Bioreactor Design and Analysis
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Lecture 09
Design of Fed Batch Bioreactors - Part 2

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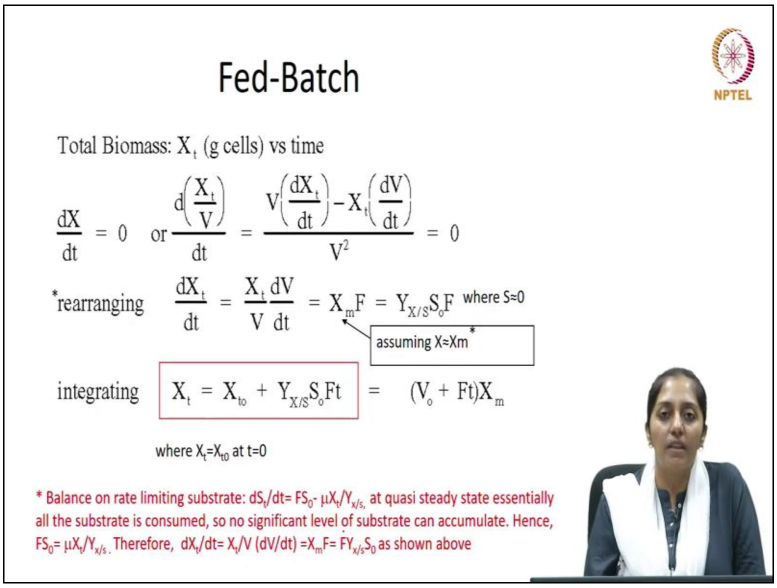

Fed-Batch

Total Biomass: X_t (g cells) vs time

$$\frac{dX}{dt} = 0 \quad \text{or} \quad \frac{d\left(\frac{X_t}{V}\right)}{dt} = \frac{V\left(\frac{dX_t}{dt}\right) - X_t\left(\frac{dV}{dt}\right)}{V^2} = 0$$

*rearranging $\frac{dX_t}{dt} = \frac{X_t}{V}\frac{dV}{dt} = X_m F = Y_{X/S} S_o F$ where S≈0

assuming X≈Xm*

integrating $\boxed{X_t = X_{to} + Y_{X/S} S_o F t} = (V_o + Ft) X_m$

where $X_t = X_{t0}$ at t=0

* Balance on rate limiting substrate: $dS_t/dt = FS_0 - \mu X_t / Y_{x/s}$, at quasi steady state essentially all the substrate is consumed, so no significant level of substrate can accumulate. Hence, $FS_0 = \mu X_t / Y_{x/s}$. Therefore, $dX_t/dt = X_t/V\ (dV/dt) = X_m F = F Y_{x/s} S_0$ as shown above

Now at quasi steady state we know that the biomass concentration is not changing with time. It was a variable and this is now at steady state so no change dX by dt is 0. However the amount of biomass in a fed batch process will keep changing with time because the volume is changing. So let us see how does it change? So let us assume the total biomass as X t at any given time t. And we know at quasi steady state dX by dt is equals to 0.

Now this X can be written as X t which is the amount of cells in the numerator divided by the volume at that time let us assume it is V. So now dX can be expanded as X t by V as given here. Now this differential X t by V has been further expanded because X t and V both are variables. So then it has been further expanded as V multiplied by dX t by dt minus X t times dV by dt and divided by V square this is how the differential is done for the two variable X t by V.

And we know that this is 0 for quasi steady state. So this corresponds to the numerator is also equals to 0 so therefore your dX t by dt will become equal to X t by b from the numerator here will become X t by V dV by dt. Now dV by dt can be replaced as F and this is X t by V some concentration. Now assuming as I said earlier the purpose of the batch is to maximum cell concentration in the fed batch process.

So let us assume it to be X m which will be what then at constant yield of the biomass. Let us assume by X by S which is theoretical maxima. So in terms of that we can write it as Y X by S into S 0 this can be the maximum biomass concentration achieved and S 0 was the initial substrate. So this means S is nearly equal to 0 which is quasi steady state as the substrate is coming in it is getting consumed.

So there is no net substrate then only you can assume maximum biomass production. So your S residual is nearly equal to 0 for this maximum biomass possible. So now this equation can be written in the form of YX by S S 0 into F. So now if we integrate X t which was dX t by dt so now with the limits of X t0 and X t, so X t0 is the initial amount of biomass present S 0 is the feed substrate concentration F is the constant feed flow rate.

So then this becomes a function of time with F YX by S S 0 and X t0 known,YX by S into S 0 X t0 would be what? X m into V 0 + X m Ft. So this X m into V 0 was X t0 which was the initial amount of biomass. Where at the initial point where the substrate concentration was S 0 volume was V 0 so the cell concentration was X t0 by multiplied by V 0. We will end up in the same scenario if we do a balance for the rate limiting substrate.

Let us see it here. This is the rate of accumulation of the substrate at any time t which is equal to the inlet substrate concentration the rate at which the substrate is coming inside the reactor and the rate at which the substrate is getting utilized. So this is a substrate balance equation S t is the amount of substrate at time t, X t was the amount of biomass at time t and S 0 is the substrate concentration and F is the volumetric flow rate.

So at quasi steady state all the substrate is getting consumed. So there is no significant level of substrate which can get accumulated. So then in that case your FS 0 so this goes to 0 and your FS 0 will become equal to mu X t by YX by S. So if FS 0 is equals to mu X t by YX by S then dX t by dt can be written as X t by V dV by dt. So we are multiplying and dividing so then this becomes X m into F which is F multiplied by X m was YX by S multiplied by S 0.

So now this equation X t is equals to X t0 plus YX - S 0 F t this demonstrates that once the quasi steady state has reached this is how the biomass, although the biomass concentration is not going to change with time inside the reactor. But the amount of biomass with time is going to change inside the reactor as a function given here, where X t0 is the start during the quasi once the quasi steady state has reached.

So at this point once the quasi study state has reached the biomass assuming it is your maximum biomass concentration and then we continue to operate the system for the maximum biomass concentration all the time. So that it does not change with time at steady state. So your X t0 is your volume starting volume at quasi steady state multiplied by the maximum biomass concentration which is YX by S into S 0.

So this is the initial amount of biomass once the quasi steady state has reached and now with time at quasi steady state this is how X multiplied by Ft this is how your X t is going to change with time. Now let us do a substrate balance. So if we do a substrate balance this is the rate at which the substrate is getting accumulated inside the reactor. This is the rate at which the substrate is coming inside the reactor.

And this is the rate at which the substrate is getting utilized inside the reactor. At quasi steady state the amount of substrate coming inside the reactor is instantly getting utilized and there is no net substrate getting accumulated inside the reactor. Hence your dS t by dt can be assumed as zero whatever substrate is getting coming inside is getting consumed. So there is no more accumulation of substrate. Hence your FS 0 becomes equal to the term mu X t by YX by S as shown above here.

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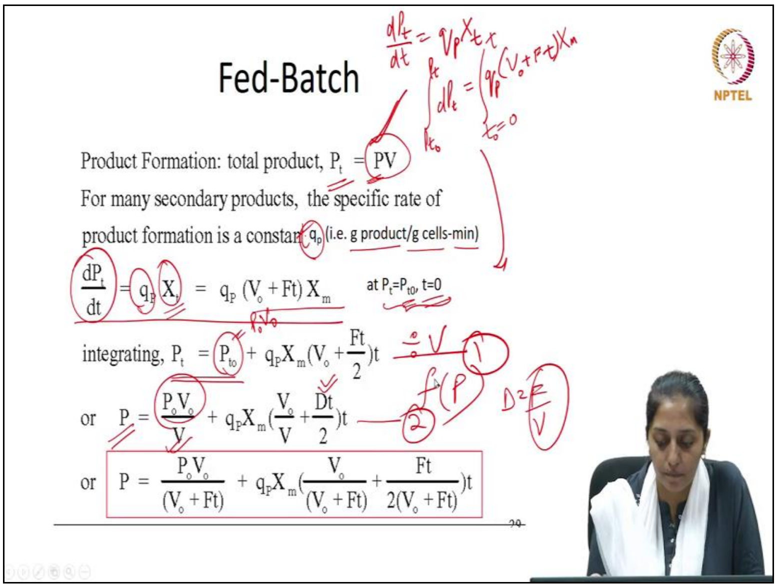

Fed-Batch

Product Formation: total product, $P_t = PV$

For many secondary products, the specific rate of product formation is a constant q_p (i.e. g product/g cells-min)

$$\frac{dP_t}{dt} = q_p X_t = q_P (V_o + Ft) X_m \quad \text{at } P_t = P_{t0},\ t=0$$

$$\text{integrating, } P_t = P_{to} + q_P X_m \left(V_o + \frac{Ft}{2}\right)t$$

$$\text{or} \quad P = \frac{P_o V_o}{V} + q_P X_m \left(\frac{V_o}{V} + \frac{Dt}{2}\right)t$$

$$\text{or} \quad \boxed{P = \frac{P_o V_o}{(V_o + Ft)} + q_P X_m \left(\frac{V_o}{(V_o + Ft)} + \frac{Ft}{2(V_o + Ft)}\right)t}$$

Now let us formulate how the product concentration is going to change in a fed batch process at quasi steady state? Now the total product concentration or the amount of proton product would be let us assume P t the product concentration is P. So the amount can be obtained by multiplying P times V, V is the volume at time t. Now the specific rate of product formation for most secondary metabolite is said to be constant.

The amount of product formed cell or biomass per time. The amount the rate at which the product is forming is equal to specific product rate multiplied by the amount of biomass at that time this is what q p stands for. So therefore if in place of X t we expand from the previous derivation we can write being a quasi steady state. It will be a function of time X m and F assuming that the fed batch process is running at its maximum biomass concentration at quasi steady state.

Now with the limits that at the beginning of the quasi steady state the amount of product is P t0 and this beginning of the quasi steady state the time is assumed to be zero. If we integrate now this equation and put the limits it will become P t is equal to P t0 plus so with respect to t the t has been taken common let us do this for clarity. So the equation was dP t by dt is equal to q p times X t.

So if we integrate and put the limits P t0 dP t is equals to this is specific product formation rate which I said so we can assume that and in place of X t it has been expanded as V 0 times Ft multiplied by X m and the limits as t0 to t and this t0 is 0. So here this will become from here we can write it as P t - P t0 is equal to q p. So this X m is broad near to q p and this becomes t square by 2, so the t and this was V 0 into t so the t has also been taken out common. So now I hope you can understand how we have reached to this equation.

Now further simplifying it rather than keeping in terms of the amount of product we will reconvert it into the concentrations because this is what we are measuring inside the reactor. So in terms of product concentration this will become equal to P is equals to so what we will do we will divide it throughout with a volume V. So this now becomes equal to P ah which we may call as rather than saying it as P t because then if this becomes amount.

So we will call it as P now, the concentration at time t and this goes to the right hand side. So P t can be written as initial product concentration multiplied by the initial volume which is known divided by the V + q p X m V 0 by V so V has been taken inside the brackets and this F by V then becomes D by 2 multiplied by now that you have understood this equation. From this itself as I said we will divide the entire equation by V to make it as a function of product concentration.

So this becomes product concentration at time t and P t0 further can be written in terms of product concentration as P 0 V 0 as given here divided by V because the entire equation has been divided by V and this V has been brought inside the brackets. So the F by V which came here we know D is equals to F by V. So F by V has been replaced as D here. And rest is kept as it is so we end up in this equation.

Now further expansion V we know is a function of time for a constant feed flow rate system assuming the constant flow rate as F, so it has been further written as V 0 + Ft here throughout the equation. So now we know how the product concentration will change with time for a quasi steady state fed batch process.