BOGDAN FEDELES: Hello, and welcome to 5.07 Biochemistry on MIT OpenCourseWare. I'm Dr. Bogdan Fedeles. Let's metabolize some problems. This series of videos is meant to supplement some of the other materials on the site, and to give you a more in-depth and more interactive take on some of the topics covered in 5.07 Biochemistry. Specifically, we're going to be working together through one problem from each problem set from this course.

Today we're discussing the very first homework problem of 5.07, which is problem one of problem set one. This problem is meant to give you a better sense of the scales and dimensions of the cellular environment. Specifically, we're going to be asking questions like, how big is this cell? What is the volume of a cell? And how many molecules of a given protein are inside a cell?

One fundamental idea introduced in this problem is that the cellular environment is very crowded. Things inside the cell are very tightly packed. Now take a look at this picture in your book. As you see here, the constituents of a cell, like proteins, enzymes, the organelles, metabolites, are all in very close proximity to each other.

Now, this is also reflected in the concentration that we're given for the proteins inside the cell. The problem tells us there are 350 milligrams per milliliter of protein. Or in other words, 350 grams per liter. Now this is a very high number in the context of biochemistry. Basically, if you think one liter is 1,000 grams then 350 grams of that is protein. So we have 350 grams, 35%, of a cell is protein. And only 60% to 65% is water. Therefore, as the problem says, when we're doing in-vitro experiments using dilute solutions we rarely recapitulate what actually happens inside the cell.

Now how big is a mammalian cell? As you will see, sizes of cells in an organism vary considerably. At one extreme we have very tiny cells like endothelial cells, red blood cells. These are very, very small. On the other end, we have reproductive cells, like the egg, which is 100 to 200 microns in diameter. Or even cells that can stretch for centimeter, like the muscle cells and certain nerve cells.

In this problem, we're going to be dealing with the red blood cells, one of the most abundant cells in the body. As you can see in this very colorful picture, a red blood cell can be approximated by a cylinder 6 to 8 microns in diameter. So knowing that, we can actually calculate some dimensions of the red blood cells, such as the total volume and their surface area.

Now here is a cylinder by which we approximate a red blood cell. And let's say the cylinder has the height, h, and the radius, r. From our problem we know h is about 2 microns and r, well we know the diameter is 6 to 8 microns. So r is going to be, let's go with the middle, 3.5 microns. Now as you remember from geometry, then the volume of the cylinder is going to be pi r squared h, which when we substitute our units, we're going to get about 77 cubic microns. All right. We'll come back to discussing the units in a little bit.

Now the surface area is just going to be the area surrounding the cylinder plus the two circles-- the top and the bottom. So the two circles are 2 pi r squared plus the surrounding area is going to be 2 pi r h. And that comes out to be about 120.95 square microns.

Now how much is really one cubic micron? Let's try to relate it to a unit that we're more familiar such as liter. Well, one milliliter is actually one cubic centimeter. One microliter is one cubic millimeter.

Now, one cubic micrometer, it's like a billion times smaller than 1 microliter. One microliter is already a million times smaller than a liter, so this is really 10 to the minus 15 liters is 1 cubic micrometer. Which is 10 to the minus 15 is the femto units. It's like one femtoliter. Now 77 femtoliters is an incredibly small volume. But as we'll see next when we look at bacteria, bacteria are even smaller.

Now, let's take a look at a Staph aureus cell. Now Staphylococcus aureus is a very common bacteria that we often find on our skin or in our respiratory tract. Now this is the same bacteria that you might have heard in that acronym MRSA, or Methicillin-Resistant Staph Aureus. Now, this MRSA is a pathogenic bacteria that can cause a lot of problems in the hospitals nowadays, because it is resistant to most of the antibiotics that we have.

Now, here's a picture of Staph aureus. As you can see, it's a spherical cell. And of course this pretty purple color is added in. This is just a electron micrograph picture of a colony of Staph aureus bacteria. So for it too we can calculate the volume of the cell and the surface area.

If we assume Staph aureus to be a sphere, of radius r, we are told r is 0.6 microns. Then we can calculate the volume of the cell. The volume is simply going to be 4 pi r cubed over 3. And if we plug-in the numbers, we're going to get 0.11 cubic micrometer.

Similarly for the surface area, it's a surface area of a sphere. It's 4 pi r squared. And the units come out to 1.13 square microns. Now 0.11 cubic microns. And we said a cubic micron is one femtoliters, like 10 to minus 15 liters. So 0.11 cubic micrometers is 110 times 10 to minus 18 liters. Now the prefix for 10 to minus 18 that's atto. So it's 110 attoliters. So this is an incredibly small volume.

So by calculating the volume and the surface area of these cells, we've essentially answered part 1 and part 2 of this problem.

Now next we're going to explore the relationship between the volume and the surface area of the cell.

As you know from geometry, the volume typically varies with the cube of the radius, whereas the surface area varies only with the square of the radius. Therefore, as the radius of an object increases the ratio of surface area over volume will decrease because the volume increases quicker. Now, this is exactly what we observe with cells. Therefore, for a red blood cell surface area over volume it's going to be 12,095 square microns over 77 cubic microns. That comes out to about 1.6 inverse microns.

Now for a Staph aureus cell, surface area over volume is going to be 1.13 square microns over 0.11 cubic microns. That's approximately 10. Why is this important? It's because the surface area of a cell controls how fast molecules can go in and out of the cell. It essentially controls the flux of molecules across the cell membrane.

Now, if the surface area of a volume is a large number, it means the molecules can access that volume fairly quickly and efficiently. But as you can see, the bigger the cell, the smaller the surface area of a volume number becomes. And therefore, for big cells molecules will have a hard time and will take a long time to get inside the cell or out of the cell. That's why nature has designed ways to transport molecules, to make them achieve the right concentration efficiently.

Now this is why, in the case of bigger cells, such as the eukaryotic cells or mammalian cells, in our case the red blood cells, nature has evolved transport mechanisms by which it can deliver small molecules throughout the entire volume of the cell. One example of such transfer molecules is hemoglobin, which is used to deliver oxygen. This is what we're going to take a look at next.

We are given that hemoglobin constitutes 95% of the proteins in the red blood cells. So let's calculate the concentration of hemoglobin in a red blood cell.

Now let's start with the average protein concentration in the cell, which we mentioned earlier, which was 350 milligrams per milliliter. Now if 95% of this is hemoglobin, then the concentration of hemoglobin is going to be about 322 milligrams per milliliter. Now I'm going to abbreviate hemoglobin as Hb.

We're told that hemoglobin has a molecular weight of 67,000 Daltons, which is another way of saying 67,000 grams per mole. So then the concentration of hemoglobin is going to be 322 milligrams per 67,000. Grams per mole is the same as milligrams per millimole and per milliliter. The grams go away and we get 0.0048. It's going to be millimole per milliliter and that's the same as mole per liter. That's the molar concentration. Or we can write it 4.8 millimolar.

Now this is a pretty important range to keep in mind, because the most abundant proteins such as hemoglobin, are going to be in the low millimolar range. Most of the other proteins are going to be in the micromolar range in a cell.

Now let's calculate how many molecules of hemoglobin we have in the red blood cell. So we calculated before that the volume of a red blood cell is actually 77 femtoliters. That's once again 77 times 10 to minus 15 liters. Now we know in this volume the concentration of hemoglobin is 4.8 millimolar. So we can calculate the number of moles. So the new number of moles is going to be the concentration times the volume.

So we have 4.8 millimolar times 77 times 10 to minus 15 liters equals-- now of course, millimolar-- we have to transform this back into molar. We have mole per liters. The liters are going to cancel out so we're going to get moles. And it's 369, or so, times 10 to minus 18 moles. Remember 10 to minus 18 that's attomoles. So 369 attomoles of hemoglobin we have in a red blood cell.

Now we know one mole contains the Avogadro numbers of molecules. So if you multiply this with the Avogadro number, we should get the actual number of molecules. So number of molecules is just Avogadro number times number of moles, and Avogadro number is approximately 6.022 times 10 to the 23rd power, so a gigantic number, times 369 times 10 to minus 18 moles. We're going to get about 2.2 times 10 to the 8 molecules. Or in other words, this is 220 million molecules.

So the problem was telling us about a Google search in which we came up for different numbers and one of them was 2,000, one of them was 200 million, so obviously the answer we got, 220 million, is closer to the 200-300 million molecules that our Google search returned. That's the answer for that part of the problem.

Finally, let's see how the size of a hemoglobin molecule compares to the size of a cell. We're told hemoglobin is roughly spherical in shape, with a diameter of about 55 Angstrom. Now as you recall from Intro to Chemistry, one Angstrom is 10 to the minus 10 meters. That's 0.1 nanometer. So our radius here is going to be half the diameter, so it's 27.5 Angstrom is 2.75 nanometers.

So the volume of a hemoglobin molecule is going to be 4 pi r cubed over 3. And with plugging in 2.75 nanometers. So it's going to come up to be 8.7 times 10 to the minus eighth cubic microns.

Now, you remember the volume of a red blood cell was 77 cubic microns, so if you look at the relationship between the two, how many volumes of a hemoglobin can we fit in a red blood cell? Well, we just divide the volume of the red blood cell to the volume of the hemoglobin. 77 over 8.7 times 10 to the minus eighth. Both are cubic microns. And that gives us 8.8 times 10 to the eight molecules.

So this is 880 million molecules of hemoglobin would fit in the volume of a red blood cell. If only hemoglobin would be in there.

Obviously this number is an overestimation, because when you're packing spherical objects, they're not going to pack very tightly with each other. And as we said, the shape is only approximately spherical, but nevertheless it's on the same order of magnitude as the 200- 300 million molecules of hemoglobin that we calculated earlier based on the concentration.

So from both the volume standpoint and concentration standpoint we now have calculated how many molecules of hemoglobin can fit in a red blood cell. This result we just got actually highlights a very important take home message, which is, if we look at the molecular and atomic scale, it is as distant from the cellular scale as the cellular scale is different from the macroscopic scale.

Now if we take one milliliter of blood, we find a few billion red blood cells inside it. Now within each red blood cell we find hundreds of millions of molecules such as hemoglobin.

That's it for this problem. I hope you now have a better sense of the sizes and scales relevant for biochemistry and cell biology in general. Keep in mind our discussion of the surface area to volume ratio and why as the cell size gets bigger, we need transport mechanisms to make sure the nutrients and metabolites get to where they need to go efficiently. Also keep in mind some of the concentration ranges that we discussed, as these will become very important in understanding the biological significance of some of the constants that we're going to calculate for enzymes later in the course.