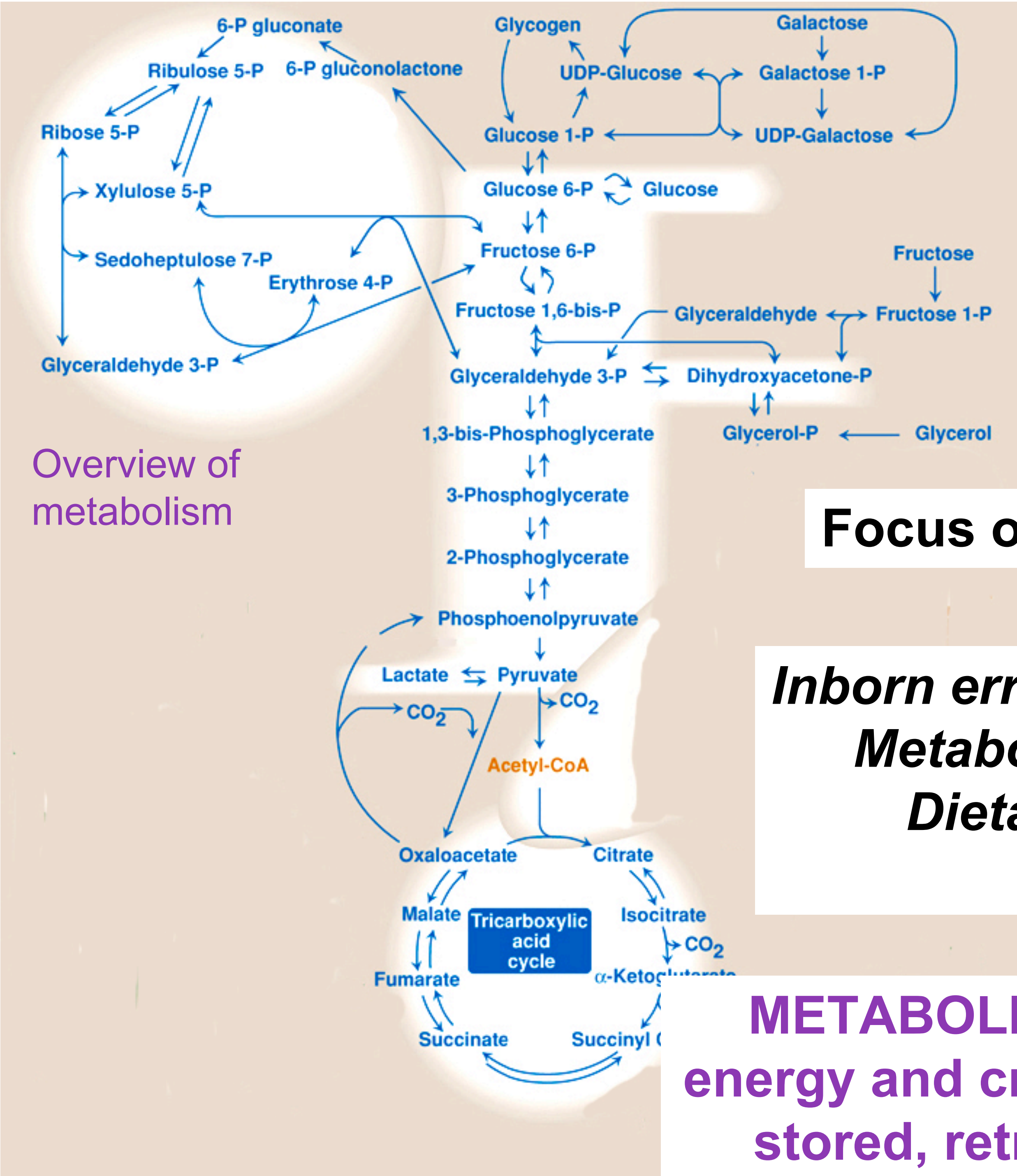



Overview of metabolism

**Focus on carbohydrates:**

***Inborn errors of metabolism***
***Metabolic syndromes***
***Dietary disorders***

**METABOLISM - understand how energy and critical compounds are stored, retrieved, and generated**

# Key knowledge base & conceptual questions

- Classify carbohydrates according to their definitions
- Discuss isomeric properties of carbohydrates
- Draw structures of the most common carbohydrates
- Discuss digestion of dietary carbohydrates

# Carbohydrates

- Most abundant organic molecules in nature
- Sugars are aldehydes or ketones with two or more -OH groups
- Products of photosynthesis

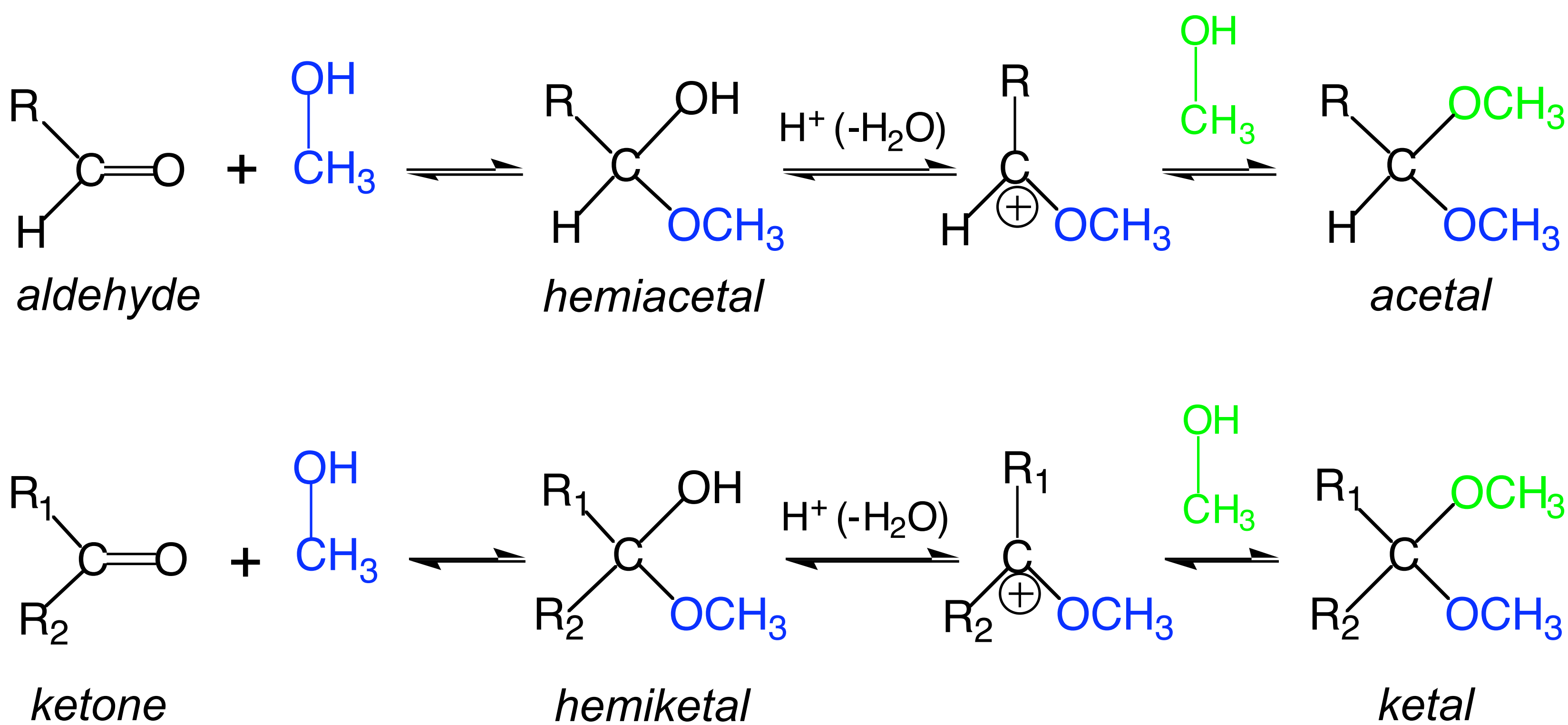
$$n\,CO_2 + n\,H_2O \xrightarrow{h\nu} (CH_2O)_n + n\,O_2$$

- Empirical formula
  - For simple carbohydrates, $(CH_2O)_n$
  - Can be incorporated in nucleic acids and coenzymes as well as associated with proteins and lipids

# Carbohydrate reactions

*In living systems, an important class of reactions for sugars are reactions with an alcohol. These involve:*

- *Formation of hemiacetals and hemiketals*
- *Formation of acetals and ketals*



# Carbohydrate Function in Living Systems

- *Energy source*
  - Cellular energy

$$(CH_2O)_n + n\,O_2 \xrightarrow{\text{ATP}} CO_2 + n\,H_2O$$

  - Storage form of energy
- *Structural element*
  - Cell walls of bacteria
  - Exoskeleton of many insects
  - Fibrous cellulose of plants
- *Intercellular communication*
  - Cell membrane components
  - Cell surface antigens

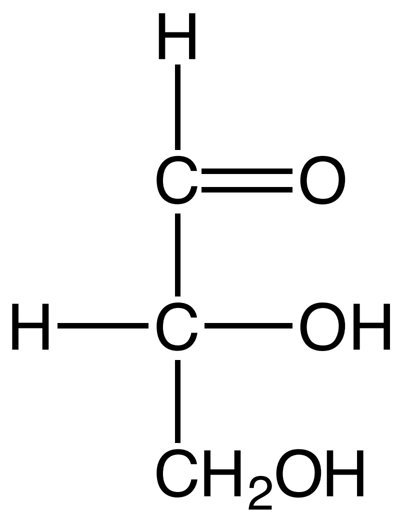
# Carbohydrate Classification: Monosaccharides

"Simple sugars"

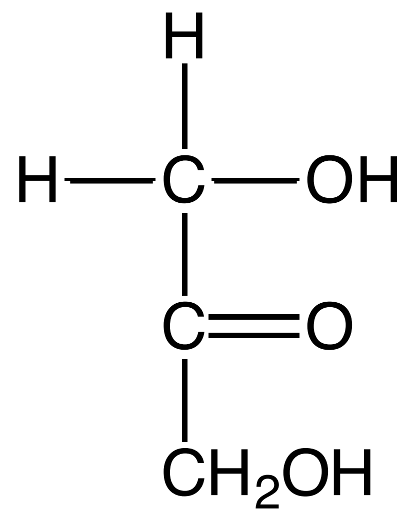
Polyhydroxy aldehydes or ketones that can't easily be further hydrolyzed

| 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 |

# Monosaccharides: Trioses $(CH_2O)_3$



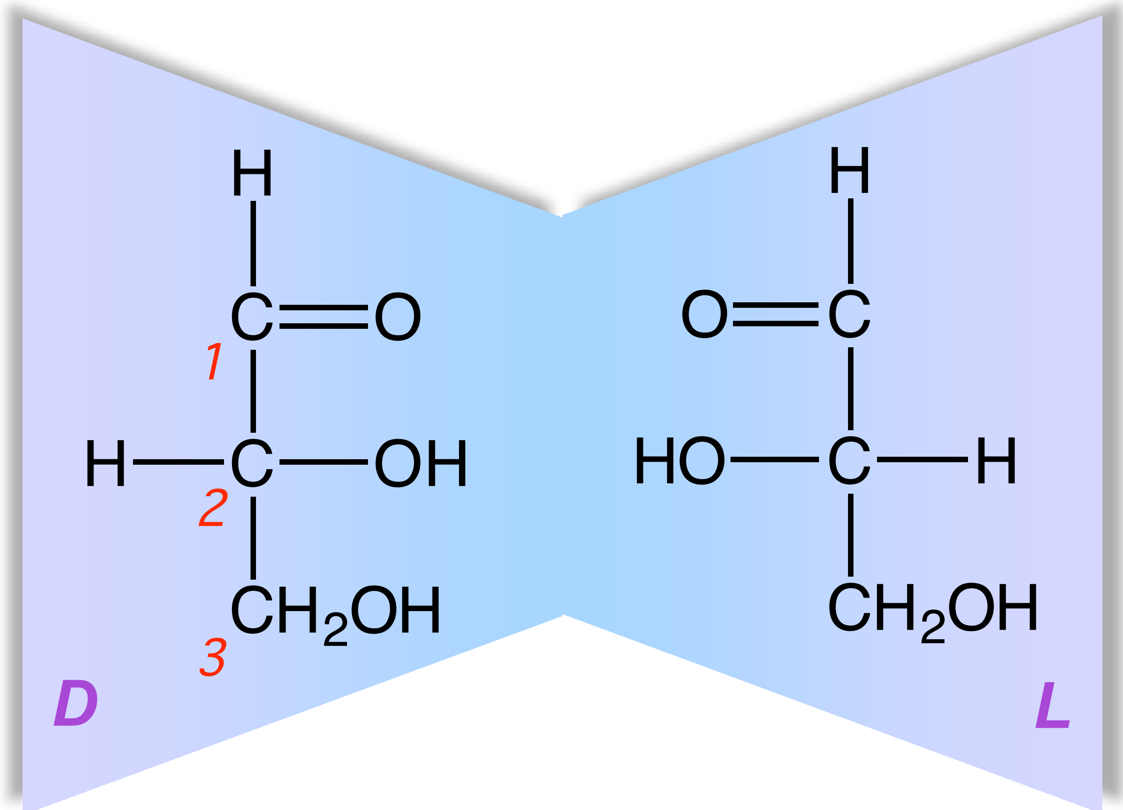

glyceraldehyde




dihydroxyacetone

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

# Monosaccharides: Trioses $(CH_2O)_3$

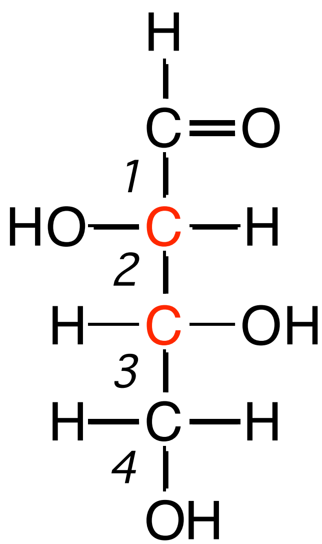



Glyceraldehyde has 1 chiral center.
(C with 4 different substituents)

The center may be D or L.

Enantiomer = mirror image

# Monosaccharides: Tetroses $(CH_2O)_4$




threose

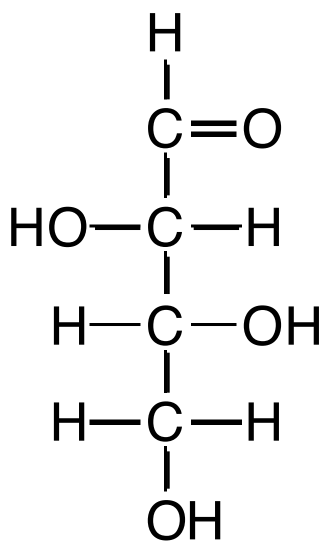
*Aldo-tetroses have 2 chiral centers.*

*The prefix D or L refers to the orientation about the chiral carbon farthest from the carbonyl group.*

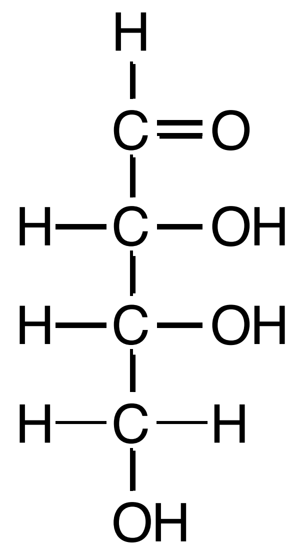
*The C3 carbon provides the orientation of threose for enantiomeric names.*

*Related molecules with different orientations around the C2 carbon have different names.*

# Monosaccharides: Tetroses $(CH_2O)_4$



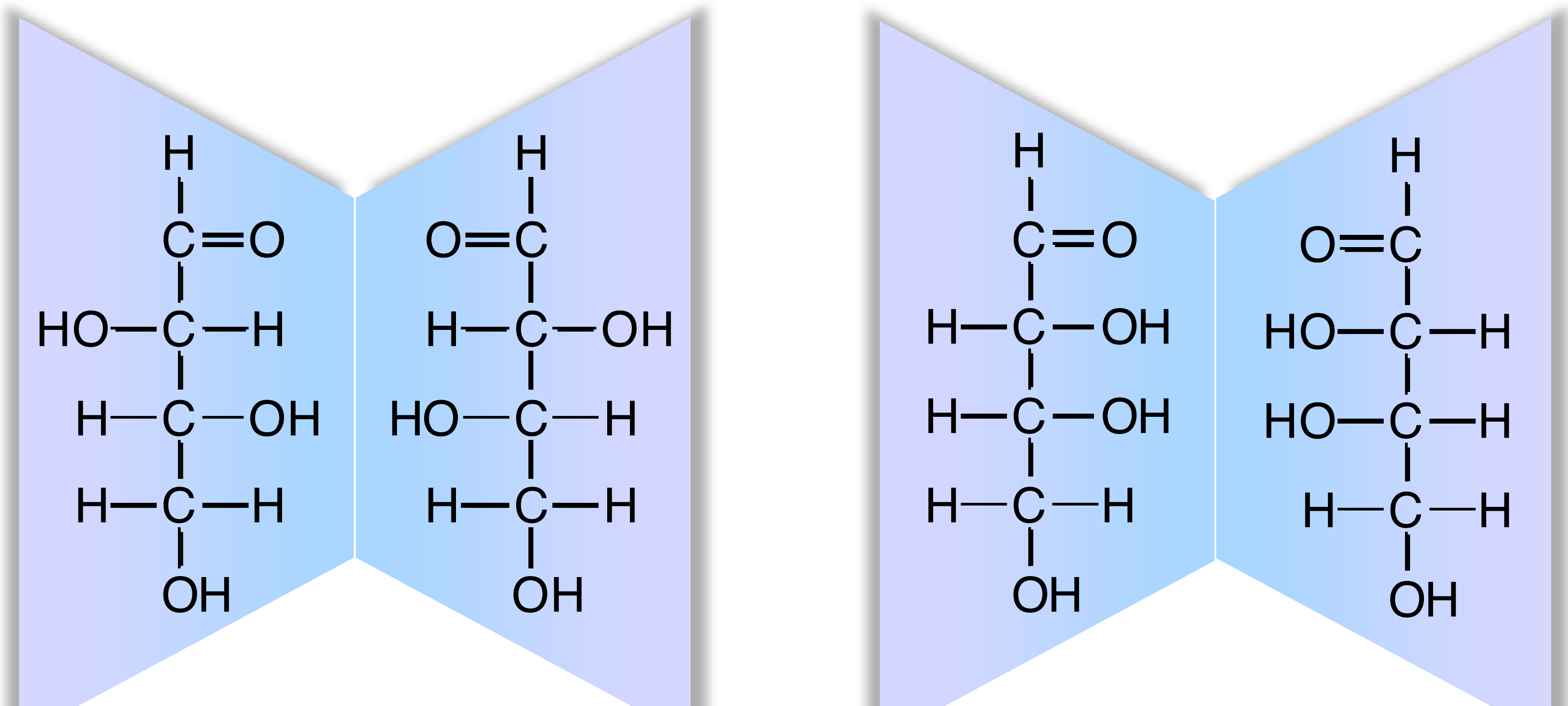
threose



erythrose

*Result: Aldo-tetroses come in two types.*
*Threose and erythrose are diastereoisomers.*
*($2^n$ stereoisomers, where n = number of chiral centers)*

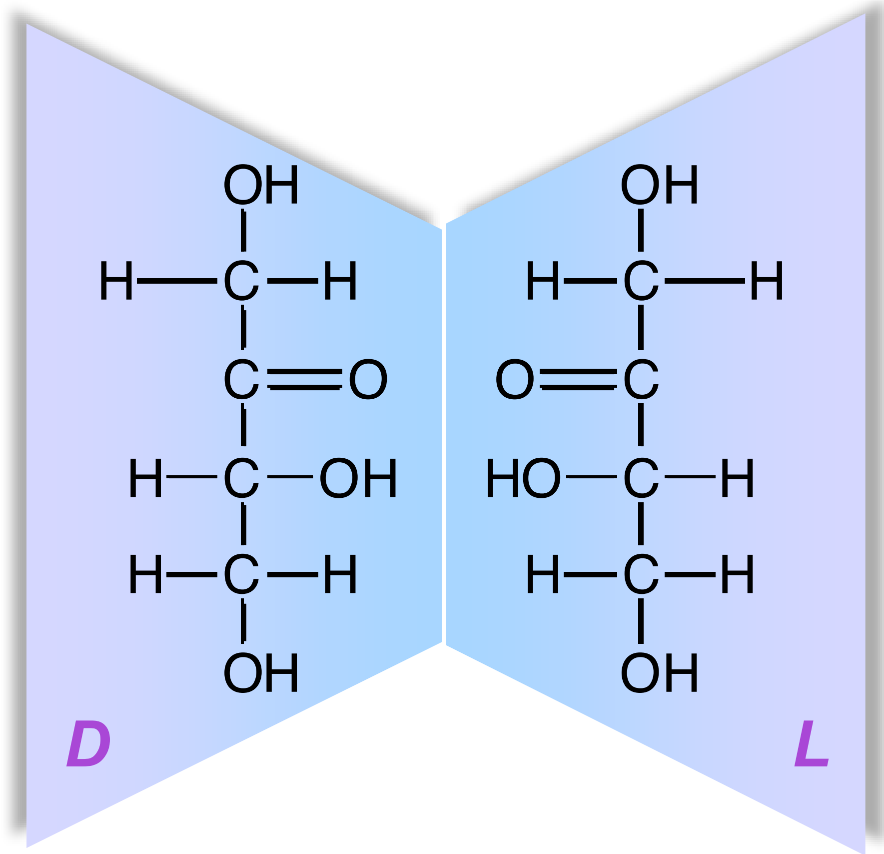
# Monosaccharides: Tetroses $(CH_2O)_4$



D-threose L-threose D-erythrose L-erythrose

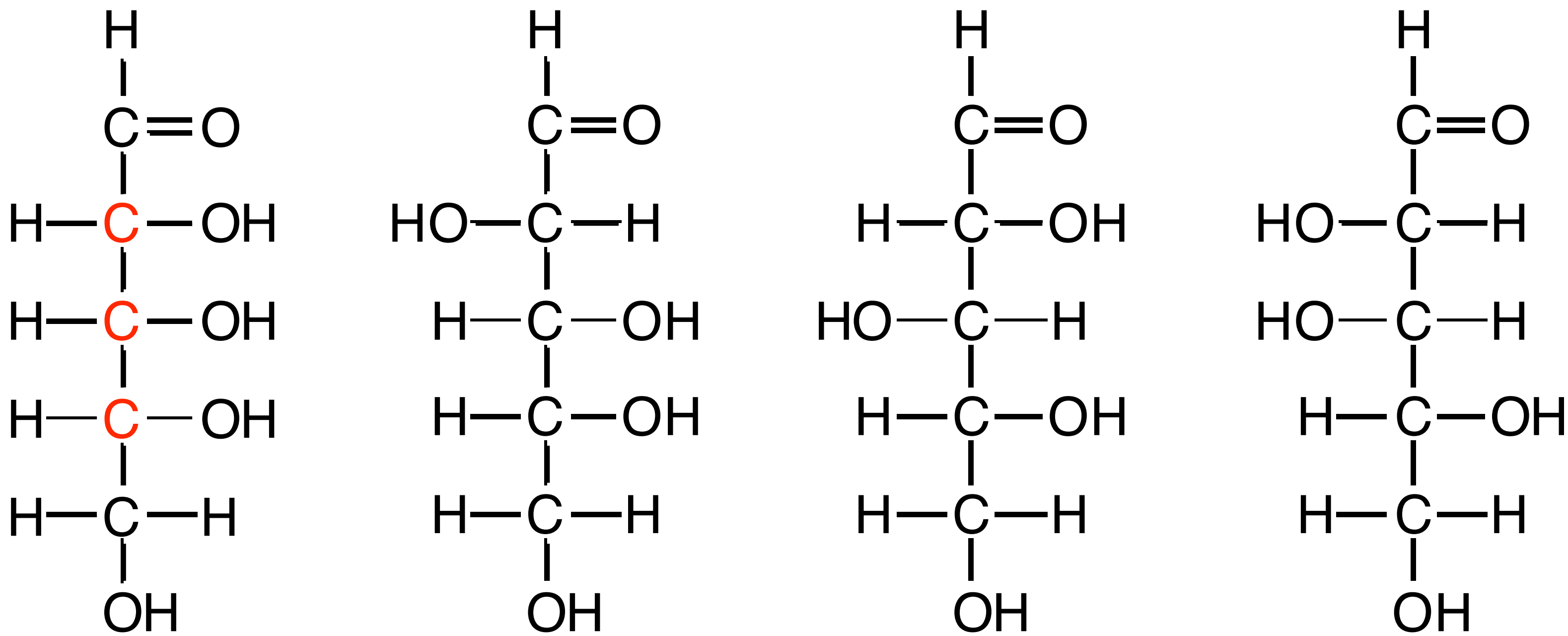
*Aldo-tetroses have 2 chiral centers and 4 stereoisomers.*
*($2^n$ stereoisomers, where $n$ = number of chiral centers)*

# Monosaccharides: Tetroses $(CH_2O)_4$




*Keto-tetroses: Erythrulose has only one chiral carbon, and thus only one pair of enantiomers.*

# Monosaccharides: Pentoses $(CH_2O)_5$



D-arabinose D-xylose D-lyxose

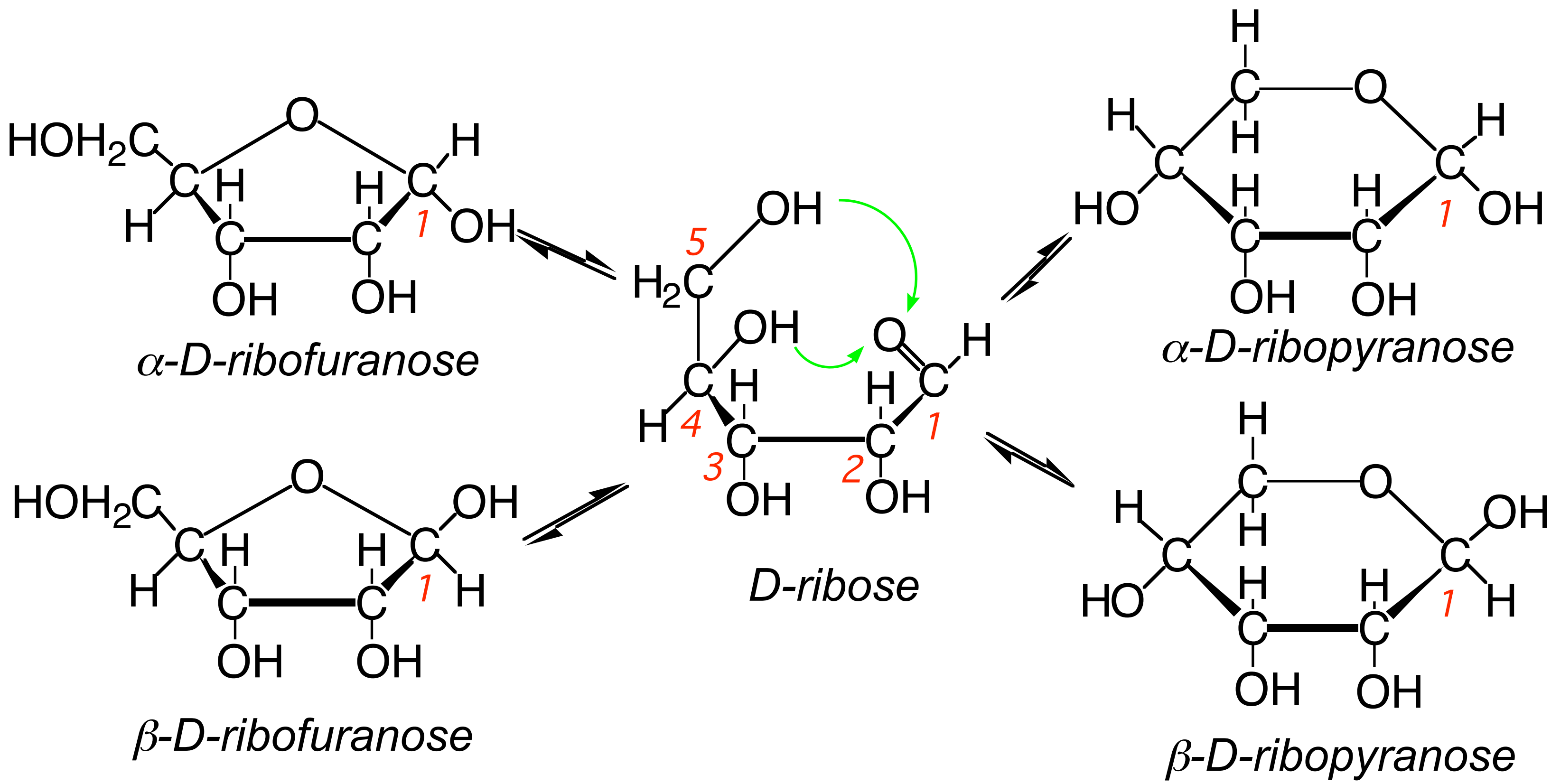
*Aldo-pentoses have 3 chiral carbons.*

*$2^3$ = 8 stereoisomers, I.e. 4 pairs of enantiomers*

# Monosaccharide cyclization

When n > 5, monosaccharides form stable ring structures.
Aldols form internal 'hemiacetals' (alcohol + aldehyde $\longrightarrow$ hemiacetal)

Cyclization produces a new chiral center.
Therefore, 2 cyclic stereoisomers are formed, $\alpha$ and $\beta$, differing in configuration at C-1, and called anomers.

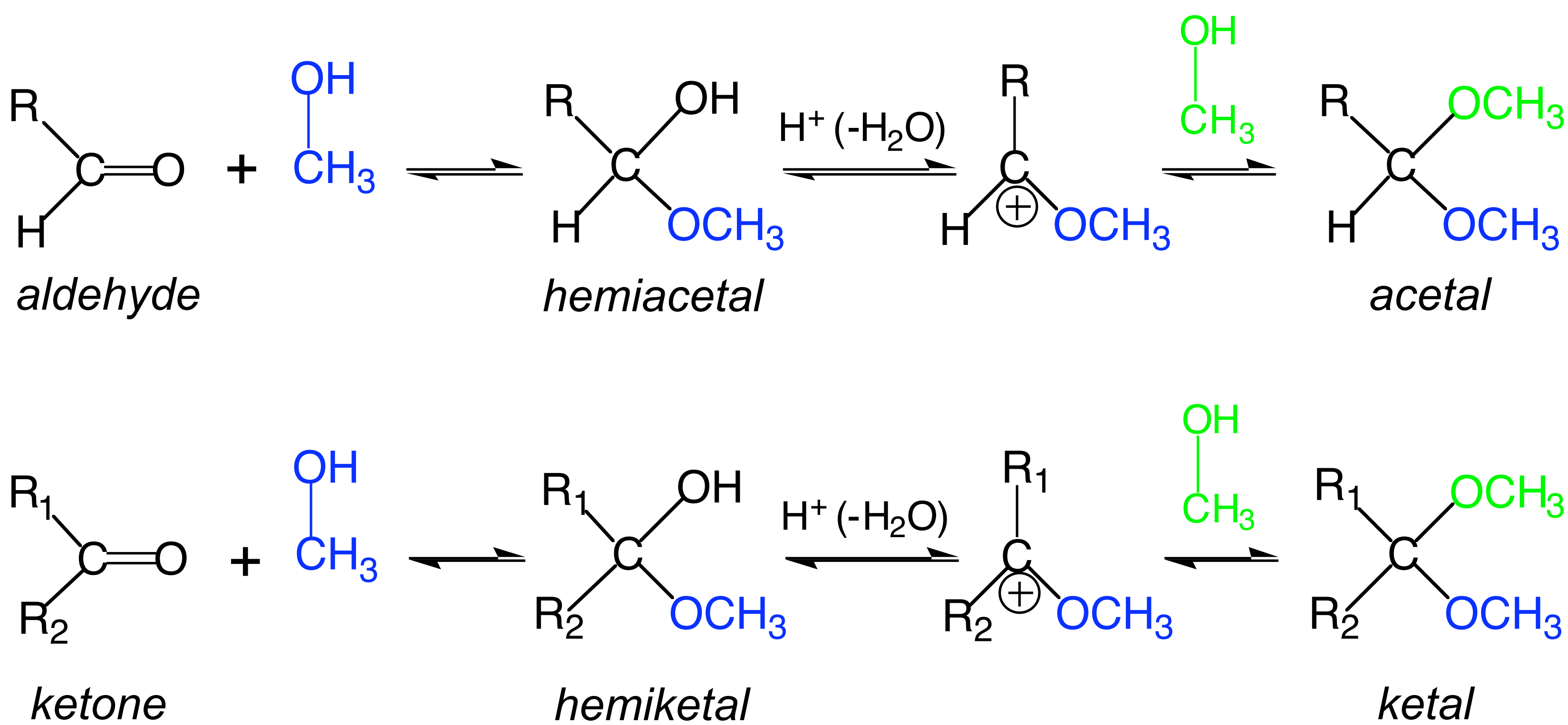


# Carbohydrate reactions

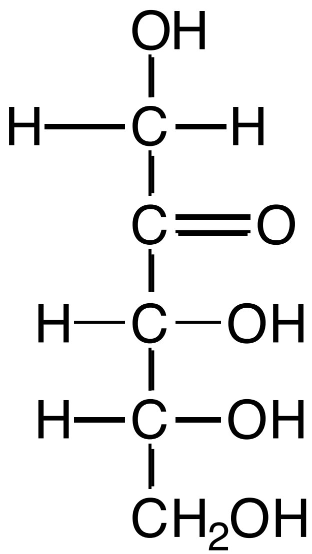
- *Formation of hemiacetals and hemiketals*

  *Important hemiacetals and hemiketals are* ***intra****molecular.*

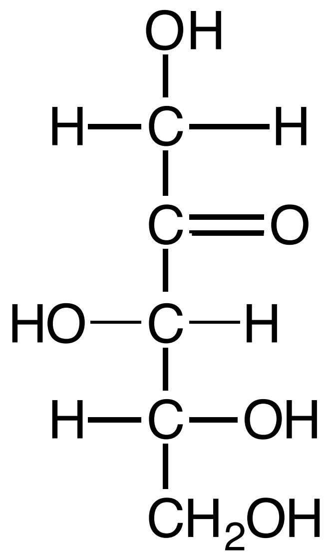
  *Intramolecular hemiacetals and hemiketals are essential for the formation of monosaccharide rings.*



# Monosaccharides: Pentoses $(CH_2O)_5$

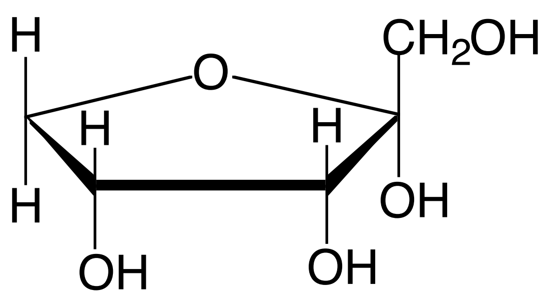



D-ribulose




D-xylulose

*Keto-pentoses have 2 chiral carbons, and thus 4 stereoisomers and 2 enantiomer pairs.*

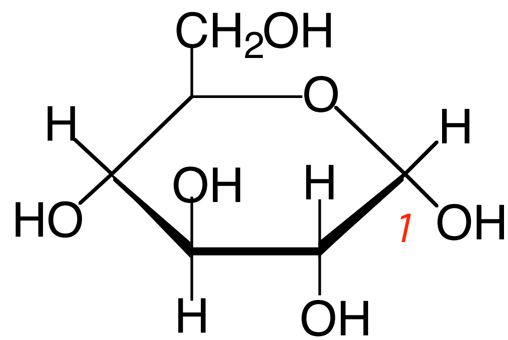



α-D-ribulose

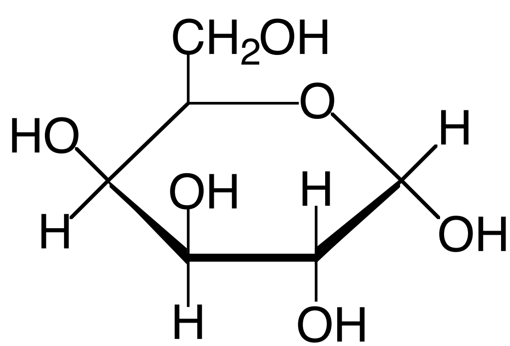
*Cyclization forms an internal 'hemi-ketal'.*

# Monosaccharides: Hexoses $(CH_2O)_6$

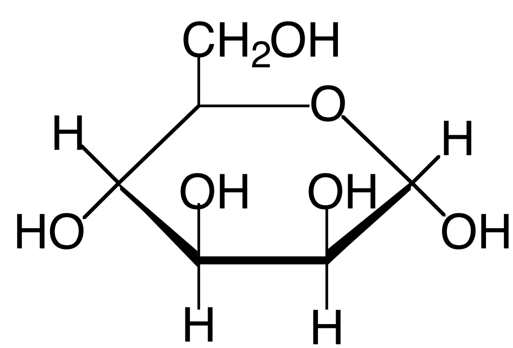
*Aldo-hexoses have 4 chiral carbons, and thus 16 stereoisomers and 8 enantiomer pairs.*
*Cyclization of aldo-hexoses leads to pyranose forms, which may be α or β at C-1 (anomers).*




β-D-glucoopyranose




β-D-galactopyranose

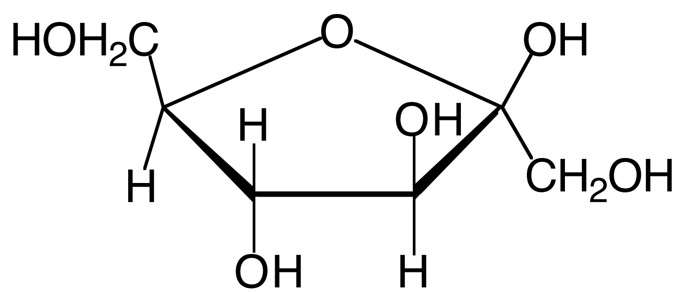



β-D-mannopyranose

# Monosaccharides: Hexoses $(CH_2O)_6$

*Keto-hexoses have 3 chiral carbons, and thus 8 stereoisomers and 4 enantiomer pairs.*

*Cyclization of keto-hexoses leads to furanose forms, which may be $\alpha$ or $\beta$ at C-1 (anomers).*




β-D-fructofuranose

Heptoses $(CH_2O)_7$ and octoses $(CH_2O)_8$ do exist, but they are rare in nature

# Summary of carbohydrate isomerism nomenclature

## Configurational isomers:

| *ISOMER* | *DEFINITION* | *EXAMPLE* |
|---|---|---|
| enantiomers | stereoisomers that are mirror images of one another | D-threose & L-threose |
| diastereoisomers | stereoisomers that are not enantiomers of one another | D-threose & D-erythose |
| anomers | stereoisomers of ring structures - they differ in configuration about C-1 | α-D-glucopyranose & β-D-glucopyranose |
| epimers | D-sugars differing in configuration at a single chiral center | D-glucose & D-mannose |

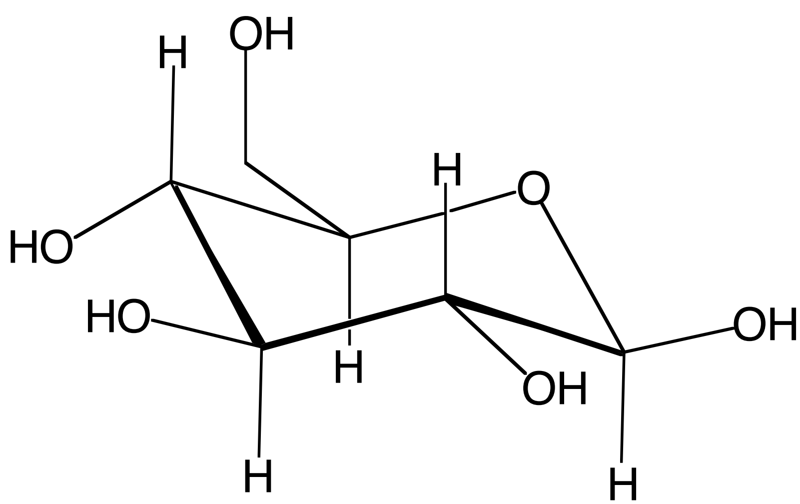
## Conformational isomers

molecules with the same stereochemical configuration, but differing in 3-dimensional conformation

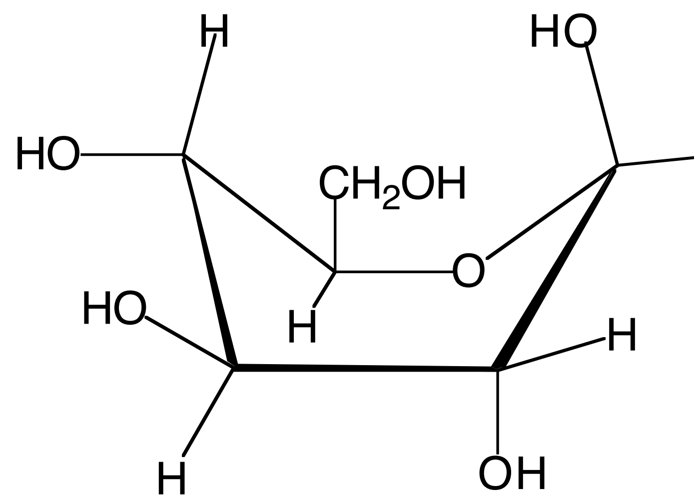
chair & boat form of β-D-glucopyranose

# Conformational isomers

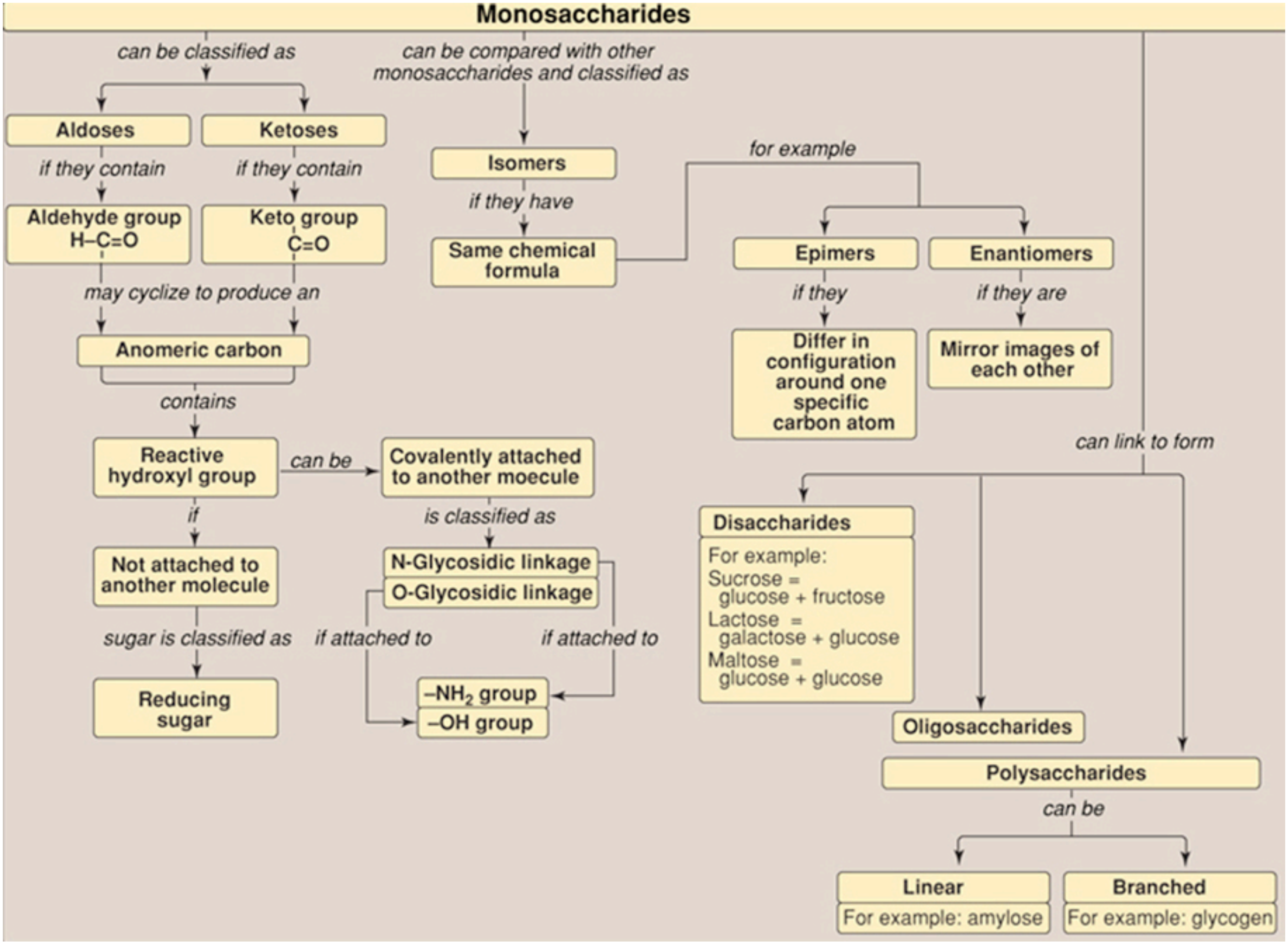
*Conformations of pyranose rings:  chair and boat*




β-D-glucopyranose
**chair form**




β-D-glucopyranose
**boat form**

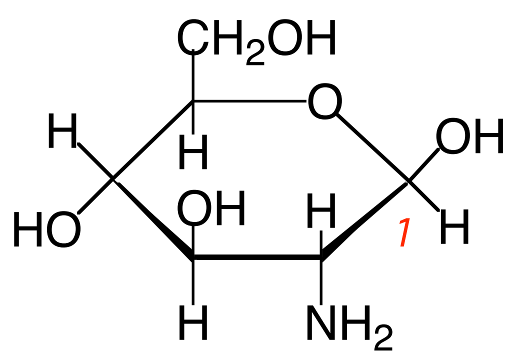

Monosaccharides
can be classified as
Aldoses
Ketoses
if they contain
if they contain
Aldehyde group H–C=O
Keto group C=O
may cyclize to produce an
Anomeric carbon
contains
Reactive hydroxyl group
can be
Covalently attached to another moecule
is classified as
N-Glycosidic linkage
O-Glycosidic linkage
if attached to
if attached to
–NH2 group
–OH group
if
Not attached to another molecule
sugar is classified as
Reducing sugar
can be compared with other monosaccharides and classified as
Isomers
if they have
Same chemical formula
for example
Epimers
Enantiomers
if they
if they are
Differ in configuration around one specific carbon atom
Mirror images of each other
can link to form
Disaccharides
For example:
Sucrose = glucose + fructose
Lactose = galactose + glucose
Maltose = glucose + glucose
Oligosaccharides
Polysaccharides
can be
Linear
For example: amylose
Branched
For example: glycogen

# Derivatives of monosaccharides

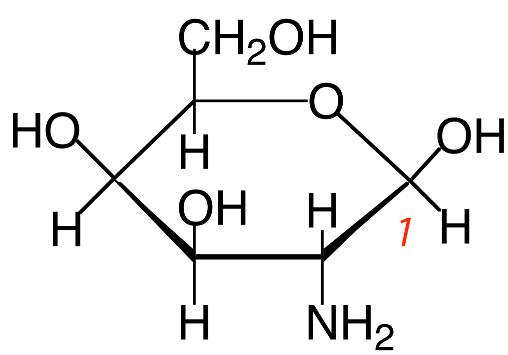
- *May be produced by replacing an -OH group* ***with*** *another substituent*
- *May be produced by attaching* ***to*** *an -OH group of another substituent*

*Examples:*

***1. Amino sugars***




β-D-glucosamine




β-D-galactosamine

# Derivatives of monosaccharides

**2. *Phosphate esters***

*ATP*

*nucleic acids*

*glyceraldehyde-3-phosphate*
*glucose-1-phosphate*
*glucose-6-phosphate*
*fructose-6-phosphate*

*Hydrolysis to yield sugar +* $P_i$ $\Delta G^{o\prime}$ *= -12 to -20 kJ/mol*

*Therefore, ATP can act as a phosphate donor to these sugars and the phosphosugar hydrolysis can drive other coupled, unfavorable reactions.*

*The phosphate esters of sugars can behave as 'activated' compounds in some metabolic reactions.*

# Glycosidic bonds

*Simple sugars are linked in glycosidic bonds to form disaccharides and polysaccharides.*

*In disaccharides and polysaccharides,*

1. *The glycosidic bond is formed by elimination of water between one anomeric hydroxyl of a cyclic monosaccharide, and the hydroxyl group of a second sugar.*
2. *The glycosidic bond is named for*
   a) *The configuration ($\alpha$ or $\beta$) of the -OH at the anomeric carbon,*
   b) *The number of the anomeric carbon*
   c) *The number of the carbon in the other linked, sugar unit*

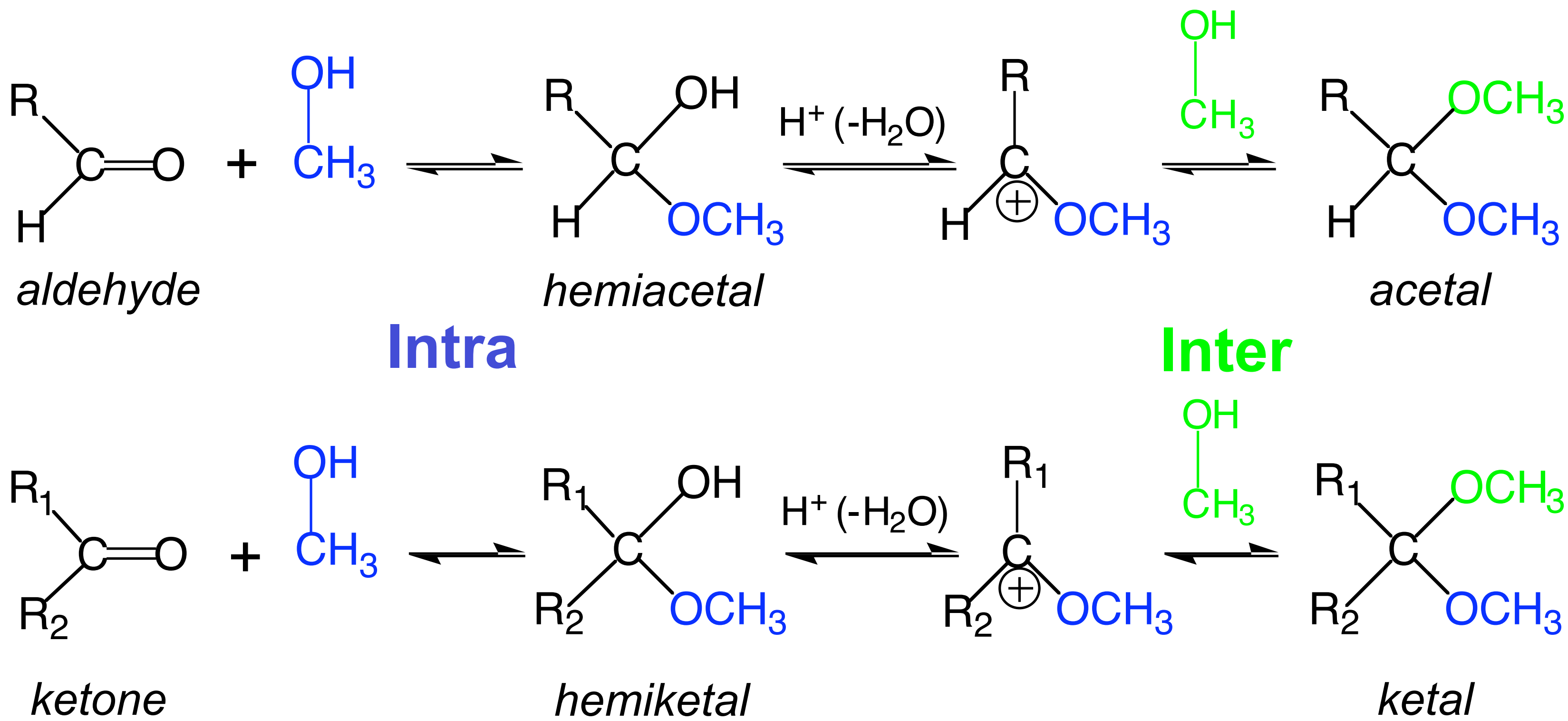
*Example: lactose = galactose-$\beta$(1 $\rightarrow$ 4)-glucose*

# Carbohydrate reactions

- *Formation of acetals and ketals*

  *The important acetals and ketals are glycosides.*

  *When the 2nd alcohol is another sugar, the compound is a disaccharide and the linkage is called a glycosidic bond.*



# Carbohydrate reactions

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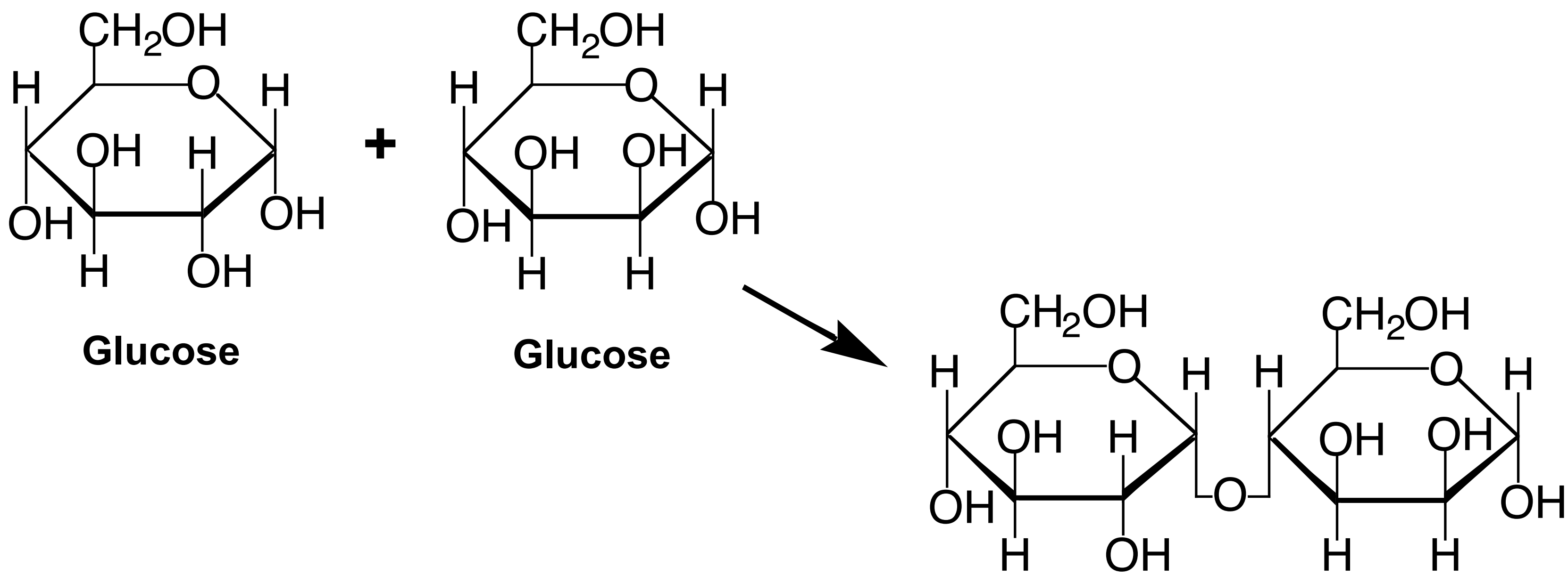



**Maltose**

glucose-α(1→4)-glucose

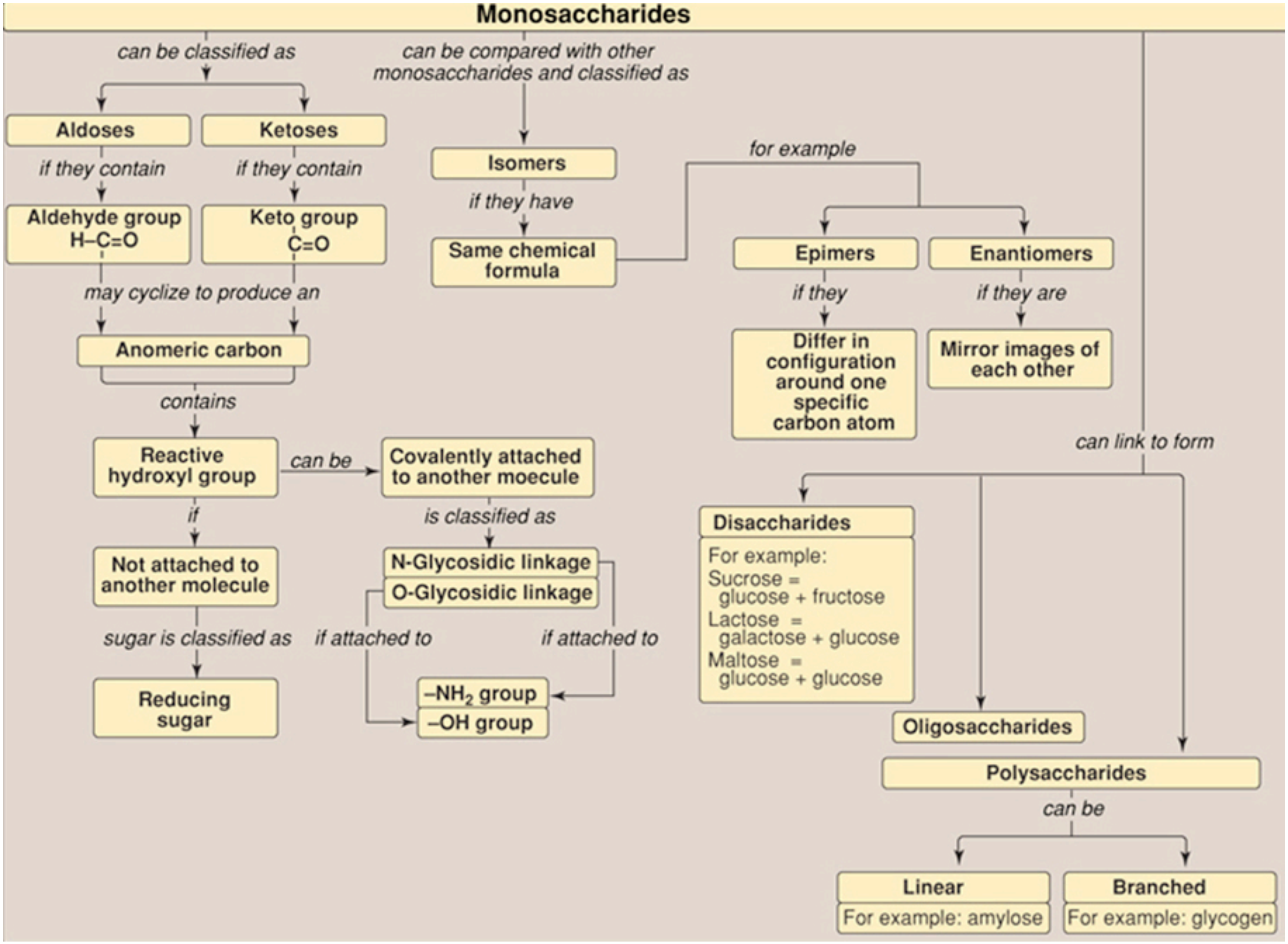
# Glycosidic bonds

*In disaccharides and polysaccharides,*

3. *The sugar unit with a free anomeric carbon is the* ***'reducing'*** *end of the disaccharide or polysaccharide.*

   *The sugar unit with its anomeric carbon tied up in the glycosidic linkage is called the '****non-reducing'*** *end.*

*'Reducing' = has a potentially free aldehyde group in the linear form (not cyclized).*
*A free aldehyde can be oxidized by oxidizing agents such as alkaline copper (II) which gives a red color when it reacts with aldoses to give* $Cu_2O$.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if
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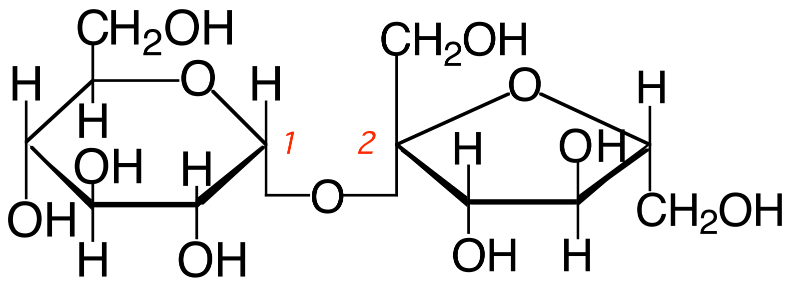
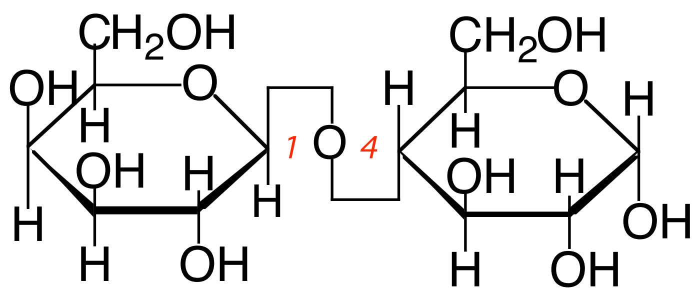
sugar is classified as
Reducing sugar
is classified as
N-Glycosidic linkage
O-Glycosidic linkage
if attached to
if attached to
–NH2 group
–OH group
can be compared with other monosaccharides and classified as
Isomers
if they have
Same chemical formula
for example
Epimers
Enantiomers
if they
if they are
Differ in configuration around one specific carbon atom
Mirror images of each other
can link to form
Disaccharides
For example:
Sucrose = glucose + fructose
Lactose = galactose + glucose
Maltose = glucose + glucose
Oligosaccharides
Polysaccharides
can be
Linear
For example: amylose
Branched
For example: glycogen

# Disaccharides



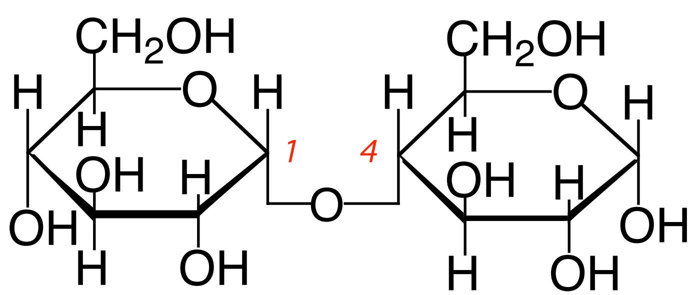
**Sucrose**
glucose-α(1→2)-glucose

cleaved by sucrase



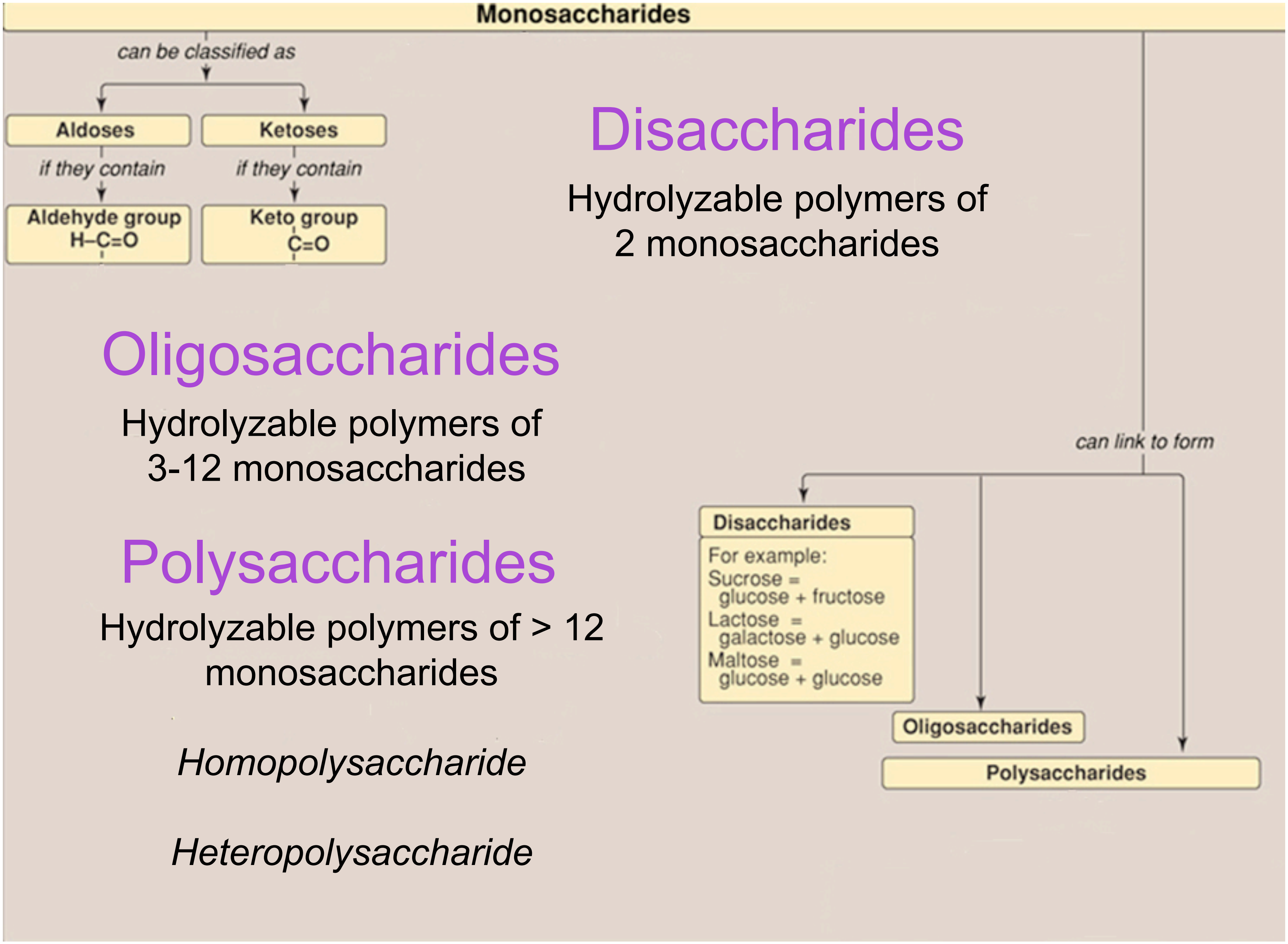
**Lactose**
galactose-β(1→4)-glucose

cleaved by lactase



**Maltose**
glucose-α(1→4)-glucose

cleaved by maltase




# Disaccharides

Hydrolyzable polymers of
2 monosaccharides

# Oligosaccharides

Hydrolyzable polymers of
3-12 monosaccharides

# Polysaccharides

Hydrolyzable polymers of > 12
monosaccharides

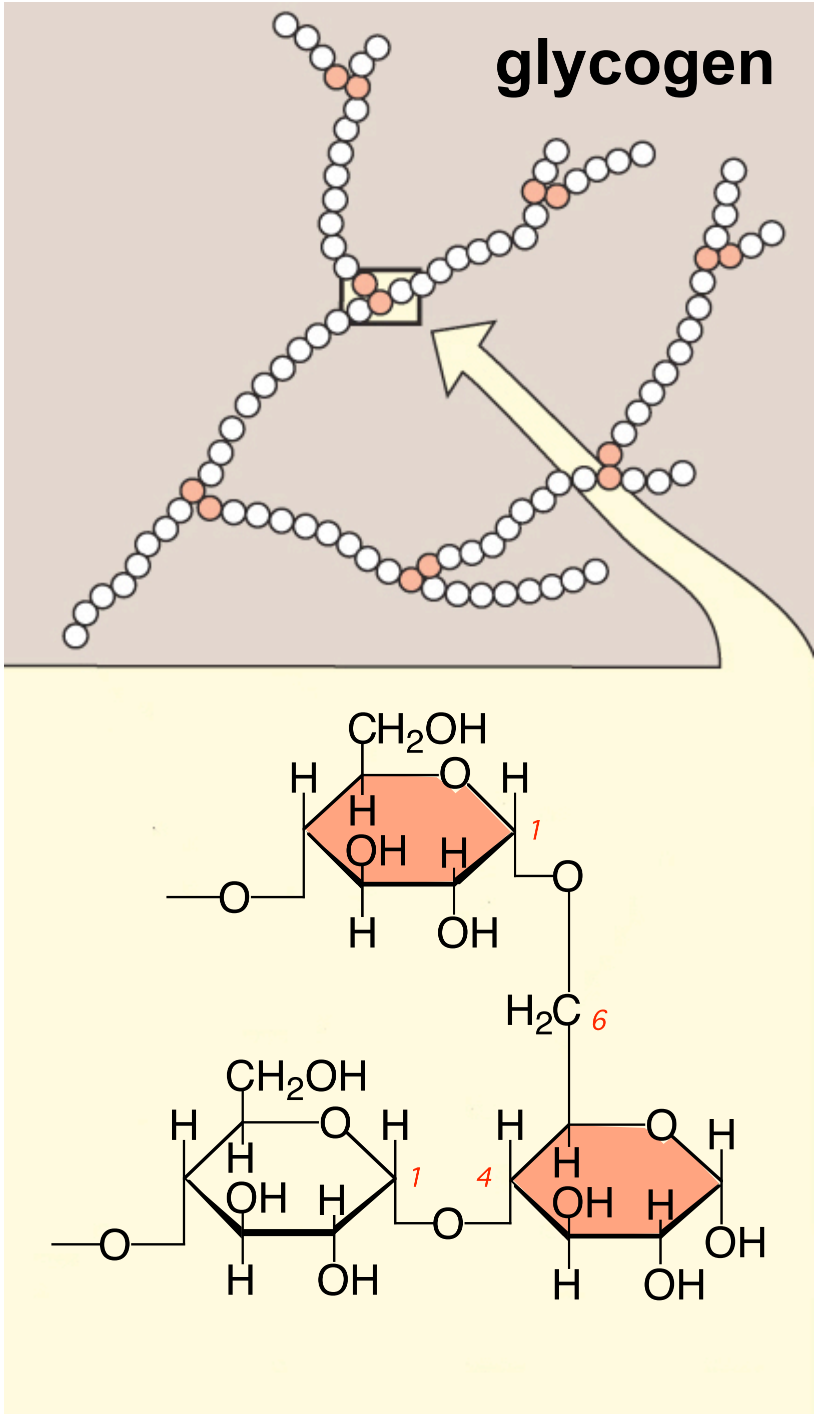
*Homopolysaccharide*

*Heteropolysaccharide*

# Polysaccharides

| Type of polysaccharide | Function | Building units | Glycosidic bond linkage |
|---|---|---|---|
| Glycogen | Storage in animals | Branched polymer of glucose | $\alpha$1,4 and $\alpha$1,6 |
| Starch | Storage in plants | Unbranched or branched polymer of glucose | $\alpha$1,4 (amylose)<br>$\alpha$1,6 (amylopectin) |
| Cellulose | Structure in plants | Unbranched polymer of glucose | $\beta$1,4 |

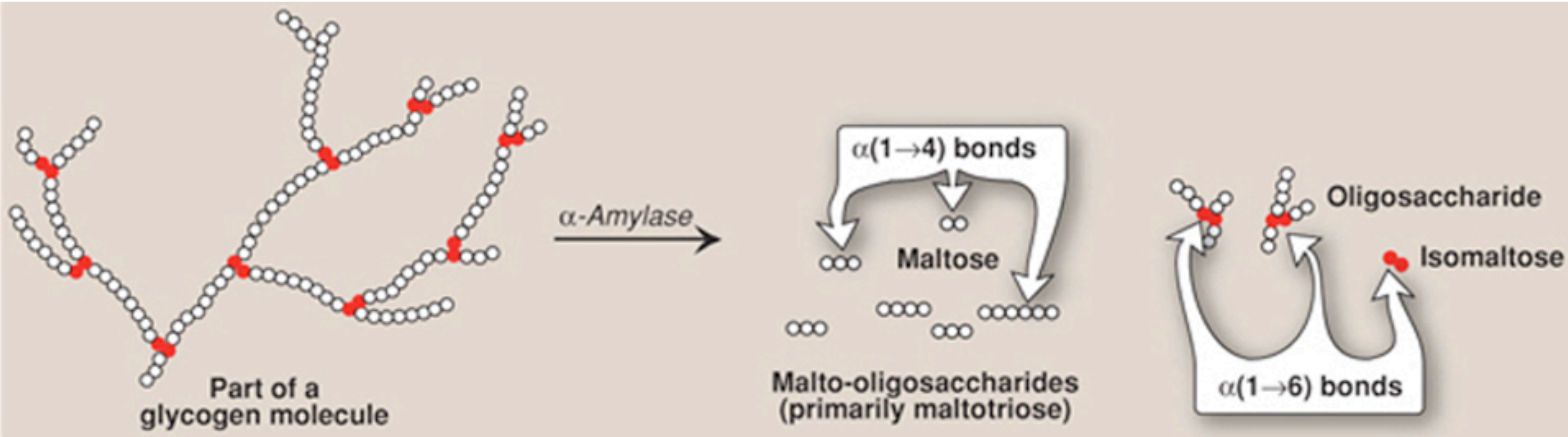
# Polysaccharides: glycogen



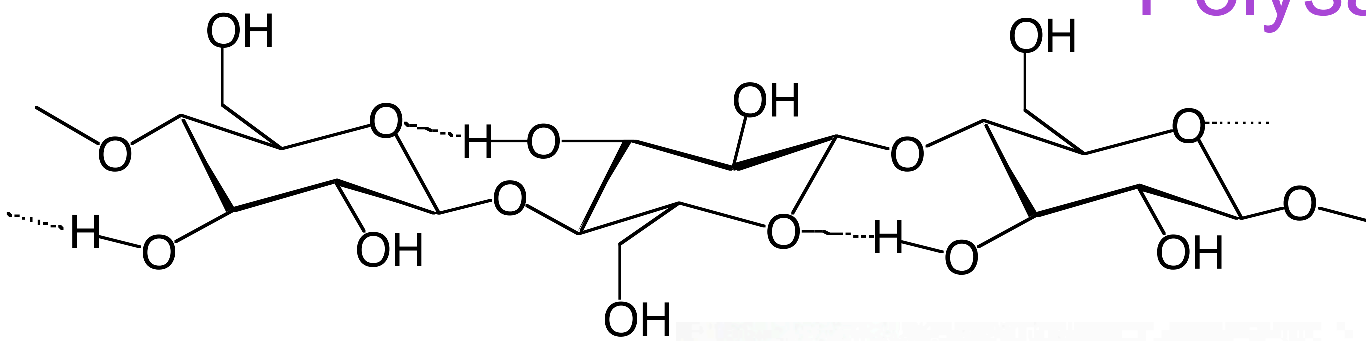

Some polysaccharides are branched.

Chemical bonds at the branch points are different from those in the linear polysaccharide.

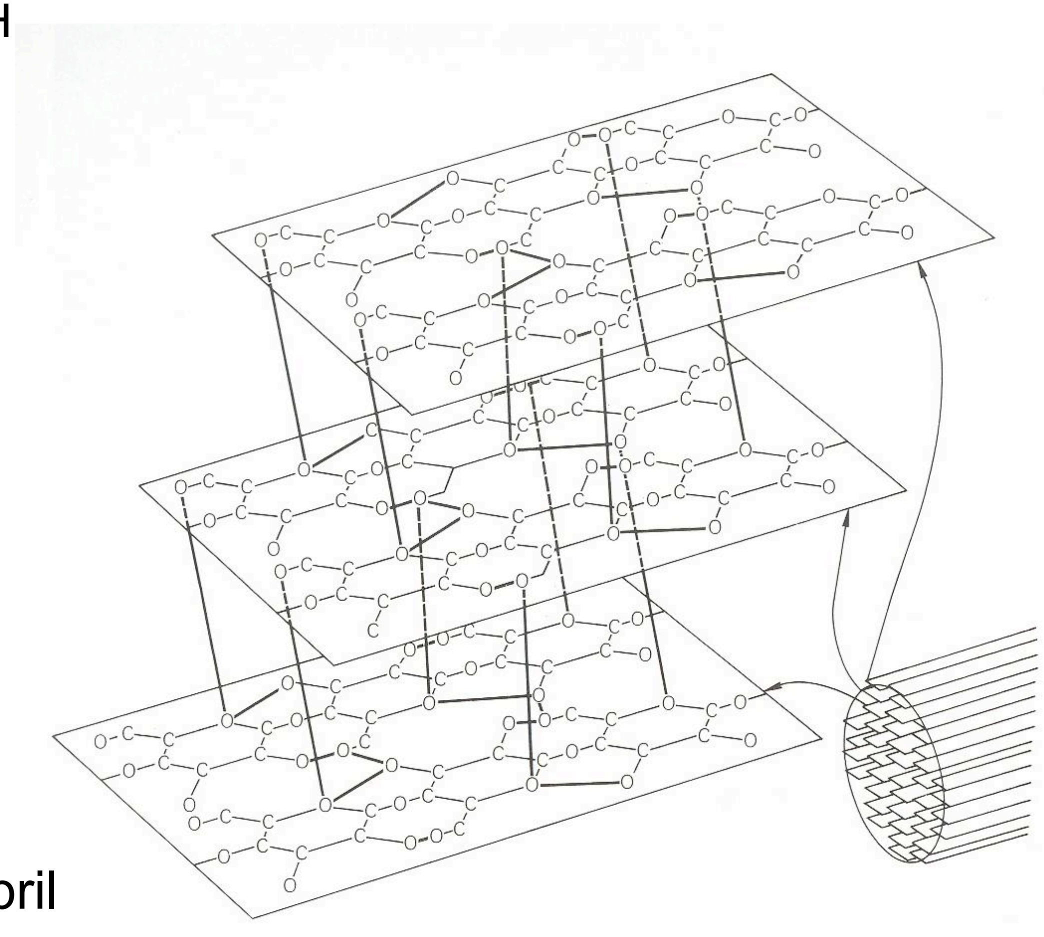
# Polysaccharides:  glycogen breakdown



# Polysaccharides: cellulose



β–1,4 linkages



Model of cellulose molecules in a microfibril

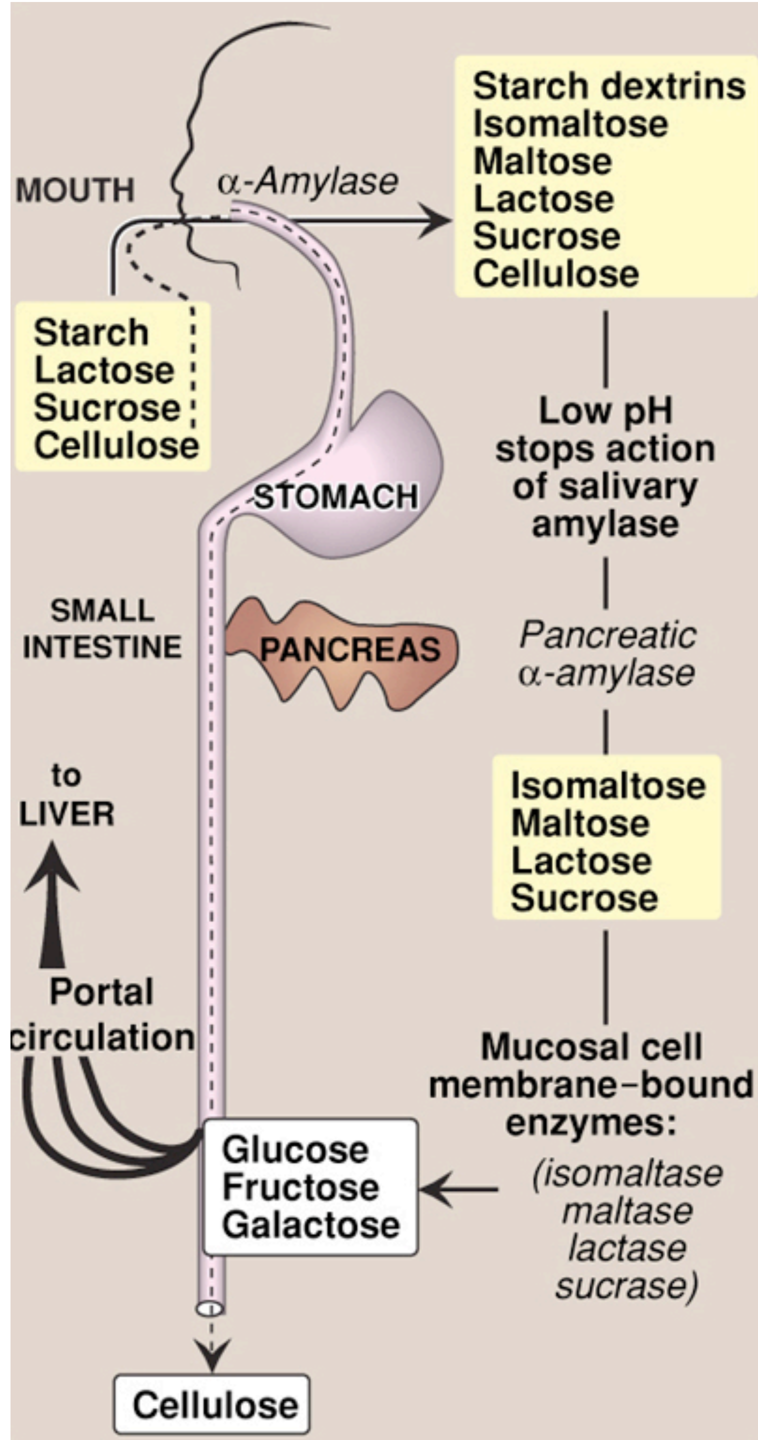
# Dietary carbohydrates

*Digestible*
- Starch
- Sucrose
- Glucose and fructose
- Lactose

*Non-digestible by humans*
- Cellulose
- Other plant polysaccharides

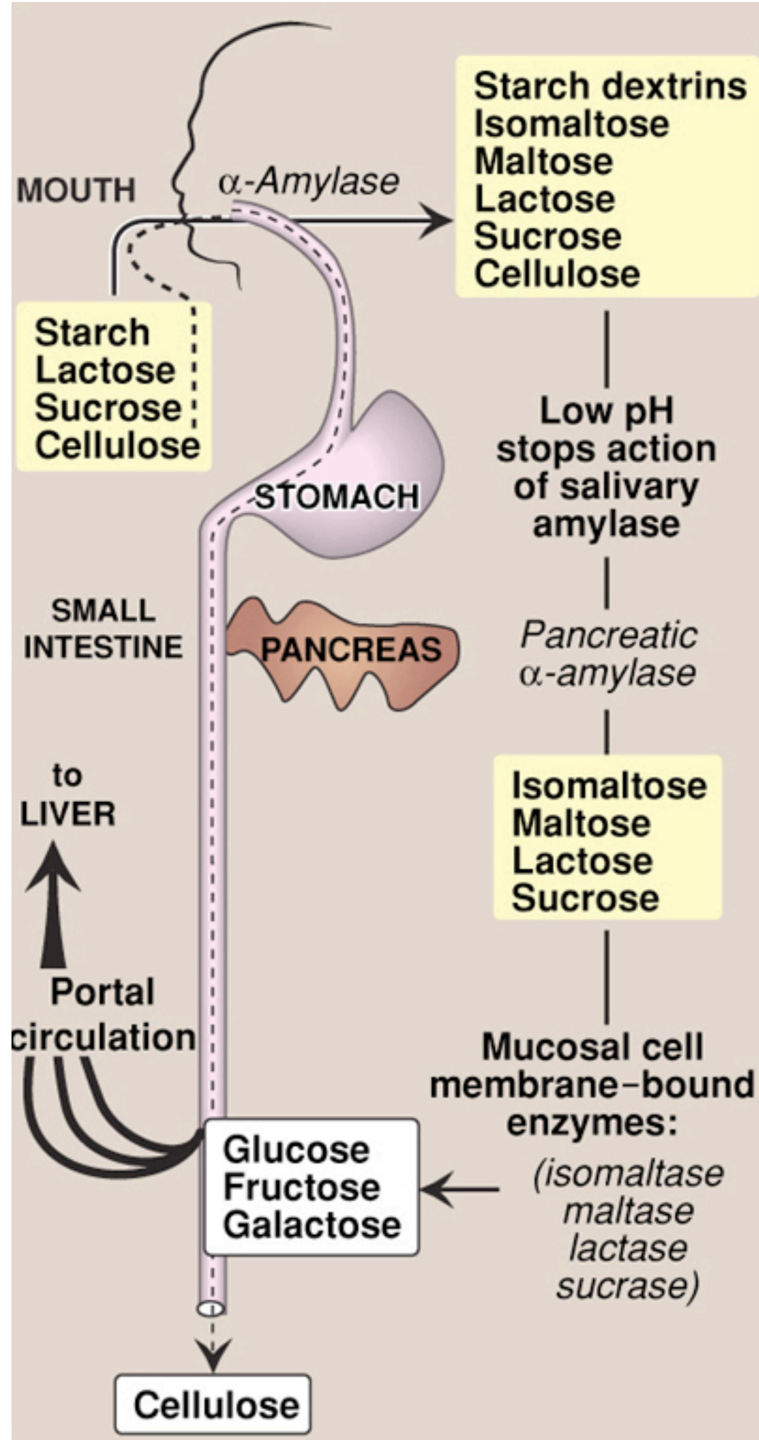
Only monosaccharides are absorbed into the bloodstream from the gut.

Digestion of carbohydrates involves their hydrolysis into monosaccharides



# Digestive enzymes

| Enzyme | Substrate | Products |
|---|---|---|
| α-Amylase | Starch, glycogen | Oligosaccharides |
| Dextrinase | Oligosaccharide | Glucose |
| Isomaltase | α-1,6-glucoside | Glucose |
| Maltase | Maltose | Glucose |
| Lactase | Lactose | Galactose, glucose |
| Sucrase | Sucrose | Fructose, glucose |



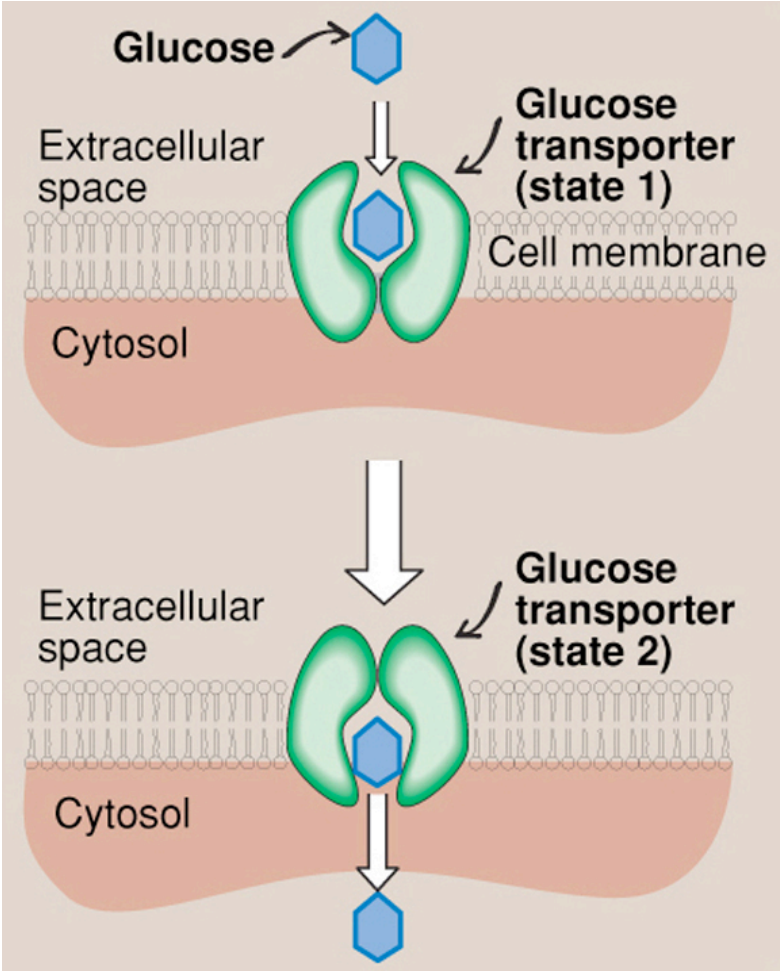
# Monosaccharide absorption by intestinal mucosal cells

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***