Transport Phenomena in Biological Systems
Prof. G.K. Suraishkumar
Department of Biotechnology Bhupat and Jyoti Mehta School of Biosciences building
Indian Institute of Technology, Madras

Lecture - 70
LPOS Optimization and Costs

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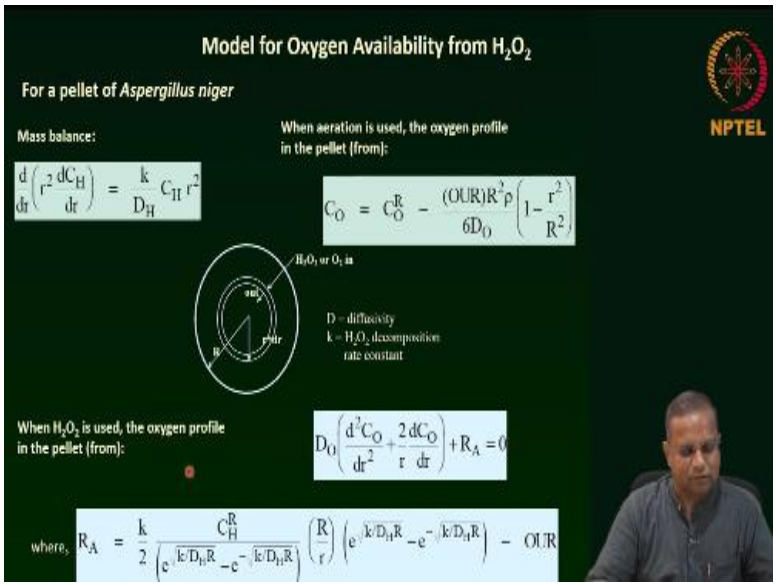

Welcome back this is the summary of what we saw in the previous class, it is nice to see it all in one format shown you the paper first to give you the entire set of details and now I am kind of summarizing here for a pellet of *Aspergillus niger* we said we represented the pellet as a sphere and then we did shell balances here. So hydrogen peroxide or oxygen is coming in from the outside to the inside.

D is the diffusivity and k is the hydrogen peroxide decomposition rate constant. You do mass balance when such a situation arises with hydrogen peroxide this is what remains from the balance you could either do a shell balance or use the equation appropriately and here this is the when aeration is used the oxygen profile directly comes from the application of the solution of the balanced equation; then when hydrogen peroxide is used the oxygen profile is something like this.

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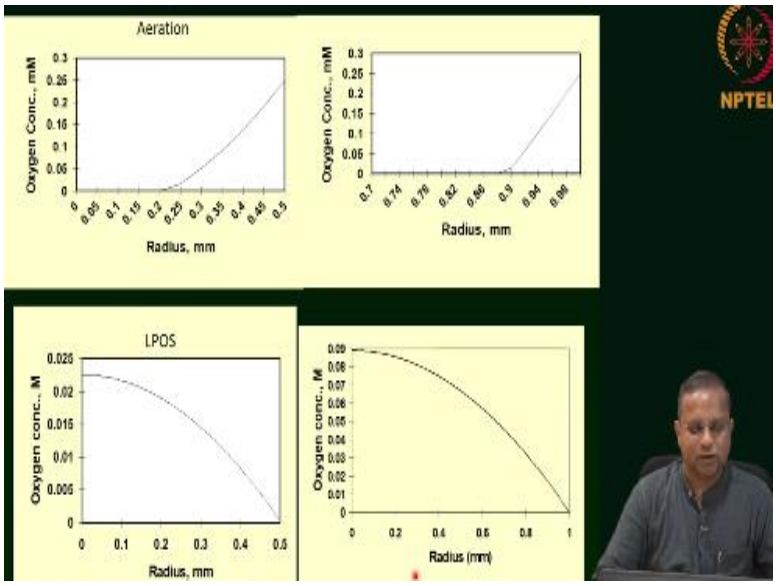

And this one gave us an idea of the oxygen concentration when aeration was used and here we get earlier, I showed you the hydrogen peroxide profiles here the oxygen concentration when LPOS uses just the reverse it is pretty much 0. When it comes in because hydrogen peroxide is coming it needs to be broken down and then oxygen released and that is taken up by the cells, here you find that there is enough oxygen at the center point of this cell whereas a huge region is devoid of oxygen when aeration was used.

So that way LPOS becomes very handy, just the size of the pellets were different in these cases. So this was what we saw in the previous paper, in this class let us look at another aspect of this I thought I will give you some details regarding the methodology itself.

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And some of the costing aspects, so that you appreciate how the costing was done I did briefly mention the costing in the first lecture of application to research aspects, but let me give you the basis in this chapter. The paper that we will talk about today is productivity improvement in Xanthan gum fermentation using multiple substrate optimization. Some parts of the introduction bio processes are often operated in fed-batch mode before that this was published in 2003 in biotechnology process again.

The authors are Chaitali Mandal, he was my second PhD student. Mangesh Kapadi one of our other PhD students myself and professor Gudi who is my colleague in IIT Bombay. Bio processes

are often operated in the fed batch mode to reduce the substrate inhibition and enhance product concentrations. Optimal operation of the fed batch process is preferred to obtain higher productivity and yields and to increase product purity.

Optimal operation can be achieved through closed loop estimation and control strategies which regulate the operation along the profiles that are obtained through optimal control theory from a control point of view this has been written. optimization of fed batch fermentations by the application of optimal control theory has therefore been an area of active research at that time and so on and so forth, this is all about optimization.

This work is concerned with the development of optimal control profiles for multiple substrates in fed-batch fermentation subject to several constraints. The system of focus is the fed batch fermentation for Xanthan gum production by *Xanthomonas campestris* and novel method of oxygen supply through liquid phase hydrogen peroxide addition has been used for the system with a view to overcome limitations of aeration due to high gas liquid transport resistance.

Other substrates that are crucial to the fermentation are the glucose and nitrogen levels and in this work we proposed and experimentally evaluate methods for optimal addition of all these three substrates with a view to maximize Xanthan Gum production. The problem is typically abounded this is getting into too much detail for this course. So the process model the production of xanthan Gum by *Xanthomonas campestris.*

And so on a mass balance for hydrogen peroxide in the medium considering that the flux of hydrogen peroxide in the cell is proportional to the difference of hydrogen peroxide concentration between the medium and the cell. In this case we are using a transfer coefficient approach. And there is a balance that has been written with the appropriate system taken into account a balance of the hydrogen peroxide concentration considering the cell as a system yielded the following material balance.

The specific growth rate dependent on had in peroxide concentration and so on has been modeled as this, the product formation has been modeled as this; this is the glucose mass balance this is the

nitrogen mass balance and so on. And this was formulated as an optimal control problem experiments done and the good results shown. Let me tell you since it is more of control I am not too sure how much of a background you have in control let me not get into the control details of this paper.

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What I am going to do is go back to the presentation and show you some summary of the results from our point of view.

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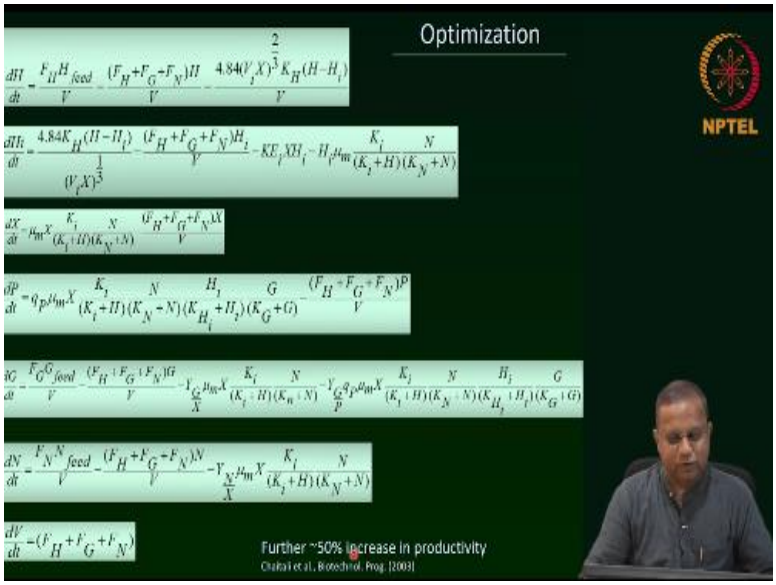

So here this was the optimization balances, all these are balances this is the accumulation term and these are the various input output and so on so forth terms. All these were it and when the optimization was done with the details given in that paper there was an increase in productivity by about 50%. So we have a better method of oxygen supply not just that you go about optimizing based on the known behaviors and so on so forth we got a further 50% increase in productivity that was experimentally shown. So that was that and;

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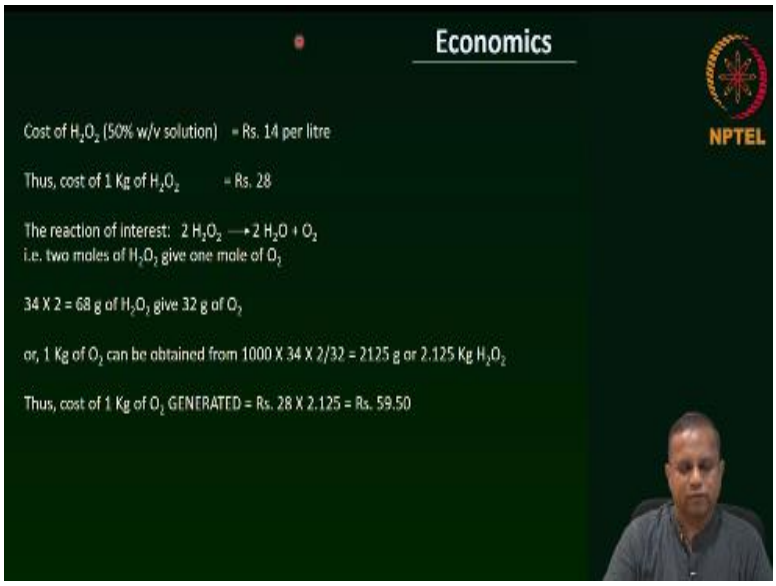

What I wanted to discuss also was the economics of the liquid phase oxygen supply strategy it might be interesting to know this also. The cost of hydrogen peroxide which is available in barrels from national peroxide and so on who as 50% weight or volume solution is still around 14 rupees per liter or it might be a little I think I checked about a year ago it was close to that it is not very different this was a long time ago by the way this was 15 years ago 15 more like 17 years ago.

The cost of 1 kg of hydrogen peroxide therefore is 28 rupees you can work out this the reaction of interest is hydrogen peroxide giving you water and oxygen two moles of methane peroxide giving you one mole of oxygen. And therefore 68 grams, because the molecular mass of hydrogen peroxide is 34, 62 moles gives you 1 mole of oxygen therefore 68 grams that is molar mass into the number of moles of hydrogen peroxide give you 1 mole or 32 grams of oxygen.

Or 1 kg of oxygen can be obtained by (1000 * 34 * 2)/32 essentially manipulating this or 2.125 kg of hydrogen peroxide. That is the cost of 1 kg of oxygen generated is about rupees 59.50. If you just consider the generation alone without any other considerations but that is not a fair comparison.

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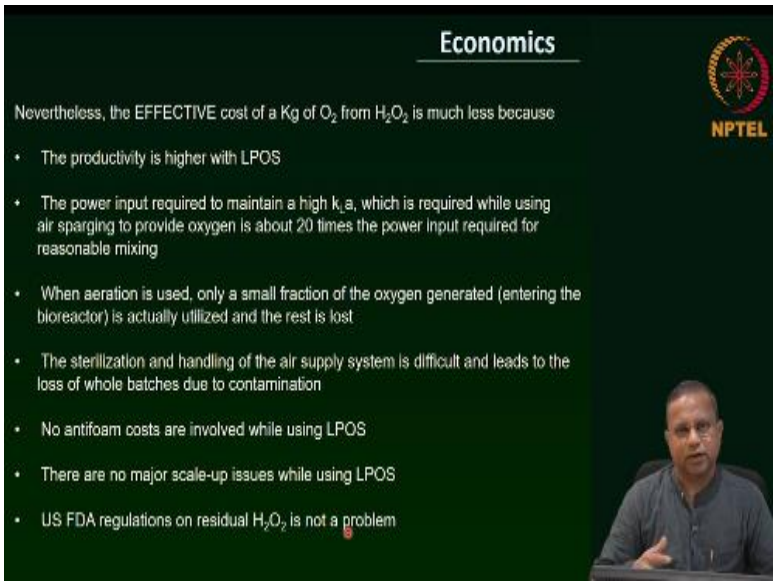

The effective cost of a kg of oxygen from hydrogen peroxide is much less because the productivity is higher with LPOS as we have already seen we have shown that in 15 systems by that by the time the power input required to maintain high k_La, remember volumetric mass transfer coefficient high k_La which is required while using air sparging to provide oxygen is about 20 times the power input required for a reasonable mixing.

So the power requirement is far less the power costs fare less when aeration is used only a small fraction of oxygen generated that is entering the bioreactor is actually utilized and the rest is lost. What do I mean by this? You know when you have aeration you provide air through bubbles into the bioreactor the oxygen from the bubbles gets out into the medium in the time that the bubbles stay in the liquid.

When they come to the surface and when they disperse you no longer have the access to the oxygen that is available in that bubble, therefore it gets lost. So a significant fraction gets lost when you are doing this, the sterilization and handling of the air supply system is difficult and leads to loss of whole batches due to contamination this is also a problem there are no antifoam costs involved while using LPOS there is no forming.

Therefore no anti foam needs to be added and there are no major scales up issues while using LPOS because mixing is the only factor you are not worried about k_La and so on so forth. This are

a lot more complex to scale up and LPOS is mixing is quite easy to scale up comparatively. And the regulations on residual hydrogen peroxide is not a problem because whatever hydrogen peroxide is added it is gone, it is completely gone by the sets.

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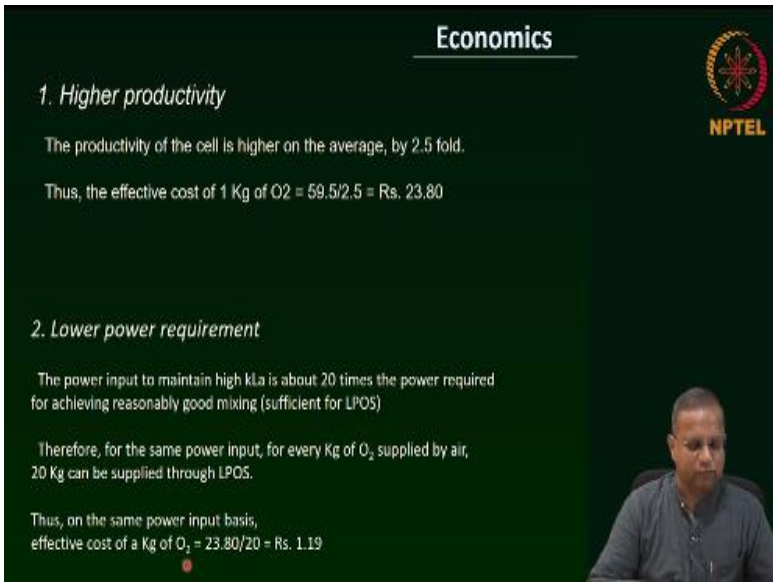

Therefore if you take one at a time and look at what is happening first the higher productivity, the productivity of the cell is higher on the average by about 2 and half fold that we are already shown. Therefore the effective cost of 1 kg of oxygen drops. So the same amount of oxygen you are getting much more product, so you ready to look at it from a product point of view so the product cost drops almost 2.5 fold comes to 23.80. So the oxygen costs for a kilogram of oxygen comes to 23.80.

We talked about lower power requirement about 20 fullness the power input to maintain high k_La is about 20 times the power required for achieving reasonably good mixing with a sufficient for the liquid phase oxygen supply strategy. Therefore for the same power input every for every kg of oxygen supplied by air 20 kg can be supplied through LPOS, that is what it means. Therefore on the same power input basis the cost effective cost of a kilogram of oxygen drops 20 fold even further to 1.19 rupees.

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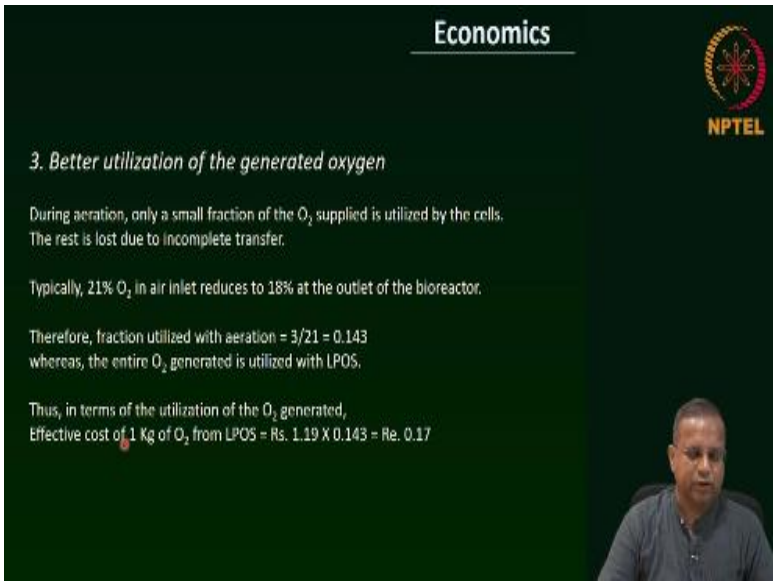

We consider probably one or two more better utilization of the generated oxygen during aeration as I mentioned only a small fraction of the oxygen supplied is utilized the rest of lost with the bubbles. Let us just not due to incomplete transfer from the bubbles to the thing and then the bubbles will go up to the headspace and then they are lost. Typically, 21% of oxygen in Inlet air reduces to only 18% of the outlet of the bioreactor it is well known.

So you are utilizing only 3% of the 21% that is I am sorry the 21% you are utilizing only 3% of the total it is 21% till 18% therefore fraction utilized is 3 by 21 or 0.143, 14.3% whereas the entire oxygen generated as utilized with a liquid phase oxygen supply strategy. That is a term of the utilization of the oxygen generated effective cost of 1 kg of oxygen from LPOS drops even further to about 0.17 paisa per kilogram of oxygen.

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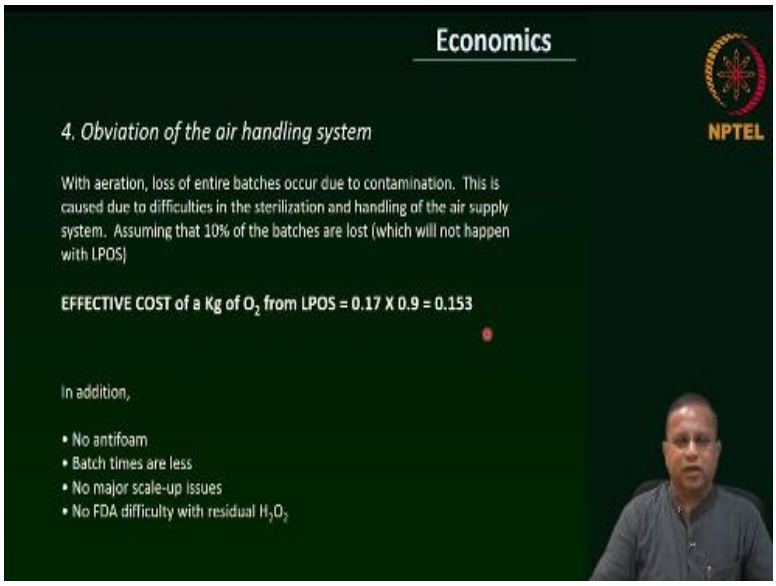

And then you have a obviation of the air handling system which leads to loss of entire batches. When aeration loss of entire batches occur due to contamination this is caused due to difficulties in the sterilization and handling of the air supply system assuming that 10% of the batches are lost which will not happen with LPOS. The effective cost of a kilogram of oxygen from LPOS is 0.153 or 15.3 paisa per kilogram of oxygen at that time the cost of oxygen from air may need compressors filters and so on so forth was about rupees 2 per gram of oxygen.

It can go even further down, in this analysis we have not considered the advantage of using no antifoam batch times being less, no major scale-up issues, no FDA difficulty with residual hydrogen peroxide and so on so forth. Even by considering these it has come down to a very affordable 15.3 paisa per kilogram of oxygen. I think we can stop with that for today for this lecture, we will continue when we meet next, see you then.