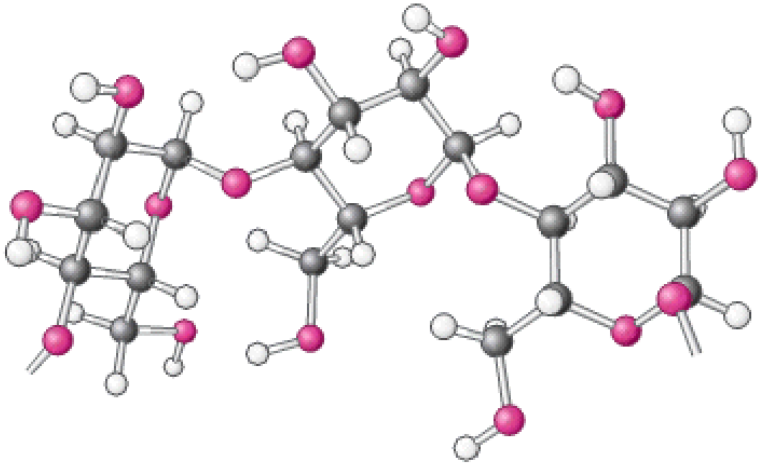
CARBOHYDRATES

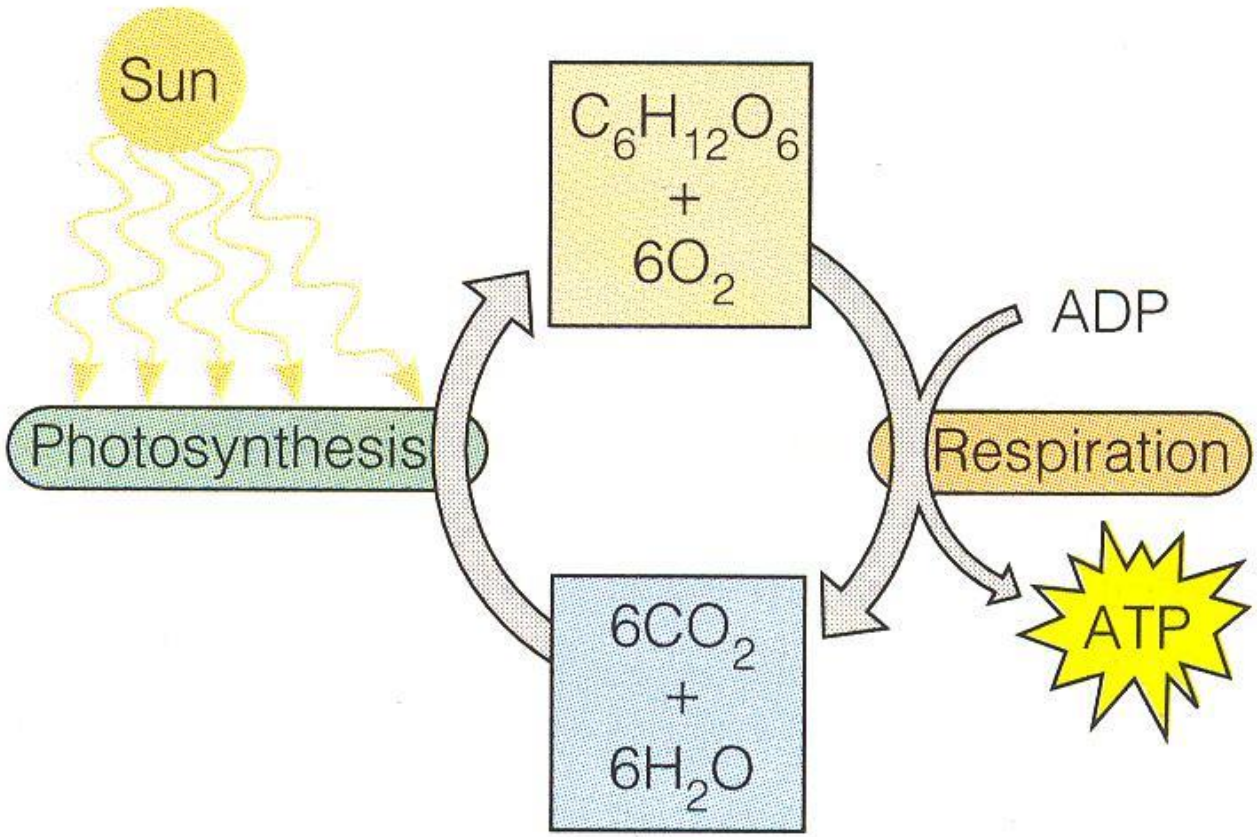
- Carbohydrates are the most abundant biomolecules on Earth.



- Carbohydrates are polyhydroxy aldehydes or ketones, or substances that yield such compounds on hydrolysis.

- Many, but not all, carbohydrates have the empirical formula (CH2O)n; some also contain nitrogen, phosphorus, or sulfur.

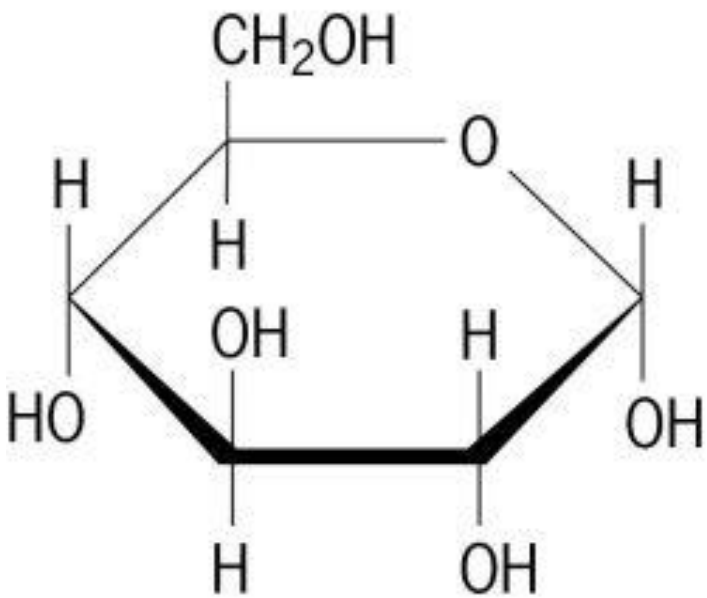
❖Each year, photosynthesis converts more than 100 billion metric tons of CO_2 and H_2O into cellulose and other plant products.



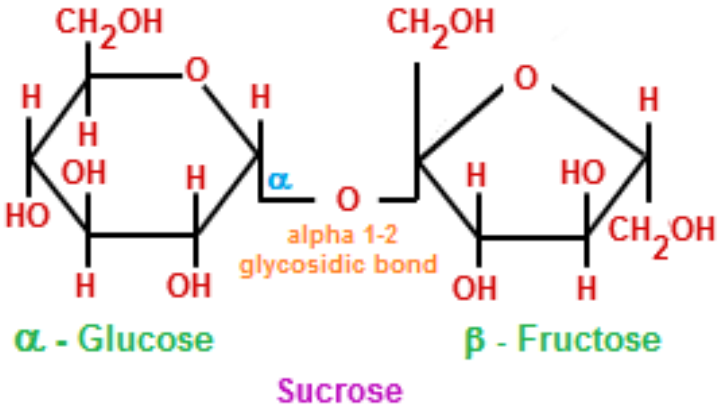
Functions of Monosaccharides

- Certain carbohydrates (sugar and starch) are a dietary staple in most parts of the world, and the oxidation of carbohydrates is the central energy-yielding pathway in most nonphotosynthetic cells.
- Carbohydrate polymers (also called glycans) serve as structural and protective elements in the cell walls of bacteria and plants and in the connective tissues of animals.
- Other carbohydrate polymers lubricate skeletal joints and participate in recognition and adhesion between cells.
- Complex carbohydrate polymers covalently attached to proteins or lipids act as signals that determine the intracellular destination or metabolic fate of these hybrid molecules, called glycoconjugates.

- There are three major size classes of carbohydrates: monosaccharides, oligosaccharides, and polysaccharides.
- **Monosaccharides**, or simple sugars, consist of a single polyhydroxy aldehyde or ketone unit.
- The most abundant monosaccharide in nature is the six-carbon sugar D-glucose, sometimes referred to as dextrose.
- Monosaccharides of four or more carbons tend to have cyclic structures.

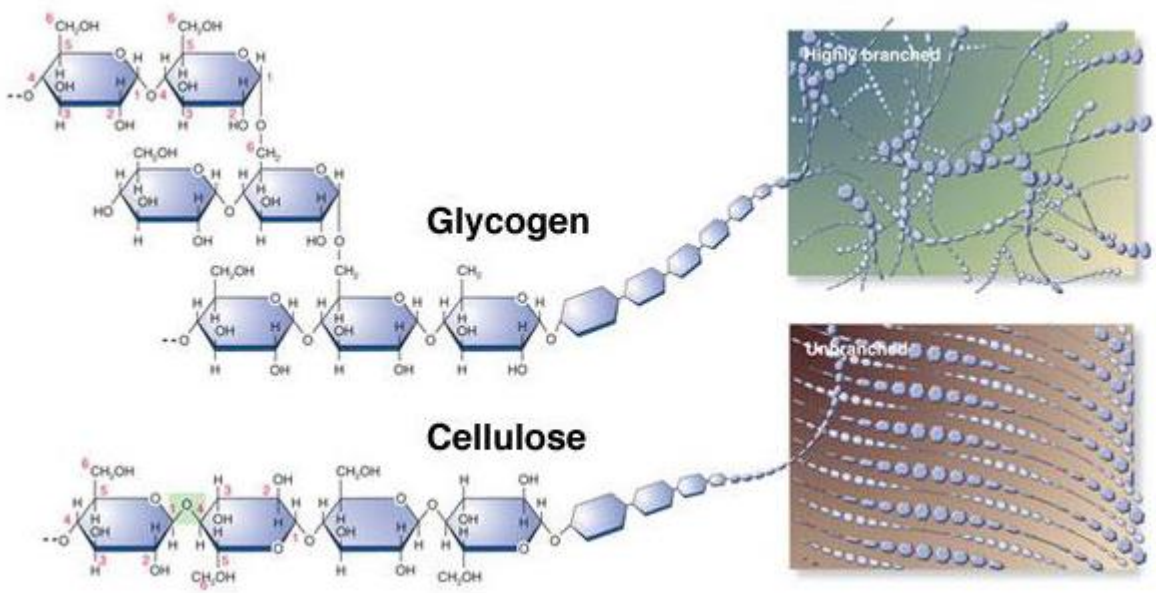


- **Oligosaccharides** consist of short chains of monosaccharide units, or residues, joined by characteristic linkages called glycosidic bonds.
- The most abundant are the disaccharides, with two monosaccharide units.
- Typical is sucrose (cane sugar), which consists of the six-carbon sugars D-glucose and D-fructose.



- All common monosaccharides and disaccharides have names ending with the suffix "-ose."
- In cells, most oligosaccharides consisting of three or more units do not occur as free entities but are joined to nonsugar molecules (lipids or proteins) in glycoconjugates.

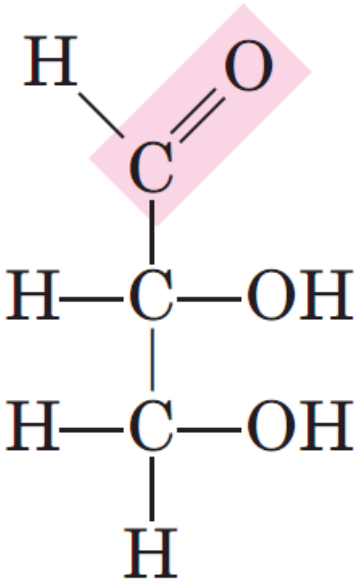
- The **polysaccharides** are sugar polymers containing more than 20 or so monosaccharide units; some have hundreds or thousands of units.
- Some polysaccharides, such as cellulose, are linear chains; others, such as glycogen, are branched.
- Both glycogen and cellulose consist of recurring units of D-glucose, but they differ in the type of glycosidic linkage and consequently have strikingly different properties and biological roles.



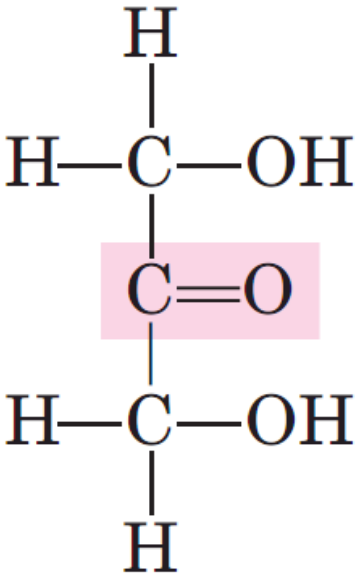
Monosaccharides

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

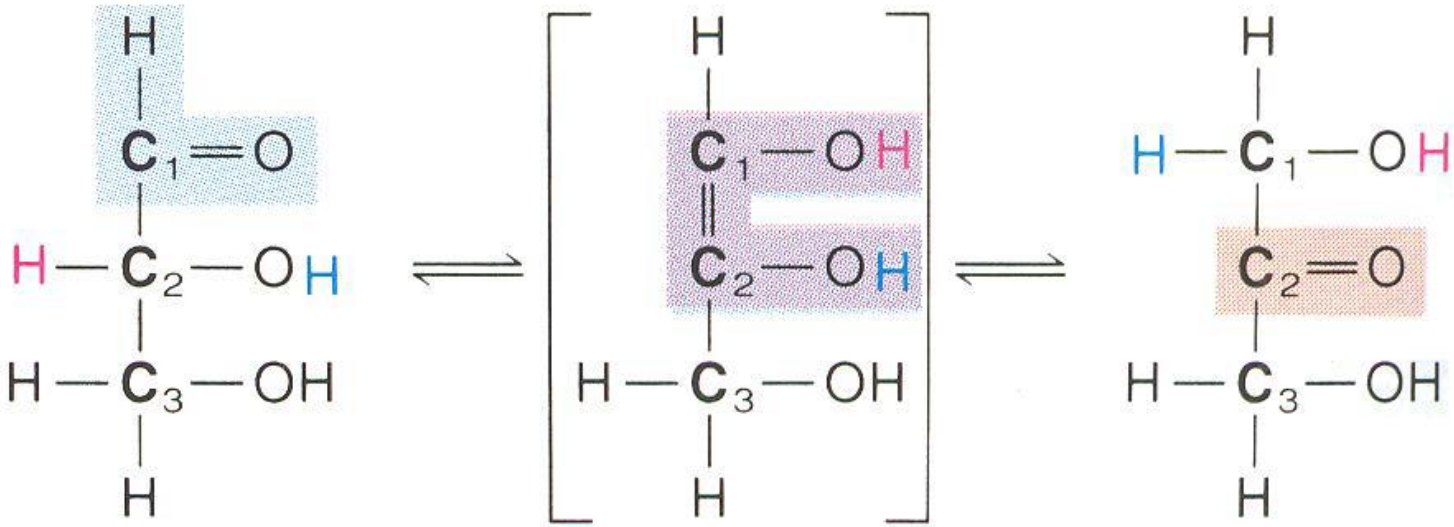
❖The simplest monosaccharides are the two three-carbon trioses: glyceraldehyde, an aldotriose, and dihydroxyacetone, a ketotriose



Glyceraldehyde, an aldotriose



Dihydroxyacetone, a ketotriose



D-Glyceraldehyde (aldotriose) | Enediol intermediate | Dihydroxyacetone (ketotriose)

❖These two compounds are structural isomers, tautomers, and could be turn each other via enediol intermediate.

❖Monosaccharides are colorless, crystalline solids that are freely soluble in water but insoluble in nonpolar solvents. Most have a sweet taste.

❖Monosaccharides with four, five, six, and seven carbon atoms in their backbones are called, respectively, tetroses, pentoses, hexoses, and heptoses.

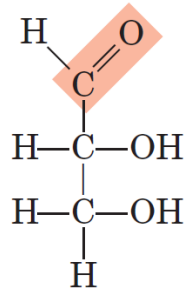
Number of Carbon	**Name**	**Aldehyde**	**Ketone**
3	Triose	Glyceraldehyde	Dihydroxyacetone
4	Tetrose	Erythrose	Erythrulose
5	Pentose	Ribose, Xylose	Ribulose, Xylulose
6	Hexose	Glucose, Galactose, Mannose	Fructose, Sorbose
7	Heptose		Heptulose

Monosaccharides Have Asymmetric Centers

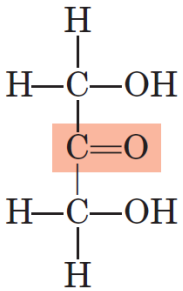
❖All the monosaccharides except dihydroxyacetone contain one or more asymmetric (chiral) carbon atoms and thus occur in optically active isomeric forms.

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

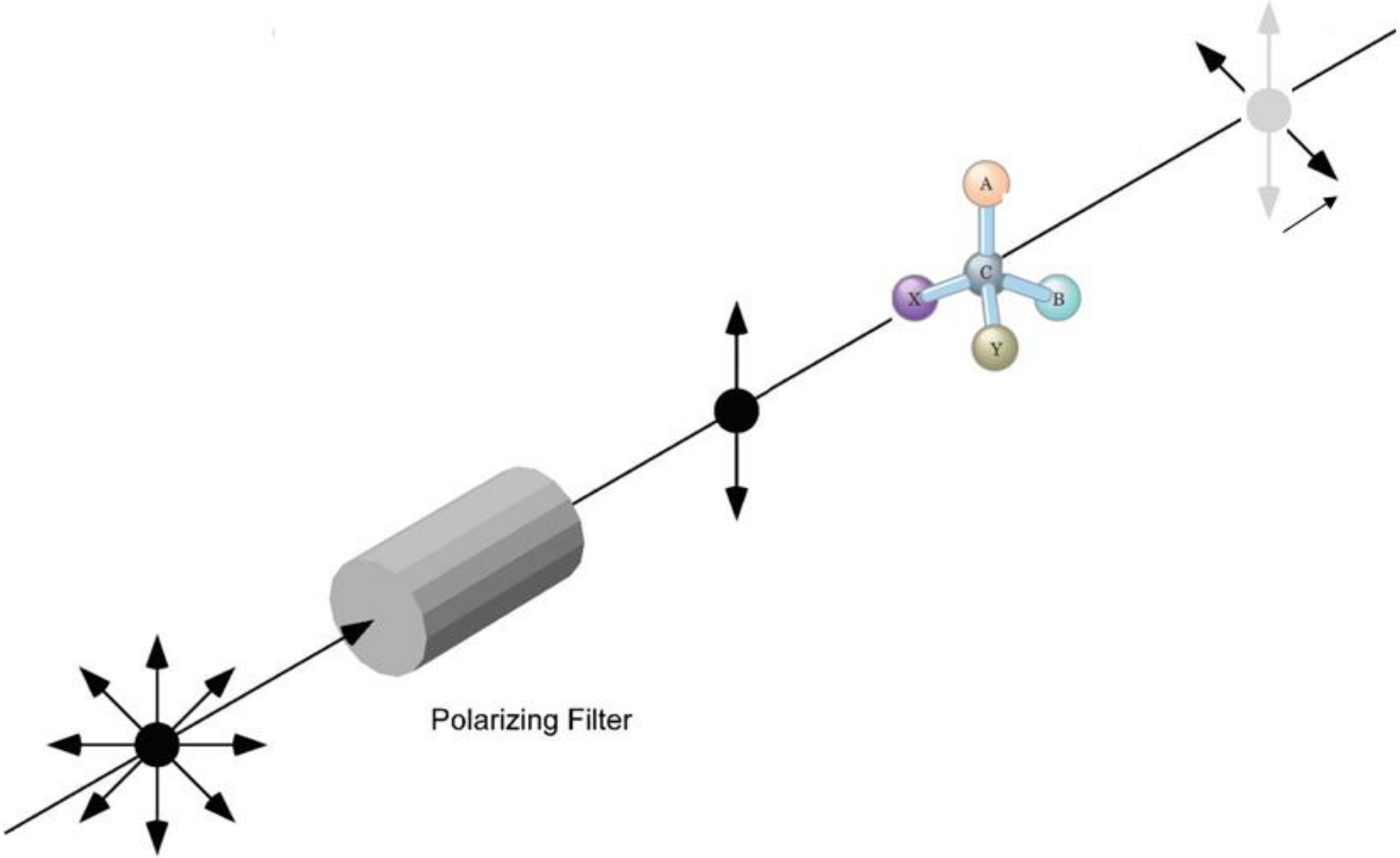
❖The simplest aldose, glyceraldehyde, contains one chiral center (the middle carbon atom) and therefore has two different optical isomers, or enantiomers.

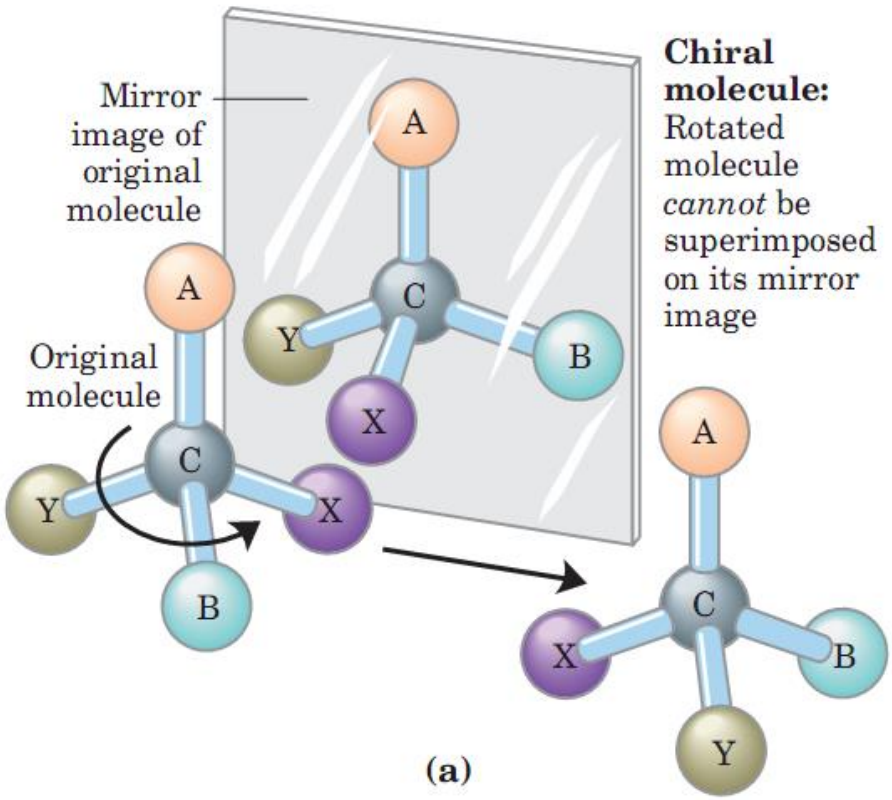


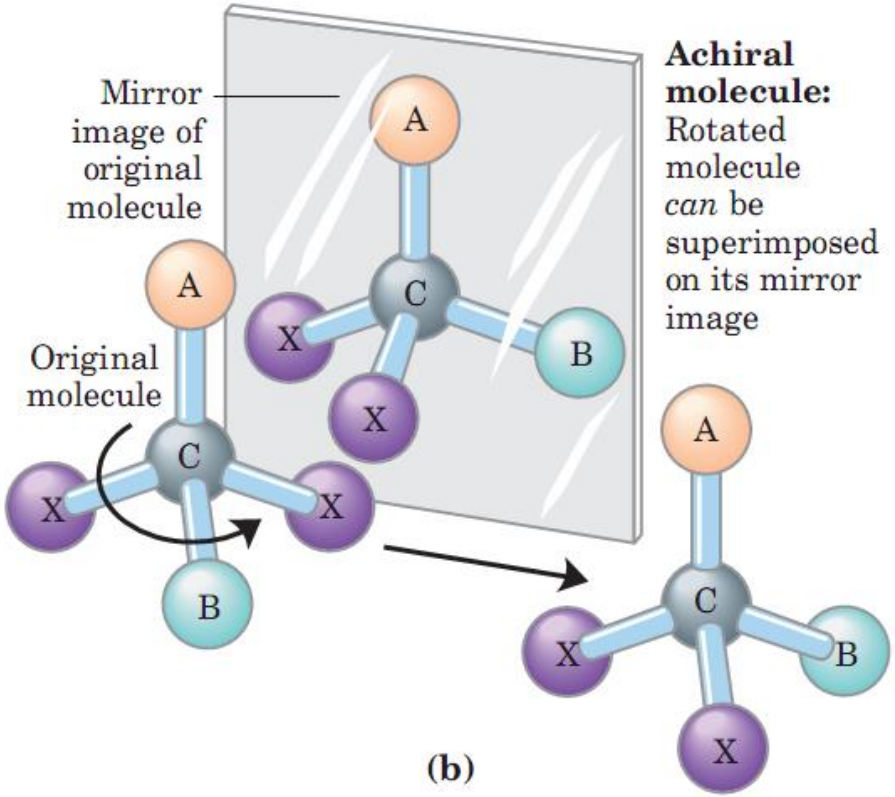
D-Glyceraldehyde, an aldotriose

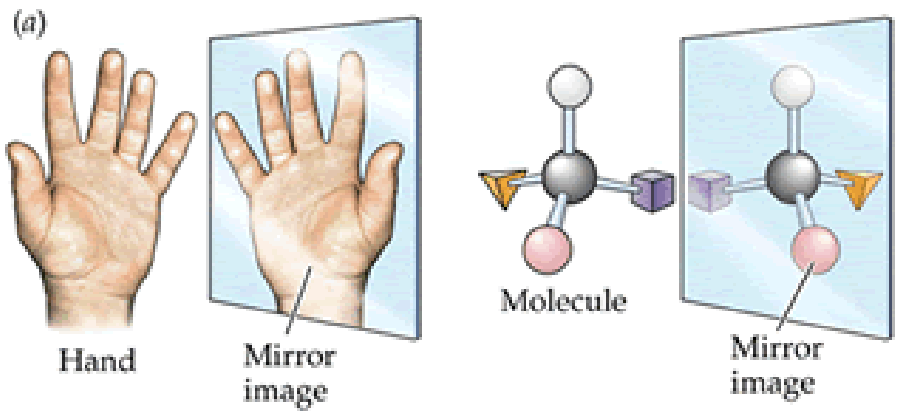


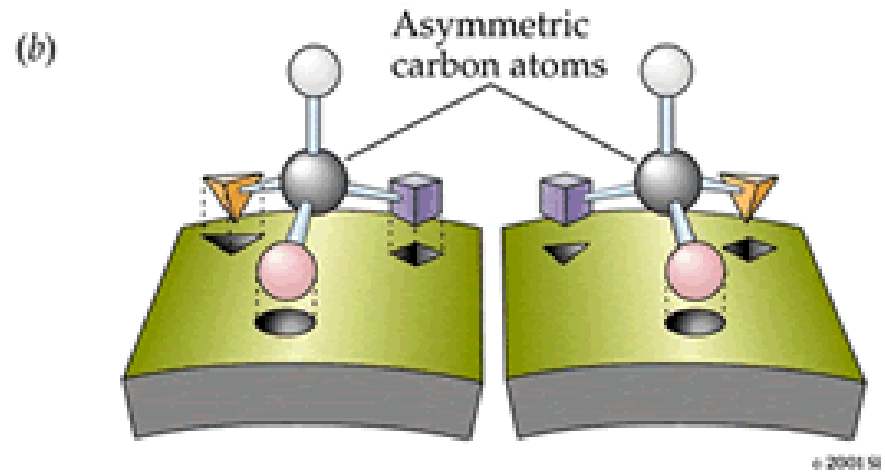
Dihydroxyacetone, a ketotriose

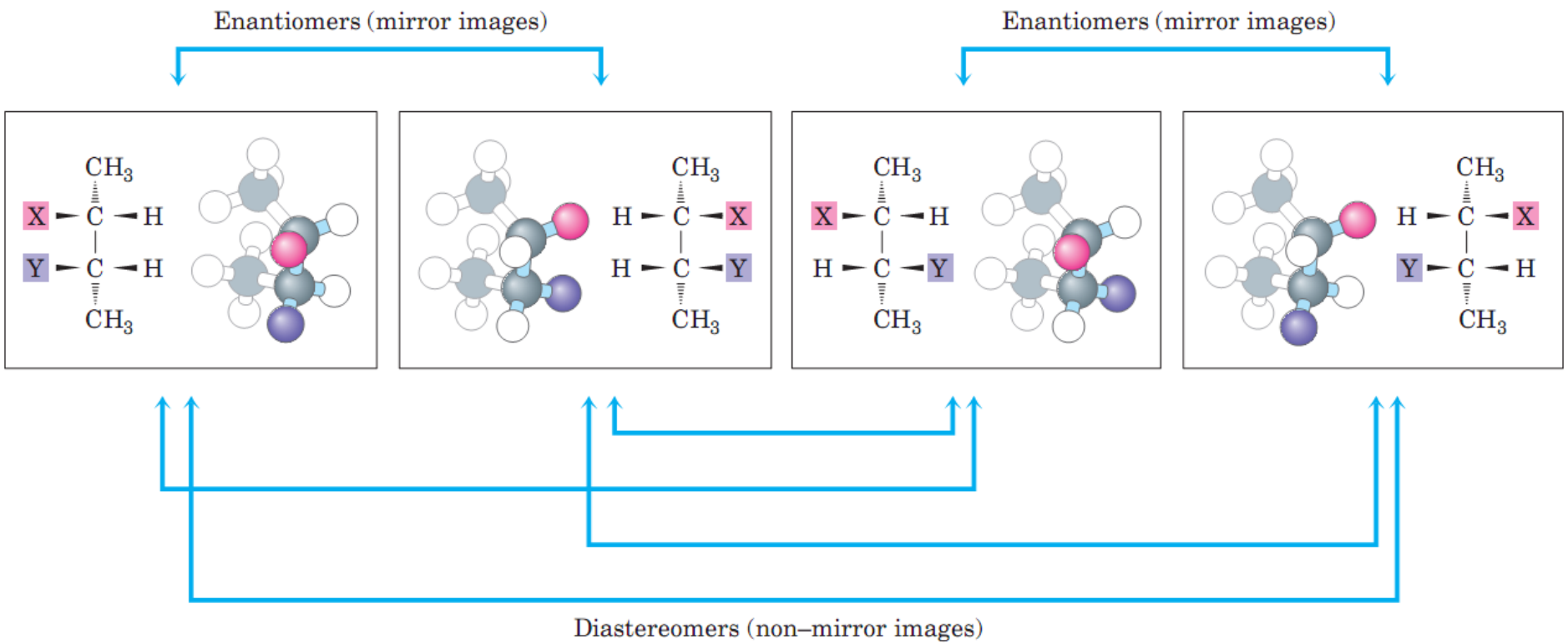

A
C
X
B
Y
Polarizing Filter


Mirror image of original molecule
Original molecule
A
C
Y
B
X
Chiral molecule: Rotated molecule *cannot* be superimposed on its mirror image
(a)


Mirror image of original molecule
Original molecule
A
C
X
B
Achiral molecule: Rotated molecule *can* be superimposed on its mirror image
(b)

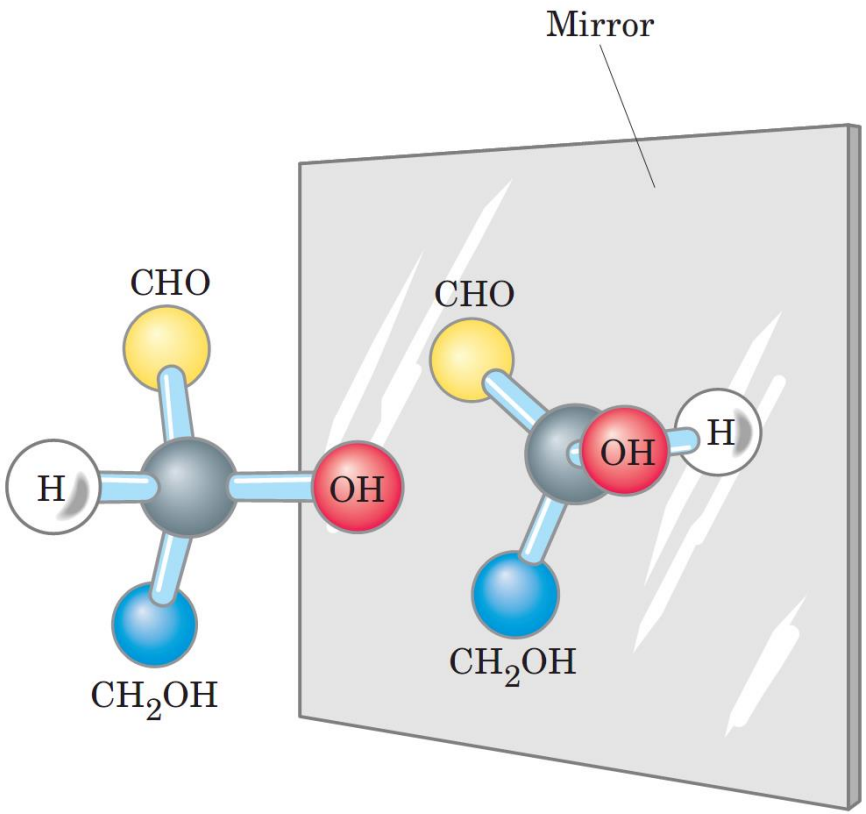

(a)
Hand
Mirror image
Molecule
Mirror image


(b)
Asymmetric carbon atoms

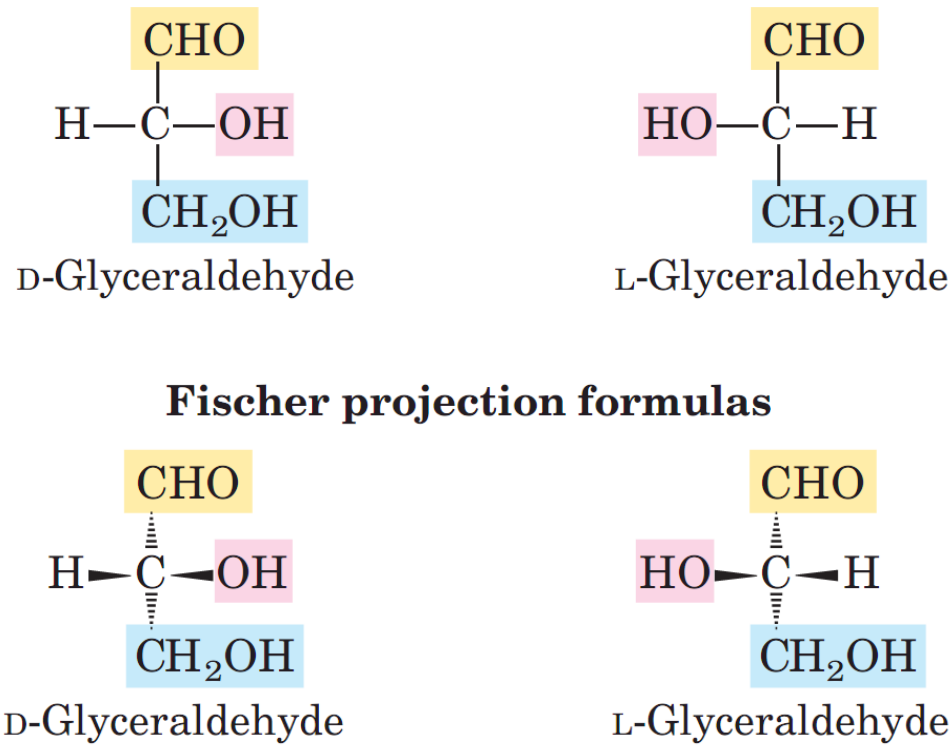

Enantiomers (mirror images)
Enantiomers (mirror images)
Diastereomers (non–mirror images)

❖To represent three-dimensional sugar structures on paper, we often use Fischer projection formulas.

❖In Fischer projection formulas, horizontal bonds Project out of the plane of the paper, toward the reader; vertical bonds project behind the plane of the paper, away from the reader.



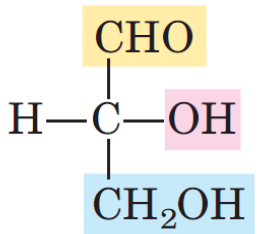
Ball-and-stick models



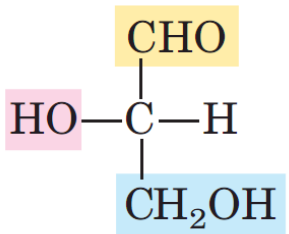
Perspective formulas

❖The stereoisomers of monosaccharides of each carbon-chain length can be divided into two groups that differ in the configuration about the chiral center most distant from the carbonyl carbon.

❖Those in which the configuration at this reference carbon is the same as that of D-glyceraldehyde are designated D isomers, and those with the same configuration as L-glyceraldehyde are L isomers.



D-Glyceraldehyde

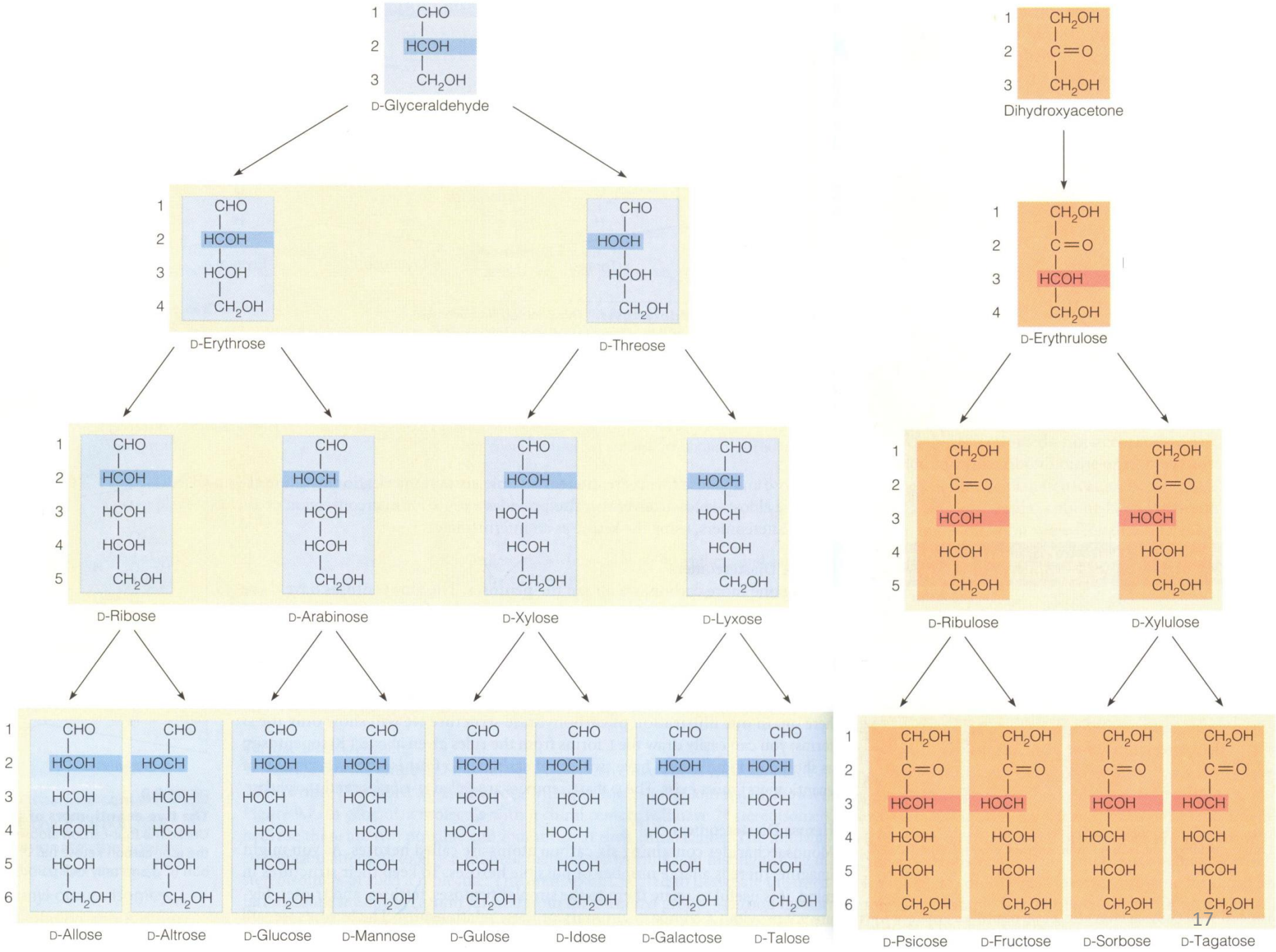


L-Glyceraldehyde

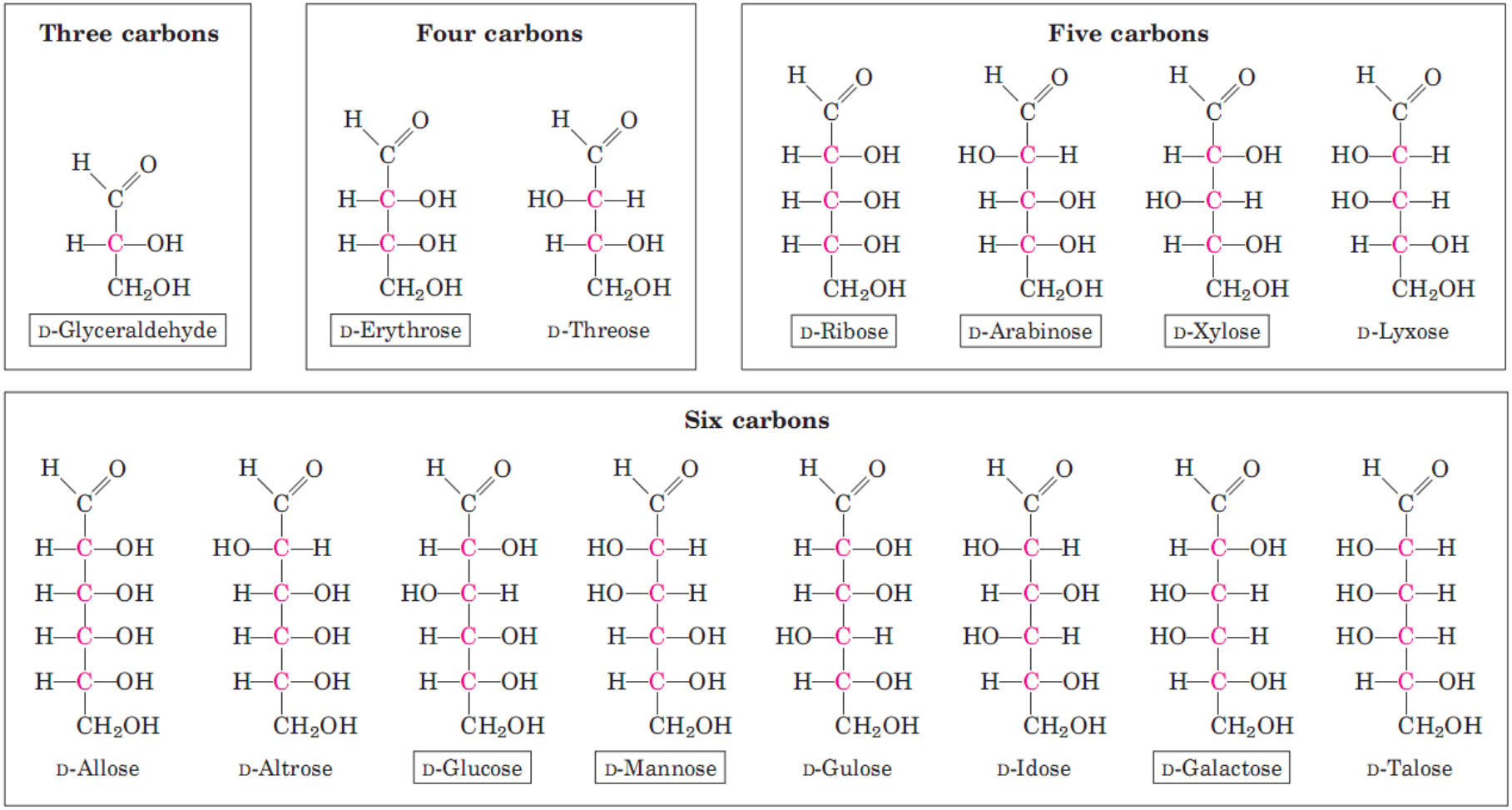
Fischer projection formulas

❖In other words, when the hydroxyl group on the reference carbon is on the right (dextro) in a projection formula that has the carbonyl carbon at the top, the sugar is the D isomer; when on the left (levo), it is the L isomer.

❖Most of the hexoses of living organisms are D isomers.

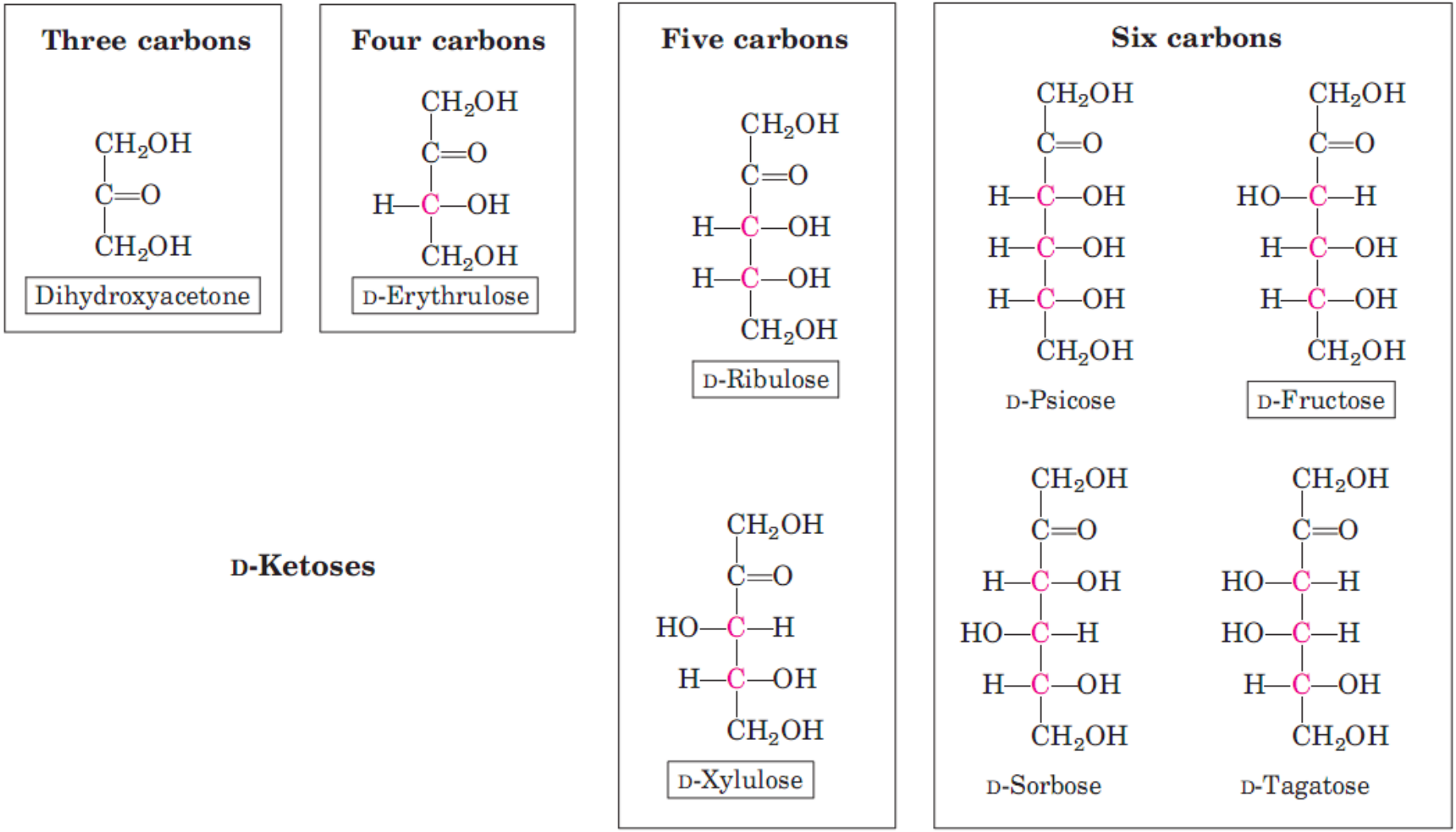

D-Glyceraldehyde
Dihydroxyacetone
D-Erythrose
D-Threose
D-Erythrulose
D-Ribose
D-Arabinose
D-Xylose
D-Lyxose
D-Ribulose
D-Xylulose
D-Allose
D-Altrose
D-Glucose
D-Mannose
D-Gulose
D-Idose
D-Galactose
D-Talose
D-Psicose
D-Fructose
D-Sorbose
D-Tagatose

Fisher Projection Formulas of D-Aldoses

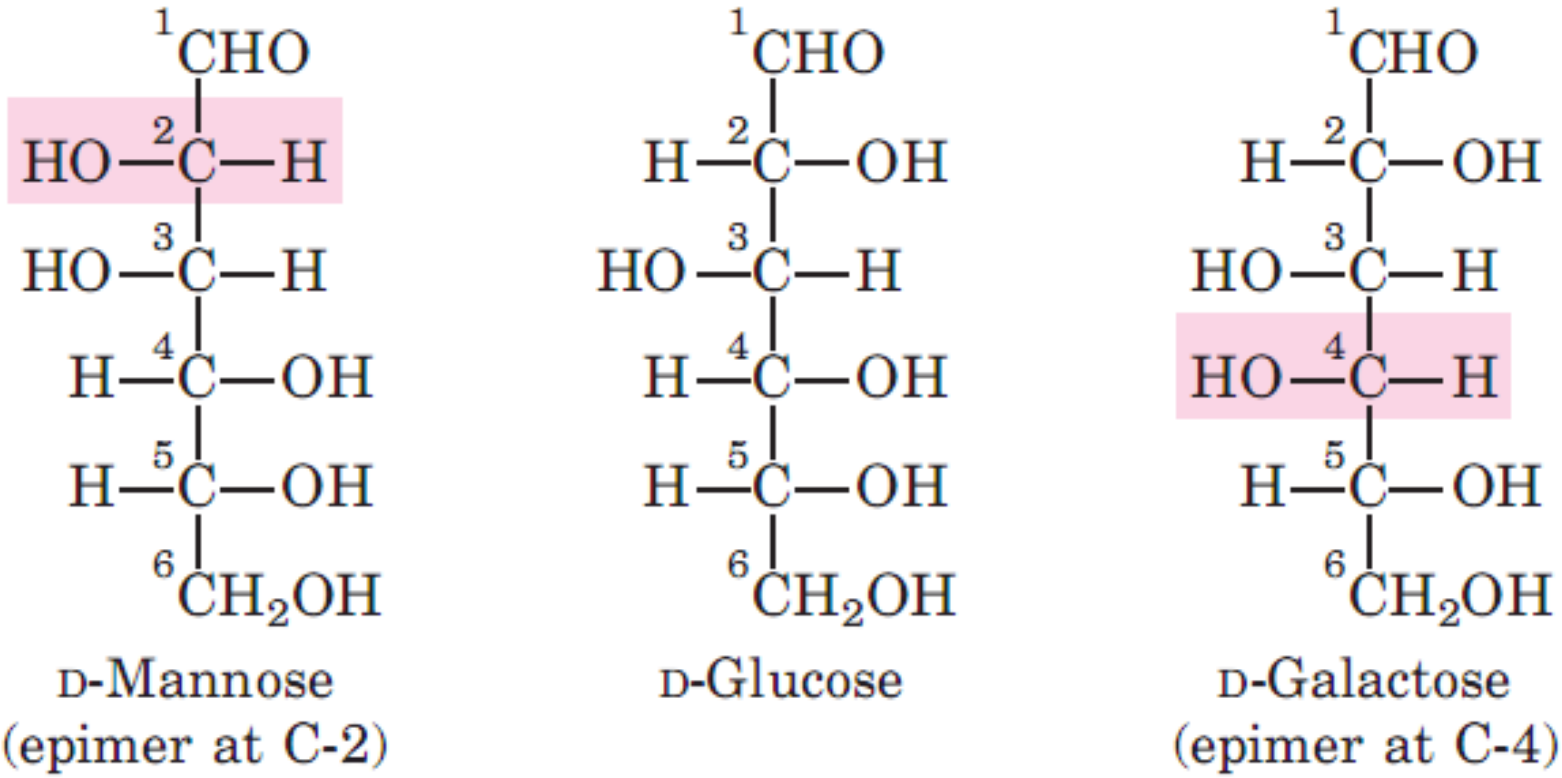


D-Aldoses

Fisher Projection Formulas of D-Ketoses



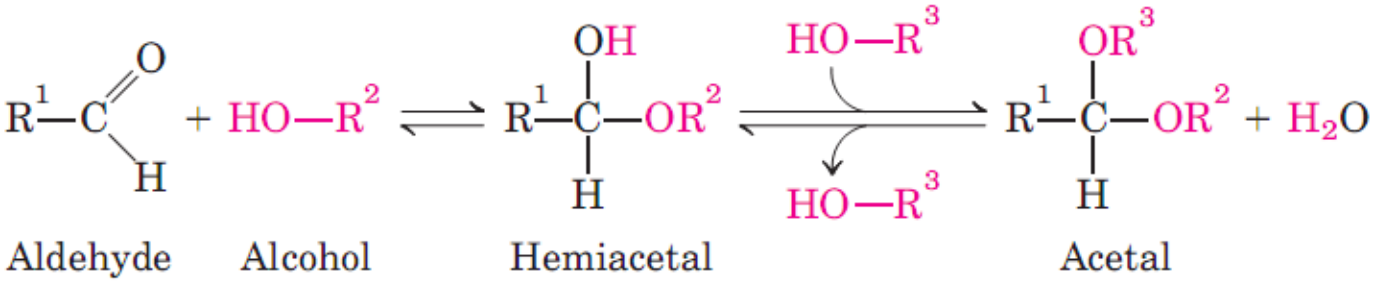
❖Two sugars that differ only in the configuration around one carbon atom are called epimers; D-glucose and D-mannose, which differ only in the stereochemistry at C-2, are epimers, as are D-glucose and D-galactose (which differ at C-4).

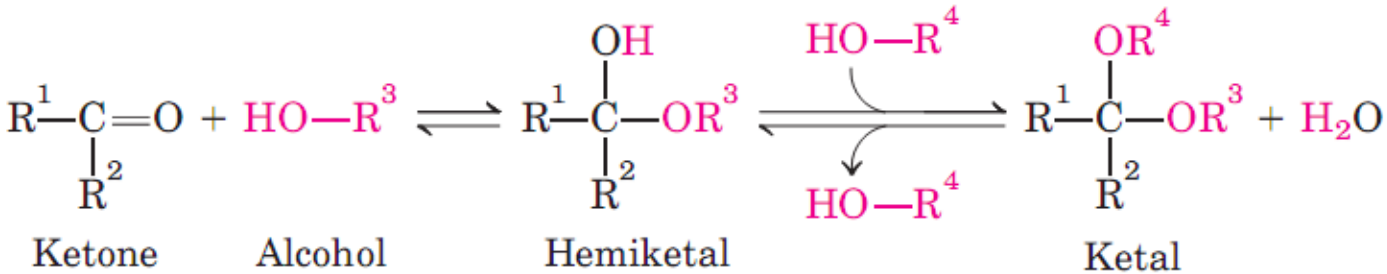


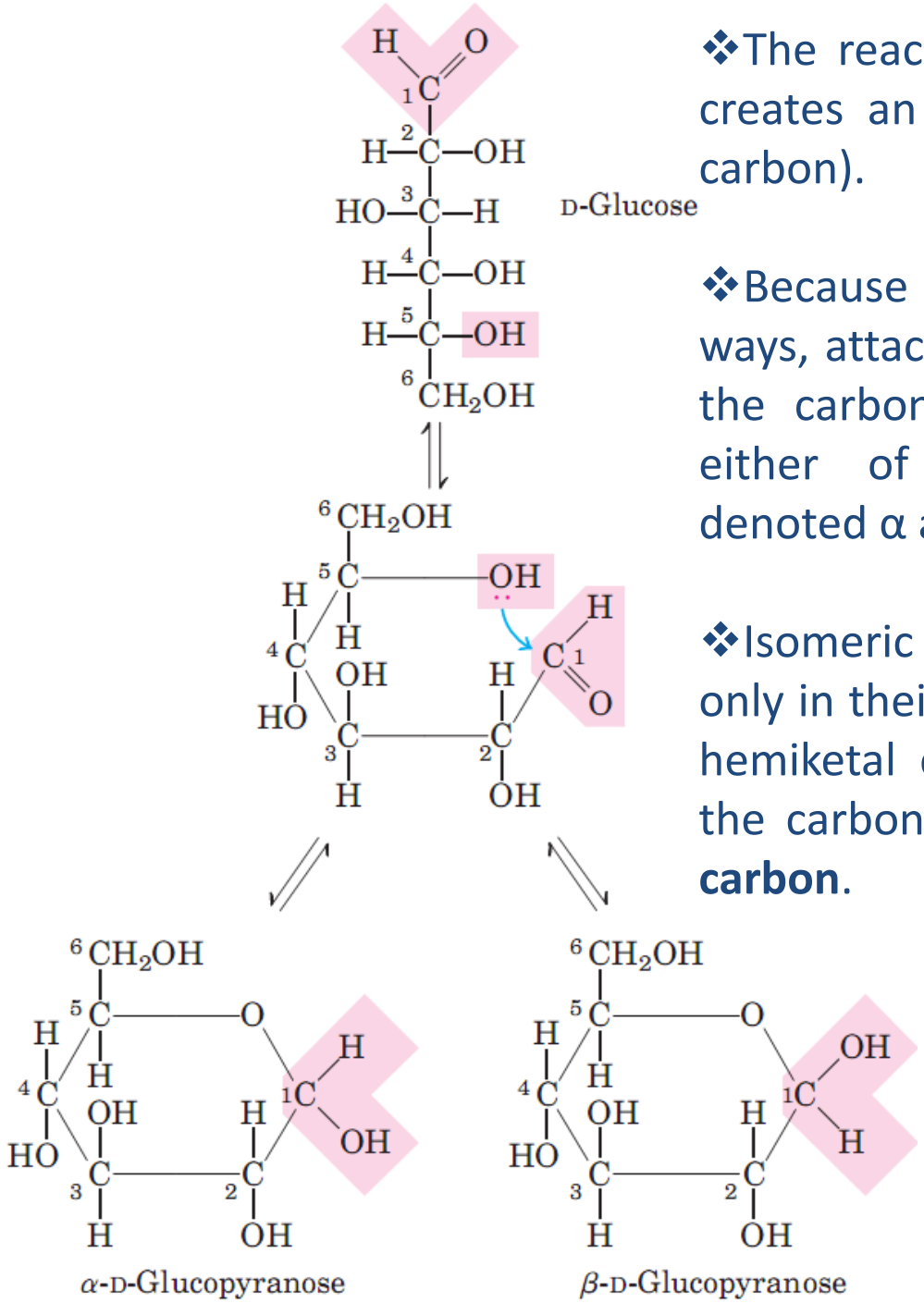
The Common Monosaccharides Have Cyclic Structures

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

❖The formation of these ring structures is the result of a general reaction between alcohols and aldehydes or ketones to form derivatives called hemiacetals or hemiketals.







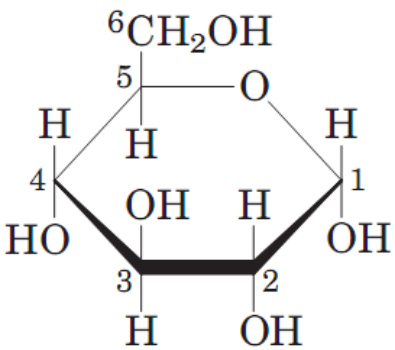
❖The reaction with the first molecule of alcohol creates an additional chiral center (the carbonyl carbon).

❖Because the alcohol can add in either of two ways, attacking either the “front” or the “back” of the carbonyl carbon, the reaction can produce either of two stereoisomeric configurations, denoted α and β.

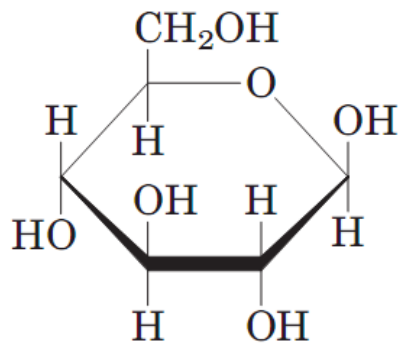
❖Isomeric forms of monosaccharides that differ only in their configuration about the hemiacetal or hemiketal carbon atom are called **anomers**, and the carbonyl carbon atom is called the **anomeric carbon**.

❖Six-membered ring compounds are called **pyranoses** because they resemble the six-membered ring compound pyran.

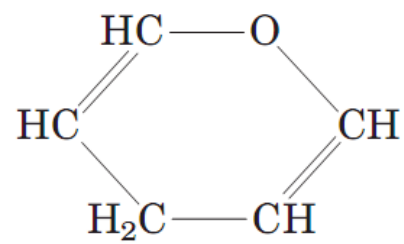
❖Ketohexoses (such as fructose) also occur as cyclic compounds where hydroxyl group at C-5 reacts with the keto group at C-2, forming a five-membered ring compounds, **furanose**.



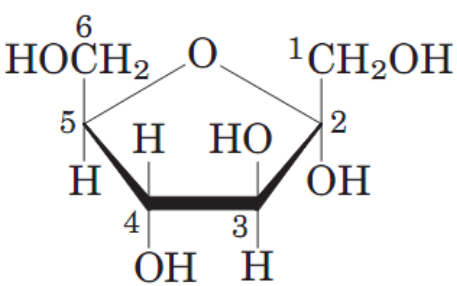
α-D-Glucopyranose



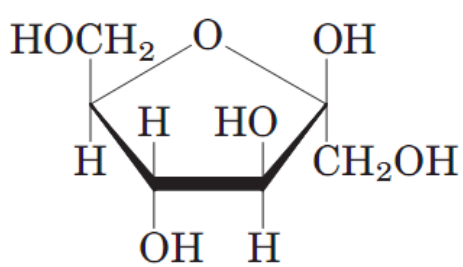
β-D-Glucopyranose



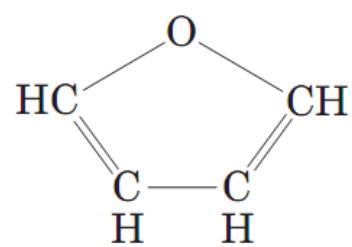
Pyran



α-D-Fructofuranose



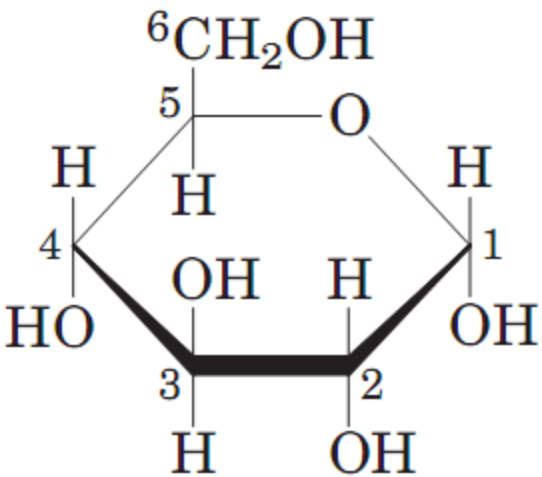
β-D-Fructofuranose



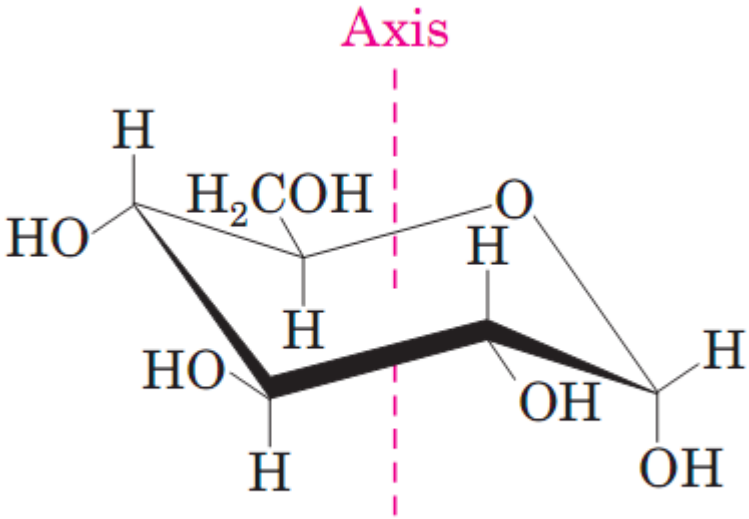
Furan

❖Cyclic sugar structures are more accurately represented in Haworth perspective formulas than in the Fischer projections commonly used for linear sugar structures.

❖In Haworth projections the six-membered ring is tilted to make its plane almost perpendicular to that of the paper, with the bonds closest to the reader drawn thicker than those farther away



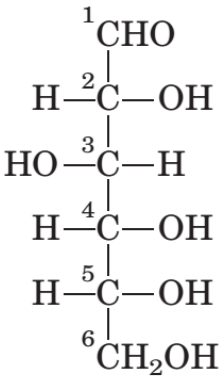
α-D-Glucopyranose



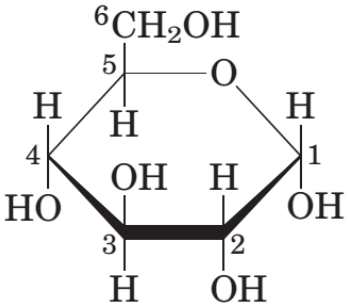
α-D-Glucopyranose

❖To convert the Fischer projection formula of any linear D-hexose to a Haworth perspective formula showing the molecule's cyclic structure;

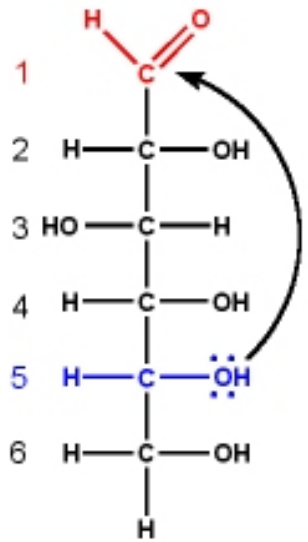
- draw the six-membered ring,
- number the carbons in a clockwise direction beginning with the anomeric carbon,
- then place the hydroxyl groups.
- If a hydroxyl group is to the right in the Fischer projection, it is placed pointing down in the Haworth perspective and vice versa.
- The terminal —CH_2OH group projects upward for the D-enantiomer, downward for the L-enantiomer.
- The hydroxyl on the anomeric carbon of a D-hexose is on the same side of the ring as C-6, the structure is β.



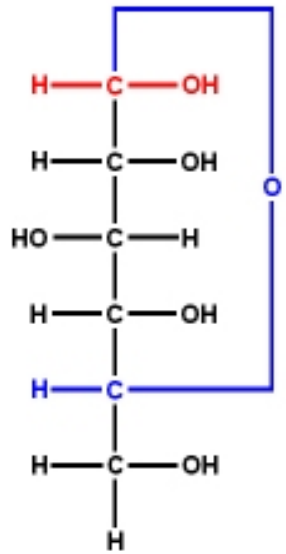
D-Glucose
Fischer projection



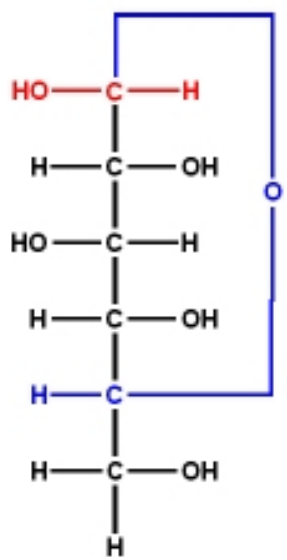
α-D-Glucopyranose
Haworth perspective



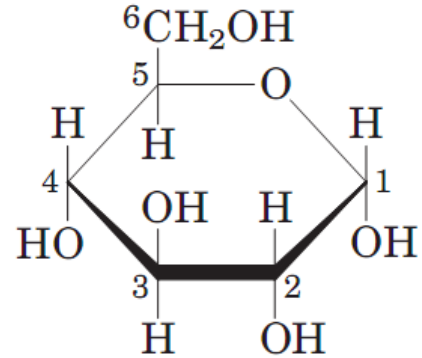
D-Glucose



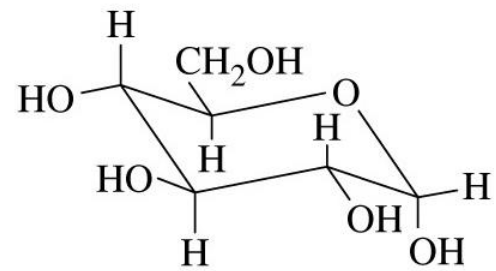
α-D-Glucopyranose



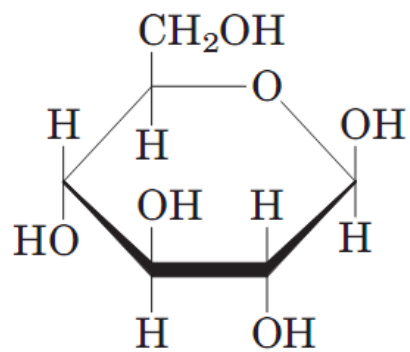
β-D-Glucopyranose



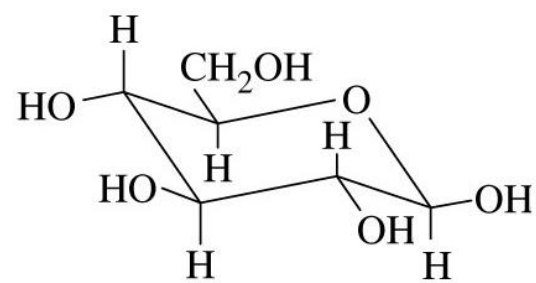
α-D-Glucopyranose



α-D-Glucopyranose



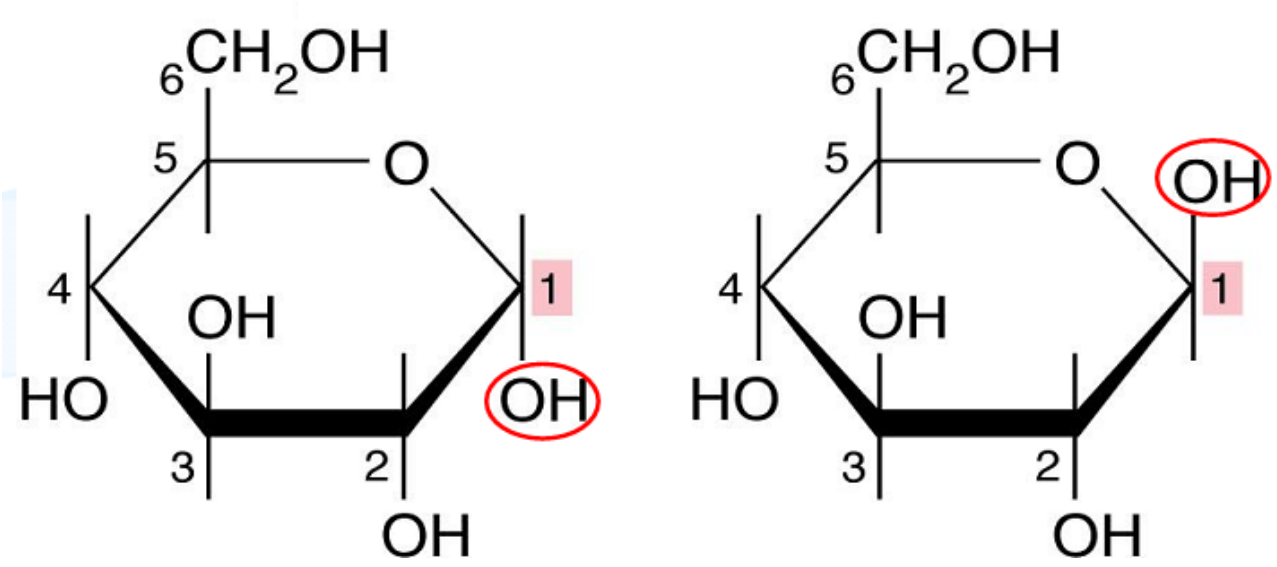
β-D-Glucopyranose

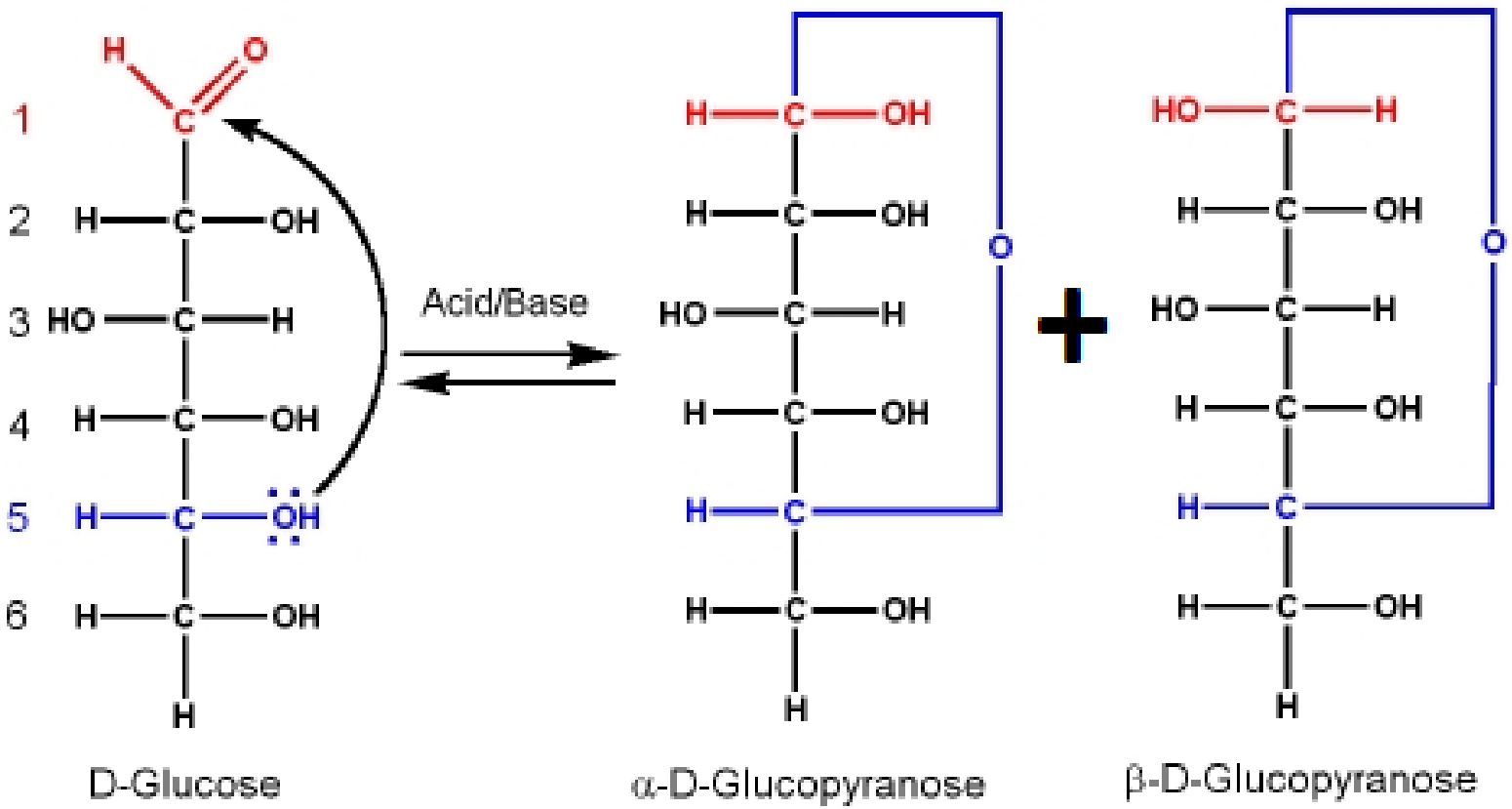


β-D-Glucopyranose

❖The α and β anomers of D-glucose interconvert in aqueous solution by a process called **mutarotation**, in which one ring form (say, the α anomer) opens briefly into the linear form, then closes again to produce the β anomer.

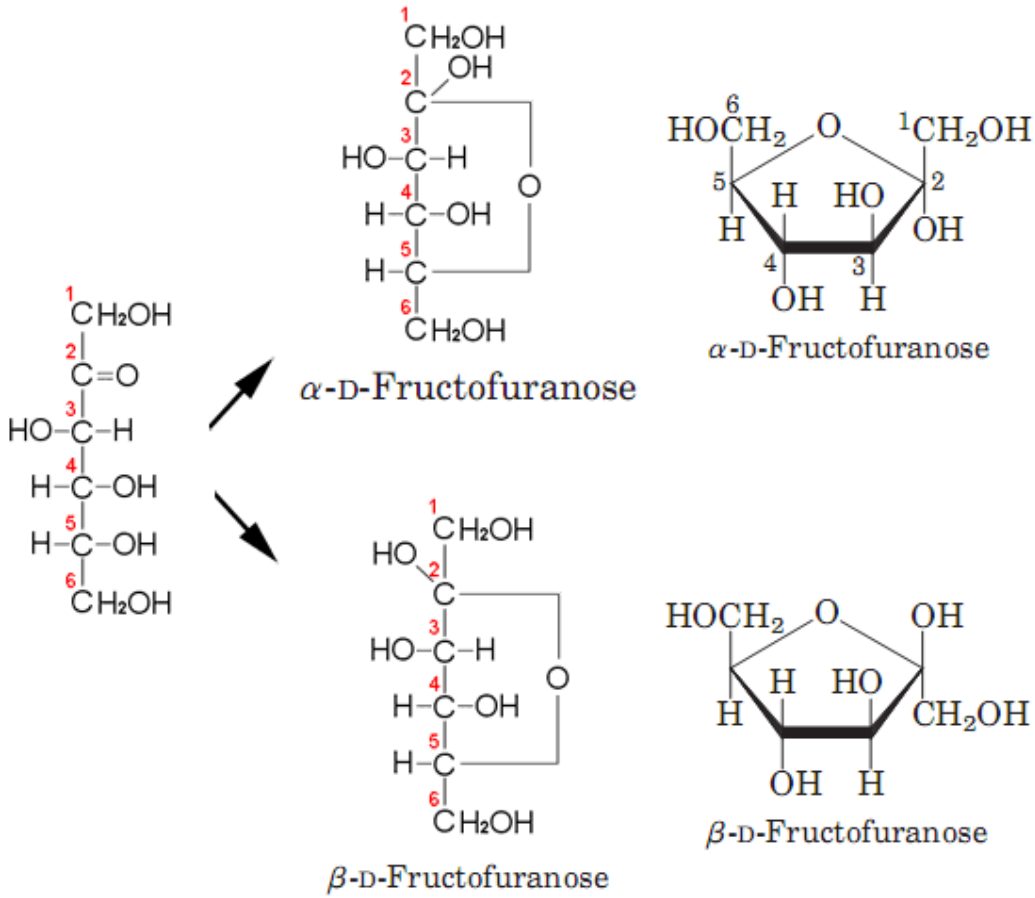
❖Thus, a solution of α-D-glucose and a solution of β-D-glucose eventually
❖form identical equilibrium mixtures having identical optical properties. This mixture consists of about one-third α-D-glucose, two-thirds β-D-glucose, and very small amounts of the linear and five-membered ring (glucofuranose)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




Acid/Base
D-Glucose
α-D-Glucopyranose
β-D-Glucopyranose

❖Ketohexoses (such as fructose) also occur as cyclic compounds with α and β anomeric forms.

❖In these compounds the hydroxyl group at C-5 (or C-6) reacts with the keto group at C-2, forming a furanose (or pyranose) ring containing a hemiketal linkage



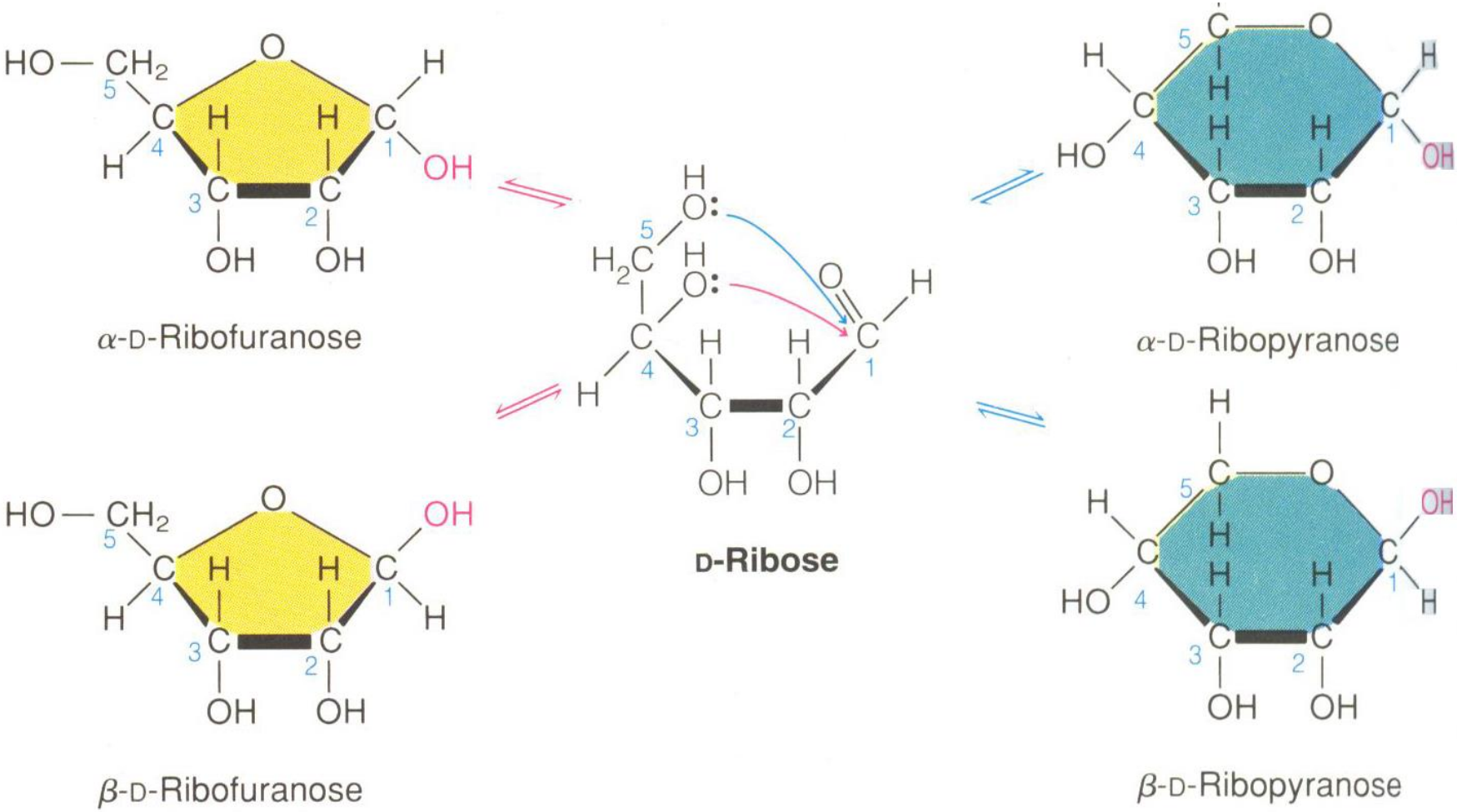

α-D-Ribofuranose
β-D-Ribofuranose
D-Ribose
α-D-Ribopyranose
β-D-Ribopyranose

TABLE 9.2 Relative amounts of tautomeric forms for some monosaccharide sugars at equilibrium in water at 40°C

	Relative Amount (%)				
Monosaccharide	α-Pyranose	β-Pyranose	α-Furanose	β-Furanose	Total Furanose
Ribose	20	56	6	18	24
Lyxose	71	29	—[a]	—[a]	<1
Altrose	27	40	20	13	33
Glucose	36	64	—[a]	—[a]	<1
Mannose	67	33	—[a]	—[a]	<1
Fructose	3	57	9	31	40

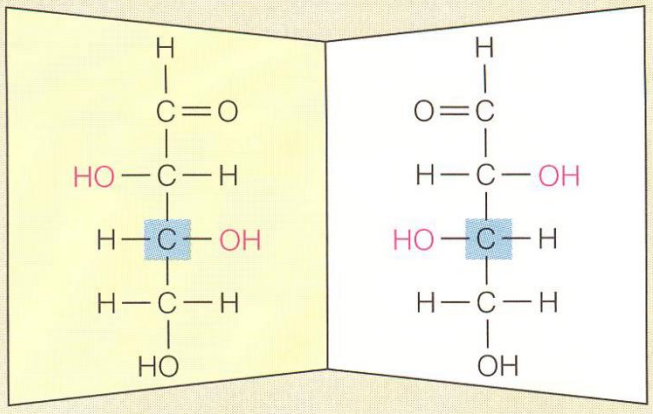
Note: In all cases, the open-chain form is much less than 1%. For data on other sugars, see S. J. Angyal, The composition and conformation of sugars in solution, *Angew. Chem.* (1969) 8:157–226.

[a]Much less than 1%.

Configurational isomers

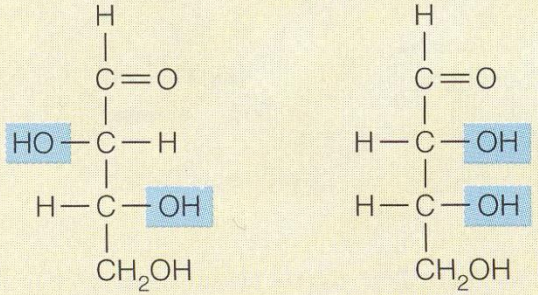
Enantiomers
Stereoisomers that are mirror images of one another

The boxed asymmetric carbon (farthest from aldehyde) determines D/L designation



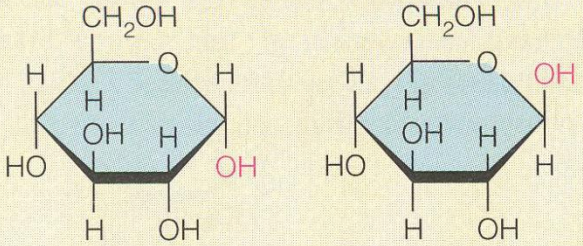
D-Threose L-Threose

Diastereomers
Stereoisomers that are not mirror images of one another



D-Threose D-Erythrose

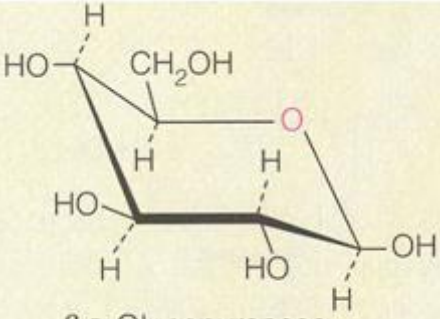
Anomers
Stereoisomers that differ in configuration at the anomeric carbon



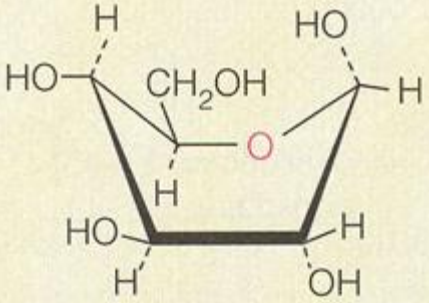
α-D-Glucopyranose β-D-Glucopyranose

Conformational isomers

Molecules with the same stereochemical configuration, but differing in three-dimensional conformation



β-D-Glucopyranose chair form



β-D-Glucopyranose boat form

Monosaccharide Derivatives

❖In addition to simple hexoses such as glucose, galactose, and mannose, there are a number of sugar derivatives in which a hydroxyl group in the parent compound is replaced with another substituent, or a carbon atom is oxidized to a carboxyl group.

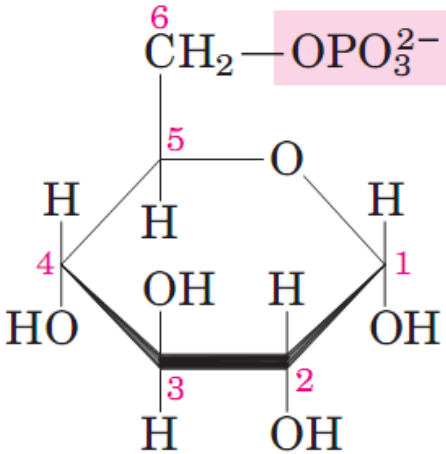
❖These derivatives have important roles in metabolism and classified as;

- Phosphate esters
- Amino sugars
- Deoxy sugars
- Acids and lactons
- Sugar alcohols (alditols)

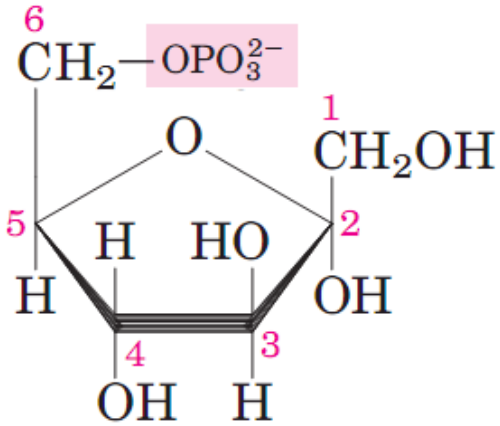
Phosphate esters

❖In the synthesis and metabolism of carbohydrates, the intermediates are very often not the sugars themselves but their phosphorylated derivatives.

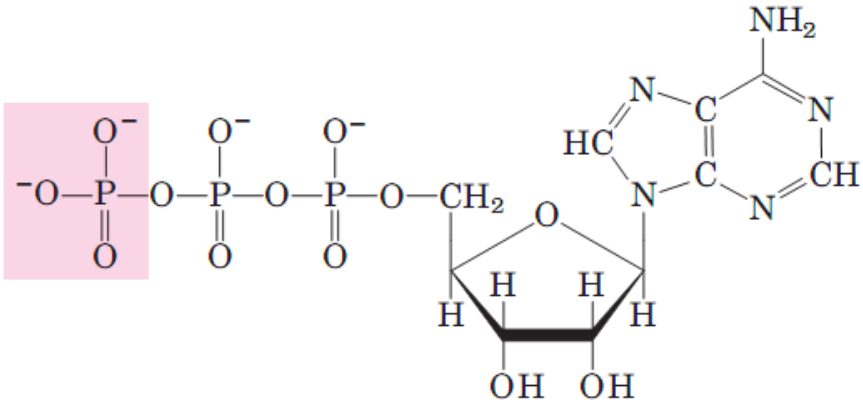
❖ Condensation of phosphoric acid with one of the hydroxyl groups of a sugar forms a phosphate ester, as in glucose 6-phosphate.



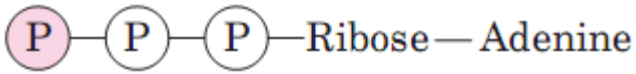
Glucose 6-phosphate



Fructose 6-phosphate



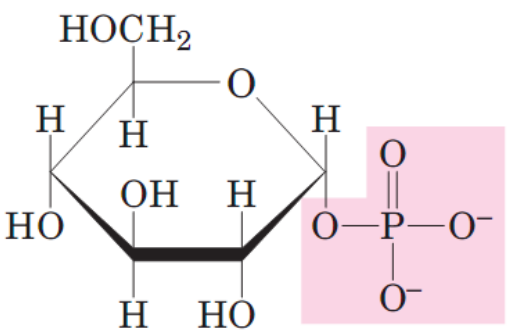
Adenosine triphosphate (ATP)



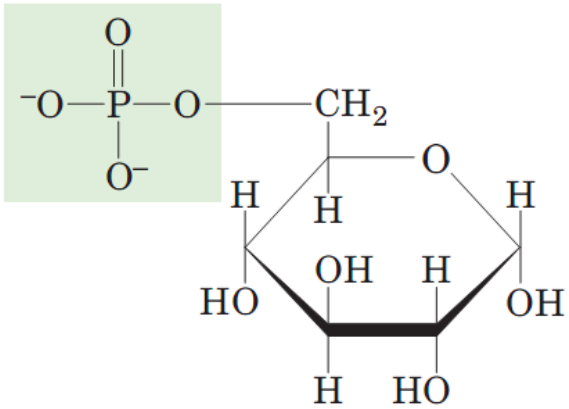
❖Sugar phosphates are relatively stable at neutral pH and bear a negative charge.

❖One effect of sugar phosphorylation within cells is to trap the sugar inside the cell.

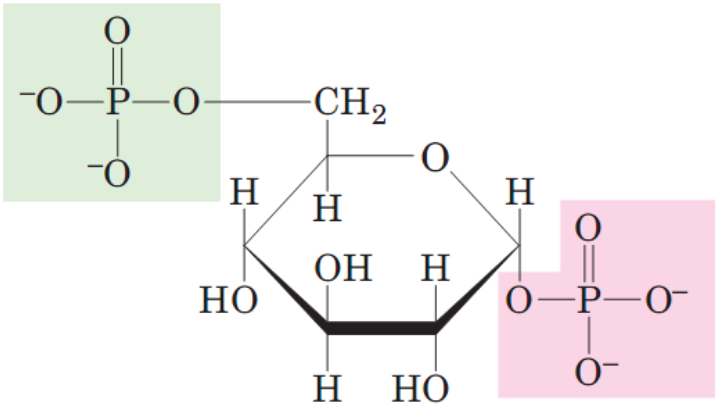
❖Phosphorylation also activates sugars for subsequent chemical transformation.



Glucose 1-phosphate



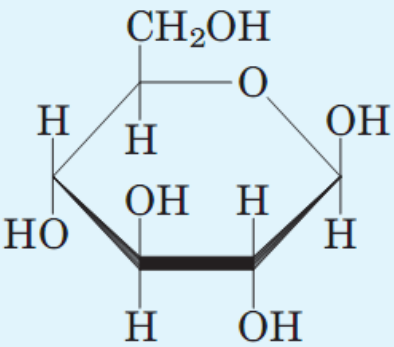
Glucose 6-phosphate



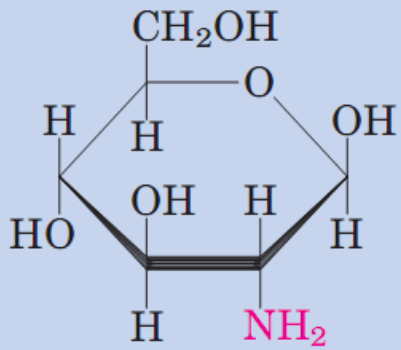
Glucose 1,6-bisphosphate

Amino Sugars

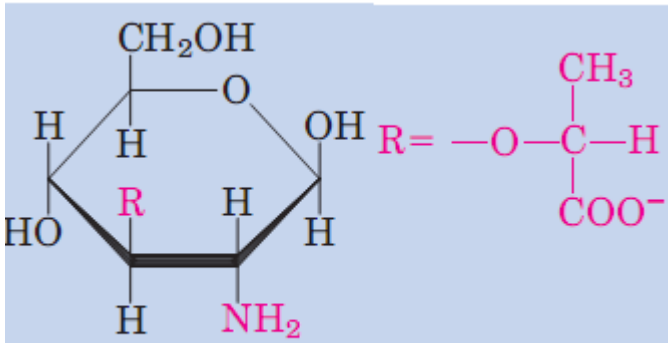
❖In glucosamine, galactosamine, and mannosamine, the hydroxyl at C-2 of the parent compound is replaced with an amino group.



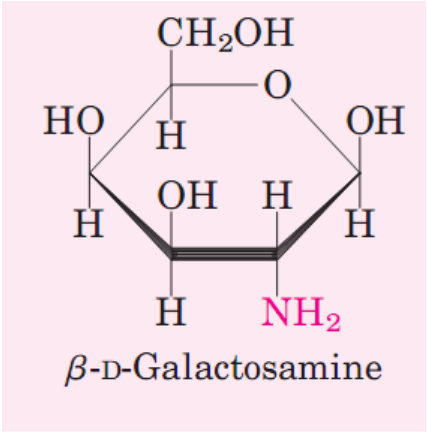
β-D-Glucose



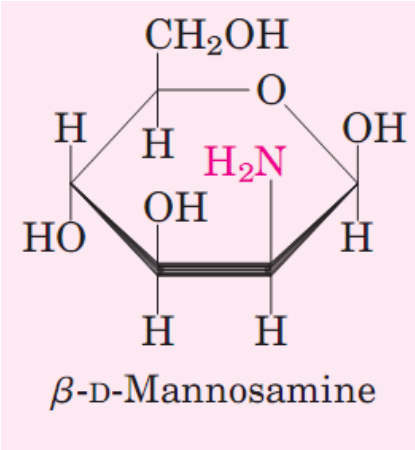
β-D-Glucosamine



Muramic acid



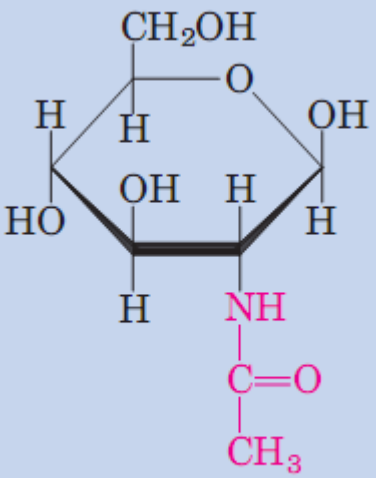
β-D-Galactosamine



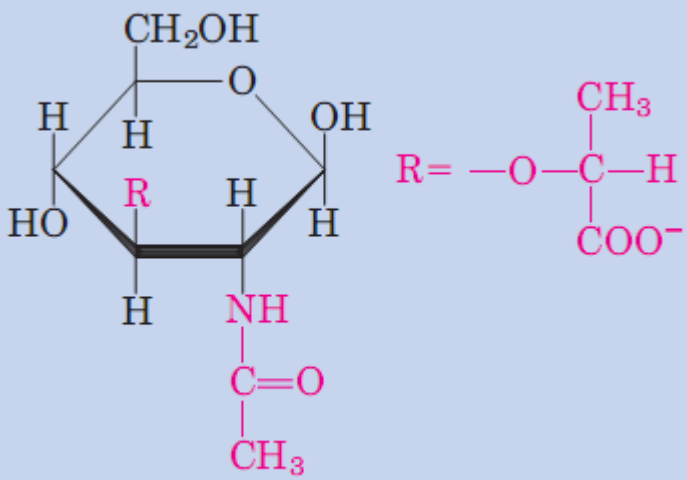
β-D-Mannosamine

❖The amino group is commonly condensed with acetic acid, as in N-acetylglucosamine.

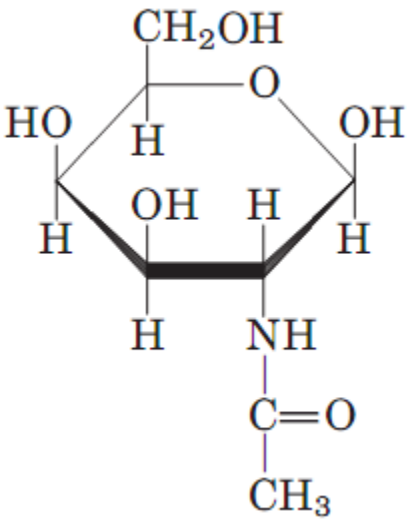
❖This glucosamine derivative is part of many structural polymers, including those of the bacterial cell wall.



N-Acetyl-*β*-D-glucosamine



N-Acetylmuramic acid

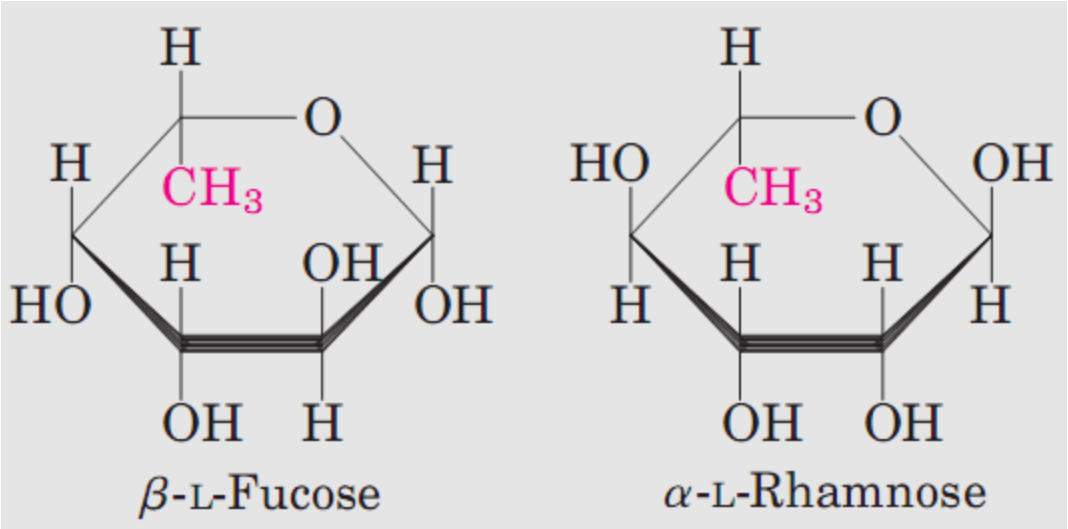


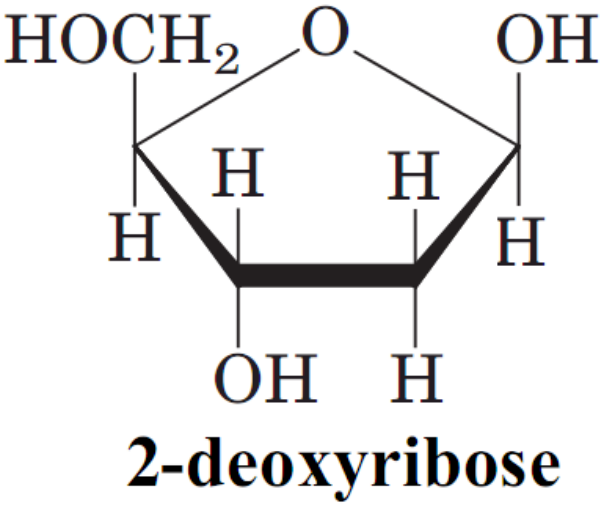
N-Acetyl-β-D-galactosamine

Deoxy Sugars

❖The substitution of a hydrogen for the hydroxyl group at C-6 of L-galactose or L-mannose produces L-fucose or L-rhamnose, respectively.

❖L-Fucose is found in the complex oligosaccharide components of glycoproteins and glycolipids; L-rhamnose is found in plant polysaccharides



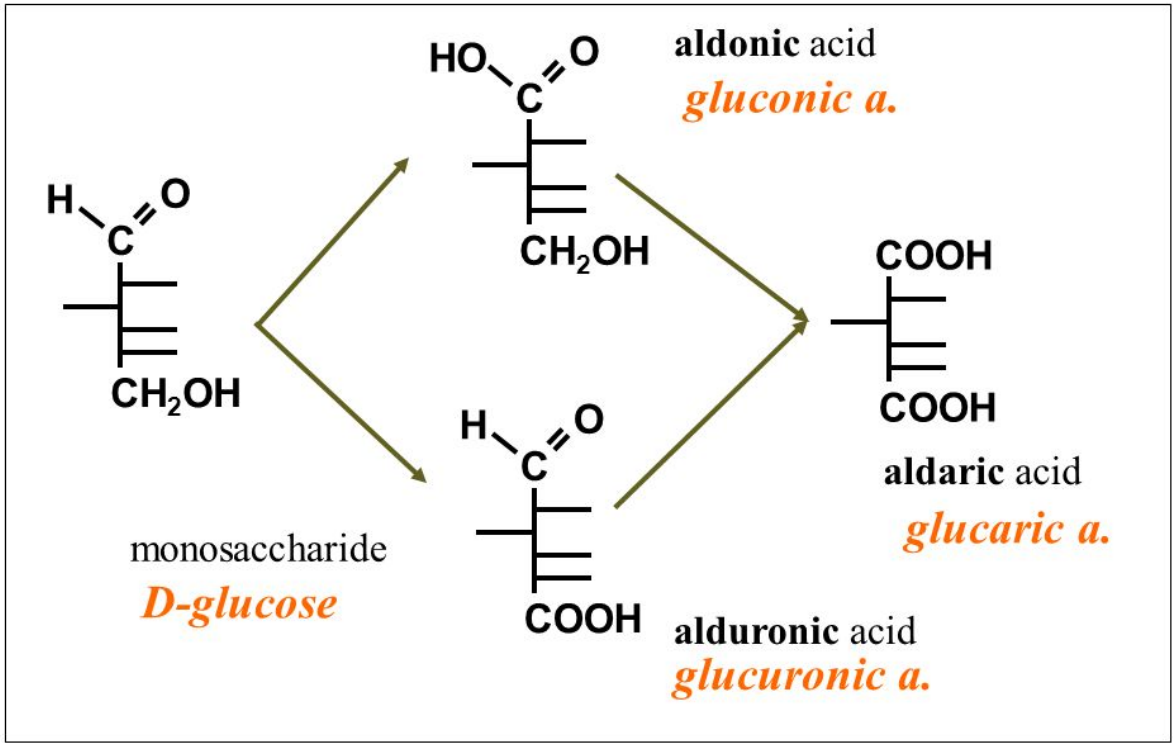


Sugar acids and lactons

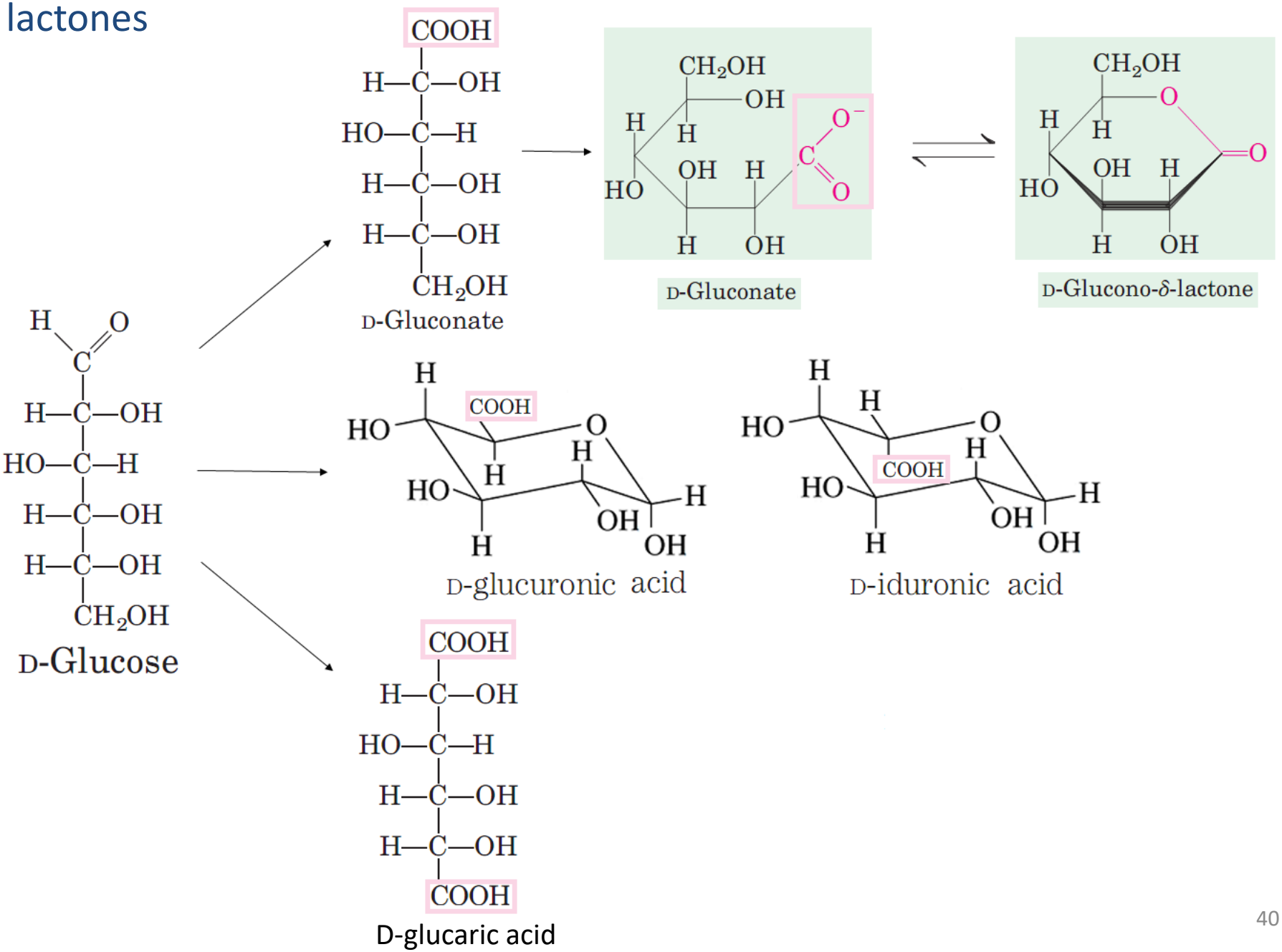
❖Oxidation of the carbonyl (aldehyde) carbon of an aldose to the carboxyl level produces aldonic acids.

❖Oxidation of the carbon at the other end of the carbon chain, C-6 of aldoses, forms the corresponding uronic acids.

❖If both carbons oxidizes, aldaric acids form.

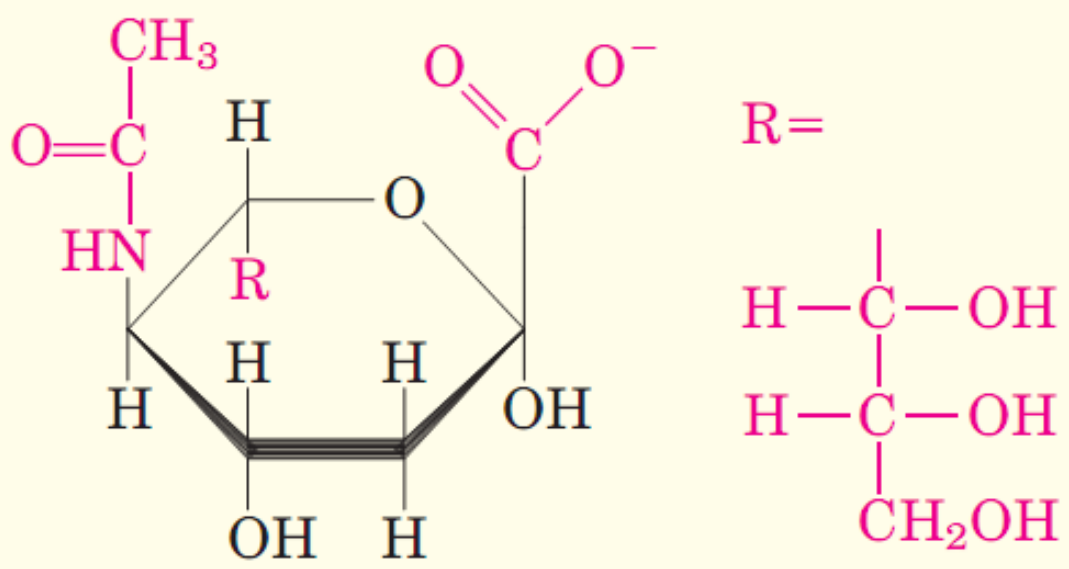


❖Both aldonic and uronic acids form stable intramolecular esters called lactones



❖The sialic acids are a family of sugars with the same nine-carbon backbone.

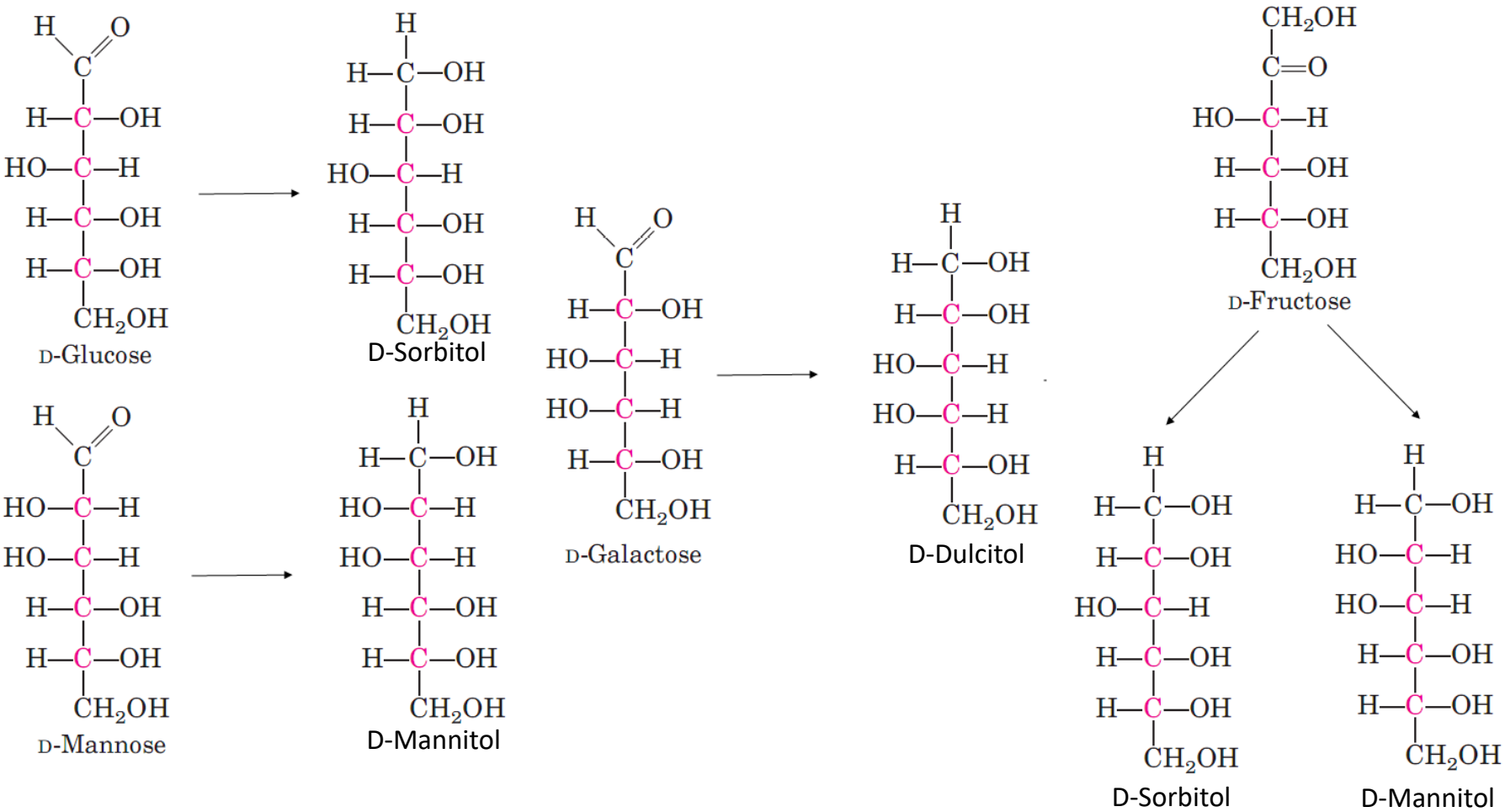
❖One of them, N-acetylneuraminic acid (often referred to simply as "sialic acid"), is a derivative of N-acetylmannosamine that occurs in many glycoproteins and glycolipids on animal cell surfaces, providing sites of recognition by other cells or extracellular carbohydrate-binding proteins



N-Acetylneuraminic acid
(a sialic acid)

Şeker Alkolleri (Alditoller)

❖When carbonyl group of a sugar reduced to alchohol, alditols form.



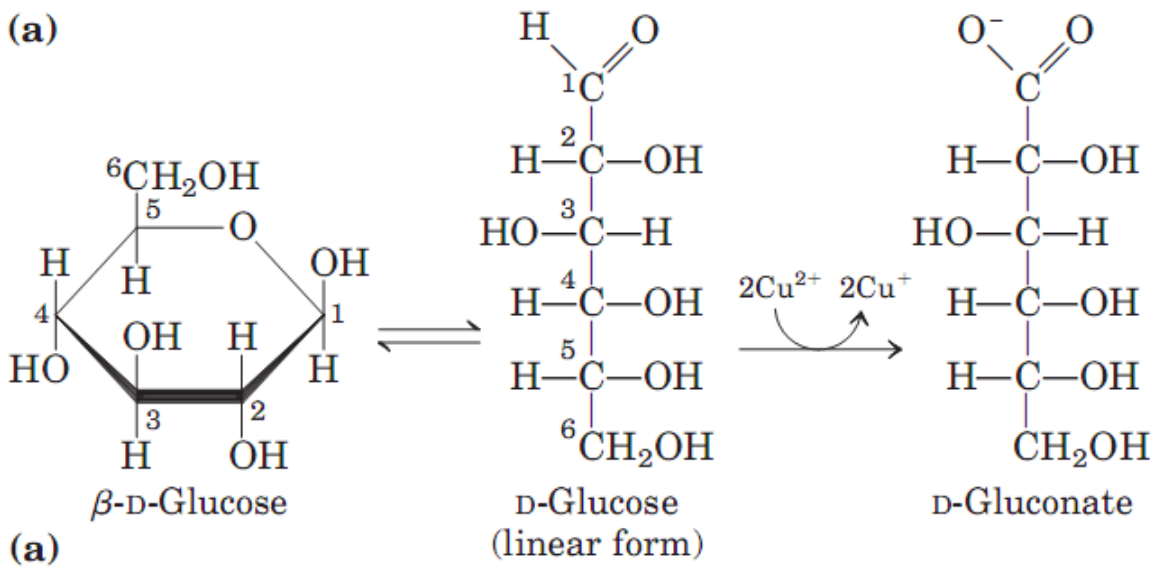
Reactions of Monosaccharides

Redox Reactions

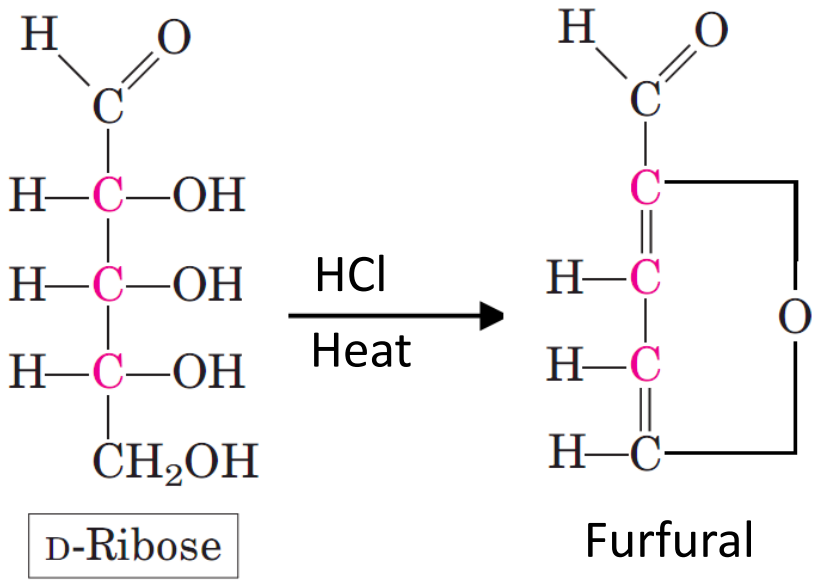
❖Monosaccharides can be oxidized by relatively mild oxidizing agents such as cupric ion.

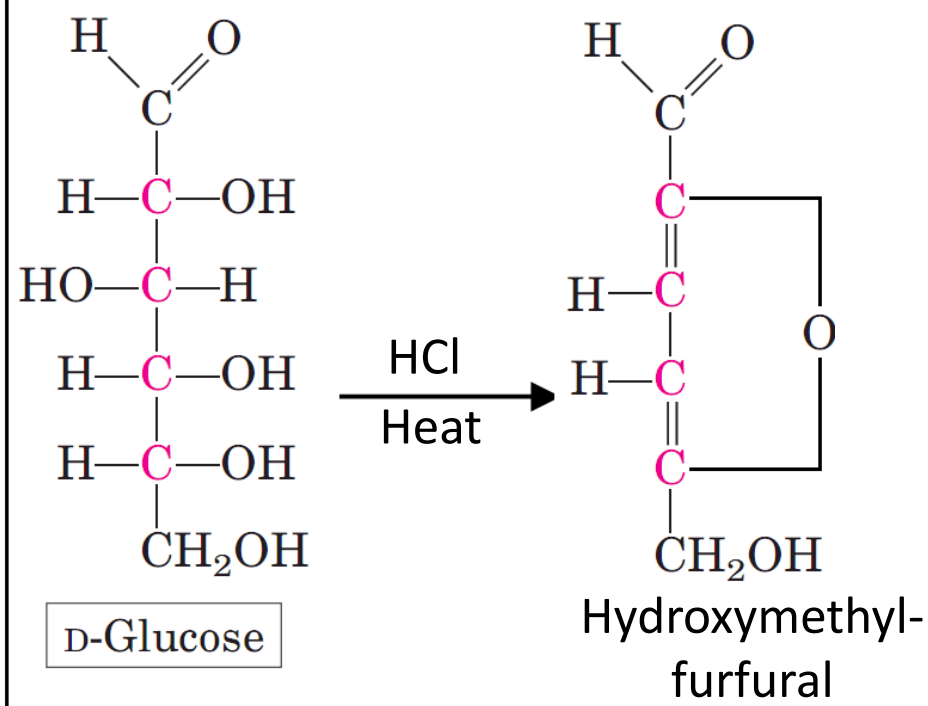
❖Glucose and other sugars capable of reducing cupric ion are called reducing sugars.

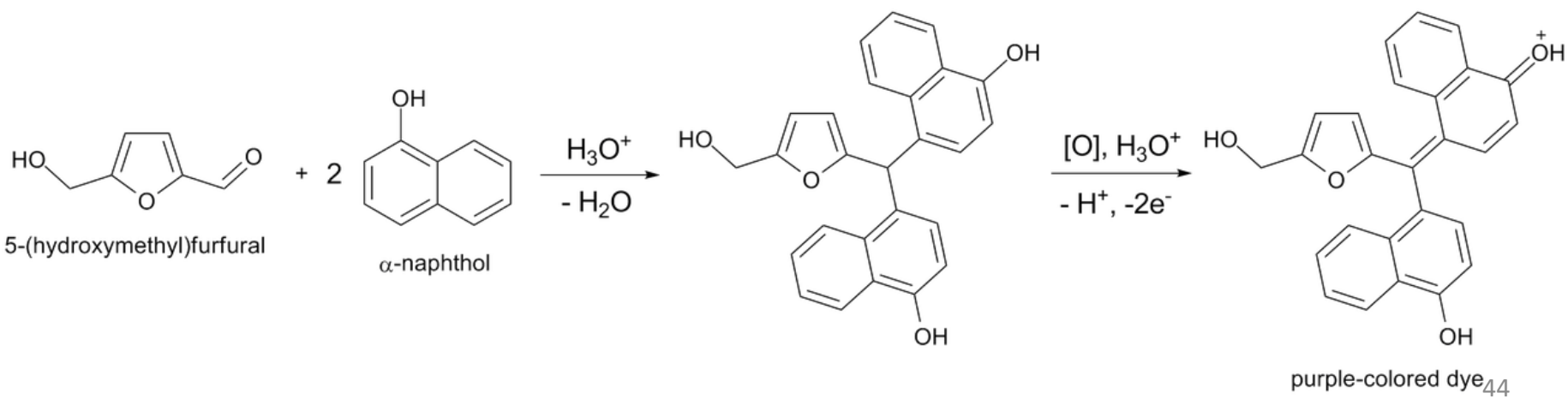
❖Cupric ion oxidizes glucose and certain other sugars to a complex mixture of carboxylic acids and this is the basis of Fehling's reaction.



Dehydration reactions

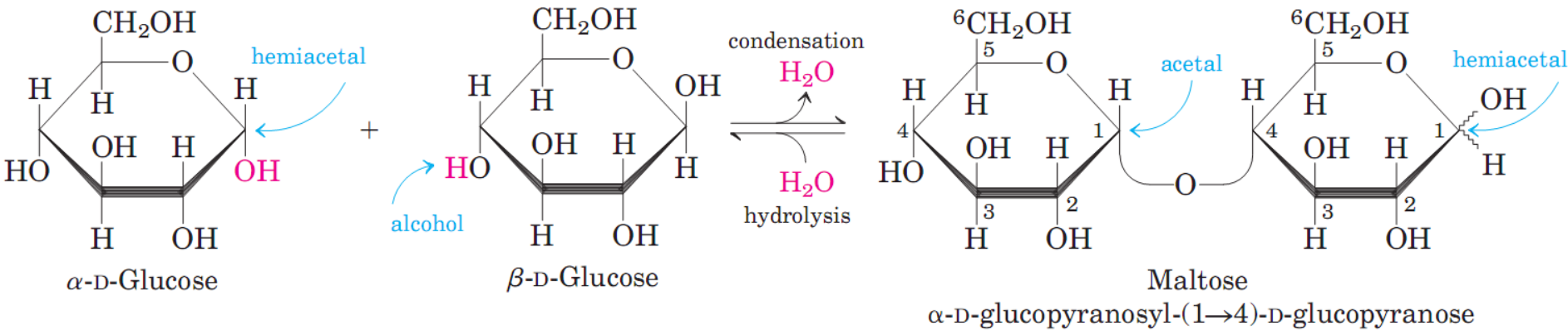






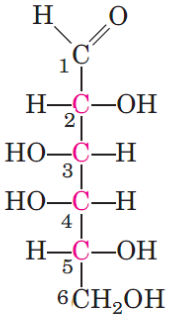
Disaccharides

❖Disaccharides (such as maltose, lactose, and sucrose) consist of two monosaccharides joined covalently by an O-glycosidic bond, which is formed when a hydroxyl group of one sugar molecule, typically cyclic, reacts with the anomeric carbon of the other.

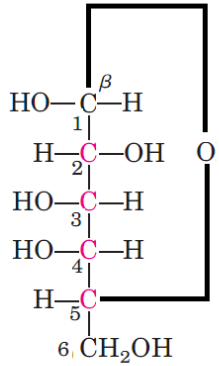


❖This reaction represents the formation of an acetal from a hemiacetal (such as glucopyranose) and an alcohol (a hydroxyl group of the second sugar molecule).

❖Resulting compound is called a glycoside.

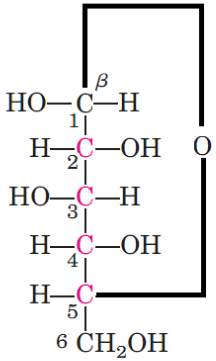


D-Galactose

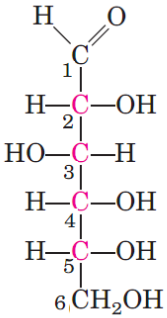


β-D-galactopyranose

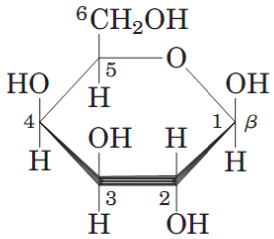
+



β-D-glucopyranose

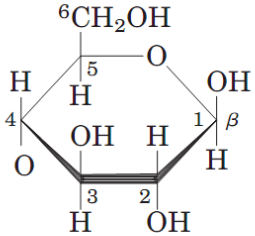


D-Glucose

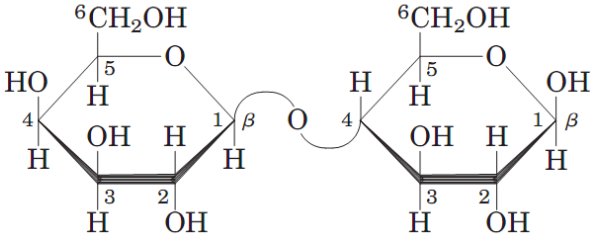


β-D-galactopyranose

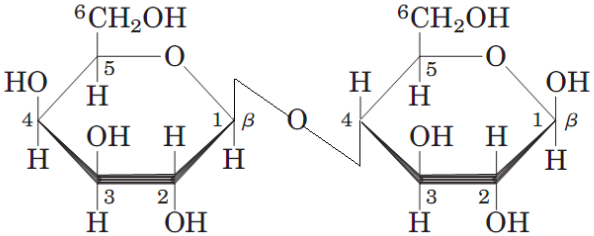
+



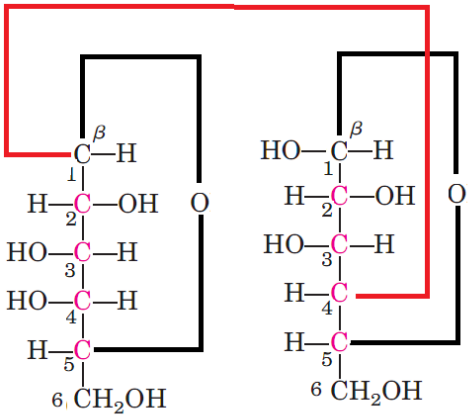
β-D-glucopyranose



Lactose (β form)
β-D-galactopyranosyl-(1→4)-β-D-glucopyranose
Gal(β1→4)Glc



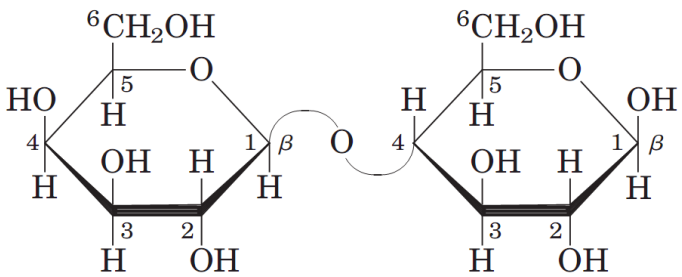
Lactose (β form)
β-D-galactopyranosyl-(1→4)-β-D-glucopyranose
Gal(β1→4)Glc



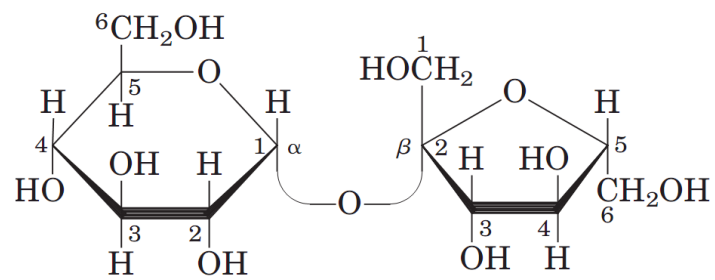
Lactose (β form)
β-D-galactopyranosyl-(1→4)-β-D-glucopyranose
Gal(β1→4)Glc

❖Glycosidic bonds are readily hydrolyzed by acid but resist cleavage by base.

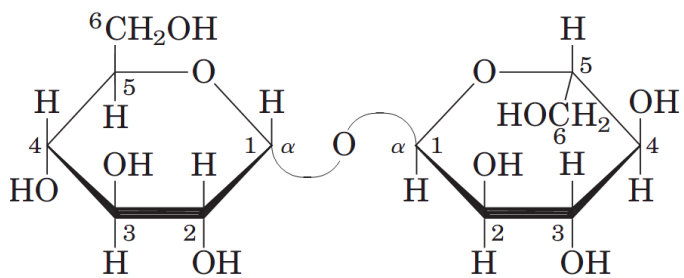
❖Thus disaccharides can be hydrolyzed to yield their free monosaccharide components by boiling with dilute acid.



Lactose (β form)
β-D-galactopyranosyl-(1→4)-β-D-glucopyranose
Gal(β1→4)Glc



Sucrose
α-D-glucopyranosyl β-D-fructofuranoside
Glc(α1↔2β)Fru

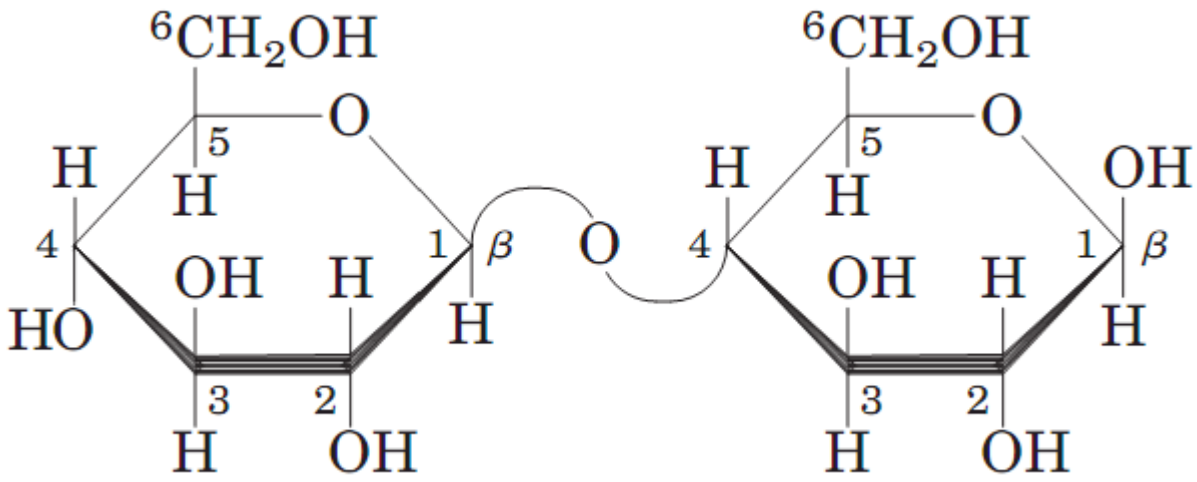


Trehalose
α-D-glucopyranosyl α-D-glucopyranoside
Glc(α1↔1α)Glc

❖The oxidation of a sugar by cupric ion occurs only with the linear
❖form, which exists in equilibrium with the cyclic form(s).

❖When the anomeric carbon is involved in a glycosidic bond, the easy interconversion of linear and cyclic forms is prevented.

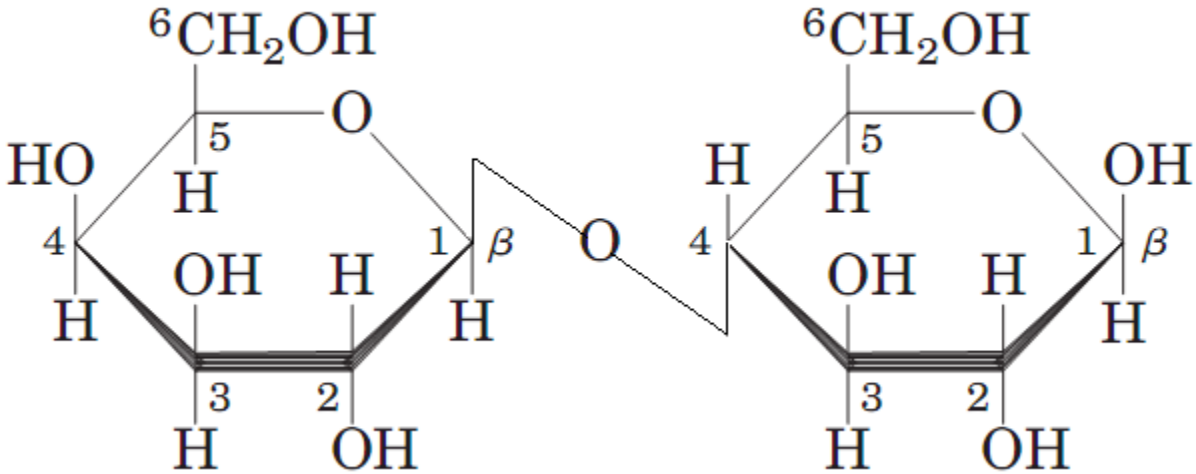
❖In describing disaccharides or polysaccharides, the end of a chain with a free anomeric carbon (one not involved in a glycosidic bond) is commonly called the reducing end.



Cellobiose

Naming of the Disaccharides

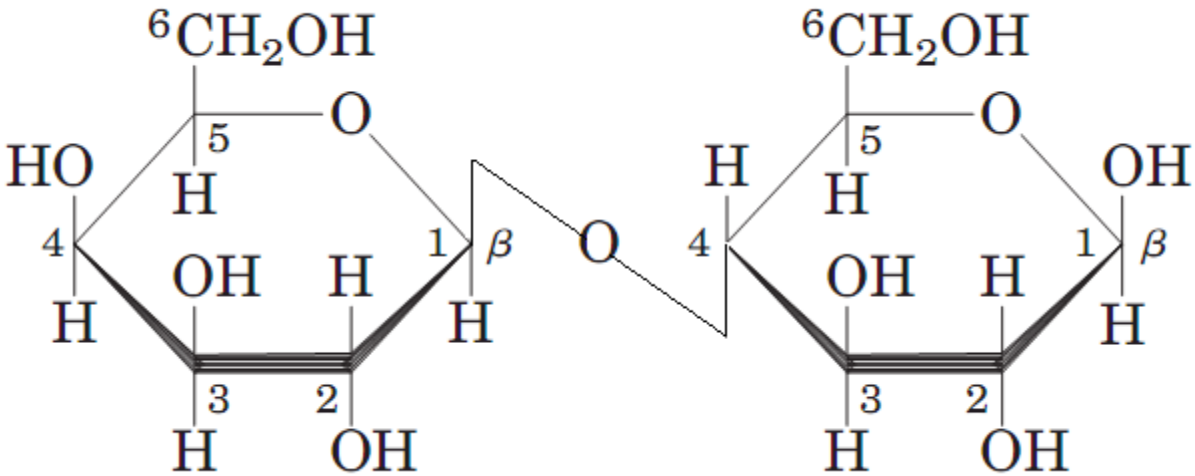
❖By convention, the name describes the compound written with its non-reducing end to the left, and we can “build up” the name in the following order.



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

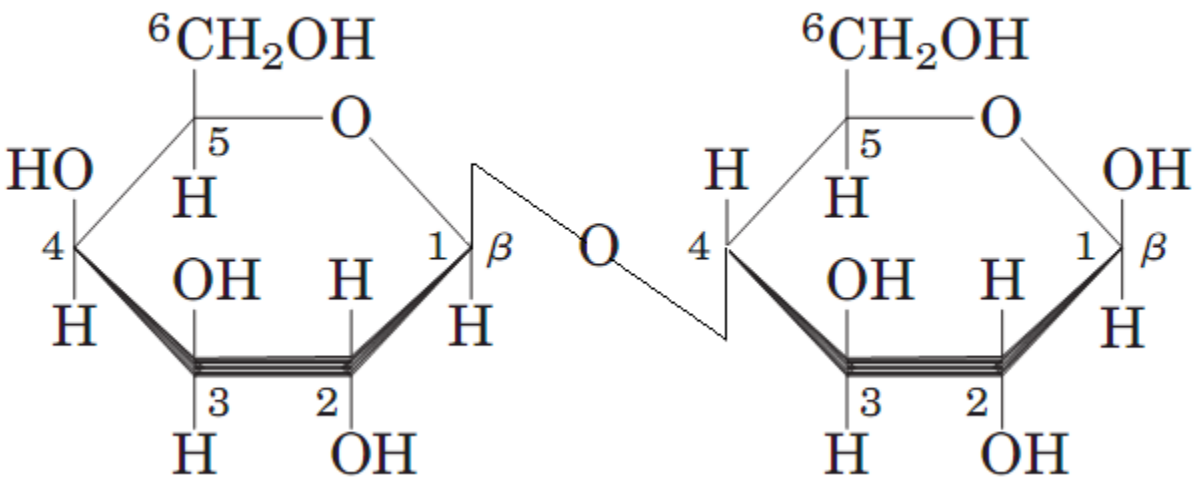
❖ β-

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



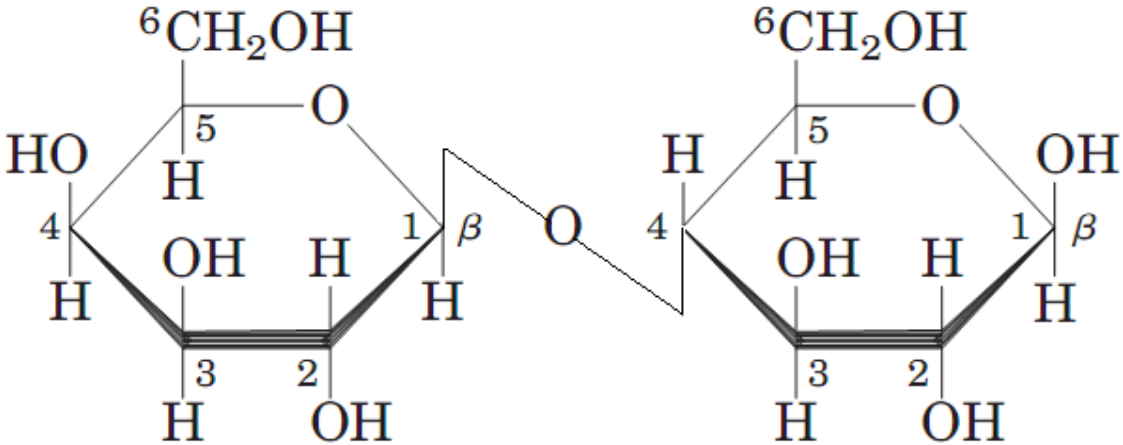
❖β-D-galactopyranosyl

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



❖β-D-galakcopyranosyl-(1→4)

❖(4) Name the second residue.



❖The name of this disaccharide is β-D-galactopyranosyl-(1→4)-β-D-glucopyranose, or commonly known as lactose.

❖It could be abbreviated as Gal(β1→4)-Glc.

❖If there is a third residue, describe the second glycosidic bond by the same conventions.

❖To shorten the description of complex polysaccharides, three-letter abbreviations or colored symbols for the monosaccharides are often used.

TABLE 7–1 Symbols and Abbreviations for Common Monosaccharides and Some of Their Derivatives

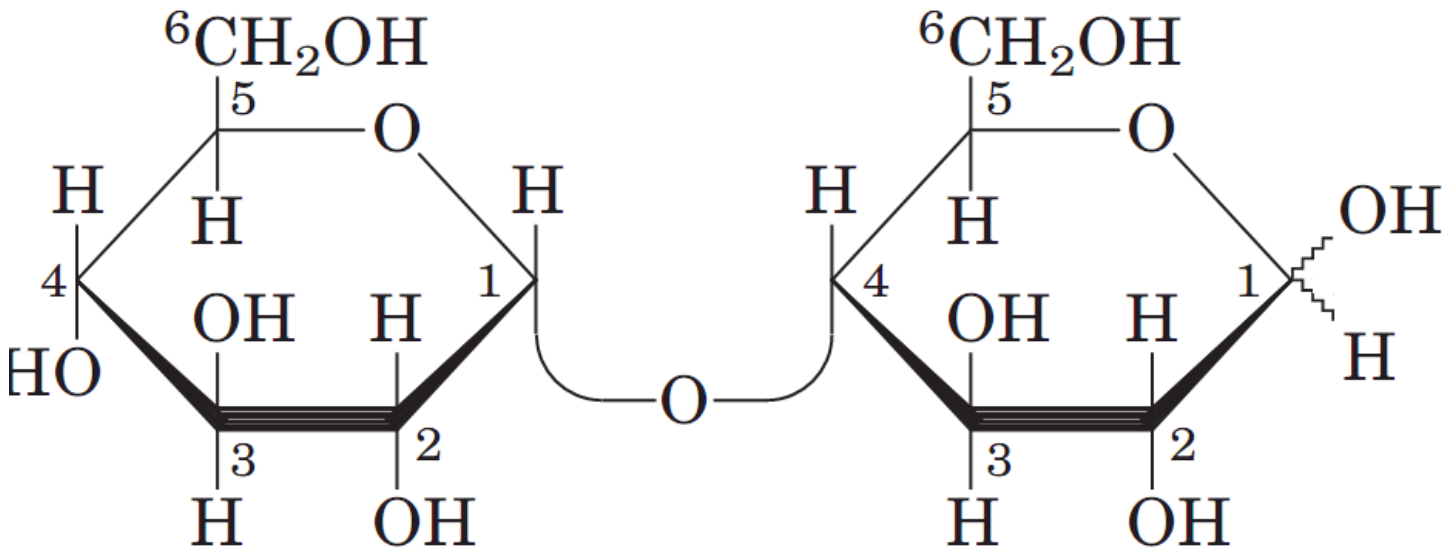
Abequose	Abe	Glucuronic acid	GlcA
Arabinose	Ara	Galactosamine	GalN
Fructose	Fru	Glucosamine	GlcN
Fucose	Fuc	*N*-Acetylgalactosamine	GalNAc
Galactose	Gal	*N*-Acetylglucosamine	GlcNAc
Glucose	Glc	Iduronic acid	IdoA
Mannose	Man	Muramic acid	Mur
Rhamnose	Rha	*N*-Acetylmuramic acid	Mur2Ac
Ribose	Rib	*N*-Acetylneuraminic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

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

Maltose

❖The disaccharide maltose contains two D-glucose residues joined by a glycosidic linkage between C-1 (the anomeric carbon) of one glucose residue and C-4 of the other.

❖Because the disaccharide retains a free anomeric carbon, maltose is a reducing sugar.



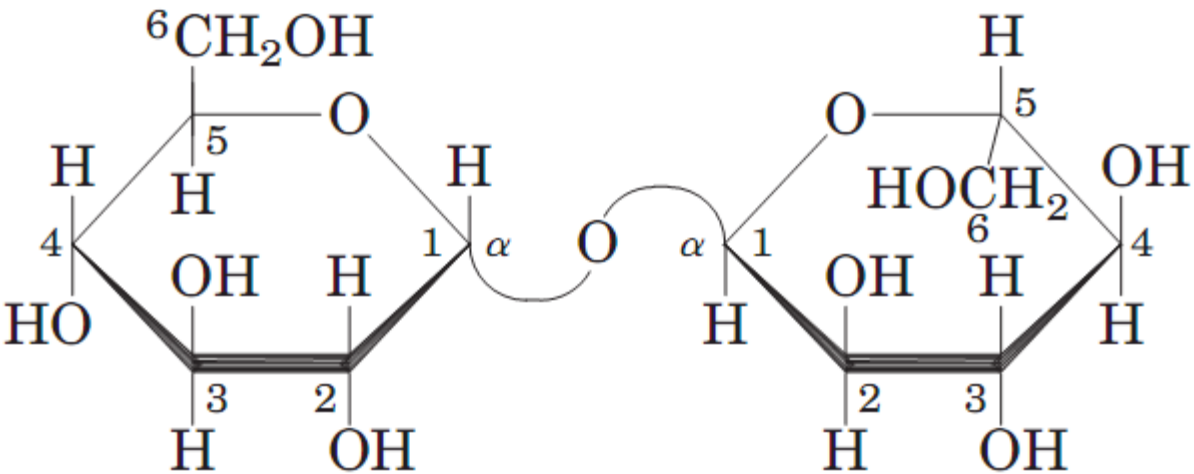
Maltose

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

Trehalose

❖Trehalose, Glc(α1←→1α)Glc, is a nonreducing sugarand a major constituent of the circulating fluid (hemolymph) of insects, serving as an energy-storage.

❖Mushrooms are the commercial source of the trehalose.

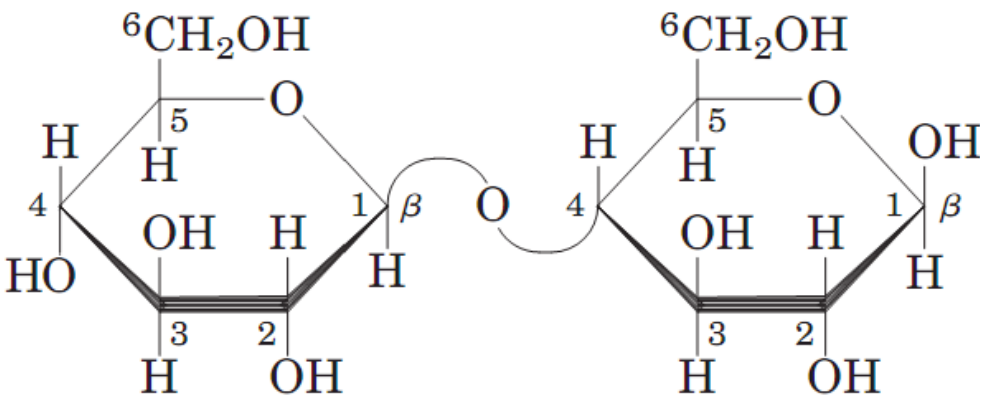


Trehalose
α-D-glucopyranosyl α-D-glucopyranoside
Glc(α1↔1α)Glc

Cellobiose and Gentiobiose

❖Cellobiose be obtained by enzymatic or acidic hydrolysis of cellulose and cellulose rich materials such as cotton, jute, or paper.

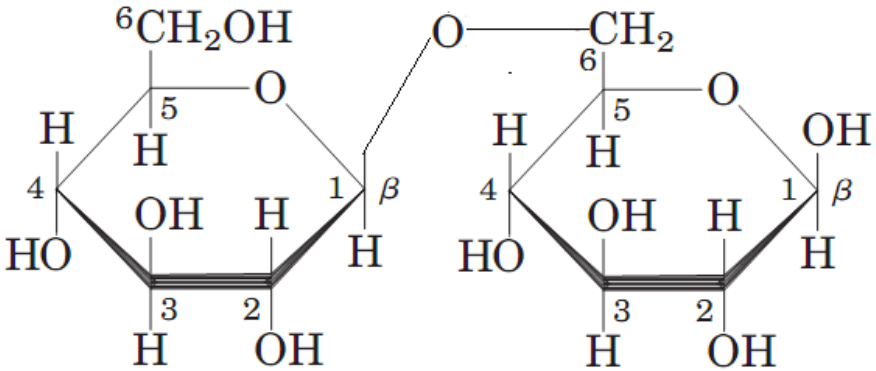
❖Gentiobiose is incorporated into the chemical structure of crocin, the chemical compound that gives saffron its color. It is a product of the caramelization of glucose



Cellobiose

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

Glu(β1→4)Glu



Gentiobiose

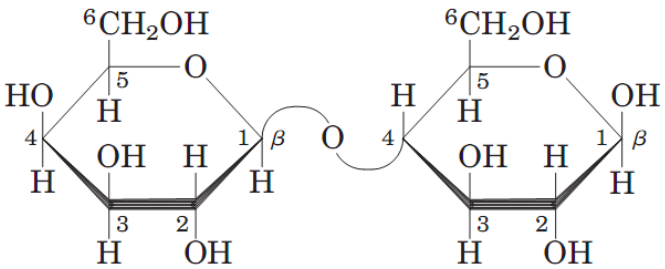
β-D-glucopyranosyl-(1→6) β-D-glucopyranose

Glu(β1→6)Glu

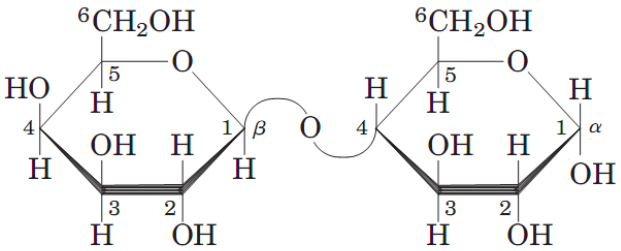
Lactose

❖Lactose is a reducing disaccharde that found in milk and consist of D-glucose and D-galactose.

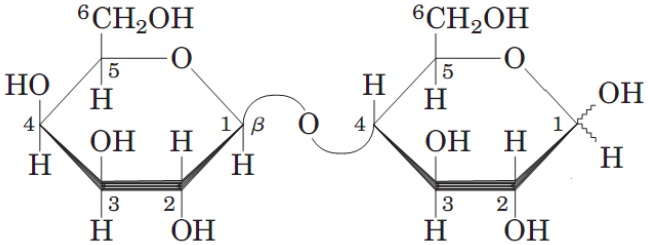
❖Lactose could be in α or β form.



Lactose (β form)
β-D-galactopyranosyl-(1→4)-β-D-glucopyranose
Gal(β1→4)Glc



Lactose (α form)
β-D-galactopyranosyl-(1→4)-α-D-glucopyranose
Gal(β1→4α)Glc



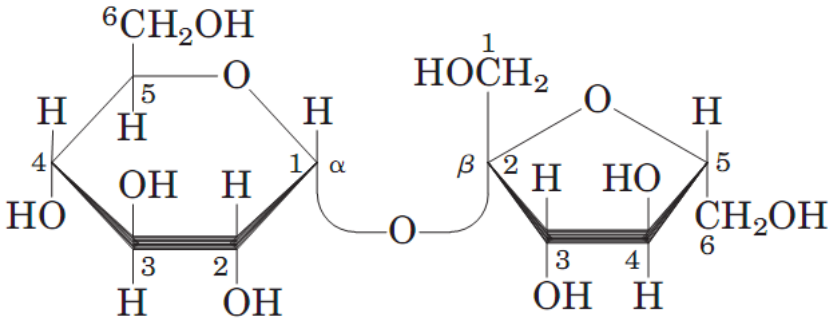
Lactose

Sucrose

- Sucrose (table sugar) is a disaccharide of glucose and fructose.

- It is formed by plants but not by animals.

- In contrast to maltose and lactose, sucrose contains no free anomeric carbon atom; and therefore it is a nonreducing sugar.



Sucrose
α-D-glucopyranosyl β-D-fructofuranoside
Glc(α1↔2β)Fru

- The abbreviated name of sucrose is either Glc(α1→2β)Fru or Fru(2β ←→1α)Glc.

- Sucrose is a major intermediate product of photosynthesis; in many plants it is the principal form in which sugar is transported from the leaves to other parts of the plant body.

Invert Sugar

❖Invert sugar is a mixture of glucose and fructose obtained from the acid (citric or ascorbic) hydrolysis of sucrose as well as the invertase enzyme.

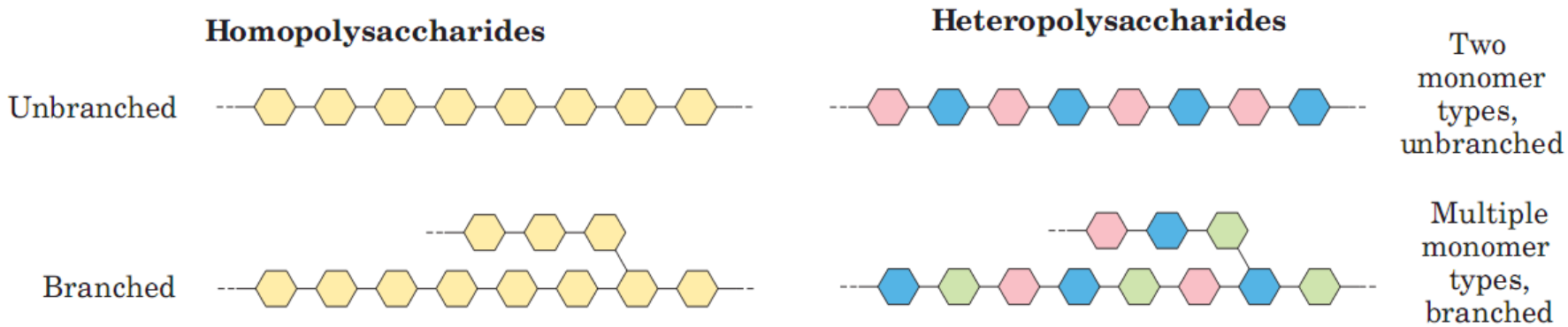
❖It is sweeter and tends to crystalize less than sucrose and fructose.

Polysaccharides

- Most carbohydrates found in nature occur as polysaccharides, polymers of medium to high molecular weight.

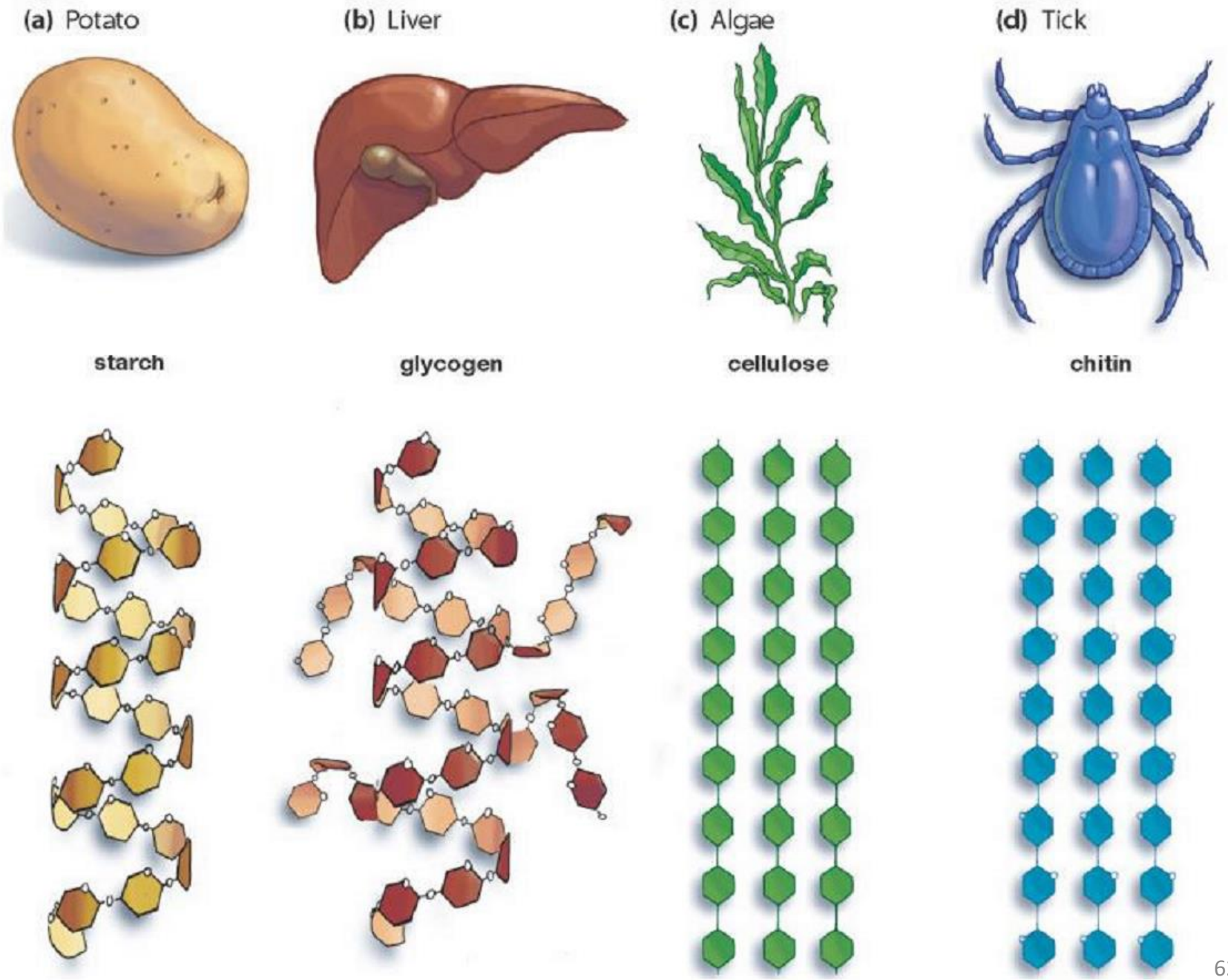
- **Polysaccharides**, also called **glycans**, differ from each other;
  - in the identity of their recurring monosaccharide units,
  - in the length of their chains,
  - in the types of bonds linking the units, and
  - in the degree of branching.

❖**Homopolysaccharides** contain only a single monomeric species; **heteropolysaccharides** contain two or more different kinds.



❖Some homopolysaccharides serve as storage forms of monosaccharides that are used as fuels; starch and glycogen are homopolysaccharides of this type.

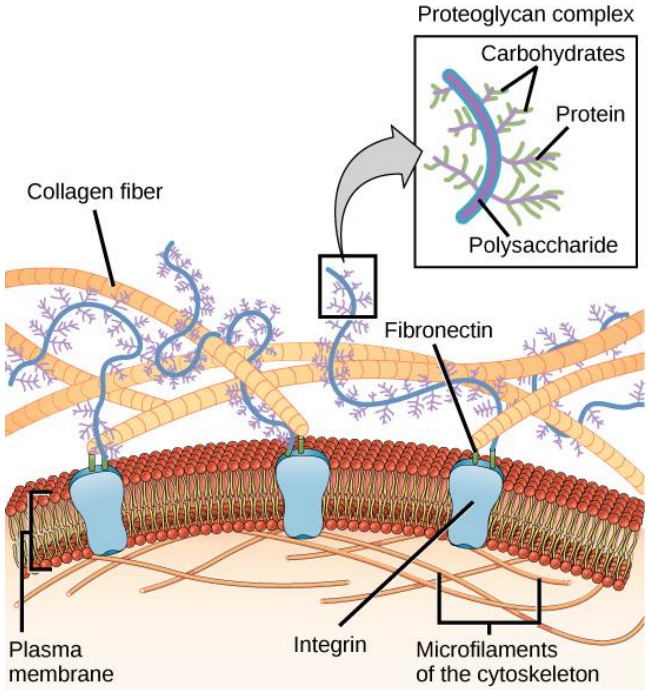
❖Other homopolysaccharides (cellulose and chitin, for example) serve as structural elements in plant cell walls and animal exoskeletons.


(a) Potato
(b) Liver
(c) Algae
(d) Tick
starch
glycogen
cellulose
chitin

❖Heteropolysaccharides provide extracellular support for organisms of all kingdoms.

❖For example, the rigid layer of the bacterial cell envelope (the peptidoglycan) is composed in part of a heteropolysaccharide built from two alternating monosaccharide units.

❖In animal tissues, the extracellular space is occupied by several types of heteropolysaccharides, which form a matrix that holds individual cells together and provides protection, shape, and support to cells, tissues, and organs.



❖Unlike proteins, polysaccharides generally do not have defining molecular weights.

❖This difference is a consequence of the mechanisms of assembly of the two types of polymer.

❖Proteins are synthesized on a template (messenger RNA) of defined sequence and length, by enzymes that follow the template exactly.

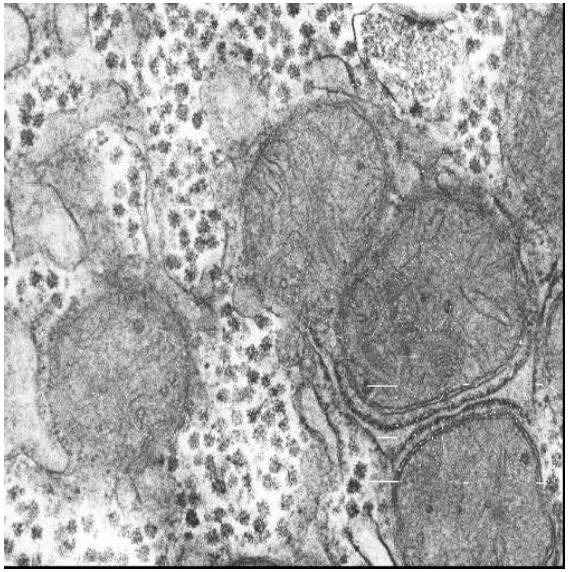
❖For polysaccharide synthesis there is no template; rather, the program for polysaccharide synthesis is intrinsic to the enzymes that catalyze the polymerization of the monomeric units, and there is no specific stopping point in the synthetic process; the products thus vary in length.

Storage Homopolysaccharides

❖The most important storage polysaccharides are starch in plant cells and glycogen in animal cells.

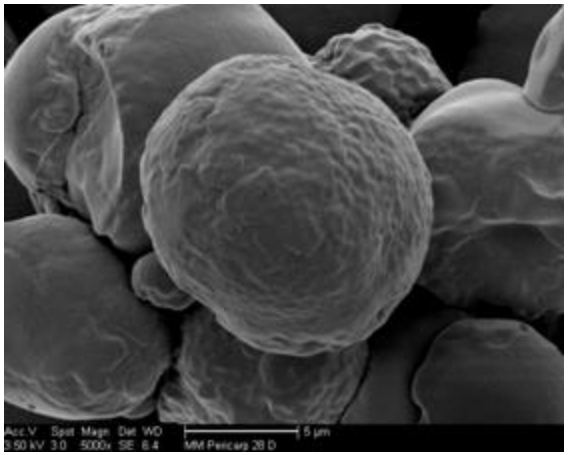
❖Both polysaccharides occur intracellularly as large clusters or granules.

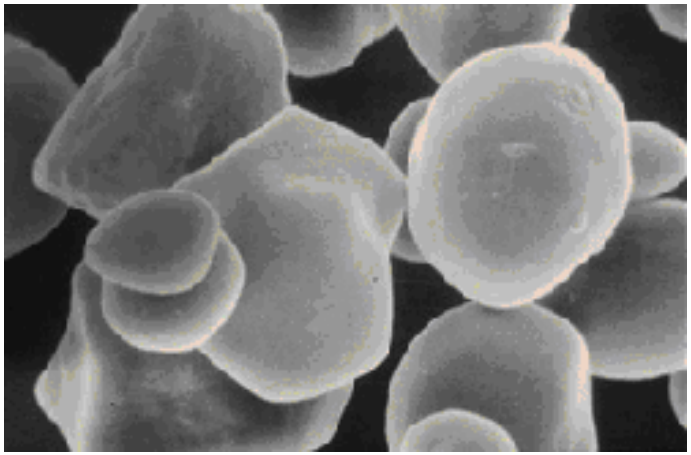
❖Starch and glycogen molecules are heavily hydrated, because they have many exposed hydroxyl groups available to hydrogen-bond with water.



Starch

❖Most plant cells have the ability to form starch, and starch storage is especially abundant in tubers (underground stems), such as potatoes, and in seeds.



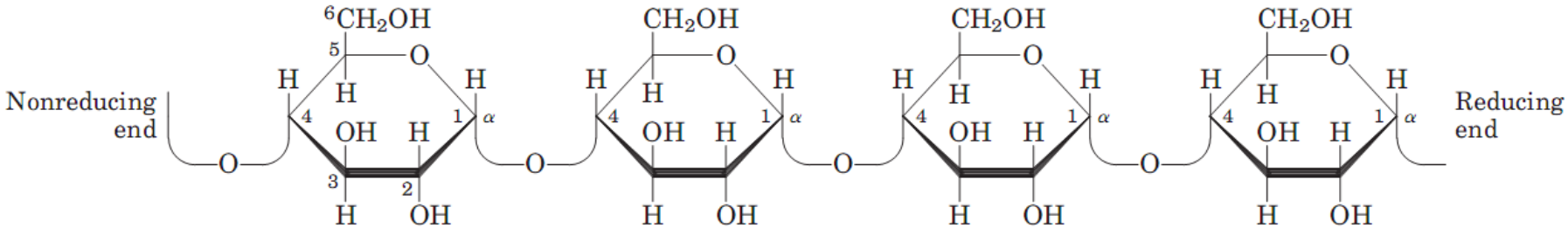


Starch granules from tomato fruit and corn.

❖Starch contains two types of glucose polymer, amylose and amylopectin.

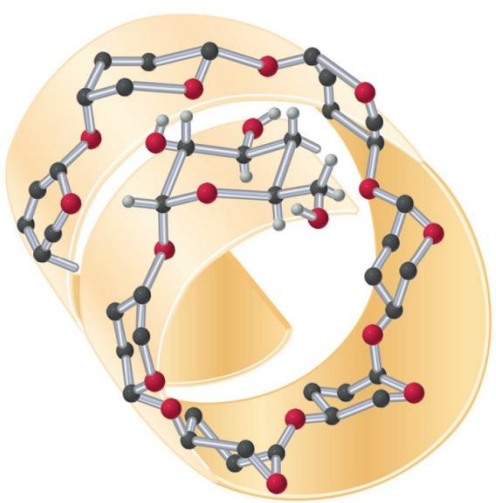
Amylose

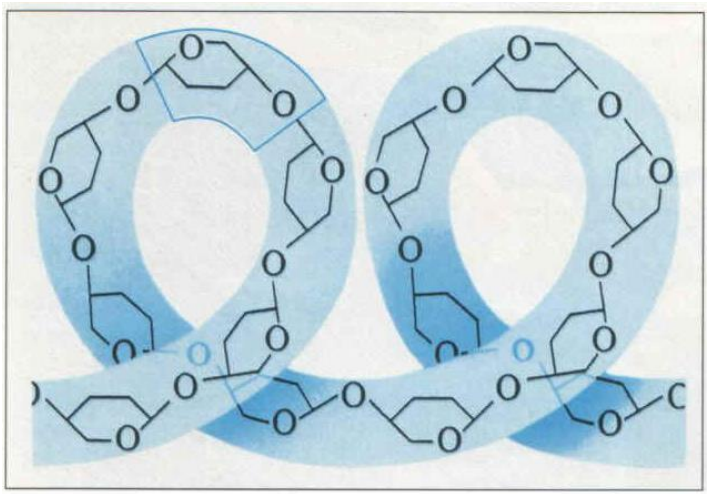
❖Amylose consists of long, unbranched chains of D-glucose residues connected by (α1→4) linkages (as in maltose).



(a) amylose

❖Since its structurally similar, it is easier for amylose to have a secondary structure.



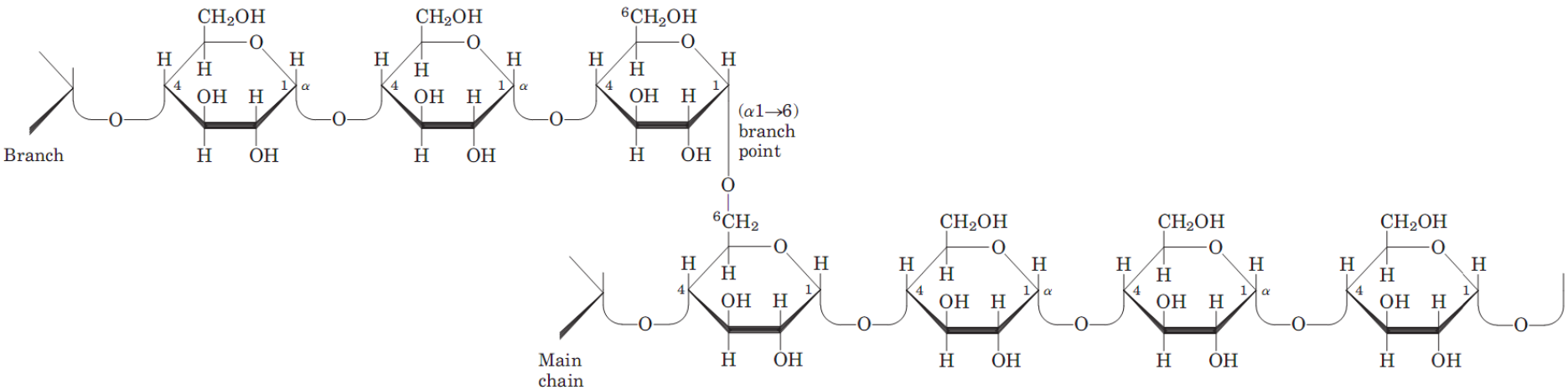


Amilopektin

❖Amylopectin also has a high molecular weight (up to 200 million) but unlike amylose is highly branched.

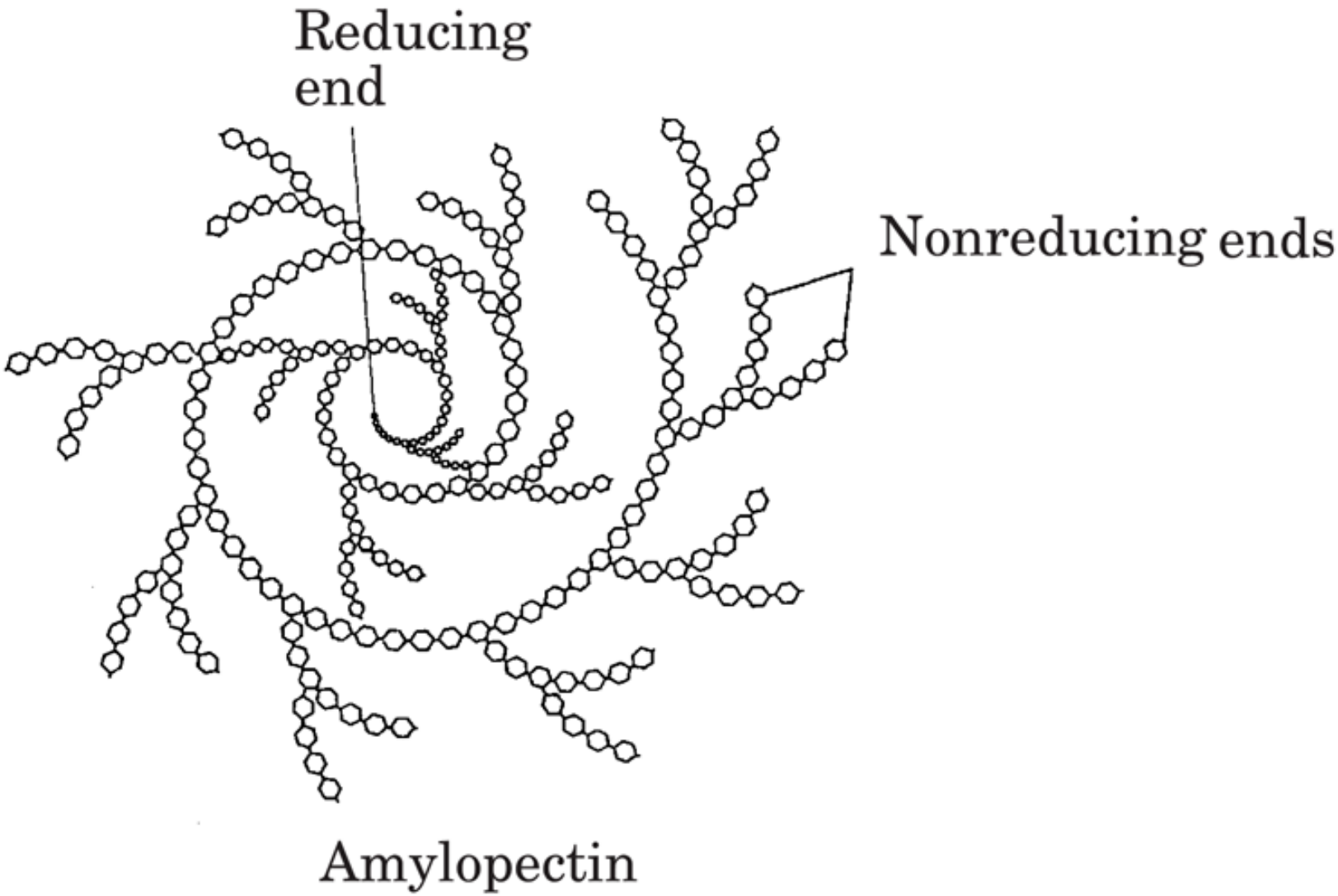
❖The glycosidic linkages joining successive glucose residues in amylopectin chains are (α1→4);

❖the branch points (occurring every 24 to 30 residues) are (α1→6) linkages.

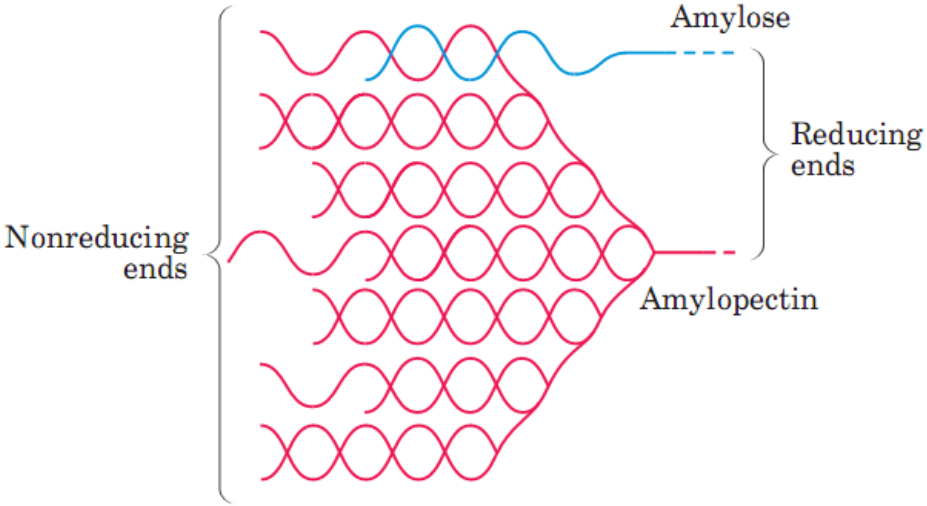


(b) Amylopectin

❖Highly branched amylopectin does not have a secondary structure.



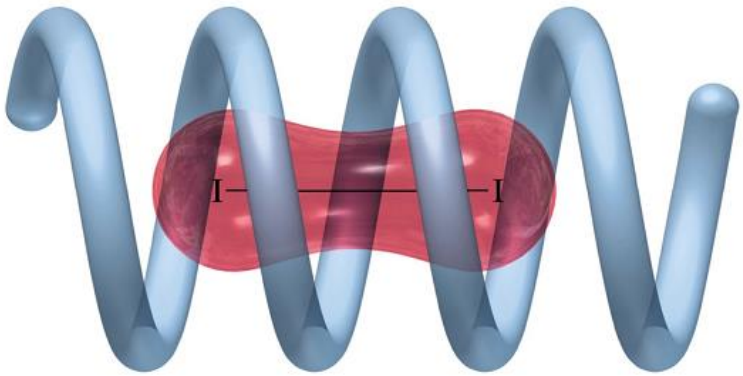
❖Natural starch consist of (10-20%) amylose and (80-90%) amylopectin.



(c)

❖Amylopectin dispersed colloidally in hot water whereas amylose is soluble.

❖Amylose is responsible for deep blue color of iodine reaction of starch.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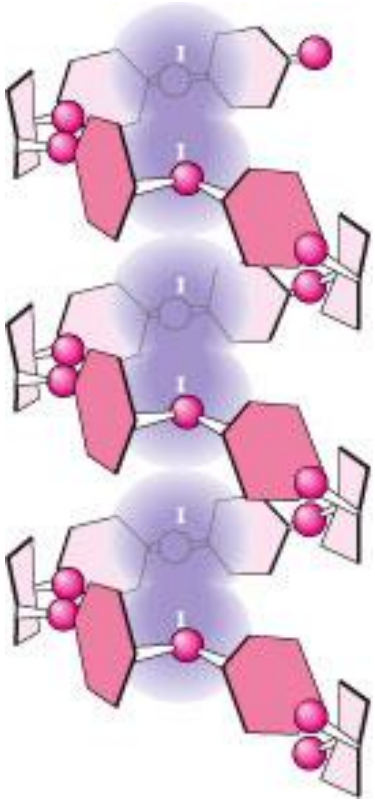
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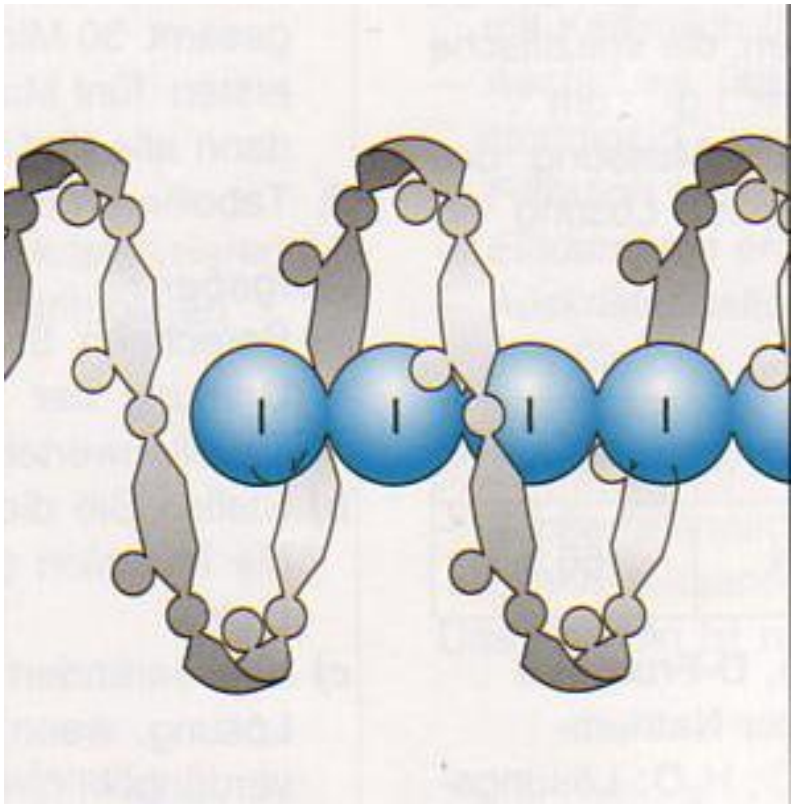
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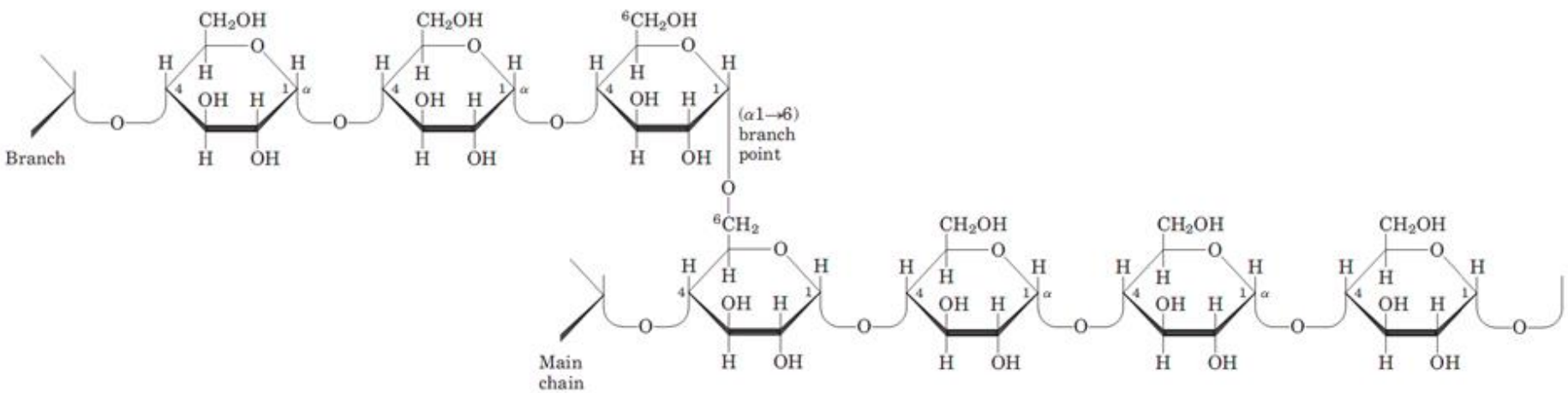
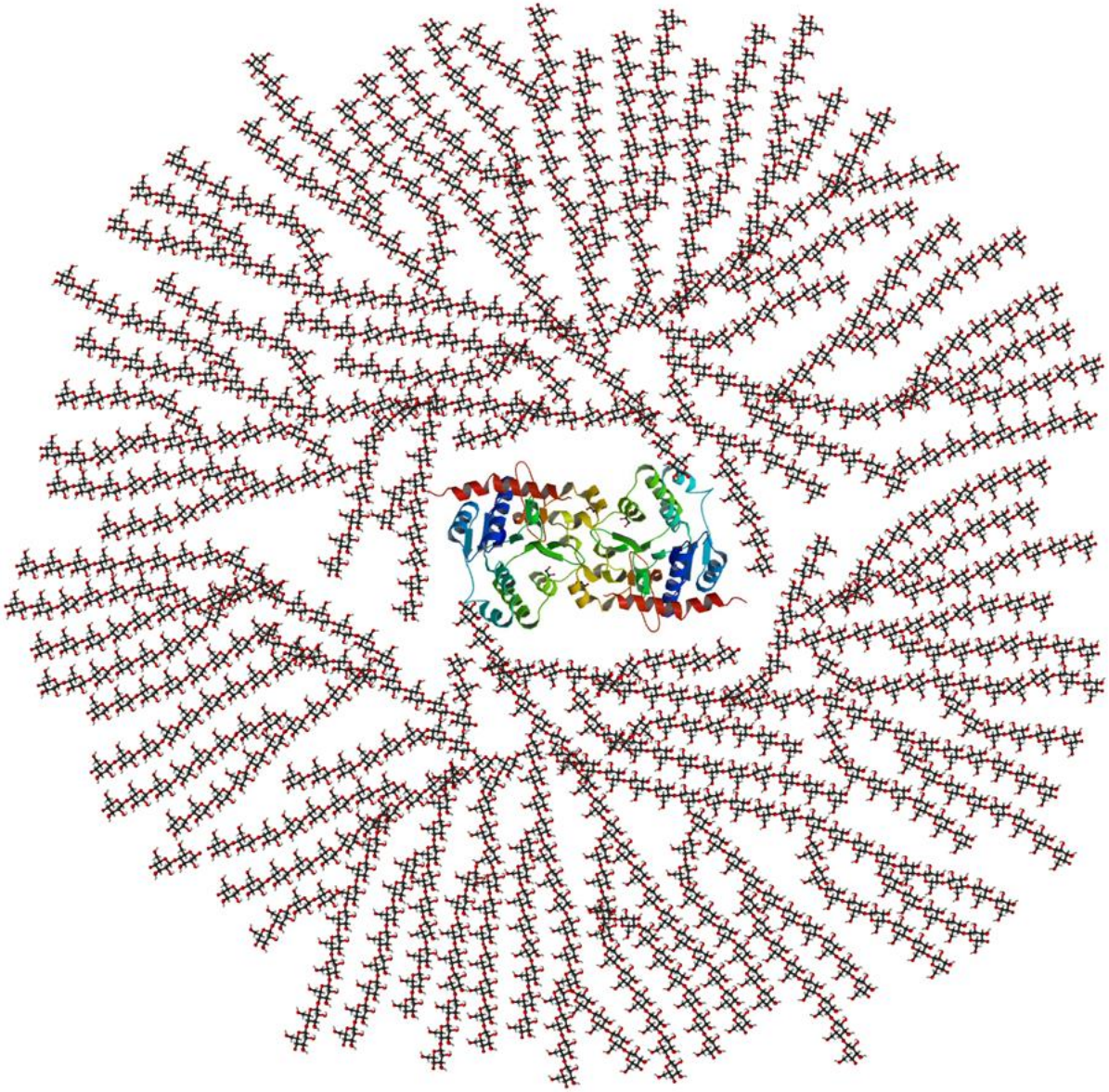
Glycogen

❖Glycogen is the main storage polysaccharide of animal cells.

❖ Like amylopectin, glycogen is a polymer of (α1→4) linked subunits of glucose, with (α 1→6) linked branches.

❖However, glycogen is more extensively branched (on average, every 8 to 12 residues) and more compact than starch.





Structure of glycogenin and glycogen.

❖Because each branch in glycogen ends with a non-reducing sugar unit, a glycogen molecule with n branches has n+1 non-reducing ends, but only one reducing end.

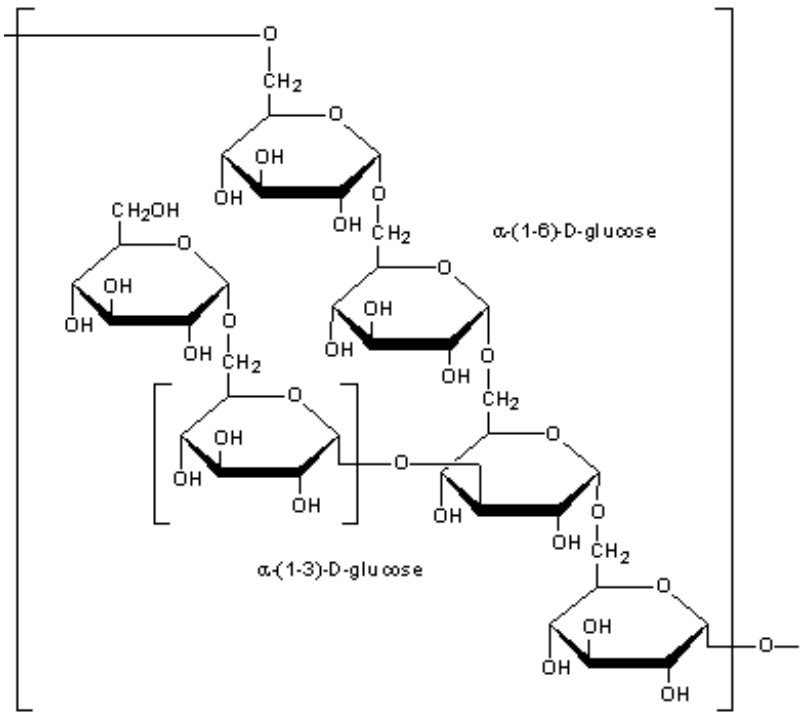
❖When glycogen is used as an energy source, glucose units are removed one at a time from the non-reducing ends.

❖Degradative enzymes that act only at non-reducing ends can work simultaneously on the many branches, speeding the conversion of the polymer to monosaccharides.

❖Due to the high osmolarity of glucose, glycogen is more suitable to be the intracellular storage of energy.

Dextrans

❖Dextrans are bacterial and yeast polysaccharides made up of (α1→6)-linked poly-D-glucose; all have (α1→3) branches, and some also have (α1→2) or (α1→4) branches.



❖Dental plaque, formed by bacteria growing on the surface of teeth, is rich in dextrans, which are adhesive and allow the bacteria to stick to teeth and to each other.

❖Dextrans also provide a source of glucose for bacterial metabolism.

❖Synthetic dextrans are used in several commercial products (for example, Sephadex) that serve in the fractionation of proteins by size-exclusion chromatography

Structural Homopolysaccharides

Cellulose

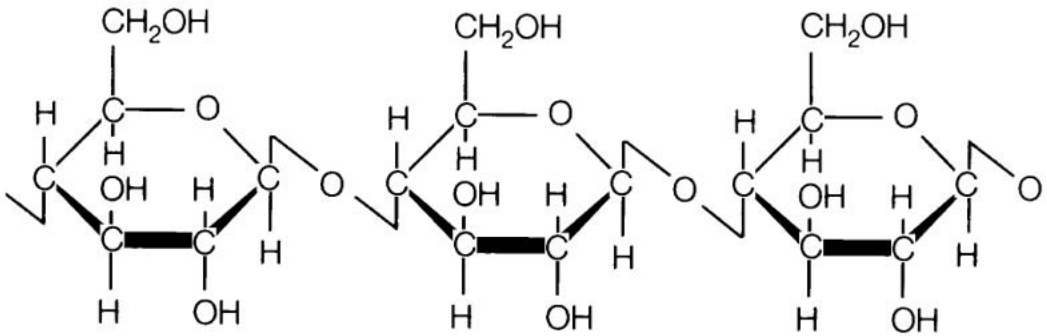
❖**Cellulose**, a fibrous, tough, water-insoluble substance, is found in the cell walls of plants, particularly in stalks, stems, trunks, and all the woody portions of the plant body.

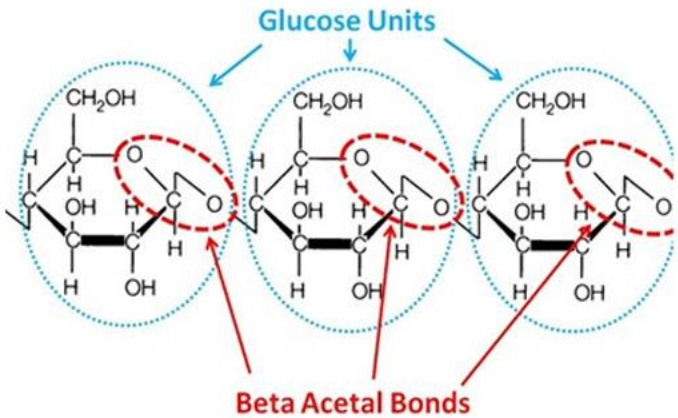
❖Cellulose constitutes much of the mass of wood, and cotton is almost pure cellulose.

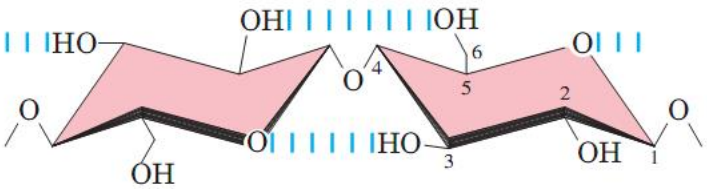
❖Like amylose, the cellulose molecule is a linear, unbranched homopolysaccharide, consisting of 10,000 to 15,000 D-glucose units.

❖But there is a very important difference: in cellulose the glucose residues have the β configuration, whereas in amylose the glucose is in the α configuration.

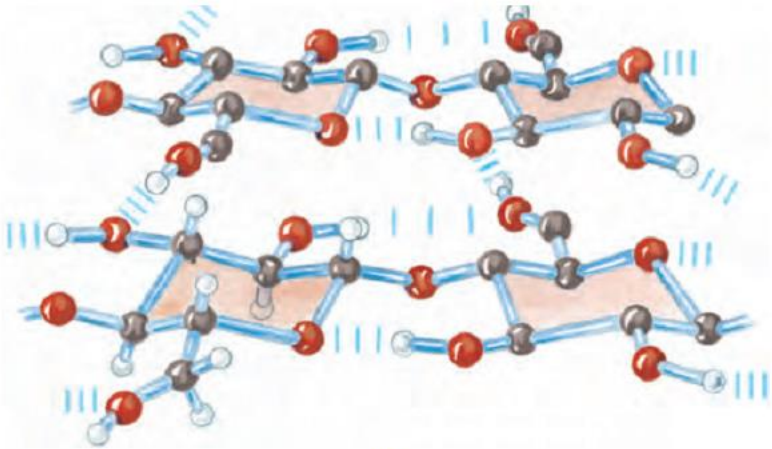
❖The glucose residues in cellulose are linked by (β1→4) glycosidic bonds, in contrast to the (α1→4) bonds of amylose.







(a)



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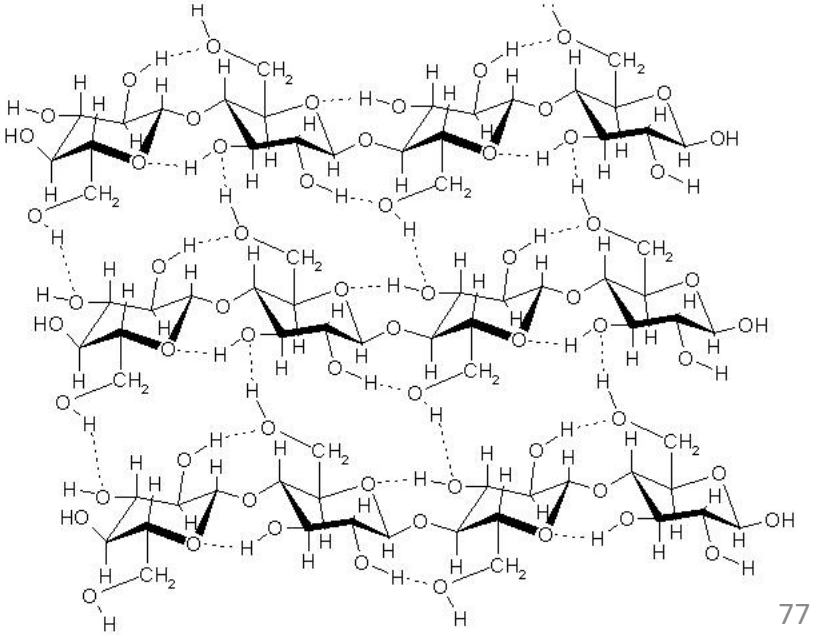
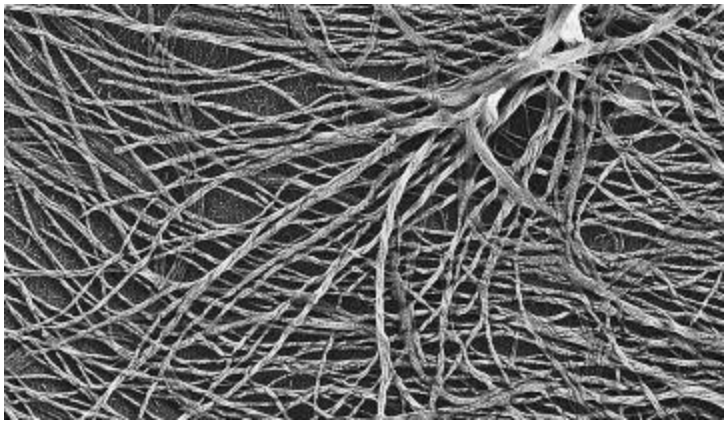
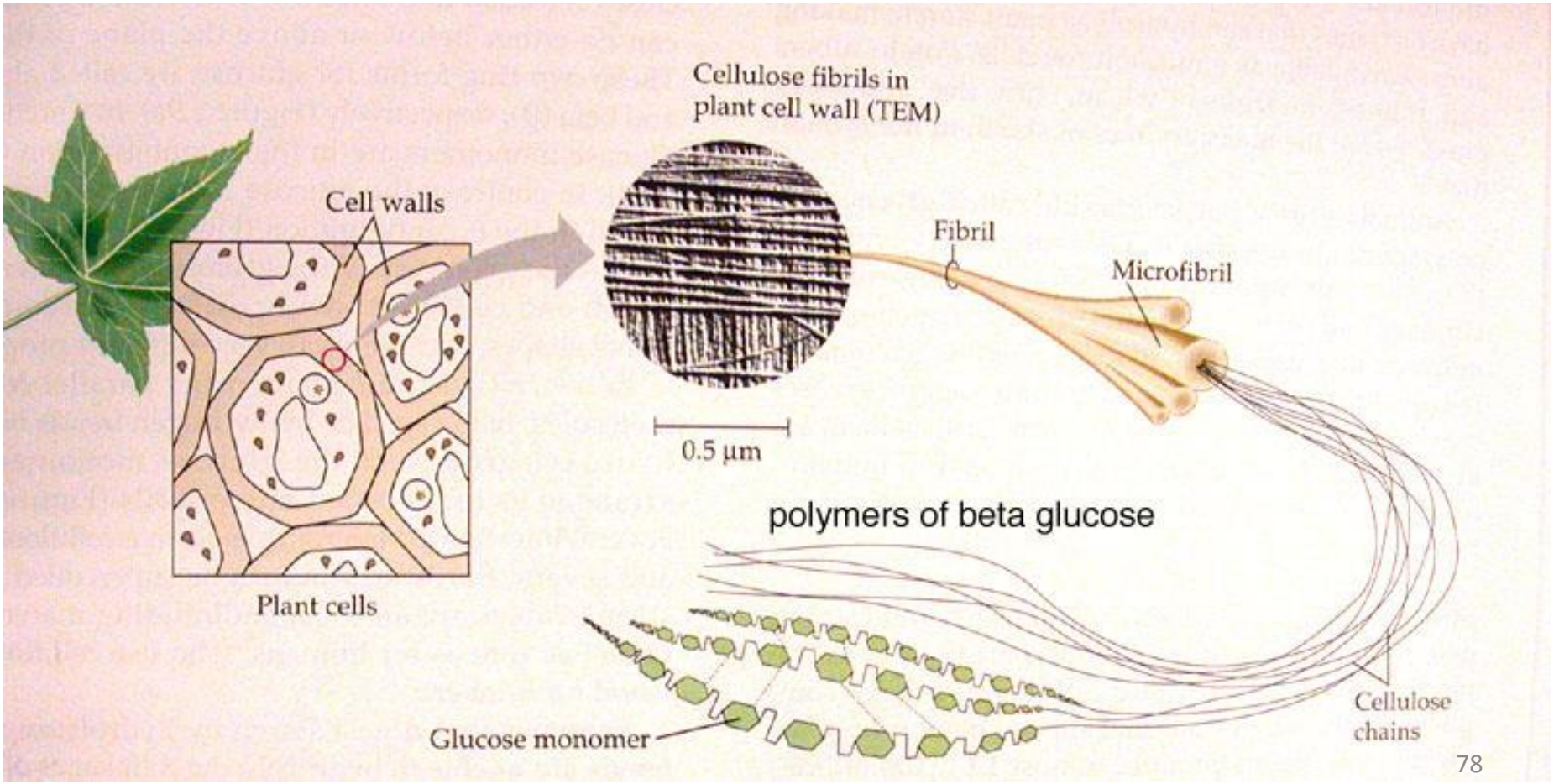





Cellulose fibrils in
plant cell wall (TEM)
Cell walls
Fibril
Microfibril
0.5 µm
polymers of beta glucose
Plant cells
Glucose monomer
Cellulose
chains

❖Glycogen and starch ingested in the diet are hydrolyzed by α-amylases and glycosidases, enzymes in saliva and the intestine that break (α1→4) glycosidic bonds between glucose units.

❖Most vertebrate animals cannot use cellulose as a fuel source, because they lack an enzyme to hydrolyze the (β1→4) linkages.

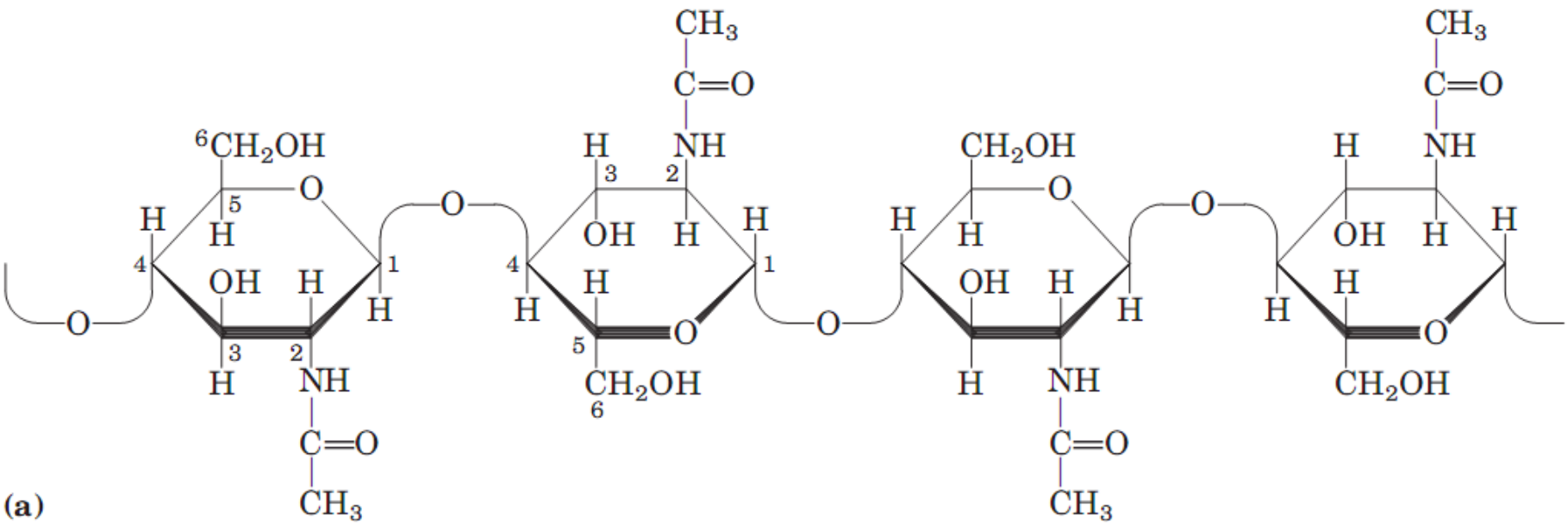
❖Termites readily digest cellulose (and therefore wood), but only because their intestinal tract harbors a symbiotic microorganism, *Trichonympha*, that secretes cellulase, which hydrolyzes the (β1→4) linkages.

❖There is one important exception to the absence of cellulase in vertebrates: ruminant animals such as cattle, sheep, and goats harbor symbiotic microorganisms in the rumen (the first of their four stomach compartments) that can hydrolyze cellulose, allowing the animal to degrade dietary cellulose from soft grasses

Chitin

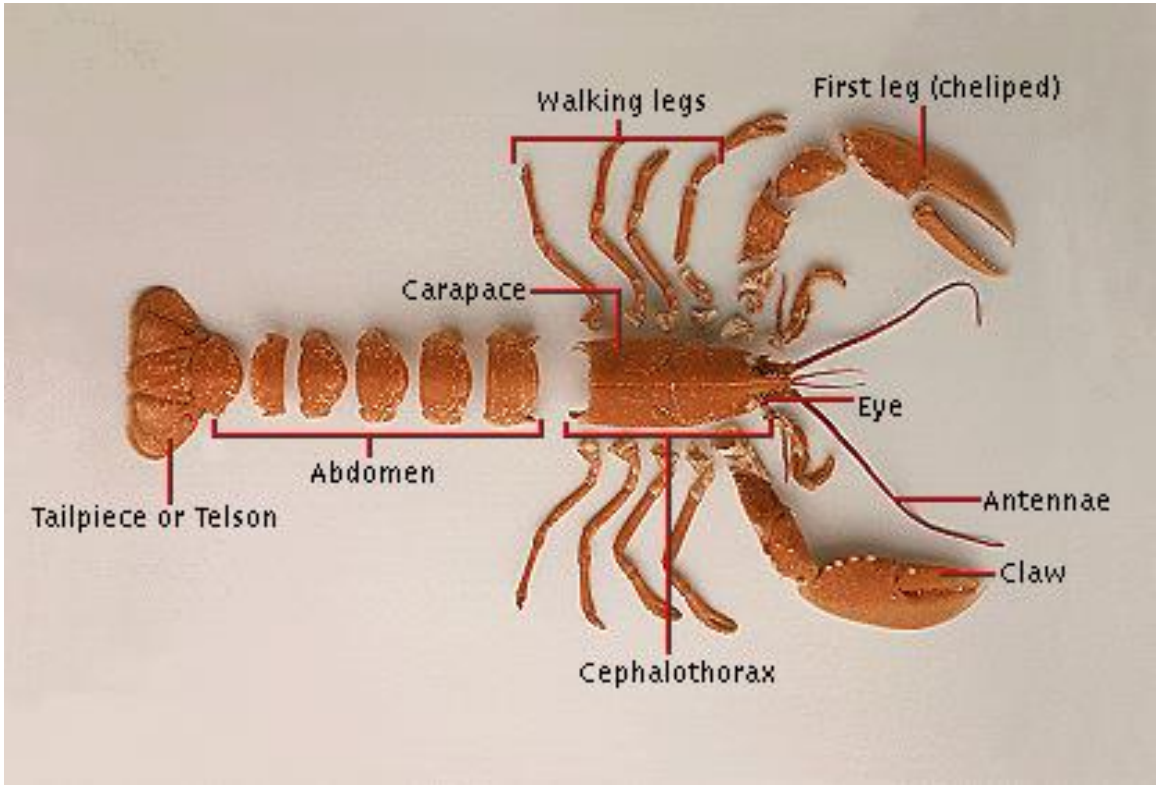
❖Chitin is a linear homopolysaccharide composed of N-acetylglucosamine residues in (β1→4) linkage.

❖The only chemical difference from cellulose is the replacement of the hydroxyl group at C-2 with an acetylated amino group.



❖Chitin forms extended fibers similar to those of cellulose, and like cellulose cannot be digested by vertebrates.

❖Chitin is the principal component of the hard exoskeletons of nearly a million species of arthropods—insects, lobsters, and crabs, for example— and is probably the second most abundant polysaccharide, next to cellulose, in nature



3-D Structures of Homopolysaccharide

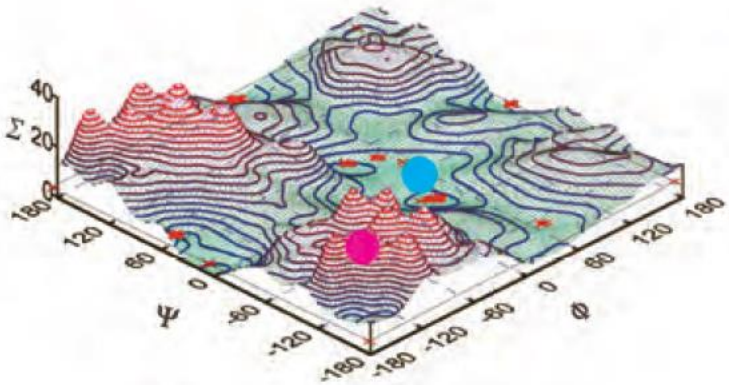
❖The folding of polysaccharides in three dimensions follows the same principles as those governing polypeptide structure:

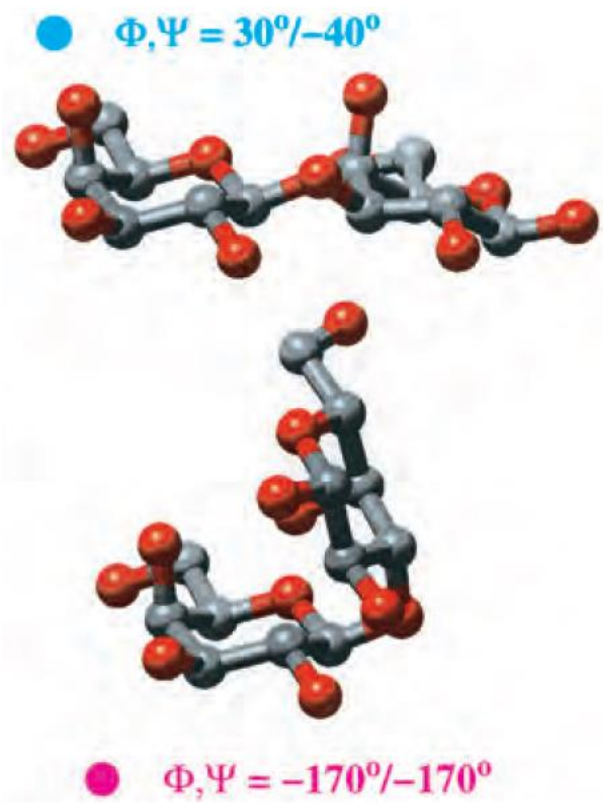
❖subunits with a more-or-less rigid structure dictated by covalent bonds form three-dimensional macromolecular structures

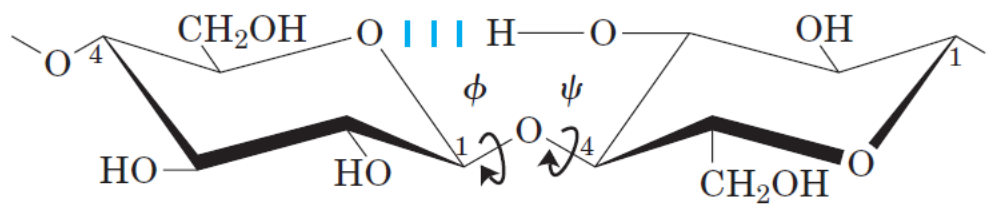
❖that are stabilized by weak interactions within or between molecules, such as hydrogen bonds and hydrophobic and van der Waals interactions, and,

❖for polymers with charged subunits, electrostatic interactions.

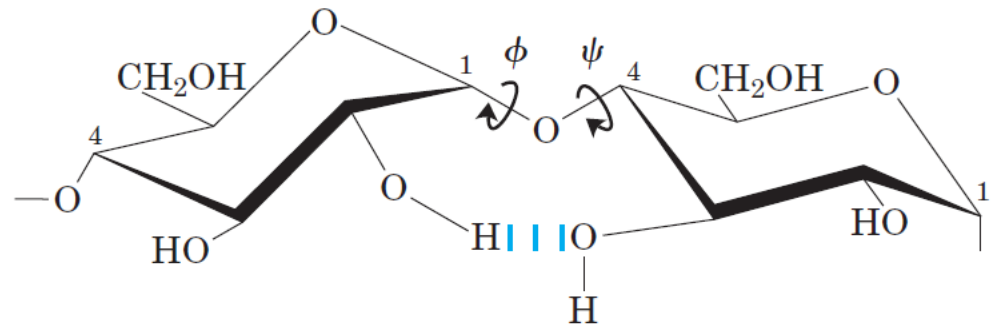
❖Because polysaccharides have so many hydroxyl groups, hydrogen bonding has an especially important influence on their structure.



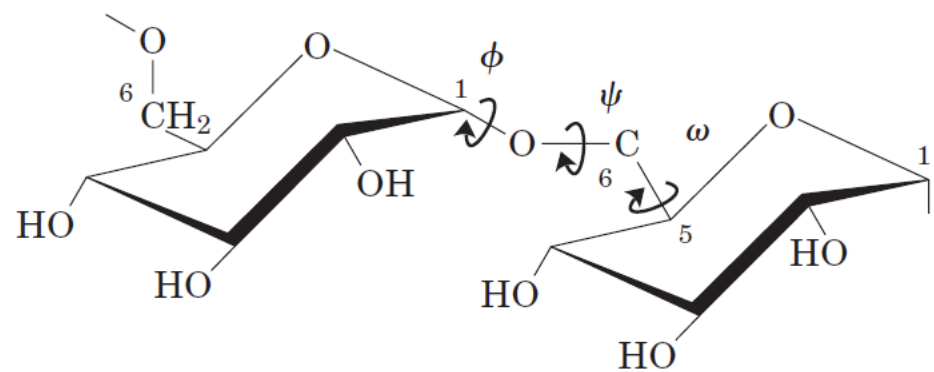




Cellulose
(β1→4)Glc repeats



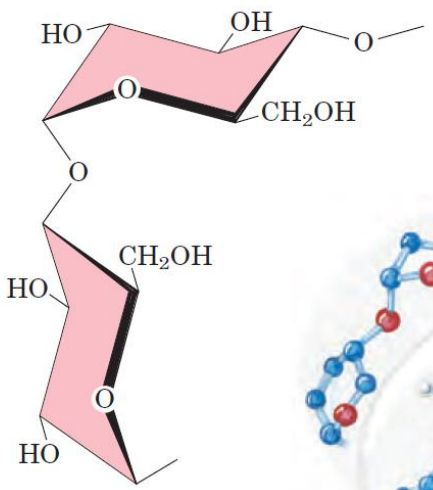
Amylose
(α1→4)Glc repeats



Dextran
(α1→6)Glc repeats, with (α1→3) branches

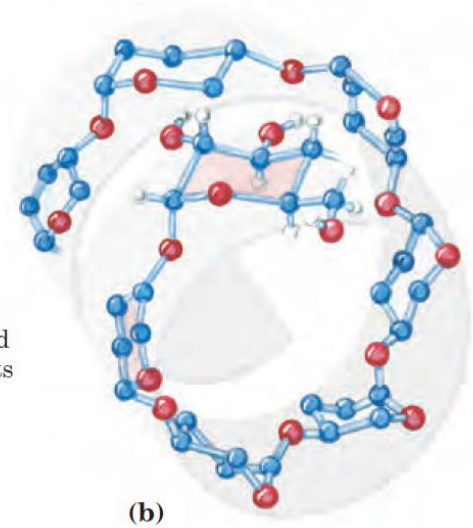
❖The most stable three-dimensional structure for the (α1→4)-linked chains of starch and glycogen is a tightly coiled helix, stabilized by interchain hydrogen bonds.

❖For cellulose, the most stable conformation is that in which each chair is turned 180° relative to its neighbors, yielding a straight, extended chain.

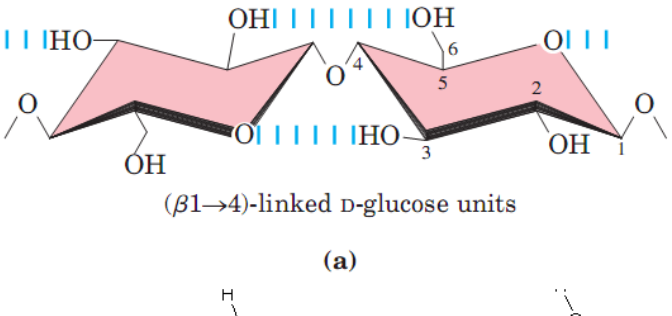


(α1→4)-linked D-glucose units

(a)

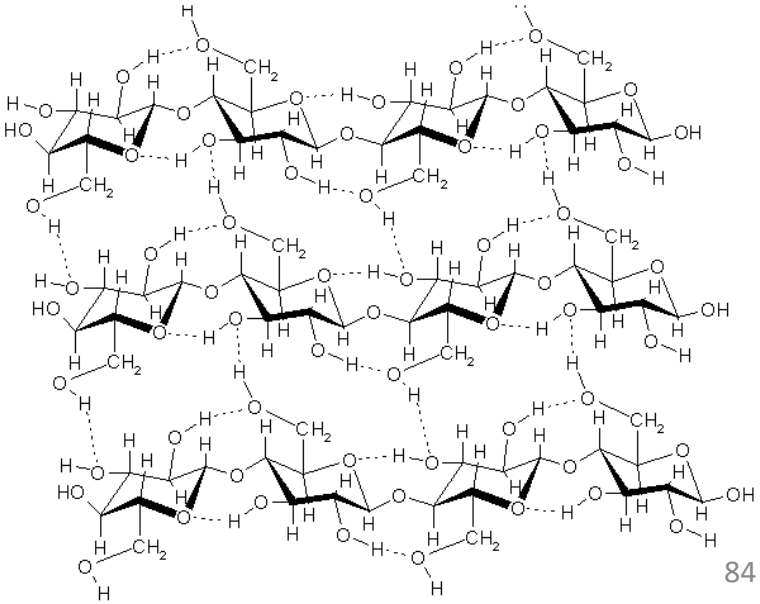


(b)



(β1→4)-linked D-glucose units

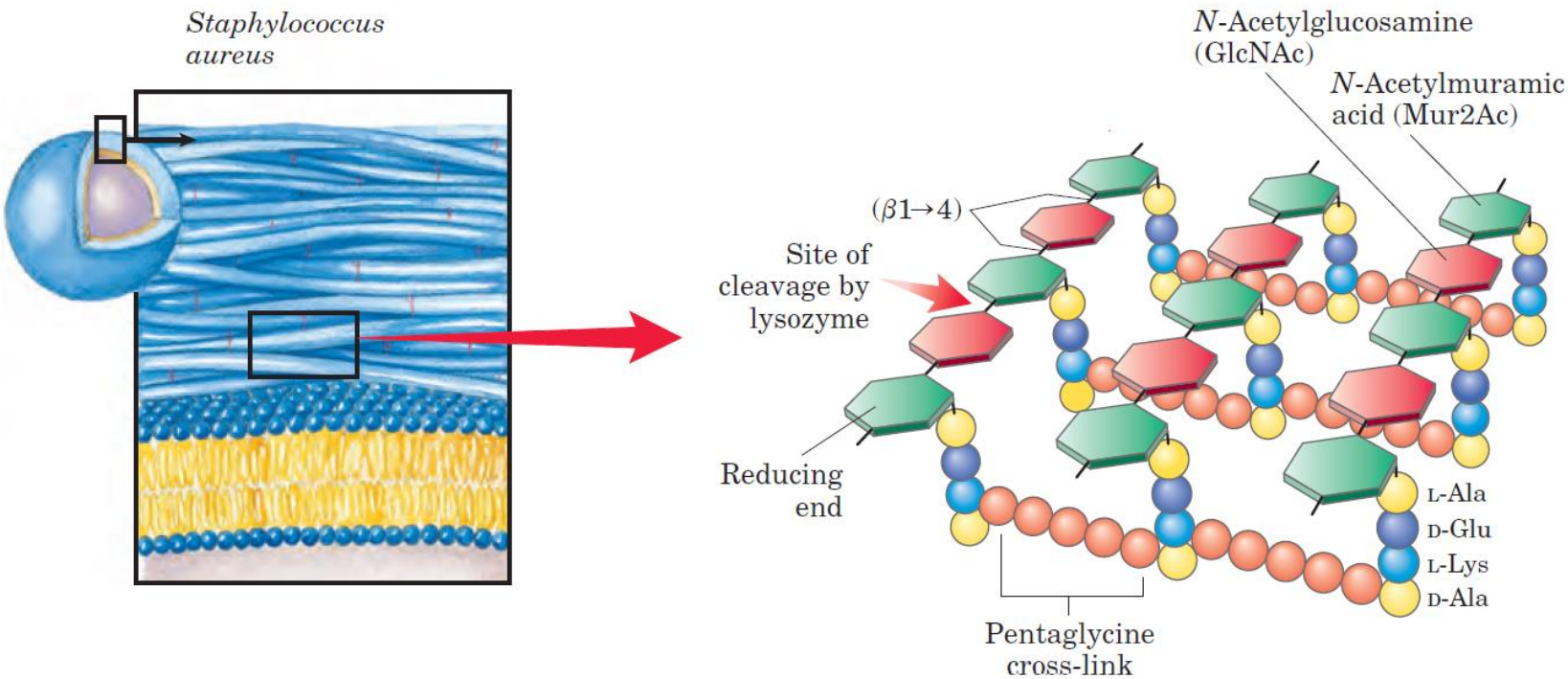
(a)

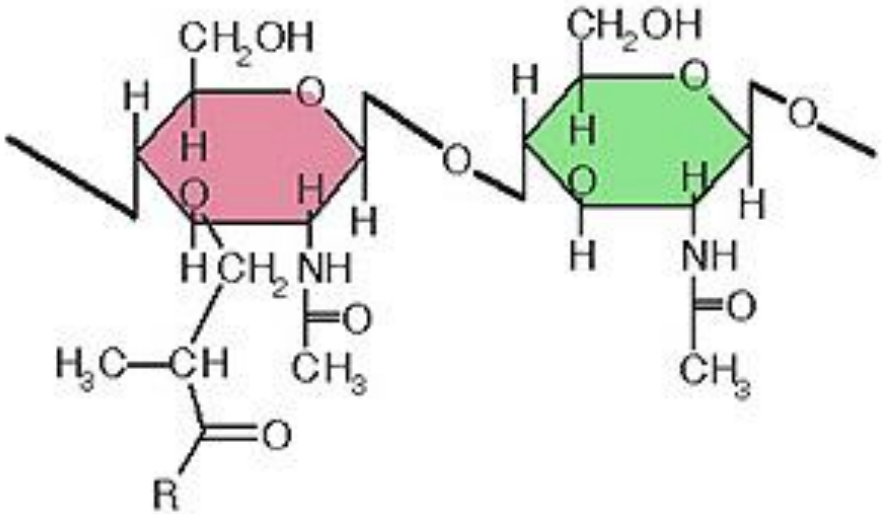


Heteropolysaccharides

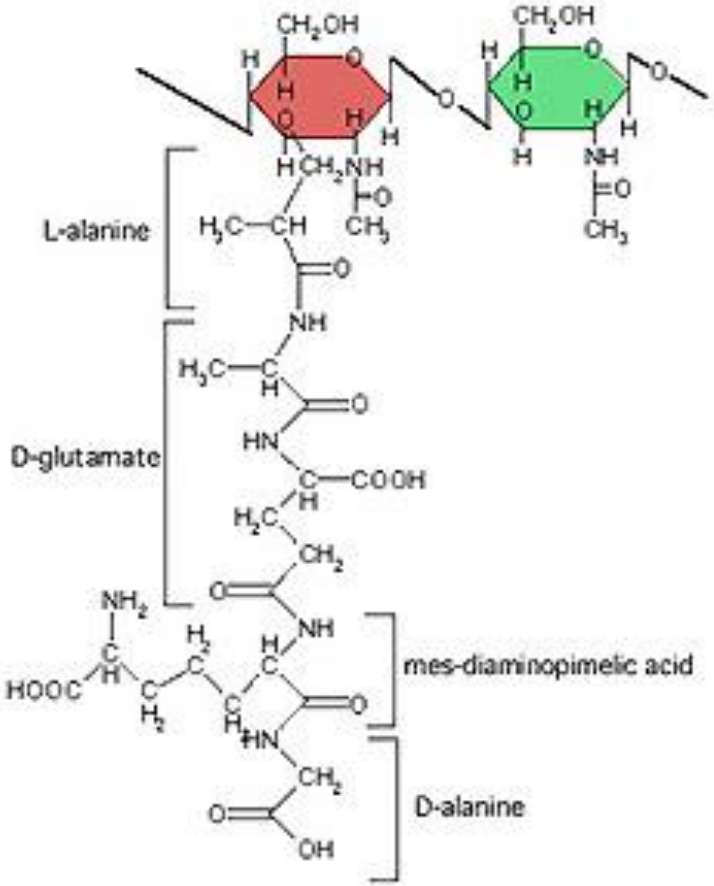
❖The rigid component of bacterial cell walls (peptidoglycan) is a heteropolymer of alternating (β1→4)-linked N-acetylglucosamine and N-acetylmuramic acid residues

❖The enzyme lysozyme kills bacteria by hydrolyzing the (β1→4) glycosidic bond between N-acetylglucosamine and N-acetylmuramic acid





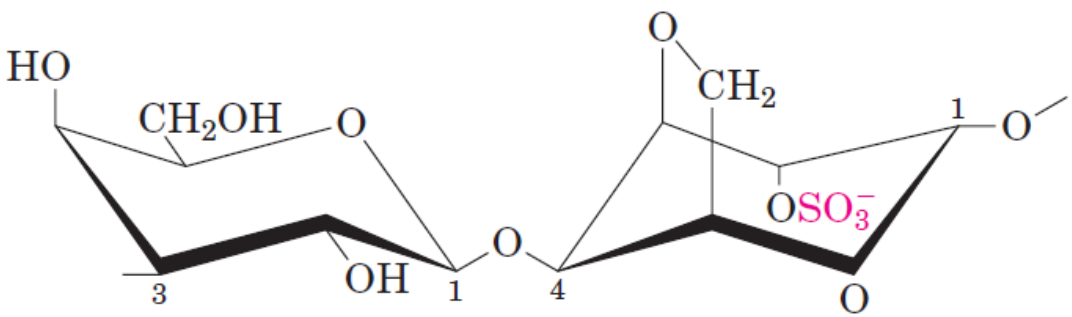
N-acetylmuramic acid-N-acetylglucosamine



Agar

❖Certain marine red algae, including some of the seaweeds, have cell walls that contain agar, a mixture of sulfated heteropolysaccharides made up of D-galactose and an L-galactose derivative ether-linked between C-3 and C-6.

❖Agar is a complex mixture of polysaccharides, all with the same backbone structure but substituted to varying degrees with sulfate and pyruvate.



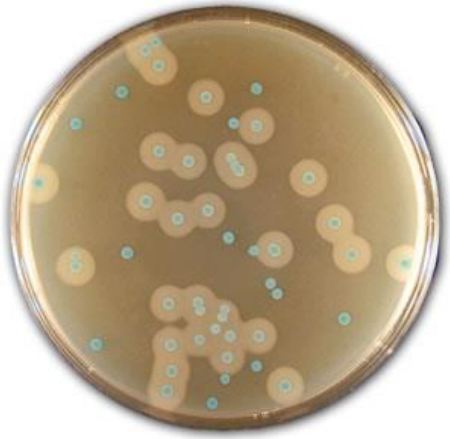
Agarose

3)D-Gal(β1→4)3,6-anhydro-L-Gal2S(α1 repeats

❖Agarose is the agar component with the fewest charged groups (sulfates, pyruvates).

❖The remarkable gel-forming property of agarose makes it useful in the biochemistry laboratory.

❖When a suspension of agarose in water is heated and cooled, the agarose forms a double helix: two molecules in parallel orientation twist together with a helix repeat of three residues; water molecules are trapped in the central cavity.



❖These structures in turn associate with each other to form a gel—a three-dimensional matrix that traps large amounts of water.

Glycosaminoglycans

❖The extracellular space in the tissues of multicellular animals is filled with a gel-like material, the extracellular matrix (ECM), also called ground substance, which holds the cells together and provides a porous pathway for the diffusion of nutrients and oxygen to individual cells.

❖The ECM that surrounds fibroblasts and other connective tissue cells is composed of an interlocking meshwork of heteropolysaccharides and fibrous proteins such as fibrillar collagens, elastins, and fibronectins.

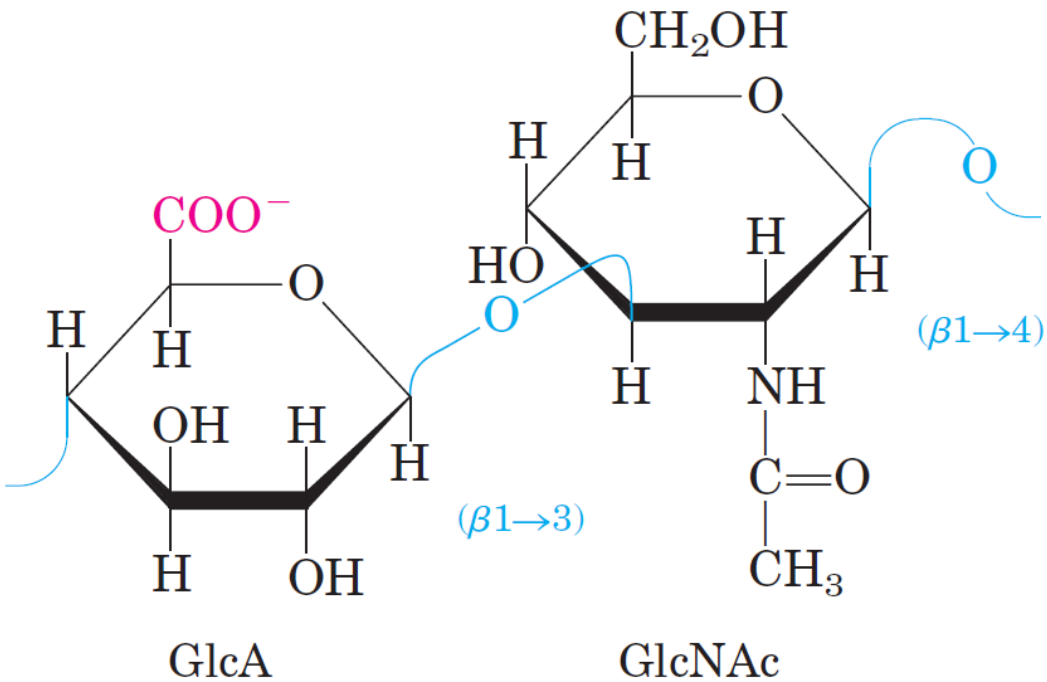
❖Basement membrane is a specialized ECM that underlies epithelial cells; it consists of specialized collagens, laminins, and heteropolysaccharides.

❖These heteropolysaccharides, the glycosaminoglycans, are a family of linear polymers composed of repeating disaccharide units

Hyaluronic acid

❖The glycosaminoglycan hyaluronan (hyaluronic acid) contains alternating residues of D-glucuronic acid and N-acetylglucosamine.

Glycosaminoglycan	Number of disaccharides per chain	Repeating disaccharide
Hyaluronate	~50,000	



❖Hyaluronan forms clear, highly viscous solutions that serve as lubricants in the synovial fluid of joints and give the vitreous humor of the vertebrate eye its jellylike consistency.

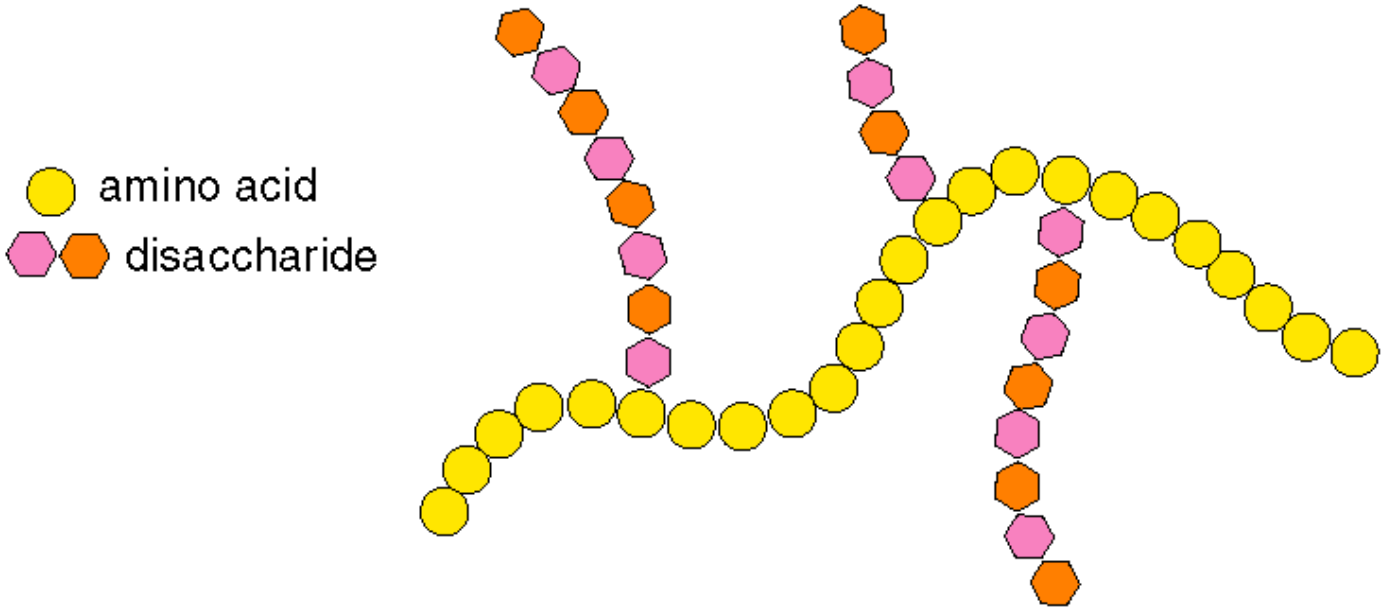
❖Hyaluronan is also a component of the extracellular matrix of cartilage and tendons, to which it contributes tensile strength and elasticity as a result of its strong noncovalent interactions with other components of the matrix.

❖Hyaluronidase, an enzyme secreted by some pathogenic bacteria, can hydrolyze the glycosidic linkages of hyaluronan, rendering tissues more susceptible to bacterial invasion.

❖In many animal species, a similar enzyme in sperm hydrolyzes an outer glycosaminoglycan coat around the ovum, allowing sperm penetration.

❖Other glycosaminoglycans differ from hyaluronan in three respects:

- they are generally much shorter polymers,
- they are covalently linked to specific proteins (proteoglycans), and,
- one or both monomeric units differ from those of hyaluronan.

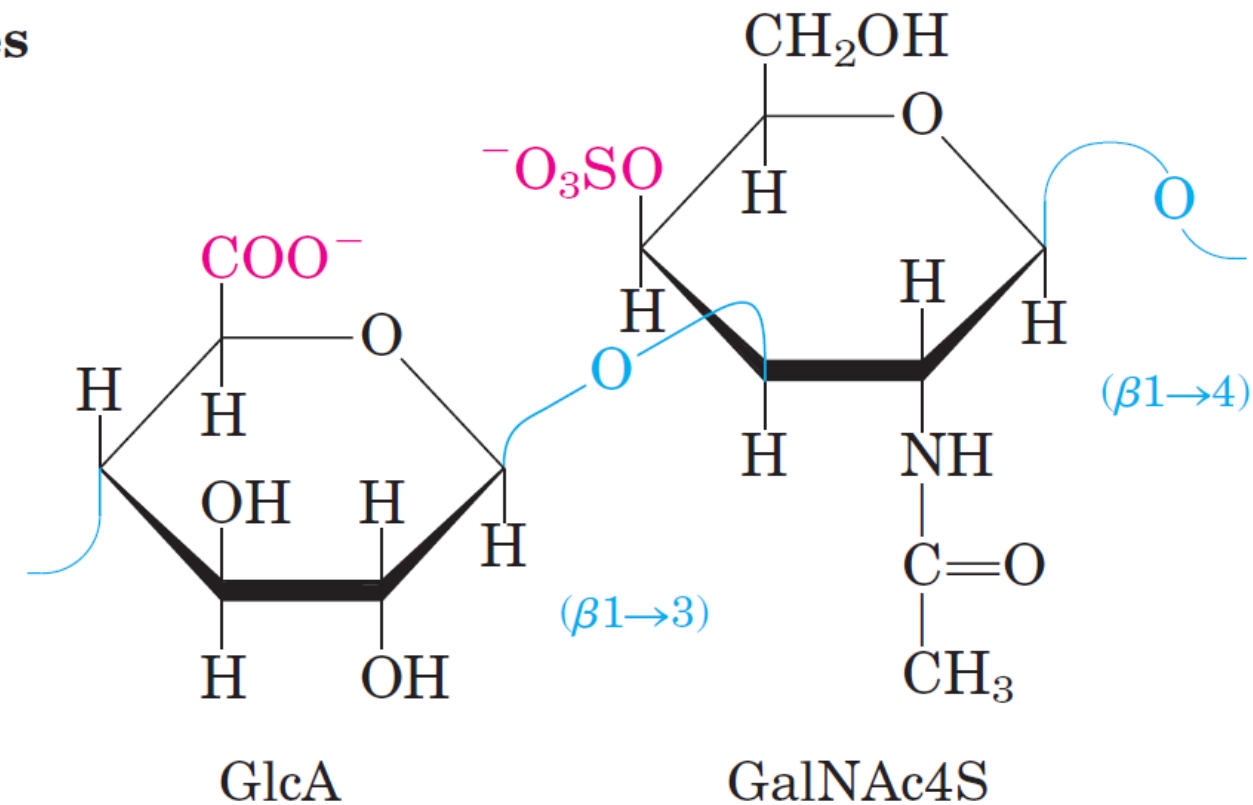


Chondroitin sulfate

❖Chondroitin sulfate contributes to the tensile strength of cartilage, tendons, ligaments, and the walls of the aorta.

Glycosaminoglycan	Number of disaccharides per chain
Chondroitin 4-sulfate	20–60

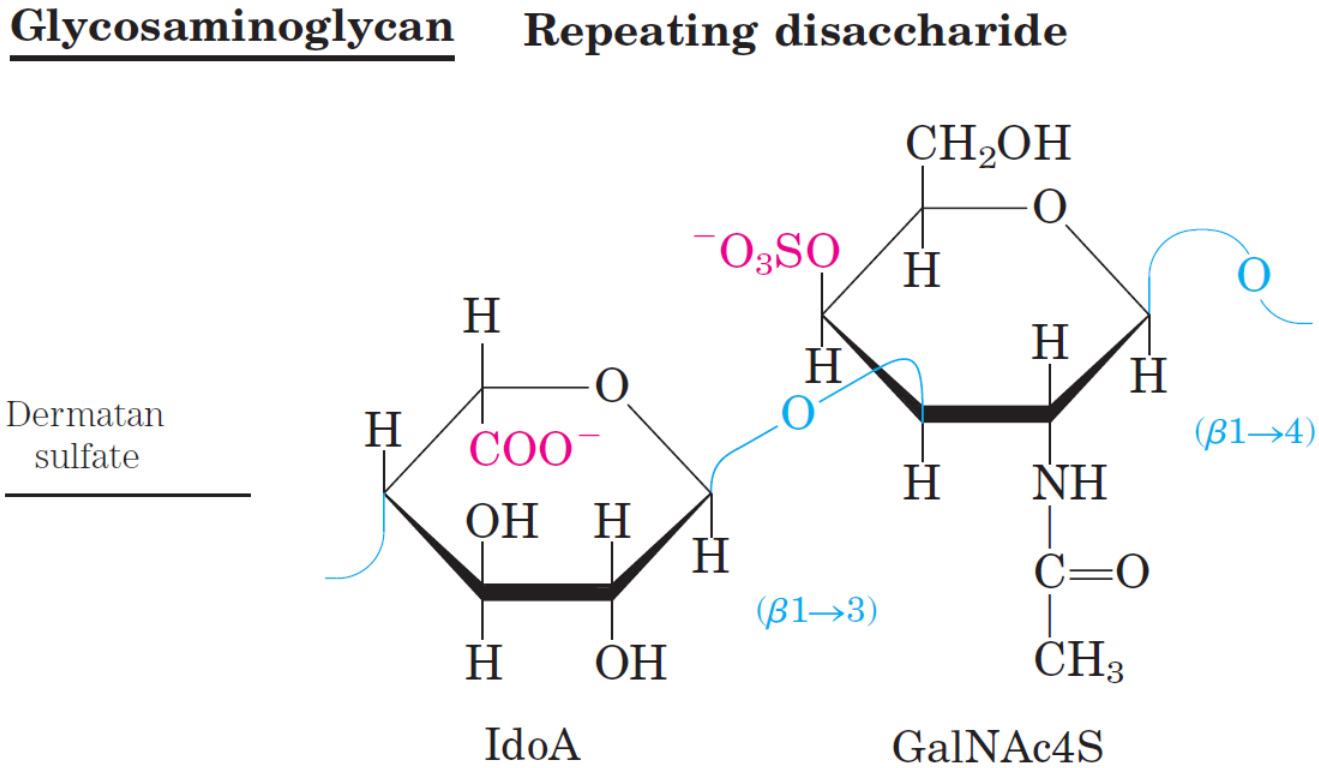
Repeating disaccharide



Dermatan Sülfat

❖Dermatan sulfate contributes to the pliability of skin and is also present in blood vessels and heart valves.

❖In this polymer, many of the glucuronate residues present in chondroitin sulfate are replaced by their 5-epimer, L-iduronate (IdoA).



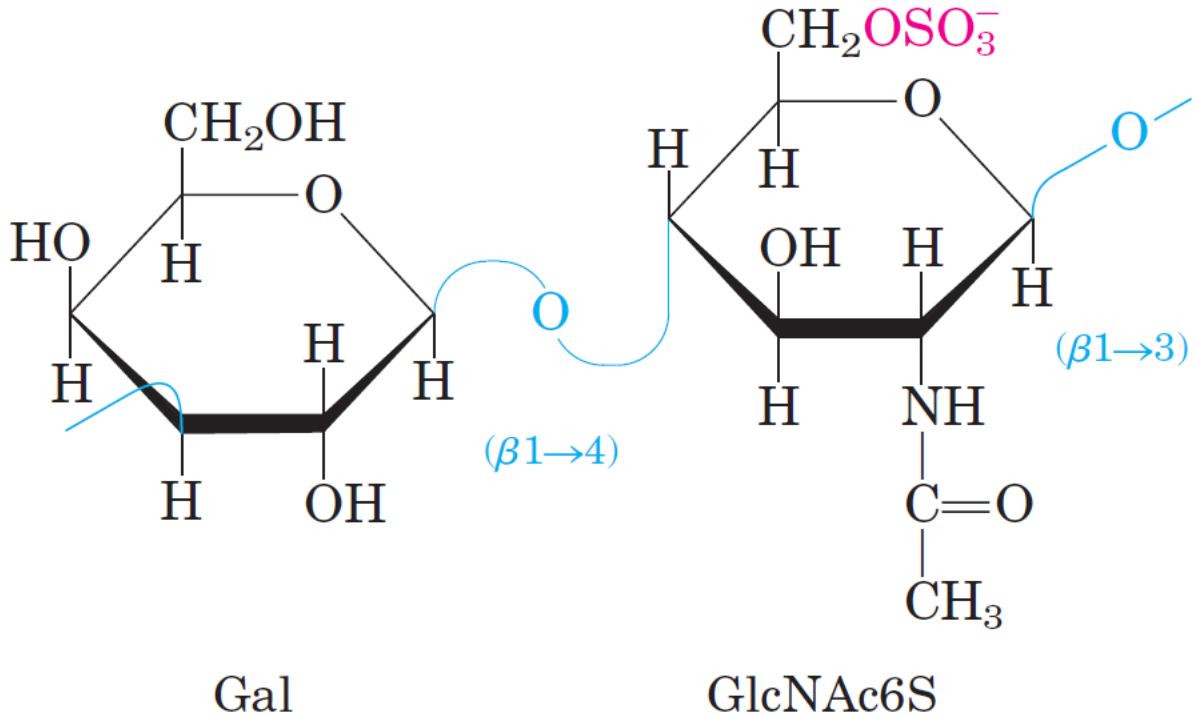
Keratan sulfates

❖Keratan sulfates have no uronic acid and their sulfate content is variable.

❖They are present in cornea, cartilage, bone, and a variety of horny structures formed of dead cells: horn, hair, hoofs, nails, and claws.

Glycosaminoglycan	Number of disaccharides per chain
Keratan sulfate	~25

Repeating disaccharide



Heparan sulfate

❖ Heparan sulfate is produced by all animal cells and contains variable arrangements of sulfated and nonsulfated sugars.

❖Heparin is a fractionated form of heparan sulfate derived mostly from mast cells (a type of leukocyte). Heparin is a therapeutic agent used to inhibit coagulation

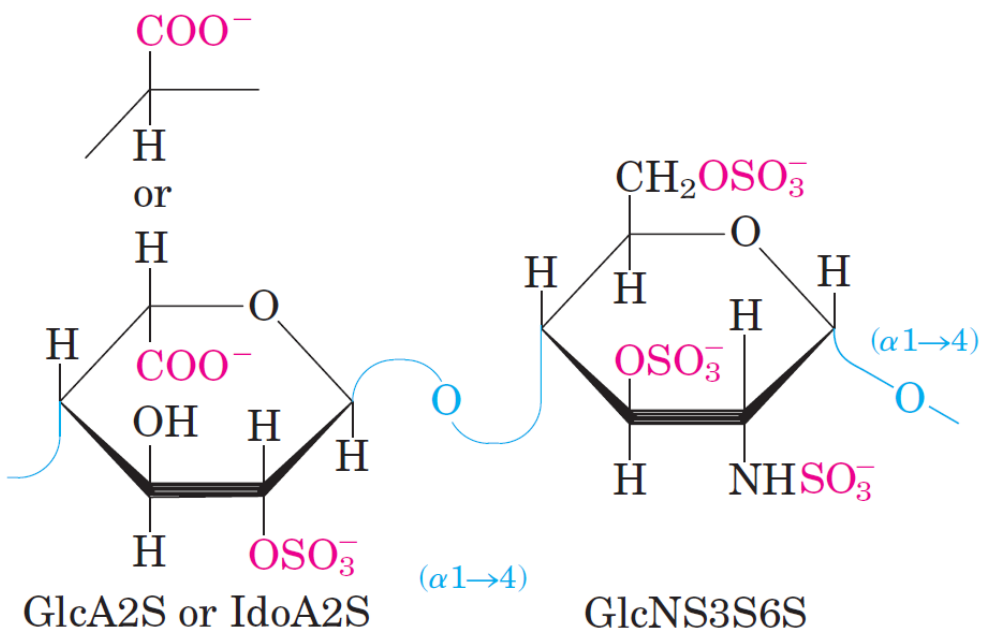
Glycosaminoglycan	Number of disaccharides per chain	Repeating disaccharide
Heparin	15–90	

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
Hyaluronate (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

Glycoconjugates

❖In addition to their important roles as stored fuels (starch, glycogen, dextran) and as structural materials (cellulose, chitin, peptidoglycans), polysaccharides and oligosaccharides are information carriers.

❖Some provide communication between cells and their extracellular surroundings;

❖others label proteins for transport to and localization in specific organelles, or for destruction when the protein is malformed or superfluous;

❖and others serve as recognition sites for extracellular signal molecules (growth factors, for example) or extracellular parasites (bacteria or viruses).

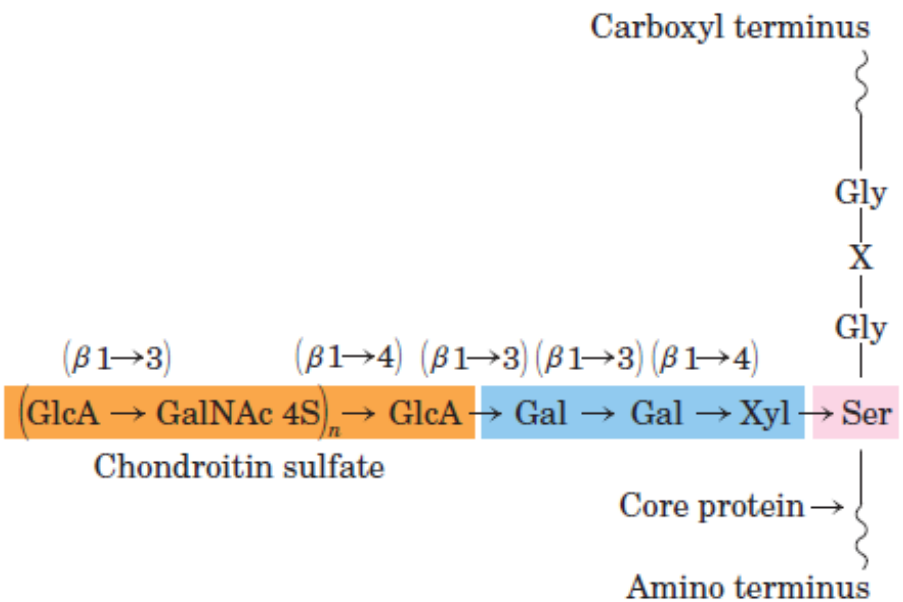
❖On almost every eukaryotic cell, specific oligosaccharide chains attached to components of the plasma membrane form a carbohydrate layer (the glycocalyx), several nanometers thick, that serves as an information-rich surface that the cell shows to its surroundings.

❖These oligosaccharides are central players in cell-cell recognition and adhesion, cell migration during development, blood clotting, the immune response, wound healing, and other cellular processes.

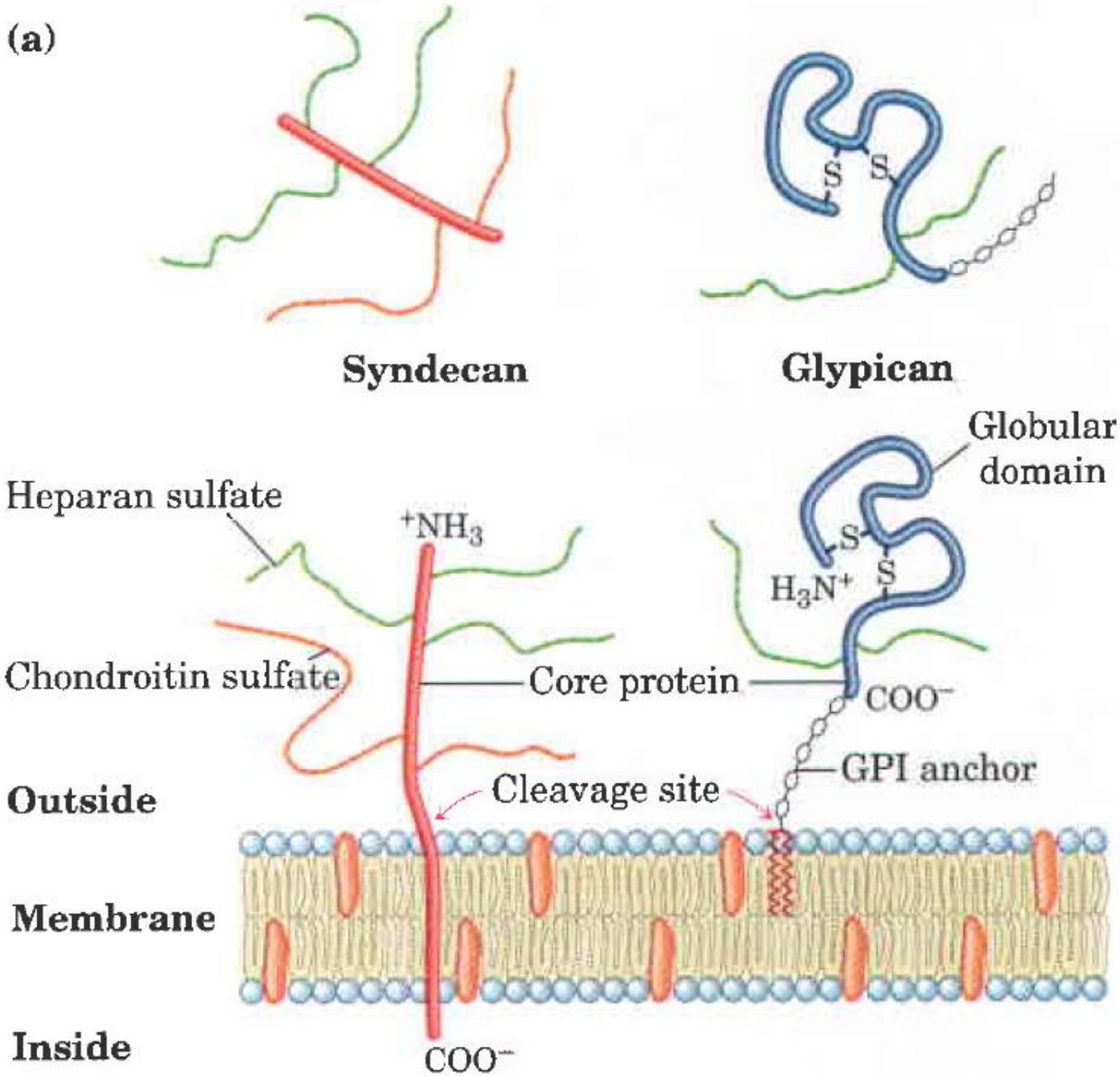
❖In most of these cases, the informational carbohydrate is covalently joined to a protein or a lipid to form a glycoconjugate, which is the biologically active molecule

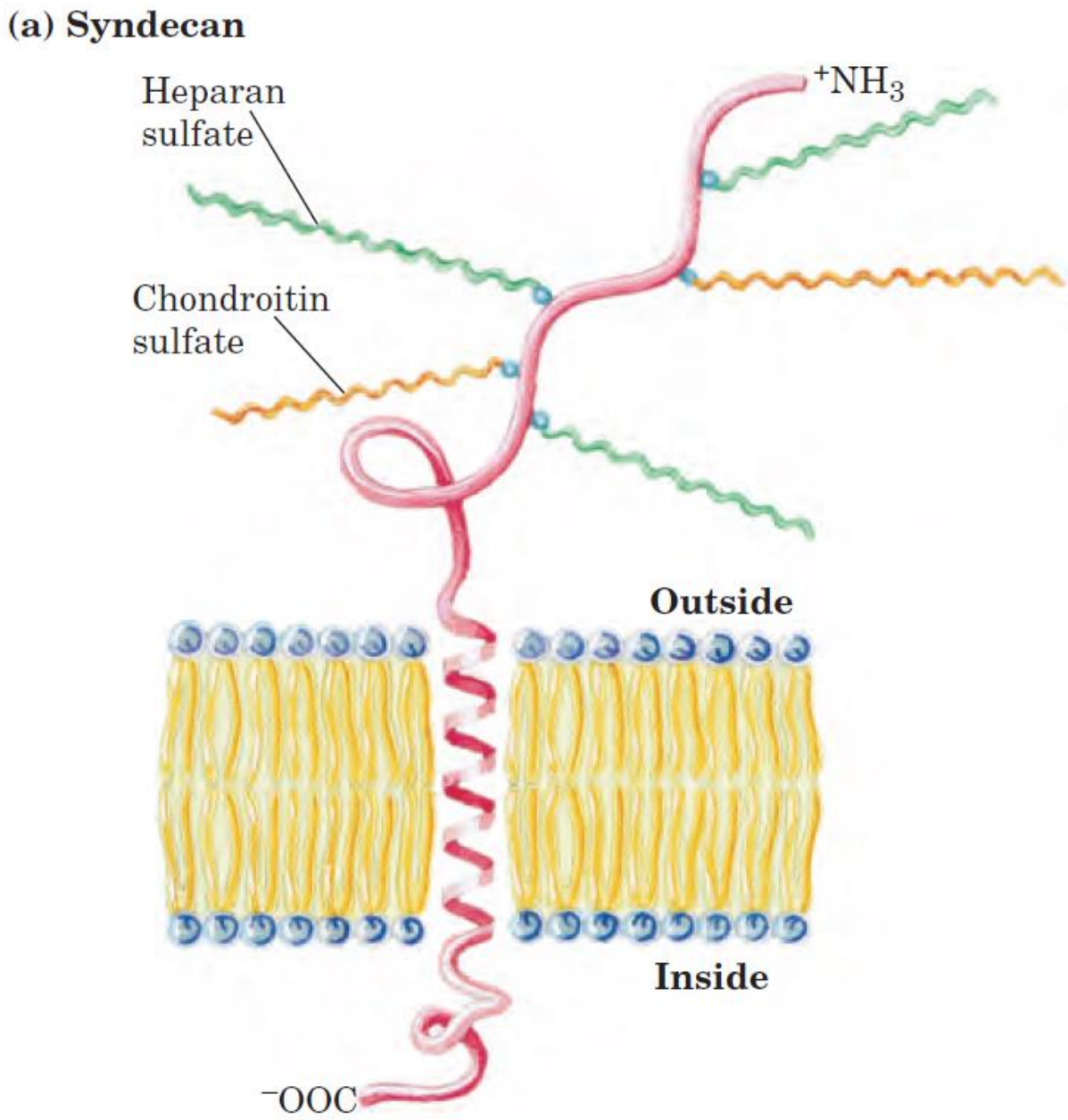
❖**Proteoglycans** are macromolecules of the cell surface or extracellular matrix in which one or more sulfated glycosaminoglycan chains are joined covalently to a membrane protein or a secreted protein.

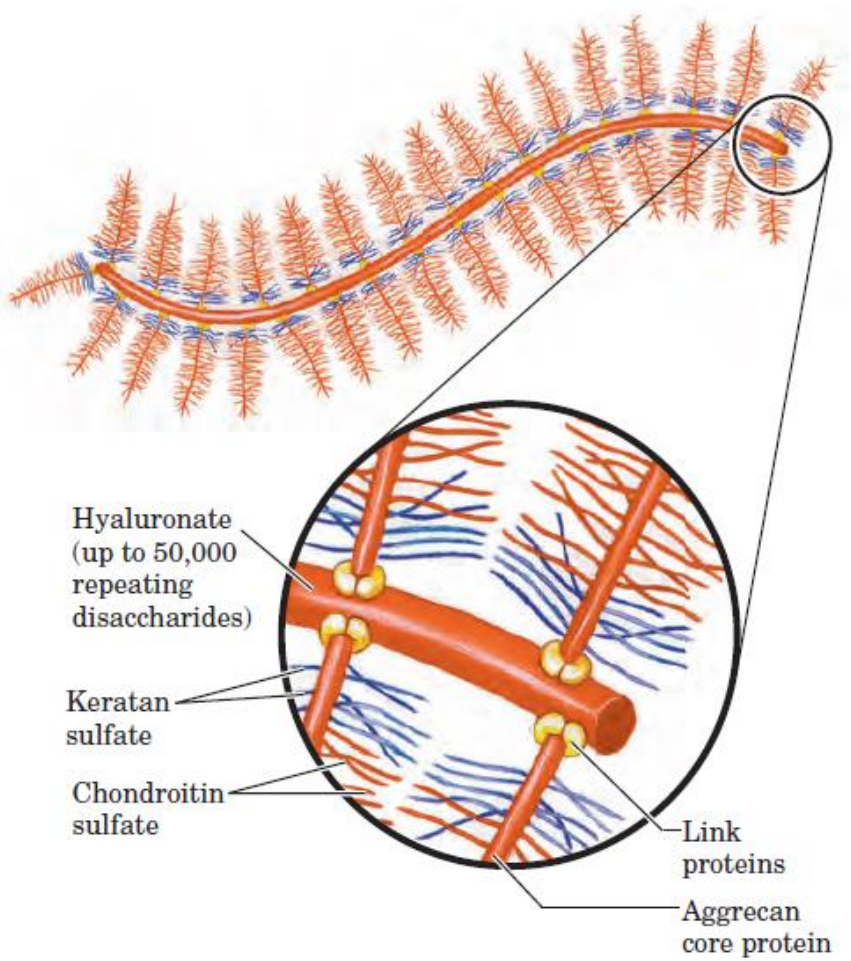
❖The glycosaminoglycan chain can bind to extracellular proteins through electrostatic interactions between the protein and the negatively charged sugar moieties on the proteoglycan.



❖Proteoglycans are major components of all extracellular matrices.


(a)
Syndecan
Glypican
S
S
Globular domain
Heparan sulfate
+NH3
S
S
H3N+
Chondroitin sulfate
Core protein
COO−
GPI anchor
Cleavage site
Outside
Membrane
Inside
COO−


(a) Syndecan
Heparan sulfate
$^{+}NH_3$
Chondroitin sulfate
Outside
Inside
^{-}OOC



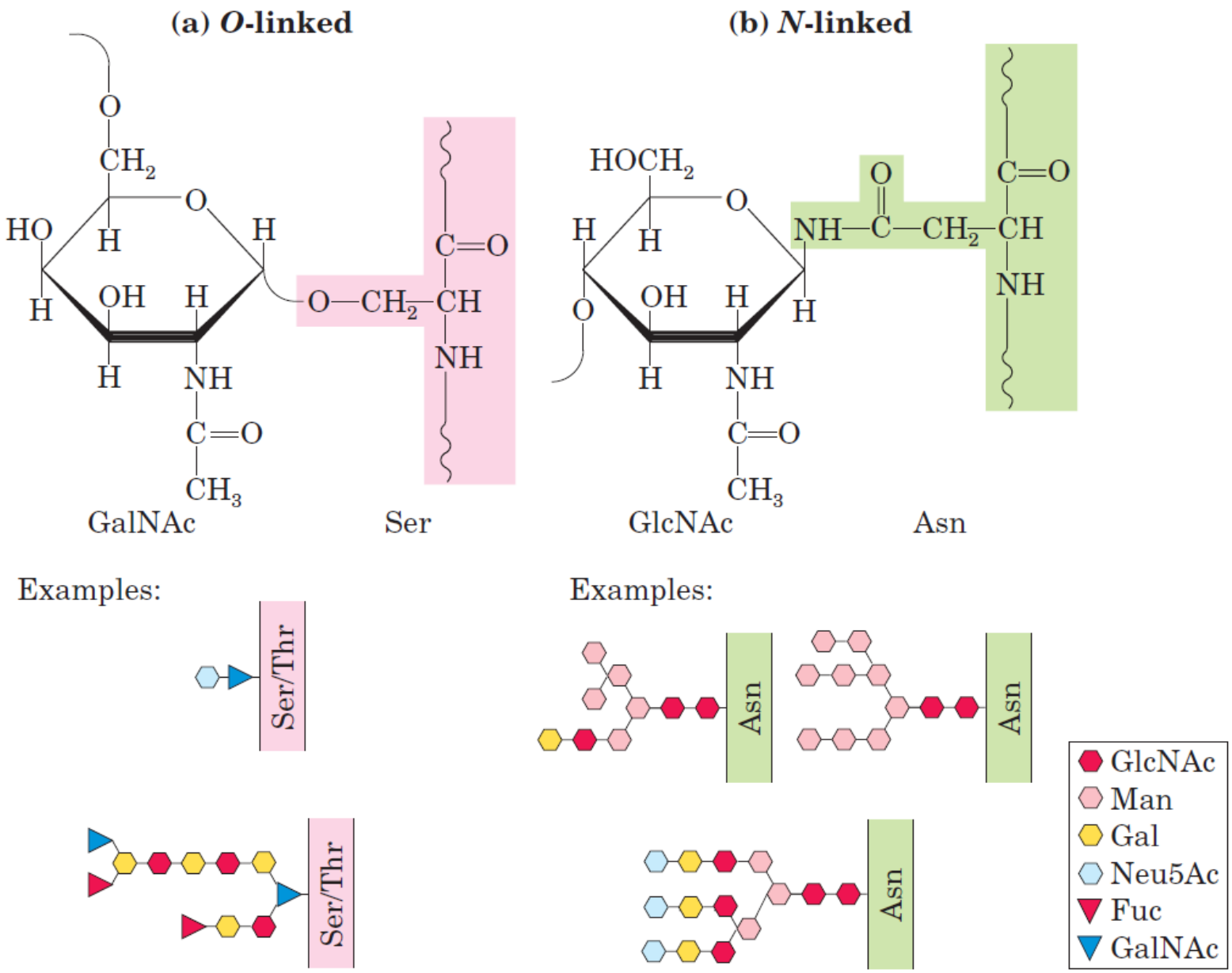
❖Some proteoglycans can form **proteoglycan aggregates**, enormous supramolecular assemblies of many core proteins all bound to a single molecule of hyaluronan.

❖**Aggrecan** interacts strongly with collagen in the extracellular matrix of cartilage, contributing to the development, tensile strength, and resilience of this connective tissue

❖**Glycoproteins** have one or several oligosaccharides of varying complexity joined covalently to a protein.

❖They are usually found on the outer face of the plasma membrane (as part of the glycocalyx), in the extracellular matrix, and in the blood. Inside cells they are found in specific organelles such as Golgi complexes, secretory granules, and lysosomes.

❖The oligosaccharide portions of glycoproteins are very heterogeneous and, like glycosaminoglycans, they are rich in information, forming highly specific sites for recognition and high affinity binding by carbohydrate-binding proteins called lectins.

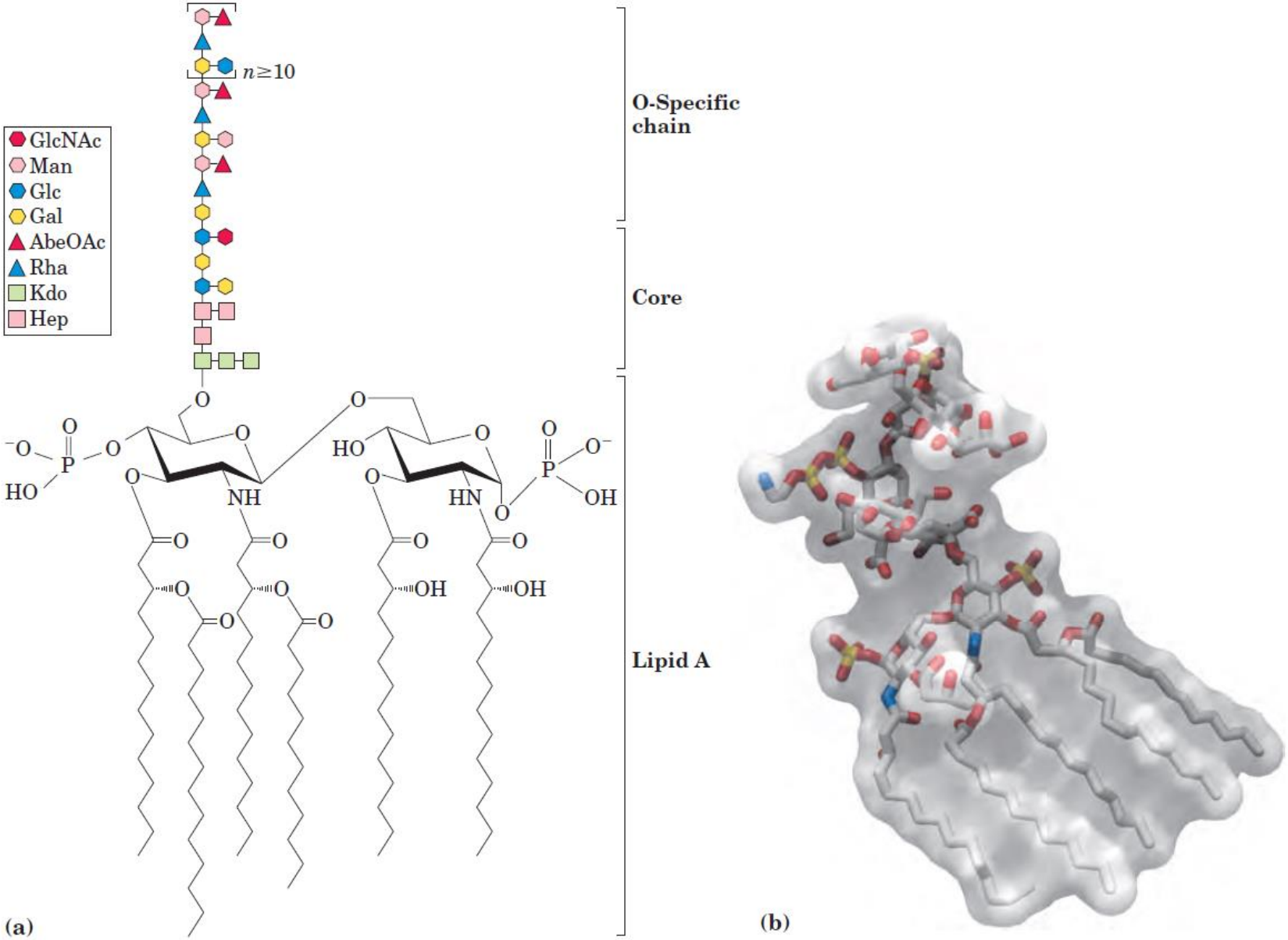

(a) O-linked
(b) N-linked
GalNAc
Ser
GlcNAc
Asn
Examples:
Ser/Thr
Ser/Thr
Examples:
Asn
Asn
Asn
GlcNAc
Man
Gal
Neu5Ac
Fuc
GalNAc

❖**Glycosphingolipids** are plasma membrane components in which the hydrophilic head groups are oligosaccharides.

❖As in glycoproteins, the oligosaccharides act as specific sites for recognition by lectins.

❖The brain and neurons are rich in glycosphingolipids, which help in nerve conduction and myelin formation.

❖Glycosphingolipids also play a role in signal transduction in cells.


GlcNAc
Man
Glc
Gal
AbeOAc
Rha
Kdo
Hep
n≥10
O-Specific chain
Core
Lipid A
(a)
(b)