OK. So today we're going to spend a little bit of time on some elementary chemistry just to develop our language that we use with one another. And so when I say hydrogen bond, you don't stare blankly at me and scratch your heads. Many of you have had this already.

For many of you this is a review, but it's a useful review.

We believe here at MIT of teaching things two or three times often, the same subject matter, but at increasing levels of sophistication.

So I do this without apology. Our first issue here is how are atoms and molecules held together? And the most familiar way by which atoms and molecules are held together is, of course, the covalent bonds. And covalent bonds have an energy of roughly 80 kilocalories per mole. And that's a rather strong energy to hold together two atoms because the energy, the thermal energy, that is the energy at, let's say, body temperature is about 0.6 kilocalories per mole. And, therefore, if you had a bond, if there was something holding things together that was in this range or two or three or four times higher then the simple thermal energy at room temperature or at body temperature would be sufficient to break apart such a bond. But, in fact, this energy, the energy of a covalent bond is so much higher that it's highly unlikely that thermal energy is going to break apart a preexisting covalent bond. And I was just reading yesterday about how people were analyzing the mitochondrial DNA from some Neanderthal bones which were dug up. The last Neanderthal lived around 30,000 years ago, our recently demised cousins.

And they were analyzing the DNA sequences. And they got out of those analyses stretches of DNA that were 200, 300 nucleotides long.

And that really is stunning testimonial to the fact that under very difficult conditions, nonetheless, complex biological molecules are able to survive over astounding periods of time, indeed those that are held together by the covalent bonds like this.

Of course, you remember the film Jurassic Park where they used PCR reaction to resurrect the DNA of dinosaurs. That's a bit of a fantasy since dinosaurs left us, I guess, about 150 million years ago, something like that. There's a big difference, obviously, between 300,000 and 150 million year ago.

Now, the fact is if you look at the way that molecules are actually hooked up, for instance, let's look at a water molecule here.

Ideally there should be no charge on this molecule.

And, in fact, there is no net charge. But the truth of the matter is, if one wants to get frank, that oxygen molecules, and we always are here, that oxygen molecules have a greater affinity for electrons than do hydrogen atoms, i.e.,

they are electronegative.

And, therefore, what this means is that the swarms of electrons that are holding all this together at the orbitals are drawn more closely to the oxygen and the hydrogen atoms, i.e., the protons are relatively willing to give up their electrons. And what this means is that there's an unequal distribution. And, as a consequence, there is a fraction of a negative charge here at this end of the molecule and there are fractions of positive charges here because it's not as if they've totally given up the electrons, but the electrons are shifted more in this direction. And this molecule is therefore called a polar molecule by virtue of the fact that here it has a positive pole and here it has a negative pole. There are other pairs of molecules which are relatively equally electronegative.

For example, here, if we have a carbon and a hydrogen, these two atoms are roughly equally matched in terms of their ability to pull electrons away, one from the other. And, as a consequence, there is no net shifting of charge.

And keep in mind that this delta I show here is only a fraction of an electronic charge. It's not the entire electronic charge moved over. But this has important consequences for the entire biochemistry that we're about to get into both today and on Monday. Important because polar molecules, such as water like this, are able to dissolve certain compounds.

And nonpolar molecules, which have large arrays of these kinds of bonds or carbon-carbon bonds, these are relatively insoluble in water, and that has important consequences for the organization of biological membranes. We might have a carbonyl bond here, that is a C going to an O via a double bond. And here we have, once again, a situation where the oxygen is far more avid in terms of its willingness and interest in pulling electrons toward itself.

And, therefore, the carbon gives up a little bit of the electron cloud and it becomes slightly electropositive.

Whereas, the oxygen atom becomes slightly electronegative.

Now, the fact of the matter is that there are also other bonds that are noncovalent and are much less energetic. For example, let's talk for a moment about a hydrogen bond.

And it's perhaps easiest to demonstrate a hydrogen bond by looking at the structure of two neighboring water molecules in a solution of water of all things. And, the fact of the matter is, let's say we draw one water molecule down here and one water molecule down here. What will happen is that this oxygen atom over here by virtue of its electronegativity will have a certain affinity for pulling this hydrogen atom toward itself. And, in fact, what actually happens in real life, whatever that is at the molecular level, is that this hydrogen atom may actually be bouncing back and forth between these two oxygens. It may be rapidly an interchange between them. This interchange

causes a strong association between two neighboring water molecules. And, indeed, represents the reason why water does not vaporize at room temperature because the water molecules have a strong affinity or an avidity for one another.

And, therefore, just to take some illustrations out of the book, this is the way it's illustrated in the book.

Probably good to have a screen down. And here you can see the way that water molecules are actually arrayed in water. This is the lower illustration here. Just to indicate to you that the hydrogen atoms are not really the possession, the ownership of one molecule of water. They're just constantly being exchanged back and forth. And this back and forth exchange, this sharing of a hydrogen atom is what enables a hydrogen bond of roughly 5 kilocalories of energy per mole to hold things together.

5 kilocalories is not much. It's only one order of magnitude above 0.6 rather than being two orders of magnitude.

And, therefore, if one raises the temperature to the level of boiling, if the temperature is high enough, the thermal energy is high enough to rip apart these kinds of associations.

Now, if we were to go back here to look at this carbonyl atom we would find the following sort of situation. Here we have this unequal sharing of electropositive and electronegative bonds.

Let's put an acidic group like this. This is a carboxylic acid right here. Here we see a carbon bond to a hydroxyl here via this oxygen atom. Here, once again, we have an electronegative atom. And, in fact, if we talk about an ionized acid, normally in the absence of ionization there would be a net zero charge right here. But at neutral pH it may well be the case that the association, for various reasons, between this oxygen and this hydrogen will allow the hydrogen, or rather the proton, the nucleus of the hydrogen atom to just wander away.

And, therefore, we can imagine there could be a net negative charge here. A whole, this has one full electron, electronegative charge here, the charge of one electron, and this proton will have ionized, will have left the carboxylic group in which it originated, and now we have an ionized acid group. Either before or even after this ionization, there is a strong affinity of the carboxyl group with the water around it because let's look at what happened before the ionization occurred. This carbon here is strong and electronegative. And, therefore, it will participate in hydrogen bonding to the water solvent here, i.

., this proton will be shared a bit between the oxygen of the water molecule and the oxygen right here. Similarly, here this oxygen will be slightly electronegative for the reasons I've just described.

And here, once again, there may be some weak hydrogen bonding going on.

Although, not as effective as over here where we have a double-bond where we have a lot of concentration of a cloud of electrons pulled towards the oxygen atom. And this begins to give us clues as to why certain molecules are soluble in water and others are insoluble.

For example, if we look at aliphatic compounds.

Let's look at a compound that's structured like this.

I guess most people would call this pentane. And we can call it that, too. And this has no electronegativity or positivity by virtue of the equal affinities of these two kinds of atoms, that is the hydrogen and the carbons for electrons. And as a consequence, this will not be able to form any hydrogen bonds with a solvent around it if the solvent happens to be water.

So there's not good bonding here. And this will, in fact, also if one puts this in a solution of water, this will cause all the water molecules to line up in a certain way, almost a quasi-crystal around the aliphatic molecule. They'll be ordered in a certain layer around the aliphatic molecule without being able to form any strong hydrogen bonds with them. And this ordering represents a loss of chaos, a loss of entropy. Entropy is chaos. It's disorder.

It's what happens, let's say, at 10:55 when we all leave the room, all of a sudden order becomes chaotic. And here, before this lining up occurred, the water molecules were chaotically arrayed throughout the solvent. After this lining up occurred there was a loss of entropy, there was a loss of chaos.

And thermodynamics tells us that generally the ordering of molecules is disfavored. And consequently we now have two reasons why this molecule doesn't like to be in the midst of water.

First of all, it's unable to form hydrogen bonds with the solvent.

And second of all there is a decrease in the entropy, in the chaos that occurs when this molecule directly confronts water.

And because of those two reasons it turns out that this molecule doesn't like to be in water. The aliphatic molecule, as one would call this in organic chemistry, doesn't like to be in water. And a dislike of water is often called its hydrophobicity, or we often call it hydro, might as well spell it right, hydrophobic, i.e., it really hates to be in water.

In fact, class, there's a second meaning for hydrophobia, or hydrophobic has a second meaning.

Every five years I ask a class to see who knows what the second meaning of hydrophobia is. This is really obscure. Sorry?

Rabies, right. The TAs aren't allowed to answer that.

If somebody has rabies, at one stage of rabies, almost near the terminal stage, the individual becomes hydrophobic because he or she doesn't like to drink water, for reasons that are obscure at least to me. Now, conversely, molecules that have carboxyl group on it would be called hydrophilic.

And, as we'll see over this lecture and the next one, these hydrophobic and hydrophilic tendencies tend to have great affects on the overall behavior of molecules. Let's, for example, imagine a situation where we have a long aliphatic tail like this. In fact, these tails can go on in certain aliphatic compounds. They can go on for 20 or even 30 carbons. And at the end of this, let's just put arbitrarily a carboxyl group. And let's say we ionized it.

So here's an acidic group that's ionized. It's shed its proton.

It's actually acquired a negative charge. And now we have something, this molecule is a bit schizoid. Because on one end of it, it loves to be in water, the other end of it hates to be in water.

And this has strong affects. It's sometimes called amphipathic, but we don't need to worry about that word. And, therefore, this carboxyl head loves to stick its head, to immerse its head in water. And these things, the aliphatic portion hates to be in water. Now, as a consequence of these rather conflicted feelings that these molecules have about water, we can ask the question what happens when we put such molecules actually into water? And what we see here is the following. That if we were to construct, for example, a molecule of the sort that has here, in this case we're talking about a molecule that has two hydrophobic tails. We'll get into its detailed structure shortly, but just imagine for a moment two long hydrophobic tails out here ended with a hydrophilic head.

And under such situations, if we put thousands of these or millions of these molecules into a solution of water, what we will then see is, no pointer? All right. Pointer?

All right. What we will then see is that the hydrophilic head groups, which are here depicted in red, will point their way outwards, they will want to stick their heads in water.

And conversely the hydrophobic tails fleeing from the water will actually associate one with the other. And so you have a structure that's called, in this case, an a micelle where you form this little globular sphere where the lipid tails are tucked inside.

And, therefore, are actually being shielded from any direct exposure to water. This structure down here, the lipid bilayer, is actually, as we will discuss in greater detail shortly, the overall topology of the way most biological membranes are organized.

In fact, virtually all of them. Why is that? Because biological membranes separate two hydrophilic or two aqueous spaces.

Thank you, sir. A gentleman you are. So here is an aqueous space and here is an aqueous space. And as we see the hydrophilic heads are immersed or sticking their heads into the hydrophilic space.

This is called a lipid bilayer. And, obviously, it's highly effective for separately these two aqueous compartments.

In eukaryotic cells, as I mentioned last time, there is an enormous premium placed on separating and segregating different aqueous compartments which is invariably achieved through the device of constructing these lipid bilayers. Here's a vesicle. A vesicle is more complicated than a micelle. Because if you look at the membrane lining the vesicle, you see it's actually a lipid bilayer, but one that in 3-dimensional space is actually a sphere. And in the case of this vesicle, we can well imagine that on the inside of the vesicle water is kept, can be stored, and on the outside of the vesicle water can be stored.

And many of the membranes that we see within the cytoplasms themselves are actually constructed on this kind of design.

So when we draw, for example, in this case the Golgi apparatus, which I mentioned to you in passing last time we met, each one of these membranes here, it's obviously drawn as a double line, but whenever you see a membrane indicated, implicit in that drawing is the fact that each one of these membranes is actually a bilayer. There are never any monolayers of lipids in living cells. Each one of these vesicles you see here is actually a lipid bilayer with an aqueous inside and, once again, aqueous on the outside. Again, much of the thermodynamic stability that allows these vesicles to remain intact rather than just diffuse apart is created by these hydrophilic and hydrophobic forces which tie such molecules together or will rip them apart.

Now, in truth there are yet other kinds of forces that govern the affinity of molecules to one another. For example, let's imagine a situation where we have an ionized acid group of the sort we just talked about before. Now, by the way, here, let's say I'll draw the negative charge on one of these two oxygens, if you can see that. But the truth is that the electrons are swarming back and forth, and so the negative charge is shared equally, the negative one electron charge is shared equally between these two oxygen atoms. And this is obviously an area of great electronegativity. Independent of that, let's imagine up here we have a basic group, let's say an amine group over here. And, the fact of the matter is, amine groups, NH2 groups, that's what an amine is, here's an amine group. This is a carboxylic group.

And the amine group, which is used very often in biochemistry, actually has an affinity. It has an unpaired set of electrons on the nitrogen, and so it likes to attract protons to it, which makes it, causes it to be called basic.

And this attraction, the scavenging of protons, perhaps from the water, will obviously give this whole group here a net positive charge, a charge equal to the charge of one proton. Here, once again, we can imagine this is hydrophilic because this charge group can once again also associate quite intimately with aqueous solvent.

Now, independent of any other forces that might exist here, indeed one could imagine situations where there is a sharing of a proton.

And, therefore, a hydrogen bond formed between these two. Independent of that is the simple electrostatic interaction of these two groups. That is the mutual attraction of positive and negative groups, one to the other. And the electrostatic interactions, you cannot quantify exactly how many kilocalories a mole there is because the energetic value in electrostatic interaction is equal to one over r squared where r is the distance between these two charged groups. And obviously the further apart you get the weaker the attraction with one another. There are also what are called van der Walls interactions. There are largely of interest to a very small community of biochemists.

You probably will never, you may never hear this term again in your life. And van der Waals interactions come from the fact that if we were to have, for example, two molecules over here which are not normally charged in any way, let's just talk about two aliphatic chains again. And I won't put in all the protons and everything, but just imagine a situation like this. What will happen is that because of the fluctuations of electrons, because the electrons are swimming around here all the time, moving from one area to the next they're never equally distributed homogenously over a long period of time, there will be brief instance in time, microseconds or even nanoseconds when there happens to be more electrons over here than right here.

Just by chance. And this area of unequal distribution of electrons will in turn induce the opposite kind of electron shift in a neighboring molecule down here.

Obviously, depending on the distance between them.

But the negative here will repel electrons down here.

The positive here will attract electrons down here.

And so you will have these two quasi-polar arrangements here and here, very ephemeral, that is lasting for a very short transient period of time. But, nonetheless, sufficient to give a very weak interaction between these two molecules which may persist only for a microsecond and then be dissipated because the charges then redistributed once again.

And, as a consequence of that, one has very weak interactions which, in the great scheme of things, play only a

very minor role in the overall energy which holds molecules together. Now, with that background in mind, let's begin to elaborate on it, on how we can make molecules that have interesting properties that enable them, among other things, to participate in the construction of lipid bilayers, which will be the first object of our attentions today in terms of actual biochemistry.

So here's a fatty acid. We see that up here. I, in effect, drew you the structure of a fatty acid up here already once before. And what we can see is through a linkage known as esterification we can create this molecule. So what do I mean by esterification? Well, in this case we're talking about a situation here where we have a carbon atom over here like this with a hydroxyl group. You see it over here. And what we're doing is we're dehydrating this, we're pulling out one net molecule of water. And each time we do that, on three separate occasions, what we end up doing is to create instead of this is to create a covalent bond between these two.

And so the end product of dehydrating this, pulling out one net molecule of water is that we end up with a structure that looks like this.

And you see that happening on at least three different occasions, here, here and here. Well, actually, I should put a carbon over here.

So here we have three esterifications.

The hydroxyl group in each case is reacting with a carboxyl group here pulling out one water, and each case creating what's called triacylglyercol or triglyceride. Triglyceride refers to the fact that we started here with a glycerol and we have now esterified it.

Now, in fact, there are two directions here in this kind of reaction. Esterification is the kind of linkage that we just showed here. And the truth is that vast numbers of biochemical linkages are made by esterification reactions and reversed by reactions that are called simply hydrolysis.

And, in this case, what we're referring to is the fact that if one were to reintroduce a water molecule into each of these three linkages, one, two and three, we would break the bond and cause this entire structure to revert to the two precursors that existed or preexisted prior to these three esterification reactions.

And time and again you'll see, over the next weeks, that esterification reactions are important for constructing different kinds of molecules. Now, the fact of the matter is we can do other kinds of modifications of a glycerol like this.

Here what we've done, instead of adding a third fatty acid, note what was done here. Here through an esterification, let's look up at this one here, instead of adding a third fatty acid, we've saved, we've reserved one of

the three groups of the glycerol.

Here's what we saw just before. We've saved one of the three groups of the glycerol and put on instead this highly hydrophilic phosphate group, once again through a dehydration reaction, an esterification reaction. And now what we've done is add insult to injury because in the absence of this phosphate it would have a hydroxyl here which is mildly hydrophilic. But now look how strongly charged this is. Here are two negative charges, one electron each. And this is already a bit electronegative.

So here we have an extremely potent hydrophilic entity.

And here the degree of schizophrenia between one end of the molecule and the other is greatly exaggerated. Here, in fact, this is extremely hydrophilic.

And, as a consequence of that, this really likes to stick its head inside water. And when we therefore talk about, we draw the images of different kinds of membranes, like this I showed you before the two tails. Here you saw the two tails I drew before in that diagram.

Here's what we can imagine they actually look like in more real molecular terms. And the hydrophilic heads sticking in the water, this is just repeating what we saw before, become even more hydrophilic if we look at a molecule like this.

Let's look at this thing here. Here's a very long hydrophobic tail.

Here are the two glycerols once again. Here is the phosphate.

And keep in mind that phosphate obviously has these extra oxygens.

Phosphate can react with more than just one partner, the glycerol down here. In this case we've added this group up here. And this group up here is, once again, this happens to be a serine which is an amino acid, this also happens to be quite hydrophilic. Here's our old friend the basic amino group. Here's the carboxyl group. This is a bit hydrophobic, CH2. And then we once again have the hydrophilic head here.

And, therefore, we imagine, if we look at what's called a space-filling model, and a space-filling model really is intended to show us what one imagines if one had this vision, which we don't have, how much space each of these atoms would actually take up if one were able to see them.

And here we see this space filling model. This lipid molecule here is actually slightly kinked with its hydrophilic head tucked into the water space. And so here's actually the way that many biological membranes look in terms of the way that they are constructed.

Now, the fact of the matter is this also affords the cell the ability to segregate contents on one or the other side of whatever lipid bilayer it happens to have constructed. And here we can see about the semi-permeability, how permeable these membranes are to different kinds of molecules. Permeability obviously refers to the ability of this membrane to obstruct or to allow the migration of molecules from one side to the other.

Ions, and these ions we see right here are obviously highly hydrophilic by virtue of their charge. That's explains, in fact, why, for example, table salt goes so readily into solution, because it readily ionizes into sodium, NA and CL, which then are avidly taken up by the water molecules.

So these are highly hydrophilic ions. And the questions is, can they go from one side of the membrane to the other?

And the answer is absolutely not or highly improbably. Why?

Because these are so highly hydrophilic, the water molecules love to gather around them and form hydrogen bonds and electrostatic bonds with them. And if one of these ions ventures over here, it's going from an area where it's warmly embraced by the solvent molecules to an area where these molecules intensely dislike these ions. And, therefore, thermodynamically the entrance of any one of these ions into the membrane, into the hydrophobic portion of the membrane is highly disfavored, which makes the membrane essentially, for all practical purposes, impermeable. The same can be said of glucose which happens to be a carbohydrate. We'll talk about it shortly. But it's also nicely hydrophilic. It also can go in water. In fact, it can go through. And it's actually the case, to my knowledge, that one doesn't really understand to this day why lipid bilayers are reasonably permeable to water.

You would say, well, water shouldn't be able to go through. It clearly doesn't have to have a net positive or negative charge, but the physical chemist, if you asked them why does water, why is water able to go through lipid bilayers? They'll say, well, we've been working on that and we'll get you an answer in the next five or ten years. And they said that 40 years ago and 30 years ago, and they're still saying it. And we don't really understand why water goes through, which is an embarrassment because here's one of the fundamental biochemical properties of living matter that is poorly understood. Gases can go right through.

And amino acids, ATP, glucose 6 phosphate, highly hydrophilic, can also not go through. Now, the advantage of this is that a cell can accumulate large concentrations of these molecules either on the inside or it can pump them to the outside. In other words, it can create great gradients in the concentrations of different kinds of ions. For example, in many cells, the concentration of calcium, CA++ is a thousand times higher on the outside of the cell than on the inside of the cell which is a testimonial to how impermeable these lipid bilayer membranes are.

The fact of the matter is I'm fudging a little bit here because in the lipid bilayers of the plasma membrane of the cell, the outer membrane of the cell that we talked about in passing last time, there are ion pumps which are constantly working away pumping ions from one side to the other overcomes the little bit of leakage which may have occurred if a calcium ion happens to have snuck through in one direction or the other. And we end up expending a lot of energy to keep these ion gradients in appropriate concentrations on the outside and the inside. In fact, virtually all the energy that is expended in our brain, almost all of it is expended to power the ion pumps which are constantly insuring that the concentrations of certain ions on the outside and the inside of neurons are kept at their proper respective levels.

It could therefore be that actually more than half of our metabolic burden every day is expended just keeping the ions segregated on the outside and inside of cells. For example, potassium is at high levels inside cells, sodium is at high levels outside cells, just to site some arbitrary examples. There are also, by the way, as I mentioned last time, channels.

And channels are actually just little doughnut shaped objects which are placed, inserted into lipid bilayers in the plasma membranes and just allow for the passive diffusion of an ion through them, through the doughnut hole enabling an ion, so if here's the lipid bilayer, not showing its two things, these kinds of doughnut shaped protein aggregates will allow the passage of ions in one direction or another. And here energy is not being expended to enable this passage. It may just be through diffusion.

If there's a higher concentration of ion on side of the lipid bilayer and a lower one on this side, this diffusion will allow the ion to migrate through the bore of the ion channel from one side to the other.

In fact, even though this does not involve the expenditure of energy on the part of the cell, the cell may actually use a gating mechanism to open or close these channels.

When the channels are closed then the ions cannot move through.

When the channels are gated open then diffusion can take over and insure the transfer, the transportation of ions from one side to the other. Now, having said that, we can begin to look at yet other higher level structures.

Here, by the way, is a better drawing than the one I provided you.

This comes from your book of what a vesicle looks like.

Here's what it looks like under the electron microscope and here's what it looks like when a talented rather than hapless and hopeless artist like myself tries to draw it. So let's just say that's our intro into lipids and membranes.

And let's move onto the next layer of complexity. And the next layer of complexity in terms of molecules represents carbohydrates.

And when we talk about a carbohydrate amongst ourselves we're talking about a molecule which, roughly speaking, has one carbon atom for every water molecule. And we'll shortly indulge ourselves in talking about all kinds of different carbohydrate molecules.

Here is really one of the most important carbohydrate molecules, glucose. And what should we note about glucose?

Well, the first thing you should see is that glucose has six carbon atoms. And, therefore, as a consequence it's called a hexose. We're going to talk about pentoses very shortly. They only have five, to state the obvious. Glycerol, which we talked about before, is also considered in one sense a carbohydrate, but it's been called by some people a triose.

It only has three carbon atoms. And you can imagine, therefore, in principal that there are certain biochemical mechanisms which indeed exist which enable one to join two glycerol molecules, one to the other, to create something like a hexose, glucose.

In fact, what we see from this drawing, expertly drawn by yours truly, is that the hexose molecule isn't really a linear molecule in solution. What happens is that because of various steric and thermodynamic forces it likes to cyclize. So let me just mention, I've just used two words that are useful to know about.

Steric or stereochemistry refers to the 3-dimensional structure of a molecule. And, obviously, the stereochemistry of a molecule is dictated by the flexibility with which participating atoms can form bonds, whether we have a trivalent atom like nitrogen or a tetravalent atom like carbon or a monovalent like hydrogen. And these structures, the stereochemistry is dictated both by what atoms are present here and by thermodynamic considerations which cause this particular hexose, indeed virtually all hexoses, to cyclize. When I say cyclize, obviously I mean to form a circular structure. Here we note one thing.

You can see how the hydroxyl here actually attacks the positively charged carbon here in order to form this cyclic structure.

You see one of the six points on this hexagonal structure here is oxygen. It's not carbon at all. So there is one oxygen and five carbons. And one of the carbons is relegated, is exiled to outside of the circle. It's sometimes called an extracyclic because it's sticking out from the actual circle. And this is the structure in which glucose actually exists inside cells. And, in fact, there is, in truth, two alternative ways by which glucose can cyclize, whether the oxygen attacks the carbon on the carbonyl group underneath or on top.

And you see that gives us two alternative structures.

What's different about them? Well, if we think about this hexose as existing in a plane, or the hexagon is in a plane In this case the oxygen is above the plane and the hydrogen is below the plane. With equal probability you can have these two atoms reversed where hydrogen is now above the plane and hydroxyl is below the plane. And both of these structures, these alternative structures can fairly be considered to be glucose. Now, let's get a little bit more complicated. Here we have fructose and we have galactose.

And what we see here is, by the way, that we have exactly the same number of carbon atoms and hydrogen atoms and oxygen atoms but they're hooked up slightly differently. And here now we begin to get very picky about the disposition, the orientation of these different kinds of hydroxyls and hydrogens.

And note, by the way, here that in many cases one doesn't even put in the H for the hydrogen. It's just implied by the end of this line. And here, if you were to look at this, you'll see here now we have two extra cyclic carbons.

Here's galactose which is yet another hexose.

These are all hexoses, but their stereochemistry creates quite different kinds of structures. And it turns out that this stereochemistry is extremely important. These molecules function very differently, one from the other.

And, for example, to the extent that glucose is used in different kinds of energy metabolism and to the extent that galactose is not, there must be certain biochemical mechanisms in which one has catalysts, the catalysts that we call enzymes that ensure that one can convert one of these hexoses through an enzyme into, let's say a less useful one into a more useful one, glucose, which can readily be burnt up by the energy-generating machinery. Here we've gone yet another order of magnitude more complex because we've gone from a monosaccharide, i.e., one or another hexose, to a disaccharide. And here's common table sugar.

And here you see that it's formed once again through an esterification reaction, i.e. there is a dehydration reaction between this hydroxyl here and this hydroxyl here.

And biochemists take the orientation of these hydroxyl and hydrogen groups very seriously. Now, you can say they're a bit obsessive. Indeed they probably are.

But, nonetheless, we can admit that the specific orientations of all these things dictate very importantly the difference between here, in this case sucrose, and in this case lactose. Why is this important? Well, this is the sugar in milk sugar. This is the dominant sugar in milk sugar, lactose. And half the world, as adults, cannot absorb this.

All kinds of unpleasant things happen when they actually drink milk. How many people here are lactose intolerant? It's nothing to be ashamed of. I'm married to a very lactose intolerant person. She's otherwise very nice.

The fact is that the enzyme to break down lactose, it's an enzyme which is called lactase. And here we have yet another nomenclature item. So lactase is the enzyme which breaks down lactose. And, by the way, this is just the harbinger of many other enzymes we're going to talk about in the future that end in A-S-E. Whereas, carbohydrates, many of them end in O-S-E, as you've already sensed.

So it turns out that the enzyme lactase is made in large amounts by most mammals very early in life. Why? To be able to breakdown the milk sugar that comes in their mother's milk.

But once mammals are weaned there's no reason on earth for them to continue to make lactase, in their stomach for example.

And, as a consequence, in most mammals the production of lactase is shut down later in life. And for some weird quirk of human history, a significant proportion of humanity has learned how to retain the ability to make lactose through adulthood. And, as a consequence, people can go and have ice cream until the age of 70, 80 or 90 without becoming very bloated. And we don't need to get into all the details, but you can begin to imagine. And what happens is, therefore, the lactase enzyme is shut down in their stomach.

It depends. Sometimes they lose it at the age of 10 or 15 or 20.

And then, for the rest of their lives, whenever they have a milk containing product, in fact, my son is also lactose intolerant. I'm surrounded by these people. Again, he is otherwise a tolerant person but he's lactose intolerant.

So this lactose molecule will go into the stomach, it will remain undigested, it will remain a disaccharide instead of being cleaved into two monosaccharides.

The two monosaccharides are no problem because they can readily be interconverted. The galactose can be readily converted into glucose, and glucose is the universal currency of carbohydrate energy. And so this disaccharide passes through the stomach unaltered and it gets into the intestines, in the small intestine and the large intestine.

And it turns out we have more bacterial cells in our gut than we have our own cells in the rest of the body. Imagine that.

And there are a lot of bacteria that are waiting around in the gut for just a little gulp of lactose. And they never get it because most people break down their lactose long before it gets into the intestine.

But here we have these lactose intolerant people.

The disaccharide gets into the gut and the bacteria go to town.

They've been waiting around for years, decades for a little bit of lactose. And now it finally arrives and they go to town, ad they start metabolizing it and they ferment and they produce lots of gas and other kinds of byproducts. And, as a consequence, this makes people very uncomfortable. Just to show you, now, the fact is that lactose intolerance people can perfectly well break down sucrose, obviously. This is one of the great energy sources from plants. But they cannot break this down.

And I emphasize that point to indicate that the stereochemical differences between different kinds of carbohydrates makes a very important difference. An enzyme like sucrase will break down the sucrose but it will not touch lactose.

So there's a high degree of stereospecificity as it's called in the trade. Here we now go to another step forward that we're going to pursue in much greater detail next time.

Because here, for the first time, we talk about polymerization. We're making polymers. Where the large number of hydroxyl groups on these monosaccharides affords one many opportunities to make very long linear aggregates end-to-end like this or even side branches. If you imagine that each one of these hydroxyls, in principle, represents a site for possible esterification, i.e., the formation of a bond to a neighboring side chain.

Here we see these two linear chains and here we see the branch which is afforded, which is made possible by the availability of these unutilized hydroxyl side chains which are just waiting around to participate, if the opportunity allows them, in some kind of esterification reaction to form a covalent bond. Here is, by the way, glycogen, which is the way we store a lot of sugar in our liver.

Here's a starch, which is what we get from many plants. And here's another very interesting polysaccharide.

It's called cellulose. And we cannot digest cellulose, but termites can. And why they can is something we'll have to wait until next time to learn about. Have a great weekend. See you on Monday.