PROFESSOR: All right. So here's the box score from the celebration on Monday. Class average improved considerably. A number of people moved from the sad face to the smiley face. I would still tell anybody who is down over here that the final exam is coming, and if you perform well on the final exam, we'll take a look at the overall performance of the semester. So get in and talk to us, if you want to, to see what we can do to help you succeed here. But it takes a little bit of effort on your part as well.

I think that's all I want to say. There will be a weekly test, a weekly minor celebration on Tuesday, as normal.

So today we're going to start the last of two units. We have two units left before the end of the semester. And this one is biochemistry. And it's one of these integrative topics that's going to bring together a lot of the material that we've looked at in the past.

And biochemistry overview, it's the chemistry of living organisms. And the first thing to point out is that biochemistry is governed by the same laws that apply to inanimate matter. And apropos of that, I'd like to read something that was written by the Nobel Prize winner, Richard Feynman.

"If in some cataclysm, all of scientific knowledge were to be destroyed, and only one sentence passed on to the next generations of creatures, what statement would contain the most information in the fewest words? I believe that it is the atomic hypothesis, or the atomic factor, whatever you wish to call it, that all things are made of atoms. Little particles that move around in perpetual motion, attracting each other when they are a little distance apart, but repelling upon being squeezed into one another."

So that's the first thing to point out. That it's the same chemistry that we've been learning up until now. And in fact, I think I've got a a slide that captures the-- there's the Feynman quote, the last part of it.

Second thing is, by way of introduction, you see a boom around us today in biotech. And what is the biotech? It's the molecular biology, it's the commercialization of molecular biology. Biology, when I was your age, was classification, taxonomy, naming things and figuring out what bin they fit into. Today it's not that. It's molecular biology. Well, what's the molecular science? Molecular science is chemistry, and it's solid state chemistry. Biology is solid state chemistry. We are solid state devices made of soft matter with an endoskeleton that's ceramic, and so on. But we are solid state devices. So this is solid state chemistry and material science, and that's why we talk about it in 3.091.

And why now? Why is the biochem revolution only now? Well, it has to do with complexity. You can think about complexity from the standpoint of materials, and in fact, lay out the ages of man. The Stone Age. The Stone Age precedes the Bronze Age. Why? Because stone is found in nature naturally. To use stone requires only to cut it and change its shape. But you make bronze, you have to engage in chemical processing. There's a chemical conversion that requires a higher level of societal sophistication. And then iron follows bronze. Why? Because iron melts at a higher temperature, so you have to have a higher level of technology in order to make the furnaces and to conduct the reduction reaction to extract iron.

And then comes polymers. Polymers, the birth of synthetics, come when? First polymers were around, what, 1829, when the pharmacist was playing with the styrene. And then it explodes in the 20th century. And then mid-century we get silicon. And silicon is even more sophisticated, because we had to understand quantum mechanics to even understand that we needed silicon. We could convert beach sand into silicon back in 1500, but who knew what to do with silicon in 1500?

And then finally comes the end of the 20th century, and now we're dealing with this stuff. So that sort of puts things in perspective.

So what we're going to do today is start the treatment of biomolecules. And the first thing I want to say, is we're going to be talking about macromolecules but not polymers. So all polymers are macromolecules, but all macromolecules are not polymers. What's the difference? In polymers, we have a common repeat unit, whereas in the life sciences, Mother Nature is a polymer engineer gone wild. She takes different functional groups and puts them at every stage along the way, as opposed to polyethylene, where it is the same functional group at every stop. So it is exploded polymer chemistry, macromolecular chemistry.

So there's four classifications of biomolecules. The proteins, carbohydrates, lipids, nucleic acids. And we're going to look at three of the four. We'll start today with proteins. We will study lipids and nucleic acids, but in the time allowed, we're going to lose the sugars. So you'll take 7.012 or something to satisfy the Institute biology requirement, you'll go much more deeply into it. But I think you're going to have very good preparation after three lectures here, and you'll be able to put together a lot of the material that we've looked at prior.

So the first thing we're going to look at is proteins. Proteins are macromolecules, and they're formed by polymerization of monomers known as amino acids. So before we can talk about proteins, we're going to first look at amino acids. So let's do that. And amino acids are substances that have the following skeletal structure. I'm going to start a new board for this.

So this is the basic skeletal structure of the amino acid. It's got a central carbon, sp3 hybridized with four struts on

it. Down in the lower left corner, we have the amino group, which is nitrogen and two hydrogens. So there's one, two, three bonds off the nitrogen, and I want to emphasize but it's still got this unpaired set of electrons, which we know makes this thing a Bronsted base. And it's going to have a site here for proton attachment. And that's a big feature here in amino acids. So this is the amino group. And it acts as a Bronsted base. So it's a proton attachment site.

Second strut is hydrogen in every amino acid. The third site, over here, is the carboxylic acid end, and that's carbon with a double bond, and one, two, three, four, all right? Every carbon needs four struts, and the fourth one has the OH. And this is the H that can fall off. So this is the proton donor here. This is carboxylic acid end.

So this is three of the four ends of the carbon bonds are fixed in all amino acids. And then the fourth one is free to be specified. This is all R. R is a placeholder. It stands for the substituent. This is the substituent. And this is nature's choice. So you can put anything here. There are hundreds of amino acids. There are only 20 seen in protein. But anything that goes up here, with this structure, is an amino acid. I don't care. You could put a cyanide up here, for all I care. It'll still qualify as a amino acid if these other three sites are filled in the following matter. So 20 seen in amino acids. 20 of those in amino acids.

And now I want to look at the substituents and break those into categories. So there's four categories of substituents. In other words, the 20 here can be broken into four categories. Four categories of R. And we can group those by their chemical properties. The first group, I took this from one of the other texts. Yeah, this is from one of the other texts. So there's the 20 amino acids.

So I'm now highlighting some of the ones that are nonpolar. So what do you see there? The nonpolar ones, you see for R. The R group is above here. so? This is just plain hydrogen, which is nonpolar There's a methyl group, CH3, so that's alanine. Here's a methylene with two methyls, so this is alanine, and so on and so forth. So the different groups hang off that R position at the top. So these are nonpolar, and this also is characterized by being hydrophobic. So that end becomes hydrophobic when we use nonpolar group.

The second option is to have polar substituents. And some of them even have hydrogen bonding capability. That's the second category. And of course those are going to be hydrophilic.

The third group is charged. The third group actually has a charge end, which becomes a negative ion in aqueous solution. And these are going to be strongly hydrophilic. And also--

[BREAK IN VIDEO]

PROFESSOR: Number nine, number nine, number nine. Can you hear? Yes? Yeah, that's good. Hydrophilic and acidic. The acoustics here today are very different, huh? We're missing a few bodies. We need to put the crash

test dummies in here, and then we'll have the same acoustic sound.

All right. And then the fourth category gives you a cation, R plus, in aqueous solution, which then, strongly hydrophilic and basic. So we'll go through.

Now, our bodies can synthesize only 10 of the 20 amino acids, and then the other 10 we have to get from diets. So when you look at some of these fad diets, you might want to check and make sure you're getting all of the proper nutrients.

Now another of the structural features of amino acids that's important is chirality. Chirality is a feature of amino acids. And what is chirality? I'll show you by way of example. Chirality talks about handedness. Comes from the Greek word for glove. So let me show you molecules that have the chirality that distinguishes them.

So I'm going to give an example with alanine. With alanine, the R-substituent group is equal to the methyl, CH3. So I'm going to put CH3 up here for the substituent, and then the other three stations are as we know them to be. So there's the amino group, there's the hydrogen, and here's the carboxylic acid.

And note, look at the compact notation here. We write COOH. This O is not bonded to the O next to it. Both O's are bonded to the carbon, but this is compressed notation. COOH, and then this. So this is alanine, and I could just as easily write the molecule in the following manner. I would still satisfy the requirement that I have an amino group, a hydrogen group, a carboxylic acid group. Actually, if I want to get really fancy in chemistry, I could write it this way. COOH, and everybody knows H can't bond to two species. In fact, it's the carbon here. But it's OK. It's compressed and in the methyl group up here.

And what you notice is that the molecule on the left is distinguishable from the molecule on the right. These are not the same molecule, even though the same substituents are here, and the other features are preserved. This cannot be superimposed. So you could distinguish these two. If I just threw them on the floor, you'd be able to pick them up and say, one has the amino group in this orientation, and if I put the other one, with the methyl above and the hydrogen below, I will have the amino group on the other side.

And these things also are optically active. And through their optical activity, we give them their names. And so let's take a look here. All right. This is just a little bit more of the amino acids.

And actually, one of our former 3.091 TAs, Andrew Magyar, who just defended his PhD thesis. I was on his committee, and he did a splendid job, and used his 3.091 principles to get through his advanced biology.

This is a list which is going to be part of the PDF that I'll post. But there are 20 amino acids, and as you know, there are 26 letters in the alphabet we use in English. And so if you want to write them in compressed form, you

just use one of these letters. There's the three-letter notation as well, so ALA is alanine.

And in the past, I used to have contests in 3.091 to ask students to give me the airports, if these were three-letter airport codes. You see, it always comes around Thanksgiving, and people are busy heading to-- and it turns out that 19 of the 20 amino acids have airport codes that correspond to the amino acid three-letter abbreviations, with the exception of glutamine, GLN. There's no airport that has GLN as its thing. That's a piece of trivia that will get you the last wedge in Trivial Pursuit. And then this is the one-letter abbreviation.

So Andrew has put them in this form. So there again, I have the basic, the acidic, the aliphatic are the ones that are nonpolar. And this is another way to look at it. And here's the base structure, and here's the whole thing in monochrome. All right. So that's part of the thing.

OK. So here's what I'm talking about. The mirror plane. So this box can be mirrored as shown. But as soon as you put a distinguishing mark in the lower right-hand corner here, the box on the left is not superimposable to the box on the right. They are distinguishable. And so these things will have different chemical reactivities, not melting point boiling point, but how they react with other molecules.

So here's the chirologics. Your gloves are chiral. If you try to put your right-handed glove on your left hand, it's a poor fit, whereas the flask here is achiral.

And now here are some molecules, just to show you how this translates into chemistry. So this molecule is chiral, this molecule is not chiral. And it has to do with the number of positions that are distinguishable.

And how does this fit into the grand scheme of things? It's sort of a form of stereoisomerism, isn't it? Remember, we looked at the geometric isomers. Here's an example. This is dichloroethylene. We looked at butene. But here we've got cis-isomer, here we've got the trans-isomer, where the chlorines are on opposite sides of the double bond here. They're on the same side of the double bond here. These are types of optical isomers. These are the mirror images, the same functional groups, but in this case, in one orientation, the plus enantiomer, here's the minus enantiomer.

They're called enantiomers because it comes from the Greek word for mirror. So we're using the Greek word for glove and the Greek word for mirror. Now we'll talk about the optical activity, and then we'll take a few notes.

So what's the optical activity? It turns out that if you put these in aqueous solution, they will cause the polarization vector of light to rotate. So here's a cartoon that shows a light source with unpolarized light, and then the light goes through a polarizer, which then forces only vertically polarized light. In other words, the electric factor is in the vertical orientation. And so now this electric vector enters this tube containing an aqueous solution of

something that has optical activity. And the degree of rotation is proportional, obviously, to the concentration of the chiral species, and also the path length. So if you have a dilute solution on a long path, or a concentrated solution on a short path, it's the number of collisions. And ultimately, you have a degree of rotation, et cetera.

And so based on how the electric vector changes is how we got the names for the various enantiomers, because we've got to name them somehow. Otherwise we can't distinguish one from the other.

So it turns out that the way I've drawn this one, with the amino group in the lower right, and the carboxylic acid group in the lower left, causes the electric vector to rotate clockwise. So I'm going to write h nu, just so that you know, or if you want to put the electric vector or something. It rotates page to the right, and so the Latin word for right is *dexter.* So this is called dextrorotatory. This is the dextrorotatory enantiomer. So now you've got really nice terminology to use at the table over the Thanksgiving turkey, all right? So this is the D-form, D-circle, or, as every right-handed person knows when speaking to a left-handed person, this is the positive direction, OK?

And now this one causes an anti-clockwise, or counterclockwise rotation of light in an aqueous solution of this. And rather than use *sinister,* which is the Latin word for left, and it has all these negative connotations, they went to the Slavic, and shows levorotatory. So this is levorotatory, L-form, or minus N, with apologies to the left-handed people in the audience. That's what it's called.

OK. So these are called enantiomers, and hence, you understand the choice of Man in the Mirror for the opening music.

So 19 of the 20 amino acids are chiral. The only one that's non-chiral, the only non-chiral amino acid, is glycine. Glycine has hydrogen as a substituent. So now you have hydrogens above and below, an amino acid here, and carboxylic acid here. And this one is achiral. This is achiral. So the other 19 so that's 95% of the amino acids, are chiral, and they exhibit this interesting behavior.

Now the other interesting piece is that only the L-enantiomer-- by and large, there a few exceptions that you can find. There's some research on this, trying to find, always the exception. But by and large, only the L-enantiomer of amino acids are found in proteins. So there's no preference in nature for synthesizing one over the other, but somehow, somewhere, a long time ago, there was a preference given to the L-enantiomer. And so all of us have the L-enantiomer present in the proteins in our bodies. So I'm going to say only, but you know that there's always going to be some exception here. But by and large, only the L-enantiomer of amino acids found in proteins. And you're going to see the protein synthesis in a moment, and try to figure out why that happened.

By the way, carbohydrates, which we're not going to talk about-- carbohydrates are chiral as well. And in sugars, only the D-enantiomer of amino acids found in sugars. And you'll see later, this is all important in terms of a lock

and key mechanism. And there are some L-sugars. L-sugars you know as invert sugars. And our bodies don't recognize invert sugars. Our body apparatus requires that there be D-sugars.

There's some science fiction novella I read many years ago about this group of people that's marooned on the proverbial desert island, and it's lush with vegetation, and they're eating all of these fruits and vegetables and wasting away. And at the end of the novel, it comes to be known that this island, because it was isolated, somehow, back in time, the plant life there had the opposite enantiomer, and so their biological apparatus didn't recognize anything. They were eating all this stuff, and it was just going right through them with no nutrient value. So if you're ever marooned, check! Find out which enantiomer you're eating! Otherwise you're wasting your time.

Honey has the L-sugar, because bees have a different biological apparatus.

Now, when we synthesize these things chemically, we can get both enantiomers coming out of the synthetic apparatus unless we take pains not to. And so when both enantiomers are present, we call that specimen, that's term racemic. So you have both the dextrorotatory and levorotatory present.

Now, normally we take the five minutes at the end to talk about chemistry in the world around us, but this is, you know, day before Thanksgiving holiday, and we've got a natural entry point here. I want to talk about what the consequence here is for human health that drives directly from chirality.

About 40 years ago, there was a drug developed in Europe called thalidomide. And it was developed by a German firm called Chemie Gruenenthal. If I can just spell it. And it was developed as an anticonvulsant. And it was a sedative, and it had fantastic properties. Namely, that it was something that you could use in treatment of people who are very depressive, but they couldn't kill themselves with this. If you tried to overdose with thalidomide, you would simply go into a sleep, and then you could be rescued

Well, that was its original intention. Just by accident, it was discovered by various people who were using it that it was a very fine palliative for morning sickness. And so women started using it in the first trimester of their pregnancies in order to calm their morning sickness.

And so there were calls for the importation of this drug to the United States. And the FDA said no. And of course there was an outcry from women's groups that said, oh, the FDA is just a bunch of men that are insensitive to women's health issues. Let's speed this stuff up, let's get it over here. They're using it in Europe. What are we doing?

It turns out that this was during the time of President John Kennedy, and he had appointed the first woman director of the FDA. And she said, it hasn't been tested thoroughly. We're not importing it to the United States. People got on airplanes, they used post office, what have you. They brought it into the United States, and it was

used widely in the United States, And then subsequently was discovered that this is a teratogen, which causes severe mutation of the DNA, and children being born minus limbs. There were grotesque deformities.

And so the position of the FDA was right. So you say, well, but didn't they test this stuff? And they did. Well, didn't they test it on animal models? And they did.

Turns out the animal models that they used lacked a certain enzyme that's present in our bodies, that converts thalidomide downstream into something that's a teratogen. It's a really, really sad story. It turns out now, knowing what we know, only one of the enantiomers of thalidomide causes birth defects. Not both. So racemic thalidomide was loaded with both palliative and toxic components. And so this is a powerful lesson of getting the-- avoiding the toxic enantiomer.

And also, there may be people here who are opposed to animal testing. And I understand your concerns. But we're far from being able to sit with the Shroedinger equation and a supercomputer and predict the metabolic activity of these drugs. And so this is the dilemma for people. Do you want to test it or not? Do you want to get these things--?

It's actually coming back now, in the treatment of HIV-AIDS. It's being used as part of a cocktail with other medications. But now we know not to give the racemic form, but only to give a particular enantiomer.

Another one that is a chiral molecule is Ritalin, which is used, among other things, for the treatment of ADHD. And there are some negative side effects of the use of Ritalin. And again, it's being discovered that it's only one of the enantiomers that has the negative side effects.

And so the whole question of chiral molecules is a very, very hot topic in chemical research. And so, how do you how direct the synthesis to get to one enantiomer and not the other? Catalysis. Again, which is something that is very important and not very well understood. Highly empirical, still. So all of those lessons that we've learned are very important.

I think there's a cartoon here that actually shows-- all right, so here's the example. This is a molecule that's chiral, and it's very primitive. You've got a square and a triangle and a circle and so on. And you see, both of these have the same chemical properties. But when you're looking at this in terms of biological activity in the human body, you can think about a lot of these interactions as lock and key.

Now, there aren't these little holes here. It's not putting a square peg in a round hole versus what are they really trying to model here? They're trying to model the types of secondary reactions. So for example, there could be a polar center here, and this could be charged negatively, and this could be charged positively, and so they will be

attracted coulombically. Maybe this has a polar end, and this has a dipole, and they'll be attracted. Maybe this is nonpolar, and this is nonpolar, so they all fit, whereas if you turn it around, you've got something that's positively charged here, and this thing's a dipole, there's no adhesion. So that's where this lock-and-key idea comes into play. And so what we're going to do later on is to figure out how to match things up in terms of dipole-dipole interactions, coulombic interactions, and so forth.

OK. So what are the properties now? Let's look at the properties of these things as just straight chemicals. So we had amino acid, I had the solid neutral form of the amino acid. What are its properties? Not the protein. Properties of the amino acid.

OK. So first of all, they are solids at room temperature. And why would we do that? Well, because look. You've got hydrogen bonding capability here, and that hydrogen bonding capability allows it to form bonds great enough to overcome thermal energy.

Molecules like this, do you think they form crystalline solids or amorphous solids? They're small enough that-- this one looks a lot like methane, doesn't it? Looks like methane with a couple of extra things. But from a distance, it's a sphere. maybe A little bit oblate, but it's a sphere. So these things form crystalline solids as opposed to amorphous solids.

Their optical properties, I've already shown you. They're colorless.

They're not good absorbers. Where's the covalent bonds with tight electrons? So there's no reason to have excitation and color.

And then, they're moderately soluble in water. And that water chemistry is what we're going to turn to next.

So now I want to look at how they behave in water. And where I'm going with this is to show you the first stages of how we animate matter. Because I talk about inanimate matter. We are animate matter. Where does the animation come from? What's the chemical origin of our animation? How is it that I can do this? See, you're looking at changes in the conformation of a polymer. That's all you're doing. You're saying, well, how-- he's moving fast. What's the Debye frequency? It's 10 trillion times a second. 10 trillion times a second the atoms vibrate in my body, and the speed at which I'm rotating my hand, compared to 10 trillion times a second, very slow, right?

Which actually explains why we talk at the speed we do. And why is it that a human being can only run-- or not only run, but runs at the speed that he or she does? It has to do with the chemistry. With the Debye frequency, and what the skeleton can do-- I mean, why aren't human beings 40 feet tall? I mean, stand back here and-- all right-- we're going to create this universe. Why are we this tall, and not 40 feet tall? Because make a skeleton 40

feet tall would be chemically very difficult. It's all chemistry. The rest, as we know, is stamp collecting.

OK, so now let's look at the properties of the amino acids and water. So I'm going to write them again in a different form. So here I'm going to put the H2N. Here's the amino acid N. Here's the central carbon. And I'm going to put the hydrogen, instead of writing it down here, this is the carbon with its little hydrogen. This is the carboxylic acid N, and then the substituent group is above. So this is again the thing.

By the way, there are two carbons here, agreed? And the central carbon is also known as the alpha-carbon. This is the alpha-carbon. That's the beta-carbon, I bet. All right. So now what I'm going to do is, I'm going to dissolve this in water at neutral pH. And what happens? What happens is that once this thing solvates, the proton falls off the carboxylic end and comes over and attaches to that electron pair at the amino acid end. And we end up with this, at neutral pH. H3NCHCOO, and the substituent is a spectator here.

Well, I lost a proton, so this is locally negative. And I gained a proton with its charge over here. So this is locally positive. I conserve charge. This is not neutral and this is not neutral, but it has a negative end and a positive end, and it's not a dipole. I mean, this is negative ion-like and this is positive ion-like. So let's say, net neutral locally positive and negative.

And just as we've fallen in love with some German terminology for words like *bremsstrahlung,* we have a German word for this one. This is like a twin ion, or it's like a hermaphrodite dual gender, so this is called *zwitterion.* It's got both genders, if you like. It's positive and negative. OK. So there's zwitterion.

And this is the way that we start to introduce the dynamic behaviors. So now I'm going to show you how to make something come to life. So what we're going to do, is we're going to show how this zwitterion can respond to changes in its environment.

And we're going to invoke in order to do is to say that to impart animation, we invoke the le Chatelier principle. It's sort of like Newton's third law for chemistry. You know Newton's third law. Every action, there's a reaction. So le Chatelier was a French engineer, but his name is associated with an important chemical principle. And it basically says that if you disturb a chemical system, the chemical system will respond in such a way as to minimize the disturbance.

So the example I'm going to give is, I'm going to start with a neutral pH, and I'm going to change the pH. And then the zwitterion is going to respond to minimize the disturbance. In other words, if I drop the pH, zwitterion is going to try to raise the pH back to what it was before. And in doing so, I think you're going to start to see how we can get animation.

So it's sort of like that a chemical disturbance-- this is the le Chatelier principle. Chemical disturbance is mitigated by a chemical response.

So here's the example that we're going to use. We're going to say, let's take something and radically change the pH. So let's drop the pH. So drop a pH means, the proton concentration is going to go up.

So how would zwitterion respond if it wants to reduce the proton concentration? Well, it's going to try to gobble up the protons. Well, how's it going to do that? Well, we know that there's a proton attachment site. Look, there's a proton attachment site at the carboxylic acid end. How do we know? Because it used to have a proton there. So it's going to go and vacuum up protons to try to bring the pH back to what it was before.

So let's look at that reaction. So here's H3NCHCOO minus plus. So this is neutral zwitterion. And what it's going to do in response to the increase in proton concentration is try to gobble these up. And the following is the result. That proton is now going to attach here, and cap that negative end. So now we've got a proton on this end, and we've added a proton at the other end.

So what's happened to the neutrality of zwitterion? It's lost! Now zwitterion is net positive, but we've started gobbling up protons. So this reaction is called protonation. And the reverse reaction is deprotonation.

And this is messy, all these darn characters. So I'm going to write the neutral zwitterion as just HA. There's the proton here, and the rest of this stuff is just details. So that's A. So HA plus H plus gives me this thing here, which is HAH plus there. Isn't that cleaner? That's a lot easier to read.

And we can write an equilibrium constant for that reaction. I'm going to call this reaction 1. In reaction 1, I can write K1. And it's written, the convention is that you always write the reaction constant for the deprotonation reaction. So I'm going to write the reaction constant for this reaction from right to left. So that's going to be this. H plus over HA divided by concentration of HA H plus.

And then we're going to bring Sorensen to the party, and take logarithms, and make it nice and clean. As we know, when Sorensen enters the room, he straightens things out. And so this will then become PK, and if I take the log base 10 of this, I'm going to end up with minus log base 10 of H, which then will be PH. And then this flips over with the minus sign, and becomes log base 10 of the ratio of protonated zwitterion over deprotonated zwitterion.

And this is known as the Henderson-Hasselbalch equation. And what does it answer? It answers the question, you tell me what the pH of the system is, and I'll tell you what the ratio of protonated to deprotonated is, because the PK is the function of the R group. So different R groups have different PKAs, and they'll respond differently. Some are very aggressive, and some are not so aggressive.

And look at what happens. At one end, when we have neutral pH, we have all of the zwitterions sitting here. And as we go to higher and higher pH, more and more of the neutral zwitterion converts to the protonated zwitterion. And in the extreme, when I've got very, very high proton concentration, I will protonate all the zwitterion. I'll protonate it out of existence. And the only amino acid that exists is fully protonated.

So I've got a sliding scale from 100% deprotonated to a 100% protonated. Well, somewhere along this scale is 50-50. And what happens when I've got equal amounts of protonated to deprotonated? That means the concentration of protonated equals the concentration of deprotonated. I have the log of 1, which is 0, and that's the pH at PK1.

So now you see physically what PK1 means. It's the pH at which you're halfway in between, which makes sense. If I wanted to characterize something, it has values between 0 and 100, I'd give you the value at 50, and you know, it varies around 50. Either 50 plus 50, 50 minus 50. So that's what the PK is. Good.

Now let's do the same thing for the opposite side. Let's, instead of a sudden drop in pH, let's look at a sudden rise in pH.

Now you see, just to finish the point. Look at what happens here. What I'm trying to show you is that this change in pH caused this molecule to change. you I mean, this could be in your stomach. And now you drink some coffee, or you drink some cola, and the pH goes way, way down, because you've drunk something that's acidic. Well, there are functional groups in the lining of your stomach that are going to now start protonating. And when they protonate, they're going to change. This could have been bonding to something, right? COO minus could've been bonding to some other molecule that's locally plus. When the proton comes in here and caps it, that bond is broken! And that's the beginning of animation. So that when I drink something, and all of a sudden, my stomach goes into action. Well, we're going to have to process this stuff. Have to turn on some switches here. It's not my brain that's doing it! It's not that the brain gets all these sensor signals. We couldn't function that way. We're functioning just by these things acting right there at the site.

This is the origin of animation. I'm telling you that this is the secret of life. I can't tell you the meaning of life. You have to go somewhere else to answer that question. But I can tell you where life comes from. There it is.

So now, sudden rise in pH, this means that the proton concentration goes way down. See, zwitterion is like one of these friends you might have. Do you have any friends that are, what do you call them, rescuers? You know, if they see anything wrong, they're the ones that get involved? They've got to help everything? In the extreme, they're quite meddlesome.

Well, this is what zwitterion is like. See, zwitterion sees a sudden drop in pH and goes, I'm zwitterion! I can help! I know what to do, because I'm zwitterion! I fix things! And I'm conflict-averse, I don't like this!

OK. Imagine you are zwitterion. So here's zwitterion, sitting there, minding its own business

[BREAK IN AUDIO]

PROFESSOR: --for a minute. Why? Because it's in a neutral pH solution. Minding its own business. That's a chemical joke.

All right. So there's zwitterion, just sitting there, minding his own business. And all of a sudden, the pH rises, and the proton concentration drops. So now we've got an abundance of hydroxyls. We're in an aqueous solution. So the zwitterion looks around and says, I've got to fix this, but there's no hydroxyl attachment site! So the zwitterion can't gobble up the hydroxyls. So what's the zwitterion do instead? Instead, it starts shedding protons. Because if it sheds protons, then what can happen is, if it forms this plus proton, then the proton can react with hydroxyl to form water, and then shoot the pH back to near neutrality. So let's dump the proton here, and we'll just end up with H2 and CHCOO minus with the R group.

So this is deprotonation in order to address the sudden rise in pH. And now we can write a K2. Let's call this reaction 2, and with K2, since it's a deprotonation reaction right away, we can just go ahead and write, this is going to be H plus. And what's left? This is just a denuded, deprotonated zwitterion, just the A minus, all over neutral zwitterion. And it looks like this.

And we can invoke Sorensen and get PK2 equals pH plus log base 10 of the neutral zwitterion over the deprotonated zwitterion. And there you go. And then, of course, that 50-50 concentration of deprotonation, the pH gives you the value of PK2.

And now, at one end, I get deprotonated. The other end, I get fully protonated, right in the middle. I get the 100% zwitterion. I said at neutral pH, but that doesn't mean 7. It means the pH at which this particular species is stable. And that's different from 7, and it's somewhere in between, isn't it? Because if I go to very acidic solutions, I will start to protonate. If I go to alkaline solutions, I'll deprotonate. So somewhere in between.

And that somewhere in between is called the isoelectric point. The isoelectric point is the place at which we get the neutral. So that's HAmax. The concentration of this is maximal at the isoelectric point, and that's called P sub I, and that's given by PK1 plus PK2, divided by 2. And that's it.

You don't have to run it. We're done. Thank you.

OK. So this is the simple story. It gets more complicated if, for example, the R group can protonate or deprotonate. So now we got two or three-ring circus. It gets more interesting. But this is the start, and there's some homework problems that will help you muddle through.

OK. So I think this is a good place to switch into the final five minutes. So here's the titration curve. I'll show that at the beginning of the next lecture.

OK. So now let's talk about kinetics. And the extreme in kinetics, I said, is an explosion. And we're coming upon December 6, which is the anniversary of the largest explosion in the history of the world before the nuclear age. And it occurred in 1917, and Halifax Harbor, Canada, at that time was a British colony, and therefore Canada's foreign policy was dictated by Britain, which was involved in a war. And there was a French supply ship and a relief ship, and they collided in Halifax Harbor. This is what the French supply ship had on it. Notice 20,000 tons of TNT.

At 8:45 AM, the Mont-Blanc is hit by the Imo. But the TNT was not ignited, and instead we ended with sparks and a fire.

By the way, this is TNT. If you look, this is toluene. Toluene is methylbenzene. It's just the methyl group. And this is trinitrotoluene. And if you go to Wikipedia, Wikipedia gives this formula, which is wrong. The methyl group is missing here. Just a word to the wise. Be careful when you use that tool, I put in quotation marks. Because it's worth about as much as you pay for it, which is why we teach you to use the bibliographic things. OK, so there it is, right here. I didn't make this up. Look at this. Completely wrong.

Anyway, so what happens?

"The crew of the Mont-Blanc, aware of their cargo, immediately took the lifeboats, screaming warnings that no one heeded. They rode for Dartmouth"-- this is across the channel from Halifax-- "leaving the now furiously burning ship to drift towards Halifax, propelled in that direction by the Imo's impact. The Mont-Blanc drifted by a Halifax Pier, brushing it and setting it ablaze. Members of the Halifax Department responded quickly, and were positioning their engine up to the nearest hydrant when the Mont-Blanc disintegrated in a blinding white flash, creating the biggest man-made explosion before the nuclear age." It was 9:05 a.m. on a Thursday morning.

"Over 1,900 people were killed immediately. Within a year, the figure climbed to well over 2,000. Around 9,000 were injured, many permanently. 325 acres, almost all of North End Halifax was destroyed. Much of what was not immediately leveled burned to the ground, aided by what are stockpiles of coal in cellars. As for the Mont-Blanc, all 3,000 tons of her were shattered into little pieces that were blasted far and wide. The barrel of one of her cannons landed three and a half miles away. Part of her anchor shank, weighing half a ton, flew two miles in the

opposite direction. Windows shattered 50 miles away, and the shock wave was felt even in Sydney, on Cape Breton Island, 270 miles to the northeast.

"There was about 20 minutes between the collision and the explosion. It was enough time for spectators, including many children, to run to the waterfront to watch the ship burning, thus coming into close range."

I mean, they were little kids, and it's a fire, and the fire engines are coming! It's fun! It's more interesting than going to school, right?

"It was enough time for others to gather at windows. Office workers came to the windows, and with the explosion, the glass shattered and blinded them.

"Not surprisingly, the hospitals weren't able to cope with so many wounded. There was also a desperate need for housing, and the misery was compounded"-- are you ready for this?-- "by the blizzard that struck the city the following day, dumping 16 inches of snow over the ruins.

"With astounding speed, relief efforts were set in motion. Money poured in from as far away as China and New Zealand, Canadian Government gave--" blah, blah, blah.

"But most Haligonians"-- which is what you call a denizen of Halifax-- "most Haligonians remember the generosity of the state of Massachusetts, which donated $750,000 of money and goods, and gave unstintingly in volunteer assistance through the Massachusetts Halifax Relief Committee."

People from the hospital district here got on trains, and went up there to assist, especially from Mass Eye and Ear, to assist the people that had been blinded.

"Starting in 1971, to this day, Halifax sends an annual Christmas tree to the city of Boston in gratitude."

And there are specifications on what the tree should look like, and how big it should be, and so on, and they bring it over to Boston Commons. So if, in the days that come, when you get back from Thanksgiving, if you happen to be across the river and you see something that's about 45 feet high and it looks like it came from Canada, this is what it is. And it's all about the Halifax explosion. OK. There you go.

All right. Well, have a nice weekend. We'll see you on Monday.