Carbohydrates

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Biomolecules

- Four major classes of biomolecules:
  1. Carbohydrates
  2. Nucleic Acids
  3. Proteins
  4. Lipids

What are Carbohydrates?

- Organic molecule found in nature.
- Constituting one of the four major classes of biomolecules.
- Carbohydrates are the most abundant compounds found in nature.
- Each year, photosynthesis converts more than 100 billion metric tons of CO_2 and H_2O into cellulose and other plant products.
- Carbohydrates are polyhydroxy aldehydes or ketones, or substances that yield them on hydrolysis.

What are Carbohydrates?

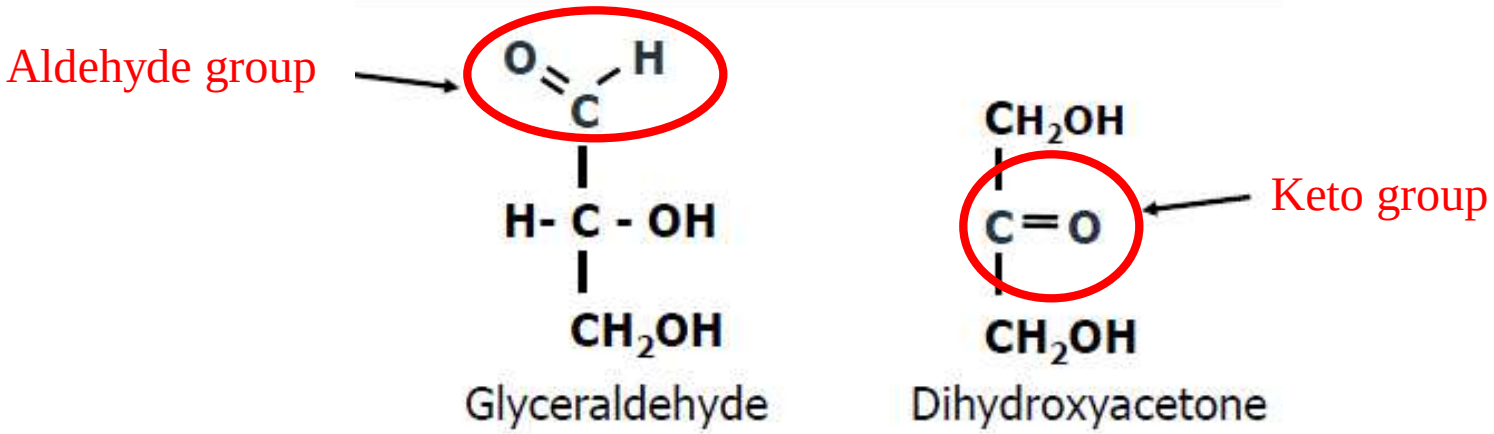
- They have the empirical formula $(CH_2O)_n$ (Exceptions contain nitrogen, phosphorus, or sulfur).
- There are Three major size classes of carbohydrates: Monosaccharides, Oligosaccharides, and Polysaccharides
- Word "saccharide" is derived from the Greek *sakcharon*, meaning "sugar".
- The **term —carbohydrate** comes from the observation that when you heat sugars, you get carbon and water (hence, *hydrate of carbon).*

Function

1. A **storage form** of energy in the body.
2. Cell **surface recognition receptors** (by other cells, hormones, viruses)
3. Cell **surface antigens**, e.g. blood groups.
4. Gastric **glycoprotein** (mucin) contains more than 60% carbohydrate.
5. A **structural component** of many organisms: a) cell walls of bacteria b) exoskeleton of insects c) cellulose of plants.
6. **Intermediates** in the biosynthesis of other basic biochemical entities (fats and proteins)
7. **Associated with other entities** such as glycosides, vitamins and antibiotics.
8. Participate in biological transport, cell-cell recognition, activation of growth factors, modulation of the immune system, lubrication of skeletal joints.

Functional Group Classification

- Carbohydrate with an aldehyde group: Aldose
- Carbohydrate with a ketone group: Ketose



- Both can be written as $C_3H_6O_3$ or $(CH_2O)_3$

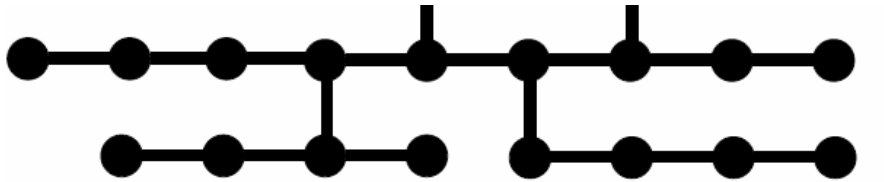
Classification

They are classified according to the number of structural units into:

1. **Monosaccharides**- the simplest carbohydrates that can not be hydrolyzed into simpler units.

2. **Oligosaccharides**- produce two to ten monosaccharide units on hydrolysis

3. **Polysaccharides**- produce more than 10 monosaccharide units on hydrolysis.



Monosaccharides

- Colorless, sweet taste, crystalline solids, freely soluble in water but insoluble in non-polar solvents.
- In the **open-chain form**, one of the carbon atoms is double-bonded to an oxygen atom to form a carbonyl group; each of the other carbon atoms has a hydroxyl group.
- If the carbonyl group is at an end of the carbon chain (that is, in an aldehyde group) the monosaccharide is an **aldose;** if the carbonyl group is at any other position (in a ketone group) the monosaccharide is a **ketose.**

Examples

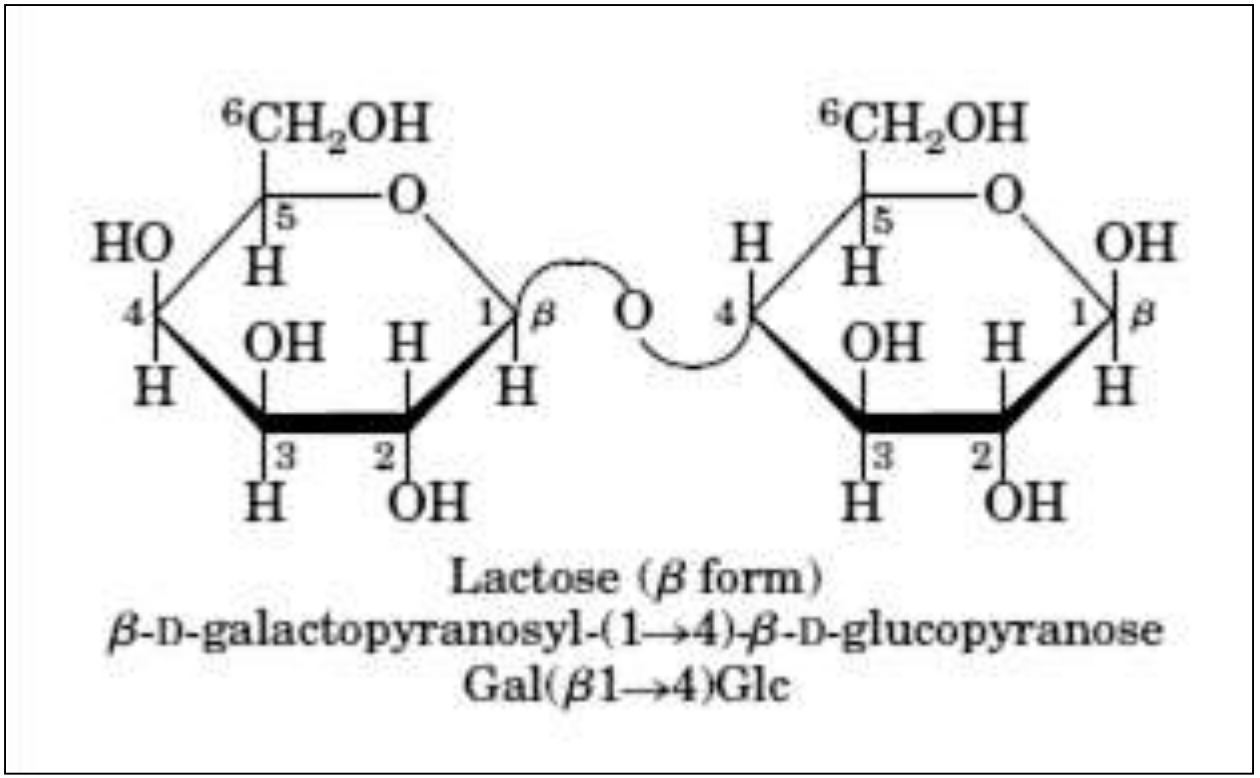
Functional Group	Sugar Class	No of Carbons	Name of Sugar
Aldehyde	Aldose	3 (aldotriose)	Glycerose
		4 (aldotetrose)	Erythrose
		5 (aldopentose)	Ribose
		6 (aldohexose)	Glucose
			Galactose
			Mannose
Ketone	Ketose	3 (ketotriose)	Dihydroxyacetone
		4 (ketotetrose)	Erythrulose
		5 ketopentose)	Xylulose
		6 (ketohexose)	Fructose
		7 Ketopeptose	Sedoheptulose

Glycosidic bond

- Glycosidic **bonds between sugars** are named according to the numbers of the connected carbons and the position of the anomeric hydroxyl group of the sugar.
- The **anomeric centre** of a sugar is a stereocentre created from the **intramolecular formation of an acetal (or ketal) of a sugar hydroxyl group and an aldehyde (or ketone) group**.
- If the anomeric hydroxyl group is in α configuration the link is α- bond and if it's in β, the link is β- bond.

Glycosidic bond

- Example : In **lactose** β1 of galactose bind to C4 of glucose by β1→4 galactosidic bond.



Oligosaccharides

- Hydrolyzable
- They consist of 2-10 monosaccharide units.
- Most important oligosaccharides are disaccharides
- **Disaccharides** are condensation products of two monosaccharide units.
- E.g.
  - ✓ Maltose = glucose + glucose
  - ✓ Sucrose = fructose + glucose
  - ✓ Lactose = galactose + glucose
  - ✓ Trehalose = glucose + glucose

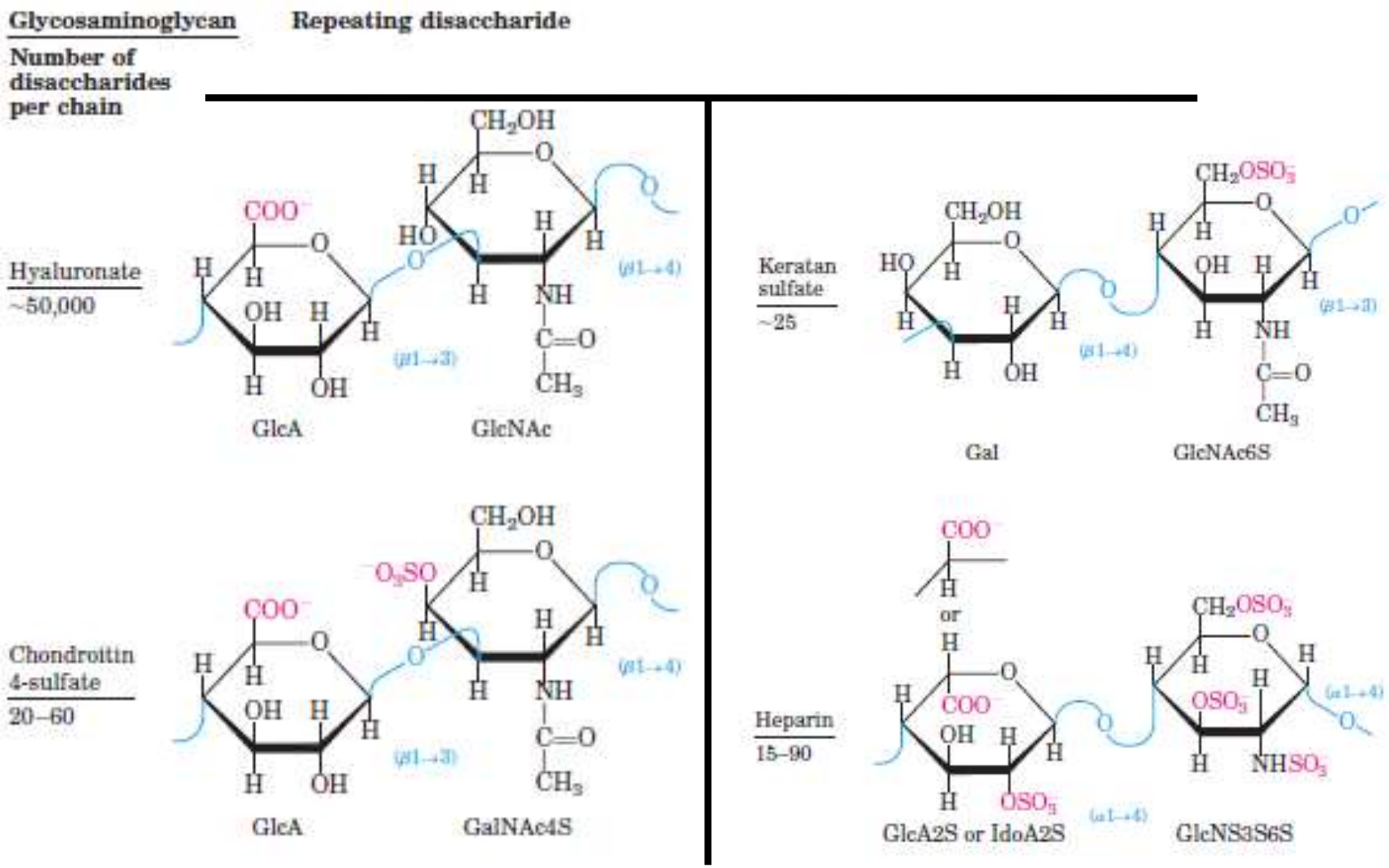
Oligosaccharides

- The disaccharides can be classified into homo disaccharides and hetero disaccharides.
  - **Homo disaccharides:** are formed of the same monosaccharide units

    Eg: maltose, trehalose.
  - **Hetero disaccharides:** are formed of different monosaccharide units

    Eg: sucrose, lactose.

Oligosaccharides



Polysaccharides

- Most carbohydrate found naturally are polysaccharide
- Polymers of medium to high molecular weight.
- Polysaccharides are also called **glycans.**
- They **differ from each** other in the identity of their recurring monosaccharide units, in the length of their chains, in the types of bonds linking the units, and in the degree of branching.
- There are **two major categories** of polysaccarides : Homopolysaccharides and Heteropolysaccharides

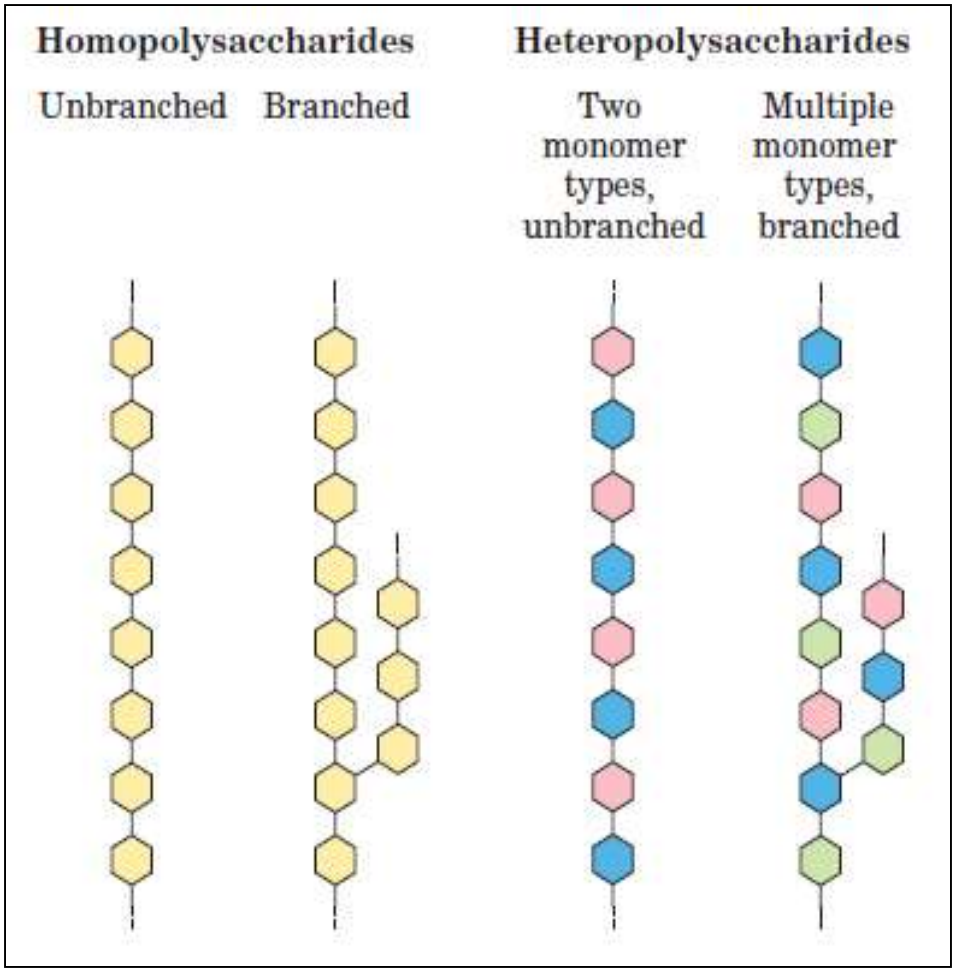
Polysaccharides

- **Homopolysaccharides**: a single type of monomer.

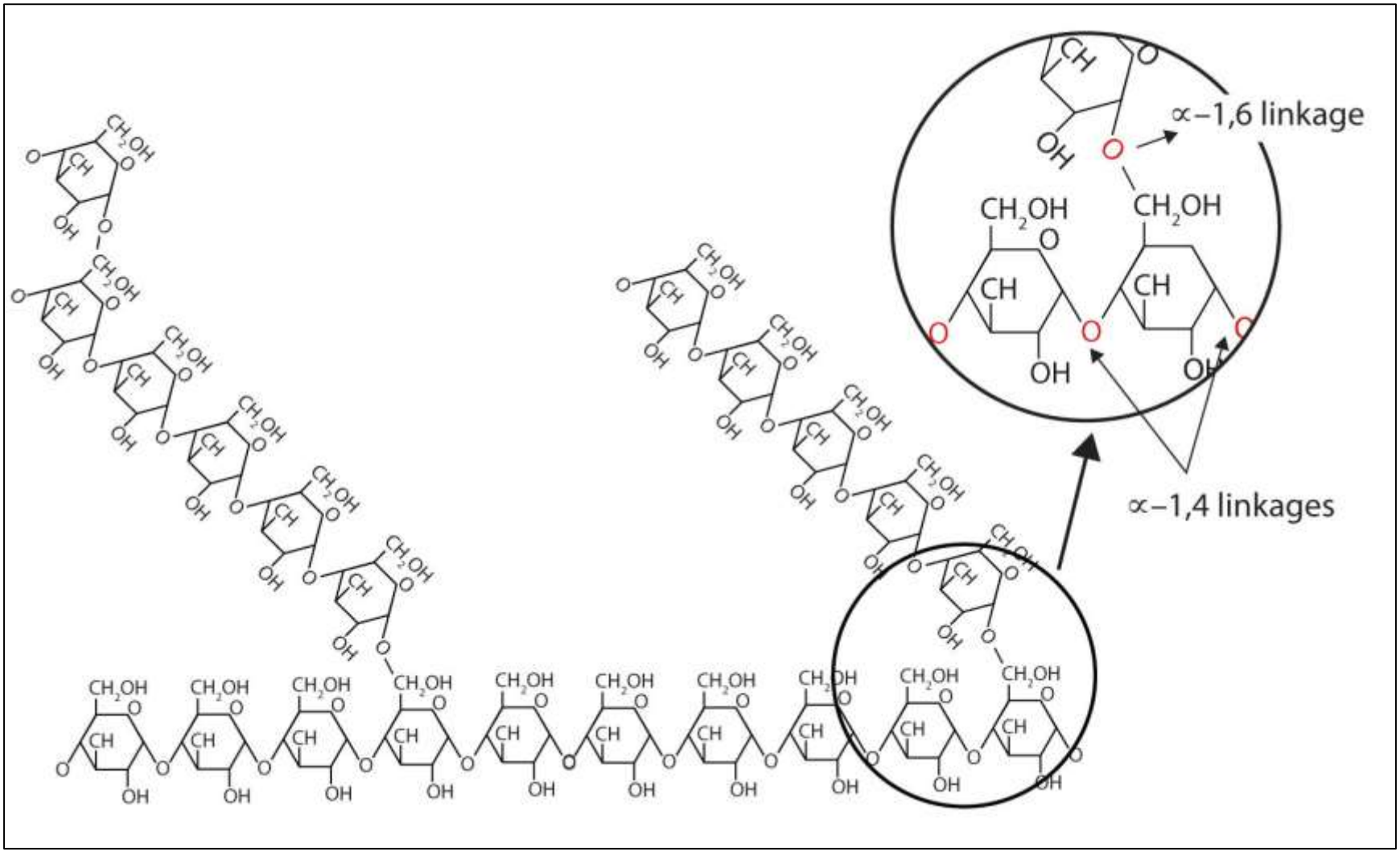
  Eg: starch, glycogen, chitin

- **Heteropolysaccharides**: two or more different kinds.

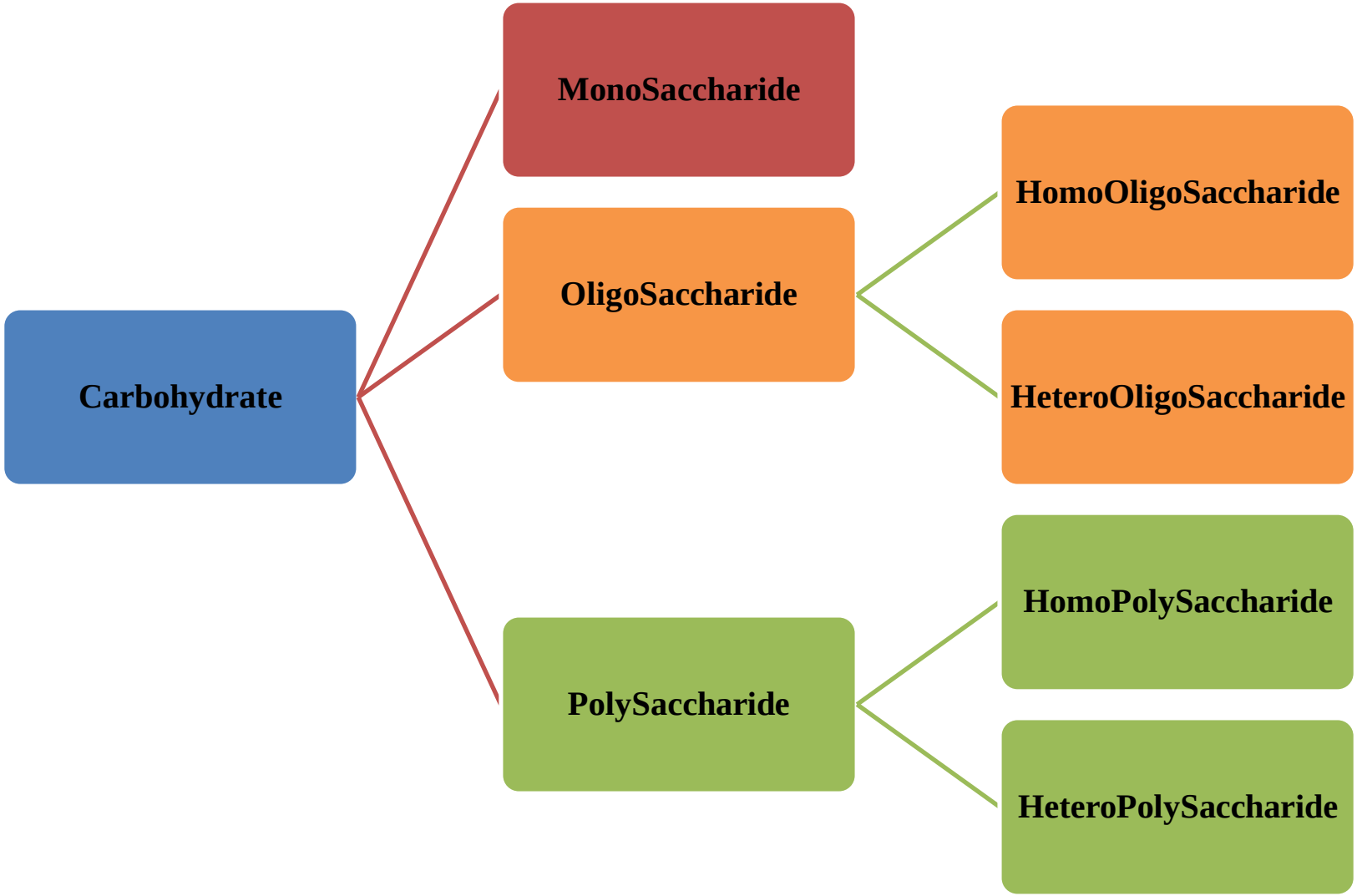
  Eg: Glycosaminoglycans, Proteoglycans, Glycoproteins



Polysaccharides



Classification



Heteropolysaccharides

Types

- **Proteoglycans** (Mucopolysaccharides) : consist of protein with a repeating polysaccharide unit.

  (First isolated from mucin so called mucopolysaccharides.)

- **Glycoproteins** : Proteins which has less than 100 saccharide residues.
- **Glycosaminoglycans**: a proteoglycan with the protein portion removed.

Glycosaminoglycans(GAGs)

- These molecules are long unbranched polysaccharides containing a repeating disaccharide unit.
- GAGs are highly **negatively charged molecules, with extended conformation that imparts high viscosity to the solution.**
- GAGs are located primarily on the **surface of cells or in the extracellular matrix (ECM).**
- A long with the high viscosity of GAGs comes **low compressibility, which makes these molecules ideal for a lubricating fluid in the joints.**

Glycosaminoglycans(GAGs)

- At the same time, their **rigidity provides structural integrity to cells and provides passage ways between cells, allowing for cell migration.**
- The disaccharide units contain either of two modified sugars, called **amino sugars** N-acetylgalactosamine (GalNAc) or N-acetylglucosamine (GlcNAc), and an **acidic sugar** uronic acid such as glucuronic acid or iduronic acid**.**
- The amino group is usually acetylated. This eliminates the positive charge.

Glycosaminoglycans(GAGs)

- In some glycosaminoglycans, one or more of the hydroxyls of the amino sugar is **esterified with sulfate.**
- The combination of these sulfate groups and the carboxylate groups of the uronic acid residues gives the glycosaminoglycans a very high density of negative charge.
- Keratan sulfate is an exception in which galactose is present, instead of an acidic sugar.
- Hyaluronic acid does not contain sulfate.

Negative charge

- The negative charge serves **two purpose** :

1. In the glomerular basement membrane, heparin sulfate's negative charge is responsible for the selectivity of the basement membrane which prevents the albumin from being excreted through the pores.
2. The negative charge attracts positively charged sodium ions which will Osmotically drag water. They hold excess water and gives the gel like elastic consistency of the extracellular matrix.

GAGs

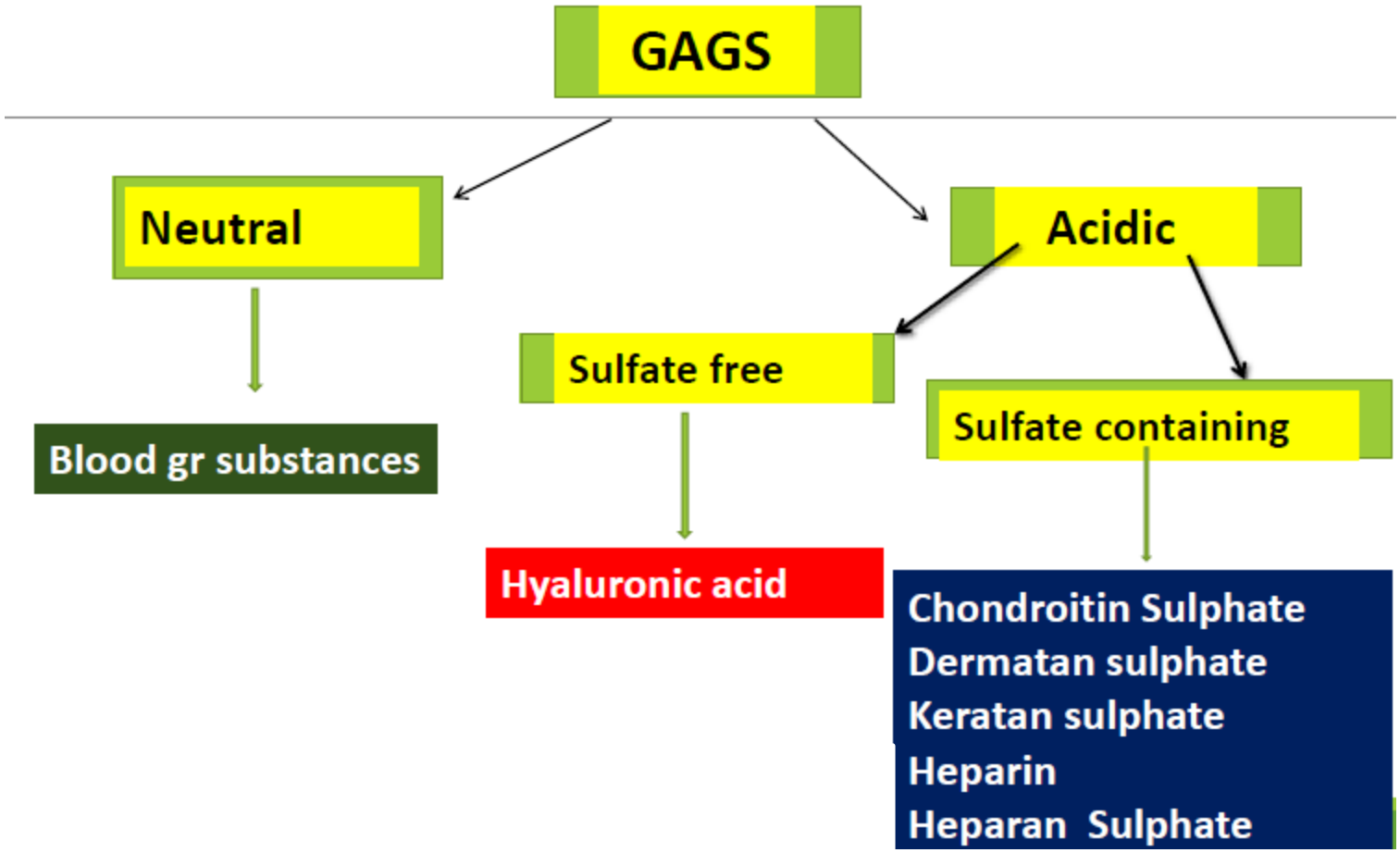
- The GAGs differ from each other:

  ✓ Monomeric(acidic & amino sugar) composition
  ✓ Degree & location of sulfation
  ✓ Type of glycosidiclinkages
  ✓ Chain length of the disaccharides
  ✓ Nature of the core protein
  ✓ Their tissue distribution
  ✓ Their biologic functions

Functions

- Structural support to connective tissue.
- GAGs form matrix or ground substance that stabilizes and supports the cellular and fibrous components of tissues.
- Plays an important role in mediating cell-cell interactions
- Their slippery consistency makes them suitable for a lubricant action in joints.

Classification of GAGs



Proteoglycans

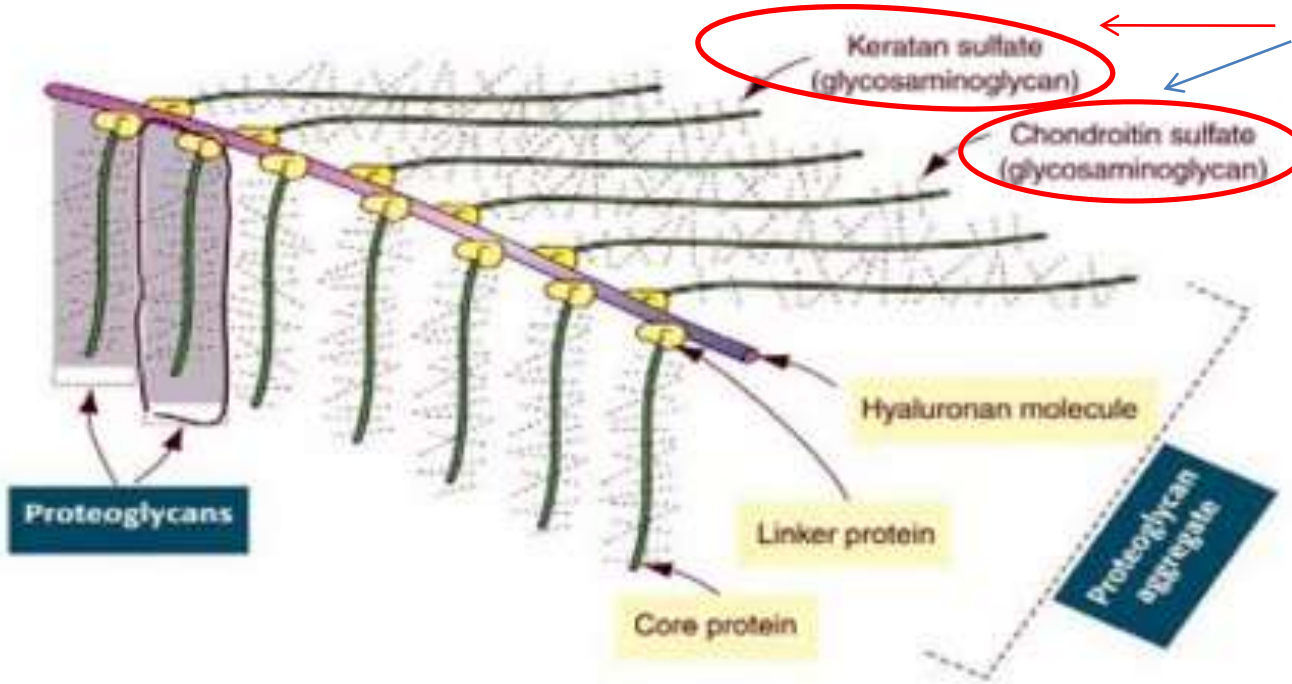
- Proteoglycans are proteins that are covalently bonded at multiple sites to heteropolysaccharides, known as glycosaminoglycans.
- Hyaluronic acid is a unique one among the GAGs as it does not contain any sulfate group and is non-covalently linked with proteoglycans in the ECM.
- The physiological properties of proteoglycans are determined by the type of GAGs attached to it.
- **Proteoglycans = GAGs + Core proteins**

Proteoglycans

- They vary in tissue distribution, nature of the core protein and glycosaminoglycans attached, and function.
- The proteins bound covalently to glycosaminoglycans are called **“core proteins”**
- The amount of carbohydrate in a proteoglycan is usually much greater than is found in a glycoprotein and may comprise up to 95% of its weight.

Proteoglycans

- **Proteoglycans** are complex extracellular macromolecules consisting of a multidomain core protein to which is attached one or more glycosaminoglycan (GAG) chains.



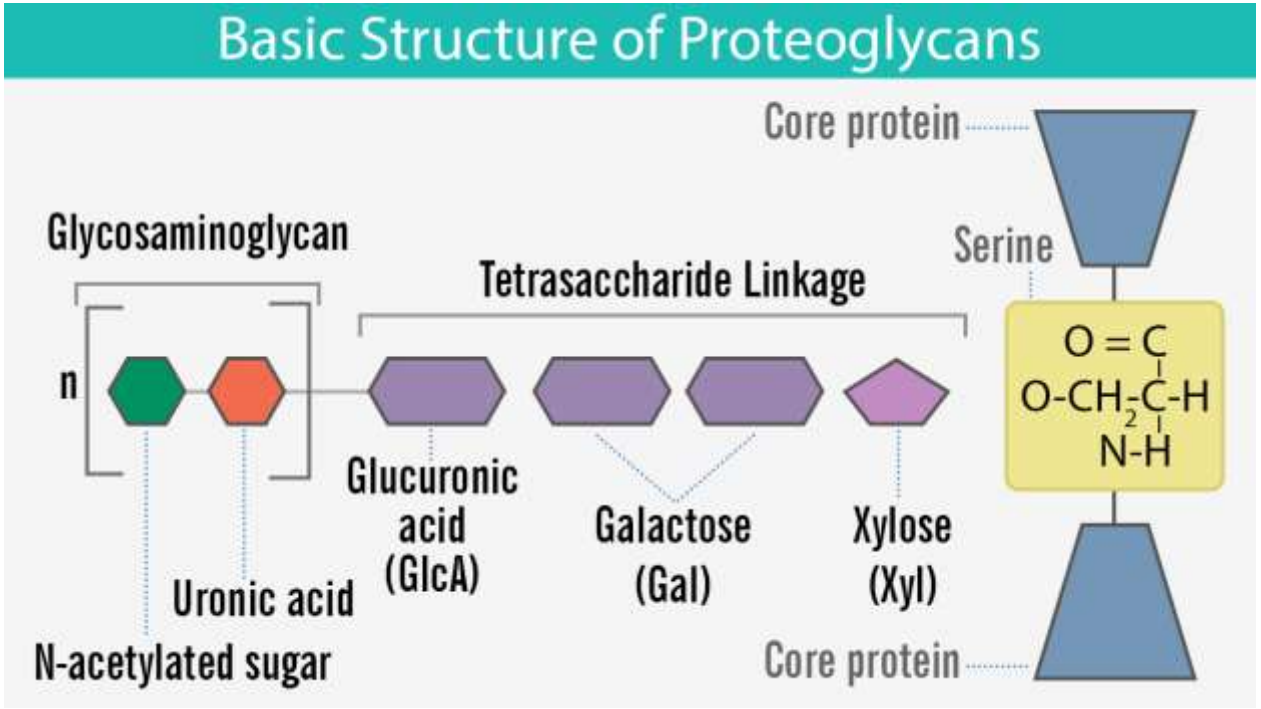
The GAGs extend perpendicularly from the core in a brush-like structure.

Structure

- Proteoglycans are composed of two basic molecules, core protein and glycosaminoglycans.
- The core protein may contain serine residues; these residues act as a point of attachment to which different glycosaminoglycans attach.
- The glycosaminoglycans attach to the core proteins perpendicularly and give rise to a brush-like structure.
- Their attachment in most but not all proteoglycans is through a tetrasaccharide linker that consist of glucuronic acid(GlcA), two galactose(Gal) and a xylose(Xyl) residue via glycosidic bonds.

Structure

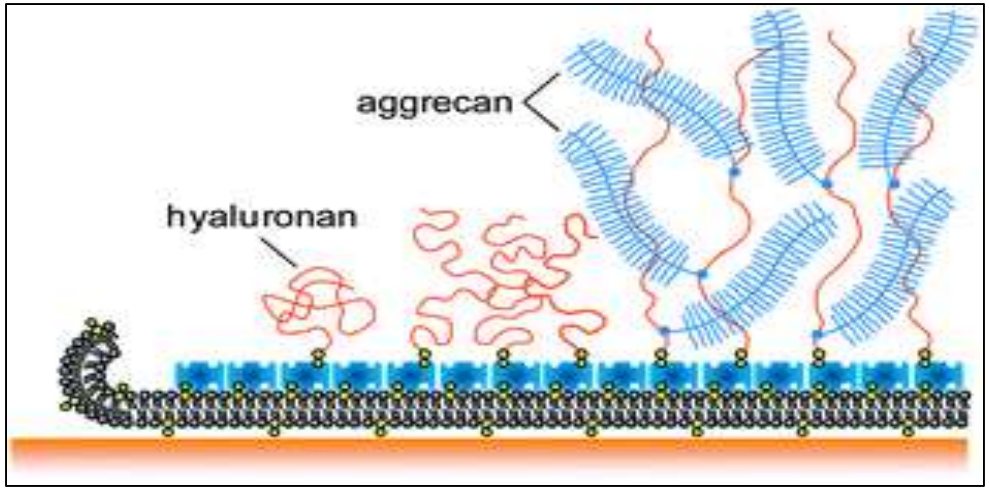
- And some glycosaminoglycans are linked to the protein core of proteoglycans through a trisaccharide linkage that lacks the GlcA residue.

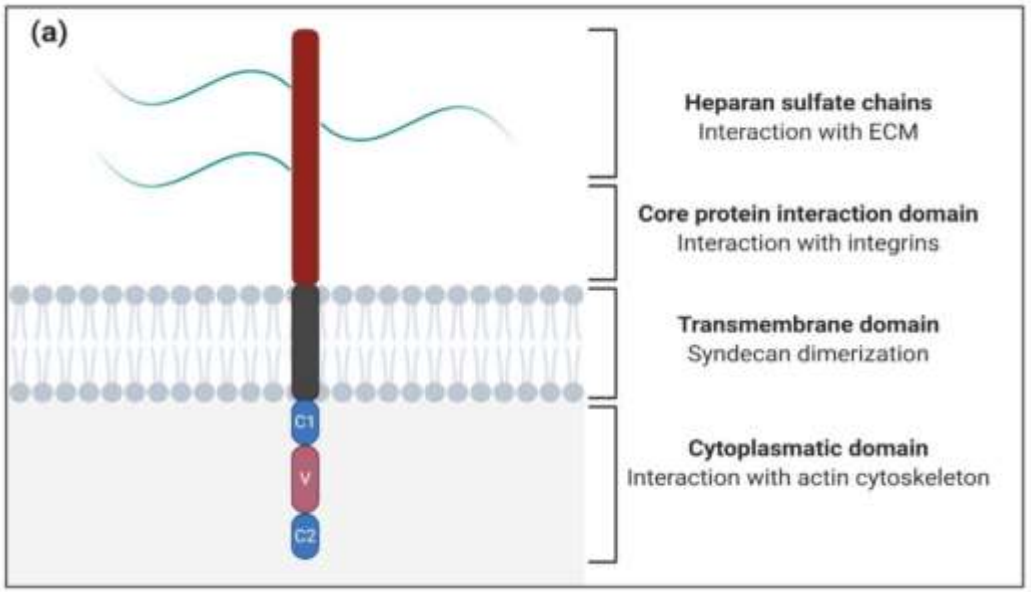


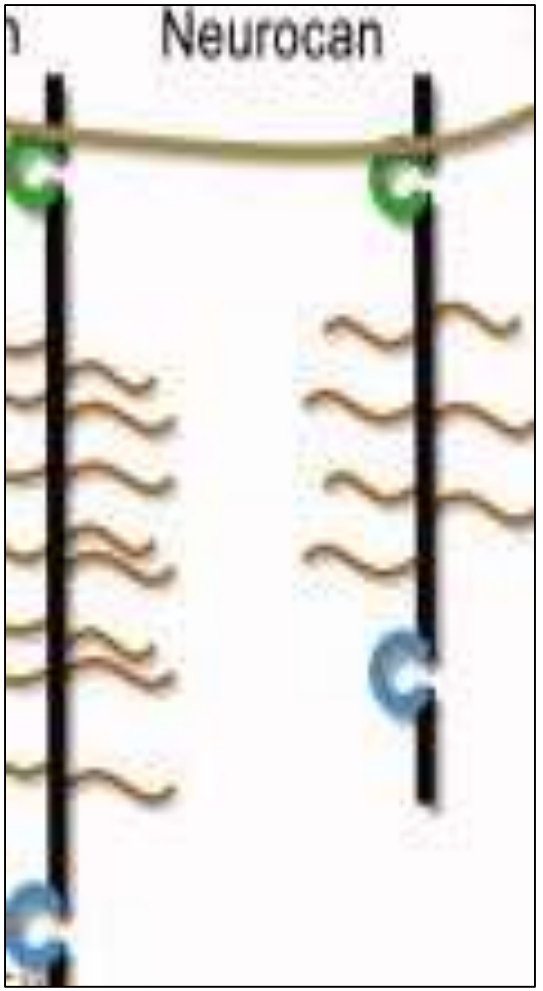
Examples

- **Agrecan-** one of the largest proteoglycan found in cartilage has more than hundred GAG's chains.
- **Syndecan-** a core protein allows three to five heparin sulfate and chondroitin sulfate GAGs chains attach to them. syndecans are transmembrane domain proteins which act as a co receptor for variety of signaling molecules such as fibroblast growth factors, endothelial growth factors etc.
- **Neurocan-** core protein are members of chondroitin sulfate proteoglycans and they contain neurocan core protein which has chondroitin sulfate GAG'S attach to them. They are component of the extracellular matrix and involve in cell migration and adhesion.

Examples


aggrecan
hyaluronan


(a)
Heparan sulfate chains
Interaction with ECM
Core protein interaction domain
Interaction with integrins
Transmembrane domain
Syndecan dimerization
Cytoplasmatic domain
Interaction with actin cytoskeleton
C1
V
C2


Neurocan

Glycoproteins

- **Glycoproteins have one or several oligosaccharides of varying complexity joined covalently to** a protein.
- They are found on the outer face of the plasma membrane, in the extracellular matrix, and in the blood.
- Inside cells they are found in specific organelles such as Golgi complexes, secretory granules, and lysosomes.

Glycoproteins

- The oligosaccharide portions of glycoproteins are less monotonous than the glycosaminoglycan chains of proteoglycans.
- **They are rich in information, forming highly specific sites for recognition of signals and highaffinity binding by other proteins by cell receptors.**
- There are 3 major classes of glycoproteins: **O-linked, N-linked** and **GPI linked**

3 major classes

1. those containing an O-glycosidic linkage (ie,**O-linked), involving the hydroxyl side** chain of serine/ threonine or hydroxylysine & hydroxyproline and a sugar such as *N-acetyl galactosamine or or galactose or xylose (GalNAc-Ser[Thr])*
2. those containing an N-glycosidic linkage (ie, **N-linked), involving the amide** nitrogen of asparagine or lysine and *N-acetyl glucosamine (GlcNAc- Asn)*
3. Glycosylphosphatidylinositol-anchored glycoprotein (**GPI-anchored, or GPI linked). C terminal a.a is linked to carbohydrate man-man-man glucosamine** through ethanolamine and is again linked to the outer leaflet of plasma membrane through inositol.

Examples

Glycoprotein(s)	*Major function(s)*
Collagen	Structure
Hydrolases, proteases, glycosidases	Enzymes
Ceruloplasmin	Transport
Immunoglobulins	Defense against infection
Synovial glycoproteins	Lubrication
Thyrotropin, erythropoietin	Hormones
Blood group substances	Antigens
Fibronectin, laminin	Cell-cell recognition and adhesion
Intrinsic factor	Absorption of vitamin B_{12}
Fibrinogen	Blood clotting

Difference

Proteoglycan	Glycoprotein
GAGs are covalently attached to a protein (95 % sugar)	Primarily of protein with small amount of carbohydrates
Sugar chain are longer (100 or more sugars)	Short oligosaccharide chain (>20)
Linear , unbranched	Highly Branched
Disaccharide repeats	Do not have repeat sequence

THANK YOU