PROFESSOR: Today, we're going to talk about a very exciting subject regarding molecules. And this subject has to do with metals in biology. Metals in biology, by the way, is actually the name of one of the Gordon research conferences. So if you get excited about this topic, you can go to the Gordon research conference web page and apply to attend the conference next summer and learn about the latest developments in metals in biology.

One of the things I want to impart to you today has to do with where we usually find metals inside of biomolecules. So that leads me to talk a little bit about nature's ligands. In biological chemistry, we find that molecules sometimes are quite a bit larger than we're used to looking at in synthetic small-molecule chemistry.

So I'm going to talk about nature's ligands today at sort of two levels of size. Going to talk first about the porphyrin ligand. And then next, we're going to talk about proteins.

OK. First this porphyrin ligand is one of the most pervasive small-molecule hosts for metal ions within biomolecules. And it's really quite a remarkable ligand type. And I'd like you to appreciate it at the level of being able to draw the structure of it and to see just how this system can provide a host for metal atoms.

It is a system that has four nitrogens that it can donate to a metal center. So it's a tetradentate ligand. We talked about bidentate ligands earlier in the semester. This is a tetradentate ligand that nature uses to hold metal ions very tightly where it wants them in a biomolecule.

And first you draw the four nitrogens at the corners of a square. And now we're

drawing in the carbon parts of the molecule. You can draw four vertical lines like that and four horizontal lines like this. And then what we're going to do is, at each of the four corners of this square-shaped molecule, we're going to go ahead and complete five-membered rings. Like that.

And then finally, we have four more carbons to add to this structure. And those four carbons are at the top, bottom, and left, and right, like this. OK.

So you can see that the porphyrin ligand is a large ring-shaped macrocycle. And where can a metal ion go? It can go right in the center.

If you are going to figure oxidation states that involved a porphyrin molecule, then you would need to know the charge like we know that one chloride is in a metal complex. It carries a one minus charge. And you need to know how many charges the porphyrin ligand would carry if a metal were in there, so that you could figure the oxidation state and the d-electron count for the metal that would be inserted into the porphyrin.

And to do that, we first recognize that if you isolate a porphyrin without the metal in there, then two of the four nitrogens have hydrogens attached. OK? And also this is a system-- you'll remember the graphite structure that we looked at last time that had all these p orbitals perpendicular to the plane of the molecule. And similarly, this is an unsaturated molecule that has lots of pi bonding going on with the carbon p orbitals that are perpendicular to the plane of the blackboard here. So it can be a quite flat molecule, but as you'll see it can ruffle as well when it carries out its biological function.

And so we'll go ahead and draw in the double bonds. And this is the part where people sometimes get messed up because one thing we don't want to do is draw five bonds to a carbon atom. OK? And if you see a structure that's drawn that way, you know that someone has made a mistake because they violated the octet rule. All right?

So let's draw in, starting here at the upper left, we'll put in a double bond here, and

here, and here. And then this is where it gets interesting because I could put a double bond here now or here because this carbon's going to need a double bond. I'm going to choose to put it here, and then I'm going to use symmetry across the way to put one there.

And having done that, I can now go here, here, here, here, and-- so I didn't use symmetry across the way. This is much easier to do and it's small. OK.

So now you can see that these two nitrogens here would have lone pairs that point into the center of the porphyrin ligand and same across the way by symmetry there. And then when we remove these two hydrogens as H plus and insert a metal ion, you'll see that the porphyrin is actually behaving as a dianion. When a metal ion and-- most typically, we're going to see that the metal that appears at the center of a porphyrin ligand is an iron center.

And so the nitrogens provide four lone pairs in the plane of the molecule that are directed at the metal center. So that's four out of the six positions for an octahedron all in the same plane. And because of the rigid delocalized structure of the porphyrin ligand, what we find is that a metal center that is in a porphyrin is very difficult to take out of the porphyrin because these lone pairs are forced at all times to converge on the same point which is the metal ion.

OK. You know that I enjoy giving lectures using shock. But sometimes when the molecules are really big, it's easier to use a computer to portray them quickly. And that's what we're going to do today, assuming my computer participates and cooperates with me today.

And what I really want to do is to go through and show you a tour of six really important metalloproteins. And all of these, you'll see the heme plays an important role, the iron in a porphyrin. This unit together, when an iron is located inside of a porphyrin, that is referred to as heme. So you can have other metals in there, and then it's not called a heme anymore, but that would be very similar structurally.

OK. So I'm going to take advantage of some really nice summaries that have been

put together on the protein data bank website. So since the first crystal structure was determined for a protein, the structural information has been collected and put together in one site so that researchers all over the world can take advantage of this information to advance science and medicine. And since 2000, the protein data bank has been collecting information about certain biomolecules and putting out one new little short story or vignette each month. So you have their Molecule of the Month portion of the protein data bank website. So each month, you can go and look and see which new molecule has been added and learn more about it.

And I want to start out here with myoglobin. OK. And I'm going to give you this website information online associated with today's notes. So you're going to see that myoglobin was the first protein structure.

There are many different ways to represent protein molecules. Protein chains are composed of linear polimers of the naturally occurring amino acids with polypeptide chains. And they can sometimes be very, very large in length, and then they fold up and make three-dimensional shapes. And these are big ligands for metal ions. And what you're going to see is that in many of the most important proteins, the place where the reaction's actually happened is that the metal center that's embedded somewhere in the protein chain as it has folded up around it to modulate function.

OK. So this is a pretty small protein-- myoglobin is. It's an oxygen storage protein. So as you know, diatomic molecules like dioxygen are important for life on Earth, and O2 in particular-- not only do we have hemoglobin that we'll talk about next, but there are also oxygen storage molecules like this myoglobin molecule. And this was the first structure that was determined, and that happened in 1960.

So we've been getting information at the molecular level about how biomolecules work really since 1960 using x-ray diffraction techniques. So first, a worker in this area has to obtain a large quantity of the protein in question, get it purified, and then find conditions under which it will grow single crystals so that you can impinge upon it with an x-ray beam and then looked at the intensities of the diffracted x-ray beams and then work back to solve the crystal structure and find out what arrangement of

atoms in 3D space could have given rise to that pattern of diffraction intensities. And that was first done for a protein in 1960.

You might find it interesting that this protein was isolated from sperm whales. OK? Sperm whale muscles. And in order to get a protein pure, as I said, you need a lot of it. And the muscles of sperm whales are very large indeed, and so these workers were able to collect large amounts of this red protein myoglobin from sperm whale muscles in order to finally get enough in pure form to crystallize and solve the crystal structure.

And since this is involved in oxygen storage and you know that whales and other marine mammals can dive below the ocean surface for long periods of time, they need to store lots of oxygen so that they can use their muscles during the length of a long dive. And this protein is very abundant in muscles. It gives meat its red color and so forth. The color is coming from the heme units that are embedded in the myoglobin. And I'll step through a little bit of this, but I would like to actually show you some more of the features of this.

You'll see as you go through this website, there are both static and interactive ways to look at metalloproteins. And sometimes the polypeptide chain composed of the amino acids is just represented here as sort of a tube, so you can see the polymer has wrapped up. And here they've chosen to represent the heme unit as spheres to highlight it and accentuate it.

And in this first structure of myoglobin, there was not an O2 molecule bound to the heme unit. Instead, there was a water molecule bound to the iron center of the heme unit. And then down here, they rotate the structure perpendicular so you can appreciate the square nature of the heme unit together with when viewed edge on, its flat nature. So that's the structure here. And you can see how this myoglobin molecule, this big protein polymer, has folded up like a clam to grasp this heme unit that inside of it will bind O2 and store it when oxygen comes to it.

And so later structures of myoglobin have been carried out that do show you the position of the O2 molecule. And in these two representations that we are given

here, we first see, once again, the heme unit as spheres and the protein side chain just as tubes. And then this representation in the bottom, all the protein side chain atoms themselves are represented as spheres. And you can see that when that's the case, you can tell that the atoms of the protein ligand really fill up space very well. And what they're showing you with this circle here is the location beneath that side chain of the dioxygen molecule inside there.

And so they're trying to give you the idea that when O2 is on the heme unit inside the myoglobin, the myoglobin protein matrix actually covers that up. And so in order for the O2 molecule to get into the heme and also to exit from the metalloprotein, this thing has to be flexible enough to open up and allow the dioxygen molecule to exit from its chamber inside the metalloprotein.

OK. Now next, I would like to go over to the site where we're actually able to look at things interactively. And you need to be able to enter the code for the protein in question.

And so this is a structure of the myoglobin molecule that was obtained at molecular or atomic resolution. So one of the parameters that you'll see when people discuss protein structures is the resolution to which the data have permitted the structure to be determined. And the best quality structures, the ones where we know most precisely where the atoms are, are the ones that have very low resolution numbers. In other words, this one, if you looked at the introductory web page there so that the resolution was at the level of one angstrom.

OK? So we're talking on the order of carbon-carbon bond distances so that you can actually see all the individual atoms quite clearly. And this has to do with the quality of the crystal and how large was the angle at which you could collect spots from the diffracted x-rays as they came off of the crystal.

And so this is nice. This one requires Java. That's why I was not able to use Athena today. But actually, I come in here, and I see that the Athena terminal is down anyway, so this was a good choice as it turns out. And this is nice because you can actually zoom on these structures.

One thing you notice is that this was crystallized with sulfate present in the medium, so there was some buffer present. And it had sulfate, and the sulfates crystallized together with the protein chains. And as we look at representations of proteins, you'll appreciate that this representation shows the polypeptide backbone as these ribbons. And that emphasizes that when proteins fold and go into a three-dimensional shape that they need for their function, they can usually do so either by making coils like this that look like springs-- these are called helices. Or they can just form random coils as you can see out here.

And oftentimes you have these helices that are like long springy tubes that are then connected at their termini by coils of the protein side chain. And then, of course, here embedded within this structure is our heme unit. And one thing if you look at this one pretty closely, you'll be able to see that this heme is a little more interesting, a little more complicated, than the one that I drew on the board here because the one I drew on the board was assumed to have just hydrogens at each of these carbon positions at the periphery of the molecule.

But when we look at the one that's actually been found in myoglobin at atomic resolutions-- so you see this one is actually with the O2 molecule present. For some reason, no bond drawn there, but that's OK. We've talked a lot about molecular representations, and we understand what's going on here. It's that people have decided that we would represent the atoms over here without any detail at all just showing them as ribbons.

And then here we're going to look at the atom positions. And you can see the five-membered ring here, here, here, and here at each nitrogen corner of the heme unit. There's the iron center.

And then, notice that the substituents, instead of being just hydrogen or organic, there's a carbon here. This looks like a methyl group perhaps. And this one looks like an ethyl group or maybe a vinyl group here if this is one of the etioporphyrin ligand types.

And then coming out here, we have CH2, CH2. We have something that looks like it might be a ketone residue since we have a single oxygen on a carbon there, or alternatively, it could be some other oxygenated residue. But over here, you see that there's a link to this five-membered ring of the heme. You have a couple of methylenes and then a carboxylate residue.

And so when you investigate these structures, these metal complexes that are embedded in the protein usually are held in position, both by the way the protein folds up around the heme unit, but also because, in this case, the heme unit is connected to residues like this carboxylic acid residue that can hydrogen bond to specific residues on the protein side chain. So if we were to look at the atoms involved in the side chain right over here that's next to this carboxylate residue, this probably has some hydrogen bond acceptor that is interacting with this carboxylate residue-- and same over here-- to hold this heme unit in its desired position or in its required position for function. So please keep that in mind as you go ahead and look at different structures in the database.

And now let's go to the 2003 description of hemoglobin. This is rather nice. OK.

So myoglobin was a pretty small protein having a single heme unit. And hemoglobin is much more interesting. It actually has four big pieces that come together, and it has four heme units in it.

OK. And as you go through this website, you'll find out about why blood is red versus blue. It's actually red in the oxygenated form and blue in the deoxygenated form. And there are many crystal structures of different hemoglobins and mutants of hemoglobins in the database and both with and without the oxygen molecules.

There's a discussion here of artificial blood. And as you'll see what the premise is here for the design of artificial blood motivated by a desire to have blood available for transfusions and so forth that would not be contaminated, would be just synthetic-- would be just pure hemoglobin in fact. But what happens is that without the protective casing of the red blood cell, the four parts of the hemoglobin molecule fall apart from each other, and they don't do their function properly anymore.

And we'll learn more about the function in a moment. So people have actually made mutants wherein you make covalent bonds between the four different subunits of the hemoglobin so that they can't fall apart. And that's one of the approaches to the synthesis of artificial blood.

And then this is a rather nice little video which comes from two different hemoglobin crystal structures. If you imagine different crystal structures, like crystal structure of hemoglobin when it has O2 bound verses when it does not have O2 bound, as snapshots of the molecule in motion, then you can generate a little movie like this one shown here from the experimental data on the crystal structure. And so the really remarkable thing here is that-- see when the O2 molecule is bound to the heme, then the protein itself, this large unit that is comprised of four parts, as one confirmation, one structure, and it changes quite a bit. You see how much it is moving around when the dioxygen molecule comes off of the heme. And that is related very much to its function.

In fact, it turns out that, in hemoglobin, when the deoxyhemoglobin arrives at a place in your body where there is a lot of oxygen, the first O2 molecule binding event is very difficult to achieve because it involves a big change in the structure of the entire protein molecule. But once that first O2 molecule has bound, the whole protein molecule has changed its structure such that the next three hemes take up their O2 molecules rapidly in rapid fire succession after the first one has done it.

So the heme goes into a place of high-oxygen concentration and it rapidly loads up with four O2's. And then it moves on. And then when it gets to a location that needs oxygen, the first one comes off, and then the next three fire off in rapid succession because of the change in the protein shape. And so hemoglobin is, therefore, very good at collecting four O2 molecules at a time and then delivering them to where they're needed.

And this is just a beautiful example of the way protein crystallography can teach us about mechanisms of biomolecules. OK. And then also you can learn about disease mechanisms in the data bank here because this is from a different crystal structure

where a mutation has occurred in the protein side chain of the hemoglobin.

So this is one hemoglobin molecule. And it turns out that when that mutation is present, unfortunately, it causes hemoglobin molecules to aggregate and stick together and clump together like that. And that phenomenon is associated with diseases like sickle cell anemia. OK?

So the structure of the protein is changed when one residue of the amino acid side chain is changed to a different amino acid. And then these things all aggregate together instead of forming nice disks as normal red blood cells do. They stick together and form these different shapes that are not good at functioning the way they're supposed to.

And then here is a close-up on where the action takes place in the hemoglobin molecule. And this, again, is from the two crystal structures that we were talking about-- the one that has the oxygen molecule bound to the iron of the hemoglobin and the one that does not. And one thing that you'll notice is that when the O2 molecules is absent, this iron in yellow represented here as this yellow sphere is sort of dipping down on one side of the hemoglobin-- the heme plane toward the nitrogen of this histidine. So this is part of the amino acid protein side chain. And a histidine residue has this Lewis space group here that is coordinated to the iron.

And so in that form, this is a five-coordinate metal center with five ligands of square pyramidal geometry. It's an octahedron missing one of those six ligands. And then when the O2 ligand comes in and binds and becomes the sixth ligand in the coordination sphere of the iron, the iron responds to that by moving up to the other side of the porphyrin plane, and it draws with it the histidine ligand.

So the iron moving up pulls the histidine up. And that structural change at the iron center is then propagated throughout the amino acid side chain to which this is connected and then, ultimately, throughout the entire protein to give you that huge conformational change that we saw when O2 is bound versus when it's not. So the coordination chemistry of the iron here is really controlling the peptide confirmation and the function of this protein.

OK. So these bio molecules actually accumulate quite a lot of the concepts that we've talked about all semester. And that phenomenon is going to continue as I take you through a tour of a couple more of these important molecules.

Now the first one was a small one that we looked at, myoglobin, and I'm going to continue that sort of progression by now talking about another small protein. This one may even remind you in its appearance of myoglobin. But instead of serving to store O2, like myoglobin, cytochrome c, which has a single heme unit in it here, serves as a shuttle for electrons. OK?

The pathway that electrons take in the whole process of respiration in organisms is really quite fascinating. We require reducing agents. We eat food. Those are reducing agents. And then we go ahead and burn that fuel using the oxygen molecule.

And that's where we get our energy. We don't burn the fuel literally by having us burst into flames, but we do it in a controlled manner, in a stepwise manner. And we take advantage of those steps to carry out the processes of life.

And so there are proteins like these small cytochrome c proteins that are developed expressly for the purpose of moving electrons from one place in the body to another. So it's like a little electron shuttle protein. And these are just two views of it.

And if you read this part of the website, you'll also learn that this one has remained virtually unchanged over eons. It's a very ancient protein. OK.

And this picture shows you cytochrome c protein and where it picks up its electrons and then where it goes to drop them off. So here's an enormous protein relative to cytochrome-- cytochrome c is the little teeny one here with just a single heme unit. OK?

Look at this thing. This thing is-- I don't know what this looks like, but it looks like a bizarre-shaped entity, shall we say. And this yellow stripe that goes across the page here is actually a membrane. So proteins are often classified as to whether they are

membrane proteins-- meaning that they don't move around. But they're embedded or fixed in a membrane with one part of their molecule on one side of the membrane and the other part of the molecule up on the other side of the membrane and then the part of the molecule that's actually located within the membrane, and then non-membrane proteins like cytochrome c that are actually mobile and can move about within a cell. And cytochrome c goes over to this large protein which has lots of different cofactors shown here in red which incidentally are hemes themselves.

And so this molecule-- the big protein here embedded in the matrix is called cytochrome bc1. And it is a protein involved in this process of respiration. It is producing electrons. And cytochrome c comes over here, and as you can see, it fits really well into this spot right here on cytochrome bc1.

And that's a feature of protein-protein interactions that they often contain residues on their surface that are hydrogen bonding residues, for example, that make their surfaces complimentary. And it means that when cytochrome c comes in into cytochrome bc1, it actually locks in in one particular way. And this complex between cytochrome c and cytochrome bc1 has been crystallized. And the crystal structure of it's in the database, and that's where we get this representation shown here. So you can actually go through-- if you're a crystallographer-- and look at all the different complimentary interactions that holds cytochrome c into place on cytochrome bc1 when it docks there.

And what I'm going to tell you in a moment is that as electrons are originating within cytochrome bc1 here, they have a pathway through which they move and they get up into this heme unit. And then when cytochrome c docs, the heme unit within it can get close enough to this heme unit that their wave functions can overlap, and the electron can tunnel right across into the cytochrome c which accepts it. And then it goes off, and it's looking for this protein next which has also been crystallized and characterized in the database. And we'll talk about it next. This is called cytochrome C oxidase because it oxidizes the reduced form of cytochrome c.

And let me just say that probably one thing we won't have on the final will be working the molecular orbital diagram of this molecule. As you can see, we've got up to a position here where the number of orbitals is kind of prohibitive to do that sort of thing. Now you can understand why the computational chemists have quite a big challenge as they try to understand at a molecular level all of the processes of life and, really, a long way from doing that actually.

When people attempt to do that these days, they're usually making some big approximations with the protein side chain because that's the electronically uninteresting part of the system. Where the metals are is where everything is happening. Let's go down here and see what else we can learn.

OK. Here's a close-up with a different representation of when cytochrome c molecule docs on to the cytochrome bc1 complex. And here we've got the polypeptide chain of cytochrome c represented as these pink tubes, and then as these yellow tubes down here, this little part of the cytochrome bc1 molecule that is reaching up to interact with cytochrome c. And here's the heme unit of cytochrome bc1 that is right at the surface of that protein so that it can overlap it's wave function with the heme unit of cytochrome c to permit an electron to transfer and reduce cytochrome c.

OK. And so now we'll go on to cytochrome c oxidase. OK.

So in reading about cytochrome c oxidase, you're going to learn more about oxygen. And this piece of today's story, together with the one that I'm going to go to next, which will be with respect to photosystem one and photosystem two, are sort of the two ends of the chain of respiration. Because with photosynthesis, that we'll talk about next, we use light energy to create O2. And most organisms on the planet have these cytochrome so that they can use O2. In fact, what they do is they take electrons that are derived from food and get energy by combining them with oxygen, reducing them-- reducing the oxygen molecule-- to water, and at the same time pushing protons across a membrane which stores energy that can be used for other processes like building up ATP.

And so, the cytochrome c oxidase is getting its electrons from cytochrome c and it's using those electrons to reduce the O2 molecule. And for that reason, cytochrome c oxidase should have somewhere in it a place for the dioxygen molecule to bind. Just like is the case for hemoglobin. We found out where oxygen binds in hemoglobin. And notice that as you go through they'll make an analogy here to charging of a battery or actually of a capacitor as you're reducing the O2 molecules with these electrons coming in from the cytochrome c shuttle, and making water and pushing protons across a membrane that is being likened to charging a battery or charging a capacitor.

And this is a membrane-bound protein just like the bc1 complexes. And here's a nice graphic that shows a number of the important cofactors. A cofactor is just something that's an integral part of a protein but isn't part of the amino acid backbone of the polypeptide chain. And usually it's something like a heme, but here not only do we have hemes, but here's a heme that is thought to be involved in the electron transport chain within the cytochrome C oxidase molecule. And over here is a heme that is thought to be important in binding the O2 molecule. And also this one has copper.

So these 3D transition elements are turning out to be pretty important in biology. The iron is frequently the site for the binding of a diatomic molecule, but look at this. This structure that's in the Cambridge database here, its PDB entry 1OCO, actually has a carbon monoxide ligand bonded to the iron in the active site where O2 is supposed to bind when this enzyme functions. So this is a poisoned form of the enzyme. CO comes in and binds and shuts this enzyme down, and that's what they were able to purify and crystallize and get the 3D structure of.

And then here you have a heme iron which interacts with the carbon end of carbon monoxide. And then positioned over here, and also ligated by residues from the protein side chain, is copper, referred to as copper b. So this is a copper ion. And that means that when a diatomic molecule goes in and binds to the heme at one end, it's other end is binding simultaneously to copper b. And that diatomic molecule is serving as a bridge between two metal ions-- the iron heme and the copper b up

here.

And then also up here is a copper a site, where you have a pair of coppers. And this site is referred to and thought to be the port of entry of the O2 molecule into cytochrome c oxidase. That O2 somehow comes in and may bind here first, but then go over here and electrons are coming in through this other heme unit into the one that binds the O2 and ends up reducing it to generate water. So that is a really pretty picture of how complicated the machinery of an enzyme can be to take advantage of all this lovely transition element chemistry and redox chemistry to carry out life function.

And also-- let's see-- OK, so what they're doing here is analyzing this. This cytochrome c oxidase is composed of a number of different protein chains that are all packed together into the overall complex, and they're coloring each of these residues a little differently here. And then when you get down to the bottom of this page, they're comparing a subunit of cytochrome c oxidase to an actual cytochrome c oxidase that is found in bacteria molecules. Bacteria organisms. So bacteria have their own cytochrome c oxidases and this looks like the central core of our cytochrome c oxidases.

And the idea is that mitochondria in cells may, at some point way, way back in evolution, have been the result of bacterial invaders into cells. And then these bacteria became integral parts of ourselves, and we added new proteins on and elaborated to change the function as we deemed necessary through evolution. But these ways of comparing structures of simpler or ancient proteins to ones that are more modern is an interesting way to learn about how life has evolved on this planet.

OK, and-- so cytochrome c oxidase is a pretty remarkable protein. And I want to see if I can get this thing up interactively because the structure is quite impressive. And I'm using this carbon monoxide substituted variant. When these structures have many thousands of atoms, sometimes these things take a little while to load. So hopefully this won't take too long.

The viewer that-- there are actually several viewers that you can choose from on this protein data bank web page, and they possess features that allow you to turn on or turn off different parts of the molecule. You can subtract away the cofactors, or subtract away some of the loops or the helices, and that allows you to explore the structure in quite some detail. Now, each of these are different protein residues, different residues of this enormous protein. So let's come down here, zoom in a little bit. OK, if I notice that-- there I can subtract away the coils that hold together the various loops, OK? Or you can take away, in fact, all of those things.

And notice the cofactors themselves are these heme units and they have some interesting and complicated side chains. But they're the same sort of heme units in general that we see in myoglobin or in cytochrome c. OK? Let's see . Actually-- there are orientations of this molecule that you can access that shows you how this thing fits nicely into a membrane. This is one of them. You see all these different helices that are aligned with one another.

This is the part of the cytochrome c oxidase that resides in the membrane. And all of these residues are lipophilic, so they interact with the non-polar interior of the membrane very well allowing this protein to just stay in as part of the membrane. And then these loops that extend on one side of the membrane or onto the other contain polar residues that would prefer to interact with water or with charged things in solution. And so that's an important aspect of the way a membrane protein like this is the structured. If I could just take away the loops here, the coil, that becomes quite clear.

So now, with the few minutes we have left, I'm going to go ahead and talk about photosystem I and II at the other end of the chain of respiration where organisms are actually-- you know, they realize that eventually you would run out of all the food on the planet and everything would die. And so they learned to absorb light and to use light energy to carry out processes of life instead of just using the energy that you get when you add electrons to water, to two oxygen and make water. And so let's go look first at photosystem I.

Photosystems I and II are different parts of the photosynthetic pathway and of the electron utilization chain, electron transfer chain. And what you see is that photosystem I and II are both going to be membrane proteins. These, incidentally, are usually much harder to obtain in large quantities and much harder to crystallize, and their structures much harder to characterize. So there are a lot of important membrane proteins whose structures are not very well known yet. In photosystem I it's a trimer. There's one piece right here, it's shaped like a big disk. Here's another piece and here's another piece. And then if you flip it by 90 degrees to look at it edge-on you can see here it is sitting in the membrane.

And these have colorful cofactors. These now have porphyrins, many porphyrins, that contain instead of iron, contain magnesium. And these are the chlorophylls that are present in here as light gathering entities. And then-- OK. OK, with this picture I can tell you quite a bit about photosystem I. Here, you can see, is the part of the molecule that is embedded in the membrane. And what we have is the ability to extract electrons from a molecule that is hard to oxidize.

OK, so in photosystem II you'll see that the source of electrons is water. And so photosystem II is capable of pulling electrons out of water, generating dioxygen, the most important photosynthetic reaction on our planet. In the case of photosystem I, the source of the electrons, instead of being water, is a little protein called plastocyanin. So plastocyanin comes up here and it is oxidized. And it's a little bit like the LED we talked about last time, because what happens is there's a pair of heme units here, they're not hemes of chlorophylls, the special pair, that when light energy is absorbed and excitation occurs, it sends an electron to high energy.

And normally, after such an absorption of light occurs, that electron would just drop back down and the molecule would go back to its ground state. But what this molecule has been built to do is to take that high energy electron and descend it through a series of redox active molecules. And it actually goes all the way through here, and these are little iron four s four cubes. So these are beautiful little inorganic molecules, Fe4 S4 cubes. The electron pathway goes through these redox active units and jumps from one of these Fe S4 cubes to another, and finally jumps out to

a protein that docks up here to accept it, which is a ferredoxin protein.

So after light comes in and you get a high energy electron, you get a hole, the hole is filled through oxidation in the case of photosystem I and plastocyanin in the case of photosystem II of water, and so the chain goes. Now, having run out of time here, I will talk about photosystem II at the beginning of next hour.