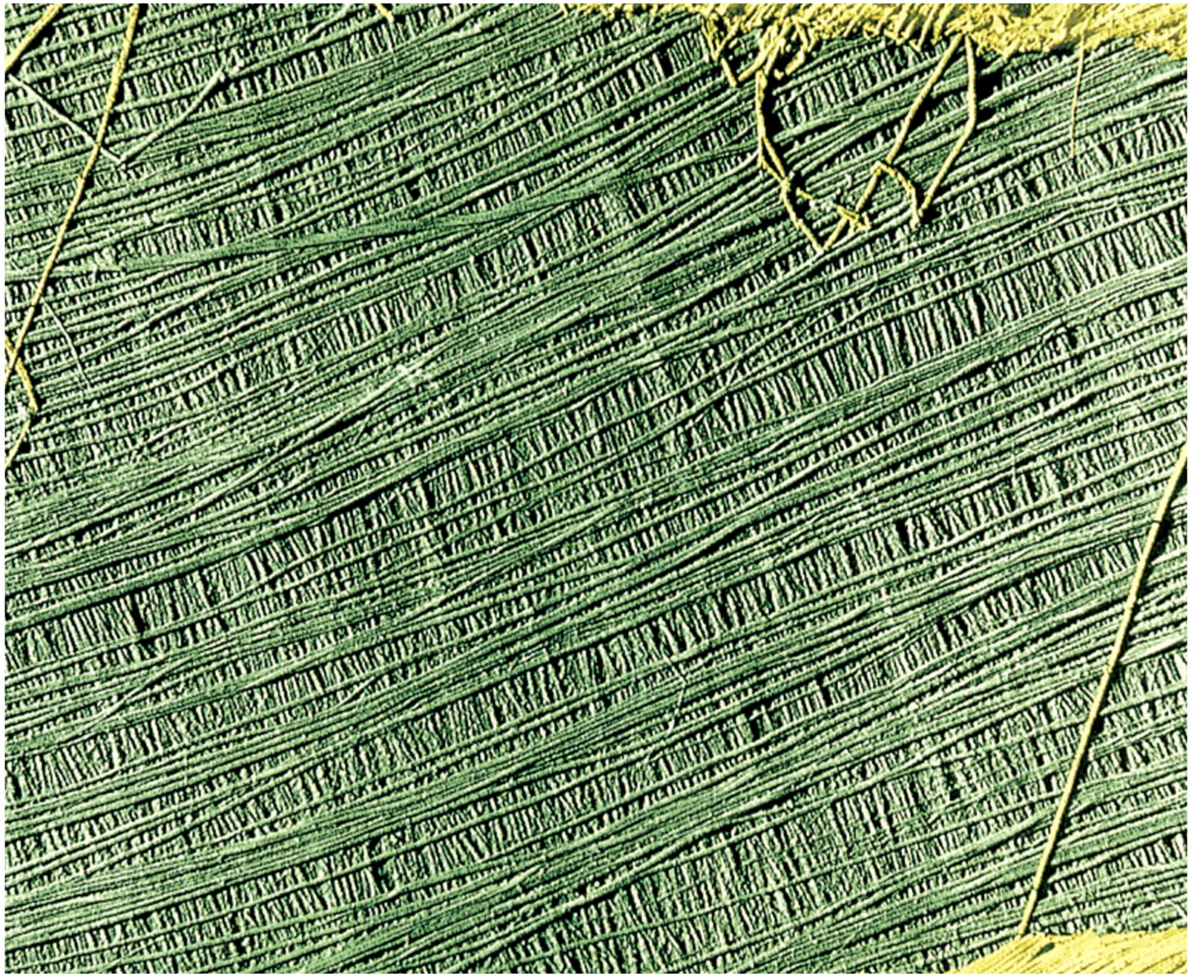
Carbohydrates

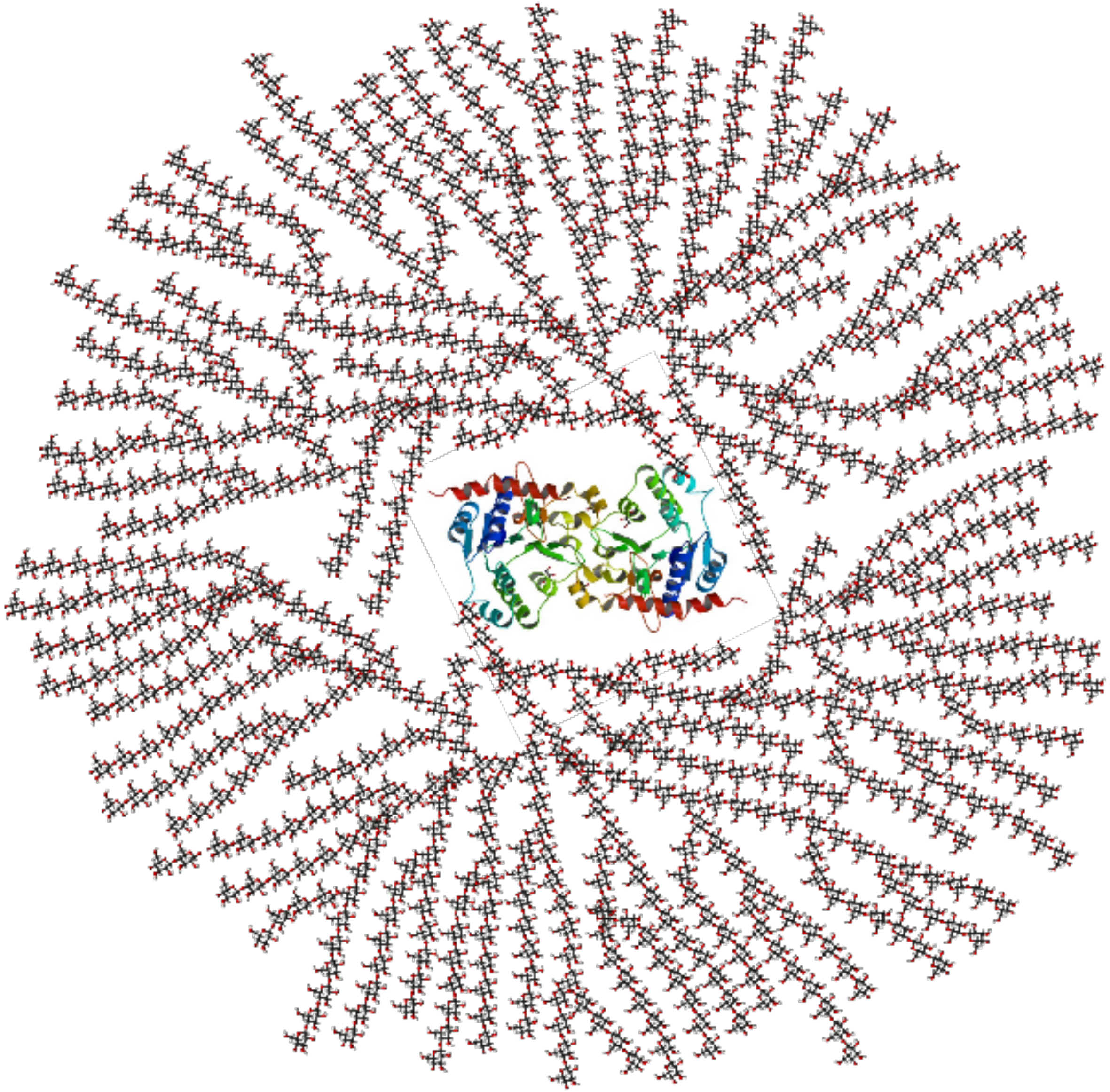
Prof. F. Malatesta

cellulose fibers in the
cell wall of a plant cell

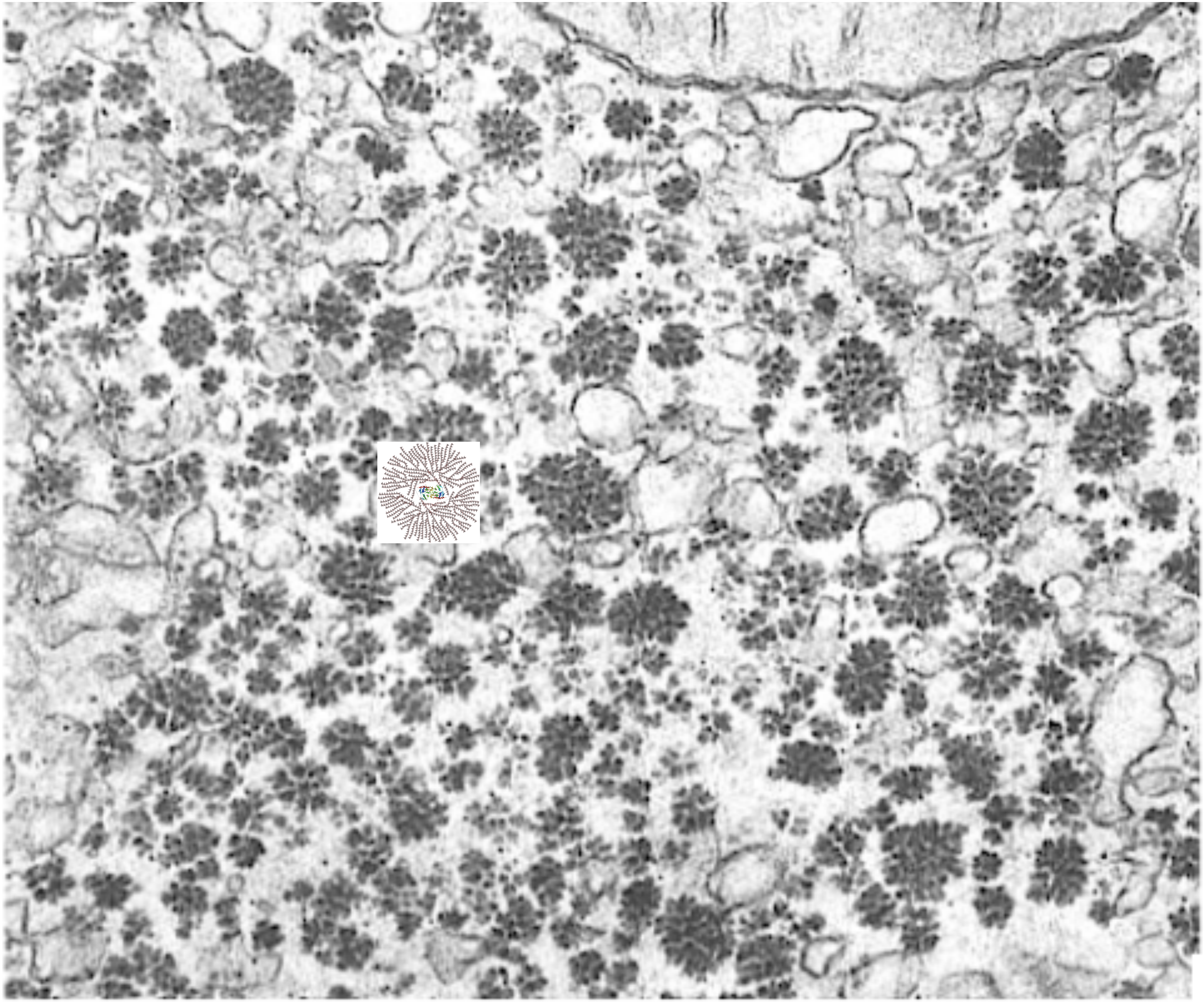


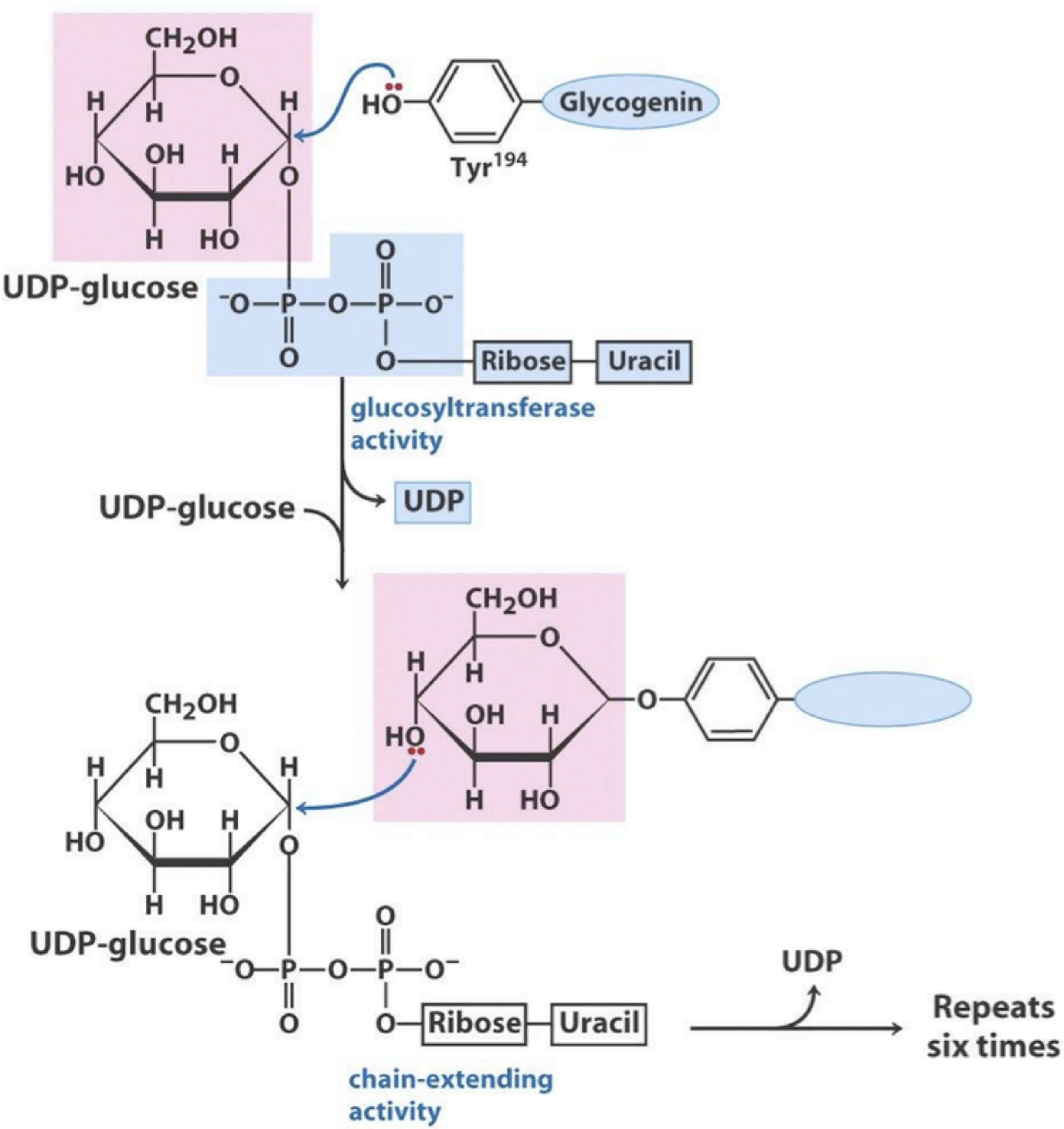
cotton

The glycogen-glycogenin complex



Glycogenin is a protein that functions as a primer for the *ex-novo* synthesis of a glycogen molecule.





UDP-glucose
Glycogenin
Tyr194
Ribose
Uracil
glucosyltransferase activity
UDP-glucose
UDP
UDP-glucose
Ribose
Uracil
UDP
Repeats six times
chain-extending activity

The multiple functions of carbohydrates

Primarily synthesized by photosynthesis: chlorophylls and other photosynthetic pigments absorb energy, produce ATP and NADPH, used to reduce CO_2 to form triose phosphate, starch and sucrose, etc..

$$6\ CO_2 + 6\ H_2O + \text{light} \rightarrow C_6H_{12}O_6 + 6\ O_2.$$

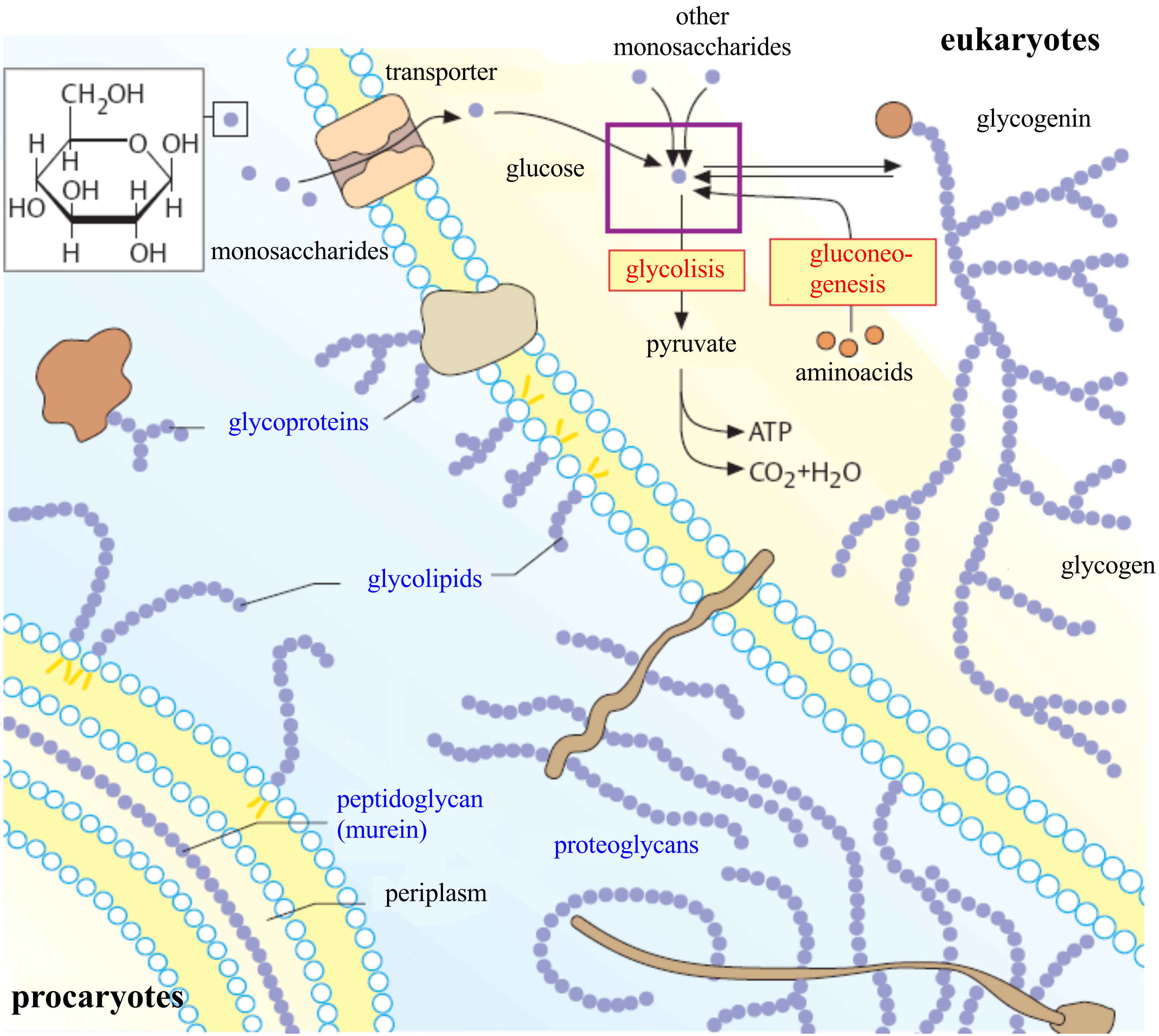
Major source of energy

Structural function

Nucleic acids components

Involved in the signal transduction pathways among cells

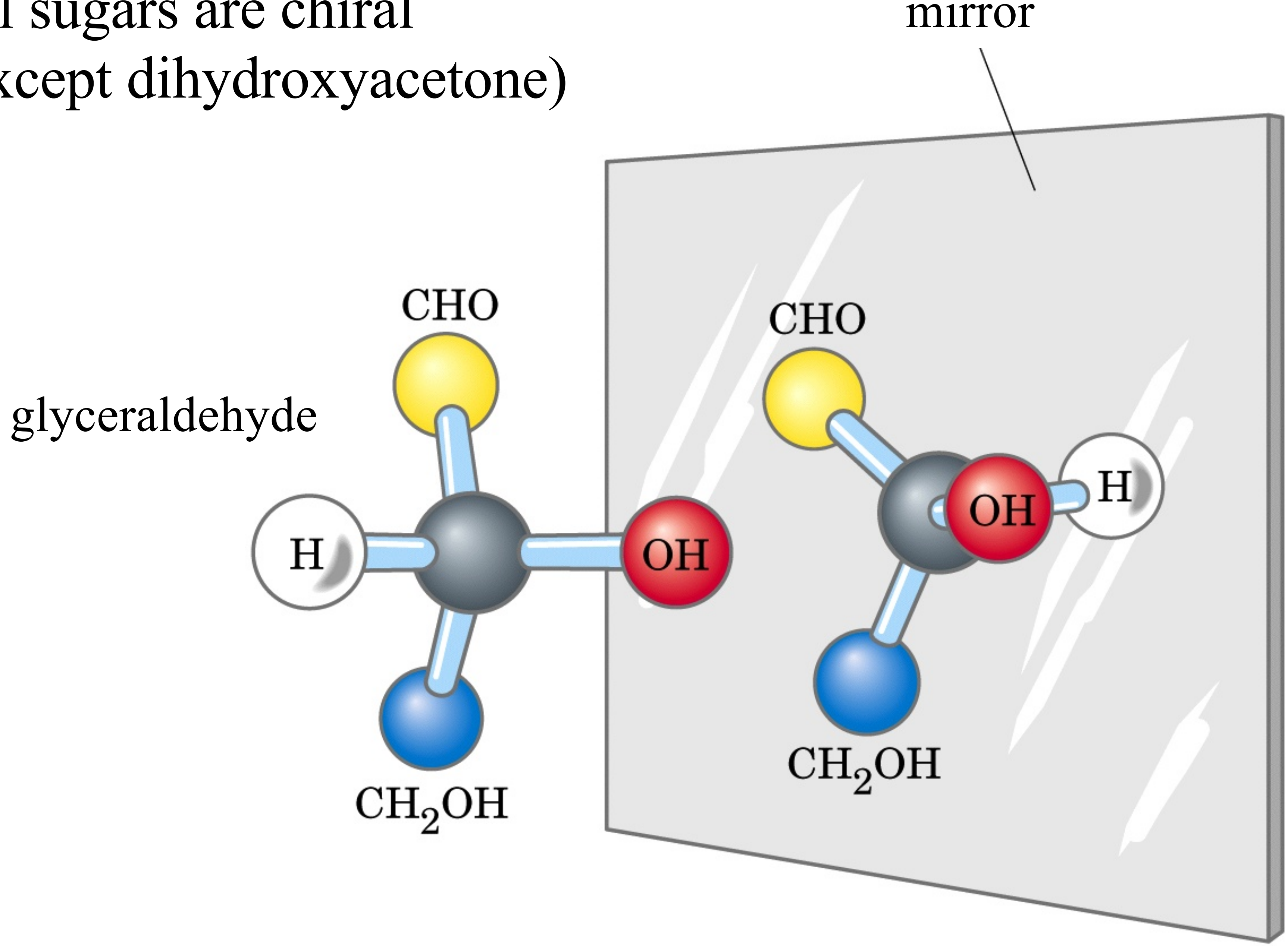
The multiple functions of carbohydrates



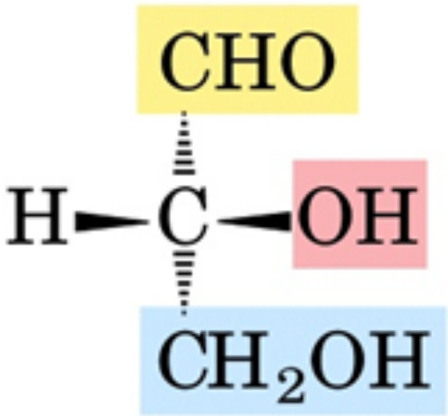
Sugars

- synonymes: carbohydrates & saccharides
- chemically: poly-oxyaldehydes or poly-oxyketones
- monosaccharides: they are not broken down into simpler compounds by hydrolysis (aldoses and ketoses)
- polysaccharides: polymers of monosaccharides
- constitutional formula $(CH_2O)_n$ $n \geq 3$
- are chiral molecules
- role: energetic, structural, genetic, signal transduction

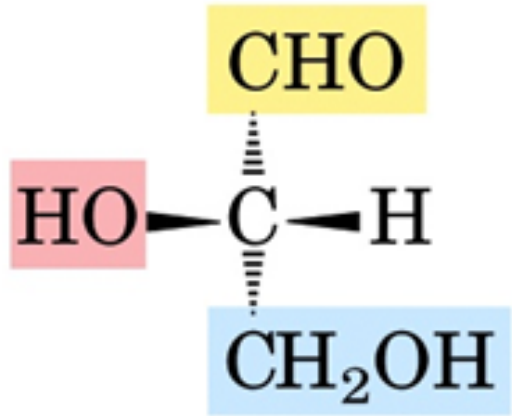
All sugars are chiral (except dihydroxyacetone)



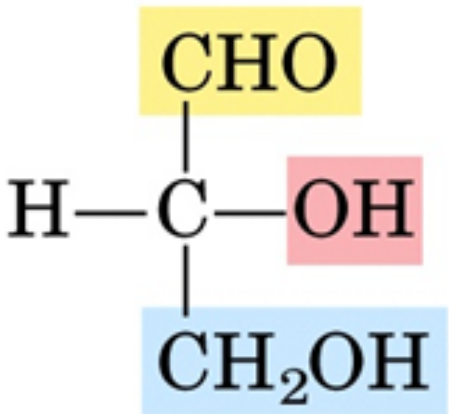
Fischer projections

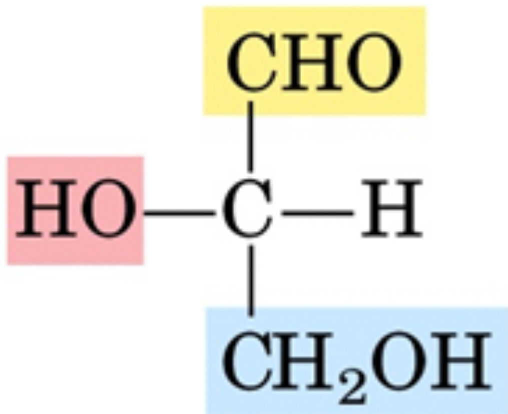


D-glyceraldehyde



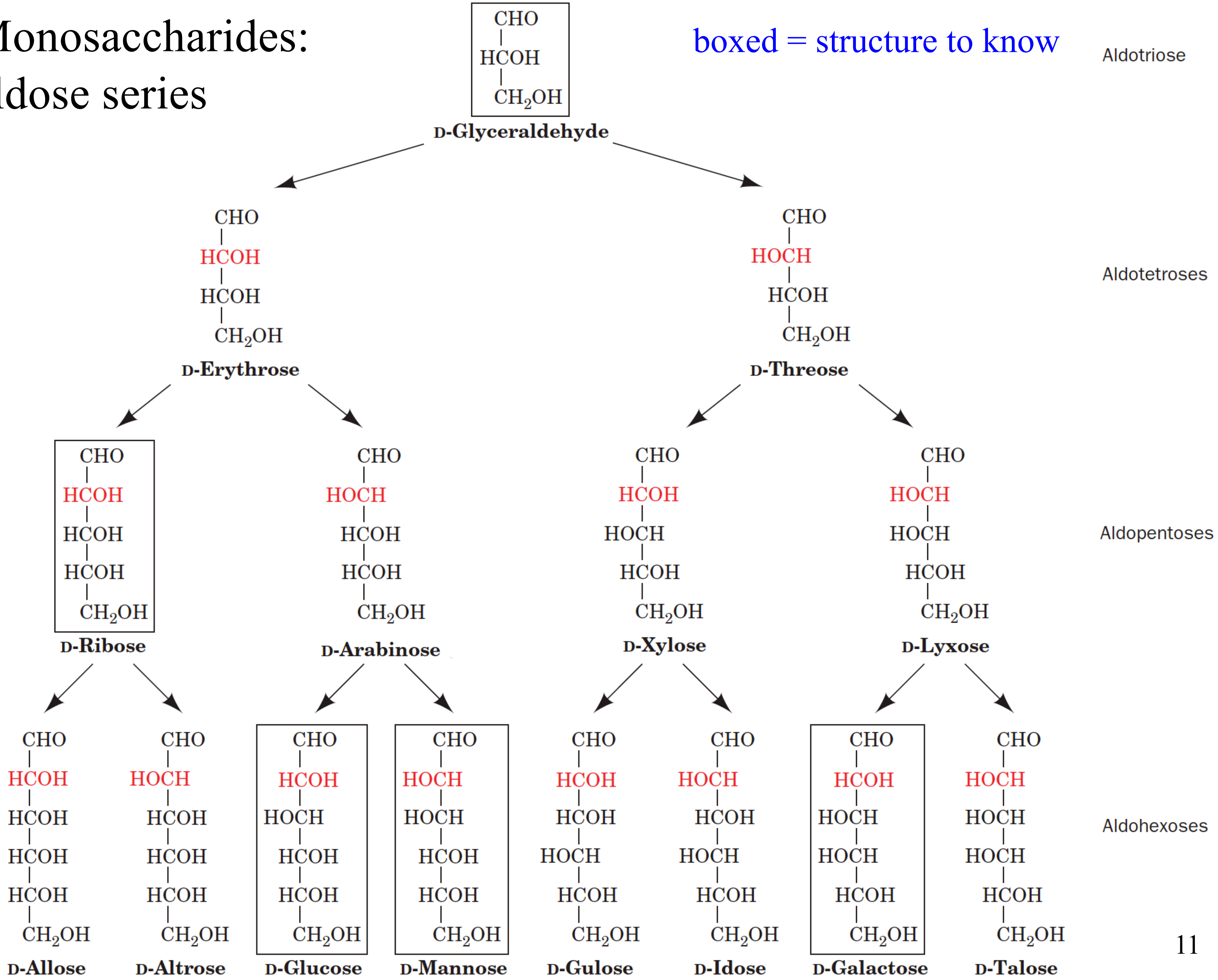
L-glyceraldehyde



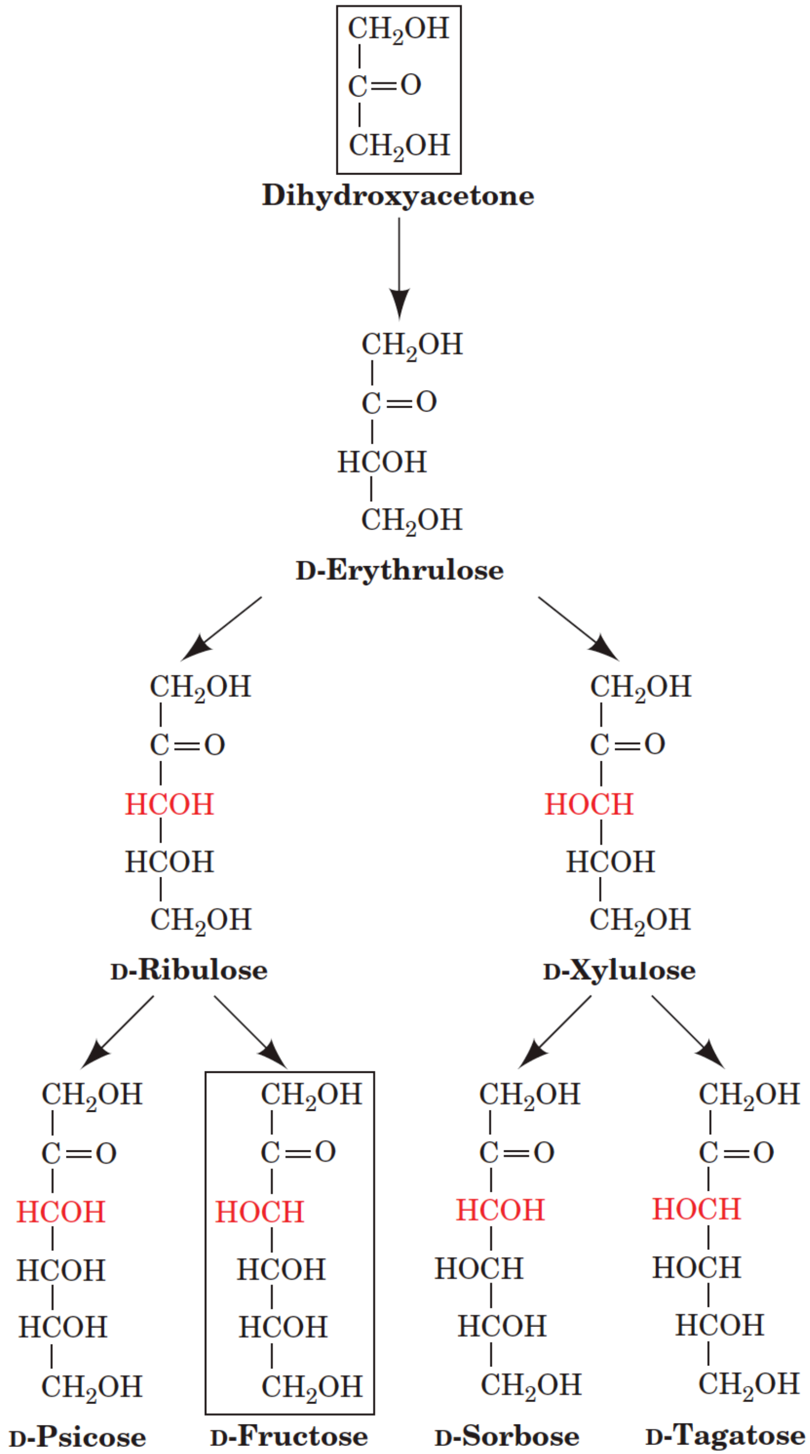


Monosaccharides: aldose series

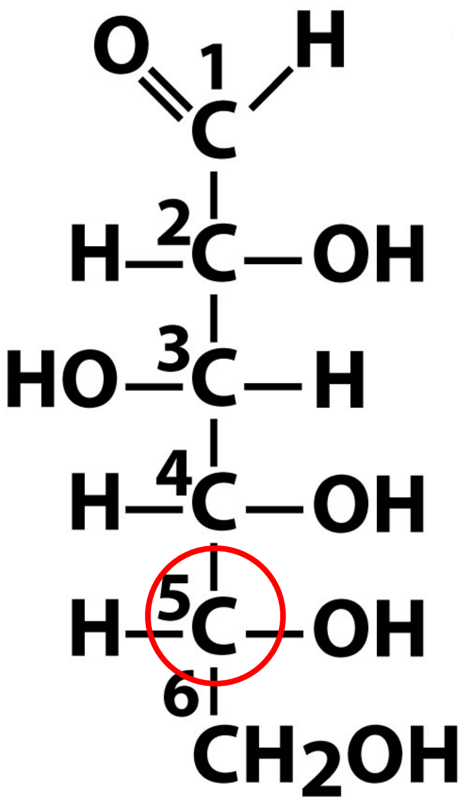
boxed = structure to know



Monosaccharides:
ketose series

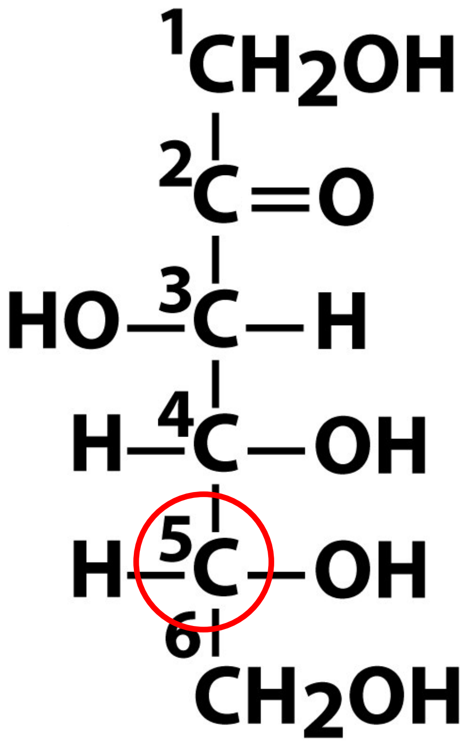


an aldohexose



D-glucose

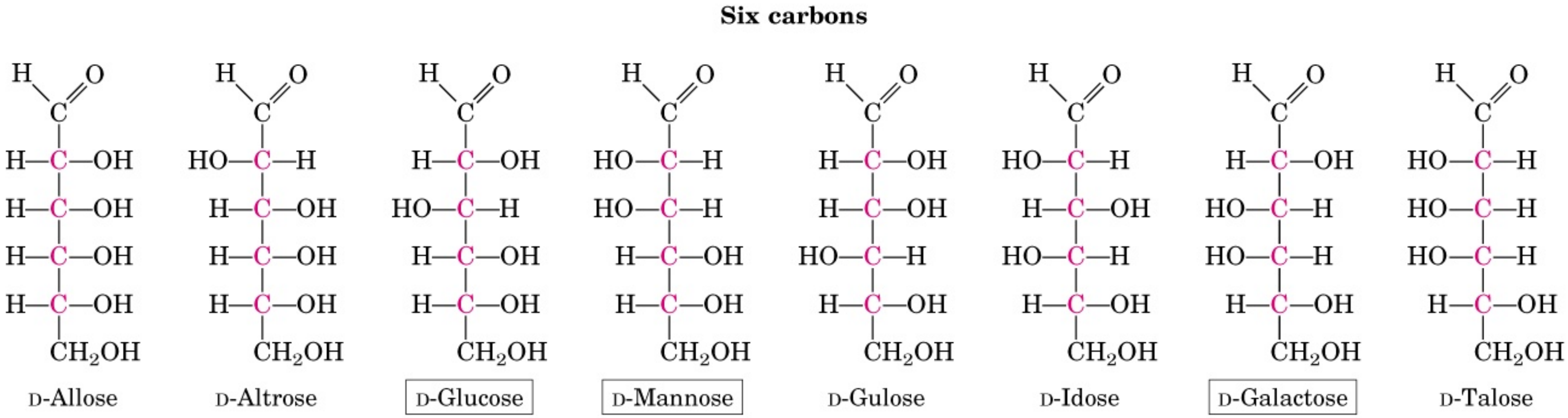
a ketohexose



D-fructose

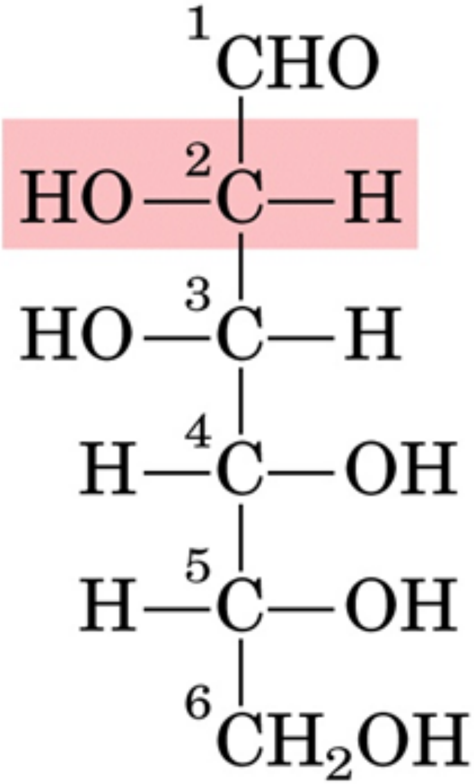
The indicated absolute configuration ("D-glucose") refers to the asymmetric carbon atom further from the aldehyde (ketone) function

How many stereoisomers are possible?

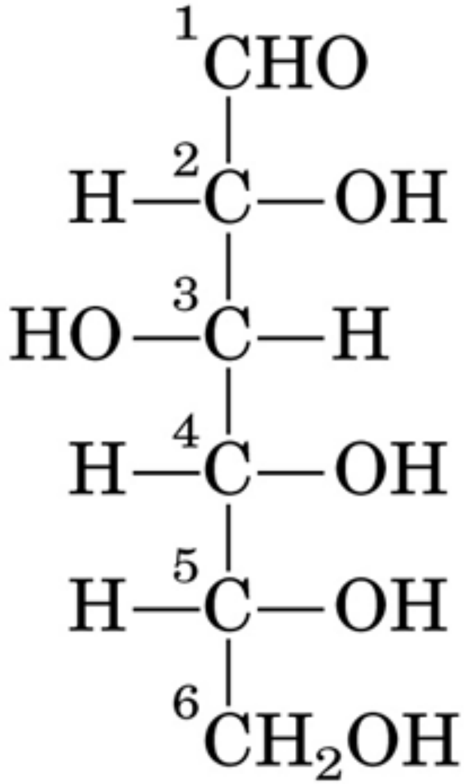


for n asymmetric carbons there are 2^n isomers

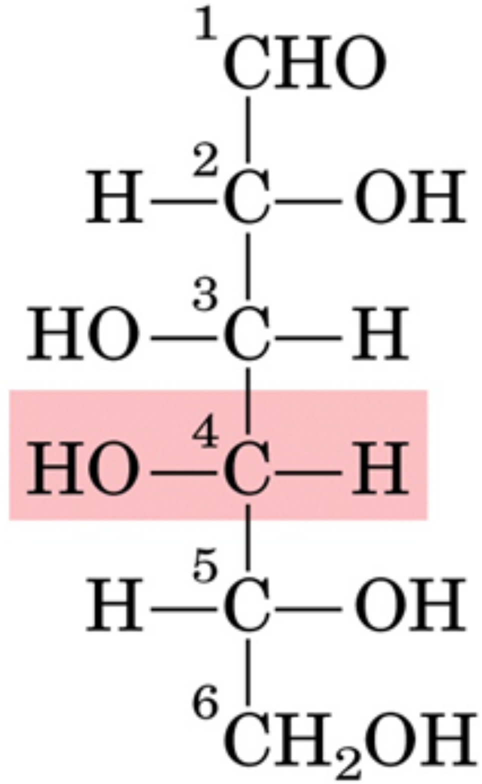
Epimers



D-mannose
(a C-2 epimer)



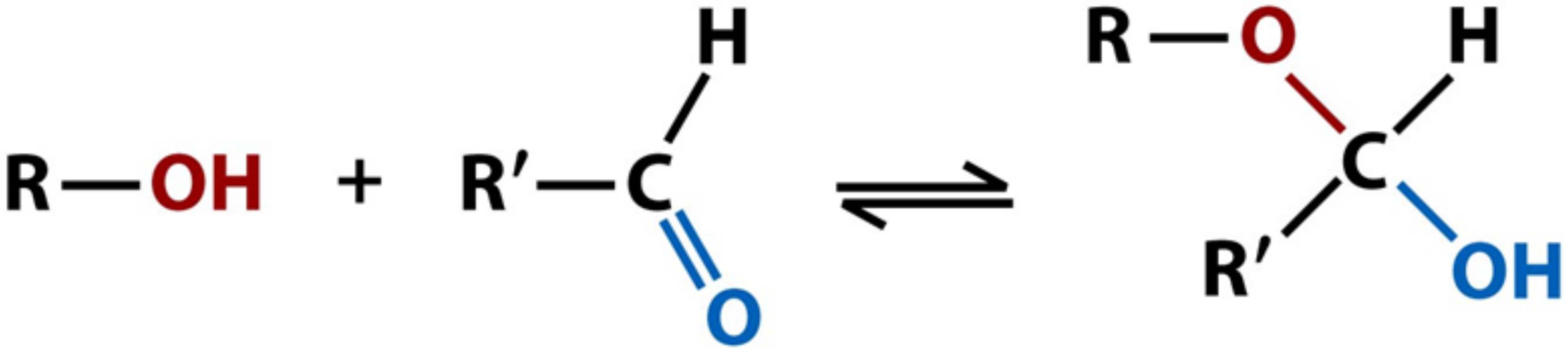
D-glucose



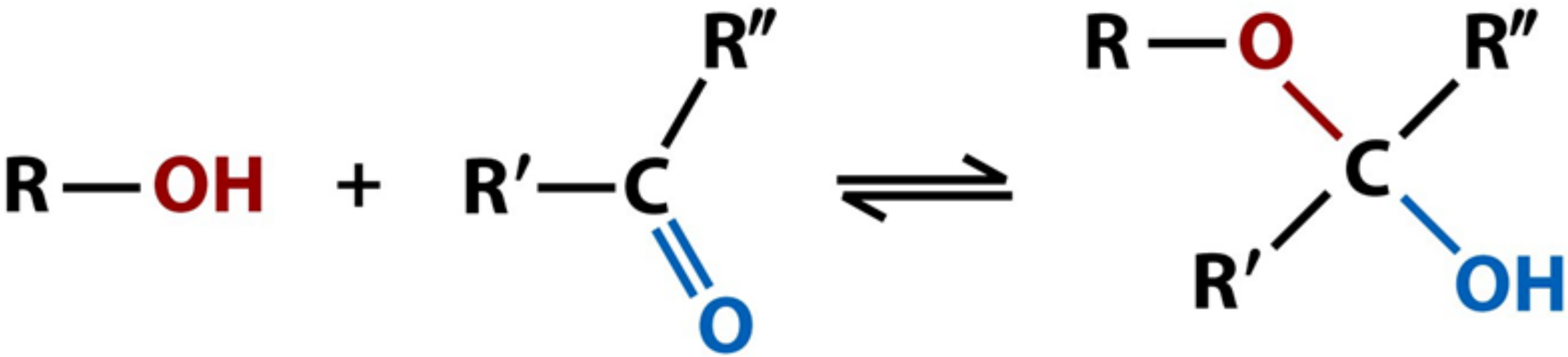
D-galactose
(a C-4 epimer)

They are diastereoisomers presenting a different configuration at a single stereocenter, in a molecule that has at least 2 chiral centers

Alcohols react with the carbonyl groups of aldoses and ketoses to form **hemiacetals** and **hemiketals**, respectively



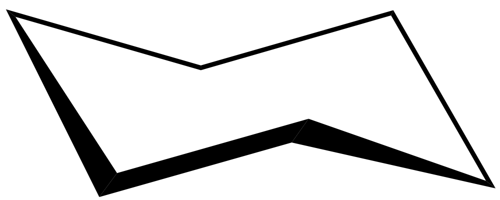
alchol aldehyde hemiacetal



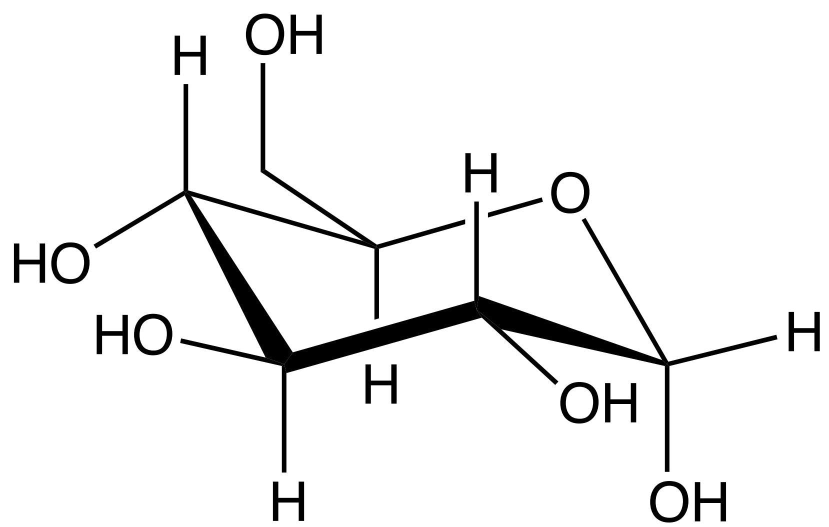
alchol ketone hemiketal

Haworth projections

It is a way to represent monosaccharides through a simplified three-dimensional perspective.
The perspective effect is obtained by highlighting with a thicker line the chemical bonds positioned closer to the observer.



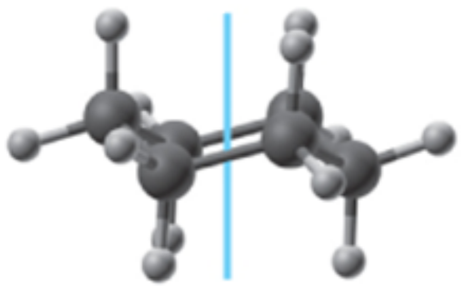
cyclohexane

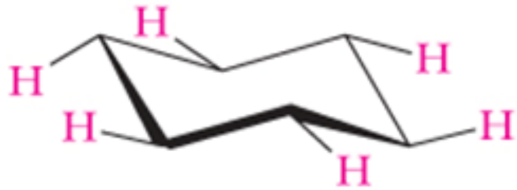


α-D-glucopyranose

In cyclohexane the ring tension is removed by adopting a chair conformation

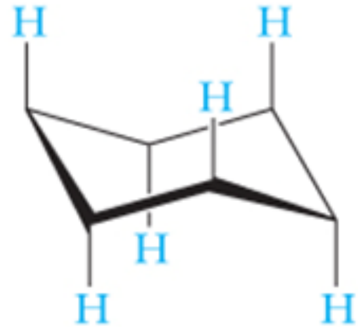
axis





6 equatorial C-H bonds

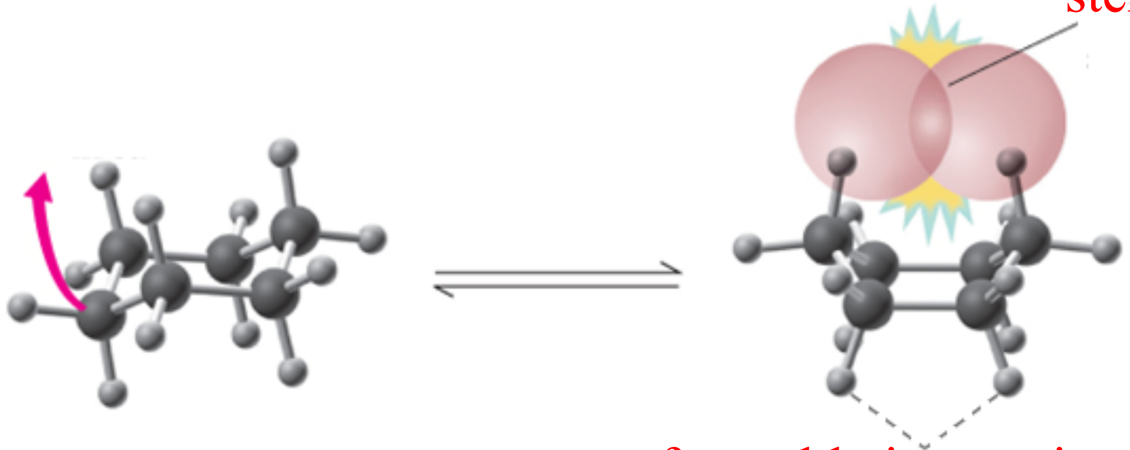
6 axial C-H bonds



The chair conformation is the most stable because the staggered arrangement of each C-C pair is free of torsional stresses and has less steric repulsion.

steric clash

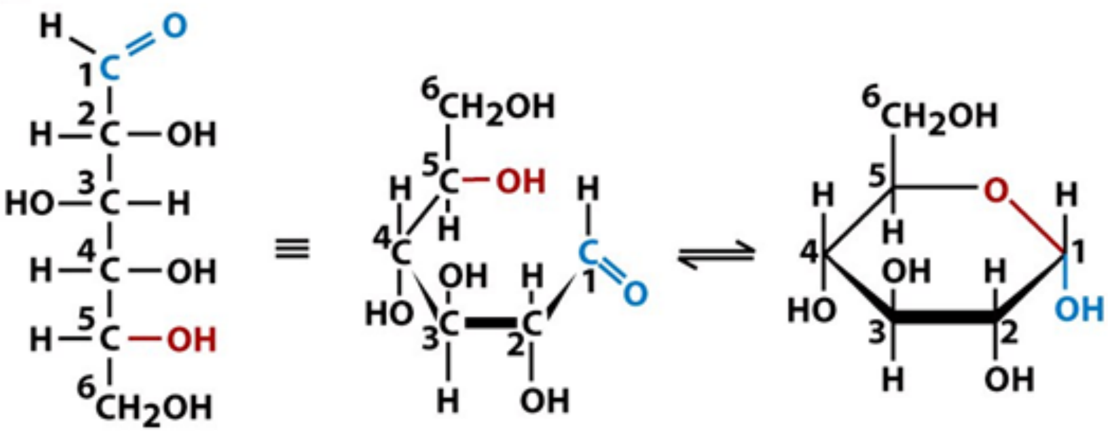
chair conformation

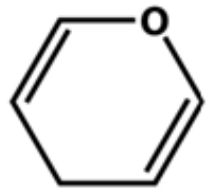


boat conformation

unfavorable interaction between eclipsed hydrogens

In the aldoses and ketoses, the hemiacetals and the hemiketals respectively, are formed by an intramolecular reaction between an alcoholic function and the carbonyl function.

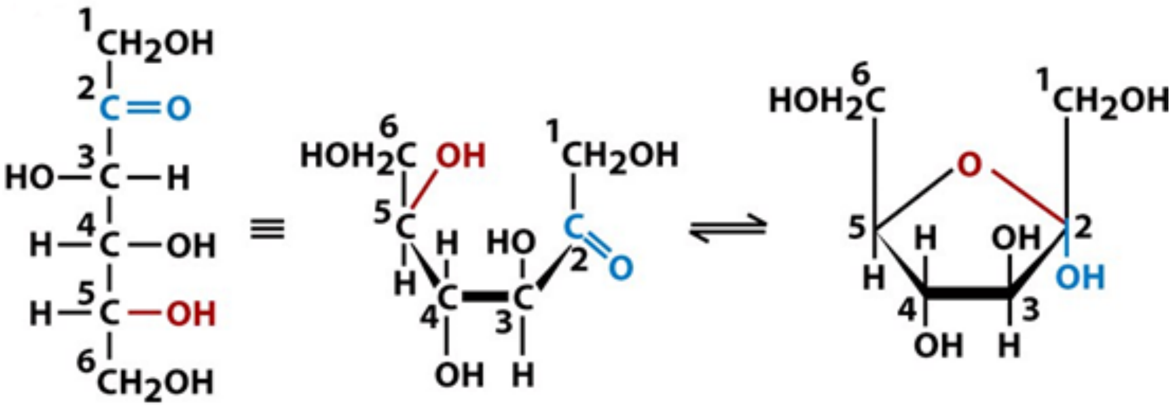




D-glucose
(open form)

α-D-glucopyranose
(Haworth projection)

pyran

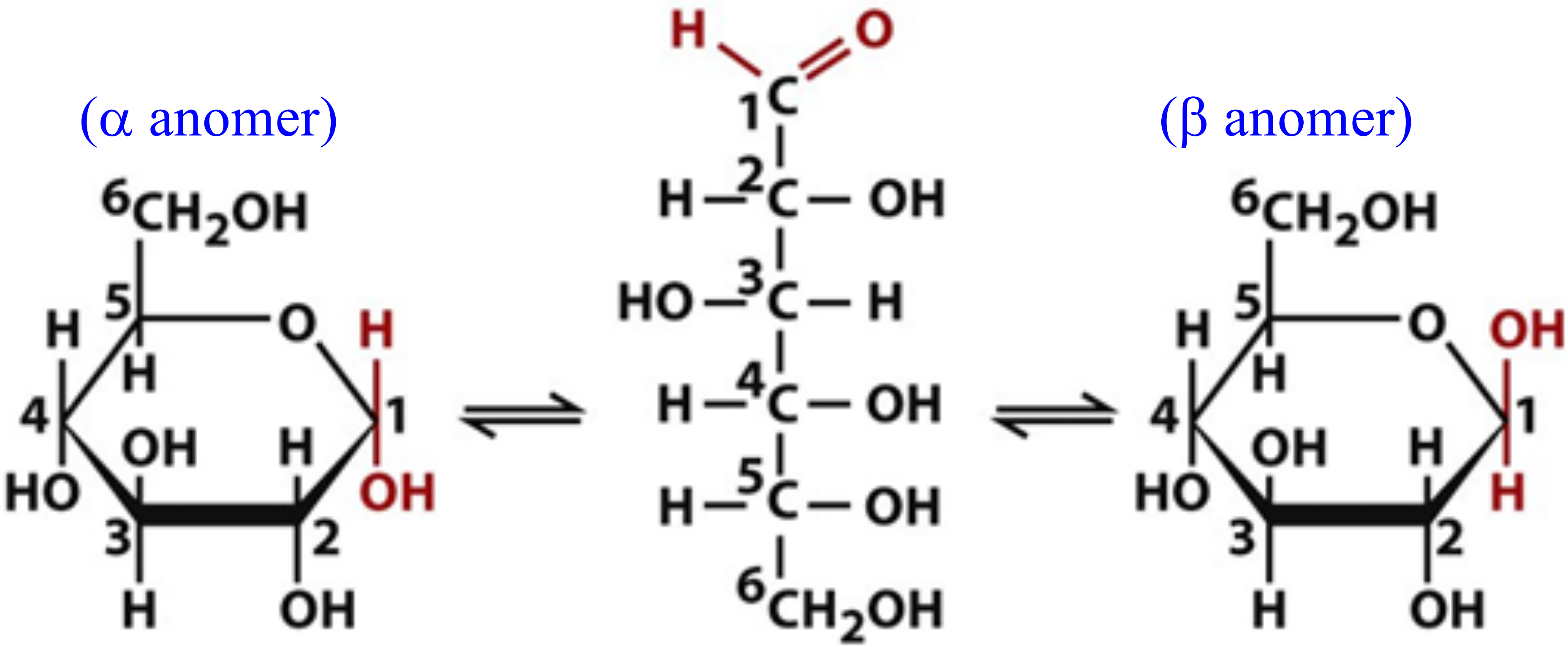


furan

D-fructose
(open form)

α-D-fructofuranose
(Haworth projection)

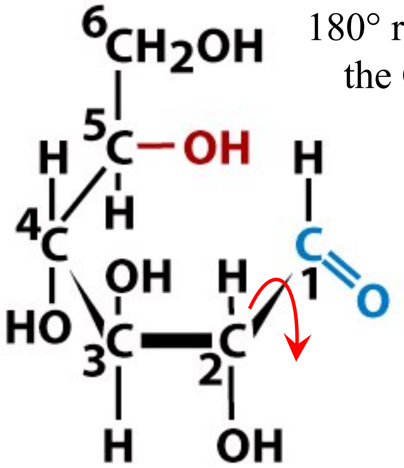
When a monosaccharide undergoes cyclization, the carbonyl carbon (anomeric C) turns into a chiral center with 2 possible configurations. The two stereoisomers which differ in the configuration of the anomeric carbon are called anomers.



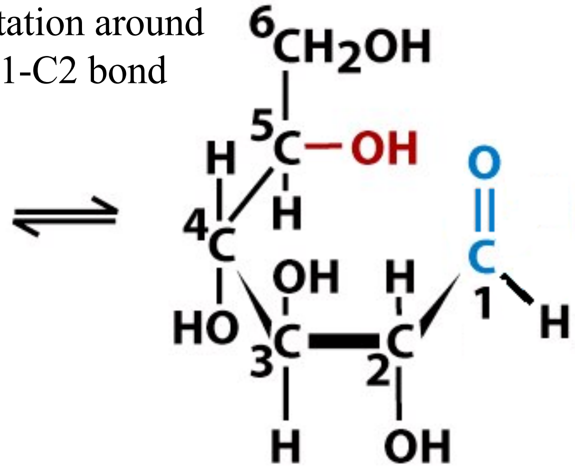
(α anomer) (β anomer)

α-D-glucopyranose β-D-glucopyranose

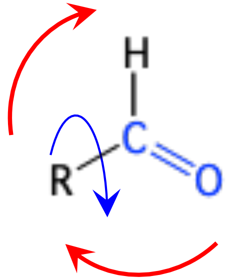
The carbonyl group is prochiral



180° rotation around
the C1-C2 bond



Priority decreases clockwise

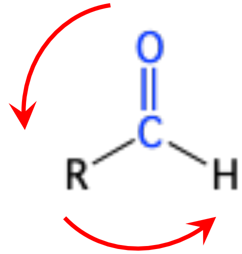


re side

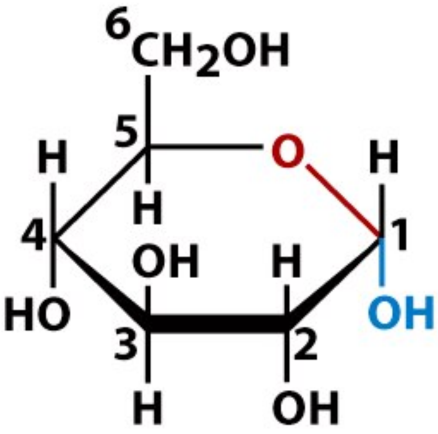
attack from
the *si* side

attack from
the *re* side

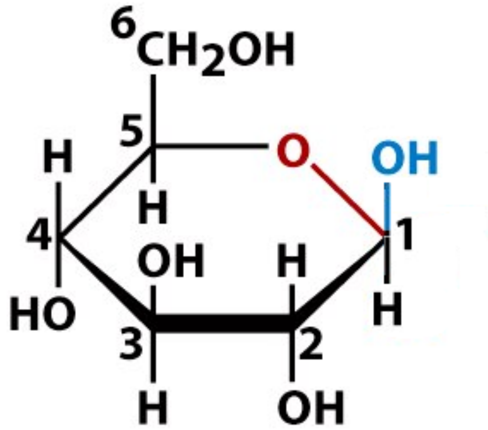
180° rotation around
the C1-C2 bond



si side



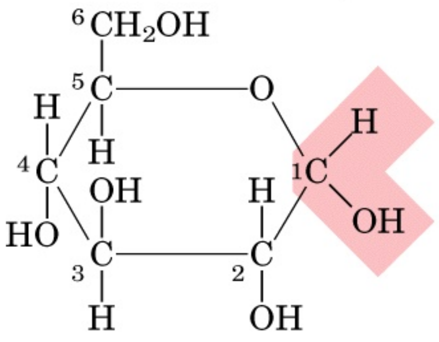
α anomer



β anomer

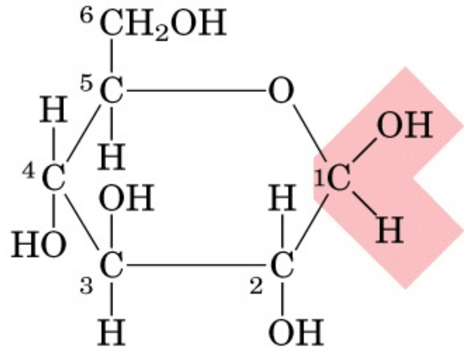
Mutarotation is the variation of the specific rotation at 25 °C ($\alpha'_{25°}$), as a function of time, starting from *pure anomeric forms*.

crystallization in 70% EtOH in H_2O

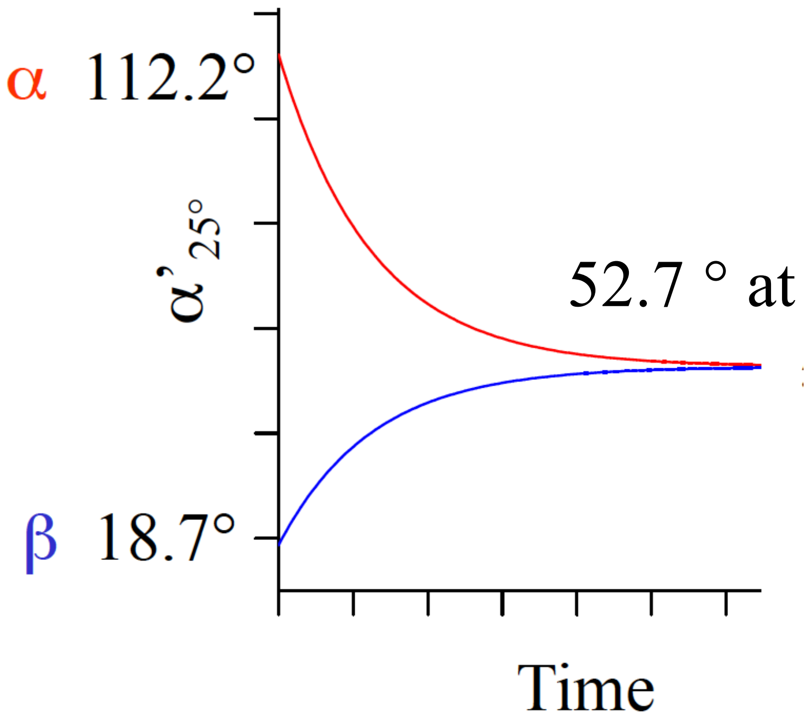


α

crystallization in acetic acid or pyridine



β



52.7 ° at equilibrium

$$\begin{cases} f_\alpha \cdot 112.2 + f_\beta \cdot 18.7 = 52.7 \\ f_\alpha + f_\beta = 1 \end{cases}$$

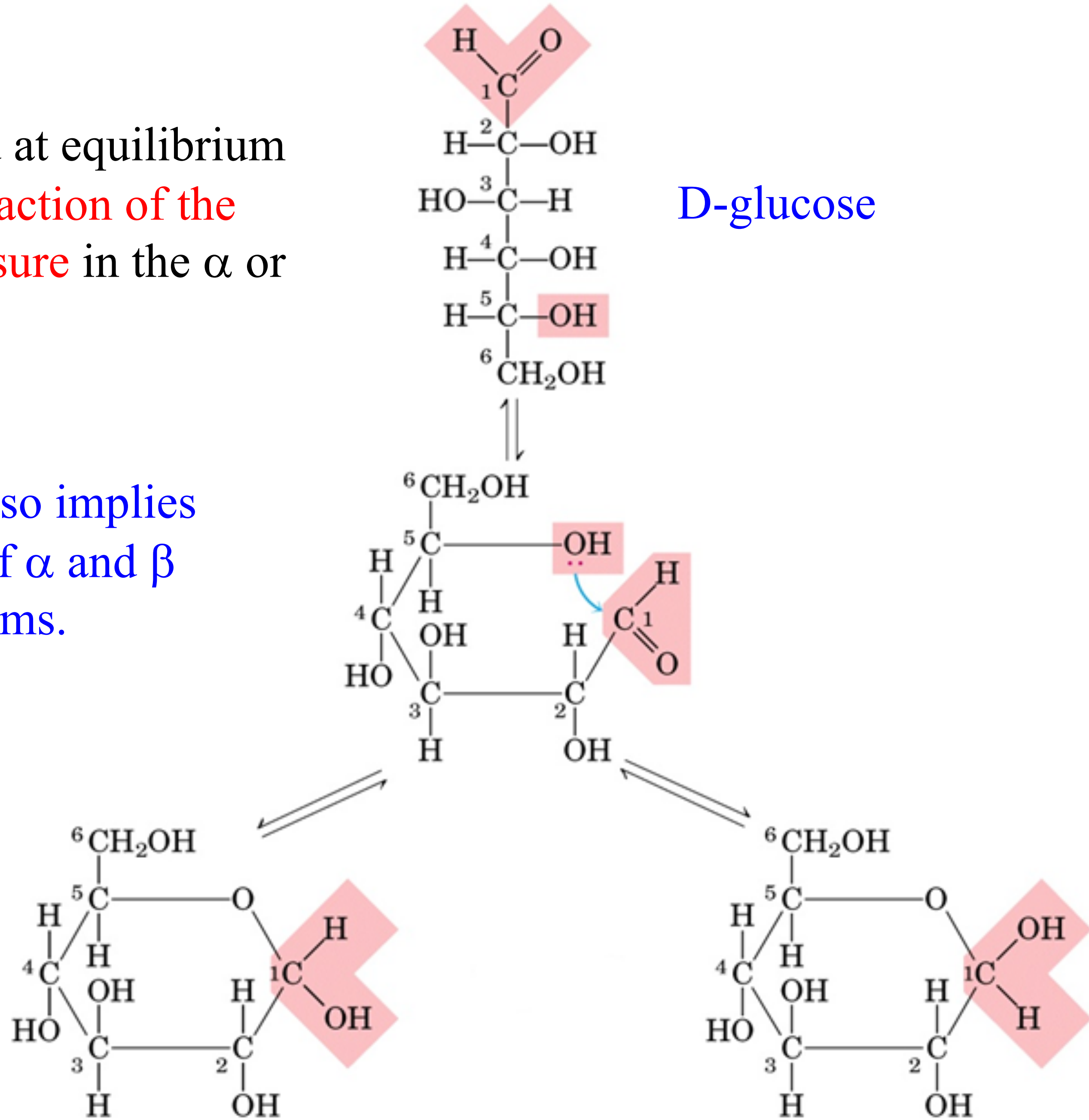
$$f_\alpha \approx 36\%$$
$$f_\beta \approx 64\%$$

The value of 52.7 ° measured at equilibrium is the result of the opening reaction of the hemiacetal ring and of re-closure in the α or β anomeric forms.

The value of $\alpha'_{25°}$ = 52.7 ° also implies the presence in the mixture of α and β pyanoside and furanoside forms.

The mixture contains:

- 0.02% open form
- 30% α pyranoside form
- 61% β pyranoside form
- the rest of α and β furanoside forms.

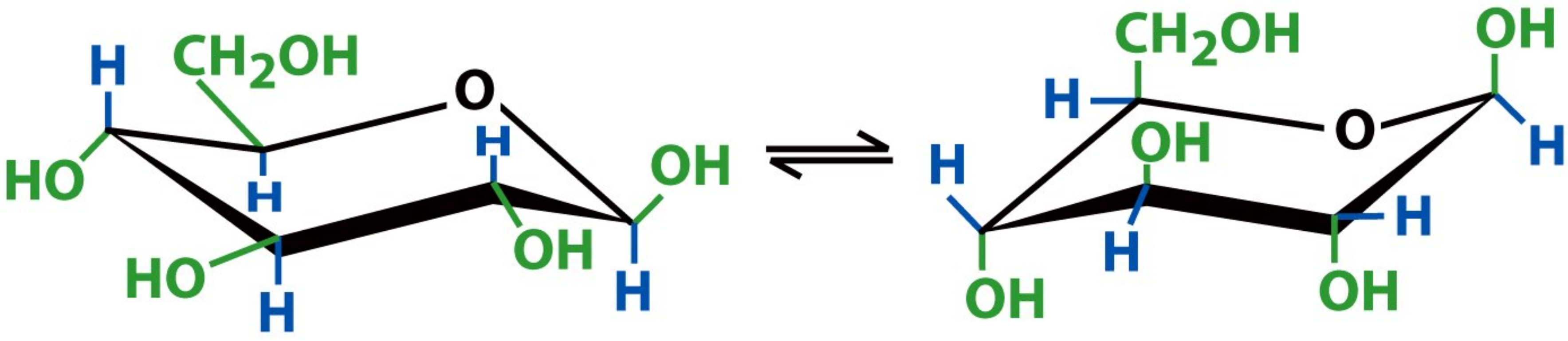


D-glucose

α-D-glucopyranose

β-D-glucopyranose

All carbon atoms in the 5 or 6-term rings are hybridized sp^3.
Of the 2 possible chair conformations the most stable (predominant) is that arrangement in which the more voluminous ring substituents of the occupy equatorial positions, rather than the axial ones

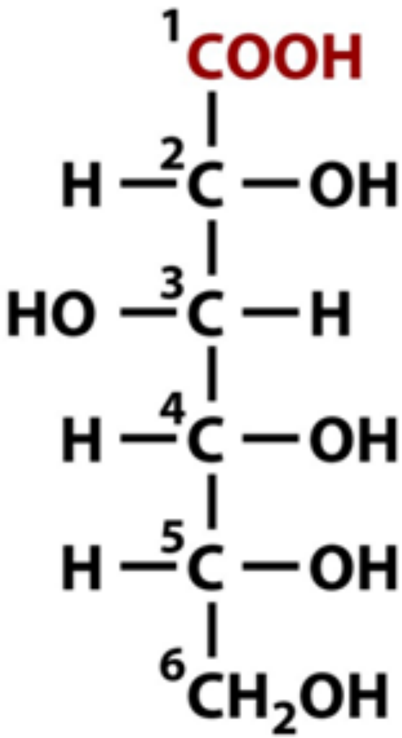


most stable conformation

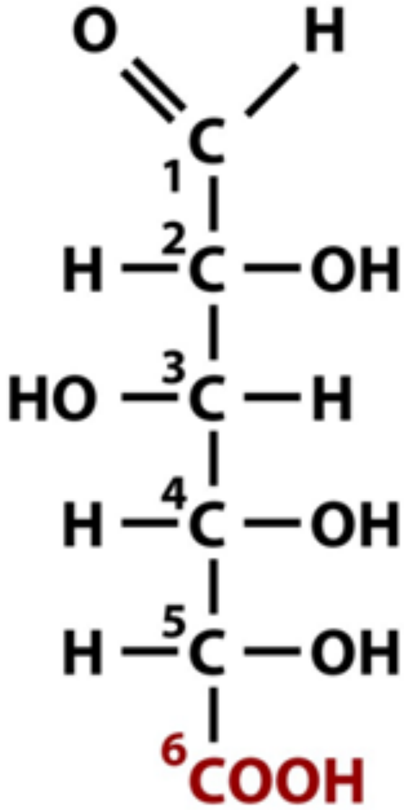
Only in glucose all 5 substituents other than H can arrange simultaneously in equatorial positions!

Sugar derivatives (typical reactions of aldehydes and ketones)

Oxidation reactions (chemical or enzymatic): aldonic, uronic, aldaric acids



D-gluconic acid



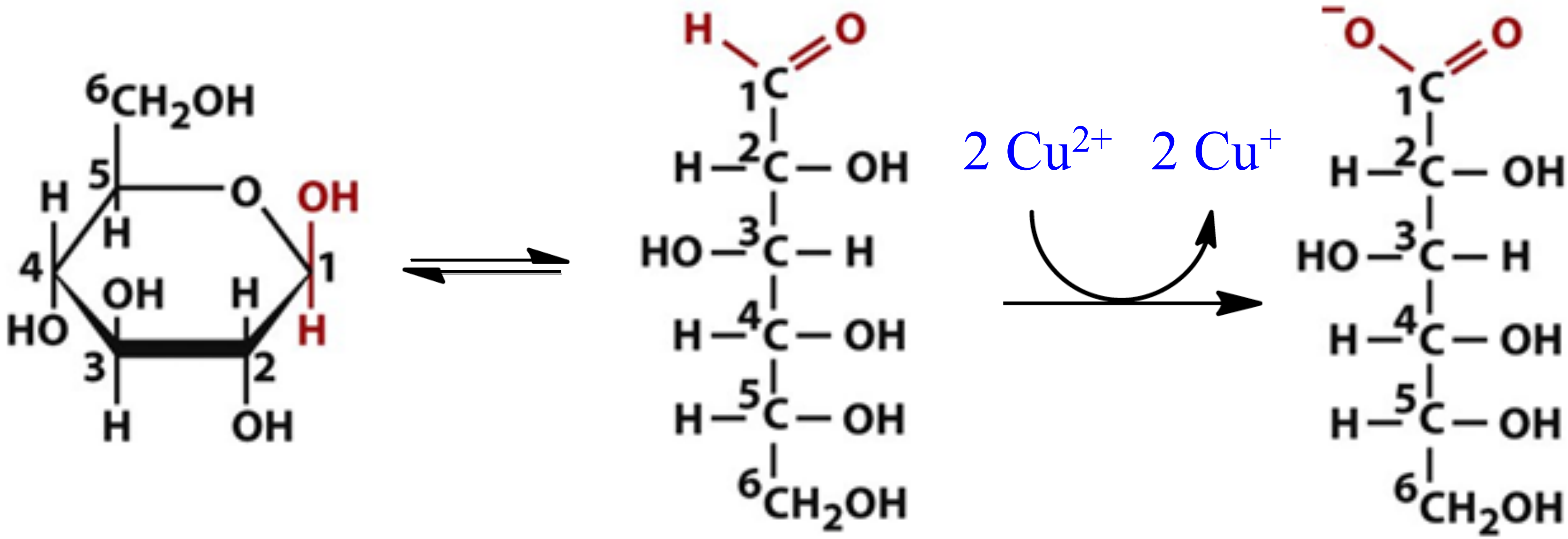
D-glucuronic acid

Reducing sugars

Fehling's reagent (Cu^{2+})

Tollens' reagent (Ag^{+})

Any sugar having a free hemiacetal or hemiketal function is called a reducing sugar.

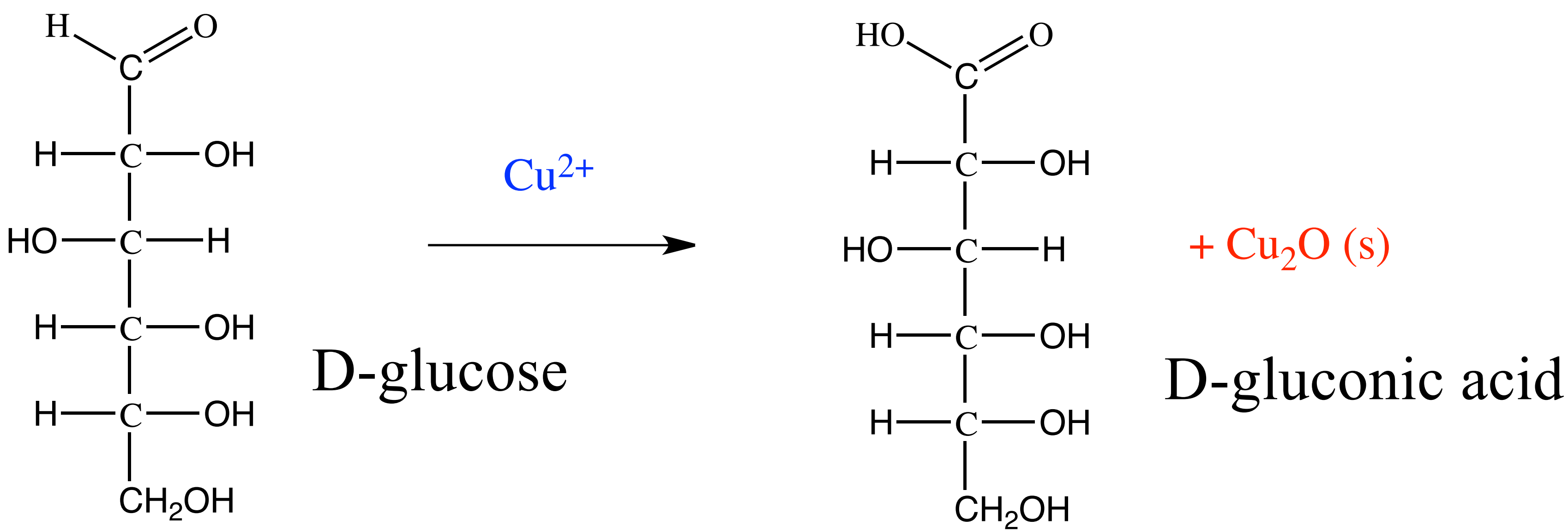


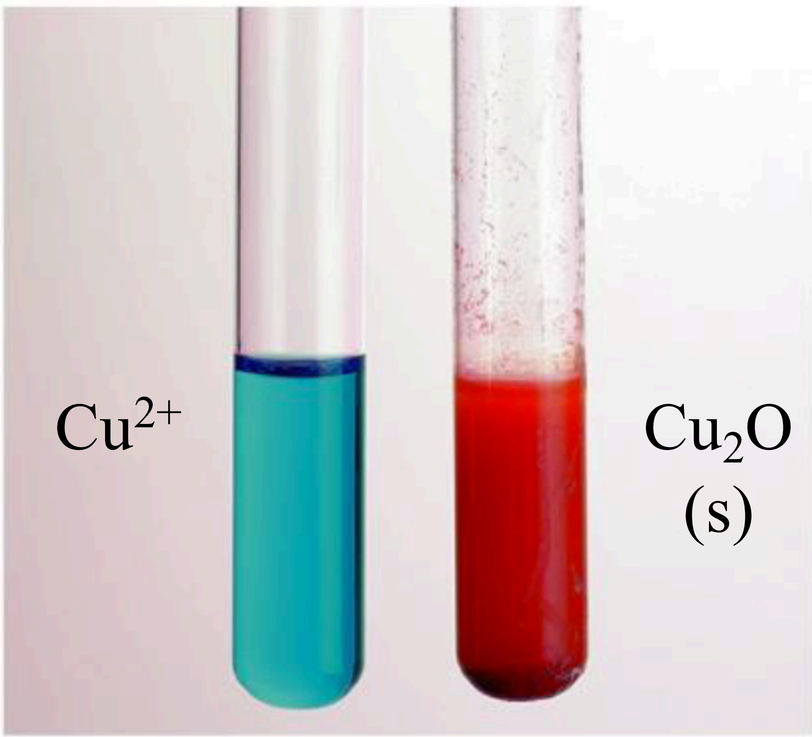
β-D-glucopyranose D-glucose D-gluconic acid

Tollens' reagent (Ag^+)

$$2\,[Ag(NH_3)_2]^+ + RCHO + H_2O \rightarrow 2\,Ag(s) + 4\,NH_3 + RCOOH + 2\,H^+$$

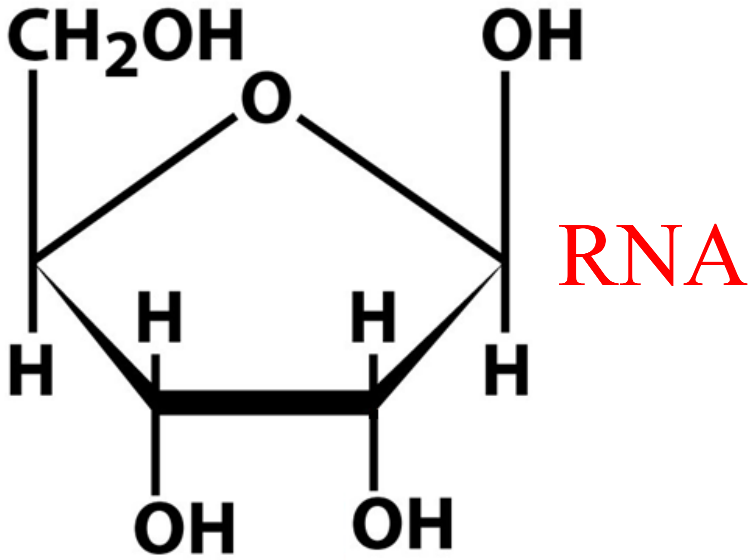
Fehling's reagent (Cu^{2+})



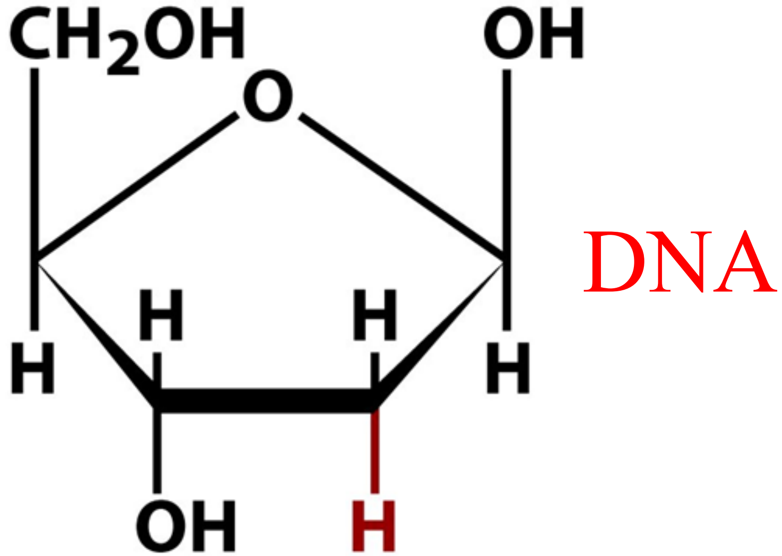


Sugar derivatives

Deoxy sugars

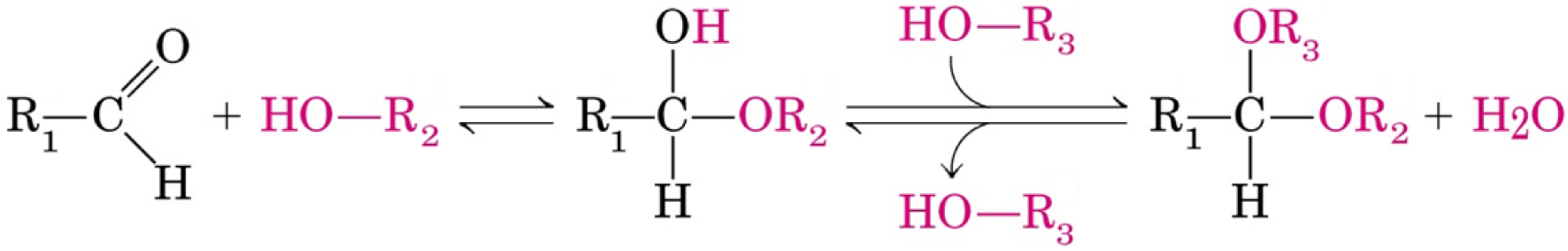


β-D-ribofuranose
(D-ribose)

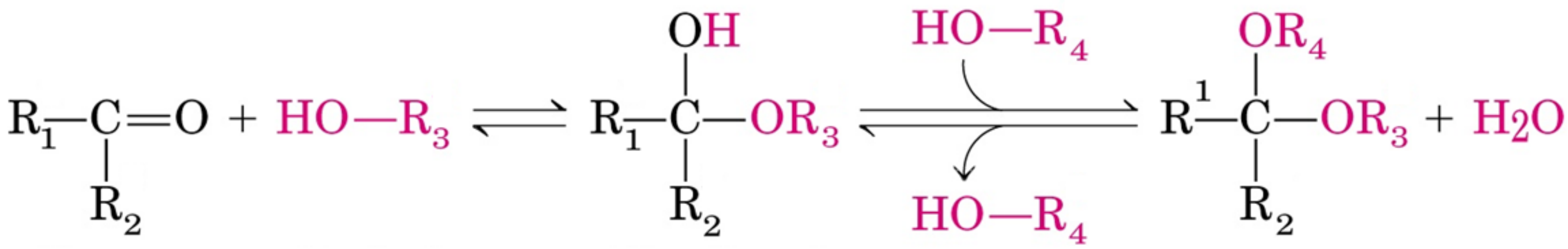


β-D-2-deoxyribofuranose
(D-2-deoxyribose)

The glycosidic bond

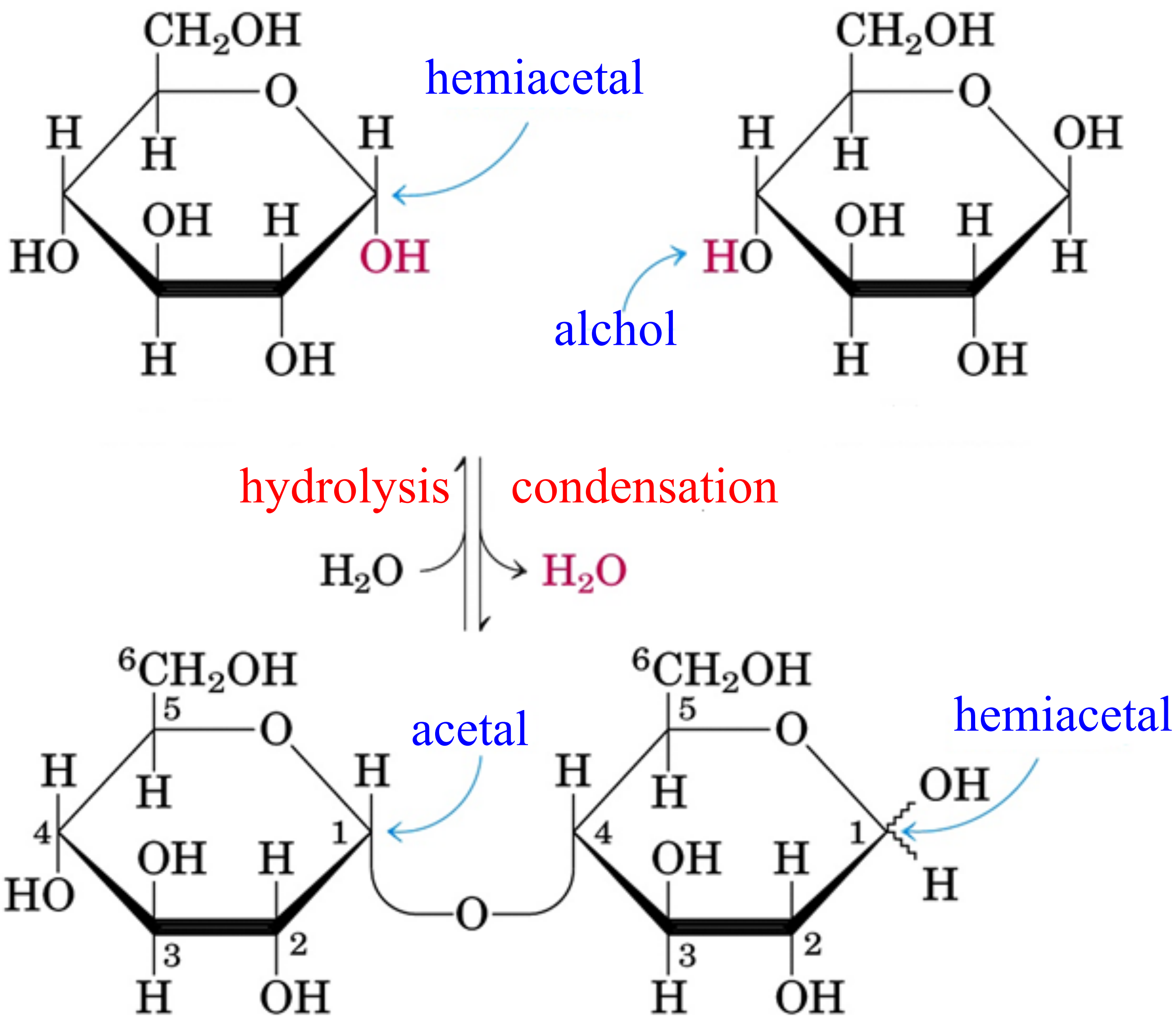


aldehyde alchol hemiacetal acetal



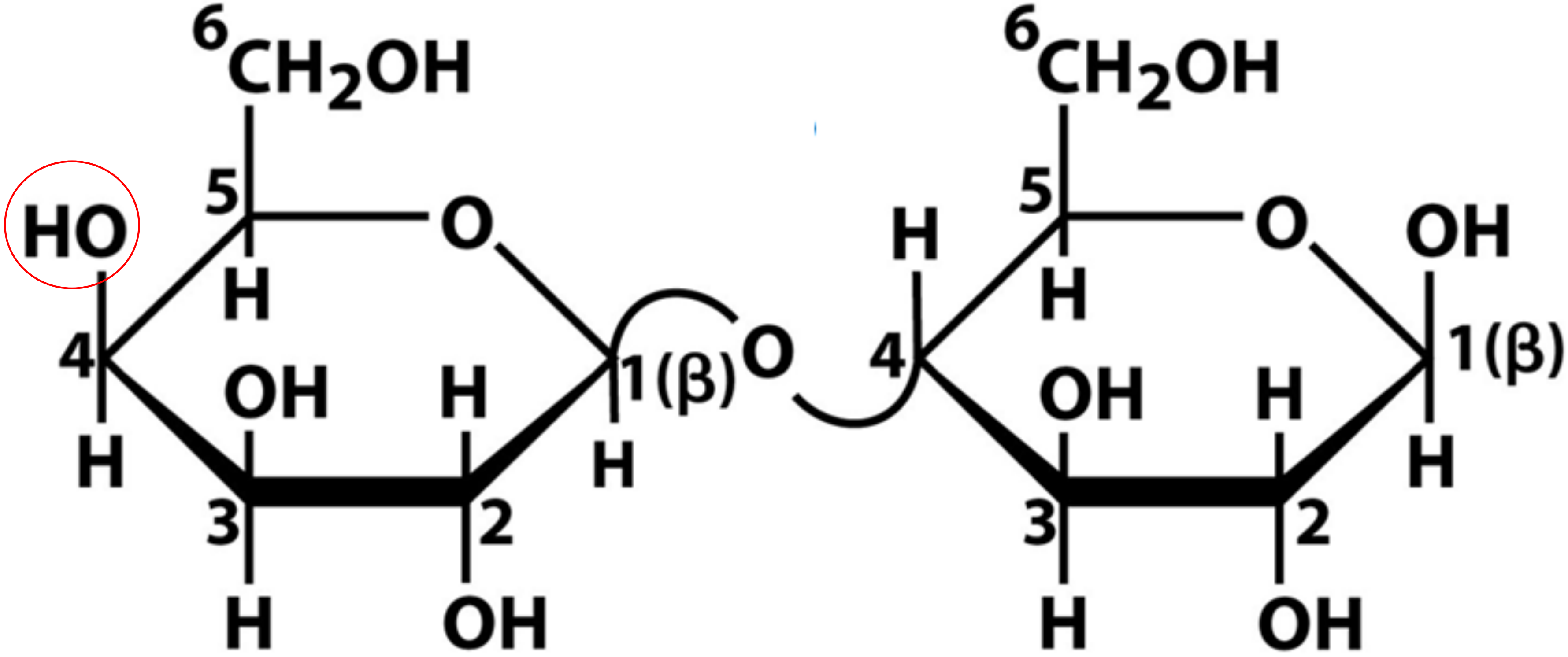
ketone alchol hemiketal ketal

The glycosidic bond



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

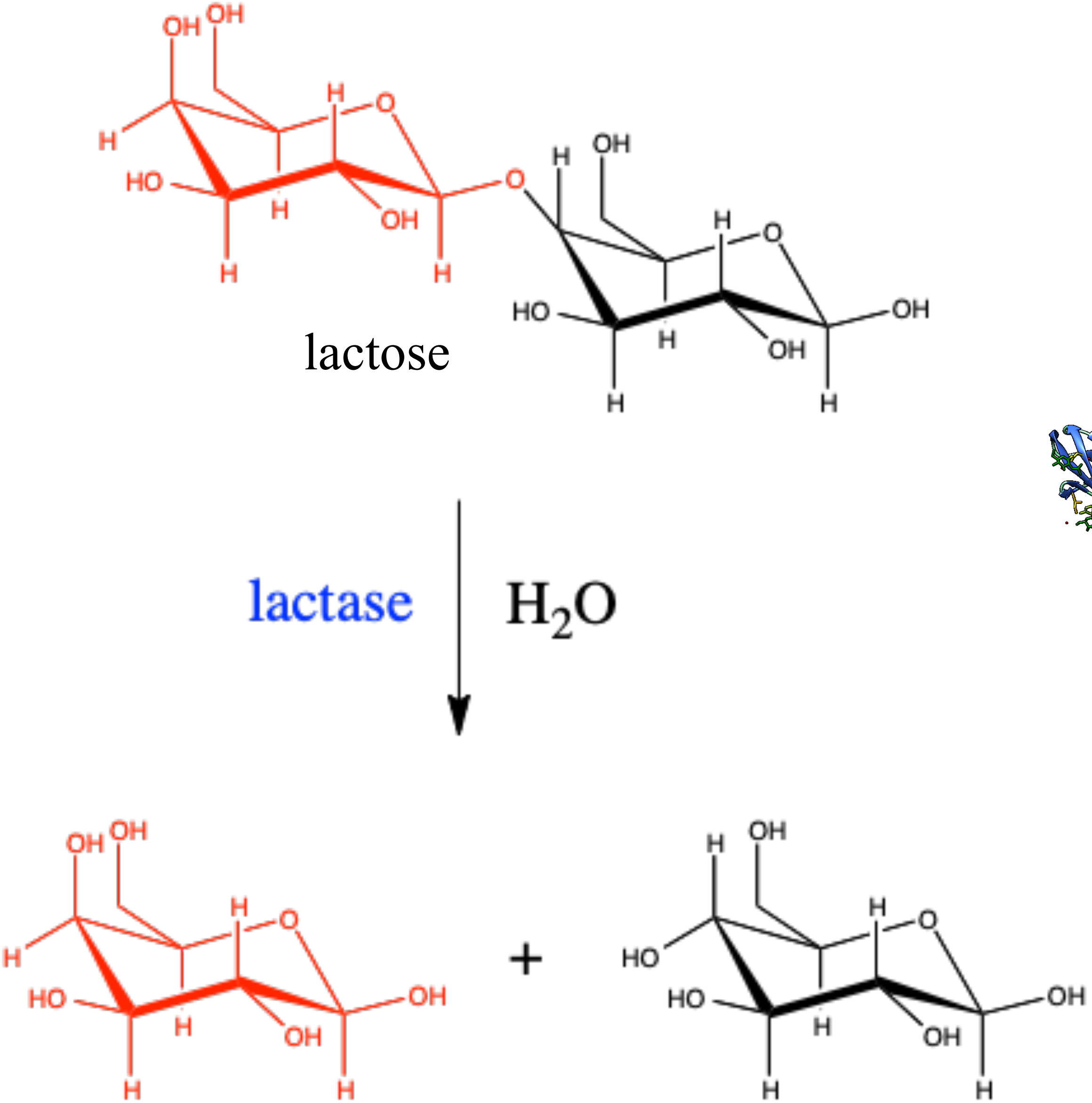
Disaccharides: lactose



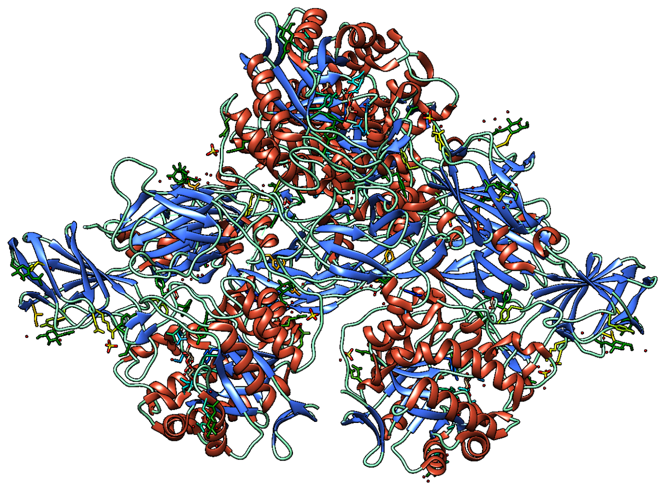
galactose glucose

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

Lactase (lactose galactohydrolase)

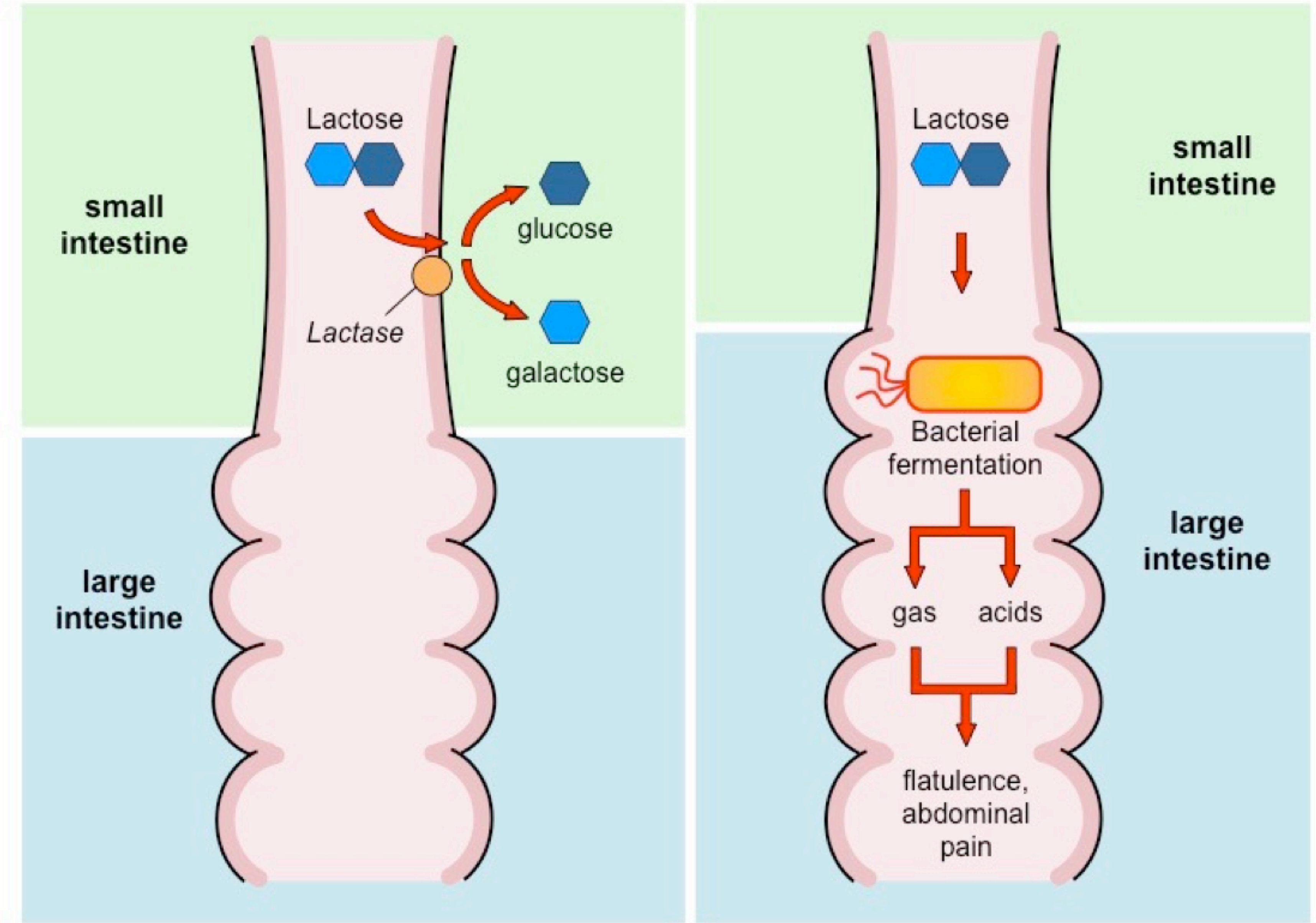


β-D-galactose β-D-glucose

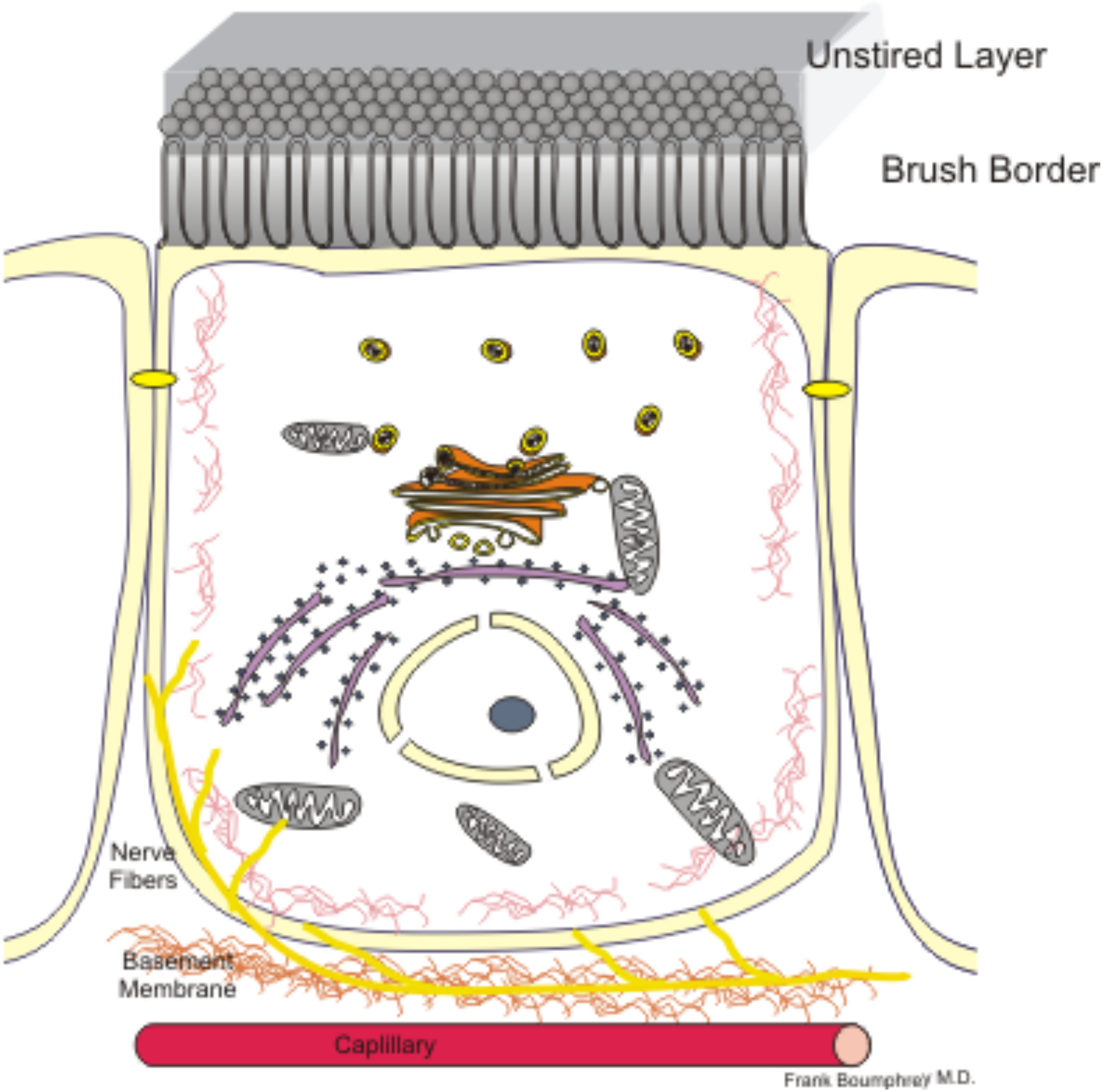


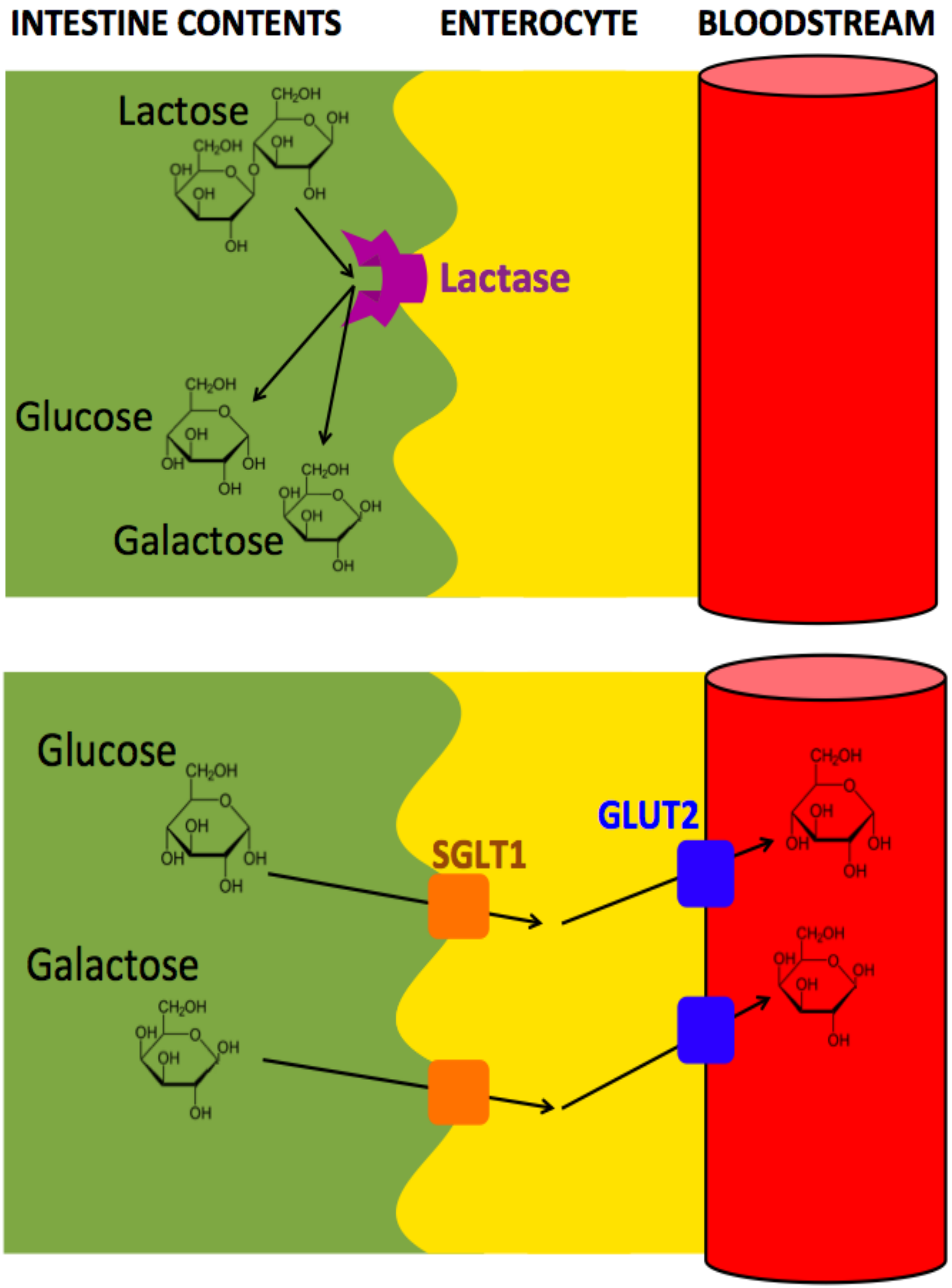
pdb: 3THC

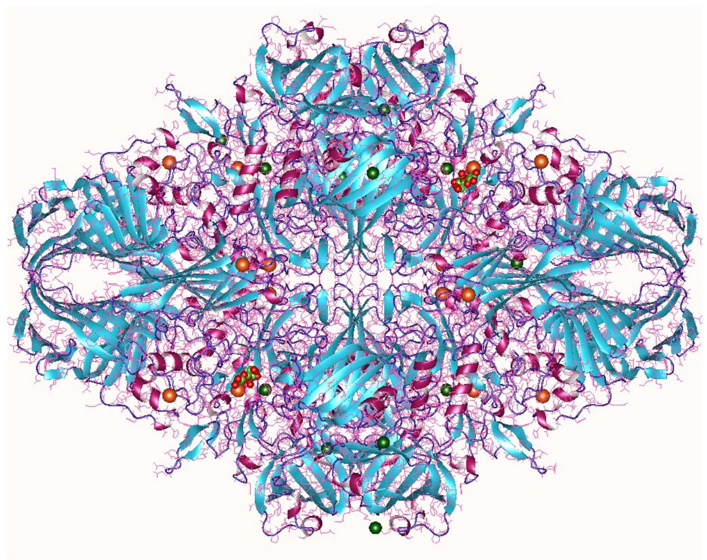
Lactose intolerance is due to the lack of enzyme lactase in the brush border of small intestine to break lactose down into glucose and galactose



Enterocytes





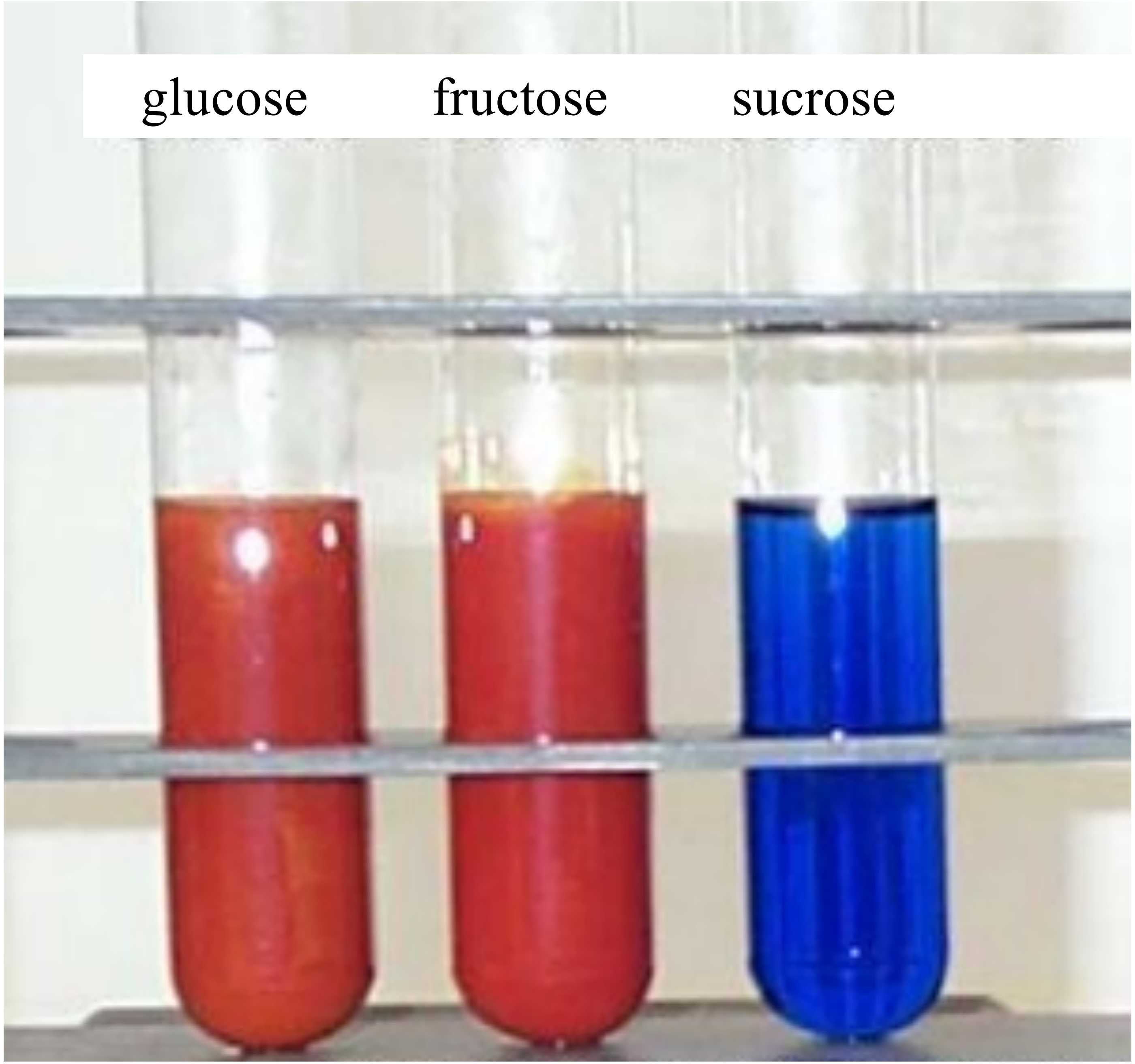


lactase

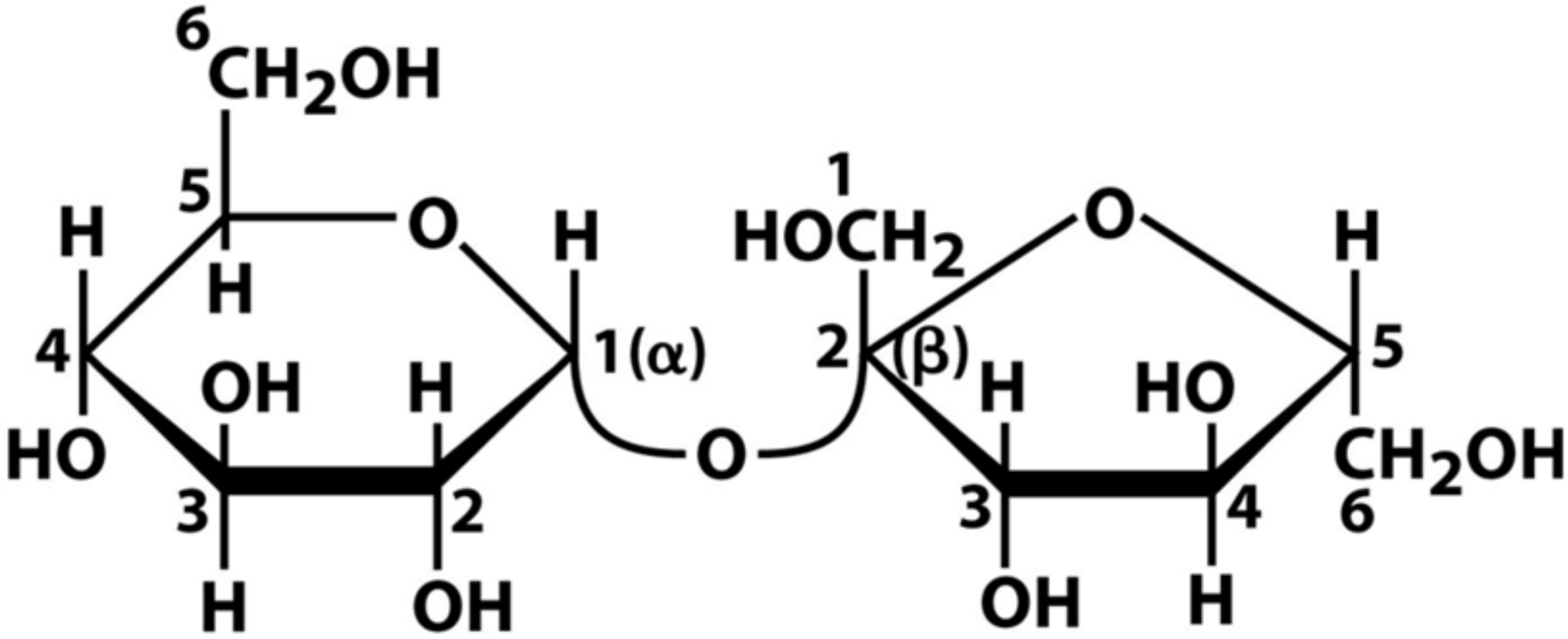
SGLT1: sodium-glucose linked transporter 1

GLUT2: glucose transporter 2

Sucrose: Fehling-negative sugar



Disaccharides: sucrose



glucose fructose

α-D-glucopyranosyl-(1→2)-β-D-fructofuranose

The bond involves the aldehyde function (C-1) of glucose and the ketone function (C-2) of fructose.
Since both reducing functions are involved in the 1 → 2 glycosidic bond, sucrose is a non-reducing sugar.

Polysaccharides

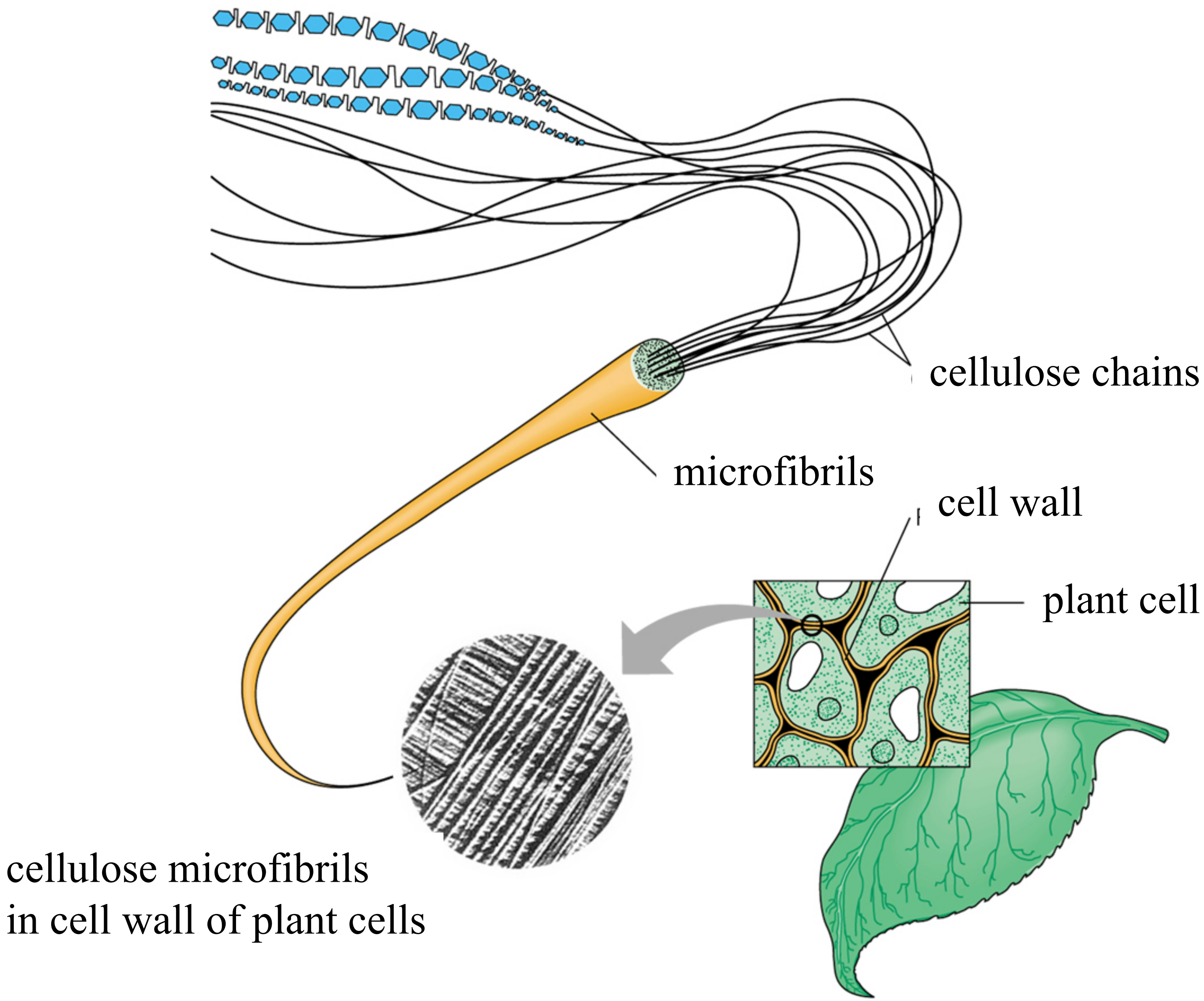
Structures and Roles of Some Polysaccharides

Polymer	Type*	Repeating unit†	Size (number of monosaccharide units)	Roles
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 to 30 residues	Up to 10^6	
Glycogen	Homo-	(α1→4)Glc, with (α1→6)Glc branches every 8 to 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
Peptidoglycan	Hetero-; peptides attached	4)Mur2Ac(β1→4) GlcNAc(β1	Very large	Structural: in bacteria, gives rigidity and strength to cell envelope
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

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

†The abbreviated names for the peptidoglycan and hyaluronate repeating units indicate that the polymer contains repeats of this disaccharide unit, with the GlcNAc of one disaccharide unit linked β(1→4) to the first residue of the next disaccharide unit.

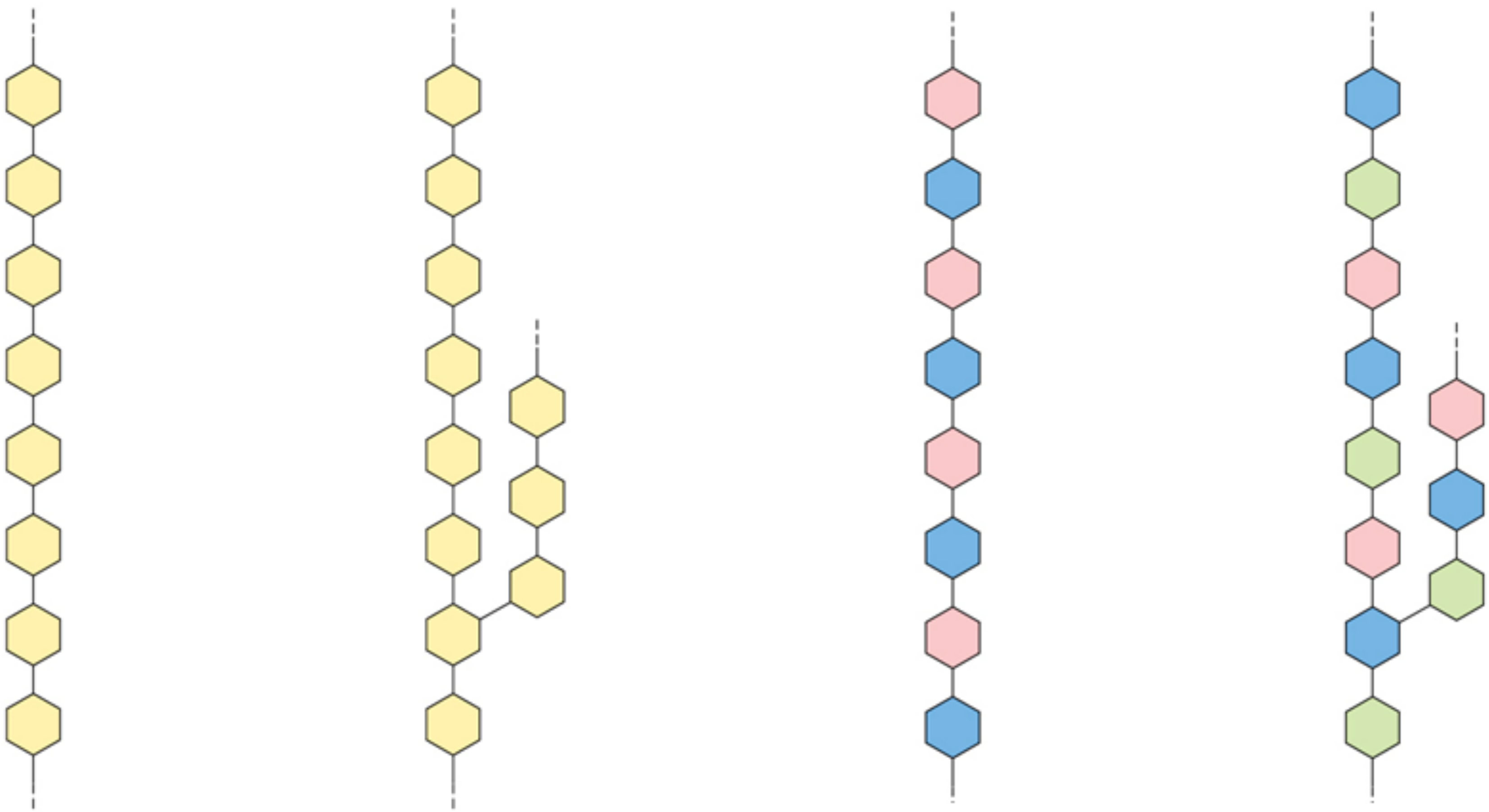
Polysaccharides



homopolysaccharides

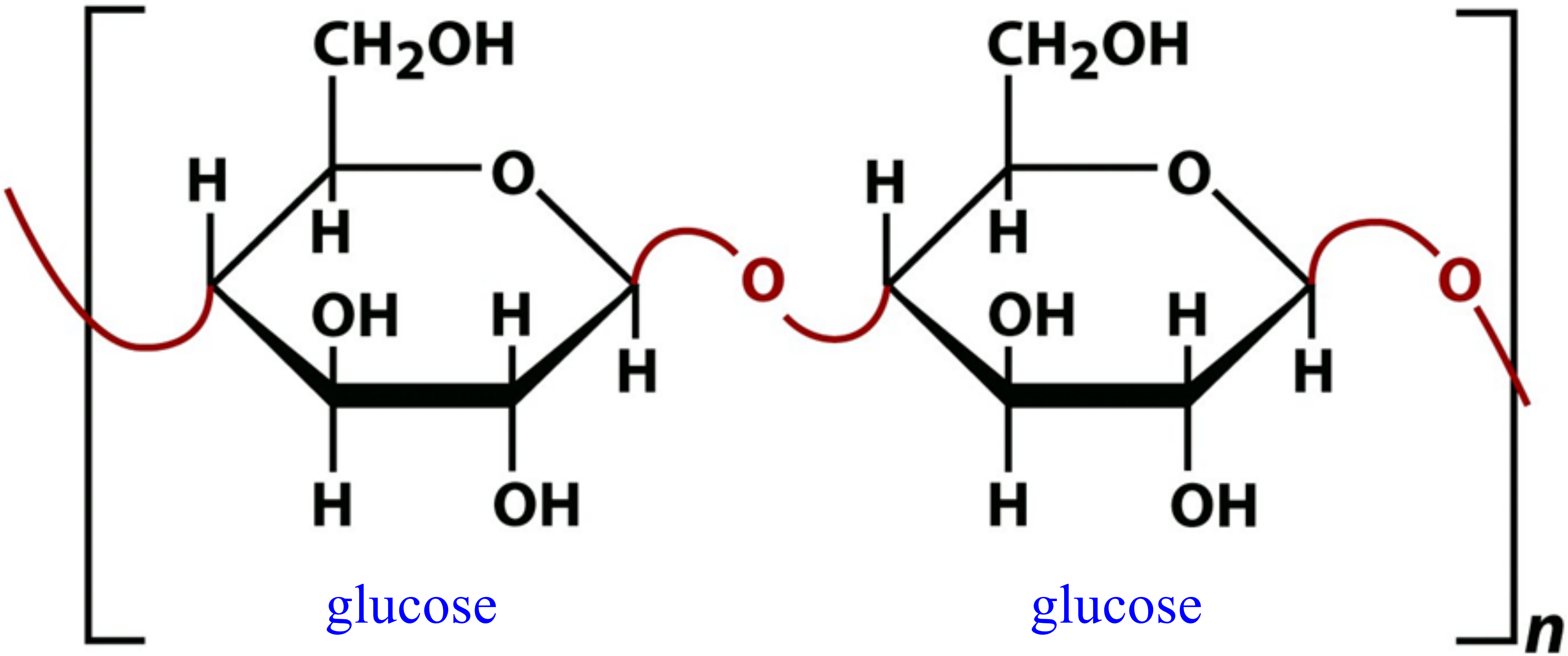
heteropolysaccharides

linear branched linear branched



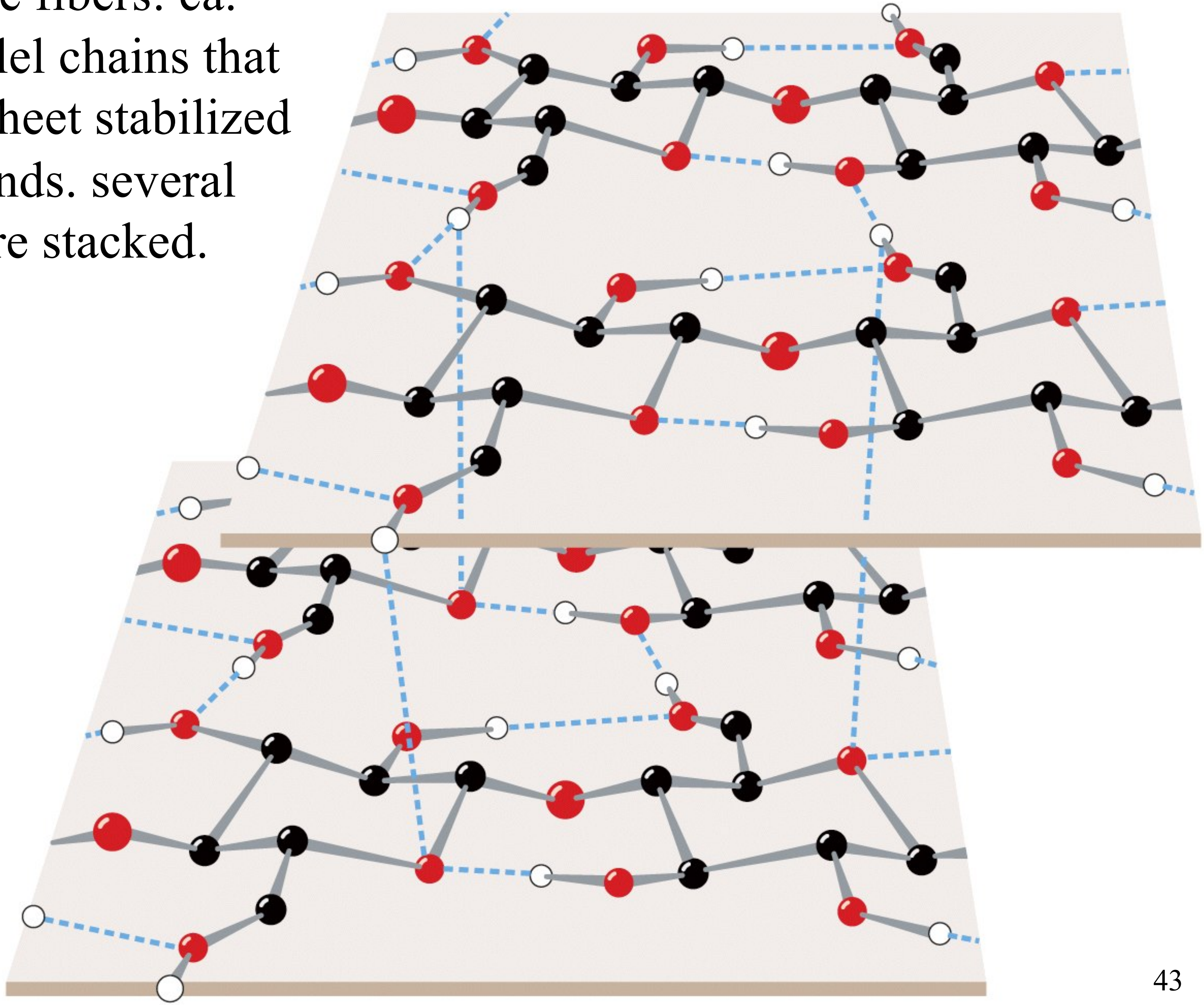
Structural polysaccharides: cellulose

basic disaccharide: cellobiose

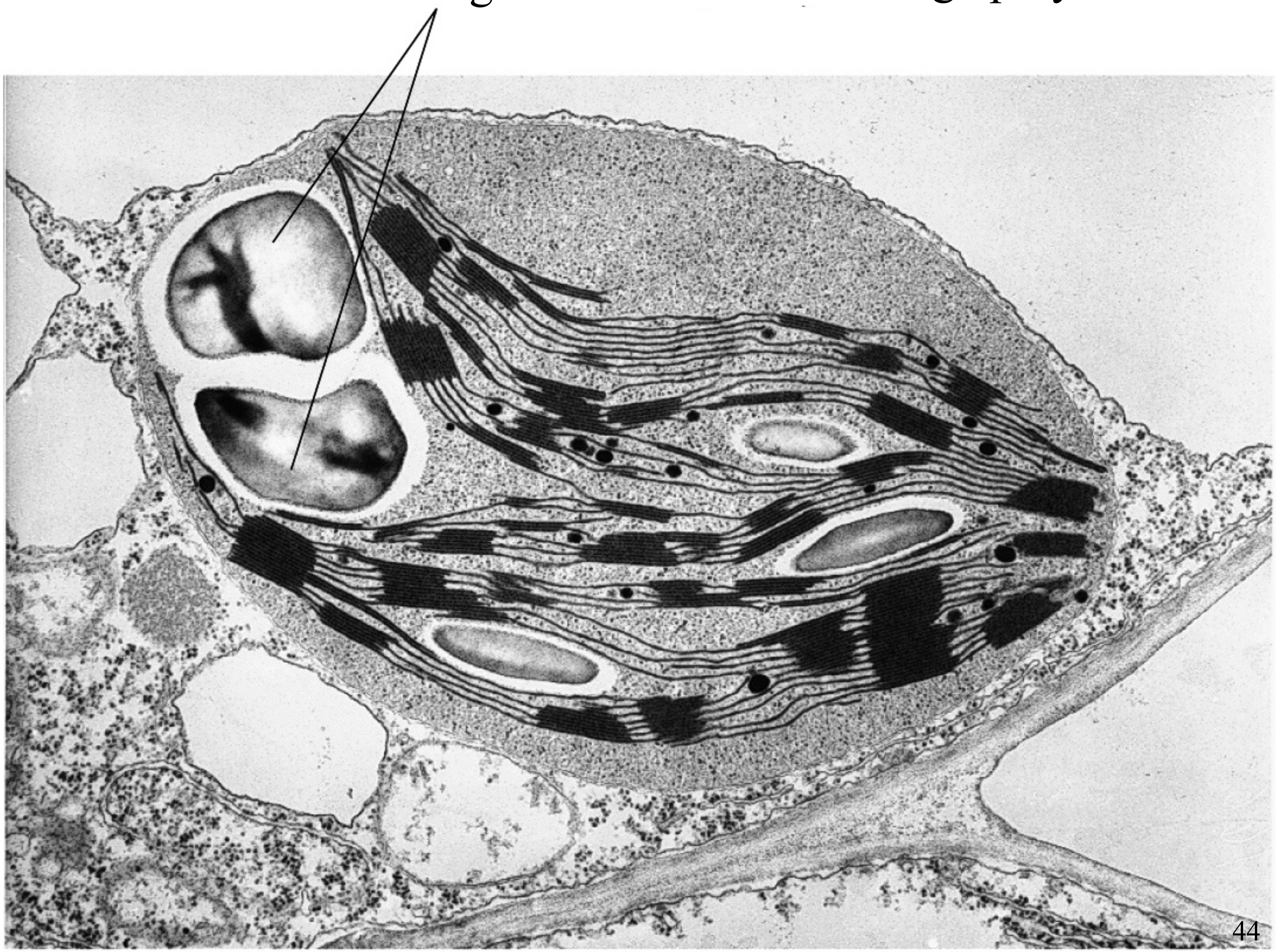


β (1→ 4) glycosidic bond

Cellulose fibers: ca. 40 parallel chains that form a sheet stabilized by H bonds. several sheets are stacked.

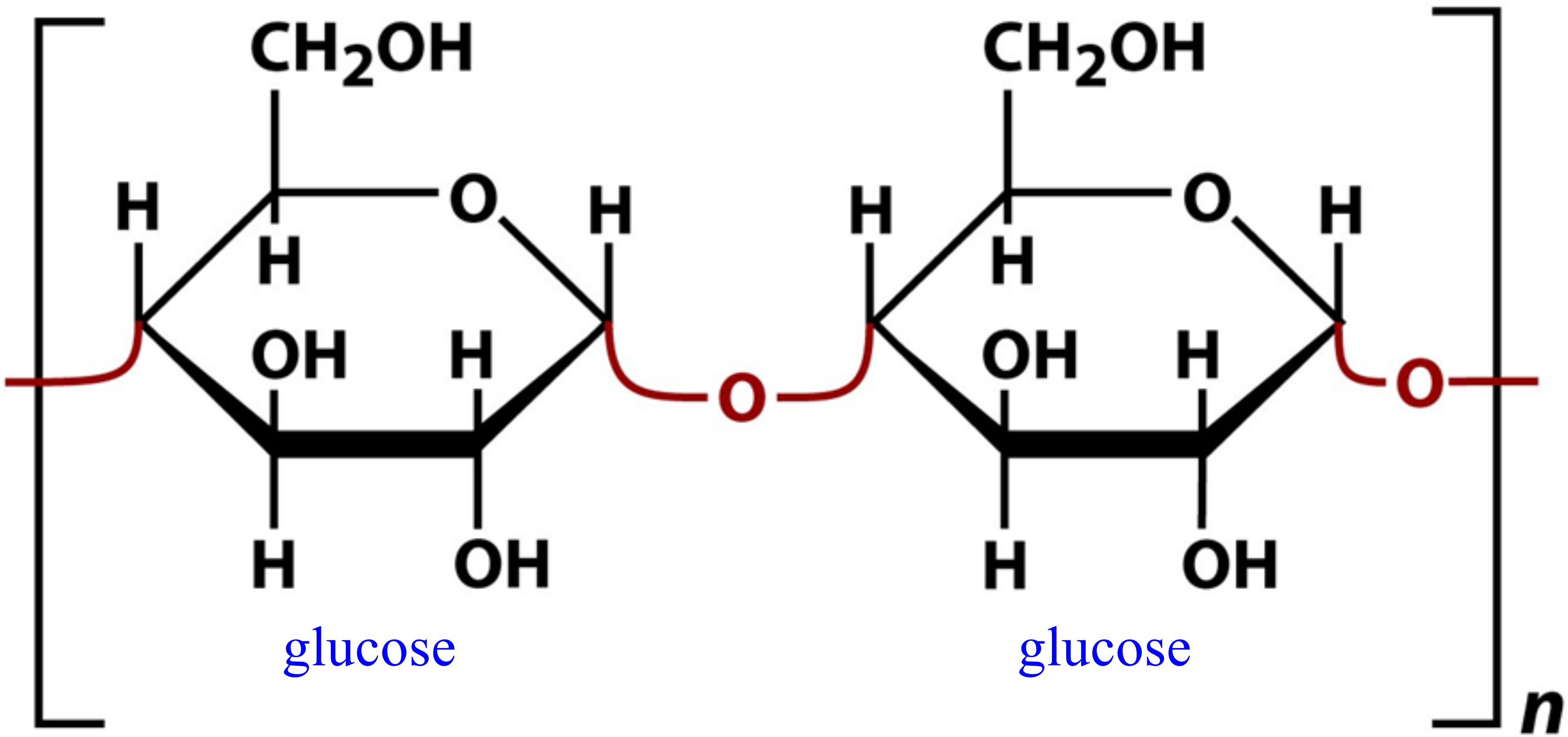


Storage polysaccharides



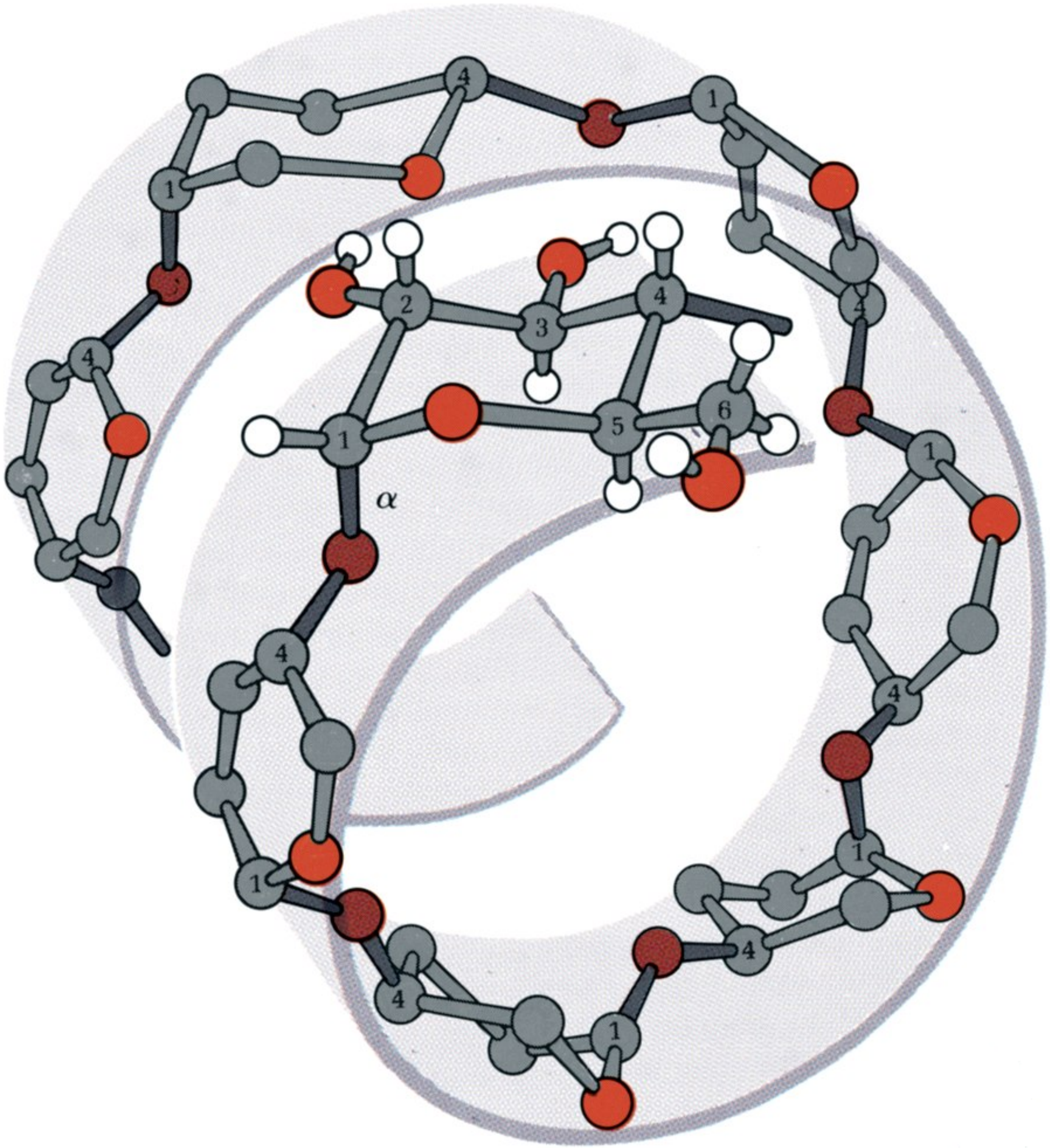
Storage polysaccarides: α-amylose

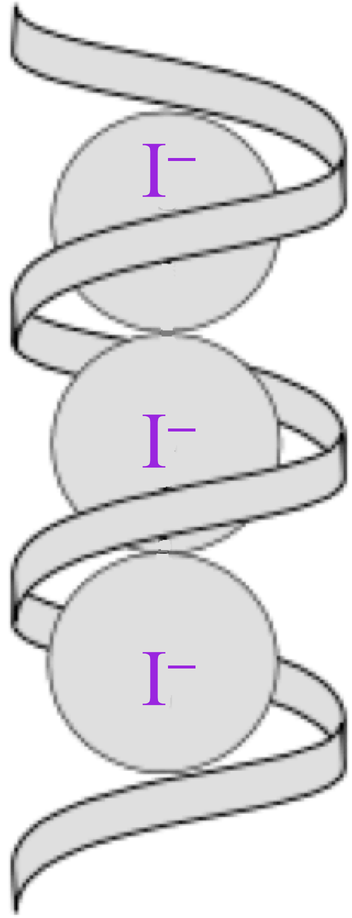
basic disaccharide: maltose



α(1→ 4) glycosidic bond

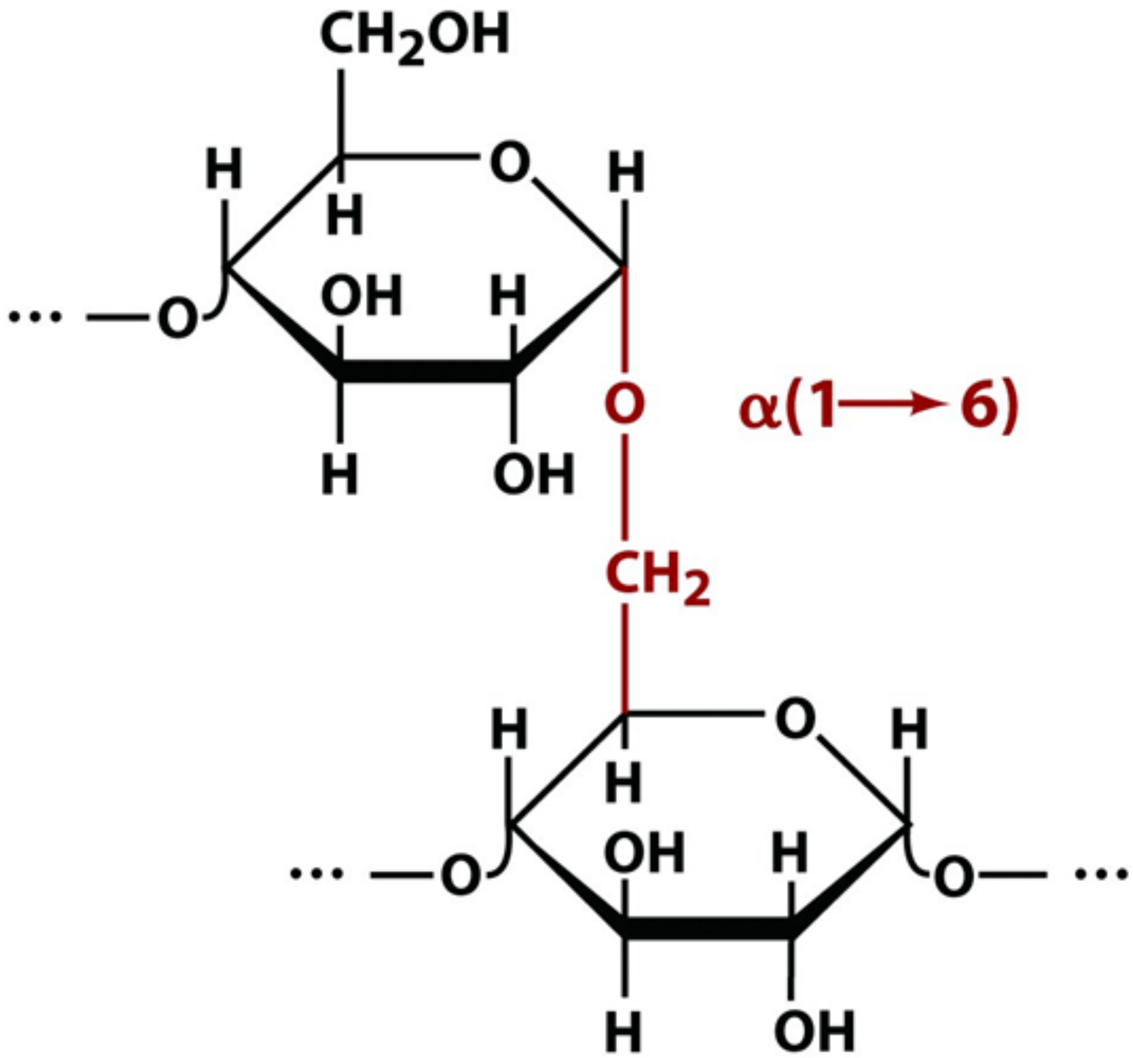
α-amylose forms a left-handed helix



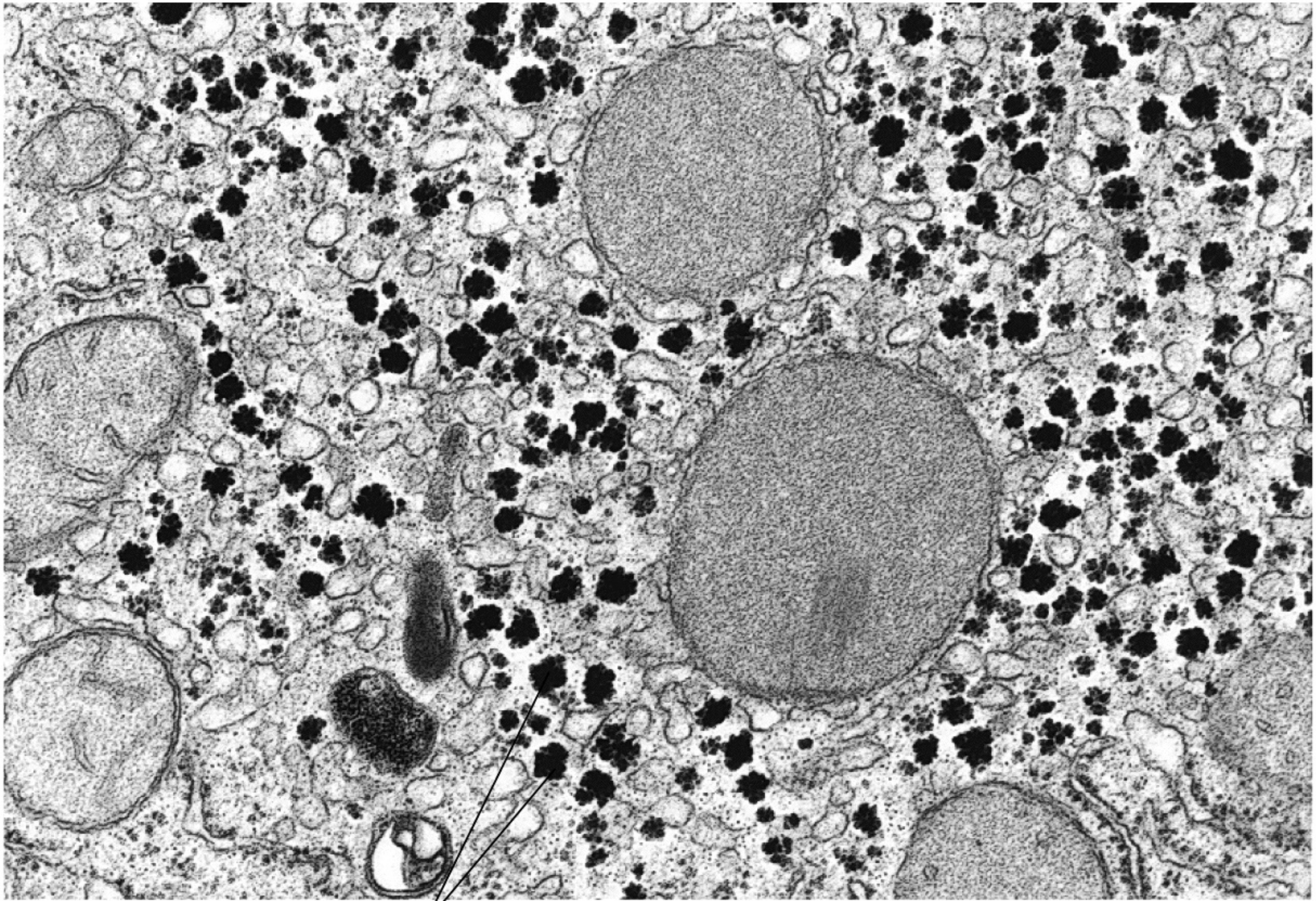


blue iodine-amylose complex

Storage polysaccharides: amylopectin & glycogen

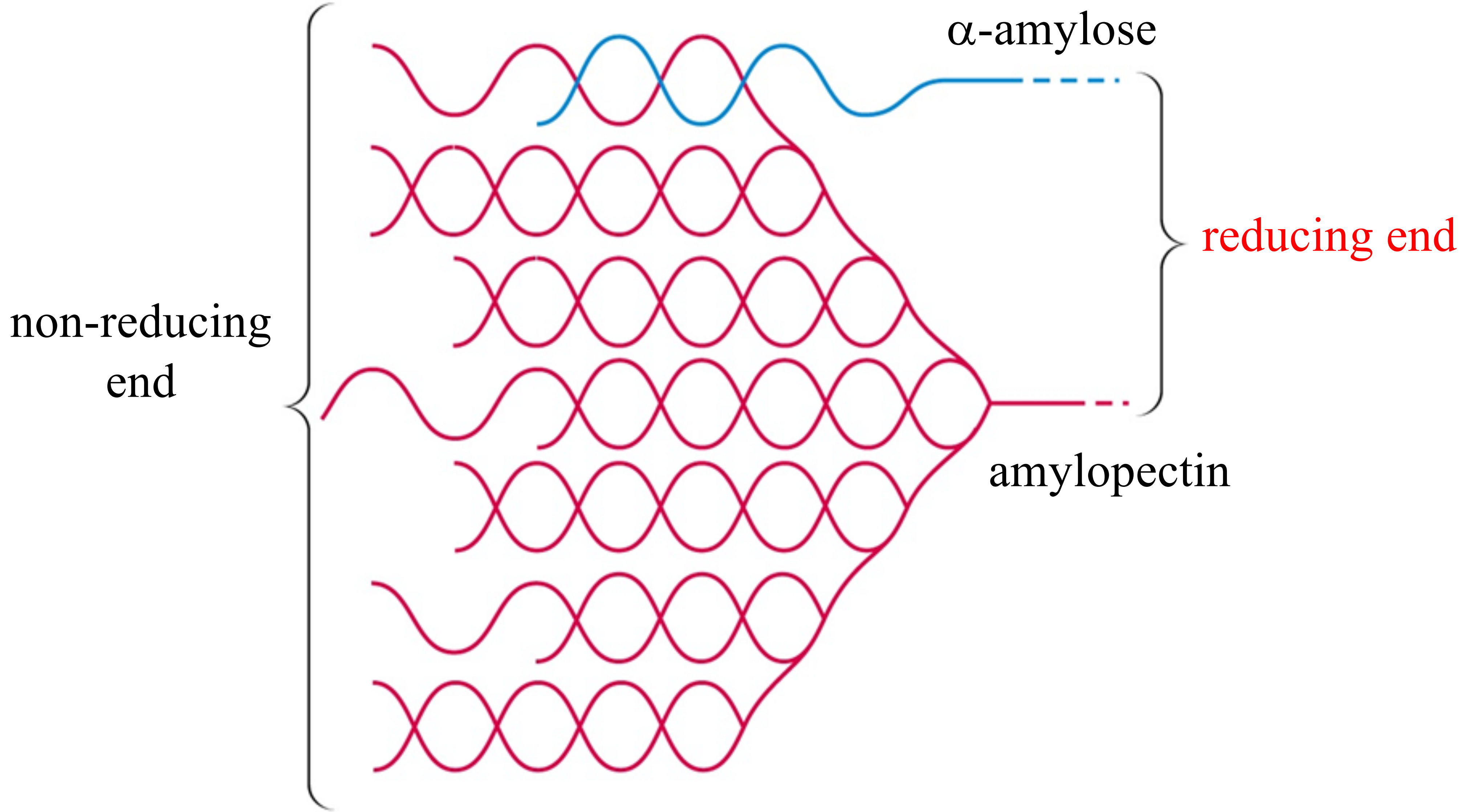


α (1→ 4) glycosidic bond with α (1→ 6) branching



glycogen granules

How many reducing ends does amylopectin (and glycogen) have?



How many reducing ends does amylopectin (and glycogen) have?