Carbohydrate metabolism

Any biochemistry textbook may work, e.g.

Lippincott's Illustrated Reviews, Biochemistry, 3rd ed,
Chapters 7-8,10-14

Roskoski, Biochemistry, 1st ed,
Chapters 7, 10, 25

Berg, Tymoczko, Stryer, 6th ed,
Chapters 11, 16, 20, 21

CARBOHYDRATES

Learning objectives:

Classify carbohydrates according to their definitions

Discuss isomeric properties of carbohydrates

Draw structures of the most common carbohydrates

Discuss digestion of dietary carbohydrates

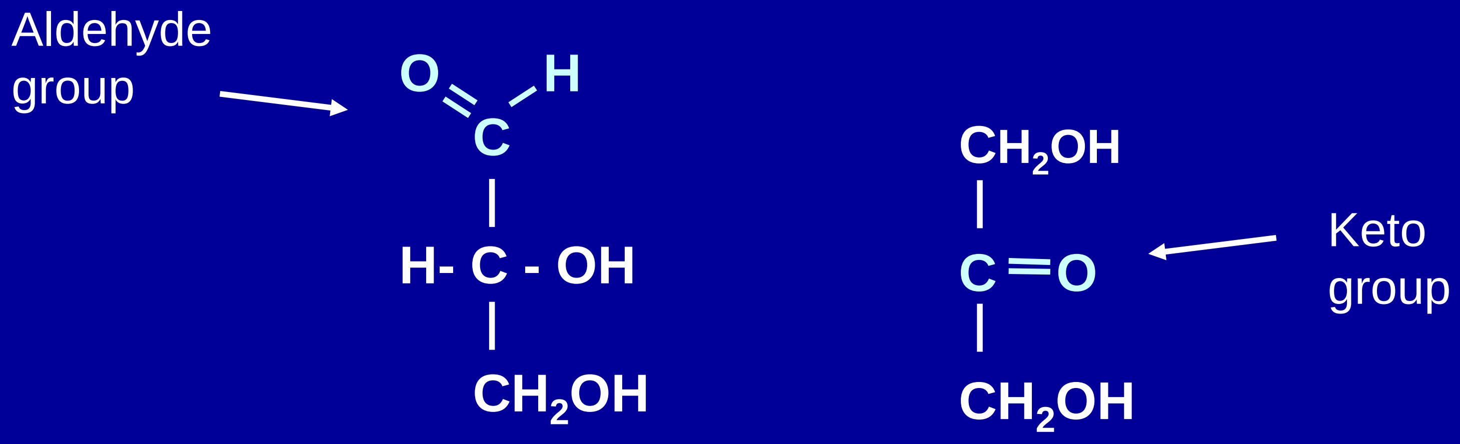
Sept. 2007

CARBOHYDRATES

- The most abundant organic molecules in nature
- Provide a significant fraction of the energy in the diet of most organisms
- Important source of energy for cells
- Can act as a storage form of energy
- Can be structural components of many organisms
- Can be cell-membrane components mediating intercellular communication
- Can be cell-surface antigens
- Can be part of the body’s extracellular ground substance
- Can be associated with proteins and lipids
- Part of RNA, DNA, and several coenzymes (NAD^+, $NADP^+$, FAD, CoA)

CARBOHYDRATES

Polyhydroxy aldehydes or ketones,
or substances that yield these compounds on hydrolysis

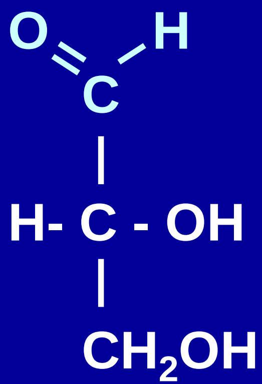


Glyceraldehyde   Dihydroxyacetone

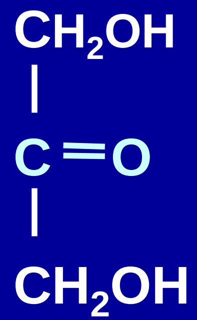
Carbohydrate with an aldehyde group: Aldose
Carbohydrate with a ketone group: Ketose

CARBOHYDRATES

Polyhydroxy aldehydes or ketones,
or substances that yield these compounds on hydrolysis



Glyceraldehyde



Dihydroxyacetone

Both can be written $C_3H_6O_3$ or $(CH_2O)_3$

Empirical formula of many simpler carbohydrates: $(CH_2O)_n$
(hence the name hydrate of carbon)

Monosaccharides

Polyhydroxy aldehydes or ketones that can’t easily be further hydrolyzed
“Simple sugars”

Number of carbons	Name	Example
3	Trioses	Glyceraldehyde
4	Tetroses	Erythrose
5	Pentoses	Ribose
6	Hexoses	Glucose, Fructose
7	Heptoses	Sedoheptulose
9	Nonoses	Neuraminic acid

Oligosaccharides

Hydrolyzable polymers of 2-6 monosaccharides

Disaccharides composed of 2 monosaccharides
Examples: Sucrose, Lactose

Polysaccharides

Hydrolyzable polymers of > 6 monosaccharides

Homopolysaccharides:
polymer of a single type of monosaccharide
Examples: Glycogen, Cellulose

Heteropolysaccharides:
polymer of at least 2 types of monosaccharide
Example: Glucosaminoglycans

ISOMERISM

<u>Structural isomers</u>

Compounds with the same molecular formula but with different structures

<u>Functional group isomers</u>

with different functional groups

E.g. glyceraldehyde and dihydroxyacetone

<u>Positional isomers</u>

with substituent groups on different C-atoms

E.g.

COO^{-}-$CHOPO_3^{-}$-CH_2OH and COO^{-}-CHOH-$CH_2OPO_3^{-}$

2-Phosphoglycerate   3-Phosphoglycerate

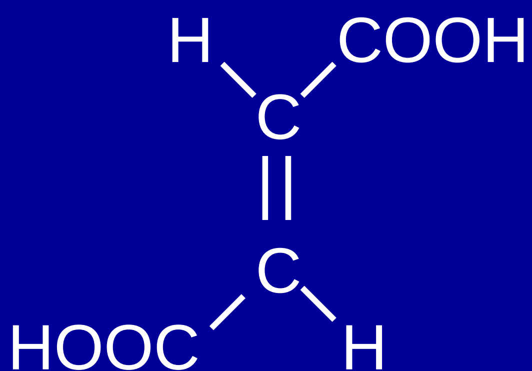
ISOMERISM

<u>Stereoisomers</u>

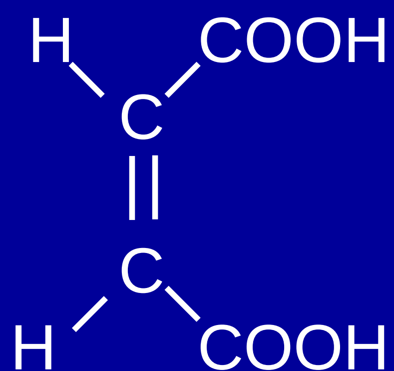
Compounds with the same molecular formula, functional groups, and position of functional groups but with different conformations

<u>*cis-trans* isomers</u>

with different conformation around double bonds



Fumaric acid (*trans*)



Maleic acid (*cis*)

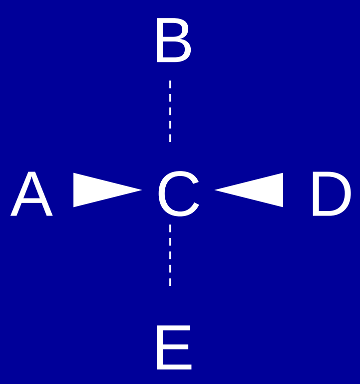
ISOMERISM

Stereoisomers

Compounds with the same molecular formula, functional groups, and position of functional groups but with different conformations

optical isomers

with different conformation around chiral or asymmetric carbon atoms



The carbon C is asymmetric if A, B, D, and E are four different groups

The four different groups A, B, D, and E can be arranged in space around the C-atom in two different ways to generate two different compounds

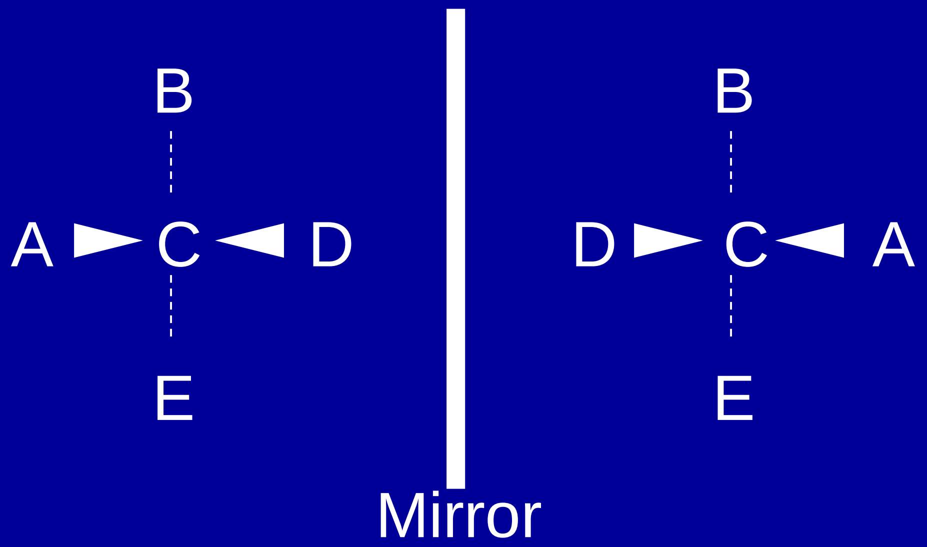
ISOMERISM

<u>Stereoisomers</u>

Compounds with the same molecular formula, functional groups, and position of functional groups but with different conformations

<u>optical isomers</u>

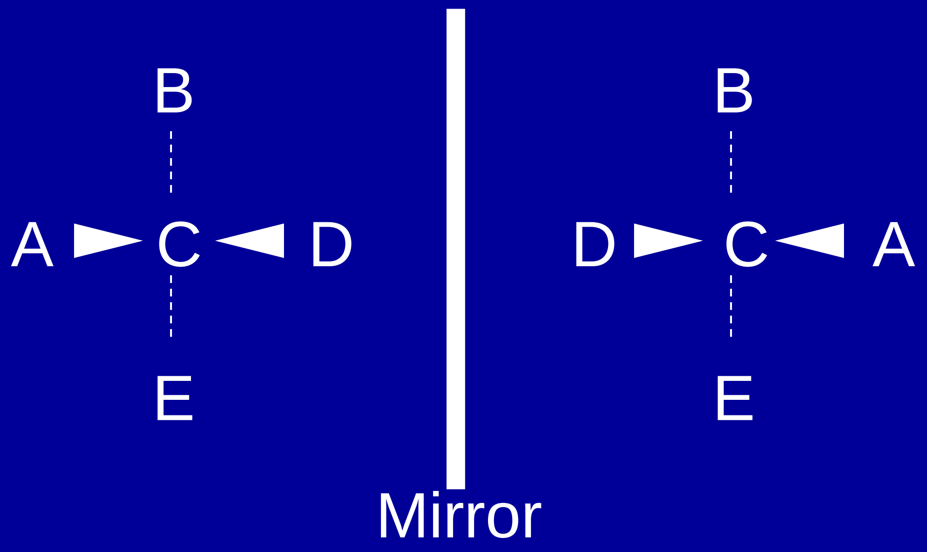
with different conformation around chiral or asymmetric carbon atoms



The mirror images can't be superimposed on each other, i.e. they are different

The mirror image isomers constitute an ***enantiomeric pair***; one member of the pair is said to be the ***enantiomer*** of the other

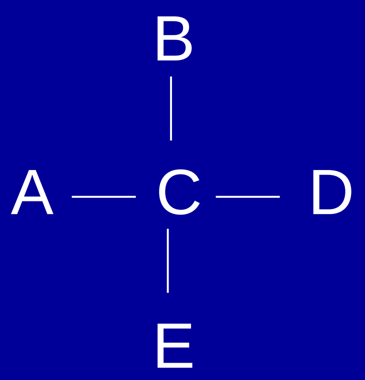
ISOMERISM



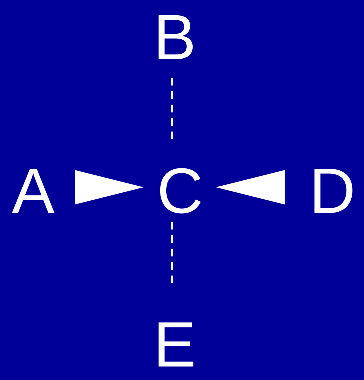
One member of an ***enantiomeric pair*** will rotate a plane of polarized light in a clockwise direction.
It is said to be *dextrorotatory* which is labelled (+)

The other member of the pair will then rotate the light in a counterclockwise direction.
It is said to be *levorotatory* which is labelled (-)

ISOMERISM

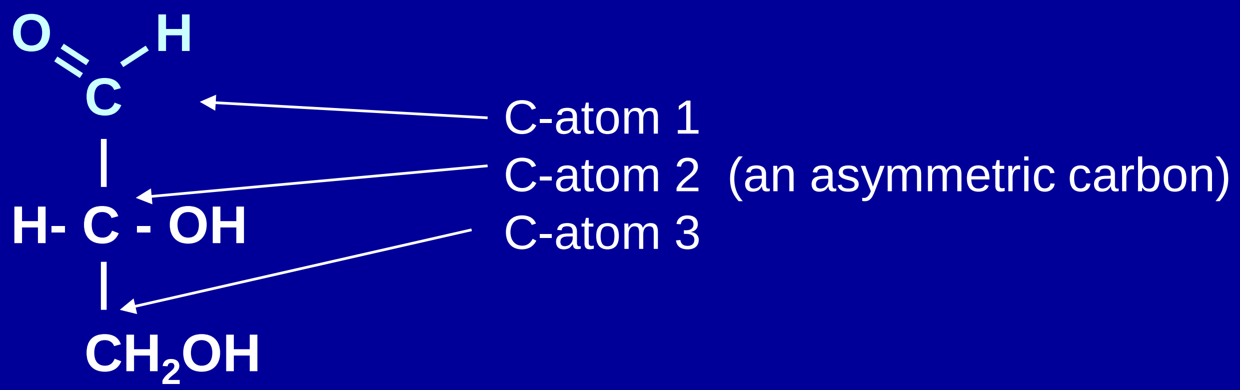


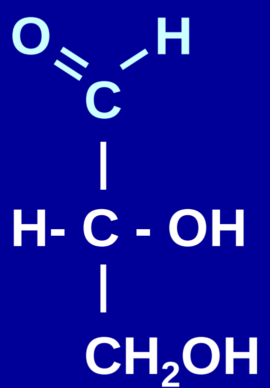
Fischer projection formula



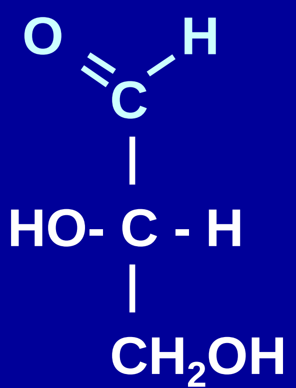
Perspective formula

Reference compound for optical isomers is the simplest monosaccharide with an asymmetric carbon: glyceraldehyde

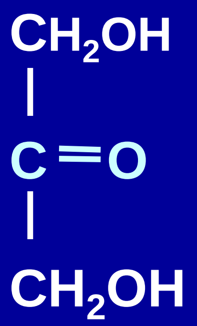




D-Glyceraldehyde



L-Glyceraldehyde



Dihydroxyacetone

D-Glyceraldehyde is assigned to be the isomer that has the hydroxyl group on the right when the aldehyde group is at the top in a Fischer projection formula.

It is also dextrorotatory, so it is also D(+)-Glyceraldehyde

If a compound has n asymmetric carbon atoms then there are 2^n different optical isomers

Number of carbon atoms	Aldose/Ketose	Number of asymmetric carbon atoms	Number of optical isomers
3	Aldose	1	2
4	Aldose	2	4
5	Aldose	3	8
6	Aldose	4	16
3	Ketose	0	-
4	Ketose	1	2
5	Ketose	2	4
6	Ketose	3	8

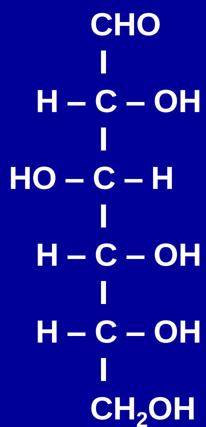
D & L designate absolute configuration of the asymmetric carbon atom farthest from the aldehyde or ketone group

D-Erythrose	L-Erythrose	D-Threose	L-Threose
CHO	CHO	CHO	CHO
|	|	|	|
H – C – OH	OH – C – H	OH – C – H	H – C – OH
|	|	|	|
H – C - OH	OH – C - H	H – C - OH	OH – C - H
|	|	|	|
CH_2OH	CH_2OH	CH_2OH	CH_2OH

D-Erythrose **L-Erythrose** **D-Threose** **L-Threose**

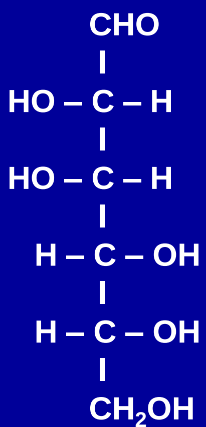
Optical isomers that are not enantiomers are *diastereomers*

Diastereomers that differ by their configuration on a single asymmetric carbon are *epimers*



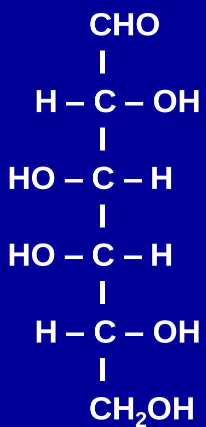
D-Glucose

$C_6H_{12}O_6$



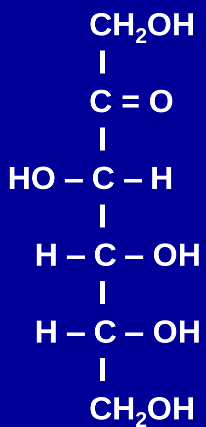
D-Mannose

$C_6H_{12}O_6$



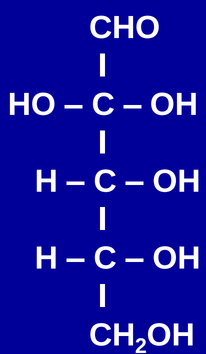
D-Galactose

$C_6H_{12}O_6$



D-Fructose

$C_6H_{12}O_6$



D-Ribose

$C_5H_{10}O_5$

Reactions involving aldehyde and keto groups in carbohydrates

$$\text{Aldehyde + Alcohol} \rightleftharpoons \text{Hemiacetal}$$

$$\text{Ketone + Alcohol} \rightleftharpoons \text{Hemiketal}$$

With ring formation involving the aldehyde- or ketone-carbon atom, this carbon atom also becomes asymmetric, giving two possible isomers called *anomers*

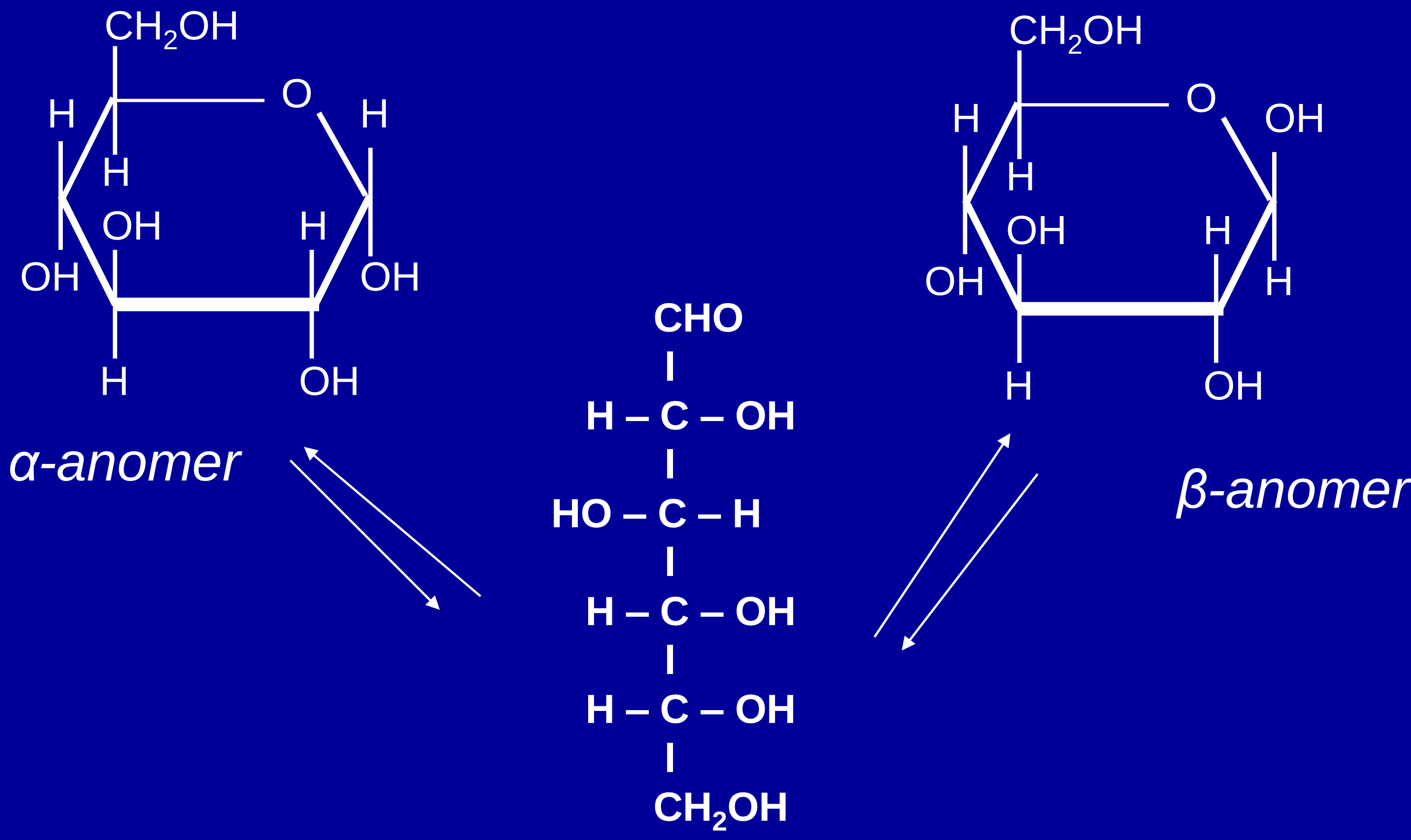
The carbon atom is the *anomeric* carbon
The hydroxyl group bound to the anomeric carbon is the *anomeric* hydroxyl group.

In Haworth formulas of D-pentoses and D-hexoses,
the *α-anomer* has the anomeric hydroxyl written below the ring plane
the *β-anomer* has the anomeric hydroxyl written above the ring plane

6-membered ring: Pyranose

5-membered ring: Furanose

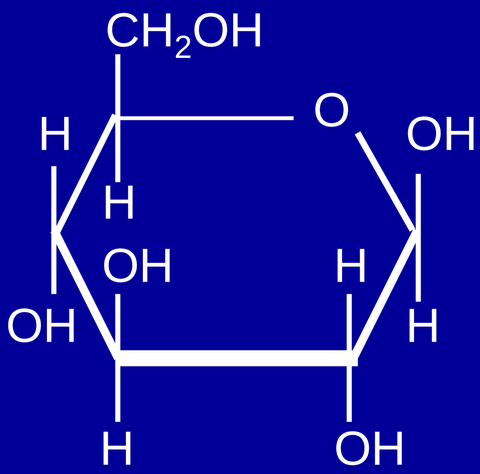
Mutarotation: Spontaneous conversion of one anomer to the other



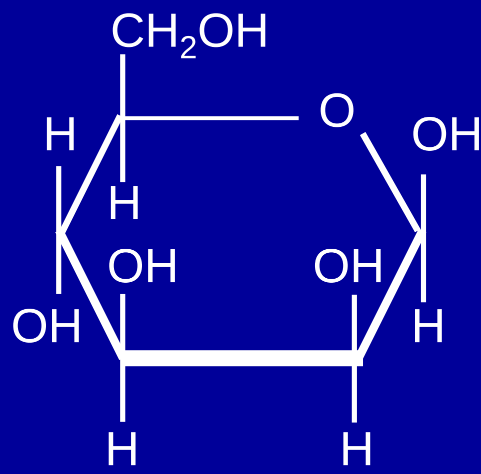
D-Glucose

Equilibrium: 36% α-anomer, 63% β-anomer, <1% open-chain form

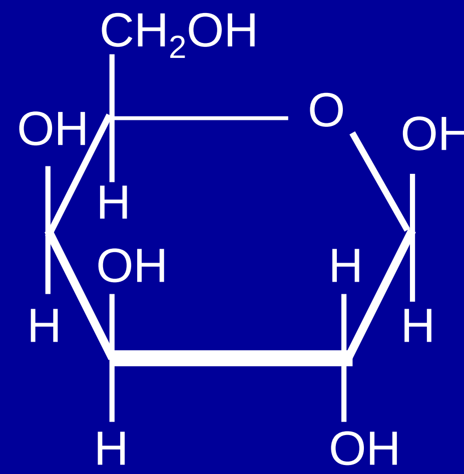
Learn (know) these structures



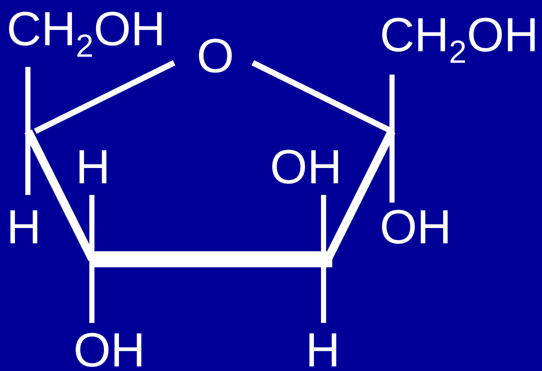
D-Glucopyranose



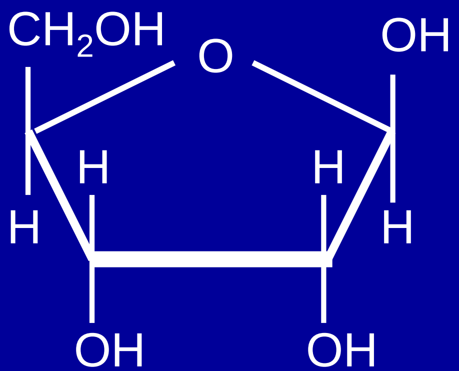
D-Mannopyranose



D-Galactopyranose



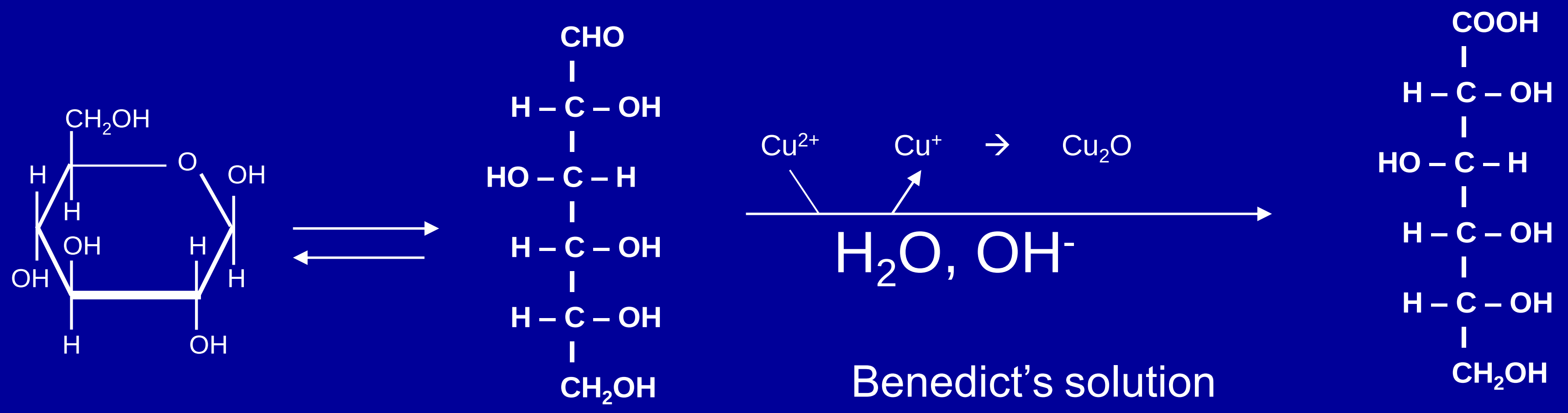
D-Fructopyranose

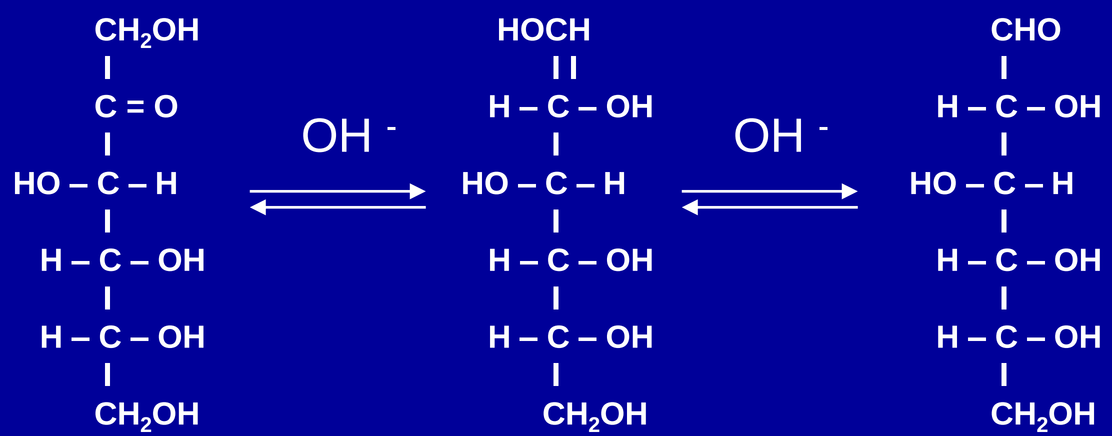


D-Ribofuranose

Reducing sugars

Carbohydrate with a free or potentially free aldehyde or ketone group





D-Fructose **Enediol** **D-Glucose**

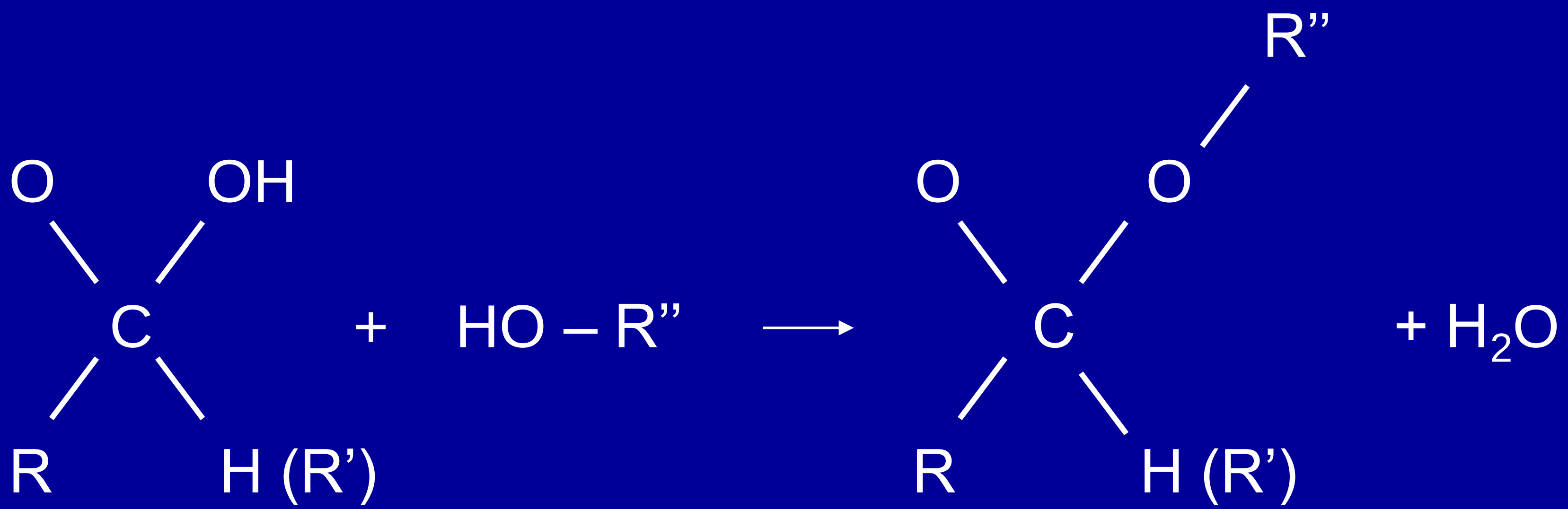
Glycosidic bonds

Bond formed between the anomeric carbon of a carbohydrate and the hydroxyl oxygen atom of an alcohol (O-glycosidic bond) or the nitrogen of an amine (N-glycosidic bond)

Glycosidic bonds between monosaccharides yields oligo- and polysaccharides

After glycosidic bond formation, the ring formation involving the anomeric carbon is stabilized with no potentially free aldehyde or keto groups

O-glycosidic bonds



Hemiacetal (Hemiketal)   Alcohol   Acetal (Ketal)   Water

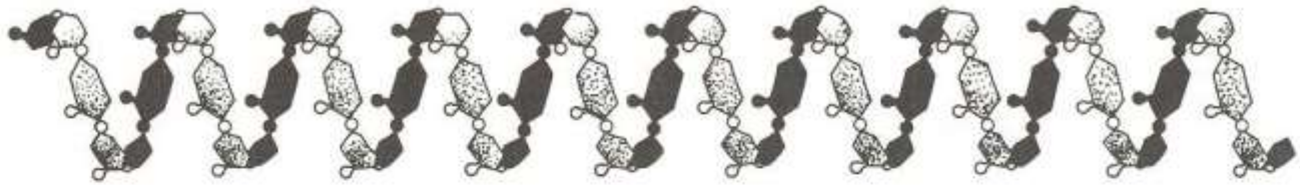
Glycosidic bonds

Lactose:	β-D-galactopyranosyl-(1→4)- D-glucopyranose
Maltose:	α-D-glucopyranosyl-(1→4)- D-glucopyranose
Isomaltose:	α-D-glucopyranosyl-(1→6)- D-glucopyranose
Sucrose:	α-D-glucopyranosyl-(1→2)- D-fructofuranose

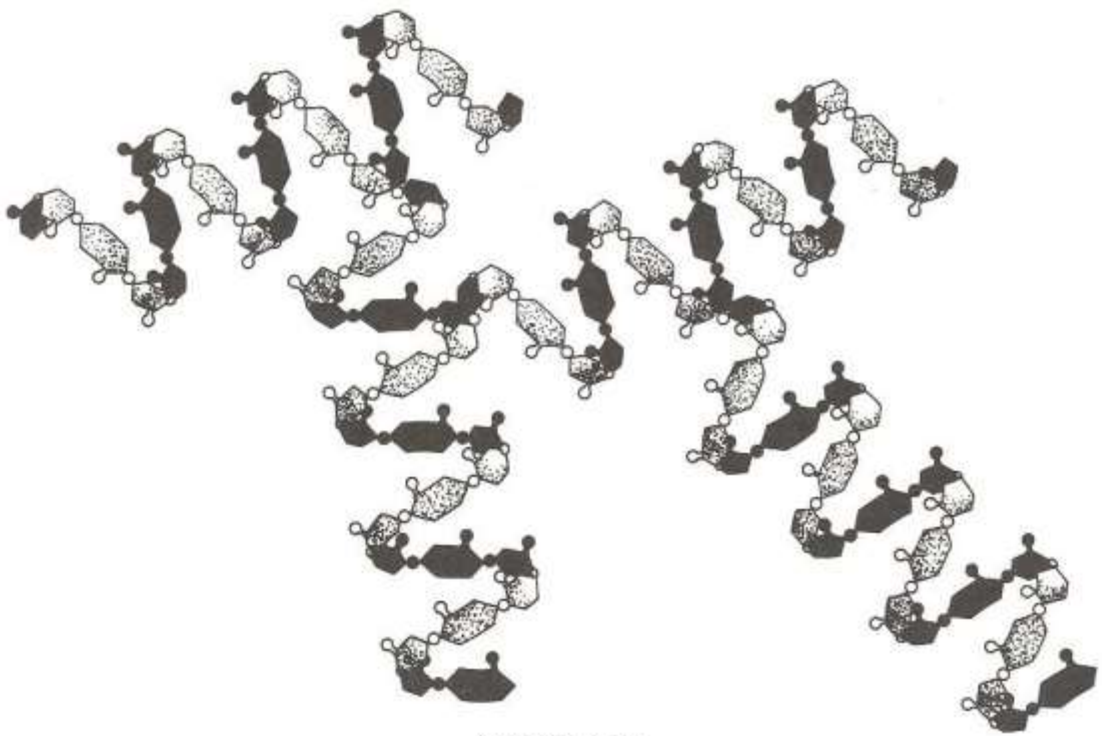
Glycosidic bonds

Lactose, glucose and isomaltose are reducing sugars with a non-reducing and reducing end

Sucrose is a non-reducing sugar

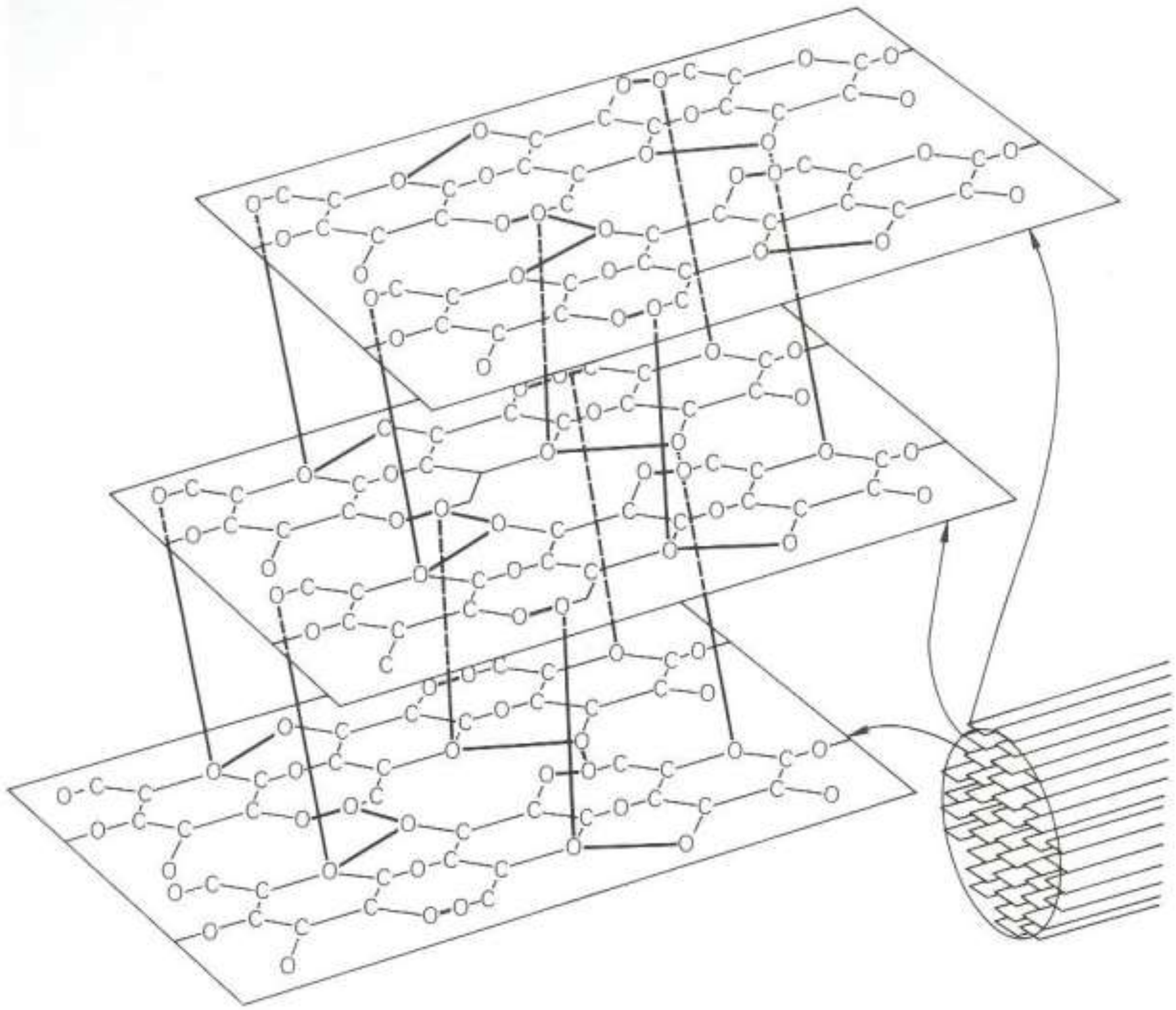


AMYLOSE



AMYLOPECTIN

Model of cellulose molecules in a microfibril



Glucosaminoglycans

Large complexes of negatively charged heteropolysaccharide chains

Typically associated with a small (<5%) amount of protein forming proteoglycans

Properties

- Can bind large amounts of water
- Gel-like matrix
- Viscous
- Lubricating
- Shock absorbing

Glucosaminoglycans

Repeating disaccharide units [acidic sugar – amino sugar]$_n$

o

Amino sugar is D-glucosamine or D-galactosamine with the amino group usually acetylated
Acidic sugar is D-gluconic acid or L-iduronic acid
Hydroxyl or amino groups may be sulfated

Carboxyl groups and sulfate groups make glycosaminoglycans negatively charged at physiological pH

Carbohydrates of glycoproteins

Glycoproteins contain less carbohydrate than proteoglycans.

Carbohydrates can be attached to the amide nitrogen in the side chain of asparagine (N-linkage) or to the hydroxyl oxygen of serine or threonine (O-linkage)

Carbohydrates of glycoproteins

Cell-surface molecules

- antigen determinants
- mediator of cell-cell interaction
- attachment sites for vira

Carbohydrates of glycoproteins

Most proteins in serum are glycosylated

Example: Erythropoietin

Glycosylation enhances stability of erytropoietin in blood

Carbohydrates of glycoproteins

Several monosaccharide building blocks
(e.g. glucose, galactose, mannose, N-acetyl glucosamine, N-acetyl galactosamine, N-acetyl mannoseamine, fucose, N-acetylneuraminic acid)

Branching

Several possible glycosidic bonds

Several potential glycosylation sites in glycoproteins

} Great structural complexity!

Dietary carbohydrates

- Starch
- Sucrose
- Glucose and fructose
- Lactose

} Digestible

- Cellulose
- Other plant polysaccharides

} Non-digestible by humans

Only monosaccharides are absorbed into the bloodstream from the gut.

Digestion of carbohydrates involves their hydrolysis into monosaccharides

Digestive Enzymes

Enzymes for carbohydrate digestion

Enzyme	Source	Substrate	Products
α-Amylase	Salivary gland Pancreas	Starch, glycogen	Oligosaccharides
Dextrinase	Small intestine	Oligosaccharides	Glucose
Isomaltase	Small intestine	α-1,6-glucosides	Glucose
Maltase	Small intestine	Maltose	Glucose
Lactase	Small intestine	Lactose	Galactose, glucose
Sucrase	Small intestine	Sucrose	Fructose, glucose

Lactase deficiency produces lactose intolerance

Absorption of monosaccharides by intestinal mucosal cells

Major monosaccharides

Glucose, galactose, fructose

Entry into mucosal cells from intestinal lumen

Active transport of glucose and galactose with a concurrent uptake of Na^+ ions

Facilitated transport of fructose via transporter protein GLUT-5

Entry into the portal circulation from mucosal cells

Facilitated transport via transporter protein GLUT-2

Blood glucose concentrations

Measured in mmol/L = mM or in mg/dL

Conversion factor: 1 mM = 18 mg/dL

Normal plasma glucose concentrations roughly
3.9 – 8.3 mM

Hypoglycemia: < 2.2 mM

Diabetes: > 7.0 mM (fasting)
> 11.1 mM 2 h after ingestion of 75 g glucose

All cells can use glucose as an energy source
Brain cells and erythrocytes require glucose as an energy source