Chapter 11 Lecture Notes: Carbohydrates

Educational Goals

1. Given a *Fischer projection* of a monosaccharide, classify it as either **aldoses** or **ketoses**.

2. Given a *Fischer projection* of a monosaccharide, classify it by the number of carbons it contains.

3. Given a *Fischer projection* of a monosaccharide, identify it as a **D-sugar** or **L-sugar**.

4. Given a *Fischer projection* of a monosaccharide, identify **chiral carbons** and determine the *number of stereoisomers* that are possible.

5. Identify *four* common types of **monosaccharide derivatives**.

6. Predict the products when a monosaccharide reacts with **a reducing agent** or with *Benedict's reagent*.

7. Define the term **anomer** and explain the difference between α and β *anomers*.

8. Understand and describe **mutarotation**.

9. Given its *Haworth projection*, identify a monosaccharide either a **pyranose** or a **furanose**.

10. Identify the **anomeric carbon** in *Haworth structures.*

11. Compare and contrast **monosaccharides**, **disaccharides**, **oligosaccharides**, and **polysaccharides.**

12. Given the structure of an oligosaccharide or polysaccharide, identify the **glycosidic bond**(s) and characterize the glycosidic linkage by the bonding pattern [for example: β(1⟶4)].

13. Given the *Haworth structures* of two monosaccharides, be able to draw the **disaccharide** that is formed when they are connected by a **glycosidic bond**.

14. Understand the difference between **homopolysaccharides** and **heteropolysaccharides**.

15. Compare and contrast the *two components* of **starch**.

16. Compare and contrast **amylopectin** and **glycogen**.

17. Identify **acetal** and **hemiacetal** bonding patterns in carbohydrates.

An Introduction to Carbohydrates

Carbohydrates are quite abundant in nature. More than *half of the carbon* found in living organisms is contained in carbohydrate molecules, most of which are contained in plants.

The primary reason for such an abundance is that a carbohydrate is produced by a series of chemical reactions that we call *photosynthesis*.

Energy from sunlight is used by plants to provide energy to drive the photosynthesis process. In the photosynthesis process, carbon dioxide and water are converted to oxygen gas and a *carbohydrate* called *glucose*.

Plants can use *glucose* to produce the ATP molecules that are needed to do the work necessary for life.

Plants store excess glucose as *starch*, for later use.

Animals obtain energy that is stored in *starch* by eating plants, or by eating animals that ate plants or had herbivores in their food-chain.

Carbohydrates are also referred to as _____ or _____.

Monosaccharides

_____ are the smallest carbohydrates and serve as the building blocks of larger carbohydrates.

- They are also referred to as _____ *sugars*.

Monosaccharides have the general chemical formula of $C_n(H_2O)_n$; where **n** (the number of carbon atoms) can be *three* to *seven*.

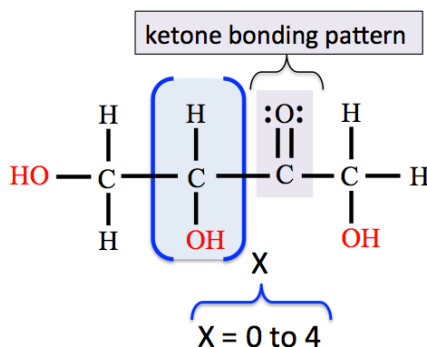They are *polyhydroxyl* **aldehydes** or **ketones**:

- Monosaccharides contain either an _____ group *or* a _____ bonding pattern.

- Monosaccharides contain *more than one* _____ (OH) *group*.

A monosaccharide that contains an *aldehyde group* is called an _____.

A monosaccharide that contains the *ketone bonding pattern* is called a _____.
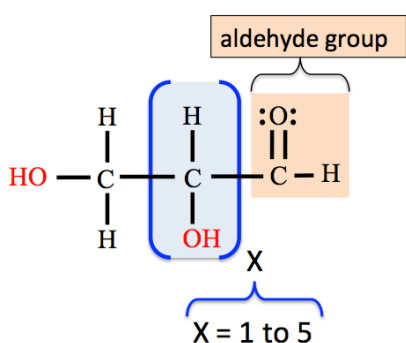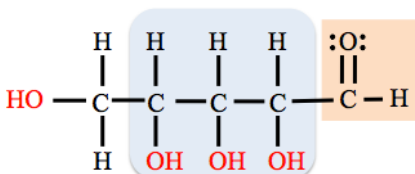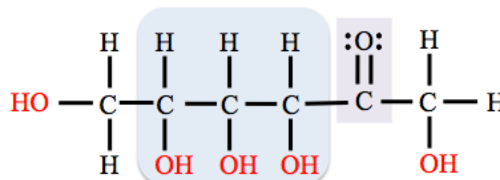

general form of an aldose

general form of a ketose

Note that the group in the parenthesis can repeat.
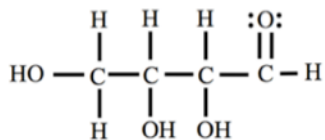

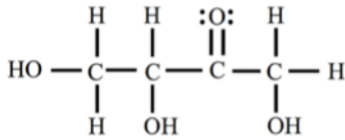an aldose structure where X = 3

a ketose structure where X = 3

Understanding Check:

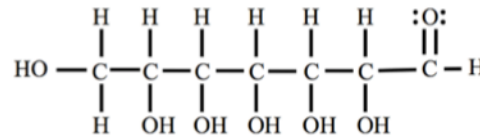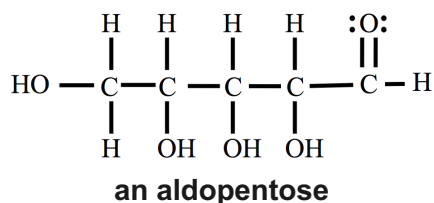Classify each of the following monosaccharides as either an *aldose* or a *ketose*

a.

b.

c.

2

Monosaccharides can be classified according to the **number of** _____they contain.

Number of Carbons	Classification
3	triose
4	tetrose
5	pentose
6	hexose
7	heptose

A monosaccharide may also be classified by _____ the number of carbons _____ whether it is an **aldose** or a **ketose**.
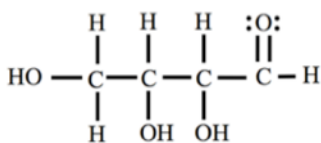
- This is done by using the prefix "_____" for aldoses, or "_____" for ketoses, in front of "triose," "tetrose," "pentose," "hexose," or "heptose."

  - For example, an **aldose** that contains **five** carbons is an **aldopentose**.

$$HO-\underset{\underset{H}{|}}{\overset{\overset{H}{|}}{C}}-\underset{\underset{OH}{|}}{\overset{\overset{H}{|}}{C}}-\underset{\underset{OH}{|}}{\overset{\overset{H}{|}}{C}}-\underset{\underset{OH}{|}}{\overset{\overset{H}{|}}{C}}-\overset{\overset{:O:}{||}}{C}-H$$
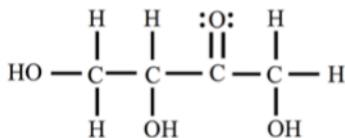
an aldopentose

Understanding Check:

Classify each of the following monosaccharides using the prefix "aldo" for aldoses, or "keto" for ketose, in front of " triose," "tetrose," "pentose," "hexose," or "heptose."

a.

$$HO-\underset{\underset{H}{|}}{\overset{\overset{H}{|}}{C}}-\underset{\underset{OH}{|}}{\overset{\overset{H}{|}}{C}}-\underset{\underset{OH}{|}}{\overset{\overset{H}{|}}{C}}-\overset{\overset{:O:}{||}}{C}-H$$

b.

$$HO-\underset{\underset{H}{|}}{\overset{\overset{H}{|}}{C}}-\underset{\underset{OH}{|}}{\overset{\overset{H}{|}}{C}}-\overset{\overset{:O:}{||}}{C}-\underset{\underset{OH}{|}}{\overset{\overset{H}{|}}{C}}-H$$

c.

$$HO-\underset{\underset{H}{|}}{\overset{\overset{H}{|}}{C}}-\underset{\underset{OH}{|}}{\overset{\overset{H}{|}}{C}}-\underset{\underset{OH}{|}}{\overset{\overset{H}{|}}{C}}-\underset{\underset{OH}{|}}{\overset{\overset{H}{|}}{C}}-\underset{\underset{OH}{|}}{\overset{\overset{H}{|}}{C}}-\overset{\overset{:O:}{||}}{C}-H$$
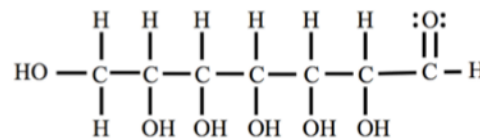

Stereochemistry of Monosaccharides

Except for the *ketotriose*, **monosaccharides** contain ____ _____ *one chiral carbon*.

Recall, that a chiral carbon is a carbon that is surrounded by *four **different** groups*.

Molecules with just **one** chiral carbon have a pair of *geometric isomers* called *enantiomers*.

Enantiomers have the same atomic connections, but a different three-dimensional arrangement of atoms, and are *nonsuperimposable mirror images* of each other.

If a molecule has _____ *than one chiral carbon*, then it will have *more than one* pair of enantiomers.

If a monosaccharide has **n** chiral carbons, then it will have 2^n stereoisomers. For example, if a molecule has *three* chiral carbons, then it will have $2^3 = (2 \times 2 \times 2) =$ **8** stereoisomers (*four* pairs of enantiomers).

Nonsuperimposable Mirror Images: *Enantiomers*
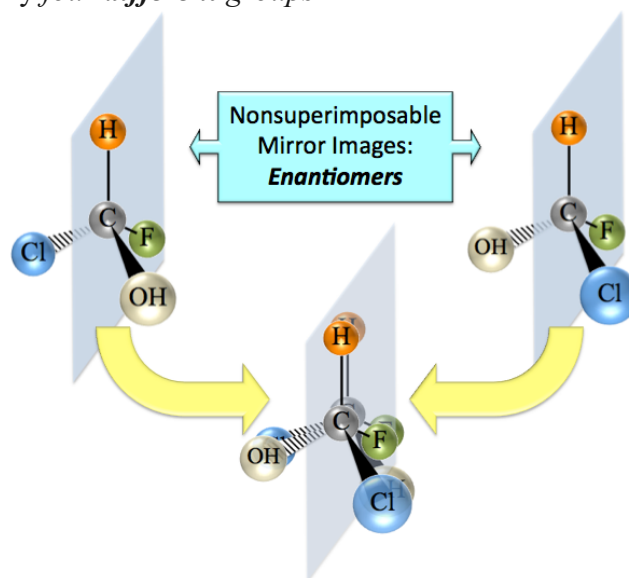
Example: How many stereoisomers are possible for the monosaccharide shown below?
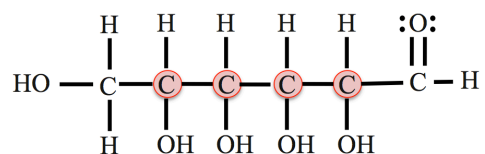
**Solution:** Identify the number of *chiral carbons*, and then calculate the number of stereoisomers.

- There are *four* chiral carbons in this molecule. The chiral carbons are highlighted in the structure below.

Since this monosaccharide structure has *four* chiral carbons, there are $2^4 = (2 \times 2 \times 2 \times 2) = $ **16 possible stereoisomers (*eight pairs of enantiomers*).**

We found that there are **16** different molecules (stereoisomers) that share this molecular formula **and** structural formula.

Most of the physical properties of these **16** stereoisomers are quite similar; however, the way they each behave in _____ *systems* can be very _____.

Let's consider the three dimensional arrangement of the atoms in the smallest monosaccharide, *glyceraldehyde*. Glyceraldehyde has only _____ *chiral carbon*.
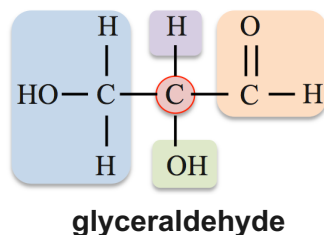
glyceraldehyde

Since there is *one* chiral carbon in glyceraldehyde, then there are $2^n = 2^1 = 2$ stereoisomers (one pair of enantiomers/nonsuperimposable mirror images).

the pair of glyceraldehyde enantiomers
(nonsuperimposable mirror images)
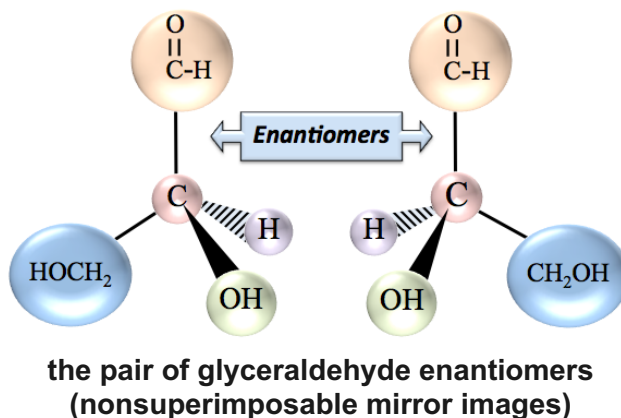
In order for professionals in healthcare, engineering, and science fields to discuss and depict the various monosaccharide stereoisomers, it is necessary to be able to draw two-dimensional (flat) structural formulas on a page or computer display, such that they still contain the ***three-dimensional information*** particular to each stereoisomer.

In previous chapters, we used the **wedge and dash system** to retain the three-dimensional information on a flat surface.

4

For monosaccharides, _____ _____ are used for this purpose.

Fischer Projections

Fisher projections are related to an imaginary "_____" that would be produced if a *chiral carbon* and its four bonded groups were placed in a *particular orientation* between a light source and a surface.

In Fischer projections, *chiral carbons are* _____ *to be at the* _____ *of a vertical and horizontal line*.

Fischer's choice of the particular orientation of the chiral carbon and its four groups was arbitrary, *any* orientation could have been used; *however*, for consistency, one specific orientation needed to be chosen.

The chosen orientation of a chiral carbon and the four groups that are bonded to it *relative to the drawing surface/page in all Fischer Projections* is as follows:

The *bonds* from the *chiral carbon* to the _____ *carbon* atoms *point at a downward angle*, and their shadows form _____ *lines* on the Fischer projection.

- In this model, these are the bonds from the *chiral carbon* to groups **Y** and **W**.

The *bonds* from the *chiral carbon* to *the _____ carbon groups* **point at an upward angle**, and their shadows form _____ *lines* on the Fischer projection.

- In this model, these are the bonds from the *chiral carbon* to groups **X** and **Z**.

For *aldoses*, the *aldehyde group* is positioned at the end of the molecule that is closest to the top of the page (position **W**).

For *ketoses*, the *carbonyl carbon* is positioned as close as possible to the end molecule that is nearest the top of the page.
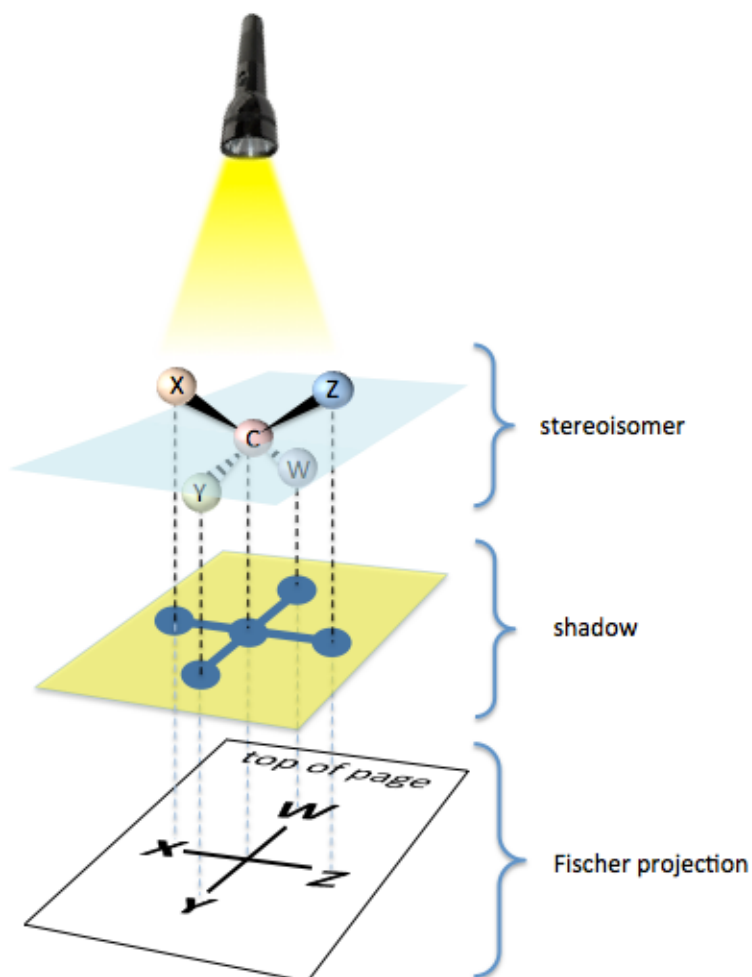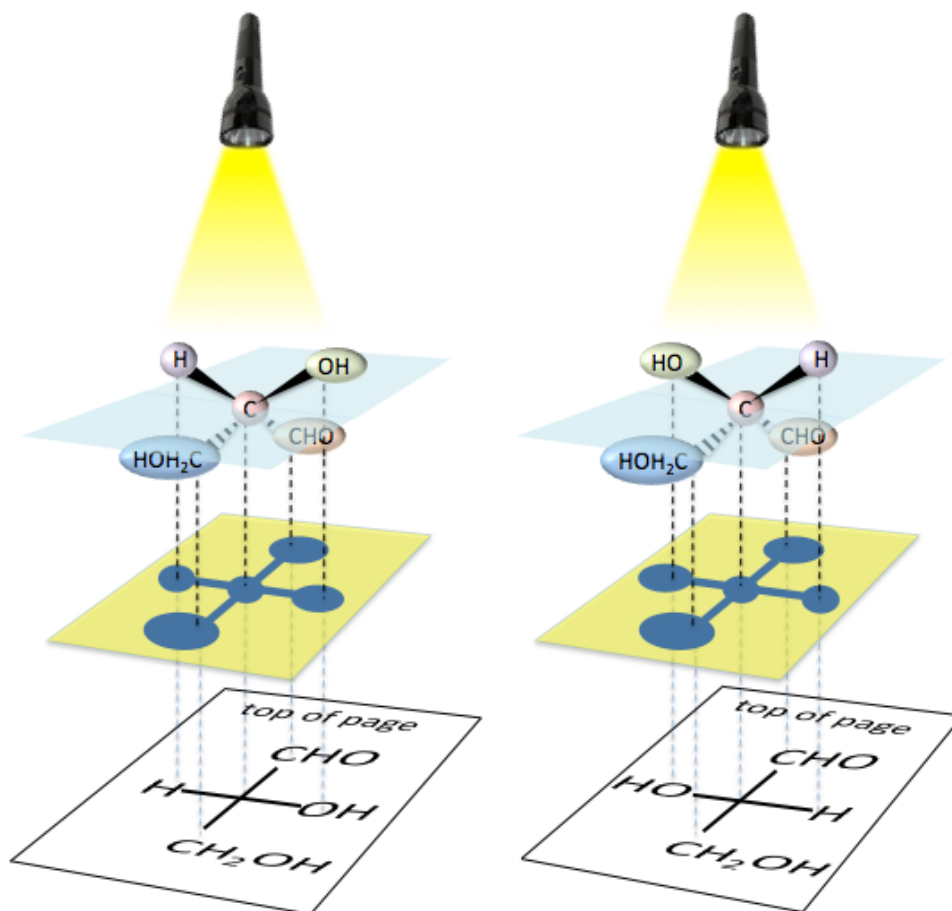
Let's consider the **Fischer projections** for both of the *glyceraldehyde* stereoisomers.

Recall that *glyceraldehyde* has **one chiral carbon**.

Because the **other two carbons** in *glyceraldehyde* are **not chiral**, shorthand notation is used to simplify the structure.

glyceraldehyde

The *aldehyde group* is represented by "**CHO.**"
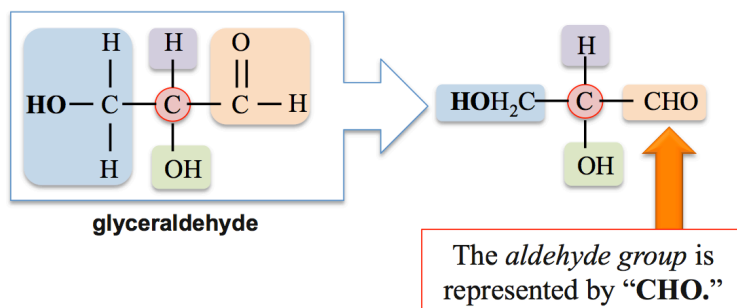
The derivation for the Fischer projections of glyceraldehyde's enantiomers is illustrated below.

The Fischer projections for the two enantiomers of glyceraldehyde are:
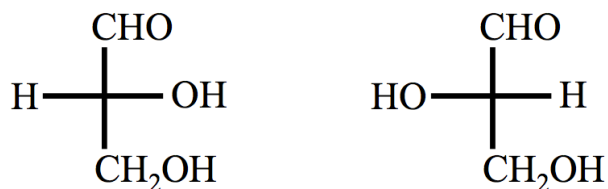
We do not need to draw the bonds around the top or bottom carbon atoms because they are **not chiral**.

Note that we draw the hydroxyl groups that are on the **left-hand side** of Fischer projections as "**HO.**"

For monosaccharides with **more than one** chiral carbon, Fischer projections must be drawn (or interpreted) by considering the orientation around _____ of the **chiral carbons**.

This is done one chiral carbon at a time. As an example, let's consider aldotetroses, which contain **two chiral carbons**:
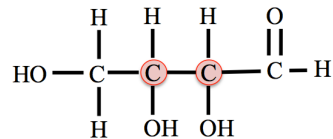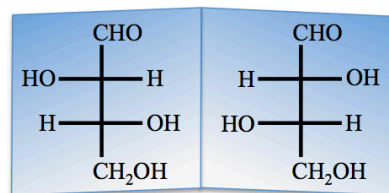

an aldotetrose

Since aldotetroses each have **two** chiral carbons, there are $2^2 = (2 \times 2) = $ **4 stereoisomers** (**two pairs of enantiomers**).
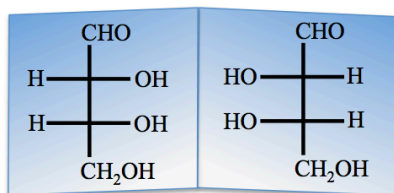
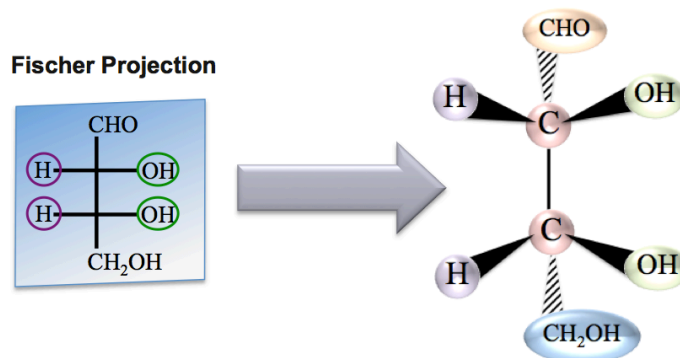**an enantiomer pair**
(mirror images)

an enantiomer pair
(mirror images)

Note that the hydrogen (**H**) and the hydroxyl group (**OH**) positions are reversed on chiral carbons for each particular enantiomer pair.

Implication of a Fischer Projection:

Wedge and Dash Representation

Fischer Projection

Understanding Check: An aldopentose contains **three chiral carbons**, and therefore there are $2^3 = 8$ aldopentose stereoisomers. Draw Fischer projections of the **eight** stereoisomers.
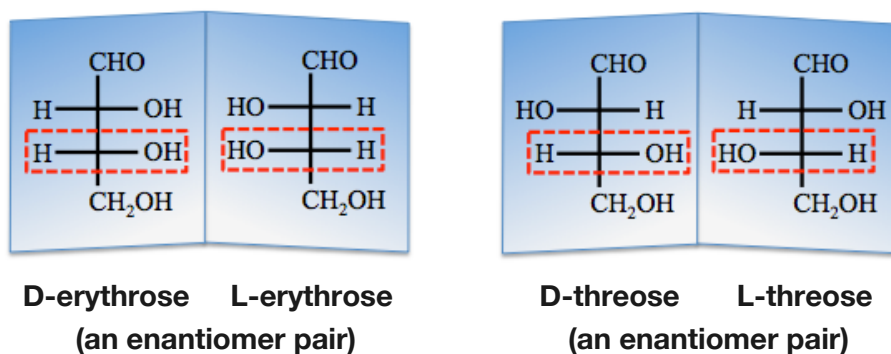
D- and L- Designations for Monosaccharides

Carbohydrates are most often referred to by their *common names*, all of which use the "_____" suffix.

- A *common name* is assigned to each pair of enantiomers.

In order to differentiate the *two* individual monosaccharides of an enantiomer pair, 'D-' or 'L-' designations are used with the common name.

- The 'L-' designation is used for the enantiomer in which **the *chiral carbon* that is furthest from the top of the Fischer projection** has its _____ *group* on the _____.

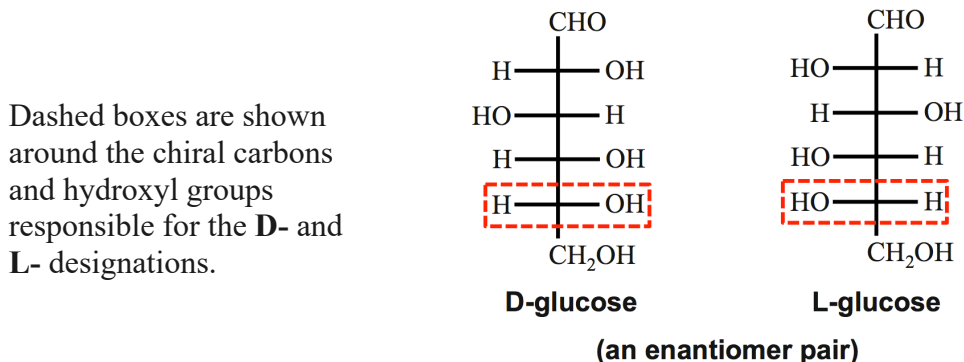- The 'D-' designation is used for the _____ *enantiomer* of the pair.

D-erythrose   L-erythrose   **D-threose   L-threose**
(an enantiomer pair)   **(an enantiomer pair)**

Monosaccharides with the **L-** designation are sometimes referred to as "**L-sugars**," and those with the **D-** designation are sometimes referred to as "**D-sugars**."

Monosaccharides are produced in living organisms by chemical reactions, some of which require enzymes that can only produce _____ particular enantiomer.

For example, the stereoisomer of *glucose* that is made in photosynthesis is **D-glucose**.

Fischer projections for both of the glucose enantiomers are shown below.

Dashed boxes are shown around the chiral carbons and hydroxyl groups responsible for the **D-** and **L-** designations.

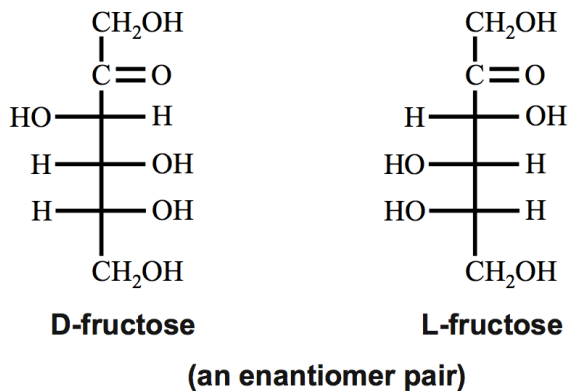**D-glucose**   **L-glucose**

(an enantiomer pair)

The glucose enantiomer pair (D-glucose and L-glucose) are *two* of the *sixteen* aldohexose stereoisomers.

- There are *seven* more aldohexose enantiomer pairs that can be drawn by varying the positions of the **H** and **OH** on each side of a Fischer projection.

- These seven other *enantiomer pairs* are differentiated from glucose, and each other, by their *common names*.
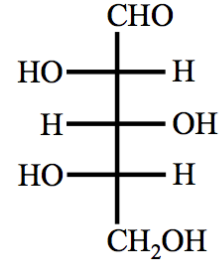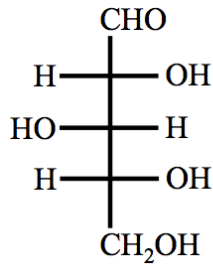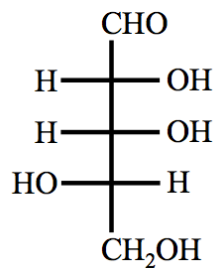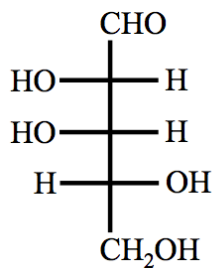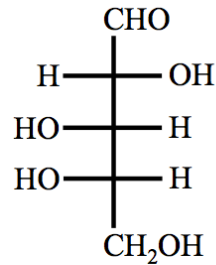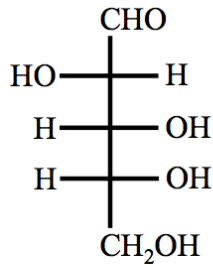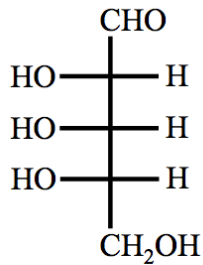
I *do not* require my students to memorize the common names and structures for particular monosaccharides, however, you should check with your own instructor to see if you are required to do so.

An example of a _____ is **fructose**. **D-Fructose** is one of our major dietary carbohydrates.

```
      CH₂OH                CH₂OH
       C=O                  C=O
  HO──┼──H            H──┼──OH
   H──┼──OH          HO──┼──H
   H──┼──OH          HO──┼──H
      CH₂OH                CH₂OH
    D-fructose           L-fructose
```

D-fructose   **L-fructose**

(an enantiomer pair)

Understanding Check

Classify each of the eight stereoisomers shown below as either **D-** or **L-** stereoisomers.

```
     CHO              CHO              CHO              CHO
 H──┼──OH       HO──┼──H        HO──┼──H        H──┼──OH
 H──┼──OH       HO──┼──H         H──┼──OH      HO──┼──H
 H──┼──OH       HO──┼──H         H──┼──OH      HO──┼──H
    CH₂OH           CH₂OH           CH₂OH           CH₂OH


     CHO              CHO              CHO              CHO
HO──┼──H        H──┼──OH        H──┼──OH       HO──┼──H
HO──┼──H        H──┼──OH       HO──┼──H         H──┼──OH
 H──┼──OH      HO──┼──H         H──┼──OH      HO──┼──H
    CH₂OH           CH₂OH           CH₂OH           CH₂OH
```

9
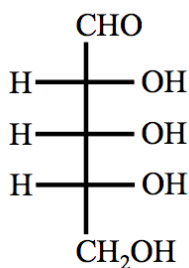
The Cyclic Forms of Monosaccharides

When monosaccharides that contain five to seven carbons are in aqueous solutions, they can undergo a reaction in which they _____ their bonding pattern to form _____ structures.

It is a **reversible** reaction in which the _____ **form** is interconverted with the _____ **form**.

- **Example:** The *cyclization* rearrangement reaction is shown below for a **D-glucose** molecule.


D-glucose
Fischer projection
(open-chain form)

D-glucose
Haworth projection
(cyclic form)
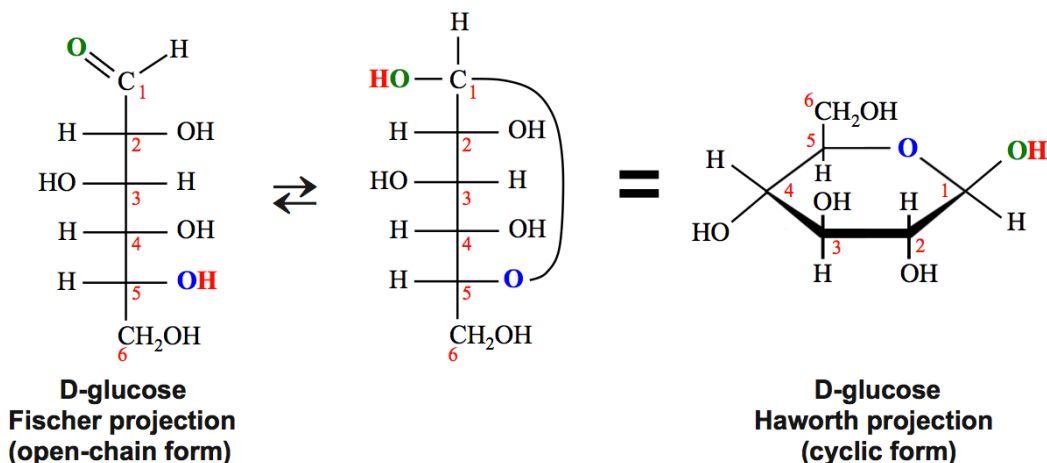
The **cyclic form** is *lower in energy* and is therefore the predominant form.

- In most solutions, the equilibrium ratio of **cyclic form** to **open-chain form** is about *one hundred* to *one*.

The *side view structures* of cyclic monosaccharides (above, right), are called _____ **projections** or **Haworth structures**.

- The carbon atoms that form the ring are not drawn explicitly, but are implied to occur where lines/bonds meet.

To help you understand the *three-dimensional* implications of Haworth projections, I have drawn a ball-and-stick model that shows the actual geometry/bond angles of the cyclic form of D-glucose, next to its Haworth Projection representation:

ball-and-stick model
**(actual molecular geometry)**

Haworth projection
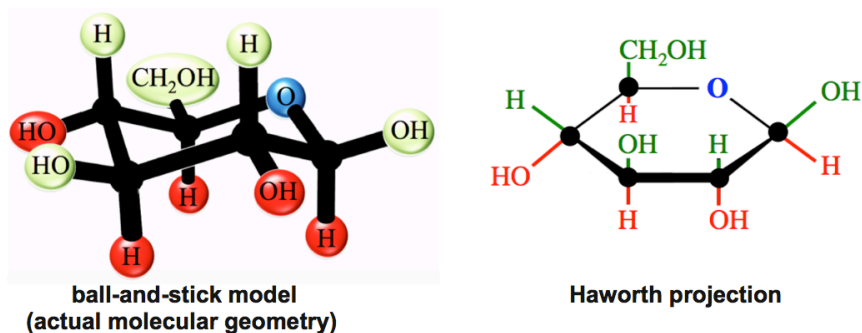
- I used large black dots at the ring-carbon positions in both structures.
- Each ring-carbon is bonded to **two** *other ring-atoms **and** **two** *other groups*.
- Groups that are oriented *upward* relative to the ring-carbons are shaded *green*.
- Groups that are oriented *downward* from ring-carbons are shaded *red*.

The rearrangement/cyclization reaction of a monosaccharide is actually a form of the *hemiacetal formation* reaction that you learned about at the end of the previous chapter.

Let's take a moment to review that reaction.

A *hemiacetal* is a molecule that contains *both* an **OR** group *and* **OH** group that are bonded to the *same* carbon.
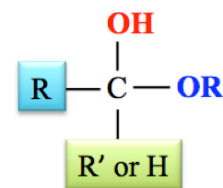
general form of a hemiacetal

An *aldehyde or a ketone* will react with an *alcohol* to form a **hemiacetal**.

The **OR"** from the *alcohol* forms a bond to the *carbonyl-carbon* of the aldehyde or ketone, the **H** from the *alcohol* bonds to the *carbonyl-oxygen*, and the carbonyl group's double bond is changed to a single bond.

aldehyde or ketone   alcohol   hemiacetal
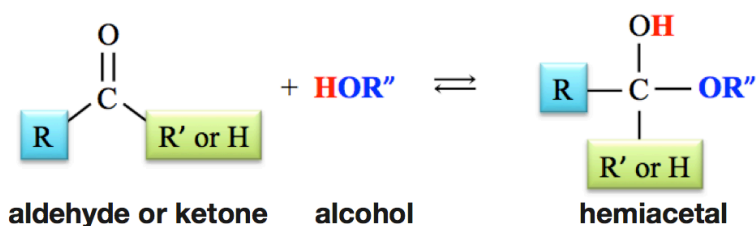
Now let's think about how this reaction can occur **for a monosaccharide.**

A *hemiacetal* is formed when a monosaccharide's *hydroxyl group* reacts with its *carbonyl group*.

D-glucose
(open-chain form, drawn curved)

D-glucose
(cyclic form)
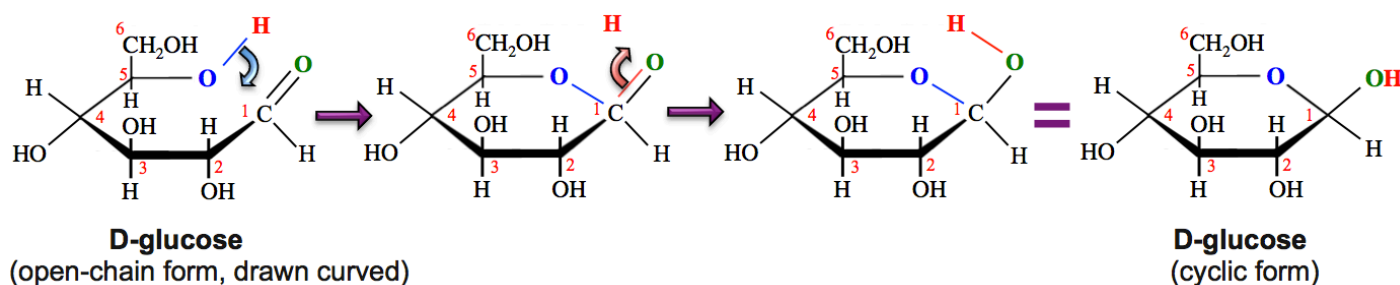
- The *hydroxyl group* is added "across" the carbonyl double bond.

D-glucose
(cyclic form)
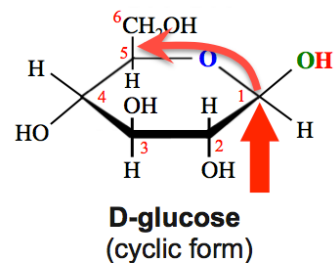
Note that, beginning at carbon number **1** and moving *counter-clockwise*, as indicated by the **red arrow**, the **OR** bonding pattern is seen.

When the **OR** bonding pattern occurs in this way, *forming a ring*, the

molecule is referred to as a _____ *hemiacetal.*
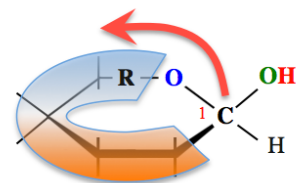
An example of the cyclization of a **ketose** (*fructose*) is shown below.

D-fructose
Fischer projection
(open-chain form)

D-fructose
Haworth projection
(cyclic form)
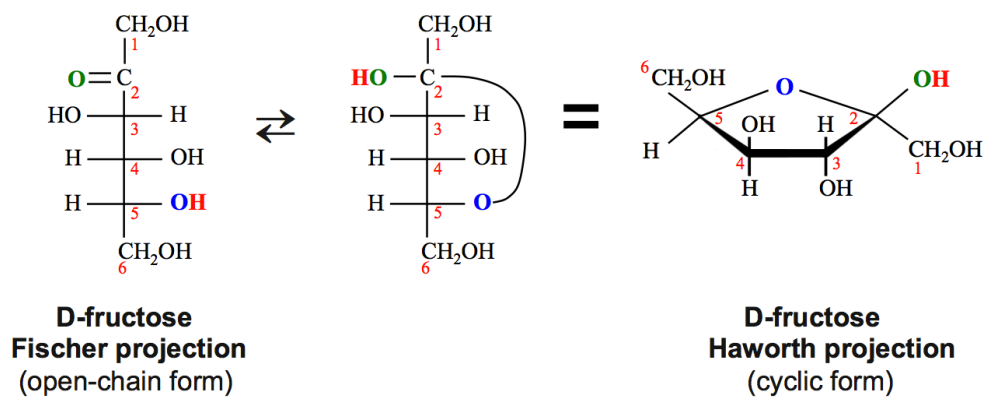
The most common cyclic monosaccharide structures are _____ and _____ member rings.

Cyclic monosaccharides with five-member rings are called _____, and those with six-member rings are called _____.

- These terms are often used as *suffixes* when naming cyclic monosaccharide structures.

  - **Examples:**

A six-member ring

D-glucopyranose
(a pyranose)

A five-member ring

D-fructofuranose
(a furanose)

12
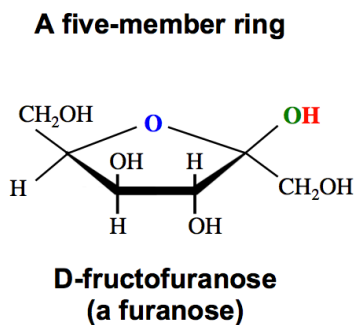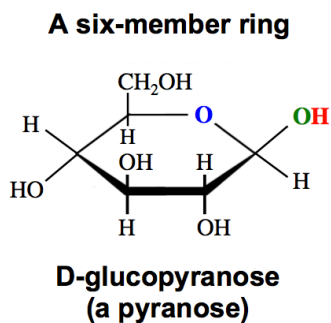
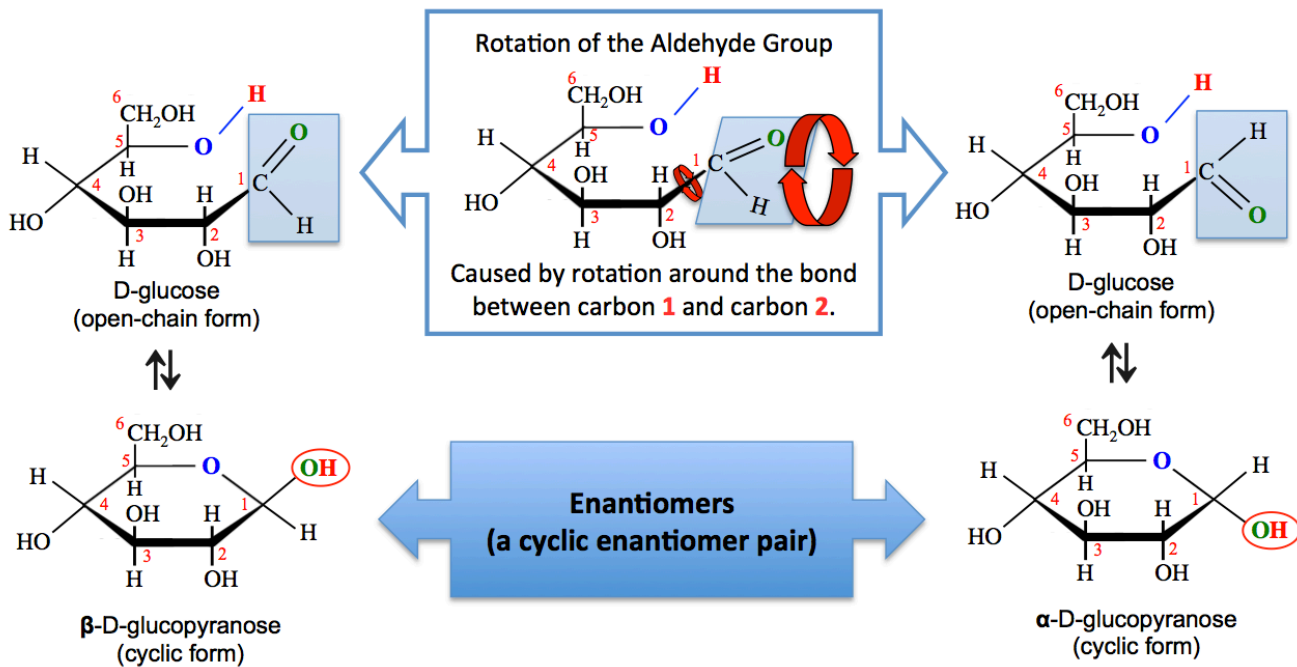The cyclization reaction is reversible; the *cyclic form* interconverts with the *open-chain form* when monosaccharides are in _____.

Each time that the *open-chain form* is converted to the *cyclic form*, one of two cyclic **enantiomers** will be formed.

- **Example:** The *cyclization* of D-glucose.

In the open-chain form of D-glucose that is shown in **top-left** of the illustration above, the carbonyl group (**C=O**) is oriented **upward** from the ring; therefore, when the *cyclic hemiacetal* is formed (**bottom, left**), the *new* hydroxyl group (**OH**) will be oriented **upward** from carbon number **1**. *Free rotation* occurs around single bonds in the open-chain form (as depicted in the box in the **top-middle** of the illustration). Rotation around the bond between carbon number **1** and carbon number **2** of the open-chain form causes the carbonyl group to, at times, be oriented **downward** from the ring (as seen in the open-chain form in the **top-right** of the illustration). In this arrangement, when the cyclization reaction occurs, the cyclic hemiacetal is formed with the *new* hydroxyl group (**OH**) oriented **downward** from carbon number **1** (as seen in the **bottom-right** structure of the illustration).

The formation of either of two different cyclic structures, **a *cyclic enantiomer pair*,** is possible because of the **four different groups** bonded to a ***chiral hemiacetal carbon*** (the carbon which contains an **OH** and an **OR**).

This carbon is called the _____ *carbon*.

The cyclic enantiomers are *almost identical*; the **only** difference is that the bonding pattern around the *anomeric carbons* are mirror images.

13
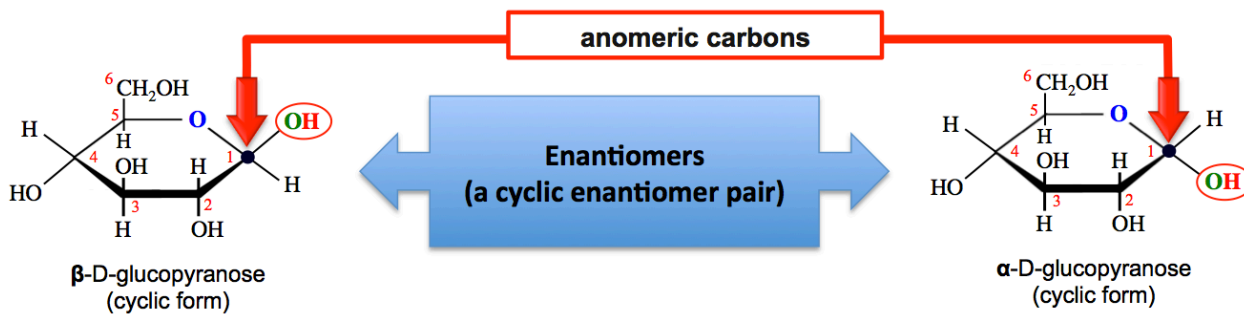
The sugar produced in photosynthesis, and almost all of the other monosaccharides found in plants and animals, are **D-sugars**. At some point in the history of Earth, nature showed a preference for **D-sugars**.
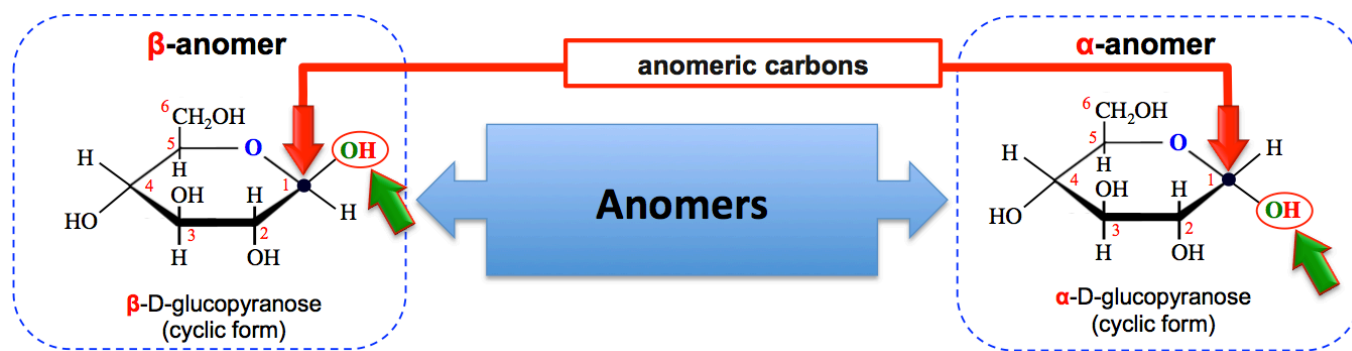
For the *remainder of this course*, you will only see **D-sugars**.

It is easy to identify the *anomeric carbon* in a Haworth projection of a D-sugar; it is the ring-carbon to the _____-*hand side* of the *ring-_____*.

The two enantiomers that can be formed during the cyclization process are called _____.

They are classified, based on the orientation of the _____ *group* (**OH**) on the *anomeric carbon*, as the **α-anomer** or the **β-anomer**.

- The **α-anomer** has the **OH** on the anomeric carbon oriented _____ from the ring.
- The **β-anomer** has the **OH** on the anomeric carbon oriented _____ from the ring.

β-anomer — β-D-glucopyranose (cyclic form) / anomeric carbons / Anomers / α-anomer — α-D-glucopyranose (cyclic form)

The conversion from **α-anomer**, to the ***open-chain form***, then to the **β-anomer** (and vice versa) is called

_____.

The formation of **β-anomers** or **α-anomers** also occurs, for the same reason, for ***ketoses***.

- For example, the cyclization of *D-fructose* results in the formation of two possible **anomers**, as shown below.

anomeric carbons

β-anomer (β-D-fructofuranose)   α-anomer (α-D-fructofuranose)
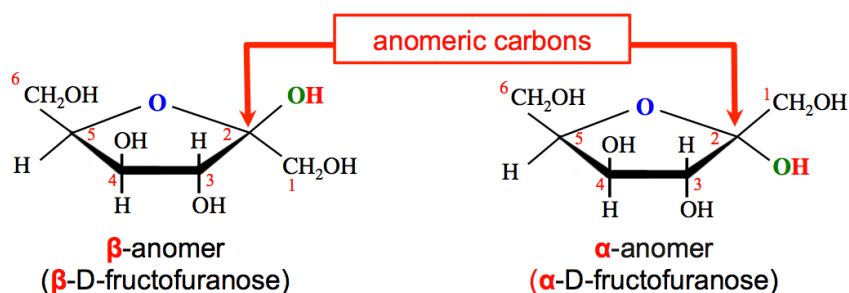
Understanding Check: For the molecules shown below,
   a) Classify each of the molecules as either a **pyranose** *or* a **furanose**.
   b) Label the **anomeric carbon**.
   c) Classify each as either a **β-anomer** *or* an **α-anomer**.

14
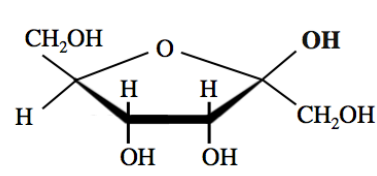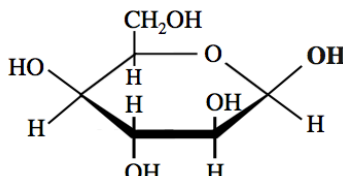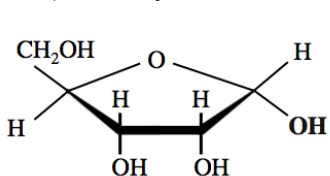
I would like you to be able to do the following on an examination:

Given a **Haworth projection** of a **D-**monosaccharide:

1. Identify the molecule as a **pyranose** or a **furanose**.
2. Identify the **anomeric** carbon.
3. Identify the molecule as the **β-anomer** or the **α-anomer**.
4. Understand the definition of **mutarotation**.
5. Understand how the three-dimensional arrangement of atoms in a monosaccharide (as seen in a ball-and-stick model) is implied by a **Haworth projection**.

Summary of Monosaccharides Stereochemistry
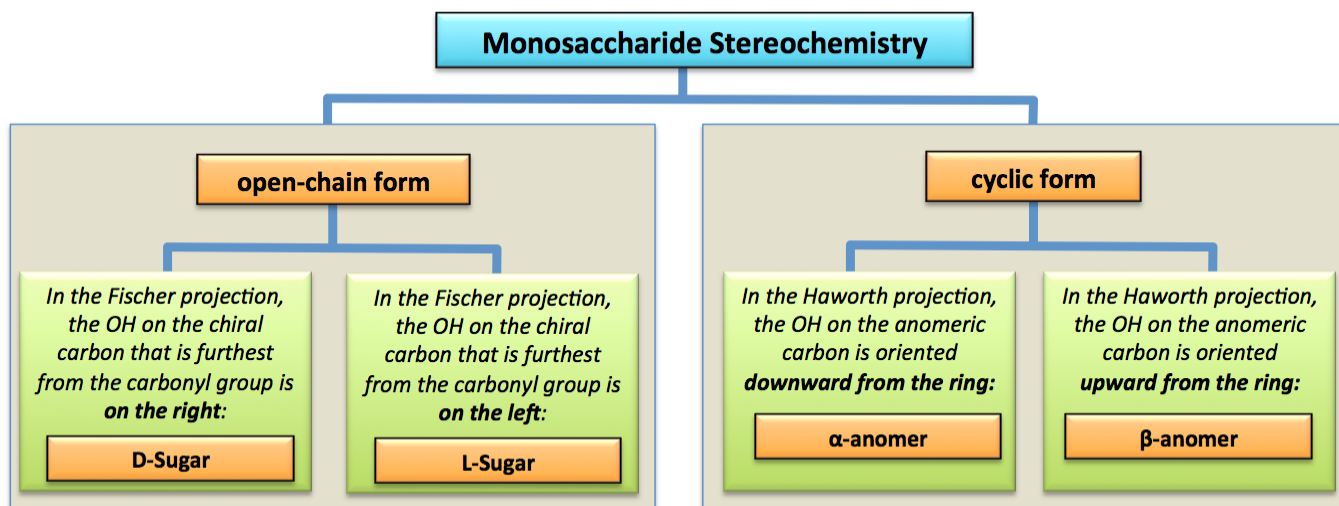
Monosaccharide Derivatives and Reactions

Monosaccharide derivatives are compounds that are _____ from monosaccharides.

I will introduce you to *four* classes of monosaccharide derivatives:

1) **Amino Sugars**
2) **Carboxylic Acid Sugars**
3) **Alcohol Sugars**
4) **Deoxy Sugars**

Amino Sugars

In an **amino sugar**, a hydroxyl group (**OH**) of a monosaccharide has been replaced by an _____ *group* (**NH₂**).

An example of an amino sugar is **D-glucosamine**. *D-Glucosamine* is derived when the hydroxyl group on carbon number **2** of *D-glucose* is replaced by an *amino group*.
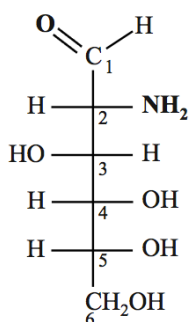
open‑chain D‑glucosamine

Like monosaccharides, *amino sugars* undergo *mutarotation*.
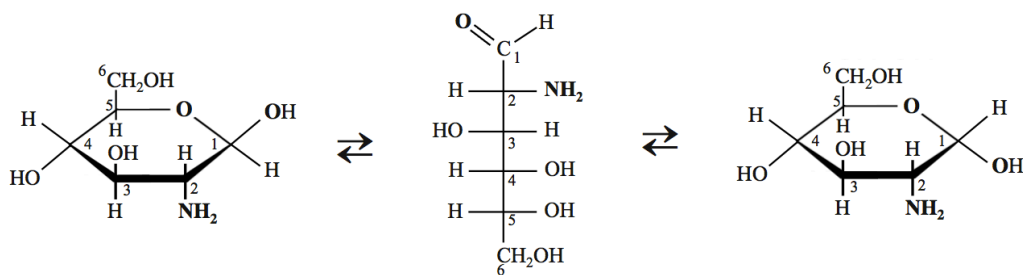
β‑D‑glucosamine   **open‑chain D‑glucosamine**   **α‑D‑glucosamine**

D-Glucosamine of the larger monosaccharide-containing polymers that make up the exoskeletons of crustaceans (e.g. shrimp, lobster, crab) and other arthropods. D-glucosamine is purified for commercial use by processing exoskeletons or other organic material that contains it. Although it has been deemed safe for human consumption and sold as a "dietary supplement," its *actual effectiveness* in the treatment of any health/medical condition, according to the US National Institutes of Health, *has not been established*.

Carboxylic Acid Sugars

In a **carboxylic acid sugar**, an aldehyde group (**CHO**) of a monosaccharide has been replaced by a
_____ *group* (**COOH**).

This is done by a reaction that you have previously seen, *oxidation* of *aldehydes* to *carboxylic acids*.

- **Example:** *D-glucose* can be **oxidized** to produce *D-gluconic acid*:

This *oxidation of aldoses* reaction was used for about 50 years in the measurement of blood sugar levels.

Stanley Benedict first discovered and published a method in which a solution containing Cu^{2+} ions acts as an oxidizing agent in the conversion of _____ to *carboxylic acid sugars*.

This solution is now referred to as _____ *reagent*.

It is used as a test for aldoses since it will oxidize the aldehyde groups *but* _____ *the hydroxyl groups* **or** the *ketone bonding patterns*.

Cu^{2+} ions appear clear-blue when in solution. If a sample that contains an *aldose* is placed in a test tube that contains hot Benedict's reagent, the Cu^{2+} will be reduced to Cu^{1+}. The Cu^{1+} then reacts with hydroxide to form a colored solid. As the aldose concentration in a sample increases, more of the colored solid is made and the color of the Benedict's test goes from blue to green to orange to red to brown. When a color change is observed, we say that it is a "positive" test.
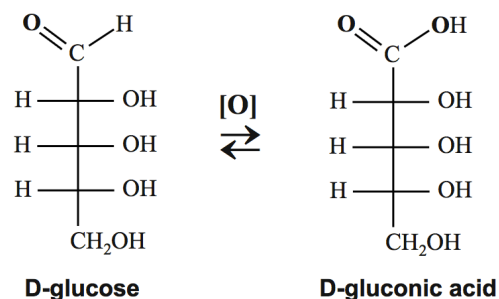
Exception: Although *fructose* is a **ketose** (*not an aldose*), it gives a positive Benedict's test result.

Sugars that produce a color change in Benedict's reagent are called "_____ _____,"
since they reduce Cu^{2+} to Cu^{1+}.

Because Benedict's reagent is *not specific* for D-glucose, which is the important blood sugar species in diabetes monitoring, its use in most medical diagnostic work has been replaced by glucometers. Glucometers are much more specific in sensing *only* D-glucose since they are based on a naturally-occurring enzyme which only catalyzes a reaction of D-glucose.

> **Understanding Check:** Draw the Fischer projection of the *carboxylic acid sugar* that is formed when the aldehyde group of D-ribose (shown below) is oxidized.
>
> **D-ribose**
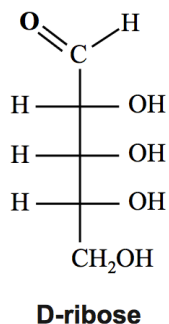
Alcohol Sugars

Alcohol sugars, sometimes called "**sugar alcohols**," are derived when the carbonyl group (**C=O**) of a monosaccharide is **reduced** to a _____ (OH) **group**.

This is done by a reaction that you have previously seen, **reduction** of *aldehydes* and *ketones* to *alcohols*.

- Example of the reduction of a monosaccharide (*D-glucose*) to form an *alcohol sugar* (*sorbitol*):

$$
\begin{array}{ccc}
\text{O} \diagdown \diagup \text{H} & & \text{CH}_2\text{OH} \\
\text{C} & & \\
\text{H} - \text{OH} & & \text{H} - \text{OH} \\
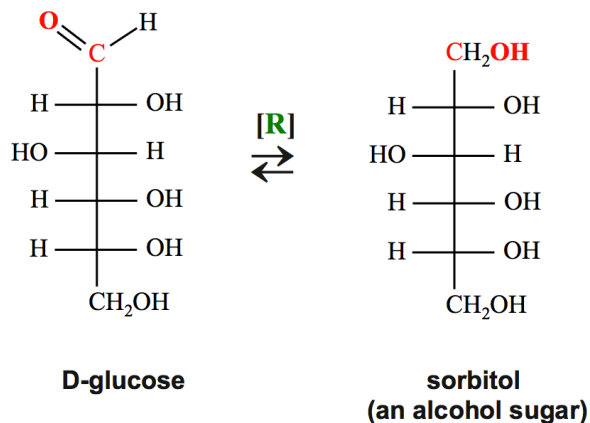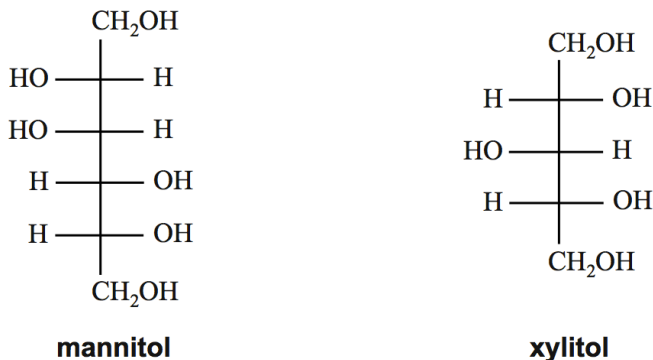\text{HO} - \text{H} & \underset{\rightleftarrows}{[\text{R}]} & \text{HO} - \text{H} \\
\text{H} - \text{OH} & & \text{H} - \text{OH} \\
\text{H} - \text{OH} & & \text{H} - \text{OH} \\
\text{CH}_2\text{OH} & & \text{CH}_2\text{OH} \\
\textbf{D-glucose} & & \textbf{sorbitol} \\
& & \textbf{(an alcohol sugar)}
\end{array}
$$

Alcohol sugars are used in the food and beverage industry as thickeners and sweeteners. Unlike sugars, alcohol sugars cannot be metabolized by oral bacteria, and therefore do not cause tooth decay. Unfortunately for chefs, alcohol sugars do not caramelize, as do natural sugars.

Sorbitol can be manufactured by the reduction of *D-glucose* and it also occurs naturally in pears, peaches, prunes, and apples. *Sorbitol* is used as a sugar substitute, mostly to replace natural sugars in order to prevent tooth decay. It is not so effective as a dietary aid because it can be metabolized by humans for energy. On a per gram basis, it provides 65% of the energy of natural sugars, yet is only 60% as sweet as table sugar (*sucrose*). *Sorbitol* is used in toothpaste, mouthwash, and chewing gum. It is also used, in greater quantities, as an orally or rectally administered laxative.

- Other examples of alcohol sugars are *mannitol* and *xylitol*:

$$
\begin{array}{cc}
\text{CH}_2\text{OH} & \text{CH}_2\text{OH} \\
\text{HO} - \text{H} & \text{H} - \text{OH} \\
\text{HO} - \text{H} & \text{HO} - \text{H} \\
\text{H} - \text{OH} & \text{H} - \text{OH} \\
\text{H} - \text{OH} & \text{CH}_2\text{OH} \\
\text{CH}_2\text{OH} & \\
\textbf{mannitol} & \textbf{xylitol}
\end{array}
$$

Mannitol is used as a sweetener and has many applications in medicine. It is frequently used as a filler in the production of tablets of medicine.

Xylitol is used as a sweetener in chewing gum. Like other alcohol sugars, it is unusable by oral bacteria. However, unlike the other alcohol sugars, *xylitol* aids in the recalcification of teeth.

Understanding Check: Draw the Fischer projection of the **alcohol sugar** that is formed when D-ribose (shown below) is **reduced**.
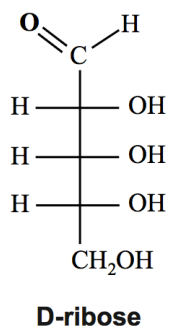
D-ribose

Deoxy Sugars

Deoxy sugars are derived when a hydroxyl group (OH) in a monosaccharide is replaced by a _____ *atom*.

- **Example:** D-*2-deoxyribose* (a deoxy sugar) is derived when the hydroxyl group on carbon number **2** of D-ribose (a monosaccharide) is replaced by a **hydrogen atom**:

D-ribose
(a monosaccharide)

D-2-deoxyribose
(a deoxy sugar)
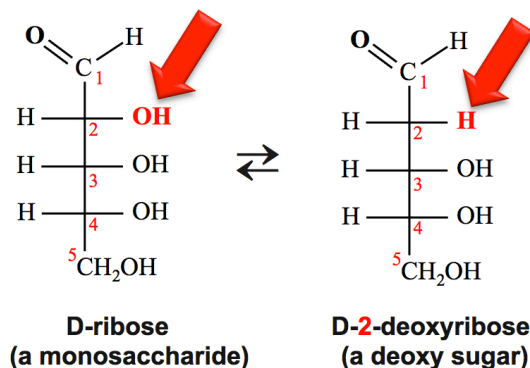
The "**2**" in D-**2**-deoxyribose indicates the carbon position where a hydrogen (**H**) replaces a hydroxyl group (**OH**) of the D-ribose monosaccharide.

Like monosaccharides, *deoxy sugars* undergo *mutarotation*.

α-D-2-deoxyribofuranose

D-2-deoxyribose
(a deoxy sugar)

β-D-2-deoxyribofuranose
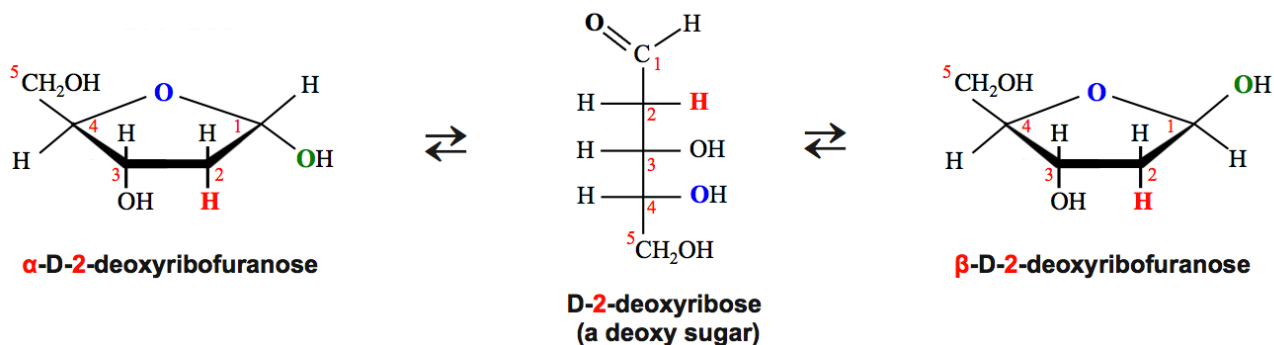
D-**2**-deoxyribofuranose is one of the residues that make deoxyribonucleic acids (DNA).

D-2-deoxyglucose is currently being used in the development of anticancer strategies.

Using the Fischer projection of **D-glucose** (shown below) as the *starting point*, draw the **Fischer projection** of D-2-deoxyglucose.

D-glucose
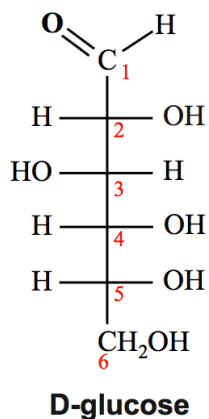
Table for the Review of Monosaccharide Derivatives

Monosaccharide Derivative	Defining Structural Trait
Amino Sugar	A hydroxyl group (OH) of a monosaccharide is replaced by an amino group (NH_2)
Carboxylic Acid Sugar	The aldehyde group (CHO) of an aldose is oxidized to a carboxyl group (COOH).
Alcohol Sugar	The carbonyl group (C=O) of a monosaccharide is reduced to a hydroxyl (OH) group
Deoxy Sugar	A hydroxyl group (OH) of a monosaccharide is replaced by a hydrogen.

Understanding Check:

Identify each of the molecules shown below as either a monosaccharide, amino sugar, carboxylic acid sugar, alcohol sugar, or a deoxy sugar.
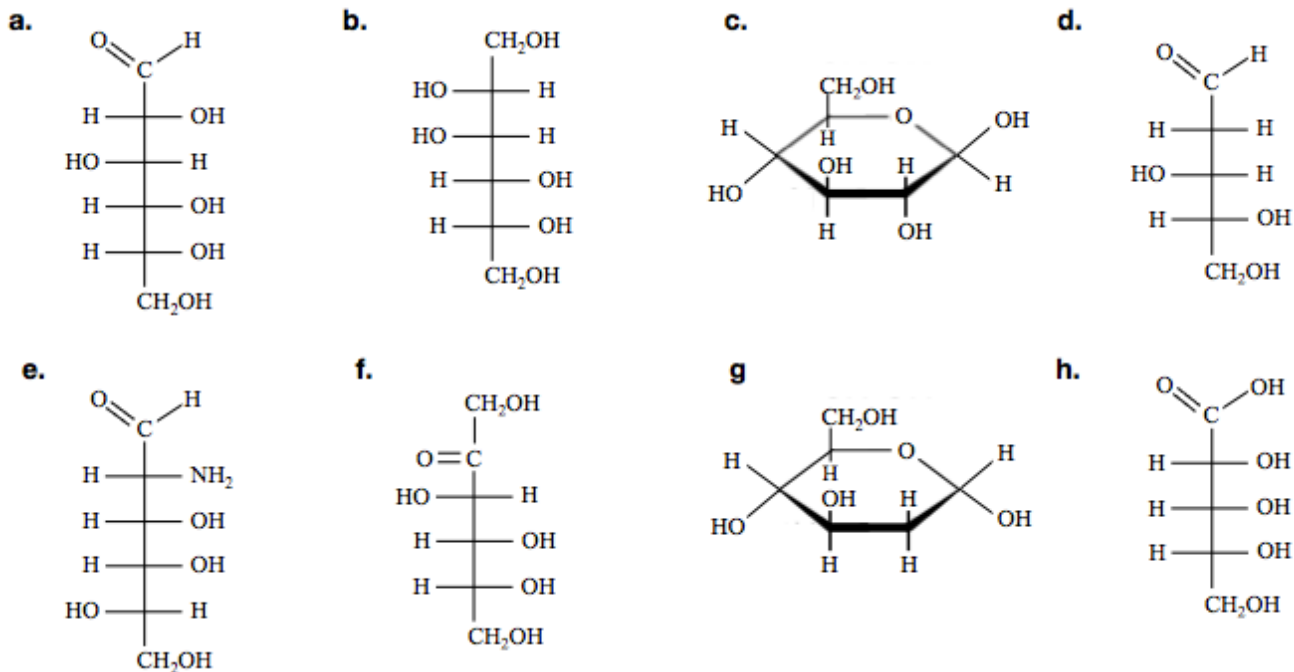
a.

$$O=C-H$$
H —— OH
HO —— H
H —— OH
H —— OH
CH_2OH

b.

CH_2OH
HO —— H
HO —— H
H —— OH
H —— OH
CH_2OH

c.

CH_2OH ... OH
H, ... H
OH H ... H
HO
H OH

d.

$$O=C-H$$
H —— H
HO —— H
H —— OH
CH_2OH

e.

$$O=C-H$$
H —— NH_2
H —— OH
H —— OH
HO —— H
CH_2OH

f.

CH_2OH
$O=C$
HO —— H
H —— OH
H —— OH
CH_2OH

g

CH_2OH ... H
H, ... H
OH H ... OH
HO
H H

h.

$$O=C-OH$$
H —— OH
H —— OH
H —— OH
CH_2OH

Carbohydrates can be classified into three major groups based on their size:

1) **monosaccharides**

2) **oligosaccharides**

3) **polysaccharides**

Oligosaccharides

Oligosaccharides are molecules that are made when _____ to _____ *monosaccharides* chemically bond to each other.

Molecules from particular organic families (such as monosaccharides) are referred to as "_____" when they bond together to form a large molecule.

Oligosaccharides are often subcategorized by the number of monosaccharide *residues* that they contain.

- For example, an oligosaccharide that is composed of *two* monosaccharide *residues* is called a

  _____.

- Likewise, an oligosaccharide made from *three* monosaccharide *residues* is called a

  _____.

21

Let's consider the bond formed between two **α-D-glucose** monosaccharides.

I will sometimes use **large black dots** at the position of the *anomeric carbons* in order to draw your attention to them.

Step 1: An **H** atom is removed from the hydroxyl group (**OH**) *that is bonded to the anomeric carbon* of the left-most residue, and an **OH** is removed from *any carbon* in the right-most residue.

- The **H** and **OH** that were removed form a water molecule.

Step 2: Draw a *new bond* from the oxygen (**O**) that remains on the *anomeric carbon* in the left-most residue **to the** carbon from which the **OH** was removed in the right-most residue.

- This *new bond* is oriented in the same direction as *was* the bond to **OH** that was removed.

maltose (a disaccharide)
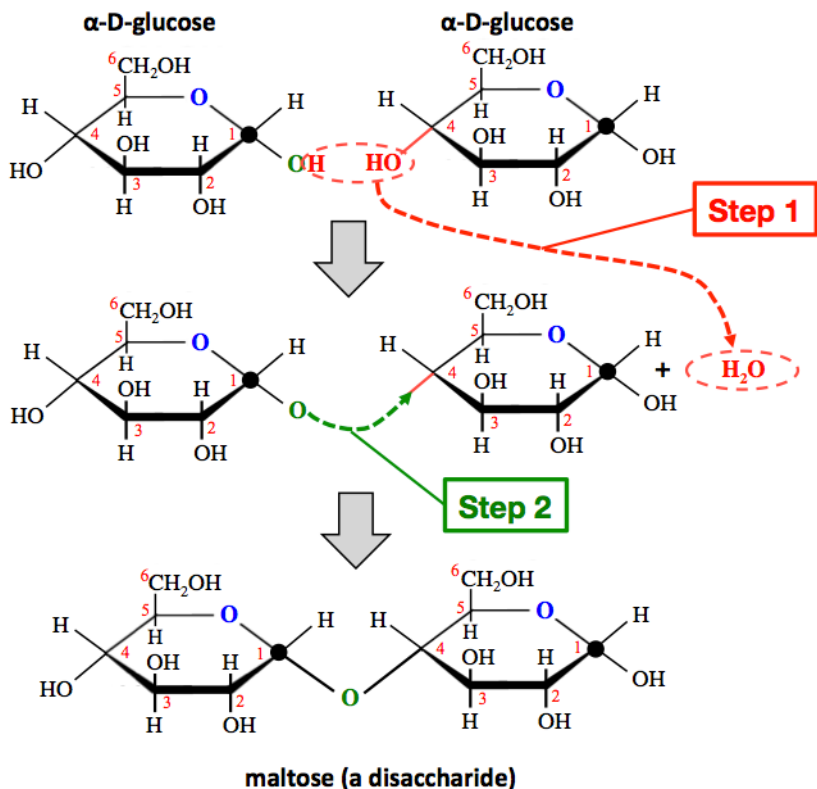
This method can be used to form a bond *between any two sugar residues*.

The *disaccharide* that is formed in *this* example is called **maltose**.

Maltose is found in malt, which is purified from germinated grains. Brewers interrupt the barley grain germination to obtain what is referred to as *malted barley*. Malted barley has a high concentration of *maltose*, which is fermentable, and therefore used in making beer and some other adult beverages. It is also used as a sweetener and thickener in frozen beverages called "malts."

The covalent bonding pattern linking the *anomeric carbon* of one residue to an *oxygen*, then to a carbon in the *other* sugar residue is referred to as a _____ _____.
(even though it actually contains *two* single bonds)

a *glycosidic bond*

maltose (a disaccharide)
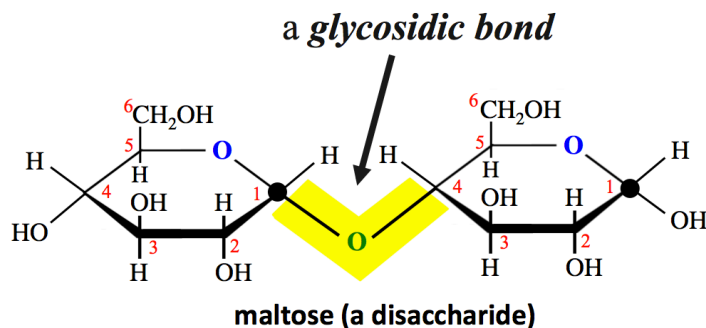
The Glycosidic Bond

Glycosidic bonds are described using **alpha (α)** or **beta (β).**

- The **alpha (α)** designation indicates that the bond *from the anomeric carbon to the oxygen* (**O**) *in the glycosidic bond* is oriented _____ from the ring.

- The **beta (β)** designation indicates that the bond *from the anomeric carbon to the oxygen* (**O**) *in the glycosidic bond* is oriented _____ from the ring.
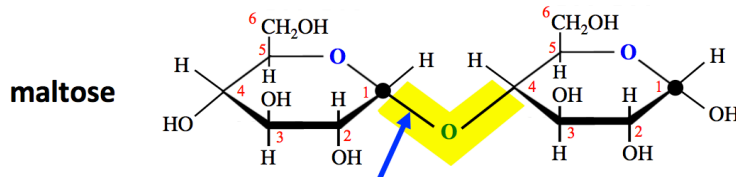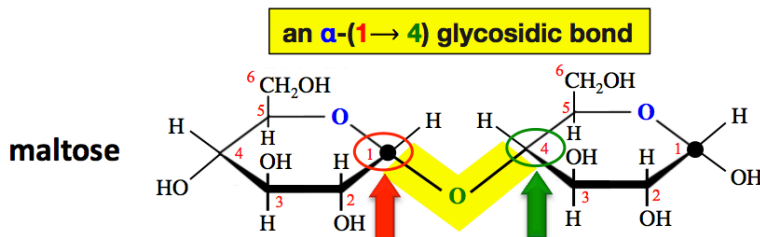

Maltose has the "**α**" designation because the bond *from the anomeric carbon to the oxygen* (**O**) *of the glycosidic bond* is oriented *downward* from the ring.

A glycosidic bond is characterized by its **α/β** orientation, *and* a description of _____ *two carbons are linked* by the glycosidic bond.

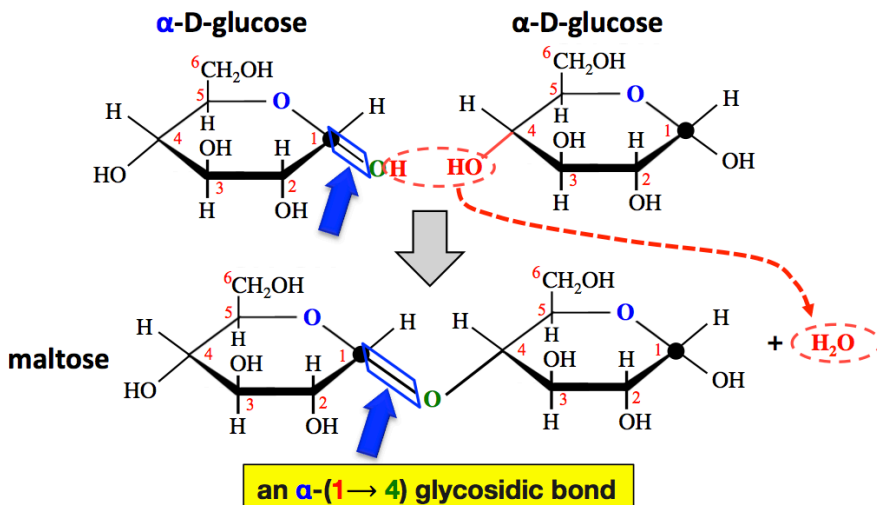For example, the glycosidic bond in *maltose* is classified as **α-(1→4).**

The numbers and arrow that are seen in the parenthesis (the "**1→4**" in the case of *maltose*) begins with the position number of the ***anomeric carbon*** where the glycosidic bond **originates**, then the arrow followed by the carbon position number where the glycosidic bond **terminates** in the *other* residue.

Maltose has the **(1→4)** designation because the ***glycosidic bond*** links the *anomeric* carbon (carbon number **1**) to carbon number **4** of the *other* residue.
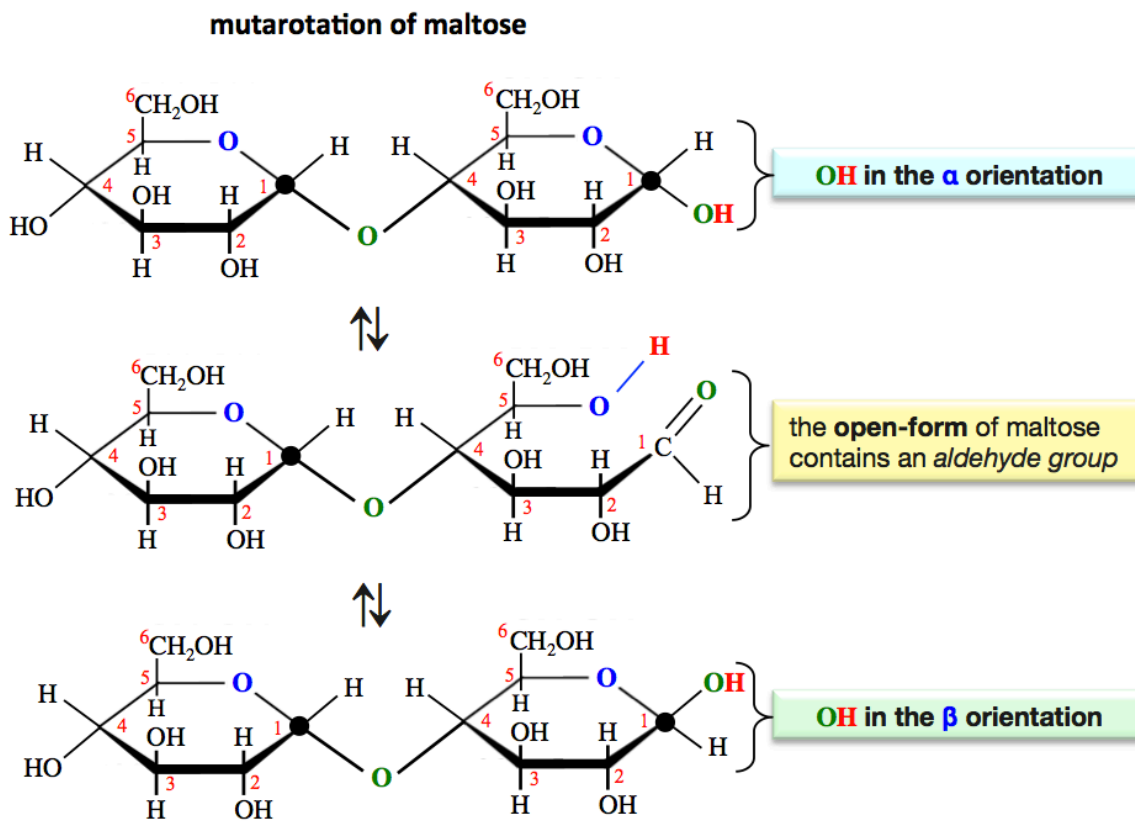
Note that the glycosidic bond in *maltose* has the **α** designation because it was constructed from **α**-monosaccharides.

Later in this video, you will see that a glycosidic bond constructed from **β**-monosaccharides will have the **β** orientation.

23

maltose

This residue can no longer interconvert between open-chain and cyclic forms.
- It is "locked" in the cyclic form.

acetal
carbon bonded to two OR groups.

hemiacetal
carbon bonded to to an OR and an OH group

This residue can undergo **mutarotation**
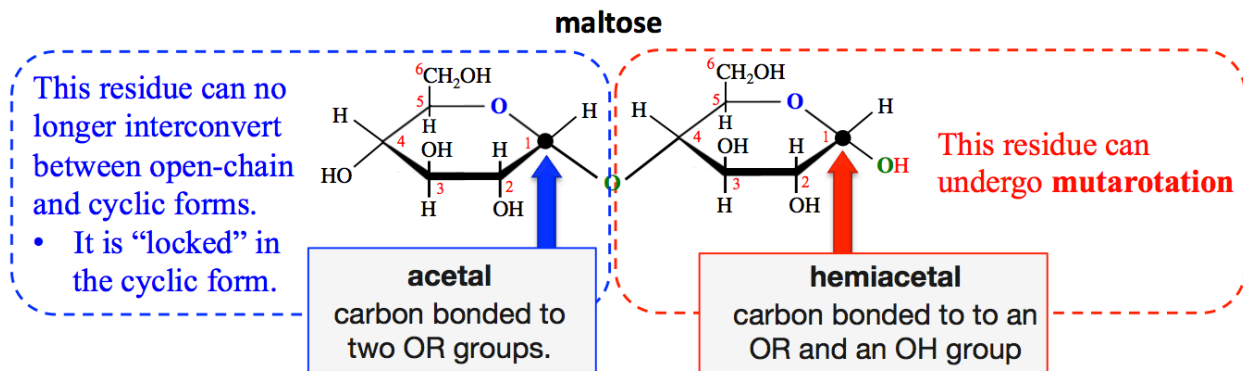
Oligosaccharides, such as maltose, *with a residue that contains a hemiacetal anomeric carbon* will interconvert (*mutarotate*) between closed anomers and an open-form.

mutarotation of maltose

OH in the α orientation

the **open-form** of maltose contains an *aldehyde group*

OH in the β orientation

Note that the mutarotation **does not** change the **α/β** designation of a glycosidic bond.

If the **open-chain form** of an oligosaccharide contains an *aldehyde group*, it will give a positive _____ test.

24

Let's now visualize the way that a glycosidic bond connects two **β-D-glucose** monosaccharides.

- We will use the same two steps as we did for the formation of a disaccharide in our previous example.

Step 1: An **H** atom is removed from the hydroxyl group (**OH**) *that is bonded to the anomeric carbon* of the left-most residue, and an **OH** is removed from *any carbon* in the right-most residue.

The **H** and **OH** that were removed form a water molecule.

Step 2: Draw a *new bond* from the oxygen (**O**) that remains on the *anomeric carbon* in the left-most residue **to** the carbon from which the **OH** was removed in the right-most residue.

- This *new bond* is oriented in the same direction as *was* the bond to **OH** that was removed.

The *disaccharide* that is formed in *this* example is called **cellobiose**.
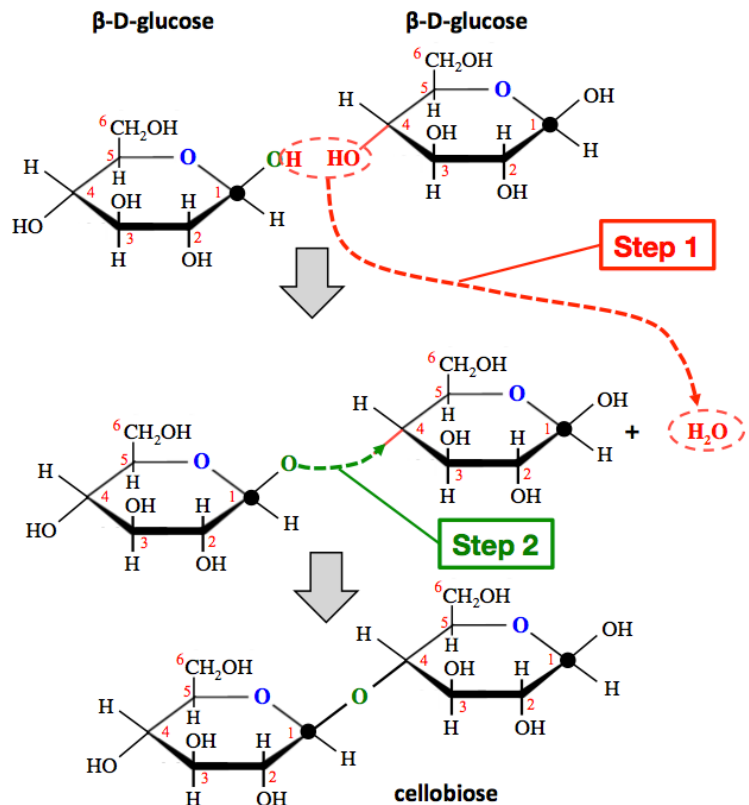
β-D-glucose   β-D-glucose

Step 1

Step 2

cellobiose

Cellobiose has the "**β**" designation because the bond *from the anomeric carbon to the oxygen (O) of the glycosidic bond* is oriented **upward** from the ring.

Cellobiose has the (1→4) designation because the glycosidic bond links the anomeric carbon (carbon number 1) to carbon number 4 of the other residue.

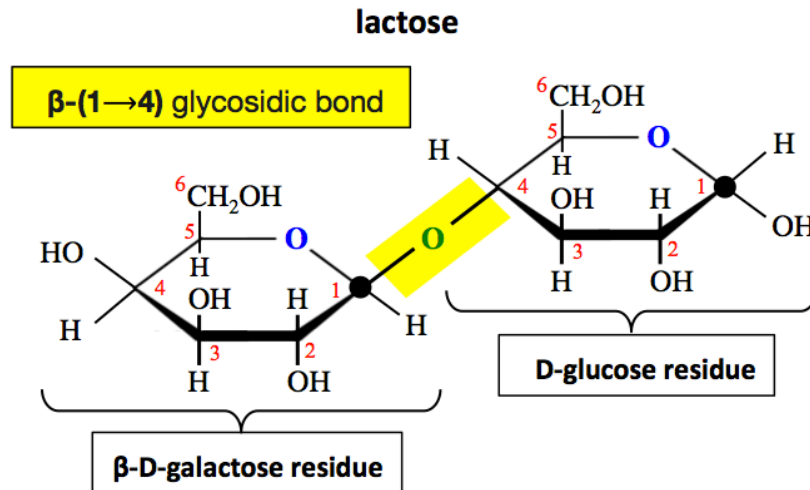**β-(1→ 4) glycosidic bond**

cellobiose (a disaccharide)
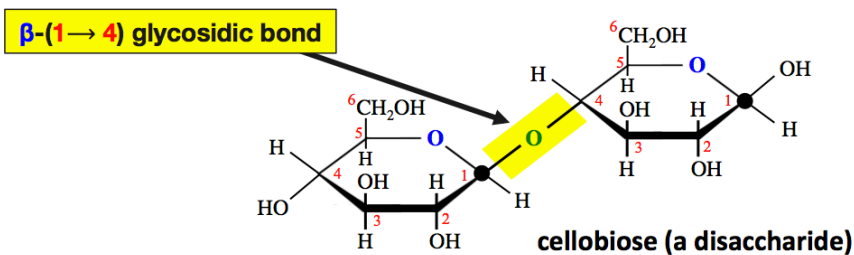
Note that since we began with **β-** monosaccharides, the glycosidic bond, necessarily, has the **β** orientation.

β-D-glucose   β-D-glucose

cellobiose

25
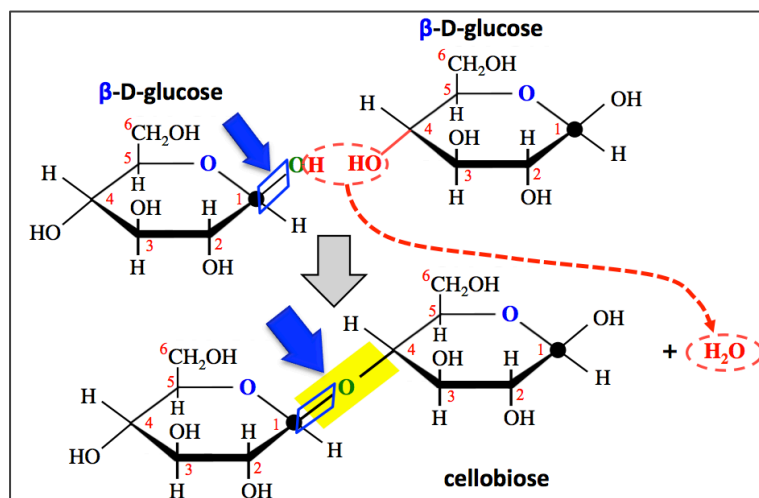
Examples of Other Oligosaccharides

Lactose is a disaccharide that contains a β-D-galactose residue bonded to a D-glucose residue by a **β-(1→4)** glycosidic bond.

lactose

Most of us have an enzyme, called lactase, that will break *galactose*-glucose **β-(1→4)** glycosidic bonds so that we can digest and metabolize *lactose*. Lactose is a nutrient that is found in milk and dairy food made from milk. A small percentage of individuals are born with a mutation in the gene that is responsible for the production of the lactase enzyme, and are therefore unable to metabolize lactose. This condition is called **congenital lactose intolerance**. In many mammals, including humans, production of the lactase enzyme ceases at a very young age, this condition is known as **primary lactose intolerance**.

Over the last five to ten thousand years, human populations have evolved a genetic variant in a "lactose persistence DNA sequence" that allows them to continue to produce the lactase enzyme, and therefore continue *lactose* metabolism into adolescence and adulthood. The presence of this DNA variation was evolutionarily beneficial and has spread to about half of the world's population. Individuals who lack the lactose persistent DNA variation suffer from *primary lactose intolerance*. Both congenital and primary lactose intolerance results in the build-up of undigested lactose in the large intestine. Intestinal bacteria ferment the lactose and produce gases such as carbon dioxide, hydrogen, and methane. The presence of these gases is quite uncomfortable since it results in flatulence and bloating. In order for individuals with lactose intolerance to enjoy dairy foods, they can add the lactase enzyme (produced by fungi or yeast) directly to their food or ingest it in tablet form. Milk that has been supplemented with the yeast lactase enzyme is sold in many countries for lactose intolerant consumers.

Sucrose, also referred to as "*table-sugar*" or just "*sugar*," is a *disaccharide* formed from an α-D-glucose residue and a **β**-D-fructose residue.
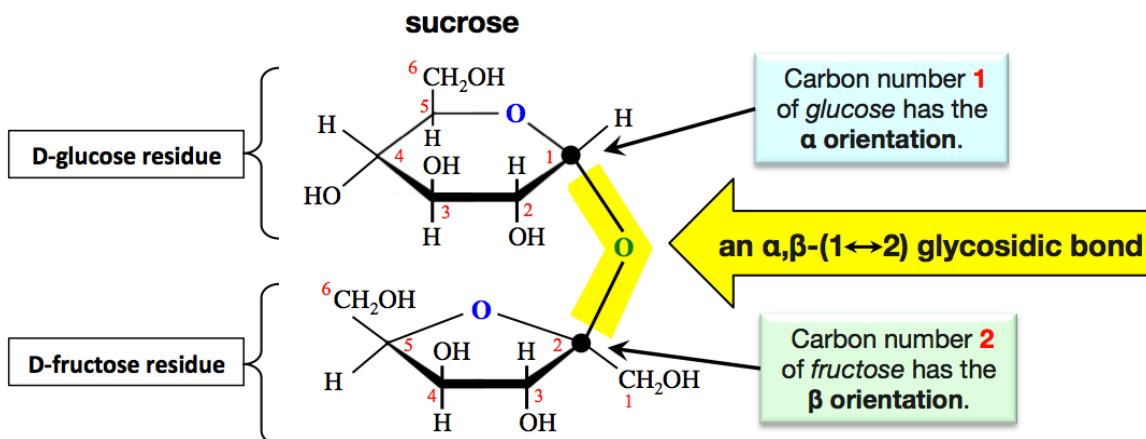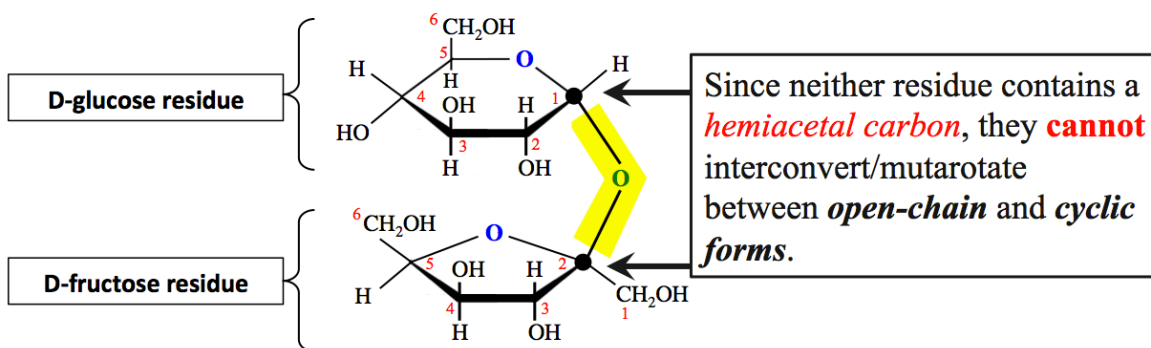
sucrose

Its glycosidic bonding pattern is a bit different from the ones that you have seen so far because it involves *two anomeric carbons*.

The glycosidic bond in sucrose links the *anomeric carbon* in the glucose residue to the *anomeric carbon* in the fructose residue.

- Note that the *anomeric carbon* in the D-fructose residue is carbon number **2**.

The glycosidic bond in *sucrose* is classified as **α,β-(1⟷2)**.

- This is because the stereochemistry at the anomeric carbon of the *glucose* residue (position number **1**) has the **α** orientation, and the anomeric carbon of the *fructose* residue (position number **2**) has the **β** orientation.

- The double arrow (⟷) used in this notation indicates that the glycosidic bond is between *two anomeric carbons*.


Both residues are "locked" in their *cyclic forms*.

For this reason, *sucrose*, *unlike* the other disaccharides that you have seen, will give a _____ Benedict's test and is therefore ***not*** classified as a **reducing sugar**.


Sucrose is consumed in relatively large quantities because of its desired "sweet" taste. It is manufactured by purification from sugar cane or sugar beets. Overconsumption of sucrose has been linked to tooth decay and obesity.

Examples of oligosaccharides that contain **more than two** monosaccharide residues are **raffinose** (a trisaccharide) and **stachyose** (a tetrasaccharide).

- **Raffinose** is made from a *galactose*, a *glucose*, and a *fructose* residue.

raffinose
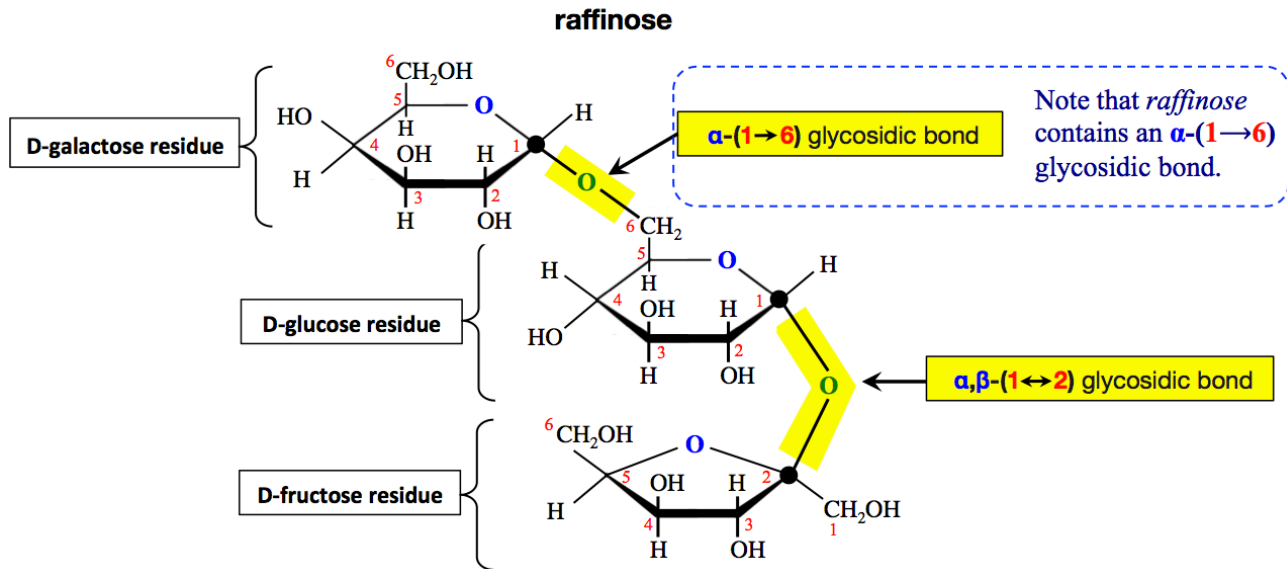
- It is categorized as a _____ because it contains **three** monosaccharide residues.

- **Stachyose** is made from **two** *galactose* residues, a *glucose* residue, and a *fructose* residue.
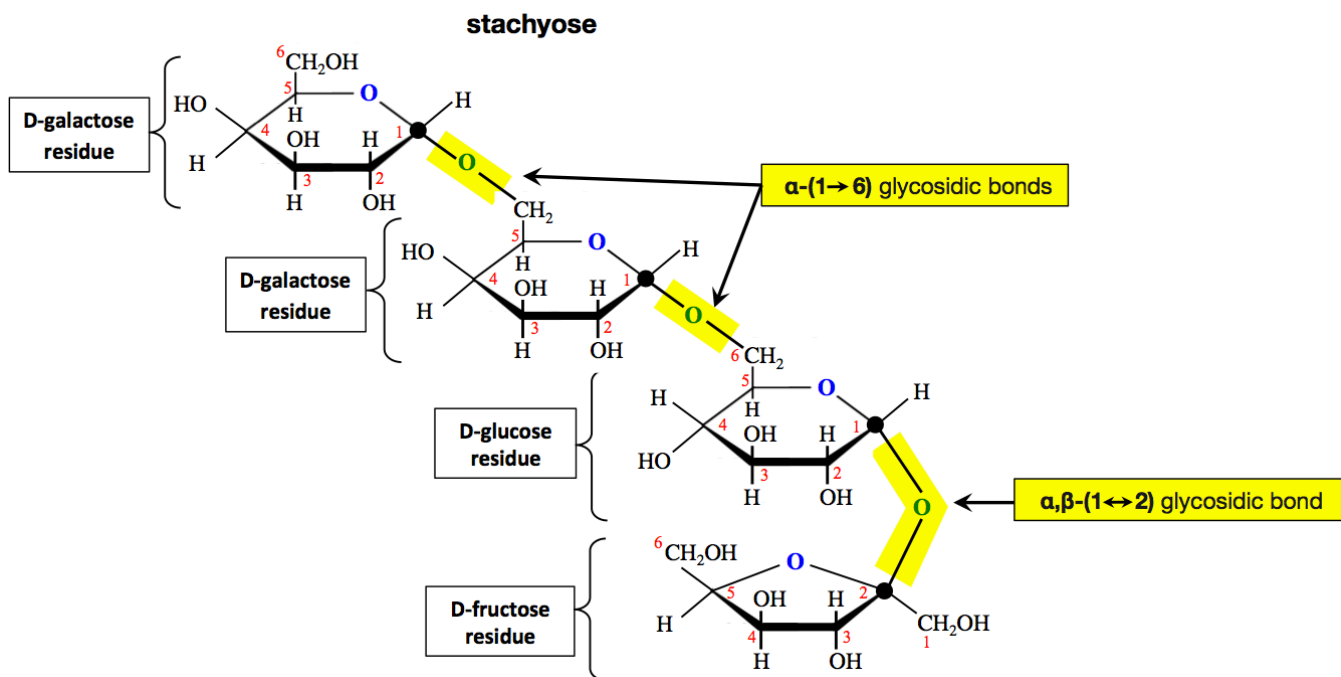
stachyose

- It is categorized as a _____ because it contains **four** monosaccharide residues.

Raffinose and **Stachyose** are found together in many foods, most notably legumes (e.g. beans and peanuts) and cruciferous vegetables (e.g. broccoli, cauliflower, brussels sprouts, and cabbage). Monogastric (single stomach) animals, including humans, pigs, and poultry, cannot completely digest *raffinose* or *stachyose* because we do not have the enzyme, α-galactosidase, that is needed to break their α-galactose glycosidic bonds. Because *raffinose* and *stachyose* pass through the digestive track without being completely digested, they can be fermented by digestive microbes to produce gases. To avoid the discomfort of bloating and flatulence associated with such gases, the α-galactosidase enzyme can be taken as a nutritional supplement (marketed by Prestige Holdings Inc.) using the brand name of Beano.
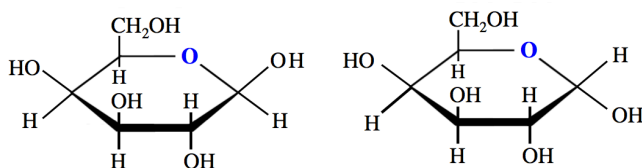
Understanding Check

Classify each of the highlighted glycosidic bonds using the **alpha "α-(X→Y)"** *or* **beta "β-(X→Y)"** designation.
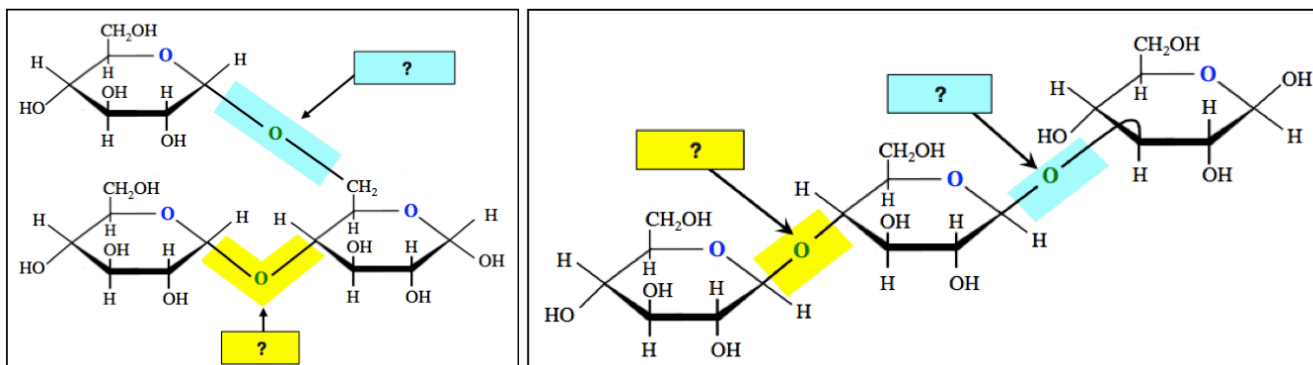
Understanding Check

Draw the disaccharide that is formed when the two monosaccharide molecules below are connected by a **β-(1→4)** glycosidic bond.
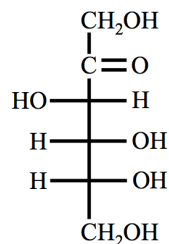
Sweeteners

A sweetener is a compound that is added to food in order to impart the sweet taste of sucrose, but with significantly fewer calories.

Sweeteners can be classified as "_____ *sweeteners*" or "_____ *sweeteners*."

- *Natural sweeteners* are carbohydrates, *naturally* occurring carbohydrate derivatives, or other *naturally* occurring non carbohydrate compounds.

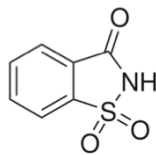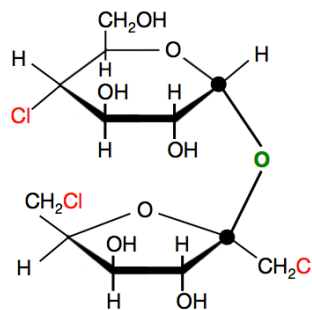   - **Example** of a *natural sweetener*: fructose

D-fructose

- *Artificial sweeteners* do not occur in nature; they are *synthesized* in commercial laboratories.

    - The structural formulas of some *artificial sweeteners* are shown below.
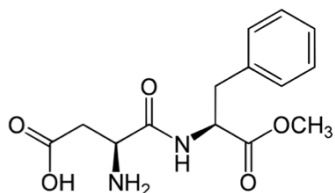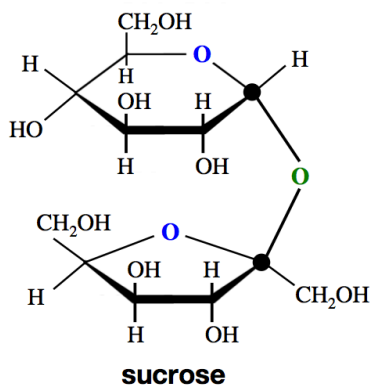
| **aspartame** (Equal, NutraSweet) | **saccharin** (Sweet'N Low) | **sucralose** (Splenda) |

sucrose

Sucrose is the reference standard for "sweetness."

A "*sweetness value*" of **100** is assigned to sucrose, and then *other* sweeteners are assigned *sweetness values* relative to the taste of the same mass of sucrose.

Sweetness Relative to the Same Mass of Sucrose	
Sweetener	**Sweetness Value**
Natural Sweeteners	
Fructose	170
Xylitol (an alcohol sugar)	100
Glucose	75
Sorbitol (an alcohol sugar)	55
Maltose	32
Galactose	30
Lactose	15
Stevia (a plant extract)	25,000
Artificial Sweeteners	
Sucralose (Splenda, Kaltame)	60000
Saccharin (Sweet'N Low)	30000
Aspartame (Equal, NutraSweet)	18,000

The sweeteners that are currently approved for sale in the US are: stevia, aspartame, sucralose, neotame, acesulfame potassium (Ace-K), saccharin, and advantame.

Although there are **rumors** to the contrary, *none of these sweeteners*, artificial or natural, *have ever been shown to cause cancer in humans.*

Carbohydrates can be classified into three major groups based on their size:

1) **monosaccharides**
2) **oligosaccharides**
3) **polysaccharides**

Polysaccharides

Polysaccharides are composed of ***more than*** _____ residues.

- The residues can be monosaccharides **or** monosaccharide derivatives.

Polysaccharides are often subcategorized as either **homopolysaccharides** or **heteropolysaccharides**.

- *Homopolysaccharides* are composed of ***only*** _____ ***type*** *of* residue.

- *Heteropolysaccharides* are composed of _____ ***than one type*** of residue

Homopolysaccharides

Example of a Homopolysaccharide: Cellulose

Cellulose is composed of multiple D-glucose residues (only), bonded to each other by **β-(1→4)** glycosidic bonds.
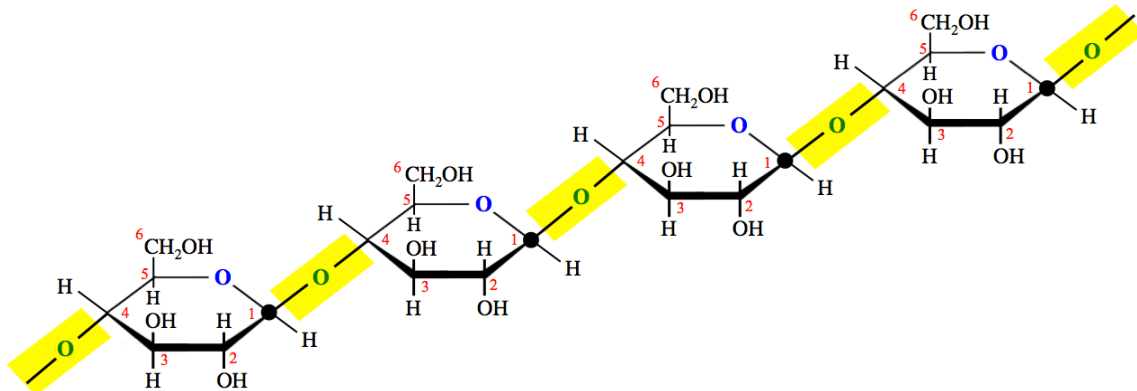
The structure shown above represents a ***small section*** of a *cellulose* molecule.

- A *cellulose* molecule contains *hundreds* (sometimes *thousands*) of glucose residues.

Cellulose is found in the cell walls of green plants, some algae, and oomycetes.

Cellulose accounts for approximately 45% of the mass of dry wood and about 90% of the mass of cotton fibers.

The major industrial use for *cellulose* is the production of paper.

Humans lack the enzyme necessary to break the *glucose-glucose* β-(1→4) glycosidic bond, therefore we cannot metabolize cellulose to get energy. It is for this reason that we do not eat paper, cotton, wood, and many other plants. Some animals (ruminants and termites) are able to metabolize cellulose, not because they produce an enzyme that can break the *glucose-glucose* β-(1→4) glycosidic bond, but because they contain bacteria in their digestive track that can do so. In humans, dietary *cellulose* acts as a bulking agent for feces, and eases defecation. When consumed, it is classified as a ***dietary fiber.***

Much of the rigidity of plant cell walls comes from the strong intermolecular forces, especially hydrogen bonding, that are present between the very long and straight cellulose molecules that lie next to each other in a side-by-side fashion.

Example of a Homopolysaccharide: Starch

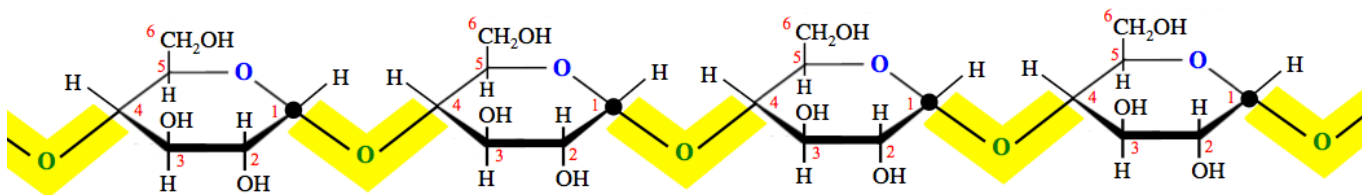**Starch** is a common component of plants.

- The excess *glucose* produced in photosynthesis is stored as *starch* in plants.

Starch is composed of _____ different polysaccharides, both of which are ***homopolysaccharides***.

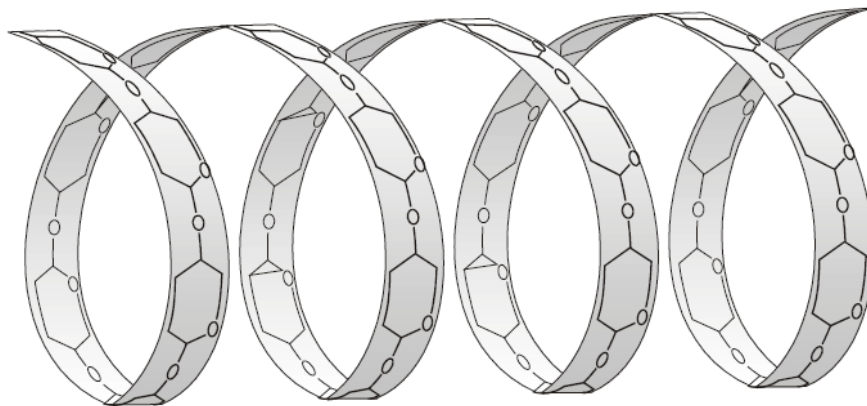The two components of *starch* are _____ and _____.

Amylose

Amylose is composed of multiple D-glucose residues (only), bonded to each other by **α-(1→4)** glycosidic bonds.

The structure shown above represents a ***small section*** of an amylose molecule. An *amylose* molecule contains *hundreds* to many *thousands* of D-glucose residues.

Note that *amylose* and *cellulose* have the same bonding pattern except for the **α** vs. **β** orientation of their glycosidic bonds.

- The difference in stereochemistry (**α** vs. **β**) in *amylose* vs. *cellulose* makes a big difference in our ability to digest these two compounds. Humans (and many other animals) have digestive enzymes (called amylases) that are capable of breaking *glucose-glucose* **α-(1→4)** glycosidic bonds.

- The difference in stereochemistry (**α** vs. **β**) *does* result in a significant difference in the three-dimensional arrangement of the residues. While *cellulose* molecules are relatively straight, the residues in amylose form a helical coil (helix) as illustrated below.

Amylopectin

The second component of starch, ***amylopectin***, is also a *homopolysaccharide* composed of multiple D-glucose residues (only), bonded to each other by **α-(1→4)** glycosidic bonds (as in *amylose*) **with other chains of D-glucose that _____ from carbon number 6**.

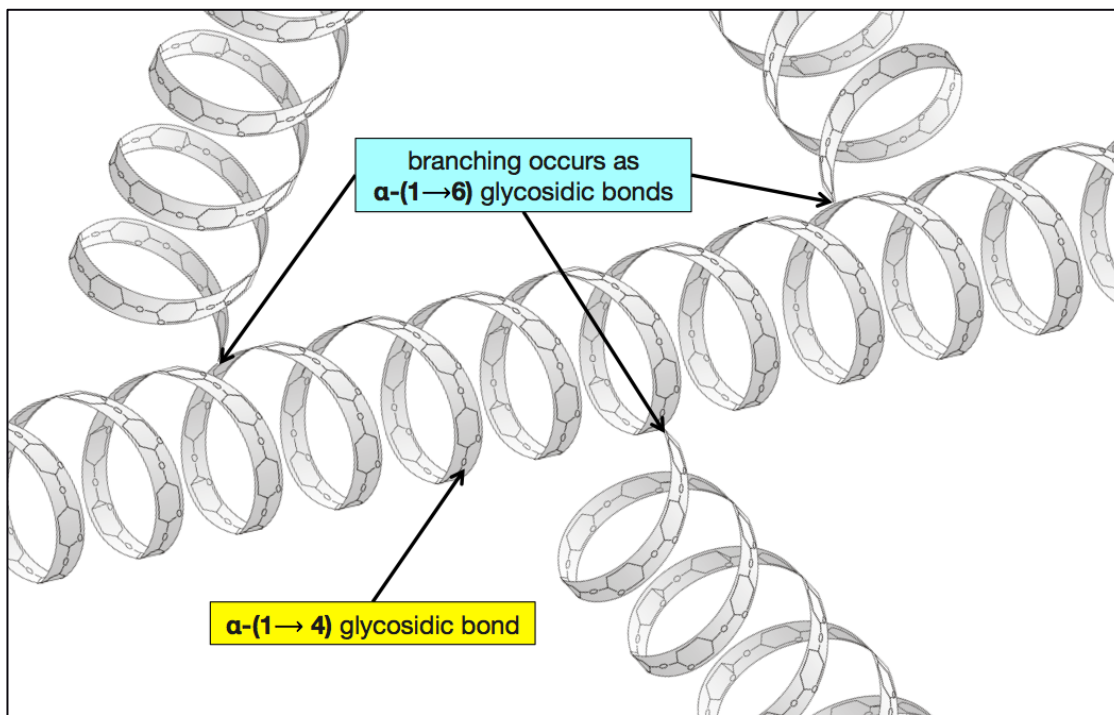The branching occurs as an **α-(1→6)** glycosidic bond, as shown below.
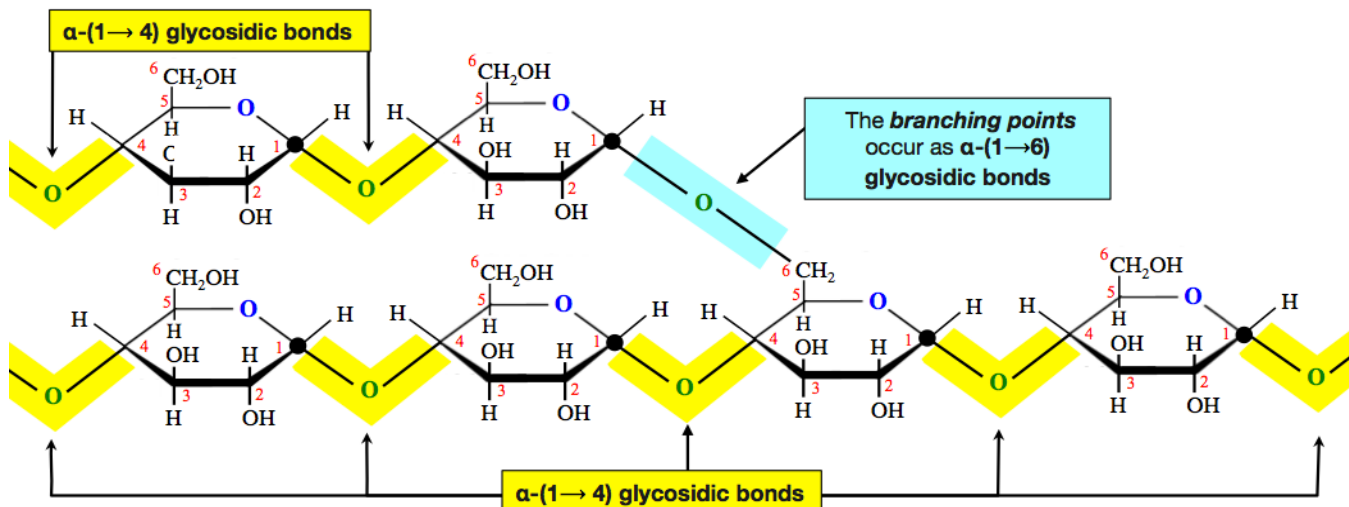
The structure shown here represents a ***small section*** of an *amylopectin* molecule. An *amylopectin* molecule typically contains 2,000 to 200,000 D-glucose residues.

Branching usually occurs every **24 to 30 glucose residues** in *amylopectin*, as illustrated below.

Because of branching, *amylopectin* molecules have a large number of *endpoints*. Since the *amylase digestive enzymes* attach to starch molecules at the endpoints, *amylopectin* can be digested more quickly than *amylose*. Starch contains about 70-80% *amylopectin* and 20-30% *amylose*. One of the three *amylase digestive enzymes* is capable of breaking the branching **α-(1→6)** glycosidic bonds.

Example of a Homopolysaccharide: Glycogen

Plants store excess glucose as *starch*; animals and fungi store excess glucose as **glycogen**.

Glycogen is a ***homopolysaccharide*** composed of multiple D-glucose residues (only).

It is almost identical to *amylopectin*, the only difference is that it ***branches more*** _____.

- Branching in *glycogen* usually occurs every **8 to 10 glucose residues**.

In humans, *glycogen* is made and stored primarily in liver and muscle cells.

Understanding Check: Amylose vs. Amylopectin

Identify the following as properties of either **amylose**, **amylopectin**, **or** *both* **amylose** and **amylopectin**.

    a. contains **α-(1→4)** glycosidic bonds
    b. homopolysaccharide
    c. contains glucose residues only
    d. contains **α-(1→6)** glycosidic bonds
    e. contains branching points
    f. more quickly digested (amylose or amylopectin?)

Understanding Check: Amylose vs. Cellulose

Identify the following as properties of either amylose, cellulose, or **both** amylose *and* cellulose.

    a. contains **α-(1→4)** glycosidic bonds
    b. contains glucose residues only
    c. found in plants
    d. has a helical structure
    e. is a homopolysaccharide
    f. contains **β-(1→4)** glycosidic bonds
    g. can be digested by humans
    h. is a major component of cell walls

Understanding Check: Glycogen vs. Amylopectin

Identify the following as properties of either glycogen, amylopectin, or **both** glycogen *and* amylopectin.

    a. contains **α-(1→4)** glycosidic bonds
    b. contains glucose residues only
    c. contains **α-(1→6)** glycosidic bonds
    d. contains branching points
    e. is a homopolysaccharide
    f. produced by plants
    g. produced by animals
   h. branching occurs more frequently (glycogen *or* amylopectin)

Heteropolysaccharides

Heteropolysaccharides are composed of *more than one type* of residue.

The residues can be *monosaccharides* and/or *monosaccharide derivatives*.

Example of a Heteropolysaccharide: Hyaluronic acid

Hyaluronic acid contains *D-glucuronic acid* and *N-acetyl-D-glucosamine* residues, connected to each other in the bonding pattern shown below.
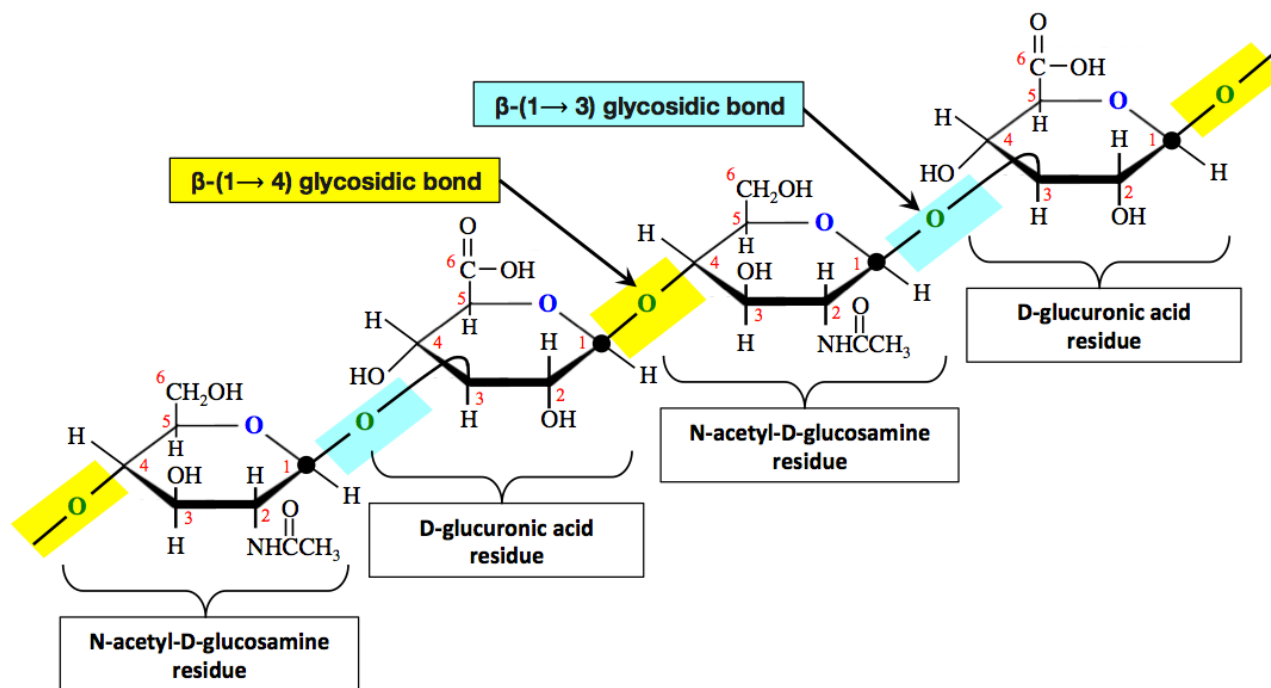
The D-glucuronic acid and N-acetyl-D-glucosamine residues are connected by alternating **β-(1→4)** and **β-(1→3)** glycosidic bonds.

The structure shown above represents only a ***small section*** of a *hyaluronic acid* molecule, *which* can contain *up to* about 50,000 residues.

Hyaluronic acid is found in the lubricating fluid that surrounds joints, and also in the vitreous humor inside the eye.

Review: Homopolysaccharides vs. Heteropolysaccharides

Homopolysaccharides contain *only one type* of residue.

Heteropolysaccharides contain *more than one type* of residue.

Summary of Carbohydrate Classification

Carbohydrates

- Contains 3-7 carbon atoms
- Contains *2 to 10* monosaccharide residues
- Contains *more than 10* monosaccharide residues

Monosaccharides
- Contains *an aldehyde group* → Aldoses
- Contains *a ketone bonding pattern* → Ketoses

Oligosaccharides

Polysaccharides
- Contains *only one type* of residue → Homopolysaccharides
- Contains *more than one* type of residue → Heteropolysaccharides