6. Carbohydrates

Carbohydrates are aldehyde or ketone compounds with multiple hydroxyl groups. They make up most of the organic matter on Earth because of their extensive roles in all forms of life

Chapter 4: Outline

6.1 Monosaccharides are aldehydes and ketones with multiple hydroxyl groups

6.2 Complex carbohydrates are formed by linkage of monosaccharides

6.3 Carbohydrates can be attached to proteins to form glycoproteins

6.4 Lectins are specific carbohydrate-binding proteins

Properties of Carbohydrates

1. Carbohydrates serve as energy stores, fuels, & metabolic intermediates

2. Ribose & deoxyribose sugars form part of the structural framework of RNA & DNA

3. Polysaccharides are structural elements in the cell walls of bacteria and plants. Cellulose is the most abundant organic compound in the biosphere

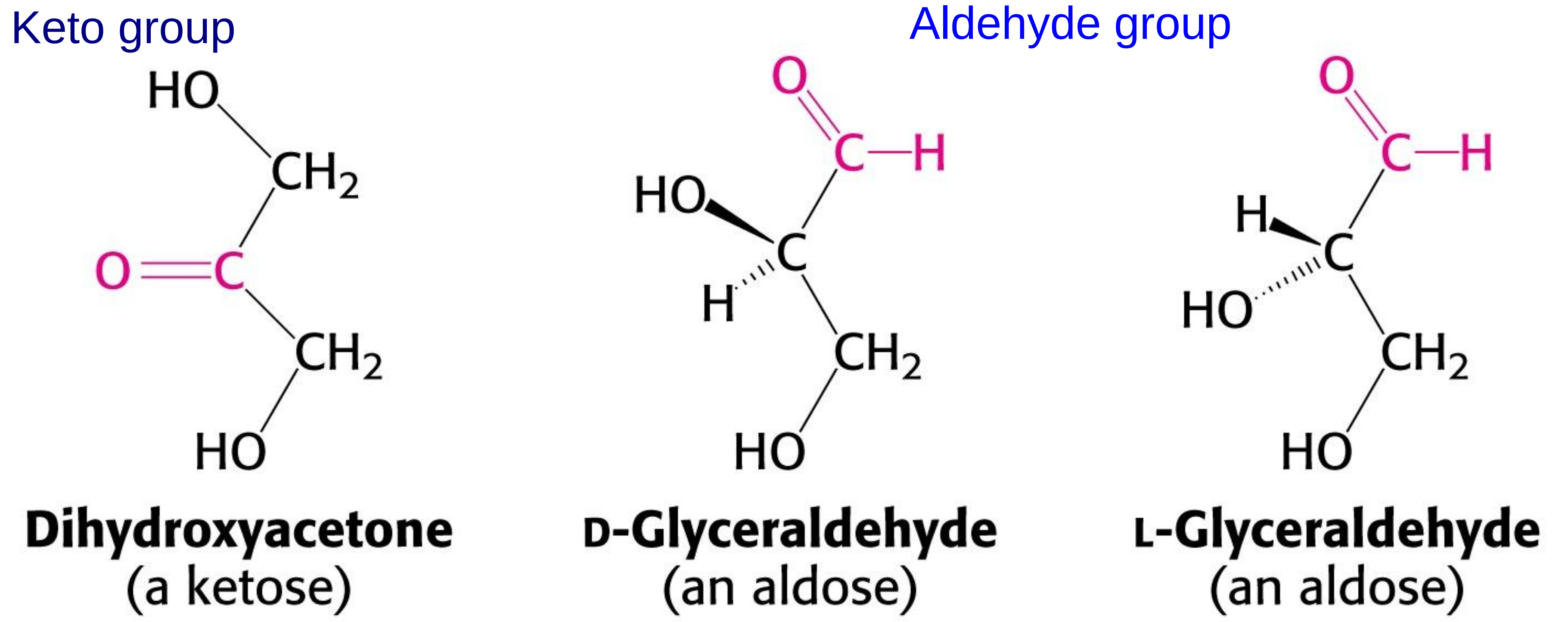
4. Carbohydrates are linked to many proteins and lipids, <u>key role in mediating interactions among cells</u> - made possible by their huge structural diversity

Monosaccharides

Simplest carbohydrates, aldehydes or ketones with two or more hydroxyl groups

Empirical formula, $(C\text{-}H_2O)_n$, literally a “carbon hydrate”

Smallest monosaccharides are trioses (n = 3)

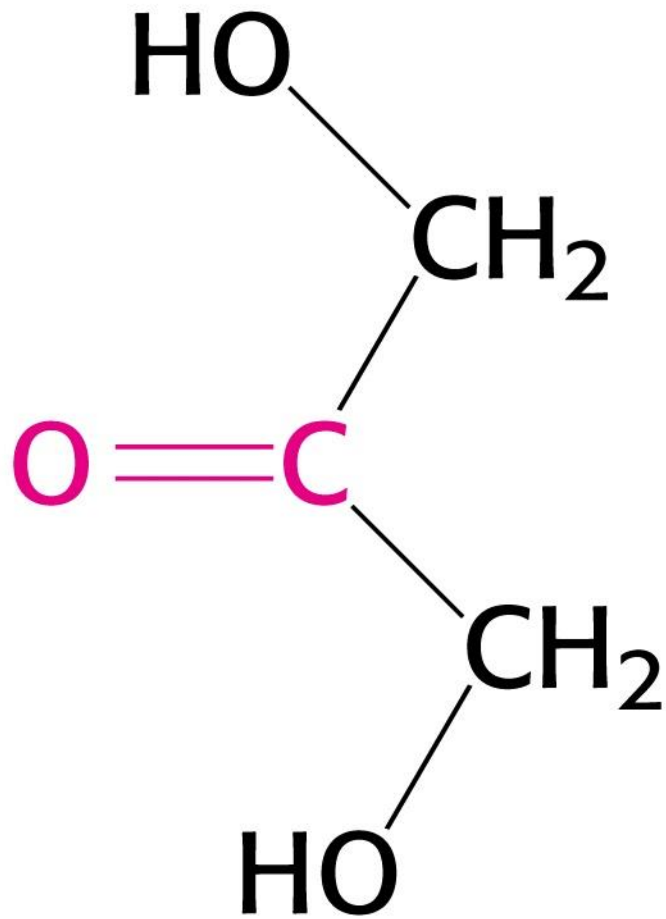


Glyceraldehyde has 1 asymmetric C, thus,
2 stereoisomers (D- & L-), are enantiomers, mirror images of each other

Dihydroxyacetone

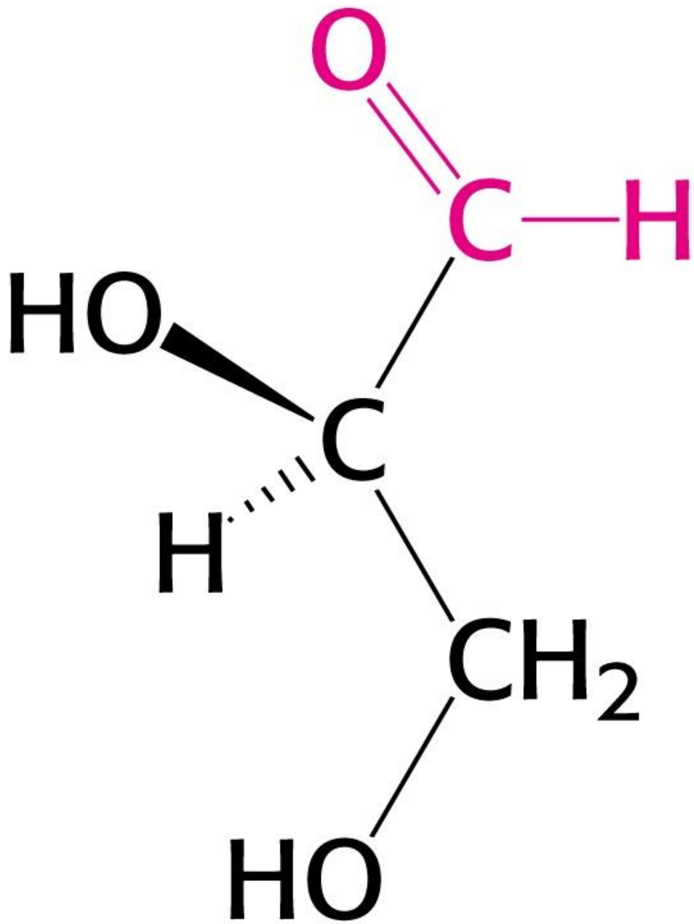
No asymmetric carbon

Keto group



Dihydroxyacetone
(a ketose)

D-Glyceraldehyde

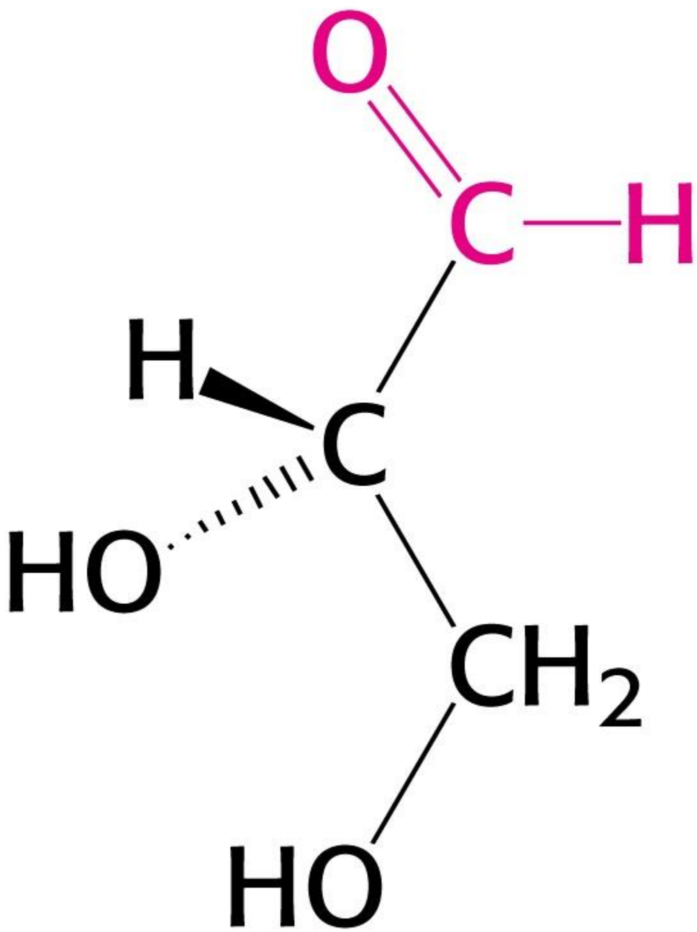


Aldehyde group

Asymmetric carbon

D-Glyceraldehyde
(an aldose)

L-Glyceraldehyde

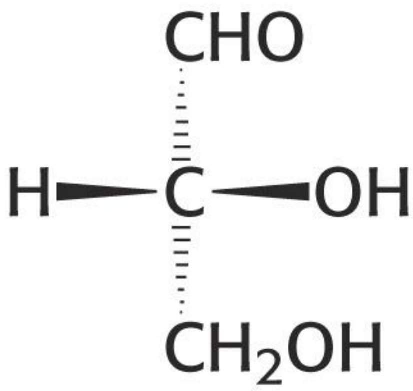


Aldehyde group

Asymmetric carbon

L-Glyceraldehyde
(an aldose)

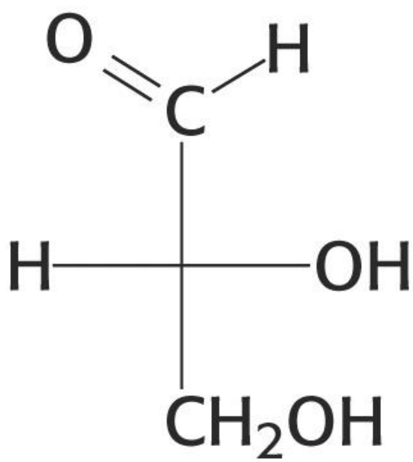
Fischer Projections



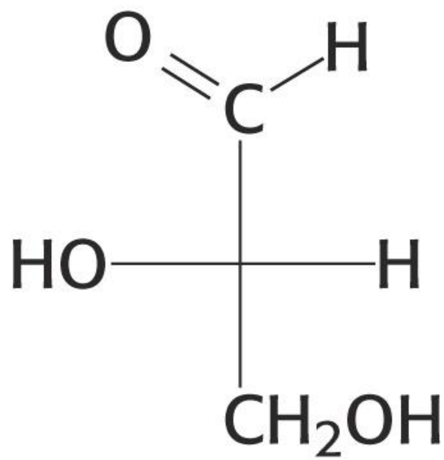
Stereochemical relations:

Horizontal bonds; in front of page plane

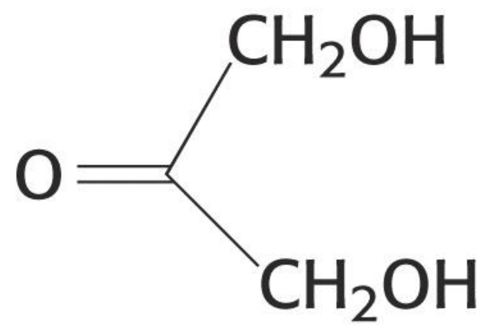
Vertical bonds; behind plane



D-Glyceraldehyde



L-Glyceraldehyde



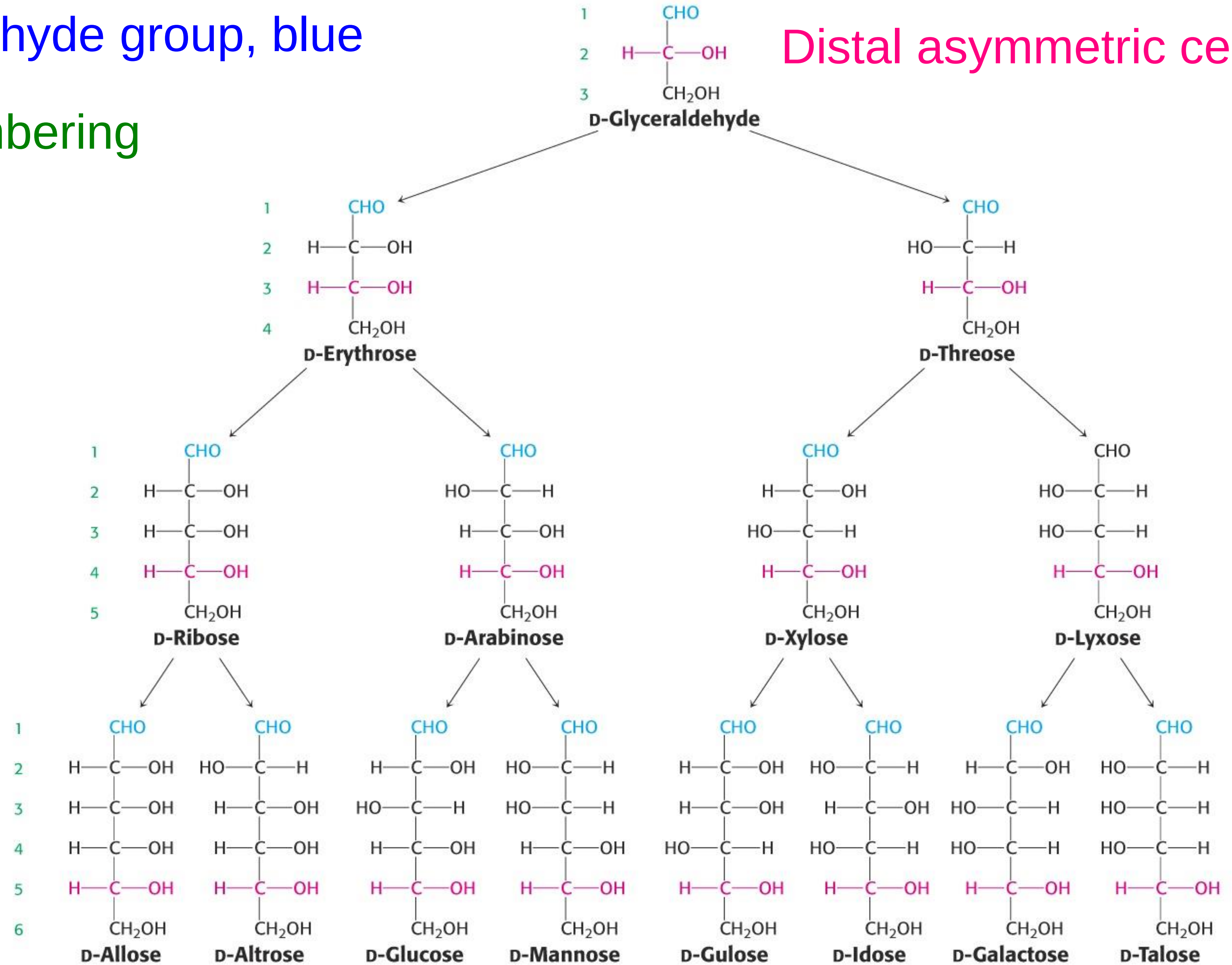
Dihydroxyacetone

D-Aldoses (3,4,5, & 6 carbons)

Aldehyde group, blue

Numbering

Distal asymmetric center

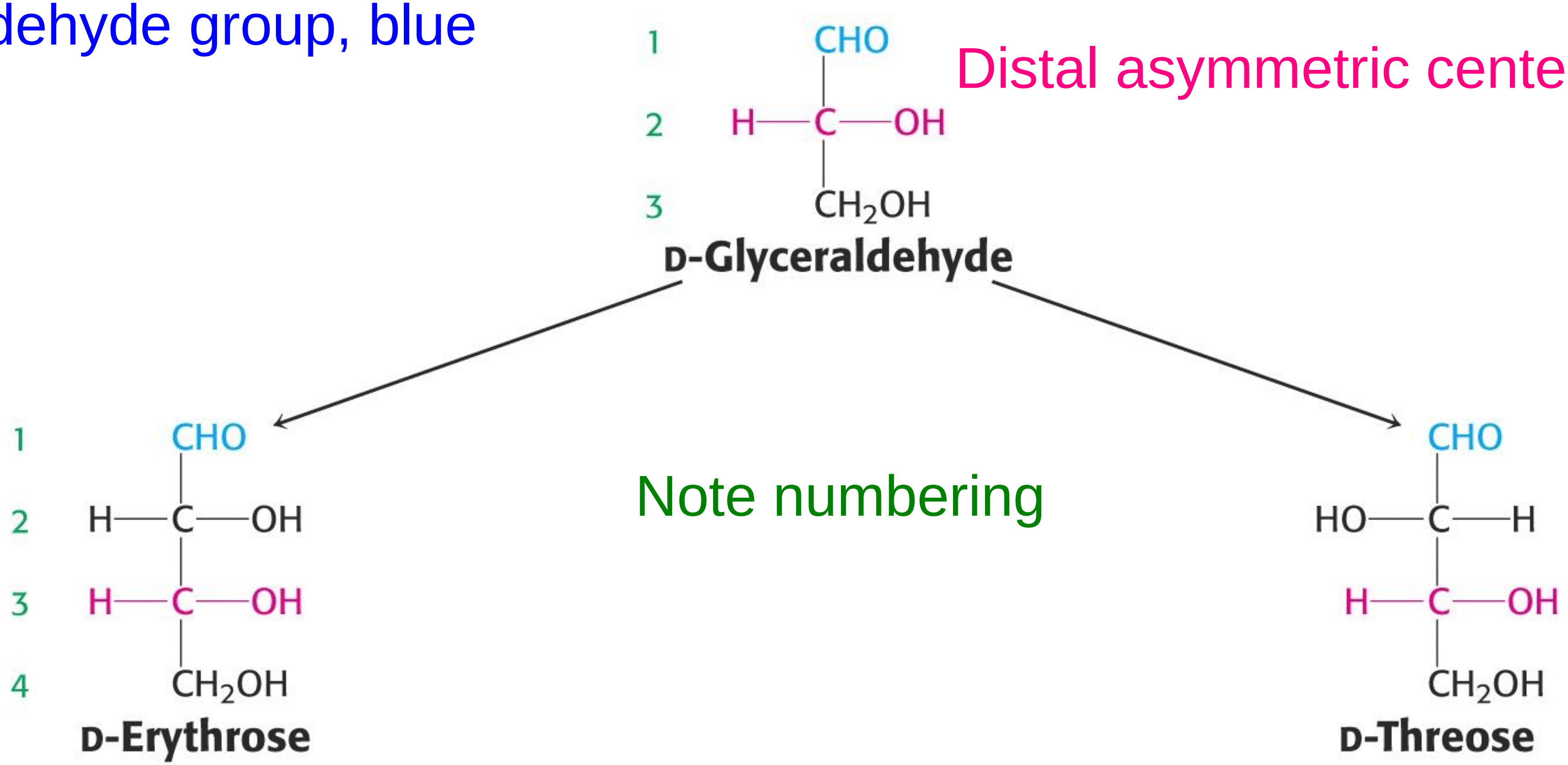


Triose & tetroses

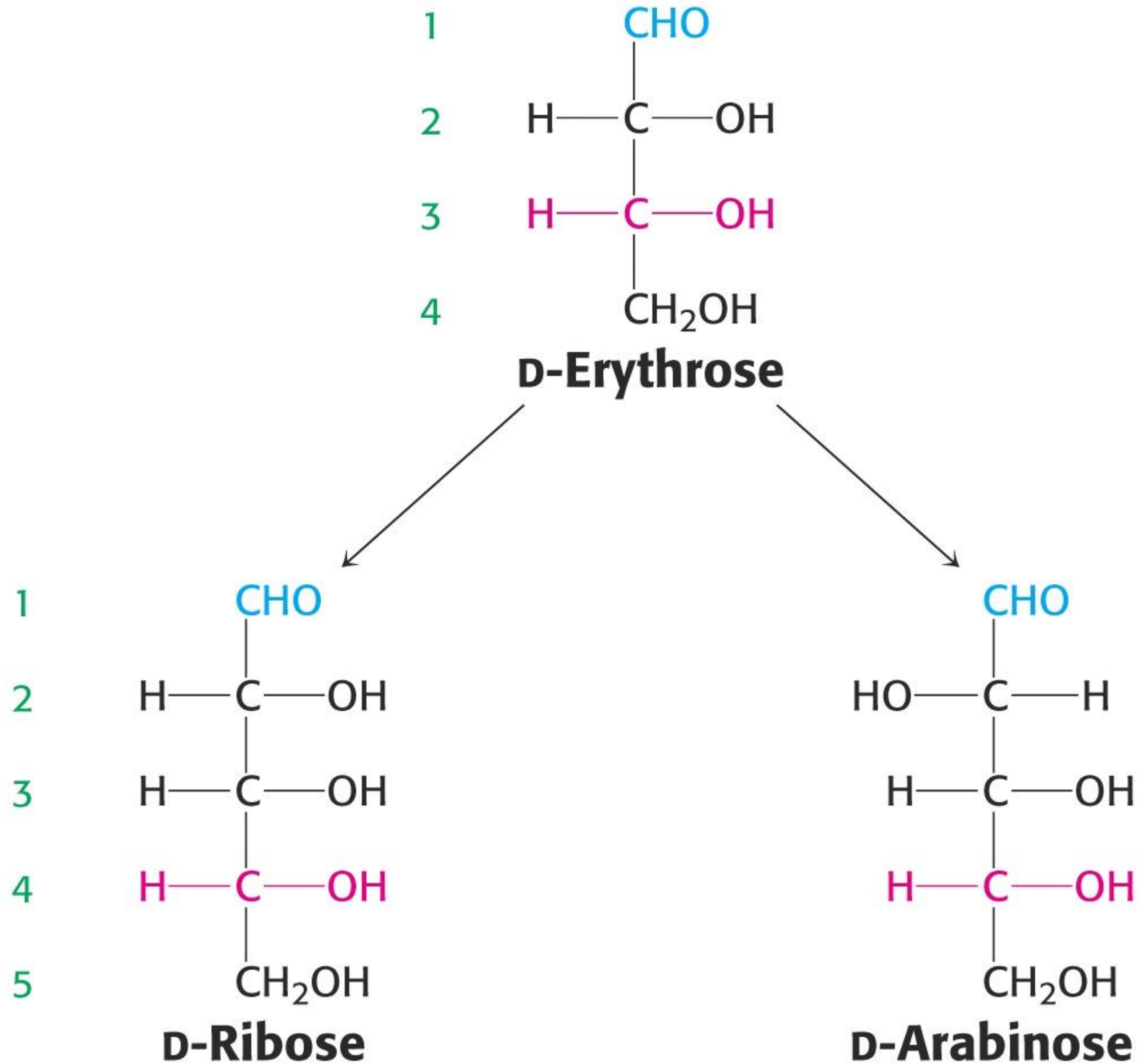
Aldehyde group, blue

Distal asymmetric center

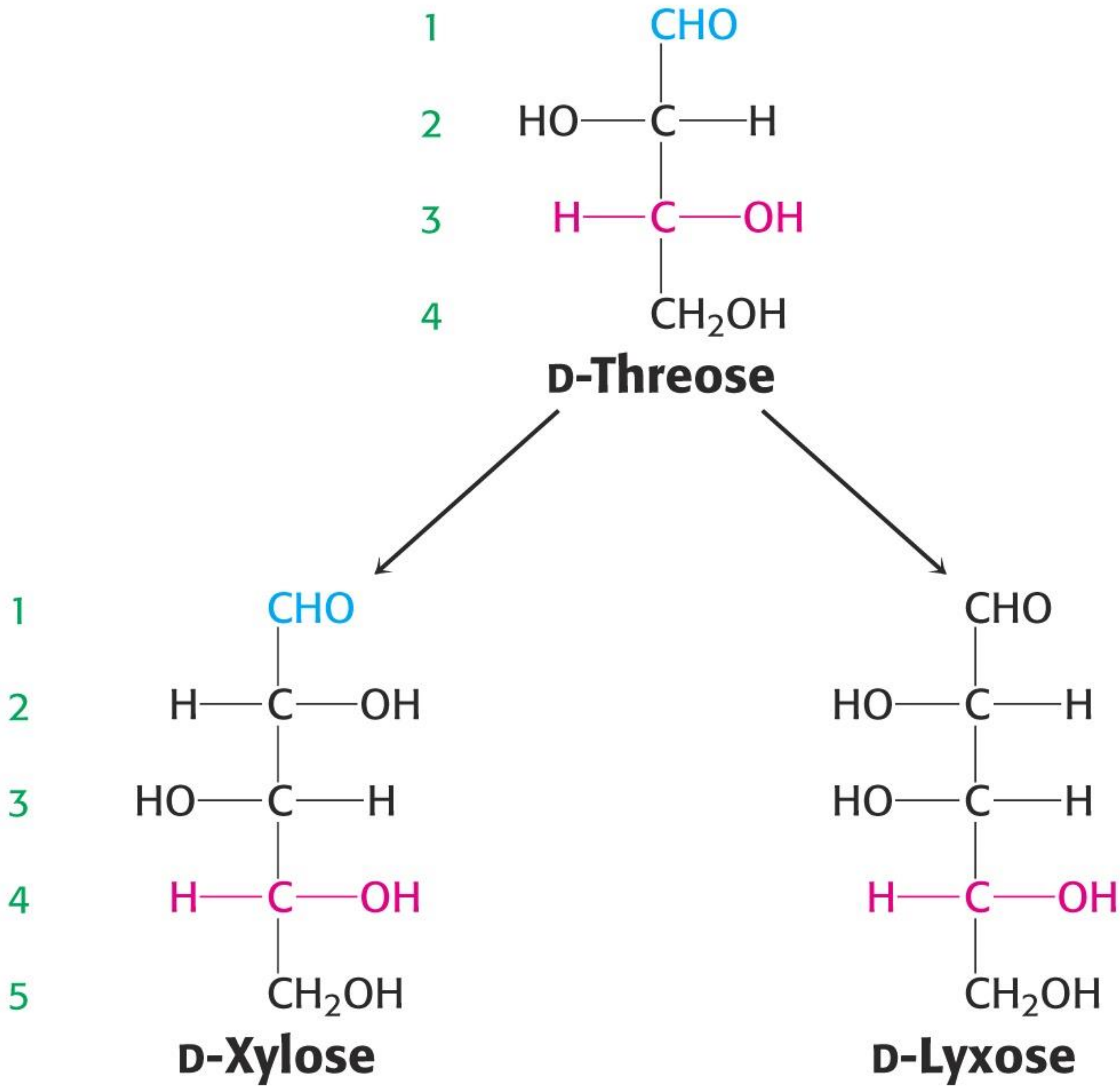
Note numbering



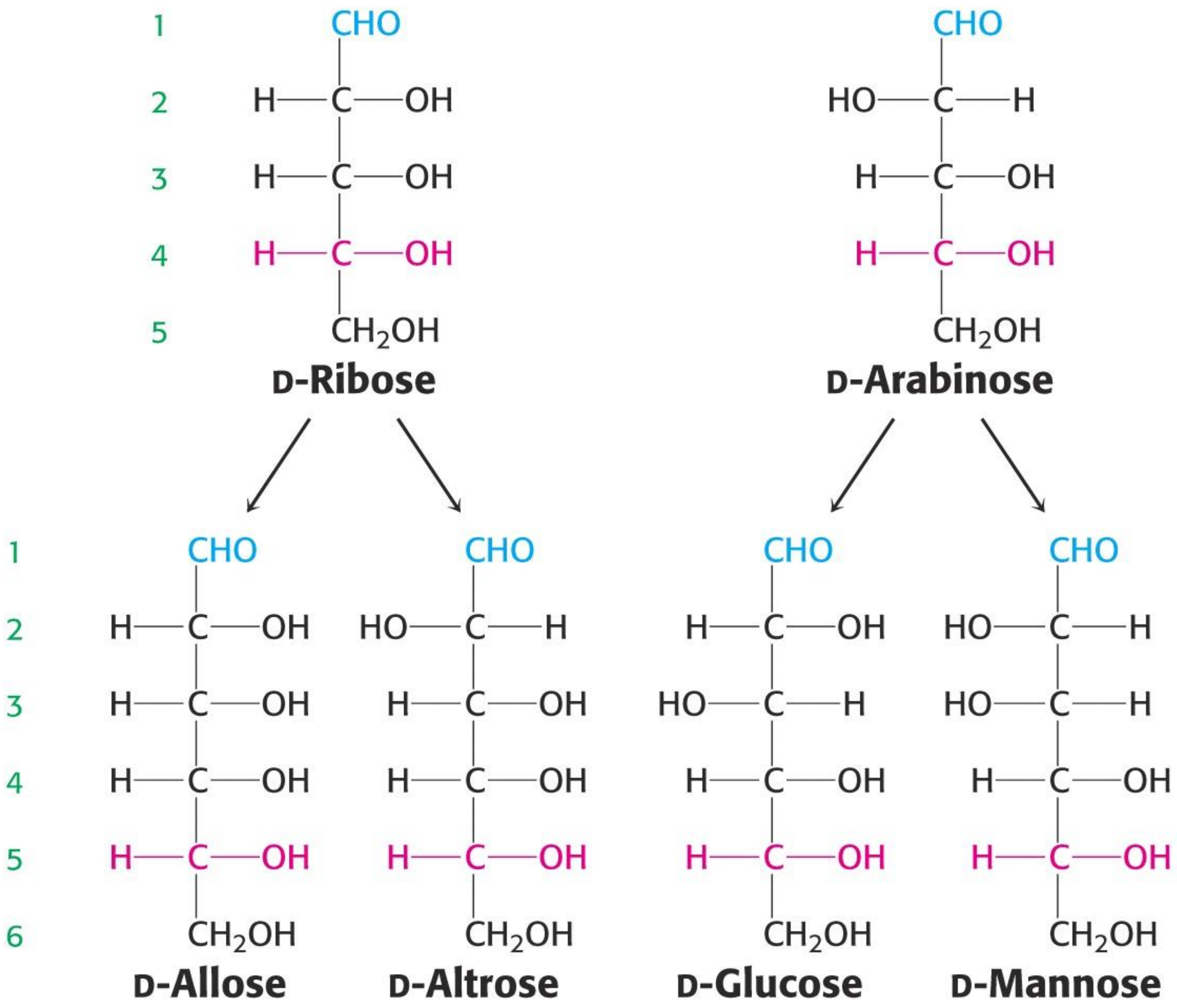
Tetrose & Pentoses



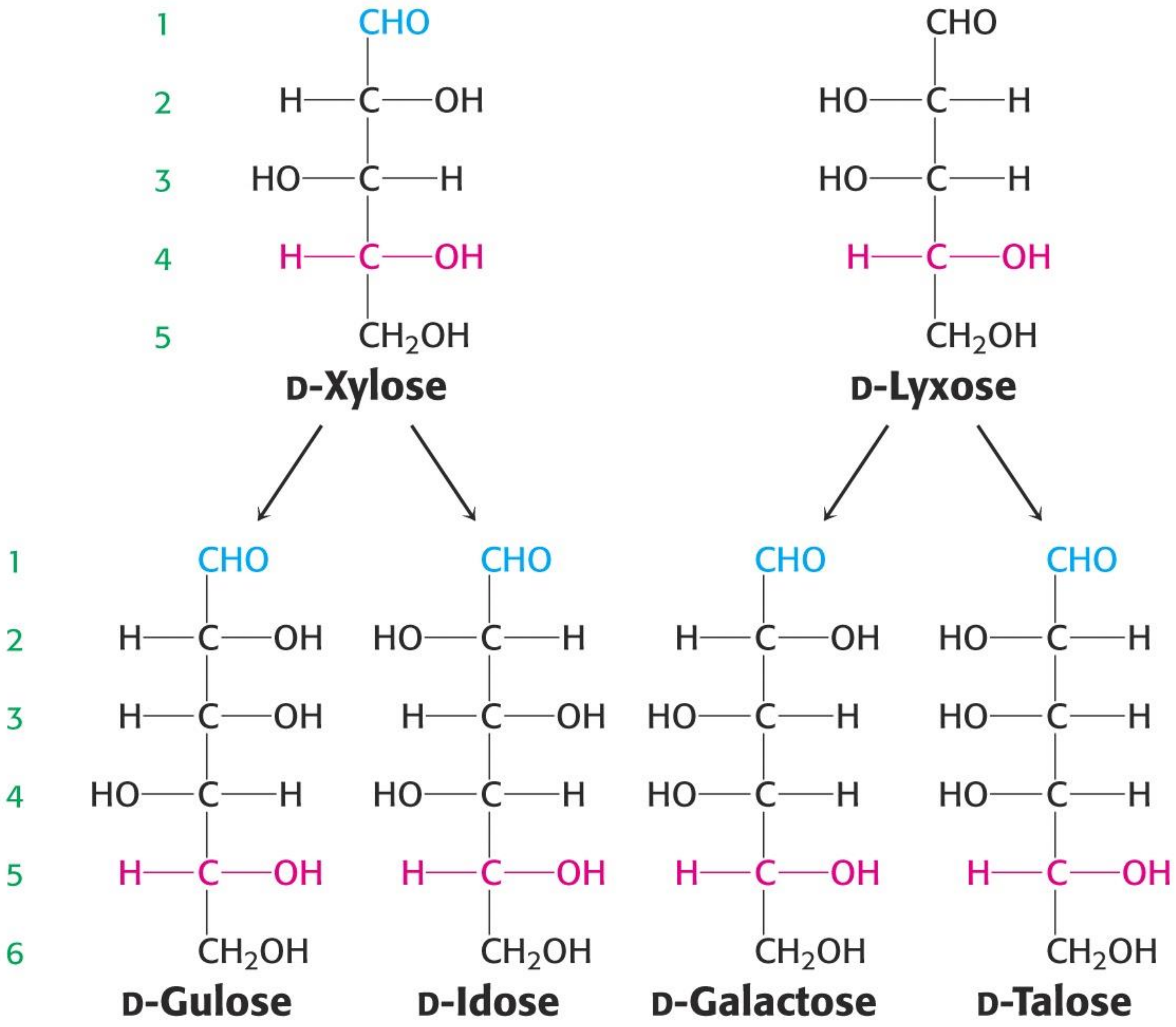
Tetrose & Pentoses



Pentoses & Hexoses



Pentoses & Hexoses

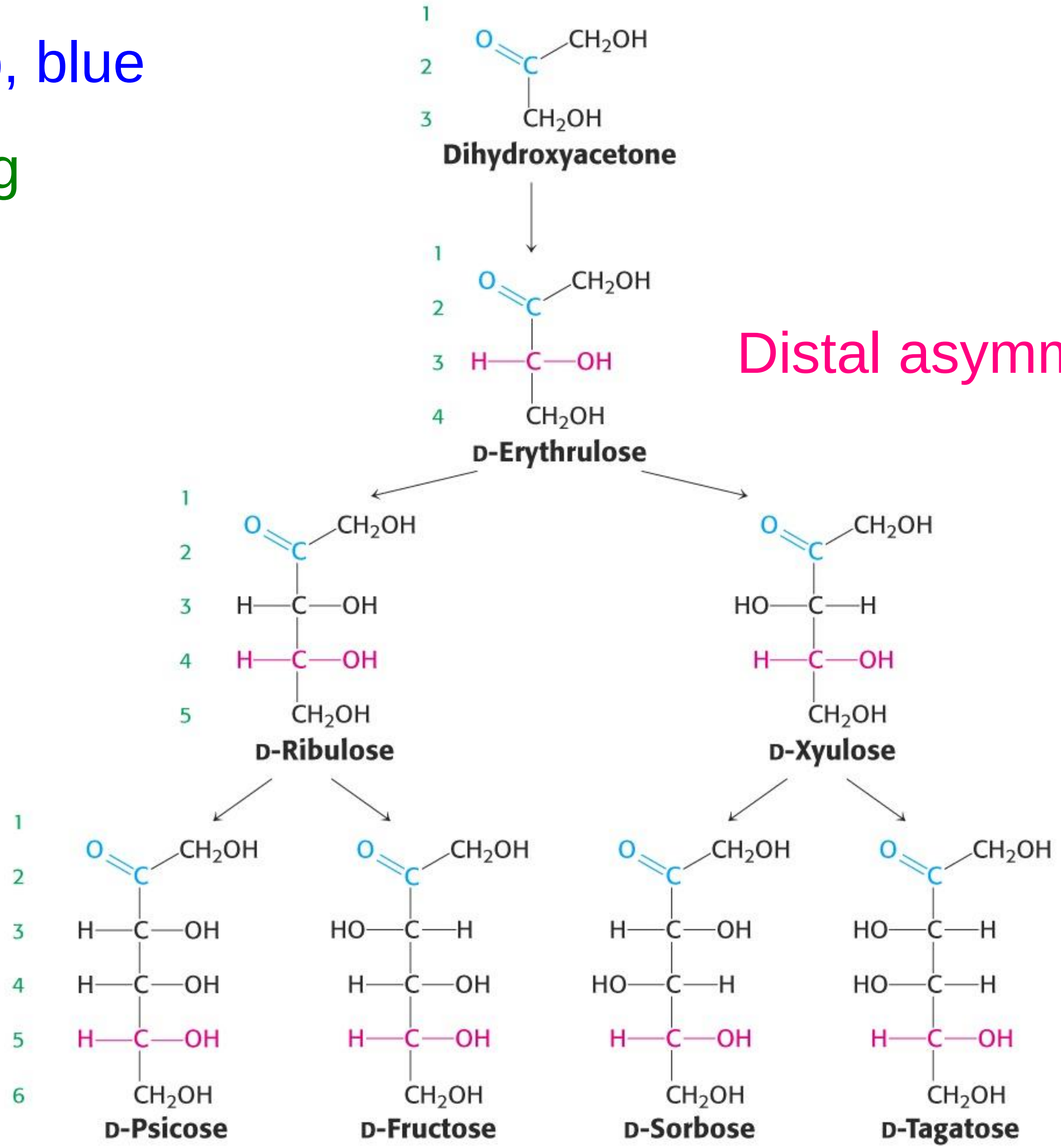


D-Ketoses (3,4,5, & 6 carbons)

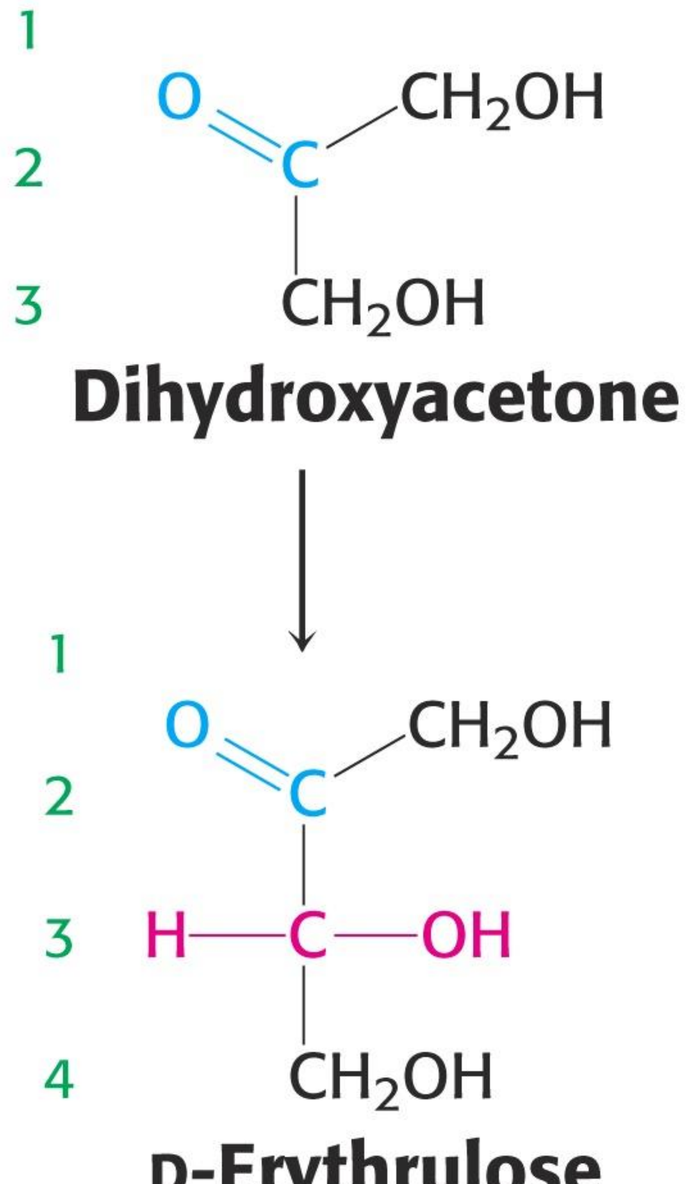
Keto group, blue

Numbering

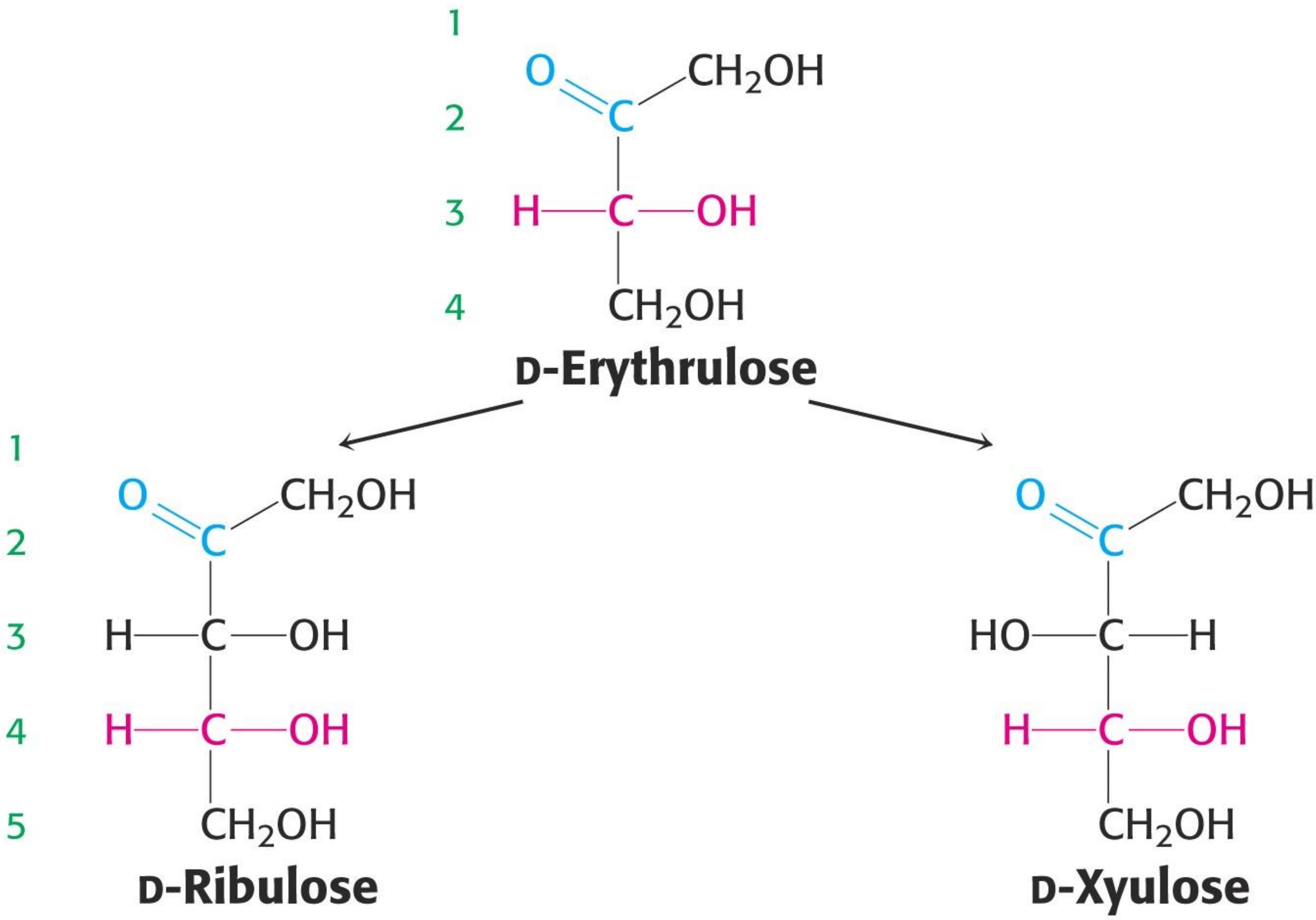
Distal asymmetric center



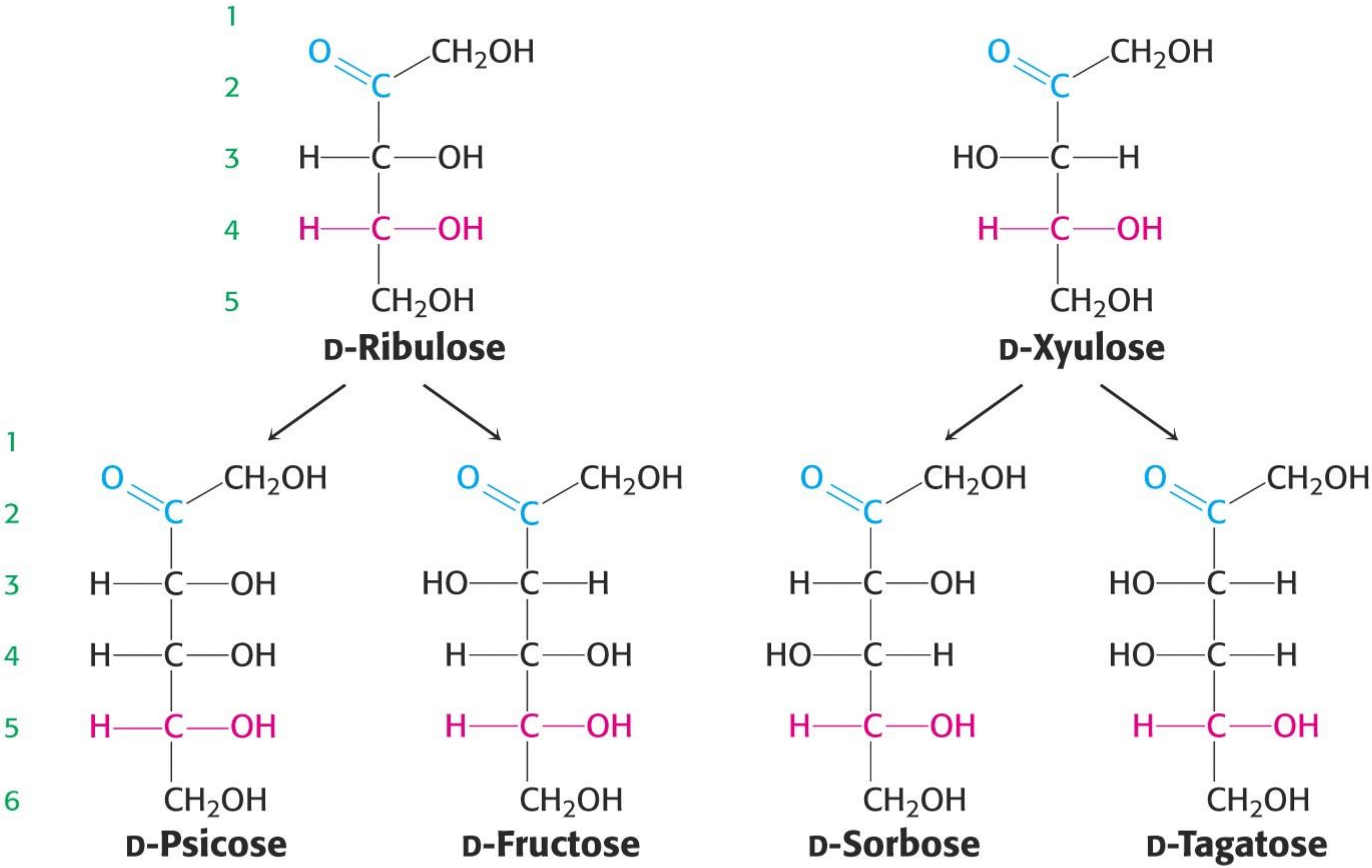
Triose & tetrose



Tetrose & Pentoses

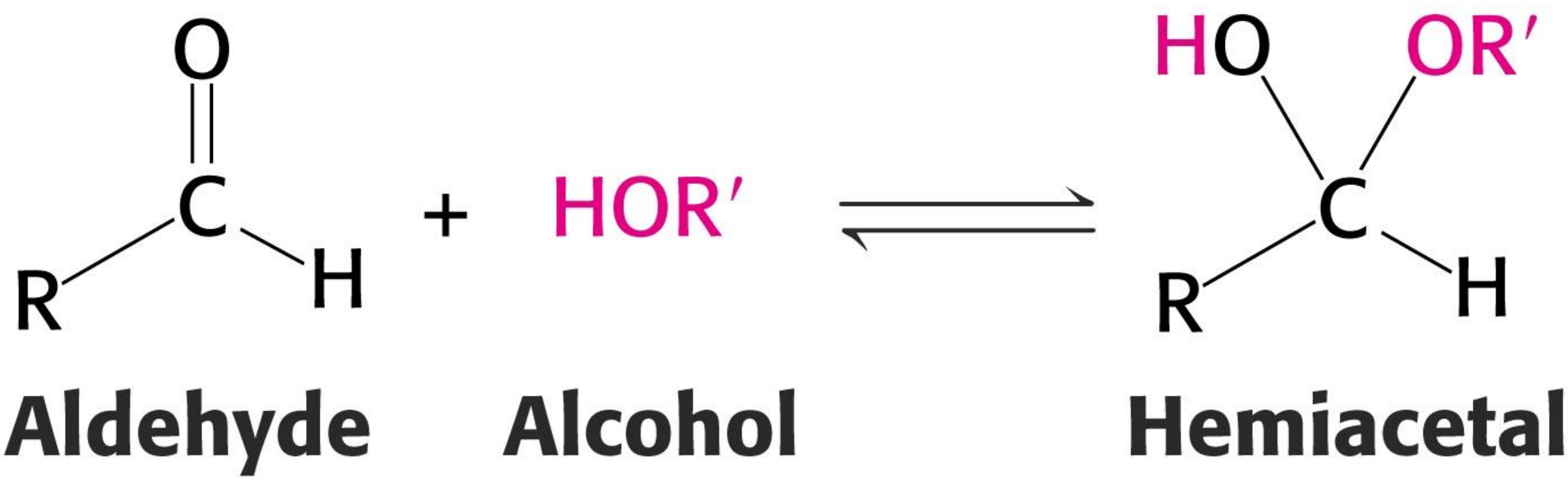


Pentoses & Hexoses



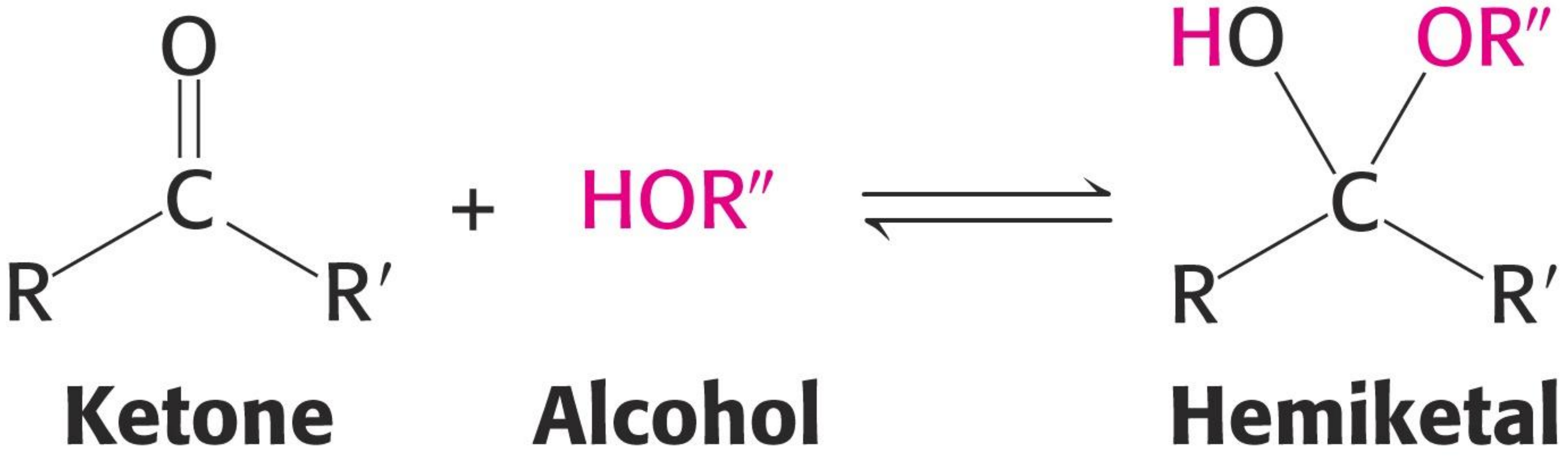
Aldehydes cyclize (pentoses & hexoses)

An aldehyde can react with an alcohol to form a hemiacetal



Ketones cyclize (pentoses & hexoses)

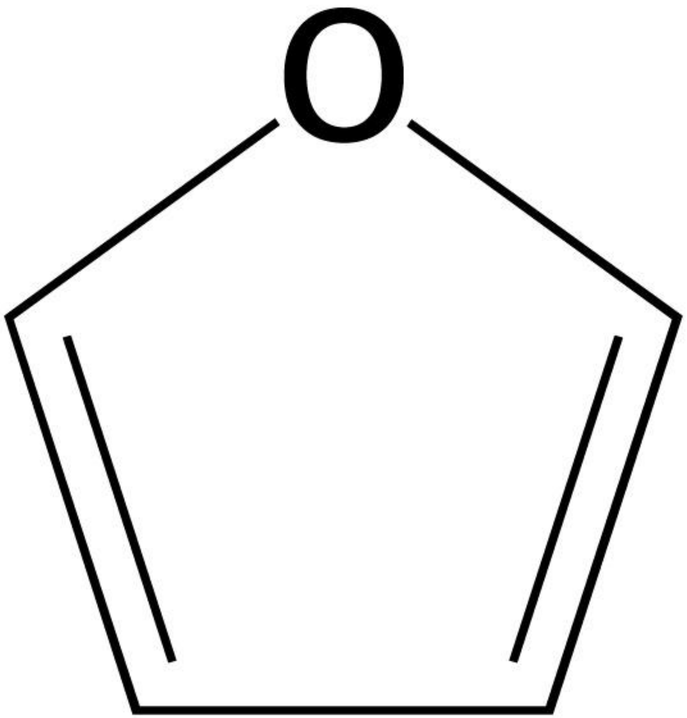
A ketone can react with an alcohol to form a <u>hemiketal</u>



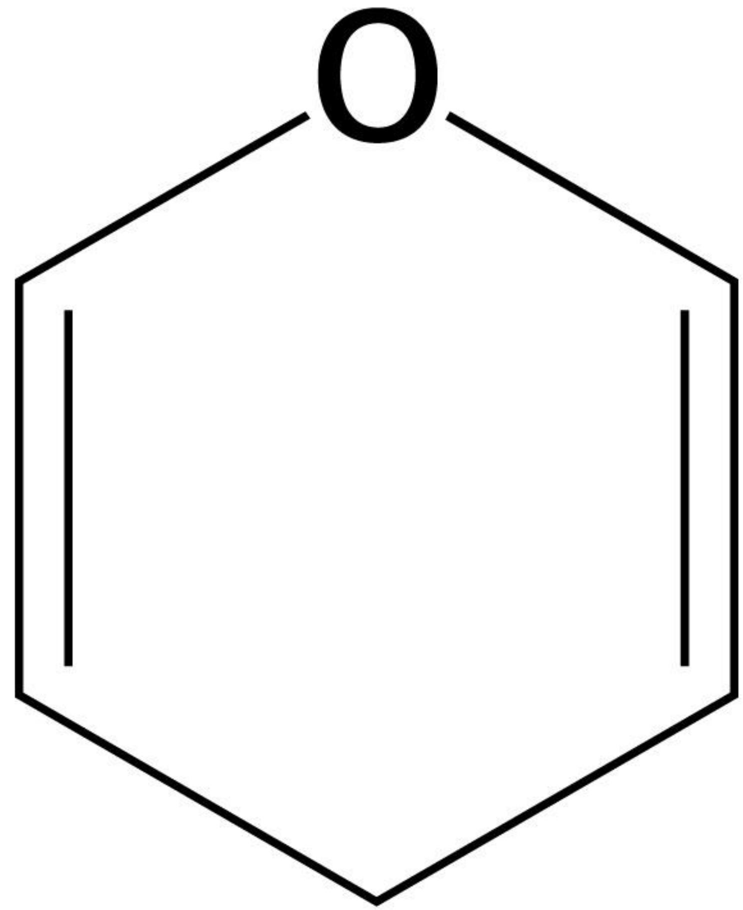
5 & 6 membered rings

Furanose

Pyranose

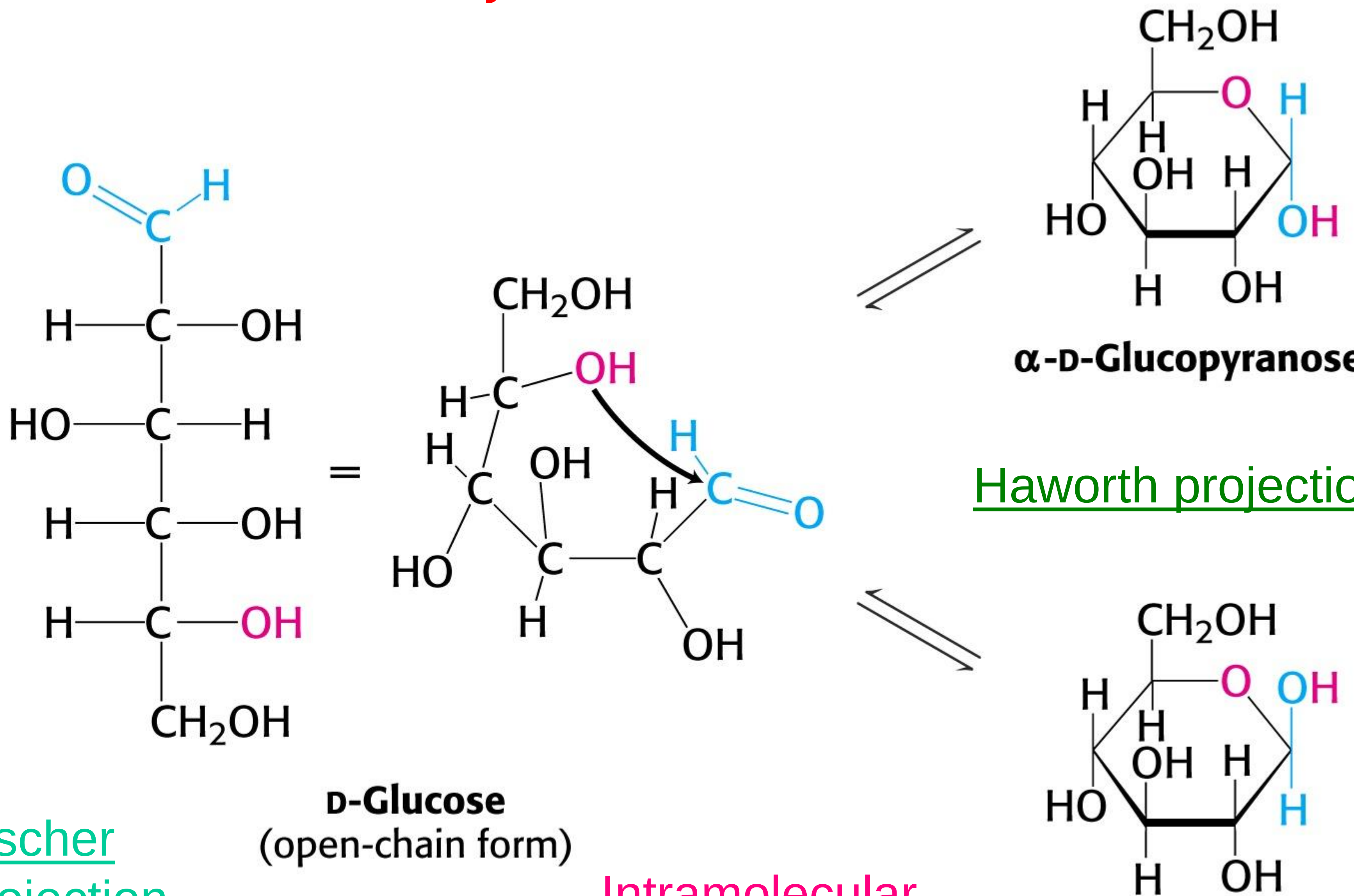


Furan



Pyran

Pyranose formation



D-Glucose
(open-chain form)

α-D-Glucopyranose

β-D-Glucopyranose

Haworth projection

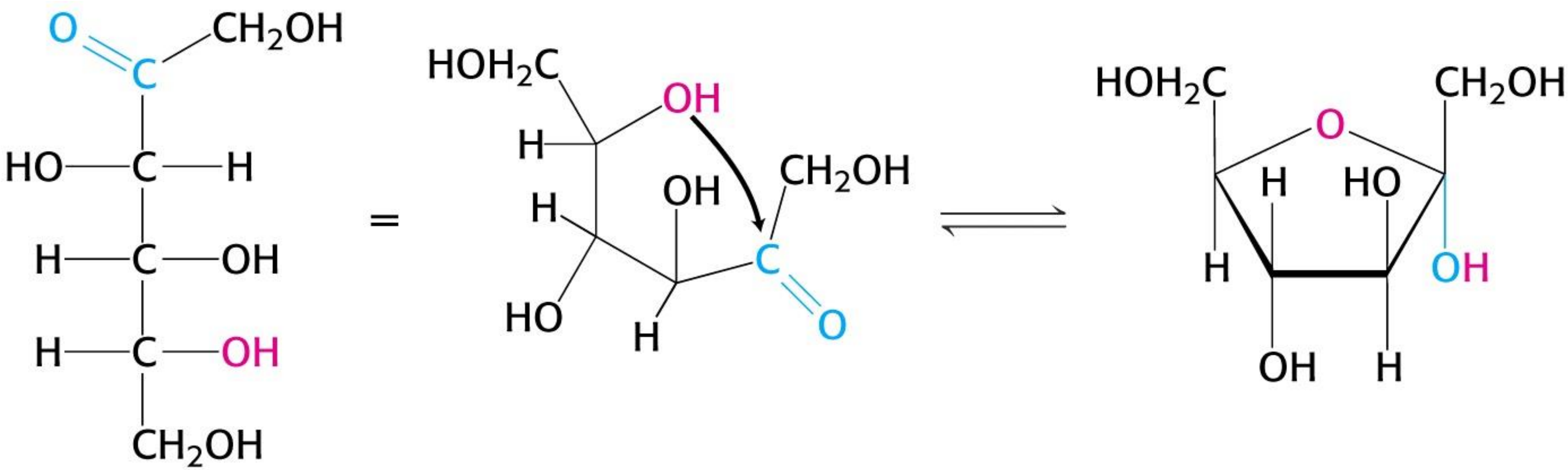
Fischer projection

Intramolecular hemiacetal,
2 anomers, α & β at C1

D & L enantiomers at C5

Furanose formation (from hexose)

Haworth projection



D-Fructose
(open-chain form)

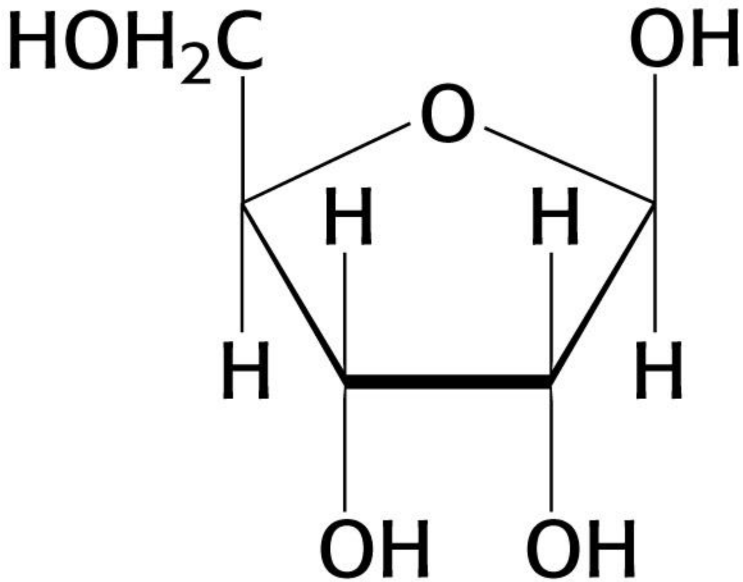
α-D-Fructofuranose
(a cyclic form of fructose)

Fischer projection

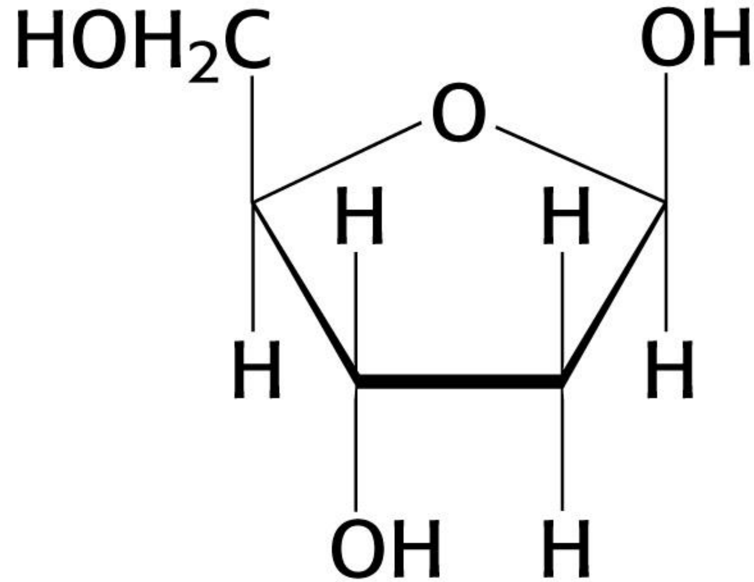
Intramolecular hemiketal,
2 anomers, α & β at C2

D & L enantiomers at C5

Furanose formation (from pentoses)



D-Ribose



2-Deoxy-D-ribose

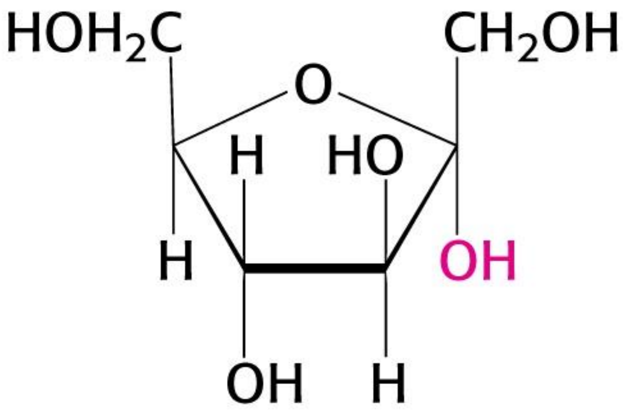
C-1 is anomeric carbon,

α-anomer, OH below ring plane

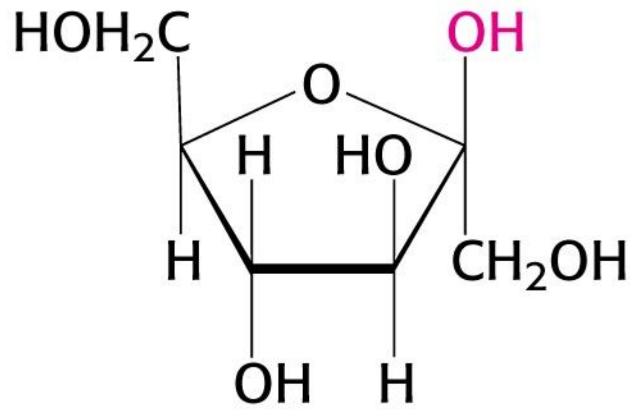
β-anomer, OH above the plane

D & L enantiomers at C4

Fructose ring structures

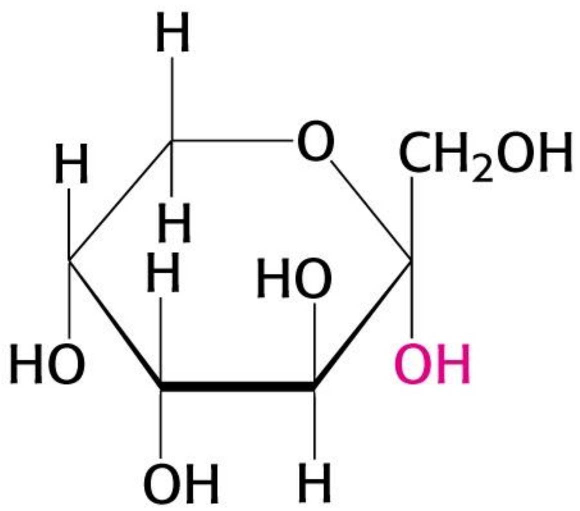


α-D-Fructofuranose

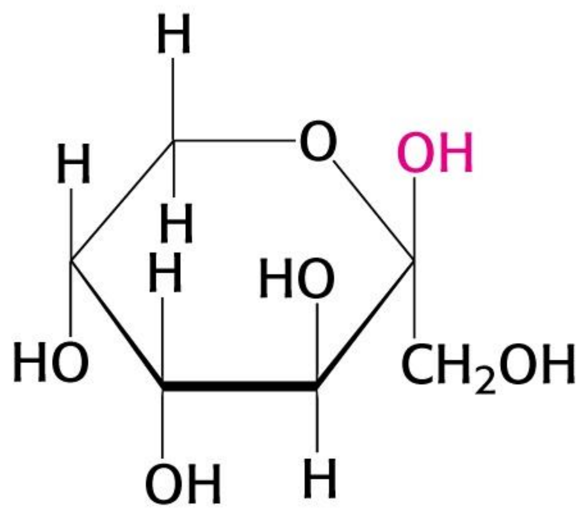


β-D-Fructofuranose

C5 to C2 bond



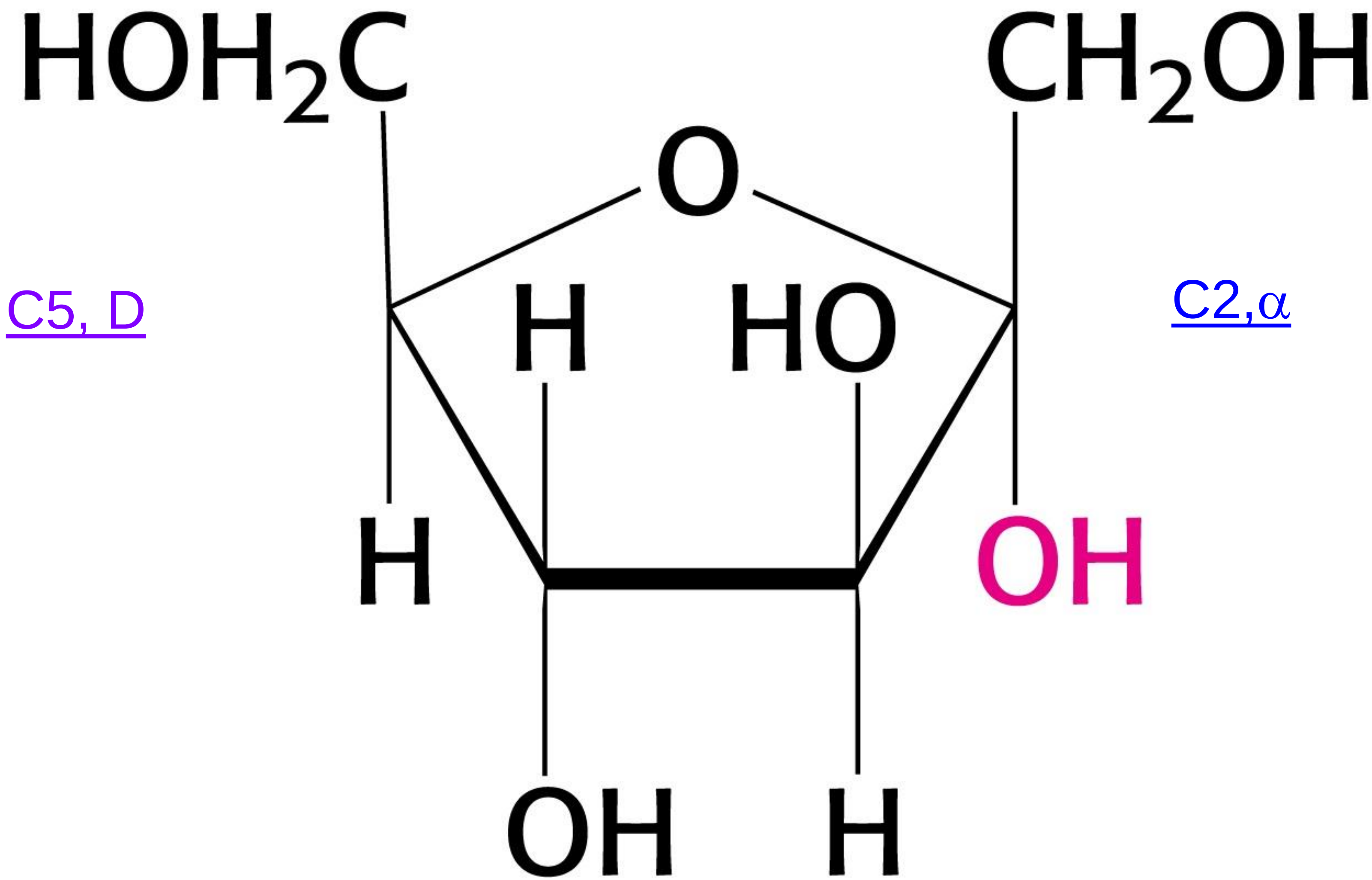
α-D-Fructopyranose



β-D-Fructopyranose

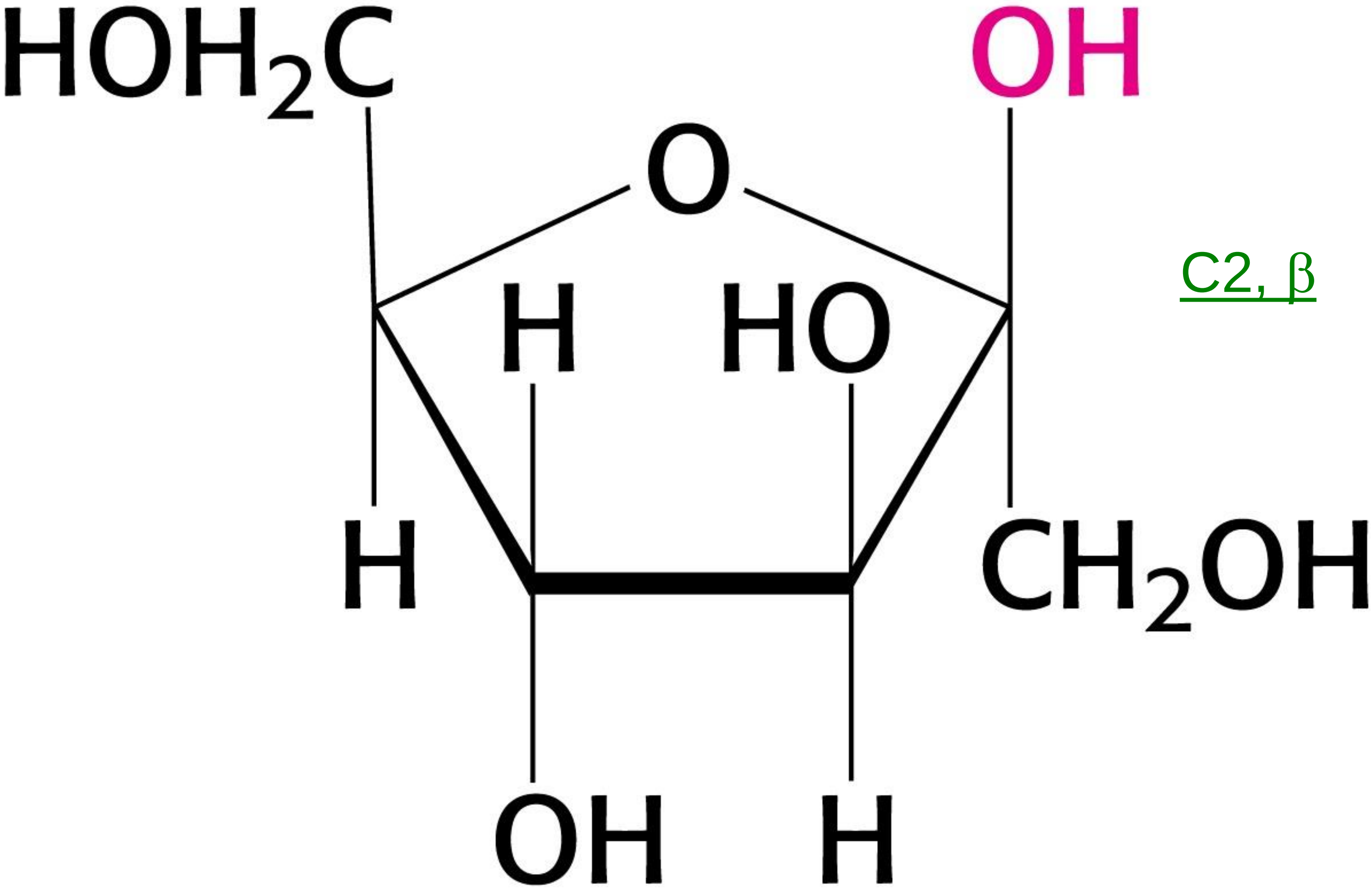
C6 to C2 bond

α-D-Fructofuranose



α-D-Fructofuranose

β-D-Fructofuranose

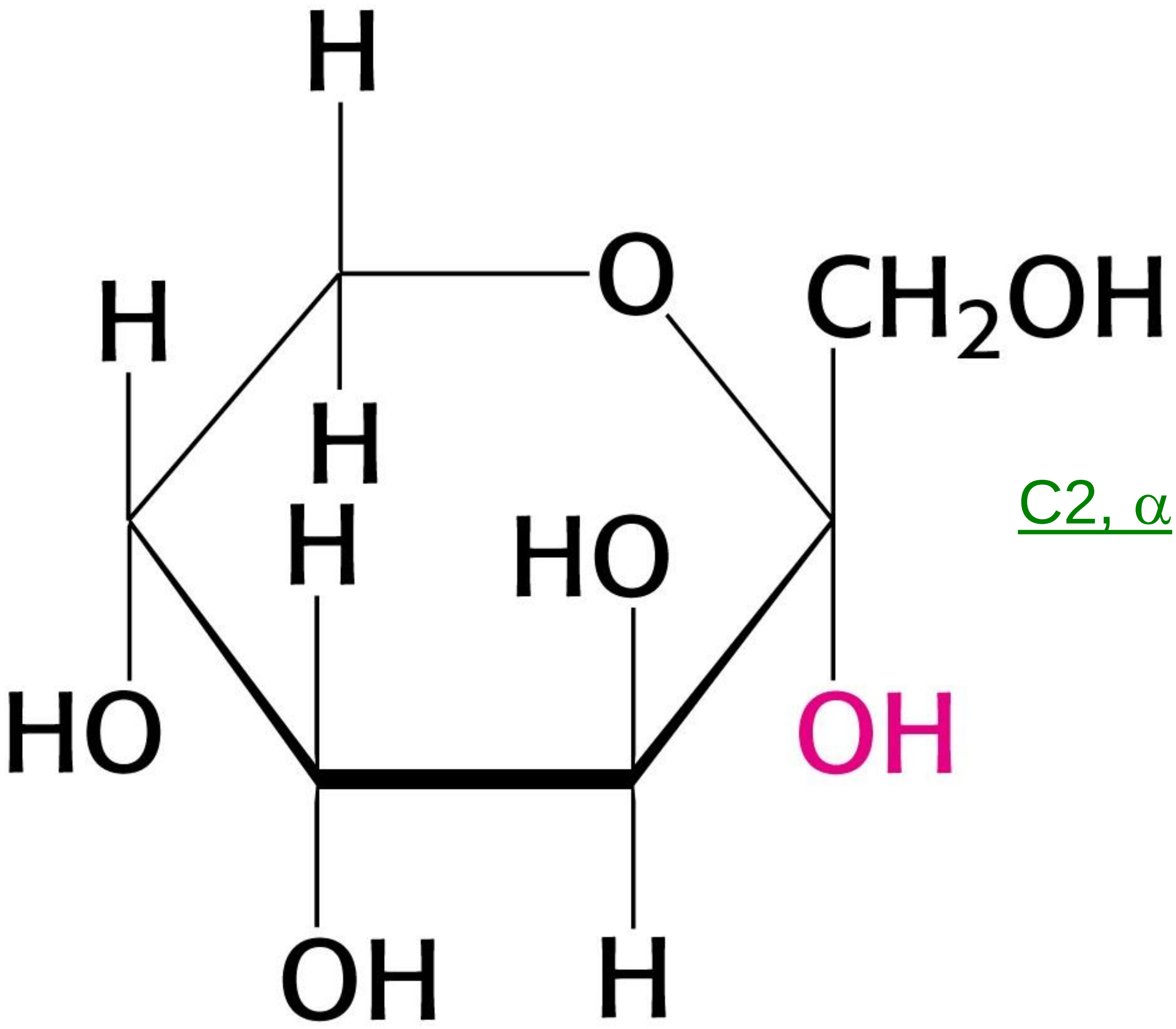


C2, β

β-D-Fructofuranose

α-D-Fructopyranose

[C5, D](#)

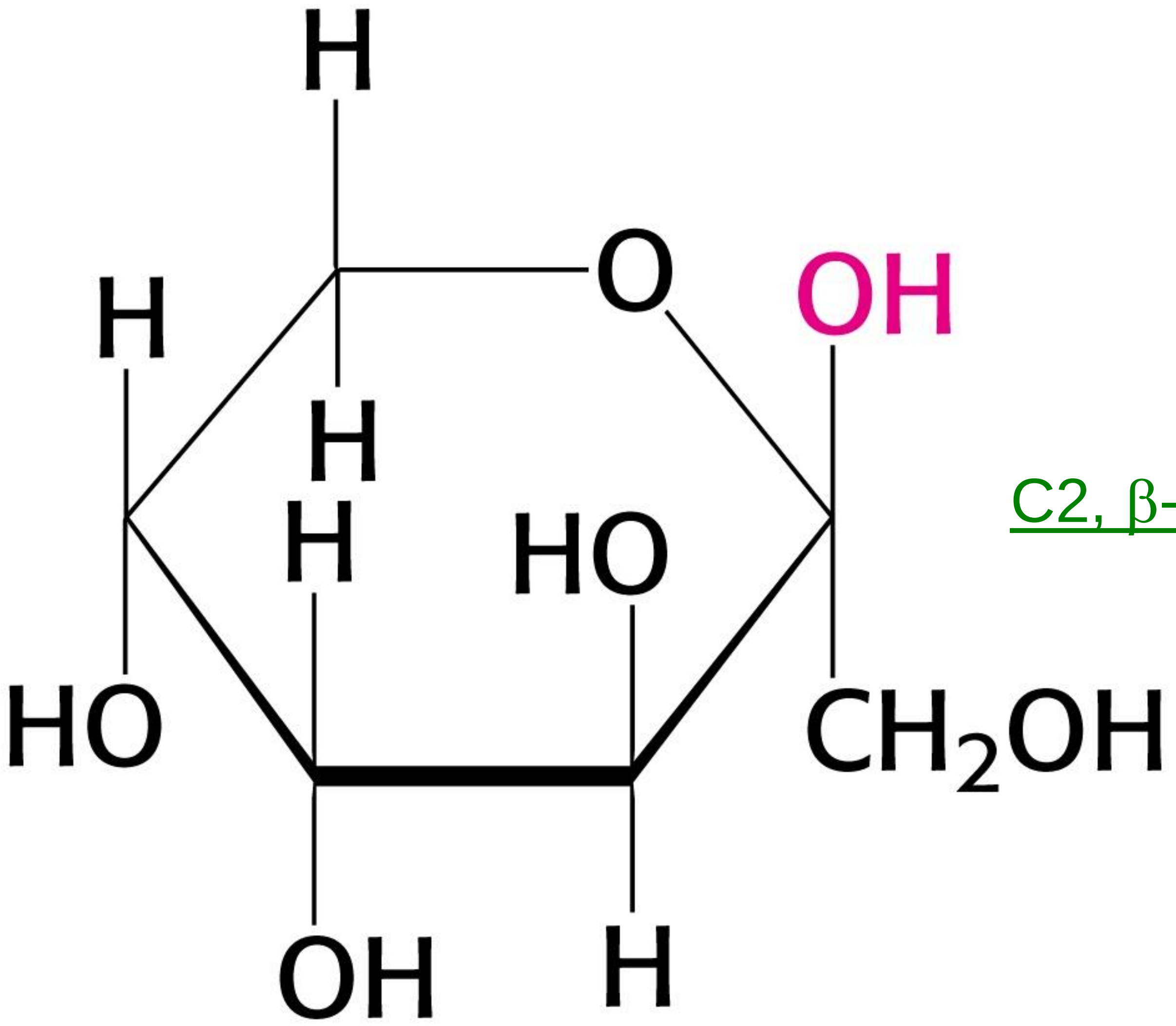


[C2, α](#)

α-D-Fructopyranose

β-D-Fructopyranose

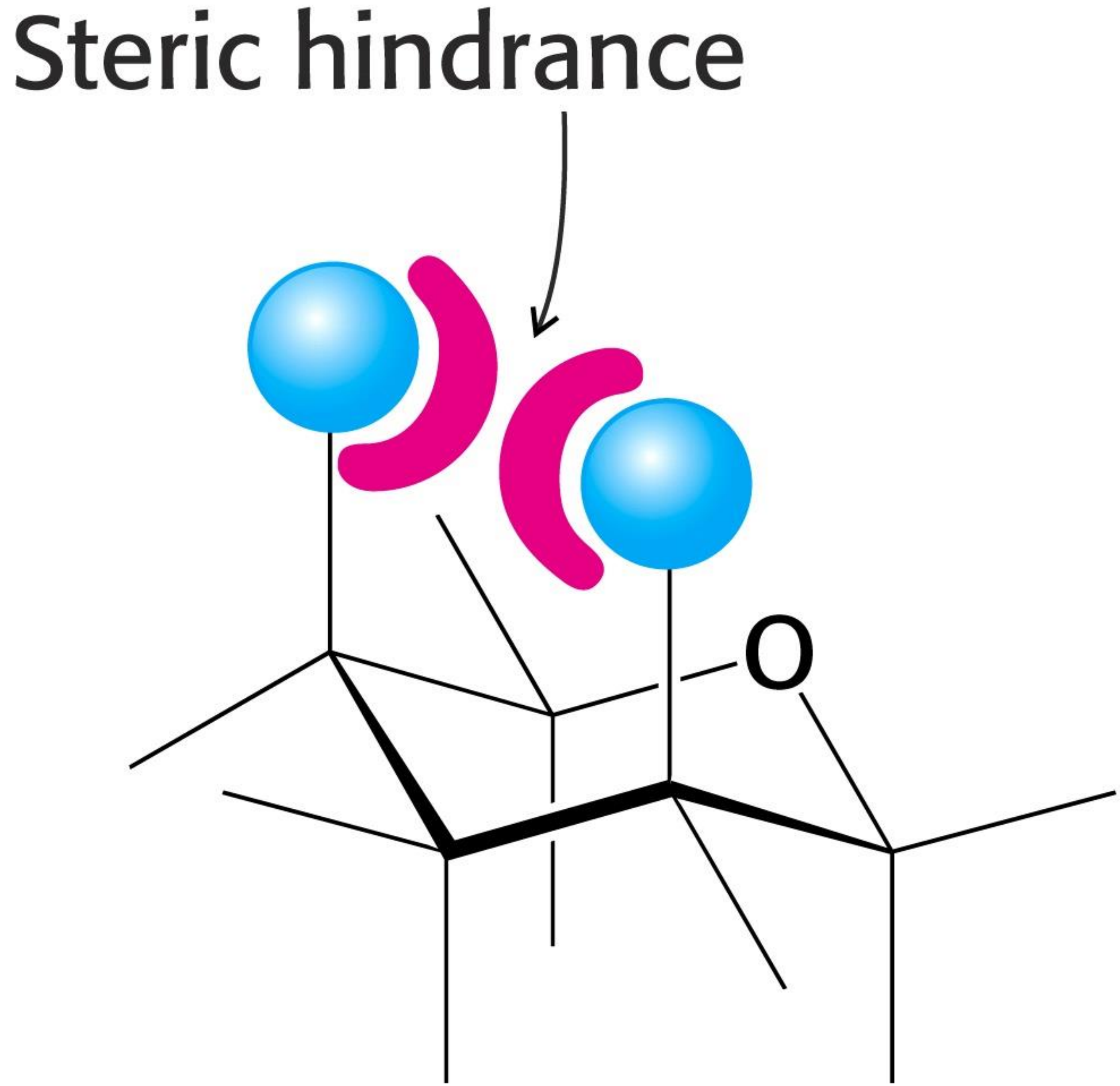
C5, D



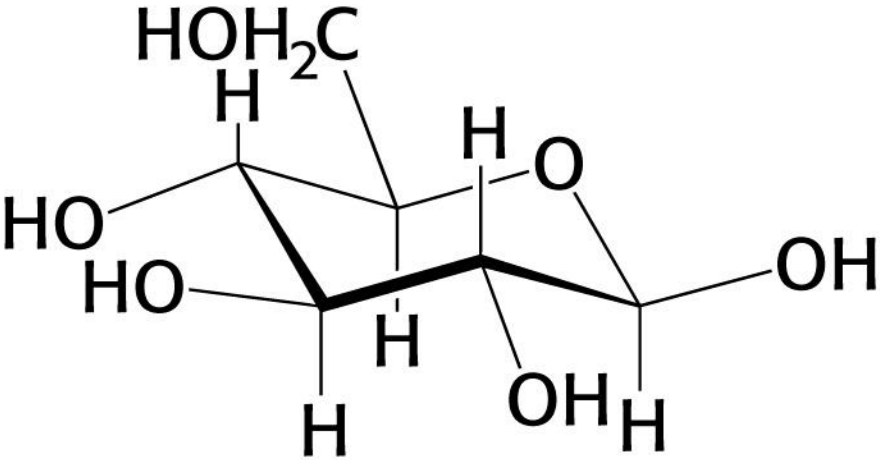
C2, β-anomer

β-D-Fructopyranose

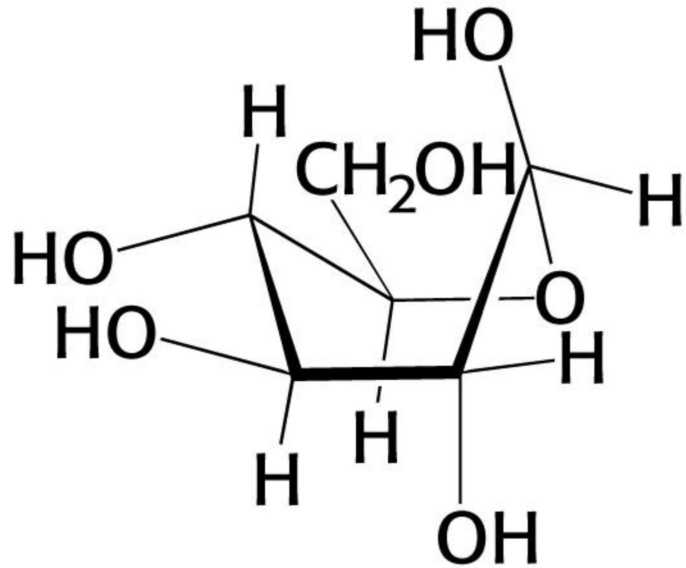
Pyranose ring not planer



Chair & Boat forms



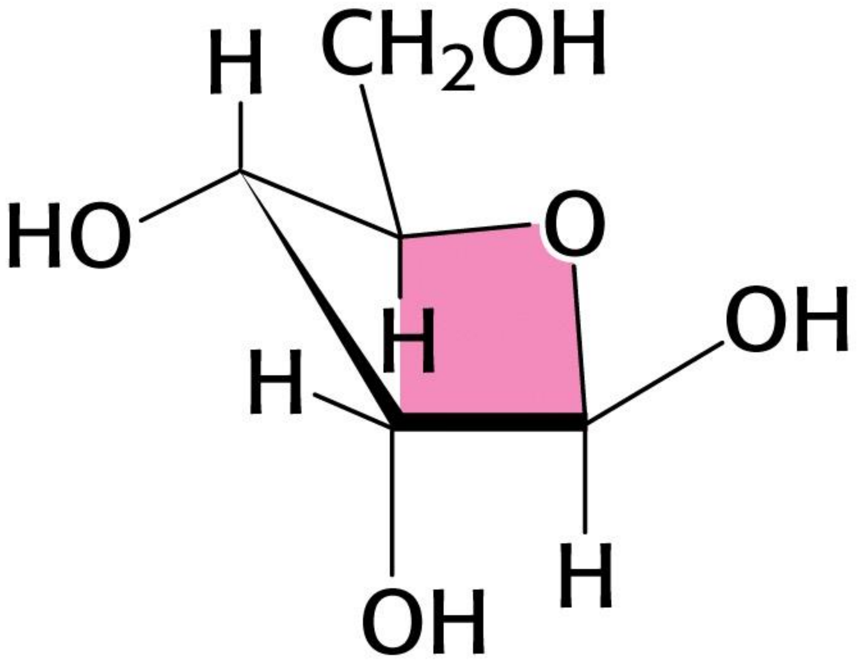
Chair form



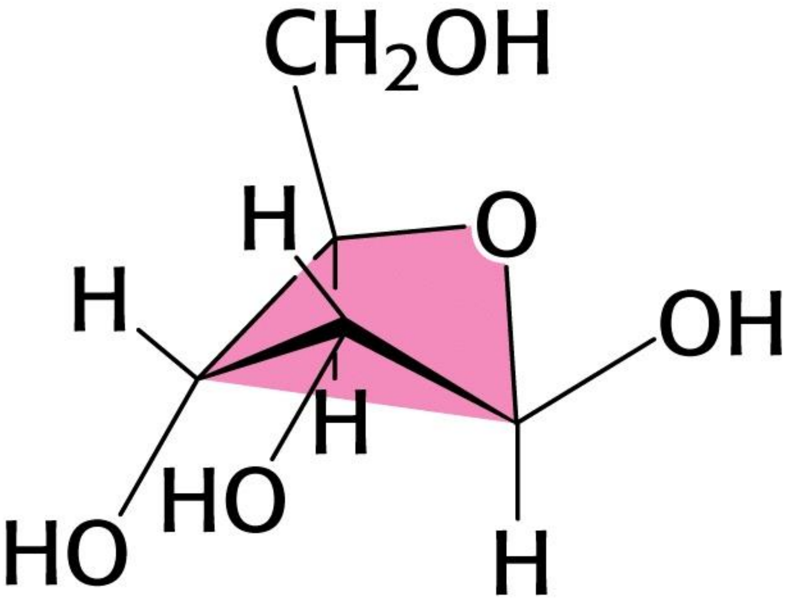
Boat form

Furanose ring not planer

Envelope form of β-D-ribose



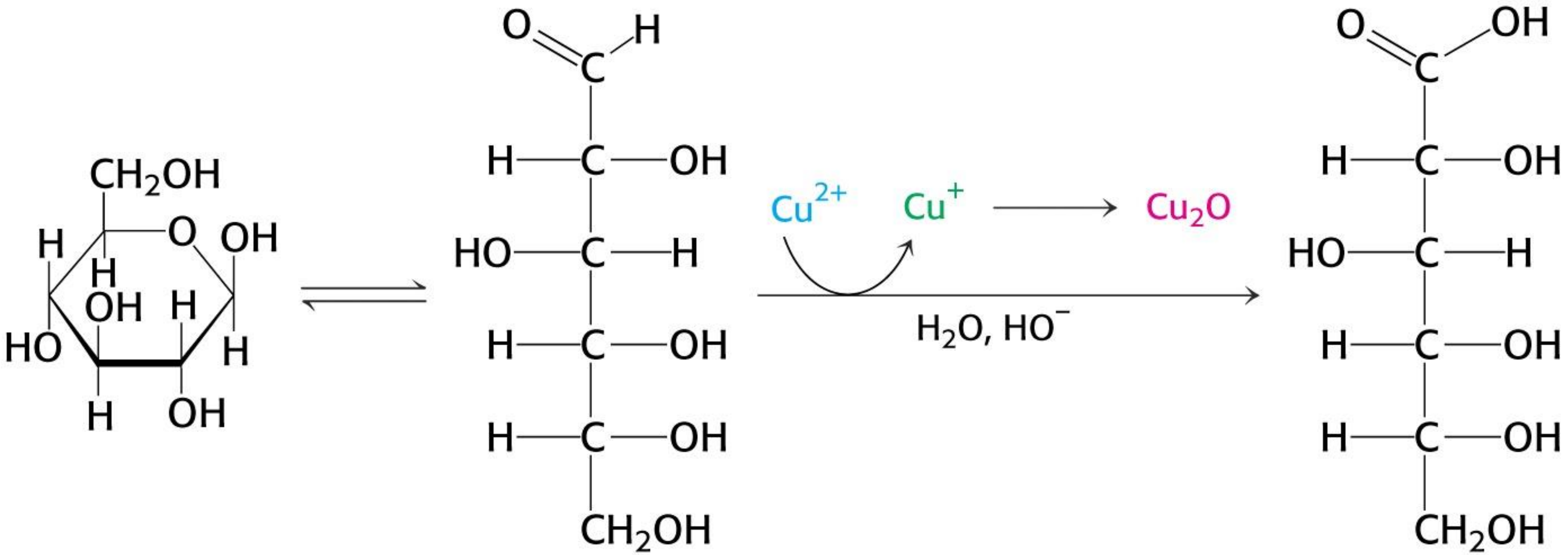
C_3-endo



C_2-endo

Reducing sugars

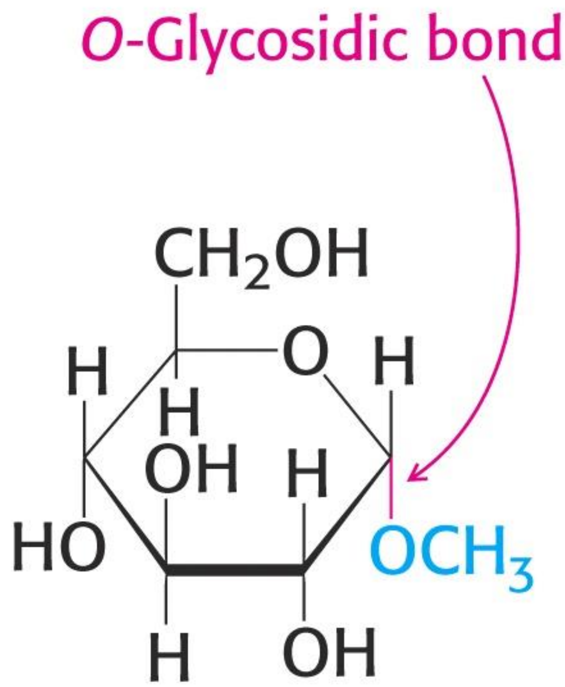
Solution of cupric ion, Cu^{2+} (Fehling's solution), test for reducing sugars such as glucose



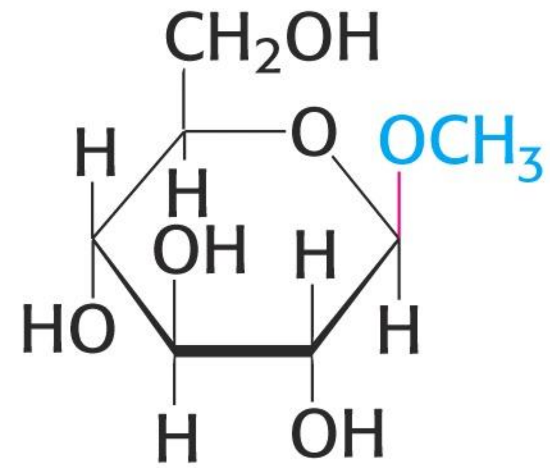
Free aldehyde group is oxidized

Glycosidic bonds

Monosaccharides can react with alcohols & amines



Methyl α-D-glucopyranoside

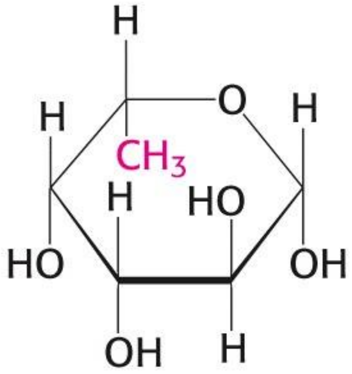


Methyl β-D-glucopyranoside

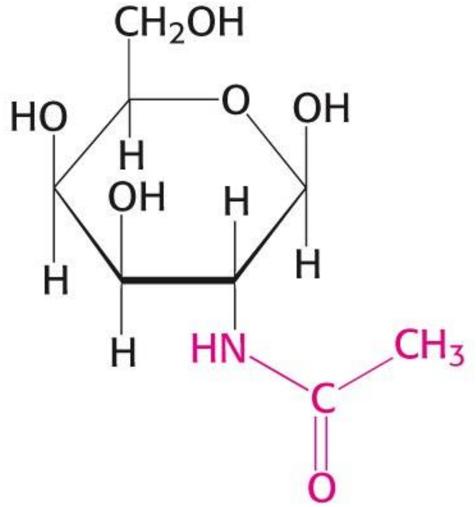
D-glucose + methanol (acid-catalyzed), two products, α & β

Modified monosaccharides

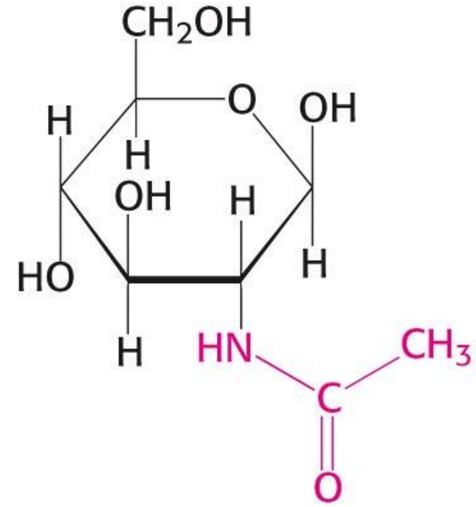
Frequently expressed on cell surfaces



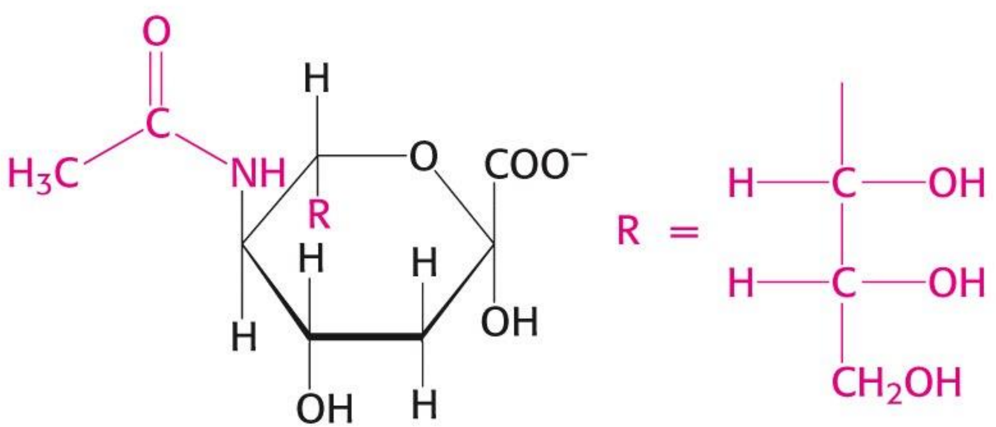
β-L-Fucose (Fuc)



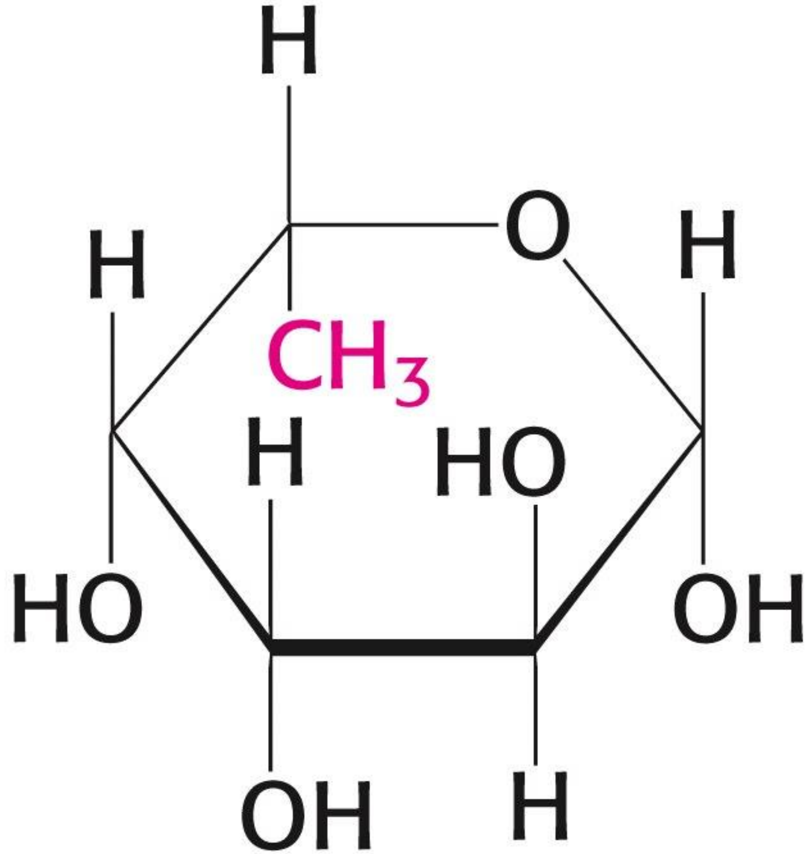
β-D-Acetylgalactosamine (GalNAc)



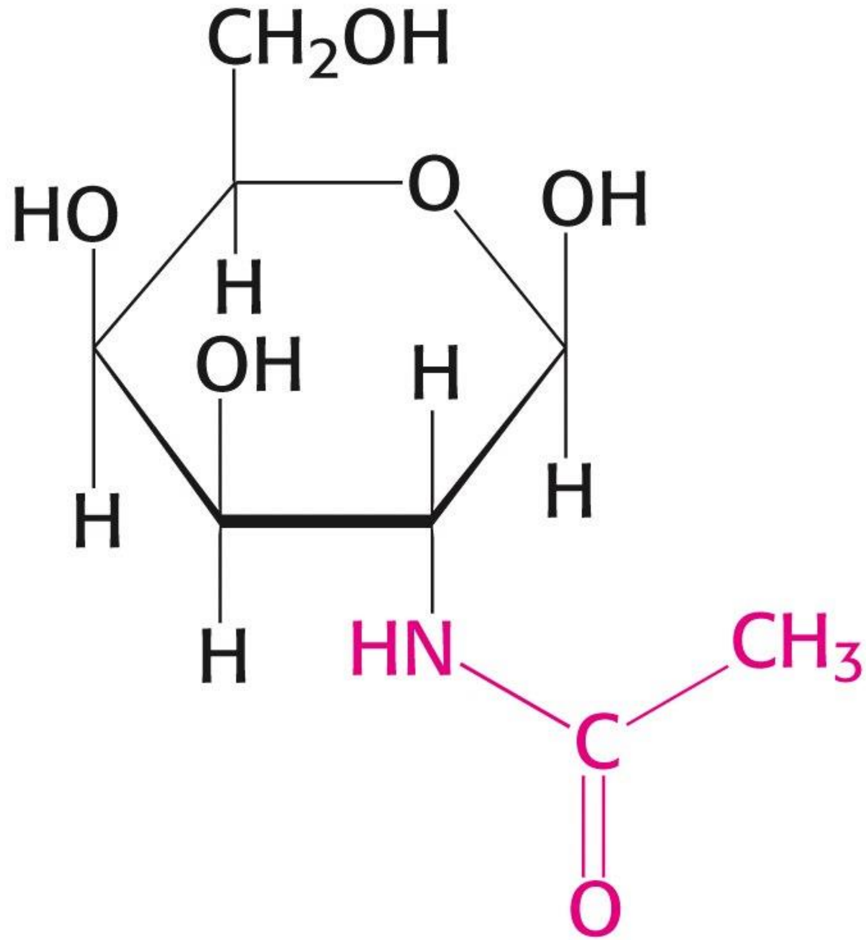
β-D-Acetylglucosamine (GlcNAc)



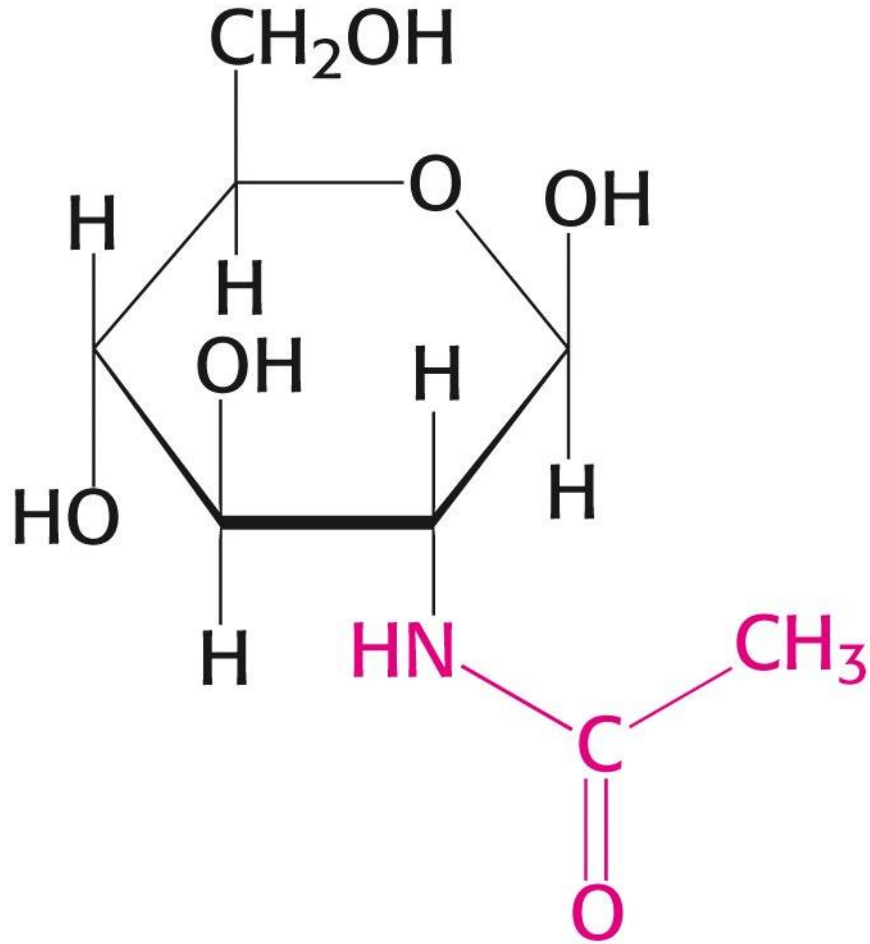
Sialic acid (Sia) (*N*-Acetylneuraminate)



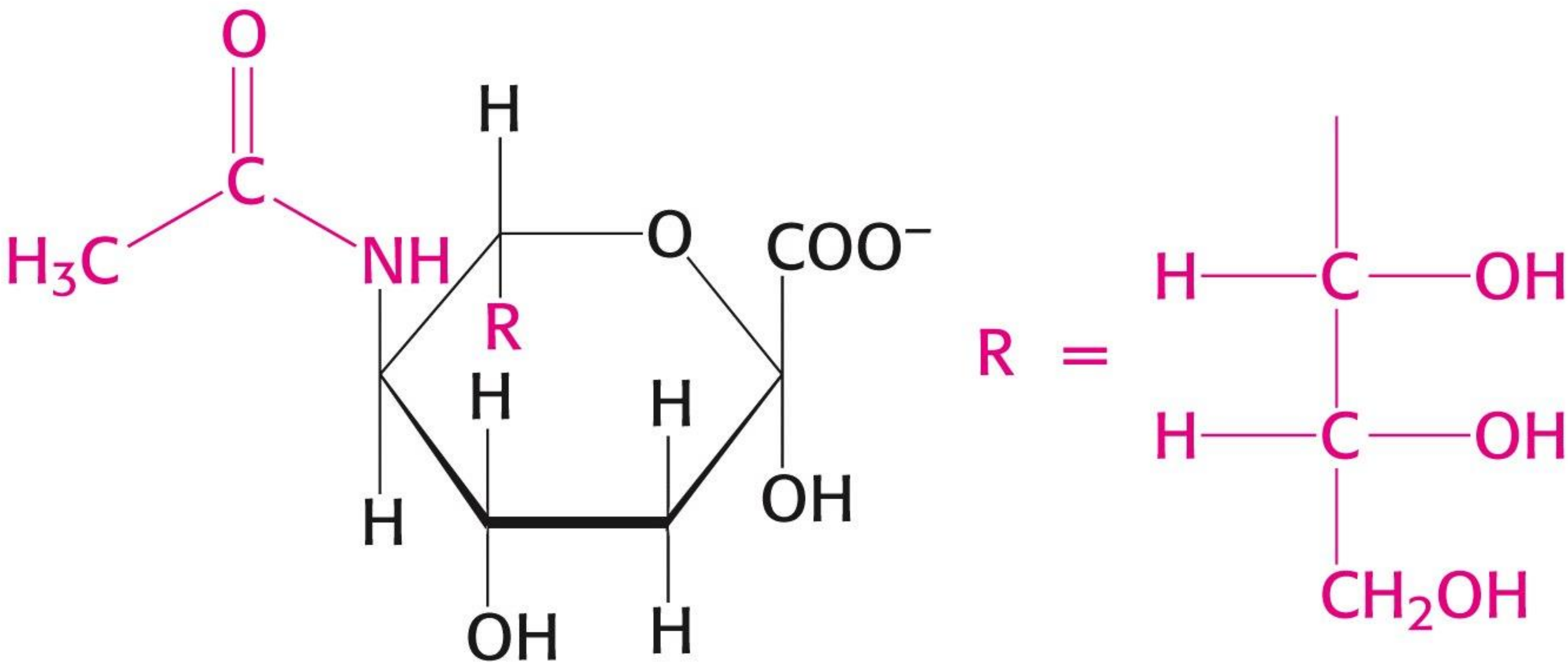
β-L-Fucose
(Fuc)



β-D-Acetylgalactosamine (GalNAc)



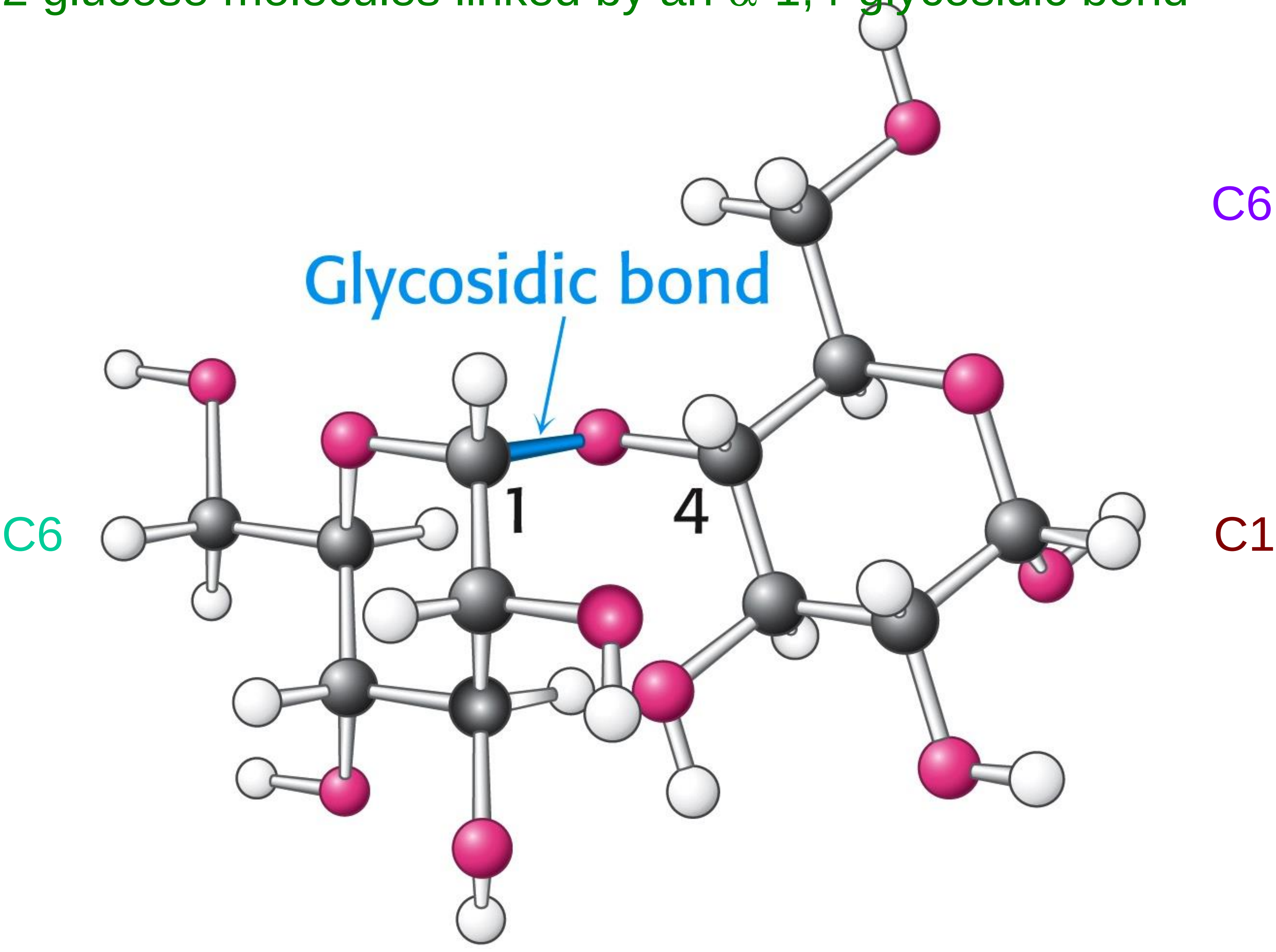
β-D-Acetylglucosamine (GlcNAc)



Sialic acid (Sia)
(*N*-Acetylneuraminate)

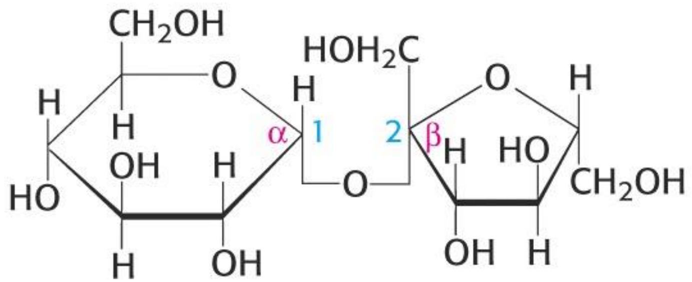
Linkage of monosaccharides: Maltose, a disaccharide

2 glucose molecules linked by an α-1,4-glycosidic bond

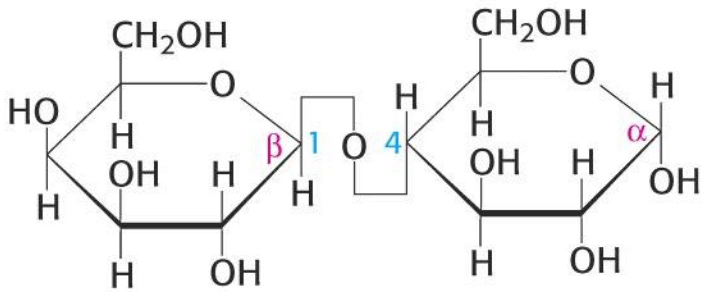


Common disaccharides

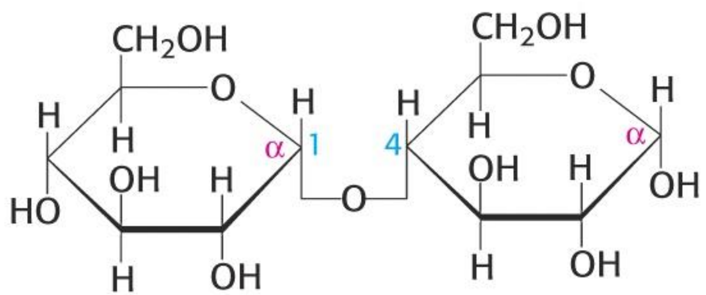
Common dietary components



Sucrose
(α-D-Glucopyranosyl-(1 → 2)-β-D-fructofuranose

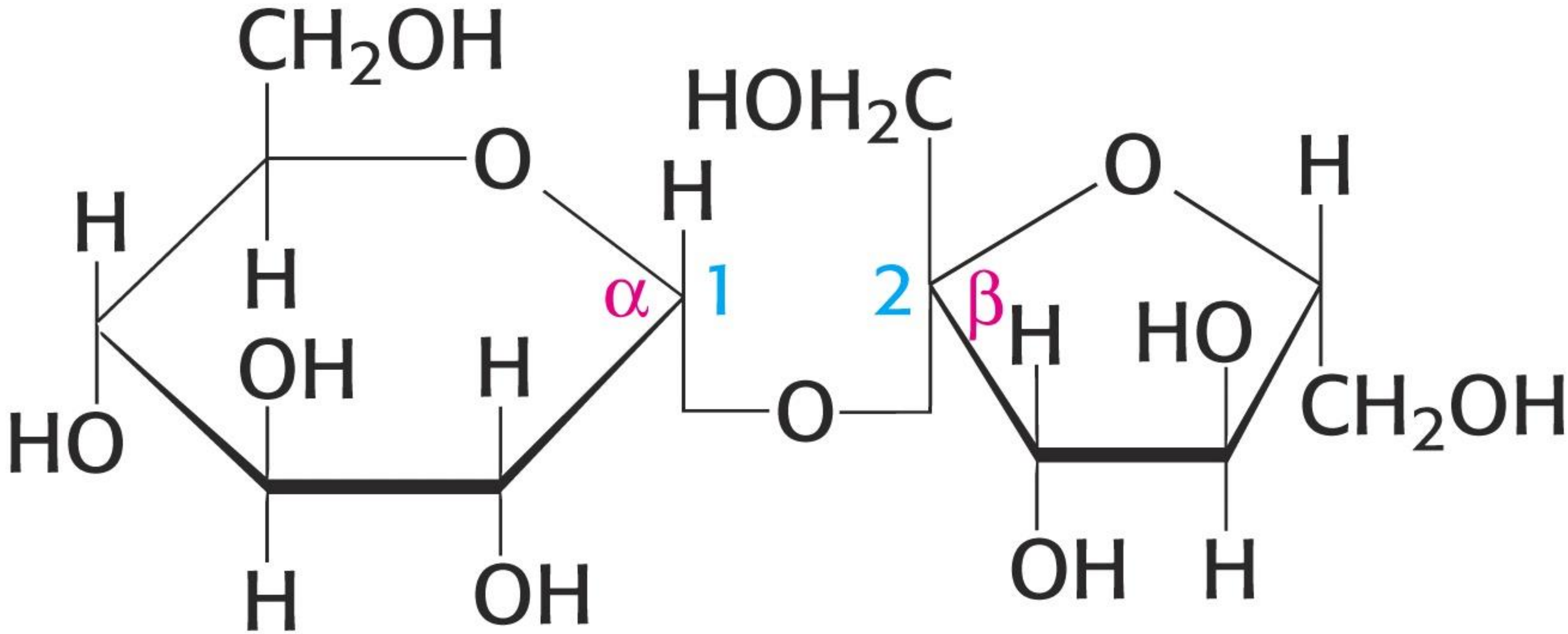


Lactose
(β-D-Galactopyranosyl-(1 → 4)-α-D-glucopyranose



Maltose
(α-D-Glucopyranosyl-(1 → 4)-α-D-glucopyranose

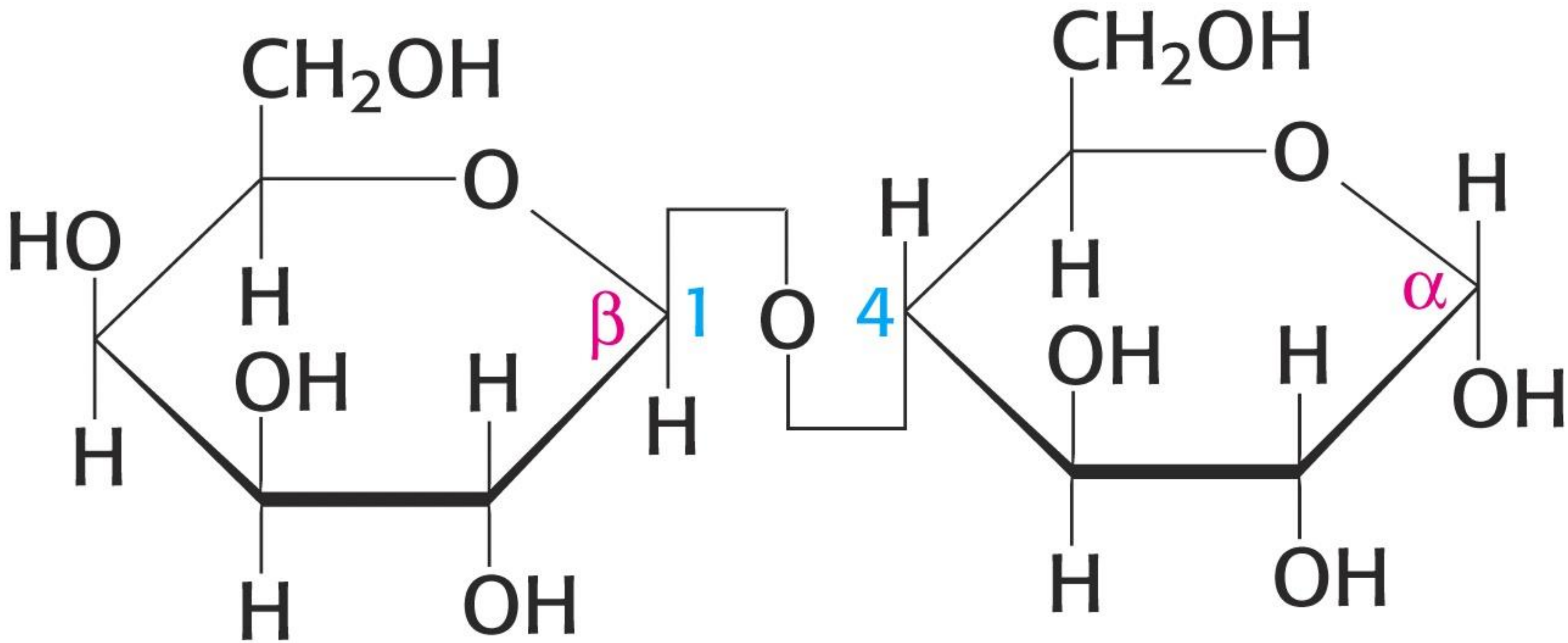
Sucrose (table sugar from cane or beet)



Sucrose
(α-D-Glucopyranosyl-(1 → 2)-β-D-fructofuranose

Hydrolyzed by sucrase

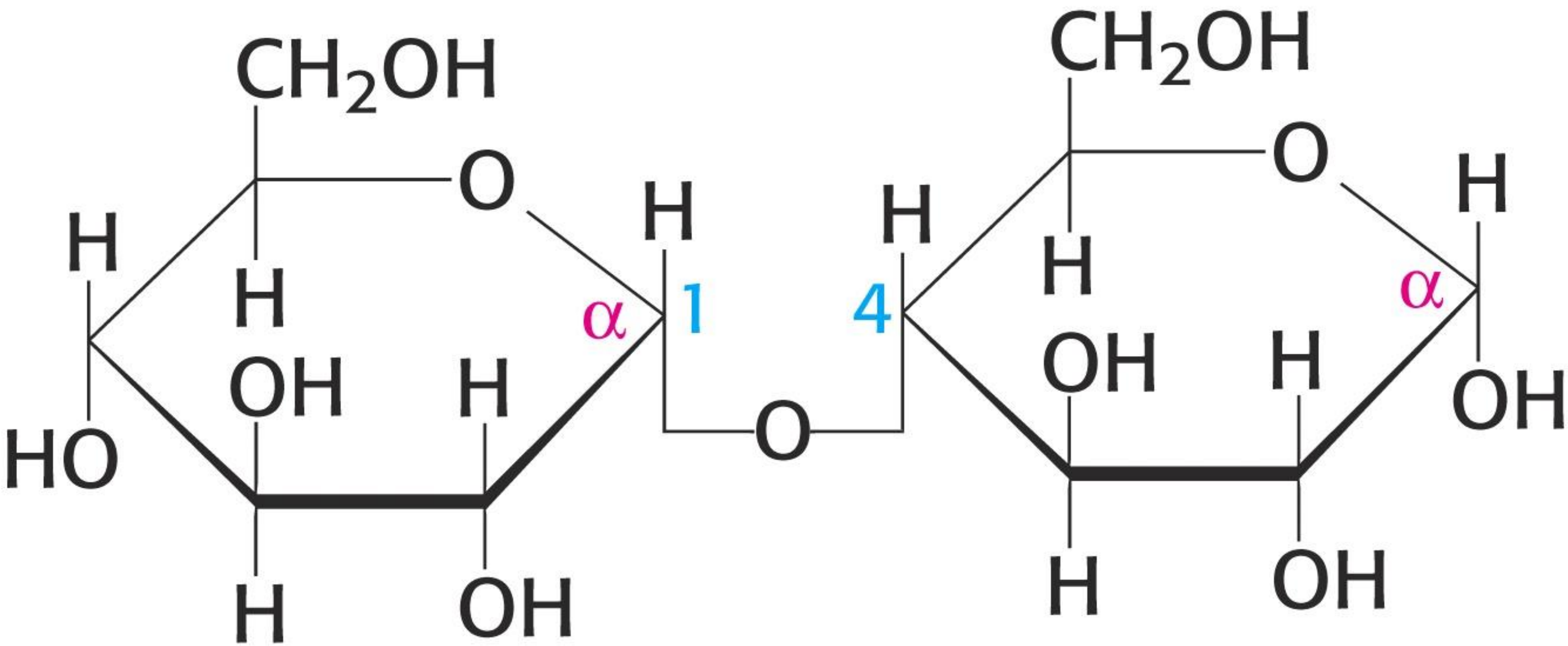
Lactose (from milk)



Lactose
(β-D-Galactopyranosyl-(1→4)-α-D-glucopyranose

Hydrolyzed by lactase in humans,
& by β-galactosidase in bacteria

Maltose (from starch hydrolysis)

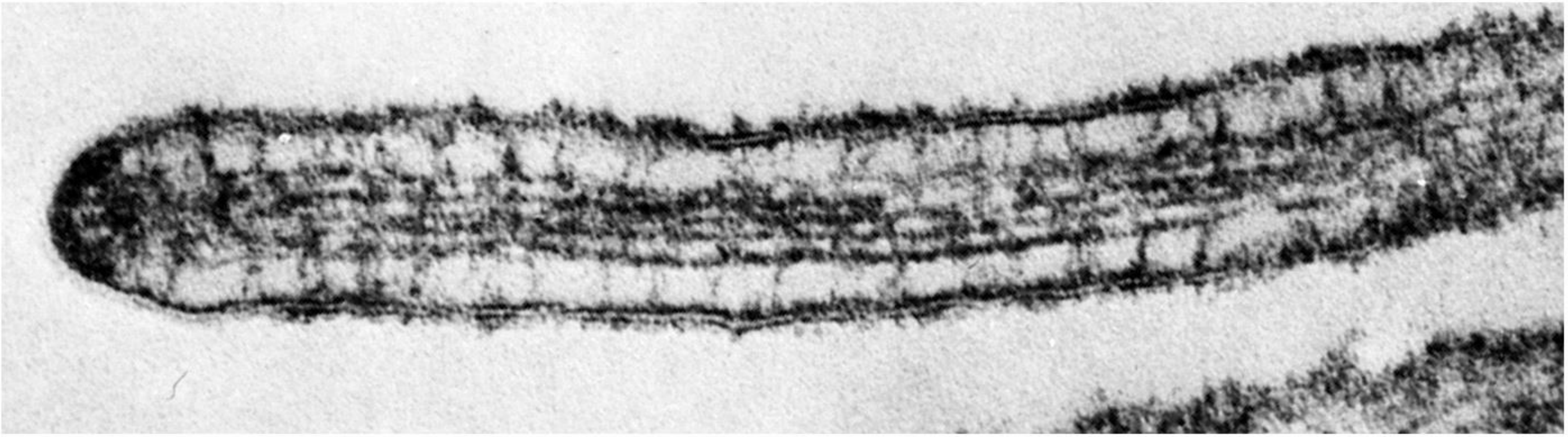


Maltose
(α-D-Glucopyranosyl-(1→4)-α-D-glucopyranose

Hydrolyzed by maltase

EM of microvillus (in small intestine)

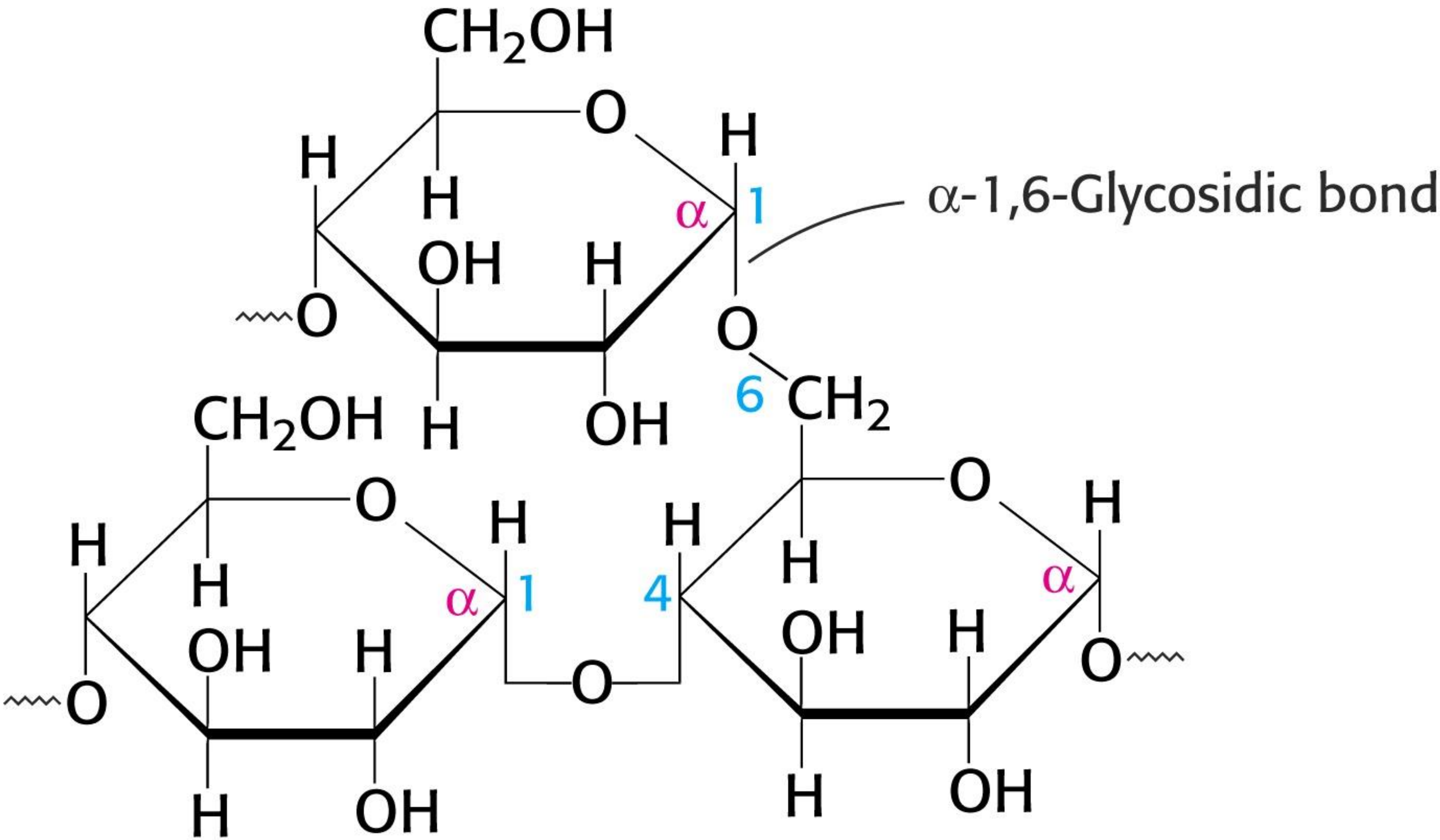
Sucrase, lactase, & maltase, located on microvilli (project from outer face of plasma membrane of intestinal epithelial cells)



Polysaccharides: Glycogen (branch points)

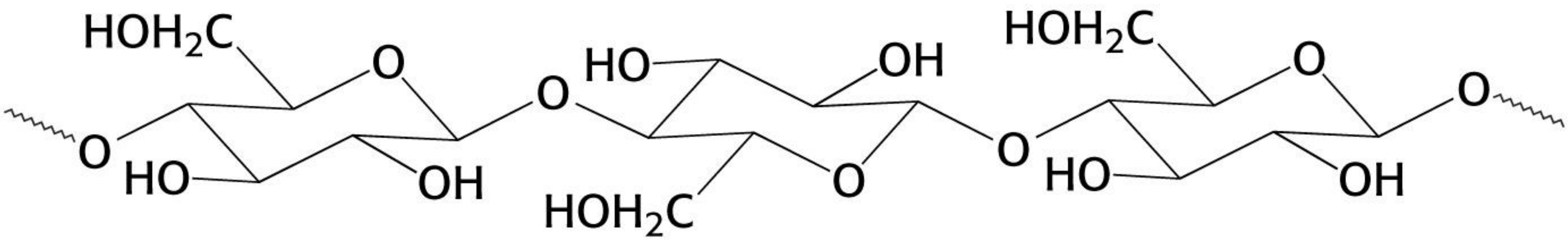
Glycogen is highly branched

Glucose store



Branch every 10 glucose units (approx)

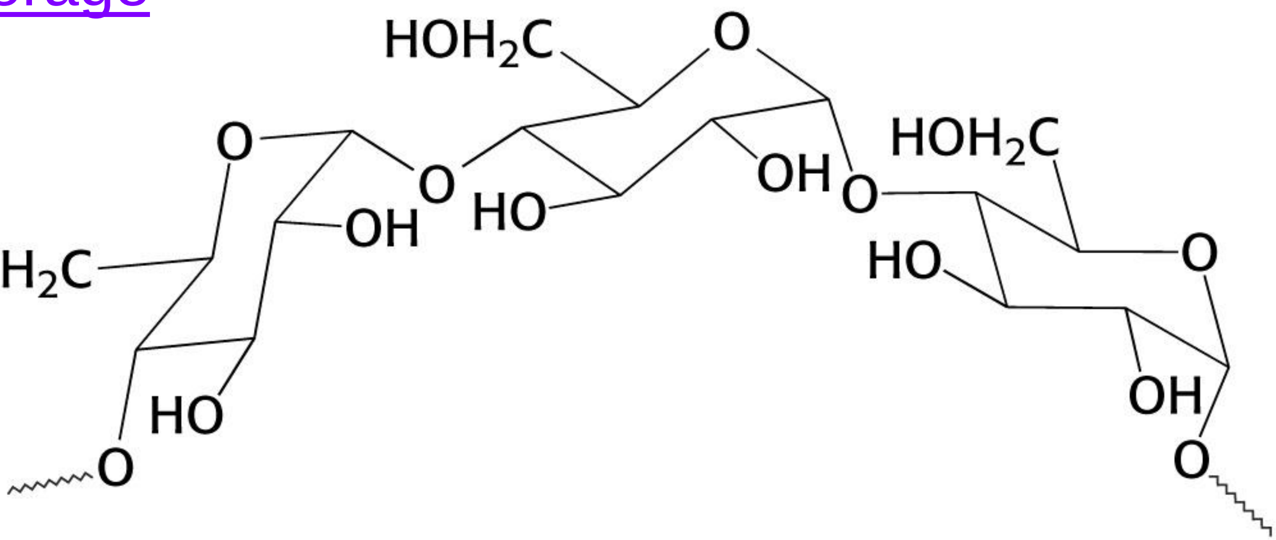
Glycosidic bonds determine structure



Cellulose
(β-1,4 linkages)

Straight chains,
good for structure

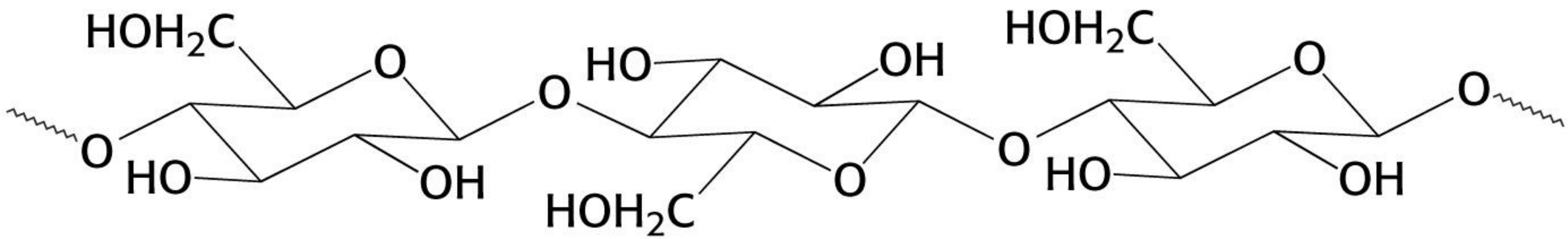
Bent chains,
good for storage



Starch and Glycogen
(α-1,4 linkages)

Cellulose

Major structural polymer of plants,
one of the most abundant organic compounds in the biosphere



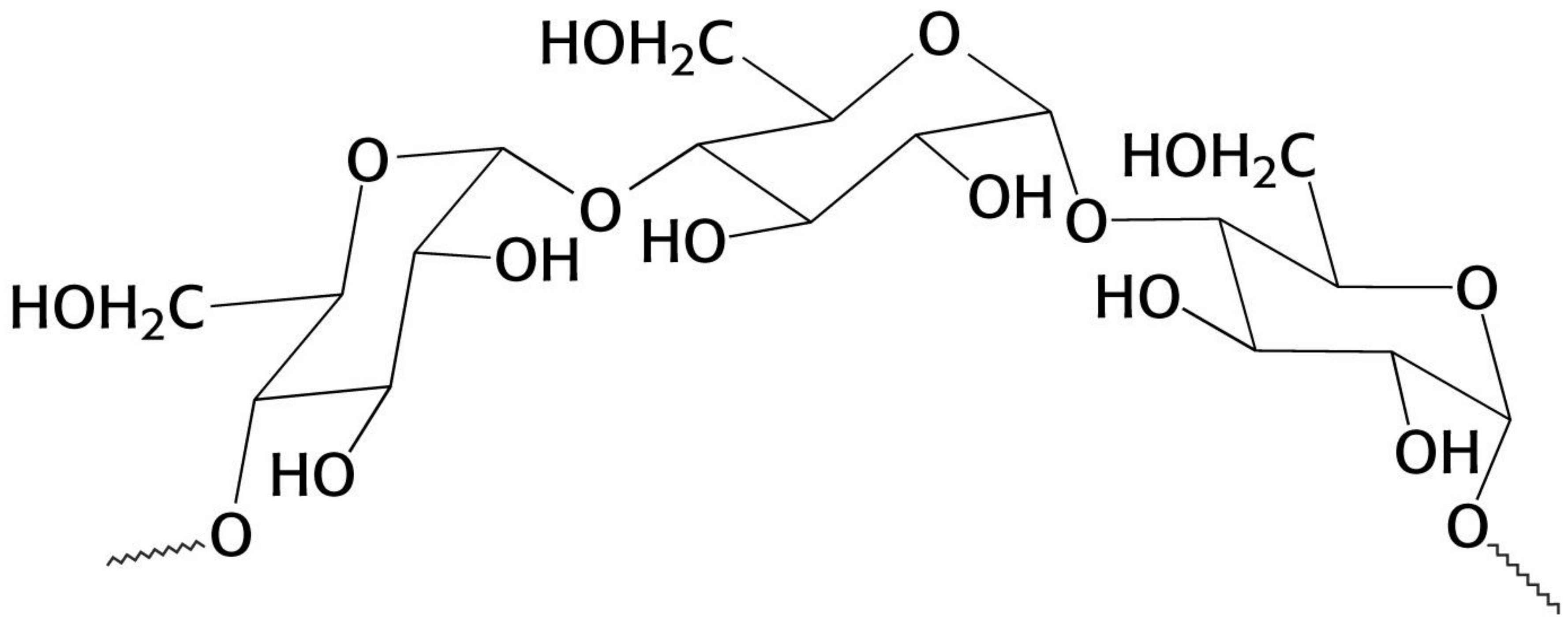
Cellulose
(β-1,4 linkages)

Straight chain polymer of glucose,
Fibrils formed by parallel chains, held by hydrogen bonds

Mammals lack cellulases, cannot digest wood or vegetable fibers,
bacteria hydrolyze it in the rumen

Starch & glycogen (homopolymers)

Open helix, accessible stores of sugar,
starch in plants, glycogen in animals



Starch and Glycogen
(α-1,4 linkages)

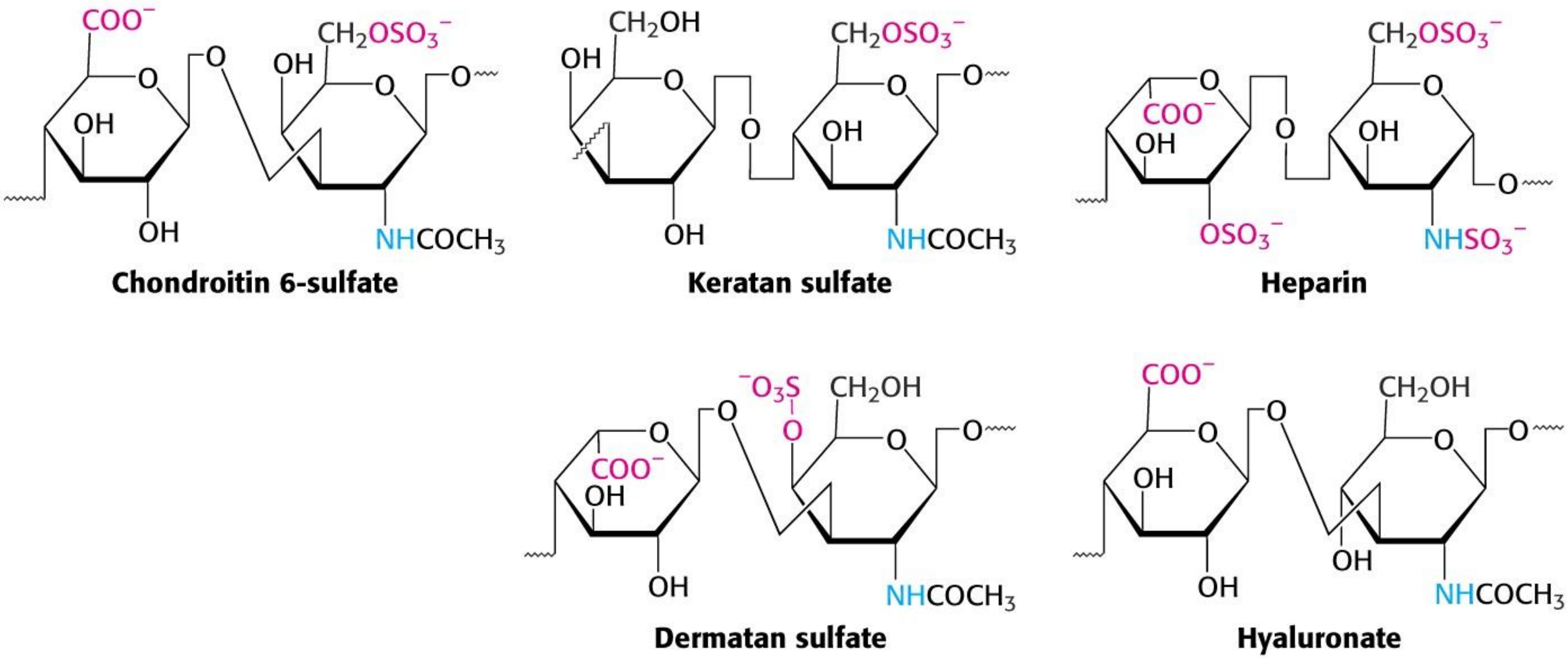
Glycogen, highly branched,
(every 10 glucose units)

Starch, two forms,
Amylose - unbranched,
Amylopectin - branched (every 30 glucose units)

Glycosaminoglycans, Anionic Polysaccharides

Made of repeating disaccharide units, containing a derivative of an amino sugar, glucosamine or galactosamine

At least 1 of the sugars has a negatively charged carboxyl or sulfate group

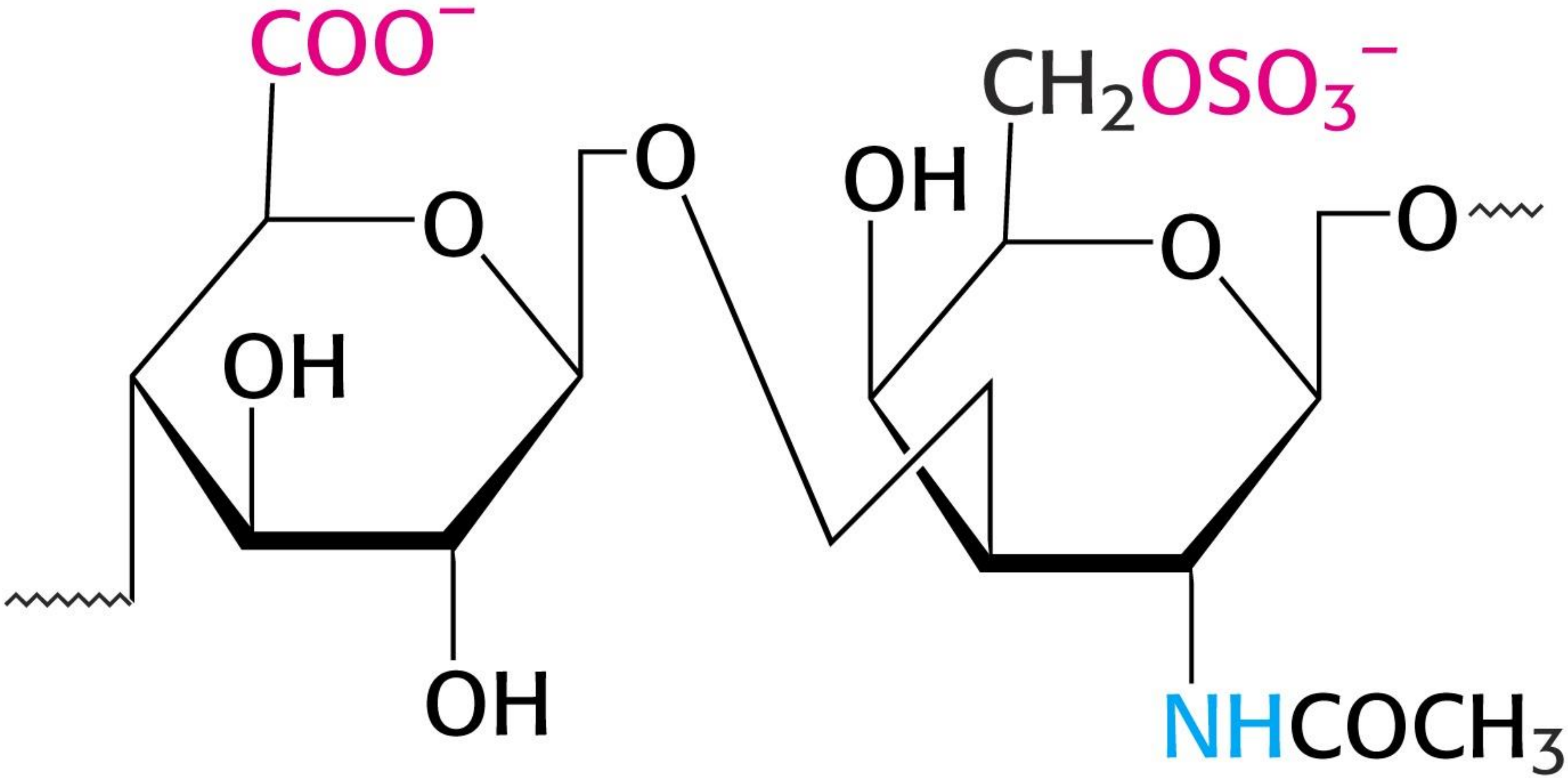


Usually attached to proteins to form proteoglycan (95% carb)

Proteoglycan functions

- Lubricants for mucous membranes & connective tissue
- Structural components in connective tissue
- Mediate adhesion of cells to extracellular matrix
- Bind factors that stimulate cell proliferation

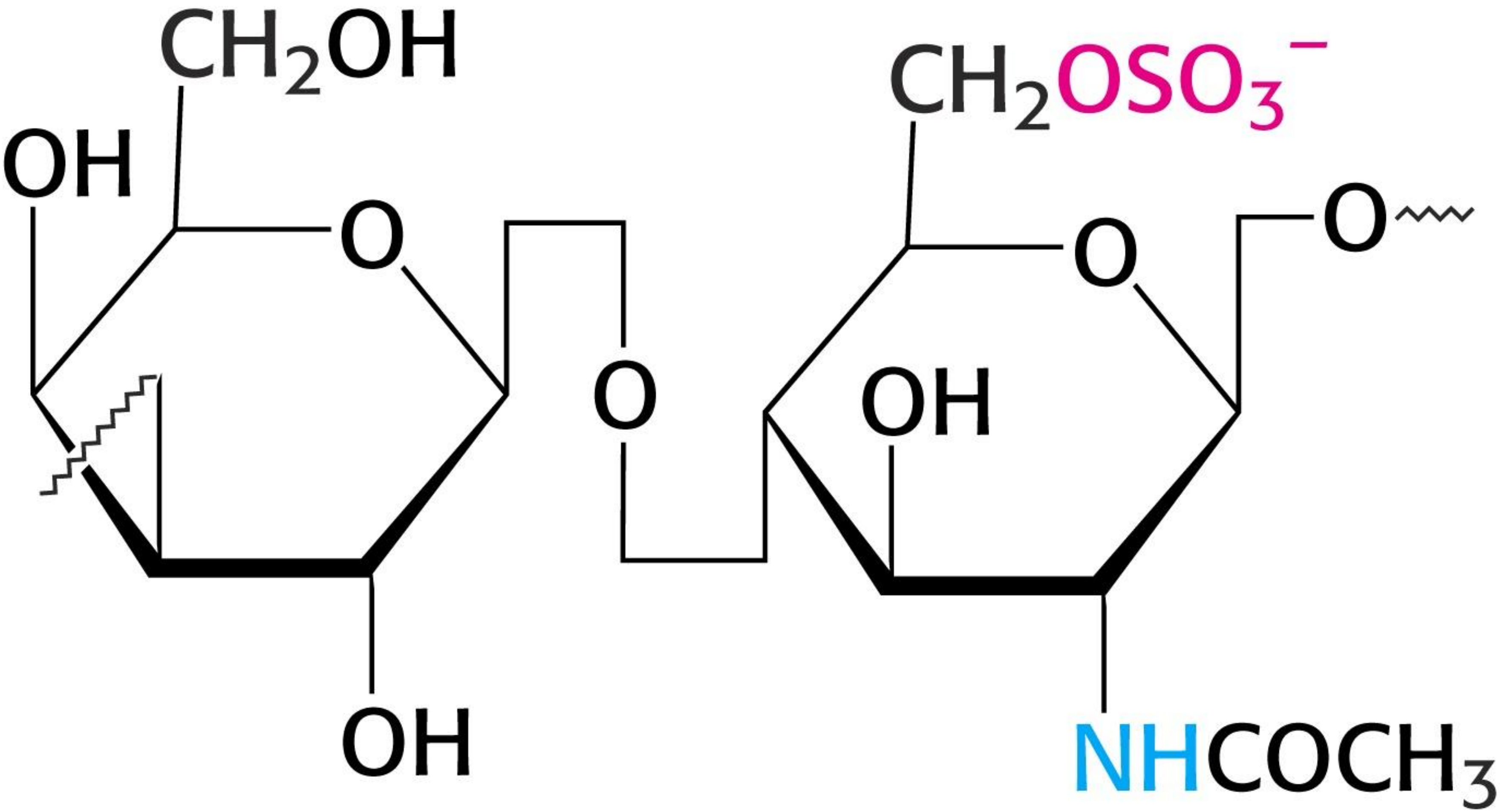
Chondroitin 6-sufate



Chondroitin 6-sulfate

Found in cartilage

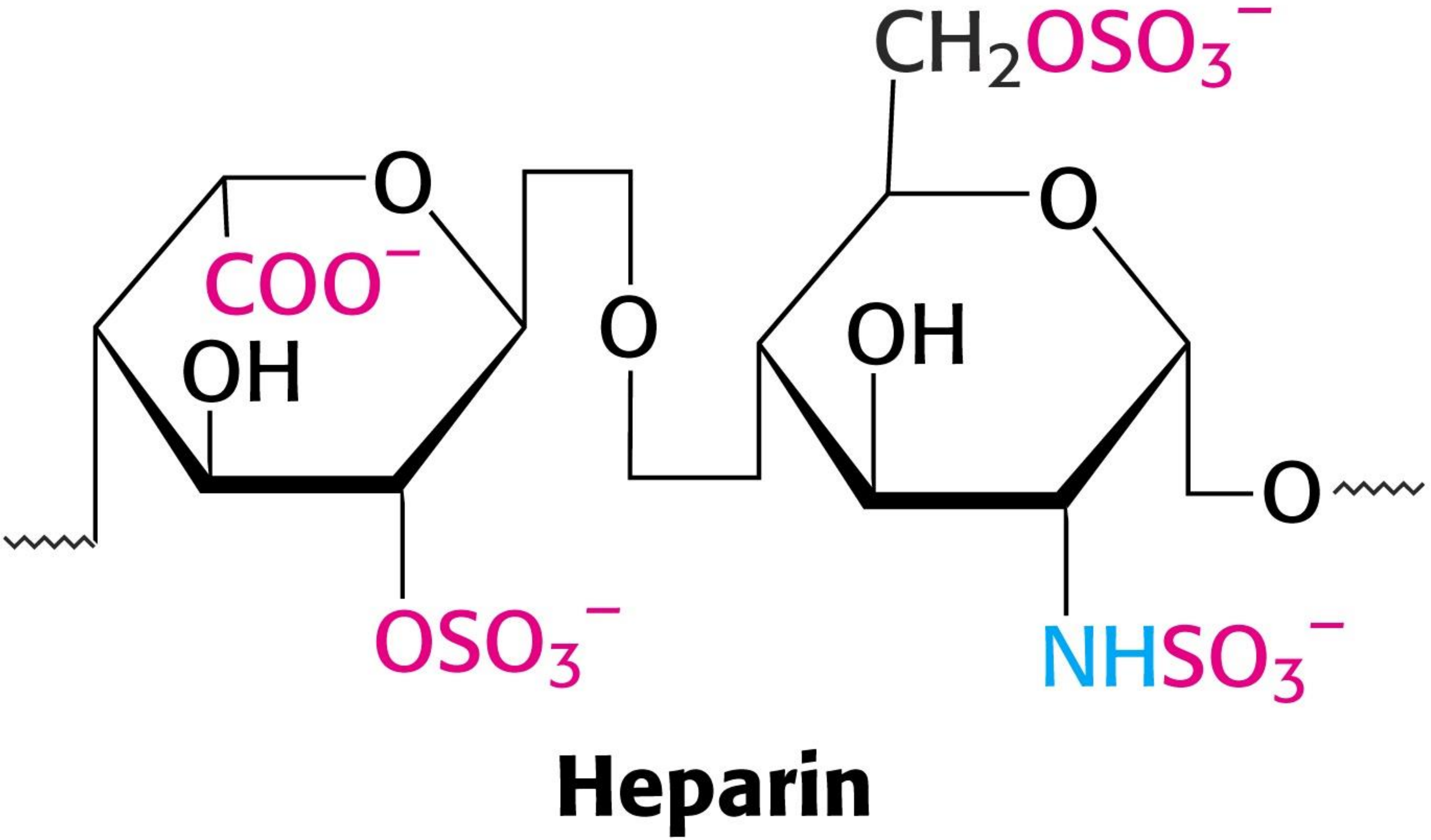
Keratan sulfate



Keratan sulfate

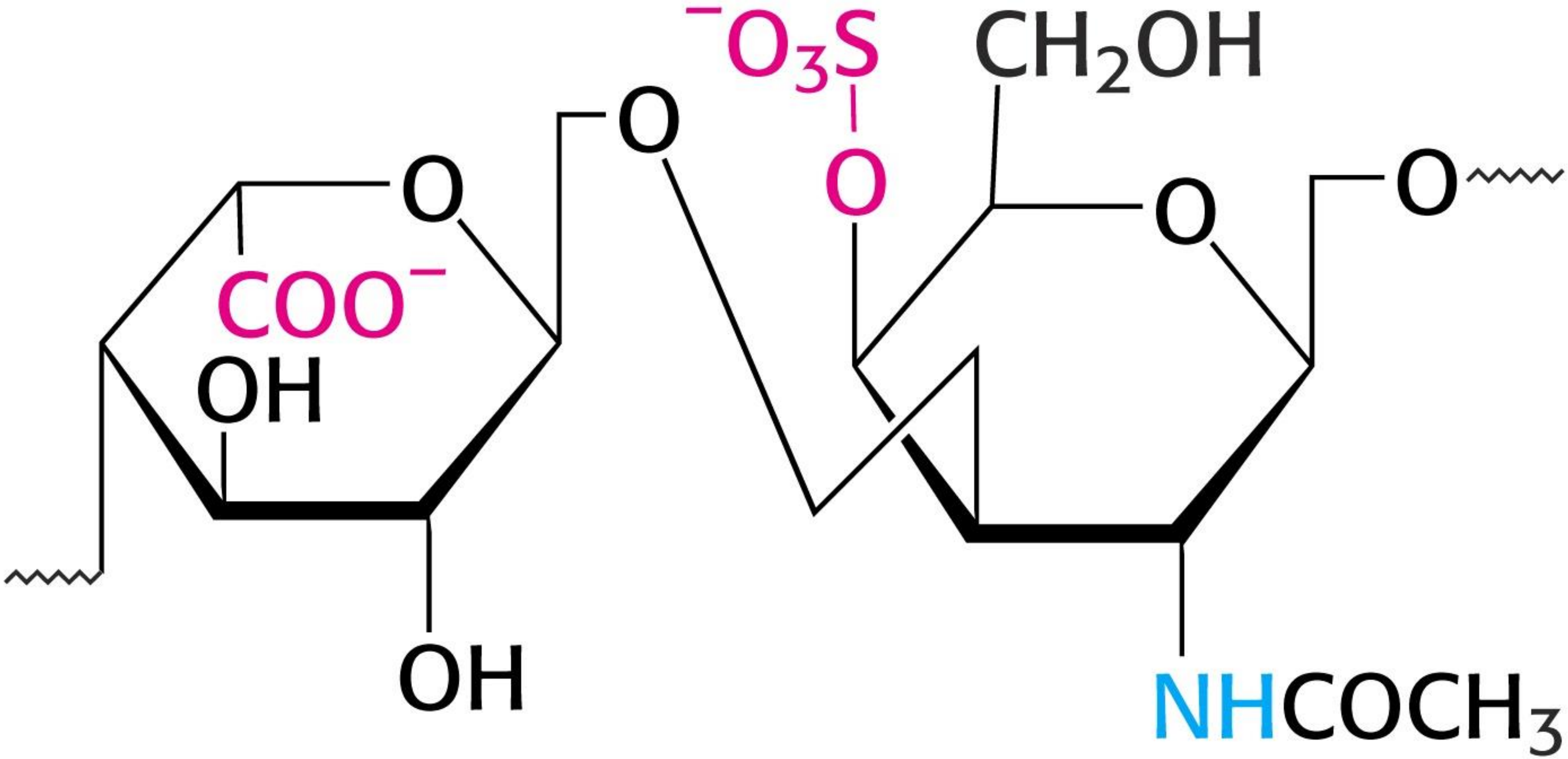
Found in hair, nails, etc

Heparin



Anticoagulant used to prevent blood clotting

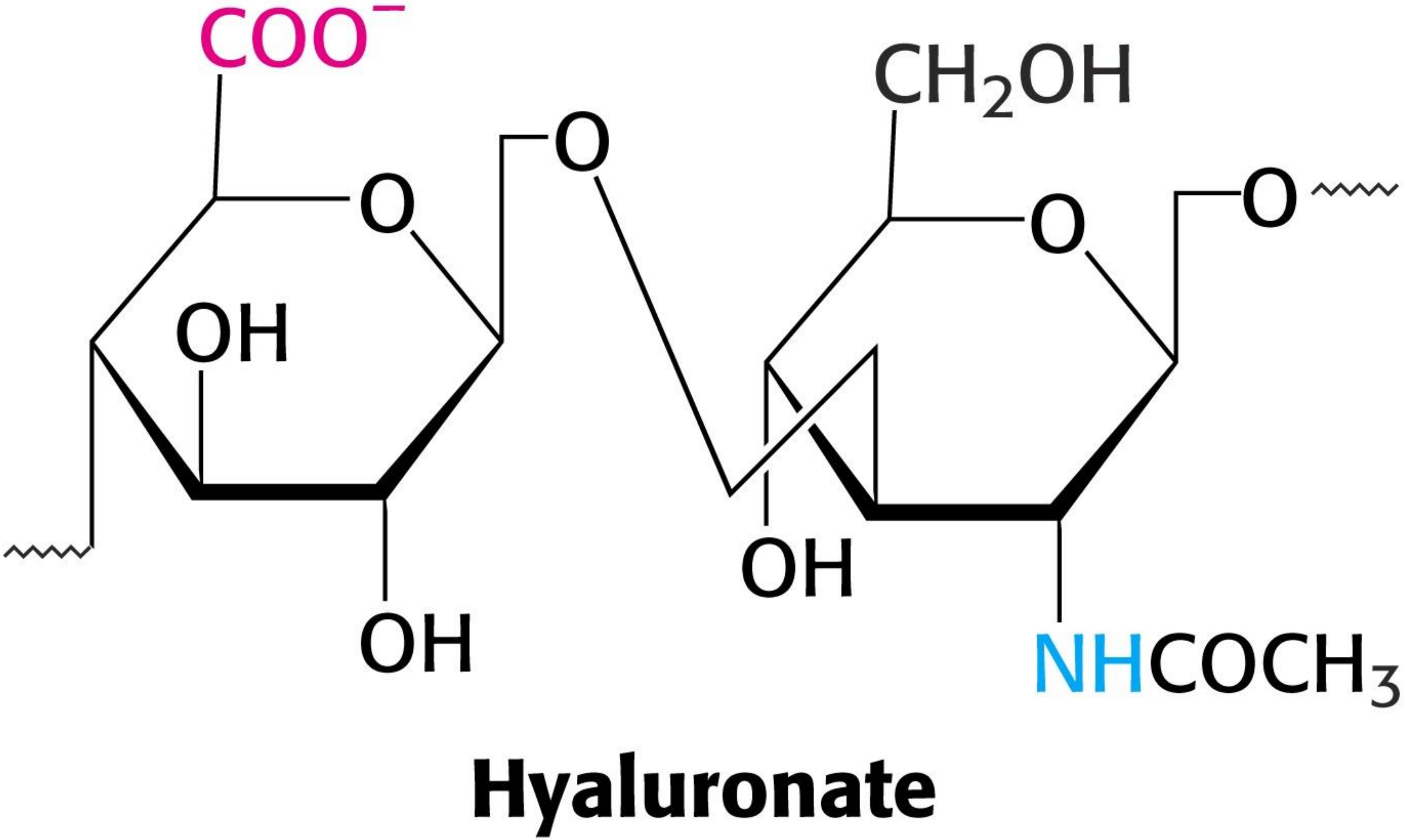
Dermatan sulfate



Dermatan sulfate

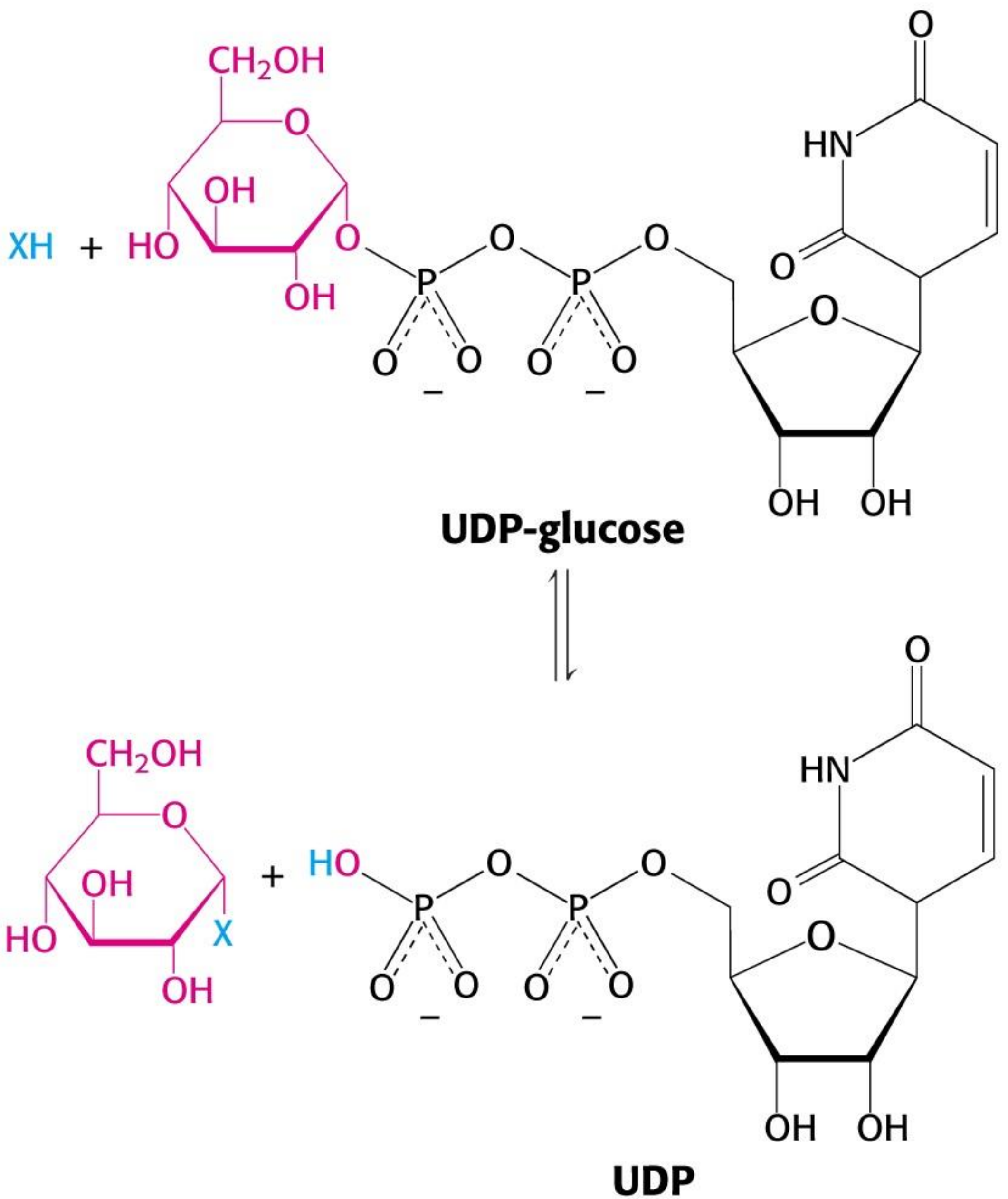
Found in skin

Hyaluronate



Found in connective tissue & serves as lubricant

Oligosaccharide synthesis: Glycosyltransferases



Catalyze formation of glycosidic bonds,

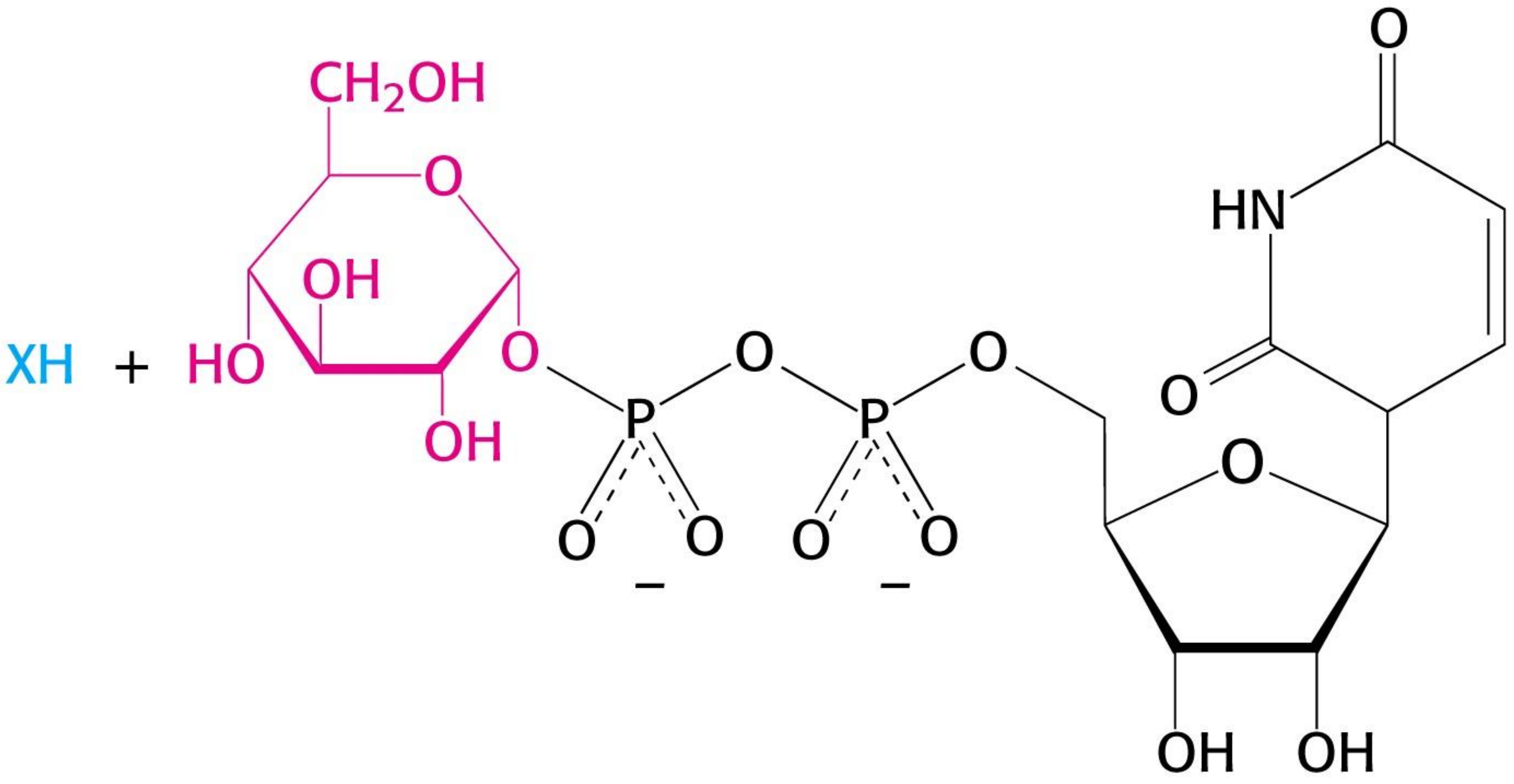
Each enzyme specific to sugar,

Therefore, many enzymes required

Unlike nucleic acid or protein biosynthesis, no template used

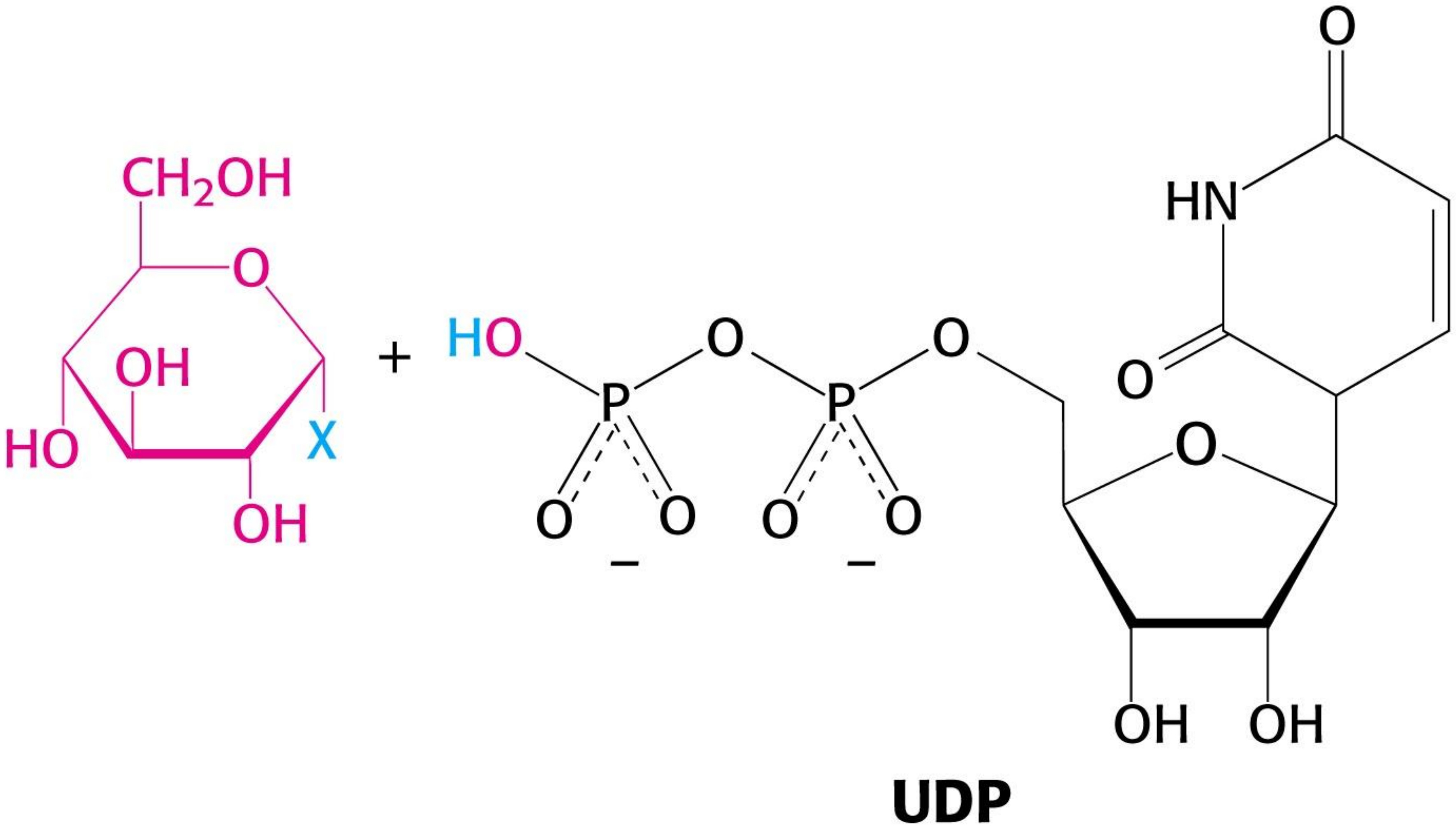
Activated sugar nucleotide

Important intermediates in many processes

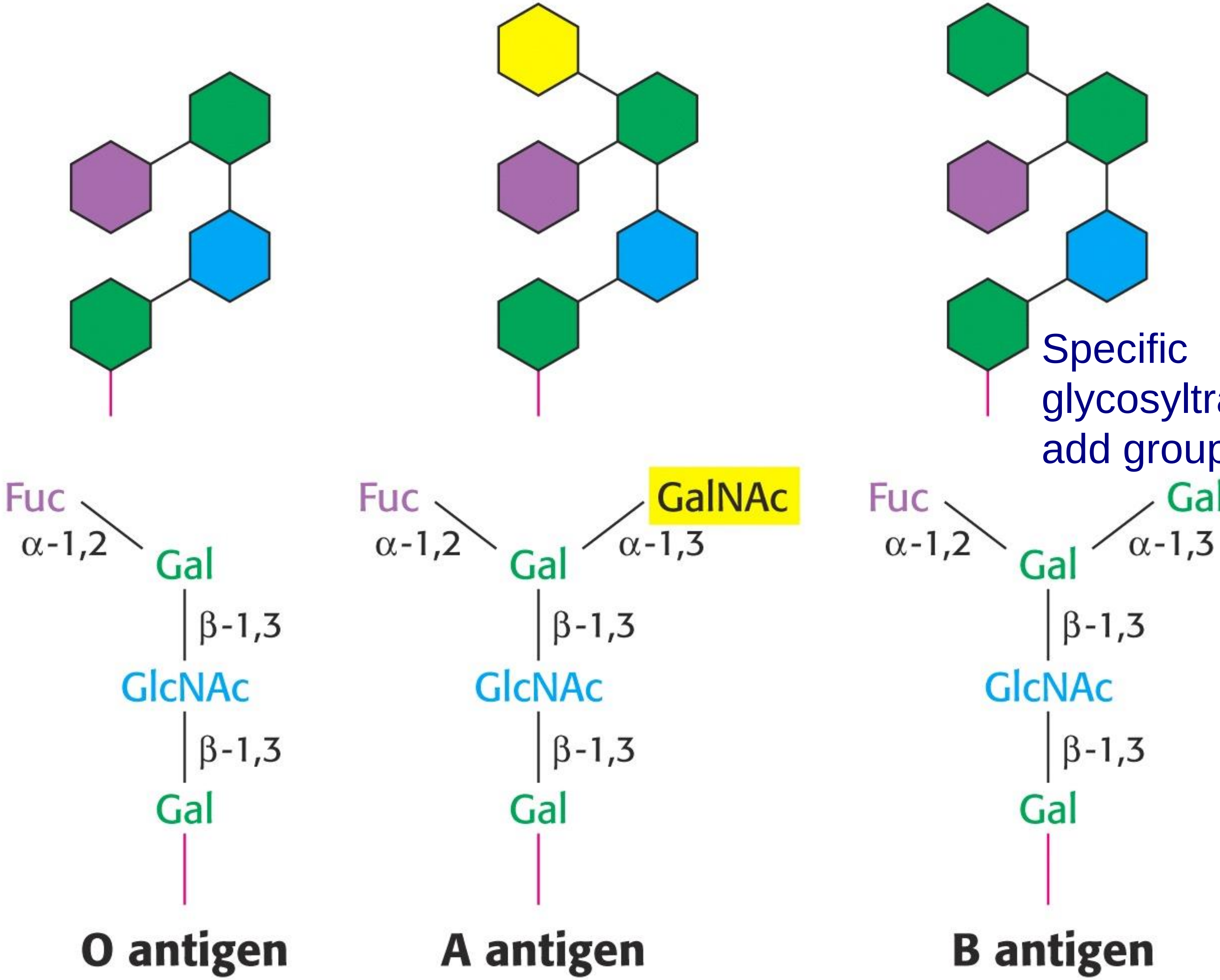


UDP-glucose

Glycosidic bond formed



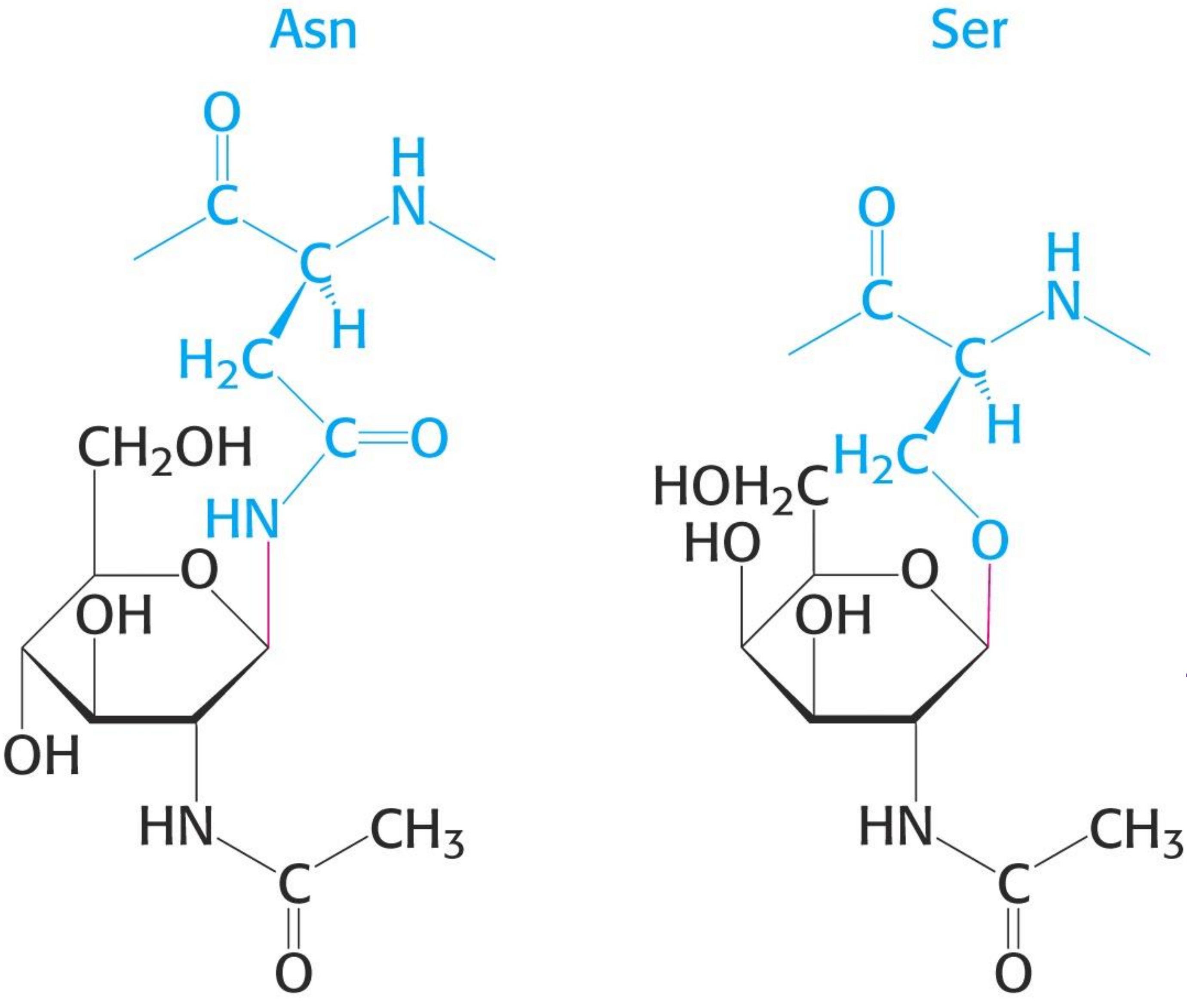
A, B, & O oligosaccharide antigens (blood groups)



Specific glycosyltransferases add group to O antigen

Foundation oligo(frameshift mutant gene), one from each parent

Glycoproteins (small % of carbs), glycosidic bonds



N-linked GlcNAc **O-linked GalNAc**

N-linked, Asn
in ER & Golgi

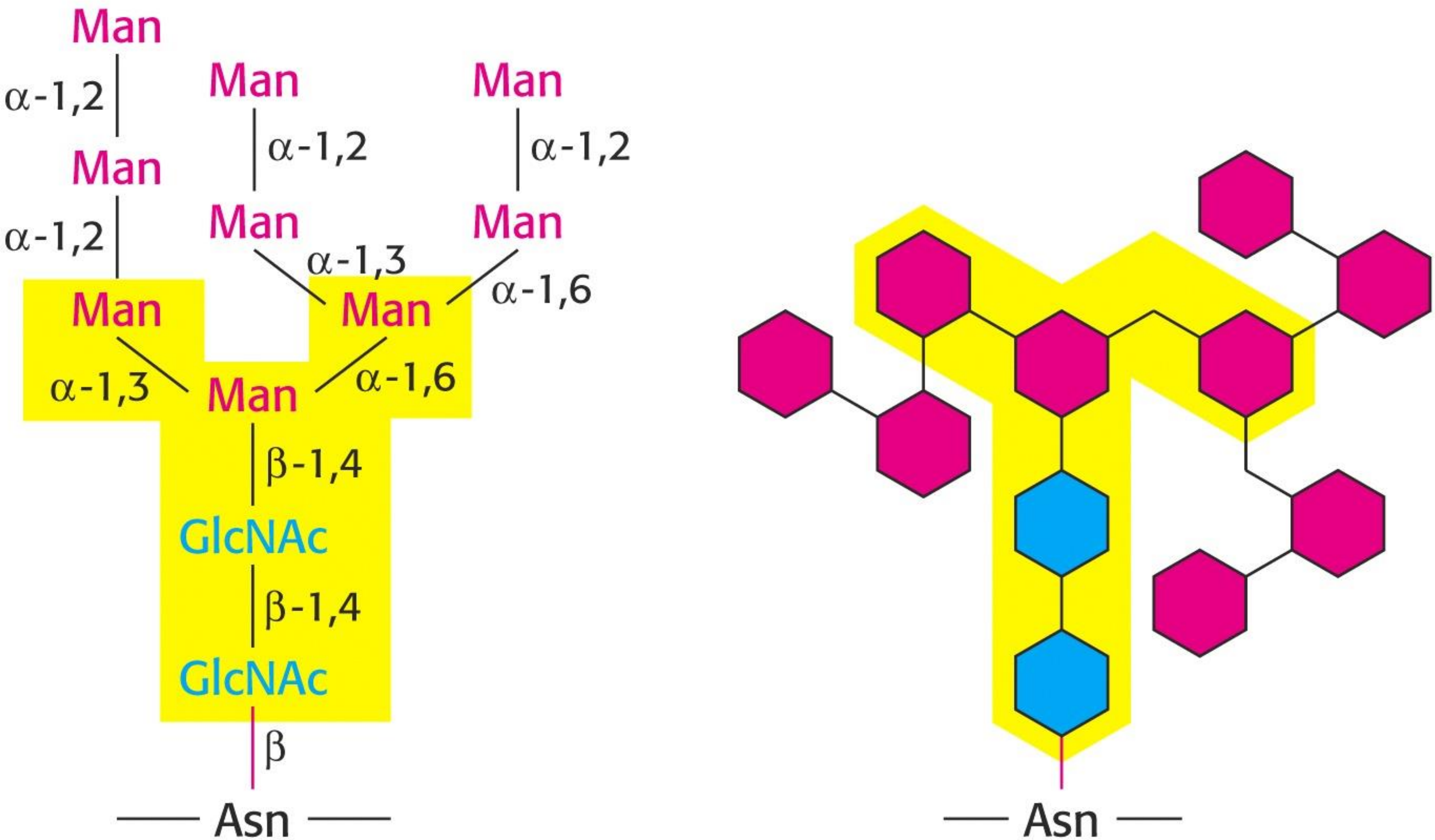
O-linked, Ser, Thr
in Golgi only

Components of
cell membranes,
adhesion,
binding of sperm
to eggs

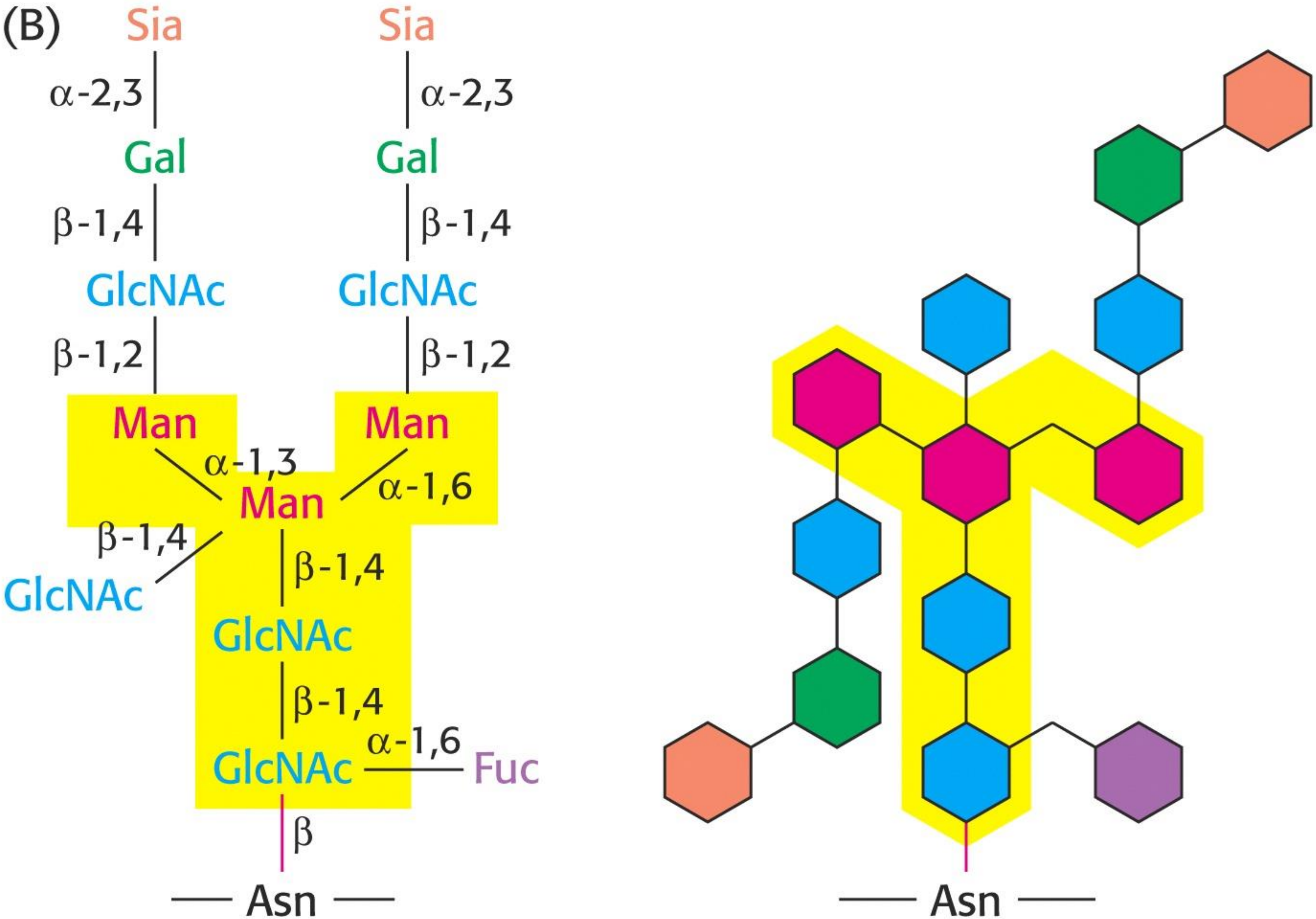
Some soluble
proteins also

N-linked oligos, high mannose type

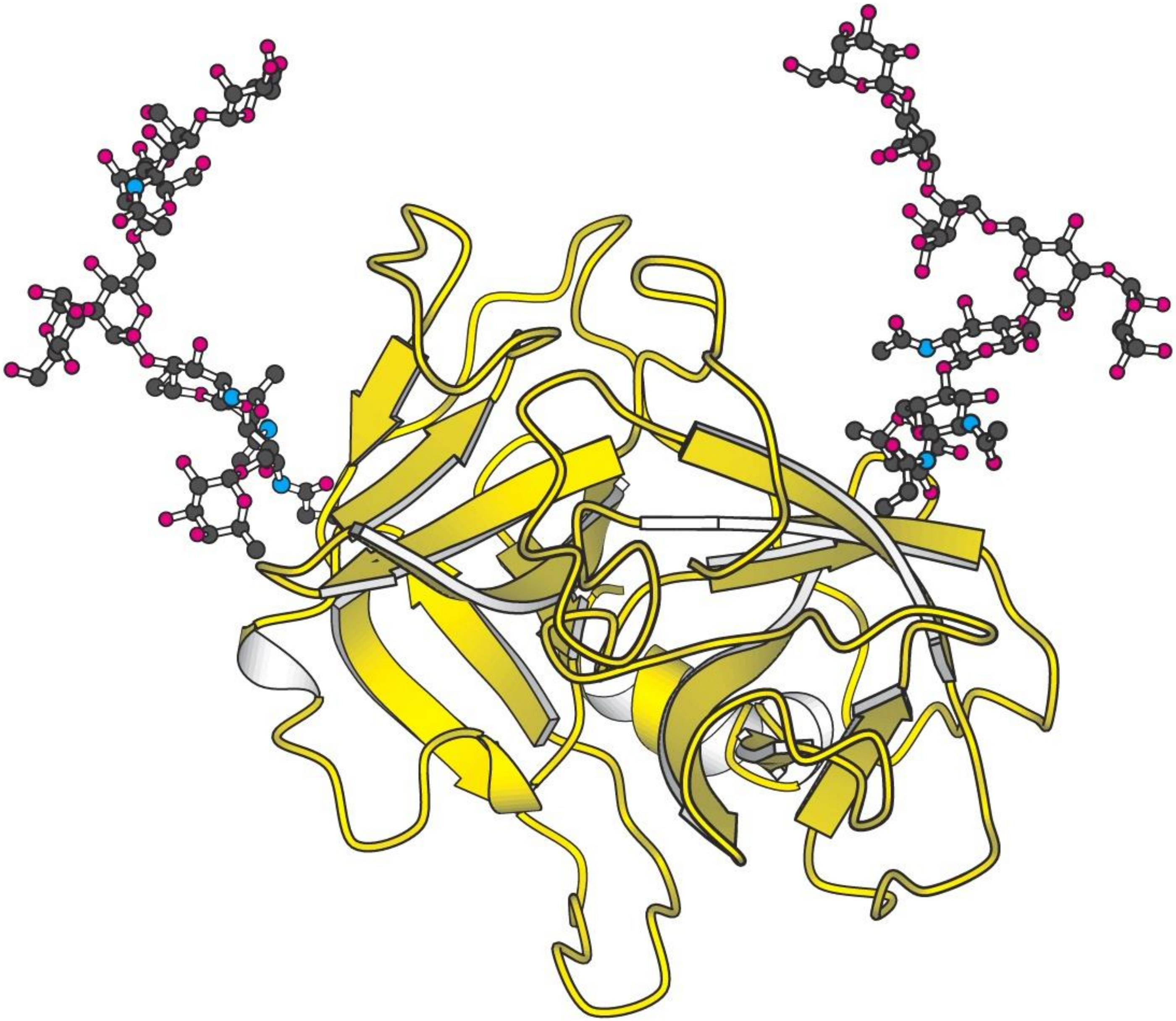
(A)



N-linked oligos, complex

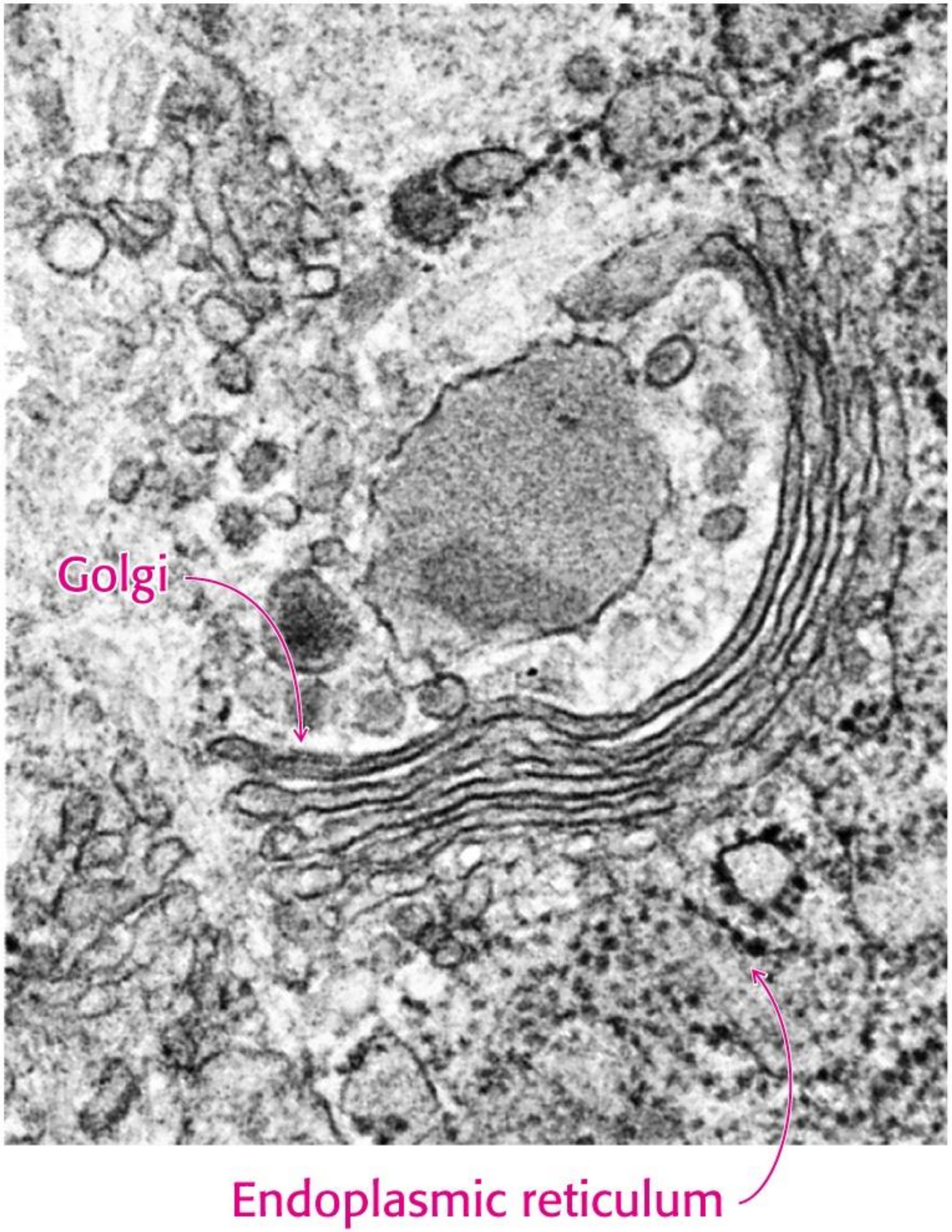


Elastase, secreted glycoprotein in serum



Most proteins in blood serum are glycoproteins

ER & Golgi complex



Where proteins are glycosylated following synthesis on ribosomes

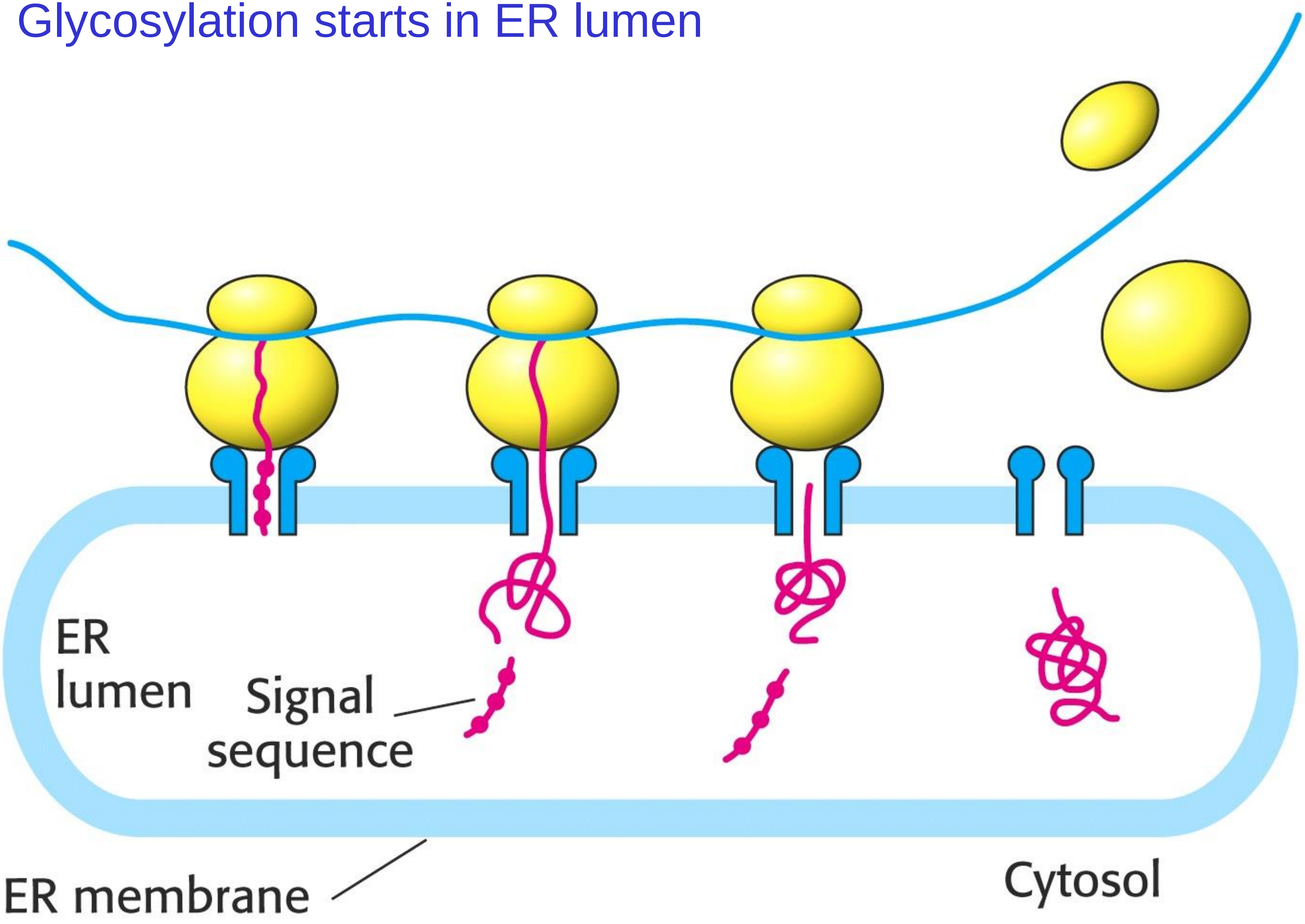
N-linked in ER
O-linked in Golgi

Black dots on ER are ribosomes

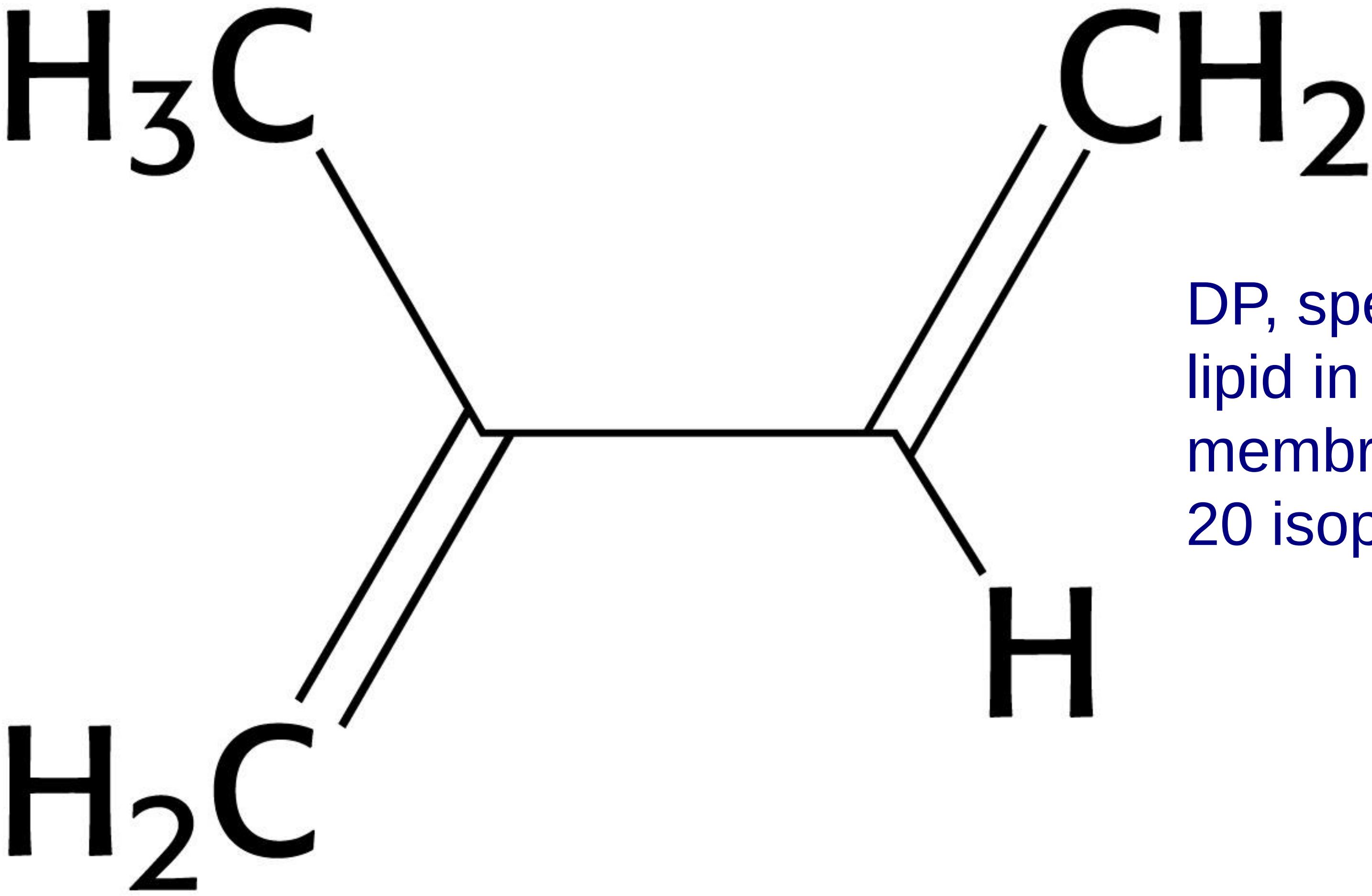
Electron micrograph

Transport into ER

Glycosylation starts in ER lumen



Repeating unit of Dolichol Phosphate (in ER membrane)

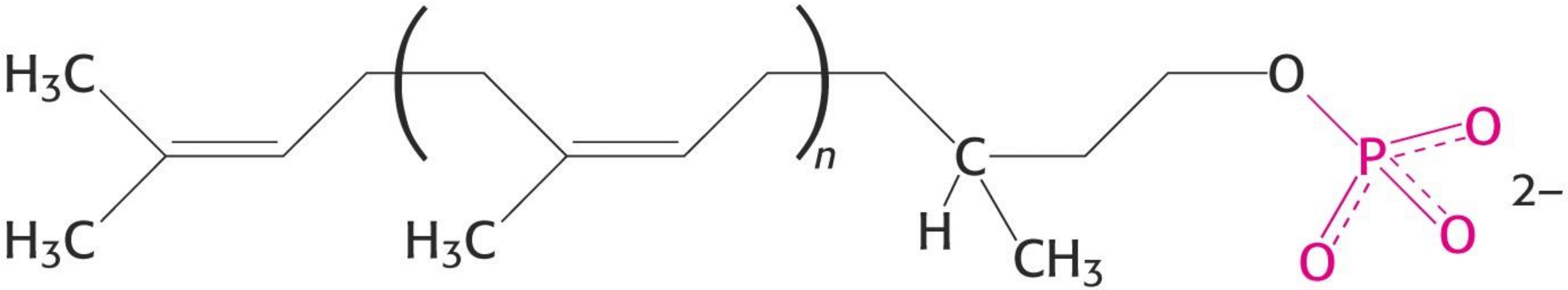


DP, specialized lipid in ER membrane - up to 20 isoprene

Isoprene

Dolichol phosphate

In ER membrane, phosphate group on cytoplasmic face



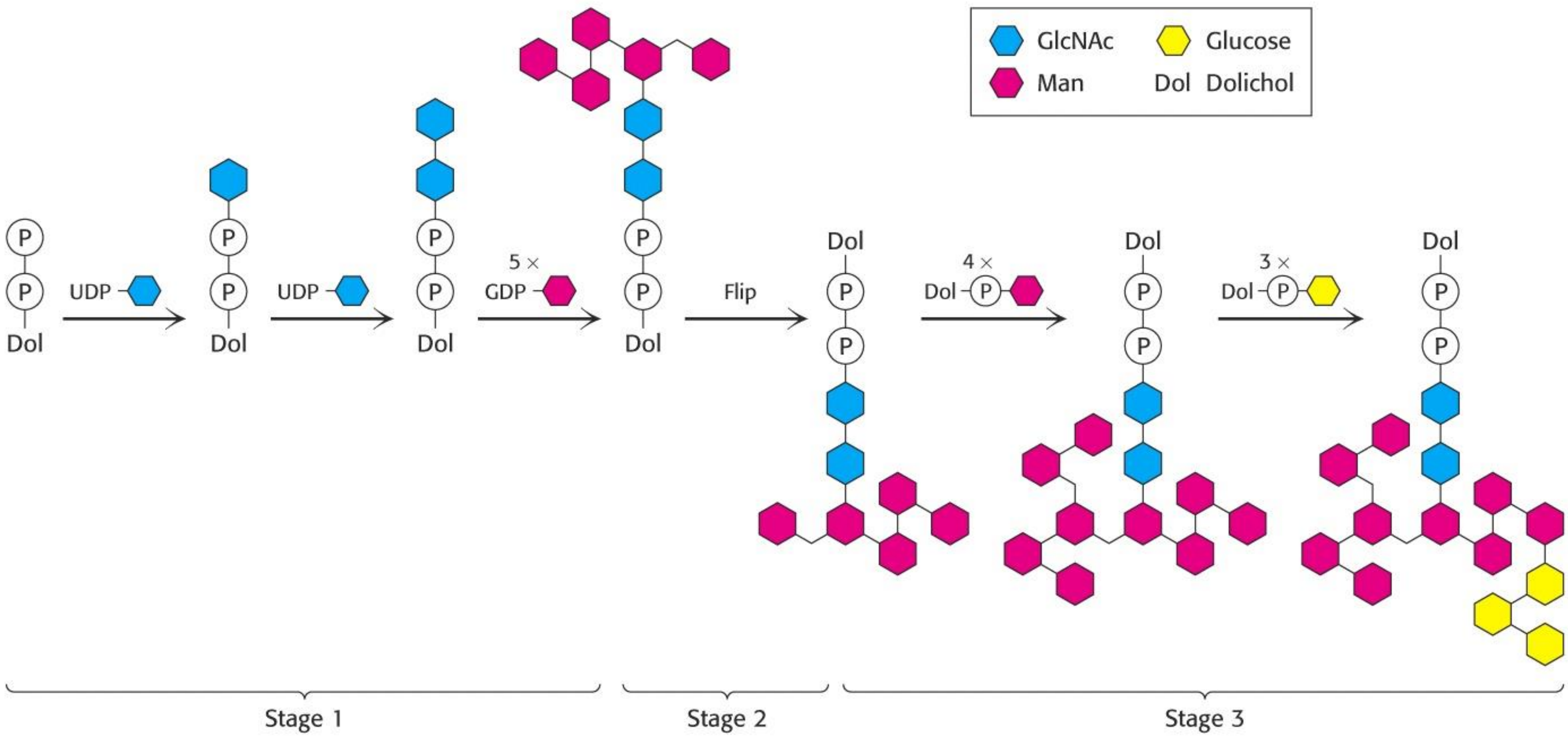
$n = 15–19$

Dolichol phosphate

A lipid molecule on which oligosaccharides are assembled prior to protein glycosylation

Assembly of N-linked oligos on Dol-P

Three stages

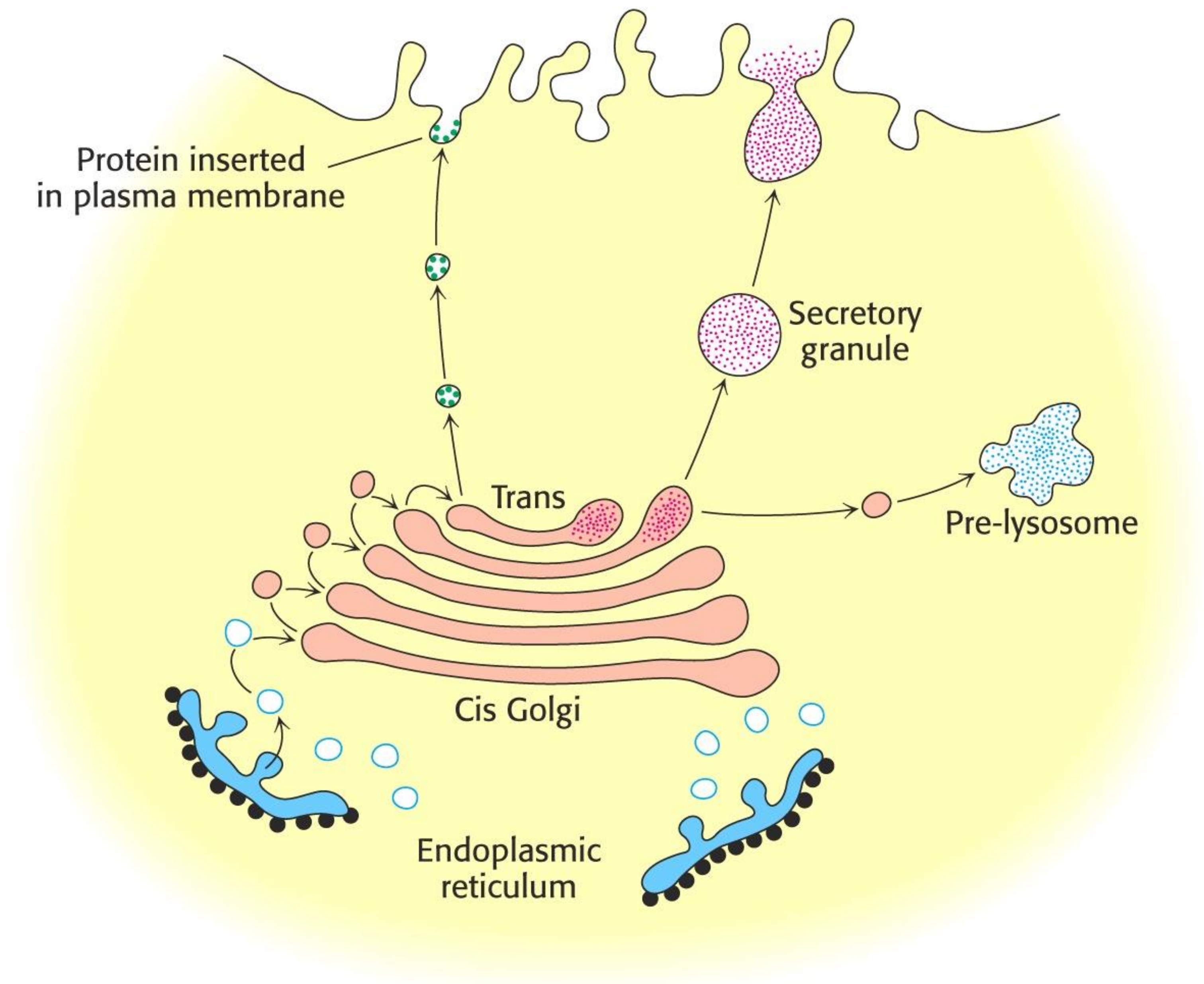


Cytoplasmic

Flip

ER lumem

Golgi complex, sorting center



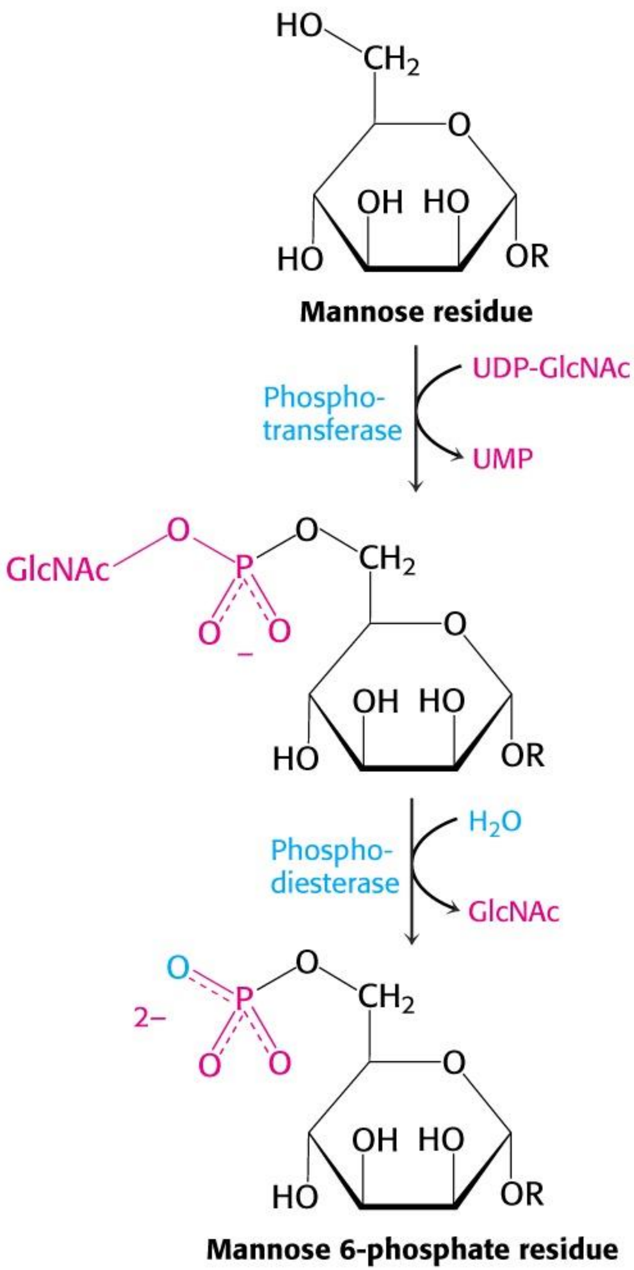
Targets proteins to,

Lysosomes,

Secretory vesicles,

Plasma membrane

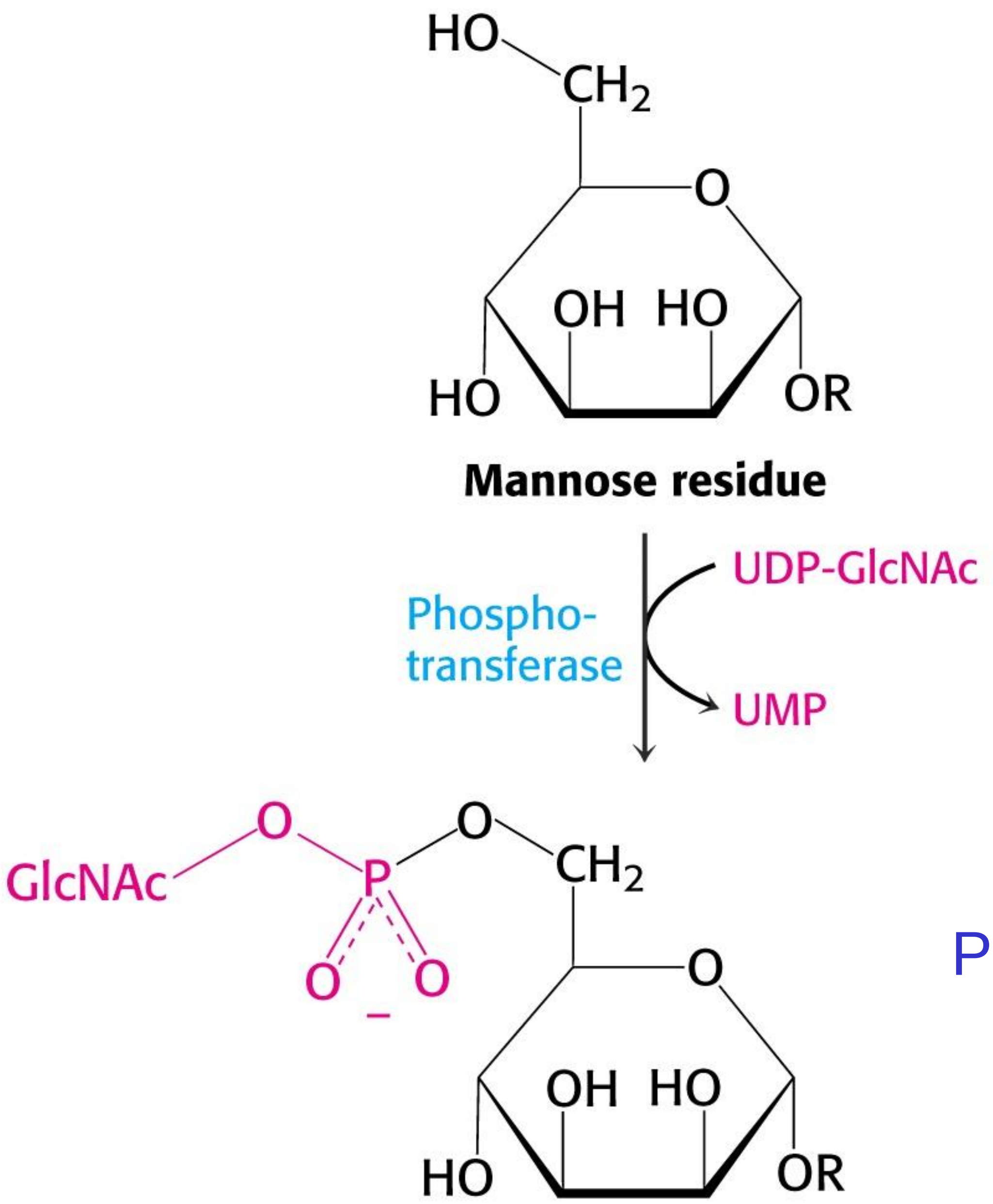
Mannose 6-phosphate marker



Modification of mannose residue in the oligo as a marker for targeting to Lysosomes

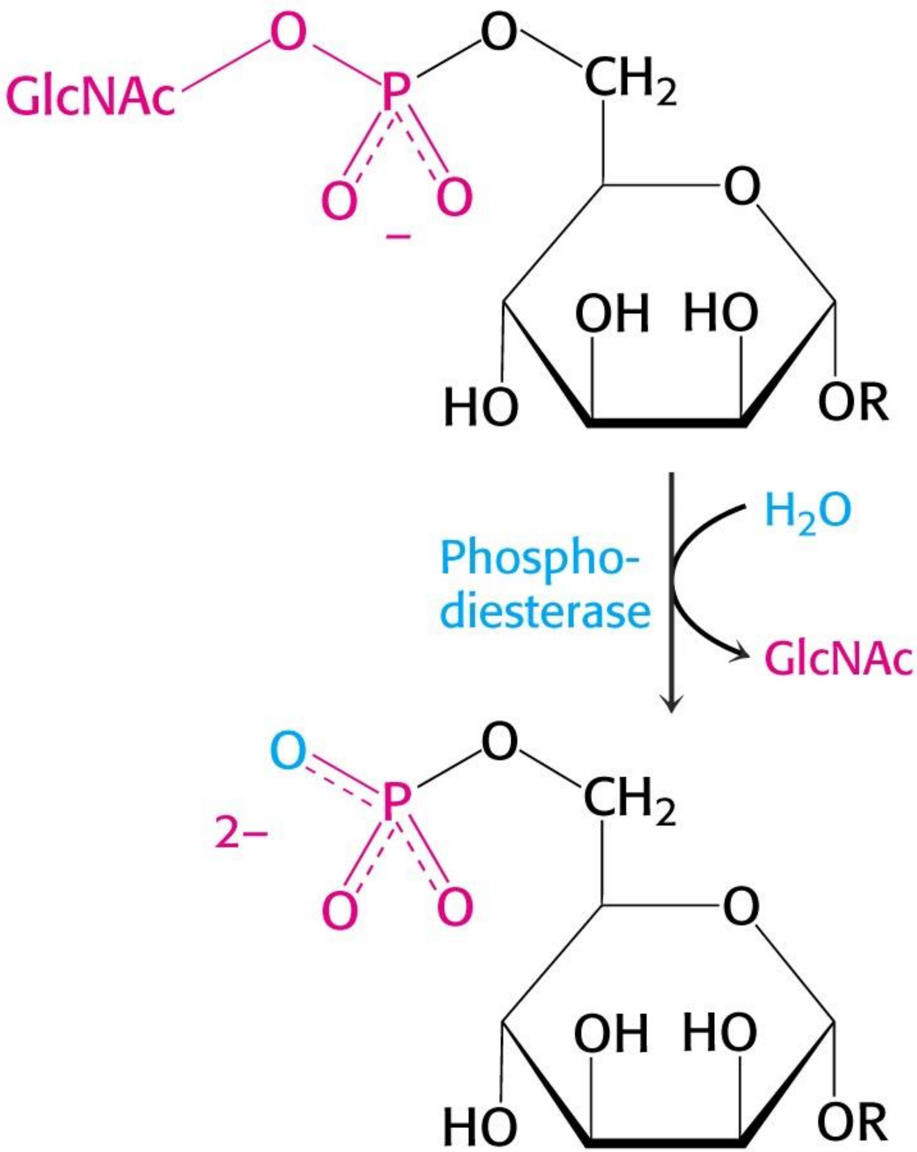
Done in cis Golgi compartment

Step one



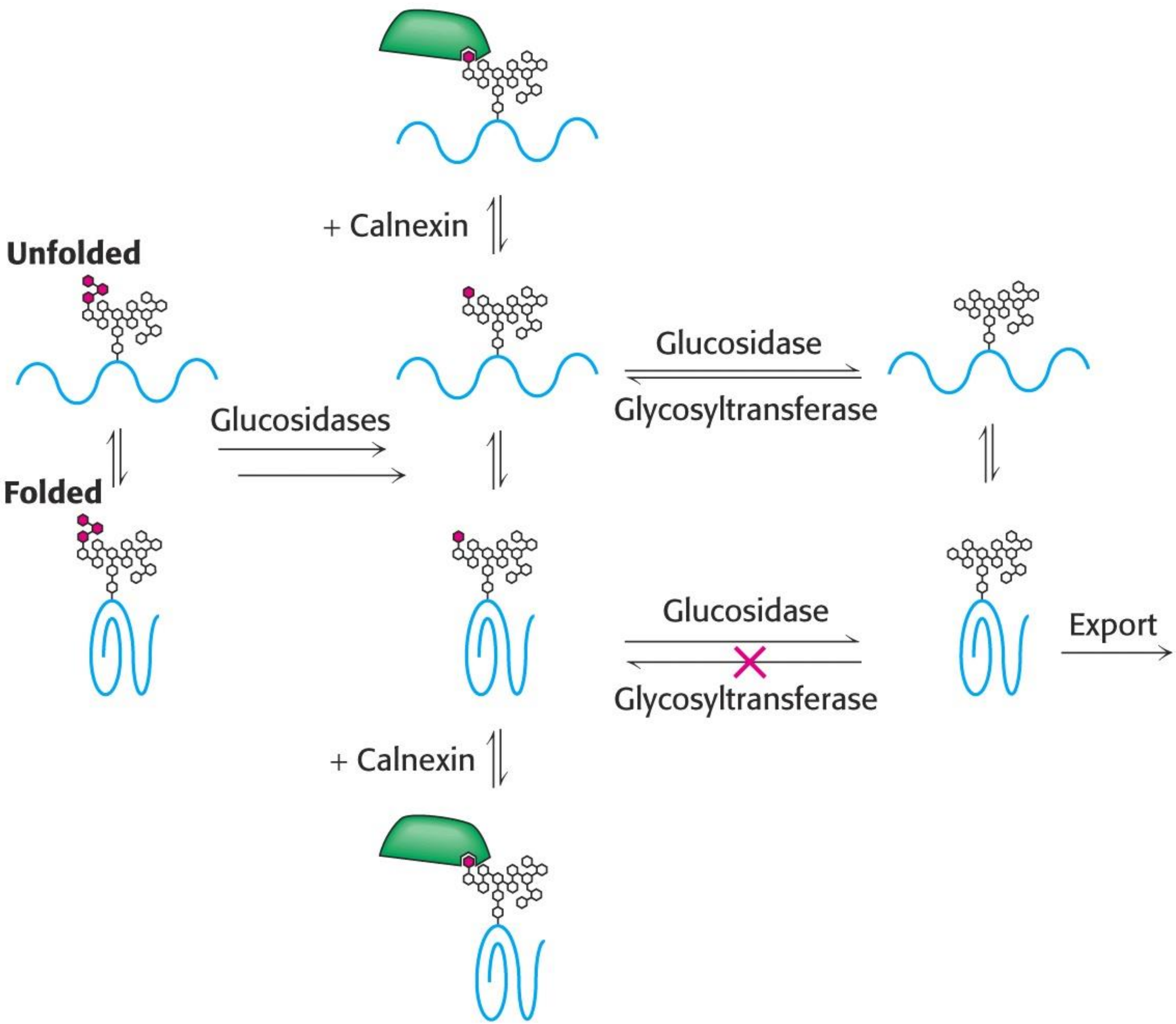
Phospho-N-acetylglucosamine

Step two



Mannose 6-phosphate residue

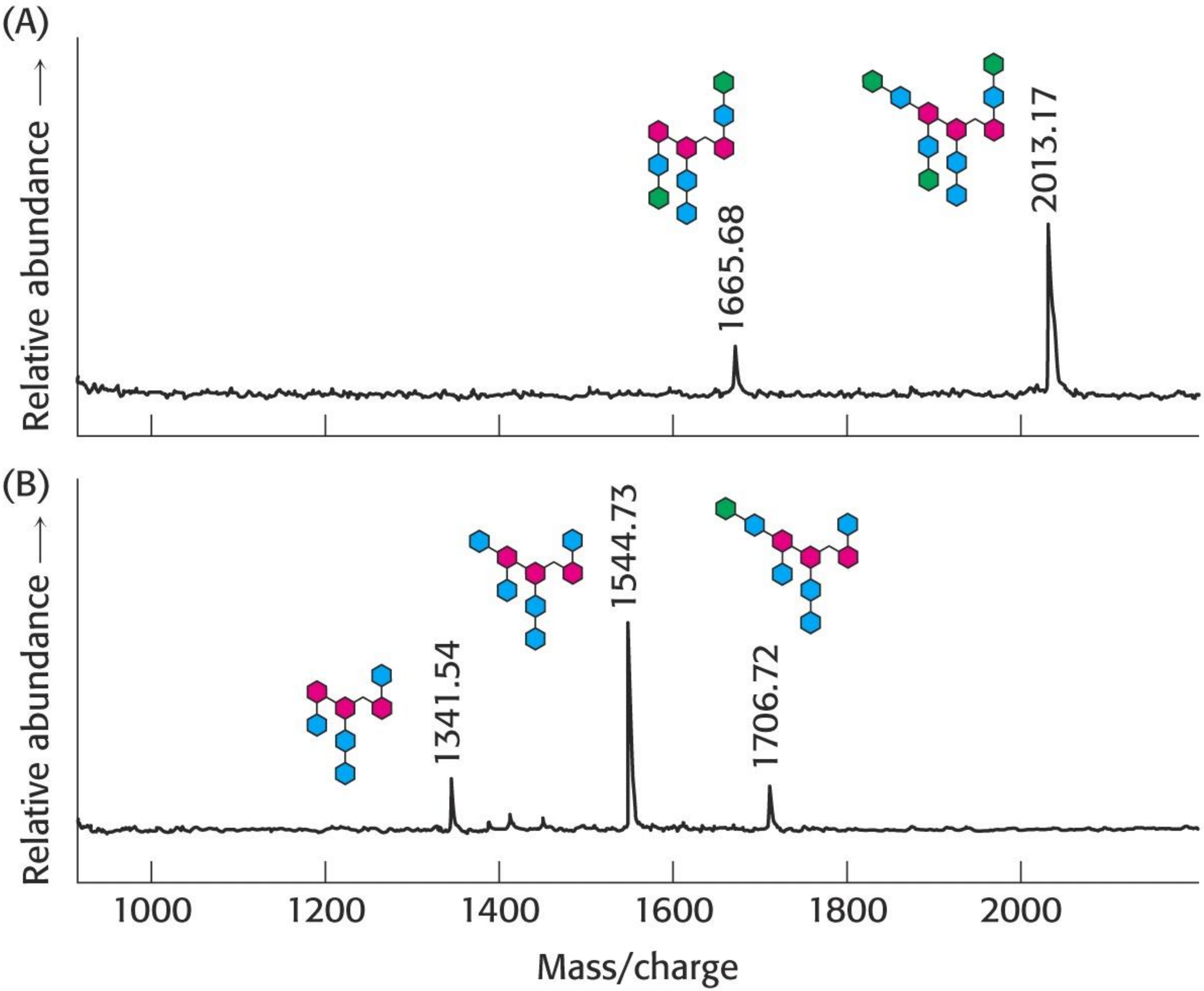
Quality control of protein folding in ER



Calnexin, & (calreticulin) chaparone Proteins

Carbohydrates carry information

Oligo structure by mass spectrometry



Plant lectins, binding selectivities

Three plant lectins bind different oligos

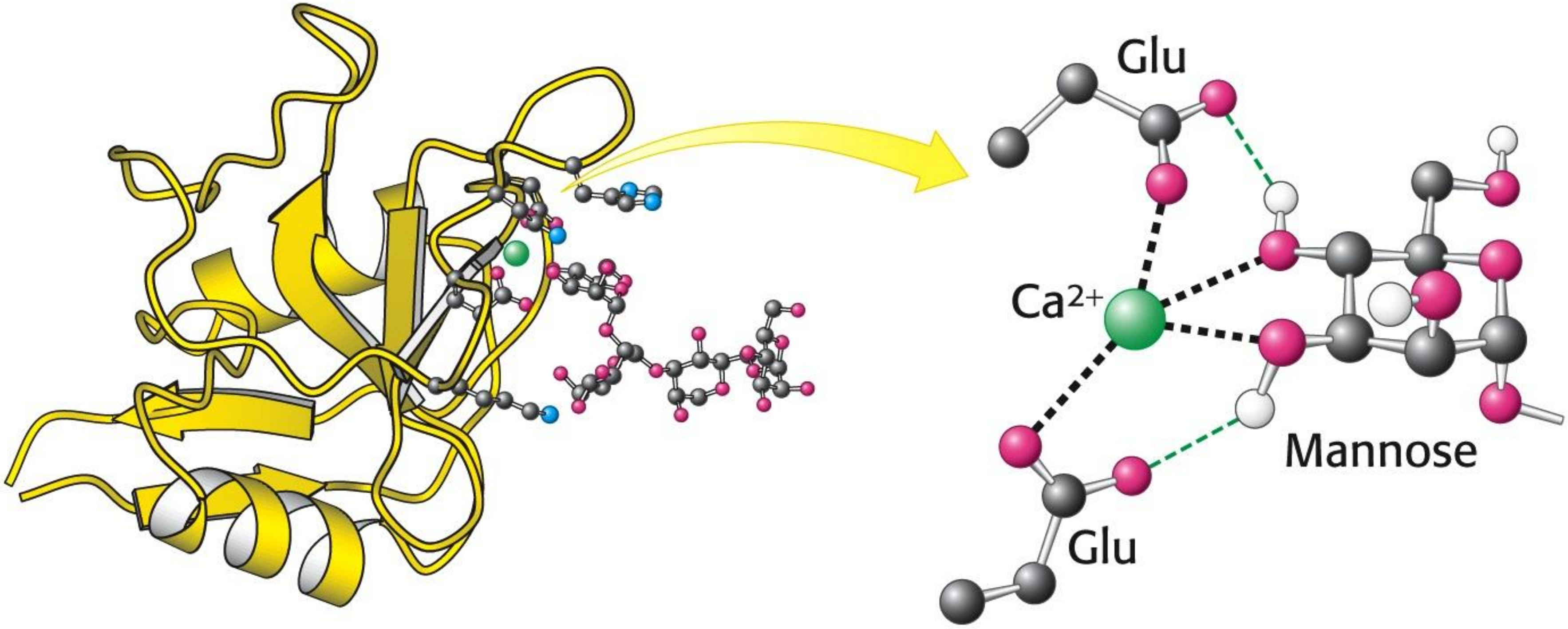
serve as insecticides

Binds to wheat germ agglutinin **Binds to peanut lectin** **Binds to phytohemagglutinin**

Animal lectin, C-type carb-binding domain

Animal cell lectins facilitate cell-cell contact

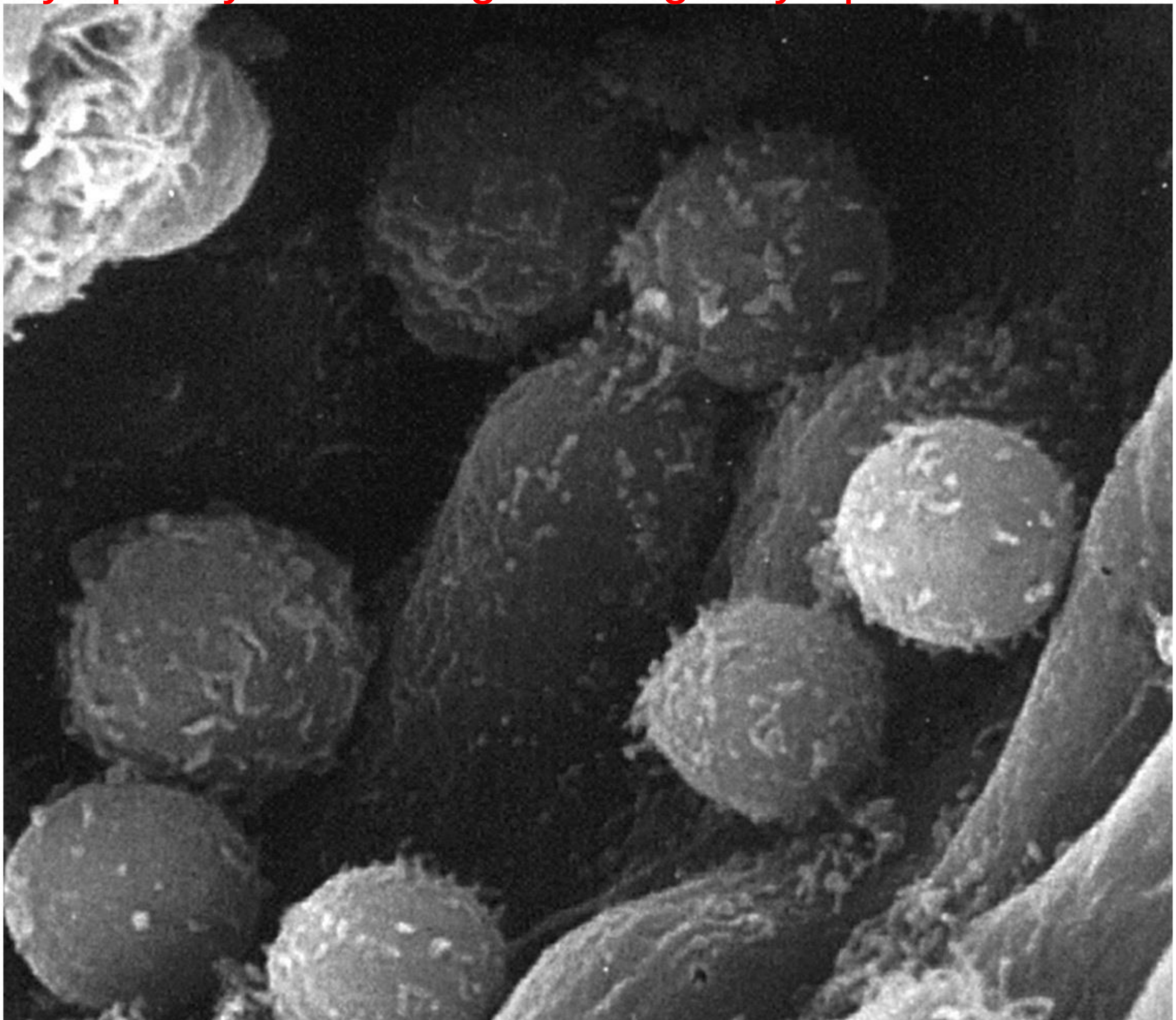
Lectin binding sites on surface of one cell interacts with carbs displayed on surface of another cell (like Velcro)



In animal cell C-type lectins, Ca^{2+} ion acts as a bridge between protein and sugar residue of oligo

Selectins, C-type lectins

Lymphocytes binding to lining of lymph nodes



Bind immune-system cells to targets,

L- to lymph-node vessels,

E- to endothelium,

P- to blood platlets

Influenza hemagglutinin

Binds to sialic acid residues on target cell surface,

Inside cell, viral protein, neuraminidase, cleaves glycosidic bond;
a promising target for anti-influenza agents