

Welcome to the CARBOHYDRATE section  
of BCMB8020

Please pick up the 5 handouts

Before next class please read

Class Text: Chapter 7: pages 356-381 &  
Chapter 23 pages 852-862

(Biochemistry, third Edition by Voet and Voet, 2004, Wiley).

Articles by Rudd *et al.*, 2004;  
Shearer and Graham (2004);  
James *et al.*, 2003.

Today these articles will be given out in class. All future required reading, as well as optional reading, will be available as pdf files on the website <http://cell.ccr.cu.edu/~dmohnen/bcmb8020/list.html>



Carbohydrates- General Review

- Functions
- Introduction and definition monosaccharides
- Aldoses and Ketoses
- Cyclic glycosyl residues, Haworth Projections
- Modified monosaccharides
- Glycosidic bond
- Disaccharides
- Polysaccharides
- Peptidoglycans
- Proteoglycans
- Glycoproteins

Carbohydrates

- \* **most abundant organic molecule on earth**
- \* **polyhydroxy aldehydes or ketones** (or yield these upon hydrolysis)
- \* **functions:** energy storage (glycogen, starch)  
metabolic intermediates (ATP, coenzymes)  
part of DNA & RNA  
structural elements in cell walls of bacteria, fungi & plants  
exoskeleton of arthropods  
extracellular matrix of animals  
cell-cell communication/signalling

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- Individual monomeric units are called **monosaccharides**  $(CH_2O)_n$  where  $n \geq 3$
- oligosaccharides** (contain 2-20 monosaccharides)  
**disaccharides** (two linked monosaccharides)
- polysaccharides** ( $> 20$  monosaccharides)
- pure mono- & disaccharides are water-soluble, colorless in solution & sweet
- two classes of monosaccharides:** aldoses & ketoses

**Glycoconjugate:** carbohydrate derivative where carbohydrate(s) are linked to a peptide, protein or lipid (i.e. **proteoglycans, peptidoglycans, glycoproteins, glycolipids**)

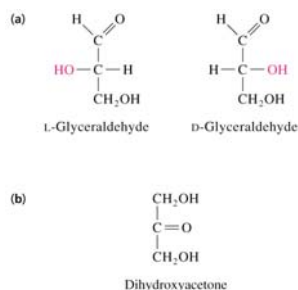
**Glycan:** carbohydrate polymer

**Stereoisomers:** compounds with the same molecular formula but different spatial arrangement of their atoms

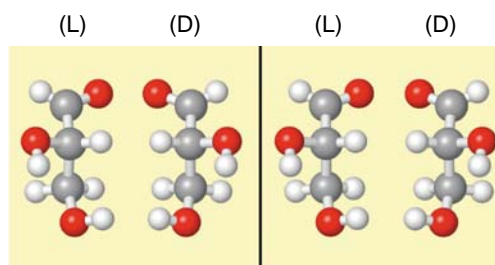
**D & L sugars** differ only in steric arrangement of atoms about central C. They are non-superimposable mirror images (i.e. **enantiomers**)

They differ in orientation of the crystals, in directions in which solutions rotate polarized light, and in selectivity of reaction with other asymmetric molecules

### Fischer projections of: (a) L- and D-glyceraldehyde, (b) dihydroxyacetone



### Stereo view of L- and D-glyceraldehyde



<u>N (# of Cs)</u>	<u>Name</u>	<u>Example</u>
3	triose	
4	tetrose	
5	pentose	
6	hexose	

For sugars with >1 asymmetric (chiral) carbon, D & L refer to chiral C furthest from aldehyde (or ketone) & correspond to D & L glyceraldehyde

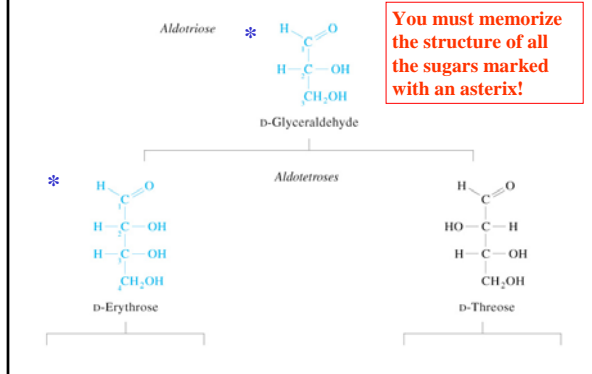
# of stereoisomers =  $2^n$  where n = # of chiral C's

**Epimer:** stereoisomers that differ in configuration at only one chiral center

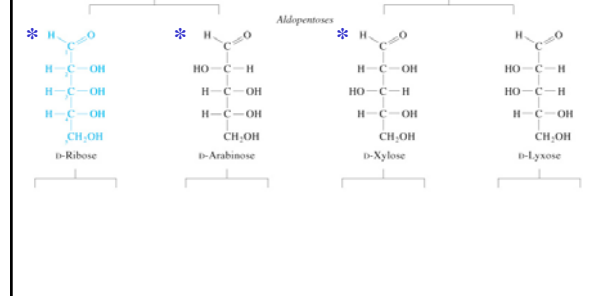
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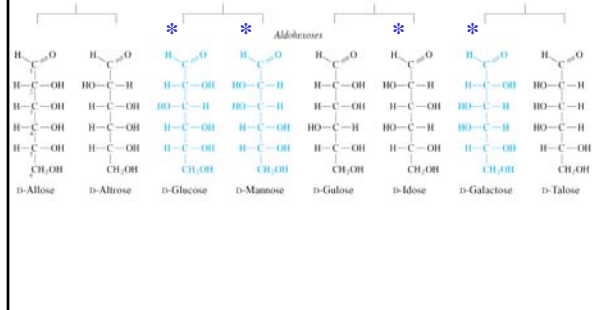
**Fig. 11-1 Structure of the 3-6 carbon D-aldoses**  
(blue are the most common)



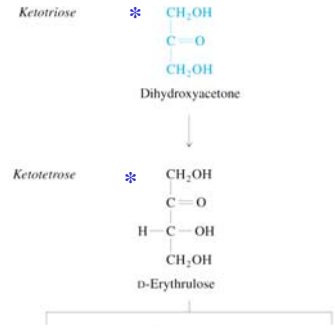
**Fig. 11-1 (aldoses continued)**



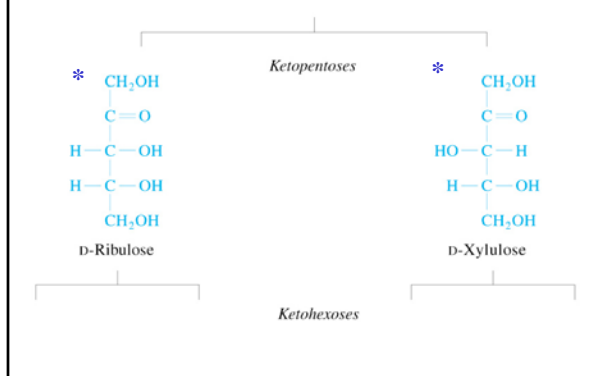
**Fig 11-1 (aldoses continued)**



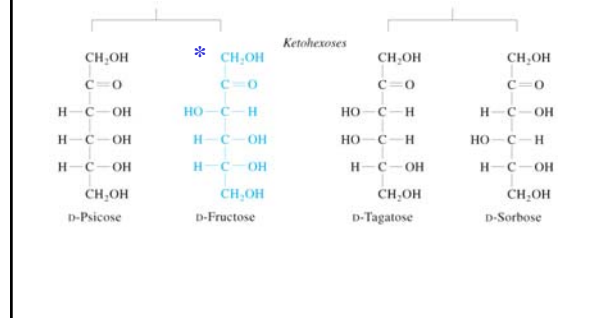
**Fig 11-2 Fisher projections of the 3 to 6 carbon D-ketoses** (blue structures are most common)



**Fig. 11-2 (ketoses continued)**

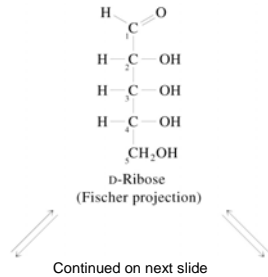


**Fig 11-2 (ketoses continued)**

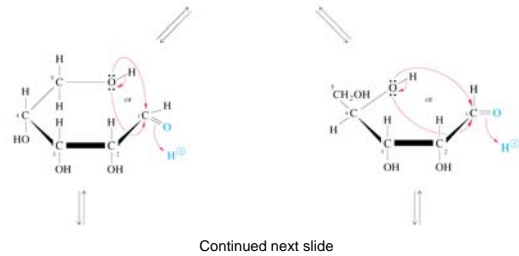




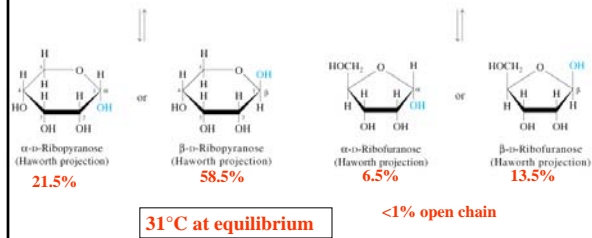
**Cyclization of D-ribose to form  $\alpha$ - and  $\beta$ -D-ribofuranose and  $\alpha$ - and  $\beta$ -D-ribofuranose**



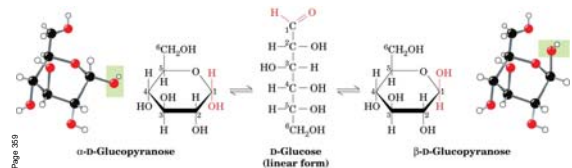
**(Cyclization of D-ribose continued)**



**(Cyclization of D-ribose continued)**

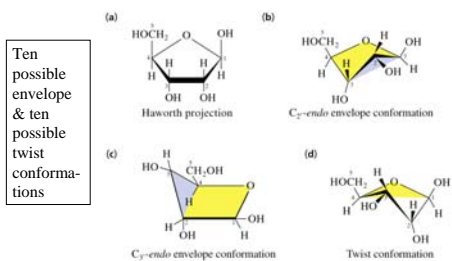


**Figure 11-5** The anomeric monosaccharides  $\alpha$ -D-glucopyranose and  $\beta$ -D-glucopyranose, drawn as both Haworth projections and ball-and-stick models.

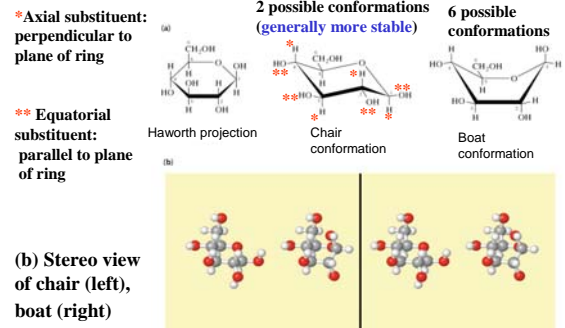


**Conformations of Monosaccharides**

**Figs. 11-6 & 11-7** Conformations of  $\beta$ -D-ribofuranose

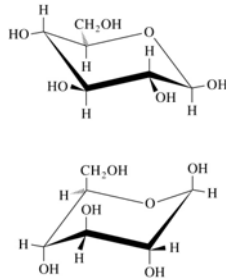


**Fig 11-6** Conformations of  $\beta$ -D-glucopyranose



**Fig 11-6 Conformations of  $\beta$ -D-glucopyranose**

- Top conformer is more stable because it has the bulky hydroxyl substituents in equatorial positions (less steric strain)



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## Derivatives of Monosaccharides

- Many sugar derivatives are found in biological systems
- Some are part of monosaccharides, oligosaccharides or polysaccharides
- These include sugar phosphates, deoxy and amino sugars, sugar alcohols and acids

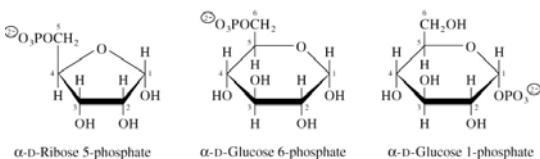
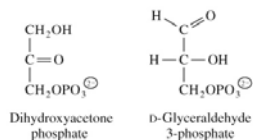
**TABLE 8.1** Abbreviations for some monosaccharides and their derivatives

Monosaccharide or derivative	Abbreviation
<b>Pentoses</b>	
Ribose	Rib
Xylose	Xyl
<b>Hexoses</b>	
Fructose	Fru
Galactose	Gal
Glucose	Glc
Mannose	Man
<b>Deoxy sugars</b>	
Abcquose	Abc
Fucose	Fuc
<b>Amino sugars</b>	
Glucosamine	GlcN
Galactosamine	GalN
N-Acetylglucosamine	GlcNAc
N-Acetylgalactosamine	GalNAc
N-Acetylneuraminic acid	NeuNAc
N-Acetylmuramic acid	MurNAc
<b>Sugar acids</b>	
Glucuronic acid	GlcUA
Iduronic acid	IdoA

**You must know these abbreviations for selected monosaccharides and their derivatives**

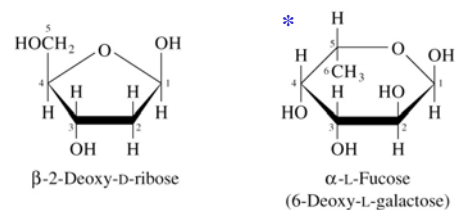
## Sugar Phosphates

Some important sugar phosphates



## Deoxy Sugars

- In deoxy sugars an H replaces an OH
- Deoxy sugars

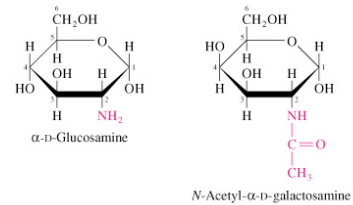


## Amino Sugars

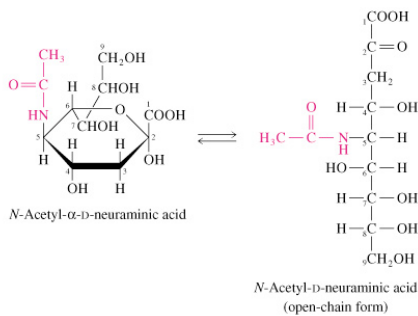
- An amino group replaces a monosaccharide OH
- Amino group is sometimes acetylated
- Amino sugars of glucose and galactose occur commonly in glycoconjugates

**Fig 11-16** Several amino sugars

- Amino and acetylamino groups are shown in red



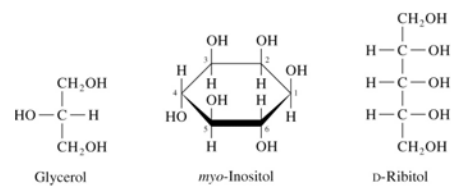
**Sialic acids** (e.g. neuraminic acid) are important in animal glycoproteins (formed from ManNAc + pyruvate)



## Sugar Alcohols (polyhydroxy alcohols)

- Sugar alcohols: carbonyl oxygen is reduced

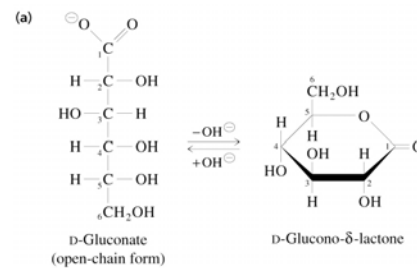
Several sugar alcohols



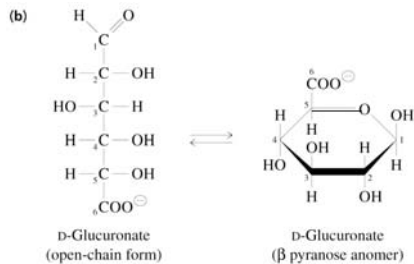
## Sugar Acids

- Sugar acids are carboxylic acids
- Produced from aldoses by:
  - (1) Oxidation of C-1 to yield an **aldonic acid**
  - (2) Oxidation of the highest-numbered carbon to an **alduronic acid**

**Fig 11-9** Sugar acids derived from glucose



## Uronic acids result from oxidation of the primary alcohol group



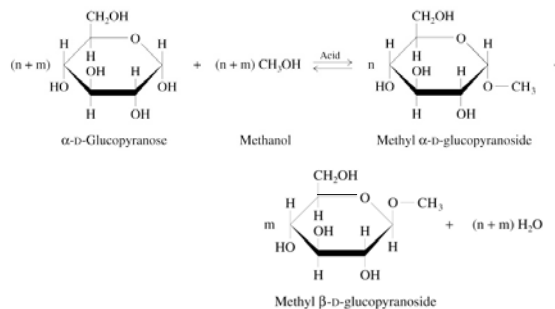
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## Disaccharides and Other Glycosides

- **Glycosidic bond** - primary structural linkage in all polymers of monosaccharides
- **Glucosides** - glucose provides the anomeric carbon
- **Glycoside** – a general term meaning that a carbohydrate provides the anomeric carbon

## Fig 8.19 Glucopyranose + methanol yields a glycoside

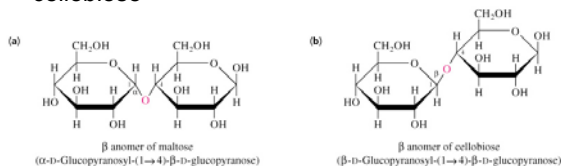


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## Structures of Disaccharides

### Fig 11-12 Structures of (a) maltose, (b) cellobiose

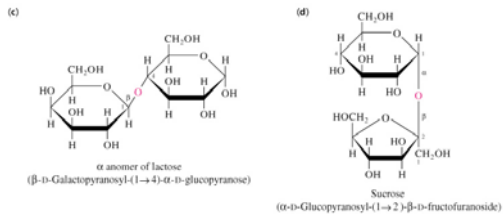


Maltose is a hydrolysis product of amylose (starch)

Cellobiose is a degradation product of cellulose

## Structures of Disaccharides (continued)

Fig. 11-12 Structures of (c) lactose, (d) sucrose



Lactose is an abundant disaccharide in milk

Sucrose: table sugar, most abundant disaccharide in nature, synthesized only in plants

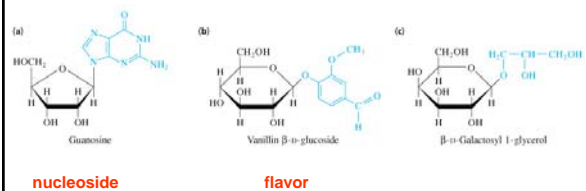
## Reducing and Nonreducing Sugars

- Carbohydrates with a reactive carbonyl (i.e. aldoses with free C1; ketoses with a free C2) are called **reducing sugars** because they can reduce metal ions (e.g.  $\text{Cu}^{2+}$ ,  $\text{Ag}^+$ )
- Carbohydrates with no free anomeric Carbon are called **non-reducing sugars** (e.g. sucrose)

## Nucleosides and Other Glycosides

- Anomeric carbons of sugars can form glycosidic linkages with alcohols, amines and thiols
- Aglycone**: nonsugar molecule attached to the anomeric sugar carbon
- Glycoside**: compound containing glycosidic bonds
- Aglycone + sugar = glycoside

## Structures of three glycosides



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## Polysaccharides

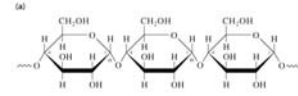
- Homoglycans** - homopolysaccharides containing only one type of monosaccharide
- Heteroglycans** - heteropolysaccharides containing residues of more than one type of monosaccharide
- Lengths and compositions of a polysaccharide may vary within a population of these molecules

## Starch and Glycogen

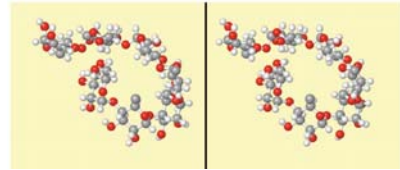
- D-Glucose is stored intracellularly in polymeric forms
- Plants and fungi - starch
- Animals and some bacteria - glycogen
- Starch is a mixture of amylose (unbranched) and amylopectin (branched)

**Fig 11-17 Structure of amylose**

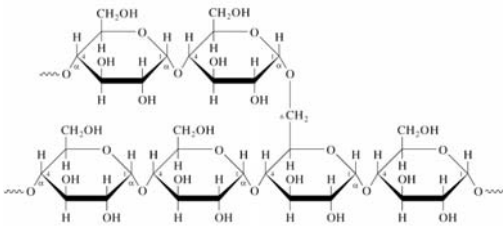
- (a) Amylose is a linear polymer of D-glucose in an  $\alpha$ -1,4-linkage; DP of 100-1000



- (b) Assumes a left-handed helical conformation in water



**Fig 11-18 Structure of amylopectin**



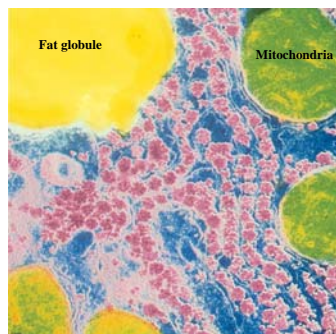
Amylopectin is amylose strands connected by an  $\alpha$ -1,6-linkage; DP of 300-6000

### Comparison of between amylopectin and glycogen

- Both are energy storage forms of glucose
- Both are strands of  $\alpha$ -1,4-linked glucose connected by  $\alpha$ -1,6-linkages
- **Amylopectin:** found in plants; DP 300-6000, crystallin, present in starch granules,  $\alpha$ -1,6-linkages branches occur 1/25 residues
- **Glycogen:** found in animals; DP  $\leq$  50,000, NOT crystallin,  $\alpha$ -1,6-linkages branches occur 1/8 to 1/12 residues

**Figure 11-19 Photomicrograph showing the glycogen granules (pink) in the cytoplasm of a liver cell.**

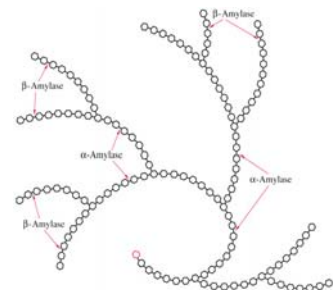
Up to 10% of the weight of the liver can be glycogen



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### Action of $\alpha$ - and $\beta$ -amylase on amylopectin (both cleave $\alpha$ -1,4-glucan)

- $\alpha$ -amylase cleaves random internal  $\alpha$ -(1-4) glucosidic bonds (i.e. **endoglycanase**)
- $\beta$ -amylase acts on nonreducing ends, **exoglycosidase**, releases dimers



**Figure 11-13** Electron micrograph of the cellulose fibers in the cell wall of the alga *Chaetomorpha melagonium*.

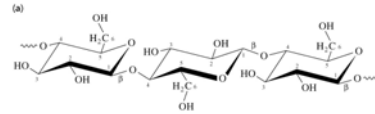


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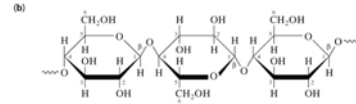
**Cellulose:** most abundant organic molecule on earth, DP 300 - >15,000, synthesized by plants & some bacteria, cell wall polysaccharide

**Fig 11-14** Structure of cellulose ( $\beta$ -1,4-linked glucose homopolymer

(a) Chair conformation

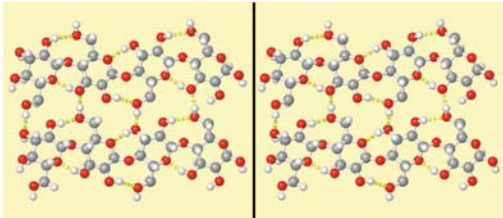


(b) Haworth projection



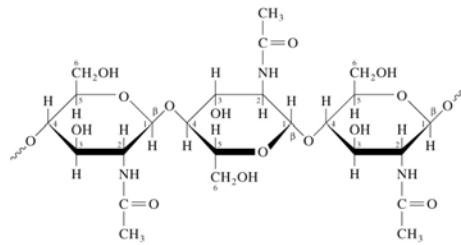
**Fig 11-15** Stereo view of cellulose fibrils  
Individual cellulose chains interact to give cellulose microfibrils and bundles

- Intra- and interchain H-bonding gives strength



**Fig 11-16** Structure of chitin: exoskeleton of spiders & crustaceans, & in cell wall of some fungi & algae

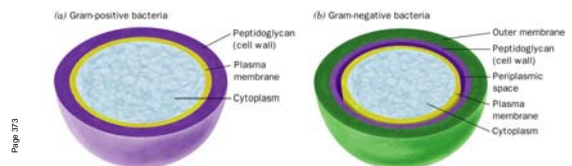
- Repeating units of  $\beta$ -(1-4)GlcNAc residues



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**Figure 11-23** Schematic diagram comparing the cell envelopes of (a) gram-positive bacteria and (b) gram-negative bacteria.

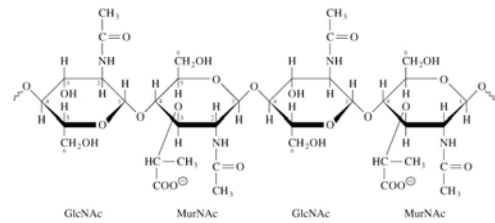


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## Peptidoglycans

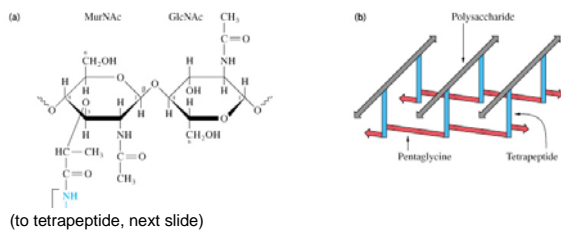
- **Peptidoglycans** - heteroglycan chains linked to peptides
- Major component of bacterial cell walls
- Heteroglycan composed of alternating GlcNAc and N-acetylmuramic acid (MurNAc)
- $\beta$ -(1  $\rightarrow$  4) linkages connect the units

**Fig 11-24** Glycan moiety of peptidoglycan

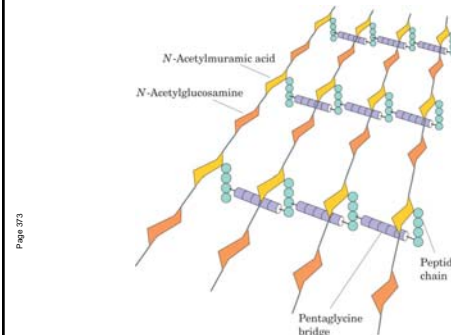


**Fig 11-24** Structure of the peptidoglycan of *S. aureus* (gram positive bacteria cell wall peptidoglycan)

(a) Repeating disaccharide unit, (b) Cross-linking of the peptidoglycan macromolecule

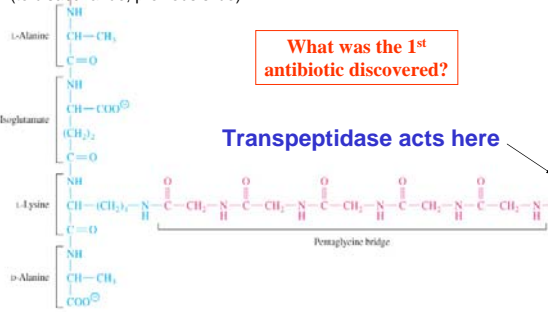


**Figure 11-24b** Chemical structure of peptidoglycan. (b) The *S. aureus* bacterial cell wall peptidoglycan.



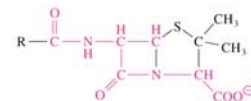
**Fig. 11-24** (continued)

(to disaccharide, previous slide)

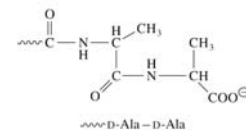


## Penicillin inhibits a transpeptidase involved in bacterial cell wall formation

- **Fig 11-25** Structures of penicillin and -D-Ala-D-Ala



- Penicillin structure resembling -D-Ala-D-Ala is shown in red



## Carbohydrates- General Review

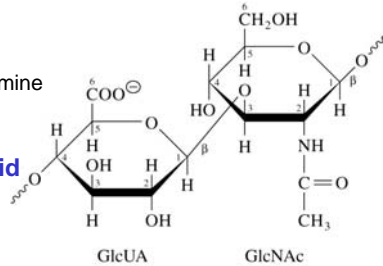
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- Glycoproteins

## Proteoglycans

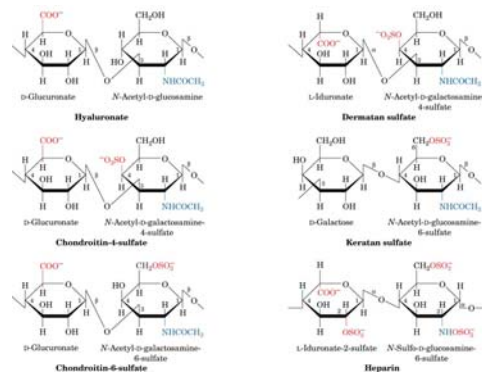
- **Proteoglycans** – glycosaminoglycan (~95%)-carbohydrate-protein conjugates. Often found in ECM. Function as lubricants, cell-cell adhesion, messengers, & give tensile strength & elasticity to soft tissues
- **Glycosaminoglycans (GAGs)**- unbranched heteroglycans of repeating disaccharides (many sulfated hydroxyl and amino groups)
- Disaccharide components include: (1) amino sugar (D-galactosamine or D-glucosamine), (2) an alduronic acid

**Fig 11-20 Repeating disaccharide of hyaluronic acid**

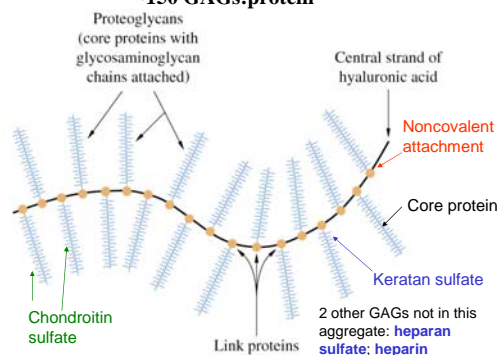
- GlcUA = D-glucuronate
  - GlcNAc= N-acetylglucosamine
- hyaluronic acid is GAG not attached to protein**



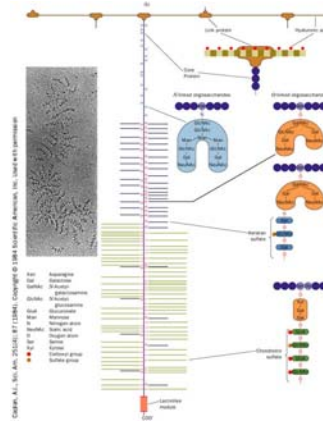
**Figure 11-20 The disaccharide repeating units of the common glycosaminoglycans.**



**Fig 11-22 Proteoglycan aggregate in cartilage ~150 GAGs:protein**



**Figure 11-22**  
**Proteoglycans. (a)** Electron micrograph showing a central strand of hyaluronic acid. **(b)** Bottlebrush model of the proteoglycan aggregate.



**Table 11-1 Properties of Some Proteoglycans.**

Proteoglycan	Approximate Core Protein Molecular Mass (kD)	Glycosaminoglycan Type (Number) <sup>a</sup>
<i>Proteoglycans interacting with hyaluronic acid</i>		
Aggrecan	220	CS (~100), KS (~30)
Versican	265–370	CS/DS (10–30)
Neurocan	136	CS (3–7)
<i>Proteoglycans of the basal laminae</i>		
Perlecan	400–467	Heparan sulfate/CS (3)
Agrin	250	Heparan sulfate (3)
Bamacan	138	CS (3)
<i>Small leucine-rich proteoglycans</i>		
Decorin	40	DS/CS (1)
Fibromodulin	42	KS (2–3)
Osteoglycin	35	KS (2–3)

<sup>a</sup>Abbreviations: CS, chondroitin sulfate; DS, dermatan sulfate; KS, keratan sulfate.  
Source: Iozzo, R.V., *Annu. Rev. Biochem.* 67, 611, 626, and 624 (1998).

## Lipo-oligosaccharides and oligosaccharides can serve as signal molecules

Specific lipo-oligosaccharides are produced by nitrogen-fixing bacteria that interact specifically with certain plants (i.e. legumes) to form root nodules. These lipo-oligosaccharides resemble chitin oligomers with specific modifications.

## Carbohydrates- General Review

- Introduction and definition monosaccharides
- Aldoses and Ketoses
- Cyclic glycosyl residues, Haworth Projections
- Modified monosaccharides
- Glycosidic bond
- Disaccharides
- Polysaccharides
- Peptidoglycans
- Proteoglycans
- Glycoproteins

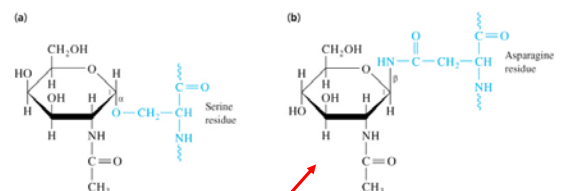
## Glycoproteins

- Proteins that contain covalently-bound oligosaccharides
- O-Glycosidic and N-glycosidic linkages
- Oligosaccharide chains exhibit great variability in sugar sequence and composition
- **Glycoforms** - proteins with identical amino acid sequences but different oligosaccharide chain composition

## Four subclasses of O-glycosidic linkages

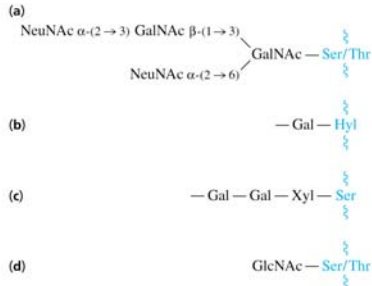
- (1) GalNAc-Ser/Thr (most common)
- (2) 5-Hydroxylysine (Hyl) to D-galactose (unique to collagen)
- (3) Gal-Gal-Xyl-Ser-core protein (in proteoglycans)
- (4) GlcNAc to a single serine or threonine

## O-Glycosidic and N-glycosidic linkages

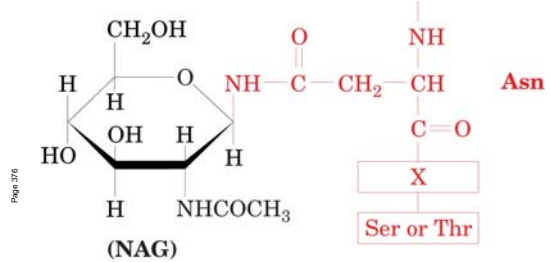


**Consensus sequence for N-glycosylation: Asn-X-Ser/Thr**

### Four subclasses of O-glycosidic linkages

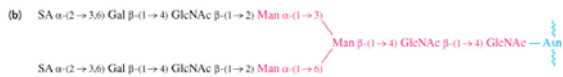
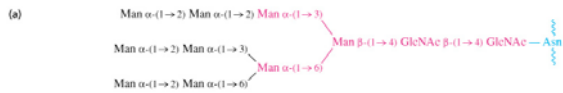


**Figure 11-29a** N-Linked oligosaccharides. (a) All N-glycosidic protein attachments occur through a  $\beta$ -N-acetylglucosamino-Asn bond to Asn-X-Ser/Thr.



### Structures of N-linked oligosaccharides

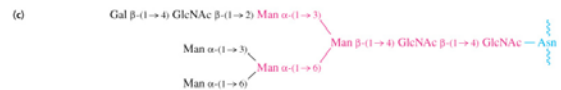
#### High mannose type



#### Complex type

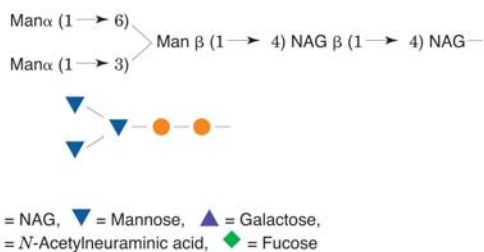
(continued)

#### Hybrid type

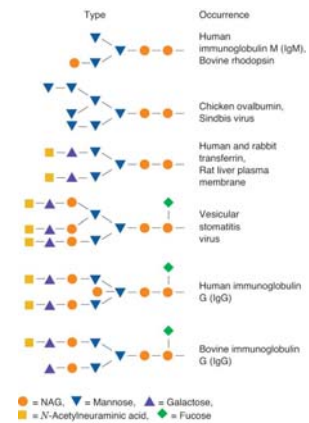


The oligosaccharides attached to proteins may alter physical properties such as size, shape, solubility, or stability, may effect folding, and/or may have biological roles

**Figure 11-29b** N-Linked oligosaccharides. (b) N-Linked oligosaccharides usually have the branched (mannose)<sub>3</sub>(NAG)<sub>2</sub> core shown.

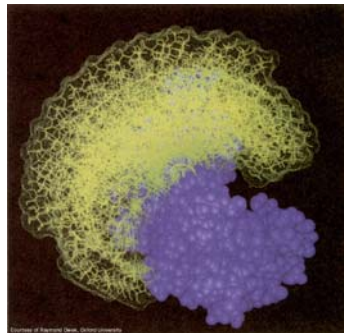


**Figure 11-29c** N-Linked oligosaccharides. (c) Some examples of N-linked oligosaccharides.



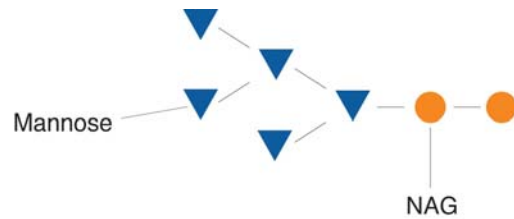
**Figure 11-31** Model of oligosaccharide dynamics in bovine pancreatic ribonuclease B (RNase B).

Oligosaccharides on glycoconjugates are mobile and flexible. Allowed conformations of one specific high mannose oligosaccharide on RNase B is shown.



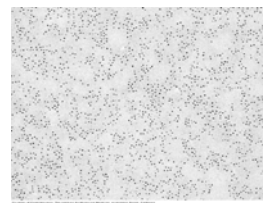
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**Figure 11-32** The microheterogeneous N-linked oligosaccharide of RNase B has the (mannose)<sub>5</sub>(NAG)<sub>2</sub> core shown.

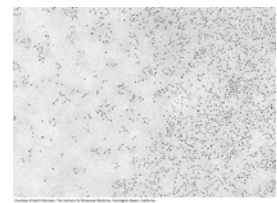


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Oligosaccharide portions of various glycoconjugates are cellular markers that mediate a variety of intercellular interactions



**Figure 11-33a** The surfaces of (a) a normal mouse cell as seen in the electron microscope.



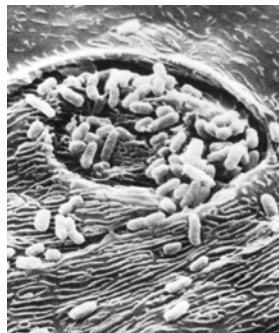
**Figure 11-33b** The surfaces of (b) a cancerous cell as seen in the electron microscope.

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Both cells were labeled with ferritin-labeled lectin concanavalin A. The lectin is evenly dispersed on the normal cell but is aggregated into clusters on the cancerous cell.

**Figure 11-34** Scanning electron micrograph of tissue from the inside of a human cheek.

The first step in bacterial infection is binding of *E. coli* to mannose residues present on the cheek cells.



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