CHAPTER 7

Carbohydrates and Glycobiology

Xianming Deng

BIOCHEMISTRY

Outline
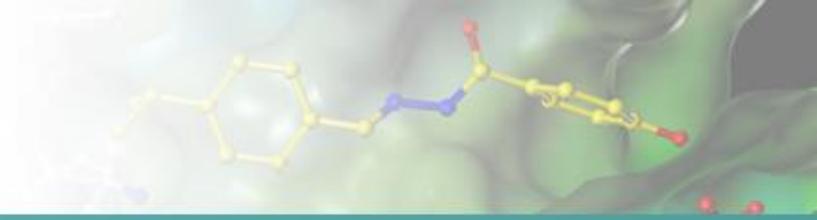
❑ **Introduction to Carbohydrates**
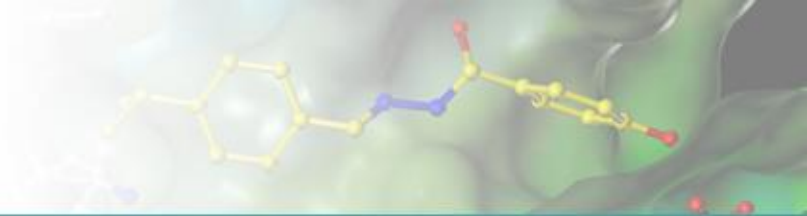
❑ **Monosaccharides**

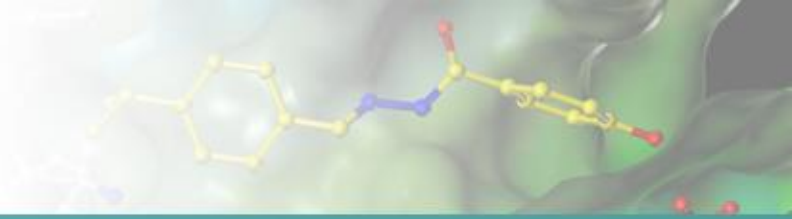❑ **Disaccharides**

Carbohydrates

➢ **Carbohydrates in ordinary life**

- Carbohydrates include not only   sugar, but also the starches that we find in foods, such as bread, pasta, and rice.
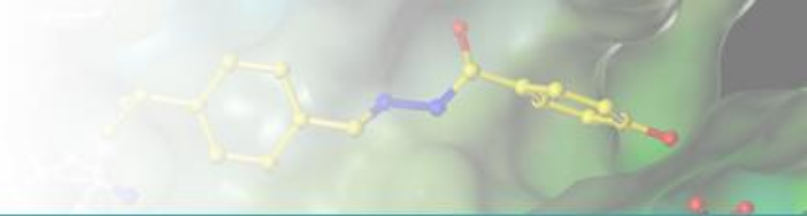
Carbohydrates

➢ **Carbohydrates in ordinary life**

- The term "**carbohydrate**" comes from the observation that when you heat sugars, you get carbon and water (hence, ***hydrate of carbon***).

- Carbohydrates are composed of units that comprise an equivalent of one water molecule for each carbon atom, **$(CH2O)_n$**

Carbohydrates

➢ **Carbohydrates** or **saccharides** (saccharo is Greek for "sugar") are polyhydroxy aldehydes or ketones, or substances that yield such compounds on hydrolysis.
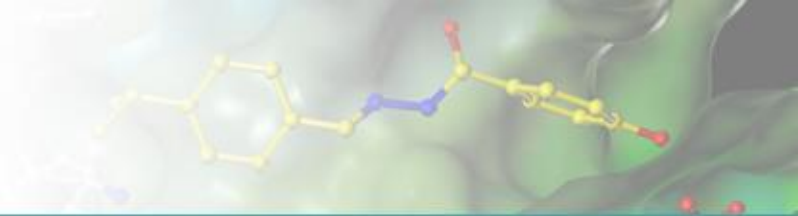
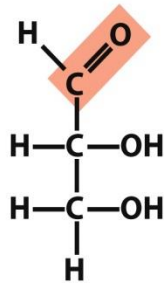**Three** major size classes of carbohydrates:

Monosaccharides

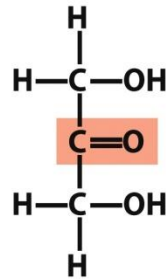**Oligosaccharides**
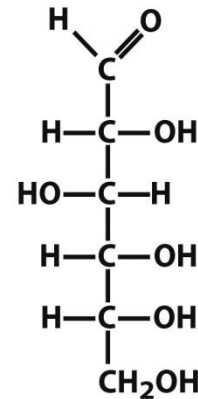
Polysaccharides

Carbohydrates

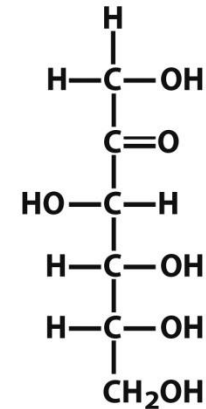- **Monosaccharides** are the simplest of the carbohydrates

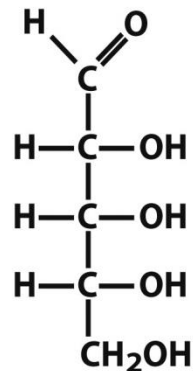Glyceraldehyde, an aldotriose

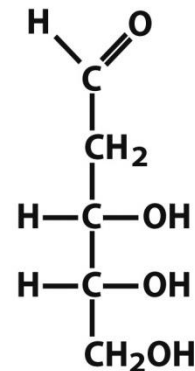Dihydroxyacetone, a ketotriose

D-Glucose, an aldohexose

D-Fructose, a ketohexose

D-Ribose, an aldopentose

2-Deoxy-D-ribose, an aldopentose

Carbohydrates

- **Disaccharides** consist of two monosaccharide units linked together by a covalent bond (e.g., sucrose（蔗糖））

Sucrose
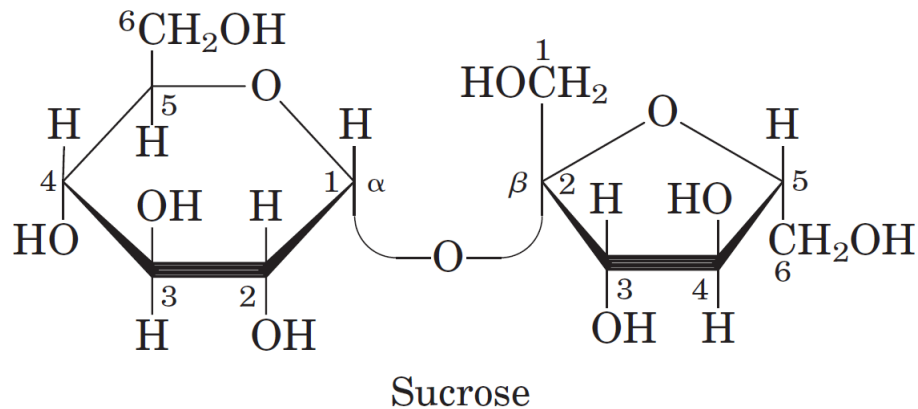
- **Oligosaccharides** contain from 3 to 10 monosaccharide units (e.g., raffinose).

Carbohydrates

- **Polysaccharides** contain very long chains of hundreds or thousands of monosaccharide units, which may be either in **straight** or **branched** chains (e.g., cellulose, glycogen, starch).

Carbohydrates

➢ **Biological functions of carbohydrates:**

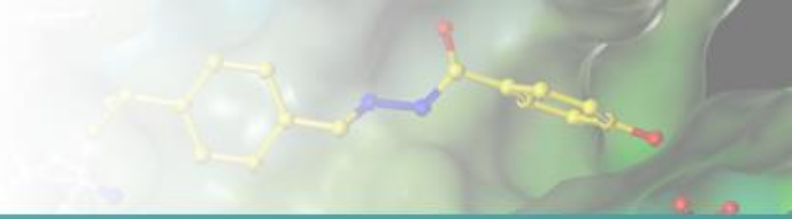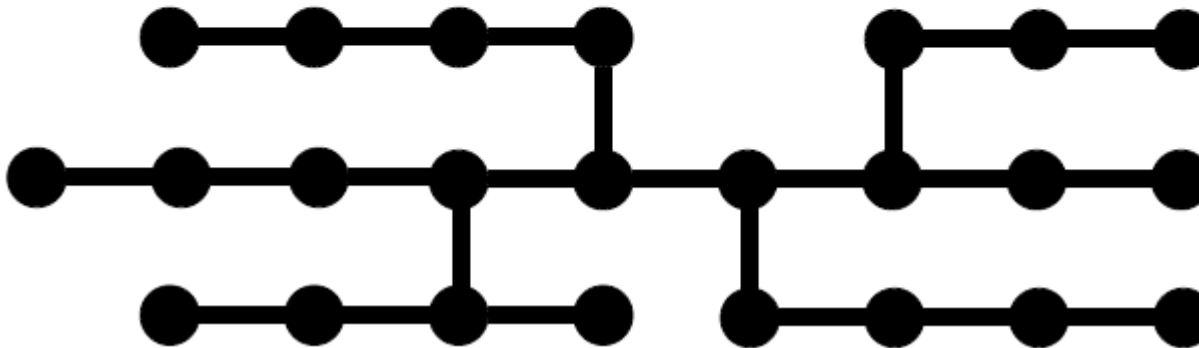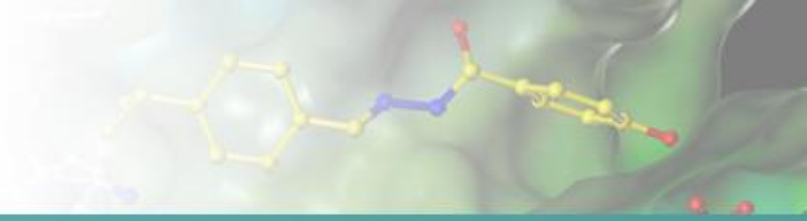- Carbohydrates are the most abundant biomolecules on Earth.

- Oxidation of carbohydrates is the central energy-yielding pathway in most nonphotosynthetic cells.

- Carbohydrate polymers (also called glycans) serve as structural and protective elements in the cell walls of bacteria and plants and in the connective tissues of animals.

- Carbohydrate polymers lubricate skeletal joints and participate in recognition and adhesion between cells.

- Complex carbohydrate polymers covalently attached to proteins or lipids act as signals.

Monosaccharides

The simplest of the carbohydrates that are either aldehydes or ketones with two or more hydroxyl groups.

- Unbranched carbon chains linked by single bonds form the backbones of monosaccharides.

- One of the carbon atoms is double-bonded to an oxygen atom to form a **carbonyl** group; each of the other carbon atoms has a hydroxyl group.

- If the carbonyl group is at an end of the carbon chain (aldehyde group) the monosaccharide is an **aldose**.

- if the carbonyl group is at any other position (ketone group) the monosaccharide is a **ketose**.

carbonyl group C=O

Glyceraldehyde, an aldotriose
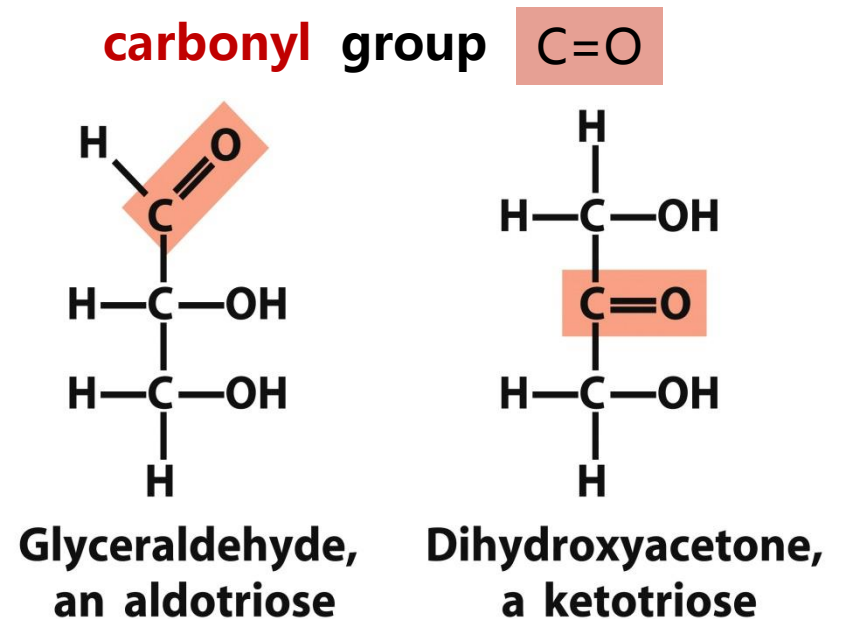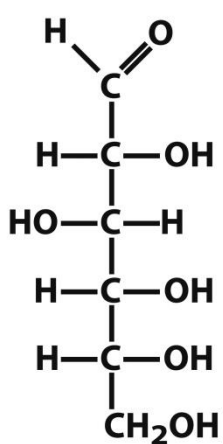
Dihydroxyacetone, a ketotriose

Figure 7-1a
Lehninger Principles of Biochemistry, Sixth Edition
© 2013 W. H. Freeman and Company

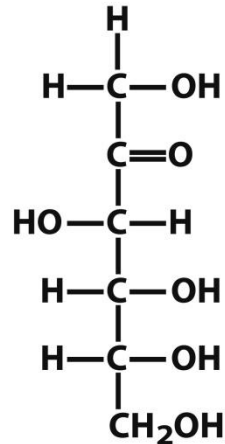The simplest monosaccharides: three-carbon **trioses**

> **Monosaccharides are classified according to the number of carbon atoms they contain**
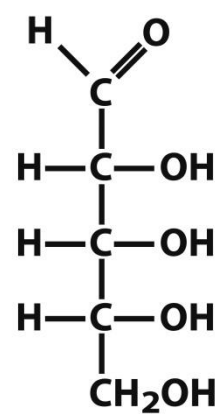
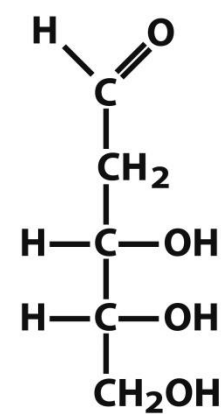| No. of carbon atoms	3	4	5	6	7
	triose	tetrose	pentose	hexose	heptose
Aldoses	aldotriose	aldotetrose	aldopentose	aldohexose	aldoheptose
ketoses	ketotriose	ketotetrose	ketopentose	ketohexose	ketoheptose

D-Glucose, an aldohexose

D-Fructose, a ketohexose

D-Ribose, an aldopentose

2-Deoxy-D-ribose, an aldopentose

> **Monosaccharides have asymmetric centers**

All the monosaccharides **EXCEPT** dihydroxyacetone (the simplest ketose) contain one or more asymmetric (chiral) carbon atoms and thus occur in optically active isomeric forms.
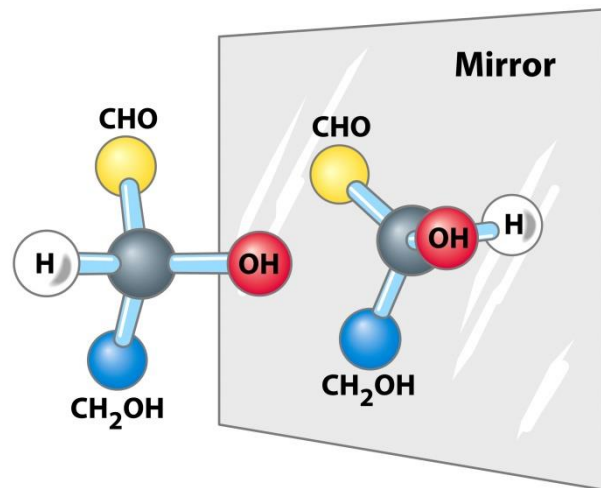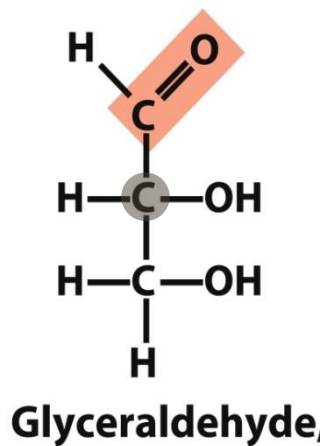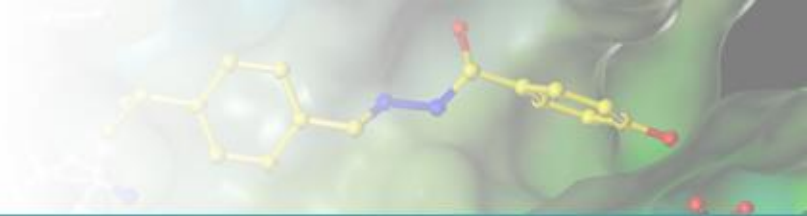
Glyceraldehyde (he simplest aldose) contains one chiral center (the middle carbon atom) and therefore has two different optical isomers, or **enantiomers(对映异构体).**
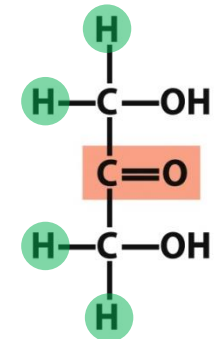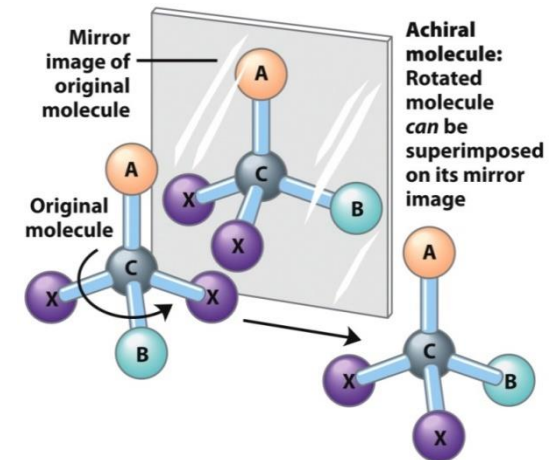
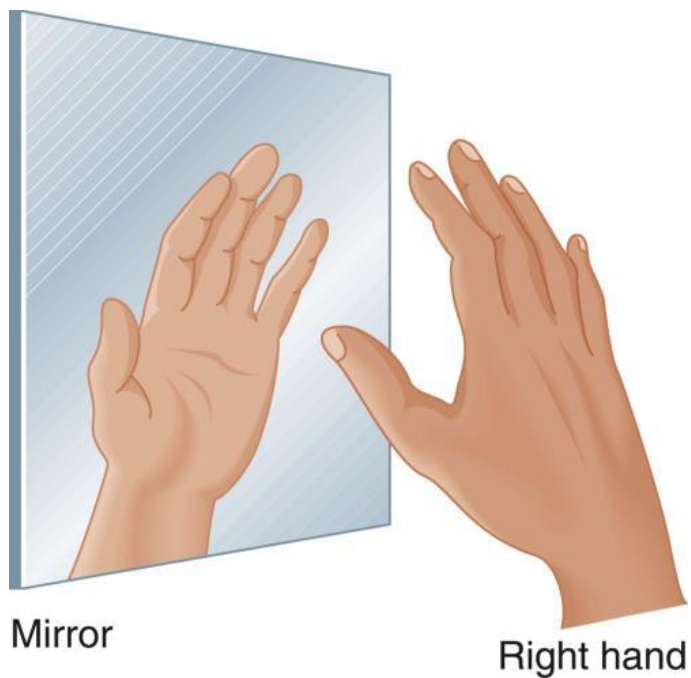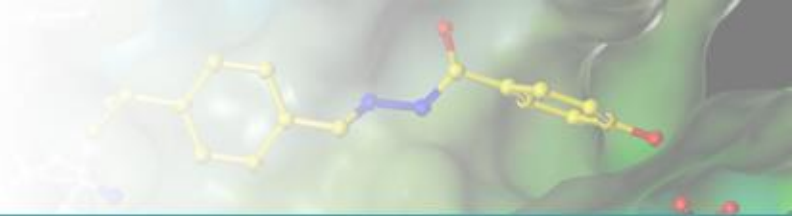# Chirality and Handedness

Chiral molecules have the same relationship to each other that your left and right hands have when reflected in a mirror.

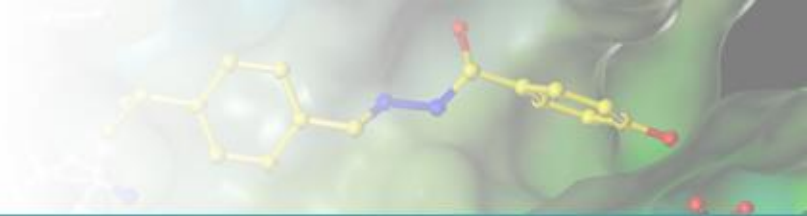Mirror   Right hand

Stereoisomers

Stereoisomers are isomeric molecules that have the same molecular formula and sequence of bonded atoms (constitution), but that differ *only* in the three-dimensional orientations of their atoms in space.[

➢ **Enantiomers** are two stereoisomers that are related to each other by a reflection: They are mirror images of each other, which are non-superimposable.

➢ **Diastereomers** are stereoisomers not related through a reflection operation. They are not mirror images of each other. These include **meso compounds**, **cis–trans (E-Z) isomers**, and **non-enantiomeric optical isomers**.

Enantiomers

- Glyceraldehyde is a **_chiral molecule_** — it cannot be superimposed on its mirror image. The two mirror-image forms of glyceraldehyde are **enantiomers** of each other.

  - Have the same physical properties, except for the direction in which they rotate polarized light.
  - Different enantiomers of a compound may have substantially different biological effects.
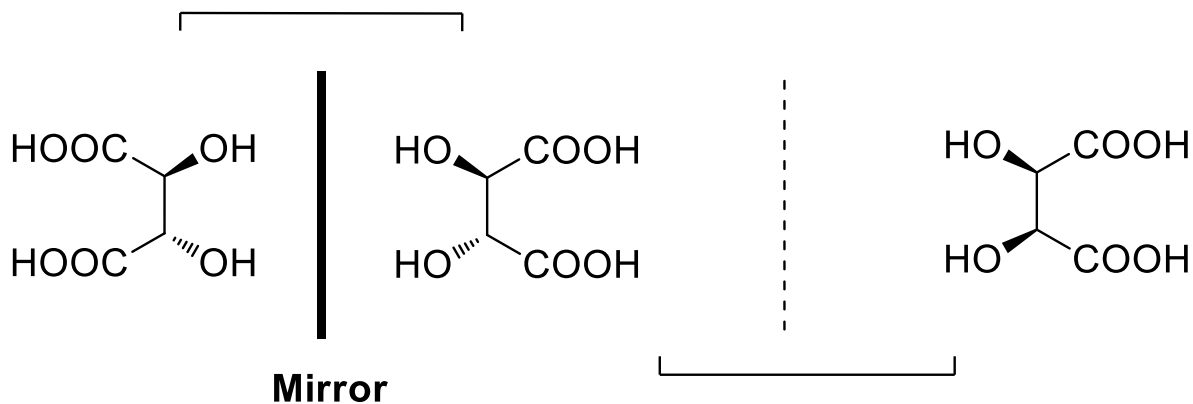 - In nature, only one enantiomer of most chiral biological compounds, such as amino acids.

$$CHO$$

$$HO-C-H$$

$$CH_2OH$$

L-glyceraldehyde

$$CHO$$

$$H-C-OH$$

$$CH_2OH$$

D-glyceraldehyde
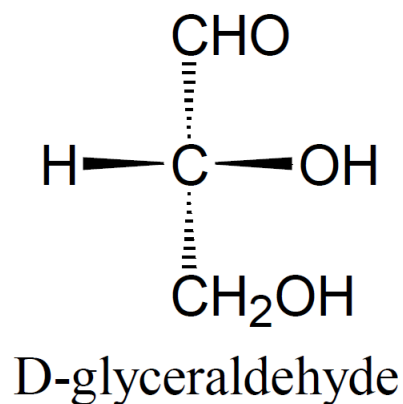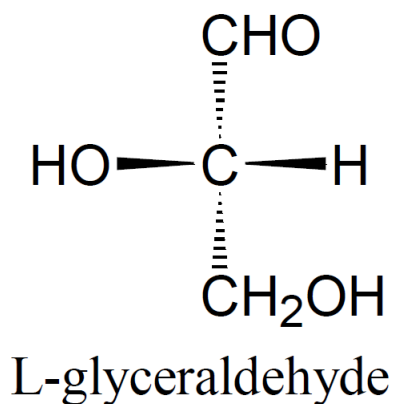
L-, D- Configuration?

Diastereomers

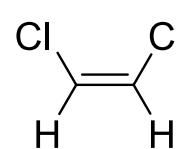These include: **meso compounds**, **cis–trans (E-Z) isomers**, and **non-enantiomeric optical isomers**.
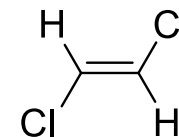– Diastereomers seldom have the same physical properties.

Enantiomers

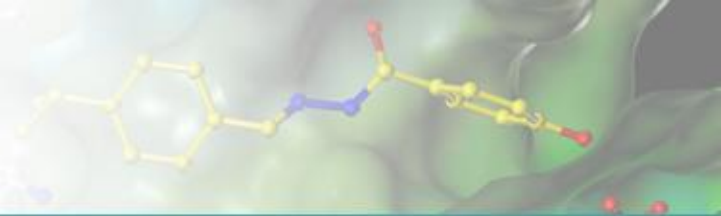**Mirror**

Diastereomers

cis–trans (E-Z) isomers

Z-

E-

- **Epimers (**差向异构体**)**

Two sugars that differ only in the configuration around one carbon atom are called **epimers**; D-glucose and D-mannose, which differ only in the stereochemistry at C-2, are epimers, as are D-glucose and D-galactose (which differ at C-4).
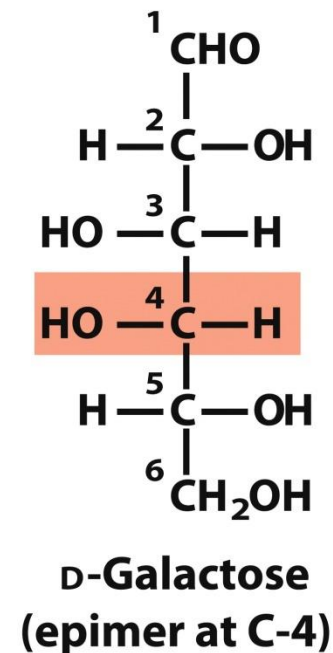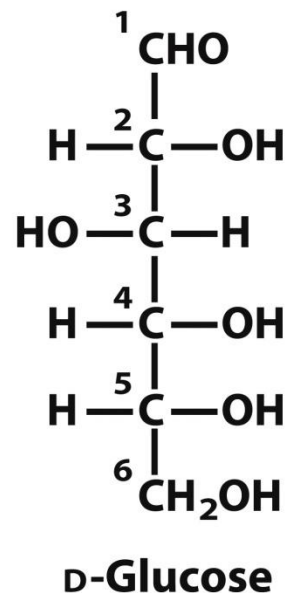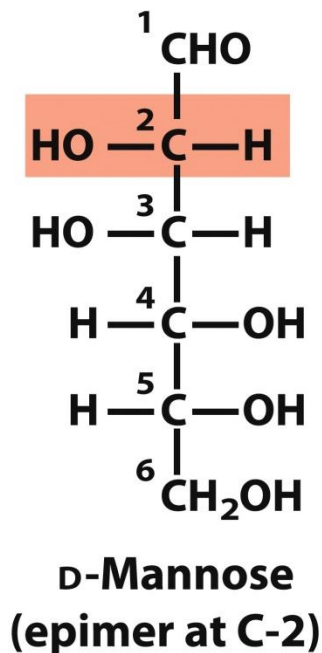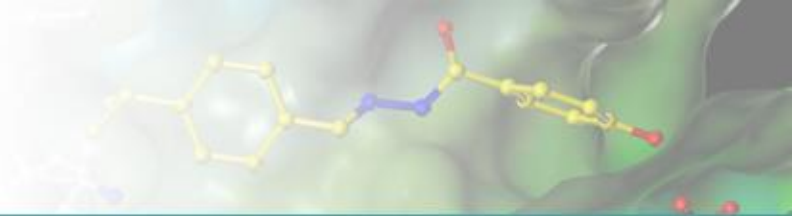

D-Mannose
(epimer at C-2)

D-Glucose

D-Galactose
(epimer at C-4)

Figure 7-4
Lehninger Principles of Biochemistry, Sixth Edition
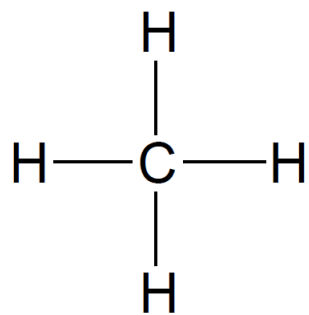© 2013 W. H. Freeman and Company

Chiral Carbons

- *Chiral objects* cannot be superimposed on their mirror images — e.g., hands, gloves, and shoes.

- *Achiral objects* can be superimposed on the mirror images — e.g., drinking glasses, spheres, and cubes.

- Any carbon atom which is connected to four different groups will be chiral, and will have two nonsuperimposable mirror images; it is a **chiral carbon** or **a center of chirality**.

  – If any of the two groups on the carbon are the same, the carbon atom cannot be chiral.

- Many organic compounds, including carbohydrates, contain more than one chiral carbon.
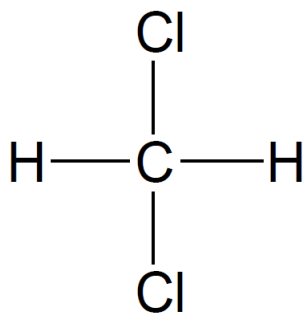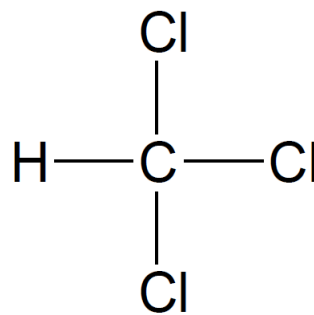
Identify the chiral carbon atoms (if any) in each of the following molecules:
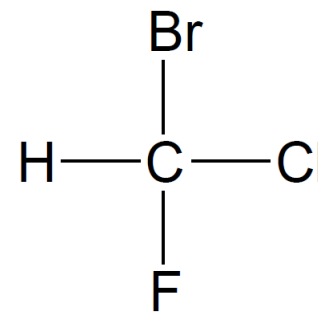
(A)　　　　　　　(B)　　　　　　　(C)　　　　　　　(D)
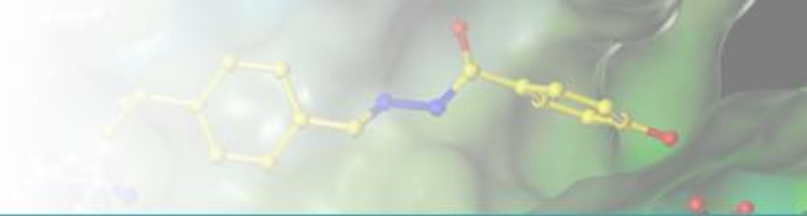
Examples: Chiral Carbon Atoms

(A)

$CH_3 - C - CH_3$ with OH above and H below

(B)

$CH_3 - C - CH_2Cl$ with OH above and H below

(C)

$CH_3 - C - CH_2CH_3$ with OH above and H below

(D)

(A)

$CH_3 - C - CH_2CH_3$ with O (double bond) above

(B)

HO — cyclohexane ring

(C)

HO — tetrahydropyran ring (O in ring)
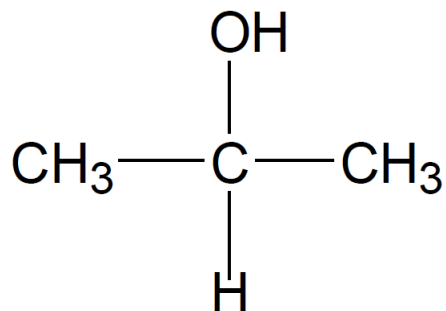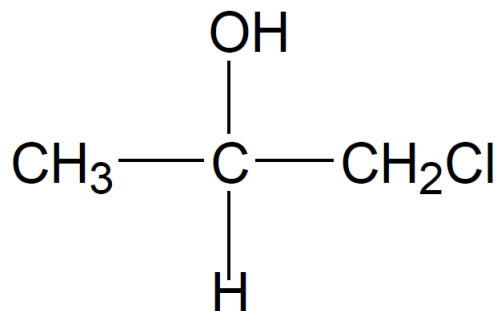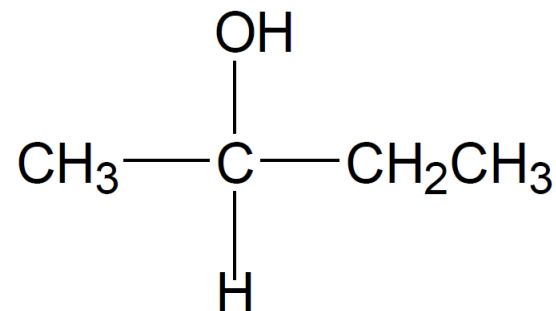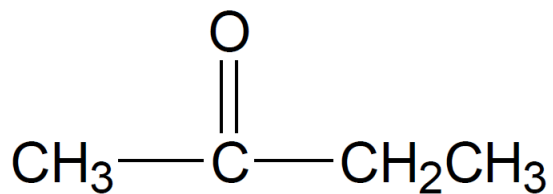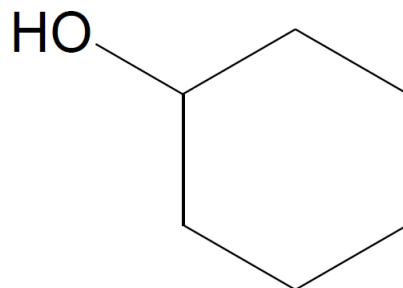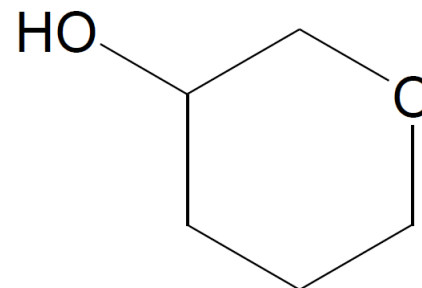
Identify the chiral carbons (if any) in the following carbohydrates:

erythrose

glucose
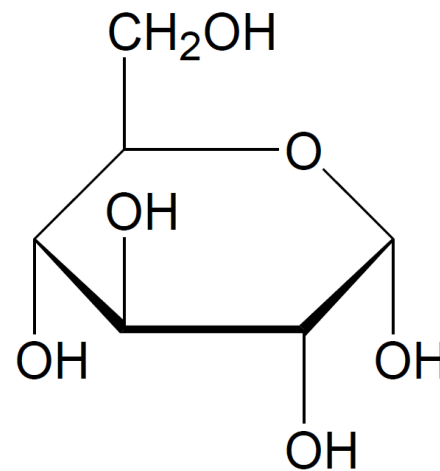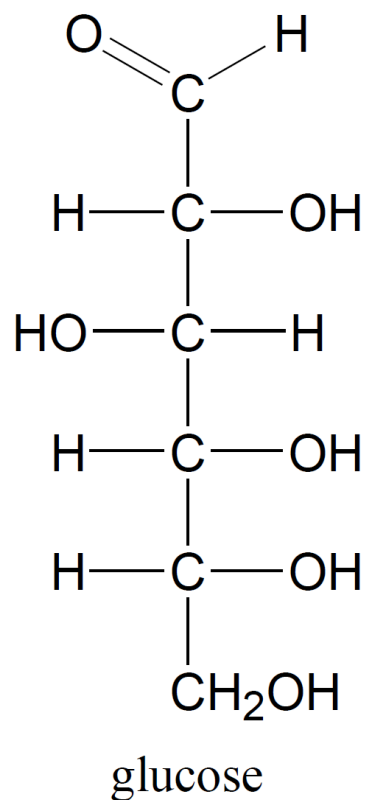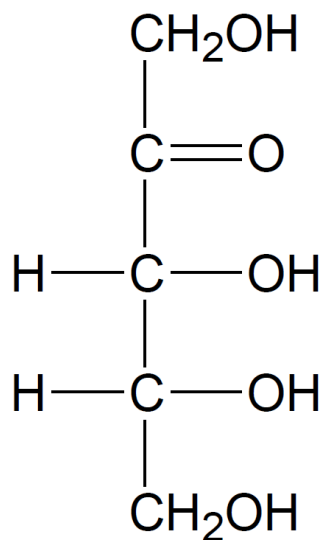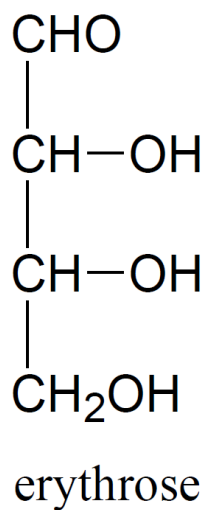
2^n Rule

- When a molecule has more than one chiral carbon, each carbon can possibly be arranged in either the right-hand or left-hand form, thus if there are n chiral carbons, there are 2n possible stereoisomers.

Maximum number of possible stereoisomers = 2^n
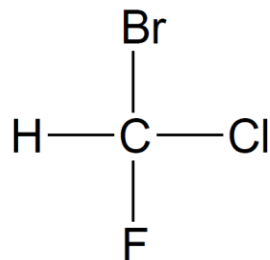
$2^1 = 2$ possible stereoisomers
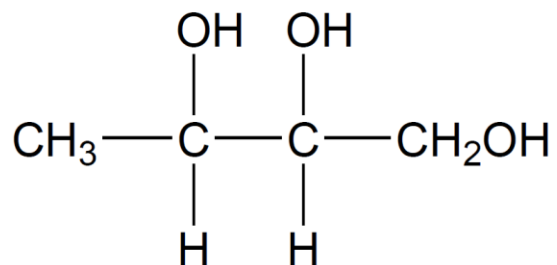
$2^2 = 4$ possible stereoisomers

What is the maximum number of possible stereo-isomers of the following compounds?

What is the maximum number of possible stereo-isomers of the following compounds?

CH$_3$

CH$_3$

HO
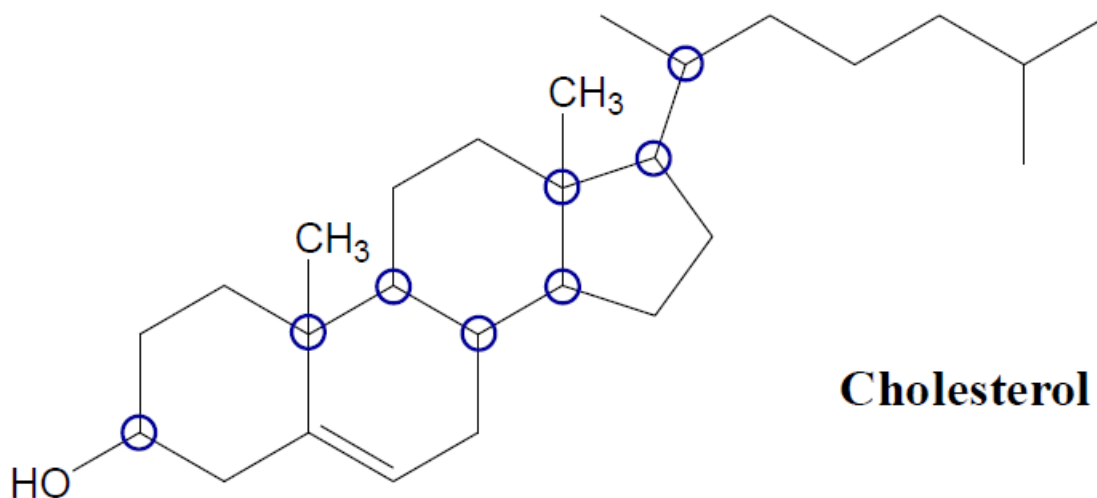
Cholesterol

$2^8 = 256$ possible stereoisomers.

But Nature makes only one!
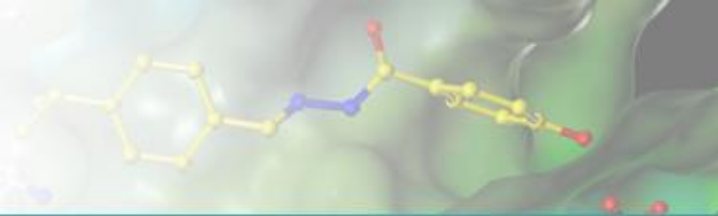
Optical Activity

Molecules which rotate the plane of polarized light are **optically active**.

– A **levorotatory** (–) substance rotates polarized light to the left [e.g., *l-glucose; (-)-glucose].*
– A **dextrorotatory** (+) substance rotates polarized light to the right [e.g., *d-glucose; (+)-glucose].*
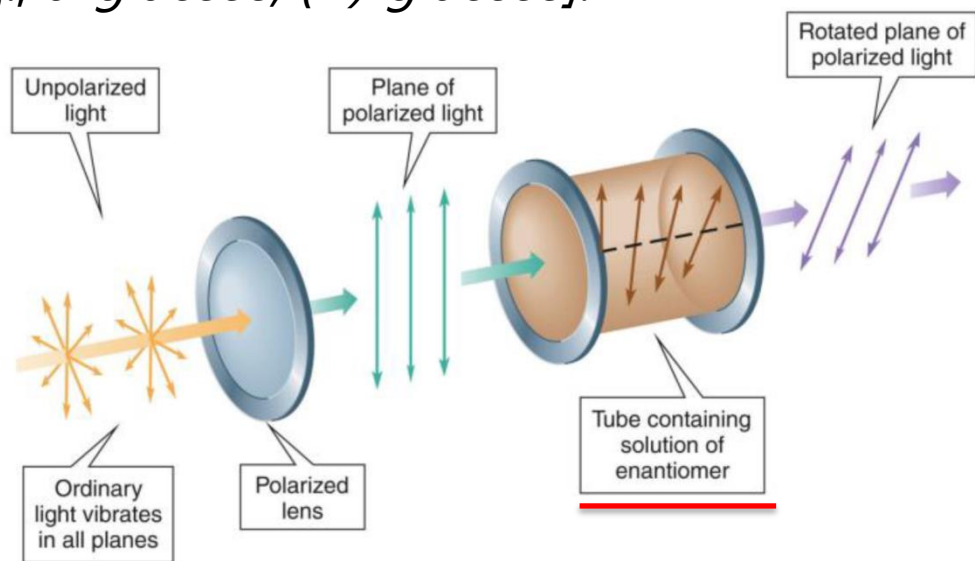
What's So Great About Chiral Molecules?

Many biologically important molecules are chiral and optically active. Often, living systems contain **only one** of the possible stereochemical forms of a compound, or they are found in separate systems.

– L-lactic acid is found in living muscles; D-lactic acid is present in sour milk.

– In some cases, one form of a molecule is beneficial, and the enantiomer is a poison (e.g., **thalidomide**).

– Humans can metabolize D-monosaccharides but not L-isomers; only L-amino acids are used in protein synthesis.

Thalidomide （反应停事件）

In the late 1950s and early 1960s, more than 10,000 children in 46 countries were born with deformities such as **phocomelia** as a consequence of thalidomide use.
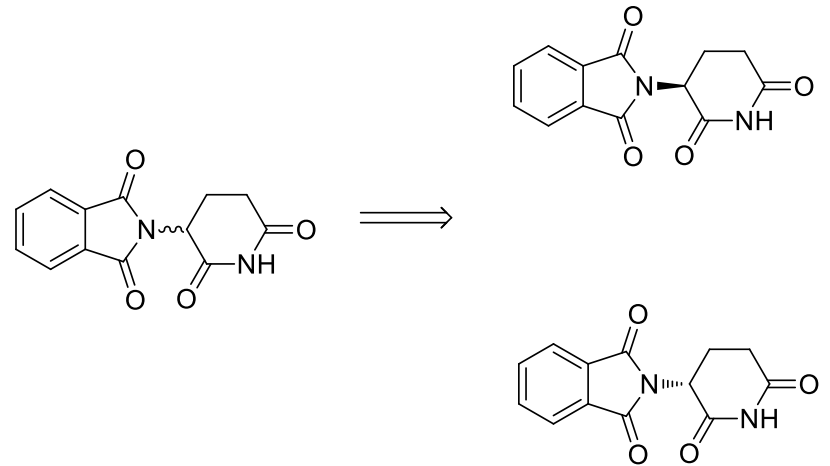
Phocomelia
(海豹肢症畸形儿)

Thalidomide analog
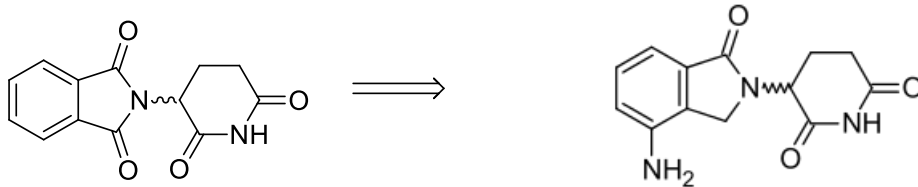
Lenalidomide

Use for :

➢ Multiple myeloma （**多发性骨髓瘤**）

➢ Myelodysplastic syndrome （**骨质增生异常综合症**）

➢ Other cancer treatment in clinical trial.
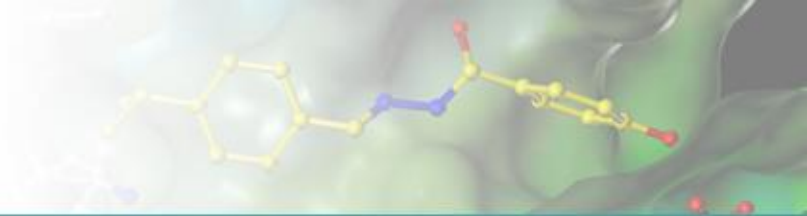
Fischer Projections

Fischer projections are a convenient way to represent mirror images in two dimensions.

Place the carbonyl group at or near the **top** and the last achiral CH_2OH at the **bottom**.

L = Left

```
        CHO
         |
  HO—C—H
         |
      CH₂OH
  L-Glyceraldehyde
```

```
        CHO
         |
   H—C—OH
         |
      CH₂OH
  D-Glyceraldehyde
```

D = Right

Fischer projection formulas

Naming Stereoisomers

When there is more than one chiral center in a carbohydrate, look at the chiral carbon **farthest** from the carbonyl group: if the hydroxy group points to right when the carbonyl is "up" it is the **D-isomer,** and when the hydroxy group points to the left, it is the **L-isomer**.

L-erythrose

D-erythrose

Examples: Fischer Projections

Draw Fischer projections of D and L lactic acid:

$$CH_3-\overset{\overset{\displaystyle CO_2H}{|}}{CH}-OH$$

Draw Fischer projections of D and L alanine:

$$CH_3-\overset{\overset{\displaystyle NH_2}{|}}{CH}-CO_2H$$
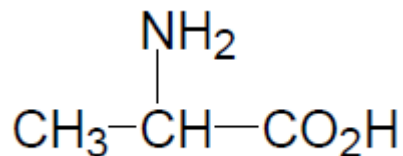
Given the structure for D-glucose, draw the structure of L-glucose:

```
          CHO
           |
   H ——————|—————— OH
           |
  HO ——————|—————— H
           |
   H ——————|—————— OH
           |
   H ——————|—————— OH
           |
         CH₂OH
```

D-glucose

Identify the following compounds as D or L isomers, and draw their mirror images.

lyxose

fructose
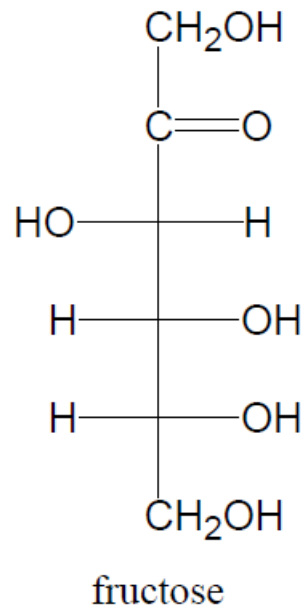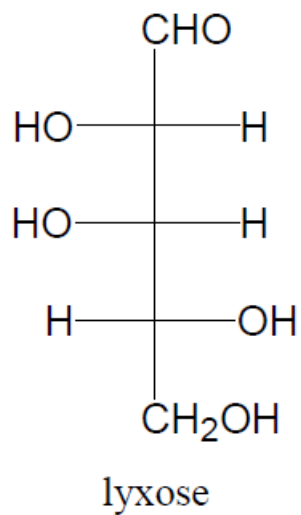
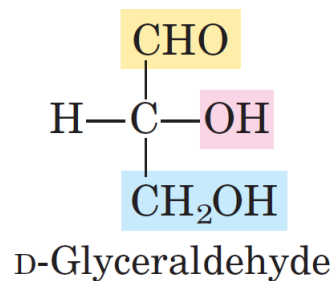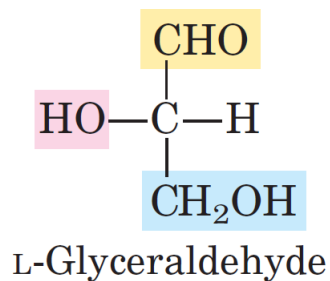- **Glyceraldehyde is conventionally designated as the D or L isomer**

Fischer projection formulas are a convenient way to represent mirror images in two dimensions.
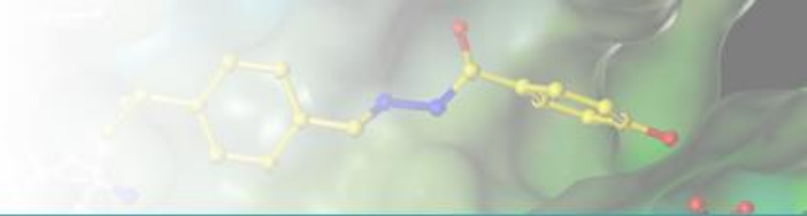
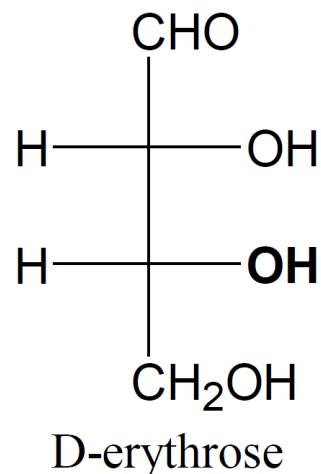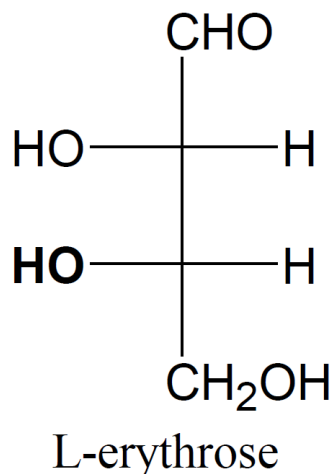Place the carbonyl group at or near the **top** and the last achiral CH$_2$OH at the **bottom**.
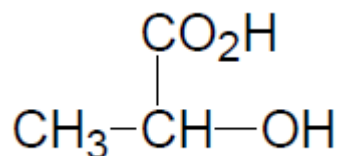
In Fischer projection formulas, horizontal bonds project out of the plane of the paper, toward the reader; vertical bonds project behind the plane of the paper, away from the reader.

L = Left (*levo*),   **D** = Right (*dextro*)

D-Glyceraldehyde   L-Glyceraldehyde
Fischer projection formulas
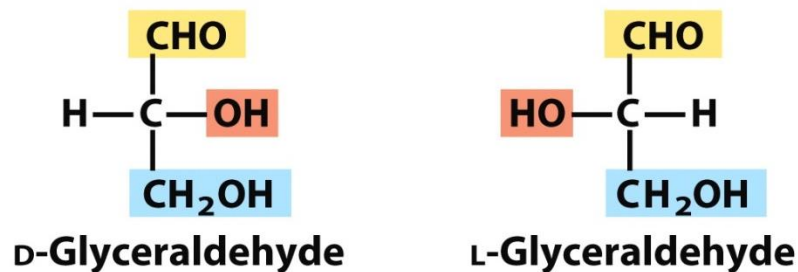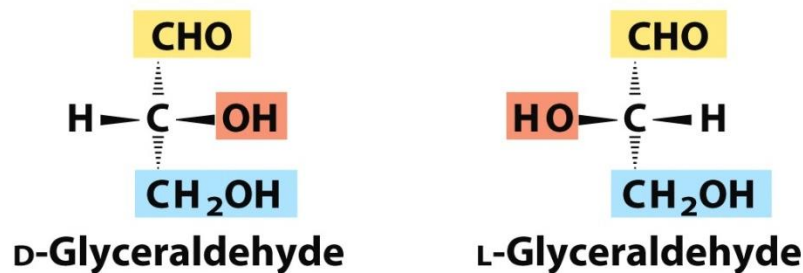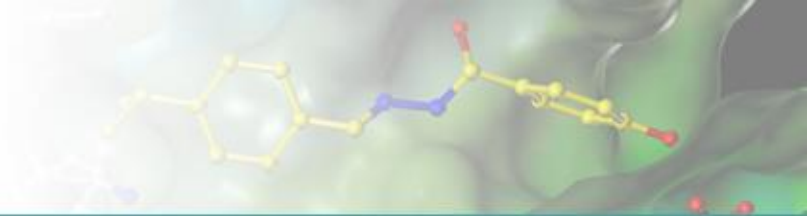
D-Glyceraldehyde   L-Glyceraldehyde
Perspective formulas

In perspective formulas, the wide end of a solid wedge projects out of the plane of the paper, toward the reader; a dashed wedge extends behind.

- The stereoisomers of monosaccharides are divided into **D** or **L** isomers based on the configuration of the **reference carbon** (the chiral center *most distant* from the carbonyl carbon).

  D isomer: the hydroxyl group on the reference carbon is on the **right** (*dextro*) in a projection formula, in which the configuration at this is the same as that of D-glyceraldehyde.

  L isomer: the hydroxyl group on the reference carbon is on the **left** (*levo*) in a projection formula, in which the configuration at this is the same as that of L-glyceraldehyde.

- In general, a molecule with n chiral centers can have 2^n stereoisomers, among which half are D isomers and the other half are L forms.

- Most of the hexoses of living organisms are D isomers. **Why D isomers?**

L-**Arabinose**
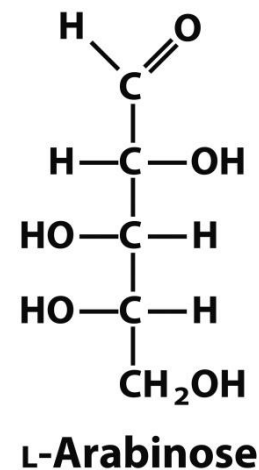
L form sugars also exist naturally

➤ **The common monosaccharides have cyclic structures**

• **Formation of hemiacetals and hemiketals.**

Figure 7-5
Lehninger Principles of Biochemistry, Sixth Edition
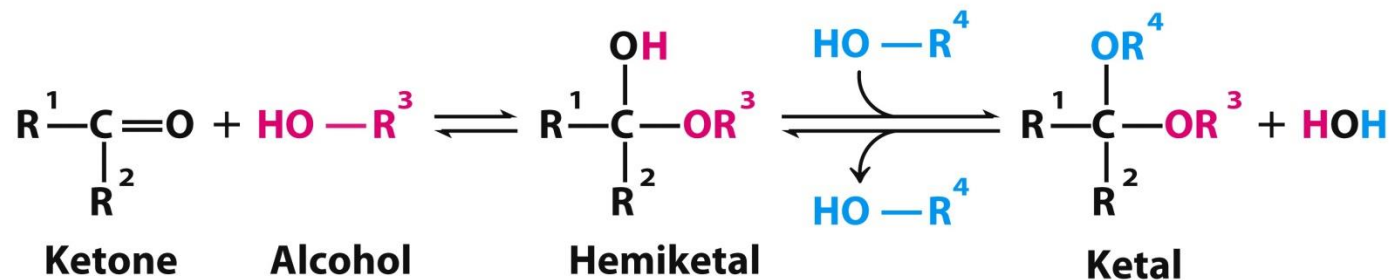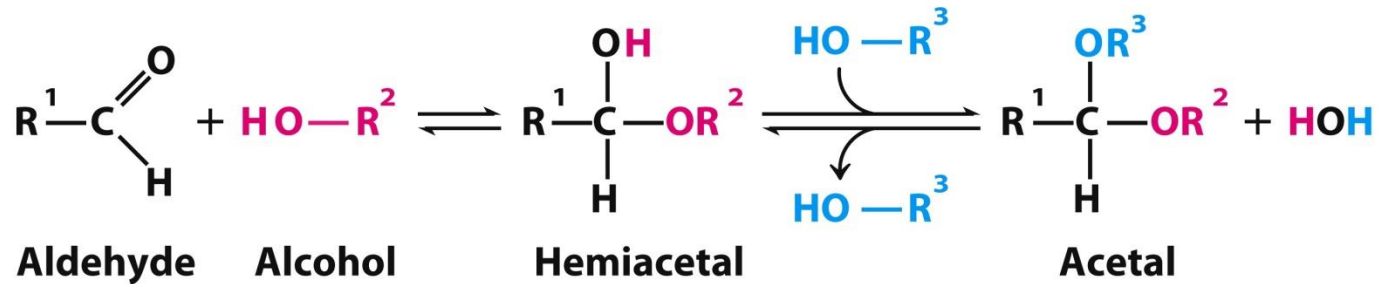© 2013 W. H. Freeman and Company

Two molecules of an alcohol can add to a carbonyl carbon

- **Formation of the two cyclic forms of D-glucose**

  In aqueous solution, **aldotetroses** and all monosaccharides with **five or more** carbon atoms in the backbone occur predominantly as **cyclic** (ring) structures in which the carbonyl group has formed a covalent bond with the oxygen of a hydroxyl group along the chain, as a result of formation of **hemiacetals** or **hemiketals.**

  Anomers（异头物） are isomeric forms of monosaccharides that differ only in their configuration about the hemiacetal or hemiketal carbon atom, and the carbonyl carbon atom is called the **anomeric carbon**.
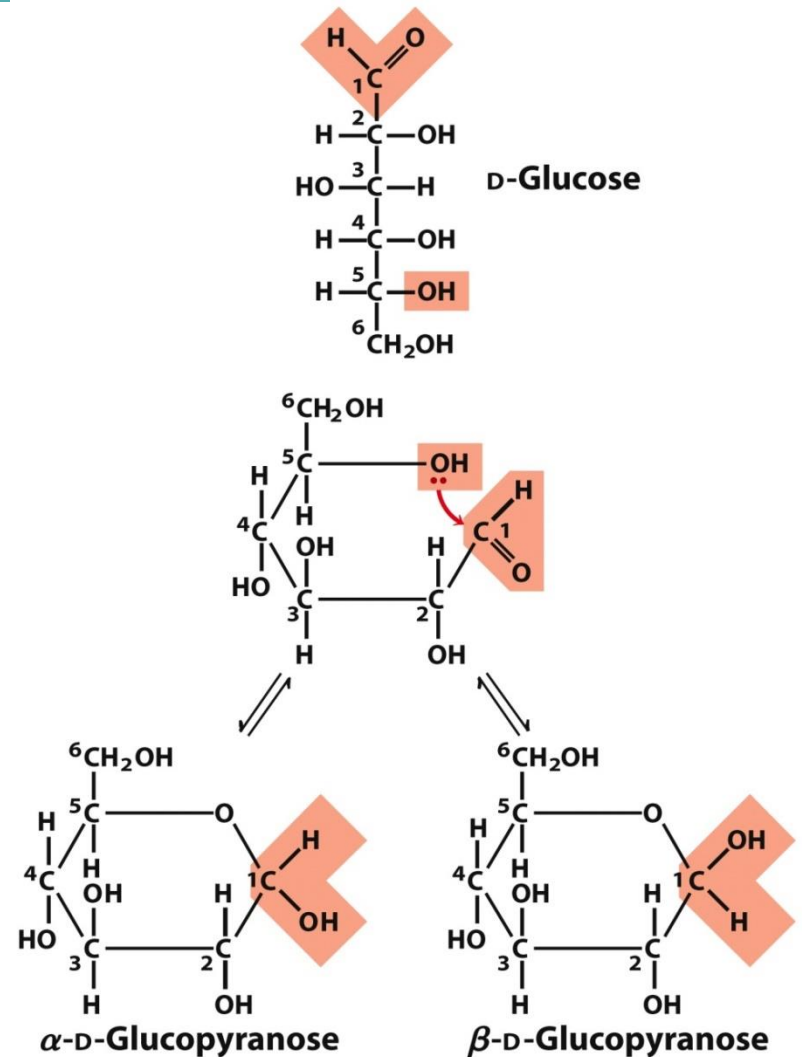
The reaction produces α and β two stereoisomeric configurations.
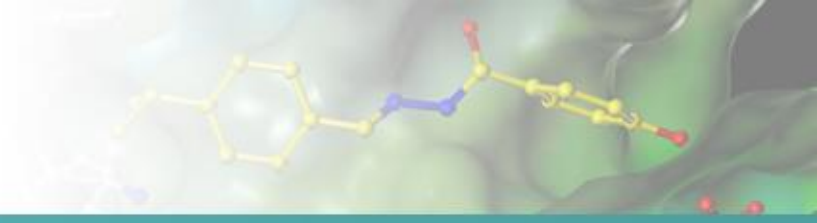
- **D-Fructose Anomers**

- **Pyran and furan**

Pyran is a six-membered heterocyclic, **non-aromatic** ring, consisting of five carbon atoms and one oxygen atom and containing two double bonds.

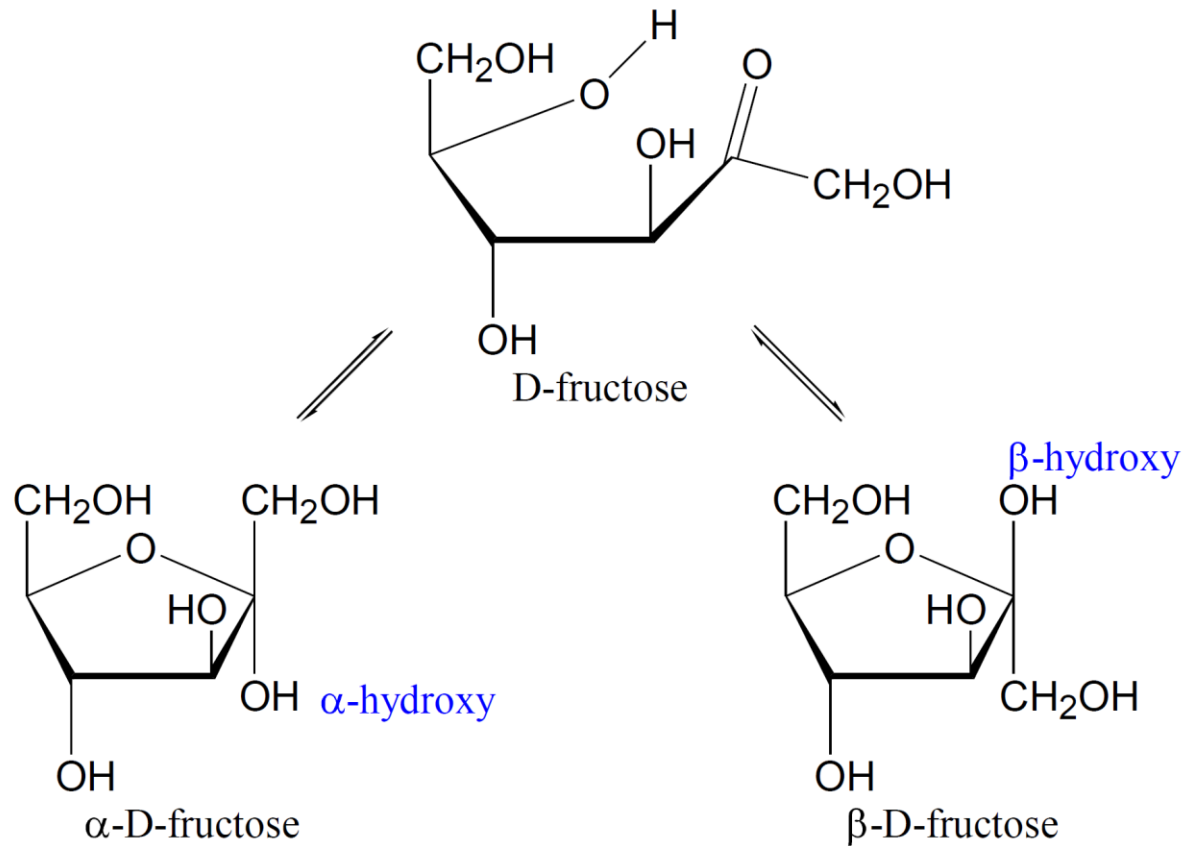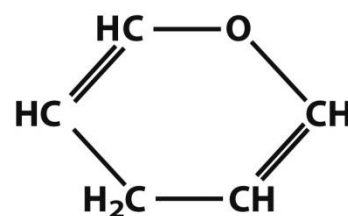**Furan** is a heterocyclic organic compound, consisting of a five-membered **aromatic** ring with four carbon atoms and one oxygen.

Pyran

吡喃
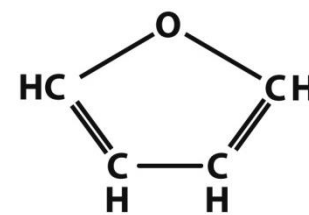
Furan

呋喃

Aromaticity is used to describe a **cyclic** (ring-shaped), **planar** (flat) molecule with a ring of **resonance bonds** that exhibits more stability than other geometric or connective arrangements with the same set of atoms.

Aromatic molecules are very stable, and do not break apart easily to react with other substances. Organic compounds that are not aromatic are classified as aliphatic compounds—they might be cyclic, but only aromatic rings have special stability (low reactivity).

- **Pyranoses and Furanoses**

Monosaccharides form six-membered ring compounds are called **pyranoses** because they resemble pyran.
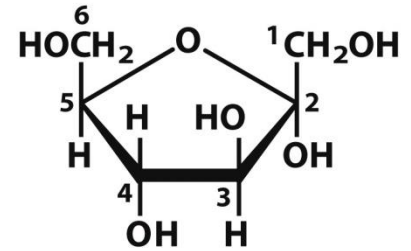
Monosaccharides form five-membered ring compounds are called **furanoses** because they resemble furan.

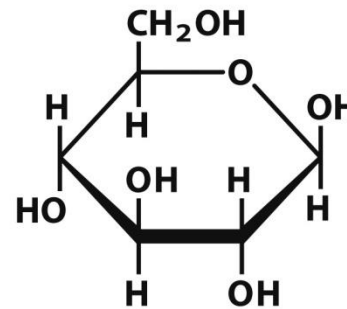D-glucose forms α-**D-glucopyranose** and β-**D-glucopyranose**.

D-Fructose forms the furanose ring; the more common anomer of this is β-**D-fructofuranose**.

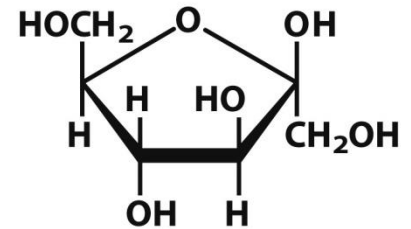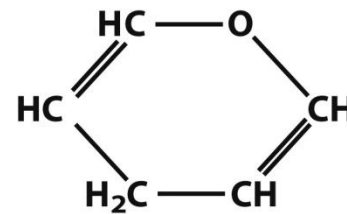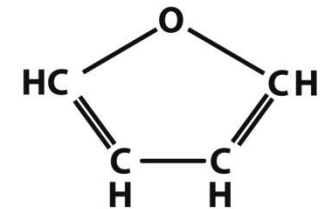α-D-Glucopyranose
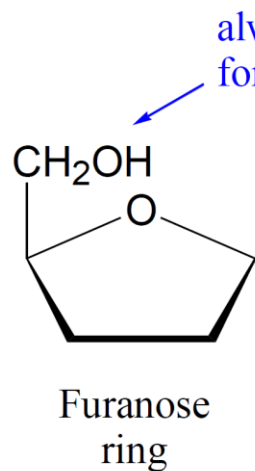
α-D-Fructofuranose

β-D-Glucopyranose

β-D-Fructofuranose

Pyran

Furan

吡喃

呋喃

- **Haworth perspective formulas** are used to represent cyclic sugar structures

D-Glucose
Fischer projection

α-D-Glucopyranose
Haworth perspective
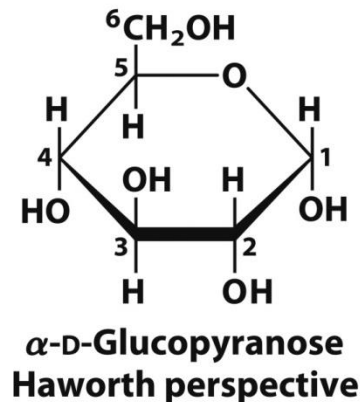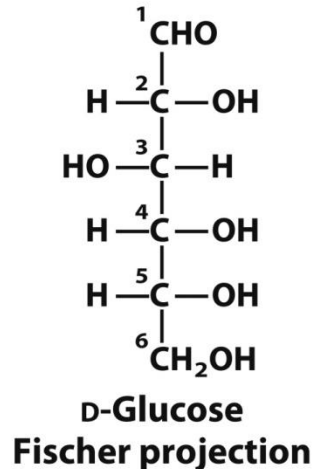
always above ring
for D-saccharides

CH$_2$OH

CH$_2$OH

Furanose
ring
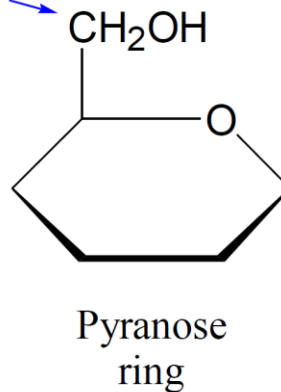
Pyranose
ring

- **Draw furanose and pyranose rings**

1) Draw ring (4 or 5 carbons and one oxygen at the upper right);

2) Number the **C** in a clockwise direction beginning with the anomeric one;

3) Place the -OH groups below the plane of the ring if it is to the right in the Fischer projection, place -OH groups above the plane if it is to the left in the Fischer projection;

4) The terminal -CH$_2$OH group projects upward for the D-enantiomer, downward for the L-enantiomer.

5) When the anomeric -OH of a D-hexose is on the same side of the ring as C-6, the structure is by definition β; when it is on the opposite side from C-6, the structure is α.

- **Mutarotation** is the change in the optical rotation because of the change in the equilibrium between two anomers.

One ring form of D-glucose opens briefly into the linear form, then closes again to produce the other anomer.

Haworth structures

α-D-glucose
36%

D-glucose
0.02%
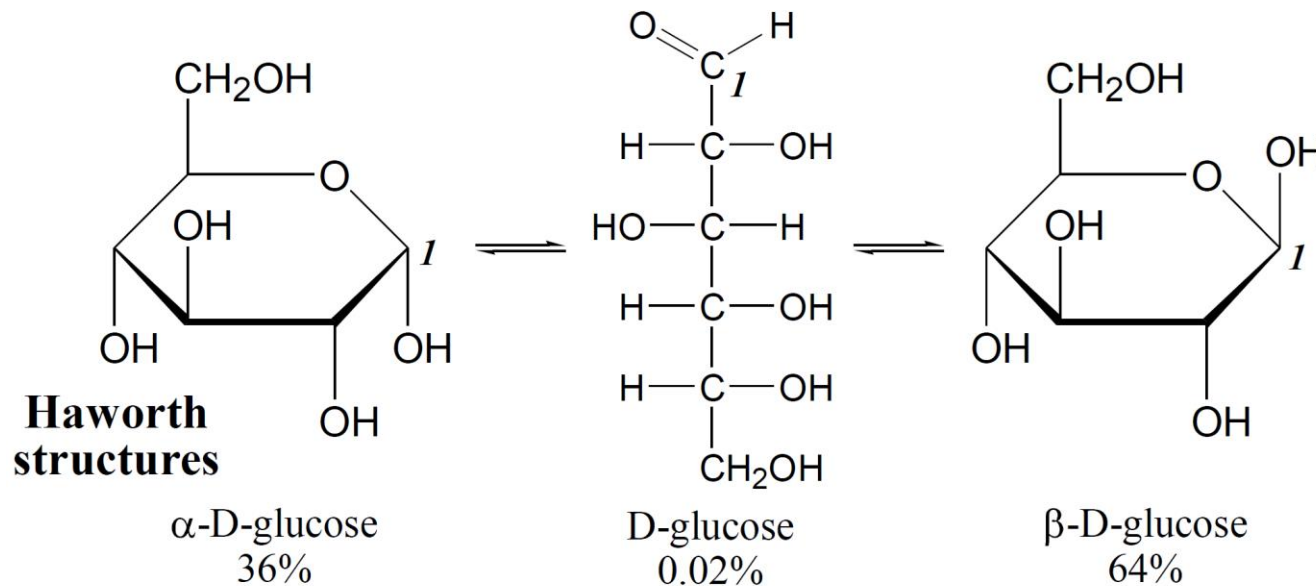
β-D-glucose
64%

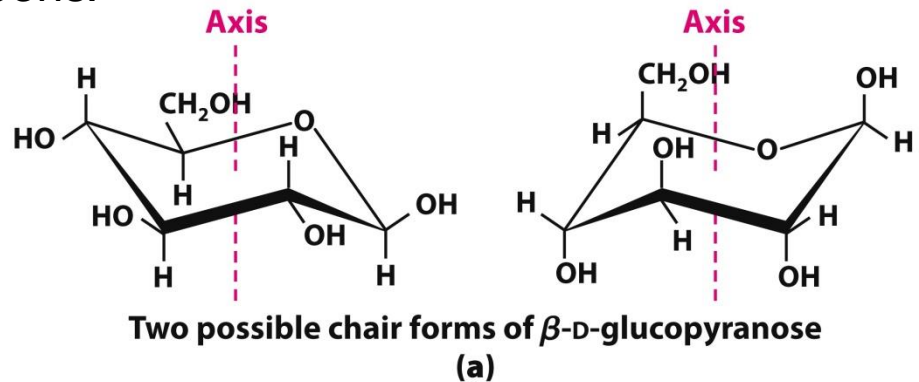Solution of α-D-glucose and a β-D-glucose eventually form identical equilibrium mixtures having identical optical properties. This mixture consists of about one-third α-D-glucose, two-thirds β-D-glucose, and very small amounts of the linear and five-membered ring (glucofuranose) forms.

- **Conformational formulas of pyranoses**

  The six-membered pyranose ring is not planar, but tends to assume either of two "chair" conformations. Interconversion of the two chair forms (which are *conformers*) does not require bond breakage and does not change configurations at any of the ring carbons.

  Two *conformers* of β-D-glucopyranose are not readily interconvertible; an input of about 46 kJ/mol is required to force the interconversion of chair forms.

  The preferred chair conformation of α-D-glucopyranose.

Two possible chair forms of β-D-glucopyranose
(a)

α-D-Glucopyranose
(b)
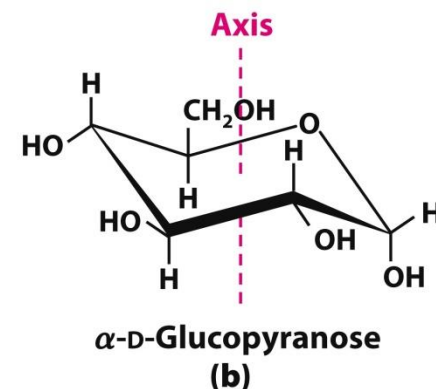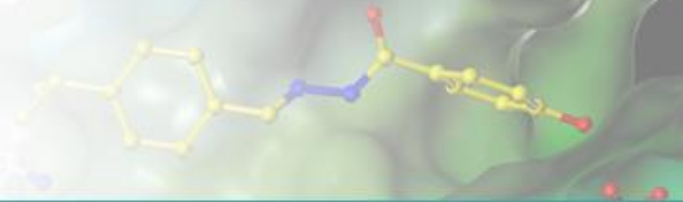
Organisms contain a variety of hexose derivatives

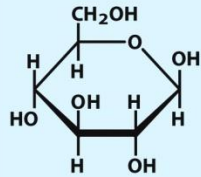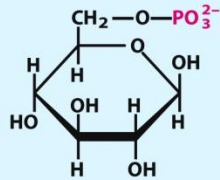There are a number of sugar derivatives in which a hydroxyl group in the parent compound is replaced with another substituent, or a carbon atom is oxidized to a carboxyl group.

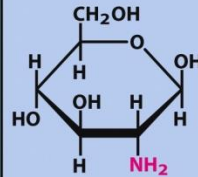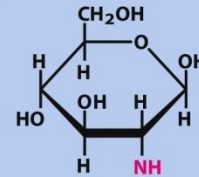**Some hexose derivatives important in biology**

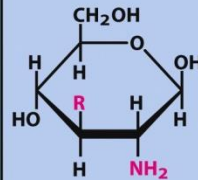## TABLE 7–1 Symbols and Abbreviations for Common Monosaccharides and Some of Their Derivatives
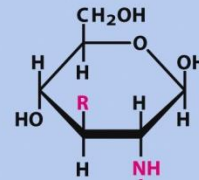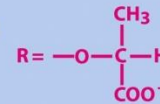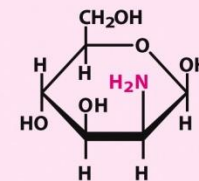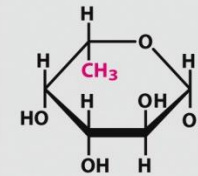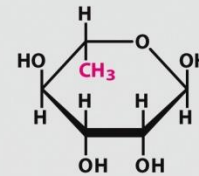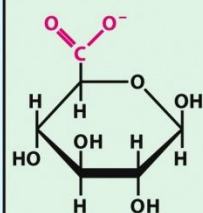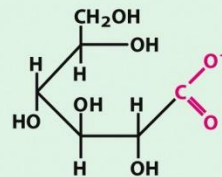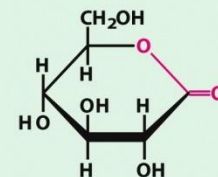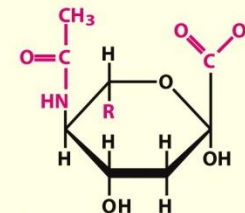
Abequose	Abe	Glucuronic acid	◆ GlcA
Arabinose	Ara	Galactosamine	◨ GalN
Fructose	Fru	Glucosamine	◨ GlcN
Fucose	▲ Fuc	*N*-Acetylgalactosamine	◻ GalNAc
Galactose	◯ Gal	*N*-Acetylglucosamine	◼ GlcNAc
Glucose	● Glc	Iduronic acid	◇ IdoA
Mannose	● Man	Muramic acid	Mur
Rhamnose	Rha	*N*-Acetylmuramic acid	Mur2Ac
Ribose	Rib	*N*-Acetylneuraminic acid (a sialic acid)	◆ Neu5Ac
Xylose	★ Xyl		

Note: In a commonly used convention, hexoses are represented as circles, *N*-acetylhexosamines as squares, and hexosamines as squares divided diagonally. All sugars with the "gluco" configuration are blue, those with the "galacto" configuration are yellow, and "manno" sugars are green. Other substituents can be added as needed: sulfate (S), phosphate (P), *O*-acetyl (OAc), or *O*-methyl (OMe).
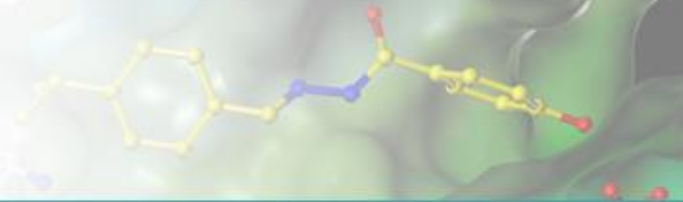
➢ **Physical properties of monosaccharides**

- Most monosaccharides have a sweet taste (fructose is sweetest, 73% sweeter than sucrose)

Table 7.2 The relative sweetness of sugars (sucrose = 1.00)

Sugar	Relative Sweetness	Type
Lactose	0.16	Disaccharide
Galactose	0.22	Monosaccharide
Maltose	0.32	Disaccharide
Xylose	0.40	Monosaccharide
Glucose	0.74	Monosaccharide
Sucrose	1.00	Disaccharide
Invert sugar	1.30	Mixture of glucose and fructose
Fructose	1.73	Monosaccharide

Box 7-2 figure 1
Lehninger Principles of Biochemistry, Sixth Edition
© 2013 W. H. Freeman and Company
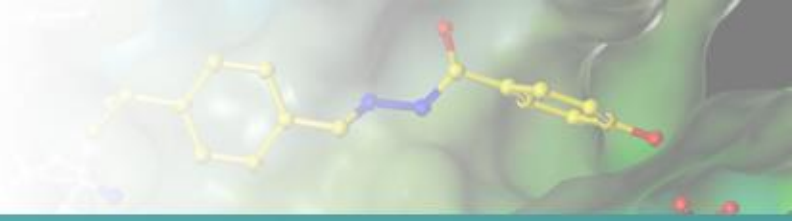
- They are solids at room temperature.

- They are *extremely soluble in water:*

  - Despite their high molecular weights, the presence of large numbers of OH groups make the monosaccharides much more water soluble than most molecules of similar MW.

  - Glucose can dissolve in minute amounts of water to make a syrup (1 g/ml in H_2O).

➢ **Chemical reactions of monosaccharides**

- **Oxidation of monosaccharides**

Aldehydes and ketones that have an OH group on the carbon next to the carbonyl group react with a basic solution of Cu^{2+} (**Benedict's reagent or Fehling's reagent**) to form a red-orange precipitate of copper oxide (Cu_2O).
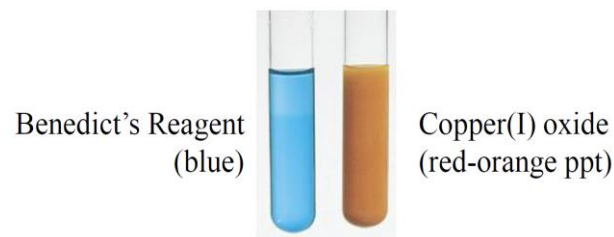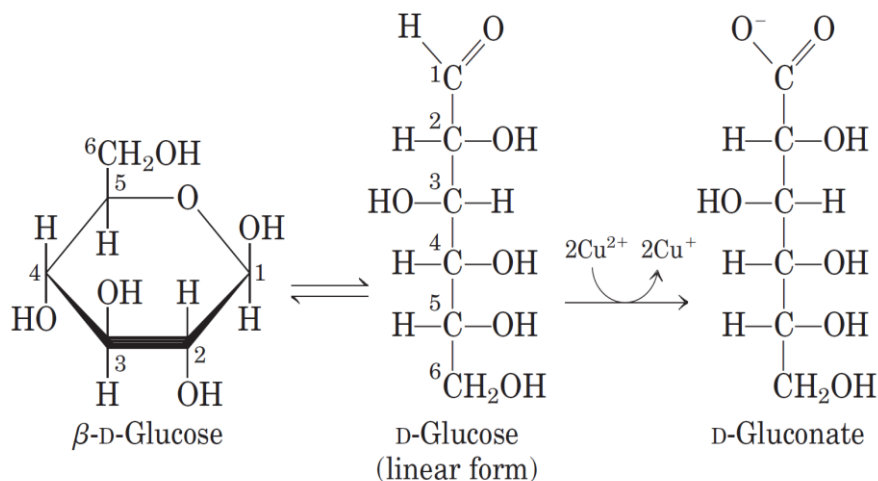
定性非定量的反应

Sugars that undergo this reaction are called **reducing sugars** (All monosaccharides are reducing sugars). The oxidation of a sugar by cupric ion occurs only with the linear form, which exists in equilibrium with the cyclic form(s).
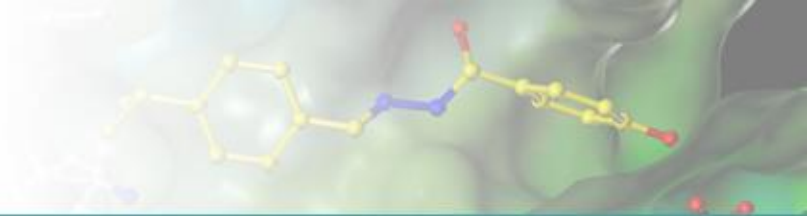
- **Formation of phosphate esters**

Phosphate esters can form at the 6-carbon of aldohexoses and ketohexoses

glucose 6-phosphate

fructose 6-phosphate
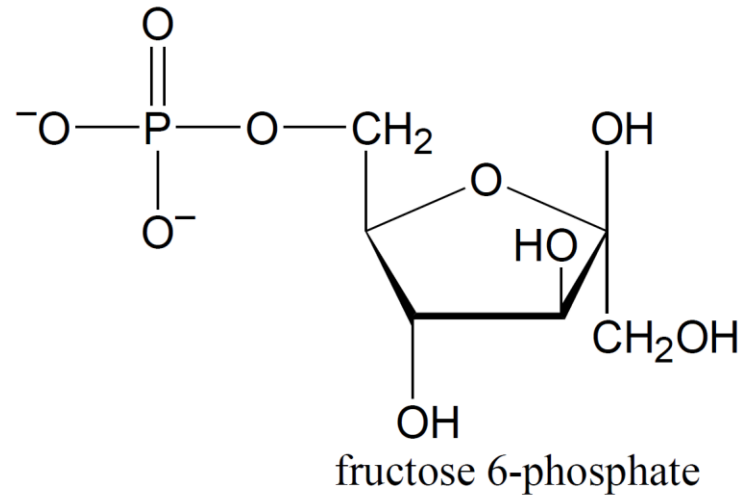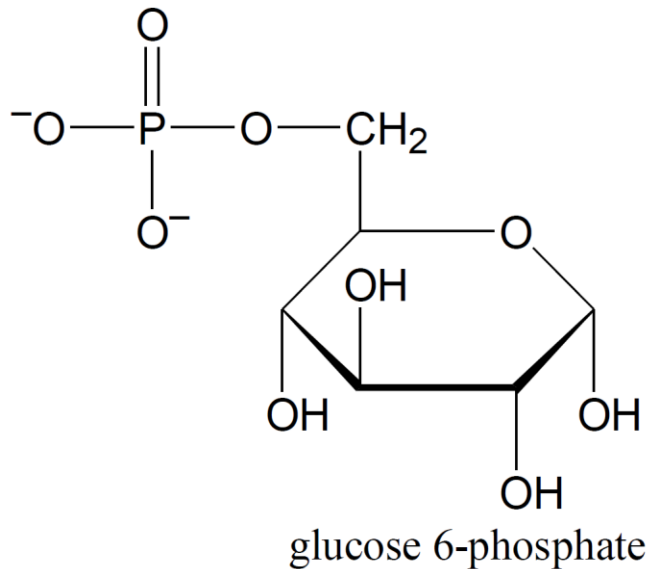
Phosphate esters of monosaccharides are found in the sugar-phosphate backbone of **DNA** and **RNA**, in **ATP**, and as intermediates in the metabolism of carbohydrates in the body.

- **Formation glycosidic bond**

  The hemiacetal and hemiketal forms of monosaccharides can react with alcohols to form acetal and ketal structures called **glycosides** (糖苷). The new carbon-oxygen bond is called the **glycosidic linkage**.

methyl α-D-glycopyranoside

α-D-glucose + CH₃OH $\xrightarrow{\text{H}^+}$

methyl β-D-glycopyranoside
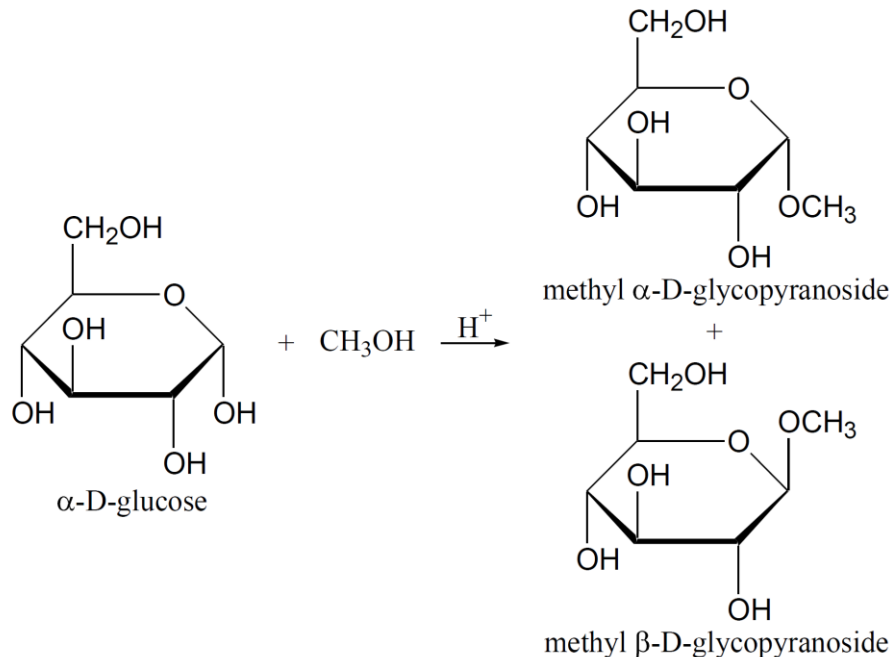
Glycoside can not open up to the open-chain form.

Not reducing sugars!

When anomeric carbon is involved in a glycosidic bond, the interconversion of linear and cyclic forms is prevented. Because the carbonyl carbon can be oxidized only when the sugar is in its linear form, formation of a glycosidic bond renders a sugar nonreducing.

Disaccharides

Disaccharides (such as maltose, lactose, and sucrose) consist of two monosaccharides joined covalently by an **O-glycosidic bond**, which is formed when a hydroxyl group of one sugar molecule, typically cyclic, reacts with the anomeric carbon of the other.
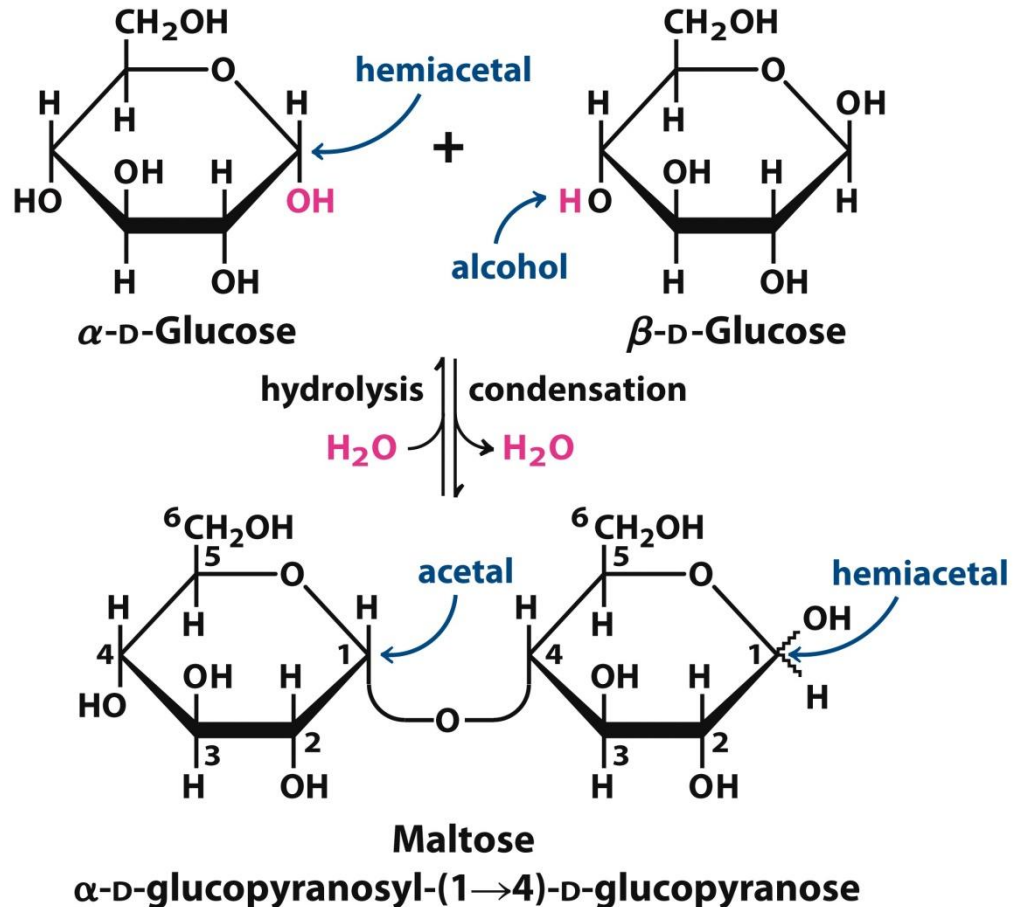
Glycosidic bonds are readily hydrolyzed by acid but resist cleavage by base.

- **Reducing end**

  In describing disaccharides or polysaccharides, the end of a chain with a free anomeric carbon (one not involved in a glycosidic bond) is commonly called the **reducing end**.

Maltose

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

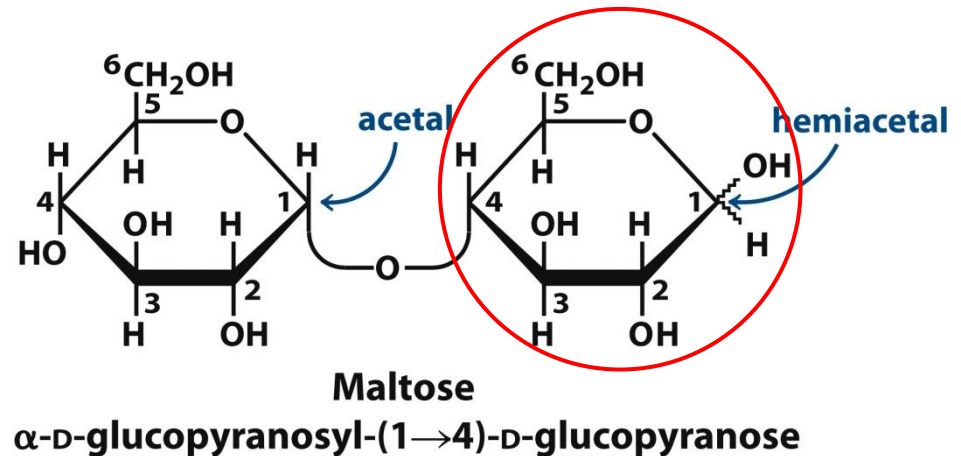The disaccharide **maltose** contains two D-glucose residues joined by a glycosidic linkage between C-1 (the anomeric carbon) of one glucose residue and C-4 of the other. Because the disaccharide retains a free anomeric carbon (C-1 of the glucose residue on the right), maltose is a reducing sugar. The configuration of the anomeric carbon atom in the glycosidic linkage is α. The glucose residue with the free anomeric carbon is capable of existing in α– and β-pyranose forms.

➤ **Rules to name disaccharides and more complex oligosaccharides**

(1) Give the configuration (α or β) at the anomeric carbon joining the first monosaccharide unit (on the left) to the second.

Maltose

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

Glc(α1→4)Glc

(2) Name the nonreducing residue; to distinguish five and six-membered ring structures, insert "furano" or "pyrano" into the name.

(3) Indicate in parentheses the two carbon atoms joined by the glycosidic bond, with an arrow connecting the two numbers; for example, (1→4) shows that C-1 of the first-named sugar residue is joined to C-4 of the second.

(4) Name the second residue. If there is a third residue, describe the second glycosidic bond by the same conventions.
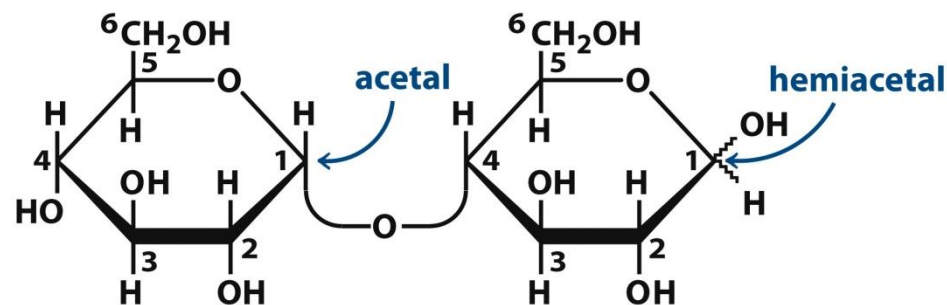
From nonreducing end to reducing end

- **Other common disaccharides**

Lactose: *galactose* and *glucose*
The anomeric carbon of the glucose residue is available for oxidation, and thus lactose is a reducing disaccharide.
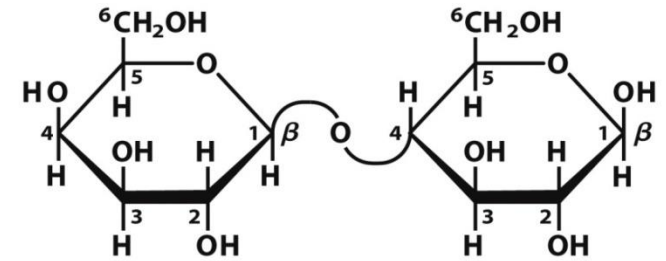The abbreviated name is Gal(β1→ 4)Glc.

Sucrose: *glucose* and *fructose*
Both anomeric carbons are involved in the glycosidic bond, sucrose is therefore a nonreducing sugar.
The abbreviated name of sucrose is either Glc(α1↔2β)Fru or Fru(β2↔1α)Glc.

Trehalose: *glucose* and *glucose*
Like sucrose, trehalose is a nonreducing sugar.
The abbreviated name is Glc(a1↔1a)Glc .

Lactose (β form)
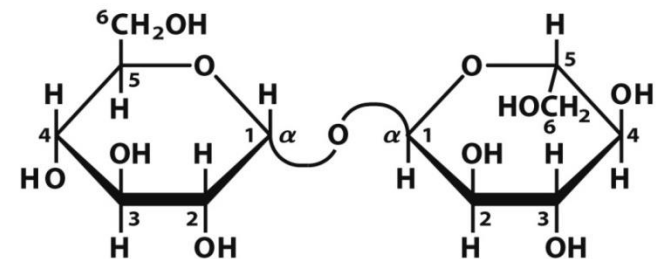β-D-galactopyranosyl-(1→4)-β-D-glucopyranose
Gal(β1→4)Glc
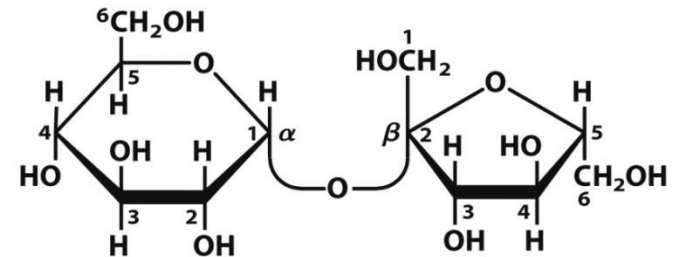
Sucrose
β-D-fructofuranosyl α-D-glucopyranoside
Fru(2β↔α1)Glc ≡ Glc(α1↔2β)Fru

Trehalose
α-D-glucopyranosyl α-D-glucopyranoside
Glc(α1↔1α)Glc

Important Monosaccharides

CH₂OH   OH
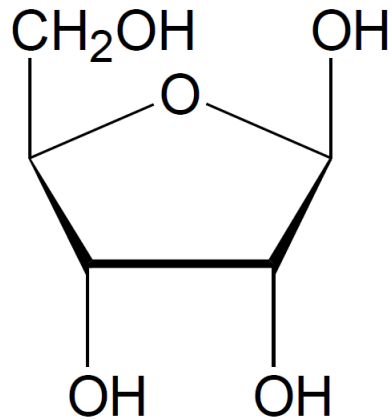
β-D-ribose
Forms the sugar backbone of
ribonucleic acid (RNA)

CH₂OH   OH
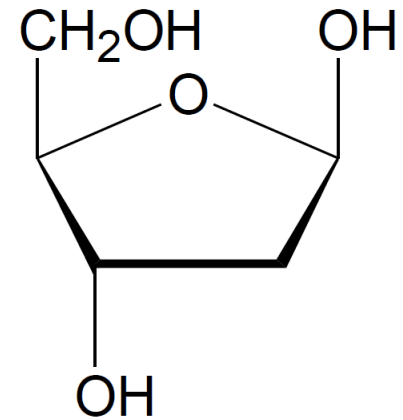
β-D-deoxyribose
Forms the sugar backbone of
deoxyribonucleic acid (DNA)

Important Monosaccharides

CH₂OH

OH

O

OH

OH
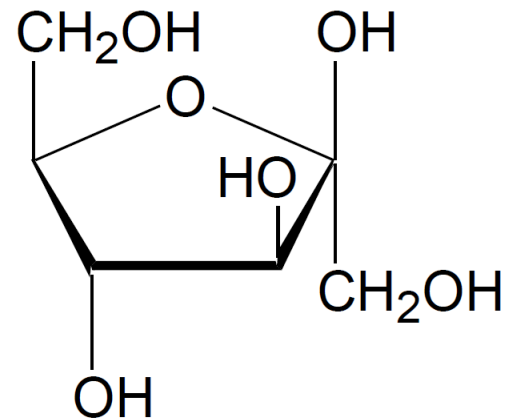
OH

OH
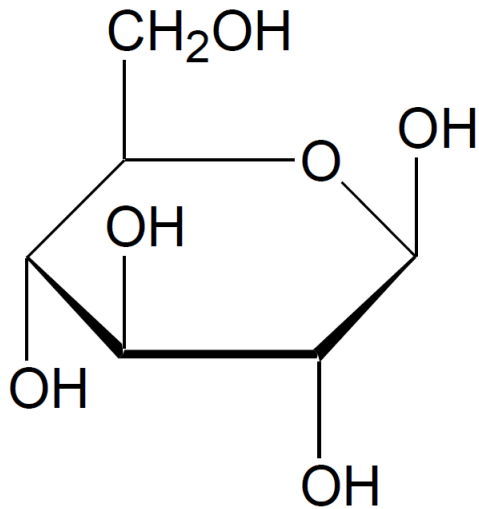
β-D-glucose

Also known as *dextrose* and *blood sugar*; present in honey and fruits. Glucose is metabolized in the body for energy. Other sugars absorbed into the body must be converted to glucose by the liver.

CH₂OH   OH

O

HO

CH₂OH

OH

β-D-fructose

Also known as *levulose* and *fruit sugar*. Fructose is the sweetest of the monosaccharides. It is present in honey (1:1 ratio with glucose), fruits, and corn syrup. It is often used to sweeten foods, since less fructose is needed to achieve the same degree of sweetness.
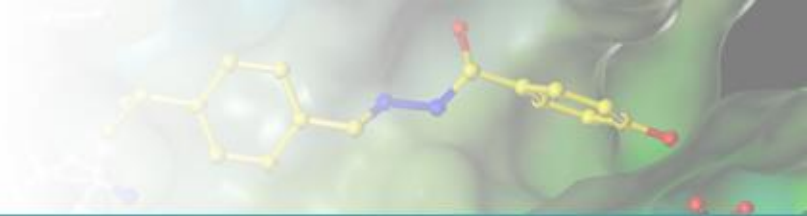
Take home messages …

✓ **Key concepts of carbohydrate**

 monosaccharides, oligosaccharides, polysaccharides, (CH2O)n

✓ **Monosaccharides**

 Aldose/Ketose, Chirality, Pyranoses/Furanoses…

Identify the structures below as being the α- or β- **forms**, and draw the structure of their anomers:

ribose

galactose