Ch. 9 - Carbohydrates & Glycobiology

- Mono- and disaccharides (simple sugars)
- Oligosaccharides (informational molecules)
- Polysaccharides (Energy stores, cell structures)
- Glycoconjugates
  - Proteoglycans
  - Glycoproteins
  - Glycolipids & lipopolysaccharides
- Lectins
  - Carbohydrate-binding proteins

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3 major size classes

- Monosaccharides
  - Single units
- Oligosaccharides
  - 2 - 20 monosaccharide units
- Polysaccharides
  - > 20 monosaccharide units

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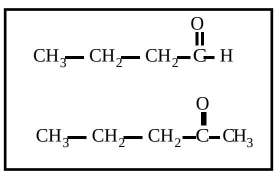
Monosaccharides & Disaccharides

Aldehydes

Ketones



Each with multiple hydroxyl (-OH) groups

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Carbon atoms attached to -OH groups often chiral centers

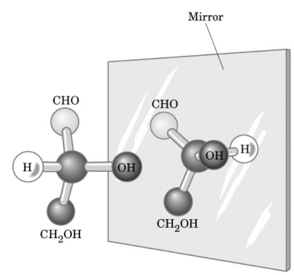

Fig 9.2 **Ball-and-stick models**

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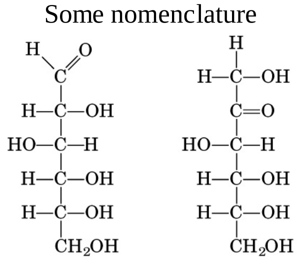
Some nomenclature



D-Glucose, an aldohexose

D-Fructose, a ketohexose

Fig 9.1 **(b)**

- Aldose - monosaccharide derivative of <u>aldehyde</u>
- Ketose - monosaccharide derivative of <u>ketone</u>

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Most monosaccharides have 3-7 carbons

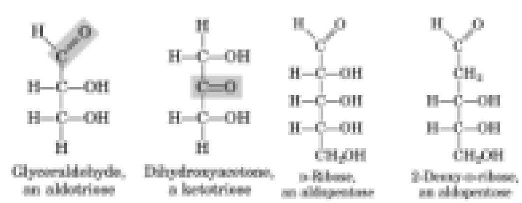

Fig 9.1 (a) (c)

- 3C = triose 4C = tetrose 5C = pentose
- 6C = hexose 7C = heptose, etc.

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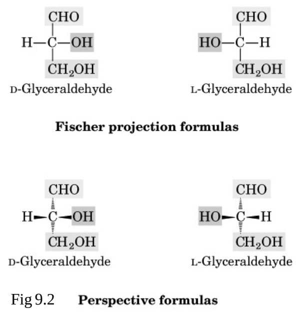
Stereoisomerism



Glyceraldehyde is reference molecule for defining D- or L- stereoisomers

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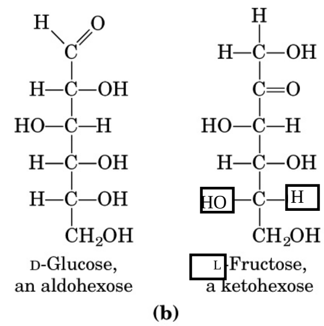
D- or L- configuration ?



Use carbon most distant from carbonyl carbon

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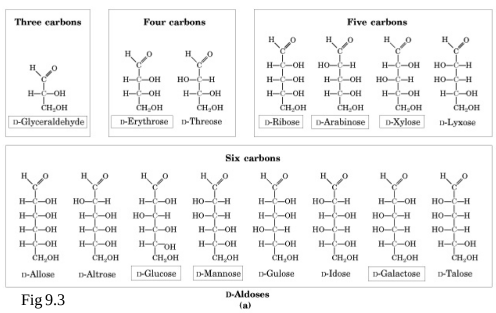
Molecules with "n" chiral centers have 2^n stereoisomers



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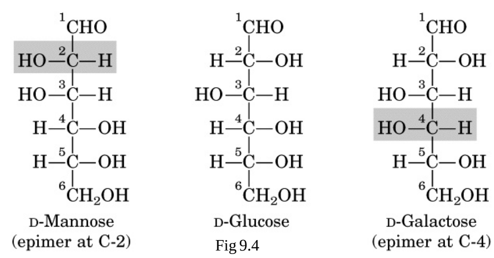
"Epimers" = monosaccharides which differ in configuration around a single carbon



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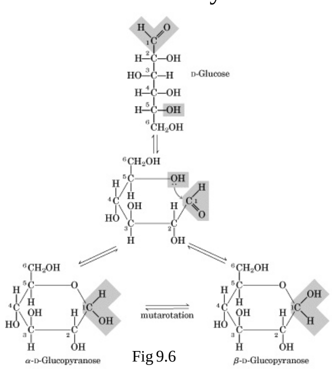
Monosaccharides have cyclic structures



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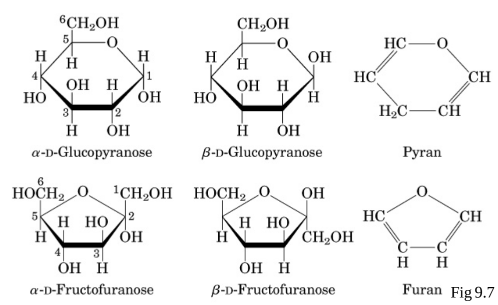
6-member ring compounds = "pyranoses"



5 member ring compounds = "furnanoses"

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Hexose derivatives

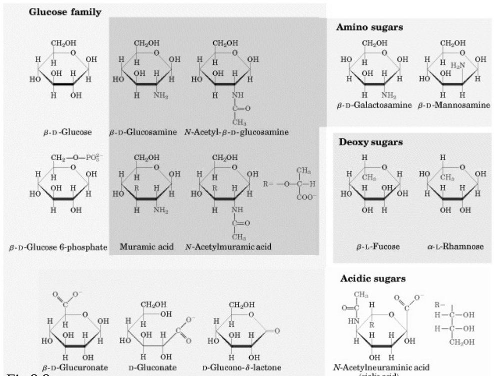

Fig 9.9

Disaccharides & glycosidic bonds

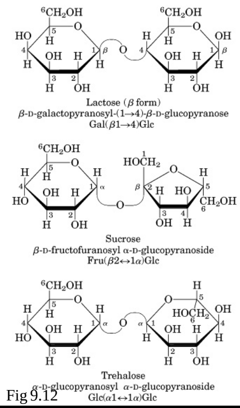

Fig 9.12

Glycosidic bond formation

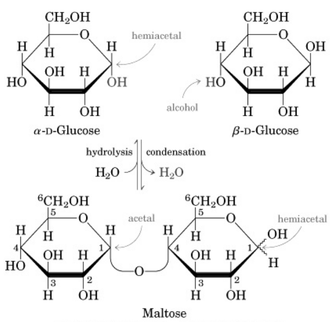

Fig 9.11 α-D-glucopyranosyl-(1→4)-D-glucopyranose

Polysaccharides

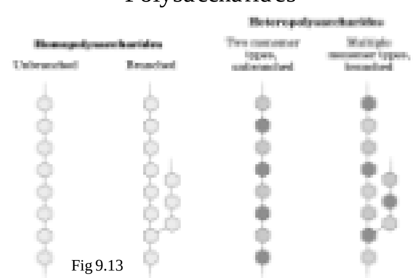

Fig 9.13

- Identity of monosaccharide units
- Length of chains
- Degree of branching
- Types of glycosidic bonds (α1-4) (β1-4) (α1-6) etc.

Starch - plant carb storage

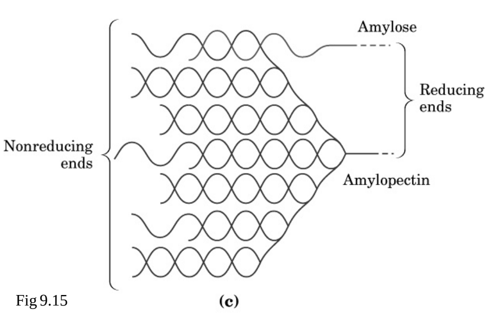

Fig 9.15

Combination of (α1-4) and (α1-6) linkages

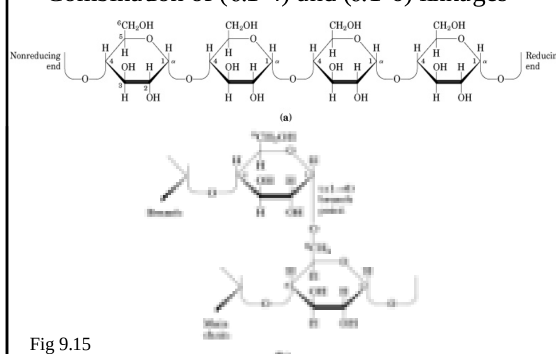

Fig 9.15

Branching speeds utilization of glucose

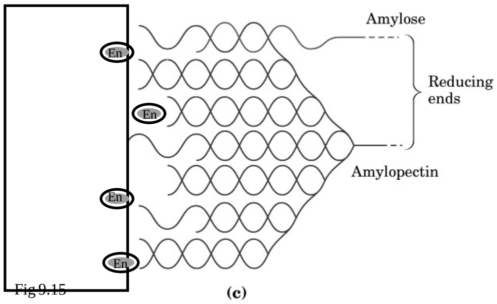

Fig 9.15

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Storing glucose as polymers makes "colligative sense"

Polymers reduce difference in osmotic pressure b/w interior & exterior of cell

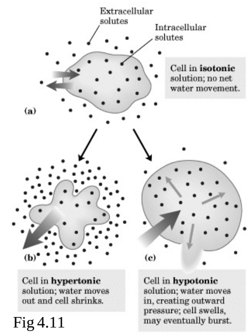

Fig 4.11

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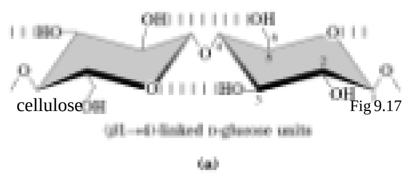
Polysaccharides: Cellulose



cellulose Fig 9.17

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3D structure: Starch vs. Cellulose

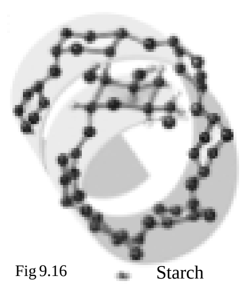

Fig 9.16 Starch

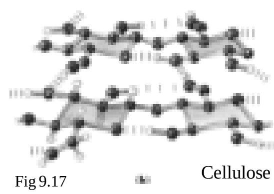

Fig 9.17 Cellulose

Result of α vs β glycosidic bonds

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Chitin - hard exoskeletons

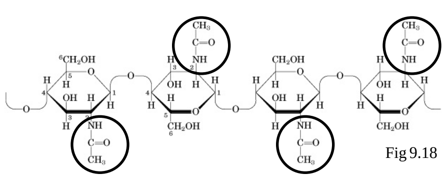

Fig 9.18

(β1-4) glycosidic linkages

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Polysaccharide-petide linkages - "peptidoglycans"

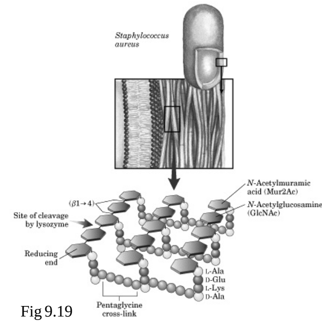

Fig 9.19

Alternating (β1-4) linked N-acetylglucosamine & N-acetylmuramic acid

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Polysaccharides - Glycosaminoglycans

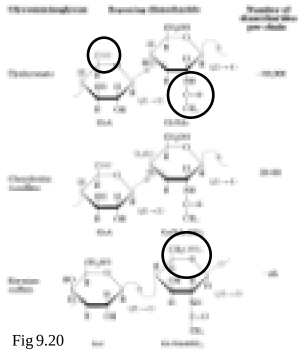

Fig 9.20

Polymers of alternating uronic acid and amino sugars 25

Diverse roles for polysaccharides

table 9–2

Structures and Roles of Some Polysaccharides

Polymer	Type*	Repeating unit†	Size (number of monosaccharide units)	Roles
Starch				Energy storage: in plants
Amylose	Homo-	(α1→4)Glc, linear	50–5,000	
Amylopectin	Homo-	(α1→4)Glc, with (α1→6)Glc branches every 24 to 30 residues	Up to 10^6	
Glycogen	Homo-	(α1→4)Glc, with (α1→6)Glc branches every 8 to 12 residues	Up to 50,000	Energy storage: in bacteria and animal cells
Cellulose	Homo-	(β1→4)Glc	Up to 15,000	Structural: in plants, gives rigidity and strength to cell walls
Chitin	Homo-	(β1→4)GlcNAc	Very large	Structural: in insects, spiders, crustaceans, gives rigidity and strength to exoskeletons
Peptidoglycan	Hetero-; peptides attached	4)Mur2Ac(β1→4) GlcNAc(β1	Very large	Structural: in bacteria, gives rigidity and strength to cell envelope
Hyaluronate (a glycosamino-glycan)	Hetero-; acidic	4)GlcA(β1→3) GlcNAc(β1	Up to 100,000	Structural: in vertebrates, extracellular matrix of skin and connective tissue; viscosity and lubrication in joints

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

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

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Glycoconjugates

- Carbohydrates covalently linked to peptides, proteins or lipids
- Variety of physiological roles
  - Cell-Cell recognition, adhesion or migration
  - Blood clotting
  - Immune response
  - Wound healing

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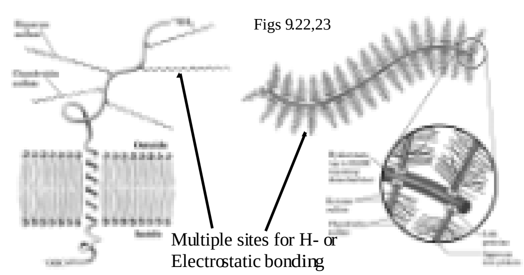
Proteoglycans

Figs 9.22,23



Multiple sites for H- or Electrostatic bonding

"core proteins" covalently linked to glycosaminoglycans

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Glycoproteins

Carbohydrate portions smaller, more structurally diverse than glycosaminoglycans

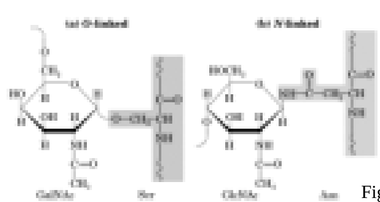

Fig 9.25

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Biological advantages of glycosylation

- Hydrophilic clusters of -OH, SO_4^-, COO^-, etc.
  - Influence on protein structure and/or folding
- Possible Protection from proteolytic degradation
  - Structural/charge barrier to proteases
- Structural diversity of oligosaccharide "labels"
  - Protein destination
  - Hormone/protein receptors
  - Cell and protein "age" indicators

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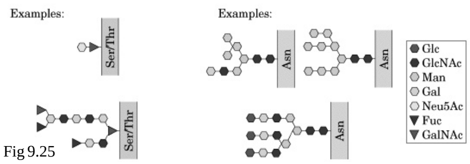

Fig 9.25

- Monosaccharides
- Glycosidic linkages (α,β, 1-4, 2-3, etc.)
- "glycoforms" - same protein, different oligosacc's 31

Glycolipids & lipopolysaccharides

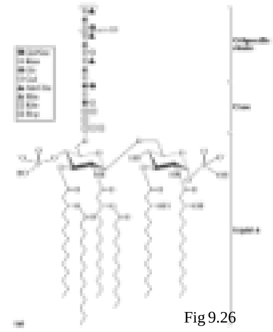

Fig 9.26

Lipids covalently bound to complex oligosacc chains

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Glycoconjugates & the extracellular matrix

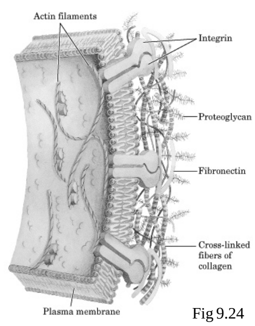

Fig 9.24

Cell-cell adhesion & communication

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Lectins - <u>proteins</u> that bind carbohydrates with high affinity & specificity

- Identification of old proteins
- Vectoring immune cells to sites of infection
- Means of infection or attachment by microbial pathogens
  - *H. pylori* (gastric ulcers)
  - Cholera toxin
  - Whooping cough
  - Influenza virus

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Oligosaccharides in adhesion and recognition

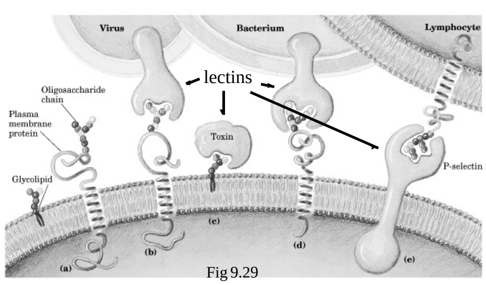

Fig 9.29

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Carbohydrates - summary

- Cyclized, polyhydroxy aldehydes or ketones
  - Monosaccharides
  - Oligosaccharides
  - Polysaccharides
- Monosaccharides have <u>></u> 1 asymmetric carbon
  - Exist in stereoisomeric forms (D- or L-)
  - Multiple chiral centers is the norm
  - Furanoses = 5-membered rings
  - Pyranoses = 6-membered rings

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- Furanoses & pyranoses occur in anomeric α and β forms - differences in configuration about hemiacetal or hemiketal carbon
- Many hexoses derivatized by adding amino, acetyl or sulfate groups
- Oligo- and polysaccharides consist of monosaccharides joined by glycosidic bonds
  - (α1-4), (β1-4) etc.

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- Oligo- and polysaccharide diversity:
  - Composition (mono's)
  - Molecular weight (no. mono's)
  - Glycosidic linkages
  - Degree of branching
- Oligo- and polysaccharide roles:
  - Energy storage
  - Structural (cellulose, chitin, glycosaminoglycans)
  - Information (labels)
  - Protein structure & stability (folding, protease protection)

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- Glycoconjugates:
  - Proteoglycans
  - glycoproteins
  - glycolipids/lipopolysaccharides
- Proteoglycans
  - More "glycan" than "protein"
  - Glycosaminoglycan-proteins of extracellular matrix
  - Cell-cell adhesion
- Glycoproteins
  - More "protein" than "glycan"
  - Structurally diverse oligos
  - Secreted proteins, "labels", cell surface interactions

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- Glycolipids/lipid polysaccharides
  - Outer surface of cell membranes
  - Cell labels
  - Recognition sites for protein binding
- Lectins
  - Carbohydrate-binding proteins
  - Mediate cell-cell interactions
    - Pathogens
    - Immune system, etc.

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