>> Steven Langjahr: Complex organic molecules are complex by virtue of their size, their molecular weight. And there are two categories that we introduced on Monday. Proteins. Proteins have a very exalted, sort of lofty reputation. Don't we think highly or protein, like it's some magic molecule? And indeed proteins have a illustrious list of functions that we'll get to in a moment. But fundamentally they are organic molecules. They're made of subunits, that is they're made of many amino acids which are connected together, connected together by covalent bonds. And it takes about 50, at least 50 amino acids to create a bona fide protein. Most proteins are way larger than that, but at a minimum, 50. And these are constructed from 20 different amino acids that typically part of your diet, part of your supplements that you might be taking, or whatever. So they're readily available. In this diagram, which you need not memorize, we're simply showing, side by side, two arbitrary amino acids. And let's look at a typical amino acid in terms of its chemistry. Notice at one end it has a nitrogen and two hydrogens. That's called an amine group. And at the other end it has a carboxyl group, C double O, that is O, O, H, a carboxyl group. This then is the standard structure, the basic requirement for an amino acid. And there are how many different amino acids?

>> [Inaudible].

>> Steven Langjahr: So they're different, not because of this, but because of R which a side group of various other carbon-based units. So if we take two amino acids, side by side, and link them together, we create a covalent bond as you can see here between the carbon of one and nitrogen of the next. This is not just a covalent bond; it's a special kind of covalent bond which is found here in protein. It's called a peptide bond. So essentially proteins are made by linking together hundreds, usually hundreds, of amino acids and the linkage is between the amino group of one and the carboxyl group of the next, forming a kind of covalent bond, a specific type called a peptide bond. Just to remind you, what is a covalent bond, what's going on there to actually create that bond – sharing of electrons. Good. So in this case it's sharing between carbon and nitrogen. Proteins, of course, are huge in terms of their length and they get very floppy and tend to interact with themselves, creating pretzel-like arrangements which have a specialized three dimensional shape or confirmation which really dictates what that protein can do. I'm not sure what this is but it came to me in some sort of gift package. But I looked at it and said, "Well, there's a protein." It's a bunch of plastic pieces but if you play with it, you can twist it up into a lot of fun little shapes, just like a – ? Protein. And so what a protein can do is a function of its amino acid sequence, and, ultimately, a function of its shape. We're going to find that that's very important because if the shape is distorted, just like a key that doesn't fit a lock, then, of course, it's not going to work. As we leave this category, there's a long list of important cellular functions for proteins. And I can remind you of a few that you recall from anatomy. Remember actin and myosin? Were they proteins? Associated with what sort of cell?

>> [Inaudible].

>> Steven Langjahr: Uh-oh. You forgot. Actin and myosin are in muscle cells. So certainly some proteins are valuable to make muscle contraction possible: Skeletal, cardiac, smooth muscle. And certainly also many hormones are made of protein. A few that come to mind would be insulin and glucagon. But not all hormones are protein. We mentioned the other day that some hormones are steroids, lipids, in fact. Also to be mentioned are cell structures, that is cell membranes, as we'll learn tonight, are at least partially constructed of water in soluble proteins. You've all heard the term antibodies. Not antibiotic, anti what?

>> [Inaudible].

>> Steven Langjahr: Bodies. Antibodies are naturally formed proteins that give you resistance to disease. You have antibodies to tetanus. You have antibodies to polio. So certainly defense, body defense is made possible by antibodies. And the biggest functional category are enzymes which we've yet to really discuss but that will be our topic Monday and also our entire lab on Tuesday. Enzymes are metabolic catalysts. They make reactions happen faster than they otherwise could. And so simply put, life as we know it would be impossible without the catalytic properties of enzymes. All enzymes are proteins. Are all proteins enzymes? Clearly not because cell structure, antibodies, muscle contraction, and some hormones are further examples of protein functions. We always want to leave a little room for a discussion of solubility. And what was that rule or question that had to be answered to dig at water solubility?

>> [Inaudible].

>> Steven Langjahr: All right. So here's the truth: Some proteins are polar and some are not. So what does that lead you to conclude? Some proteins are water soluble, some are not. The protein that makes up your nails and your hair, it's called keratin. Is that water soluble? Well, mine is because every time I shampoo it just dissolves but yours is probably not. I'm joking. And then there's protein in the blood. Maybe you recall albumen and fibrinogen. These are water soluble proteins. Certainly actin and myosin, we mentioned those are part of muscle and they're not water soluble. If they were, then the whole muscle would just melt away so there are many examples. In short, some proteins are water soluble, some are not. And it's all based upon whether or not the molecule is polar or not. So if the molecule is charges, or polar, then water solubility is presumed. Let's leave protein and move into our final rather astounding category, nucleic acids. Nucleic acids are so-called because they were first discovered where in the cell? Where do you think based on the name?

>> [Inaudible].

>> Steven Langjahr: In the nucleus. And the two most famous, two important nucleic acids by name, I'm sure you know, the abbreviations RNA and DNA. But fundamentally what are nucleic acids? What are they composed of? What are the subunits? They're basically strands of thousands, tens of thousands of subunits called nucleotides. And so here in this two dimensional diagram we

boxed up a nucleotide. A given nucleotide consists of a sugar, either ribose or deoxyribose; a phosphate group, PO4; and one of four or five so-called nitrogenous bases. So as you look to this brief sketch, you see how many nucleotides linked together here? There's one, two, and what? Three. And this goes on and on. So certainly this representation is not a nucleic acid because, by definition you need what? You need – ?

>> [Inaudible].

>> Steven Langjahr: Thousands. But it's a good start. So nucleic acids, both DNA and RNA, are made of these subunits called nucleotides. I'm sure this molecule here needs no introduction. It's iconic. It's featured on billboards and magazine covers. Of course we're talking about deoxyribonucleic acid. I made that one myself from PVC at Home Depot. I'm so proud. And this little thing represents the subunits. What are the subunits? Nucleotides. So this would be the sugar. This would be the phosphate group. This would be one of the many nitrides in this basis which are linked and cause this molecule to form a kind of ladder, as you see. Naturally we'll spend a lot more time with this molecule because its form and function is critical for genetic information and also for protein synthesis. But let's move on. Essentially these nucleotides are linked together and they are between the phosphate group of one and sugar of the next. In case that's not clear, this is a sugar, this black piece, right. This is a phosphate. Sugar what? Phosphate. Sugar, phosphate. So the linkage of nucleotides is between the sugar of one and the phosphate of the next. This creates incredibly complex molecules which also have some very recognizable, very functionally significant configurations, specifically a double helix versus a single helix. A double helix is a twisted ladder as illustrated in my gargantuan model there. A single helix is familiar to you in a child's toy. What's that thing of steel that you pull apart and watch it march downstairs? A slinky. If you pull that apart, it is a single what? A single helix. Double, single. DNA, of course, is the iconic double helix. RNA is mostly a single helix as we'll see. And so, side by side in this two dimensional drawing we recognize and distinguish DNA from RNA. But what do they have in common? They are nucleic acids therefore they're made of what subunits? Nucleotides. The differences are in the nature of the nucleotides and certainly also the overall appearance and design of the molecule itself. We'll have a lot more to say about these molecules. For now we can certainly remind you that these are large organic molecules, indeed they are the largest organic molecules in the cell. And they are the most – what's the word here? Stable. What's the opposite of stable? Unstable. Would you like your DNA to be stable or unstable? Would you like to be the same person tomorrow that you are today? You think so. So it makes sense that these molecules are rather durable. But, that said, not unable to change. That is, we know that when these molecules do change, drastic consequences can occur. I'm speaking of the M-word. I suppose you're catching my drift.

>> [Inaudible].

>> Steven Langjahr: Mutation, which, of course, is not welcome in many set-

tings. Functions for DNA and RNA are two-fold which we've already mentioned. First, these molecules direct, and control, and make possible protein synthesis. This might seem like a simple statement but it couldn't be more important. What a cell can do, what a cell can't do is a function of the proteins that it has. And what determines the protein that a cell can make obviously is the DNA. Aside from that we know that DNA is used in the process of sexual reproduction so that we pass our DNA, that is we combine our DNA with our mate and that creates an offspring which is in then a combination of DNA from mother and father. So genetic information and the direction of protein synthesis. What about water solubility? What's the question you need to ask?

>> [Inaudible].

>> Steven Langjahr: Is it polar? And the answer is it is. So both DNA and RNA are water soluble which is perhaps a little bit odd, that is you might be thinking, "Well, wait a minute. If it's water soluble, then it would just dissolve in water." Yes, it does. But that doesn't mean it breaks up. Can something dissolve in water and still be chemically intact? Think of this: Does glucose dissolve in water? Is it still sweet? Is it still C6H12O6? So dissolving in water does not mean that it breaks into atomic particles or anything. DNA is indeed water soluble. Later in this course you're going to extract DNA from your own cheek cells and you'll find that you can't see DNA as long as it's in water because it's water what?

>> [Inaudible].

>> Steven Langjahr: So to get it to become visible to our eyes, we have to put it in alcohol where it is insoluble. So this may seem like a unimportant fact, but it's interesting that DNA is and remains completely water soluble. Now there's a final category here which is sort of miscellaneous which means things that don't fit the big four. What are the big four categories of organic molecules?

>> [Inaudible].

>> Steven Langjahr: Carbohydrates.

>> [Inaudible].

>> Steven Langjahr: Fats, proteins, and now, nucleic acids. Some, some molecules are indeed organic but don't nicely fit into any of those four categories. So these are called intermediates because they're precursors, subunits, or combinations of various smaller organic molecules. And alcohol is an organic molecule and your body makes certain kinds of alcohols. Organic acids and bases, some of which are part of the DNA molecule as we've mentioned. Lipoproteins, obviously a combination of what? What's the name imply? Lipo proteins, combinations of fats and proteins. And nucleoproteins, apparently a combination of nucleic acids and proteins. So that's why these are in this category, this intermediate category because the essentially combination molecules. They lead to the formation of more complex or they might be precursors I should say to other types of organic molecules. So with that now concluded,

we're going to transition without any real fanfare into our next major consideration for the rest of tonight: The nature and design of cell membranes. We're going to talk about the composition of cell membranes. We're going to talk about the architecture of cell membranes. And the functions of cell membranes as much as we can describe with what we know today. So the properties of cell membranes are fascinating. And certainly from the outset we'd have to agree and be impressed by the fact that the cell is defined by the cell membrane which really dictates what goes in and out of the cell. Yesterday we gave a word for at least the porosity properties of cell membranes. What word did we use to describe their permeability? Semipermeable, selectively permeable. And that's intuitively obvious, that is we know things have to get into the cell, we know things have to leave. So that may be true but we'll elaborate on the nature of that permeability as we move through this topic. So first, what can we say about the membrane structure? You might say, well, we probably have a pretty good photograph of cell membranes so we'll just take a picture and we'll go from there. In fact, it's not that easy because the cell membrane is a very thin thing and the molecular scale is such that even our most powerful microscopes are bound to disappoint here. Way before we were even able to take photos of cell membranes there was naturally an attempt to at least sort of tease out the composition of cell membranes. Easy to do. You just put cells in a blender and then you essentially destroy the cells and you pour out the stuff and you figure out what then the cell membrane must have been made of. And a long time ago this recipe was revealed. Some membranes are made of 50% protein, 45% lipid, and the rest essentially carbohydrate, monosaccharide chains, as it turns out. Now maybe that's interesting, maybe not. We do see that the lipid category is further delineated. It's not triglyceride. It's phospholipid. And also a smattering of this steroid called cholesterol. So although this is true and has been confirmed time and time again, it doesn't really give us any real insight to the design of the membrane. It's kind of like driving through an area where houses are being constructed where you see lumber stacked there, where you see dry wall, and cement, and all sorts of building materials. So you know what the house is going to be built of but just looking at those materials, do you have any idea of what the house is going to look like? Any idea about its architecture? Not at all. So this doesn't really give us any clue as to the architecture, only the basic chemistry, the basic composition of the membrane. So what about the architecture? Are we left to speculate or can we at least start with photographs that we've taken? We have. This is the best photograph ever taken of a cell membrane. And you're disappointed I'm sure. In fact it's hard to know what it even is. I'll give you this much: This is the outside of the cell and that's the inside of the cell. The best photograph ever taken. All we can really tease out of this is that apparently it's got two sides; that is two membranes just like a sandwich. And that, of course, has been confirmed over and again. But yet we've never seen the molecules. We know these molecules are there so we have to rely on their known chemical behavior to sort of speculate as to how they actually come together. So a long, long time ago it was deduced that cell membranes are indeed two-sided lipid sheets with proteins apparently embed-

ded in them just as doorways are embedded in the wall of a building. And this mosaic, this model, which has been reproduced and essentially spruced up in textbooks, is essentially the modern version of what cell membranes look like on a molecular level. The key player, the basic backbone of a cell membrane are these molecules which you can see and remember are phospholipids. Now a phospholipid is just like a triglyceride; that is it's made of a glycerol, two fatty acids, but in place of the third fatty acid it has a phosphate group. Now the phosphate group confers charge, electric charge, and therefore, instead of the molecule being neutral, it has some electric charge which is called the charged polar end. What do we know about charge and its relationship to water solubility? Any molecule which is charged or polar will have an affinity for, that is an attraction to, water. In this simple diagram we show water, H2O, on the outside of the cell. We show water, H2O, on the inside of the cell. And why are these phospholipids lined up so neatly side by side? These are essentially making contact with, forming what sort of bonds with water molecules?

>> [Inaudible].

>> Steven Langjahr: Hydrogen bonds. Now why don't these molecules just disappear in the water entirely? Well, they do have a charge end, but they have a what? A uncharged neutral end. So perhaps in biology these sort of funny descriptions are recalled. The charged end is said to be hydrophilic and the neutral end is said to be hydrophobic. And that is what keeps these molecules from just disappearing, completely dissolving in the water, both on the outside and on the inside. They line up and form a film, F-I-L-M, which is a double layered film with phospholipid heads pointing outside and phospholipid heads pointing inside. The important thing about this reality is the fact that each of these phospholipids is not bonded to the one next to it at all. So although it's hard to animate this, if you were to push right here, would this be stiff or would it be rather floppy and flexible?

>> [Inaudible].

>> Steven Langjahr: Because there is no rigidity, no bond between this phospholipid and that. So it is indeed very filmy, very soft. If you could jump on a cell membrane, it would be like jumping on a waterbed in that it would give and move pretty much like this model which is a commercial attempt to show what we're talking about. Maybe from where you're seated it's hard to see but we have these Styrofoam balls with these red tails on them. So what are the Styrofoam balls meant to be?

>> [Inaudible].

>> Steven Langjahr: Charged polar ends. And the red tails are the uncharged non-polar. The non-polar tails are hydrophobic. The Styrofoam balls are hydrophilic. And as I shake or move this container, you get the idea that this is indeed very fluid, very flexible because of this design. That then is the known basic construction of a cell membrane: A two-sided lipid sheet with embedded proteins. Here's another fancy artist's conception, again showing the phospho-

lipids as we've described them. But notice protruding through here like hotdog buns, are these protein molecules which I've compared already to a doorjamb. Does a doorjamb go through this wall? Does it sort of frame it up? And the obvious suggestion here is that these proteins serve as channels, pathways, in other words, doorways into or out of the cell. Indeed they're called protein channels because they're channels made of protein. These designs can get really fun if you look at other attempts to describe them. Here again we see the phospholipid backbone. In this model we see cholesterol mentioned. We mentioned that it's also a part of this lipid fraction there. Cholesterol embedded inside here tends to make this tighter, tends to seal it better, tends to make it stronger, and therefore cholesterol has that significance to the cell membrane. But these larges globs here are protein, some of which serve as pathways, some of which serve as receptor sites for various activities, various responses that the cell may have. So what you have on your page shows, again, this hydrophilic arrangement of phospholipids nudging up to these yellow guys. What are the yellow guys?

>> [Inaudible].

>> Steven Langjahr: Water. And is water on the inside? Sure. Outside? Yeah. And so this creates the fluid film which has two distinct sides. Penetrating, indeed poking through to the outside and inside, are these protein molecules, some of which are for doorways, some of which dictate the passage of ions or other molecules, some of which provide receptor sites for activities, recognition of other molecules, and so on. So as we leave this architectural description, we want to say in conclusion that this design is completely self-assembling. If you put phospholipids in water, this will happen spontaneously. It doesn't take any outside intervention because these molecules spontaneously line up, that is the hydrophilic heads line up with the water, and the hydrophobic tails stay away from water, therefore creating a membrane which essentially defines the cell on all sides. And, interestingly, this membrane has a fair degree of tolerance for stretch. And if it is injured, it can – what's this word here? – it can reseal. You could almost imagine that, at least with this model. You can see it's sort of moving there. If I took the top off, and I don't want to do it, but if I stuck my finger, would I be able to easily move through these two parts of the membrane? But if I pulled my finger out, would everything come right back together? So that's what we mean by the capacity to reseal. It's not indestructible, as we saw yesterday. Can this membrane be blown apart with too much internal pressure? And we describe that as cytolysis or hemolysis, osmotic hemolysis as it applies to the red blood cell. So not indestructible, but certainly quite durable, capable of forming spontaneously, capable of resealing with minor assaults. So this leads us to the next topic. What about the known functions of the cell membrane? How does it do what it does? What are some of the astounding capabilities of cell membranes? It is, of course, a membrane made of lipid, a lipid bilayer. So as we speculate on what molecules would pass easily, we're not surprised to read that this membrane is very permeable, readily permeable, completely permeable to all neutral molecules. I mean, after all what's it made of? Mostly it's made of

phospholipid. And you've heard the expression perhaps that like dissolves like. So if it's made of lipid, would it accommodate lipid? Would lipid molecules or other neutral molecules be able to go right through? And the answer is yes. So, in short, anything that is neutral, any molecule which is non- what? Non- ?

>> [Inaudible].

>> Steven Langjahr: Polar has no trouble getting through the cell membrane at all. But when it comes to other molecules which are polar, there's quite a limited permeability, we say selectively permeable. And in ways that we're about to describe, this permeability variation is a function of the molecules in question and the means by which they go through the cell. This simple bar graph is indeed simple but it provides at least an introduction to where we're going. On the vertical axis we see permeability, zero to 100%. And based on what you read there, what kinds of molecules enjoy no impediment, that is have no impediment to passage? Which kind of molecules readily and completely pass through the cell membrane?

>> [Inaudible].

>> Steven Langjahr: Neutral lipid soluble molecules, a fact we've already discussed. But what about polar molecules? We see that those have trouble, certainly not free permeability. And the next two columns, blue and green, show the difference between what is it? Small polar molecules and what?

>> [Inaudible].

>> Steven Langjahr: Large polar molecules. So first, do polar molecules have the ability to get through? Yes. Better or worse than lipids? Worse. And is there any further information here? What's the only difference between a small polar molecule and a large polar molecule? Size. So clearly these two facts suggest that apparently size is a factor, just like we can only drive certain things through that door. Can you drive a motorcycle through that door? Can you drive a car through that door? Not easily. So this information suggests that however these polar molecules are getting through, size seems to be a factor. It also points to the fact that most ions share a higher degree of permeability than the larger polar molecules. So how does this fit with what we know to be the design of these membranes, specifically the protein channels which we alluded to? Protein channels are called that because they're made of protein, protein which spans – that means punctures all the way through from the inside out. And as such, they permit the passive diffusion of specific ions from – or I should say down a concentration gradient from a what?

>> [Inaudible].

>> Steven Langjahr: High to low. Protein channels are often compared to gates because a gate can be what?

>> [Inaudible].

>> Steven Langjahr: Opened or closed. In this illustration we see the protein channel apparently open. Over here it's apparently closed. We call this gating. And so these channels are indeed gated. They're opening or closing triggered by various factors allowing for the passage of ions. What allows these ions to pass is the channel. But what determines the direction in which these ions move? Why would they move predominantly out? Why would they move predominantly in? What dictates that is not anything but the simple what? Concentration. So if there's a higher concentration of an ion out here, if allowed to, it would then move down a concentration gradient provided the channel is open and certainly disallowed when the channel is closed. Protein channels do not carry protein. They're called protein channels because they're made of protein. Their design is to control the influx or efflux of charged atoms, i.e., ions. The next kind of transport is much more sophisticated and involves what are called carrier molecules. Not protein channels, but something more akin to a revolving door that you might see at a hotel. In this enlargement we see the cell membrane. Once again, the protein channel which we've just discussed. But on either side an imaginary depiction of what are called carrier molecules. Carrier molecule make possible what's called carrier mediated transport. Mediated means to assist. CMT, carrier mediated transport, is what is responsible for the transport of small and especially large polar molecules which would have no chance to enter the cell by any other means. Remember, protein channels are not intended for large molecules. They are there simply for the entry or the loss of ions. But yet our graph shows us that there are large molecules entering or leaving the cell and they do it by CMT. What's that?

>> [Inaudible].

>> Steven Langjahr: Carrier mediated transport. This graphic is, of course, static but it's attempting to show that large polar molecules can bind to particular sites on these carriers and then that carrier can somehow bring that molecule in or move in such a fashion that it moves it out. Again, something like a revolving door at a hotel where you're more or less escorted in and out. Michelle?

[Inaudible]

Well, these are large polar molecules. This is meant to be a small polar molecule. And so clearly in this illustration these guys would not be accommodated by this particular carrier. A good question because carriers are very specific and we'll come to that topic pretty much right now. There's two types of CMT. What's that? Carrier mediated transport. The first is called facilitated diffusion, as opposed to passive diffusion. We mentioned that a moment ago. Passive diffusion means the molecules are moving on their own from a what? High to low. Facilitated diffusion involves some kind of escort, some sort of assistance. Facilitated diffusion requires and utilizes the help of carrier molecules but still these molecules obey or otherwise can only escort these molecules not up, but what? Down a concentration gradient. This, then, enables this process to occur without any effort, without any energy expenditure. So facilitated diffusion used

no cellular energy. In other words, it doesn't gobble up ATP, a molecule we'll be dwelling quite a bit on later. Some examples of organic molecules which are transported this way, first, glucose. Glucose is an organic molecule, yes? Fairly large and therefore no way to get through the protein channels. Remember, these are reserved for ions alone. But intuitively is glucose able to access cells? Does glucose get into the cell? Yes. Turns out it does so through facilitated diffusion, escorted then by the involvement of carriers but not requiring the use of ATP. Now here's a curious thought as apparently glucose moves into the cell, why? Not because the cell needs it. Apparently because there must be a high concentration of glucose what? On the outside favoring the passive movement that is the facilitated movement of glucose into the interior. But is it possible for glucose to leave cell if there were a high concentration of glucose developed there? The answer's yes. But that rarely happens. And it's a simple reality. When glucose comes into the cell, does it accumulate there or does it get used to make chemical energy? So the gradient almost always favors, not the loss of glucose, but the entry of glucose. In short, can glucose go both ways through the cell membrane? Yes. But which way does it normally go? Outside to in, escorted there by these carrier molecules. And the same, the same applies to nucleotides. Nucleotides are the subunits of what? Subunits of nucleic acids. And they're brought in, again, not because the cell needs them, but because there's a high concentration of nucleotides where? Outside. Why doesn't that concentration build as those nucleotides come in? What happens to these nucleotides, they're not broken down but they are used almost immediately to make what?

>> [Inaudible].

>> Steven Langjahr: So there's always this gradient which favors the entry of nucleotides just as it favors the entry of glucose. Second kind of CMT, active transport. A word like active is the opposite of one like passive and so active implies there's some physical action going on here which is quite involved. In other words, effort is being expended. And that's indicated by the remarkable difference of active transport. It moves molecules not down a concentration gradient, but what? Up a concentration gradient. That's like pushing a bowling ball up a hill, certainly requires effort. And, therefore, this kind of mechanism is often referred to as a pump such as something that pulls water out of the ground or oil out of the ground. Is effort or energy required to do that? Certainly. And the energy that's used is this cellular currency, this energy known as ATP. This energy is necessary to break the bond, break the attachment of the molecule being carried with the carrier that is assisting in this movement. Examples of active transport include the entry of amino acids. Amino acids are the building blocks of what?

>> [Inaudible].

>> Steven Langjahr: Why do cells need amino acids? What are they going to make from amino acids? Protein. Is there a constant synthesis of proteins going on in most cells? Yes. Is there a hunger, is there an appetite then for amino acids? Yes. And this process is particularly valuable because it can

move amino acids from a what? From a low concentration inside the cell to where there may be a high concentration. This helps to stockpile, helps to build up, and therefore make available a large inventory of amino acids. This is also the mechanism which explains what we introduced yesterday. We said sodium ions get into the cell rather easily but there's a mechanism in the membrane which literally pumps, actually pushes those sodium ions out. And so now we're reminding you that that is active transport, the removal of sodium ions which is not without expense. And what is the cost, what is the expense involved in active transport?

>> [Inaudible].

>> Steven Langjahr: ATP. So at this point we could come up with a simple, well, couple of scenarios. What if the cell were short of ATP? Never mind all the things that might come to mind, let's just take this one at a time. If the cell didn't have any ATP, or short supply, would it be able to acquire amino acids as well as it should? Therefore, what would suffer? If cells can't get amino acids, they can't make?

>> Protein.

>> Steven Langjahr: And if they can't make protein, they can't synthesize enzymes, or antibodies, or whatever. You can see that would be devastating. And what about sodium? Active transport doesn't bring sodium in. Active transport puts sodium out. What if ATP were unavailable to do that? Would sodium get in? Yes. Would it be pumped out? No. So where would the sodium accumulate? Inside the cell. What would that do to the cell [inaudible] concentration over time?

>> [Inaudible].

>> Steven Langjahr: And what would water do as the result?

>> [Inaudible].

>> Steven Langjahr: And what would the cell do as the result?

>> [Inaudible].

>> Steven Langjahr: So you can see that the removal of sodium ions protects the cell from that osmotic pressure which would be fatal to a cell. That is called cytolysis or hemolysis as the case may be. So certainly active transport is important, at least in these two examples. Active transport also incidentally actually moves some potassium ions in. And I know this is abstract right now, but the balance between sodium out and potassium in really helps establish the electrical properties of a cell, especially a nerve cell. Before we finish this, before we move on, there's a couple of things to say about both forms of CMT. CMT? Carrier mediated transport. What are the two forms? Facilitated diffusion, active transport. Both of these exhibit something called carrier specificity. And they both exhibit something called carrier saturation. Let's talk about each of these ideas. Down here we have an attempt to illustrate each of these concepts.

On the left carrier specificity. These geometric units here are meant to be protein carriers. And the spattering of shapes out here represent the very numerous types of organic molecules that are available or otherwise here. Based on what you see, these three carriers are the same and essentially, apparently, they are dedicated to, specific to, able to carry only which of these kinds of molecules? Only these square guys. Will they carry the circles? No. Will they carry the triangles? No. What's that concept called?

>> [Inaudible].

>> Steven Langjahr: Carrier specificity. It's really rather simple. The carriers that carry glucose are not going to carry what? Nucleotides. The notion is carrier specificity. It's important to realize incidentally that these carriers are a protein and they can be installed, that is they can be beefed up or removed just like a rancher might install gates or take gates out. In other words, the number of carriers is subject to change. But at any given moment the number of carriers is pretty well fixed which leads us to this next idea, something called carrier saturation. The word saturation we use a lot. If you take a sponge, a kitchen sponge, and you put water in it and you can't get it to hold any more water, you might say, "Well, it's – ." What? Saturated. So the word is not unfamiliar. But this idea can be confused because we're not talking about cell saturation, we're talking about carrier saturation. The best way to illustrate that I think is with a graph of this concept and its limitations. So a simple set of coordinates whereas here on the vertical axis we'll have uptake of something and then here on the horizontal axis we'll have the concentration of that something. So what does that mean? If we increase the concentration of the molecules that are available for transport, will their uptake be increased accordingly? If we add a greater amount, a higher concentration of these molecules, will that result in a greater uptake? Yes. But although that is true to a degree, the greater the outside concentration, the greater the what? Is this going to go up indefinitely in a linear fashion like that or will there be some point where that stops increasing in this straight line fashion? What would cause this to change? Would it do this? Would it do this? Or would it do that at some point? X, Y, Z? Z. And when that level occurs, when adding more causes no further uptake, what's the explanation? We're adding more and adding more but we're not seeing any further increase in the uptake of these molecules. What's the explanation? Is the cell full? Is the cell saturated? No. What's saturated is what? Carriers. I know this is a silly analogy but I always think of it. But it happens every time I go to the grocery store and then we have check-out saturation, you know what I mean? Not getting that? You want to get out of there, right. Why is there this long line? What's the [inaudible], what's the problem, what the hold up? The number of checkers. And so that's essentially an example of that. So the uptake of these molecules is limited, not by the capacity of the cell, but by the number of available what? Carriers. If own an amusement park and you want to invite people in, what's the better way to get them in and make them happy? You going to have one entrance or a lot of entrances? A lot of entrances. So in that sense carrier saturation simply reflects

a limited capacity, a limited number of available carriers. The carriers are busy. The carriers are occupied. They're working at their fullest capacity. And there is no way to overcome carrier saturation except by what? Can we build and install more carrier molecules? Yes. An actual example is something as basic as exercise. Do muscle cells need glucose? Yes. What do you think happens to the carrier molecules that transport glucose if you exercise? Does the cell make more of these carriers or less? More. And therefore allows the uptake of more what? Glucose. So this is quite appropriate, quite logical. And only points to the fact that carrier saturation is a temporary limitation that can be adjusted through activities of the cell, through activities of the body. We've covered a lot and so let's pause before moving on and reflect on what we've said. What's the cell membrane made of ?

>> [Inaudible].

>> Steven Langjahr: Phospholipid. A little bit of cholesterol in there but those molecules, those hydrophilic and hydrophobic molecules, create the basic flexible container known as the cell membrane. Is the membrane perforated by these doorways? Yes. These are called protein channels. Do they carry protein? No. They allow the transport, they allow the diffusion of I-word, ions. They can be opened and closed, said to be gated. Aside from that we have other proteins that don't form channels. Other proteins form carrier molecules. We spoke of carrier specificity. What's that mean in your own words? This carrier is specific. That means it carries what? That but not what? That. All molecules that are involved in CMT exhibit some degree of potential saturation, meaning they have a limit to their ability to do what they do because they become essentially involved, occupied, and completely overwhelmed. This dictates the overall uptake of molecules. Okay. Quick questions then. Which of these types allows for the passive diffusion of ions?

>> [Inaudible].

>> Steven Langjahr: Protein channels. Which of these accounts for the cell's acquisition of nucleotides? Which of these facilitate a diffusion? Which of these is accountable, or accounts for the acquisition of amino acids? Active transport. Which of these can move molecules up a concentration gradient? Up a concentration gradient. Active transport. Which of these does not require energy? Facilitated diffusion. Which does? Active transport. So all of these things really assert the magical and incredible properties of the cell membrane. It's not just a bag which encloses cytoplasm. Ooh, I forgot I had this little graphic. Watch this, it's kind of fun. Well, okay. It's not that fun. So that's meant to show how it spins it in. But remember, and incidentally, facilitated diffusion, is that a one-way or a two-way street?

>> Two-way.

>> Steven Langjahr: It's two-way. Can it take molecules from the inside out? Yes. Outside in? Yes. What determines which way? Concentration gradient, nothing more. Finishing up with a final property of cell membranes, some-

thing you knew but deserves a special merit badge so to speak because it's quite, quite stunning to witness because it is something that is photographed and you can see videos and actual animations of it. This is a cell, happens to be a white blood cell, a macrophage, photographed over a minute consuming, actually taking in and destroying a bacterium. The name of that process I'm sure you know is called phagocytosis. But phagocytosis is just part of a process that is more generically known as endocytosis. Endocytosis is essentially the internalization of something on the outside, something that's relatively huge and it may not be just a molecule but actually a microorganism as in the case illustrated here. My simple graphic is just that, simple. There's the cell. And then here's some stuff. And then the membrane is actually puckering in and aggressively internalizing it. The name of that process is endocytosis. It is subdivided into two forms depending upon the nature of the material being moved. If the material is solid and bulky, then it's called phagocytosis. If it's liquid, then it's called pinocytosis. But essentially this process takes things from the outside and moves them in by actual aggression, actual physical change in shape of the cell membrane which requires that this membrane be actually dynamic, actually capable of reaching out, surrounding, and then pinching off, internalizing this material. Cells that are famous for this are the white cells, especially so-called macrophages. And this is an actual scanning electron micrograph of a macrophage apparently tackling something that's bigger than it really should try. It would be like you trying to swallow a two by four. But anyway, it's dumb enough to think that it can do it. And so it's attempting to do what? Attempting the process of phagocytosis. What does this achieve? Why is it important? Well, it provides defense against infectious agents more often than not. And so white blood cells have a reputation for providing this kind of defense against infection. The opposite of endocytosis is exocytosis. And that was easy for me to animate because if I already had this, I just had to spin it in reverse. So exocytosis is essentially surrounding something in the cell, essentially putting a bag around it and then kicking it out the door. It's kind of like what you do at home? Don't you bag your trash? Then you throw it out the door, more or less? Exocytosis. And this requires the same degree of effort by the cell. And, needless to say, energy is involved in both of these processes. But it provides a means to expel molecules that are made in the cell. And not only molecules made in the cell, but something rather astounding that you might recall from anatomy. A red blood cell, does it have a nucleus or not?

>> [Inaudible].

>> Steven Langjahr: No. Did the cells that led to that mature red blood cell at one time have a nucleus?

>> [Inaudible].

>> Steven Langjahr: What happens to that nucleus is that literally it gets kicked out. And the reason for that you might have been told in anatomy, is that the nucleus is just excess baggage. After all, the red blood cell has to fold and fit through tiny spaces. Would the nucleus be an asset or a liability in doing

that? So the nucleus is removed in the final stages of the creation of a red blood cell. And this is a photograph of that event. It doesn't seem like, it looks maybe bizarre. This is the cell. This is the what? Nucleus which is being kicked out through the process of exocytosis. Pretty incredible something that large can actually be thrown out of the cell and allow the cell then to reseal, reform, and carry on the functions that we know red blood cells can do. But far and away the most important example of exocytosis is something that's happening in your brain and throughout your nervous system every nanosecond of your existence. You know about nerve cells. You know that they do not physically touch. There's a gap called the synaptic cleft. And even from anatomy or biology you know that on the presynaptic side there are these containers of molecules, containers called synaptic vesicles containing neurotransmitters: Serotonin, acetylcholine, epinephrine, norepinephrine, et cetera. And these molecules are being sprayed, that is released into the synaptic cleft through what process?

>> [Inaudible].

>> Steven Langjahr: Exocytosis. In fact, if this process fails, and it sometimes does, then obviously there'd be no communication between that cell and the other. Does this lead to devastating neurological diseases, things such as Parkinson's, or schizophrenia, or so on? So it's impossible to overestimate then the importance of exocytosis. And it's incredible, not only that it happens, but that it happens so quickly. These molecules are released and incidentally these same molecules that are active on the postsynaptic cell then turn around and get what? Get reabsorbed by endocytosis to then make available for exocytosis. So certainly neurons testify to the importance of endo and exocytosis. That's it. That's it for tonight. Quite enough. So if you have questions? Great. Just to remind you, what's going to show up on the webpage on Saturday?

>> [Inaudible].

>> Steven Langjahr: All right. Also you should be doing these review questions. And where are the answers to those review questions?

>> [Inaudible].

>> Steven Langjahr: Well, they're going to be on a flash drive that you give me and they won't be if you don't so. I'll be happy to do that tonight if you have a flash drive with you. You have one of those? Just let me finish this, please, and I'll be with you in a sec.