

CHEM 153A Week 5

Aidan Jan

February 4, 2025

Carbohydrates

- **Carbohydrates** = aldehydes or ketones with at least two hydroxyl groups, or substances that yield such compounds on hydrolysis
- many carbohydrates have the empirical formula $(\text{CH}_2\text{O})_n$
- **monosaccharides** = simple sugars, consisting of a single polyhydroxy aldehyde or ketone unit
 - Example: D-glucose
- **disaccharides** = oligosaccharides with two monosaccharide units
 - Example: sucrose (D-glucose and D-fructose)
- **Oligosaccharides** = short chains of monosaccharide units, or residues, joined by glycosidic bonds
- **Polysaccharides** = sugar polymers with 10+ monosaccharide units
 - Examples: cellulose (linear), glycogen (branched)

Functions of Carbohydrates

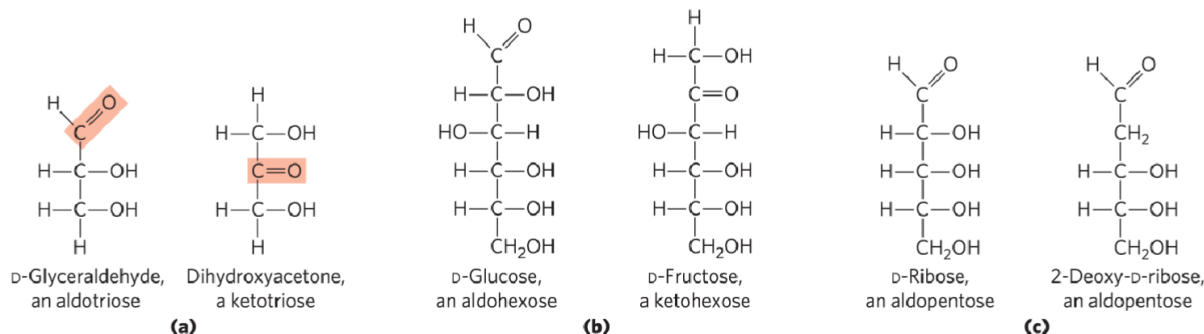
- Energy sources (e.g., large polymers for energy storage)
- Protein targeting
- Cell identification/recognition (e.g., determination of blood type)
- Protection/structure (e.g., cell walls and insect shells)
- Components of other biomolecules (e.g., antibiotics, enzyme cofactors, nucleic acids, etc.)
- Other (e.g., lubrication in joints)

From previous courses:

- What a carbohydrate is
- Different kinds of sugars (mono-, di-, poly-)
- Basic structures of a few monosaccharides
- Basic nomenclature
 - Aldoses vs. Ketoses (functional group)
 - C_3 = triose
 - C_4 = tetraose
 - C_5 = pentose
 - C_6 = hexose

Aldoses and Ketoses

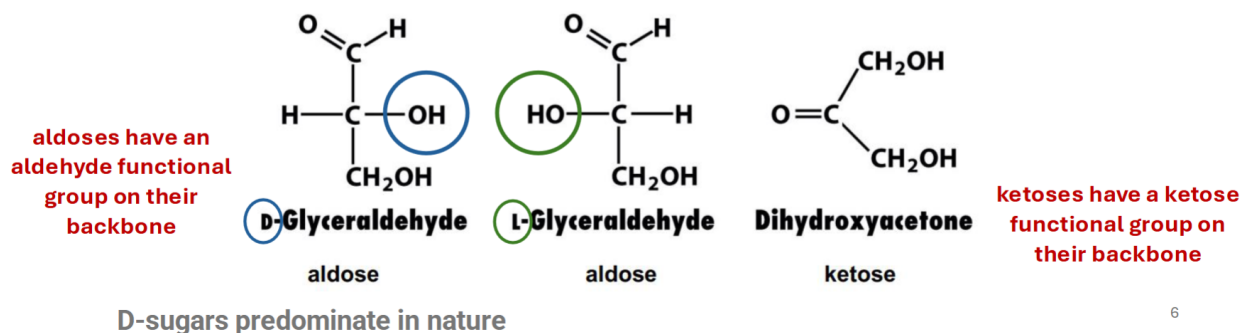
- **aldose** = carbonyl group is at an end of the carbon chain (in an aldehyde group)
- **ketose** = carbonyl group is at any other position (in a ketone group)



Nelson & Cox, *Lehninger Principles of Biochemistry*, 8e, © 2021 W. H. Freeman and Company

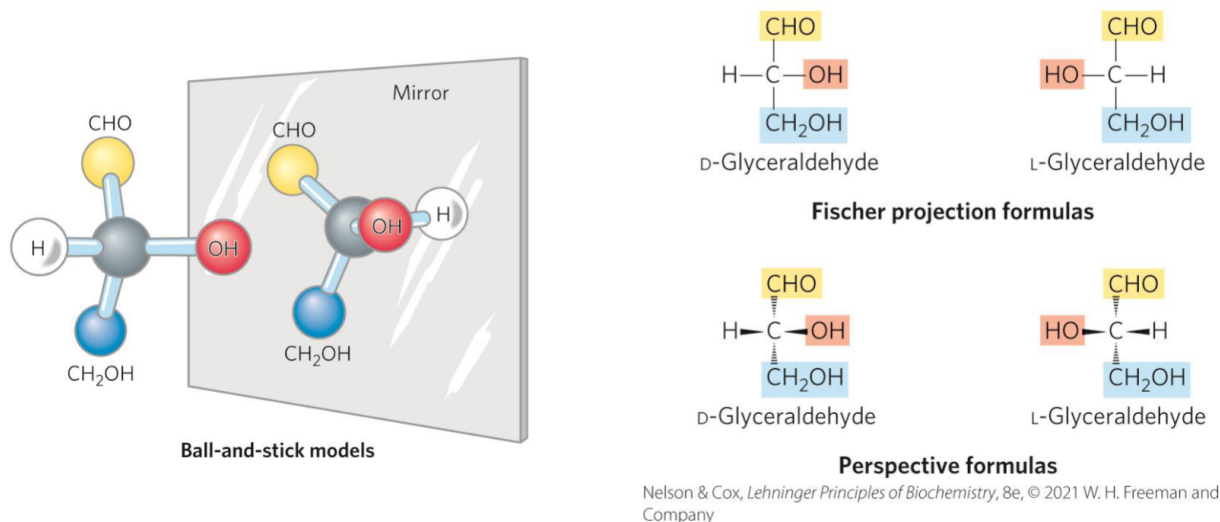
Basic Trioses - D and L

- The below structures are all **trioses** (three carbon sugars) - basically the simplest sugars possible
- For n stereocenters, there are 2 possible stereoisomers (making 2^n stereoisomers total)
- Glyceraldehyde has 1 stereocenter, hence 2 stereoisomers, notated as D and L
 - If the OH on the last chiral carbon points to the right, the sugar is D
 - If the OH on the last chiral carbon points to the left, the sugar is L



6

Enantiomers of Glyceraldehyde



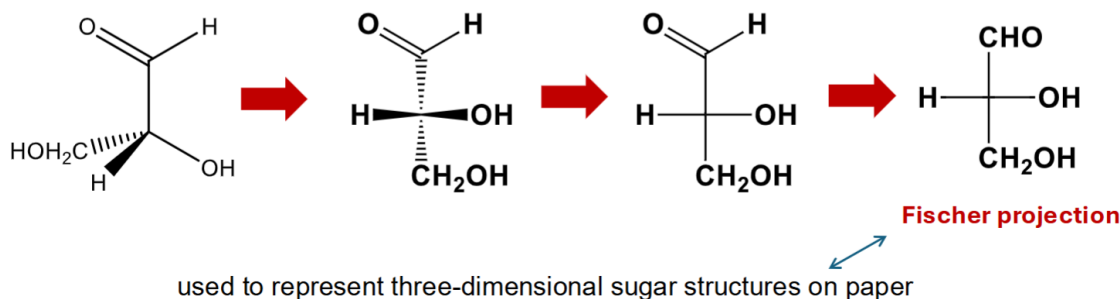
D Isomers and L Isomers

- **reference carbon** = chiral center *most distant* from the carbonyl carbon
- two groups of stereoisomers:
 - D isomers = configuration at reference carbon is the same as D-glyceraldehyde
 - * on the right (dextro) in a projection formula
 - * most hexoses of living organisms
 - L isomers = configuration at reference carbon is the same as L-glyceraldehyde
 - * on the left (levo) in a projection formula

Fischer Projection Review

- **Fischer projections are the preferred representation of linear carbohydrates**
- Vertical lines represent dashes angled away from you
- Horizontal lines represent wedges angled towards you
- Fischer projections of longer sugars are set up in such a way as to easily transition to cyclic molecules

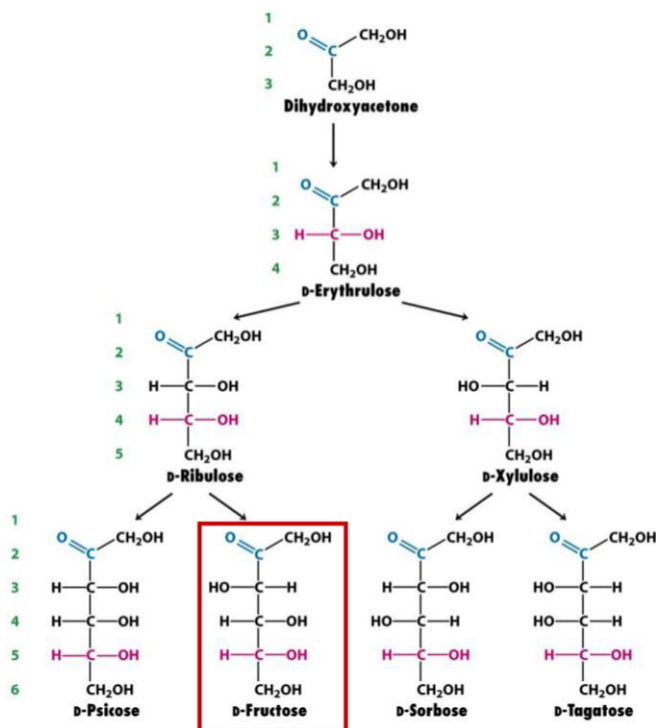
D-(+)-glyceraldehyde



Ketose Family

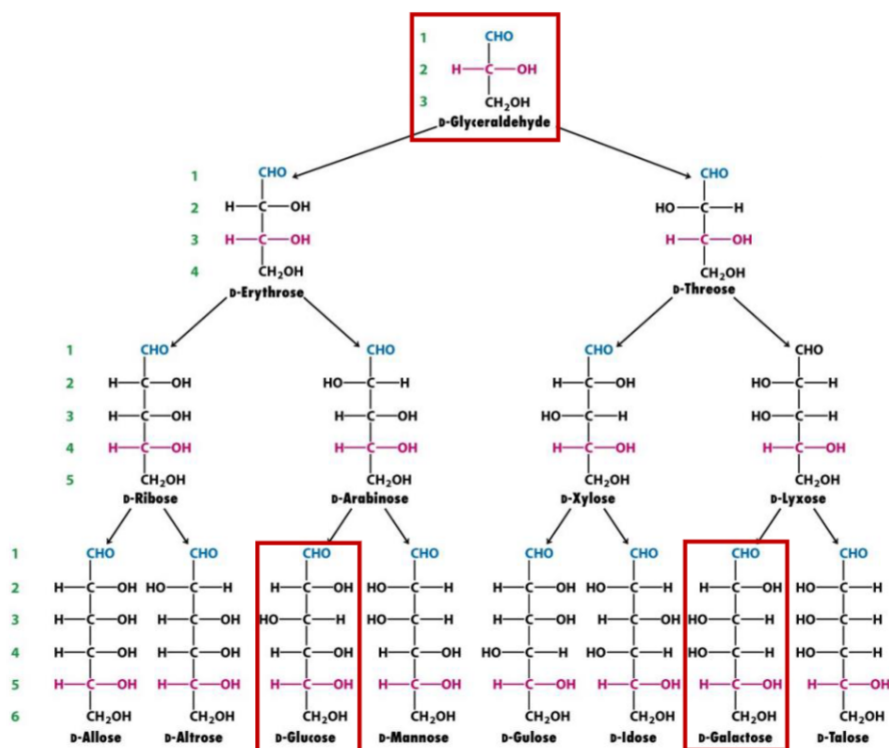
The carbons of a sugar are numbered beginning at the end of the chain nearest the carbonyl group

- C₃ = triose
- C₄ = tetraose
- C₅ = pentose
- C₆ = hexose



3 stereocenters, so 2^3 stereoisomers, but we're excluding L sugars so $8/2 = 4$.

Aldose Family

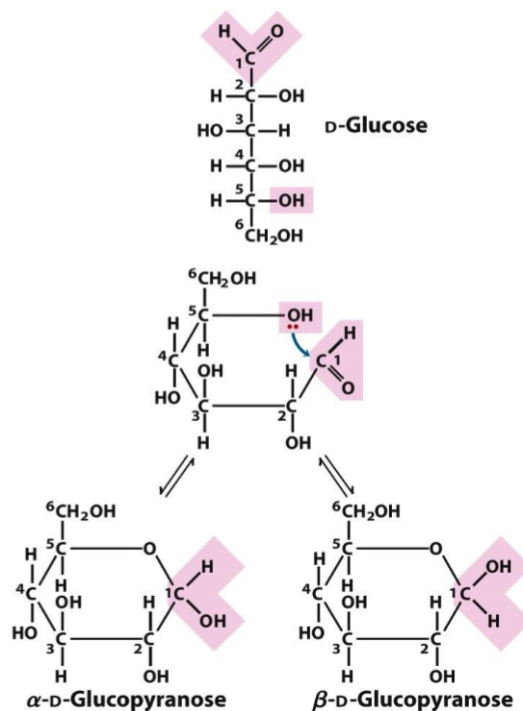


The Common Monosaccharides Have Cyclic Structures

- in aqueous solution, aldotetroses and all monosaccharides with 5+ backbone carbon atoms occur as cyclic structures
 - covalent bond between the carbonyl group and the oxygen of a hydroxyl group → cyclic hemiacetal
- Linear sugars cyclize via intramolecular hemiacetal formation
- Favored ring sizes: 5- and 6-membered rings (furanoses and pyranoses)

Formation of the Two Cyclic Forms of D-Glucose

- Reaction between the aldehyde group at C-1 and the hydroxyl group at C-5 forms a **hemiacetal linkage**
- **mutarotation** = the interconversion of α and β anomers



Mutarotation is the interconversion of α and β anomers

Cyclization of Monomeric Sugars

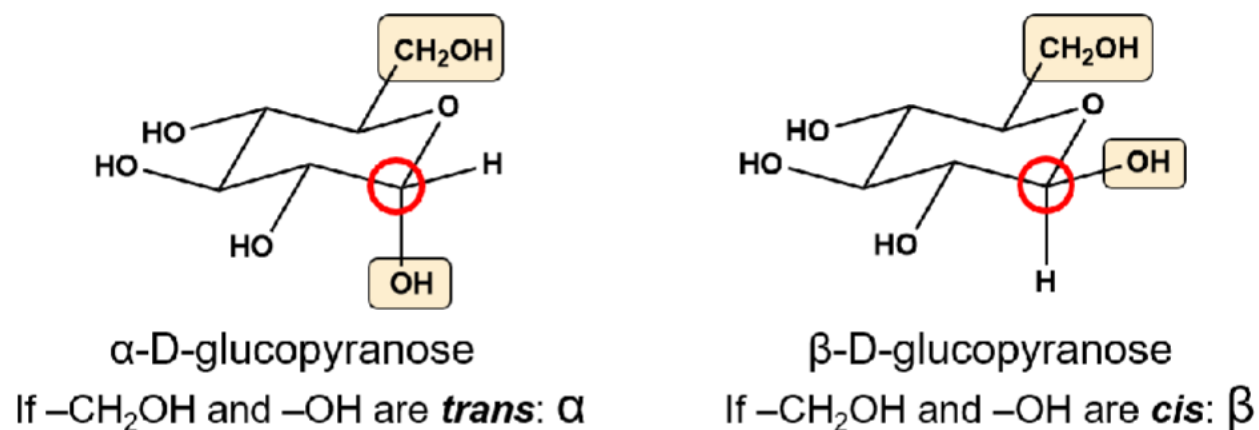
- Previous linear molecule had four stereocenters
 - **Cyclization generates a new stereocenter at C_1**
- Two possibilities can form, α and β anomers
 - Notation denotes whether -OH is on the same side of ring as C_6
 - * α is opposite side
 - * β is same side
- For D-sugars, C_6 is above the ring so always the same behavior
 - α , -OH is down (trans)
 - β , -OH is up (cis)
- Cyclization is a **reversible** process
 - This means anomers can interchange
 - * This is called **mutarotation**
 - **C_1 is now the anomeric carbon**

Mutarotation

- In aqueous solution, cyclic sugars like glucose exist in equilibrium with their open-chain form.
- When a sugar molecule opens up, **the hemiacetal bond at the anomeric carbon is broken**, forming the linear aldehyde (or ketone) form.
- This open-chain form can then reclose to form either the α - or β -anomer.

- The direction from which the hydroxyl group attacks the carbonyl carbon determines whether the -OH at the anomeric carbon ends up in the axial (α) or equatorial (β) position. Under acidic or basic conditions, this equilibrium is established more rapidly, but it occurs spontaneously even in pure water. Thus, mutarotation is the chemical process by which the configuration at the anomeric center interconverts, switching the α - and β -anomeric forms.

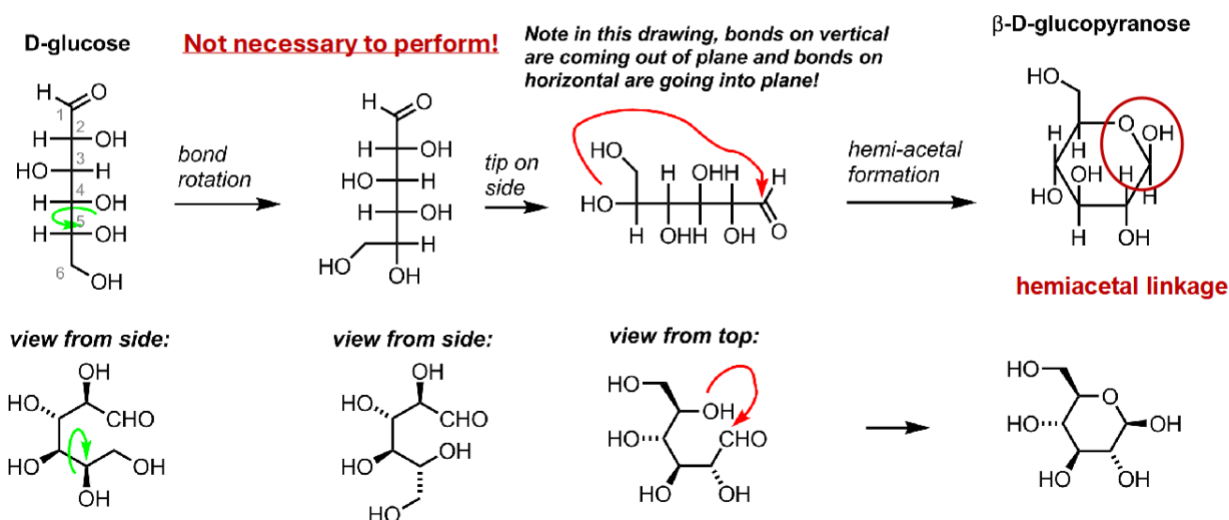
Cyclization of monomeric sugars produces either of two stereoisomeric configurations: α and β



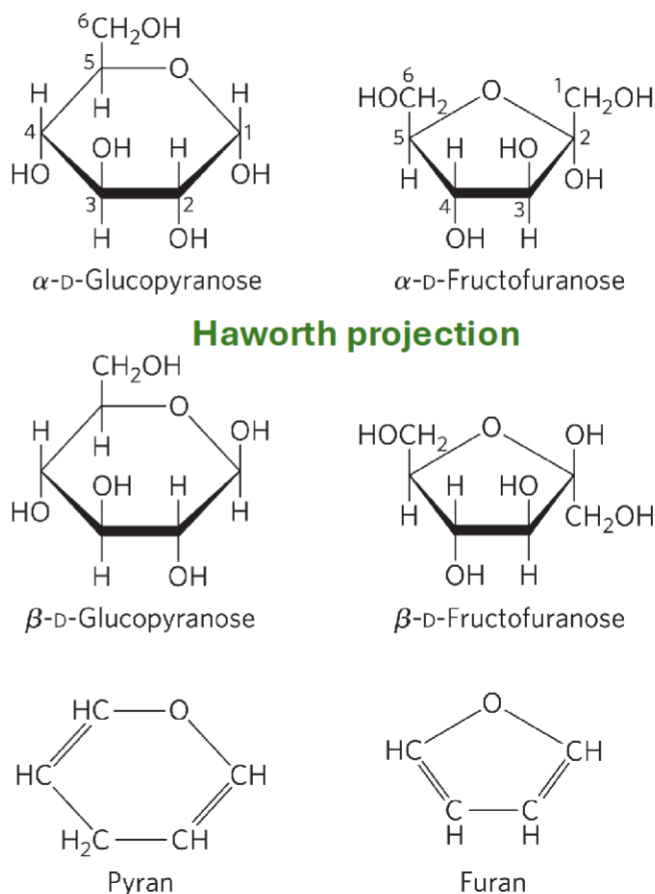
The anomeric carbon serves as the **connection** to other monosaccharides

The **anomeric carbon** is highly reactive because it retains some of the original reactivity of the carbonyl group from the linear form. This makes it ideal for forming **glycosidic bonds**, which are the covalent linkages between sugars or between a sugar and another molecule (such as a protein or lipid)

Cyclization of Linear Monosaccharides Mechanism



Pyranoses and Furanoses



- Six-membered ring compounds are called **pyranoses** because they resemble the six-membered ring compound pyran. The systematic names for the two ring forms of D-glucose are therefore α -D-glucopyranose and β -D-glucopyranose
- Ketohexoses (such as fructose) also occur as cyclic compounds with α and β anomeric forms. In these compounds, the hydroxyl group at C-5 (or C-6) reacts with the keto group at C-2 to form a **furanose** (or pyranose) ring containing a hemiketal linkage.
- D-Fructose readily forms the furanose ring the more common anomer of this sugar in combined forms or in derivatives is β -D-fructofuranose

Furanoses can exist in equilibrium with pyranoses

[FILL 19]

Hemoglobin Glycation

(so named to distinguish it from glycosylation, the enzymatic transfer of glucose to a protein)

- A person's glycated hemoglobin fraction (HbA1c) reflects the average concentration of glucose in the blood (AG) over the past 2-3 months and is the gold standard measure for establishing risk for diabetes-related complications in patients with type 1 or type 2 diabetes

[FILL 20] [FILL 21, edited, combined]

Glycosidic Bond Formation

- **Glycosidic bonds** are covalent bonds that form between the hemiacetal group of a carbohydrate and a hydroxyl group on another compound (for us, other carbohydrates)
- This is how disaccharides, oligosaccharides, and polysaccharides form
 - Glycosidic bonds are notated with: The carbon they come from, the carbon they're going to, and the α/β arrangement (determined by the anomeric carbon)

[FILL 22]

Nomenclature for Glycosidic Bonds

- Anomeric Configuration:
 - α : In a Haworth projection of a D-pyranose, the -OH on the anomeric carbon is positioned on the side opposite the CH_2OH group (typically shown "down" or in an axial orientation)
 - β : The -OH on the anomeric carbon is on the same side as the CH_2OH group (typically shown "up" or in an equatorial orientation)
- Linkage Positions:
 - The notation (e.g., 1 \rightarrow 4) indicates that the bond forms between the anomeric carbon (C1) of one sugar and a specific carbon (e.g., C4) on the adjacent sugar
 - Other common linkages include:
 - * 1 \rightarrow 6: For example, in glycogen, the main chain is formed by α (1 \rightarrow 4) linkages with branch points at α (1 \rightarrow 6) bonds
 - * 1 \rightarrow 2: In sucrose, the glycosidic bond links the anomeric carbon of glucose to the anomeric carbon of fructose (commonly described as α -D-glucopyranosyl-(1 \rightarrow 2)- β -D-fructofuranoside)
- Examples:
 - Amylose (starch): Composed of α (1 \rightarrow 4) glycosidic bonds
 - Cellulose: Consists of β (1 \rightarrow 4) glycosidic bonds
 - Glycogen: Features α (1 \rightarrow 4) bonds in its main chain with α (1 \rightarrow 6) bonds at branch points
 - Sucrose: Has an α (1 \rightarrow 2) glycosidic bond linking the two monosaccharides

[FILL 24]

Note that the glycosidic bond can be alpha or beta, and that the second carbohydrate can be linked at any of the carbon atoms that contain an -OH. The glycosidic bond is named as alpha or beta, followed by numbers that correspond to the locations of the carbons involved in the glycosidic bond.

Polysaccharides

Monomeric subunits, monosaccharides, serve as the building blocks of large carbohydrate polymers. The specific sugar, the way the units are linked, and whether the polymer is branched determine its properties and thus its function

- Most carbohydrates in nature occur as polysaccharides ($M_r > 20000$)
- also called **glycans**

[FILL 24]

Homopolysaccharides and Heteropolysaccharides

- **Homopolysaccharides** = contain only a single monomeric sugar species
 - Serve as storage forms and structural elements
- **Heteropolysaccharides** = contain 2+ kinds of monomers
 - provide extracellular support

[FILL 26]

Polysaccharides Generally Do Not Have Defined Lengths or Molecular Weights

- This distinction between proteins and polysaccharides is a consequence of the mechanisms of assembly
- There is no template for polysaccharide synthesis
- The program for polysaccharide synthesis is intrinsic to the enzymes that catalyze the polymerization of monomer units

The sequences of complex polysaccharides are determined by the intrinsic properties of the biosynthetic enzymes that add each monomeric unit to the growing polymer.

Some Homopolysaccharides are storage forms of fuel

- storage polysaccharides = starch in plant cells and glycogen in animal cells
- **starch and glycogen molecules are heavily hydrated because they have many exposed hydroxyl groups available to hydrogen bond**

Starch (Amylose)

- **Amylose (starch)** is a polysaccharide of α -D-glucose that's used for **energy storage in plants**
- Standard 1,4 linkage, no branches
- Human enzymes can break down α linkages and utilize for energy

[FILL 28]

Starch (amylose) isn't a straight chain!

- On average, 8 glucose residues per turn.

[FILL 29]

Glycogen

- **Glycogen** is a polysaccharide of α -D-glucose that's used for **energy storage in animals**
- Main linkage is 1,4 but after 8-10 residues there's a 1,6 linkage as well
- Multiple branches reduce time it takes for breakdown and utilization
- Human enzymes can more easily break down α linkages

[FILL 30] [FILL 31]

Glycogen isn't a straight chain either!

[FILL 32]

Some Homopolysaccharides Serve Structural Roles

Cellulose = tough, fibrous, water-insoluble substance

- linear, unbranched homopolysaccharide, consisting of 10000 to 15000 D-glucose units
- glucose residues have the β configuration
- linked by ($\beta 1 \rightarrow 4$) glycosidic bonds
- animals do not have the enzyme to hydrolyze ($\beta 1 \rightarrow 4$) glycosidic bonds

[FILL 33-L]

Chitin = linear homopolysaccharide composed of *n*-acetylglucosamine residues in ($\beta 1 \rightarrow 4$) linkage

- Acetylated amino group makes chitin more hydrophobic and water-resistant than cellulose

[FILL 33-R]

Cellulose

- **Cellulose** is a polysaccharide of β -D-glucose that's used **for structure in plants**
- Human enzymes can't break down β linkages! No way to use for energy
- **Cellulose has an alternating structure!** (every other glucose is inverted)
- Cellulose chains can form strong intrachain and interchain hydrogen bonds: High tensile strength

[FILL 34] [FILL 35]

Chitin

- **Chitin** is a polysaccharide of N-acetyl-D-glucosamine connected through a $\beta(1 \rightarrow 4)$ linkage
- Structure of chitin differs from cellulose because of acetamide groups
- Also has alternating structure and strong interchain/intrachain hydrogen bonding

[FILL 36]

It is a **structural polysaccharide** found in the exoskeletons of **insects, crustaceans** (like crabs and shrimp), and the **cell walls of fungi**. Chitin is the second most abundant polysaccharide in nature after cellulose.

[FILL 37]

Lipids and Membranes

[FILL 1]

Lipids

- **Lipids** are a class of organic compounds that are **insoluble in water**, and soluble in organic solvents
 - Note that this is a definition based around solubility, not so much structure
- Energy storage: Longer term in comparison with carbohydrates (hydrocarbon tails store lots of energy)
- Structural components: Cell membranes! (e.g., phospholipid bilayer)
- Signaling molecules: Both intracellular and intercellular (e.g., testosterone)

Lipidomics Seeks to Catalog All Lipids and their Functions

LIPID MAPS Lipidomics Gateway = database analogous to the Protein Data Bank

- has its own classification system of eight chemical categories

[FILL 4]

Lipids Overview

[FILL 5]

Fatty Acids

- **Fatty acids** are carboxylic acids with aliphatic chains (hydrocarbon chains) ranging from 4 to 36 carbons long (C4 to C36)
- In some fatty acids, this chain is unbranched and fully saturated (contains no double bonds)
- In others, the chain contains one or more double bonds. A few contain three-carbon rings, hydroxyl groups, or methyl-group branches
- A **polyunsaturated** fatty acid contains **more than one double bond** in its backbone
- Naturally occurring components of triacylglycerols and phospholipids

[FILL 6]

Cis and Trans Configuration

[FILL 7]

Unsaturated fats have one or more **double bonds** between carbon atoms. These double bonds can exist in two configurations:

- **Cis configuration:** The hydrogen atoms attached to the carbon atoms of the double bond are on the **same side** of the molecule. This creates a kink in the fatty acid chain, making it more difficult for the fats to pack together tightly. Cis fats are generally liquid at room temperature (e.g., oils)
- **Trans configuration:** The hydrogen atoms are on **opposite sides** of the double bond, resulting in a straighter chain, similar to saturated fats. This straight structure allows trans fats to pack together tightly, making them more solid at room temperature

Common Patterns in Fatty Acids

Several naming schemes exist for fatty acids:

- most common fatty acids have even numbers of carbon atoms in an unbranched chain of 12 to 24 carbons: **the mode of synthesis, which involves successive condensations of two-carbon (acetate) units**
- In **monosaturated** fatty acids, the double bond is usually between **C-9 and C-10** (Δ^9)
- in **polyunsaturated** fatty acids:
 - the double bonds are usually Δ^{12} **and** Δ^{15}
 - double bonds are usually separated by a methylene group
- double bonds are usually in the cis configuration

Nomenclature for Unbranched Fatty Acids

- the chain length and number of double bonds, separated by a colon
- numbering begins at the carboxyl carbon
- positions of double bonds are indicated by Δ and a superscript number

[FILL 9]

Polyunsaturated Fatty Acids (PUFAs)

- **polyunsaturated fatty acids (PUFAs)** = contain more than one double bond in their backbone
 - **omega-3** ($\omega - 3$) **fatty acids** = double bond between C-3 and C-4 relative to the most distant carbon (ω)
 - **omega-6** ($\omega - 6$) **fatty acids** = double bond between C-6 and C-7 relative to ω

[FILL 10]

PUFAs and Human Nutrition

- humans must obtain the **omega-3** PUFA α -linolenic acid (ALA; 18:3($\Delta^{9,12,15}$)) **from their diet**
- humans use ALA to synthesize:
 - eicosapentaenoic acid (EPA; 20:5($\Delta^{5,8,11,14,17}$))
 - docosahexaenoic acid (DHA; 22:6($\Delta^{4,7,10,13,16,19}$))
- the optimal dietary ratio of omega-6 and omega-3 PUFAs is between 1:1 and 4:1

EPA and **DHA** are essential omega-3 fatty acids that play critical roles in **reducing inflammation**, supporting **cardiovascular health**, **brain function**, **eye health**, and **immune regulation**. DHA is particularly important for brain development and structure, while EPA is more involved in reducing inflammation and maintaining heart health.

Naming Fatty Acids

- Several naming schemes exist for fatty acids
 - **Omega Naming:**
 - The of carbons in the fatty acid (e.g., 18)
 - The of double bonds (2 or 3, for our examples)
 - The position of the first double bond from the methyl end (e.g., 6 and 3)
 - * Omega (ω) carbon is the final carbon in the fatty acid chain. We'll count backwards from ω to the first carbon in the double bond.

[FILL 12, edited]

Omega Naming

[FILL 13]

Fatty acid MPs - Length

[FILL 15]

Melting Points of Fatty Acids

At room temperature:

- saturated fatty acids have a waxy consistency
- unsaturated fatty acids are oily liquids
- extent of packing depends on degree of saturation: kinks disrupt packing

Fully saturated fatty acids in the extended form pack into nearly crystalline arrays, stabilized by extensive hydrophobic interaction. The presence of one or more fatty acids with cis double bonds (red) interferes with this tight packing and results in less stable aggregates.

[FILL 17]

Fatty acid MPs - Unsaturation

- Melting points decrease as we increase unsaturation
- Has implications for biological regulation of membranes

[FILL 17]

Triacylglycerols (TAGs)

- **Triacylglycerols** are esters derived from glycerol and three fatty acids
- Constitute $\approx 90\%$ of dietary lipids, and the vast majority of fat in the body
- **Major form of metabolic energy storage in humans:**
 - Glycogen (the storage form of glucose in the body) < 200 **grams** of in most people
 - Human body fat is measured in whole percentages (**kilograms**)

[FILL 20]

Triacylglycerols Provide Stored Energy

- vertebrates store triacylglycerols as lipid droplets in adipocytes (fat cells)
- plants store triacylglycerols in the seeds
- Carbohydrates (like glycogen) are **short-term** storage, TAGs are **long-term** storage.

More on TAGs

- Less oxidized than carbohydrates and amino acids (more reduced \rightarrow better energy storage)
 - CH_4 (most reduced) \rightarrow CO_2 (most oxidized)
- AG Composition:
 - Simple TAGs: All three fatty acids are identical
 - Mixed TAGs: Contain different fatty acids

[FILL 21]

In biochemistry, a molecule that is more reduced carries a greater number of electrons that can be transferred to another acceptor (for instance, in an oxidation reaction). When such a molecule is oxidized, those electrons are released, allowing the cell to harness energy (e.g., through cellular respiration). Therefore, a more reduced molecule has a higher potential to yield energy upon oxidation.

TAG Catabolism

- TAGs are broken down during **lipolysis**, generating glycerol and three fatty acids
- The resulting fatty acids are then fed into **beta oxidation** (catabolic cycle that oxidizes the fatty acid - reducing $\text{NAD}^+/\text{FAD}^-$ and generates acetyl-CoA)
 - During beta-oxidation, fatty acids are sequentially broken down through a series of reactions. **These reactions shorten the fatty acid chain by two carbons each cycle.**
 - Fatty acids go through cycles until they are spent (**i.e., the longer the fatty acid, the more energy it can produce: more carbons = more oxidation cycles → More ATP**)

Lipids vs. Polysaccharides

[FILL 23]

- **Lipids** are ideal for **long-term energy storage** in a compact, water-free form, but they are slower to access and require oxygen to be metabolized.
- **Polysaccharides** are better for **short-term, quick energy** due to their rapid mobilization, ability to function anaerobically, and role in immediate energy needs, despite their lower storage efficiency.
- **Polysaccharides** are stored as large polymers to avoid increasing osmotic pressure; however, when broken down into glucose units, they can increase osmotic pressure, especially if rapidly mobilized.
- **Lipids** do not affect osmotic pressure due to their hydrophobicity and storage in non-aqueous environments, making them ideal for high-capacity energy storage without impacting cellular water balance.

Eicosanoids - Local Hormones

- **Eicosanoids** are a family of biologically active molecules derived from arachidonic acid (specifically an arachidonate phospholipid)
- Considered "local" hormones - all autocrine and paracrine signaling:
 - **Paracrine Signaling:** Hormone acts on **neighboring cells** (prostaglandins released in response to tissue damage act on nearby cells to mediate inflammation)
 - **Autocrine Signaling:** Hormones act on the **same cell** that produced them (certain **growth factors** can act on the cells that secrete them to regulate cell growth or survival)

[FILL 24, edited]

Sterols - Global Hormones

- **Sterols** are a subset of steroids that play several roles in eukaryotes
 - Components of membranes
 - Signaling compounds
- "Global" hormones, also known as **endocrine hormones:** signaling molecules that are released into the **bloodstream** and travel throughout the body to exert their effects on **distant target organs** or tissues
- Bind to nuclear receptors

[FILL 25]

A diet rich in certain types of fatty acids, particularly saturated fats and trans fats, can contribute to cardiovascular problems and lead to vein or artery clogging due to several factors, including:

Build-Up of Plaque in Arteries (Atherosclerosis):

- **Saturated fats** (commonly found in animal products like butter, cheese, and fatty meats) and **trans fats** (found in processed and fried foods) can raise levels of **low-density lipoprotein (LDL)** cholesterol in the blood
- High levels of **LDL cholesterol** can lead to the formation of **plaque** (a mixture of cholesterol, fats, calcium, and other substances) on the walls of arteries
- This plaque build-up narrows the arteries and **restricts blood flow**, which is called **atherosclerosis**. Over time, this can cause the arteries to harden and lose flexibility, making it difficult for blood to flow through smoothly.