Lehninger

SIXTH EDITION

Principles of Biochemistry

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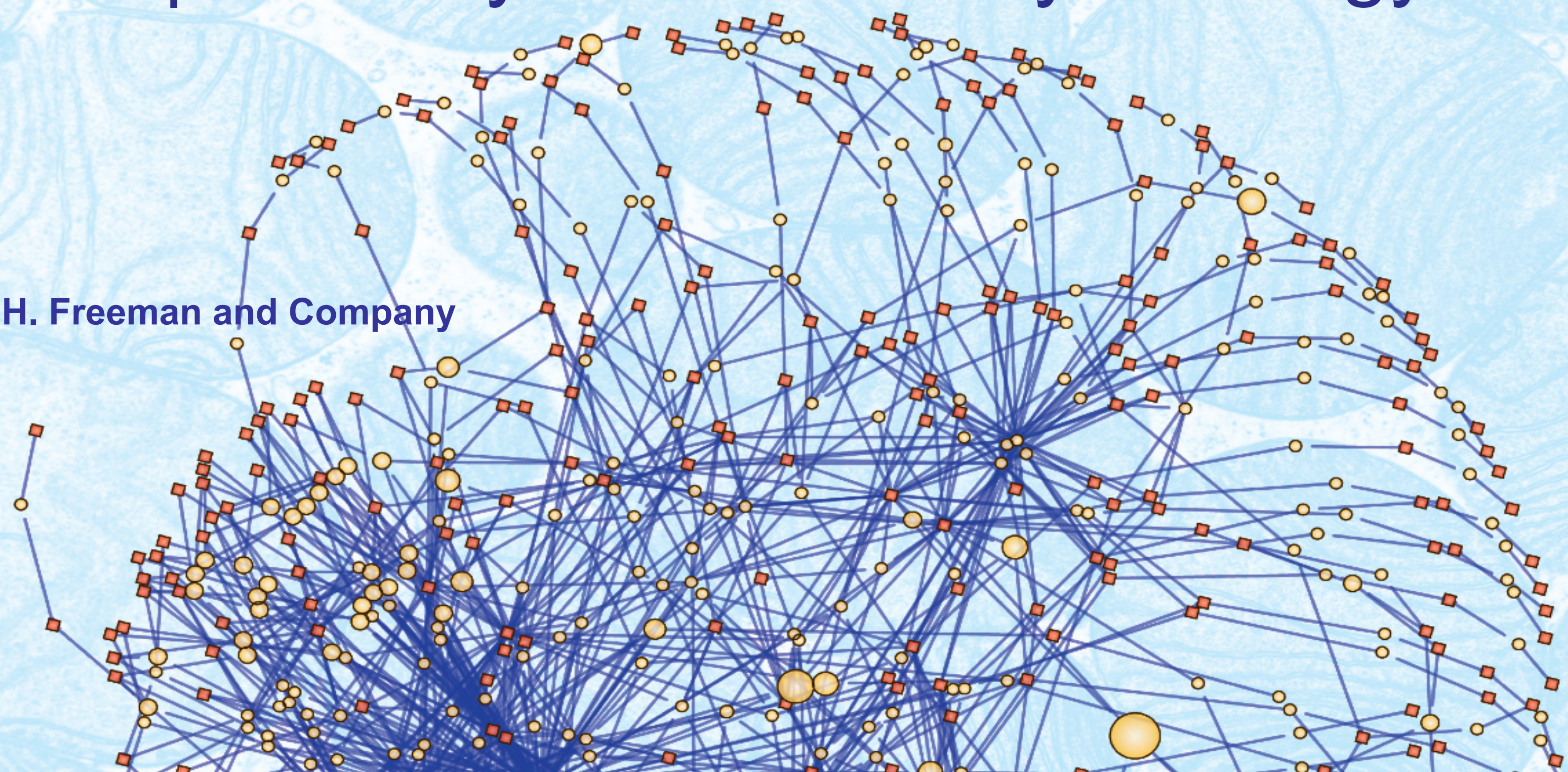
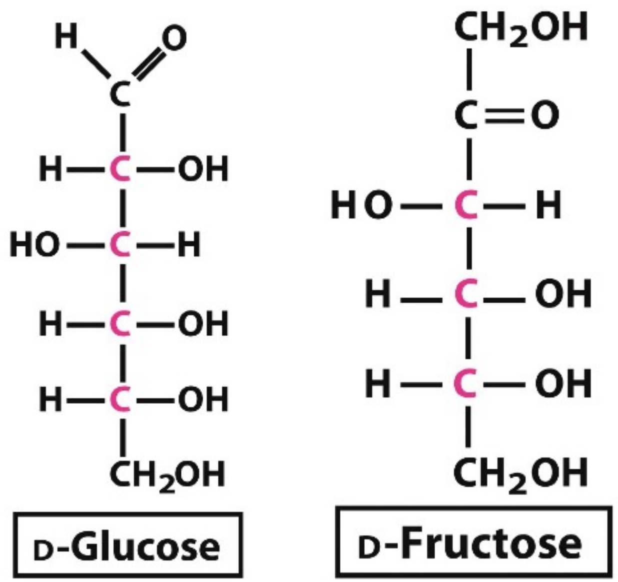
7 | Carbohydrates and Glycobiology



Carbohydrates

- Polyhydroxy aldehydes or ketones
  - Many but NOT all have formula $C_n(H_2O)_n$
  - Some also contain N, P or S
- Produced from CO_2 and H_2O via photosynthesis in plants
- Three major classes (many end with -ose)
  - <u>Mono</u>saccharide (one-sugar)
  - <u>Di</u>saccharide (two-sugar)
  - <u>Poly</u>saccharide (many-sugar)



$C_6H_{12}O_6$ $C_6H_{12}O_6$

Week 7 Carbohydrates and Glycobiology

7.1 Monosaccharides and Disaccharides

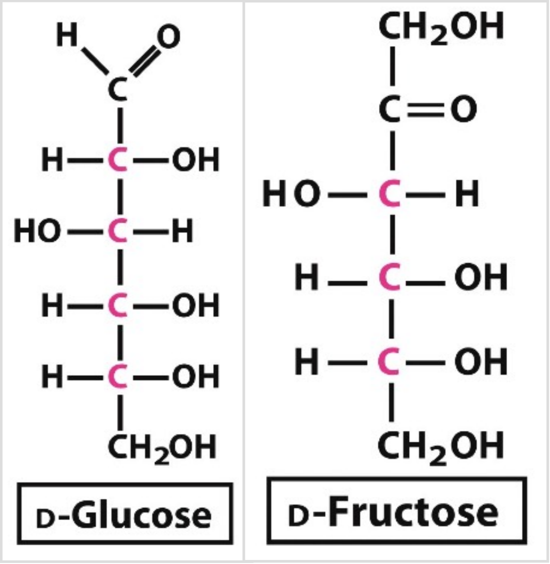
7.2 Polysaccharides

7.3 Glycoconjugates

7.4 Carbohydrates as Informational Molecules

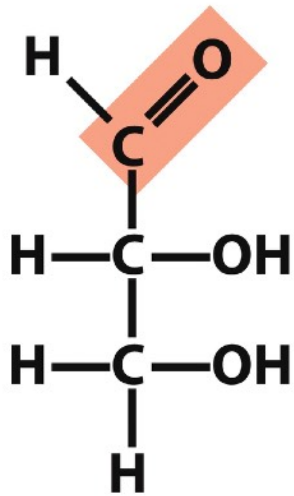
Monosaccharide

- Freely soluble in water (H-bonds).
  - Glucose solubility: 91 g in 100 mL water.
  - Sucrose solubility: 200 g in 100 mL water.
- Unbranched carbon chain.
  - Carbon atoms linked by single bonds.
  - One C double-bonded to O (carbonyl group).
  - Each of the other C atoms has a hydroxyl group (-OH).

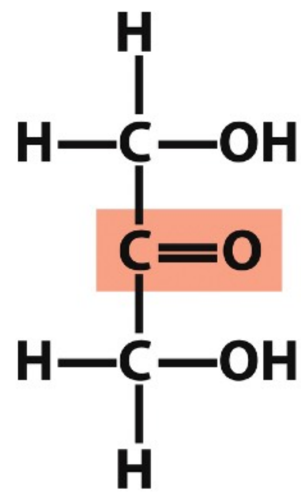


Aldoses and Ketoses

- An aldose contains an aldehyde functionality
  - **Carbonyl group** at the end of carbon chain.
- A ketose contains a ketone functionality
  - **Carbonyl group** at any other position.

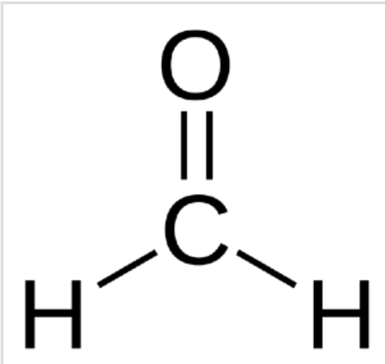


Glyceraldehyde,

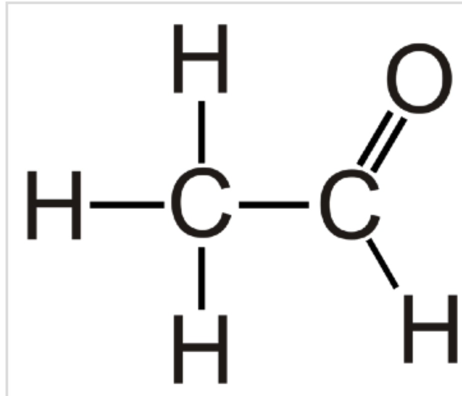


Dihydroxyacetone,

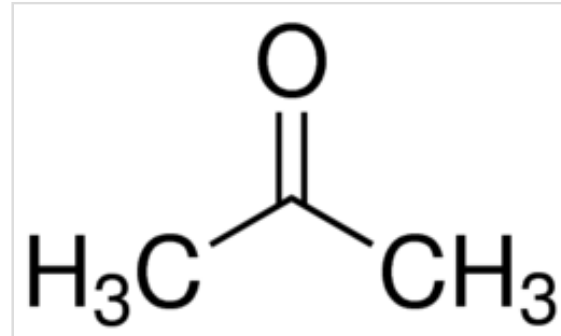
Aldehyde, Ketone and Glycerol



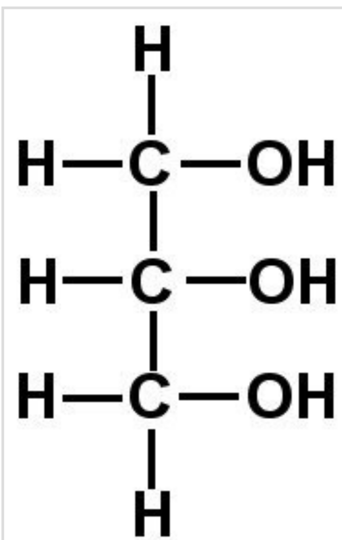
formaldehyde



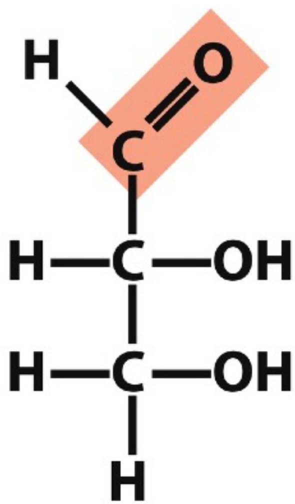
acetaldehyde



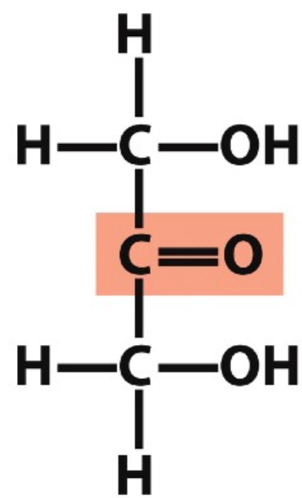
acetone



glycerol

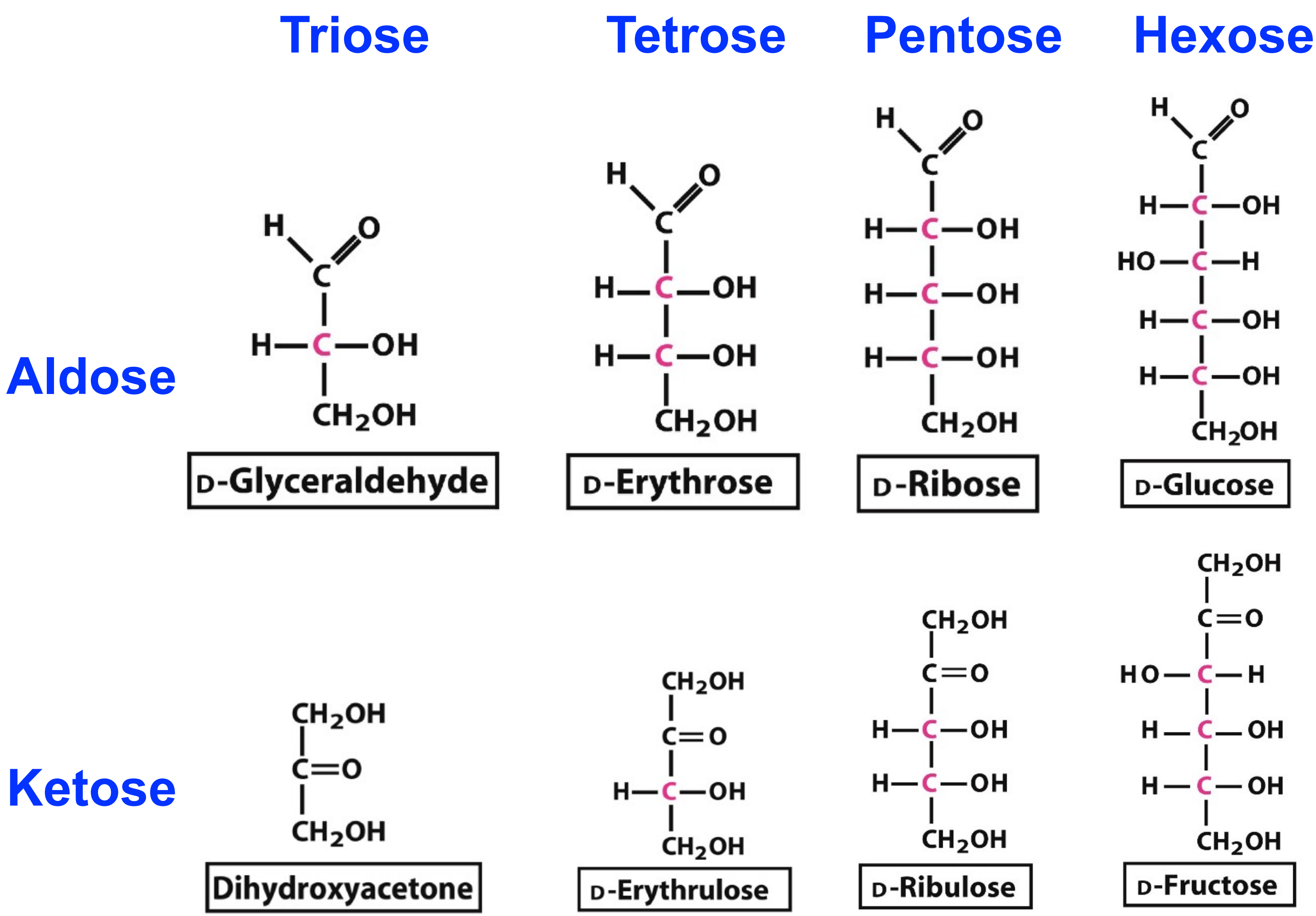


Glyceraldehyde,



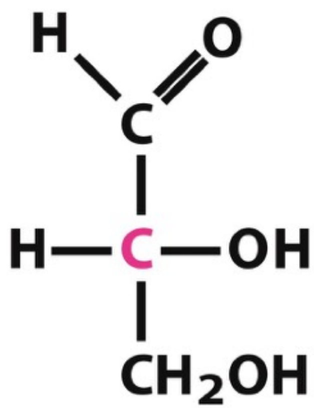
Dihydroxyacetone,

Three-Carbon Sugars and More

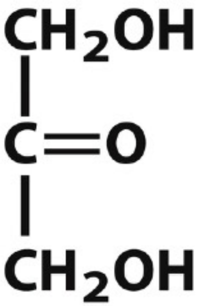


Monosaccharides Have Chiral Centers

- All monosaccharides except dihydroxyacetone have one or more chiral (asymmetric) carbon atoms.
- The simplest aldotriose, glyceraldehyde, contains one chiral center.
  - Glyceraldehyde has two isomers called enantiomers.
  - Enantiomers are mirror images of each other.

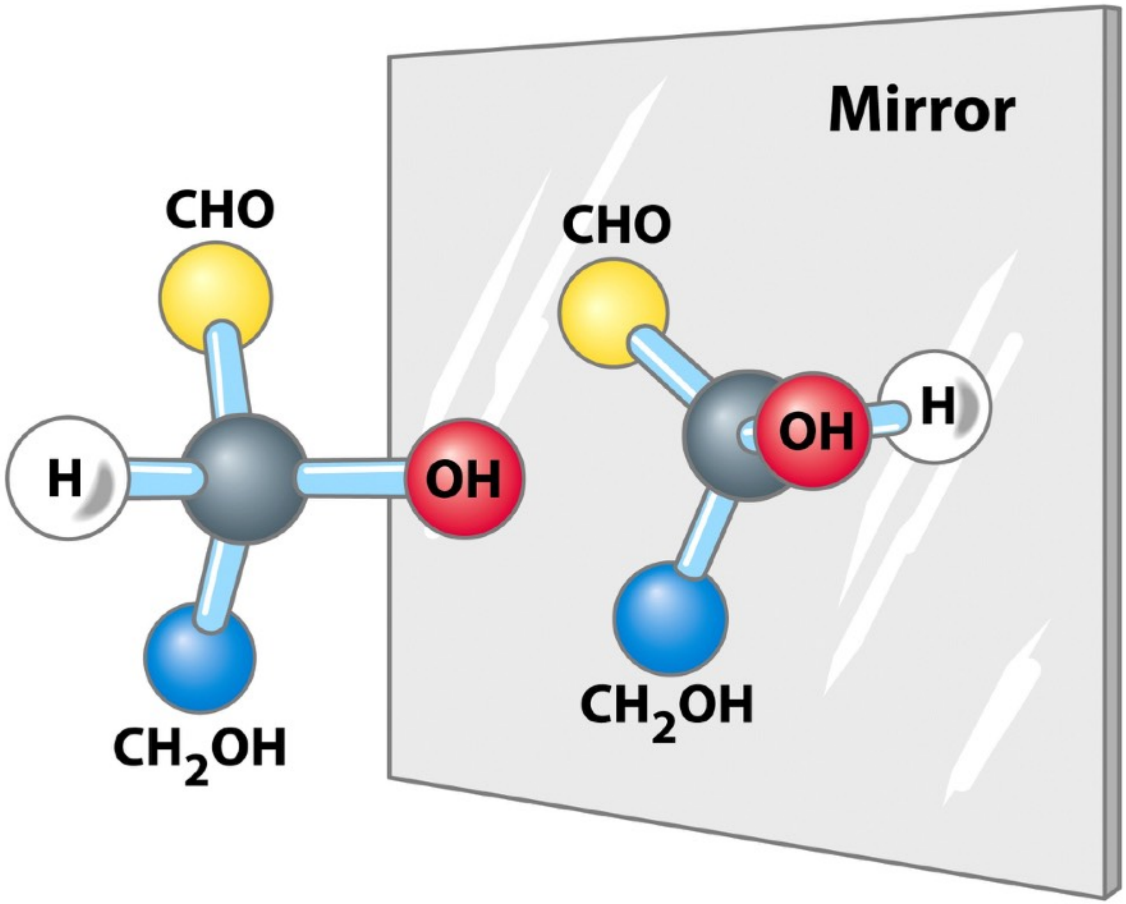


D-Glyceraldehyde



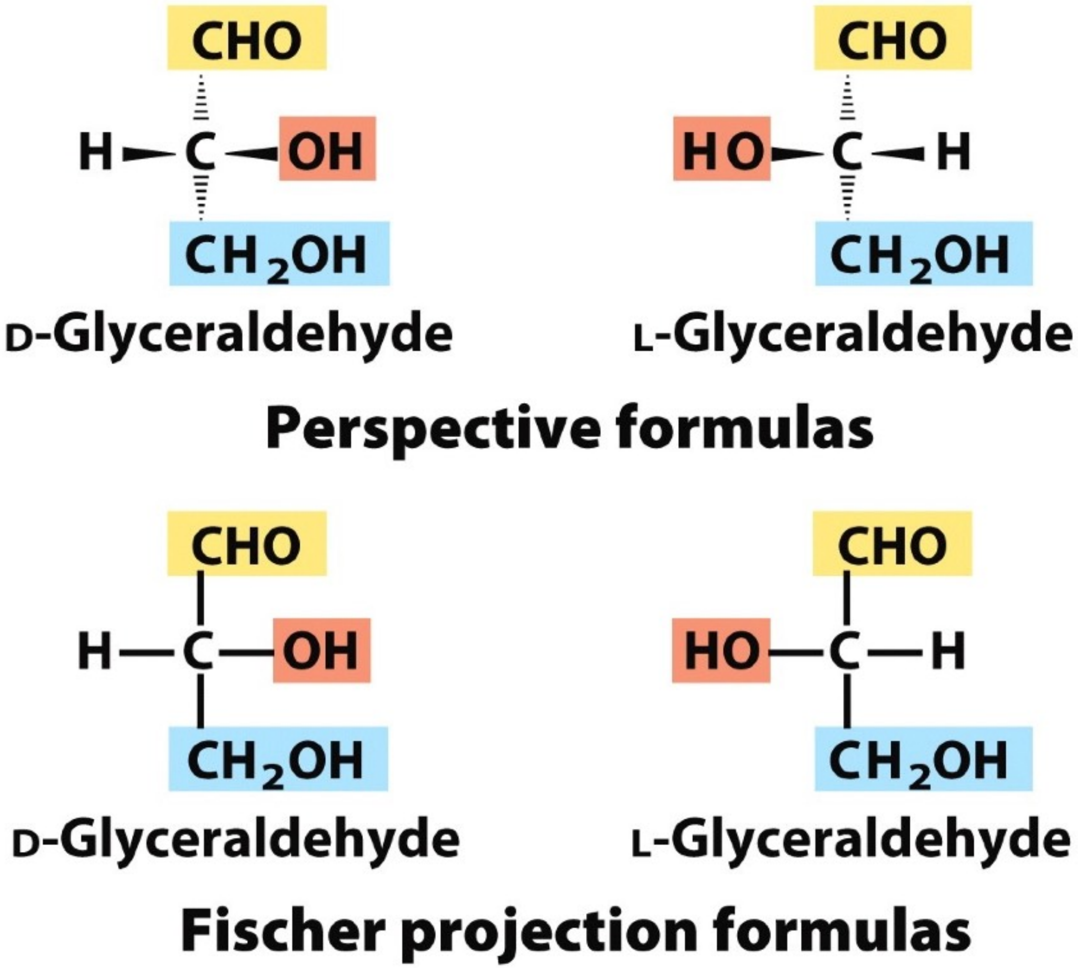
Dihydroxyacetone

Ways to Represent Two Enantiomers 1



Ball-and-stick models

Ways to Represent Two Enantiomers 2

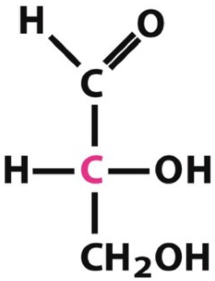


- Chiral compounds can be drawn using perspective formulas.
- However, chiral carbohydrates are usually represented by Fischer projections.
- Horizontal bonds are pointing toward you; vertical bonds are projecting away from you.

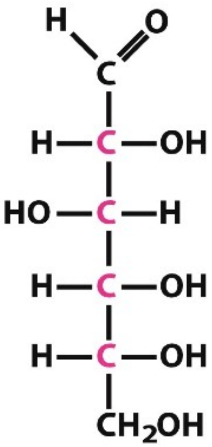
Number of Stereoisomers

In general, a molecule with *n* chiral centers can have 2^n different stereoisomers.

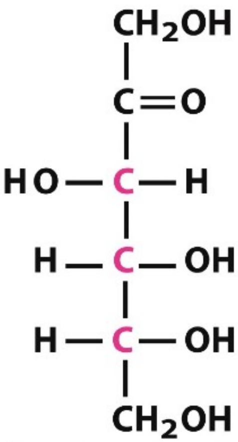
- Glyceraldehyde has **1 chiral center**, and therefore 2 stereoisomers (D-glyceraldehyde and L-glyceraldehyde).
- Aldohexose has **4 chiral centers**, and therefore 16 stereoisomers.
- Ketohexose has **3 chiral centers**, and therefore 8 stereoisomers.



D-Glyceraldehyde



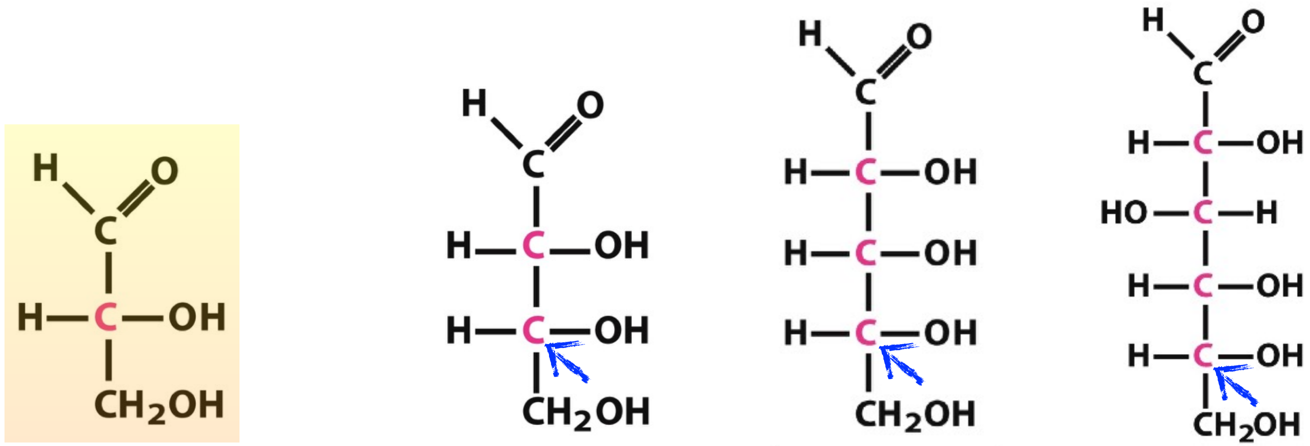
D-Glucose



D-Fructose

D-Stereoisomer or L-Stereoisomer?

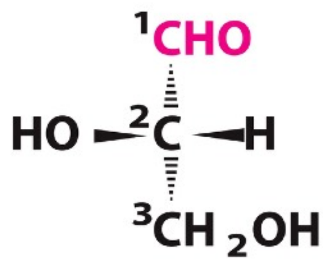
- Reference carbon
  - Chiral center most distant from carbonyl carbon.
- Reference molecule
  - D-isomers have the same configuration at the reference carbon as **D-glyceraldehyde** (-OH group on the right).
- Most hexoses in living organisms are **D stereoisomers**.



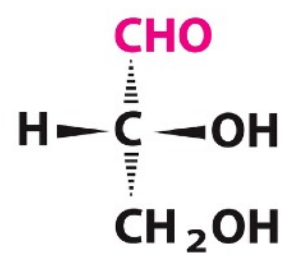
D-Glyceraldehyde D-Erythrose D-Ribose D-Glucose

All Amino Acids Are Chiral Except Gly

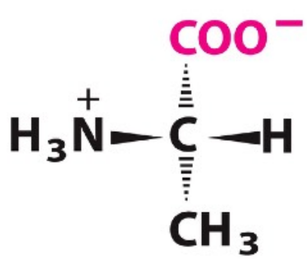
- DL system.
  - Compare with glyceraldehyde.
  - Absolute configuration only.
  - Not optical properties.
  - Only L isomers found in proteins
- RS system.



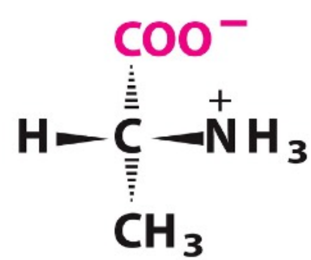
L-Glyceraldehyde



D-Glyceraldehyde



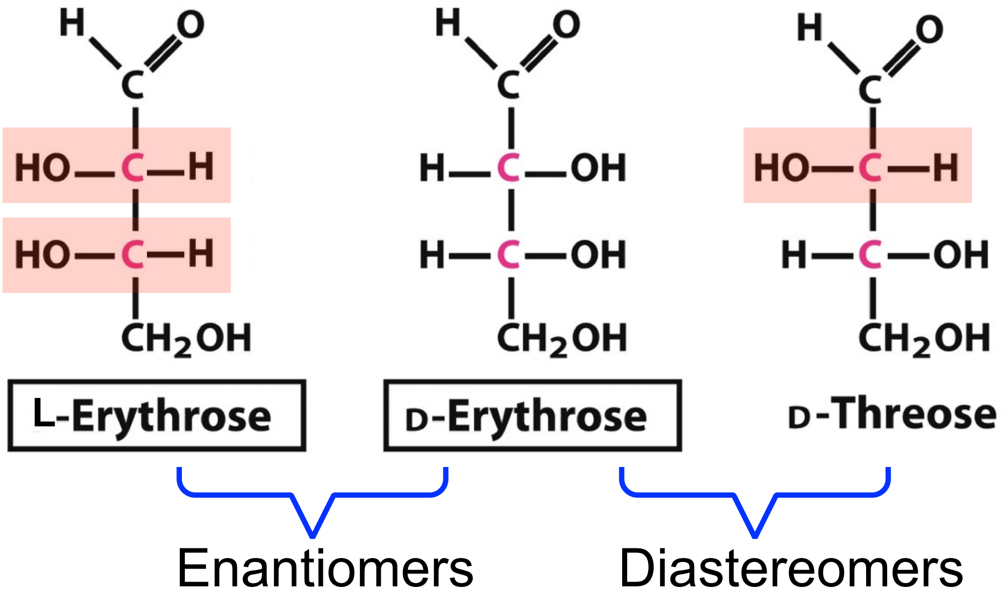
L-Alanine



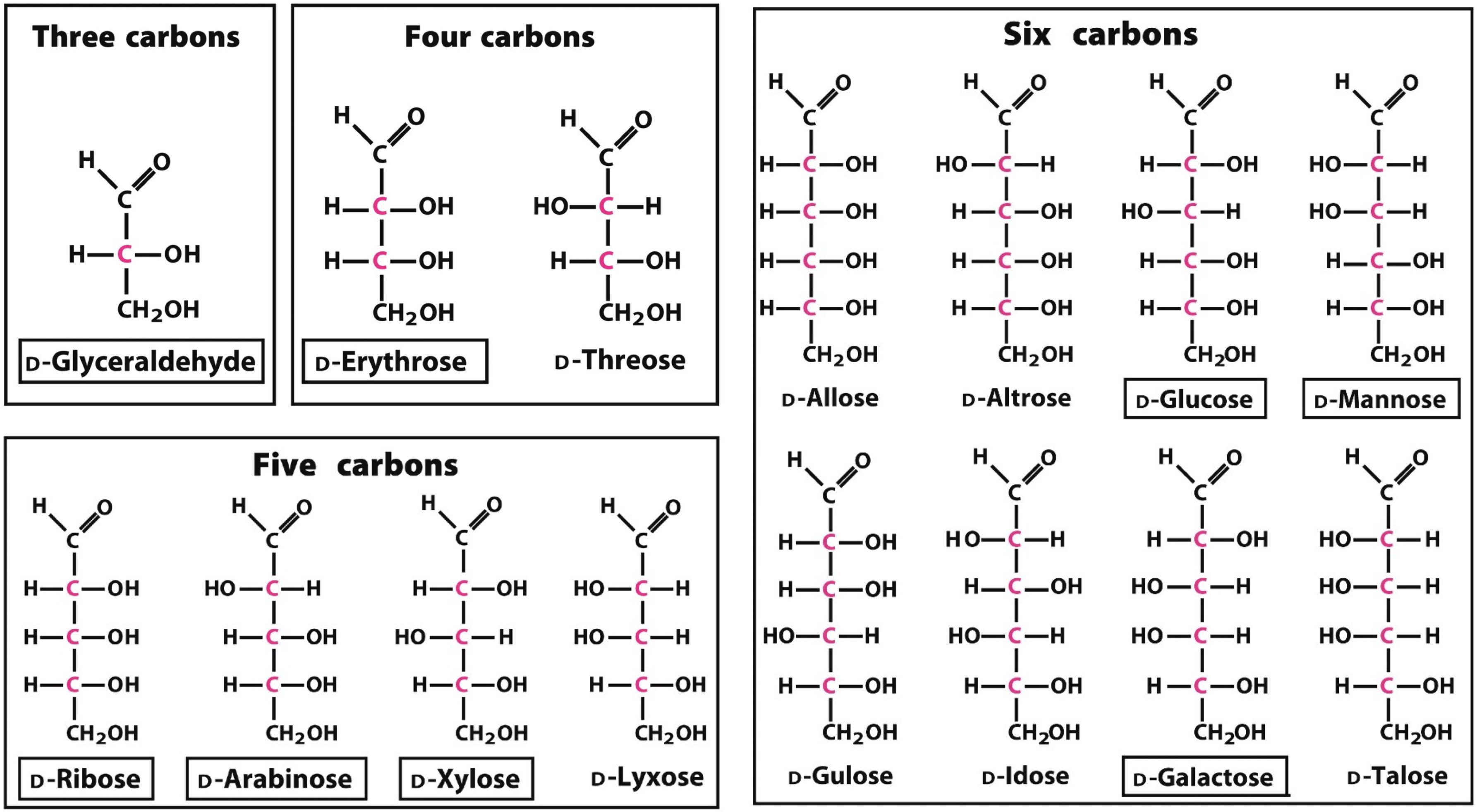
D-Alanine

Enantiomer and Diastereomer

- Enantiomers: stereoisomers that are mirror images.
- Diastereomers: stereoisomers that are NOT mirror images.
- Enantiomers have similar physical properties.
- Diastereomers have different physical properties.
  - L- and D-erythrose have the same water solubility.
  - Water solubilities of erythrose and threose are different.

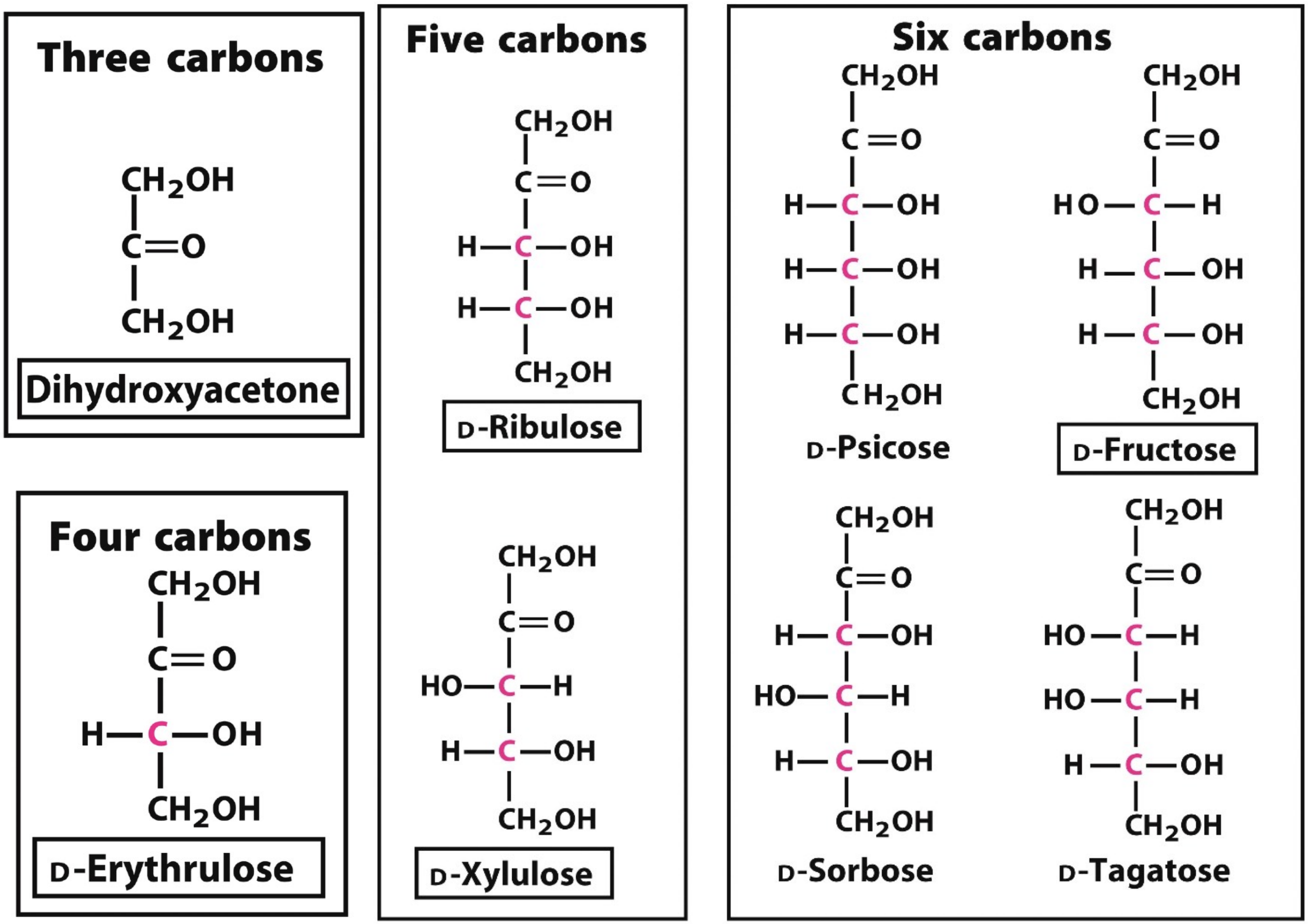


Aldoses



boxed: common in nature.

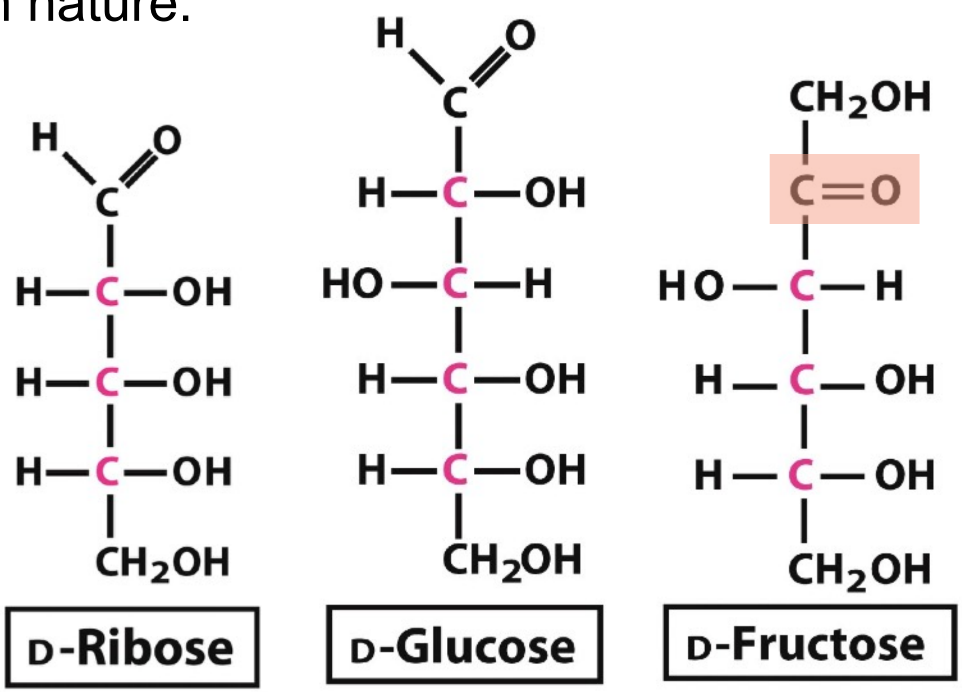
Ketoses



Erythrose->Erythrulose. Ribose->Ribulose. Xylose->Xylulose.

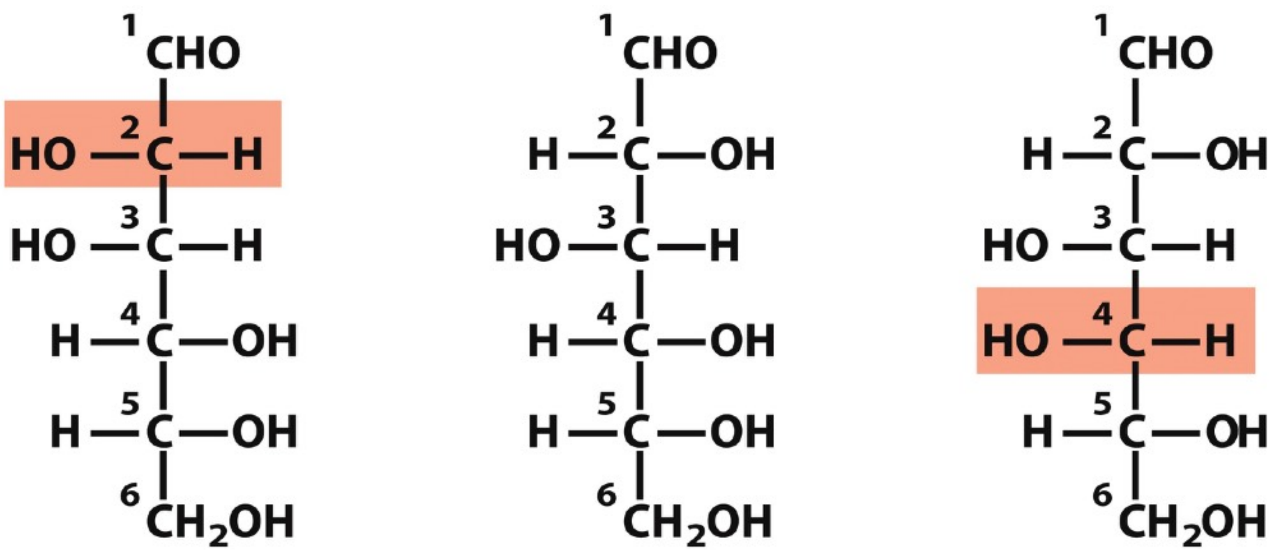
Structures to Know

- Ribose is the standard **five-carbon** sugar (pentose).
  - Component of nucleic acid.
- Glucose is the standard **six-carbon** sugar (hexose).
  - Most common aldohexose in nature.
- Fructose is the **ketose form** of glucose.
  - Most common ketohexose in nature.



Epimer

- Epimers are two sugars that differ **only in configuration around one carbon atom**.
- Configurations at all the other chiral centers are identical.

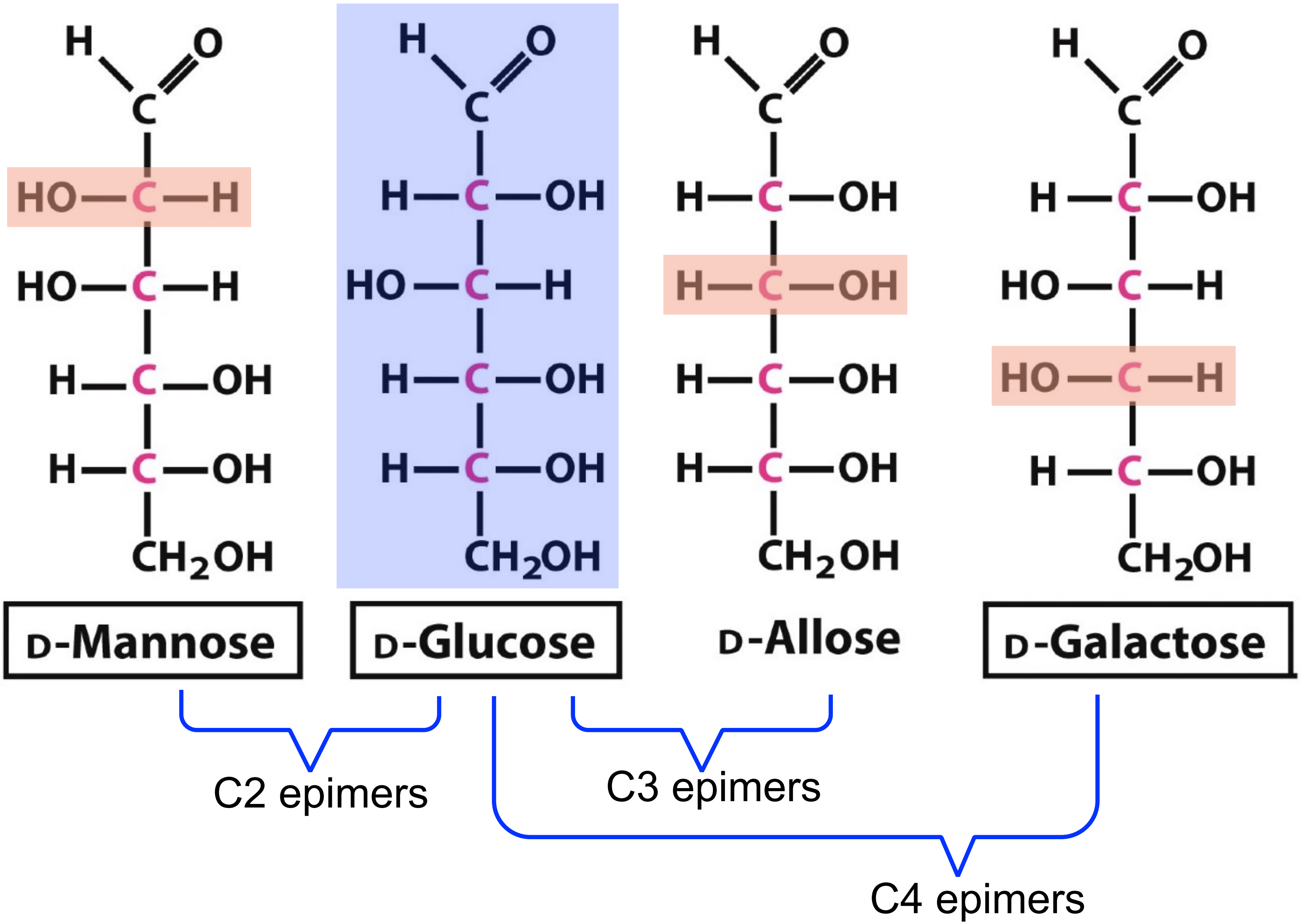


D-Mannose (epimer at C-2)

D-Glucose

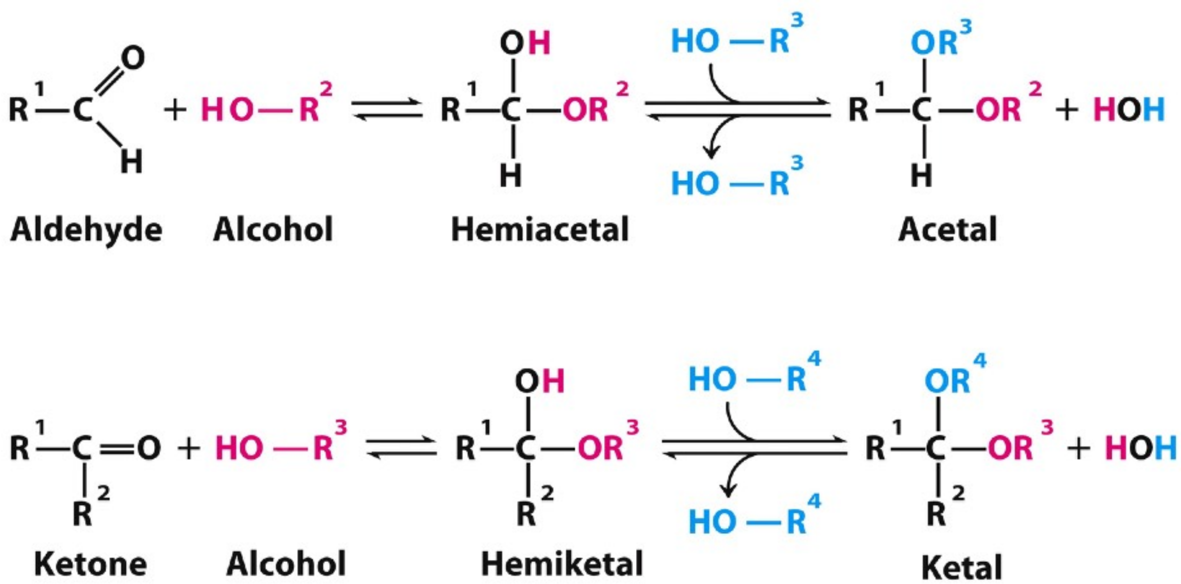
D-Galactose (epimer at C-4)

Epimers of D-glucose



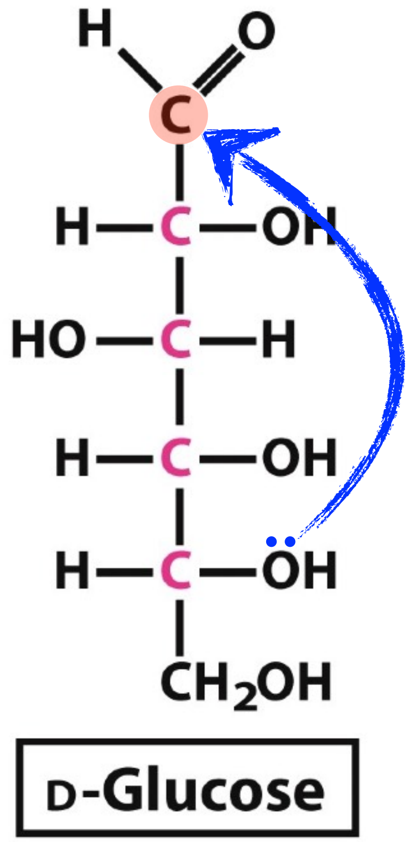
Hemiacetals and Hemiketals

- Aldehyde and ketone carbons are electrophilic. Alcohol oxygen atom is nucleophilic.
- When aldehydes are attacked by alcohols, **hemiacetals** form ("hemi-" means "half").
  - Further attack by alcohols produces acetals.
- When ketones are attacked by alcohols, **hemiketals** form.
  - Further attack by alcohols produces ketals.



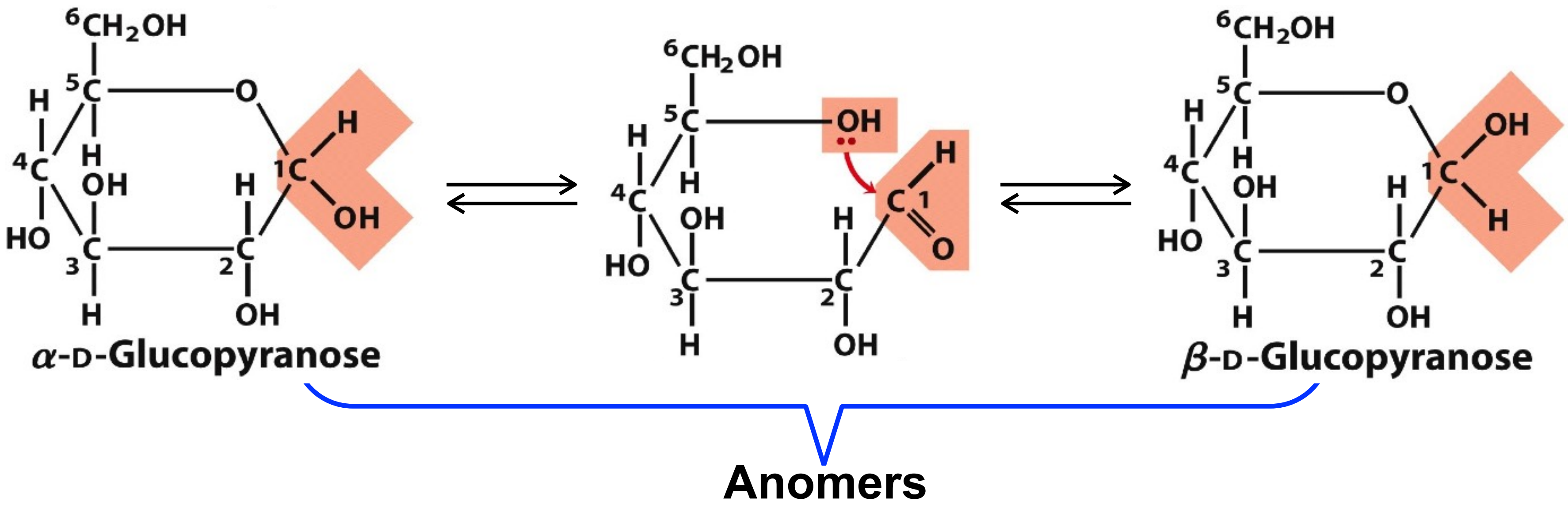
Cyclization of Monosaccharides

- Monosaccharides are polyhydroxy aldehydes or ketones.
  - Have hydroxyl oxygen atoms as nucleophiles.
  - Have carbonyl carbon atoms as electrophiles.
- Pentoses and hexoses readily undergo **intramolecular cyclization**.
- The former carbonyl carbon becomes a new chiral center, called the <u>anomeric carbon</u> (carbon #1 in glucose).



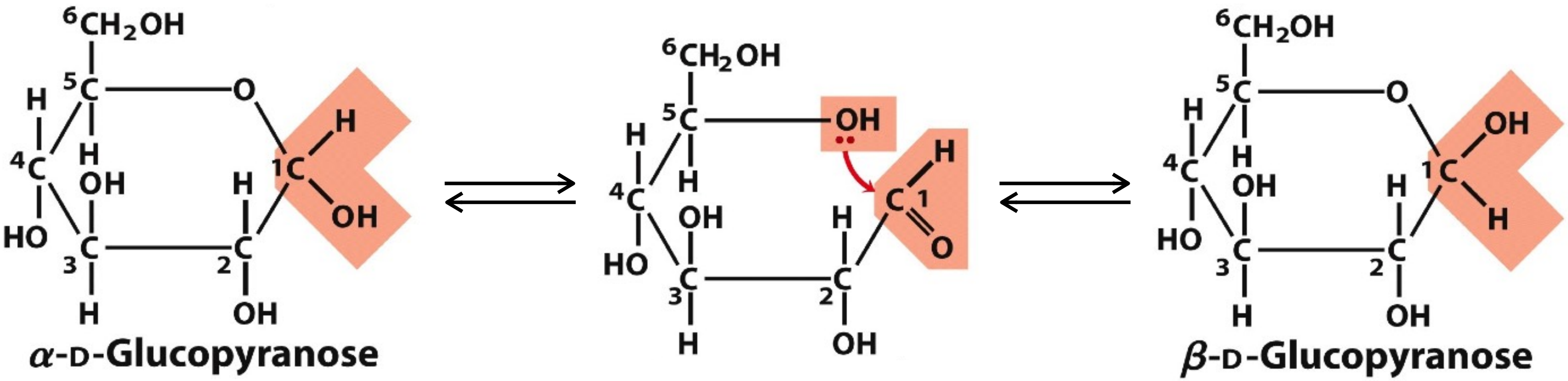
Cyclization of Monosaccharides

- The former carbonyl oxygen becomes a **hydroxyl group**; the position of this group determines if the anomer is α or β.
- If the hydroxyl group is on the opposite side (trans) of the ring as the CH_2OH moiety, the configuration is α.
- If the hydroxyl group is on the same side (cis) of the ring as the CH_2OH moiety, the configuration is β.



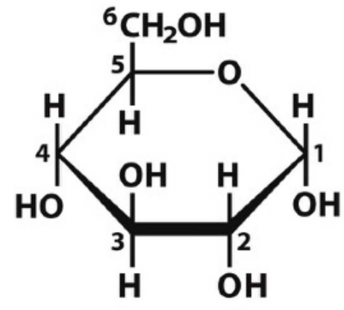
Mutarotation

- The α and β anomers of D-glucose interconvert in aqueous solution by a process called **mutarotation**.
  - One ring form opens briefly into linear form.
  - Linear form closes to produce the other ring form.
- At equilibrium.
  - 1/3 α-D-glucose.
  - 2/3 β-D-glucose.
  - Very small amounts of linear form and five-membered ring (glucofuranose) form.

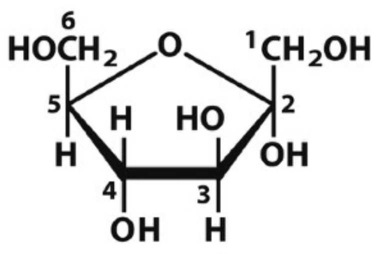


Pyranose and Furanose

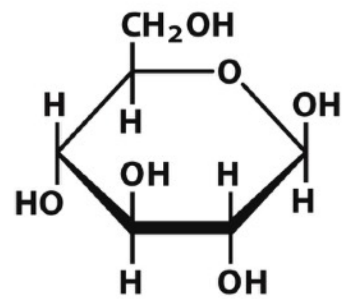
- Pyranose
  - Six-membered
  - Contains oxygen
  - Sugar ring
- Furanose
  - Five-membered
  - Contains oxygen
  - Sugar ring



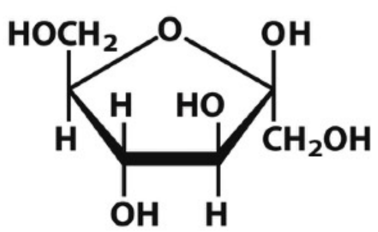
α-D-Glucopyranose



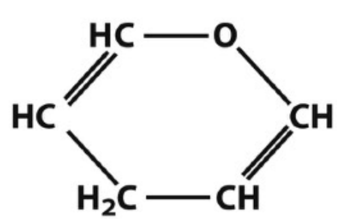
α-D-Fructofuranose



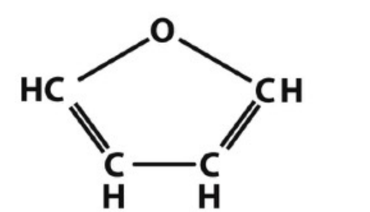
β-D-Glucopyranose



β-D-Fructofuranose

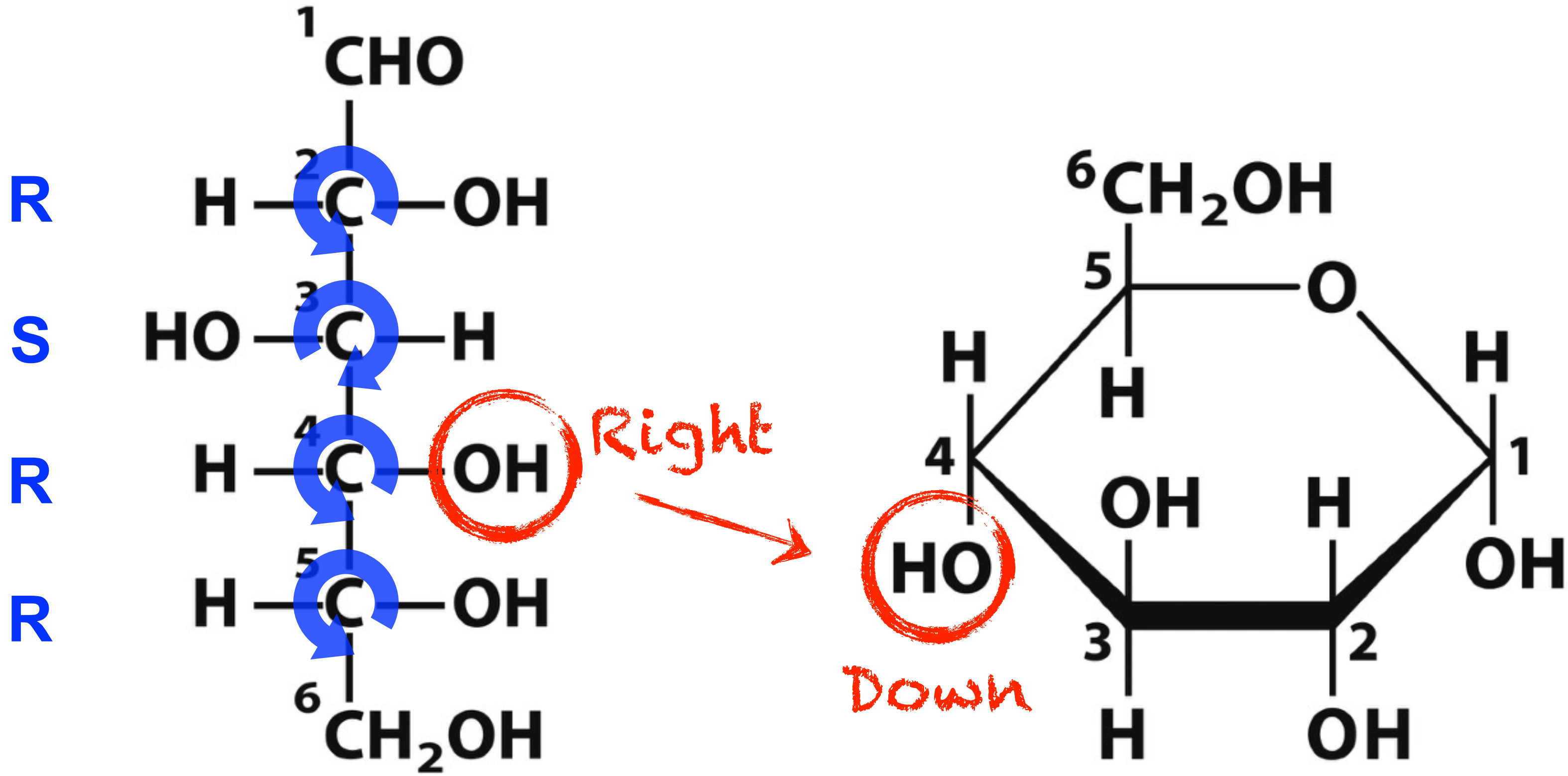


Pyran



Furan

Fischer Projection vs. Haworth Perspective



D-Glucose
Fischer projection

α-D-Glucopyranose
Haworth perspective

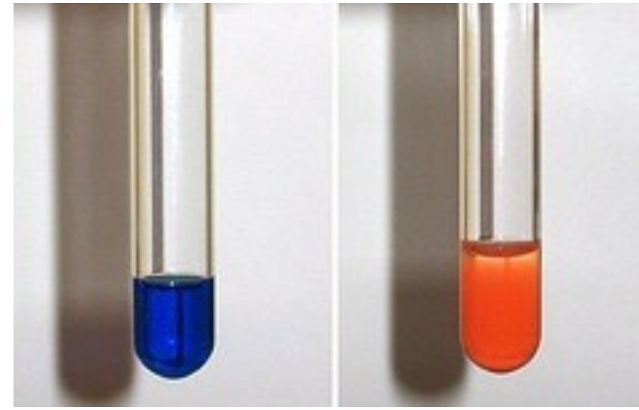
Linear structure

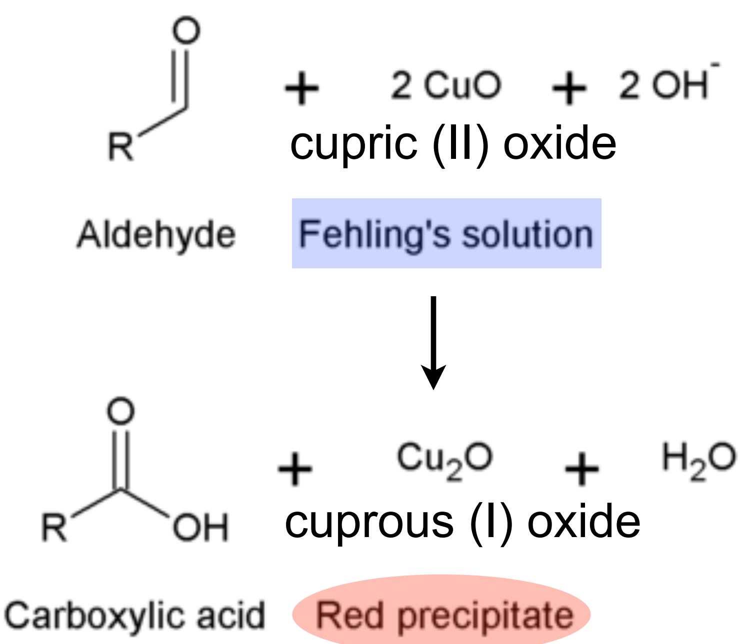
Cyclic structure

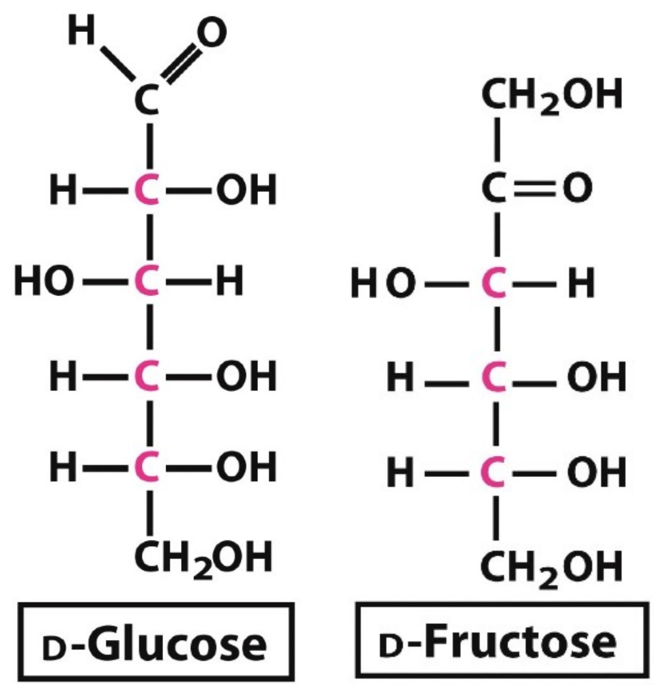
Systematic IUPAC name (2*R*,3*S*,4*R*,5*R*)-2,3,4,5,6-Pentahydroxyhexanal

Reducing Sugars

- **Monosaccharides are reducing sugars.**
  - All aldoses, such as glucose.
  - All alpha-hydroxyl ketoses, such as fructose.
  - Positive in Fehling's reaction.

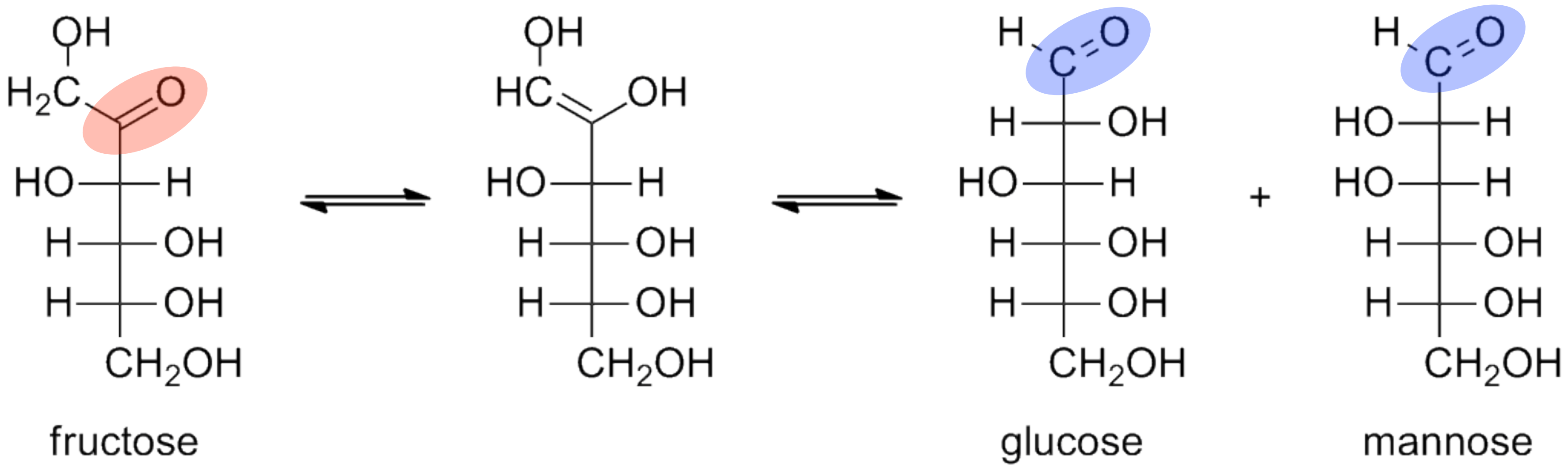




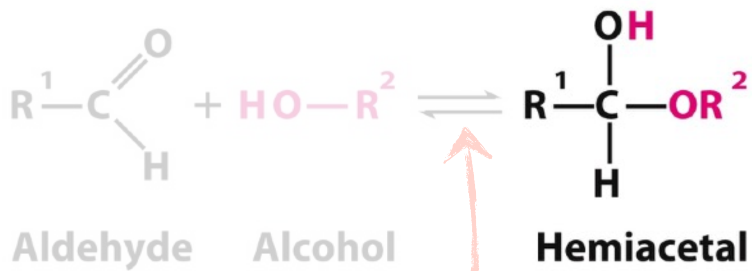


Why is Fructose a Reducing Sugar?

- Fructose, a ketose, is readily isomerized to a mixture of aldoses (glucose and mannose) under basic conditions.



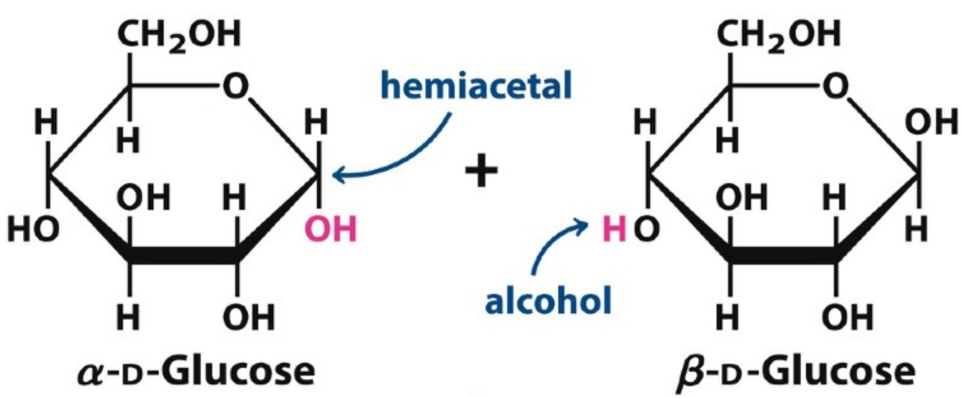
Disaccharides



Monosaccharide Cyclization

Two sugar molecules can be joined.

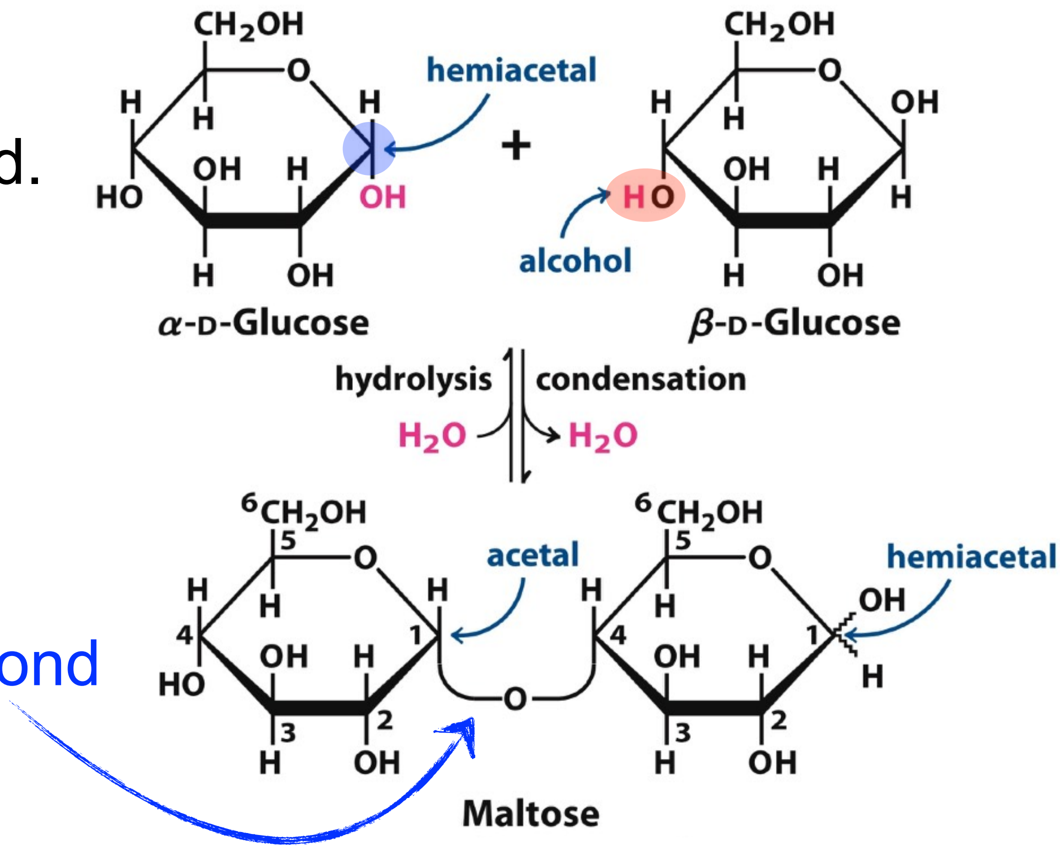
- One sugar acts as a hemiacetal.
- The other sugar acts as an alcohol.



Disaccharides Contain a Glycosidic Bond

- Two sugar molecules can be joined via a glycosidic bond between an anomeric carbon and a hydroxyl group.
- One molecule of water is eliminated.
- Hemiacetal is converted to acetal.

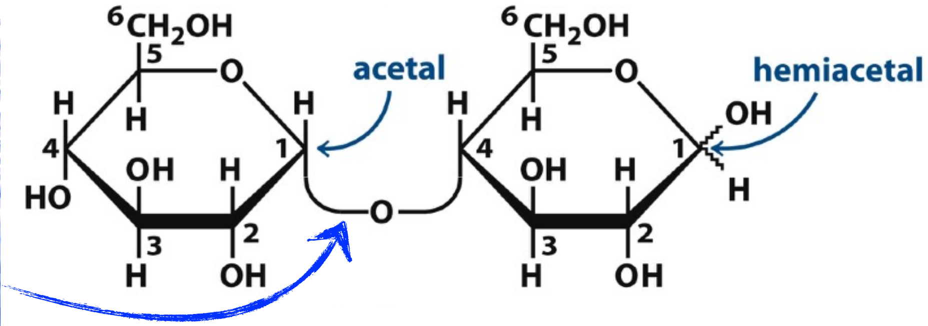
glycosidic bond

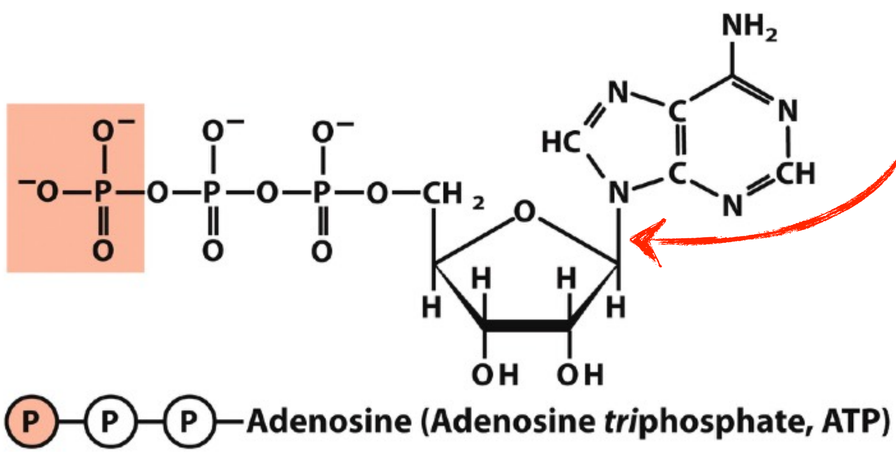


Glycosidic Bond

***O*-glycosidic bond**

anomeric carbon connected to an oxygen atom.

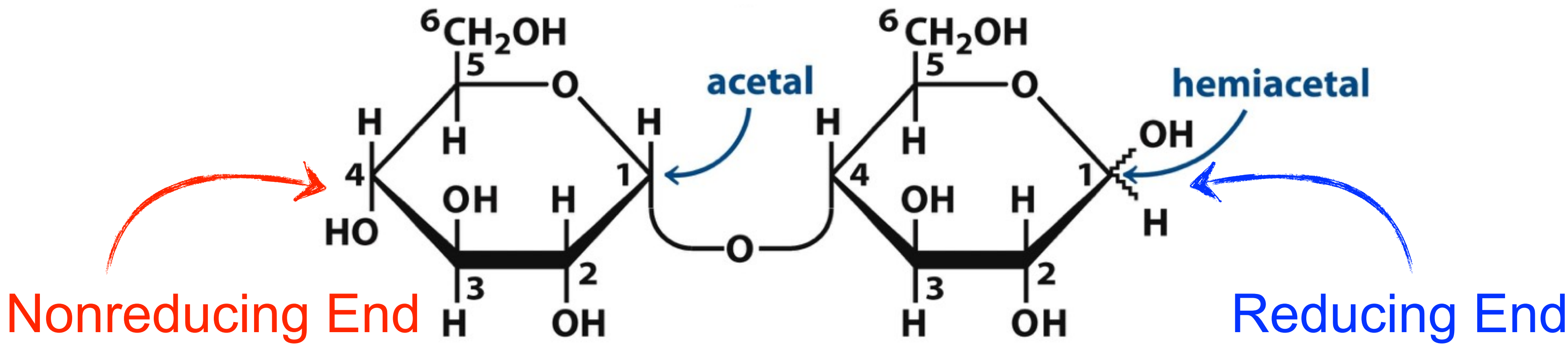




***N*-glycosidic bond**

anomeric carbon connected to a nitrogen atom.

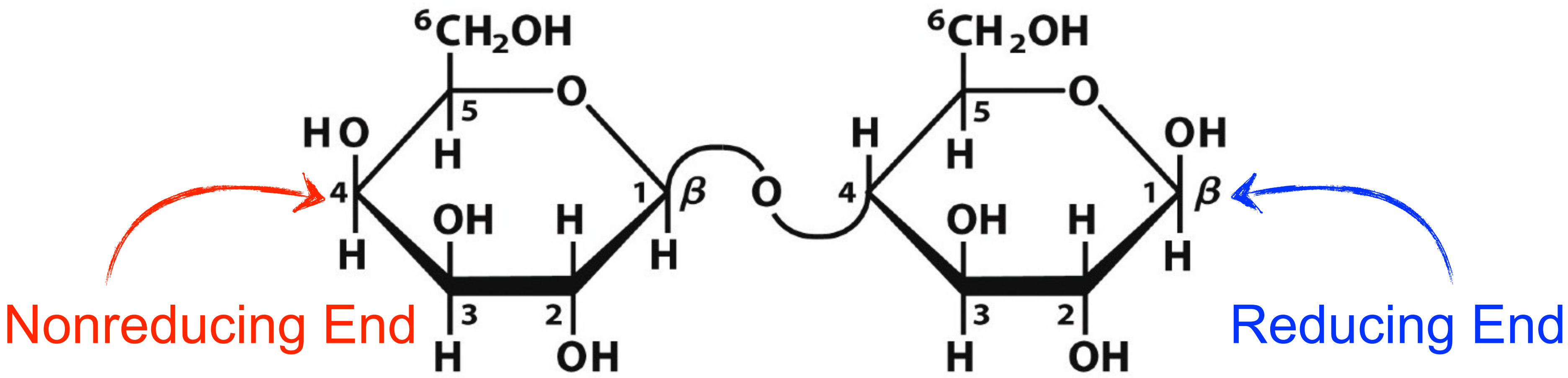
Maltose is a Reducing Disaccharide



- First monomer (glucose) is nonreducing.
    - Anomeric carbon involved in the glycosidic linkage (acetal)
    - Cannot convert between linear and cyclic form.
- Second monomer (glucose) is reducing.
    - Anomeric carbon NOT involved in the glycosidic linkage (hemiacetal)
    - **Can still convert between linear and cyclic form.**
    - Wavy lines indicate structure may be α or β (can be interconverted).

Lactose is a Reducing Disaccharide

- Lactose occurs naturally in milk (gives sweetness).
- Lactose is made of two monosaccharides.
  - Galactose and glucose.
- Lactose is a reducing disaccharide.
  - Anomeric carbon in galactose involved in glycosidic bond.
  - Anomeric carbon in glucose is available for oxidation.

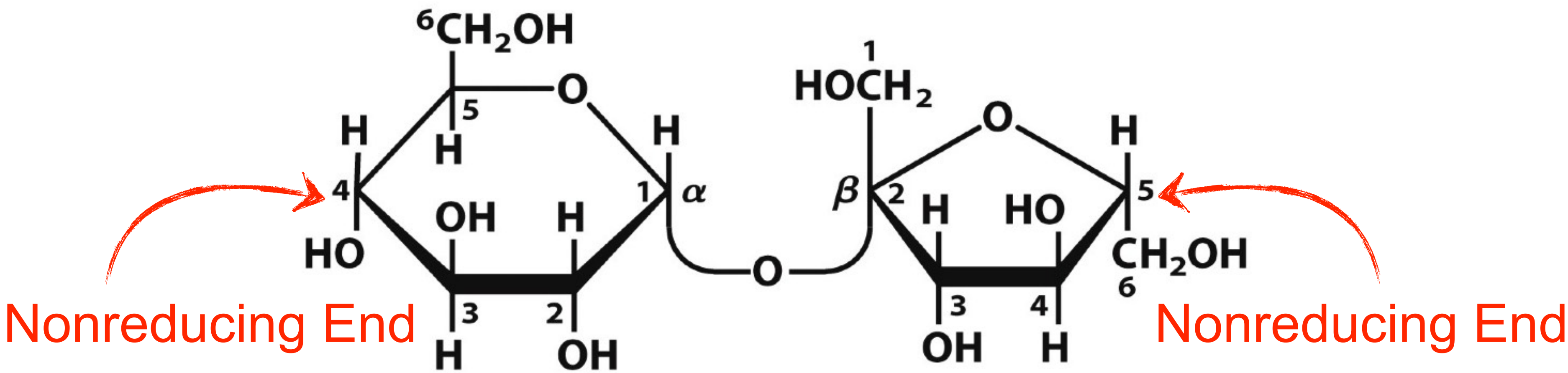


Lactose (β form)

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

Sucrose is a Nonreducing Disaccharide

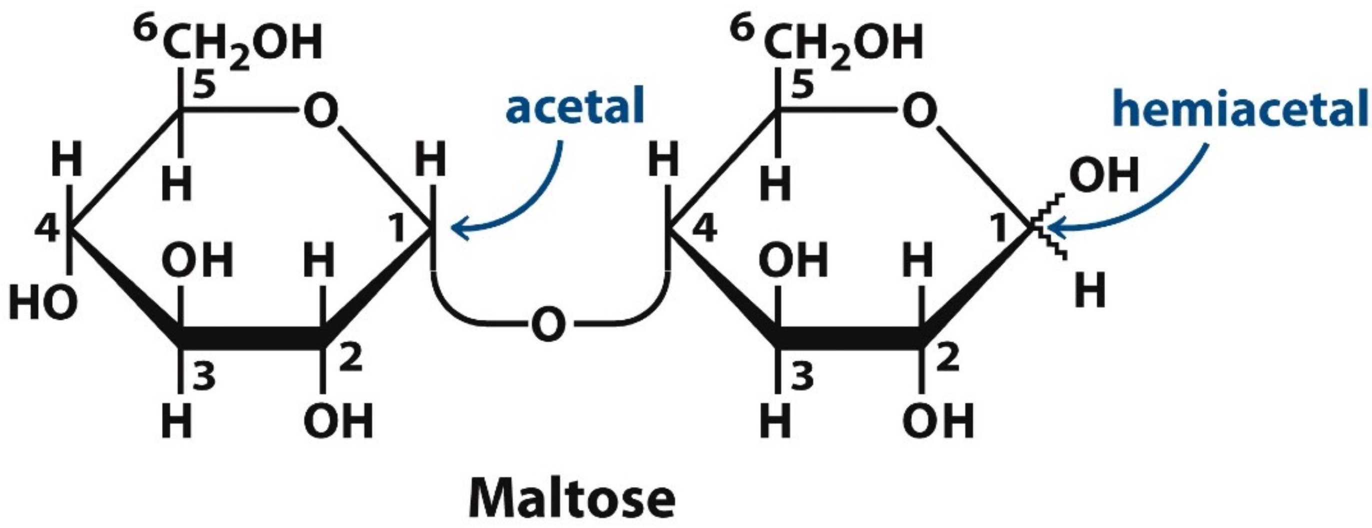
- Sucrose is produced by plants but not by animals.
- Sucrose is made of two monosaccharides.
  - Glucose and fructose.
- Sucrose is a nonreducing disaccharide.
  - Anomeric carbon (C #1) in glucose involved in glycosidic bond.
  - Anomeric carbon (C #2) in fructose involved in glycosidic bond.



Sucrose

β-D-fructofuranosyl α-D-glucopyranoside

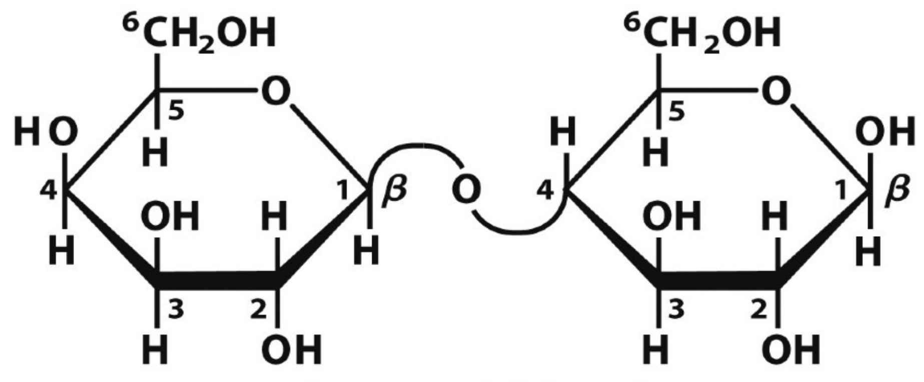
Disaccharide Nomenclature 1



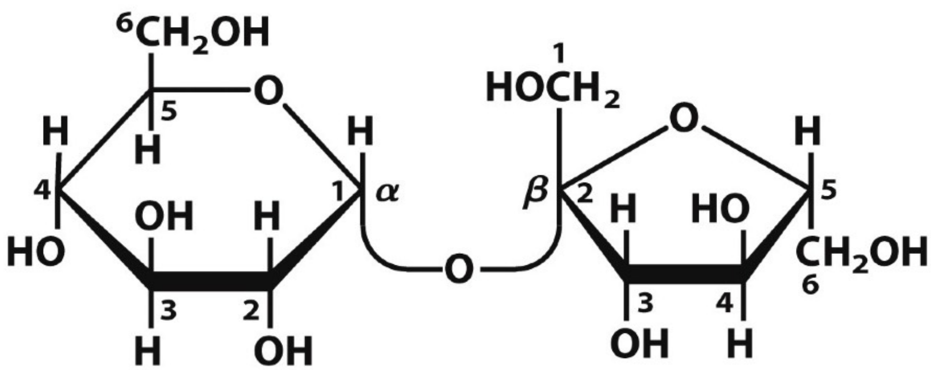
α-D-glucopyranosyl-(1→4)-D-glucopyranose

1. Name of 1st monosaccharide. Name of 2nd monosaccharide. —> Glc Glc
2. Electrophile -> nucleophile. —> Glc->Glc
3. Carbons involved in glycosidic bond. —> Glc(1->4)Glc
4. Configuration of anomeric carbon. —> Glc(α1->4)Glc

Disaccharide Nomenclature 2



1. Gla Glc
2. Gal->Glc
3. Gal(1->4)Glc
4. Gal(β1->4)Glc



1. Glc Fru
2. Glc<->Fru
3. Glc(1<->2)Fru
4. Glc(α1<->2β)Fru

Summary 7.1 Mono- and Disaccharides

- Sugars (saccharides) contain one aldehyde or ketone group and two or more hydroxyl groups.
- Monosaccharides generally contain several chiral centers, and exist in different stereochemical forms.
    - Fischer projection. Perspective formula.
    - Enantiomer. Diastereomer. Epimer.
    - Monosaccharide cyclization. Hemiacetal. Hemiketal.
    - Haworth perspective. Anomer. Anomeric carbon. Mutarotation.
    - Reducing sugar.
- Disaccharide. Acetal. Glycoside. Glycosidic bond. Nonreducing sugar. Nomenclature.

Week 7 Carbohydrates and Glycobiology

7.1 Monosaccharides and Disaccharides

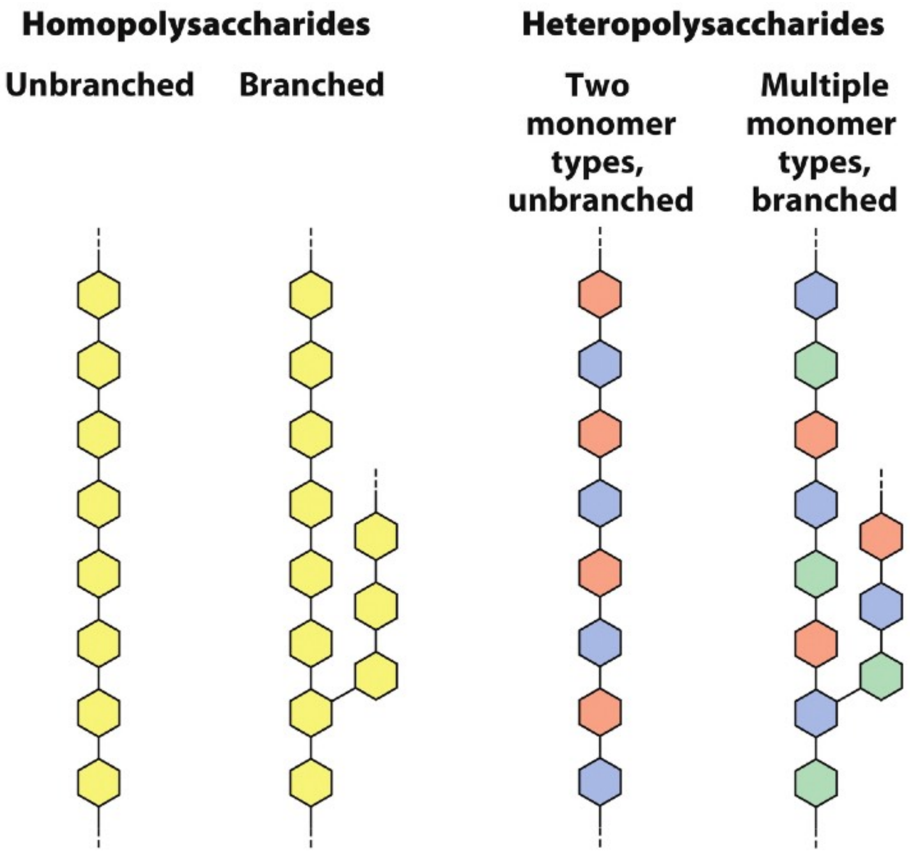
7.2 Polysaccharides

7.3 Glycoconjugates

7.4 Carbohydrates as Informational Molecules

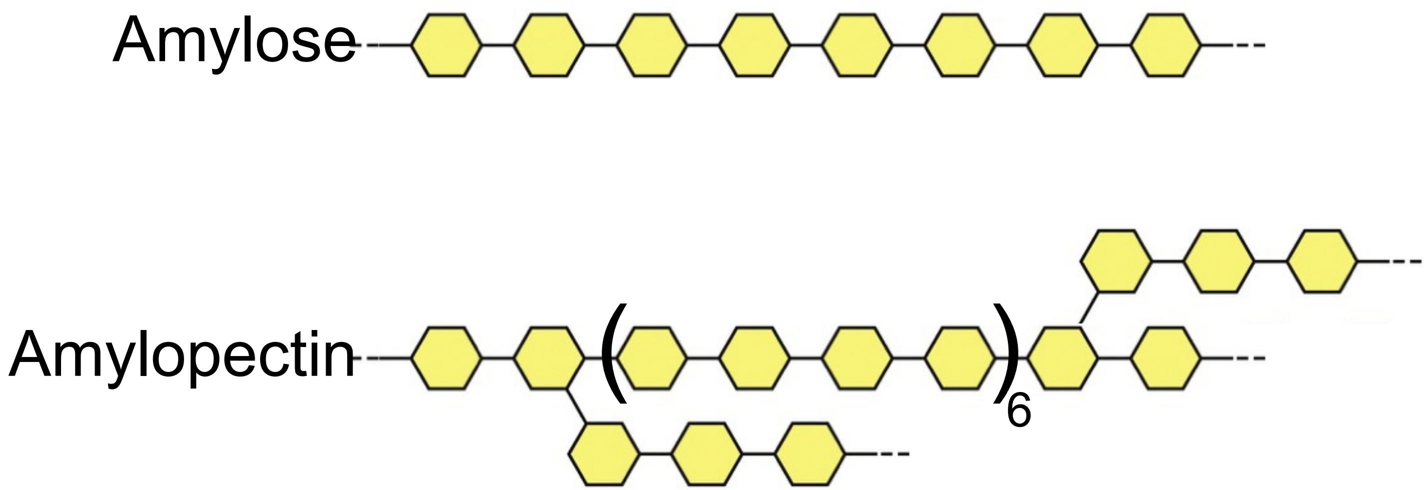
Polysaccharides

- Polysaccharides, also called glycans, are polymers of monosaccharides
- Homopolysaccharides
  - Single monomer
  - Linear or branched
- Heteropolysaccharides
  - Two or more monomers
  - Linear or branched

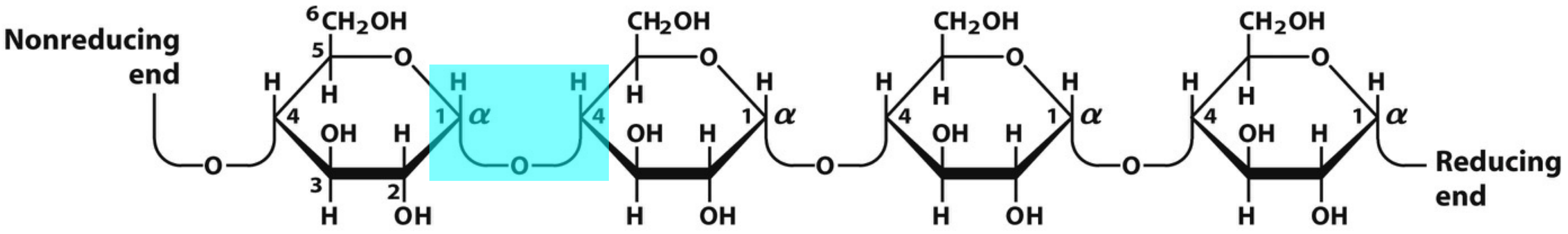


Starch is Homopolysaccharide

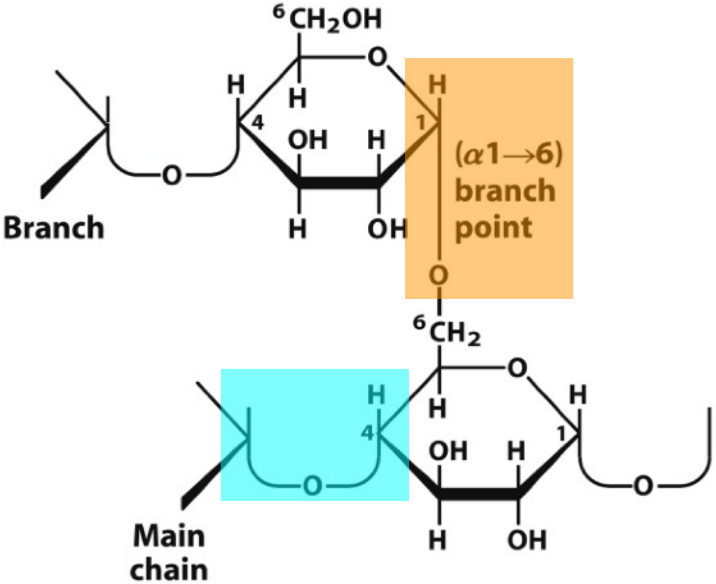
- Main **storage** polysaccharide in plants
- A mixture of two homopolysaccharides of **α-D-glucose**
  - Amylose is an **unbranched** linear polymer
  - Amylopectin is **branched**, and the branch points occur every 24 - 30 residues



Starch Contains Two Types of Linkages



Amylose

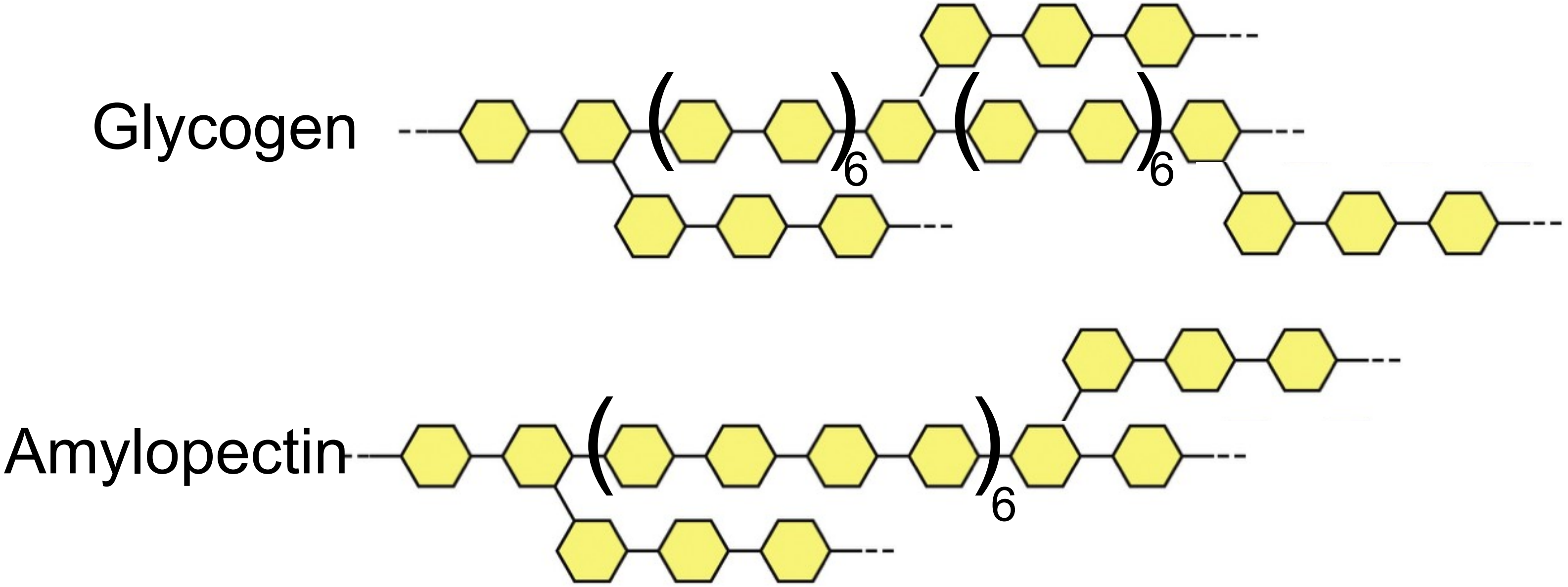


Amylopectin

- In amylose, glucose residues are connected by **(α1->4)** linkages
- In amylopectin, main chain has **(α1->4)** linkages and branch points have **(α1->6)** linkages

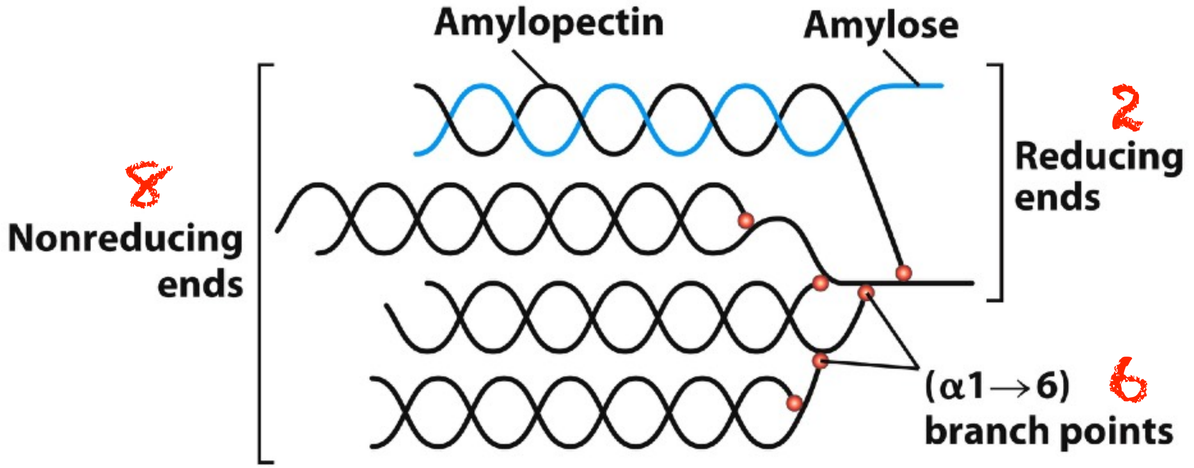
Glycogen is Homopolysaccharide

- Main **storage** polysaccharide in animals.
- Glycogen is similar to amylopectin.
  - Polymer of **α-D-glucose** monomers.
  - (α1->4)-linked main chain and (α1->6)-linked branches.
- More extensively branched than amylopectin.
  - Branch points every 8 - 12 residues.



Nonreducing Ends in Starch and Glycogen

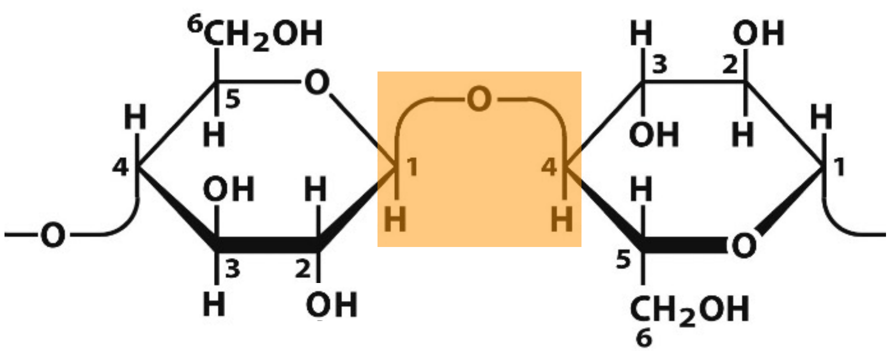
- One amylose molecule has one reducing end and one nonreducing end.
- One amylopectin or glycogen molecule with *n* branches has one reducing end and *n + 1* nonreducing ends.
- **Digestive enzymes act only at nonreducing ends, and can work simultaneously on many branches.**



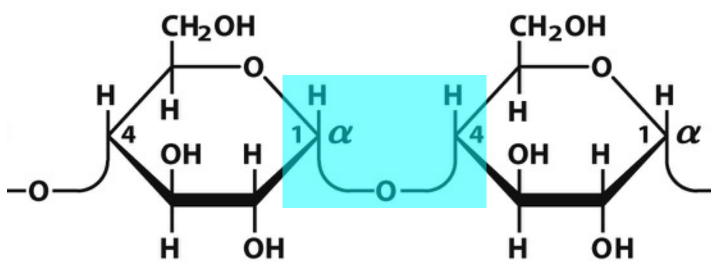
Reducing Ends + Branches = Nonreducing Ends

Cellulose is Homopolysaccharide

- Found in cell walls of plants.
  - Constitutes much of mass of wood.
  - Cotton is almost pure cellulose.
- Linear, unbranched homopolysaccharide of glucose (like amylose).
  - **(β1->4) linkage**
  - For comparison, **(α1->4) linkage** in amylose



Cellulose



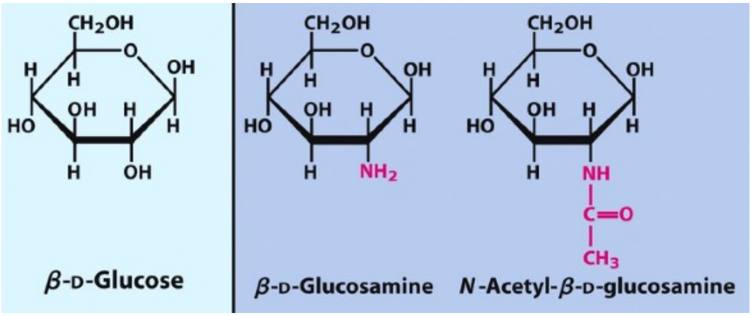
Amylose

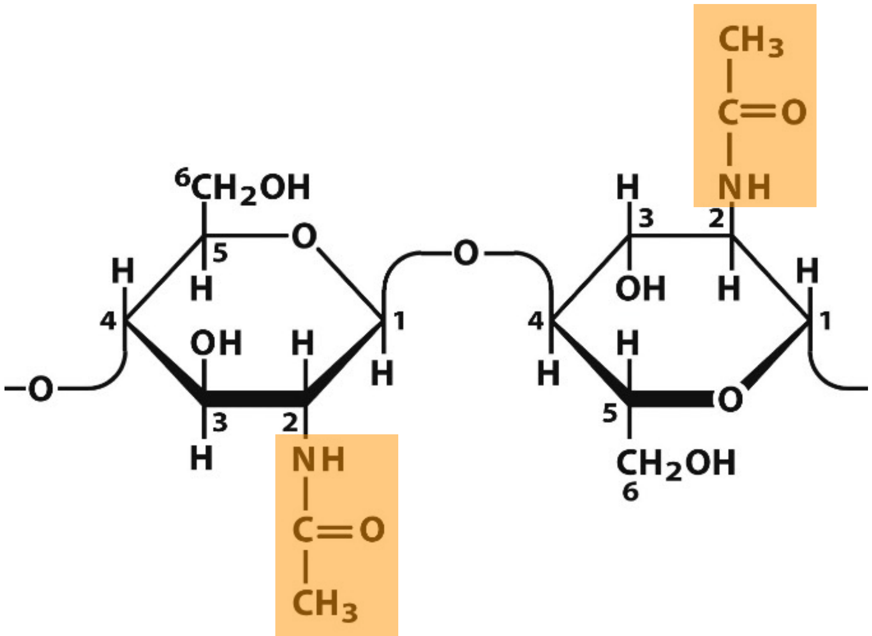
Cellulose Metabolism

- Most animals do NOT have enzymes that break (β1->4) glycosidic bonds, and so cannot digest cellulose.
  - Have enzymes that break (α1->4) glycosidic bonds.
  - Can digest starch and glycogen.
- Fungi and bacteria have cellulase, and so they can digest wood.
- Ruminants (cattle, sheep, and goats) and termites live symbiotically with microorganisms that produces cellulase.
  - Ruminants can convert cellulose in grass to sugar in milk.
  - Termites can eat wood and so cause damage to buildings.

Chitin is Homopolysaccharide

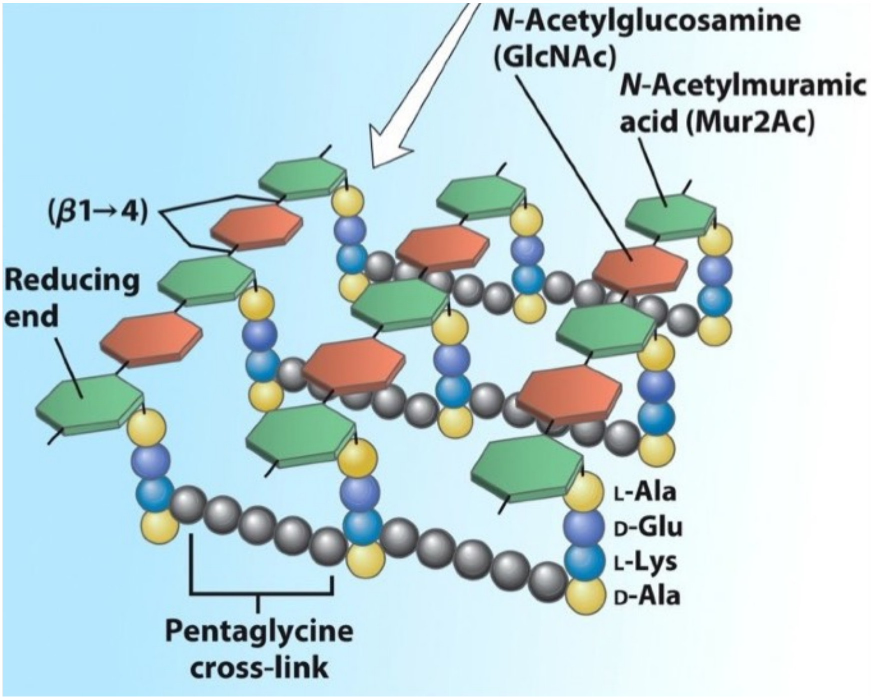
- Linear, unbranched homopolysaccharide.
  - (β1->4) linkage.
  - Composed of **N-acetylglucosamine** residues.
- Found in exoskeletons of insects, spiders, and crabs.
  - Cannot be digested by animals.

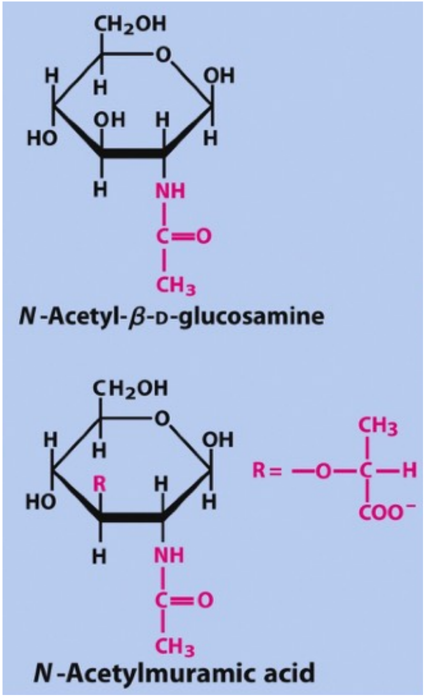




Heteropolysaccharide in Peptidoglycan

- Peptidoglycan contains linear, unbranched heteropolysaccharide.
  - (β1->4) linkage.
  - Alternating **N-acetylglucosamine** and **N-acetylmuramic acid** residues.
  - Cross-linked by short peptides.
- Found in bacterial cell wall.



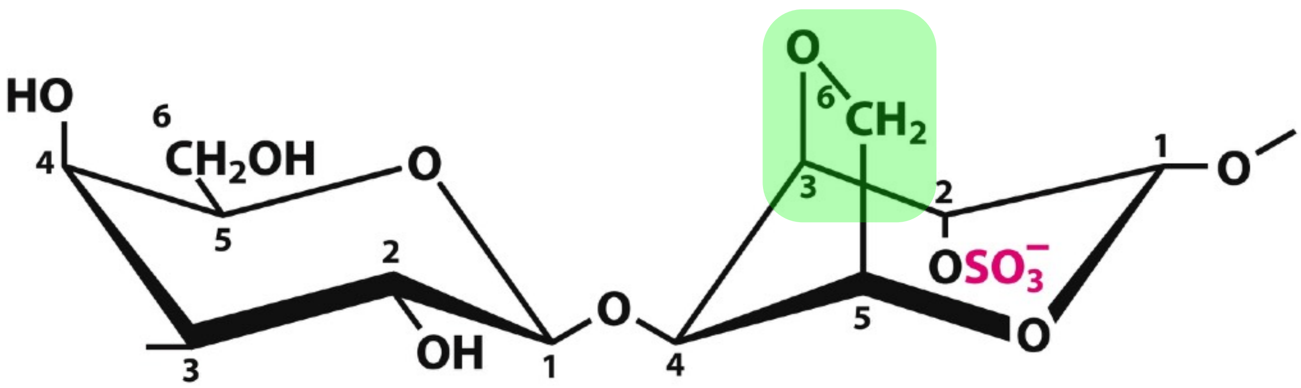


GlcNAc

Mur2Ac

Agarose is Heteropolysaccharide

- Linear, unbranched heteropolysaccharide.
  - (α1->3) linkage between disaccharide repeating units.
  - Repeating unit consists of **D-galactose** and **L-galactose derivative**.
  - **Ether bridge** and **sulfate ester**.
  - (β1->4) linkage between D-galactose and L-galactose derivative.
- Found in cell walls of red algae, including some seaweeds.



D-galactose **L-galactose derivative**

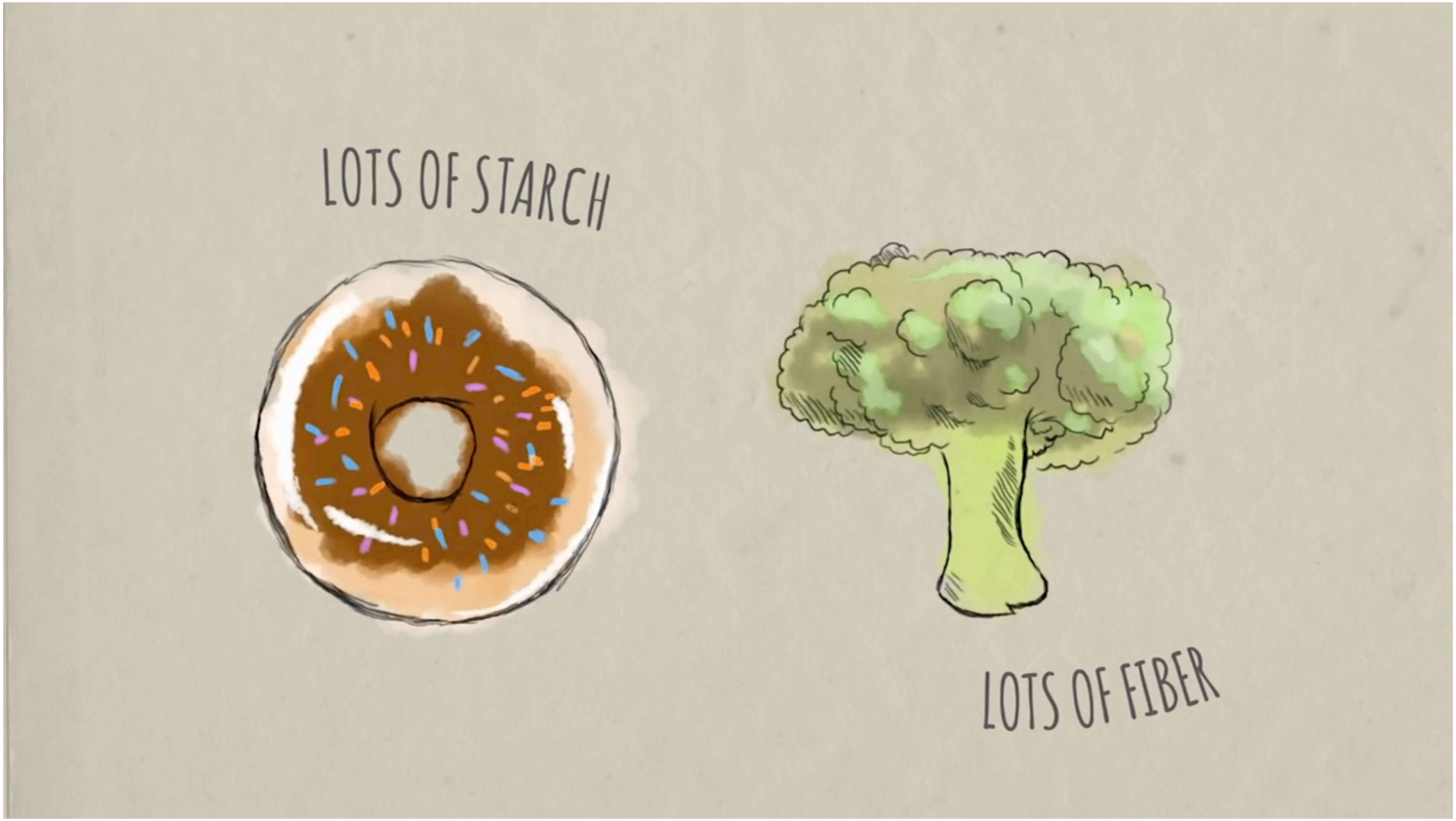
Summary of Some Polysaccharides

Polymer	Type*	Repeating unit†	Roles/significance
Starch			Energy storage: in plants
Amylose	Homo-	(α1→4)Glc, linear	
Amylopectin	Homo-	(α1→4)Glc, with (α1→6)Glc branches every 24–30 residues	
Glycogen	Homo-	(α1→4)Glc, with (α1→6)Glc branches every 8–12 residues	Energy storage: in bacteria and animal cells
Cellulose	Homo-	(β1→4)Glc	Structural: in plants, gives rigidity and strength to cell walls
Chitin	Homo-	(β1→4)GlcNAc	Structural: in insects, spiders, crustaceans, gives rigidity and strength to exoskeletons
Peptidoglycan	Hetero-; peptides attached	4)Mur2Ac(β1→4) GlcNAc(β1	Structural: in bacteria, gives rigidity and strength to cell envelope
Agarose	Hetero-	3)D-Gal(β1→4)3,6-anhydro-L-Gal(α1	Structural: in algae, cell wall material

Summary 7.2 Polysaccharides

- Polysaccharides serve as stored fuel (starch and glycogen) and as structural components of cell walls (cellulose, chitin, peptidoglycan, and agarose).
- Homopolysaccharides starch and glycogen consist of glucose with (α1->4) linkages. Homopolysaccharides cellulose and chitin are composed of glucose derivatives with (β1->4) linkages.
- Heteropolysaccharides peptidoglycan and agarose contain disaccharide repeating units: glucose derivatives and galactose derivatives.

How Carbohydrates Impact Health



Week 7 Carbohydrates and Glycobiology

7.1 Monosaccharides and Disaccharides

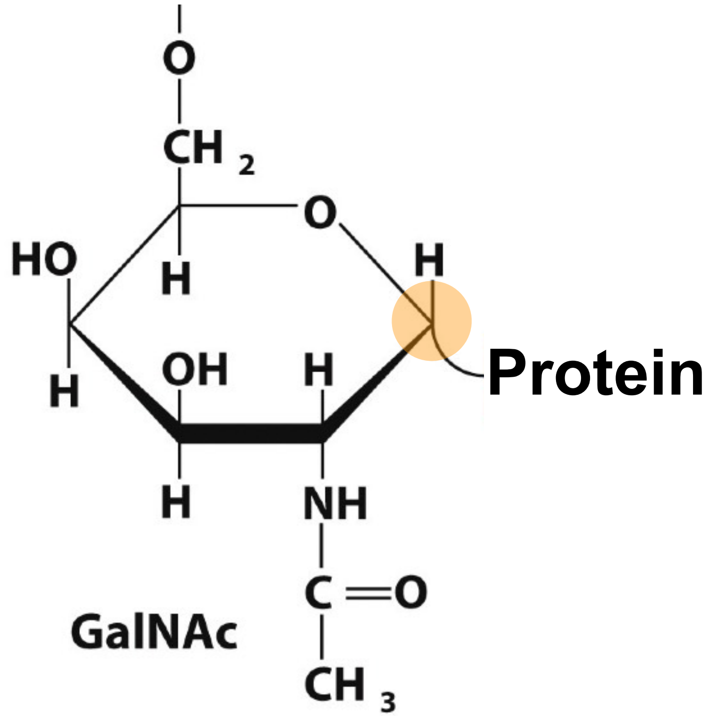
7.2 Polysaccharides

7.3 Glycoconjugates

7.4 Carbohydrates as Informational Molecules

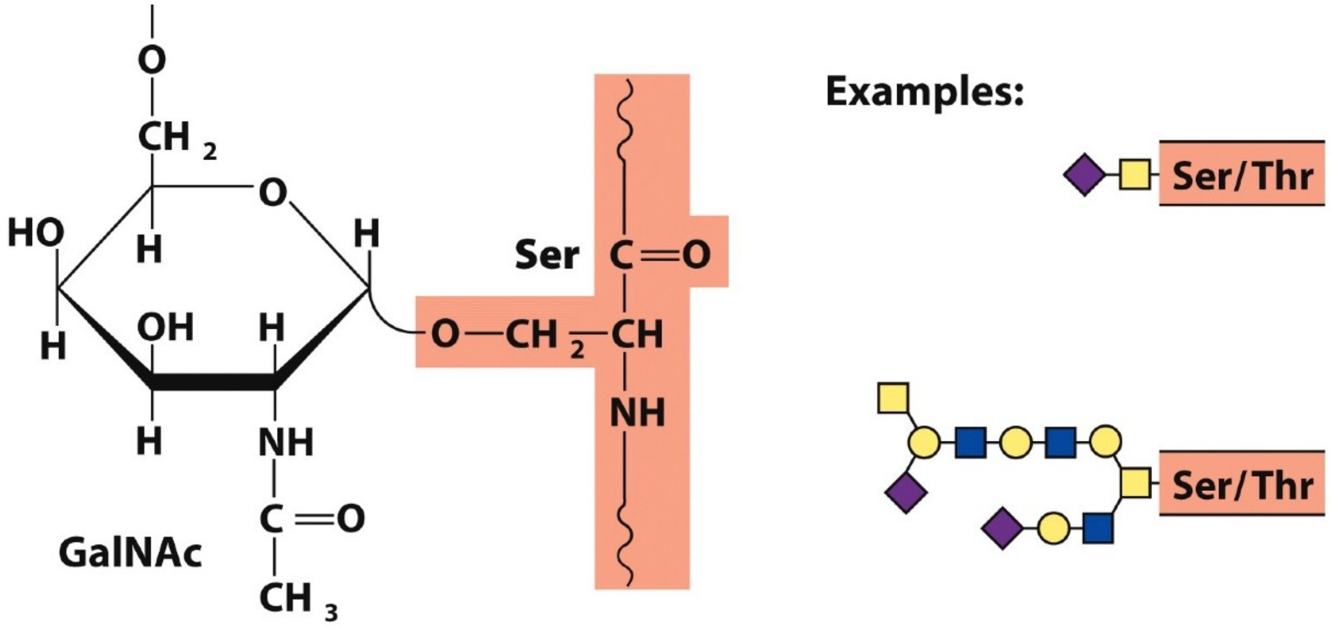
Glycoprotein

- A protein with small oligosaccharides attached
  - Carbohydrate attached via its **anomeric carbon**.
  - Glycosidic bond between carbohydrate and protein.
  - Glycosylation important in regulation of protein activity.



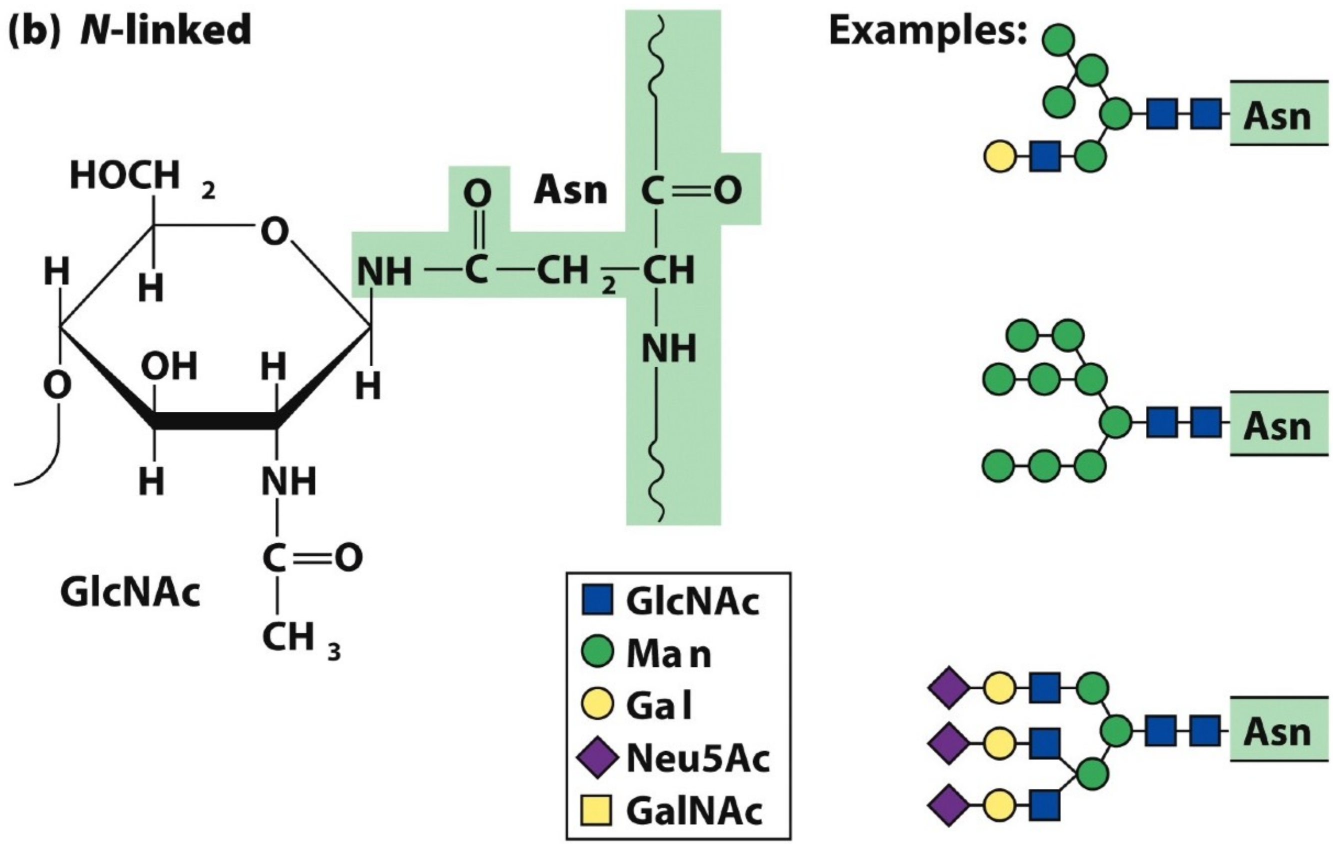
O-Glycosidic Bond

Hydroxyl oxygen (Ser/Thr) reacts with anomeric carbon.



N-Glycosidic Bond

Amide nitrogen (Asn) reacts with anomeric carbon.



Example of Glycoprotein: Mucin

- Heavily glycosylated protein.
  - Water-holding capacity.
- Present in most secretions such as saliva and snail slime.
- Give slipperiness.

Beauty Benefits of Snail Slime?

- Keep hydrated.
  - Snails do not like sunlight and appear in rainy days.
- Chemical barrier.
  - Hold water and maintain temperature.
- You never know what the snail has crawled over.
- Snail is the host of many parasites.

Week 7 Carbohydrates and Glycobiology

7.1 Monosaccharides and Disaccharides

7.2 Polysaccharides

7.3 Glycoconjugates

7.4 Carbohydrates as Informational Molecules

Informational Molecule

- A 100-residue polysaccharide vs. a 100-residue polypeptide.
- The number of structurally different polysaccharides is far greater than the number of different polypeptides.
  - All peptides are linear and there is only one way to connect two residues.
  - Polysaccharides can be linear or branched, α- or β-linked, joined 1->4, 1->6, etc.

Common Monosaccharides and derivatives

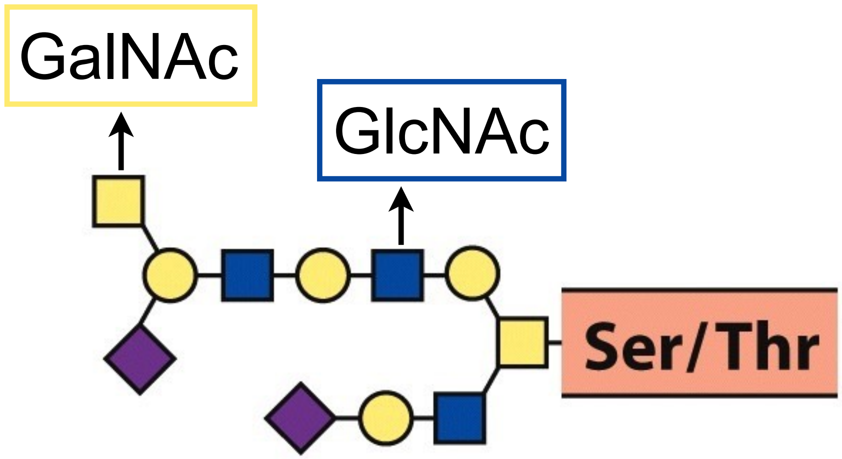
Abequose	Abe	Glucuronic acid	GlcA
Arabinose	Ara	Galactosamine	GalN
Fructose	Fru	Glucosamine	GlcN
Fucose	Fuc	*N*-Acetylgalactosamine	GalNAc
Galactose	Gal	*N*-Acetylglucosamine	GlcNAc
Glucose	Glc	Iduronic acid	IdoA
Mannose	Man	Muramic acid	Mur
Rhamnose	Rha	*N*-Acetylmuramic acid	Mur2Ac
Ribose	Rib	*N*-Acetylneuraminic acid (a sialic acid)	Neu5Ac
Xylose	Xyl		

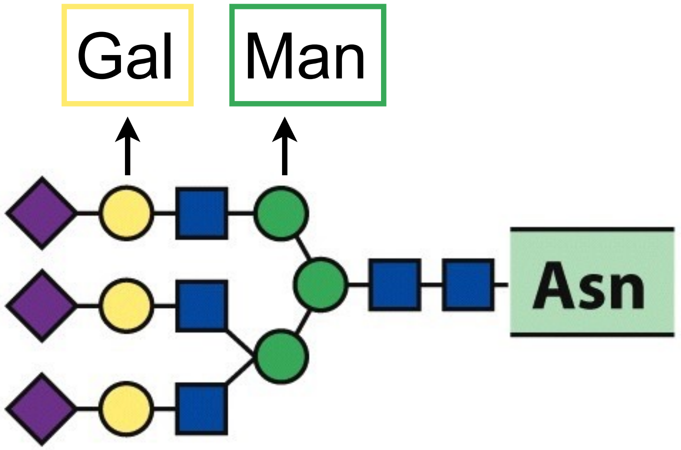
Standard Amino Acids

Glycine	Gly G	Serine	Ser S
Alanine	Ala A	Threonine	Thr T
Proline	Pro P	Cysteine[¶]	Cys C
Valine	Val V	Asparagine	Asn N
Leucine	Leu L	Glutamine	Gln Q
Isoleucine	Ile I	Lysine	Lys K
Methionine	Met M	Histidine	His H
Phenylalanine	Phe F	Arginine	Arg R
Tyrosine	Tyr Y	Aspartate	Asp D
Tryptophan	Trp W	Glutamate	Glu E

Sugar Code

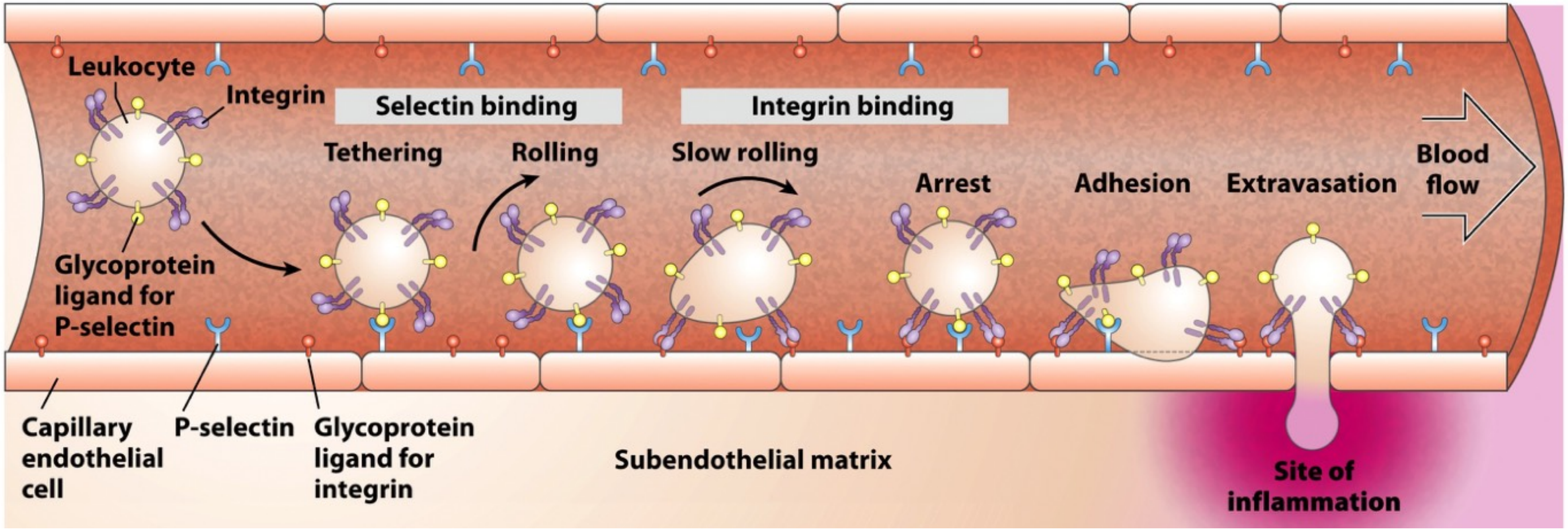
- Cells use carbohydrates to encode important information.
- Such information is used in many biological processes such as:
  - Protein targeting.
  - Cell-cell interaction.
- Lectins are proteins that read sugar code.
  - Carbohydrate-binding proteins.
  - **Highly specific.**
  - May bind a soluble carbohydrate or the sugar part of a glycoprotein.





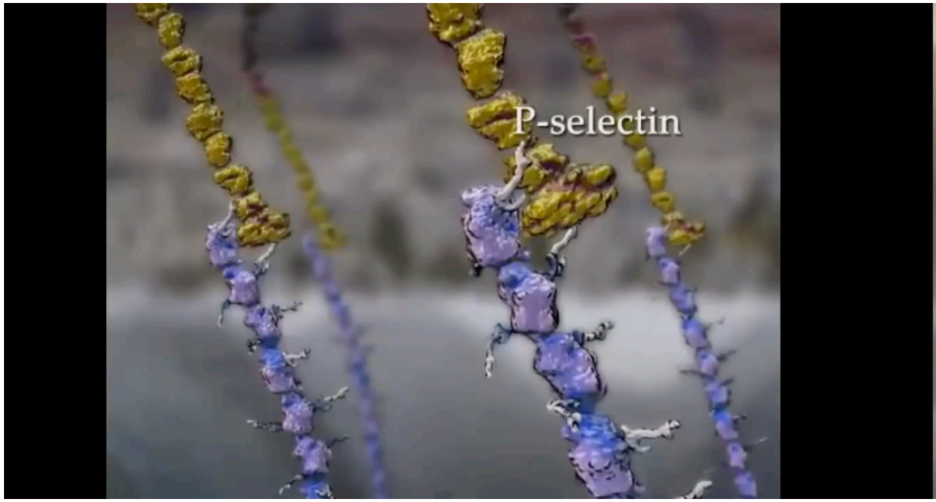
Selectins Mediate Cell-Cell Recognition

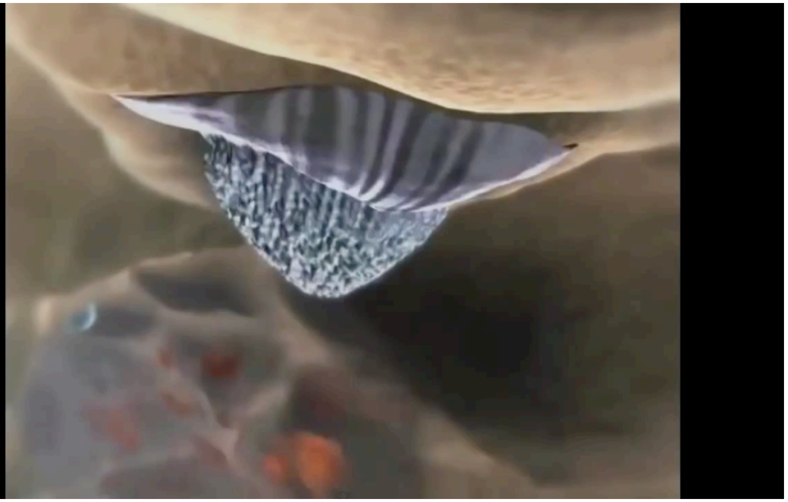
- Selectins are a family of plasma membrane lectins.
- Mediate movement of leukocytes to site of inflammation.
  - Selectin interacts with a specific oligosaccharide of a glycoprotein.
  - Capillary endothelial cells capture leukocytes.
  - Leukocytes move to infection site and initiate immune attack.



Selectins in Leukocyte Extravasation

- P-Selectin on endothelial cells interacts with a glycoprotein on leukocytes.
  - Red blood cells are carried away at high velocity by a strong blood flow.
  - Leukocytes roll slowly on endothelial cells.
  - Existing interactions are broken and new ones are formed.
- Leukocytes migrate through blood vessel wall into inflamed tissue.
  - These strong interactions immobilize rolling leukocytes at site of inflammation.
  - Profound reorganization of cytoskeleton.
  - The leukocyte insert itself between endothelial cells.





Summary 7.3 and 7.4

- Glycoproteins contain oligosaccharides covalently linked to Ser/Thr or Asn residues. Many cell surface proteins and secreted proteins are glycoproteins.
- The number of ways to assemble a polysaccharide is greater than the number of ways to assemble a protein or nucleic acid. Glycans are more information-dense.
- Lectins are highly specific carbohydrate-binding proteins. Lectins are commonly found on cell surface, and mediate interaction with other cells.

Example Question

Which of the following monosaccharides is *not* an aldose?

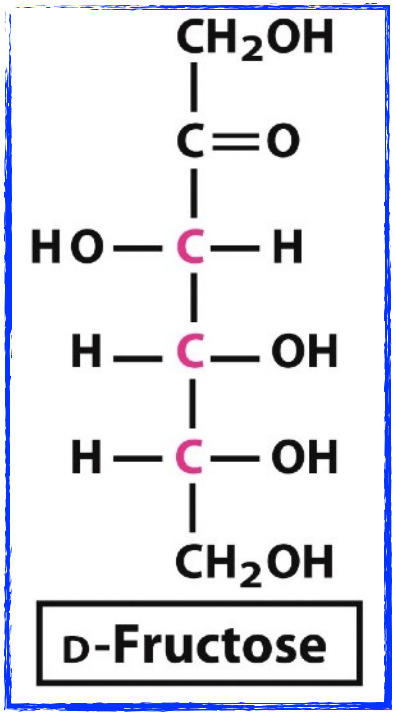
A) Galactose

B) Fructose

C) Glucose

D) Glyceraldehyde

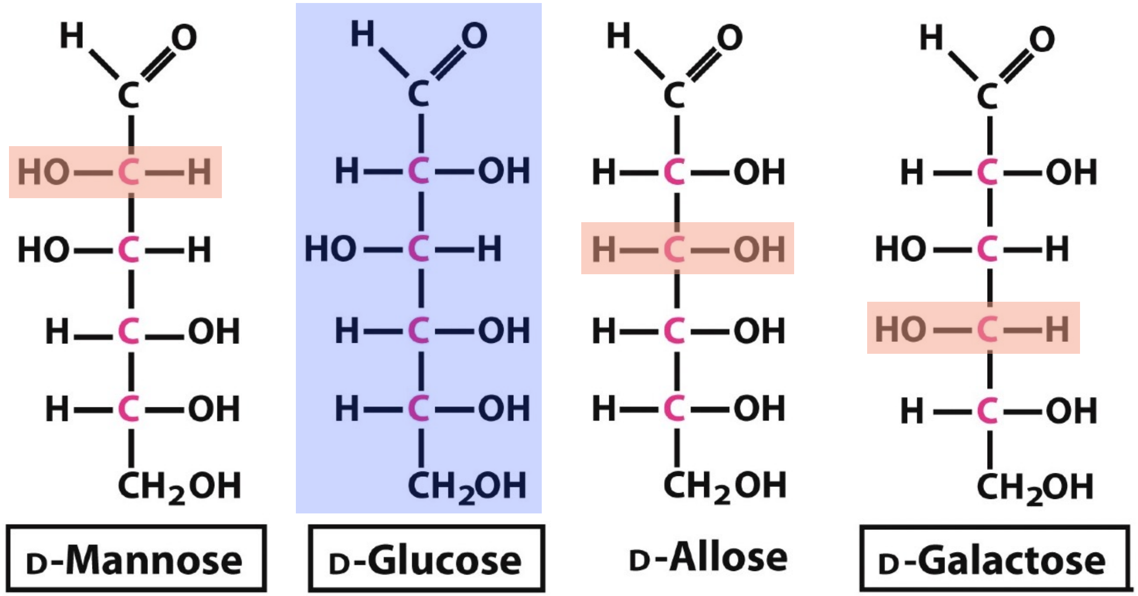
E) Ribose



Example Question

Which of the following is an epimeric pair?

A) D-glucose and D-glucosamine
B) D-glucose and D-mannose
C) D-glucose and L-glucose
D) D-lactose and D-sucrose
E) L-mannose and L-fructose



Example Question

When the linear form of glucose cyclizes, the product is a(n):

A) hemiketal.
B) glycoside.
C) hemiacetal.
D) acetal.
E) oligosaccharide.

Example Question

Which of the following pairs is interconverted in the process of mutarotation?

A) D-glucose and D-fructose
B) D-glucose and D-galactose
C) D-glucose and D-glucosamine
D) D-glucose and L-glucose
E) α-D-glucose and β-D-glucose

Example Question

Following complete hydrolysis of a sample of glycogen and a sample of cellulose, which of the following is *true*?

A) The cellulose sample has a higher ratio of α-D-glucose than the glycogen sample.
B) The cellulose sample contains only α-D-glucose.
C) Both samples consist of a mixture of α-D-glucose and β-D-glucose.
D) The glycogen sample has a higher ratio of α-D-glucose than the cellulose sample.
E) The glycogen sample contains only β-D-glucose.

Example Question

Explain why all mono- and disaccharides are soluble in water.

Example Question

Define what enantiomers are (in 20 words or fewer).

Define what epimers are (in 20 words or fewer).

Define what a pyranose is (in 20 words or fewer).

Define what a ketose is (in 20 words or fewer).

Example Question

Match these molecules with their biological roles.

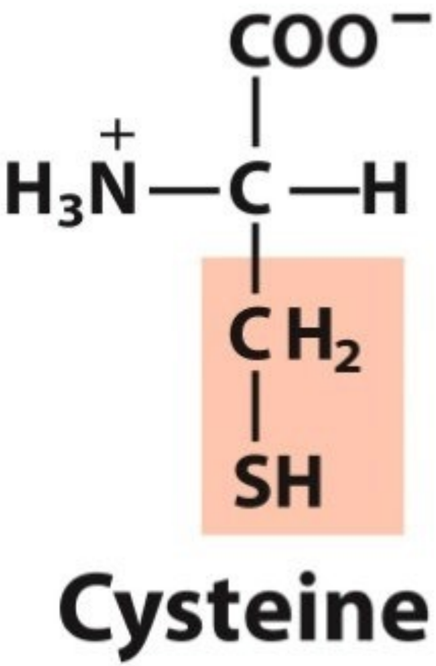
(a) glycogen	__ exoskeleton of insect
(b) cellulose	__ carbohydrate storage in plant
(c) chitin	__ carbohydrate storage in animal liver
(d) peptidoglycan	__ structural component of plant cell wall
(e) starch	__ structural component of bacterial cell wall

Example Question

Describe one biological advantage of storing glucose units in *branched* polymers (glycogen, amylopectin) rather than in linear polymers.

The enzymes that act on these polymers to generate glucose for metabolism **act only on their nonreducing ends**. With extensive branching, there are more such ends for enzymatic attack than would be present in the same quantity of glucose stored in a linear polymer. In effect, **branched polymers increase the substrate concentration for these enzymes**.

Two Sulfur-Containing Amino Acids



Amino acid
for 7th week