Carbohydrates

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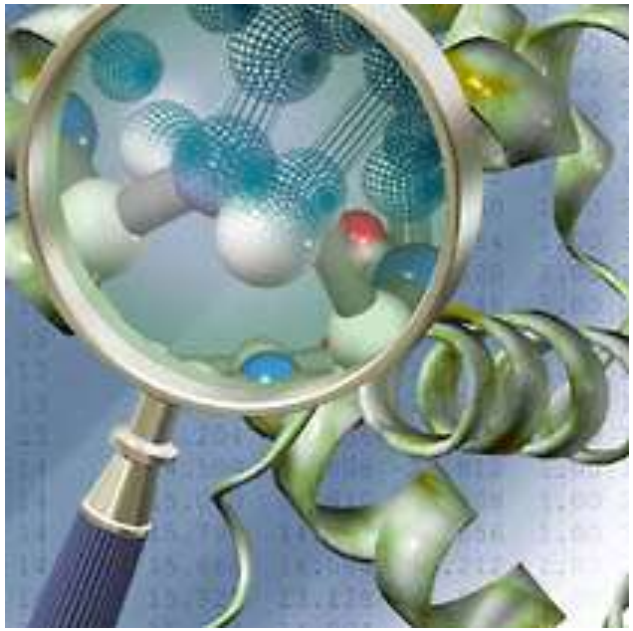
Department of Biochemistry



Introduction

- carbohydrates are the most abundant biomolecules on Earth.

- What is the biological importance of carbohydrates?

Carbohydrate Functions

- **provide the majority of energy** in most organisms.

- **serve as metabolic intermediates**

- **are structural components of cell walls & cell membrane**

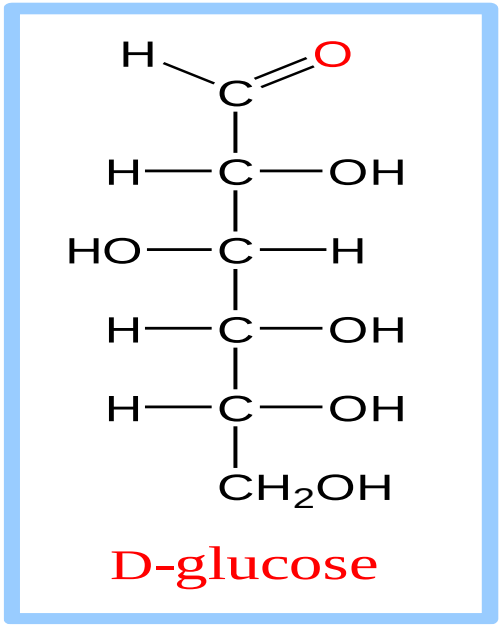
Carbohydrate Functions, Cont……..

-ribose, 2-deoxy ribose are **component of the nucleotides**.

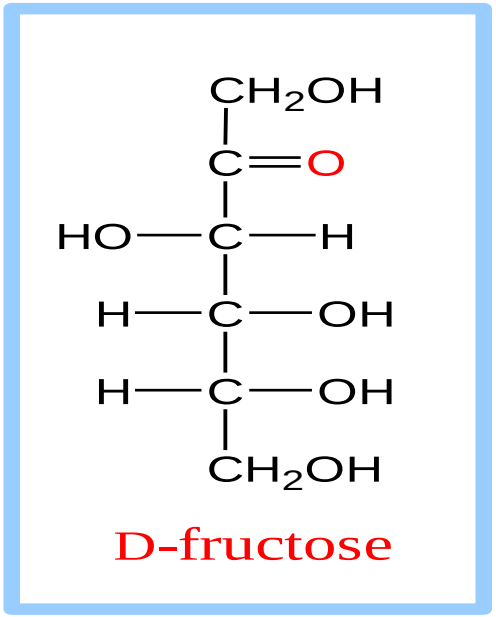
- play roles **in lubrication, immunity and cellular intercommunication**

Chemical Structure

- Carbohydrates are ***polyhydroxyaldehydes*** or ***polyhydroxyketones*** , or substances that yield such compounds on hydrolysis.



D-glucose



D-fructose

Chemical Structure, Cont……..

- Carbohydrates are made of carbon, hydrogen, and oxygen atoms, always in a ratio of 1:2:1

- Many, but not all, carbohydrates have the empirical formula $\mathbf{(C\ H2O)_n}$. Some also contain nitrogen, phosphorus, or sulfur.

Carbohydrate Classification

- Monosaccharides - consist of a single polyhydroxy aldehyde or polyhydroxy ketone units.

- Oligosaccharides - a few (2-10) monosaccharides covalently linked.

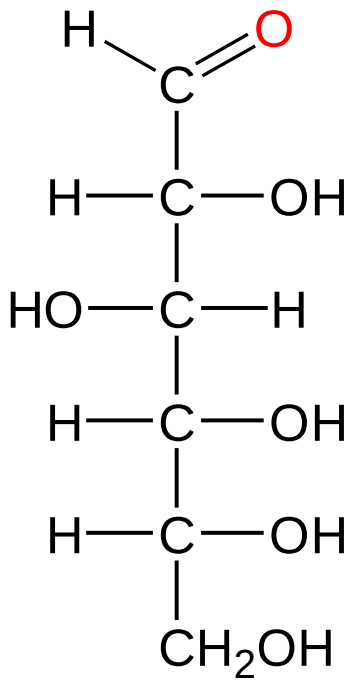
  Disaccharides - 2 monosaccharides covalently linked

- Polysaccharides - polymers consisting of chains of monosaccharide or disaccharide units.

Monosaccharides

Aldoses (e.g., glucose) have an aldehyde group at one end.

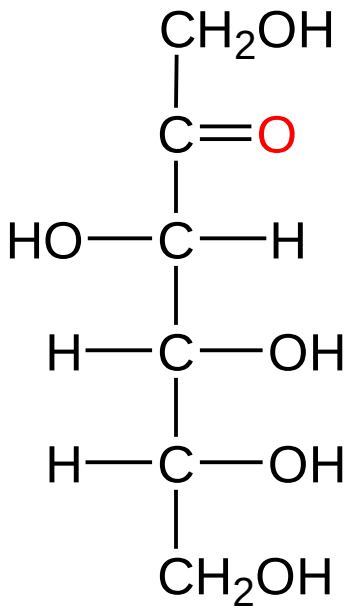
Ketoses (e.g., fructose) have a keto group, usually at C2.



D-glucose

Open chain forms
(Fischer projections)

Carbons are numbered sequentially with the aldehyde or keton group assigned the lowest possible number



D-fructose

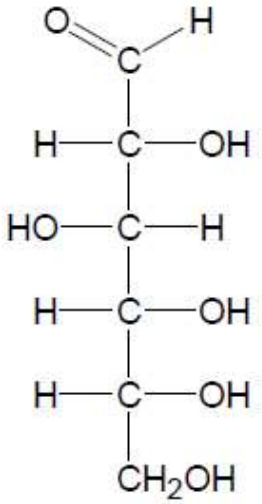
Nomenclature

Functional group

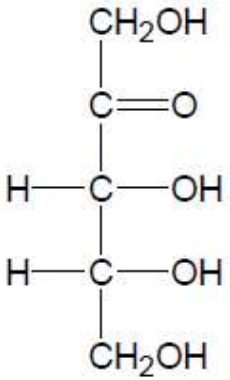
Number of carbons	**Aldehyde**	**Ketone**
4	Tetrose	Tetrulose
5	Pentose	Pentulose
6	Hexose	Hexulose
7	Heptose	Heptulose
8	Octose	Octulose

Classification of Monosaccharides

- Thus, glucose is an **aldohexose** (aldehyde + 6 Cs) and ribulose is a **ketopentose** (ketone + 5 Cs)



glucose
an **aldohexose**



ribulose
a **ketopentose**

Representative Monosaccharides

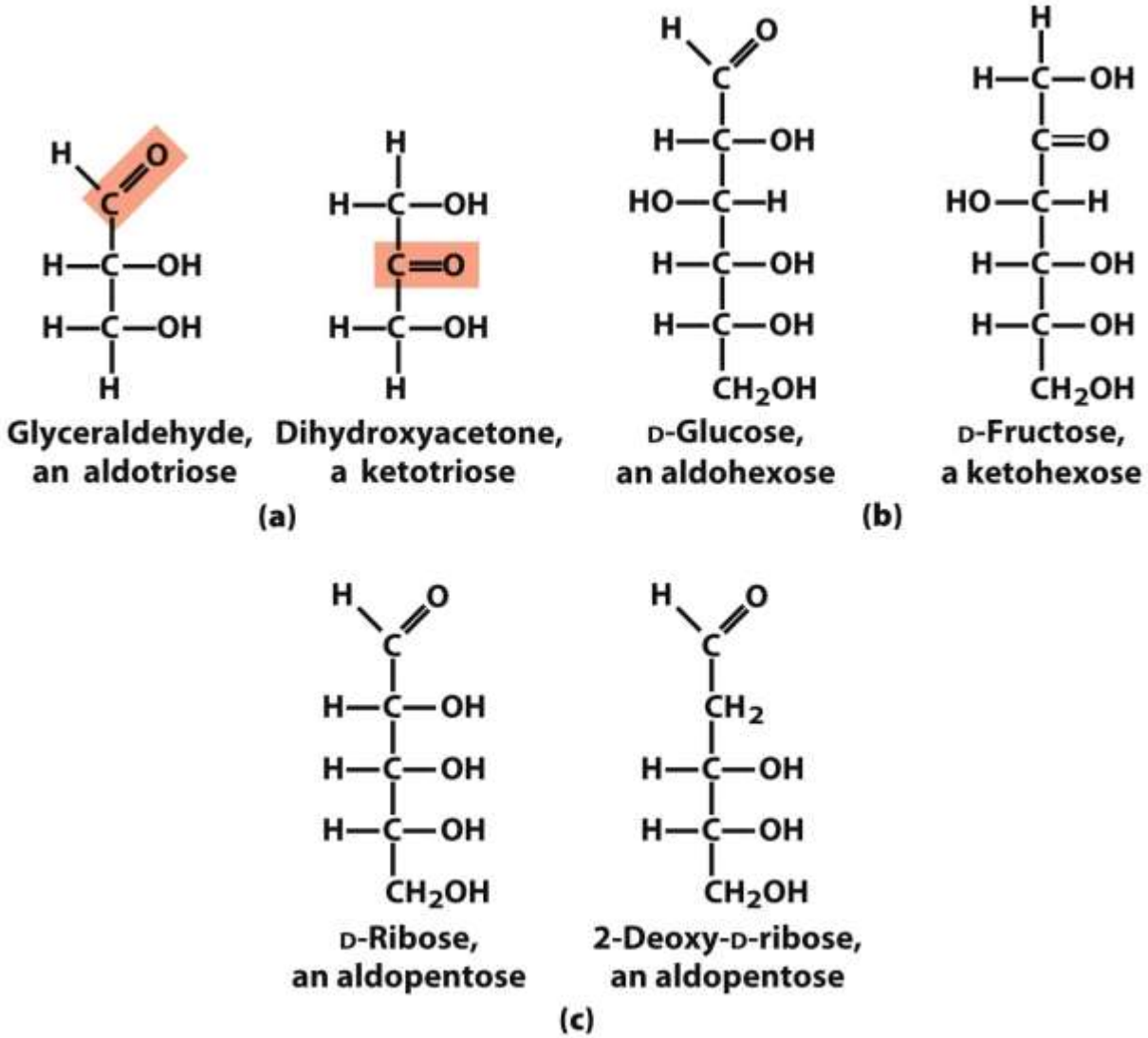


Figure 7-1
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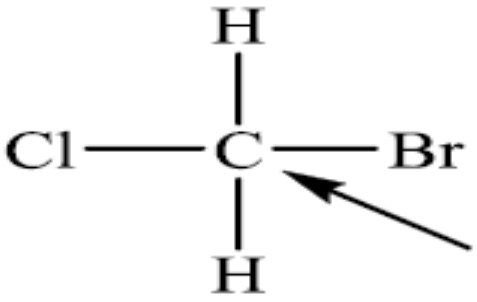
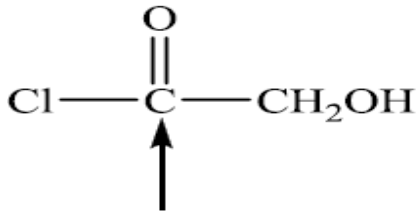
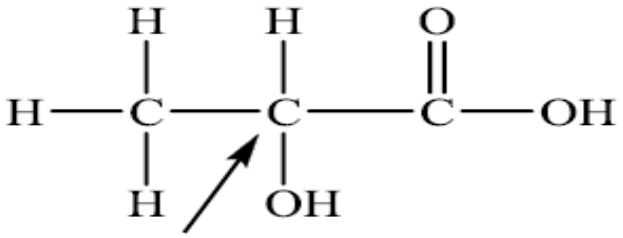
Asymmetric (chiral) carbon



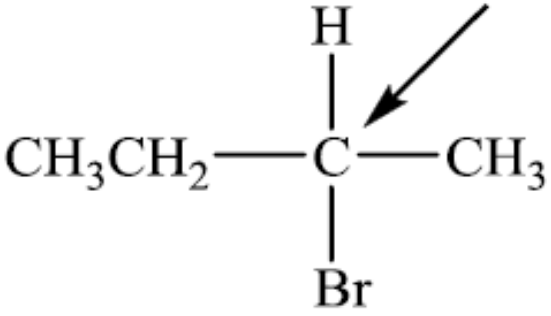
a)



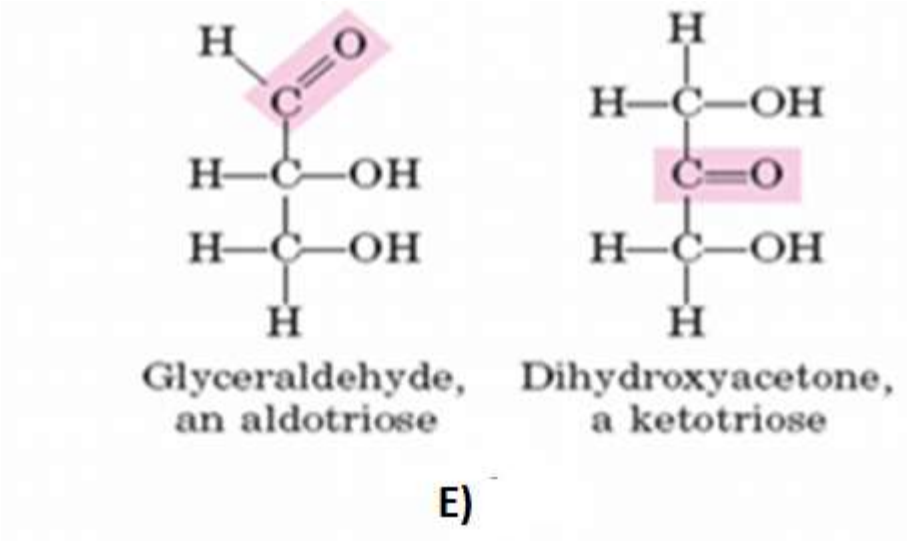
b)



d)



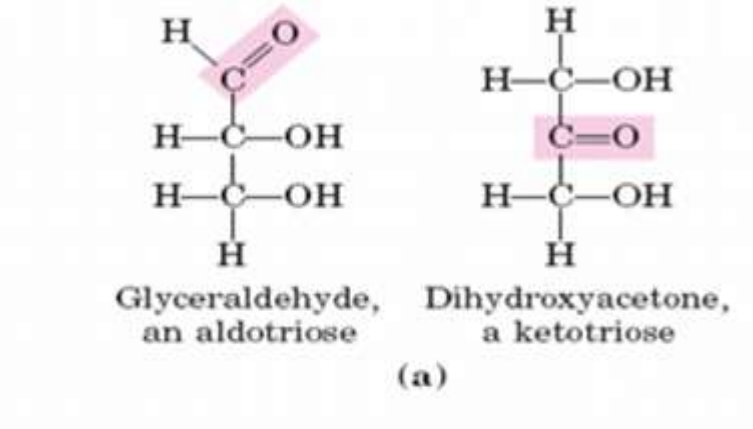
c)

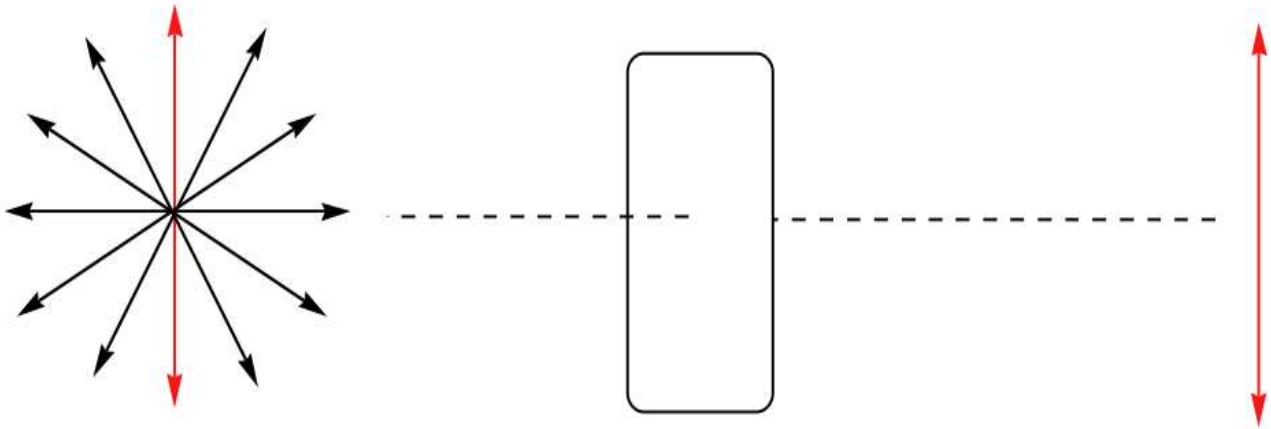


E)

Monosaccharaides Have Asymmetric Centers

- All the monosaccharides except dihydroxyacetone contain one or more asymmetric (chiral) carbon atoms and thus occur in optically active isomeric forms.

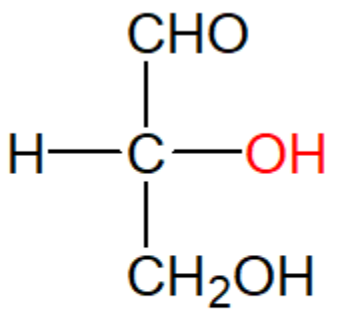




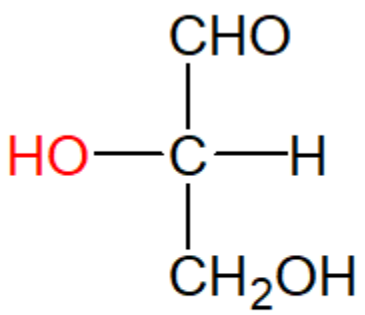
randomly oriented light polarizing filter plane-polarized light

Cont…….

- The simplest aldose, **glyceraldehyde**, contains one chiral canter (the middle carbon atom) and therefore has two different optical isomers, or **enantiomers.**



D-glyceraldehyde

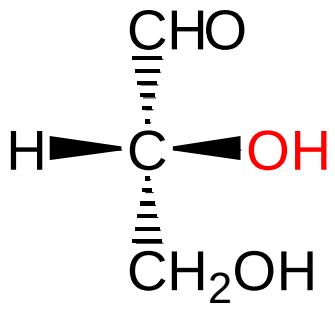


L-glyceraldehyde

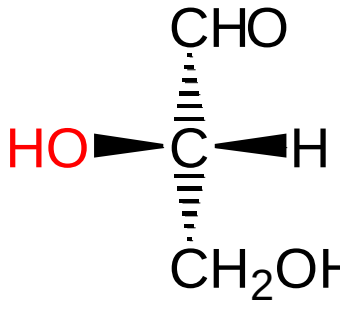
D vs L Designation

D & L designations are based on the configuration about the single asymmetric C in glyceraldehyde.

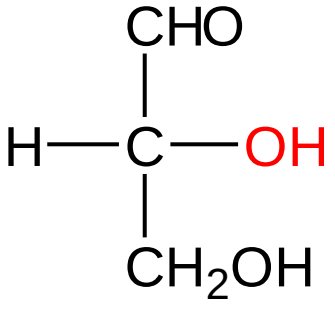
The lower representations are Fischer Projections.



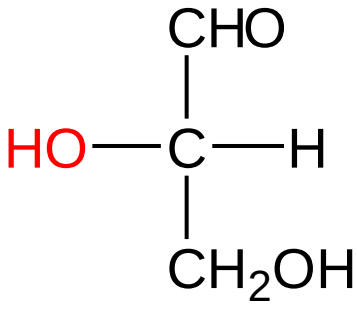
D-glyceraldehyde



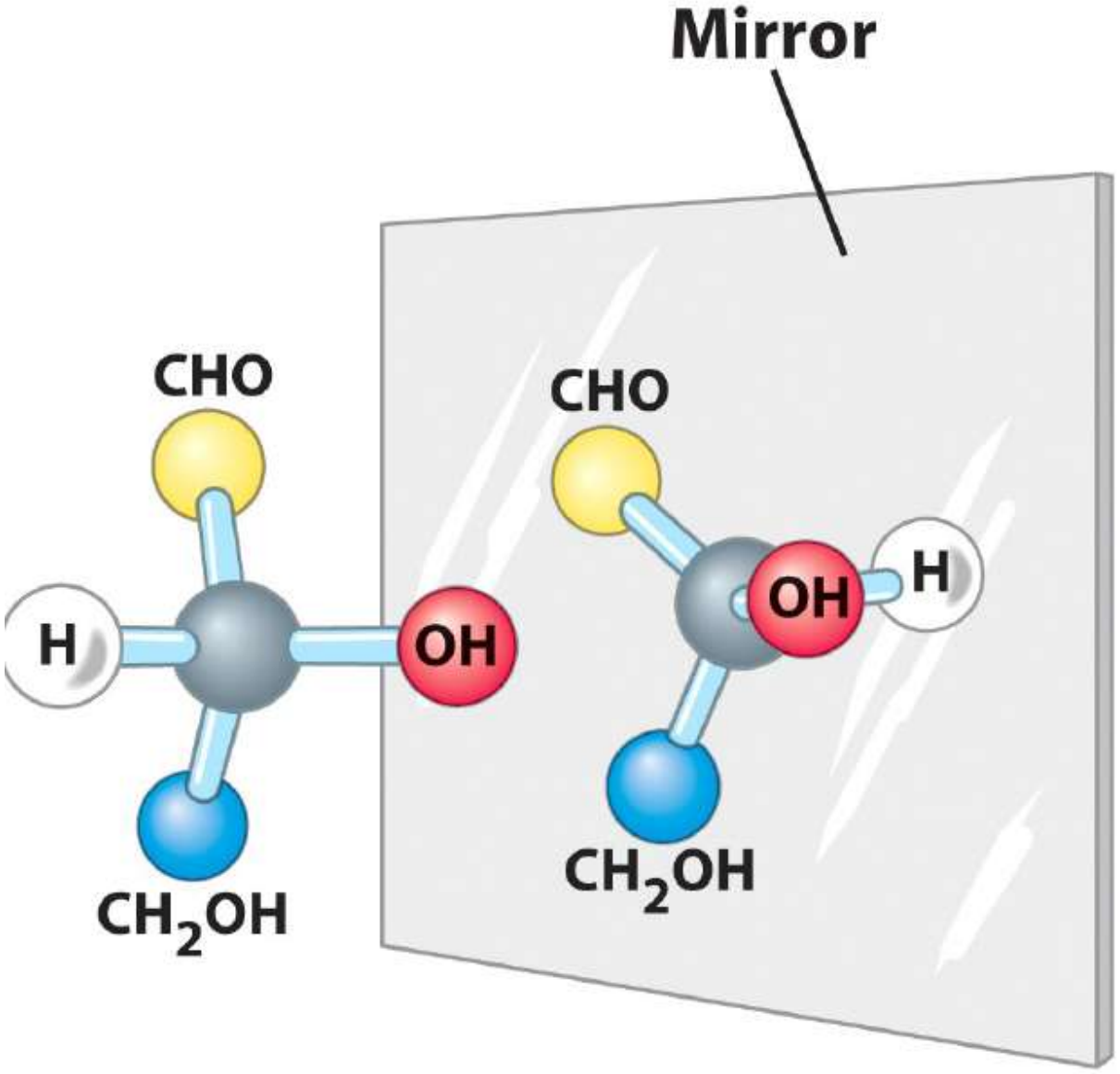
L-glyceraldehyde



D-glyceraldehyde



L-glyceraldehyde

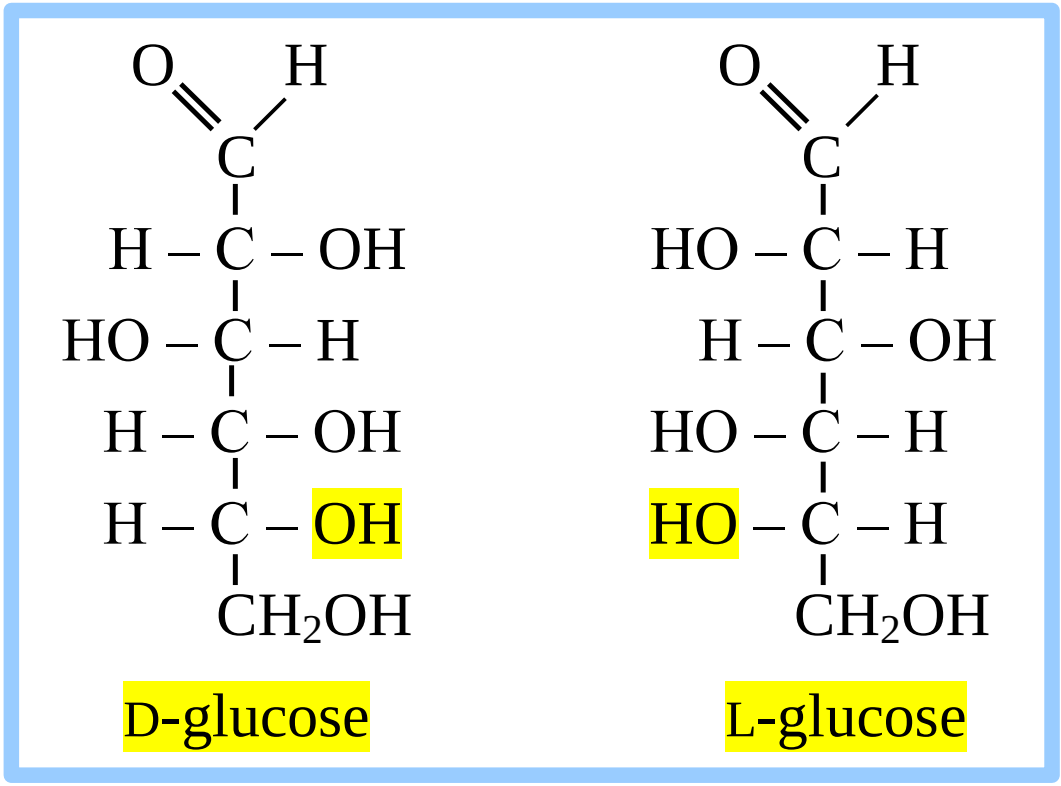


Ball-and-stick models

Sugar Nomenclature

For sugars with more than one chiral center, **D** or **L** refers to the asymmetric **C** farthest from the aldehyde or keto group.

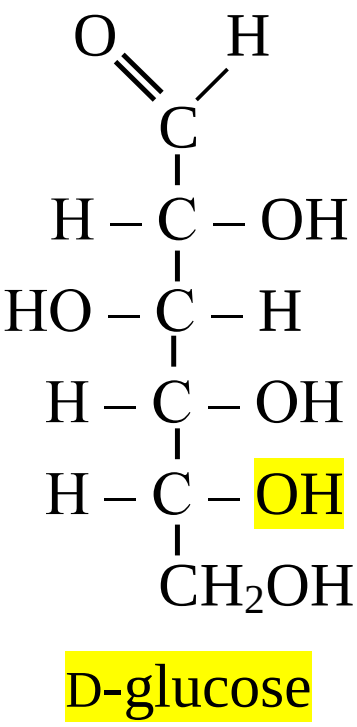
Most naturally occurring sugars are D isomers.



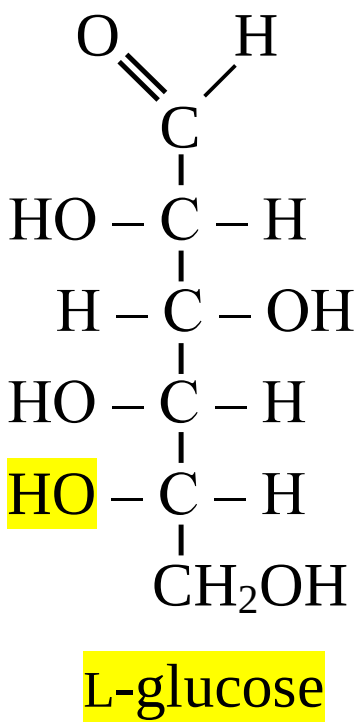
D & L sugars are mirror images of one another.

They have the same name, e.g., D-glucose & L-glucose.

Other stereoisomers have unique names, e.g., glucose, mannose, galactose, etc.



D-glucose

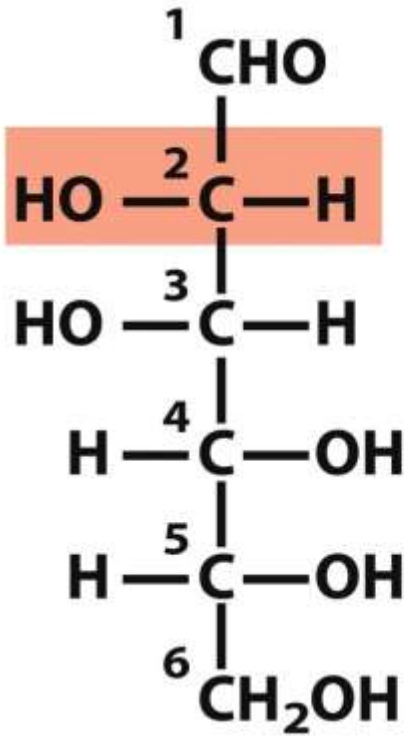


L-glucose

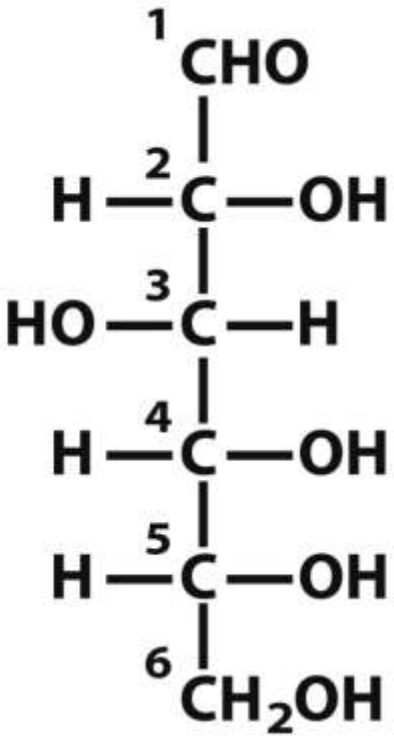
The number of stereoisomers is 2^n, where n is the number of asymmetric centers.

The 6-C aldoses have 4 asymmetric centers. Thus there are 16 stereoisomers (8 D-sugars and 8 L-sugars).

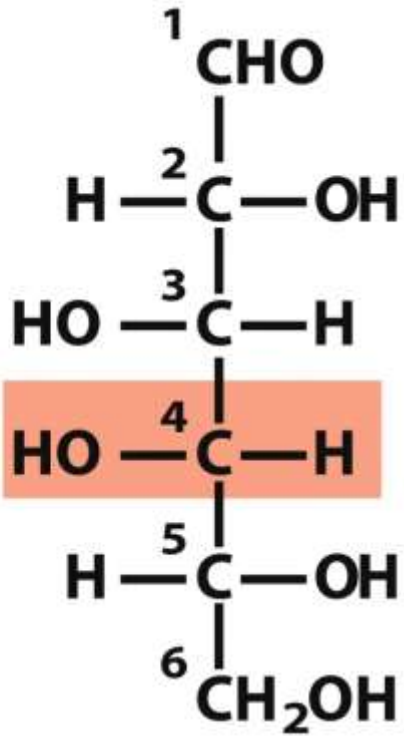
Mannose and Galactose are epimers of Glucose



D-Mannose
(epimer at C-2)



D-Glucose



D-Galactose
(epimer at C-4)

Figure 7-4
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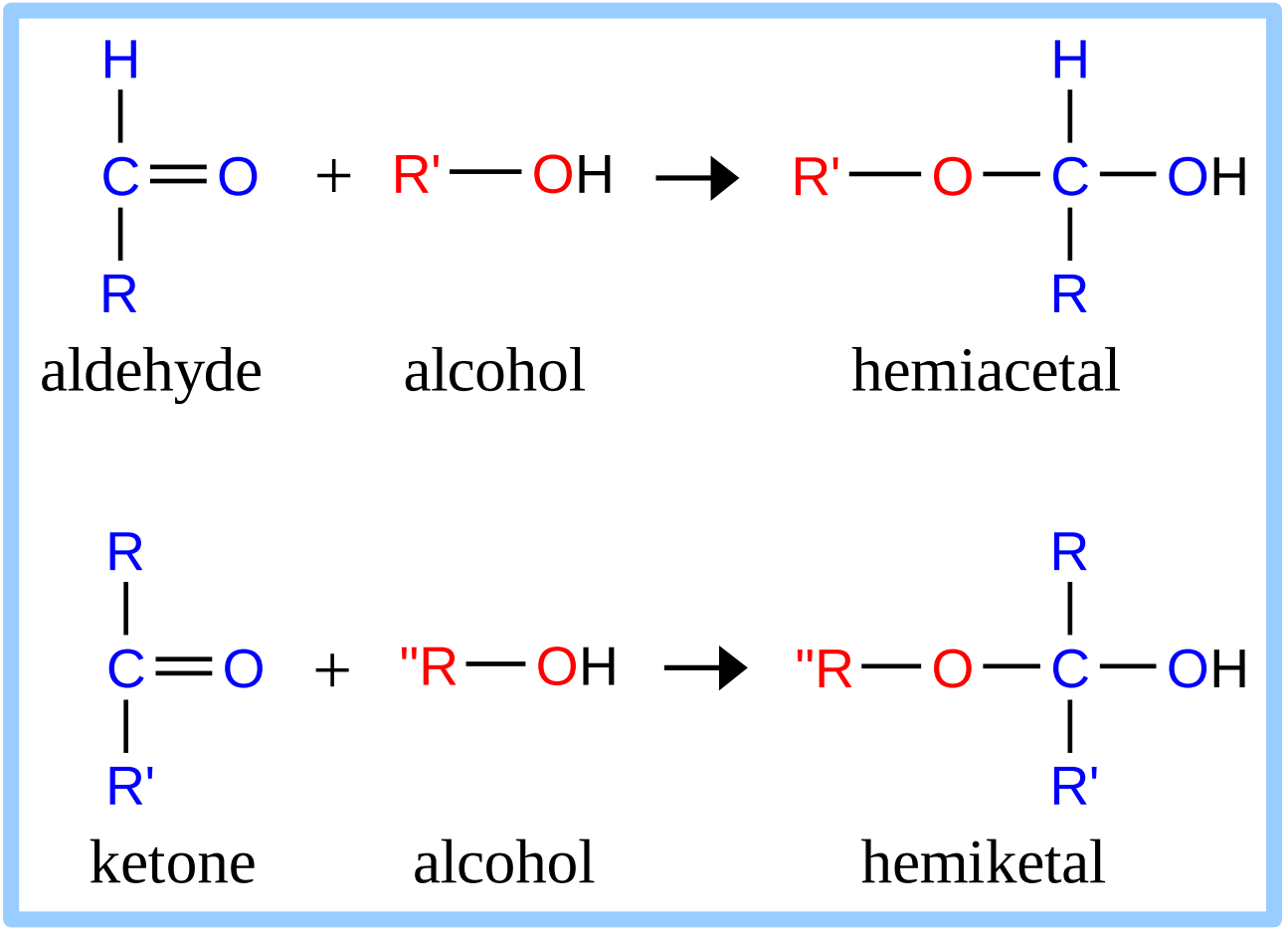
Hemiacetal & hemiketal formation

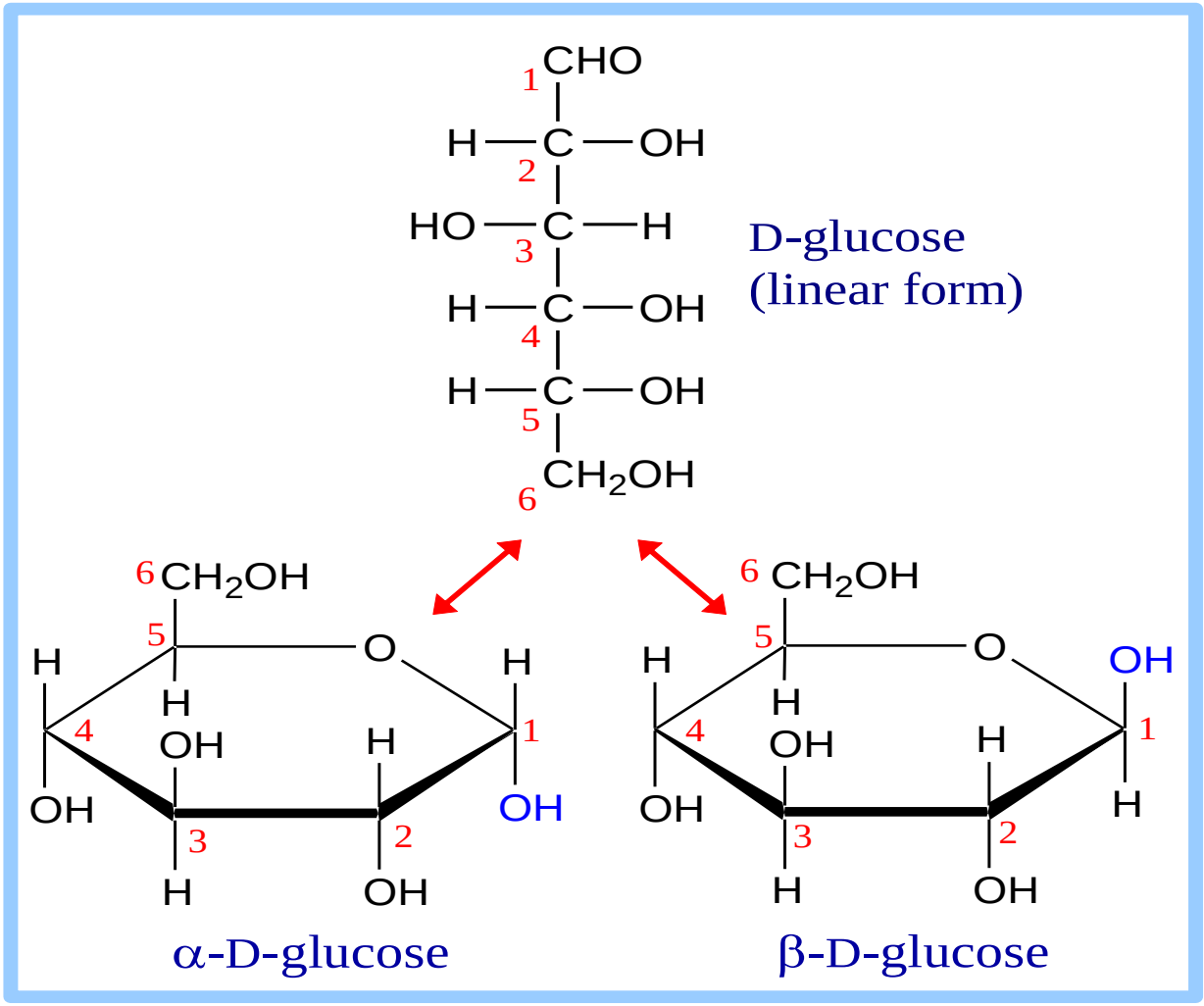
An aldehyde can react with an alcohol to form a hemiacetal.

A ketone can react with an alcohol to form a hemiketal.



Pentoses and hexoses can cyclize as the ketone or aldehyde reacts with a distal OH.

Glucose forms an intra-molecular hemiacetal, as the C1 aldehyde & C5 OH react, to form a 6-member pyranose ring, named after pyran.



These representations of the cyclic sugars are called Haworth projections.

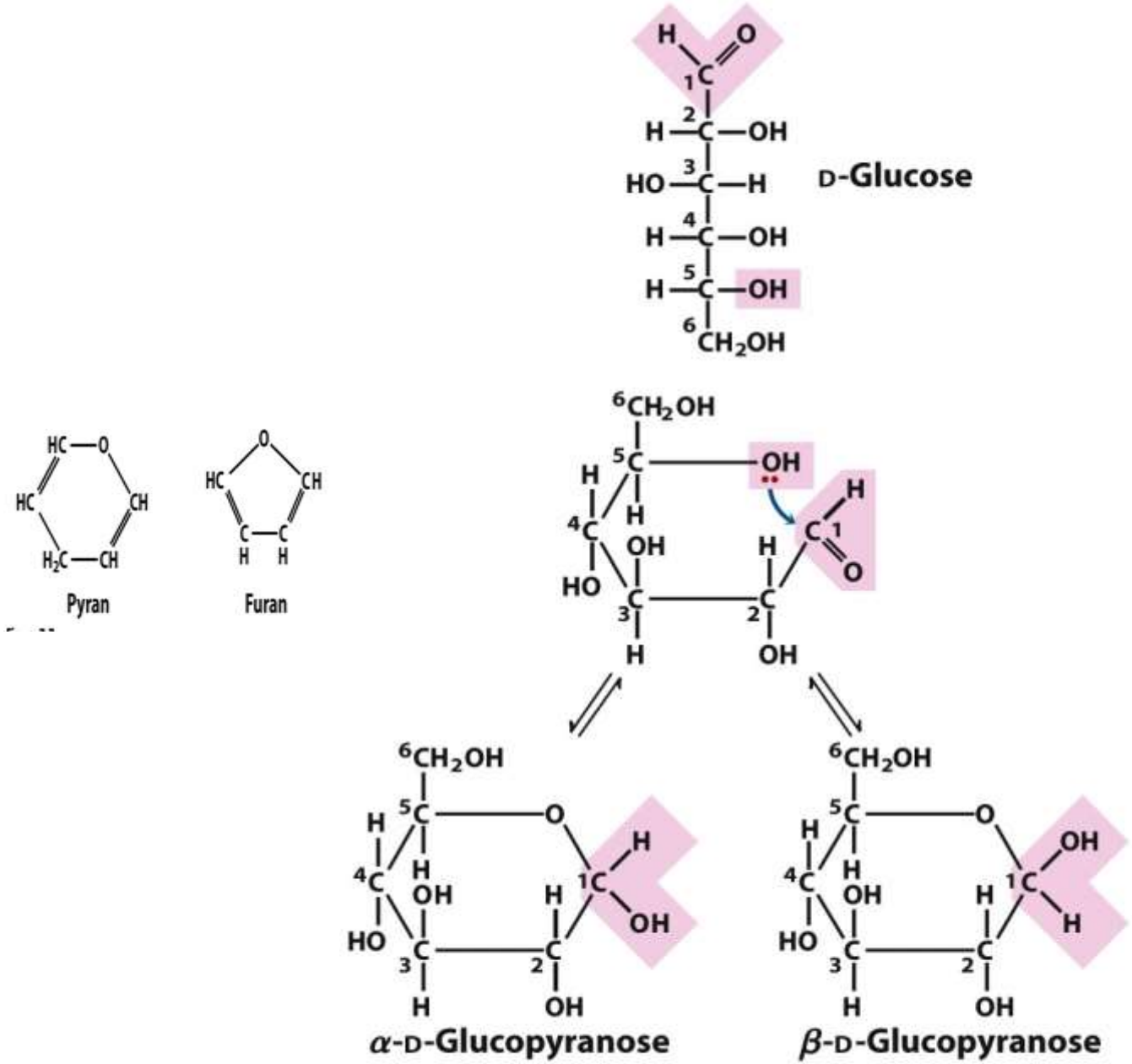


Figure 7-6

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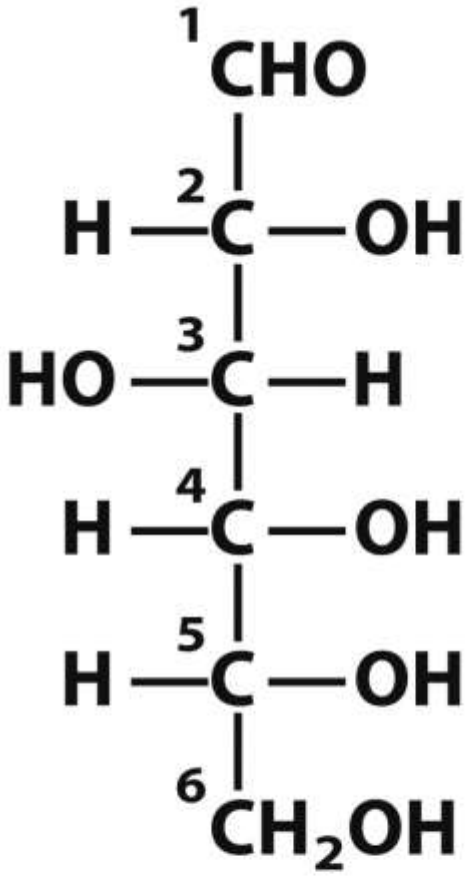
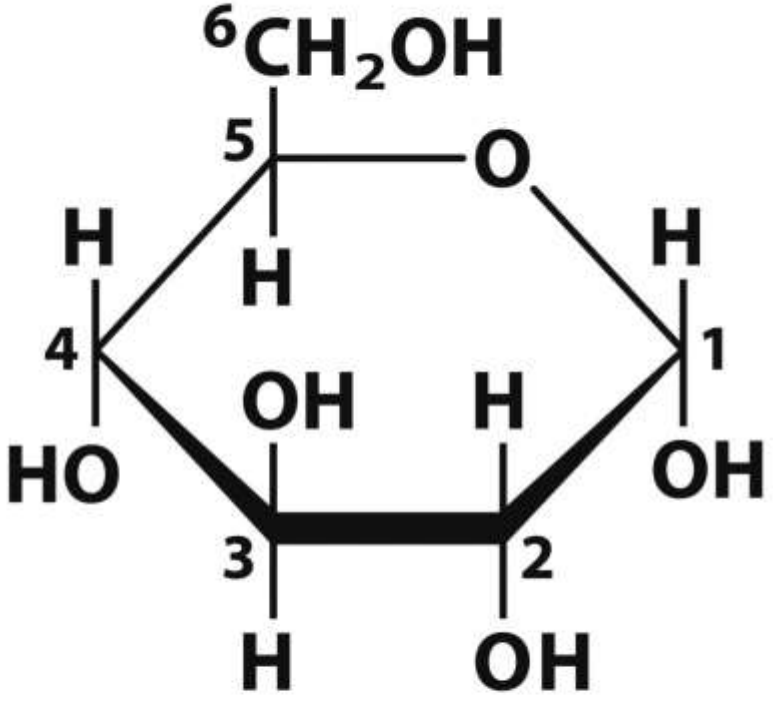
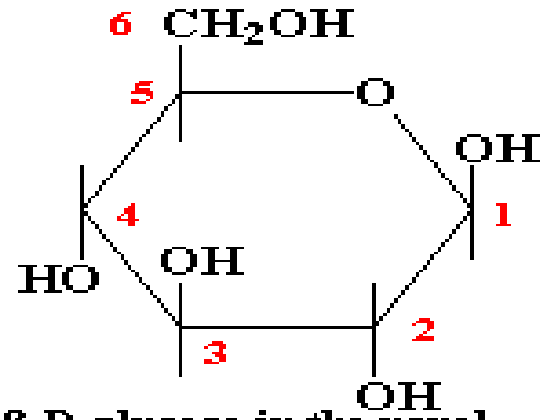


D-Glucose
Fischer projection

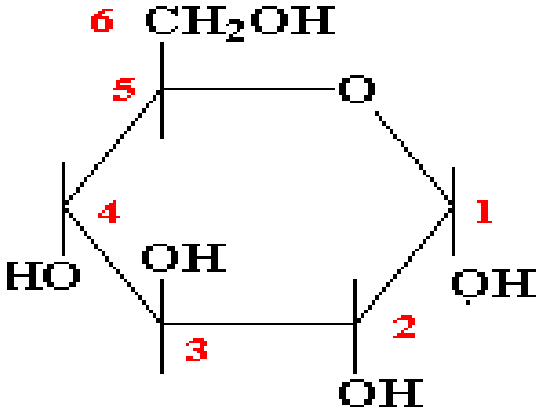


α-D-Glucopyranose
Haworth perspective

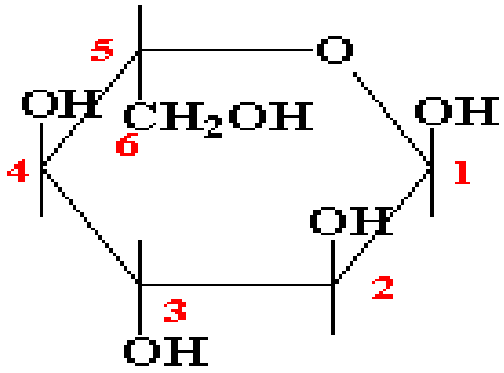
Unnumbered 7 p247
Lehninger Principles of Biochemistry, Sixth Edition



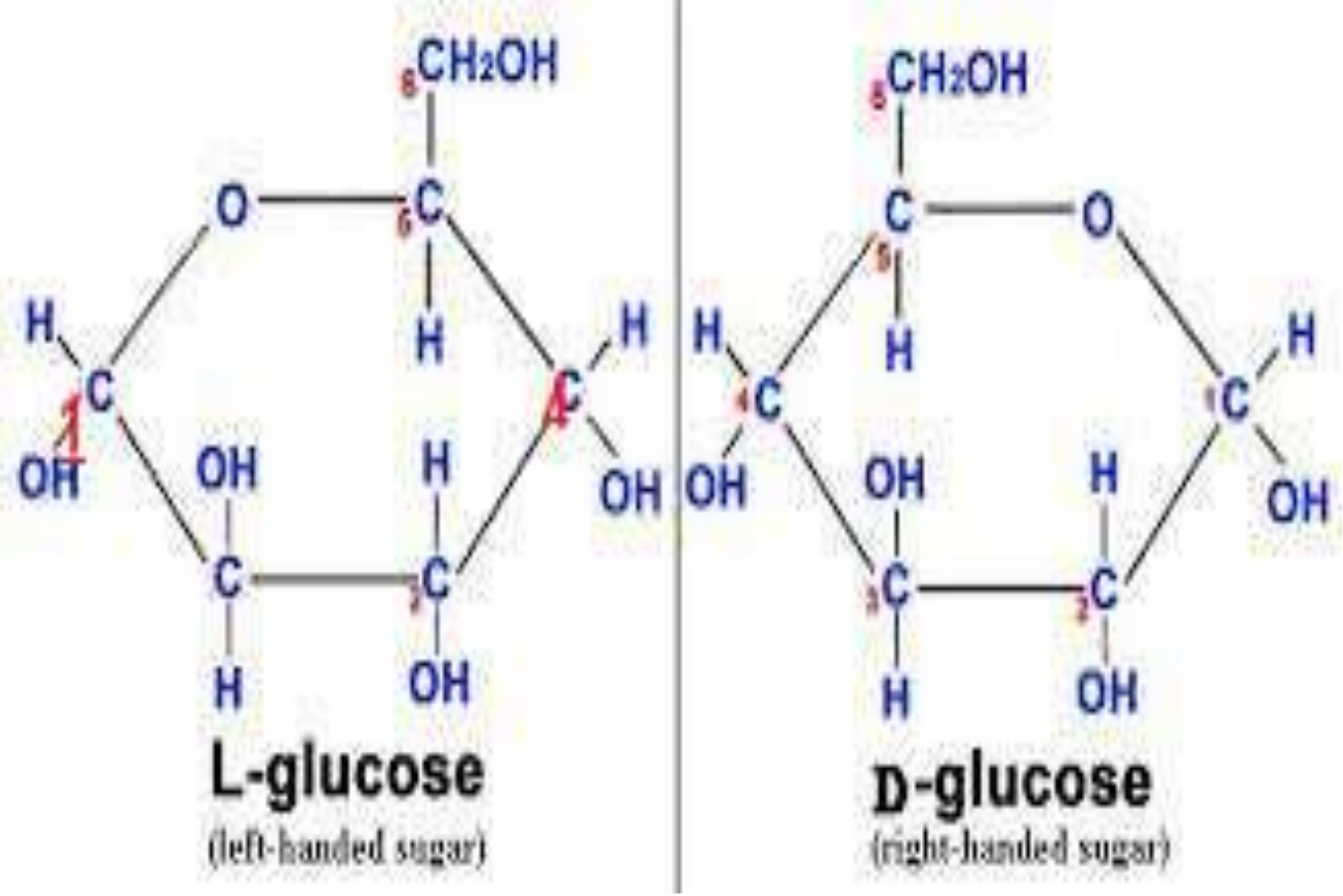
β-D-glucose in the usual abbreviated format

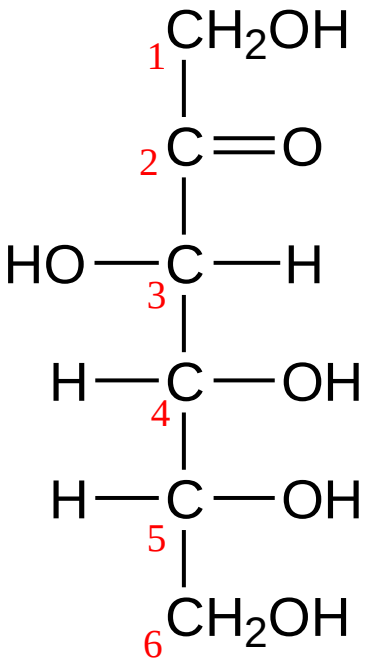


α-D-glucose

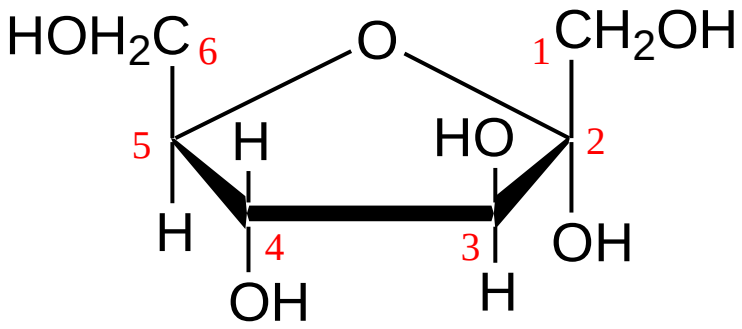


α-L-glucose: note that the C1 hydroxyl points up for this enantiomer.


CH2OH
O
H
OH
OH
H
OH
H
OH
H
L-glucose
(left-handed sugar)
CH2OH
O
H
OH
OH
H
OH
H
D-glucose
(right-handed sugar)



D-fructose (linear)



α-D-fructofuranose

Fructose forms either

- a 6-member pyranose ring, by reaction of the C2 keto group with the OH on C6, or
- a 5-member furanose ring, by reaction of the C2 keto group with the OH on C5.

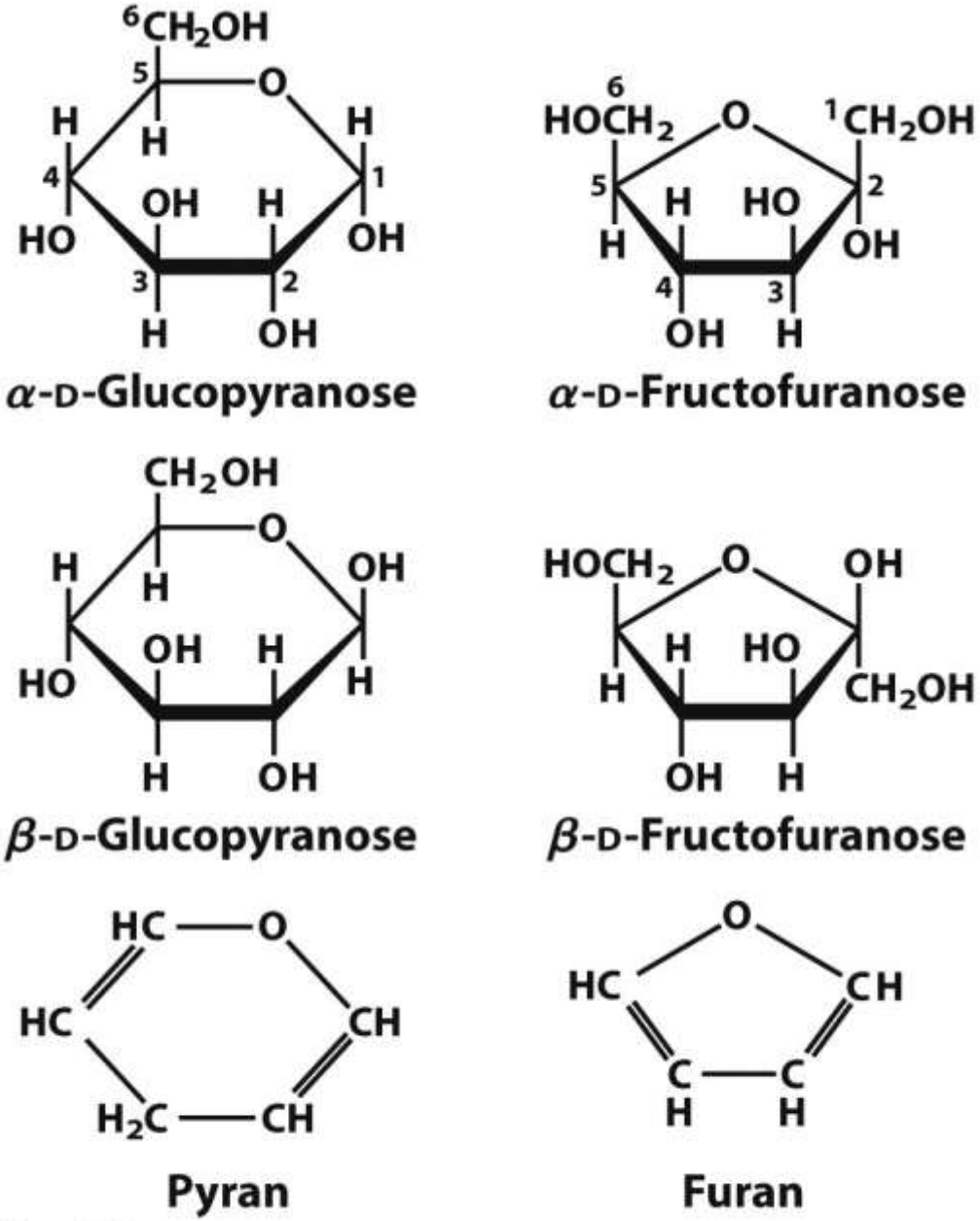


Figure 7-7
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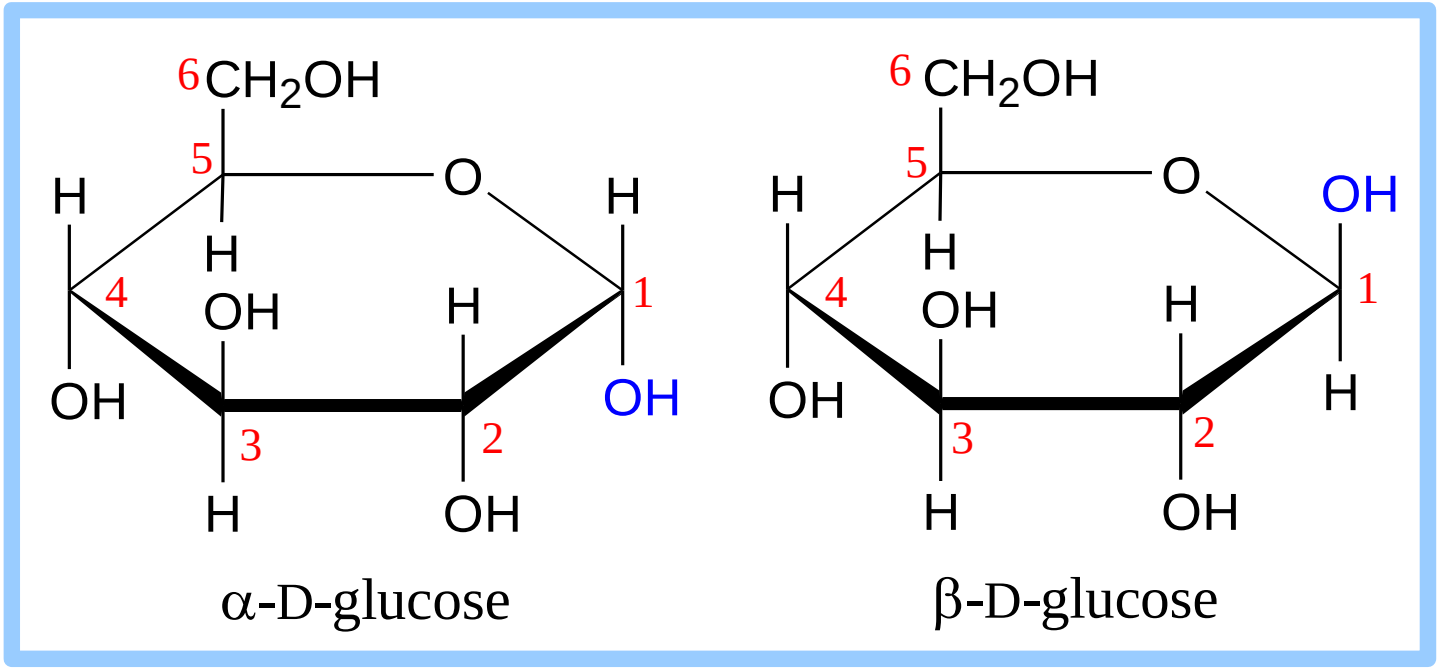
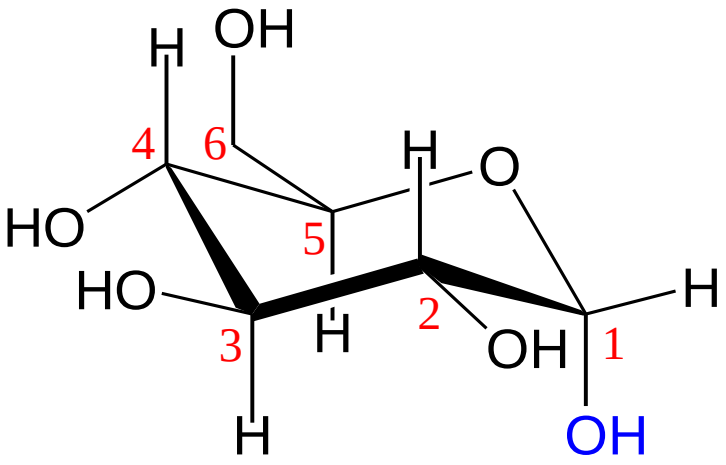


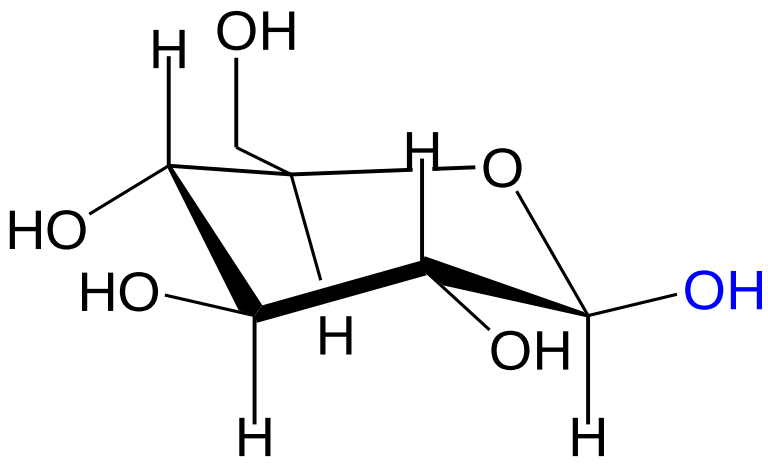
Cyclization of glucose produces a new asymmetric center at C1. The 2 stereoisomers are called anomers, α & β.

Haworth projections represent the cyclic sugars as having essentially planar rings, with the OH at the anomeric C1:

- α (OH below the ring)
- β (OH above the ring).



α-D-glucopyranose



β-D-glucopyranose

Because of the tetrahedral nature of carbon bonds, pyranose sugars actually assume a "chair" or "boat" configuration, depending on the sugar.

The representation above reflects the chair configuration of the glucopyranose ring more accurately than the Haworth projection.

Sugars as reducing agent

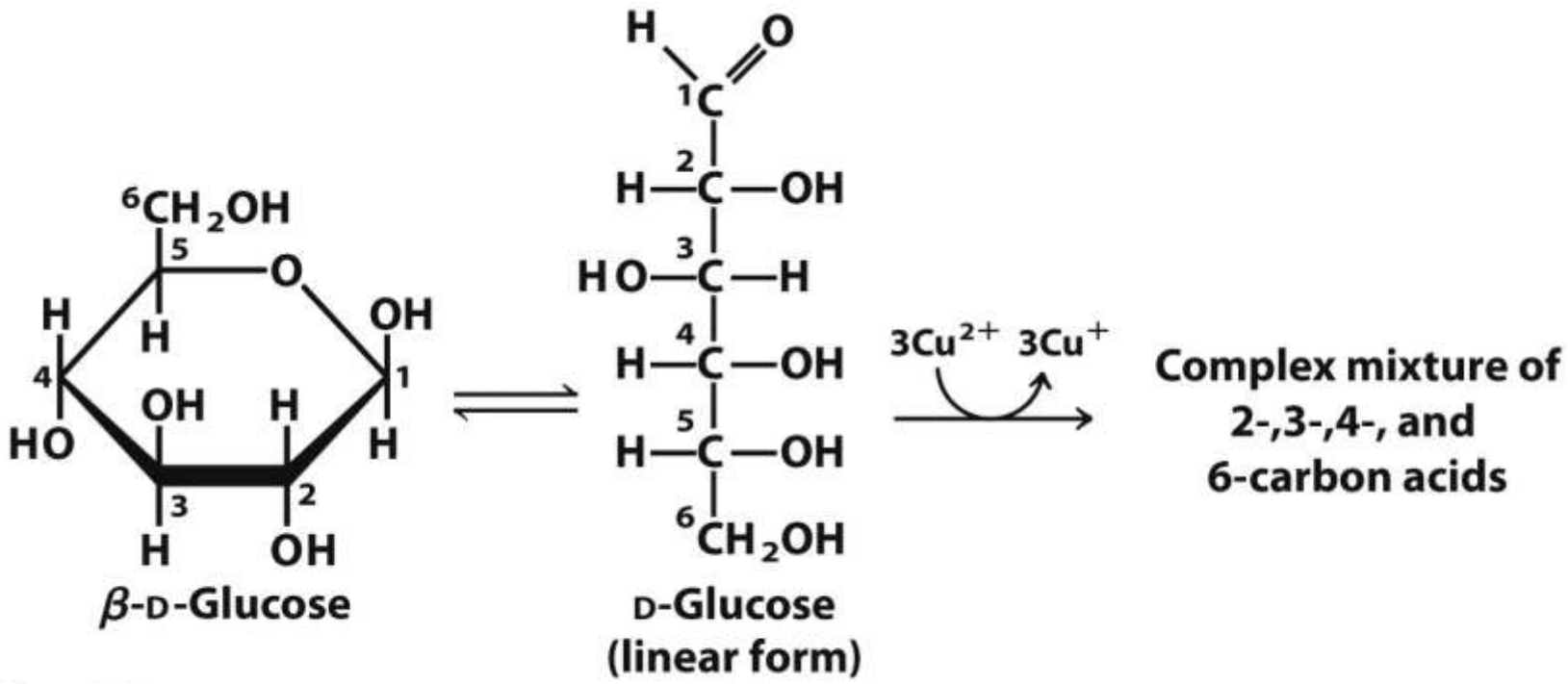


Figure 7-10
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Box 7-1 figure 1
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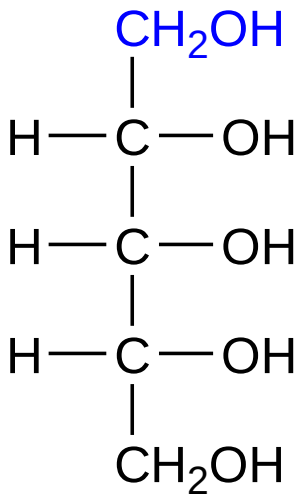
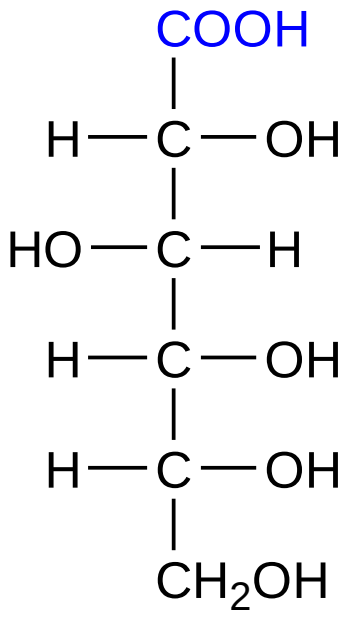
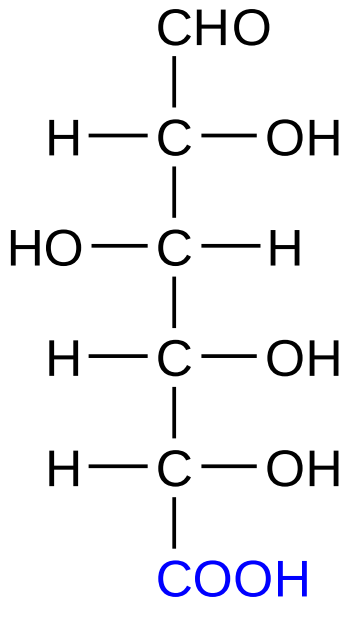
Sugar derivatives



D-ribitol



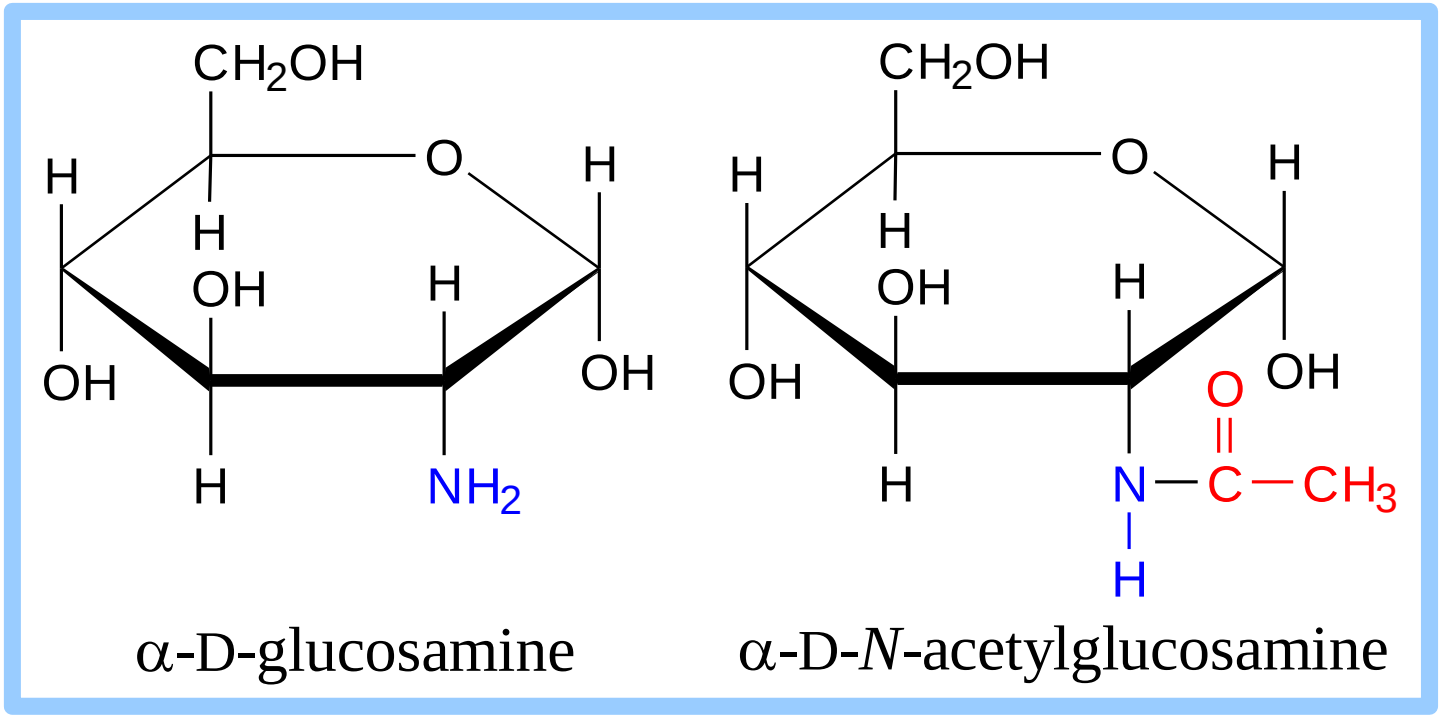
D-gluconic acid



D-glucuronic acid

- sugar alcohol - lacks an aldehyde or ketone; e.g., ribitol.
- sugar acid - the aldehyde at C1, or OH at C6, is oxidized to a carboxylic acid; e.g., gluconic acid, glucuronic acid.

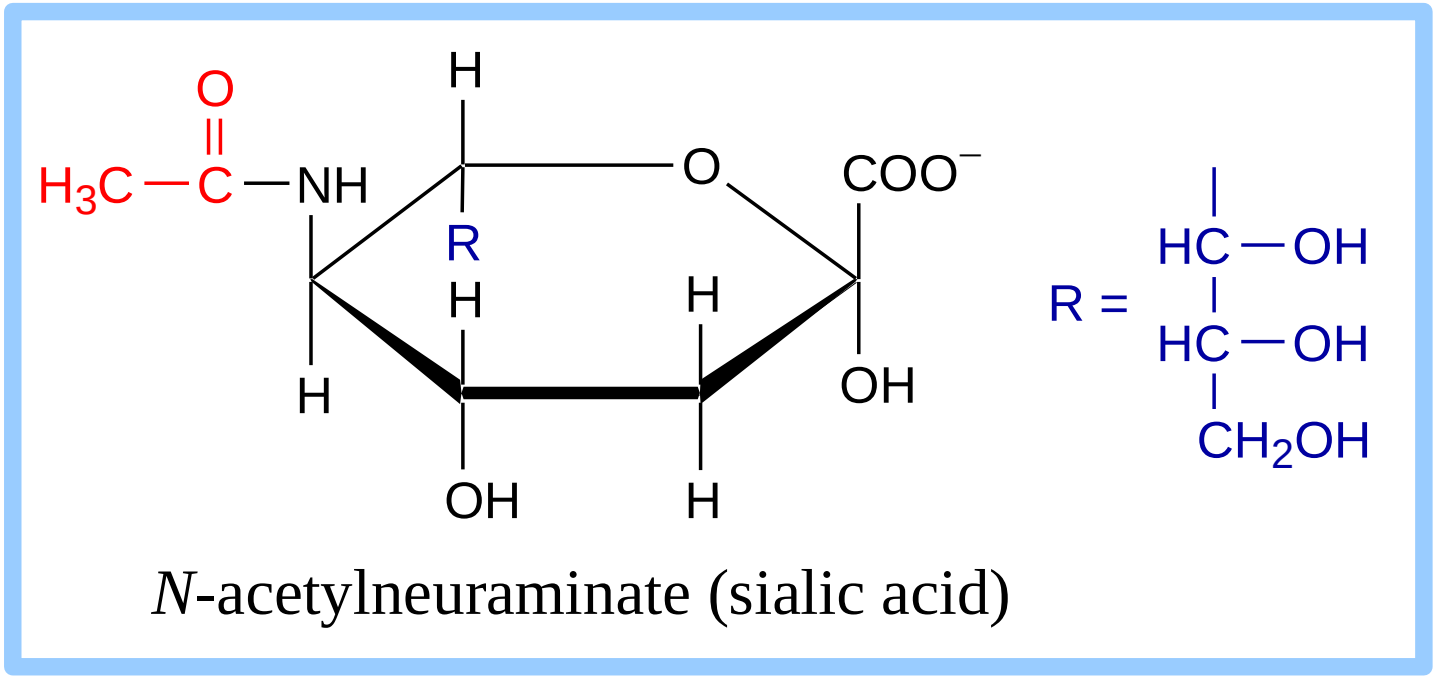
Sugar derivatives



α-D-glucosamine α-D-*N*-acetylglucosamine

amino sugar - an amino group substitutes for a hydroxyl. An example is glucosamine.

The amino group may be acetylated, as in *N*-acetylglucosamine.



N-acetylneuraminate (sialic acid)

N-acetylneuraminate (N-acetylneuraminic acid, also called sialic acid) is often found as a terminal residue of oligosaccharide chains of glycoproteins.

Sialic acid imparts negative charge to glycoproteins, because its carboxyl group tends to dissociate a proton at physiological pH, as shown here.

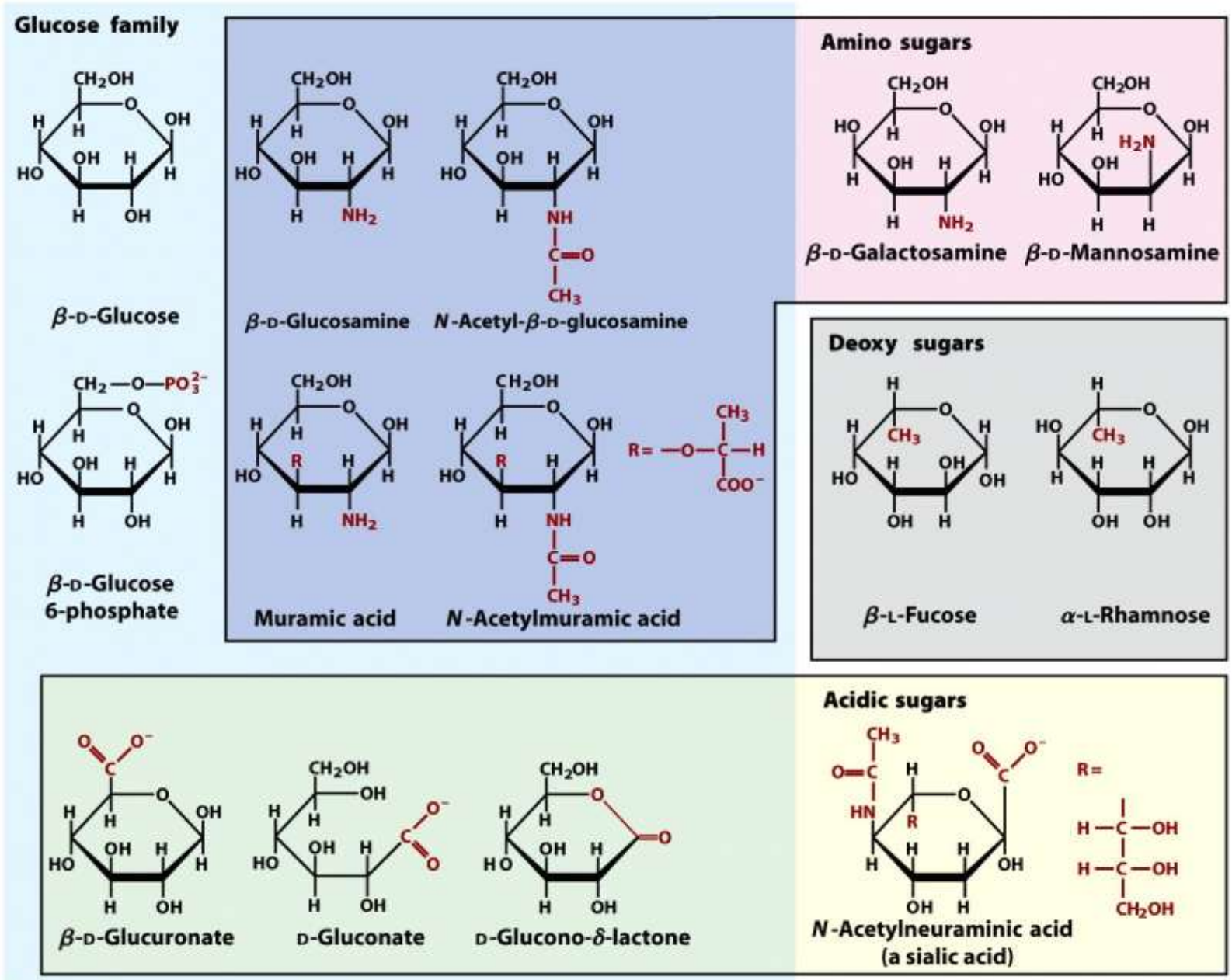


Figure 7-9

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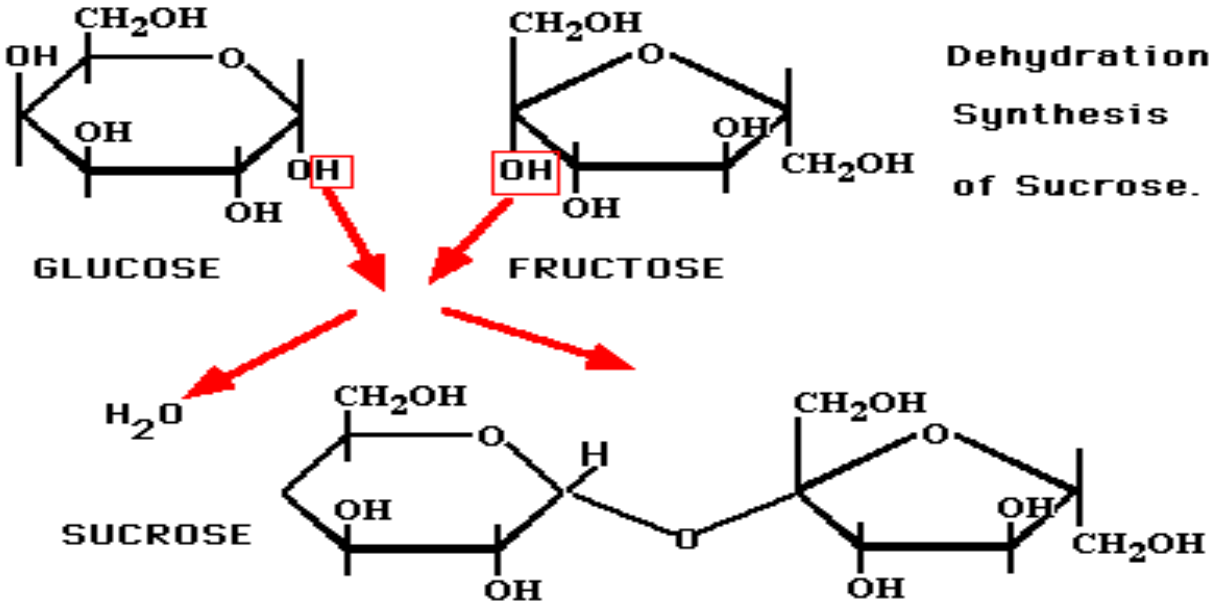
Glycosidic Bonds

The anomeric hydroxyl and a hydroxyl of another sugar or some other compound can join together, splitting out water to form a glycosidic bond:

R-OH + HO-R' → R-O-R' + H_2O



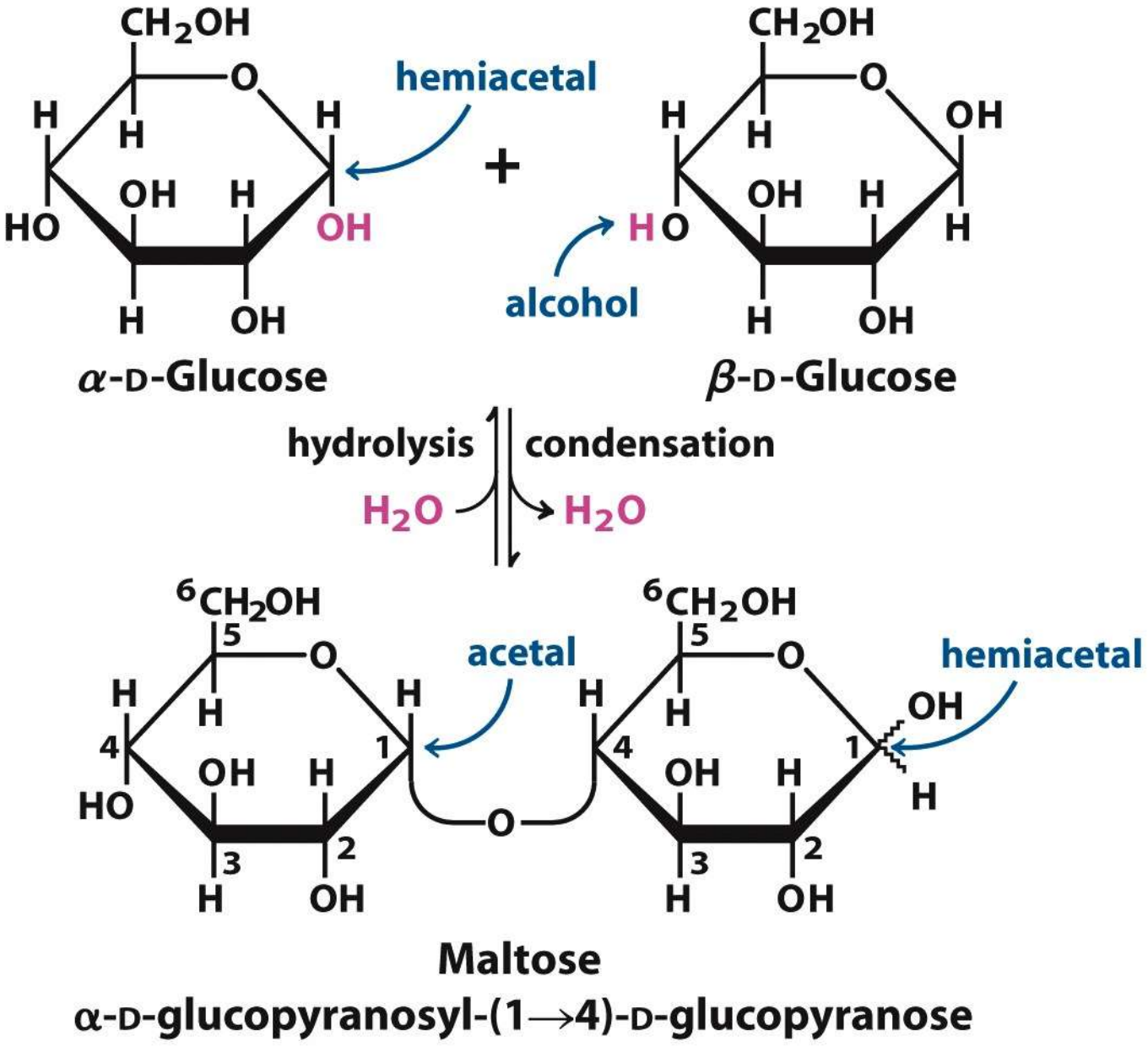


Figure 7-11
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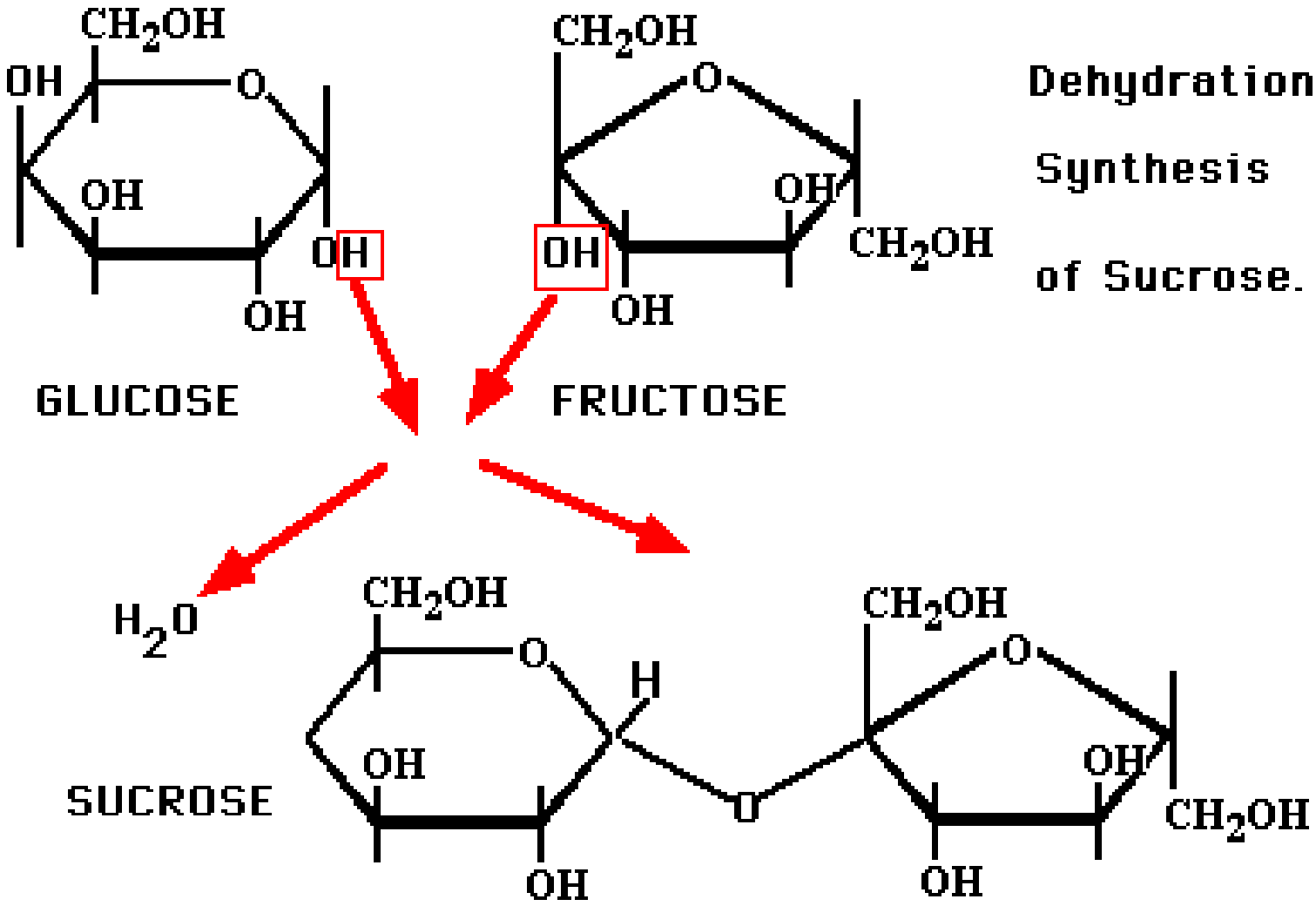
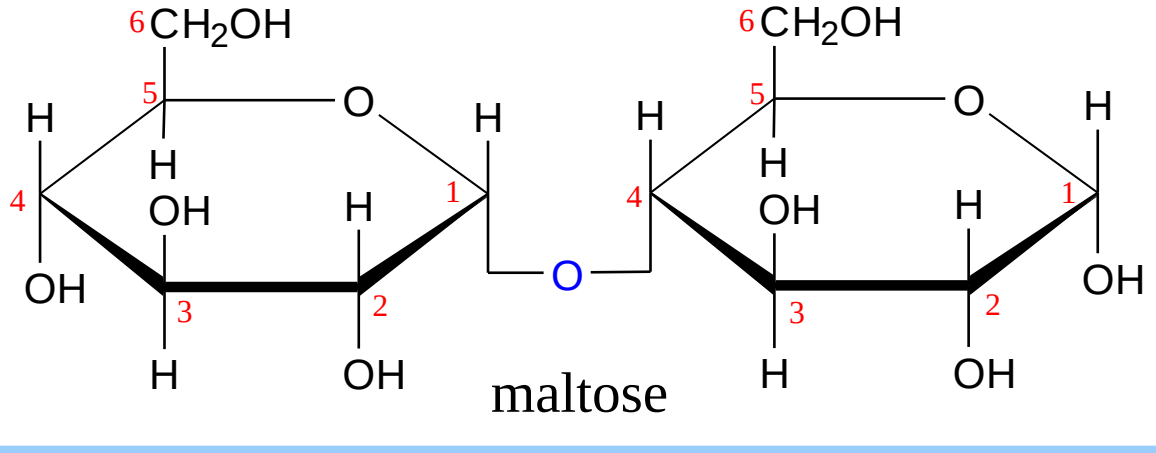
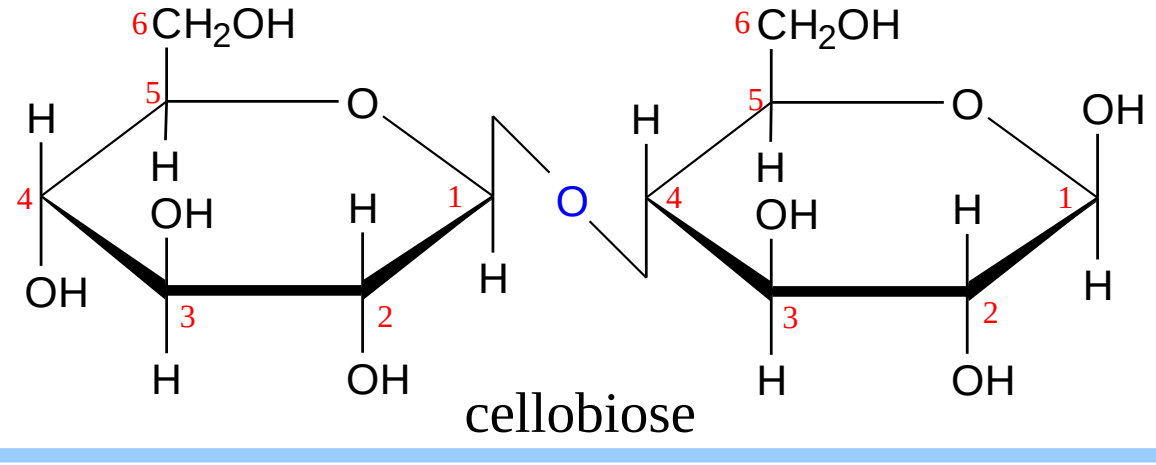

CH2OH
OH
O
OH
OH
OH
GLUCOSE
CH2OH
O
OH
OH
OH
CH2OH
FRUCTOSE
Dehydration
Synthesis
of Sucrose.
H2O
SUCROSE
CH2OH
O
H
OH
OH
O
CH2OH
O
OH
OH
CH2OH

Disaccharides:

Maltose, a cleavage product of starch (e.g., amylose), is a disaccharide with an $\alpha(1\rightarrow 4)$ glycosidic link between C1 - C4 OH of 2 glucoses.

It is the **α** anomer (C1 O points down).





Cellobiose, a product of cellulose breakdown, is the otherwise equivalent **β** anomer (O on C1 points up).

The $\beta(1\rightarrow 4)$ glycosidic linkage is represented as a zig-zag, but one glucose is actually **flipped over** relative to the other.

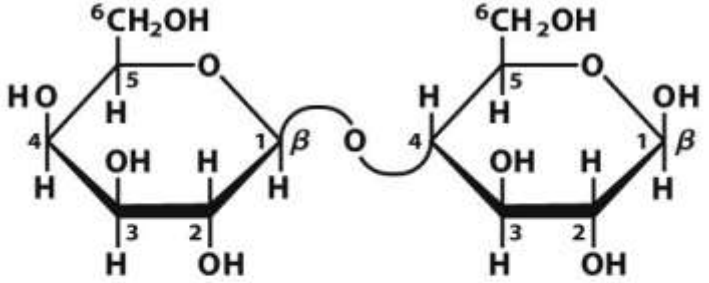
Other **disaccharides** include:

- **Sucrose**, common table sugar, has a glycosidic bond linking the anomeric hydroxyls of glucose & fructose.

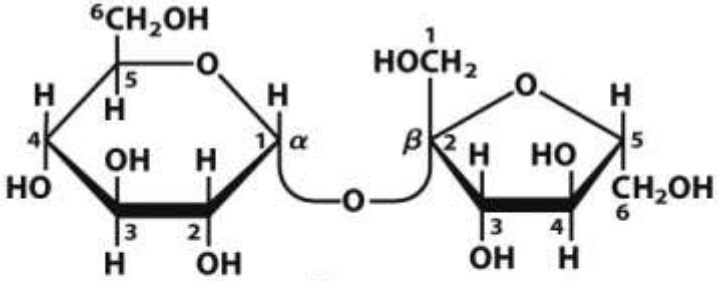
  Because the configuration at the anomeric C of glucose is α (O points down from ring), the linkage is α(1→2).

  The full name of sucrose is α-D-glucopyranosyl-(1→2)-β-D-fructopyranose.)

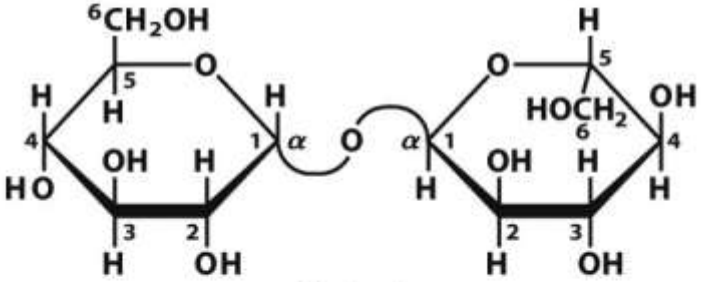
- **Lactose**, milk sugar, is composed of galactose & glucose, with β(1→4) linkage from the anomeric OH of galactose. Its full name is β-D-galactopyranosyl-(1→ 4)-α-D-glucopyranose



Lactose (β form)
β-D-galactopyranosyl-(1$\rightarrow$4)-β-D-glucopyranose
Gal(β1$\rightarrow$4)Glc



Sucrose
β-D-fructofuranosyl α-D-glucopyranoside
Fru(2$\beta\leftrightarrow\alpha$1)Glc $\equiv$ Glc(α1$\leftrightarrow$2β)Fru



Trehalose
α-D-glucopyranosyl α-D-glucopyranoside
Glc(α1$\leftrightarrow$1α)Glc

Figure 7-12
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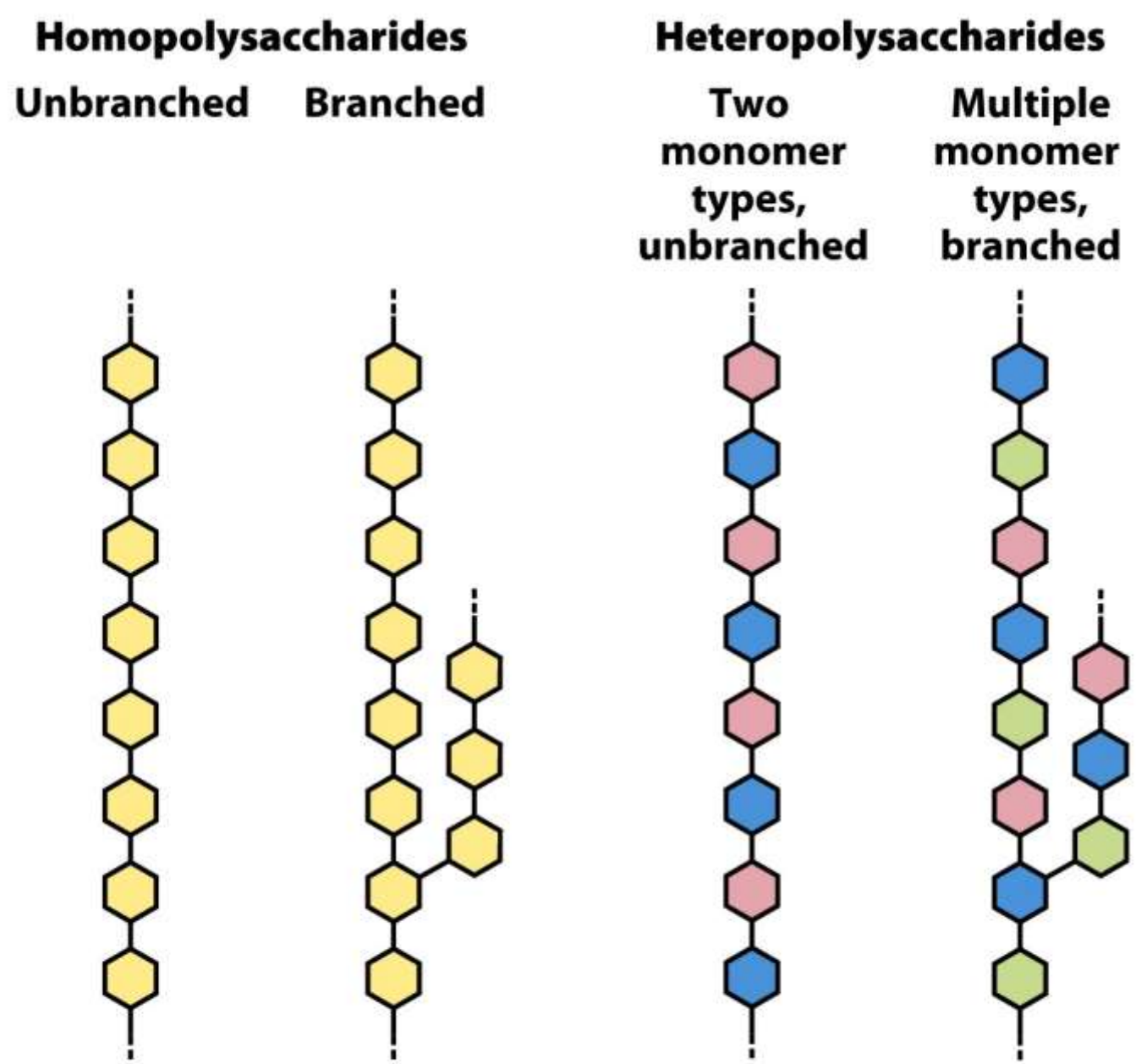
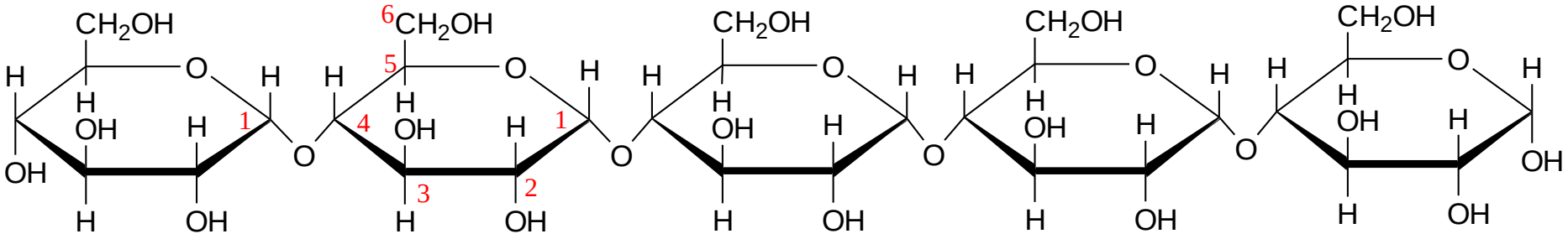


Figure 7-13
Lehninger Principles of Biochemistry, Fifth Edition



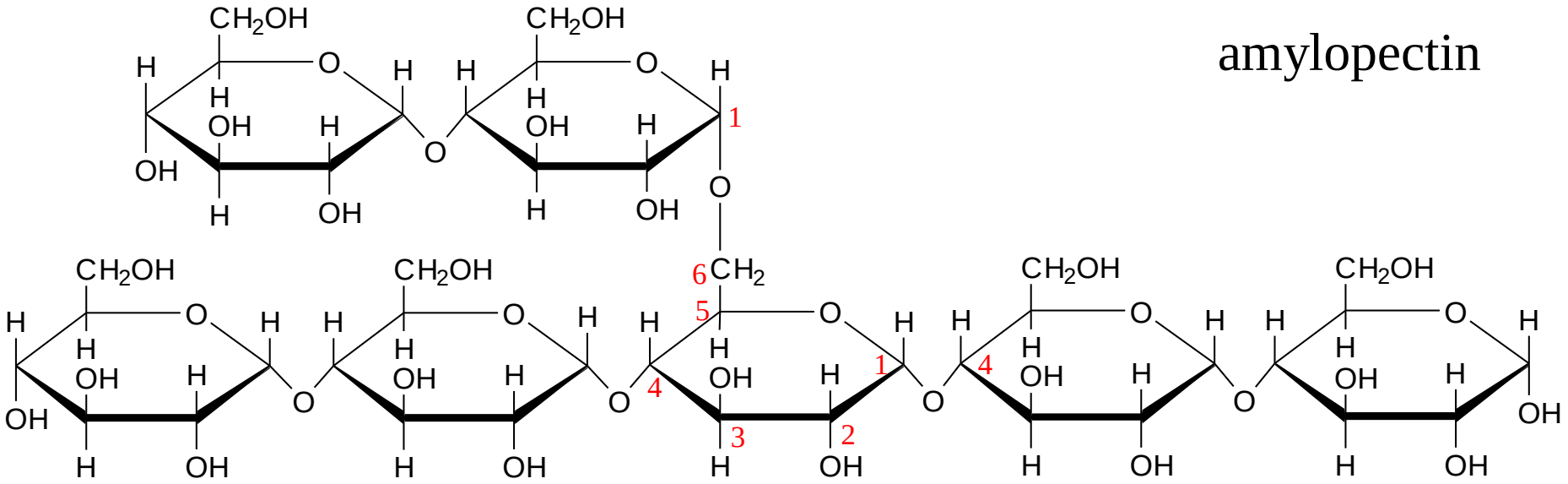
Polysaccharides:

Plants store glucose as **amylose** or **amylopectin**, glucose polymers collectively called starch.

Glucose storage in **polymeric** form **minimizes osmotic effects**.

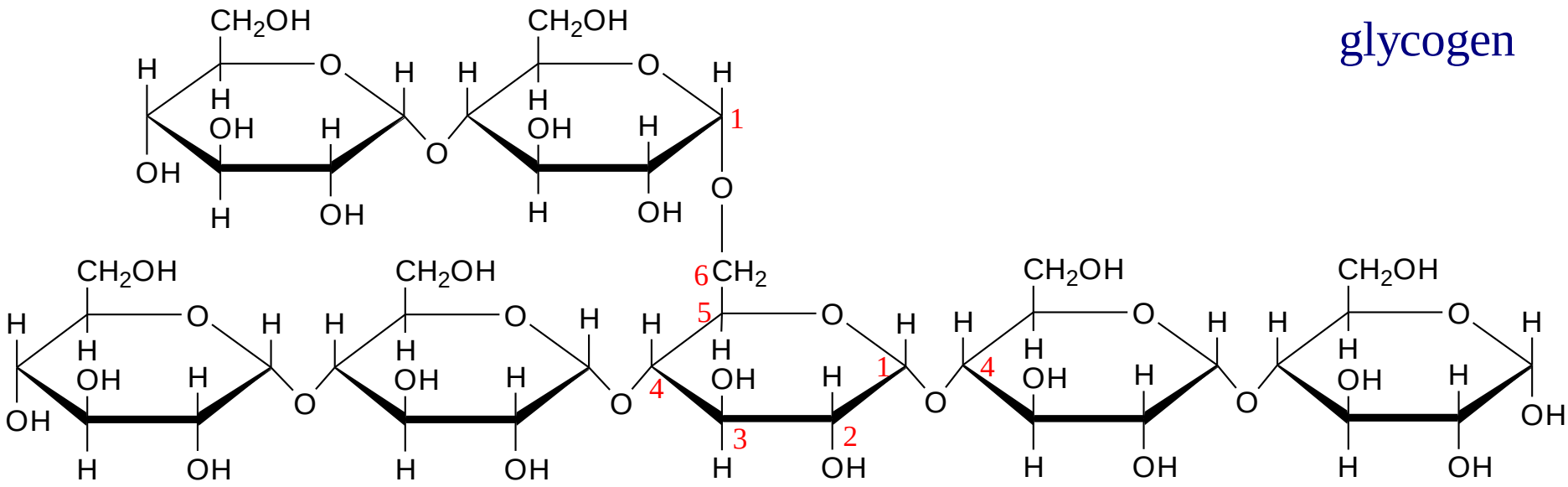
Amylose is a glucose polymer with **α(1→4)** linkages.

The end of the polysaccharide with an anomeric C1 not involved in a glycosidic bond is called the **reducing end**.



Amylopectin is a glucose polymer with mainly α(1→4) linkages, but it also has **branches** formed by α(1→6) linkages. Branches are generally longer than shown above.

The branches produce a compact structure & provide multiple chain ends at which enzymatic cleavage can occur.

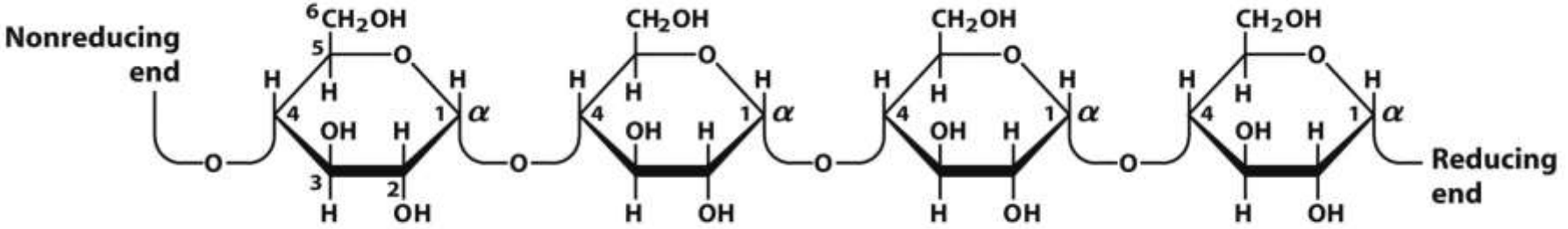


Glycogen, the glucose storage polymer in **animals**, is similar in structure to amylopectin.

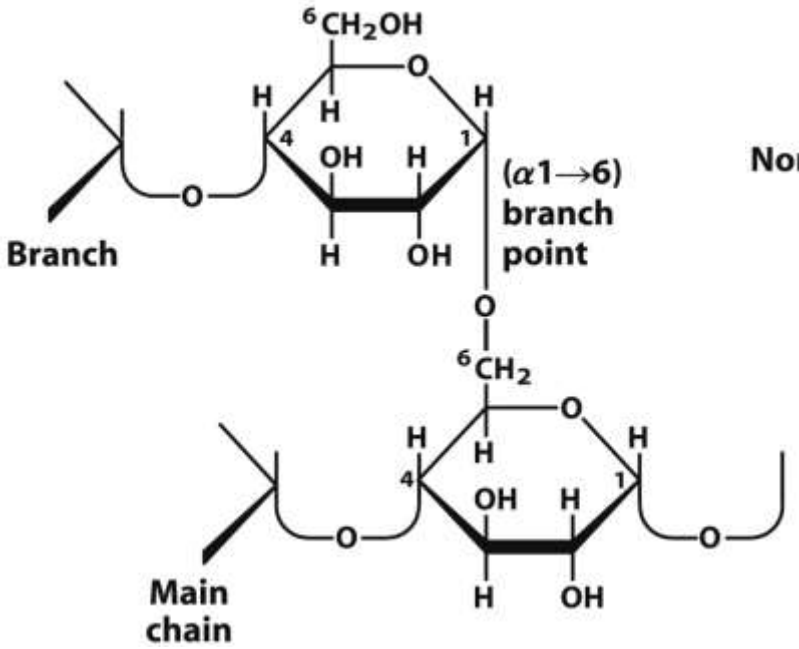
But glycogen has **more** $\alpha(1\rightarrow6)$ **branches**.

The highly branched structure permits rapid glucose release from glycogen stores, e.g., in muscle during exercise.

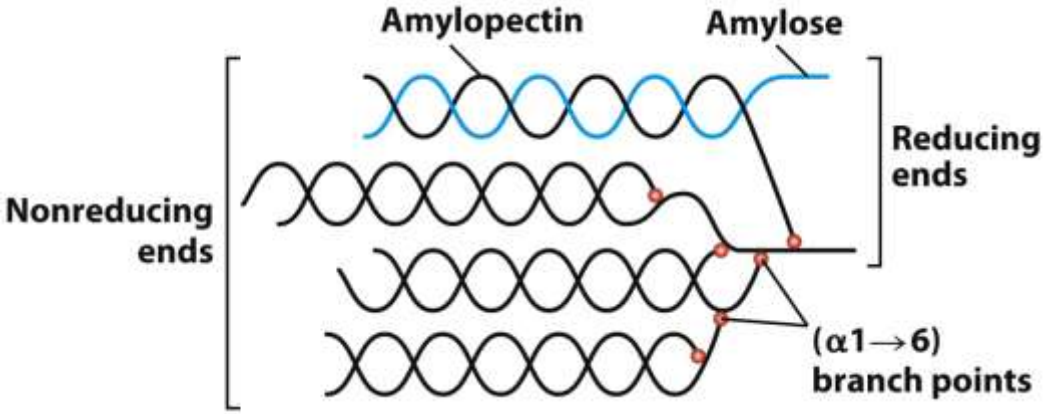
The ability to rapidly mobilize glucose is more essential to animals than to plants.



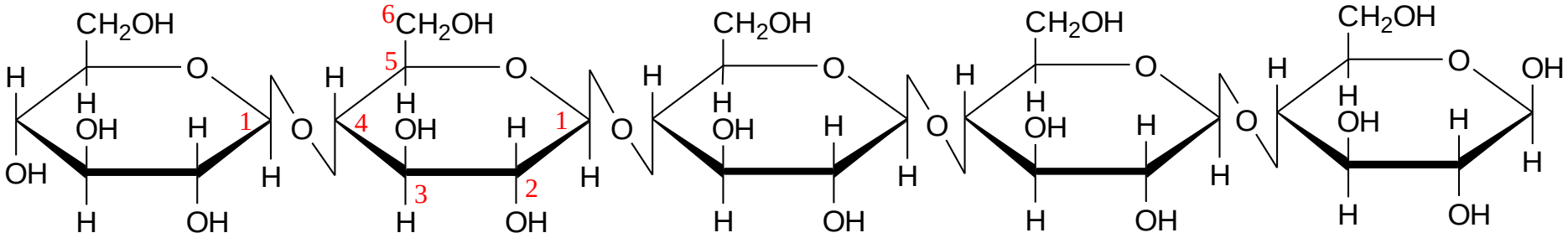
Amylose



Amylopectin and Glycogen



Starch Structure

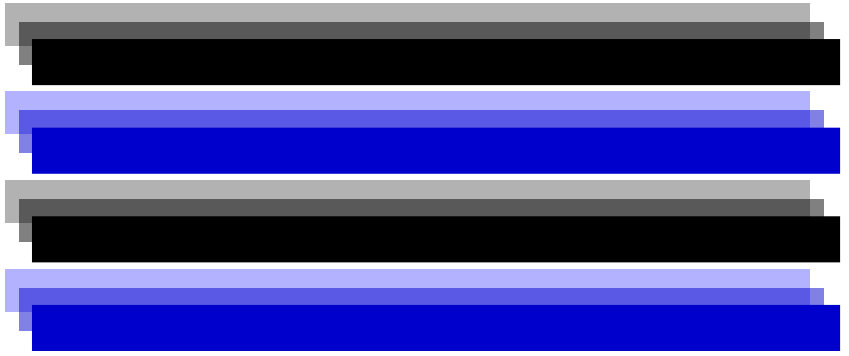


cellulose

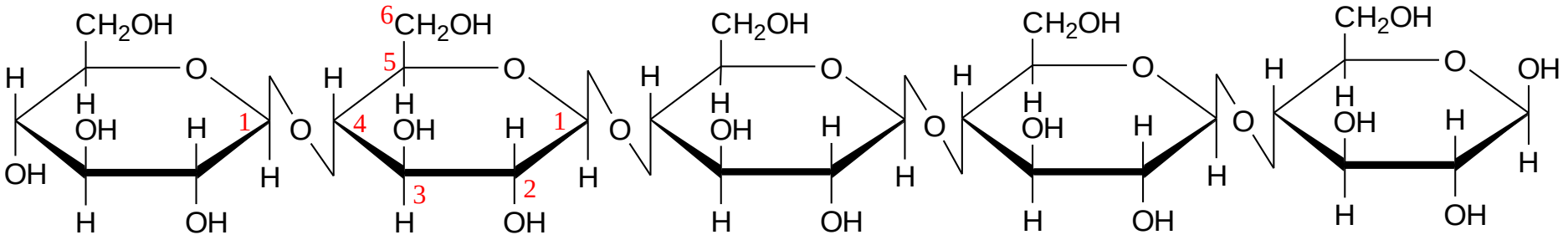
Cellulose, a major constituent of plant cell walls, consists of long linear chains of glucose with β(1→4) linkages.

Every other glucose is flipped over, due to β linkages.

This promotes intra-chain and inter-chain H-bonds and van der Waals interactions, that cause cellulose chains to be straight & rigid, and pack with a crystalline arrangement in thick bundles - microfibrils.



Schematic of arrangement of cellulose chains in a microfibril.



cellulose

Multisubunit **Cellulose Synthase** complexes in the plasma membrane spin out from the cell surface microfibrils consisting of 36 parallel, interacting cellulose chains.

These **microfibrils** are very **strong**.

The **role** of cellulose is to impart strength and rigidity to plant cell walls, which can withstand high hydrostatic pressure gradients. Osmotic swelling is prevented.

Cellulose

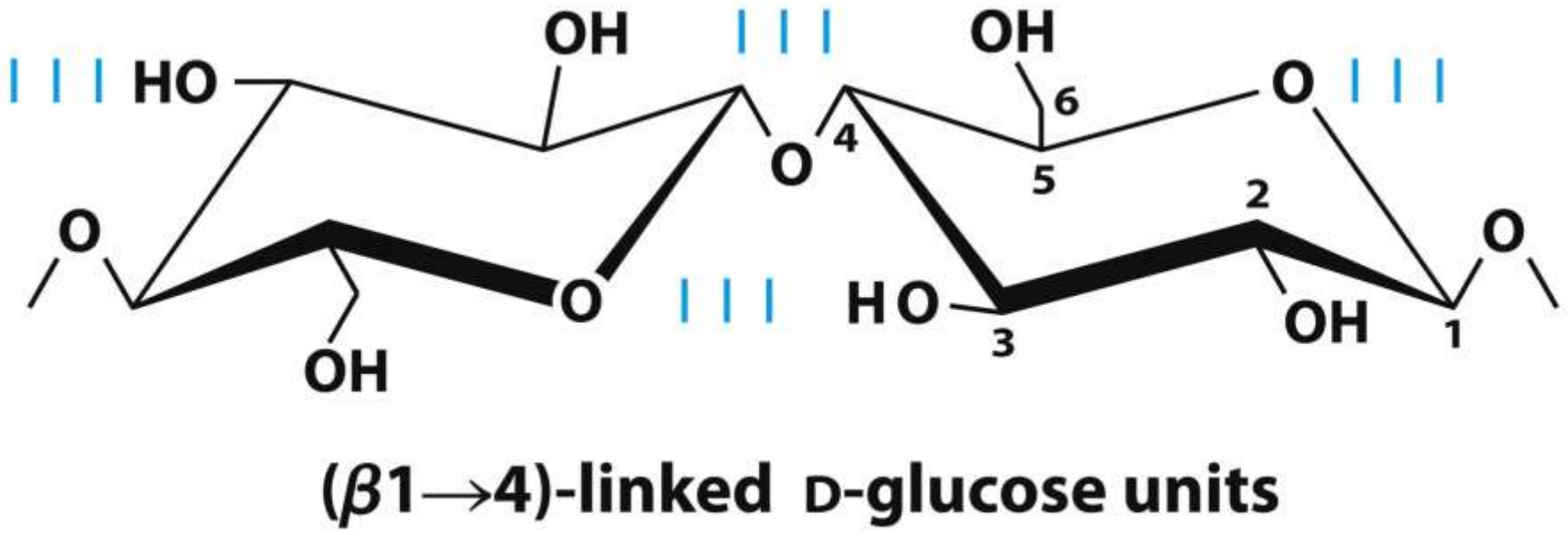


Figure 7-14
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French Fries versus Fiber

Humans digest starch and glycogen ingested in their diet using α-amylases, enzymes that hydrolyze (α 1$\rightarrow$4) glycosidic bonds.

Humans cannot hydrolyze (β1$\rightarrow$4) linkages of cellulose. Therefore cellulose is not a fuel source for humans. It is fiber.

Certain microorganisms have cellulases, enzymes that hydrolyze (β 1$\rightarrow$4) linkages of cellulose.
Cattle have these organisms in their rumen.
Termites have them in their intestinal tract.

Chitin is the principal component of the exoskeleton of arthropods like insects, lobsters, and crabs

Linear homopolysaccharide of N-acetylglucosamine in β(1→4) linkage

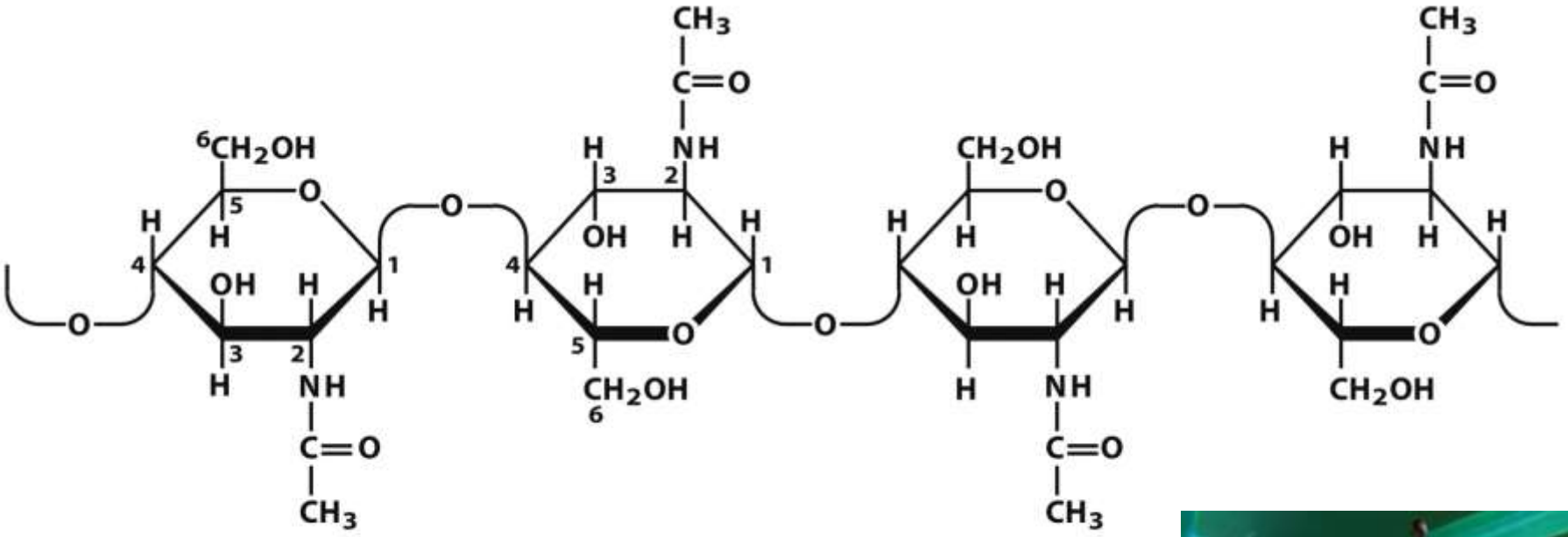

Figure 7-16a
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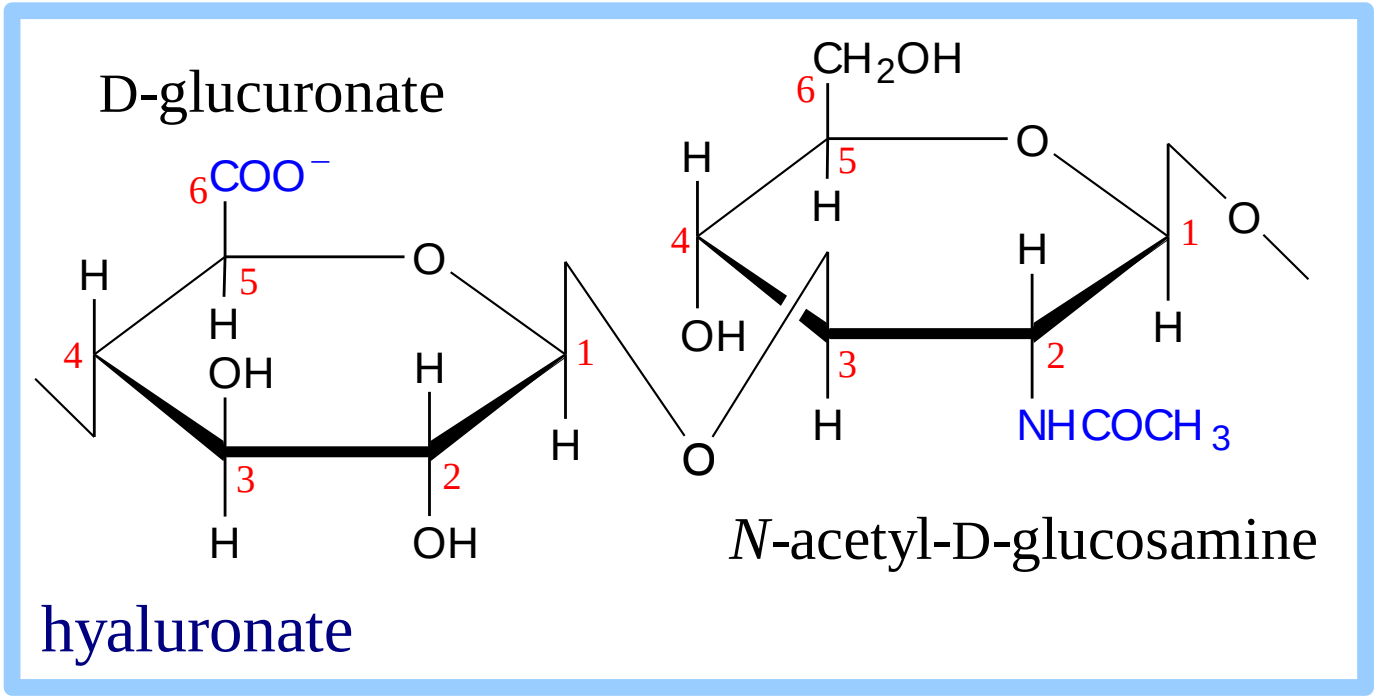
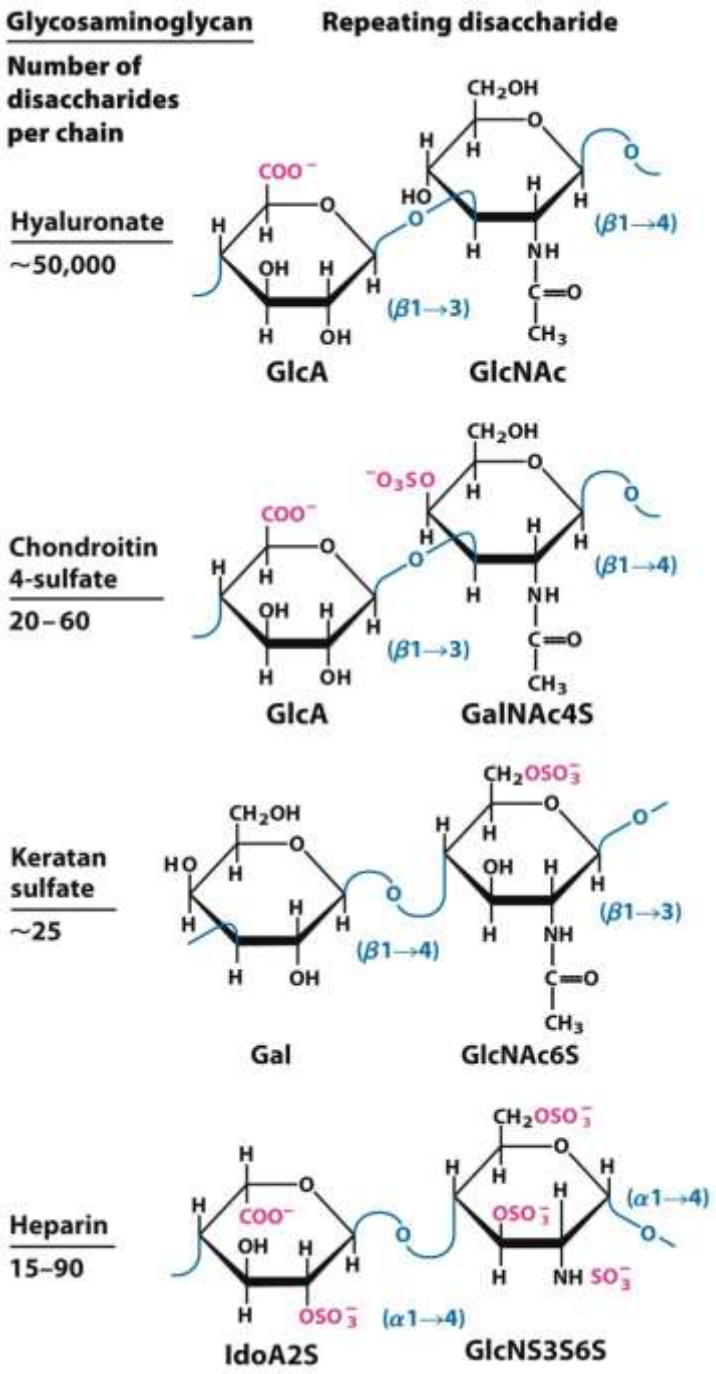


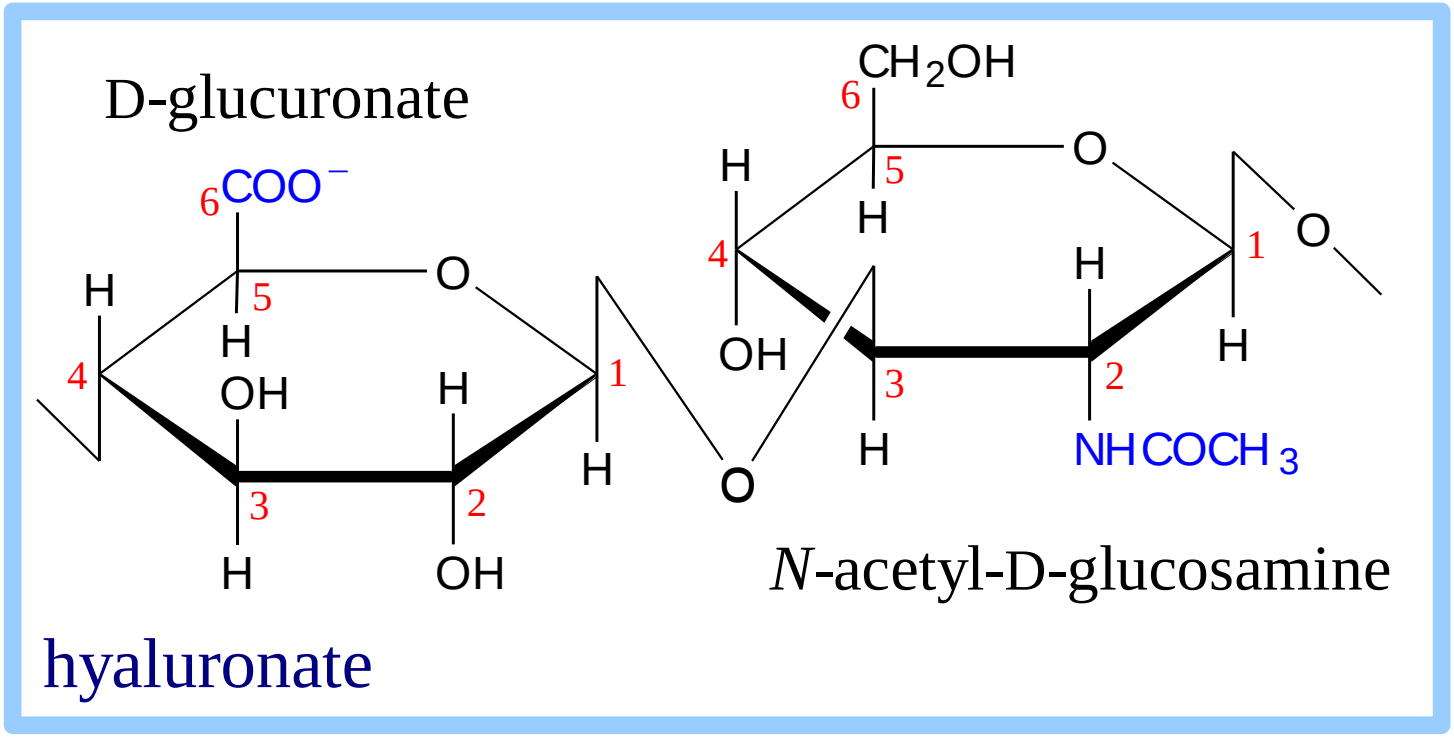
Glycosaminoglycans (mucopolysaccharides) are linear polymers of **repeating disaccharides**.

The constituent monosaccharides tend to be **modified**, with acidic groups, amino groups, sulfated hydroxyl and amino groups, etc.

Glycosaminoglycans tend to be **negatively charged**, because of the prevalence of acidic groups.



Glycosaminoglycans are found in the extracellular matrix



Hyaluronate (hyaluronan) is a **glycosaminoglycan** with a repeating disaccharide consisting of 2 glucose derivatives, glucuronate (glucuronic acid) & *N*-acetyl-glucosamine.

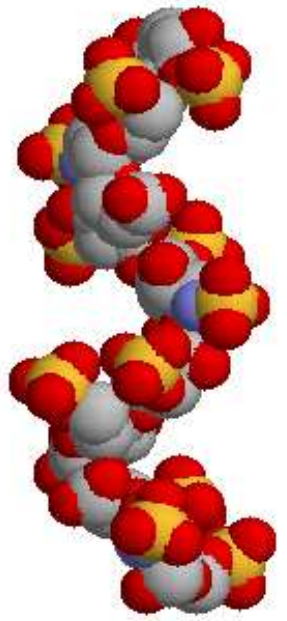
The glycosidic linkages are β(1→3) & β(1→4).

Heparin, a soluble glycosaminoglycan found in granules of mast cells, has a structure similar to that of heparan sulfates, but is more **highly sulfated**.

When released into the blood, it inhibits clot formation by interacting with the protein antithrombin.

Heparin has an **extended helical conformation**.

PDB 1RID

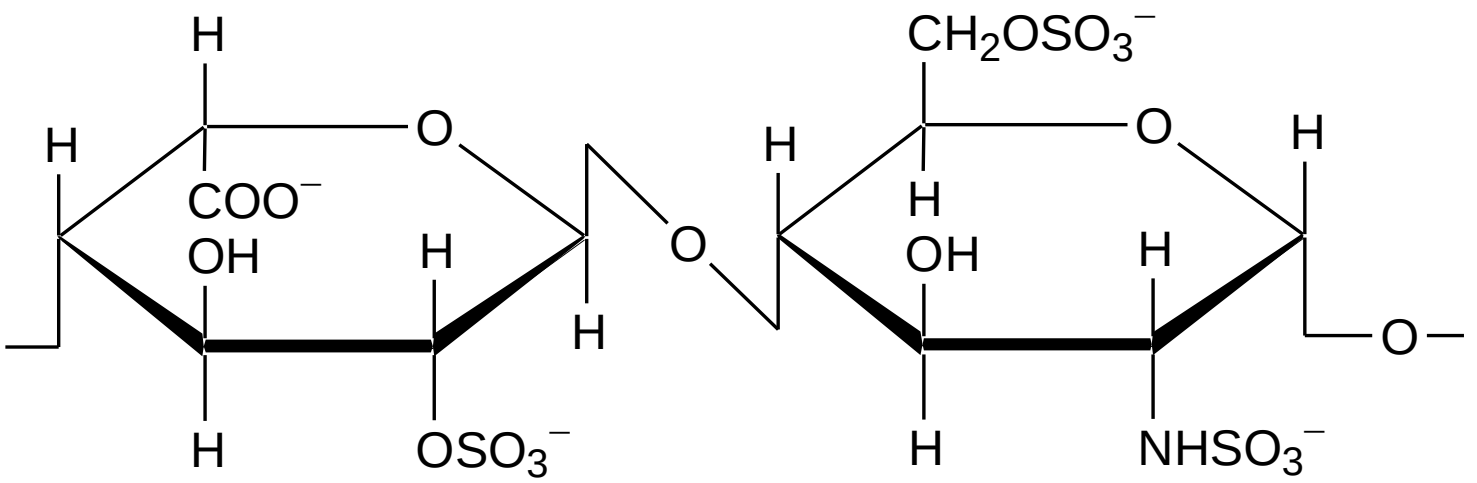


heparin: $(IDS\text{-}SGN)_5$

C O N S

Charge repulsion by the many negatively charged groups may contribute to this conformation.

Heparin shown has 10 residues, alternating IDS (iduronate-2-sulfate) & SGN (N-sulfo-glucosamine-6-sulfate).



heparin or heparan sulfate - examples of residues

Heparan sulfate is initially synthesized on a membrane-embedded core protein as a polymer of alternating ***N*-acetylglucosamine** and **glucuronate** residues.

Later, in segments of the polymer, glucuronate residues may be converted to the sulfated sugar **iduronic acid**, while *N*-acetylglucosamine residues may be deacetylated and/or sulfated.

TABLE 7–2 Structures and Roles of Some Polysaccharides

Polymer	Type*	Repeating unit†	Size (number of monosaccharide units)	Roles/significance
Starch				Energy storage: in plants
Amylose	Homo-	(α1→4)Glc, linear	50–5,000	
Amylopectin	Homo-	(α1→4)Glc, with (α1→6)Glc branches every 24–30 residues	Up to 10^6	
Glycogen	Homo-	(α1→4)Glc, with (α1→6)Glc branches every 8–12 residues	Up to 50,000	Energy storage: in bacteria and animal cells
Cellulose	Homo-	(β1→4)Glc	Up to 15,000	Structural: in plants, gives rigidity and strength to cell walls
Chitin	Homo-	(β1→4)GlcNAc	Very large	Structural: in insects, spiders, crustaceans, gives rigidity and strength to exoskeletons
Dextran	Homo-	(α1→6)Glc, with (α1→3) branches	Wide range	Structural: in bacteria, extracellular adhesive
Peptidoglycan	Hetero-; peptides attached	4)Mur2Ac(β1→4) GlcNAc(β1	Very large	Structural: in bacteria, gives rigidity and strength to cell envelope
Agarose	Hetero-	3)D-Gal(β1→4)3,6-anhydro-L-Gal(α1	1,000	Structural: in algae, cell wall material
Hyaluronan (a glycosamino-glycan)	Hetero-; acidic	4)GlcA(β1→3) GlcNAc(β1	Up to 100,000	Structural: in vertebrates, extracellular matrix of skin and connective tissue; viscosity and lubrication in joints

*Each polymer is classified as a homopolysaccharide (homo-) or heteropolysaccharide (hetero-).

†The abbreviated names for the peptidoglycan, agarose, and hyaluronan repeating units indicate that the polymer contains repeats of this disaccharide unit. For example, in peptidoglycan, the GlcNAc of one disaccharide unit is (β1→4)-linked to the first residue of the next disaccharide unit.

Table 7-2

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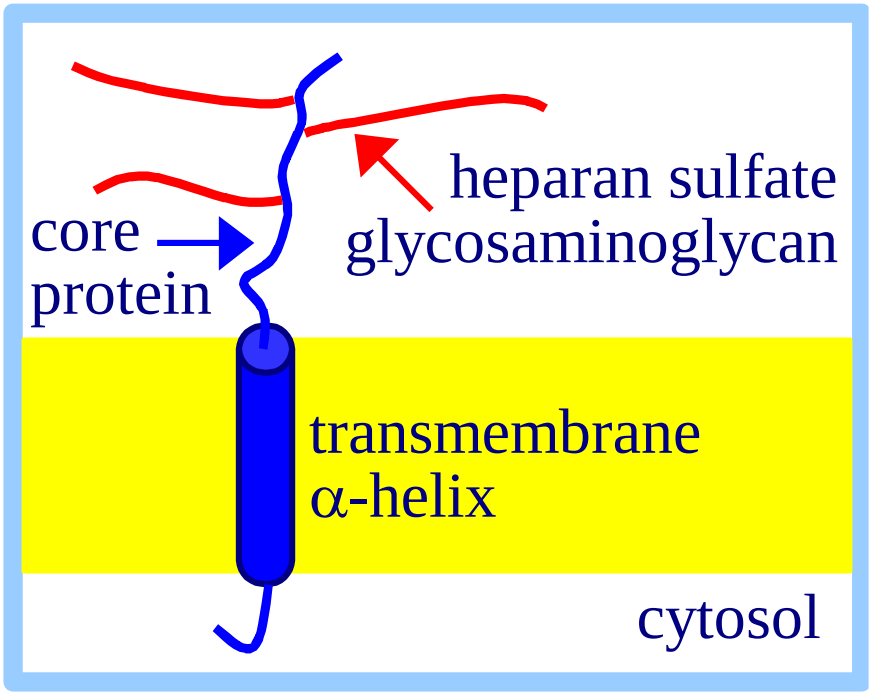

Proteoglycans are **glycosaminoglycans** that are covalently linked to serine residues of specific **core proteins**.

The glycosaminoglycan chain is synthesized by sequential addition of sugar residues to the core protein.

Cellular location of carbohydrates

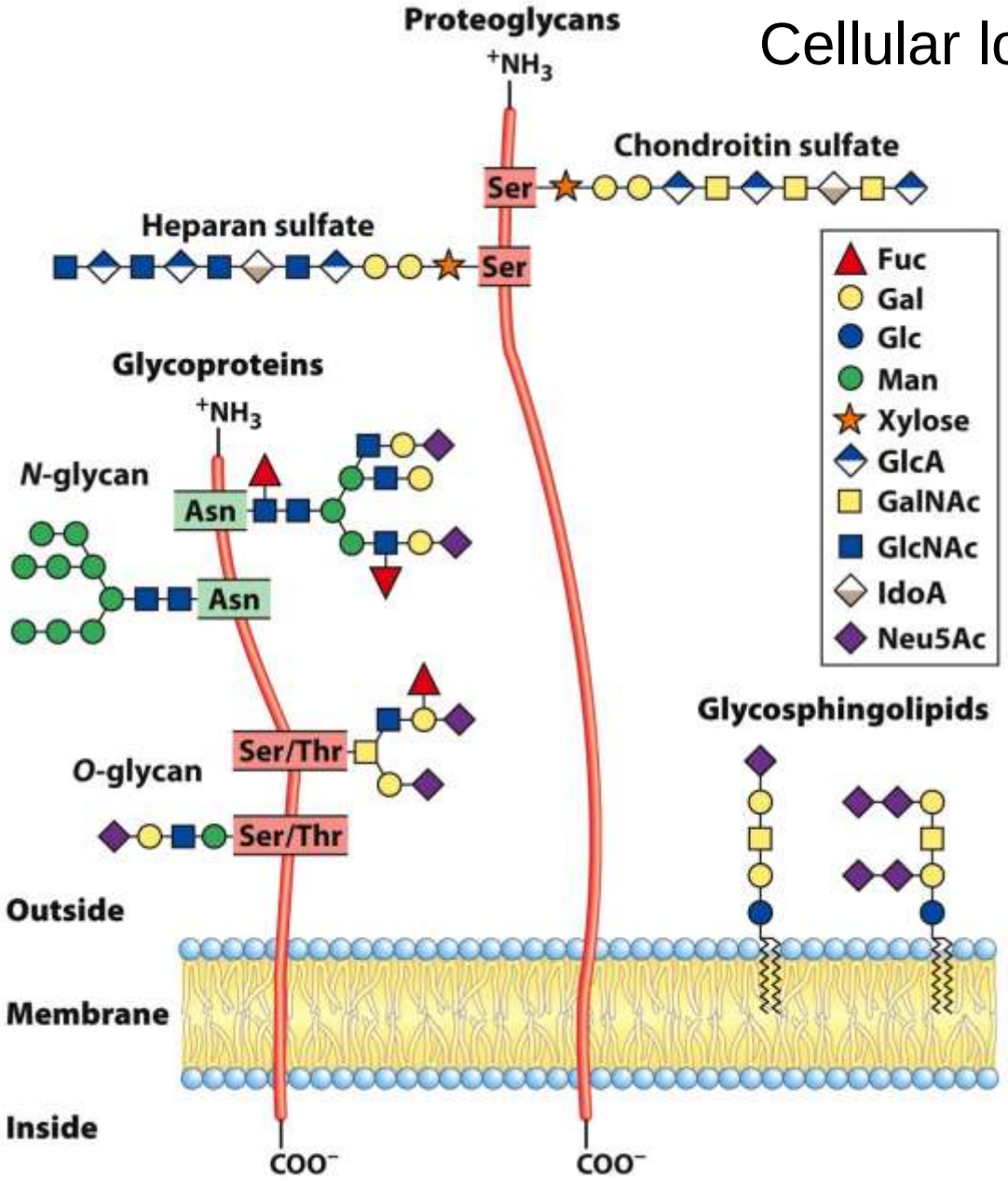

Figure 7-24
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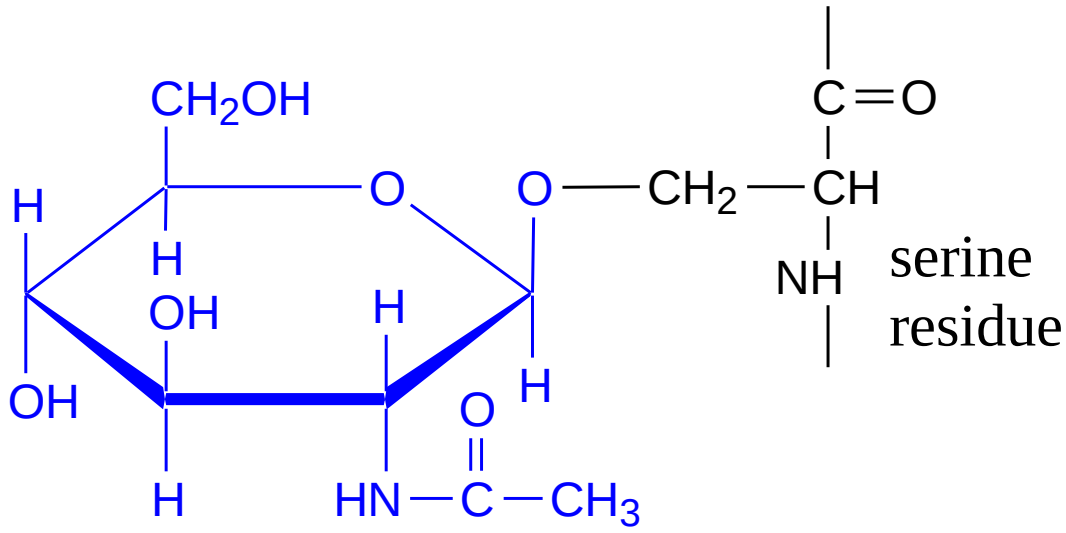
Oligosaccharides that are covalently attached to proteins or to membrane lipids may be linear or branched chains.

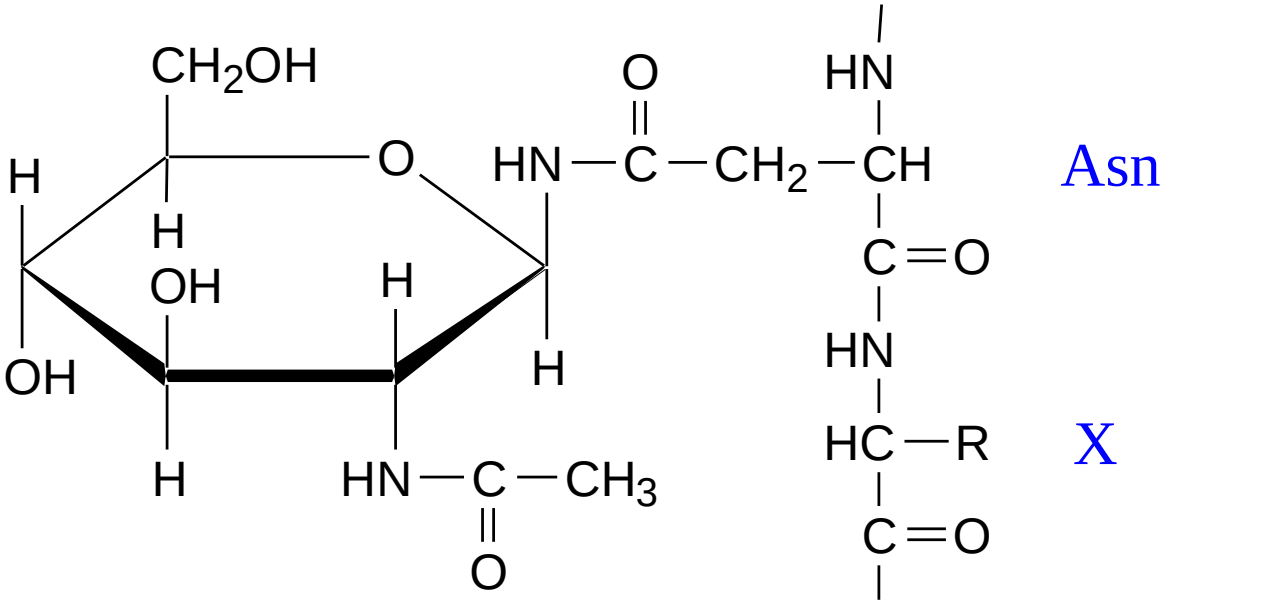


β-D-*N*-acetylglucosamine

O-linked oligosaccharide chains of glycoproteins vary in complexity.

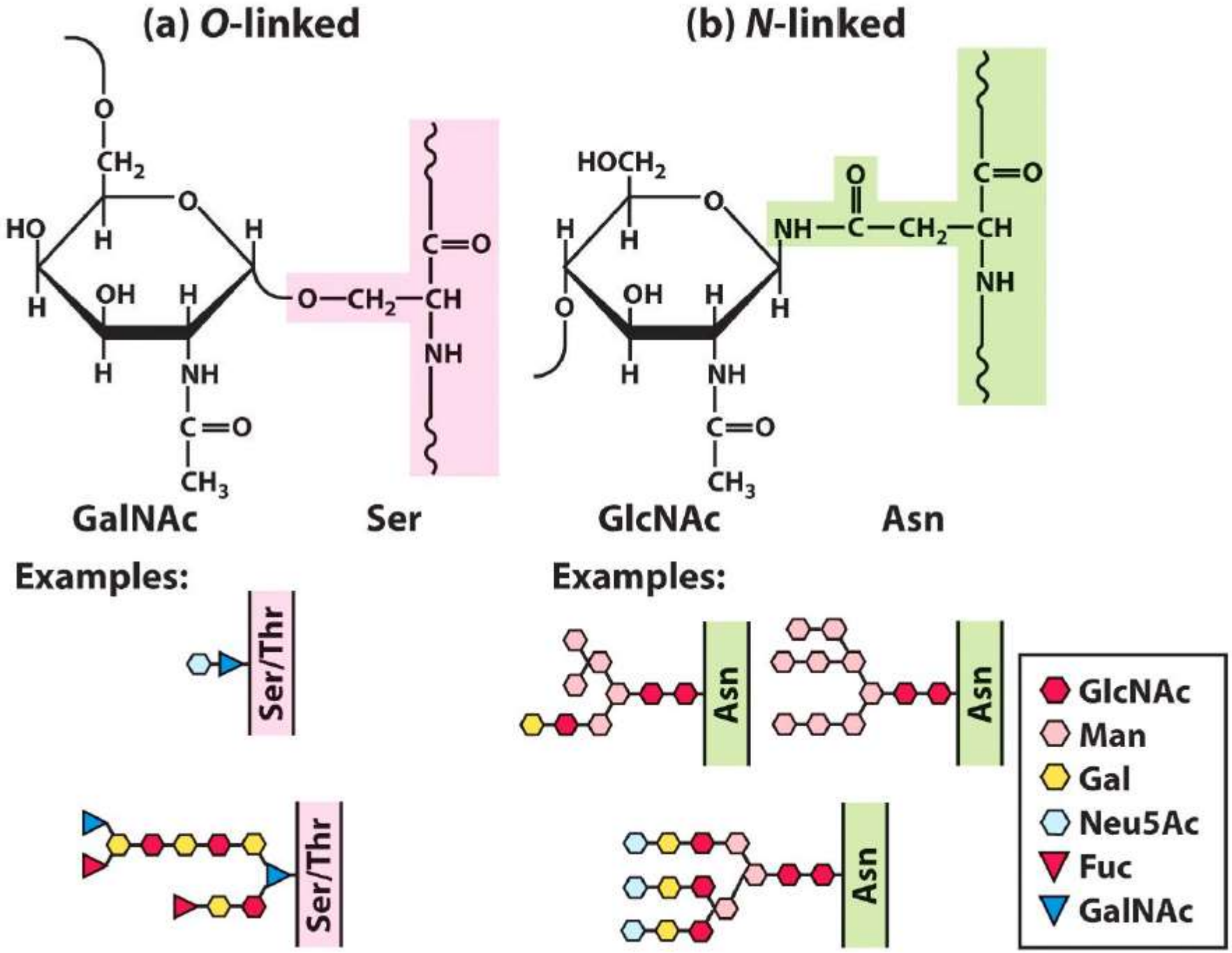
They link to a protein via a glycosidic bond between a sugar residue & a **serine or threonine OH**.

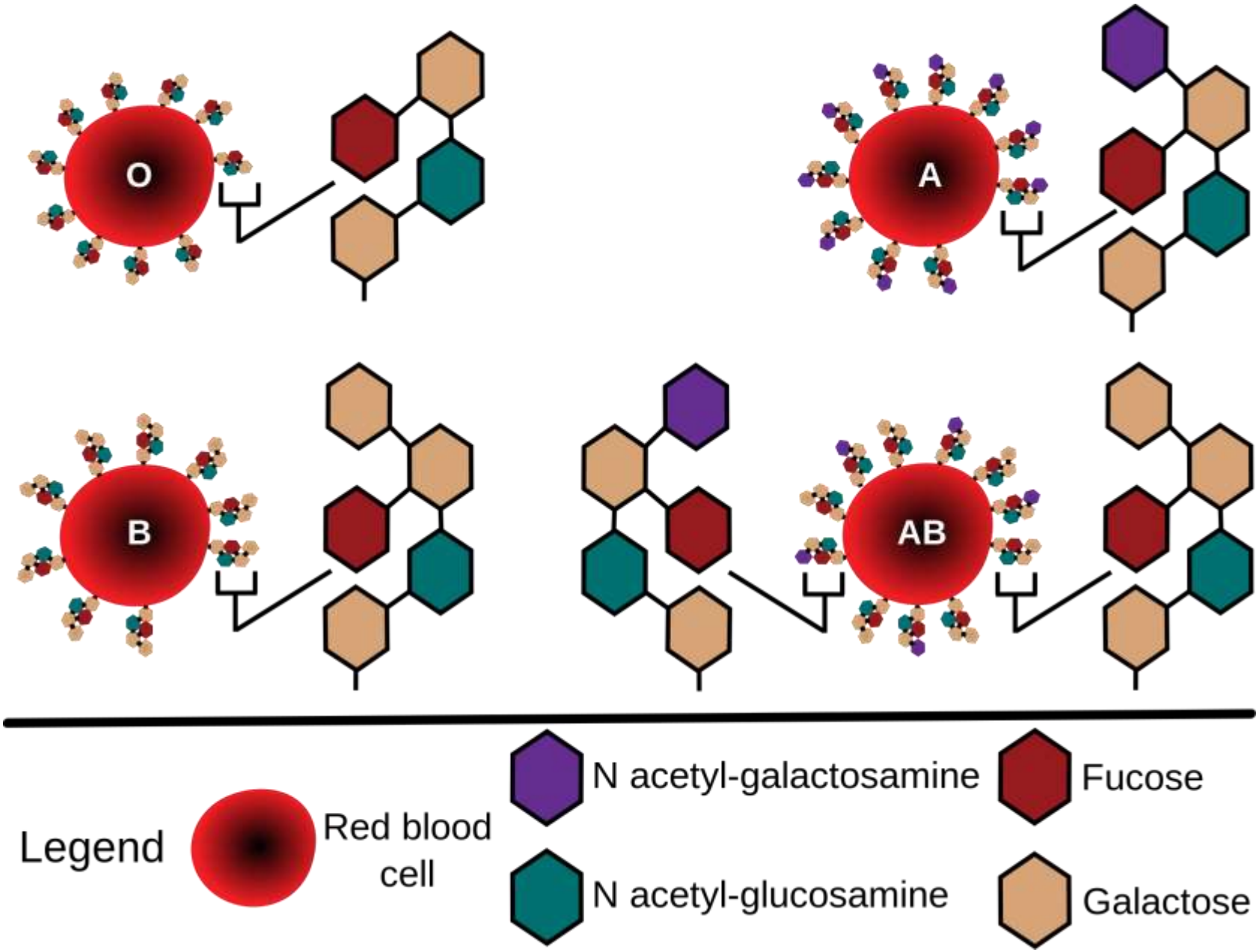
O-linked oligosaccharides have roles in **recognition**, **interaction**, and **enzyme regulation**.



***N*-linked oligosaccharides** of glycoproteins tend to be complex and branched.

First ***N*-acetylglucosamine** is linked to a protein via the side-chain N of an asparagine residue in a particular 3-amino acid sequence.


(a) O-linked
(b) N-linked
GalNAc
Ser
GlcNAc
Asn
Examples:
Examples:
Ser/Thr
Ser/Thr
Asn
Asn
Asn
GlcNAc
Man
Gal
Neu5Ac
Fuc
GalNAc


O
A
B
AB
Legend
Red blood cell
N acetyl-galactosamine
Fucose
N acetyl-glucosamine
Galactose

Blood group antigens are specific classes of oligosaccharides that may be bound to proteins, lipid, or membranes of RBC.

Before a patient can be given a blood transfusion or tissue transplantation, the blood or tissue types must be matched with the donor.

Use of mismatched blood could be fatal to the pateint.

Glycation

- The nonenzymatic reaction of glucose with a primary amino group in hemoglobin begins with

(1) formation of a Schiff base, which

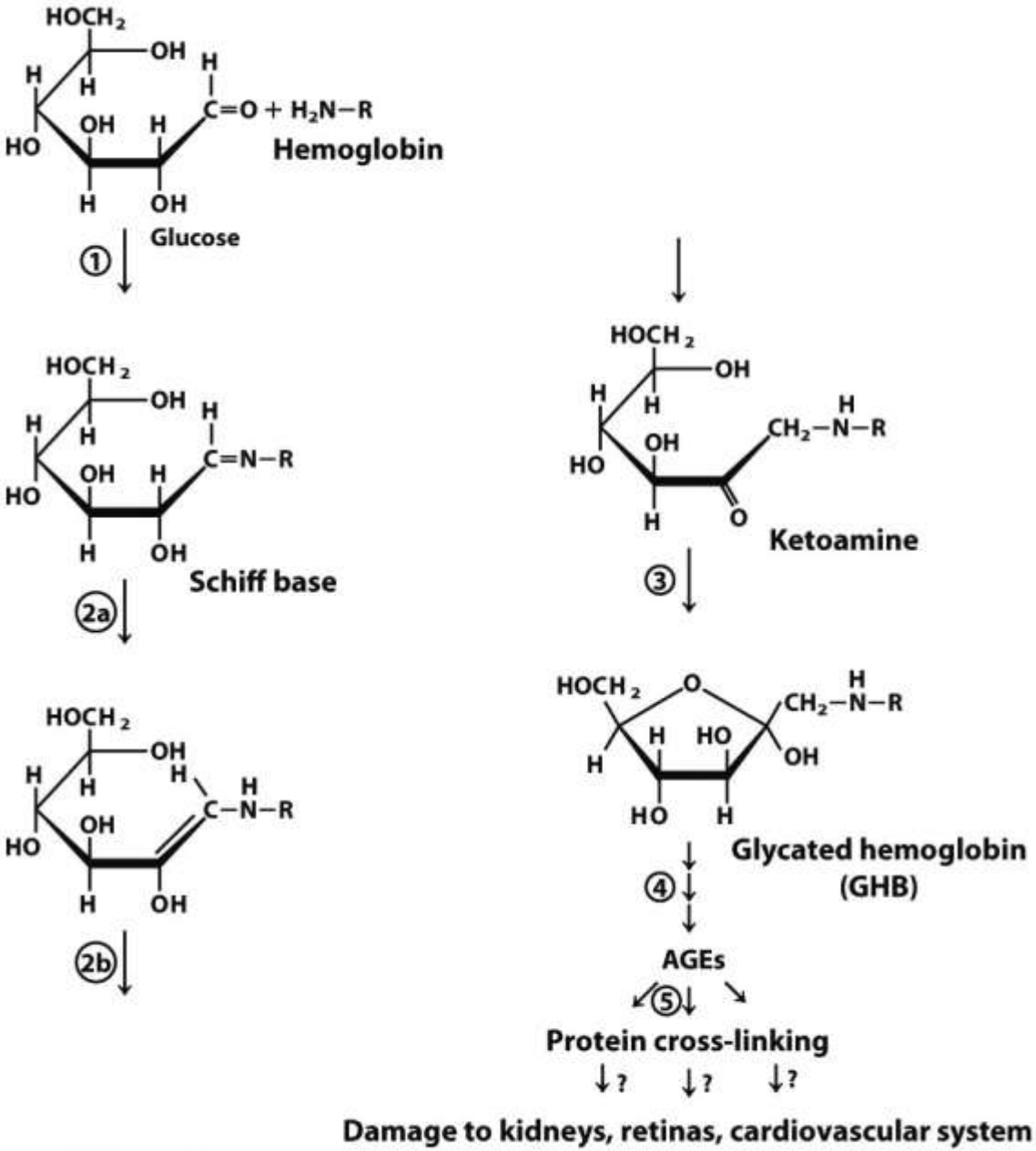
(2) undergoes the Amadori rearrangement to generate a stable product;

(3) this ketoimine can further cyclize to yield GHB.

Glycation

(4) Subsequent reactions generate advanced glycation end products (AGEs), such as ε-*N*-carboxymethyllysine and methylglyoxal, compounds that:

(5) can damage other proteins by cross-linking them, causing pathological changes.



Box 7-1 figure 2

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