PROFESSOR: So again, the equivalence point is where you've added all of the moles of your strong base that you need to convert all the moles you had of the weak acid to its conjugate base. So if we have this type of problem, a strong base titrating a weak acid, the pH is going to be greater than 7 at this equivalence or stoichiometric point.

And we can see that in the plot. Here is pH 7, little arrow going up indicating it's going to be greater than 7. And that's because we have just the conjugate base left at this point.

So again, pH depends on the property of the salt that's formed at the equivalence point. And when it is a weak acid being titrated with a strong base-- and that's what we have here, weak acid, strong base-- you're going to get a salt and water. But this salt, now, is going to have basic properties. And we saw this before that sodium has no effect on pH. Things in group 1 are not going to have any effect on pH.

But HCO2- is a conjugate base of a weak acid. It is a weak base itself. So this is going to be basic. And so that's why the pH is going to be greater than 7. Remember, salt and water problems really break down to weak acid and water or weak base and water problems, depending on what went into a form that particular salt.

So when you're doing these problems, and if you're on the exam and you get to the end and you know that the pH should be greater than 7, but the pH you calculated, for some reason and you don't know where you made the mistake, is less than 7. If you say to me, this doesn't make sense. It should be greater than 7, because it should be basic at this point, should just have conjugate base around, you will get points back for recognizing that the answer you gave me can't be right.

So always pay attention to what answer you're getting. Does that answer make sense? I really care more about that people understand what's going on, than they can do the math perfectly in a very short amount of time.

But you'll often be asked to calculate the pH. So let's think about how we would calculate the

pH. We know it's greater than 7, but what is it exactly for this problem.

And to do that, we need to first know what the volume is going to be. What volume of that strong base do we need to add to reach the stoichiometric or equivalence point? So we had in the beginning 2.5 times 10 to the minus third moles of our weak acid.

So that means that at the stoichiometric point, we're going to form that number of moles of conjugate base. And that also means that to do that we need to add that number of moles of the strong base. So we need to add 2.5 times 10 to the minus third moles of our strong base. We know the concentration in the strong base, 0.15 molar. So we can calculate that the volume we need is 16.7 milliliters.

Now, the total volume to get to the stoichiometric point was 25-- that's what we had originally-- plus this 16.74, so 41.7 milliliters or 0.0417 liters. We can calculate the molarity of the conjugate base that's formed. How many moles in this total volume gives us a molarity of 0.0600 molar.

And now, we can go ahead and solve the problem. But why don't you tell me how we're going to solve the problem. What are we going to use to solve this problem? Let's just do 10 more seconds.

Yep, so Kb, and so if we look at this problem for a minute, so this is, again, the type of problem, it's a weak base problem. We've converted all the weak acid we had to its conjugate base, because we added enough moles of the strong base to convert all the weak acid to the conjugate base. So the equivalence point, all we have is the weak base. So this is a base and water problem.

So we write our base plus water going to the conjugate acid plus hydroxide. And when it's a base and water problem, you should have hydroxide on the other side. So we can set up this expression. We get 0.06 molar minus x, x plus x.

And we can use Kb to solve the problem. And Kb, in this case, is 5.6 times 10 to the minus 11th. That's going to be equal to x squared over 0.0600 minus x. So if I was given Ka and I now need Kb, what do I use to convert Ka and Kb?

AUDIENCE: [INAUDIBLE].

PROFESSOR: Right. And you can use Kw to solve it, yep. So we can easily convert between these two. Not a

problem.

So this is how you would do the problem. And always remember, ask yourself what type of problem it is. If it's weak base and water, you want a Kb. So can I use Henderson-Hasselbalch for this?

AUDIENCE: No.

PROFESSOR: No, I can't. And you should not as well. So what do you do after this? We should be able to go from here. We're not going to go through all the steps.

We can simplify, pretend x is small, make sure x is small. And in this case, x is quite small of 1.83 times 10 to the minus sixth molar. From that, we have to remember that x, now, is the hydroxide ion concentrations. So we're going to calculate pOH first and then calculate pH by subtract 14.00 minus pOH to get us the pH.

And now, it's 8.26. That's above 7. That number makes sense. If I had stopped and forgotten what x was and realized the pH was 5.74, I should have realized there was a problem there. So weak base in water problem.

So we go up here. That's Point S, the stoichiometric point. We have a pH of 8.26. Now, we've added this little E at the end. We're just going to think about the last type of problem you might see, which is past the equivalence point.

So here, you are at a volume beyond the volume needed to get you to the equivalence point. And at this point, you have your conjugate base in solution. But you're adding a lot of concentrated base of sodium hydroxide to that solution.

So the amount of the conjugate base that you have there is really not going to contribute to pH anymore, not compared to the pH change that's going to be caused by just putting extra strong base into solution. So the pH is really going to be determined by the excess amount of any OH you have. And you can pretty much forget all the work you just did in calculating what the pH was due to the conjugate base, because that's going to be overwhelmed by this. And I'll show you that that's true.

So what this is then is a strong base in water problem. So beyond the equivalence point now, we're a strong base and water problem. So how do we do this? And we saw this already, but we'll just review it one more time.

So we're 5 mills past the equivalence point. So we're going to figure out how many extra moles of OH we added. 5 mills times our concentration, so we have 7.5 times 10 to the minus fourth moles that are extra.

And now, we need to calculate the concentration. And we have to remember our volume. So we added 5 extra mills. We had 25 to begin with. And we use 16.7 to get to the equivalence point. And so when you have the whole volume in there, you can calculate that your concentration is 0.016 molar OH.

Then from that, we can calculate pOH. And from that, we calculate pH. And it's 12.21. And just to convince you that it was OK that I forgot all about that conjugate base-- remember, the concentration that we had calculated of OH that is due to that weak base in solution? This number, really small compared to that number.

And if you want to be very particular, you can add this to this before calculating this. But it's really not going to give you-- to the number of significant figures you have, it's not going to make any difference whatsoever. So this is a strong base in water problem. We're only going to think about how many moles extra of OH do we have, and what is the total volume, and then you're done.

So now, we've done this whole curve. We started at the beginning. It was a weak acid problem down here. We went into the buffering region. We can use Henderson-Hasselbalch here.

We can do a very simple calculation at the half equivalence point, pH equals pKa. Then at the stoichiometric point, we're a weak base problem. And then we're a strong base problem. So you can now do the same thing the other way. Yeah, question.

AUDIENCE: What if you were given a problem like, figure out what the buffering region was? We never calculated E.

PROFESSOR: Yes, right. So we skipped E, because there was a lot of different points. Yeah, so if you are in a region where you have both conjugate acid, conjugate bass, you can assume that's in the buffering region. So you need to have both to be in the buffering region, if the problem only has your weak acid in water and initially you have sort of zero of the other.

But if you've added some of the strong acid, strong base, that means you've converted some, but you know you're not at the equivalence point yet. You can assume a buffer problem. And

then pretty much, it's kind of in the buffering region, unless it's right here or right there.

So pretty much anywhere in here, you can assume it's going to be a buffer problem. And when you do the subtraction, you should see that you had your weak acid. And you've converted some to the conjugate. And you can see that you have amounts of both when you do that subtraction. And when you have concentrations of both, then you're in the buffering region.

AUDIENCE: So you would go from B to F?

PROFESSOR: So you would do D the same way that you did B. Yeah, that would be the same. And then if you want to make sure that you're not there-- but you should know that when you start the problem, because when you start doing these problems, you're going to calculate, say, how much moles of the weak acid you had. And then you calculate how many moles of the base you added. And if they're equal, then you're like, oh, I'm not in the buffering region. I'm at the equivalence point. If they're not equal, if the number of moles you've added are lesser the strong base but non-zero, then you're in the buffering region.

Any other good questions? And we're not going to go the other direction. We're not going to do all the points in the other one. But there's a problem set for that.

But I'm not going to leave acid-base quite yet. We're almost there, but not quite yet, because I've got to say a little more about pKa's. So pKa's are not just important in titration problems. And I want to share with you one of my favorite videos about why pKa's are important.

[VIDEO PLAYBACK]

- My name is Samuel Thompson. I'm a rising senior at MIT. And for the past three years, I've been working with Alice Ting. My project is in the field of chemical biology, which means that I'm a tool maker. And I've been making tools to allow people to look at proteins.

We want to see where they are, what they're doing, what they're interacting with. But all proteins and all cells are completely transparent whenever you look at them under a microscope. So we use an enzyme to attach an organic molecule-- a very, very small molecule-- to the protein, so that we get the same fluorescent output. We see a bright light whenever we shine laser light on it and look at it under a microscope.

After some very complicated research, we came up with a very basic problem in our design. We had a mismatch between our probe and the pH of the cells. Cells typically exist at about

7.2 to 7.5 pH.

That's what's healthy for them. They need that. And if you go outside those boundaries, they're very unhealthy, and they behave abnormally. And the pKa of our probe is also 7.5.

pKa is the point where any sort of species is half protonated, half deprotonated. And our probe needs to be deprotonated. It needs to be in some sort of basic solution compared to its pKa in order for it to be visible, in order for it to glow.

Since our pKa of our fluorescent molecule and the pH of the cells exactly match up, that means that our probe is half protonated, half deprotonated. This is a huge problem for our labeling, because it immediately means that we're at 50% efficiency. We couldn't get more than half of these molecules to glow. And we couldn't see more than half of our proteins.

Our solution was to change the pKa of the probe. So we changed to a different molecule that's very, very similar and we hoped would work with our system but has a much lower pKa, 3.5, which allows us to work through all these neutral pHs and these physiological pHs and still be very bright and still be completely deprotonated.

A lot of diseases are caused by mutations, which change where proteins go. It either locks them into a specific compartment or puts them in places that they don't need to be. I hope that my work can be used by other people to study their own systems. They can use my process to label that protein and then look at disease cells and find out where that protein is and what it's doing. Hopefully, this can be used to unlock the keys to new therapeutic methods and medicine.

[END PLAYBACK]

PROFESSOR: So that was Samuel-- he graduated; he's now at UCSF in graduate school-- and talking about his research in Alice Ting's lab. Samuel was my academic advisee. He's a chemistry major. And then in the later part of graduate school, he actually switched and did research in my lab.

And so that was one of my favorite videos. And I miss Samuel. Anyway so it shows an undergraduate, just like you, caring about pKa's So that's why it's one of my favorites.

So let's do a couple of clicker questions related to Samuel's video. And so now, consider, what if the pKa of the probe had been 10? How much of it would glow at physiological pH? What can you say about that probe? 10 more seconds.

So let's take a look at the answer. So most of it-- not much of it is going to be glowing is the answer to that part. And let's just look at why that is true for a minute. So this is what Samuel talked about in his video that, at pH 7-- the physiological pH, they had one probe where the pKa was equal to the pH they were using.

And so as Samuel told you, if we think about Henderson-Hasselbalch, that's going to mean that the ratio of HA to A is going to be equal to 1. It's one to one. And so that's going to mean only 50% maximum efficiency. And so here you see that when the pH is equal to the pKa, you have equal moles of HA as you have A minus. So you're not going to have more-- you can't possibly have more than 50% efficiency, 50% more glowing.

But then in their design strategy, what they did was they used another molecule with a different pKa, one of 3.5. And now, the pH is much greater than the pKa. And so as you go above, pH above the pKa, you get more and more deprotonated species. So if you use Henderson-Hasselbalch here, you could calculate the ratio is 1 to 8,000. So you're going to have a lot of glowing probe under those circumstances.

And then the clicker question that I just asked you is, what happens then if your pKa was 10? So now, you have a situation where the pH is below the pKa. And if we did the math, we would see that the ratio now of protonated to deprotonated is 400 to 1, so very little glowing.

So this is an important thing to think about in doing these other kinds of problems. When the pH equals the pKa, you have equal amounts of HA and A minus; pHs above, more deprotonated; pHs below, more protonated.

So let's try one more clicker question. And see now thinking about the pKa's of three different groups here for this amino acid, which structure would you get? Should this amino group be protonated or deprotonated, NH3 or NH2, OH or O minus, and OH or O minus here?

Let's just take 10 more seconds. I know a lot of people aren't done, but we have a demo that we need to get to and a t-shirt vote to get to. Not bad.

[LAUGHTER]

Oh, we have no answer to it. But it is D. So this is the structure. So here, for these two, we have pKa's that are high. They're above the pH, so we expect them to be protonated. And here, we have a pKa that's below the pH, so we expect that to be deprotonated. So again, you

want to think about, how does the pKa relate to the pH.

So that is now the end of the acid-bases, end of Exam 3 material.