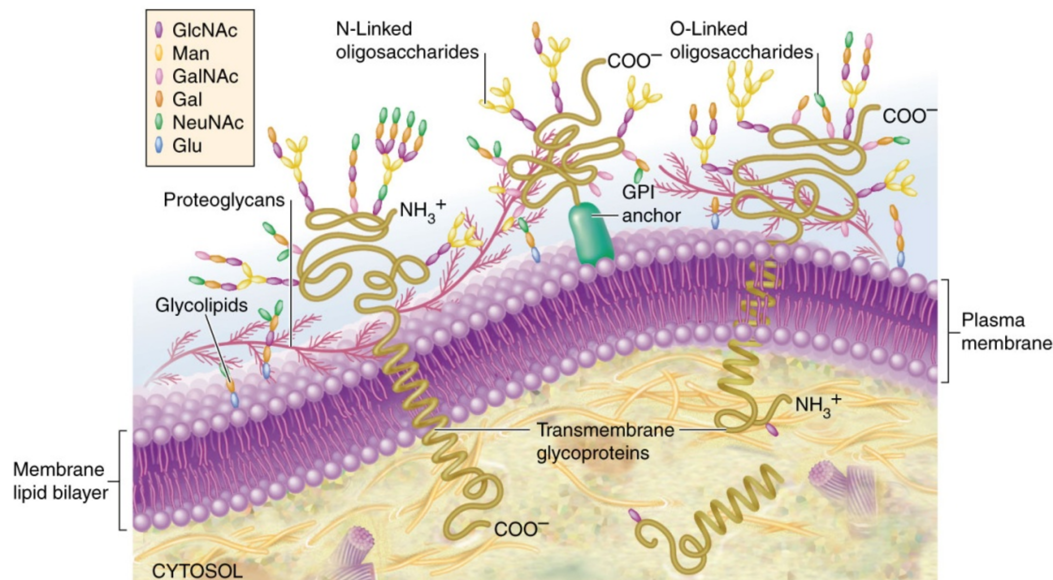
Chapter 7

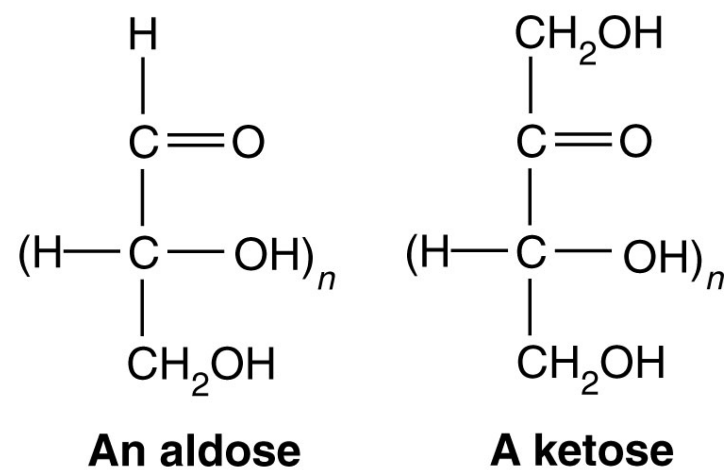
Overview

- **Carbohydrates** – main ingredient for energy production
  - Most abundant biomolecule in nature
  - Direct link between solar energy & chemical energy
  - Glucose – our main energy source



From McKee and McKee, *Biochemistry*, 5th Edition, © 2011 Oxford University Press

- **Carbohydrate:** polyhydroxyaldehyde or polyhydroxyketone, most abundant biomolecules in nature, biological functions include
  - **Energy sources – glucose**
  - **Structural elements – cellulose & chitin in plants & insects**
  - **Cellular communication & identity**
  - **Precursors in production of other biomolecules**
  - **Monosaccharides** - simple sugars
    - **Aldoses** - aldehyde functional group
    - **Ketoses** - ketone functional group
    - Building blocks of all carbohydrates
    - General formula $\mathbf{C_nH_{2n}O_n}$ or $(CH_2O)_n$ where **n** varies from 3 – 8
  - **Oligosaccharides** – 2-10 monosaccharides
  - **Polysaccharides** - >10 monosaccharides



- Carbohydrates are also classified by the number of carbon atoms they contain
  - Trioses, tetroses, pentoses, and hexoses
    - Most abundent in living cells are hexoses and pentoses
    - Class names often combine information about carbon number and functional group
- Glyceraldehyde contains a stereocenter on #2 C (chiral); exists as a pair of enantiomers
  - Chiral carbon – asymmetric carbon in molecule having mirror-image form
  - Enantiomers - Mirror-images stereoisomers

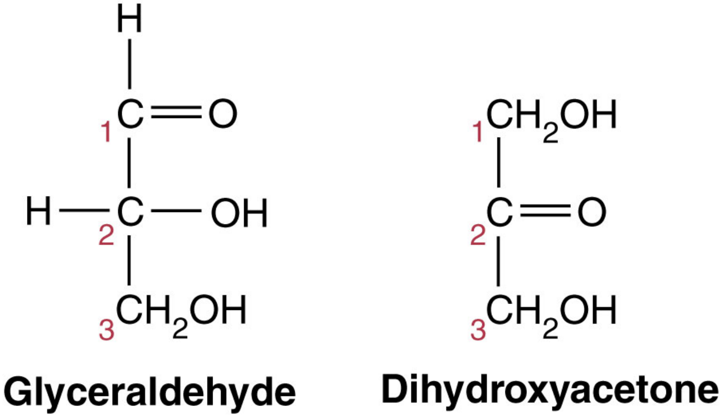
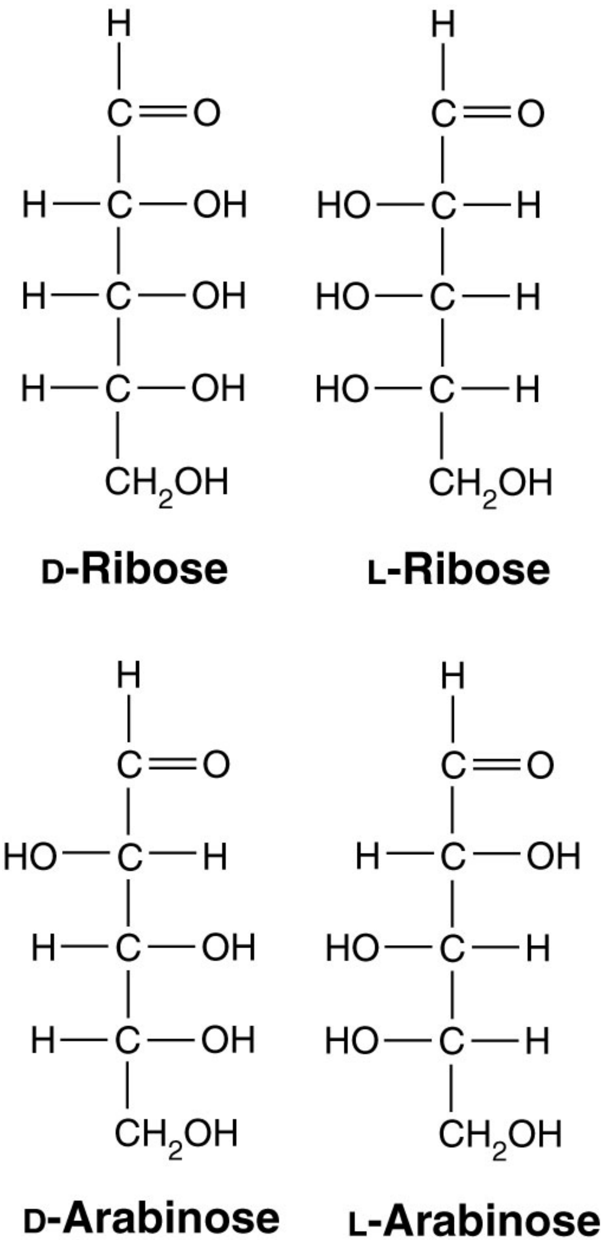


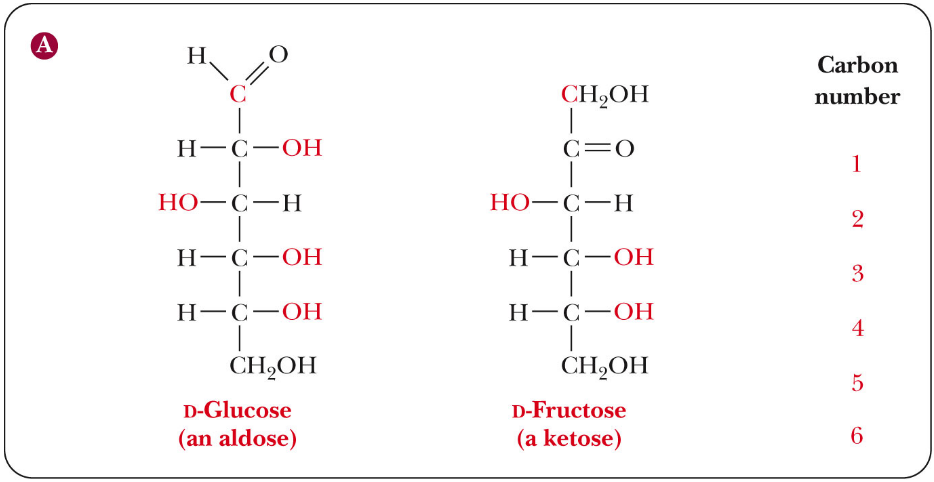
Figure 7.2 Glyceraldehyde (an Aldotriose) and Dihydroxyacetone (a Ketotriose)

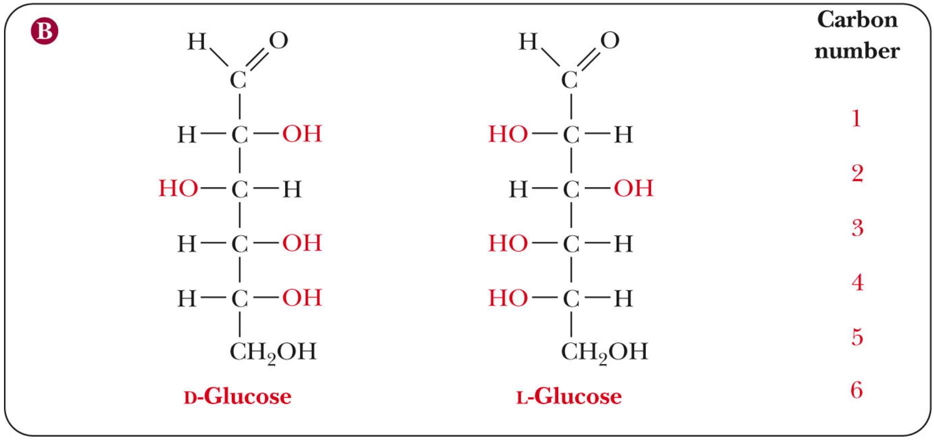


- **3-C sugars have 1 chiral C so only 2 enanitomers; more chiral C more possible stereoisomers**
- **Diastereomers:** stereoisomers that are not mirror images
  - example: D-ribose (-OHs on right); L-ribose (-OHs on left)
  - example: D-arabinose and L-arabinose
    - **Epimers:** diastereomers that differ from each other in configuration at only one chiral carbon

Figure 7.4 The Optical Isomers D- and L- Ribose and D- and L- Arabinose

- **Fischer projection:** 2-D representation shows tetrahedral stereo-centers
  - Carbons - numbered starting most highly oxidized C, top
  - D- or L- configuration - determined by arrangement on C-5
  - D-glucose, hydroxyl on right; L-glucose hydroxyl on left





Cyclic Structure of Monosaccharides

- Cyclization - interaction between functional groups on distant carbons
  - C1 to C5, to make a cyclic **hemiacetal**
  - Cyclization using C2 to C5 results in **hemiketal** formation.
- Carbonyl carbon is new chiral center and becomes an **anomeric carbon**

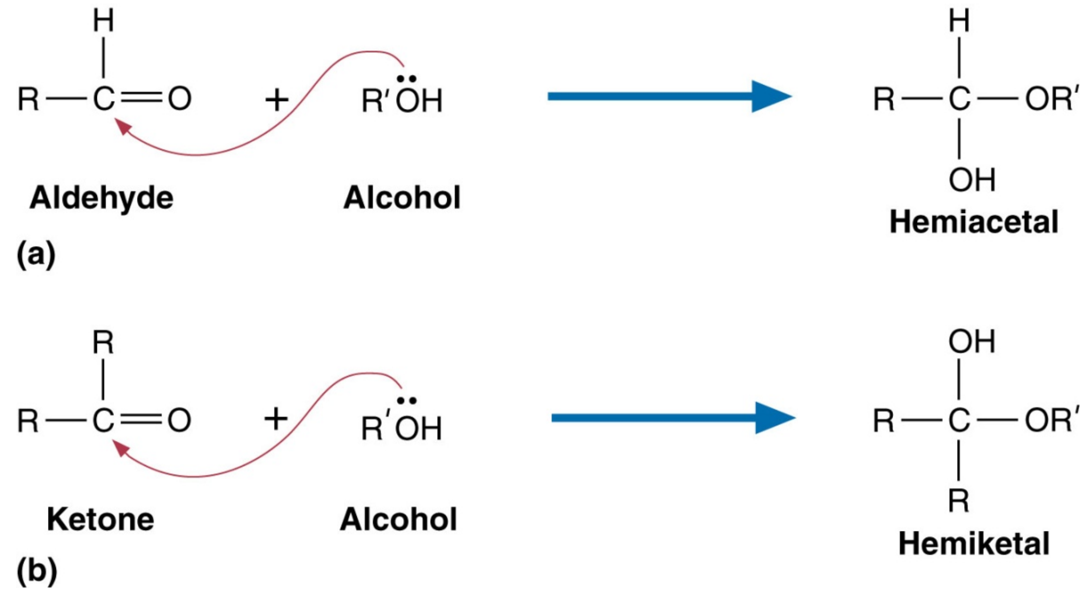
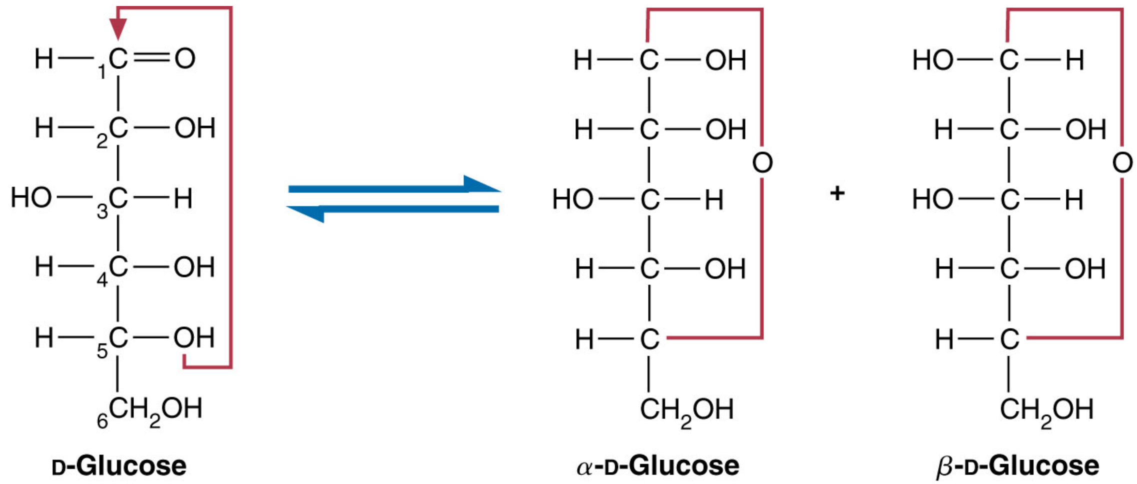


Figure 7.5 Formation of Hemiacetals and Hemiketals

From McKee and McKee, *Biochemistry*, 5th Edition, © 2011 Oxford University Press

Figure 7.6 Monosaccharide Structure



- Two possible diastereomers from cyclization are called **anomers**
  - α-D-glucose – OH on R; β-D-glucose – OH on L
- 5- and 6-membered hemiacetals are represented as planar pentagons or hexagons
  - Commonly written with the anomeric carbon (C1) on right; hemiacetal oxygen to the back right
  - D-sugar form, when the anomeric hydroxyl is up it gives a β-anomeric form (right above) while down gives the α-anomeric form (left)

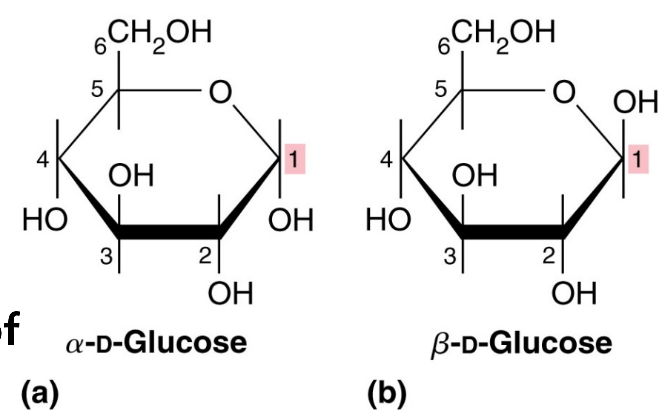
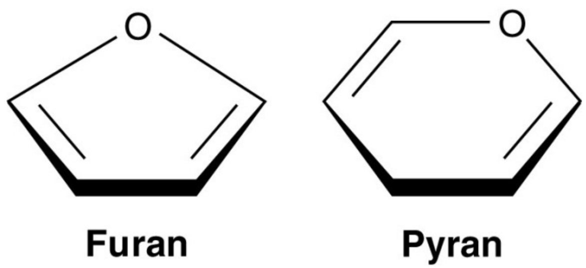


Figure 7.7 Haworth Structures of the Anomers of D-Glucose

Figure 7.8 Furan and Pyran



- Five-membered rings are called **furanoses** and six-membered rings are **pyranoses**
- Cyclic form of fructose is fructofuranose, while glucose in the pyranose form is glucopyranose

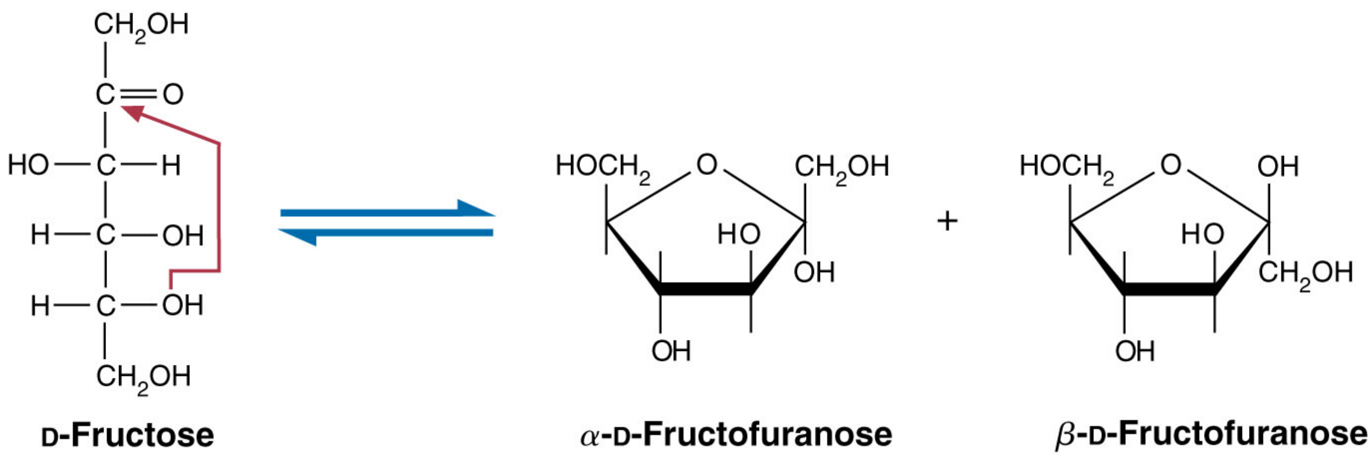
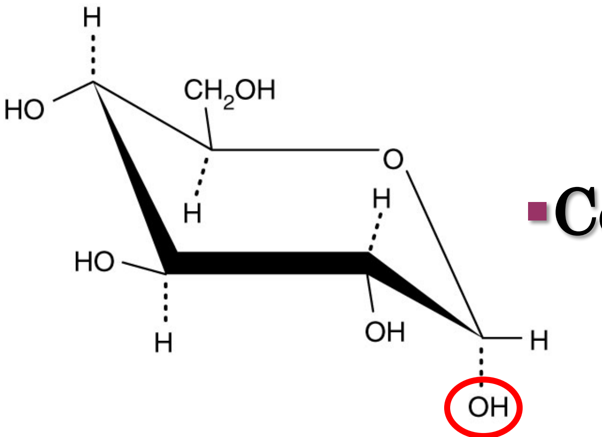
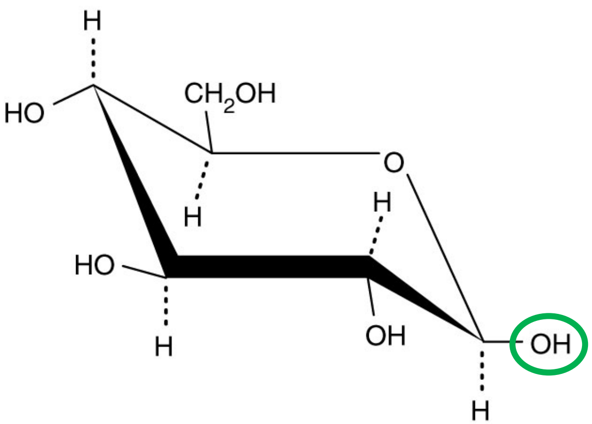


Figure 7.9 Fischer and Haworth Representations of D-Fructose



α-D-Glucopyranose



β-D-Glucopyranose

Figure 7.10 α- and β-D-glucose

- **Conformational Structures**
  - Furanoses are close to planar
    - ✓ Haworth projection adequately represent
  - Pyranoses more accurately represented as strain-free chair conformation
    - ✓ α-D-Glucopyranose - OH on anomeric C down/back
    - ✓ β-D-Glucopyranose – OH on anomeric C on plane/right

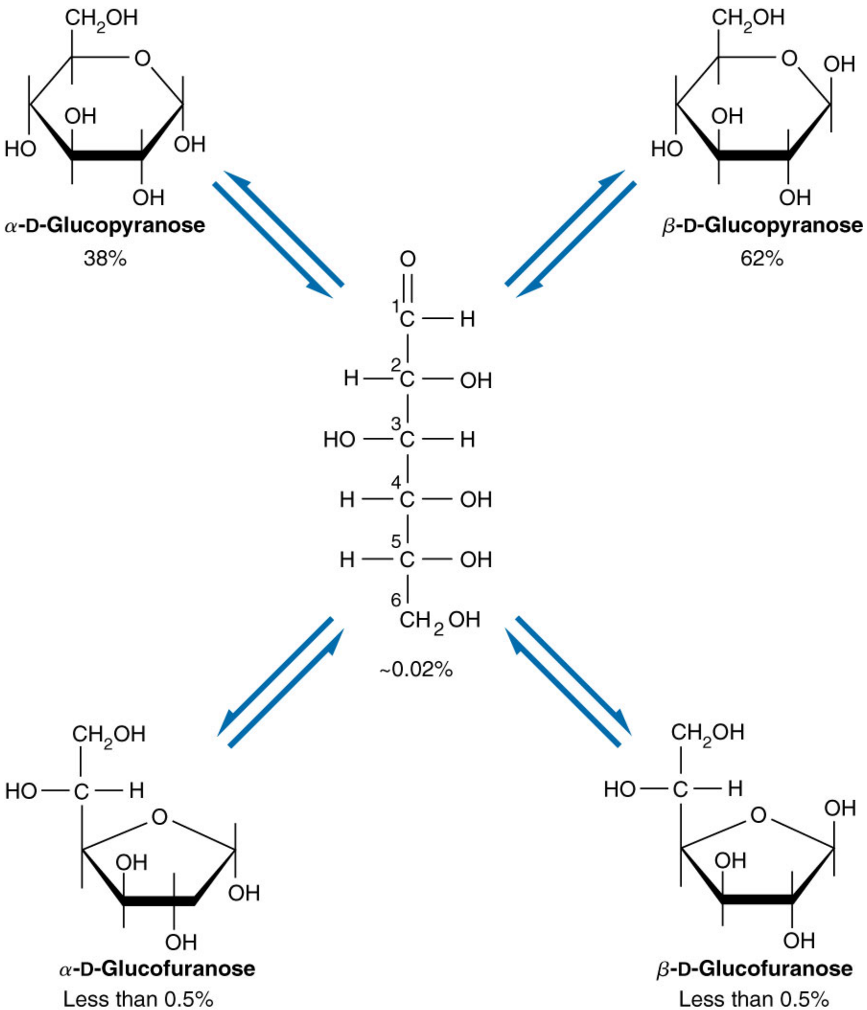
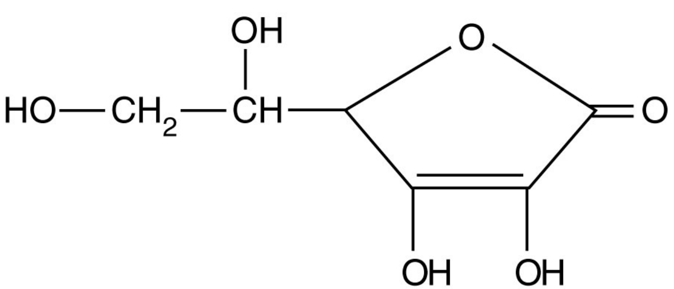


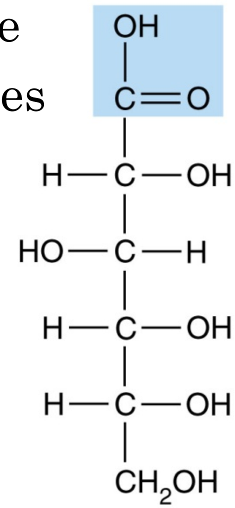
Figure 7.11 Equilibrium Mixture of D-Glucose

- **Mutarotation**
  - α- and β-forms of monosaccharides are readily interconverted in aqueous environments
  - Spontaneous process produces an equilibrium mixture of α- and β-forms in both furanose and pyranose ring structures
    - Open chain form can participate in redox reactions

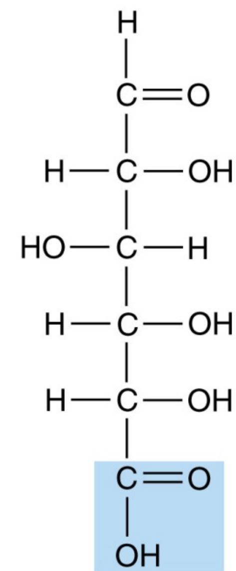
- **Oxidation**—undergo several oxidation reactions in presence of metal ions or certain enzymes
  - Oxidation of aldehyde group yields **aldonic acid**
  - Oxidation of terminal CH_2OH group yields **uronic acid**
  - Oxidation of both groups yields **aldaric acid**
  - **Lactone** -produced if the carbonyl groups of aldonic or uronic acids react with an OH group in the same molecule
    - Readily produced in nature - **L-ascorbic acid** (vitamin C)
    - Vitamin C is a powerful reducing agent, protects cells from reactive oxygen and nitrogen species



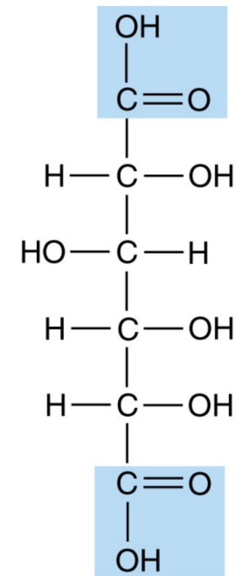
Ascorbic acid



D-Gluconic acid



D-Glucuronic acid



D-Glucaric acid

Reduction – aldehyde and ketone groups yields sugar alcohols, **alditols**

- **Reducing sugars** - reduced by weak, oxidizing agents such as Benedict's reagent
  - Needs open chain - all aldoses are reducing sugars
    - ketoses (fructose) are reducing sugars also, due to isomerization

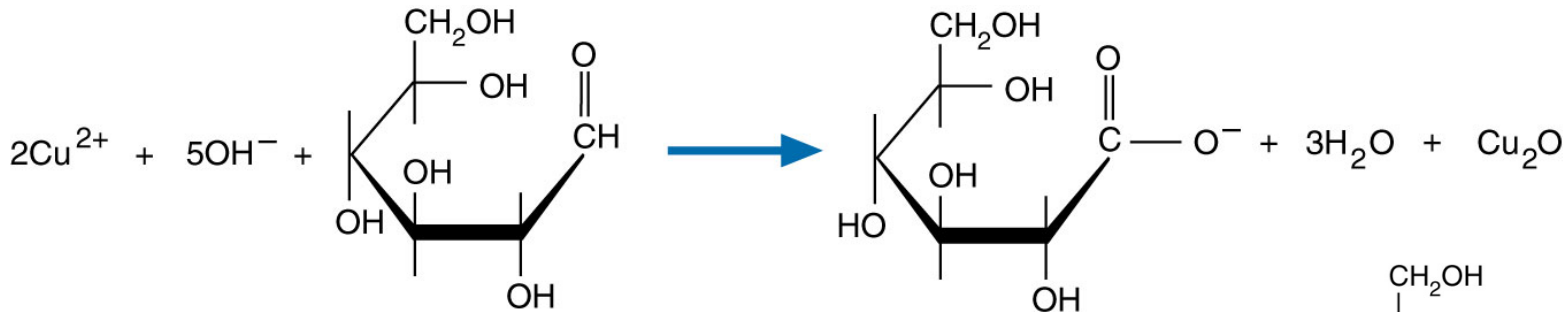
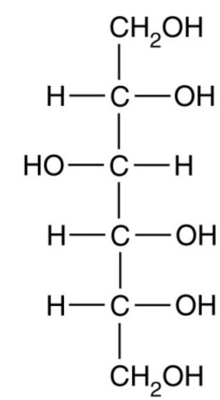


Figure 7.14 Reaction of Glucose with Benedict's Reagent

- Alditols - used in commercial food processing and in pharmaceuticals (e.g., sorbitol can be used to prevent moisture loss)



D-Glucitol

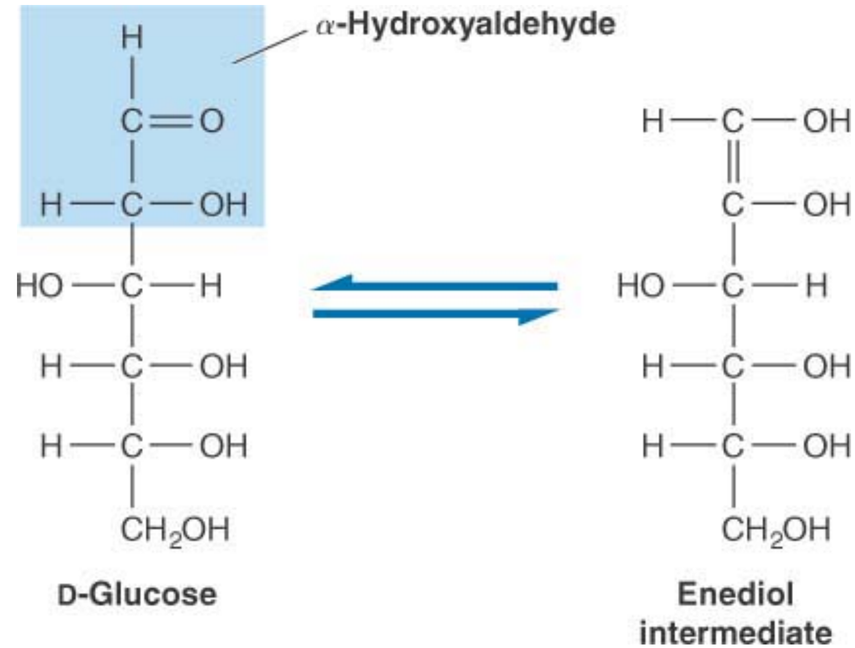


Figure 7.16 Isomerization of D-Glucose to Form D-Mannose and D-Fructose

- **Isomerization** - undergo several types of isomerization
  - D-glucose incubated in an alkaline solution for several hours produces two isomers: D-mannose and D-fructose
  - Both involve an **enediol** intermediate

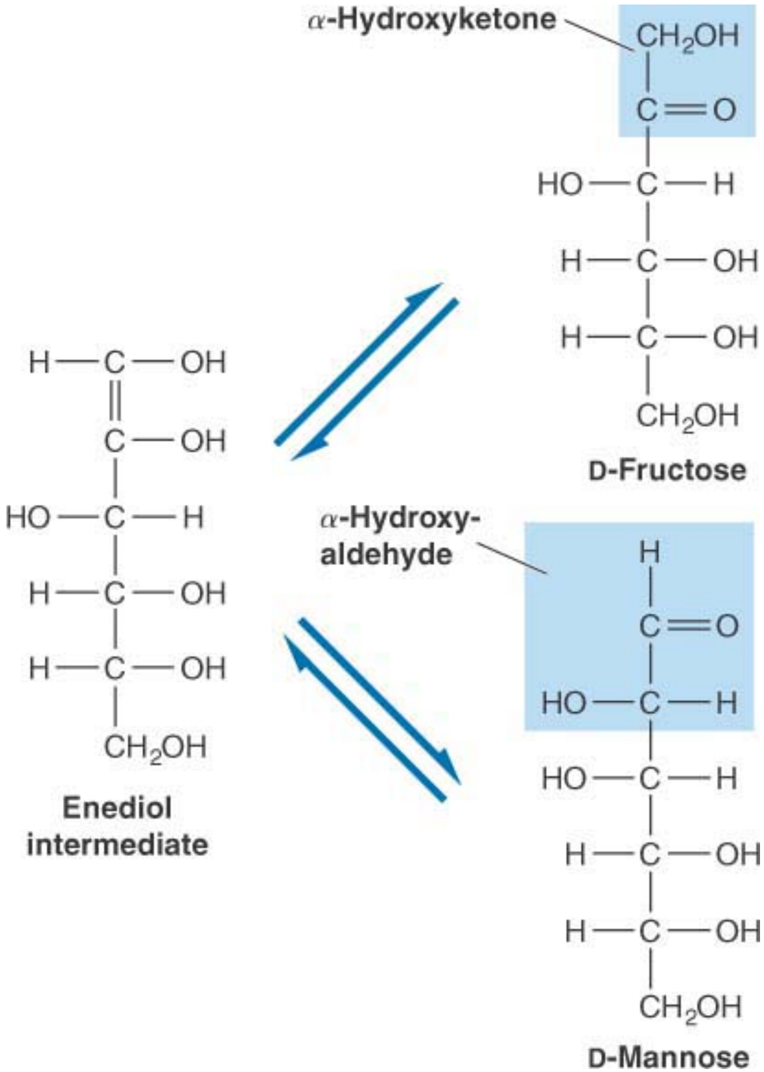
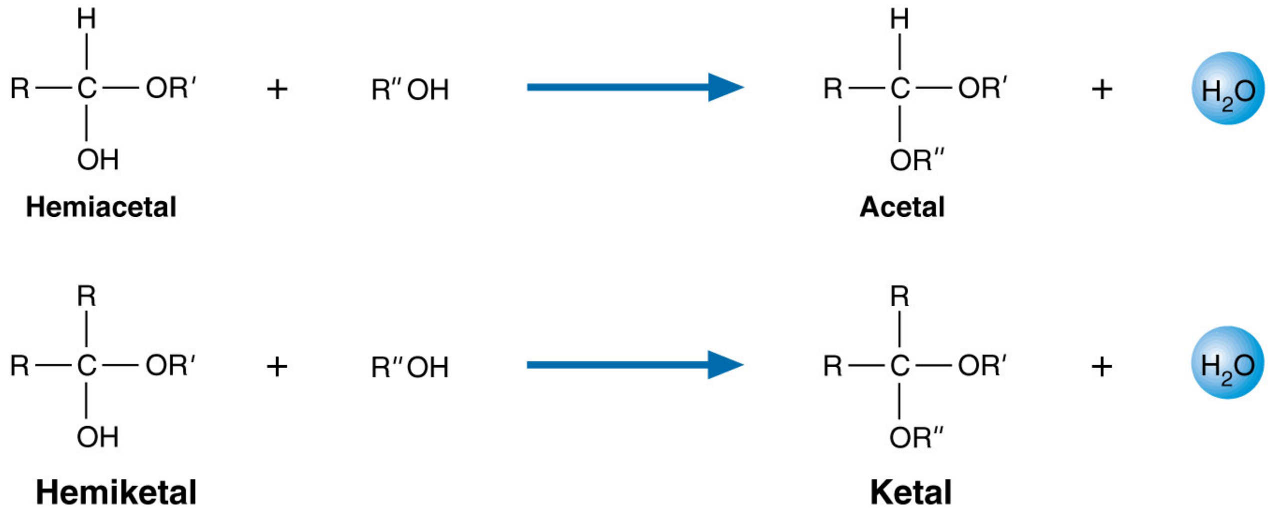


Figure 7.16 Isomerization of D-Glucose to Form D-Mannose and D-Fructose

- Transformation of glucose to fructose is an **aldose-ketose interconversion**
- Transformation of glucose to mannose is referred to as **epimerization**

- **Esterification** - free OH groups of carbohydrates can be converted to esters by reactions with acids
  - Can dramatically change a sugar's chemical and physical properties
  - Phosphate and sulfate esters most common in nature
    - ✓ Phosphate esters are formed during reactions with ATP
    - ✓ Sulfate esters – found predominantly in the proteoglycan components of connective tissue
      - ✓ Participate in forming of salt bridges between carbohydrate chains

Figure 7.17 Formation of Acetals and Ketals



- **Glycoside Formation**—hemiacetals and hemiketals react with alcohols to form the corresponding **acetal** and **ketal**
  - Cyclic hemiacetal or hemiketal form reacts with an alcohol a **glycosidic linkage** is formed, compound a **glycoside**
    - ✓ Chemically an ether, ROR'
    - ✓ Naming of glycosides specifies the sugar component – glucose and fructose are glucoside and fructoside
- **Disaccharide** – acetal linkage between hemiacetal hydroxyl of 1 monosaccharide & hydroxyl of another
- **Polysaccharides** – many monosaccharides linked together

- **Glycosylation Reactions** attach sugars or glycans (sugar polymers) to proteins or lipids
  - Catalyzed by glycosyl transferases
    - Glycosidic bonds are formed between anomeric carbons in certain glycans and oxygen or nitrogen of other types of molecules, resulting in N- or O-glycosidic bonds
- **Glycation** is reaction of reducing sugars with nucleophilic nitrogen atoms in a nonenzymatic reaction
  - Most researched is the nonenzymatic glycation of protein (**Maillard reaction**)
  - Schiff base that forms rearranges to a stable ketoamine, called Amadori product
  - Can further react to form advanced glycation end products (AGEs)
    - Promote inflammatory processes and involved in age-related diseases

Section 7.1: Important Monosaccharides

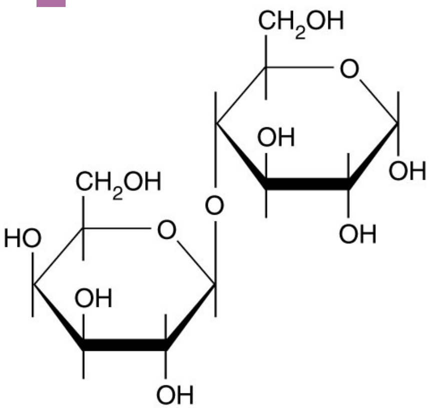
- **Glucose (D-Glucose)** —originally called dextrose, it is found in large quantities throughout the natural world
  - Primary fuel for living cells
  - Preferred energy source for brain cells and cells without mitochondria (erythrocytes)
  - Dietary sources: plant starch, disaccharides lactose, maltose, sucrose
- **Fructose (D-Fructose) -** fruit sugar, because of its high content in fruit
  - Per-gram basis, it is twice as sweet as sucrose; often used as a sweetening agent in processed food
  - Sperm use fructose as an energy source
- **Galactose** is necessary to synthesize a variety of important biomolecules
  - Important biomolecules - lactose, glycolipids, phospholipids, proetoglycan, glycoproteins
  - **Galactosemia** is a genetic disorder resulting from a missing enzyme in galactose metabolism

Section 7.1: Monosaccharide Derivatives

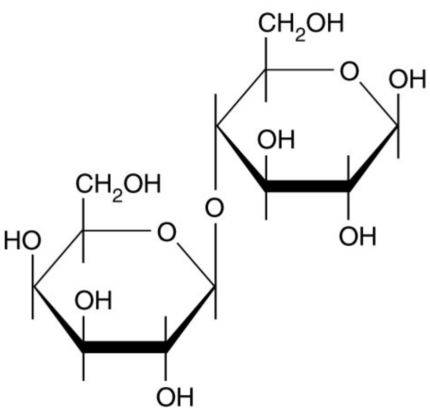
- **Uronic Acid -** α-D-glucuronate (7.24a) and its epimer β-L-iduronate (7.24b) are important in animals
  - D-Glucuronic acid is used in the liver to improve water solubility to remove waste molecules
- **Amino Sugars -** a hydroxyl group (usually on carbon 2) is replaced with an amine group
  - D-Glucosamine (a) and D-galactosamine (b) are most common and often attached to proteins or lipids
- **Deoxy Sugars -** have an –OH replaced by an –H or $–CH_3$
  - 2-deoxy-D-ribose (7.25b) is pentose sugar of DNA; fucose (7.25a) part of ABO blood group determinants

- **Lactose (milk sugar)** - reducing sugar, found in milk
  - Galactose linked to glucose (β(1,4) linkage)
  - Lactose intolerance results from lactase deficiency
    - ✓ Inability to break down lactose to galactose & glucose
- **Maltose (malt sugar)** – intermediate of starch hydrolysis
  - α(1,4) linkage between two molecules of glucose
  - Does not exist freely in nature
- **Cellobiose** is a degradation product of cellulose
  - Two molecules of glucose linked with a β(1,4) glycosidic bond
  - Does not exist freely in nature
- **Sucrose** – cane or beet sugar; nonreducing sugar
  - Glucose linked to fructose by an α,β(1,2) glycosidic bond
  - Glycosidic bond occurs between both anomeric carbons

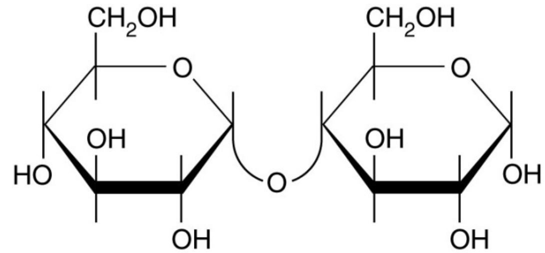
Section 7.2: Disaccharides



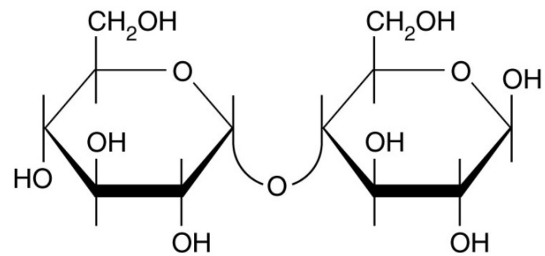
α-Lactose



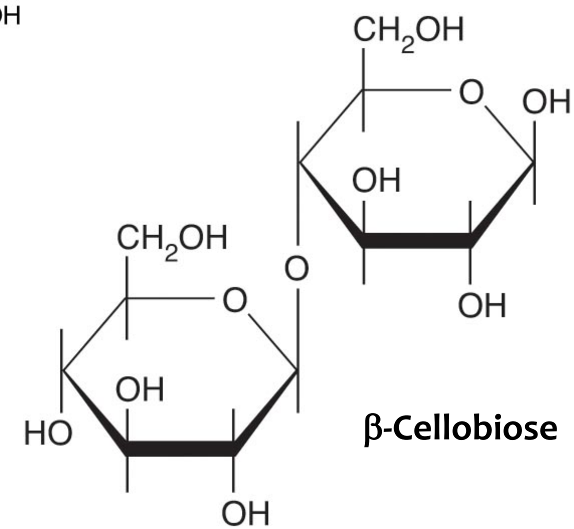
β-Lactose



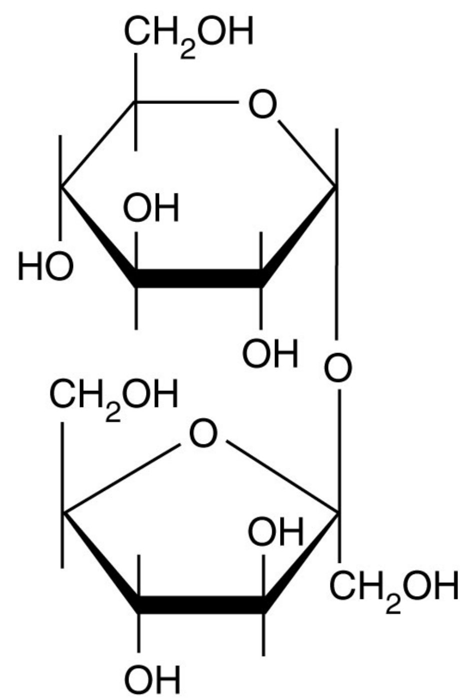
α-Maltose



β-Maltose



β-Cellobiose



Sucrose

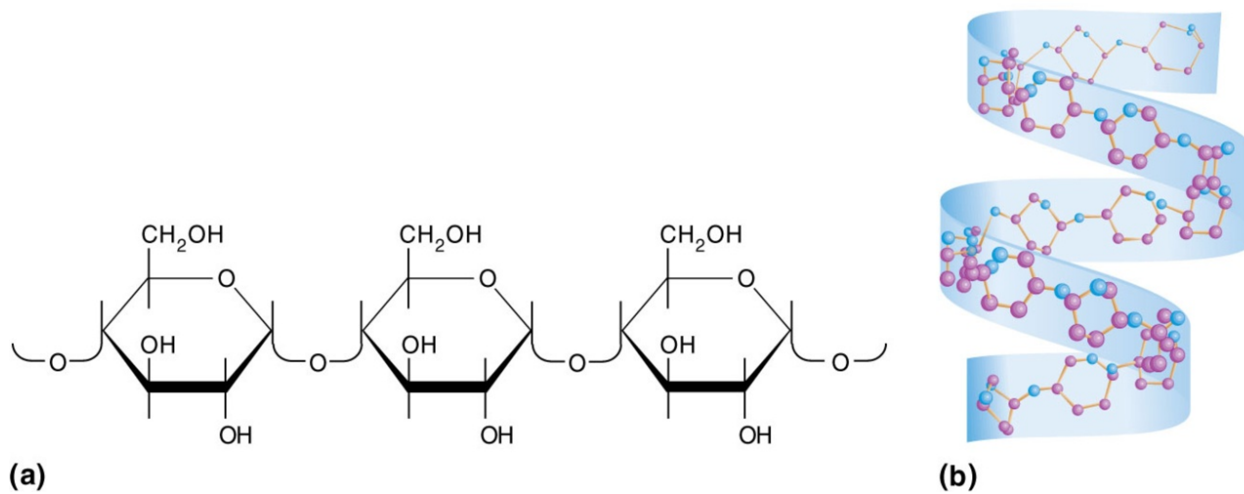
- Polysaccharides (**glycans**) - large numbers of monosaccharides connected by glycosidic linkages
  - Can be linear or branched
  - Two classes: **homoglycans** and **heteroglycans**
  - Smaller glycans -2 to 10 monomers called oligosaccharides
  - Most often attached to polypeptides as glycoproteins
    - N-linked by N-glycosidic bond with asparagine R amide nitrogen
    - O-linked through serine or threonine R group hydroxyl

- **Homoglycans**
  - Found in starch, glycogen, cellulose, and chitin (glucose monomer)
  - **Starch** and **glycogen** are energy storage molecules while chitin and cellulose are structural
  - **Chitin** is part of the cell wall of fungi and arthropod exoskeleton
  - **Cellulose** is the primary component of plant cell walls
    - ✓ Most abundant organic substance on earth
  - No fixed molecular weight - size is a reflection of the metabolic state of the cell producing them

Section 7.3: Polysaccharides

- **Starch** - energy reservoir of plant cells; significant source of carbohydrate in the human diet
  - **Amylose** - long, unbranched chains of D-glucose with α(1,4) linkages
    - Contains thousands of glucose monomers - molecular weight from 150,000 to 600,000 Da
  - **Amylopectin** - branched polymer containing both α(1,6) and α(1,4) linkages
    - Branch points occur every 20 to 25 residues; α1,6 linkages

Amylose



From McKee and McKee, *Biochemistry*, 5th Edition, © 2011 Oxford University Press

- **Glycogen** - carbohydrate storage molecule in animals; greatest abundance in liver and muscle cells
  - Up to 8–10% of the wet weight of liver cells and 2–3% in muscle cells
  - Similar in structure to amylopectin, with more branch points
  - More compact and easily mobilized than other polysaccharides

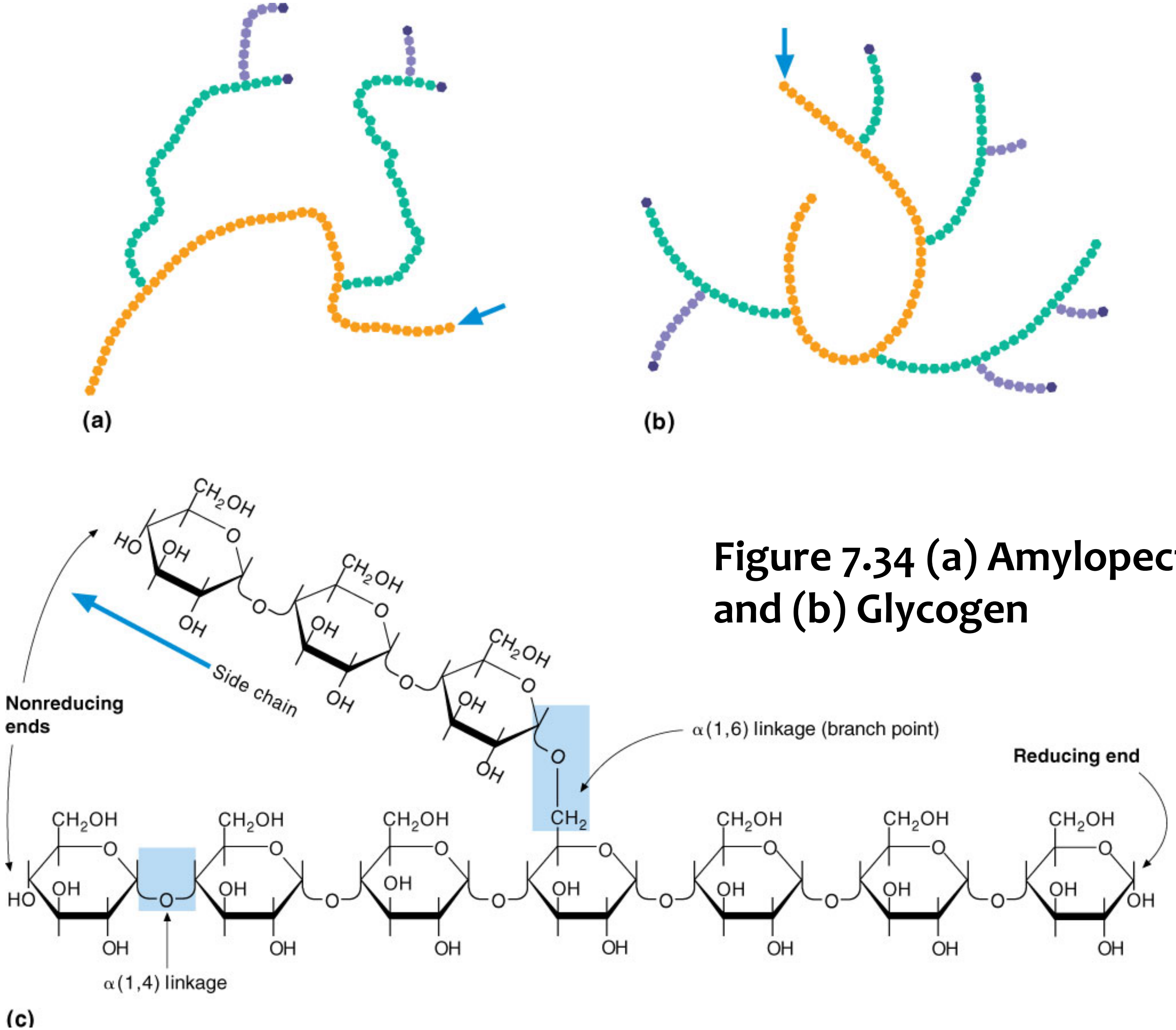
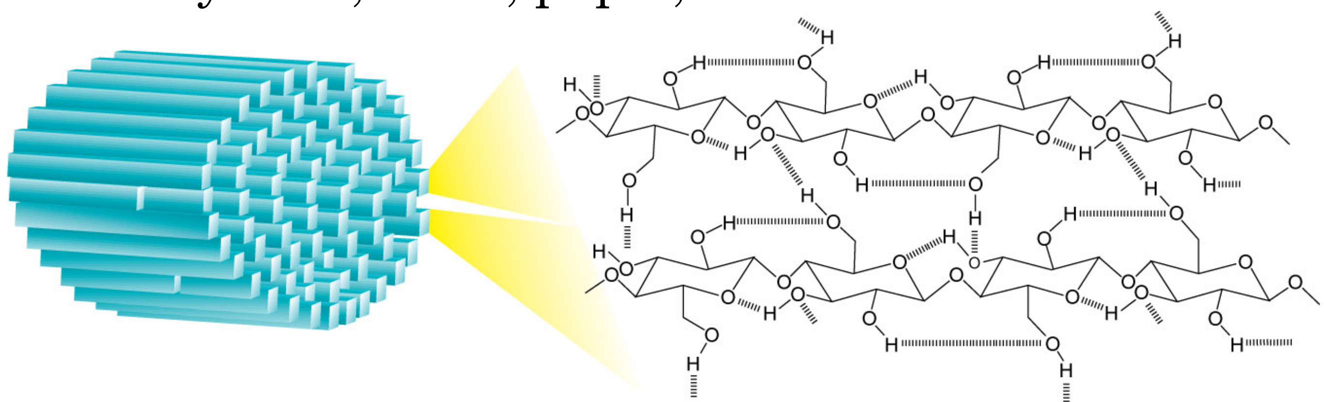


Figure 7.34 (a) Amylopectin and (b) Glycogen

- **Cellulose** - D-glucopyranosides linked by β(1,4) glycosidic bonds
  - Most important structural polysaccharide of plants (most abundant organic substance on earth)
  - Pairs of unbranched cellulose molecules (12,000 glucose units each) are held together by hydrogen bonding to form sheetlike strips, or **microfibrils**
    - Each microfibril bundle is tough and inflexible with a tensile strength comparable to that of steel wire
    - Important for dietary fiber, wood, paper, and textiles

Cellulose Microfibrils



- **Heteroglycans** – high molecular weight; consisting of more than 1 type of monosaccharide; linkages to proteins
  - N-linked (**N-glycans**) are linked via a β-glycosidic bond
  - O-linked (O-glycans) have a disaccharide core of galactosyl-β-(1,3)-N-acetylgalactosamine linked via an α-glycosidic bond to the hydroxyl of serine or threonine residues
  - Glycosaminoglycans (GAGs) – linear polymers with repeating disaccharide units
    - Five classes: hyaluronic acid, chondroitin sulfate, dermatan sulfate, heparin & heparin sulfate, keratin

- **Glycoconjugates** –carbohydrates linked to proteins and lipids
- **Proteoglycans**
  - Distinguished by their high carbohydrate content (about 95%)
  - Occur on cell surfaces or are secreted to the extracellular matrix

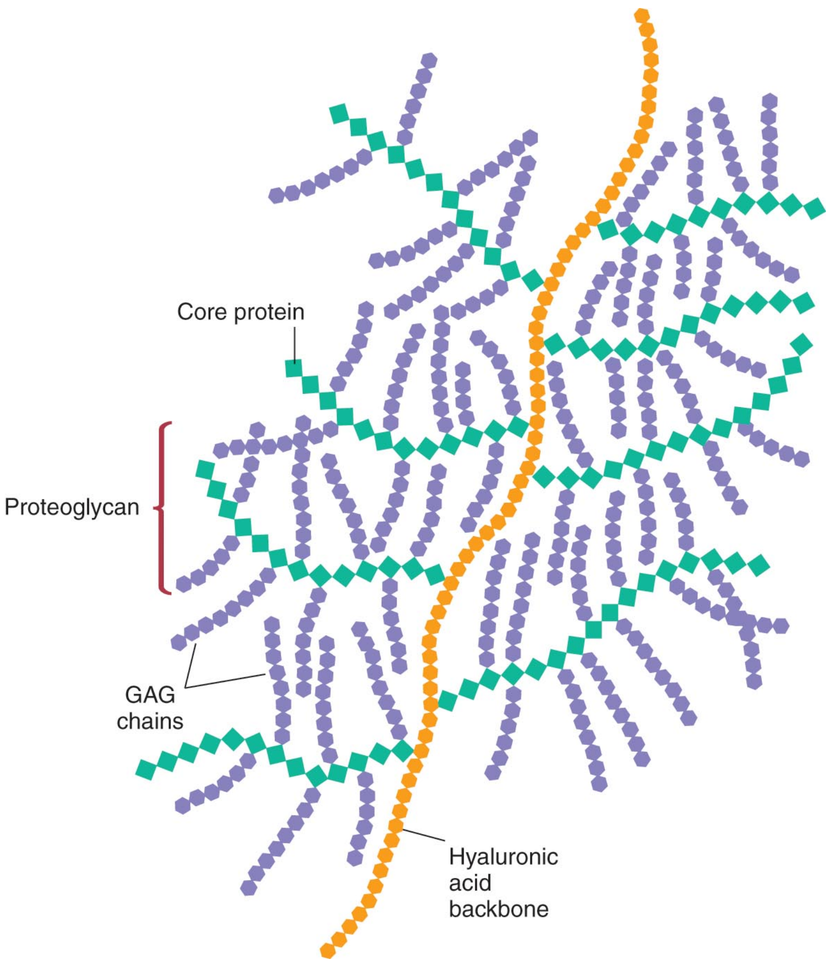


Figure 7.37 Proteoglycan Aggregate

- **Proteoglycans**
  - All contain GAG chains that are linked to core proteins by N- and O-glycosidic bonds
    - Aggrecan is an example of a type of proteoglycan that is found in abundance in cartilage
      - A core protein linked to over 100 chondroitin sulfate and 40 keratin sulfate chains
      - Up to 100 aggrecans are in turn attached to hyaluronic acid to form a proteoglycan aggregate
  - Roles in organizing extracellular matrix and are involved in signal transduction
  - Metabolism involved in many genetic disorders
    - Hurler's syndrome – enzyme deficiency

- **Glycoproteins**
  - Defined as proteins covalently linked to carbohydrates through N- and O-linkages
    - Several addition reactions in the lumen of the endoplasmic reticulum and Golgi complex are responsible for final N- linked oligosaccharide structure
    - O-glycan synthesis occurs later, probably initiating in the Golgi complex
  - Carbohydrate could be 1%–85% of total weight
    - ✓ Usually linked to serine, threonine or asparagine
- **Glycoprotein Functions**
  - Metal-transport proteins transferrin & ceruloplasmin
  - Blood-clotting factors
  - Proteins involved in cell destruction during immune reactions
  - Hormones - signaling

Section 7.5: The Sugar Code

- Living organisms require large coding capacities for information transfer
  - Profound complexity of functioning systems
  - To succeed as a coding mechanism, a class of molecules must have a large capacity for variation
  - Glycosylation is the most important posttranslational modification in terms of coding capacity
  - More possibilities with hexasaccharides than hexapeptides
  - In addition to their immense combinatorial possibilities; relatively inflexible, perfect for precise ligand binding
- **Lectins**
  - **Lectins**, or carbohydrate-binding proteins, are involved in translating the sugar code
  - Bind specifically to carbohydrates via hydrogen bonding, van der Waals forces, and hydrophobic interactions

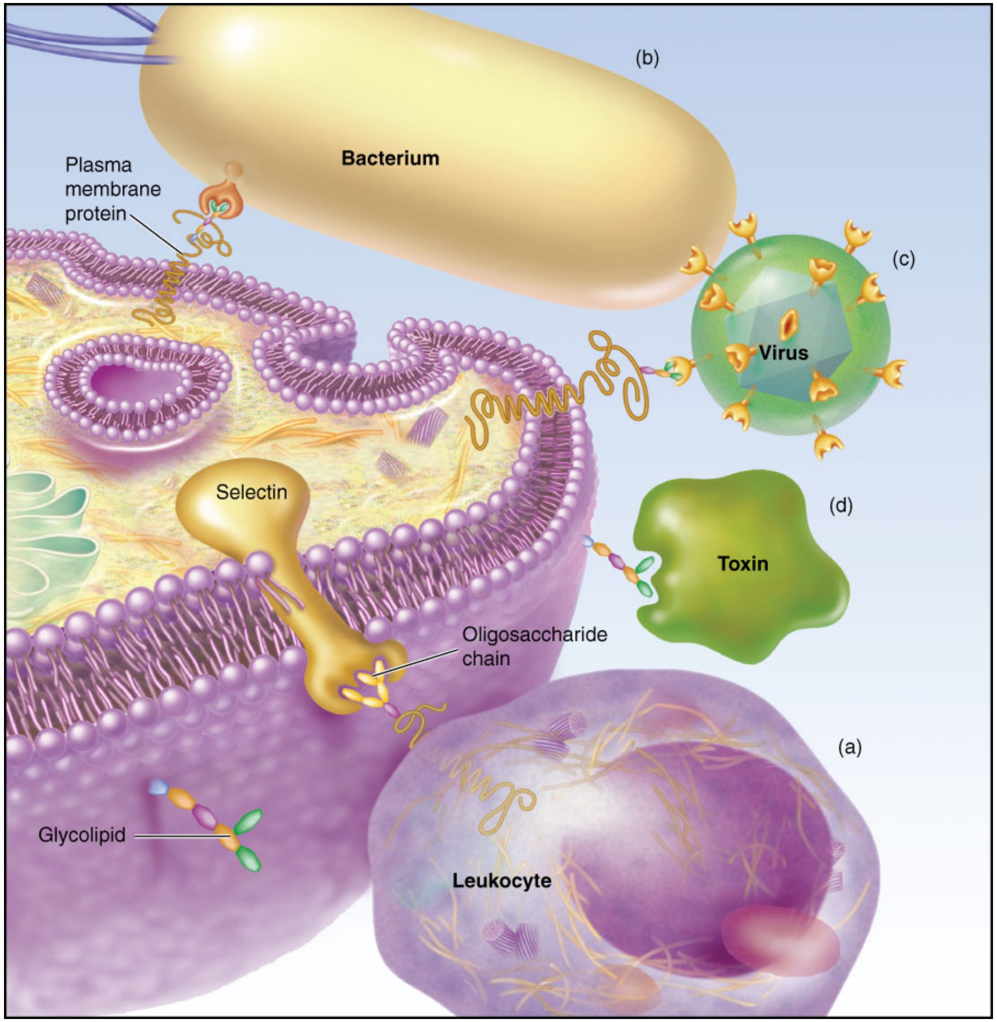


Figure 7.39 Role of Oligosaccharides in Biological Recognition

- **Lectins Continued**
  - Biological processes include binding to microorganisms, binding to toxins, and involved in leukocyte rolling

- **The Glycome**
  - Total set of sugars and glycans in a cell or organism
  - Constantly in flux depending on the cell's response to environment
  - There is no template for glycan biosynthesis; it is done in a stepwise process
  - **Glycoforms** can result based upon slight variations in glycan composition of each glycoprotein