

So the big issue that I was trying to take on yesterday, and this is of really fundamental importance to biology, is that you saw from that molecular composition of cells 80% water. Of the rest of it about 50% of what's there by mass is protein. Proteins do most of the really interesting stuff in the cell. They're the ones that are able to catalyze specific chemical reactions with all this amazing chemistry that's needed for life to take place at physiological conditions. They are structural components of the cells. They are all kinds of amazing machines. I showed you the little flagellar motor that turns it, but that's just one of many, many nano machines that are necessary for life. They have exquisite specificity when you get sick and you get an immune response. You develop antibodies and other cells that are able to recognize exactly some piece of that virus or bacterium that has infected you and mount an immune response. But all of the things that are doing that are proteins. And the sort of, most of you I think know that, as we've sort of said that amino acids are just a chain, one amino acid joined to another amino acid to another amino acid and so on. And so the backbone, that peptide bond that I showed the other day is absolutely regular piece of backbone. And what gives the amino acids their character is the side chain that hangs off. And you'll have different side chains hanging off depending on what the amino acid is. And you will not have to memorize all of those structures. But the important thing is that these various amino acids fit into chemical categories that give them properties. They either have a plus charge and a negative charge, they're hydrophobic, they don't like to go with water, they are polar, they cannot interact with water and so on. And it's clear from a couple of your comments, some of you are why are we going through all of this? Well, the reason we're going through all of this is all amino acids look like this. It doesn't matter. They're going to be an enzyme, a part of a motor, a structural part of yourselves. They all consist of the same backbone made up of those 20 amino acids. And what gives these, makes the proteins so important is the ultimate 3-dimensional structure. I'm not sure what this sound is. OK. Let's try standing back here. What gives all of these proteins their individual character is how this chain of amino acids, you could just think of them like this, folds up into some 3-dimensional structure that ultimately is able to do the biological function that we're trying to understand. And one of the real holy grails still in biology is how to look at the sequence of amino acids that constitute a protein and figure out what the 3-dimensional structure is. It's one of the holy grails that hasn't been solved. One of you may have a key insight that will solve this. If we could do that it would really be a huge advance, because what you can get out of the genome sequences is you can read the sequence of every gene and you can predict the sequence of amino acids in the protein. But all it tells you is the linear sequence of the amino acids. It doesn't tell you what the 3-dimensional structure is. And how an amino acid gets from the sort of floppy chain linear structure to the 3-dimensional thing is complicated. And you have to understand several kinds of forces. And so I introduced a few terms. When we think about protein structure, the primary structure, that's just the linear sequence -- -- of amino acids. So valine followed by a tryptophan, followed by a proline, followed a threonine, whatever it would be. That doesn't tell you very much. Then the first key part of understanding how proteins get to a 3-dimensional structure was the discovery of what's termed secondary structure. And these are the thing I introduced to you to the other day. There are two important ones. An alpha helix and a beta sheet. And this is a propensity of a certain string of amino acids in this linear sequence to adopt one of two very common protein structures. And the important thing about these elements, the alpha helices and the beta sheets is they are not dependent on the side chain. So they are not. They are instead dependent on hydrogen bonds -- -- between N-H and the carbon double bond oxygen in the backbone. And that was how Linus Pauling figured out originally the alpha helix. He decided to ignore all the side chains. And he worked out that you could arrange the backbone of a protein, the peptide bonds into these repeating structures that would account for the reflections he'd seen. When we get to talking about how Watson and Crick worked out the structure, that's how they started out, too. They decided to ignore, if you will, the side chains, which are the As and Gs and Cs and Ts, which turned out to be not a productive way to go after the structure of DNA. But, in any case, that was part of what Linus Pauling did in working these out. And so those little movies I showed you, this is an alpha helix. Now, what's been done in this picture is all the side chains have been taken off. And so you can look at this in your textbook, you'll see pictures, but these hydrogen bonds are -- The amino acid is just in this helix. It's coiling around. And at regular intervals there's the opportunity for forming a hydrogen bond. And we can, with some success but certainly not certainty, predict that a particular sequence of amino acids is going to form an alpha helix. And part of what that's based on is there are some amino acids that don't fit easily into an alpha helix, so they'll disrupt one if it ever tried to form. So that's one of the elements of protein structure. So what you might get from this is the idea that somewhere along here this little piece of the linear sequence is apt to be an alpha helix. And you can represent that as this little sort of coil that you see in these 3-dimensional structures. The other one, which is the beta sheet, now that involves interactions between two pieces of, two stretches of amino acids. Maybe there was a loop in between. And then you can get interactions between them. And that, oops. Let me just go, there's the beta sheet interaction. Now, those are represented as arrows. You know, it takes two of them to go. So you've got to have, to represent a beta sheet in a 3-dimensional structure you have to have two of those broad arrows. And there was a question why were there arrows on them? Well, one of the things, I think you can see if you look at those backbones, is that both nucleic acid and protein backbones, there's a polarity. If you start in this direction, the amino terminus, it's got a particular direction. It's not symmetric. If you come back the other way you find carboxyl, amino, the alpha carbon. And you'll find it in the opposite order if you come back the other way. So there's an inherent polarity. The arrows aren't represented on here, but they are when you look at it in 3-dimensions. And you can either form beta sheets where the two strands have the same polarity or, if in a case like that where they loop back, then of course if this one was pointing in this direction as it goes through the loop then the opposite strand will be pointing in the other polarity, one going this way and one going that way. So this part is sort of helpful. You can make guesses that maybe this part has a tendency over here to form a beta sheet. but you still haven't gotten very far towards understanding

how you get to the 3-dimensional structure. And just by putting on and superimposing some amino acids onto that alpha helix then you can see what happens, that if you form an alpha helix what happens is all the side chains stick out. And now I think you can see, those of you who are engineers anyway, if you wanted to build something you have a cylinder and you can stick amino acids out that have particular chemical characteristics. And depending on the characteristics of those amino acids, whether they have charges on them or if they hate water or something, that will influence what happens to that component of the protein structure when it gets into a 3-dimensional thing. And, as I think I showed you the other day, when we caught it looking down the end on this particular example, here are a couple of aromatic amino acids right here, they're on the same side of the helix and they would hate water. Whereas, some of the other amino acids up here are ones that have charges so those would love water. So what this would look like is a cylinder part of which hated water and part of which loved water. And you might guess it folded up in 3-dimensional space. The part that hated water might fold towards the inside of the protein. And the part of the cylinder that loved water would face to the outside. So that's sort of the underlying principle. So the rest of the other forces that we had to understand in order to get to what's called the tertiary structure, this is the full 3D structure, which we can now determine by a variety of methods. X-ray crystallography of proteins is probably the most common. The NMR, for example, can be used to derive a 3-dimensional structure as well. And the other forces then that go into this are ionic forces. Someone seemed confused by this, but if you have a plus charge on this part of an amino acid and a minus charge here, if in 3-dimensional space the plus charge got somewhere near the minus charge then that would form an ionic bond. And I think most of you know enough electricity and magnetism that wouldn't surprise you that those two would be attracted. The one that I think that has been harder to understand is van der Waals interactions that we talked about the other day, which is tricky in the sense that for this course you don't particularly really need to understand the underlying chemistry. But the principal of it is that if you have a nonpolar bond, one that hasn't got any particular attraction to it, gets very, very close to another one, then the transient fluctuations in one induce something in the other one that makes them stick together. And the whole point about this is if you get two molecular surfaces that are very, very close together, about, you know, many two times the length of a covalent bond or something, then you can generate very powerful forces. Because even though each individual interaction is weak, about a quarter or a third of a hydrogen bond, summing them up can make them very, very strong. And so that's another kind of force that's important when a linear molecule is trying to figure out how in space it's going to fold up. The point of the gecko thing was it's only relatively recently been discovered that the reason those lizards can stick to walls is they have sort of incredible split ends. I noticed a couple of you came to Bob Full's talk the other day and you got to hear the full treatment. But because the hairs on their feet are so split they're very fine and the molecules are able to make very close interactions, van der Waals interactions with the surface. And that's what's holding the gecko to the wall. And there are just so many of them that it can support a whole gecko. And that's what could be the basis of, he said to me, a \$30 to \$50 billion adhesive industry, a self-cleaning dry adhesive. And it's not something magic only the gecko hair will do. You can design synthetic molecules that have the same property and are able to make these millions of van der Waals interactions. So that's two of the other things. And the final thing, which isn't really a force but goes into this, is this hydrophobic effect. And that is that if we have things, amino acids such as valine or something that doesn't like to mix with water, then when the protein folds up, the things that don't like to interact with water will kind of go together just the way if you put a lot of oil in the water it will sort of pull together. Because any time you have something that gets stuck in water, it disrupts hydrogen bonds and that's energetically unfavorable. So the things that hate water will tend to lump together. And you're all used to seeing little drops of oil and stuff floating around. And let me switch over to this other thing now. So this was just showing you one of these protein chains that's folded up into a 3-dimensional structure. This happens to be something with an enzymatic activity. But the important thing for right now is what's been colored in here are the amino acids that if you look back on the list of amino acids and what categories are, you'd see some of them are said to have hydrophobic side chains. You can see quite strikingly how the amino acids in the interior part of this protein have clustered together. They don't like to interact with water. They interact very well with each other. Just like you can mix butter and oil, they mix together very well. And so that is another factor that contributes to the 3-dimensional structure of these proteins. So understanding what proteins are all about means ultimately understanding their 3-dimensional structure. And, as I say, a big unsolved problem right at the moment is how do you get from a linear chain of amino acids to one of these 3-dimensional structures? And you can imagine with 20 different side chains there's an unbelievable number of combinations that you can make. Yet almost every protein in nature has one unique or one or two or something confirmations that takes out, out of all the kinds of things that you could do. And it's this combination of forces that does that. You know, let me just go back for one second. So the final thing that ones talks about when you're talking about proteins are quaternary structure. And what that means is when you have more than one polypeptide chain, so if we have two different proteins that interact, this is protein number one and this is protein number two, then there has to be some sort of interaction between each of these three dimensional structures in order for the proteins to stick together. Something like that flagellar motor that let's the bacteria swim, has many, many parts, all of which have to fit together just the same way all the different parts of an engine have to fit together. Now this next little movie is just a dimer. It's actually a heterodimer so it's made of two proteins. They're different but they've come together and they're interaction. So what you will first see is the 3-dimensional structure of each protein showing the alpha helices, the beta sheets, and nothing else is shown. The side chains aren't shown. The molecular surfaces aren't shown. You can just see the backbone. You'll see alpha helix a turn, some beta sheets, just the kind of stuff you were seeing the other day. But you'll see that the two proteins are together. And this is actually a movie made by Tom Schwartz who's a crystallographer who just started on our facility this fall in the biology department. It's one of the proteins he studied. And then after that he rotates it around so you can see it. After that he then puts on the side chains and then traces the surface. So this is what they call the van der Waals surface. So this is what the

protein would actually look like. And what I think you'll see from this is how incredibly well the proteins fit together. The theme I'll probably keep saying all the way through the course is biology works from fitting shapes. And things have to work incredibly well, and that's also why these van der Waals forces become so important. Because evolution has ended up making things that just go together just like a hand in a perfectly fit glove. That's the way most of these interactions are. So watch this little movie. So the light blue is one of the proteins. There's an alpha helix. There are a lot of alpha helices in this one. And the purple one is the other protein. And you can see that in between them there's an interface. And so those must be interacting. But when he superimposes now all the amino acids in the surface, now what he's going to do, he's going to pull those apart so you can see where they were interacting. Do you get the idea now of how beautifully these things have folded up in 3-dimensional space in positions so that they can fit together and work together as a machine? Just the same way if you were building a machine and you needed to have two parts that you had to join together you've got a tool thing so that the surfaces go exactly together. That's what nature does. That's also why I'm making such a deal out of this 3-dimensional structure of proteins and how it got there. I could just say it gets there by magic, but it doesn't. It's determined by this set of forces. And one of the things we cannot do at this point is predict. Here's a linear sequence of amino acids. Here's the 3D structure. That would be a huge advance in biology if one of you guys could figure out how to do that during your career. OK. So I just want to reiterate some of the things that proteins do because we'll be talking about them as we go along. One thing they do, they act as enzymes which are catalysts for biological reactions that take place under physiological conditions. And we'll give you a lot of examples of those enzymes starting very soon. They play structural roles. Our hair, our fingernails are made of protein. The hairs on the gecko's feet are made of keratin which is the same stuff our hair is made of, except they basically got a whole lot of split ends. They're finer hairs to begin with and a lot of split ends. And that's what makes these very, very fine things that can make van der Waals interactions with surfaces. They play roles in specificity. For example, I mentioned the antibodies. And we'll talk about the immune response in some detail at the end of the course. And one of the really magic things that we've come to understand in biology recently is how it is that your body has this immune system that's able to recognize literally any molecule, any molecule. It doesn't matter whether it is existed or you and your PhD thesis in chemistry synthesize something the world has never seen before, your immune system can create an antibody or something that will very, very specifically recognize that particular shape in just the same sort of way that you saw the shape on that movie. And you might think you'd need to code a zillion millions of DNA in order to do that. But there's a trick using combinatorial functions and mutation that lets your body do that. Another example, which I was showing you, that can do all sorts of little motors and machines, I showed you the bacteria swimming around. These are just *E. coli*. And you cannot see the flagellar motors, but you can see them buzzing around just under a cover slip. Some of them are stuck to the cover slip. There we go. In this one, which was taken by Howard Burge who is a professor at Harvard, I just took this off his website, you can see the bacteria swimming by having these flagella which are basically like sort of propellers more or less that they turn. Here's one where he used the strobe so you can get a little bit better view of it. And I showed you this picture in the first lecture. So that's the machine, but every single part of that machine is made of a protein that's got a very certain 3-dimensional space. And we're going to start talking about energetics, how does this cell get energy? And one of the things you might wonder is if you were to design such a nano machine how would you power it? They exist. I mean it's here. But that's why in part I'm going to start talking about energy and how cells make energy, because this is one of the things they have to do. And that was, as I said, was an average electron micrograph of a lot of those motors. So you can see that although, you know, that's the textbook thing, the actual thing is pretty much the same shape. This is not at a resolution where you can make out the individual proteins that put it together, but some of those are starting to be known in 3-dimensional detail. And I thought you might enjoy seeing this just to convince you it's a motor. In this thing, what Howard Burge did was he stuck the propeller, if you will, the flagellar to a cover slip using an antibody. And then he let them do their thing. And normally they would be turning the propeller and swimming, but if the propeller is attached the same thing would happen if you held onto the propeller of a boat and turned on the motor the boat would start twirling around. And what you're seeing here is bacterial that are twirling around because their flagellar are stuck on. And those of you who are observant will notice even that they change direction. And that's part of the system that bacteria use so they can swim towards a food source or away from another one. OK. Here's just something to let you think about it. If anybody can figure this out send me an email. Here's something else. The phenomenon I'm going to show you is due to a protein made by a soil bacterium called *Pseudomonas syringae*. You don't need to know that. It associated with plants. And what you're going to see is a little movie made by a couple of post-docs in my lab where they took pure water. And if it's pure water you can cool it below freezing. You can get it down to, I don't know, minus eight degrees centigrade and it still will be a liquid, even though you know water freezes at zero degrees centigrade. And what it has to do in order to turn into ice, somewhere you have to nucleate the formation of an ice crystal. And once it goes, going. So, anyway, what you're going to see is some super-cooled water they've made. You can see there is zero degrees there. And this is Metchitaga, one of the post-docs in my lab. That's the super-cooled water. She's taking a little bit of culture of this *Pseudomonas syringae*, and she's just going to put it in, give a little tiny squirt, a few micro-liters into that water. Now it's going all cloudy. And now you might wonder what's happening there. But, as you'll discovery, what happened is that what was liquid water is now ice. That is due to one protein that this bacterium makes and displays on its surface. And here's a controlled experiment. This is putting in a little bit of *Rhizobium meliloti*, another soil organism, and the same amount of bacteria. It didn't happen. OK. So that's due to a protein that was on the surface of that bacterium. Anybody have any idea what that could do? Send me an email. OK. There's one last class of [UNINTELLIGIBLE] macromolecule. Those are lipids. These are a little different in the sense that this is not know a long chain made by joining together subunits as you see with the proteins and nucleic acids, but putting together the parts necessary to make a lipid involve the same principle. that you end up splittina out water molecules. That's a theme you've heard over and

over again. And if we take three long chain, three fatty acids, some number of carbons -- Some number of carbons. Just some arbitrary number here. And then we take a three carbon compound that has three hydroxyl groups. Now, this is not a carbohydrate because you'll notice there's not a double bond oxygen as you saw in the carbohydrates. It's actually an alcohol that's known as glycerol. And if we split out water like this what you get is a fat, something you're familiar with from beef fat. Or if you get something like olive oil, you've heard the term unsaturated fats. Maybe you'll recall from the second lecture that if we had a single covalent bond, or if we had a double or a triple bond that was called an unsaturated bond. So if you have an unsaturated bond in here somewhere then you end up with an unsaturated fat. And most of you know probably something like beef fat is solid. If you put it in a refrigerator something like peanut oil will stay liquid. And that's because if you have just saturated side chains from this then they pack together very tightly and they will form a solid. If you put a double bond in then there's a kink in the backbone and it's hard for these things to pack together. And that's why they're called unsaturated fats. Now, there's a very particular kind of lipid that's of unbelievable importance in biology known as a phospholipid. And the reason that's so important is that that is the boundary that determines the outside of a cell. So every cell, every organism either is a single cell or is made up of multiple cells. And, as I said in the first lecture, that one of the secrets to life is having a boundary that goes around your insides it separates your insides from all the rest of the universe. And the way these membranes, as they're called, are made of is what's known as a phospholipid bilayer. And it's the same principle as before. It uses a glycerol, except that one of the fatty acids is replaced by a phosphate group that will have some kind decoration added onto it. And the other will have fatty acids at the other two positions. Now, you'll notice by splitting out water here, the kind of bond that we have created, the chemical name of this is an ester bond. And if we wanted to break it we could add water back across it. So what's important about this molecule is this part of the molecule, if you will, is water-loving because the very polar bonds here, the oxygen here would have a negative charge under physiological conditions. And this part is, if you will, water-hating. So phospholipids are often represented in the following way where this is the water-loving and then this would be the water-hating part here. And so if you take phospholipids and you just try and disperse them in water, they spontaneously self-assemble into structures that bring the water-loving parts together and the water-hating parts together. And by so doing this they form what's known as a phospholipid bilayer. And that's what this membrane is made of. Membrane of bacterial cell, membrane of our cells virtually the same thing. It has the property that is not permeable to very much. Water can get across a very limited number of other chemical compounds, but most things cannot. And so, by having this membrane, what the cell is able to do then is control who comes in and who comes out. And the way it does that is it has to put particular importers or exporters imbedded in the membrane that can carry out those functions. Because, as you would guess, any system would have to bring stuff in, get rid of waste, you'd have to be able to go back and forth. The things that do all those transports across the membrane are, what kind of molecule do you think it likely to be? If nature was going to design something that was a pump to get something in or something that would get something out, any idea what kind of molecule? Take a guess given what I've said so far. Protein. Yeah. Absolutely. And let me just sort of show you a couple little pictures here. So here's a representation of this phospholipid bilayer. This is pretty standard stuff. This is what you'd put on a blackboard. Here's in gray now the phospholipid. And here's one of these proteins, a picture of one of these proteins that functions to get things across the membrane. And hopefully what you can see now is that it's made up of a whole lot of alpha helices, and they pack together to give sort of a cylinder made up of different alpha helices that weave in out like this. And then by this sort of trick the protein is able to create a channel that runs up and down the middle of this protein that's imbedded in the membrane. And then, depending on the characteristics that channel, it can either be used to bring stuff in or get rid of it. There is a more fanciful depiction of it. This is not reality, but there you are with the water-loving parts. Here are the fatty acids going in. And this is supposed to be one of these membrane proteins. Now, this next movie is trying to pretend here that it's looking at one of these membrane proteins colored here in red as it spans the membrane. So here's looking from the membrane surface on. And now it's going to dive into this thing as it crossed the membrane. And basically what this movie is letting you do is feel like if you were the molecule that's being transported across the membrane you'd see how you'd go right down through a channel in the middle of the protein. So that's one of the underlying principals then, is that you have a phospholipid boundary that's critical for life. But then to have everything else that needs to happen the cell makes a series of proteins that function either to bring stuff in or to bring it out. Or in the case of something like the flagellar motor we talked about it has to imbed a part of the machinery right in the membrane. And one last picture I just want to show you. Usually, even on that movie, you tend to see the cell represented something like this with a membrane and every once in a while there's a protein. This is a cartoon but it is much closer to a to-scale drawing. This is an E. coli cell. Now, they have an extra membrane that we won't worry about right for the moment. But right there, this little piece that we can see little bits of, is the cell's membrane. And what this picture is showing is that this membrane is just absolutely studded with membrane proteins that are going to carry out various functions. And here actually we're seeing that motor which is imbedded both in the inner and outer membrane. And there's the motor going off. But a couple of things maybe you can take home from this is there are a lot of proteins stuck in those membranes that control what goes in and out. You also get a sense in here of how crowded the cytoplasm is. The proteins are really at amazingly high concentrations when they're inside the cytoplasm. OK. So that's sort of a quick survey. It's nothing more than a really superficial introduction to the four classes of biomolecules. But to go any farther we're going to have to think a little bit now about the characteristics of living cells. I don't know if any of you know if any of you know what this is, but this is baker's yeast. If you were making bread you know you put some yeast in it and it divides and it gives off carbon dioxide as a waste product and makes the bread rise. And what's happened in that little movie you just saw were two cells dividing to give four, and four dividing to get eight, and I don't know what we're up to here, but you can see a cell grow. That's sped up. It takes probably something closer to an hour for a cell division to take place. But this is the kind of thing that microorganisms do when they grow. is you can

start with a single cell and it will make two cells that are identical to itself and those will make four. And what happens when we start out as a single cell, we start out initially like this. And we make cells that are identical at the beginning. And those are the famous embryonic stem cells, because at this point they can become any cell in your body. And if you're a yeast it doesn't matter. Everything you make is the same. If it's a human, once you start dividing at some point cells are going to have to start making decisions and the progeny will have to start to be different of each other so that you can have something that's an eye and another cell that's in the liver and so on. And we'll talk a little bit about that as we go on. But the major point, right at this point, is that all of life involves one cell dividing and giving a couple of other cells, and then those going on. So these cells, as we've said, characteristics of organisms which are to be true at their cellular level as well is that they carry out metabolism, they undergo regulated growth. And you have a nice example of yeast undergoing regulated growth and they reproduce, which in the case of a single-celled organism is the same as cell division. For us reproducing is a lot more complicated because we have to make a whole other multicellular organism where the cells have differentiated functions, but the point about that is there has to be an unbelievable amount of synthesis. The DNA in our body, we start out with two meters in a fertilized cell, and we have ten to the fourteenth cells by the time we're an adult. So we've had to make a tremendous amount of DNA let alone protein and everything else. And something almost all of you know from your engineering background from this place is that you need energy in order to synthesize material. And what we'll start to talk about in the next phase of this course then is how do cells make energy and how do they carry out metabolism. So I'm going to, just before we do that, introduce to you very quickly, to close out here, two classes of organisms that we find in nature. We find organisms that are known as autotrophs. These are certain bacteria, and they're able to make everything they need starting with CO₂, ammonia, phosphate, water, a few things, but that's all they need. So, for example, an organism that lives, a bacterium that lives out in the open ocean is able to make everything from those very, very simple basic building blocks. Heterotrophs need to eat -- -- some things made by other organisms. An example of a heterotroph that you're familiar with, that I'm familiar with is us. You probably remember your mother reminding you, as you're about to have yet another hotdog, that it was important to eat your vitamins. The reason you need to eat vitamins, those are things we absolutely need for our life but we cannot make them ourselves. Vitamin C is one you probably know. It has an interesting history how people figured this out. It was sailors at sea got really, really sick. Their teeth would start to loosen, they would start to bleed and they would die. Some of the famous sea voyages you heard about in high school, I think the Cape of Good Hope, on that trip where that was discovered 100 out of the 160 sailors died at sea because of scurvy. Now, scurvy turns out to be due to not having vitamin C. And there was finally a guy, Lind, I'm just blanking on his first name at the moment, in about the 1700s who was a naval surgeon in the British Navy who actually figured out that if you gave sailors lemon juice that they didn't get scurvy. It was a controlled experiment. It took about 50 years. I think it was 1795 when they started to finally give the sailors lemon juice and stopped having this terrible sickness amongst their sailors. And then in about 1950 they substituted lime juice. And some of you may still know the British sailors are called limeys. And that was because of this solution they found to avoiding scurvy. And what was really happening was they were finding a way to provide vitamin C which is in fresh fruits and vegetables which wasn't part of the classic sailor diet which was sort of biscuits and dried meat during long voyages at sea. And there are several other vitamins, but the reason they're called vitamins is they're things that you body cannot make but other organisms can. The other thing that we cannot make, we can make some of our 20 amino acids, but there are eight amino acids that we cannot make, lysine, methionine, leucine, isoleucine, valine, threonine, phenylalanine and tryptophan. And this actually has consequences for us because those of you who are vegetarians probably know you have to be kind of careful about your diet. If you're eating animal protein you're getting essentially all the different amino acids, but if you're a vegetarian you have to be careful because the major food crops such as wheat and rice, for example, are very low in lysine. So if you just eat those you end up with a lysine deficiency that's not good. But, on the other hand, beans, lentils, the various leguminous plants, which also are those ones that form the special associations with bacteria that let them convert atmospheric nitrogen into ammonia, legumes are high in lysine but low in methionine. So peoples all over the world figured this out by trial and error. So the Mexican diet is rice and beans. There's a reason for it. What's happening actually is just in the rice you're low in lysine, but by having beans at the same time you're balancing out the two. Or the Native Americans in this part of the country had the three sisters with the corn, the squash and the beans. And again they were balancing out the diet by making sure that they got the various amino acids, a balance of all the amino acids that were necessary for life. It also actually was really good gardening practice because the beans were able to convert atmospheric nitrogen into ammonia, which was fertilizer, and the squash leaves shaded the ground so that the ground didn't dry out, and the corn could grow even when it was short on water. But what was really happening, as people grew without even understanding about chemistry, they were compensating for the fact that we're heterotrophs and needed to do this. So we'll start in the next lecture on trying to talk about how cells make energy and how it makes some of this amazing stuff happen.