Introduction to Biomolecules
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Lecture – 3
Stereochemistry and Properties of Water - Part – 1/2

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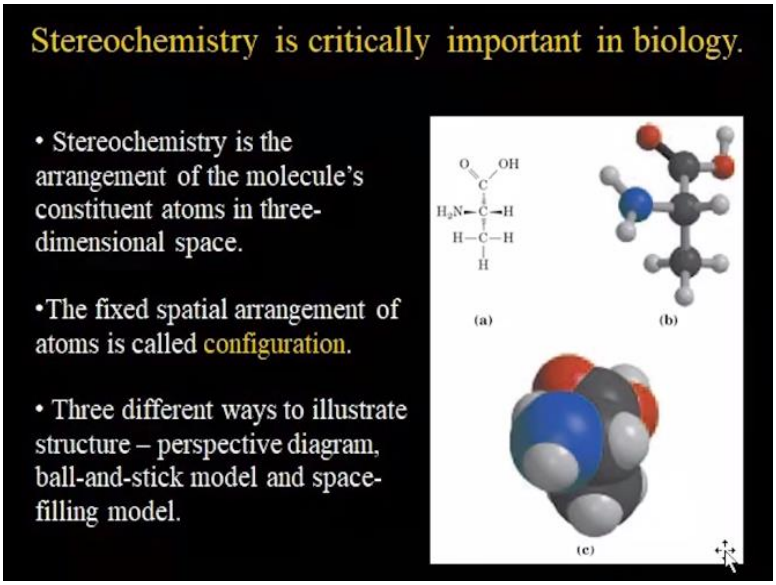

Today we are going to learn about stereochemistry. So stereochemistry is about how the constant atoms of a molecule are arranged in the three-dimensional space. So the atoms of a molecule can be arranged in different ways in a three-dimensional space and each one of the specific sequences of the such arrangement we call as a configuration. So as we see examples all of this will become very clear.

The arrangement of these atoms in a molecule we represent them in at least three major ways. One of them is the drawing that you see here or which we call as the perspective diagram. So the perspective diagram tells you what atoms are bonded to what other atoms and also about whether a given group is projecting in one direction compared to the other one. Like for example this hydrogen and these amino groups are projecting forward that is indicated by that kind of an arrow, the dark arrow.

And then some dashed one like for example the central carbon to the top one and bottom one gives you a dashed line or arrow like line that indicates that the carboxyl group and this methyl group project away from the plane. So this amino group and hydrogen project towards

you from the plane and while these project away. So these are indicated by perspective diagram, but when you go to the ball and stick model, there you get an idea of the length of the bond.

For example, what is the length between this atom and this atom, the bond length that is indicated by the length of the line and then you have angle also visible like for example the bond angle between this and this is indicated and then when you go to this space-filling model the actual space occupied by each atom which is determined by its van der Waal radius is the basis for this diagram.

So the size of each atom like for example this gray one hydrogen is small and this one is big you know nitrogen and this is carbon and this oxygen and so on this hydroxyl group here. So each of these ball shaped structures vary in their size, like hydrogen is small, nitrogen is big and that size is proportionally magnified based on their van der Waal radii. The van der Waal radii of an atom is the space into which it will not allow any other matter to come in.

So that is the basis for the space-filling model. So this is actually the closest representation of the actual molecule. So these are the three ways in which we represent the configuration. So this is a certain arrangement of these constant atoms in this molecule. So what kind of molecule is this? Can anyone guess from our first class? Amino acid, very good. So I was about to say in an online class this kind of question and the answer is difficult, but you proved me wrong that is very good. Let us move on to the next one.

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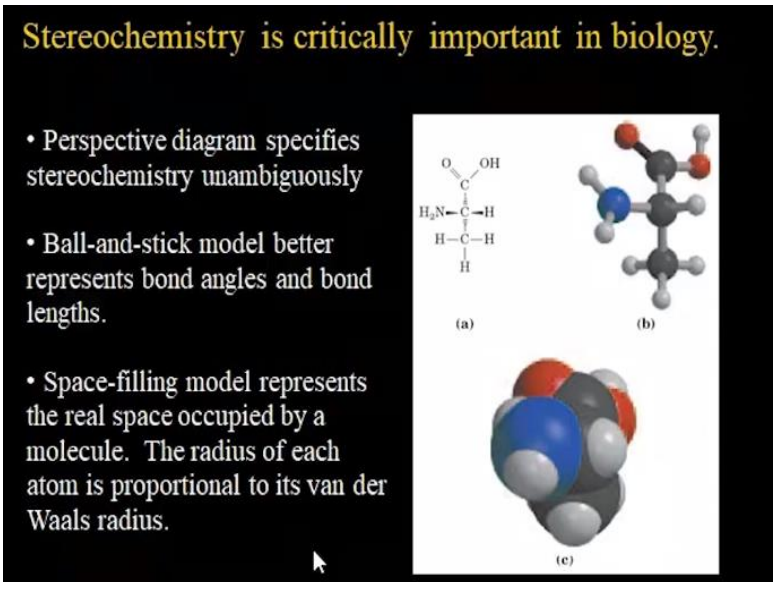

So this I just told you perspective diagram specifies stereochemistry unambiguously that is which one is away from the plane, which one is towards you from the plane, etc., and ball and stick primarily the bond length and the angle and space-filling model actual space occupied by the atoms.

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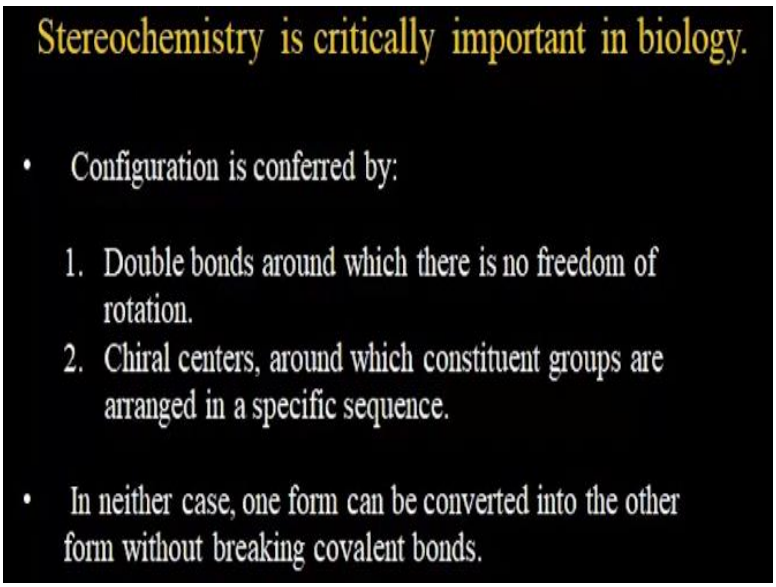

So the title keeps telling you the stereochemistry is critically important in biology that I will come to it towards the end of this part. So now let us get to the configuration. So what is the big deal? Why should I worry about the configuration? You know as long as carboxylic acid is there it is going to behave like an acid, no matter where in the molecule it is and it does not matter where it is amino group is going to behave like amino group.

But not really depending on the sequence of arrangement or which other functional group is its neighbor affects the functional group function itself. Like for example if you take the carboxylic acid group COH in acetic acid versus the same carboxylic acid group in an amino acid like glycine they do not dissociate at the same rate, they do not give up the proton at the same level. One is stronger acid than the other one.

So you can go ahead and learn about it on your own as a homework like why carboxylic acid group in glycine behaves different from carboxylic acid in acetic acid. So that is chemistry, so even functional groups depending on the arrangement in a molecule their chemical behavior itself can vary, but in biology there is something else that matters that we will talk about when we get to the end of this topic.

So first let us focus on this sequence of arrangement itself which is the configuration. So this configuration can vary primarily due to two features of a molecule. One if you have a double bond. Around the double bond there is no freedom of rotation and therefore the atoms get fixed in the three-dimensional space with reference to other constituents. So the double bond prevents rotation of the bond between the two atoms that are bonded.

Like for example C double bond C and due to that you have a specific configuration. If you do not have the double bond in between the same atoms, if it is a single bond and if you have a free rotation, then the groups will rearrange in space. So configuration really does not matter and the other one is chiral center. So you have a carbon atom with its 4 valences and if you have 4 different groups attached to it, then we call that as a chiral carbon or an asymmetric center.

And due to the differences in the 4 groups, the sequence of arrangement can give rise to a specific configuration. So the different sequence of arrangement can have different configurations and in both cases one configuration cannot be changed to another configuration without breaking a covalent bond and rejoining it, so that is the basis for configuration.

So to change the orientation in other cases where you do not have a chiral center and where you have all single bonds, the groups can actually the bonds can freely rotate and therefore the three-dimensional position of constant atoms can really change. So therefore, there is not anything to talk about a specific configuration, it is all that they are randomly changing positions.

But when you have these two situations that kind of a rearrangement cannot readily happen and therefore they are fixed in a certain orientation and therefore your specific orientations and each orientation matters and so we will see these with examples as we go.

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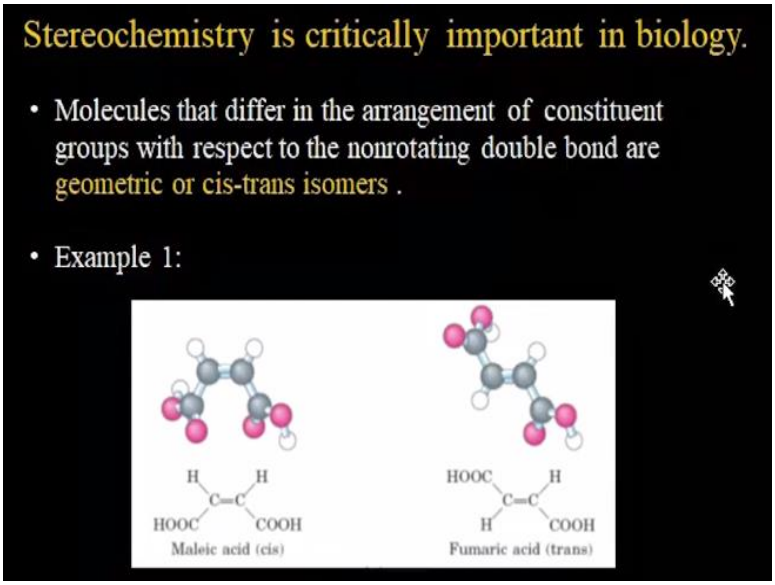

So the first one we will take up is the double bond. So here you have maleic acid with its ball and stick model and the perspective diagram below. So here you have two carbons bonded with by double bond and so you have groups attached to them. So you have two hydrogens and two carboxylic acids, so they could either be both hydrogen can be on the same side when you consider them with reference to the side where carboxylic acid groups are attached.

So I am highlighting this to make you understand that molecules do not exist the way we draw them on a piece of paper. This fear constantly comes to me because the way our textbooks are written, school textbooks, for example if you go to NCERT plus 2 textbook where they introduce polysaccharides, believe it or not polysaccharides you have already learned in your school itself.

There when they talk about polysaccharide reducing end, non-reducing end, they say the left end is the reducing end and the right end is the non-reducing end. This error is still there in the book for the last 10 years or so. So there is not anything like left and right, left of whom, right of whom, we need to think that reference. So these are molecules occupying three-dimensional space most often in a solution, so atoms can be any which way they want.

So when I say hydrogen atoms on the same side, this is with reference to the side where the carboxyl groups are, I do not mean hydrogen when they are on the top of the diagram and carboxylic acid at the bottom of the diagram. So when you have this side or this kind of an orientation you say this is cis orientation and when you have the opposite orientation like one hydrogen on the same side as another carboxyl group, then this is trans orientation.

Same side is cis, opposite side is trans and due to this sort of an arrangement around double bonded carbon atoms, we often call them cis-trans isomers or geometric isomers. So when you use these two terms you are referring to a configuration where the two configuration of a molecule differs in the arrangement of constituent groups with respect to the non-rotating double bond. So this is what you call as geometric or cis-trans isomers.

So here this reference primarily is with reference to the double bond which does not allow free rotation. The second one is the chiral carbon right, we only talked about two.

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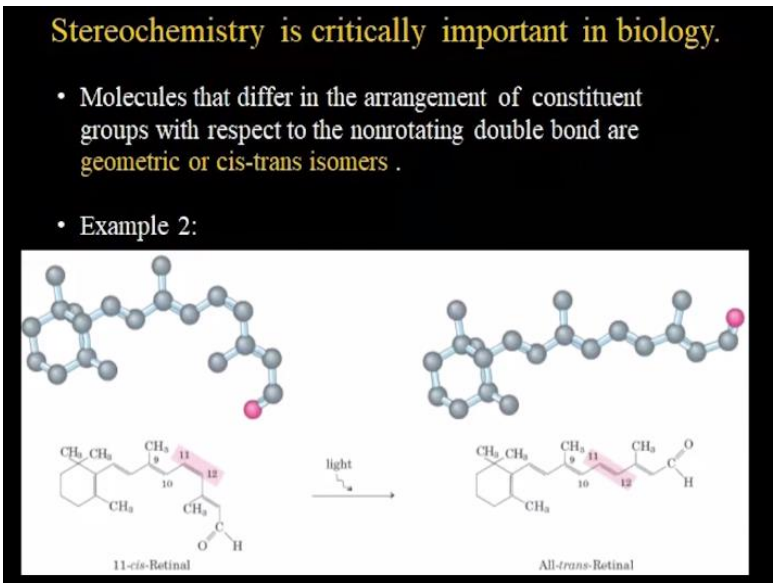

So this is another example of the geometry called cis-trans isomers which matters in biology like retinal 11 cis retinol. So here you see this double bond between the 11th and the 12th carbon in this large molecule. So when the groups this side and the groups this side bonded to this carbon and this carbon are on the same side, you call cis and when it is on the other side you call the trans all-trans retinal and 11-cis retinal.

Conversion between the two is how we sense light in our eyes. When the light falls on our eyes, the lens focuses on retina. The cells in the retina have these molecules which undergo this transformation and that transformation is what triggers the electrical signal that our optic nerve takes to the brain and where the brain decodes that and constructs the image. So you see the configuration change here is that important in biology, otherwise the functional groups are the same. So this is another example for cis-trans isomers.

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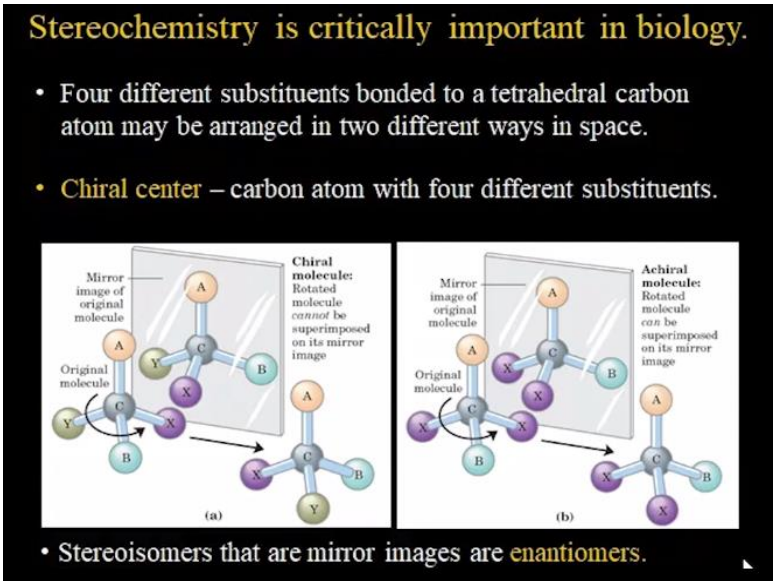

The second one is the chiral center where as shown in this figure you have a carbon atom to which you have 4 different groups attached. You have A, B, Y and X. So now if you keep a mirror next to this, let us say you made this ball and stick using really some balls and sticks, then if you keep a mirror you will get a mirror image like this and if you try to rotate this molecule it will not rotate to the same shown on the mirror so that you can superimpose.

So when the B comes correctly to orient to this but Y does not, instead X comes. So when you rotate you cannot superimpose on the mirror image of the molecule. So, this is one arrangement and when you have this sort of a situation you call that as an enantiomer. So this is based on arrangement, sequence of arrangement of constituents around a chiral carbon and instead if you have let us say 2 similar groups attached there is no asymmetry and you have symmetry.

Here the rotated one will neatly superimpose. Rotated molecule can be superimposed. So this is not chiral and here there is not any difference between the two, so there is not anything to speak of as specific configuration. While here there is a specific configuration, one is the mirror image of the other one, so two types are possible here and such a carbon is the chiral center and this sort of a mirror image structures are called enantiomers.

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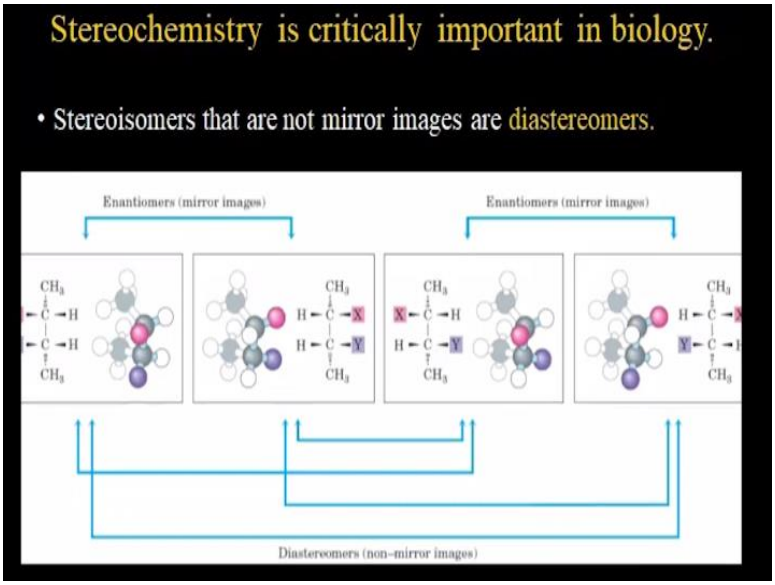

So you can have a varying orientation around a chiral carbon which need not be a mirror image and that will not be called enantiomer instead that will be called diastereomers. So you look at the molecule shown here CH3, then you have CHY and CHX. So his will be mirror image of this, but if you take this one here this is diastereoisomer, this and this like the first and the third are not mirror images although they have the same constituents but different arrangements.

Here the X and Y are attached to different sides of the two carbon atoms while here one is the mirror image of the other. So these two are enantiomers, these two are enantiomers, but these are diastereoisomers. So this becomes often very important in carbohydrate chemistry because that is where we saw these kind of arrangements.

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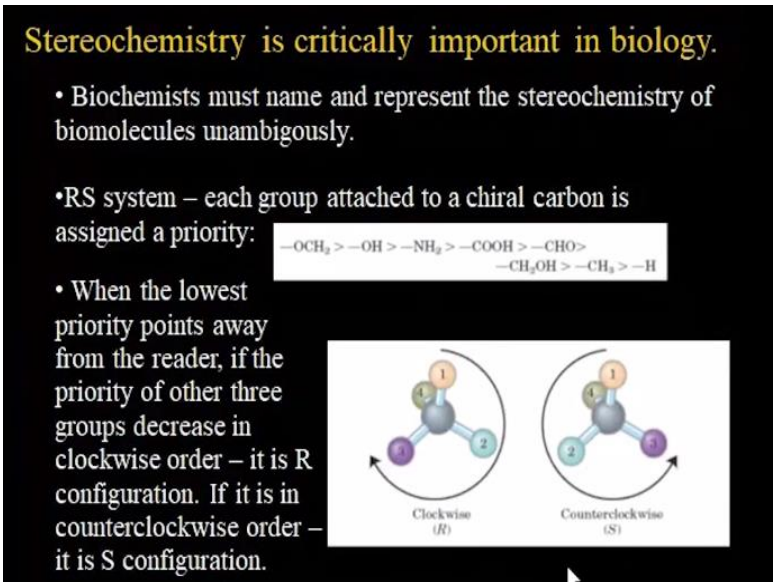

So when you have different groups attached biochemists use a system called RS to determine the orientation or the specific configuration to refer to the configuration and the way it works is it is based on priority and priority is assigned based on the functional groups like for example the hydrogen gets the lowest priority in methyl group next and so on. So this is the increasing order of priority.

Now if you take a molecule and based on this if the lowest priority points away from you like in this case 4 among 1, 2, 3, 4. These are the priority numbers, priority 1, priority 2, priority 3, and priority 4. When the priority 4 faces away from you and now the other one's priority decreases in a clockwise 1, 2, 3 then this is R configuration.

Instead when the low priority group faces away from you then the other constituents decrease priority in a counter clockwise way as shown in this then that is S configuration. So this is R configuration, this is S configuration. So this is how chemists refer to the specific configurations, alright.

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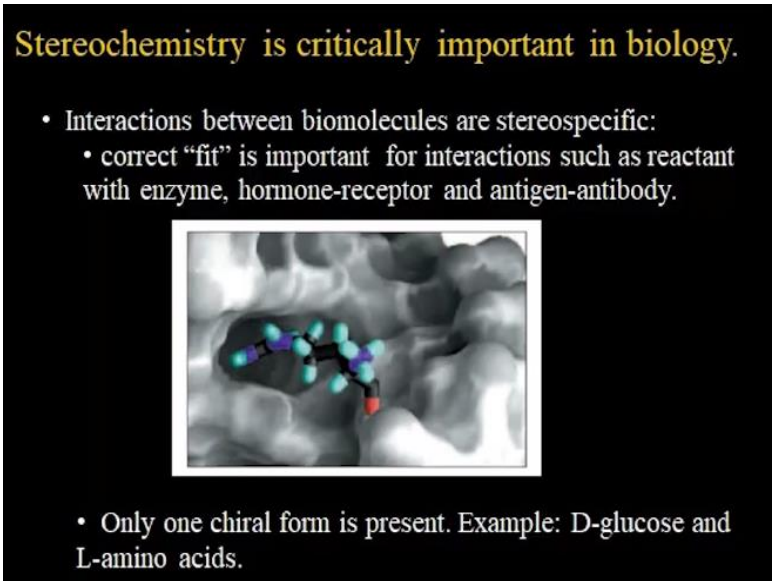

So now really the main reason why we are learning stereochemistry. So at the beginning I mentioned that even the functional group property varies depending on what other groups are attached in the same molecule. Other than that, that is like speaking relatively a minor effect, but in biology many reactions are completely dependent on the stereo specificity of the molecules, only one configuration will work.

The other configuration will not work that is primarily because the molecular shape matters for biology. It is simply not the chemical reactions of the functional groups, it is the shape of the molecule. If you take a key and a lock, let us say you have 6 levers, in all if you take 2 locks, both locks may have the same 6 levers and the key also may have those 6 different protruding structures.

The same structures but then one key will not work on the other that is because the arrangement of those protrusions are complementary to the structure inside the lock. Specific shape matters there, exactly similar logic works with molecules in biology where often times you have a ligand binding to a specific pocket on a receptor. So the receptor's shape determines which ligand or which specific configuration of a molecule can be a ligand for it.

While the other configuration of the same molecule will not be a ligand for it. As shown here, the ball and stick model of a ligand fitting to a receptor or it could even be a substrate on an enzymes active site, you know in that cavity only this arrangement of these constant atoms can fit snugly and any variation on it will not fit. So due to this, stereochemistry is really critical you know in biology it is very, very important.

Interactions between biomolecules are stereospecific like if R fits S will not; if S, R will not fit. So correct fit is important for reactions. For example, I mentioned already like the amylase enzyme in our digestive system can hydrolyze glucose, glucose, glucose in starch when it is linked alpha 1, 4. If it is beta 1, 4 as in cellulose again you have glucose, the same molecule every constant atom is identical, only the bond orientation is instead of alpha it is beta and cellulose will not be hydrolyzed by amylase.

So that is why you cannot eat leaves, you really need a starch-based food to eat and these monomers that we learnt like glucose and amino acids, I did not talk about that stereochemistry, normally we find monosaccharides deconfiguration, amino acids occur in L-amino acids, so in proteins you do not find D-amino acids or in carbohydrates you do not find L monosaccharides.

So therefore, stereochemistry matters a lot. Here are some example enzyme-substrate, hormone-receptor, antigen-antibody. So these are all very, very specific for the actual shape of the molecule.

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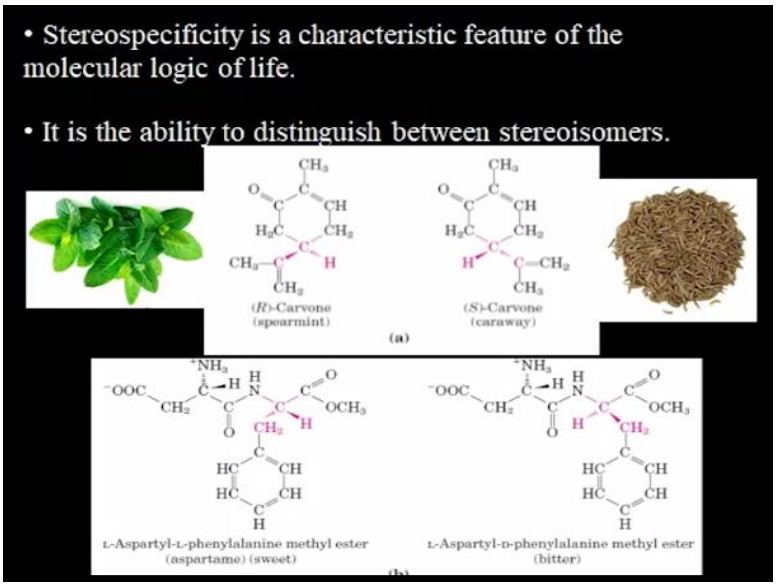

So here are some examples to make us understand in a more like everyday way. If you take the spear mint or these caraway seeds, both you know we get oils from them. Both have very different fragrance, but the fragrance comes from the same molecule carvone. In spearmint it is R orientation and in carvone it is S orientation and simply due to this the order and receptor in your nose where this carvone binds varies.

And due to that this one you smell differently from this and it is not just the smell even the taste if you take this aspartame. Aspartame is an artificial sweetener. This orientation is sweet while the other orientation L orientation is bitter and sometimes you can even test some people for example there is one molecule called PTC. Some people have a receptor it binds and they find it extremely bitter and others find it tasteless. So stereochemistry matters for all of this.

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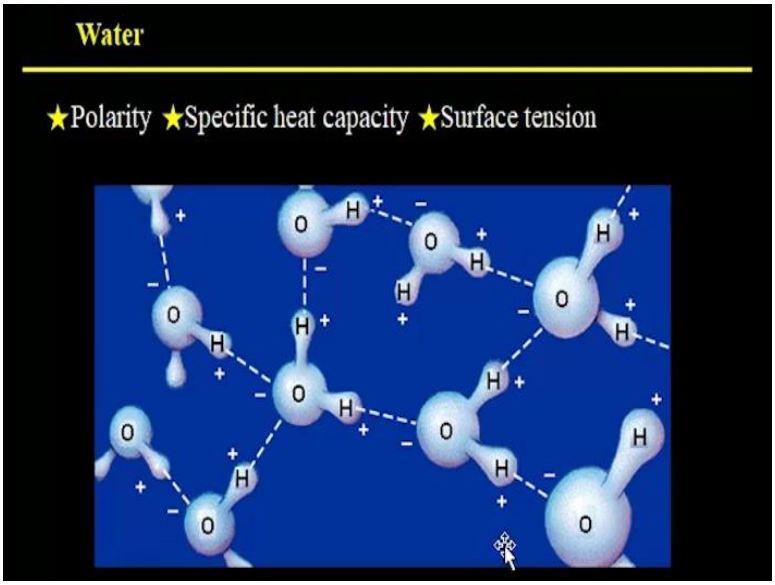

So that brings us to the end of our brief discussion on stereochemistry. So next we will move on to water. So water is extremely important like it we saw in the very first slide of the first lecture the primary constant of cell is water, 70% we found of the cell volume is one way molecular mass is made up of water. So water is very critical and all of that arises from one single feature of water, so that is what we are going to focus now.

So if you look at here I am assuming all of you know what is a hydrogen bond, but briefly to refresh your memory when you have a hydrogen atom bonded covalently to a strongly electronegative atom. So then this electronegative atom pulls the shared pairs of or pair of electrons like both electrons towards it. So the shared pair of electrons spend more time orbiting around oxygen nucleus than around the hydrogen nucleus.

So that is what we mean when we say the electronegative atom pulls the shared pair of electrons. Due to this, this atom acquires partial positive charge while the other one because its proton spends more time with the other one it is partially positively charged. So oxygen has two such bonds in water with hydrogen atoms and due to that this has delta 2 negative delta for partial charge and this is delta 1 positive charge.

So when you have that kind of polarity in a molecule, then this partial positive charge can interact with another molecule that has partial negative charge which is in this case nearby another water molecule's oxygen. So they have a weak bonding due to this partial positive and negative charges and that bond is what we call as hydrogen bonding and this is what is

crucial for all emergent properties of water and life critically depends on that property of water.

So we will discuss this as we go along. So now if you look at it this is like a body of water. Assume it is a glass of water and each molecule is bonded to the other molecule due to this. So this hydrogen to this and the other hydrogen to the other one and an oxygen can interact with two other water molecules because it has two partial positive charges and so on, it is all networks. Now if we take hydrogen bond as a chemical bond, then a body of water is a single molecule because all molecules are bonded there.

So they are essentially a single molecule and due to this nature of hydrogen bonding which is coming from the strong electronegativity of oxygen atom, you need to provide lot more heat energy to raise the temperature of a unit quantity of water by 1 degree Celsius, you know which we call as a specific heat capacity. To raise the temperature of 1 liter of water by 1 degree Celsius will be water specific heat capacity and that is higher compared to other solvents.

The reason is because much of the heat energy that you provide goes into breaking these bonds. So therefore, water actually can take up lot of heat without significantly increasing the temperature and that is why the temperature of earth's, you know its terrestrial and oculus area on the surrounding or air-filled atmosphere have a very narrow range of temperature variation.

So you do not have like –100 degrees in winter or +200 degrees in summer. It varies only a small range, in coastal place like in Chennai you have very little variation from summer to winter or daytime to nighttime and that is because the much of the heat is taken by the water which is 70% of the ocean and the coastal areas are closer to the ocean. So due to this, the temperature variation is maintained in a narrow range.

If it were not, life will not be able to exist. In winter what happens, summer I understood, then winter what happens? All these hydrogen bond formation releases energy and that energy helps the earth to be warmer. So in winter you get some heat energy from the bonding that happen in the ocean and like in water and that keeps you a little warmer and in summer the opposite.

The breaking of the bonds take up much of the heat and due to this the temperature variation of earth is maintained within a narrow range and we will also talk about surface tension. So if the molecules cling together as a result the surface tension automatically will be higher. So the molecules are not going to spread the readily, they will cling together, so water will form droplet more readily. So if you measure contact angle that will be a lot higher for water.

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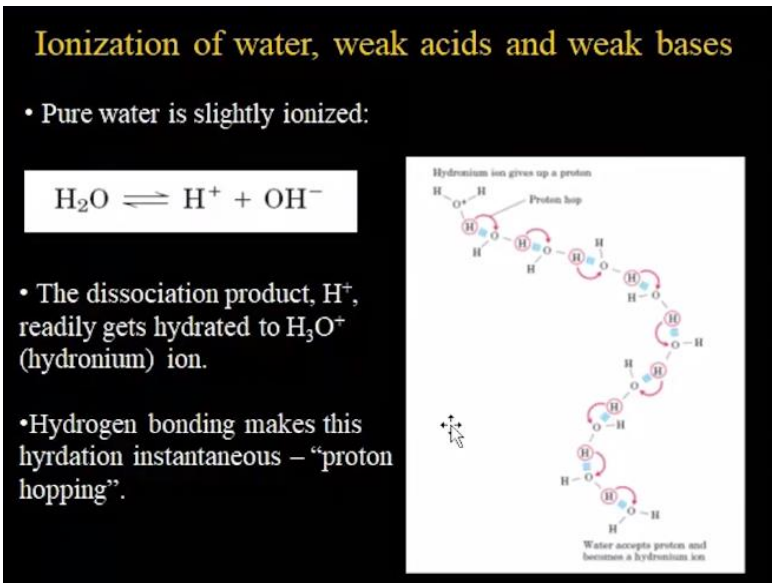

So the next one, we are not going to get too much into the physics of water coming from this hydrogen bonds, instead we are moving slowly towards the chemistry side of it because that is what is critical for us. So there we are going to look at another feature of water and then combine it along with the hydrogen bonding nature of water molecules and then see what property emerges.

So one this new property of water we are going to talk about is its ionization. So in pure water a very few molecules ionize and that is why we call it as its slightly ionized and when they ionize you have a positively charged proton or hydrogen ion and then a negatively charged hydroxyl ion, and this proton can be attached to the water molecule or hydrated leading to what we call as a hydronium ion.

This is made possible by the partial negative charge that you have it on the water and as a result the proton getting hydrated is instantaneous and when it happens and the water molecule to which it gets attached and becoming trans in the H3O is not in isolation that is hydrogen bonded to neighboring water molecules. As a result, a random spontaneously

ionized proton can hop from one water molecule to another water molecule over a long distance and that is what we call as proton hopping.

So like for example this one dissociating readily gets attached to it due to the hydrogen bonded nature of that and this hydronium ion again donates a proton and so on and it moves from one molecule to another molecule or vast distances very, very quickly and that is important for group transfer reactions in enzymes active sites. We will learn about enzymes and their active sites later.

Right now, briefly all you need to know is in the three-dimensional structure of an enzyme the functional groups attached to amino acids participate in reactions catalyzing reactions and for those few amino acids which are involved in the reaction or the pocket where the substrate binds we call that as the active site. So that is the part of the protein where the reaction actually takes place.

And in that kind of an active site protons are often abstracted or donated. and those help in the bond breaking or forming and for those purposes the quick uh proton hopping helps in the transfer of the protons.

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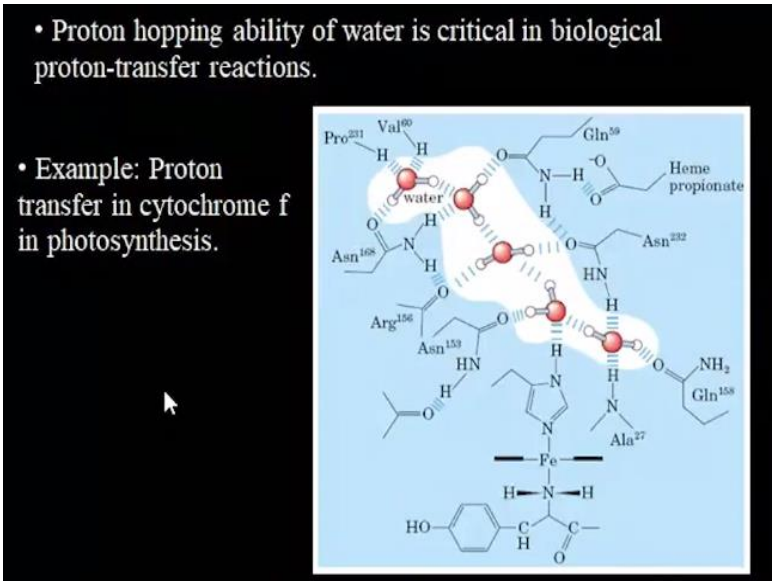

As seen in the cytochrome f this is a protein involved in photosynthesis, we will learn in great detail when we get to photosynthesis several lectures from now and in its active site for example a proton donated by this proline residue. The number indicates that is amino acid

number in that polypeptide chain and that quickly transfers via these water molecules in the active site to this glutamine at another location.

And that kind of a transfer is readily made possible by the water molecules and their ability to conduct proton hopping. So these are really fundamental concepts, so take your time in a comfortable time to recollect and understand these.

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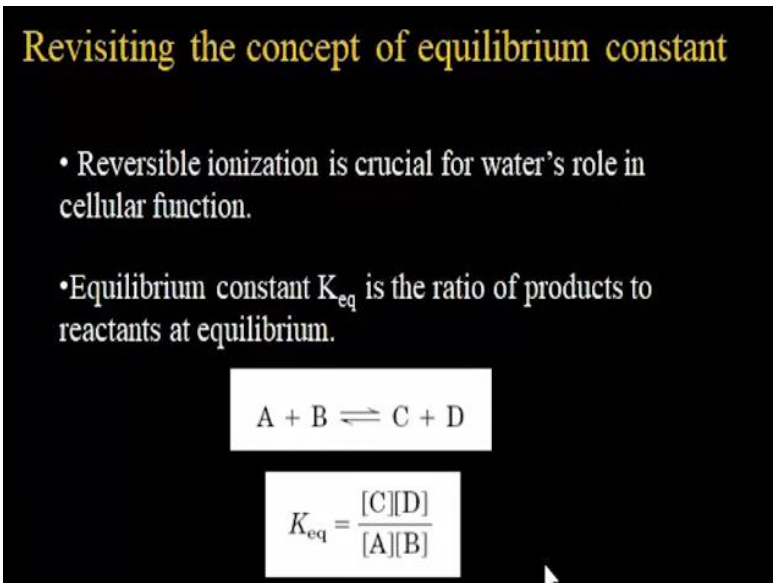

So we continue on this weak ionization of water and to proceed further about it let us recollect our memory on equilibrium constant. I am sure you have learned this long time ago A + B if they react and produce a product C + D in a reversible reaction where C + D also can give rise to A + B, then you will write rate equation.

You know rate of C D formation is proportional to A B and then you will put a rate constant and say rate of the forward reaction let us say RF equals KF reaction is directly proportional to the product of the reactants, so you will say A B and the other one you will say R reverse equals then K reverse times C times D that is what you will write and at an equilibrium both rates are the same.

If you rearrange you will get this equilibrium constant where C times D divided by A times B is the equilibrium constant. This I am sure you learned it long time ago, this is just to recollect. So if it is not clear to you, so revise your chemistry. So primarily it all comes from the basic point that rate of the reaction is directly proportional to the concentration of the reactants and here you have two of them.

So you can write two equations and when you say both are equal and then you take the constant out and rearrange you will get this. So now let us apply this to the water.

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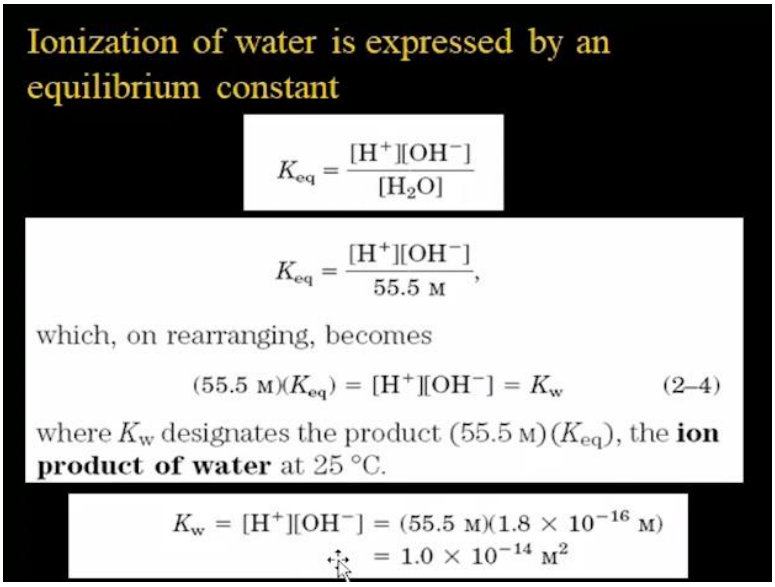

So in water dissociation, therefore this will be H+ times OH– that is concentration of hydrogen times, sorry hydrogen ion times concentration of the hydroxide divided by the water concentration. So that is the equilibrium constant for the water dissociation as we saw in this reaction. So now in pure water, water concentration is 55.5 molar. So if you take one mole and apply water's molecular weight 18, then you will find out it is 55.5 molar is the concentration of water.

So if you rearrange this, then 55.5 times equilibrium constant equals the product of the two ions and since this is constant and this is constant then you can call that as a constant Kw. So this is the constant which is equal to the product of the ions and therefore it is called ion product of water and this K equilibrium has been experimentally determined and that is 1.8 times 10 power –16.

And if you multiply that by 55.5 that is this water concentration you get 1 times 10 power –14. So this is the value of ion product of water when water is pure water, like there is nothing else it is just H2O at 25 degrees.

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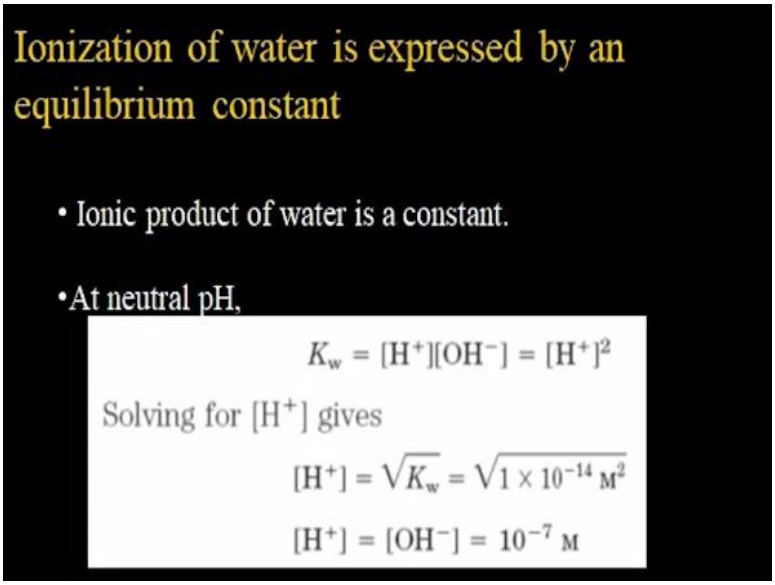

So now this can be rearranged to find what is the concentration of hydrogen and the hydroxyl ions and at equilibrium they both are at the same concentration therefore you can consider as square of one of them and therefore root of the ion product will be the concentration of either of the two. So in pure water the concentration of the protons or the concentration of hydroxyl ion is equal to 10 power –7 molar.

So this is the basis for a scheme of measuring hydrogen ion concentration which we call as the pH scale. So at neutral pH where dissociation is at equilibrium and where the concentration of one ion equals the other, the concentration of hydrogen ion equals 10 power –7 molar and this is the basis for the pH scale.

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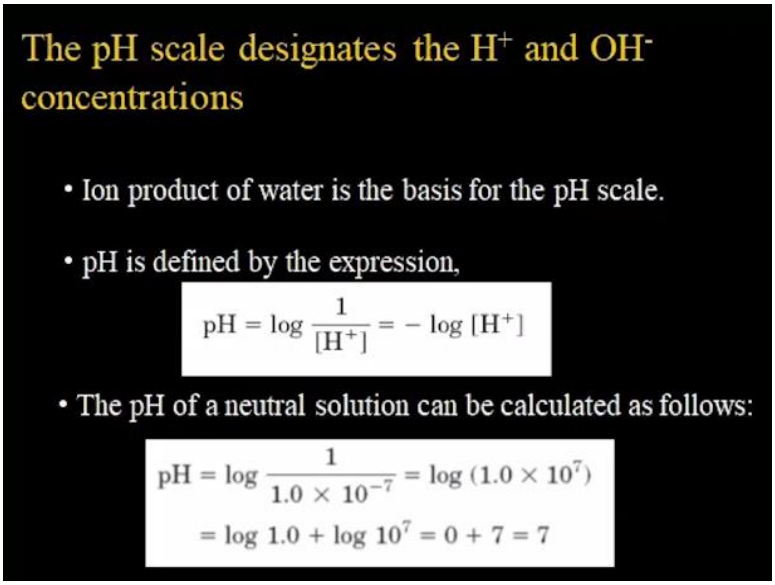

Now let us look at what is pH. So pH is defined as the negative logarithm to the base 10 of the hydrogen ion concentration, log 1 by H+ concentration. So you can rearrange and write it as minus log proton concentration and so at neutral pH, it will be this is 10 power –7and if you solve this you get 7 as the pH. So negative log to the base 10 of 10 power –7 is 7. So the neutral pH = 7.

So essentially based on this equation what you get is pH directly refers to the concentration of the hydrogen ions in a solution. It is a measure of hydrogen ion concentration and value change of 1, like 7 to 6 or say 7 to 8 means a 10 fold change because you are taking log to the base 10 here. So a solution having pH 7 and another solution having pH 8 differ in the hydrogen ion concentration by a factor of 10 fold by an order of magnitude.

So this is the basis for pH and pH is an easy way of referring to hydrogen ion concentration that is the only reason we use pH.

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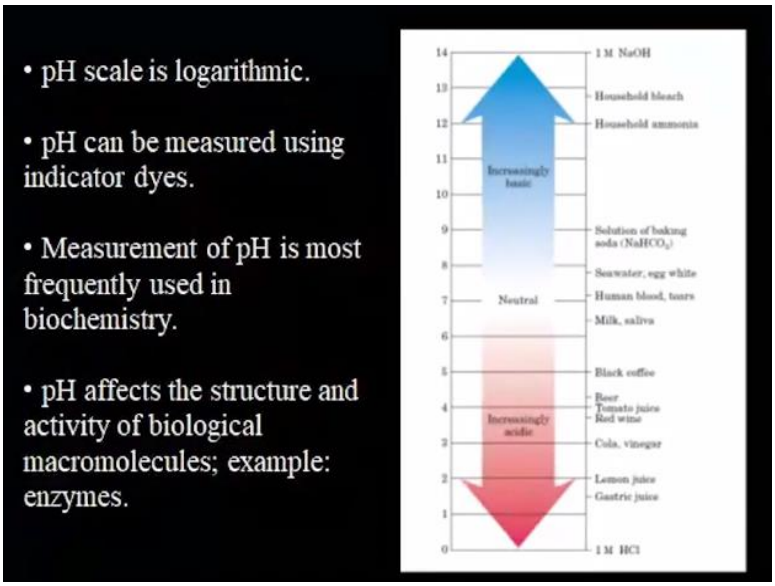

So here this diagram tells you the range of pH is of common household or laboratory common reagents you can see them, so like sodium hydroxide is very strong base. Here when we say strong base or strong acid we are referring to how readily it will dissociate like Na+ and OH. If I take 1 molar NaOH if I get 1 molar Na+ and one molar OH– meaning it completely dissociates then that is the strongest base.

Similarly if I take hydrochloric acid if 1 HCl dissociates to 1 molar proton and 1 molar chloride then I call that as strongest acid. So weak acids do not completely dissociate. So that

is the difference between strong acid and weak acid. So here you can see the different solutions that we use at home have a different range of pH. Like for example stomach gastric juice you know the juice produced in our stomach for digestion has very low pH, pH of about 1.5.

So lemon is little bit less acidic, vinegar which is primarily acetic acid and the phosphoric acid present in the beverages like coke or Pepsi that you drink they are acidic, although weaker than gastric juice and so on and as you go up milk is nearly close to neutral and then if you go here baking soda, household bleach cleaning, household ammonia, this is Colin the one you use for cleaning glasses, glass windows.

So bleach hypo it also has sodium hydroxide and that is why its pH is very very high. So there are indicator dyes where the color of the dye changes depending on the hydrogen ion concentration of the solution in which you dip them. So we use those indicator dyes to get an approximate idea of the pH and the measurement of pH is frequently used in biochemistry because most of the biochemical reactions are very sensitive to the hydrogen ion concentration.

So therefore pH is very, very central in biochemistry. So pH affects, what I mean is the hydrogen ion concentration significantly affects the structure and activity of biological molecules. A good example are enzymes. So that is why the pH is very critical for us.