Introduction To Cell Biology
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Enzymes, Carbohydrates And Lipids

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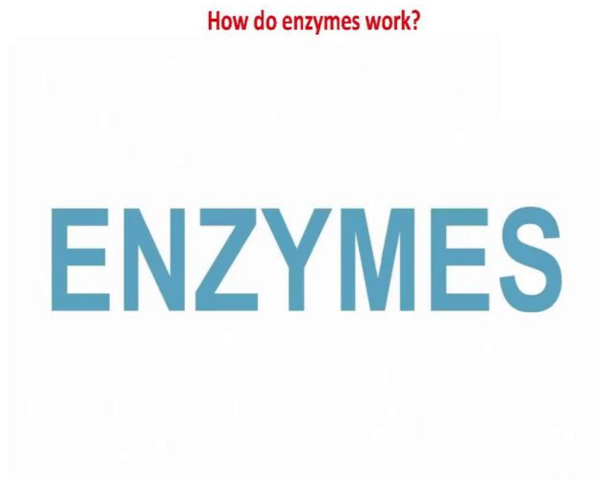
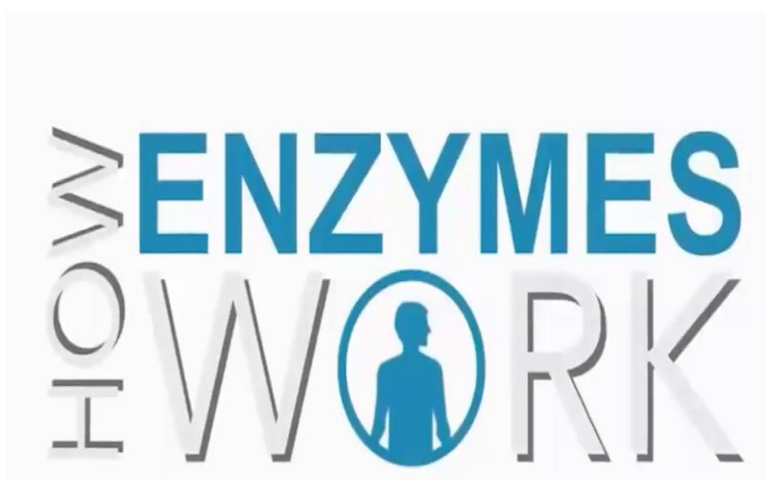
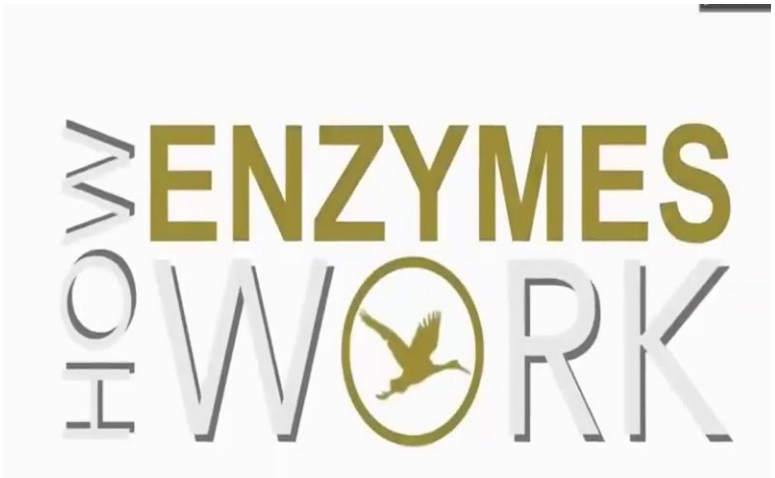




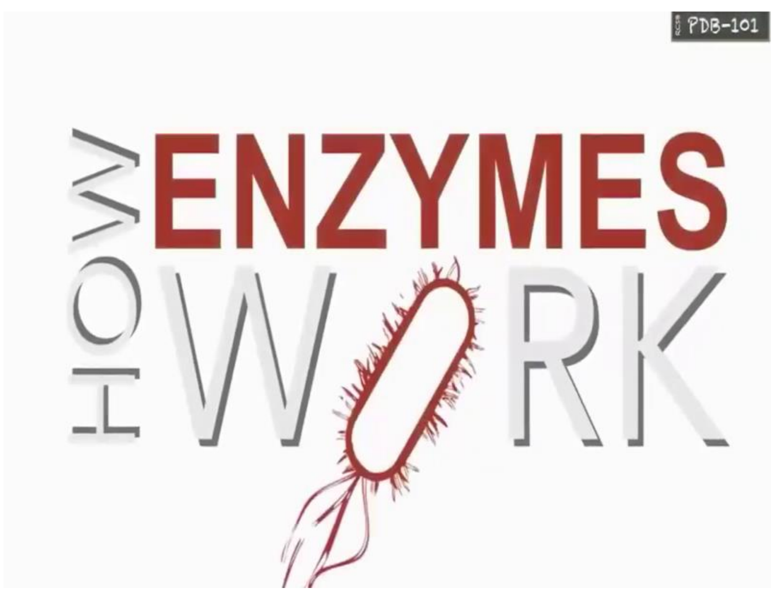
HOW ENZYMES WORK

HOW ENZYMES WORK

HOW ENZYMES WORK


HOW
ENZYMES
WORK


PDB-101
HOW
ENZYMES
WORK


PDB-101
HOW
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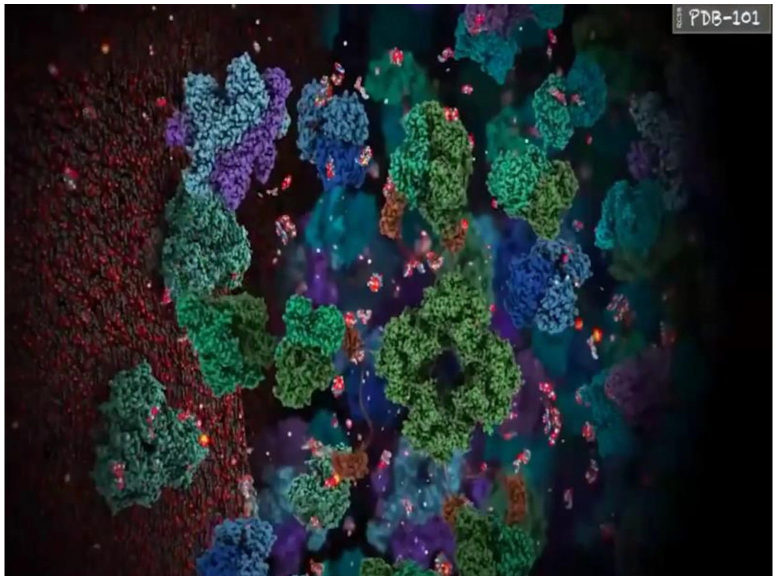
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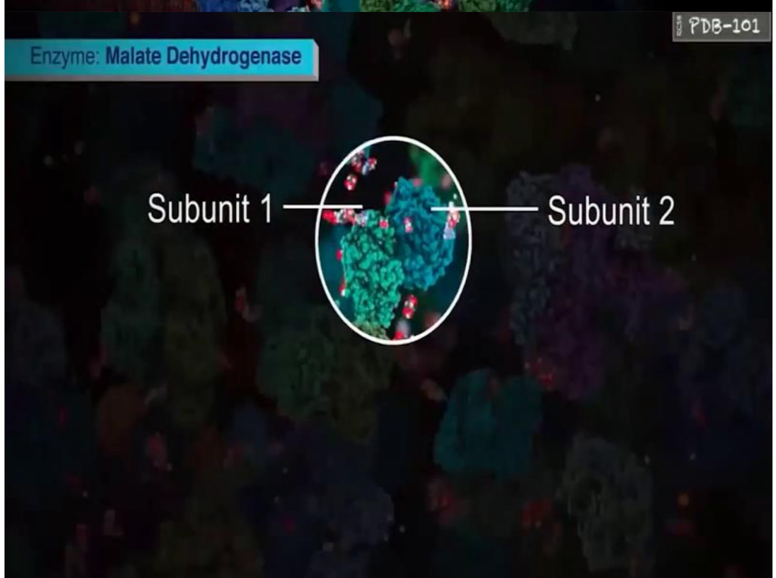
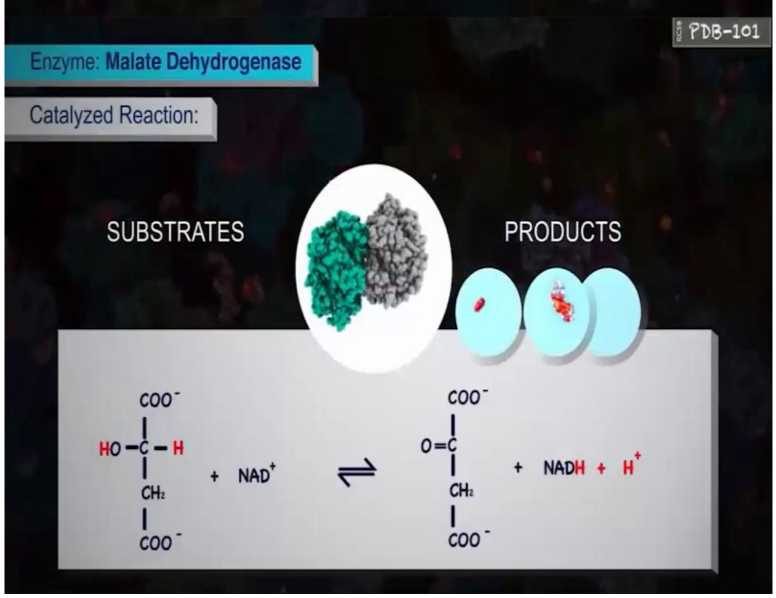
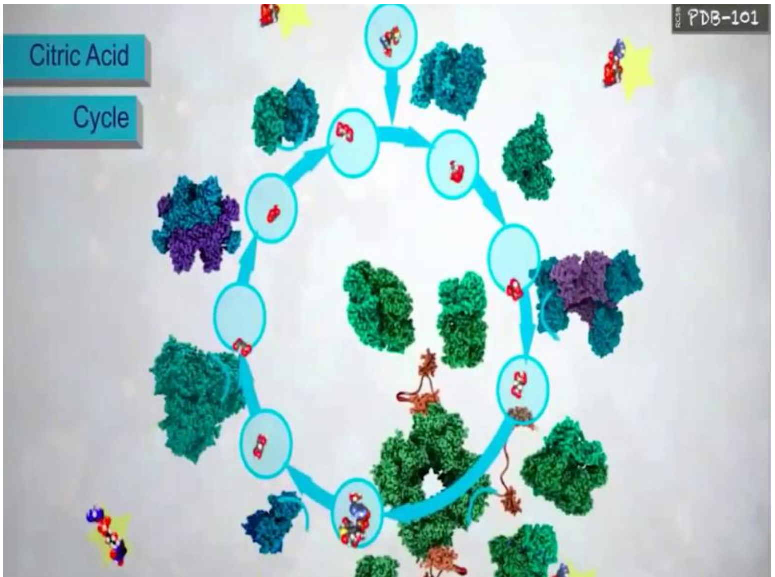
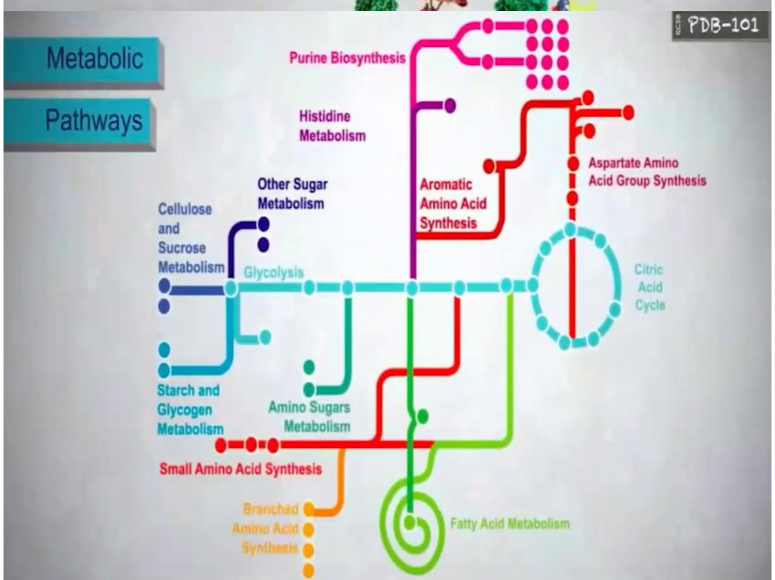
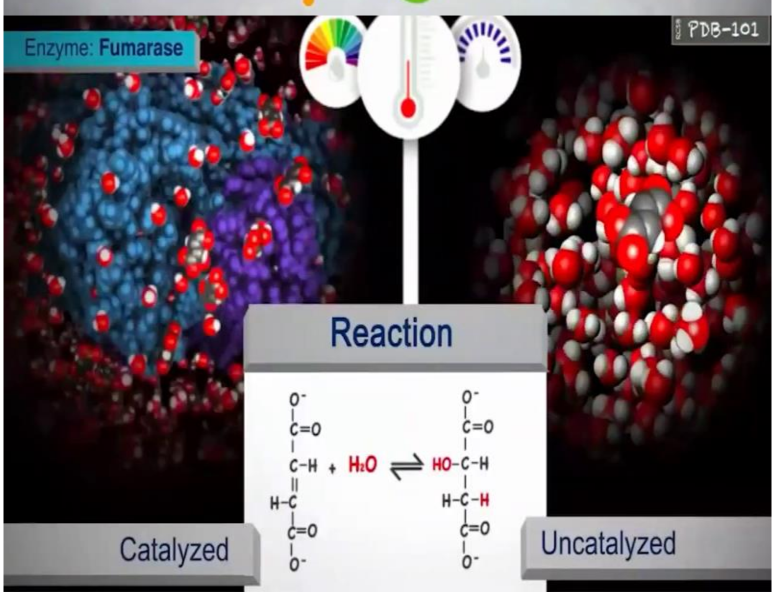

PDB-101
Enzyme: Malate Dehydrogenase
Subunit 1
Subunit 2


PDB-101
Enzyme: Malate Dehydrogenase
Catalyzed Reaction:
SUBSTRATES
PRODUCTS
COO^-
HO–C–H
CH_2
COO^-
+ NAD^+
⇌
COO^-
O=C
CH_2
COO^-
+ NADH + H^+


Citric Acid
Cycle
PDB-101


Metabolic
Pathways
PDB-101
Purine Biosynthesis
Histidine Metabolism
Aromatic Amino Acid Synthesis
Aspartate Amino Acid Group Synthesis
Other Sugar Metabolism
Cellulose and Sucrose Metabolism
Glycolysis
Citric Acid Cycle
Starch and Glycogen Metabolism
Amino Sugars Metabolism
Small Amino Acid Synthesis
Branched Amino Acid Synthesis
Fatty Acid Metabolism


Enzyme: Fumarase
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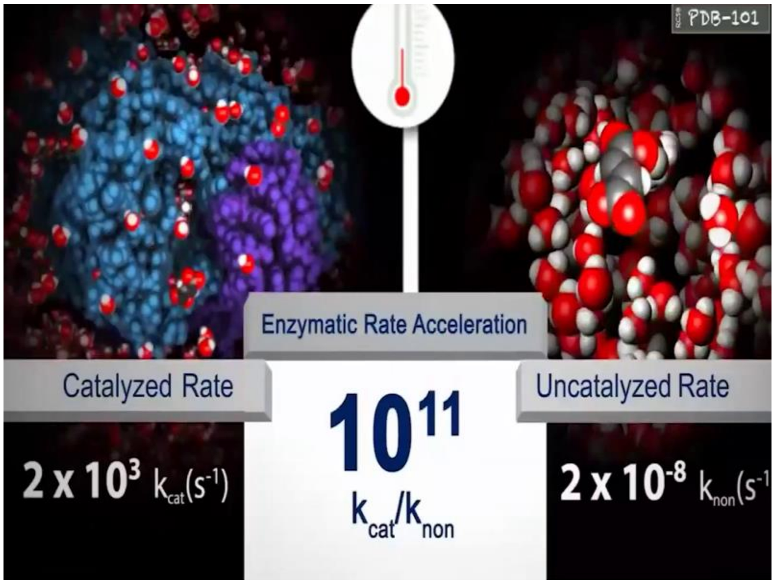
Reaction
H₂O
Catalyzed
Uncatalyzed



I am going to just show this move. Every single second inside every living cell 1000s of chemical reactions are taking place. These reactions are performed by enzymes. An enzyme is a protein that catalyzes the chemical reaction. It initiates the reaction speeds up the reaction's progress and make sure the outcome is always the same.

These enzymes often work together to form longer pathways, such as the citric acid cycle, which is a series of chemical reactions used by cells to generate energy from carbohydrates. The essential tests in life such as metabolism, protein synthesis, and cell renewal and growth are all regulated by enzymes.

The life sustaining power of enzymes lies in the fact that they catalyze reactions in mild conditions of pH, temperature, and atmospheric pressure. The rates of catalyzed reactions are millions to trillions times faster than those of the same reactions un catalyzed, speed of a reaction in the absence of enzyme, additional energy would need to be provided as heat flows the substrates and occasionally provides enough energy to trigger a reaction.

In the course of most reactions, an unstable and highly energetic transition state is formed as substrates are transformed into products. An enzyme acts as a template for the reaction binding to the substrate and holding it in the proper position to form the product. An enzyme also surrounds the substrate with reactive groups that stabilize the transition state, making it easier for the reaction to occur. To understand how enzymes work, let us take a closer look at a reaction of the citric acid cycle that is catalyzed by the enzyme Aconitase.

Aconitase binds to its substrate citrate and removes a hydroxyl group and a hydrogen atom to form an intermediate Cis-aconitate, it then adds the hydrogen hydroxyl back in slightly different positions to form the product Isocitrate.

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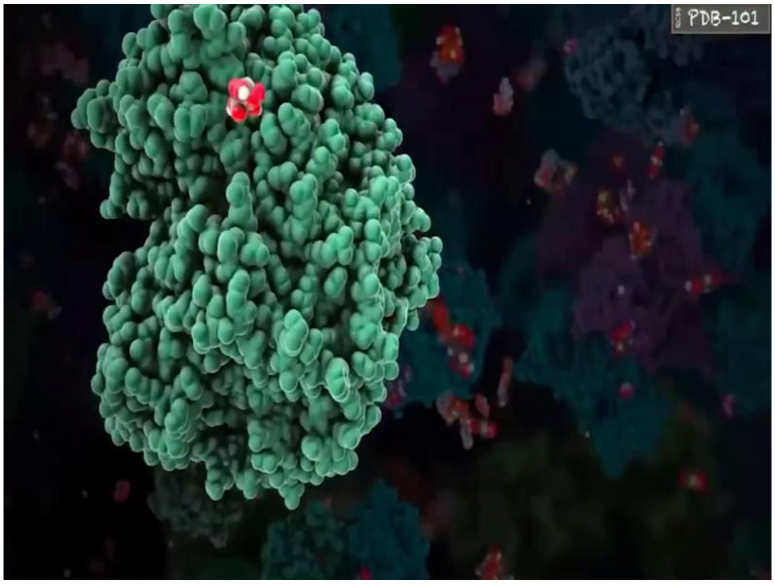

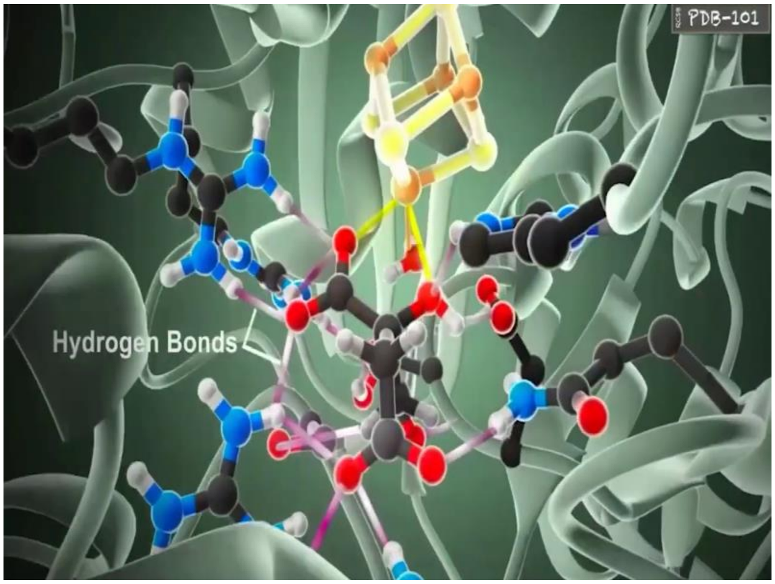

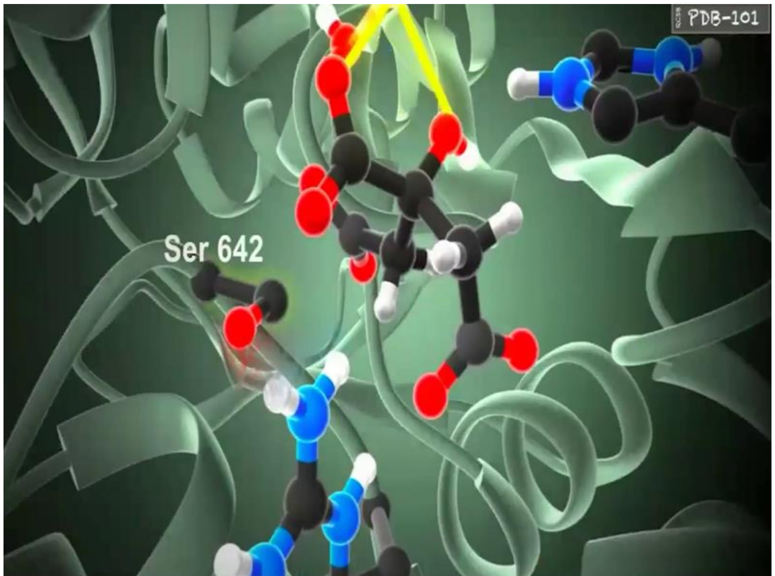
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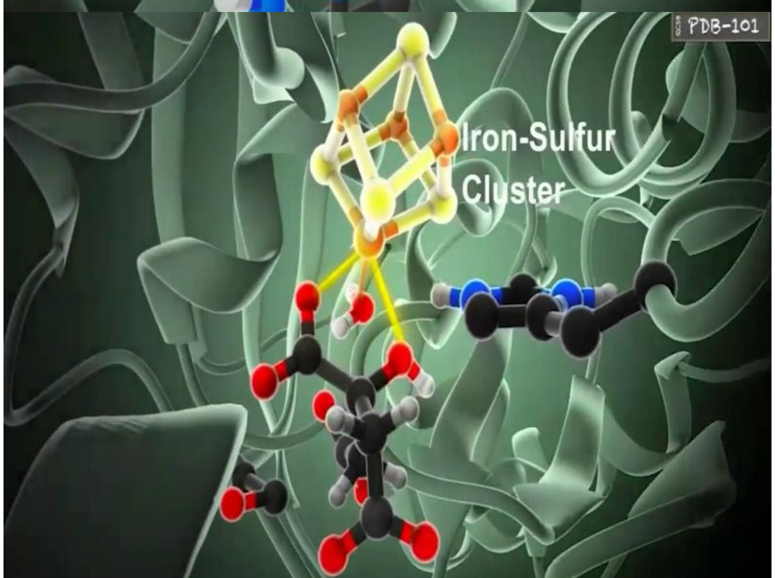
Ser 642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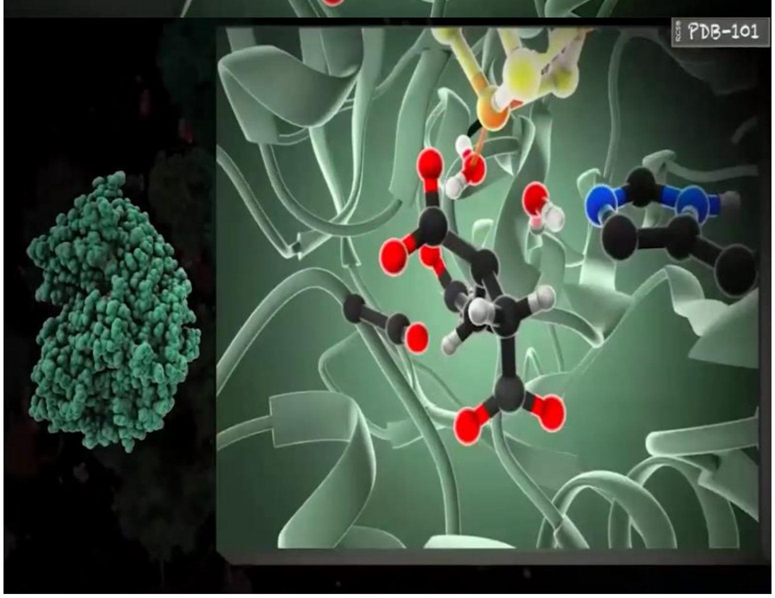
Iron-Sulfur
Cluster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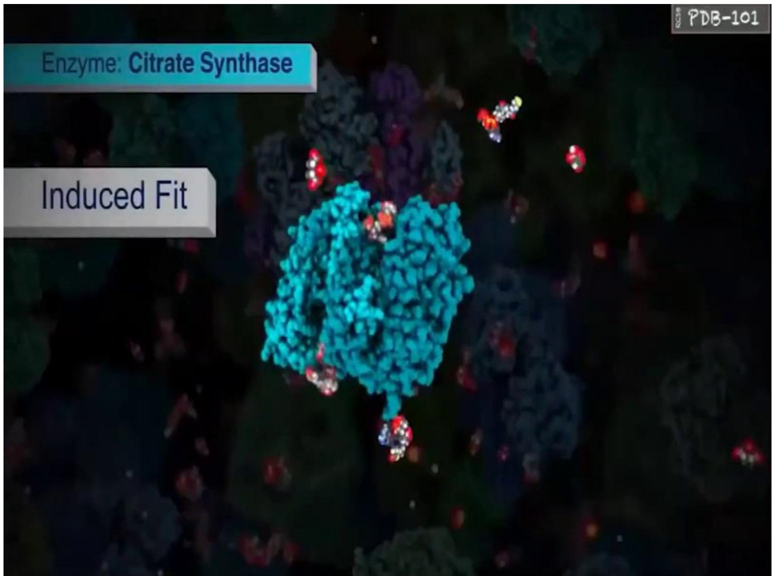

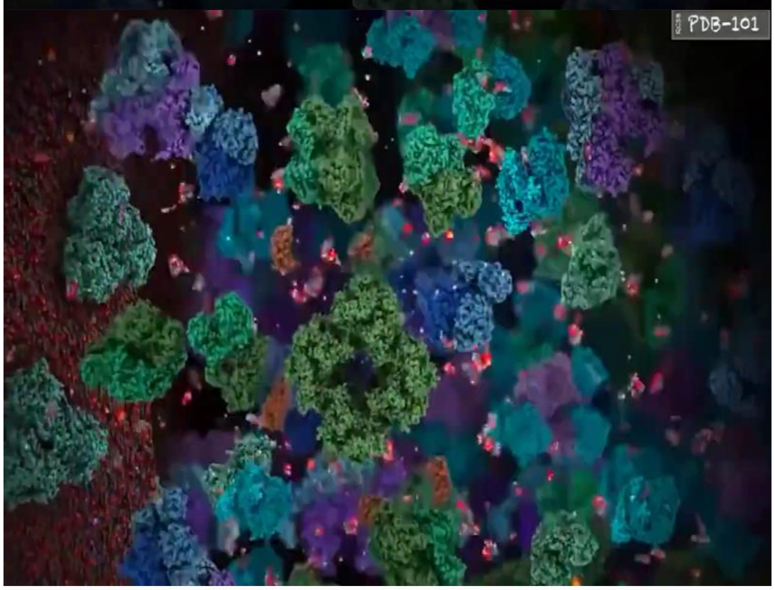

HOW ENZYMES WORK


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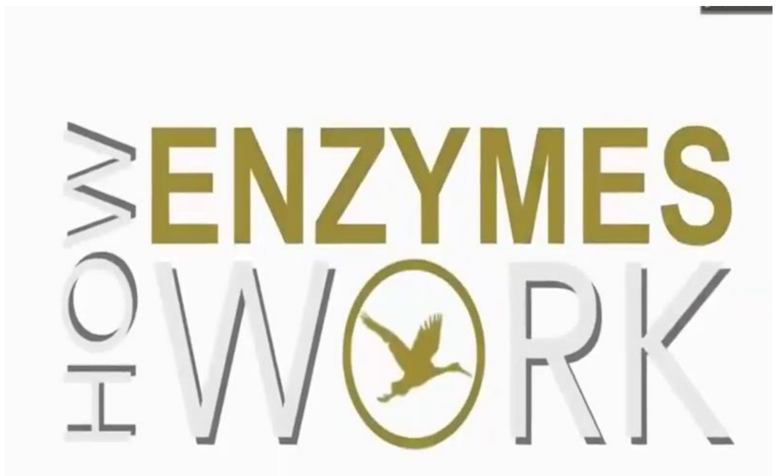
HOW
ENZYMES
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PDB-101
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In the active site, some amino acids are perfectly positioned to recognize a substrate and hold it in the optimal position for the reaction to begin, some amino acids are involved in recognizing and holding the substrate. Other amino acids are directly involved in catalysis. Histidine 101 acts as an acid by donating its proton, thanks to the chemical environment of serine 642 it can act as the base by accepting the proton from substrate.

The active site of a Aconitase also contains an iron sulfur cluster that stabilizes the substrate electrostatically and helps to position it relative to the catalytic residues. The first step in the reaction is dehydration in this step Histidine acts as an acid, protonates the hydroxyl on the substrate, allowing it to leave as a water molecule.

Serine then acts as a base extracting a hydrogen atom from the opposite side of the substrate forming the intermediate Cis-aconitate, Cis-aconitate then flips upside down and the complimentary hydration reaction is performed. In this step histidine grabs a hydrogen atom from a passing water molecule, placing the resulting hydroxyl group back onto the substrate. Serine then returns the hydrogen atom and the final product Isocitrate is released.

Notice that the enzyme itself was not changed by the reaction, it extracted a hydroxyl group and a hydrogen atom and then put them back the starting and ending in the same stage. This is the hallmark of a catalyst. When it finishes a reaction, it is ready for the next so it can perform 1000s of reactions in a row.

Notice also that the shape of an active site is often flexible. Many enzymes surround their substrates and enclosing them to form the perfect environment for reaction. Enzymes are fundamental to life on earth, working every second of every day to maintain life processes in every cell in every living creature on the planet.

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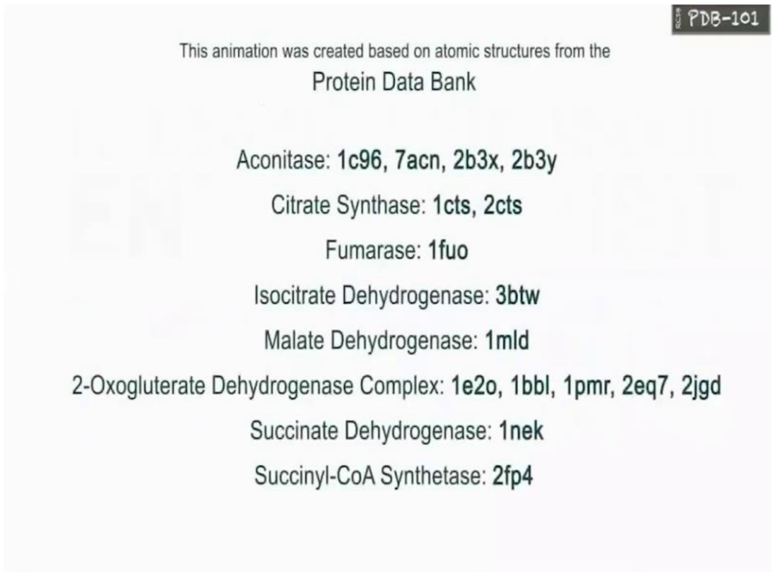

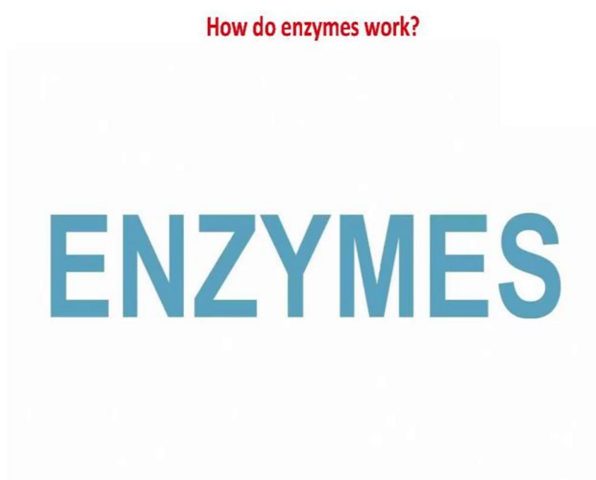

I use this movie just as a way to give you a visual impression of what each folded protein is doing inside a cell taking enzymes as an example. You should not be familiar with the idea of showing a structure using, in this case a ball and stick arrangement or using different visualization patterns.

And you could see how water surrounds the protein, how in a single reaction how the substrate enters the protein is modified by side chains, which are positioned exactly in a way to convert the substrate into its end product. And you also saw the role of water in this particular example, which is there in the active site to help in conversion of this enzyme.

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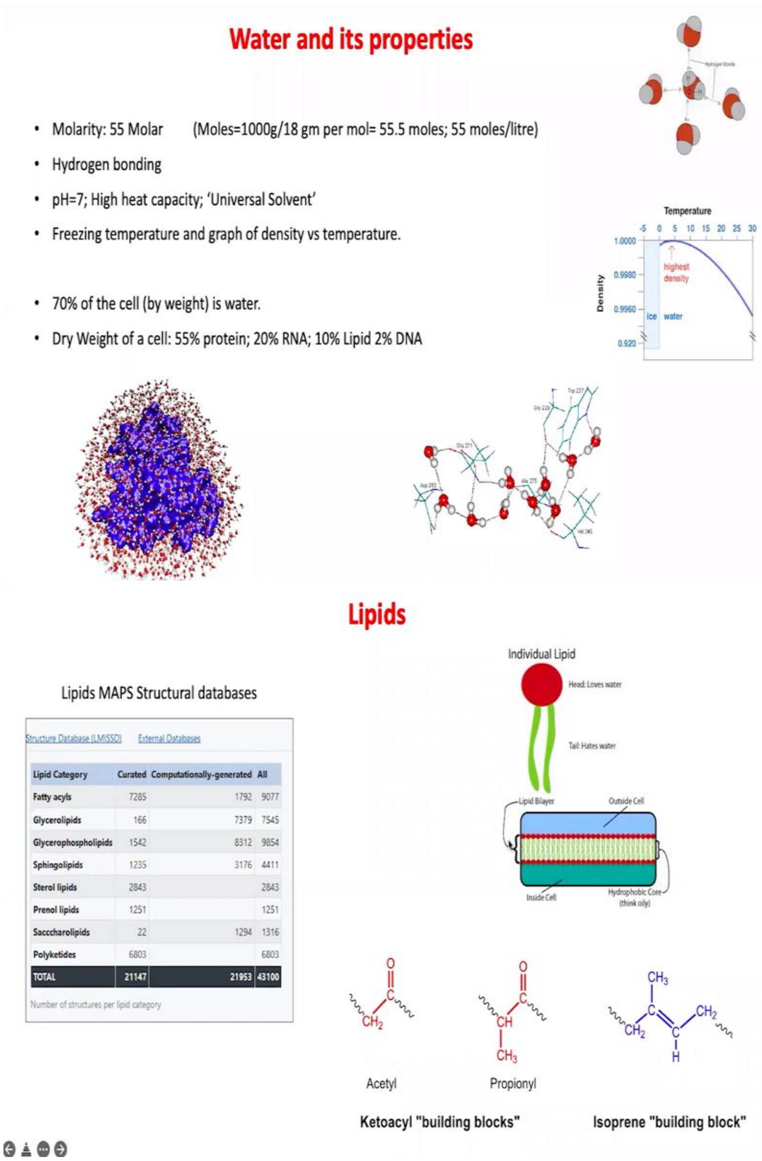

So, effectively, I want you to think a lot about water and the properties of water. In 10th, and 12th, standard, maybe 8th standard, you learned about the properties of water. And water is life. Think about water in terms of its effect on macromolecules. And the role it plays in physiology, these are some properties I have listed of water.

I have focused a lot on hydrogen bonding, do remember that in a cell 70 percent of the cell by weight is water. And also shown over here, the dry weight after you remove water. Whatever is left, how much of protein is there, how much of RNA is there, how much of lipid is there, and so on and so forth.

And here is a sort of a schematic over here, showing you water molecules, which are in the characteristic read by ball and stick arrangement, and the hydrogen bonding network they have in side chains. So, also shown on the left over here, a water molecule surrounding a globular protein structure.

So, I would not say any more about this, I do not really have the time I am going to spend the last 10 plus 10 minutes on just introducing lipids and carbohydrates. And I will not go beyond that for this course, simply because as I said, it is an introductory course. Now, lipids are not as easy to classify as nucleic acids or proteins.

They are wide ranging in the different forms they have just like the protein databank there is a map structural database, which lists the different unique lipids which have been identified. Unlike proteins, which are identified by sequencing nucleic acids by sequencing, mass-spec is usually a tool to identify different lipids of different molecular weights, different kinds, lipids are made up of these blocks, which are shown the two red ones and the blue one on the bottom.

And what I want to focus on is the fact that there are many-many classifications of lipids and this is from the maps database showing you the kinds of classifications like sphingolipids, sterol lipids, polyketides, so on and so forth. And over here is what we are going to focus on for the next 5 minutes, which is lipids in membranes.

Now, lipids in membranes are the massive bulk of lipids inside the cell, but remember, lipids are there in fat droplets, they are an energy source lipids conjugate to proteins, lipids are signaling molecules. So, lipids are there in have broad functions in the cell. But in terms of volumes, in terms of number of lipids involved in any one function is basically lipids are there in, in membranes, and this is something you have seen.

For example, phospholipids have, we draw these head tail diagrams, simplistic diagrams, head loves water tail does not love water. And the tail part mostly contains of these repeating blocks, which are carbon, hydrogen oxygen, three atoms mostly, which are hydrophobic, and shown in this picture is the usual double membrane arrangement with the head, which is polar facing outside and inside the cell, where there is an aqueous environment, and hydrophobic parts hiding from water inside the body.

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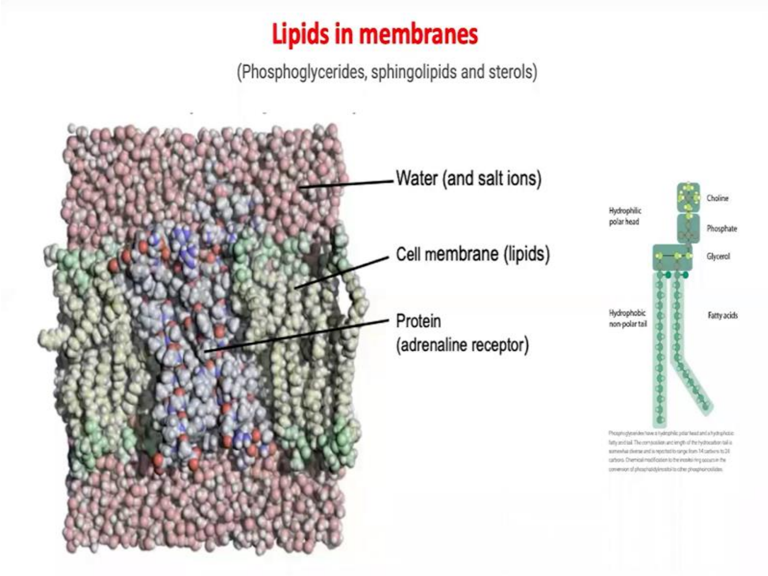

This is a sort of a schematic picture showing you membrane, which is in green and light green over here, with phospholipid with its diagrammatically, shown over here with the atoms, fatty acids in the tail, a glycerol group, a phosphate and a choline in the head part. And you can see water outside the membrane water inside the membrane, a protein embedded inside the membrane.

So, this is what the normal structure of any membrane looks like water on both sides, a double membrane in the middle, and many times proteins, especially membrane proteins sitting slap bang in the middle of the membrane, allowing communication between the two sides of the outside and the inside part of the membrane.

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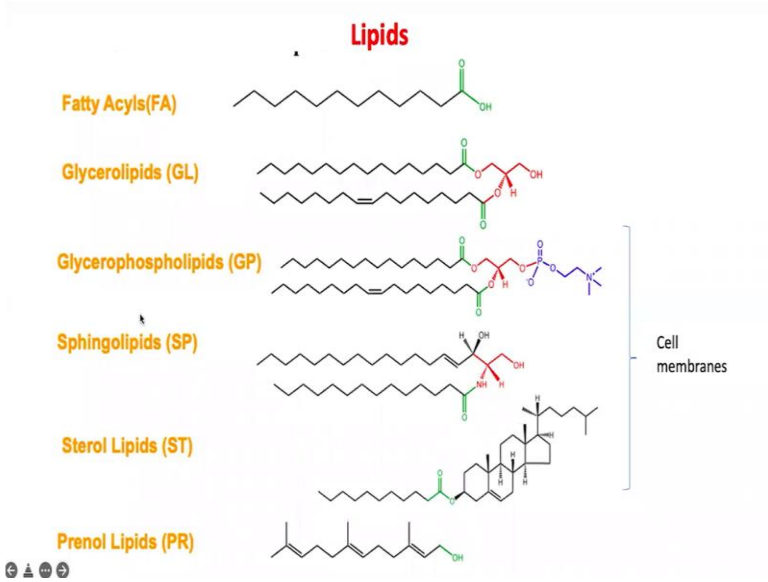

And these are just some schematic diagrams of different lipids of different classes with the carbon hydrogen oxygen groups over here, and the polar group shown in red and blue on the right hand side, with these three being mostly involved in cell membranes.

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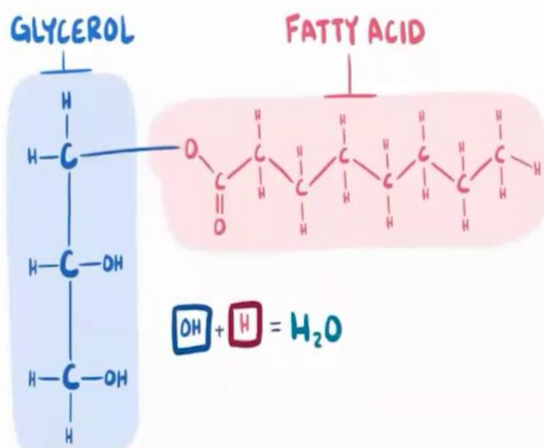
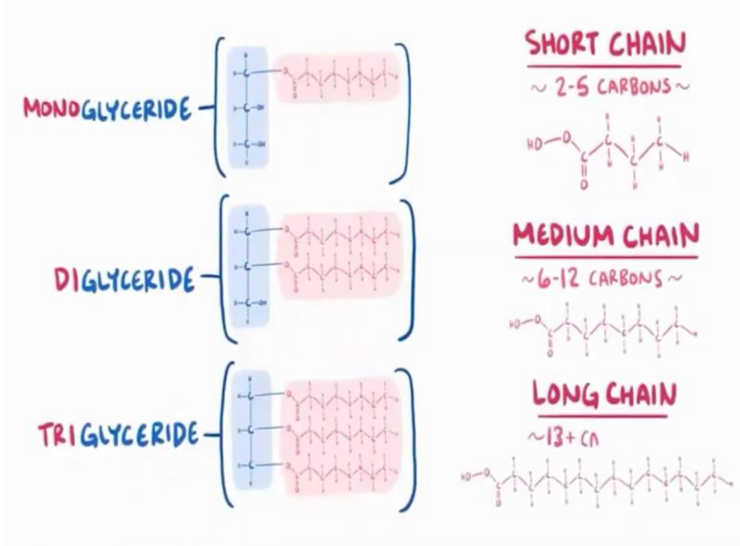
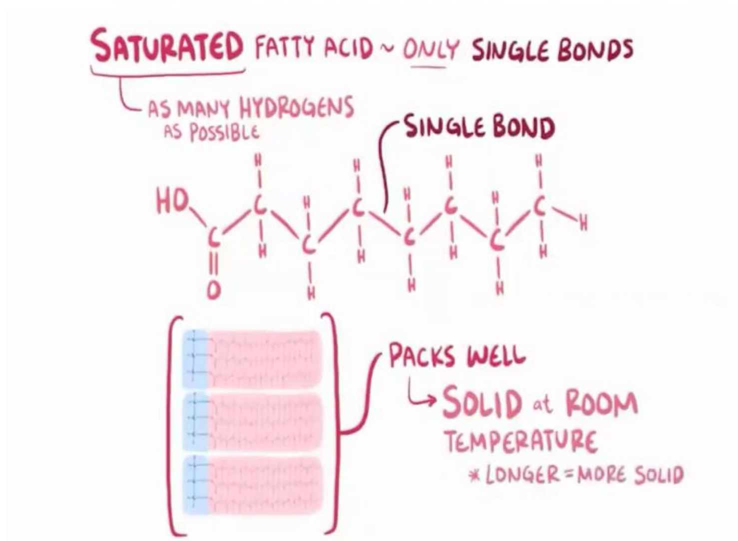
FATS ~ ESSENTIAL PART of HEALTHY DIET

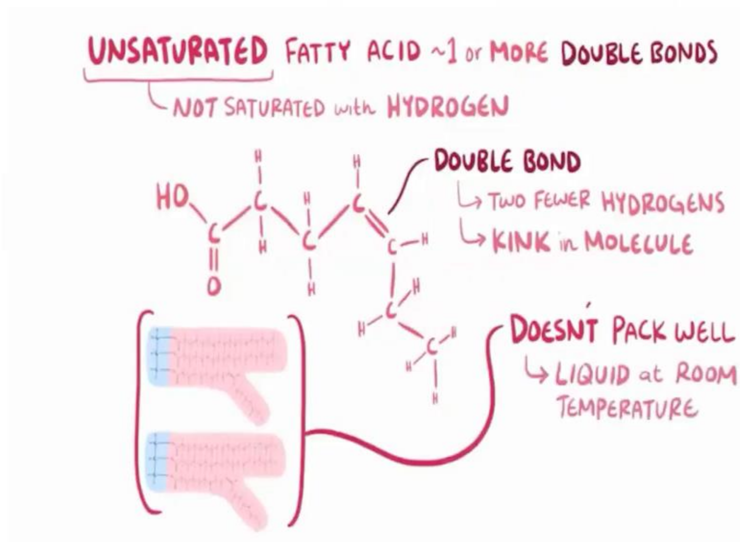
* TASTE & TEXTURE of FOODS
* **MAJOR** SOURCE of ENERGY
* CRITICAL to CELLS & TISSUES
* HELP **ABSORB VITAMINS**
* CONVERTED to PROSTAGLANDINS

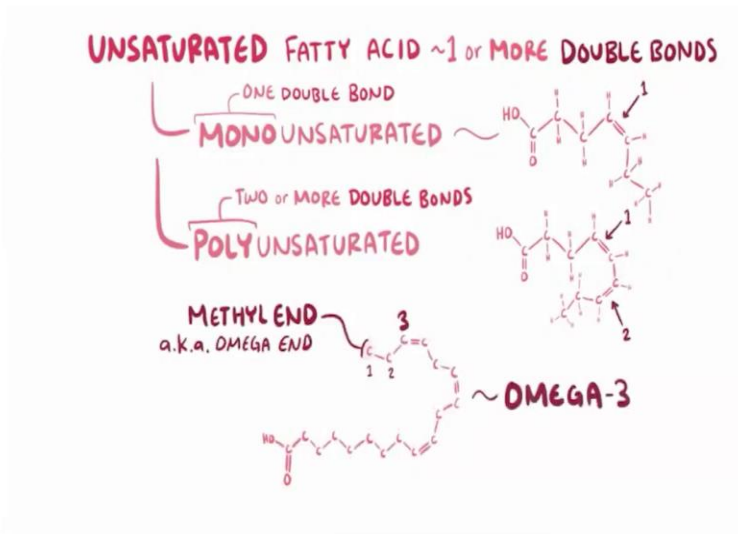
HELP CELLS COMMUNICATE

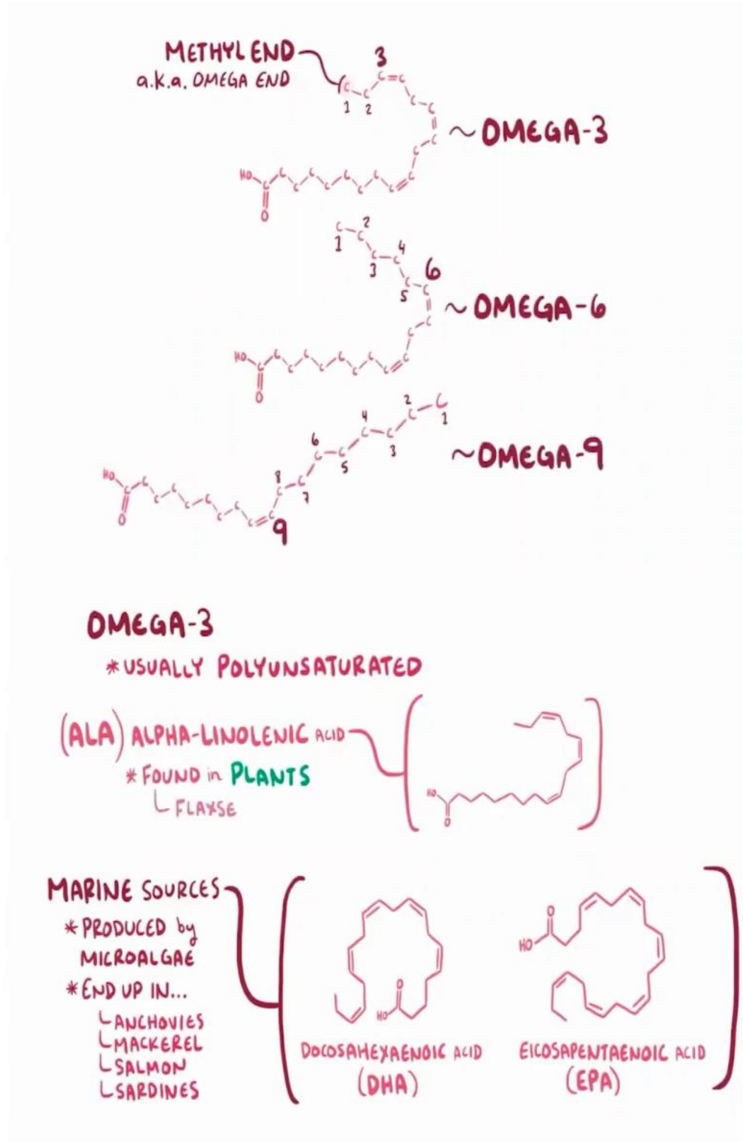



MONOGLYCERIDE
DIGLYCERIDE
TRIGLYCERIDE
SHORT CHAIN
~ 2-5 CARBONS ~
MEDIUM CHAIN
~ 6-12 CARBONS ~
LONG CHAIN
~ 13+ Cn


SATURATED FATTY ACID ~ ONLY SINGLE BONDS
AS MANY HYDROGENS AS POSSIBLE
SINGLE BOND
PACKS WELL
SOLID at ROOM TEMPERATURE
* LONGER = MORE SOLID


UNSATURATED FATTY ACID ~1 or MORE DOUBLE BONDS
NOT SATURATED with HYDROGEN
DOUBLE BOND
TWO FEWER HYDROGENS
KINK in MOLECULE
DOESN'T PACK WELL
LIQUID at ROOM TEMPERATURE


UNSATURATED FATTY ACID ~1 or MORE DOUBLE BONDS
ONE DOUBLE BOND
MONOUNSATURATED
TWO or MORE DOUBLE BONDS
POLYUNSATURATED
METHYL END
a.k.a. OMEGA END
~OMEGA-3


METHYL END
a.k.a. OMEGA END
~OMEGA-3
~OMEGA-6
~OMEGA-9
OMEGA-3
*USUALLY POLYUNSATURATED
(ALA) ALPHA-LINOLENIC ACID
*FOUND in PLANTS
FLAXSE
MARINE SOURCES
*PRODUCED by MICROALGAE
*END UP IN...
ANCHOVIES
MACKEREL
SALMON
SARDINES
DOCOSAHEXAENOIC ACID (DHA)
EICOSAPENTAENOIC ACID (EPA)

We will see a quick movie to introduce lipids. Fats are an essential part of a healthy diet. They contribute to the taste and texture of foods, like the smoothness of guacamole and the flakiness of a croissant fats are also a major source of energy and a critical component of cells and tissues. And they also help absorb essential vitamins and can be converted into other molecules like prostaglandins, which helps cells communicate with each other.

Fats have a three carbon backbone called glycerol, as well as fatty acid chains. The fatty acid chain is basically a string of carbon and hydrogen atoms. Put an OH group from the glycerol molecule binds to hydrogen from the fatty acid and H2O or water molecule gets released, and the two molecules link up. If this happens once the result is a mono glycerol, if it happens twice, it is a Diglyceride and three times makes a triglyceride.

Now there are various types of fatty acid chains, and one way to categorize them is by their length. In other words, how many carbons they have. Short chain fatty acids have 2 to 5 carbons, medium chain fatty acids have 6 to 12 carbons, and long chain fatty acids have 13 or more carbons. Fatty acid chains are also categorized by the bonds connecting the carbons in the chain.

A single bond is just one bond between the carbon atoms. And when a fatty acid chain has only single bonds, it is called a saturated fatty acid. Because it has as many hydrogen atoms as possible, or it is saturated with that. Triglycerides with saturated fatty acids are nice and straight. So, they packed together really well.

And as a result, they are usually solid at room temperature. And the longer the saturated fatty acid chain, the more likely it will be solid at room temperature. Carbons can also have double bonds between them though, and when a fatty acid has one or more double bonds, it is called an unsaturated fatty acid, because, it is not saturated with hydrogen atoms.

Probably, double bond, there are two fewer hydrogen atoms. Also, a double bond causes a kink in the molecule, so the triglycerides, does not pack together as nicely as saturated fats. As a result, unsaturated fats are usually liquid at room temperature. Unsaturated fatty acids can be further classified according to the number of their double bonds, mono unsaturated fatty acids are unsaturated fatty acids with just one double bond.

Poly unsaturated fatty acids have two or more double bonds. Also, they can be classified according to their location as well. Since all these hydrogens can get kind of crazy looking, we will just take them away for now. So, another name for the methyl end is the Omega End. And then we can count the number of carbons until the first double bond.

Since this one is 3, it would be an omega 3 fatty acid. If the double bond is 6 carbons from the end, it is an Omega 6, and if it is 9 carbons from the end, it is called omega 9. Now to make things even easier when looking at these molecules, I am just going to show the bonds.

So, omega 3 are usually poly unsaturated fatty acids, and include alpha linolenic acid or ALA Eicosapentaenoic acid, or EPA and docosahexaenoic acid or DHA. EPA and DHA are marine sources of Omega 3s. They are produced by micro algae and end up in the tissues of fish like anchovies, mackerel, salmon, and sardines. ALA is found in plants like flaxseed.

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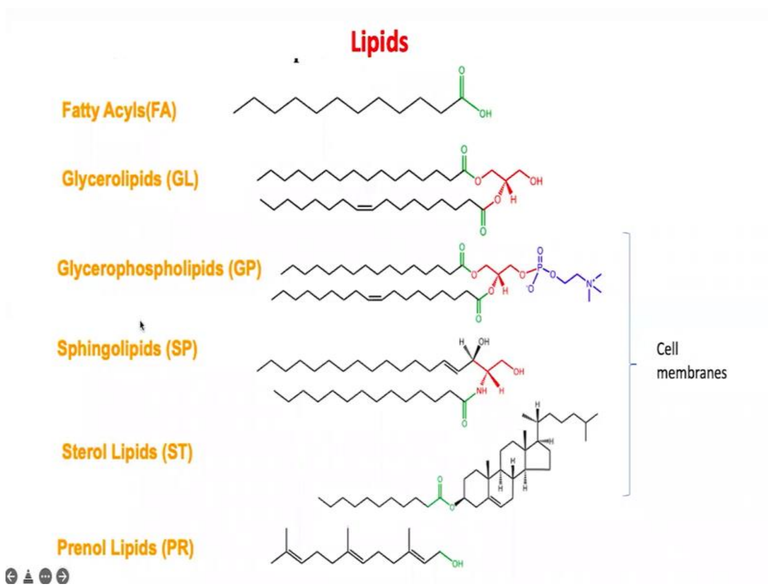

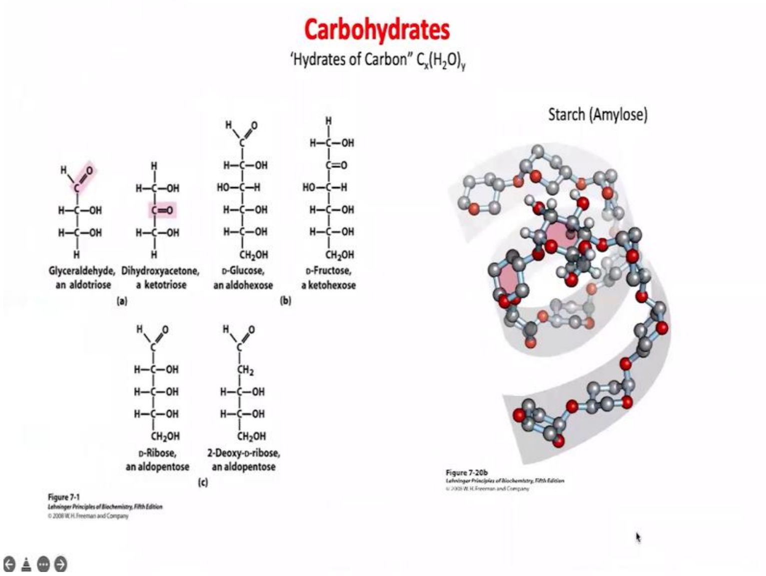

This is just to give you an idea of structure of lipids and how to draw them. I will also now end by introducing you to carbohydrates. I just want to emphasize on a few things. One is that carbohydrates can form complex structures, resembling for example, what you see in nucleic acids and proteins. This is a helical form of starch or Amylose, and again, hydrogen bonds play a very important role in this particular polymer. Let us look at a quick movie for introduction to carbohydrates.

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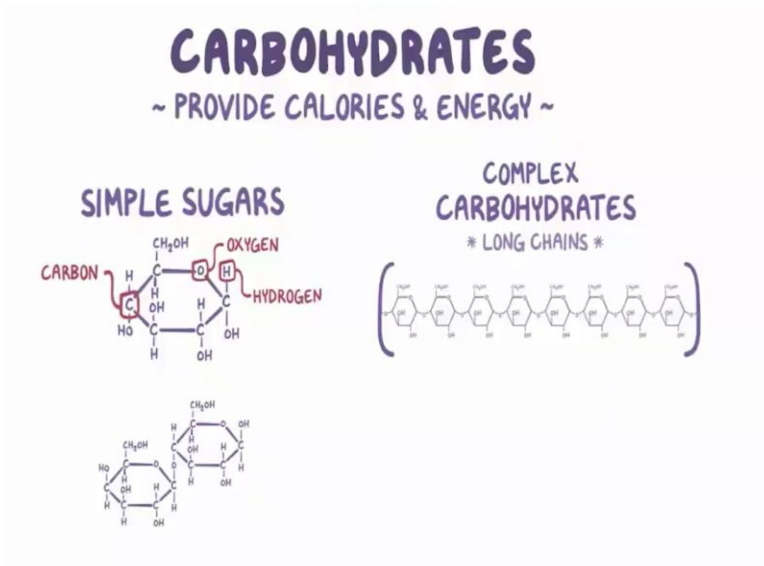
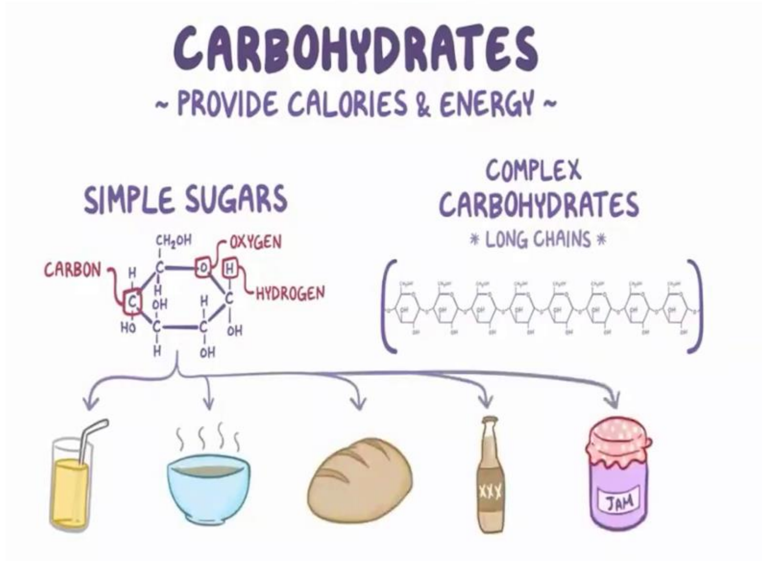
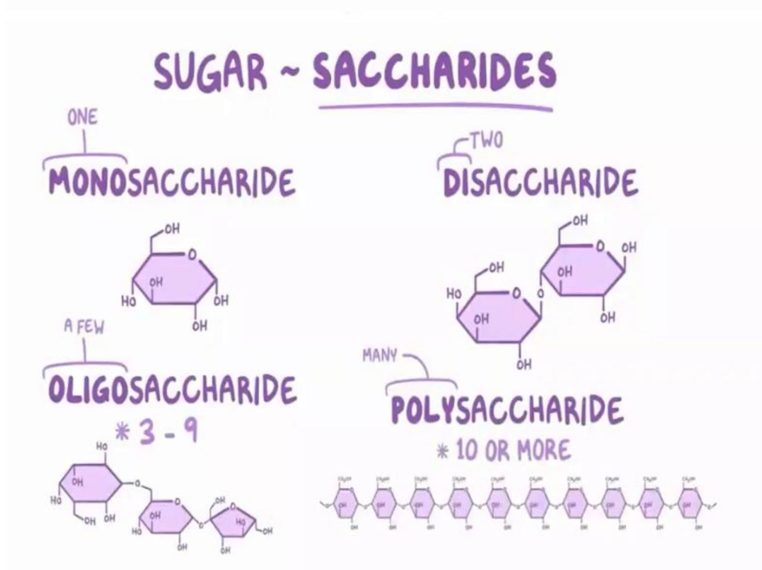



CARBOHYDRATES
~ PROVIDE CALORIES & ENERGY ~
SIMPLE SUGARS
COMPLEX CARBOHYDRATES
* LONG CHAINS *
CARBON
OXYGEN
HYDROGEN
CH2OH
JAM


MILK
FOUND NATURALLY
SUGAR-Os
ADDED
ENERGY
INGREDIENTS ~ COULD BE SOURCES OF ADDED SUGAR


SUGAR ~ SACCHARIDES
ONE
MONOSACCHARIDE
TWO
DISACCHARIDE
A FEW
OLIGOSACCHARIDE
* 3 - 9
MANY
POLYSACCHARIDE
* 10 OR MORE

Carbohydrates include both simple sugars which are little ring shaped molecules made of carbon, hydrogen and oxygen, either alone or in pairs, as well as more complex carbohydrates which are formed when these rings link up together to make long chains. Carbohydrates provide us with calories or energy and simple sugars in particular play a lot of roles in our diet. They sweeten lemonade, balance out in acidic miso soup, fuel yeast in rising dough and alcohol, and help preserve jams and jellies.

Now, sugars are found naturally in plants like fruits, vegetables, and grains, as well as animal products like milk and cheese. Added sugars are the sugars that get added to foods like cereals, catch up, energy bars and even salad dressings.

To be clear, even if the sugar being added comes from a natural source like sugar cane or honey, it is still considered an added sugar. In fact, a variety of ingredients listed on food labels might be sources of added sugars. Some of what you are probably familiar with.

Sugar actually refers to a family of molecules called saccharides. Monosaccharides were mono means one. So, one sugar molecule disaccharide, where di means two. So, two sugar molecules linked together oligosaccharides were oligo means a few. So, it is 3 to 9 sugar molecules linked together, and polysaccharides, where poly means many, so it is 10 or more sugar molecules linked together.

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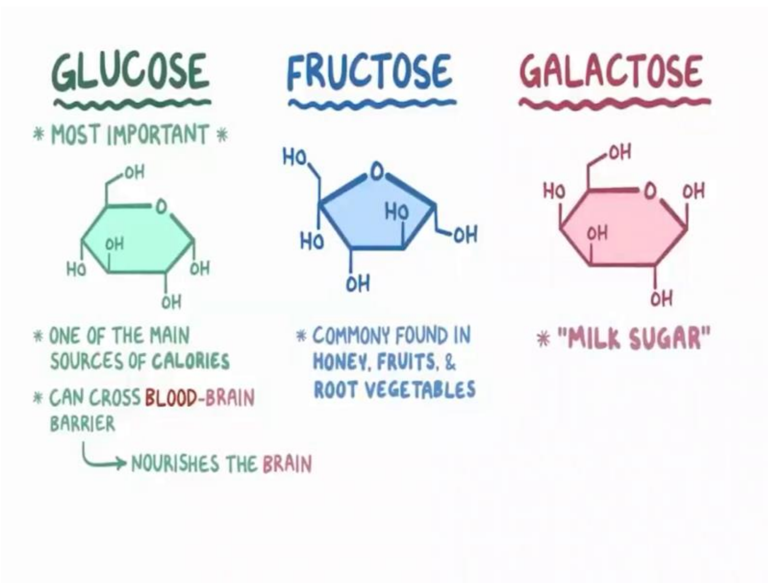

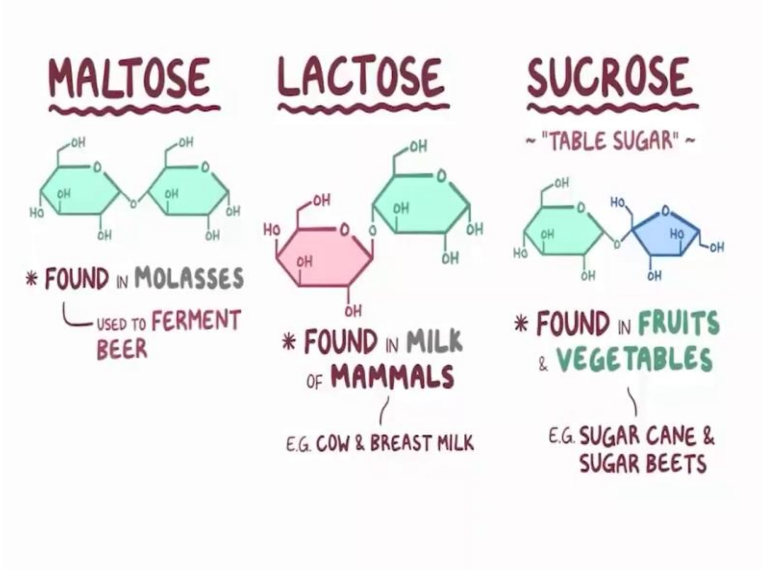

Glucose is the most important member of the sugar family, and it is a monosaccharide. It is one of the main sources of calories for the body, and is able to cross the blood brain barrier and nourishes the brain. Another monosaccharide is fructose, which is commonly found in honey, fruits and root vegetables.

Finally, there is the monosaccharide galactose known as milk sugar. It is known as milk sugar because it is only found in nature when it links with glucose to form lactose, a disaccharide found in the milk of mammals, which includes cow milk as well as human breast milk.

Sucrose, or table sugar is another disaccharide. And it is formed when fructose links up with glucose. Sucrose is found in various fruits and vegetables, with sugar cane and sugar beets having the highest quantities. Maltose is another disaccharide. And this one is two glucose molecules linked together. And it is found in molasses, which can be used as a substrate to ferment beer.

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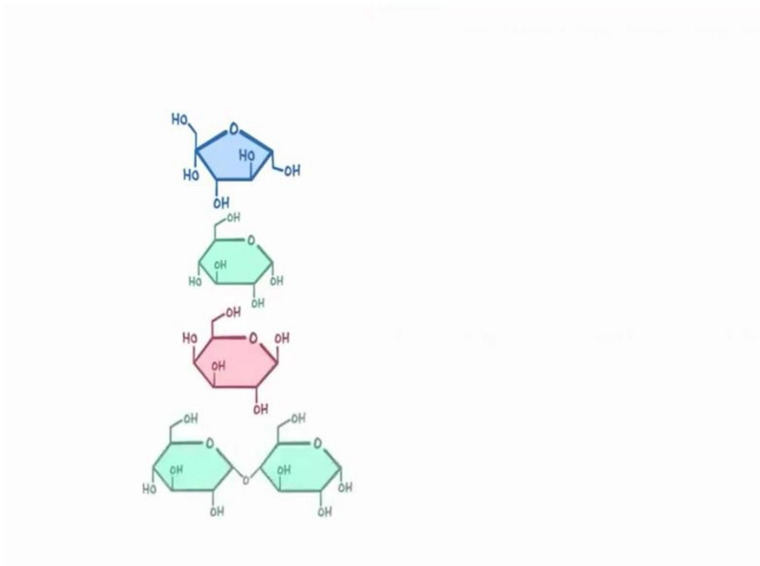

Sugars, like fructose for example, are most always found in combination with other sugars. And the combinations can be pretty different, even in seemingly similar foods.

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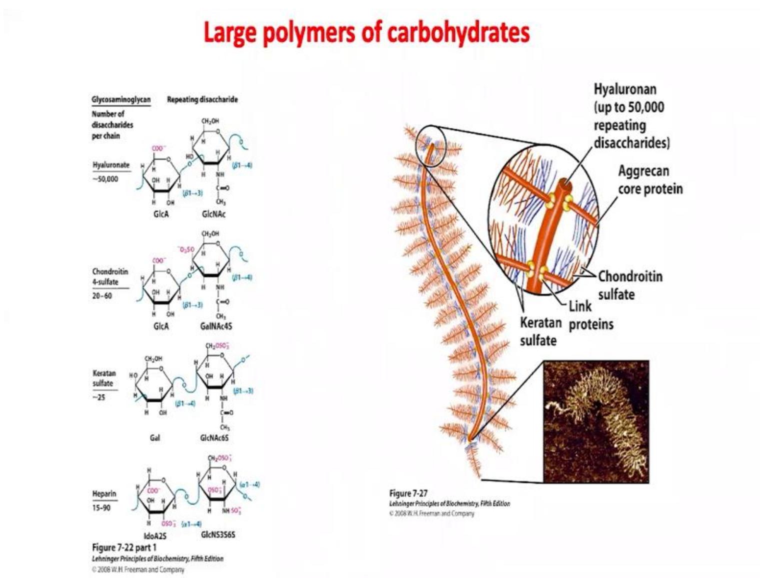

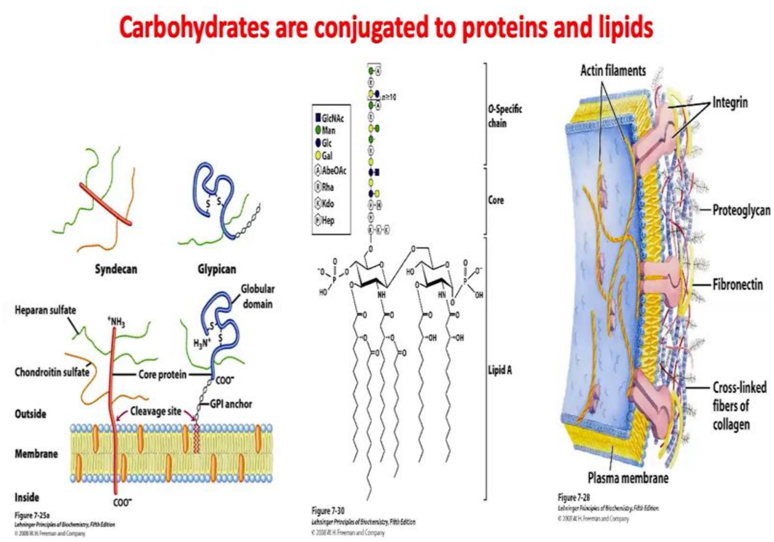

So, I am going to stop this over here. And again, I will ask you to see the rest of this movie. So, what I want to end is to emphasize that carbohydrates can form large polymers. Shown on the left are examples of four such polymers having the bonds, which were shown in the short movie I showed you, and I will take the example of Hyaluronate, which has about 50,000 repeating units of this disaccharide.

And this particular molecule and other molecules also are found on the surface of most cells. So, the surface of cells are decorated with polysaccharides. It is literally it is like looking at a forest from down from a helicopter, you will see the surface of the cell is pretty much like the land, you cannot see the land at all you only see the carbohydrates, and you will only see the protein.

There is a huge amount of crowding at the level of the surface of the cell, with proteins and carbohydrates dominating the landscape of whichever entity is trying to enter the cell from the outside. So, this is my last slide. I also want to leave you with the idea of simple carbohydrates and the polymers of carbohydrates, which you have seen, can conjugate to lipids, and they can conjugate to proteins.

And these conjugations between these three macromolecules, lipids, proteins, carbohydrates have very important functional roles. And very obviously looking from a central dogma viewpoint, these conjugations happen post translational. So, DNA does not directly code for the conjugation of a carbohydrate or a lipid to protein. But the unique sequence of amino acids has motifs, which lead to conjugation of these macromolecules to proteins.

And by conjugation between these different macromolecules, you create functional and structural entities, which are very, very different from the simple idea of proteins, lipids, or even carbohydrates. And on the right hand side, and this is the last thing I am going to say, is a structure of the plasma membrane with the bluish part on the left being the inside, showing you the polymers of actin filaments.

Which dominate the landscape of the inside of the cell, membrane proteins like integrins, sitting in the double membrane, which is made up of lipids, and as I said, a forest of carbohydrates and proteins on the surface of the cell, which effectively are pointing outwards. And any molecule coming to enter the cell or interact with the cell will first face this forest on its way to the cell. So, I will stop over here and take any questions.

Student: Sir, what does, the lipids exactly do?

Professor: So, this is what I said? Lipids do many things. They are the structural entity of membranes. So, the first thing which you will always say is that they are the membranes, which are very important to compartmentalize cells, because unless you compartmentalize cells, different enzymatic reactions will mix with each other.

So, if you want a compartment inside a cell which is at low pH, for example, to degrade proteins, you cannot afford to have a pH of 3 inside the entire cell because the cell will not be able to function. So, membranes will act as a sort of a barrier keeping this compartment separate from everywhere else. Nucleic acids are themselves in a large compartment a double membrane compartment called as the nucleus.

So, membrane proteins are very important. Now, lipids can also act as storage material which can be used for making energy. Carbohydrates can be converted into lipids. Lipids can also function as signaling entities. So, they are means if you read a textbook or a review on lipids, there will be 40-50 different things at least which lipids can do inside the cell.