Biochemical Engineering

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Lecture No. # 29

Stability of Bioreactors (Contd.)

On stability of bioreactors and we will continue from where we left, so what we did was we looked at this model of the chemostat for any generalised form of the specific growth rate mu. If you go back to your notes you will see and then we looked at that and we looked at the steady state for that and we derived the criteria using Herberts criteria, we derived the criteria for the stability of the states.

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$$A = \begin{pmatrix} \dfrac{\partial f_1}{\partial X} & \dfrac{\partial f_1}{\partial S} \\ \dfrac{\partial f_2}{\partial X} & \dfrac{\partial f_2}{\partial S} \end{pmatrix} = \begin{pmatrix} a_{11} & a_{12} \\ a_{21} & a_{22} \end{pmatrix}$$

$$\frac{\partial f_1}{\partial X} = -D + \mu \qquad\qquad \frac{\partial f_1}{\partial S} = X \frac{\partial \mu}{\partial S}$$

$$\frac{\partial f_2}{\partial X} = -\frac{\mu}{Y_{x/s}} \qquad\qquad \frac{\partial f_2}{\partial S} = -D - \frac{X}{Y_{x/s}} \frac{\partial \mu}{\partial S}$$

And then in the last 5 minutes or 10 minutes of the lecture what we did was, we put in our form of the specific growth rates being mu here as you see on the screen now and we derived the matrix because we had. So, using the Herberts criteria we had to derive the matrix A and then we have to look at the terms of the matrix and there some couple

of criteria one is that two of the terms are greater and then the product of the other two less than 0.

So, that was the criteria. So using that if you look here, we did this and I am just going to quickly go through this, this is the last thing I remember having done. So, f 1, f 2 lets go where I can show you what f 1, f 2 are my two functions.

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Stability of a chemostat :

$$\frac{dx}{dt} = D(X_0 - X) + \frac{\mu_{max}S}{k_s + S}X$$

$$\frac{dy}{dt} = D(S_0 - S) - \frac{1}{Y_{x/s}}\frac{\mu_{max}S}{k_s + S}X$$

$$f_1(X,S) = D(X_0 - X) + \frac{\mu_{max}S}{k_s + S}X$$

$$f_2(X,S) = D(S_0 - S) - \frac{1}{Y_{x/s}}\frac{\mu_{max}S}{k_s + S}X$$

So, f 1, f 2 are my two functions out here which represent the balance equation for the cell and the substrate respectively, so f 1 represents the balance equation for the cell and f 2 represents the balance equation for the substrate.

So, what we did is we took the matrix A which was del f 1, del X, del f 1, del S, del f 2 at del X, del f s 2, del S and we obtained the four terms a 1 ,a 1, a 1 1, a 1 2, a 2 1, a 2 2, so a 1 1 is this, a 1 2 is this one, a 2 1 is this and a 2 2 is this one, now next we go and apply our criteria.

$$\left| \underline{\underline{A}} - \lambda \underline{\underline{I}} \right| = 0$$

$$\begin{pmatrix} a_{11} - \lambda & a_{12} \\ a_{21} & a_{22} - \lambda \end{pmatrix} = 0$$

$$(a_{11} - \lambda)(a_{22} - \lambda) - a_{12}a_{22} = 0$$

or $\lambda^2 - (a_{11} + a_{22})\lambda + (a_{11}a_{22} - a_{12}a_{21}) = 0$

$\therefore B_1 = -(a_{11} + a_{22})$

$B_2 = (a_{11}a_{22} - a_{12}a_{21})$

$B_3 = 0$

$\Rightarrow$ for both eigenvalues to have negative real parts.

So, this is my matrix and so this is how it looks. Now for it to be stable so, this is A and A minus lambda gives the characteristic equation for the Eigen values which is this. So, this is the characteristic equation. Now, when I arrange them in terms of increasing decreasing lambda power, this is what I get and my B 1 is this and B 2 is this. So, my criteria was that B 1 has to be greater than 0. I believe greater than 0 and B 2 has to be as greater than 0 too.

$$B_1 > 0$$

$$\&\& \ \det \begin{pmatrix} B_1 & B_3 \\ 1 & B_2 \end{pmatrix} > 0$$

i.e $B_1 B_2 > 0$

i.e $B_2 > 0$

criteria : $B_1 > 0 \ \&\& \ B_2 > 0$

$\Rightarrow (a_{11} + a_{22}) < 0 \ \&\& \ (a_{11}a_{22} - a_{12}a_{21}) > 0$

So, these are my criteria. So, if you go back, this is my characteristic equation and the necessary criteria for the real parts of the roots to be negative is that both, the coefficients have to be greater than 0. So what I need to satisfy is B 1 and B 2. So, actually you know strictly speaking, it is just B 1, B 2 minus B 3, but B 3 is 0 out here because it is a 2 by 2 matrix.

So, for a 2 by 2 matrix and what I told you is that one of the things is that most of the equations that I am going to give you or you are going to do in the chemostat are 2 by 2 matrices. So, it is kind of simplifies your life all you need to do is look at the characteristic equation for lambda and then say that the 2 coefficients of the characteristic equation one for lambda to the power 1 and the other for lambda to the power 0, they both have to be positive.

So, if both the coefficients are positive then it is straight forward and ensure that the roots have real negative, but then intuitively also, you can realise that if the coefficients are positive then obviously the roots are going to be negative. Similarly, if both the coefficients are negative then the roots are going to be positive.

So, if both the coefficients are positive then the roots are negative that is all you need to remember out here. So, any time we do this, the easiest way is to create the characteristic equation for lambda, write the characteristic equation, I mean you can go do the Harveys way also you know, But I find it lot easier to actually be able to write the characters, you feel lot more confident about it to be able to write the characteristic equation for lambda and then equate or in equate rather the two coefficients to be greater than 0.

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for Monod Growth Model:

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

$$\frac{\partial \mu}{\partial S} = \frac{\mu_{max}k_s}{(k_s + S)^2} > 0 \text{ for all } S$$

from previous analysis for $S_0 < \dfrac{Dk_s}{\mu_{max} - D}$

the reaction does not take off.

so, we consider the case: $S_0 > \dfrac{Dk_s}{\mu_{max} - D}$

So, that is it. So, next what we do is, we now use a Monod Growth Model. Till now we had been using a generalised mu ==meneralised== value of mu now, we use the Monod Growth Model, because unless we use the Monod Growth Model or any other growth model we cannot come up with the specific criteria. So in the Monod Growth Model everything else remains the same, remember so all the analysis that we did till now is valid for all kinds of growth models provided you know it is just a two equation system.

So, here mu in Monod Growth Model is given by mu max S over K s plus S and so del mu del S is given as mu max K s over K s plus S square. So, as you can see straight away over here del mu del S is greater than 0. These are things that we have to quickly figure out so then del mu del S is greater than 0 for all values of S because its K s is positive mu max is positive and it is a positive number in the denominator.

So, it is greater than 0 for all values of x S. So, in the previous analysis we have shown already when we did the steady state analysis, that here what you see on the screen S naught is less than D K s over mu max plus D. If that is the case then the reaction does not happen at all. Why does the reaction does not happen at all? Because that is not enough substrate for the reaction to happen physically speaking and mathematically. What you found was that you got a unfeasible or else trivial solution. So, if you remember go back and remember that S naught greater than D K s over mu max minus D and mu max had to be greater than D. Why is mu max had to be greater than D? Because

one of the criteria for steady state was mu max equals D <mark>right</mark> the straightway, steady state criteria was mu max equals D.

Now, if mu equals D, now mu equals mu max time some number which is less than 1. So, obviously then mu max has to be greater than D. So, then the denominator is positive out here, but the reaction can only happen if S naught is greater than D K s over mu max plus D K s. So, we will consider that case only here, because there is no point considering the other cases. And if you need I will go back and show you the chart we had, you know we have a nice chart which showed here, this one see,

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for sterile feed ($X_o = 0$) :

D	$S_0 > \dfrac{Dk_s}{\mu_{max} - D}$	$S_0 < \dfrac{Dk_s}{\mu_{max} - D}$
$D < \mu_{max}$	$S_{ss} = \dfrac{Dk_s}{\mu_{max} - D}$, $X_{ss} = Y_{x/s}(S_0 - S)$	$S_{ss} = S_0$, $X_{ss} = 0$
$D > \mu_{max}$	$S_{ss} = S_0$, $X_{ss} = 0$	$S_{ss} = S_0$, $X_{ss} = 0$

So, look at this side S naught less than D K s over mu max plus D K s, these are all trivial solutions and this one you get trivial or non trivial solutions, depending on the D greater than mu max or D less than mu max. Now, D greater than mu max is not possible, just as I explained because D equals mu. So, mu equals mu max time some number which is less than one. So, obviously D has to be less than mu max so the in that region alone you can get a non trivial solution fine.

So, let us work through this all we need to do is actually find the criteria. So, we understand this, that S naught has to be greater than D K s over mu max plus D K s.

with $X_0 = 0$ (sterile feed).

$\Rightarrow$ for $D < \mu_{max}$ where $S_{ss} = \dfrac{Dk_s}{\mu_{max} - D}$

$$A = \begin{pmatrix} 0 & X_{ss}(\dfrac{d\mu}{ds}) \\ -\dfrac{D}{Y_{x/s}} & -(\dfrac{X_{ss}}{Y_{x/s}}(\dfrac{\partial \mu}{\partial S})_{ss} + D) \end{pmatrix}$$

note $a_{11} = 0$, $a_{22} < 0$ $\therefore$ $B_1 > 0$

$a_{12} = X_s(\dfrac{d\mu}{ds})_{ss} > 0$, $a_{21} = \dfrac{-D}{\mu_{max} - D}$

$-a_{12}a_{21} > 0 \therefore$ Stable Steady State

Now, let us consider the case of sterile feed. Why do we consider that? Just to make our calculations a little simpler sterile feed means X naught equals 0. Now, so again we are looking in the region of D less than mu max and S s s, S s s naught less than D K s over mu max plus K s, so in that region S s s that you get is given by D K s over mu max plus D K s that is what we got last time. And if you go back and put these values into your the values that we got into your A matrix, so A matrix is here.

So, if you go and put these values, this becomes 0. Why because, mu equals D, so this becomes 0 and the rest of them are all non 0 numbers. So, that is the only term that becomes 0, but by becoming 0 it makes a calculation quite simple because as you say this a B 2 will be simply minus a 1 2 times a 2 1 and B 1 will be simply minus a 2 2, is it clear because a 1 1 is 0 so B 1 will simply be minus a 2 2 and B 2 will simply be minus a 1 2, a 2 1, so this is my A matrix over here this term being 0.

So, a 1 1 being 0 so all I need to do is prove that I have my a 2 2 to be less than 0, because B one is minus of a 2 2 now and what else I need a 1 2 times a 2 1 the negative of that greater than 0 or in other words, a 1 2 times a 2 1 less than 0. So, my two criteria B 1 greater than 0 and B 2 greater than 0 that is, the two coefficients greater than 0 translate too because a 1 1 is 0. Just as I explained just now, translate to a 2 2 less than 0 and a 1 2 a 2 1 less than 0 that is all.

So, that would be that is criteria for stable steady state, now a 2 2 is this number over here as you can see, so minus a 2 2 is minus of this number so this number D is positive number so del mu del S is.

What is it?

Positive?

Positive, I just explained why so, this is a positive number right? This whole thing is positive, D is positive, del mu del S is positive, obviously X is positive, then Y is positive, so this whole thing put together is a negative number. So, this is automatically satisfied. Is it clear? a 2 2 less than 0 is automatically satisfied. Now the other criteria is the only one that we have to take care of.

So, this is a product of these two minus a 1 2 times a 2 1 so, D is what you will get is D times X s s over del mu, del S over Y and minus of that and there is a minus out here so this whole thing comes out to be positive so D X s s del mu, del S over Y has to be greater than 0, so that is my criteria. For greater than 0, I think I will come back to that, I think I do not have written it here clearly.

So, basically my criteria for D less than mu max is simply, del mu del S times D times X s s times Y s. Now, you are going to tell me that is it greater than 0, so you are going to tell me is that correct or not? As I told is it stable or not? And the answer is Yes, It is stable, but why? We are not going to satisfy anything, it is automatically satisfied everything is automatically satisfied for this criteria, why because, just from this, let me here just because of this del mu del S is this number mu max K s over K s plus S square which is positive for all values of S.

So automatically is that clear or do I need to explain? So, I need to explain this quickly through here. So, here a 1 2 times a 2 1 negative of that is X s s, del mu del S times D over X Y fine now D is positive, X is positive, Y is positive and del mu del S is positive, so obviously this whole thing is positive right?

So, this criteria satisfies, look over here you have a 2 2 this number has to be less than 0. So, this is positive, so obviously the negative of the whole thing is negative, so this is also satisfied automatically, clear? So, both criteria automatically satisfied, as a result

this condition is steady state is stable. The next one is the trivial state as I explained, that you know.
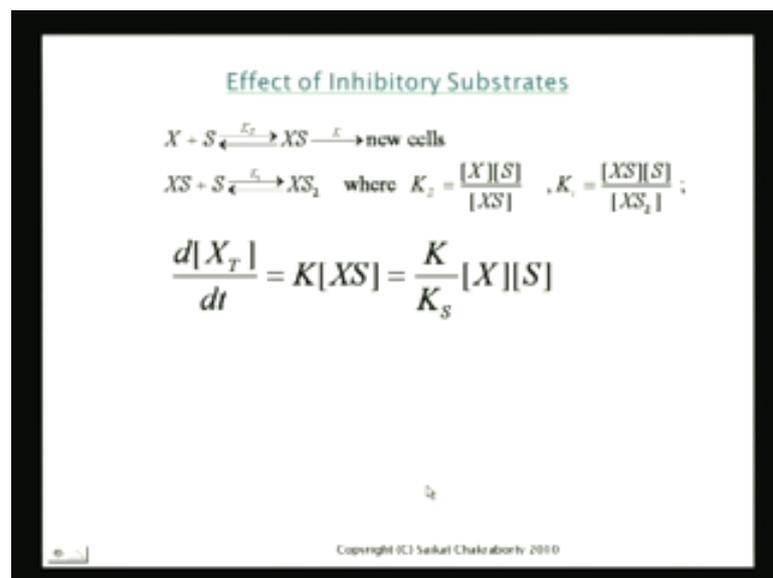
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So, D greater than mu max obviously you do not have anything, but the trivial solution, but we are still looking at the stability of it and the reason we are still looking at it the stability of it is because whether the trivial stage itself is stable, you know a trivial state means what? That nothing really happens, you let the thing go in and it just goes out, but even is that stable or does that degenerate some other unstable steady state.

So, we are trying to look at that and the A matrix is slightly different because this D is no longer equals mu. So this term is not 0, on the other hand this term turns out to be 0 when you go and do the algebra yourself. But I am not going to, you know the details of this one because this is a trivial state, but still so you get that a 1 1 plus a 2 2, when you add these two up equals this number which is less than 0. Why is that less than 0? Because D is greater than mu max.

So, if D is greater than mu max obviously 2 D is greater than mu max, 2 D is greater than mu therefore, this number is less than 0. So, this criteria is satisfied and the second one is a 1 1 times a 2 2 minus this is 0. So, the product of these two have to be greater than 0. So, this criteria again is satisfied because D is greater than mu D is greater than mu max therefore, it is greater than mu so this is positive. So, product is positive so what we figure out is that, the Trivial steady state is also stable.

So, both criteria satisfied and both lambdas are negative, so trivial steady state is also stable. Is that clear to all of you? Or do you want me to repeat any parts of it? I am going a little fast because I want to finish something. So, then next thing that we will be going to do today is that apply the same calculation, then the same process and the same mechanism that we did to multiple steady states and the case of substrate inhibition. I do not know if you have forgotten, let me remind you.

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So, this was what the case of substrate inhibition was, so till now we did the Monod Growth Model with the simple thing. Now you know, as I said that we did the case of multiple substrates and similar kind of multiple substrates.

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What we get is mu, so we can do a similar kind of analysis using multiple substrate. So, the one that I am doing is the case of substrate inhibition.

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So, the reaction for that substrate inhibition was X plus S giving X S and X S reacts with S again to give X S 2 which does not produce new cell.

So if you remember, these were the all the derivations. Let me not go through them, you know if this X t was the sum of the 3 X plus X S plus x s 2.

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$$\frac{d[X_T]}{dt} = \frac{K}{K_s}[X][S] = \frac{K}{K_s}\frac{[S]}{\left(1 + \frac{[S]}{K_s} + \frac{[S]^2}{K_i K_s}\right)}[X_T]$$

$$\mu = \frac{1}{[X_T]}\frac{d[X_T]}{dt} = \frac{\mu_{max}[S]}{\left(1 + \frac{[S]}{K_s} + \frac{[S]^2}{K_i K_s}\right)}$$

This rate of growth reaches a maximum value at $S = S_{crit}$ beyond which it declines. To find the maximum specific growth:

$$\frac{d\mu}{dS} = 0 \quad \Rightarrow \quad S_{crit} = \sqrt{K_i K_s}$$

And then we went through this and this is what we found, so why are we interested in this? Because this is the only thing that is different from the previous case, the value of mu itself, because everything the balance equations the rest of the analysis everything is same. So if you remember the reason, we did it in the previous classes, we went up and did all the analysis without putting in any value of mu at all. The reason we did that is because the basic equations irrespective of the form of mu as a same, right?

So, whatever form of mu we take, be it substrate inhibition, be it multiple substrates, you know other kinds of inhibitors does not be a problem at all. We can just put in that form, everything into that form. So, let us go back here so you see it is a, this is my form mu which is mu max S, 1 plus K s plus this term you know apart from Monod. You have this extra term of S square over K i, K s, so what do you think you know? So this is not important for us. So, what do you think the innovate is because you see that del mu del S could be 0, but we will come to that later.

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Substrate Inhibition and Multiple Steady States.

$$\mu = \frac{\mu_{max} S}{k_s + S + \dfrac{S^2}{k_i}}$$

Balance equation:

$$\frac{dX}{dt} = -DX + \frac{\mu_{max} S}{k_s + S + \dfrac{S^2}{k_i}} X \text{ (sterile feed)}$$

$$\frac{dS}{dt} = D(S_0 - S) - \frac{1}{Y_{x/s}} \left(\frac{\mu_{max} S}{k_s + S + \dfrac{S^2}{k_i}} X \right)$$

So, what do you think? Even if I ask you that so these are basic equations, what would be the effect of substrate inhibition on the system? What do you think would be the effect? What do you think would be the effect of substrate inhibition? These equations are written for sterile feed, I have written it down there. What we got last time, let us review what we got last time without the substrate inhibition is that there is one trivial state and one non trivial state and both are stable, that is what we found, if I do a quick review.

So, first question is two questions. What do you think in terms of, what you will get in terms of trivial states and non trivial states? a and b is that? What do you think about their stability just an intuition, we will work out the whole thing you know whole maths in the rest of the class, but just some intuition.

Multiple (( ))

Yes, multiple states in a way. Last time also you had multiple states, because you had a trivial state and a non trivial state. So, two states that was still multiple, but what do you mean by multiple states here? How many states? I mean that is, it should be a easy answer because what happens to the order of the equation?

Increases?

Increases by?

By 1 order of magnitude in S, so from 2 to 3 so how many.

3 yes, So that is the straight answer for the second order. Last time you had a second order equation, you got two steady states. This time you have a cubic equations so obviously, you are going to have three steady state so that is one part of the answer and the other part obviously, you cannot tell without doing the analysis. But what do you, what can you tell you now?

What are the intuition telling you, what happens when there are three states?

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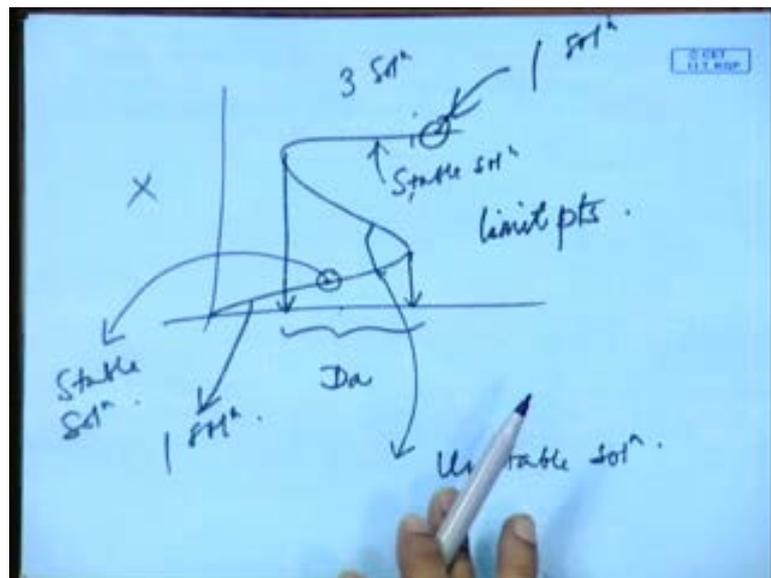
Yes, so let me show you this, you know, I think I have drawn this diagram several times before, so let us say this is X conversion just like here something like that and this is the reactor Damkohler number which depends on the residence time of the chemo stat, exactly the same thing, so this is how it is going to be, so these are.

What are these called? I have told you this before.

Still, what does the name mathematically?

So, limit points they may or may not be ignition or extension depends on the catalyst and stuffs like that, you know, if you are doing a chemical reaction, but in mathematically the generate term for these is limit points. So, why this was important is because between these limit points in this region of this limit points, you have three solutions and beyond that one solution and one solution.

So, between this only you have the cubic solution. What it means is that, when we solve it, you will see that outside the certain range in the of the parameter, there is a single solution because you know the determinant goes off, determinant goes to 0 or something like that typically the determinant goes to 0 and the outside range and you end up with a single solution and within that you have just three solutions, if I look at the stuff again.

So, limit points these two and this is the ignited branch, this is the stable solution,a middle one and this is the stable solution. So, the bottom branch is the is the stable solution, the top branch is a stable solution and the middle branch is an unstable solution. Why is it an unstable? Is because, if you for some reason going to the unstable branch and allow the system to stay there it will either go to the top branch of the ignited branch or go to the bottom branch or the extinguish branch depending on whichever is closer to, it does not stay there for very long.

So, your aim is never to operate close to the unstable branch and how do you ensure that? As an engineer for example, you have to operate your plant or your reactor in a certain parameter range, parameter range means say, residence time or liquid volume or the substrate concentration, whatever it is, how will you ensure that it does not go to the unstable branch? You choose your parameters such that, it does not go to the unstable branch, right? How do you choose?

How do you choose your parameters such that it does not go with the unstable branch?
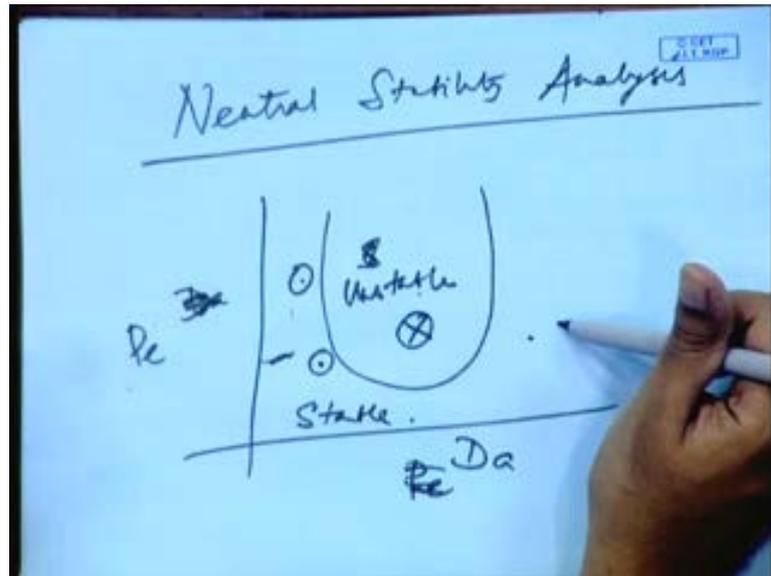
Yes, but there is a procedure for that and that is called, let me see if you have heard of this Neutral Stability and that is exactly what we are doing now. What it does is, basically it draws you, essentially draw this in the parametric plain. For example, see here, it could be in the plain of Damkohler number verus Pekkle number, something like that or Pekkle number here.

Let us say, Pekkle number here and Damkohler number here, then what it gives you? It gives you a curve like this because from here this diagram that I drew now how do you know? You never know for otherwise, what you have to do if you choose every Damkohler number, go and make some simulations, find out whether your solution is in the stable branch or unstable branch.

That is a complete waste of your time, you cannot keep doing it. So what you need to do is, you need to isolate or figure out in the parametric plain of Pekkle versus Damkohler. Whether the system is going to be stable or unstable so this is the part where it can be unstable and the system is stable here, which means that you choose parameter such that it stays in the middle of this range, it stays within this stable path. It could be the other way around also, it could be that inside is stable or outside this is unstable very unlikely or typically you know because of Pekkle increases it becomes unstable. So, but there is a possibility that it can happen, stable can be inside and unstable can be outside.

So, our aim to do this, you know our engineering aim to do all this analysis is to be able to come up with this Neutral Stability Diagram. So that we do not have to do the calculations every time we can figure out in the parametric space. What part is stable and what part is unstable as a result as soon as you know in the reactor, as soon as you choose your parameters, you know your flow rate. Damkohler and Pekkle number between them contain all the parameters, essentially you know flow rate volume of the reaction reactor, reaction time, the size of the, you know the diffusion length scale in the reactor and the diffusion coefficient of the species in the reactor.

So, all these parameters are contained between the Pekkle and Damkohler number. So, if you look here. So, essentially that you choose your Pekkle and Damkohler such that your system stays here or here or here and does not go anywhere here so, that is your range. So, you can directly choose the parameters you do not have to do calculations all the time, once you get the Neutral Stability Curve, this curve once and for all you can directly choose your parameter and make sure that is in the stable value. So, that is our aim, not to just solve one problem, not to just solve for the steady state and analysis stability of the steady state, but to get a Neutral Stability Curve, so that you can use that at all times.

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So, that is what we are trying to do over here. So, as I discussed that this being a Cubic equation this will have three solutions. And out of these three solutions, it turns out one

will be a trivial solution and the two would be non trivial solutions, so then we have to look at the stability of these solutions.

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Trivial Steady State: (1) $X_{ss} = 0$, $S_{ss} = S_0$

Non Trivial SS: (2) $S_{ss} = \dfrac{k_I}{2D}\{(\mu_{max} - D) \pm [(\mu_{max} - D)^2 - \dfrac{4D^2 k_s}{k_I}]^{0.5}\}$

$X_{ss} = Y_{x/s}(S_0 - S_{ss})$

So, the trivial solution as we have looked before, it is simply going to be X s s equals 0 and S s s equals S naught and the non trivial solutions, if you solve these you know so how do I solve this, remember what we did was we did a invariance right? We did an invariance.

So, you multiply this by the this second equation by Y and add these two up and as a result these term will go, then you can express X as a function of S and then you put it back over here and then solve it. So, you solve it by the method of invariance and this is what you get, this is to only remind you, Valid for mu max greater than D, this is mu max not equal to D rather this is valid for mu max not equals to D, why is this valid for mu max not equals D? Because mu max equals D what will happen is this squadratic form, Remember the you taken out the Trivial solution, you have a Cubic equation to start with you, take out one of the solutions which is the trivial solution then you have a quadratic form. So, this is the quadratic form you are solving. So, if you know this thing is like the Cubic form, it will be some S times a 1 square plus a 2 S plus a 3 equals 0.

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So, this is the form once you put that, so this will give you the sorry this is not S, S minus S naught so this part will be the trivial solution this is trivial which will give you S equals S naught and this is the non trivial part. So, this is a quadratic you can solve, but what I am trying to say is that a 1 equals mu max minus D. So, what you need to do is when mu max equals D then you need to drop this completely from the equation itself. Do not solve the quadratic and then try to settle around because it will come in the denominator or something then the whole thing will blow up.

So, if mu max equals D then just drop this term completely and then you have a linear and you have just one single solution which is you know, given here. So, this solution over here is for mu max for a 1 equals 0 then this is given by K 1 K s. So, if I can go back to the screen now.

Trivial Steady State: (1) $X_{ss} = 0$, $S_{ss} = S_0$

Non Trivial SS: (2) $S_{ss} = \dfrac{k_I}{2D}\{(\mu_{max} - D) \pm [(\mu_{max} - D)^2 - \dfrac{4D^2k_s}{k_I}]^{0.5}\}$

$$X_{ss} = Y_{x/s}(S_0 - S_{ss})$$

three solutions are expected when

$D = \mu_{max}$ when $S_{ss} = \sqrt{k_I k_s}$

N.B two solutions given by (2) provided that

$(\mu_{max} - D) > 2D\sqrt{\dfrac{k_s}{k_I}}$

So, the Non Trivial solution is given by S S equals K I over 2 K D this term mu max minus D plus minus this determinant and X s s. So, this is let my S s s and X s s is obtained as S naught minus S s s times Y, because there is no material balance right? So, if S naught minus S has been consumed then Y times that would be give you the amount of cells that has been formed.

So, for mu as I said for a 1 equals 0 the first coefficient equals 0 or for D equals mu max S s s is square root of K s K s over K i. So, the two solutions that you get over here these two so non trivial solutions are provided that mu max minus D is greater than this or in other words the discriminant is greater than 0 this discriminant is positive, so you get this so mu max minus D is 2D is it correct.

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Stability of above steady staes:

$$\mu = \frac{\mu_{max} S}{k_s + S + S^2/k_1}$$

$$\frac{d\mu}{ds} = \frac{\mu_{max}(k_s k_1 - S^2)}{(k_s + S + S^2/k_1)^2}$$

let us cosider the non trivial states i.e $X_0 \neq 0$

hence, $-DX + \mu X = 0$

$\mu = D$

Now, what we have are essentially my three states for the special case where mu max equals d I have this state, but apart from that essentially for all other cases these are my three states.

Now, what I have to do is I have to look at the stability of three states, predictably your trivial state is going to be steady stable predictably, but we will still have to, we will still check that, so what is my, you know, difference that I need to do? Everything is same or again as before, only my mu is different so, I need to calculate my del mu del s. Now what we have looked at the three states, what do you suspect in terms of the stability of the states? Something Yes, I think already said that one of the solutions is going to be unstable and the other two are going to be stable. Yes, That is what I also suspect, but can you create a reason for that. What could be the reason for that? What was the driving force the last time we did for the normal case? What was the driving force behind making these solutions stable both the solutions it turned out were stable, but what was the driving force? What is the reason for that?

D was greater than mu max? No, D has to be always greater than mu max for feasible solution to exist. Is D is now greater than mu it is not going to work.

(( )).

, correct the reason behind that was del mu del S was always positive, but if you remember from the last time we did in the growth model del mu del S was not always positive, it goes to positive and then goes to 0 and then decreases, right? If you remember, so it turned out that if del mu del S were not positive last time for example, then the system would be unstable.

So, what we can predict or intuit I mean, it is not mandatory that exactly mathematically we get, but you know we have to always couple some kind of intuition with the mathematics. So, what we intuit is that for the region where the specific growth rate decreases with substrate the system is going to be unstable. And physically if you think of it makes sense that if you increasing the amount of substrate by the specific growth rate decreasing that is the really worrying case, right? Physically speaking and that probably is the reason where there are sources of instability. So, let us try and look at it.

So, this is the first thing you will say is mu over here with the inhibition term in there and this is my del mu del s or d mu d s over here and which could be negative or positive depending on the numerator, because the denominator is always positive. It is the numerator which can go negative or positive. So, depending on whether S is greater than square root of k i k s, all less than square root of k i k s, then you have trouble, if f equals square root of k i k s then you have then what do you have?

Trivial solutions.

Not the trivial solution, Trivial solution is 0 this is that solution d equals mu max and S equals s square root of k s and k s k s. Trivial solution is this one, let us not confuse trivial solution with this, this is trivial solution, these are non trivial solutions are special case of the non trivial solution, is this one where d equals mu max. Is it clear Lisa? Is there any problem understand? This is probably the hardest thing we have done in this till now, but if there is a problem just stop me and so the special case of the non trivial solution is S square root equals square root of k i k s, but in general we have the trivial solution and two non trivial solutions.

So out of the non trivial solution there is one possibility of S being equal to k i k s in which case del mu del S would equal 0, right? That is one possibility, but that is a exceptional possibility a special case, but in general k i k s would have to be greater than 0 or less than 0. So, depending on whether it is greater than 0 so square root of k i k s

greater than S or square root of K I K s less than S, so square root of k i k s is greater than S and we probably think that the system is going to be stable fine.

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So, we consider the non trivial states over here and for the non trivial states the mu equals D for this trivial state is not necessary, but for the non trivial state mu equals D. Do you remember we had X times mu minus D equals 0 so, for trivial state this is X equals 0 for non trivial state mu equals D, right? Because these are things if you remember,

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A remains same as in chemostat (with no inhibition)

$$\underline{\underline{A}} = \begin{pmatrix} 0 & X_{ss}(\frac{d\mu}{ds})_{ss} \\ \frac{-D}{Y_{x/s}} & -(\frac{X_{ss}}{Y_{x/s}}(\frac{d\mu}{ds})_{ss}+D) \end{pmatrix}$$

for stability $a_{11}+a_{22}<0$ & $a_{11}a_{22}-a_{12}a_{21}>0$

$\therefore \frac{X_{ss}}{Y_{x/s}}(\frac{d\mu}{ds})_{ss}+D>0$ $D\frac{X_{ss}}{Y_{x/s}}(\frac{d\mu}{ds})_{ss}>0$

for $\frac{d\mu}{ds}>0$, $S_{ss}^2 < k_s k_I$ $\therefore$ condition for stability $S_{ss}<\sqrt{k_s k_I}$

if this is satisfied then stability condition $(a_{11}a_{22}-a_{12}a_{21})$ also holds.

So, this matrix A that we have, this is the same matrix that we have remember? Exactly same, as what we did last time, because we still have a generalised form of mu, we have not put in our mu into it. Now we are going to put in our mu into it so stability criteria was a 1 1 plus a 2 2 less than 0 or in other words, this term to be negative and the other one is a 1 1 a 2 2 minus a 1 2 a 2 1 greater than 0 and in other words, the product of these two terms to be positive.

Now, to remind you again the last time we had a advantage because del mu del S was greater than 0. So, we could conclude directly that yes if del mu del S is 0 than greater than positive then of course, this whole term is going to be negative. Similarly, del mu del S is positive then of course, the product of these two terms is going to be greater than 0, right? Is it clear to everybody?
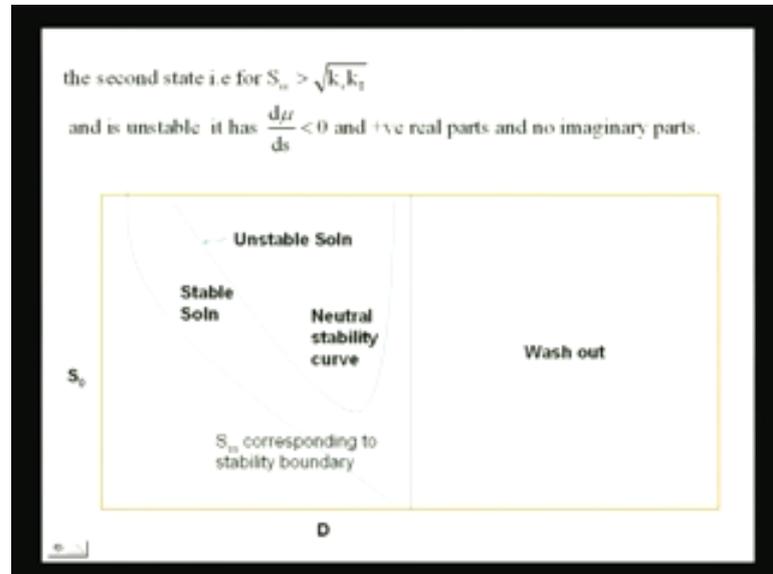
So, this we could conclude that directly, now we cannot conclude that directly and we have to depend on the, on a case by case basis. So, this is my criteria now so del mu del S times X over Y plus D should be greater than 0 and this one will lead to del mu del S times D X over Y should be greater than 0 fine now for del mu del S greater for del mu del S to be greater than 0 my S square. As I just showed s square has to be less than k i k s square has to be less than k i k s so that is my stability criteria, essentially that s has to be lesser than this is what we have intuited just by looking at the equation itself we had intuited this.

So, my stability criteria is that s has to be less than square root of k i k s and you can go back and check all rest of it you know, you can put over here, you can do the rest, I have skipped that calculation, but the differentiation is already there you can put go and put back over here, but you know, coming back to this model one of the things you need to, though I do not kind of ask you, I mean I am not suggesting that you do that in the exam I want you to put the stability criteria a 1 1 plus a 2 2 greater than less than 0 and the other two terms a 1 1 minus a 2 2 minus a 1 2 a 2 1 greater than 0 and then come through it.

But at the end of the day, if you think, come to think of it what is your stability criteria is essentially coming down to del mu del S should be greater than 0, right? Is it correct? You do all the calculations and I do not suggest that you do not do the calculations in the test or something, you do the calculations to show that you know everything and this is

the proper way, but check on your calculation essentially would be what to find out, what is my criteria such that del mu del S is positive. So, at the end of the day that is what matters, but then again do not go and write it straight away, derive it.

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the second state i.e for $S_o > \sqrt{k_i k_{ii}}$

and is unstable it has $\frac{d\mu}{ds} < 0$ and +ve real parts and no imaginary parts.

Unstable Soln

Stable Soln

Neutral stability curve

Wash out

S_0

S_{ss} corresponding to stability boundary

D

So, this what you see on the screen is now my Neutral Stability Curve. The thing that I had been trying to get and look what I have over here is s naught over d so this is a major difference between what I showed you, this multiple solution curve that is called known as Difurcation diagram. The one that I just showed you here, this one if I can go to the, yes,
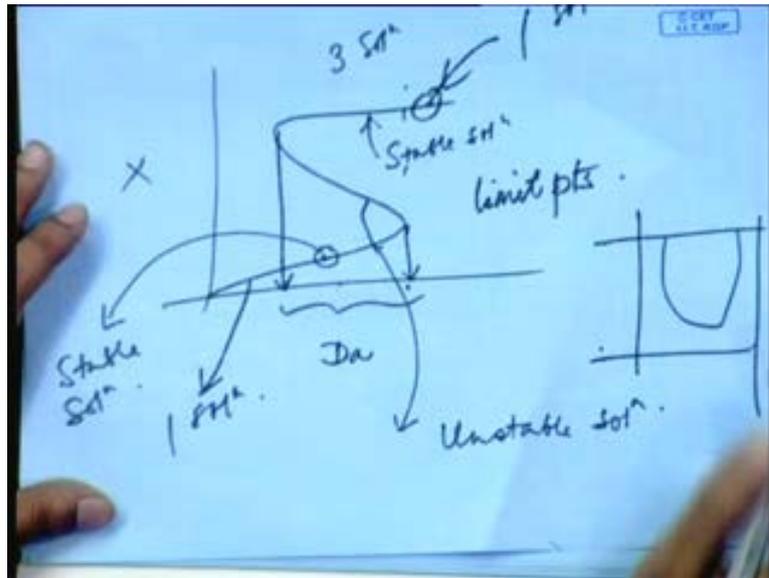
So, this is my Bifurcation diagram and my Neutral Stability Curve, would be this now I need to draw a fresh diagram and over the Bifurcation Curve and the Neutral Stability Curve together and there is something I want you to help me here.
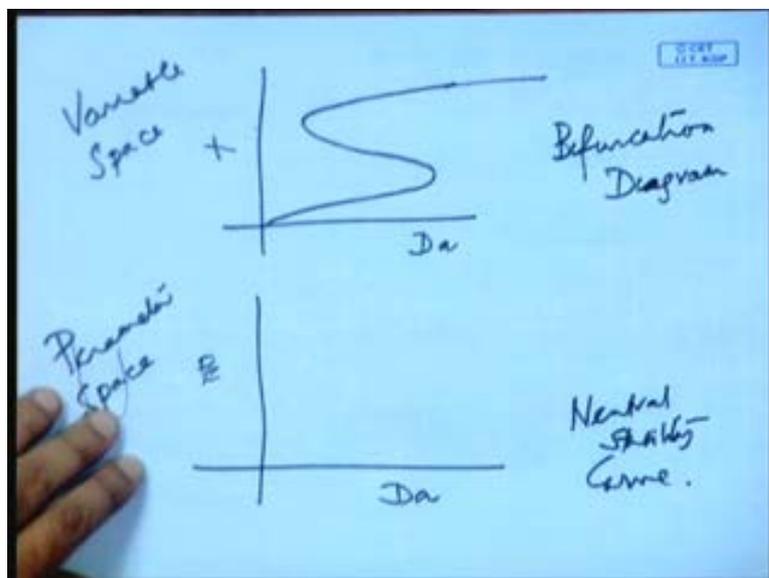
So, as you can see that the extinguish branch essentially saturates, you know over time it kind of saturates are over Damkohler number, let us say this is Damkohler and this is the conversion X. Now I want you to tell me, help me with how the Mutual Stability Curve is going to look like. So this is my Bifurcation diagram, I want you to help me with how

my neutral stability curve would look like, how it look like it would have a, (( )) would look similar to what I told you like this, what I drew over here, but where would this (( )), how would I place that?

So, let us say my Neutral Stability Curve in the again X axis is still D a, but y axis is Pekkle. Do you understand? Do you discern the difference in the terms of the axis for the bifurcation and the Neutral Stability Curve? The major difference is that Bifurcation Curve is drawn in the Variable Space. Neutral Stability Curve is drawn in the parameter space. So, this is the variable space and this is drawn in the parameter space and there is, so, Variable space means one variable versus a parameter, there is, this is, in the parameter space which means two parameters and then there is another kind of plot, what is it called? Where two variables you would haveand you draw one variable versus another for let us say, in this case if I want to draw X versus s space.

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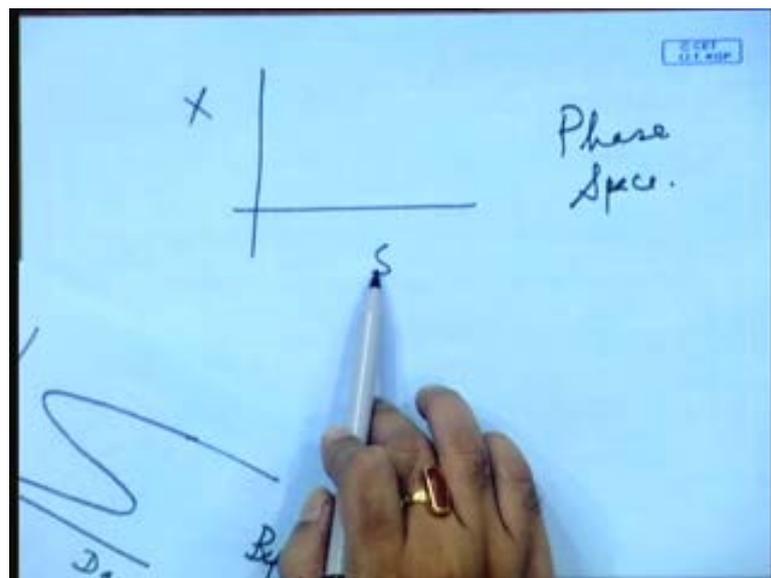
What is this called? What is it?

I do not remember.

You do not remember? Who remembers? It is called the phase space, see if the variable space here, the parameter space here and the phase space is where both the variables are drawn against each other. And so, this is something that is important and you have to understand this. Although I explained it before that you draw you necessarily draw the

Neutral Stability Curve in the parameter space and not in the variable space or the phase space. The reason you do that is because you are not interested in what the value of that, do you understand? What I am trying to say, you not interested in what the value of the parameter variable is going to be. You are interested in what parameter should you operate your reactor in. You are not interested whether X is going to be 0.9 or 0.8 or 0.7 or 0.6, that is not your concern. You are not even interested whether it is going to be ignited or extinguished? That is an important question by the way, that you know if you look at this bifurcation diagram over here this is the ignited branch in this extinguish branch. It is important actually to figure out whether the system is going to operate in the ignited branch or the extinguished branch. Why because, you want it to operate in the Ignited branch.

Ignited branch, Yes, because you want product, you know you would not run a reactor without generating product, so if you are in the extinguish branch you hardly generate any product. So that is important, but more important than that is, whether the system is stable or unstable. So, that is why the more important thing is the Neutral Stability go. First come stability, once the system is stable then you worry about whether you are generating enough product or not enough product. You understand what I am to trying to say, so first is stability,

So, once the system is stable there are two possibilities that the system could be in the ignited branch or in the extinguish branch, if you look over here as we discussed that this length the bottom length is stable the top leg is stable, but the middle leg is unstable. So, even when the system is stable there is still a possibility of it being the ignited branch or in the extinguish branch and you want it in the ignited branch, right? So, I will come to that. Also how to figure that out? But your first criteria is, stability.

So, now you tell me that I have explained so much now, you tell me that how do I draw my neutral stability curve between the limit point?

Between the limit point, so this is how we draw line over here and line over here and numerical stability curve will be like this will be like this and then like this. So, this is the system is unstable over here and stable over here, so this corresponds to this branch, corresponds to this branch over here corresponds to this branch corresponds to this and the middle branch corresponds to this, so the two limit points correspond to the two

horizontal. So, two limit points correspond to the two vertical limits. Please remember these all things, so the two limit points correspond to the two vertical limits of the neutral stability curve.

So, now my problem is solved. So, I now know that what part is stable and what part is unstable. I can choose my criteria such that it is stable, now how do I choose whether it goes to the steady state or to the ignited state, extinguish state? That also I can choose from the Neutral Stability curve. If you look here, so if I choose something around this point then it will be in the ignited state, just say after this vertical second vertical length. so it will go to the ignited state. So, if I choose something out here, in the towards my left hand corner, complete left hand corner then it will go to the extinguish state.

So, I want my two things, I want my system to be stable, I want it to have attained maximum you know, to give maximum product. So, which means that first it has to be either on the ignited and the extinguish branch and the second would it should be in be the ignited branch.

So, this Neutral Stability Curve is the very useful thing in a way because, let me choose my parameters my flow rate, my reactor size, my reaction rate, my diffusion coefficient everything such that say, I choose something like this, this would be probably the optimum choice, because it makes sure that it is stable or you can go here it make sure it is stable and make sure it is in the ignited branch, is that clear to all of you?

Now, let us go back to the screen. So, this was a generic thing I showed and this is the actual thing. So, this is the wash out case, so in other words the Trivial solution. Trivial solution means that no product is being formed. So, not really worried about this and this is my Neutral Stability Curve. Looks like and you know if there is a essentially vertical limit. Also it goes up a little bit so many a times, it is little sharp. Sometimes it is kind of flattened, all these things happen, but you go a little up. And then a kind of sharp and so, this is my unstable solution is middle in the inside here above and the rest of the system is stable solution. What is this line over here? This line is not properly drawn, actually it should touch this due line over here.

So, any how this line over here corresponds to, it is written here the steady state value of the substrate, so this is not a part of the, let me not confuse you, any which way this is, this blue line over here, is the bottom line. This one is not a part of the Neutral stability

curve. It is just concentration plot or substrate plot relating to this value, so do not worry so much about this line, just worry about this one. So, this is my neutral stability curve. And as we concluded that the system goes unstable not just with multiple inhibition. In general the system goes unstable well when del mu del S is negative and then it we end up having positive real roots.

So, for del mu del S negative, this is the part the unstable solution and for del mu del S positive, everything here below is stable. So, this is your first encounter with neutral stability curves, right?

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now for, $a_{11} + a_{22} \leq 0$ and $a_{11}a_{22} - a_{12}a_{21} > 0$

$$\frac{X_{ss}}{Y_{X/s}}(\frac{d\mu}{dS})_{ss} + D \leq 0 \quad (a)$$

$$\frac{DX_{ss}}{Y_{X/s}}(\frac{d\mu}{dS})_{ss} < 0 \quad (b)$$

inserting $(\frac{d\mu}{dS})_{ss} = \frac{\mu_{max}(k_s k_I - S_{ss}^2)}{(k_s + S_{ss} + S_{ss}^2/k_I)^2}$

So, just want to make sure that everybody understand. If there is any question on Neutral Stability Curve, you can ask me now or may be a minute later also, this is the overall stability curve.

And, this is the details of the calculation that I skipped, you know all those calculations I skipped you can go through these calculations, you want me to go through or just not very kind of Trivial.

So, essentially we have skipped the calculation because I just showed that del mu del s greater than 0 is stable. So, but this is the hard way going through all the details and in everything. So, this is the better picture. Now, I have of the this unstable and this is a so. So, these are rates in gram per litre and d so what essentially it tells me if you look at this Neutral Stability Curve. If I want to be in the stable region then it gives me numbers on two of the parameters, one is the S naught the initial substrate concentration I use and the second one is the D or D is the inverse of the residence time or in other words residence time itself.

So, what it tells me is that what should be the size of the reactor or you know size cum flow rate? So, residence time is ratio of these two a and b would be what would be my initial substrate concentration, this is what it tells me. So, that I can pick so if you look at the curve here so I can pick any point over here for example, I pick a point over here so that the system is stable and I know that for my S naught for this system to be stable . If my S naught is this my dilution rate has to be this or in other case if my reactor is given to me, you cannot make changes to explore rate and its size then I pick my s naught initial substrate concentration such that it is in the stable zone.

$$\mu_{max} = 1hr^{-1}$$
$$k_s = 0.05 gm/l$$
$$k_1 = 0.5 gm/l$$
$$D > 06125 hr^{-1}(\text{wash out trivial solution})$$
note $S_{ss} < S_0$ for non trivial solution.

So, if you need you can go through the calculations on your own so if you need to feel comfortable with it you can go, as I told you know there is this state, one s is outside the quadratic. So, these are the values in mu max is hour inverse so these values are in a way important. If you actually want to plot it so as you can see that the reaction mu max is sort of you know gives you the reaction rate and that is of the order of hours and so rate is 0.6125 the dilution rate is also of the order of hour inverse and you ensure that these less than mu max over here.

So, these less than mu max that is ensured number one and number two they are of the same order, they follow the stability criteria. So, that is in a way concludes our discussion on the stability of these states. Now you know some assignments you might want to do on your own is that these stability criteria that I show over here is for the inhibition, but let us go back. So, this stability criteria that you obtained over here is for all possible values of mu.

So, some of the things that you might want to do is look at how you change your mu and that how it changes the stability of the system. Now it may be little boring to do, that to start with because this is with the maths, but once you go through the maths and you essentially will come out so one of the things you might want to tell me, is that whether our intuition that for all del mu del S greater than less than 0 is the system unstable, that is the question I posed to you? For different if I go through this one let us say here, so

system like this for all kinds of del mu del s less than 0 is the system unstable this system or any other system, any other kind of growth model we have. I mean a lot of different growth models we have studied if I remember.

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So, and the Monod, Malthusian logistics all these different growth models are here so one question a that I posed to you is that, are for all these growth models if the system unstable for del mu del S less than 0, a and b is that even if is unstable. What kind of solutions face you get? What kind of Neutral Stability Curves and in the parametric space that you get? And this is something that you might want to look at in at home or something like that. And you know it is important, to we just did these two particular cases the Monod growth model one of the easy things you can do is simply do the Modified Monod growth model which is very straight forward same as Monod growth model almost, because there is not much effective except for that k s naught here, but if you take this model for example, how does it change your whole system?

And how does it change the Neutral Stability Curve in the Neutral Stability Space? The reason I am talking about this is see, till the point we write the basic equation for the system and keep any mu out there and do our analysis it is all valid, but you have to realise that the growth model when we put in is an artificial thing. Do you understand what I am trying to say the growth model itself is an artificial thing the balance equations

with any mu in there is the real thing because things are happening that way, but the growth model is an artificial thing.

So, it could be that I can choose growth model number one and you can choose growth model number two for the system and we should not come up with wholly different criteria for neutral stability. Do you understand what I am saying because at the end of the day, irrespective of what I engineer number one chooses growth model and engineer number two chooses different growth model the system should still run, so you might want to check with different kind of growth models and try and see that whether the Neutral Stability Curve that you get is similar or different.

So, we will stop here and tomorrows lecture I think if there are any questions on Neutral Stability. And if there is what you might want to do is think about it and ask me in the beginning of the class next class that is one possibility that is I think, because this is probably one of the hardest things. We did this calculations and everything in this course, so is there anything you want to ask at this point unintuitive stability or so we will save it for tomorrow, if there is any question I will stop you know may be towards the end of next lecture we will spare a few minutes and go through and we will start a new chapter in the next class. Thanks.