Aspects of Biochemical Engineering
Prof. Debabrata Das
Department of Biotechnology
Indian Institute of Technology, Kharagpur

Lecture – 56
Process Control of the Biochemical Processes

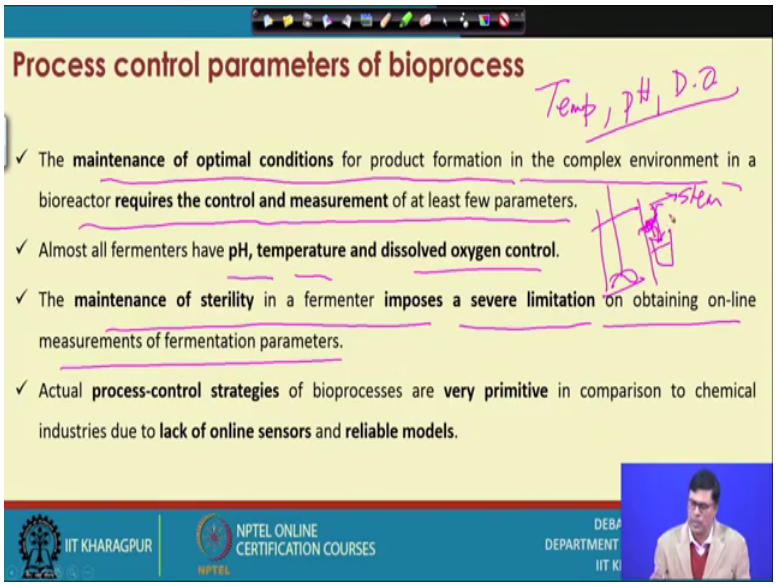
Welcome back to my course Aspects of Biochemical Engineering. Now, in the last lecture I try to discuss the industrial fermentation process and the material analysis. Now, when you discuss the industrial fermentation process we have come across the several things we have come across the bioreactor, bioreactor is the vital things because where the biochemical reaction take place and I told you that main issue is that how to maintain the sterility of that particular process.

So, that our desired organism can grow in that particular environment and to get the desired amount of product and for doings so, I have already shown you in the last lecture that different different type of control controllers are used.

Now, in this lecture we are going to discuss the process control of the biochemical processes that what are the different process control that we use in the biochemical process as you know the chemical and biochemical industry both the different type of process control is required to give the optimum environment, so, that we can maximize the product formation.

So, this particular lecture we with main purpose is to what are the give you the detail information what are the different control system we use how we how it function and all this information I try to share with you.

(Refer Slide Time: 01:50)



Now, first let me let me tell you that process control parameters that involve in the in this bioprocess the maintain the optimum conditions for product formation in the complex environment in a bioreactor required the control and measurement of at least the few parameters that I told you.

Suppose we know that or your organism they are very sensitive to temperature the environment the temperature pH dissolve oxygen that plays very important role am I right if it is there away fermentation process though that you have to mention that.

So, to maintain that that what are the different control systems required almost all fermenters having the pH temperature dissolved oxygen control though the maintenance of the sterility in a fermenter impose a severe limitations on obtaining online measurement of the fermentation parameters.

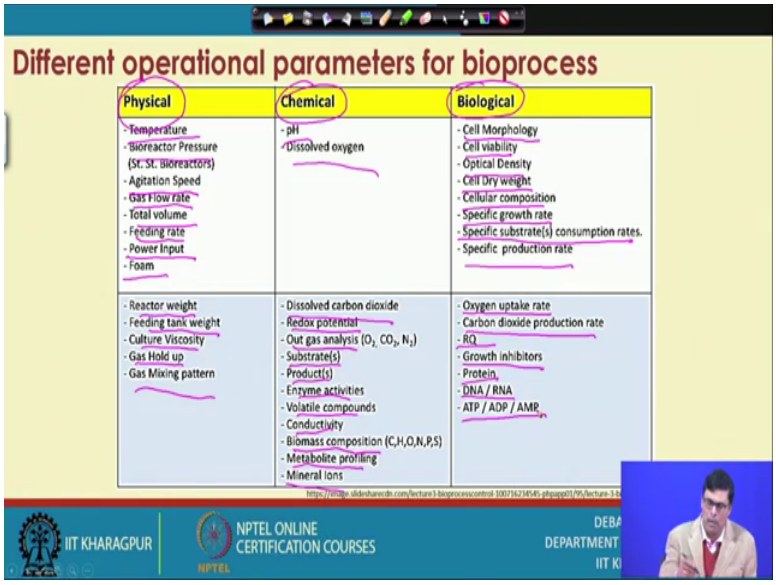
So, whenever we draw the sample whenever do anything in the system we always consider the sterility of the process the how we can, but draw the sample also I can I can give the a typical example suppose this is a this is a fermenter and this is suppose this is your drawing the sample.

So, you basically do we have here suppose here we have one bulb and here is there is the life steam line you know steam line you know life steam line.

The first we press the steam in this pipe line just to ensure the line is hundred percent straight lines then we draw the draw the this we open this bulb and take it in the test tube and then close it and again we draw various a press the steam, so, that just to make the ensure that pipeline in straight lines. So, you know that sterility part we try to maintain in this particular fermentation process.

Actual the process controls strategy of bioprocess are very primitive in compression to the chemical industry due to lack of online sensor and reliable models. So, this is another problem that we have. Now, let us let us see that.

(Refer Slide Time: 04:07)



What are the different operational parameters that we have in the bioprocess, now we can divide into three different categories. So, one is called physical parameter, another called chemical parameter, another is the biological parameter am I right.

Now, physical parameter means what the first parameter that come in picture that is the temperature and second parameter is the bio reactor pressure because what pressure is maintained because usually our biological system operated close to one atmospheric pressure agitation speed we cannot increase the agitation speed to high because if a, if we mostly we use the mechanical agitator if we increase the agitation speed it gives some kind of shearing effect and if there is shearing effect that will hamper the growth of the microorganism.

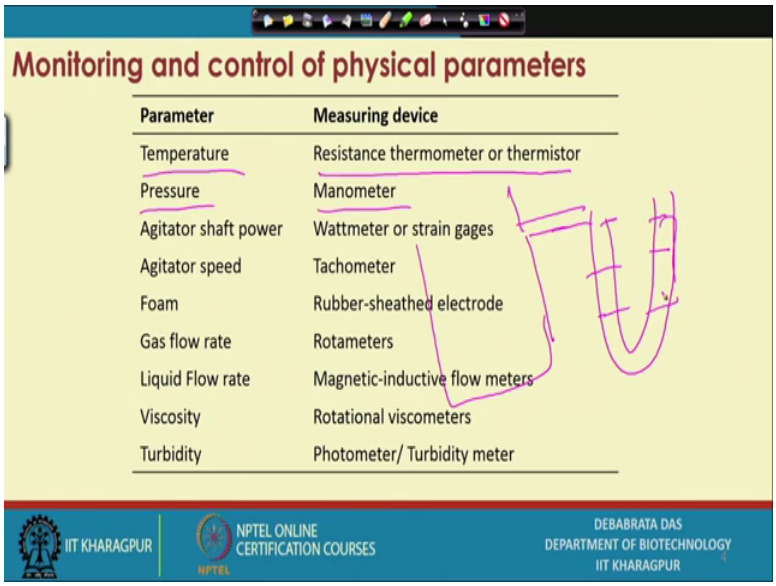
Then gas slow rate because the what you call air flooded that we important the total volume that is very important then total volume we also monitor that how you maintain the monitor the total volume we can monitor either by using watch glass or by using some kind of sensor sensing device; nowadays available that from that we can find it out the feeding rate we can find out that that power improved, we can calculate and the foam that the that that is the things that is the parameters we have we have in this fermentation system.

Then other things is the reactor weight the feeding tank weight the culture viscosity gas holding up and the gas mixing pattern. So, these are the this is this undergoing the physical technique and chemical we have pH and dissolved oxygen and another things we have dissolved carbon dioxide redox potential, we have out gas analysis, sub state product enzyme, activity volatile compounds conductivity, biomass composition metabolites profile and the mineral the ions.

So, different parameters we can estimate seeing the bioprocess and biological we have cell morphology, cell viability, optical density, cell dry weight, and cellular composition, specific growth rate, specific sub state consumption rate, and the specific product formation rate then we have we have oxygen uptake rate, carbon dioxide production rate, respiratory quotient then we have growth inhibitor protein DNA RNA ATP, ADP and AMP that.

So, this are the different parameters we can we can may be used for the offering the different bioprocesses.

(Refer Slide Time: 07:00)

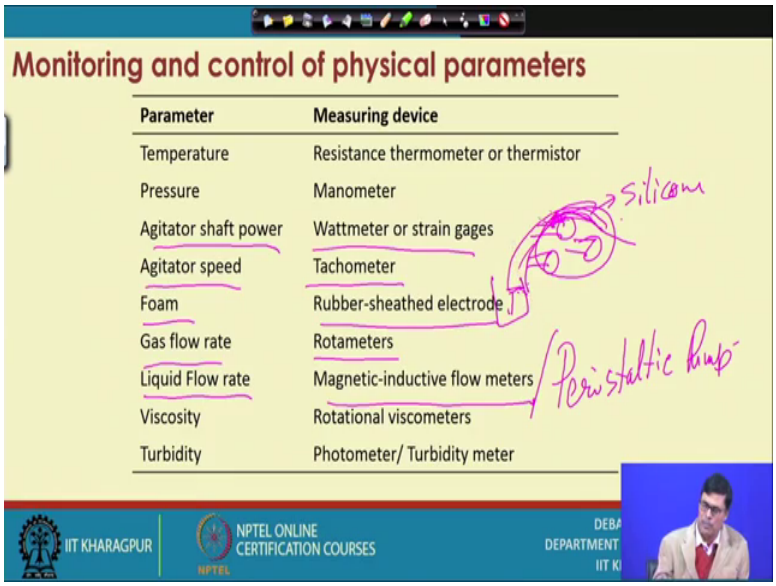


Now, let us see that how we monitor the physical parameters like you know that temperature let us say for example, that is the we use the resistance thermometer or thermistor because I told you it is basically the bimetallic am I right. Now, we know the expansion characteristics of the metal that where depends on it varies on the depends on the conductivity am I right.

So, depending on this conductivity of the metals the expansion and contraction that takes place and from that we can monitor the temperature this is what you call a resistance thermometer and, but here we do not use the mercury thermometer.

The pressure we use the manometer is very very small technique that we have we know; this manometer this we put the liquid and suppose this is connected with your the reactor that you know that this is the reactor that we have and then this pressure difference that will find out from that we can calculate what is the pressure inside the reactor that we can we can calculate.

(Refer Slide Time: 08:16)



Then agitator shaft power this watt meter that we can we have a or string as the we can use. Agitator speed can be a estimated by using tachometer because in our day to day life we also use we have seen that in our in our car and other things we if you want to find out the what is the speed of the wheel that we can find out with the help of tachometer.

Foam is the rubber sheathed electrode that is used and gas flow meter we have already told rotameter is used and rotameters we have a flow (Refer Time: 08:47) we will discuss in details and liquid flow rate as a magnetic inductive flow, but here I want to point out in the following biochemical industry we use the peristaltic pump.

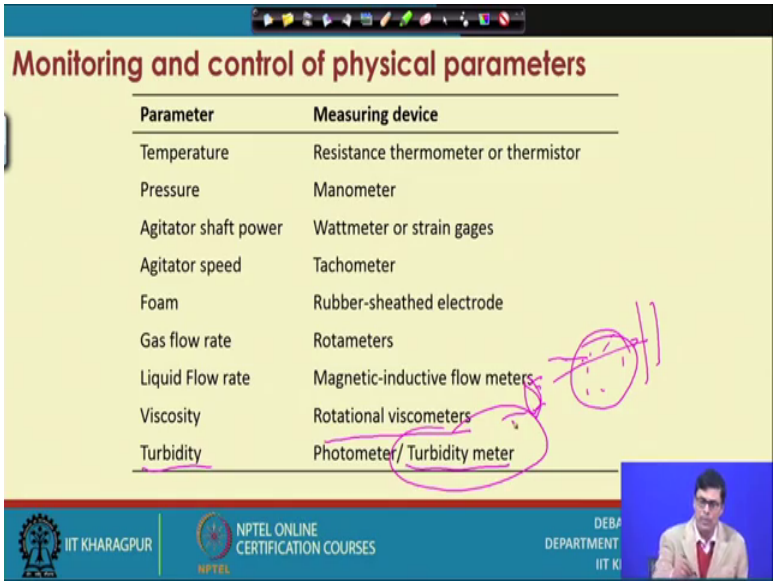
Now, what is peristaltic pump, peristaltic pump is a kind of you know that you know you have kind of that you know that or that that you have this is rod is there and here you what you do? You put the pipe round this and it rotates like this and it follow the principle just like a stopper you know that we have we have in the stopper what you do we press it to take the air out and when we, when they immerge in the water the with the release it then with the vacuum the water will suck into the tube that you know.

So, you know this is like this. So, when this have to move then it press this tube this is mostly made of silicon tube silicon tube you know that. So, when you press it takes the air out and then it again air this way then it creates a partial vacuum here.

So, that that if it is a connected with the somewhere the water tank or liquid tank then water will be suck in and why you why it use in this biochemical process because nothing is expose to the atmosphere everything remain inside the pipeline.

So, we can maintain the sterility very easily viscosity may be if a major with the help of viscometer

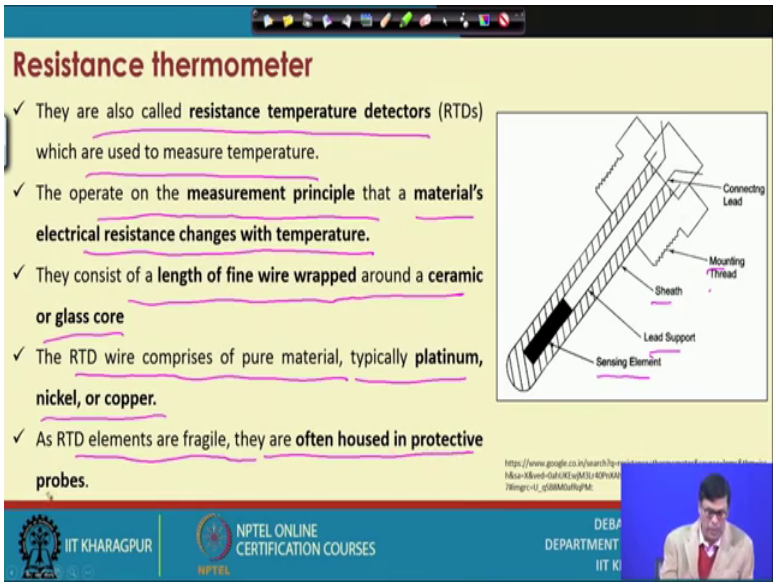
(Refer Slide Time: 10:30)



We have we know the Brookfield viscometer is largely used turbidity is used by turbidometer and turbidometer and calorimeter is little bit different. The turbidometer we is a that the what OD we determine on the basis of that you know scattering of the light particles like the, suppose if the if the particles is there your light will be scattered like this and you know that when you have you have detected here.

This is the light source we have here then we find out how much of light is penetrating this from that we can find out what is the density of the cell present in the sample.

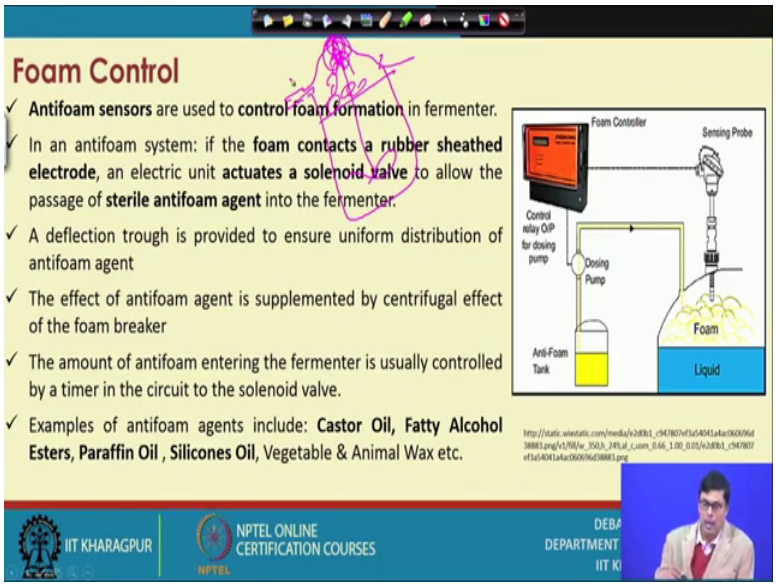
(Refer Slide Time: 11:19)



Now, this is how the resistance thermometer looks this is the. This is the this is the sensing elements and this is the lead support sheath and mounting thread and connecting lead now the they are also called the resistant temperature detector which are used to measure the temperature the operator on the on the measurement of principle that materials element resistance changes with temperature as I pointed out the resistant changes with respect to temperature that we measured.

They consisted of length of fine wire wrap around the ceramic and glass core and RDT wire comprises of pure material typically platinum, nickel, and copper. RDT is a element is are fragile and they are often housed in a protective probes. So, this is the this is RDT resistant temperature detector.

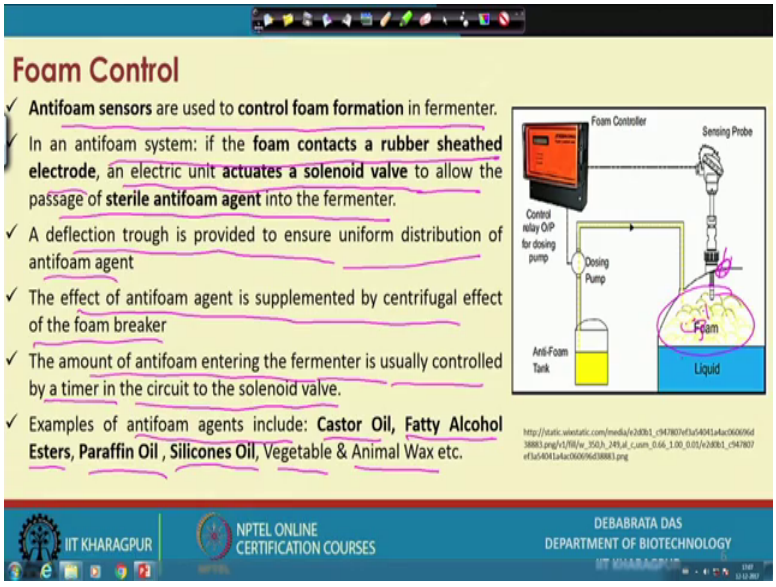
(Refer Slide Time: 12:30)



Next is the foam control next is the foam control which is which is the common feature of any biochemical industry foam formation and as I have why it is very much required because you see that that in the fermenter see suppose this is the fermenter and if you have foam formation and I told you that here you have mechanical seal.

Now, if we allow the foam to build up it will enter the mechanicals seal and rupture the mechanical seal and if you rupture the mechanical seal then all air will enter into the system as per the system.

(Refer Slide Time: 13:06)



So, foam control is the antifoam sensor are used to the control the foam in the fermenter, anti foam system is foam contact in the rubber sheathed electrode and electric circuit actuated a solenoid valve to allow the passage of sterile antifoam agent into the reactor.

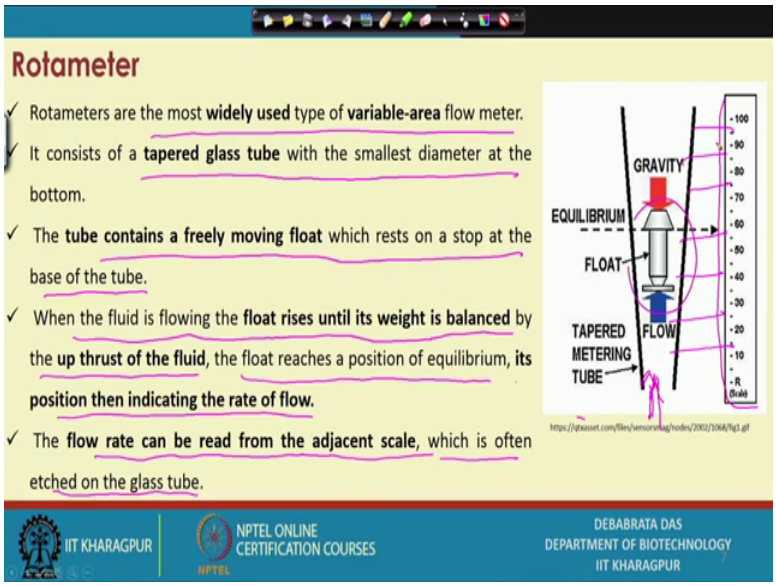
So, there is a current what is solenoid valve, solenoid valve is a electrically controlled valve. So, if a as soon as that you know that this sensor the sensing then is go through the here sensing is there. So, it will it will immediately that it will it will open this solenoid valve and put the antifoam oil into the reactor and when it puts in the reactor this foam will be subside and if a foam subside then it will not effect your mechanical seal at all.

A deflection trough provided to ensure the uniform distribution of the antifoam agent. The effect of antifoam agent is supplemented by centrifugal effect of the foam breaker the amount of antifoam entering the fermenter is usually controlled by a timer in the circuit to the solenoid valve.

Example of the antifoam agent includes the Castrol oil, Fatty Alcohol Ester, Paraffin oil and Silicone oil, vegetable or animal wax etcetera or I can I can tell you that in our in our day to day life if you look in the kitchen that when we cook anything that we particularly cook pulses we find lot of home formation is there and we heat the pulses in the water we will and to subside the foam we add some kind of oil.

So, similarly in the fermentation industry we can we use different type of oil may be vegetable oil, may Castor oil we have Paraffin oils, Silicon oil, vegetable oil and, but you know that the type of oil we use is varies from the industry to industry. Now, rotameter because rotameter is kind of float.

(Refer Slide Time: 15:14)

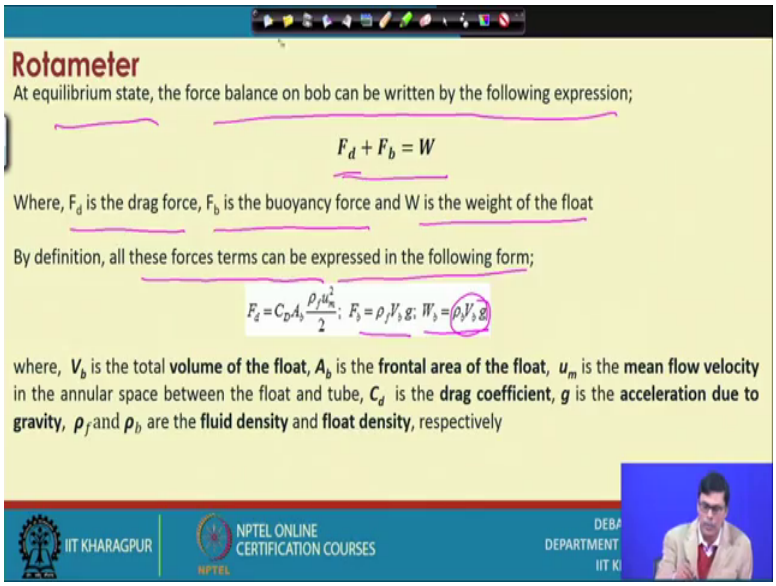


That you know see here that this is the float this is gravity float. So, when you when you press suppose you are pressing your air you throw this though it make a I know that that you know pressure.

So, rotameter is the most widely used variable area of flow meter the tapered glass tube was smallest diameter at the bottom tube contains the freely moving float the rest on a top of at the base of the tube and when the fluid is flowing float rises until its weight is balance and by the up thrust of the fluid the float reaches a position equilibrium and its position then indicated in the rate of flow the rate of rate the flow rate can be read and adjusted in the scale which is often which is in a glass tube.

The main advantage of the rotameter is that suppose you increase the air velocity then flow rate is increases then your float will rise and this is liner scale am I right. So, you can easily monitor that at different flow rate that what. So, you can control your flow rate very easily that is why the rotameter is used in the fermentation industry for controlling the flow of the fluid.

(Refer Slide Time: 16:40)

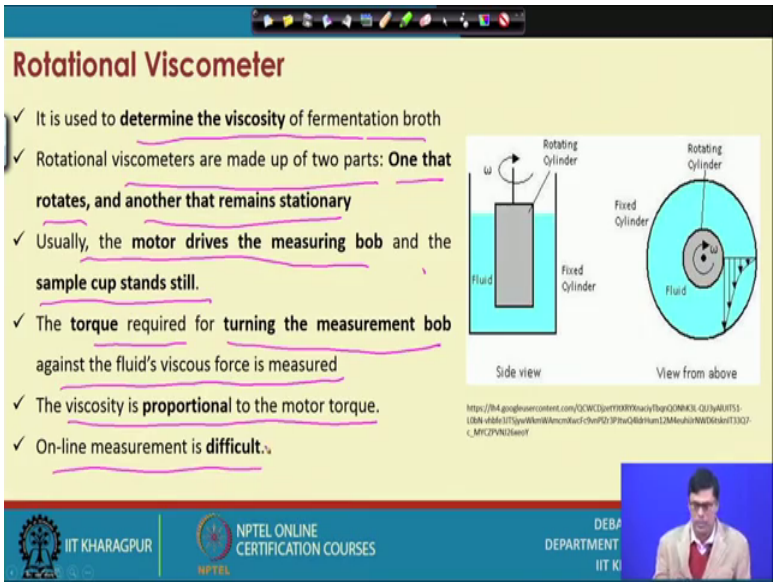


Now, the we are talking about the equilibrium state the force balance on a bob is written in the following expression F d plus F b equal to W, what is the F d is the drag force F d is the balance force of the float and W is the weight of the float.

So, you know that this should be equal to this under equilibrium condition this should be equal to this and by definition all form of force term can be expressed in the following form the F d equal to C D A b into rho f u m square by 2 F d can be expressed like this and W is the just that the weight.

So, this is how we can find it out the rotational viscometer.

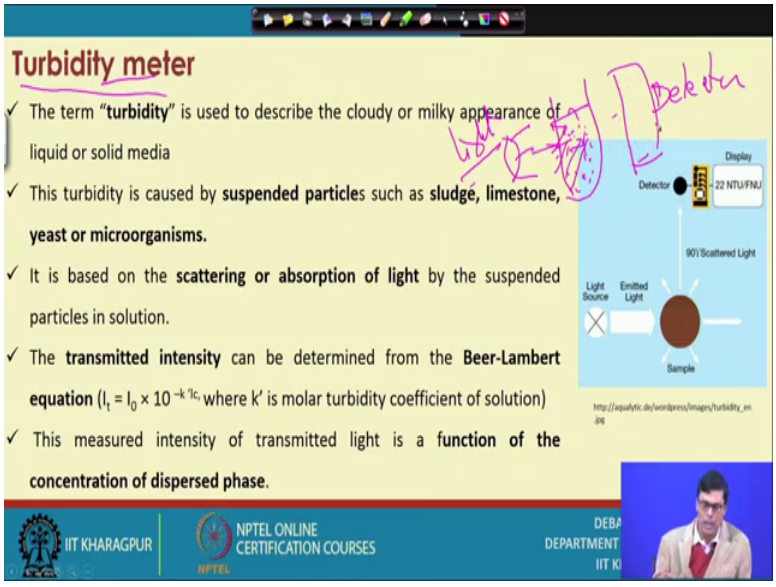
(Refer Slide Time: 17:30)



Which is used for the viscosity of the fluid particularly we know that that brookfield viscometer that is used for the measuring the viscosity of the fluid that determination of the viscosity of the fermentation broth, rotational viscometers are made a made up of two part, one that rotates another that remains stationary.

Usually the motor drive the measuring bob and the and the sample cup stands still, the torque required for turning measure bob against the fluid viscous force is measured the viscosity is proportional to the motor torque on line measurement is difficult.

(Refer Slide Time: 18:14)



Now, another thing is the turbidity meter I try to explain the turbidity meter because this is we know that principles of calorimeter. What is the principle of calorimeter suppose this is the light source this is light source and we keep a solution here and we pass a particular wavelength of light and we measure the intensity of light here you know am I right this is the detector and this is the light source.

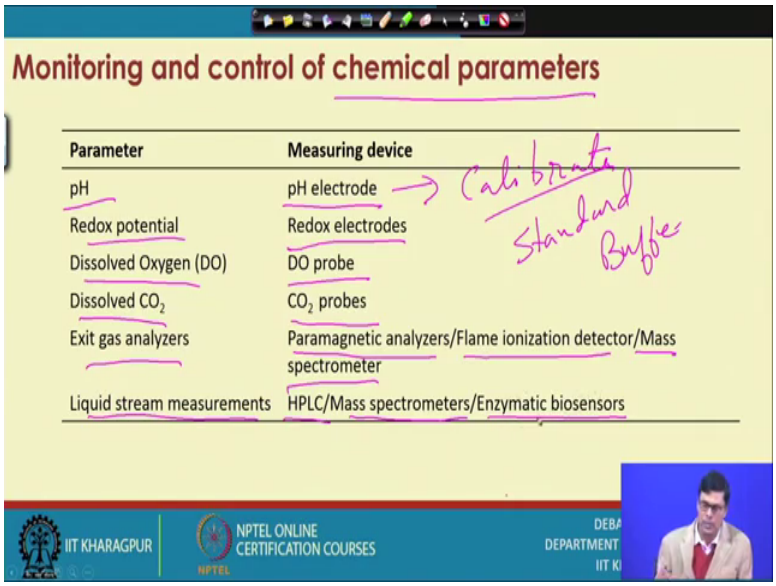
A particular wavelength or we find out we through the scanning we find out that what wavelength you have maximum absorption and that wave length we do that in case of calorimeter, but in case of turbidity meter what we do this is the this is the that. So, in case of calorimeter it is due to absorption light absorption, now here it is not absorption the part is the organism is this particle.

So, you know light will scattered you know it will strike here it will strike here like this if the density is small if that that you know less light will penetrate through this tube. So, your light density measurement here will be less. So, here the term turbidity is used to describe the cloudy or milky appearance of the liquid or the solid media, this turbidity is caused the due to suspension of particle like sludge, lime stone, yeast or microorganism is it based on scattering or absorption of light by the suspended particles.

The transmission that transmitted intensity can be determined by the Beer-Lambert equation that I t equal to I 0 into 10 to the power minus k into n c where k is the molar turbidity coefficient of the solution this measured intensity of transmitted light is a function of the concentration of the disperse phase.

So, this is how we measured the how much light has been emitted that you know that we measured by this a turbidometer this indicate the concentration of cells present in the particular medium.

(Refer Slide Time: 20:35)

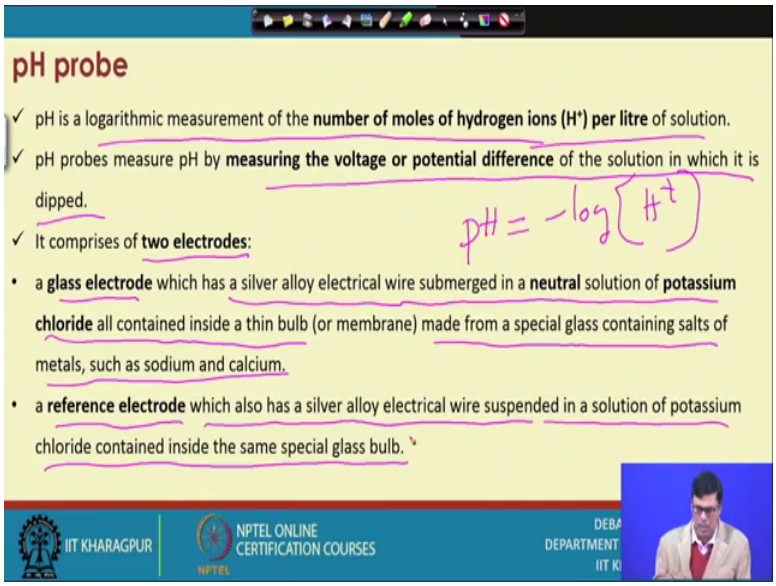


The then question come this all physical parameter then let us come to the chemical parameter we have pH I told you the pH probe is used and for pH monitoring.

Now, whenever you we use any kind of pH probe first we shall have to calibrate the calibrate with the standard buffer with the with the standard buffer the we calibrate that then we put the sample and we find it out the redox potential also measured the kind of oxidation reduction potential of the liquid dissolve oxygen probe; when measured with the help of dissolve oxygen DO probe the dissolve oxygen dissolve carbon dioxide by carbon dioxide probe exist gas analysis can be done by paramagnetic analysis of flame ionization detector and mass spectrometer.

Now, liquid stream measurement by HPLC mass spectro meter and enzymatic biosensor that is used for liquid stream measurement. Suppose I want to measure the how much glucose is there we use the some kind of glucose sensor just to find out how much glucose is there in the outgoing liquid; Now, pH probe that take the instance.

(Refer Slide Time: 21:54)

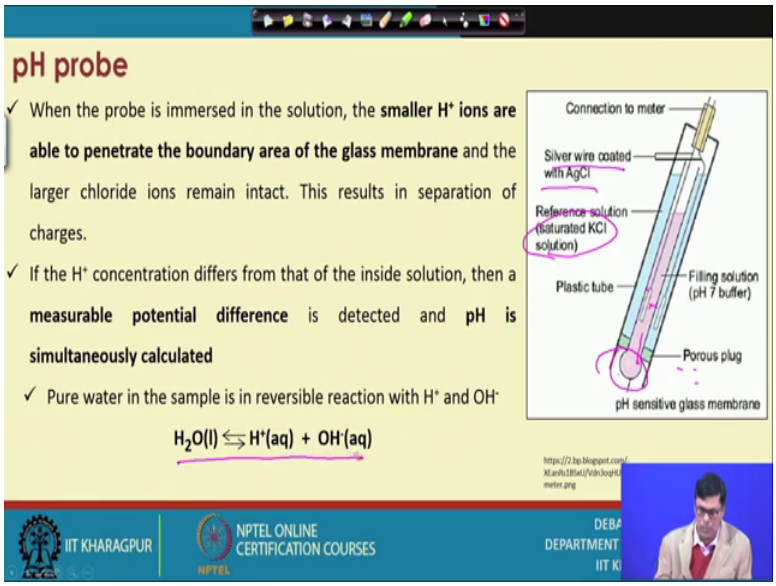


The pH is a logarithmic measurement of the number of moles of moles of hydrogen ion per liter. So, pH how you can write pH equal to minus log into hydrogen ion concentration am I right.

So, this is what is written there the pH probe measure the pH by measuring the voltage of potential difference of the solution in which it is dipped. So, whatever that you know this kind of device we have either mostly we use the potentiometrically, potentiometrically means voltage difference is comprised of two electrode.

One is glass electrode which is silver alloy electrical wire submerge in a neutral solution of potassium chloride, all content inside the thin bulb and made from a is special glass containing salts metal such as the sodium or calcium reference electrode which also a silver alloy electrical wire suspended in a solution of potassium chloride contained inside the same special glass bulb.

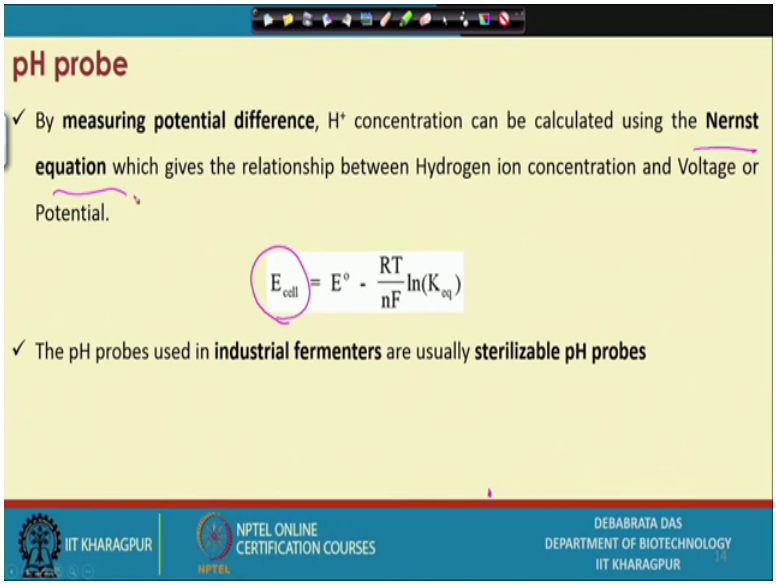
(Refer Slide Time: 23:12)



So, this is how this pH probe looks and this is how it is there that you know this is the filling solution this is the electrolyte that we have you can see this is the electrolyte that this is the plastic tubes and this is the electrolyte solution saturated KCl solution and here you have a the silver wire coated with a AgCl.

And this is the electrode to electros we have and this is the porous glass and this is when you touch the liquid then you sense here and measure the pH of the solution and this reaction is like this that H2O is the hydrogen ion plus OH ion the aqueous solution.

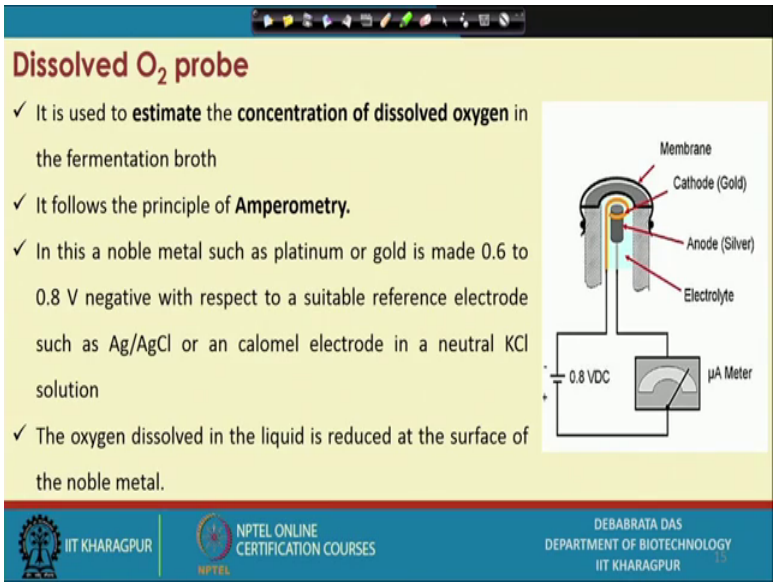
(Refer Slide Time: 23:54)



Now, pH probe how you can calculate this potential we can the E a that potential difference equal to E a E cell equal to E 0 minus R T divide by n F l n, K e k is the equilibrium constant, am I right? If you know the equilibrium constant of that particular that ion compression process this is called Nerst equation on the basis of we can find out the what is the voltage that we have.

This is how it pH probe is function. Now, dissolve oxygen probe.

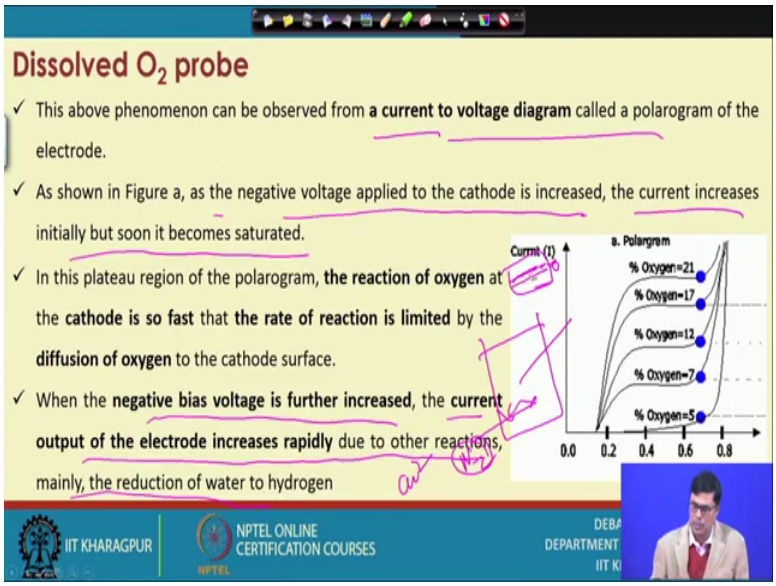
(Refer Slide Time: 24:30)



It looks like this is the membrane this is the cathode which is made of gold and the anode this is made of silver and this is the electrolyte that we have and we measured on the basis of amperometrically and we measure heat.

So, here your pH we measure on the basis of potentiometric and this we measured on the basis of amperometric, amperometric means with the help of micro emitter.

(Refer Slide Time: 25:00)

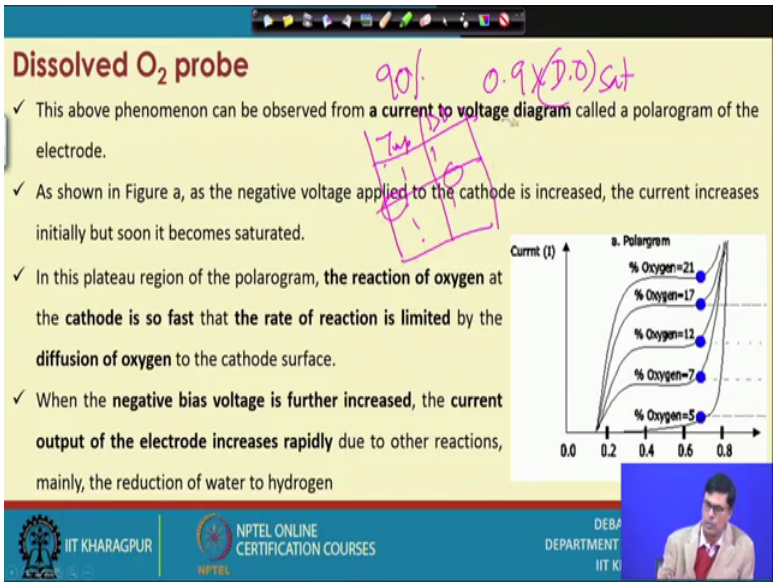


Now, the above phenomena if you look at can be measured by current to voltage diagram this is a this is like this is negative balance. We can have this kind of structure that we correlation, we have the negative voltage apply to the cathode is increased the current increases initially, but soon it becomes saturated.

The when the negative bias voltage is further increased the current output of the electrode increases rapidly due to the other reactions; mainly now one thing I want to tell here how we celibate this to dissolve oxygen probe first in the fermenter where suppose this is the DO probe first we sparge nitrogen and just to drive all the oxygen out and when your monitor shows the that your results is constant that we adjust to 0 and then we this is replaced by air and you will find the dissolved oxygen concentration increases and when this constants the number is constant then that we fix as the 100.

So, your still lies into between 0 to 100 and 100 stands for the saturated dissolve oxygen concentration, suppose the reading is 90, 90 is 90 percent 90 percent means if you have 0.9 into saturated dissolve oxygen concertation DO that is saturation that concentration.

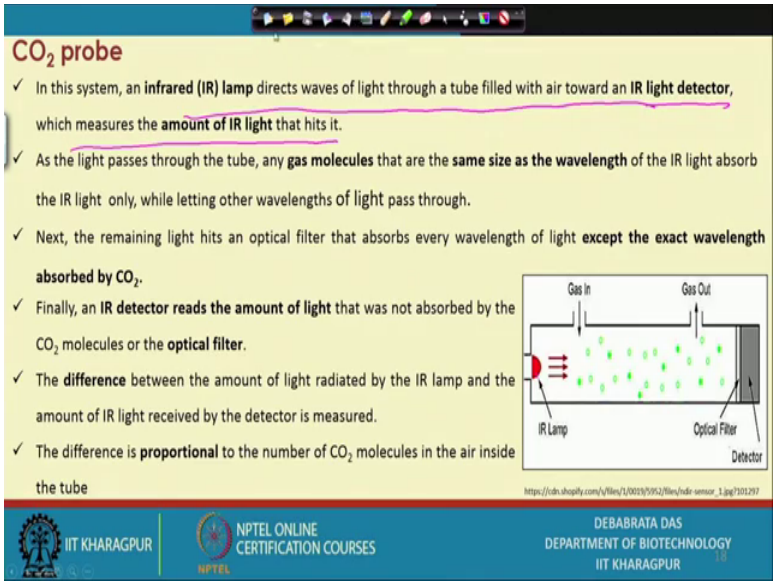
(Refer Slide Time: 26:17)



So, if we have any kind of chemical log book we will find the table where we will find that different temperature what is the saturated DO concertation.

So, if you know that if you know your temperature of operation if you know dissolve oxygen concentration. So, you can easily find out the what is the DO concentration this is how it monitored this is.

(Refer Slide Time: 26:51)

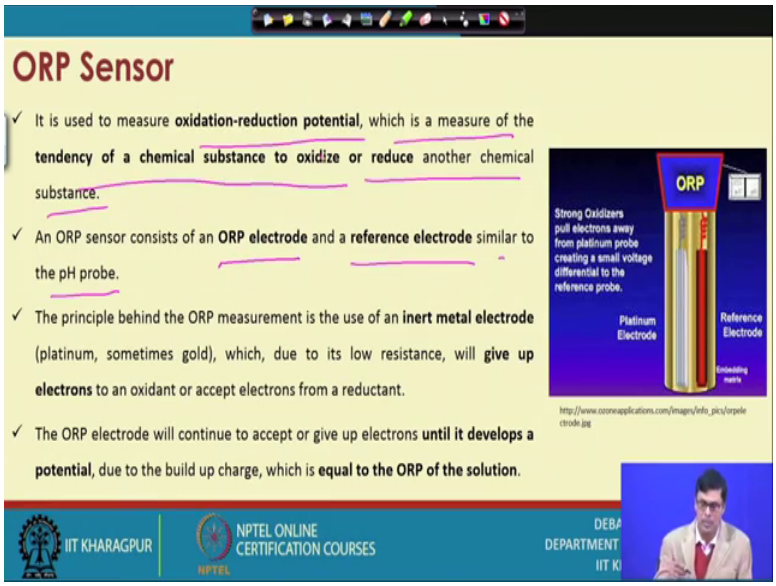


This is how it is done am I not going in details. The similarly we can find out the carbon dioxide probe for that that how you can monitor this is this is the infrared lamp detected

the wave of light through the tube and filled with air and IR light detector is used which is measured the amount of IR light that hit is.

So, this is like this IR lamp is there and you find out were gas in and gas out when this is the detected from the detector; we can find out what is the concentration that we have.

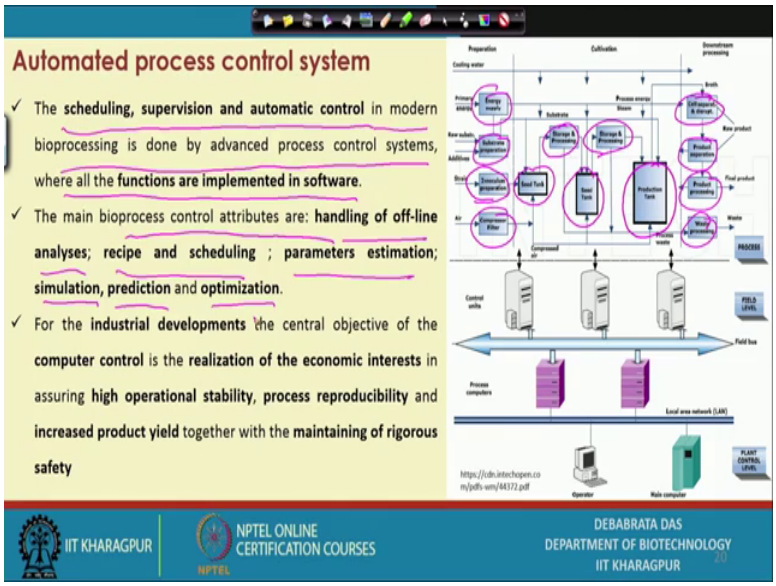
(Refer Slide Time: 27:28)



Now, this is the oxidation reduction potential that we have which is measured by the tendency of the chemical substance to oxidize or reduce to another chemical substance. Sometime it is very much required in case of fermentation process the concentrate of OPR electrode and reference electrode similar to the pH probes.

So, pH probe and this sometimes the we have both the with the pH probe club with this with the oxygen reduction potential, but both the thing oxidation reduction potential and pH probe from the same probe sometime we estimate it the same principles more or less we use here.

(Refer Slide Time: 28:08)



Now, this is the automated process control system that we have that is used in the fermentation industry. Now, if you look at the scheduling supervisor and automation control in modern bio-processing is done by advance process control system for all function are a implemented in software.

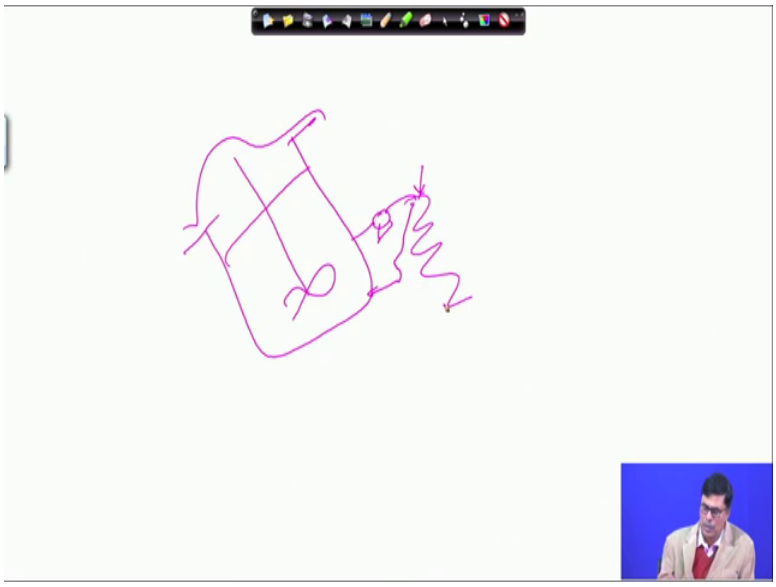
Now, I want to tell here that you know that most of the industry they have pneumatic control system, pneumatic control means special regulating system. So, we can we can we can have a control modules that you know from that we can we can have all the information that we have that.

As for examples this is the production tank we have am I right and this is the storage and processor this is the seat tank that we have, this is storage and processor this is again a this is the seat tank and this is the (Refer Time: 29:06) preparation this is the compression filter, this is sub state preparation, this is the energy supply, this is the cell separation and disruption, this is the product separation product processing, waste processing.

So, these are the different a units we have. So, we have different control units we have the we require all the control system for the different pH. We use that it is a main purpose of bio bioprocess control attributes the handling of off line analysis off line means we take the material out then analyze and recipe and scheduling and parameter estimation the assimilation and prediction and optimization.

So, we monitor from outside we take the sampler I can give the example of online that you know that we have we have two types of analytical system we have, we have online and off line as per examples that suppose in a reactor

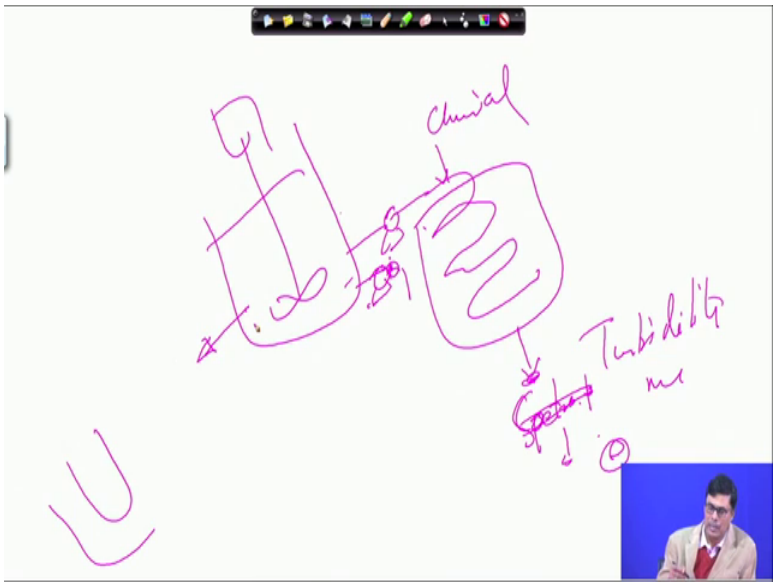
(Refer Slide Time: 30:15)



I can explain that you know like this suppose in a reactor if you wanted to have some kind of online analysis; how we can do that, how we can do the online analysis.

So, what you can have we can have a pump here though here we can have some kind of you know thus a since you so, you can have a bypass line here. So, you can connect it with like this.

(Refer Slide Time: 30:44)



So, here that I hope that it is not written properly to let me tell you we draw the sample with the help of pump. It goes to the analyzer like this then this is a control environment you pose some kind of chemicals then suppose you have calorimeter or spectrophotometer spectro photometer or let us assume this is turbidometer turbido turbidity meter.

So, we can easily find out that what is the cell density and this information is connected with this pump. Another pump here that we set the pump in such a way if the turbidity cross such an limit then this pump will be on and take the material out from the system. This is the how we can do the online monitoring system, now these we can do it off line you can draw the sample out and analyze here you know you have turbidometer and in the turbidometer you can find out and then on the basis of offline analysis you can draw the, you can take the material out.

So, two type of analyzing device we have one in online and another is offline. For the industrial development the central objective of the computer control is to realize the economic interest in assuring the high operational stability processes reproducibility and increase product yield together with maintaining the rigorous safety. So, this is the main purpose for why we required this automatic control with the industrial purpose.

We now most of the industry they operated automatically because their man power requirement in the process drastically reduce because we have seen that I when I discuss

the batch process and continuous process we have seen that in case of continuous process their productivity is more high and not only that that you know the man requirement for the operation of the continuous process is one tenth as compared to the batch process.

So, this is how this control system place very effective role in case of biochemical industry. So, in this particular lecture I give you the overall idea that what are different control system we have mostly it can be divided in the three different ways, one is physical, another is chemical and biological and there are and different parameters because all parameters it is not possible to discuss in this lecture that depending on the your interest you can do that.

As per example suppose you want to monitor the glucose concentration in the fermentation broth, we can use the glucose sensor and you can find out when the glucose concentration cross after certain limit you take the material out. The or you know you can use some kind of product sensor; I can the you can find out that how much product is formation is there from that you can when the product the I can give the example of if that cell mass concentration can be estimated with the help of turbidity meter and when your OD value reach up to certain level that you know then you ensure that your cell concentration leads to the desired level then you take the material out.

This is how we can operate the system and we have different type of control unit we have temperature control, we have pH control, we have do control, we have that agitates speed control, we have antifoam oil we can control. There are different type of control system we use to make the system the operative and to make proper environmental condition and provide desired conditions; So, that we can maximize our product formation.

Thank you very much.