Bioreactors

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Lecture - 03
Solution to PP 1.1

Welcome to lecture number 3 in this NPTEL online certification course on bioreactors, a 10-hour course. In the first two lectures, we got introduced to what bioreactors were, what kind of products they make, what are the common types of bioreactors that are used, what are the modes of operation, predominantly batch, continuous and semi batch, or fed batch; and then, we started looking at some details. The first aspect that we looked at was how to have a clean slate, because, we said, we kill all organisms that are there. We create a clean slate, and then we introduce the organisms of our interest into the bioreactor, which produces the product of interest to us.

To achieve the clean slate, there are three methods possible, three main methods possible. Temperature based, or chemicals based, chemical vapors and so on, or radiation based, gamma, UV, and things like that. Then, we saw thermal sterilization, the temperature based aspect, in some detail, so that we had enough information to be able to design a-priori, the sterilization process. That is the whole point about analyzing and so on. It also gives us a lot of insights, but the practical aspect is to be able to design appropriate processes. Let me open this particular presentation.

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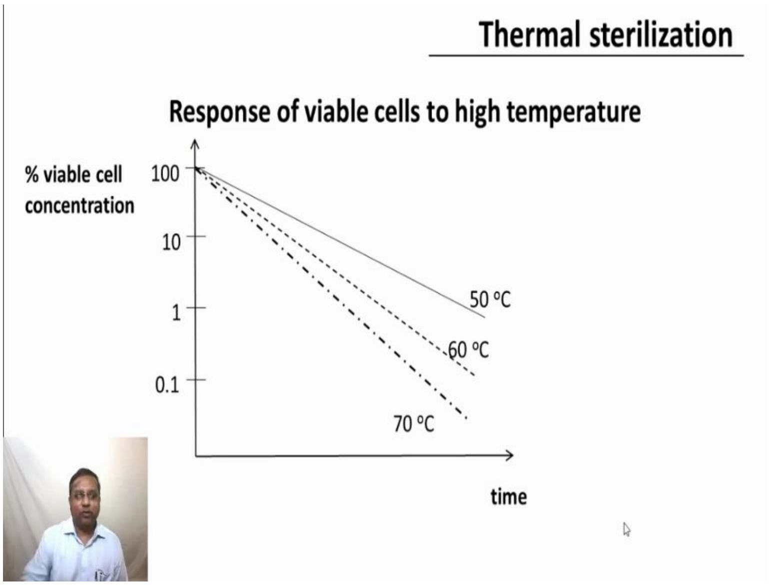

This is what we saw, the thermal sterilization, the response of viable cells to high temperature. We have on the y axis the percent viable cell concentration on a log scale, versus time on the x axis, and the relationship is linear when this is on a log scale. Also, we said that, the decrease, the slope of the decrease, increases as the temperature increases. This is the kind of response that we were trying to analyze.

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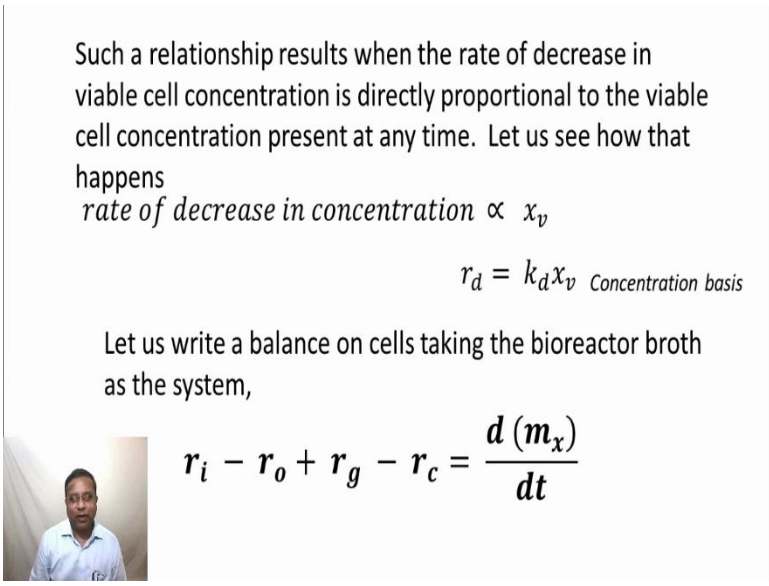

We said that we could analyze this situation, if we considered the rate of decrease in concentration to be directly proportional to the concentration of viable cells; a sort of a first order relationship. Using that, and the fact that this operation is happening in a batch bioreactor, we wrote a balance for it, and arrived at, let me get there; this was the governing equation, d d t of x v is minus k d into x v.

$$\frac{d\,(x_v)}{dt} = -\,k_d x_v$$

And if you solve this, we would get ln of x v naught by x v equals k d t. That gives you the time there.

$$\ln\left(\frac{x_{v0}}{x_v}\right) = k_d\, t$$

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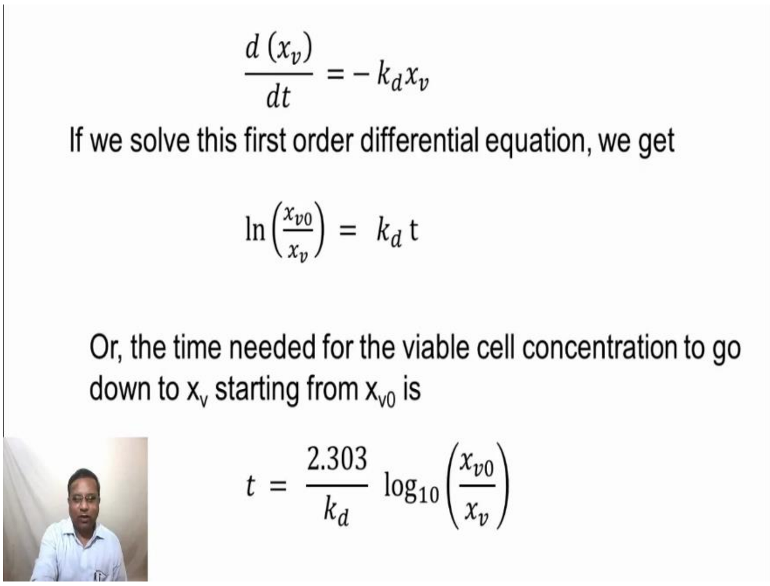

The time needed for the viable cell concentration to go down to x v, starting from x v naught is 2.303 by k d log to the base 10 x v naught by x v.

$$t = \frac{2.303}{k_d} \log_{10}\left(\frac{x_{v0}}{x_v}\right)$$

As you can realize, this is natural log, log to the base e; when we convert that to log to the base 10, you have a factor of 2.303. But, otherwise, this is essentially this equation transposed. The main thing here is that, we have the time that is necessary for the viable cell concentration to go down from x v naught to x v, under certain set of conditions, which is characterized by this death constant k d, or the sterilization constant k d. So, this is what we arrived at. And then, we also looked at something called a decimal reduction rate, which is the time that is required for a 10-fold decrease in viable cell concentration, at a given temperature.

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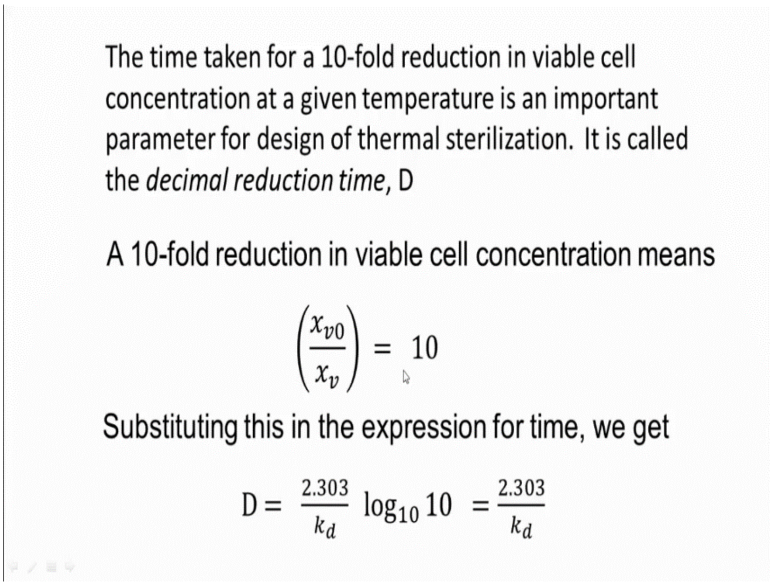

For a 10-fold reduction, all we needed to do was, replace x v naught by x v to be 10,

$$\left(\frac{x_{v0}}{x_v}\right) = 10$$

And then, we got the decimal reduction time D as 2.303 by k d.

$$D = \frac{2.303}{k_d}$$

At this point, a problem was assigned, the practice problem 1.1.

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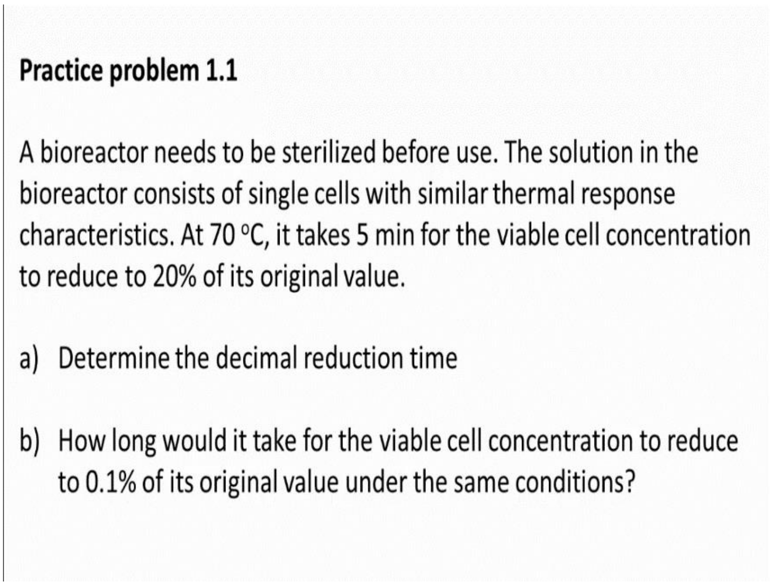

It read, a bioreactor needs to be sterilized before use. The solution in the bioreactor consists of single cells with similar thermal response characteristics. At 70-degree C, it takes 5 minutes for the viable cell concentration to reduce to 20 percent of its original value. A, determine the decimal reduction time, and b, how long would it take for the viable cell concentration to reduce to 0.1 percent of its original value, under the same conditions. This was the question that was, or the problem that was assigned, when we pretty much finished up the previous lecture, lecture number 2. I hope you would have had a chance to work this out. I will, as promised earlier, work out problems that are assigned in the beginning of the next lecture. We will start this lecture by solving this problem first.

Let me first talk a little bit about problem solving.

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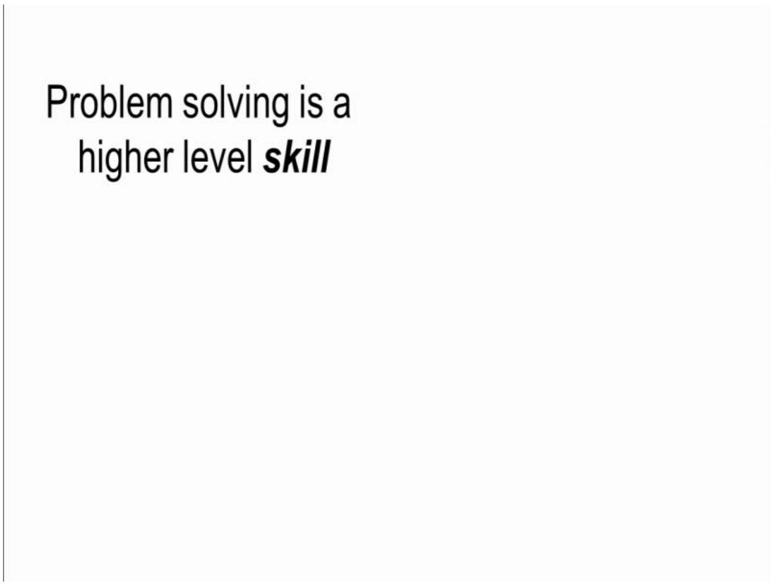

Problem solving is a higher level skill. It is the same way as somebody being able to either sing well, or dance well, or play a game well, or come what may, you think of skills, and you have a certain association with it. Similarly, problem solving is also a skill; in fact, it is a higher level skill in the cognitive domain. Some people would be naturally good at it, as are some people who have a natural ability in music, in dance, and so on and so forth. If you have the natural ability, then this initial part, or the details of the problem solving, may not be very necessary for you. You are already at a good level. I think you should continue with whatever you are doing, assign, do the problems that are assigned, and you should be fine.

However, in my experience, I have found that, most people do not have problem solving as their natural skill. It is necessary for us to pick up that skill, because it is necessary for this profession. And, if you do not have a natural skill, but you need to do something, then you need to pick it up. To pick it up, of course, we practice, we put an effort and then, we get to a certain level, of being able to do problems. I am sure, with consistent good effort, you would be able to solve problems. We will limit ourselves to what are called closed ended problems in this course. Closed ended problems are problems in which everything that is needed for the solution of the problem is either given in the problem statement, or is known through material in your notes, and so on and so forth. This is distinct from open ended problems that may not have all the information that is required stated in the problem, or known; you might need to extend a few things, and then get information from other sources, literature and so on, and then solve the problem.

In fact, in my regular courses, I do assign, a semester long, open ended problem to solve, a problem to be solved over the entire length of the semester. It is a very good learning experience for the students. This format does not allow us to do that effectively. So, let us, at least look at closed ended problem solving for this course.

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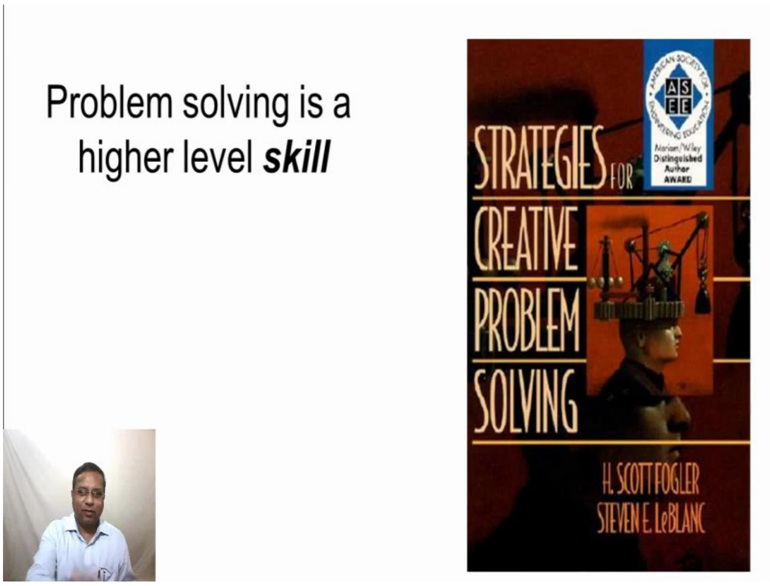

If you are interested in knowing, or in developing the problem solving skill in a systematic fashion, you may want to look at this book. This is, the title of the book is, Strategies for Creative Problem Solving. The authors are Scott Fogler and Steven E LeBlanc. This is a good book. You might want to take a look at that book, if you want to know a little more about problem solving; if you really want to get into it, and become an expert with sustained effort.

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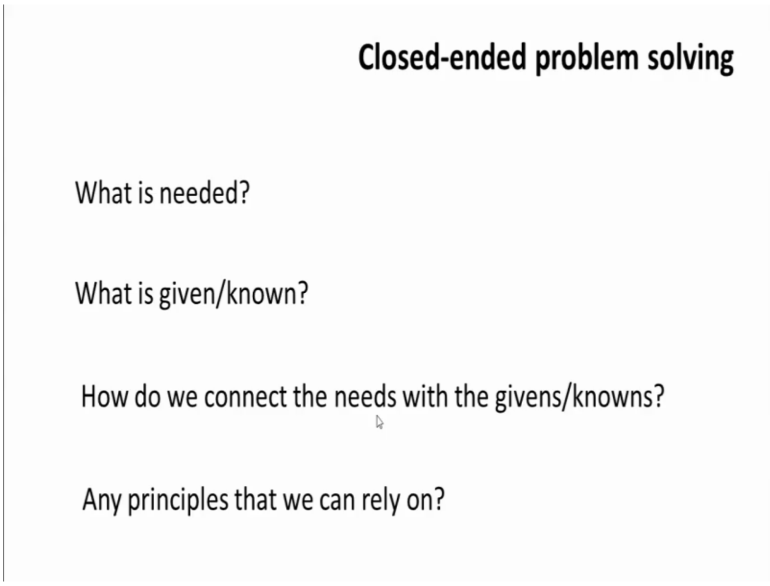

With that, let me go onto how we are going to go about closed ended problem solving. The first question to ask is, what is needed. What does the problem want us to find? Once that is clear, write it down; then, ask the question, what is given, or known, through the problem, through the material that is relevant to the problem, that was covered in the lectures, and so on. Once both those are clear, then, we will ask the question, how do we connect the first one with the second one? How do we connect the needs of this particular problem with the givens, or knowns, in this problem? And while doing that, we will also ask, are there any basic principles that we can rely on, to be able to solve this problem? In fact, while presenting the solution, I am going to use only the first 3, what is needed, what is given or known, how do we connect the needs with givens and knowns, and take this as a part of the third aspect; that is how I am going to do it. Now, let us go about solving the problem that is posed.

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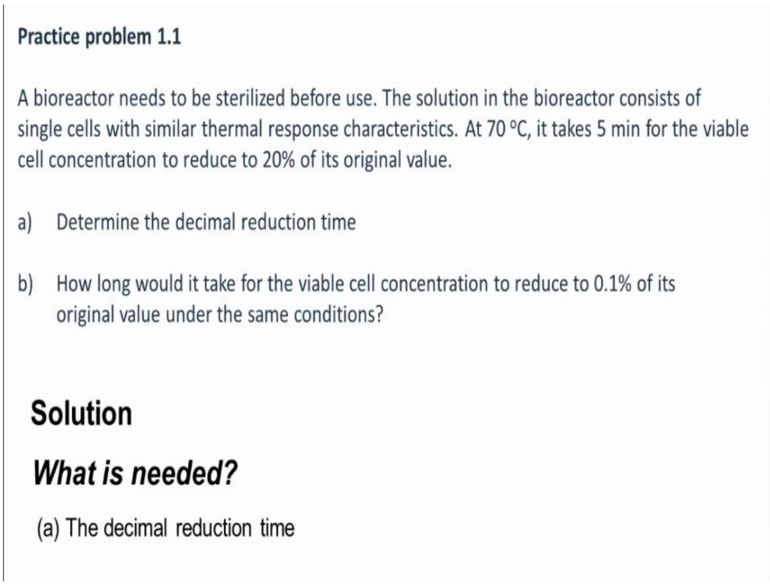

We have already read this. We need to find the decimal reduction time in part a, and in part b, how long would it take for the viable cell concentration to reduce to 0.1 percent of its original value. Some information is given.

The solution, in the bioreactor consists of single cells with similar thermal response characteristics. Therefore, you can assume linear dependence of the log of the viable cell concentration with time, as we saw in class, sorry, the lecture. And also, it says that, at 70-degree C, it takes 5 minutes for the viable cell concentration to reduce to 20 percent of its original value. Having seen this, let us go about the solution. First question, as we said was, what is needed. Let us take one part of it, after another; part a, the decimal reduction time. So, that is clear.

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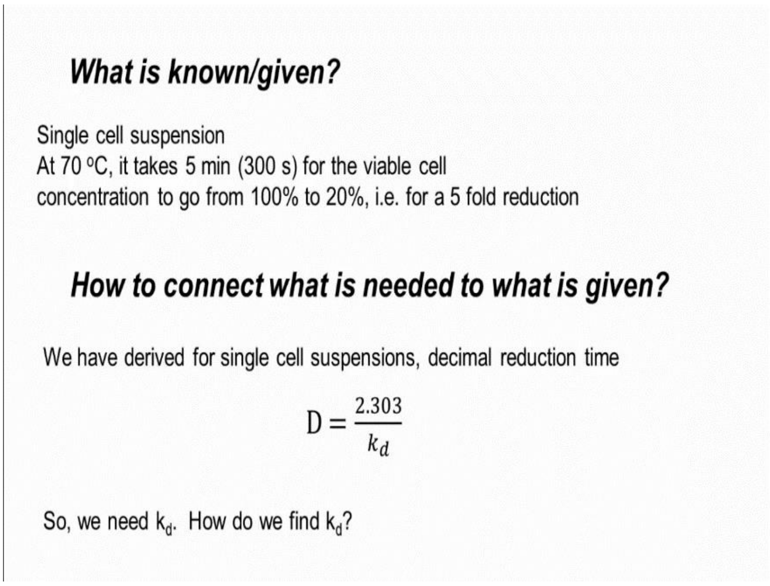

So, let us ask the second question; what is known, or given? We know that, it is a single cell suspension; we discussed this earlier too. And also, we know that at 70-degree C, it takes 5 minutes or 300 hundred seconds for the viable cell concentration to go from 100 percent to 20 percent. Or, in other words, a 5-fold reduction, takes 300 seconds. You see that, I have converted this 5 minutes into 300 seconds, ok.

It is usually good to work in a consistent system of units, whatever that might be, and for the purposes of this course, we will mostly use the SI units, and that is the reason why I have converted 5 minutes to 300 hundred seconds. It is good to do this a-priori and then, go about the actual solution, or beforehand, and go about the actual solution. Then, the third main question, how to connect what is needed to what is given. If you think about it, I am sure, quite a lot of you would have solved this. You think about it. We have derived the decimal reduction time, which we also reviewed a few minutes ago, as 2.303 by k d.

$$D = \frac{2.303}{k_d}$$

Therefore, we need k d. If we have k d, we can find out D, which is the decimal reduction time, which is what is required in part a.

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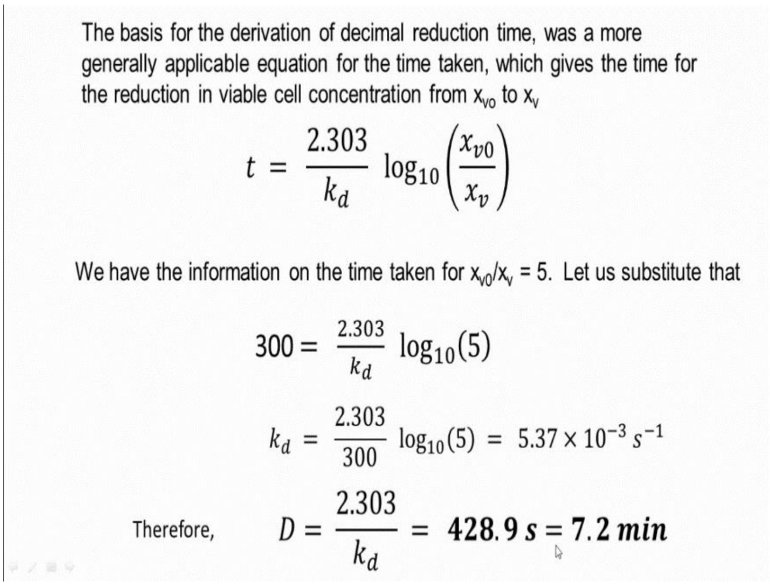

How do you find k d? To do that, let us go back and look at the basis for the derivation of decimal reduction time. We, I think we went through it during the review process. So, let me just say, this gives the time for the reduction and viable cell concentration from x v naught to x v. We had derived the time to be 2.303 by k d, log to the base 10 x v naught by x v.

$$t = \frac{2.303}{k_d} \log_{10}\left(\frac{x_{v0}}{x_v}\right)$$

We have the information on the time taken for x v naught by x v to be 5.

$$\frac{x_{v0}}{x_v} = 5$$

In other words a 5 fold reduction, from 100 percent to 20 percent. So, that if you substitute here, in other words, this is, becomes 5, right. So, we need 5 minutes or 300 seconds for a 5-fold reduction. Therefore, 300 equals 2.303 by k d log 5 to the base 10.

$$300 = \frac{2.303}{k_d} \log_{10}(5)$$

So, k d is the only variable here, and k d, if we transpose this, or essentially multiply both sides of the equation, you can do the same things to both side of, both sides of the equation, that you know; if we multiply this side by k d, and this side also by k d, we get, and divide this side by 300 and this side also by 300, we get k d equals 2.303 by 300 log 5 to the base 10, which turns out to be 5.37 into 10 power minus 3 second inverse.

$$k_d = \frac{2.303}{300} \log_{10}(5) = 5.37 \times 10^{-3}\, s^{-1}$$

I would like you to verify this particular answer. If you have this answer, fine, but please verify. I have deliberately not verified my answers during the solution process alone. I have done that for the exam questions, and so on, but during the, in a demonstration of the solutions of the problems, the practice problems that are assigned, I have deliberately not verified my answers. If you find an error, please point it out; that will be a nice exercise for you. Now that we have k d, we can find the decimal reduction time as 2.303 by k d, which turns out to be 2.303 by 5.37 into 10 power minus 3, or 428.9 seconds; because this was in second inverse, we get this in seconds. If we divide this by 60, we get 7.2 minutes.

$$D = \frac{2.303}{k_d} = \frac{2.303}{5.37 \times 10^{-3}\, s^{-1}} = 428.9\, s = 7.2\, min$$

Therefore, it takes 7.2 minutes for a 10-fold reduction in the viable cell concentration under these conditions.

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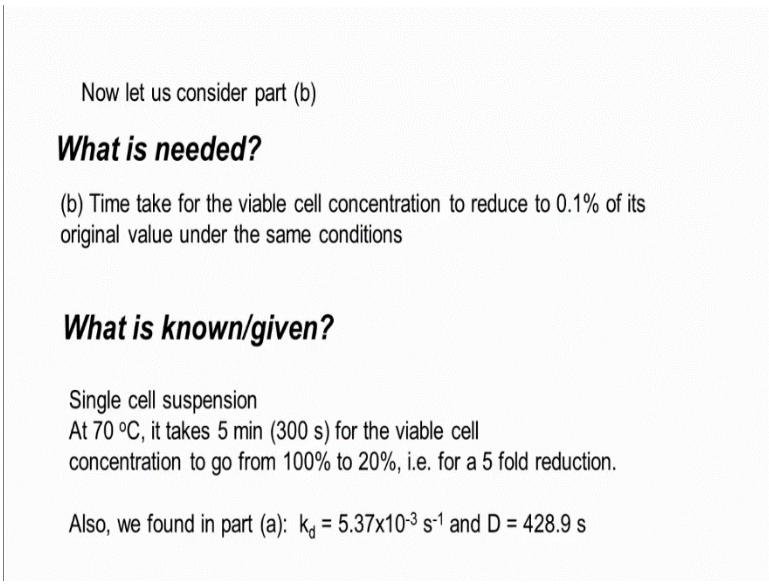

Now, let us consider part b. Again, we will ask the same questions; what is needed? The time taken for the viable cell concentration to reduce to 0.1 percent of its original value under the same conditions. What is known, or given? Single cell suspension, the same as earlier, at 70-degree C, it takes 300 seconds for the viable cell concentration to go from 100 percent to 20 percent. And also, we found in part a, the value of k d, and the value of the decimal reduction time; this is what is known.

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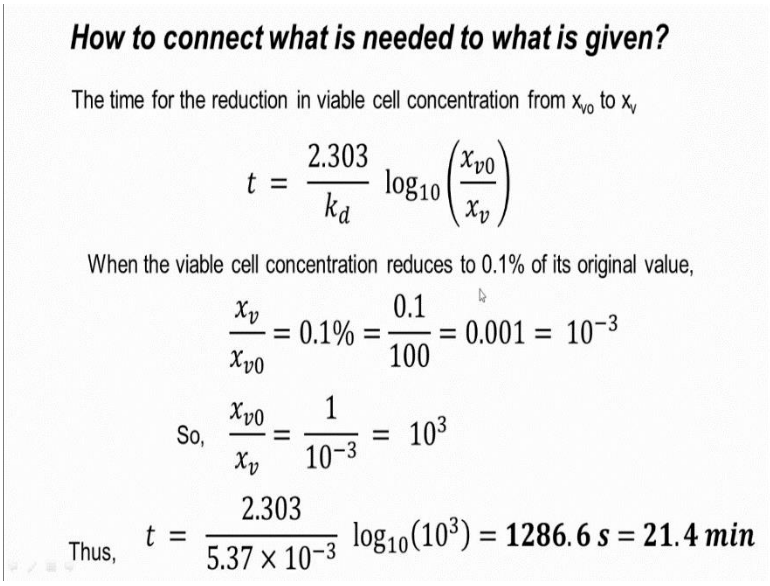

How do we connect, what is known to what is given. The time for reduction in viable cell concentration from x v naught to x v we have already derived and seen earlier also; that equals 2.303 by k d, log to the base 10 of x v naught by x v.

$$t = \frac{2.303}{k_d} \log_{10}\left(\frac{x_{v0}}{x_v}\right)$$

When the viable cell concentration reduces to 0.1 percent of its original value, this is the condition that is of interest to us in problem b. We know that x v naught by x v, sorry, x v by x v naught is 0.1. If x v by x v naught is 0.1, percent this is; this is percent, if we convert it into fraction, this will turn out to be 0.1 by 100; you know, percentage is always out of 100. So, fraction is, when we need the fraction, we need to divide it by 100, this is 0.001, or 10 power minus 3.

$$\frac{x_v}{x_{v0}} = 0.1\% = \frac{0.1}{100} = 0.001 = 10^{-3}$$

So, x v naught by x v, if we flip it around, it will be 1 by 10 power minus 3, or 10 power 3.

$$\frac{x_{v0}}{x_v} = \frac{1}{10^{-3}} = 10^3$$

And thus, the time required for the viable cell concentration to reduce to 0.1 percent of its original value would be just substitution of the various known aspects now, into this equation; 2.303 by 5.37 into 10 power minus 3 log to the base 10 of 10 power 3. That turns out to be 1286.6 seconds, or 21.4 minutes.

$$t = \frac{2.303}{5.37 \times 10^{-3}\ s^{-1}} \log_{10}(10^3) = 1286.6\ s = 21.4\ min$$

This is one way to solve the problem. I have shown you all these steps. Hopefully, you understood these steps, and if you be at it, if it is not natural to you and if you be at it, I am sure you will be able to solve closed ended problems. I think we will finish off lecture 3 with this. These lectures would be of variable times. They will all add up to around 10 hours. The, each lecture would be of variable time. We will meet in the next lecture, lecture 4. See you then.