CARBOHYDRATES AND GLYCOBIOLOGY,

Ch-7

Dr. Rula Abdul-Ghani

1) Energy:

   CHO oxidation central energy–yielding pathway.

2) Structural and protective elements:

   insoluble polymers in cells walls of bacteria, connective tissue of animals, plants (cellulose)

3) participate in biological transport, Adhesion and cell-cell recognition, modulation of the immune system

4) intermediates in the biosynthesis of other basic biochemical entities (fats and proteins)

5) Determine fate/ intracellular location of hybrid molecules / Glycoconjugates = complex CHO covalently attached to lipids/ proteins

Carbohydrates = sugars = saccharides
polyhydroxy aldehydes / ketones most have empirical formula $(CH_2O)_n$. may contain sulfur, nitrogen, phosphorous e.g. in deoxysugars, aminosugars

Three major classes:

1)Monosaccharides / simple sugars: (-ose)

single polyhydroxy aldehyde / ketone unit.
most abundant = D-glucose
> 4C → cyclic structure

2) Oligosaccharides: (-ose)

joined chain of mono joined by glycosidic bond
most abundant disaccharides e.g. sucrose= glucose+fructose

In cells oligo >3 mono don't occur free but joined to lipid/protein

3) Polysaccharides:

>20 till hundreds/ thousands mono.
linear chain (cellulose) or branched (glycogen)

Monosaccharides:

Colorless, crystalline solids, soluble in water, sweet taste.

Simplest aldehyde / ketone with 2 hydroxyl groups.

Trioses, tetroses, pentoses, hexoses, heptoses

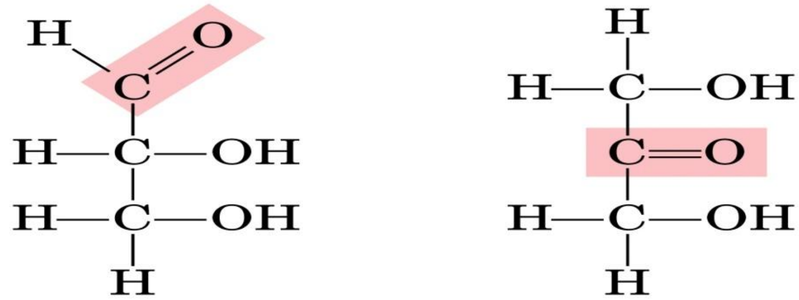
Many C atoms are chiral centers→ stereoisomers.

Two families of Monosaccharides:

Aldoses: if carbonyl group at an end of the C chain.

Ketoses: if carbonyl group at any other position of the C chain

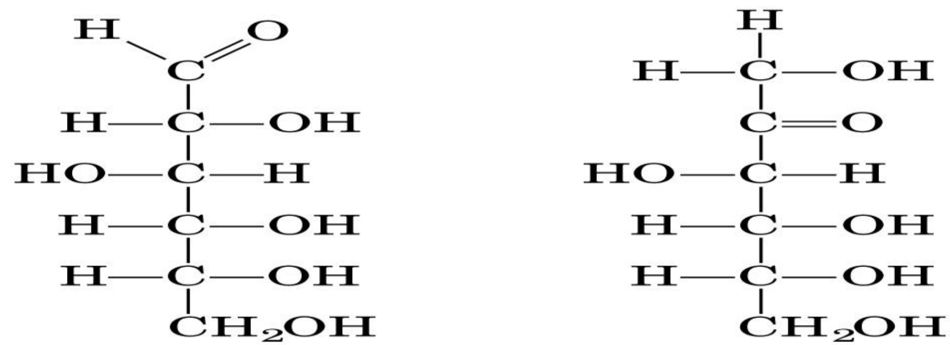
Trioses:
Simplest Monosaccharides



Glyceraldehyde, an aldotriose — Dihydroxyacetone, a ketotriose

(a)

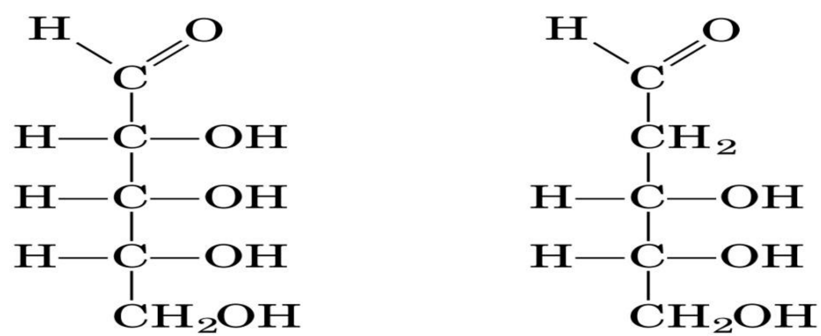
Hexoses:
Most common mono in nature



D-Glucose, an aldohexose — D-Fructose, a ketohexose

(b)

Pentoses:
Components of nucleotides and nucleic acids.



D-Ribose, an aldopentose — 2-Deoxy-D-ribose, an aldopentose

(c)

By convention:

Two isomers D- and L-

OH- group on the reference C on the right = D-isomer.

OH- group on the reference C on the left = L-isomer.

Fischer projection formulas

Molecule with n chiral centers

have 2^n sterioisomers.

Glyceraldehyde $2^1 = 2$

Aldohexose = $2^4 = 16$

Perspective formulas

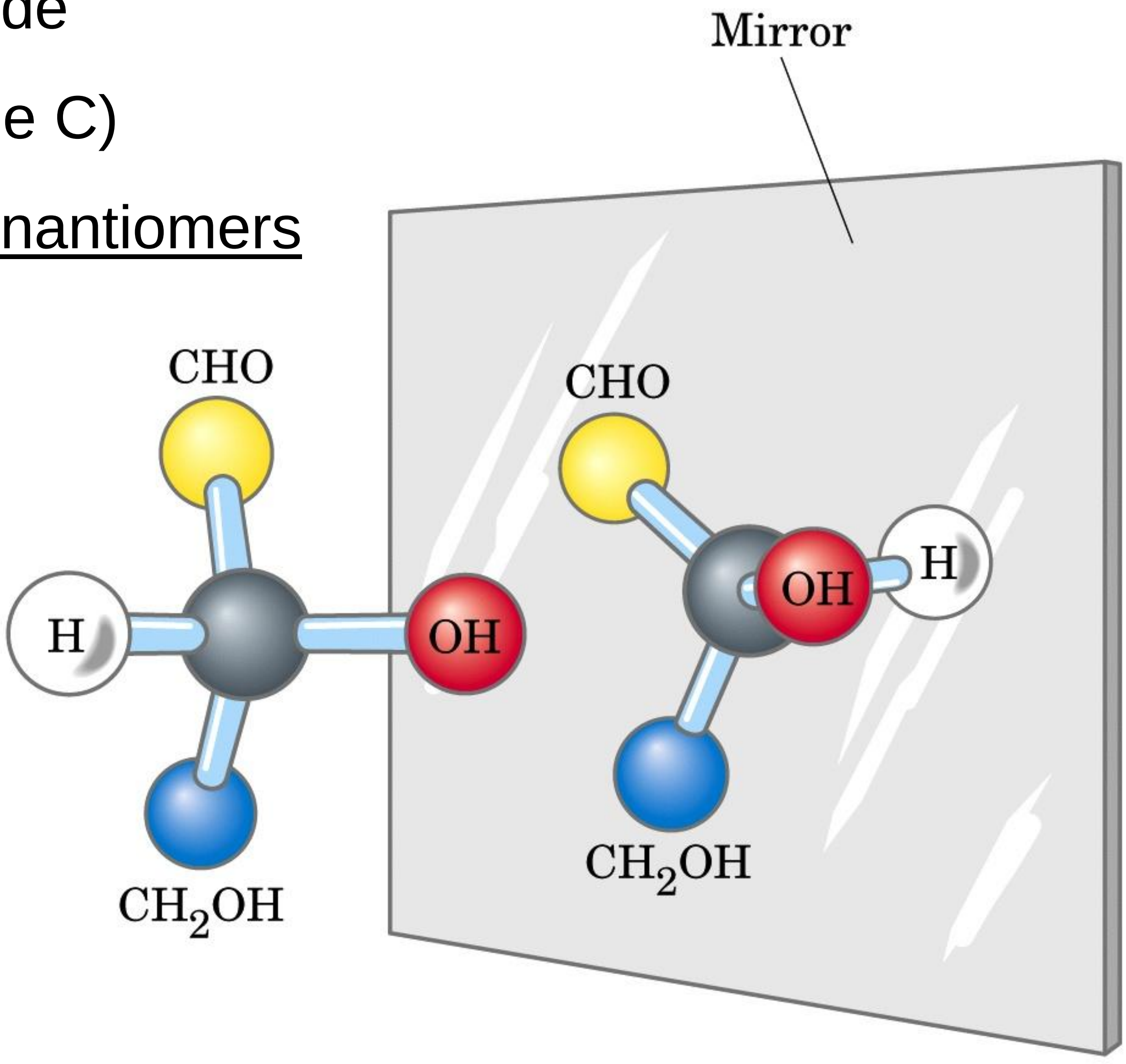
All mono except DHAP has one/more asymmetric chiral centers.

Simplest = glyceraldehyde

One chiral center (middle C)

→2 different isomers / enantiomers

→ Mirror images.



Ball-and-stick models

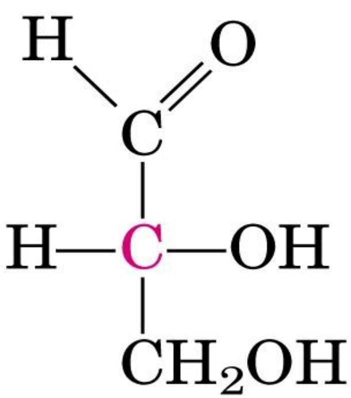
Aldoses:

Carbon numbering :

begin at the end of the chain nearest to carbonyl group

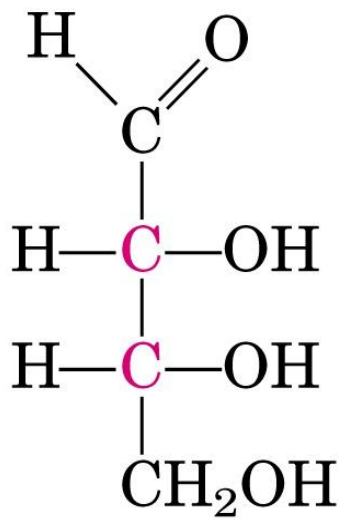
C = chiral center

Three carbons

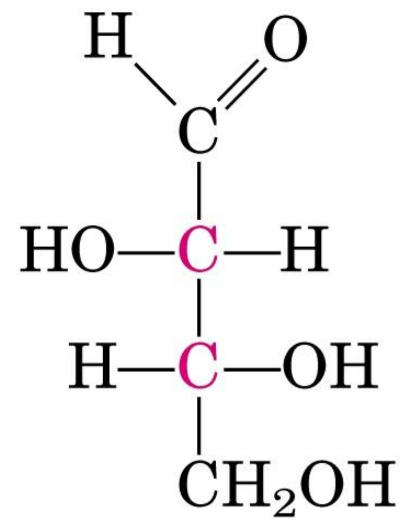


D-Glyceraldehyde

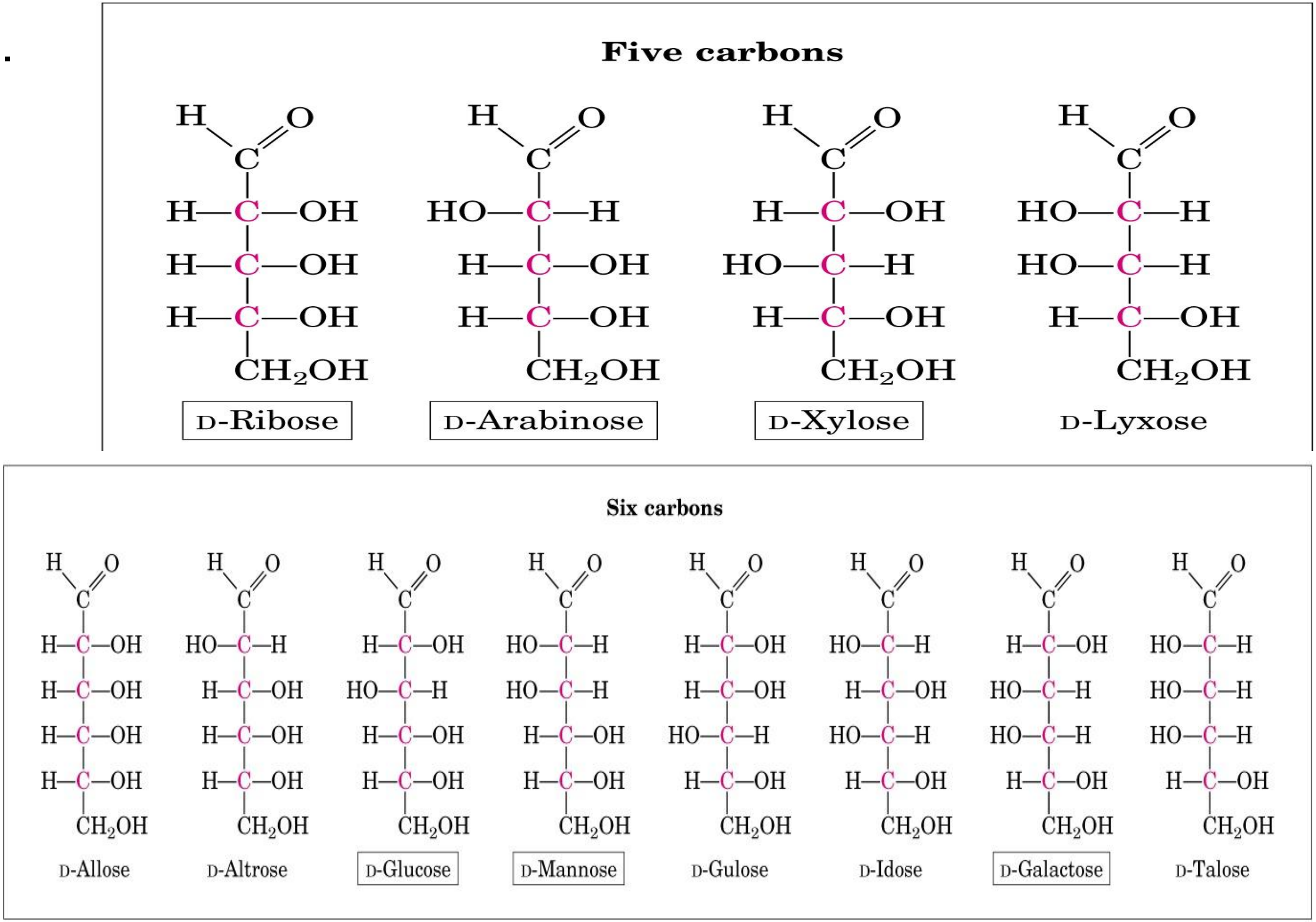
Four carbons



D-Erythrose



D-Threose


Five carbons
D-Ribose
D-Arabinose
D-Xylose
D-Lyxose
Six carbons
D-Allose
D-Altrose
D-Glucose
D-Mannose
D-Gulose
D-Idose
D-Galactose
D-Talose

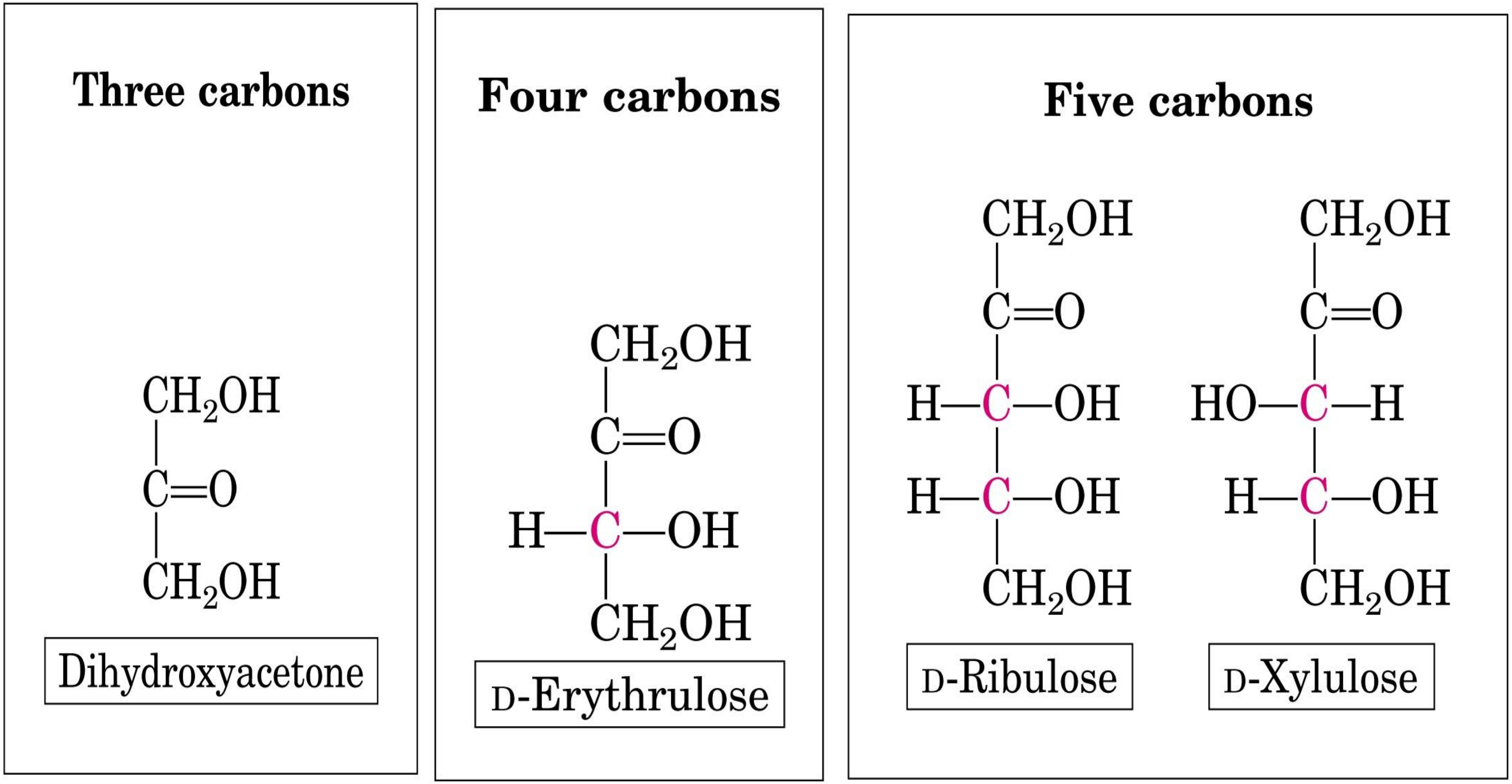
D-Aldoses
(a)

Sterioisomers

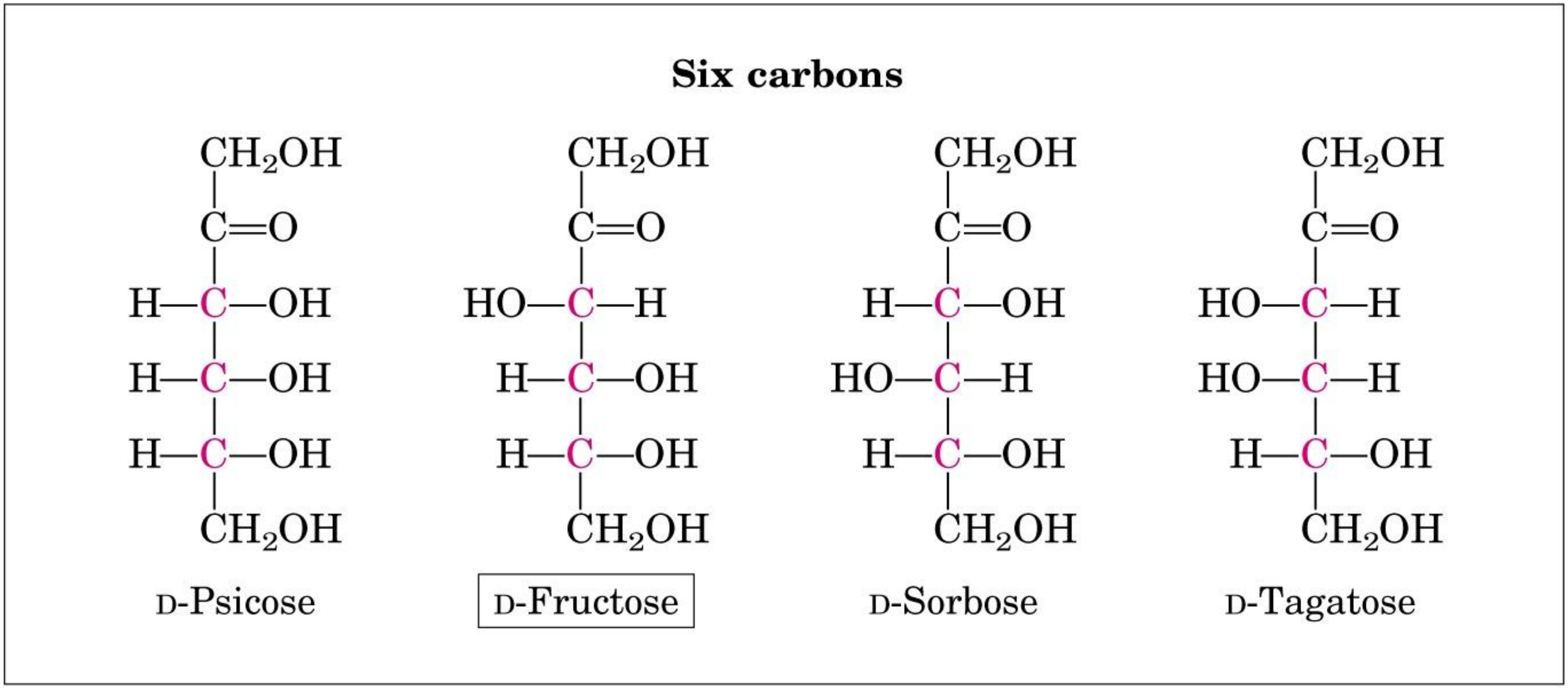
Divided into 2 groups (D , L) that differ in configuration about chiral center most distant from the carbonyl carbon = REFERENCE Carbon.

Ketoses:

Four- and five- carbon ketoses has the suffix – “ul”



Ketohexoses named differently:

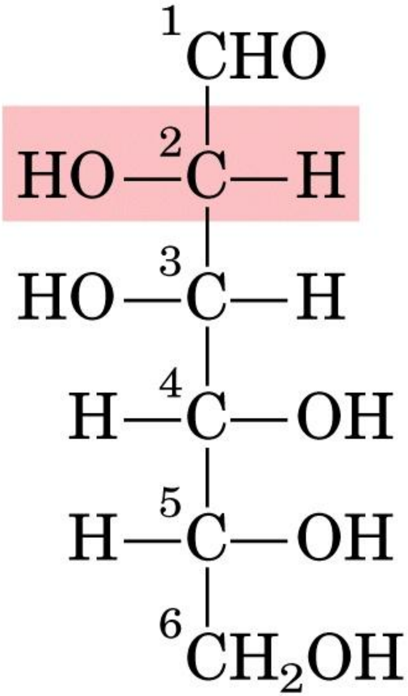


D-Ketoses
(b)

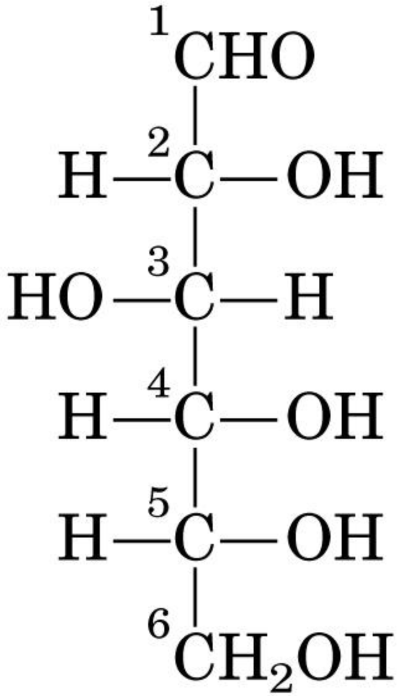
Epimers :

Two sugars that differ only in configuration of one chiral center.

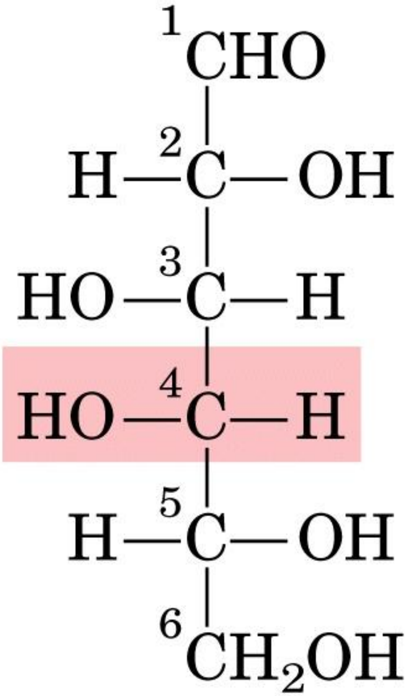
Epimers of D- glucose:



D-Mannose
(epimer at C-2)

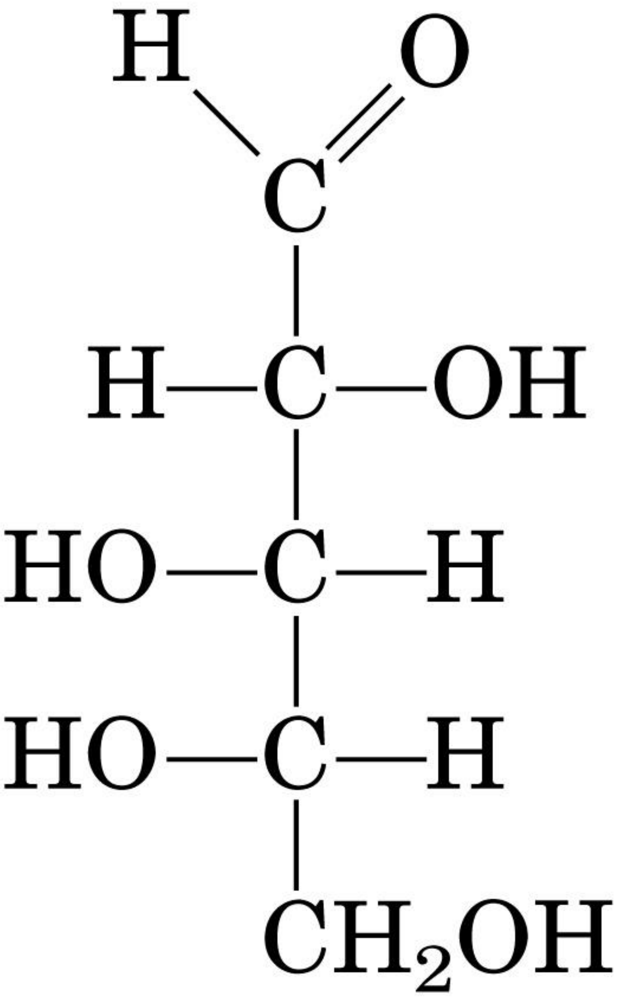


D-Glucose



D-Galactose
(epimer at C-4)

Some sugars exist in nature as L- isomers e.g L-arabinose and components of glycoconjugates.



L-Arabinose

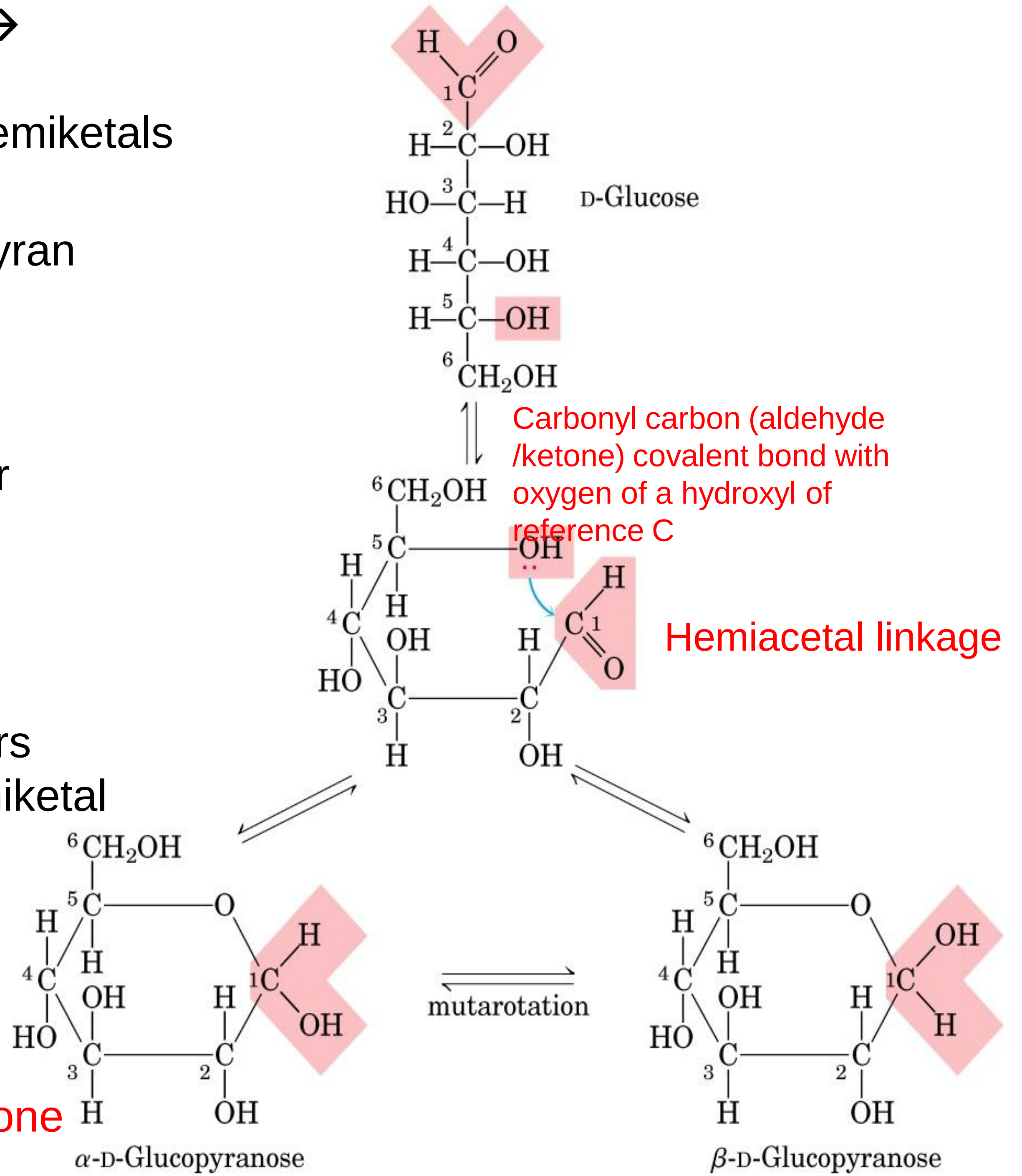
Mono >4C in aqueous soln →
cyclic /ring structure.
Form internal hemiacetals/hemiketals

Glucopyranose resembles pyran
(6-membered ring)

Anomers:
Isomeric forms of mono differ only in configuration at hemiketal/ hemiacetal C

Mutarotation:
Interconversion bw 2 anomers (α and β) of hemiacetal/ hemiketal

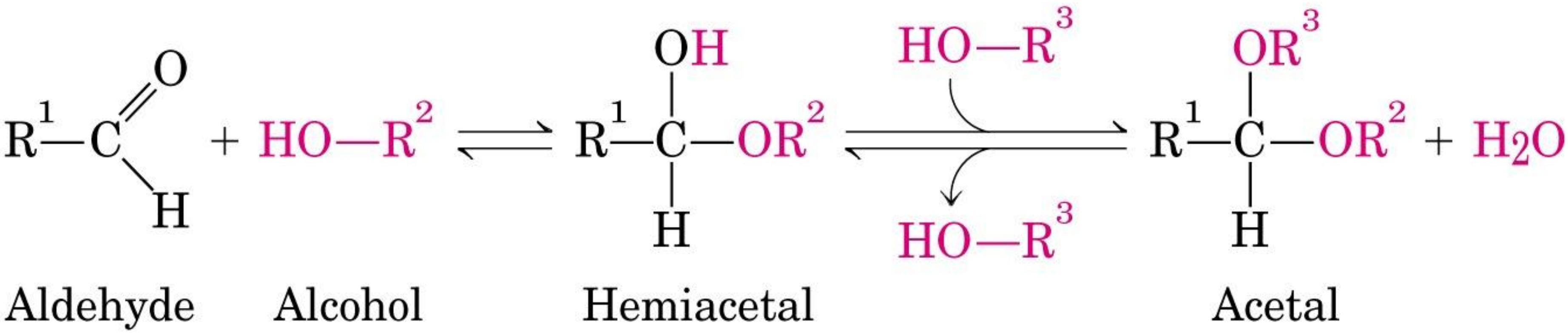
In aqueous soln.
1/3 α + 2/3 β +
+ very small amount linear
C1 = anomeric carbon α / β originally from aldehyde/ ketone



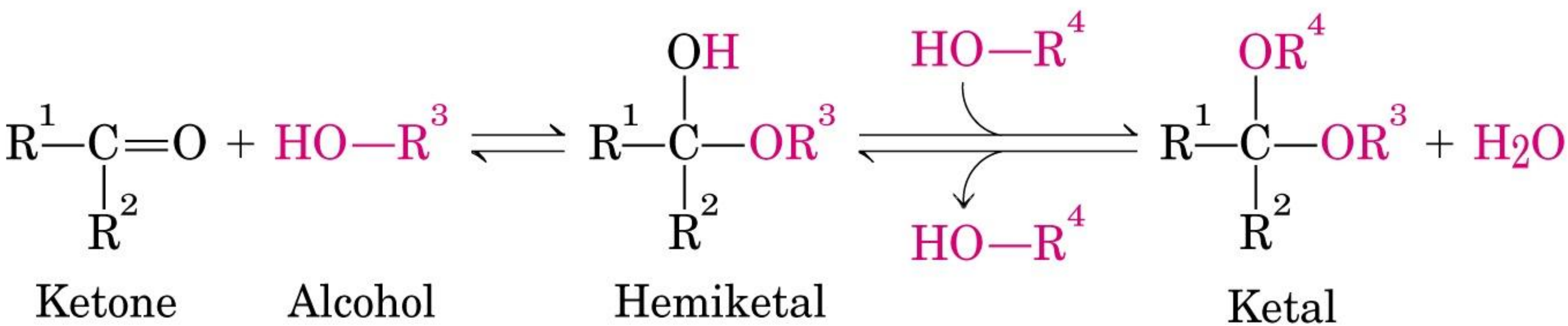
Hemiacetal & hemiketal formation.

An aldehyde can react with an alcohol → hemiacetal.

A ketone can react with an alcohol → hemiketal.



Substitution of another alcohol
(another sugar)→Glycosidic bond

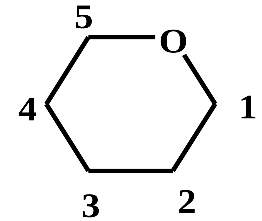


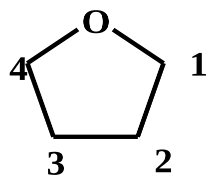
Pyranoses and furanoses:

β - anomers more common.

Haworth perspective formulas:

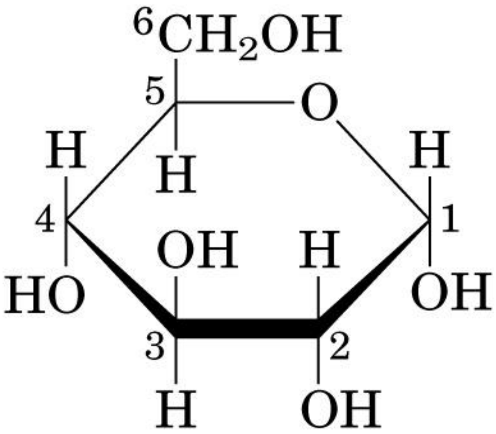
show the steriochemistry of ring forms of mono.



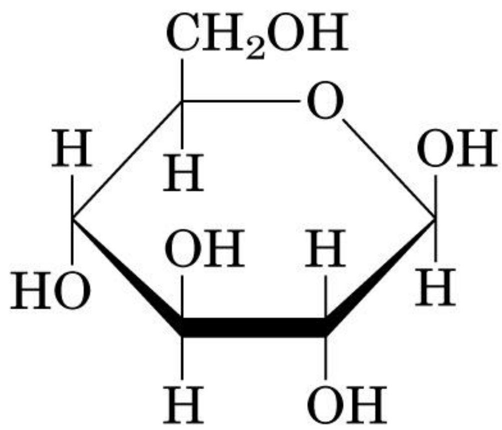


α (OH below the ring)

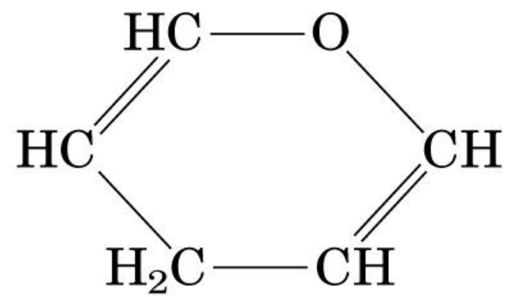
β (OH above the ring).



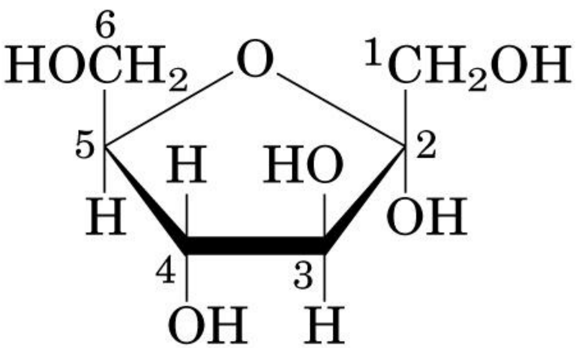
α-D-Glucopyranose



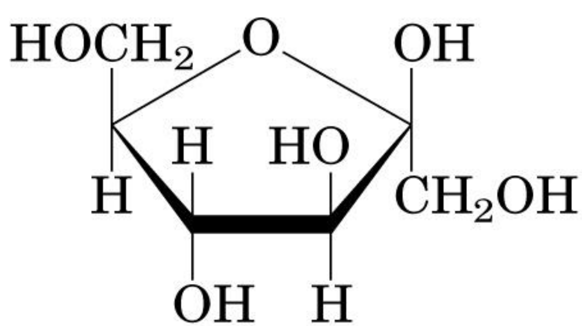
β-D-Glucopyranose



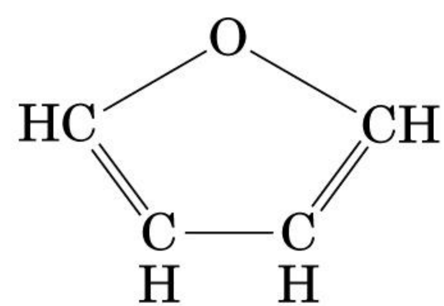
Pyran



α-D-Fructofuranose



β-D-Fructofuranose

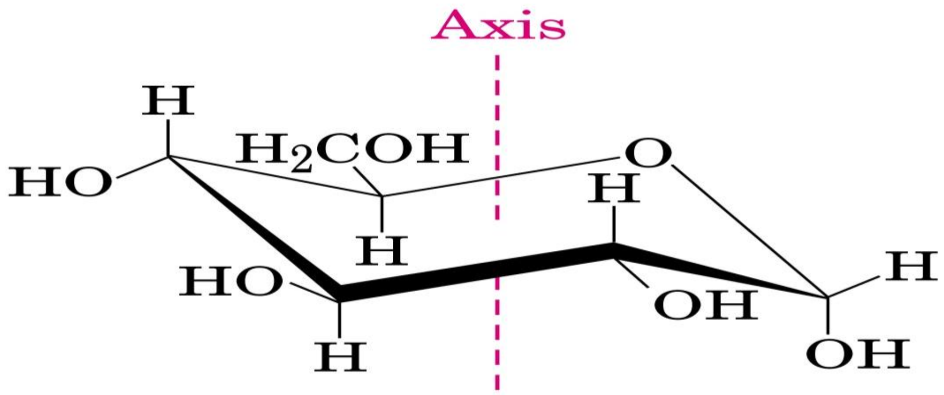


Furan

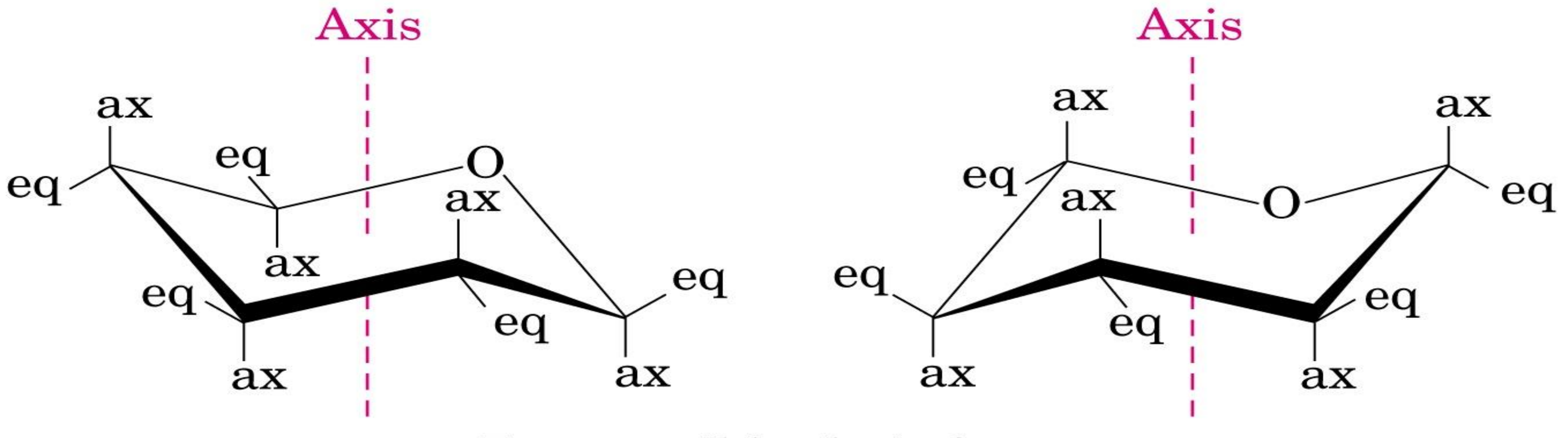
Six-membered pyranose ring is not planar,

Chair/ boat conformation.

ax= axial, eq = equatorial



α-D-Glucopyranose
(b)



Two possible chair forms
(a)

Structural representation of sugars

- Fisher projection & Perspective formulas : straight chain representation.
- Haworth projection: simple ring structure.
- Conformational representation: chair & boat configurations.

Sugar derivatives:

1) Amino sugars

Hydroxyl group→ replaced with another substitute

N-acetylglucosamine→ structural polymer in bacterial cell wall.

2)Deoxy sugars

Substitution of OH- to H

3) Acidic sugars

Carbon atom→ oxidized to a carboxyl group.

Aldonic acid (e.g gluconic acid):oxidation at C1

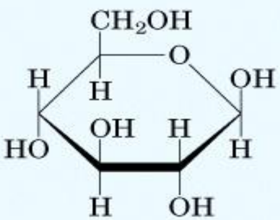
Uronic acid (e.g glucoronic acid): oxidation at C6

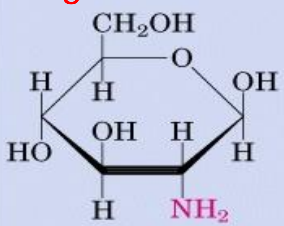
4) Phosphorylated sugars (metabolic intermediates,nucleic acids

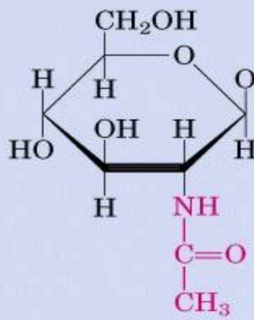
Activate the sugar for rxn, trap sugar in cell

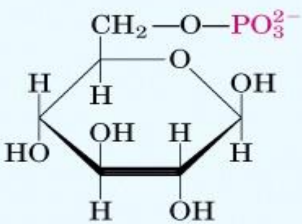
C2 hydroxyl → amino group→glucosamine
Condensed with acetic acid→ N-acetyl glucosamine

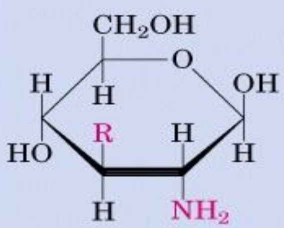
Glucose family

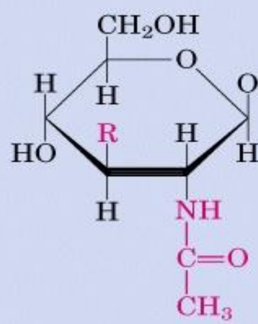

β-D-Glucose

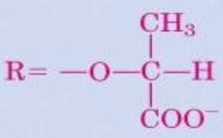

β-D-Glucosamine


N-Acetyl-β-D-glucosamine

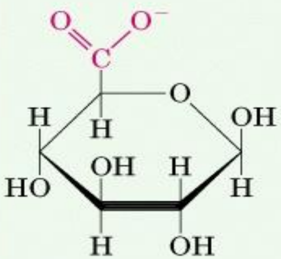

β-D-Glucose 6-phosphate

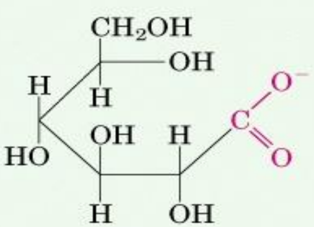

Muramic acid

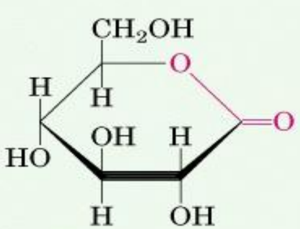

N-Acetylmuramic acid



Lactic acid ether linked to O at C3

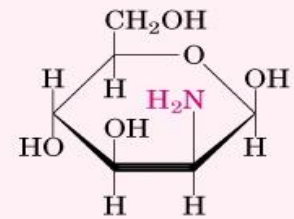

β-D-Glucuronate


D-Gluconate

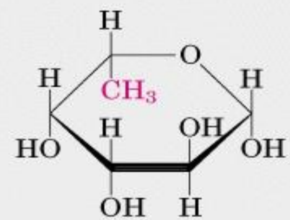

D-Glucono-δ-lactone

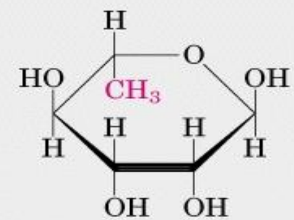
Amino sugars


β-D-Galactosamine


β-D-Mannosamine

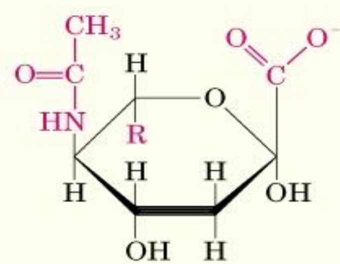
Deoxy sugars

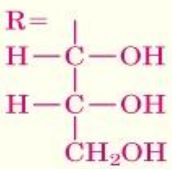

β-L-Fucose


α-L-Rhamnose

Glycoproteins +glycolipids(plant)

Acidic sugars



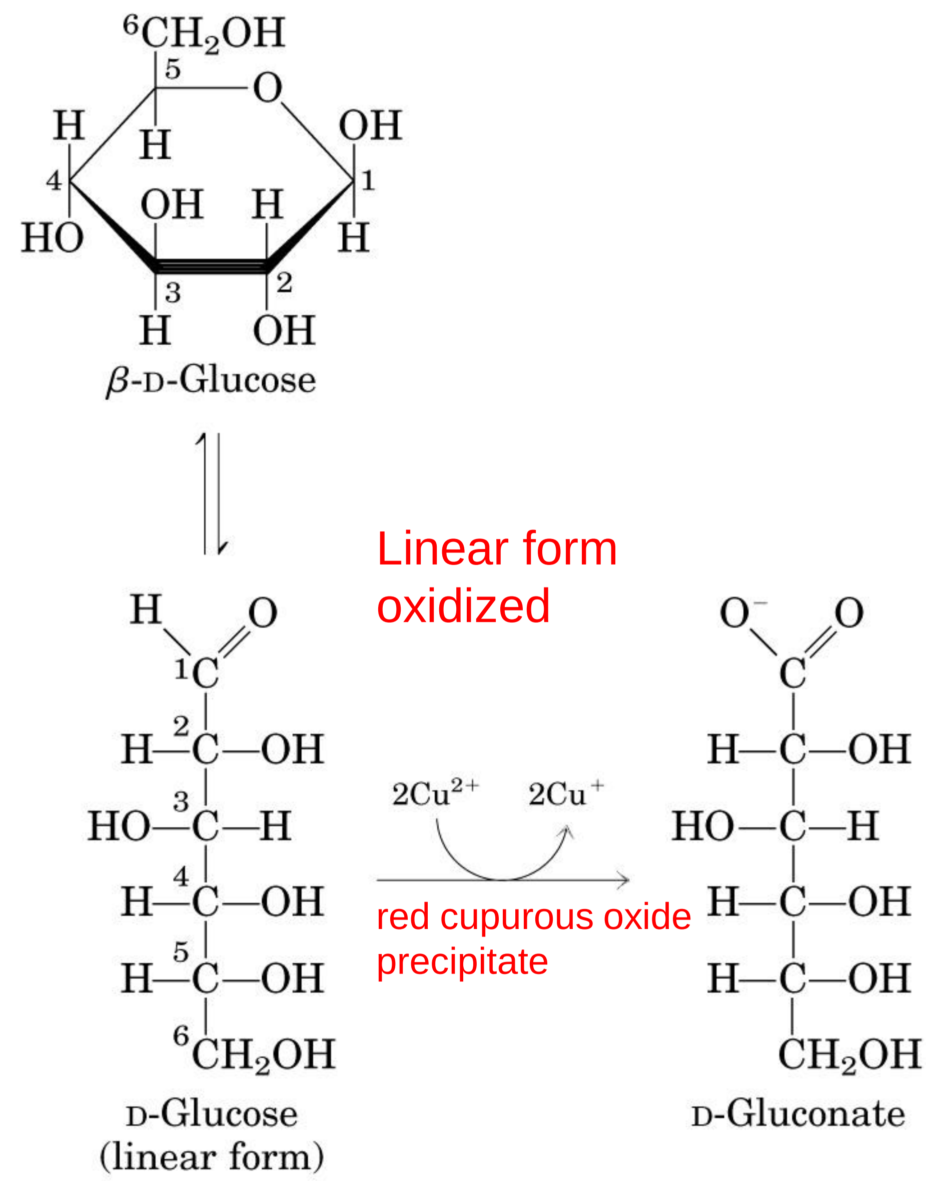

N-Acetylneuraminic acid
(sialic acid)

Mono oxidized by mild oxidizing agent cupric Cu^{2+} or ferrric Fe^{2+}

Sugars capable of reducing→ reducing sugars

The basis of Fehling`s rxn = Qualitative test for presence of reducing sugars.

Used previously for [Glc] in blood and urine + Diagnosis of DM.



(a)

Glucose oxidase:

More sensitive way to measure [Glc] in blood.

$$\text{D-Glucose} + O_2 \xrightarrow{\text{glucose oxidase}} \text{D-Glucono-}\delta\text{-lactone} + H_2O_2$$

(b)

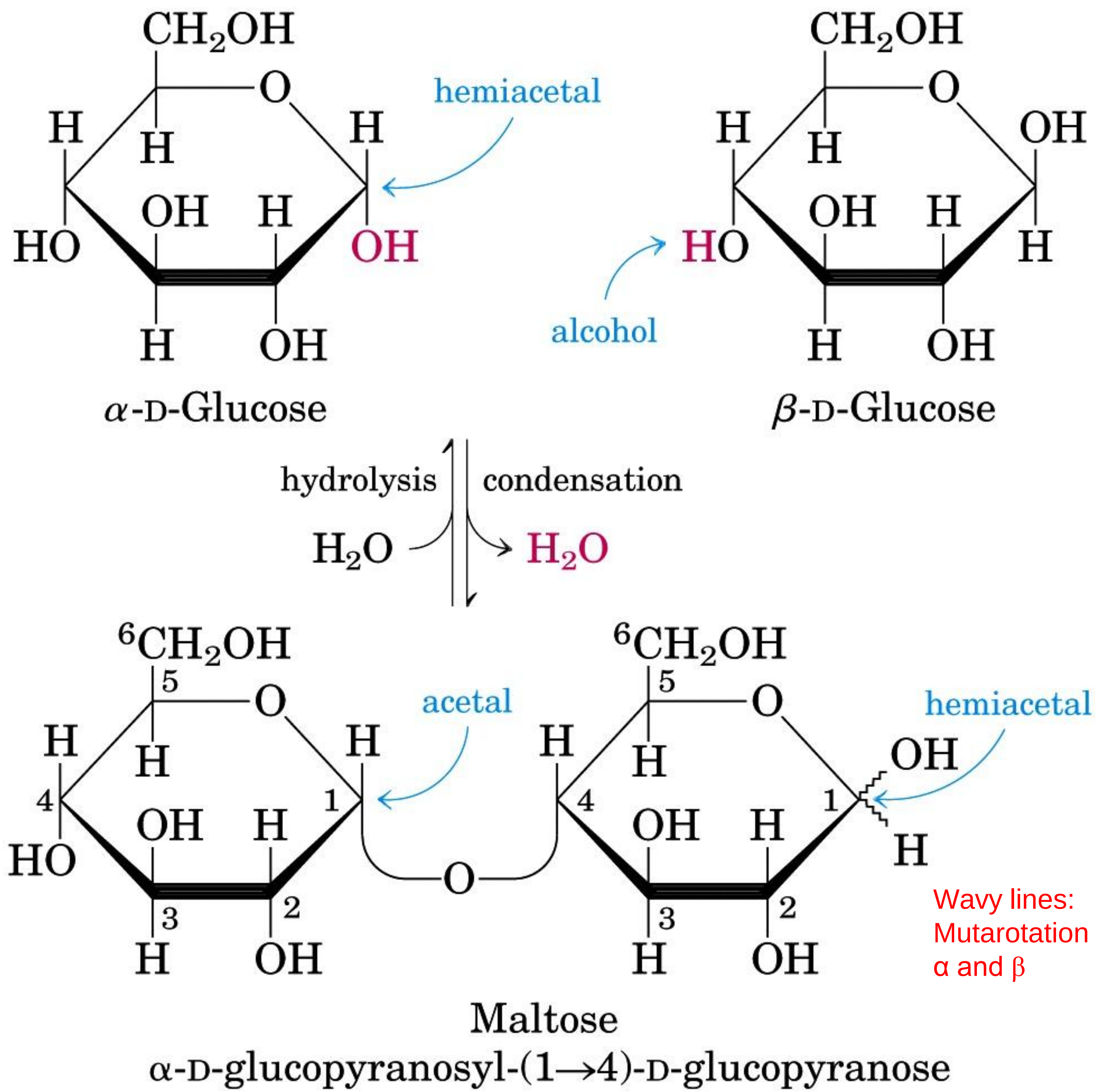
A second enzyme is needed peroxidase

H_2O_2 →→ colored product measured by spectrophotometer.

Formation of Disaccharide: lactose, maltose, sucrose

O-glycosidic bond formed when OH- group of one mono reacts with anomeric C1 of the other.

Hydroxyl at C1 = reducing end not involved in glycosidic bond.
→reducing sugar



Some common disaccharides:

Common name
Full systematic name
Abbreviation

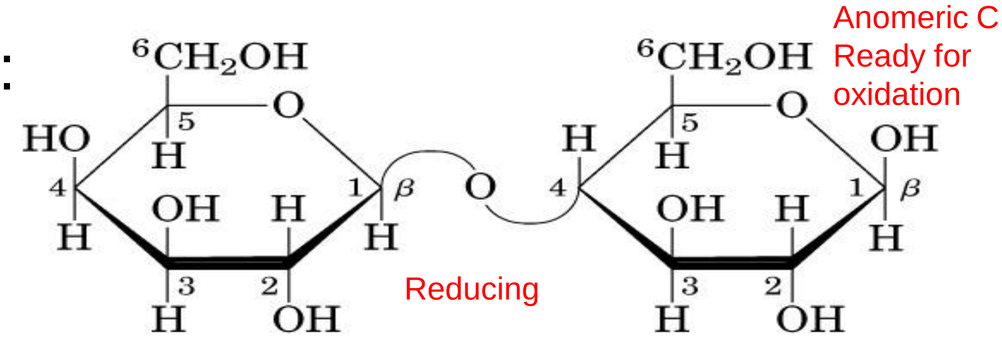
Lactose occur naturally in milk

Sucrose (table sugar)
Sucrose = non reducing sugar

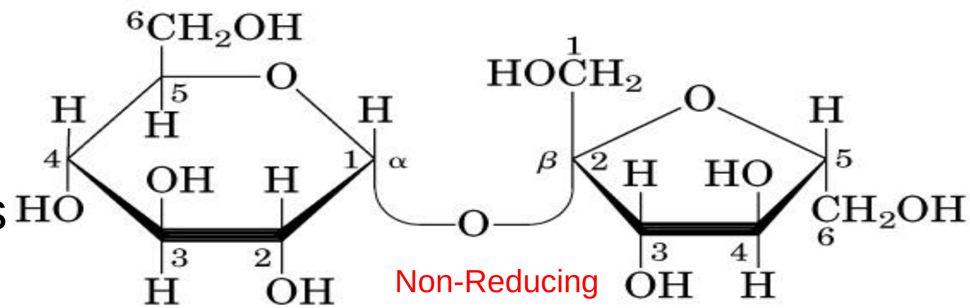
Trehalose energy storage in insects

Double headed arrow connects anomeric C

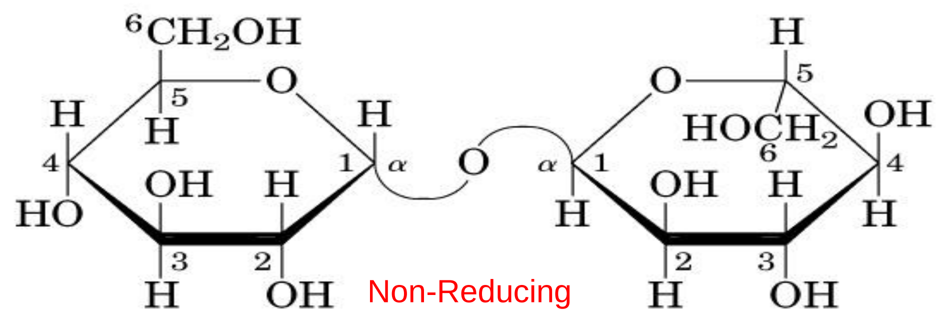
Nonreducing disacchaarides
= glycosides



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



Sucrose
β-D-fructofuranosyl α-D-glucopyranoside
Fru(β2↔1α)Glc



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

To shorten name of polysaccharides, mono are abbreviated:

table 9–1

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	Muramic acid	Mur
Mannose	Man	*N*-Acetylmuramic acid	Mur2Ac
Rhamnose	Rha	*N*-Acetylneuraminic acid (sialic acid)	Neu5Ac
Ribose	Rib		
Xylose	Xyl		

Polysaccharides = glycans differ in

1) Chain length

2) Identity of repeating mono

3) Type of bonds linking subunits

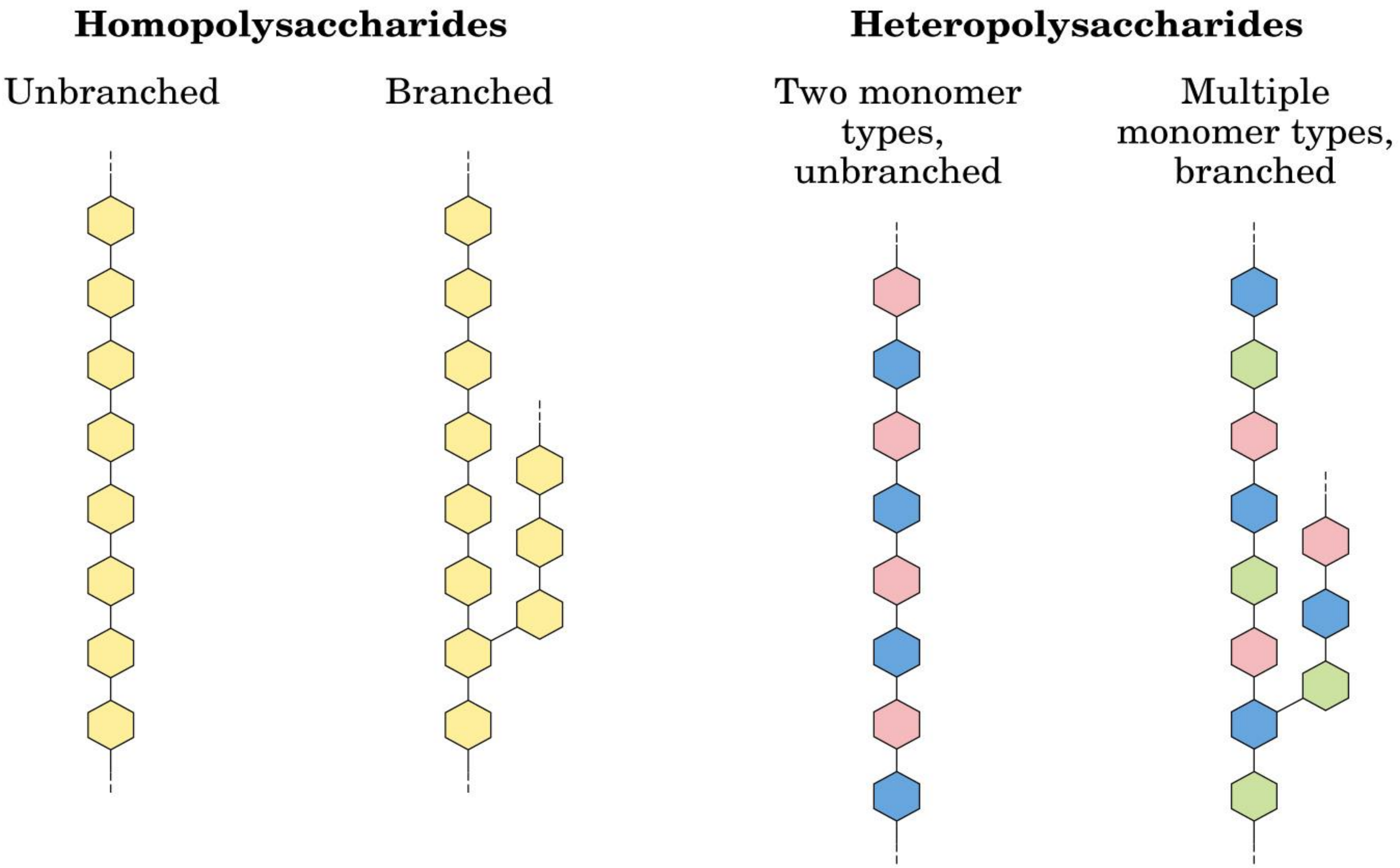
4) Degree of branching

A) Storage forms used as fuel : starch, glycogen, dextran.
B) Structural element in plant cell wall and animal exoskeleton cellulose, chitin.

Unlike proteins:
No definite M. wt.
No template for polysaccharide synthesis.

Homopolysaccharide : a single type of monomer.

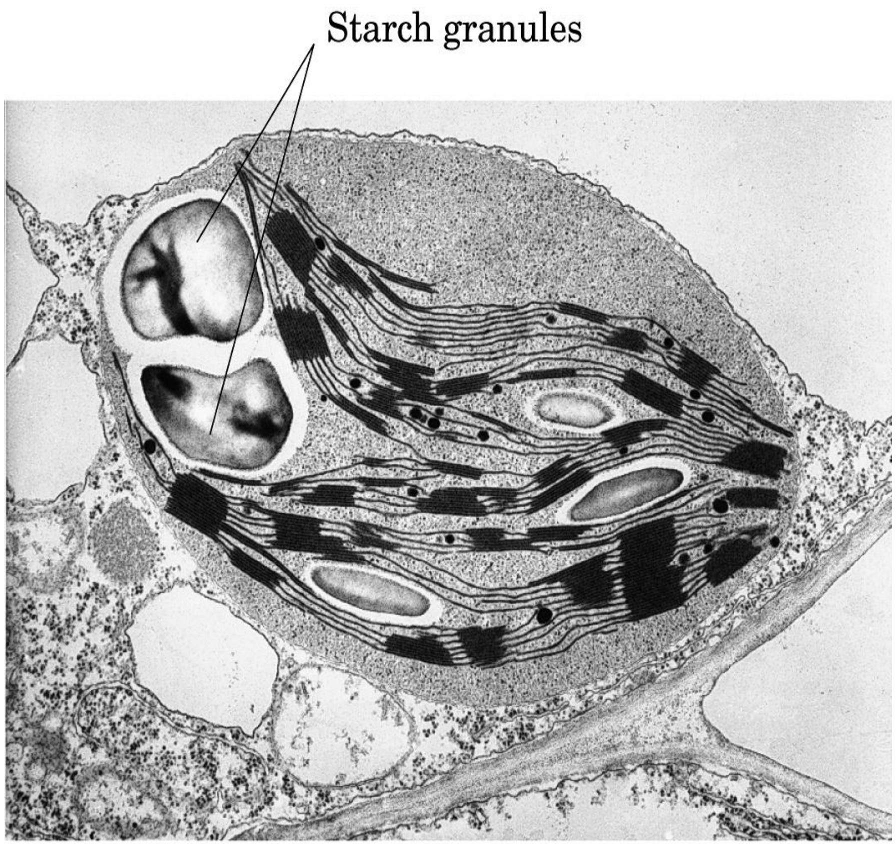
Heteropolysaccharide : two / more different types.



Starch and Glycogen occur intracellularly as large clusters/granule

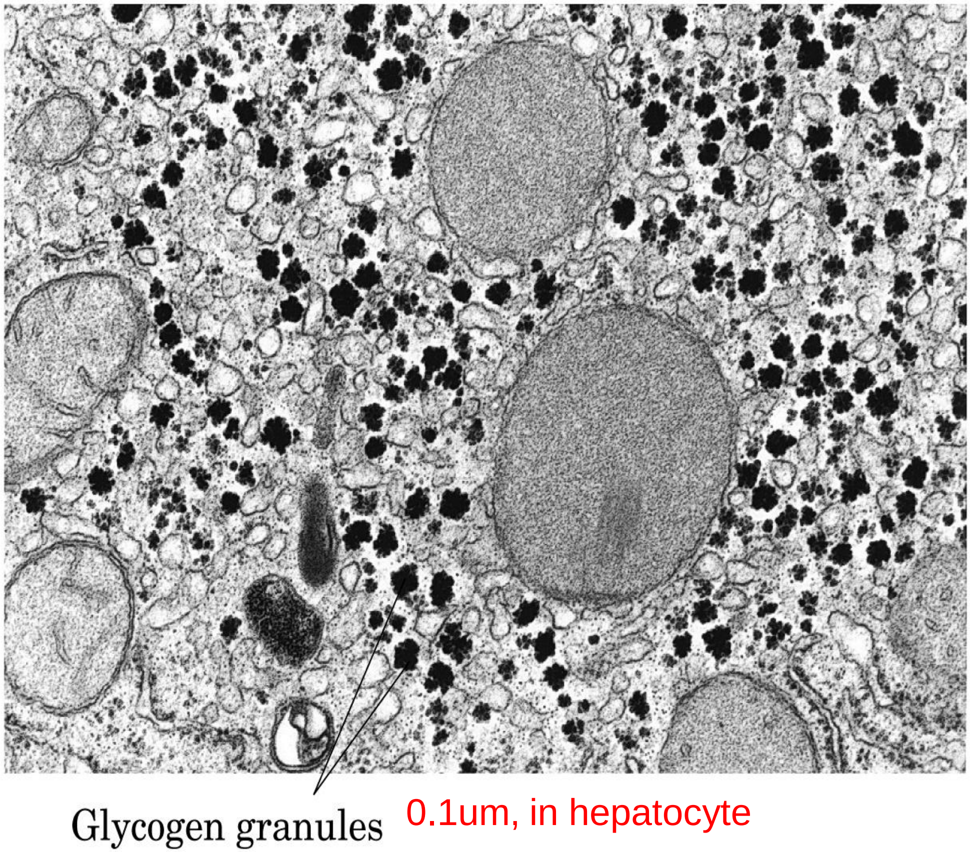
Heavily hydrated due to many hydroxyl →H-bond with water.

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



Starch granules in a chloroplast: 1um

(a)



0.1um, in hepatocyte

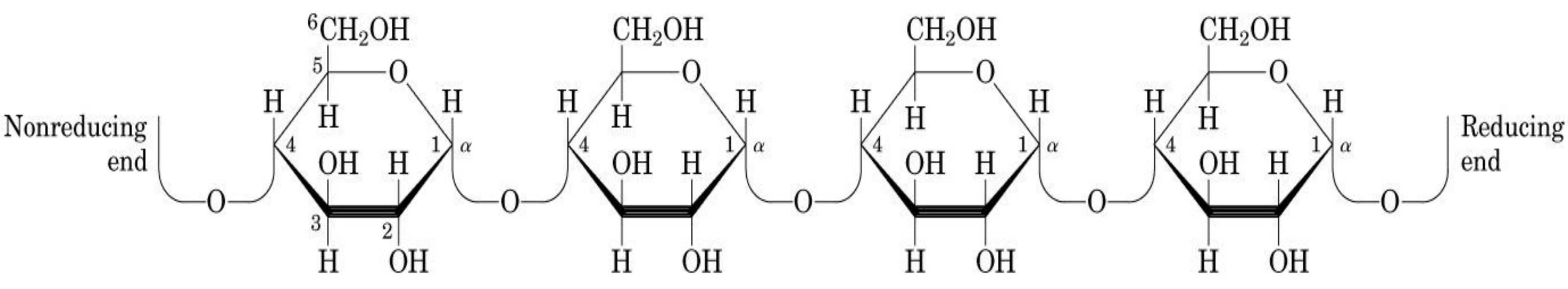
(b)

Starch contain 2 types of glucose polymers:

Amylose & Amylopectin.

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

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



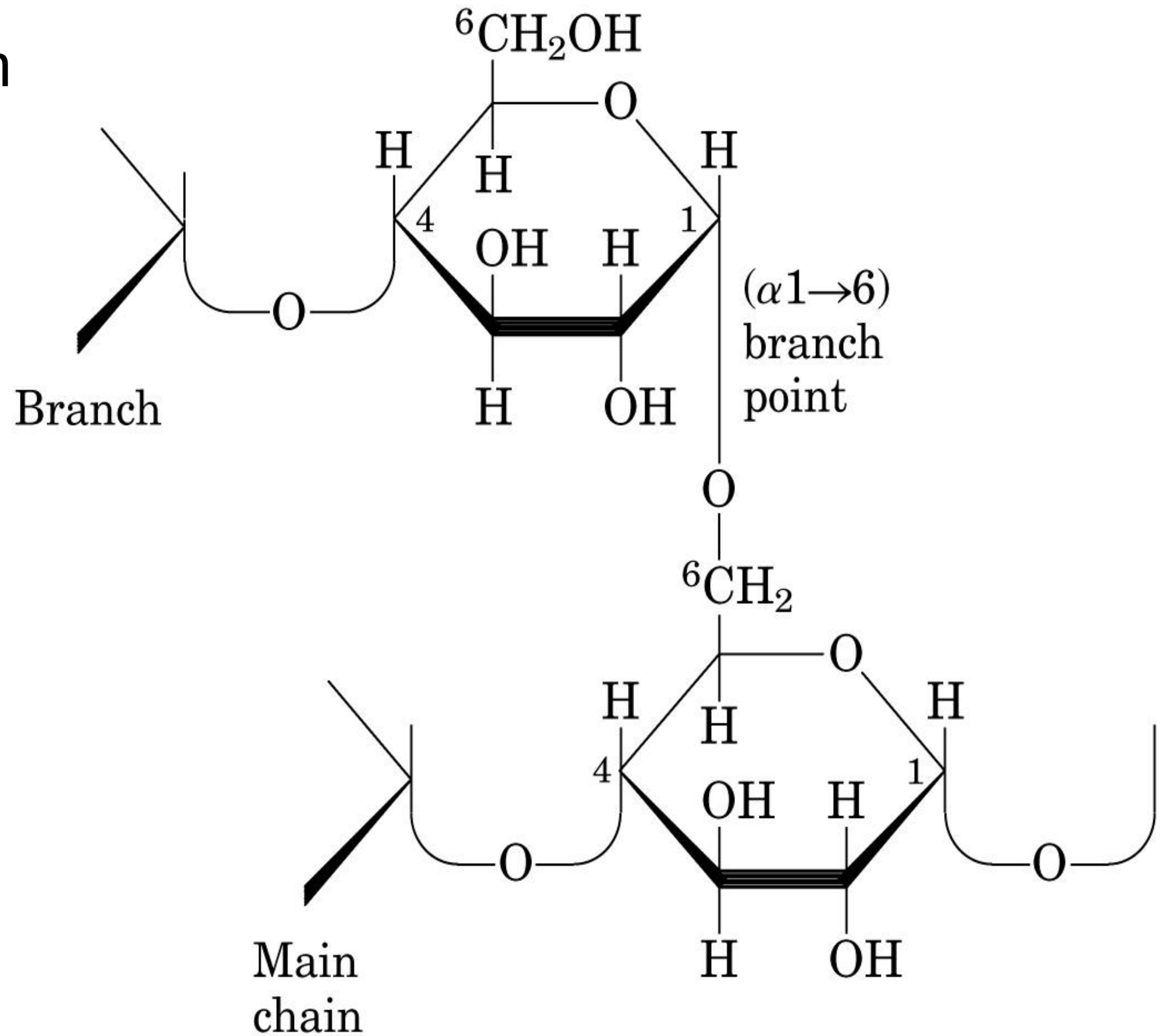
(a)

2) Amylopectin:

A glucose polymer with α(1→4) linkages + α(1→6) **branches.**

Branching produce a compact structure &

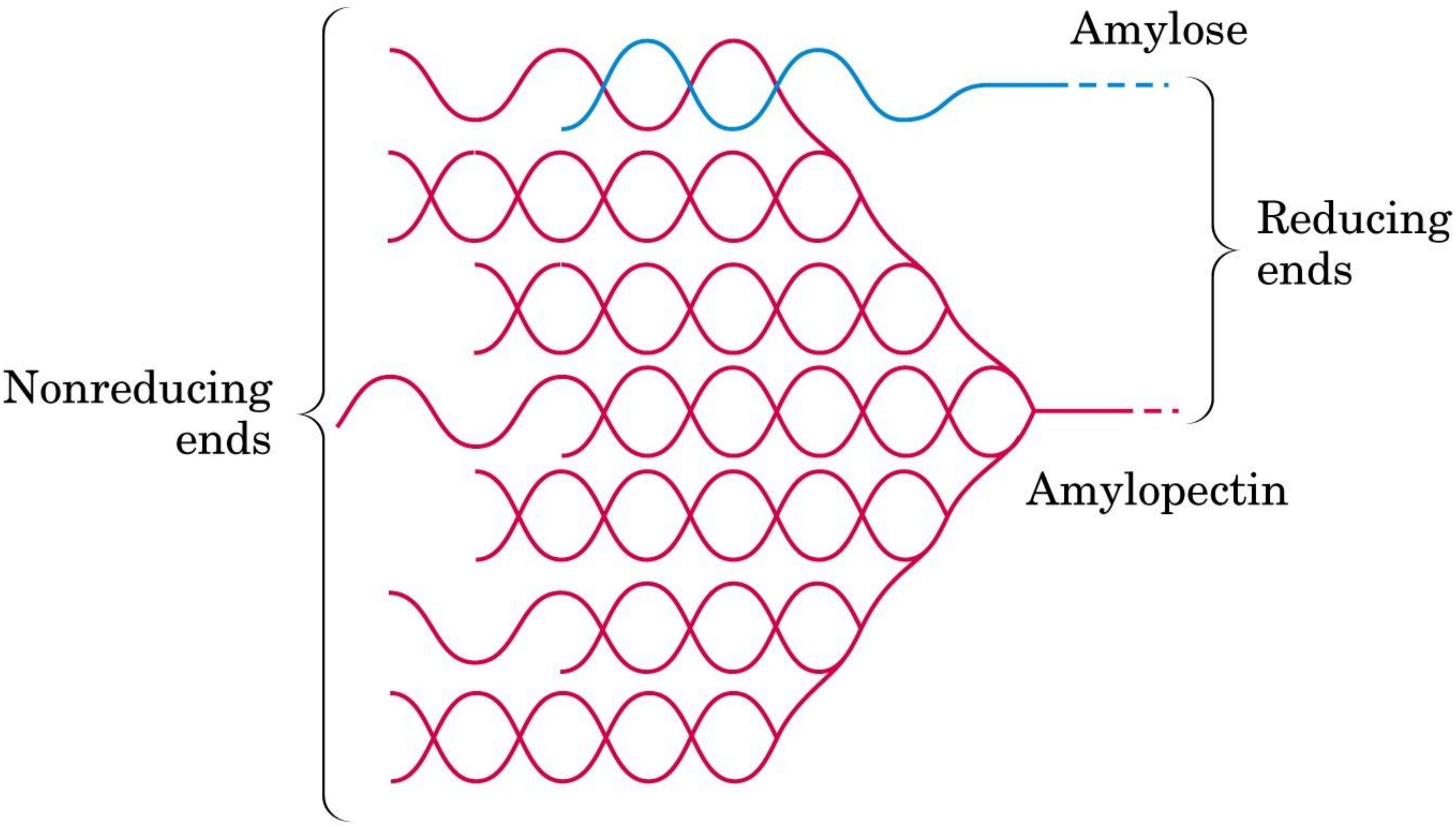
multiple chain ends at which enzymatic cleavage can occur.



(b)

Cluster of amylose + amylopectin →starch

Amylopectin form double helical structures with itself / Amylose.



(c)

Glycogen (animal starch)

- contains α(1,4) links + α(1,6) branches every 8-12 glucose unit.

- similar in structure to amylopectin but glycogen **more branched**

- stored in muscle and liver.

- hydrolyzed by saliva and intestinal secretions α, β amylases.

- hydrolyzed in cell by glycogen phosphorylase.

The highly branched structure permits:

1) rapid glucose release from glycogen stores, e.g. in muscle during exercise 2) increase solubility 3) more compact structure.

Dextran:

-Bacterial and yeast polysaccharide.

- polymer of glucose α(1→6)and branches of α(1→2) or α(1→3) or α(1→4).

-Dental plaque rich in Dextran.

Homopolysaccharides that provide structural role:

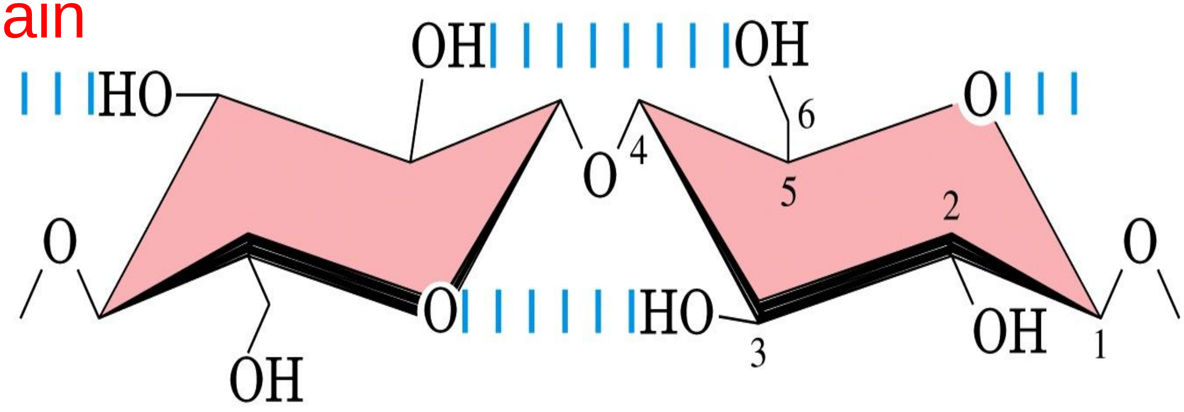
Cellulose

- Most abundant of all CHO in nature.
- A major constituent of plant cell walls.
- Consists of long linear chains of β-D-Glc linked with $\beta(1 \rightarrow 4)$ linkages.
- Humans lack E to hydrolyze cellulose (break β $1 \rightarrow 4$ linkage).
- Fungus and bacteria has cellulase.
- Cattle (sheep, goat) camel, giraffe have bacteria in intestinal tract that secrete cellulase.

Two units of cellulose chain

Every other Glc is flipped over, due to β linkages

This promotes intra-chain and inter-chain H-bonds



(β1→4)-linked D-glucose units

(a)

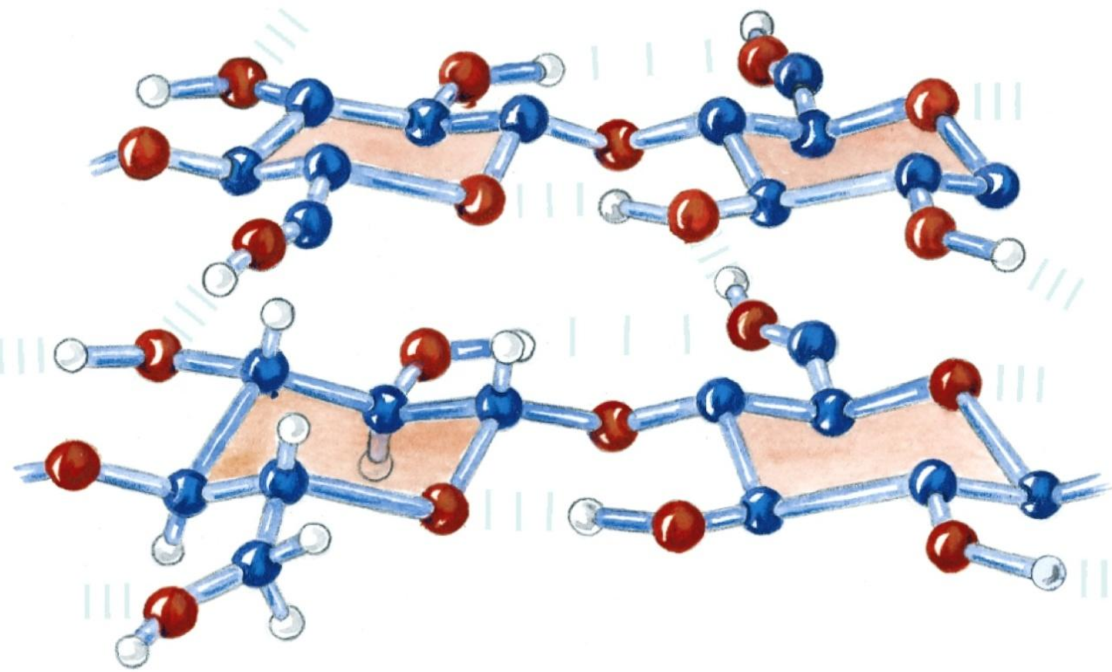
Two parallel cellulose chains

Straight extended chain.

<u>All OH- ready for H-bond</u>.

Several chains lying side by side

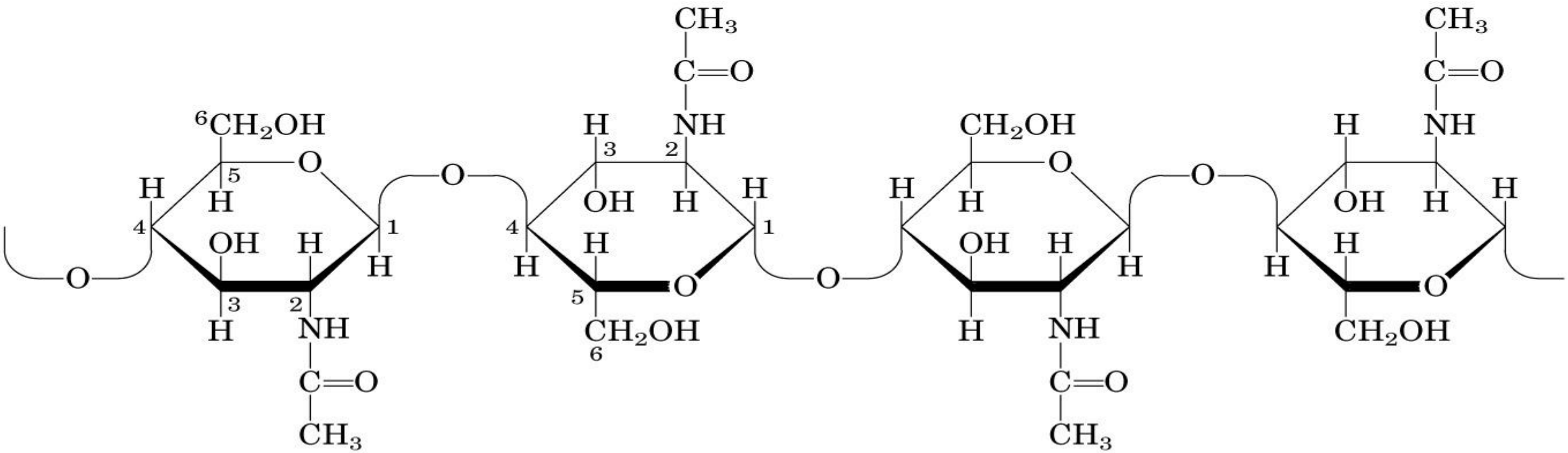
→ straight stable fibers of great tensile strength → paper, insulating tiles, cardboard.



(b)

Chitin

- the 2nd most abundant CHO polymer.
- present in the cell wall of fungi and exoskeletons of lobster, crab, insects and spiders.
- Linear homopolysaccharide (βLinkage) of GlcNAc at C2 hydroxyl (only difference from cellulose)
- Forms extended fibers like cellulose.
- Cant be digested by vertebrates.



- Chitin is used to make a strong and flexible surgical thread that decomposes after the wound or incision heals.

Steric factors and H-bond and Homopolysaccharides folding:

Polysaccharides stabilized by H-bond, hydrophobic, Van der waals interaction & for charged subunits electrostatic interactions

Starch & Glycogen → helical structure with intrachain H-bond.

Cellulose & Chitin → long straight strands interact with neighbor.

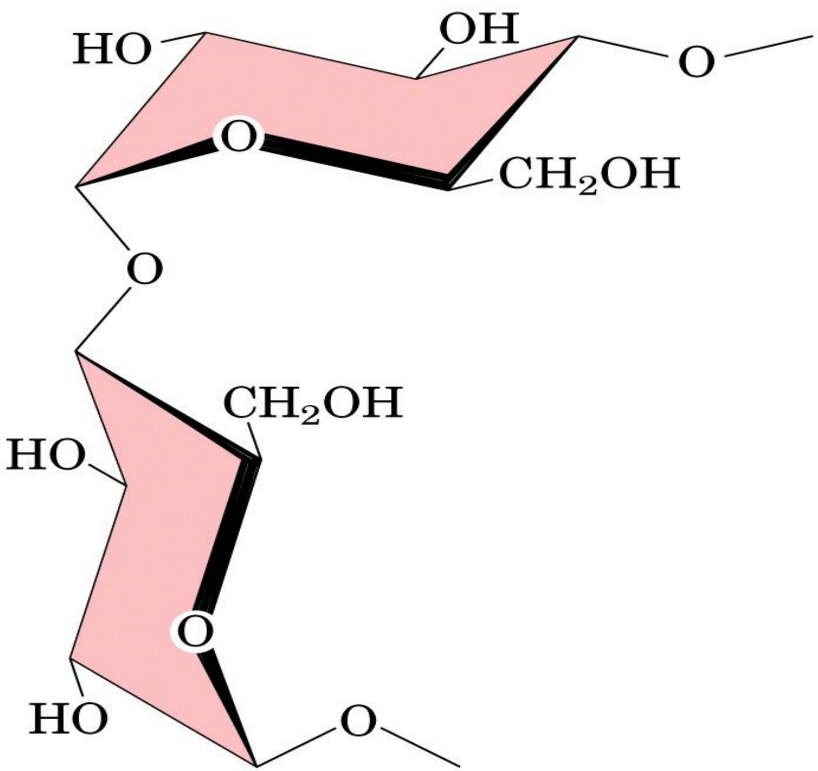
The structure of starch (amylose):

Polysaccharide chains are curved, rather than linear

This α 1→4 linkage causes the polymer to have tightly coiled helical structure.

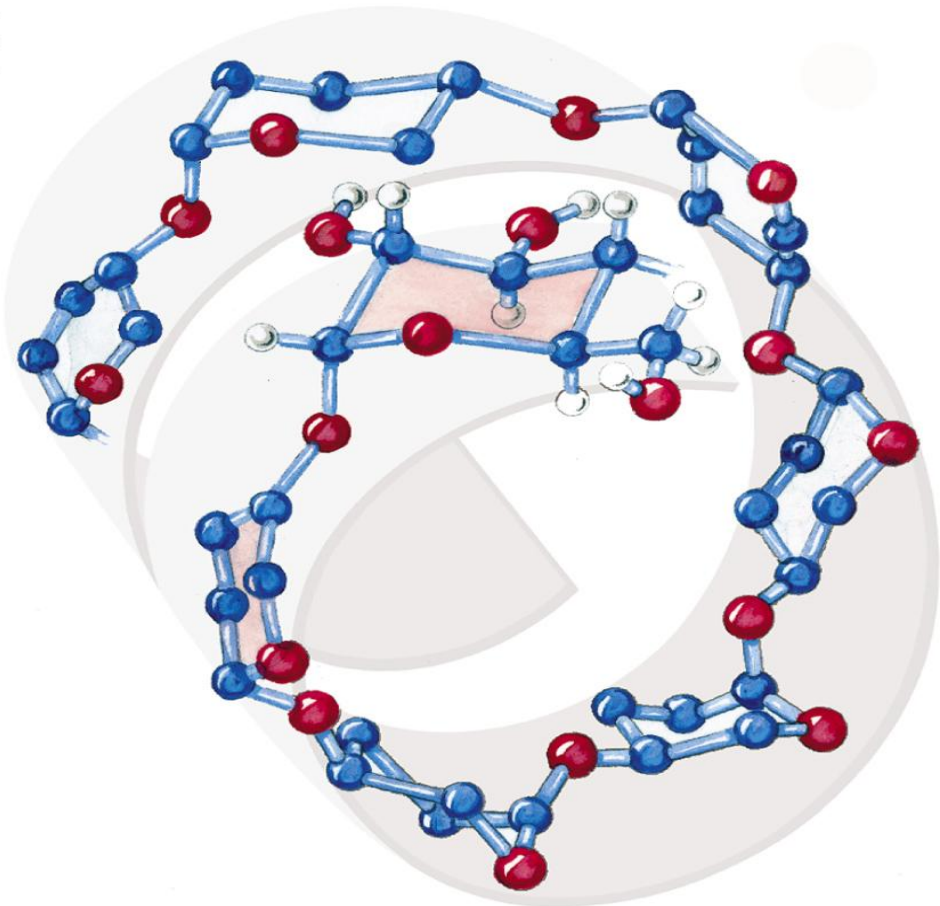
→ most stable 3 dimensional structure.

These dense compact structures form dense granules of starch / glycogen.



(α1→4)-linked D-glucose units

(a)

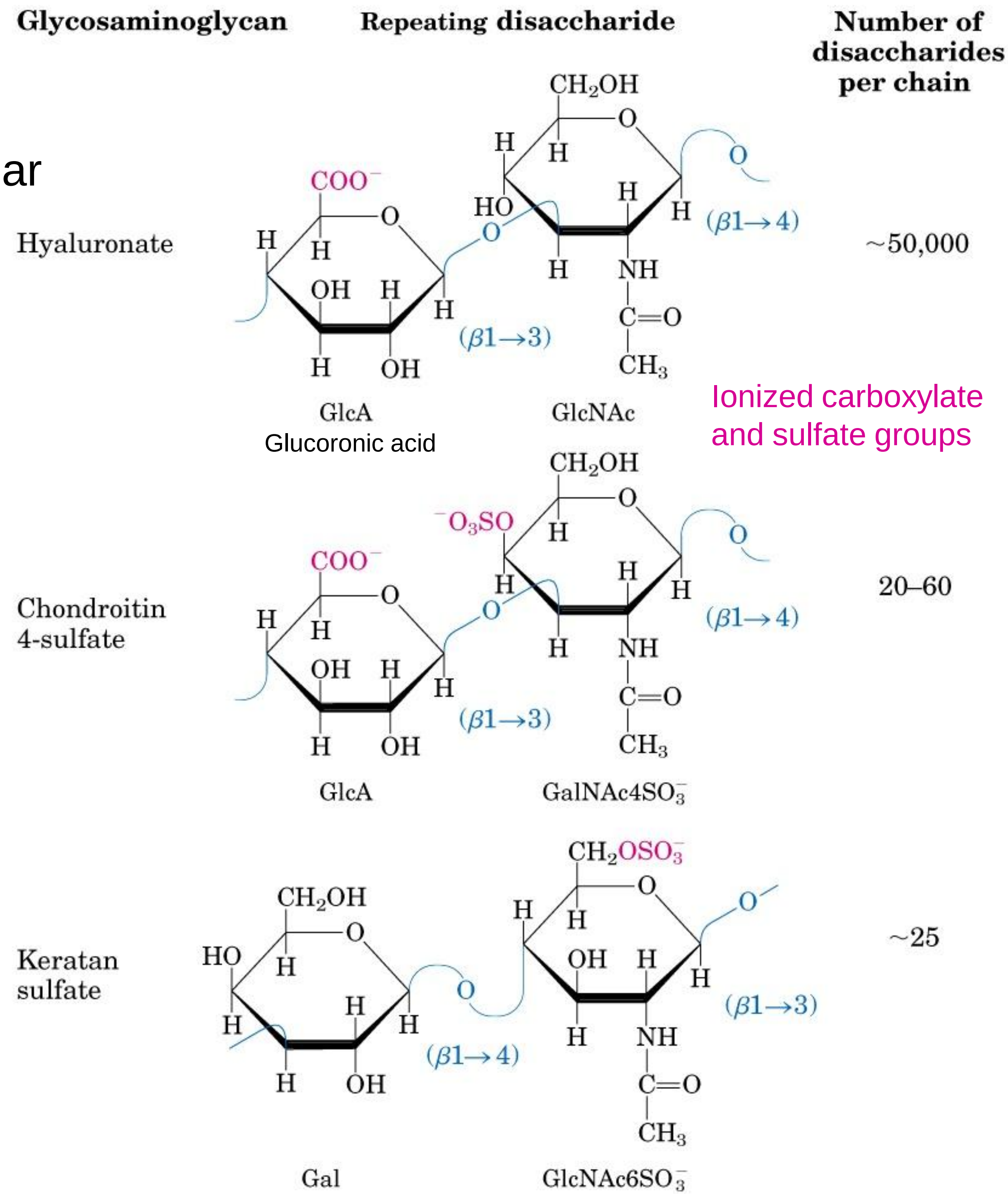


(b)

Glycosaminoglycans of extracellular matrix:

Gel like material of extracellular space, holds cells together + porous pathway for nutrients and oxygen transport.

Meshwork of heteropolysaccharide + fibrous proteins (collagen)



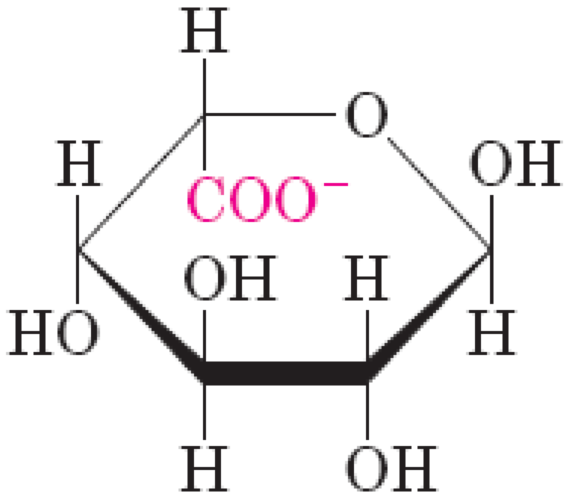
Repeating disaccharide in glycosaminoglycans:

one GlcNAc / GalNAc the other uronic acid (IdoA /GlcA).

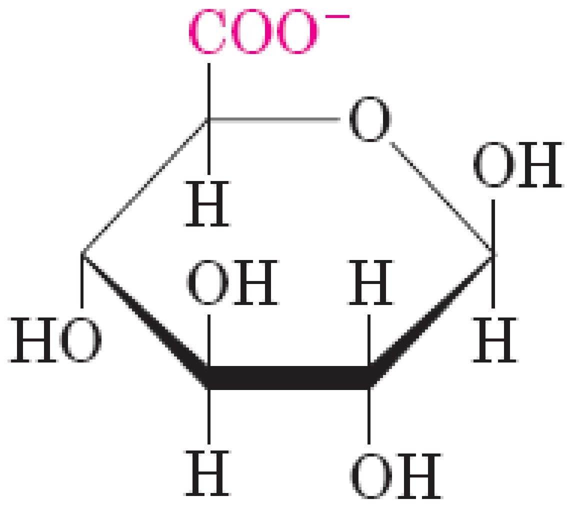
Sulfate esters give these polymers large –ve charge.

Glycosaminoglycans provide :

adhesiveness, viscosity, strength to extracellular matrix.



β-L-Iduronate
(IdoA)



β-D-Glucuronate
(GlcA)

Glycosaminoglycans Are Heteropolysaccharides Of The Extracellular Matrix

1) Hyaluronic acid - *hyalos* "glass" , clear highly viscous soln

-Lubricants in joints , jelly-like material of the eye.

-Component of connective tissue cartilage, skin → strength & elasticity

-In bacteria hyaluronidase → hydrolyse glycosidic bond in tissues → more susceptible to bacterial invasion.

-Similar E in sperm act on glycosaminoglycan coat of ovum.

2) Chondroitin sulfate*chondros* "cartilage"
Tensile strength of cartilage, tendon, ligament, and walls of the aorta

3) Dermatan sulfate
- skin, blood vessels, and heart valves

4) Keratan sulfate *keras* "horn"
- cornea, Cartilage, bone, horn, hair, hoofs, nails and claws

5) Heparin -*hepar* "liver" natural anticoagulant made in mast cells
- bind antithrombin, then bind and inhibit thrombin.