7 Carbohydrates and Glycobiology

Carbohydrates

- **carbohydrates** = aldehydes or ketones with at least two hydroxyl groups, or substances that yield such compounds on hydrolysis
- many carbohydrates have the empirical formula $(CH_2O)_n$

Some carbohydrates contain sulfur

- Produced from CO_2 and H_2O via photosynthesis in plants
- Range from as small as glyceraldehyde (M_w = 90 g/mol) to as large as amylopectin (M_w > 200,000,000 g/mol)
- Can be covalently linked with proteins and lipids

Carbohydrates are no restricted to specific structures

تحقيق، إنجاز

- Fulfill a variety of functions, including:
  - energy source and energy storage
  - structural component of cell walls and exoskeletons → Wood contain carbohydrates cellulose
  - informational molecules in cell-cell signaling

Classes of Carbohydrates

- **monosaccharides** = simple sugars, consist of a single polyhydroxy aldehyde or ketone unit
  - example: D-glucose

= Monosaccharides connection is condensation reaction

- **disaccharides** = oligosaccharides with two monosaccharide units
  - example: sucrose (D-glucose and D-fructose)
    Lactose (glucose and galactose
- **oligosaccharides** = short chains of monosaccharide units, or residues, joined by glycosidic bonds
- **polysaccharides** = sugar polymers with 10+ monosaccharide units
  - examples: cellulose (linear), glycogen (branched)

P2

Clicker Question 1

A(n) ________ is a(n) ________ with two monosaccharide units.

A. oligosaccharide; polysaccharide
B. polysaccharide; oligosaccharide
C. disaccharide; oligosaccharide
D. disaccharide; polysaccharide

Clicker Question 1, Response

A(n) _________ is a(n) _________ with two monosaccharide units.

C. disaccharide; oligosaccharide

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.

7.1 Monosaccharides and Disaccharides

P1 Principle 1

Carbohydrates can have multiple chiral carbons; the configuration of groups around each carbon atom determines how the compound interacts with other biomolecules. As we saw for L-amino acids in proteins, with rare exceptions, biological evolution selected one stereochemical series (D-series) for sugars.

Stereoisomerism in Sugars

- sugar stereoisomers arise because many of the carbon atoms to which the hydroxyl groups are attached are ***chiral centers***

- enzymes that act on sugars are stereospecific

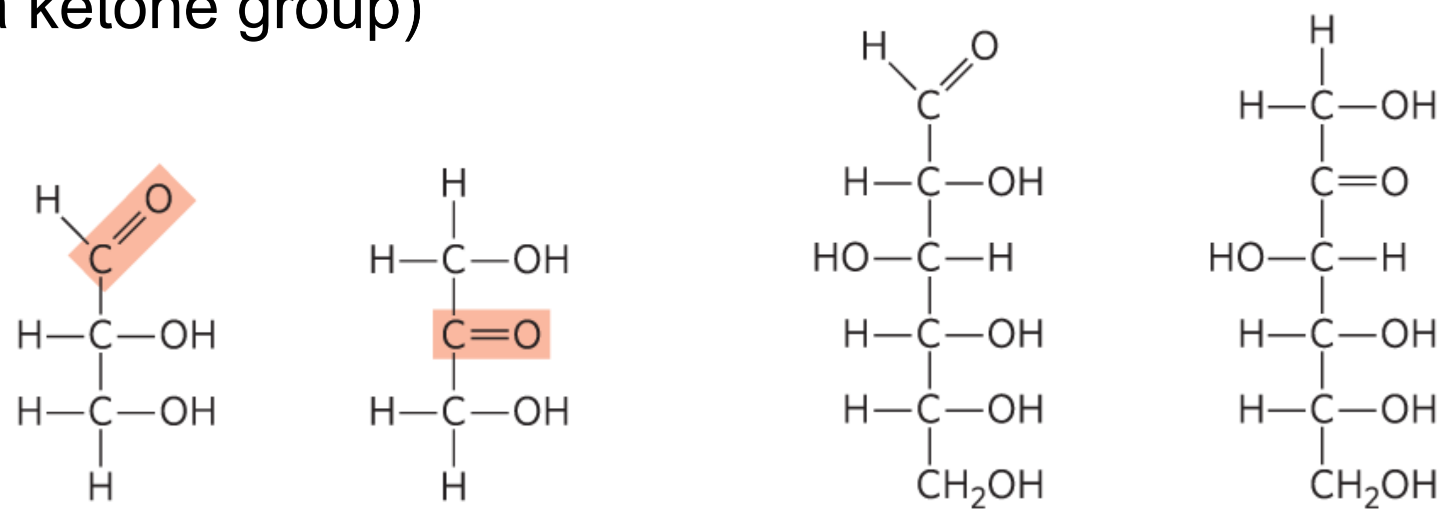
The Two Families of Monosaccharides Are Aldoses and Ketoses

- backbones of monosaccharides:
  - unbranched carbon chains with single bonds linking all carbon atoms
  - one of the carbon atoms is double-bonded to an oxygen atom to form a carbonyl group
  - other carbon atoms are bonded to a hydroxyl group

Aldoses and Ketoses

- **aldose** = carbonyl group is at an end of the carbon chain (in an aldehyde group)

- **ketose** = carbonyl group is at any other position (in a ketone group)



D-Glyceraldehyde, an aldotriose

Dihydroxyacetone, a ketotriose

(a)

D-Glucose, an aldohexose

D-Fructose, a ketohexose

(b)

P1

Clicker Question 2

What chemical feature determines if a sugar is an aldose or a ketose?

A. the direction of rotation of polarized light
B. the position of the carbonyl carbon
C. if the enantiomers resemble either glyceraldehyde or dihydroxyacetone
D. if the epimers differ in configuration around one carbon or more than one carbon

Clicker Question 2, Response

What chemical feature determines if a sugar is an aldose or a ketose?

B. the position of the carbonyl carbon

The backbones of common monosaccharides are unbranched carbon chains in which all the carbon atoms are linked by single bonds. In this open-chain form, one of the carbon atoms is double-bonded to an oxygen atom to form a carbonyl group. If the carbonyl group is at an end of the carbon chain, the monosaccharide is an aldose. If the carbonyl group is at any other position, it is a ketose.

Monosaccharide Carbon Backbone

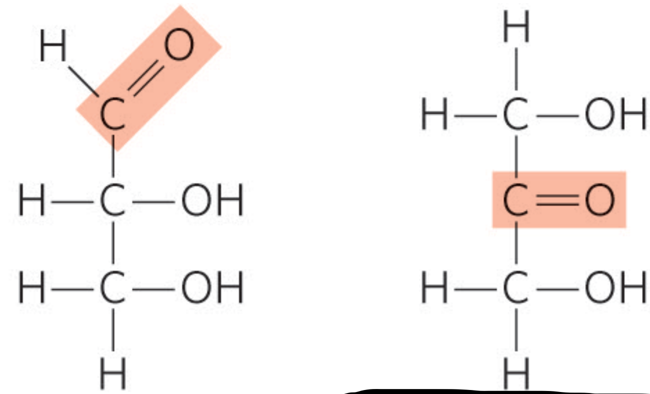
- 3 C → triose
- 4 C → tetrose
- 5 C → pentose
- 6 C → hexose
- 7 C → heptose

Trioses

- trioses = simplest monosaccharides, three carbon backbone

Chiral molecule at C2

Not chiral molecule



D-Glyceraldehyde, an aldotriose

Dihydroxyacetone, a ketotriose

(a)

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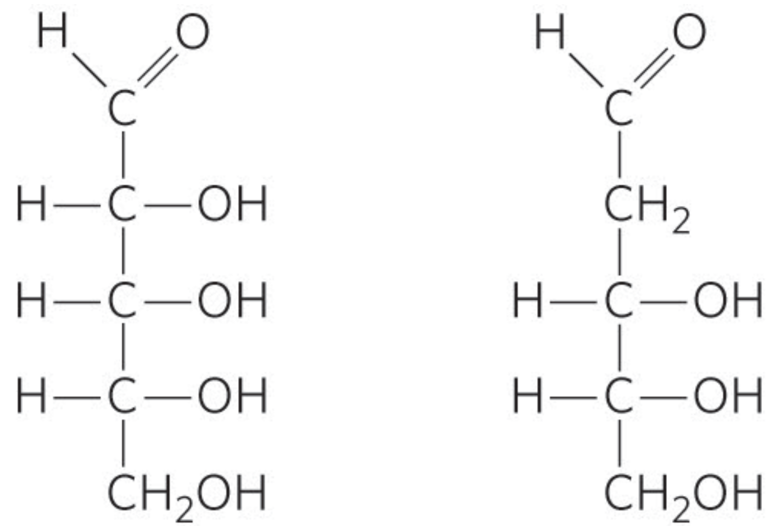
Only monosaccharide that is achiral

Tetroses and Pentoses

- tetroses = four carbon backbone
- pentoses = five carbon backbone

component of RNA

component of DNA



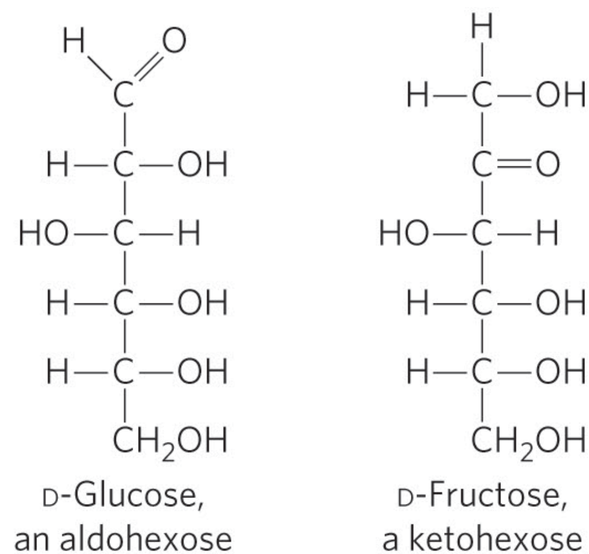
D-Ribose, an aldopentose

2-Deoxy-D-ribose, an aldopentose

(c)

Hexoses and Heptoses

- hexoses = six carbon backbone
- heptoses = seven carbon backbone



(b)

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P1

Clicker Question 3

Glucose is a monosaccharide with a(n):

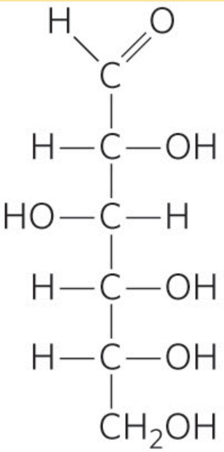
A. aldehyde functional group and six carbons.
B. ketone functional group and six carbons.
C. aldehyde functional group and seven carbons.
D. ketone functional group and seven carbons.

Clicker Question 3, Response

Glucose is a monosaccharide with a(n):

A. aldehyde functional group and six carbons.

Glucose is an aldohexose, a monosaccharide with an aldehyde functional group and six carbons.



D-Glucose,
an aldohexose

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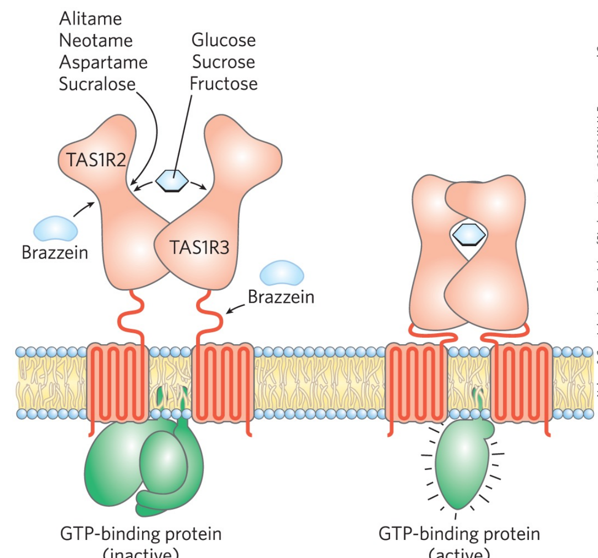
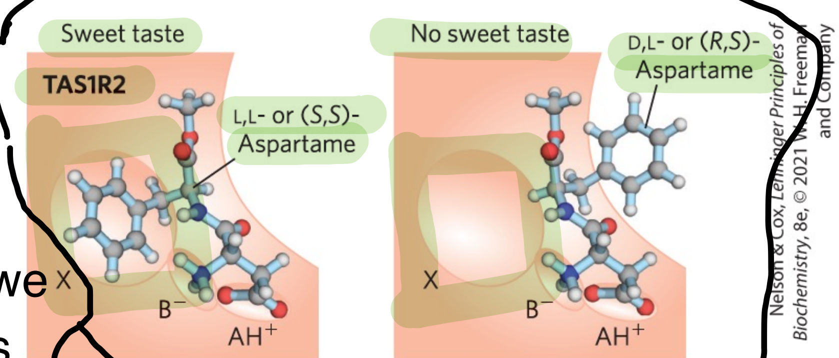
What Makes Sugar Sweet?

- *TAS1R2* and *TAS1R3* encode sweet-taste receptors
- binding of a compatible molecule generates a “sweet” electrical signal in the brain
  – requires a steric match





*Why syrup is more sweetness than sugar?
Our suger is disaccharide sucrose, in syrup, we break the sucrose to form monosaccharides fructose and glucose, and monosaccharides binds to receptors better than disaccharides

P1

Clicker Question 4

Why does (*R,S*)-aspartame NOT stimulate the sweet receptor?

A. Site AH^+ cannot bind the partially negative oxygen of the carboxylic acid.
B. Site B^- cannot hydrogen bond with the amine nitrogen.
C. Site X cannot accommodate the hydrophobic benzene ring.
D. None of the sites can interact with (*R,S*)-aspartame.

Clicker Question 4, Response

Why does (*R*,*S*)-aspartame NOT stimulate the sweet receptor?

C. Site X cannot accommodate the hydrophobic benzene ring.

The steric match must be correct to stimulate the sweet receptor. Site X is oriented perpendicular to AH^+ and $B^–$ and can accommodate the hydrophobic benzene ring of (*S*,*S*)-aspartame. However, Site X cannot accommodate the hydrophobic benzene ring of (*R*,*S*)-aspartame.

Monosaccharides Have Asymmetric Centers

- all monosaccharides (except *dihydroxyacetone*) contain 1+ chiral carbon atom
  - occur in optically active isomeric forms

- **enantiomers** = two different optical isomers that are mirror images

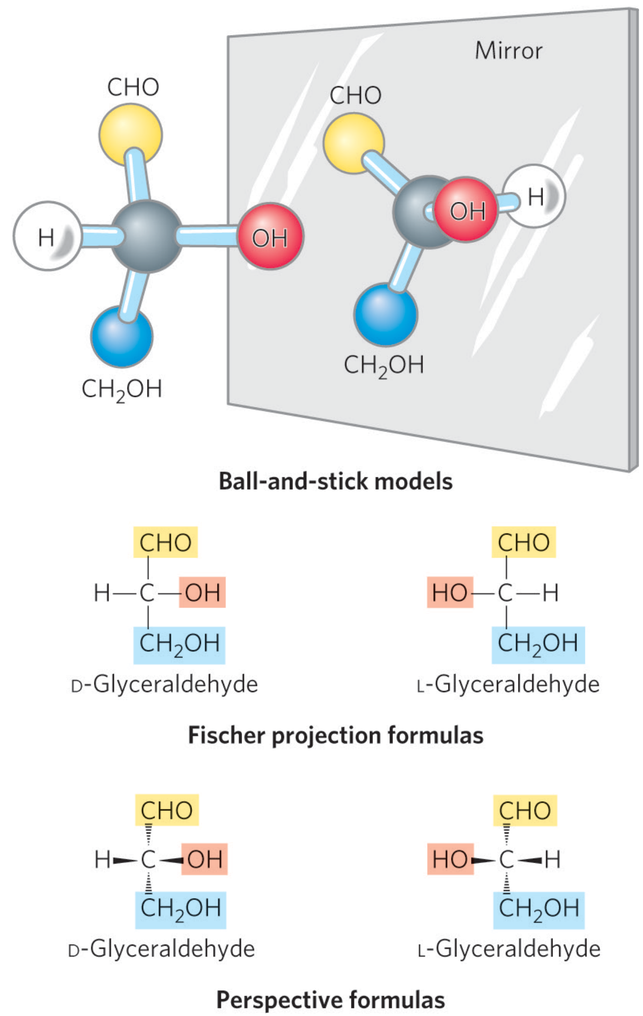
- a molecule with *n* chiral centers can have 2^n stereoisomers

Fischer Projection Formulas

- used to represent three-dimensional sugar structures on paper
- bonds drawn horizontally indicate bonds that project out of the plane of the paper
- bonds drawn vertically project behind the plane of the paper

Fischer projection formulas

Enantiomers of Glyceraldehyde



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Numbering Carbons of a Sugar

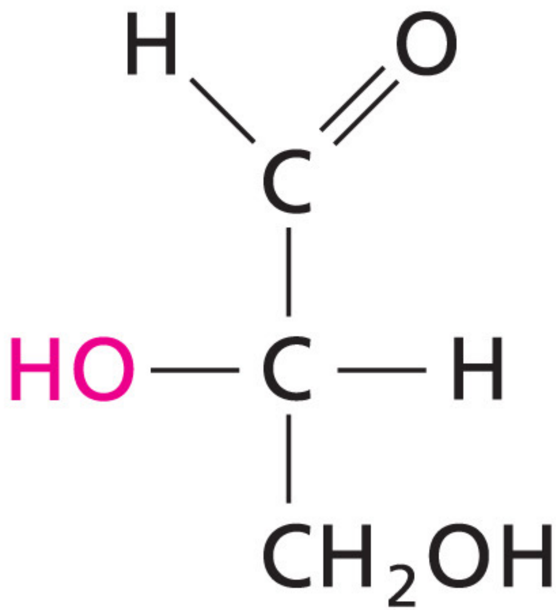
- carbons are numbered beginning at the end of the chain near the carbonyl group

D Isomers and L Isomers

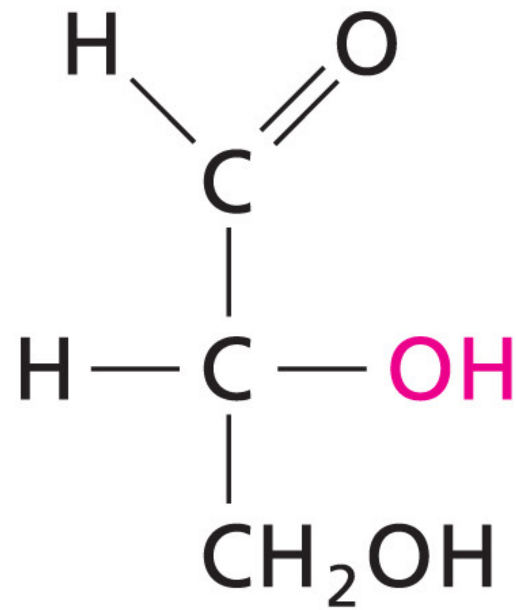
بعيد

- reference carbon = chiral center *most distant* from the carbonyl carbon

- two groups of stereoisomers:
  - D isomers = configuration at reference carbon is the same as D-glyceraldehyde
    - on the right (*dextro*) in a projection formula
    - most hexoses of living organisms
  - L isomers = configuration at reference carbon is the same as L-glyceraldehyde
    - on the left (*levo*) in a projection formula



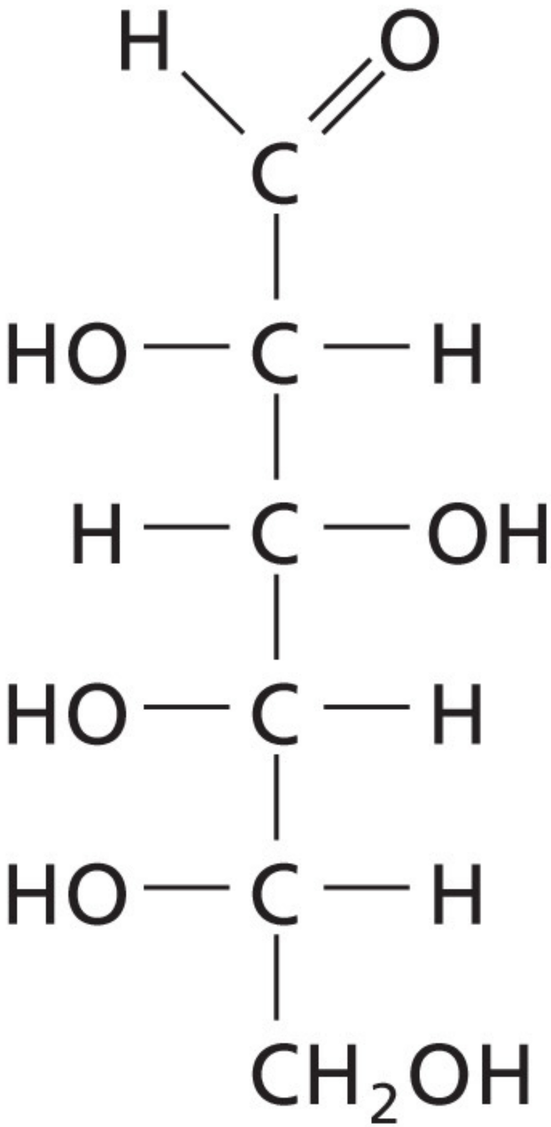
L-Glyceraldehyde



D-Glyceraldehyde

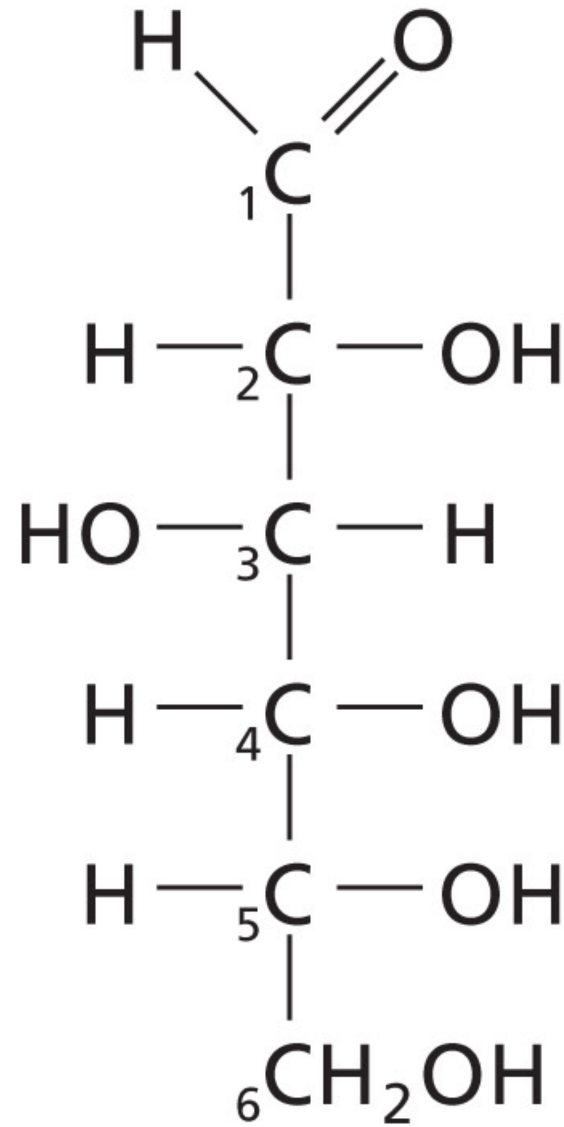
Non-
superimposable
mirror images

Four chiral centers



L-Glucose

Non-superimposable mirror images



D-Glucose

P1

Clicker Question 5

Which statement is false regarding the enantiomers of glyceraldehyde?

A. The enantiomers of glyceraldehyde are mirror images of each other.
B. Because glyceraldehyde contains one chiral center, it has two enantiomers.
C. In the Fischer projection formula for D-glyceraldehyde, the hydroxyl group is on the right.
D. Glyceraldehyde does not occur in optically active isomeric forms.

Clicker Question 5, Response

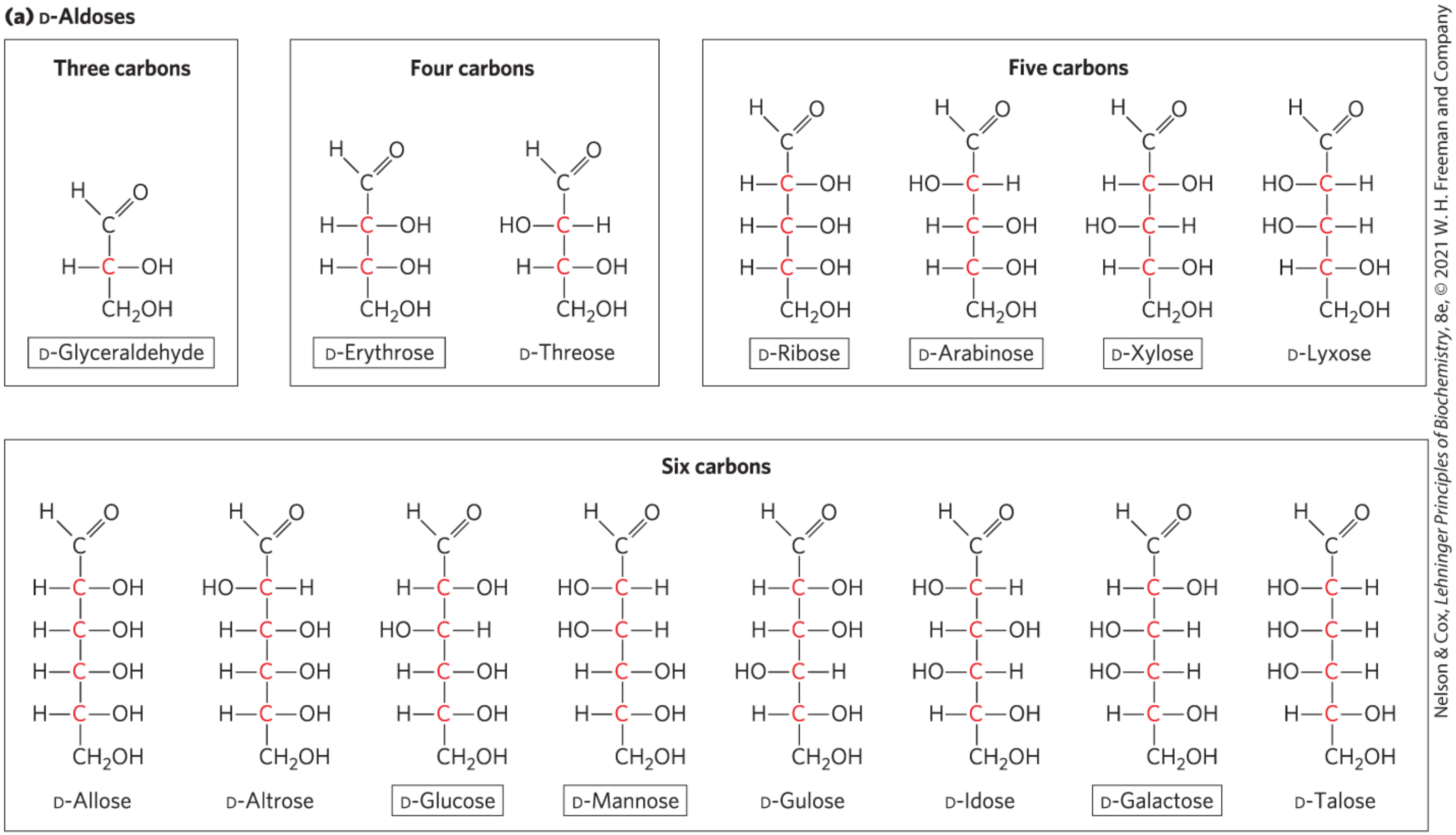
Which statement is false regarding the enantiomers of glyceraldehyde?

D. Glyceraldehyde does not occur in optically active isomeric forms.

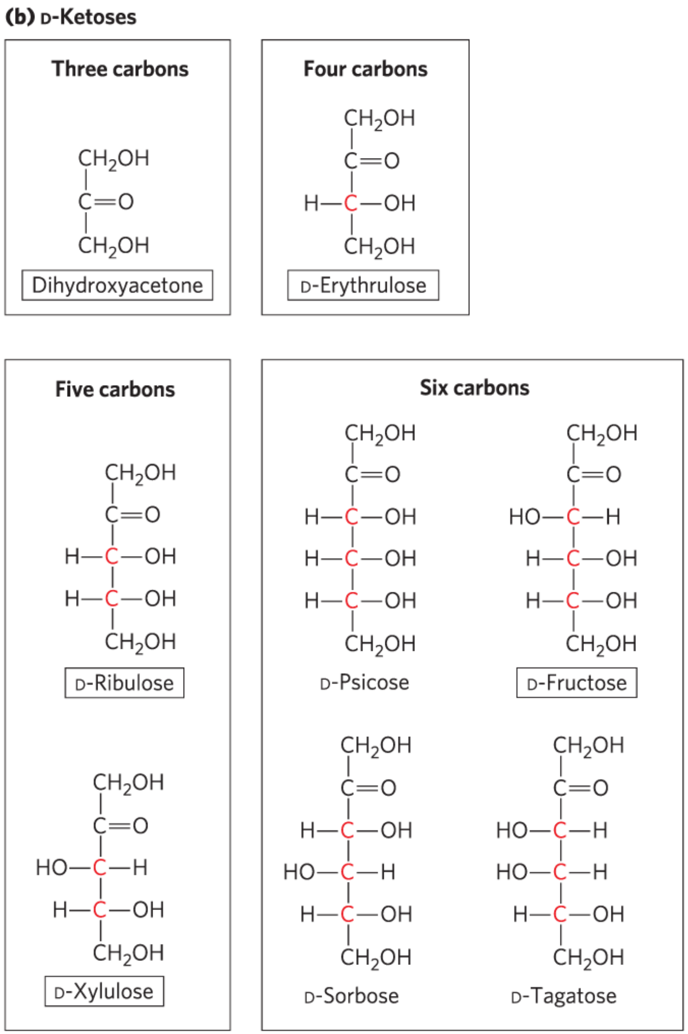
All the monosaccharides except dihydroxyacetone contain one or more asymmetric (chiral) carbon atoms and thus occur in optically active isomeric forms. The simplest aldose, glyceraldehyde, contains one chiral center (the middle carbon atom) and therefore has two different optical isomers, or enantiomers.

D-Aldoses

(a) D-Aldoses

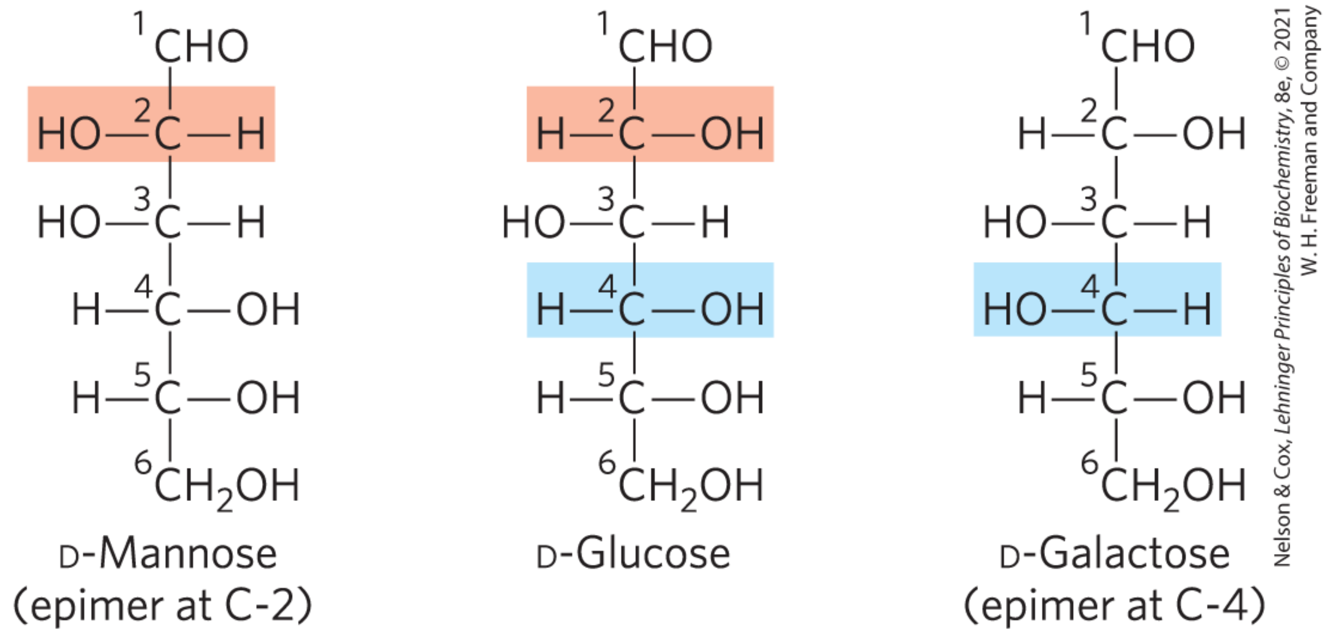


D-Ketoses


(b) D-Ketoses
Three carbons
CH2OH
C=O
CH2OH
Dihydroxyacetone
Four carbons
CH2OH
C=O
H—C—OH
CH2OH
D-Erythrulose
Five carbons
CH2OH
C=O
H—C—OH
H—C—OH
CH2OH
D-Ribulose
CH2OH
C=O
HO—C—H
H—C—OH
CH2OH
D-Xylulose
Six carbons
CH2OH
C=O
H—C—OH
H—C—OH
H—C—OH
CH2OH
D-Psicose
CH2OH
C=O
HO—C—H
H—C—OH
H—C—OH
CH2OH
D-Fructose
CH2OH
C=O
H—C—OH
HO—C—H
H—C—OH
CH2OH
D-Sorbose
CH2OH
C=O
HO—C—H
HO—C—H
H—C—OH
CH2OH
D-Tagatose

Epimers

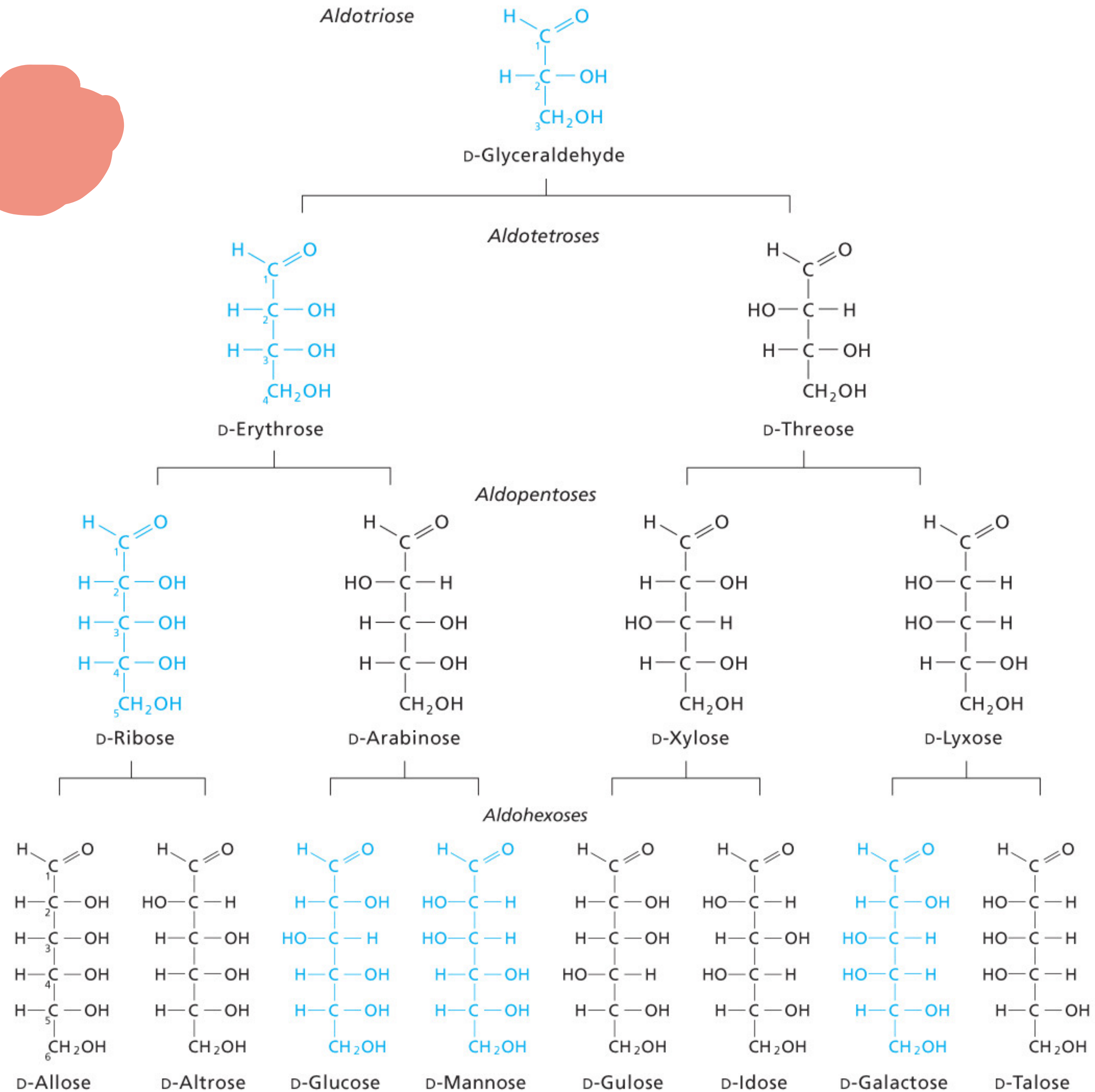
- **epimers** = two sugars that differ only in the configuration around one carbon atom

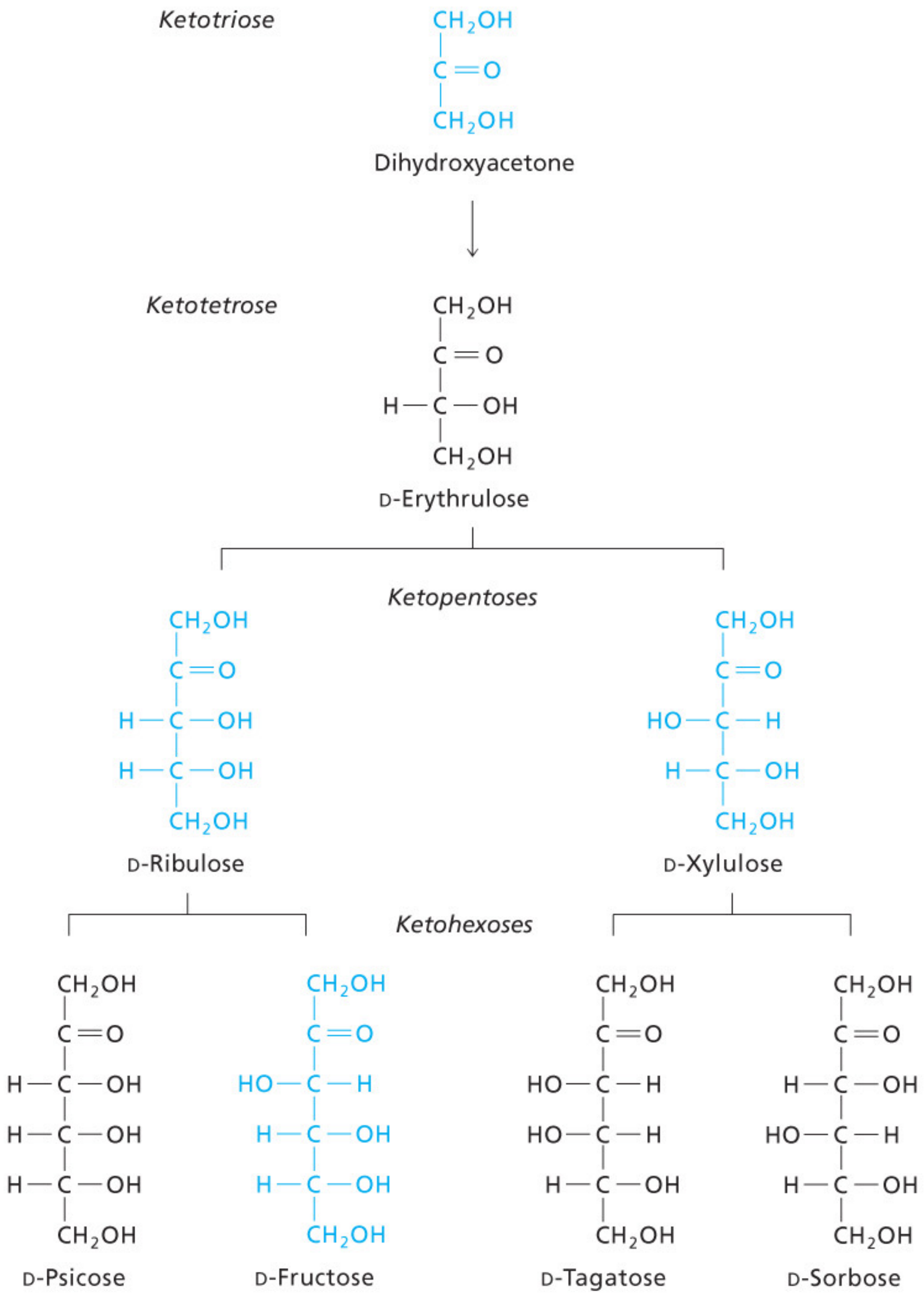


- D-Mannose and D-galactose are both epimers of D-glucose.
- D-Mannose and D-galactose vary at more than one chiral center and are diastereomers, but not epimers.

Structures to Know

- Glyceraldehyde & dihydroxyacetone are the standard three-carbon sugars
- Ribose is the standard five-carbon sugar
- Glucose is the standard six-carbon sugar
- Galactose is an epimer of glucose
- Mannose is an epimer of glucose
- Fructose is the ketose form of glucose


Aldotriose
D-Glyceraldehyde
Aldotetroses
D-Erythrose
D-Threose
Aldopentoses
D-Ribose
D-Arabinose
D-Xylose
D-Lyxose
Aldohexoses
D-Allose
D-Altrose
D-Glucose
D-Mannose
D-Gulose
D-Idose
D-Galactose
D-Talose


Ketotriose
Dihydroxyacetone
Ketotetrose
D-Erythrulose
Ketopentoses
D-Ribulose
D-Xylulose
Ketohexoses
D-Psicose
D-Fructose
D-Tagatose
D-Sorbose

The Common Monosaccharides Have Cyclic Structures

- in aqueous solution, aldotetroses and all monosaccharides with 5+ backbone carbon atoms occur as cyclic structures
  - covalent bond between the carbonyl group and the oxygen of a hydroxyl group

P1

Clicker Question 6

A monosaccharide with a ketone functional group and seven carbons:

A. can never exist in cyclic form.
B. is a ketoheptose.
C. is the monosaccharide found in RNA but not DNA.
D. has a single chiral center.

Clicker Question 6, Response

A monosaccharide with a ketone functional group and seven carbons:

B. is a ketoheptose.

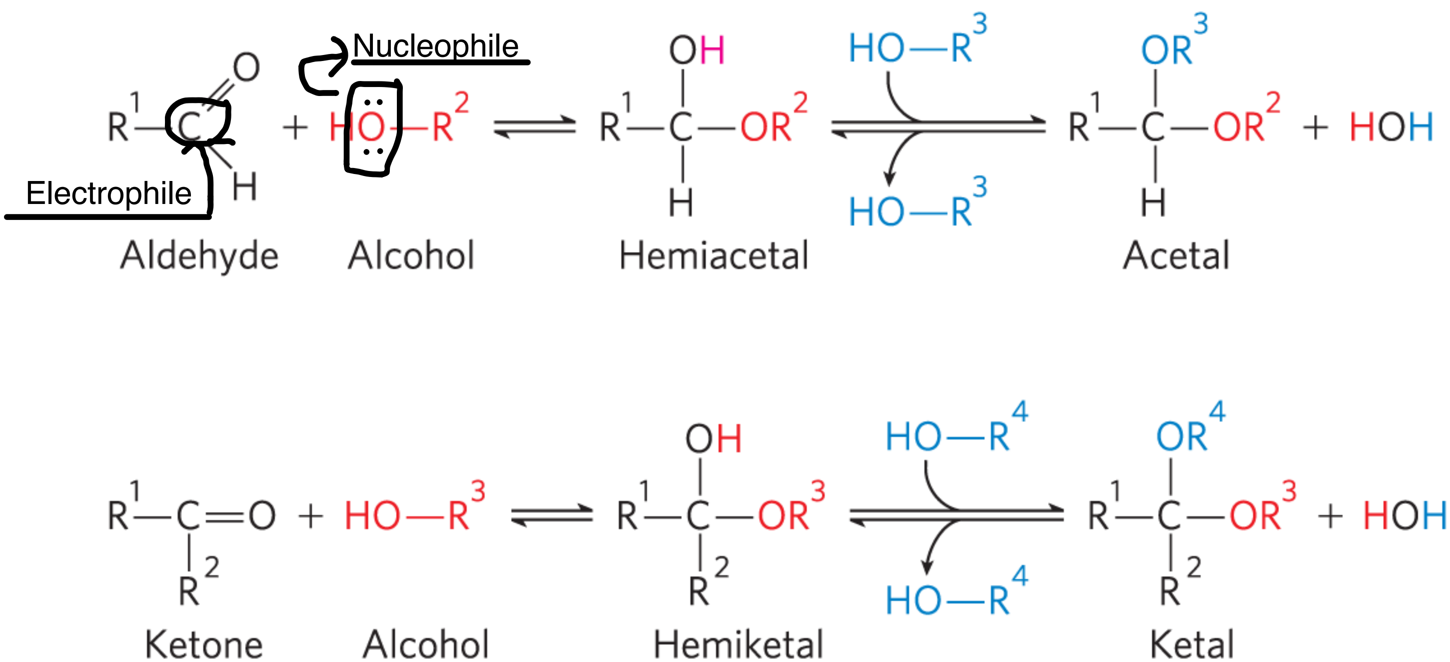
Monosaccharides with seven carbon atoms in their backbones are called heptoses. A ketose of this chain length is a ketoheptose.

Hemiacetals and Hemiketals

- **hemiacetals** or **hemiketals** = derivatives formed by a general reaction between alcohols and aldehydes or ketones
  - product of the first alcohol molecule addition
  - a five- or six-membered ring forms if the —OH and carbonyl groups are on the same molecule

- **acetal** or **ketal** = product of the second alcohol molecule addition
  - forms a glycosidic bond

Formation of Hemiacetals and Hemiketals



α and *β* Stereoisomeric Configurations

- reaction with the first alcohol molecule creates an additional chiral center (the carbonyl carbon)
- produces either of two stereoisomeric configurations: *α* (*trans*) and *β* (*cis*)
- **anomers** = isomeric forms of monosaccharides that differ only in their configuration about the hemiacetal or hemiketal carbon atom
- **anomeric carbon** = the carbonyl carbon atom

P1

Clicker Question 7

What name is given to monosaccharides that differ in configuration about the hemiacetal carbon atom?

A. enantiomers
B. isomers
C. epimers
D. anomers

Clicker Question 7, Response

What name is given to monosaccharides that differ in configuration about the hemiacetal carbon atom?

D. anomers

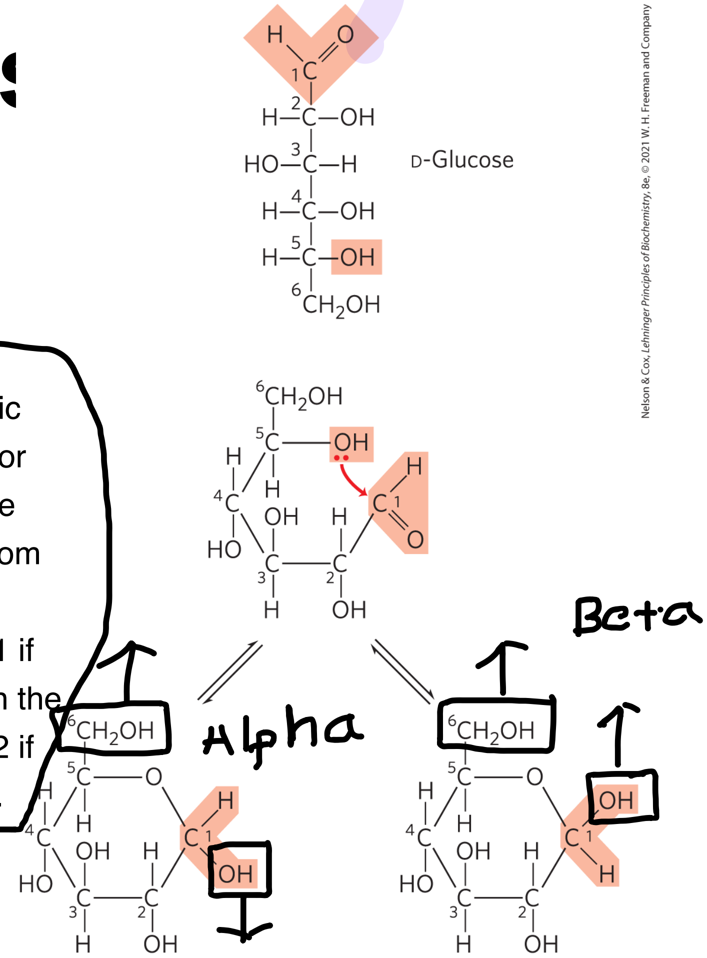
Isomeric forms of monosaccharides that differ only in their configuration about the hemiacetal or hemiketal carbon atom are called anomers.

Formation of the Two Cyclic Forms of D-Glucos

- reaction between the aldehyde group at C-1 and the hydroxyl group at C-5 forms a hemiacetal linkage

- **mutarotation** = the interconversion of α and β anomers

Anomers are cyclic monosaccharides or glycosides that are epimers, differing from each other in the configuration of C-1 if they are aldoses or in the configuration at C-2 if they are ketoses.



α-D-Glucopyranose

β-D-Glucopyranose

If the *hydroxyl group* is on the *opposite side* (trans) of the ring as the *CH_2OH* moiety the configuration is α

In the *hydroxyl group* is on the *same side* (cis) of the ring as the *CH_2OH* moiety, the configuration is β

P1

Clicker Question 8

Cyclization of monosaccharides:

A. is the reaction of hemiketal or hemiacetal formation.
B. is irreversible.
C. creates *α* and *β* epimers.
D. only occurs in hexoses.

Clicker Question 8, Response

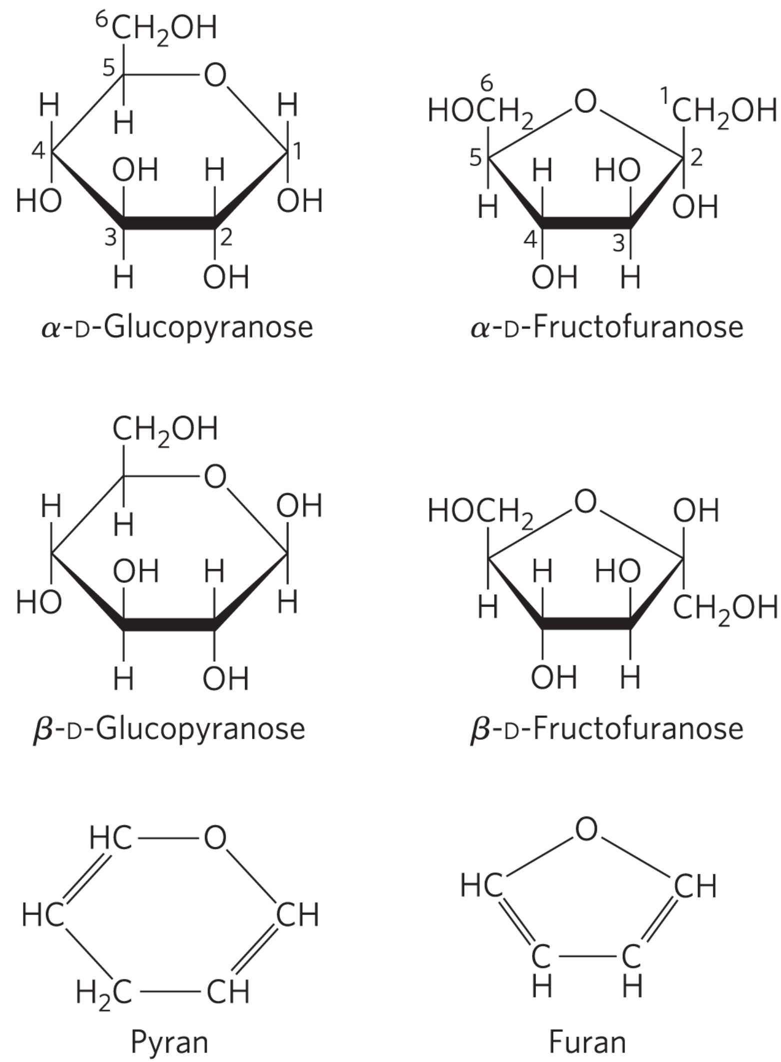
Cyclization of monosaccharides:

A. is the reaction of hemiketal or hemiacetal formation.

In aqueous solution, 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 in the same sugar molecule. 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.

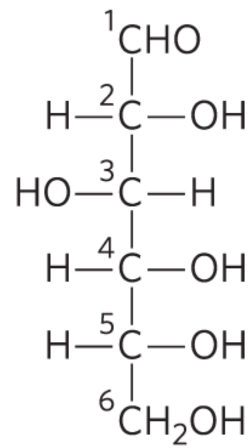
Pyranoses and Furanoses

- **pyranoses** = six-membered ring compounds
  - form when the hydroxyl group at C-6 reacts with the keto group at C-2
- **furanoses** = five-membered ring compounds
  - form when the hydroxyl group at C-5 reacts with the keto group at C-2

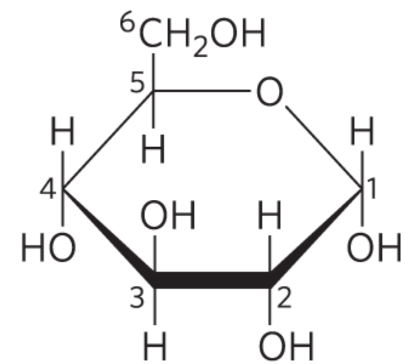


Haworth Perspective Formulas

- **Haworth perspective formulas** = more accurate representation of cyclic sugar structure than Fischer projections
  - six-membered ring is يميل tilted to make its plane almost perpendicular to that of the paper
  - bonds closest to the reader are drawn thicker than those farther away



D-Glucose
Fischer projection



α-D-Glucopyranose
Haworth perspective

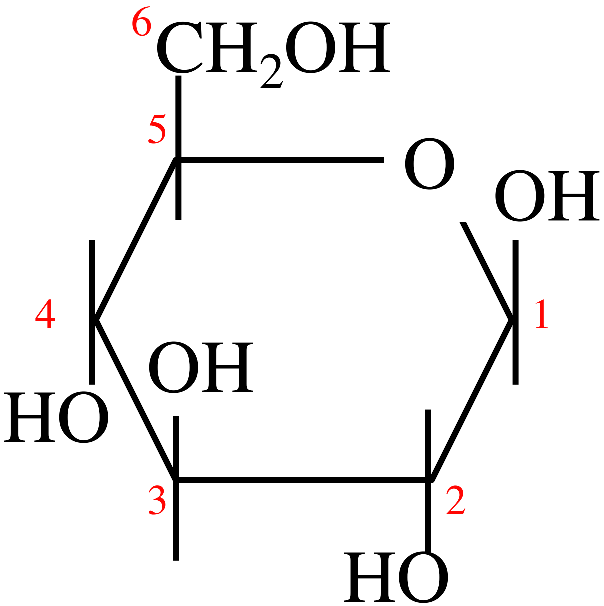
Converting D-Hexose Fischer Projections to Haworth Perspective Formulas

- step 1: draw the six-membered ring (five carbons, and one oxygen at the upper right)
- step 2: number the carbons in a clockwise direction beginning with the anomeric carbon
- step 3: place the hydroxyl groups
  - hydroxyl groups on the right in a Fischer projection are placed pointing down and those on the left are placed pointing up

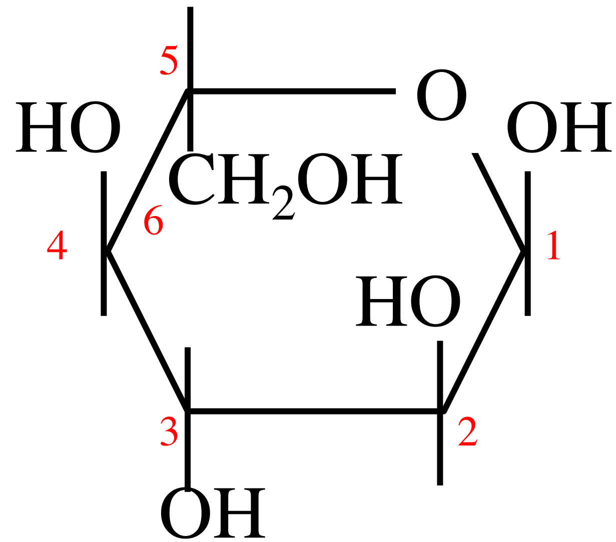
Converting D-Hexose Fischer Projections to Haworth Perspective Formulas, Continued

- step 4: place the terminal —CH_2OH group
  - projects upward for the D enantiomer, downward for the L enantiomer
- step 5: place the anomeric hydroxyl group
  - for a *β* structure, the hydroxyl group is placed on the same side of the ring as C-6
  - for an *α* structure, it is placed on the opposite side

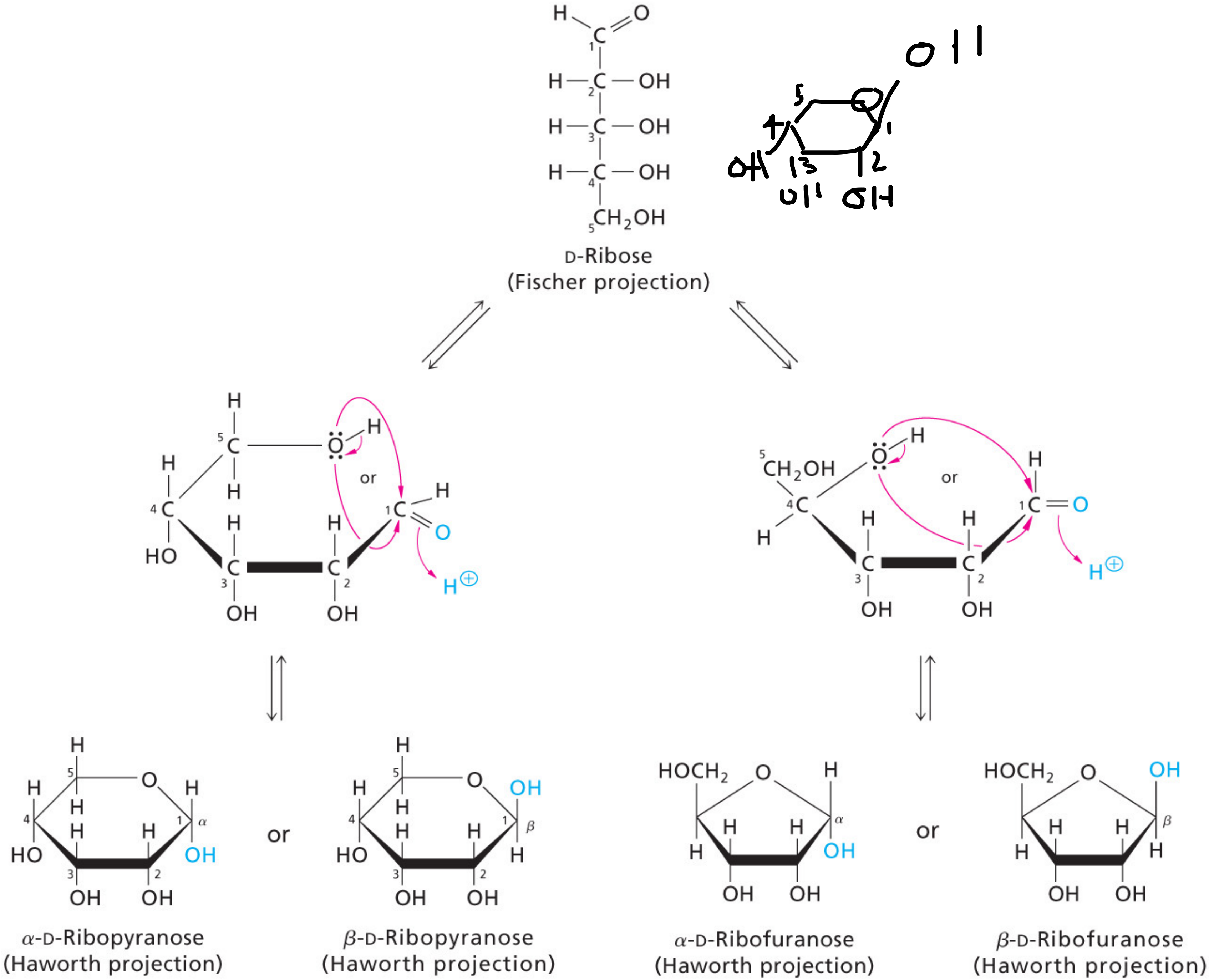
Example



β-D-glucose
(C^1-OH points up,
cis to C^6H_2OH)



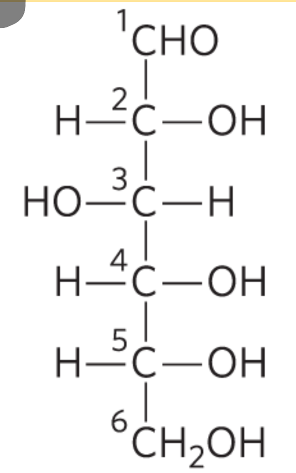
α-L-glucose
(C^1-OH points up,
trans to C^6H_2OH)


D-Ribose
(Fischer projection)
or
or
α-D-Ribopyranose
(Haworth projection)
or
β-D-Ribopyranose
(Haworth projection)
α-D-Ribofuranose
(Haworth projection)
or
β-D-Ribofuranose
(Haworth projection)

P1

Clicker Question 9

Using the Fischer projection of D-glucose, identify which statement is true of the Haworth perspective formula of *α*-D-glucopyranose.



D-Glucose
Fischer projection

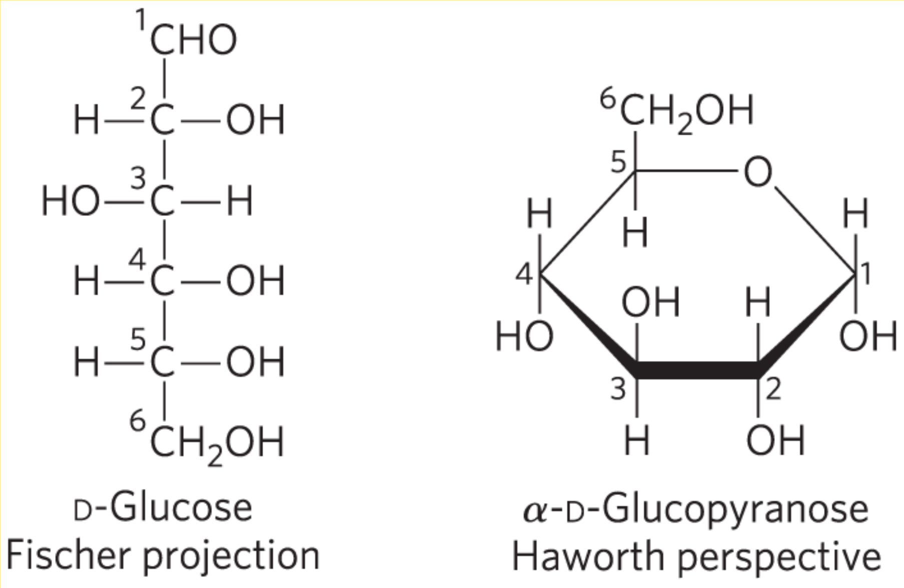
A. The terminal —CH_2OH group projects downward.
B. The anomeric hydroxyl is on the opposite side from C-6.
C. The hydroxyl group on C-2 is placed pointing up.
D. The cyclic structure is a five-membered ring.

Clicker Question 9, Response

Using the Fischer projection of D-glucose, identify which statement is true of the Haworth perspective formula of α-D-glucopyranose.

B. The anomeric hydroxyl is on the opposite side from C-6.

For an α structure, the anomeric carbon (C-1) has its hydroxyl group placed on the opposite side from C-6.



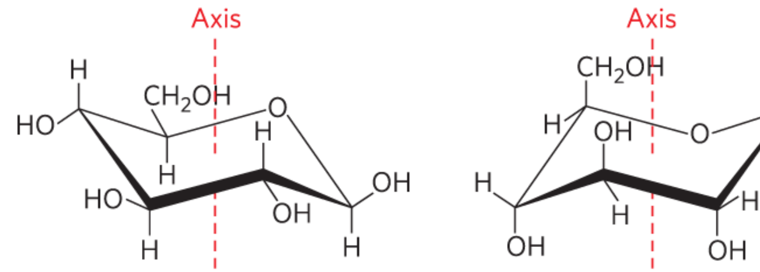
P5 Principle 5

يفترض، يتخذ

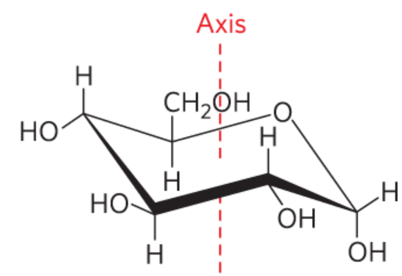
Polysaccharides assume three-dimensional structures with the lowest-energy conformations, determined by covalent bonds, hydrogen bonds, charge interactions, and steric factors. Starch folds into a helical structure stabilized by internal hydrogen bonds; cellulose assumes an extended structure in which intermolecular hydrogen bonds are more important.

Conformational Formulas of Pyranoses

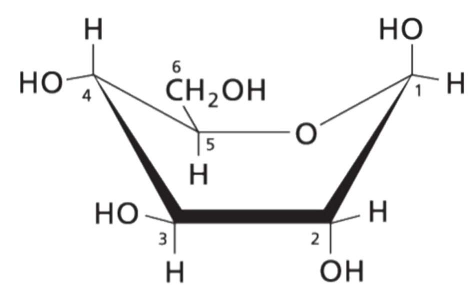
- pyranose rings tend to assume either of two "chair" conformations (rarely "boat" conformation)
  - interconvertible without breaking covalent bonds
  - requires energy input



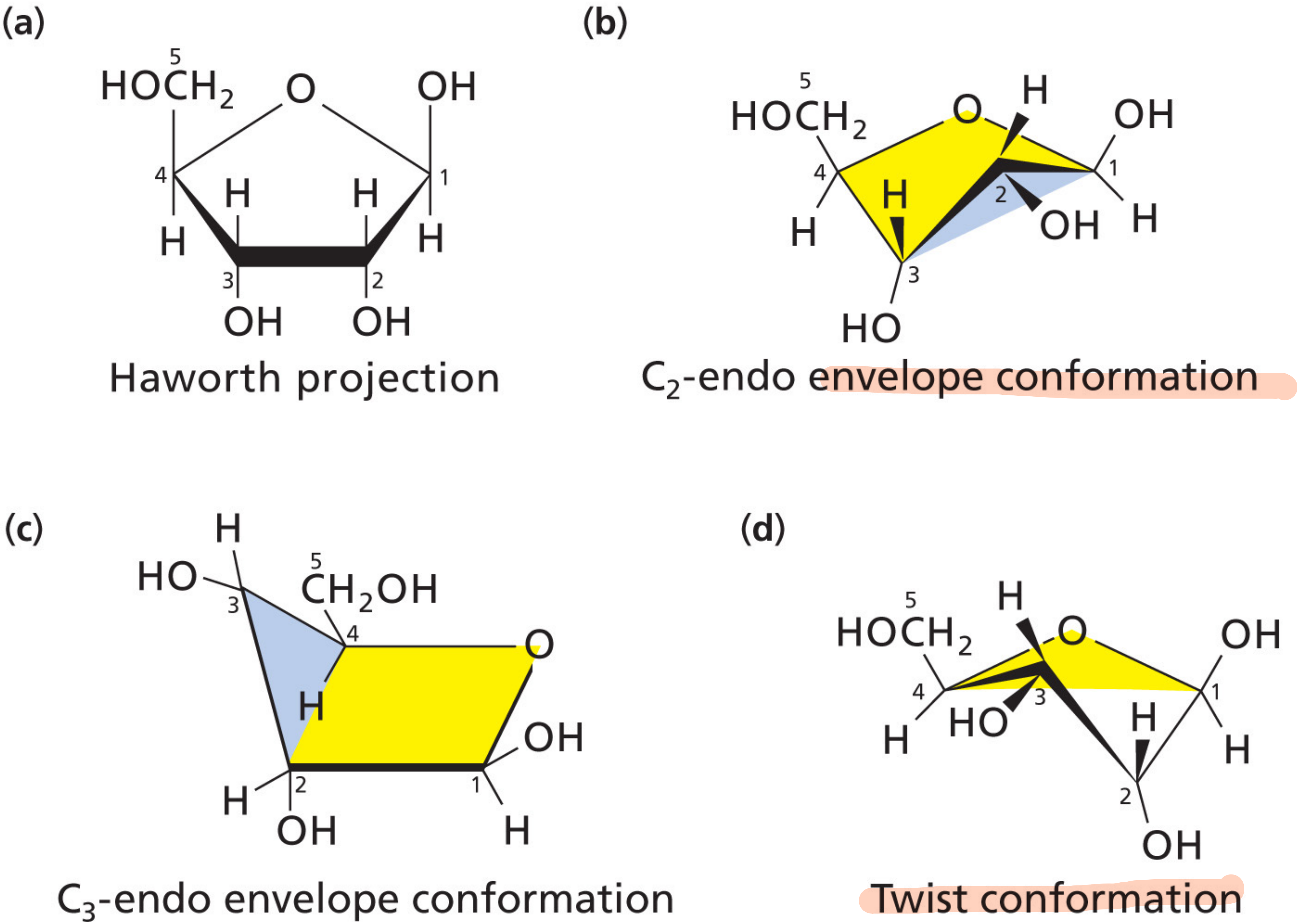
Two possible chair forms of β-D-glucopyranose
(a)



α-D-Glucopyranose
(b)

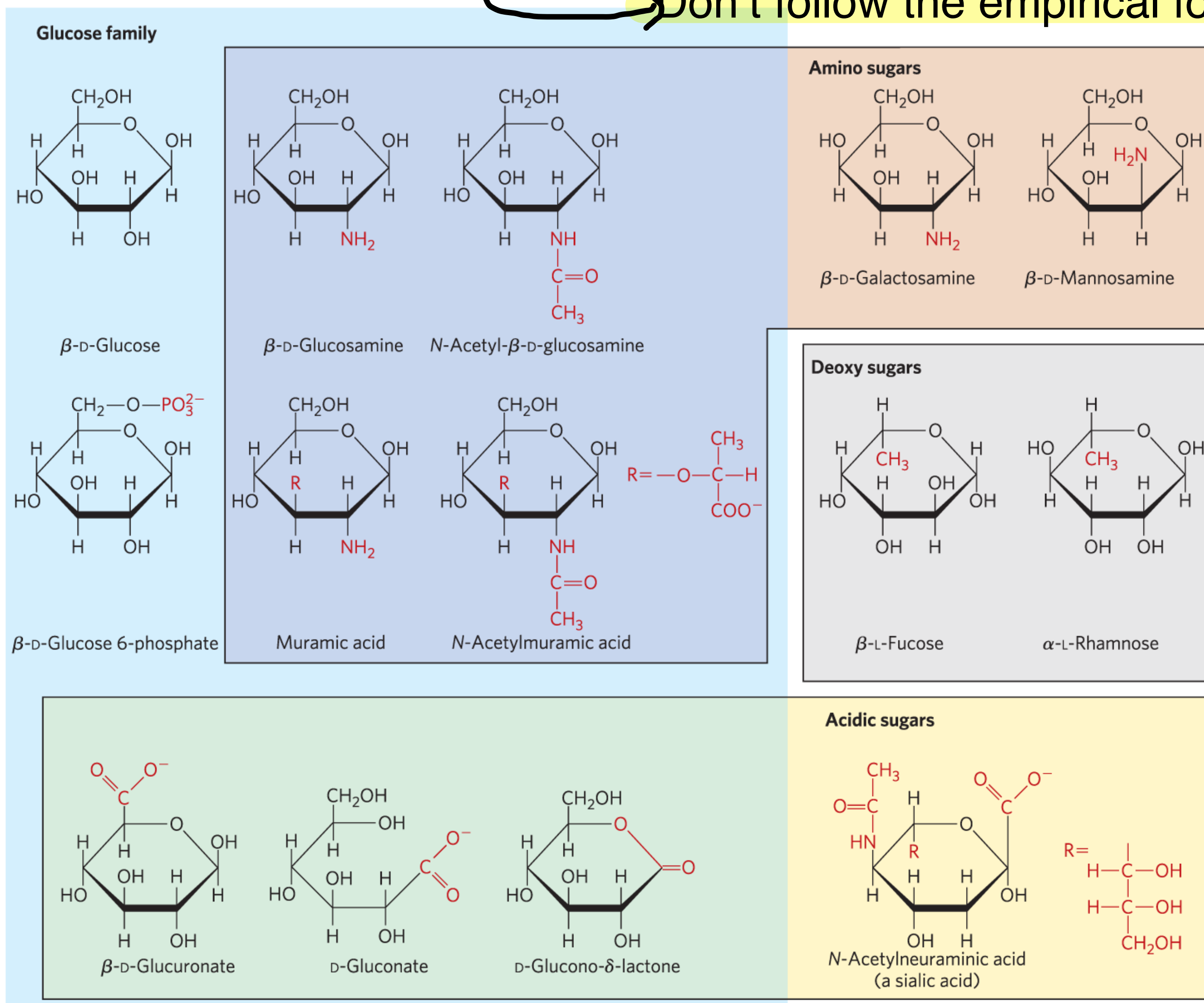


Boat conformation


(a)
HOCH2
O
OH
H
H
H
H
OH
OH
Haworth projection
(b)
HOCH2
O
H
OH
H
OH
H
H
HO
C2-endo envelope conformation
(c)
H
HO
CH2OH
O
H
OH
H
OH
H
C3-endo envelope conformation
(d)
HOCH2
H
O
OH
HO
H
H
H
OH
Twist conformation

Organisms Contain a Variety of Hexose Derivatives

→Don't follow the empirical formula of sugar



Aldonic and Uronic Acids

الشكل الذي يتكون بعد

- **aldonic acids** = form following oxidation of the carbonyl carbon of aldoses
- **uronic acids** = form following oxidation at C-6
- both form stable intramolecular esters called lactones

Phosphorylated Derivatives

- some sugar intermediates are phosphate esters
  - example: glucose 6-phosphate
- stable at neutral pH and bear a negative charge
- functions to trap sugar inside the cell because most cells do not have membrane transporters for phosphorylated sugars

Sugars That Are, or Can Form, Aldehydes Are Reducing Sugars

- **reducing sugars** = undergo a characteristic redox reaction where free aldehyde groups react with Cu^{2+} under alkaline condition
  - reduction of Cu^{2+} to Cu^{+} forms a قرميد brick-red precipitate

- ketoses that can tautomerize to form aldehydes are also reducing sugars

Chain-Ring Equilibrium and Reducing Sugars

- The ring forms exist in equilibrium with the open-chain forms
- Reducing sugars have a free anomeric carbon
- Aldehyde can reduce Cu^{2+} to Cu^{+} (Fehling's test)
- Aldehyde can reduce Ag^{+} to Ag^{0} (Tollens' test)
- Allows detection of reducing sugars, such as glucose (by measuring the amount of oxidizing agent reduced by a sugar solution, the sugar concentration can be estimated)

The cuprous ion (Cu^+) produced forms a red cuprous oxide precipitate.

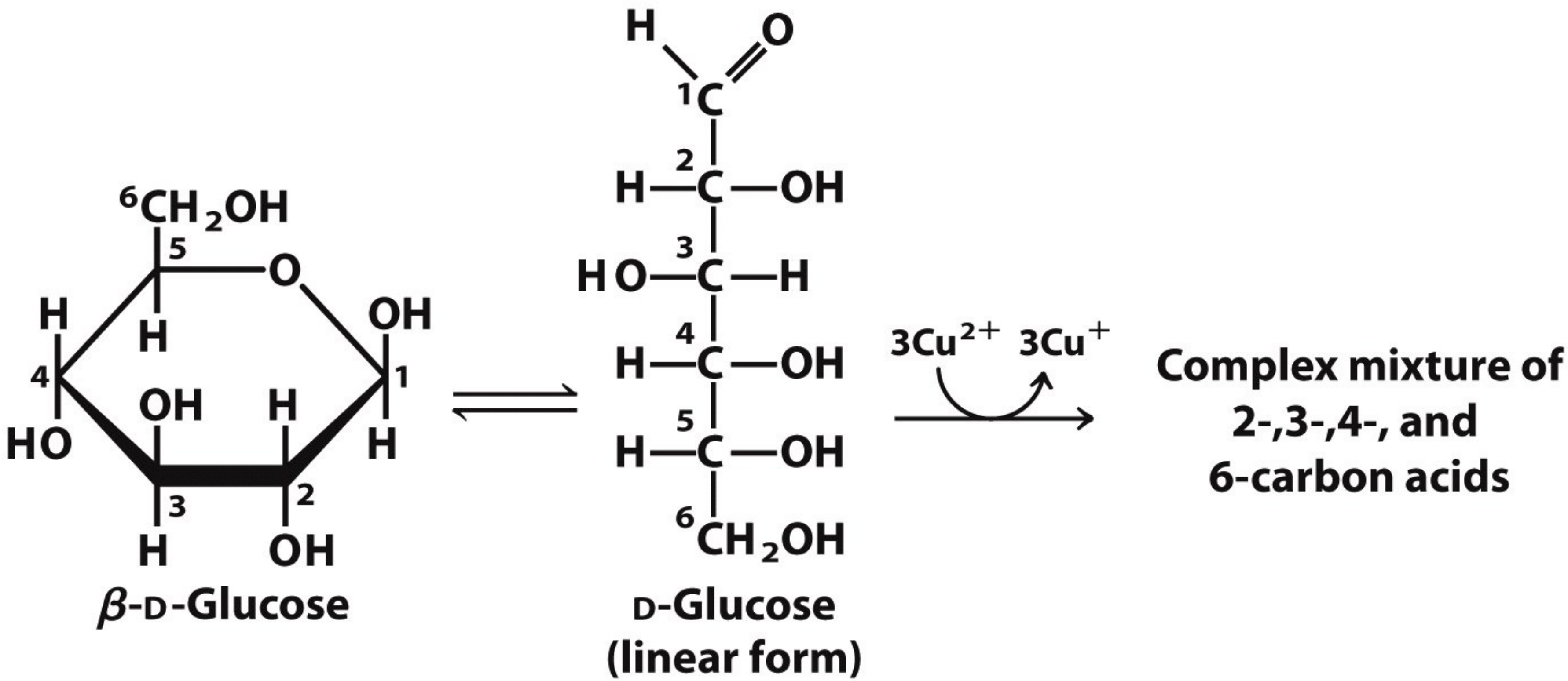


Figure 7-10
Lehninger Principles of Biochemistry, Fifth Edition

P1 Clicker Question 10

Which reaction is one that is NOT common of glucose?

A. mutarotation
B. oxidation to an aldonic acid
C. oxidation to an uronic acid
D. oxidation by reducing sugars

Clicker Question 10, Response

Which reaction is one that is NOT common of glucose?

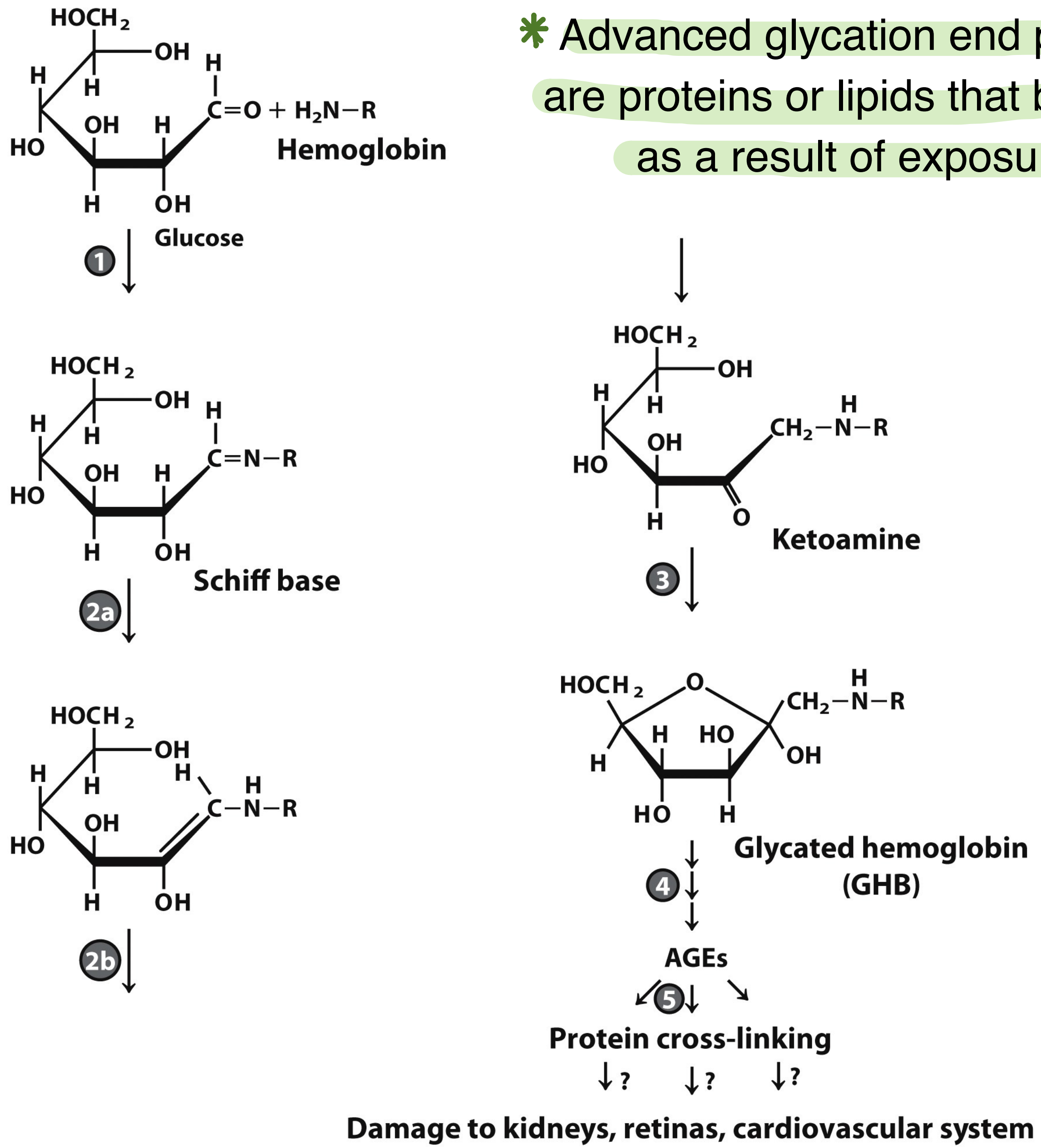
D. oxidation by reducing sugars

Glucose does not undergo oxidation by reducing sugars. Glucose itself is a reducing sugar. Free aldehyde groups in glucose undergo a characteristic redox reaction with Cu^{2+} under alkaline conditions. As glucose is oxidized from aldehyde to carboxylic acid, Cu^{2+} is reduced to Cu^{+}, which forms a brick-red precipitate.

Blood glucose measurements in the diagnosis and treatment of diabetes

- Untreated diabetes has several long-term consequences: kidney failure, cardiovascular disease, blindness (العمى), impaired wound healing, etc.
- Average $[glc]_{blood}$ (Abbreviation of glucose) over days can be measured because of a nonenzymatic reaction between glc and primary amino groups in Hb
- The amount of glycated Hb (GHb) reflects the average $[glc]_{blood}$ over the circulating lifetime of RBC (~120 days)
- Normal levels ~5% of Hb is GHb
- Diabetic people may have it as high as 13%
- Advanced glycation endproducts (AGEs) contribute to the long term problems associated with diabetes

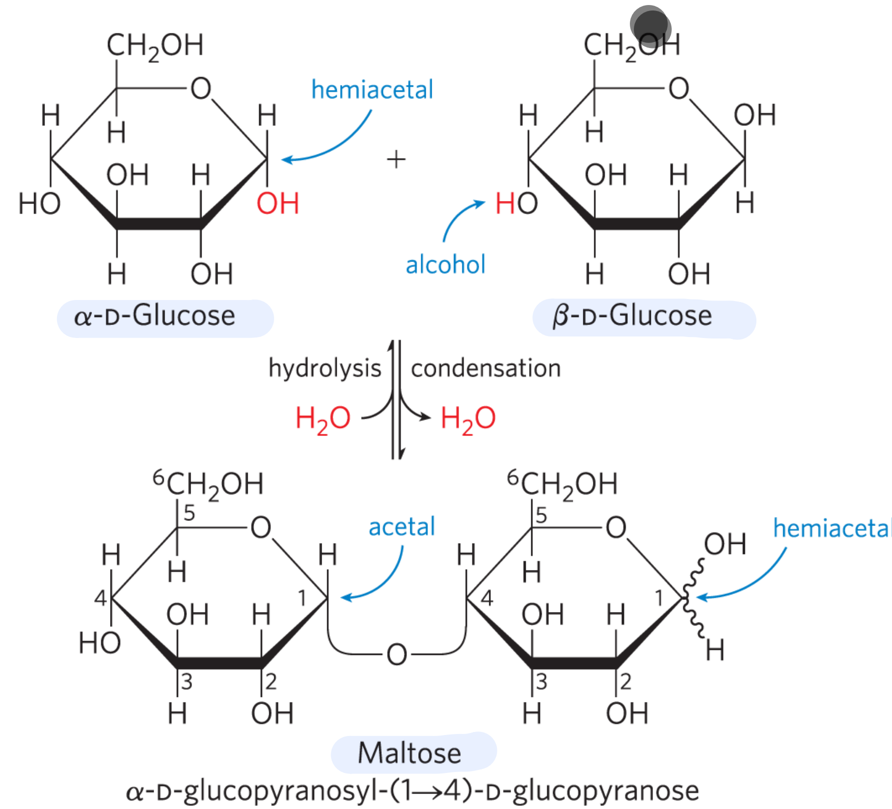
* Advanced glycation end products (AGEs) are proteins or lipids that become glycated as a result of exposure to sugars



Box 7-1 figure 1
Lehninger Principles of Biochemistry, Sixth Edition

O-Glycosidic Bonds

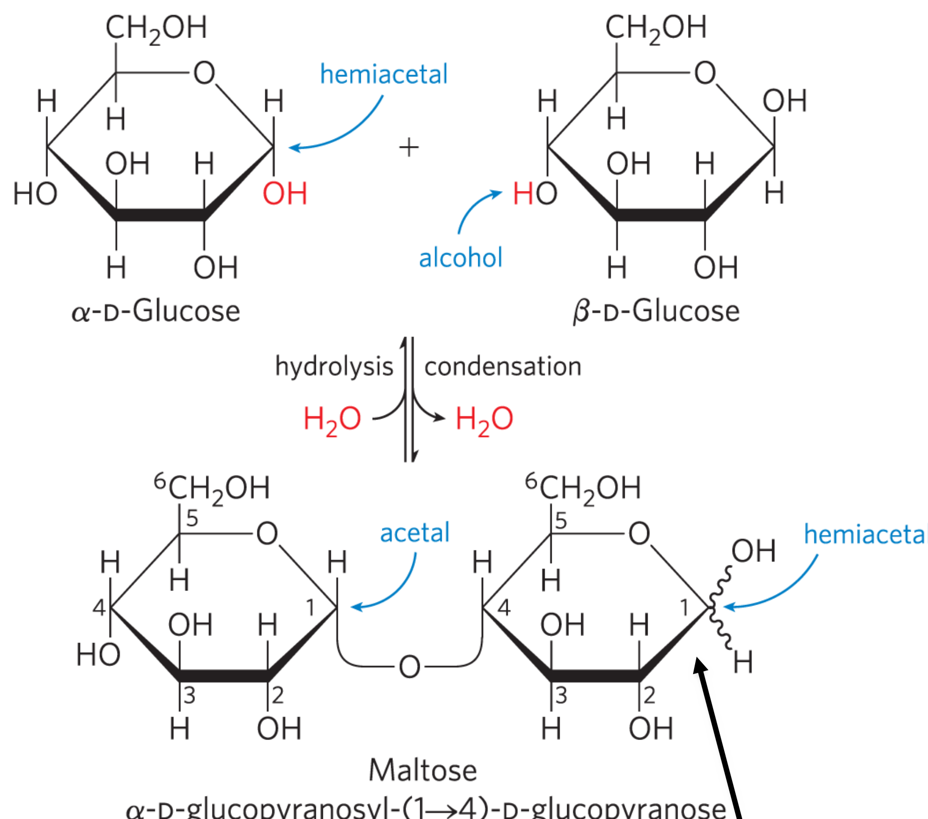
- ***O*-glycosidic bond** = covalent linkage joining two monosaccharides
  - formed when a hydroxyl group of one sugar molecule reacts with the anomeric carbon of the other
  - The resulting compound is a **glycoside**
  - readily hydrolyzed by acid



The Reducing End

- formation of a glycosidic bond يجعل renders a sugar nonreducing

- **reducing end** = the end of a disaccharide or polysaccharide chain with a free anomeric carbon



Free anomeric carbon

P1

Clicker Question 11

What term is given to carbohydrates linked by their anomeric carbons?

A. nonreducing sugars
B. glycosides
C. anomers
D. hemiketals

Clicker Question 11, Response

What term is given to carbohydrates linked by their anomeric carbons?

A. nonreducing sugars

When the anomeric carbon is involved in a glycosidic bond, the easy interconversion of linear and cyclic forms is prevented. Formation of a glycosidic bond therefore renders a sugar nonreducing.

Naming Reducing Oligosaccharides

- step 1: with the nonreducing end on the left, give the configuration (*α* or *β*) at the anomeric carbon joining the first unit to the second

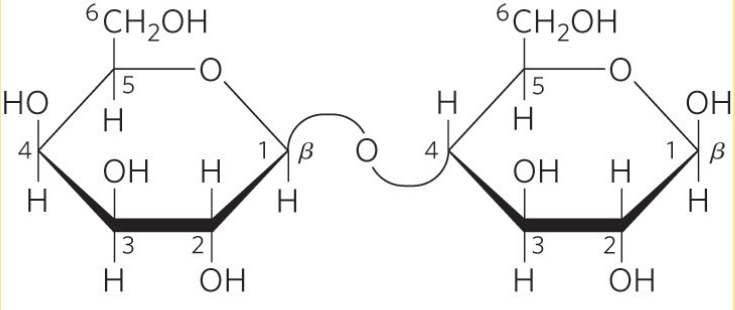
- step 2: name the nonreducing residue using “furano” or “pyrano”

- step 3: indicate in parentheses the two carbon atoms joined by the glycosidic bond, with an arrow connecting the two numbers

- step 4: name the second residue and repeat for additional residues

P1 Clicker Question 12

Following the convention for naming reducing oligosaccharides, what is the name of lactose, as shown.

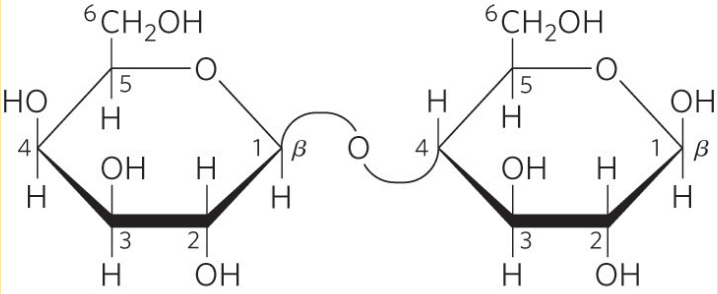


Lactose (*β* form)
β-D-galactopyranosyl-(1→4)-*β*-D-glucopyranose
Gal(*β*1→4)Glc

A. *α*-L-glucopyranose-(1→6)-*α*-L-galactopyranosyl
B. *β*-D-glucopyranose-(1→4)-*β*-D-galactopyranosyl
C. *β*-D-galactopyranosyl-(1→4)-*β*-D-glucopyranose
D. *α*-L-galactopyranosyl-(1→6)-*α*-L-glucopyranose

Clicker Question 12, Response

Following the convention for naming reducing oligosaccharides, what is the name of lactose, as shown.



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

C. *β*-D-galactopyranosyl-(1→4)-*β*-D-glucopyranose

The image is drawn with the nonreducing end on the left. The anomeric carbon joining the first unit to the second is *β* and the nonreducing unit is the six-membered ring D-galactose. A (1→4)-glycosidic bond links the two monosaccharides together. The second residue is the six-membered ring D-glucose.

Symbols and Abbreviations for Monosaccharides and Derivatives

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		

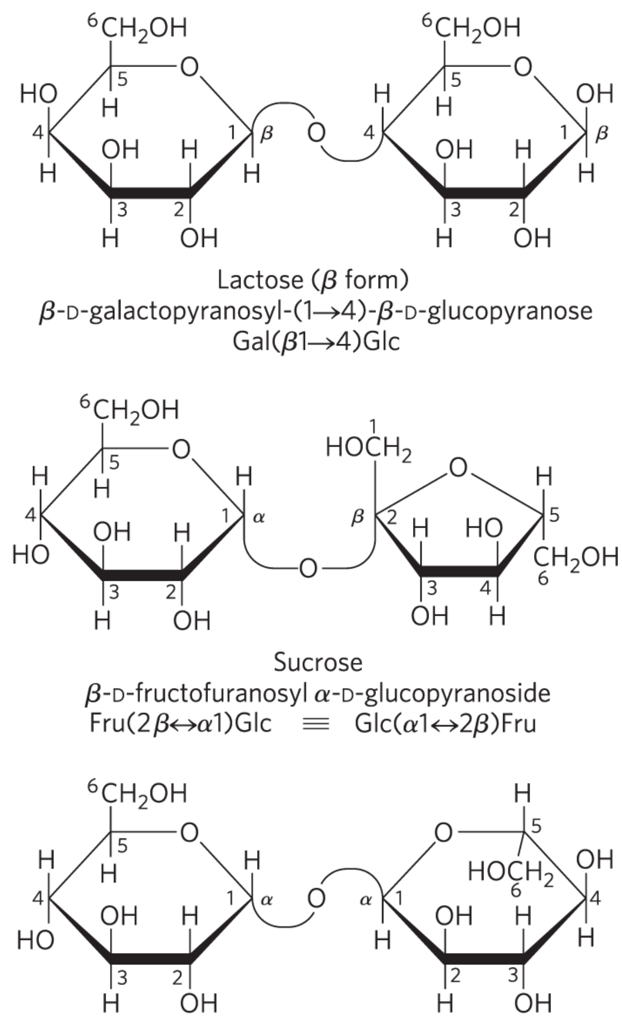
Note: In a commonly used convention, hexoses are represented as circles, *N*-acetylhexosamines as squares, and hexosamines as squares divided diagonally. All sugars with the "gluco" configuration are blue, those with the "galacto" configuration are yellow, and "manno" sugars are green. Other substituents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

Three Common Disaccharides

- lactose is a reducing disaccharide

- sucrose and trehalose are nonreducing sugars

*Abbreviations
- Glc —> glucose
- Gal—> galactose
- Fru—> fructose
- Man —> mannose
- GlcN —> N-acytelglucoseamine



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

Sucrose
β-D-fructofuranosyl α-D-glucopyranoside
Fru(2β↔α1)Glc ≡ Glc(α1↔2β)Fru

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

P1

Clicker Question 13

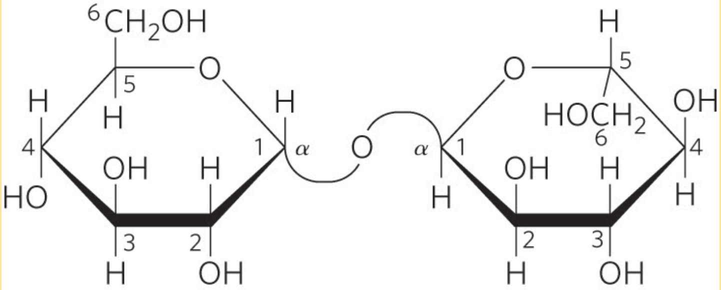
Which of these sugars is nonreducing?

A. trehalose
B. glucose
C. maltose
D. lactose

Clicker Question 13, Response

Which of these sugars is nonreducing?

A. trehalose



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

When the anomeric carbon is involved in a glycosidic bond, the easy interconversion of linear and cyclic forms is prevented. Formation of a glycosidic bond therefore renders a sugar nonreducing. Trehalose is a disaccharide of D-glucose that is a nonreducing sugar.

P1 Clicker Question 14

Which item is NOT associated with disaccharides?

A. *O*-glycosidic linkages
B. formation of a ketal or acetal
C. never having free anomeric carbons
D. sucrose

Clicker Question 14, Response

Which item is NOT associated with disaccharides?

C. never having free anomeric carbons

In describing disaccharides and polysaccharides, the end of a chain with a free anomeric carbon (one not involved in a glycosidic bond) is called the reducing end. There are a number of disaccharides with free anomeric carbons, including glucose and lactose.

7.2 Polysaccharides

P2 Principle 2

Monomeric subunits, monosaccharides, serve as the building blocks of large carbohydrate polymers. The specific sugar, the way the units are linked, and whether the polymer is branched determine its properties and thus its function.

Polysaccharides

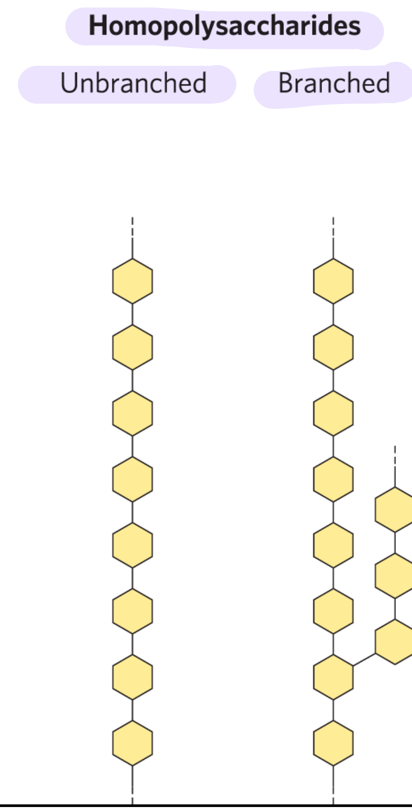
- most carbohydrates in nature occur as polysaccharides (M_r > 20,000)

- also called **glycans**

YouTube Video:

1) Carbohydrates & sugars – biochemistry (Osmosis)

Homopolysaccharides and Heteropolysaccharides



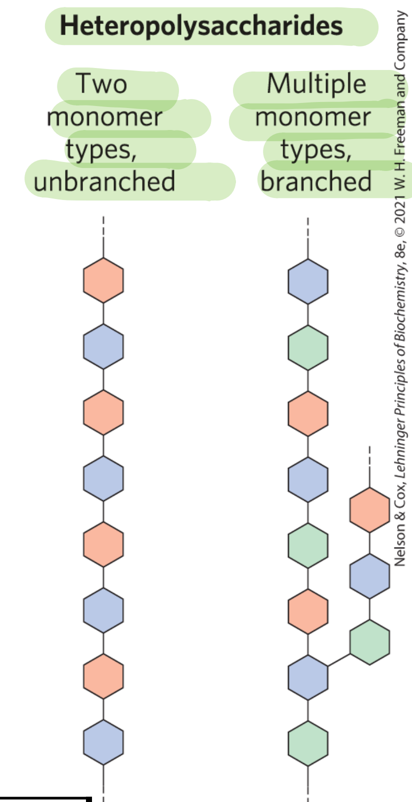
- **homopolysaccharides** = contain only a single monomeric sugar species
  - serve as storage forms and structural elements
  - Can be branched or linear

Can be:

1) Storage forms of monosaccharides, used for fuel (starch and glycogen)
2) Structural elements in plant cell walls and animal exoskeletons (cellulose and chitin)

Homopolysaccharides and Heteropolysaccharides

- **heteropolysaccharides** = contain 2+ kinds of monomers
  - provide extracellular support
  - Can be branched or linear



Provide extracellular support for organisms of all kingdoms,

E.g.

1) Bacterial cell envelope is composed in part of a heteropolysaccharide
2) Extracellular matrix in animal cells

P2

Clicker Question 15

Which statement is false regarding homopolysaccharides and heteropolysaccharides?

A. Homopolysaccharides contain a single monomeric sugar species.
B. Some homopolysaccharides serve as structural elements in animal exoskeletons.
C. Heteropolysaccharides serve as storage forms of monosaccharides that are used as fuel.
D. In animal tissues, the extracellular space is occupied by several types of heteropolysaccharides.

Clicker Question 15, Response

Which statement is false regarding homopolysaccharides and heteropolysaccharides?

C. Heteropolysaccharides serve as storage forms of monosaccharides that are used as fuel.

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

P4 Principle 4

The sequences of complex polysaccharides are determined by the intrinsic properties of the biosynthetic enzymes that add each monomeric unit to the growing polymer. This is in على النقيض contrast with DNA, RNA, and proteins, which are synthesized on templates that direct their sequence.

Polysaccharides Generally Do Not Have Defined Lengths or Molecular Weights

الفرق

- this distinction between proteins and polysaccharides is a consequence of the mechanisms of assembly
- there is no template for polysaccharide synthesis
- the program for polysaccharide synthesis is intrinsic to the enzymes that catalyze the polymerization of monomer units

Some Homopolysaccharides Are Storage Forms of Fuel

- storage polysaccharides = starch in plant cells and glycogen in animal cells

رطبة جداً

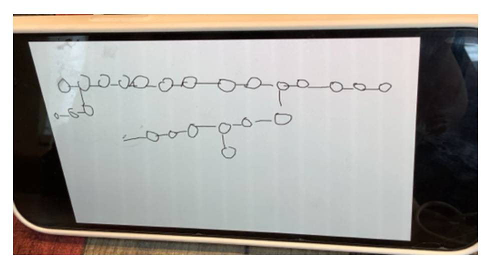
- starch and glycogen molecules are heavily hydrated because they have many exposed hydroxyl groups available to hydrogen bond

Starch and Glycogen

* We can digest starch and glycogen

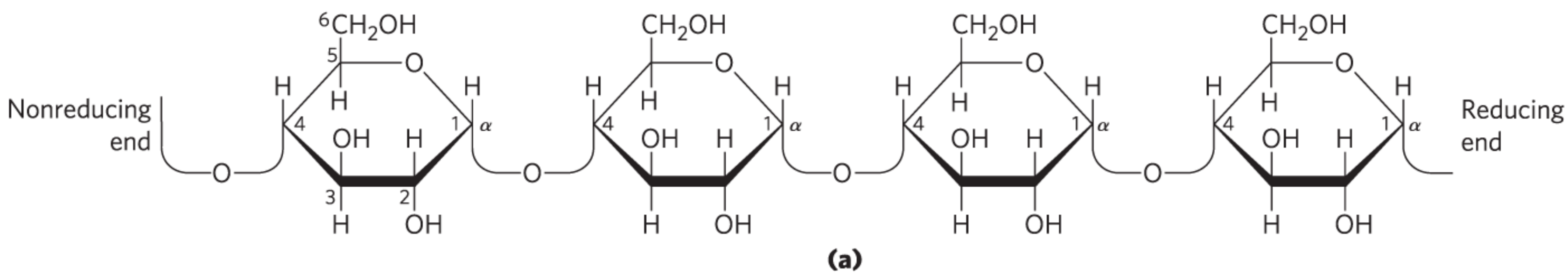
- **starch** = contains two types of glucose polymer, amylose and amylopectin
  - amylose = long, unbranched chains of D-glucose residues connected by $(\alpha 1 \rightarrow 4)$ linkages
  - amylopectin = larger than amylose with $(\alpha 1 \rightarrow 4)$ linkages between glucose residues and highly branched due to $(\alpha 1 \rightarrow 6)$ linkages At each 24-30 residue

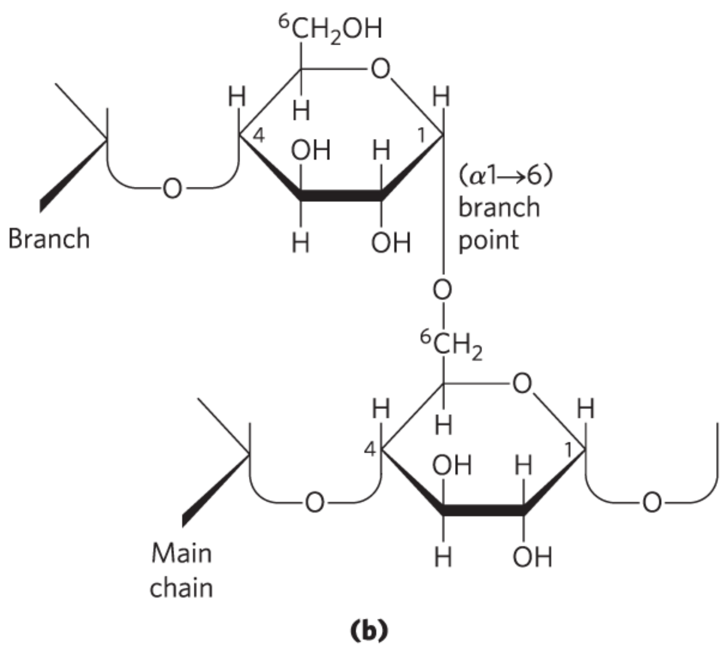
- **glycogen** = polymer of $(\alpha 1 \rightarrow 4)$-linked glucose subunits, with $(\alpha 1 \rightarrow 6)$-linked branches At each 8-12 residue
  - more extensively branched
  - more compact than starch



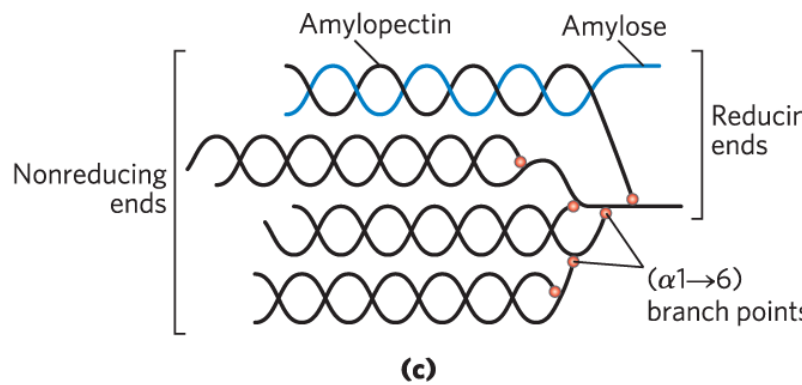
Structure of Starch and Glycogen

*All enzymes that make or break glycogen work at nonreducing end





Glycogen and amylopectin have one reducing end but many nonreducing ends (a polymer with n branches has n + 1 nonreducing ends and only 1 reducing end)



P2

Clicker Question 16

What *O*-glycosidic bond is commonly found in amylose, amylopectin, and glycogen?

A. (β1→4)
B. (α1→6)
C. (β1→6)
D. (α1→4)

Clicker Question 16, Response

What *O*-glycosidic bond is commonly found in amylose, amylopectin, and glycogen?

D. (α1→4)

Amylose, amylopectin, and glycogen all contain (α1→4) linkages joining successive glucose residues.

P2

Clicker Question 17

A glycogen molecule with 28 branches has how many nonreducing and reducing ends?

A. 28 nonreducing ends and 28 reducing ends
B. 29 nonreducing ends and 1 reducing end
C. 1 nonreducing end and 29 reducing ends
D. 1 nonreducing end and 1 reducing end

Clicker Question 17, Response

A glycogen molecule with 28 branches has how many nonreducing and reducing ends?

B. 29 nonreducing ends and 1 reducing end

Because each branch of glycogen ends with a nonreducing sugar unit, a glycogen molecule with *n* branches has *n* + 1 nonreducing ends, but only one reducing end. Thus, a glycogen molecule with 28 branches has 29 nonreducing ends and 1 reducing end.

P3 Principle 3

Storage of low molecular weight metabolites in polymeric form avoids the very high osmolarity that would result from storing them as individual monomers. If the glucose in liver glycogen were monomeric, the glucose concentration in liver would be so high that cells would swell and lyse from the entry of water by osmosis.

Storage of Glucose as Polymers Avoids High Osmolarity

- hepatocytes in the fed state store glycogen equivalent to a glucose concentration of 0.4 M

- 0.4 M glucose in the cytosol would برفع elevate the osmolarity
  - the resulting osmotic entry of water might تمزق rupture the cell

* Osmotic pressure depend on the number of molecules, not size of it

P3 Clicker Question 18

Why is it logical for sugars to be added to only one end of glycogen, making them excellent molecules for glucose *storage*?

A. Because the other end of the molecule is anchored to a membrane with a lipid.
B. Because it is the reducing end, and a reduction reaction is the mechanism for adding the sugar.
C. Because it has the hemiacetal carbon, the one carbon to which more sugars can be attached.
D. Because there are many nonreducing ends on one molecule, allowing rapid glucose storage and release.

Clicker Question 18, Response

Why is it logical for sugars to be added to only one end of glycogen, making them excellent molecules for glucose *storage*?

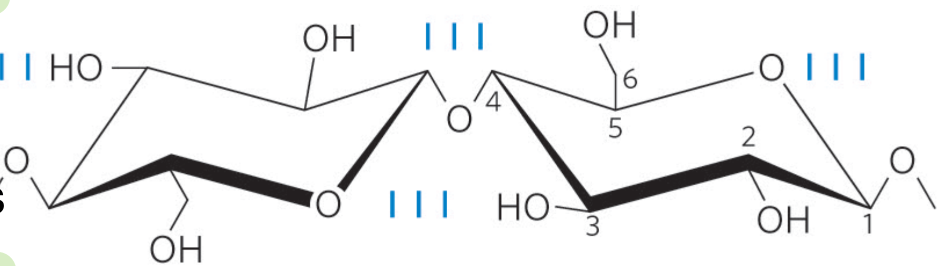
D. Because there are many nonreducing ends on one molecule, allowing rapid glucose storage and release.

A glycogen molecule with *n* branches has *n* + 1 nonreducing ends. When glycogen is used as an energy source, glucose units are removed one at a time from the nonreducing ends. Degradative enzymes that act only at nonreducing ends can work simultaneously on the many branches, speeding the conversion of the polymer to monosaccharides.

Some Homopolysaccharides Serve Structural Roles

- **cellulose** = tough, fibrous, water-insoluble substance
  - linear, unbranched homopolysaccharide, consisting of 10,000 to 15,000 D-glucose units
  - glucose residues have the *β* configuration
  - linked by (*β*1→4) glycosidic bonds
  - animals do not have the enzyme to hydrolyze (*β*1→4) glycosidic bonds

*The only difference between amylose and cellulose that are the amylose has α configuration but cellulose has β configuration



(*β*1→4)-linked D-glucose units

P5 Clicker Question 19

Even though amylose and cellulose are made of similar homopolysaccharide chains, they have very different properties. Why?

A. The *β*-glycosidic linkage of glucose molecules in cellulose form interchain and intrachain hydrogen bonds that produce straight, stable fibers that exclude water.
B. Cellulose is composed of galactose, while amylose is composed of glucose.
C. The *α*-glycosidic linkage of glucose molecules in amylose causes it to form helices that exclude water.
D. Amylose makes a linear polymer which cannot make hydrogen bonds.

Clicker Question 19, Response

Even though amylose and cellulose are made of similar homopolysaccharide chains, they have very different properties. Why?

A. **The *β*-glycosidic linkage of glucose molecules in cellulose form interchain and intrachain hydrogen bonds that produce straight, stable fibers that exclude water.**

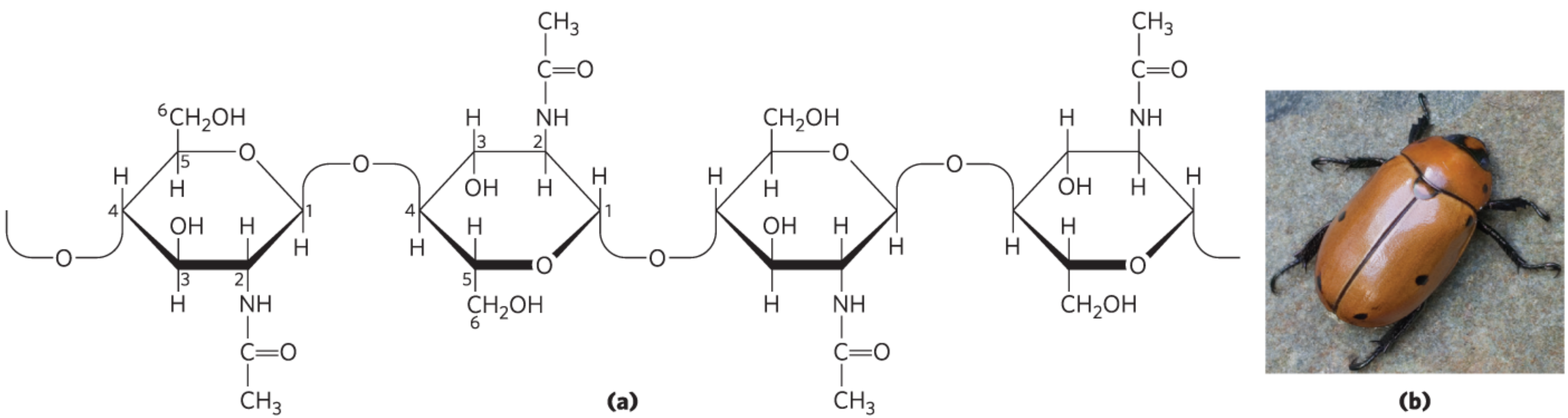
The glucose residues in cellulose are linked by (*β*1→4) glycosidic bonds, allowing for the formation of interchain and intrachain hydrogen bonds.

Chitin

Produce exoskeleton in insects

we can't digest chitin

- **chitin** = linear homopolysaccharide composed of *N*-acetylglucosamine residues in (β1→4) linkage
  - acetylated amino group makes chitin more hydrophobic and water-resistant than cellulose



(a) (b)

(b) Paul Whitten/Science Source.

* Chitin is more hydrophobic than cellulose because it contain a amide group instead of hydroxy group

P5 Clicker Question 20

Why are chitin and cellulose hydrophobic and essentially insoluble in an aqueous media?

A. Because polymers of these molecules pack so tightly together, there is no geometric space left for water.
B. Because they form many internal hydrogen bonds, they leave no sites for binding to water.
C. Because there are no enzymes that can break the beta linkages.
D. Because the linear polymer cannot make hydrogen bonds.

Clicker Question 20, Response

Why are chitin and cellulose hydrophobic and essentially insoluble in an aqueous media?

B. Because they form many internal hydrogen bonds, they leave no sites for binding to water.

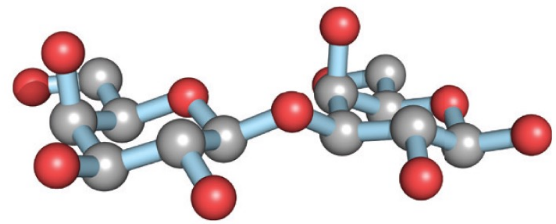
The residues in chitin and cellulose are both linked by (β1→4) linkages, allowing for the formation of internal hydrogen bonds.

Steric Factors and Hydrogen Bonding Influence Homopolysaccharide Folding

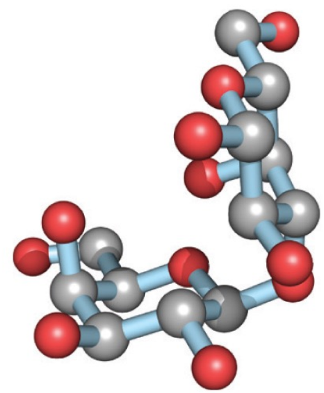
- three-dimensional structures stabilized by weak interactions within or between molecules
  - hydrogen bonding is especially important due to the high number of hydroxyl groups in polysaccharides
- free rotation about both C—O bonds linking the residues is limited by steric hindrance by substituents

Different Energetic Conformation of a Disaccharide

- bulkiness and electronic effects at the anomeric carbon place قيد constraints on φ and ψ



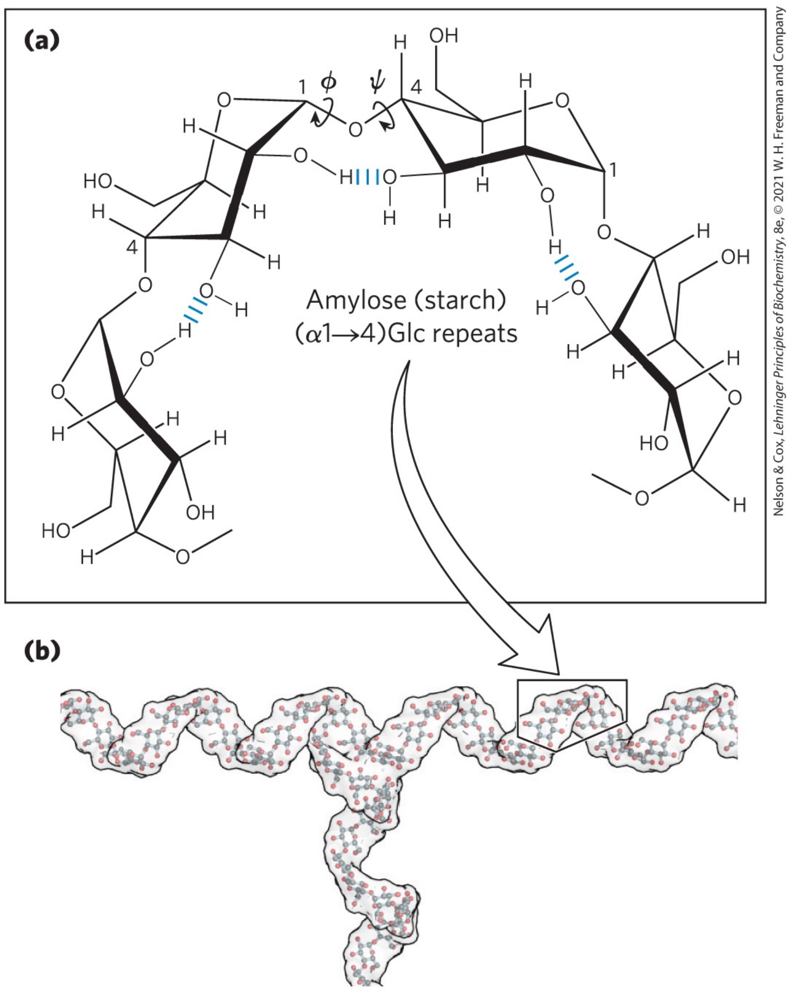
Low-energy conformation is extended and maximizes H-bonding.



High-energy conformation is sterically hindered.

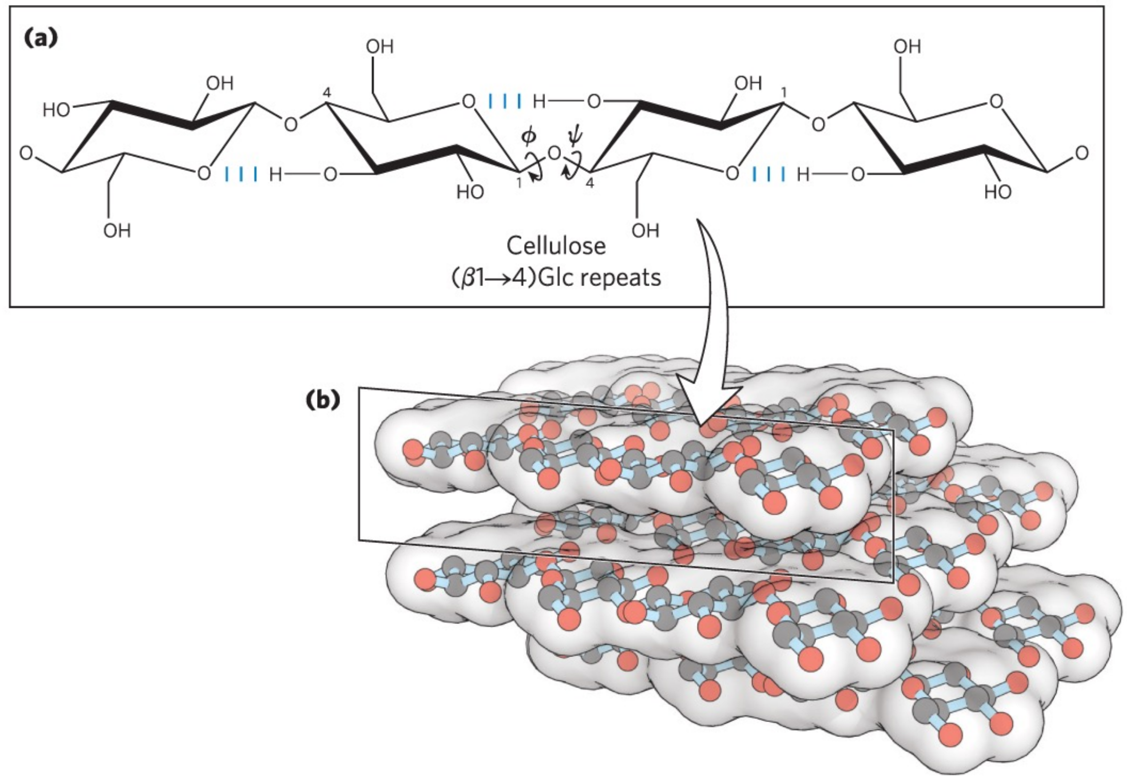
Helical Structure of Starch and Glycogen

- most stable three-dimensional structure for the (α1→4)-linked chains of starch and glycogen
  - six residues/turn



Linear Structure of Cellulose

- most stable conformation is a straight, extended chain
  - each chair is turned 180° relative to its neighbors



P2

Clicker Question 21

Polysaccharides:

A. do not fold into three-dimensional structures.
B. are glycans.
C. must be homopolysaccharides.
D. are never branched.

Clicker Question 21, Response

Polysaccharides:

B. are glycans.

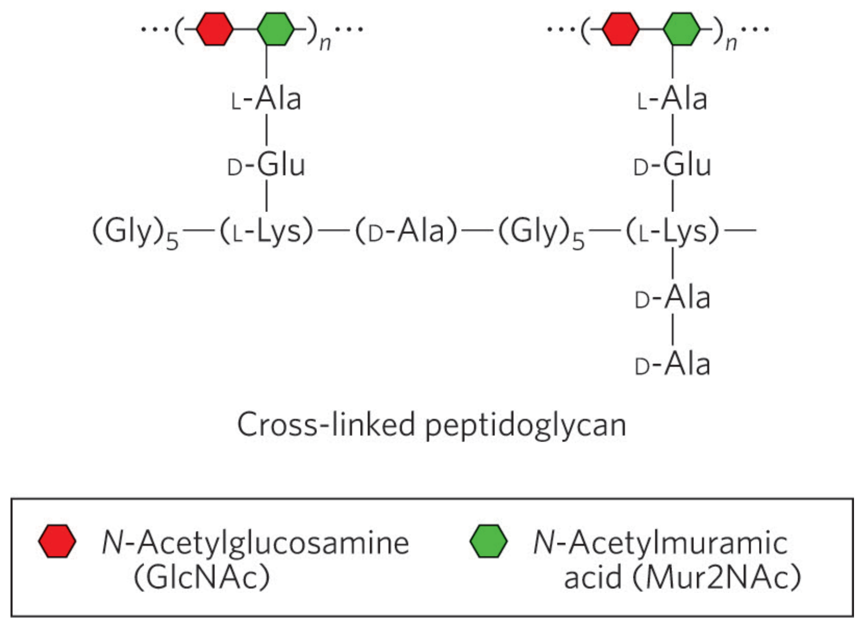
Polysaccharides are also called glycans.

Peptidoglycan Reinforces the Bacterial Cell Wall

We can't digest peptidoglycan

One of the rare compounds that contain L isomer and D isomer

- peptidoglycan = rigid component of bacterial cell walls
  - heteropolymer of alternating (β1→4)-linked *N*-acetylglucosamine and *N*-acetylmuramic acid residues
  - cross-linked by short peptides



Nelson & Cox, *Lehninger Principles of Biochemistry*, 8e, © 2021 W. H. Freeman and Company

✱ Peptidoglycan is heteropolysaccharides

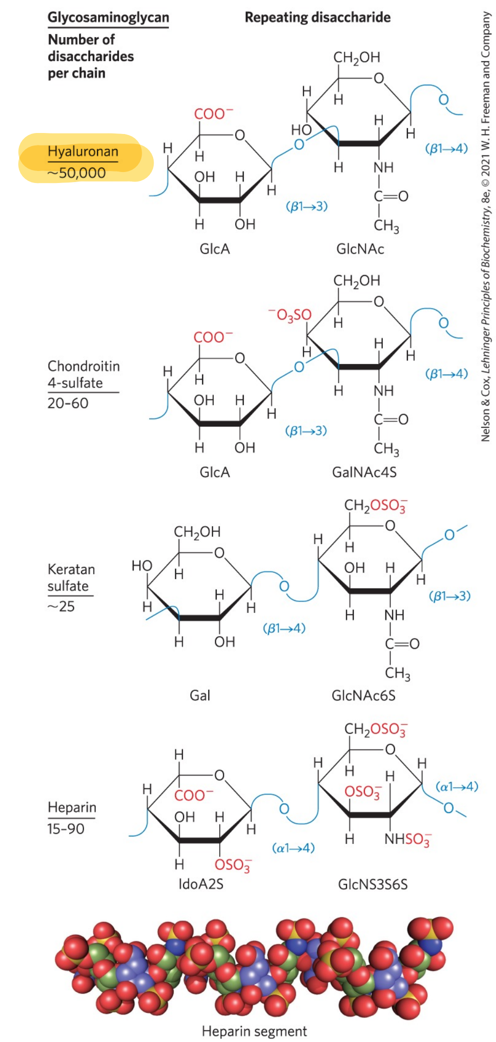
Glycosaminoglycans Are Heteropolysaccharides of the Extracellular Matrix

- **extracellular matrix (ECM)** = gel-like material in the extracellular space of tissues that holds cells together and provides a porous pathway for nutrient and O_2 diffusion
  متشابكة
  - composed of an interlocking meshwork of heteropolysaccharides (ground substance) and fibrous proteins

- basement membrane (specialized ECM) also contains heteropolysaccharides

Repeating Units of Glycosaminoglycans of ECM

- **glycosaminoglycans** = heteropolysaccharides in ECM
  - linear polymers composed of repeating disaccharide units
  - one monosaccharide is always either *N*-acetylglucosamine or *N*-acetylgalactosamine and the other is usually a uronic acid
  - unique to animals and bacteria
  - some contain esterified sulfate groups



*Glycosaminoglycans contain different types of bond (α and β) between different carbon(such as 1-3 and 1-4).

Types of Glycosaminoglycans

- **hyaluronan** (hyaluronic acid) = alternating residues of D-glucuronic acid and *N*-acetylglucosamine

سائل زلالي

*Very important in joints because it have a big role in synovial fluid.

- **chondroitin sulfate, dermatan sulfate, keratan sulfate,** and **heparan sulfate** differ from hyaluronan in three respects:
  - generally much shorter polymers
  - covalently linked to specific proteins (proteoglycans)
  - one or both monomer units differ from hyaluronan

الشد

- provide viscosity, adhesiveness, and tensile strength to the extracellular matrix

P2

Clicker Question 22

Which characteristic is NOT one that is true of glycosaminoglycans?

A. found in extracellular matrix
B. always contain sulfates
C. are heteropolysaccharides
D. are disaccharide repeat units

Clicker Question 22, Response

Which characteristic is NOT one that is true of glycosaminoglycans?

B. always contain sulfates

The glycosaminoglycans, are a family of linear polymers composed of repeating disaccharide units. Some, but not all, glycosaminoglycans contain esterified sulfate groups.

Heparan Sulfate

- contains variable, nonrandom arrangements of sulfated and nonsulfated sugars

- sulfated residues gives the molecule the ability to interact specifically with proteins

Heparin

- highly sulfated, intracellular form of heparan sulfate produced primarily by mast cells

- used as a therapeutic agent to inhibit coagulation of blood through its capacity to bind the protease inhibitor antithrombin

قدرة

* Heparin is the most negatively charged biological compound

* Heparin bind to protease that break down antithrombin —> antithrombin bind to thrombin—> thrombin doesn't work —> fibrinogen will not convert to fibrin—> blood will no coagulated

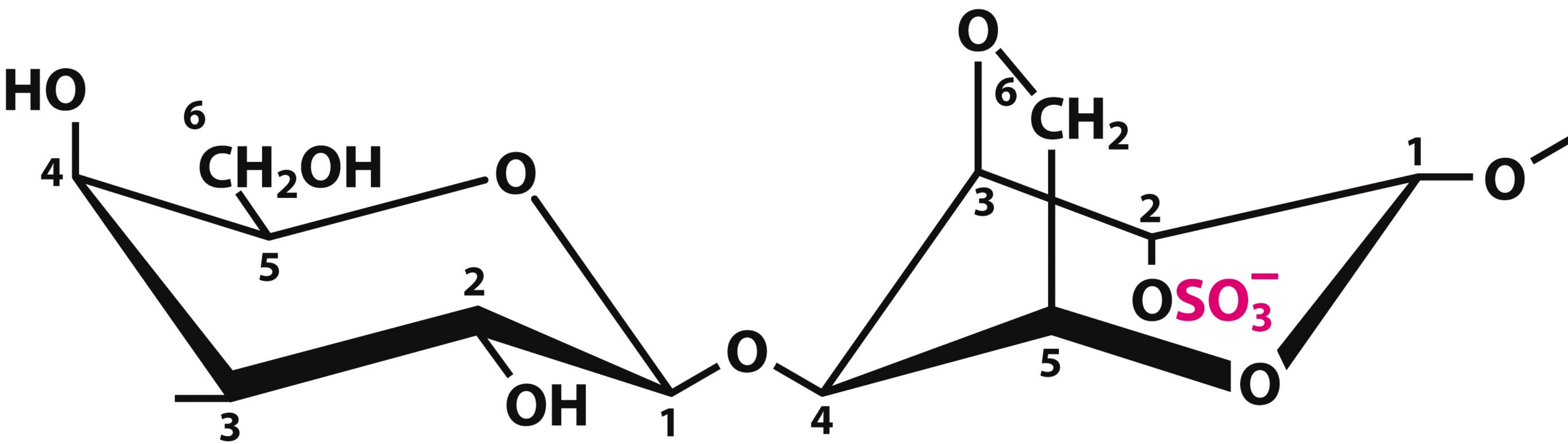
Dextrans

- Bacterial and yeast polysaccharides
- $(\alpha 1 \rightarrow 6)$-linked poly-D-glucose
- All units have $(\alpha 1 \rightarrow 3)$ branches
- Some have also $(\alpha 1 \rightarrow 2)$ or $(\alpha 1 \rightarrow 4)$ branches
- Dental plaque ترسبات (formed by bacteria on the surface of teeth) is rich in dextrans

Agar and Agarose

- Agar is a complex mixture of complex hetereopolysaccharides composed of **agarose** and **agaropectin** (containing modified galactose units)
- Agar serves as a component of cell wall in some seaweeds الأعشاب البحرية
- Agar solutions form gels that are commonly used in the laboratory as a surface for growing bacteria
- Agar is also used for capsules in which some drugs and vitamins are packaged
- Agarose solutions form gels that are commonly used in the laboratory for separation DNA by electrophoresis

Agar and Agarose



Agarose

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

Figure 7-21
Lehninger Principles of Biochemistry, Sixth Edition

Table 8.2 Structures of some common polysaccharides

Polysaccharide[a]	Component(s)[b]	Linkage(s)
Storage homoglycans		
Starch		
Amylose	Glc	α-(1 → 4)
Amylopectin	Glc	α-(1 → 4), α-(1 → 6) (branches)
Glycogen	Glc	α-(1 → 4), α-(1 → 6) (branches)
Structural homoglycans		
Cellulose	Glc	β(1 → 4)
Chitin	GlcNAc	β(1 → 4)
Heteroglycans		
Glycosaminoglycans	Disaccharides (amino sugars, sugar acids)	Various
Hyaluronic acid	GlcUA and GlcNAc	β(1 → 3), β(1 → 4)

[a]Polysaccharides are unbranched unless otherwise indicated.

[b]Glc, Glucose; GlcNAc, *N*-acetylglucosamine; GlcUA, D-glucuronate.

Structure and Roles of Some Polysaccharides

Table 7-2 Structures and Roles of Some Polysaccharides

Polymer	Type	Repeating unit	Size (number of monosaccharide units)	Roles/significance
Starch: Amylose	Homo-	(α1→4)Glc, linear	50-5,000	Energy storage: in plants
Starch: Amylopectin	Homo-	(α1→4)Glc, with (α1→6)Glc branches every 24-30 residues	Up to 10^6	Energy storage: in plants
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
Hyaluronan (a glycosaminoglycan)	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

P2 Clicker Question 23

The glycosaminoglycan hyaluronan:

A. is a homopolysaccharide.
B. consists of alternating residues of D-glucuronic acid and *N*-acetylglucosamine.
C. is covalently linked to specific proteins.
D. is a much shorter polymer than heparin.

Clicker Question 23, Response

The glycosaminoglycan hyaluronan:

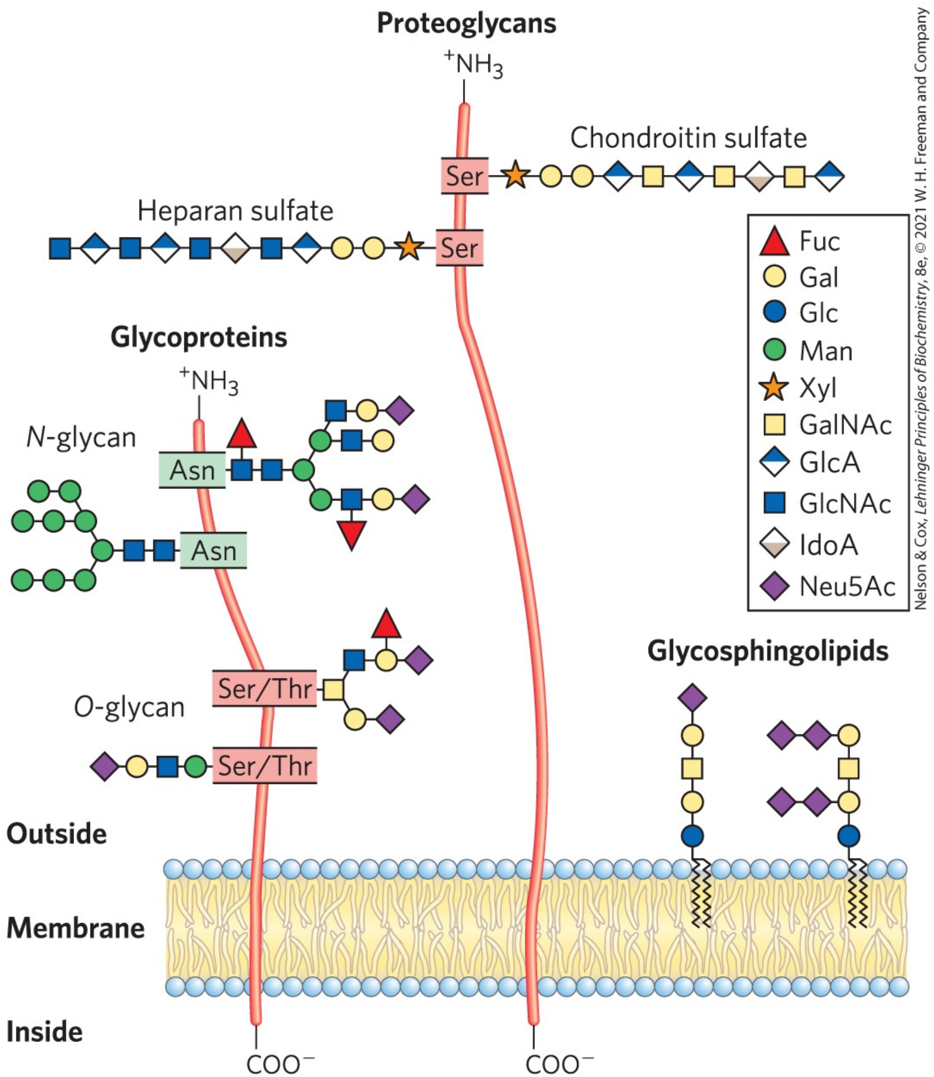
B. consists of alternating residues of D-glucuronic acid and *N*-acetylglucosamine.

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

7.3 Glycoconjugates: Proteoglycans, Glycoproteins, and Glycolipids

Glycoconjugate

- **glycoconjugate** = biologically active molecule consisting of an informational carbohydrate joined to a protein or lipid



Proteoglycans

- **proteoglycans** = macromolecules of the cell surface or ECM consisting of 1+ sulfated glycosaminoglycan chain(s) joined covalently to a membrane protein or secreted protein
  - major component of all extracellular matrices

*The difference between proteoglycans and glycoproteins

= Glycoproteins is a protein surrounded by sugars

= Proteoglycans is auger surrounded by protein

Glycoproteins

Produce in Golgi apparatus

- **glycoproteins** = have one or several oligosaccharides joined covalently to a protein
  - found on the outer face of the plasma membrane, in ECM, in blood, and in organelles (Golgi complexes, secretory granules, and lysosomes)
  - oligosaccharide portions are heterogenous and rich in information

Glycolipids and Glycosphingolipids

- **glycolipids** = plasma membrane components in which the hydrophilic head groups are oligosaccharides

- **glycosphingolipids** = class of glycolipids with specific backbone structure
  - neurons are rich in glycosphingolipids
  - play a role in signal transduction

* blood type depend on glycosphingolipids.

≡ in our red blood cells, there are lipids have suger groups.

- If we have enzyme that add galactose to lipid. Blood type B
- If we have enzyme that add N-acetylgalactoseamine to lipid. Blood type A
- If we have the 2 enzymes. Blood type AB
- If we don't have any of 2 enzymes. Blood type O

P2

Clicker Question 24

Which statement about glycoconjugates is false?

A. The glycosaminoglycan chain of the proteoglycan can bind to extracellular proteins through electrostatic interactions.
B. Glycolipids are found in specific organelles, such as Golgi complexes.
C. Glycosphingolipids play a role in signal transduction.
D. The oligosaccharide portions of glycoproteins are very heterogeneous.

Clicker Question 24, Response

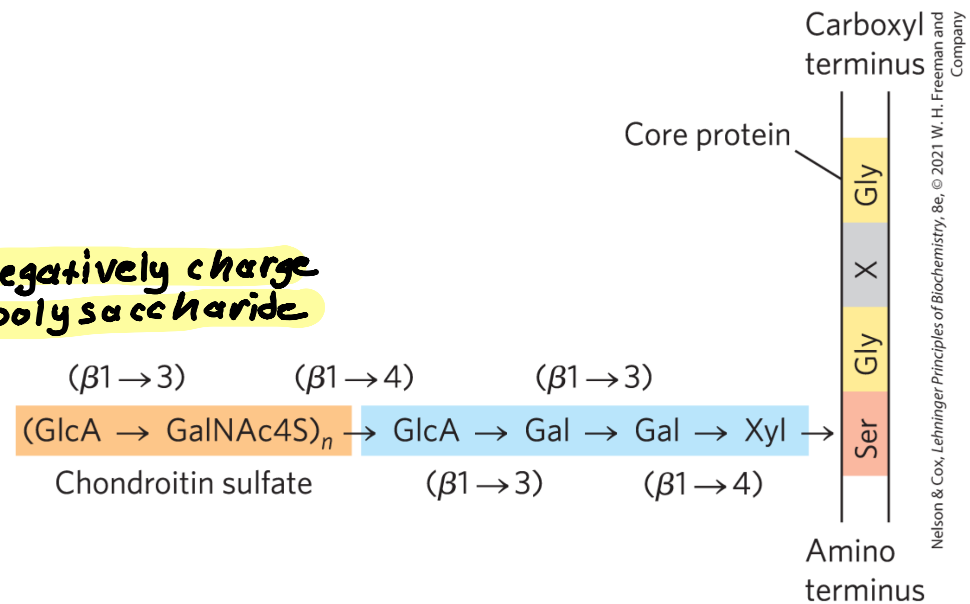
Which statement about glycoconjugates is false?

B. Glycolipids are found in specific organelles, such as Golgi complexes.

Inside cells, glycoproteins are found in specific organelles such as Golgi complexes (where the oligosaccharide moieties are added to the proteins), secretory granules, and lysosomes. Glycolipids are plasma membrane components in which the hydrophilic head groups are oligosaccharides.

Proteoglycans Are Glycosaminoglycan-Containing Macromolecules of the Cell Surface and Extracellular Matrix

- proteoglycan unit = "core protein" with covalently attached glycosaminoglycan(s) → negatively charge polysaccharide
- tetrasaccharide linker connects to glycosaminoglycan to a Ser residue of the protein

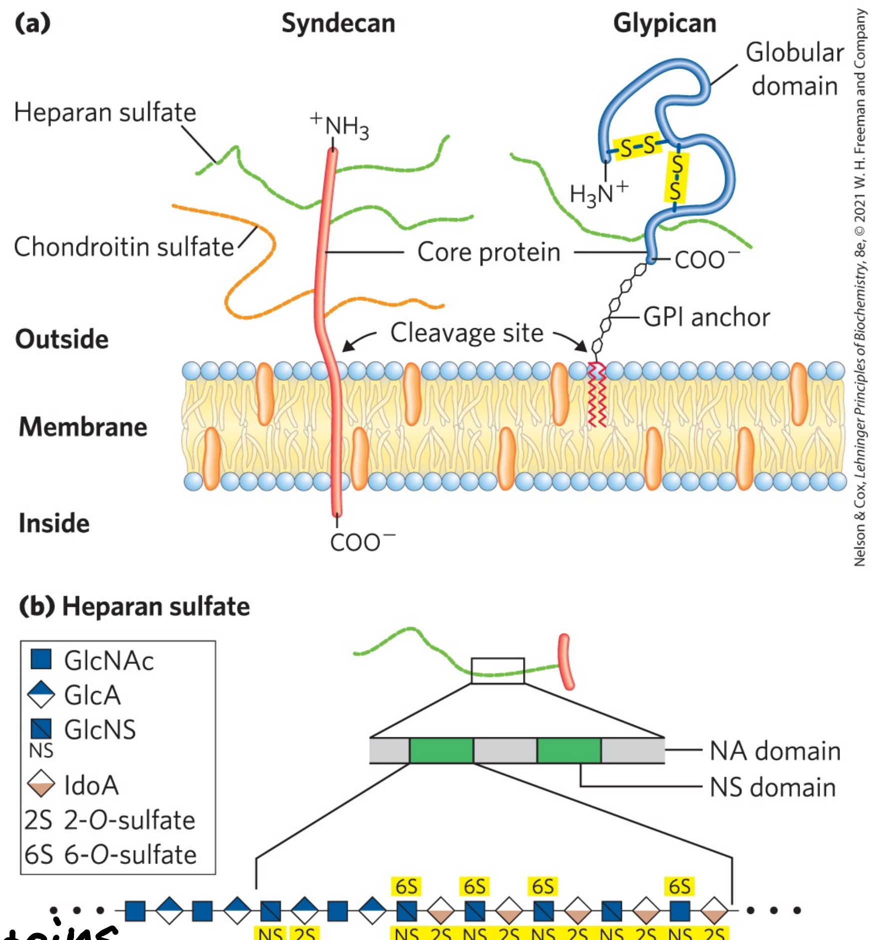


Two Families of Membrane Heparan Sulfate Proteoglycans

- **syndecans** = single transmembrane domain and an extracellular domain bearing 3–5 chains of heparan sulfate and chondroitin sulfate

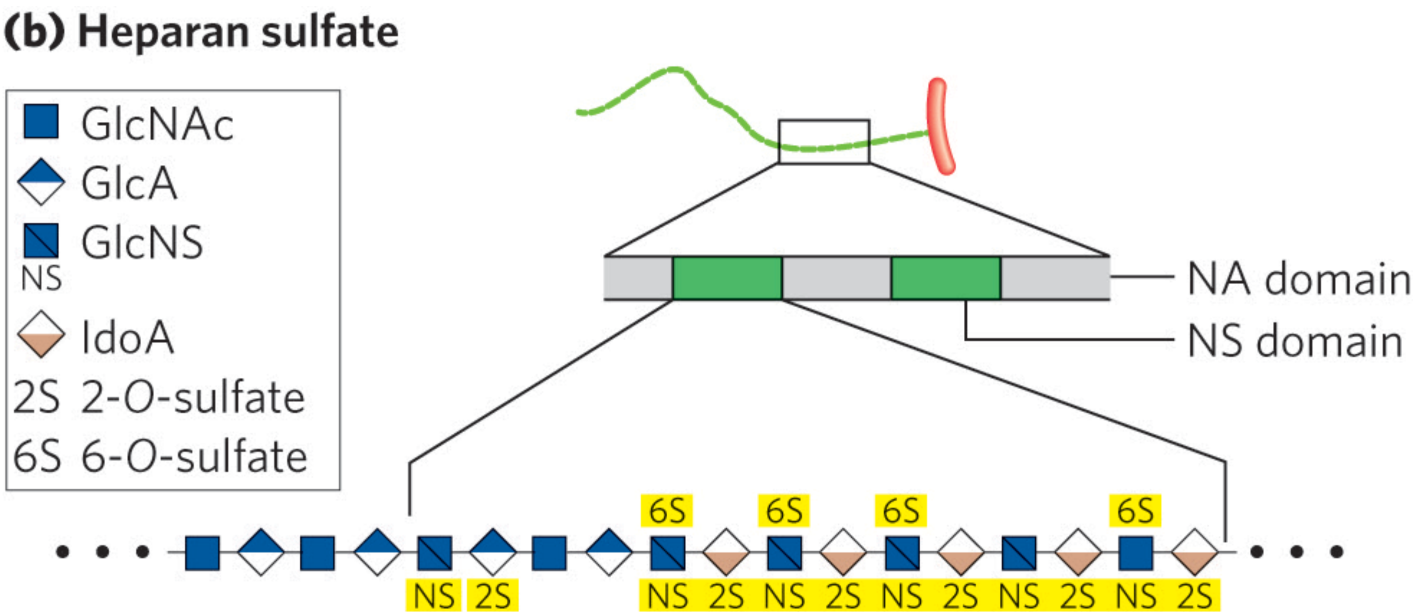
- **glycipans** = attached to the membrane by a GPI anchor (a *g*lycosylated derivative of the membrane lipid *p*hosphatidyl*i*nositol)

bond between glycolipids and glycoproteins.



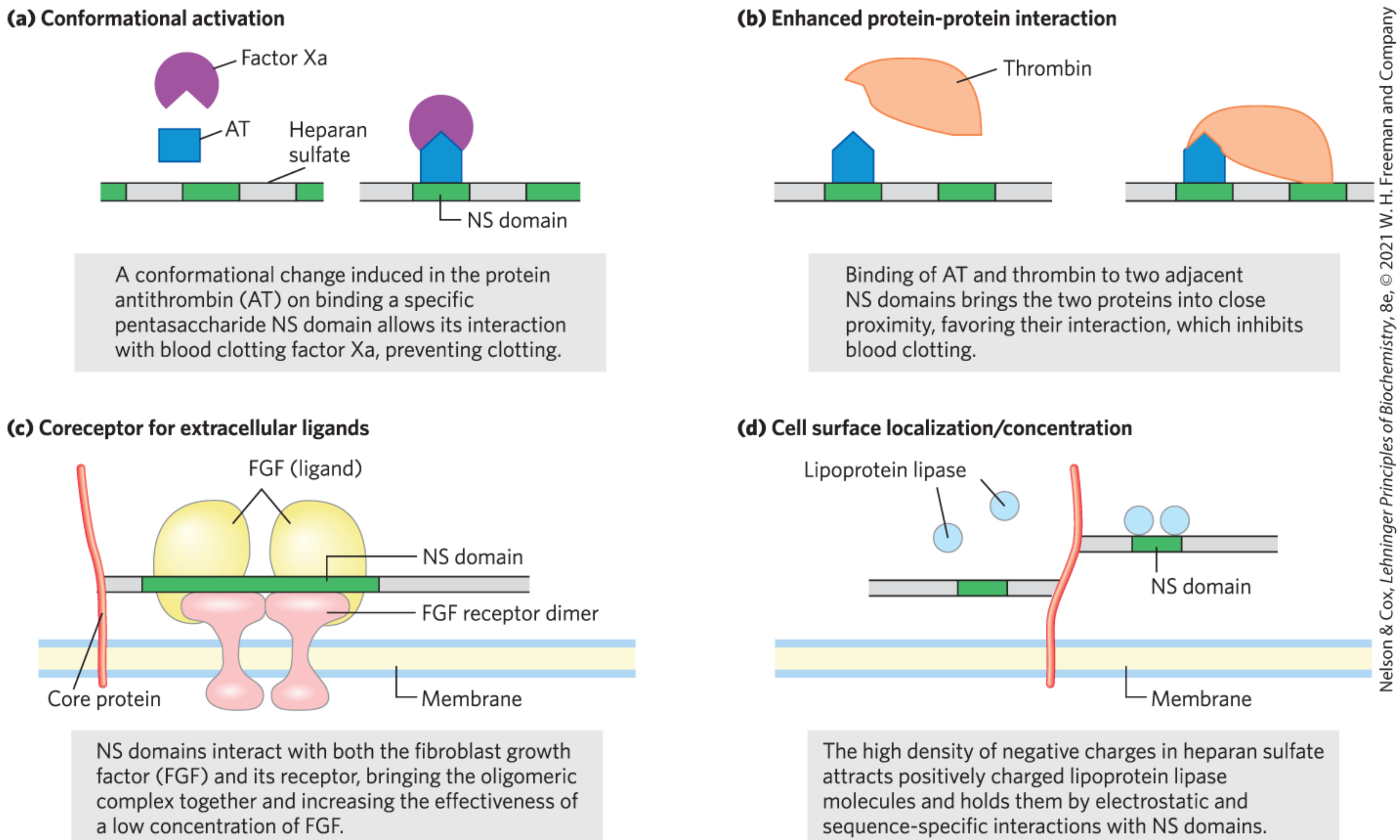
NS Domains

- NS domains = highly sulfated domains that alternate with domains having unmodified GlcNAc and GlcA residues



Nelson & Cox, *Lehninger Principles of Biochemistry*, 8e, © 2021 W. H. Freeman and Company

Four Types of Protein Interactions with NS Domains of Heparan Sulfate



P2

Clicker Question 25

Which statement about proteoglycans is false?

A. They contain protein.
B. They can affect ligand-receptor interactions.
C. They are always extracellular.
D. They contain glycosaminoglycans.

Clicker Question 25, Response

Which statement about proteoglycans is false?

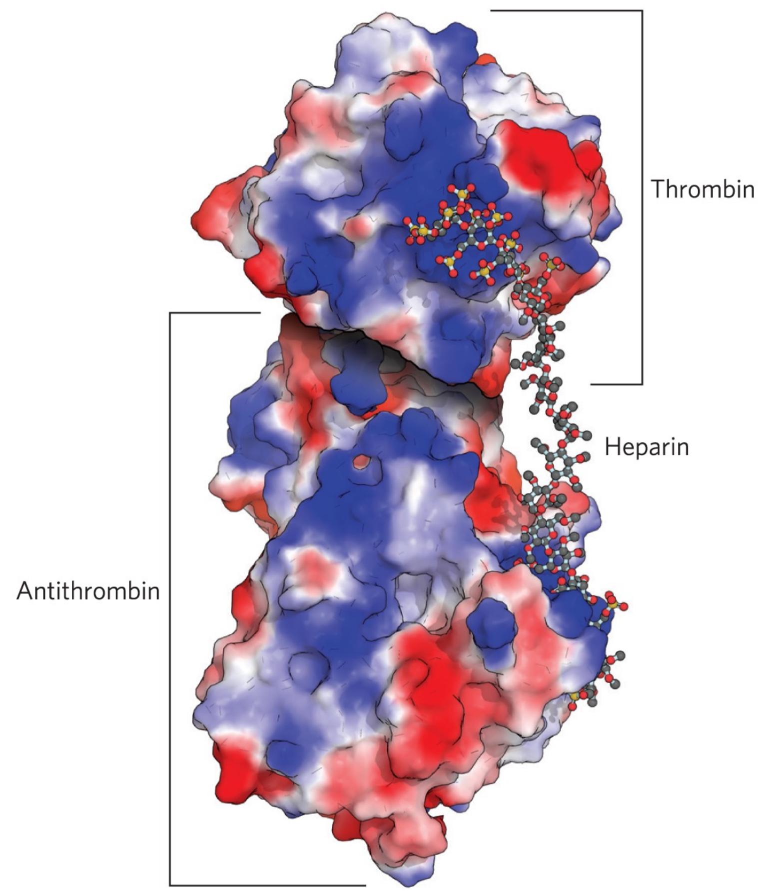
C. They are always extracellular.

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

Heparan Sulfate Enhancement of the Binding of Thrombin to Antithrombin

- antithrombin binds to and inhibits the protease thrombin only in the presence of heparan sulfate

- both proteins are rich in Arg and Lys residues
  - interact electrostatically with the sulfates of the glycosaminoglycans

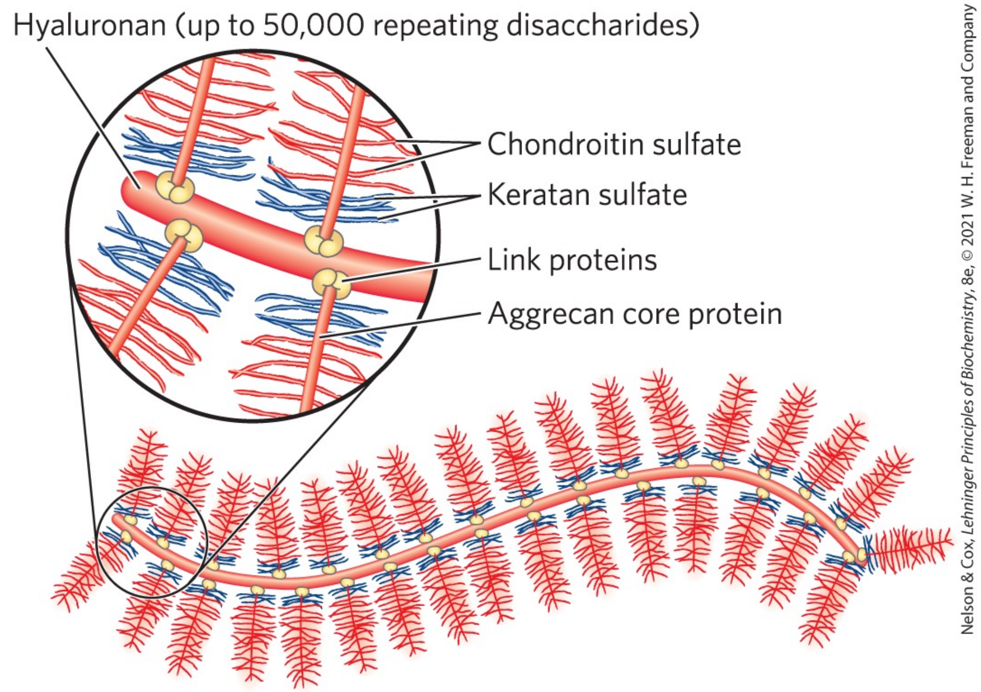


Positively charged regions

Proteoglycan Aggregates

- **proteoglycan aggregates** = supramolecular assemblies of many core proteins all bound to a single molecule of hyaluronan

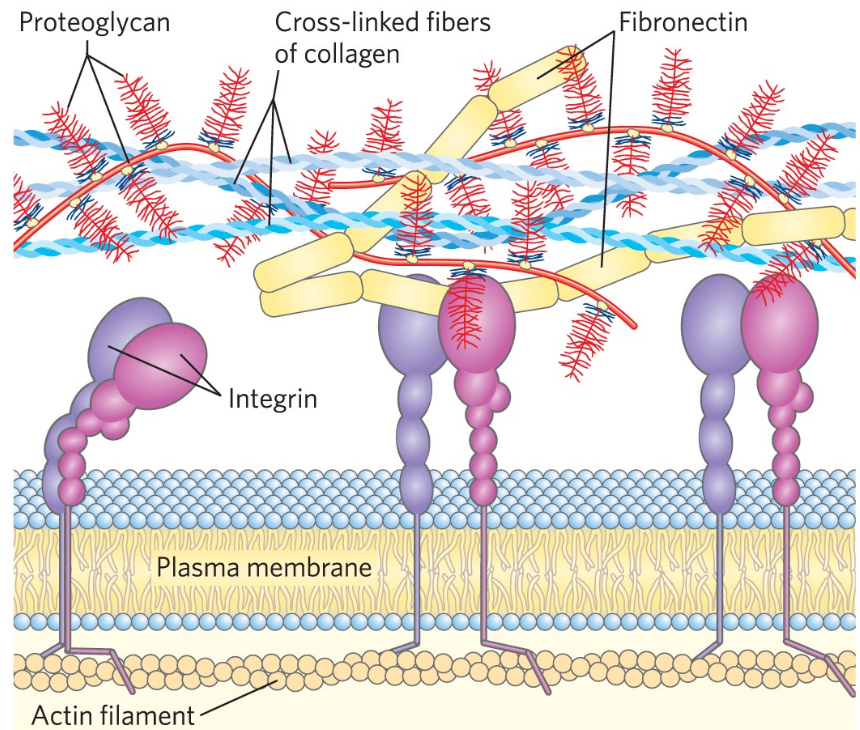
- aggrecan interacts strongly with collagen in the ECM of cartilage



Fibronectin and Integrins

→ link protein

- **fibronectin** = has separate domains to bind fibrin, heparan sulfate, and collagen
  - contain the conserved RGD sequence (Arg–Gly–Asp) to bind **integrins**



- **integrins** = mediate signaling between cell interior and ECM molecules

P7

Principle 7

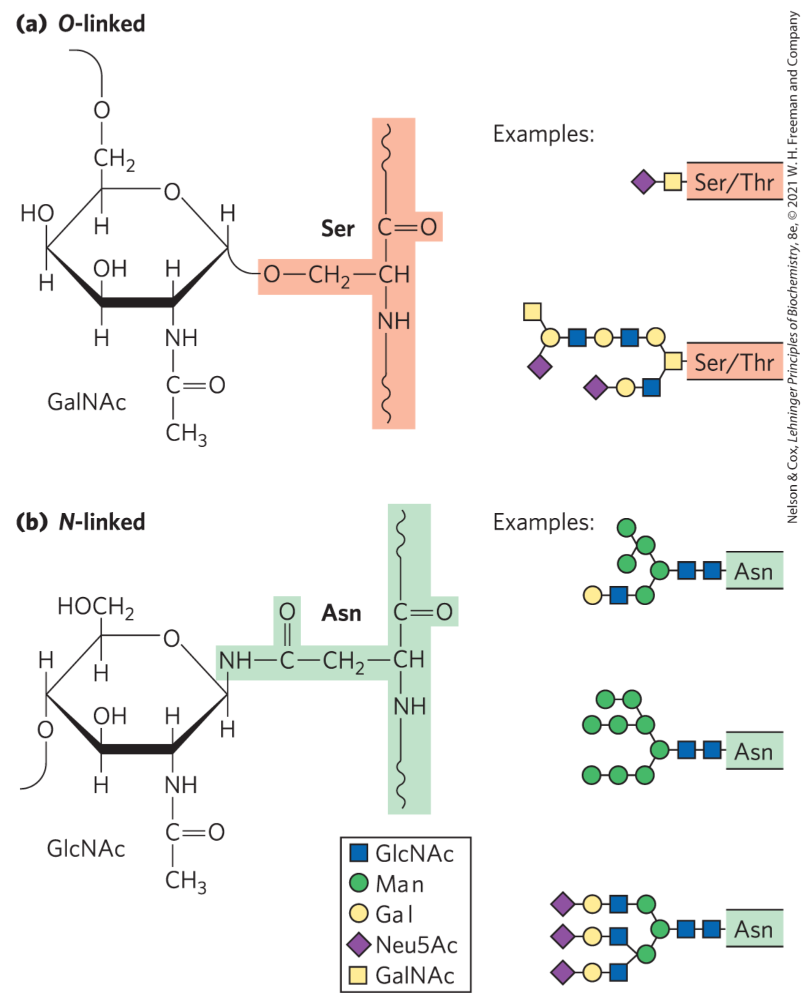
An almost infinite variety of discrete structures can be built from a small number of monomeric subunits. Even short polymers, when arranged in different sequences, joined through different linkages, and branched to specific degrees, present unique faces recognized by their molecular partners.

Purpose of Interactions between Cells and the ECM

- interactions between cells and the ECM:
  - anchor cells to the ECM, providing the strength and elasticity of skin and joints الهجرة
  - provide paths that direct the migration of cells in developing tissue
  - convey information in both directions across the plasma membrane

Glycoproteins Have Covalently Attached Oligosaccharides

- two types of attachments:
  - *O*-linked = a glycoside bond joins the anomeric carbon of a carbohydrate to the —OH of a Ser or Thr residue
  - *N*-linked = an ***N*-glycosyl bond** joins the anomeric carbon of a sugar to the amide nitrogen of an Asn residue



P2 Clicker Question 26

A laboratory is studying the binding properties of a glycoprotein on the plasma membrane. What amino acids should they analyze for the presence of branched heteropolysaccharides?

A. Ser, Thr, and Tyr
B. Ser, Thr, and Asn
C. Trp, Tyr, and Phe
D. Lys, His, and Arg

Clicker Question 26, Response

A laboratory is studying the binding properties of a glycoprotein on the plasma membrane. What amino acids should they analyze for the presence of branched heteropolysaccharides?

B. Ser, Thr, and Asn

Glycoproteins are carbohydrate-protein conjugates. The carbohydrate is attached at its anomeric carbon through a glycosidic link to the —OH of a Ser or Thr residue (*O*-linked), or through an *N*-glycosyl link to the amide nitrogen of an Asn residue (*N*-linked).

Examples of Glycoproteins

- **mucins** = secreted or membrane glycoproteins
  - can contain large numbers of *O*-linked oligosaccharide chains
  - present in most secretions

- proteins of the blood
  - examples: immunoglobulins (antibodies), follicle-stimulating hormone, luteinizing hormone, and thyroid-stimulating hormone

- milk proteins
  - example: major whey protein *α*-lactalbumin

The Biological Advantages of Adding Oligosaccharides to Proteins

- covalently attached oligosaccharides:
  - influence the folding and stability of the proteins
  - provide critical information about the targeting of newly synthesized proteins
  - allow specific recognition by other proteins

P2 Clicker Question 27

Glycoproteins:

A. contain unbranched oligosaccharides.
B. are sometimes intracellular.
C. have oligosaccharides covalently attached to aspartate residues.
D. are a small fraction of the total number of proteins in a human cell.

Clicker Question 27, Response

Glycoproteins:

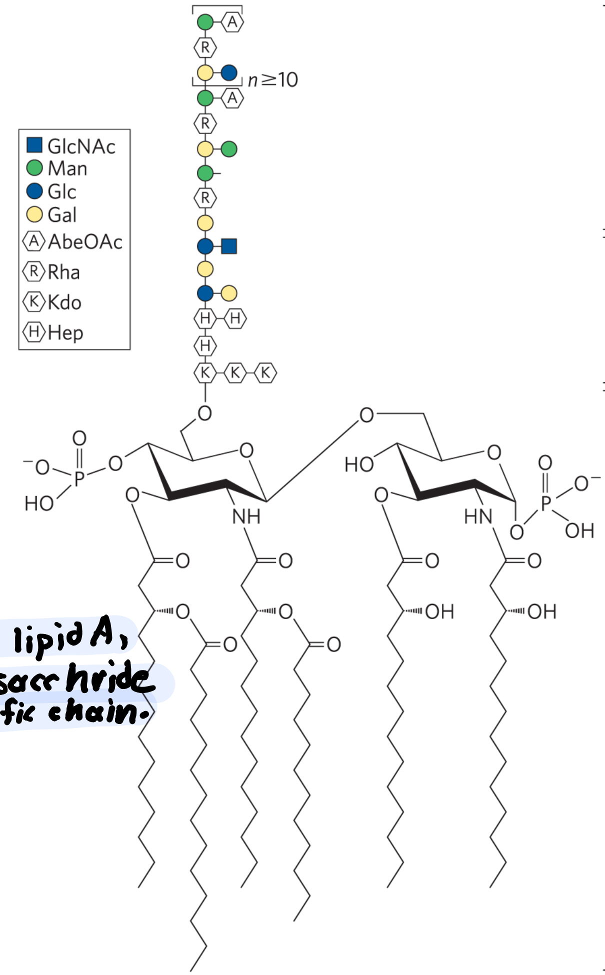
B. are sometimes intracellular.

Many of the proteins secreted by eukaryotic cells are glycoproteins, including most of the proteins of blood. Some of the proteins secreted by the pancreas are glycosylated, as are most of the proteins contained in lysosomes.

Glycolipids and Lipopolysaccharides Are Membrane Components

- **gangliosides** = membrane lipids of eukaryotic cells in which the polar head group is a complex oligosaccharide containing a sialic acid and other monosaccharide residues

- **lipopolysaccharides** = composed of lipid A, core of oligosaccharide, and O-specific chain. dominant surface feature of the outer membrane of gram-negative bacteria



P2 Clicker Question 28

Which of these is NOT a glycoconjugate?

A. trehalose
B. syndecan
C. glypican
D. glycosphingolipid

Clicker Question 28, Response

Which of these is NOT a glycoconjugate?

A. trehalose

A glycoconjugate is a biologically active molecule in which an informational carbohydrate is covalently joined to a protein or a lipid. Trehalose is a disaccharide of glucose.

P2 Clicker Question 29

Oligosaccharides are:

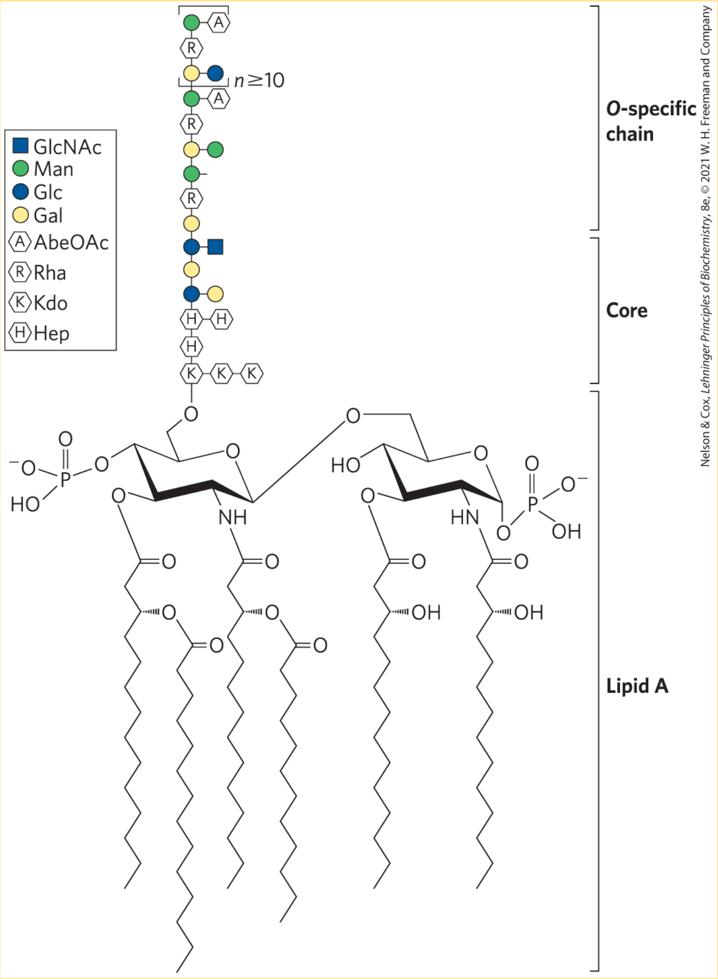
A. never found in mucins.
B. classified as a *N*- or *O*-linked when found in gangliosides.
C. found in bacterial lipopolysaccharides.
D. never attached to hormones.

Clicker Question 29, Response

Oligosaccharides are:

C. found in bacterial lipopolysaccharides.

The lipopolysaccharides of *S. typhimurium* contain six fatty acids bound to two glucosamine residues, one of which is the point of attachment for a complex oligosaccharide. *E. coli* has similar but unique lipopolysaccharides.



7.4 Carbohydrates as Informational Molecules: The Sugar Code

P6

Principle 6

Molecular complementarity is central to function. The recognition of oligosaccharides by sugar-binding proteins (lectins) results from a perfect fit between lectin and ligand.

The Challenge of Glycobiology

- glycobiology = the study of the structure and function of glycoconjugates

- the challenge is to understand how cells use specific oligosaccharides to encode information about:
  - intracellular targeting of proteins
  - cell-cell interactions
  - cell differentiation and tissue development
  - extracellular signals

Oligosaccharide Structures Are Information-Dense

- branched structures, not found in nucleic acids or proteins, are common in oligosaccharides

- almost limitless variety of oligosaccharides due to differences in:
  - stereochemistry and position of glycosidic bonds
  - type and orientation of substituent groups
  - the number and type of branches

Lectins Are Proteins That Read the Sugar Code and Mediate Many Biological Processes

- **lectins** = bind carbohydrates with high specificity and with moderate to high affinity

- functions:
  - cell-cell recognition
  - signaling
  - adhesion
  - intracellular targeting of newly synthesized proteins

Selectins

- **selectins** = family of plasma membrane lectins that mediate cell-cell recognition and adhesion in a wide range of cellular processes
  - move immune cells through the capillary wall
  - mediate inflammatory responses
  - mediate the rejection of transplanted organs

الرفض

P5 Clicker Question 30

Which statement about selectins is false?

A. They mediate cell-cell recognition.
B. They are involved in the movement of immune system cells.
C. They can be involved in the process rejection of transplanted organs.
D. They are intracellular.

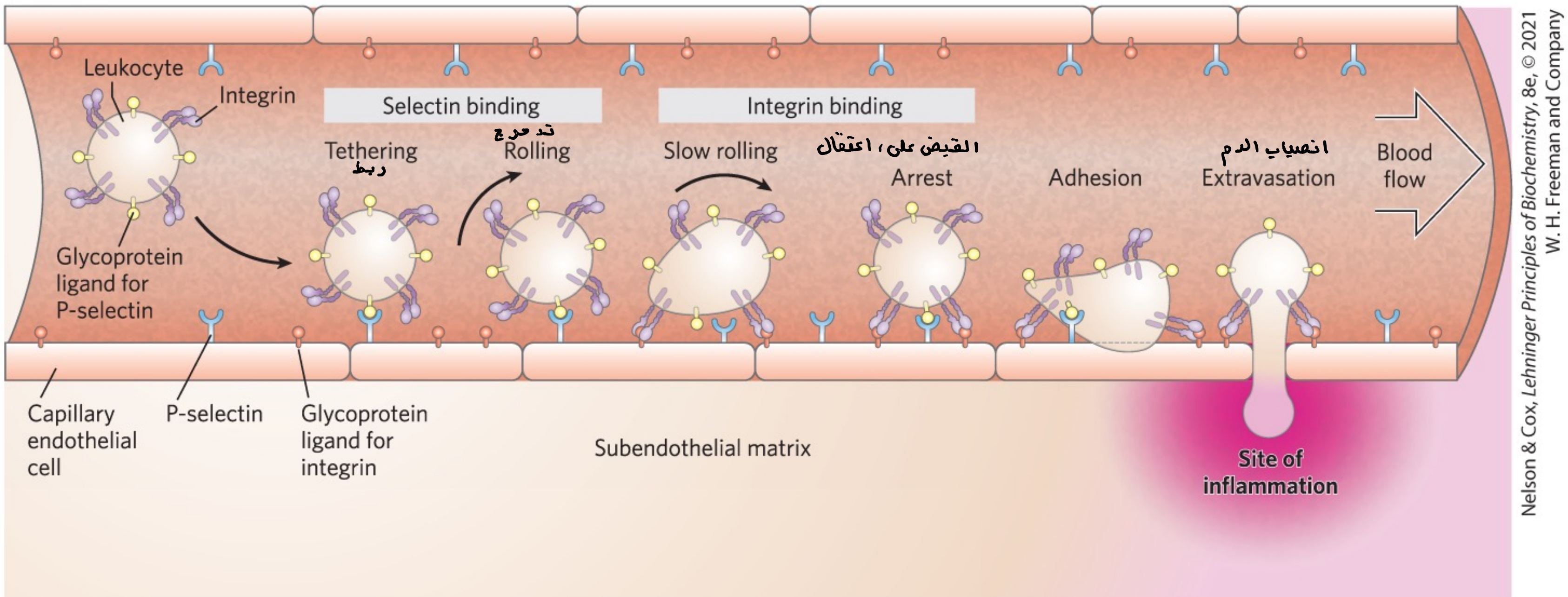
Clicker Question 30, Response

Which statement about selectins is false?

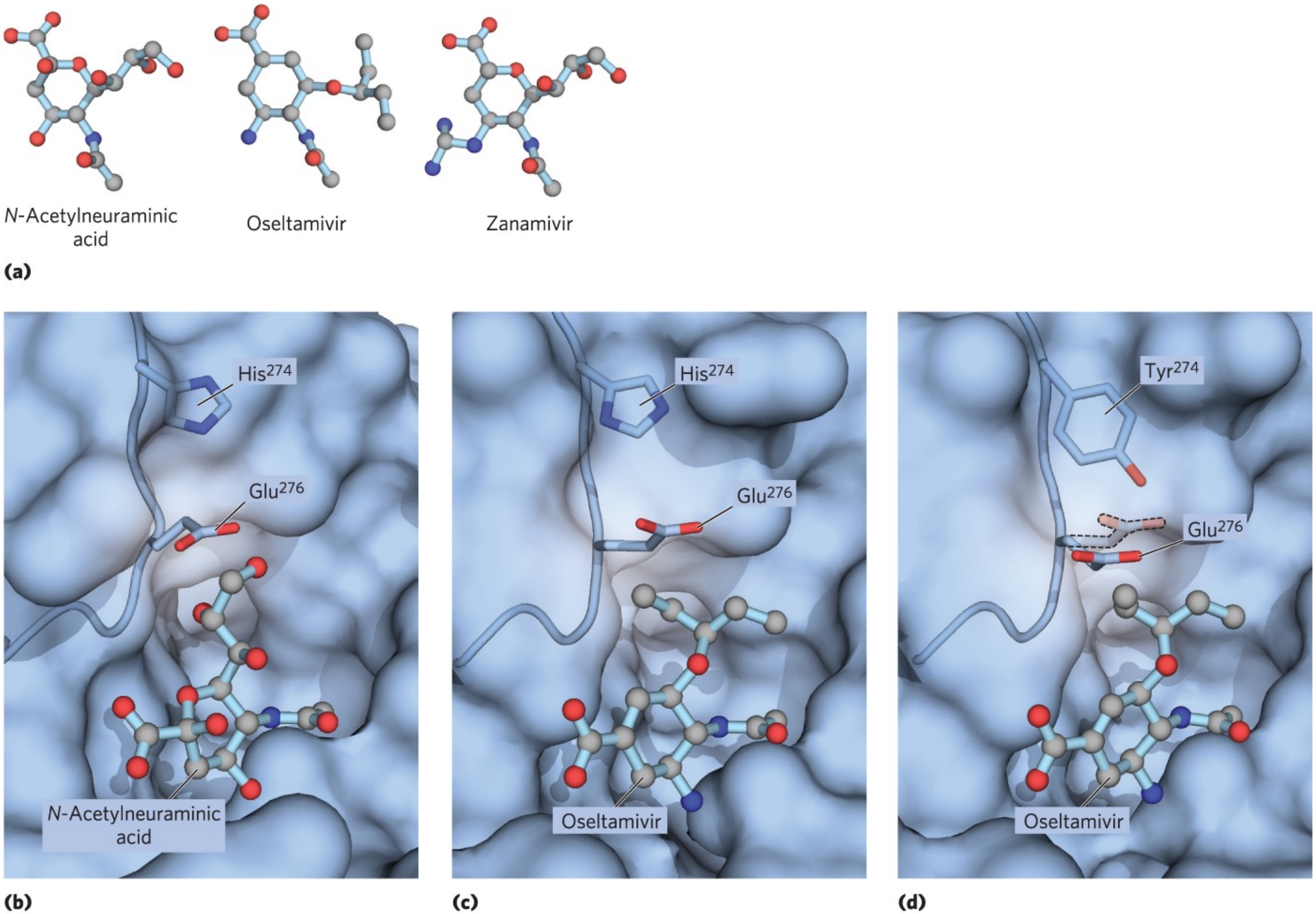
D. They are intracellular.

Selectins are a family of plasma membrane lectins that mediate cell-cell recognition and adhesion in a wide range of cellular processes.

Role of Lectin-Ligand Interactions in Leukocyte Movement



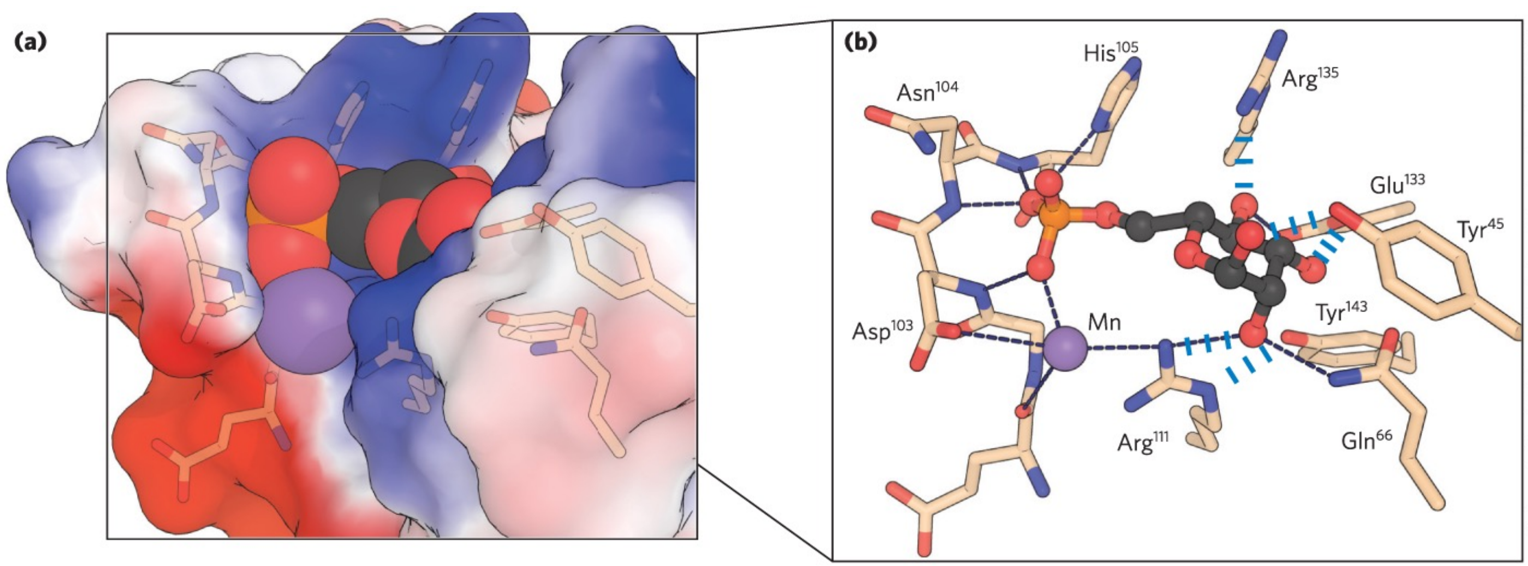
Binding Site on Influenza Neuraminidase



Lectin-Carbohydrate Interactions Are Highly Specific and Often Multivalent

دقيق

- subtle molecular complementarity allows interaction only with the lectin's correct carbohydrate binding partners

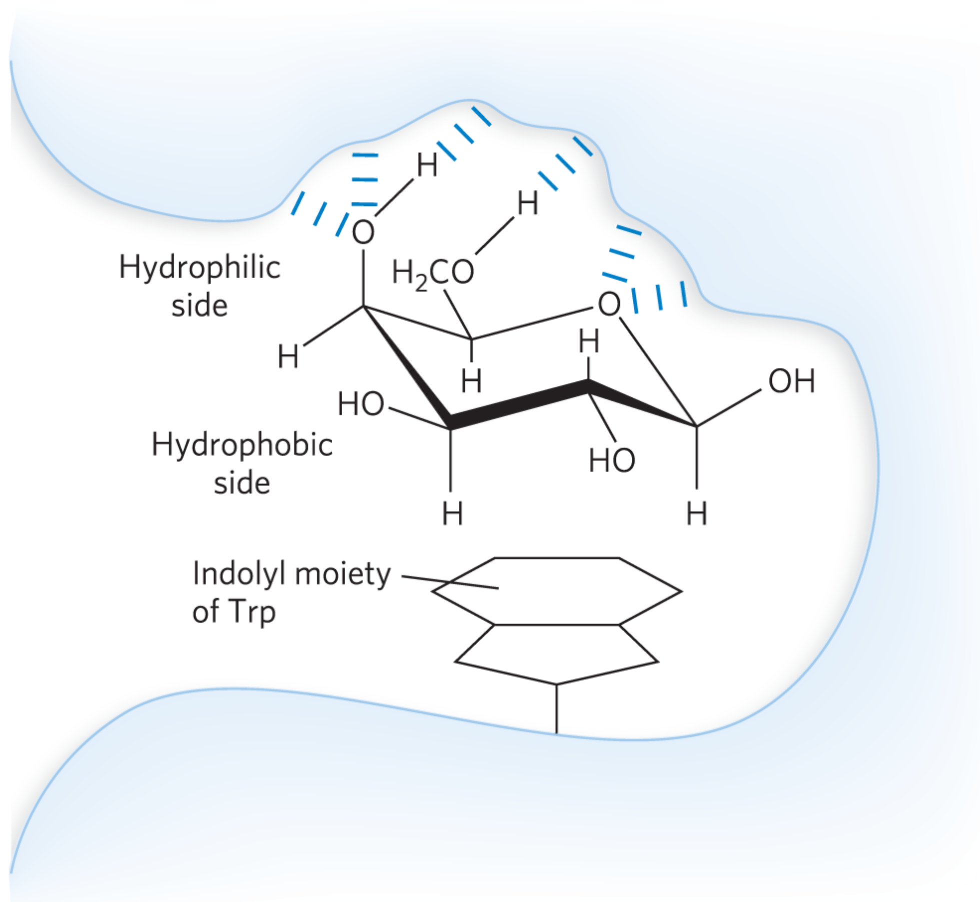


Lectin Multivalency

- lectin multivalency = single lectin molecule has multiple carbohydrate binding domains
  - increases effective affinity

Interactions of Sugar Residues Due to the Hydrophobic Effect

- many sugars have a more polar side and a less polar side



P5

Clicker Question 31

Lectins:

A. often bind their ligands via multiple weak interactions.
B. bind their ligands with relatively low specificity.
C. prevent viruses from binding to their target cells.
D. are carbohydrates that bind to receptor proteins.

Clicker Question 31, Response

Lectins:

A. often bind their ligands via multiple weak interactions.

Many sugars have a more polar side and a less polar side; the more polar side hydrogen-bonds with the lectin, while the less polar side undergoes interactions with nonpolar amino acid residues through the hydrophobic effect. The sum of all these interactions produces high-affinity binding and high specificity of lectins for their carbohydrate ligands.

Biological Interactions Mediated by the Sugar Code