


Bioreactor Design and Analysis
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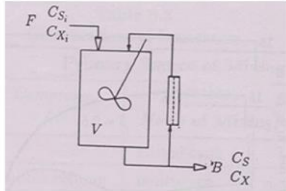
Lecture 16
Design of Continuous Bioreactors - Part 4


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Continuous Reactor with cell Recycle



$F C_{Si} - B C_{Xi} + V \mu C_x = V dC_x/dt$
 $\beta D = \beta / \tau = \mu$, at steady state with sterile feed
 β = bleeding ratio = B/F
 At steady state $\beta D = \mu$ at no cell recycle i.e. at $\beta = 1$, $D = \mu$
 Assuming monod's kinetics
 $C_x = \beta K_d / (\tau \mu_{max} - \beta)$
 It is valid only for $\tau \mu_{max} > \beta$ and $C_x = Y_{x/s} (C_{Si} - \beta C_{Sj}) / \beta$
 If $\beta < 1$ then Dilution rate can be increased more than μ_{max} without washout till some higher value equivalent to μ_{max} / β





James M. Lee, Biochemical Engineering, Prentice Hall, 1992

So, in another setup of continuous recycle continuous reactor with cell recycle. If you can see the schematic here on the screen for a continuous reactor running at a steady state with the recycle stream. Here the cell separator device is after the bleeding stream. So bleeding stream is the stream of the recycle which is being let out. So this is being done in order to find the conditions so that we can run still the system at steady state.

So let us find the condition. So in this case B is the volumetric flow rate of the bleeding stream and let us assume that the volumetric flow rate of the bleeding stream is related to the incoming flow rate by a factor beta. So now let us do a mass balance across this system. Now because nothing is known about the volumetric flow rate or flow rate of the system exiting this and how much is going as a recycle.

So we can place the system boundary as I have shown with these red dots. And let us do a mass balance across the system boundary. So if we do a mass balance across this system boundary the first term shown here in equation one $F C_{xi}$ is the rate at which the biomass is entering the boundary layer or boundary. The second term $B C_x$ is the rate at which the

biomass is leaving the system boundary plus $V \mu C_x$ is the rate at which there is growth happening in this system. This net is equal to the accumulation of the biomass in the reactor.

So the rate at which now at steady state we want to assume that the accumulation rate is zero. So, if we do the rearrangement and we consider beta as B/F then at steady state you will find βD is equal to μ now with no recycle which means beta is equal to 1 this is a simple scenario of D is equal to μ in a cstr running at a steady state. Assuming Monod's kinetics in this case the steady-state substrate concentration which is exiting the reactors can be given as equation two.

So if we assume in μ is equal to βD that it is following Monod's kinetics μ can be replaced as $\mu_{max} C_s$ upon $C_s + K_L$ and on the it is β times t . So if you do the rearrangement you reach to equation 2 where $1/D$ is τ which is the residence time. Now if you see the denominator this is valid only when $\tau \mu_{max}$ is greater than β . So therefore, your μ_{max} should be greater than β times t .

So which means that for β is equal to 1 there is no recycle is not it. So for no washout to happen the dilution rate always has to be less than μ_{max} . But if β is a fraction less than 1 then dilution rate can be increased more than μ_{max} and still we can avoid washout because here β times t where β is a fraction will still remain less than μ_{max} in the denominator. Then your steady state biomass concentration in terms of yield coefficient can be given as $C_{si} - \beta C_s$.

So if we need to determine the value of D at which the washout can happen in the system for a given value of β then $\tau \mu_{max}$ is to be greater than β . So your μ_{max} be greater than β/D and your dilution rate has to be less than μ_{max} by β given any value of β . So this is the dilution rate at which the washout can happen in this system.

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Endogenous respiration



Adding term for endogenous respiration gives

$$D = \frac{\mu_{\max} S}{S + K_s} - k_d$$

$$\mu = D + k_d$$

$$S = \frac{(D + k_d) K_s}{\mu_{\max} - D - k_d}$$

$$X = Y_{x/s} (S_0 - S) \frac{D}{D + k_d}$$



So let us see if there is endogenous respiration then how do we take into account that term in a continuous reactor. So in a continuous system we know that at steady state D is equals to μ where μ in case of endogenous respiration will be the net specific growth rate and when there is endogenous respiration it will be actual specific growth rate minus K_d . We have done already earlier where K_d is the rate constant for endogenous respiration.


So therefore your actual specific growth rate can be written as D plus K_d and the steady state substrate we know it is related to $D K_s$ upon $\mu_{\max} - D$. So in this case μ we can write it as $\mu_{\max} S$ upon S plus K_s Monod's saturation constant is equals to D plus K_d . If we do the rearrangement here we will get the equation the expression given here for S and x can be given as $Y_{x/s} (S_0 - S) \frac{D}{D + k_d}$ and here it is x multiplied by D plus K_d .

So now we know that $Y_{x/s}$ is dx by dt by ds by dt . So if we expand this for the system your $Y_{x/s} ds$ by dt is equals to dx by dt which is μ times x and here it is in a container system it is dx and here ds by dt is nothing but consumption rate is $D s_0$ minus $D s$ and $Y_{x/s}$ and there is a sterile feed. So now your x becomes for a continuous system can be given as $Y_{x/s} (S_0 - S)$.

So now similarly, if you do it for an endogenous respiration then the ds by dt the rate at which the substrate is getting consumed for growth is nothing but $D S_0$ minus $D S$ and this is equal to dx by dt which is the rate of growth is your μ times x where μ is your net specific growth rate which will be D plus K_d into x . So your dx by dt can be given as D plus

K_d multiplied by x . So therefore your Y_x by s is equal to D plus K_d times x upon $D S_0$ minus S . Further rearranging as we need to find the x it will be Y_x by s D times S_0 minus S divided by D plus K_d times. So this is the expression for the biomass.

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$$\left[\frac{ds}{dt} \right]_{total} = \left[\frac{ds}{dt} \right]_m + \left[\frac{ds}{dt} \right]_g + \left[\frac{ds}{dt} \right]_p$$

Substrate balance equation for a chemostat is

$$D(S_0 - S) - \frac{1}{Y_x} (D + k_d) X = 0$$


The yield coefficient varies with dilution rate for $k_d > 0$



Now we know that the substrate which is getting consumed it is not only getting consumed for growth but it is also getting consumed for maintenance and product formation. So for maintenance it comes under the endogenous metabolism. So we will then do a substrate balance equation for the chemostat. So then if we do that you will see equation one this is the rate at which substrate is coming in rate at which the substrate is going outside the reactor and this is the rate of consumption for the substrate in growth.

Assuming net growth where K_d is your endogenous metabolism and there is no accumulation steady state so this is 0. And therefore, you will observe that you can find an expression same as was given in the earlier slide. For x , so for determining x you can do a substrate balance across the chemostat. So now you can see that the yield coefficient in a chemostat varies with dilution rate for an endogenous metabolism present.

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$$D(S_0 - S) - \frac{1}{Y_{X/S}} (D + k_d) X = 0$$

$$D\left(\frac{S_0 - S}{X}\right) - \frac{D}{Y_{X/S}} - \frac{k_d}{Y_{X/S}} = 0$$

$$D\left(\frac{1}{Y_{X/S}^{AP}}\right) - \frac{D}{Y_{X/S}} - \frac{k_d}{Y_{X/S}} = 0$$

$$\left(\frac{1}{Y_{X/S}^{AP}}\right) = \frac{1}{Y_{X/S}} + \frac{k_d}{Y_{X/S} \cdot D}$$

$$\left(\frac{1}{Y_{X/S}^{AP}}\right) = \frac{1}{Y_{X/S}} + \frac{m_S}{D}$$


So, if endogenous metabolism is present then the yield coefficient varies with the dilution rate. We will see how it varies with the dilution rate. So if you see the equation the first line $D(S_0 - S)$ minus S this is the first term is the rate at which the substrate is coming inside. The second term D multiplied by S is the rate at which the substrate is going out and this is the rate at which the substrate is getting consumed in case of endogenous metabolism.

So in the second line this has been expanded and the entire equation one has been divided by X . So once you divide it by X then your actual yield coefficient or theoretical yield coefficient is given as $S_0 - S$ by X is not it. So this we will call it as the apparent yield coefficient which means what we measure X is the biomass which is in the outlet stream or inside the reactor concentration and $S_0 - S$ will be the substrate consumed.

Then $Y_{X/S}$ is your theoretical yield coefficient and if you expand you will find that this is how the apparent yield coefficient or the actual yield coefficient which you measure experimentally is related to the theoretical yield coefficients which is the kinetic constant by a factor. So this entire k_d by $Y_{X/S}$ has been replaced by a coefficient m_S which is called as maintenance coefficient.

So your $Y_{X/S}$ theoretical is related to apparent yield by this factor. So as the dilution rate keeps on increasing your $Y_{X/S}$ apparent will keep on decreasing.

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• From chemostat data, plot $\frac{1}{Y_{X/S}}$ measured vs $1/D$ to get m_s and $Y_{X/S}$ maximum.

NPTEL

So you can see the plot your apparent yield coefficient which you measure as a function of the residence time. So as residence time increases which means the dilution rate decreases the y apparent yield coefficient also decreases. So this is the plot which has been made here. So $1/Y_{AP}$ is y and in terms of $1/D$ as x so your intercept is your $1/Y_{X/S}$ theoretical and your slope is m_s which is $K_d/Y_{X/S}$ which is equal to your maintenance coefficient.

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Deviation from ideality

- In mycelial fermentation or during production of polysaccharides, the fermentation broth may become viscous and pose difficulty to complete mixing in the reactor.
- Also, certain cells tend to grow as films on the solid surfaces of the bioreactors and its components.
- At industrial scale there are incomplete mixed regions in a chemostat.
- A segregated reactor model can be used to analyze an incompletely mixed continuous-flow fermenter.

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Now let us see a deviation from ideality. Like for example in mycelial fermentations now in mycelial fermentations or during production of polysaccharides for example the fermentation broth may become viscous and therefore pose difficulty to complete mixing in the reactor. Sometimes certain cells they tend to grow as films on the solid surface of the reactors and its component. At industrial scale there are incomplete mixed regions in a chemostat. So then in

that case a segregated reactor model can be used to analyze this incompletely mixed continuous flow fermenter.

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- A simple two-compartment model of a Chemostat culture is used where the reactor is divided into two regions:
- A well mixed region and a stagnant region.
- Feed and effluent streams pass through the well mixed region I and mass exchange takes place between two regions.
- The biomass and substrate balances for both regions at steady state result in eqns:
 - Region 1: $X_1=Y(S_0-S_1)$ substrate balance
 - Region 2: $X_2-X_1=Y(S_1-S_2)$ substrate balance
 - Region 1: Biomass balance, $X_2+\alpha/D' \mu_m [S_2/K_s+S_1]X_1=(1+D/D')X_1$
 - Region 2: Biomass balance $X_1+(1-\alpha)/D' \mu_m [S_2/K_s+S_2]X_2=X_2$

So there is a well known model which is called as two compartment model a simple model for a chemo start culture which can be used in such a scenario. Where the reactor is divided into two regions. A well-mixed region and a stagnant region. So if you see the schematic shown on the slide the field and the effluent streams they pass through the well-mixed region which has been given a subscript one.

And mass exchange happens between the two regions which is the well mixed and the stagnant region. The stagnant region the variables are shown with the subscript two. So if you do the biomass and substrate balance for both the regions and steady state we will end up in equations given here. They have done substrate balance first. So let us see the region 1 which is with the subscript one the substrate balance has been done.

And this system is at steady state so then your x_1 will become equal to the yield coefficient multiplied by the inlet minus outlet substrate concentrations which is a normal chemostat. Now for the region 2 if you do the substrate balance and with the same notations shown here you will end up in equation 2. So maybe you can take 3 and 4 as assignments and you can take home this assignment do a biomass balance across the two regions region 1 and region 2 and see if you are able to end up in equation 3 and 4.