PROFESSOR: So what I want to do today is-- I want to introduce this to you very quickly-- is-- and I was going to show you this at the end of the last class-- if we simply go to the far end of the scale, the picometer scale-- you see carbon. I'm not going to start you with carbon, that is a little dull.

But over the next few weeks-- few classes, rather, because we have to do this in fast order-- we will cover details of carbohydrates, amino acids nucleosides, and phospholipids and how those building blocks are put together-- their properties, their ability to interact and engage in non-covalent interactions with other molecules and the ability to make polymers out of some of these, such as the nucleosides and the amino acids and the carbohydrates, which then start to create the richness of life.

We will also discuss today the super molecular chemistry of phospholipids as they make micelles and lipid bilayers, which are the key boundary of cells. So this is very important. And then in the following week, we'll go to some of the bigger things like proteins, nucleic acid, polymers-- for example, here's RNA. So the course will literally do this-- take you from one end of the scale to the other. So I want you to get a sense of these dimensions.

I want to mention one sort of fairly stupid thing with respect to how chemists and biochemists talk about certain metrics, certain distances that are pertinent to biology and biochemistry. Engineers tend to talk about micrometers and nanometers. There is one unit that chemists and biologists use quite a lot, it's the Angstrom after a Finnish or Sw-- no, not Finnish. I think it was a Norwegian. And that is equivalent-- 10 Angstrom equals 1 nanometer.

So when you're looking at scales, we tend to talk about Angstrom because they're a convenient number. But don't get fooled by this. It can be a little bit confusing because it's 10 to the negative 10. So a nanometer is 10 to the negative 9, you know that quite frequently. Picometer-- 10 to the negative 12, micrometer-- negative 6. But the Angstrom is just a funny unit we use a lot, and it's 10 to the negative 10. So just to make sure there's no ambiguity about that particular detail, OK? All right.

So today's lecture will focus on the molecules of life. And in particular, I'm going to, through the next few classes, introduce you to the various molecules of life.

But first of all, we have to do a little bit to understand chemical bonding. And in particular, we

want to look at both covalent and non-covalent bonding because covalent bonding is important-- it's the structure, it's the framework. But non-covalent bonding is what gives us dynamics. These are much weaker forces that can be broken and remade very readily that are essential for things like forming the DNA duplex, folding your proteins, associating the lipid bilayer. All of those are non-covalent forces and they are dynamic because they're weak, you can break one relatively easily as long as you're ready to make another one in its place.

So I will spend a little bit of time on that. And then today, we'll talk about lipids and membranes.

But first of all, let me introduce you to some of the molecules of life in this rendition that's done by David Goodsell at Scripps. So up in the top corner here, you look at 2.3 is the three dimensional structure of a protein. It's folded into a globular state through non-covalent forces. I brought a little 3D model of a protein for you to look at and take a look at later. That was one of the suggestions I made. You could coordinate printing a 3D model as one of your later projects.

We will learn about the forces that hold the polymer together-- the covalent forces. But then the non-covalent forces that make globular structures that are very important for function. They're not much use as unraveled spaghetti. They're way more useful as their three dimensional structure.

Down here in the corner is a carbohydrate. It really looks pretty pathetic in this rendition, but carbohydrates have a lot of value, particularly in energy storage but also in things like the extracellular matrix and as entities that signal information between cells. There's a lot of communication done by cell surface carbohydrates.

Over here you see the canonical structure of double stranded DNA. We'll look at the covalent structure of those single strands, but then we'll focus in on the non-covalent interactions that make the double-stranded DNA and store genetic information which is also central to life.

And then lastly on this, but we'll cover this today, is a lipid bilayer. It's a fascinating supramolecule structure that really is at the heart of how all your cells are held in a compartment surrounded by a lipid bilayer.

So by the time we start talking about those, you'll understand the forces that put in place that lipid bilayer that arguably-- and I've read articles that say this-- that the evolution of lipid

bilayers is as important as the genetic code. Because if cells did not have a surrounding, did not have an inside where you could concentrate reagents and macromolecules and do biochemistry, life wouldn't exist in the same way.

OK, so let's take a look at the composition of living systems. And remarkably, we are about 75% water. So most proteins are very hydrated. There's a lot of water in cells. There's a lot of water outside of cells in the matrix. And really, we sort of survive weird. We survive in an aqueous environment.

And the thing that you also want to think about is when we think about non-covalent forces, these are forces put in place in water. We don't live on a far distant planet where we're in sort of liquid methane or anything like that. So water is critical to life. The establishment of the hydrosphere when Earth first formed, the evolutionary events that happen after that were really hand in hand with the fact that it was an aqueous environment. Because forces are different whether they are in hydrophobic environments or hydrophilic environments. And really, you'll start to get appreciation for that as we move forward.

So this basically suggests that if I put one of you in a giant desiccator and pumped out all the water I could possibly pull out, there'd be about sort of-- depending on your weight-- 40 pounds of things left behind. Of what's left behind, the majority of it is going to be biological macromolecules-- whoops. And then the rest of it, that little sliver, are things like ions and small molecules-- calcium, magnesium, iron, manganese, those small inorganic ions as well as small molecule metabolites that are involved in central metabolism.

Let's now look at the macromolecules and their sort of proportions relative to each other. The smallest sliver of the lipids, which we'll talk about today. Then you have the nucleic acids that are critical for information storage. You have proteins, which make the largest piece of the pie. And carbohydrates, which are is the 25%.

So you can see how important carbohydrates are because of their proportion being relatively large. The lipid proportion, though, is small but absolutely critical, harking back to the membrane bilayer. Because if we didn't have the membrane bilayer, once again, we wouldn't have life in the same way that we have it now. So that gives you a sense of the relative proportions of things.

And frankly, when I discuss the macromolecules, I really like to start with lipids because of the membrane bilayer, but because their structures are comparatively simple relative to amino

acids and nucleic acids. So we can get a few of the basics of the chemical structures down and how we render them on paper so that we can do that with lipids, which are a little simpler.

Now life, to a chemist, they have to sort of worry about this entire mess of the periodic table. But the good news for you is for biological systems, we deal with very focused components of the periodic table. So those biological macromolecules are made up largely of only six elements-- hydrogen, carbon, nitrogen, and oxygen, phosphorus, and sulfur.

So that makes the amount of stuff you need to know about basic covalent structures way more simple than it is for the average chemist who has to worry about everything down here in the nether regions and-- whoops, what are you doing? And the things that are radioactive, all kinds of other things. You don't have to worry about any of that. So the covalent bonding we will talk about is amongst those six different elements. And they make up 98% of the cellular mass.

And then the other components that are important in cells are some metal ions-- the alkali and [? alkalia ?] elements. So sodium, magnesium, potassium, calcium-- those are all quite important in life. And then these transition metal ions that are really important in enzyme catalysis, for example. But we will not cover very much of that. But those are what are known as trace elements that are very-- transition metal elements that are very important for biochemistry.

And then last of all, there are some rogue ones that there's even smaller amounts in physiologic systems. These are things like chromium, molybdenum, and tungsten, selenium, and iodine. And of those, certain of these elements only are found in totally bizarre organisms. So for example, you and I don't have much molybdenum and tungsten, I don't think, unless it slipped in there by accident. But you and I definitely need selenium and iodine as trace elements. Does anyone know where iodine comes and figures most prominently? Yeah?

AUDIENCE: Thyroid.

PROFESSOR: Thyroid, absolutely. So the thyroid hormone is a small organic molecule with several iodines in it. And we need-- absolutely need-- iodine in our diet in order to build the thyroxine hormone that deals with a lot of aspects of metabolism. So we don't need a lot. And if we get too much, it's bad for you. But we definitely need traces of these elements.

Now I will spend a very small amount of time just laying down the basics of organic chemistry

bonding. Now who have you either taken the chemistry GIR or had high school chemistry quite recently? Is that pretty much all of you? And now if you didn't put your hand up, don't worry. We're here to bring you up to speed if you need it. Frankly, if you just know what's on the next two or three slides, you're in great shape. All the information that you need has been condensed . But if it's a little bit out of nowhere, you could come see me in office hours and I can just run through things for you and we can just get you up to speed. There is no need for pre-knowledge, I just need an idea of how much pre-knowledge you have.

So when we talk about covalent bonding and start to think about the elements that are critical for life, it's important to consider the electronic structures of these elements and why they happen to be the chosen elements, OK? The most important thing about hydrogen, carbon, nitrogen, oxygen, phosphorus, and sulfur is they love to make covalent bonds. A lot of metal ions form salts, you know-- sodium chloride or many other different salts. But covalent bonds are the main structure of all macromolecules. Strong bonds between elements, such as these six in particular-- these six-- where they share electrons in covalent bonds rather than form ionic interactions where somebody gives an electron to someone else and you have a plus-minus type interaction.

So these shared bonds are important for life. So it's good to understand why hydrogen, carbon, nitrogen, and oxygen, and then phosphorous and sulfur are so important.

In order to understand the covalent bonding of these elements, it's useful to know the electronic configuration, but you could live without that. The most important thing is that covalent bonds, such as the one between carbon and hydrogen here, reflect a shared pair of electrons-- one from the hydrogen, one from the carbon-- to make a stable covalent bond. Because of its electronic configuration, carbon is neutral when it has four covalent bonds.

Nitrogen is neutral when it has three covalent bonds. But there's an extra lone pair of electrons that are not forming bonds in neutral nitrogen. And oxygen is neutral when it has two covalent bonds. These could be with hydrogen, they could be with carbon, they could be with several of the other elements.

For carbon, we don't deal with charged states of carbon because they're pretty high energy. They may be high energy intermediates in an enzyme catalyzed reaction, but they're not sitting there as high energy intermediates in your macromolecules.

The key thing you want to notice is for all of these elements, the valence shell is complete with

eight electrons. But these lone pairs-- and I-- or bunny ears, as people like to call them-- really feature very prominently in biochemistry and biology because they are places for hydrogen bonding interactions. So we run a lot on electrostatic hydrogen bonding and hydrophobic interactions. If we know where the lone pair electrons are, we know one part of a hydrogen bonding interaction.

It turns out that in biology, we're mostly at pH 7 or in that range except for a few sub cellular compartments. But at pH 8, nitrogen lone pair of electrons will pick up a proton to become a positively charged nitrogen. And you'll mostly see that as a positively charged. So the side chain of lysine, which has an NH 3, an NH 2 at the very end of a carbon chain, is most commonly protonated and positively charged. So it could be involved in an interaction. So we can consider both the neutral and the positively charged state of nitrogen.

For oxygen, that oxygen lone pair can pick up a proton to form the hydronium ion. So that's a positively charged OH group. So it would have an extra proton, using up a lone pair and three hydrogens, or it could give up a proton to form the hydroxide ion. And those are the states of oxygen that are most common. So in that, we've kind of dispatched those first four of the six elements.

Phosphorus and sulfur are a little tricky, but there is some good news. Sulfur copies oxygen, so you don't really have to worry too much about sulfur. You'll just consider it to really be sort of an older sibling of oxygen where all the chemistry is very, very similar. Sulfur, or the negatively charged sulfur anion, are both important.

Phosphorus is different. Phosphorus does not tend to show up in the version that copies nitrogen. It is capable of adopting higher oxidation states. And all of the phosphorus you meet in biochemistry for the most part-- there's a few odd things in weird organisms-- is going to be in the form of an oxidized form of phosphorus, which generally has one, two, three, four, five bonds to phosphorus. It can take on a higher oxidation state. And you will see phosphorus.

Phosphorus in the phosphate form is absolutely essential to life because it's the place where we store a ton of reactivity for the reactions of nucleotides, adenosine triphosphate, adenosine diphosphate, the phosphodiester backbone in nucleic acids, phosphorylation of amino acids to form phosphoproteins. It's always in this state with all the extra oxygens and that configuration of bonds, OK? If you know this, you've got a lot of the covalent bonds under control.

So any questions about this? Is everyone all right? I know it might be-- it's probably a refresher for most of you.

The next thing I just briefly want to mention is the most typical functional groups that occur in biological molecules. And you may, say, well, what does it mean, functional group? Usually it's a place where the action happens. If you have a large molecule that's a bunch of carbon-carbon and carbon-hydrogen covalent bonds, there's not a lot going on unless you can really rip those bonds apart, but they're high energy. But functional groups are oftentimes where chemistry happens or biochemistry happens.

So there's the OH hydroxyl. We, as chemists and biochemists, will tend to use an R where we mean something else. So we don't write out a whole structure, we would just put R OH equals-- I'm going to just say anything. So for example, if R was CH 3, CH 2, you would have ethanol. But I'm keeping it more generic.

The next functional group that is important is the carboxylate group, or the carboxyl group. Looks like this. Now when we look at these molecules, you always want to sort of think where the lone pair electrons are. There's two on oxygen, two on oxygen, two on oxygen. So that actually shows you where the rest of the electrons are. This is the carboxyl group.

But in nature, in physiologic systems, this shows up most commonly in its anionic form. That's important because when we start to think of interactions between enzymes and their substrates, or the folding of proteins, we're thinking of something with a negative charge, not a neutral. So this group loses a proton to form the carboxylate group. And if you want to know where the lone pairs are now, that's what they look like. So those are two of the key ones.

Let's now go to nitrogen. That is the neutral amine. But as I just mentioned to you, that will very commonly pick up a proton and be in the positively charged state.

Now when I show you both of those guys in the positively charged state, what you could immediately tell me is that if I have an amino acid with one of these groups and a nearby amino acid with one of these groups, they could form an electrostatic interaction between themselves-- plus and minus complementing each other. So if you know the charge states, you're much better off because you can tell where non-covalent types of ionic or electrostatic interactions occur. So these are very important.

Then there's the phosphate group-- it's often ionized-- and the sulfhydryl group. So

phosphate-- the sulfhydryl group is also called the thiol group. And I'm sure I've spelt that wrong because hydryl-- they look like that. And the most common state of the sulfhydryl-- well, not the most common-- can also appear as the anionic structure. So that's the basic functional groups.

Now there are two more functional group assemblies that you will see a lot in physiologic systems that are basically composites of some of these structures. Because when we have single building blocks, we need to join them to each other through different types of chemistries. So I want to show you the types of chemistry that you get by forming a composite of hydroxyl and a carboxyl group and a composite of a carboxyl group and an amide. Because the polymer that's the protein polymer has building blocks that have a means and carboxyls, but they're all put together into what polymeric structure where those groups have been joined in a condensation polymer.

So let me just show you what those look like. And then we'll be done with the functional groups. So there are-- the first one-- because I've drawn them in this order, OK-- is the amide. And the other one is the ester. When you do these two reactions, if you do them in the lab, they're called condensation reactions because as you form that bond, you kick out a molecule of water.

These are really important new functional groups to you because your proteins are held together by amide groups. In fact, they're so important in proteins, we often call them peptide groups. You'll see more about that on Monday.

And the esters are really important. For example, in derivatives of glycerol that make fatty acids or phospholipids, you'll see esters occurring again and again.

The other composite group that you can also see is with the phosphate plus an alcohol. And what that group looks like is as follows. And you're going to see this sort of endlessly in nucleic acids. Let's keep the charges all even here. And this is what's known as the phosphate ester. OK, and that is yet another condensation where you kick out water.

All right, so let's just run back to this image. And we can sum it all up. Those are all the groups that I just described to you. And if you want, you can go back and put lone pairs of electrons on everything. And then the composite groups that I want to mention to you in particular are the amide and the ester. And they're very important in physiologic systems. They are the bond that holds together the biopolymer in many cases. Not shown on this picture is the phosphate

ester-- I've added that this year because it's kind of important-- is a similar condensation reaction between phosphorus and an alcohol, and that in particular is the bond you'll see that holds together nucleic acids.

And now one sort of thing that we won't go into a lot of detail-- I want you to notice that this nitrogen here has a lone pair of electrons. It picks up a proton very readily. The amide nitrogen is not so willing to pick up a proton because it messes up the rest of its chemistry. So that nitrogen in an amide tends to be observed as a neutral. However, that hydrogen can be involved in hydrogen bonds. OK, any questions about that before we move on to non-covalent bonds? Is everything clear?

Now I try to put everything in one place so you have it in front of you. What I've put on those two slides is what you need to know about organic covalent bonding. It doesn't go beyond it. I will say there's a tiny bit of memorization, but once you commit that stuff to memory, you're in a good place with respect to understanding how the molecules of life are put together. OK.

Now what is more important to me once we've put those structures in place is non-covalent bonding. Because to me, non-covalent bonding is synonymous with dynamics-- forces that can be readily broken and reassembled, broken and reassembled. The energy, the strength of a typical bond between two carbons or a carbon and a hydrogen is on the order of 90 to 100 kilocalories per mole. It takes a lot to break those bonds. We can't break them at will to go and do some biological activity.

But the range of energies of the non-covalent bonds are far more modest. They range from-- so this is covalent. But the non-covalent range from 1, maybe to about 10 kilocalories per mole. So when you think about those forces, they're readily broken and made, broken and made. And what's so amazing about protein and nucleic acid structure is that you can gradually break a bond while you're making another non-covalent bond so you can have the dynamics of the structure that define a lot of its functional properties.

Because structures are dynamic, an enzyme that's a composite of a lot of non-covalent interaction combined a substrate can gradually form a set of covalent bonds with that substrate but then can start changing the shape of that structure and that shape in order to go through a catalytic cycle to do chemistry and then to liberate products. That is all driven by changes in non-covalent bonding. Subtle changes that occur without big energy barriers that would be necessary to break the covalent bonds.

So shown at the top here, you see the average bond energy of covalent bonds. This small number is something, for example, between two chlorines. That's a pretty weak bond. But of course, we don't have a lot of them running around. So really, carbon-hydrogen, carbon-carbon, they're at the higher end-- about 100 kilocalories, 80 kilocalories per mole.

The other important interactions, though, that make up the non-covalent interactions are as follows. So the first important one is the ionic bond. It is also called a salt bridge or an electrostatic interaction. Why we give three names for this probably comes from which type of chemist decided to define them. They are all the same things. They are basically interactions between a positively charged entity, a protonated amine; and a negatively charged entity, a deprotonated carboxylate.

Those are about the strongest of the non-covalent bonds, but it's very variable because it depends a lot on their environment. If those two entities are in a hydrophobic environment, they're going to charge right for each other to form a strong electrostatic interaction. But if those are out in water, each of those groups could be solvated by water and they'd have to give up solvation in order to form a good electrostatic interaction. When we talk about protein folding, we'll go into that in a little bit more detail.

So the reason why this says very variable is not to drive you crazy. It's just they're very variable. But they will still range, I would say, from 2 to 10 kilocalories. Come on. So those are important-- easy to pick out. The strongest of the set. If Dr. Ray gives you a problem set and starts asking you to pick out non-covalent interactions, that's the one you take care of straight away because it is the most obvious.

The next most important, though, is the hydrogen bond. Now hydrogen bonds have been known to mystify people for years because people are like, how do I pick these things out, how do I pick these things out? I'm going to give you a foolproof way of picking out hydrogen bonds so you will never be at a loss for hydrogen bonds, OK.

Well, how do we recognize them? They are between hydrogens that are on electronegative elements such as oxygen-- of course, there's other things attached here-- or on nitrogen, or on sulfur. So all of those three functional groups can serve as hydrogen bond donors. They can give a proton in a hydrogen bond and share that proton between a hydrogen bond acceptor, OK. So these are all going to be known as donors. So you can recognize them.

This-- carbon is not a hydrogen bond donor. Carbon's got his hydrogen and he's not giving it away to anybody for love or money. Its holding on tight. So this is not a hydrogen bond donor. OK?

Now what are the hydrogen bond acceptors are places where that hydrogen would want to sit-- yes.

AUDIENCE: There's the two lines next to it--

PROFESSOR: Actually, they just read-- they could be double or they could be single, but I was just putting them so that you see that the nitrogen has one, two, three bonds to it. OK, yeah. It could alternatively also be the form of nitrogen-- just to confuse you-- that has an extra proton that could be the protonated version because that can still be a hydrogen bond donor. OK.

Now what are the hydrogen bond acceptors? They are any place where you have a lone pair. So let's just think of a carbonyl group-- two lone pairs. A hydroxyl group-- two lone pairs. A nitrogen that is not protonated-- one lone pair. Those are the hydrogen bond acceptors. So as long as you know your structures in the functional groups and you know where the lone pairs are, you can figure out where there could be a hydrogen bond. So all of these types are acceptors. OK.

So in protein biochemistry, for example, those kinds of hydrogen bonding is very, very important to form the three-dimensional structures of proteins. And the reason why is because in a protein, proteins are made up of amide bonds where this Hn can be a donor, this O can be an acceptor, and you can get networks of hydrogen bonding interactions to establish structures of proteins. When a small molecule binds to a protein, it may look to fit in a place where it can maximize electrostatic interactions and the hydrogen bonding interactions.

So we'll ask you to start to be able to pick out hydrogen bonding. So here you saw the electrostatic interaction. Here is a typical hydrogen bonding interaction between a hydroxyl and a carbonyl group. I couldn't spot that very readily unless I remembered that there were lone pairs of electrons there, OK.

The other two ty-- any questions about that? Any questions about hydrogen bonding? Are you comfortable with thinking you could derive your way to figuring out where they are? You'll see them used a lot, so they'll become more and more familiar to you as you move forward. OK, good.

The last two types of interactions are the hydrophobic interactions and van der Waals forces. I never get the spelling right, but I'll get the concepts over you.

Now hydrophobic interactions are incredibly important. So when you think of folding a protein driven solely by electrostatic interactions and hydrogen bonding, you have a bit of a problem because all of those groups are hydrogen bonded to water. So you'd have to get rid of the water before they could make interactions with each other. Does that makes sense? Because we are in water. We're folding in water.

Hydrophobic interactions are really great because they want to form in water. If you're making, you know, a batch of salad dressing, oil and vinegar, and you shake it up, what happens? It separates. The oil goes to the top, the vinegar goes to the bottom. Why? Because of hydrophobic interactions in the oil phase.

So if you have a large protein that has a bunch of hydrophobic groups, they will want to collapse out of the water to interact with each other. And then hydrogen bonding and electrostatic will fall into place. So hydrophobic interactions are a very important and vital force in nature in the non-covalent bonding. And those are literally interactions amongst molecules that have a lot of CH and CC bonds.

The final force that's shown up there is the van der Waals force. And we don't worry too much about that, but it is simply the interaction between very weakly polarized carbon-hydrogen or other types of bonds where there's a little bit of a dipole between the bond and they form little dipolar interactions. But mostly, I think you really want to focus on the electrostatic, the hydrogen bond, and the hydrophobic. These are more minor and it's a little bit of a subtlety.

So let's focus on those three. All right, so with that said, the key thing for you-- what do you need to be able to do is understand them and recognize them in complex systems.

Lastly I'm just going to leave this. It's going to stay in your notes. We in biochemistry tend to use line angle drawings. It's kind of complicated to draw these sort of great big things with all the hydrogens and oxygen and stuff spelled out, so we use the line angled drawing. There's some shown here for different molecules. And the rules are laid out so that you can go and just figure out, do a bit of practicing, and just figure out the line angle drawing and what it means.

Basically, every line represents a bond, every vertex represents a carbon atom. But what you

do show on the drawings are the non-carbon atoms. So for example, oxygen, or nitrogen. And when you show, you imply the hydrogens that are bonded to carbon but you have to show the hydrogens that are on nitrogen or oxygen, for example, and you have to figure out what your charged state might be. So I'm going to leave you with that. All right. OK.

So what we've learned so far is these basic forces in biology are critical for the assembly of the building blocks of biological macromolecules. What I want to talk to you about now-- and we'll probably, because I've spent a little bit of time on that, spill over a little more to next week-- but I'm going to talk to you about the first class of macromolecules, which are the lipids.

So what makes something a lipid? These are the most sort of complicated mixture of biological molecules. And formally, they're not really macromolecules. They're small molecules.

But what's common to all of them is that they are very rich in carbon-carbon and carbon-hydrogen bonds because all of these-- the line angle drawings of all of these would suggest to you that the dominant feature of all these molecules is a bunch of CC and CH ions, which makes the molecules quite hydrophobic. There are no functional groups there. And they behave very differently. For example, they would have a tough time dissolving in water in some cases. And so this complicated looking set of molecules can be distilled out as being very rich in carbon-hydrogen and carbon-carbon bonds. And we call those collectively lipids.

And they have a lot of different functions. So for example, triglycerides, such as shown here, with three ester bonds are storage for energy-- things like estradiol, things like steroids. They have this 6-6-6-5 arrangement of rings. All your steroid hormones kind of look like that. A lot of CH bonds. There are some vitamins. So for example, retinol is a vitamin. It's also a lipid. And then there are the phospholipids shown down here.

I just briefly want to mention a little bit about retinal and retinol, which are crucial. Retinol is a critical vitamin. It comes actually from carotene, which is a molecule that you find in a lot of orange and yellow fruits, such as carrots.

But the oxidized product of retinol is this lipid called retinal, which is central to the process of vision. So retinal binds to proteins that sit in the membrane. When light shines on them, the shape of the retinal changes. It goes from a particular configuration of the double bond to a different one. The shape just changes, and that sends a signal to your brain. So lipids are important, absolutely essential, in vision and sight because they are involved in the signaling process because their shapes change and send signals.

Other types of lipids-- so these things-- and we call them fatty acids mostly because they are greasy long-chained acids with a long hydrophobic tail and a hydrophilic end group here. These molecules are also what are known as amphipathic because they have a sort of split personality. They have a hydrophobic moiety and a hydrophilic moiety. Whenever you see amphi at the beginning of a word, it means in both. So both hydrophilic and lipophilic. So these are important.

And these are very important components. You probably heard a lot of press about some of the fatty acids and how bad trans fats are for you and how you should be careful to make sure your diet is rich in cis fats rather than trans fats because the trans fats are contributors to coronary heart disease. So you may wonder, what's the relationship between heart disease and these two types of lipophilic components which are in the body? So let me describe to you that relationship. Remember that cis fats are rich in things like the nut oils and fruit oils, such as olive oil.

So coronary heart disease is associated with trans fats. What's the linkage, what's the biology in that? So the story is related to cholesterol. Cholesterol is a critical component in our membranes. The trouble is we have to be able to move cholesterol around. But it's so hydrophobic it doesn't dissolve in water, OK? So in the body, your cholesterol is moved around in the form of lipoproteins that bind to the cholesterol and take it to the different organs where it is needed, all right?

And so the lipoproteins can either be low density and associate with cholesterol, or they can be high density, and those also associate with cholesterol. The high density lipoproteins are kind of large. In fact, they're fairly agile. They don't stick to arteries and vessels, and they can be excreted in the liver or move around the bloodstream without any problem.

It's the low density ones that are problems because they're low density and they kind of stick to the walls of your arteries and start making buildups and then plaques, which contribute to heart disease. So the low density ones have cholesterol, but they're very small, sticky, and it's a physical interaction with your blood vessels and they start to clog your arteries.

What's the relationship to saturated and trans fats? It's that they increase the low density lipoprotein in preference to the high density. So if you have a lot of trans fats, you make a lot of low density lipoproteins, it's trying to carry cholesterol around, but it gets stuck to your blood

vessels and you start to clog your blood vessels. That contributes to heart disease.

So these lipophilic molecules are important. They are places to store energy. They are critical to hormones and signaling, for example. But there are some complications with disease because certain types of fatty acids contribute to heart disease. Yeah.

AUDIENCE: Is it a lower density if it doesn't have a bend in it?

PROFESSOR: No, no. the density is of the entire physical particle. It's a nanoparticle that would show a different density respective to how it floats in water. So the density is really the physical metric of the entire particle as opposed to just the molecule. It might be different because of the way it compacts, but the important thing about the trans fats is that they really contribute to making the protein that forms the low density particles. OK, all right.

So I'm just going to introduce these-- not quickly, but I'll show you some cool images at the beginning of the next class. This is the last group of lipidic molecules, and they are actually-- whoops-- esters and phosphoesters of fatty acids with glycerol. This is a small molecule that forms esters through its oxygen to these long chains and also to phosphate. And these contribute to really important functions in the body.

They are also amphipathic because they have a hydrophobic component and a hydrophilic component. And we often draw them in a shorthand form like this to represent this head group and these tails. And I want to just leave you with this wonderful image of the sorts of supramolecular structures that these kinds of phospholipids can form.

So supramolecular is a very important term in biology as it is in engineering-- supramolecular. It means it's a structure that's above the molecular level. It's an aggregation of different molecules to make a super molecule with different properties from the individual components.

Phospholipids self-assemble-- and that's another important term-- into supramolecular structures that are very, very important in living systems. Some of them just are useful in other sorts of engineering approaches, such as liposomes and micelles, but the most important supramolecular structure of a phospholipid is the lipid bilayer that surrounds your cells. And what happens is you simply put those molecules-- the phospholipids in water and they will self-assemble on their own into these supramolecular structures.

Whether they form micelles or liposomes or bilayers is dependent very much on the tails of the lipids-- what sorts of shapes and structures you get. But in physiology-- in human physiology--

the phospholipids that we have want to form these bilayer structures that have incredibly important properties. Most importantly that they are semi-permeable and they can wrap, form the boundary to certain cells.

So I will continue with the final discussion of this on Monday before we move forward to the amino acids, peptides, and proteins. And I just quickly want to move you to ask you for Monday to try to catch a read of the section 3.2 in the text if you have a chance. It'll give you a nice preview.