Lecture 2

BT 203

Biochemistry

3-0-0-6

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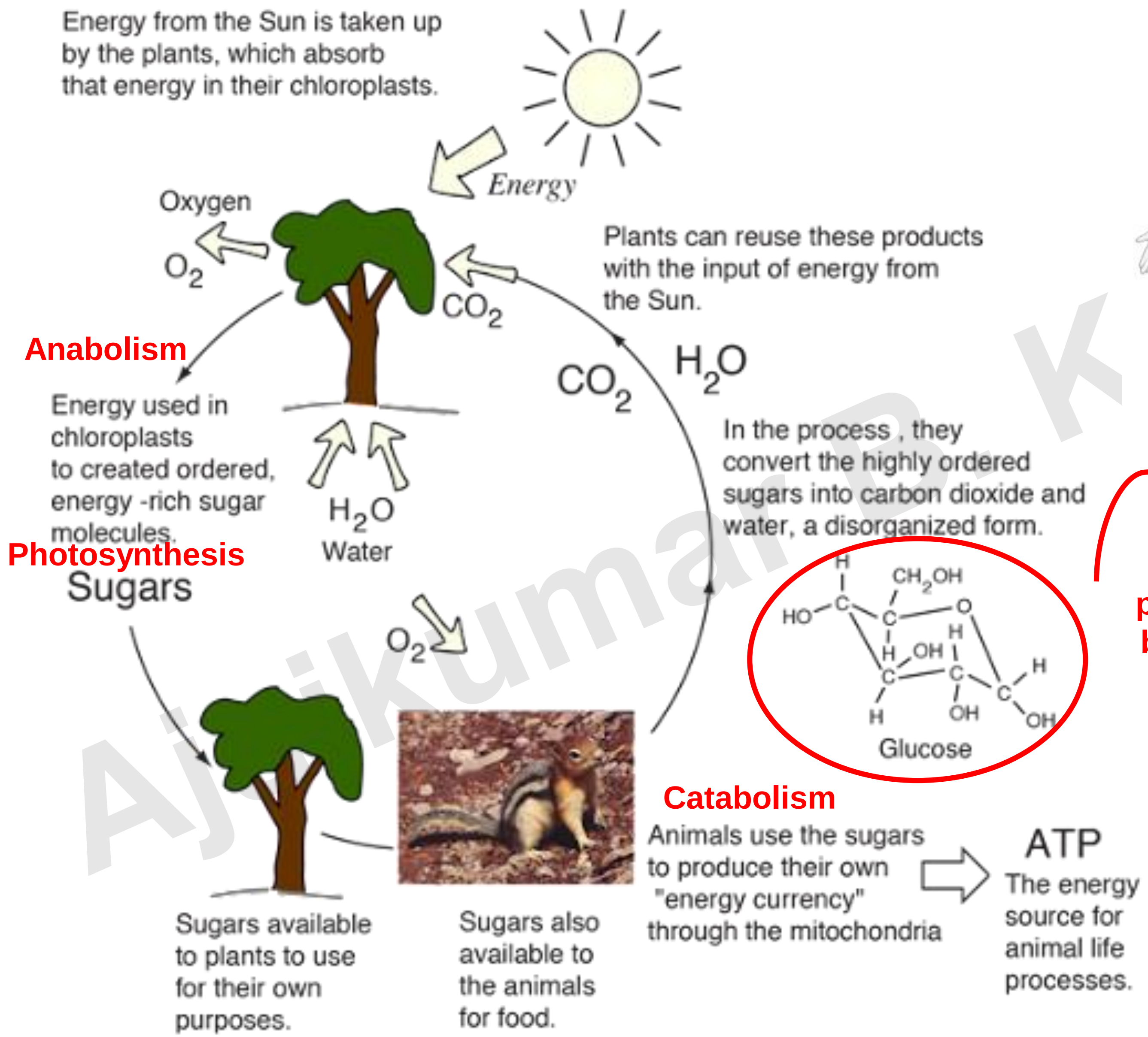
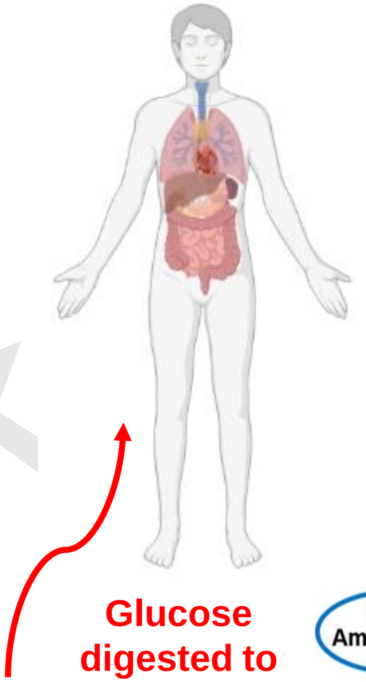
Important questions:

- How does the energy from sunlight we use for our day to day life?
- What are the major types of biomolecules that build up our cells, tissues, organs and body?
- What are the different levels of organization in our body?
- What are the different types of cells and tissues of our body?
- What are the different organ systems of our body?
- Why we call living organisms as highly complex machines?

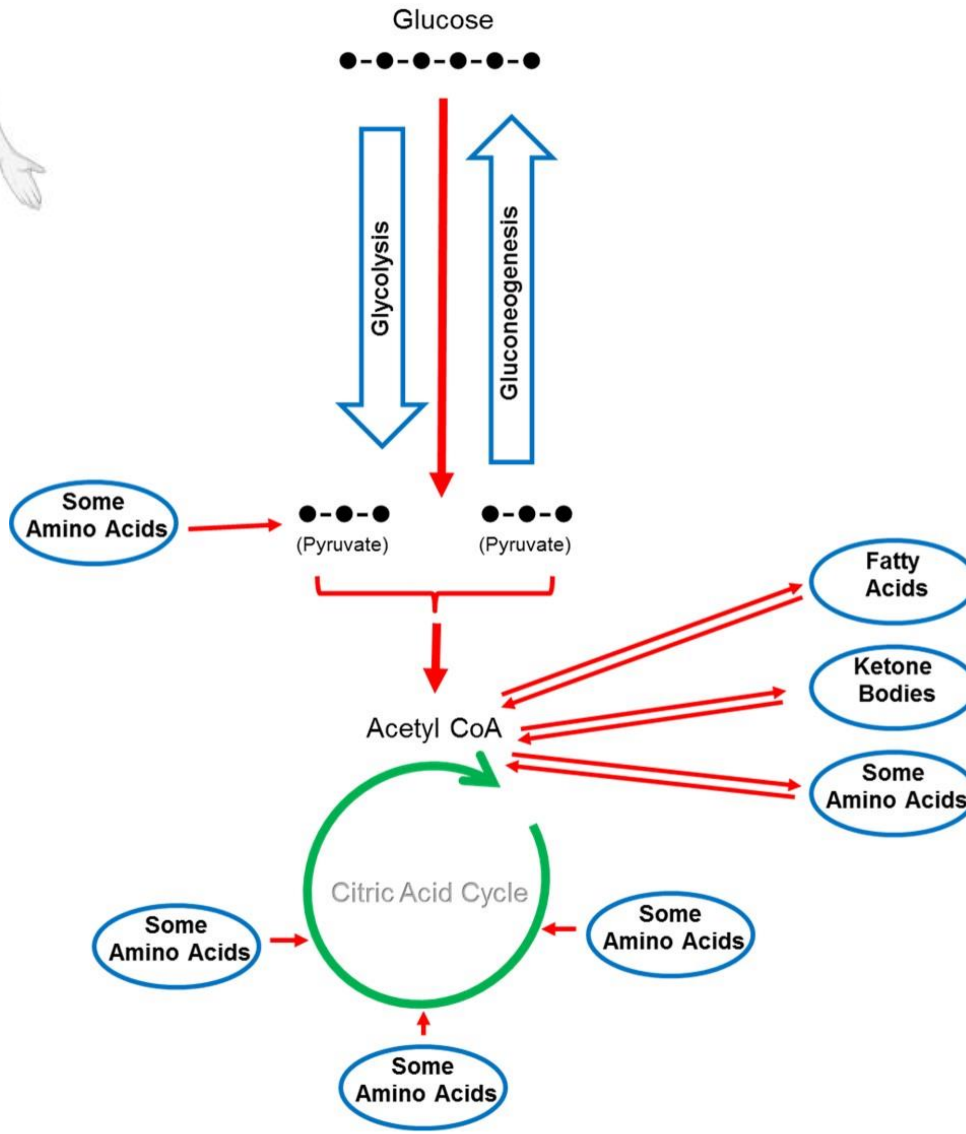
Energy Cycle





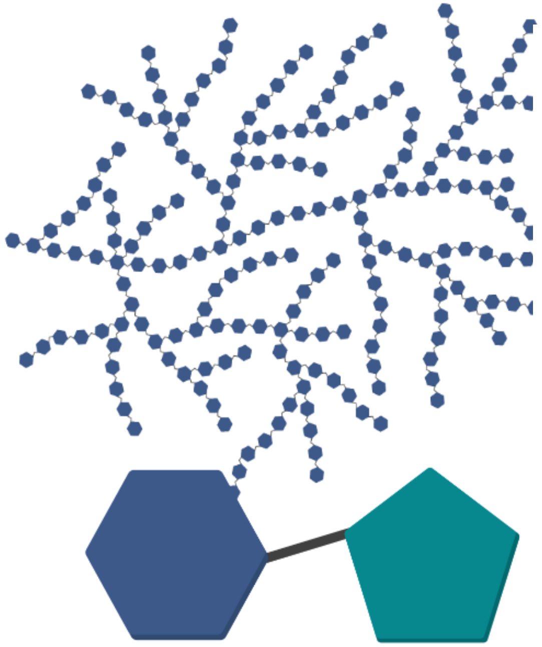
Glucose digested to produce other biomolecules

Glucose is the primary molecule of life

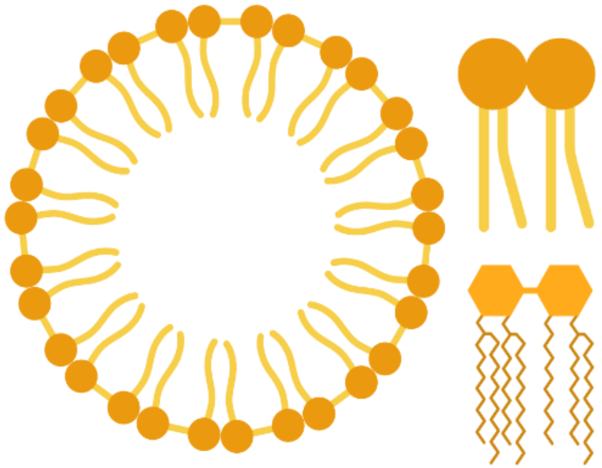


Building Blocks of Life

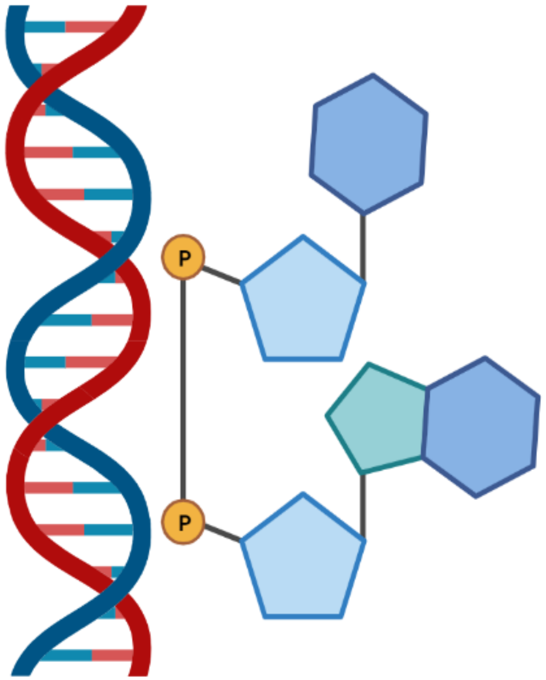
Carbohydrates



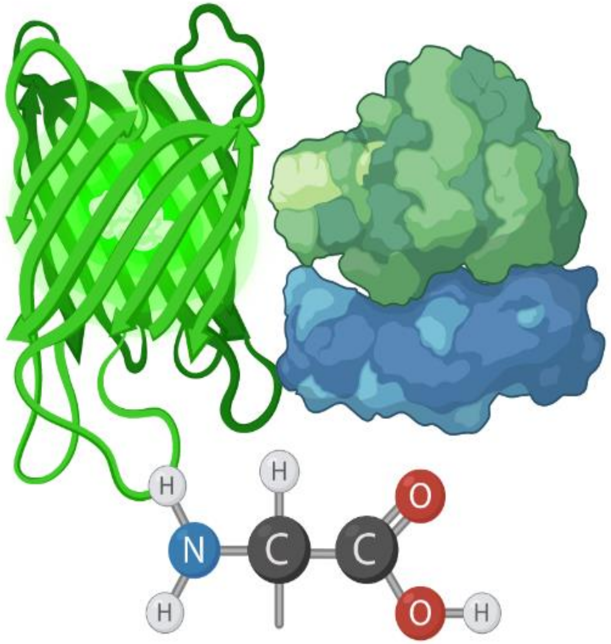
Lipids



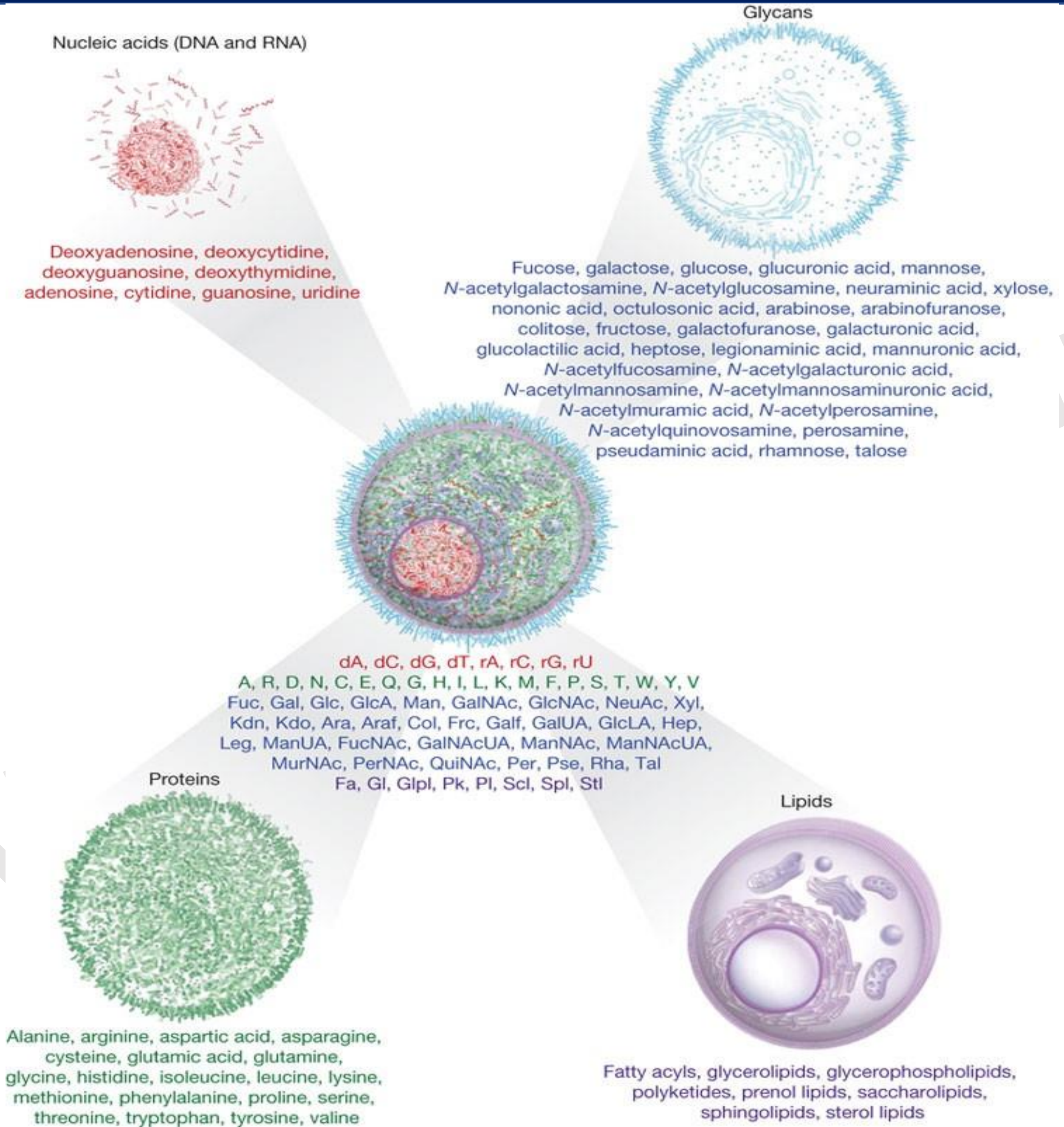
Nucleic Acids



Proteins



Building Blocks of Life

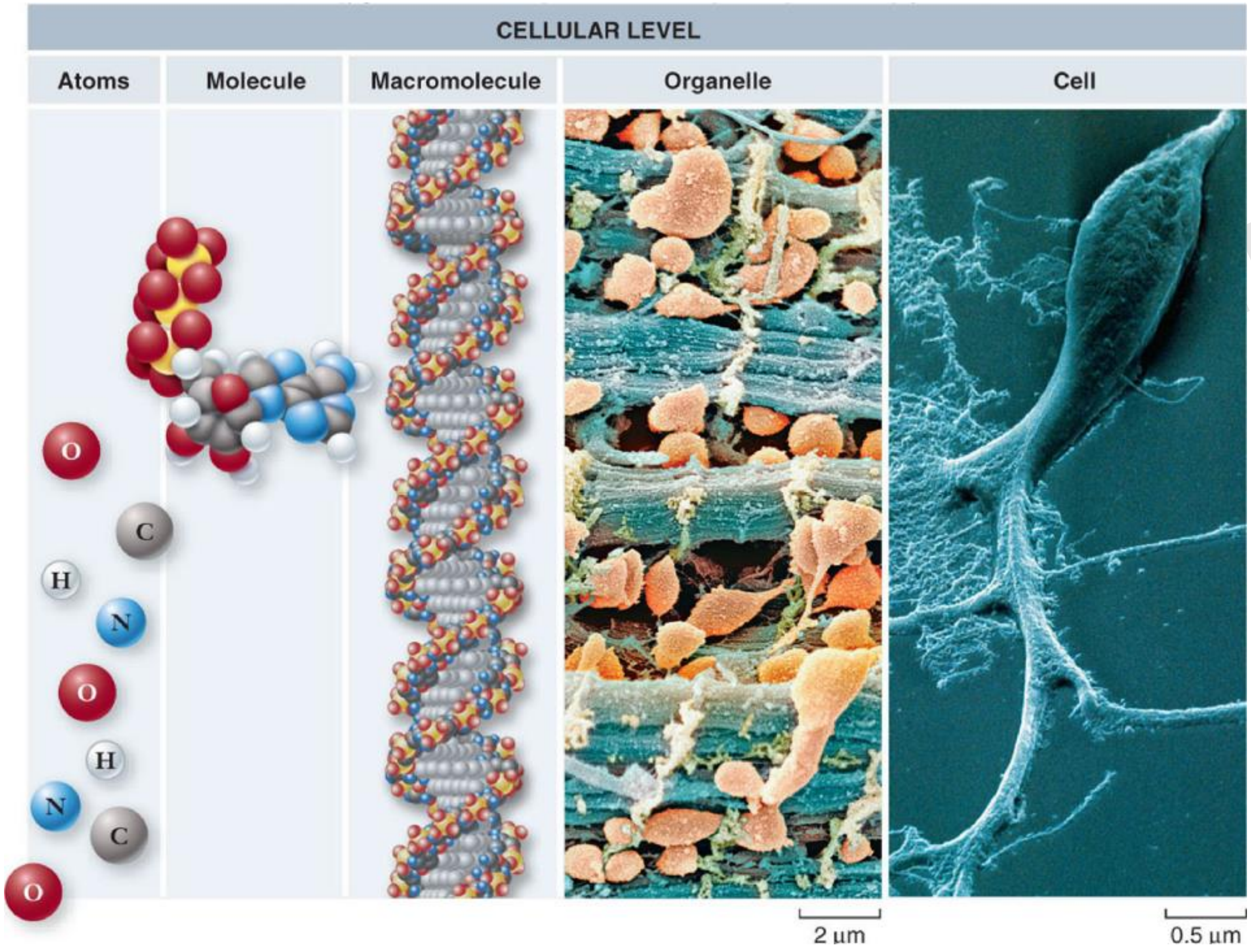


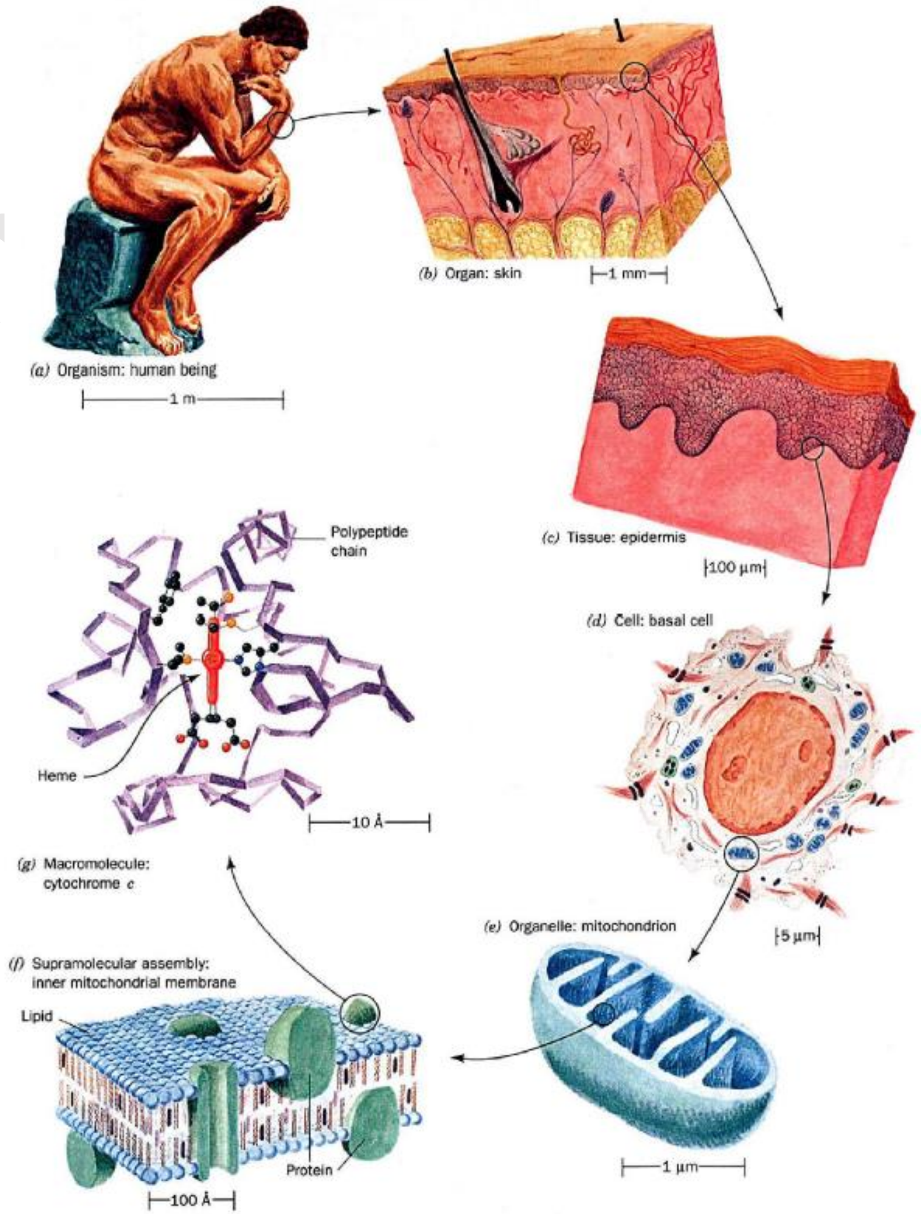
68 molecules formed from the fundamental four bio-molecules that form cells

- 20 natural amino acids used in the synthesis of proteins
- 32 carbohydrate molecules are the precursor of the major glycans present
- 8 major lipid families contributing to all the lipids present in the cells
- 8 nucleic acids in building the genetic code of life- DNA, RNA

Source: Marth, J. A unified vision of the building blocks of life. *Nat Cell Biol* **10,** 1015 (2008). https://doi.org/10.1038/ncb0908-1015

Levels of Organization

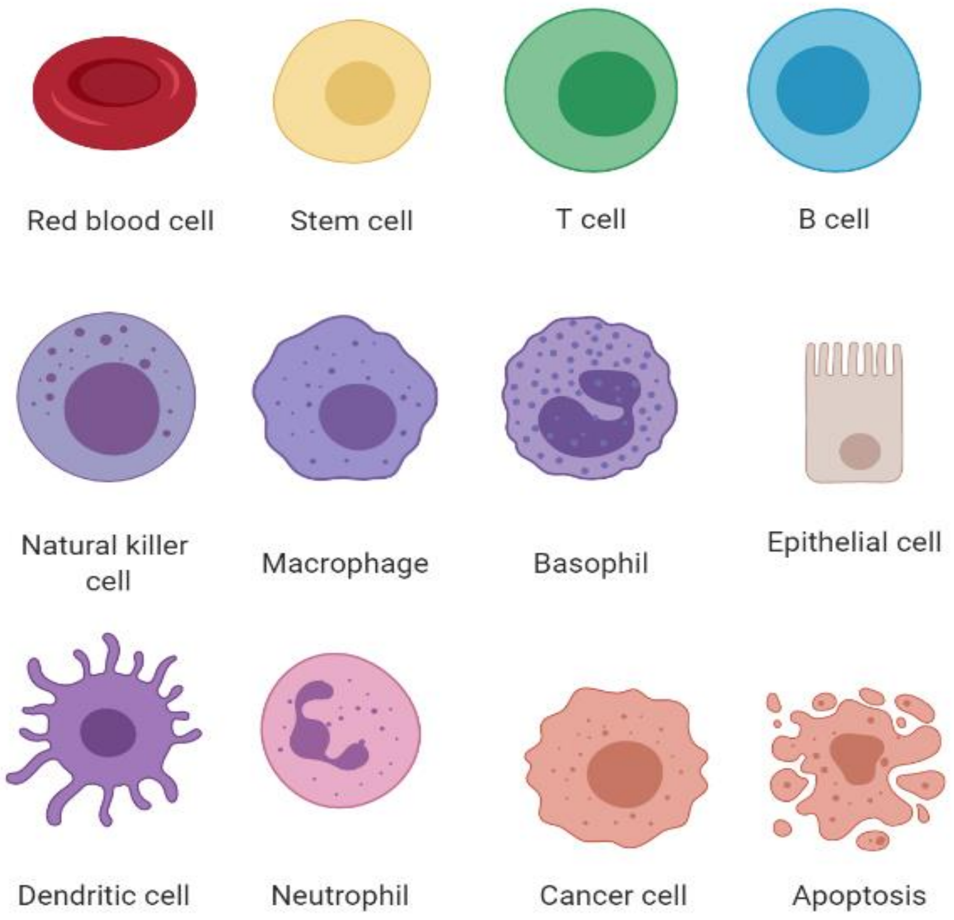




Different Cells and Tissues of Our Body

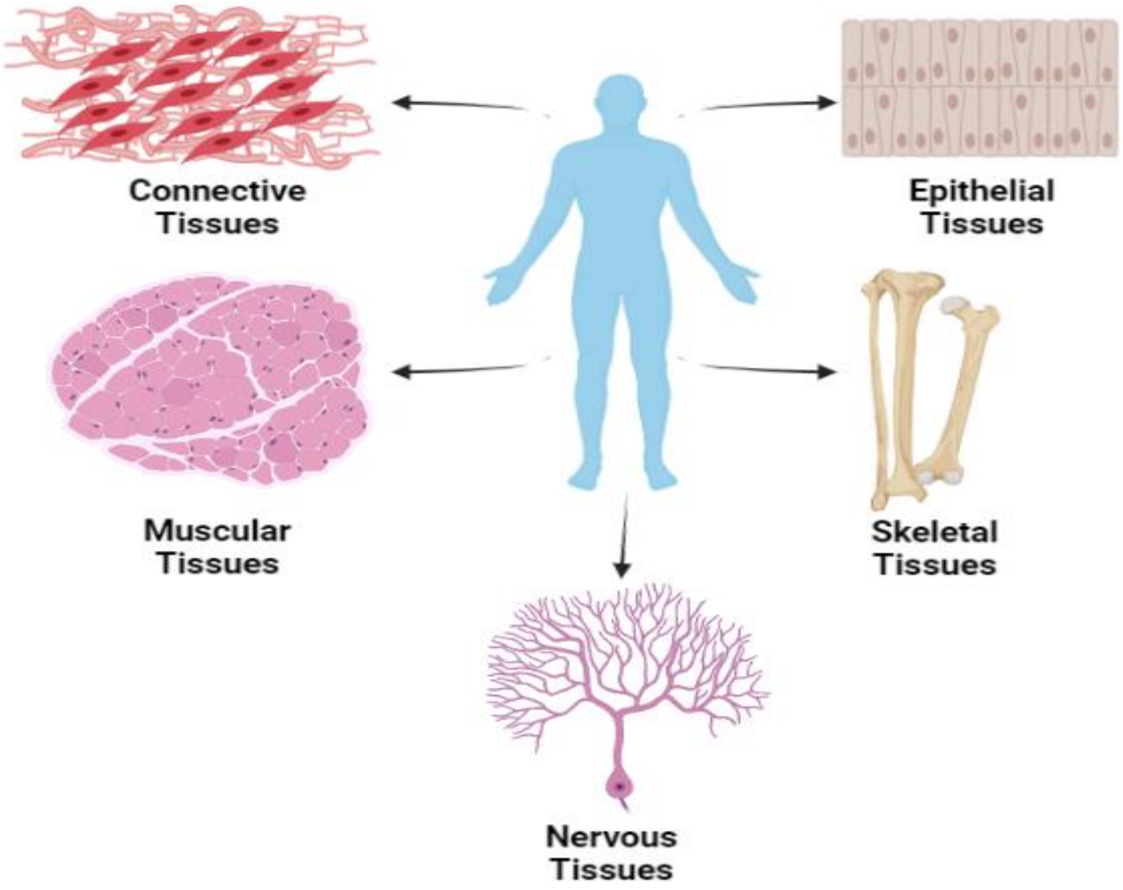
Types Cells

- ❖ 37.3 trillion cells
- ❖ 200 different cell types



Tissues

- ❖ Connective , epithelial, Muscle and Nervous tissues
- ❖ Gluteus Maximus-largest muscle
- ❖ Masseter-Strongest muscle



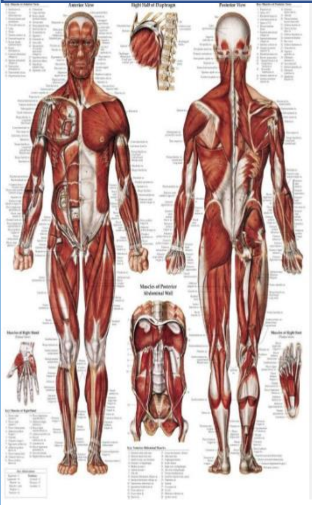
Organ System

Skeletal System

Consists of
- 206 bones
- Cartilage
- Ligaments

Main Functions
- Provide Structure
- Protects Internal Organs

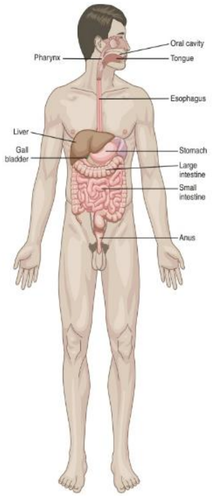
Muscular System



Consists of
- 600 muscles

Main Functions
- Supports the body
- Allows movement

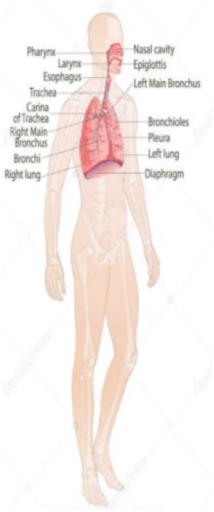
Digestive System



Consists of
- Oral cavity
- Esophagus
- Stomach
- Intestine
- Rectum

Main Functions
- Digestion
- Absorption
- Secretion

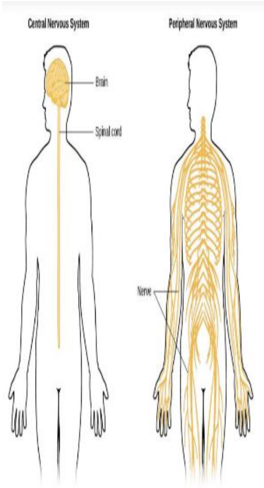
Respiratory System



Consists of
- Nose
- Trachea
- Lungs

Main Functions
- Gas exchange
- Acid-base balance
- Defense and metabolism
- phonation

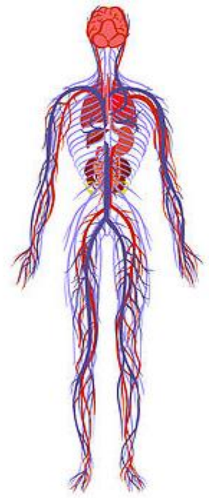
Nervous System



Consists of
- Brain
- Spinal cord
- 7 trillion nerves

Main Functions
- Sensation
- Integration
- Response

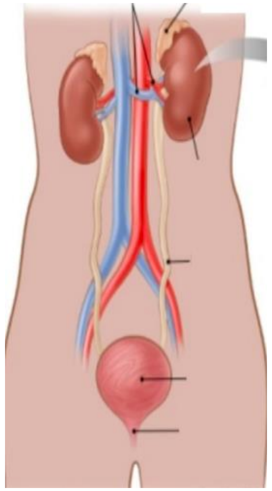
Circulatory System



Consists of
- Heart
- Blood vessels
- Blood
- Lymphatic system

Main Functions
- Transports …. to and from the tissues

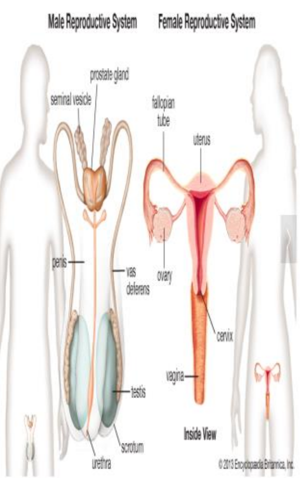
Urinary System



Consists of
- Skin
- Liver
- Kidneys
- lungs

Main Functions
- Excretion
- Acid-base balance

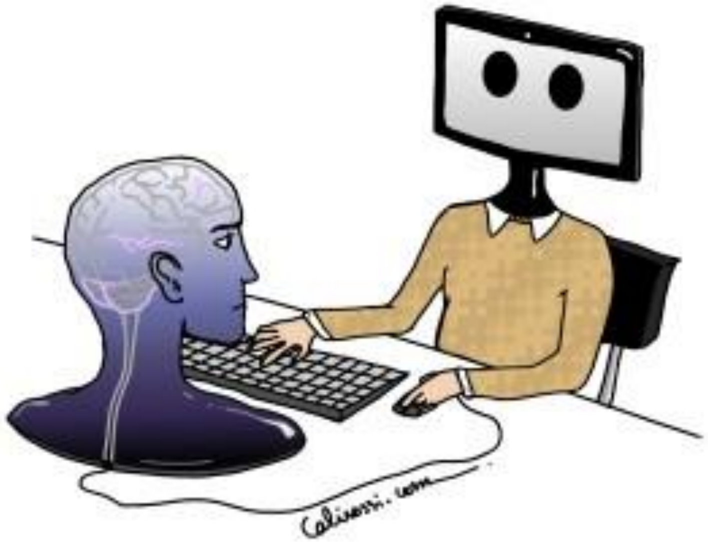
Reproductive System

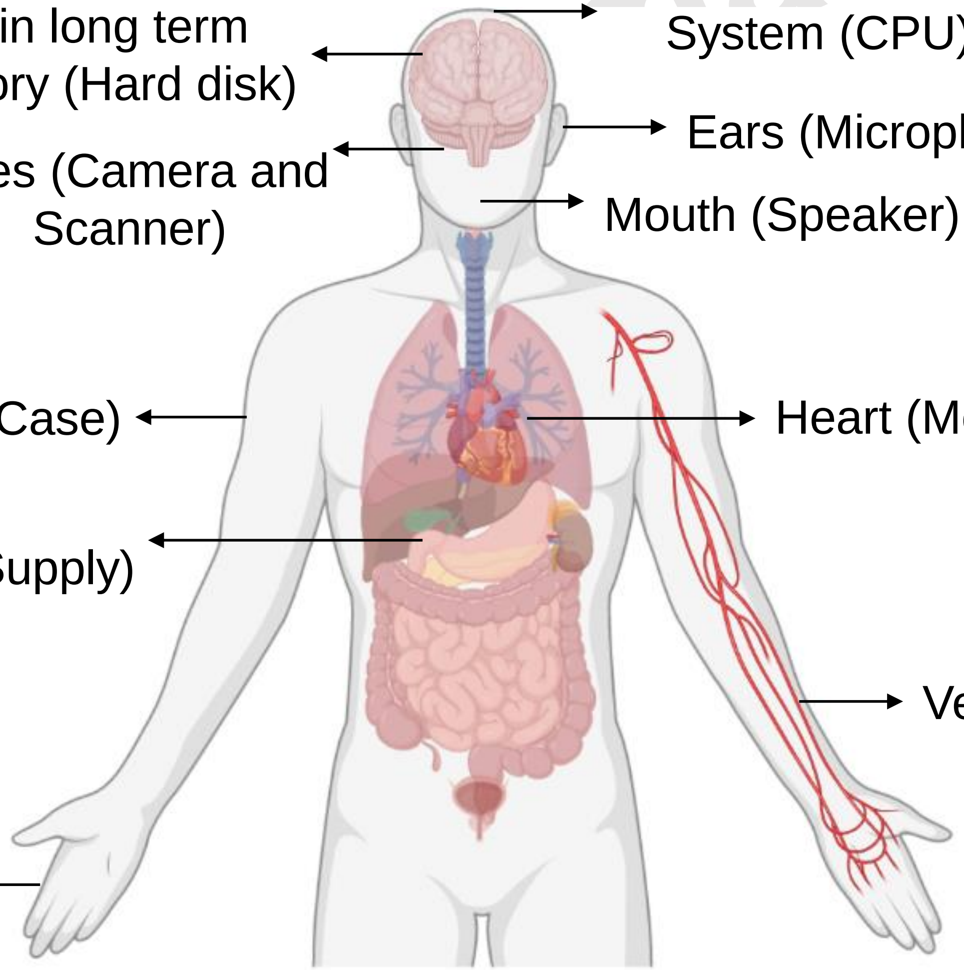


Consists of
- Uterus
- Ovaries
- Prostate
- testes

Main Functions
- Sexual development
- Reproduction

Is Human Body a Machine ??





Key Concepts

- Energy Cycle
- Types of biomolecules- Carbohydrates, Lipids, Nucleic Acids, Proteins
- Levels of Organization
- Types of organs, tissues and cells
- Facts about human body

Lecture -2

Slide 3:

As you are well aware about the energy cycle of life, where the light from the sun, the primary source of energy is utilized by the plants to produce energy rich sugar molecules. This is done by a process of photosynthesis in the chloroplast of plant leaves, which we will be discussing in detail in the subsequent classes. After which the animals eat the plants and catabolize the sugars in a process of oxidative phosphorylation to produce the ATP molecule, the energy currency of life. Glucose the primary energy source for most of the living organism in the plant can be catabolize to form other major building blocks of the body.

Apart from producing ATP, glucose can be further utilized by the other process of the body to produce fatty acids, amino acids which are the precursor molecules

How many of you know that glucose is not the only source of energy in our body?

Ans: During fasting or prolonged dieting, lipids and even proteins are metabolized to produce the energy required for sustenance at a cost. We will cover this interesting phenomenon in the integration of metabolism where we will see how all the process in the body is interlinked and tightly regulated.

Slide 4:

As indivisible units of life, the cells of all organisms consist of four fundamental macromolecular components: nucleic acids (including DNA and RNA), proteins, lipids and carbohydrates.

Carbohydrates are your body's main source of energy: They help fuel your brain, kidneys, heart muscles, and central nervous system. For instance, fiber is a carbohydrate that aids in digestion, helps you feel full, and keeps blood cholesterol levels in check. Your body can store extra carbohydrates in your muscles and liver for use when you're not getting enough carbohydrates in your diet.

Lipids serve as metabolic fuels alternative to glucose. Apart from being energy reserve for body, they serve as structural components of biological membranes and as biologically active molecules exerting a wide range of regulatory functions, For example: the lipophilic bile acids aid in lipid emulsification during digestion of fats

Nucleic acids are an important class of macromolecules found in all cells and viruses. The functions of nucleic acids have to do with the storage and expression of genetic information. Understanding how genes are read by the cell and used to create proteins creates enormous opportunities for understanding disease

Proteins are the most abundant macromolecule present in the cells. Every cellular process involves protein and it's the main source of structural and functional integrity of cells. The basic structure of protein is a chain of amino acids.

We will discuss each type of bio-macromolecule, its types, metabolism and its importance in biology in details in the subsequent classes.

Slide 5:

There are 68 molecules that contribute to the synthesis and primary structures of the 4 fundamental macromolecular components of all cells: nucleic acids, proteins, glycans and lipids. DNA and RNA are produced from the 8 nucleosides. Although deoxyribose (d) and ribose (r) are saccharides, they are an integral part of the energetically charged nucleoside building blocks that are used to synthesize DNA and RNA. There are 20 natural amino acids used in the synthesis of proteins. Glycans/carbohydrates derive initially from 32, and possibly more, saccharides used in the enzymatic process of glycosylation and are often attached to proteins and lipids, although some exist as independent macromolecules. Lipids are represented by 8 recently classified categories and contain a large repertoire of hydrophobic and amphipathic molecules. The number of molecular building blocks does not directly infer the relative structural complexity of the repertoire of each component

Slide 6:

Before you begin to study the different structures that from the human body, it is helpful to consider its basic architecture; that is, how its smallest parts are assembled into larger structures. It is convenient to consider the structures of the body in terms of fundamental levels of organization that increase in complexity: subatomic particles, atoms, molecules, organelles, cells, tissues, organs, organ systems, organisms.

To study the chemical level of organization, scientists consider the simplest building blocks of matter: subatomic particles, atoms and molecules. All matter in the universe is composed of one or more unique pure substances called elements, familiar examples of which are hydrogen, oxygen, carbon, nitrogen, calcium, and iron. The smallest unit of any of these pure substances (elements) is an atom. Atoms are made up of subatomic particles such as the proton, electron and neutron. Two or more atoms combine to form a molecule, such as the water molecules, proteins, and sugars found in living things. Molecules are the chemical building blocks of all body structures.

A human cell typically consists of flexible membranes that enclose cytoplasm, a water-based cellular fluid together with a variety of tiny functioning units called organelles. In humans, as in all organisms, cells perform all functions of life. A tissue is a group of many similar cells (though sometimes composed of a few related types) that work together to perform a specific function. An organ is an anatomically distinct structure of the body composed of two or more tissue types. Each organ performs one or more specific physiological functions. An organ system is a group of organs that work together to perform major functions or meet physiological needs of the body.

Slide 7:

Cells are the basic unit of life on earth. Humans are made up of trillions of cells. Cells can be thought of as tiny packages that contain minute factories, warehouses, transport systems, and power plants. They function on their own, creating their own energy and self-replicating.

Different cell types can look wildly different, and carry out very different roles within the body. For instance, a sperm cell resembles a tadpole, a female egg cell is spherical, and nerve cells are essentially thin tubes. Despite their differences, they often share certain structures; these are referred to as organelles- nucleus. Plasma membrane, lysosomes, mitochondria, endoplasmic reticulum, golgi apparatus.

A tissue is a group of cells that have similar shape and function.
There are 4 basic types of tissue: connective tissue, epithelial tissue, muscle tissue, and nervous tissue.

1) Connective tissue is the most abundant tissue type in our body. It connects other cells and tissues together. It is typically found in our bones, cartilage, adipose, collagen, blood and many other areas in our body
2) Epithelial tissue - It is found in the lining of our stomach, intestines, trachea, and any other passageways in our body as a form of protection, absorption of nutrients, and secretion of fluids
3) Muscle tissue tissue allows for movement by receiving signals (excitable tissue) to contract our muscles. This results in being able to move our arms, helping with food moving through the digestive system, and allowing our heart to contract
4) Nerve tissue Nervous tissue conducts and transmits signals (excitable tissue) throughout our body to other muscles and glands. This forms a great way of communication between different organs in the body to maintain homeostasis

Slide 8:

Organ System

The tissues combine to form organs. An organ is a part of body which performs definite function. The final units of organization in the body are called systems. A system is a group of organs ach of which contributes its share to the function of the body as a whole.

Human body consists of 8 major organ systems.

Facts about our organ system

Skeletal system:

Inside our body there are 206 bones. Babies are born with 300 bones. It’s not those bones disappear as we grow older. Instead, these tiny bones fuse together to form the larger bones of the skeletal system. Each bone plays an important role in mechanics of your body and if one bone is broken, all the bones around it can not function properly.

There are 2 types of bones- 1) Cortical bone- made of hard and dense bone -ex. Femur or thighbone
2) Trabecular bone- soft and spongy-ex. Pelvis or hip bone

The skeletal system is not very common- only 10% of the species on earth are vertebrates including humans and rest 90% are invertebrates.

Muscular System:

There are more than 600 muscles in our body including those muscles in the arms and legs as well as muscles deep inside your body.
There are three types of muscles-

1) skeletal muscle: Connected to bones via tendons. Predominantly involved in movement, providing structural support and maintaining posture
2) Smooth muscle- found in different organs of our body-ex. digestive organs, respiratory organs. They are involuntary.
3) Cardiac muscle-Found only in the heart. That allows the heart to beat.

The largest muscles in the body is gluteus maximus of buttocks and the smallest muscles are tympani and stapedius of inner ear. The hardest working muscle is in the heart-it pumps around 2500 gallons of blood per day.
Busiest muscle is in your eye -in an hour of reading eye muscles makes 10,000 coordinated movements

Digestive System:
The digestive system includes structures that form the alimentary canal and the accessory organs of digestion. The alimentary canal is a single continuous tube that includes the oral cavity, pharynx, esophagus, stomach, and intestines. It is also called the digestive tract or the gastrointestinal (GI) tract.
Digestion breaks down large compounds in food and liquids into smaller molecules that can be absorbed into the bloodstream. The absorbed nutrients include carbohydrates, protein, fats, minerals, and vitamins. They are processed, then delivered throughout the body and used for energy, growth, and cell repair.
The six major activities of the digestive system are ingestion, propulsion, mechanical breakdown, chemical digestion, absorption, and elimination. First, food is ingested, chewed, and swallowed. Next, muscular contractions propel it through the alimentary canal and physically break it down into tiny particles. Digestive fluids chemically break down the nutrients from food into molecules small enough for absorption. Finally, indigestible substances are eliminated as waste.

Respiratory System:

The respiratory organs include:

- **Mouth and nose:** Openings that pull air from outside your body into your respiratory system.
- **Pharynx (throat):** Tube that delivers air from your mouth and nose to the trachea (windpipe).
- **Trachea:** Passage connecting your throat and lungs.
- **Bronchial tubes:** Tubes at the bottom of your windpipe that connect into each lung.
- **Lungs:** Major component of respiratory system**.** Two organs that remove oxygen from the air and pass it into your blood.

In humans, the average breathing, or respiratory rate, mostly depends on age. A newborn's normal breathing rate is about 40 to 60 times each minute and may slow to 30 to 40 times per minute when the baby is sleeping. The average resting respiratory rate for adults is 12 to 16 breaths per minute, and up to 40 to 60 breaths per minute during exercise.

Nervous System:

Nervous system comprises of

1) Central nervous system- i.e. Brain and spinal cord
2) Peripheral nervous system-i.e. neurons

The nervous system is the body's communication system. The human body contains billions of nerve cells -about 100 billion in the brain and 13.5 billion in the spinal cord.

These nerve cells take in information through the body's senses: touch, taste, smell, sight, and sound. The brain interprets these sensory cues to understand what's going on outside and inside the body. This allows a person to use their body to interact with their surrounding environment and control their body functions.

Circulatory System:

It includes the heart, blood vessels and blood, and is vital for fighting diseases and maintaining homeostasis. The system's main function is to transport blood, nutrients, gases and hormones to and from the cells throughout the body.

The circulatory system in the human body stretches about 66,000 miles, which is more than two and a half times the circumference of the Earth.

Blood is a liquid tissue: fluid makes up more than half; plasma, white and red blood cells make up the remainder. Red blood cells (erythrocytes) are the body's cellular lungs; their job is to supply oxygen to every cell and remove carbon dioxide. Each hemoglobin molecule in the red blood cell can carry four oxygen molecules. The hemoglobin in red blood cells scoops up oxygen molecules in oxygen-rich tissues such as the lungs, and then releases them in oxygen-deprived tissues throughout the body. Each second, we lose about 3 million red blood cells only to be replaced by the same number produced in the bone marrow.

Urinary System:

Our urinary tract consist of two kidneys, two ureters, a bladder, and a urethra.

Kidneys act as filters to clean waste from blood and make urine. Each kidney has one million filtering units called nephrons. Together, nephrons filter about a half of a cup of blood per minute. This translates to about 45 gallons per day. By the time you are 40 years old, your kidneys have filtered blood volume equivalent to an Olympic-size pool! And for an average 150- to 180-pound adult, the kidneys filter all the blood in their body once every 38 to 48 minutes. That is all the blood in our body is filtered 40 times through kidneys everyday. And the human bladder can stretch to hold 400mLof urine.

Reproductive System:

Males produce the smallest human cell — the sperm, which is only 5 micrometers including the sperm's "tail."

A female's ovum, is the largest human cell, which is about 120 micrometers in diameter

Slide 9:

After learning how the body is constituted, can we compare human body with a machine? As most of you may know, that human body contains layers after layers of complexity, some even say that it is the most complicated and sophisticated machinery present.

Just step back and take a few minutes to think about how amazingly similar our bodies can be to that of a computer.

For example: Web cam detect light and send signals through the optic lens to the visual and the computer to the CPU. Just exactly like how the eyes works sending visual signals to the brain through optic nerves.

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Lecture 3

BT 203

Biochemistry

3-0-0-6

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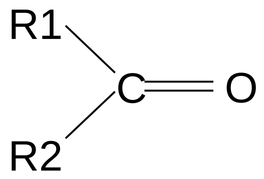
Key Questions

- What are carbohydrates?
- What are the different types of carbohydrates?
- What are the different types of representation a carbohydrate have?
- What are the structural representation of carbohydrates?
- How does carbohydrates forms rings like structures?
- What type of tests are required to detect the carbohydrates?
- What are the types of disaccharides?

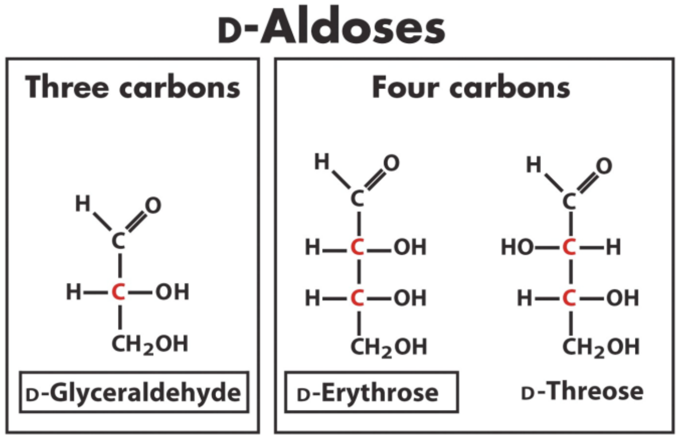
Carbohydrates

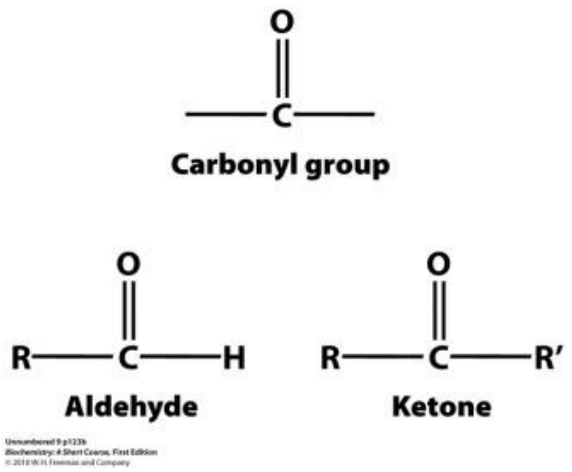
They are important for energy storage, cell-cell signaling and cell wall structures.

- Most have the formula (CH2O)n
- **Three major classes of carbohydrates: mono, oligo, poly saccharides**
- Monosaccharides are single sugars and can be divided into 2 groups: aldoses, which have aldehyde groups, and ketoses, which have ketone groups.



Aldehyde is a carbonyl (C=O) where One R grp is H
Ketone is a carbonyl where No R grp is H





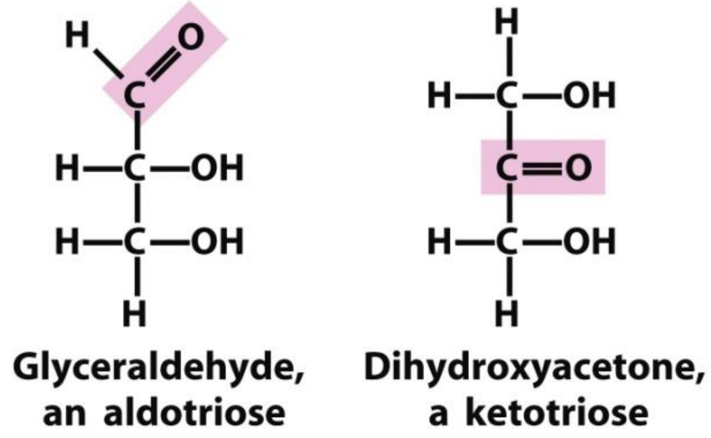


Figure 7-1a
Lehninger Principles of Biochemistry, Fifth Edition
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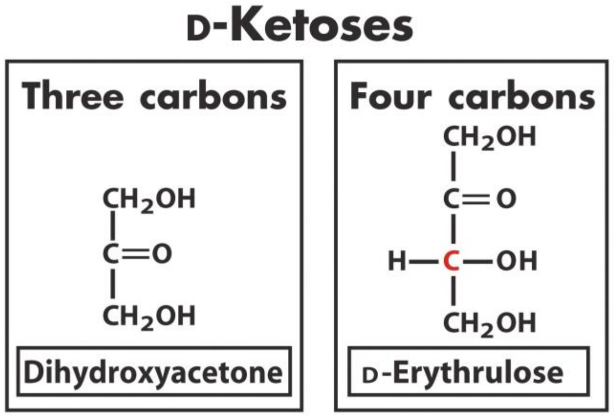


Types of monosaccharides

Aldoses

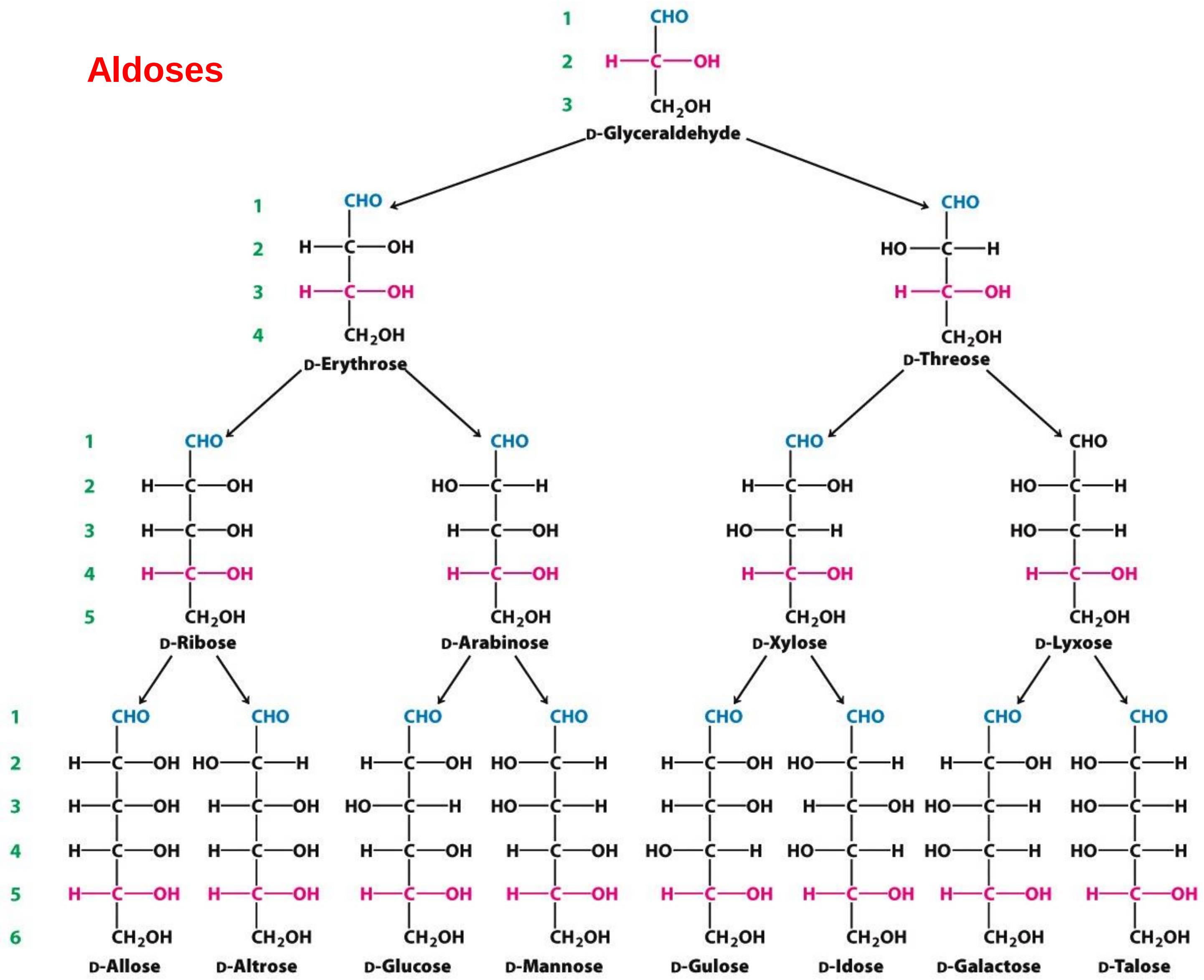


Figure 9.2
Biochemistry: A Short Course, First Edition

Ketoses

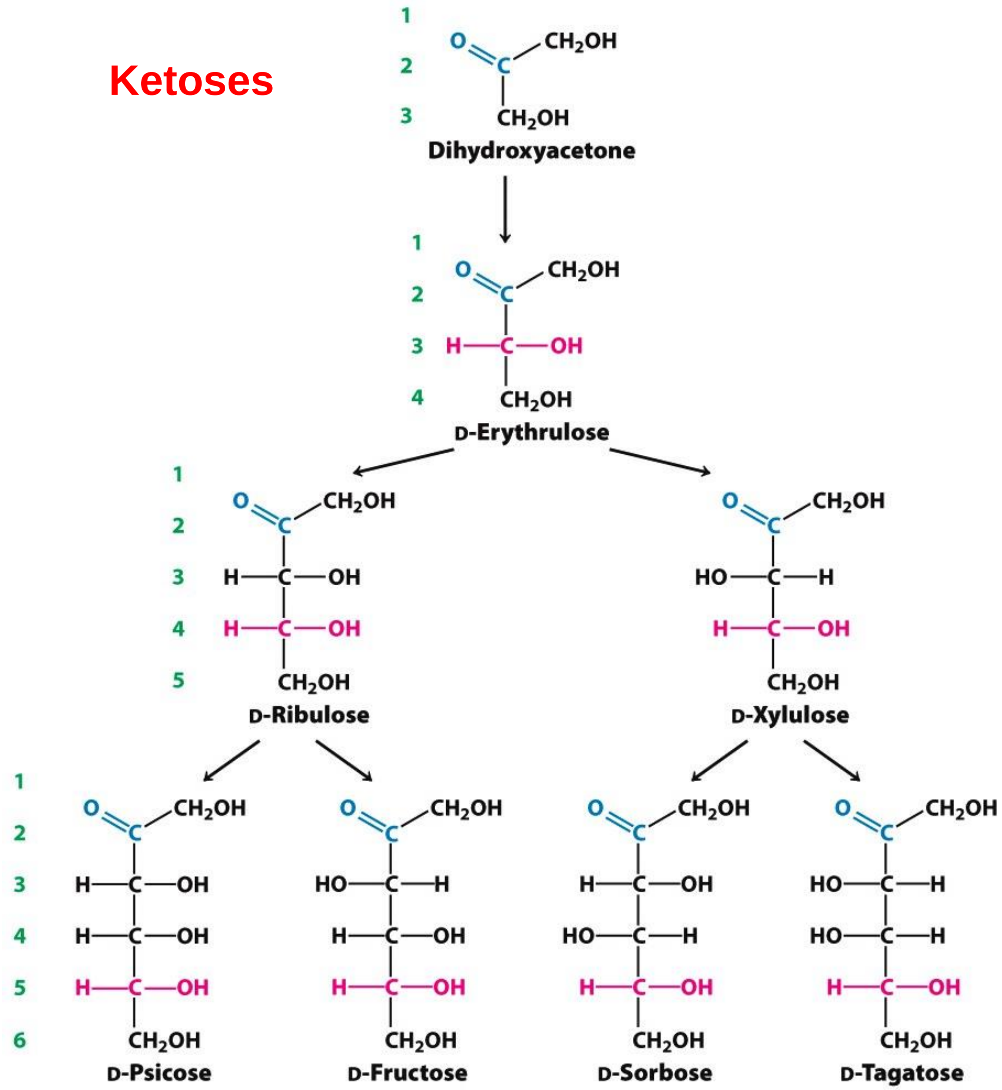
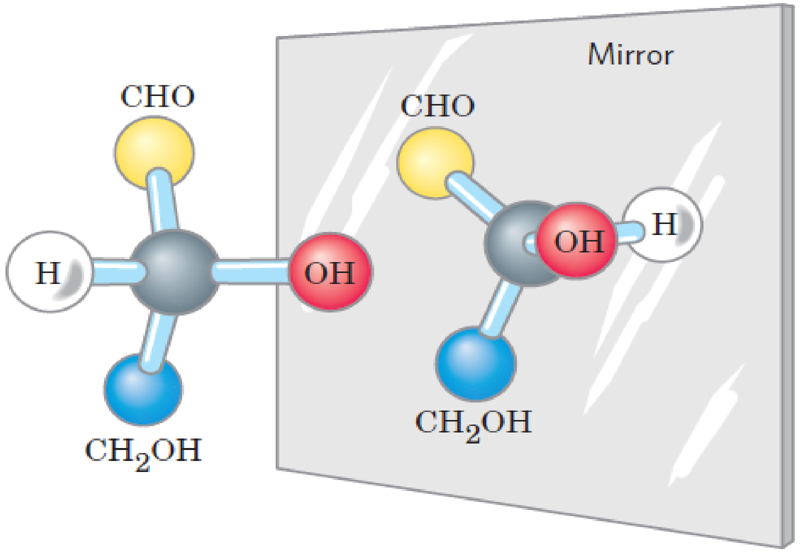


Figure 9.3
Biochemistry: A Short Course, First Edition

Monosaccharides



Ball-and-stick models

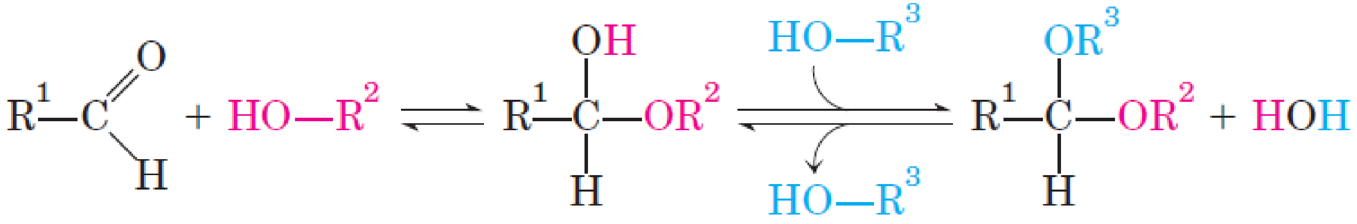
D-Glyceraldehyde L-Glyceraldehyde

Fischer projection formulas

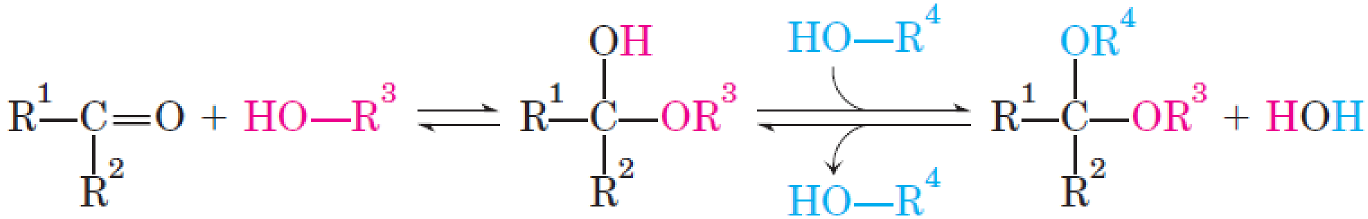
D-Glyceraldehyde L-Glyceraldehyde

Perspective formulas

Formation of hemiacetals and hemiketal



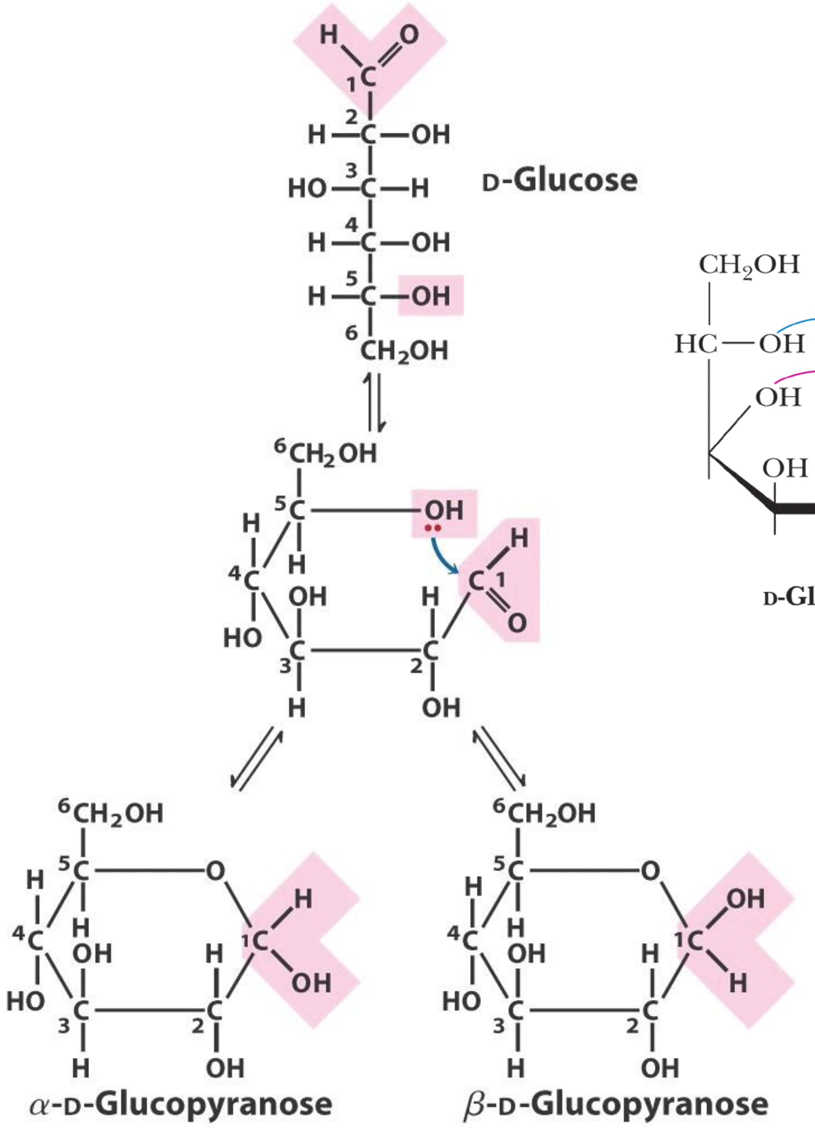
Aldehyde Alcohol Hemiacetal Acetal

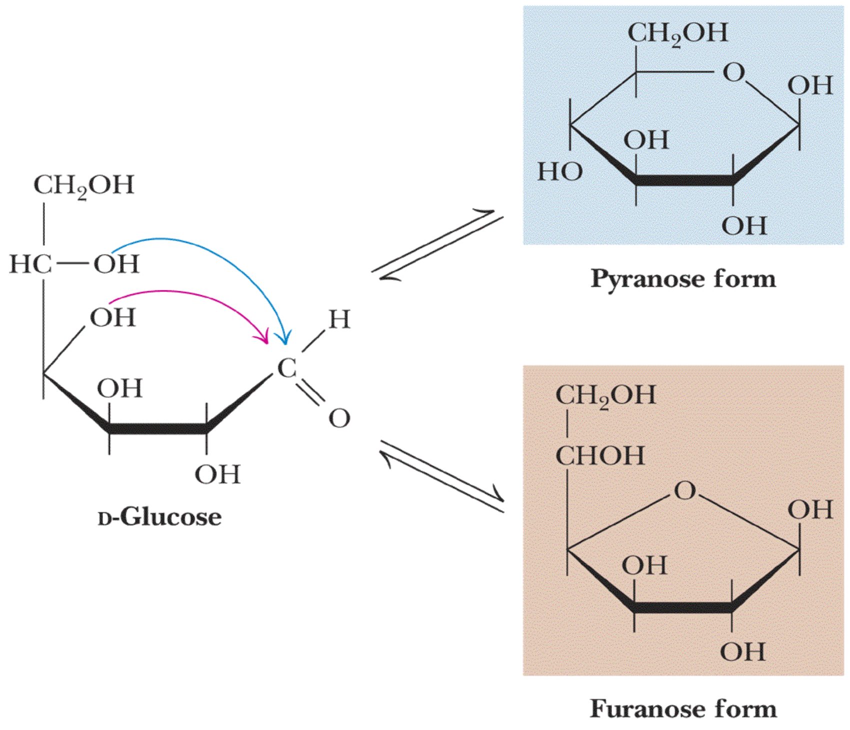


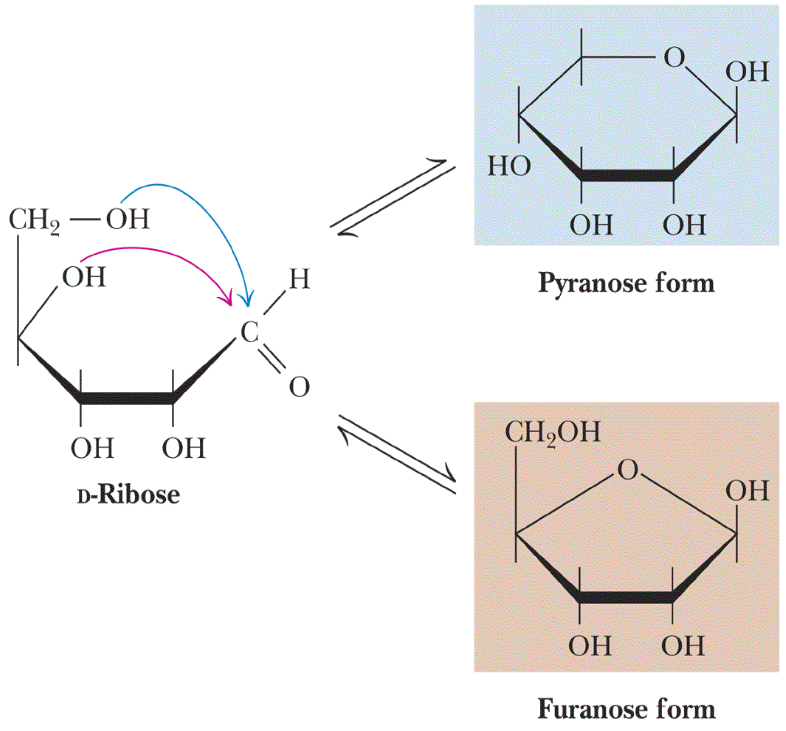
Ketone Alcohol Hemiketal Ketal

An aldehyde or ketone can react with an alcohol in a 1:1 ratio to yield a hemiacetal or hemiketal, respectively, creating a new chiral center at the carbonyl carbon. Substitution of a second alcohol molecule produces an acetal or ketal. When the second alcohol is part of another sugar molecule, the bond produced is a glycosidic bond.

Different conformations of monosaccharides





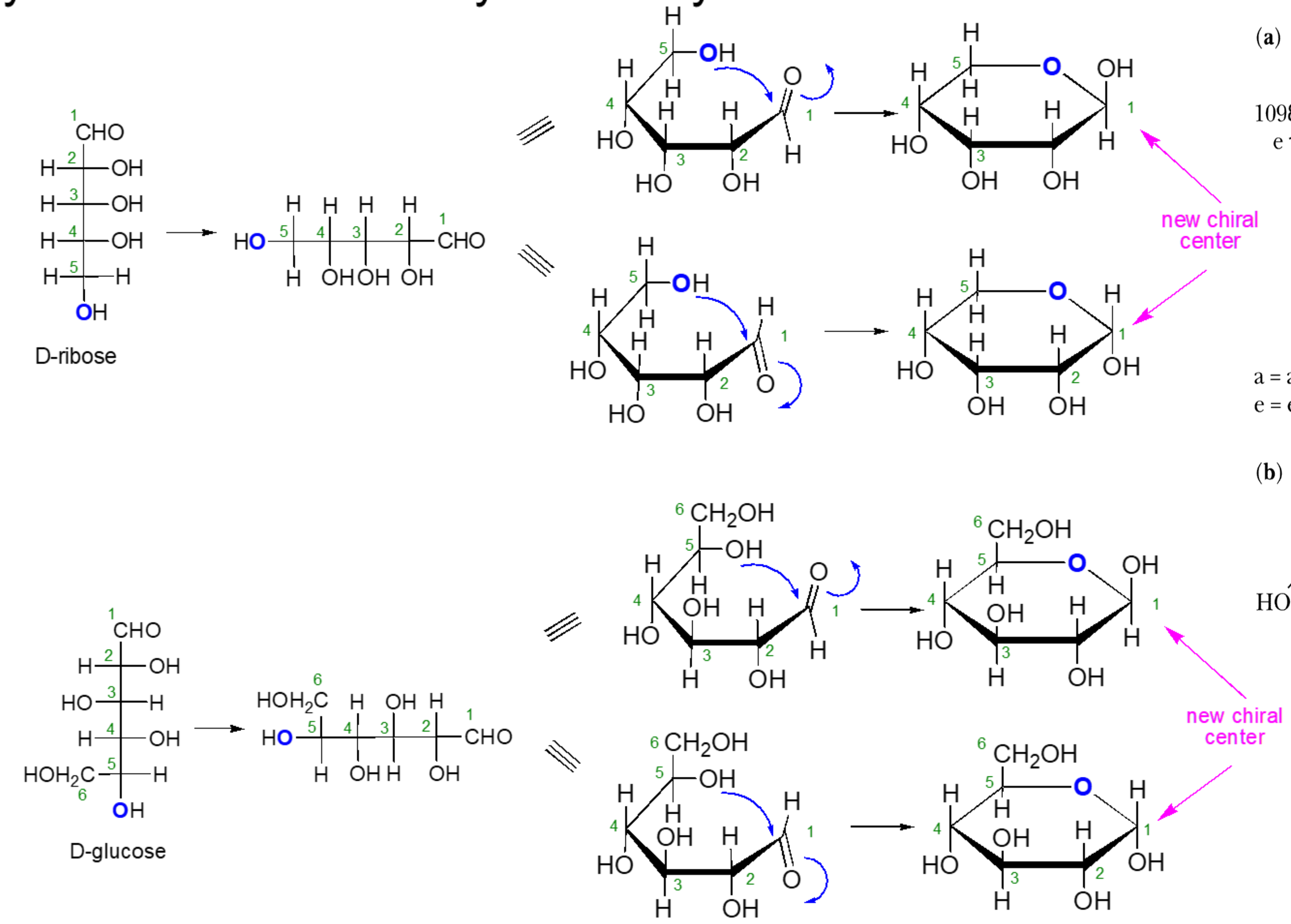


In aqueous solution, monosaccharides with five or more C atoms in the backbone occur as cyclic (ring) structures in which the carbonyl group has formed a covalent bond with the O of a hydroxyl group along the chain. These 6-membered ring compounds are called **pyranoses**. These rings form due to a general reaction that occurs between alcohols and aldehydes or ketones to form derivatives called
hemiacetals or **hemiketals**.
Anomers are isomeric forms of monosaccharides that differ only in their configuration about the hemiacetal or hemiketal C.

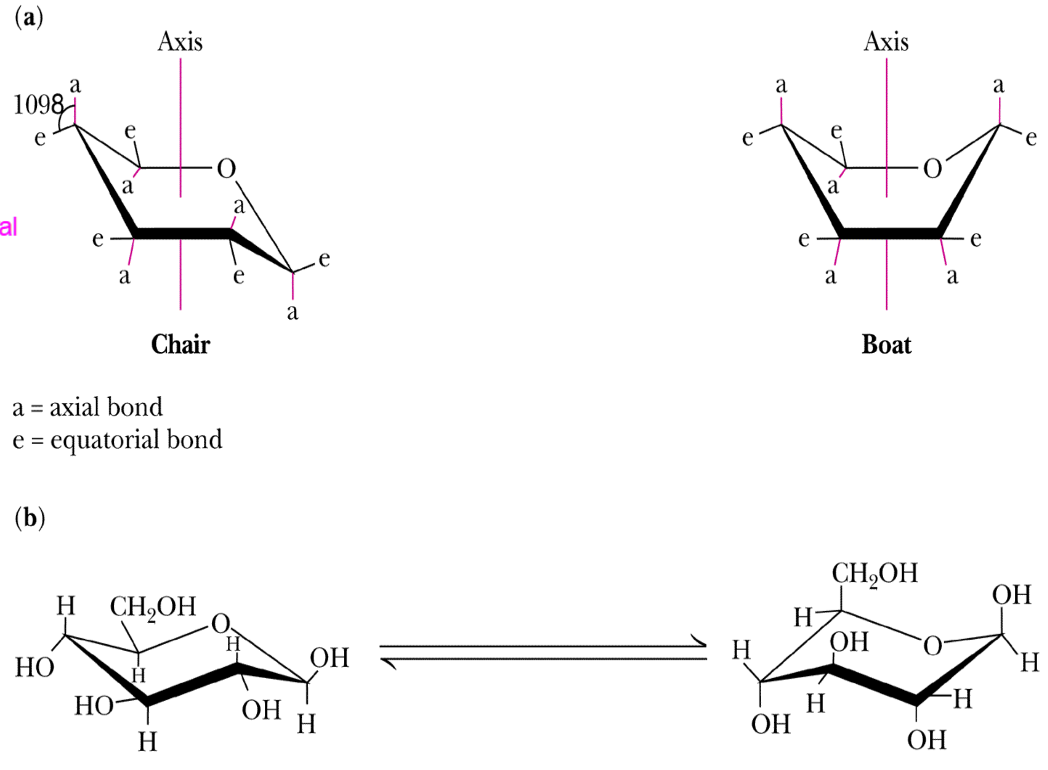
Ajaikumar B. Kunnumakkara

Different conformations of monosaccharides

Cyclic Forms of Carbohydrates: Pyranose Forms.

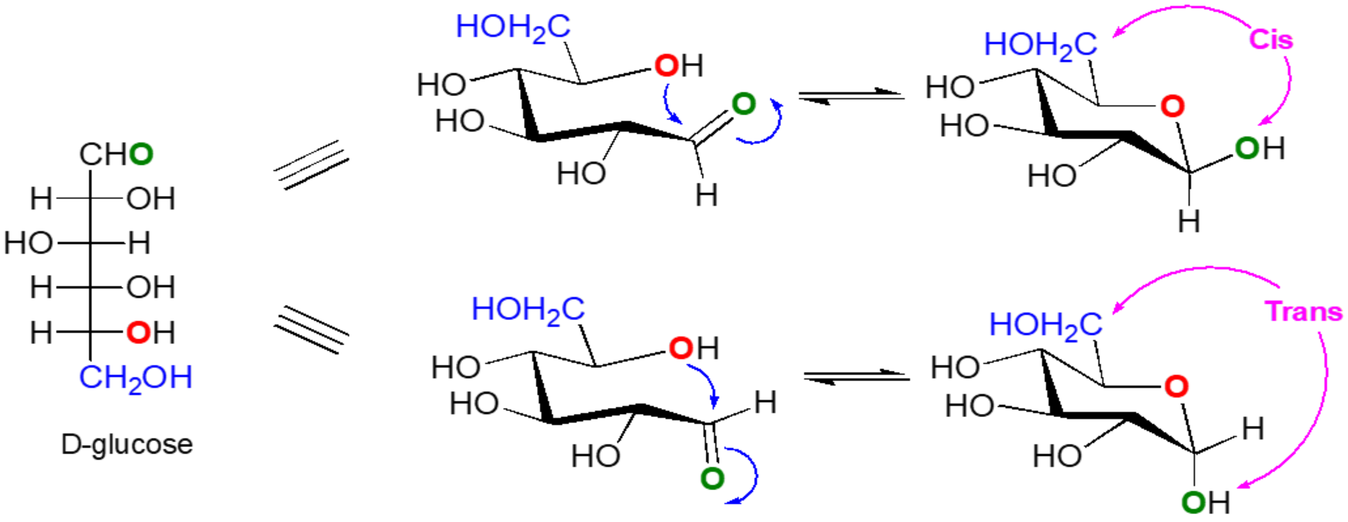


Chair and boat conformations of a pyranose sugar



Different types of monosaccharides

Mutarotation and Anomeric Effect

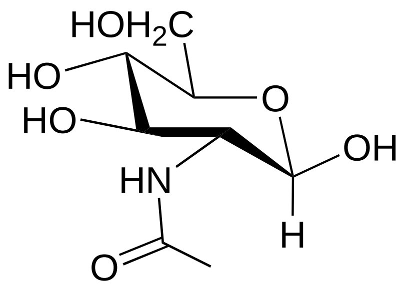


D-glucose

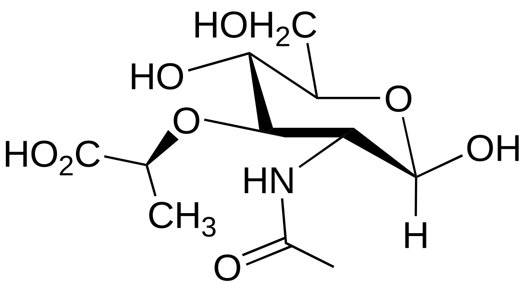
β-D-Glucopyranose (64%)
(β-anomer: C1-OH and CH_2OH are cis)

α-D-Glucopyranose (36%)
(α-anomer: C1-OH and CH_2OH are trans)

Amino Sugars

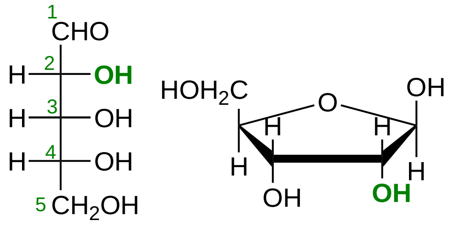


N-acetyl-D-glucosamine
(GlcNAc or NAG)

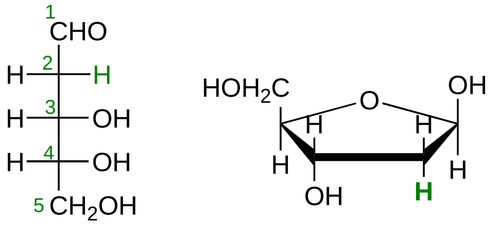


N-Acetylmuramic acid
(MurNAc)

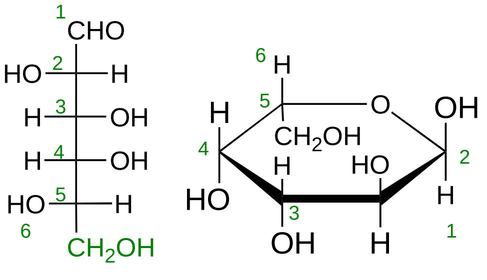
Deoxy Sugars



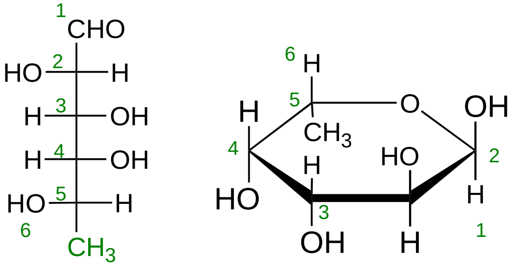
D-ribose



2-Deoxy-D-ribose



L-Galactose



6-Deoxy-L-Galactose
(fucose)

Sugars are reducing agents

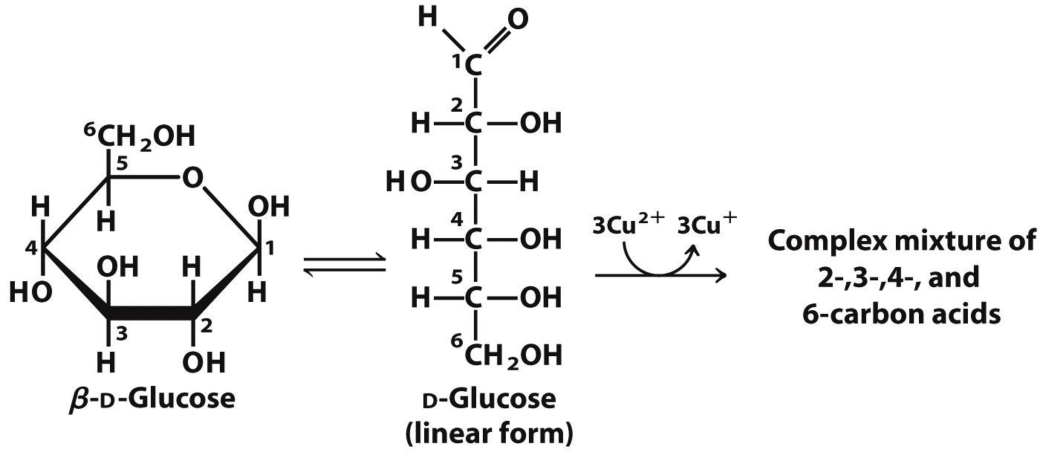
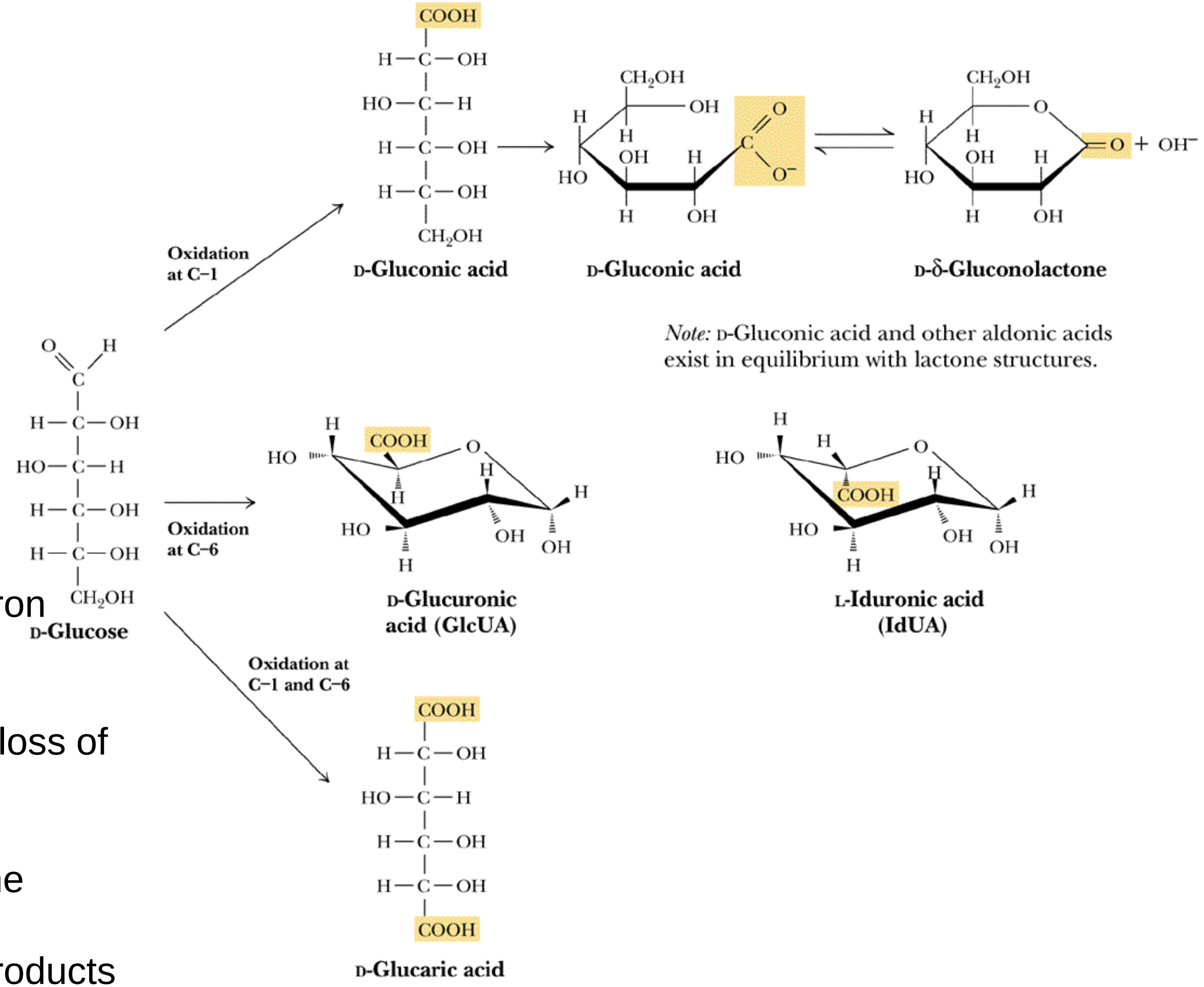


Figure 7-10
Lehninger Principles of Biochemistry, Fifth Edition



- Oxidation is electron loss, reduction is electron gain
- Reducing agent is electron donor, oxidizing agent is electron acceptor.
- Gain of an electron by atom/molecule is called reduction, loss of electron is oxidation.
- Oxidation of the anomeric carbon of glucose under alkaline conditions.
- The reaction with Cu^{2+} is complex, yielding a mixture of products

Terminology

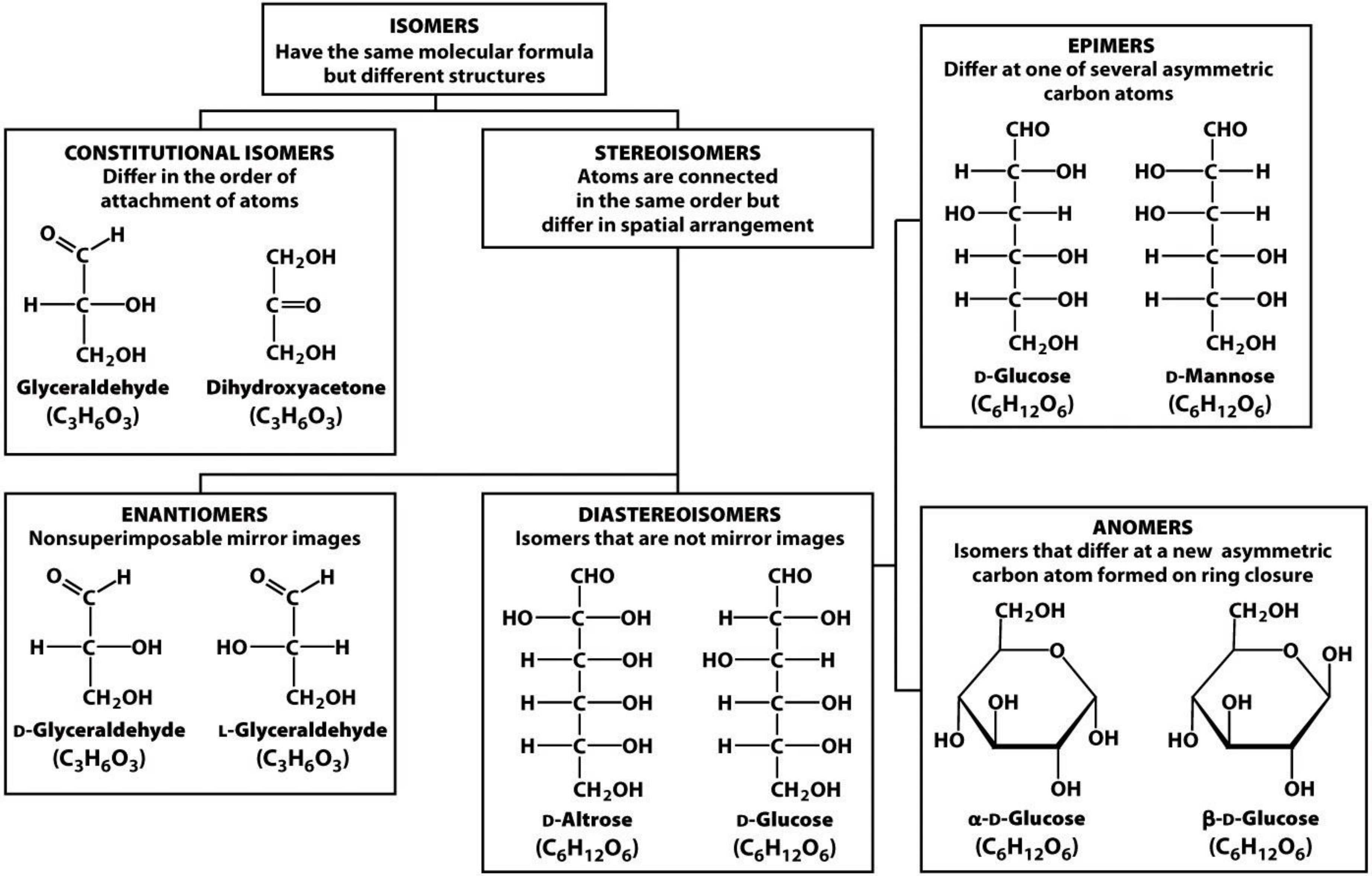


Figure 9.1
Biochemistry: A Short Course, First Edition

- Isomers
- Constitutional isomers
- Stereoisomers
- Enantiomers
- Diastereoisomers
- Epimers
- Anomers

Important hexoses in biology

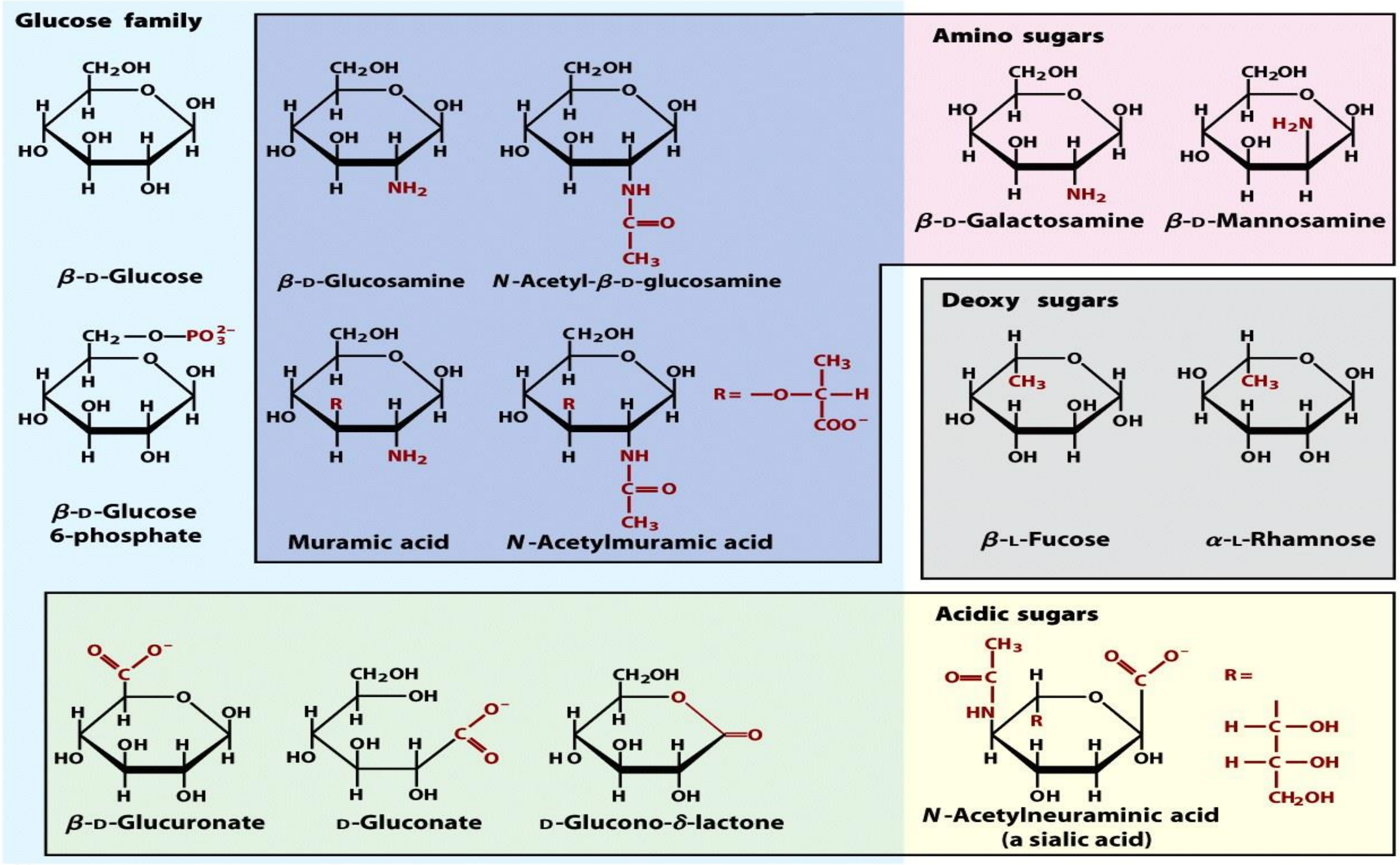
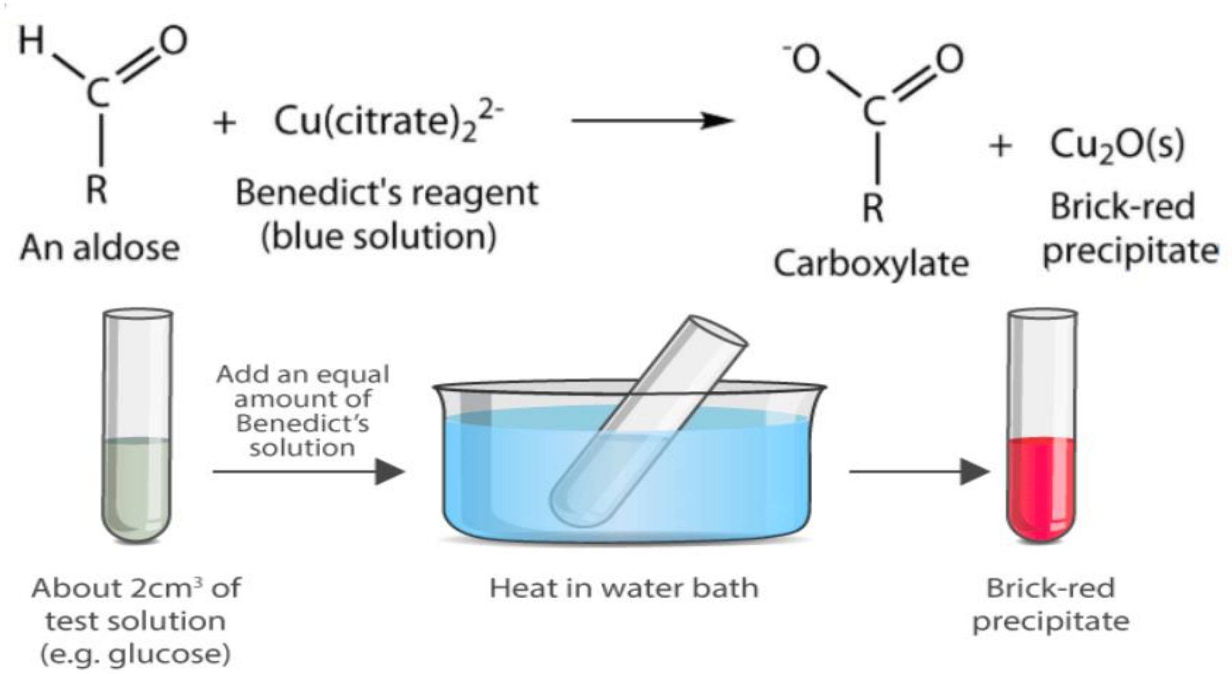


Figure 7-9
Lehninger Principles of Biochemistry, Fifth Edition

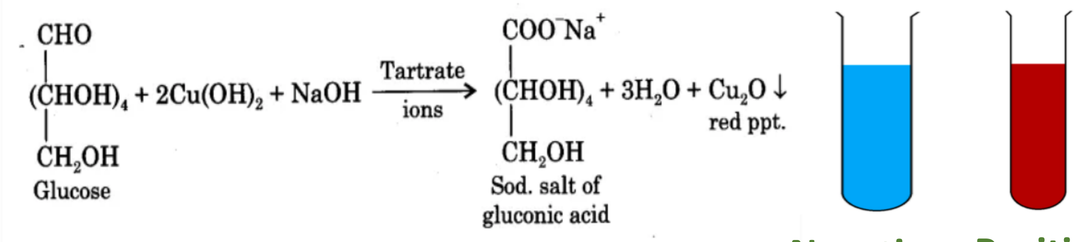
How do you find the presence of carbohydrate in given solution?

Benedict's Test



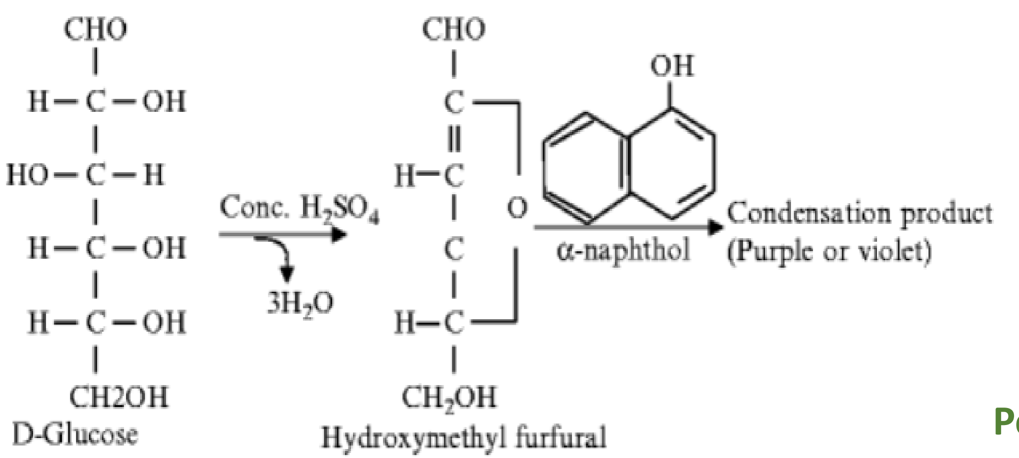
Positive

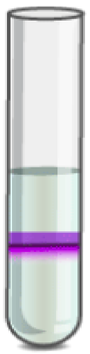
Fehling's Test



Negative Positive

Molisch's Test





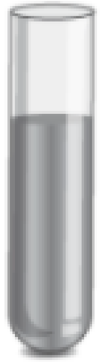
Positive

Tollen's Test

$$NH_4OH + AgNO_3 \longrightarrow NH_4NO_3 + Ag(OH)$$

$$2Ag(OH) \longrightarrow Ag_2O + H_2O$$

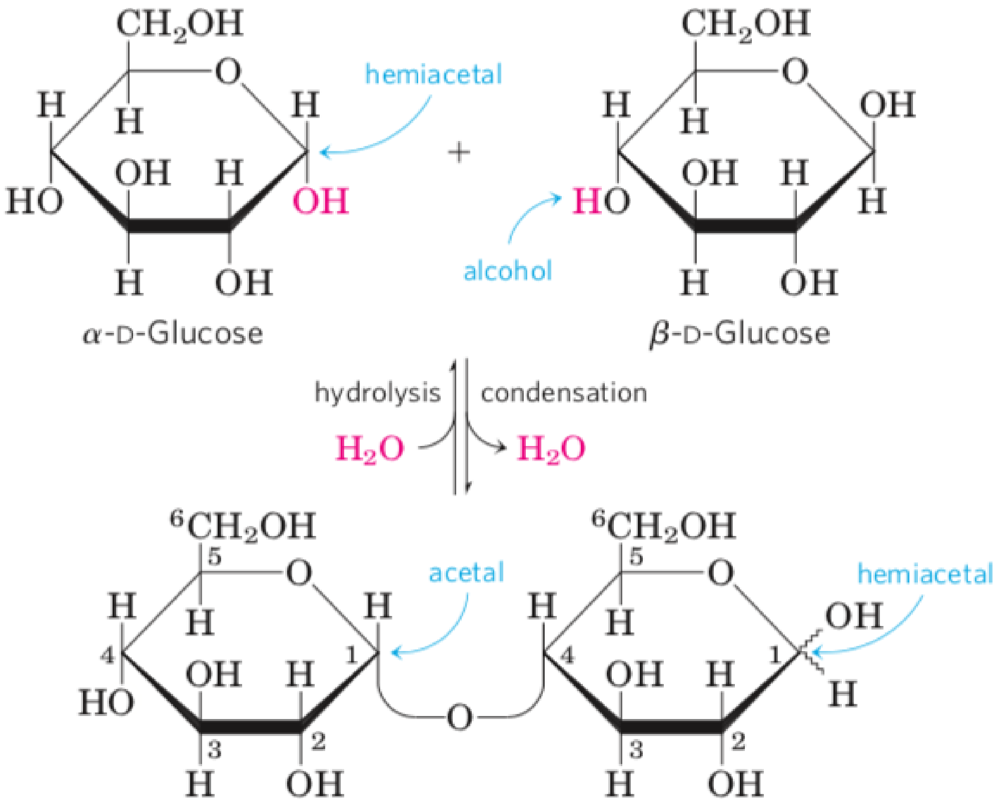
$$\underset{\text{Glucose}}{\begin{array}{c} CH_2OH \\ | \\ (CHOH)_4 \\ | \\ CHO \end{array}} + Ag_2O \longrightarrow \begin{array}{c} CH_2OH \\ | \\ (CHOH)_4 \\ | \\ COOH \end{array} + \underset{\substack{\text{Silver} \\ \text{mirror}}}{2Ag}$$



Disaccharides

Glycosidic Bonds

- α- 1→4 linkage

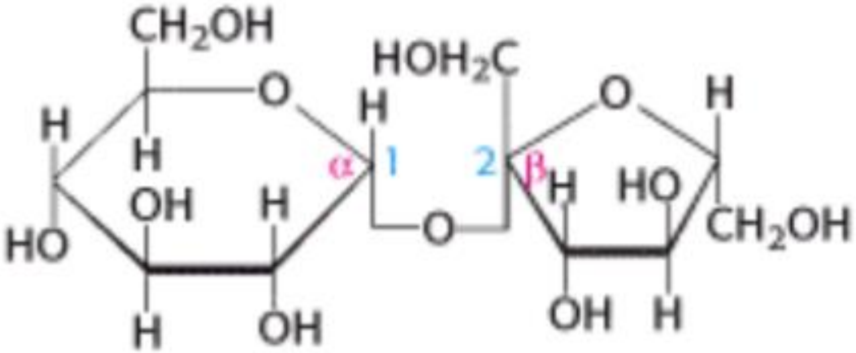


Maltose

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

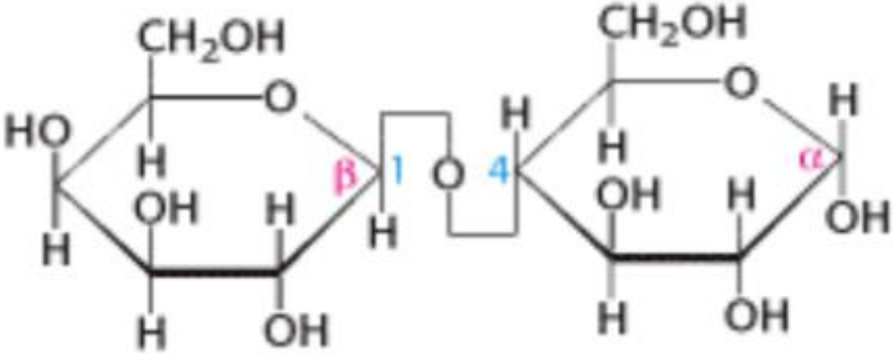
Glycosidic Bonds

- α- 1→4 linkage
- β 1→4 linkage



Sucrose

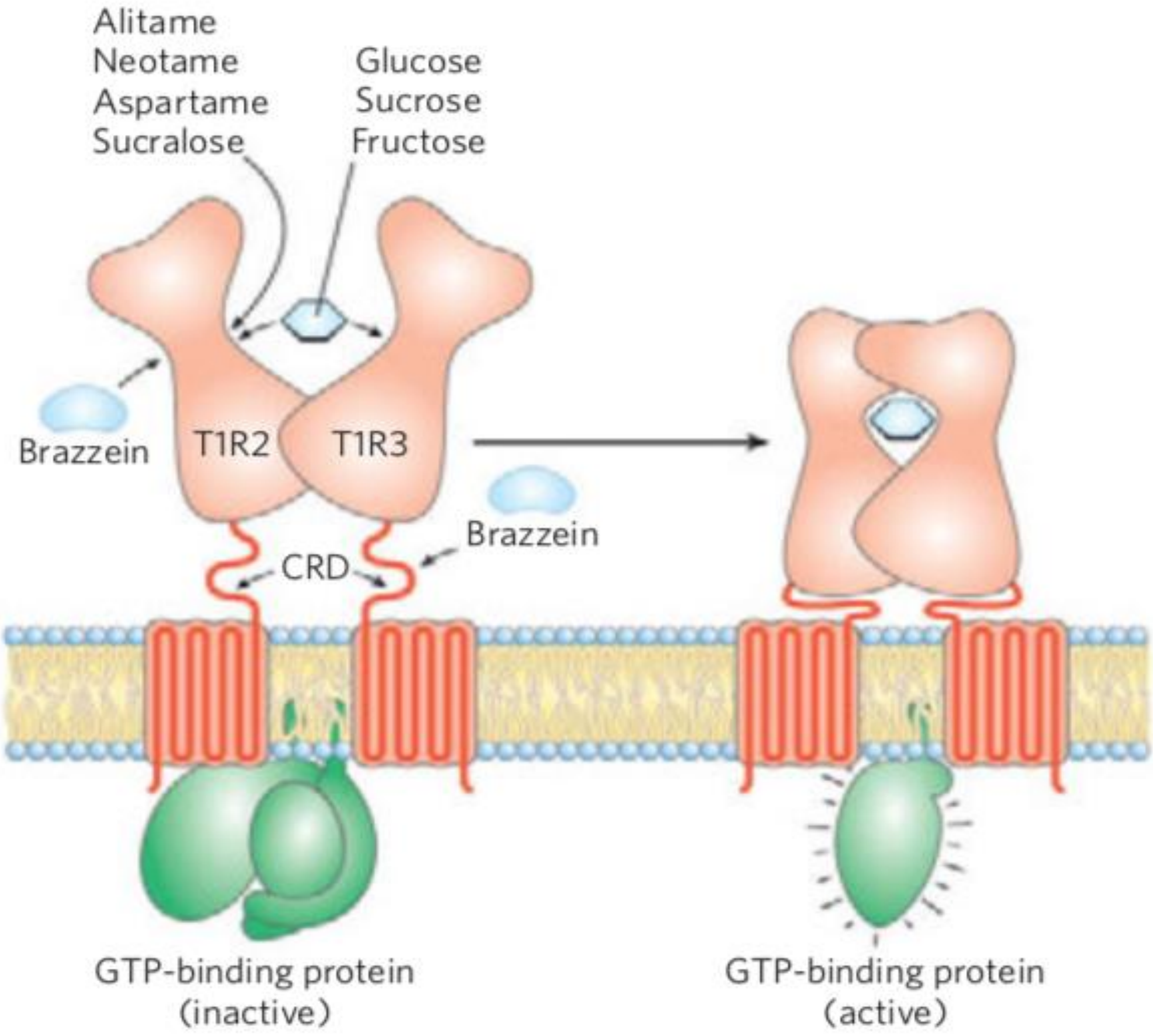
α-D-glucopyranosyl-(1→2)-β-D-fructopyranose



Lactose

β-D-galactopyranosyl-(1→4)- α -D-glucopyranose

Sugar is Sweet???



- ✓ Sweet – One among the five flavors
- ✓ Two genes- TIR2 & TIR3 encodes sweetness receptors
- ✓ Activation of GTP-binding protein triggers the signal

Key Concepts

- **Carbohydrates and its functions**
- **Different types of carbohydrates**
- **Structural representation of carbohydrates**
- **Tests required to detect the carbohydrates**

<u>BT203: Biochemistry</u>

<u>Lecture: 3</u>

<u>Slide 3</u>

Importance of Carbohydrates: Carbohydrates are one of the most abundant molecules on the plant. Carbohydrates (sugar and starch) are a dietary staple in most parts of the world, and the oxidation of carbohydrates is the central energy-yielding pathway. It serves as <u>structural and protective elements</u> in the cell walls of bacteria and plants. Other carbohydrate polymers lubricate skeletal joints and participate in recognition and adhesion between cells.

Definition: Carbohydrates are polyhydroxy aldehydes or ketones, or substances that yield such compounds on hydrolysis. There are three major size classes of carbohydrates: monosaccharides, oligosaccharides,and polysaccharides (the word “saccharide” is derived from the Greek *sakcharon*, meaning “sugar”).

Monosaccharides, or simple sugars, consist of a single polyhydroxy aldehyde or ketone unit. **Oligosaccharides** consist of short chains of monosaccharide units, or residues, joined by characteristic linkages called glycosidic bonds. **Polysaccharides** are sugar polymers containing more than 20 or so monosaccharide units.

The backbones of common monosaccharides are unbranched carbon chains in which all the carbon atoms are linked by single bonds. If the carbonyl group is at an end of the carbon chain (that is, in an aldehyde group) the monosaccharide is an aldose; if the carbonyl group is at any other position (in a ketone group) the monosaccharide is a ketose. The simplest monosaccharides are the three-carbon trioses: glyceraldehyde

<u>Slide 4</u>

Monosaccharides with four, five, six, and seven carbon atoms in their backbones are called, respectively, tetroses, pentoses, hexoses, and heptoses. There are aldoses and ketoses of each of these chain lengths: aldotetroses and ketotetroses, aldopentoses and ketopentoses, and so on. The hexoses, which include the aldohexose D-glucose and the ketohexose D-fructose are the most common monosaccharides in nature—the products of photosynthesis, and key intermediates in the central energy-yielding reaction sequence in most organisms.

All the monosaccharides except dihydroxyacetone contain one or more asymmetric **(chiral) carbon atoms** and thus occur in optically active isomeric forms.

<u>Slide 5</u>

To represent three-dimensional sugar structures on paper, we often use Fischer projection formulas. In Fischer projection formulas, horizontal bonds project out of the

plane of the paper, toward the reader; vertical bonds project behind the plane of the paper, away from the reader.
When the hydroxyl group on the reference carbon is on the right (dextro) in a projection formula that has the carbonyl carbon at the top, the sugar is the D isomer; when on the left (levo).
Most of the hexoses of living organisms are D isomers. Why only D isomers? You guys look into this and can come up with the answers. We will discuss it in the next class

In fact, in aqueous solution, aldotetroses and all monosaccharides with five or more carbon atoms in the backbone occur predominantly as cyclic (ring) structures in which the carbonyl group has formed a covalent bond with the oxygen of a hydroxyl group along the chain. The formation of these ring structures is the result of a general reaction between alcohols and aldehydes or ketones to form derivatives called hemiacetals or hemiketals.

To make it happen an aldehyde or ketone can react with an alcohol in a 1:1 ratio to yield a hemiacetal or hemiketal, respectively, creating a new chiral center at the carbonyl carbon. Substitution of a second alcohol molecule produces an acetal or ketal. When the second alcohol is part of another sugar molecule, the bond produced is a glycosidic bond.

<u>Slide 6</u>

As in the previous slide, we saw how hemiacetal or hemiketal is formed by the reaction of molecule of alcohol.
The reaction with the first molecule of alcohol creates an additional chiral center (the carbonyl carbon). Because the alcohol can add in either of two ways, attacking either the “front” or the “back” of the carbonyl carbon, the reaction can produce either of two stereoisomeric configurations, denoted
Example: D-glucose exists in solution as an intramolecular hemiacetal in which the free hydroxyl group at C-5 has reacted with the aldehydic C-1, rendering the latter carbon asymmetric and producing two possible stereoisomers, designated α and β.

Six-membered ring compounds are called pyranoses because they resemble the six-membered ring compound pyran. Similarly, 5 membered ring compounds are called as furanoses.
D-glucose and D-ribose both can cyclize in two ways forming either furanose or pyranose structures

Cyclic sugar structures are more accurately represented in Haworth perspective formulas than in the Fischer projections commonly used for linear sugar structures. In Haworth projections the six-membered ring is tilted to make its plane almost perpendicular to that of the paper, with the bonds closest to the reader drawn thicker than those farther away.

<u>Slide 7</u>

Reaction between the aldehyde group at C-1 and the hydroxyl group at C-5 forms

a hemiacetal linkage, producing either of two stereoisomers, the α and β anomers, which differ only in the stereochemistry around the hemiacetal carbon. This reaction is reversible.
This slide depicts the reaction of hemiacetal and hemiketal to form ring like structures.

Haworth perspective formulas are commonly used to show the stereochemistry of ring forms of monosaccharides. However, the six membered pyranose ring is not planar, as Haworth perspectives suggest, but tends to assume either of two “chair” conformations. To interconvert α and β configurations, the bond involving the ring oxygen atom would have to be broken, but interconversion of the two chair forms (which are conformers) does not require bond breakage and does not change configurations at any of the ring carbons.

<u>Slide 8:</u>

The α and β anomers of D-glucose interconvert in aqueous solution by a process called mutarotation, in which one ring form (say, the α anomer) opens briefly into the linear form, then closes again to produce the β anomer. Thus, a solution of α -D-glucose and a solution of β -D-glucose eventually form identical equilibrium mixtures having identical optical properties.

The α and β -anomers are in equilibrium, and interconvert through the open form. The pure anomers can be isolated by crystallization. When the pure anomers are dissolved in water they undergo mutarotation, the process by which they return to an equilibrium mixture of the anomer.

Deoxy Sugars. Carbohydrates that are missing a hydroxy group

Amino Sugars. Carbohydrates in which a hydroxyl group is replaced with an $-NH_2$ or -NHAc group

<u>Slide 9:</u>

Monosaccharides can be oxidized by relatively mild oxidizing agents such as cupric (Cu^{2+}) ion. The carbonyl carbon is oxidized to a carboxyl group. Glucose and other sugars capable of reducing cupric ion are called reducing sugars. Cupric ion oxidizes glucose and certain other sugars to a complex mixture of carboxylic acids. This is the basis of Fehling’s reaction, a semi-quantitative test for the presence of reducing sugar that for many years was used to detect and measure elevated glucose levels in people with diabetes mellitus. Other oxidations at different carbon position yields other glycans.

<u>Slide 10:</u>

This is the terminology slides of topics so far covered, so as you people get an idea of the various terminologies present in the carbohydrate biochemistry.

<u>Slide 11:</u>

In addition to simple hexoses such as glucose, galactose, and mannose, there are a number of sugar derivatives in which a hydroxyl group in the parent compound is replaced with another substituent, or a carbon atom is oxidized to a carboxyl group. In amino sugars, an —NH2 group replaces one of the —OH groups in the parent hexose. Substitution of —H for —OH produces a deoxy sugar; note that the deoxy sugars shown here occur in nature as the L isomers. The acidic sugars contain a carboxylate group, which confers a negative charge at neutral pH. D-Glucono-δ-lactone results from formation of an ester linkage between the C-1 carboxylate group and the C-5 (also known as the δ carbon) hydroxyl group of D-gluconate.

Slide 12:

Tests for Carbohydrates

Benedict's Test

This test is given by reducing sugars. in alkaline medium, sodium carbonate converts glucose to enediol and this enediol reduce cupric to cuprous forming cuprous hydroxide. This solution is kept in sodium citrate and on boiling, red precipitate of cuprous oxide is formed. The appearance of red precipitate confirms the presence of carbohydrates.

Fehling's Test

This test is given by reducing sugars. To the aqueous solution of carbohydrate fehling's solution is added and heated in water bath. Formation of red precipitate confirms the presence of reducing sugars. The copper ions present in fehling's solution in +3 state is reduced to +2 oxidation state and in alkaline medium it is precipitated as red cuprous oxide.

Molisch's Test

Molisch's test is a general test for carbohydrates. This test is given by almost all of the carbohydrates. In this test, concentrated sulfuric acid converts the given carbohydrate into furfural or its derivatives, which react with α-naphthol to form a purple-colored product.

Polysaccharides and glycoproteins also give a positive reaction.

Tollen's Test

This test is given by reducing sugars. Carbohydrates react with Tollens reagent and forms a silver mirror on the inner walls of the test tube. This confirms the presence of reducing sugars. Silver ions are reduced to metallic silver

The appearance of silver mirror confirms the presence of reducing sugars.

Slide 13:

Disaccharides:

Disaccharides as the name says (di- means two) consists of two monosaccharide residues joined covalently called glycosidic bond.

There are two types of glycosidic linkages-

O-glycosidic - which is formed when a hydroxyl group of one sugar molecule reacts with the anomeric carbon of the other. This reaction represents the formation of an acetal from a hemiacetal and an alcohol.

N-glycosyl bonds - join the anomeric carbon of a sugar to a nitrogen atom in glycoproteins

Glycosidic bonds are readily hydrolyzed by acid but resist cleavage by base. Thus, disaccharides can be hydrolyzed to yield their free monosaccharide components by boiling with dilute acid.

When the anomeric carbon is involved in a glycosidic bond, the easy interconversion of linear and cyclic forms is prevented. Because the carbonyl carbon can be oxidized only when the sugar is in its linear form, formation of a glycosidic bond renders a sugar nonreducing. In describing disaccharides or polysaccharides, the end of a chain with a free anomeric carbon is commonly called the reducing end.

The disaccharide maltose contains two D-glucose residues joined by a glycosidic linkage between C-1 -the anomeric carbon- of one glucose residue and C-4 of the other. Because the disaccharide retains a free anomeric carbon C-1 of the glucose residue on the right, maltose is a reducing sugar. The configuration of the anomeric carbon atom in the glycosidic linkage is α. The glucose residue with the free anomeric carbon is capable of existing in α- and β-pyranose forms.

The disaccharide lactose- yields D-galactose and D-glucose on hydrolysis. It occurs naturally in milk. The anomeric carbon of the glucose residue is available for oxidation, and thus lactose is a reducing disaccharide.

Sucrose or table sugar- is a disaccharide of glucose and fructose. It is formed by plants but not by animals. In contrast to maltose and lactose, sucrose contains no free anomeric carbon atom; the anomeric carbons of both monosaccharide units are involved in the glycosidic bond. Sucrose is therefore a nonreducing sugar. And this stability toward oxidation makes it a suitable molecule for the storage and transport of energy in plants.

Slide 14:

Sugar is sweet:

Sweetness is one of the 5 basic flavors which humans can taste.

Sweet taste is detected by protein receptors in the plasma membranes of gusta- tory cells in the taste buds on the surface of the tongue. In humans, two closely related genes (*T1R2* and *T1R3*) encode sweetness receptors. When a molecule with a compatible structure binds these receptors on a gustatory cell’s extracellular domain, it triggers a series of events in the cell including activation of GTP-binding protein that lead to an electrical signal being sent to the brain that is interpreted there as “sweet.”

Other classes of compounds that also bind the sweet receptors: the amino acids glycine, alanine, and serine are mildly sweet and harmless; nitrobenzene and ethylene glycol have a strong sweet taste, but are toxic. Several natural products are extraordinarily sweet: stevioside, a sugar derivative isolated from the leaves of the stevia plant (*Stevia rebaudiana* Berton), is several hundred times sweeter than an equivalent amount of sucrose (table sugar), and the small (54 amino acids) protein brazzein, isolated from berries of the Oubli vine (*Pentadiplandra brazzeana* Baillon) in Gabon and Cameroon, is 17,000 times as sweet as sucrose on a molar basis. Presumably the sweet taste of the berries encourages their consumption by animals, which then disperse the seeds geographically so new plants may be established.

There is great interest in the development of artificial sweeteners as weight reduction aids compounds that give foods a sweet taste without adding the calories found in sugars. The artificial sweetener aspartame demonstrates the importance of stereochemistry in biology. When the steric match is correct, the sweet receptor is stimulated and the signal “sweet” is conducted to the brain. When the match is not correct, the sweet receptor is not stimulated.

XXXXXXXXXXXXX

Lecture 4

BT 203

Biochemistry

3-0-0-6

Prof. Ajaikumar B. Kunnumakkara

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Key Questions

- **What are polysaccharides?**
- **What are the different types of polysaccharides?**
- **What are the biological relevance of polysaccharides?**
- **What are the different special glycans present in the body?**
- **What are the various approaches for carbohydrate analysis?**

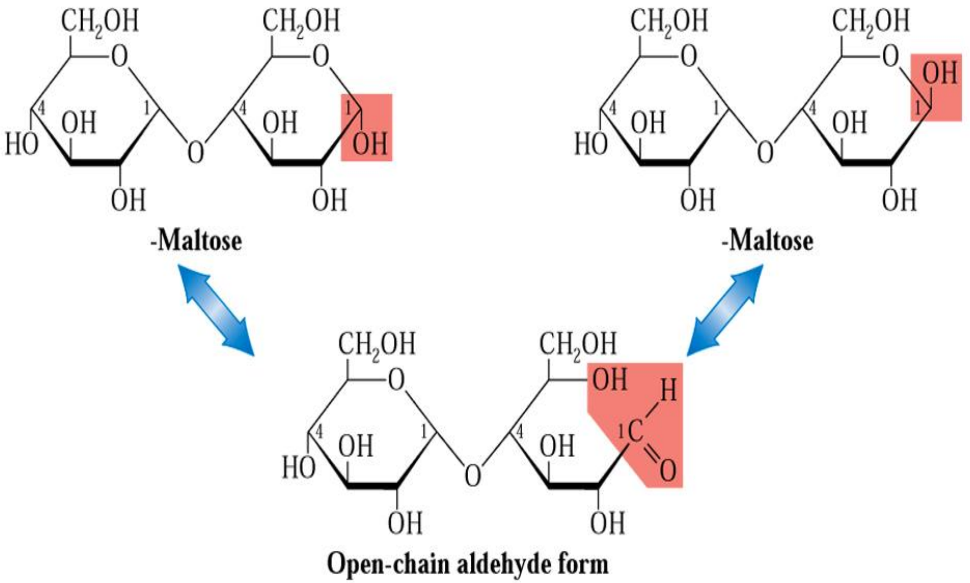
Glycosidic bonds:

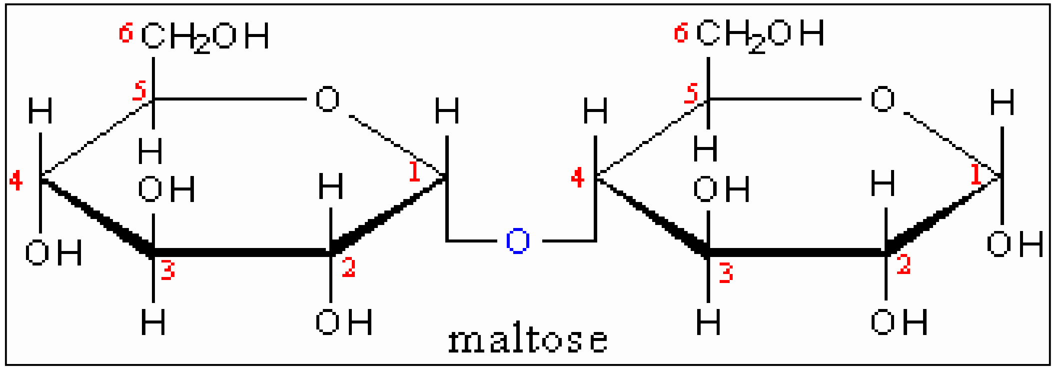
The **hydroxyl group** and a **hydroxyl group** of *another* sugar or other compound can join together, splitting out water to form a **glycosidic bond**.

$$\mathbf{R\text{-}OH + HO\text{-}R' \rightarrow R\text{-}O\text{-}R' + H_2O}$$

glycosidic linking helps form disaccharides, oligosaccharides, and polysaccharides from rings of monosaccharides

Glycosidic linkage





Alpha (1→4) glycosidic linkage of 2 D-Glucose molecules

- Formation of disaccharides is like glycoside formation (condensation raction)
  - Monosaccharide + alcohol --> glycoside + H_2O
  - Monosaccharide + monosaccharide --> disaccharide + H_2O

Disaccharide	glycosidic linkage	Reducing?	Human Digestion
Maltose	α(1-4)	yes	easily
Cellobiose	β(1-4)	yes	no
Lactose	β(1-4)	yes	usually
Sucrose	α,β(1-2)	no	yes

Polysaccharides

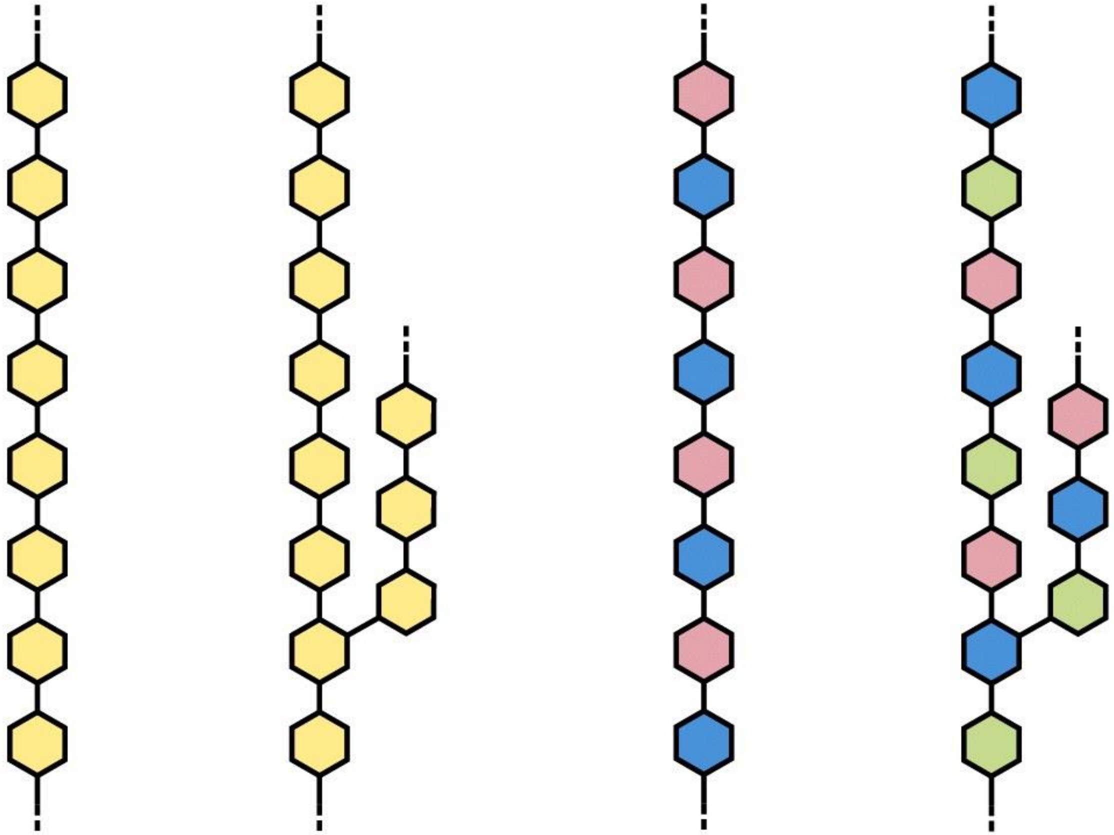


Figure 7-13
Lehninger Principles of Biochemistry, Fifth Edition

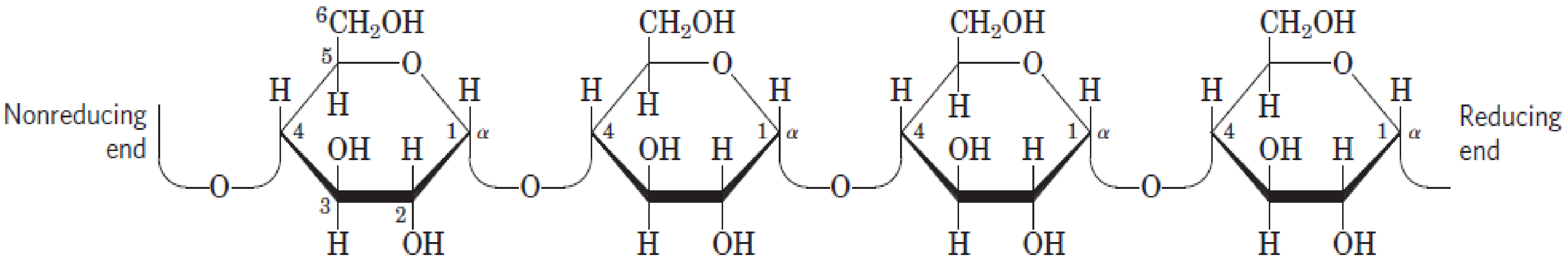
TABLE 8.2 Structures of some common polysaccharides

Polysaccharide[a]	Component(s)[b]	Linkage(s)
Storage homoglycans		
Starch		
Amylose	Glc	α-(1→4)
Amylopectin	Glc	α-(1→4), α-(1→6) (branches)
Glycogen	Glc	α-(1→4), α-(1→6) (branches)
Structural homoglycans		
Cellulose	Glc	β(1→4)
Chitin	GlcNAc	β(1→4)
Heteroglycans		
Glycosaminoglycans	Disaccharides (amino sugars, sugar acids)	Various
Hyaluronic acid	GlcUA and GlcNAc	β(1→3), β(1→4)

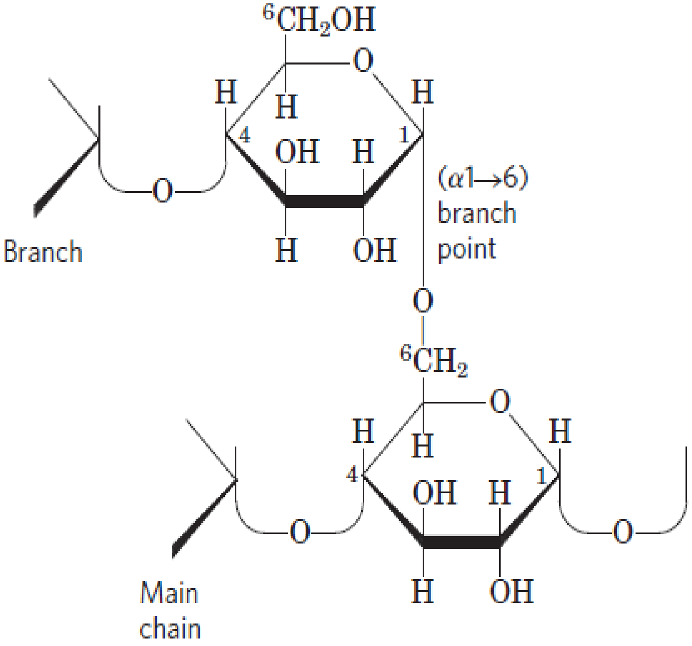
[a] Polysaccharides are unbranched unless otherwise indicated
[b] Glc, Glucose; GlcNAc, *N*-acetylglucosamine; GlcUA, D-glucuronate.

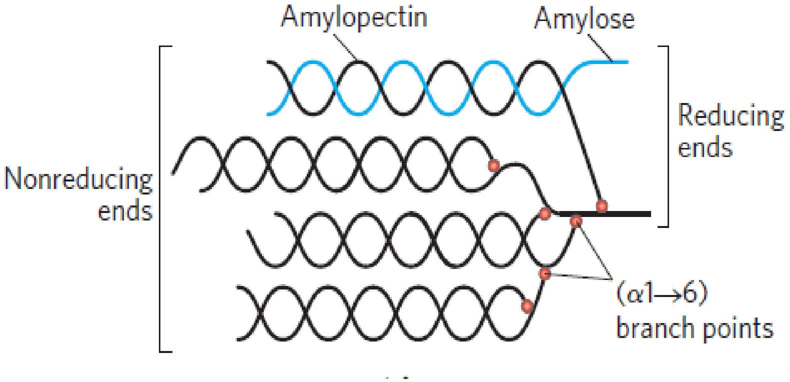
Starch and Glycogen

- Main sources of starch are rice, corn, wheat, potatoes and cassava
- A storage polysaccharide
- White and amorphous, tasteless
- Insoluble in cold water
- Gives dextrins during incomplete hydrolysis
- Starch is used as a recipient, a binder in medications to aid the formation of tablets.
- Industrially it has many applications such as in adhesives, paper making, biofuel, textiles
- Amylose 20% and 80% amylopectin



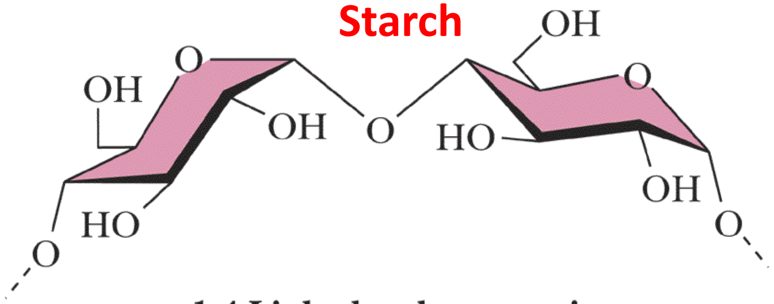
(a) Amylose





Starch

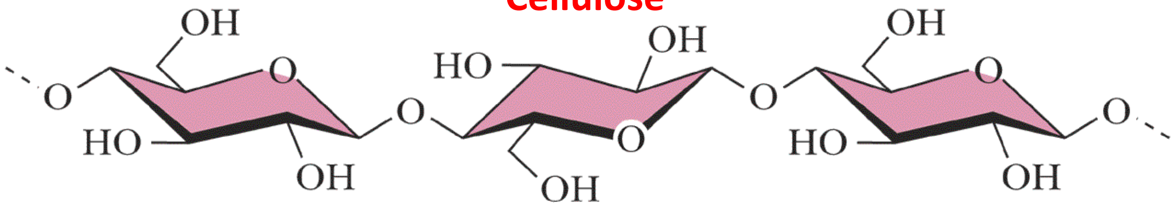
Starch



α-1,4-Linked D-glucose units

(a)

Cellulose

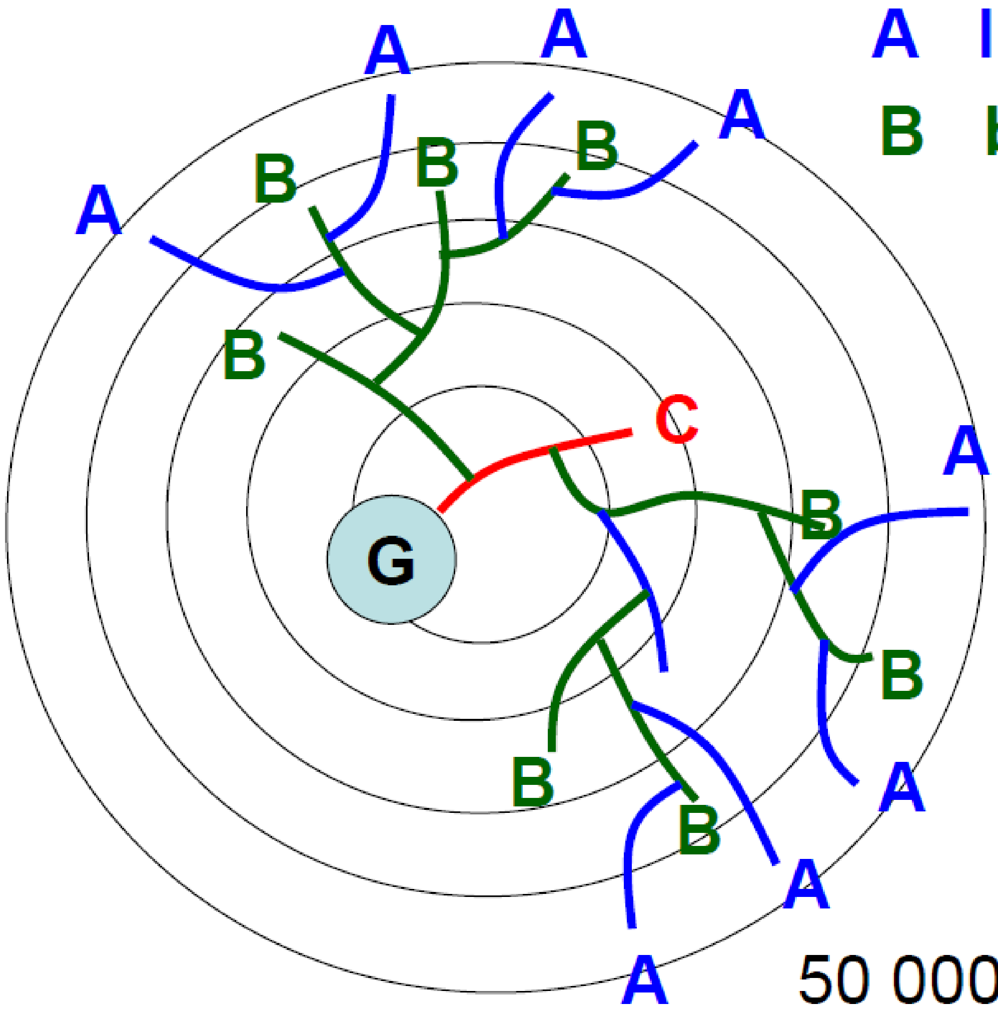


β-1,4-Linked D-glucose units

(b)

Amylose	Amylopectin
1. It has simple unbranched structure 2. It is soluble in water 3. It has alpha-1,4 glycosidic linkage 4. It is easily dispersed in water 5. It gives blue colour with iodine	1. It has a branched chain structure 2. It is insoluble in water 3. It has alpha 1,4-glycosidic and alpha 1,6-glycosidic linkage 4. It is not easily dispersed in water 5. It gives purple colour with iodine

Glycogen: The Perfect Molecule



A linear

B branched

All chains of same length (11~15 Glc/chain)

2 branching points/B chain

12 layers

Optimized !!
Thank you,
Natural Selection!

50 000 glucose units

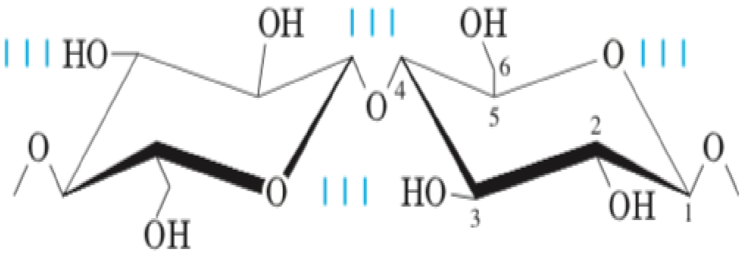
2 000 non-reducing ends

The Pursuit of Perfection by A. Cornish-Bowden

Homopolysaccharides

Cellulose

- β - 1→4 linkage



(β1→4)-linked D-glucose units

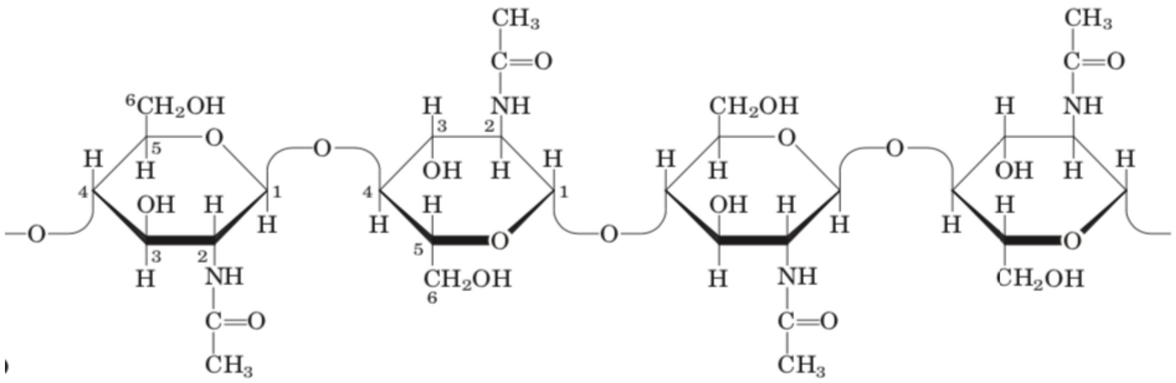
- ✓ Fibrous
- ✓ Water-insoluble
- ✓ Cell wall of plants
- ✓ Cotton-pure cellulose
- ✓ Linear molecule
- ✓ Consists of 10,000-50,000 D-glucose units

- ✓ Cellulose is digested by- cellulase
- ✓ Vertebrates lack cellulase
- ✓ Symbiotic relationship with Trichonympha, helps termites to digest cellulose
- ✓ Similarly, ruminants such as sheep, cattle, goats harbor intestinal microbes to digest cellulose

Trichonympha

Chitin

- N-acetyl-D-glucosamine in β - 1→4 linkage

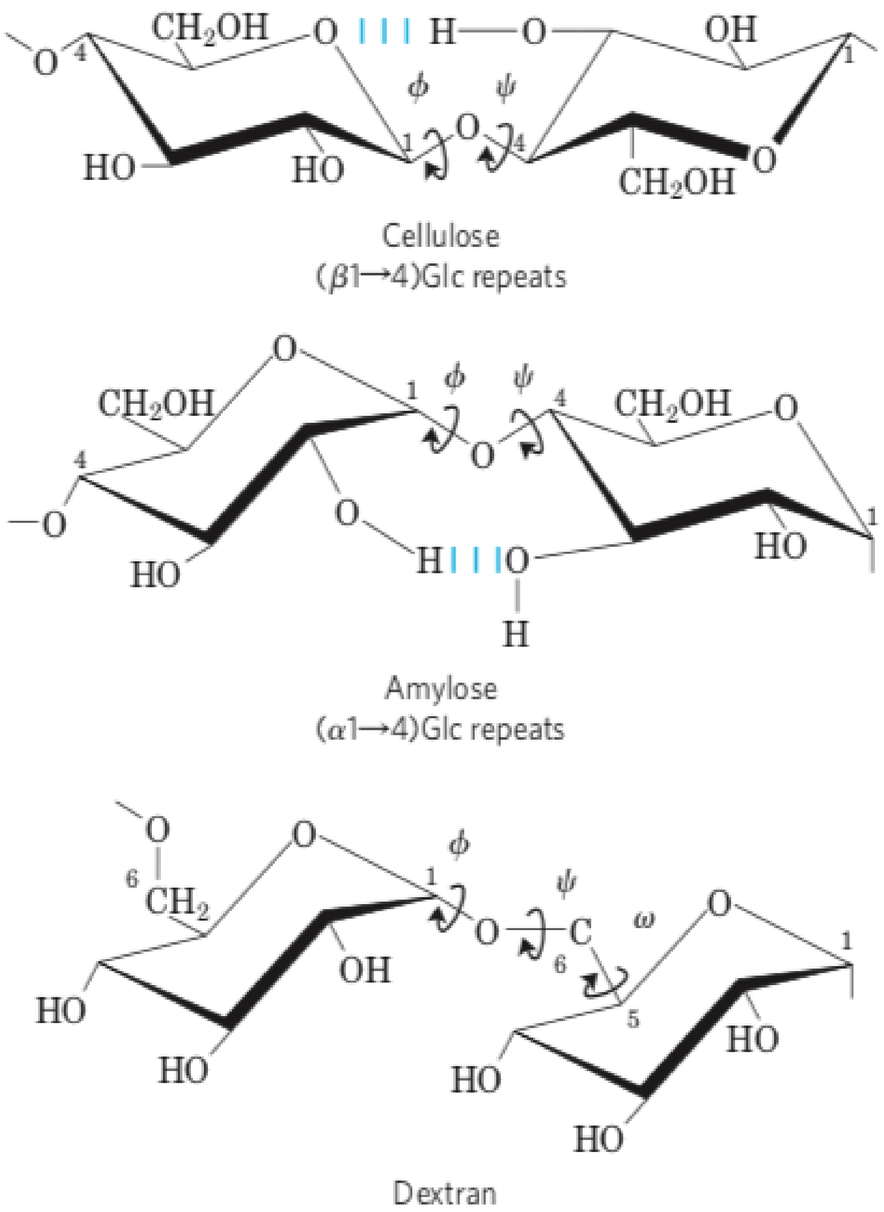


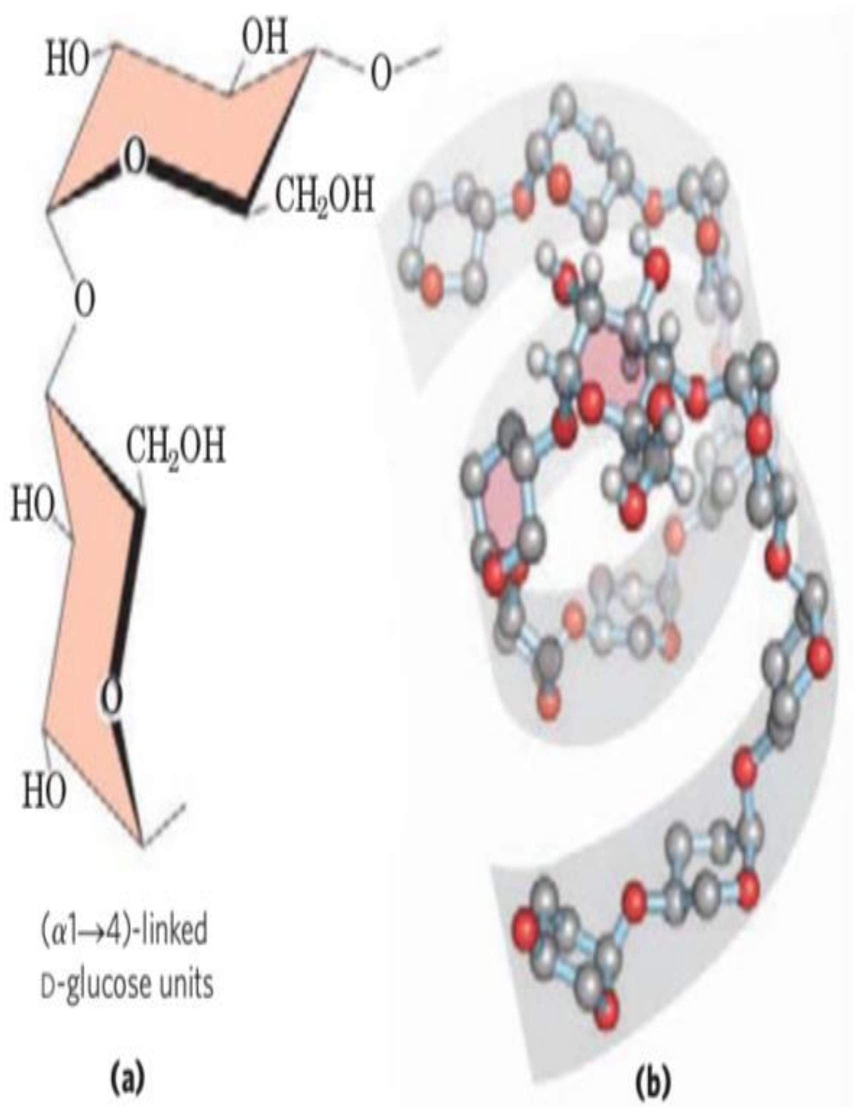
- ✓ Linear molecule
- ✓ Differs from cellulose by the presence of acetylated amino group at C-2
- ✓ Cannot be digested by vertebrates
- ✓ Principal compound of exoskeleton of – insects, lobsters, crabs

June beetle

Homopolysaccharide Folding

- ❖ Hydrogen Bonding
- ❖ Hydrophobic interactions
- ❖ Van der waals interactions
- ❖ Steric hindrance
- ❖ Dihedral angles
- ❖ Most stable structure of glycogen and starch is tightly coiled helix stabilized by hydrogen bonds
- ❖ Amylose- Each residue forms 60^0 angle with preceding residue-six residue per turn
- ❖ Cellulose-forms 180^0-linear chain-straight supramolecular structure with great tensile strength



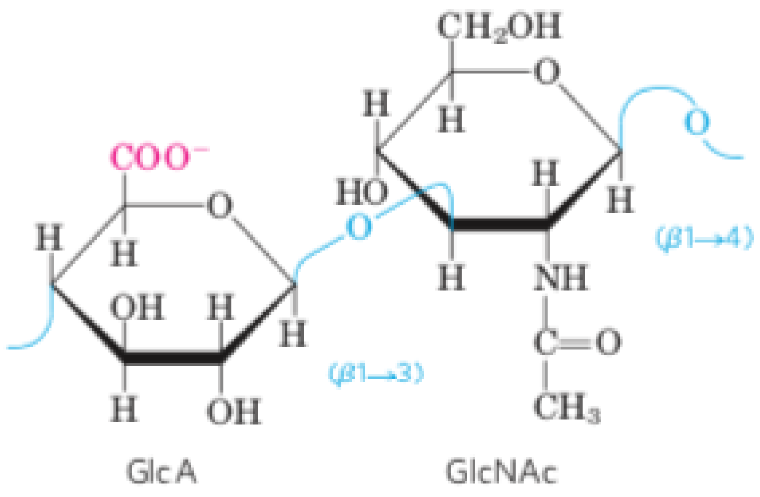


Glycosaminoglycans

- Glycosaminoglycans also known as mucopolysaccharides are heteropolysaccharides
- Linear polymers composed of repeating disaccharides
- Not found in plants
- One of the two monosaccharide is always either N-acetylglucosamine or N-acetylgalactosamine
- Other monosaccharide is generally a uronic acid

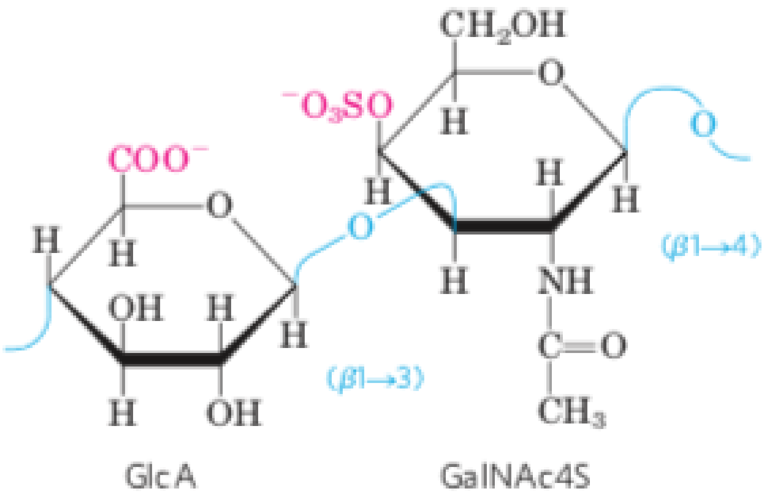
Hyaluronan

- ✓ Contains alternating residues of D-glucuronic acid and N-acetylglucosamine
- ✓ Up to 50,000 repeats of basic disaccharide units
- ✓ Function: Lubricant in synovial joint, consistency of vitreous humor, component of ECM, cartilage, tendons
- ✓ Hyaluronidase in sperm hydrolyzes outer cover of ovum allowing sperm penetration



Chondroitin Sulfate

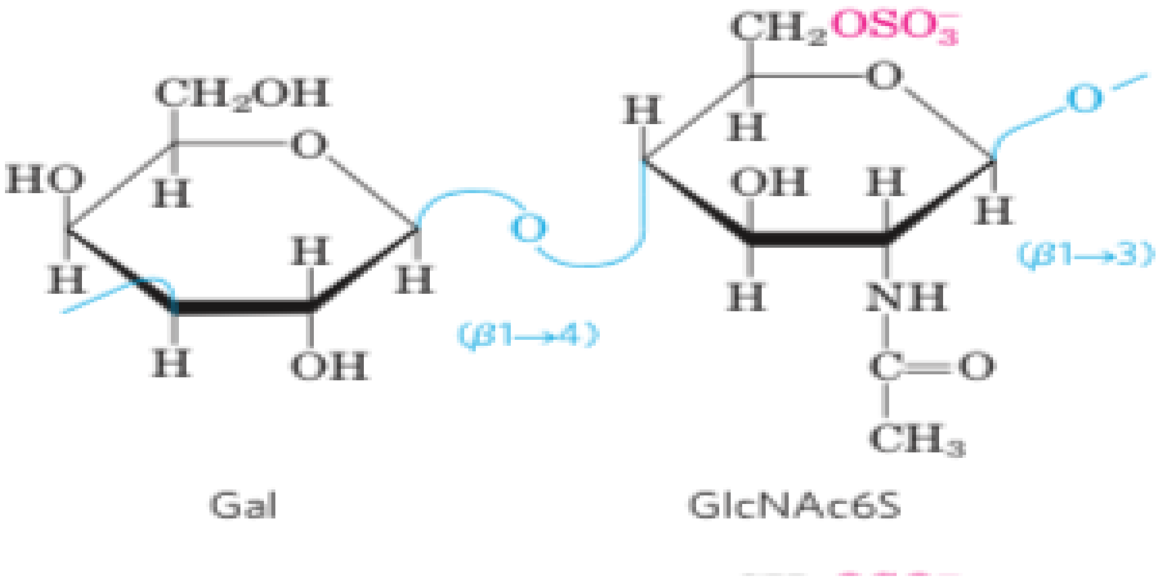
- ✓ Contains repeating units of D-glucuronic acid beta 1,3- N-acetyl galactosamine sulfate
- ✓ Each disaccharide unit is attached to the nest by beta-1,4 linkage
- ✓ Function: Contributes to tensile strength of cartilage, ligaments, tendons and walls of aorta



Glycosaminoglycans

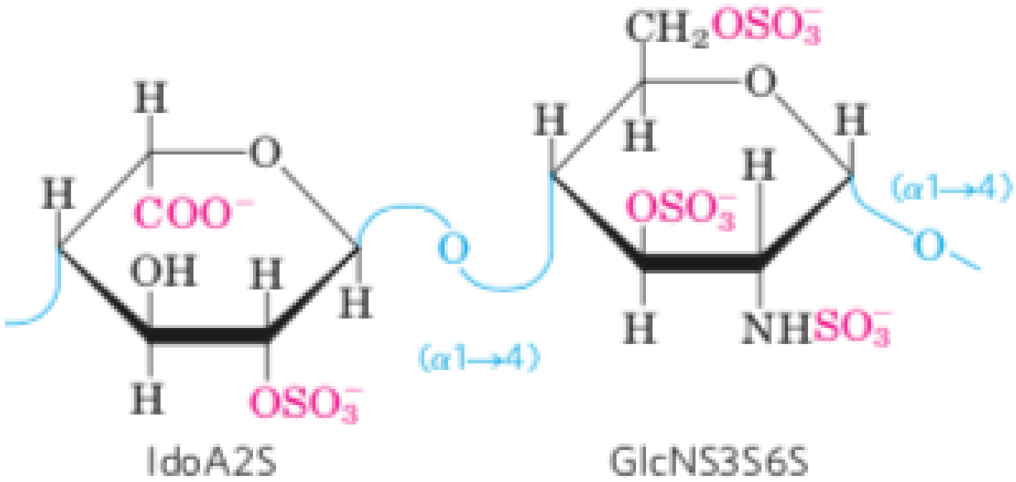
Keratan sulfate

- ✓ Contains repeating units of galactose and N-acetyl glucosamine in beta linkage
- ✓ No uronic acid
- ✓ Present in cornea, cartilage, bone, horn, hair, hoof, nails and claws



Heparan sulfate

- ✓ Produced by all animal cells; Contain variable arrangements of sulfated and nonsulfated sugars
- ✓ Interacts with large number of ECM components, various enzymes and factors in plasma
- ✓ Heparin (anti-coagulant) fractionated form of heparan-widely used when collecting blood for clinical studies
- ✓ Heparin activates antithrombin III which in turn inactivates thrombin, factor X and factor IX



Summary

- Polysaccharides serve fuel source
- Play structural roles
- Strengthens the exoskeletons of arthropods.
- Dextran forms an adhesive coat around certain bacteria
- Glycosaminoglycans- extracellular heteropolysaccharides
- These polymers provide- viscosity, adhesiveness, and tensile strength to the extracellular matrix

Polymer	Type*	Repeating unit[†]	Size (number of monosaccharide units)	Roles/significance
Starch				Energy storage: in plants
Amylose	Homo-	($\alpha1\rightarrow4$)Glc, linear	50–5,000	
Amylopectin	Homo-	($\alpha1\rightarrow4$)Glc, with ($\alpha1\rightarrow6$)Glc branches every 24–30 residues	Up to 10^6	
Glycogen	Homo-	($\alpha1\rightarrow4$)Glc, with ($\alpha1\rightarrow6$)Glc branches every 8–12 residues	Up to 50,000	Energy storage: in bacteria and animal cells
Cellulose	Homo-	($\beta1\rightarrow4$)Glc	Up to 15,000	Structural: in plants, gives rigidity and strength to cell walls
Chitin	Homo-	($\beta1\rightarrow4$)GlcNAc	Very large	Structural: in insects, spiders, crustaceans, gives rigidity and strength to exoskeletons
Dextran	Homo-	($\alpha1\rightarrow6$)Glc, with ($\alpha1\rightarrow3$) branches	Wide range	Structural: in bacteria, extracellular adhesive
Peptidoglycan	Hetero-; peptides attached	4)Mur2Ac($\beta1\rightarrow4$)GlcNAc($\beta1$	Very large	Structural: in bacteria, gives rigidity and strength to cell envelope
Agarose	Hetero-	3)D-Gal($\beta1\rightarrow4$)3,6-anhydro-L-Gal($\alpha1$	1,000	Structural: in algae, cell wall material
Hyaluronan (a glycosamino-glycan)	Hetero-; acidic	4)GlcA($\beta1\rightarrow3$)GlcNAc($\beta1$	Up to 100,000	Structural: in vertebrates, extracellular matrix of skin and connective tissue; viscosity and lubrication in joints

BT 203: Biochemistry

Lecture-4

Slide 3

After learning about monosaccharides and disaccharides, now we will learn how are complex carbohydrates formed.

Most carbohydrates found in nature occur as polysaccharides, polymers of medium to high molecular weight (Mw. 20,000). Polysaccharides, also called glycans, differ from each other in the identity of their recurring monosaccharide units, in the length of their chains, in the types of bonds linking the units, and in the degree of branching.

Homopolysaccharides contain only a single monomeric species whereas heteropolysaccharides contain two or more different kinds. Some homopolysaccharides **serve as storage forms of monosaccharides** that are used as fuels; starch and glycogen are homopolysaccharides of this type. Other homopolysaccharides (cellulose and chitin, for example) **serve as structural elements in plant cell walls and animal exoskeletons**. Heteropolysaccharides provide extracellular support for organisms of all kingdoms.

The table depicts the different types of polysaccharides with their components and linkages.

Slide 4:

This slide talks about the starch and glycogen structural units, and what are their functions. The most important storage polysaccharides are starch in plant cells and glycogen in animal cells.

Starch is storage polysaccharide, main sources of starch are rice, corn, wheat, potatoes and cassava.

Starch contains two types of glucose polymer, amylose and amylopectin. Amylose consists of long, unbranched chains of D-glucose residues connected by (α1- 4) linkages (as in maltose). Such chains vary in molecular weight from a few thousand to more than a million.

Amylopectin also has a high molecular weight (up to 200 million) but unlike amylose is highly branched. The glycosidic linkages joining successive glucose residues in amylopectin chains are (α1- 4); the branch points (occurring every 24 to 30 residues) are (α1- 6) linkages.

Glycogen is the main storage polysaccharide of animal cells. Like amylopectin, glycogen is a polymer of (α1-4)-linked subunits of glucose, with (α1- 6)-linked branches, but glycogen is more extensively branched (on average, every 8 to 12 residues) and more compact than starch. Glycogen is especially abundant in the liver, where it may constitute as much as 7% of the wet weight.

Slide 5: In this slide, we will discuss about the difference between the amylose and amylopectin, as both are the building blocks for the most important storage molecules for plant and animal kingdom.

Slide 6: Glycogen is considered as the wonder molecule, because each branch in glycogen ends with a nonreducing sugar unit, a glycogen molecule with n branches has n 1 1 nonreducing ends, but only one reducing end. When glycogen is used as an energy source, glucose units are removed one at a time from the nonreducing ends.

Why not store glucose in its monomeric form?

It has been calculated that hepatocytes store glycogen equivalent to a glucose concentration of 0.4 M. The actual concentration of glycogen, which is insoluble and contributes little to the osmolarity of the cytosol, is about 0.01 μM. If the cytosol contained 0.4 M glucose, the osmolarity would be threateningly elevated, leading to osmotic entry of water that might rupture the cell. Furthermore, with an intracellular glucose concentration of 0.4 M and an external concentration of about 5 mM (the concentration in the blood of a mammal), the free-energy change for glucose uptake into cells against this very high concentration gradient would be prohibitively large.

Slide 7:

Cellulose, a fibrous, tough, water-insoluble substance, is found in the cell walls of plants, particularly in stalks, stems, trunks, and all the woody portions of the plant body. Cellulose constitutes much of the mass of wood, and cotton is almost pure cellulose. Like amylose, the cellulose molecule is a linear, unbranched homopolysaccharide, consisting of 10,000 to 15,000 D-glucose units. But there is a very important difference: in cellulose the glucose residues have the beta configuration whereas in amylose the glucose is in the alpha configuration. The glucose residues in cellulose are linked by (beta-1,4) glycosidic bonds, in contrast to the (alpha -1,4) bonds of amylose. This difference causes individual molecules of cellulose and amylose to fold differently in space, giving them very different macroscopic structures and physical properties. The tough, fibrous nature of cellulose makes it useful in such commercial products as cardboard and insulation material, and it is a major constituent of cotton and linen fabrics. Cellulose is also the starting material for the commercial production of cellophane and rayon.

Vertebrates cannot digest the cellulose???

Glycogen and starch ingested in the diet are hydrolyzed by alpha-amylases and glycosidases, enzymes in saliva and the intestine that break (alpha-1,4) glycosidic bonds between glucose units. Most vertebrate animals cannot use cellulose as a fuel source, because they lack an enzyme to hydrolyze the (beta-1,4) linkages. Termites readily digest cellulose, but only because their intestinal tract harbors a symbiotic micro- organism, *Trichonympha*, that secretes cellulase, which hydrolyzes the (beta-1,4) linkages. There is one important exception to the absence of cellulase in vertebrates: ruminant animals such as cattle, sheep, and goats harbor symbiotic microorganisms in the stomach that can hydrolyze cellulose, allowing the animal to degrade dietary cellulose from soft grasses, but not from woody plants.

Chitin is a linear homopolysaccharide composed of *N*-acetylglucosamine residues in (beta-1, 4) linkage. The only chemical difference from cellulose is the replacement of the hydroxyl group at C-2 with an acetylated amino group. Chitin forms extended fibers like those of cellulose, and like cellulose cannot be digested by vertebrates. Chitin is the principal component of the hard exoskeletons of nearly a million species of arthropods—insects, lobsters, and crabs, for example— and is probably the second most abundant polysaccha- ride, next to cellulose, in nature; an estimated 1 billion tons of chitin are produced each year in the biosphere.

Slide 8:

The folding of polysaccharides in three dimensions follows the same principles as those governing polypeptide structure: subunits with a more-or-less rigid structure dictated by covalent bonds form three-dimensional macromolecular structures that are stabilized by weak interactions within or between molecules, such as hydrogen bonds and hydrophobic and van der Waals interactions, and, for polymers with charged subunits, electrostatic interactions. Because polysaccharides have so many hydroxyl groups, hydrogen bonding has an especially important influence on their structure. There is, in principle, free rotation about both COO bonds linking the residues, but as in polypeptides, rotation about each bond is limited by steric hindrance by substituents. The most stable three-dimensional structure for the (alpha-1, 4)-linked chains of starch and glycogen is a tightly coiled helix, stabilized by interchain hydrogen bonds. For cellulose, the most stable conformation is that in which each chair is turned 1808 relative to its neighbors, yielding a straight, extended chain. All —OH groups are available for hydrogen bonding with neighboring chains. With several chains lying side by side, a stabilizing network of interchain and intrachain hydrogen bonds produces straight, stable supramolecular fibers of great tensile strength. This property of cellulose has made it a useful substance to civilizations for millennia. Many manufactured products, including papyrus, paper, cardboard, rayon, insulating tiles, and a variety of other useful materials, are derived from cellulose. The water content of these materials is low because extensive interchain hydrogen bonding between cellulose molecules satisfies their capacity for hydrogen-bond formation.

Slide 9:

Glycosaminoglycans, are a family of linear polymers composed of repeating disaccharide units. They are unique to animals and bacteria and are not found in plants. One of the two monosaccharides is always either *N*-acetylglucosamine or *N*-acetylgalactosamine; the other is in most cases a uronic acid, usually D-glucuronic or L-iduronic acid. Some glycosaminoglycans contain esterified sulfate groups. The combination of sulfate groups and the carboxylate groups of the uronic acid residues gives glycosaminoglycans a very high density of negative charge. To minimize the repulsive forces among neighboring charged groups, these molecules assume an extended conformation in solution, forming a rodlike helix in which the negatively charged carboxylate groups occur on alternate sides of the helix. The extended rod form also provides maximum separation between the negatively charged sulfate groups. The specific patterns of sulfated and nonsulfated sugar residues in glycosaminoglycans provide for specific recognition by a variety of protein ligands that bind electrostatically to these molecules.

The glycosaminoglycan **hyaluronan** (hyaluronic acid) contains alternating residues of D-glucuronic acid and *N*-acetylglucosamine. With up to 50,000 repeats of the basic disaccharide unit, hyaluronan has a molecular weight of several million; it forms clear, highly viscous solutions that serve as lubricants in the synovial fluid of joints and give the vitreous humor of the vertebrate eye its jellylike consistency Hyaluronan is also a component of the extracellular matrix of cartilage and tendons, to which it contributes tensile strength and elasticity as a result of its strong noncovalent interactions with other components of the matrix. Hyaluronidase, an enzyme secreted by some pathogenic bacteria, can hydrolyze the glycosidic linkages of hyaluronan, rendering tissues more susceptible to bacterial invasion. In many animal species, a similar enzyme in sperm hydrolyzes an outer glycosaminoglycan coat around the ovum, allowing sperm penetration.

Chondroitin sulfate-Greek *chondros*, “cartilage”- contributes to the tensile strength of cartilage, tendons, ligaments, and the walls of the aorta. Dermatan sulfate -Greek *derma*, “skin”- contributes to the pliability of skin and is also present in blood vessels and heart valves. In this polymer, many of the glucuronate residues present in chondroitin sulfate are replaced by their 5-epimer, L-iduronate (IdoA).

Slide 10:

Keratan sulfates-Greek *keras*, “horn”-have no uronic acid and their sulfate content is variable. They are present in cornea, cartilage, bone, and a variety of horny structures formed of dead cells: horn, hair, hoofs, nails, and claws.

Heparan sulfate -Greek *he p̄ar*, “liver”- is produced by all animal cells and contains variable arrangements of sulfated and nonsulfated sugars. The sulfated segments of the chain allow it to interact with many proteins, including growth factors and ECM components, as well as various enzymes and factors present in plasma. Heparin is a fractionated form of heparan sulfate derived mostly from mast cells. Heparin is a therapeutic agent used to inhibit coagulation through its capacity to bind the protease inhibitor antithrombin. Heparin binding causes antithrombin to bind to and inhibit thrombin, a protease essential to blood clotting. The interaction is strongly electrostatic; heparin has the highest negative charge density of any known biological macromolecule. Purified heparin is routinely added to blood samples obtained for clinical analysis, and to blood donated for transfusion, to prevent clotting.

Slide 11:

Summary

- Polysaccharides (glycans) serve as stored fuel and as structural components of cell walls and extracellular matrix.
- The homopolysaccharides starch and glycogen are stored fuels in plant, animal, and bacterial cells. They consist of D-glucose with (alpha -1,4) linkages, and both contain some branches.
- The homopolysaccharides cellulose, chitin, and dextran serve structural roles. Cellulose, composed of (beta 1,4)-linked D-glucose residues, lends strength and rigidity to plant cell walls. Chitin, a polymer of (beta-1,4)-linked *N*-acetylglucosamine, strengthens the exoskeletons of arthropods. Dextran forms an adhesive coat around certain bacteria.
- Homopolysaccharides fold in three dimensions. The chair form of the pyranose ring is essentially rigid, so the conformation of the polymers is determined by rotation about the bonds from the rings to the oxygen atom in the glycosidic linkage.
- Starch and glycogen form helical structures with intrachain hydrogen bonding; cellulose and chitin form long, straight strands that interact with neighboring strands.
- Glycosaminoglycans are extracellular heteropolysaccharides in which one of the two monosaccharide units is a uronic acid (keratin sulfate is an exception) and the other an *N*-acetylated amino sugar.
- Sulfate esters on some of the hydroxyl groups and on the amino group of some glucosamine residues in heparasain and in heparan sulfate give these polymers a high density of negative charge, forcing them to assume extended conformations.
- These polymers (hyaluronan, chondroitin sulfate, dermatan sulfate, and keratan sulfate) provide viscosity, adhesiveness, and tensile strength to the extracellular matrix

Lecture 5

BT 203

Biochemistry

3-0-0-6

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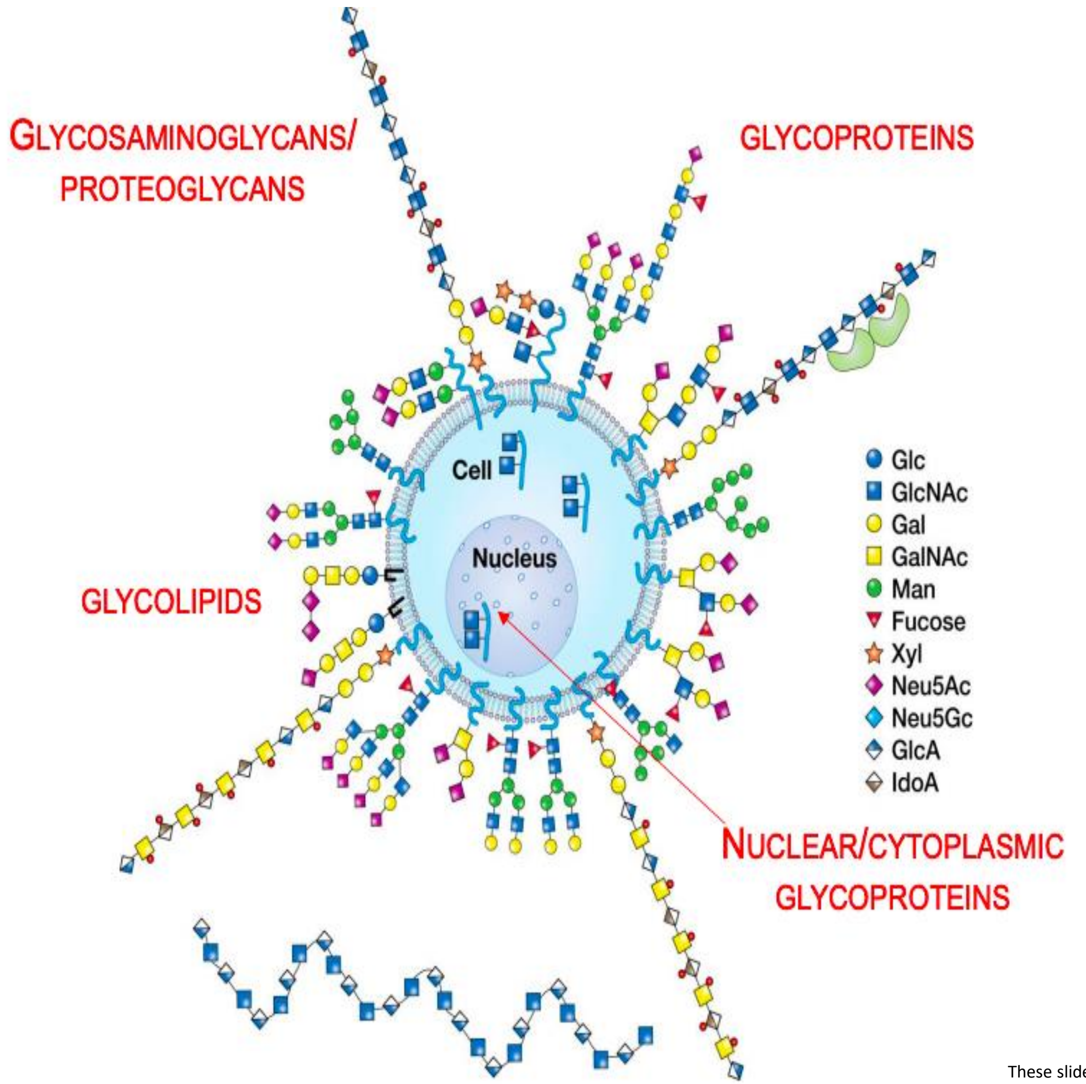
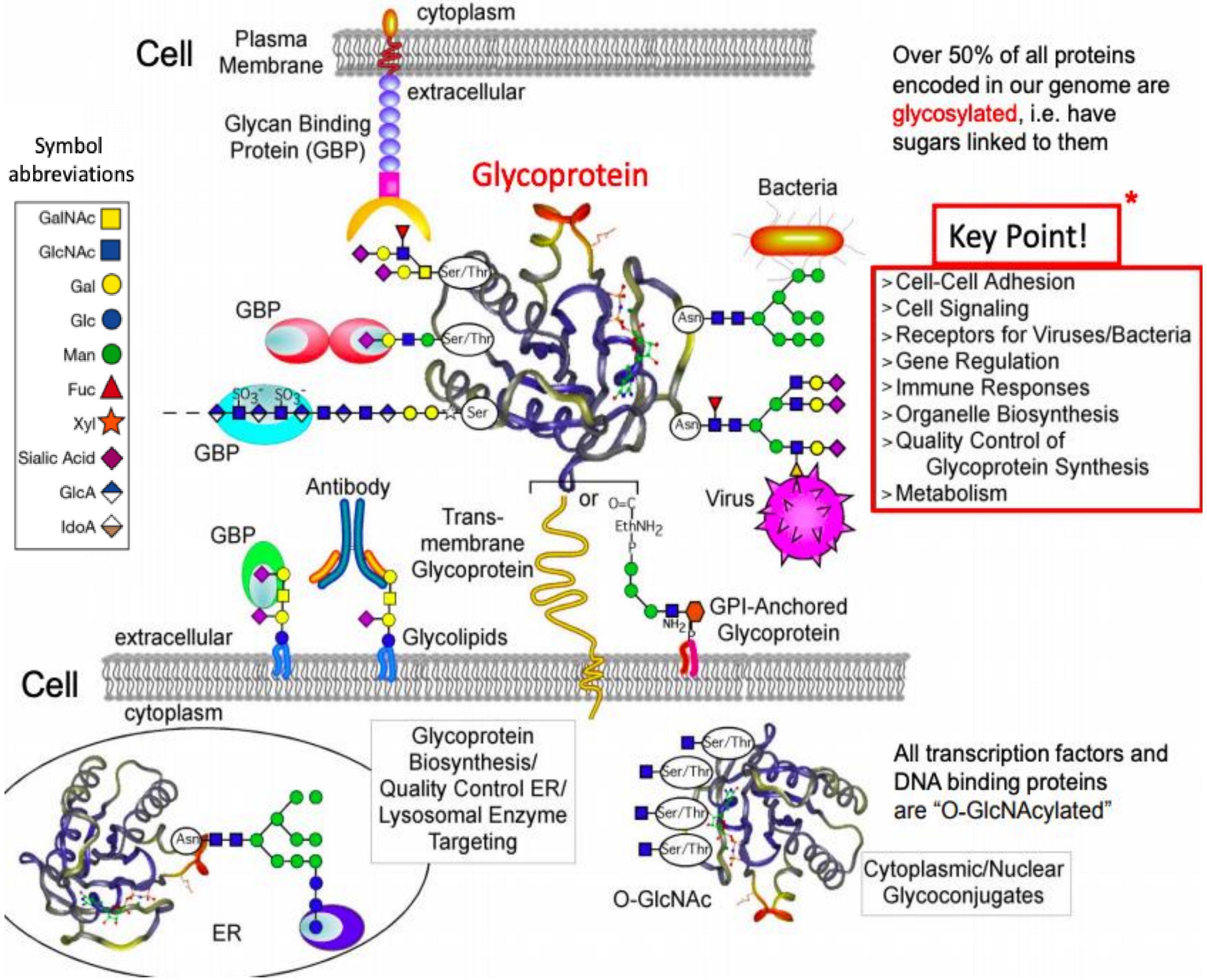
Key Concepts

- What are glycoconjugates?
- What are the different types of glycoconjugates?
- What are the biological functions of glycoconjugates?
- What determines your blood group?
- What are diseases associated with glycoconjugates?

Glycoconjugates

- ✓ Covalent linkage of oligosaccharide and protein or lipid to form conjugates-biologically active molecule
- ✓ Involved in cell to cell communication, cell signaling, cell adhesion and migration, blood clotting and wound healing





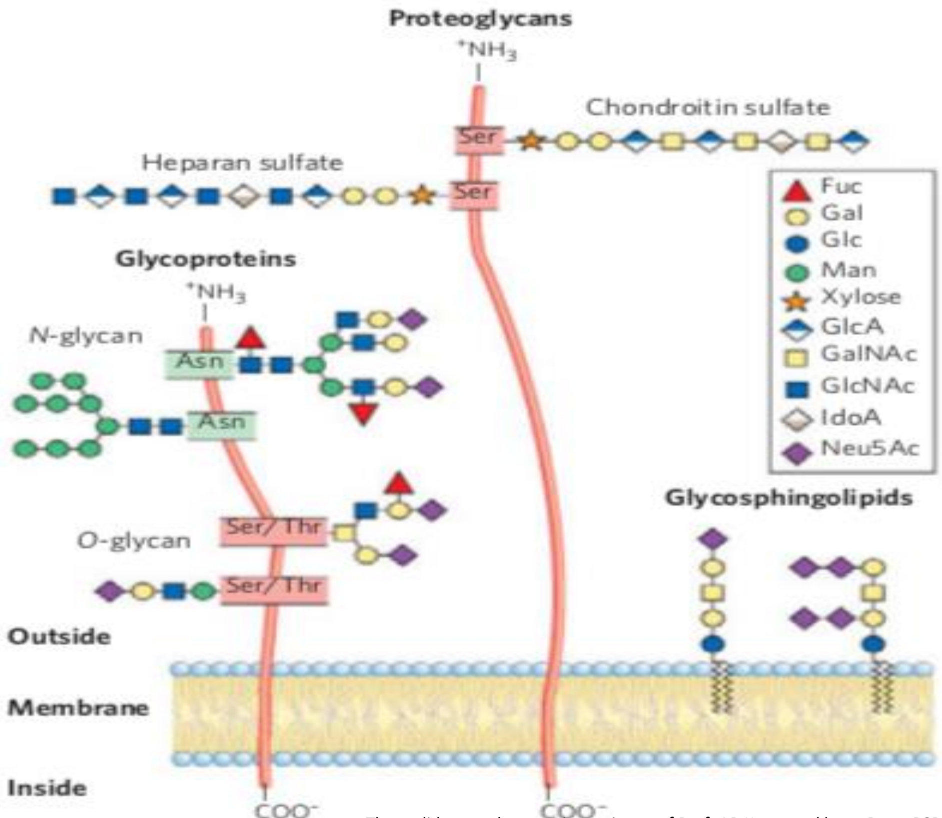
Proteoglycans

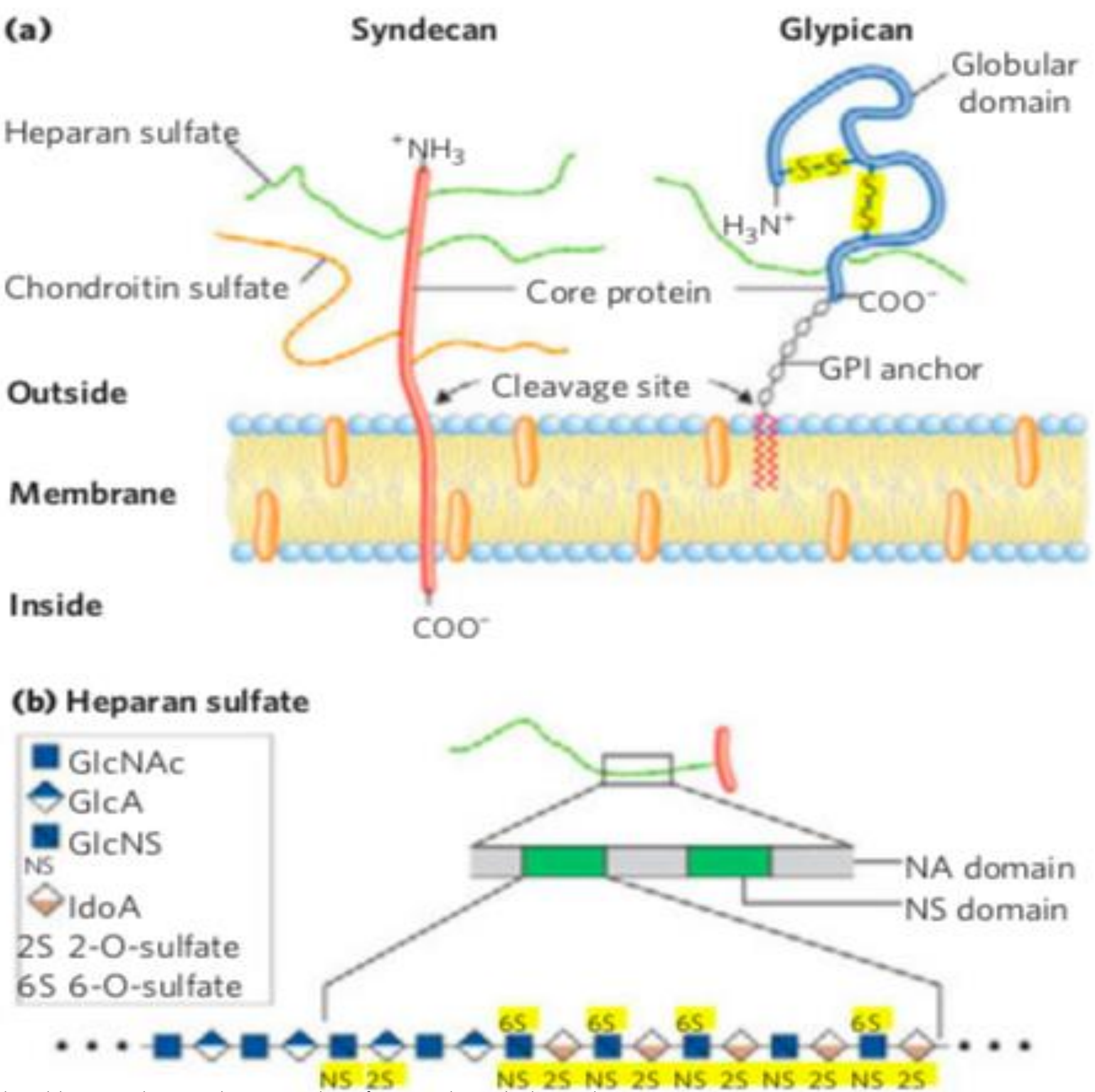
Proteoglycans:

- Core protein covalently attached to glycosaminoglycans
- Point of attachment is "Serine"
- 2 major types of heparan sulfate proteoglycans

a. Syndecans

b. Glypicans



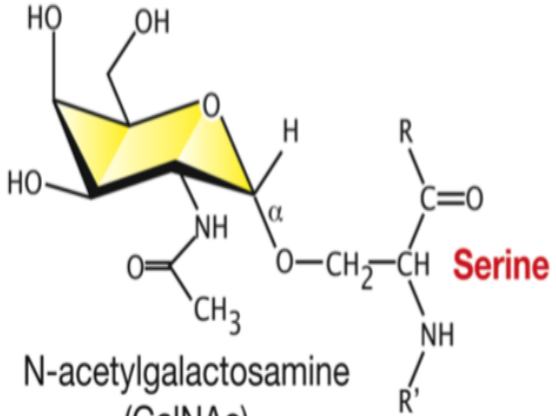


Glycoproteins

Two major glycosidic linkages in glycoproteins

O-Glycan (to Serine and Threonine)

Typical O-glycan Linkage
GalNAcα1-Ser/Thr

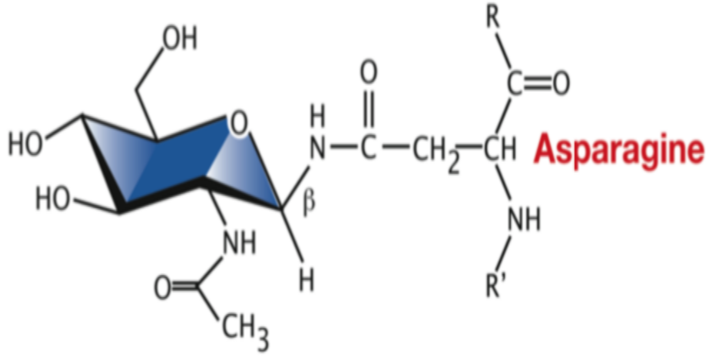


N-acetylgalactosamine (GalNAc)

No consensus sequence, but modified Serine or Threonine (Ser/Thr) residues are often adjacent or near Pro residues

N-Glycan (to Asparagine)

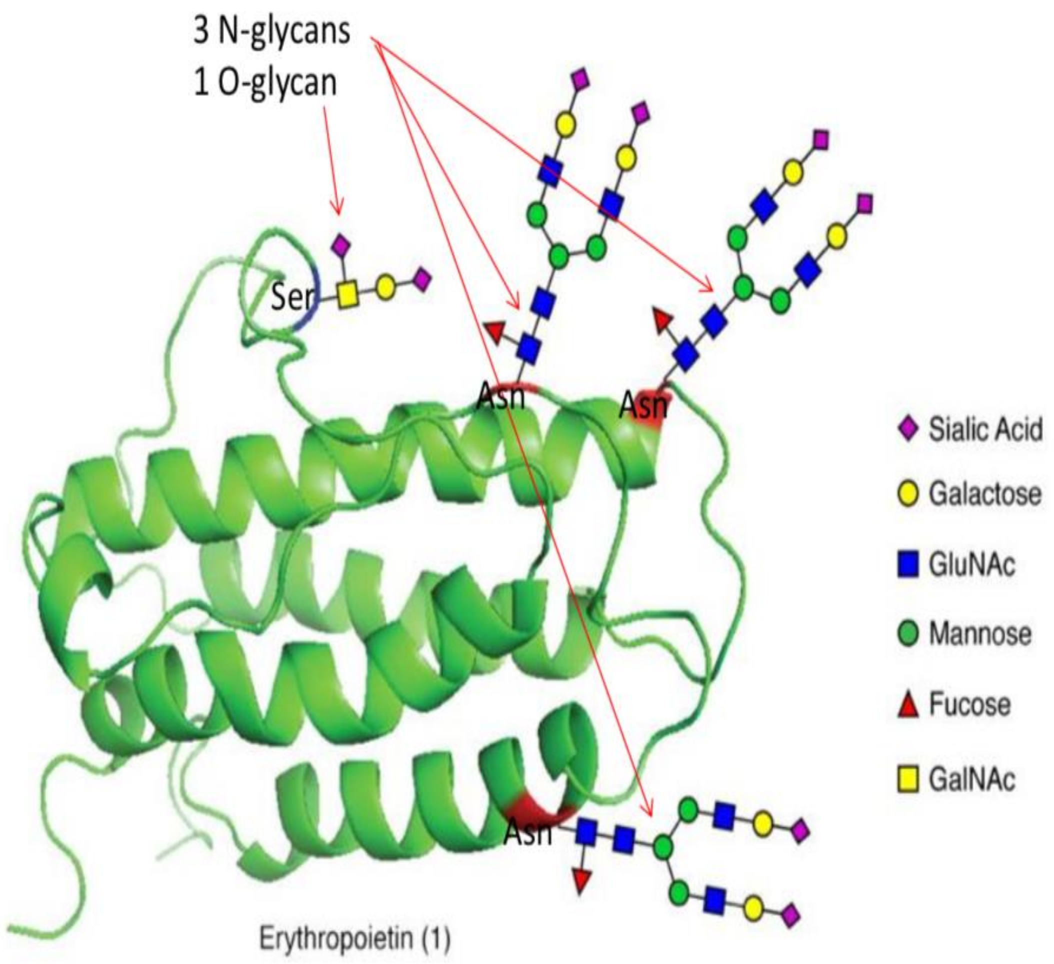
Typical N-glycan Linkage
GlcNAcβ1-Asn



N-acetylglucosamine (GlcNAc)

Always in consensus sequence
---Asn-X-Ser/Thr---
Where X = any amino acid except Pro

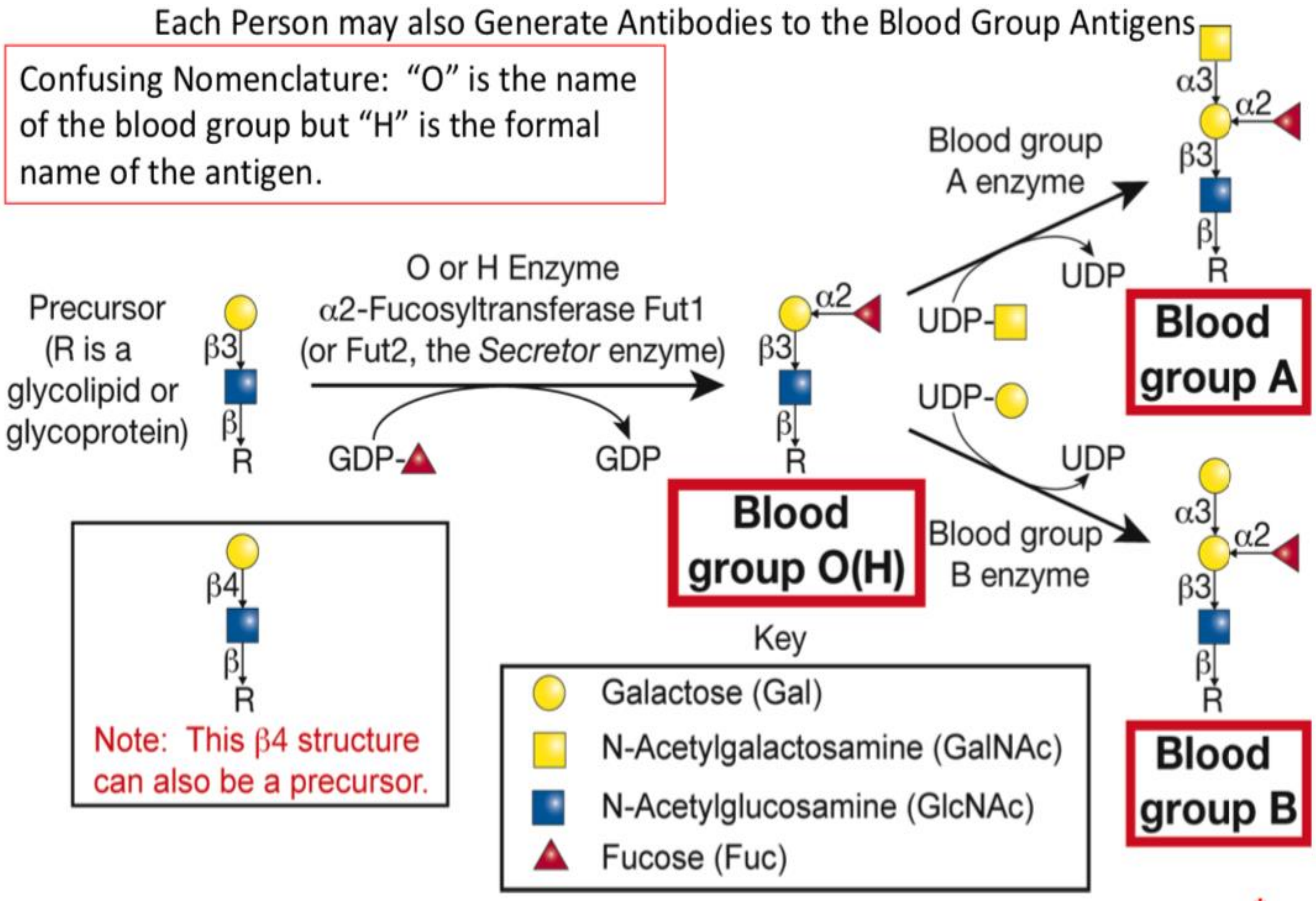
Erythropoietin is a glycoprotein hormone



Your blood group is decided by carbohydrates

Blood Type	Erythrocyte antigens	Serum antibodies that can agglutinate other erythrocytes
A	A	Anti-B
B	B	Anti-A
AB	A &B	none
O	H	Anti-A & Anti-B

- ABO(H) blood group antigens are proteins containing carbohydrate structures synthesized in Golgi apparatus of megakaryocytes
- People with blood group 'O' are universal red cell donors and people with blood group AB are universal red cell recipients.

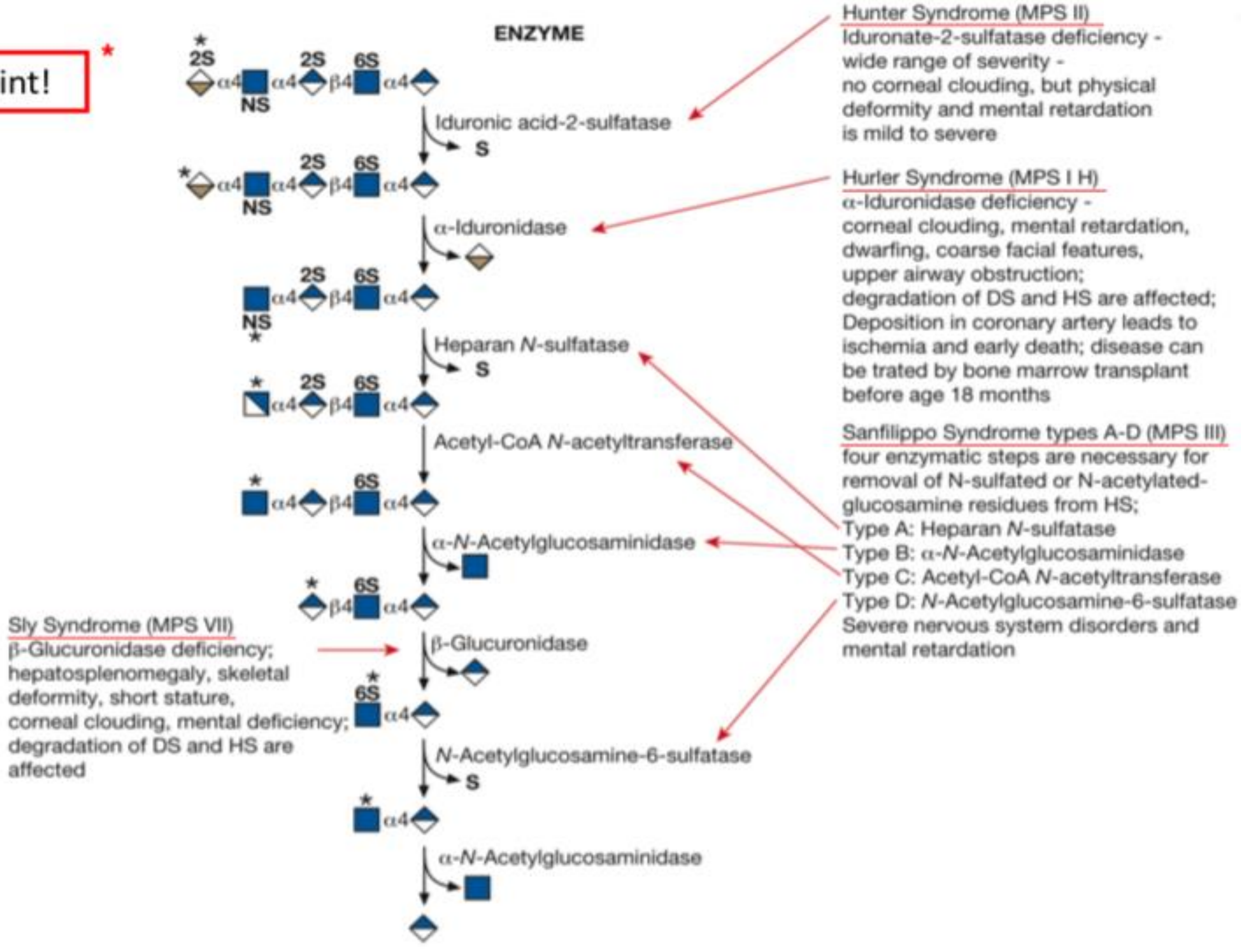


Key Point! – ABO are different carbohydrate structures on red blood cells

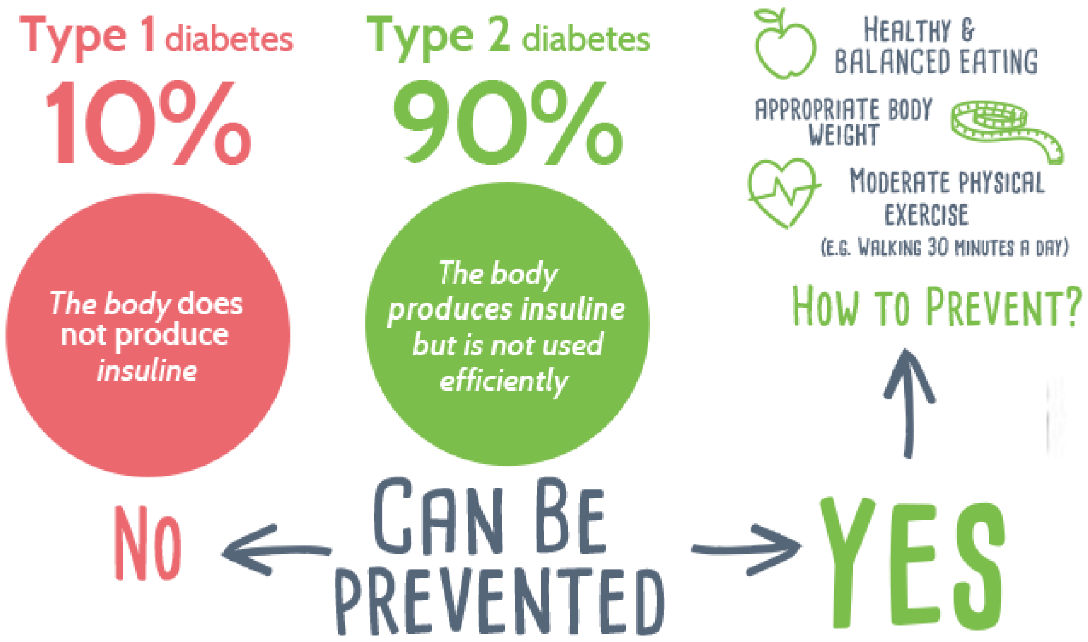
Mucopolysaccharidoses (Lysosomal Storage Diseases-LSDs)

- Inherited metabolic diseases characterized by deficiency of glycohydrolase
- Results in accumulation of glycosaminoglycans
- Causes permanent progressive cellular, organ and system damage and mental development
- Defects in degradation of glycolipids are also associated with LSDs-Ex: Tay Sachs disease
- Tay Sachs is caused by the mutation in hexosaminidase and results in the accumulation of ganglioside and is characterized by fatal deterioration of brain function

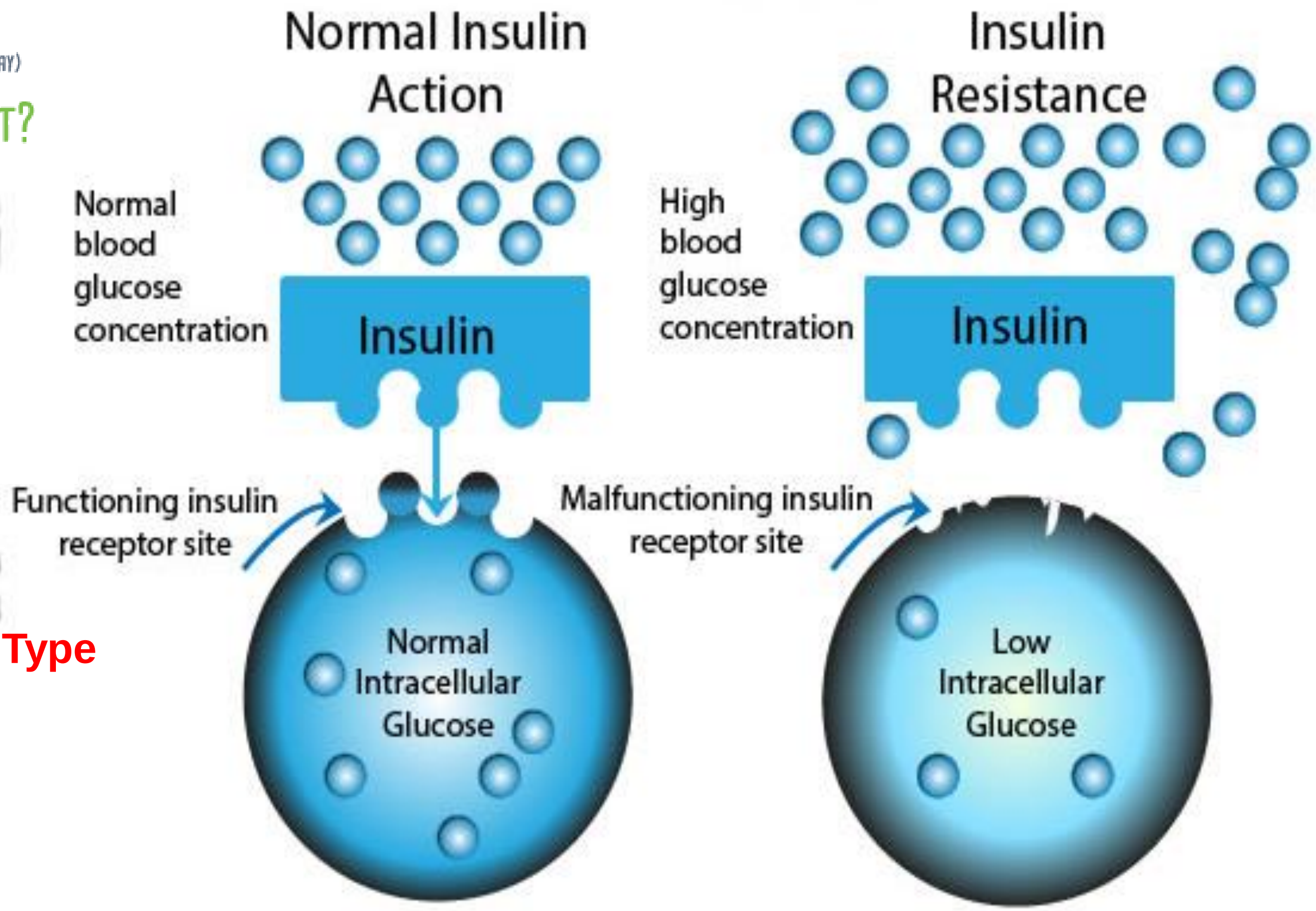
Key Point! *



Diabetes



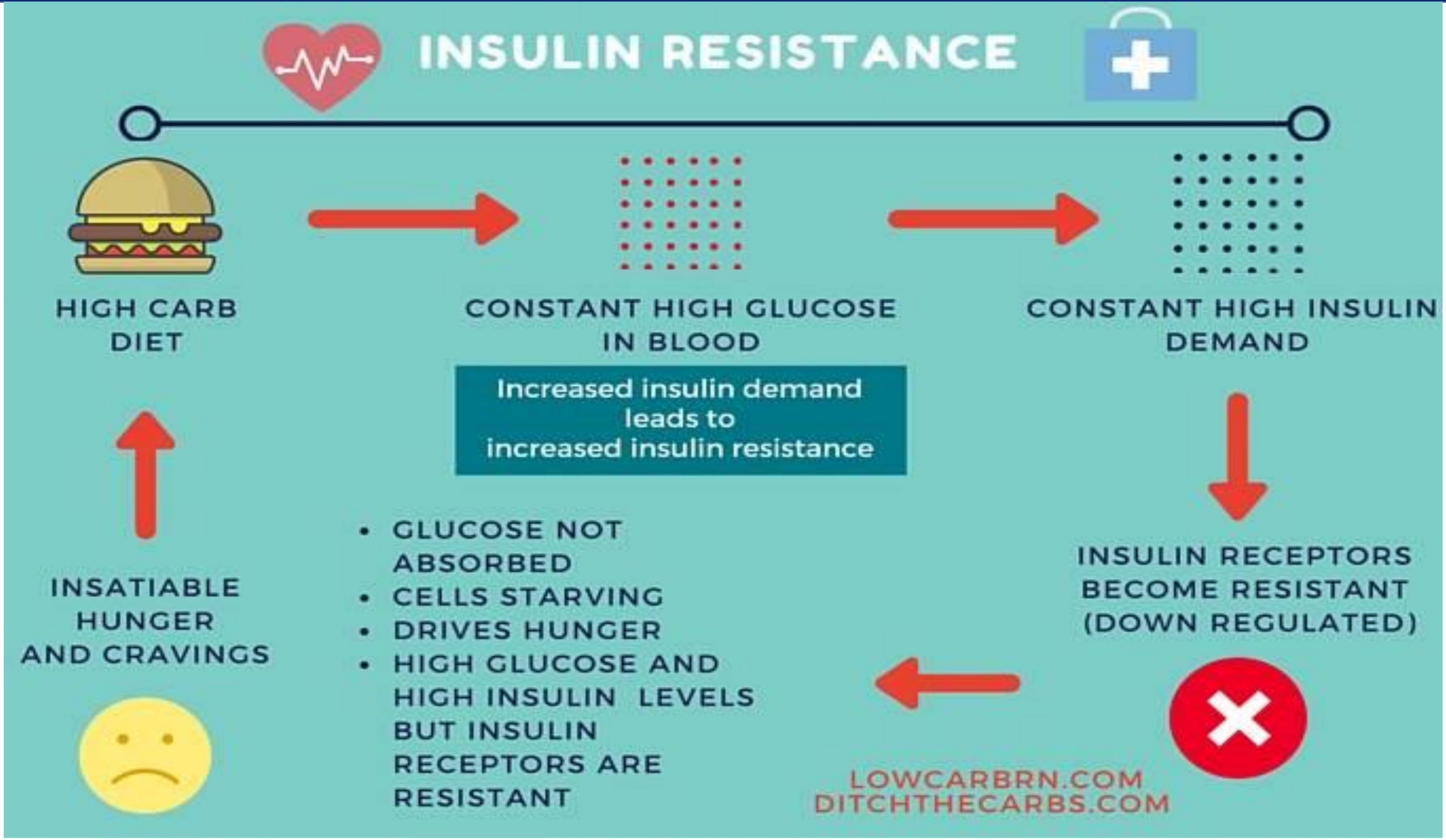
Mechanism of Insulin Resistance



- ✓ **Type 1 and Type 2 diabetes, More prevalent is the Type 2 diabetes**
- ✓ **Type 2 diabetes- body cannot process the sugar**
- ✓ **Major issues in the insulin pathway where insulin receptor malfunctions leading to low glucose concentration in the cell**

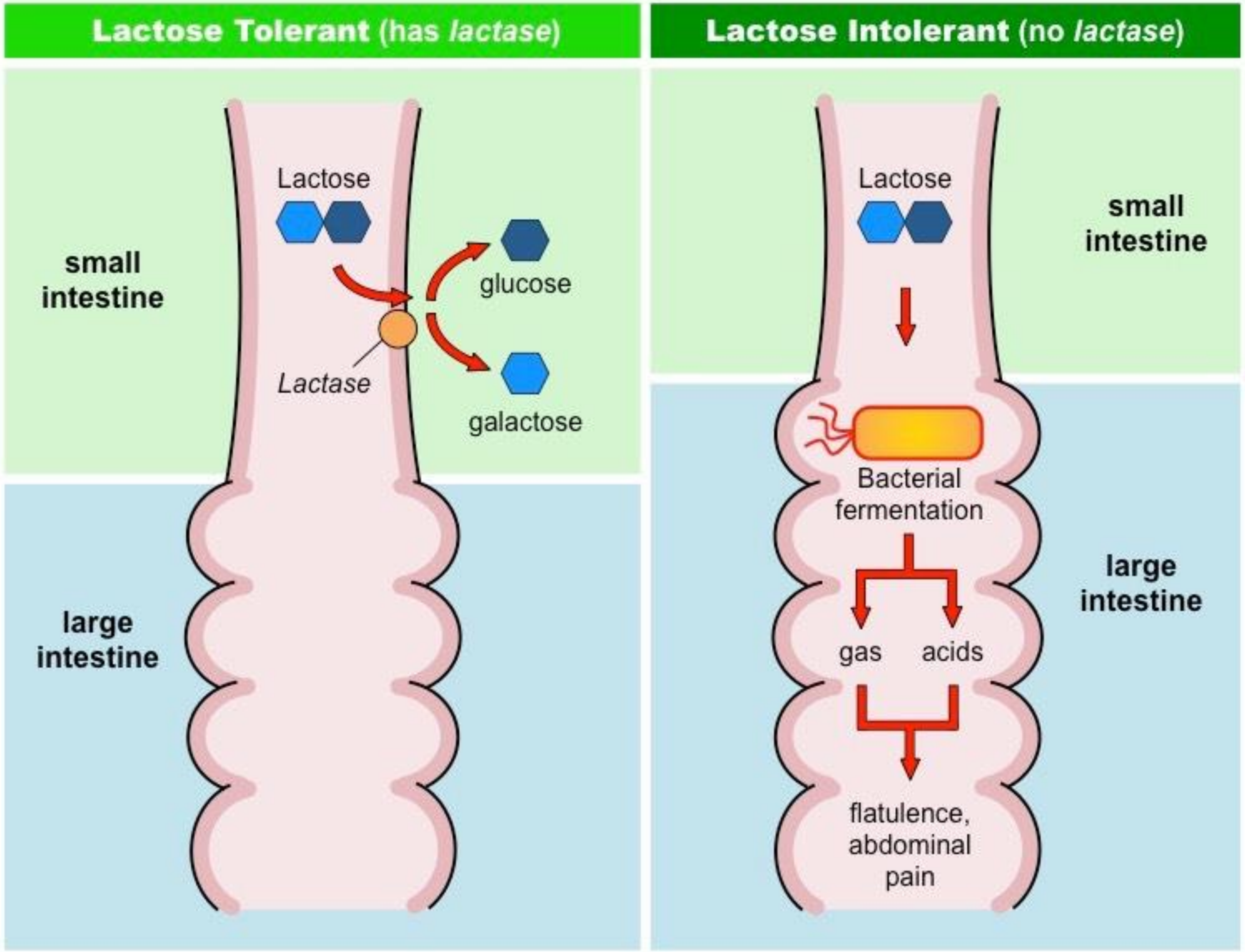
Source- http://www.med.soton.ac.uk/mooc/science/changet21.html

Diabetes- High Carb and Low carb Diet



Lactose Intolerance

- ✓ Lactose or milk sugar found in the milk of mammals - 4-6% in cow's milk and 5-8% in human milk.
- ✓ Lactose intolerance is the inability to digest significant amounts of lactose, the predominant sugar of milk
- ✓ Inability results from a shortage of the enzyme lactase
- ✓ Lactase breaks down the lactose, milk sugar, into glucose and galactose that can then be absorbed into the bloodstream.



Source-https://sites.google.com/site/lactoseintolerancemtwn9156283/1

<u>BT 203: Biochemistry</u>

Lecture: 5

Slide 3:

On almost every eukaryotic cell, specific oligosaccharide chains attached to components of the plasma membrane form a carbohydrate layer (the glycocalyx). This layer is several nanometers thick, that serves as an information-rich surface that the cell shows to its surroundings.

Proteoglycans are macromolecules of the cell sur- face or extracellular matrix in which one or more sulfated glycosaminoglycan chains are joined covalently to a membrane protein or a secreted protein. The glycosaminoglycan chain can bind to extracellular proteins through electrostatic interactions between the protein and the negatively charged sugar moieties on the proteoglycan. Proteoglycans are major components of all extracellular matrices

Glycoproteins have one or several oligosaccharides of varying complexity joined covalently to a protein. They are usually found on the outer face of the plasma membrane (as part of the glycocalyx), in the extracellular matrix, and in the blood. Inside cells they are found in specific organelles such as Golgi complexes, secretory granules, and lysosomes. The oligosaccharide portions of glycoproteins are very heterogeneous, and, like glycosaminoglycans, they are rich in information, forming highly specific sites for recognition and high- affinity binding by carbohydrate-binding proteins called lectins. Some cytosolic and nuclear proteins can be glycosylated as well.

Glycosphingolipids are plasma membrane com- ponents in which the hydrophilic head groups are oligo- saccharides. As in glycoproteins, the oligosaccharides act as specific sites for recognition by lectins. The brain and neurons are rich in glycosphingolipids, which help in nerve conduction and myelin formation. Glycosphingolipids also play a role in signal transduction in cells

These oligosaccharides are central players in cell-cell recognition and adhesion, cell migration during development, blood clotting, the immune response, wound healing, and other cellular processes. In most of these cases, the informational carbohydrate is covalently joined to a protein or a lipid to form a **glycoconjugate**, which is the biologically active molecule.

Slide 4:

Mammalian cells can produce 40 types of proteoglycans. These molecules act as tissue organizers, and they influence various cellular activities, such as growth factor activation and adhesion. The basic proteoglycan unit consists of a "core protein" with covalently attached glycosaminoglycan(s). The point of attachment is a Serine residue, to which the glycosaminoglycan is joined through a tetra-saccharide bridge. The Ser residue is generally in the sequence –Ser–Gly–X–Gly– (where X is any amino acid residue), although not every protein with this sequence has an attached glycosaminoglycan. Many proteoglycans are secreted into the extracellular matrix, but some are integral membrane proteins.

There are two major families of membrane heparan sulfate proteoglycans.

Syndecans have a single transmembrane domain and an extracellular domain bearing three to five chains of heparan sulfate and in some cases chondroitin sulfate.

Glypicans are attached to the membrane by a lipid anchor, a derivative of the membrane lipid phosphatidylinositol (see Fig. 11–15).

Both syndecans and glypicans can be shed into the extracellular space. A protease in the ECM that cuts close to the membrane surface releases syndecan ectodomains (those domains outside the plasma mem- brane), and a phospholipase that breaks the connection to the membrane lipid releases glypicans. These mechanisms provide a way for a cell to change its surface features quickly. Shedding is highly regulated and is activated in proliferating cells, such as cancer cells. Proteoglycan shedding is involved in cell-cell recognition and adhesion, and in the proliferation and differentiation of cells. Numerous chondroitin sulfate and dermatan sulfate proteoglycans also exist, some as membrane-bound entities, others as secreted products in the ECM

Slide 5:

Two major types of glycosylation of proteins can occur

1. O-glycosylation and proteins are O-Glycans

   In this, sugars are attached to oxygen, typically on serine or threonine, but very rarely on tyrosine and other non-canonical amino acids such as hydroxylysine and hydroxyproline. No consensus sequences are quired but modified Ser or Thr residues are often adjacent to each other or near the Pro residue.

2. N-glycosylation:

   In this, sugars are attached to nitrogen typically on the amide chain of asparagine. Always require consensus sequence “---Asn-X-Ser/Thr---" where X can be any amino acid except Pro.

A very good example of glycoprotein is a hormone -erythropoietin synthesized mainly by kidney. It stimulates red cell production and is involved in the development of erythroid lineage from multipotent progenitors. Nonhematopoietic roles of erythropoietin includes vasoconstriction-dependent hypertension, stimulating angiogenesis, and promoting cell survival via activation of EPO receptors resulting in anti-apoptotic effects on ischemic tissues

Slide 6:

- ABO(H) blood group antigens are carbohydrate structures synthesized on glycoproteins and glycolipids in the Golgi apparatus of red blood cell precursors, megakaryocytes, and many types of epithelial cells, and occur on cell surfaces and in secretions. Biosynthesis occurs through a series of enzymatic reactions that add a single sugar from a nucleotide sugar donor to an acceptor as shown
- Nucleotide sugars used: GDP-Fucose, UDP-Galactose, UDP-N-acetylgalactosamine
- The products of the reactions of Fut1 (H-enzyme) or Fut2 (secretor enzyme) become the acceptors for the Blood group A or B enzymes, to create the human A or B antigens, respectively

- People with blood group A, have both the A enzyme and the Fut1 enzyme, whereas people with blood group B, have the B enzyme and the Fut1 enzyme.
- People with blood group O(H) lack the A and B enzyme and have Fut1 enzyme.
- The secretor H structure is inherited independently (Fut2) and some people are non- secretors (meaning no blood antigens are in saliva, etc.), and some are secretors, where they can make blood group antigens in secretion

Antigens on erythrocytes and antibodies to blood groups

Blood Type	Erythrocyte antigens	Serum antibodies that can agglutinate other erythrocytes
A	A	Anti-B
B	B	Anti-A
AB	A &B	none
O	H	Anti-A & Anti-B

Universal donors: “O”

Universal recipients: “AB”

Slide 7:

The mucopolysaccharidoses (lysosomal storage diseases or LSDs) are a group of inherited metabolic diseases in which a defective or missing glycohydrolase enzyme causes accumulation of complex sugars (GAGs in many cases) to accumulate in harmful amounts in the body's cells and tissues.

This accumulation causes permanent, progressive cellular damage that affects appearance, physical abilities, organ and system functioning, and, in most cases, mental development.

Depending on the type of mucopolysaccharidosis (MPS (x)), affected individuals may have normal intellect or may be profoundly retarded, may experience developmental delay, or have severe behavioral problems.

Physical symptoms generally include coarse or rough facial features, thick lips, an enlarged mouth and tongue, short stature with a disproportionately short trunk (dwarfism), abnormal bone size or shape (and other skeletal irregularities), thickened skin, enlarged organs such as the liver or spleen, hernias, and excessive body hair growth

Slide 8:

Let's talk about one of the most important chronic diseases affecting worldwide i.e., diabetes.

Diabetes is a chronic (long-lasting) health condition that affects how your body turns food into energy.

Most of the food you eat is broken down into sugar (also called glucose) and released into your bloodstream. When your blood sugar goes up, it signals your pancreas to release insulin. Insulin acts like a key to let the blood sugar into your body's cells for use as energy. If you have diabetes, your body either doesn't make enough insulin or can't use the insulin it makes as well as it should. When there isn't enough insulin or cells stop responding to insulin, too much blood sugar stays in your bloodstream. Over time, that can cause serious health problems, such as heart disease, vision loss, and kidney disease. There are different types of diabetes like Type 1 and Type 2 diabetes. Type 1 diabetes is thought to be caused by an autoimmune reaction (the body attacks itself by mistake) that stops your body from making insulin. Approximately 5-10% of the people who have diabetes have type.

With type 2 diabetes, your body doesn't use insulin well and can't keep blood sugar at normal levels. About 90-95% of people with diabetes have type 2. It develops over many years and is usually diagnosed in adults. Type 2 diabetes is more prevalent than Type 1 diabetes.

Mechanism of Insulin resistance- Initially, the body is insulin resistant - this means that even though the pancreas is producing insulin, the cells in the body do not respond to it normally. It is not totally understood why this happens but it may be due to defective cellular pathways including binding of insulin to its receptor where it triggers its actions, dysfunctional signals sent from receptor binding, or due to overeating, the insulin receptors are all fully bound with insulin and so insulin can have no additional effects as there are no spare insulin receptors.

Insulin resistance affects many of the organs in the body, including liver, muscle and adipose tissue that are important for regulation of glucose homeostasis. Insulin resistance also affects other organs such as the ovaries (polycystic ovary syndrome) and the blood vessels (contributing to heart disease, and vascular diseases such as stroke and peripheral vascular disease).

Some people with type 2 diabetes do not ever need insulin treatment but require medicines that make their cells respond better to insulin.

In many people with type 2 diabetes, the β cells work extra hard to produce more insulin to try to overcome the insulin resistance. This leads to exhaustion of the β cells and their destruction, and a reduction in the amount of insulin produced. This is why some people with type 2 diabetes require treatment with insulin. In type 2 diabetes, the timeline for insulin requirement is variable or they may not require insulin ever.

Slide 9:

With diabetes, the body can't effectively process carbohydrates. Normally, when you eat carbs, they're broken down into small units of glucose, which end up as blood sugar.

When blood sugar levels go up, the pancreas responds by producing the hormone insulin. This hormone allows blood sugar to enter cells. In people without diabetes, blood sugar levels remain within a narrow range throughout the day. For those who have diabetes, however, this system doesn't work in the same way. This is a big problem, because having both too high and too low blood sugar levels can cause severe harm. There are several types of diabetes, but the two most common ones are type 1 and type 2 diabetes. Both of these conditions can occur at any age. In type 1 diabetes, an autoimmune process destroys the insulin-producing beta cells in the pancreas. People with diabetes take insulin several times a day to ensure that glucose gets into the cells and stays at a healthy level in the bloodstream.

In type 2 diabetes, the beta cells at first produce enough insulin, but the body's cells are resistant to its action, so blood sugar remains high. To compensate, the pancreas produces more insulin, attempting to bring blood sugar down. Over time, the beta cells lose their ability to produce enough insulin. Of the three macronutrients — protein, carbs, and fat — carbs have the greatest impact on blood sugar management. This is because the body breaks them down into glucose.

Therefore, people with diabetes may need to take large doses of insulin, medication, or both when they eat a lot of carbohydrates.

What’s more, low carb diets seem to work well in the long term when people stick to them. In one study, people with type 2 diabetes ate a low carb diet for 6 months. Their diabetes remained well managed more than 3 years later if they stuck to the diet

Slide 10:

The diminished ability to digest lactose (commonly found in dairy products such as: milk, cream and cheese) is called lactose intolerance. When lactose enters our bodies, the lactose is commonly digested and broken down by an enzyme by the name of lactase. Lactase is manufactured by the cells that exist in the lining of our small intestines. If lactose-based products are consumed by lactose intolerant suffers, there is a strong likelihood that they will experience abdominal discomfort from bloating, diarrhoea, nausea and flatulence.

A majority of suffers with reduced lactase levels do somewhat hang onto some lactase activity and can consume varying quantities of products containing lactose suffering little to no symptoms.