

HAZEL SIVE: Another truism of biochemistry is that many of the molecules within cells are very large. And they're called macromolecules, to indicate this. So macromolecules. So these are often -- Biological molecules are often macromolecules. And these macromolecules are often polymers-- not always-- where a polymer is some kind of repeat of a monomer "n" times.

And in formation of macromolecules, there are two kinds of reactions that you need to know. They are called condensation and hydrolysis reactions. And they go something like this. Condensation reactions form bonds. Hydrolysis reactions break bonds.

And condensation reactions go something like this. If we call the monomer M, there would be a monomer with a hydroxyl group that interacts with another monomer that has a hydroxyl group. And the outcome of that would be a bond between the two monomers, with the release of water.

And the flip of that, during a hydrolysis reaction, is exactly the opposite, where this dimer here, M-O-M, where there's an ether bond between the two monomers as I've drawn it, called different things-- we'll talk about that-- adds water and then is broken down into two monomers. And so you should know a condensation and a hydrolysis reaction, because every reaction that we talk about in this course and in much of biochemistry involves either condensation or hydrolysis reactions. Often, both condensation or hydrolysis require energy, sometimes that they release it. So often, both often require energy in order to proceed. Okay.

Very good. Let's move then to the second topic that I'd like to discuss today, which is the first big class of macromolecules, the lipids. Lipids are a fascinating class of macromolecules essential for life. They comprise about 5% of the dry mass of a cell, the dry mass referring to the mass remaining after the water has been removed. And lipids are crucial-- and we discussed this briefly last lecture-- for formation of the membranes around the cell and around the various organelles.

So lipids are required for membranes. They also serve as major energy stores for the cells. Their bonds are very energy rich. They are also involved in various signaling processes. We'll touch on this today and later in the course. And of course, they are involved in insulation, both in keeping the whole organism warm-- if it's an animal, during winter-- but also in insulating nerve cells as nerve cells transmit their signals by insulating them, kind of like an electrical wire is insulated by plastic.

The condensation reactions that form during lipid formation often involve synthesis of things called triglycerides. And triglycerides are formed from glycerol. And I'm going to warn you that my chemical structures are going to be casual. We assume that you have enough chemistry that if you know that I write CH_2OH , you actually know that the hydrogens are sticking out around the carbon.

Okay? That's my contract with you. We assume you know enough chemistry to deal with that. If you don't, then please come and see me or Dr. Sinha.

And to that glycerol is added a fatty acid. And the fatty acid has got a hydroxyl group attached to a carbonyl, which is attached to a long-chain hydrocarbon, where n is 16 to 20. And this guy here is called a fatty acid.

And out of the addition of glycerol and the fatty acid-- I'm going to put a line between the two so that you can see the difference-- comes something called a triglyceride. And I'm going to draw this for just one of the glycerol carbon atoms. And then the same thing is true for all the others.

So you'll have CH_2 at the end, and then a condensation reaction. And we're going to write et cetera here, being casual about this. And out of this comes this triglyceride.

This reaction is a condensation reaction. It eliminates water. It's a condensation reaction. And it's also a transesterification, where you can see the ester bond formed in the triglyceride.

I'm going to notate triglycerides in a slightly different way. I'll show you this in a

moment. But let's take a look at a picture here so you can see what it actually looks like.

Here's glycerol, from your book. And here is a fatty acid. And here are the reactive species interacting to give you a condensation reaction and joining up the glycerol to the fatty acid. And the glycerol then serves as a backbone to have these three chains of fatty acid. Hence the name triglycerides.

Lipids are not, strictly speaking, polymers. And so what I said about macromolecules being polymers really doesn't hold for lipids. But the other principles do.

One of the things about lipids is that they can be modified. And they can be modified by replacing one of the fatty acid chains with something that is polar. So if you look at this triglyceride, you can see at a glance that it is really hydrogens and carbons.

It's very non-polar. There's a couple of oxygens up here. But there are so few relative to the molecule that really this is a very non-polar molecule.

But you can change the properties of lipids in an extraordinary way by replacing one of the fatty acid chains with something polar. And that is particularly done in phospholipids. And we're going to now draw a triglyceride in a different way, in shorthand, where the glycerol is going to have a horizontal bar and the fatty acid chains are going to emanate as vertical lines.

The triglyceride, your classic one, is hydrophobic because it is non-polar. But you can also take one of those side chains, or one of those fatty acid chains, and replace it with a phosphate group. So you can replace one fatty acid with a phosphate, which is highly charged. And then you get something like this, where the blob is the phosphate group.

Phospholipids are the things which make cell membranes. And they make cell membranes because they are on one end polar, and on the other end they're non-polar. And so here on the top end, they are polar and hydrophilic. And then the bottom part is non-polar.

And this causes them to self-associate so that the polar groups face water and the non-polar groups face one another. And these will spontaneously form a lipid bilayer, the thing that surrounds all of the cell and all of the organelles. So they will go and spontaneously associate into a bilayered membrane, which we can draw like this, using our shorthand notation.

And what I've done is to now put the hydrophobic or the non-polar bits facing one another. And these polar bits are now interacting with water. So these are hydrophilic-- which I'm going to hyphenate. And they are indeed interacting with water.

Let's look at some pictures to exemplify this. Here is the chemical structure of a phospholipid. They're the long-chain fatty acids. And here's the phosphate group. This is actually a modified phosphate group.

It's got a choline moiety, which makes it even more polar. And here you go with this little bit sticking out. So you can see the shape of the molecule has changed. And also its electronegativity has changed.

And here are these molecules that spontaneously form this lipid bilayer, the phospholipid membrane, with all the hydrophilic parts sticking out and touching water on either side and the hydrophobic parts interacting with one another. I want to really make a point that this is not a double membrane. This is a single membrane.

We talked last time about mitochondria and the nucleus having double membranes around them. That would be two of these. This thing that we've got up here is a single membrane. This is what all cell membranes and organelle membranes look like. That's an important thing to realize.

The last thing I want to mention -- Actually, the last thing I want to mention about triglycerides is that there are a couple of different kinds of triglyceride chains which are very important medically. And you've heard of them. There are saturated fats,

where the triglyceride chains have got all single carbon atoms. And all of these completely saturated-- in other words, there are no double bonds.

Triglycerides with these types of chains tend to pack tightly. And this gives them the property of chemical stability and confers on them a high melting point. So saturated fats are often solid. And this is bad. These are bad for you.

In contrast, unsaturated fats are sometimes good for you and sometimes not. So unsaturated fats all have, somewhere, a carbon double bond. There are two kinds of unsaturated fats. There are cis-unsaturated fats, where-- let's just put in some extra bonds here-- where the other bonds that are available to the carbons are on the same side of the molecule.

And you remember that there's no free rotation around a double bond. So if that molecule looks like that, it is stuck that way. If it synthesized that way, it's stuck that way.

On the other hand, there are trans-unsaturated fats, where the additional valencies of carbon are on opposite sides of the molecule. Cis fats-- I'll show you a slide in a moment-- so these have got double bonds. The cis fats pack poorly because they are kinked. And these have got a low melting point. And these are good for you.

The trans-fats, however, are much more like the saturated fats, and they pack tightly, et cetera, high melting point. And they are particularly bad for you. Trans-fats are very seldom found in nature. They are found in Twinkies and other gourmet treats.

All right, let's look at some structures here from your book. Saturated fats, you can see the chains are all straight, and they pack very tightly. Cis-unsaturated fats, here's a bend in the chain, and this makes the molecules pack loosely. This is a steric, a spatial, consideration.

And then if you look at trans and cis fats, here's oleic acid. It's the same carbon chain. But trans-oleic acid has a straight chain, cis-oleic has a bend.

They're both unsaturated fats. And the question that I am sure you have seen is whether or not trans fat should be removed from all food, and how that can be done, and why it is bad for you. And now it's required that there are ingredients posted on various food so that you know what you're eating.

And I'm going to tell you a little bit about why trans fat is bad for you. But I have to introduce to you another lipid and another class of lipids in order to do so. And that's not the only reason that I'm going to introduce this other class of lipids. I'm going to do it because it's a very important class.

So a second class of lipids that we should consider beyond the triglycerides are the steroids. Steroids share a common ring structure. They are lipids with a common ring structure. And I have the slide up so you can look at it even now.

Their precursor is cholesterol. And cholesterol is, in fact, not bad. It is an essential lipid. And it's essential both for formation of the membrane, and all membranes, and it is also crucial for signaling.

And if an organism develops without cholesterol, it develops with one eye. You lack the whole midline that divides you into two more or less bilaterally symmetric parts. So cholesterol is a very essential component.

Other things that come from lipids are vitamin D, much in the news also with regard to preventing inflammation, and various hormones. Their structure's on the board -- on the screen. And you can see, in green, the common ring structure with various other groups attached, which give these different steroidal lipids their particular structures. And we'll come back to the notion of cholesterol and why it's both essential but-- let me annotate here-- too much is bad. All right.

In the news a lot are steroids androgens, a particular class of artificial androgens are normal steroids. But there is a class of artificial steroids. Here's one, tetrahydrogestrinone, which is used by athletes. It is mostly undetectable.

The tests for anabolic steroids used by athletes are actually very high tech. And this one is very difficult to detect. And it makes the question of whether particular

athletes have used steroids rather difficult to answer unequivocally.

Too much cholesterol -- I should be using the screen.

Too much cholesterol leads to a condition called atherosclerosis, where cholesterol is deposited in the arteries. Here it is. And this literally physically blocks up the artery, causes the blood to clot, and leads to heart attacks.

And here's an artery that's OK-- well, actually it's not quite, there. You can see it's being injected with contrast, and there's a little place where it's not OK. And here's one which is completely occluded by an atherosclerotic plaque.

What's the deal with cholesterol? Cholesterol is used for membranes and signalling. But it also is carried through the body by a component called low-density lipoprotein. And this low-density lipoprotein, or LDL, is deposited in the arteries, where it plugs them and leads to heart attack.

If cholesterol binds high-density lipoproteins, a different kind of a transport molecule, then the excess cholesterol is excreted by the liver, and you're good. You're well. Turns out, through complicated reasons, that trans fat and saturated fat increases the levels of this bad, low-density lipoprotein and thereby increases heart attacks.

I should note that most cholesterol is made by you. 80% of your cholesterol is made by you. 20% you get from food. So eating a low cholesterol diet usually doesn't do much for cholesterol levels. You actually have to interfere with synthesis, which is what the various drugs called statins do.

All right. So enough about lipids. Let us move to our third topic today, another fascinating and important set of macromolecules, the carbohydrates. Carbohydrates make up about 25% of the dry mass of a cell . They're used as an energy source, as a carbon source to build other molecules. And they also encode information, as in your blood type, which I will try to touch on in a few moments.

Their chemical formula is much simpler and is polymeric, unlike the lipids. $(CH_2O)_n$,

or if you like, more informatively, $(\text{H-C-OH})_n$. And because of the hydroxyl group, carbohydrates are pretty much always hydrophilic.

The monomer of carbohydrates is called a monosaccharide. And there can be polymers that are two monomers or multiple monomers. So the monomer-- and you should know this-- is called a monosaccharide, where saccharide sounds like saccharin. That means sugar.

And there can be dimers, which would be a small polymer, which would be a disaccharide. And then you can also get long sugars, which would be polysaccharides. A monosaccharide, for example, would be glucose. A disaccharide, sucrose. And a polysaccharide, glycogen in animals or cellulose in plants.

All right. Let's look at the condensation reaction that is responsible for making carbohydrates. It's a simple condensation reaction, at least on the board. It requires careful orchestration by the cell, but on the board it's easy to draw.

One carbohydrate plus another carbohydrate-- I'm not going to put all the side groups on, but you understand there are other side groups here or another carbon there, giving rise to-- with the release of water. So here is a condensation reaction. And this bond that forms in carbohydrates-- I'm actually going to add the next carbons on here, instead of X. I apologize for erasing here, but let's put some carbons here rather than X because that will be clearer.

But the bond between two monomers is called a glycosidic bond. And that designates that it is found in carbohydrates. Carbohydrates can isomerize. That means the same chemical formula can change its shape, can change the organization of its atoms, and can isomerize between the ring and a linear structure.

And carbohydrates can also be modified. They remain hydrophilic in general, but there are many modifications which are rather crucial to their function. They can get, for example, phosphate groups or amino groups. And this will change their particular properties.

Let's look at some slides. And then I want to tell you about a very fascinating and important example of carbohydrates as an information source. So here's glucose as straight chain and glucose as a ring.

If you're not familiar with looking at chemical structures-- I keep forgetting that is my usual board. But let's look at this one because it's brighter. If you're not familiar with looking at chemical structures, if you see these dark areas in a molecule, it means that the molecule is coming out of the board towards you. So it gives a bit of three-dimensionality to that molecule.

And here are the condensation reactions involved in the formation of maltose, which is a glucose disaccharide. And here is the glycosidic linkage. The atoms in carbohydrates get particular numbers.

It is the carbon atoms that get particular numbers. And next lecture, that is going to become very important when we talk about nucleic acids. And here is sucrose, a dimer of glucose and fructose.

Now, depending on the orientation of these bonds between the saccharides, between the monomers, they may or may not be able to be broken by the enzymes, by the chemicals in your body that are involved in hydrolysis reactions. So sucroses can be broken down pretty much by everyone. But lactose, which is the galactose-glucose dimer has got a glycosidic bond which has a particular shape. And that particular shape is only recognized by people who have a molecule called lactase-- we'll talk about this in a couple of lectures-- which is able to break this chemical bond here. And if you're lactose intolerant, the reason you get stomach ache and so on is because you get accumulation of this disaccharide, and it has side effects on your digestive system.

All right. So I want to tell you now about a really fascinating example of information as encoded by carbohydrates. We will have much more to say about carbohydrates as we go along. But I'm going to tell you about information-- particularly here, because we won't talk about it very much more.

One example of carbohydrates giving information is in your blood type. So for blood type, there are specific carbohydrates for each. But there is the same core set of molecules, which is then modified to give you the different blood groups, to four blood groups.

This is a representation of the four blood groups. They are called O, A, B, and AB. And you probably know which one you are. I am A.

One of those blood groups is really valuable. It's called O. And it's valuable because anyone could receive this blood in a transfusion. And anyone can because it's kind of your basic blood type.

It contains an H group, which is the basic sugar information on blood cells. And all of the other blood groups also contains this basic information, but they contain other sugars as well, here indicated by purple. The key to these different sugars is indicated below.

But O can be given to any kind of person because you do not have antibodies against this particular H group. Because everyone's got it. So O is the only blood group where, when you put it into anyone, there are not antibodies-- which you'll learn about later in the course-- that will then attack the blood cells and cause massive blood clots and deaths.

When people donate blood, 3/4 of it is not O. After a time, blood is thrown away from blood banks because it's not usable forever. And a lot of this type, A, B and AB blood, is thrown away. And so investigators have been asking for a long time whether they couldn't remove these extra sugars from AB, B, and A, and turn those bloods into type O, which would then be useful for everyone.

It turns out that's kind of difficult to do. But a few years ago, a group did come up with what may be a solution. It still hasn't been proved, even though this was a few years ago. It takes a long time.

Here's a different representation of the sugars on blood types. Here's group A and group B. And there are enzymes-- there you see, office hours. I'm not kidding. It's

on my calendar. All right.

There are substances, enzymes, we'll talk about which can actually remove some of these sugars off groups A and B and convert them into group O. These substances, these enzymes, were isolated by Liu et al. When you see this at the bottom-- Here's a piece of education.

Often I will show you something, and in the bottom right-hand corner it will say "Liu et al" or "Jones et al" and a date. That refers to a publication. This group was able to convert group type A and type B into a type O. And they are now working on a machine which can convert type A, AB, and B blood into type O.

And we'll stop there.