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1.1 **REVIEW**: SYMMETRY AND **ASYMMETRY OF ORGANIC** MOLECULES

Structural isomers: have the same chemical formula but differ in their structures.

Stereoisomers: have the same chemical formula but differ in the orientation of their atoms in space.

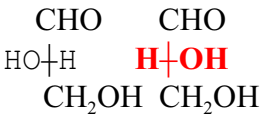
Conformations: various arrangements in space obtained by rotating an atom or a group around a bond or by twisting the molecule (without breaking any bonds).

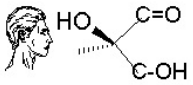
Configurations: various arrangements in space obtained by changing the points of attachment of chemical groups (bonds must be broken to pass from one configuration to another configuration).

1.2 **Molecular asymmetry:** When the arrangement of identical substituents is such that the molecule and its image in a mirror are not superposable - > the molecule and its image are two stereoisomers (TWO DIFFERENT STRUCTURES!).

The two **configurations of glyceraldehyde** (drawn according to the Fische convention in which **vertical bonds are behind the plane of the page**, i.e., *stick into the plane of the paper* and **horizontal bonds are in front of the plane** of the page, i.e., *Point towards you!*).

L-form D-form





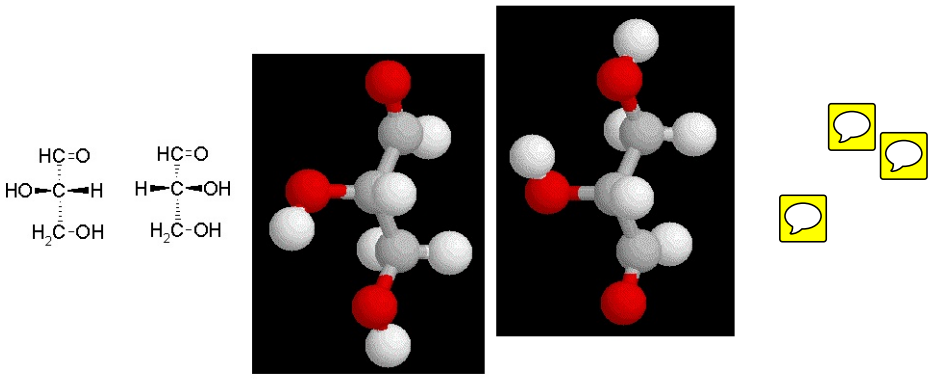
Naming with the Fischer convention: Align chain or molecule so that
oxidized end is **up** and **pointing away from you**
other end of chain or molecule is **down** and **pointing away from you**.

Molecule is called **D** if functional group is in your right hand, **L** if in left.

On your model: -Red=bond to oxidized end, -Green=bond to tail, -Blue= bond to OH

Relevance of the two configurations

When two of the bonds going to carbon 2 are aligned in the in the same way for each configuration, this FORCES the other two bonds to be on opposite ends in each configuration.



Conclusion : the two structures are different

These two stereoisomers are called **optical isomers**, or **enantiomers**

Importance: life is stereospecific!

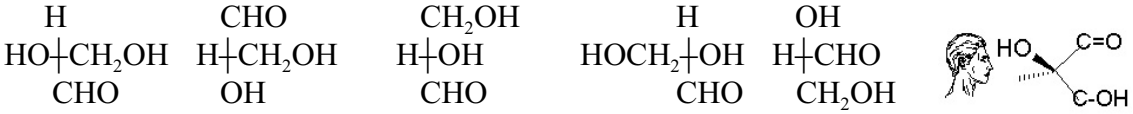
Asymmetrical carbons: when a carbon atom is attached to four atoms or groups which are all different from each other, there is the possibility of having two configurations .

A **chiral** molecule is a molecule which contains such an asymmetry. Such molecules are said to be optically active.

The asymmetrical carbon is called a **chiral centre** and the molecule has the property of **chirality**.

A mixture of two isomers in equal quantities (obtained in a chemical synthesis) is called a **racemic mixture**. The **resolution** of a racemic mixture is the physical separation of the two components.

.Q#1.2a In biochemistry, chiral centres are often produced by enzymatic reactions and they are not necessarily lined up according to the Fischer convention. Since life is stereospecific, a biochemist needs to be able to judge configurations. Identify the following depictions of glyceraldehyde as D or L:



(A) (B) (C) (D) (E)

If you can not do this by looking at the structure, you need to learn to do it for this course!

To learn: make a model of one carbon with four bonds (piece of styrofoam and four toothpicks is ok). Label bonds as in D-glyceraldehyde. Try to fit model to structure drawn on paper by rotating it appropriately.

If model fits, structure on paper is a D. If it does not fit, structure on paper is an L.

Q#1.2b Imagine that you have a human shape molecular size robot that approaches carbon 2 of glycerol ($CH_2OH.CHOH.CH_2OH$) from the side that the H and OH bonds are on, then seizes the H of carbon 2 in his left hand and the OH of C2 in his right hand. With his mouth the robot then seizes the OH on the carbon
that is sticking up in his face and oxidizes it to an aldehyde. Will the robot produce D-glyceraldehyde, L-glyceraldehyde or a racemic mixture of the two?

Q#1.2c What is the general size of the robot? mm? um? nm? pm? ...

1.3 **Identifying enantiomers**

1.3.1 **Polarized light**

Principle: Any molecule that is not identical to its mirror image will cause a rotation of polarised light.

When a beam of **polarized light** passes through a solution containing a chiral molecule, the angle of the light will change.

One isomer will turn the light to the right (this isomer is dextrorotatory and indicated by a + or a d), the other isomer gives the same amount of deviation but to the left (this isomer is levorotatory and indicated by a - or a l). -> A **racemic mixture** has no optical activity.

One cannot calculate the intensity or the direction (d,l) of the optical activity. The intensity varies according to conditions under which it is measured (pH, ionic force).

Note: **Geometrical isomers** (**cis-trans**) are also stereoisomers but they do not contain chiral centres - > They do not have optical activity.

1.3.2 **Enzymes and enantiomers**

Since the two structures are different, enzymes readily distinguish them: if an enzyme works on one isomer *it will not work on the other*.

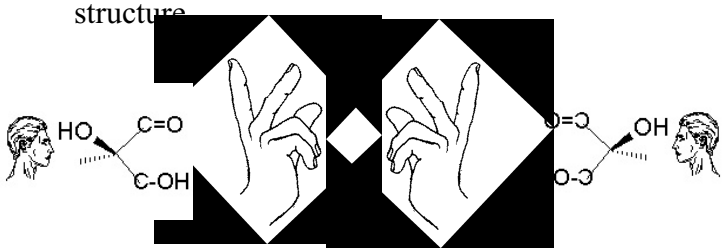
A biological synthesis therefore always gives only one isomer (because *life is stereospecific!*).

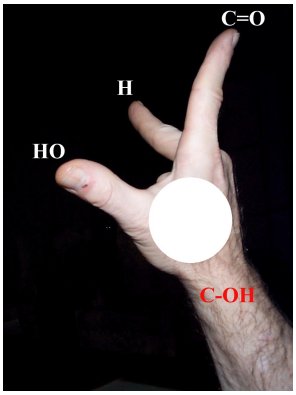
Q#1.3: Why is life stereospecific?

1.4 Nomenclature for the configurations:

1.4a The ***"biochemistry"*** **system (Fischer nomenclature):** For sugars and amino acids the configuration is expressed relative to the configuration of glyceraldehyde.
The letters D and L are used to designate the two configurations.

Using one's hand for Fischer nomenclature {not in book}:
Bend the hand at the wrist and use the first three fingers to model a tetragonal carbon. One determines the configuration of an unknown by comparing one's hands with the structure.





To have the assignments for the fingers, one can use

*When my forearm comes from the end and my fingers are **AAA**,*
***D** ("the") sugars are my right hand, amino acids are a **L**eft hand away.*

in which, for amino acids, AAA means: 1. **A**mino 2. **A**cid 3. **A**lpha-hydrogen
and for sugars, AAA means: 1. **A**lcohol 2. **A**ldehyde 3. **A**-hydrogen

1.4b The *chemistry* system (RS nomenclature) {pg 74}:
This is for your reference: You do not need to know it for this course...
~~The absolute configuration of each chiral centre is indicated by the letters R (rectus) or S (sinister). The order of the atoms is determined using the atomic number and by going from the smallest atom (or group) to the heaviest one.~~

~~Using one's hand for RS nomenclature:~~
~~To have the positions of the fingers:~~

~~*When I point at bonds by decreasing weight, with forearm as space or heaviest,*~~
~~*First my right hand reaches re or is R, then my left is S or first points to pro-S.*~~

NOTE: The Fischer nomenclature and the RS nomenclature are based on different premises
-> THERE IS NO EQUIVALENCE BETWEEN THE TWO SYSTEMS!

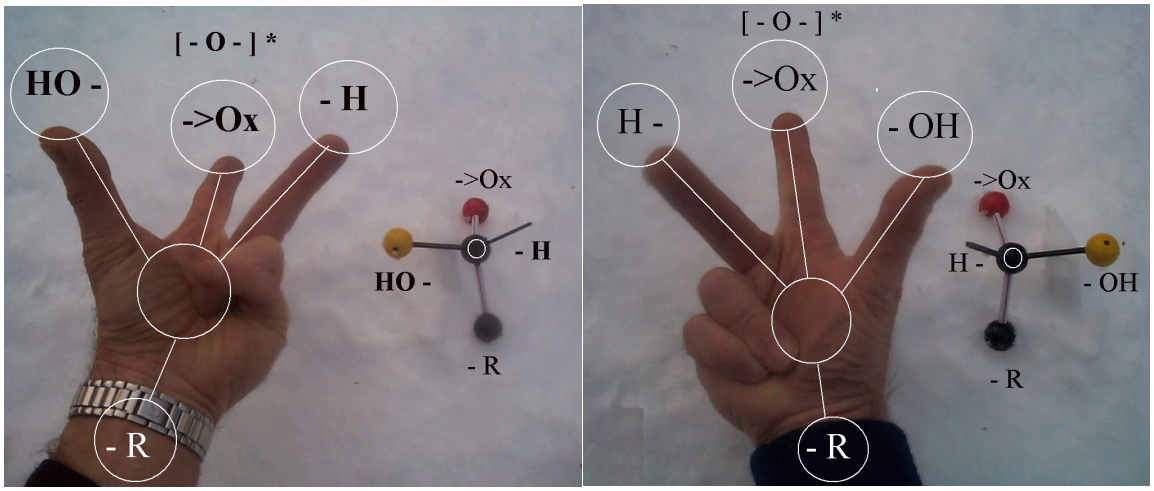
Summarizing questions:
Q#1.4a Question #1.2 stated: "*In biochemistry, chiral centres are often produced by enzymatic reactions*". What type of enzymatic reactions will produce chiral centres?

Q#1.4b Exception to section 1.3.2! There are enzymes that will act on both the D and the L form of a compound.... Explain how this can happen.

1.4c DETAILS, TIPS AND EXTENSION OF THE **AAA** HAND SYSTEM

Imagining the hand as a carbon atom: Imagine your palm as the carbon. Your forearm is the bond going to the R group. Your first three fingers are the other three bonds. With the palm of your hand facing you, BEND your wrist away from you. SPREAD your three fingers as much as possible and point the OUTER TWO FINGERS TOWARDS YOURSELF.

The two configurations of glyceraldehyde AND OF THE HAND....



* Use this finger for the ring O of a pyranose or furanose when fitting to an anomeric carbon (Easy to remember with the faulty logic: "*this oxygen is more oxidized, it has two bonds to carbons*"

Note: When there is no hydrogen on the carbon (such as the anomeric carbon of fructose), if you start systematically, by default the "hydrogen finger" will point to carbon 1.

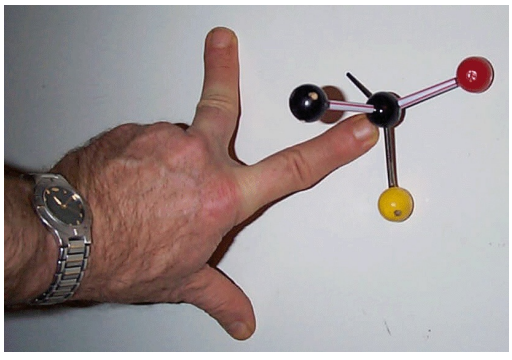
Tip for fitting your hand model to structures seen on paper: Your wrist does not have 360° rotation and you will break it if you try to twist too much in the wrong direction!

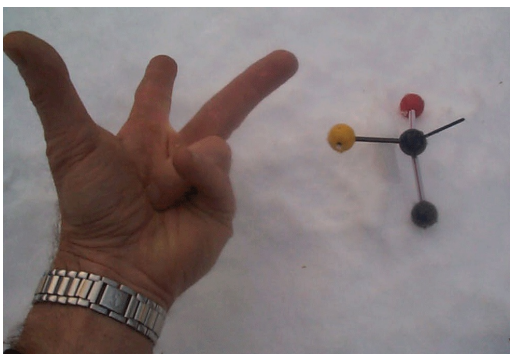
Start with the R group: If it is below the page, start from below and point hand upward;
if it is above the page, point into the page.

In all cases: when the second finger does not align, it is the other structure.

H
$HOCH_2$┼CHO
OH

CHO
HO┼H
CH_2OH





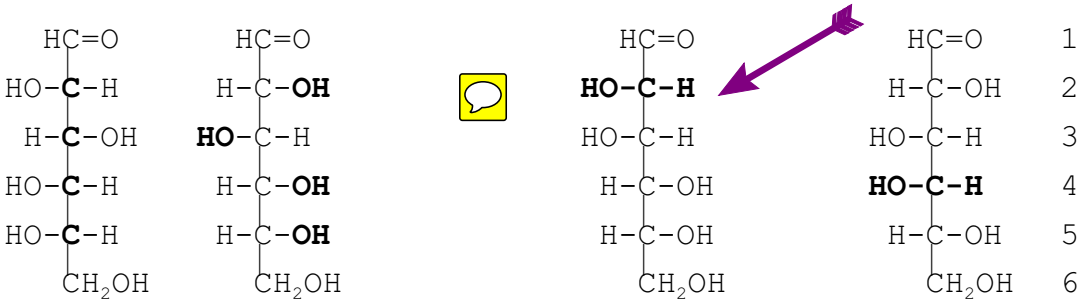
1.5 STEREOISOMERS WITH **SEVERAL CHIRAL CENTRES {Chap 9}**

1.5.1 Words:

Enantiomers contain one or more chiral centres, all of opposite chirality. One is D, the other L. Two enantiomers are non superposable mirror images of each other.

Diastereoisomers: a pair of stereoisomers which are not enantiomers. They contain **more than one chiral center** but **not all** the centres are **of opposite chirality.**
Two diastereoisomers are not mirror images of each other.

Epimers: a pair of diastereoisomers in which one centre is of opposite chirality.
Two epimers are not mirror images of each other.



L-GLUCOSE D-GLUCOSE D-MANNOSE D-GALACTOSE

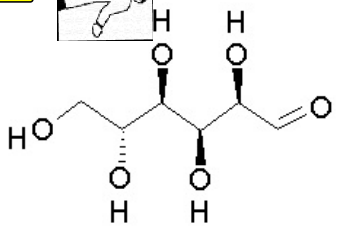
Reminder: the Fischer convention is: at each carbon horizontal bonds go towards you (i.e, out of the plain of the paper), vertical bonds go away from you (into the plane of the paper).

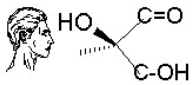
L-glucose and D-glucose are enantiomers.	mirror images
D-mannose and D-galactose are diastereoisomers.	some differences
D-glucose and D-mannose are epimers (at C-2).	one difference
D-glucose and D-galactose are epimers (at C-4).	one difference

Q#1.5a When two hydroxyl groups on adjacent carbons complex with the anion periodate (IO_4^-), the reagent oxidatively cleaves the carbon-carbon bond between the two carbons. Both OHs must be in the plane of the C-C bond. Will this ion cut the four compounds above identically? Which one will be cut the most? Which the least?

Q#1.5b Assume that the first molecule above, L-glucose, has the 3D structure depicted by the drawing; we will call this a front view. What is the shape of the backbone if you were viewing it from the side (imagine that you are in the plane of the paper to the right or left of the molecule: Line? Zig-zag? Circle? Spiral? Helix?

Q#1.5c Which of the above sugars is identical to:
Reminder: In zig-zag drawings, the carbon backbone is in the plane of the paper, the substituents are above or below!
And Hs are not put in!





✎!!

2. CARBOHYDRATES

(Monosaccharides and polysaccharides) "sugars" {Chap 9}

\2Ce2 2d4 1D5

2.1 Definition:

Small organic chain (C3 to C7) with a hydroxyl grouping on almost every carbon; usually one of carbons is an aldehyde or a ketone. These small chains can be used as sub-units to form polymers.

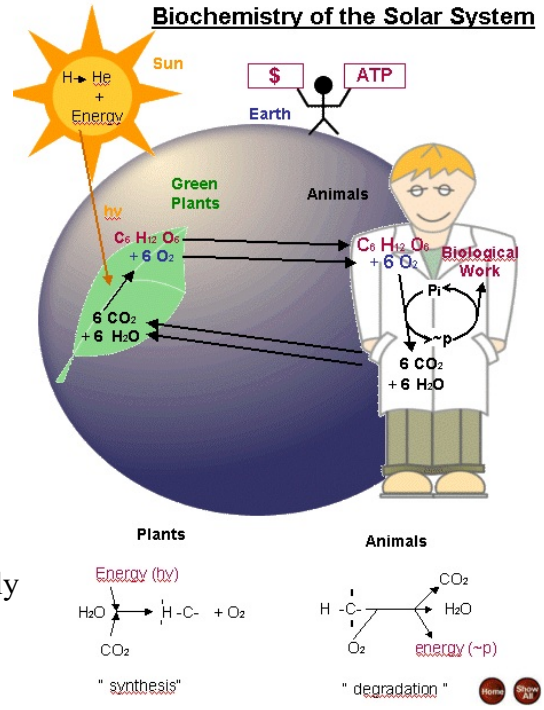
- > Any product with the *general* formula $C_x(H_2O)_x$ < - > X---|---C---|---Y (OH; H; n)

Result: Sugars will make a lot of hydrogen bonds with water

Abundance: the most abundant biomolecules on the planet

Role: I - **energy source**
II - structural
III - information
IV - metabolic intermediates
V - active substances

- > involved in almost all the vital functions



Energy source: The brain requires a constant supply of glucose (a C6 sugar) and blood glucose is carefully maintained at about 5 mM.

Q#2.1a How does the glucose concentration compare to the concentration of 1) of H^+ ?
2) water?

Q#2.1b Assume that you need 400 g of glucose a day to stay alive.
How long will you survive using just the glucose found in your blood?
Your blood volume is 5 l. Do this problem using ONLY the information found on this page.

Classification:

monosaccharides - monomers

monosaccharides and disaccharides are considered as "**simple sugars** ".

oligosaccharides - 2 to 10 units

polysaccharides - >10 units

homopolymers = AAAA

heteropolymers = ABABAB

Nomenclature:

General name of simple sugars (mono and disaccharides): the name finishes with "ose ".

Functional group: (in addition to the alcohol group)

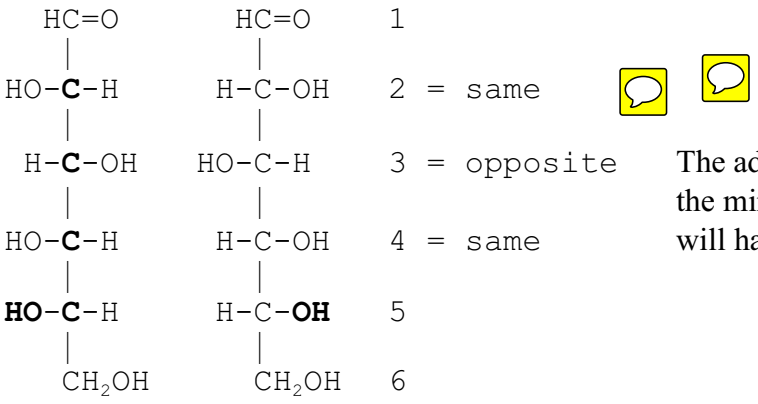
aldehyde = > **aldose** ketone = >**ketose**

Number of carbons in sugar: C3 = triose C4 =tetrose C5 = pentose C6 = hexose

Oligosaccharides: three units = trisaccharide, four units = tetrasaccharide, etc.

D and L :The chiral carbon which is furthest away from the oxidized end (called the reference carbon) is used to decide if a sugar is called D or L. If it has the same configuration as the chiral carbon of D-glyceraldehyde the sugar is D and vice versa. The DL nomenclature is **only** used for this carbon!

Specific name of sugar: In a Fischer projection, all the **other** carbons are compared to the reference carbon (are they the same configuration or the opposite configuration?) and the sugar is given a historic name based on the configurations that are observed (next page).



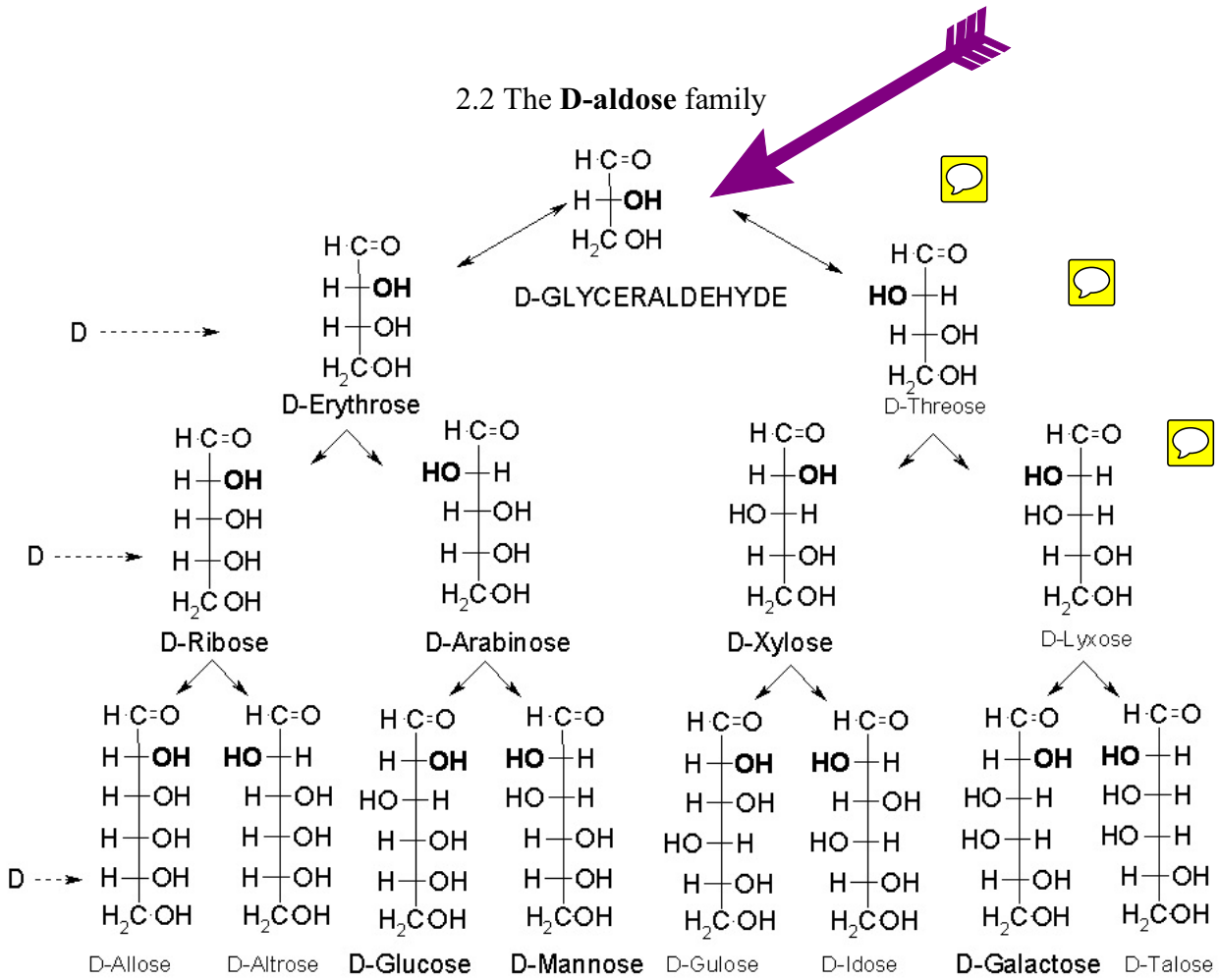
The advantage of this system is that the mirror images of a sugar will have the same name.

L-GLUCOSE **D**-GLUCOSE

Monosaccharides are grouped into two families:

1) **aldoses** (they have an aldehyde group) 2) **ketoses** (they have a ketone group)

2.2 The **D-aldose** family



The vertical arrows show epimers. Sugars important in nature are in bold type. Mirror images of these sugars will be the L-aldose family. They are rare in nature.

Sugars to know:

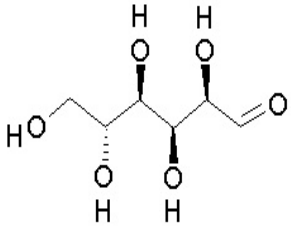
glucose (it is your SOS molecule, the one your body calls for emergencies; SOS also giving the configurations as one goes down the molecule: **S**ame (configuration at C2 as at the D-carbon), **O**pposite (configuration at C3 to that at the D-carbon) **S**ame (configuration at C4 as the D-carbon).

mannose (epimer of D-glucose at first chiral centre, "*man-nose*"-> turn the *nose*, first OH of SOS)

galactose (epimer of D-glucose at "last" chiral centre: last because if configuration at C5 is changed then it would be an L-sugar; "*gala-toes*"-> turn the *toes*, the last carbon of SOS)

Q#2.2a Without going back to previous page: What is the weight of all the glucose (5 mM) in your blood (5l)?

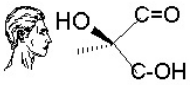
#Q2.2b Name this sugar ---------->



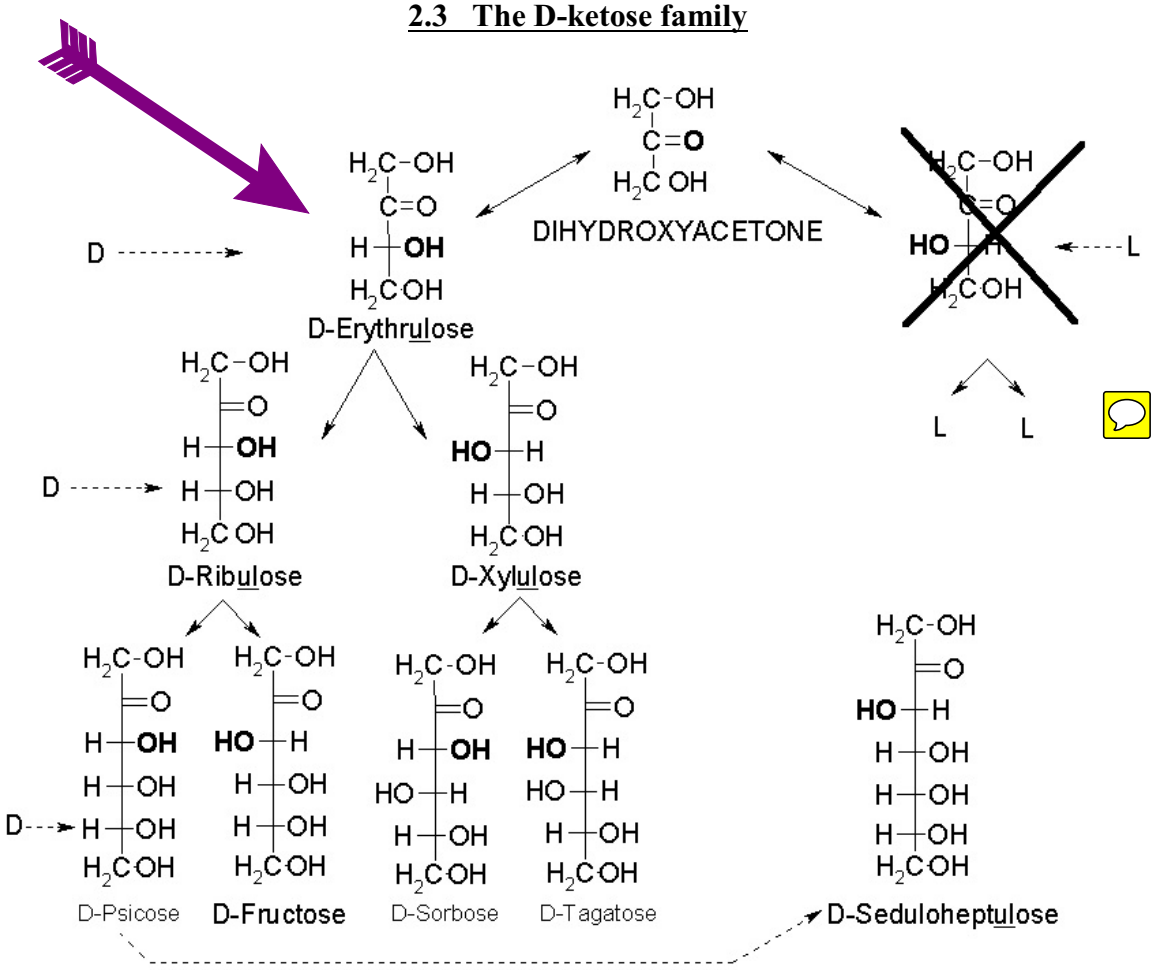
Draw mannose the same way:

Draw galactose " " :

Draw L-glucose " " :



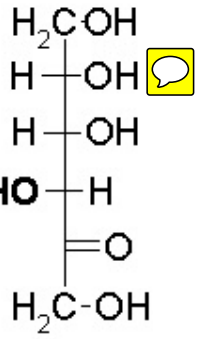
2.3 The D-ketose family



The ketoses are named by adding " ul " (underlined above) to the name of the corresponding aldose. But often historical names exist...

Vertical arrows indicate epimers. Sugars important in nature are in bold type.

Sugar to know: fructose (= the "ketose form of glucose ")

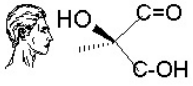


Q#2.3a Name this sugar : <----------

Q#2.3b This sugar is: freely soluble in water? quite soluble? poorly soluble? slightly soluble? more soluble in alcohol than in water?

Q#2.3c If you chemically reduced the C=O of glucose and fructose to OH, would both give the same product? Different products?

Q#2.3d What differences would you expect if you used an enzyme to carry out the reduction described in Q#2.3c?



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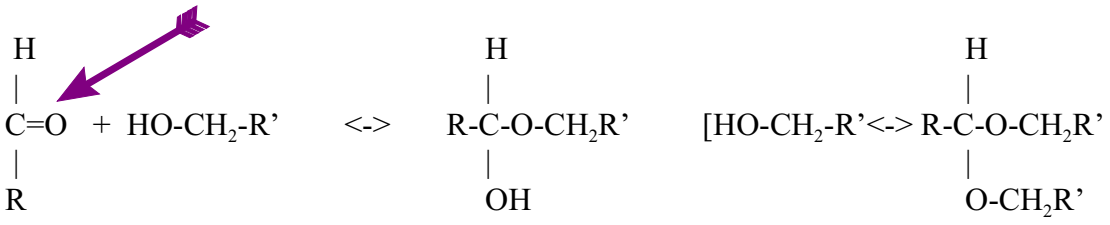
2.4 THE CYCLIC SHAPE OF MONOSACCHARIDES

\2Ce3 3j26 2d4 1D5

2.4.1 Organic chemistry review

Reaction 1 *Reaction 2*

Aldehyde + Alcohol -> **hemi-acetal** [+ alcohol -> **acetal**]



Ketone + Alcohol -> hemiketal [+ alcohol -> ketal]

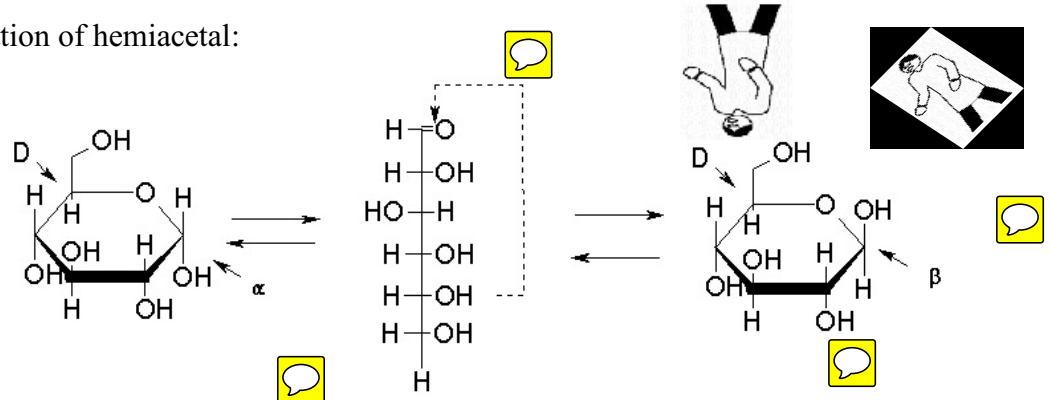
2.4.2 THE STABLE FORM OF THE ALDOHEXOSES is an internal hemi-acetal: THE **CYCLIC HEMIACETAL FORMED WITH C5!**

For sugars, this **6 atom** ring is called a **pyranose** ring.

Haworth projection: This drawing of the ring uses the convention that the bottom of the ring is in front of the plan of paper while the top of the ring is behind the plan.

There are two possibilities for the hemi-acetal :-> Carbon 1 becomes chiral!

Formation of hemiacetal:



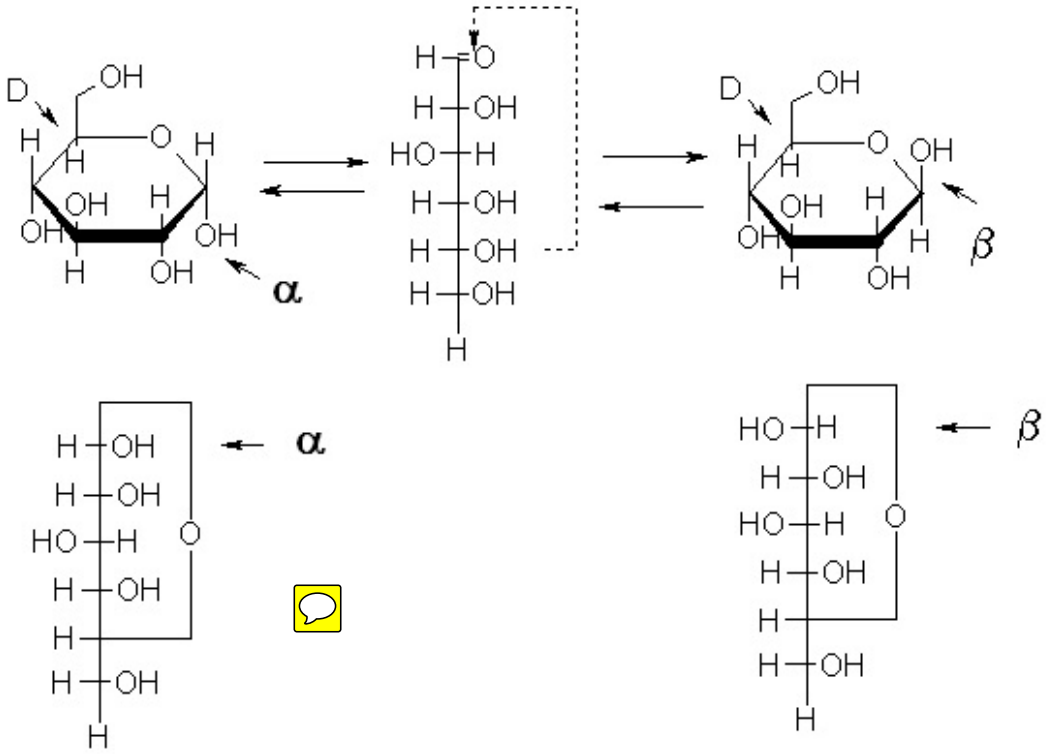
α-D-glucopyranose Reaction β-D-glucopyranose

The carbon which becomes chiral (C-1) is called the anomeric carbon; the two isomers are called **anomers**:

An α isomer (α anomer) is when the C1 hydroxyl group has the same orientation as the reference carbon IN A FISCHER PROJECTION (for this structure, it means that the C1 hydroxyl is on the side of the ring that is opposite to carbon 6).

A β isomer (β anomer) is when the C1 hydroxyl group has the opposite orientation of the reference carbon IN A FISCHER PROJECTION (for this structure, it means that the C1 hydroxyl is on the same side of the ring as carbon 6).

NOMENCLATURE OF THE ANOMERS = as always the Fischer projection!



α-D-glucopyranose β-D-glucopyranose

Note: Anomer designations, like sugar names, are a relative designation: they are based on the configuration of the last chiral atom (the reference carbon).

Q#2.4.2a For the definition of anomers most texts state (Voet pg 359): "*In the α anomer, the OH substituent of the anomeric carbon is on the opposite side of the sugar ring from the CH_2OH group at the chiral centre that designates the D or L configuration....*" This definition will sometimes give the wrong result. Compare it to what I gave you above and identify in which situation this textbook definition will give the wrong result!
Mathews pg 318 ln 4: "*In all D-monosaccharides, the -CH2OH is above the ring.*" !!!

In solution, an **equilibrium** exists between the two anomers, but the reaction is slow.

Mutarotation is the reaction which leads to the equilibrium
(at equilibrium glucose is = 1/3 α + 2/3 β).

The linear form **almost** does not exist (but it is the intermediate in the mutarotation reaction!)

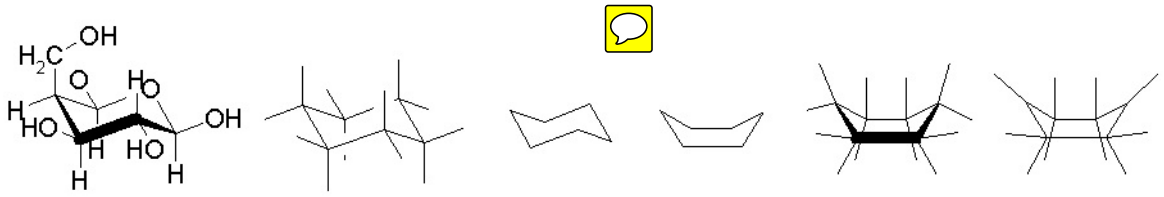
Mutarotation will not occur (" the equilibrium will not exist ") when the OH at C-1 is blocked or substituted (Review: this means that there is no free H on the anomeric O)..

Q#2.4.2b The crystalline form of glucose is α-D-glucopyranose. Since it is prepared from a solution that contains both anomers, why is the crystalline form of glucose α-D-glucopyranose and not a mixture of the two anomers?

Q#2.4.2c Suppose you wanted to prepare crystalline β-D-glucopyranose. What would you propose?

Q#2.4.2d What is the biggest atom that you could fit inside a pyranose ring: H, Li, Na, K, Rb, Cs, Fr ?

Conformations of the pyranoses (Review: saturated 6 member ring, e.g., cyclohexane)



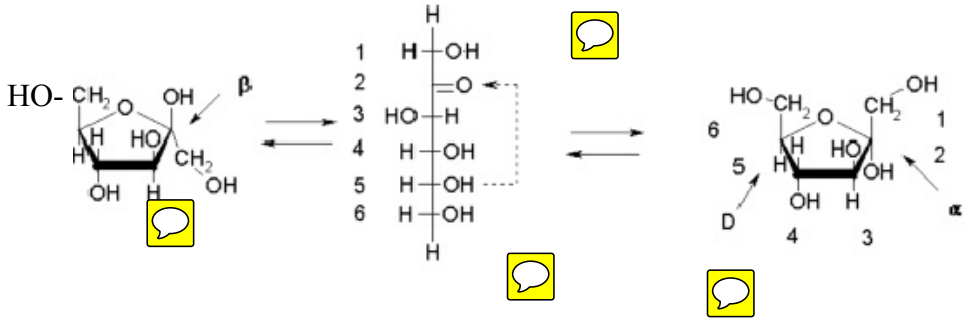
<---------- chair ----------> <---------- boat ---------->

Which conformation will occur in solution? Depends on the substituents!

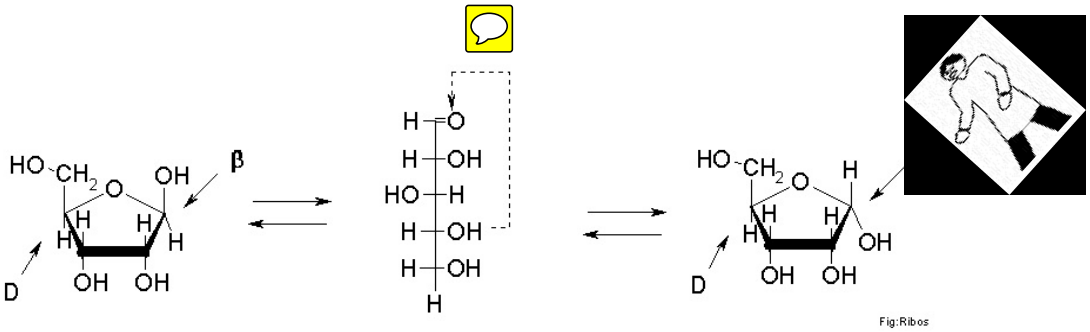
2.4.3 The STABLE FORM of ALDOPENTOSES and the *biological* form of CETOHEXOSES is A **FIVE** ATOM ring

This ring is called a **furanose.**

The conventions used for the pyranoses are also used for the furanoses (Haworth projection, anomeric carbon, anomers).



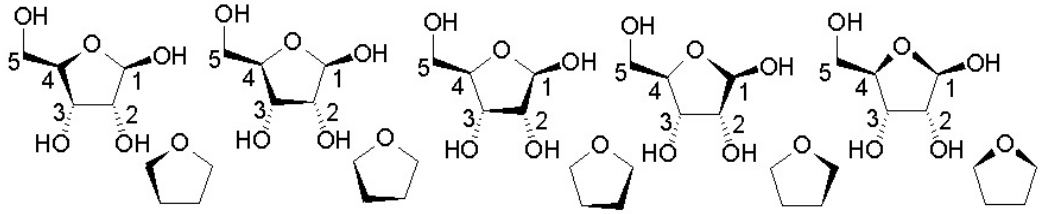
β-D-Fructofuranose D-Fructose α-D-Fructofuranose



β-D-Ribose D-Ribose α-D-Ribose

Q#2.4. What is the mistake on the middle structure shown above?
Think RNA and DNA! Go to Aldose family page...

Conformations of the furanoses: The envelope structure of a saturated 5 atom ring (Review cyclopentane)



Q#2.4.3a Question that summarizes everything to this point: At equilibrium, glucose and fructose solutions contain both the furanose forms and the pyranose forms. Draw the **five** compounds that exist in each of these solutions. If you saw one of these cycles inverted or upside down, would you recognise it? Practise converting all of them to the linear form...
If you were asked why fructopyranose has a ring carbon with just two hydrogens and no free OH, could you explain?

Q#2.4.3b Free fructose (the sweet taste of honey) is mainly β-D-pyranose yet the fructose found in most biological compounds is ONLY the furanose form (illustrated above and in most textbooks). Explain.

2.5 PROPERTIES OF MONOSACCHARIDES

-**Color**: Q# 2.5a What is the color of a solution of D-mannose? L-mannose?

-Density: Q#2.5b You are looking at a box that measures 0.25 m x 0.41 m x 0.1 m that is full of a sugar.

Can you pick it up or will you destroy your back?

-Solubility: Very soluble (but not charged) They form hydrogen bonds.

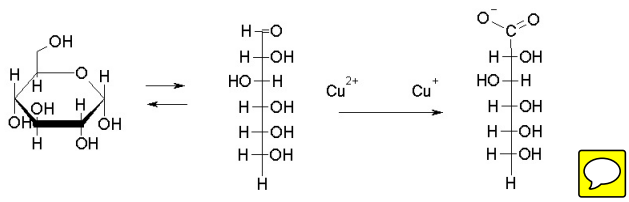
-Can be crystallized

-Taste: Sweet taste for most

-Optical activity Q#2.5c Which sugars will not have optical activity? Consider the products of Q#2.3c!

2.6 CHEMISTRY

2.6.1 Mild oxidation a) **chemical** : Fehling's test (= a classification system for sugars)

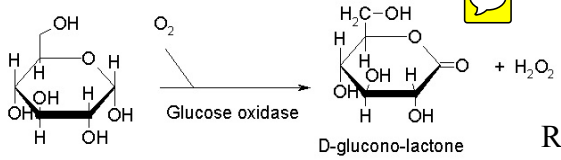


A positive test (one sees the red color of cuprous oxide)means that the sugar has a free aldehyde or ketone. Such sugars are called **reducing sugars**.

Glucose ----------> Gluconic acid (note that it has a charge)

Nomenclature: any aldose with an oxidized C1 becomes an aldonic acid,
e.g., mannose -> mannonic acid.

Mild oxidation b) **enzymatic** : Glucose oxidase
(current method used to identify and measure glucose)



The product is a **lactone** and has no charge.

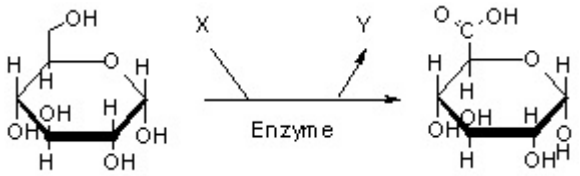
Reminders: a lactone is just a cyclic ester.
Ester = acid + alcohol

Q#2.6.1a Is carbon 1 more oxidised in gluconic acid or in glucono-lactone?

Q#2.6.1b What type of reaction is needed to convert glucono-lactone to gluconic acid? Oxidation? Reduction?

Q#2.6.1c To identify glucose in blood, what is the advantage of the glucose oxidase test compared to the Fehling test?

2.6.2 The oxidation of the primary alcohol group (found on carbon 6): An important oxidation in biology:



This oxidation gives glucuronic acid

Nomenclature: any aldose with an oxidized C6 becomes an alduronic acid,
e.g., mannose -> mannuronic acid.

Q#2.6.2a Give the properties of X and Y. Remember: nothing is magic....

Q#2.6.2b Liver attaches glucuronic acid (with a glycoside bond) to waste compounds that contain a lot of hydrogens ("Yellow" babies happen when this reaction does not occur). What would this accomplish? What is the advantage of using glucuronate compared to glucose?

2.6.3 Reduction

D-glucose ---> ["H_2"] HO-C

CH_2OH
C-OH
C-OH
C-OH
CH_2OH

D-sorbitol

general reaction:

Aldose ---> ["H_2"] **alditol**

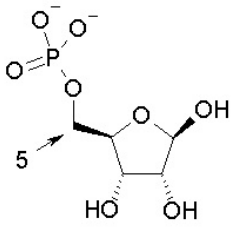
Note: alditols will exist only in linear form.

Q#2.6.3 You carry our a chemical reduction of fructose.
Result: All the product will be D-sorbitol? Half will be D-sorbitol and half L-sorbitol? None will be D-sorbitol? Half will be D-sorbitol?

An enzyme carries out the same reduction. Result?

2.6.4 BIOLOGY: Esterification of the **alcohol functions** is a key reaction for the handling of sugars.

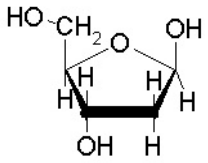
Alcohol + acid - > esters



Ribose + "phosphoric ----> ribose-5-phosphate
acid"

Other derivatives of biological importance:

deoxysugars = a hydroxyl group is replaced by a hydrogen.
= the carbon is reduced

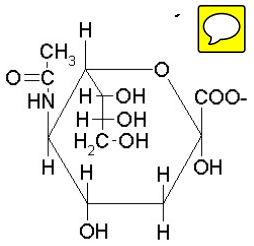


β-D-2-deoxyribose

amino sugars, **sulfo** sugars, etc...

Q#2.6.4a What question would you ask the person who asked you to draw glucosamine (amino-glucose)?

Q#2.6.4b Use the words and the 4 sugars that you are supposed to know to unambiguously describe the structure on the right.



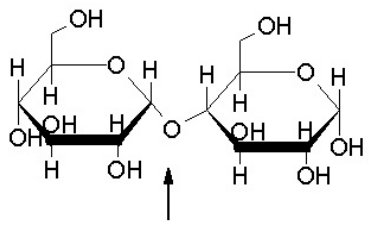
2.7 BOND **BETWEEN** SUGARS:

The most common bond is between the alcohol of one sugar and the free alcohol of the hemiacetal (or hemiketal) of the other sugar (this gives an acetal or a ketal, 2.4.1):

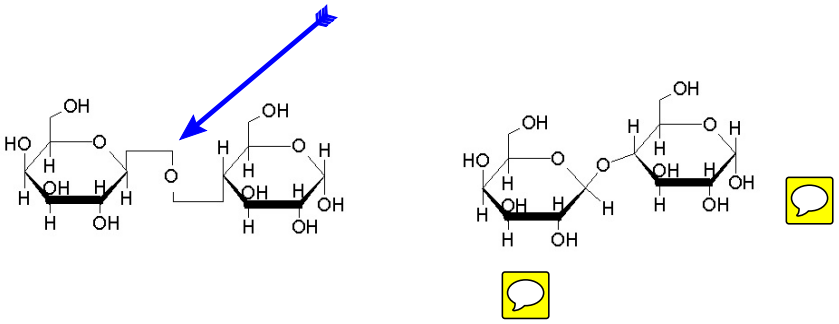
This bond is called a **glycosidic bond.**

Q# 2.7a What kind of reaction made this bond? Will this reaction produce a lot of energy?

α-1,4 Bond
Example: The disaccharide, maltose is two molecules of glucose linked by a α-glycosidic bond between C-1 and C-4



β-1,4 Bond Example: Lactose
lactose is a galactose linked to a glucose with a β-1,4 bond

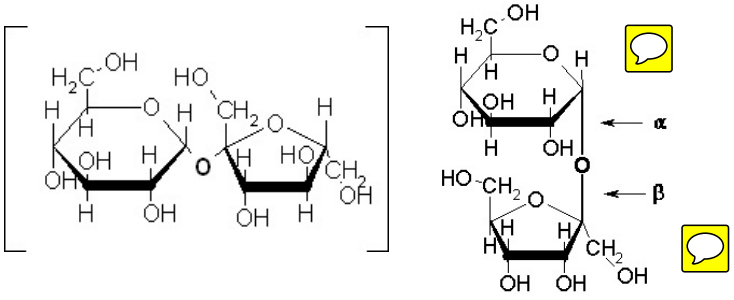


α-1,β-2 Bond Example: **Sucrose** is a bond between the C-1 of glucose and C-2 of fructose

Sucrose is normal table sugar (a plant sugar)

It is the the α-anomer of glucose linked to the β-anomer of fructose.

There is **no free anomeric carbon**
- > a negative Fehling test
- > sucrose is not a reducing sugar.



Q#2.7b Did you spot the error on the structure on the right?

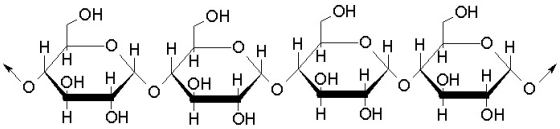
Glycoside: When the glycosidic bond links a sugar with a compound that is not a sugar, the resulting product is called a glycoside.

2.8 **POLYSACCHARIDES** *"carbohydrates" "sugar polymers"* \2Ce4 2d4 1D5

2.8) Polysaccharides used as energy stores : starch (plants) and glycogen (animals)

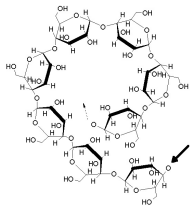
2.8.1) STARCH (a store of energy in plants)
is a mixture of amylose (15-20%) and amylopectin (80-85%)

Amylose:
a linear chain
of glucose units
linked with α-1,4 bonds
for 100 to 1000 residues

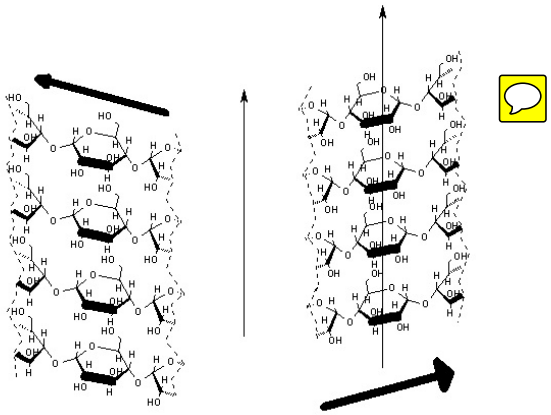


The structure is a helix ----->

a helix with six residues per turn ---------->
(*looked at from above*)



a helix that is left handed:
(*Looked at from the side*) ---------->



Left handed Right handed

Handedness of a helix

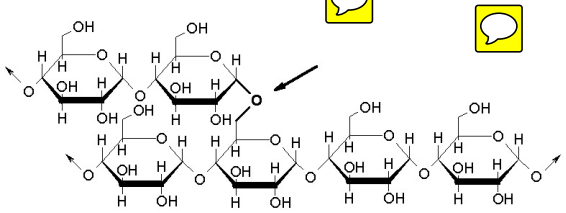
One way to tell handedness is to imagine the helix as a staircase:
Does the staircase turn right or left?

In the chem or pharmaceutical lab: In the starch test for iodine: iodine inserts into the helix and this gives the blue color.

Q#2.8.1 What is the mirror image of a right handed helix? (You could look at this page in the mirror)

Amylopectin (the branched form of starch):

Chains of glucose
(α-1,4 bonds)
with branching (α-1,6 bonds)
at every 24-30 residues.

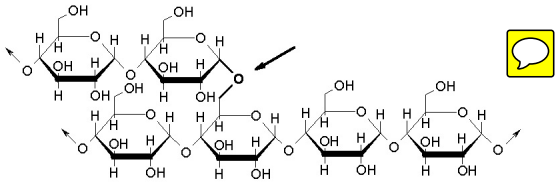


Size varies from 300 to 10,000 residues
- > insoluble....

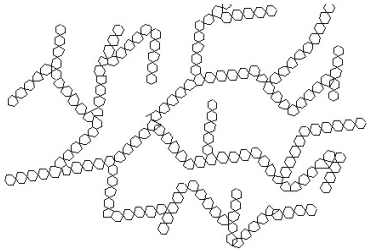
Starch is stored as starch granules (~ 1 μm) in plant cells.

2.8.2 GLYCOGEN: An energy store in **animals** (liver and muscle) and in bacteria. Sometimes called animal starch.

Chains of glucose
(α-1,4 bonds)
with branching(α-1,6 bonds)
at every 8-12 residues.



The structure is therefore more compact than that of amylopectin.



Up to 600,000 residues of glucose per molecule!
Stored in the cytoplasm in 0.1 μm granules.

Q#2.8.2a The Merck Index states that glycogen "does not reduce Fehling's solution." Explain why it does not.

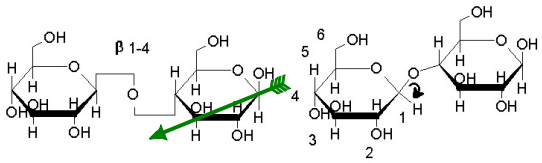
Q#2.8.2b Glycogen has more residues than starch. Why are glycogen granules smaller than starch granules? Would you expect to see glycogen granules in an electron micrograph of your liver cell? Why? Why not?

Q#2.8.2c What is the advantage of storing glucose as glycogen? Why not just store free glucose in your liver?

Q#2.8.2d In grouse like birds, glycogen is 0.4% of the flight muscle. Glucose use during panic flight is 100 micromoles/min/g muscle. How long can a game bird fly before it has to land due to lack of glucose?

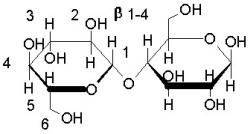
2.9) STRUCTURAL POLYSACCHARIDES : cellulose and chitin

2.9.1 CELLULOSE: constitutes the cell walls of plants.
It is a half of the carbon in the biosphere.
but vertebrates cannot digest cellulose!

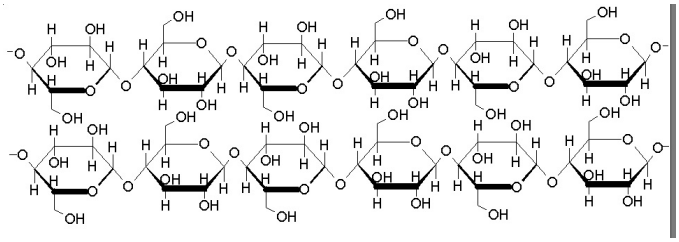


It is a linear chain of glucose units
(like amylose);
but the bonds are **β**-1,4

one glucose residue is rotated compared to the next,
this puts the two rings in the "same" plane ---------->



- > this gives long straight chains:



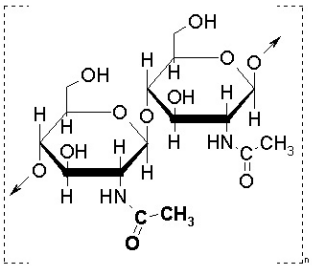
One can consider cellulose as a polymer of glucose dimers.

Hydrogen bonds between the chains consolidate the structure.

Cellulose is insoluble in water.

Q# 2.9.1 Under optimal conditions, bamboo can grow at a rate of 0.3m per day. The stems are cellulose fibers. How many sugar per second are added to each fibre at this growth rate? You could estimate the length of one residue by drawing it and using your C-C bond reference to estimate the length but to save you time I will give you the value given in the book : 0.45 nm is the length of a glucose residue. (which you will immediately round off to 0.5 nm so that you can do the calculation without using a calculator...)

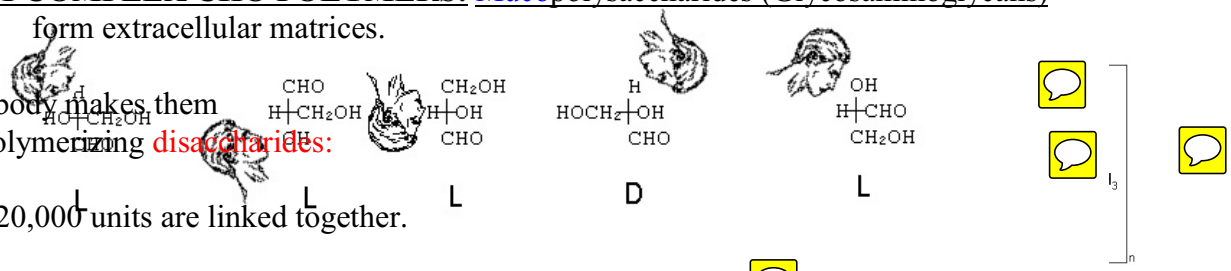
2.9.2 CHITIN: structure of the shells of invertebrates
(the exoskeleton of insects and shellfish).



A linear N-acetyl-glucosamine polymer :
the amine is at C-2,
the bond is (**β**-1,4)

2.10.1 COMPLEX CHO POLYMERS: Mucopolysaccharides (Glycosaminoglycans) form extracellular matrices.

The body makes them by polymerizing disaccharides:



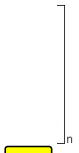
50 - 20,000 units are linked together.

Commonly used disaccharides:

Hyaluronic acid

Dermatan

glucuronic acid linked to
N-acetyl-glucosamine
or N-acetyl-galactosamine.



Slimy, mucus like consistency because they are long and associated with a lot of water.

Chondroitin-4-sulfate

Heparin

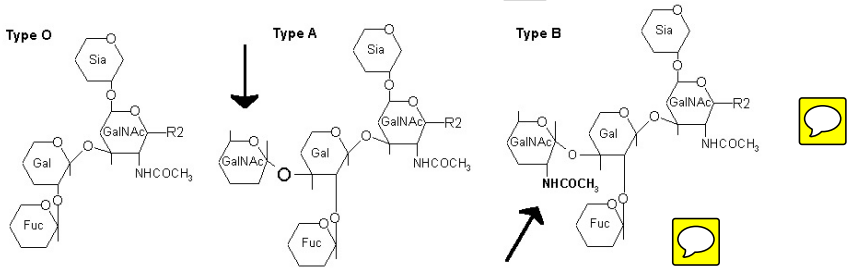
Do not memorize these four specific names and structures: However can you describe them with words you have learned up to this point (see question Q#2.6.4b)? Could you draw them if you were given that type of description?

2.10.2 COMPLEX POLYMERS ATTACHED TO PROTEINS: proteoglycans (or **mucoproteins**)

Mucopolysaccharides (previous section) are usually attached to proteins giving **proteoglycans** or **mucoproteins**. They are used for lubrication, for the damping of shocks and to make complex structures. Polysaccharide constitutes the bulk of these molecules.

Glycoproteins are proteins which contain a "small" amount of sugar. These molecules contain mostly protein. [Glycolipid: a lipid that contains sugars.]

Example:
The ABO blood group antigens



R on the figure is either a protein or a lipid.

Gal = galactose Sia = sialic Fuc = fucose (a deoxy sugar)

CONCLUDING REMARK FOR CARBOHYDRATE SECTION:

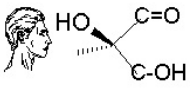
Note that polysaccharides have sizes that are not well defined.

The other biological polymers (nucleic acids and proteins) have **exact lengths**!

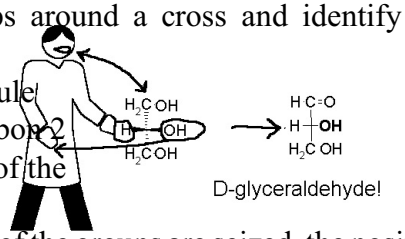
\2Ce5 2d3 1D5

. Appendix I: Answers to sugar questions

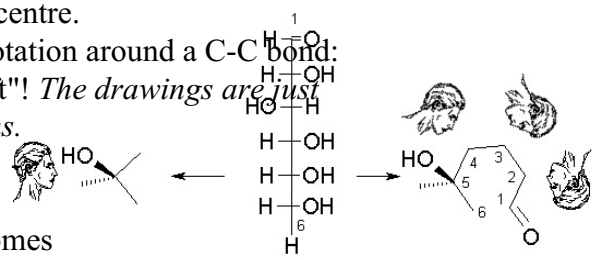
Q#1.2a



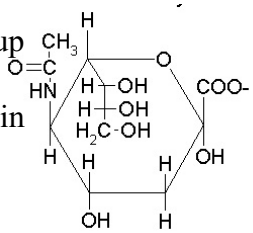
If you need more practice, randomly position groups around a cross and identify the configuration. There are 24 ways to draw this carbon!



#1.2b Only D-glyceraldehyde. With the way the molecule is held only one of the terminal carbons will be up. Carbon 2 of glycerol is said to be **prochiral**: a reaction with one of the two identical substituents converts it to a chiral group.
Two identical substituents = prochiral. Note: When two of the groups are seized, the position of the other two groups is totally defined. Name another type of prochiral group (answer at #1.6).
#1.2c nm. This is the scale of molecules. A key reference value for biochem and organic chem is the length of a carbon-carbon bond (0.15 nm). Knowing this ruler you can *estimate* the size of ANY molecule.
#1.3 Because enzymes are little robots! See #1.2b
#1.4a Any reaction that converts a prochiral group to one with four different substituents. See Q#1.2b
#1.4b The enzyme does not seize the chiral centre.
#1.5a Identically! Reminder: There is free rotation around a C-C bond: Any OH can be "on the right" or "on the left"! *The drawings are just a convention used to show the configurations.*



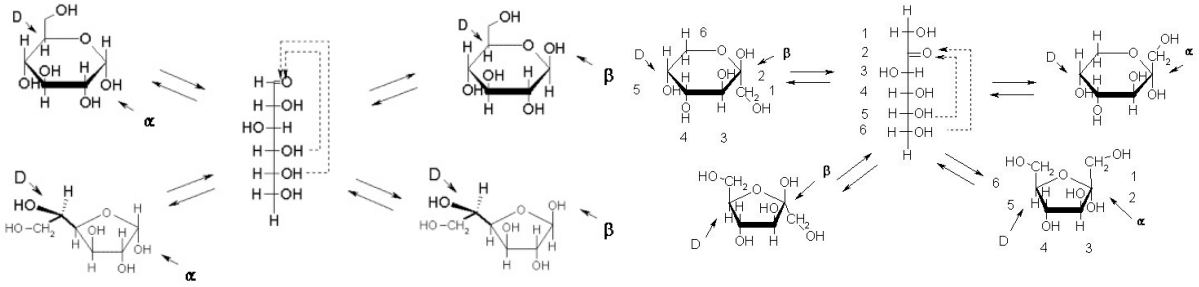
#1.5b a circle -> -> -> ->
#1.5c D-glucose
#1.6 Any carbon that with one reaction becomes a carbon with four different substituents: ketone, double bond, ring carbon, imine, etc...
#1.7 a coat of negative charges
#2.1a Water = 1000/18 = 55 M : about 10,000 x more concentrated. H^+ : pH 7 = 10^{-7} M : about 10,000 x less concentrated. Definitely enough water to make H-bonds with glucose!
#2.1b Blood contains 5 mM x 5l = **25 mMol**. Mol Weight $C_6(H_2O)_6$ = (6x12=72) + (6x18 = 108) = 180 ≈ 200 (rounded off for quick math). 400 g ÷ "200" g/mol = 2 mol/day = 2000 mMol/day. 2000mMol/day ÷ "25 hr/day" (for quick math) = **80 mMol/hr**. 80/25 ≈ 1/3 of an hour! But you will pass out before that: blood glucose can not drop to 0.
#2.2a Even with the structures available, it is not worth changing the method of estimation: do as in #2.1b: 25 mMol x "200" mg/mMol = 5,000 mg = 5g
#2.2b Glucose. For mannose change the configuration at C2, for galactose for C4, for L-glucose change all the chiral centres. Reminder: Find the reference carbon first! Then look at other things...
#2.3a L-fructose It is drawn upside down.
#2.3b All the OHs = polar group on every carbon -> freely soluble
#2.3c Since chemical reduction gives both configurations, a half of the reduction products obtained from fructose will be identical to the single reduction product obtained from glucose.
#2.3d Glucose: no difference. Fructose: only one of the two isomers would be made.
#2.4.2a When the hydroxyl on the DL carbon is not involved in the ring forming reaction. Example: the compound on the right, called a sialic group (Sia), is found in large amounts on the surface of your cells. The CH_2OH definition would call this a β anomer. This is wrong! Using the definition in



the notes you will correctly identify it as the α anomer.
For another example of the weakness of the definition, see fructopyranose (Q#2.4.3a)
#2.4.2b Crystals form as deposits of the same structure when a product precipitates from a saturated solution. Since the crystal is α-D-glucopyranose, the solubility of the α-anomer must be lower. Since an equilibrium exists, more α-anomer will be made from β as the crystal grows. This will give just one anomer in the crystal.
#2.4.2c Try to modify the solution so that β-D-glucopyranose is the less soluble of the two.
#2.4.2d None of them! Look at it in CHIME. Remember your ruler: see Q#1.2c

Haworth Wire frame Stick Ball and stick Space filling (Van der Waals radii)

#2.4.3a



#2.4.3b Enzymes chose this form and incorporate it into biological compounds in a manner that does not allow mutarotation to occur (see 2.4.2). For an example see sucrose (2.7).
#2.5a Sugars have no extensive resonance (or atoms with d-orbitals) and they should be, and are, "colorless" (in visible light), which means white. Traces of color are due to contaminants or to the start of degradation reactions (usually oxidations). Keep this principle in mind when opening biochemicals!
#2.5b 25 cm x 40 cm x 10 cm = size of a bag of cement or big bag of sugar -> you can lift it. If the density is reasonable! .25 x .4 x .1 = 0.01 m^3 = 10 kg if it were water. Organic chemicals have low densities (C,H,O,N). Fats float (lot of hydrogen), sugars sink (lot of oxygen) -> densities will be "around" 1. Most interesting biochemicals and organics (*interesting means with C,H,O,N*) are about 1.5
#2.5c Racemic mixtures. And also when the sugar is identical to its mirror image: this can happen when there is an internal plane of symmetry, i.e., one half of the molecule is a mirror image of the other half (called meso compounds). Mannitol is like this (see 2.6.3), it's a sugar found in plants.
#2.6.1a Same in both! In case of doubt, review the oxidation levels of carbon. Lactones and hemiacetals are often missed or mixed up... In case of doubt, draw the linear form (see Q#2.43a)
#2.6.1b No change in carbon oxidation level (#2.6.1a). The lactone is an ester -> hydrolysis will open it.
#2.6.1c An enzyme is specific and will detect only glucose. Fehling's will pick up all

reducing sugars.
#2.6.2a No magic: the oxidizing power must come from somewhere: an oxidation accompanies a reduction. X must be an oxidizing agent, Y is the reduced form of X.
#2.6.2b Makes them more soluble -> easier to excrete. (Lots of hydrogens = not very soluble.) Glucuronic is charged thus solubulizes more than glucose.
#2.6.3 Both configuration will be obtained at C2 -> half will be D-sorbitol. The enzyme makes only one isomer
#2.6.4a "What carbon is the amine on?" (Usually amines are on C2)
#2.6.4b It is the α-pyranose of a D-keto- nanose (9 carbons; if your Latin is a little rusty, just say "nine"-ose). C1 is oxidized to the carboxyl level, C3 is a deoxy and C5 is N-acetyl substituted. Carbons 5 to 8 have the configuration of mannose (Guess how this molecule is made?). Or you could say that in a Fischer projection, the other chiral centres all have the same configuration as the DL carbon except for carbons 5 & 6. Now if you read your description, could you draw the compound? The simple name for this compound is a sialic group (see Q#2.4.2a) : Many sialic acid groups are linked through glycoside bonds to other sugars on the surface of your membranes. What property will these groups confer to the surface of your cells? Answer at #2.10.
#2.7a The usual: removal of water. See page B-3 2. No! It's synthesis. It will cost energy...
#2.7b Fructose has the wrong configuration at carbon 3
#2.8.1 a left handed helix. One helix will turn polarized light one way, the other the other way.
#2.8.2a Below the sensitivity of the procedure: the entire glycogen molecule has only one reducing end.
#2.8.2b A 1 μm starch granule must contain <u>many</u> molecules of starch. Yes (electron micrographs often contain a 1 μm scale bar). Under the electron microscope you see glycogen as black dots in a liver cell.
#2.8.2c Does not raise the osmotic pressure. If it was stored as free glucose, a liver cell would be 0.4 M! This could burst the cell. It would also make it very hard to take up glucose from blood.
#2.8.2d 0.4% = 4 mg/g tissue = 4000 ug/g ÷ "200" ug/umol (MW of a C6 sugar see Q#2.1b) = 20 umol/g ÷ 100 uMol/min = 1/5 of a minute! Since the time is so short, was it worth doing accurate calculations?
#2.9.1 300 mm/day ÷ "25"hours/day ≈ 12 mm/hr, ÷ 60 min/hr ≈ 0.2 mm/min = 200 um/min ÷60s/min ≈ 3 um/s = 3000 nm/s ÷ 0.5 nm/residue ≈ 6000 residues/s. Without rounding off the value is 7700 residues/s.
#2.10 a negative charge.

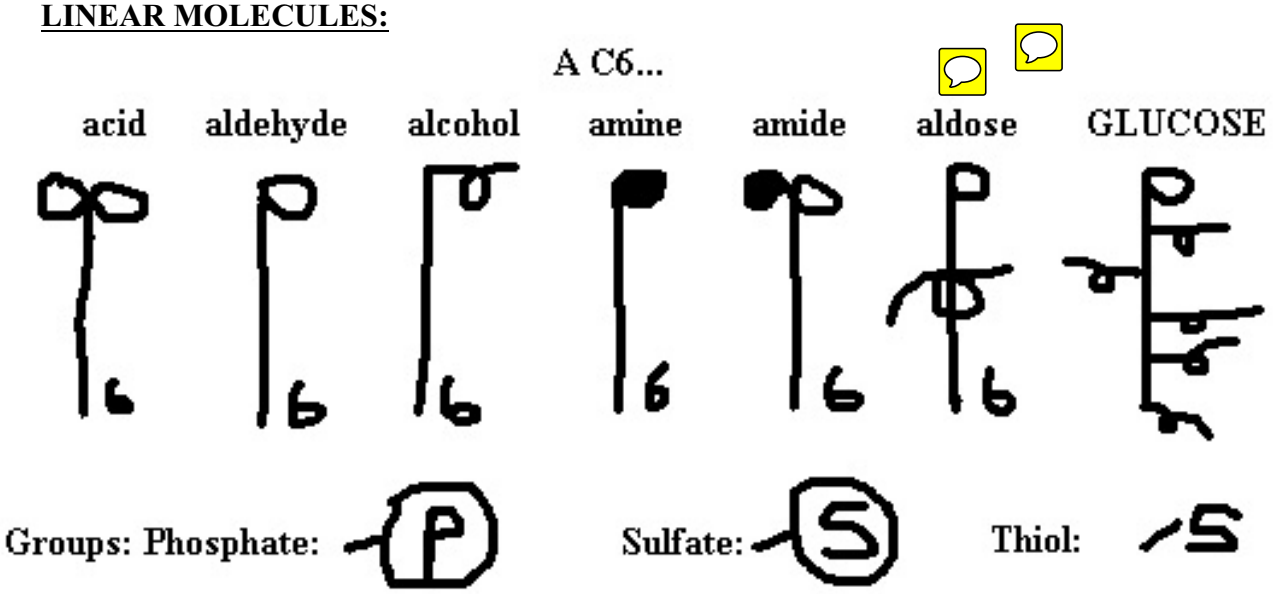
Reminder:

On your model: -Red=bond to oxidized end, -Green=bond to tail, -Blue= bond to OH

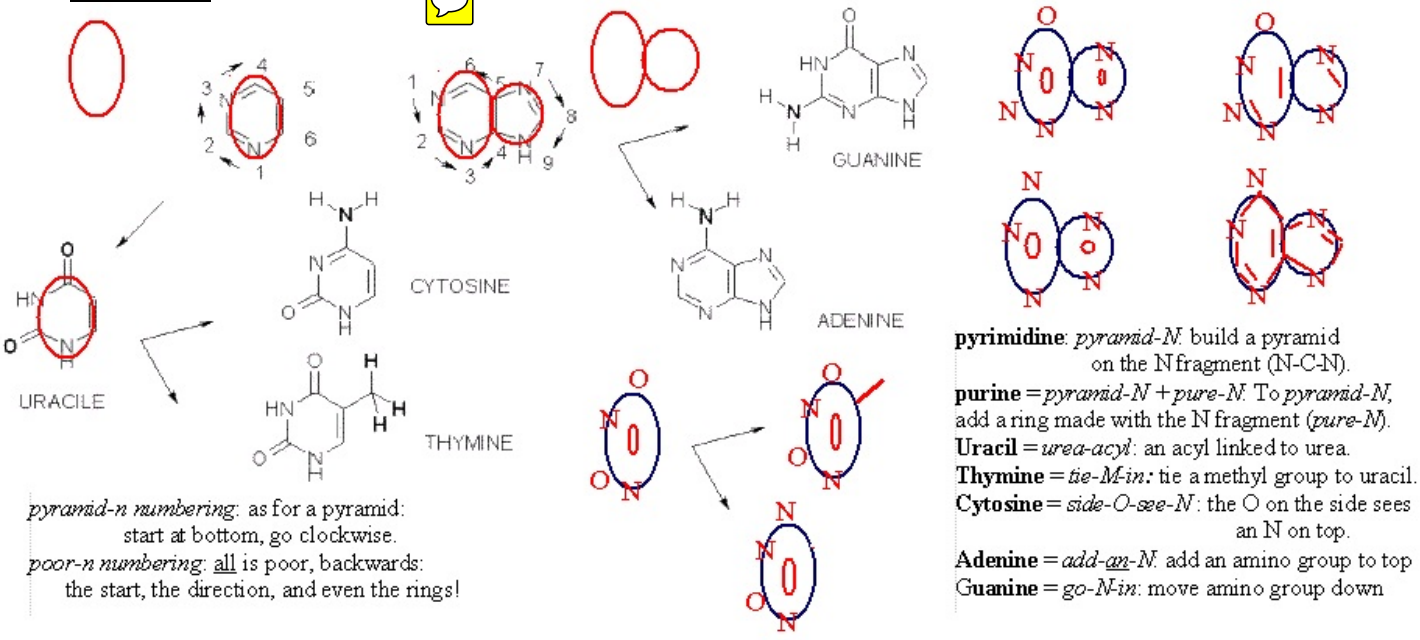
Normal osmotic pressure = 300 mOsM (150 mM KCl)

Appendix II: **AN EASY AND RAPID SHORTHAND SYSTEM FOR BIOMOLECULES**

LINEAR MOLECULES:



CYCLES:



pyramid-n numbering: as for a pyramid: start at bottom, go clockwise.
poor-n numbering: all is poor, backwards: the start, the direction, and even the rings!

pyrimidine: *pyramid-N*: build a pyramid on the N fragment (N-C-N).
purine = *pyramid-N* + *pure-N*: To *pyramid-N*, add a ring made with the N fragment (*pure-N*).
Uracil = *urea-acyl*: an acyl linked to urea.
Thymine = *tie-M-in:* tie a methyl group to uracil.
Cytosine = *side-O-see-N*: the O on the side sees an N on top.
Adenine = *add-an-N*: add an amino group to top
Guanine = *go-N-in*: move amino group down

SUGARS: