BOGDAN FEDELES: Hi, everyone. Welcome to 5.07 Bio Chemistry Online. I'm Dr. Bogdan Fedeles. I'm going to help you work through some more biochemistry problems today.

I have here question 2 of Problem Set 8. Now, this is the question I put together to get you thinking about the electron transport chain. As you know, the electron transport chain is a fundamental redox process through which we convert the chemical energy of the covalent bonds into an electrochemical gradient.

This electrochemical gradient is like a battery, and it can be used inside the cell to generate, for example, ATP, which is the energy currency of the cell, or it can be dissipated to generate heat. We're going to see both of these modes in action in this problem.

Now in most organisms, the electron transport chain helps to transfer electrons all the way to molecular oxygen. However, in this problem, we're dealing with an organism that lives deep inside the ocean where the atmospheric oxygen is not available. And it turns out this organism transfers its electrons to sulfate. Sulfate is the final electron acceptor.

Part A of this problem asks us to write the order of the electron carriers as they would function in an electron transport chain for this organism. Now, for a number of redox processes, the problem provides a table with the electrochemical reducing potentials, as you see here.

Now, I've selected the ones that are mentioned in the problem, and I put them into a smaller table here. As you can see, we're dealing with cytochrome A, B, C, C1. This is the flavin mononucleotide. This is the sulfate, the fine electron acceptor, and ubiquinol.

Now, on this column here we have the redox potential, which are the electrochemical reduction potentials denoted by epsilon, or e0 prime. Now, e0, as you know from physical chemistry or physics, denotes the electrochemical potential in standard conditions. However, in biochemistry, we use the e0 prime notation to denote that the pH is taken into account, and it's not what you would expect, like of hydrogen ion's concentration equals 1 molar, but rather it's a pH of 7. The hydrogen ion's concentration equals 10 to the minus 7.

So therefore, these numbers are adjusted to correspond to pH 7. The electrochemical potentials we see in this table are reduction potentials, and they tell us how easy it is to reduce a particular species. Therefore, the higher the number, the easier it is to reduce that particular species and the more energy the reduction of that species will generate.

Therefore, the electron transport chain will go from the species that hardest to be reduce towards the species that are easiest to be reduced. Therefore, the order of the electron carriers will be from the ones that have the lowest reductive potential to the ones that have the highest reductive potential.

So now if we're going to sort all these electron carriers in order of their potential, we're going to get the following order as you see here. So the electrons are going to flow from the flavin into the coenzyme Q, and then the electrons are going to flow coenzyme Q to cytochrome B, and then Cytochrome C1, C, A, and sulfate.

And as you can see, flavin has a negative reduction potential. It's like the hardest to be reduced. And the next one is ubiquinol. It's barely positive. And then the highest number is sulfate 0.48 volts.

Now, let's take a closer look how the electrons are going to be transferred through this proposed electron transport chain. In the first reaction, here we have the flavin, I've written the flavin adenine dinucleotide, FADH2, the reduced version, is going to be converted to the oxidized FAD version of it. And in this redox reaction, we're going to use the coenzyme Q, the oxidized version and reduce it in the process. So the electrons get transferred from FADH2 to coenzyme Q.

Now, in the next reaction, the reduced version of coenzyme Q is going to get oxidized back to coenzyme Q and in the process cytochrome B is going to go from its oxidized form to its reduced form. Now, this process continues with every single step, every single electron carrier up until we get to the sulfate where the reduced form of the cytochrome A will donate its electrons to the sulfate, and sulfate would get reduced to its reduced form. It's called sulfite.

So if we were to draw how the electrons move through this chain, the electrons are going to start at FADH, and then they're going to be transferred to coenzyme Q in the reduced form. And then coenzyme Q is going to pass it to the cytochrome B. That's going to be in its reduced form. And then cytochrome B is going to pass it to cytochrome C1, and then cytochrome C, cytochrome A, and finally, they're going to end up in sulfite.

Another thing to notice here is that except for the initial flavin and the final electron acceptor, sulfate, all the other intermediates get regenerated. So we go from the oxidized version to the reduced version and back to the oxidized version. So all these electron carriers are going to be sufficient only in catalytic amounts.

So the only thing that gets consumed is the FADH2 and the sulfate. These are two reactants. And we get in this reaction FAD and sulfite.

What we just said will help us segue into the Part B of the problem, which asks us to calculate how much energy do we get by converting one molecule of FADH2 and one molecule of sulfate into FAD and sulfite, respectively. Now as we pointed out here, only the FADH2 and sulfate are consumed in this reaction. All the other electron carriers are recycled and regenerated in the course of the electron transport chain.

In order to calculate the energy, it's useful first to write the half reaction of the redox processes. Here are the two half reactions of this redox process. FADH2 gets oxidized through FAD and donates its two electrons. And the epsilon, or e0 prime is minus 0.22 volts. Now, this is the potential from the table, and that's a reduction potential. The equation as written is an oxidation, and therefore, the potential that we need to take into account is the minus of this one.

Sulfate is then going to accept the two electrons and going to get reduced to the sulfite and water. And the electrochemical potential for this is 0.48 volts. So now when we add these two together, we get the overall process where FADH2 gets oxidized by sulfate to generate FAD and sulfite. And the electromotive force is just the mathematical sum of these two keeping in mind that this has to be taken as a negative sign. Because, again, as written, this is an oxidation and this the potential for the reduction reaction. So electromotive force is actually 0.7 volts.

Now, we can easily convert from the electromotive force to a delta g0 prime value, and the relationship is written here, delta g0 prime. It's minus nF delta e0 prime and is the number of electrons in the process as we see here. Two, F is the Faraday's constant and delta e0 prime is going to be the electromotive force. And if we go through the number crunching, we get a delta g0 prime minus 135 kilojoules per mole.

Notice because it's a negative number that means there's a spontaneous process as written. And as you know, the negative delta g will correspond to a positive electromotive force.

Now, we're just one step away from calculating how much ATP we can produce with this energy. As you know, we generate ATP out of ADP and phosphate, and this is the reaction that's catalyzed by ATP synthase. And it takes about 30.5 kilojoules per mole to form ATP out of ADP and phosphate. Therefore, the 135 kilojoules per mole that we generated from 1 mole of FADH2, it's going to be enough for about 4 molecules of ATPs.

This is in contrast, which was the normal processes that use oxygen as their final electron acceptor where out of one FADH2 molecule, will generate at most 2 molecules of ATP. So in some ways, sulfate is actually a better electron acceptor and can give us more energy.

Part C of these problem deals with a culture of this microorganism in the lab. And we're adding to this culture dinitrophenol, a compound we're told has a pKa of about 5.2. So let's explore what happens to the electron transport chain of the organism when we add dinitrophenol.

Here I put together a cartoon representation of the electron transport chain of our organism. So as you can see here, this is the extracellular environment. This is the outer membrane. This is the inner membrane where we have all these complexes I denoted here with these rectangles of the electron transport chain.

And FADH2, for example, is going to donate its electrons. They're going to be passed along all the way to sulfate. And in the process, protons are going to get pumped into this intermembrane space.

Now, these protons can be used in the ATP synthase as they travel back into the intercellular space. Their energy can be used to convert ADP and organophosphate to ATP as we just discussed in Part 2.

Now, to this organism, we said we're going to add dinitrophenol. Here is the structure of dinitrophenol. And we're told the pKa of this proton, right here, the pKa is about 5.2. When this compound diffuses through the membrane, it's going to go through this intermembrane space, which has a very low pH and also in the intercellular space in the cytosol, which has a much higher pH.

So because pKa 5.2, it's a relatively low, much lower than 7, pKa, in the intermembrane space where it's more acidic, it's going to be protonated. So we can write, for example, dinitrophenol OH in equilibrium with dinitrophenol O minus plus a proton.

Now, because here we have a lot of protons, this equilibrium will be shifted to the left. That is the protonated form of dinitrophenol. However, here in the cytosol, the NPOH, it's going to be in the same equilibrium O minus plus H plus. But because the pH is fairly high, that is there are not a lot of protons, this equilibrium is going to be shifted to the right. This equilibrium is going to be shifted to the left.

So now look what happens. So because this equilibrium has shifted to the left, it's going to keep soaking up a lot of these protons. Then the neutral dinitrophenol molecule is going to diffuse through the membrane as such and enter the intercellular space to cytosol where it's going to be deprotonated. The equilibrium is shifted to the right.

So in effect, dinitrophenol is going to carry the protons from the intermembrane space inside the cell. Now it's going to do that in parallel with the protons that are going to be flowing through the ATP synthase to generate ATP. So in effect, we're discharging this battery where the concentration of protons is basically our electrochemical gradient. It's going to be discharging the battery without producing ATP.

So as you know, if you short circuit a battery, the battery is going to heat up because you're discharging an electrochemical gradient. Similarly, dinitrophenol, by taking these protons from the intermembrane space and bringing them inside into the intercellular space, it's going to be generating heat. Therefore, we can answer Part C by saying that the medium in which these cells are growing is going to heat up when we add dinitrophenol to it.

The processes described in this problem are fairly universal. Now, in eukaryotes, like more evolved organisms, they would happen in the mitochondria. Now, if you look back at this diagram, if this was the double membrane of the mitochondria, this would be the inside of the cell that contains the mitochondria, this would be the intermembrane space, and this will be the inside of the mitochondria or the mitochondrial matrix.

Similarly, by adding a compound like dinitrophenol, who can dissipate the electrochemical gradient in the mitochondria and cause the cell to heat up. In fact, this process is actually used by a number of organisms to generate heat instead of chemical energy, or ATP. For example, the brown fat cells in newborns in mammals have a special protein that allows to dissipate this electrochemical gradient in the mitochondria to generate heat.

Another good example is the seeds of many plants. When they germinate, they actually generate a lot of heat that can be used to melt the ice or the snow around them. That's why some of the plants can start growing even before the snow has melt in the early spring.

I hope that working through this problem will help you understand better the inner workings of an electron transport chain and how it can convert the chemical energy of chemical bonds into an electrochemical gradient, which can then be used to generate high energy compounds like ATP. Or it can be dissipated to generate heat.