

Bioreactor Design and Analysis
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Lecture 11
Design of Fed Batch Bioreactors - Practice Problems - Part 2

Welcome back students so today we are going to do some problems on fed batch reactors. Let us begin with the first problem.

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Problem 1



For the production of penicillin, high cell density cultivation is carried out in a laboratory bioreactor. The bioreactor is operated in a fed batch mode with an initial medium volume of 0.6 litres. The maximum specific growth rate of the microorganism is 0.3/h, the yield of biomass from glucose is 0.5 g/g and K_s is 0.1 g/l. The concentration of growth rate limiting substrate glucose in the medium is 100 g/l. The reactor is initially inoculated with 1.5 g/l of cells and allowed to grow in a batch mode till substrate is virtually exhausted. Then, medium flow is started at a rate of 0.2 l/h and the fed batch operation is continued under quasi-steady state conditions.

A. Determine the concentration of glucose in the vessel at $t=2$ h at quasi-steady state.

B. Determine the concentration and total amount of biomass in the vessel at $t=2$ h (at quasi steady state).

C. If q_p is 0.2 g penicillin/g cells/h and $P_0=0$, determine the product concentration in the vessel at 2h.

D. At 2h, 400 ml of the product is with drawn and the fed batch operation continued as before till 4 h. What will be the product concentration at 4 h?



So we will try to do some practice with these problems. If you see on the slide the problem states that for the production of penicillin high density cultivation is carried out in a laboratory bioreactor. The bioreactor is operated in a fed batch mode with an initial medium volume of 0.6 liters. The maximum specific growth rate of the microorganism is 0.3 hour inverse the yield coefficient of biomass with respect to the substrate which is glucose here is given as 0.5 gram per gram.

And the Monod saturation constant is 0.1 grams per liter. The concentration of growth rate limiting substrate glucose in the medium is 100 grams per liter. The reactor is initially inoculated with 1.5 grams per liter of cells and allowed to grow in a batch mode till substrate is virtually exhausted. Then medium flow is started at a rate of 0.2 liter per hour and the fed batch operation is continued under quasi steady-state conditions.

Now let us see the first part of the problem determine the concentration of glucose in the vessel at t is equals to 2 hours of quasi steady state.

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Solution

a) Fed batch is operated when the cell density is high and virtually all of the substrate gets utilized.

So that $\frac{dx}{dt} \approx 0$

At those conditions, $D \approx \mu$

So it can be substituted into Monod's kinetics,

$$\mu = \frac{\mu_{max} S}{S + K_s}$$

$s \approx \frac{DK_s}{\mu_{max} - D}$

At $t=2h$, $V = V_0 + F \cdot t = 1L$


$= 0.6 + 0.2 \times 2 = 1L$

$D = \frac{0.2 L/h}{1L}$

So, substituting the values, $s = 0.2 g/L$

$D = \frac{F}{V} = \frac{0.2 L/h}{1L}$

$= 0.2$



Let us first list down what all is given to us and the conditions of steady state or rather quasi steady state in a fed batch operation. Now steady state or pseudo steady state in fed batch means that there is going to be no accumulation of biomass or substrate happening inside the reactor which means as seen on the slide if you can see on the slide dx by dt will be nearly 0 and also your ds by dt .

And under such a condition your specific growth rate as we had done earlier in our theory classes for fed batch cultivations that the correlation between the sub specific growth rate and the dilution rate is as shown here that both become equal. Now if the culture is following Monod's kinetics then and applying the conditions of steady state which is μ is equals to D . So this is Monod's model and now if we substitute D in place of μ and rearrange this equation to find S .

Your S in terms of D and the model parameters is obtained as shown here which I have underlined with the curly bracket. Now it is said that at t is equals to 2 hour we need to determine the biomass. So given the initial volume and the time of 2 hours and the volumetric flow rate we can find the final volume. So now if you do the rearrangement we know that in this equation the dilution rate is equal to F by V , F is given to us as 0.2 liter per hour and volume is 1 liter then at 2 hours.

So V naught was 0.6 liters F was 0.2 and time in 2 hours so then your final volume becomes one liter. So now if this 1 liter is substituted at 2 hours here for the volume then the dilution rate comes out to be 0.2. Now the residual substrate or at steady state what will be the substrate concentration in the reactor we can find out using this expression. So if you substitute the value of D the residual substrate concentration or the steady state substrate concentration comes out to be 0.2 grams per liter, which is your answer of the part 1.

Now let us see part 2 which is B here. Determine the concentration and total amount of biomass in the vessel at t is equals to 2 hours of quasi steady state.

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b) At quasi steady state and at high cell density, $s \ll s_0$ and also applying $D \approx \mu$

Substituting this in the mass balance equation for biomass gives,

$$X = (X_0 + Y_{X/S} S_i) V_0 + (Y_{X/S} S_i F) t_{fb}$$

$$X = (1.5 + 100 * 0.5) * 0.6 + (0.5 * 100 * 0.2) * 2$$

$$= 50.9 \text{ g}$$

Handwritten notes on the slide include:

- $x = Y_{X/S} S_i$
- $\frac{dx}{dt} = F S_i - \frac{\mu X}{Y_{X/S}}$
- $\frac{dV}{dt} + S \frac{dV}{dt} = F S_i - \frac{\mu X}{Y_{X/S}}$
- $S \approx 0 \Rightarrow \frac{\mu X}{Y_{X/S}} = F(S_i - S)$
- $D(S_i - S) = \frac{\mu X}{Y_{X/S}}$
- $\mu = D$

Now quasi steady state, now it is given now it is 0.2 grams per liter and we started with 100 grams per liter. So we can assume it is nearly finished. So your steady state biomass concentration at quasi steady state can be given as applying D is equals to μ can be given as $Y X$ by $S S i$ assuming that steady state. So if we do a substrate balance at steady state we can determine the value of X .

So let us do the substrate balance here. So at steady state we know μ is equal to D by the biomass balance. So if we substitute this here in this equation. Now S is nearly 0 which was 0.2. So we can say that X is $Y X$ by S into $S i$. So this is how with substrate balance for fed batch reactor we have been able to achieve if residual substrate concentration is nearly zero. Further assuming then the steady state biomass concentration is $S i$ times $Y X$ by S where $S i$ is the inlet or feed substrate concentration.

We have done in the fed batch reactors theory classes that amount of biomass for a fed batch although the concentration remains the same for a pseudo steady state fed batch system. However the amount of biomass will keep changing as a function of time the flow rate of the feed. So you can see that in this equation. So $X_{naught} + Y_{X \text{ by } S} \frac{S - S_i}{S_i}$ is into V_{naught} is nothing but if you remember the problem statement.

It is given here that the reactor is initially inoculated with 1.5 grams per liter of cells and allowed to grow in batch mode till the substrate is virtually exhausted. So we can determine in this batch how much biomass will be generated before it is converted to fed batch. So X_{naught} is the initial concentration the starter culture and the batch is continued till all the substrate is exhausted given the yield coefficient of biomass with respect to substrate the final biomass will be nothing but using the yield coefficient correlation for batch it is $Y_{X \text{ by } S} \times (S - S_{naught})$ where S_{naught} stands for initial values.

So your X will become $X_{naught} + Y_{X \text{ by } S} \times (S - S_{naught})$ where S is nearly finished so as shown here your X the amount so here X_{prime} let us say so here X is amount what we were writing here was concentration. So if we want to convert it into amounts we will have to multiply it with the volume of the system at the end of the batch. So this $Y_{X \text{ by } S} \times (S - S_{naught}) + X_{naught}$ concentration is at the end of the batch multiplied by the initial volume at the start of the fed batch or end of the batch which was 0.6 liters before the feeding started.

So this is what has been done here this will be the initial amount of biomass present at the beginning of the fed batch and then as the feeding will continue it will change to keep running at the state where S is nearly zero and t_{fb} is the time for which the feeding is being done and F is the volumetric flow rate of the feed and S_i is the feed substrate concentration. So then your X will be changing as this which is the amount of biomass this comes out to be 50.9 grams.

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c) The concentration of product is given by
Specific rate of product formation is given by

$$\frac{dP^t}{dt} = q_p X^t$$

Where P^t is the total amount of product in the culture
Substituting $X = (V_0 + Ft)X_m$, we have

$$\frac{dP^t}{dt} = q_p X_m (V_0 + Ft)$$

Where X_m is maximum concentration of biomass

Integrating,



$$P^t = P_0^t + q_p X_m \left(V_0 + \frac{Ft}{2} \right) t$$

In terms of product concentration,

$$P = \frac{P_0 V_0}{V_0 + Ft} + q_p X_m t \left(\frac{V_0}{V_0 + Ft} + \frac{Ft}{2(V_0 + Ft)} \right)$$

$p_0 = 0$; $q_p = 0.2$ g penicillin/gcell.h
Therefore, $p = 16.288$ g/L

Handwritten notes:
 $P^t = X^t$
 $= X (V_0 + Ft)$
 $dP^t = q_p X_m (V_0 + Ft) dt$
 $V = V_0 + Ft$

Let us see the third part if the specific product formation rate is 0.2 grams penicillin per gram cell per hour and P naught is equal to 0 determine the product concentration in the vessel at 2 hours. So the specific product formation rate is nothing but 1 by X dp by dt so here P t and X t stand for the amount of product and amount of biomass at time t . So if X t is nothing but the biomass concentration multiplied by the volume at that time t .

And these biomass concentrations for the pseudo steady state with nearly substrate concentration are 0 which means it is maximum biomass concentration. So we can write it as y X by S s I multiplied by b naught plus Ft into q p is dP t by dt . Now here if the maximum biomass concentration is known then fine otherwise it can also be obtained if S i is known. So here it has been integrated to get the function of P with respect to time.

So once we integrate we can get this X m is constant add steady state and this is what we had derived the expression already in fed batch classes. So we can determine the product amount and then divided by the volume at time t which is V naught + Ft to get the amount of product concentration at time t .

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After 2 h, 400 mL is removed, so the volume is back to 0.6 L but the cell concentration is 50.9 g/L.

NPTEL

$$X_2 = 0.6 \times 50.9 + (0.5 \times 100 \times 0.2) \times 2$$


$$= 50.54 \text{ g and } V = 1 \text{ L at 4h,}$$

so $x_2 = 50.54 \text{ g/L}$

$$p_2 = 16.288 \times 0.6 + 0.2 \times 0.2 (0.6 + 0.2) \times 50.54$$

$$= 25.95 \text{ g/L}$$

Handwritten notes include: $V = V_0 + Ft = 0.6 + 0.2 \times 2 = 1 \text{ L}$, $t = 2 \text{ h}$, $q/p \times X$, and $q/p \times V_0$.



Let us see the fourth part at 2 hours 400 ml of the product is withdrawn and the fed batch operation is continued as before till 4 hours. So after 2 hours of quasi steady state 400 ml of the product is removed. So the volume goes back to 600 ml and then it is further continued in fed batch mode till four hours okay. So then we are asked to calculate the product concentration at 4 hours.

So after 2 hours of quasi steady state 400 ml is removed. So we know that the volume from 1 liter will go back to 0.6 liters at t is equals to 2 hour. However because it is at quasi steady state the biomass concentration is 50.9 grams per liter and then so this becomes the initial point for again fed batch to start. So your amount of biomass which will be obtained after four hours of feeding can again be obtained by the expression we had used here this equation here.

We will use the same expression. So if you now the only difference is this will change to the value at 2 hours so this is volume at 2 hours and this is the biomass concentration at 2 hours. So multiplying by the volume this is the amount of biomass at 2 hours and this is nothing but F the substrate concentration in the feed point 2 is F and 0.5 was $Y X$ by S and t is because still till 4, t is equal to 4 hour and we had started at t is equals to 2 hour where the removal happened and the volume reduced to 0.6 from 1 liter.

So how long the feed was done? The feed was done for another 2 hours. So here the t value is 2 hours we will come to know the amount of biomass which we can obtain at the end of 4th hour which is 50.54 grams and V is V naught plus Ft . So this was $0.6 + 0.2$ into time is 2

hours. So this is again one liter after 2 hours of feeding. So now once we know the final volume after 2 hours of feeding at fourth hour and the amount of biomass the concentration would be biomass amount divided by the volume at that point.

So in the reactor it will be 50.54 grams per liter. Similarly we will calculate the concentration of product which comes out to be 20.95 grams per liter. So here if you see 16.28 was the product concentration at t is equals to 2 hours and the volume at that point was 0.6 liters because 400 ml has been removed. So amount of product can be obtained by multiplying the volume with the product concentration at t is equals to 2 hours which remains the same even after the removal of 400 ml.

So q_p is given to us as 0.2 which is given here. So if you see put it in the expression given here your amount of product is $P_{naught} + q_p \times X \times (V_{naught} + F_t \times t)$. In terms of concentration if we rewrite this equation it will come out to be as shown here. So your final concentration of product will be the the initial concentration multiplied by the initial volume divided by the final volume plus q_p the final biomass concentration time the initial volume plus F_t .

So if we substitute all this so here we know the final volume was again one liter so $V_{naught} + F_t$ here gets automatically cancelled. So this will end up into P_{naught} and V_{naught} is nothing but your initial amount of product divided by. So all this is one. So in for this problem this can be simplified as shown here as $P_{naught} \times V_{naught} + q_p \times X$ which is here the steady state concentration multiplied by the time 2 hour.

So this is a typo here the time 2 hours and in the brackets we have $V_{naught} + F_t$ by 2 so F is 0.2 time is 2 hours by 2. So we have $0.6 + 0.2$ inside the brackets as shown here. This is your final biomass concentration and this 0.2 it is a typo it is 2. So this will give you 25.95 grams per liter as product concentration at t is equals to 4 hours.