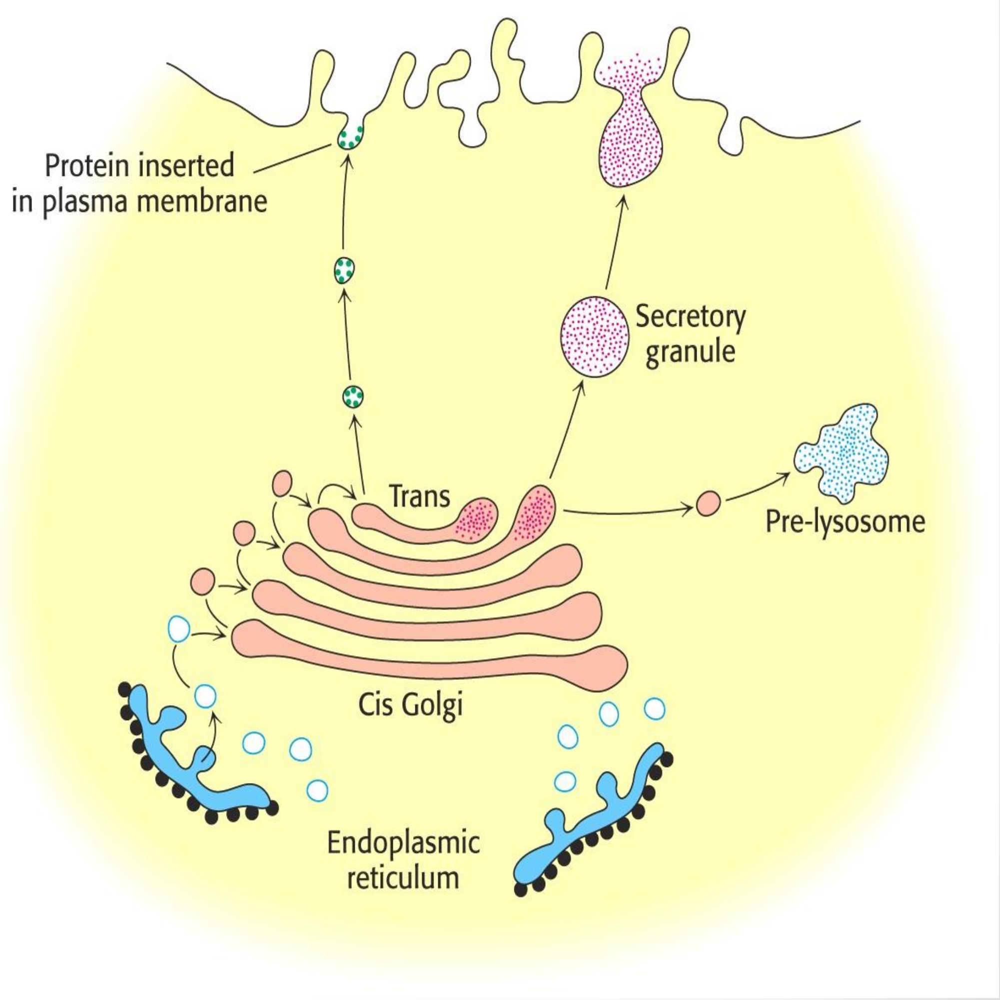
Glycosylation

Glycosylation
X
Glycation

Glycosylation begins in the cisterns of the **endoplasmic reticulum** and continues in the **Golgi apparatus**.

The attached saccharides change the conformation of the proteins. This is of particular importance when considering **protein-protein interactions** such as those that occur between protein ligands and their cognate receptors .

The attached saccharides significantly serve to distribute proteins to the plasma membrane, secretory granules and to subcellular organelles (lysosomes). **Many of them are signal molecules** (hormones, cytokines)



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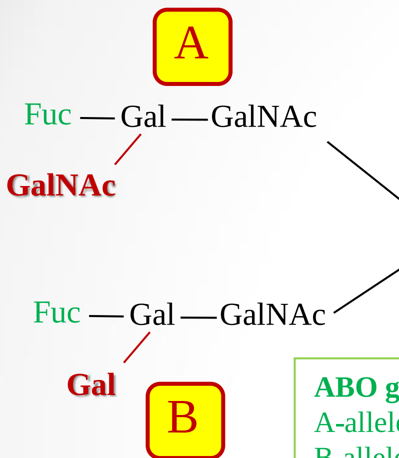
GLYCOLIPIDS

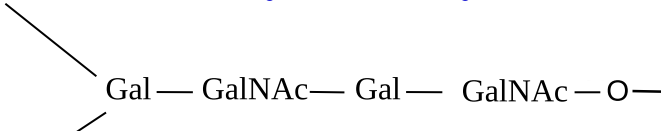
Blood groups

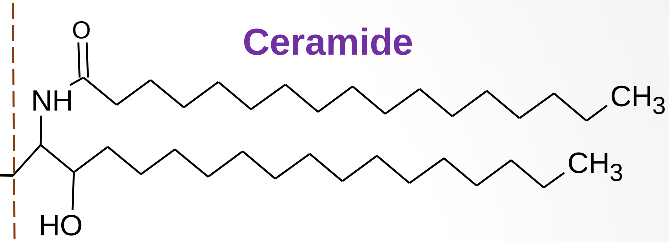
Blood groups ABO system is based on the presence of special monosaccharide substituents fucose, N-acetyl galactosamine (GalNAc , A) and galactose (Gal, B) on the **saccharide part of the membrane glycolipids** and glycoproteins.

Further details are given on the following slide.

Lipid layer of the cell membrane

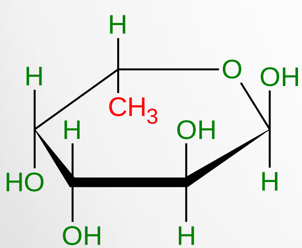






ABO genes
A-allele … N-acetylgalactosamine glycosyltranferase
B-allele … galactose glycosyltransferase
O-allele ….no active trasnsferase
H-gene …..fucosyltransferase

Fuc ……………..…….substance H
Fuc + GalNAc ……….substance A
Fuc + Gal …………….substance B



Fucose
(6-deoxy-L-galactose)

GROUP	1st branch with fucose	2nd branch with fucose	Antibodies in plasma	Comment
O	-	-	Anti-A Anti-B	H subatance is present only or fucose even misses out
A	GalNAc	GalNAc	Anti-B	-
B	Gal	Gal	Anti-A	-
AB	GalNAc	Gal	None	-

GLYCOLIPIDS

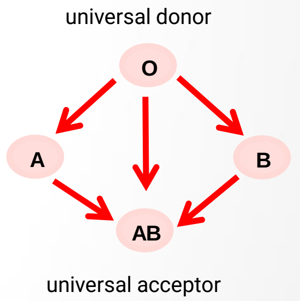
Blood ABO system

Membranes of red blood cells (and other cells) contain a number of blood group antigens. The most studied are antigens A and B. They are glycolipids and glycoproteins, the important structure of which is an oligosaccharide called substance H (antigen H). At the end of the chain, substance H has an unusual derivative of L-galactose called fucose. Substance H is a precursor of antigen A and B; the addition of N-acetyl galactosamine (GalNAc) gives antigen A and the addition of galactosamine (Gal) gives antigen A.

Specific glycosyltranferases are responsible for the synthesis of the mentioned antigens: fucosyltransferase, N-acetylgalactosamine glycosyltranferase and galactose glycosyltransferase..
The presence of the fucose in the antigen H structure is essential.
The enzymes N-acetylgalactosamine glycosyltranferase and galactose glycosyltransferase do not work without fucosyl substituent.

The affiliation of a person to a certain blood group is given of his ABO gene alleles
A-allele … N-acetylgalactosamine glycosyltranferase
B-allele … galactose glycosyltransferase
O-allele … no active transferase
H-gene ….fucosyltransferase

ABO incompatibility reaction
Anti-A and anti-B antibodies are present in the blood plasma against those antigens that are not present in the individual‘s.
If erythrocytes were administered during transfusion with antigens against which the recipient has antibodies in the plasma,
hemolysis strokes, hemocoagulation, and, after depletion of coagulation factors, bleeding would occur.



Glycolipids are binding sites for bacteria and bacterial toxins

Specific saccharides of glycolipids, glycoproteins and proteoglycans of tissue cells a recognised by **bacterial proteins adhesines.** Also the toxins secreted from bacteria (including tetanus toxin and botulinum toxin also bind to specific cellular glycolipids. These events are cirical for bacterial colonization and infection.

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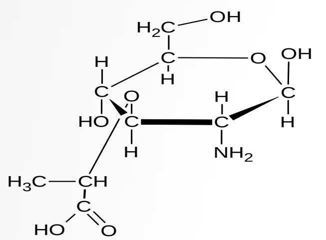
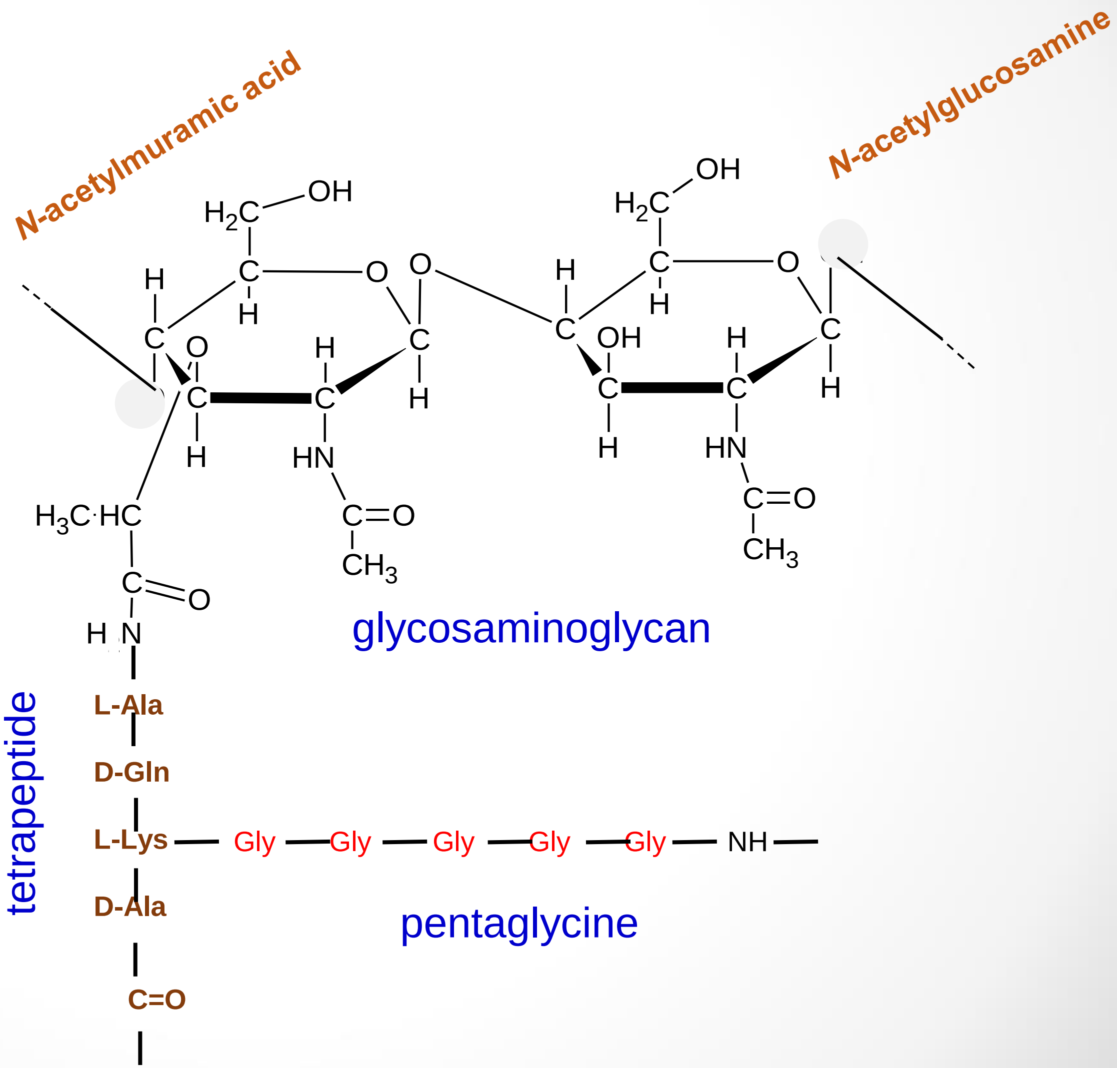
Peptidoglycan (muropeptide)

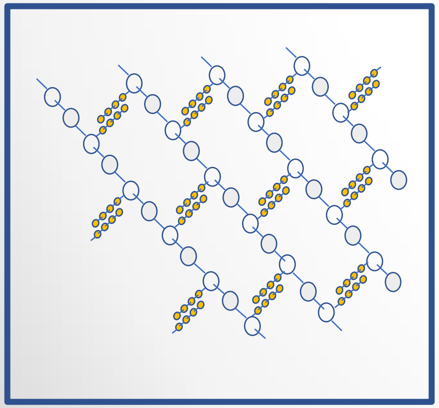
Bacterial cell wall (structural support) is network composed of **peptides** (pentaglycines and tetrapeptides) and of **glycosaminoglycan**



Muramic acid

Ether of lactic acid and glucosamine



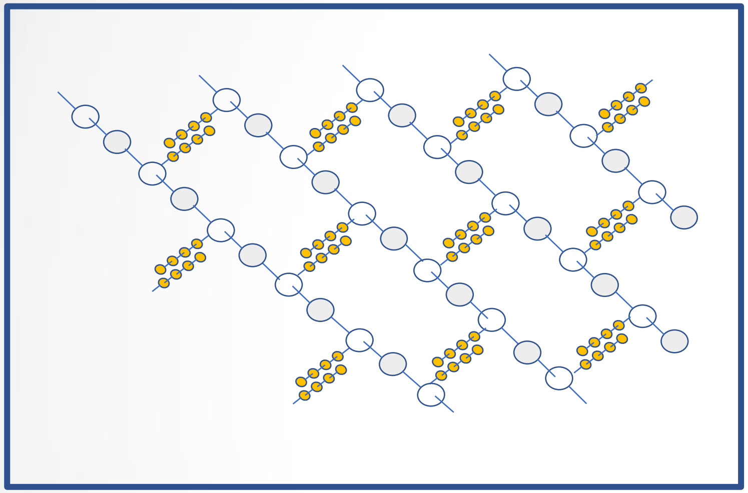


Bacterial cell wall

(pentaglycines omitted)

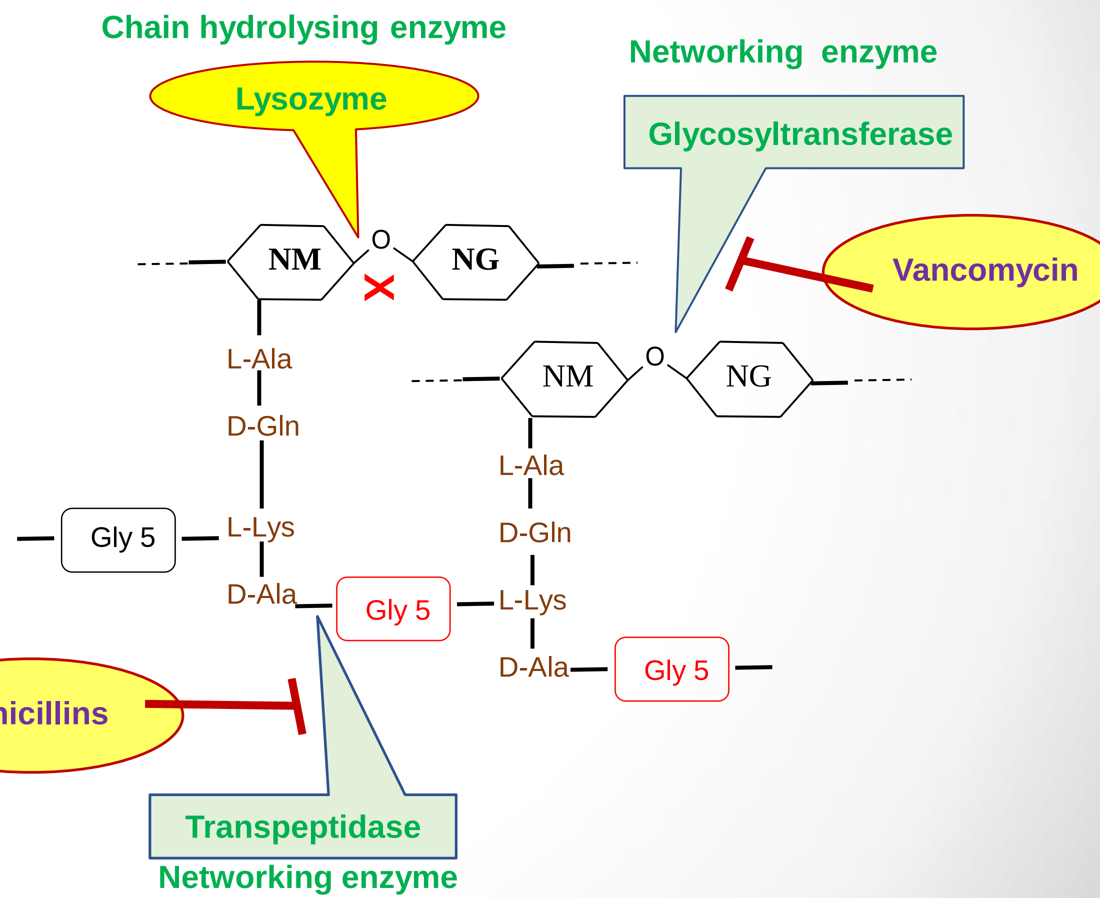
Peptidoglycan (muropeptide)

Synthesis of peptidoglycan network is catalysed by the glycosyltransferase and transpeptidase, which can serve as a target of various antibacterial medicaments



Bacterial cell wall

(pentaglycines omitted)

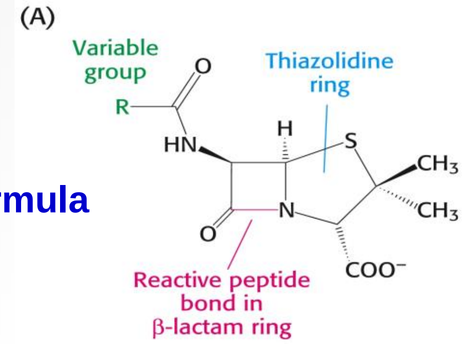


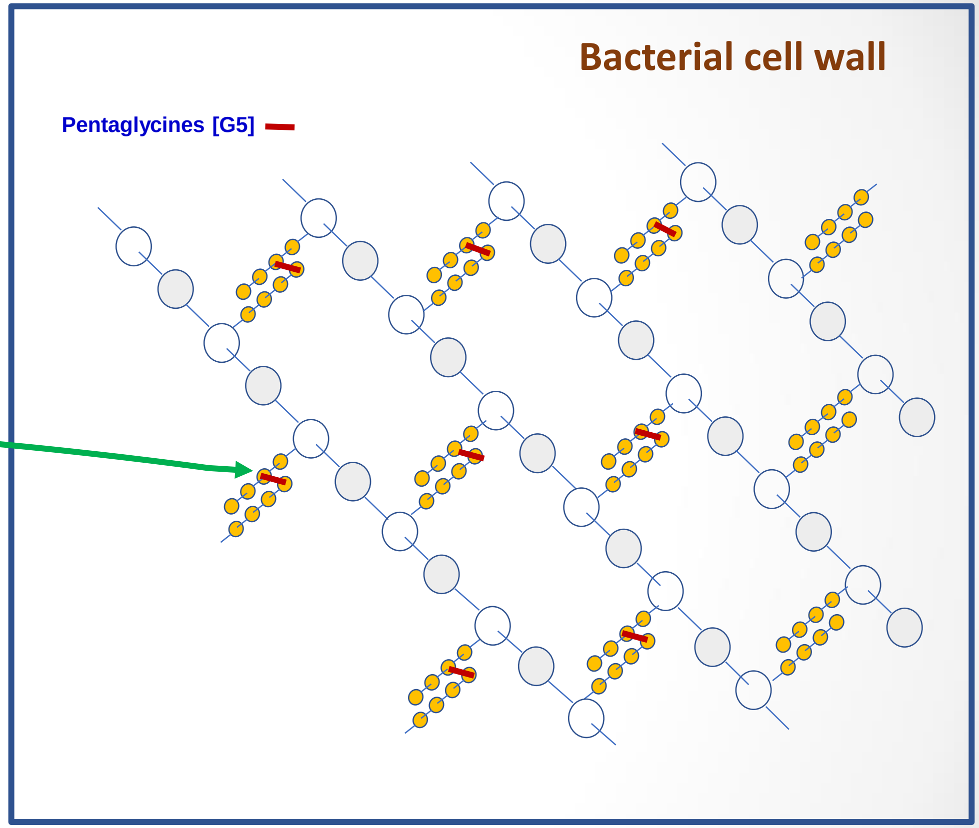
A **lysosome** is a cell organelle x **lysozyme** is bactericidal **hydrolase** in tears, eggs, human milk and mucus.

Penicillin

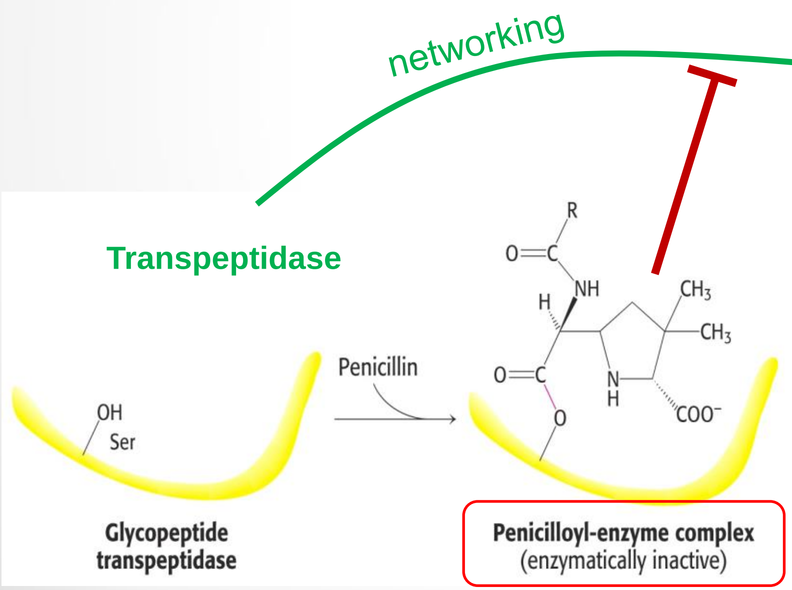
Mechanism of bactericidal activity = inhibition of transpeptidase

Penicillin formula





Transpeptidase



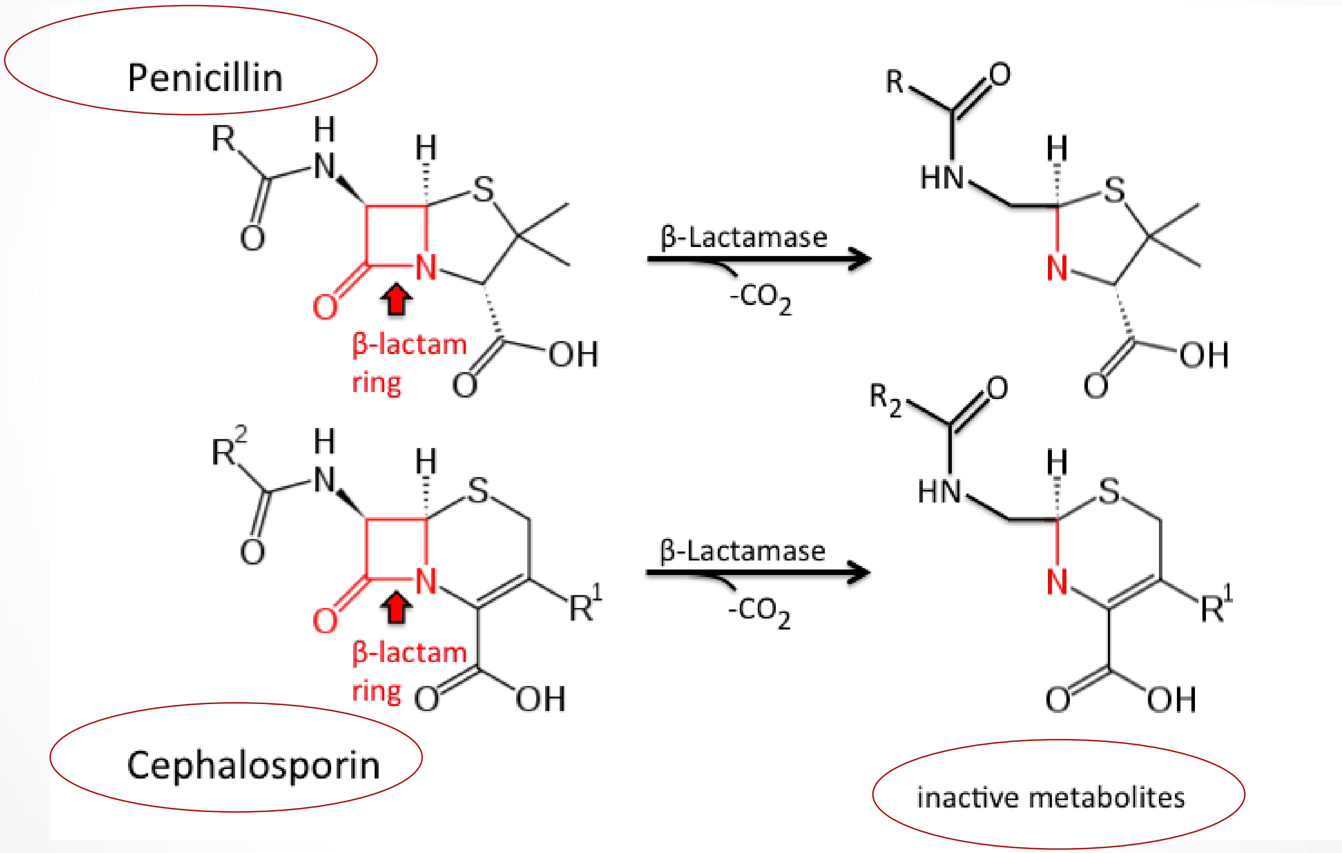
Inhibition of networking

Penicillin inhibits joining of pentaglycines to tetrapeptides

Berg J.M., Tymoczko J.L. Clarke N,D, Stryer L., Biochemistry, W.H.Freeman and Company 2002 (adapted)

Beta-lactamases

Enzymes produced by bacteria. They open the lactam ring and provide **bacterial resistance** to β-lactam antibiotics such are penicillins.



Antibiotic pharmacology https://tmedweb.tulane.edu/pharmwiki/doku.php/antibiotic_pharmacology

Pathogenetic role of saccharides (examples)

Blood groups

Antibiotic target

Diabetes mellitus

Diagnostic significance

Tooth caries

Dental caries

is caused mainly by two factors:

1. **adherence of food to the teeth** containing saccharides sucrose, fructose and glucose

2. few specific species of bacteria in this biofilm. Especially *Streptococcus mutants and Lactobacillus species* are able to produce **high levels of lactic acid** by glycolysis and related metabolic pathways. Simultaneously they are resistant to low pH (acidic environment) in contrary to enamel and dentin which are demineralized.

20190514_BP_NM_superfinal.pdf (muni.cz)

Thank you for your attention

Literature

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